Lars-Peter Kamolz
Marc G. Jeschke
Raymund E. Horch
Markus Küntscher
Pavel Brychta
Editors

Handbook of Burns Volume 2

Reconstruction and Rehabilitation

Second Edition

Springer

Handbook of Burns Volume 2

Lars-Peter Kamolz • Marc G. Jeschke
Raymund E. Horch • Markus Küntscher
Pavel Brychta
Editors

Handbook of Burns Volume 2

Reconstruction and Rehabilitation

Second Edition

Springer

Editors
Lars-Peter Kamolz
Division of Plastic, Aesthetic and Reconstructive Surgery
Department of Surgery, Medical University of Graz
Graz
Austria

Raymund E. Horch
Department of Plastic and Hand Surgery
University Hospital of Erlangen
Friedrich-Alexander University of Erlangen-Nürnberg
Erlangen
Germany

Pavel Brychta
Department of Burns & Reconstructive Surgery
Masaryk University
Brno
Czech Republic

Marc G. Jeschke
Ross Tilley Burn Centre
Sunnybrook Health Sciences Centre
Toronto
ON
Canada

Markus Küntscher
Department of Plastic and Hand Surgery
Evangelische Elisabeth Klinik Krankenhau
Berlin
Germany

ISBN 978-3-030-34510-5 ISBN 978-3-030-34511-2 (eBook)
https://doi.org/10.1007/978-3-030-34511-2

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Severe burn injuries are maybe not the most common injuries occurring on a daily basis; however, it is estimated that within North America approximately 300,000–500,000 patients are hospitalized annually due to a burn-related injury and that worldwide approximately 500,000–1,000,000 people die due to a burn-related injury. Once a burn injury has occurred, it is one of the most severe forms of any injury, inducing a complex cascade of various responses including inflammatory, hypermetabolic, immune, as well as infectious responses. These responses interact with each other and are extremely complex and difficult to treat. Specialized centers, protocolized treatment, multi-center trials, and close collaborations improved morbidity and mortality after severe burn injury over the last two decades. However, a vast morbidity and mortality postburn still occur and represent one of the major problems in burn treatment.

One of the major characteristics of burn injury that has been evolving over the last decade is that a burn injury is not treated and healed once the wounds are healed. This used to be a landmark that no longer exists. Various studies have indicated that a burn injury and its pathophysiologic sequelae persist for at least 5–10 years, and not only in terms of scarring, infection, metabolism, and various other responses. Therefore, this leads to the importance of the current two volumes of these burn books. It has been speculated and hypothesized that early intervention and alleviation of these detrimental responses benefit in terms of clinical outcomes; therefore, the individual book chapters focus on the treatment and complexity of each of these responses to improve outcomes.

We re-edited and worked over the two books to include novel aspects of burn. We now focus more on quality of life, mental health, and novel technologies. The up-to-date chapters provide evidence-based medicine and current state-of-the-art treatments for any practitioner dealing with acute burn wounds, chronic burn wounds, and all other types of burn wounds. The second volume will then delineate the importance for long-term treatment as it describes the reconstructive and alternative approaches of long-term treatments postburn.

This is unique and therefore will hopefully improve the outcome of burn patients by guiding various kinds of burn practitioners from nursing, physicians, occupational therapy, physical therapy, pharmacy, and so forth. The focus of each chapter is not only to give an overview but also to "summarize" current best treatments and to make it easy for each reader to easily access the treatment options and knowledge.

We hope that these books will raise as much enthusiasm as it has for its contributors.

Graz, Austria — Lars-Peter Kamolz
Toronto, ON, Canada — Marc G. Jeschke
Erlangen, Germany — Raymund E. Horch
Berlin, Germany — Markus Küntscher
Brno, Czech Republic — Pavel Brychta

Contents

Part I

Psychological Aspects and Long Time Consequences

1 Acute Stress Disorder and Post-traumatic Stress Disorder in Individuals Suffering from Burn Injury

Brent W. Smith and Walter J. Meyer

1.1 Introduction

Burn injuries present unique social, emotional, and behavioral challenges to many burn survivors. While some burn survivors experience few, if any, negative psychological reactions, others experience increases in anxiety, poor body image, sleep disturbances, post-traumatic stress, and other difficulties. Even relatively small, superficial burn injuries may result in elevated levels of psychological distress in the short term. Poor psychological functioning in burn survivors is associated with a number of poor social and psychological outcomes, and can negatively impact motivation and treatment adherence. Effective management of psychological distress allows burn survivors to more fully focus on their recovery and to resume a normal life.

While burn survivors may experience many types of psychological distress, a common form of distress for both adults and children involves traumatic stress. This chapter will discuss two diagnoses associated with traumatic stress: acute stress disorder and post-traumatic stress disorder. An overview of factors related to these disorders will be presented, including common comorbid disorders and risk factors. Evidence-based assessment measures and treatment modalities (both pharmacological and non-pharmacological) will be discussed. The chapter ends with a brief overview of post-traumatic growth and future research directions.

B. W. Smith · W. J. Meyer (✉)
Department of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, TX, USA

Department of Psychological and Psychiatric Services, Shriners Hospitals for Children, Galveston, TX, USA
e-mail: bresmith@shrinenet.org; wmeyer@utmb.edu

1.2 Definition and Symptoms

Traumatic events are defined as "shocking and emotionally overwhelming situations that may involve actual or threatened death, serious injury, or threat to physical integrity" [1]. Reactions to traumatic events, such as burns, vary considerably from person to person. Many individuals experience symptoms of traumatic stress. Such symptoms include anxiety, fear, nightmares, intrusive thoughts, re-experiencing the trauma, sleep difficulties, and hypervigilance, among others. Traumatic stress reactions following a burn may be relatively mild and transient. For example, a child may experience intense anxiety and may frequently express fear about the event, but these symptoms may quickly subside over the course of a few days. Alternatively, some burn survivors experience functional impairment due to numerous intense, lasting traumatic stress symptoms. These individuals may warrant a diagnosis of either Acute Stress Disorder (ASD) or Post-Traumatic Stress Disorder (PTSD) depending on the number and severity of the symptoms, as well as the amount of time that has passed since the event. ASD is a relatively new diagnosis, first recognized in the DSM-IV in 1994. PTSD has been recognized as a disorder since 1980, first appearing in the DSM-III. Tables 1.1 and 1.2 provide a summary of the diagnostic criteria for ASD and PTSD according to the DSM-5. For full diagnostic criteria practitioners should consult the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [2].

The criteria for these disorders are similar in many ways, although dissociative symptoms are given greater emphasis in the ASD criteria. The core difference between the two disorders is one of timing: ASD is diagnosed within 30 days following the traumatic event, while PTSD is diagnosed when symptoms have been present more than 1 month.

It should be noted that failure to meet full diagnostic criteria for ASD or PTSD *does not* indicate lack of clinically significant risk and/or distress. Subthreshold PTSD symptoms are associated with a number of negative outcomes, including functional impairment, depression, and suicidal

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_1

Table 1.1 Acute stress disorder

Criterion A (required)	Exposure to actual or threatened death, serious injury, or sexual violation
Criterion B (nine required)	Presence of the following symptoms from any of the five categories of intrusion, negative mood, dissociation, avoidance, and arousal *Intrusion symptoms* • Recurrent, involuntary, and intrusive distressing memories • Recurrent distressing dreams related to the event • Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event were recurring • Intense or prolonged psychological distress or marked physiological reactions in response to triggers related to the event *Negative mood* • Persistent inability to experience positive emotions *Dissociative symptoms* • Altered sense of the reality of one's surroundings or oneself • Inability to remember an important aspect of the traumatic event *Avoidance symptoms* • Efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event • Efforts to avoid external reminders that arouse distressing memories, thoughts, or feelings about the event *Arousal symptoms* • Sleep disturbance • Irritable behavior and angry outbursts, often expressed as verbal or physical aggression toward people or objects • Hypervigilance • Problems with concentration • Exaggerated startle response
Additional requirements (all required)	• Symptoms occur within 3 days to 1 month • Symptoms create distress or functional impairment (e.g., social, occupational) • Symptoms are not due to medication, substance use, or other illness

Table 1.2 Post-traumatic stress disorder

Criterion A (one required)	The person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence, in the following way(s): • Direct exposure to the event • Witnessing the trauma • Learning that a relative or close friend was exposed to a trauma • Indirect exposure to aversive details of the trauma, usually in the course of professional duties
Criterion B (one required)	The traumatic event is persistently re-experienced, in the following way(s): • Intrusive thoughts • Nightmares • Flashbacks • Emotional distress after exposure to traumatic reminders • Physical reactivity after exposure to traumatic reminders
Criterion C (one required)	Avoidance of trauma-related stimuli after the trauma, in the following way(s): • Trauma-related thoughts or feelings • Trauma-related reminders
Criterion D (two required)	Negative thoughts or feelings that began or worsened after the trauma, in the following way(s): • Inability to recall key features of the trauma • Overly negative thoughts and assumptions about oneself or the world • Exaggerated blame of self or others for causing the trauma • Negative affect • Decreased interest in activities • Feeling isolated • Difficulty experiencing positive affect
Criterion E (two required)	Trauma-related arousal/reactivity that began or worsened after the trauma, in the following way(s): • Irritability or aggression • Risky or destructive behavior • Hypervigilance • Heightened startle reaction • Difficulty concentrating • Difficulty sleeping
Additional requirements (all required)	• Symptoms last for more than 1 month • Symptoms create distress or functional impairment (e.g., social, occupational) • Symptoms are not due to medication, substance use, or other illness

ideation [3]. In addition, several studies have indicated that the criteria for ASD may be overly strict, and that many children who do not qualify for a diagnosis of ASD nonetheless report clinically significant post-traumatic stress [4, 5]. Treating providers should ensure that traumatic stress symptoms are treated in all burn survivors, not just those who meet criteria for a diagnosis of ASD or PTSD.

1.3 Prevalence

Both ASD and PTSD are frequently diagnosed following a traumatic event. Prevalence of each disorder varies by several factors, including sex and type of traumatic event [6]. Both diagnoses are relatively common in burn survivors, as well as in the parents of children who have been burned.

1.3.1 ASD

Various studies have found rates of ASD in adults following a traumatic event to range from 6% to 33% [7]. Similar to adult findings, various rates of ASD in children have been found depending on the traumatic event. Child survivors of motor vehicle accidents show rates of ASD from 8% to 17%, while 21% of child victims of assault developed the disorder [4, 8]. Significant numbers of children and adults exposed to trauma may develop subsyndromal ASD [4, 9]. One weakness in the literature on ASD is the scarcity of studies using DSM-5 criteria. Only one published study investigating ASD prevalence in a youth sample using updated DSM-V criteria was identified, where 14.2% of children admitted to an emergency department following a traumatic event met DSM-V criteria for ASD [5].

ASD is relatively common in burn survivors. In adult burn survivors, researchers have found rates of ASD ranging from 2% to 30% [10, 11]. In children who have sustained burns, rates of ASD ranging from 8% to 31% have been found [12, 13]. These rates of ASD persist despite regimented medication management for anxiety [12]. However, existing studies of ASD in adult and pediatric burn survivors utilize DSM-IV criteria. More research on DSM-5 ASD prevalence in burn populations is needed.

1.3.2 PTSD

In contrast to ASD, there is an abundance of research regarding PTSD in both adults and children. Lifetime PTSD rates range from 6% to 9% in the USA, with PTSD rates increasing substantially for individuals exposed to multiple traumatic events [6]. Fortunately for survivors, PTSD symptoms tend to decrease over time. A review of longitudinal studies found a mean prevalence rate of PTSD of 29% 1 month following a generic trauma, which decreased to 17% 12 months later [14]. However, while most individuals experience a reduction of symptoms over time, a minority of those diagnosed with PTSD continue to experience chronic post-traumatic symptoms. About 16% of children and adolescents develop PTSD following a traumatic event [15]. Similar to adults, rates of PTSD in children vary according to type of trauma, with interpersonal trauma resulting in PTSD rates of up to 33% in females [15].

PTSD is a common diagnosis in burn survivors, although it appears to be more common in adult burn survivors than in children. PTSD may originate from the traumatic experience of being burned, but may also be related to the trauma of painful procedures (such as bathing/debridement) and severe physical complications (e.g., frequent pain, contractures, severe scarring) which occur post-burn [16]. In adult burn survivors, the prevalence of PTSD varies with the amount of time that has elapsed since the burn. Between 3% and 35% of adults develop PTSD during hospitalization, while up to 40% meet criteria for PTSD 3–6 months post-burn, 9–45% meet criteria for PTSD 1 year post-burn, and 7–25% meet criteria for PTSD more than 2 years post-burn [11]. Rates of PTSD in child burn survivors range from 2% to 19% [17, 18]. PTSD can even occur in very young children, with 10% of young burn survivors (aged 1–4 years old) diagnosed with the disorder [19].

For practitioners working with children, it is important to recognize that parents and other caregivers are at high risk for both ASD and PTSD. Researchers have found rates of clinically significant acute stress in up to 50% of mothers and 27% of fathers in the first month following a child's injury [20]. Significant post-traumatic stress symptoms continue in many parents as their child heals, with 47% of parents experiencing such symptoms 3 months post-burn [21]. High levels of anxiety in parents, in turn, are related to increased parent–child conflict [21], which may lead to increased distress in the child. Clinicians should be aware of the high likelihood of post-traumatic stress symptoms in parents, and should encourage parents to seek support and mental health treatment in order to ensure that they are psychologically healthy and able to support their recovering child.

1.4 Comorbidity

PTSD is highly comorbid with other psychological disorders, with a lifetime history of at least one other disorder present in 79% of women with PTSD and 88% of men with PTSD [22]. The most common comorbid disorders include depressive disorders, other anxiety disorders, and substance use disorders [23]. PTSD is also strongly associated with

suicidal behavior, even when controlling for other mental disorders [24]. In children, comorbid conditions can include anxiety, mood, sleep, learning, attention, and conduct problems [25].

The comorbidity of PTSD with other disorders is unclear in burn populations. However, burn survivors frequently experience other types of psychological distress, including depression, anxiety, adjustment difficulties, and impaired body image. Further research is needed on comorbidity of PTSD and ASD with other psychiatric disorders.

1.5 Risk Factors for the Development of Post-traumatic Stress

Several pretrauma risk factors for PTSD have been identified following a general traumatic event, including sex (women are up to twice as likely as men to develop PTSD following a traumatic event), prior trauma exposure, pretrauma mental health disorders, and personality factors, such as neuroticism and avoidant coping [6, 26]. PTSD is also inversely correlated with household income [27]. The intentionality of the traumatic event is important in the development of PTSD, with victims of an intentional trauma (e.g., an assault) more likely to develop PTSD than individuals exposed to a non-intentional trauma (e.g., a natural disaster). While this finding was not specific to burn-related trauma, it is likely that individuals who have been intentionally burned are at a higher risk of developing post-traumatic stress, although further research in this area is needed. After the traumatic event, individuals with PTSD are at higher risk for substance use disorders, as they may attempt to self-medicate the painful symptoms of PTSD [23].

A number of risk factors specific to the development of post-traumatic stress symptoms in burn survivors have been identified. The perceived threat to one's life during the traumatic event was found to be the most powerful predictor of adult post-traumatic stress in a recent review of the burn literature [11]. Moderately predictive factors included intrusion symptoms during acute care and severity of pain. Other predictive factors include low socioeconomic status, being unmarried, a history of previous psychiatric disorders, dissociative episodes during the burn injury event, and the development of additional mental health problems during the acute care period [11]. Appearance-related distress is also linked to a number of post-traumatic stress symptoms, notably intrusive thoughts and hyper-arousal [28]. In children, body image concerns are directly related to the development of post-traumatic stress, as are poor support systems and parental stress [13, 29, 30]. Burn size and type do not appear to be particularly predictive of PTSD [11, 31].

Alternatively, several protective factors have been identified which reduce the likelihood of developing a post-traumatic stress-related disorder following a burn injury. These protective factors include good social functioning, positive relationships, absence of feelings of shame, engagement in leisure activities, and positive appraisals about the future [11]. In our experience, small, close-knit communities also appear to serve as protective factor, possibly due to the large amount of social support received from such communities.

Of note, many studies have found that a diagnosis of ASD is only moderately useful in predicting later PTSD in non-burn populations [4, 5, 32]. This holds true for pediatric burn populations as well, with the prevalence of PTSD similar in children who had significant ASD symptoms and those who did not [33, 34]. In adult burn populations, however, researchers have found ASD to be predictive of later PTSD [10, 35, 36]. Dissociative [36] and avoidant [10] symptoms of ASD are particularly predictive of later PTSD in adults.

1.6 Assessment

When assessing ASD and PTSD in burn survivors, it is important to utilize a multi-method, multi-informant approach. While various types of validated screening instruments and semi-structured interviews are useful for obtaining a greater understanding of post-traumatic symptomatology, no one measure should be relied upon for diagnosis. Patients may minimize symptoms due to fears of stigmatization, or may lack insight into their behavior. Validated measures are best used along with a clinical interview, observation of patient behavior, and information from other sources as available (e.g., parent report, medical record, inpatient nursing observations). The US Department of Veteran Affairs' National Center for PTSD keeps an updated list of trauma and PTSD assessment measures for children and adults, which can be found at https://www.ptsd.va.gov/professional/assessment/all_measures.asp.

1.6.1 ASD

There is currently a relative lack of measures for assessing acute stress disorder based on updated DSM-5 criteria. For measures based on DSM-IV criteria, the Acute Stress Disorder Interview (ASDI) and Acute Stress Disorder Scale (ASDS) have been shown to have strong psychometric properties [37]. The ASDI is a structured clinical interview, while the ASDS is a self-report measure that correlates highly with symptom clusters found in ASDI [38, 39]. Both measures are based on adult samples and are not burn-specific measures.

There are several instruments utilized frequently in children with burn injury, both of which are based on DSM-IV criteria. The Acute Stress Disorder Symptom Checklist [40] is 12-item instrument that was developed in a pediatric burn

intensive care unit to expedite the assessment of post-traumatic distress. This scale is for in-hospital use and does not assess avoidance. The Child Stress Reaction Checklist has a Burn Version (CSRS). It is a 36-item observer-report instrument that measures acute stress and post-traumatic symptoms in children [41].

When working with children, it is important to thoroughly interview both the caregiver and the child. Research involving non-burned children has found that parent–child agreement on ASD symptoms is poor, with children more likely than parents to report disassociation and re-experiencing symptoms [42]. Parent reports were also about half as likely as child reports to meet diagnostic criteria for ASD [42]. Care should be taken to ensure that children are given the opportunity to report their symptoms.

1.6.2 PTSD

PTSD must be assessed carefully, as many symptoms overlap with other disorders. What differentiates PTSD from other disorders is (1) the presence of a traumatic event and (2) the relation of re-experiencing symptoms (e.g., flashbacks, nightmares) to that event [6]. There are a number of updated evidence-based assessment measures for assessing PTSD based on DSM-5 criteria. Structured interviews for adults include the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5), which is freely available online from the U.S. Department of Veteran Affairs' National Center for PTSD (www.ptsd.va.gov) [43], as well as the Structured Clinical Interview for DSM-5 (SCID-5) [44]. A commonly used self-report measure of PTSD symptomatology is the PTSD Checklist for DSM-5 (PCL-5), a 20-item measure which can be completed in 5–10 min [45]. Like the CAPS-5, the PLC-5 is freely available from www.ptsd.va.gov.

Structured interviews for children include the Clinician-Administered PTSD Scale for DSM-5—Child/Adolescent Version and the UCLA Child/Adolescent PTSD Reaction Index for DSM-5 [46, 47]. The PTSD Reaction Index is available in English, Spanish, and German. One freely available, easily administered measure based on DSM-5 criteria is the Child and Adolescent Trauma Screen (CATS) [48]. The CATS contains both self-report and parent-report versions and is suitable for children aged 3–17. It is available in English, German, Norwegian, and Spanish, with partial translations in several other languages [49]. For children who have been burned, the Burn Version of the Child Stress Reaction Checklist can assist in assessing post-traumatic stress symptoms [41].

In contrast to ASD, children and parents are more likely to agree on the prevalence of PTSD symptoms present in trauma-exposed children; however, there are still many differences in child/parent perceptions of symptoms and symptom severity [42]. It is important that both the child and the caregiver be interviewed before making a diagnosis of PTSD.

1.6.3 Assessment Considerations

When assessing post-traumatic stress, it is important to keep in mind several factors that can significantly impair the validity of the assessment results. These include impairments to the patient's mental status and/or delirium, pain, time, and culture. In addition, practitioners may also be faced with considerations involving time constraints and cost.

1.6.3.1 Mental Status and Delirium

Delirium is a state which develops over a short period of time (hours to days) and which tends to fluctuate. It involves (1) disturbances in attention (e.g., difficulty sustaining, focusing, or shifting attention) and awareness, as well as (2) changes in cognition, such as memory deficits, language or perceptual deficits, and disorientation [2]. There are relatively few studies examining the prevalence rate of delirium in burned patients. The existing literature, however, indicates that delirium is common in the acute care phase. For example, researchers found at least one episode of delirium occurring in 77% of ventilated adult burn patients [50].

Patients who develop PTSD are more likely than those without the diagnosis to experience an episode of delirium [51]. Therefore, ascertaining the presence of delirium is important because, if left untreated, the experience can impact psychological recovery. Before proceeding with formal psychodiagnostic assessment, it is essential to determine the individual's mental status (e.g., orientation to person, place, and time). If the patient presents with a poor mental status (e.g., confused, not oriented), then delirium should be considered. Since the evaluation and treatment of delirium is very different from that of ASD or PTSD, distinguishing delirium is very important. Delirium can be formally assessed using validated measures such as the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) for adults [52], the Pediatric CAM-ICU for children ages 5–17 [53], and the Preschool CAM-ICU for children younger than 5 years [54].

If symptoms of delirium are present, it is key to first rule-out potential medical causes (e.g., fever, metabolic disruption, blood pressure abnormalities, drug effects). Delirium is usually an early reaction that occurs during the immediate post-burn phase when patients may be intubated, heavily medicated with narcotic analgesics, overstimulated, or sleep and/or sensory deprived. These factors make reliable diagnoses of delirium difficult. In addition to medical causes, a patient's pain level may also confound a diagnosis of delirium. For this reason, adequate pain management must be vigorously addressed first. Pain-reducing medications, such

as opiates and methadone, are associated with a reduced risk of developing delirium, possibly through the reduction of pain [50].

1.6.3.2 Pain

Pain is often a large part of the post-burn experience and, if not controlled adequately, can be an overwhelming symptom. The physical and psychological manifestations of pain symptoms can appear very similar to that of anxiety and/or depression [55]. Furthermore, increases in severity of pain and number of pain locations are associated with an increase in symptoms of depression and anxiety [56]. This relationship is bidirectional, with increases in mood symptoms associated with higher odds of disabling, limiting pain [57]. Control of pain decreases the stress response, lowering cortisol and catecholamines. Better pain management during the acute phase of care is associated with a reduction in post-traumatic stress symptoms [58, 59]. In addition, when pain is well managed, patients are better able to participate in the assessment process and are less likely to exhibit pain-related mood symptoms that can interfere with a diagnosis of PTSD or ASD.

1.6.3.3 Time

Finding adequate patient time to conduct an evaluation can be difficult, particularly in inpatient settings. Patients' days are often very busy with surgeries, tubbing, rehabilitation, etc. To further compound this, medications given before and/or during the activities can leave the patient fairly sedated or drowsy afterward. However, it is important to prioritize frequent assessment of patients, as a significant portion of burn survivors, even those with small burn injuries, experience psychiatric symptoms [35, 60]. Mental health practitioners must work collaboratively with other members of the treatment team to ensure the team understands the important nature of trauma-related screening and assessment, and that adequate time is reserved for such activities.

1.7 Treatment

Left untreated, post-traumatic stress can result in a number of problematic outcomes. In the acute phase, post-traumatic stress symptoms such as re-experiencing, dissociation, negative mood, and aggression can interfere with treatment of the patient's wounds, physical and occupational therapy, and other aspects of the treatment regimen. In the long term, researchers have found that adults and children with untreated post-traumatic stress are likely to continue experiencing unwanted, disruptive post-traumatic stress symptoms [61, 62]. In addition, they report lower than average quality of life, increased depressive symptoms, and higher health care costs [61, 62]. Thankfully, there are a number of psychotherapeutic and pharmacological therapies that have been proven effective in reducing post-traumatic stress symptoms in trauma survivors. Psychotherapy for PTSD leads to a large initial improvement from baseline, and more than half of patients who complete cognitive-behavioral-related treatments experience significantly reduced symptomatology [63]. Treatment goals for those with ASD or PTSD symptoms include reducing symptom severity, preventing or treating trauma-related comorbid conditions, improving adaptive functioning, restoring a sense of safety, limiting generalization of the danger experienced as a result of the traumatic event, and preventing relapse [64].

1.7.1 Initial Intervention

In the acute phase post-injury, the focus tends to be on crisis intervention. This can include supportive services, case management, and psychoeducation about the possible symptoms and course of post-traumatic stress. During this time, individuals are encouraged to rely on their innate strengths and support system. This alone may reduce the need for further psychological intervention [64].

Another aspect of early intervention includes frequent pain assessment and aggressive management of the patient's pain and anxiety. Ratcliff et al. [12] found a 25% reduction in the incidence of ASD with pediatric burn patients since the implementation of a structured pain protocol. In addition, these researchers found that an increase in the use of morphine and benzodiazepine across an eight-year span was correlated with a simultaneous decrease (from 12.1% to 8.7%) in PTSD symptoms. This benefit of managing pain with higher doses morphine was also confirmed in a later study conducted with very young children [59].

1.7.2 Cognitive-Behavioral Therapies

The prevailing method of treatment for post-traumatic distress has been psychotherapy. A large body of research indicates that interventions based on cognitive-behavioral principles are the most effective form of psychotherapy [65]. These interventions include cognitive processing therapy (CPT), prolonged exposure (PE), eye movement desensitization and reprocessing (EMDR), and for children, trauma-focused cognitive-behavioral therapy (TF-CBT) [65–68].

A large component of each of these therapies involves exposure. Patients are exposed in a gradual manner to a feared stimulus, most often the memory of the traumatic event itself or stimuli surrounding the traumatic event (e.g., sights, sounds, or smells). This exposure may be done in vivo or through imaginal procedures. In vivo exposure involves presenting the client with the actual feared stimulus.

Examples include a child who was burned in a fire involving isopropyl alcohol gradually learning to open, smell, and then touch an alcohol wipe; or a child traumatized by her post-burn bathing procedures gradually unlearning her fear of water/bathing. Imaginal exposure is more commonly used and may take many forms, including storytelling, writing, and imagining re-experiencing the traumatic event. During exposure exercises patients use a variety of techniques, depending on the therapeutic approach, to modulate their emotions, relax their bodies, and more adaptively process the event cognitively. Ideally, survivors' feelings of safety and competence are increased during this process, as feared stimuli transition from overwhelming and terrifying to manageable, if still unpleasant.

While exposure is a large component of the treatment of PTSD, is does not occur in isolation. Treatment typically begins with psychoeducation, which helps patients understand what post-traumatic stress is and how it is commonly experienced following a traumatic event. Psychoeducation may also instill hope, as patients learn about the effectiveness of treatment. Treatment also generally involves relaxation strategies, which are taught and practiced before any repeated exposure begins. Such strategies may include diaphragmatic breathing, progressive muscle relaxation, and/or mindfulness techniques, and allow the patient to modulate certain physiological and psychological symptoms related to trauma exposure. Finally, treatment involves addressing distorted or maladaptive thoughts through cognitive restructuring, socratic questioning, thought classification, and other methods commonly used in general cognitive-behavioral therapy.

A few modifications are made when treating children with a TF-CBT approach. First, when working with children, it is essential that a parent or some other stable, trusted adult is involved in treatment. Researchers have long found the presence of competent adult caregivers to be a protective, supportive buffer for children who have experienced trauma [69, 70]. Exposure components of TF-CBT should generally not be engaged in until safety is established (e.g., the patient is no longer in the acute stage of recovery). In addition, skills related to relaxation, affect modulation, and cognitive coping should be taught and repeatedly practiced before beginning exposure exercises begin. Parents and other caregivers, including nurses, physical and occupational therapists, and other professionals, can assist in reinforcing some of these strategies after being educated by the treating clinician. In contrast to exposure, these components of TF-CBT are often appropriate to begin during the acute stage, provided the patient is cognitively intact.

Finally, clinicians are encouraged to assess post-traumatic stress symptoms with a standardized assessment instrument at baseline and periodically throughout treatment. This allows clinicians to ensure that patients are making measurable progress during treatment. If patients are not making progress or begin showing prolonged increases in symptomatology, alternative forms of treatment should be considered. Temporary increases in anxiety and fear should be expected shortly before beginning exposure exercises; however, these symptoms should remit after the exposure exercise has been completed. It can be helpful to draw patients' attention to the ways in which their fear/anxiety levels typically lessen as a function of exposure.

1.7.3 Other Psychosocial Interventions

While cognitive-behavioral therapies have been the most rigorously tested and have been proven effective in reducing post-traumatic stress symptoms, a number of other approaches are available for individuals who are either unsuitable for cognitive-behavioral treatment due to variables such as age or intellectual functioning, or who do not respond to cognitive-behavioral intervention.

Very young children may not have the verbal skills, cognitive development, or self-awareness needed to participate in CBT. For these children, play therapy may be more developmentally appropriate [71]. This approach allows indirect or symbolic expressions of emotion and events through the use of dolls, toys, art, and/or music. Play therapy can be considered an age-appropriate form of exposure therapy.

Interpersonal psychotherapy (IPT) is a time-limited, evidence-based intervention for depression [72]. In recent years, researchers have found that IPT can be effective in reducing post-traumatic stress symptoms. A randomized 14-week control trial compared IPT to prolonged exposure in adults, and found both were effective in reducing post-traumatic stress symptoms [67]. In addition, dropout rates among individuals with a comorbid diagnosis of depression were much lower for the IPT group (20%) than the PE group (50%). While IPT has not yet been studied in burn populations, it may be useful as an alternative approach for burn survivors who do not respond to other, more well-established treatments.

Finally, providing burn survivors with a strong support system is crucial in both acute and long-term recovery [30]. While it can be difficult for friends and family to see their loved one suffering, the emotional support they provide is extremely important to the patient's psychological recovery. Family and friends, particularly parents of pediatric patients, can also be trained to assist in specific types of psychosocial support, such as providing support and grounding to the patient during flashbacks or when he/she experiences intrusive images, reminding the patient to use relaxation skills, and prompting the patient use learned CBT skills (positive self-talk, reframing, etc.).

1.7.4 Medication

Acutely burned patients may initially not be able to fully engage in psychotherapy. Robert et al. [40] stated that the "acutely burned patient is often too physically impaired to engage in counseling, unable to focus cognitively, developmentally unable to process emotions verbally, or too distraught or agitated to verbalize emotions. Thus, psychopharmacologic treatment may be the only option" (p. 255). Medications, while not originally developed for treatment of ASD/PTSD, can be helpful in controlling these symptoms [2, 73].

After the Vietnam War, PTSD was recognized as a major sequelae of the war and a need for treating thousands of troops was appreciated. At the same time, a number of new antidepressants became available. These medications proved to be effective in treating the symptoms of PTSD. Tricyclic antidepressants, such as imipramine, and monoamine oxidase inhibitors were effective in some studies at 67–100% [74–76]. In the 1990s, the selective serotonin reuptake inhibitor (SSRI) fluoxetine was introduced as therapy and also found to be effective [77–79]. That was followed by other SSRIs and serotonin norepinephrine reuptake inhibitors (SNRIs) were also found to be effective [80–83]. The only SSRIs that have been supported consistently by double blind placebo control studies have been sertraline and paroxetine and the one SNRI similarly supported is venlafaxine [80, 84]. Fluoxetine has received only inconsistent support [85].

In addition, imipramine and fluoxetine have been found to significantly reduce ASD symptoms in more than 80% of the subjects [86]. In that study of 130 children, children with very large burns (>60% TBSA) did not respond as consistently as those with smaller burns. Robert et al. [40] demonstrated that imipramine was superior to chlorohydrate. However, the benefit of antidepressants could not be replicated in a subsequent study utilizing a randomized double blind match controlled study which compared medication with placebo [87]. This study suggests that ASD will often disappear on its own without intervention. Perhaps the 2 days of symptoms required for the diagnosis is not long enough to substantiate the diagnosis of ASD.

For symptoms of ASD and PTSD, SSRIs, because of their safety, are often the first medication utilized [80, 88]. There is also evidence to suggest that benzodiazepines and/or morphine will also reduce such symptoms [89]. However, the use of benzodiazepines has produced mixed results [90]. In our experience, burn patients often develop symptoms of ASD and/or PTSD in spite of receiving benzodiazepines for anxiety at that time [40]. Anticonvulsants have been used as second-line medications [91, 92]. Depakote has not been found to be helpful [93]. Antipsychotics like risperidone has been reported to be an effective adjunctive therapy for patients receiving SSRI [94–97]. These results have not always been reproducible [91]. Pregabalin has been used to augment antidepressants for PTSD [98]. Sedative antidepressants such as mirtazapine can effectively augment SSRI therapy of PTSD, particularly the associated sleep problems such as nightmares [86]. Other types of medications such as quetiapine or prazosin can fulfill the same role [99, 100]. Quetiapine has also been effective by itself in the treatment of PTSD [101–103].

The immediate post-trauma administration of adrenergic antagonists, such as propranolol, has demonstrated mixed results in the short and long term. The theory behind utilizing a medication such as propranolol is based on the idea that post-traumatic stress is characterized by atypical neuronal activation [104]. Interrupting the brain and nervous systems' natural reaction to "overlearn" the physiological response to a memory may be beneficial in the treatment of ASD/PTSD [105, 106]. This pairing of non-threatening stimuli with unpleasant stimuli is thought to be increased by prolonged production of beta-adrenergic chemicals [107]. Studies to date are limited and have found mixed results on the benefit of propranolol on ASD and PTSD in adults and children (e.g., [95, 108–111]). Failure to demonstrate an effect may be in the timing of propranolol administration. The closer to the time of the trauma the more effective it seems to be. Using a different class of medication, sertraline, Stoddard et al. have attempted to block the starting of ASD [112]. Their double blind placebo controlled study administered 25–150 mg/day in 6–20-year-olds for a 24 week period. They did demonstrate that the sertraline was more effective than placebo in preventing ASD symptoms. Further studies are definitely needed.

1.8 Post-traumatic Growth

While a burn can result in significant psychosocial difficulties, many individuals also experience personal and social growth as a result of such traumatic injuries. Such growth is termed "post-traumatic growth" (PTG). Broadly speaking, PTG is defined as positive psychological change resulting from experiencing a traumatic event [69, 113]. Examples include greater appreciation for life, greater personal strength, recognition of new opportunities, religious or spiritual growth, and improved interpersonal relationships [114]. Several studies have documented post-traumatic growth occurring in many adult burn survivors, and have identified predictors of PTG including active coping and social support [115, 116]. Several other studies have reviewed the literature on PTG in burn survivors and have identified future directions for research and practice [117, 118]. While positive outcomes in pediatric burn survivors have been documented, PTG has not yet been specifically examined in this population. There is a need for further research regarding the factors associated with PTG in both adult and pediatric burn survivors.

1.9 Summary and Conclusions

The experience of being burned, as well as some aspects of hospitalization for those with severe burns, can be traumatizing for many individuals. Special care is needed to assist individuals in their recovery over both the short and long term. A multidisciplinary, trauma-informed approach to treatment is recommended. While some patients recover without functionally impairing emotional distress, many experience ASD, PTSD, and/or clinically impactful subsyndromal post-traumatic stress symptoms. Adequate pain and anxiety management during the acute phase of treatment can aid in the prevention of ASD and PTSD development. Symptoms should be assessed through a multi-method, multi-informant approach using well-validated instruments. ASD and PTSD, as well as subsyndromal post-traumatic stress symptoms, may be treated through the use of evidence-based, trauma-informed cognitive-behavioral interventions (e.g., PE, CPT, or TF-CBT), as well as through the use of pharmacotherapy (e.g., antidepressants and anxiolytics). However, no convergent treatment has been established to date. More research is needed to determine the most effective intervention protocol to address these potentially debilitating symptoms.

References

1. International Society for Traumatic Stress Studies. ISTSS—what is traumatic stress? Washington, DC: ISTSS; 2016. http://www.istss.org/public-resources/what-is-traumatic-stress.aspx. Accessed 26 Apr 2017.
2. Baker DG, Nievergelt CM, Risbrough VB. Posttraumatic stress disorder: emerging concepts of pharmacotherapy. Expert Opin Emerg Drugs. 2009;14(2):251–72.
3. Marshall RD, Olfson M, Hellman F, Blanco C, Guardino M, Struening EL. Comorbidity, impairment, and suicidality in subthreshold PTSD. Am J Psychiatry. 2001;158(9):1467–73.
4. Kassam-Adams N, et al. Acute stress symptoms in children: results from an international data archive. J Am Acad Child Adolesc Psychiatry. 2012;51(8):812–20.
5. Meiser-Stedman R, McKinnon A, Dixon C, Boyle A, Smith P, Dalgleish T. Acute stress disorder and the transition to posttraumatic stress disorder in children and adolescents: prevalence, course, prognosis, diagnostic suitability, and risk markers. Depress Anxiety. 2017;34(4):348–55.
6. Sareen J. Posttraumatic stress disorder in adults: impact, comorbidity, risk factors, and treatment. Can J Psychiatry. 2014;59(9):460.
7. US Department of Veteran Affairs, National Center for PTSD. Acute stress disorder. Washington, DC: National Center for PTSD; 2016. https://www.ptsd.va.gov/professional/treatment/early/acute-stress-disorder.asp. Accessed 2 May 2017.
8. Meiser-Stedman R, Dalgleish T, Smith P, Yule W, Glucksman E. Diagnostic, demographic, memory quality, and cognitive variables associated with acute stress disorder in children and adolescents. J Abnorm Psychol. 2007;116(1):65–79.
9. Kangas M, Henry JL, Bryant RA. The relationship between acute stress disorder and posttraumatic stress disorder following cancer. J Consult Clin Psychol. 2005;73(2):360–4.
10. Difede J, et al. Acute stress disorder after burn injury: a predictor of posttraumatic stress disorder? Psychosom Med. 2002;64(5):826–34.
11. Giannoni-Pastor A, Eiroa-Orosa FJ, Fidel Kinori SG, Arguello JM, Casas M. Prevalence and predictors of posttraumatic stress symptomatology among burn survivors: a systematic review and meta-analysis. J Burn Care Res. 2016;37(1):e79–89.
12. Ratcliff SL, et al. The effectiveness of a pain and anxiety protocol to treat the acute pediatric burn patient. Burns. 2006;32(5):554–62.
13. Stoddard FJ, et al. Acute stress symptoms in young children with burns. J Am Acad Child Adolesc Psychiatry. 2006;45(1):87–93.
14. Santiago PN, et al. A systematic review of PTSD prevalence and trajectories in DSM-5 defined trauma exposed populations: intentional and non-intentional traumatic events. PLoS One. 2013;8(4):e59236.
15. Alisic E, et al. Rates of post-traumatic stress disorder in trauma-exposed children and adolescents: meta-analysis. Br J Psychiatry. 2014;204(5):335–40.
16. Schneider JC, et al. The long-term impact of physical and emotional trauma: the station nightclub fire. PLoS ONE. 2012;7(10):e47339.
17. Landolt MA, Buehlmann C, Maag T, Schiestl C. Brief report: quality of life is impaired in pediatric burn survivors with posttraumatic stress disorder. J Pediatr Psychol. 2009;34(1):14–21.
18. Thomas CR, Blakeney P, Holzer CE, Meyer WJ. Psychiatric disorders in long-term adjustment of at-risk adolescent burn survivors. J Burn Care Res. 2009;30(3):458–63.
19. Stoddard FJ, et al. Posttraumatic stress disorder diagnosis in young children with burns. J Burn Care Res. 2017;38(1):e343–51.
20. Bakker A, Van Loey NEE, Van der Heijden PGM, Van Son MJM. Acute stress reactions in couples after a burn event to their young child. J Pediatr Psychol. 2012;37(10):1127–35.
21. Hall E, et al. Posttraumatic stress symptoms in parents of children with acute burns. J Pediatr Psychol. 2006;31(4):403–12.
22. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry. 1995;52(12):1048–60.
23. Brady KT, Killeen TK, Brewerton T, Lucerini S. Comorbidity of psychiatric disorders and posttraumatic stress disorder. J Clin Psychiatry. 2000;61(Suppl 7):22–32.
24. Nepon J, Belik S-L, Bolton J, Sareen J. The relationship between anxiety disorders and suicide attempts: findings from the National Epidemiologic Survey on alcohol and related conditions. Depress Anxiety. 2010;27(9):791–8.
25. Caffo E, Belaise C. Psychological aspects of traumatic injury in children and adolescents. Child Adolesc Psychiatr Clin N Am. 2003;12(3):493–535.
26. Tolin DF, Foa EB. Sex differences in trauma and posttraumatic stress disorder: a quantitative review of 25 years of research. Psychol Bull. 2006;132(6):959–92.
27. Sareen J, Afifi TO, McMillan KA, Asmundson GJG. Relationship between household income and mental disorders: findings from a population-based longitudinal study. Arch Gen Psychiatry. 2011;68(4):419–27.
28. Shepherd L. A pilot study exploring the relationship between trauma symptoms and appearance concerns following burns. Burns. 2015;41(2):345–51.
29. Saxe G, et al. Risk factors for acute stress disorder in children with burns. J Trauma Dissociation. 2005;6(2):37–49.
30. Yu BH, Dimsdale JE. Posttraumatic stress disorder in patients with burn injuries. J Burn Care Rehabil. 1999;20(5):426–33; discussion 422–5.
31. Rosenberg M, et al. Immediate and long-term psychological problems for survivors of severe pediatric electrical injury. Burns. 2015;41(8):1823–30.
32. Bryant RA. Acute stress disorder as a predictor of posttraumatic stress disorder: a systematic review. J Clin Psychiatry. 2011;72(2):233–9.

33. Brown RC, et al. Predicting the transition from acute stress disorder to posttraumatic stress disorder in children with severe injuries. J Pediatr Health Care. 2016;30(6):558–68.
34. Rosenberg L, et al. Does acute stress disorder predict subsequent posttraumatic stress disorder in pediatric burn survivors? J Clin Psychiatry. 2015;76(11):1564–8.
35. McKibben JBA, Bresnick MG, Wiechman Askay SA, Fauerbach JA. Acute stress disorder and posttraumatic stress disorder: a prospective study of prevalence, course, and predictors in a sample with major burn injuries. J Burn Care Res. 2008;29(1):22–35.
36. Van Loey NEE, Maas CJM, Faber AW, Taal LA. Predictors of chronic posttraumatic stress symptoms following burn injury: results of a longitudinal study. J Trauma Stress. 2003;16(4):361–9.
37. Gibson LE. Acute stress disorder – PTSD. Washington, DC: National Center for PTSD; 2016. https://www.ptsd.va.gov/professional/treatment/early/acute-stress-disorder.asp. Accessed 10 Jun 2017.
38. Bryant RA, Moulds ML, Guthrie RM. Acute stress disorder scale: a self-report measure of acute stress disorder. Psychol Assess. 2000;12(1):61–8.
39. Bryant RA, Harvey AG, Dang ST, Sackville T. Assessing acute stress disorder: psychometric properties of a structured clinical interview. Psychol Assess. 1998;10(3):215–20.
40. Robert R, Meyer WJ, Villarreal C, Blakeney PE, Desai M, Herndon D. An approach to the timely treatment of acute stress disorder. J Burn Care Rehabil. 1999;20(3):250–8.
41. Saxe G, et al. Child stress disorders checklist: a measure of ASD and PTSD in children. J Am Acad Child Adolesc Psychiatry. 2003;42(8):972–8.
42. Meiser-Stedman R, Smith P, Glucksman E, Yule W, Dalgleish T. Parent and child agreement for acute stress disorder, posttraumatic stress disorder and other psychopathology in a prospective study of children and adolescents exposed to single-event trauma. J Abnorm Child Psychol. 2007;35(2):191–201.
43. Weathers F, Blake D, Schnurr P, Kaloupek D, Marx B, Keane T. The clinician-administered PTSD scale for DSM-5 (CAPS-5). Washington, DC: National Center for PTSD; 2013. Interview available Natl. Cent. PTSD www.ptsd.va.gov.
44. First M, Williams J, Karg R, Spitzer R. Structured clinical interview for DSM-5 disorders, clinician version (SCID-5-CV). Arlington, VA: American Psychiatric Association; 2015.
45. Weathers F, Litz B, Keane T, Palmieri P, Marx B, Schnurr P. The PTSD checklist for DSM-5 (PCL-5). 2013. Washington, DC: National Center for PTSD; 2014. Scale available Natl. Cent. PTSD. www.ptsd.va.gov.
46. Elhai JD, et al. Psychometric properties of the UCLA PTSD reaction index. Part II: investigating factor structure findings in a national clinic-referred youth sample. J Trauma Stress. 2013;26(1):10–8.
47. Steinberg AM, et al. Psychometric properties of the UCLA PTSD reaction index: part I. J Trauma Stress. 2013;26(1):1–9.
48. Sachser C, et al. International development and psychometric properties of the child and adolescent trauma screen (CATS). J Affect Disord. 2017;210:189–95.
49. Goldbeck L. Instructions for the CATS. n.d. https://ulmer-onlineklinik.de/course/view.php?id=1701. Accessed 10 Jun 2017.
50. Agarwal V, et al. Prevalence and risk factors for development of delirium in burn intensive care unit patients. J Burn Care Res. 2010;31(5):706–15.
51. Patterson DR, Everett JJ, Bombardier CH, Questad KA, Lee VK, Marvin JA. Psychological effects of severe burn injuries. Psychol Bull. 1993;113(2):362–78.
52. Ely EW, et al. Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit (CAM-ICU). Crit Care Med. 2001;29(7):1370–9.
53. Smith HAB, et al. Diagnosing delirium in critically ill children: validity and reliability of the pediatric confusion assessment method for the intensive care unit. Crit Care Med. 2011;39(1):150–7.
54. Smith HAB, et al. The preschool confusion assessment method for the ICU: valid and reliable delirium monitoring for critically ill infants and children. Crit Care Med. 2016;44(3):592–600.
55. Main CJ, Spanswick CC. Pain management: an interdisciplinary approach. Amsterdam: Elsevier Health Sciences; 2000.
56. Gerrits MMJG, van Oppen P, van Marwijk HWJ, Penninx BWJH, van der Horst HE. Pain and the onset of depressive and anxiety disorders. Pain. 2014;155(1):53–9.
57. de Heer EW, et al. The association of depression and anxiety with pain: a study from NESDA. PLoS ONE. 2014;9(10):e106907.
58. Saxe G, et al. Relationship between acute morphine and the course of PTSD in children with burns. J Am Acad Child Adolesc Psychiatry. 2001;40(8):915–21.
59. Stoddard FJ, et al. Preliminary evidence for the effects of morphine on posttraumatic stress disorder symptoms in one- to four-year-olds with burns. J Burn Care Res. 2009;30(5):836–43.
60. Tedstone JE, Tarrier N. An investigation of the prevalence of psychological morbidity in burn-injured patients. Burns. 1997;23(7):550–4.
61. Goenjian AK, Walling D, Steinberg AM, Karayan I, Najarian LM, Pynoos R. A prospective study of posttraumatic stress and depressive reactions among treated and untreated adolescents 5 years after a catastrophic disaster. Am J Psychiatry. 2005;162(12):2302–8.
62. Priebe S, et al. Consequences of untreated posttraumatic stress disorder following war in former Yugoslavia: morbidity, subjective quality of life, and care costs. Croat Med J. 2009;50(5):465–75.
63. Bradley R, Greene J, Russ E, Dutra L, Westen D. A multidimensional meta-analysis of psychotherapy for PTSD. Am J Psychiatry. 2005;162(2):214–27.
64. Ursano RJ, et al. Treatment of patients with acute stress disorder and posttraumatic stress disorder. Washington, DC: American Psychiatric Association; 2010.
65. Institute of Medicine Committee on Treatment of PTSD. Treatment of posttraumatic stress disorder: an assessment of the evidence. Washington, DC: National Academy of Sciences; 2008.
66. Cary CE, McMillen JC. The data behind the dissemination: a systematic review of trauma-focused cognitive behavioral therapy for use with children and youth. Child Youth Serv Rev. 2012;34(4):748–57.
67. Markowitz JC, et al. Is exposure necessary? A randomized clinical trial of interpersonal psychotherapy for PTSD. Am J Psychiatry. 2015;172(5):430–40.
68. Watts BV, Schnurr PP, Mayo L, Young-Xu Y, Weeks WB, Friedman MJ. Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. J Clin Psychiatry. 2013;74(6):e541–50.
69. Kilmer RP, Gil-Rivas V, Griese B, Hardy SJ, Hafstad GS, Alisic E. Posttraumatic growth in children and youth: clinical implications of an emerging research literature. Am J Orthopsychiatry. 2014;84(5):506–18.
70. Masten AS, Best KM, Garmezy N. Resilience and development: contributions from the study of children who overcome adversity. Dev Psychopathol. 1990;2(4):425–44.
71. Goodyear-Brown P. Play therapy with traumatized children. Hoboken, NJ: John Wiley & Sons; 2010.
72. de Mello MF, de Jesus Mari J, Bacaltchuk J, Verdeli H, Neugebauer R. A systematic review of research findings on the efficacy of interpersonal therapy for depressive disorders. Eur Arch Psychiatry Clin Neurosci. 2005;255(2):75–82.
73. Reinblatt SP, Riddle MA. The pharmacological management of childhood anxiety disorders: a review. Psychopharmacology. 2007;191(1):67–86.
74. Davidson J. Vintage treatments for PTSD: a reconsideration of tricyclic drugs. J Psychopharmacol. 2015;29(3):264–9.
75. Frank JB, Kosten TR, Giller EL, Dan E. A randomized clinical trial of phenelzine and imipramine for posttraumatic stress disorder. Am J Psychiatry. 1988;145(10):1289–91.
76. Southwick S, Yehuda R, Giller E Jr, Charney D. Use of tricyclics and monoamine oxidase inhibitors in the treatment of PTSD: a quantita-

tive review. Catecholamine Funct Post-Trauma Stress Disord Emerg Concepts. 1994;1994:293–305.
77. Nagy LM, Morgan CA, Southwick SM, Charney DS. Open prospective trial of fluoxetine for posttraumatic stress disorder. J Clin Psychopharmacol. 1993;13(2):107–13.
78. Shay J. Fluoxerine reduces explosiveness and elevates mood of Vietnam combat vets with PTSD. J Trauma Stress. 1992;5(1):97–101.
79. van der Kolk BA, et al. Fluoxetine in posttraumatic stress disorder. J Clin Psychiatry. 1994;55(12):517–22.
80. Bernardy NC, Friedman MJ. Pharmacological management of posttraumatic stress disorder. Curr Opin Psychol. 2017;14:116–21.
81. Brady K, et al. Efficacy and safety of sertraline treatment of posttraumatic stress disorder: a randomized controlled trial. JAMA. 2000;283(14):1837–44.
82. Seedat S, et al. Comparison of response to a selective serotonin reuptake inhibitor in children, adolescents, and adults with posttraumatic stress disorder. J Child Adolesc Psychopharmacol. 2002;12(1):37–46.
83. Simon NM, et al. Paroxetine CR augmentation for posttraumatic stress disorder refractory to prolonged exposure therapy. J Clin Psychiatry. 2008;69(3):400–5.
84. Davidson J, Rothbaum BO, Tucker P, Asnis G, Benattia I, Musgnung JJ. Venlafaxine extended release in posttraumatic stress disorder: a sertraline- and placebo-controlled study. J Clin Psychopharmacol. 2006;26(3):259–67.
85. Lee DJ, Schnitzlein CW, Wolf JP, Vythilingam M, Rasmusson AM, Hoge CW. Psychotherapy versus pharmacotherapy for posttraumatic stress disorder: systemic review and meta-analyses to determine first-line treatments. Depress Anxiety. 2016;33(9):792–806.
86. Schneier FR, et al. Combined mirtazapine and SSRI treatment of PTSD: a placebo-controlled trial. Depress Anxiety. 2015;32(8):570–9.
87. Robert R, et al. Treating thermally injured children suffering symptoms of acute stress with imipramine and fluoxetine: a randomized, double-blind study. Burns. 2008;34(7):919–28.
88. Yehuda R, McFarlane A. PTSD is a valid diagnosis: who benefits from challenging its existence? Cranbury Township, NJ: Psychiatric Times; 2009.
89. Saxe GN, et al. Pathways to PTSD, part I: children with burns. Am J Psychiatry. 2005;162(7):1299–304.
90. Marshall RD, Pierce D. Implications of recent findings in posttraumatic stress disorder and the role of pharmacotherapy. Harv Rev Psychiatry. 2000;7(5):247–56.
91. Jeffreys MD. Atypical antipsychotics and anticonvulsants in the treatment of PTSD: treatment options that include cognitive behavioral therapies. In: A practical guide to PTSD treatment: pharmacological and psychotherapeutic approaches. Washington, DC: American Psychological Association; 2015. p. 89–99.
92. Berger W, et al. Pharmacologic alternatives to antidepressants in posttraumatic stress disorder: a systematic review. Prog Neuro-Psychopharmacol Biol Psychiatry. 2009;33(2):169–80.
93. Davis LL, Davidson JRT, Ward LC, Bartolucci A, Bowden CL, Petty F. Divalproex in the treatment of posttraumatic stress disorder: a randomized, double-blind, placebo-controlled trial in a veteran population. J Clin Psychopharmacol. 2008;28(1):84–8.
94. Hamner MB, Faldowski RA, Ulmer HG, Frueh BC, Huber MG, Arana GW. Adjunctive risperidone treatment in post-traumatic stress disorder: a preliminary controlled trial of effects on comorbid psychotic symptoms. Int Clin Psychopharmacol. 2003;18(1):1–8.
95. Pastrana Jiménez JI, Catalina Romero C, García Diéguez N, Lopez-Ibor Aliño JJ. Pharmacological treatment of acute stress disorder with propranolol and hypnotics. Actas Esp Psiquiatr. 2007;35(6):351–8.
96. Meighen KG, Hines LA, Lagges AM. Risperidone treatment of preschool children with thermal burns and acute stress disorder. J Child Adolesc Psychopharmacol. 2007;17(2):223–32.
97. Rothbaum BO, Killeen TK, Davidson JRT, Brady KT, Connor KM, Heekin MH. Placebo-controlled trial of risperidone augmentation for selective serotonin reuptake inhibitor-resistant civilian posttraumatic stress disorder. J Clin Psychiatry. 2008;69(4):520–5.
98. Pae C-U, Marks DM, Han C, Masand PS, Patkar AA. Pregabalin augmentation of antidepressants in patients with accident-related posttraumatic stress disorder: an open label pilot study. Int Clin Psychopharmacol. 2009;24(1):29–33.
99. Raskind MA, et al. A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in combat veterans with post-traumatic stress disorder. Biol Psychiatry. 2007;61(8):928–34.
100. Byers MG, Allison KM, Wendel CS, Lee JK. Prazosin versus quetiapine for nighttime posttraumatic stress disorder symptoms in veterans: an assessment of long-term comparative effectiveness and safety. J Clin Psychopharmacol. 2010;30(3):225–9.
101. Kozaric-Kovacic D, Pivac N. Quetiapine treatment in an open trial in combat-related post-traumatic stress disorder with psychotic features. Int J Neuropsychopharmacol. 2007;10(2):253–61.
102. Villarreal G, et al. Efficacy of quetiapine monotherapy in posttraumatic stress disorder: a randomized, placebo-controlled trial. Am J Psychiatry. 2016;173(12):1205–12.
103. Hamner MB, Deitsch SE, Brodrick PS, Ulmer HG, Lorberbaum JP. Quetiapine treatment in patients with posttraumatic stress disorder: an open trial of adjunctive therapy. J Clin Psychopharmacol. 2003;23(1):15–20.
104. Southwick SM, Paige S, Morgan CA, Bremner JD, Krystal JH, Charney DS. Neurotransmitter alterations in PTSD: catecholamines and serotonin. Semin Clin Neuropsychiatry. 1999;4(4):242–8.
105. Debiec J, LeDoux JE. Noradrenergic signaling in the amygdala contributes to the reconsolidation of fear memory: treatment implications for PTSD. Ann N Y Acad Sci. 2006;1071:521–4.
106. Pitman RK, Delahanty DL. Conceptually driven pharmacologic approaches to acute trauma. CNS Spectr. 2005;10(2):99–106.
107. Marmar CR, Neylan TC, Schoenfeld FB. New directions in the pharmacotherapy of posttraumatic stress disorder. Psychiatry Q. 2002;73(4):259–70.
108. Brunet A, Orr SP, Tremblay J, Robertson K, Nader K, Pitman RK. Effect of post-retrieval propranolol on psychophysiologic responding during subsequent script-driven traumatic imagery in post-traumatic stress disorder. J Psychiatr Res. 2008;42(6):503–6.
109. McGhee LL, Maani CV, Garza TH, Desocio PA, Gaylord KM, Black IH. The effect of propranolol on posttraumatic stress disorder in burned service members. J Burn Care Res. 2009;30(1):92–7.
110. Sharp S, Thomas C, Rosenberg L, Rosenberg M, Meyer W. Propranolol does not reduce risk for acute stress disorder in pediatric burn trauma. J Trauma. 2010;68(1):193–7.
111. Rosenberg L, et al. Does acute propranolol treatment prevent posttraumatic stress disorder, anxiety, depression in children with burns? J Child Adolesc Psychopharmacol. 2018;28(2):117–23.
112. Stoddard FJ, et al. A randomized controlled trial of sertraline to prevent posttraumatic stress disorder in burned children. J Child Adolesc Psychopharmacol. 2011;21(5):469–77.
113. Picoraro JA, Womer JW, Kazak AE, Feudtner C. Posttraumatic growth in parents and pediatric patients. J Palliat Med. 2014;17(2):209–18.
114. Tedeschi RG, Calhoun LG. Posttraumatic growth: conceptual foundations and empirical evidence. Psychol Inq. 2004;15(1):1–18.
115. Baillie SE, Sellwood W, Wisely JA. Post-traumatic growth in adults following a burn. Burns. 2014;40(6):1089–96.
116. Rosenbach C, Renneberg B. Positive change after severe burn injuries. J Burn Care Res. 2008;29(4):638–43.
117. Askay SW, Magyar-Russell G. Post-traumatic growth and spirituality in burn recovery. Int Rev Psychiatry. 2009;21(6):570–9.
118. Attoe C, Pounds-Cornish E. Psychosocial adjustment following burns: an integrative literature review. Burns. 2015;41(7):1375–84.

Long-Term Outcomes Following Burn Injuries

2

Shelley A. Wiechman

2.1 Introduction

As a result of the declining length of inpatient hospitalization after major burn injuries, patients are being discharged with multiple, long-term physical and psychological challenges, such as ongoing pain, intensive physical therapy, contractures, amputations, and psychological distress. These challenges can persist for many years, requiring specialty multidisciplinary burn care. Issues associated with long-term adjustment have been recognized as a priority for research and clinical practice. In this chapter, we will begin by using a biopsychosocial model to examine various factors of long-term burn recovery. We will also discuss various aspects of emotional distress, pain, pruritus, sleep, and body image issues, and conclude with recommendations for treatment.

2.2 The Biopsychosocial Model of Recovery

A person's response to stress is a function of their personality style and coping mechanisms and how these interact over time with the environmental factors that are present. Univariate models are insufficient to explain a person's response to a burn injury and their long-term outcomes. More sophisticated, theory-driven biopsychosocial models are needed to explain outcomes of burn injury. Researchers have identified pre-burn psychological disorders, injury characteristics (e.g., burn size and location, acute pain levels), lack of social support, and ineffective coping styles as risk factors for poor post-injury adjustment [1].

S. A. Wiechman (✉)
Department of Rehabilitation Medicine, University of Washington School of Medicine, Seattle, WA, USA
e-mail: wiechman@uw.edu

2.2.1 Pre-burn Emotional and Physical Health

A person's pre-burn level of physical and emotional functioning can greatly impact their course of recovery from their ICU stay to years beyond discharge. For example, those patients with substance abuse disorders, diabetes, COPD, and other medical comorbidities have lower survival rates, longer lengths of stay, and fair poorer overall. The available research largely supports the impression that individuals with burns severe enough to warrant hospital care often have pre-existing chaos and dysfunction in their lives. In several reviews of the literature, it was found that the incidence of mental illness and personality disorders was higher in burn unit patients than the general population [2–4]. For example, Patterson et al. [3], estimated that the presence of premorbid psychiatric disorders ranged between 28% and 75%, higher than expected in the general population. These disorders include depression, personality disorders, and substance abuse. Another study by Patterson et al. [5] found patients with burn injuries scored higher on premorbid levels of psychological distress, anxiety, depression, and loss of behavioral and emotional control when compared to a national normative sample. These studies also found that individuals with pre-existing psychopathology often cope with hospitalization through previously established, dysfunctional and often disruptive patterns. Such dysfunctional coping styles, in turn, had an adverse impact on hospital course that increased length of stay and led to more serious psychopathology upon discharge and throughout their outpatient recovery.

2.2.2 Injury Characteristics

Researchers have begun to focus on potential variables from acute hospitalization that may have a long-term impact on adjustment [6, 7]. Total Burn Surface Area (TBSA), length

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_2

of hospitalization, and days spent in the ICU or on a ventilator have been used as indicators of the severity of a burn injury. Research on the relation between these variables and outcomes has been equivocal. Patterson et al. [3] cautioned against using TBSA as the sole predictor of emotional outcome, citing studies that have shown significant emotional distress in persons with relatively small burns, and little to no distress in persons with large burns. High inpatient pain levels have also been found to lead to long-term distress. The amount of pain that a person reports in the hospital supersedes both the size of their burn and the length of hospitalization as predictors of long-term outcome at six months, one year, and two years post discharge [6, 8]. Location of the burn has been found to predict adjustment, with those persons with burns on their face or hands showing more emotional distress than those with more hidden burns [9].

2.2.3 Coping

In the general literature on coping, Lazarus and Folkman [10] proposed a comprehensive model of stress and coping that is based on the notion that a person's appraisal of the demands and consequences of a situation and the amount of control they perceive to have over the situation will lead to selection of a particular coping strategy. A number of organizing terms have been used to categorize coping styles [11]. The extent to which a coping strategy involves approaching a particular stressor, versus avoiding the stressor, is a widely used classification [12]. For instance, active strategies such as problem-solving, information seeking, and social support seeking can be construed as approach-oriented coping, and strategies that involve disengagement, denial, or distraction can be viewed as avoidance-oriented efforts. Neither approach-oriented nor avoidance-oriented coping behaviors are inherently adaptive or maladaptive; coping effectiveness is better determined by the characteristics of the individual and the situation [10]. However, reviews of the literature on coping with chronic illness have suggested that approach-oriented coping styles are more favorable towards physical and emotional health outcomes in medical populations [13].

Some research has suggested that the selection of a specific coping strategy will depend on the individual's appraisal of the amount of control they have over the situation. For example, if a person appraises the situation as being more controllable, then they will use a strategy in which they will attempt to actively problem-solve or mobilize resources; if they appraise low levels of control, then they will likely employ strategies in which they distract their attention away from the stressor [14]. Little research has attempted to characterize the adaptiveness of specific coping strategies in burn patients over time. It is also unknown if a person can be taught a specific coping style, especially when under such considerable stress as recovering from a burn injury.

2.2.4 Emotional Distress

The first year or two following a burn injury seems to be a time of substantial distress [3, 15–18]. Clearly, mood disorders [9, 15, 19–23] and anxiety disorders [15, 19, 20, 22, 24, 25] are the most common symptoms of distress; however, patients may also experience a myriad of other problems, including sleep disturbance [26–28], body image concerns [29], and sexual problems [30, 31]. It is important to recognize that although patients may not meet full DSM-V criteria for a diagnosis of the disorder, individual symptoms can cause a great deal of distress and should be treated [32, 33].

2.2.5 Post-traumatic Stress Disorder

The reported frequency of acute stress disorder (ASD) following a burn injury ranges from 11% to 32% of patients [20, 34–39]. While the frequency of post-traumatic stress disorder (PTSD) is approximately 23–33% of patients 3–6 months after a burn injury [34, 40], that percentage ranges from 15% to 45% at one year following the injury [15, 20, 37, 41]. In contrast, community-based studies show that the lifetime prevalence of persons with PTSD is 1–14% [42]. The large variability in reported rates of diagnosed ASD/PTSD is likely due to differences in measurement strategies and measurement timepoints. However, most researchers and clinicians agree that even if patients do not meet a formal diagnosis of ASD or PTSD, the majority of burn survivors are having at least some of the symptoms of this disorder (e.g., nightmares, intrusive thoughts, hypervigilance, avoidance) that negatively impacts their quality of life. When identifying possible risk factors for the development of PTSD, pre-existing anxiety or depressive disorders are associated with an increased risk of developing PTSD. Further, the baseline symptoms of ASD at discharge and at 1 month predict presence of PTSD at 1 year [43], suggesting that symptoms do not decrease over time if left untreated. In addition, burn patients who have a comorbid diagnosis of PTSD are higher utilizers of medical services. Injury-related characteristics such as total body surface area burned and the location of the injury have repeatedly failed to predict who will suffer from such trauma. In contrast, issues such as the patient's mental health history, social support, and coping style hold significant promise as predictive factors. We recommend a screening tool such as the Post-Traumatic Stress Disorder Symptom Checklist – Civilian version (PSCL-C) [44] to identify those suffering from symptoms of PTSD.

2.2.6 Depression

Research that has attempted to identify rates of depressive disorders following a burn injury has been fraught with challenges. In their comprehensive review, Thombs and colleagues [45] found that most of the studies have been at single centers with small sample sizes with poor rates of recruitment and retention. In addition, the multiple approaches and measures used have led to a wide variation in reported rates of depressive symptoms and diagnosable disorders. For example, the range of reported symptoms in the first year after a burn injury is 2–22% and the prevalence rate after one year is 3–54% [46]. There seem to be much lower prevalence rates of depression when a structured interview is used as compared to a standardized measure. But even when standardized measures are used, the rates vary widely. The most common standardized measures are the Hospital Anxiety and Depression Scale (depression subscale) (HADS) [47] and the Beck Depression Inventory (BDI) [48]. The HADS does not include questions with somatic symptoms, but the BDI does. Oftentimes it is difficult to differentiate between what symptoms can be attributed to the medical disorder and what are somatic symptoms of depression, which could account for the higher reported rates of depression when using the BDI versus the HADS. The general consensus among the medical community is that if a person meets criteria for a DSM-V diagnosis, they should be diagnosed and treated, even if symptoms can be accounted for by the medical condition. This approach is known as the inclusive approach. The rationale behind this approach is that the origin of symptoms is less important than the distress that they are causing and patients will benefit from treatment. Typically, patients are underdiagnosed for mental health disorders in the medical setting and are overlooked for treatment that could enhance their quality of life [49]. In recent years, the 9-item Patient Health Questionnaire [50] has been recommended for use as a screening tool in primary care and other medical specialty clinics and may prove to be useful in the burn setting.

Several studies have also found that depression rates tend to be stable from discharge to at least the first year following a burn injury [21]. Although it is commonly assumed that these rates will decrease after the first year, no longitudinal studies have looked at depression rates longer than 1 year post-injury. Thombs et al. [46] found seven studies that reported on risk factors for depression following a burn injury. As mentioned earlier, many of the identified risk factors encompass premorbid functioning, such as employment status, medical illness, and prior depression. Those who suffered from depressive symptoms in the year prior to the burn injury were five times more likely to be diagnosed with a mood disorder at hospital discharge [15]. Other risk factors include female gender, and a visible burn [9]. Although research in this area has been fraught with methodological problems making it difficult to pin down actual rates of depressive disorders, the ABA quality consensus committee recommends a brief screen for depressive symptoms during the inpatient hospitalization, at discharge and at follow-up clinic visits [51]. Referrals to mental health professionals can be made for more in-depth assessments if warranted by the responses on the screening tool.

2.2.7 Pain

Burn pain varies greatly from patient to patient, shows substantial fluctuation over time, and can be unpredictable due to the complex interaction of physiologic, psychosocial, and premorbid behavior issues [52]. Burn pain that is reported after the initial injury is not reliably correlated with the size or depth of a burn. Specifically, a patient with a superficial (second degree) burn may show substantially more pain than one with a full thickness (third degree) burn, due to both physical factors (e.g., location and mechanism of the injury, individual differences in pain threshold and tolerance, response to analgesics) and psychologic factors (e.g., previous pain experiences, anxiety, depression). As a result, it is critical to realize that predicting the amount of pain or suffering a patient will experience based on the nature of, or the physiologic response to, their burn injury is not possible, and furthermore, the patient's pain experience can change dramatically over the course of both inpatient and outpatient care. It is also important to note that pain can continue well beyond wound healing.

Chronic pain is defined as pain that lasts longer than six months or remains after all burn wounds and skin graft donor sites have healed. The mechanisms and treatment of chronic burn pain are inadequately studied and poorly understood. Although most acute burn pain results from tissue damage, it is important to be aware that pain from nerve damage may also be present, particularly in severe injuries associated with extremity amputations, and represent an anatomic source for chronic burn pain complaints. Because there are identifiable sensory changes in patients who suffer burn injuries, it is unclear as to whether or not these patients' pain should be defined as chronic pain or is simply an ongoing form of acute or neuropathic pain. Regardless of the label used to classify post-burn injury chronic pain, ongoing pain has the potential to have a significant negative impact on the quality of life of burn survivors.

Malenfant et al. [53] found evidence for changes in the central nervous system that could maintain pain for years after a burn wound has healed. They found that significant sensory losses and sensory changes were found not only in burn sites but also in the non-injured areas. Tactile sensibility deficits were significantly associated with the presence of

painful sensations. This was greatest in deep burn injuries that required skin grafting.

Choiniere et al. [54] interviewed 104 burn survivors who were 1–7 years post-burn injury. The mean time since burn injury was 37 months, and the mean Total Burn Surface Area (TBSA) was 19%. Surprisingly, 35% reported ongoing pain. Of those reporting pain, 75% said it interfered with work, 56% said it interfered with sleep, and 67% reported interference with social functioning. In a sample of 236 burn survivors 1–9 years post-burn injury with a mean time since injury of 47 months, and a mean TBSA of 20%, Malenfant et al. [53] found a similar rate of patients with ongoing pain (36%). Work interference was reported by 67% of those with pain, 36% reported sleep difficulties, and 47% reported disturbance in social activities. Recently, Schneider et al. [55] reviewed the natural history of neuropathic-like pain after a burn injury. Over a 2-year period they found 72 patients in their outpatient clinic that described symptoms consistent with neuropathic pain. The average pain rating was 7/10 and persisted for more than 1 year after the injury. In this study, gabapentin and steroid injections were used to treat the pain about one-third of the time. Other interventions included rest, massage, use of pressure garments, and elevation.

Finally, Dauber [56] mailed out a survey to members of a burn survivor support group and of the 358 respondents, 52% reported ongoing pain, 66% said that it interfered with their rehabilitation, and 55% said the pain interfered with their daily lives. Respondents in this study also reported that thoughts of the accident and depression made their pain worse. In these studies, TBSA and skin grafting have been the only predictors of chronic pain. The majority of respondents had not tried relaxation, imagery, or hypnosis. It is important to note that the average length of time since the burn injury in two of these studies was 3–4 years. This is well past the one-year time frame that medical professionals believe it takes for burn injuries to be completely healed.

In order to provide comprehensive and consistent analgesic care for burn patients, many burn centers advocate a structured approach to burn analgesia that incorporates both pharmacologic and nonpharmacologic therapies, targets the specific clinical pain settings unique to the burn patient and yet can be individualized to meet specific patient needs and institutional capabilities. Such structured protocols help to avoid both the undertreatment of burn pain and concerns regarding opioid addiction. A discussion of specific pharmacological protocols used to treat burn pain is beyond the scope of this article and can be found elsewhere [57, 58].

2.2.8 Nonpharmacological Chronic Burn Pain Management

Two approaches that have been empirically tested for chronic pain include hypnosis and cognitive behavior therapy. Although hypnosis involves much more than just avoidance or distraction, the end result is often similar in that this technique takes a person's focus off of the painful procedure they are undergoing. Hypnosis is an altered state of consciousness characterized by an increased receptivity to suggestion, ability to alter perceptions and sensations, and an increased capacity for dissociation. It is believed that the dramatic shift in consciousness that occurs with hypnosis is the cornerstone of an individual's ability to change their awareness of pain [59]. Hypnosis involves several stages, including building clinician–patient rapport, enhancing relaxation through deep breathing, suggestions for deepening the hypnotic state and narrowing their attention, providing posthypnotic suggestions, and alerting [60]. The posthypnotic suggestions allow us to do hypnosis at any time prior to the painful procedure, thus eliminating the need for our presence during the procedure. We typically use a rapid induction analgesia format described by Patterson [60] and originally published by Barber [60], but there are numerous scripts for hypnotic analgesia that can be used directly or with improvisation. However, the technique should only be used by trained clinicians who can assess the risks and benefits of this powerful technique.

Cognitive restructuring is frequently used as a coping technique for patients with chronic pain [61, 62]. However, there are reports in the literature of using this technique for various type of pain, including that from dental work and surgical procedures [63]. A handful of studies have looked at this approach with burn pain [64, 65]. Catastrophizing has been found to have the largest link between thoughts and pain. This distorted thinking style exaggerates any sensation of pain, or setback, and becomes a point of perseveration for the patient. For example, a minor setback in therapy following a planned surgery (such as a contracture release), a wound infection, or simple fatigue, can turn into thoughts such as "I can't take this anymore; I have to start all over again; I will never recover."

The first step in cognitive restructuring is to identify and stop negative, catastrophizing thoughts. Thoughts such as "this is really going to hurt" and "I can't handle this pain" only lead to an increase in anxiety and a subsequent increase in pain. Patients can learn to recognize these negative thoughts and stop them, perhaps by picturing a stop sign or red light in their mind. They can also distract themselves by turning their attention to another topic. Children as young as seven years of age have been taught to use this technique successfully [64, 66].

Ideally, we want patients to transform their catastrophic thoughts into a positive statement. This is known as reappraisal or reframing. For example, they may change the thoughts in the above example to "I have been through this wound care procedure before and it did not hurt as much as I thought it would," or " I have a very high pain tolerance and can cope with whatever will happen." Patients may also ben-

efit from being taught the difference between "hurt" and "harm" when interpreting their pain sensations [67]. Specifically, an increase in pain is often a good sign with respect to burn wound healing. As discussed early in the chapter, deep (third degree) burns often destroy nerve endings and limit the capacity for nociception. In deep burns that begin to heal or in more shallow burns, skin buds develop that are highly innervated and sensitive to pain and temperature. Explaining this healing process to patients can help them to understand the nature of their pain and to reframe negative thoughts into reassuring, positive ones.

2.2.9 Sleep

Sleep problems are one of the most common complaints of burn patients once they are discharged from the hospital, yet likely one of the most undertreated. Sleep problems are best viewed as a symptom rather than a disease and are frequent even in the absence of burn injury, affecting up to 50% of normal adults in the USA [68]. Addressing sleep in a general population as insomnia can lead to distress, impaired functioning, increased accidents, and decreased work productivity [69, 70]. With burn survivors, poor sleep can affect issues such as therapy performance, pain control, adjustment, and even wound healing. Thus, addressing sleep after burn injuries is an important issue to address in addition to the variety of other complications survivors have to face.

A burn injury and its treatment present a multitude of factors that can interfere with sleep. Early in care, the hospital setting and nature of care can be highly disruptive factors. Frequent painful and intrusive treatments, noisy settings, metabolic imbalance, and awakening to take vital signs are the rule rather than the exception. As wounds heal, pruritus (itch) can become extremely unpleasant, in addition to the pain. Anxiety and depression can also interrupt sleep in themselves, but the medication to control burn-related complications such as pruritus, pain, and depression also has an impact on sleep. It is not surprising then that patients with burn injuries will experience impaired sleep for long periods of time, first from the issues associated with hospitalization and later as a function to the transition home.

Given all of these factors, it is not surprising that the few studies that have been done on sleep quality with burn survivors reflect high levels of disruption. Rose and colleagues [71] followed 82 children with severe burn injuries and reported serious sleep disturbance one year after injury. Sleep disturbances included nightmares, bedwetting, and sleepwalking. Approximately 63% of the sample complained of needing daytime naps, which is far greater than the norm. The few studies that have monitored polysomnogram (PSG) in burn survivors have reported increased total sleep time, decreases in stage 3 and 4 sleep, decreased rapid eye movement (REM) sleep, and increased arousals when compared to age-matched controls [72–74].

With respect to treatment for sleep disorders after burn injuries, there is little question that healthcare professionals entertain pharmacologic options far too early and to the exclusion of more benign options. Clinicians should work with the patients on nonpharmacologic interventions before turning to this option. Nonpharmacologic options include sleep hygiene, stimulus control, sleep restriction, relaxation therapy, cognitive-behavioral therapy, and light therapy. Sleep hygiene interventions include changing the environment (e.g., quiet rooms), reducing daytime naps, establishing regular sleep/wake schedules, reducing stimulants from late afternoon to prior to bedtime when appropriate (e.g., caffeine, candy, nicotine, alcohol), decreasing stimuli at night (e.g., internet, TV), and proper timing of food and exercise. Stimulus control involves creating the bed as a stimulus for sleep by having the patient go to bed only when sleepy and removing competing stimuli from the bedroom (e.g., television), sleep restriction focuses on having the patient remain in bed only when asleep. Cognitive-behavioral therapy can help patients work with the dysfunctional thoughts that disrupt sleep, relaxation therapy is self-explanatory, and light therapy can address disruption of circadian rhythms. A full review of the medications used to treat sleep disorders after a burn injury is reported by Jaffe and Patterson [28].

2.2.10 Pruritus

Pruritus continues to be one of the most common and distressing complications following a burn injury. Pruritus can be severe and interfere with sleep, daily activities and can reopen wounds due to scratching. Post-burn pruritus also tends to be cyclical in that it begins in the early stages of wound healing, peaks at 6 months post-burn and declines after the first year following the injury [75]. Pruritus occurs in both healed and grafted skin, but is more intense where hypertrophic scarring has formed. There is a paucity of evidence-based research in this area, although a plethora of pharmacological and nonpharmacological interventions have been proposed in smaller scale studies. Recently, there has been a greater understanding of the physiological mechanisms underlying pruritus in burn injuries. For example, it is largely believed that pruritus from burns stems from inflammation, dryness and damage to the skin, as well as nerve damage/regeneration [76]. Two review articles on evidence-based treatments for post-burn pruritus have been published recently [77, 78]. Both reviews have found some potentially promising treatments for post-burn pruritus and will be summarized in the table below. Bell and Gabriel [77] used the Practice Guidelines for Burn Care 2006 [78] to classify the studies. They found the most promising treatments with the

strongest study designs to be selective antihistamine receptor agonists (Cetirizine/Cimetidine) and the pulse dye laser. Across studies, any antihistamine administration appeared to be better than no administration, but no single antihistamine worked effectively all of the time. Pulse dye laser treatments were used for intense itching in smaller areas with three treatments at one-month intervals; the effects lasted up to 12 months [79]. Combinations of the various treatments may also be more effective than single treatments from one modality [80]. Authors caution that the evidence is based on smaller scale studies and larger, prospective, randomized controlled trials need to be conducted.

2.2.11 Body Image

Burn injuries can cause significant changes in appearance, whether from scarring, contractures, changes in skin pigmentation, or amputations. The impact that these physical changes have on self-esteem and body image has only recently been studied [81–83]. The majority of research on body image has focused on eating disorders or congenital differences (e.g., cleft palate) and there has been little study on acquired changes in appearance (e.g., trauma, burns, etc.). Across disability groups (craniofacial abnormalities, amputations, burns, SCI), there is a wide range of individual differences in terms of coping with visible disfigurement. Specifically, Egan et al. [84] estimated that 30–50% of individuals with visible differences may experience psychological difficulty at some time. This highlights the fact that the majority of individuals adjust to their scars well and can go on to develop an appreciation for their body. Several studies of risk factors for the development of poor body image found that burn characteristics, such as the visibility of the scar, and objective severity of a disfigurement do not predict the extent of distress or negative body image [84]. Instead, personal characteristics such as depression, female gender, and coping style best predicted body image dissatisfaction [81–83].

An additional predictor of body image dissatisfaction is the importance that a patient placed on their appearance before the burn injury. If a person did not place much importance on their appearance before the burn, they tend to be much less distressed by scarring [81] . As such, viewing the visible difference as only a small part of their lives seems to be critical in developing body appreciation. Family and unconditional acceptance play a large role in this process. Parents can help children learn to talk about their scars in a casual way and model positive social responses towards teasing or other stigmatization. Developing hobbies, talents and exploring other aspects of identity (not just physical appearance) will help individuals to put their appearance in perspective. This might be challenging in western society where physical appearance is paramount. It would be beneficial to the field to put more focused research efforts on those people with visible differences who go on to develop a strong body appreciation. Most treatments to address body image concerns have focused on cognitive-behavioral strategies to address a person's appraisal of their appearance, to teach adaptive coping strategies, and to introduce social skills that enhance self-esteem and improve social competence [85, 86]. Two of these programs are the Changing Faces program in Great Britain [87] and the BEST program in the US [88]. Both of these programs include a hospital-based image enhancement and social skills program, along with a series of publications for patients dealing with aspects of scarring and changes in appearance. These programs teach survivors a number of adaptive behaviors in response to the inevitable negative societal responses to a change of appearance.

There has been recent attention on the concept of body appreciation, defined broadly as love and acceptance of one's body and appreciation of its uniqueness and the function it performs [89]. The concept of body appreciation is distinctly different than that of body dissatisfaction, and interventions to promote body image appreciation may be slightly different than CBT approaches for body dissatisfaction. More research needs to be conducted in this area with our burn population. We do a disservice to our patients if we exclusively focus on alleviating symptoms of body image disturbance without recognizing opportunities to promote body image appreciation.

2.2.12 Return to Work

Returning to work is a major step towards reintegration following a burn injury. Research has shown that the sooner a person can return to work, the more likely they are to return to work and the better state of mental health. Returning to work can be an important part of therapy as it forces a person to get up, out of the house and be active daily. Work can improve mood and improve quality of sleep. The burn team can set a person up for success in this area by encouraging them to contact their employer as soon as possible following the injury and assist with filling out any necessary paperwork. It is rare that a person with a burn injury qualifies for either short- or long-term disability. A gradual return to work plan is recommended that includes consideration of light duty options as soon as possible after discharge, as well as returning to work for a couple of hours for a short time, then progressing to half days and finally full days. Returning to work in the middle of a typical work week can ease the transition as there are only a couple of days of work until the weekend and then they can rest and start again the following week. Patients should be encouraged to consult their state's employment rules, especially if it is an injury that occurred on the job.

2.2.13 Return to School

Similar to returning to work, the sooner a child can return to school, the better they do emotionally and physically. Public schools are mandated to provide accommodations when needed. This may entail allowing a child to wear splints and pressure garments during the day and getting assistance with range of motion exercises. Accommodations for physical education classes might also be necessary for a short time. It is rare that a child would need home schooling or to change schools as a result of their injury. The Phoenix Society has developed a program entitled, "The Journey Back," for parents, teachers, and hospital staff who are assisting a child with a positive return to school after a burn injury. It is important that the child be prepared for questions and comments from classmates about their injury. Healthcare providers and parents need to discuss different questions and scenarios with the child and rehearse appropriate responses prior to returning to school.

Signature Programs of the Phoenix Society

- A peer support program (Phoenix SOAR).
- A secure and moderated online support group (Phoenix Connect).
- A program to assist with school re-entry (The Journey Back).
- An annual international conference for both adults and teen burn survivors and their families (World Burn Congress).
- A comprehensive set of tools that offers practical ways to handle teasing, questions, and various social interactions after a burn injury (Beyond Surviving: Tools for Thriving).
- Finally, a variety of online courses for burn recovery.

2.3 Summary

A biopsychosocial model of burn outcomes can be useful to guide our understanding of the long-term outcomes of burn survivors. The ongoing rehabilitation issues that burn survivors face are complex and can include physical, emotional, social, and vocational challenges. The distress of the injury does not end when patients leave the hospital. Problems with anxiety, depression, sleep, pruritus, and body image can continue for years. All can impact a patient's ability to return to an acceptable quality of life. Further, we have facilitated two burn survivor focus groups this past year to ascertain barriers to returning to an acceptable quality of life. Unanimously, survivors felt isolated once they were discharged from the outpatient clinic services and felt that the secondary conditions mentioned above were not being addressed by their primary care providers, particularly those in more rural communities [52, 53]. They expressed a desire to have more burn-specific interventions once they returned home. The multidisciplinary team approach to care that has long been practiced by inpatient rehabilitation and inpatient burn units should continue after discharge. Patients will continue to benefit from the expertise provided by both burn surgeons and physiatrists, as well as services from a vocational counselor, social workers, physical and occupational therapists and psychologists. Connecting patients and families with the Phoenix Society is critical. The Phoenix Society is a national advocacy group that provides programs and support services for both burn survivors and their families. Finally, more research needs to focus on effective treatments for the various issues that burn survivors face. Treatment interventions for these issues must be sophisticated and flexible enough to account for the large variability in causes of distress.

Summary Box

A biopsychosocial model of burn outcomes can be useful to guide our understanding of the long-term outcomes of burn survivors. The ongoing rehabilitation issues that burn survivors face are complex and can include physical, emotional, social, and vocational challenges. The distress of the injury does not end when patients leave the hospital. Problems with anxiety, depression, sleep, pruritus, and body image can continue for years. All can impact a patient's ability to return to an acceptable quality of life. Patients will continue to benefit from the expertise provided by both burn surgeons and physiatrists, as well as services from a vocational counselor, social workers, physical and occupational therapists and psychologists. Connecting patients and families with the Phoenix Society and other groups of peers is critical. Finally, more research needs to focus on effective treatments for the various issues that burn survivors face. Treatment interventions for these issues must be sophisticated and flexible enough to account for the large variability in causes of distress.

Acknowledgement Funding support: NIDILRR grant 90DP0029. NIH grant R01 GM042725.

References

1. Wiechman SA, Hoyt M, Patterson DR. Using a biopsychosocial model to understand long-term outcomes in persons with burn injuries. Arch Phys Med Rehabil. 2018;101(1S):S55–62.

2. Kolman PBR. The incidence of psycholopathology in burned adult patients: a critical review. J Burn Care Rehabil. 1983;4:430–6.
3. Patterson DR, Everett JJ, Bombardier CH, et al. Psychological effects of severe burn injuries. Psychol Bull. 1993;113(2):362–78.
4. Patterson DR, Jensen M. Hypnosis and clinical pain. Psychol Bull. 2003;129(4):495–521.
5. Patterson DR, Finch CP, Wiechman SA, et al. Premorbid mental health status of adult burn patients: comparison with a normative sample. J Burn Care Rehabil. 2003;24(5):347–50.
6. Patterson DR, Tininenko J, Ptacek JT. Pain during burn hospitalization predicts long-term outcome. J Burn Care Res. 2006;27(5):719–26.
7. Noronha DO, Faust J. Identifying the variables impacting post-burn psychological adjustment: a meta-analysis. J Pediatr Psychol. 2007;32(3):380–91.
8. Ptacek JT, Patterson DR, Montgomery BK, et al. Pain, coping, and adjustment in patients with severe burns: preliminary findings from a prospective study. J Pain Symptom Manage. 1995;10:446–55.
9. Wiechman SA, Ptacek JT, Patterson DR, et al. Rates, trends, and depression following burn injuries. J Burn Care Rehabil. 2001;22(6):417–24.
10. Lazarus RS, Folkman S. Stress, appraisal and coping. New York, NY: Springer; 1984.
11. Taylor SE, Stanton AL. Coping resources, coping processes, and mental health. Annu Rev Clin Psychol. 2007;3:377–401.
12. Suls J, Fletcher B. The relative efficacy of avoidant and non-avoidant coping strategies: a meta-analysis. Health Psychol. 1985;4(3):249–88.
13. Stanton AL, Revenson TA, Tennen H. Health psychology: psychological adjustment to chronic disease. Annu Rev Psychol. 2007;58:565–92.
14. Folkman S, Lazarus RS. An analysis of coping in a middle-aged community sample. J Health Soc Behav. 1980;21:219–39.
15. Fauerbach J, Lawrence J, Haythornthwaite J, et al. Pschiatric history affects post trauma morbidity in a burn injured adult sample. Psychosomatics. 1997;38:374–85.
16. Fauerbach JA, McKibben J, Bienvenu OJ, et al. Psychological distress after major burn injury. Psychosom Med. 2007;69(5):473–82.
17. Edwards RR, Magyar-Russell G, Thombs B, et al. Acute pain at discharge from hospitalization is a prospective predictor of long-term suicidal ideation after burn injury. Arch Phys Med Rehabil. 2007;88(12 Suppl 2):S36–42.
18. Ullrich PM, Askay SW, Patterson DR. Pain, depression, and physical functioning following burn injury. Rehabil Psychol. 2009;54(2):211–6.
19. Fukunishi I. Relationship of cosmetic disfigurement to the severity of posttraumatic stress disorder in burn injury or digital amputation. Psychother Psychosom. 1999;68(2):82–6.
20. Madianos MG, Papaghelis M, Ioannovich J, et al. Psychiatric disorders in burn patients: a follow-up study. Psychother Psychosom. 2001;70(1):30–7.
21. Ptacek J, Patterson D, Heimbach D. Inpatient depression in persons with burns. J Burn Care Rehabil. 2002;23(1):1–9.
22. Tedstone JE, Tarrier N. An investigation of the prevalence of psychological morbidity in burn-injured patients. Burns. 1997;23(7-8):550–4.
23. Williams EE, Griffiths TA. Psychological consequences of burn injury. Burns. 1991;17(6):478–80.
24. Bauer K, Hardy P, Van Sorsten V. Posttraumatic stress disorder in burn populations: a critical review of the literature. J Burn Care Rehabil. 1998;19:230–40.
25. Ehde D, Patterson D, Wiechman S, et al. Post-traumatic stress symptoms and distress one year after burn injury. J Burn Care Rehabil. 2000;21(2):105–11.
26. Boeve SA, Aaron LA, Martin-Herz SP, et al. Sleep disturbance after burn injury. J Burn Care Rehabil. 2002;23(1):32–8.
27. Lawrence J, Fauerbach J, Eudell E, et al. Sleep disturbance following burn injury: a frequent yet understudied complication. J Burn Care Rehabil. 1998;19:480–6.
28. Jaffe S, Patterson DR. Treating sleep problems in patients with burn injuries: practical considerations. J Burn Care Rehabil. 2004;25(3):294–305.
29. Fauerbach JA, Heinberg LJ, Lawrence JW, et al. Effect of early body image dissatisfaction on subsequent psychological and physical adjustment after disfiguring injury. Psychosom Med. 2000;62(4):576–82.
30. Bianchi TL. Aspects of sexuality after burn injury: outcomes in men. J Burn Care Rehabil. 1997;18(2):183–6; discussion 182.
31. Wiechman Askay SA, Patterson DR. Psychological rehabilitation in burn injuries. In: Frank RG, Rosenthal M, Caplan B, editors. Handbook of rehabiliation psychology. 2nd ed. Washington, DC: American Psychological Association; 2009.
32. Fauerbach JA, Lawrence JW, Munster AM, et al. Prolonged adjustment difficulties among those with acute posttrauma distress following burn injury. J Behav Med. 1999;22(4):359–78.
33. Patterson DR, Ptacek JT, Cromes F, et al. The 2000 Clinical Research Award. Describing and predicting distress and satisfaction with life for burn survivors. J Burn Care Rehabil. 2000;21(6):490–8.
34. Difede J, Ptacek JT, Roberts J, et al. Acute stress disorder after burn injury: a predictor of posttraumatic stress disorder? Psychosom Med. 2002;64(5):826–34.
35. Bryant R. Predictors of post-traumatic stress disorder following burn injury. Burns. 1996;22:89–92.
36. Fleming MP, Difede J. Effects of varying scoring rules of the Clinician Administered PTSD Scale (CAPS) for the diagnosis of PTSD after acute burn injury. J Trauma Stress. 1999;12(3):535–42.
37. Lambert JF, Difede J, Contrada RJ. The relationship of attribution of responsibility to acute stress disorder among hospitalized burn patients. J Nerv Ment Dis. 2004;192(4):304–12.
38. Ehde DM, Patterson DR, Wiechman SA, et al. Post-traumatic stress symptoms and distress following acute burn injury. Burns. 1999;25:587–92.
39. Van Loey NE, Maas CJ, Faber AW, et al. Predictors of chronic posttraumatic stress symptoms following burn injury: results of a longitudinal study. J Trauma Stress. 2003;16(4):361–9.
40. El Hamaoui Y, Yaalaoui S, Chihabeddine K, et al. Post-traumatic stress disorder in burned patients. Burns. 2002;28(7):647–50.
41. Difede J, Barocas D. Acute intrusive and avoidant PTSD symptoms as predictors of chronic PTSD following burn injury. J Trauma Stress. 1999;12(2):363–9.
42. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
43. McKibben JB, Bresnick MG, Wiechman Askay SA, et al. Acute stress disorder and posttraumatic stress disorder: a prospective study of prevalence, course, and predictors in a sample with major burn injuries. J Burn Care Res. 2008;29(1):22–35.
44. Weathers F, Litz B, Herman D, Huska J, Keane T. The PTSD Checklist (PCL): reliability, validity, and diagnostic utility. San Antonio, TX: Paper presented at the Annual Convention of the International Society for Traumatic Stress Studies; 1993.
45. Thombs BD, Bresnick MG, Magyar-Russell G. Depression in survivors of burn injury: a systematic review. Gen Hosp Psychiatry. 2006;28(6):494–502.
46. Thombs BD, Bass EB, Ford DE, et al. Prevalence of depression in survivors of acute myocardial infarction. J Gen Intern Med. 2006;21(1):30–8.
47. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–70.
48. Beck A, Steer RA, Brown G. BDI-II manual. 2nd ed. San Antonio, TX: The Psychological Corporation; 1996.

49. Wiechman SA, Kalpakjian CZ, Johnson KL. Measuring depression in adults with burn injuries: a systematic review. J Burn Care Res. 2016;37(5):e415–26.
50. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606–13.
51. Gibran NS, Wiechman SA, et al. Summary of the 2012 ABA burn quality consensus conference. J Burn Care Res. 2013;34(4):361–85.
52. Perry S, Heidrich G. Management of pain during debridement: a survey of U.S. burn units. Pain. 1982;13(3):267–80.
53. Malenfant A, Forget R, Amsel R, et al. Tactile, thermal and pain sensibility in burned patients with and without chronic pain and paresthesia problems. Pain. 1998;77(3):241–51.
54. Choiniere M, Melzack R, Papillon J. Pain and parathesia in patients with healed burns: an exploratory study. J Pain Symptom Manage. 1991;6:437–44.
55. Schneider JC, Harris NL, El Shami A, et al. A descriptive review of neuropathic-like pain after burn injury. J Burn Care Res. 2006;27(4):524–8.
56. Dauber A, Osgood PF, Breslau AJ, et al. Chronic persistent pain after severe burns: a survey of 358 burn survivors. Pain Med. 2002;3(1):6–17.
57. Faucher L, Furukwaw K. Practice guidelines for the management of pain. J Burn Care Rehabil. 2006;27(5):659–68.
58. Summer GJ, Puntillo KA, Miaskowski C, et al. Burn injury pain: the continuing challenge. J Pain. 2007;8(7):533–48.
59. Barber J. A brief introduction to hypnotic analgesia. In: Barber J, editor. Hypnosis and suggestion in the treatment of pain. A clinical guide. New York, NY: W.W. Norton & Company; 1996. p. 3–33.
60. Patterson DR. Burn pain. In: Barber J, editor. Hypnosis and suggestion in the treatment of pain. New York, NY: W. W. Norton & Company; 1996. p. 267–302.
61. Holzman AD, Turk DC. Pain management. Oxford: Pergamon Press; 1986.
62. Turk DC, Meichenbaum D, Genest M. Pain and behavioral medicine: a cognitive-behavioral perspective. New York, NY: Guilford Press; 1983.
63. Langer E, Janis I, Wolfer J. Reduction of psychological stress in surgical patients. J Exp Soc Psychol. 1975;11:165–9.
64. Thurber CA, Martin-Herz SP, Patterson DR. Psychological principles of burn wound pain in children. I: theoretical framework. J Burn Care Rehabil. 2000;21(4):376–87; discussion 375.
65. Everett J, Patterson DR, Chen AC. Cognitive and behavioral treatments for burn pain. Pain Clin. 1990;3(3):133–45.
66. Zeltzer L. Pain and symptom management. In: Bearson DJ, Mullhern RK, editors. Pediatric psychooncology: psychological perspectives on children with cancer. New York, NY: Oxford University Press; 1994. p. 61–83.
67. Fordyce WE. Behavioral methods for chronic pain and illness. C.V. Mosby: St. Louis, MO; 1976.
68. Ancoli-Israel S, Roth T. Characteristics of insomnia in the United States: results of the 1991 National Sleep Foundation Survey I. Sleep. 1999;22(2):S347–53.
69. Chesson A, Hartse K, Anderson W, et al. Practice parameters for the evaluation of chronic insomnia. An American Academy of Sleep Medicine report. Standards of Practice Committee of the American Academy of Sleep Medicine. Sleep. 2000;23(2):237–41.
70. Weyerer S, Dilling H. Prevalence and treatment of insomnia in the community: results from the Upper Bavarian Field Study. Sleep. 1991;14(5):392–8.
71. Rose M, Sanford A, Thomas C, et al. Factors altering the sleep of burned children. Sleep. 2001;24(1):45–51.
72. Gottschlich MM, Jenkins M, Mayes T, et al. Lack of effect of sleep on energy expenditure and physiologic measures in critically ill burn patients. J Am Diet Assoc. 1997;97(2):131–9.
73. Gottschlich MM, Jenkins ME, Mayes T, et al. The 1994 Clinical Research Award. A prospective clinical study of the polysomnographic stages of sleep after burn injury. J Burn Care Rehabil. 1994;15(6):486–92.
74. Robertson CF, Zuker R, Dabrowski B, et al. Obstructive sleep apnea: a complication of burns to the head and neck in children. J Burn Care Rehabil. 1985;6(4):353–7.
75. Ahee AM, Smith SJ, Pliska-Matyshak G, et al. When does itching start and stop post-burn? J Burn Care Rehabil. 1999;20(1 Pt 2):S187.
76. Goutos I, Dziewulski P, Richardson PM. Pruritus in burns: review article. J Burn Care Res. 2009;30(2):221–8.
77. Bell PL, Gabriel V. Evidence based review for the treatment of post-burn pruritus. J Burn Care Res. 2009;30(1):55–61.
78. Gibran NS. Practice guidelines for burn care, 2006. J Burn Care Res. 2006;27(4):437–8.
79. Allison KP, Kiernan MN, Waters RA, et al. Pulsed dye laser treatment of burn scars. Alleviation or irritation? Burns. 2003;29(3):207–13.
80. Baker RA, Zeller RA, Klein RL, et al. Burn wound itch control using H1 and H2 antagonists. J Burn Care Rehabil. 2001;22(4):263–8.
81. Fauerbach JA, Heinberg LJ, Lawrence JW, et al. Coping with body image changes following a disfiguring burn injury. Health Psychol. 2002;21(2):115–21.
82. Lawrence JW, Fauerbach JA, Heinberg L, et al. Visible vs hidden scars and their relation to body esteem. J Burn Care Rehabil. 2004;25(1):25–32.
83. Abdullah A, Blakeney P, Hunt R, et al. Visible scars and self-esteem in pediatric patients with burns. J Burn Care Rehabil. 1994;15(2):164–8.
84. Egan K, Harcourt D, Rumsey N. A qualitative study of the experiences of people who identify themselves as having adjusted positively to a visible difference. J Health Psychol. 2011;16(5):739–49.
85. Fauerbach J, Spence R, Patterson D. Adult burn injury. In: Sarwer D, Goldwyn R, Pruzinsky T, et al., editors. Psychological aspects of reconstructive and cosmetic plastic surgery: clinical, empirical, and ethical perspectives. Philadelphia, PA: Lippincott Williams and Wilkins; 2006.
86. Pruzinsky T, Cash TF. Integrative themes in body-image development, deviance, and change. In: Cash TF, Pruzinsky T, editors. Body images: development, deviance, and change. New York, NY: Guilford Press; 1990. p. 337–49.
87. Partridge J. When burns affect the way you look. London: Changing Faces; 1997.
88. Kammerer B. BEST program provides key to successful community reintegration. Burn Support News. 2010;Winter:1–4.
89. Tylka TL, Wood-Barcalow NL. What is and what is not positive body image? Conceptual foundations and construct definition. Body Image. 2015;14:118–29.

Part II

Skin Architecture and Burn Wound Healing

Skin Architecture and Function

3

Adelheid Elbe-Bürger and Gabriel Hundeshagen

3.1 Skin Structure

The human skin accounts for about 15% of the total adult body weight and is the largest organ. It exerts multiple crucial functions. It forms a protective barrier; shields our muscles, internal organs, and body fluids from bacteria, viruses, ultraviolet light, and other environmental aggressors; protects the body from dehydration or massive absorption of water; functions as a thermoregulator and sense organ; and plays a crucial cell-mediated immunity. The skin contains tissues of various origins (epithelial, connective, vascular, muscular, and nervous) which are organized in three layers: epidermis (outermost layer), dermis, and the hypodermis (consisting of adipose tissue that connects the dermis to underlying skeletal components) (Fig. 3.1). The epidermis and its appendages are of ectodermal origin, whereas the dermis and the hypodermis are of mesenchymal origin. The epidermis and dermis are connected by the dermal-epidermal junction, which is synthesized by basal keratinocytes and dermal fibroblasts. The skin is not developed homogeneously and shows regional variations in thickness and distribution of epidermal appendages [1, 2].

A. Elbe-Bürger
Division of Immunology, Allergy and Infectious Diseases (DIAID), Department of Dermatology, Medical University of Vienna, Vienna, Austria
e-mail: adelheid.elbe-buerger@meduniwien.ac.at

G. Hundeshagen (✉)
Department of Hand, Plastic and Reconstructive Surgery, Burn Trauma Center, BG Trauma Center Ludwigshafen, University of Heidelberg, Ludwigshafen, Germany

Department of Surgery, Shriners Hospital for Children, University of Texas Medical Branch, Galveston, TX, USA

3.2 Epidermis

The epidermis is a stratified, non-vascularized epithelium that undergoes a continuous process of renewal and loss through cell replication in its basal compartment and desquamation at the surface. The primary source of cell renewal is proliferation and differentiation of stem cells [3–5]. However, there seems to be some plasticity between stem cells and their early progeny, as most basal keratinocytes maintain their regenerative potential and are capable of regenerating epidermis [6]. Evidence has been provided that commitment to differentiation does not prohibit keratinocytes from re-entering the cell cycle, de-differentiation, and acquiring "stemness," suggesting that epidermis can use different strategies for homeostasis and tissue regeneration [7].

Many cell types can be found in the epidermis, the majority (~90%) of which are keratinocytes. They undergo morphological and biochemical differentiation (keratinization), resulting in the production of corneocytes that shed from the skin surface with time (~30 days). There are other distinct cell populations which have specific functions such as Langerhans cells (LCs, resident immune cells), melanocytes (production of melanin), Merkel cells (mediators of mechanotransduction), and infrequent T cells.

The epidermis consists of a multilayered sheet of keratinocytes (from the bottom up) interspersed by hair follicles [1]. The stratum basale (also known as stratum germinativum) is a single layer of cells attached to a noncellular basal membrane that separates the epidermis from the dermis. It consists mostly of basal keratinocytes, Merkel cells, and melanocytes. The stratum spinosum (5–15 layers) contains irregular polyhedral keratinocytes with limited capacity for cell division and LCs. This cell layer provides the mechanical strength necessary to resist physical trauma. The stratum granulosum (1–3 layers) contains flattened, polyhedral keratinocytes producing keratohyalin granules. Tight junctions in this layer play an essential role in fluid retention [8]. The stratum corneum contains many sheets of flattened, nonviable, scale-like corneocytes responsible for actual mechanical

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_3

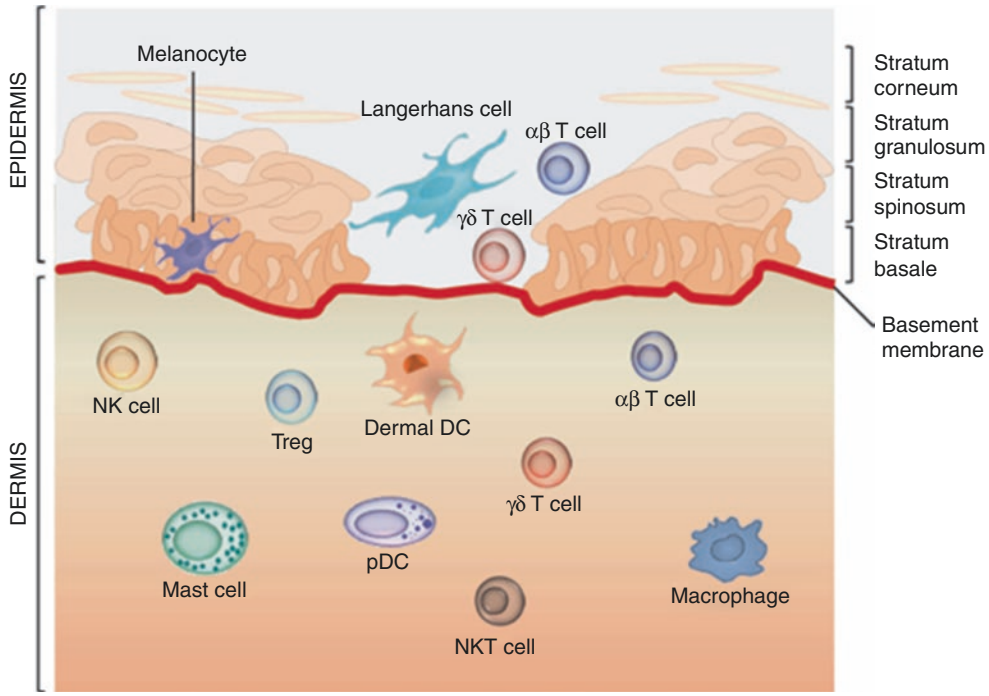


Fig. 3.1 Structure of the skin—the different layers and cell types. Collagen, elastin, and other components of the extracellular matrix of the dermis and the hypodermis are not represented. The stratum lucidum usually present in thick epidermis such as palms and soles is not included; it is normally located between the stratum granulosum and stratum corneum and consists of flattened cells with no nuclei. Merkel cells are not represented either (designed by Marion Prior)

shielding of the skin [9] (Fig. 3.1). In some body areas (i.e., palmo-plantar regions), an additional layer is located between the stratum granulosum and the stratum corneum—the stratum lucidum [10]. The thickness of the epidermis varies among body areas [thinnest sites: face, trunk (20–60 μm), thicker areas: arms, legs, back of hand, upper foot (40–80 μm), thickest sites: soles of the feet, fingertips (160–560 μm)] [11]. Lastly, the epidermis contains the superficial part of the eccrine sweat glands.

3.3 Dermis

Underneath the epidermis is the dermis—a considerably thicker (2–4 mm) layer that can be divided into a papillary (superficial) and a reticular (deep) portion. Its supportive, compressible and elastic connective tissue protects epidermis, its appendages and the nervous and vascular plexuses. The dermis contains an extracellular matrix composed of fibrous and non-fibrous proteins and inorganic matter: glycoproteins (i.e., laminin, fibronectin), proteoglycans (versican, perlecan), glycosaminoglycans (i.e., keratin sulfate, heparin, chondroitin), water, and hyaluronic acid [1, 2]. Collagen (mainly types I and III, also IV and VII) provides the skin with tensile strength and tissue integrity, whereas elastin provides elasticity and resiliency. A wide network of blood vessels provides nutrient supply for the stratum basale of the epidermis, lymphatic vessels, nerve endings, sweat glands, excretory glands (sebaceous, eccrine, and apocrine), muscles, hair follicles, nails, as well as resident and trafficking cells [1]. The main cell type of the dermis is the fibroblast. The dermis also hosts cells of the immune system such as interstitial dendritic cells (DCs), plasmacytoid DCs, macrophages, mast cells, natural killer (NK) cells, and T cells [TCR $\alpha\beta^+$ T cells (T helper 1 (T_H1) cells, T_H2 cells, $CD8^+$ T cells, T_H17 cells), regulatory T cells (Tregs), natural killer T (NKT) cells, and TCR $\gamma\delta^+$ T cells] (Fig. 3.1) [12–14]. Dermal thickness varies depending on the anatomic region (back, palms, and soles have thicker dermis than the eyelids).

3.4 Hypodermis (Subcutaneous Fat, Panniculus Adiposus)

The hypodermis is a subcutaneous tissue and in fact not part of the skin. It connects the dermis to the underlying bones or muscles, stores lipids, regulates body temperature, insulates and cushions the body. The main cell type is the adipocyte showing pericellular expression of S100 protein and vimentin [2]. Fibroblasts, mast cells, sweat gland endings, vessels, and nerves contribute to the formation of the corresponding dermal plexuses.

3.5 Skin (Stem) Cells: A Promising Source for Tissue Engineering and Regenerative Medicine?

Therapeutic applications of stem cells in regenerative medicine are anticipated to be part of clinical medicine soon. With regard to skin, the focus of stem cell research is and will be on the epidermis and the hair follicle. Under normal

conditions, the interfollicular epidermis and sebaceous glands are constantly self-renewing, while the hair follicles undergo cyclic changes of growth, involution, and resting phases [15, 16]. For hair follicle stem cells, it has been described that they not only reside in the stem cell niche called "bulge" and express CD34, cytokeratin 15, CD200 [17–22] and retain DNA or histone labels [23–25], but that they are also present in other areas [26–29]. Most recently, Hans Clevers and his group found that a stem cell cluster in a hair follicle, characterized by the expression of leucine-rich repeat-containing G protein-coupled receptor 6 (Lgr6), a close homolog of the Lgr5 marker for stem cells in the small intestine and colon, resides directly above the hair bulge and gives rise to all cell lineages of the mouse skin [30]. In experiments with wounded mice, they found that Lrg6 stem cells around the wound initiated wound repair [30]. The isolation of the human variant could dramatically improve clinical trials in patients. Today we are already able to grow new skin in vitro using skin cells from patients with severe burns, but the new hairless skin is often dry and fragile. With the discovery of the "mother" stem cell, it could be possible to re-establish the normal anatomy and function of the skin and its appendages in burn and wound patients.

Mesenchymal stem cells (MSCs) residing within the dermis were first isolated in 2001 and named "skin-derived precursors" (SKPs). They have the capacity to differentiate into adipocytes, osteocytes, chondrocytes, smooth muscle cells, neurons, glia cells such as Schwann cells as well as hematopoietic cells of myeloid and erythroid lineage [31–43]. Pending a more in-detail investigation they also seem to be able to differentiate into insulin-producing pancreatic cells, keratinocytes, hepatocytes, and other cells [44–46]. The dermal papillae of hair follicles represent the likely anatomical niche for these multipotent dermal cells [32, 47–51]. Because of their easy isolation and culture, multipotency, and highly expansive properties, dermal MSCs have the potential to function as a readily accessible, autologous source for several therapeutic applications. These include the treatment of graft-versus-host disease, idiopathic pulmonary fibrosis, systemic lupus erythematosus, arthritis, neurodegenerative disorders, traumatic spinal injury, and others [52, 53]. The most immediate impact can be expected in the field of wound healing. In the treatment of burn injury, the advent of cultured epithelial autografts (CEA) in the 1980s sparked the lasting interest in "cell-supported" wound healing [54, 55]. In recent years, MSCs isolated from subcutaneous adipose tissue have been transferred to woundbeds successfully via direct injection, spraying, or enclosed in various synthetic and biomaterials [56–58]. Many studies have suggested a contribution of MSCs to reconstituting skin in cutaneous wounds through improved vascularization and re-epithelialization, but problems related to harvest, expansion, storage, and cost need resolution before MSCs can become a standard clinically [59–61].

A newer technology has been developed to de-differentiate and reprogram adult somatic cells (in the skin from keratinocytes, dermal fibroblasts, dermal papilla cells, etc.) into a stem cell-like state which have been named induced pluripotent stem (iPS) cells. Originally performed in mice and later established also in humans, researchers induced pluripotency through selective gene transfer [62–66]. Such lines could be expanded indefinitely and could differentiate to form numerous kinds of different tissues. Even though several limitations currently preclude their use in a clinical setting, this discovery opens up the possibility of generating patient-specific pluripotent cells for autologous regenerative medicine.

3.6 Keratinocytes: Immune Competent Epithelial Cells

The predominant cell type of the epidermis is the keratinocyte with morphological variations within epidermal layers. Keratinocytes of the stratum basale are anchored by hemidesmosomes to the basement membrane that separates the epidermis from the dermis (Fig. 3.1). Adjacent keratinocytes of all layers are generally interconnected by desmosomes, tight junctions, and adherens junctions. Basal keratinocytes contain melanosomes, to store the skin color pigment melanin, which is synthesized by melanocytes. The basal layer contains stem cells and cycling keratinocytes, expressing proliferation antigens such as Ki67 and PCNA. The stratum corneum consists of corneocytes which are devoid of a nucleus and of cytoplasmic organelles and are shed from the skin surface, thus contributing to the barrier function of the skin. Keratins (K) are fibrous proteins belonging to the family of intermediate filaments and are parts of the cytoskeleton. Their primary function is to protect epithelial cells from mechanical and non-mechanical stresses that would result in cell death. Other emerging functions include cell signaling, stress response and apoptosis induction, as well as unique functions that are keratin specific and tissue specific. Two types of keratins can be distinguished, based on their pH value: Type 1 keratins are acidic, whereas type 2 keratins are neutral/basic [67, 68]. Keratinocytes express keratin polypeptides in pairs, composed of a type 1 and a type 2 keratin. Within normal epidermis, K5 and K14/K15 are expressed in basal keratinocytes, whereas K1 and K10 are expressed in suprabasal keratinocytes. Stratum granulosum cells express K2 and K11, and those in the plantar region express K9 [69].

Keratinocytes function as immune sentinels. They can recognize foreign and potentially harmful agents such as conserved pathogen-associated molecular patterns (PAMPs) which are shared by numerous microorganisms, danger-associated molecular patterns such as toxins and irritants and ultraviolet light through a variety of pattern recognition receptors (PRRs). These include Toll-like receptors

(TLRs), nucleotide-binding domains, leucine-rich repeat (NLRs) proteins, scavenger receptors, and C-type lectin receptors and are instrumental in both launching innate immune responses and influencing adaptive immunity of the skin as well as being pivotal mediators in infectious and inflammatory skin diseases [70–75]. TLR activation triggers signaling pathways that result in the production of antimicrobial peptides, cytokines, chemokines, and costimulatory molecules, which induce inflammatory responses and protective immunity against pathogens [14, 74, 76]. Originally recognized for their expression on immune cells, TLRs have also been identified on keratinocytes. Basal keratinocytes express TLR2/TLR4 mRNA and proteins and suprabasal keratinocytes express TLR1–5, TLR7, and TLR10 mRNA [77–79], suggesting that keratinocytes in different layers of the epidermis also express different TLRs. Recent studies suggest that rather than stimulating inflammation in response to injury, some commensal organisms actually help to limit the inflammatory response by acting as negative regulators of TLR3 signaling [80]. Another reason for the natural resistance to commensals is a "barrier" consisting of antimicrobial peptides and proteins, which are produced either constitutively or upon induction through various stimuli (β-defensins, RNase 7, psoriasin, cathelicidin LL-37) [81–83].

In unperturbed skin, keratinocytes produce only few cytokines such as interleukin (IL)-1, IL-7, and transforming growth factor (TGF)-β. However, they alert the host to delivery of certain noxious stimuli (trauma, non-ionizing radiation, chemicals) through production of a plethora of proinflammatory and immunomodulatory cytokines [IL-1, -6, -7, -10, -12, -15, -17, -18, -20, tumor necrosis factor (TNF)-α], chemokines [CC chemokine ligand (CCL)2, CCL5, CCL27, CXC-chemokine ligand (CXCL)8], and colony-stimulating factors [granulocyte-colony stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF)] [84]. This activation has multiple consequences. It causes the migration of cells into and out of the skin, has systemic effects, influences keratinocyte proliferation and differentiation, and affects the production of other cytokines [85]. More specifically, activated keratinocytes attract several cell types into the skin such as LC precursors via the expression of CCL20 [86, 87]. They can also recruit effector T cells to the skin by expressing CCL20, CXCL9–11, whereas neutrophils are attracted through CXCL1 and CXCL8 [88]. The fact that keratinocytes respond to cytokines through the expression of multiple receptors, clearly demonstrates that their functional properties can be regulated by cells of the immune system.

Keratinocytes also secrete neuropeptides, eicosanoids, reactive oxygen species, complement and related receptors. These mediators have potent inflammatory and immunomodulatory properties [85]. Dysregulation and abnormal expression of inflammatory mediators or their receptors in keratinocytes are relevant to the pathogenesis of chronic inflammatory skin diseases such as psoriasis, atopic dermatitis, and allergic contact dermatitis.

3.7 Melanocytes: Pigment Cells with Immune Properties

Human skin exists in a wide range of different colors and gradients. This is due to the presence of a chemically inert and stable pigment known as melanin, the biosynthesis of which takes place in melanocytes within membrane-bound organelles known as melanosomes. The latter can be divided into four maturation stages, determined by their structure and the quantity, quality and arrangement of the melanin produced. Melanocytes transfer melanosomes through their dendrites to adjacent keratinocytes, where they form caps that protect the keratinocyte from harmful ultraviolet light and other environmental stimuli [89]. The anatomical relationship between keratinocytes and melanocytes is known as the "epidermal melanin unit" [1]. Melanocytes represent 2–5% of all epidermal cells, descend from neural crest and migrate into the basal cell layer of the epidermis where they are regularly distributed [2, 90] (Fig. 3.1). Each melanocyte is in contact with ~40 keratinocytes in the basal and suprabasal layers [1]. They have a dendritic morphology and express S100, bcl-2, vimentin, c-kit/CD117, and other markers [2, 69, 91]. The density of melanocytes is constant in human skin. Various skin colors result from different quantities of produced and stored melanin [92]. Human melanocytes are not simply pigment-producing cells but also have phagocytic capacity and secrete a number of cytokines such as IL-1, IL-3, IL-6, GM-CSF, TNF-α, and TGF-β [90, 93]. It has been shown that melanocytes express a panel of TLRs (1–4, 6, 7 and 9), most of which are also functional [94]. These properties can turn melanocytes into active mediators of dermal innate immunity.

3.8 Merkel Cells: Essential for Light-Touch Responses

The skin is a sensory organ. Four main classes of sensory receptors in mammalian skin mediate different aspects of the sense of touch [95]. One of these specialized structures, the Merkel cell–neurite complex, is thought to be important for two-point discrimination and the detection of texture, shape, and curvature [96]. The receptor complex consists of Merkel cells, a distinct cell population located in the basal layer of the epidermis and in the epithelial sheath of hair follicles [69], and the afferent somatosensory fibers that innervate them. Merkel cell–neurite complexes are found in touch-

sensitive areas of the skin including whisker follicles, glabrous (hairless) skin surfaces such as the hands and feet, and specialized epithelial structures in the hairy skin called touch domes [97]. Since their discovery in 1875, the functions of Merkel cells are still unclear. Using Merkel cell-deficient mice, it has been shown recently that they are required for the characteristic neurophysiological response of Merkel cell–neurite complexes to tactile stimuli [98]. Merkel cells are characterized by dense-core granules that contain a variety of neuropeptides, plasma membrane spines, and cytoskeletal filaments consisting of cytokeratins like K20 and desmosomes [99, 100]. Furthermore, Merkel cells express many components of the presynaptic machinery and transcription factors involved in neuronal cell fate determination [101]. Their density shows regional variations [102]. In hair follicles, Merkel cells are rarely associated with nerve endings, whereas those in the epidermis are in close contact with terminal nerves. Merkel cells not in close association with nerve terminals have an endocrine function [99, 103, 104].

Two hypotheses used to heat up an intense controversy about the developmental origin of Merkel cells [99, 103, 104]. The neural crest hypothesis proposes that Merkel cells are derived from neural crest stem cells based on the finding that they synthesize neuropeptides, express presynaptic molecules and proneural transcription factors, and from observations in lineage-tracing experiments in animals [105–107]. The epidermal origin hypothesis is based on their location in the basal layer and the presence of cytokeratin 20, the observation of their temporal appearance, and their presence in the epidermis before the appearance of other neural crest derivatives such as nerve endings of the skin [108–113]. Genetic lineage tracing and conditional knockout techniques provided conclusive evidence for an epidermal origin of Merkel cells [114, 115]. With this definitive assignment of the origin of this cell population, insights into the pathogenesis of human diseases such as Merkel cell carcinoma could be possible [116].

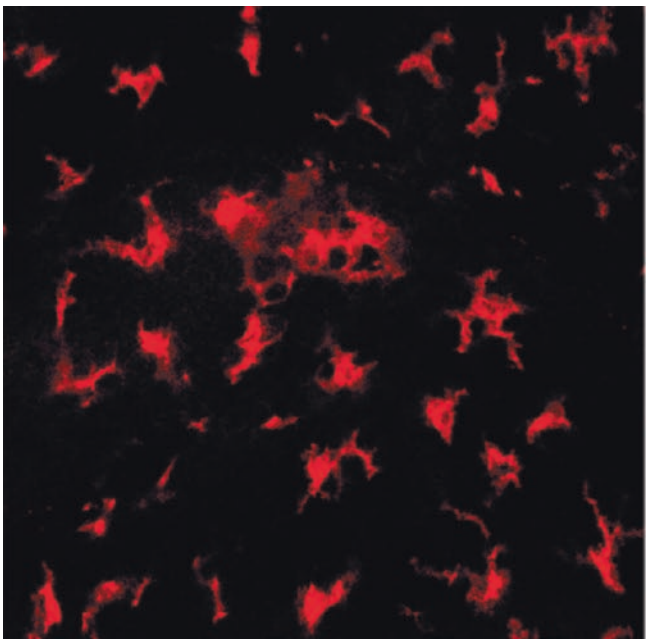
3.9 Dendritic Cells: Key Regulators of the Immune Response

DCs—the most potent antigen-presenting cells (APCs)—translate innate to adaptive immunity [117]. They are present in an immature state in minute numbers (1–3%) in most peripheral tissues. Encounter with antigens or other stimuli by phagocytosis, macropinocytosis, and receptor-mediated endocytosis causes their migration towards T cell rich areas of the secondary lymphoid organs via afferent lymphatics. During this migration process, DCs mature, lose their ability to capture antigens and acquire the capacity to present antigens to naive T cells, which then start to proliferate [118, 119]. To avoid an excessive immune response, activated T cells can induce apoptosis in DCs by expressing Fas Ligand, TNF-α 4, and TNF-related apoptosis-inducing ligand (TRAIL) [120]. DCs can direct a T cell-mediated adaptive immune response towards a type-1 and/or type-2 reaction [121] and have the unique ability to cross-present antigens to naive T cells [122]. Depletion of DCs, as has been associated with immunosuppressed states after severe burn injury or sepsis, leaves the organism prone to bacterial infection and its local and systemic sequelae [123, 124]. Lymphoid and myeloid progenitor cells express fms-like tyrosine kinase ligand (Flt3L) receptors, which mediate DC expansion through proliferation and differentiation [125]. It has been shown in murine models that prophylactic replenishment of systemic DC through Flt3L administration during the immunosuppressed post-burn state significantly enhances the host response to bacterial wound infection and systemic pathogen dissemination [126, 127]. This finding, next to underscoring the importance of DC in mounting a sufficient initial immune response, may indicate future therapeutic approaches that target the host's immune system rather than specific pathogens. Beyond traits relating to immunity, DCs are involved in the induction of tolerance in the thymus and in lymphoid organs [117, 119, 128]. A small number of DCs move from the periphery to the lymph nodes, even in the absence of invading pathogens in the steady state [122]. These tolerogenic DCs neither activate T cells nor lead to a clonal expansion, because of the release of IL-10 and catabolizing enzyme ideolamine 2,3-dioxygenase (IDO) which enable T cell anergy, T cell death, and Treg cell proliferation [129]. Even though a remarkable phenotypic heterogeneity of DCs has been long recognized, it has been only possible to clearly relate DC phenotype to DC function in a few instances. In the skin, DCs can be divided according to their anatomical localization. In the epidermis one can detect LCs, and in the dermis interstitial DCs.

3.10 Langerhans Cells: Required for Induction of Immunity and/or Tolerance?

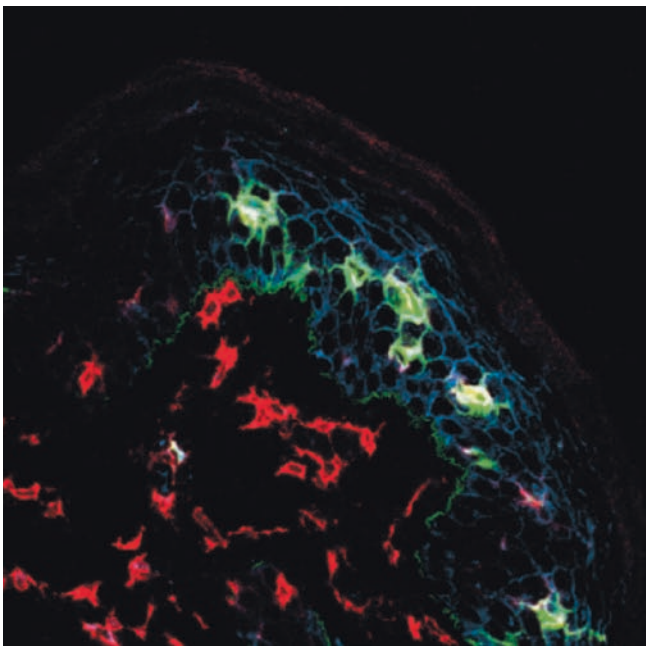
Paul Langerhans, a medical student in Berlin, who was especially interested in the anatomy of cutaneous nerves, inoculated gold into human skin and discovered in 1868 a population of dendritically shaped cells in the epidermis which he deemed nerve cells [130]. More than one century later it was appreciated that he discovered leukocytes which are now recognized as a member of the DC system. Landmark publications and several excellent reviews on skin DCs have been published over decades and are discussed and cited by Nikolaus Romani et al. in a noteworthy review [131].

LCs represent the most striking example of an extensively studied tissue DC subpopulation. They reside in basal and



CD45

Fig. 3.2 LCs form a dense network in the epidermis as visualized here with an anti-CD45 staining on an epidermal human sheet (Courtesy of Christopher Schuster, MD)



CD45 x CD207/Laminin5 x CD1a

Fig. 3.3 CD45$^+$ (red) cells with a dendritic morphology are present in the epidermis and dermis. CD1a$^+$ (blue) and CD207$^+$ (green) cells, presumably LCs, are located in the epidermis as demonstrated in a human skin tissue section (Courtesy of Christopher Schuster, MD)

suprabasal epidermal layers and mucosa epithelium and extend their protrusions, known as dendrites, through the tight seals between keratinocytes to comprise a dense network that covers the entire body surface (Fig. 3.2). LCs account for 3–5% of epidermal cells and originate from hematopoietic stem cells in the bone marrow [132–135]. The defining marker for LCs is an intracytoplasmic organelle, known as Birbeck granule, with a tennis-racket or, more often, rod-shaped morphology [136]. In humans, LCs also express a characteristic set of cell surface molecules such as membrane ATPase (CD39), CD1 a (important for presentation of microbial lipid antigens), E-cadherin/CD324 (mediates LC attachment to keratinocytes), Langerin/CD207 (responsible for the generation of Birbeck granules), CC chemokine receptor (CCR)6 (responsible for LC migration to the epithelium), and the skin-homing antigen named cutaneous lymphocyte-associated antigen (CLA) (Fig. 3.3) [85]. Furthermore, LCs are equipped with a large array of conserved PRRs including TLRs, C-type lectin receptors, and NLRs that recognize microbial products as well as other intracellular danger signals [78, 137–141]. The poor reactivity of LCs to various PAMPs may potentially explain why commensal bacteria do not continuously trigger inflammation in skin. It is conceivable that keratinocytes may initially respond instead of LCs and then secrete cytokines to modulate LC functions indirectly [142]. LCs are also characterized by the absence of the macrophage mannose receptor (MMR/CD206), DC-SIGN/CD209 and the coagulation factor XIIIa, molecules that can be found on dermal APCs (Fig. 3.4) [85].

For a long time it was believed that LCs are continually replenished by circulating hematopoietic bone marrow-derived precursor cells during adult life. Elegant studies from Miriam Merad and her colleagues have shown that LCs are maintained locally independently of circulating precursors in the steady state [143]. Over the years, several researchers have confirmed this finding and evidence has been provided that this happens via self-renewal and/or specialized local LC precursors as reviewed by Romani et al. [131]. For example, CD14$^+$ LC precursors reside in the human dermis [144] and it has been shown that their migration step into the epidermis is controlled by the release of keratinocyte-derived macrophage-inflammatory protein-3α/CCL20 and CXCL14 [86, 87, 145].

In contrast, under conditions of inflammation (infection [146], contact sensitizers [147], physical damage from heat [148], gentle tape stripping [149], ultraviolet and ionizing radiation [150, 151], chemokine stimuli [152], or exposure to TLR agonists [138, 153]) LCs leave the epidermis. In a mouse model, it has been shown that LCs are replaced by circulating Gr-1$^+$ monocytes in a M-CSFR-dependent manner [154].

As TGF-β is critical for LC development [155–159] and the production of TGF-β in developing prenatal human epidermis correlates with the appearance of markers such as

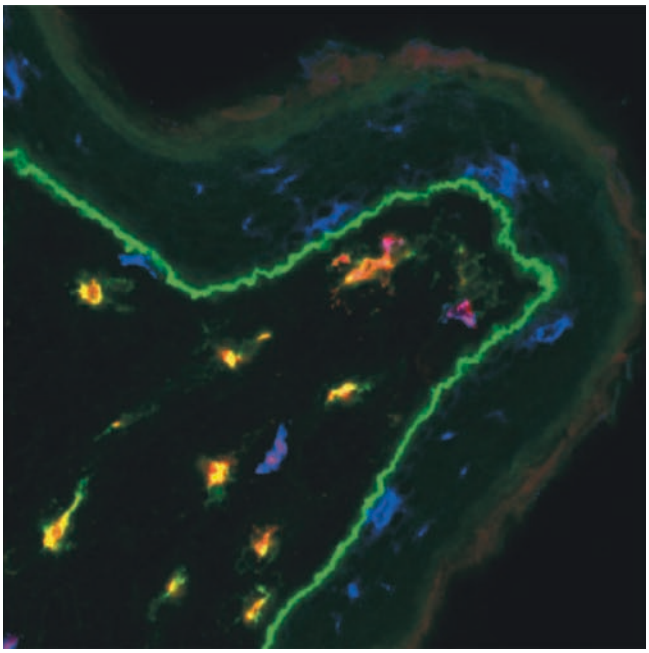


Fig. 3.4 Dendritic-appearing cells expressing monocyte/macrophage markers such as CD206 (red) and CD209 (green) are only located in the dermis and not in the epidermis. CD1c$^+$ (blue) cells exist in the epidermis and dermis. An Alexa Fluor 488-labeled Laminin 5/332 (green) mAb visualizes the dermo-epidermal junction (Courtesy of Christopher Schuster, MD)

CD207 and CD1 a [160], it is possible that TGF-β also plays an important role for the acquisition of the LC phenotype in human epidermis. In addition, the increasing staining intensity of these markers in prenatal human skin may reflect the consistently increasing total amount of TGF-β in the developing epidermis [160].

Despite years of intensive research, the function of LCs remains enigmatic. Three LC-deficient mouse models established by independent groups have begun to challenge the dogma that there is a requirement for LCs for the induction of certain types of cell-mediated immune responses such as contact hypersensitivity [161–163]. Rather than establishing an exact role for LCs, the groups found unchanged, diminished or enhanced contact hypersensitivity using their mouse models, implying that LCs may have regulatory/downregulating properties that serve to contain and constrain adaptive immune responses in the skin. Other observations provide evidence for a strong immunogenic function of LCs under certain conditions. Thus, their role in the skin immune system seems to be manifold, depending on the state of the skin condition (steady state versus inflammation), the doses of antigens, the type of pathogen, and other variables as proposed by Romani et al. [131]. Several questions remain unsolved, and new questions have arisen as a result of this recent progress.

3.11 Dermal Dendritic Cell Subsets: Possessors of Diverse Functions

The human dermis contains three distinct subsets of APCs. HLA-DR^{bright}CD1a$^+$CD14$^-$CD1b$^+$CD1c$^+$CD207$^-$ DCs, HLA-DR^{bright}CD1a$^-$CD14$^+$ DCs, and HLA-DR^{dim}CD1a$^-$CD14$^+$CD1c$^-$FXIIIa$^+$CD163$^+$ dermal macrophages [164–171]. CD1a$^+$CD14$^-$ DCs are located close to lymphatic vessels in the upper layers of the dermis and are clearly distinct from migrating LCs [165, 166]. They can induce the proliferation of allogeneic T cells, although less efficient than LCs [171, 172]. CD14$^+$ cells include both migratory DCs and nonmigratory macrophages and evidence has been provided that they are from distinct lineages [166]. CD14$^+$ dermal DCs are able to prime CD4$^+$ T cells into cells that can induce naive B cells to perform an isotype-switch and to become cells secreting large amounts of immunoglobulins, thereby controlling humoral immunity [172]. Some rare migrating LCs, expressing markers such as CD1 a, CD1 b, CD207, and CD208, can be identified in healthy human dermis [164, 165, 173, 174].

Plasmacytoid DCs are present but rare in healthy human skin [175], while lesional skin samples from patients with psoriasis vulgaris and contact dermatitis contain high numbers of these cells [176]. They express IL-3Rα/CD123, blood dendritic cell antigen (BDCA)-4/CD304 and, the only exclusive marker for plasmacytoid DCs, BDCA-2/CD303. A special feature of plasmacytoid DCs is that they express a wide range of TLRs which makes them very competent to recognize microbial pathogens. Furthermore, they are potent producers of type I interferons during viral infection [177].

In mice, but not yet in humans, a novel CD207$^+$ DC subset has recently been described in the dermis. Some of the major immune functions historically assigned to LCs are now recognized as being performed with greater efficiency by these cells and other dermal DC cell subsets [178–181].

In conclusion, the diverse range and function of skin APCs, even though not entirely clear, has significant implications most particularly for the development of novel human vaccines [172].

3.12 Resident Skin T Cells: Important Mediators of Skin Homeostasis and Pathology

T cells mediate the body's immune responses through a variety of functions. Depending on the type of infection, T cells react by secreting specific cytokine patterns, which provide important signals to other subsets of immune cells. It has been suspected for a long time that T cells are also present in healthy human skin [182]. Approximately one million T cells are present per 1 cm^2 of normal human

adult skin, resulting in 20 billion T cells per individual, which is more than twice the total number of T cells in the blood [183]. Initially, it was thought that T cells circulate between the skin and skin-draining lymph nodes and thus can quickly respond to antigen challenges [184, 185]. It has been shown, however, that skin is steadily colonized by long-lived populations of memory T cells [186–189] and it has been proposed that these cells but not recruited T cells have a major role in skin immune homeostasis and pathology [190].

The vast majority of skin-associated T cells in normal adult human skin are located in the dermis, whereas only small numbers reside in the epidermis. Nearly all skin-resident T cells express TCR αβ heterodimers. TCR $\gamma\delta^+$ T cells make up a small proportion of the total T cells in the skin [191–193]. Fewer than 5% of T cells resident in normal adult human skin are $CD45RA^+$ naive T cells, whereas over 95% are CD45RO memory T cells. Most express the skin-homing addressin CLA which is the ligand for E- and P-selectin. Skin-specific memory T cells acquire skin-homing properties after a process known as imprinting, which involves contact with tissue-derived DCs and lymph node stromal cells [194, 195]. Thus, effector T cells are programmed during differentiation to migrate to the tissue from which their cognate antigen was originally derived. While the distribution of naive and memory T cells in adult peripheral blood is quite similar to the skin, only 10% of the $CD3^+$ blood cells are positive for CLA [196, 197]. To regulate the trafficking of T cells to cutaneous sites, chemokine receptors play an important role. Approximately 50% of CLA^+ T cells express CCR8 and only a subset expresses CCR7 and CCR10 [145, 196, 198, 199]. Vitamin D has been proposed to have a crucial role in the direction of memory T cells to the skin via upregulation of CCR10 expression [200].

In the dermis, T cells are preferentially located around postcapillary venules and are often situated just beneath the dermo-epidermal junction of adjacent cutaneous appendages. TCR $\alpha\beta^+$ cells are primarily single positive for CD4 or CD8 co-receptors, showing either an equal distribution or preference for the $CD4^+$ subset [201].

Epidermal T cells account for about 2% of the $CD3^+$ population in normal skin [201–203]. They primarily reside within the basal and suprabasal keratinocyte layer often in close apposition to LCs, allowing for close interaction [203]. The epidermal TCR $\alpha\beta^+$ T cell population is primarily represented by single $CD4^+$ or $CD8^+$ cells [202, 204]. Spetz et al. have shown not only that $CD8^+$ TCR αβ-bearing epidermal T cells express the CD8αα homodimer at higher frequencies compared with peripheral blood, but have also found $CD4^-CD8^-$TCR $\alpha\beta^+$ cells in the epidermis [204]. A minor population of epidermal T cells display TCR γδ heterodimers. Most of them are negative for CD4 and CD8 markers [203, 205, 206].

Conclusive data is sparse regarding the function of TCR $\gamma\delta^+$ T cells in human skin. Increased numbers have been shown in a wide range of human skin pathologies. TCR $\gamma\delta^+$ skin T cells primarily express the Vδ1 chain, whereas TCR $\gamma\delta^+$ T cells in peripheral blood express the Vδ2 chain [197]. It has been proposed that $V\delta1^+$ skin T cells act as immune sentinels by responding to stressed epithelial cells, thus controlling epithelial cell integrity [207]. Human TCR $\gamma\delta^+$ epidermal T cells produce growth factors such as insulin-like growth factor 1 upon activation and contribute to the effective healing of acute wounds [197].

The immune system not only has to mount immune responses to pathogens but also maintain tolerance to self and non-self antigens. Tregs which are characterized by the expression of the transcription factor FOXP3 maintain self-tolerance and function by suppressing the activation, cytokine production, and proliferation of other T cells [208]. Clark et al. have described that between 5% and 10% of the T cells resident in normal human skin are $FOXP3^+$ Tregs [12, 209]. These cells not only protect against autoimmune reactions to self antigens and assist in the resolution of cutaneous inflammation, but unfortunately, can also protect tumors from immune detection, allow latent infections to persist and can dysfunction under conditions present in inflammatory diseases [210].

Lastly, NK cells are present in the dermis and express receptors for homing to noninflammed skin and for recognition of allogeneic tumor cells [191].

3.13 Dermal-Epidermal Junction: Laden with Multiple Functions

The dermal-epidermal junction is a complex and continuous basal membrane (Fig. 3.1) along the epidermis and skin appendages, including sweat glands, hair follicles, and sebaceous glands. From the surface to the bottom, the dermal-epidermal junction can be divided into three zones: the keratin filament-hemidesmosome complex of basal cells, the lamina lucida, and the lamina densa [211, 212]. The major components of all basal membranes are collagenous and non-collagenous glycoproteins and proteoglycans such as collagen IV, laminins, nidogens, perlecan, fibulins, and fibronectin [213–215]. Collagen IV is a heterotrimer of three α chains each of which contains three distinct domains [214, 216]. Laminins are very large heterotrimeric glycoproteins (600–950 kDa) composed of an α, β, and γ chain [215]. To date, five distinct α, four β, and three γ laminin chains have been identified that can combine to form 15 different isoforms. As the old nomenclature from laminin 1 to laminin 15 (according to their discovery) appeared impractical, a new simplified nomenclature, based on the chain composition and the number of each chain is used today. For example, the

major laminin of the epidermal basement membrane, the previous laminin 5, with an α-chain composition α3β3γ2, is now called laminin 332 [217, 218] and can be detected on frozen tissue specimens by a specific antibody (Fig. 3.4). The function of laminins is not yet fully understood, but through interactions with other surface components they control cellular activities such as adhesion, migration, and proliferation [217, 219]. Some molecules demonstrate a restricted distribution. For example, collagens VII and XVII are associated with skin but are not found in glomerular and alveolar membranes. Based on ultrastructural and biochemical studies, several functions have been proposed for the basement membrane. It may be a structural source for the secure attachment and polarity of the epidermal basal cells and may have a barrier function, separating the dermis and epidermis. Furthermore, the basement membrane is most likely responsible for a firm attachment of the dermis to the epidermis through a continuous system of structural elements and modifies several cellular functions [211, 212].

Acknowledgements I thank Marion Prior and Karin Pfisterer (Department of Dermatology, Vienna) for editorial comments and Nikolaus Romani and Patrizia Stoitzner (Department of Dermatology, Innsbruck) for their continued help with "skin-related" questions. Supported by the Jubiläumsfonds der Österreichischen Nationalbank (Nr. 12 958) and a research grant of the Austrian Science Fund (FWF, P19 474-B13).

References

1. Costin GE, Hearing VJ. Human skin pigmentation: melanocytes modulate skin color in response to stress. FASEB J. 2007;21:976–94.
2. Kanitakis J. Anatomy, histology and immunohistochemistry of normal human skin. Eur J Dermatol. 2002;12:390–9.
3. Blanpain C, Fuchs E. Epidermal homeostasis: a balancing act of stem cells in the skin. Nat Rev Mol Cell Biol. 2009;10:207–17.
4. Blanpain C, Horsley V, Fuchs E. Epithelial stem cells: turning over new leaves. Cell. 2007;128:445–58.
5. Potten CS, Booth C. Keratinocyte stem cells: a commentary. J Invest Dermatol. 2002;119:888–99.
6. Li A, Pouliot N, Redvers R, Kaur P. Extensive tissue-regenerative capacity of neonatal human keratinocyte stem cells and their progeny. J Clin Invest. 2004;113:390–400.
7. Mannik J, Alzayady K, Ghazizadeh S. Regeneration of multilineage skin epithelia by differentiated keratinocytes. J Invest Dermatol. 2010;130:388–97.
8. Segre JA. Epidermal barrier formation and recovery in skin disorders. J Clin Invest. 2006;116:1150–8.
9. Elias PM. Stratum corneum defensive functions: an integrated view. J Invest Dermatol. 2005;125:183–200.
10. Fuchs E. Scratching the surface of skin development. Nature. 2007;445:834–42.
11. Tobin DJ. Biochemistry of human skin–our brain on the outside. Chem Soc Rev. 2006;35:52–67.
12. Clark RA, Kupper TS. IL-15 and dermal fibroblasts induce proliferation of natural regulatory T cells isolated from human skin. Blood. 2007;109:194–202.
13. Kryczek I, Bruce AT, Gudjonsson JE, Johnston A, Aphale A, Vatan L, Szeliga W, Wang Y, Liu Y, Welling TH, Elder JT, Zou W. Induction of IL-17^{+} T cell trafficking and development by IFN-gamma: mechanism and pathological relevance in psoriasis. J Immunol. 2008;181:4733–41.
14. Nestle FO, Di MP, Qin JZ, Nickoloff BJ. Skin immune sentinels in health and disease. Nat Rev Immunol. 2009;9:679–91.
15. Alonso L, Fuchs E. The hair cycle. J Cell Sci. 2006;119:391–3.
16. Fuchs E. Skin stem cells: rising to the surface. J Cell Biol. 2008;180:273–84.
17. Blanpain C, Lowry WE, Geoghegan A, Polak L, Fuchs E. Self-renewal, multipotency, and the existence of two cell populations within an epithelial stem cell niche. Cell. 2004;118:635–48.
18. Inoue K, Aoi N, Sato T, Yamauchi Y, Suga H, Eto H, Kato H, Araki J, Yoshimura K. Differential expression of stem-cell-associated markers in human hair follicle epithelial cells. Lab Investig. 2009;89:844–56.
19. Lyle S, Christofidou-Solomidou M, Liu Y, Elder DE, Albelda S, Cotsarelis G. The C8/144B monoclonal antibody recognizes cytokeratin 15 and defines the location of human hair follicle stem cells. J Cell Sci. 1998;111:3179–88.
20. Morris RJ, Liu Y, Marles L, Yang Z, Trempus C, Li S, Lin JS, Sawicki JA, Cotsarelis G. Capturing and profiling adult hair follicle stem cells. Nat Biotechnol. 2004;22:411–7.
21. Ohyama M, Terunuma A, Tock CL, Radonovich MF, Pise-Masison CA, Hopping SB, Brady JN, Udey MC, Vogel JC. Characterization and isolation of stem cell-enriched human hair follicle bulge cells. J Clin Invest. 2006;1(16):249–60.
22. Trempus CS, Morris RJ, Bortner CD, Cotsarelis G, Fair-cloth RS, Reece JM, Tennant RW. Enrichment for living murine keratinocytes from the hair follicle bulge with the cell surface marker CD34. J Invest Dermatol. 2003;120:501–11.
23. Braun KM, Niemann C, Jensen UB, Sundberg JP, Silva-Vargas V, Watt FM. Manipulation of stem cell proliferation and lineage commitment: visualisation of label-retaining cells in wholemounts of mouse epidermis. Development. 2003;130:5241–55.
24. Cotsarelis G, Sun TT, Lavker RM. Label-retaining cells reside in the bulge area of pilosebaceous unit: implications for follicular stem cells, hair cycle, and skin carcinogenesis. Cell. 1990;61:1329–37.
25. Tumbar T, Guasch G, Greco V, Blanpain C, Lowry WE, Rendl M, Fuchs E. Defining the epithelial stem cell niche in skin. Science. 2004;303:359–63.
26. Ito M, Kizawa K, Hamada K, Cotsarelis G. Hair follicle stem cells in the lower bulge form the secondary germ, a biochemically distinct but functionally equivalent progenitor cell population, at the termination of catagen. Differentiation. 2004;72:548–57.
27. Jensen KB, Collins CA, Nascimento E, Tan DW, Frye M, Itami S, Watt FM. Lrig1 expression defines a distinct multipotent stem cell population in mammalian epidermis. Cell Stem Cell. 2009;4:427–39.
28. Jensen UB, Yan X, Triel C, Woo SH, Christensen R, Owens DM. A distinct population of clonogenic and multipotent murine follicular keratinocytes residing in the upper isthmus. J Cell Sci. 2008;121:609–17.
29. Nijhof JG, Braun KM, Giangreco A, van Pelt C, Kawamoto H, Boyd RL, Willemze R, Mullenders LH, Watt FM, De Gruijl FR, van Ewijk W. The cell-surface marker MTS24 identifies a novel population of follicular keratinocytes with characteristics of progenitor cells. Development. 2006;133:3027–37.
30. Snippert HJ, Haegebarth A, Kasper M, Jaks V, van Es JH, Barker N, van de Wetering M, van den Born M, Begthel H, Vries RG, Stange DE, Toftgard R, Clevers H. Lgr6 marks stem cells in the hair follicle that generate all cell lineages of the skin. Science. 2010;327:1385–9.
31. Fernandes KJ, Kobayashi NR, Gallagher CJ, Barnabe-Heider F, Aumont A, Kaplan DR, Miller FD. Analysis of the neurogenic potential of multipotent skin-derived precursors. Exp Neurol. 2006;201:32–48.
32. Fernandes KJ, McKenzie IA, Mill P, Smith KM, Akhavan M, Barnabe-Heider F, Biernaskie J, Junek A, Kobayashi NR, Toma JG, Kaplan DR, Labosky PA, Rafuse V, Hui CC, Miller FD. A dermal

niche for multipotent adult skin-derived precursor cells. Nat Cell Biol. 2004;6:1082–93.
33. Gingras M, Champigny MF, Berthod F. Differentiation of human adult skin-derived neuronal precursors into mature neurons. J Cell Physiol. 2007;210:498–506.
34. Hunt DP, Jahoda C, Chandran S. Multipotent skin-derived precursors: from biology to clinical translation. Curr Opin Biotechnol. 2009;20:522–30.
35. Hunt DP, Sajic M, Phillips H, Henderson D, Compston A, Smith K, Chandran S. Origins of gliogenic stem cell populations within adult skin and bone marrow. Stem Cells Dev. 2010;19:1055–65.
36. Joannides A, Gaughwin P, Schwiening C, Majed H, Sterling J, Compston A, Chandran S. Efficient generation of neural precursors from adult human skin: astrocytes promote neurogenesis from skin-derived stem cells. Lancet. 2004;364:172–8.
37. Kroeze KL, Jurgens WJ, Doulabi BZ, van Milligen FJ, Scheper RJ, Gibbs S. Chemokine-mediated migration of skin-derived stem cells: predominant role for CCL5/RANTES. J Invest Dermatol. 2009;129:1569–81.
38. Lavoie JF, Biernaskie JA, Chen Y, Bagli D, Alman B, Kaplan DR, Miller FD. Skin-derived precursors differentiate into skeletogenic cell types and contribute to bone repair. Stem Cells Dev. 2009;18:893–906.
39. McKenzie IA, Biernaskie J, Toma JG, Midha R, Miller FD. Skin-derived precursors generate myelinating Schwann cells for the injured and dysmyelinated nervous system. J Neurosci. 2006;26:6651–60.
40. Toma JG, Akhavan M, Fernandes KJ, Barnabe-Heider F, Sadikot A, Kaplan DR, Miller FD. Isolation of multipotent adult stem cells from the dermis of mammalian skin. Nat Cell Biol. 2001;3:778–84.
41. Toma JG, McKenzie IA, Bagli D, Miller FD. Isolation and characterization of multipotent skin-derived precursors from human skin. Stem Cells. 2005;23:727–37.
42. Yang LY, Zheng JK, Liu XM, Hui GZ, Guo LH. Culture of skin-derived precursors and their differentiation into neurons. Chin J Traumatol. 2004;7:91–5.
43. Zhao Z, Liao L, Cao Y, Jiang X, Zhao RC. Establishment and properties of fetal dermis-derived mesenchymal stem cell lines: plasticity in vitro and hematopoietic protection in vivo. Bone Marrow Transplant. 2005;36:355–65.
44. Lysy PA, Smets F, Sibille C, Najimi M, Sokal EM. Human skin fibroblasts: from mesodermal to hepatocyte-like differentiation. Hepatology. 2007;46:1574–85.
45. Medina RJ, Kataoka K, Takaishi M, Miyazaki M, Huh NH. Isolation of epithelial stem cells fromdermis by a three-dimensional culture system. J Cell Biochem. 2006;98:174–84.
46. Shi CM, Cheng TM. Differentiation of dermis-derived multipotent cells into insulin-producing pancreatic cells in vitro. World J Gastroenterol. 2004;10:2550–2.
47. Biernaskie J, Paris M, Morozova O, Fagan BM, Marra M, Pevny L, Miller FD. SKPs derive from hair follicle precursors and exhibit properties of adult dermal stem cells. Cell Stem Cell. 2009;5:610–23.
48. Hoogduijn MJ, Gorjup E, Genever PG. Comparative characterization of hair follicle dermal stem cells and bone marrow mesenchymal stem cells. Stem Cells Dev. 2006;15:49–60.
49. Hunt DP, Morris PN, Sterling J, Anderson JA, Joannides A, Jahoda C, Compston A, Chandran S. A highly enriched niche of precursor cells with neuronal and glial potential within the hair follicle dermal papilla of adult skin. Stem Cells. 2008;26:163–72.
50. Jahoda CA, Whitehouse J, Reynolds AJ, Hole N. Hair follicle dermal cells differentiate into adipogenic and osteogenic lineages. Exp Dermatol. 2003;12:849–59.
51. Lako M, Armstrong L, Cairns PM, Harris S, Hole N, Jahoda CA. Hair follicle dermal cells repopulate the mouse haematopoietic system. J Cell Sci. 2002;115:3967–74.
52. Sellheyer K, Krahl D. Cutaneous mesenchymal stem cells: current status of research and potential clinical applications. Hautarzt. 2010;61:429–34.
53. Sun L, Akiyama K, Zhang H, Yamaza T, Hou Y, Zhao S, Xu T, Le A, Shi S. Mesenchymal stem cell transplantation reverses multiorgan dysfunction in systemic lupus erythematosus mice and humans. Stem Cells. 2009;27:1421–32.
54. Wood FM, Kolybaba ML, Allen P. The use of cultured epithelial autograft in the treatment of major burn injuries: a critical review of the literature. Burns. 2006;32(4):395–401.
55. Sood R, Roggy D, Zieger M, Balledux J, Chaudhari S, Koumanis DJ, et al. Cultured epithelial autografts for coverage of large burn wounds in eighty-eight patients: the Indiana University experience. J Burn Care Res. 2010;31(4):559–68.
56. Hamrahi VF, Goverman J, Jung W, Wu JC, Fischman AJ, Tompkins RG, et al. In vivo molecular imaging of murine embryonic stem cells delivered to a burn wound surface via Integra® scaffolding. J Burn Care Res. 2012;33(2):e49–54.
57. Falanga V, Iwamoto S, Chartier M, Yufit T, Butmarc J, Kouttab N, et al. Autologous bone marrow-derived cultured mesenchymal stem cells delivered in a fibrin spray accelerate healing in murine and human cutaneous wounds. Tissue Eng. 2007;13(6):1299–312.
58. Supp DM, Boyce ST. Engineered skin substitutes: practices and potentials. Clin Dermatol. 2005;23(4):403–12.
59. Fu X, Li H. Mesenchymal stem cells and skin wound repair and regeneration: possibilities and questions. Cell Tissue Res. 2009;335:317–21.
60. Stoff A, Rivera AA, Sanjib BN, Moore ST, Michael NT, Espinosa-de-Los-Monteros A, Richter DF, Siegal GP, Chow LT, Feldman D, Vasconez LO, Michael MJ, Stoff-Khalili MA, Curiel DT. Promotion of incisional wound repair by human mesenchymal stem cell transplantation. Exp Dermatol. 2009;18:362–9.
61. Ghieh F, Jurjus R, Ibrahim A, Geagea AG, Daouk H, El Baba B, et al. The use of stem cells in burn wound healing: a review. Biomed Res Int. 2015;2015:e684084.
62. Aasen T, Raya A, Barrero MJ, Garreta E, Consiglio A, Gonzalez F, Vassena R, Bilic J, Pekarik V, Tiscornia G, Edel M, Boue S, Izpisua Belmonte JC. Efficient and rapid generation of induced pluripotent stem cells from human keratinocytes. Nat Biotechnol. 2008;26:1276–84.
63. Takahashi K, Tanabe K, Ohnuki M, Narita M, Ichisaka T, Tomoda K, Yamanaka S. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. Cell. 2007;131:861–72.
64. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell. 2006;126:663–76.
65. Tsai SY, Clavel C, Kim S, Ang YS, Grisanti L, Lee DF, Kelley K, Rendl M. Oct4 and klf4 reprogram dermal papilla cells into induced pluripotent stem cells. Stem Cells. 2010;28:221–8.
66. Yu J, Vodyanik MA, Smuga-Otto K, Antosiewicz-Bourget J, Frane JL, Tian S, Nie J, Jonsdottir GA, Ruotti V, Stewart R, Slukvin II, Thomson JA. Induced pluripotent stem cell lines derived from human somatic cells. Science. 2007;318:1917–20.
67. Coulombe PA, Omary MB. 'Hard' and 'soft' principles defining the structure, function and regulation of keratin intermediate filaments. Curr Opin Cell Biol. 2002;14:110–22.
68. Fuchs E. Keratins and the skin. Annu Rev Cell Dev Biol. 1995;11:123–53.
69. Kanitakis J. Immunohistochemistry of normal human skin. Eur J Dermatol. 1998;8:539–47.
70. Curry JL, Qin JZ, Bonish B, Carrick R, Bacon P, Panella J, Robinson J, Nickoloff BJ. Innate immune-related receptors in normal and psoriatic skin. Arch Pathol Lab Med. 2003;127:178–86.
71. Iwasaki A, Medzhitov R. Regulation of adaptive immunity by the innate immune system. Science. 2010;327:291–5.

72. Maytin EV. Differential effects of heat shock and UVB light upon stress protein expression in epidermal keratinocytes. J Biol Chem. 1992;267:23189–96.
73. McGirt LY, Beck LA. Innate immune defects in atopic dermatitis. J Allergy Clin Immunol. 2006;118:202–8.
74. McInturff JE, Modlin RL, Kim J. The role of toll-like receptors in the pathogenesis and treatment of dermatological disease. J Invest Dermatol. 2005;125:1–8.
75. Ting JP, Duncan JA, Lei Y. How the noninflammasome NLRs function in the innate immune system. Science. 2010;327:286–90.
76. Akira S, Uematsu S, Takeuchi O. Pathogen recognition and innate immunity. Cell. 2006;124:783–801.
77. Baker BS, Ovigne JM, Powles AV, Corcoran S, Fry L. Normal keratinocytes express Toll-like receptors (TLRs) 1, 2 and 5: modulation of TLR expression in chronic plaque psoriasis. Br J Dermatol. 2003;148:670–9.
78. Flacher V, Bouschbacher M, Verronese E, Massacrier C, Sisirak V, Berthier-Vergnes O, Saint-Vis B, Caux C, Dezutter-Dambuyant C, Lebecque S, Valladeau J. Human Langerhans cells express a specific TLR profile and differentially respond to viruses and Gram-positive bacteria. J Immunol. 2006;177:7959–67.
79. Song PI, Park YM, Abraham T, Harten B, Zivony A, Neparidze N, Armstrong CA, Ansel JC. Human keratinocytes express functional CD14 and toll-like receptor 4. J Invest Dermatol. 2002;119:424–32.
80. Lai Y, Di NA, Nakatsuji T, Leichtle A, Yang Y, Cogen AL, Wu ZR, Hooper LV, Schmidt RR, Von AS RKA, Huang CM, Ryan AF, Gallo RL. Commensal bacteria regulate Toll-like receptor 3-dependent inflammation after skin injury. Nat Med. 2009;15:1377–82.
81. Lai Y, Gallo RL. AMPed up immunity: how antimicrobial peptides have multiple roles in immune defense. Trends Immunol. 2009;30:131–41.
82. Schauber J, Gallo RL. Expanding the roles of antimicrobial peptides in skin: alarming and arming keratinocytes. J Invest Dermatol. 2007;127:510–2.
83. Schröder JM. Epithelial antimicrobial peptides: innate local host response elements. Cell Mol Life Sci. 1999;56:32–46.
84. Grone A. Keratinocytes and cytokines. Vet Immunol Immunopathol. 2002;88:1–12.
85. Modlin RL, Kim J, Maurer D, Bangert C, Stingl G. Innate and adaptive immunity in the skin. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, editors. Fitzpatrick's dermatology in general medicine. 7th ed. New York, NY: McGraw Hill; 2007. p. 95–114.
86. Charbonnier AS, Kohrgruber N, Kriehuber E, Stingl G, Rot A, Maurer D. Macrophage inflammatory protein 3alpha is involved in the constitutive trafficking of epidermal Langerhans cells. J Exp Med. 1999;190:1755–68.
87. Dieu-Nosjean MC, Massacrier C, Homey B, Vanbervliet B, Pin JJ, Vicari A, Lebecque S, Dezutter-Dambuyant C, Schmitt D, Zlotnik A, Caux C. Macrophage inflammatory protein 3alpha is expressed at inflamed epithelial surfaces and is the most potent chemokine known in attracting Langerhans cell precursors. J Exp Med. 2000;192:705–18.
88. Albanesi C, Scarponi C, Giustizieri ML, Girolomoni G. Keratinocytes in inflammatory skin diseases. Curr Drug Targets Inflamm Allergy. 2005;4:329–34.
89. Kobayashi N, Nakagawa A, Muramatsu T, Yamashina Y, Shirai T, Hashimoto MW, Ishigaki Y, Ohnishi T, Mori T. Supranuclear melanin caps reduce ultraviolet induced DNA photoproducts in human epidermis. J Invest Dermatol. 1998;110:806–10.
90. Salmon JK, Armstrong CA, Ansel JC. The skin as an immune organ. West J Med. 1994;160:146–52.
91. Norris A, Todd C, Graham A, Quinn AG, Thody AJ. The expression of the c-kit receptor by epidermal melanocytes may be reduced in vitiligo. Br J Dermatol. 1996;134:299–306.
92. Jimbow K, Quevedo WC Jr, Fitzpatrick TB, Szabo G. Some aspects of melanin biology: 1950–1975. J Invest Dermatol. 1976;67:72–89.
93. Mattei S, Colombo MP, Melani C, Silvani A, Parmiani G, Herlyn M. Expression of cytokine/growth factors and their receptors in human melanoma and melanocytes. Int J Cancer. 1994;56:853–7.
94. Yu N, Zhang S, Zuo F, Kang K, Guan M, Xiang L. Cultured human melanocytes express functional toll-like receptors 2–4, 7 and 9. J Dermatol Sci. 2009;56:113–20.
95. Johnson KO. The roles and functions of cutaneous mechanoreceptors. Curr Opin Neurobiol. 2001;11:455–61.
96. Lumpkin EA, Bautista DM. Feeling the pressure in mammalian somatosensation. Curr Opin Neurobiol. 2005;15:382–8.
97. Halata Z, Grim M, Bauman KI. Friedrich Sigmund Merkel and his "Merkel cell", morphology, development, and physiology: review and new results. Anat Rec A Discov Mol Cell Evol Biol. 2003;271:225–39.
98. Maricich SM, Wellnitz SA, Nelson AM, Lesniak DR, Gerling GJ, Lumpkin EA, Zoghbi HY. Merkel cells are essential for light-touch responses. Science. 2009;324:1580–2.
99. Boulais N, Misery L. Merkel cells. J Am Acad Dermatol. 2007;57:147–65.
100. Moll I, Kuhn C, Moll R. Cytokeratin 20 is a general marker of cutaneous Merkel cells while certain neuronal proteins are absent. J Invest Dermatol. 1995;104:910–5.
101. Haeberle H, Fujiwara M, Chuang J, Medina MM, Panditrao MV, Bechstedt S, Howard J, Lumpkin EA. Molecular profiling reveals synaptic release machinery in Merkel cells. Proc Natl Acad Sci U S A. 2004;101:14503–8.
102. Lacour JP, Dubois D, Pisani A, Ortonne JP. Anatomical mapping of Merkel cells in normal human adult epidermis. Br J Dermatol. 1991;125:535–42.
103. Lucarz A, Brand G. Current considerations about Merkel cells. Eur J Cell Biol. 2007;86:243–51.
104. Moll I, Roessler M, Brandner JM, Eispert AC, Houdek P, Moll R. Human Merkel cells–aspects of cell biology, distribution and functions. Eur J Cell Biol. 2005;84:259–71.
105. Grim M, Halata Z. Developmental origin of avian Merkel cells. Anat Embryol (Berl). 2000;202:401–10.
106. Szeder V, Grim M, Halata Z, Sieber-Blum M. Neural crest origin of mammalian Merkel cells. Dev Biol. 2003;253:258–63.
107. Winkelmann RK. The Merkel cell system and a comparison between it and the neurosecretory or APUD cell system. J Invest Dermatol. 1977;69:41–6.
108. Cheng Chew SB, Leung PY. Ultrastructural study of the Merkel cell and its expression of met-enkephalin immunoreactivity during fetal and postnatal development in mice. J Anat. 1994;185:511–20.
109. Moll I, Lane AT, Franke WW, Moll R. Intraepidermal formation of Merkel cells in xenografts of human fetal skin. J Invest Dermatol. 1990;94:359–64.
110. Moll I, Moll R. Early development of human Merkel cells. Exp Dermatol. 1992;1:180–4.
111. Moll I, Moll R, Franke WW. Formation of epidermal and dermal Merkel cells during human fetal skin development. J Invest Dermatol. 1986;87:779–87.
112. Narisawa Y, Hashimoto K. Immunohistochemical demonstration of nerve-Merkel cell complex in fetal human skin. J Dermatol Sci. 1991;2:361–70.
113. Vielkind U, Sebzda MK, Gibson IR, Hardy MH. Dynamics of Merkel cell patterns in developing hair follicles in the dorsal skin of mice, demonstrated by a monoclonal antibody to mouse keratin 8. Acta Anat (Basel). 1995;152:93–109.
114. Morrison KM, Miesegaes GR, Lumpkin EA, Maricich SM. Mammalian Merkel cells are descended from the epidermal lineage. Dev Biol. 2009;336:76–83.

115. Van Keymeulen A, Mascre G, Youseff KK, Harel I, Michaux C, de Geest N, Szpalski C, Achouri Y, Bloch W, Hassan BA, Blanpain C. Epidermal progenitors give rise to Merkel cells during embryonic development and adult homeostasis. J Cell Biol. 2009;187:91–100.
116. Sidhu GS, Chandra P, Cassai ND. Merkel cells, normal and neoplastic: an update. Ultrastruct Pathol. 2005;29:287–94.
117. Steinman RM, Hemmi H. Dendritic cells: translating innate to adaptive immunity. Curr Top Microbiol Immunol. 2006;311:17–58.
118. Banchereau J, Briere F, Caux C, Davoust J, Lebecque S, Liu Y-J, Pulendran B, Palucka K. Immunobiology of dendritic cells. Annu Rev Immunol. 2000;18:767–811.
119. Steinman RM. Dendritic cells: versatile controllers of the immune system. Nat Med. 2007;13:1155–9.
120. Leibbrandt A, Penninger JM. RANK/RANKL: regulators of immune responses and bone physiology. Ann N Y Acad Sci. 2008;1143:123–50.
121. Toebak MJ, Gibbs S, Bruynzeel DP, Scheper RJ, Ruste-meyer T. Dendritic cells: biology of the skin. Contact Dermatitis. 2009;60:2–20.
122. Mutyambizi K, Berger CL, Edelson RL. The balance between immunity and tolerance: the role of Langerhans cells. Cell Mol Life Sci. 2009;66:831–40.
123. Pène F, Zuber B, Courtine E, Rousseau C, Ouaaz F, Toubiana J, et al. Dendritic cells modulate lung response to *Pseudomonas aeruginosa* in a murine model of sepsis-induced immune dysfunction. J Immunol. 2008;181(12):8513–20.
124. Jeschke MG, Chinkes DL, Finnerty CC, Kulp G, Suman OE, Norbury WB, et al. Pathophysiologic response to severe burn injury. Ann Surg. 2008;248(3):387–401.
125. Wu L. A Flt3L encounter: mTOR signaling in dendritic cells. Immunity. 2010;33(4):580–2.
126. Bohannon J, Cui W, Cox R, Przkora R, Sherwood E, Toliver-Kinsky T. Prophylactic treatment with Fms-like tyrosine kinase-3 ligand after burn injury enhances global immune responses to infection. J Immunol. 2008;180(5):3038–48.
127. Toliver-Kinsky TE, Cui W, Murphey ED, Lin C, Sherwood ER. Enhancement of dendritic cell production by Fms-like tyrosine kinase-3 ligand increases the resistance of mice to a burn wound infection. J Immunol. 2005;174(1):404–10.
128. Steinman RM, Banchereau J. Taking dendritic cells into medicine. Nature. 2007;449:419–26.
129. Morelli AE, Thomson AW. Tolerogenic dendritic cells and the quest for transplant tolerance. Nat Rev Immunol. 2007;7:610–21.
130. Langerhans P. Über die Nerven der menschlichen Haut. Virchows Arch. 1868;44:325–37.
131. Romani N, Clausen BE, Stoitzner P. Langerhans cells and more: langerin-expressing dendritic cell subsets in the skin. Immunol Rev. 2010;234:120–41.
132. Frelinger JG, Hood L, Hill S, Frelinger JA. Mouse epidermal Ia molecules have a bone marrow origin. Nature. 1979;282:321–3.
133. Katz SI, Tamaki K, Sachs DH. Epidermal Langerhans cells are derived from cells originating in bone marrow. Nature. 1979;282:324–6.
134. Perreault C, Pelletier M, Landry D, Gyger M. Study of Langerhans cells after allogeneic bone marrow transplantation. Blood. 1984;63:807–11.
135. Volc-Platzer B, Stingl G, Wolff K, Hinterberger W, Schnedl W. Cytogenetic identification of allogeneic epidermal Langerhans cells in a bone marrowgraft recipient. N Engl J Med. 1984;310:1123–4.
136. Birbeck MS, Breathnach AS, Everall JD. An electron microscopic study of basal melanocytes and high level clear cells (Langerhans cell) in vitiligo. J Invest Dermatol. 1961;37:51–64.
137. Kummer JA, Broekhuizen R, Everett H, Agostini L, Kuijk L, Martinon F, van Bruggen R, Tschopp J. Inflammasome components NALP 1 and 3 show distinct but separate expression profiles in human tissues suggesting a site-specific role in the inflammatory response. J Histochem Cytochem. 2007;55:443–52.
138. Peiser M, Koeck J, Kirschning CJ, Wittig B, Wanner R. Human Langerhans cells selectively activated via Toll-like receptor 2 agonists acquire migratory and $CD4^+$ T cell stimulatory capacity. J Leukoc Biol. 2008;83:1118–27.
139. Renn CN, Sanchez DJ, Ochoa MT, Legaspi AJ, Oh CK, Liu PT, Krutzik SR, Sieling PA, Cheng G, Modlin RL. TLR activation of Langerhans cell-like dendritic cells triggers an antiviral immune response. J Immunol. 2006;177:298–305.
140. Takeuchi J, Watari E, Shinya E, Norose Y, Matsumoto M, Seya T, Sugita M, Kawana S, Takahashi H. Down-regulation of Toll-like receptor expression in monocyte-derived Langerhans cell-like cells: implications of low-responsiveness to bacterial components in the epidermal Langerhans cells. Biochem Biophys Res Commun. 2003;306:674–9.
141. Van der Aar AM, Sylva-Steenland RM, Bos JD, Kapsenberg ML, de Jong EC, Teunissen MB. Loss of TLR2, TLR4, and TLR5 on Langerhans cells abolishes bacterial recognition. J Immunol. 2007;178:1986–90.
142. Asahina A, Tamaki K. Role of Langerhans cells in cutaneous protective immunity: is the reappraisal necessary? J Dermatol Sci. 2006;44:1–9.
143. Merad M, Manz MG, Karsunky H, Wagers A, Peters W, Charo I, Weissman IL, Cyster JG, Engleman EG. Langerhans cells renew in the skin throughout life under steady-state conditions. Nat Immunol. 2002;3:1135–41.
144. Larregina AT, Watkins SC, Erdos G, Spencer LA, Storkus WJ, Beer SD, Falo LD Jr. Direct transfection and activation of human cutaneous dendritic cells. Gene Ther. 2001;8:608–17.
145. Schaerli P, Willimann K, Ebert LM, Walz A, Moser B. Cutaneous CXCL14 targets blood precursors to epidermal niches for Langerhans cell differentiation. Immunity. 2005;23:331–42.
146. Eidsmo L, Allan R, Caminschi I, van Rooijen N, Heath WR, Carbone FR. Differential migration of epidermal and dermal dendritic cells during skin infection. J Immunol. 2009;182:3165–72.
147. Weinlich G, Heine M, Stössel H, Zanella M, Stoitzner P, Ortner U, Smolle J, Koch F, Sepp NT, Schuler G, Romani N. Entry into afferent lymphatics and maturation in situ of migrating murine cutaneous dendritic cells. J Invest Dermatol. 1998;110:441–8.
148. Ghaznawie M, Papadimitriou JM, Heenan PJ. The repopulation of murine Langerhans cells after depletion by mild heat injury. Br J Dermatol. 1999;141:206–10.
149. Holzmann S, Tripp CH, Schmuth M, Janke K, Koch F, Saeland S, Stoitzner P, Romani N. A model system using tape stripping for characterization of Langerhans cell-precursors in vivo. J Invest Dermatol. 2004;122:1165–74.
150. Cummings RJ, Mitra S, Foster TH, Lord EM. Migration of skin dendritic cells in response to ionizing radiation exposure. Radiat Res. 2009;171:687–97.
151. Janssens AS, Pavel S, Out-Luiting JJ, Willemze R, de Gruijl FR. Normalized ultraviolet (UV) induction of Langerhans cell depletion and neutrophil infiltrates after artificial UVB hardening of patients with polymorphic light eruption. Br J Dermatol. 2005;152:1268–74.
152. Villablanca EJ, Mora JR. A two-step model for Langerhans cell migration to skin-draining LN. Eur J Immunol. 2008;38:2975–80.
153. Ban E, Dupre L, Hermann E, Rohn W, Vendeville C, Quatannens B, Ricciardi-Castagnoli P, Capron A, Riveau G. CpG motifs induce Langerhans cell migration in vivo. Int Immunol. 2000;12:737–45.
154. Ginhoux F, Tacke F, Angeli V, Bogunovic M, LoubeauM DXM, Stanley ER, Randolph GJ, Merad M. Langerhans cells arise from monocytes in vivo. Nat Immunol. 2006;7:265–73.
155. Annes JP, Munger JS, Rifkin DB. Making sense of latent TGFbeta activation. J Cell Sci. 2003;116:217–24.

156. Borkowski TA, Letterio JJ, Farr AG, Udey MC. A role for endogenous transforming growth factor β1 in Langerhans cell biology: the skin of transforming growth factor β1 null mice is devoid of epidermal Langerhans cells. J Exp Med. 1996;184:2417–22.
157. Jaksits S, Kriehuber E, Charbonnier AS, Rappersberger K, Stingl G, Maurer D. CD34+ cell-derived CD14+ precursor cells develop into Langerhans cells in a TGFbeta 1-dependent manner. J Immunol. 1999;163:4869–77.
158. Kaplan DH, Li MO, Jenison MC, Shlomchik WD, Flavell RA, Shlomchik MJ. Autocrine/paracrine TGFbeta1 is required for the development of epidermal Langerhans cells. J Exp Med. 2007;204:2545–52.
159. Strobl H, Riedl E, Scheinecker C, Bello-Fernandez C, Pickl WF, Rappersberger K, Majdic O, Knapp W. TGF-β1 promotes in vitro development of dendritic cells from CD34+ hemopoietic progenitors. J Immunol. 1996;157:1499–507.
160. Schuster C, Vaculik C, Fiala C, Meindl S, Brandt O, Imhof M, Stingl G, Eppel W, Elbe-Bürger A. HLA-DR+ leukocytes acquire CD1 antigens in embryonic and fetal human skin and contain functional antigen-presenting cells. J Exp Med. 2009;206:169–81.
161. Kaplan DH, Kissenpfennig A, Clausen BE. Insights into Langerhans cell function from Langerhans cell ablation models. Eur J Immunol. 2008;38:2369–76.
162. Kimber I, Cumberbatch M, Dearman RJ. Langerhans cell migration: not necessarily always at the center of the skin sensitization universe. J Invest Dermatol. 2009;129:1852–3.
163. Merad M, Ginhoux F, Collin M. Origin, homeostasis and function of Langerhans cells and other langerin-expressing dendritic cells. Nat Rev Immunol. 2008;8:935–47.
164. Angel CE, Chen CJ, Horlacher OC, Winkler S, John T, Browning J, MacGregor D, Cebon J, Dunbar PR. Distinctive localization of antigen-presenting cells in human lymph nodes. Blood. 2009;113:1257–67.
165. Angel CE, George E, Brooks AES, Ostrovsky LL, Brown TLA, Dunbar PR. CD1a+ antigen-presenting cells in human dermis respond rapidly to CCR7 ligands. J Immunol. 2006;176:5730–4.
166. Haniffa M, Ginhoux F, Wang XN, Bigley V, Abel M, Dimmick I, Bullock S, Grisotto M, Booth T, Taub P, Hilkens C, Merad M, Collin M. Differential rates of replacement of human dermal dendritic cells and macrophages during hematopoietic stem cell transplantation. J Exp Med. 2009;206:371–85.
167. McLellan AD, Heiser A, Sorg RV, Fearnley DB, Hart DN. Dermal dendritic cells associated with T lymphocytes in normal human skin display an activated phenotype. J Invest Dermatol. 1998;111:841–9.
168. Nestle FO, Zheng XG, Thompson CB, Turka LA, Nickoloff BJ. Characterization of dermal dendritic cells obtained from normal human skin reveals phenotypic and functionally distinctive subsets. J Immunol. 1993;151:6535–45.
169. Ochoa MT, Loncaric A, Krutzik SR, Becker TC, Modlin RL. "Dermal dendritic cells" comprise two distinct populations: CD1+ dendritic cells and CD209+ macrophages. J Invest Dermatol. 2008;128:2225–31.
170. Turville SG, Cameron PU, Handley A, Lin G, Pohlmann S, Doms RW, Cunningham AL. Diversity of receptors binding HIV on dendritic cell subsets. Nat Immunol. 2002;3:975–83.
171. Zaba LC, Fuentes-Duculan J, Steinman RM, Krueger JG, Lowes MA. Normal human dermis contains distinct populations of CD11c+BDCA-1+ dendritic cells and CD163+FXIIIA+ macrophages. J Clin Invest. 2007;117:2517–25.
172. Klechevsky E, Morita R, Liu M, Cao Y, Coquery S, Thompson-Snipes L, Briere F, Chaussabel D, Zurawski G, Palucka AK, Reiter Y, Banchereau J, Ueno H. Functional specializations of human epidermal Langerhans cells and CD14+ dermal dendritic cells. Immunity. 2008;29:497–510.
173. Angel CE, George E, Ostrovsky LL, Dunbar PR. Comprehensive analysis of MHC-II expression in healthy human skin. Immunol Cell Biol. 2007;85:363–9.
174. Angel CE, Lala A, Chen CJ, Edgar SG, Ostrovsky LL, Dunbar PR. CD14+ antigen-presenting cells in human dermis are less mature than their CD1a+ counterparts. Int Immunol. 2007;19:1271–9.
175. Bangert C, Friedl J, Stary G, Stingl G, Kopp T. Immunopathologic features of allergic contact dermatitis in humans: participation of plasmacytoid dendritic cells in the pathogenesis of the disease? J Invest Dermatol. 2003;121:1409–18.
176. Wollenberg A, Wagner M, Gunther S, Towarowski A, Tuma E, Moderer M, Rothenfusser S, Wetzel S, Endres S, Hartmann G. Plasmacytoid dendritic cells: a new cutaneous dendritic cell subset with distinct role in inflammatory skin diseases. J Invest Dermatol. 2002;119:1096–102.
177. Colonna M, Krug A, Cella M. Interferon-producing cells: on the front line in immune responses against pathogens. Curr Opin Immunol. 2002;14:373–9.
178. Bursch LS, Wang L, Igyarto B, Kissenpfennig A, Malissen B, Kaplan DH, Hogquist KA. Identification of a novel population of Langerin+ dendritic cells. J Exp Med. 2007;204:3147–56.
179. Ginhoux F, Collin MP, Bogunovic M, Abel M, Leboeuf M, Helft J, Ochando J, Kissenpfennig A, Malissen B, Grisotto M, Snoeck H, Randolph G, Merad M. Blood-derived dermal langerin+ dendritic cells survey the skin in the steady state. J Exp Med. 2007;204:3133–46.
180. Nagao K, Ginhoux F, Leitner WW, Motegi S, Bennett CL, Clausen BE, Merad M, Udey MC. Murine epidermal Langerhans cells and langerin-expressing dermal dendritic cells are unrelated and exhibit distinct functions. Proc Natl Acad Sci U S A. 2009;106:3312–7.
181. Poulin LF, Henri S, de Bovis B, Devilard E, Kissenpfennig A, Malissen B. The dermis contains langerin+ dendritic cells that develop and function independently of epidermal Langerhans cells. J Exp Med. 2007;204:3119–31.
182. Andrew CE, Andrew NV. Lymphocytes in the normal epidermis of the rat and man. Anat Rec. 1949;104:217–41.
183. Clark RA, Chong BF, Mirchandani N, Yamanaka K, Murphy GF, Dowgiert RK, Kupper TS. A novel method for the isolation of skin resident T cells from normal and diseased human skin. J Invest Dermatol. 2006;126:1059–70.
184. Kupper TS, Fuhlbrigge RC. Immune surveillance in the skin: mechanisms and clinical consequences. Nat Rev Immunol. 2004;4:211–22.
185. Streilein JW. Skin-associated lymphoid tissues (SALT): origins and functions. J Invest Dermatol. 1983;80:12s–6s.
186. Boyman O, Hefti HP, Conrad C, Nickoloff BJ, Suter M, Nestle FO. Spontaneous development of psoriasis in a new animal model shows an essential role for resident T cells and tumor necrosis factor-α. J Exp Med. 2004;199:731–6.
187. Conrad C, Boyman O, Tonel G, Tun-Kyi A, Laggner U, de Fougerolles A, Kotelianski V, Gardner H, Nestle FO. Alpha1beta1 integrin is crucial for accumulation of epidermal T cells and the development of psoriasis. Nat Med. 2007;13:836–42.
188. Gebhardt T, Wakim LM, Eidsmo L, Reading PC, Heath WR, Carbone FR. Memory T cells in nonlymphoid tissue that provide enhanced local immunity during infection with herpes simplex virus. Nat Immunol. 2009;10:524–30.
189. Wakim LM, Waithman J, van Rooijen N, Heath WR, Carbone FR. Dendritic cell-induced memory T cell activation in nonlymphoid tissues. Science. 2008;319:198–202.
190. Boyman O, Conrad C, Tonel G, Gilliet M, Nestle FO. The pathogenic role of tissue-resident immune cells in psoriasis. Trends Immunol. 2007;28:51–7.

191. Ebert LM, Meuter S, Moser B. Homing and function of human skin gammadelta T cells and NK cells: relevance for tumor surveillance. J Immunol. 2006;176:4331–6.
192. Foster CA, Elbe A. Lymphocyte subpopulations of the skin. In: Bos JD, editor. Skin immune system (SIS). 2nd ed. Boca Raton, NY: CRC Press; 1997. p. 85–108.
193. Tamaki K, Sugaya M, Tada Y, Yasaka N, Uehira M, Nishimoto H, Nakamura K. Epidermal and dermal gamma-delta T cells. Chem Immunol. 2001;79:43–51.
194. Edele F, Molenaar R, Gutle D, Dudda JC, Jakob T, Homey B, Mebius R, Hornef M, Martin SF. Cutting edge: instructive role of peripheral tissue cells in the imprinting of T cell homing receptor patterns. J Immunol. 2008;181:3745–9.
195. Mora JR, Cheng GY, Picarella D, Briskin M, Buchanan N, Von Andrian U. Reciprocal and dynamic control of CD8 T cell homing by dendritic cells from skin-and gut-associated lymphoid tissues. J Exp Med. 2005;201:303–16.
196. Clark RA, Chong B, Mirchandani N, Brinster NK, Yamanaka K, Dowgiert RK, Kupper TS. The vast majority of CLA^+ T cells are resident in normal skin. J Immunol. 2006;176:4431–9.
197. Toulon A, Breton L, Taylor KR, Tenenhaus M, Bhavsar D, Lanigan C, Rudolph R, Jameson J, Havran WL. A role for human skin-resident T cells in wound healing. J Exp Med. 2009;206:743–50.
198. Campbell JJ, Murphy KE, Kunkel EJ, Brightling CE, Soler D, Shen Z, Boisvert J, Greenberg HB, Vierra MA, Goodman SB, Genovese MC, Wardlaw AJ, Butcher EC, Wu L. CCR7 expression and memory T cell diversity in humans. J Immunol. 2001;166:877–84.
199. Homey B, Alenius H, Muller A, Soto H, Bowman EP, Yuan W, McEvoy L, Lauerma AI, Assmann T, Bune-mann E, LehtoM WH, Yen D, Marxhausen H, To W, Sedgwick J, Ruzicka T, Lehmann P, Zlotnik A. CCL27-CCR10 interactions regulate T cell-mediated skin inflammation. Nat Med. 2002;8:157–65.
200. Sigmundsdottir H, Butcher EC. Environmental cues, dendritic cells and the programming of tissue-selective lymphocyte trafficking. Nat Immunol. 2008;9:981–7.
201. Bos JD, Zonneveld I, Das PK, Krieg SR, van der Loos CM, Kapsenberg ML. The skin immune system (SIS): distribution and immunophenotype of lymphocyte subpopulations in normal human skin. J Invest Dermatol. 1987;88:569–73.
202. Bos JD, de Boer OJ, Tibosch E, Das PK, Pals ST. Skin-homing T lymphocytes: detection of cutaneous lymphocyte-associated antigen (CLA) by HECA-452 in normal human skin. Arch Dermatol Res. 1993;285:179–83.
203. Foster CA, Yokozeki H, Rappersberger K, Koning F, Volc-Platzer B, Rieger A, Coligan JE, Wolff K, Stingl G. Human epidermal T cells predominately belong to the lineage expressing αβ T cell receptor. J Exp Med. 1990;171:997–1013.
204. Spetz AL, Strominger J, Groh-Spies V. T cell subsets in normal human epidermis. Am J Pathol. 1996;149:665–74.
205. Alaibac M, Morris J, Yu R, Chu AC. T lymphocytes bearing the γδ T-cell receptor: a study in normal human skin and pathological skin conditions. Br J Dermatol. 1992;127:458–62.
206. Groh V, Porcelli S, Fabbi M, Lanier LL, Picker LJ, Anderson T, Warnke RA, Bhan AK, Strominger JL, Brenner MB. Human lymphocytes bearing T cell receptor γδ are phenotypically diverse and evenly distributed throughout the lymphoid system. J Exp Med. 1989;169:1277–94.
207. Holtmeier W, Kabelitz D. Gammadelta T cells link innate and adaptive immune responses. Chem Immunol Allergy. 2005;86:151–83.
208. Sakaguchi S. Naturally arising Foxp3-expressing $CD25^+CD4^+$ regulatory T cells in immunological tolerance to self and non-self. Nat Immunol. 2005;6:345–52.
209. Clark RA, Huang SJ, Murphy GF, Mollet IG, Hijnen D, Muthukuru M, Schanbacher CF, Edwards V, Miller DM, Kim JE, Lambert J, Kupper TS. Human squamous cell carcinomas evade the immune response by down-regulation of vascular E-selectin and recruitment of regulatory T cells. J Exp Med. 2008;205:2221–34.
210. Clark RA. Skin-resident T cells: the ups and downs of on site immunity. J Invest Dermatol. 2010;130:362–70.
211. Eady RA, McGrath JA, McMillan JR. Ultrastructural clues to genetic disorders of skin: the dermal-epidermal junction. J Invest Dermatol. 1994;103:13S–8S.
212. Keene DR, Marinkovich MP, Sakai LY. Immuno-dissection of the connective tissue matrix in human skin. Microsc Res Tech. 1997;38:394–406.
213. Erickson AC, Couchman JR. Still more complexity in mammalian basement membranes. J Histochem Cytochem. 2000;48:1291–306.
214. Timpl R. Macromolecular organization of basement membranes. Curr Opin Cell Biol. 1996;8:618–24.
215. Yurchenco PD, Amenta PS, Patton BL. Basement membrane assembly, stability and activities observed through a developmental lens. Matrix Biol. 2004;22:521–38.
216. Myllyharju J, Kivirikko KI. Collagens, modifying enzymes and their mutations in humans, flies and worms. Trends Genet. 2004;20:33–43.
217. Aumailley M, Bruckner-Tuderman L, Carter WG, Deutzmann R, Edgar D, Ekblom P, Engel J, Engvall E, Hohenester E, Jones JC, Kleinman HK, Marinkovich MP, Martin GR, Mayer U, Meneguzzi G, Miner JH, Miyazaki K, Patarroyo M, Paulsson M, Quaranta V, Sanes JR, Sasaki T, Sekiguchi K, Sorokin LM, Talts JF, Tryggvason K, Uitto J, Virtanen I, von de Mark K, Wewer UM, Yamada Y, Yurchenco PD. A simplified laminin nomenclature. Matrix Biol. 2005;24:326–32.
218. Hallmann R, Horn N, Selg M, Wendler O, Pausch F, Sorokin LM. Expression and function of laminins in the embryonic and mature vasculature. Physiol Rev. 2005;85:979–1000.
219. Miner JH, Yurchenco PD. Laminin functions in tissue morphogenesis. Annu Rev Cell Dev Biol. 2004;20:255–84.

Burn Wound Healing: Pathophysiology

4

Luc Teot, Sami Otman, Antonio Brancati, and Rainer Mittermayr

4.1 Introduction

Burn injuries represent a specific wound entity with unique clinical features which range from the difficulty of initial assessment to the long-term tendency to develop pathologic scars. For long time considered as acute wounds, burns are in fact wounds showing a long-term evolution transforming them into chronic wounds, if inadequately managed. The pathophysiological changes in the burn wound are characterized by effects caused by heat per se and complex superimposed local as well as systemic alterations. Due to profound disturbances of the immunostatus in general burn wounds are highly susceptible to infections upon completed keratinization. A common consensus among burn specialists emerges considering that a burn wound has to be covered within a period of 2–3 weeks, justifying a dogma of rapid excision and grafting, a surgical approach popularized by surgeons since the 1970s. In fact, burn wounds which remained unhealed for several weeks or months either due to skin graft infection or by accumulation of the high level of proteases included the wound after 3–4 weeks of non-healing.

4.2 Local Biological Events Occurring After Burns

The skin is supposed to be the largest organ realizing multiple functions. It maintains not only a physical but also an immunological protective barrier conserving the organism against physical abrasion, bacterial invasion, dehydration, and ultraviolet radiation. Body temperature is kept constant by adaptation of the blood flow in the dermal plexus in conjunction with the tight regulation of fluid homeostasis via the sweet glands (thermoregulation). The skin contains abundant nerve endings and receptors that detect stimuli related to temperature, touch, pressure, and pain (sensation). Finally it defines also the personal features of the social appearance. Exogenous aggressors such as burns result in either the loss or disruption of some or all of these functions.

Jackson first described three zones of burn injury [1].

1. *Zone of coagulation*: The area of maximum impact is located at the center of the wound and is characterized by irreversible tissue loss. Coagulation and denaturation of the constituent proteins and loss of plasma membrane integrity are observed, with a necrosis visible at the center of injury.
2. *Zone of stasis*: In the surrounding zone of stasis a compromised tissue perfusion could be observed, ranging from critical capillary vasoconstriction to ischemia. This zone may be easily transformed into necrosis due to the accumulated effects of decreased perfusion, edema, and infection. However, when correctly managed these changes may be preserved.
3. *Zone of hyperemia*: The outer periphery of the burn wound represents the zone of hyperemia characterized by viable cells and vasodilatation mediated by local inflammatory mediators. Tissue within this zone usually recovers completely unless complicated by infection or severe hypoperfusion.

Secondary to the tissue loss in the zone of coagulation due to direct heat induced protein denaturation, especially the zone of stasis and hyperemia further contribute to the local pathology of the burn injury. An intense activation of toxic inflammatory mediators such as oxidants and proteases further damages skin and capillary endothelial cells, thus aggravating severity of trauma by inducing further ischemic tissue necrosis [2].

Immediately after burn, microvessels in the mentioned zones lose their capacity to keep fluids apart from the interstitial area. Loss of fluid and proteins is intense and contemporary to shift in the ionic content of the cells. This induced ischemia could lead to an increase in depth and the

L. Teot (✉) · S. Otman · A. Brancati · R. Mittermayr
Burns Unit, Wound Healing Unit, Lapeyronie Hospital, Montpellier University Hospital, Montpellier Cedex, France

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_4

aggravation of tissue loss. This microvascular injury is of dual origin, on one side due to the intensity of thermal injury and on the other hand due to vasoconstrictive substances. The microcirculatory changes induced by the thermal impact may be also related to an excessive hydrostatic pressure. The hypovolemic shock as well as the coexistent tissue trauma by itself create the burn shock, a specific situation, which increases the entire body inflammatory response and turning it into an accelerated multi-organ failure. The hypermetabolic response of burns injury should be managed accurately [3].

4.2.1 Inflammation

The inflammatory response following thermal injury is characterized by specific differences in comparison to the "normal" wound healing process. It is controlled by a large number of mediators originating from the major plasma enzyme systems and released from different kinds of leucocytes. Fast-acting mediators, such as vasoactive amines and the products of the kinin system, modulate the immediate response. The early phase of post-burn edema seems to be partly mediated by the vasoactive histamine [4]. It was shown that in thermal injury an increased activation of the kinin system occurs [5]. This may be attributed to excessive activation of the Hageman factor (F XII) [6], which not only leads to increased activation of the kallikrein-bradykinin system but also has consequences on the arachidonic acid cascade, complement cascade, and the coagulation-fibrinolytic cascades. However, bradykinin as a product from the kinin system considerably contributes to the local edema formation due increased venular dilation and permeability.

On the other hand, the biosynthesis of the metabolites from the arachidonic acid cascade, specifically prostaglandins, prostacyclin, and thromboxane A2, is also increased [7]. In this context, prostacyclin could lead to perpetuation of burn edema formation, and thromboxane A2 may be responsible for vasoconstriction and local ischemia in burned tissue.

The alternative pathway to activate the complement system in burns seems to be favored although an activation by inflammation burn injuries local biological events inflammation hydroxyl radicals have been shown also [8]. Depletion of complement components takes place, early after thermal injury, concomitant with reduction in the serum opsonic activity for various bacteria [9]. Increased levels of the activated complement components C3a and C5a (anaphylatoxins) in the plasma of burn patients are considered to regulate polymorphonuclear leucocytes function in these patients [10].

A hypercoagulability in thermally damaged tissue has been observed 2–3 hours following scalding due to a pronounced activation of the coagulation cascade [11]. These findings correlate well with the increase of kinins in the lymph, indicating that the Hageman factor may serve as a common activator of the kinin and the coagulation-fibrinolytic system.

As soon as leucocytes have arrived at the site of injury or infection, they release mediators which control the later accumulation and activation of other cells. Cytokines are involved in both inflammation and immunity. These mediators regulate the amplitude and duration of the inflammatory response and have multiple overlapping regulatory actions. Among the number of cytokines released by activated platelets, IGF-1 was to be reduced and correlated with the burn surface area [12]. This lower IGF-1 level may contribute to the impaired wound healing in these patients. IGF-1 also lowers protein oxidation in patients with thermal injury.

In this context, the function of various cell types as a main source of such cytokines is also modified by the thermal impact.

Polymorphonuclear cells show dysfunction in chemotaxis, phagocytosis, oxidative metabolism, granular enzyme contents and intracellular killing. A proposed mechanism is an overall systemic catabolism of the contractile actin protein in these cells. One consequence could include a predisposition for infectious complications [13].

Immunosuppression is often seen in severe thermal injury [14]. In this context, the cell-mediated immunity (lymphocytes) is usually severely impaired. The lymphocyte subpopulations were shown to be altered following injury by means of flow cytometry, where all T-lymphocyte subpopulations decrease (CD4 lymphocytes within 48 h and a larger proportion of CD8 cells for the following 3 weeks). B-lymphocytes and CD16 (natural killer cells), however, were found to be unchanged following thermal injury. In addition, a severe thermal injury is of such a magnitude that the extent of immunosuppression appears to be greater than following other forms of trauma.

Mast cells also secrete a broad range of substances including chemoattractants (TNF-α, IL-8, LTB4, PAF), vasoactivators (histamine, PAF, kininogenase), and spasmogens (histamine, PGD2, LTC4, LTD4) [15]. Thus, following thermal injury the chemoattractants released from mast cells directly contribute to the recruitment and interstitial migration of leucocytes. Furthermore, the mast cell-dependent arteriolar constriction that produces temporary reduction of blood flow immediately after tissue injury may provide favorable hemodynamic conditions for blood clotting and leucocyte migration.

Monocytes (upon activation termed as macrophages) release beside others IL-1 and TNF-a having a stimulatory effect on T cells but also an influence of the control of remote functions (production of, e.g., acute phase proteins, IL-6, and fever) [16]. On the other hand, they induce the thermal impact changes in skin proteins which have a specific effect on monocyte IL-1 secretion. It has been suggested that blood

monocytes are superstimulated following severe burns in vivo and produce large amounts of IL-1 leading to exhaustion of monocyte function.

4.2.2 Edema

Edema occurring during the first 24 h is by itself a source of secondary induced lesions. During the first day after injury, extravasation occurs in both the burned skin and the non-burned tissues. The amount of edema in burned skin depends on the type and extent of injury, but also on the type and degree of resuscitation administered. When burns involve large areas, edema is intense and creates important secondary lesions in the surrounding zones. Chemical mediators (cytokines) as discussed previously are intensively released into the burn lesion during the first 24 h. Large amounts of histamine are released into the burn area from mast cells, increasing vessel permeability in the early stage. Prostaglandins are released from burned tissues and act as potent vasoactive mediators. Serotonin, coming from platelets, is also released in the burn area. Its role is supposed to increase hydrostatic pressure by limiting the vein diameter. Bradykinin plays also a substantial role in the inflammatory process and has important effects in terms of edema formation. However, the role of these mediators remains poorly understood, and anti-mediators used in clinical situations do not substantially affect the edema formation. Free oxygen radicals are released in large amounts after trauma in general and burns in particular. Antioxidants have been shown to be partially efficient in reducing the extent of edema formation [17].

Kramer and Herndon [18] analyzed the factors interrelating the physiological determinants of transmicrovascular fluid flux, and could determine that edema is a resulting factor of several items (increased capillary filtration, capillary pressure, interstitial hydrostatic pressure, osmotic reflection coefficient, plasma colloid osmotic pressure, and interstitial colloid osmotic pressure).

4.2.3 Burn Wound Conversion

Burn wound conversion is also attributed to the secondary consequences of burn injury (Fig. 4.1). As a unique property of burn injury, the wound extension shows dynamic characteristics in the sub-acute post-burn phase. Burn wounds initially assessed as superficial could further progress into deep(er) lesions involving previously unburned adjacent tissue. A multitude of associated factors are related to an overexpression of vasoactive and inflammatory mediators. An imbalance between vasodilatory and vasoconstrictory prostanoids potentially could threaten the viability of tissue in the zone of stasis [19]. However, also vasodilation is implicated in the progression of the burn wound. Upregulation of inducible nitric oxide synthase causes peripheral vasodilation in the hyperemia and stasis zone, thus perpetuating inflammation. Moreover, transcription factor nuclear factor KB (NF-κB), which is also upregulated, induces increased downstream production of many inflammatory cytokines [20].

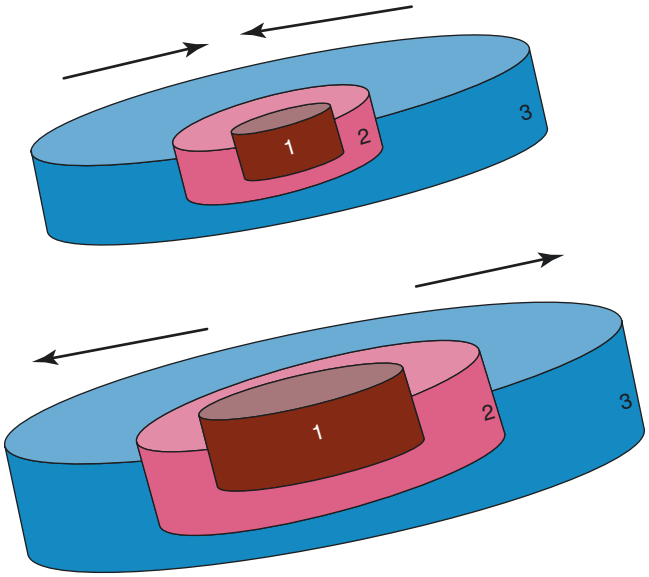


Fig. 4.1 Thermal burns covering limited areas (above) show recovery due to re-epithelialization after adequate management (arrows indicate recovery by re-epithelialization). If the burn wound exceeds a certain surface area (below), burn wound conversion is observed due to an overexpression of vasoactive and inflammatory mediators (arrows indicate progression of tissue downfall). (1) Zone of coagulation, (2) Zone of stasis, (3) Zone of hyperemia

Toxic secondary products of activated xanthine oxidase as well as neutrophils, including hydrogen peroxide, superoxide, and hydroxyl radicals, appear to directly damage dermal structures. A concomitant decrease in the physiological antioxidant mechanisms (e.g., superoxide dismutase, catalase, glutathione, α-tocopherol, and ascorbic acid levels) further impairs the local defense.

Hypoperfusion secondary to edema formation may also be linked to the conversion phenomenon. Increased vessel permeability whether as a reactive consequence of various factors (e.g., prostaglandins, bradykinin, histamine) or cell-toxic oxygen radicals causes an interstitial fluid shift exacerbating hypoperfusion in vulnerable tissue, specifically in the zones of stasis and hyperemia [2].

Elevated levels of bradykinin are not only responsible for increased vascular permeability but also cause hypercoagulation, thus resulting in microthrombosis. In combination with the procoagulant properties of thermal energy, bradykinin may stimulate microthrombosis in the zone of stasis and, as such, contribute to the burn wound progression.

4.3 Evolution of the Burn Wound and Local Consequences of Burns

Burn wounds do not represent a static wound condition with determinate wound depth just after the thermal aggression.

If temperatures of a minimum of 45 °C for 1 min are needed to create a deep burn, an exposure to a temperature of 100 °C for only 1 s leads to the same lesion. During the first 24 h, several factors may lead to a local degradation. Jackson could distinguish three different zones: the burn lesion itself; an adjacent area of stasis; and the periwound area filled with edema. Depending on the general evolution of the patient and the local treatment, the zone of stasis may create an obstacle to revascularization and could emerge as an origin of secondary worsening of the burn wound.

On the contrary, a rigorous management of both the local wound and the general condition of the patient is of good prognosis factor. The burn impact induces a catecholamine surge, a hypermetabolic response, a shock. Adapted resuscitation measures may prevent a fatal outcome in severe burns. This period is at high risk of development of a local delay in healing leading to infection. Locally the most important factor impairing healing (as well as life threatening) remains infection. The general management of infection will be combined to a local use of a large variety of topical antimicrobials.

Common germs responsible for local infections are multiple and are sometimes difficult to treat. Rigorous isolation protocols and the use of new types of antibiotics (e.g., vancomycin and piperacillin/tazobactam) are capable to reduce both the local and the systemic infectivity of the multidrug resistant *Staphylococcus aureus*. *Pseudomonas aeruginosa* and Acinetobacter are the main gram negative germs, on which colistin seems to act efficiently. Candida, Aspergillus, and Fusarium are the most frequently encountered fungal pathogens, on which amphotericin B and voriconazole may sufficiently act. These germs interfere with the wound healing process and could further contribute to the extent of the necrotic tissue [21].

Hypergranulation may be observed when burns are not appropriately managed. Granulation tissue is present over large burns areas where epidermization is lacking. Hypergranulation is an obstacle to epidermization. An adapted local management using corticosteroid will limit overgrowth and stabilize the granulation tissue at the same level than the surrounding epidermis.

Burns generate a high level of inflammation, impairing the whole healing process and in particular epidermization. However, epidermization should be obtained as fast as possible. Deep burns will need to be covered using surgical procedures of reconstructive skin surgery like skin grafts or flaps. More superficial wounds should be subjected to a quick surgical coverage using a combination of dermal and epidermal replacement. This constitutes the best local solution to obtain a stable non-retractile scar. Total thickness skin grafts offer this type of solution, but the scarcity of sources especially in large burned individuals makes them unavailable to recover extended areas. Partial thickness skin grafts offer a good covering alternative in most clinical routine cases, subject to the condition that rehabilitation is started rapidly. When used on highly retractile areas like joints in fingers, the hand or wrist areas, the use of partial thickness skin graft may lead to retractile scars. The foot needs a dermal replacement thick enough to prevent hyperkeratosis and/or secondary dermabrasions. Nevertheless, one difference observed between burns and chronic wounds is that in chronic wounds the capacity for re-epidermization is linked to the general condition of the patient, whose slow recovery issues to a very slow re-epidermization process. In chronic burns, epidermization is sometimes more difficult to achieve than in any other type of wound.

The last biological stage in burn healing is maturation of the wound, a period of time which describes the process of tissue remodeling resulting in a mature scar. This phase usually lasts for approximately 12 months, although sometimes prolonged (up to 2 years or longer in children, or in specific anatomical locations with high mechanostimulation, like the intermammary folds in women). On the other hand is an adequate mechanostimulation of scars, a well-accepted therapeutic approach to counteract the myofibroblast cell proliferation [22]. However, careful attention has to be drawn on adapted mechanical forces to manage scars resulting from burns sufficiently. Pathological scars are supposedly related to a disorder of wound healing [23]. The tendency to develop pathological scarring is more pronounced in burns of thermal origin. Joint retractions are often clinically observed when rehabilitation was not done correctly. Rehabilitation is mandatory to prevent pathological burns wound maturation.

If a burn wound is not adequately treated ending up in a chronic burn wound, healing will eventually also occur due to an intense skin contraction certainly as a consequence to the prolonged and intensive inflammatory process. These situations are still observed in emerging countries, issuing to extensive retractile scars, sources of important functional loss, particularly on the extremities. When burns occur early in life, these scars are source of intense deformities and irreversible loss of function (hand, wrist, elbow, shoulder being sometimes retracted together). These skin deformities generate in children an imbalance on the growing areas of bones at the extremities, thus possibly resulting in irreversible changes in the skeletal shape.

4.4 General Factors Influencing the Burn Wound Evolution

Skin lesions begin to appear after a heat exposure between 45 °C (1 h) and 70 °C (a few seconds). A series of consider-

ations in the wound management of thermal injuries should be taken into account.

4.4.1 Types of Burns

Origin of burns can be thermal, electric, or chemical.

- Thermal burns constitute the major group with an incidence of 80% and present a specific profile. They are considered not only as wounds but also as a general disease with subsequent consequences on thermal regulation, glycemia control, immunological status, myocardial function, and pulmonary hypertension. The resulting scars after thermal burns also present a higher tendency to develop hypertrophy and following congestion could last for a long period of time, longer than in any other type of burn injury.
- Electrical burns show a special feature, with two different types of lesion:
- Flash burns, where the electrical current is spread on the surface of the skin. These lesions look like thermal burns.
- Electrical passage burns show an entry point and an exit point, mostly found on the hand and the foot, the source of electricity being hung in the palm of the hand, the current running into the body, looking for a contact with earth, and exiting at the foot level. The heart may be also affected, with potential cardiac arrest due to a resonance effect between the amperage of the electrical current and the cardiac His bundle.
- Chemical burns often present a combination of chemical toxic effects on skin and thermal consequences. Bases and acids may attack the skin and the underlying tissues. The more concentrated the more invasive are the lesions, with a remnant effect sometimes which renders a simple lavage not sufficient for stopping progression of lesions towards the depth of the tissues. The development of amphotere solutions (Diphoterine gel, to be applied over mucosae as well as over skin lesions [24]), capable to react with both acid and basic aggressive products, has limited the interest of the "principle of neutralization" proned some decades ago. This attitude was more to rinse the fresh burns with a reverse base acid solution equivalent in concentration.

4.4.2 The Systemic Response to Local Burns

The release of cytokines and other inflammatory mediators at the site of injury has a systemic effect (Fig. 4.2) if burns involve more than 20% of total body surface area (TBSA). Severe alterations of the cardiovascular function may determine the degree of the burn shock, an abnormal physiologic

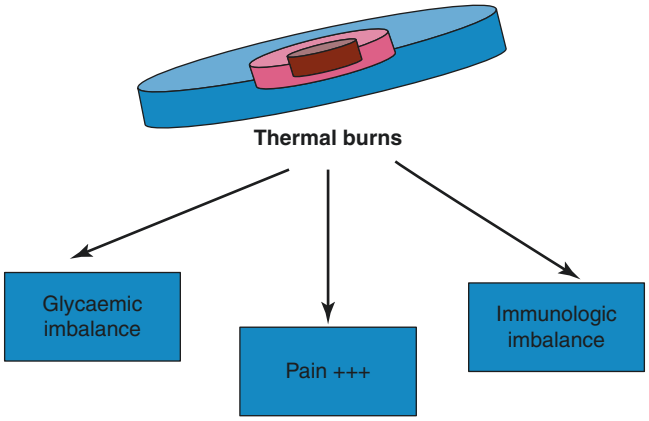


Fig. 4.2 Extended burn wounds (>20% TBSA) lead to a systemic response involving multiple organs and functional systems potentially leading to the burn shock

state in which tissue perfusion is insufficient to maintain adequate delivery of oxygen and nutrients and removal of cellular waste products [25].

4.4.3 Influence of Immediate Care on Burn Wounds

The quality of immediate care has an important influence on the outcome of the burn wound. A superficial second degree burn observed during the initial evaluation can turn into a deep second degree burn the day after (burn wound conversion), either due to a poor general management or because the general condition worsens in the resuscitation unit. Problems inherent to immediate burn care will not be developed in this chapter; however, it is important to keep the importance of adapted resuscitation protocols during the initial stage in mind. Application of systemic antimicrobials is also of importance and has to be considered when dealing with general infections originating from the burn wound.

4.4.4 Pathophysiological Consequences of Choice of Strategies Concerning Burn Wound Healing

In third degree burns, the strategy should remain univocal. Early excision and skin grafting were adopted by most of the physicians since the last 30 years (Fig. 4.3). Nowadays the question is more which skin substitute is sufficiently able to minimize the scarring process. Dermal replacement is a real issue to prevent functional damages and cosmetic consequences. Options like choosing a two-step procedure (delayed skin graft after a period of dermal re-vascularization) or a single step procedure (immediate skin grafting after application of a dermal substitute) are linked to the angioge-

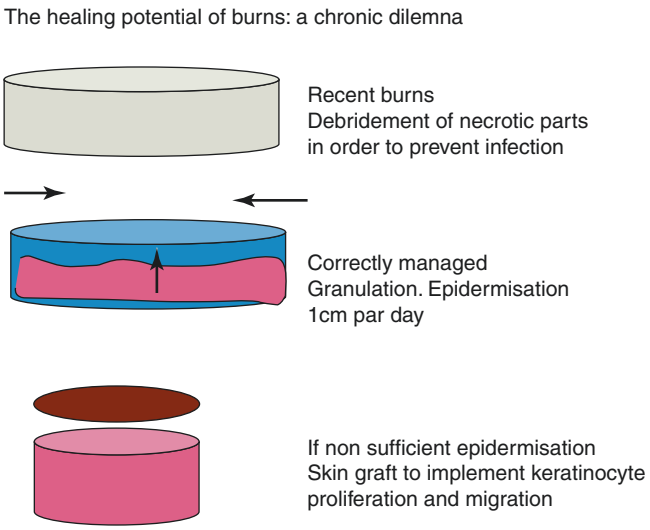


Fig. 4.3 The healing potential of burns

netic capacities of the excised recipient wound bed to penetrate and to re-vascularize the inert material, sufficiently nourishing the freshly applied skin graft [26].

In second degree burns, difficulties concerning the adequate assessment and management of the infection risk still persist:

- Assessment of burns is considered to be insufficiently precise in more than 40% of the cases evaluated by the specialists, especially during the first 3 days post-burn. Hereby, primarily the assessment of the burn depth is at high risk to a false diagnosis. Some clinical key elements could be helpful to accurately evaluate the depth of the burn lesion initially. Superficial burns are characterized by severe pain at gauze passage, uniform redness of the surface, and vulnerability to bleeding. In contrast, deep second degree burns show a red-white aspect, a nonhemorrhagic surface, and only a moderate pain at gauze passage.
- The adapted dressing should prevent in this period a pejorative evolution towards infection, and cover this risk. Topical antimicrobials are still first choice in the local treatment, and the most used agent is silver sulfadiazine cream.
- A pending question is to change habits in using large quantities of antiseptics, still largely used in order to prevent infection in this situation, and abandon or change to milder concentrations as proposed in some new solutions like biguanides? It is still too early to answer these questions and large trials should be done in order to check the capacities of these new strategies to control infection and prevent skin damages.

4.5 Conclusion

The pathophysiology of burn wounds is univocal for limited surfaces, and becomes dual when the TBSA is important, with a vicious circle between local and systemic effects. In this situation, the local lesion will be aggravated by the intense inflammatory process and the impaired vascularization secondary to the large amount of edema. These changes, combined with local consequences of the general poor condition, create a rapid degradation of the patient's status, leading to the burn shock.

Early resuscitation, an adapted local management, and the systematic prevention of infection (local and general) should be realized early and combined with an aggressive debridement of deep burnt areas.

References

1. Jackson DM. The diagnosis of the depth of burning. Br J Surg. 1953;40:588–96.
2. Kao CC, Garner WL. Acute burns. Plast Reconstr Surg. 2000;105:2482–92.
3. Williams FN, Herndon DN, Jeschke MG. The hypermetabolic response to burn injury and interventions to modify this response. Clin Plast Surg. 2009;36:583–96.
4. Friedl HP, Till GO, Trentz O, Ward PA. Roles of histamine, complement and xanthine oxidase in thermal injury of skin. Am J Pathol. 1989;135:203–17.
5. Arturson G. The plasma kinins in thermal injury. Scand J Clin Lab Invest Suppl. 1969;107:153–61.
6. Arturson G. Pathophysiology of the burn wound and pharmacological treatment. The Rudi Hermans lecture, 1995. Burns. 1996;22:255–74.
7. Zweifach BW. Dynamic sequelae of the acute inflammatory process: a state-of-the-art review. In: Little RA, Frayn KN, editors. The scientific basis for the care of the critically ill. Manchester: Manchester University Press; 1986.
8. Gelfand JA, Donelan M, Burke JF. Preferential activation and depletion of the alternative complement pathway by burn injury. Ann Surg. 1983;198:58–62.
9. Bjornson AB, Altemeier WA, Bjornson HS. Complement, opsonins, and the immune response to bacterial infection in burned patients. Ann Surg. 1980;191:323–9.
10. Davis CF, Moore FD Jr, Rodrick ML, Fearon DT, Mannick JA. Neutrophil activation after burn injury: contributions of the classic complement pathway and of endotoxin. Surgery. 1987;102:477–84.
11. Edery H, Lewis GP. Kinin-forming activity and histamine in lymph after tissue injury. J Physiol. 1963;169:568–83.
12. Moller S, Jensen M, Svensson P, Skakkebaek NE. Insulin-like growth factor 1 (IGF-1) in burn patients. Burns. 1991;17:279–81.
13. Sko-Seljavaara S. Granulocyte kinetics in burns. J Burn Care Rehabil. 1987;8:492–5.
14. O'Sullivan ST, O'Connor TP. Immunosuppression following thermal injury: the pathogenesis of immunodysfunction. Br J Plast Surg. 1997;50:615–23.
15. Gordon JR, Burd PR, Galli SJ. Mast cells as a source of multifunctional cytokines. Immunol Today. 1990;11:458–64.

16. Schwacha MG. Macrophages and post-burn immune dysfunction. Burns. 2003;29:1–14.
17. Demling RH. The burn edema process: current concepts. J Burn Care Rehabil. 2005;26:207–27.
18. Kramer GC, Herndon DN, Linares HA, Traber DL. Effects of inhalation injury on airway blood flow and edema formation. J Burn Care Rehabil. 1989;10:45–51.
19. Robson MC, Del Beccaro EJ, Heggers JP. The effect of prostaglandins on the dermal microcirculation after burning, and the inhibition of the effect by specific pharmacological agents. Plast Reconstr Surg. 1979;63:781–7.
20. Rawlingson A. Nitric oxide, inflammation and acute burn injury. Burns. 2003;29:631–40.
21. Branski LK, et al. Emerging infections in burns. Surg Infect. 2009;10:389–97.
22. Desmouliere A, Chaponnier C, Gabbiani G. Tissue repair, contraction, and the myofibroblast. Wound Repair Regen. 2005;13:7–12.
23. Shih B, Garside E, McGrouther DA, Bayat A. Molecular dissection of abnormal wound healing processes resulting in keloid disease. Wound Repair Regen. 2010;18:139–53.
24. Hall AH, Cavallini M, Mathieu L, Maibach HI. Safety of dermal diphoterine application: an active decontamination solution for chemical splash injuries. Cutan Ocul Toxicol. 2009;28:149–56.
25. Keck M, Herndon DH, Kamolz LP, Frey M, Jeschke MG. Pathophysiology of burns. Wien Med Wochenschr. 2009;159:327–36.
26. Bloemen MC, van Leeuwen MC, van Vucht NE, van Zuijlen PP, Middelkoop E. Dermal substitution in acute burns and reconstructive surgery: a 12-year follow-up. Plast Reconstr Surg. 2010;125:1450–9.

Part III

Scar Assessment, Treatment and Rehabilitation

Scar Assessment

5

Pauline D. H. M. Verhaegen, Martijn B. A. van der Wal, Esther Middelkoop, and Paul P. M. van Zuijlen

5.1 Scar Assessment Tools

Scars may lead to an array of functional, cosmetic, and psychological consequences. Scar tissue is usually distinguished from normal skin by an aberrant color, increased thickness, irregular surface area, and poor functional quality, caused by loss of pliability and contraction or expansion of the surface area. All separate scar features are relevant and attribute to the quality and general opinion on a scar.

An ideal assessment of a scar should include both subjective and objective aspects [1]. Scar assessment scales are frequently used to generate a systematic judgment by observers on the following aspects: color, thickness, relief, pliability, and the surface area. A judgment by the patient is obligatory to include pruritus and pain in the assessment. These items are particularly relevant when scars become hypertrophic [2]. Complaints and cosmetic disfigurement caused by scars may lead patients to suffer from psychosocial problems, which in turn may result in a decreased quality of life [3]. Both subjective and objective measurements of scar features are nowadays mandatory to practice evidence-based medicine. Therefore, in this chapter an overview will be given of the most important subjective and objective measurement tools for scar evaluation.

5.2 Scar Features

Color: Generally, disturbance in the color of a scar is created by the components vascularization and pigmentation. Vascularization or erythema is caused by an increase of capillary blood flow. In the early maturation phase, an increase in redness is an indicator of scar activity (Fig. 5.1a). Secondly, pigmentation is caused by a decrease or increase of melanin produced by melanocytes of the epidermis. Erythema usually diminishes after several months or sometimes years, whereas pigmentation mismatching often remains (Fig. 5.1b).

Thickness: An increase in scar thickness, e.g., hypertrophy, can be a frequent and cosmetically disfiguring sequela

Pauline D.H.M. Verhaegen and Martijn B.A. van der Wal contributed equally to this work.

Pauline D. H. M. Verhaegen
Association of Dutch Burn Centres Beverwijk, Beverwijk, The Netherlands
Department of Plastic, Reconstructive, and Hand Surgery, Red Cross Hospital Beverwijk, Beverwijk, The Netherlands
Burn Centre, Red Cross Hospital Beverwijk, Beverwijk, The Netherlands
Department of Plastic, Reconstructive, and Hand Surgery, Academical Medical Centre Amsterdam, Amsterdam, The Netherlands

M. B. A. van der Wal
Association of Dutch Burn Centres Beverwijk, Beverwijk, The Netherlands
Burn Centre, Red Cross Hospital Beverwijk, Beverwijk, The Netherlands

E. Middelkoop
Association of Dutch Burn Centres Beverwijk, Beverwijk, The Netherlands
Burn Centre, Red Cross Hospital Beverwijk, Beverwijk, The Netherlands
Department of Plastic, Reconstructive, and Hand Surgery, VU Medical Centre Amsterdam, Amsterdam, The Netherlands

P. P. M. van Zuijlen (✉)
Association of Dutch Burn Centres Beverwijk, Beverwijk, The Netherlands
Department of Plastic, Reconstructive, and Hand Surgery, Red Cross Hospital Beverwijk, Beverwijk, The Netherlands
Burn Centre, Red Cross Hospital Beverwijk, Beverwijk, The Netherlands
Department of Plastic, Reconstructive, and Hand Surgery, Academical Medical Centre Amsterdam, Amsterdam, The Netherlands
Department of Plastic, Reconstructive, and Hand Surgery, VU Medical Centre Amsterdam, Amsterdam, The Netherlands

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_5

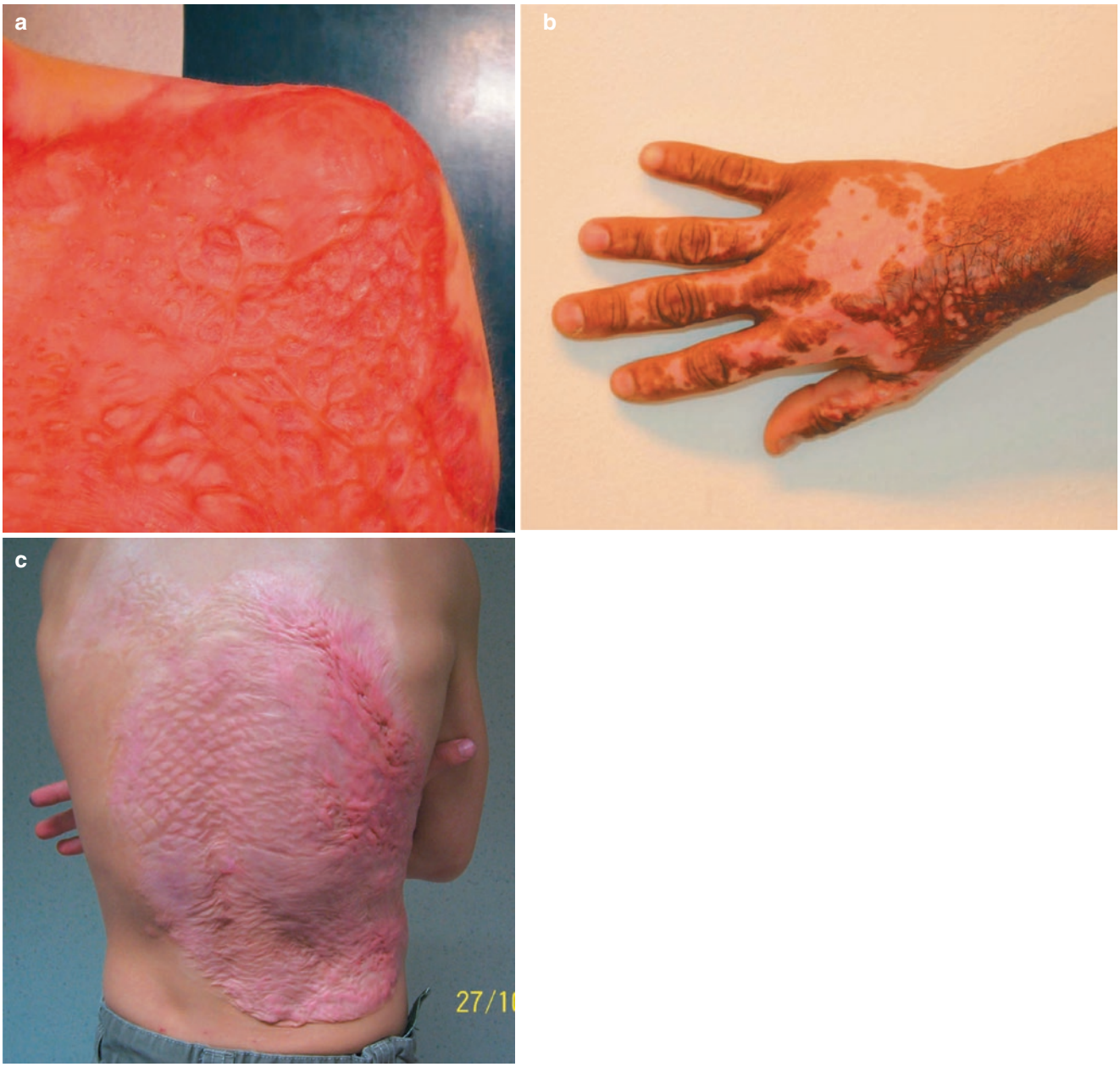


Fig. 5.1 (**a**) A red and raised scar after a burn injury of the shoulder. (**b**) Hypopigmentation after a burn injury of the hand. (**c**) Relief of a matured burn scar after skin transplantation of the back

of scarring (Fig. 5.1a). Hypertrophic scars are often misdiagnosed as keloids. The difference between the two is that keloids proliferate beyond the boundaries of the original lesion, while hypertrophic scars become raised, but stay within their confines [4]. In addition, hypertrophic scars typically decrease in thickness over time as opposed to keloids, which may have phases of reactivation [5].

Relief: Previous research has shown that the overall opinion of a scar, given by a clinician, is significantly influenced by relief [6]. Surface irregularities of a scar are especially seen after burn treatment, when a skin transplantation is needed and a meshed split skin graft is applied on the burned area. Often the areas in between the meshed split skin graft become raised [7]. As shown in Fig. 5.1c, such irregularities will remain.

Pliability: Loss of pliability is a major cause of functional impairment. Especially when a scar is situated adjacent to joints, scar stiffness may result in a limited range of motion. In addition, loss of pliability in the facial region will often cause asymmetry and an altered or diminished facial expression.

Surface area: In clinical practice, surface area is measured by planimetry. Planimetry is useful for calculating the wound

size, but also for calculating the percentage of a scar that becomes hypertrophic, hypopigmentated, or the extent of scar contraction or expansion over time. Scars may contract in time, which regularly leads to scar contracture (Fig. 5.2). In these cases, reconstructive surgery may be required. On the contrary, in linear scars expansion of the scar is frequently seen, which results in a broader scar and a less aesthetical result (Fig. 5.3). The extent of scar contraction or expansion is often used as an outcome parameter in research.

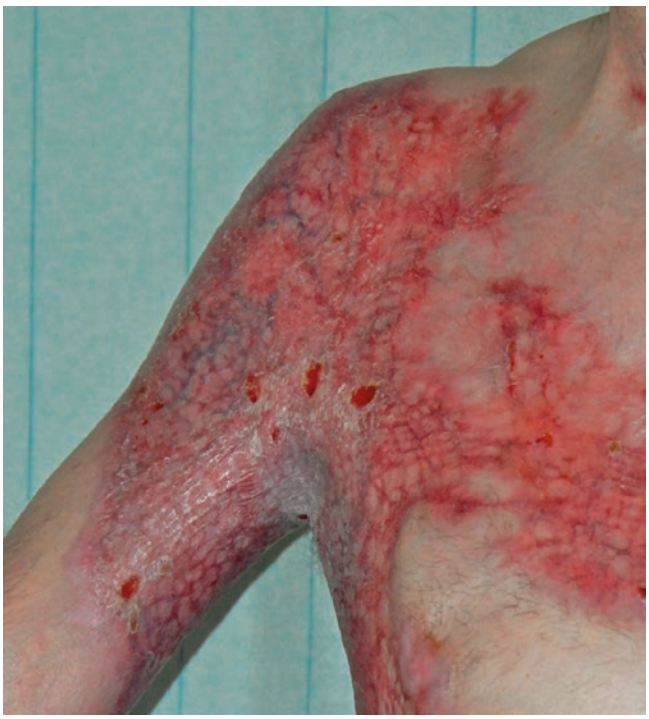


Fig. 5.2 Scar contracture after burn injury of the axilla with limited range of motion

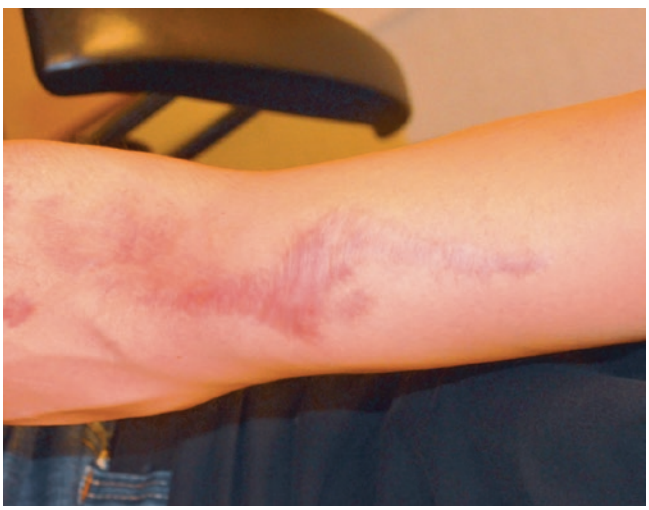


Fig. 5.3 Expansion of a linear scar on the upper arm

Although an increasing number of subjective and objective tools have become available, there is no general agreement as to the most appropriate tool(s) for scar evaluation [8]. In this chapter, subjective scar assessment scales and objective scar assessment tools are critically reviewed with respect to the concepts of internal consistency, level of agreement, reliability, validity, and feasibility.

5.2.1 Clinimetrical Principles

Requirements for both subjective and objective measurement tools are *reliability*, *validity,* and *feasibility*. Reliability refers to the reproducibility of measurements or ratings by observers [9]. An intraclass correlation coefficient (ICC) higher than 0.7 is considered a minimum requirement for reliable results [10]. The validity refers to the exactness of the measurements or ratings [11], i.e., do they measure what we want to measure? A Pearson's correlation coefficient higher than 0.6 is considered as good, ranging from 0.3 to 0.6 as moderate, and lower than 0.3 as weak [12]. Feasibility of a measurement tool refers to its convenience, effectiveness, price, and ease of use. It is hereby relevant to determine if the measurement tool can be used in a clinical or research setting.

Subjective measurement tools, e.g., scar assessment scales, can consist of either *nominal*, *ordinal*, or *categorical* variables. *Nominal* scales assign items to groups or categories. No ordering of the items is implied and they do not provide quantitative information (e.g., sex, race, etc.). In *ordinal* scales, the numbers assigned to objects represent the rank order (e.g., first, second, third, etc.) of the entities assessed. However, the interval between the numbers is not necessarily equal. *Categorical* scales are a nominal and ordinal scale combined into one. Combination can either be numerical (e.g., 1, 2, 3, etc.) or quantitative (e.g., normal skin, slightly hypertrophic, hypertrophic, keloid).

Clinimetrical parameters for scar assessment scales specifically are the *Cronbach's alpha* and *Cohen's Kappa or Weighted Kappa*. The Cronbach's alpha describes the internal consistency of a scale, which generally gives an idea whether several items that propose to measure the same general construct also produce similar scores. Results are considered good if the Cronbach's alpha ranges between 0.7 and 0.9. If the Cronbach's alpha is higher than 0.9, redundant items are included and a lower score than 0.7 means that no internal consistency has been reached [10]. The Cohen's Kappa or Weighted Kappa refers to the level of agreement between observers. The Cohen's Kappa is used in nominal scales and the Weighted Kappa is used for ordinal scales. Its cutoff points are determined according to Landis et al.: a Kappa above 0.6 is considered substantial and above 0.8 almost perfect [13].

5.3 Subjective Scar Assessment Scales

Scar assessment scales are questionnaires that have been developed to give an overall impression of a scar. In general, these scales are free of charge and easy to use which makes them very accessible in clinical practice. Ideally they should include the most important scar features described above. A drawback of assessment scales is its subjective nature. They are filled out by the observer or sometimes by the patient and are therefore susceptible to confounding factors. These factors may include (in)experience of an observer or patient and the psychological component, related to scarring which influences the judgment of the patient.

In the past decades, several attempts have been made to create an appropriate scale and mostly their origin is found in the assessment of burn scars. In 1988, Smith et al. were the first to show that *cosmetic disfigurement after burns* could be measured reliably [14]. Although this scale was far from perfect due to the fact that four raters were required to obtain reliable ratings, it inspired several authors to create a more suitable questionnaire for scars.

In 1990, Sullivan et al. introduced a new scar scale, which became known as the *Vancouver Scar Scale (VSS)* [15]. Again, this scale was designed to measure burn scars and included most scar parameters such as pigmentation, vascularity, pliability, and scar height (thickness). After being modified by Baryza et al. [16] for a better interobserver reliability, it became the most commonly used scale worldwide.

As stated by Sullivan et al., the VSS was still far from perfection and some problems were encountered. First, some important scar characteristics such as pain and itching were absent, since they concentrated on clinician's judgment rather than patient scores. Secondly, not all the variables in the VSS concerned ordinal data. The parameter pigmentation scored 0 for normal, 1 for hypopigmentation, 2 for mixed pigmentation, and 3 for hyperpigmentation. Although the scale was originally designed to show the degree of a pathological condition, it is often used to numerically indicate the absolute severity of a burn scar, with a high score indicating a worse scar. No evidence is found in literature that hypopigmentation should be considered a less severe condition than hyperpigmentation in scarring. In most cases, the opinion will be guided by the patient's normal skin appearance: e.g., a hypopigmented scarred area is considered worse in dark skin compared to pale skin. Thirdly, not all variables add the same number to the score, while no evidence was provided why one parameter should add more or less to the score. Finally, two observers were required to obtain reliable data, which limits its clinical ease of use.

Beausang et al. proposed a new quantitative scale which is often referred to as the *Manchester Scar Assessment Proforma* or *Manchester Scar Scale* (MSS) [17]. It was considered to be more complete compared to the VSS and better suited for linear scars. Because it was difficult for observers to distinguish vascularization from pigmentation, they combined these two components by referring to "color mismatching" with the ranking of none, slight, obvious, and gross mismatch. Additionally, an overall global assessment was made using the Visual Analogue Scale (VAS). Still, the patients' component was lacking and multiple observers were necessary for the scale to have an acceptable reliability.

A scale by Yeong et al., named the *Seattle Scale*, was designed for clinical use and for photographic assessment. A drawback of this scale was that the parameter pigmentation was given a negative value when a scar was hypopigmentated, suggesting that less pigmentation could improve the appearance of the scar [18].

In 1998, Crowe et al. introduced the *Hamilton Scale* which was specially designed to evaluate photographs of scars. It was shown to have a "substantial" to "almost perfect" reliability and novice therapists were as reliable as scar experts in the use of this scale [18, 19].

One of the most recently developed and upcoming scar scales is the *Patient and Observer Scar Assessment Scale (POSAS)* [6]. It consists of an observer and a patient component and contains the most important scar parameters used in previous scar scales. The observers score vascularization, pigmentation, pliability, thickness, and relief, while the patients score color, pliability, thickness, relief, itching, and pain. All these parameters are scored in a 10-step scale making it possible to measure a mean score, even while using merely some of the components of the scale, needed for specific purposes. It was first tested on burn scars and also became useful for the evaluation of linear scars after modification by van de Kar et al. in 2005 [20]. Both the VSS and the POSAS were found to be valid. However, in a direct comparison the POSAS was shown to be more consistent, reliable, and feasible than the VSS, making it more useful for clinical purpose.

In the same year, a new scale using photograph analysis was introduced, named the *Matching Assessment of Scars and Photographs* (MAPS) [21]. This scale was a modification of the Seattle Scale and the negative scoring system persisted, making it impossible for the observer to add the different components and obtain an overall score. Nevertheless a good reliability was found, except from vascularization and it also showed that extensive training of the observers was not necessary.

Table 5.1 gives an overview of the abovementioned scar assessment scales.

Table 5.1 An overview of scar assessment scales and their relevant clinimetrical parameters

Scale (authors + references)	Clinically or photographs assessed and by observer/ patient	Included items	Observers used/required	Tested on	Reliability		Validity
					Intra-observer	Inter-observer	
Cosmetic Disfigurement Scale [14]	Photographs and observer	1. Irregularity 2. Thickness 3. Discolorization 4. Overall clothed 5. Overall non-clothed	4	Burn scars	ICC: Irregularity: 0.89; thickness: 0.91 Color: 0.85 Overall clothed: 0.98 Overall non-clothed: 0.94	ICC: (averaged) irregularity: 0.78 thickness: 0.79 Color: 0.72 Overall clothed: 0.94 Overall non-clothed: 0.86	–
VSS [15]	Clinically and observer	1. Pigmentation 2. Vascularity 3. Pliability 4. Height	3	Burn scars	Not measured	Mean kappa: each observer pair: 0.5 (±0.1)	–
VSS with additional tool [16]	Clinically and observer	1. Pigmentation 2. Vascularity 3. Pliability 4. Height	3	Burn scars	Not measured	Overall ICC: 0.81 Cohen's kappa: Pigmentation: 0.61 Vascularity: 0.73 Pliability: 0.71 Height: 0.56	–
Seattle Scale [18]	Photographs and observer	1. Surface 2. Border height 3. Thickness 4. Color	8	Burn scars	Not measured	ICC: Surface: 0.94 Border height: 0.95 Thickness: 0.90 Color: 0.85	–
Manchester Scar Scale [17]	Photographs and observer	1. Color 2. Contour 3. Texture 4. Distortion	10	Surgical scars, hypertrophic scars, and keloid scars	Mean CV: 7.8–14.8%	Overall correlation coefficient (Spearman's rho): 0.87	Correlation with histology findings Contour: $R^2 = 0.62$ Texture: $R^2 = 0.69$
Hamilton Scale [19]	Photographs and observer	1. Height 2. Irregularity (proportion of scar) 3. Vascularity 4. Color	2	Burn scars	Cohen's kappa: height: 0.75–0.79 Irregularity: 0.75–0.76 Vascularity: 0.66–0.72 Color: 0.72–0.90	Cohen's kappa: Height: 0.82–0.84 Irregularity: 0.80–0.89 Vascularity: 0.73–0.78 Color: 0.80–0.72	–
Modified VSS [22]	Clinically and observer	1. Pigmentation 2. Vascularity 3. Pliability 4. Height	3	Burns scars and surgical scars	Not measured	ICC: Pigmentation: 0.20 Vascularity: 0.41 Pliability: 0.42 Height: 0.36	–

Table 5.1 (continued)

Scale (authors + references)	Clinically or photographs assessed and by observer/ patient	Included items	Observers used/required	Tested on	Reliability		Validity
					Intra-observer	Inter-observer	
POSAS [6]	Clinically and observer and patient	*Observer*: 1. Vascularity 2. Pigmentation 3. Thickness 4. Relief 5. Pliability *Patient*: 1. Pain 2. Itching 3. Color 4. Stiffness 5. Thickness 6. Irregularity	1	Burn scars	Internal consistency (Cronbach's alpha) Observer: 0.69 Patient: 0.76	ICC: Observer score: 0.73 (0.62–0.82)	Correlation observer scale with VSS Spearman's rho = 0.89
MAPS [21]	Photographs and observer	1. Surface 2. Border height 3. Thickness 4. Color 5. Pigmentation	3	Burn scars	ICC: Surface: 0.40 Border height: 0.79 Thickness: 0.82 Color: 0.79	ICC: Surface: 0.25–0.38 Border height: 0.63–0.70 Thickness: 0.60–0.74 Color: 0.5–0.71	–
Modified POSAS [20, 23]	Clinically and observer and patient	*Observer*: 1. Vascularity 2. Pigmentation 3. Thickness 4. Relief 5. Pliability 6. Surface area *Patient*: 1. Pain 2. Itching 3. Color 4. Stiffness 5. Thickness 6. Irregularity	1	Burn scars, surgical scars	Internal consistency (Cronbach's alpha) Observer: 0.86 and 0.77 Patient: 0.90 and 0.74	ICC observer: Vascularity: 0.81 and 0.62 Pigmentation: 0.71 and 0.73 Thickness: 0.72 and 0.39 Relief: 0.67 and 0.79 Pliability: 0.65 and 0.48 Surface area: 0.83	Correlation observer scale with VSS Spearman's rho = 0.38

VSS Vancouver Scar Scale, *POSAS* Patient and Observer Scar Assessment Scale, MAPS matching assessment of scars and photographs

5.3.1 Importance of Different Scar Features on the General Impression

Previous research has shown that the parameters color, thickness, and relief influence the observers' general opinion of a burn scar the most [6]. The patients' opinion is predominantly influenced by itching and thickness of the scar. When testing the POSAS on the assessment of linear scars, it was shown that especially the parameters redness, pigmentation, relief, and contraction or expansion of the surface area influenced the observers' general opinion. Again, the patients' opinion was predominantly influenced by itching and thickness of the scar [20].

5.4 Objective Measurement Tools

5.4.1 Color

Color evaluation raises several practical problems, e.g., observers are not always able to make a good distinction between the two components vascularization and pigmentation. Also color-blinded observers will have a great difficulty in answering these questions in scar assessment scales. This underlines the importance of objective color measurement tools in scar evaluation; however, not all objective tools have this discriminative ability. At present, the most common objective method of measuring skin color is referred to as

reflectance spectroscopy. Color is determined by measuring the intensity of light reflected from specific wavelengths. Within this principle, two different types of devices can be distinguished: the tristimulus reflectance colorimetry and the narrow-band spectrophotometry.

Tristimulus reflectance colorimetry was developed to objectively represent color in a manner the human eye perceives it. The level of light reflected through three broad wavelength filters is determined. In 1976, a color model based on human perception was established by the Commission Internationale de l'Eclairage (CIE) [24, 25]. Several devices integrated these values into their systems where any color can be described by three values: L*, the lightness; a*, the amount of green or red; and b*, the amount of yellow or blue. In practice, the L* expresses the relative brightness of the color, a* the redness, and b* the pigmentation of the skin. Examples of tristimulus devices are the Colorwalk colorimeter (Photofolt, UMN Electronics, Indianapolis, IN), the Micro Color (DR Bruno Lange GmbH, Düsseldorf, Germany), the Labscan XE (Hunter Associates Inc., Texas, USA), and the Minolta Chromameter CR-200 and CR-300 (Minolta Camera Co., Ltd., Osaka, Japan).

The *Minolta Chromameter* is the most commonly used colorimeter for the color assessment of both normal and scarred skin [26–29]. On normal skin, the device was shown to have an excellent intra-observer reliability for all three parameters (L*, a*, b*) with very low standard error of mean (SEM) values. It also showed a good to excellent inter-observer reliability, inter-instrument and day-to-day reliability and it can therefore be used by a single observer [30]. On scarred skin, the reliability was good for the three parameters and increased up to excellent when the measurement was performed by four observers. The measurement for redness correlated significantly but weakly with the POSAS. As far as pigmentation was concerned, an unacceptably low correlation was found compared to the pigmentation score of the VSS. It was stated by the authors that this lack of correlation might be related to the poor agreement of the observers in the assessment scale, especially with highly vascularized scars. It was hypothesized that the vascularization of the scar could mask the pigmentation of the scar and this was confirmed by post-hoc analysis when the agreement and correlation improved at lower vascularized scars [31]. Although this device links to a computer, it performs relatively good in a clinical setting due to the connecting cable that gives the investigator an acceptable range of motion.

The *Labscan XE* is a full-scanning spectrophotometer that has been tested for its reliability and validity on scars. Although the inter-observer reliability for redness was only moderate, the results did seem to correlate well with the redness parameter of the VSS. The pigmentation measurements were more reliable, but a sufficient correlation with the pigmentation value b* could not be found. This device is also limited for clinical purposes because it is too big to be positioned correctly over body regions such as the neck, the back, and the chest [32].

Narrow-band spectrophotometry devices were developed to measure skin or scar redness and pigmentation in the form of erythema and melanin. This method was first described by Diffey and Farr and is based on the differences in light absorption of red and green by hemoglobin and melanin [33–35]. These differences result in a certain intensity of reflected light which can be measured. Blood is colored red because hemoglobin absorbs much green light and reflects red light, while melanin is colored brown because it absorbs light of all wavelengths. The erythema index (E) is defined as $E = 100 \times \log$ (intensity of reflected red light/intensity of reflected green light) and the melanin index (M) is defined as: $M = 100 \times \log$ (1/intensity of reflected red light). The *DermaSpectrometer* (Cortex Technology, Hadsund, Denmark), the *Mexameter* (Courage and Khazaka, Cologne, Germany), and the *Erythema meter* (Dia-stron, Andover, United Kingdom) are examples of narrow-band reflectometers.

The *DermaSpectrometer* is a handheld tool, which makes it very feasible in general practice. It is equipped with a 6 mm diameter probe which is placed on the skin. After pressing the shutter button, the results are immediately displayed. The Derma Spectrometer was found to have a good reliability on normal and scarred skin, although a relatively high variation of day-to-day repeatability (8–22%) was seen for the erythema index on normal skin [31, 36]. Oliveira et al. found a good correlation between the erythema and melanin values of the DermaSpectrometer with the VSS scores for respectively redness and pigmentation [37]. This was later confirmed by Draaijers et al. for redness (compared with the POSAS), but they failed to show an acceptable correlation with pigmentation [31].

The *Mexameter* has to be linked to a computer, making it less suited for clinical purposes. However, the cable between the device and the probe gives the investigator an acceptable range of motion. The probe is equipped with 16 light-emitting diodes that send light at three defined wavelengths: 568 nm (green), 660 nm (red), 880 nm (infrared). The reflected light is measured through the abovementioned principle and is immediately displayed. Recent work by Nedelec et al. showed good intra- and inter-observer reliability values of the erythema and melanin index when using this device on normal and scarred skin [38, 39]. In addition, only a moderate correlation of the erythema index with the subscale vascularization of the modified VSS was found and there was a weak correlation of the melanin index with the pigmentation score [39].

The DermaSpectrometer and the Mexameter have been compared in vitro and in vivo on normal skin. The repeatability as well as the sensitivity of these two instruments was

good. Both measurement devices were able to characterize skin color and to quantify small skin color changes [36]. On scarred skin, a comparison with the DermaSpectrometer has not been made.

Different types of tristimulus devices have been compared with narrow-band devices on normal skin [36, 40]. On scarred skin, Draaijers et al. compared the Minolta Chromameter with the DermaSpectrometer [31]. Although the Minolta gave the most reliable values, the DermaSpectrometer seemed to be more feasible in clinical practice and was therefore preferred.

In summary, the tristimulus colorimeter is capable of measuring all scar colors, whereas the narrow-band reflectometers are designed for measuring the intensity of erythema and pigmentation. On scarred surface both types of devices seem reliable, but neither the tristimulus nor the narrow-band devices seem able to perform measurements with an acceptable correlation with the gold standard. The DermaSpectrometer is the most feasible tool, but it has recently been withdrawn from the market. We conclude that there is no objective tool available for the analysis of scar color that measures redness and pigmentation in a reliable and valid way. Until further research is performed, the Minolta Chromameter and the Mexameter seem the best devices available for measuring scar color.

5.4.2 Thickness

When measuring thickness of a scar it is important to distinguish clinical thickness from histological thickness. Clinically, thickness is usually measured through comparing the height of the scar with the normal surrounding skin, while the histological thickness might differ because of bulky connective tissue, especially in immature scars.

A skin biopsy remains the gold standard to measure scar thickness but it is infrequently applied in the clinical setting because of its invasive character. Ultrasound has been shown to be reproducible and accurate in the determination of the thickness of normal and scarred skin [38, 39, 41, 42]. Today, in combination with the appropriate software, it is possible to create a three-dimensional image, including measurements of thickness, area, and volume of the scar tissue. This method is often used for the analysis of scar thickness after burns or surgical treatments [43–45]. The *Tissue Ultrasound Palpation System (TUPS)* (Biomedical Ultrasonic Solutions, Hong Kong) and the *Dermascan C* (Cortex Technology, Denmark) are frequently used devices.

The *TUPS* is a portable ultrasound machine which is connected to a probe that is equipped with an ultrasound transducer with both a transmitter and receiver at the tip. It was proven to have a high inter-observer and test-retest reliability, but it only seemed to correlate moderately with the VSS that was used to test its concurrent validity [46]. A phantom study by Du et al. showed that the TUPS was able to measure the volume of a scar with a 90% accuracy [47].

The Dermascan C is a high-frequency (10–50 MHz), high-resolution ultrasound scanner that captures and reproduces detailed images of the skin or scar. It is able to penetrate to a depth up to 15 mm, making it accessible for the measurements of most common scars. A good inter-observer and excellent intra-observer reliability was found on scarred surfaces and measurements could also be reliably repeated the next week. The validity of the Dermascan C was tested and a statistically significant Spearman's Rho correlation of 0.41 and 0.50 was found between the total thickness of the instrument and the VSS subscale for height [39].

In 2007, a new scanning technique for accurate volume measurements of keloids was introduced [48]. The *Vivid 900* (Konica-Minolta, Milton Keynes, United Kingdom) is a non-contact scanning device that combines photography and laser technology for volume assessment using RapidForm 2004 3D reverse modelling software. This scanner is not portable and relatively expensive, making it less accessible for small centers. Although no reliability test was performed, the results seemed to correlate positively with the total score of the Manchester scar scale. Then again, whether a correlation of scar volume with a total scar score is desirable, remains debatable.

Magnetic Resonance Imaging (MRI) has been shown to accurately and reliably measure the thickness of normal skin [49]. This technique has not been applied for measuring scar thickness. Moreover, this method is very expensive and time-consuming.

After reviewing the available evidence, ultrasound seems the first choice tool for measuring scar thickness. It is convenient in use and found to be accurate and reliable for the evaluation of scar thickness. Because the Dermascan C showed a slightly higher correlation with the VSS compared to TUPS, this device would be our first choice for this purpose.

5.4.3 Relief

Surface irregularities, also referred to as relief, can be measured by various measurement tools. A selection of the most important, non-invasive, objective measurement tools is reviewed below.

Most objective relief measurement methods measure the skin topography indirectly by using a negative replica of the skin [50–54]. SILFLO® silicon polymer (Flexico Developments Ltd., Hertfordshire, United Kingdom) is most widely used and previous studies have proven its reliability and reproducibility [55]. First, liquid silicone is placed onto the area of interest and mixed with a hardener in a fixed posi-

tion. After the replica is hardened, which takes 1 min to 24 h, a negative print of the skin or scar is generated. To assess the relief, further investigation needs to be done on these replicas, which may include *Mechanical, Optical, Laser, Transparency, or Interference Fringe Projection Profilometry.*

The *Mechanical Profilometry* technique, which is also referred to as the stylus method, is a relief measuring method, which generates digitized data from a stylus that runs over a replica [56–58]. Relief can be measured up to several millimeters [55]. Even though mechanical profilometry has a high reliability, its feasibility is low, because of a long drying and measuring time of 24 h and 8 min, respectively. In addition, it is uncertain whether this method would be suitable and reliable for measuring scar relief, since it has only been used to assess the depth of wrinkles, skin dryness, and atopic dermatitis in unscarred skin.

Optical Profilometry is a relief measuring method, which works by the detection of black and white reflections by light irradiation. This light irradiation is caused by differences in depth and angle of the replica. In a short time period, the image is processed by a high-resolution black and white video or CCD (Charge-Coupled Device) camera, which is projected on a computer and analyzed by using specialized software [59, 60]. This system is able to measure relief up to 6 mm [55], which makes it suitable to quantify scar relief. However, the optical profilometry method, which previously has shown good reliability on normal skin [59, 61], should first be tested on its reliability on scars before clinical use would be advocated.

Laser Profilometry is a relief measuring method, which is based on the principle of light amplification and reflection from a skin replica [62, 63]. After reflection of light from the replica, the laser is focused by a movable lens. These movements of the lens, which are proportional to the relief of the replica, are registered digitally and calculated by a specialized software program. This software program displays a three-dimensional picture, on which calculations such as the Fourier analysis can be performed [62]. The maximum vertical measuring range is 10 mm. Laser profilometry is a very accurate and reliable method for relief measurements on normal skin [63]. However, reliability for measurements of scars and validity have not been assessed. In addition, its feasibility is low because of a long measurement time (10–30 min), high costs, and complexity in use. Therefore, laser profilometry is not recommended for use in a clinical setting, but may be used for research purposes.

Transparency Profilometry can be performed by using the Visiometer (Courage and Khazaka, Cologne, Germany) [64–66]. This measurement principle is based on light transmission through a thin replica of silicone of which the light absorption is known. The Visiometer measures reliably between a vertical range of 10 and 361 μm [64], but since relief in scars and relief of deeper wrinkles often exceeds 361 μm, this method will most likely not be useful for measurements of scar relief. Moreover, its validity has never been assessed.

Interferometry, also referred to as *Interference Fringe Projection Profilometry* (Breuckmann, Meersburg, Germany), consists of calculating a phase image from interference fringe image projection. The phase image gives access to the altitude at each point. By calculating the phase difference between the phase of the replica and that of the reference plane, the relief of the replica is obtained [67]. The Dermatop® system and the Toposurf® software are used to generate the data. The interferometry measurements showed good accuracy and reliability. Research showed that in the evaluation of micro-and macrorelief interferometry was considered more feasible than the other four profilometry methods, which have been discussed above [68]. Since the vertical measurement range has not been mentioned, it remains unclear whether it would be suitable for measurements of scar relief.

Besides indirect measurements of topography, which use skin replicas, skin topography can also be measured directly. The *PRIMOS* (Phases shift Rapid In vivo Measurement Of the Skin, GFMesstechnik GmbH, Teltow, Germany) is a non-contact measurement tool which assesses relief. It is able to measure skin relief with a vertical range up to 10 mm. First, a parallel digital stripe pattern is projected onto the skin and the reflected light is absorbed by a CCD-chip of a high-resolution camera. Subsequently, a digital three-dimensional image is achieved which is evaluated by use of a specialized software program [69]. The PRIMOS is a feasible measurement tool: generating the image and processing the data is an easy and short procedure compared to the measurement methods that analyze negative skin replicas. Currently, the reliability and validity of the PRIMOS for scar relief measurements are being tested [70].

Relief measurement tools should be subdivided into tools which are applicable on irregularities of normal skin and tools applicable on scar relief. Transparency Profilometry and Interferometry are able to precisely measure skin microrelief, which can be relevant for the evaluation of therapies for dermatological diseases or for the cosmetic industries. Mechanical, optical, and laser profilometry could be more useful for quantifying macrorelief of scars. However, because of low feasibility these methods have a limited application in a clinical setting, but could be used for research purposes. The PRIMOS, which is a more feasible measurement tool, may very well be suitable for the quantification of scar relief in a clinical setting.

5.4.4 Elasticity

The mechanical qualities of the skin are well appreciated and studied. Experimental models identified the most important mechanical skin characteristics, which are tensile strength,

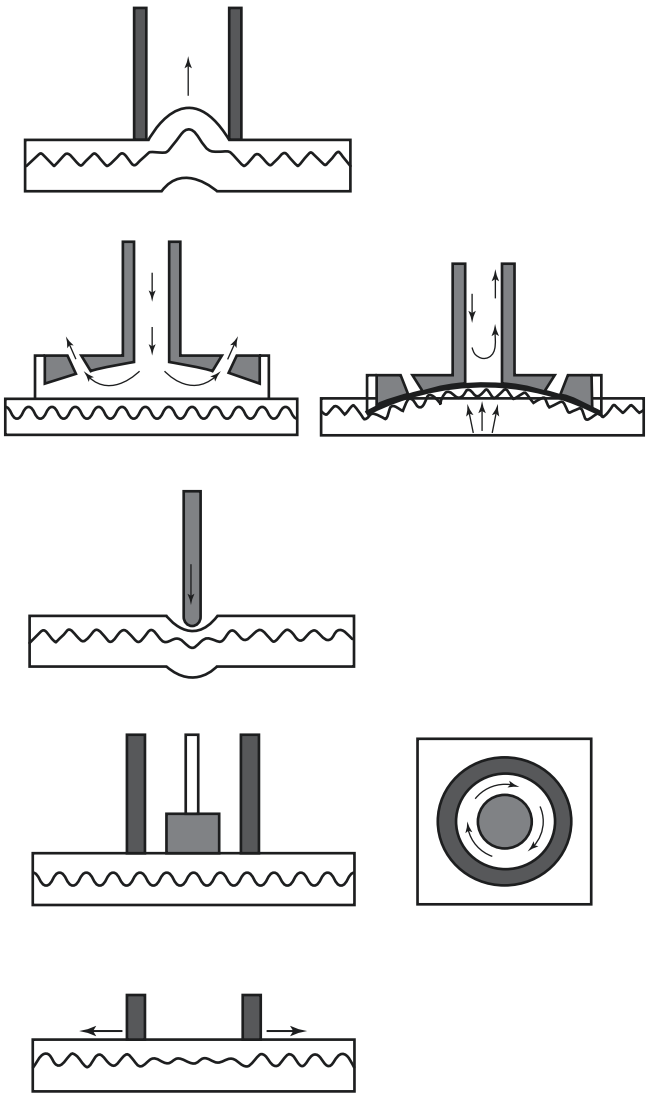


Fig. 5.4 Schematic drawings of the mechanisms based on the type of load on the skin: suction by the Cutometer and DermaLab (*above*), pressure by the Pneumatonometer (*second from above*), pressure by the Durometer (*center*), torsion (*second from below*) by the Dermal Torque Meter, and tension by the Elastometer and Extensometer (*below*). The working mechanism of the Pneumatonometer (*second from above*) is based on air that normally flows through the system (*left panel*).This system is blocked at a certain pressure (*right panel*)

ultimate extension, and stress-strain curves [71]. Tools that measure these mechanical qualities will be discussed by the following four subcategories, which are based on the type of load on the skin: suction, pressure, torsion, and tension. In Fig. 5.4, these types of load are visualized and explained.

5.5 Suction Methods

The most frequently described elasticity measurement tool is the *Cutometer® Skin Elasticity Meter* 474 and 575, with its latest MPA 580 version (Courage and Khazaka Electronic GmbH, Cologne, Germany). During the measurement constant negative pressure is used for a short period, alternated with periods of normal pressure. This pressure is exerted over a small area of the skin, which ranges from 2 mm to 8 mm, depending on the diameter of the probe. The probe with a 6 mm aperture provides the most precise measurements of the dermal elasticity [72]. When the Cutometer was tested on normal skin, reliable results were obtained [73]. In addition, the Cutometer was found to have a good reliability for measurements on both sclerodermal skin [74] and scars [75, 76]. Validity of the Cutometer has been assessed, which showed a weak to moderate correlation with the pliability score of the POSAS [75].

The *DermaLab®* (Cortex Technology, Hadsund, Denmark) [77], which has replaced the Dermaflex® [78–81], measures the stress that is needed to achieve an elevation of the skin of 1.5 mm. Its measuring aperture is 10 mm, which is larger than the aperture of the Cutometer (2–8 mm). Therefore, these devices measure different mechanical qualities of the skin: a smaller measuring aperture (Cutometer) predominantly measures qualities of the epidermis and the superficial dermis, whereas a larger measuring aperture (DermaLab) measures the dermis itself together with the sliding mobility of the junction between dermis and the layer of the subcutaneous fat [73]. Both measurement devices with a small and larger measuring aperture are of relevance in the scar evaluation. However, one should realize that dependent on this measuring aperture different mechanical qualities are measured. The reliability, validity, and feasibility of the DermaLab have been sparsely examined: only one report has shown that the DermaLab measures less accurately than the Dermaflex [77]. Therefore, before applying the DermaLab in the evaluation of scars more clinimetrical research needs to be performed.

5.6 Pressure Methods

Tonometry is a measurement method which was originally developed to determine the intraocular pressure. Later, tonometry was used to quantify firmness and flexibility of skin and scars [82]. It is composed of an air flow system, a built-in sensor, and a membrane that makes contact with the skin surface. When applied to the skin, the amount of pressure that is needed to lock the system is measured. The measurement is displayed on a dial indicator. The *Cicatrometer*, *Pneumatonometer*, *Tissue Tonometer*, and *Durometer* are all tonometers which work by the same measurement technique. The *Cicatrometer* (University of California, San Diego, USA) is the first type of tonometer which has been used to assess burn scars [82]. Subsequently, the *Pneumatonometer* (Medtronic Solan, Jacksonville, USA) was described and assessed on its validity: a moderate correlation with the pliability score of the VSS was shown in the measurement on

burn scars [83]. Later, the *Tissue Tonometer* (Flinders University Biomedical Engineering Department, Adelaide, Australia) was developed, which showed an excellent intra-observer reliability on burn scars [84]. The assessment of its validity showed a moderate correlation with the pliability score of the VSS [84].

The latest version of the Tonometer is called the *Durometer* (Rex Gauge Company Inc., Glenview, USA), which was originally designed to measure the hardness of material. Later, the durometer was used in the assessment of skin hardness in scleroderma [85], lipodermatosclerosis [86], and skin induration in venous diseases [87]. In multiple trials, the Durometer was tested on sclerodermal skin with excellent reliability and good validity [88–90]. However, its reliability and validity for scars have not been investigated yet, but probably would be similar to the reliability and validity that has been found for the Tissue Tonometer and Pneumatonometer. The primary disadvantage of tonometry is that the measurement is influenced by the hardness of the underlying tissue. Therefore, it is less suitable for anatomical locations where bony structures are situated directly under the skin (i.e., the hand, fingers, or face) [85].

5.7 Torsion Methods

The *Dermal Torque Meter* (Dia-stron, Andover, United Kingdom) is a commercially available measurement tool that assesses elasticity via torsional force onto the skin [91–93]. It has a rotating flat disk which is placed in contact with the skin surface. This disk applies a rotational force along the plain of the skin surface. The rotational load is applied by a motor with controllable voltage and allows adjustment of the torque. A ring guard was constructed circumferentially to the disk leaving a strip of skin in between. The Dermal Torque Meter has been applied for the evaluation of normal skin [94] and burn scars [95], but no data on its reliability have been reported. Validity of measurements on normal skin has been evaluated, which showed a poor correlation with the Cutometer measurements [96]. Since reliability is unknown and torsion methods are not transferable to suction techniques, their suitability for scar assessment has yet to be determined.

5.8 Tension Methods

The following measurement tools work by measuring the skin deformation, after tension is exerted in the horizontal plane of the skin. The *Elastometer* (Washington University, St. Louis, USA) is a handheld measurement tool that has been developed for extension evaluation by distracting two loci of skin [97]. It has been used to measure normal skin and hypertrophic burn scars. Another measurement tool which works by the same technique of skin extension is the *Extensometer* (University of Hong Kong, Hong Kong, China) [98]. A known rate of extension is applied to the skin via double-sided adhesive tape on two metal tabs. The skin extension related to the load intensity is displayed in a graph. The Extensometer has been used in the assessment of elasticity of normal skin and hypertrophic scars [99]. Unfortunately, reliability and validity of these type of measurement tools have not been examined.

In conclusion, we advise the Cutometer as the first choice for elasticity measurements, since this measurement tool is feasible and measures reliably, with a reasonable validity. Other possibilities could include Tonometry, which is both reliable and valid for measurements on scars. Unfortunately, Tonometry will be biased by the hardness of structures underneath the skin. Measurement tools that work by torsion and tension methods at present do not have a major role in the scar assessment armamentarium, because minimum requirements (reliability and validity) have not been investigated or have not been met.

5.8.1 Surface Area: Planimetry

The most simple and commonly used method of planimetry is tracing the scar or wound margins. In 1992, Bryant et al. described the *Transparent Acetate Wound Perimeter Tracing* (Labelon Projection Transparencies, Braintree, United Kingdom) [100, 101]. The wound is traced on a transparent grid paper and subsequently the observer counts the number of squares that fall within the tracing and calculates the area. This technique was found to be reliable, valid, and feasible for quick wound assessment [102–104]. Beside tracing a wound or scar, it is also possible to cut out this trace and use the *Weighing Method* (Transparency Film, Scotch 3M, St Paul, USA, and Gram-atic® Balance, Mettler Instrument Corporation, Hightstown, USA) [100], whereby the weight has a linear correlation with the surface area. This method was found to be reliable, but is less practical because the observer first needs to determine the mass/cm^2 and secondly needs a precise weighing scale. Moreover, tracing, cutting out this trace, and weighing could introduce extra variation into the measurements. Overall, cautiousness should be preserved in the tracing technique, since it appeared that the greatest source of error in wound tracings was in the tracings themselves rather than in the determination and calculation of the final wound area [100, 105].

More sophisticated surface area measurements can be done by *Computer Assisted Planimetry*. The wound or scar is traced on any kind of transparent sheet, followed by digitizing this sheet and analyzing the scanned sheet by a computer program. Various computer programs exist to

determine the real area [106–109]. Another example of computer assisted planimetry is tracing on a digital computerized tablet, e.g., a sonic digitizer or Visitrak (Smiths and Nephew, London, United Kingdom), which is a reliable way of area determination. However, these tablets can be very expensive and costs may rise up to several thousand dollars [105, 110]. Validity of computer assisted planimetry has not been reported to date.

Another frequently used and simple method of planimetry is photography. The use of photography has been applied in *Photogrammetry* and *Stereophotogrammetry*. In Photogrammetry, a calibrated grid is projected on the film image. The camera is held on a standard distance from the image of interest. In 1986, Bulstrode et al. found this technique to have an excellent reliability [111]. In 2004, van Zuijlen et al. found planimetry by photography (using a calibrated grid which is projected on the film image) to be valid and reliable, even more reliable than tracing on transparent sheets, except for extremely curved body parts [112]. Because difficulties remain in converting a three-dimensional image into a two-dimensional image, stereophotogrammetry has been developed. Stereophotogrammetry is Photogrammetry, which is extended by the use of two cameras. These cameras generate a more precise reconstruction of the area of interest. Stereophotogrammetry was found to be a reliable and valid measurement tool, which is more accurate than tracing or simple photography [113]. Although this tool measures very accurately, the use in clinical practice is limited because it is expensive, time-consuming and requires specialistic skills [108].

Eventually, in planimetry various more extensive imaging techniques can be used, such as *Ultrasound*, *Computed Tomography*, and *Magnetic Resonance Imaging* [1, 114, 115]. From these images, a three-dimensional computer reconstruction can be generated [115]. However, their applicability is limited by a low feasibility, very high costs, and potential inaccuracy because of movement of the area of interest. In addition, these measuring techniques have not been properly assessed on their reliability and validity.

In surface area measurements, two important problems must be taken into account: the first problem is that the borders of the wound or scar may become unclear, which may cause a broader variation in measured surface area. The second problem is that extremely curved body parts and areas with skin folds may influence the measurements that are done by the use of photography. In 2004 this was demonstrated by Van Zuijlen et al., who found that for extremely curved body parts planimetry by photography was less reliable than the tracing method [112]. Planimetry of circumferential wounds or scars may cause similar problems.

In summary, for surface area measurements we advocate the use of reliable, inexpensive, and uncomplicated methods which are clinically validated and can be applied without limitation.

Overall, we recommend the photographic technique as a standard evaluation method for wounds or scars which are not subjected to curved body parts and skin folds: digitized measurements show better results than manual tracing, because the greatest measurement errors lie in the manual tracing done by the observers [100, 105]. However, for extremely curved body parts, large surface areas, and locations, which are difficult to measure, the most feasible and advocated method would remain the manual tracing method, either on metric paper or on transparent sheets.

Table 5.2 gives an overview of the abovementioned scar assessment tools.

Table 5.2 An overview of scar assessment tools and their relevant clinimetrical parameters

	Inter-observer reliability normal skin	Inter-observer reliability scars	Validity scars	Price[a]	Clinical application
Color					
DermaSpectrometer	Redness: CV < 22% Pigmentation: CV < 4% [36]	Redness: 1 obs: 0.72; 4 obs: 0.91 Pigmentation: 1 obs: 0.94; 4 obs: 0.98	Redness: 0.50[b] Pigmentation: 0.32[b] [31]	Not commercially available anymore	[116, 117] No scars
Labscan XE	Redness: 0.92 Pigmentation: 0.95–0.96 [32]	Redness: 0.50 Pigmentation: 0.88–0.99 [43]	Redness: 0 .72 with VSS Pigmentation: 0.50–0.83[b] with VSS [43]	$26,455	–
Mexameter	Redness: 0.97 Pigmentation: 0.99 [39]	Redness: 0.82–0.97 Pigmentation: 0.95–0.98 [39]	Redness: 0.52–0.65[b] with VSS [39] Pigmentation: 0.37–0.50[b] with VSS [39]	$14,205	[118–121] No scars
Minolta Chromameter CR-200	Redness: CV < 10% Pigmentation: CV < 1% [36]	Redness: 1 obs: 0.75; 4 obs: 0.92 Pigmentation: 1 obs: 0.73–0.89; 4 obs: 0.91–0.97	Redness: 0.42[b] with POSAS [31] Pigmentation: 0.23–0.24[b] with POSAS [31]	Not commercially available anymore	[44, 117]

Table 5.2 (continued)

	Inter-observer reliability normal skin	Inter-observer reliability scars	Validity scars	Price[a]	Clinical application
Minolta Chromameter CR-300	Redness: 1 obs: 0.92 Pigmentation: 1 obs: 0.97–0.99 [29]	–	–	Not commercially available anymore	[29, 122]
Thickness					
Dermascan C	0.85 [39]	0.89–0.91 [39]	0.41–0.50[b] with height score VSS [39]	$ > 41,775	[123]
TUPS	–	0.84 [46]	0.34[c] with height score VSS [46] 0.42[c] with total score VSS [46]	$16,480	[43, 124]
Vivid 910 (volume)	–	–	0.63[c] with total score MSS [48]	$67,950	[125] No scars
Relief					
Mechanical Profilometry	CV < 0.5% [56]	–	–	Unknown	[50] No scars
Optical Profilometry	CV < 3% [61]	–	–	Unknown	–
Laser Profilometry	–	–	–	Unknown	[63] No scars
Transparency Profilometry	Normal skin not assessed metal plates: CV < 10% [64]	–	–	Visiometer: $16,480	[65, 123] No scars
Interferometry	CV < 4% [68]	–	–	$111,435	[126, 127] No scars
PRIMOS	0.74 [70]	0.82 [70]	0.53–0.70[c] with relief score POSAS [70]	$42,320	[69, 128]
Elasticity					
Cutometer	1 obs: 0.75–0.85; 4 obs: 0.93–0.96 [75]	1 obs: 0.35–0.76; 4 obs: 0.68–0.93 [75]	0.29–0.53[b] with pliability score POSAS [75]	$5575	[129, 130]
Dermaflex	CV: 60.7–23.2%	–	0.38–0.44[c] with DermaLab [77]	Not commercially available anymore	[77, 131] No scars
DermaLab	CV: 44.4–57.8%	–	0.38–0.44[c] with Dermaflex [77]	$6440	–
Tonometry	0.82–0.91 [89]	Sclerodermal skin: 0.95 [132]	0.57[d] with VSS [83] 0.442–0.457[c] with VSS [84]	$405–820	[37, 83–85, 132]
Dermal torque meter	–	–	Poor[d] with Cutometer [96]	$14,690	[95, 96]
Elastometer	–	–	–	Not commercially available anymore	[97]
Extensometer	–	–	–	Not commercially available anymore	[99]
Surface area					
Transparent acetate wound perimeter tracing	0.48–0.88 [112]	–	Good[d] [112]	$ < 5	[104, 133, 134] No scars
Weighing method	–	–	–	$1680–6800	[100] No scars
Computer assisted planimetry	–	–	–	Visitrak: Not commercially available anymore	[133, 135, 136] No scars
Photogrammetry	0.72–0.93 [112]	–	Good[d] [112]	Unknown	[37] No scars
Stereophotogrammetry	–	0.98[c] [113] (wounds)	–	Unknown	[108] No scars

Obs observer, *CV* coefficient of variation in % ((Highest value − Lowest value)/Lowest value) × 100
[a]Prices based on the exchange rate of April 2010
[b]Spearman's rho correlation coefficient
[c]Pearson's correlation coefficient
[d]Correlation coefficient unknown

5.9 Conclusion

In the future decades, the role of reliable and valid scar assessment tools will become more prominent. In this chapter, several measurement tools that may be considered for scar assessment are described.

In general, objective scar measurements are preferred over subjective scar assessment scales. However, subjective scar assessment scales performed by observers have several advantages. They are convenient, cheap, and give semi-quantitative information along several clinical parameters. Moreover, they can be performed in outpatient clinics, as they require little time to complete. On the other hand, several available assessment scales require more than one observer to obtain good reliability and to reduce the measuring error of a single observer.

It is debatable whether evaluation of all scar features (color, thickness, relief, pliability, and surface area) is necessary for a complete scar assessment scale. However, only after many years of experience with a certain scar assessment scale such lists may be shortened, because the relevance of parameters first needs to be evaluated for different scar categories in different patient groups.

Measuring devices provide objective parameters and make errors that are usually consistent and predictable. The best scar measuring devices in terms of reliability and validity are yet to be determined for many of the parameters that bear importance for research goals.

Furthermore, it should be taken into account whether the measurement tool can be used in a clinical setting, where the time element is highly important and anyone should be able to perform the measurement, or on the other hand, in a research setting, where more time is available and more specialized observers carry out the measurements.

In this chapter, we systematically discussed methods to access scar formation that are considered relevant to research involving scars. Surprisingly, only few scar assessment tools have been studied sufficiently. Of course, there is no need to perform the entire array of clinical analyses in a single study. The aim of a study must dictate the methodology and the preferred methods of evaluation.

References

1. Powers PS, Sarkar S, Goldgof DB, Cruse CW, Tsap LV. Scar assessment: current problems and future solutions. J Burn Care Rehabil. 1999;20(1 Pt 1):54–60.. discussion 53
2. Van Loey NE, Bremer M, Faber AW, Middelkoop E, Nieuwenhuis MK. Itching following burns: epidemiology and predictors. Br J Dermatol. 2008;158(1):95–100.
3. Bock O, Schmid-Ott G, Malewski P, Mrowietz U. Quality of life of patients with keloid and hypertrophic scarring. Arch Dermatol Res. 2006;297(10):433–8.
4. Peacock EE Jr, Madden JW, Trier WC. Biologic basis for the treatment of keloids and hypertrophic scars. South Med J. 1970;63(7):755–60.
5. Brissett AE, Sherris DA. Scar contractures, hypertrophic scars, and keloids. Facial Plast Surg. 2001;17(4):263–72.
6. Draaijers LJ, Tempelman FR, Botman YA, Tuinebreijer WE, Middelkoop E, Kreis RW, van Zuijlen PP. The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation. Plast Reconstr Surg. 2004;113(7):1960–5; discussion 1966–7.
7. Herd AN, Hall PN, Widdowson P, Tanner NS. Mesh grafts—an 18 month follow-up. Burns Incl Therm Inj. 1987;13(1):57–61.
8. Ferguson MW, Whitby DJ, Shah M, Armstrong J, Siebert JW, Longaker MT. Scar formation: the spectral nature of fetal and adult wound repair. Plast Reconstr Surg. 1996;97(4):854–60.
9. Streiner DL, Norman GR. Reliability. In: Health measurement scales. 4th ed. Oxford: Oxford University Press; 2008. p. 167–210.
10. Nunnaly JC. Psychometric theory. 2nd ed. New York: McGraw-Hill; 1978.
11. Streiner DL, Norman GR. Validity. In: Health measurement scales. 4th ed. Oxford: Oxford University Press; 2008. p. 247–76.
12. Andresen EM. Criteria for assessing the tools of disability outcomes research. Arch Phys Med Rehabil. 2000;81(12 Suppl 2):S15–20.
13. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159–74.
14. Smith GM, Tompkins DM, Bigelow ME, Antoon AY. Burn-induced cosmetic disfigurement: can it be measured reliably? J Burn Care Rehabil. 1988;9(4):371–5.
15. Sullivan T, Smith J, Kermode J, McIver E, Courtemanche DJ. Rating the burn scar. J Burn Care Rehabil. 1990;11(3):256–60.
16. Baryza MJ, Baryza GA. The Vancouver scar scale: an administration tool and its interrater reliability. J Burn Care Rehabil. 1995;16(5):535–8.
17. Beausang E, Floyd H, Dunn KW, Orton CI, Ferguson MW. A new quantitative scale for clinical scar assessment. Plast Reconstr Surg. 1998;102(6):1954–61.
18. Yeong EK, Mann R, Engrav LH, Goldberg M, Cain V, Costa B, Moore M, Nakamura D, Lee J. Improved burn scar assessment with use of a new scar-rating scale. J Burn Care Rehabil. 1997;18(4):353–5.. discussion 352
19. Crowe JM, Simpson K, Johnson W, Allen J. Reliability of photographic analysis in determining change in scar appearance. J Burn Care Rehabil. 1998;19(2):183–6.
20. van de Kar AL, Corion LU, Smeulders MJ, Draaijers LJ, van der Horst CM, van Zuijlen PP. Reliable and feasible evaluation of linear scars by the patient and observer scar assessment scale. Plast Reconstr Surg. 2005;116(2):514–22.
21. Masters M, McMahon M, Svens B. Reliability testing of a new scar assessment tool, matching assessment of scars and photographs (MAPS). J Burn Care Rehabil. 2005;26(3):273–84.
22. Nedelec B, Shankowsky HA, Tredget EE. Rating the resolving hypertrophic scar: comparison of the Vancouver scar scale and scar volume. J Burn Care Rehabil. 2000;21(3):205–12.
23. Truong PT, Lee JC, Soer B, Gaul CA, Olivotto IA. Reliability and validity testing of the patient and observer scar assessment scale in evaluating linear scars after breast cancer surgery. Plast Reconstr Surg. 2007;119(2):487–94.
24. Weatherall IL, Coombs BD. Skin color measurements in terms of CIELAB color space values. J Invest Dermatol. 1992;99(4):468–73.
25. Westerhof W. CIE colorimetry. In: Serup J, Jemec E, editors. Handbook of non-invasive methods and the skin. Boca Raton, FL: Taylor and Francis; 1995.
26. Guarrera M, Brusati C, Rebora A. Topical metronidazole does not abate UVB-induced erythema. Dermatology. 2001;203(2):121–3.

27. Ngo K, Goldstein D, Neligan P, Gilbert R. Colorimetric evaluation of facial skin and free flap donor sites in various ethnic populations. J Otolaryngol. 2006;35(4):249–54.
28. Swope VB, Supp AP, Cornelius JR, Babcock GF, Boyce ST. Regulation of pigmentation in cultured skin substitutes by cytometric sorting of melanocytes and keratinocytes. J Invest Dermatol. 1997;109(3):289–95.
29. Van den Kerckhove E, Stappaerts K, Fieuws S, Laperre J, Massage P, Flour M, Boeckx W. The assessment of erythema and thickness on burn related scars during pressure garment therapy as a preventive measure for hypertrophic scarring. Burns. 2005;31(6):696–702.
30. Van den Kerckhove E, Staes F, Flour M, Stappaerts K, Boeckx W. Reproducibility of repeated measurements on healthy skin with Minolta Chromameter CR-300. Skin Res Technol. 2001;7(1):56–9.
31. Draaijers LJ, Tempelman FR, Botman YA, Kreis RW, Middelkoop E, van Zuijlen PP. Colour evaluation in scars: tristimulus colorimeter, narrow-band simple reflectance meter or subjective evaluation? Burns. 2004;30(2):103–7.
32. Li-Tsang CW, Lau JC, Liu SK. Validation of an objective scar pigmentation measurement by using a spectrocolorimeter. Burns. 2003;29(8):779–84.
33. Diffey BL, Oliver RJ, Farr PM. A portable instrument for quantifying erythema induced by ultraviolet radiation. Br J Dermatol. 1984;111(6):663–72.
34. Diffey BL, Farr PM, Oakley AM. Quantitative studies on UVA-induced erythema in human skin. Br J Dermatol. 1987;117(1):57–66.
35. Farr PM, Diffey BL. Quantitative studies on cutaneous erythema induced by ultraviolet radiation. Br J Dermatol. 1984;111(6):673–82.
36. Clarys P, Alewaeters K, Lambrecht R, Barel AO. Skin color measurements: comparison between three instruments: the Chromameter(R), the DermaSpectrometer(R) and the Mexameter(R). Skin Res Technol. 2000;6(4):230–8.
37. Oliveira GV, Chinkes D, Mitchell C, Oliveras G, Hawkins HK, Herndon DN. Objective assessment of burn scar vascularity, erythema, pliability, thickness, and planimetry. Dermatol Surg. 2005;31(1):48–58.
38. Nedelec B, Correa JA, Rachelska G, Armour A, LaSalle L. Quantitative measurement of hypertrophic scar: interrater reliability and concurrent validity. J Burn Care Res. 2008;29(3):501–11.
39. Nedelec B, Correa JA, Rachelska G, Armour A, LaSalle L. Quantitative measurement of hypertrophic scar: intrarater reliability, sensitivity, and specificity. J Burn Care Res. 2008;29(3):489–500.
40. Shriver MD, Parra EJ. Comparison of narrow-band reflectance spectroscopy and tristimulus colorimetry for measurements of skin and hair color in persons of different biological ancestry. Am J Phys Anthropol. 2000;112(1):17–27.
41. Alexander H, Miller DL. Determining skin thickness with pulsed ultra sound. J Invest Dermatol. 1979;72(1):17–9.
42. Tan CY, Statham B, Marks R, Payne PA. Skin thickness measurement by pulsed ultrasound: its reproducibility, validation and variability. Br J Dermatol. 1982;106(6):657–67.
43. Li-Tsang CW, Lau JC, Chan CC. Prevalence of hypertrophic scar formation and its characteristics among the Chinese population. Burns. 2005;31(5):610–6.
44. Niessen FB, Spauwen PH, Robinson PH, Fidler V, Kon M. The use of silicone occlusive sheeting (Sil-K) and silicone occlusive gel (Epiderm) in the prevention of hypertrophic scar formation. Plast Reconstr Surg. 1998;102(6):1962–72.
45. Wang GQ, Xia ZF. Transplantation of epidermis of scar tissue on acellular dermal matrix. Burns. 2009;35(3):352–5.
46. Lau JC, Li-Tsang CW, Zheng YP. Application of tissue ultrasound palpation system (TUPS) in objective scar evaluation. Burns. 2005;31(4):445–52.
47. Du YC, Lin CM, Chen YF, Chen CL, Chen T. Implementation of a burn scar assessment system by ultrasound techniques. Conf Proc IEEE Eng Med Biol Soc. 2006;1:2328–31.
48. Taylor B, McGrouther DA, Bayat A. Use of a non-contact 3D digitiser to measure the volume of keloid scars: a useful tool for scar assessment. J Plast Reconstr Aesthet Surg. 2007;60(1):87–94.
49. Richard S, Querleux B, Bittoun J, Jolivet O, Idy-Peretti I, de Lacharriere O, Leveque JL. Characterization of the skin in vivo by high resolution magnetic resonance imaging: water behavior and age-related effects. J Invest Dermatol. 1993;100(5):705–9.
50. Barbenel JC, Makki S, Agache P. The variability of skin surface contours. Ann Biomed Eng. 1980;8(2):175–82.
51. Hatzis J. The wrinkle and its measurement-a skin surface profilometric method. Micron. 2004;35(3):201–19.
52. Makki S, Barbenel JC, Agache P. A quantitative method for the assessment of the microtopography of human skin. Acta Derm Venereol. 1979;59(4):285–91.
53. Sampson J. A method of replicating dry or moist surfaces for examination by light microscopy. Nature. 1961;191:932–3.
54. Sarkany I. A method for studying the microtopography of the skin. Br J Dermatol. 1962;74:254–9.
55. Leveque JL. EEMCO guidance for the assessment of skin topography. The European expert group on efficacy measurement of cosmetics and other topical products. J Eur Acad Dermatol Venereol. 1999;12(2):103–14.
56. Kautzky F, Dahm MW, Drosner M, Köhler LD. Direct profilometry of the skin: its reproducibility and variability. J Eur Acad Dermatol Venereol. 1995;5:15–23.
57. Linde YW, Bengtsson A, Loden M. 'Dry' skin in atopic dermatitis. II. A surface profilometry study. Acta Derm Venereol. 1989;69(4):315–9.
58. Tronnier H, Heinrich U. Untersuchungen zur Messung der Hautoberfläche. Hautnah Derm. 1991;6:80–6.
59. Corcuff P, De Rigal J, Leveque JL. Image analysis of the cutaneous relief. Bioeng Skin Newslett. 1982;4:16.
60. Serup J, Keiding J, Fullerton A, Gnidecka M, Gnidecki R. High-frequency ultrasound examination of skin: introduction and guide. In: Serup J, Jemec GBE, editors. Handbook of non-invasive methods and the skin. Boca Raton, FL: CRC Press; 1995. p. 239–56.
61. Fischer TW, Wigger-Alberti W, Elsner P. Direct and non-direct measurement techniques for analysis of skin surface topography. Skin Pharmacol Appl Skin Physiol. 1999;12(1–2):1–11.
62. Muller U. Roughness (measured by profilometry: mechanical, optical and laser). In: Berardesca E, Elsner P, Wilhelm KP, Maibach HI, editors. Bioengineering of the skin: methods and instrumentation. Boca Raton: CRC Press; 1995. p. 97.
63. Saur R, Schramm U, Steinhoff R, Wolff HH. Structure analysis of the skin surface using computer-assisted laser profilometry. New method for the quantitative assessment of roughness structure of the skin. Hautarzt. 1991;42(8):499–506.
64. De Paepe K, Lagarde JM, Gall Y, Roseeuw D, Rogiers V. Microrelief of the skin using a light transmission method. Arch Dermatol Res. 2000;292(10):500–10.
65. Fluhr JW, Gehring W, Gloor M. Analyse der Hautrauhigkeit bei Personen unterschiedlicher Alters-gruppen mit dem Visiometer. Akt Dermatol. 1995;21:151–6.
66. Fluhr JW, Bettinger J, Gloor M. Skin Visiometer SV 400 zur Hautrauhigkeitsmessung: EDV-gestutzte Transmissions-Profilometrie. Kosmet Med. 1996;18:42–7.
67. Altmeyer P, Erbler H, Kromer T, Duwe HP, Hoffmann K. Interferometry: a new method for no-touch measurement of the surface and volume of ulcerous skin lesions. Acta Derm Venereol. 1995;75(3):193–7.
68. Lagarde JM, Rouvrais C, Black D, Diridollou S, Gall Y. Skin topography measurement by interference fringe projection: a technical validation. Skin Res Technol. 2001;7(2):112–21.
69. Friedman PM, Skover GR, Payonk G, Kauvar AN, Geronemus RG. 3D in-vivo optical skin imaging for topographical quantitative assessment of non-ablative laser technology. Dermatol Surg. 2002;28(3):199–204.

70. Bloemen MCT, van Gerven MS, van der Wal MBA, Verhaegen PDHM, Middelkoop E. An objective measuring device for surface roughness in skin and scars. J Am Acad Dermatol. 2010;64(4):706–15.
71. Vogel HG. Mechanical measurements of skin. Acta Derm Venereol. 1994;185:39–43.
72. Barel AO, Courage W, Clarys P. Suction method for measurement of skin mechanical properties: the Cutometer®. Handbook of non-invasive methods and the skin. Boca Raton, FL: CRC Press Inc; 1995. p. 335–40.
73. Pierard GE, Nikkels-Tassoudji N, Pierard-Franchimont C. Influence of the test area on the mechanical properties of skin. Dermatology. 1995;191(1):9–15.
74. Enomoto DN, Mekkes JR, Bossuyt PM, Hoekzema R, Bos JD. Quantification of cutaneous sclerosis with a skin elasticity meter in patients with generalized scleroderma. J Am Acad Dermatol. 1996;35(3 Pt 1):381–7.
75. Draaijers LJ, Botman YA, Tempelman FR, Kreis RW, Middelkoop E, van Zuijlen PP. Skin elasticity meter or subjective evaluation in scars: a reliability assessment. Burns. 2004;30(2):109–14.
76. Fong SS, Hung LK, Cheng JC. The cutometer and ultrasonography in the assessment of postburn hypertrophic scar – a preliminary study. Burns. 1997;23(Suppl 1):S12–8.
77. Pedersen LK, Hansen B, Jemec GBE. Mechanical properties of the skin: a comparison between two suction cup methods. Skin Res Technol. 2003;9:111–5.
78. Elsner P, Wilhelm D, Maibach HI. Mechanical properties of human forearm and vulvar skin. Br J Dermatol. 1990;122(5):607–14.
79. Pedersen LK, Jemec GB. Plasticising effect of water and glycerin on human skin in vivo. J Dermatol Sci. 1999;19(1):48–52.
80. Serup J, Northeved A. Skin elasticity in localized scleroderma (morphoea). Introduction of a biaxial in vivo method for measurement of tensile distensibility, hysteresis, and resilient distension of diseased and normal skin. J Dermatol. 1985;12(1):52–62.
81. Serup J, Northeved A. Skin elasticity in psoriasis. In vivo measurement of tensile distensibility, hysteresis and resilient distension with a new method. Comparison with skin thickness as measured with high-frequency ultrasound. J Dermatol. 1985;12(4):318–24.
82. Katz SM, Frank DH, Leopold GR, Wachtel TL. Objective measurement of hypertrophic burn scar: a preliminary study of tonometry and ultrasonography. Ann Plast Surg. 1985;14(2):121–7.
83. Spann K, Mileski WJ, Atiles L, Purdue G, Hunt J. The 1996 clinical research award. Use of a pneumatonometer in burn scar assessment. J Burn Care Rehabil. 1996;17(6 Pt 1):515–7.
84. Lye I, Edgar DW, Wood FM, Carroll S. Tissue tonometry is a simple, objective measure for pliability of burn scar: is it reliable? J Burn Care Res. 2006;27(1):82–5.
85. Falanga V, Bucalo B. Use of a durometer to assess skin hardness. J Am Acad Dermatol. 1993;29(1):47–51.
86. Romanelli M, Falanga V. Use of a durometer to measure the degree of skin induration in lipodermatosclerosis. J Am Acad Dermatol. 1995;32(2 Pt 1):188–91.
87. LeBlanc N, Falabella A, Murata H, Hasan A, Weiss E, Falanga V. Durometer measurements of skin induration in venous disease. Dermatol Surg. 1997;23(4):285–7.
88. Kissin EY, Schiller AM, Gelbard RB, Anderson JJ, Falanga V, Simms RW, Korn JH, Merkel PA. Durometry for the assessment of skin disease in systemic sclerosis. Arthritis Rheum. 2006;55(4):603–9.
89. Merkel PA, Silliman NP, Denton CP, Furst DE, Khanna D, Emery P, Hsu VM, Streisand JB, Polisson RP, Akesson A, Coppock J, van den Hoogen F, Herrick A, Mayes MD, Veale D, Seibold JR, Black CM, Korn JH. Validity, reliability, and feasibility of durometer measurements of scleroderma skin disease in a multicenter treatment trial. Arthritis Rheum. 2008;59(5):699–705.
90. Seyger MM, van den Hoogen FH, de Boo T, de Jong EM. Reliability of two methods to assess morphea: skin scoring and the use of a durometer. J Am Acad Dermatol. 1997;37(5 Pt 1):793–6.
91. Barbenel JC, Evans JH. The time-dependent mechanical properties of skin. J Invest Dermatol. 1977;69(3):318–20.
92. Finlay B. Dynamic mechanical testing of human skin 'in vivo'. J Biomech. 1970;3(6):557–68.
93. Finlay B. The torsional characteristics of human skin in vivo. Biomed Eng. 1971;6(12):567–73.
94. Leveque JL, de Rigal J, Agache PG, Monneur C. Influence of ageing on the in vivo extensibility of human skin at a low stress. Arch Dermatol Res. 1980;269(2):127–35.
95. Boyce ST, Supp AP, Wickett RR, Hoath SB, Warden GD. Assessment with the dermal torque meter of skin pliability after treatment of burns with cultured skin substitutes. J Burn Care Rehabil. 2000;21(1 Pt 1):55–63.
96. Murray BC, Wickett RR. Correlations between dermal torque meter, cutometer, and dermal phase meter measurements of human skin. Skin Res Technol. 1997;3:101–6.
97. Bartell TH, Monafo WW, Mustoe TA. A new instrument for serial measurements of elasticity in hypertrophic scar. J Burn Care Rehabil. 1988;9(6):657–60.
98. Stark HL. Directional variations in the extensibility of human skin. Br J Plast Surg. 1977;30(2):105–14.
99. Clark JA, Cheng JC, Leung KS. Mechanical properties of normal skin and hypertrophic scars. Burns. 1996;22(6):443–6.
100. Bohannon RW, Pfaller BA. Documentation of wound surface area from tracings of wound perimeters. Clinical report on three techniques. Phys Ther. 1983;63(10):1622–4.
101. Bryant RA. Acute and chronic wounds: nursing management CV. St. Louis, MO: Mosby; 1992.
102. Ferrell BA, Artinian BM, Sessing D. The Sessing scale for assessment of pressure ulcer healing. J Am Geriatr Soc. 1995;43(1):37–40.
103. Liskay AM, Mion LC, Davis BR. Comparison of two devices for wound measurement. Dermatol Nurs. 1993;5(6):434–41.
104. Thomas AC, Wysocki AB. The healing wound: a comparison of three clinically useful methods of measurement. Decubitus. 1990;3(1):18–25.
105. Wysocki AB. Wound measurement. Int J Dermatol. 1996;35(2):82–91.
106. Anthony D, Barnes E. Pressure sores. One measuring pressure sores accurately. Nurs Times. 1984;80(36):33–5.
107. Cutler NR, George R, Seifert RD, Brunelle R, Sramek JJ, McNeill K, Boyd WM. Comparison of quantitative methodologies to define chronic pressure ulcer measurements. Decubitus. 1993;6(6):22–30.
108. Johnson M, Miller R. Measuring healing in leg ulcers: practice considerations. Appl Nurs Res. 1996;9(4):204–8.
109. Kim NH, Wysocki AB, Bovik AC, Diller KR. A microcomputer-based vision system for area measurement. Comput Biol Med. 1987;17(3):173–83.
110. Coleridge Smith PD, Scurr JH. Direct method of measuring venous ulcers. Br J Surg. 1989;76(7):689.
111. Bulstrode CJ, Goode AW, Scott PJ. Stereophotogrammetry for measuring rates of cutaneous healing: a comparison with conventional techniques. Clin Sci (Lond). 1986;71(4):437–43.
112. van Zuijlen PP, Angeles AP, Suijker MH, Kreis RW, Middelkoop E. Reliability and accuracy of techniques for surface area measurements of wounds and scars. Int J Low Extrem Wounds. 2004;3(1):7–11.
113. Frantz RA, Johnson DA. Stereophotography and computerized image analysis: a three-dimensional method of measuring wound healing. Wounds. 1992;4:58–64.

114. Hendrix RW, Calenoff L, Lederman RB, Nieman HL. Radiology of pressure sores. Radiology. 1981;138(2):351–6.
115. Wood FM, Currie K, Backman B, Cena B. Current difficulties and the possible future directions in scar assessment. Burns. 1996;22(6):455–8.
116. Groth L, Serup J. Cutaneous microdialysis in man: effects of needle insertion trauma and anaesthesia on skin perfusion, erythema and skin thickness. Acta Derm Venereol. 1998;78(1):5–9.
117. Takiwaki H, Overgaard L, Serup J. Comparison of narrow-band reflectance spectrophotometric and tristimulus colorimetric measurements of skin color. Twenty-three anatomical sites evaluated by the Dermaspectrometer and the Chroma meter CR-200. Skin Pharmacol. 1994;7(4):217–25.
118. Levy JL, Pons F, Agopian L, Besson R. A double-blind controlled study of a nonhydroquinone bleaching cream in the treatment of melasma. J Cosmet Dermatol. 2005;4(4):272–6.
119. Li YH, Chen JZ, Wei HC, Wu Y, Liu M, Xu YY, Dong GH, Chen HD. Efficacy and safety of intense pulsed light in treatment of melasma in Chinese patients. Dermatol Surg. 2008;34(5):693–700; discussion 700–691.
120. Moon SJ, Kim DK, Chang JH, Kim CH, Kim HW, Park SY, Han SH, Lee JE, Yoo TH, Han DS, Kang SW. The impact of dialysis modality on skin hyperpigmentation in haemodialysis patients. Nephrol Dial Transplant. 2009;24(9):2803–9.
121. Pierard-Franchimont C, Pierard GE. A double-blind placebo-controlled study of ketoconazole + desonide gel combination in the treatment of facial seborrheic dermatitis. Dermatology. 2002;204(4):344–7.
122. Kim MS, Rodney WN, Cooper T, Kite C, Reece GP, Markey MK. Towards quantifying the aesthetic outcomes of breast cancer treatment: comparison of clinical photography and colorimetry. J Eval Clin Pract. 2009;15(1):20–31.
123. Lee HK, Seo YK, Baek JH, Koh JS. Comparison between ultrasonography (Dermascan C version 3) and transparency profilometry (skin Visiometer SV600). Skin Res Technol. 2008;14(1):8–12.
124. Li-Tsang CW, Lau JC, Choi J, Chan CC, Jianan L. A prospective randomized clinical trial to investigate the effect of silicone gel sheeting (Cica-care) on post-traumatic hypertrophic scar among the Chinese population. Burns. 2006;32(6):678–83.
125. Kau CH, Cronin A, Durning P, Zhurov AI, Sandham A, Richmond S. A new method for the 3D measurement of postoperative swelling following orthognathic surgery. Orthod Craniofac Res. 2006;9(1):31–7.
126. Lagarde JM, Rouvrais C, Black D. Topography and anisotropy of the skin surface with ageing. Skin Res Technol. 2005;11(2):110–9.
127. Li L, Mac-Mary S, Marsaut D, Sainthillier JM, Nouveau S, Gharbi T, de Lacharriere O, Humbert P. Age-related changes in skin topography and microcirculation. Arch Dermatol Res. 2006;297(9):412–6.
128. Jacobi U, Chen M, Frankowski G, Sinkgraven R, Hund M, Rzany B, Sterry W, Lademann J. In vivo determination of skin surface topography using an optical 3D device. Skin Res Technol. 2004;10(4):207–14.
129. Cua AB, Wilhelm KP, Maibach HI. Elastic properties of human skin: relation to age, sex, and anatomical region. Arch Dermatol Res. 1990;282(5):283–8.
130. Vloemans AF, Soesman AM, Suijker M, Kreis RW, Middelkoop E. A randomised clinical trial comparing a hydrocolloid-derived dressing and glycerol preserved allograft skin in the management of partial thickness burns. Burns. 2003;29(7):702–10.
131. Pedersen L, Jemec GB. Mechanical properties and barrier function of healthy human skin. Acta Derm Venereol. 2006;86(4):308–11.
132. Corica GF, Wigger NC, Edgar DW, Wood FM, Carroll S. Objective measurement of scarring by multiple assessors: is the tissue tonometer a reliable option? J Burn Care Res. 2006;27(4):520–3.
133. Lagan KM, Dusoir AE, McDonough SM, Baxter GD. Wound measurement: the comparative reliability of direct versus photographic tracings analyzed by planimetry versus digitizing techniques. Arch Phys Med Rehabil. 2000;81(8):1110–6.
134. Langemo DK, Melland H, Hanson D, Olson B, Hunter S, Henly SJ. Two-dimensional wound measurement: comparison of 4 techniques. Adv Wound Care. 1998;11(7):337–43.
135. Gethin G, Cowman S. Wound measurement comparing the use of acetate tracings and Visitrak digital planimetry. J Clin Nurs. 2006;15(4):422–7.
136. Sugama J, Matsui Y, Sanada H, Konya C, Okuwa M, Kitagawa A. A study of the efficiency and convenience of an advanced portable wound measurement system (VISITRAK). J Clin Nurs. 2007;16(7):1265–9.

Burn Scar Treatment

6

Luc Teot, Sami Otman, Antonio Brancati, and Rainer Mittermayr

6.1 Physiological Scarring

Scar formation is considered as an integrative part of the complex and dynamic process of normal physiological wound healing to restore skin integrity following injury and is referred to as the maturation phase. This phase is dominated by fibroblasts. The pivotal feature of this process is the synthesis, deposition, and remodeling of collagen, the major structural substance of connective tissue. The collagen deposition in normal wound healing peaks by the third week after injury. Collagen remodeling is characterized by a (balanced) continuous synthesis and degradation of collagen and is observed already early during the wound healing process. The degradation of wound collagen is controlled by a variety of enzymes such as collagenases (e.g., MMP-1) derived from granulocytes, macrophages, keratinocytes, and fibroblasts. On the other hand, the expression and activity of collagenases is tightly controlled by cytokines.

Wound contraction is a further inherent part of wound healing and is presented by an ongoing process resulting in part from the proliferation of a specialized fibroblast population termed as myofibroblasts containing myofilaments (α-SMA, desmin).

Overall, it has to be mentioned that scar tissue is never as strong as normal, uninjured skin. For the first 3–4 weeks after injury, the wound can easily be re-opened by minimal trauma. After 6 weeks, the scar has attained approximately half of its final strength. During the next 12 months, the scar gradually increases its ability to withstand injury, but it never attains normal strength (for review, see [1]).

6.2 Pathological Scarring

In some individuals, however, and particularly in burn victims, some of the wound healing processes may lead to production of overabundant extracellular matrix, resulting in abnormal scar formation, which is of altered composition (e.g., misbalanced collagen I/III ratio) and organization (e.g., nonlinear oriented collagen bundles). Causative factors which are implicated in pathological scar formation are a prolonged and subsequently dysregulated inflammatory phase, a misbalance between pro- and anti-fibrogenic factors, and the involvement of specific cell subpopulations.

Especially extended and deep wounds eliciting systemic responses, features of severe burn wounds, are prone to develop pathological scarring. While superficial burn wounds heal in a normal timely manner resulting in minimal scarring, deeper burns often result in pathological (hypertrophic) scarring necessitating further intervention. This is due to the fact that the majority of epidermal and dermal regenerative structures such as basal membrane, appendices, and hair follicles are destroyed and healing can only occur from the wound edges, thus prolonging phases of wound healing. It was clinically shown that wounds which are not healed within a 3 weeks period have a high risk potential of hypertrophic scarring, independent of age, site, and genetic predisposition [2]. Additionally, dermal fibroblasts were found to exhibit similar characteristics as fibroblasts cultured from hypertrophic scars, expressing higher TGF-β1, CTGF (connective tissue growth factor), and α-SMA levels [3–5].

Following the (thermal) impact the initial formed fibrin matrix serves as a scaffold for migrating cells. However, inadequate fibrin removal due to suppressed fibrinolysis controlled by the activity tissue plasminogen inhibitor-1 (is upregulated by TGF-β1 and downregulated TGF-β3) impedes healing and might lead to fibrosis [6, 7]. Burns but also infected wounds (burn wounds are at high risk for infections) exaggerate especially the inflammatory phase, thus leading to a misbalance in favor of a pro-fibrogenic status.

L. Teot (✉) · S. Otman · A. Brancati · R. Mittermayr
Burns Unit, Wound Healing Unit, Lapeyronie Hospital, Montpellier University Hospital, Montpellier Cedex, France

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_6

Potential cytokines which are discussed in this context are PDGF, TGF-β, IGF-1, and IL-4.

PDGF is a degranulation product of platelets early during wound healing and is elevated in hypertrophic scar tissue. It has been shown as a potent promoter of fibroblast proliferation, extracellular matrix production, and the induction of the myofibroblast phenotype [1].

TGF-β is a cytokine well characterized as a fibrogenic factor and exists in three isoforms (TGF-β1–3). Following burn injury, TGF-β1 and 2 stimulate their own synthesis in an autocrine fashion and attract neutrophils, monocytes as well as fibroblasts. In fibroblasts, they stimulate the synthesis of collagen, fibronectin, and certain glycosaminoglycans partly via Smad transduction pathway [8].

TGF-β1 downregulates decorin, important for normal collagen fibrillogenesis, and upregulates versican and biglycan. Neovascularization is enhanced while different proteinases are modulated (MMP-1 downregulation).

In hypertrophic scars of post-burn patients, TGF-β is upregulated locally and systemically [9].

A further factor which is also increased in hypertrophic scars is IGF-1, a cytokine with mitogenic activity on fibroblasts and endothelial cells with collagen synthesis stimulation of dermal fibroblasts [10]. Furthermore, it also decreases the expression of collagenase, thus aggravating the abnormal collagen deposition seen in hypertrophic scars [11].

Clinically, it has been well recognized that injuries associated with prolonged immune responses, such in burns, are predisposed to developing abnormal scarring. Therefore it is hypothesized that not the severity of inflammation predisposes to hypertrophic scarring but the type of immune response. The two subsets of CD41 cells present in wound healing, Th1 and Th2 cells, show antagonistic activity. While Th1 cytokine expression results in an antifibrotic phenotype (e.g., increased collagenase), Th2 cytokine profile results in pro-fibrotic milieu.

Studies evaluating the cytokine profile after burn injury show reduced Th1 cytokine synthesis (e.g., IL-2, IFN-γ) and increased Th2 cytokine profile [12, 13].

Th3, a further subtype of CD41 T-cells, is also pro-fibrotic, and was shown to be elevated in burn patients [14].

Therefore, it seems that early after burn injury a "Th2 immune response" leads to the pro-fibrotic Th3 cells which are capable to induce fibrosis, while inhibiting the antifibrotic Th1 activity [15].

Recently, a newly identified cell population has been implicated in the pathophysiology of hypertrophic scars following thermal injury [16–18]. They exhibit both monocyte- and fibroblast-like characteristics and originate from the bone marrow. They are thought to play a role in tissue repair by several mechanisms (e.g., ECM secretion, antigen presentation, cytokine production, angiogenesis). It is discussed that this cell population contributes to the myofibroblasts. In the peripheral blood of burn patients, an increased percentage of fibrocytes were found compared to controls [17]. It was further shown that this fibrocytes from burned patients are able to modify dermal fibroblast function to increase the secretion for TGF-β and CTGF (connective tissue growth factor), a factor stimulating the proliferation of fibroblasts and ECM protein synthesis and which may mediate many of the pro-fibrotic effects of TGF-β [19, 20].

There are many factors which lead in the outlined scar pathophysiology. In general, a higher prevalence of abnormal scarring is observed in burn patients (dependent upon burn extension), especially when caused by flame. The burn location is also implied as a risk factor for pathological scar formation. However, both sexes show equal distribution, but hypertrophy is more common in children. Race as a risk factor is also discussed in the literature, with black patients bearing a higher risk compared to others.

To summarize, a lot of various factors of the normal physiological wound healing cascade are altered in a manner that finally result in abnormal scarring, which is primarily characterized by excessive disorientated collagen deposition.

6.3 Scar Classification and Grading

Classifying scars is essential for choosing the right treatment regime. Several approaches try to differentiate the pathological scars according to their appearance, histological patterns, and clinical symptoms. Recently, a schema was proposed by Mustoe et al. [21] with modified standard terminology to be clinically as relevant as possible (Table 6.1).

On the other hand, also a number of different grading systems were developed, in an effort to adjust treatment to the stage of the scar. The Vancouver Scar Scale is probably the most common and widely used, evaluating the burn scar in an objective manner subsequently providing assistance in prognosis and management.

However, to prevent the development of unsatisfactory outcomes such as hypertrophic scarring or keloids, clinicians should already initially develop a routine scar assessment program during the first 3 months after complete healing has occurred [22].

6.4 Scar Treatment

Pathological scarring is seen in more than 50% of healed deep burns, thus making it an important entity in the long-term run of burn victims. Several clinical as well as experimental attempts focus this specific problem ranging from conservative biophysical measures, surgical treatment, to pharmacological interventions.

Table 6.1 Scar classification from Mustoe et al. [21]

Scar type	Description
Mature scar	A light-colored, flat scar
Immature scar	A red, sometimes itchy or painful, and slightly elevated scar in the process of remodeling. Many of these will mature normally over time and become flat, and assume a pigmentation that is similar to the surrounding skin, although they can be paler or slightly darker
Linear hypertrophic (e.g., surgical/traumatic) scar	A red, raised, sometimes itchy scar confined to the border of the original surgical incision. This usually occurs within weeks after surgery. These scars may increase in size rapidly for 3–6 months and then, after a static phase, begin to regress. They generally mature to have an elevated, slightly rope-like appearance with increased width, which is variable. The full maturation process may take up to 2 years
Widespread hypertrophic (e.g., burn) scar	A widespread red, raised, sometimes itchy scar that remains within the borders of the burn injury
Minor keloid	A focally raised, itchy scar extending over normal tissue. This may develop up to 1 year after injury and does not regress on its own. Simple surgical excision is often followed by recurrence. There may be a genetic abnormality involved in keloid scarring. Typical sites include earlobes
Major keloid	A large, raised (>0.5 cm) scar, possibly painful or pruritic and extending over normal tissue. This often results from minor trauma and can continue to spread over years

According to the current knowledge of abnormal pathological scarring therapeutic approaches can target (1) the mechanical properties of wound repair, (2) misbalance between collagen synthesis and degradation, and (3) the altered inflammatory response.

6.4.1 Scar Prevention

Prevention of a pathological event is usually more effective than treating them which is additionally often unsatisfying and associated with additional burden to health care expenses. As previously mentioned, thermal injuries especially when extended in area and depth are prone to hypertrophic scarring and could potentially benefit from preventive burn scar management. However, focusing on burn treatment, prevention or treatment of pathological scarring can be conceptually and practically similar especially when considering the high percentage of pathological scarring in burns. Therefore, treatment regimes which are used as preventive means could also be used in treating manifest pathologies and vice versa.

Many preventive (and) treatment strategies have proven their efficacy due to extensive clinical use, applied whether as single or as a combination therapy. However, only few have reached a certain evidence-based medicine level.

6.4.2 Surgical Treatment Options

6.4.2.1 Surgery: Prevention

A well-accepted classification system of burn injuries is oriented on the extent of the skin component involved. Second (dermal) degree burns are additionally subdivided in superficial or deep. In the first, necrosis occupies only the upper (superficial) dermis, with unaffected reticular dermis. These burns are usually managed conservatively (without excision and grafting) due to the good healing prognosis as well as low incidence of abnormal scarring.

In contrast, in deep dermal burns, necrosis involves the reticular dermis and the zone of stasis further extends deep into the dermis. These burns are generally best treated with excision and grafting, which can reduce the risk of long-term complications such as hypertrophic scarring and burn contractures [23].

Full-thickness (third-degree) burns involve the entire dermis and are generally managed with excision and grafting.

Degree of scarring is strongly dependent on the duration of healing and thus on the residues of dermal components (= burn depth). In particular, deep wounds (full-thickness wounds or wounds with considerable dermal component involvement) are considered to heal unlikely within 21 days, and Deitch et al. showed a significantly enhanced risk of abnormal scarring if the wound is persistent for 10 days and that this risk rise to 80% for wounds which show delayed healing beyond day 21 [2].

Therefore, each burn which is expected to take more than 3 weeks to heal (especially with knowledge of high risk scar formers) should be considered to be early skin grafted. Again, clinical correct assessment of the burn is mandatory to draw conclusions regarding the expected healing time.

Excision of burn wounds with an adequate technique and control of blood loss followed by early wound closure, primarily with autologous skin grafts, could effectively decrease severity of hypertrophic scarring, contraction, and allows faster rehabilitation [24, 25].

Skin grafts are widely accepted as a standard method in covering extended excised burn and scar areas. Over the past decades, great advances were made regarding the technique and tools for skin graft harvesting as well as graft meshing. Skin graft could generally be divided in subgroups dependent on the amount of dermis involved. Split-thickness skin grafts, thin or thick, include only a portion of the dermis, whereas full-thickness skin grafts consist of the epidermis and the entire dermal layer.

It is the thickness which determines also the postoperative degree of wound contraction. Normally, the thinner the skin graft applied the higher the degree of contraction which may occur at the recipient site. This is of clinical importance which skin graft should be used in which location. Split-thickness skin grafts are more suitable to cover large burn

areas or large defects originating from excised abnormal scars without involving mobile joint surfaces.

Split-thickness grafts also have significant disadvantages that must be considered. Split-thickness grafts are more fragile (dependent on whether thin, intermediate, or thick is chosen), especially when applied over areas with few underlying nutritional support. The contraction is more pronounced, lacks elasticity and grows adequately with the individual. They tend to be abnormally pigmented, either pale or white, or alternatively hyper-pigmented, particularly in darker-skinned individuals.

On the other hand, full-thickness skin grafts, which tend to less contraction, are particularly used over joints, in the face and in defects of the hand. Additionally, for smaller (profound) burns with sufficient donor sites or locations susceptible for contraction and scarring sheet grafts can be considered as a valuable tool.

However, the follow-up management has to be carefully carried out due to the possibility of hematoma and seroma accumulation underneath this sheet grafts compromising graft survival with potentially graft loss.

Skin grafts can be further subdivided into sheet (unmeshed) and meshed grafts. Meshed grafts are fenestrated using mesh ratios ranging from 1: 1 to 4:1, thus enabling to cover larger defect areas. The risk of hematoma or seroma formation is minimized due to the drainage via the fenestration. However, meshed grafts again show a certain degree of contraction and scarring (according to the mesh pattern) with prolonged healing times dependent on the ratio used, because of lacking dermal components in the mesh interstices. Further means such as allografts or other biological dressings can be applied over higher meshed grafts to prevent desiccation.

In areas where functional as well as cosmetic results are favorable such as face, neck, and hands, sheet grafts are to prefer over meshed grafts.

6.4.2.2 Surgery: Treatment

Surgical excision of hypertrophic scars or keloids is a common management option whether to release associated scar contraction or to improve esthetical appearance. Small lesions can be excised in total and closed primarily but using essential principles to avoid re-scarring. This includes minimizing trauma to the dermal edges, avoidance of excessive wound traction, adequate amount of suture material in the right location, and avoidance of wound tension. However, in larger areas of abnormal scarring, which are more common in burned patients, with considerable contractions, partial release of this contraction should be considered. Coverage of the resulting defect could be realized using skin graft of flaps. Flaps are more effective than grafting in terms of prevention re-contraction.

However, excision alone for example of keloids without additional measures may result in a recurrence rate as high as 90%. Therefore, adjunctive treatment modalities are recommended for hypertrophic scars as well as in the treatment of keloids, which are discussed later.

Additional surgical techniques to treat hypertrophic scars are Z- or W-plasty to release scar tension. A profound treatment should achieve both excision with narrowing the scars and change of the direction of the scars realized by Z- or W-plasty. The main principle of the Z-plasty is the extension of a reduced distance and the main scar axis is changed parallel to skin creases. The W-plasty causes a disruption of the scar, thus making it less conspicuous. Every other scar shank can be positioned within the skin creases.

In keloids, however, simple excision is inadequate due to the stimulation of additional collagen synthesis, thus resulting in fast and often more pronounced recurrences. Therefore, an intramarginal surgical excision is highly recommended to prevent this collagen synthesis. Moreover, especially in keloids, surgical therapy should be combined with adjuvant therapies, which were already shown to lower recurrence rates.

Stretching forces to wounds are considered to substantially contribute to abnormal scarring. Tension at the wound borders compromises microvascular perfusion, prolongs inflammation, and increases time of healing resulting in enhanced fibroplasias. Thus special attention has to be drawn on preventing these avoidable risk factors. However, wounds prone to tension forces can be effectively physically supported by intradermal sutures for at least 6 weeks. Recently, a new suture material (V-Loc®, Covidien) was introduced that allows distributing the tension throughout the wound by grasping the tissue at multiple points that spreads the tension across the wound. Moreover, due to the design with unidirectional, circumferential shallow barbs it allows avoiding knotting and reduces foreign body material with associated complications. Some recent studies [26, 27] were published, with promising results in terms of cost-efficacy.

6.5 Dermal Substitutes

An intact basal membrane and the source of keratinocytes, like hair follicles and skin appendages are essential in re-epithelialization and wound healing. Additionally, the dermis is recognized to play a pivotal role in contraction. Scars of limited depth normally preserve elasticity. Contrarily, loss of dermal components in deep wounds results in the absence of elasticity, and fibroblastic cell proliferation issuing to hypertrophy and contraction.

The recent development of dermal substitutes could open a place for their use in pathologic scar prevention. Multiple devices, integrating different technologies, are now proposed for use in burns and reconstructive surgery. These artificial dermis formed either by a single layer of product (to be

immediately covered by skin grafts) or a double layer (a collagen-based product covered by a film, to be repopulated before a second procedure of skin grafting), some of them being of allogenic origin, or derived from synthetic compounds, sometimes having been previously repopulated by cells (fibroblasts, keratinocytes, or both). Extensive researches are still to be done, both in fundamental research and in clinical trials dermal substitutes burn scar treatment dermal substitutes establishing the real benefit of these technologies.

6.5.1 Bilayer Non-cellularized Dermal Regeneration Templates

Integra® was the first artificial dermis launched on the market in the 1990s. Composed of bovine collagen (prion-free, containing glycosaminoglycans), bilayer Integra® is covered with a thin layer of silicone that prevents collagen desiccation. In a two-step procedure, first full laminar adhesion is essential to initiate angiogenesis and remodeling which is characterized by a neodermis constituting an intermediate layer between the skin graft and the underlying wound bed. The second surgical procedure is performed when the collagen has been re-vascularized (within 3 weeks if no adjunct negative-pressure therapy is implemented, or 10 days if TPN is employed). Following removal of the silicone layer, a split-thickness sheet graft is placed onto the scaffold. This technique has recently been proposed as an alternative method of covering burns with large surface areas [28].

Renoskin® is a bilayer artificial dermis. Like Integra®, it comprises a collagen layer covered with a thin layer of silicone. It is used in deep burns, and more recently in all reconstructive surgical applications. Renoskin® appears to improve the flexibility of scar tissue.

Hyalomatrix® promotes the formation of budding tissue formed by hyaluronic acid which enables skin grafting after 1–2 weeks. The dermis formed in this manner is impregnated with hyaluronic acid, the graft takes more effectively and the underlying area is improved (elasticity and flexibility are enhanced) [29, 30].

6.5.2 Single-Layer Cellularized Dermal Regeneration Templates

Pelnac® is a porcine tendon collagen, neutralized and freeze-dried, available as sponge membranes. After debridement, the artificial dermis is applied to wounds, and ointment-impregnated gauze is applied to prevent wound desiccation. The adapted atelocollagen sponge promotes the early infiltration of mononuclear cells and fibroblasts and better growth of connective tissue strands and epithelium. Consequently, abundant granulation tissue develops on the wound surface, over which free skin grafting can be performed after about 2 weeks [31].

Matriderm® is an original matrix consisting of collagen and elastin. Available as a flexible sheet it adepts to the wound shape. Once applied, it exerts a mild hemostatic effect through suction of the underlying tissue. Matriderm® can be applied to viable sub-cutaneous cell tissue, tendons, or bony tissue. In a one-step procedure, Matriderm® is first applied as a dermal sub-layer followed by the skin graft. The usage of a thin skin graft is preferred, and initial results show clear benefits of this artificial skin in terms of ease of use and elasticity [32, 33].

Single-layer Integra® is composed of collagen and glycosaminoglycans. It exhibits the same properties as classic Integra®, but has no silicone layer, making it suitable for immediate application of a thin skin graft (one-step procedure).

Alloderm™, Strattice, and Permaform are derived from porcine dermis. These products may be used as solid thick structures. Their capacity of being penetrated by vessels is lower than the previous ones. Used in dura matrix replacement, they can be proposed as fixation devices for abdominal wall reconstruction or internal brass in mammary ptosis or after breast reduction.

Gliader™ has recently been proposed by the Dutch skin bank. Clinical indications are burns coverage and trauma. The device is immediately covered using skin grafts during the same surgical procedure or some days after.

6.6 Non-surgical Treatment Options

Among a long list of proposals, some of them are considered now as a classical approach, like silicone gel sheets, with some evidence behind, others are gaining evidence like 5-FU [34] injections and Avotermin (TGF-β3) [35].

6.6.1 Adhesive Tapes

Multidirectional tension on wounds is meanwhile recognized as an important pathophysiological factor in developing abnormal scarring. Eliminating such stretching forces on wounds can be easily achieved by applying microporous hypoallergenic paper tapes [36].

This enables to control the wound tension forces and prevent hypertrophic scarring. Treatment should be initiated early after surgery and maintained for several weeks, as maximum strength of a scar is only achieved after at least 12 weeks post wounding [37].

Although the exact mechanism of efficacy is unknown, a dual working hypothesis is suggested. The mechanical influence similar to that using pressure garments seems to be

obvious and second may be an occlusive component analogous to the treatment with silicone gel sheets.

Nevertheless, paper tapes are non-invasive, inexpensive with minimal demands on patients and could be therefore used as a preventive mean at least in low risk patients.

6.6.2 Pressure Garments

It was in the late 1960 when pressure treatment arose as a therapeutic standard means to prevent and treat abnormal scarring in burned patients [38]. Mechanisms which are discussed to be involved in the effects of pressure therapy are decreased scar blood flow, decreased edema formation, decreased protein deposition including chondroitin sulfate, and increased lysis. Once edema formation is decreased, it lowers also the measured pressure and increases scar tissue temperature which is regarded to pertain positive effects. Increased temperature, even by 1 °C, will significantly increase collagenolysis and scar maturation [39–42].

The garments should be applied as soon as possible after the acute and subacute burn treatment.

Recommendations regarding the pressure which should be applied range between 24 and 30 mmHg for 6–12 months, although these recommendations are largely based on empiric clinical findings. Typically the garments which are used are custom-made from an elastic material with a high content of spandex. The use could be limited in difficult anatomic locations such as flexures or areas of high mobility (e.g., joints). Furthermore, patient discomfort could lead to a major problem with reports of non-compliant patients from 8.5% to 59% [40, 41].

A recently conducted meta-analysis on the effectiveness of pressure garment therapy for the prevention of abnormal scarring after burn injury was unable to demonstrate a difference to control scars [43].

6.6.3 Silicone Gel Sheeting

Since the early 1980s, silicone gel sheeting became popular in the treatment of scar pathologies and has now good evidence in efficacy as demonstrated by several studies as a safe and effective management option [44–50].

More than 60 silicone elastomeric products have been marketed since 1990 [51].

Although the exact mechanism of silicone gel sheeting on improvement of abnormal scars is uncertain, several hypothesis are proposed.

Possible mechanisms include increased temperature, hydration caused by occlusion of the underlying skin, increased oxygen tension, direct action of the silicone oil, and polarization of the scar tissue caused by the negative static electric charge generated by movement of the silicone [52–56].

The use of silicone gel sheeting is recommended to begin soon after the wound is entirely epithelialized and these sheets should be worn for at least 12 h/day for a minimum of 2 months. Unfavorable events such as pruritus, rash, maceration, and odor can be managed by temporary interruption of treatment and regular washing of the sheet and the scar.

Many clinicians adopt a multimodal approach to the treatment and prevention of hypertrophic and keloid scars.

6.6.4 Corticosteroids

Intralesional corticosteroid injections are already used since the mid-1960s in scar management and are able to reduce scar volume while improving pliability, height, and symptoms such as pruritus [57, 58].

Corticosteroid application has antimitotic effect on fibroblast, thus decreasing fibroblast proliferation. This diminishes the collagen synthesis, and glycosaminoglycans synthesis. Finally, it suppresses pro-inflammatory mediators by inhibition of leukocytes and monocytes [59, 60].

The most common corticosteroid which is used for the treatment of scars is insoluble triamcinolone acetonide in a concentration of 10–40 mg/ml dependent on the scar pathology (10 mg/ml every 3–6 weeks in developing hypertrophic scars; 40 mg/ml three monthly in manifest keloids) [61].

Due to the painful sensations during intralesional injection the combination with a local anesthetic such as lidocaine is recommended. Further common side effects include tissue atrophy, telangiectasia, hypopigmentation, and rebound effects [57, 62].

However, there is broad variation concerning response rates from 50% to 100% and recurrance rates between 9% to 50% [42].

Combination with other therapies such as surgery, laser, and 5-fluorouracil may improve outcome [57, 63, 64].

Because of the poor absorption of topical administered corticosteroids, usage is only of limited effect and thus preserved for superficial lesions only.

6.6.5 Radiotherapy

First reports using radiation for the treatment of keloids date back to 1906. But further evidence suggested that the monotherapy is inadequate [65] (response from 10% to 94% with keloid recurrence rate of 50–100%) [66].

Therefore radiotherapy was used in conjunction with other treatment modalities such as surgery and reported response rates varied between 65% and 99% when compared.

Proposed mode of efficacy is the direct apoptotic effect on cells in particular on fibroblast by using the suggested 15–20 Gy which should be fractionated over 5–6 treatment sessions in the early postoperative phase [67].

However, radiotherapy is still discussed controversially due to (anecdotal) reports of inducing malignancies especially when used as monotherapy. On the other hand, large studies with long-term follow-up showed no evidence to substantiate the risk of carcinogenesis [68].

Nevertheless, radiotherapy remains a valuable and effective therapeutic option in severe keloids. It is suggested that a close team workup is carried out between surgeons and radiation oncologists before excluding radiotherapy in the treatment of keloids [69].

6.6.6 Laser Therapy

Since the introduction of laser treatment in the indication of hypertrophic scars and keloids in the mid-1980s, more and more lasers with different wavelengths have been studied [70, 71].

Argon and CO_2 lasers were examined in the treatment of hypertrophic scars with initially promising results but showed during follow-up high recurrence rate [72, 73].

More recent wavelength-specific lasers such as flashlamp-pulsed dye lasers (PDL) and the non-laser intense-pulsed light source were able to improve the scar texture, erythema, size and pliability of hypertrophic scar with the consequence that this lasers were used more frequently [74–77].

Currently, the PDL wavelengths 585 and 595 nm are most frequently used for therapeutic purposes.

For neodymium:yttrium-aluminum-garnet (Nd: YAG) lasers, response rates between 36% and 47% are reported [73].

However, in a recent study determining Nd:YAG laser on keloids, nearly 60% of the keloids were flattened after one treatment session. Additionally, these patients remained free of keloid scarring in the follow-up period of 5 years [78].

A study evaluating the pulsed erbium:yttrium-aluminum-garnet laser showed efficacy in the treatment of hypertrophic and depressed scars, without serious side effects [79].

Lasers have been shown also to be effective not only in the treatment of manifest abnormal scarring but also in the prevention of hypertrophic scars. In 1996, Gaston et al. reported that a 585-nm PDL was effective in preventing the formation of hypertrophic scars in burn wounds [80].

This study is supported by other experimental studies, including incisional and burn wounds [81].

The mechanism of action by which laser irradiation improves proliferative scars is not known. Suggested theories are based on selective photothermolysis, in which the light energy emitted from a vascular laser (such as PDL) is absorbed by hemoglobin, generating heat and leading to coagulation necrosis, thus inducing local hypoxia [82, 83].

It is also suggested that hypoxia induction by laser destruction of capillaries might also alter collagen synthesis by fibroblasts and degradation through metalloproteinase release [84].

Further factors which are discussed in conjunction with scar improvement are decreased fibroblast proliferation and collagen III deposition [85].

TGF-β1 is considered to induce and modulate collagen formation and PDL treatment is associated with the down-regulation of TGF-β1 expression associated with an increase of MMP-13 (collagenase 3) activity [86].

Although lack of large controlled studies, laser therapy remains emerging technology, and further studies should be conducted to further evaluate efficacy in abnormal scar treatment.

6.6.7 Cryotherapy

Cryotherapy whether by contact or by spray using liquid nitrogen can effectively improve hypertrophic scars and keloids [87, 88].

When used as a single therapy it can result in flattening of keloids in 51–74%, although several treatment sessions are necessary [88–90].

Application of cryotherapy induces local ischemia with subsequent necrosis of the hypertrophic scar tissue [63].

Due to the common side effect of permanent hypopigmentation as well as the long postoperative healing phase between the single applications, this treatment modality is limited in general for small scars only. Other side effects include pain upon application, hyperpigmentation, and skin atrophy [87].

Recently, a new method has been developed to avoid drawbacks of the classical cryotherapy. An intralesional needle cryoprobe is inserted longitudinally in the scar axis to maximize the volume of tissue which can be frozen [88].

It was shown that a single application can achieve 50% scar volume reduction, with only mild local edema and epidermiolysis, accompanied by mild pain or discomfort.

6.6.8 5-Fluorouracil

5-Fluorouracil (5-FU), a pyrimidine analog used in chemotherapy, has been shown to be converted intracellular into its active substrate and ultimately incorporated into DNA, thus inhibiting DNA synthesis [91].

Cells with a high turn-over, such as fibroblasts in dermal wounds responsible for excessive collagen production, are preferentially targeted by 5-FU, whose proliferation is inhibited. Scar softening was reported to be faster with intralesional 5-FU than with PDL alone [92].

However, 5-FU can be also used in combination with other treatment modalities such as corticosteroids.

Intralesional injection of 5-FU 50 mg/ml in combination with triamcinolone 10 mg/ml or with a very low concentration of betamethasone (5.7 mg/ml) may promote better regression without recurrence of keloid scars smaller than 2 cm in diameter [91, 93].

Limitations of the treatment are that the injection can be painful, purpura and ulcers may occur, and that the agent is expensive [94, 95].

There is to date no consensus concerning the dosage and exposure time and further studies are needed to improve efficacy of this potential treatment.

6.6.9 Interferon

It was outlined that Th2 polarized immune response contribute to abnormal scarring, thus newer therapeutics emerged to attempt the shift towards Th1 response. A Th1 cell product—interferons, which are divided into a, b, and g, inhibit types I and III collagen synthesis by dermal fibroblasts in a dose-dependent manner [96].

It could be shown in a study on keloids that intralesional application of IFN-g is able to reduce scar size, to decrease collagen nodules and to change the orientation of the collagen bundels into a more organized way. The recurrence rate assessed after 1 year following injection was minimal [97]. This finding is supported by others which showed improved symptoms after intralesional IFN-g injection of 10–200 μg twice weekly for 4 weeks [98, 99].

However, injections are painful and may require local anesthesia. Furthermore, potential side effects include flu-like syndromes characterized by headache, diffuse myalgia, low grade temperature, and fatigue [99].

Similarly, Tredget et al. reported significant improvement of hypertrophic scars when interferon-2b is injected three times weekly. Serum TGF-b levels were also reduced and continued to be low after treatment [9].

Reports further suggest that interferon treatment is significantly better than triamcinolone acetonide injection in preventing postsurgical recurrences of keloids [100]. However, other research groups could not reproduce such low recurrence rates associated with intralesional IFN-2a application [101, 102].

Thus, further studies are required to determine if these contradictory results may be attributed to the dosage, delivery mode, differences of keloid location, or the combination of these factors.

6.6.10 Avotermin (TGF-β3)

The principle of preventing bad scarring was initiated by Renovo some years ago. Injections of TGF-β3 synthetic equivalent in the wound edges after closing the postoperative wound were initiated and analyzed in RCTs. Fergusson et al. could recently demonstrate statistical differences on a meta-analysis of those different trials [103].

6.7 Conclusion

Pathological scarring is linked to different etiologies, among them the mechanical stimulation represents an important factor. The biological abnormal behavior of fibroblasts, with signaling imbalance, is also a pathway for new biological inhibitors.

These two issues are reflected in the catalogue of potentially valid solutions for scar management.

Mechanical stabilization of the scar, hydration and injection of products supposed to slow down inflammation, and the permanence of the fibroblast proliferation are the basis of the recently proposed options in this domain. Surgical solutions like an extended use of dermal substitutes, skin grafts, flaps and the use of mechanically resistant sutures, taping the postoperative scar are also solutions having been proposed in the literature.

However, evidence is still weak and needs to be confirmed by prospective trials.

References

1. Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. Physiol Rev. 2003;83:835–70.
2. Deitch EA, Wheelahan TM, Rose MP, Clothier J, Cotter J. Hypertrophic burn scars: analysis of variables. J Trauma. 1983;23:895–8.
3. Wang J, Dodd C, Shankowsky HA, Scott PG, Tredget EE. Deep dermal fibroblasts contribute to hypertrophic scarring. Lab Investig. 2008;88:1278–90.
4. Wang R, et al. Hypertrophic scar tissues and fibroblasts produce more transforming growth factor-beta1 mRNA and protein than normal skin and cells. Wound Repair Regen. 2000;8:128–37.
5. Colwell AS, Phan TT, Kong W, Longaker MT, Lorenz PH. Hypertrophic scar fibroblasts have increased connective tissue growth factor expression after transforming growth factor-beta stimulation. Plast Reconstr Surg. 2005;116:1387–90.
6. Clark RA. Fibrin and wound healing. Ann N Y Acad Sci. 2001;936:355–67.
7. Tuan TL, et al. Increased plasminogen activator inhibitor-1 in keloid fibroblasts may account for their elevated collagen accumulation in fibrin gel cultures. Am J Pathol. 2003;162:1579–89.
8. Ignotz RA, Massague J. Transforming growth factor-beta stimulates the expression of fibronectin and collagen and their incorporation into the extracellular matrix. J Biol Chem. 1986;261:4337–45.
9. Tredget EE, et al. Transforming growth factor-beta in thermally injured patients with hypertrophic scars: effects of interferon alpha-2 b. Plast Reconstr Surg. 1998;102:1317–28.
10. Ghahary A, Shen Q, Shen YJ, Scott PG, Tredget EE. Induction of transforming growth factor beta 1 by insulin-like growth factor-1 in dermal fibroblasts. J Cell Physiol. 1998;174:301–9.
11. Ghahary A, et al. Collagenase production is lower in post-burn hypertrophic scar fibroblasts than in normal fibroblasts and

is reduced by insulin-like growth factor-1. J Invest Dermatol. 1996;106:476–81.
12. O'Sullivan ST, et al. Major injury leads to predominance of the T helper-2 lymphocyte phenotype and diminished interleukin-12 production associated with decreased resistance to infection. Ann Surg. 1995;222:482–90.
13. Horgan AF, et al. Altered gene transcription after burn injury results in depressed T-lymphocyte activation. Ann Surg. 1994;220:342–51.
14. Wang J, et al. Increased TGF-beta-producing CD4+ T lymphocytes in postburn patients and their potential interaction with dermal fibroblasts in hypertrophic scarring. Wound Repair Regen. 2007;15:530–9.
15. Ladak A, Tredget EE. Pathophysiology and management of the burn scar. Clin Plast Surg. 2009;36:661–74.
16. Yang L, et al. Identification of fibrocytes in postburn hypertrophic scar. Wound Repair Regen. 2005;13:398–404.
17. Yang L, et al. Peripheral blood fibrocytes from burn patients: identification and quantification of fibrocytes in adherent cells cultured from peripheral blood mononuclear cells. Lab Investig. 2002;82:1183–92.
18. Scott PG, Ghahary A, Tredget EE. Molecular and cellular aspects of fibrosis following thermal injury. Hand Clin. 2000;16:271–87.
19. Wang J, et al. Accelerated wound healing in leukocyte-specific, protein 1-deficient mouse is associated with increased infiltration of leukocytes and fibrocytes. J Leukoc Biol. 2007;82:1554–63.
20. Grotendorst GR. Connective tissue growth factor: a mediator of TGF-beta action on fibroblasts. Cytokine Growth Factor Rev. 1997;8:171–9.
21. Mustoe TA, et al. International clinical recommendations on scar management. Plast Reconstr Surg. 2002;110:560–71.
22. Teot L. Clinical evaluation of scars. Wound Repair Regen. 2002;10:93–7.
23. Silver GM, et al. Standard operating procedures for the clinical management of patients enrolled in a prospective study of inflammation and the host response to thermal injury. J Burn Care Res. 2007;28:222–30.
24. Ramzy PI, Barret JP, Herndon DN. Thermal injury. Crit Care Clin. 1999;15:333–52.
25. Atiyeh BS, et al. Benefit-cost analysis of moist exposed burn ointment. Burns. 2002;28:659–63.
26. Tewari AK, et al. Use of a novel absorbable barbed plastic surgical suture enables a "self-cinching" technique of vesicourethral anastomosis during robot-assisted prostatectomy and improves anastomotic times. J Endourol. 2010;24:1645–50.
27. Demyttenaere SV, et al. Barbed suture for gastrointestinal closure: a randomized control trial. Surg Innov. 2009;16:237–42.
28. Heimbach DM, et al. Multicenter postapproval clinical trial of Integra dermal regeneration template for burn treatment. J Burn Care Rehabil. 2003;24:42–8.
29. Scuderi N, et al. The clinical application of autologous bioengineered skin based on a hyaluronic acid scaffold. Biomaterials. 2008;29:1620–9.
30. Gravante G, et al. The use of hyalomatrix PA in the treatment of deep partial-thickness burns. J Burn Care Res. 2007;28:269–74.
31. Fujioka M, Fujii T. Maxillary growth following atelocollagen implantation on mucoperiosteal denudation of the palatal process in young rabbits: implications for clinical cleft palate repair. Cleft Palate Craniofac J. 1997;34:297–308.
32. Ryssel H, Gazyakan E, Germann G, Ohlbauer M. The use of MatriDerm in early excision and simultaneous autologous skin grafting in burns – a pilot study. Burns. 2008;34:93–7.
33. Haslik W, et al. First experiences with the collagen-elastin matrix Matriderm as a dermal substitute in severe burn injuries of the hand. Burns. 2007;33:364–8.
34. Wang XQ, Liu YK, Qing C, Lu SL. A review of the effectiveness of antimitotic drug injections for hypertrophic scars and keloids. Ann Plast Surg. 2009;63:688–92.
35. Ferguson MW, et al. Prophylactic administration of avotermin for improvement of skin scarring: three double-blind, placebo-controlled, phase I/II studies. Lancet. 2009;373:1264–74.
36. Reiffel RS. Prevention of hypertrophic scars by long-term paper tape application. Plast Reconstr Surg. 1995;96:1715–8.
37. Atkinson JA, McKenna KT, Barnett AG, McGrath DJ, Rudd M. A randomized, controlled trial to determine the efficacy of paper tape in preventing hypertrophic scar formation in surgical incisions that traverse Langer's skin tension lines. Plast Reconstr Surg. 2005;116:1648–56.
38. Linares HA, Larson DL, Willis-Galstaun BA. Historical notes on the use of pressure in the treatment of hypertrophic scars or keloids. Burns. 1993;19:17–21.
39. Rose MP, Deitch EA. The clinical use of a tubular compression bandage, Tubigrip, for burn-scar therapy: a critical analysis. Burns Incl Therm Inj. 1985;12:58–64.
40. Kealey GP, Jensen KL, Laubenthal KN, Lewis RW. Prospective randomized comparison of two types of pressure therapy garments. J Burn Care Rehabil. 1990;11:334–6.
41. Johnson J, Greenspan B, Gorga D, Nagler W, Goodwin C. Compliance with pressure garment use in burn rehabilitation. J Burn Care Rehabil. 1994;15:180–8.
42. Niessen FB, Spauwen PH, Schalkwijk J, Kon M. On the nature of hypertrophic scars and keloids: a review. Plast Reconstr Surg. 1999;104:1435–58.
43. Anzarut A. The evidence for and against the effectiveness of pressure garment therapy for scar management. Plast Reconstr Surg. 2007;120:1437–8.
44. Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel: a new treatment for hypertrophic scars. Surgery. 1989;106:781–6.
45. Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel for the prevention and treatment of hypertrophic scar. Arch Surg. 1991;126:499–504.
46. Cruz-Korchin NI. Effectiveness of silicone sheets in the prevention of hypertrophic breast scars. Ann Plast Surg. 1996;37:345–8.
47. Gold MH. A controlled clinical trial of topical silicone gel sheeting in the treatment of hypertrophic scars and keloids. J Am Acad Dermatol. 1994;30:506–7.
48. Berman B, Flores F. Comparison of a silicone gel-filled cushion and silicon gel sheeting for the treatment of hypertrophic or keloid scars. Dermatol Surg. 1999;25:484–6.
49. Su CW, Alizadeh K, Boddie A, Lee RC. The problem scar. Clin Plast Surg. 1998;25:451–65.
50. Poston J. The use of silicone gel sheeting in the management of hypertrophic and keloid scars. J Wound Care. 2000;9:10–6.
51. Berman B, et al. A review of the biologic effects, clinical efficacy, and safety of silicone elastomer sheeting for hypertrophic and keloid scar treatment and management. Dermatol Surg. 2007;33:1291–302.
52. Hirshowitz B, et al. Static-electric field induction by a silicone cushion for the treatment of hypertrophic and keloid scars. Plast Reconstr Surg. 1998;101:1173–83.
53. Gilman TH. Silicone sheet for treatment and prevention of hypertrophic scar: a new proposal for the mechanism of efficacy. Wound Repair Regen. 2003;11:235–6.
54. Suetak T, Sasai S, Zhen YX, Tagami H. Effects of silicone gel sheet on the stratum corneum hydration. Br J Plast Surg. 2000;53:503–7.
55. Branagan M, Chenery DH, Nicholson S. Use of infrared attenuated total reflectance spectroscopy for the in vivo measurement of hydration level and silicone distribution in the stratum corneum following skin coverage by polymeric dressings. Skin Pharmacol Appl Ski Physiol. 2000;13:157–64.
56. Musgrave MA, Umraw N, Fish JS, Gomez M, Cartotto RC. The effect of silicone gel sheets on perfusion of hypertrophic burn scars. J Burn Care Rehabil. 2002;23:208–14.
57. Manuskiatti W, Fitzpatrick RE. Treatment response of keloidal and hypertrophic sternotomy scars: comparison among intralesional

corticosteroid, 5-fluorouracil, and 585-nm flashlamp-pumped pulsed-dye laser treatments. Arch Dermatol. 2002;138:1149–55.
58. Kang N, Sivakumar B, Sanders R, Nduka C, Gault D. Intralesional injections of collagenase are ineffective in the treatment of keloid and hypertrophic scars. J Plast Reconstr Aesthet Surg. 2006;59:693–9.
59. Urioste SS, Arndt KA, Dover JS. Keloids and hypertrophic scars: review and treatment strategies. Semin Cutan Med Surg. 1999;18:159–71.
60. Sherris DA, Larrabee WF Jr, Murakami CS. Management of scar contractures, hypertrophic scars, and keloids. Otolaryngol Clin N Am. 1995;28:1057–68.
61. Brissett AE, Sherris DA. Scar contractures, hypertrophic scars, and keloids. Facial Plast Surg. 2001;17:263–72.
62. Nemeth AJ. Keloids and hypertrophic scars. J Dermatol Surg Oncol. 1993;19:738–46.
63. Boutli-Kasapidou F, Tsakiri A, Anagnostou E, Mourel-lou O. Hypertrophic and keloidal scars: an approach to polytherapy. Int J Dermatol. 2005;44:324–7.
64. Asilian A, Darougheh A, Shariati F. New combination of triamcinolone, 5-fluorouracil, and pulsed-dye laser for treatment of keloid and hypertrophic scars. Dermatol Surg. 2006;32:907–15.
65. Borok TL, et al. Role of ionizing irradiation for 393 keloids. Int J Radiat Oncol Biol Phys. 1988;15:865–70.
66. Berman B, Bieley HC. Adjunct therapies to surgical management of keloids. Dermatol Surg. 1996;22:126–30.
67. Slemp AE, Kirschner RE. Keloids and scars: a review of keloids and scars, their pathogenesis, risk factors, and management. Curr Opin Pediatr. 2006;18:396–402.
68. Malaker K, Vijayraghavan K, Hodson I, Al YT. Retrospective analysis of treatment of unresectable keloids with primary radiation over 25 years. Clin Oncol (R Coll Radiol). 2004;16:290–8.
69. Ogawa R, Yoshitatsu S, Yoshida K, Miyashita T. Is radiation therapy for keloids acceptable? The risk of radiation-induced carcinogenesis. Plast Reconstr Surg. 2009;124:1196–201.
70. Castro DJ, et al. Effects of the Nd:YAG laser on DNA synthesis and collagen production in human skin fibroblast cultures. Ann Plast Surg. 1983;11:214–22.
71. Apfelberg DB, Maser MR, Lash H, White D, Weston J. Preliminary results of argon and carbon dioxide laser treatment of keloid scars. Lasers Surg Med. 1984;4:283–90.
72. Henderson DL, Cromwell TA, Mes LG. Argon and carbon dioxide laser treatment of hypertrophic and keloid scars. Lasers Surg Med. 1984;3:271–7.
73. Abergel RP, et al. Control of connective tissue metabolism by lasers: recent developments and future prospects. J Am Acad Dermatol. 1984;11:1142–50.
74. Alster TS, Nanni CA. Pulsed dye laser treatment of hypertrophic burn scars. Plast Reconstr Surg. 1998;102:2190–5.
75. Allison KP, Kiernan MN, Waters RA, Clement RM. Pulsed dye laser treatment of burn scars. Alleviation or irritation? Burns. 2003;29:207–13.
76. Kono T, et al. The flashlamp-pumped pulsed dye laser (585 nm) treatment of hypertrophic scars in Asians. Ann Plast Surg. 2003;51:366–71.
77. Alster TS, Williams CM. Treatment of keloid sternotomy scars with 585 nm flashlamp-pumped pulsed-dye laser. Lancet. 1995;345:1198–200.
78. Kumar K, Kapoor BS, Rai P, Shukla HS. In-situ irradiation of keloid scars with Nd:YAG laser. J Wound Care. 2000;9:213–5.
79. Kwon SD, Kye YC. Treatment of scars with a pulsed Er:YAG laser. J Cutan Laser Ther. 2000;2:27–31.
80. Gaston P, Humzah MD, Quaba AA. The pulsed tuneable dye laser as an aid in the management of postburn scarring. Burns. 1996;22:203–5.
81. Liew SH, Murison M, Dickson WA. Prophylactic treatment of deep dermal burn scar to prevent hypertrophic scarring using the pulsed dye laser: a preliminary study. Ann Plast Surg. 2002;49:472–5.
82. Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. Science. 1983;220:524–7.
83. Reiken SR, et al. Control of hypertrophic scar growth using selective photothermolysis. Lasers Surg Med. 1997;21:7–12.
84. Paquet P, Hermanns JF, Pierard GE. Effect of the 585 nm flashlamp-pumped pulsed dye laser for the treatment of keloids. Dermatol Surg. 2001;27:171–4.
85. Kuo YR, et al. Activation of ERK and p38 kinase mediated keloid fibroblast apoptosis after flashlamp pulsed-dye laser treatment. Lasers Surg Med. 2005;36:31–7.
86. Kuo YR, et al. Suppressed TGF-beta1 expression is correl ated with up-regulation of matrix metalloproteinase-13 in keloid regression after flashlamp pulsed-dye laser treatment. Lasers Surg Med. 2005;36:38–42.
87. Rusciani L, Rossi G, Bono R. Use of cryotherapy in the treatment of keloids. J Dermatol Surg Oncol. 1993;19:529–34.
88. Har-Shai Y, Amar M, Sabo E. Intralesional cryotherapy for enhancing the involution of hypertrophic scars and keloids. Plast Reconstr Surg. 2003;111:1841–52.
89. Ernst K, Hundeiker M. Results of cryosurgery in 394 patients with hypertrophic scars and keloids. Hautarzt. 1995;46:462–6.
90. Layton AM, Yip J, Cunliffe WJ. A comparison of intralesional triamcinolone and cryosurgery in the treatment of acne keloids. Br J Dermatol. 1994;130:498–501.
91. Apikian M, Goodman G. Intralesional 5-fluorouracil in the treatment of keloid scars. Australas J Dermatol. 2004;45:140–3.
92. Nouri K, Vidulich K, Rivas MP. Lasers for scars: a review. J Cosmet Dermatol. 2006;5:14–22.
93. Lebwohl M. From the literature: intralesional 5-FU in the treatment of hypertrophic scars and keloids: clinical experience. J Am Acad Dermatol. 2000;42:677.
94. Gupta S, Kalra A. Efficacy and safety of intralesional 5-fluorouracil in the treatment of keloids. Dermatology. 2002;204:130–2.
95. Baisch A, Riedel F. Hyperplastic scars and keloids: part II: surgical and non-surgical treatment modalities. HNO. 2006;54:981–92.
96. Jimenez SA, Freundlich B, Rosenbloom J. Selective inhibition of human diploid fibroblast collagen synthesis by interferons. J Clin Invest. 1984;74:1112–6.
97. Granstein RD, et al. A controlled trial of intralesional recombinant interferon-gamma in the treatment of keloidal scarring. Clinical and histologic findings. Arch Dermatol. 1990;126:1295–302.
98. Pittet B, et al. Effect of gamma-interferon on the clinical and biologic evolution of hypertrophic scars and Dupuytren's disease: an open pilot study. Plast Reconstr Surg. 1994;93:1224–35.
99. Larrabee WF Jr, East CA, Jaffe HS, Stephenson C, Peterson KE. Intralesional interferon gamma treatment for keloids and hypertrophic scars. Arch Otolaryngol Head Neck Surg. 1990;116:1159–62.
100. Berman B, Flores F. Recurrence rates of excised keloids treated with postoperative triamcinolone acetonide injections or interferon alfa-2 b injections. J Am Acad Dermatol. 1997;37:755–7.
101. Wong TW, Chiu HC, Yip KM. Intralesional interferon alpha-2 b has no effect in the treatment of keloids. Br J Dermatol. 1994;130:683–5.
102. Al-Khawajah MM. Failure of interferon-alpha 2 b in the treatment of mature keloids. Int J Dermatol. 1996;35:515–7.
103. Occleston NL, Fairlamb D, Hutchison J, O'Kane S, Ferguson MW. Avotermin for the improvement of scar appearance: a new pharmaceutical in a new therapeutic area. Expert Opin Investig Drugs. 2009;18:1231–9.

The Future of Wound Documentation: Three-Dimensional, Evidence-Based, Intuitive, and Thorough

7

Michael Giretzlehner and Lars-Peter Kamolz

7.1 Medical Documentation

The Collins English Dictionary defines documentation as "the act of supplying with or using documents or references" [14]. The aim of any documentation is to make the documented facts available. In most cases, the focus of such documentations is the gathering of data itself instead of making existing data available.

The requirements for a modern wound documentation are far beyond traditional paper-based (even if converted into computer-based forms) documentation. The required medical features for wound documentation have already been well defined by experts. As stated by [8, 15], from a medical point of view, the following requirements are essential to ensure a modern and up-to-date wound documentation:

- Medical history (age of patient, wound history and wound anamnesis, social background, psychosocial situation and basic mood, attitude towards the condition, lifestyle, immune status, mobility, continence situation, blood flow, allergies, nutrition and fluid status, associated and metabolic diseases, surgeries, tumors, medication, pain, etc.)
- Wound assessment (localization, wound dimension, wound bed, exudate/transudate, smell, wound edge, neighboring areas of the wound, pain, infection, etc.)
- Wound duration and relapse number
- Therapy (compression therapy, pressure relief, movements and promotion of movements, pain therapy, therapy of wound smell and wound exudate, antiseptics, debridement, wound cleaning, wound dressings, management of malnutrition, dietary supplements, advising and education)
- General status of the patient
- Knowledge of the patients and their relatives
- Self-management of the patients and their relatives with regard to health care
- Individual schedule for measures
- Documentation of the measures and their efficacy.
- Result of a regularly carried out follow-up
- Traceability and verification of authors

7.2 Electronic Documentation

Especially if a documentation in relation to the patient's body location is needed, paper-based documentation is still in use due to the lack of possibilities in electronic documentation systems. However, paper-based wound documentation is no longer a valid alternative as the new requirements for a modern up-to-date wound documentation are far too complex.

Beside many others, Törnvall et al. confirmed a qualitative and quantitative advantage of an electronic wound documentation in a study on ulcers [13]. An electronic documentation provides better availability and evaluability of the collected data, easier exchange of information (for consultation of experts), easier access to resources, and creation of new medical knowledge. This contributes remarkably to an improved quality in wound management.

7.3 Structured Data

Advantages of free-text documentation are flexible terms, dynamic expressions, and a more effective recording by dictation. However, it has serious shortcomings: due to the linguistic variety and the lack of structure, there is no possibility for verification of quality and completeness. Free-text documentation often assumes implicit information [5] and data

M. Giretzlehner (✉)
Division of Medical Informatics, RISC, Johannes Kepler University Linz, Hagenberg im Mühlkreis, Austria
e-mail: michael.giretzlehner@risc.uni-linz.ac.at

L.-P. Kamolz (✉)
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria
e-mail: lars.kamolz@medunigraz.at

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_7

analysis beyond single patients is extremely difficult and error-prone.

A computer-assisted documentation alone does not necessarily create scientifically useful data. To ensure an optimal basis for data evaluation, a documentation system should provide clearly structured data for selection and avoid free-text documentation. This allows clear recording of facts at defined scopes, as for example the complete patient, a special condition or a single examination. Although the given information might sometimes be less extensive than in free-text documents [5], the quality of structured data is superior due to implicit context information and uniform terminology.

7.4 Wound Management

A wound must not be regarded as an isolated problem. To identify the general condition of the patient, it is important to evaluate the background of the problem situation, general medical history, information about mobility and pain, other disorders and limitations, psychic condition, etc. In complex medical cases, only the observation of a long time can bear findings of the adequacy of the current therapy approach.

Modern wound management requires multi-professional and interdisciplinary cooperation of various professions. Thus, a system is necessary, which can provide the relevant information clearly in due time and over large geographical distances.

7.5 Photo Documentation

As only the health care personnel who is directly participating in the dressing change can evaluate the status of the wound, it is essential to create high-quality photographic material as often as possible. Dressing changes often have to be done in a timely fashion, so details that might have remained unnoticed can be reviewed later on. This can help avoiding unnecessary dressing changes (i.e., just for reviewing the wound) and provide valuable information for other players in the interdisciplinary wound management team.

7.6 Data Standards

In order to enable knowledge extraction out of the collected data, it is necessary to merge them into a common data storage, with respect to all data security concerns. The merging of data from various sources is a big challenge as institutions operate different software tools, use different types of data storage structures, varying conventions, unequal time spans, diverse levels of data aggregation and different errors. Only a common established data standard and conform implementation of all systems of involved parties can address those problems appropriately [2].

7.7 Existing Documentation Systems

Despite Törnvall et al. [13] stated that filling out papers in wound documentation has plenty of shortcomings compared to a computer-assisted wound documentation, many institutions still use paper forms (or free-text-based electronic forms) for documentation and include them in the patient's file. Literature shows that most systems used in clinical practice do not meet the known requirements for a successful wound documentation. Many systems show deficits in the record of a thorough medical history of the patient [4]. Various solutions use given terms without stating their sources [4]. Most existing documentation systems do not include mechanisms to perform statistical evaluation of the collected data. Furthermore, only a few systems are able to gather data via mobile devices as for example laptops, tablet PCs, or smartphones. No existing documentation system has the ability to access evidence-based knowledge [4]. Most existing systems have a poor inter-rater reliability.

7.8 Documentation for Burn Injuries

Especially for the documentation of burns, a holistic documentation system has been developed during the last decade. It's called "BurnCase 3D" (www.burncase.at) and offers a wide library of 3D models, which can be precisely adapted for age, gender, height, and weight allowing for accurate burned surface area estimation regardless of body forms. The 3D model can be translated, rotated, and scaled along three axes. Physicians can represent burns by drawing on superimposed pictures of the burned areas onto this 3D model, allowing the burned surface areas to be automatically calculated by the system. The system enables a complete documentation of the whole treatment process from first assessment to outcome.

Parvizi et al. [10] has shown that a software tool, like BurnCase 3D, is a valid and reliable tool for the determination of percentage burned TBSA and documentation. Major improvements of modern burn care can be achieved by optimizing methods of burned TBSA determination and a complete comparable documentation set. Objective and validated documentation of wounds are needed for burn care as well as burn care research.

7.9 Research for Documentation Systems

Research for new approaches of holistic wound documentation is currently in progress by the Johannes Kepler

University Linz (RISC Software, Division of Medical informatics) in cooperation with an experienced team of physicians and nurses. Since 2002, the project team has worked on the burn injury documentation system *BurnCase 3D* [3], which is in clinical use worldwide. The aim of this follow-up research project is to make use of gained experiences and to develop a software system, which will revolutionize the documentation, evaluation, and therapeutic decisions in modern wound management.

According to the methods of action research [7], deductive and empirical methods and a synergy of practice and science in problem solving are used. These proposed solutions by science are being tested and improved in practice in the form of prototyping feedback loops.

7.10 Data Quality and Data Completeness

The research project aims to improve the quality of data acquisition by providing clear structured characteristics and collecting qualitative data with default specifications. To make terminology transparent, the system includes an encyclopedia with definitions and charts including references to their sources. Thus, the system guarantees that everyone involved in the treatment process can understand and interpret the provided data and information of the documentation correctly.

To assist in terms of completeness of the collected data, the system provides features for automatic reminding including visual feedback of obligatory fields and their status. Consequently, the users can see where essential information is missing at a glance.

7.11 Virtual Patients

Three-dimensional virtual patients adapted the physical constitution of the real patient by special computer algorithms are proved to be objective and accurate [10]. Pediatric patients are challenging due to varying size and body proportions, and appropriate proportionally correct 3D models are already available [12] (see Fig. 7.1).

Model adaptation algorithms for different body shapes are scope of currently ongoing research (see Fig. 7.2).

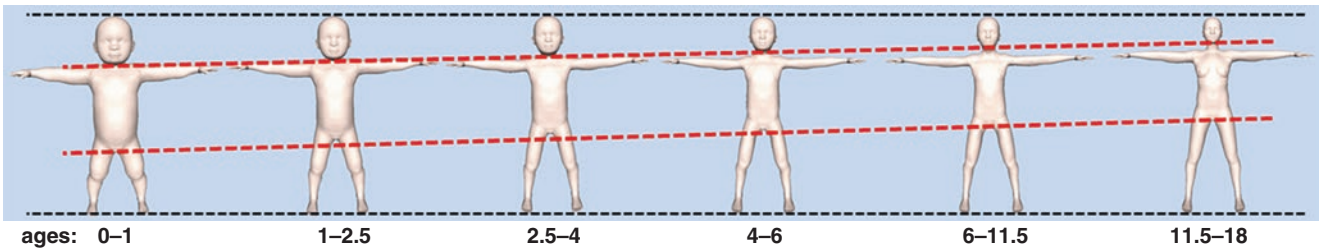


Fig. 7.1 Proportionally correct 3D models of pediatric patients

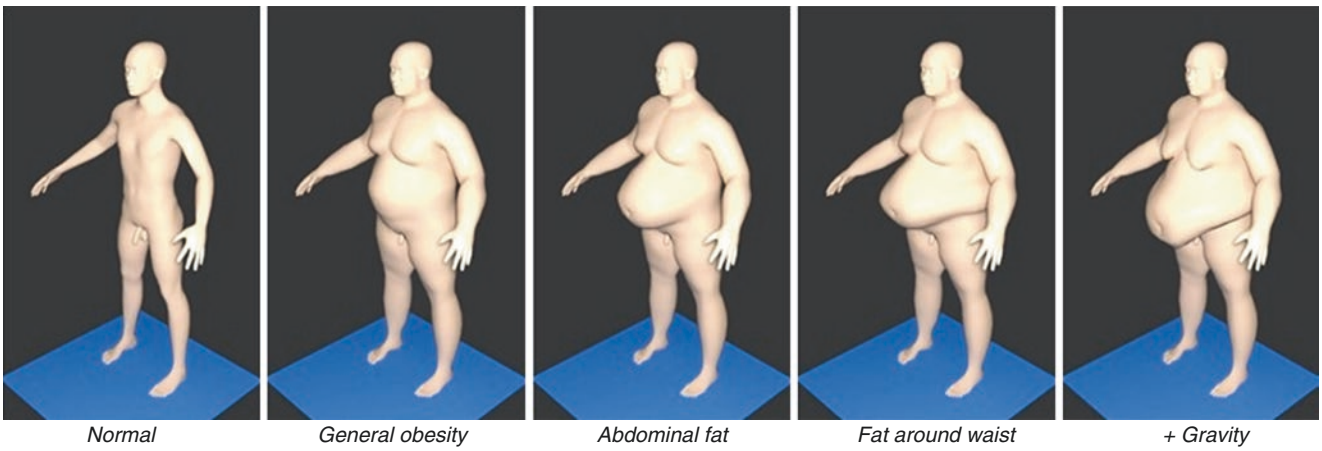


Fig. 7.2 Example for obese body shapes

7.12 Data Acquisition on Virtual Patients

Simple sketching on the virtual patients is used to document wound areas or therapy steps (see Fig. 7.3). This can be done by standard computer equipment (i.e., computer mouse) and does not demand any special hardware.

Virtual patient models provide the possibility to sketch or just drag-and-drop information about wound, dressings, clinical findings, documents, or photos. Different colors represent the types of documentation items (see Fig. 7.3). By placing items directly on body positions, swabs, or additional relevant items, wound infection and complications can be consistently documented and understood.

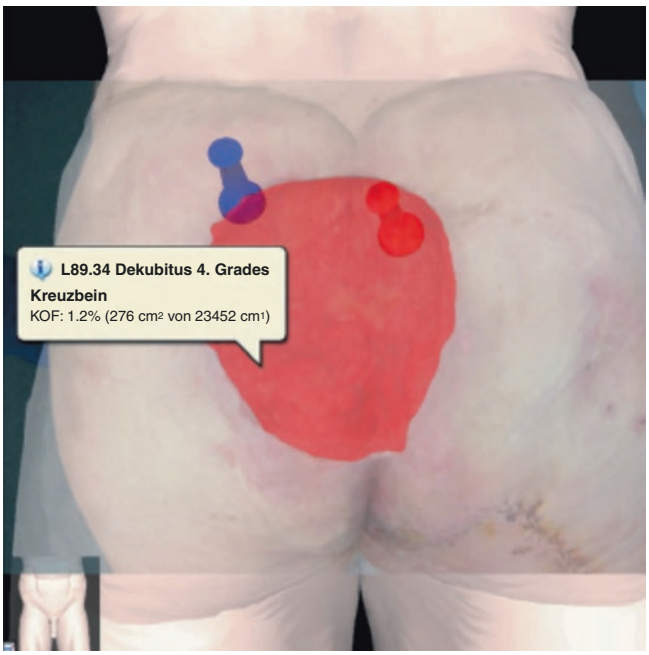


Fig. 7.3 Three-dimensional patient with wound and allocated information objects as digital photographs (blue pin) and wound swabs (red pin)

7.13 Photo Documentation on Virtual Patients

The possibility to integrate photos to the actual body localization is intuitive and beneficial. Plenty of photo documentation systems have the major drawback that it is difficult to find desired photos later on. By positioning photos directly on a virtual three-dimensional patient, they are assigned to point of time, body localization, and diagnosis automatically. This can accordingly support research and medical treatment, by easy access to pictures and their enclosed conditions. Due to the rapid development of cameras, smart devices, and 3D scanner, 3D photos are arising. However, conventional high-quality two-dimensional photos can still be considered as state of the art in medical routine. To be prepared of the up-coming improvement of 3D photos, both 2D and 3D photos can be positioned and projected to the 3D model (see Fig. 7.4).

A projection of a photo to a 3D patient model creates the ability to retain the three-dimensional character of the wound (see Fig. 7.5), which ensures an objective and quantitative evaluation of the wound. The information stored in the three-dimensional patient model can be used to derive medical codes as for example ICD (International Classification of Diseases). Documented photos should be accessible chronologically as well as an aggregated illustration of the history of each wound.

7.14 Data Analysis Beyond Single Institutions

Possibilities for data analysis make acquired data accessible and useful. Functionalities to extract data from databases, aggregate and prepare data for further evaluation without special IT-knowledge are the key to success [1]. Special improved software components can avoid technical hurdles

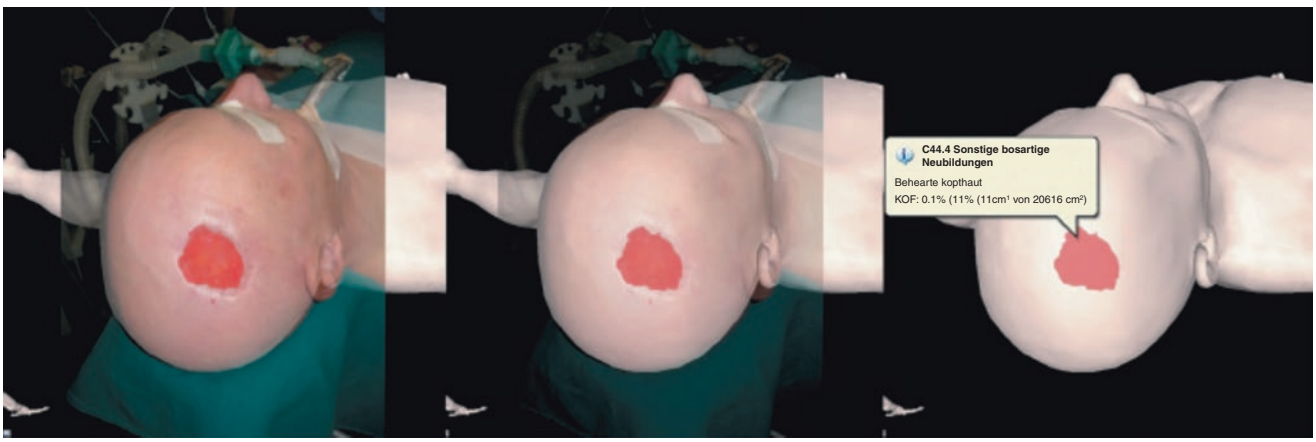


Fig. 7.4 Semi-transparent transition and transmission of wound information

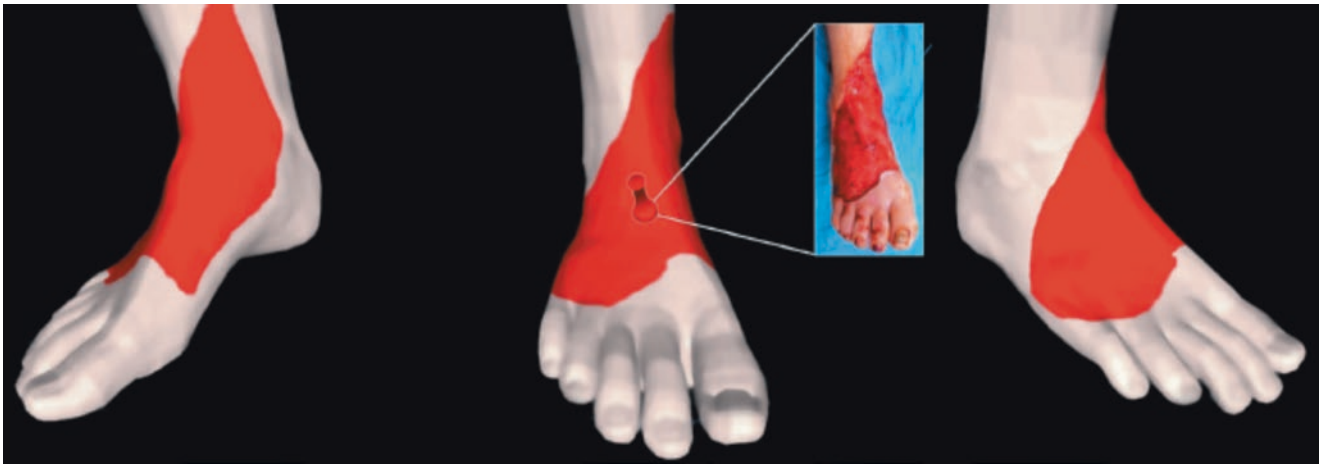


Fig. 7.5 The documentation on a 3D model retains the three-dimensionality

of data collection for studies and medical registries. Consequently, data of wound documentations is easily available to be compared and evaluated beyond single institutions. Arising multi-center data collections contain valuable information, which can serve as basis for further data-mining activities to extract knowledge and well-grounded new medical evidence.

In complicated medical cases, a second opinion or discussion with medical colleagues can bring new findings. Secure and protected transferring of the recorded patient data can provide a good overview of the situation of the patient due to complete documentation and the intuitive three-dimensional patient.

7.15 Including Evidence

The rather slow inclusion of new published evidence into medical daily routine is a well-known problem. Jonitz [6] states that new medical knowledge is generated faster than medical practice progresses. Sackett [11] defines evidence-based medicine as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients." The practice of this paradigm thus includes the need to find the best available, externally clinically relevant research results. The essential factors for such a computer aided knowledge based system are computer interpretable data and intelligent machine learning based search algorithms to find the best external clinical evidence in relevant medical scientific publication databases.

An integrated mechanism to access reliable knowledge for the patient at hand can highly contribute to increase the quality of treatment. An established standardized wound documentation and the possibility to compare collected data can contribute to an effective training of machine learning systems. The aim is to detect specific characteristics in the data and to make proposals concerning medical treatment alternatives. Applying this technique will generate possibilities to help physicians in their daily routine.

7.16 Mobile Documentation

Mobile phones are a rapidly expanding technology and facilitate the remote exchange of medical information in order to assist diagnosis and treatment [9]. Beside smart phones, tablets on basis of Android, iOS, and Windows will be more and more used for documentation. Therefore, a modern state-of-the-art computer documentation system has be able to run on different operating systems—especially for medical domains with a big number of actors (doctors, nurses, mobile wound manager, etc.). For this reason, a completely platform independent (e.g., HTML5-based) solution is needed (see Fig. 7.6).

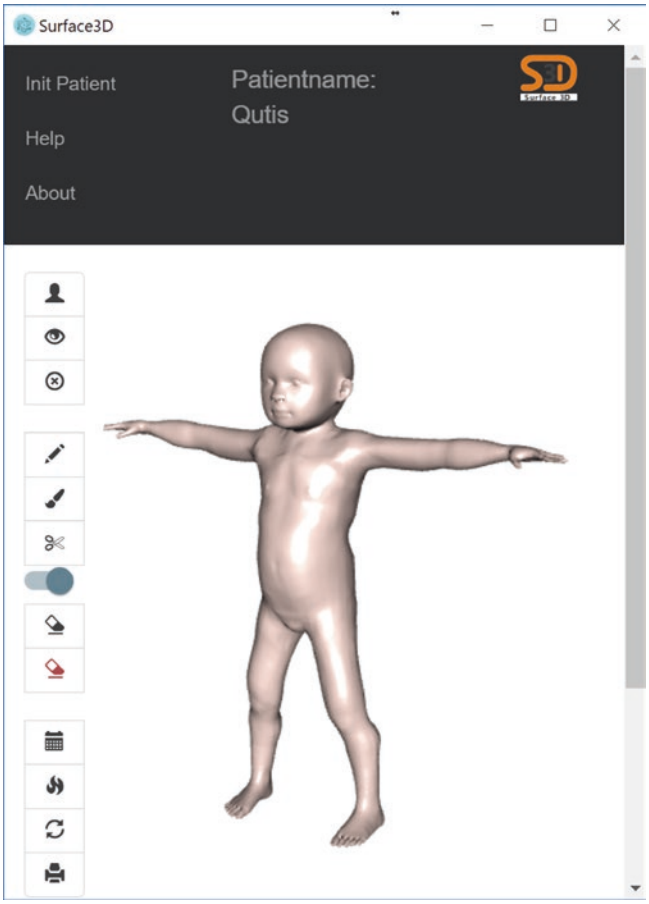


Fig. 7.6 Platform independent implementation of 3D documentation will run on Windows, MacOS, Android, and common web browsers

Summary

Various systems meet most of the required demands for a wound documentation system. However, they have shortcomings in concerns of data objectivity, data structures, missing definitions of terminologies, or data visualization. Functionalities for scientific data comparison (of more than a single medial institution) and data transfer mechanisms are rarely present but essential for advance in medicine.

A medical documentation system should be able to illustrate every single step of treatment and to present the complete condition of the patient at any point of time, over any local distance, to anyone involved in the treatment process.

By using the complete information of a high-quality documentation system, sufficient information can be extracted to optimize the treatment of the patient (e.g., avoid an unnecessary dressing change due to switchover of the health care team or general success of a therapy approach). This results in benefits for the patient (less pain, shorter healing time, etc.), reduced costs for medical institutions, and optimized outcomes.

There are ongoing research projects to solve existing problems and to provide the highest possible data quality. This can be achieved by well-structured data recording and objective three-dimensional determination of wound dimension and localization. The future of wound documentation will advance the daily routine of modern medicine and provides relevant medical information for all involved parties at stage of the treatment process.

References

1. Girardi D, Küng J, Kleiser R, Sonnberger M, Csillag D, Trenkler J, Holzinger A. Interactive knowledge discovery with the doctor-in-the-loop: a practical example of cerebral aneurysms research. Brain Inform. 2016;3:133–43. https://doi.org/10.1007/s40708-016-0038-2.
2. Giretzlehner M, Haller HL, Faucher LD, Pressman MA, Salinas J, Jeng JC. One burn, one standard. J Burn Care Res. 2014;1:1. https://doi.org/10.1097/BCR.0000000000000004.
3. Haller HL, Dirnberger J, Giretzlehner M, Rodemund C, Kamolz L. "Understanding burns": research project BurnCase 3D—overcome the limits of existing methods in burns documentation. Burns. 2009;35:311–7. https://doi.org/10.1016/j.burns.2008.07.010.
4. Hübner U, Flemming D, Schultz-Gödker A. Software zur digitalen Wunddokumentation: Marktübersicht und Bewertungskriterien. WundM. 2009;3(6):16–25.
5. Ingenerf J. Computergestützte strukturierte Befundung am Beispiel der Wunddokumentation. WundM. 2009;3(6):104–1.
6. Kunz R, Cox M. Lehrbuch evidenzbasierte Medizin in Klinik und Praxis: mit 85 Tabellen, 2., überarb. und erw. Aufl. Dt. Ärzte-Verl, Köln; 2007.
7. Österle T, Gutzwiller H. Ein Beispiel für die Analyse und das System-Design, 2. Hallbergmoos: AIT Angewandte Informations Technik; 1992.
8. Panfil E, Linde E. Kriterien zur Wunddokumentation – Literaturanalyse. Frankfurt: Hessisches Institut für Pflegeforschung; 2006.
9. Parvizi D, Giretzlehner M, Dirnberger J, Owen R, Haller HL, Schintler MV, Wurzer P, Lumenta DB, Kamolz LP. The use of teleemedicine in burn care: development of a mobile system for TBSA documentation and remote assessment. Ann Burns Fire Disasters. 2014;27(2):94–10.
10. Parvizi D, Giretzlehner M, Wurzer P, Klein LD, Shoham Y, Bohanon FJ, Haller HL, Tuca A, Branski LK, Lumenta DB, Herndon DN, Kamolz L-P. BurnCase 3D software validation study:

burn size measurement accuracy and inter-rater reliability. Burns. 2016;42:329. https://doi.org/10.1016/j.burns.2016.01.008.
11. Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ. 1996;312:71–2. https://doi.org/10.1136/bmj.312.7023.71.
12. Thumfart S, Giretzlehner M, Höller J, Ehrenmüller M, Pfurtscheller K, Haller HL, Kamolz L-P, Schmitt K, Furthner D. Proportionally correct 3D models of infants, children and adolescents for precise burn size measurement. Ann Burns Fire Disasters. 2015;28:9.
13. Törnvall E, Wahren LK, Wilhelmsson S. Advancing nursing documentation—an intervention study using patients with leg ulcer as an example. Int J Med Inform. 2009;78:605–17. https://doi.org/10.1016/j.ijmedinf.2009.04.002.
14. Publishers HC. Collins English dictionary. New York, NY: Harper Collins Publishers; 2017.
15. DNQP (Deutsches Netzwerk für Qualitätsentwicklung in der Pflege e.V.). Expertenstandard Pflege von Menschen mit chronischen Wunden, Fachhochschule Osnabrück.

8 Evaluation of Mimic Function in Patients with Facial Burns by Use of the Three-Dimensional Video-Analysis

Maria Michaelidou and Manfred Frey

Objective evaluation of facial motion has always been a challenging task. Many grading systems have been developed through the years, but they have often been inconsistently reproducible and subjective or they have not been able to take into account the three-dimensional aspect of facial movements. Facial burns cause also a functional impairment apart from the visible deformity of facial characteristics and the anticipated consequences from an aesthetic and psychosocial standpoint. The loss of facial skin and the resulting scar formation after conservative treatment or after skin grafting lead to an altered facial expression both in repose and during facial animation.

The need for development of an accurate system for evaluation of facial motion became urgent as reconstructive surgery in facial palsy progressed. The most commonly employed system for evaluation of facial movements in this setting is still the House–Brackmann scale in many centers, which was actually developed by otolaryngologists and primarily designed for the follow-up of Bell's palsy patients [1]. The scale, as such, serves as an approximate estimation of the overall state of palsy and thus serves as a tool for the total assessment of the patient, without enabling, however, precise separate and detailed information in regard to individual parts of the face. Moreover, the House–Brackmann scale is not based on actual measurements and is therefore fraught with a considerable degree of subjectivity.

Similarly, the paresis score system suggested by Stennert [2, 3] is also based on the subjective opinion of the examiner on whether each of the ten points constituting the system applies to the patient or not. Moreover, the paralyzed side is evaluated on its own without consideration of the contralateral healthy side. This leads sometimes to a faulty score of paresis, for instance when the statement upon the presence or not of a nasolabial sulcus must be marked as negative at a single patient and thereby increase the score of paresis although at this patient a nasolabial fold may not even be present at the healthy side, as in the case of young patients. Moreover, an ignoring of the contralateral healthy side in the estimation of the extent of the paresis leads to a neglect of individual patterns of smile, a problem that is best reflected when it comes to the points eight and nine of the system.

Johnson et al. described in 1994 [4–6] a quantitative method known as the maximum static response assay of facial motion for the evaluation of the success of functional free muscle transplantation in patients with chronic facial paralysis. Although the attempt to express the extent of paralysis in numbers and, thus, objectify the postoperative outcome was a well-justified one, still this method was actually projecting a three-dimensional motion into a two-dimensional distance. Gross et al. [7] showed in 1996, however, that projecting 3D into 2D data leads to loss of accuracy of measurement because three-dimensional amplitudes are significantly larger than the two-dimensional amplitudes.

First attempts to overcome the limitation of two-dimensionality of the existing evaluation systems were yielded with success in 1992, when Frey et al. introduced a new documentation system for facial movements as a basis for the International Registry for Neuromuscular Reconstruction in the face [8, 9]. The system, called VICON, enabled for the first time a three-dimensional motion analysis based on the measurement of movements of standardized static and dynamic points in the face during standardized mimic activities. Although this system was very useful for research purposes, it was too complicated for daily clinical application.

In 1994 an electronic instrument, called faciometer®, was introduced by Frey et al. in order to measure excursions of facial landmarks during animation after reconstruction in case of facial palsy [10]. The faciometer® consisted of calipers connected to a digital display, which showed the distance between the tips of the calipers [10].

Due to significant advances in computer technology, particularly in the field of image analysis, it became possible to achieve a three-dimensional analysis of a two-dimensional

M. Michaelidou (✉) · M. Frey
International Center for Facial Nerve Surgery,
Confraternität, Vienna, Austria
e-mail: office@entdecke-schoenheit.at

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_8

video taken during the course of a facial movement. This new system was completed and installed for the first time in the Laboratory for Movement and Image Analysis at the Division of Plastic and Reconstructive Surgery, Department of Surgery, Medical School of Vienna in January of 1998 [11]. Since then, the evaluation of all patients treated for facial paralysis at the abovementioned institution was performed by use of this system, which has become the standard tool for the preoperative documentation, for the planning of the treatment, and for the postoperative monitoring and evaluation of the operative outcome.

The system consists of three main components (Fig. 8.1):

- The data acquisition system which includes the following:
  - A sample mirror system, consisting of two special mirrors arranged under a constant sharp angle and a comfortable seat placed underneath of them so that the patient's head is positioned between the two mirrors in a way that complete images of the patient's face can be obtained and all marked points are seen by the camera in both mirrors at the same time.
  - A calibration grid, which is essential for the definition of the three-dimensional space prior to every recording session.
  - A digital video camera (Sony DCR-CX700E®) for the recording of the films.
  - Computer station, where the recorded sequences are transferred using DV Manager® 1.7 (FAST Multimedia mInc., Woodinville, WA, USA) and edited by a program of analysis.
- The data analyzing system with the following components:
  - Ulead®5-Video Editor software (Ulead Systems Inc., Torrance, CA, USA) for the selection of the most suitable sequences and
  - Facialis® software (Laboratory of Biomechanics of the Swiss Federal Institute of Technology, Zurich, Switzerland) for video editing.
- The data visualization system: a specially designed program for presenting the data processed through the Facialis® software, called FaciShow® (Laboratory of Biomechanics of the Swiss Federal Institute of Technology, Zurich, Switzerland). The program enables the demonstration of landmarks both in two- and in three-dimensional perspective for every single movement as well as the demonstration of excursions of landmarks at each phase of the animation (Fig. 8.2). Additionally, the whole video clip for each and every

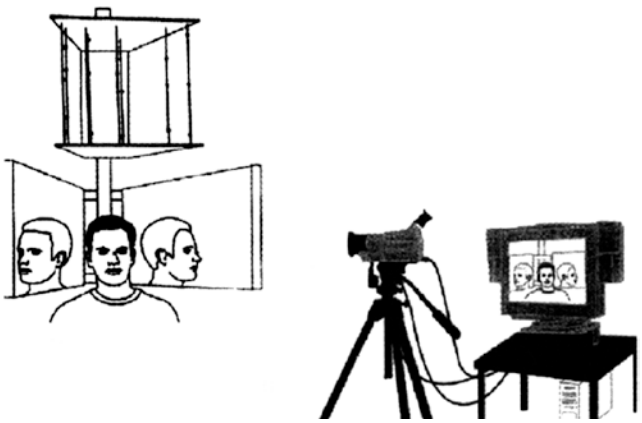


Fig. 8.1 Schema of the three-dimensional video-analysis system [11]

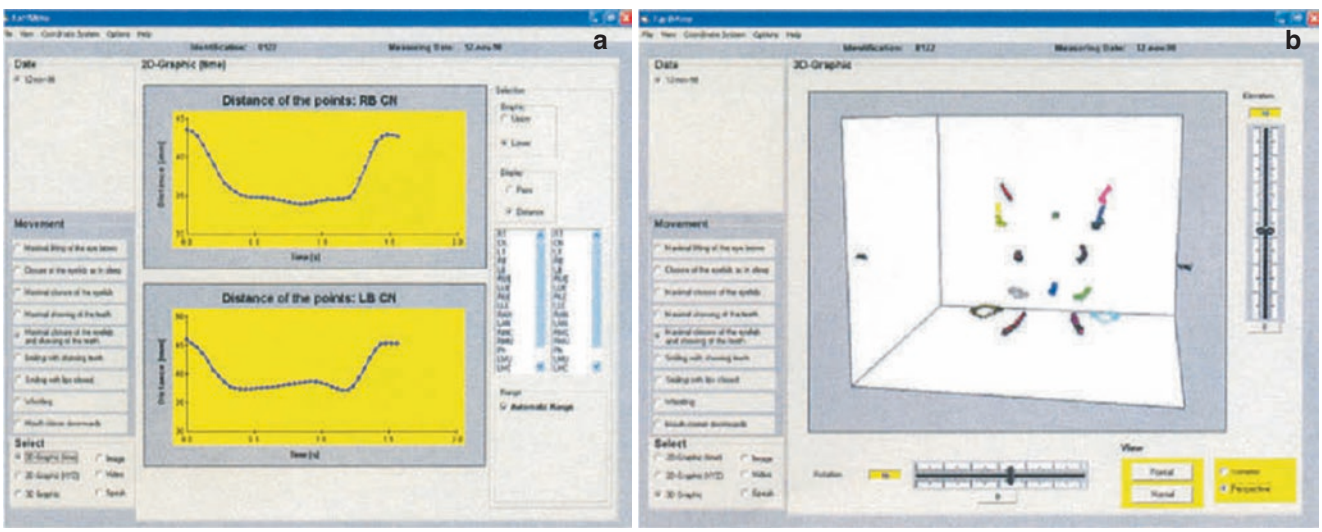


Fig. 8.2 FaciShow®: (**a**) graphical two-dimensional representation of the distances between landmarks of the face and (**b**) visualization of the movement of each landmark during the whole course of motion in a three-dimensional perspective [12]

movement can be reviewed or the picture of the patient's face both in repose and in the endpoint of every movement can be seen.

The procedure of data acquisition follows a standard pattern which has been described by Frey et al. extensively [11–15] and is cited here in summarized form.

A selection of 18 standard reproducible anatomical landmarks on the face, of which three are static and 15 are dynamic (Table 8.1 and Fig. 8.3), are marked on the patient's face. A permanent marker is used to place a 2 mm black dot at each of the dynamic landmarks. The static points are marked with a plastic light ball 5 mm in diameter. All markings, except the points central nose and philtrum, are made on both sides of the face.

Each patient is videotaped under standard conditions. All recordings are made in the same room, in the same chair and by the same examiner. Light from four 1000 W Halogen

Table 8.1 Abbreviations of the standardized facial landmarks [11]

Abbreviations of the standardized facial landmarks [11]	
Central nose	CN
Left ala of the nose	LAN
Left brow	LB
Left lower eyelid	LLE
Left mouth corner	LMC
Left midlateral point of the lower lip	LML
Left midlateral point of the upper lip	LMU
Left tragus	LT
Left upper eyelid	LUE
Philthrum	PH
Right ala of the nose	RAN
Right brow	RB
Right lower eyelid	RLE
Right mouth corner	RMC
Right midlateral point of the lower lip	RML
Right midlateral point of the upper lip	RMU
Right tragus	RT
Right upper eyelid	RUE

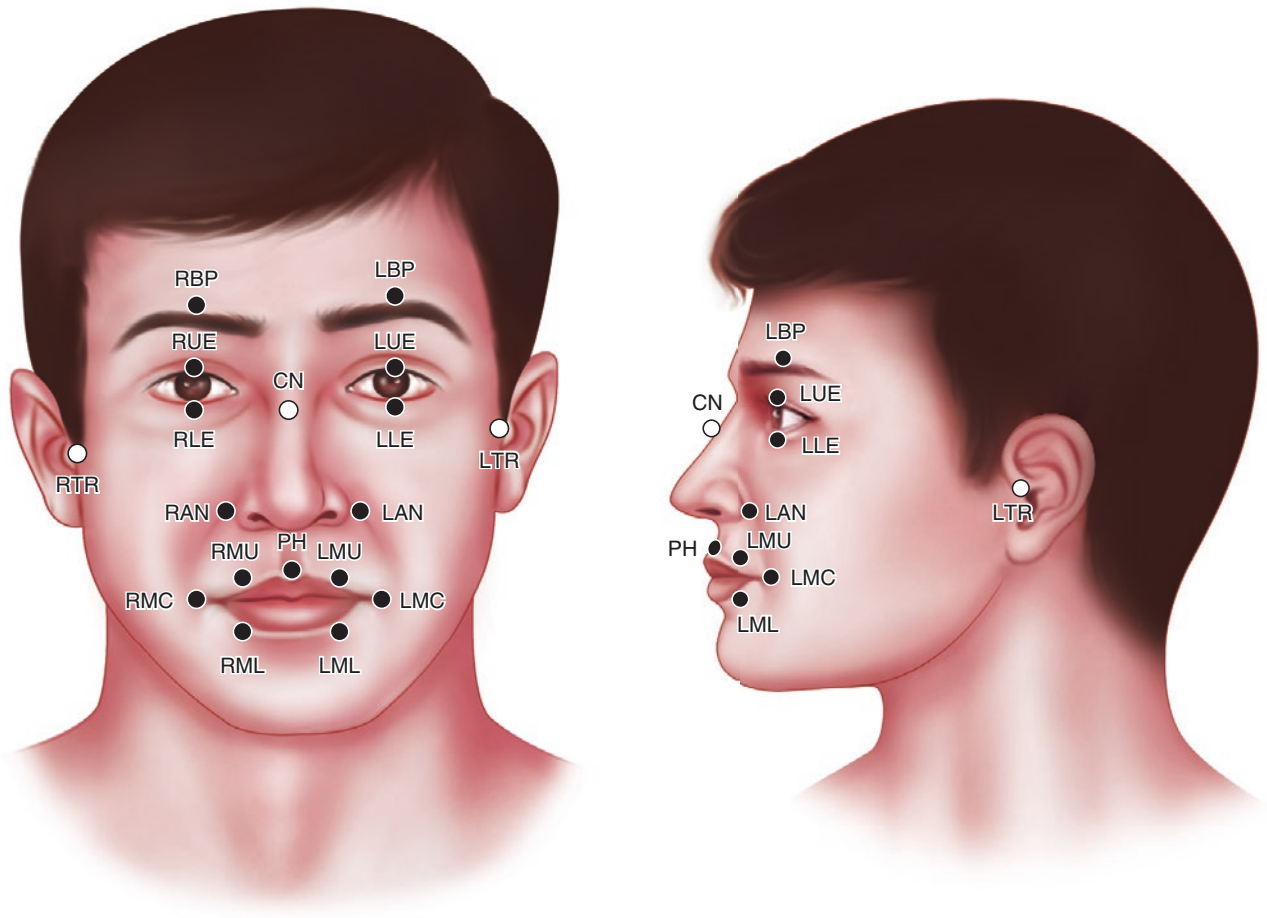


Fig. 8.3 The locations of the static and dynamic landmarks on the face in frontal and lateral view [8]

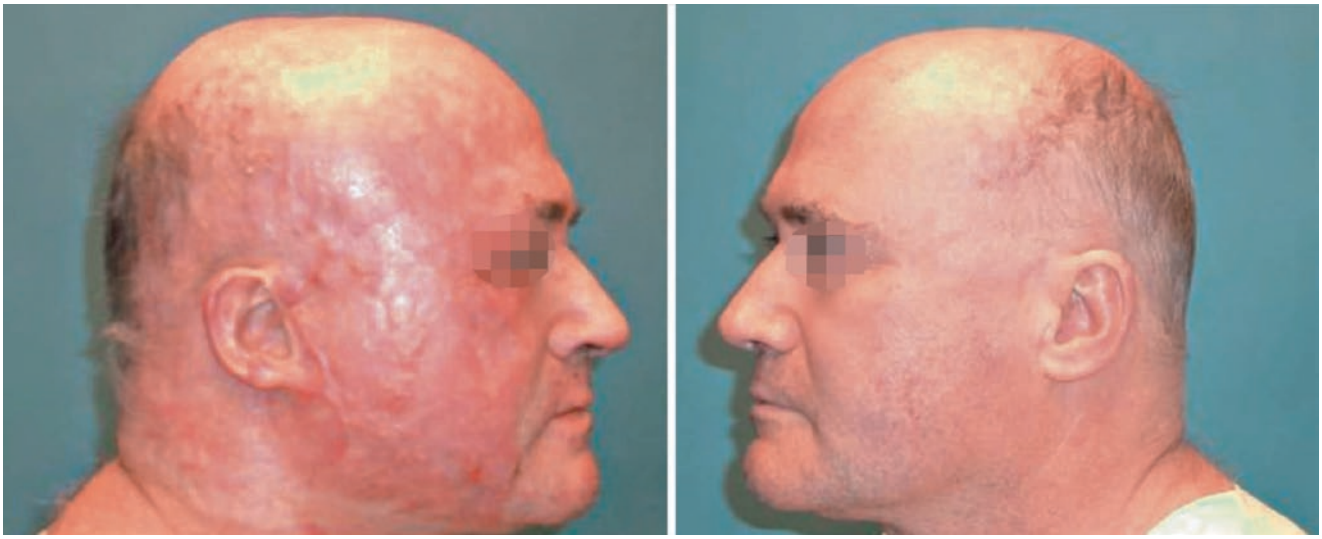


Fig. 8.4 Male patient with facial burn scars of the right hemiface from a lateral point of view [16]

Photo-optic lamps (Osram, Munich, Germany) is used to generate uniform, symmetrical and standardized lighting.

The patient sits relaxed and upright in a normal chair without head support, eyes looking forward into the camera, which is positioned 5 m away. After the patient has been positioned in the calibrated measurement field, a series of nine standardized facial animations are performed in a sequential order after a verbal signal.

Three repetitions of each set of facial animations are digitally collected through a video camera in real time with a sampling rate of 25 pictures per second and transferred to a computer, where the most suitable video sequence out of the three is edited and saved as video (.avi) and image (.uis) files. The selected data is then analyzed by the means of Facialis software [11] (Laboratory for Biomechanics, Swiss federal Institute of Technology, Zurich, Switzerland), which calculates the 3D coordinates of landmarks on the face. The processed data can then be visualized by the FaciShow software [11] (Laboratory for Biomechanics, Swiss federal Institute of Technology, Zurich, Switzerland). Two-dimensional (2D) and three-dimensional (3D) trajectories of each landmark during movement can be presented. This procedure is performed in every patient before every operative step and 6, 12, 18 and 24 months after surgery.

After having applied the system of three-dimensional video-analysis in order to evaluate results after reconstructive surgery in cases of facial palsy [15, 17, 18], we applied the system also in patients with facial burns that had been treated by excision and grafting with allogenous keratinocytes [16]. The results of facial analysis of these patients were compared with the values of healthy volunteers who had already been analyzed in the same fashion in a previous study [12]. The burn patients showed on average smaller excursions of landmarks during facial animation and higher degree of static asymmetry than healthy volunteers. As in the case of healthy volunteers, the degree of asymmetry after animation of the face was smaller than in repose, i.e., static asymmetry was higher than dynamic asymmetry [16].

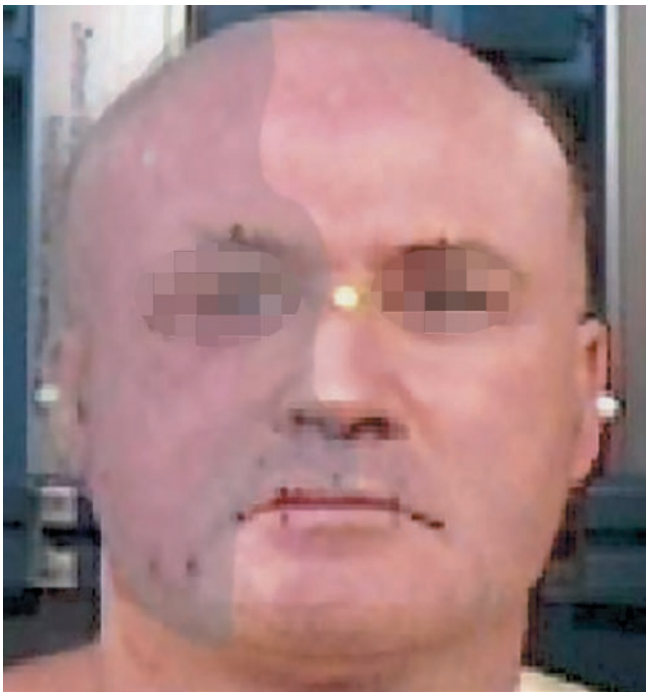


Fig. 8.5 The same patient as in Fig. 8.4 from a frontal point of view. The gray marking displays the extent of facial scar formation on the right hemiface [16]

In Fig. 8.4, a male patient with facial burns is presented and the use of the three-dimensional system of video-analysis for quantification of the impact of the resulting scars on the static symmetry of the face and the facial motion is explained. In this patient, the burn injury affects only the right hemiface (Fig. 8.5). The overall scar formation affecting the entire right hemiface leads to a lateral displacement of the mouth

Table 8.2 Distance of the tragus to the mouth corner (TR-MC) and central nose point to the middle upper lip point (CN-MU) on the right and the left hemiface in repose and at the endpoint of motion [16]

	Repose	Right hemiface			Left hemiface		Asymmetry	
		Endpoint of motion	Amplitude	Repose	Endpoint of motion	Amplitude	Repose	Amplitude
TR-MC	100.50	94.64	5.86	101.45	93.54	7.91	0.95	2.05
CN-MU	64.46	63.10	1.36	66.79	64.50	2.29	2.33	0.93

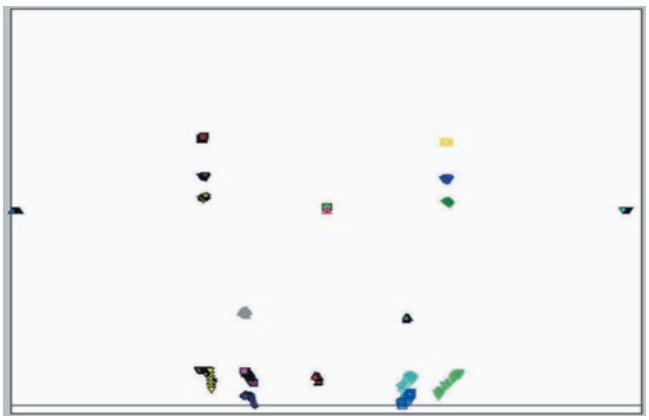


Fig. 8.6 Three-dimensional view of all static and dynamic points of the face of the patient in Figs. 8.4 and 8.5 during the motion "smiling with lips closed"

corner and a cranial displacement of the middle upper lip point on the right side. Thus, there is a shortening of the distance of the mouth corner to the tragus and a shortening of the distance of the central nose point to the middle upper lip point on the right side of the face compared to the left one. As a consequence, the amplitude of motion of the mouth corner to the tragus and of the middle upper lip point to the central nose point is shorter on the right side of the face than on the left one. The three-dimensional video-analysis confirmed these observations (Table 8.2). In Fig. 8.6, a three-dimensional view of all static and dynamic points of the face of this patient during the motion "smiling with lips closed" is displayed. A different course of motion of the corner of the mouth, the upper middle and lower middle lip point are observed on the right hemiface compared to the left one.

In future, we will consider the use of three-dimensional video-analysis in order to quantify the impact of facial scars and the impact of different concepts of treatment (conservative vs. operative treatment, reconstruction with keratinocytes vs. skin grafts vs. artificial agents such as Integra®, Matriderm®, Acticoat®) on the static symmetry of the face and on the facial motion.

References

1. House JW. Facial nerve grading systems. Laryngoscope. 1983;93:1056–69.
2. Stennert E, Limberg CH, Frentrup KP. Paralysis and secondary defect score. In: Miehkle A, Stennert E, Chilla R (eds) new aspects in facial surgery. Clin Plast Surg. 1979;6:458.
3. Stennert E, Limberg CH, Frentrup KP. Pareseund Defektheilungs-Index. HNO. 1977;25:238–45.
4. Bajaj-Luthra A, Müller T, Johnson PC. Quantitative analysis of facial motion components: anatomic and nonanatomic motion in normal persons and in patients with complete facial paralysis. Plast Reconstr Surg. 1997;99:1894.
5. Johnson PC, Brown H, Kuzon WM, Balliet R, Garrison J, Campbell J. Simultaneous quantification of facial movements: the maximal static response assay of facial nerve function. Ann Plast Surg. 1994;32:171.
6. Johnson PJ, Bajaj-Luthra A, Llull R, Johnson PC. Quantitative facial motion analysis after functional free muscle reanimation procedures. Plast Reconstr Surg. 1997;100:1710.
7. Gross MM, Trotman CA, Moffat KS. A comparison of three-dimensional and two-dimensional analyses of facial motion. Angle Orthod. 1996;66:189.
8. Frey M, Jenny A, Giovanoli P, Stüssi E. Development of a new documentation system for facial movements as a basis for the international registry for neurovascular reconstruction in the face. Plast Reconstr Surg. 1994;93:1334–49.
9. Stüssi E, Handschin S, Frey M. Quantifizierung von Gesichtsasymmetrien. Eine Methode zur Objektivierung von Beeinträchtigungen der Gesichtsmotorik: eine Pilotstudie. Biomed Tech. 1992;37:14–9.
10. Koller R, Kargül G, Giovanoli P, Meissl G, Frey M. Quantification of functional results after facial burns by the Faciometer®. Burns. 2000;26:716–23.
11. Frey M, Giovanoli P, Gerber H, Slameczka M, Stüssi E. Three-dimensional video analysis of facial movements: a new method to assess the quantity and quality of the smile. Plast Reconstr Surg. 1999;104:2032–9.
12. Giovanoli P, Tzou C-HJ, Ploner M, Frey M. Three-dimensional video-analysis of facial movements in healthy volunteers. Br J Plast Surg. 2003;56:644–52.
13. Frey M. Smile reconstruction using the gracilis muscle. Oper Techn Plast Reconstr Surg. 1999;6:180–9.
14. Frey M, Giovanoli P. The three-stage concept to optimize the results of microsurgical reanimation of the paralyzed face. Clin Plast Surg. 2002;29:1–24.
15. Frey M, Michaelidou M, Tzou CH-H, Gerber H, Stüssi E, Mittlböck M. Three-dimensional video analysis of the paralyzed face reanimated by cross-face nerve grafting and free gracilis muscle transplantation: quantification of the functional outcome. Plast Reconstr Surg. 2008;122(6):1709–22.
16. Eggert S (2010) Quantitative analyse der Gesichtsmotorik nach Verbrennungen mit dem system der Drei-Dimensionalen video-analyse. Doctoral thesis, Medical University of Vienna, Austria.
17. Michaelidou M (2004) Comparison of surgical methods for reanimation of the paralyzed face by use of 3D-video-analysis. Doctoral thesis, Medical University of Vienna, Austria.
18. Michaelidou M, Tzou CH-H, Gerber H, Stüssi E, Mittlböck M, Frey M. The combination of muscle transpositions and static procedures – a useful concept for reconstruction in the paralyzed face of the patient with limited life expectancy or who is not a candidate for free muscle transfer. Plast Reconstr Surg. 2009;123(1):121–9.

Rehabilitation and Scar Management

9

Lars-Peter Kamolz and Marc G. Jeschke

9.1 Introduction

Survival was once the key parameter of success in managing serious burns, but due to improvements concerning burn care this has changed tremendously. Today, however, the aim of all treatment activities is the return of burn patients back into their private and social life under conditions, which allow independence and social sovereignty. This goal has extended the traditional role of the burn care team beyond wound closure.

Three broad aspects are involved in this effort: rehabilitation, reconstruction, and reintegration. Modern burn care may be divided into the following four general phases [1]:

- The first phase, initial evaluation and resuscitation, occurs on days 1–3 and requires an accurate fluid resuscitation and thorough evaluation for other injuries and co-morbid conditions.
- The second phase, initial wound excision and biologic closure, includes the manoeuvre that changes the natural history of the disease. This is accomplished typically by a series of staged operations that are completed during the first few days after injury.
- The third phase, definitive wound closure, involves replacement of temporary wound covers with a definitive cover; there is also closure and acute reconstruction of areas with small surface area but high complexity, such as the face and hands.
- The final stage of care is rehabilitation, reconstruction, and reintegration. Although this begins during the resuscitation period, it becomes time-consuming and involved toward the end of the acute hospital stay.

9.2 Rehabilitation in the Critically Ill Burn Patient

Burn rehabilitation is undeniably difficult and time-consuming, but the time spent is worthwhile [2–6]. For every member of the burn team, rehabilitation must start from the time of injury on, but the final obtainable treatment goals and strategies can vary, depending on the patient's injury, age, and co-morbidities.

In critically ill patients, the primary goals of rehabilitation are:

- Limitation of the loss of range of motion (ROM)
- Oedema reduction
- Prevention of predictable contractures

If a body part is left immobile for a prolonged period of time, capsular contraction and shortening of tendon and muscle groups (which cross the joints) occur. Contractures often develop, if wounds are not closed promptly and adequately.

Several predictable contractures that occur in patients with burns can be prevented by a proper ROM, positioning, and splinting programmes [1].

- Passive ROM is best performed twice daily, with the therapist taking all joints through a full ROM (Fig. 9.1). The therapist must be sensitive to the patient's pain, anxiety, wound status, extremity perfusion, and security of the patient's airway and vascular access.
- These procedures should be performed in coordination with the ICU staff. Attention to the security of endotracheal tubes, nasogastric tubes, and arterial and central

L.-P. Kamolz (✉)
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

COREMED - Cooperative Centre for Regenerative Medicine, Joanneum Research Forschungsgesellschaft mbH, Graz, Austria
e-mail: lars.kamolz@medunigraz.at

M. G. Jeschke
Sunnybrook Health Sciences Centre, Ross Tilley Burn Centre, Toronto, ON, Canada

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_9

Fig. 9.1 Passive mobilization

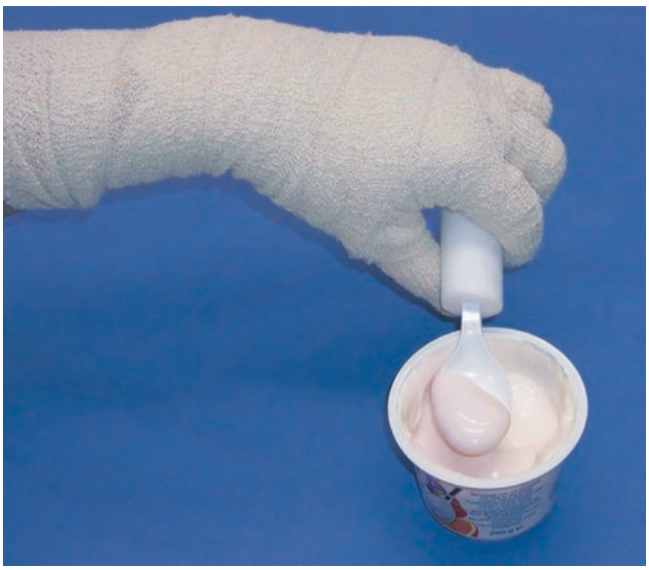


Fig. 9.2 ADL training

venous catheters is paramount, as an unexpected loss can contribute to morbidity and mortality.
- Proper antideformity positioning minimizes shortening of tendons, collateral ligaments, and joint capsules; moreover, it reduces oedema formation.
- Inspect all splints at least daily for evidence of poor fitting or pressure injury.

Oedema reduction should be encouraged from admission on. The only body system that can actively remove excess fluid and debris from the interstitium is the lymphatic system. The principles of oedema reduction should be performed:

- Compression
- Movement
- Elevation or positioning of limbs
- Maximization of lymphatic function

Beside the factors range of motion (ROM), oedema reduction, and prevention of predictable contractures, a long-term relationship has to be established with the patient and family members to ensure compliance with therapy goals and to increase the patient's morale for recovery. Moreover, adequate pain control is important for long-term compliance of the patient. The factors compliance and pain control will become even more important in the later phase of rehabilitation.

9.3 Rehabilitation in the Recovering Burn Patient

As critical illness abates and wounds progressively close, the roles of the physical and occupational therapists (as well as the demands on the patient) expand and become more difficult. Patients become more aware of what has happened to them, and they can become fearful of the therapist and the associated potentially uncomfortable procedures.

- The principal components of burn therapy [2–6] that characterize this period include the following:
  - Continued passive ROM
  - Increasing active ROM and strengthening
  - Minimizing oedema
  - ADL training (activities of daily living) (Fig. 9.2)
  - Scar management
  - Preparing for work or play or school

Long-term favourable outcome requires hard work during this period, but it is important for the therapist not to push too hard. An early programme of passive ROM greatly facilitates successful retention of normal ROM during this period. Intraoperative ROM also can be useful; in coordination with the operating room team, passive ROM can be performed between induction of anaesthesia and preparation of the surgical site. Other manoeuvres that can be used to increase the patient's tolerance for passive ROM are the timing of the ROM session at the end of the dressing changes performed under pain medication.

- Burned and grafted extremities commonly have oedema that can contribute to joint stiffness. Reducing this oedema facilitates rehabilitation efforts.
  - In the early phase, the use of self-adherent elastic will help to reduce digital oedema. Tubular elastic dressings, elastic wrap dressings, elevation, and retrograde massage also help reduce extremity oedema.
- As definitive wound closure nears and hospital discharge approaches, the focus of rehabilitation efforts becomes

practical. Performance of ADL tasks and the impending return to play/school/work are important considerations.
  - Resisted ROM, isometric exercises, active strengthening, and gait training are important objectives.
  - When treating children, it is important to use developmentally appropriate play to facilitate rehabilitation goals.
- For many burn patients, the first 18 months after discharge are more difficult than the acute stay. The principal rehabilitation goals at this time include the following:
  - Progressive ROM and strengthening
  - Evaluation of evolving problem areas
  - Specific postoperative therapy after reconstructive operations
  - Scar management

Unfortunately, it is not uncommon for ROM and strength to be lost during the first months after discharge. The burn unit team should monitor the quality of outpatient rehabilitation services during routine clinic visits at the burn unit. If the patient is losing substantial ROM and strength due to inadequate therapy, readmission for focused rehabilitation efforts is appropriate and recommended.

9.4 Non-surgical Scar Management

The treatment of scars is a big challenging process and important part in the rehabilitation programme. Scars can lead to emotional conflicts and psychosocial problems, but beside these aesthetic and emotional problems scars can cause also important functional restrictions and impairments. Due to the fact that the process of the hypertrophic scarring begins often after discharge and may last for several month and years, a need for special aftercare especially during the first 12–24 months is needed.

Although the process of the scar maturation is not fully understood yet, several approaches are propagated for non-surgical scar management.

9.4.1 Compression Therapy

As early as possible compression therapy should be performed by use of special customized compression garments (Figs. 9.3 and 9.4). Compression therapy helps to provide functionally and aesthetically satisfying scars and reduces the need for surgical scar revisions. By use of compression, good and satisfactory results can be achieved in 85% of the patients suffering from hypertrophic scars [7, 8], because as long as the scars are active, they can be influenced by compression. The exact mechanism of action is not cleared yet, but there is clear evidence that continuous pressure reduces the blood flow within the scar and thereby its activity. The metabolism of the scar is reduced and local ischemia and hypoxia is resulting in a reduced proliferation and activity of the fibroblasts and thereby of the collage synthesis [9]. Thereby excessive scaring is decreased [10].

Fig. 9.3 Custom-made compression garments

Fig. 9.4 Special compression gloves plus additional pressure for the web spaces

Wounds which heal within 14–21 days have a lower chance to develop hypertrophic scars, but if wound healing takes longer than 21 days, there is a higher chance to develop hypertrophic scars and a compression therapy is an absolutely must [10] for a period of several months (in children often also more than 2 years until the scars are mature) and should be worn 24 h daily.

The optimum compression pressure, which should be exerted onto the scar, is discussed still controversially [11–14]. A pressure of 10 mmHg is probably enough to reduce scars and a pressure more than 40 mmHg is possibly not good for the skin and can cause nerve irritations and pain. The compression pressure, which is generated with compression clothes, amounts approx. 24–28 mmHg; this is more or less identical with the capillary pressure, which amounts around 25 mmHg.

9.4.2 Pressure Pads

Problems concerning compression therapy can occur in unfavourable localizations, above all in concave surfaces, as for example in the area of the sternum and the face. These are only hardly accessible to a suitable compression treatment. Mostly, a combination with special pads (pelotte), which can exert additional pressure, is useful. Pressure pads are made from different materials as for example from silicone gel, elastomeric and different plastic materials. The used material should be chosen depending on scar maturation and on the skin status of the patient. In general, one begins with a soft, thin and elastic pad and exchanges this with the time for harder and stronger pressure-exercising pads.

9.4.3 Hydration and Silicone

Silicone has been used with great success in order to reduce hypertrophic scars; hydration or the silicone related prevention of wound desiccation appears to be the contributing mechanism. Hydration seems to inhibit the fibroblast related production of collagen and glycosaminoglycans. Silicone gel sheets can be worn 24 h daily. Beside gel sheets [8], there are also silicone gels [7] available; they are normally applied twice a day after suture removal. Both silicone sheets and gels seem to have positive influence on scare size and erythema reduction. The use is not limited to prophylactic scar treatment, but also for improving pre-existing hypertrophic scars. The advantages of this kind of the scar treatment are the easy use and the quick improvement of the clinical symptoms.

9.4.4 Lubricants and Solar Exposition

Due to the functional impairment, special skin care is needed after a burn injury. Hydration protects the skin against dryness. Special oils and creams, which do not irritate the skin, should be applied several times daily.

The patients should be cleared up thoroughly about the fact that the scars in the first year after a burn injury may be put out by no means to the direct sun. The danger of sunburn is very big and the scars will become probably darker in the sun. This discoloration is lasting and makes the scars even more remarkable. Solar cream with a solar protection factor from at least 30 as well as adequate sun protection clothing is strictly recommended [15].

9.4.5 Creams/Salves

There is a great variety of creams for conservative scar management on the market; many of them are used, but few of them enjoy medical acceptance. A lot of these creams are vitamin based or contain herbal extracts. Vitamin E, a lipid soluble antioxidant in skin has been used to reduce oxygen radicals, which alter collagen and glycosaminoglycan production. Topical Vitamin A has been used as a superficial resurfacing agent. Softening and flattening of scars are presented in the literature, but the use is not generally recommended. Other natural sources for scar improvements are on the market, but their efficacy is still under heavy discussion.

9.4.6 Scar Massage

Massage is a very good treatment option in order to improve the mobility of joints in the case of rigid scars. Rigid scar ropes are thereby dissolved and the scar becomes softer, more elastic, and more pliable. In the acute phase, only a local pressure should be applied to the scar. Furthermore, no special massage creams should be used in this early phase. If the skin tolerates friction, the scar can be manipulated by rotary and stroking movements under use of special oils and creams. It is recommended to carry out the massage at least twice daily. An electric massage device can be also used with additional heat application. Heat relaxes the tissue and raises the elasticity, so that the scars can be better mobilized. Here paraffin wax hydrotherapy and ultrasound are used with success. Conscientious scar massage can be effective in limited areas of scarring; it is also convenient, because it can be performed by family members.

9.4.7 Cortisone Treatment

In the non-surgical scar management, cortisone therapy has a firm place [16–18]; it is mainly used for the treatment of hypertrophic scars and keloids. The application of steroids can reduce collagen synthesis up to 60% [16]. Moreover, there is a significant reduction of glycosaminoglycan- and

hyaluronic acid synthesis by use of steroids. This leads to the decrease of the extracellular matrix and thereby to a scar reduction. Intralesional injections are often performed every 4–6 weeks. They can be used alone or as an adjunct to other treatment modalities. It is often used in combination with compression and/or excision and post-surgical radiation [16]. The most frequent side effects are atrophy and hypopigmentation around the injection places [17].

9.4.8 Antimitotic Drugs

A new intralesional scar treatment option is mainly based on antimitotic drugs such as bleomycin and 5-fluorouracil (5-FU).

9.4.9 Verapamil

The intralesional injection of the calcium channel blocker Verapamil seems to be a new promising option for the treatment of hypertrophic scars and keloids. In a recent study, Verapamil was injected into the wound edges directly after the scar and keloid excision [19–21].

9.4.10 Laser

Hypertrophic scars, keloids, and mild to moderate acne scars may benefit from skin resurfacing procedures using the carbon dioxide (CO_2) laser and the Nd YAG laser [22, 23].

9.4.11 Radiotherapy

Nowadays the application of radiotherapy in the conservative scar treatment is critical because of its potential side effects and risks like radiodermatitis, ulceration, and tissue atrophy, but there are also many reports available that this kind of treatment option is still useful and should be taken into account for scar treatment, especially after keloid excision [24].

9.4.12 Soft Tissue Augmentation

Atrophic and depressed scars may also benefit from filling procedures. There are different fillers available on the market. Collagen and collagen with fibroblasts are quite popular. Live cell transfer has been advocated as a long-lasting solution for tissue augmentation. Lipotransfer has become popular for scar treatment, because it seems that fat cell transfer is not only able to improve volume and contour, but also to improve skin quality [25].

9.5 Conclusions

The ultimate goal of all burn care is the reintegration of the patient into society. A few years ago, the goal of the burn team was survival of the patient and discharge was the measurement of outcome. Ideally, patients return to their families, schoolmates, and communities as if the injury had never occurred. In order to achieve this, rehabilitation and reconstruction of the seriously burned patient became important parts of today's burn care.

References

1. Sheridan RL. Burn rehabilitation. http://emedicine.medscape.com/article/318436-overview.
2. Robson MC, Smith DJ, Vander Zee AJ, et al. Making the burned hand functional. Clin Plast Surg. 1992;19(3):663–71.
3. Harden NG, Luster SH. Rehabilitation considerations in the care of the acute burn patient. Crit Care Nurs Clin North Am. 1991;3(2):245–53.
4. Pessina MA, Ellis SM. Burn management. Rehabilitation. Nurs Clin North Am. 1997;32(2):365–74.
5. Trees DW, Ketelsen CA, Hobbs JA. Use of a modified tilt table for preambulation strength training as an adjunct to burn rehabilitation: a case series. J Burn Care Rehabil. 2003;24(2):97–103.
6. Staley M, Richard R. Burn care and rehabilitation principles and practice, vol. Ch. 14. Philadelphia, PA: FA Davis; 1994. p. 380–418.
7. Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel: a new treatment of hyperthrophic scar. Surgery. 1989;106:781–7.
8. Katz BE. Silicone gel sheeting in scar therapy. Cutis. 1995;56:65–7.
9. Kischer CW. The microvessels in hypertrophic scars, keloids and related lesions: a review. J Submicrosc Cytol Pathol. 1992;24:281–96.
10. Mc Donald WS, Deitch EA. Hypertrophic skin grafts in burn patients: a prospective analysis of variables. J Trauma. 1987;27:147–50.
11. Cheng JC, Evans JH, Leung KS, et al. Pressure therapy in the treatment of post-burn hypertrophic scar – a critical look into its usefulness and fallacies by pressure monitoring. Burns. 1984;10:154–63.
12. Giele HP, Liddiard K, Currie K, et al. Direct measurement of cutaneous pressures generated by pressure garments. Burns. 1997;23:137–41.
13. Larson DL, Abston S, Willis B, et al. Contracture and scar formation in the burn patient. Clin Plast Surg. 1974;1:653–6.
14. Robertson JC, Hodgson B, Druett JE, et al. Pressure therapy for hypertrophic scarring: preliminary communication. J R Soc Med. 1980;73:348–54.
15. Huruitz S. The sun and sunscreen protection: recommendations for children. J Dermatol Surg Oncol. 1988;14(6):657–60.
16. Tang YW. Intra- and postoperative steroid injection for keloids and hyperthrophic scars. Br J Plast Surg. 1992;45:371–3.
17. Oikarinen A, Autio P. New aspects of the mechanism of corticosteroid-induced dermal atrophy. Clin Exp Derm. 1991;16:416–9.
18. Hirshowitz B, Lerner D, Moscona AR. Treatment of keloid scars by combined cryosurgery and intralesional corticosteroids. Aesthet Plast Surg. 1982;6:153–8.

19. D'Andrea F, Brongo S, Ferraro G, et al. Prevention and treatment of keloids with intralesional verapamil. Dermatology. 2002;204:60–2.
20. Lee RC, Doong H, Jellema AF. The response of burn scars to intralesional verapamil: report of five cases. Arch Surg. 1994;129:107–11.
21. Doong H, Dissanayake S, Gowrishankar TR, et al. The 1996 Lindberg award: calcium antagonists alter cell shape and induce rocollagenase synthesis in keloid and normal human dermal fibroblasts. J Burn Care Rehabil. 1996;17:497–514.
22. Alster TS, McMeekin TO. Improvement of facial acne scars by the 585 nm flashlamp-pumped pulsed dye laser. J Am Acad Dermatol. 1996;35:79–81.
23. Henderson DL, Cromwell TA, Mes LG. Argon and carbon dioxid laser treatment of hypertrophic and keloid scars. Dermatology. 1984;204:60–2.
24. Kovalic JJ, Perez CA. Radiation therapy following keloidectomy: a 20-year experience. Int J Radiat Oncol Biol Phys. 1989;17:77–80.
25. Jeong JH. Adipose stem cells and skin repair. Curr Stem Cell Res Ther. 2010;5(2):137–40.

Laser Treatment of Scars

10

Gerd G. Gauglitz and Julian Poetschke

10.1 Introduction

Scars can form as a result of surgery, trauma, or even spontaneously. In many cases, they are inconspicuous and result in little discomfort. Pathological scarring like linear or widespread hypertrophic scarring or keloids often result in pronounced functional impairments and can grossly disfigure the affected patients. Thus, effective scar therapy is paramount to rehabilitate both function and aesthetics. Well-researched and oft employed techniques for scar therapy include surgical options like scar excision, tension-relieving z- and w-plasty, skin grafting, local as well as free flaps and nonsurgical options like corticosteroid injections, pressure therapy, silicone-based wound gels and sheets, and many others. Further potential for scar treatment is offered through different laser treatment methods that have become increasingly popular throughout the last years. With a variety of different laser technologies being available, physicians require an in-depth knowledge about their individual properties and capabilities as well as their applicability for the treatment of different scar types to ensure safe and effective laser scar treatment.

10.2 Laser Technologies for Scar Treatment

Laser technologies can be divided in different subgroups through their mode of action. A common distinction would be the differentiation between ablative and nonablative lasers. While nonablative lasers commonly target different physiological (oxyhemoglobin) or artificial (tattoos) pigments, ablative lasers allow for the vaporization of tissue, thus allowing the physician to ablate, excise, and resurface the treated tissue.

10.2.1 Ablative Lasers

Through their distinctive wavelengths, the energy of ablative lasers is well absorbed by water. This allows for the vaporization of water-rich skin cells and dermal matrix compounds and thus their controlled ablation. Ablative lasers used for scar treatment include the erbium-doped yttrium aluminum garnet laser also known as the Er:YAG laser, and the carbon dioxide (CO_2) laser. The Er:YAG laser emits a wavelength of 2940 nm which place it in the infrared spectrum. The laser's energy is strongly absorbed by water and very little energy is transferred into the surrounding tissue, thus resulting in little to no heat necrosis. This is sometimes referred to as "cold ablation." It also means that coagulating blood vessels during treatment is ineffective with the Er:YAG, thus limiting its ability to ablate tissue and to influence dermal matrix regeneration and remodeling.

The CO_2 laser uses a wavelength of 10,600 nm. While its energy is also strongly absorbed by water, use of the CO_2 laser results in significant heat dispersion into the surrounding tissue. In tissue ablation, this can be used to coagulate blood vessels, thus allowing for thorough and extensive tissue resurfacing unlike with the Er:YAG laser. It also leads to significant skin tightening as heat-damaged proteins within the skin are remodeled [1]. In the past, continuous wave devices were commonly used and later replaced by pulsed units that minimized thermal damage to the surrounding tissue. Recently, ablative lasers have further been modernized by the addition of fractional treatment modes. Fractional lasers divide the laser beam into an array of smaller beams, thus leaving intact skin islets in-between the treated skin. These microthermal treatment zones (MTZs) vary in size and depth depending on the device used but can reach over 3 mm in depth with current laser technology, thus allowing for the effective treatment of thicker lesions. While fractional

G. G. Gauglitz (✉)
Department of Dermatology and Allergy, Ludwig-Maximilian-University, Munich, Germany
e-mail: gerd.gauglitz@med.uni-muenchen.de

J. Poetschke
Department of Plastic and Hand Surgery, Burn Center, Klinikum St. Georg gGmbH, Leipzig, Germany

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_10

ablative laser treatment slightly limits the treatment efficacy, it greatly enhances recovery time when compared to non-fractional ablation. Deep fractional photothermolysis has also been proven to positively influence heat-shock proteins and other agents associated with dermal matrix regeneration [2, 3].

Side effects of ablative laser treatment include swelling, erythema, skin infection, scarring, hypopigmentation as well as demarcation between treated and untreated skin [1].

10.2.2 Nonablative Lasers

One of the most popular nonablative lasers used for scar treatment is the pulsed dye laser (PDL). With a wavelength of 585 or 595 nm its target chromophore is oxygenized hemoglobin within superficial blood vessels. While absorption by the hemoglobin is stronger with the 585 nm wavelength, lasers with 595 nm are commonly favored as they allow for deeper tissue penetration. By transferring laser energy to the oxyhemoglobin, application of the laser leads to coagulation within the blood vessel which results in compromised microcirculation and decreased peripheral distribution of nutrients and most critically, oxygen. The resultant tissue ischemia and hypoxia lead to TGF-β1 suppression, which inhibits fibroblast proliferation and stimulates the expression of antifibrotic substances such as MMP-13, ERK, or p38 kinase in treated scar tissue [1, 4, 5].

Side effects of PDL treatment are commonly mild. They include purpura that usually persist for 7–14 days as well as vesicles and crusts. The severity of the side effects is typically correlated with the employed energy density. In darker skin types, persisting hyperpigmentation can occur. The occurrence, however, is less common when using 595 nm PDL treatment as compared to 585 nm lasers [6].

The neodymium-doped yttrium aluminum garnet or Nd:YAG laser commonly employs a wavelength of 1064 nm. While similar to the PDL in its mode of action, the wavelength of the Nd:YAG allows for greater tissue penetration. This however comes at a price. First, the Nd:YAG's efficacy is significantly reduced in greater depths. Second, it is not as strongly absorbed by oxyhemoglobin as the PDL's energy. Water and melanin compete with the hemoglobin as the target chromophores which can lead to heating of the surrounding tissue and thus burns and scarring as potential side effects [1]. Side effects of Nd:YAG laser treatment also include a prickling sensation during treatment as well as erythema and swelling post-treatment [7].

The erbium glass or Er:Glass laser is a nonablative laser commonly used as a fractional laser and employs wavelengths around 1500 nm within the infrared spectrum to achieve its effects. It allows for the selective distribution of heat within the subepidermal tissue, thus stimulating different intradermal proliferative pathways as well as the regeneration of a physiological matrix structure. As this laser works through the sole application of heat into the skin without damaging the epidermal barrier, down-time after treatment is commonly very low. Treatment can, however, go along with light swelling, erythema as well as post-inflammatory hyperpigmentation [8].

10.3 Laser Treatment Options for Different Scar Types

10.3.1 Linear Scars

Linear scars are most often a result of surgery. When fresh, they usually appear reddish and slightly raised and can go along with light to moderate pruritus. Usually fresh scars mature within a few months becoming flat, pale, and depigmented [9]. For improved normalization of scar height, vascularity and pliability PDL treatment has been suggested for surgical scars, starting with the day of suture removal. In split-scar studies, three treatment sessions at 4-week intervals seemed to markedly improve the aforementioned scar parameters [10, 11]. Another study on postoperative scars showed improvements through both PDL and Er:Glass laser treatment with the latter resulting in greater improvements [12]. Sobanko et al. could not discern significant differences between treated and untreated scars after one session of fractional ablative CO_2 laser treatment on the day of suture removal after a 3-month follow-up using the Vancouver Scar Scale. Nevertheless patients reported satisfaction with the laser treatment [13].

Ultimately though, while prevention of severe scarring is important and can be recommended with the onset of complete reepithelialization of the surgical wound, current guidelines recommend silicone sheeting or gels as well as onion extract containing products [6, 14–17]. While expert committees stress the potential of laser treatment for fresh postoperative scars, especially in patients with a predisposition for pathological scarring [18], more research is needed before clear recommendations can be made.

Deliberate self-harm scars are an example of linear scarring that are quite problematic for patients. They are commonly located on the volar forearms, on the abdomen or the inner thighs and even though they usually heal well and only leave slim, pale, and flat scars, their sheer number, their pattern and the associated stigma result in grave psychosocial impairment [19] of the affected patients, thus resulting in a pronounced desire for treatment.

The treatment of deliberate self-harm scars using the nonablative fractional Er:Glass laser is currently the subject of intensified research. Our study group could show that three sessions of Er:Glass laser treatment in 4-week intervals

led to statistically significant improvement of scar relief as well as POSAS (Patient and Observer Scar Assessment Scale) scores (Fig. 10.1). Quality of life in the treated patients was also significantly improved (Guertler et al., Lasers in Medical Science 2017, accepted). Standardized treatment parameters were used during each session which was divided into two passes. First, a small spot with a higher density and lower energy was employed to treat only the scars, while during the second pass, a larger spot with a reduced density but higher energy was used to treat the surrounding skin, too.

Even though these initial findings are highly encouraging, further research is required to further characterize the efficacy of Er:Glass laser treatment for deliberate self-harm scars.

10.3.2 Linear Hypertrophic Scars

Linear hypertrophic scars form within 4–8 weeks after wound closure. Common reasons for hypertrophic scar

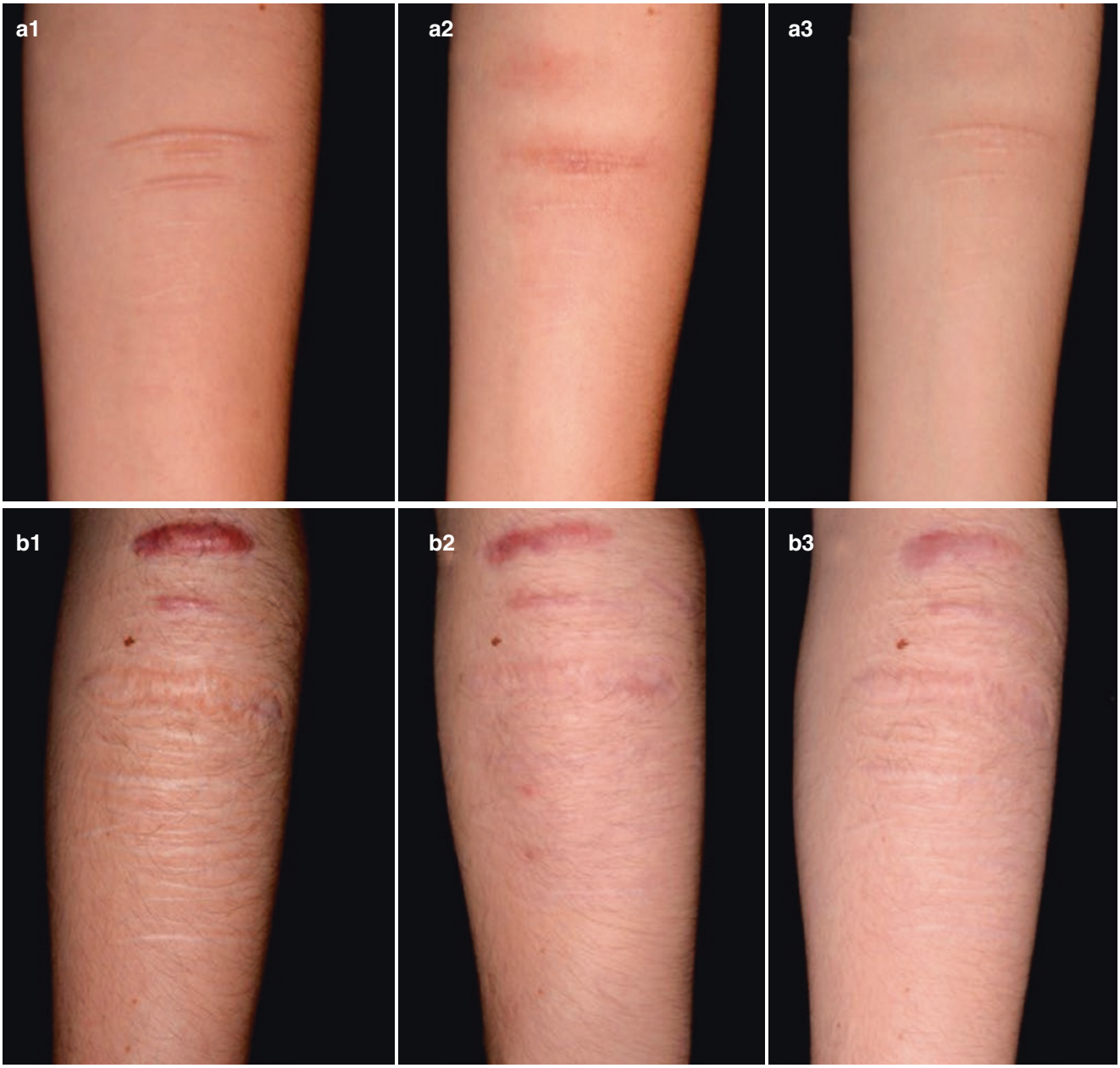


Fig. 10.1 Self-harm scars before (A1/B1), 1 month after (A2/B2), and 6 months after (A3/B3) 3 sessions of non-ablative fractional Er:Glass laser treatment (1565 nm ResurFx, M22, Lumenis Ltd., Yokneam, Israel) (Figures previously published in Guertler et al., "Objective evaluation of the efficacy of a non-ablative, fractional 1565 nm laser for the treatment of deliberate self-harm scars," Lasers in medical Science, 2017, accepted as of 1 October 2017)

formation include excess tension on the wound margins and wound infection. Their appearance is erythematous, rope-like, and bulging, and they are often associated with pruritus and pain, especially when irritated through contact or friction. They form within the margins of the original trauma and after a week-long phase of growth will eventually show steady involution after a short phase of stagnation [19]. Since linear hypertrophic scarring often regresses over time, primary laser treatment usually is not indicated. In inactive and burnt-out hypertrophic scars, however, ablative laser treatment can be considered as a second-line treatment option for scar flattening and the loosening of contractures [16]. The latter is achieved through fractional treatment, which results in a normalization of the dermal matrix architecture through the induction of heat-shock proteins, TGF-β subtypes, and matrix metalloproteinases, while regular ablative laser treatment can be employed for the ablation of burned-out scar tissue. In our experience several sessions are usually required to achieve sufficient blending of the scar into the surrounding tissue. Herein, CO_2 laser treatment seems to be more effective than Er:YAG laser treatment, potentially due to the effects of the thermal energy on dermal matrix regeneration [9, 20].

10.3.3 Widespread Hypertrophic Scars

Widespread hypertrophic scars are most commonly the result of burn trauma. They appear raised with an irregular surface, they contain rope-like scar strands and are considerably firmer and less elastic than healthy skin. They can appear erythematous as well as hypopigmented and often lack skin appendages like hair and sebaceous glands.

In addition to this, burn patients often require skin grafting, most commonly split-thickness grafts which show considerable propensity to heal hypertrophically, thus adding to larger areas of hypertrophic scarring. Furthermore, split-thickness grafts often add further to aesthetic impairments through their often apparent mesh-pattern that results from expansion of the skin graft. Widespread hypertrophic burn scars commonly go along with great aesthetic, functional, and psychosocial impairments, resulting in an often dramatic need for treatment and scar improvement.

Commonly patients with widespread burn injuries are advised to wear compression garments for at least 1 year after deep burns and especially after receiving split-thickness skin grafts.

Silicone sheets are also often used to limit hypertrophic scarring. Should widespread hypertrophic scarring occur, patients are thus far often treated using medical needling to soften scars and through dermabrasion to flatten thick scars [21].

In recent years, fractional ablative CO_2 laser treatment has been recommended as an option for widespread hypertrophic scar treatment.

Pilot studies researching the effects of fractional photothermolysis could demonstrate that such treatment modulates the concentrations of different heat-shock proteins, subtypes of the TGF-β family as well as matrix metalloproteinases leading to dermal matrix remodeling and a shift to a normalized dermal architecture [2, 3, 22–25].

After the molecular effects of fractional photothermolysis were established, multiple pilot studies on CO_2 laser treatment have shown improvements in scar texture, pliability, and clinical symptoms resulting in improved functional and aesthetic aspects and considerable patient satisfaction [2, 22, 25–31]. Levi et al. reported patient satisfaction of 96.7% with pronounced reductions of scar tightness and pruritus as well as neuropathic pain after three treatment sessions every 4 months [28].

Our study group examined the effects of one session of fractional ablative carbon dioxide laser (Lumenis Ultrapulse Encore, Lumenis Ltd., Yokneam, Israel) treatment on mature burn scars in an in-patient controlled approach. Two 10 cm by 10 cm areas of hypertrophic scarring were designated as study areas. One of them received one session of laser treatment, the other was left untreated. Treatment included three passes with the laser. During the first pass, the whole scarred area was treated using a deep fractional approach with individualized energy settings intended to allow penetration into the deep dermis (ScaarFX: 90–150 mJ/cm^2 (2–3.3 mm), Density 1%, 250 Hz). During the second pass, a small spot with a slightly reduced energy and high density was used to ablate individual fine scar strands (ActiveFX (small spot): 40–90 mJ/cm^2, high density, 300 Hz). Lastly, a large spot with a high energy but low density was used for general surface smoothening (ActiveFX (large spot): 125 mJ/cm^2, low density, 125 Hz). Through this approach and with a 6-month follow-up we could demonstrate a significant reduction in scar firmness of over 30%. The scar texture was also improved greatly showing a reduction of profile irregularities of over 30%. POSAS and VSS scores were also significantly improved as were Dermatology Life Quality Scores [32].

Fractional ablative CO_2 laser treatment has been established as a safe and effective treatment method for widespread hypertrophic burn scars. As a consequence, current guidelines for the treatment of pathological scarring recommend fractional ablative CO_2 laser treatment as a promising treatment option for widespread hypertrophic scarring (Fig. 10.2) [14, 16]. Nevertheless, while current studies have been able to characterize the effects of this treatment method, further research into possible treatment paradigms is necessary.

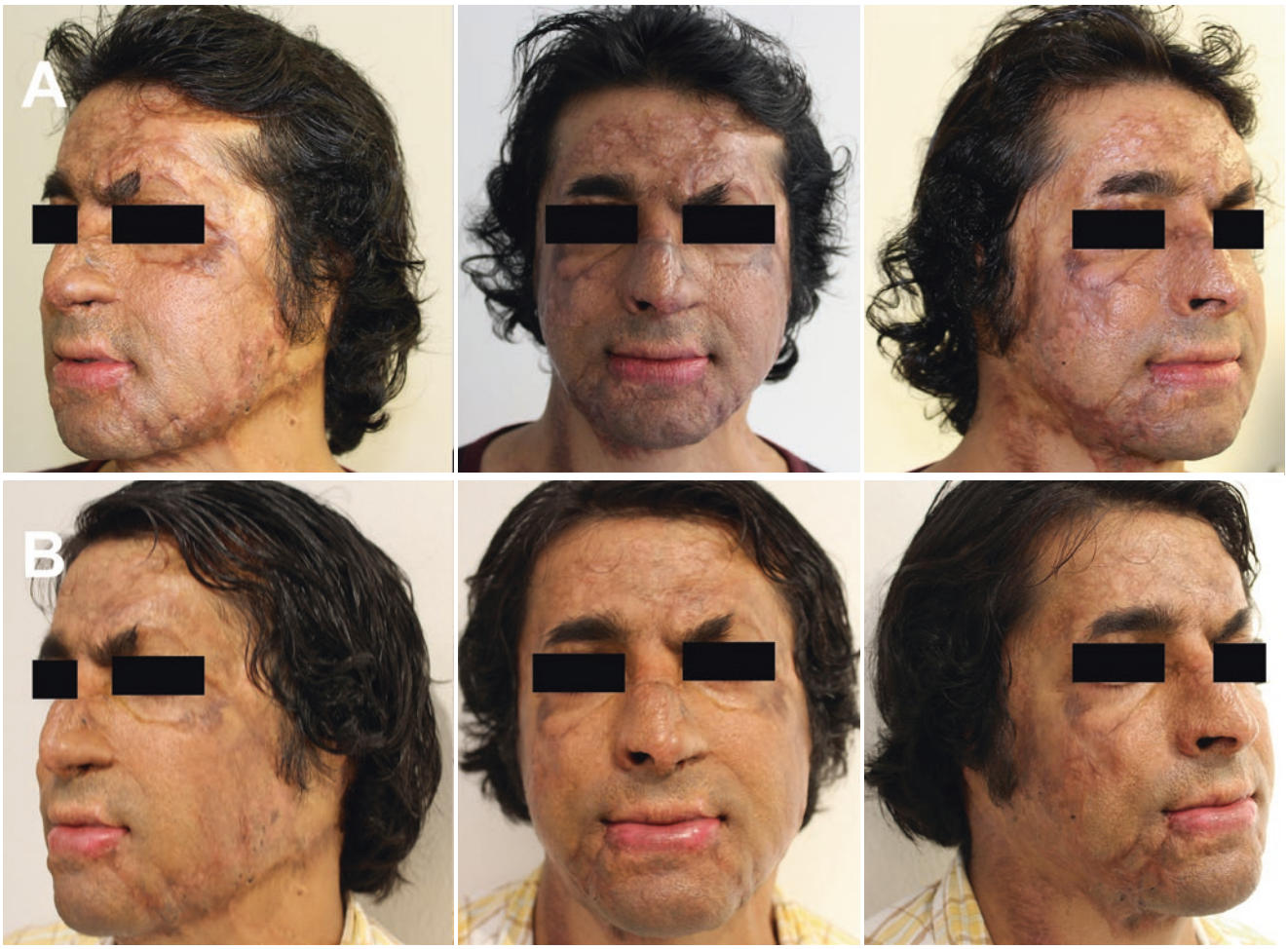


Fig. 10.2 Widespread facial hypertrophic burn scars, before (**a**) and after (**b**) multiple sessions of fractional ablative CO_2 laser treatment (Lumenis Ultrapulse Encore) using the aforementioned parameters

10.3.4 Keloids

Keloids are often mistaken for hypertrophic scars and vice versa. They appear as smooth well-demarcated, embossed tumors of the skin. They are often erythematous and show telangiectasia and sometimes ulceration. Keloids oftentimes go along with excruciating pruritus and pain, especially when irritated and can grow to enormous sizes. Keloid occurrence can be the result of trauma, surgery, or even spontaneous formation without apparent reason. Keloids can form during the early stages of wound healing, continually growing for extended periods of time or also appear years after the causative trauma. Unlike hypertrophic scars, keloids show no tendency for regression over time. Keloid occurrence is associated with darker Fitzpatrick skin types commonly found in Africans and Asians, a positive family history for keloid disease and predilection sites include the chest, shoulders, and ear lobes.

In 1995, Alster et al. described the 585 nm PDL as a significantly effective tool to improve erythema, scar height, skin surface texture, and pruritus in previously untreated keloids after two treatment sessions in 6–8 week intervals [33]. Follow-up studies by different research groups, however, struggled to reproduce the promising results by Alster et al. [34] and the overall level of evidence on the PDL's efficacy for keloid treatment remains low due to small study groups, uncontrolled designs and unstandardized treatment paradigms as well as insufficiently short follow-up periods [35]. Nevertheless, current treatment guidelines for pathological scarring recommend the PDL as a second-line treatment option in keloids that are pruritic and erythematous due to research indicating the potential of the PDL to ameliorate these symptoms (Fig. 10.3) [6, 14, 16, 36].

Nd:YAG laser treatment for keloids showed promising results in a small pilot study by Cho et al. after a 3-month

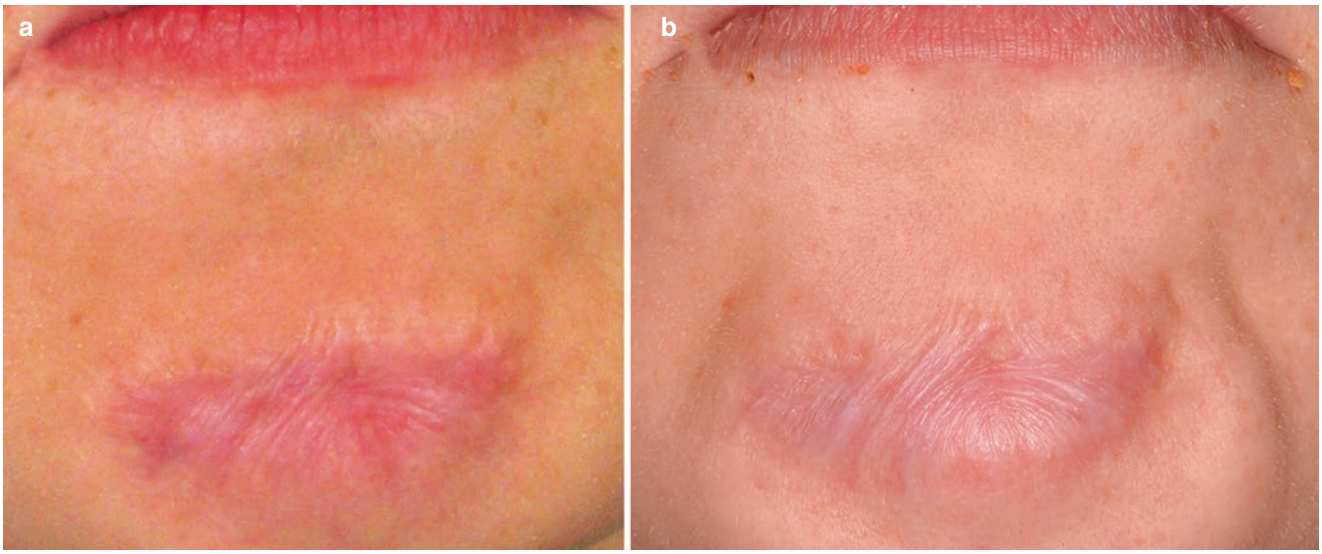


Fig. 10.3 Erythematous scar before (left) and after (right) four sessions of PDL treatment (11 J/cm^2, 30/10, 10 ms, 7 mm spot)

follow-up [7]. Koike et al., too, reported significant keloid scar improvement after monthly Nd:YAG laser treatment sessions over the course of 1 year. After 6 months of follow-up, however, over 50% of the keloids treated showed recurrence [37]. Overall the level of evidence of Nd:YAG laser treatment for keloids is relatively low, thus resulting in the omission of this treatment modality in current guidelines.

Ablative lasers play a very limited role in the therapy of keloids. Since keloids are associated with significant recurrence after treatment, scar ablation is not recommended as a standard procedure in keloids much like conventional excision. Ablative laser treatment can, however, be considered for debulking large keloids or as a secondary measure in therapy refractory scars. Then, however, it is recommended to combine laser therapy with other prophylactic measures like intralesional corticosteroid injections to decrease the probability of recurrence.

10.4 Summary

While guideline-based scar therapy is still dominated by other therapeutic means, laser therapy plays an increasingly important role in the treatment of pathological scarring. With the advent of new laser technologies, an increased availability of laser treatment, and continued scientific evaluation of new treatment forms, their role is likely to become more vital. While being an integral part in the treatment of almost every scar type except for keloids, laser treatment might soon become an option for scar prevention too, as our understanding of their influence on the wound healing cascade and potential positive influence on the normalization of the dermal architecture improves.

Laser therapy offers physicians different targeted treatment options for pathological scarring that are safe, efficacious, and comfortable to perform in an ambulatory setting, thus further adding to patient comfort. It has therefore become a staple in contemporary scar therapy that can greatly benefit patients that suffer from aesthetically and functionally debilitating scars.

References

1. Stewart N, Lim AC, Lowe PM, Goodman G. Lasers and laser-like devices: part one. Australas J Dermatol. 2013;54:173–83.
2. Dams SD, de Liefde-van Beest M, Nuijs AM, Oomens CW, Baaijens FP. Pulsed heat shocks enhance procollagen type I and procollagen type III expression in human dermal fibroblasts. Skin Res Technol. 2010;16:354–64.
3. Helbig D, Paasch U. Molecular changes during skin aging and wound healing after fractional ablative photothermolysis. Skin Res Technol. 2011;17:119–28.
4. Kuo YR, Wu WS, Jeng SF, Huang HC, Yang KD, Sacks JM, et al. Activation of ERK and p38 kinase mediated keloid fibroblast apoptosis after flashlamp pulsed-dye laser treatment. Lasers Surg Med. 2005;36:31–7.
5. Kuo YR, Wu WS, Jeng SF, Wang FS, Huang HC, Lin CZ, et al. Suppressed TGF-beta1 expression is correlated with up-regulation of matrix metalloproteinase-13 in keloid regression after flashlamp pulsed-dye laser treatment. Lasers Surg Med. 2005;36:38–42.
6. Nast A, Eming S, Fluhr J, Fritz K, Gauglitz G, Hohenleutner S, et al. German S2k guidelines for the therapy of pathological scars (hypertrophic scars and keloids). J German Soc Dermatol. 2012;10:747–62.
7. Cho SB, Lee JH, Lee SH, Lee SJ, Bang D, Oh SH. Efficacy and safety of 1064-nm Q-switched Nd:YAG laser with low fluence for

keloids and hypertrophic scars. J Eur Acad Dermatol Venereol. 2010;24:1070–4.
8. Bencini PL, Tourlaki A, Galimberti M, Longo C, Pellacani G, De Giorgi V, et al. Nonablative fractional photothermolysis for acne scars: clinical and in vivo microscopic documentation of treatment efficacy. Dermatol Ther. 2012;25:463–7.
9. Poetschke J, Gauglitz GG. Current options for the treatment of pathological scarring. J German Soc Dermatol. 2016;14:467–77.
10. Nouri K, Jimenez GP, Harrison-Balestra C, Elgart GW. 585-nm pulsed dye laser in the treatment of surgical scars starting on the suture removal day. Dermatol Surg. 2003;29:65–73; discussion 73.
11. Nouri K, Rivas MP, Stevens M, Ballard CJ, Singer L, Ma F, et al. Comparison of the effectiveness of the pulsed dye laser 585 nm versus 595 nm in the treatment of new surgical scars. Lasers Med Sci. 2009;24:801–10.
12. Tierney E, Mahmoud BH, Srivastava D, Ozog D, Kouba DJ. Treatment of surgical scars with nonablative fractional laser versus pulsed dye laser: a randomized controlled trial. Dermatol Surg. 2009;35:1172–80.
13. Sobanko JF, Vachiramon V, Rattanaumpawan P, Miller CJ. Early postoperative single treatment ablative fractional lasing of Mohs micrographic surgery facial scars: a split-scar, evaluator-blinded study. Lasers Surg Med. 2015;47:1–5.
14. Gold MH, Berman B, Clementoni MT, Gauglitz GG, Nahai F, Murcia C. Updated international clinical recommendations on scar management: part 1-evaluating the evidence. Dermatol Surg. 2014;40:817–24.
15. Gold MH, Foster TD, Adair MA, Burlison K, Lewis T. Prevention of hypertrophic scars and keloids by the prophylactic use of topical silicone gel sheets following a surgical procedure in an office setting. Dermatol Surg. 2001;27:641–4.
16. Gold MH, McGuire M, Mustoe TA, Pusic A, Sachdev M, Waibel J, et al. Updated international clinical recommendations on scar management: part 2-algorithms for scar prevention and treatment. Dermatol Surg. 2014;40:825–31.
17. Mustoe TA, Cooter RD, Gold MH, Hobbs FD, Ramelet AA, Shakespeare PG, et al. International clinical recommendations on scar management. Plast Reconstr Surg. 2002;110:560–71.
18. Anderson RR, Donelan MB, Hivnor C, Greeson E, Ross EV, Shumaker PR, et al. Laser treatment of traumatic scars with an emphasis on ablative fractional laser resurfacing: consensus report. JAMA Dermatol. 2014;150:187–93.
19. Reinholz M, Poetschke J, Schwaiger H, Epple A, Ruzicka T, Gauglitz GG. The dermatology life quality index as a means to assess life quality in patients with different scar types. J Eur Acad Dermatol Venereol. 2015;29:2112–9.
20. Choi JE, Oh GN, Kim JY, Seo SH, Ahn HH, Kye YC. Ablative fractional laser treatment for hypertrophic scars: comparison between Er:YAG and CO_2 fractional lasers. J Dermatolog Treat. 2014;25:299–303.
21. Aust MC, Knobloch K, Reimers K, Redeker J, Ipaktchi R, Altintas MA, et al. Percutaneous collagen induction therapy: an alternative treatment for burn scars. Burns. 2010;36:836–43.
22. El-Zawahry BM, Sobhi RM, Bassiouny DA, Tabak SA. Ablative CO fractional resurfacing in treatment of thermal burn scars: an open-label controlled clinical and histopathological study. J Cosmet Dermatol. 2015;14:324.
23. Laubach HJ, Tannous Z, Anderson RR, Manstein D. Skin responses to fractional photothermolysis. Lasers Surg Med. 2006;38:142–9.
24. Manstein D, Herron GS, Sink RK, Tanner H, Anderson RR. Fractional photothermolysis: a new concept for cutaneous remodeling using microscopic patterns of thermal injury. Lasers Surg Med. 2004;34:426–38.
25. Ozog DM, Liu A, Chaffins ML, Ormsby AH, Fincher EF, Chipps LK, et al. Evaluation of clinical results, histological architecture, and collagen expression following treatment of mature burn scars with a fractional carbon dioxide laser. JAMA Dermatol. 2013;149:50–7.
26. Hultman CS, Friedstat JS, Edkins RE, Cairns BA, Meyer AA. Laser resurfacing and remodeling of hypertrophic burn scars: the results of a large, prospective, before-after cohort study, with long-term follow-up. Ann Surg. 2014;260:519–29.. discussion 529-532
27. Khandelwal A, Yelvington M, Tang X, Brown S. Ablative fractional photothermolysis for the treatment of hypertrophic burn scars in adult and pediatric patients: a single surgeon's experience. J Burn Care Res. 2014;35:455–63.
28. Levi B, Ibrahim A, Mathews K, Wojcik B, Gomez J, Fagan S, et al. The use of CO_2 fractional Photothermolysis for the treatment of burn scars. J Burn Care Res. 2016;37:106–14.
29. Qu L, Liu A, Zhou L, He C, Grossman PH, Moy RL, et al. Clinical and molecular effects on mature burn scars after treatment with a fractional CO(2) laser. Lasers Surg Med. 2012;44:517–24.
30. Sever C, Uygur F, Kulahci Y, Oksuz S, Sahin C, Yuksel F. Treatment of facial burn scars with CO2 laser resurfacing and thin skin grafting. J Craniofac Surg. 2010;21:1024–8.
31. Suh D-H CK-Y, Song K-Y, et al. Revision of burn scars using ablative fractional CO_2 laser. J Am Acad Dermatol. 2012;66:AB216.
32. Poetschke J, Dornseifer U, Clementoni MT, Reinholz M, Schwaiger H, Steckmeier S, et al. Ultrapulsed fractional ablative carbon dioxide laser treatment of hypertrophic burn scars: evaluation of an inpatient controlled, standardized treatment approach. Lasers Med Sci. 2017;32:1031–40.
33. Alster TS, Williams CM. Treatment of keloid sternotomy scars with 585 nm flashlamp-pumped pulsed-dye laser. Lancet. 1995;345:1198–200.
34. Paquet P, Hermanns JF, Pierard GE. Effect of the 585 nm flashlamp-pumped pulsed dye laser for the treatment of keloids. Dermatol Surg. 2001;27:171–4.
35. Durani P, Bayat A. Levels of evidence for the treatment of keloid disease. J Plast Reconstr Aesthet Surg. 2008;61:4–17.
36. Gauglitz GG. Management of keloids and hypertrophic scars: current and emerging options. Clin Cosmet Investig Dermatol. 2013;6:103–14.
37. Koike S, Akaishi S, Nagashima Y, Dohi T, Hyakusoku H, Ogawa R. Nd:YAG laser treatment for keloids and hypertrophic scars: an analysis of 102 cases. Plast Reconstr Surg Glob Open. 2014;2:e272.

The Value of Medical Needling in Burn Scars

11

Matthias Aust, Desmond Fernandes, and Richard Bender

11.1 Introduction

Patients with burn scar deformities frequently request help to improve both the aesthetic and functional complications of their scars. There are numerous methods available for surgeons to treat burn scars, but nowadays, there is a demand for less invasive and more cost-effective procedures to give the desired benefits.

Non-invasive treatments such as silicone patches and pressure garments are important ways to control scars. Minimally invasive techniques such as cortisone injections also have a place. Surgeons have generally depended on surgical interventions such as scar excision, W- or Z-pasties, and pedicled or free skin flaps to treat contractures or severe irregular scars. The quest for better results has also led to the application of many different topical therapies such as laser resurfacing, dermabrasion and deep chemical peels.

The last-mentioned methods all follow the same principal: they are ablative, they change the scar by destroying the epidermis partially or completely and scarring the dermis. The death of tissue leads to an inflammatory response. In the process of trying to treat dermal scarring, the epidermis may be completely destroyed and replaced by a thinner epidermis with flatter rete ridges covering parallel-orientated scar collagen which is distinctive for scarred skin [1–3]. Furthermore, the skin becomes more vulnerable to infections [4].

The ideal scar treatment method would avoid ablation of the epidermis and rather promote the formation of physiological dermal collagen in a lattice pattern by initiating the expression of growth factors which are relevant for scarless wound healing and regeneration of the skin. In other words, the perfect remedy would be to remove the visible defective scarring and regenerate healthier anatomically more normal skin.

In recent years, it has been shown that it is possible to a significant degree to achieve the ideal treatment by using percutaneous collagen induction or "Medical Needling" [5–7]. Medical Needling is a minimal-invasive non-ablative procedure capable of improving scar quality and functionality by dermal reorganization with a decrease in scar collagen accompanied by an increase of physiological collagen and fibronectin as well as an increase of glycosaminoglycans. There is a decrease of trans-epidermal water loss because the epidermis is thicker, and the stratum corneum becomes a fully functional water barrier.

Approximately 20 years ago Camirand and Doucet [8] demonstrated that by simple "needle abrasion", one could get significant clinical improvement in treating white surgical scars with a tattoo artists' device. Orentreich also reported about "dermal needling or subcision" as an alternative for treating scars and wrinkles [9]. Based on these concepts, Fernandes developed the percutaneous collagen induction technique [10]. Thanks to targeted research within the last 15 years, impressive scientific data is now available which underlines the efficacy and safety of Medical Needling and why it works [5, 7, 11–15].

11.2 Science

11.2.1 How It Works

Medical Needling is repetitive puncturing of burn scars with a roller equipped with 3.0 mm long needles that penetrate into the dermal scars and cause intra dermal bleeding (see Fig. 11.1).

The needling device is repeatedly rolled over the scar in three main directions: longitudinally, diagonally and horizontally to get the best distribution of puncture holes.

M. Aust (✉)
Aust Aesthetik, Landsberg am Lech, Germany

D. Fernandes
Renaissance Surgical Clinic, Cape Town, South Africa
e-mail: info@drdes.co.za

R. Bender
Department for Plastic and Aesthetic Surgery/Hand Surgery, Bergmannsheil Buer, Gelsenkirchen, Germany

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_11

According to the extent of the scar, this procedure can last 30 min or longer. It is important to use the device with constant pressure and do the rolling in one direction at a time to prevent shear forces. The needles are solid and do not have a lumen. Hence, they pierce the skin and mainly separate the skin cells rather than destroying them (see Fig. 11.2). They penetrate the dermis 2.0 mm to a maximum of 3 mm and produce thousands of micro puncture wounds and intradermal bleeding. Some blood comes up through the channels to cause bleeding on the surface. The most important bleeding occurs in the dermis, but bleeding through the skin gives us a good idea of what is happening down below in the dermis.

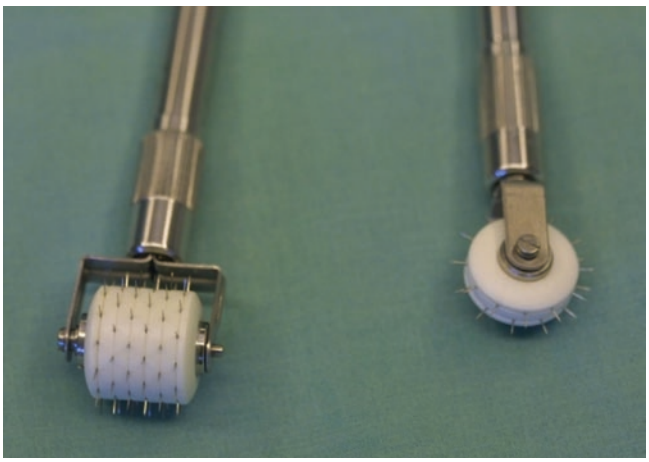


Fig. 11.1 Needling device

11.2.2 Induction of the Wound Healing Cascade

This trauma initiates the activation of the physiological wound healing cascade but with a significant difference. Normally trauma causes the temporary presence of TGF-β3, and the wound heals predominantly under the influence of TGF-β1 and -β2 which results in scar tissue. After needling, TGF-β1 and -β2 rapidly disappear from the scene, and TGF-β3 dominates which results in scarless healing and regeneration [16]. Skin needling induces a new (and as yet unrecognized) phase of regenerative healing which should not be confused with the post-traumatic inflammatory cascade. Platelets, keratinocytes and neutrophils secrete growth factors such as platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), tissue growth factor and transforming growth factor-α and -ß (TGF-α and TGF-ß). These initiate the synthesis of dermal structures such as collagen, elastin and fibronectin and also stimulate the migration of fibroblasts and keratinocytes [13, 17] The modulation of these growth factors right at the beginning signals the differences between

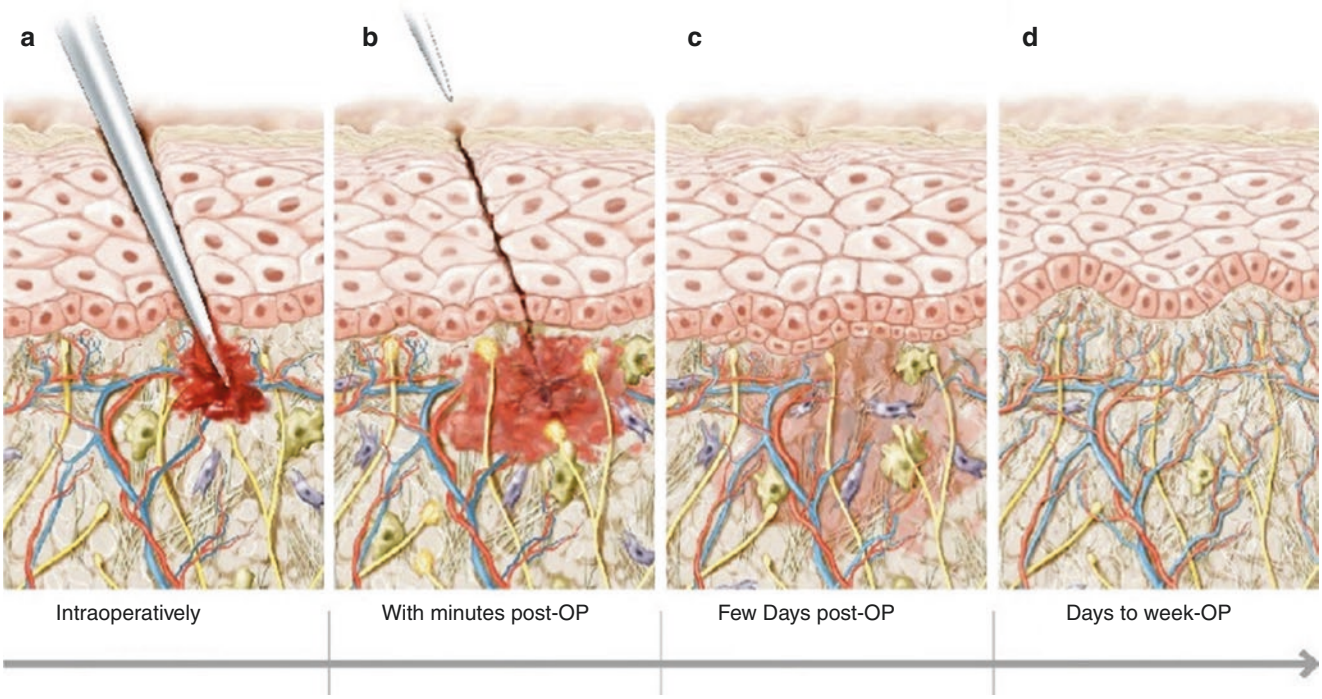


Fig. 11.2 Schematic illustration of Medical Needling and the effects on the wound. The needles pierce the epidermis and the blood vessels of the dermis, and when the needle is withdrawn, the needle tract closes and by the next day it cannot be detected histologically. Within days, collagen I and elastin are generated

this new paradigm of scarless healing versus the archetypal healing with scar formation.

11.2.3 TGF and the Induction of Collagen I

This new repair and regeneration mechanism is relevant for the formation of collagen I which is the physiological type collagen in a lattice pattern in healthy skin, whereas collagen III is more prevalent in parallel-orientated scar collagen. TGF-β3 makes a transient presence in standard surgical wounds and has largely disappeared within 24 h of injury. Typical scars, we now know, are the result of dominant activity of TGF-ß1 and -2. In contrast, TGF-ß1 and -2 levels are extremely low in scarless embryonal wound healing while the levels of TGF-ß3 are remarkably high [1, 5, 16, 18].

Medical Needling particularly influences the liberation of TGF-ß1, -ß2 and -ß3. Within days post-treatment, the levels of TGF-ß1 and -2 are significantly downregulated, whereas TGF-ß3 reaches high expression levels even beyond the initial wound healing phase [7, 13]. In support of this, the production of type I collagen was found to be increased after Medical Needling (see Figs. 11.3, 11.4 and 11.5). The changes seen in skin needling indicate a lower level of TGF-ß3 by 2 months. Ferguson's team argue that it is the initial height of the rise in concentration of TGF-ß3 that is probably the most important influence, not so much the duration of the raised levels because he points out the TGF-ß3 does not stay raised for the extended healing period [19]. Studies in humans that are as yet unpublished show that TGF-ß3 is raised after needling and become higher when needling is done at short intervals (Fernandes, personal communication).

11.2.4 Dermal Remodelling

Dermal reorganization after Medical Needling depends not only on the formation of physiological orientated collagen I but also on the inclusion of glycosaminoglycan molecules and fibronectin. This was shown in the animal model through the quantitative analysis of gene expression as well as through immunohistological analyses [12, 13, 20]. As seen in Figs. 11.12 and 11.13, the entire connective tissue framework appears thicker and denser post-treatment.

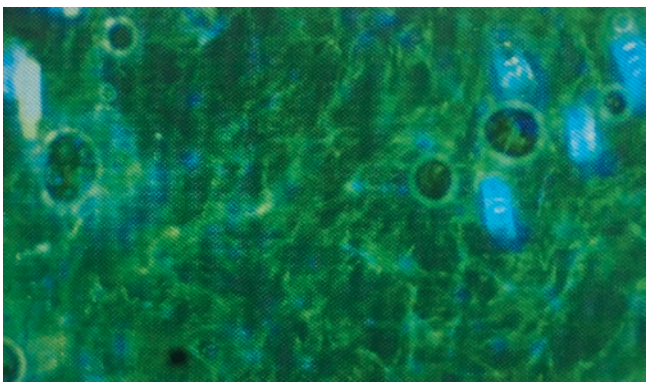


Fig. 11.4 Immunofluorescence visualization of collagen I: Staining with antibodies directed against Collagen I (Alexa488) and DAPI. Un-needled animal of the dermis failed to react with the antibodies

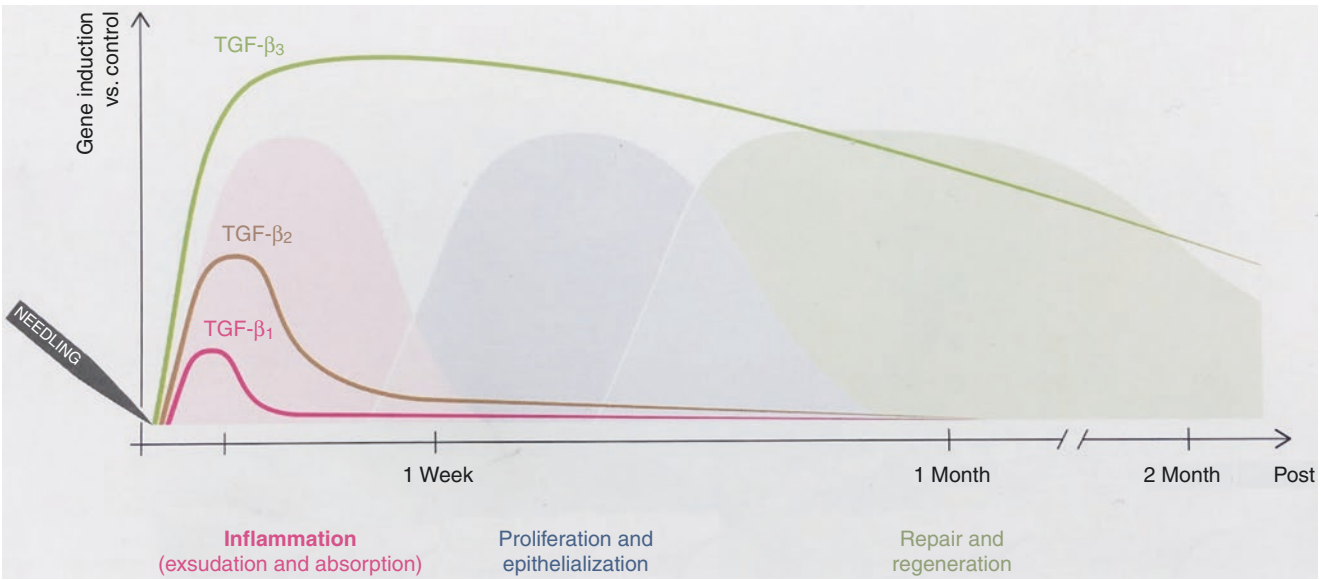


Fig. 11.3 Microarray analyses of TGF-ß1, -ß2 and -ß3 expression levels in treated animals. The induction of TGF-ß3 gene expression continues even beyond the initial wound healing phase, whereas TGF-ß1 and -ß2 are downregulated during the second week post-treatment

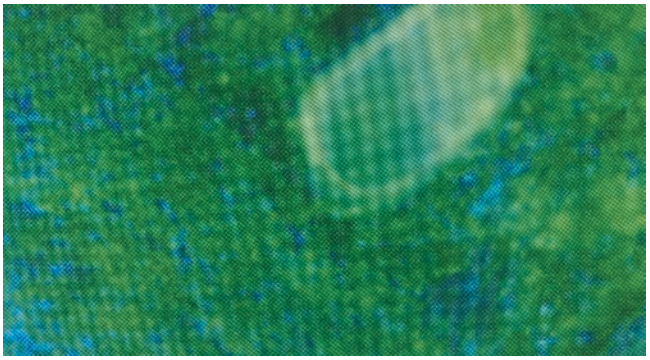


Fig. 11.5 Immunohistochemical staining, anti-collagen I. Needled animal with 8 weeks of skincare stained without primary antibody. The amount of type I collagen was qualitatively increased in treated group compared to their controls judged by the brighter fluorescence

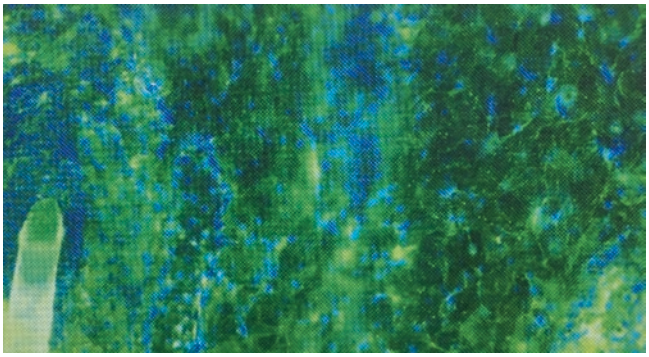


Fig. 11.7 Immunohistochemical staining, anti-elastin. Needled animal with 8 weeks of skincare stained without primary antibody. The amount of elastin was qualitatively increased in treated group compared to their controls judged by the brighter fluorescence

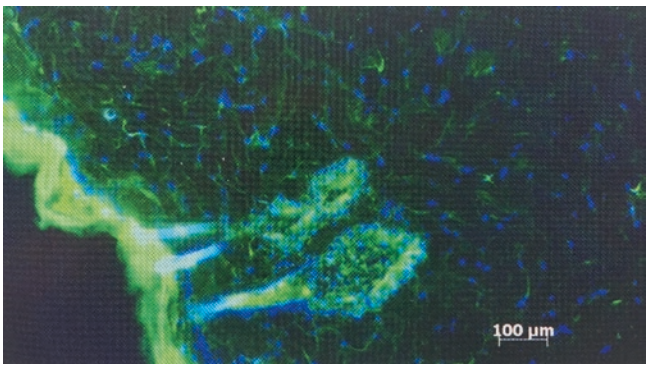


Fig. 11.6 Immunohistochemical staining, anti-elastin. Untreated animal immunofluorescence visualization of elastin: Staining with antibodies directed against elastin (Alexa488) and DAPI. Un-needled animal of the dermis failed to react with the antibodies

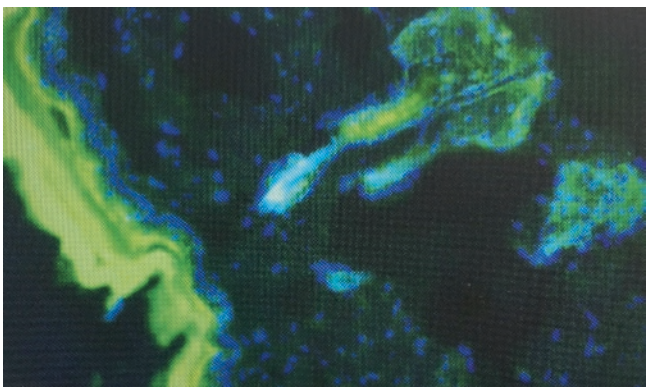


Fig. 11.8 Immunohistochemical staining, anti-VEGF. Untreated animal immunofluorescence visualization of elastin: Staining with antibodies directed against elastin (Alexa488) and DAPI. Un-needled animal of the dermis failed to react with the antibodies

11.2.5 Increase in Skin Elasticity

Moreover, the stimulation of the endogenous FGF contributes towards improved skin elasticity. As seen in Figs. 11.6 and 11.7, the amount of elastin is significantly higher after Medical Needling.

11.2.6 Normalized Perfusion

The secretion of VEGF during the healing phase stimulates angiogenesis and leads to the formation of tiny blood vessels in the corium. This helps to normalize the characteristic pathological erythema of scars after burn injuries. As seen in Figs. 11.8 and 11.9, the amount of VEGF significantly rises after Medical Needling.

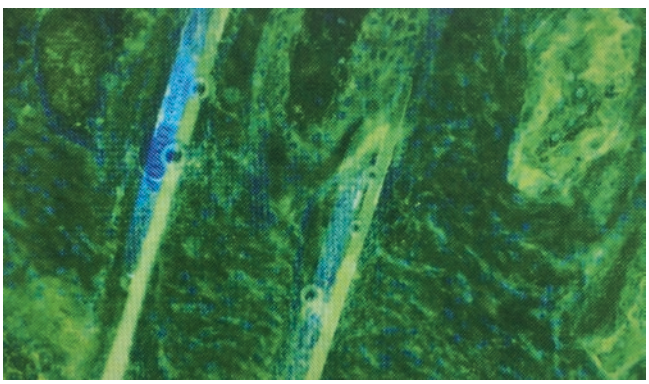


Fig. 11.9 Immunohistochemical staining, anti-VEGF. Needled animal. VEGF showed a membranous staining pattern along the intercellular junctions in the basal and suprabasal layers of the epidermis. A brighter fluorescence indicates that the amount of VEGF in the dermis is augmented in the needled groups compared to the un-needled groups

11.2.7 Increase in Skin Moisture Content

Scars often appear dry and loose due to a decrease of glycosaminoglycans with a result of reduced water retention in the skin and due to thinner epidermis with increased transepidermal water loss. Medical Needling is associated with a higher inclusion of glycosaminoglycans (see Figs. 11.10 and 11.11) and with a thicker epidermis post-treatment (see Figs. 11.12 and 11.13). Both help to maximize the moisture of the skin back to the reference of healthy skin.

11.2.8 Increase of Epidermal Thickness

In contrast to ablative treatments, the skin structures are not injured after Medical Needling. The epidermis remains physiologically intact which means that potential side effects such as inflammation, new scarring or dyspigmentation are reduced to a minimum. Furthermore, it has been shown in the animal model that the thickness of the epidermis increases up to 140% after treatment versus untreated ones [12] (see Figs. 11.12 and 11.13).

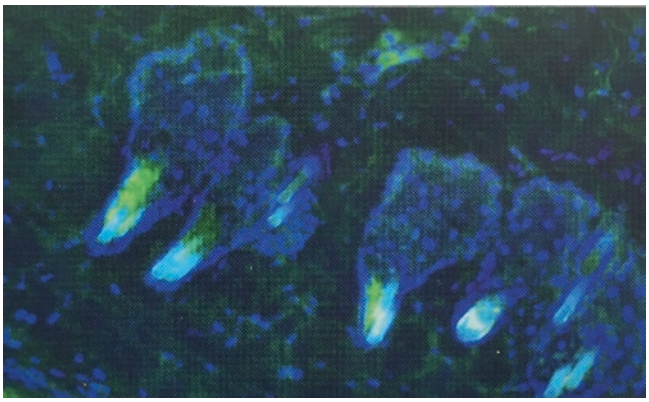


Fig. 11.10 Immunofluorescence visualization of GAGs (Alexa488-conjugated) and DAPI (representative example). Un-needled animal with 8 weeks of skincare. GAGs showed dense deposits occupying much of the dermis, leaving only isolated collagen bundles visible (white arrows)

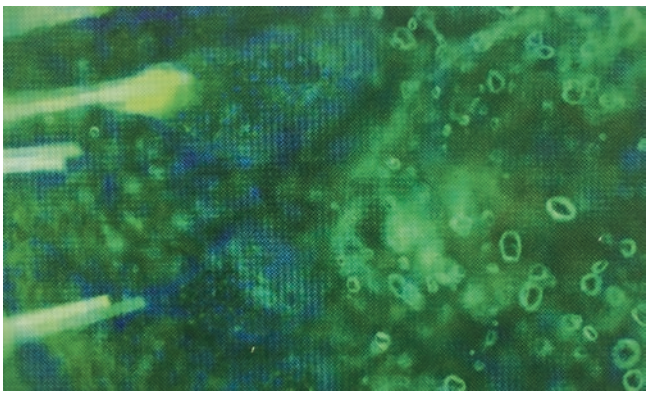


Fig. 11.11 Immunohistochemical staining, anti-GAG. Needled animal. Needled animal with 8 weeks of skincare stained without primary antibody. As observed in the PAS staining, a marked increase in the amount of GAGs was observed throughout the different needled groups in comparison to the un-needled groups

11.2.9 Role of Vitamins in Wound Healing

Maximal post Needling improvement was seen in combination with pre- and post-treatment of the skin with vitamin A and oxidants vitamin C and E (see Figs. 11.12 and 11.13).

11.2.10 No Dyspigmentation After Medical Needling

A disadvantage of ablative scar treatments is that there is an increased risk of dyspigmentation especially in darker skin

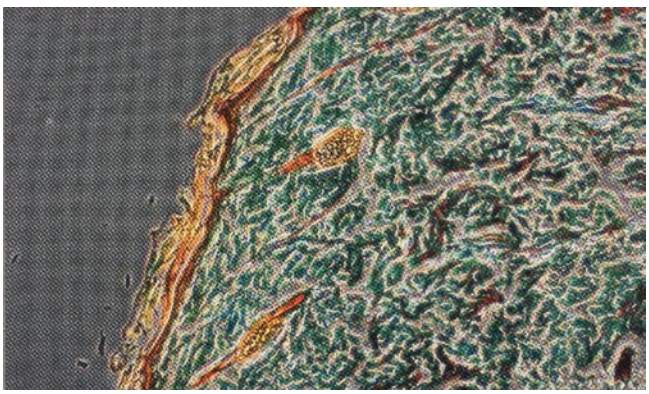


Fig. 11.12 Masson's Trichrome staining. Untreated animal (control)

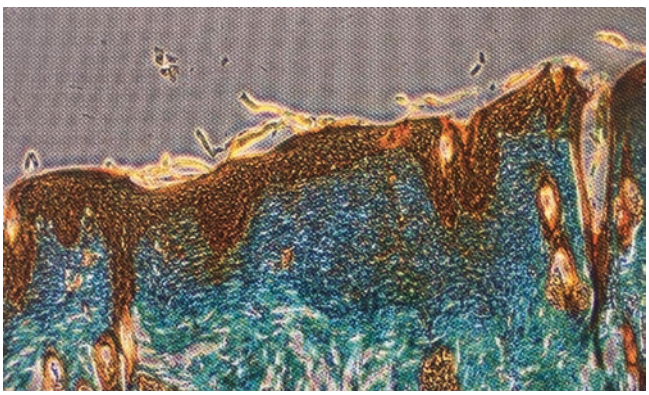


Fig. 11.13 Needled animal with 8 weeks of skincare collagen fibre bundles were increased, thickened and more loosely woven in both the papillary and reticular dermis most prominently in the needled plus skincare group (D). Elastin fibres in the dermis highly linear and the epidermal dermal interface showed regular dermal papillae; cellular polarity and normal epidermal differentiation appeared to be maintained; and the elastin network within the reticular dermis was regularly thickened and organized in all groups

types [21–23]. In 480 patients, it has been shown that there is no risk of dyspigmentation after Medical Needling [20]. Furthermore, Medical Needling does not change the number of melanocytes, but the expression levels of melanocyte-stimulating hormone (MSH) and interleukin-10 (IL-10) are modified [20]. MSH which influences the proliferation and activity of melanocytes is significantly downregulated within days after treatment. IL-10 as an anti-inflammatory cytokine is upregulated post-operatively [20]. In a subsequent study, it has been shown that it is not possible to repigment larger areas of hypopigmented skin with Medical Needling alone.

11.2.11 Repigmentation of Hypopigmented Burn Scars with Medical Needling and Non-cultured Autologous Skin Cell Suspension (NCASCS)

Currently, numerous methods are available to treat hypopigmented skin, such as split skin grafting [24, 25], lasers [26] and cultured skin cell transplantation [27–29]. In recent years, research focused additionally on non-cultured skin cell suspension. The autologous cell harvesting device is used to create a spray suspension of living autologous skin cells. These cells are harvested intraoperatively and directly applied, in suspension, to the prepared wound.

In order to prepare an area for treatment with NCASCS, the wound has been first treated by using dermabrasion or lasers which are both ablative methods. By their nature, ablative treatments remove skin structures and cells, including the basement membrane, which are replaced by a thinner epidermis with flatter rete ridges [1, 2, 29]. This initiates an inflammatory response that stimulates fibroblasts to produce parallel-oriented scar collagen instead of physiological lattice pattern collagen [1, 30]. Additionally, the risk of dyspigmentation increases after these ablative treatments due to associated damage to the melanocytes [31, 32].

An ideal wound preparation for the autologous cell suspension would be a treatment that does not destroy structures of the epidermis yet creates a conduit that allows ingress of melanocytes, which promotes the formation of physiological collagen instead of scar collagen and initiates the expression of growth factors. As we described above, Medical Needling offers all these advantages.

To combine both procedures, it is at first necessary to prepare a depigmented scar with intense medical needling. Afterwards, the autologous cell suspension is applied through a spray syringe on the wound.

The hypothesis is that the melanocytes of the cell suspension link through the epidermal canals onto the basal membrane. In a pilot study with 20 patients, it has been shown that it is possible to get marked subjective and objective improvements regarding repigmentation with the combination of Medical Needling and NCASCS [33].

11.3 Clinical Results

11.3.1 Medical Needling

See Figs. 11.14, 11.15, 11.16, 11.17, 11.18, 11.19, and 11.20.

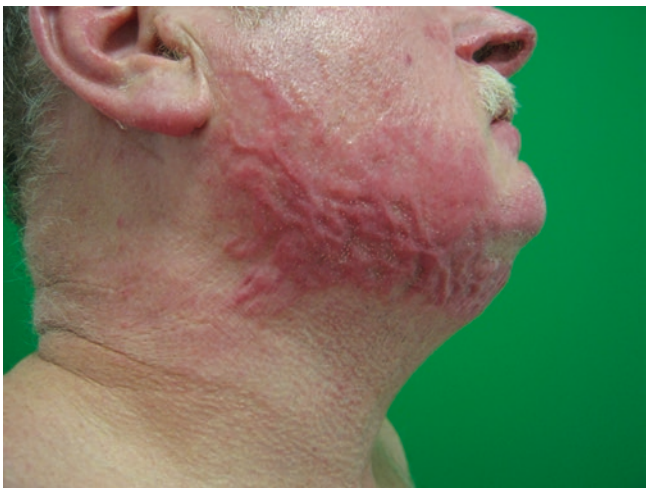


Fig. 11.14 One-month-old active burn scar due to open fire burn injury

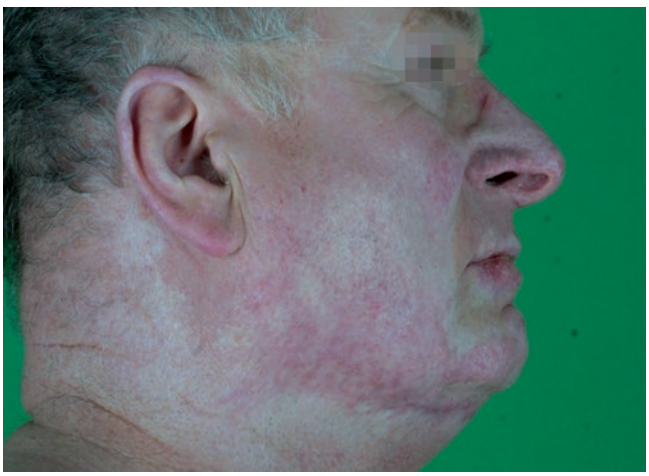


Fig. 11.15 Needling was performed 1 month after trauma (just after the epithelium was closed) Pictures show improvement of the scar 1 year post needling

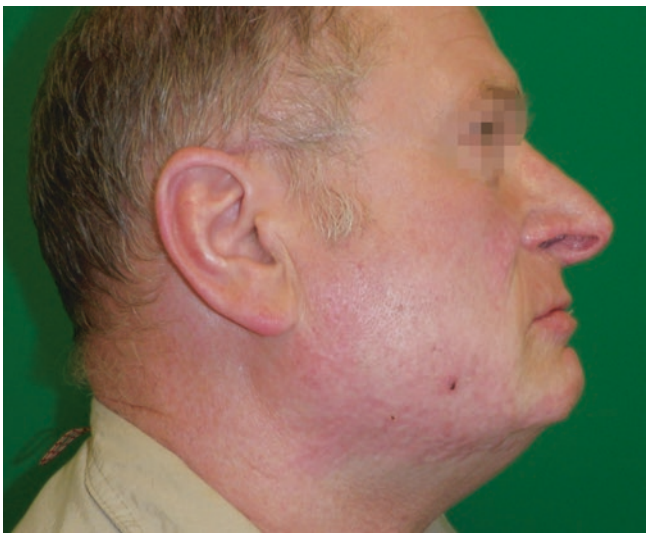


Fig. 11.16 Result after a second deep needling 1 year after the second needling (2 years post initial trauma)

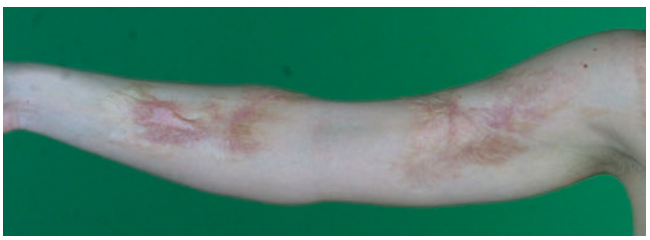


Fig. 11.17 Hypertrophic burn scar lower arm 5 years post trauma

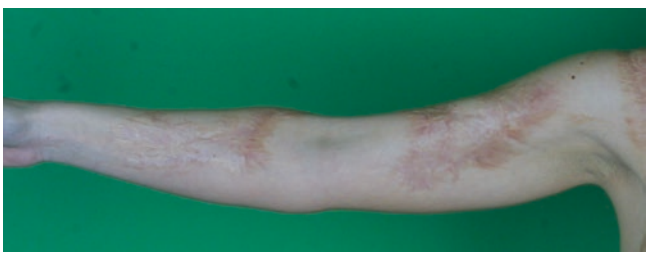


Fig. 11.18 Improvement of the hypertrophic burn scar 6 months post 3 mm needling

11.3.2 Medical Needling and NCASCS

See Figs. 11.21, 11.22, 11.23, 11.24, and 11.25.

11.4 Conclusion

Medical Needling offers a new alternative treatment for burn scars by changing pathological scar collagen with thousands of micro punctures into a scar with normal collagen. When we prick skin, we puncture blood vessels, and the release of platelets signals the release of growth factors which then improve dermal collagen, vascularization and epidermal

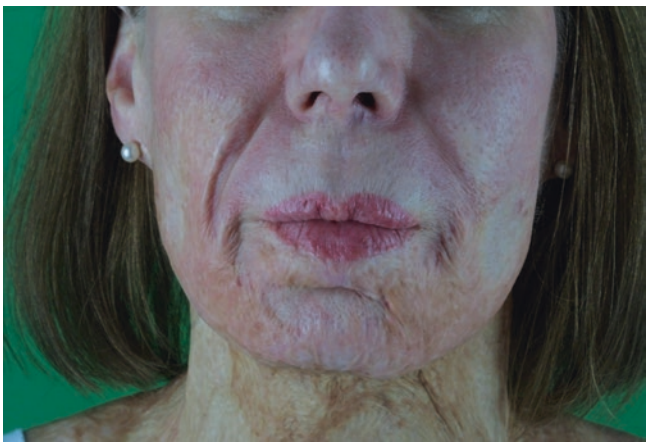


Fig. 11.19 Full face burn scars after a deep second- and third-degree burn accident, picture taken 10 years post trauma

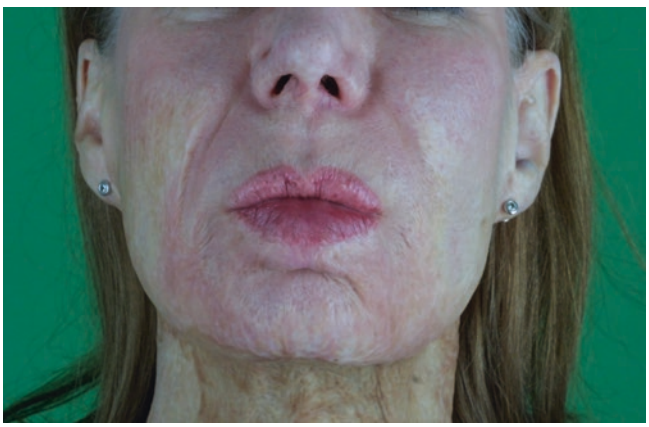


Fig. 11.20 Improvement of the skin and scar condition 6 months after a 3 mm needling of the face

thickening. Medical Needling liberates growth factors like VEGF and TGF-ß3 which initiate the replacement of parallel, packed scar collagen by physiological collagen I in a lattice orientation, with added elastin and glycosaminoglycans. The scars after Medical Needling tend to appear smoother, softer, less itchy and much less obvious. The skin becomes altogether more elastic, and as a result, contractures are also softened, and in some cases, invasive surgery to treat contractures becomes unnecessary. Skin needling is showing us that it relieves tensions in tissues and minimizes the need for Z-plasty and major flaps. Early skin needling could help avoid scar contractures which is one of the most crippling feature of burns. A significant problem arises for young girls as their breast develops, because the breast tissue is entrapped by scar tissue and does not develop properly. Skin needling is worth doing for these patients and should be done as early as possible after the burn injury. There is a good reason to believe that if we can change the spectrum of tissue healing dominated by TGF-ß1 and -ß2 in the acute phase and convert it into a regenerative phase promoted by TGF-ß3, that we

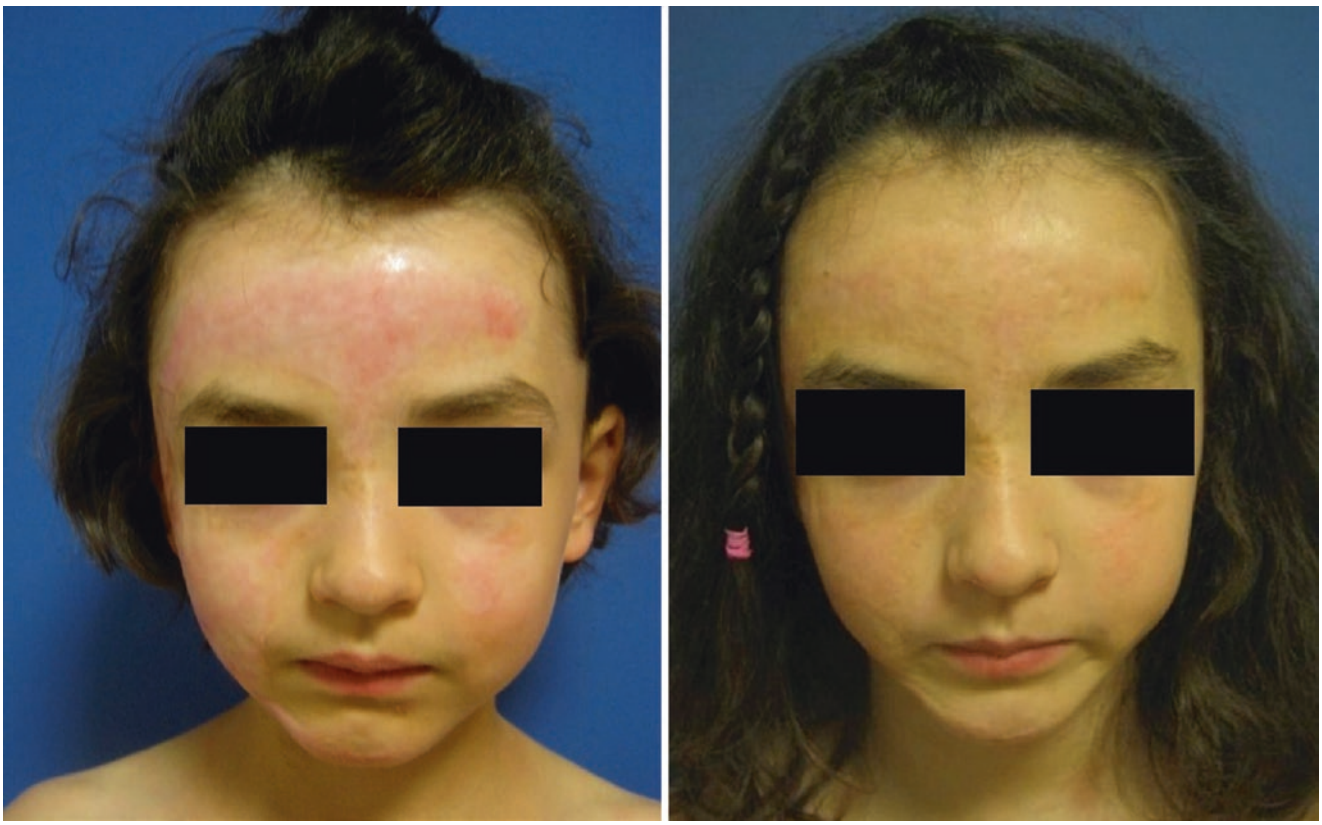


Fig. 11.21 Forehead scar with hypopigmented areas before and with better repigmentation 1 year post needling combined with NCASCS

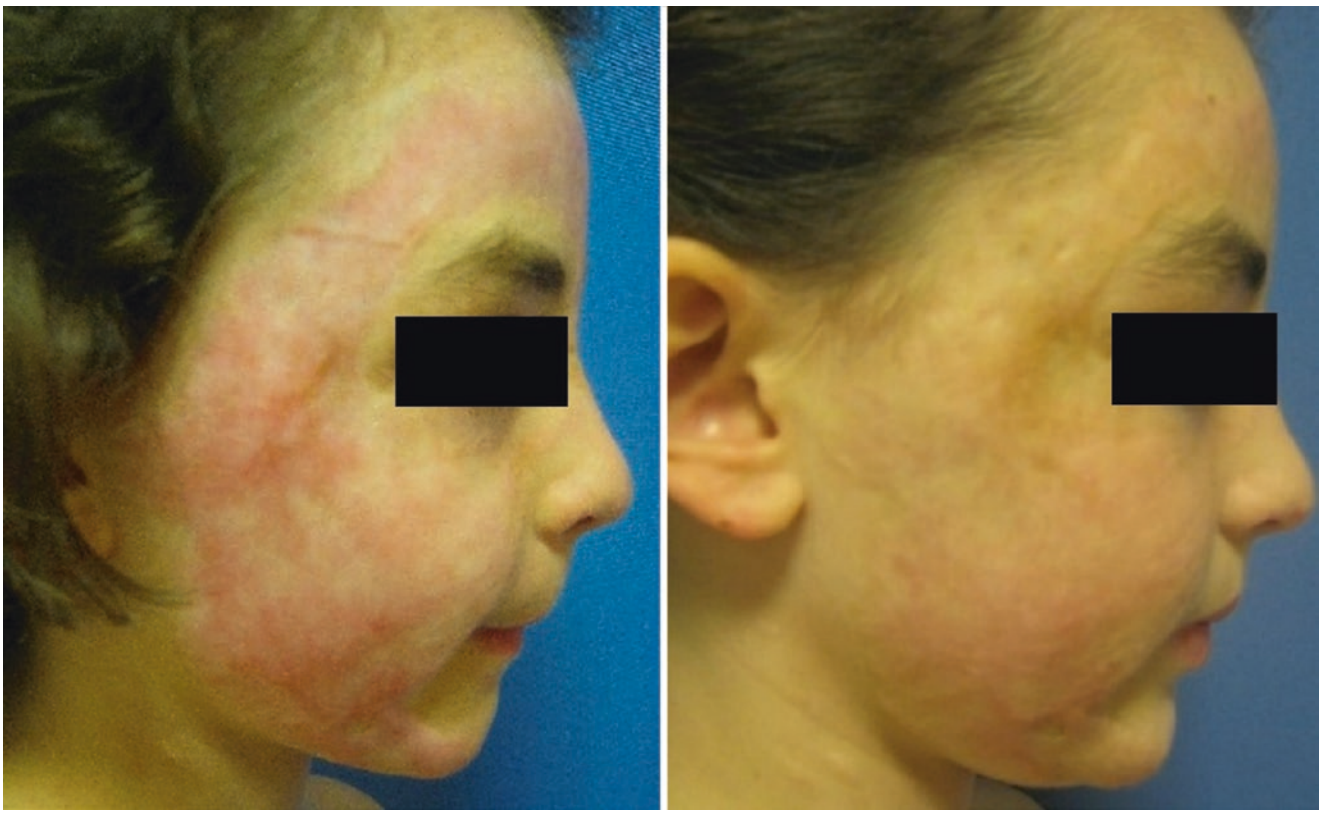


Fig. 11.22 Hypopigmented scar after hot water burn 16 months post trauma before and with better repigmentation 1 year post needling combined with NCASCS

Fig. 11.23 Hypopigmented scar lower back after burn 24 months post trauma before treatment

Fig. 11.24 Improvement of the melanin level and thereby repigmentation of the scar 1 year post treatment

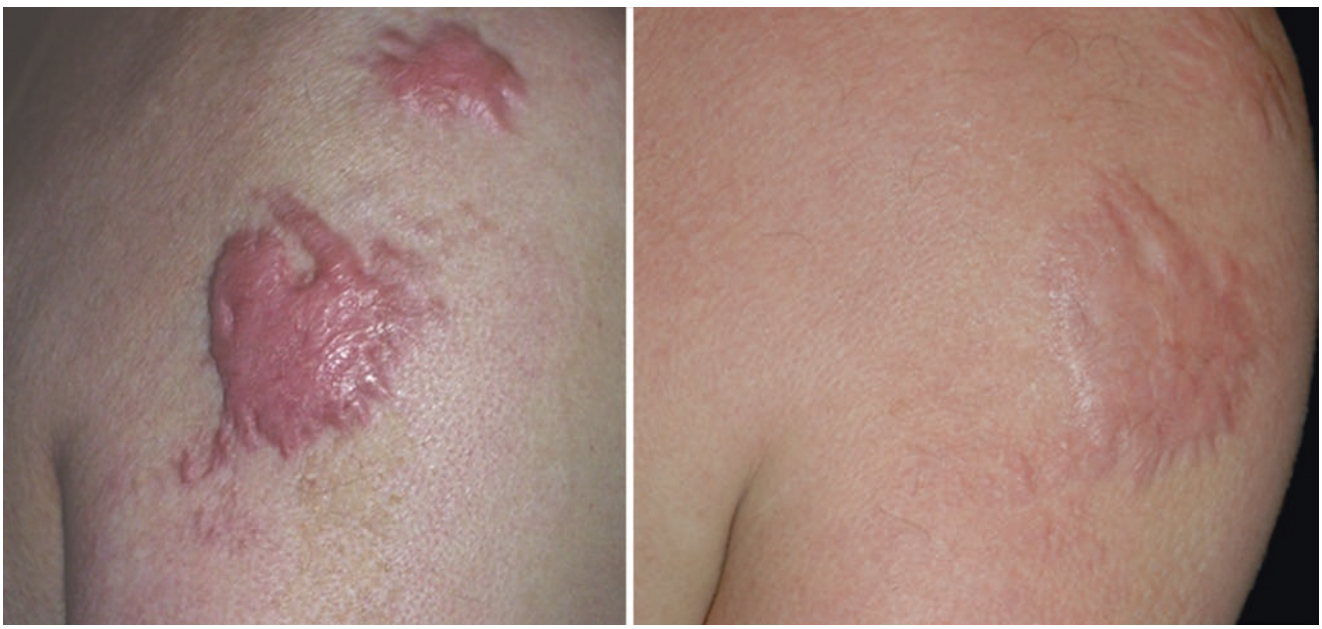


Fig. 11.25 A post-burn keloid is not the same as a true keloid, and skin needling is a convenient way to treat these scars. The result seen is after 1-year interval after one session of 3 mm needling

will have long-term effects and avoid contractures. Our experience at this stage is largely on treating well-established burns, but the authors feel that skin needling should become a part of the early management of burn scars.

For repigmentation, it offers the ideal pretreatment for non-cultured autologous skin cell transplantation. Both treatments preserve the epidermis which results in a reduced risk of new scarring or dyspigmentation.

Medical Needling offers a treatment that for the first time in medical history can cause regeneration of tissue and soften burn scars and reduce contractures. When done repeatedly and intensively, then burn-scarred tissue can seem to be almost normal unscarred skin. However, the timing probably is of utmost importance. The authors believe skin needling should be done as soon after the burn injury as is reasonable because they have had experience treating burns within a few hours to days of the initial burn injury, and it seems the earlier the needling, the greater the chance to heal with minimal scars.

Skin needling needs to be understood by clinicians treating burns, so that this valuable technique can be offered to as many burn victims as possible.

References

1. Rawlins JM, Lam WL, Karoo RO, Naylor IL, Sharpe DT. Quantifying collagen type in mature burn scars: a novel approach using histology and digital image analysis. J Burn Care Res. 2006;27(1):60–5.
2. Roy D. Ablative facial resurfacing. Dermatol Clin. 2005;23(3):549–59.. viii

3. Avram MM, Tope WD, Yu T, Szachowicz E, Nelson JS. Hypertrophic scarring of the neck following ablative fractional carbon dioxide laser resurfacing. Lasers Surg Med. 2009;41(3):185–8.
4. Costa IM, Damasceno PS, Costa MC, Gomes KG. Review in peeling complications. J Cosmet Dermatol. 2017;16(3):319–26.
5. Aust MC, Fernandes D, Kolokythas P, Kaplan HM, Vogt PM. Percutaneous collagen induction therapy: an alternative treatment for scars, wrinkles, and skin laxity. Plast Reconstr Surg. 2008;121(4):1421–9.
6. Fernandes D, Signorini M. Combating photoaging with percutaneous collagen induction. Clin Dermatol. 2008;26(2):192–9.
7. Aust MB, Fernandes SD. Illustrated guide to percutaneous collagen induction: basics, indications, use. New Malden: Quintessence Publishing; 2013.
8. Camirand A, Doucet J. Needle dermabrasion. Aesthet Plast Surg. 1997;21(1):48–51.
9. Orentreich DS, Orentreich N. Subcutaneous incisionless (subcision) surgery for the correction of depressed scars and wrinkles. Dermatol Surg. 1995;21(6):543–9.
10. Fernandes D. Percutaneous collagen induction: an alternative to laser resurfacing. Aesthet Surg J. 2002;22(3):307–9.
11. Aust MC, Knobloch K, Reimers K, Redeker J, Ipaktchi R, Altintas MA, et al. Percutaneous collagen induction therapy: an alternative treatment for burn scars. Burns. 2010;36(6):836–43.
12. Aust MC, Reimers K, Kaplan HM, Stahl F, Repenning C, Scheper T, et al. Percutaneous collagen induction-regeneration in place of cicatrisation? J Plast Reconstr Aesthet Surg. 2011;64(1):97–107.
13. Aust MC, Reimers K, Gohritz A, Jahn S, Stahl F, Repenning C, et al. Percutaneous collagen induction. Scarless skin rejuvenation: fact or fiction? Clin Exp Dermatol. 2010;35(4):437–9.
14. El-Domyati M, Barakat M, Awad S, Medhat W, El-Fakahany H, Farag H. Microneedling therapy for atrophic acne scars: an objective evaluation. J Clin Aesthet Dermatol. 2015;8(7):36–42.
15. El-Domyati M, Barakat M, Awad S, Medhat W, El-Fakahany H, Farag H. Multiple microneedling sessions for minimally invasive facial rejuvenation: an objective assessment. Int J Dermatol. 2015;54(12):1361–9.
16. Ferguson MW, O'Kane S. Scar-free healing: from embryonic mechanisms to adult therapeutic intervention. Philos Trans R Soc Lond Ser B Biol Sci. 2004;359(1445):839–50.
17. Schultz GS, Wysocki A. Interactions between extracellular matrix and growth factors in wound healing. Wound Repair Regen. 2009;17(2):153–62.
18. Bandyopadhyay B, Fan J, Guan S, Li Y, Chen M, Woodley DT, et al. A "traffic control" role for TGFbeta3: orchestrating dermal and epidermal cell motility during wound healing. J Cell Biol. 2006;172(7):1093–105.
19. Occleston NL, Fairlamb D, Hutchison J, O'Kane S, Ferguson MW. Avotermin for the improvement of scar appearance: a new pharmaceutical in a new therapeutic area. Expert Opin Investig Drugs. 2009;18(8):1231–9.
20. Aust MC, Reimers K, Repenning C, Stahl F, Jahn S, Guggenheim M, et al. Percutaneous collagen induction: minimally invasive skin rejuvenation without risk of hyperpigmentation-fact or fiction? Plast Reconstr Surg. 2008;122(5):1553–63.
21. Yamaguchi Y, Hearing VJ. Melanocytes and their diseases. Cold Spring Harb Perspect Med. 2014;4(5):a017046.
22. Alam M, Warycha M. Complications of lasers and light treatments. Dermatol Ther. 2011;24(6):571–80.
23. Vaiyavatjamai P, Wattanakrai P. Side effects and complications of fractional 1550-nm erbium fiber laser treatment among Asians. J Cosmet Dermatol. 2011;10(4):313–6.
24. Onur E. The treatment of burn scar hypopigmentation and surface irregularity by dermabrasion and thin skin grafting. Plast Reconstr Surg. 1990;85(5):754–8.
25. Kahn AM, Cohen MJ. Treatment for depigmentation following burn injuries. Burns. 1996;22(7):552–4.
26. Cho S, Zheng Z, Park Y-K, Roh MR. The 308-nm excimer laser: a promising device for the treatment of childhood vitiligo. Photodermatol Photoimmunol Photomed. 2011;27(1):24–9.
27. Stoner M, Wood F. The treatment of hypopigmented lesions with cultured epithelial autograft. J Burn Care Rehabil. 2000;21:50–4.
28. Zhang DM, Hong WS, Fu LF, Wei XD, Xu AE. A randomized controlled study of the effects of different modalities of narrowband ultraviolet B therapy on the outcome of cultured autologous melanocytes transplantation in treating vitiligo. Dermatol Surg. 2014;40(4):420–6.
29. Ross EV, Naseef GS, McKinlay JR, Barnette DJ, Skrobal M, Grevelink J, et al. Comparison of carbon dioxide laser, erbium:YAG laser, dermabrasion, and dermatome. J Am Acad Dermatol. 2000;42(1):92–105.
30. Laws RA, Finley EM, McCollough ML, Grabski WJ. Alabaster skin after carbon dioxide laser resurfacing with histologic correlation. Dermatol Surg. 1998;24(6):633–6.
31. Bernstein LJ, Kauvar ANB, Grossman MC, Geronemus RG. The short- and long-term side effects of carbon dioxide laser resurfacing. Dermatol Surg. 1997;23(7):519–25.
32. Thomas JR, Somenek M. Scar revision review. Arch Facial Plast Surg. 2012;14(3):162–74.
33. Busch KH, Bender R, Walezko N, Aziz H, Altintas MA, Aust MC. Combination of medical needling and non-cultured autologous skin cell transplantation (ReNovaCell) for repigmentation of hypopigmented burn scars. Burns. 2016;42(7):1556–66.

Principles of Autologous Fat Grafting: Current Application in Burn Wounds and Scars

12

Lukas Prantl and Alexandra Anker

12.1 Definition

Fat grafting is defined as the improvement of body contour by a multistep low-invasive procedure consisting of harvesting, preparation, and final application of refined fat tissue into a recipient site inducing regenerative processes [1, 2].

12.2 Indications and Contraindications

Autologous fat transfer has become widely accepted for an increasing number of indications. Fat grafts are primarily applied as a biocompatible filling substance for soft-tissue deficiency resulting from trauma, illness (e.g., breast cancer), or senescence as a secondary reconstructive measure [3].

Lipofilling has become a pivotal adjunctive therapeutic measure in breast reconstruction. Asymmetries or contour irregularities after the initial surgery (e.g., pedicled or free microvascular flaps, breast implants or expanders) can be corrected [4, 5]. Patients suffering from radiation injury with indurations and irregularities of the breast envelope are treated with fat grafts to smooth the skin surface and reduce adhesions [6]. In fact, in critically ill patients, complete breast reconstruction via fat mammoplasty can be considered to avoid the perioperative risks and comorbidities associated with more extensive surgeries such as free tissue transfer (e.g., in the palliative setting) [1].

According to the recently published consensus statement of the German society of plastic surgeons (DGPRAEC—Deutsche Gesellschaft für Plastische, Rekonstruktive und Ästhetische Chirurgie), the operative indication for fat grafting after lumpectomy in marked contrast to complete breast ablation should be strictly handled. After segmental mastectomy of ductal carcinoma in situ (DCIS), at least 2 years of absence of cancer recurrence is recommended before the procedure may be evaluated [1].

Likewise, patients with a hereditary predisposition for breast cancer (e.g., carriers of BRCA-1/-2 mutation, positive family history) should be treated with extreme caution only (e.g., in a controlled study setting) [6]. Postoperatively, the radiographic adjudication may be aggravated [7–9]. With regard to its oncologic safety, a recent study has shown no overall increase in locoregional or systemic cancer recurrence after fat grafting in patients with segmental or total mastectomy followed by reconstruction compared to an analogous control group treated without lipofilling. However, further analysis of this data unveiled that a specific subgroup consisting of patients treated with hormonal therapy had an increased risk of locoregional recurrence of 1.4% following lipofilling versus 0.5% without lipofilling ($p = 0.038$) [10]. Nevertheless, based on current scientific knowledge, the recurrence rate can still be considered low. Investigations in the closer future will hopefully determine the clinical significance of this increase.

Informed consent, close follow-up, and personalized breast cancer-screening regimes in accordance with the latest breast cancer guidelines (e.g., http://www.ago-online.de/en/guidelines-mamma/march-2016/) are inevitable for patients under hormonal therapy, segmental resection of DCIS, and hereditary breast cancer predisposition.

Aside from its application in oncologic breast reconstruction, micromastia, Poland syndrome, or tuberous breasts have been considered as indications for fat grafting as primary reconstructive measure (Fig. 12.1) [5, 6]. In comparison to conventional breast augmentation, implant related complications such as foreign body reaction including capsular contracture or implant rupture necessitating removal or replacement surgeries can be avoided. The unpredictability

L. Prantl (✉)
Department of Plastic, Hand and Reconstructive Surgery, University Hospital of Regensburg, Regensburg, Germany

Department of Plastic, Hand and Reconstructive Surgery, Caritas Hospital St. Josef, Regensburg, Germany
e-mail: lukas.prantl@klinik.uni-regensburg.de

A. Anker
Department of Plastic, Hand and Reconstructive Surgery, Caritas Hospital St. Josef, Regensburg, Germany

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_12

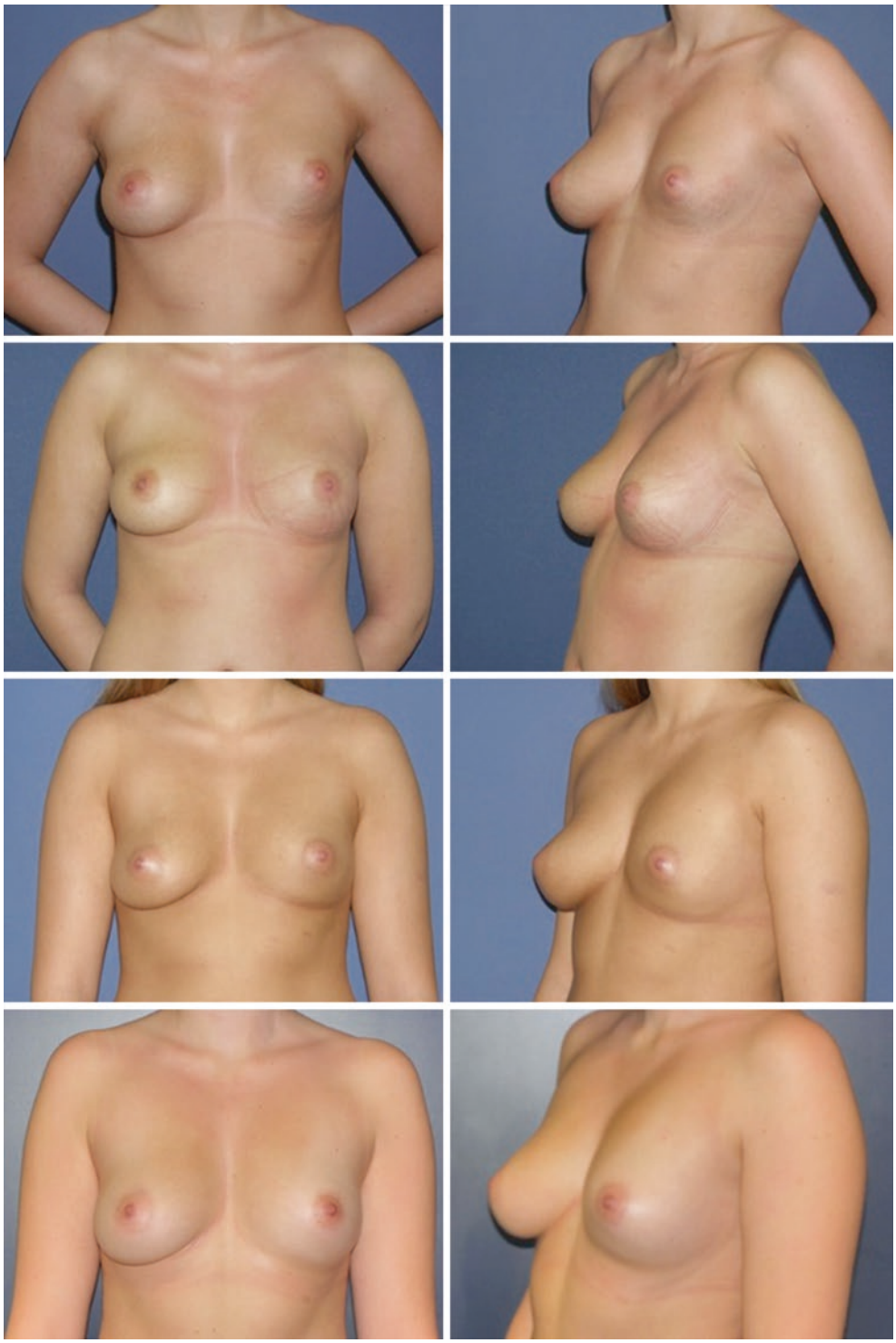


Fig. 12.1 Patient with congenital breast asymmetry before (first row) and after three sessions of autologous fat grafting (second row) with a considerable impact on breast volume, 1 year postoperatively (third row), and late results 4 years after the procedure (fourth row)

of fat volume retention and related aesthetic outcome, however, remains a challenge in autologous fat transfer procedures. As much as 40–60% of the transplanted fat grafts are typically retained [11]. In contrast, overcorrection increases the risk of fat necrosis and should be avoided [12]. Adequate volume gain along with a satisfying cosmetic result is usually achieved by serial interventions. Most authors recommend a refractory phase of 3 months minimum in between two sessions [2].

Despite this variable degree of fat intake, fat grafting is generally well accepted by the great majority of patients due to its low morbidity, tolerable downtime, and natural results.

Furthermore, autologous fat transfer has become an appreciated adjunct procedure for the low-invasive correction of residual contour deformities occurring after breast reduction or augmentation [5, 6, 13].

Aside from the breast, fat grafting has been used in multiple other body regions. The aim of volume and contour improvement has been successfully achieved in facial, gluteal, and penile volume deficiencies [6, 14–23]. HIV seropositive patients suffering from facial lipodystrophy under antiretroviral therapy were successfully treated with facial fat auto-grafting leading to aesthetic and social benefits [24].

Skin rejuvenation by placement of fat grafts and restoring fullness to atrophic subcutaneous tissue in the face or on the dorsum of the hand showed promising results (Fig. 12.2) [22, 25, 26].

Contraindications to autologous fat transfer include general limitations to surgery such as unrealistic expectations or body dysmorphic disorder, active malignancy or infection in the donor or recipient site, hematologic abnormalities or anticoagulation, as well as pregnancy and breastfeeding. In severe chronic disease states, operability might be assessed with caution [1, 27].

As mentioned before, careful consideration is indicated in patients with positive family history for breast cancer or genetic predisposition (e.g., including BRCA-1/-2 gene carriers) as well as after lumpectomy of DCIS [1, 6].

12.2.1 Fat Grafting in Burn Wounds and Scars

Recently, autologous fat transfer has gained attention in the treatment of burn scars and wounds owing to its high plasticity and scarce donor site morbidity. Improvements in scar softness, color, texture, and quality have been attributed to a favorable cytokine and growth factor profile of adipose derived stem cells (ASC) (Figs. 12.3 and 12.4) [28]. The well-known in vitro changes of cytokines, growth factors, and adhesion molecules in different co-culture models with ASC support the clinical observation that ASC have a stabilizing effect when injected into irradiated wounds and scars [29].

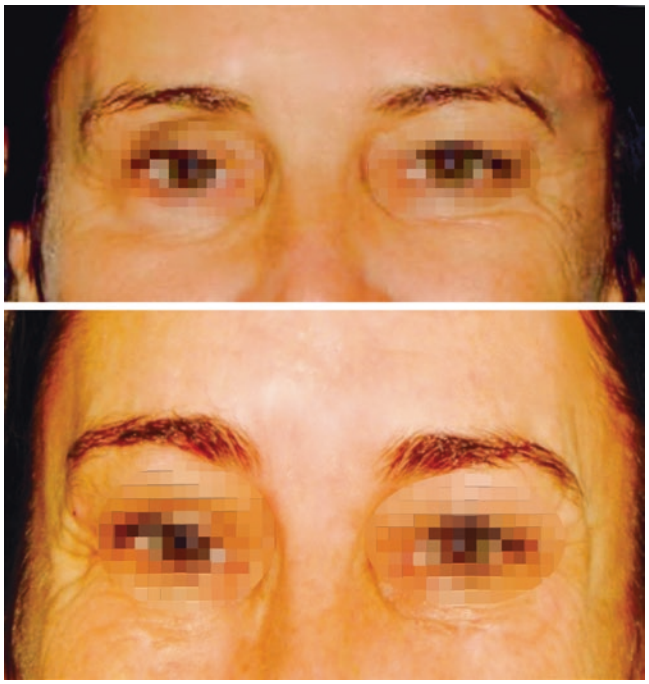


Fig. 12.2 Patient suffering from soft tissue deficiency in the right superior orbital compartment before (top) and 3 months after the lipofilling procedure (bottom)

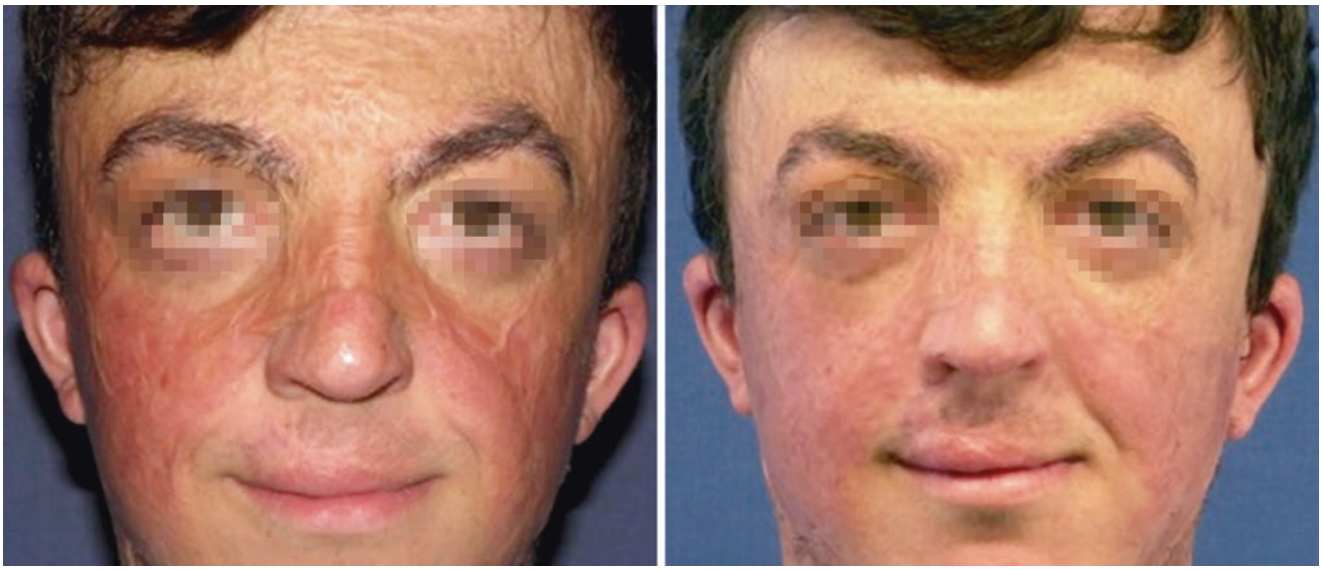


Fig. 12.3 Patient suffering from burn injury in early childhood before and after three sessions of lipofilling. Reduced redness and less scar tension are reported by the patient

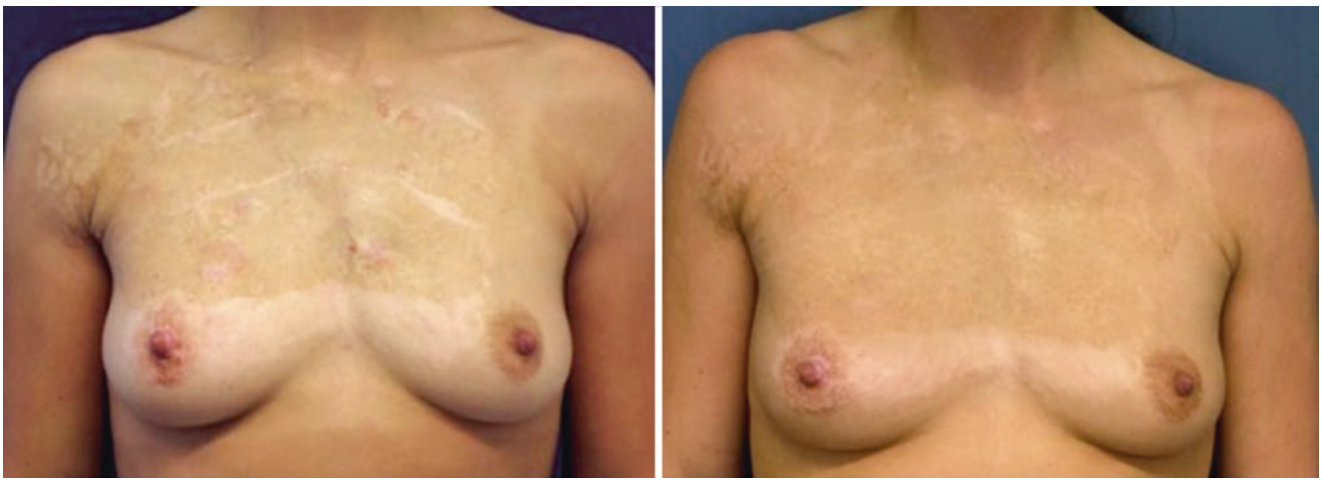


Fig. 12.4 Patient with extensive thoracic scalding requiring skin transplantation before and after autologous fat transfer. According to the patient, skin quality improved markedly with reduced tendency of laceration

Indications	
Breast reconstruction	Asymmetry or contour defects after prior reconstructive surgery (e.g., pedicled or free microvascular flaps) Indurations/radiodermatitis after radiotherapy Complete fat mammoplasty
Congenital breast deformities	Poland syndrome Tuberous breast deformities Micromastia
Soft tissue defects and contour deformities/ volume augmentation	Contour deformities resulting from trauma or illness Asymmetry or contour defects occurring after breast augmentation or reduction Asymmetry or contour defects after prior liposuction Facial atrophy (e.g., caused by antiretroviral medication) Gluteal or penile augmentation
Skin rejuvenation	Rejuvenation of the dorsum of the hand Facial rejuvenation
Burn scars and chronic wounds	Improvement of scar quality, softness, texture, and color
Relative contraindications	
Breast cancer with segmental mastectomy	Especially in case of DCIS
Hereditary predisposition for breast cancer	Positive family history BRCA-1/-2 mutation
Absolute contraindications	
Active malignancy or infection	At recipient or donor site
Hematologic abnormalities	Anticoagulation
General	Pregnancy and breastfeeding Body dysmorphic disorder Unrealistic expectations External motivation

In a controlled nude mouse model, fat grafting induced dermal hyperplasia due to increased collagen deposition compared to an untreated control site [30].

Further, investigations in chronic burn scars treated with lipofilling showed an increase in neovascularization and improved dermal organization in comparison to untreated areas. Immunohistochemical analysis confirmed a reduction of melanocytes with a corresponding decrease in hyperpigmentation and consecutive color improvement of the scar [31].

Another controlled study found enhanced skin elasticity following autologous fat transfer in cicatrices while no difference could be detected for the control group, which had been injected with saline only. Pre- and postoperative durometer analyses confirmed a significant reduction in skin hardness at 3 months follow-up in fat-grafted areas of mature burn scars [32].

Further, this regenerative effect is not limited to burn injuries. In fact, lower lid ectropion caused by chemical burn was effectively treated with autologous fat transfer. One month postoperatively, the patient presented with a considerably improved esthetic and functional aspect with the absence of xerophthalmia. Remarkably, sustainable results could be documented as long as 5 years after the procedure [33].

A few studies report beneficial effects of fat transfer providing wound coverage in acute burn injury with a potential reduction of inflammation and promotion of vascularization [34–36]. However, critical evaluation is indicated as an additional trauma is caused by harvesting fat from a healthy donor site in a critically ill patient.

Overall, studies on fat grafting in burn patients are of small sample size, and large randomized controlled trials are

missing requiring further research [35]. We face the same conflict with the increasing application of platelet-rich plasma (PRP) as single therapy or in combination with ASC. Numerous in vitro studies have proved the regenerative aspect of platelets; however, supportive clinical evidence is widely missing [37].

12.3 Technique

Autologous fat transfer is a highly elective surgery that is performed under sterile conditions by trained health professionals in an outpatient or inpatient setting. Preoperatively, patients need to be instructed in detail about the procedure itself, associated risks and complications, and the postoperative course by the surgeon and provide oral and written informed consent acknowledging their understanding. Photographic documentation of the donor and recipient sites is essential to compare postoperative results with the preoperative status and assess the absorption rate of the transplanted tissue [2].

Fat grafting is a multi-step process including (1) harvesting and (2) preparation of lipoaspirate as well as (3) injection of purified fat.

12.3.1 Harvesting

Prior to fat aspiration, small incisions of a few millimeters length, ideally hidden in creases or previous scars and placed convenient for access, are created with the tip of a scalpel No. 11. Then the donor site is prepared by infiltration of tumescent solution containing a vasoconstrictor (e.g., epinephrine, 1:200,000) for minimization of bleeding and optionally a local anesthetic for pain relief [38]. Lidocaine and articaine have recently been associated with a reduction in viability of adipocyte precursor cells. Other agents such as ropivacaine might preferably be used for tumescent anesthesia [39, 40].

The donor site is chosen preoperatively according to tissue volume and the patient's preference. To improve body contour, most commonly liposuction is performed on the abdomen, thighs, and hips.

For tissue extraction, various liposuction methods are in common use, e.g., manual syringe liposuction ("Coleman technique"), pump-assisted vacuum liposuction, water-assisted liposuction ("WAL"), ultrasound-assisted liposuction, or liposuction with the aid of harvesting devices such as LipiVage (Genesis Biosystems Inc., Lewisville, TX) [12, 26, 41–45]. No clear evidence for the superiority of any fat aspiration technique has been found to date, and it appears that all available harvesting methods are appropriate for successful autologous fat transfer [2, 46–49]. Recently adipocyte viability of up to 90% has been reported for water-assisted liposuction [1].

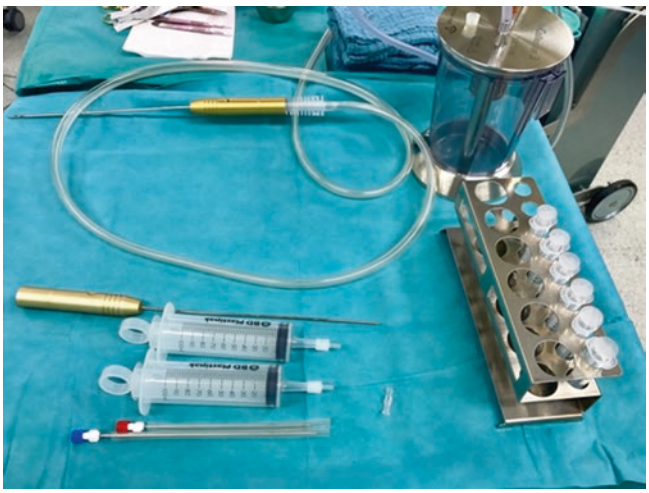


Fig. 12.5 Equipment used for fat grafting. Suction device, collection container, transfer syringe, Luer-lock syringes, and blunt infiltration cannula

Irrespective of the technique used, blunt harvesting cannulas are recommended to encourage viability of adipocytes. Cannulas with large diameters (>4 mm) may be advantageous, and low suction pressure should be administered [50–53].

To avoid exposure to the air and potential bacterial contamination, a closed, sterile system from suction device to collection container is favorable (Fig. 12.5) [1].

12.3.2 Preparation

After adequate accumulation of lipoaspirate, the tissue is transferred from the collection container into Luer-lock syringes, stored vertically upside down sitting in a grid for sedimentation for a few minutes (Fig. 12.6a, b) [54]. Under the action of gravity, the aspirate is separated into three phases, an upper oily layer from disrupted fat cells, a middle relatively pure layer containing vital adipocytes, and a lower watery layer consisting of blood and infiltration liquids [6]. The aqueous phase is discarded from the syringe to obtain a proper purified fat graft ready to inject into the recipient site (Fig. 12.6c). It has to be considered that a significant fraction of the obtained lipoaspirate is tumescent solution, erythrocytes, and other contaminants that are eliminated prior to fat injection, relevantly reducing the volume of the graft.

To separate the different phases, alternatively, the aspirated tissue is processed via filtration or centrifugation [54]. Comparative studies trying to identify the optimal technique

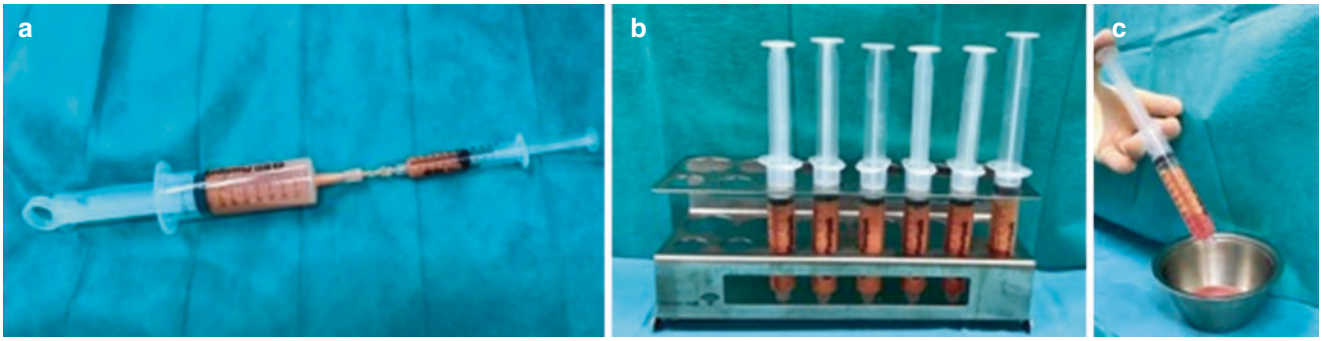


Fig. 12.6 (**a**) Fat transfer into Luer-lock syringes. (**b**) Syringes stored upside down in a tray for sedimentation. (**c**) Discarding the aqueous phase

Fig. 12.7 Blunt infiltration cannula

of fat graft preparation provided ambiguous results, and to date, none of them can be given a clear preference [25, 47, 55–57].

12.3.3 Injection

For fat placement, blunt infiltration cannulas with a single distal aperture are used. The cannulas are available with different diameters, lengths, and curves as needed for different parts of the body (Fig. 12.7) [1]. For hand and face, usually 1–3 mL Luer-lock syringes are used, for any other region (e.g. breast, gluteal region) 10 mL or even larger syringes seem to be appropriate.

Through the same incisions that were used for infiltration of tumescent solution, the cannula is inserted and a pathway is generated. While the cannula is being withdrawn, the plunger of the syringe is pressed slightly and fat is deposited. Multiple ducts in a V-shaped pattern are produced, and with each pass, about 0.5–1.0 mL of fat is placed to create a homogenously distributed three-dimensional meshwork [58].

12.3.4 Postoperative Care

A close follow-up with regular wound inspections to recognize complications such as infection promptly is indicated to ensure patient safety [2]. Patients should be prepared for a recovery period of a few days minimum. Initially, analgesic agents may be necessary. Local cooling measures promote a rapid regression of swelling and alleviate pain. Fat graft donor sites are provided with compression garments to reduce the risk of formation of hematoma and seroma [1]. At the recipient site, a slightly shaping dressing can be considered; however, direct pressure on the freshly transplanted lipoaspirate should be avoided rigorously [4, 59].

12.4 Risks and Complications

Fat grafting is generally considered a low-risk, low-morbidity surgical technique associated with tolerable pain and a short postoperative downtime.

Complications include swelling, hematoma, or seroma of the donor as well as the recipient site, whereas severe bleeding requiring emergency surgery has not been reported so far [60–62]. Infections with skin microbes occur occasionally, and rare cases of septic shock were noted [23, 60, 63].

Preoperative assessment of fat-intake rates is challenging. Graft volume loss up to 40–60% due to absorption or fat tissue necrosis is described [11, 19]. Interestingly, fat transplant hypertrophy or overgrowth was seen as an infrequent event [64, 65]. Consequently, patients' frustration is common if postoperative results do not mirror the expected outcome.

Adiponecrosis, oil cysts, or calcifications of breast tissue may develop after fat transferring [1]. These morphological irregularities may impede interpretation of breast sonogram, mammography, or MRI, thereby potentially interfering with breast cancer detection [7, 13, 60]. No reported case of delay in diagnosis or treatment of malignancy after autologous fat transplantation neither any other clear evidence was found to date; however, that strongly confirms this interference.

Unsatisfactory esthetic outcomes with scarring of stab incisions, surface contour irregularities, or asymmetry are rare [1].

Extensive thinning of the skin with the cannula at the donor and recipient site may lead to skin necrosis or laceration [1]. Nerve injury with sensory reduction or complete loss is another possible complication of fat grafting [1].

The surgeon and anesthetist must be aware of adverse drug reactions, e.g., if tumescent solution includes local anesthetic agents that rarely induce allergic symptoms [1].

According to a recent study, during lipofilling procedures, interstitial pressures are reached that exceed pressure limits defined as hazardous for fat embolism [66]. Complications such as fat embolism, as well as stroke, lipoid meningitis, pneumothorax, or septic shock as potentially life-threatening conditions, however, are depicted as isolated incidents in scientific literature databases [6, 63, 67–69]. Severe or lethal events seem to be extremely rare and causation in these singular incidents could not be fully established.

Overall, the complication rate associated with autologous fat transfer is low. Preoperatively, patients should be educated in an appropriate matter about the procedure and its associated risks.

References

1. Giunta RE, Horch RE, Prantl L, Baur EM, Herold C, Kamolz L, et al. Consensus of the Deutsche Gesellschaft der Plastischen, Rekonstruktiven und Asthetischen Chirurgen (DGPRAC) on autologous fat grafting. Handchir Mikrochir Plast Chir. 2016;48(6):337–9.
2. Prantl L, Rennekampff HO, Giunta RE, Harder Y, von Heimburg D, Heine N, et al. Current perceptions of Lipofilling on the basis of the new guideline on "autologous fat grafting". Handchir Mikrochir Plast Chir. 2016;48(6):330–6.
3. Falch BM, de Weerd L, Sundsfjord A. Maggot therapy in wound management. Tidsskr Nor Laegeforen. 2009;129(18):1864–7.
4. Missana MC, Laurent I, Barreau L, Balleyguier C. Autologous fat transfer in reconstructive breast surgery: indications, technique and results. Eur J Surg Oncol. 2007;33(6):685–90.
5. Del Vecchio DA, Bucky LP. Breast augmentation using preexpansion and autologous fat transplantation: a clinical radiographic study. Plast Reconstr Surg. 2011;127(6):2441–50.
6. Gutowski KA, Force AFGT. Current applications and safety of autologous fat grafts: a report of the ASPS fat graft task force. Plast Reconstr Surg. 2009;124(1):272–80.
7. Pulagam SR, Poulton T, Mamounas EP. Long-term clinical and radiologic results with autologous fat transplantation for breast augmentation: case reports and review of the literature. Breast J. 2006;12(1):63–5.
8. Chala LF, de Barros N, de Camargo MP, Endo E, Kim SJ, Pincerato KM, et al. Fat necrosis of the breast: mammographic, sonographic, computed tomography, and magnetic resonance imaging findings. Curr Probl Diagn Radiol. 2004;33(3):106–26.
9. Claro F Jr, Figueiredo JC, Zampar AG, Pinto-Neto AM. Applicability and safety of autologous fat for reconstruction of the breast. Br J Surg. 2012;99(6):768–80.
10. Kronowitz SJ, Mandujano CC, Liu J, Kuerer HM, Smith B, Garvey P, et al. Lipofilling of the breast does not increase the risk of recurrence of breast Cancer: a matched controlled study. Plast Reconstr Surg. 2016;137(2):385–93.
11. Niechajev I, Sevcuk O. Long-term results of fat transplantation: clinical and histologic studies. Plast Reconstr Surg. 1994;94(3):496–506.
12. Khouri RK Jr, Khouri RE, Lujan-Hernandez JR, Khouri KR, Lancerotto L, Orgill DP. Diffusion and perfusion: the keys to fat grafting. Plast Reconstr Surg Glob Open. 2014;2(9):e220.
13. Coleman SR, Saboeiro AP. Fat grafting to the breast revisited: safety and efficacy. Plast Reconstr Surg. 2007;119(3):775–85; discussion 86–7.
14. Panfilov DE. Augmentative phalloplasty. Aesthet Plast Surg. 2006;30(2):183–97.
15. Spyropoulos E, Christoforidis C, Borousas D, Mavrikos S, Bourounis M, Athanasiadis S. Augmentation phalloplasty surgery for penile dysmorphophobia in young adults: considerations regarding patient selection, outcome evaluation and techniques applied. Eur Urol. 2005;48(1):121–7; discussion 7–8.
16. Murillo WL. Buttock augmentation: case studies of fat injection monitored by magnetic resonance imaging. Plast Reconstr Surg. 2004;114(6):1606–14.. discussion 15-6
17. Harrison D, Selvaggi G. Gluteal augmentation surgery: indications and surgical management. J Plast Reconstr Aesthet Surg. 2007;60(8):922–8.
18. Monreal J. Fat tissue as a permanent implant: new instruments and refinements. Aesthet Surg J. 2003;23(3):213–6.
19. Coleman SR. Lower lid deformity secondary to autogenous fat transfer: a cautionary tale. Aesthet Plast Surg. 2008;32(3):415–7.
20. Guyuron B, Majzoub RK. Facial augmentation with core fat graft: a preliminary report. Plast Reconstr Surg. 2007;120(1):295–302.
21. Hu S, Zhang H, Feng Y, Yang Y, Han X, Han X, et al. Introduction of an easy technique for purification and injection of autogenous free fat parcels in correcting of facial contour deformities. Ann Plast Surg. 2007;58(6):602–7.
22. Pontius AT, Williams EF 3rd. The evolution of midface rejuvenation: combining the midface-lift and fat transfer. Arch Facial Plast Surg. 2006;8(5):300–5.
23. Niechajev I. Lip enhancement: surgical alternatives and histologic aspects. Plast Reconstr Surg. 2000;105(3):1173–83; discussion 84–7.
24. Domergue S, Psomas C, Yachouh J, Lesnik A, Reynes J, Goudot P, et al. Fat microinfiltration autografting for facial restructuring in HIV patients. J Craniomaxillofac Surg. 2006;34(8):484–8.
25. Butterwick KJ. Lipoaugmentation for aging hands: a comparison of the longevity and aesthetic results of centrifuged versus noncentrifuged fat. Dermatol Surg. 2002;28(11):987–91.
26. Coleman SR. Hand rejuvenation with structural fat grafting. Plast Reconstr Surg. 2002;110(7):1731–44; discussion 45–7.
27. Marwah M, Kulkarni A, Godse K, Abhyankar S, Patil S, Nadkarni N. Fat Ful'fill'ment: a review of autologous fat grafting. J Cutan Aesthet Surg. 2013;6(3):132–8.
28. Pallua N, Pulsfort AK, Suschek C, Wolter TP. Content of the growth factors bFGF, IGF-1, VEGF, and PDGF-BB in freshly harvested lipoaspirate after centrifugation and incubation. Plast Reconstr Surg. 2009;123(3):826–33.
29. Haubner F, Leyh M, Ohmann E, Pohl F, Prantl L, Gassner HG. Effects of external radiation in a co-culture model of endothelial cells and adipose-derived stem cells. Radiat Oncol. 2013;8:66.
30. Mojallal A, Lequeux C, Shipkov C, Breton P, Foyatier JL, Braye F, et al. Improvement of skin quality after fat grafting: clinical observation and an animal study. Plast Reconstr Surg. 2009;124(3):765–74.
31. Bruno A, Delli Santi G, Fasciani L, Cempanari M, Palombo M, Palombo P. Burn scar lipofilling: immunohistochemical and clinical outcomes. J Craniofac Surg. 2013;24(5):1806–14.
32. Klinger M, Caviggioli F, Klinger FM, Giannasi S, Bandi V, Banzatti B, et al. Autologous fat graft in scar treatment. J Craniofac Surg. 2013;24(5):1610–5.
33. Caviggioli F, Klinger F, Villani F, Fossati C, Vinci V, Klinger M. Correction of cicatricial ectropion by autologous fat graft. Aesthet Plast Surg. 2008;32(3):555–7.
34. Ranganathan K, Wong VW, Krebsbach PH, Wang SC, Cederna PS, Levi B. Fat grafting for thermal injury: current state and future directions. J Burn Care Res. 2013;34(2):219–26.

35. Conde-Green A, Marano AA, Lee ES, Reisler T, Price LA, Milner SM, et al. Fat grafting and adipose-derived regenerative cells in burn wound healing and scarring: a systematic review of the literature. Plast Reconstr Surg. 2016;137(1):302–12.
36. Piccolo NS, Piccolo MS, Piccolo MT. Fat grafting for treatment of burns, burn scars, and other difficult wounds. Clin Plast Surg. 2015;42(2):263–83.
37. Loibl M, Lang S, Hanke A, Herrmann M, Huber M, Brockhoff G, et al. Leukocyte-reduced platelet-rich plasma alters protein expression of adipose tissue-derived mesenchymal stem cells. Plast Reconstr Surg. 2016;138(2):397–408.
38. Moore JH Jr, Kolaczynski JW, Morales LM, Considine RV, Pietrzkowski Z, Noto PF, et al. Viability of fat obtained by syringe suction lipectomy: effects of local anesthesia with lidocaine. Aesthet Plast Surg. 1995;19(4):335–9.
39. Keck M, Janke J, Ueberreiter K. Viability of preadipocytes in vitro: the influence of local anesthetics and pH. Dermatol Surg. 2009;35(8):1251–7.
40. Keck M, Zeyda M, Gollinger K, Burjak S, Kamolz LP, Frey M, et al. Local anesthetics have a major impact on viability of preadipocytes and their differentiation into adipocytes. Plast Reconstr Surg. 2010;126(5):1500–5.
41. Ueberreiter K, von Finckenstein JG, Cromme F, Herold C, Tanzella U, Vogt PM. BEAULI—a new and easy method for large-volume fat grafts. Handchir Mikrochir Plast Chir. 2010;42(6):379–85.
42. Ferguson RE, Cui X, Fink BF, Vasconez HC, Pu LL. The viability of autologous fat grafts harvested with the LipiVage system: a comparative study. Ann Plast Surg. 2008;60(5):594–7.
43. Coleman SR. Structural fat grafting: more than a permanent filler. Plast Reconstr Surg. 2006;118(3 Suppl):108S–20S.
44. Khouri RK, Rigotti G, Cardoso E, Khouri RK Jr, Biggs TM. Megavolume autologous fat transfer: part II. Practice and techniques. Plast Reconstr Surg. 2014;133(6):1369–77.
45. Khouri RK, Rigotti G, Cardoso E, Khouri RK Jr, Biggs TM. Megavolume autologous fat transfer: part I. Theory and principles. Plast Reconstr Surg. 2014;133(3):550–7.
46. Leong DT, Hutmacher DW, Chew FT, Lim TC. Viability and adipogenic potential of human adipose tissue processed cell population obtained from pump-assisted and syringe-assisted liposuction. J Dermatol Sci. 2005;37(3):169–76.
47. Gabriel A, Champaneria MC, Maxwell GP. Fat grafting and breast reconstruction: tips for ensuring predictability. Gland Surg. 2015;4(3):232–43.
48. Rohrich RJ, Morales DE, Krueger JE, Ansari M, Ochoa O, Robinson J Jr, et al. Comparative lipoplasty analysis of in vivo-treated adipose tissue. Plast Reconstr Surg. 2000;105(6):2152–8.. discussion 9-60
49. Fisher C, Grahovac TL, Schafer ME, Shippert RD, Marra KG, Rubin JP. Comparison of harvest and processing techniques for fat grafting and adipose stem cell isolation. Plast Reconstr Surg. 2013;132(2):351–61.
50. Ozsoy Z, Kul Z, Bilir A. The role of cannula diameter in improved adipocyte viability: a quantitative analysis. Aesthet Surg J. 2006;26(3):287–9.
51. Erdim M, Tezel E, Numanoglu A, Sav A. The effects of the size of liposuction cannula on adipocyte survival and the optimum temperature for fat graft storage: an experimental study. J Plast Reconstr Aesthet Surg. 2009;62(9):1210–4.
52. Shiffman MA, Mirrafati S. Fat transfer techniques: the effect of harvest and transfer methods on adipocyte viability and review of the literature. Dermatol Surg. 2001;27(9):819–26.
53. Cheriyan T, Kao HK, Qiao X, Guo L. Low harvest pressure enhances autologous fat graft viability. Plast Reconstr Surg. 2014;133(6):1365–8.
54. Kling RE, Mehrara BJ, Pusic AL, Young VL, Hume KM, Crotty CA, et al. Trends in autologous fat grafting to the breast: a national survey of the American Society of Plastic Surgeons. Plast Reconstr Surg. 2013;132(1):35–46.
55. Botti G, Pascali M, Botti C, Bodog F, Cervelli V. A clinical trial in facial fat grafting: filtered and washed versus centrifuged fat. Plast Reconstr Surg. 2011;127(6):2464–73.
56. Khater R, Atanassova P, Anastassov Y, Pellerin P, Martinot-Duquennoy V. Clinical and experimental study of autologous fat grafting after processing by centrifugation and serum lavage. Aesthet Plast Surg. 2009;33(1):37–43.
57. Salinas HM, Broelsch GF, Fernandes JR, McCormack MC, Meppelink AM, Randolph MA, et al. Comparative analysis of processing methods in fat grafting. Plast Reconstr Surg. 2014;134(4):675–83.
58. Bucky LP, Percec I. The science of autologous fat grafting: views on current and future approaches to neoadipogenesis. Aesthet Surg J. 2008;28(3):313–21; quiz 22–4.
59. Delay E, Sinna R, Chekaroua K, Delaporte T, Garson S, Toussoun G. Lipomodeling of Poland's syndrome: a new treatment of the thoracic deformity. Aesthet Plast Surg. 2010;34(2):218–25.
60. Hang-Fu L, Marmolya G, Feiglin DH. Liposuction fat-fillant implant for breast augmentation and reconstruction. Aesthet Plast Surg. 1995;19(5):427–37.
61. Guerrerosantos J. Simultaneous rhytidoplasty and lipoinjection: a comprehensive aesthetic surgical strategy. Plast Reconstr Surg. 1998;102(1):191–9.
62. Ellenbogen R, Youn A, Yamini D, Svehlak S. The volumetric face lift. Aesthet Surg J. 2004;24(6):514–22.
63. Valdatta L, Thione A, Buoro M, Tuinder S. A case of life-threatening sepsis after breast augmentation by fat injection. Aesthet Plast Surg. 2001;25(5):347–9.
64. Miller JJ, Popp JC. Fat hypertrophy after autologous fat transfer. Ophthal Plast Reconstr Surg. 2002;18(3):228–31.
65. Latoni JD, Marshall DM, Wolfe SA. Overgrowth of fat autotransplanted for correction of localized steroid-induced atrophy. Plast Reconstr Surg. 2000;106(7):1566–9.
66. Klein SM, Prantl L, Geis S, Eisenmann-Klein M, Dolderer J, Felthaus O, et al. Pressure monitoring during lipofilling procedures. Clin Hemorheol Microcirc. 2014;58(1):9–17.
67. Yoon SS, Chang DI, Chung KC. Acute fatal stroke immediately following autologous fat injection into the face. Neurology. 2003;61(8):1151–2.
68. Ricaurte JC, Murali R, Mandell W. Uncomplicated postoperative lipoid meningitis secondary to autologous fat graft necrosis. Clin Infect Dis. 2000;30(3):613–5.
69. Feinendegen DL, Baumgartner RW, Schroth G, Mattle HP, Tschopp H. Middle cerebral artery occlusion AND ocular fat embolism after autologous fat injection in the face. J Neurol. 1998;245(1):53–4.

Exercise

13

Eric Rivas, Serina J. McEntire, Karen J. Kowalske, and Oscar E. Suman

13.1 Acute Stage

The benefits of exercise in reversing the negative consequences of bed rest have been well documented. Exercise after hospital discharge is also clearly critically important for facilitating maintenance of and/or improvements in physical function, lean body mass (LBM), and metabolic recovery following a major burn injury [1, 2]. However, the utility of exercise during critical care and acute care hospitalization following burn injury has not been fully described. The purpose of this chapter is to describe the importance of positioning, mobilization up out of bed, and aerobic exercise during the acute stage can be safely incorporated into the treatment plan following burn injury.

13.1.1 Safety and Efficacy Considerations Prior to Beginning Exercise

It is well known that bed rest has detrimental effects on psychosocial well-being [3], cardiorespiratory capacity [4], LBM [5], and bone and whole-body metabolism [5, 6], yet it is the practice across the country for most patients in the intensive care unit to be sedated and on bed rest. This leads to many complications including atelectasis, pneumonia, hypovolemia, dampened carotid baroreceptor response, orthostatic hypotension, deep venous thrombosis and pulmonary embolism, constipation and ileus, hyperglycemia and insulin resistance, muscle atrophy and deconditioning, bone demineralization, joint contractures, decubiti, depression, and decreased functional capacity [7, 8]. Clearly, these are not optimal for critically ill patients. Notably, a recent randomized trial showed that, in sedated adults on mechanical ventilation, those receiving sedation combined with exercise and mobilization (physical and occupational therapy) had fewer days on the ventilator, a lower incidence of delirium, and better function and walking distance at hospital discharge than those who received only daily sedation [9]. A study of this sort has not been conducted in patients with severe burn injury, begging the question: how do we decide who can begin getting up out of bed?

Timmerman and colleagues designed a specific decision tree that can be used as a guide. First, the managing physician needs a thorough understanding of the current medical condition, any medical comorbidities, and the patient's premorbid functional level. Obviously, the tolerance for sitting will differ between a geriatric patient and a teenager. Also, someone with premorbid tetraplegia or hemiparesis will be different than someone with no premorbid functional limitations. Other conditions like arthritis should also be taken into account [10].

The next consideration is the patient's cardiovascular reserve. At baseline, the individual's heart rate should be less than 50% of the age-predicted maximum. This may be easier to achieve and perhaps less relevant now that many burn patients are treated with beta-blockers during their acute care course. Blood pressure must be stable in the absence of pressors. Close monitoring for orthostatic hypotension is essential, as this is a common complication of bed rest. Wrapping the legs with Ace wrap may help decrease this effect. A normal electrocardiogram without signs of ischemia or unstable arrhythmia is obvious. If a patient has had a recent myocardial infarction, getting out of bed is still feasible but may

E. Rivas
Department of Kinesiology and Sport Management, Texas Tech University, Lubbock, TX, USA

S. J. McEntire
College of Nursing and Health Sciences, Valdosta State University, Valdosta, GA, USA

K. J. Kowalske
Department of Physical Medicine and Rehabilitation, University of Texas Southwestern Medical Center, Dallas, TX, USA

O. E. Suman (✉)
Department of Surgery, The University of Texas, Medical Branch, Galveston, TX, USA
e-mail: oesuman@utmb.edu

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_13

need to proceed more slowly. Other cardiac contraindications include unstable angina, severe symptomatic aortic stenosis, acute decompensated heart failure, acute myocarditis, and dissecting aneurysm [10].

Is there an adequate respiratory reserve? In general, oxygen saturation should be greater than 90% on an inspired fraction of oxygen of less than 60%. Mechanical ventilation cannot be high-frequency oscillation. Other patient factors to be considered are hemoglobin greater than 7 g/dL without active bleeding, platelet count >20,000 platelets per microliter, stable WBC count without an active acute metabolic compromising infection, and blood glucose, which should be >50 and <400 mg/dL. Patients should be afebrile, alert enough to participate, and not significantly agitated. Neurologic complications include increased intracranial pressure, actively seizing, or delirium tremors. Orthopedic limitations are unstable spine or fracture, severe osteoporosis, or unstable boney metastasis [10]. Acute deep venous thrombosis can be managed with 1 day of bed rest and pulmonary embolism with 3 days.

Lastly, the burn community must address the issue of timing of getting up after a skin graft. Numerous studies have shown that ambulation is safe on the day of grafting for a lower leg burn. Obviously, these studies were done in otherwise healthy subjects with smaller burns. Losing precious skin graft in a patient with a large burn is to be avoided, but is it worth the trade-off of additional ventilator days and a poorer outcome at hospital discharge?

Many external factors must be considered when mobilizing a crucially ill patient. Although tracheostomy is preferred, an endotracheal tube is not an absolute contraindication. Extra care must be taken to avoid dislodgement of the tube or trauma to vocal cords. Dialysis is not a contraindication, but timing the activity around dialysis is pragmatic. Temporary pacemakers have fragile wiring and may be dislodged, so they are likely a contraindication to mobility [10]. The issue of lines is somewhat controversial. Central venous catheters and arterial lines are not a contraindication.

Lastly, the issue of staffing is critically important. Many burn units have had cutbacks in therapy coverage. Future studies should show how this mobilization can decrease the number of days on the ventilator or hospital complications. This may justify the staffing essential for this activity even if it does not meet the traditional productivity criteria set for physical or occupational therapists (Table 13.1).

Table 13.1 Decision guide to start physical activities

Characteristic		Consideration
Cardiovascular reserve	50% of age-predicted maximum	Beta- blockers, orthostatic tolerance, ECG without signs of ischemia or unstable arrhythmia, recent myocardial infarction
Respiratory reserve	>90% O_2 sat; <60% FiO_2	Tracheostomy, endotracheal tube, deep vein thrombosis, pulmonary embolism
Mental stability	Alert and not significantly agitated	Neurologic complications, increased intracranial pressure, seizing, or delirium tremors
Orthopedic limitations	Unstable spine, fractures, unstable boney metastasis	Limb loss
Skin grafting	Severity and location of burns	Open wounds
Other	Hemoglobin >7 g/dL, platelet count >200,000, WBC stable, blood glucose <50 to <250 mg/dL	Care should be taken with pacemaker, central venous catheters, and arterial lines

ECG electrocardiogram, *FiO_2* inspired fraction of oxygen

13.1.2 Mobilization Protocol

Complete bed rest orders should be an exception and should be questioned if a legitimate reason is not apparent. Once the above safety criteria have been reviewed, progressive mobility can begin.

Any patient immobile for more than 3 days will be deconditioned and will require orthostatic training for upright positioning. Patients ready to begin ventilator weaning are most likely ready for mobility. All patients should be turned every 2 h while on bed rest, with good documentation if turning is contraindicated or if the patient does not tolerate it.

All patients who cannot actively participate in therapy should receive range of motion (ROM) exercise at least twice per day. Mechanically ventilated patients should have the head of the bed (HOB) elevated >30° unless contraindicated.

Readiness for and progression of activity should be evaluated on each shift. If mobilization does not occur, reasons should be clearly documented. Progressive mobilization should occur two or three times a day unless the patient meets exclusion criteria. Evaluate tolerance to activity and progress to the next step as tolerated.

Progressive Mobility Proposal [11]:

1. Elevate HOB to 45°.
2. Place the legs in a dependent position (partial chair position).
3. Elevate HOB to 65° and place the legs in full dependent position (full chair position).
4. Dangling the patient's feet with assistance once the patient is conscious and following commands. Patient's feet should be touching the floor if possible. Support torso but encourage independence.

5. Stand the patient at the bedside with support once the patient is able to lift his or her leg against gravity. The patient should bear weight.
6. Transfer the patient to a chair by pivoting or taking one or two small steps. Patient should sit up for 1 or 2 h.
7. Allow the patient to walk with assistance. The patient can use walker if needed.
8. Allow the patient to walk independently.

13.1.3 Heterotopic Ossification

Heterotopic ossification occurs in about 4% of burn patients, the majority of which are critically ill [12, 13]. The factors that contribute to heterotopic ossification is a topic of considerable debate; however, this condition is most common in patients who are critically ill and have burns with persistent open wounds [12, 14]. There is certainly a contention that significant edema fluid, prolonged sedation, and immobilization as well as numerous missed therapy treatment sessions are also contributing factors [14]. Therefore, the burn team should emphasize keeping joints moving, avoiding over sedation, and closing the wound as quickly as safely feasible.

13.1.4 Positioning

Following burn injury, placing injured tissues in a position of stretch is essential [15]. Burned tissue has a tendency to shorten, resulting in contractures, which are the single most common complication following burn injury [16]. The classic description of positioning is well known in the burn community. This includes shoulder abduction, elbow extension, wrist neutral, and metacarpal phalyngeal (MP) flexion with proximal interphalyngeal and distal interphalyngeal extension [17]. This decreases the edema in the hand, avoids tension on any exposed extensor mechanisms, and facilitates the return of MP flexion. Avoiding over abduction of the shoulders is critical to prevent stretch on the brachial plexus. Prolonged elbow flexion can produce ulnar nerve ischemia. Wrist flexion or extension may compromise the median nerve in the carpal tunnel. The lower limbs should be in slight hip abduction with rotation, with knee extension and the ankles in neutral. The frog leg position can overstretch the peroneal nerve with resultant foot drop [13, 18]. The other key for positioning is to carefully monitor for pressure points, particularly on the occiput and heel. In conjunction with positioning, the range of motion (ROM) and prolonged stretch are essential for avoiding permanent contractures [19].

Edema following resuscitation can contribute to contracture formation, particularly in the hands where significant edema can cause MP hyperextension and proximal interphalyngeal flexion [20]. This edema can also cause microvascular ischemia with subsequent neuropathy. Appropriate positioning can be utilized to help limit edema and its consequences. This leads to the question of whether more patients should undergo escharotomy. One would think that more escharotomies should be done given a neuropathy rate of 12% in major burn injury. The counter argument is that the majority of these neuropathies resolve over time without intervention [21].

We know exercise can reverse or attenuate the effects of bedrest and facilitates metabolic recovery in the late stages of burns. The above review examines the evidence for safety and efficacy of beginning exercise for patients while they are in the ICU. This is combined with evidence for safely mobilizing individuals on the day of or the day after a skin graft. Leaving burn patients in bed for days clearly affects time on the ventilator and functional outcomes. Each individual member of the burn team should be challenged to speak up on the importance of exercise in providing the best possible care for patients.

13.2 Outpatient Stage

The purpose of this section is to describe a typical exercise rehabilitation program that can be implemented once a patient has been discharged from the acute unit and into outpatient care. The mode, duration, frequency, and intensity of exercise are discussed. In addition, methods of assessing aerobic function and muscle function are described.

13.2.1 Exercise: Background

Multiple physical and functional limitations are present postburn and must be addressed in a long-term rehabilitation program. Traditionally, standard physical and occupation therapy programs for burn injuries concentrate on restoring and maintaining ROM, scar reduction, and prevention of contractures [22]. The major underlying factors that prohibit the burn patient from becoming independent in self-care, home management, work duties, and leisure activities point to limited ROM, loss of mobility, intolerance to standing or walking, pain, and decreased strength and endurance [23]. Indeed, ROM is reported to be the primary indicator for determining back to work status and impairment status [24]. However, despite participation in standard rehabilitation programs, patients experience a loss of LBM, muscle weakness, and diminished aerobic capacity [25–27]. We performed isokinetic testing of the ankle, and elbow in burned adults who had normal ROM but complained of an inability to perform job-related duties. Significant deficits in muscle strength and

Table 13.2 Characteristics of subjects and exercise functional outcome improvements from Shriners Hospitals for Children rehabilitation exercise training program

Author	N	% Male	Age (years)	TBSA burned	Training program	Peak VO_2 (%Δ)	Strength (%Δ)	LBM (%Δ)
Suman et al. [32]	16	84	10.5 ± 1	60 ± 3	A + R, 12 weeks	22.7	44	6.4
Suman et al. [33]	17	82	12.6 ± 1	60 ± 4	A + R, 12 weeks	24.3	–	–
Suman et al. [2]	11	81	11.8 ± 2	61 ± 2	A + R, 12 weeks	–	40.7	6.4
Clayton et al. [47]	24	81	11.3 ± 4	46 ± 15	A + R, 6 weeks	11.2	38.3	13.7
Clayton et al. [47]	18	82	12.3 ± 4	56 ± 13	A + R, 12 weeks	22.2	40	21.5
Hardee et al. [48]	24	80	13.0 ± 1	60 ± 2	A + R, 12 weeks	12.5	28	8.5
Wurzer et al. [49]	82	61	12.4 ± 4	56 ± 15	A + R, 12 weeks	22.5	25.3	13
Suman et al. [50]	13	70	10.5 ± 1	59 ± 3	A + R, 12 weeks	–	42.6	5.4
Mean ± SD	–	78 ± 8	11.8 ± 1	57 ± 5	–	19 ± 6	37 ± 7	11 ± 6

Data are reported as mean ± SD

TBSA total body surface, *A + R* aerobic + resistance exercise training program, VO_2 volume of oxygen, *Strength* peak torque, *LBM* total lean body mass

power were found. Despite normal ROM, these individuals were not ready to return to work, and their complaints of difficulty with job-related tasks were justified. Similarly, St-Pierre et al. [28] found that, at approximately 35 months postburn, muscle strength was 15–20% lower in adults with greater than 30% total body surface area (TBSA) burns than in age-matched controls.

Exercise has been demonstrated to be an essential component of the long-term rehabilitation program postburn. Exercise reportedly aids in controlling edema, decreased tendon adherence, joint stiffness, capsular shortening, muscle atrophy, and whole-body deconditioning [29, 30]. Also, exercise is reported to decrease the likelihood of needing additional surgical procedures to release burn scar contractures [31]. In addition, exercise training has been shown to maintain and improve LBM, augment the incorporation of amino acids into muscle proteins, increase muscle strength, increase walking distance by up to 50%, and improve cardiopulmonary capacity [1, 31].

Despite evidence that exercise training has a host of beneficial effects postburn, published reports on the effects of exercise training in burn patients are limited. de Lateur et al. [26] showed that adult burn patients had significant improvements in aerobic fitness after completion of a 12-week treadmill exercise program. Matched controls who participated in only a standard rehabilitation program did not achieve the same gains in aerobic capacity as those in the training program. Suman et al. [32] reported that a 12-week aerobic and resistance exercise program, in combination with a standard hospital rehabilitation program, significantly improved physiologic function in children with severe burns (7–17 years of age and ≥40% TBSA burned) compared to standard of care (SOC) alone. In this study, leg muscle strength was assessed using an isokinetic dynamometer test on the dominant leg extensors at a speed of 150°/s. LBM was measured using dual energy X-ray absorptiometry (DXA). In addition, peak oxygen consumption (VO_2) was measured during a standardized treadmill exercise test, and the resting energy expenditure was measured after an 8–12 h fast. All exercise testing was performed at 6 months postburn and repeated 12 weeks later. Following the 12-week intervention, muscle strength increased 44% in the exercise group compared to a 6% increase in SOC group. LBM increased approximately 6% in exercisers but was unchanged in the SOC group. Aerobic capacity increased 23% in the exercisers but decreased 1.35% in the non-exercisers. Resting energy expenditure was elevated in both the groups at baseline, but it increased an additional 15% in the SOC group, while it remained unchanged in the exercise group. In a similar population of children with burns, Suman et al. [33] also reported significant improvements in pulmonary function (maximum voluntary ventilation, MVV; forced expiratory volume, FEV_1; and forced vital capacity, FVC), treadmill time, and aerobic capacity following a 12-week aerobic and resistance exercise training program. In burned children 2–6 years of age, Neugebauer et al. [34] reported significant improvements in both passive and active ROM at the elbow and knee following a 12-week supplemental group music and movement program. In general, 6–12 weeks of concurrent (aerobic + resistance) exercise training at our institute has been found to yield improvements in peak VO_2 (~20% increase), peak torque or strength (37% increase), and total LBM (11% improvement) (see Table 13.2) because many of our subjects are male. More studies are needed to understand if females respond similarly to our exercise rehabilitation program.

Finally, it is important to note that thermal homeostasis is impaired in burn patients because of the inability of burned skin to control heat loss [35–37] coupled with an attenuated or absent sweat rate response in grafted skin [38–40]. However, this should not discourage the use of a rehabilitation exercise program. Studies have investigated exercise and temperature regulation in burned adults and found that adults with burns can tolerate exercise heat stress similarly to non-burned individuals [40–44]. In children, McEntire et al. [45, 46] found that moderate intensity exercise at room temperature was safe for children with less than 75% TBSA burns

and did not result in hyperthermia or heat illness. Thus, patients with burns who participate in regular physical exercise can gain the health-related benefits of improved flexibility, balance, stamina, and strength, all of which are needed to return to an active and independent lifestyle [26].

13.2.2 Exercise Prescription

Exercise training may be prescribed for persons with severe burns once they have been discharged from the hospital and into an outpatient setting. In addition, it is expected that the physician in charge of the patient will have given the approval to participate in an exercise rehabilitation program or will have even written the exercise prescription themselves. Exercise training is defined here as a "planned, structured and repetitive body movement done to improve or maintain one or more components of physical fitness" [51]. The exercise prescription described in this chapter is based primarily on the outpatient exercise program that has been implemented at Shriners Hospitals for Children in Galveston, Texas, for rehabilitation of severely burned children [32] and in some severely burned adults (unpublished data). This exercise program is supplemented with physical and occupational therapy. This program has been demonstrated to be beneficial in children 7–18 years old [2, 32, 52] [33] as well as in numerous adults with burns. The principles of designing exercise programs for children and adults with severe burns are based primarily on guidelines for healthy, non-burned children and adults [51, 53–58].

An initial evaluation of risk factors for and/or symptoms of chronic conditions concomitant to the burn should be performed prior to beginning exercise. Preexisting conditions may include chronic cardiovascular, pulmonary, and metabolic diseases. The objective is to obtain the necessary information to provide a safe and effective exercise rehabilitation program. Subjective data should be obtained to characterize any limitations or problems that the patient may have. A history of pre-burn physical activity as well as current medical problems, symptoms, and limitations is valuable in designing an effective exercise program. Pain or weakness during ambulation, shortness of breath, or severe fatigue may adversely affect exercise tolerance. In addition, the medications that a patient is taking may affect their ability to exercise. Following this health screening, exercise testing should be performed to evaluate the patient's exercise or physical capacity.

13.2.3 Exercise Testing

The objectives of exercise testing are multifactorial. For cardiopulmonary testing, the primary objectives are to assess physical work capacity and aerobic fitness, observe cardiorespiratory and metabolic responses, determine the basis for exercise prescription, and assess changes in fitness due to exercise training. For muscular strength testing, the primary objectives include measuring muscle strength (absolute and relative to body weight), measuring antagonist/agonist muscle ratios, assessing changes in body composition (lean mass, fat mass, and bone density), and providing a basis for exercise prescription. Exercise testing should be conducted prior to the start of any exercise rehabilitation program and at the end of such program. Sometimes, if the program is of long duration, a midpoint evaluation can be done. The patient's developmental maturity should be considered when performing exercise testing and training. We recommend a chronological age of 7 years and older, although children as young as 3–4 years of age have been tested [54]. Although we briefly describe methods of exercise testing in patients with burns, the reader should keep in mind that numerous field tests and prediction formulas exist for the estimation of both cardiopulmonary and muscle fitness [51]. Nevertheless, caution should be taken, as many have not been validated in burn populations.

13.2.3.1 Peak Oxygen Consumption or Aerobic Exercise Capacity

All patients should undergo a standardized exercise test. We use the treadmill exercise test and the modified Bruce treadmill protocol. However, other treadmill protocols such as the "Ramp Protocol" can be used [59] [51]. If it is not possible for the patient to be tested on a treadmill, a cycle ergometer or arm ergometer can also be used to evaluate or assess the physical conditioning of the patient before starting exercise rehabilitation or a training program [60]. Heart rate can easily be obtained with monitors. VO_2 should be measured if possible but requires more expensive equipment capable of indirect calorimetry, which entails continuous breath-by-breath analysis of inspired and expired gasses, flow, and volume. For the Bruce protocol, speed and grade begin at 1.7 mph and 0%, respectively. Thereafter, the speed and inclination are increased every 3 min. Patients are constantly encouraged to complete 3-min stages, and the test is terminated when peak volitional effort is achieved. Additional assessments that can be performed during the test include blood pressure, Borg's rated perceived exertion (RPE) [61], basic electrocardiogram, and spirometry. Notably, children and adolescents may lack cognitive ability or understanding of descriptors of exercise intensity associated with adult scales. Roemmich et al. have developed the Pictorial Children's Effort Rating Table (PCERT) for use in pediatric populations [62].

If indirect calorimetry is used, it is important to understand that no validated, universally accepted criteria exist in

children for the determination of peak VO_2 [63]. Therefore, we use similar standards as adults [64]. Peak values are obtained, and tests are deemed maximal once subjects signal to stop (volitional fatigue) exercise and at least three of the following criteria are met: a respiratory exchange ratio ≥1.05, leveling off in VO_2 with increasing workloads (<2 mL O_2 kg^{-1} min^{-1}), a final exercise heart rate ≥190 bpm, or a final test time between 8 and 12 min. Similar criteria have been used by others in children [63, 65]. However, we have observed that peak heart rate is limited to 175–180 bpm in severely burned children (>50–60% TBSA burned) compared to peak heart rate in age-matched children (195 to >200 bpm); therefore, caution should be taken for using for peak HR >190 as some burn children with severe burn injury may not be able to reach values that high. Once determined, peak VO_2 and peak heart rate can then be used to establish the intensity with which patients should exercise during the exercise program.

13.2.3.2 Strength Measurements

Isokinetic dynamometry strength testing can be performed to assess muscle function or to evaluate progress. If a Biodex Isokinetic dynamometer is used, the test can be done on the dominant leg extensors and/or leg with burns. Testing can be performed at varying angular velocities such as 180°/s, 150°/s, 120°/s, or 90°/s, although we recommend 150°/s based on our experience. For very young children (e.g., 7–10 years), a velocity of 180°/s might be better, as a lower velocity of 90°/s seems to be too difficult. The patients are seated and their position stabilized with a restraining strap over the mid-thigh, pelvis, and truck. All patients should be familiarized with the equipment before the actual test starts. We recommend that the procedure first be demonstrated by the administrator of the test. Second, the test procedure should be explained to the patients. Patients should then be allowed to practice the actual movement during three submaximal repetitions without a load as a warm-up. Finally, after the three submaximal warm-up repetitions, ten maximum voluntary muscle contractions (full extension and flexion) can be performed consecutively without rest in between. The number of repetitions and sets can be varied. For example, we recommend one set of ten repetitions at each velocity, with a 2-min rest interval between velocities. Values of peak torque, total work, and average power are calculated by the Biodex software system, and progress in muscle function can be monitored.

13.2.3.3 Three Repetition Maximum Test

Determining a safe and effective load for patients to use during workouts is useful before starting a resistive training program. The "repetition maximum" method can be used to determine the amount of weight or load that can be used as baseline or starting loads. We recommend that an initial three repetition maximum load (3RM) be performed prior to starting the exercise rehabilitation program. The 3RM is determined as follows. After an instruction period on correct weightlifting technique, the patient warms up with the lever arm and bar (or wooden dowel), and they are allowed to become familiar with the movement. After this, the patient lifts a weight that allows successful completion of four repetitions. If the fourth repetition is successfully achieved with correct technique, a 1-min resting period is allowed. After the resting period, patients are instructed to lift a progressively greater amount of weight or load at least four times. If the patient successfully lifts the weight for three repetitions, but the fourth repetition is not volitionally possible, because of either fatigue or inability to maintain correct technique, the test is terminated, and the amount of weight lifted from the successful set is recorded as the individual 3RM. We recommend the order of exercises to be from exercises that involve large muscle groups to ones that involve smaller muscle groups: bench press, leg press, shoulder press, leg extension, biceps curl, leg curl, and triceps curl. If 3RM cannot be obtained, we recommend that upper body exercise load be started at approximately 20% of the total body mass, and lower body exercise load be started at approximately 40% of the total body mass.

13.2.3.4 Lean Body Mass Measurements

LBM measurements should be made if possible. We assess LBM using DXA. DXA with the appropriate software measures the attenuation of two X-ray beams, one of which is high energy and one of which is low energy. These measurements are then compared with standard models of thickness used for bone and soft tissues. Subsequently, the calculated soft tissue is separated into LBM and fat mass. This is a useful tool for assessing the progress of an exercise program and perhaps nutritional interventions. However, the DXA machine is expensive. Whether other methods of measuring body composition such as underwater weighing or bioimpedance are suitable for burn patients is unknown.

13.2.3.5 Additional Testing

Major muscle and joint flexibility may be assessed using sit-and-reach or goniometry for ROM. Other tests may include gait analysis, balance, or reaction time. Sit-and-stand scores, timed walk/jog, and/or lifting exercises may be used to assess functional performance. The results of all evaluations should be used to identify problem areas, to write an exercise prescription, to design an exercise program, and to assess progress during and after an exercise program (Table 13.3).

Table 13.3 Shriners Hospitals for Children exercise rehabilitation program workouts

Aerobic workout	Specifications
Intensity	70–85% of individual peak aerobic capacity (peak VO_2) or 50–85% of heart rate reserve. Heart rate and rate perceived exertion measured at regular intervals
Duration	20–40 min (excluding warm-up and cool-down); continuous or intervals of work to rest or easy to moderate
Frequency	3–5 days per week
Mode	Treadmills, cycle ergometers, elliptical machines, arm ergometers, rowing machines. Sports such as soccer, basketball, and kickball
Resistance workout	
Exercise type	Multi-joint, assistance, and core exercises involving both the upper and lower body
Weight/load lifted and repetitions	Weeks 1–2: 50–60% of 3RM for 12–15 reps; weeks 3–6: 70–75% of 3RM for 8–10 reps; weeks 7–12: 75–85% of 3RM for 8–12 reps
Number of sets	2–3 sets
Order of exercises	Bench/chest press, leg press or squats, lat pulldown or row, leg extension, shoulder press, lunges, biceps curl, hamstring curl, triceps extension, toe raises, and core exercises (abdominals, back, or hip/gluteus). Larger muscles to smaller muscles
Type of exercises	Ten basic resistance exercises using variable resistance machines, free weights, or resistance bands: 5 for upper body, 5 for the lower body, plus 1–3 core exercises
Rest period	Approximately 1–2 min between sets
Frequency	Three days per week is recommended but may do every day if alternating upper and lower body workouts. Need to account for the type of aerobic workout

13.2.4 Exercise Programs

An example of our 12-week exercise rehabilitation program for individuals with severe burns is provided in Table 13.3. This program is implemented at hospital discharge. However, it has also been successfully implemented at 6 months postburn and up to 12 months postburn. The results of our program have been published, and the reader is referred to these for more details [47, 51, 64, 66, 67].

13.2.4.1 Aerobic Training

Intensity

To improve aerobic fitness, one must ensure that the intensity of exercise is between 65% and 95% of the peak heart rate or between 45% and 85% of the heart rate reserve (HRR) [Target heart rate = ((HR_{peak} – HR_{rest}) × % intensity desired) + HR_{rest}] [66]. HRR is the difference between the peak heart rate obtained during the maximal treadmill exercise test and resting heart rate. Others have recommended estimating peak HR when it is not possible to perform a maximal treadmill exercise test, using a simple method of estimating peak heart rate is to use the formula (220 – age) [51]. We caution using this formula in children. We have found that it is not appropriate to use this formula in children due to peak HR values in severely burned children top out at 175–180 bpm. For this reason, in this population, we recommend using RPE (see below), together with the actual heart rate obtained during a maximal exercise capacity test.

RPE can serve as a guideline for establishing exercise intensity [51, 61], and the PCERT can be used in pediatric populations [62]. RPE and PCERT are valuable indicators of exercise tolerance and intensity, and they are useful when obtaining peak heart rate is not possible or if patients are on medications that affect heart rate, such as beta-blockers. Currently, there are two commonly used RPE scales. The original or category scale rates exercise intensity on a scale of 6–20, while the revised or category-ratio scale uses a rating of 0–10. The category-ratio scale has been reported to be better understood by patients, providing the tester more valid information. An aerobic training effect and the threshold for the start of anaerobic training are achieved at a rating of "somewhat hard" to "hard," which equates to a category rating of 12–16 or a rating of 4–5 on the category-ratio scale [67]. PCERT ratings range from 1 to 10, with verbal cues ranging from "very, very easy" to "so hard I'm going to stop" and a cartoon picture of a child walking up stairs and becoming more fatigued every two steps.

Another method of evaluating exercise intensity is the "Talk Test," or the point where speech first becomes difficult. This point approximates exercise intensity almost equivocally to the ventilator threshold. The patient should be advised to exercise at an intensity where speech is comfortable. When speech becomes difficult, one can assume that exercise intensity is consistently above ventilator threshold or above the desired intensity of exercise needed for general improvements in fitness [68]. Safety and effectiveness are equally important, and the intensity should also be sufficient to result in a long-term, active lifestyle.

After discharge, children with severe burn injury have aerobic exercise capacities that are ~50% of those in age-matched non-burned children [2, 32, 33, 52]. According to normative data for non-burned healthy children aged 13–19 years available from The Cooper Institute for Aerobics Research, burned children fall into the very poor (<25 mL O_2 kg^{-1} min^{-1})-to-poor (25–31 mL O_2 kg^{-1} min^{-1}) category (using standard ratio scaling) [69]. A comparison reference for non-burned healthy children, non-trained boys and girls have a reportedly peak VO_2 of 47 and 40 mL O_2 kg min^{-1}, respectively [70, 71]. We have reported that, at hospital discharge, burned children have values in the range of 24–32 mL O_2 kg^{-1} min^{-1} [48, 72]. We also have observed that burned children walking at a slow intensity

(1.7 mph/0%, first stage of the modified Bruce protocol) are working at ~70% of their peak VO_2 and ~80% of their peak heart rate. In contrast, at that same workload, non-burned children exercise at 70% of their peak VO_2 and at ~50% of their peak heart rate. Thus, even though the work rate may seem low, caution should be taken when initially starting the prescription of exercise. We have found that 12 weeks of exercise training increases aerobic capacity to up to 80% of that seen in non-burned age-matched children. Thus, the initial exercise training workload may seem low for children with severe burn injury, but they are actually working at a greater percentage of their peak capacity than non-burned children. Monitoring perception and heart rate are important tools for gauging rehabilitation exercise prescription.

Duration

The duration and intensity of an exercise session are closely linked. For burn patients, the duration of exercise should be 5–20 min during the first week and depends on the functional status and pain tolerance of the patient. The objective should be to perform 20–60 min of aerobic exercise. This can be done continuously or intermittently (intervals), with a minimum of 10-min exercise bouts. Typically, an exercise session of 20–30 min and between 65% and 85% peak VO_2 or 40–85% of HRR (excluding warm-up and cool-down time) should induce health and fitness improvements [51]. Burn patients with low aerobic capacity or endurance may benefit from an exercise program of four to six 5-min bouts with rest periods between bouts. However, even 1-min work intervals and 1-min rest intervals for a total of 20 min will confer benefits. The duration of the exercise bout is progressively increased over time.

An aerobic exercise program should consist of warm-up, endurance, and cool-down periods. The warm-up period should consist of approximately 5–10 min of low-intensity exercises to increase body temperature and prepare the body for more strenuous work during the endurance phase. Stretching exercises were traditionally incorporated during the warm-up; however, recent evidence has shown stretching to be contraindicated at this point in the exercise session [73, 74]. Light aerobic exercise has been shown to be adequate for increasing flexibility prior to an exercise session [51]. For example, the warm-up may consist of slow, easy walking followed by moderately fast walking during the endurance phase. However, a moderate walk (3.5 mph) may be a warm-up speed for a patient that jogs at 5.5 mph during the endurance phase. Heart rate can be monitored to ensure that the warm-up activity is not too strenuous.

The objective of the endurance phase is to develop and improve cardiorespiratory or aerobic fitness. This phase should consist of 20–60 min of continuous or intermittent (minimum of 10-min bouts accumulated throughout the day) aerobic exercise. The duration depends on the intensity of the activity. For example, moderate-intensity exercise should be conducted for 30 min or more, while high-intensity, vigorous exercise should last for 20 min or more [75]. In this phase, large muscle groups should be engaged during rhythmic or dynamic exercises. Recreational activities or sports may be incorporated into this phase provided that they are of sufficient intensity and duration (minimum of 20 min) and that they complement the endurance phase.

Following the endurance phase, a cool-down period of 2–5 min is recommended to gradually return heart rate and blood pressure to resting values. These exercises should be lower intensity and may include slow walking, jogging, or stretching exercises. The cool-down is important for reducing the possibility of a hypotensive event after exercise as well as other cardiovascular complications [76].

Frequency

The optimal training frequency for improving aerobic capacity appears to 3–5 exercise sessions per week. However, deconditioned persons can improve cardiorespiratory fitness with only two exercise sessions per week [51, 75]. At 60–80% of HRR or 70–85% of peak aerobic capacity, 3–5 exercise sessions per week are sufficient to improve or maintain peak aerobic capacity. Patients with diminished aerobic capacities may benefit from multiple, short (5 days/week) exercise sessions. The number of sessions per week will vary depending on the patient's limitations and lifestyle.

Mode

The mode of exercise chosen should engage large muscle groups during rhythmic or dynamic exercise. Treadmill walking or running, cycling, elliptical trainer, and rowing are all examples of aerobic activities that engage large muscle groups and have been used for exercise in burn patients. Walking or jogging at a track or field is also appropriate. Swimming is also beneficial; however, closure of burn wounds must be ensured to minimize infection or contamination of others. Sports activities such as soccer, basketball, or tennis are also appropriate. However, care should be taken to avoid hard or extreme physical contact. Prescribing exercises that are appropriate for the patients' physical and mental developmental maturity is extremely important.

In burn patients, walking or cycling and even rowing are typically initially prescribed exercises. These activities are easy to tolerate and safe, with intensity being easy to monitor. Some patients may progress quickly through walking, jogging, and cycling programs because of the extent of the burn injury, personality, previous athletic experience, or psychosocial health. The risk of injury during high-intensity or high-impact exercises should be considered when prescribing exercise modalities, particularly in those who have functional limitations, are overweight or obese, or are novice exercisers. Cross training (participation in a variety of differ-

ent exercise modes and intensities) is desirable to increase enjoyment and compliance as well as to reduce repetitive orthopedic stresses. For children, play activity is also highly desirable and should be mixed with standard exercise training sessions.

Progression of Exercise

The duration, intensity, and transition to more difficult exercises should progress slowly to ensure the safety of the patient. This will decrease the potential for inducing excessive muscle soreness, causing new injuries, or aggravating pre-existing injuries. In addition, the patient should be educated to not move too quickly into demanding or challenging activities [2, 60]. For example, once the patient can walk 1–2 miles without fatigue or pain, they may progress to a walk/jog or jogging program. The rate of progression depends on the patient's functional capacity, medical and health status, pain tolerance, location of burns, age, activity preferences and goals, and overall tolerance to the current level of training. For burn patients, the exercise prescription can be divided into three stages of progression: initial, improvement, and maintenance [77].

The initial stage should consist of light and moderate aerobic activities (50–60% peak VO_2 or 40–60% HRR), which have a low potential for injury, muscle soreness, or pain. If the exercise is too hard or aggressive, adherence may be compromised. The amount of time spent in the initial stages varies. We recommend at least 4 weeks for initial conditioning. Exercise duration during this stage may begin with 15–20 min and progress to 30 min, at least three times per week. Deconditioned individuals should be allowed additional time to adapt at each conditioning stage. Age of the individual also needs to be considered, as conditioning may take longer in older or extremely deconditioned patients [51, 75, 77].

The goal of the improvement stage is to progressively increase the overall exercise stimulus to elicit significant improvements in aerobic fitness. This stage differs from the initial phase in that the patient is progressed at a more rapid rate. This stage usually lasts 4–5 months, during which time intensity is progressively increased within the upper half of the target range of 70–85% peak VO_2 or 40–85% HRR. In our experience with a 12-week training program for burned children 7–18 years of age, some children are able to start the improvement phase after 3–4 weeks of initial conditioning. Duration is increased consistently every 2–3 weeks until participants are able to continuously exercise at a moderate to vigorous intensity for 20–30 min. Interval training is beneficial during this stage provided that the total time engaged in moderate to vigorous activity is at least 20 min.

Once the patient has achieved the objectives of the improvement stage, the long-term maintenance of their cardiopulmonary fitness begins. At this time, the patient may not be interested in increasing the conditioning. Continuing the workout routine will maintain fitness level, improve quality of life, and reduce the risk of mortality. Re-evaluation and establishment of new goals are recommended during this phase.

13.2.4.2 Resistance or Strength Training

Strength is defined as the ability to produce force, while muscular endurance is defined as the ability to produce force over an extended time. Muscle strength and endurance play an important role in the ability to perform activities of daily living. Following a severe burn, extensive and prolonged loss of lean muscle mass occurs. Therefore, resistance training, which increases LBM, should be part of a comprehensive exercise rehabilitation program for burned individuals [32, 77].

The principles of designing a resistance training program for burned individuals are similar to those for the aerobic training program outlined above. Individuals should be educated in proper weightlifting technique, and strict rules and safety should be enforced at all times to reduce the potential for injury or accidents. Breath holding should be avoided during lifting as it may increase blood pressure, which can be dangerous. Prior to beginning a resistance training program, individuals should undergo strength testing (isokinetic or 3RM) and an evaluation to identify problem areas, prescribe exercise workloads, and track progress. Muscle strength tests are also valuable for determining return to work status [25].

Exercise Type and Order

Resistance training exercises can be divided into multijoint, assistance, and core exercises. Multijoint exercises involve one or more large muscle groups such as the chest, shoulder, back, or thigh. Assistance exercises are single-joint exercises that target smaller muscle groups such as the biceps, triceps, trapezius, and calves [77]. Core exercises are meant to strengthen and stabilize the spine, pelvis, and shoulder girdle as well as to provide a solid foundation for the movements of the extremities [78, 79]. Eccentric exercises are not recommended in burn patients because they have a higher potential to cause delayed onset muscle soreness. Severe muscle soreness may discourage participation or adherence to exercise.

For deconditioned or untrained individuals, the order of exercises should be multijoint or large muscle groups first, followed by assistance exercises [80, 81] and core exercises. In addition, alternating upper and lower body exercises allows more recovery time between exercises. In severely burned children, we have successfully implemented the following exercises into a resistance training program: bench or chest press, leg press or squat, lat pulldown or row, leg extension, shoulder press, lunges, biceps curl, hamstring curl, triceps extension, and toe raises. Core strengthening exercises follow and may include exercises such as crunches, back

extensions, pushups, plank exercises, bridging, bicycles, and hip and gluteus strength exercises. All types of equipment including variable resistant machines, free weights, resistance bands, and medicine balls are acceptable for burned individuals to use during exercise. With children, it is important that the equipment used fits their size, and this equipment may need to be adapted to support smaller body sizes.

Frequency

For severely burned individuals, we recommend 2–3 days per week of resistance training. Resistance training is often performed on alternate days as aerobic training but can be combined into the same exercise session. If the patient desires to work out every day using weights, we strongly recommend splitting the days into routines for upper body and lower body. However, the type and intensity of the aerobic workout will need to be accounted for, as doing a lower body workout on day 1 and very high-intensity aerobic workouts on 2 consecutive days may be counterproductive.

Number of Sets and Repetitions

The current recommendations for resistance training include 1–3 sets of 8–15 repetitions using exercises that target all major muscle groups [77]. For improving muscle strength and endurance, we recommend 8–15 repetitions of light-to-moderate weight in children [32] and 8–15 repetitions of moderate-to-heavy weight in burned adults. Heavy weight intensity may be possible in older children (i.e., 16 or 17 years old), but we do not believe it is required for the general improvement of muscle strength and function.

Training Load

If load is established with the 3RM method, we offer this example, which is used in our 12-week hospital exercise program for burn patients. During the first week of training, the individual is familiarized with the exercise and taught proper lifting form. The use of very light weights or a broomstick is recommended when individuals are learning new exercises. After the individual has mastered the correct form, the weight should be set at 50–60% of their 3RM, and 12–15 repetitions should be performed for 1–2 weeks. The load can then be increased to 70–75% of 3RM for 8–10 repetitions for 4–5 weeks. At weeks 7–12, the training intensity is increased to 75–85% with 8–12 repetitions.

Rest Periods

Allowing sufficient time between sets is important, so that the muscle can recover enough for the individual to perform the next set of exercises with proper form. For 10–15 repetition sets, less than 1 min of rest should be adequate, but up to 2 min is allowable. For recovery periods between resistive training sessions, we recommend at least 1 day of recovery period for any given muscle group.

Progressive Overload

Monitoring and recording an individual's workout and weights lifted during each session is important, as it allows one to continue to see improvements during the exercise program. Progressive overload may be achieved by increasing the weight, using a greater number of repetitions, or decreasing the rest periods. The 2-for-2-rule is ideal for use in deconditioned individuals or young children. In this method, once two or more repetitions can be performed above the repetition goal for two consecutive workouts for a specific exercise, then the weight should be increased for that exercise for the next training session [80, 82]. The increase in the amount of weight for an exercise is dependent on the physical condition of the individual and the area of the body (upper or lower body). In severely burned individuals, we recommend a 2- to 5-pound increase in weight for upper body exercises and a 5- to 10-pound increase for lower body exercises.

13.3 Special Considerations

For children, it is very important that machines and exercises be adapted to their size, strength level, and maturity level. We have found that traditional machine weights are often too large for children but can be modified using items such as foam blocks and seat padding to correctly position the child and accommodate their smaller statures. Adaptive equipment such as gloves, wrist or ankle weights, or elastic wraps is useful when working with patients with hand injuries or amputations. Resistance bands and medicine balls work well in deconditioned patients who do not have the strength needed to lift the minimum weight on a machine. Working with burned individuals often requires a bit of ingenuity, resourcefulness, and the ability to see outside the weight room when planning and adapting a resistance training program.

Goals for all patients should be set early in the exercise program. They should be evaluated regularly with the patient and adjusted as needed. The goals must be realistic and achievable. An intrinsic or extrinsic reward system may be implemented to help the patient achieve their goals.

An exercise rehabilitation program should be supplemented with an outpatient physical and occupational therapy program. Exercise professionals must work together to avoid duplication of services, identify areas that need attention, and provide the most comprehensive rehabilitation program for the individual patient.

Exercise should start early and as soon as possible after hospital discharge. The program should be structured and supervised by a trained professional. The ultimate goal of an exercise rehabilitation program should be to improve overall physical function. This program should be challenging,

effective, safe, and fun. One must use common sense and follow established guidelines during programming. The exercise program should also teach and promote healthy lifestyle habits to ensure that patients comply with the exercise program. The thought that "something is better than nothing" is correct, but safety should be the number one priority.

The American College of Sports Medicine (ACSM) has a manual with a list of absolute and relative contraindications to exercise and exercise testing for adults, children, and special populations [51, 75, 77]. Many of these contraindications will also apply to individuals with severe burns. This ACSM manual is a useful source of information, and one will find it helpful for use in exercise prescription and program design.

References

1. Cucuzzo NA, Ferrando A, Herndon DN. The effects of exercise programming vs traditional outpatient therapy in the rehabilitation of severely burned children. J Burn Care Rehabil. 2001;22(3):214–20.
2. Suman OE, Herndon DN. Effects of cessation of a structured and supervised exercise conditioning program on lean mass and muscle strength in severely burned children. Arch Phys Med Rehabil. 2007;88(12 Suppl 2):S24–9.
3. Ishizaki Y, et al. Psychological effects of bed rest in young healthy subjects. Acta Physiol Scand Suppl. 1994;616:83–7.
4. Convertino VA, et al. Cardiorespiratory responses to exercise after bed rest in men and women. Acta Astronaut. 1977;4(7–8):895–905.
5. Dirks ML, et al. One week of bed rest leads to substantial muscle atrophy and induces whole-body insulin resistance in the absence of skeletal muscle lipid accumulation. Diabetes. 2016;65(10):2862–75.
6. Buehlmeier J, et al. Markers of bone metabolism during 14 days of bed rest in young and older men. J Musculoskelet Neuronal Interact. 2017;17(1):399–408.
7. Convertino VA, Bloomfield SA, Greenleaf JE. An overview of the issues: physiological effects of bed rest and restricted physical activity. Med Sci Sports Exerc. 1997;29(2):187–90.
8. Kortebein P, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older adults. JAMA. 2007;297(16):1772–4.
9. Schweickert WD, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet. 2009;373(9678):1874–82.
10. Stiller K. Safety issues that should be considered when mobilizing critically ill patients. Crit Care Clin. 2007;23(1):35–53.
11. Timmerman RA. A mobility protocol for critically ill adults. Dimens Crit Care Nurs. 2007;26(5):175–9; quiz 180–1.
12. Elledge ES, et al. Heterotopic bone formation in burned patients. J Trauma. 1988;28(5):684–7.
13. Higashimori H, Carlsen RC, Whetzel TP. Early excision of a full-thickness burn prevents peripheral nerve conduction deficits in mice. Plast Reconstr Surg. 2006;117(1):152–64.
14. Klein MB, et al. Extended time to wound closure is associated with increased risk of heterotopic ossification of the elbow. J Burn Care Res. 2007;28(3):447–50.
15. Smith K, Owens K. Physical and occupational therapy burn unit protocol—benefits and uses. J Burn Care Rehabil. 1985;6(6):506–8.
16. Schneider JC, et al. Contractures in burn injury: defining the problem. J Burn Care Res. 2006;27(4):508–14.
17. Richard R, et al. Burn rehabilitation and research: proceedings of a consensus summit. J Burn Care Res. 2009;30(4):543–73.
18. Helm PA, et al. Burn injury: rehabilitation management in 1982. Arch Phys Med Rehabil. 1982;63(1):6–16.
19. Kottke FJ, Pauley DL, Ptak RA. The rationale for prolonged stretching for correction of shortening of connective tissue. Arch Phys Med Rehabil. 1966;47(6):345–52.
20. Demling RH. The burn edema process: current concepts. J Burn Care Rehabil. 2005;26(3):207–27.
21. Gabriel V, Kowalske KJ, Holavanahalli RK. Assessment of recovery from burn-related neuropathy by electrodiagnostic testing. J Burn Care Res. 2009;30(4):668–74.
22. Simons M, et al. Occupational therapy and physiotherapy for the patient with burns: principles and management guidelines. J Burn Care Rehabil. 2003;24(5):323–35; discussion 322.
23. Cheng S, Rogers JC. Changes in occupational role performance after a severe burn: a retrospective study. Am J Occup Ther. 1989;43(1):17–24.
24. Rondinelli RD, et al. Guides to the evaluation of permanent impairment. 6th ed. Chicago, IL: American Medical Association; 2008. p. 634, xxiv.
25. Cronan T, Hammond J, Ward CG. The value of isokinetic exercise and testing in burn rehabilitation and determination of back-to-work status. J Burn Care Rehabil. 1990;11(3):224–7.
26. de Lateur BJ, et al. Augmented exercise in the treatment of deconditioning from major burn injury. Arch Phys Med Rehabil. 2007;88(12 Suppl 2):S18–23.
27. Hart DW, et al. Persistence of muscle catabolism after severe burn. Surgery. 2000;128(2):312–9.
28. St-Pierre DM, et al. Muscle strength in individuals with healed burns. Arch Phys Med Rehabil. 1998;79(2):155–61.
29. Harden NG, Luster SH. Rehabilitation considerations in the care of the acute burn patient. Crit Care Nurs Clin North Am. 1991;3(2):245–53.
30. Richard R, Staley M. Burn care and rehabilitation: principles and practice. Philadelphia, PA: F.A. Davis; 1994. p. 711, xxviii.
31. Celis MM, et al. Effect of a supervised exercise and physiotherapy program on surgical interventions in children with thermal injury. J Burn Care Rehabil. 2003;24(1):57–61; discussion 56.
32. Suman OE, et al. Effects of a 12-wk resistance exercise program on skeletal muscle strength in children with burn injuries. J Appl Physiol (1985). 2001;91(3):1168–75.
33. Suman OE, Mlcak RP, Herndon DN. Effect of exercise training on pulmonary function in children with thermal injury. J Burn Care Rehabil. 2002;23(4):288–93; discussion 287.
34. Neugebauer CT, et al. Effects of a 12-week rehabilitation program with music & exercise groups on range of motion in young children with severe burns. J Burn Care Res. 2008;29(6):939–48.
35. Birke G, et al. Studies on burns. XII. Lipid metabolism, catecholamine excretion, basal metabolic rate, and water loss during treatment of burns with warm dry air. Acta Chir Scand. 1972;138(4):321–33.
36. Wilmore DW, et al. Catecholamines: mediator of the hypermetabolic response to thermal injury. Ann Surg. 1974;180(4):653–69.
37. Wilmore DW, et al. Effect of ambient temperature on heat production and heat loss in burn patients. J Appl Physiol. 1975;38(4):593–7.
38. Davis SL, et al. Impaired cutaneous vasodilation and sweating in grafted skin during whole-body heating. J Burn Care Res. 2007;28(3):427–34.
39. McGibbon B, et al. Thermal regulation in patients after the healing of large deep burns. Plast Reconstr Surg. 1973;52(2):164–70.
40. Shapiro Y, et al. Thermoregulatory responses of patients with extensive healed burns. J Appl Physiol. 1982;53(4):1019–22.
41. Pearson J, et al. Post junctional sudomotor and cutaneous vascular responses in noninjured skin following heat acclimation in burn survivors. J Burn Care Res. 2016;38(1):e284–92.

42. Ganio MS, et al. Nongrafted skin area best predicts exercise core temperature responses in burned humans. Med Sci Sports Exerc. 2015;47(10):2224–32.
43. Schlader ZJ, et al. Heat acclimation improves heat exercise tolerance and heat dissipation in individuals with extensive skin grafts. J Appl Physiol (1985). 2015;119(1):69–76.
44. Ganio MS, et al. Effect of human skin grafts on whole-body heat loss during exercise heat stress: a case report. J Burn Care Res. 2013;34(4):e263–70.
45. McEntire SJ, et al. Thermoregulation during exercise in severely burned children. Pediatr Rehabil. 2006;9(1):57–64.
46. McEntire SJ, et al. Absence of exertional hyperthermia in a 17-year-old boy with severe burns. J Burn Care Res. 2009;30(4):752–5.
47. Clayton RP, et al. Effects of different duration exercise programs in children with severe burns. Burns. 2016;
48. Hardee JP, et al. Early rehabilitative exercise training in the recovery from pediatric burn. Med Sci Sports Exerc. 2014;46(9):1710–6.
49. Wurzer P, et al. Long-term effects of physical exercise during rehabilitation in patients with severe burns. Surgery. 2016;160(3):781–8.
50. Suman OE, et al. Effect of exogenous growth hormone and exercise on lean mass and muscle function in children with burns. J Appl Physiol (1985). 2003;94(6):2273–81.
51. Pescatello LS, American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. 9th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2014. p. 456, xxiv.
52. Suman OE, Mlcak RP, Herndon DN. Effects of exogenous growth hormone on resting pulmonary function in children with thermal injury. J Burn Care Rehabil. 2004;25(3):287–93.
53. Adams RB, et al. Cardiovascular rehabilitation of patients with burns. J Burn Care Rehabil. 1990;11(3):246–55.
54. American Academy of Pediatrics Committee on Sports Medicine. Risks in distance running for children. Pediatrics. 1990;86(5):799–800.
55. Guy JA, Micheli LJ. Strength training for children and adolescents. J Am Acad Orthop Surg. 2001;9(1):29–36.
56. Gillett JG, et al. The impact of strength training on skeletal muscle morphology and architecture in children and adolescents with spastic cerebral palsy: a systematic review. Res Dev Disabil. 2016;56:183–96.
57. Barbieri D, Zaccagni L. Strength training for children and adolescents: benefits and risks. Coll Antropol. 2013;37(Suppl 2):219–25.
58. Schranz N, Tomkinson G, Olds T. What is the effect of resistance training on the strength, body composition and psychosocial status of overweight and obese children and adolescents? A systematic review and meta-analysis. Sports Med. 2013;43(9):893–907.
59. Maeder M, et al. Impact of the exercise mode on exercise capacity: bicycle testing revisited. Chest. 2005;128(4):2804–11.
60. Myers J, et al. Recommendations for clinical exercise laboratories: a scientific statement from the american heart association. Circulation. 2009;119(24):3144–61.
61. Borg GA. Perceived exertion. Exerc Sport Sci Rev. 1974;2:131–53.
62. Roemmich JN, et al. Validity of PCERT and OMNI walk/run ratings of perceived exertion. Med Sci Sports Exerc. 2006;38(5):1014–9.
63. Peyer K, Pivarnik JM, Coe DP. The relationship among HRpeak, RERpeak, and VO2peak during treadmill testing in girls. Res Q Exerc Sport. 2011;82(4):685–92.
64. Howley ET, Bassett DR Jr, Welch HG. Criteria for maximal oxygen uptake: review and commentary. Med Sci Sports Exerc. 1995;27(9):1292–301.
65. Rowland TW. Does peak VO2 reflect VO2max in children? Evidence from supramaximal testing. Med Sci Sports Exerc. 1993;25(6):689–93.
66. Howley ET. Type of activity: resistance, aerobic and leisure versus occupational physical activity. Med Sci Sports Exerc. 2001;33(6 Suppl):S364–9; discussion S419–20.
67. Foster C, et al. A new approach to monitoring exercise training. J Strength Cond Res. 2001;15(1):109–15.
68. Loose BD, et al. Consistency of the counting talk test for exercise prescription. J Strength Cond Res. 2012;26(6):1701–7.
69. Heyward VH, Gibson AL, editors. Advanced fitness assessment and exercise prescription. 7th ed. Champaign, IL: Human Kinetics; 2014. p. 537, xiv.
70. Matecki S, et al. Maximal oxygen uptake in healthy children: factors of variation and available standards. Rev Mal Respir. 2001;18(5):499–506.
71. Cooper DM, et al. Aerobic parameters of exercise as a function of body size during growth in children. J Appl Physiol Respir Environ Exerc Physiol. 1984;56(3):628–34.
72. Porter C, et al. The role of exercise in the rehabilitation of patients with severe burns. Exerc Sport Sci Rev. 2015;43(1):34–40.
73. Behm DG, Button DC, Butt JC. Factors affecting force loss with prolonged stretching. Can J Appl Physiol. 2001;26(3):261–72.
74. Kokkonen J, Nelson AG, Cornwell A. Acute muscle stretching inhibits maximal strength performance. Res Q Exerc Sport. 1998;69(4):411–5.
75. American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. Med Sci Sports Exerc. 1998;30(6):975–91.
76. Haskell WL. Cardiovascular complications during exercise training of cardiac patients. Circulation. 1978;57(5):920–4.
77. Swain DP, American College of Sports Medicine and American College of Sports Medicine. ACSM's resource manual for Guidelines for exercise testing and prescription. 7th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2014. p. 862, xv.
78. Hodges PW, Richardson CA. Contraction of the abdominal muscles associated with movement of the lower limb. Phys Ther. 1997;77(2):132–42; discussion 142–4.
79. Hodges PW, Richardson CA. Relationship between limb movement speed and associated contraction of the trunk muscles. Ergonomics. 1997;40(11):1220–30.
80. Fleck SJ, Kraemer WJ. Designing resistance training programs. 3rd ed. Champaign, IL: Human Kinetics; 2004. p. 377, xiii.
81. Stone MH, Wilson GD. Resistive training and selected effects. Med Clin North Am. 1985;69(1):109–22.
82. Baechle TR, Earle RW. Weight training: steps to success. 4th ed. Champaign, IL: Human Kinetics; 2012. p. 215, xx.

Part IV

Burn Reconstruction: Principles

Principles of Burn Reconstruction

14

Lars-Peter Kamolz and David B. Lumenta

Due to extraordinary advances concerning the understanding of cellular and molecular processes in wound healing, wound care innovations and new developments concerning burn care have been made; burn care has improved to the extend that persons with burns frequently can survive. The trend in current treatment extends beyond the preservation of life; the ultimate goal is the return of burn victims, as full participants, back into their social and business life [1, 2].

A more aggressive approach in the acute phase has led to a higher survival rates on one side, but also to a higher number of patients, who will require reconstructive surgery on the other side. Successful reconstruction requires a profound understanding of skin anatomy and physiology, careful analysis of the defect, and thoughtful considerations of different techniques suitable to execute the surgical plan [3].

14.1 From the Reconstructive Ladder to the Reconstructive Elevator

Based on the concept of the reconstructive ladder by Mathes und Nahai, new advances in the understanding of the anatomy, operative techniques, instrumentation, and surgical skills have led to the concept of the reconstructive elevator: complex procedures are no longer considered as last resort procedures only. In the quest to provide optimal form and function, it is currently accepted to jump several rungs of the ladder, due to the knowledge that some defects require more complex solutions. The goal of surgical reconstruction is restoration of preoperative function and appearance. The surgeon must reconstruct the defect with tissues that are missing and which allows defect coverage with tissues of similar contour, texture, and color [4, 5].

14.2 The Reconstructive Clockwork

In clinical daily routine, combinations of different techniques are often applied, in order to permit new reconstructive possibilities for the patient, but neither the reconstructive ladders of Mathes and Nahai in 1982 nor the reconstructive elevator permit a real combination of the different reconstructive procedures and techniques.

The image of interlocking wheels of a clockwork illustrates the integration of different reconstructive methods even more impressive than the conventional reconstructive ladder and elevator [6] (Fig. 14.1).

14.2.1 General Principles

Hypertrophic scars and scar contraction with concomitant functional impairment are the most common problems that require correction or reconstruction. Choosing the right modality depends upon several factors, e.g., the age or maturity of the scar. But also the knowledge of the healing properties of the patient (i.e., whether the patient has a tendency towards keloid or hypertrophic scarring) might help to decide on how aggressive or how conservative.

Objective assessment of deformities and functional impairment is of utmost importance for planning the right reconstructive procedure. Formulating a realistic plan to restore the functional problems requires analysis of the physical deformities and psychological disturbance of the patient. Psychiatric, psychosocial [7], and physiotherapeutic cares have to be continued while a surgical treatment plan is instituted.

L.-P. Kamolz (✉)
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

COREMED - Cooperative Centre for Regenerative Medicine, JOANNEUM RESEARCH Forschungsgesellschaft mbH, Graz, Austria
e-mail: lars.kamolz@medunigraz.at

D. B. Lumenta
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_14

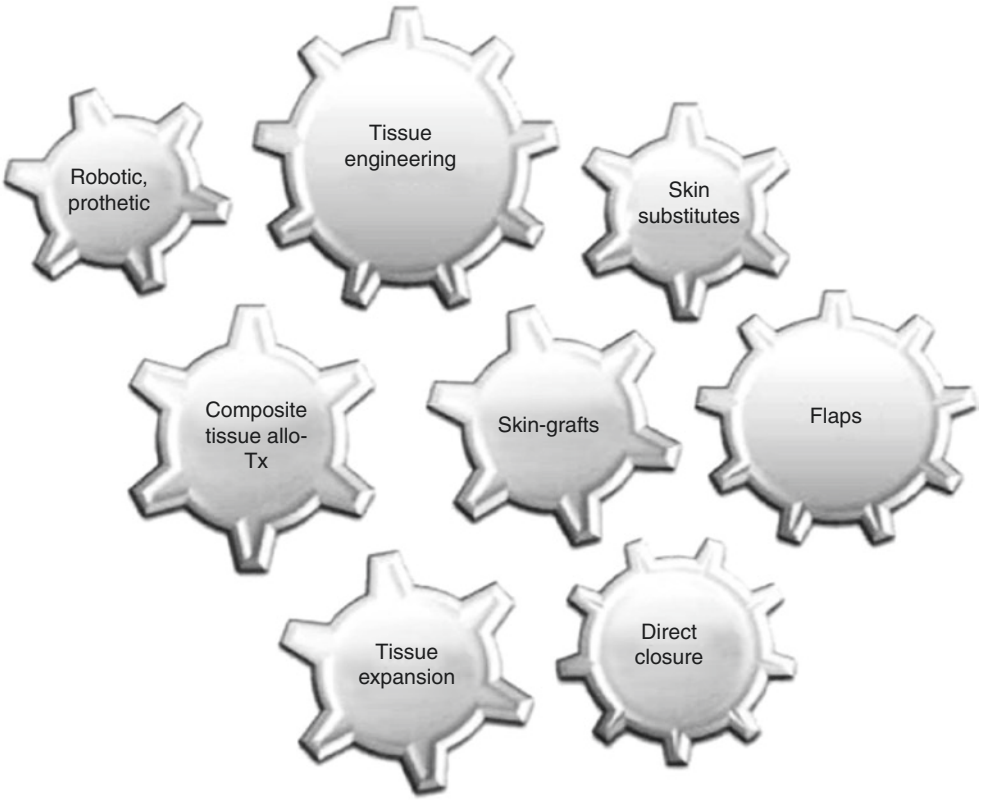


Fig. 14.1 The reconstructive clockwork: the interlocking wheels of a clockwork illustrates the integration of different reconstructive methods

14.3 Indication and Timing of Surgical Intervention

For a surgeon, making a decision *how* to operate on a patient with burn deformities is quite simple. In contrast, deciding *when* to operate on a patient can be difficult. However, the basic principle is based on the following:

- Restoring bodily deformities that impose functional difficulties must precede any surgical effort to restore the appearance.

In short, a surgeon's effort must be concentrated upon restoring the deformed bodily parts essential for physical functions, if not for patient survival. In contrast, restoration of deformed regions in general can be performed in a later phase.

It is postulated that attempts to correct burn deformities should be delayed for at least 1–2 years. During this time needed for scar maturation, an interim conservative treatment by using pressure garments and splinting is recommended to reduce scarring and to minimize joint contracture, because operating on an immature scar is technically more cumbersome and will lead to a higher number of complications. It is never too late to revise a scar, but conversely, it may be too early.

14.4 The Techniques of Reconstruction

Several techniques are routinely used to reconstruct deformities and to close defects related to the burn trauma.

Principally, they are:

- Excision techniques
- Serial excision and tissue expansion
- Skin grafting techniques with or without the use of dermal substitutes
- Local skin flaps
- Distant flaps
- Allotransplantation
- Tissue engineering
- Robotics and prosthesis

14.5 Excision Techniques

Excision with direct closure of the resultant wound is the simplest and the most direct approach in burn reconstruction. It is important to determine the amount of scar tissue that can be removed, so that the resultant defect can be closed directly. A circumferential incision is made in the line previously marked and is carried out through the full thickness of the scar down to the subcutaneous layer. In case of a keloid, an

intralesional excision might be better instead of an extralesional one in order to avoid recurrence. In order to minimize vascular supply interference along the wound edges, undermining of the scar edge should be kept to a minimum, whenever possible.

14.5.1 W-Plasty and Geometric Broken Line Closure

W-plasty [8, 9] is a series of connected, triangular advancement flaps mirrored along the length of each side of the scar, but a W-plasty, unlike a Z-plasty, does not result in an overall change in length of the scar, it makes the scar less conspicuous, and it disrupts wound contracture with its irregular pattern. As with all other procedure, it is helpful to mark the planned design prior to the operation (Fig. 14.2).

The Geometric Broken Line Closure (GBLC) is a more sophisticated scar regularization technique than the W-plasty and requires more time to execute [10–13]; unlike the W-plasty's regularly irregular pattern, which results in a somewhat predictable scar pattern that can be followed by the observer's eye, the irregular irregularity of the GBLC allows maximum scar camouflage. This is achieved by various combinations of triangles, rectangles, squares, and semicircles in differing widths and lengths along the scar (Figs. 14.2 and 14.3).

14.6 Serial Excision and Tissue Expansion

The goal of surgical reconstruction is the restoration of preoperative function and appearance. The surgeon must reconstruct the defect with tissue of similar contour, texture, and color. Surgical excision of scars relies upon recruitment of local tissue for closure of the resulting defect, and thus, adjacent skin will usually provide the best match for the defect. In areas where tissue laxity is poor or the resulting defect would be too big, tissue expansion and serial excision are useful techniques to overcome a lack of sufficient local tissue for closure. Tissue expansion allows large areas of burn scar to be resurfaced by providing tissue of similar texture and color to the defect. Moreover, it is combined with the advantage of donor site morbidity reduction. Issues and disadvantages that need to be addressed are that the technique of pre-expansion requires additional office visits for serial expansion and at least one extra surgical procedure with potential for additional complications. A significant time period between 9 and 12 weeks for progressive tissue expansion is required. Tissue expanders are very versatile tools in reconstructive burn surgery, but still, careful patient selection, correct indications and realistic treatment concepts, large experience and well-selected surgical techniques, precise instruction of the medical staff, as well as detailed and continuous education of the patients are essential [14, 15].

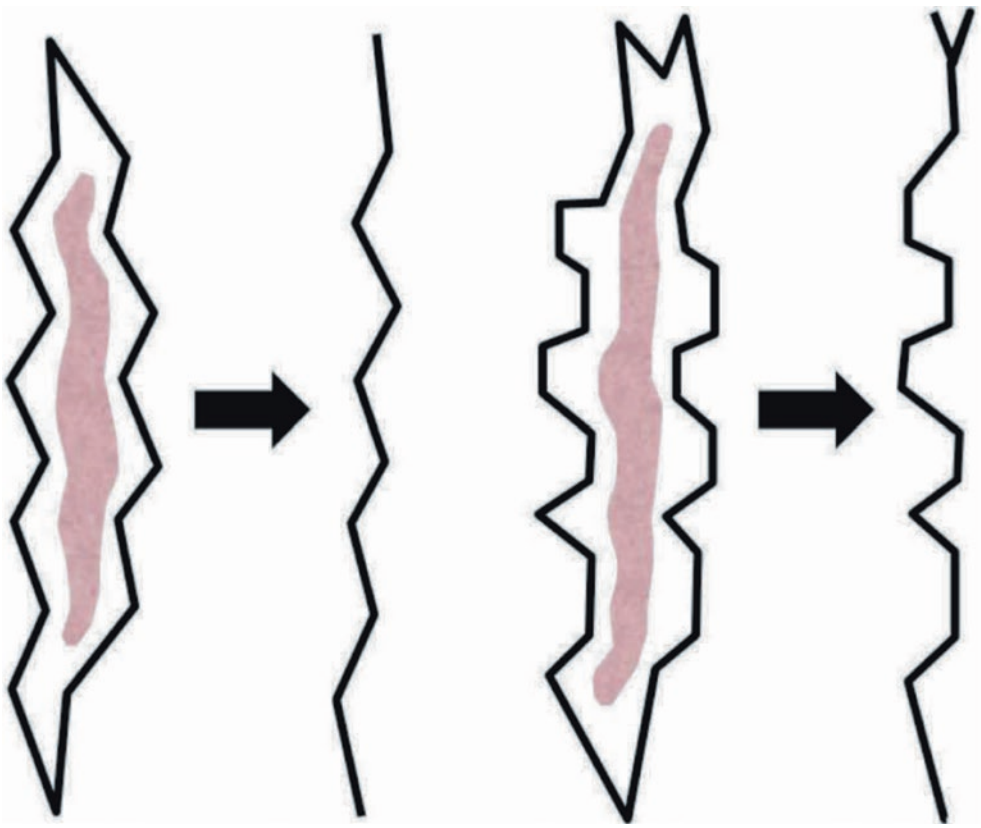


Fig. 14.2 W-plasty (left) and geometric broken line closure (right) (scar: pink)

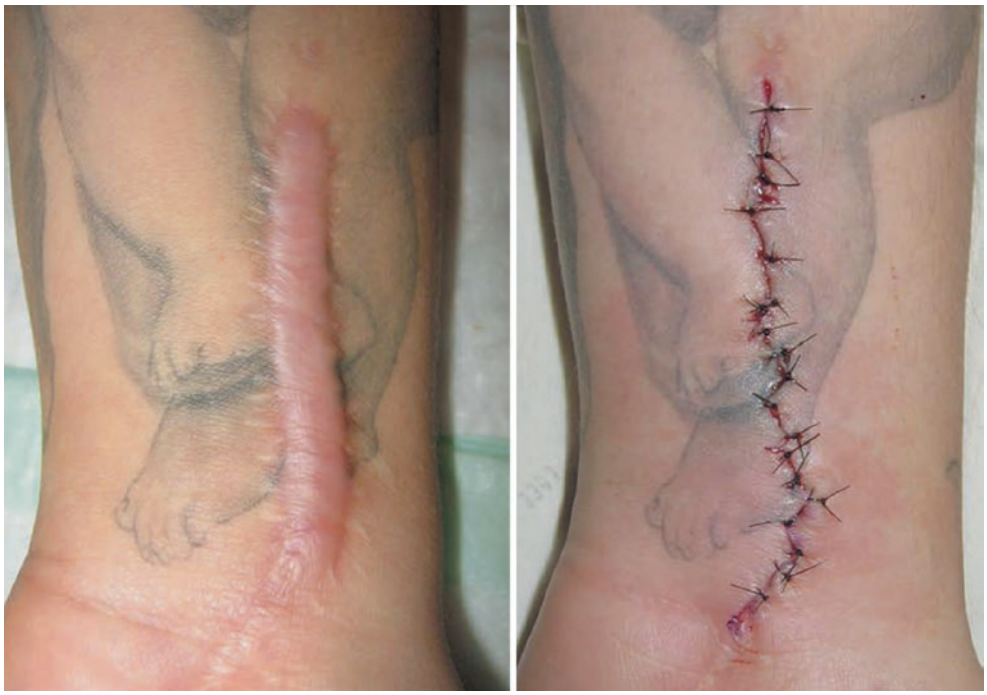


Fig. 14.3 Geometric broken line closure: clinical example

Serial excisions involve the partial excision of the scar with consecutive advancement of adjacent skin. In a series of sequential procedures, the area of a scar is completely excised. The number of procedures needed depends on the elasticity of the surrounding skin and the size of scar being excised. The primary disadvantage of this technique is the requirement for multiple operations. If more than two operations are needed, tissue expansion should be considered as an alternative treatment option.

14.7 Skin Grafting Techniques

Covering an open wound with a skin graft harvested at a various thickness is the conventional approach of wound closure. A skin graft including epidermis and dermis is defined as a full-thickness skin graft, and a piece of skin cut at a thickness varying between 8/1000 of an inch (0.196 mm) and 18/1000 of an inch (0.441 mm) is considered to be a partial- or a split-thickness skin graft. The thickness of a full-thickness skin graft is quite variable depending upon the harvest region.

In case of a full-thickness skin graft, a paper template may be made to determine the size of the skin graft needed to close a wound. The skin graft is laid down to the wound bed and is anchored in place by suturing or stapling the graft onto the wound bed. A continuous contact of the skin graft with the wound bed is essential to ensure an in-growth of a vascular network within 3–5 days and thereby for graft survival. A gauze or cotton bolster tied over a graft has been the traditional technique to anchor and to prevent fluid accumulating underneath a graft, if there is a flat and well-vascularized wound bed. In regions that are associated with a less good take rate (concave defects; regions, which are subject to repeated motion like joints) or in patients with co-morbidities that may have an impact on graft healing, other techniques [16–18], instead of the bolstering technique, are used for skin graft fixation. The use of topical negative pressure or fibrin glue can lead to better skin graft healing [16] (Fig. 14.4).

The criteria for using skin grafts of various thicknesses are mainly based on:

- The use of a thin graft is more appropriate for closing wounds with unstable vascular supply, particularly if the skin graft donor site is scarce.
- Moreover, the quality and the presence of dermis seem to have an influence on the extent of wound contraction. The extent of contraction, which is noted if a thin partial-thickness skin graft is used, is larger than using a full-thickness graft. The presence of a sufficient dermal structure could reduce wound contracture.

Skin graft in combination with a dermal substitute—For the past several years, artificial dermal substitutes have been used in order to improve skin quality, e.g., Alloderm™, Integra™ [19]; these materials, when implanted over an open wound, have been found to form a layer of close to normal dermis, thus providing a wound bed better for skin grafting and thereby better skin quality. However, the need for a staged approach to graft a wound using this technique is considered cumbersome. Matriderm™ is a new dermal matrix, which consists of collagen and elastin, and allows a single-step reconstruction of dermis and epidermis in combination with a split thickness skin graft [20–22] (Fig. 14.5).

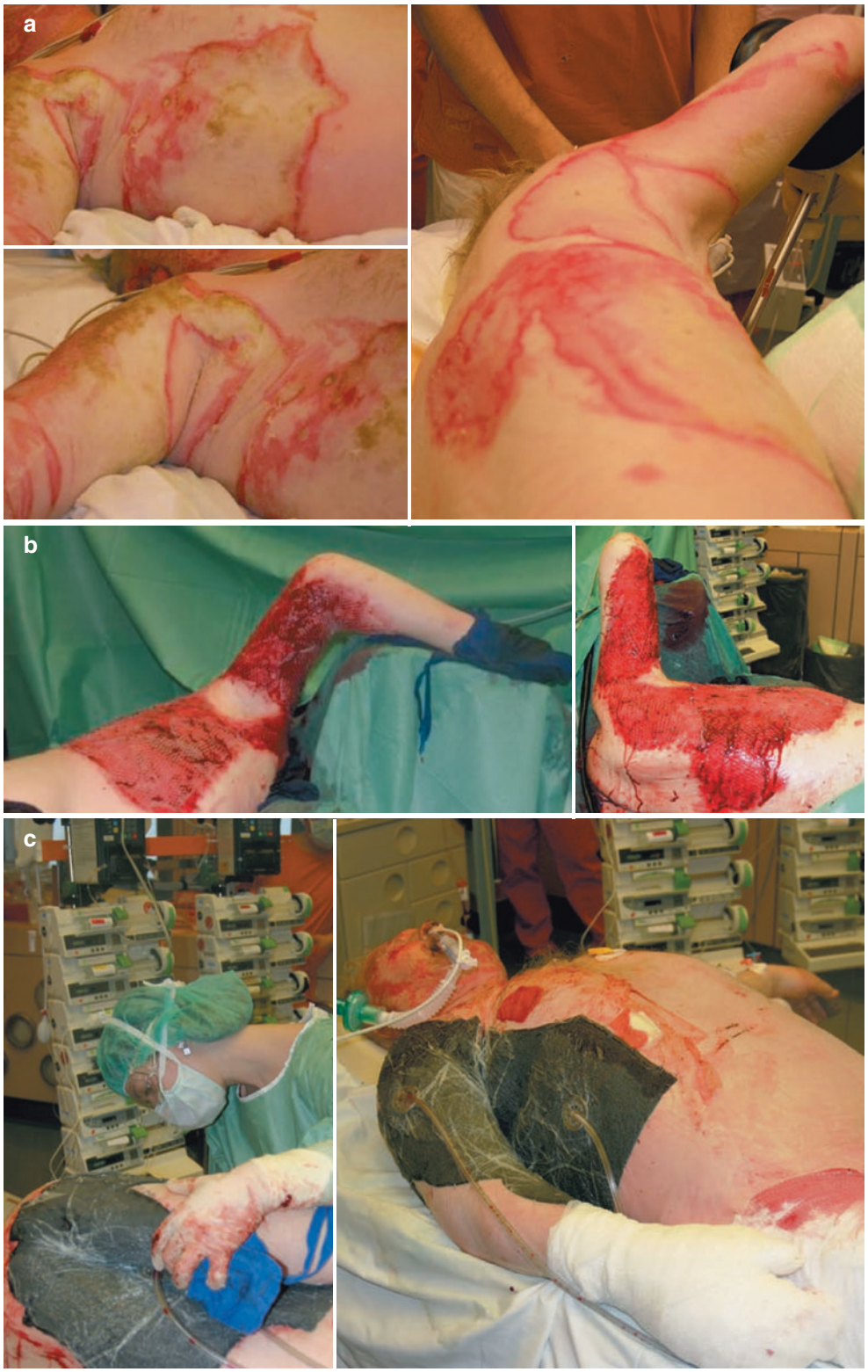


Fig. 14.4 (**a**) Dermal to full-thickness burn. (**b**) Tangential excision and grafting with 1:3 meshed skin graft. (**c**) Skin graft fixation by use of V.A.C. for 5 days. (**d**) After removal of V.A.C. dressing: 100% take rate of the skin grafts

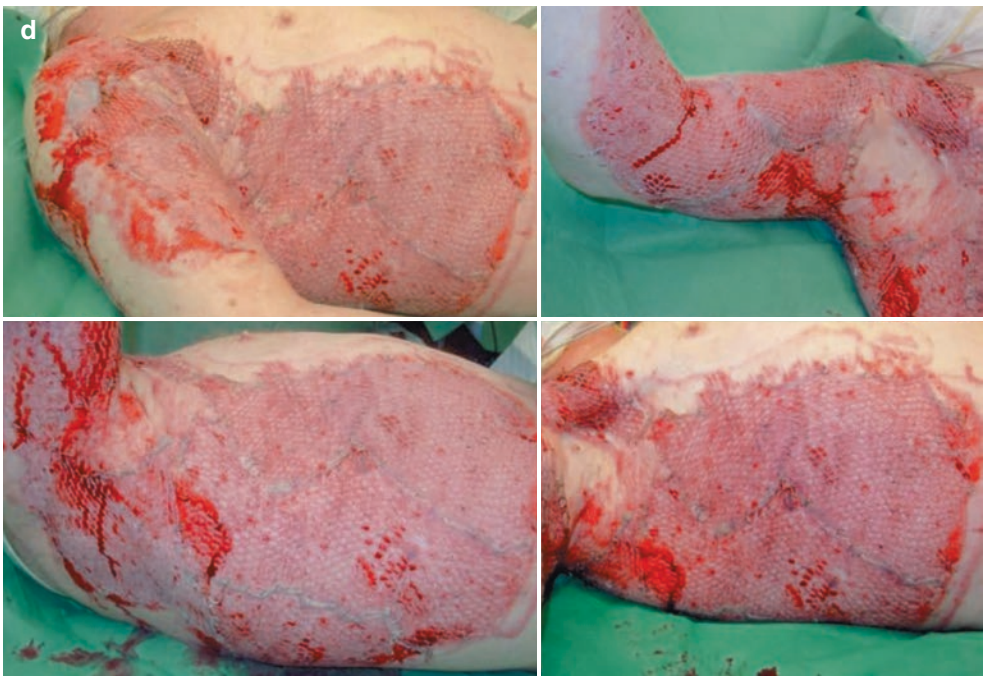


Fig. 14.4 (continued)

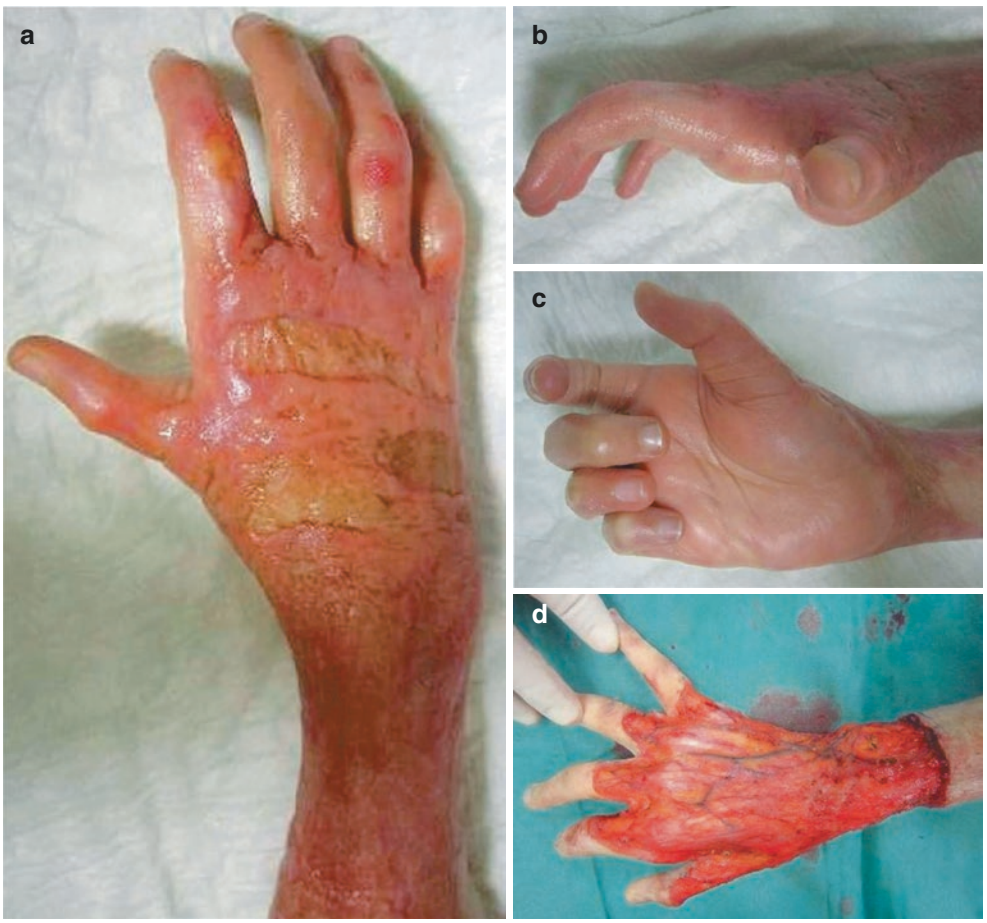


Fig. 14.5 (**a**) Hypertrophic and contracted scars (right hand). (**b**) Hyperextension in of the MCP joints. (**c**) Flexion only possible in the PIP and DIP joints, hyperextension in the MCP joints. (**d**) Complete excision of the hypertrophic and contracted scar plate. (**e**) Early results obtained by use of Matriderm® and skin graft in a single-step procedure (3 months postoperative)

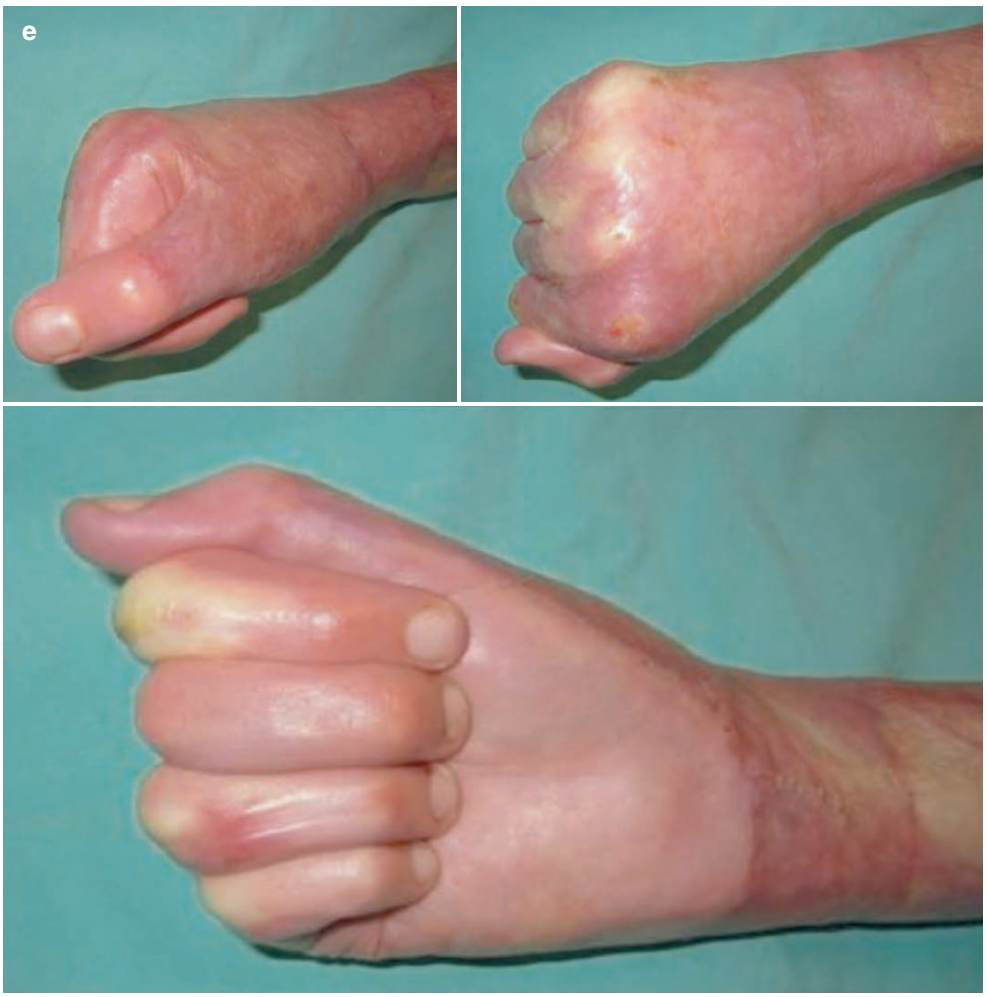


Fig. 14.5 (continued)

14.8 Local Skin Flaps

The approach using a segment of skin with its intrinsic structural components attached to cover a defect follows also the fundamental principle of reconstructive surgery to restore a destructed bodily part with a piece of like tissue. The recent technical innovation of incorporating a muscle and/or facial layer in the skin flap design, especially in a burned area, further expanded the scope of burn reconstruction as more burned tissues could be used for flap fabrication.

No single flap is optimal for every scar excision. Each individual scared area has to be analyzed for:

- Depth of the scar.
- Tissue involved.
- Availability of normal tissue for reconstruction. Based on this, the ideal flap or the combination of flaps and techniques is chosen for reconstruction.

Often-used skin flaps are the Z-plasty technique, the multiple Z-plasties, the ¾ Z-plasty technique.

14.8.1 Z-Plasty

There are three purposes to perform a Z-plasty:

- To lengthen a scar or to release a contracture
- To disperse a scar
- To realign a scar within a relaxed skin tension line

The traditional Z-plasty consists of two constant features; first there are three incisions of equal length—two limbs and a central incision. Second there are two angles of equal degree—the limbs form 60° angles with the central incision (Fig. 14.6). Ideally the central incision should be placed along the axis of the scar; alternatively the scar itself may be

completely excised with a fusiform defect acting as the central incision (Fig. 14.7).

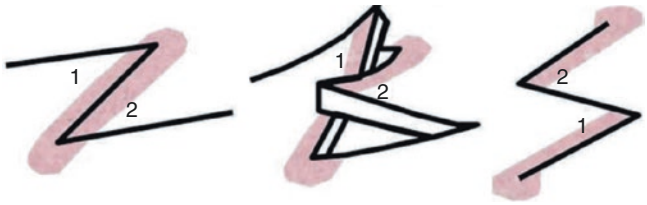


Fig. 14.6 Z-plasty (scar: pink)

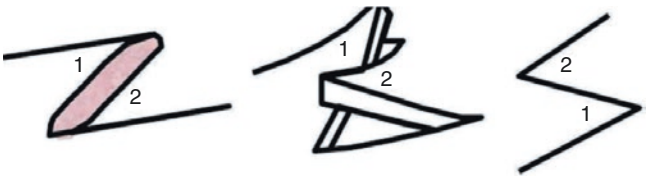


Fig. 14.7 Modified Z-plasty (scar: pink)

14.8.2 Double-Opposing Z-Plasty

Two Z-plasty incisions placed immediately adjacent to one another as mirror images will produce an incision known as a double-opposing Z-plasty (Figs. 14.8 and 14.9) The advantage of this technique is that significant lengthening can be achieved in areas of limited skin availability. Ideal indication for this technique is the release of web space contractures (Fig. 14.10).

The *¾ Z-plasty or half-Z* used to refer to a technique (Figs. 14.11 and 14.12) with one limb incision being perpendicular to the central one. The incision is created on the scar side, which creates a fissure in the scar in which a triangular flap is introduced. The length gained on the scar side is directly proportional to the width of the triangular flap.

Despite its geometric advantage in flap design, fabricating a skin flap or skin flaps for reconstruction of burn deformities is not infrequently plagued with skin necrosis. Aberrant vascular supplies to the skin attributable to the original injury and/or surgical treatment could be the factor responsible for

Fig. 14.8 Double-opposing Z-plasty (scar: pink)

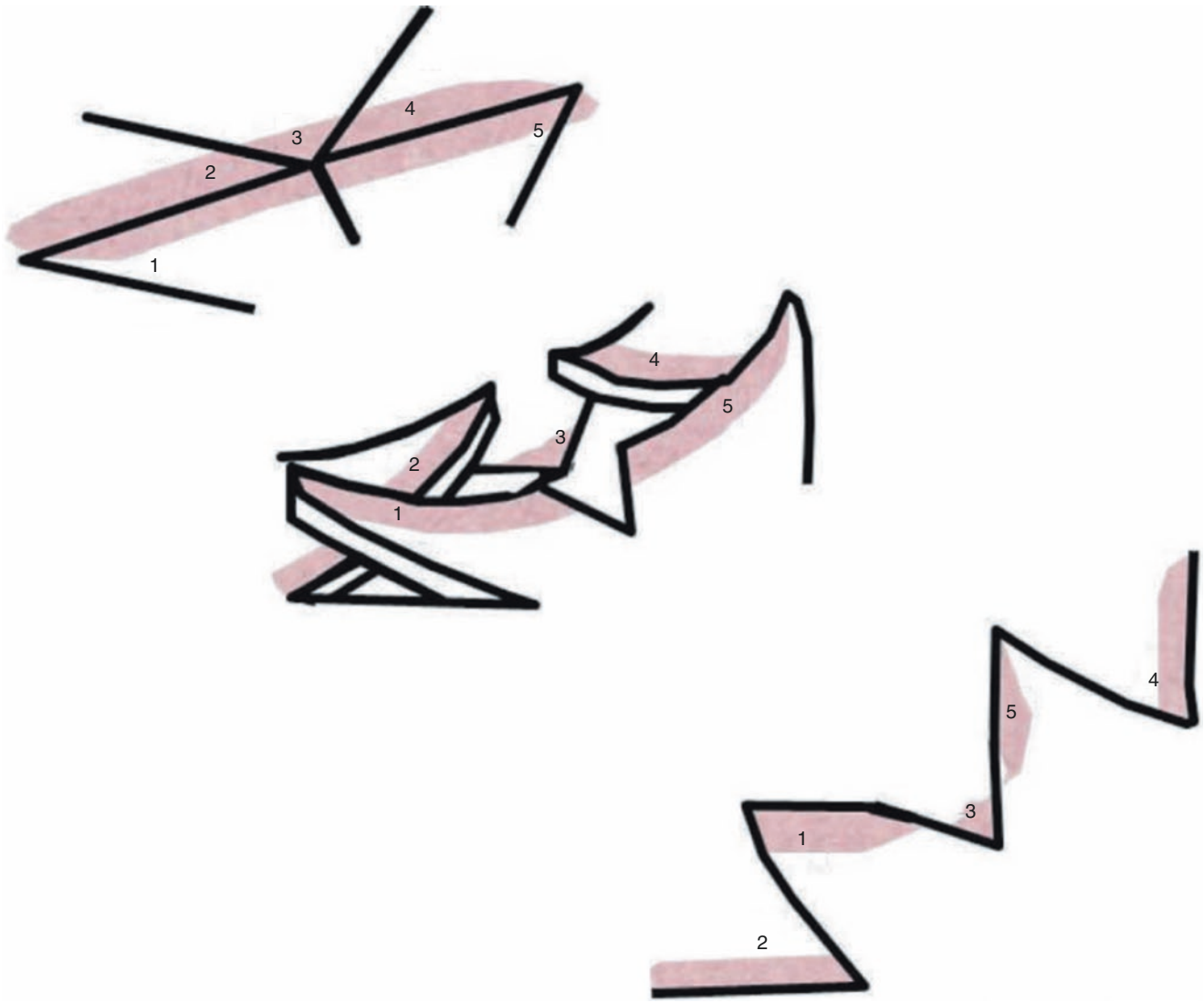


Fig. 14.9 Modified double-opposing Z-plasty (scar: pink)

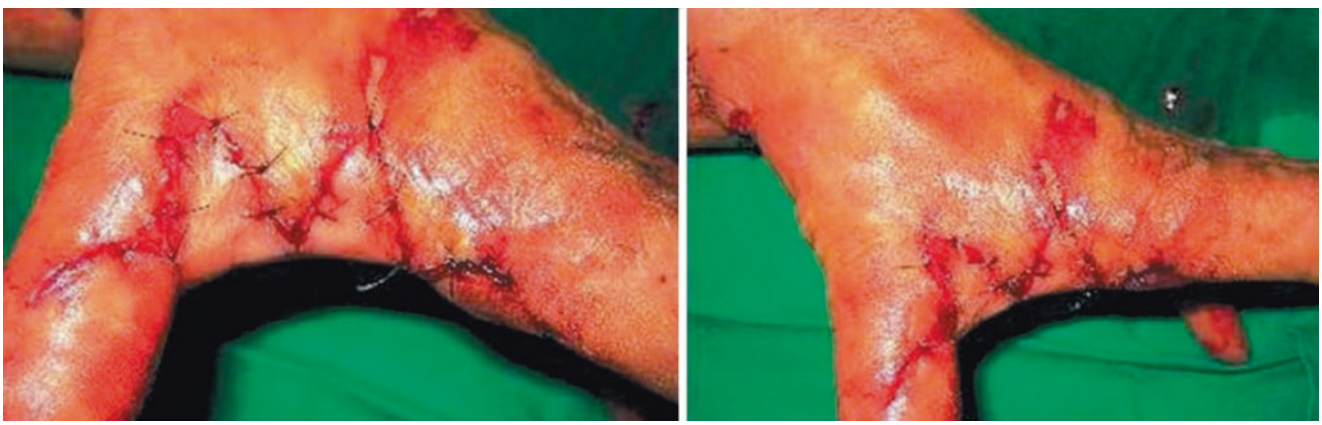


Fig. 14.10 Scar correction by use of a modified double-opposing Z-plasty (1. Web space)

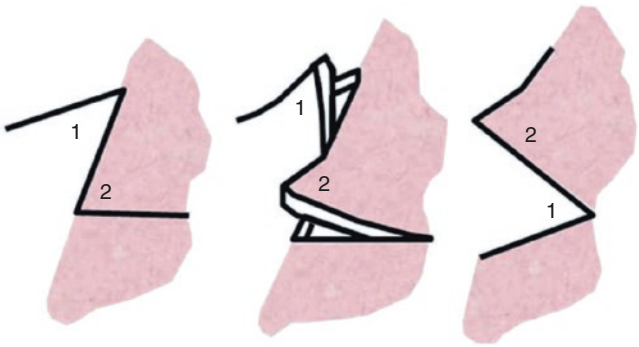


Fig. 14.11 ¾ Z-plasty or half-Z (Scar: pink)

problems. In recent years, the use of a skin flap designed to include muscle or fascia underneath has further expanded the usefulness of conventional Z-plasty and the ¾ Z-plasty techniques in burn reconstruction.

14.8.3 Musculocutaneous (MC) or Fasciocutaneous (FC) Flap Technique

Inclusion of not only the skin but also the subcutaneous tissues and fascia and muscle is necessary to fabricate a skin flap to reconstruct a tissue defect in individuals with deep

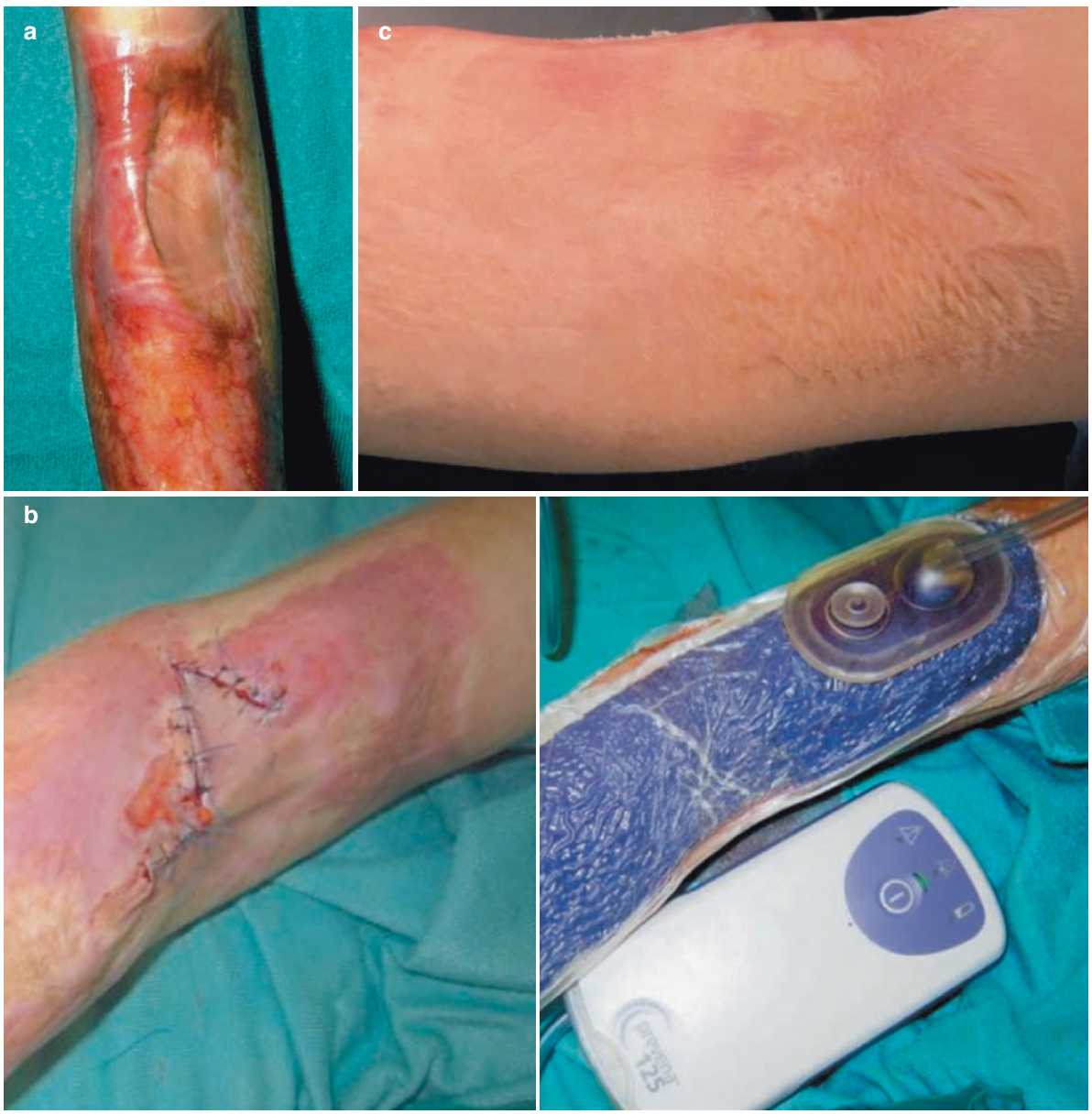


Fig. 14.12 (**a**) Scar contracture right cubita. (**b**) Correction by use of a ¾ Z-plasty, coverage with Prevena® for 6 days. (**c**) Long-time result after correction by use of a ¾ Z-plasty

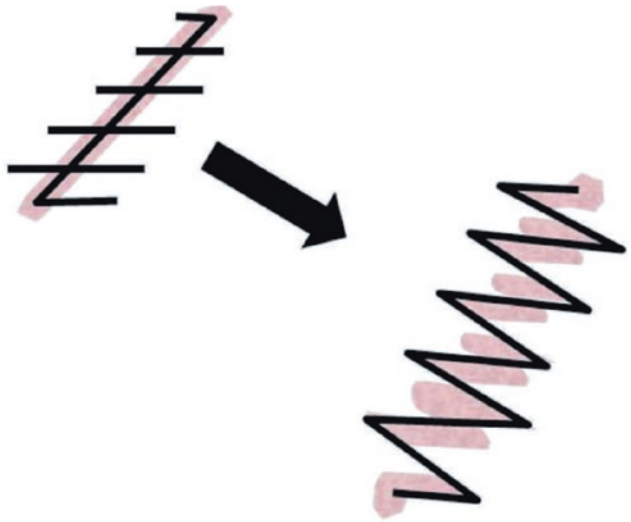


Fig. 14.13 Multiple Z-plasties (scar: pink)

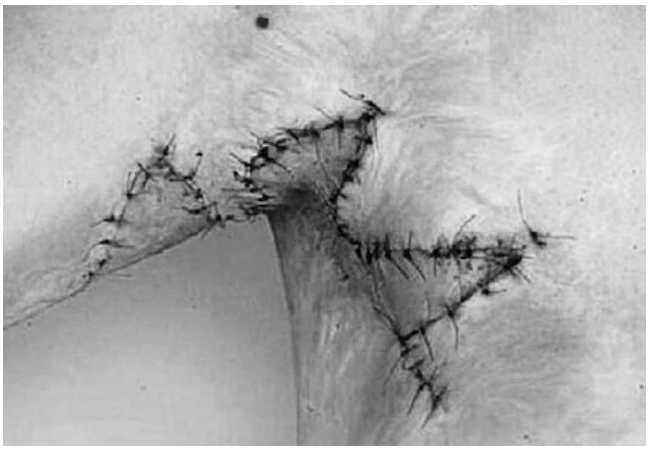


Fig. 14.14 Scar corrections by use of multiple Z-plasties (right axilla)

burn injuries. Which means, fabricating a flap in a burned area is possible, if the underlying muscle or the fascia is included in the design [23].

Moreover, multiple Z-plasties are often used for scar corrections (Figs. 14.13 and 14.14).

14.9 Distant Flaps

A distant flap involves a donor site, which is distant from the defect. The mode of transfer might be direct or microvascular. Direct flap, e.g., the forehead flap or the groin flap, involves direct approximation of the recipient bed to the donor site. These flaps all require a second operation to divide the pedicle.

14.9.1 Free Tissue Transfer

The evolution of microsurgery and free tissue transfer has dramatically expanded the functional and esthetic potential of reconstructive surgery. Due to microvascular anastomoses, free transfer of single or compound tissues and replantation of amputated parts are possible. Moreover, by using a free tissue transfer, single-step reconstructions are principally possible.

14.9.2 Perforator Flaps

Based on the septocutaneous perforator vessels, perforator flaps were developed. Song et al. described in 1984 [24] that the lateral femur region can serve not only as a skin harvest place but also as the donor side for the "antero lateral thigh (ALT) flap" based on a long pedicle. Then Koshima and colleagues from Japan refined exemplarily the ALT transfer subsequently. In 1989 Koshima introduced an abdominal skin and fat flap based on the inferior epigastric vessels and muscle perforators. Recently, the theory of perforasomes is under evaluation: every perforator contains a unique vascular territory, the perforasome [25]. This knowledge will lead to new useable pedicled and free flaps for reconstruction.

With the advent of microsurgical techniques, transplanting a composite tissue can be carried out with minimal morbidities. The regimen, in caring for burn victims, however, may be limited because of a paucity of donor materials. It is ironic that burn patients with suitable donor sites seldom require such an elaborate treatment, but those, who are in need of microsurgical tissue transplantation, are inevitably without appropriate donor sites because of extensive tissue destruction.

14.10 Composite Tissue Allo-Transplantation

"Composite tissue allotransplantation" (CTA) of parts of the face, or forearms and upper extremities [26–29], is a young area of transplantation medicine. The first clinical results are promising in comparison to the first reports of organ transplantation, although the medium-term and long-term problems, for example, tumor induction by the immunosuppression as well as chronic rejection have to be taken into account. This is not an unimportant fact, because CTA is normally not of vital importance. Nevertheless, for the affected persons, who must live in social isolation with exhausted reconstructive measures or prostheses, such operations may result a

dramatic improvement concerning quality of life. However, it is important to mention that currently only a selected small number of highly motivated patients are candidates for CTA.

14.11 Regeneration: Tissue Engineering

Tissue regeneration and tissue engineering have gained relevance for reconstructive surgery [30–32]. Recently, fat transplantation or lipo transfer is of utmost interest. Czerny transplanted in 1895 a lipoma for mamma reconstruction, and fat injection was described among other things by Eugene Holländer in 1910 within a patient with "progressive decrease of the fatty tissue." Erich Lexer dedicated in the first part of his book nearly 300 pages for free fat transfers. In 2001 it was demonstrated that beside fat cells also "adipose-derived stem cells" (ADSC) and other cell populations in the fatty tissue are usable for these purposes. The transplantation of ADSC was able to regenerate full-layered cartilage defects in the animal model [33]. The stem cell associated with fat cell transplantation in patients with a radioderm has led to improved healing. Moreover, fat cell transplantation is able to improve not only volume and contour defects but also skin quality [34–36]; thereby it seems that fat transfer will play an important part in burn reconstruction in the future.

14.12 Robotics/Prosthesis

If all reconstructive measures fail, myoelectric prostheses are a promising resort to go to. In recent years, these have been improved tremendously by introducing targeted muscle transfers (TMR) to the armamentarium of reconstructive surgery [37, 38]. Modern myoelectric prostheses have multiple degrees of freedom that mandate a complex control system to provide dependable use for the patient. Extremity reconstruction in the twenty-first century will see many new avenues to replace the loss of a limb and reconstruct the loss of function. Both biological and technical advances will provide possibilities that may well open up therapies that have been unthinkable only a few years ago. Targeted muscle reinnervation together with the provision of a myoelectric prosthesis with several degrees of freedom is such an approach and will definitely be a solid stepping stone leading to new strategies in extremity rehabilitation and reconstruction.

14.13 Summary

The regimen of burn treatment has changed drastically over the past 50 years. The regimen of an early debridement and wound coverage, initially with biological dressings and later with autologous skin grafts, enhanced the survival rate. It is, however, ironic that this improvement in survival has caused an increase of patients, who will require reconstructive surgery.

Unsightly hypertrophic scar, scar contracture, affecting particularly the joint structures, and missing bodily parts are still the most common sequelae of burn injuries today.

The difficulty concerning burn reconstruction is largely due to a lack of adequate donor sites, but due to the improvements in reconstructive surgery, better results are achievable. New areas like "composite tissue allotransplantation" of compound tissues like arms or parts of the face, prosthesis, and also regenerative medicine with "tissue engineering" have already entered the clinical routine and will improve the final results obtained by burn reconstruction.

References

1. Williams FN, Herndon DN, Hawkins HK, et al. The leading causes of death after burn injury in a single pediatric burn center. Crit Care. 2009;13(6):183.
2. Kamolz LP. Burns: learning from the past in order to be fit for the future. Crit Care. 2010;14(1):106.
3. Clark JM, Wang TD. Local flaps in scar revision. Facial Plast Surg. 2001;4:295–308.
4. Mathes S, Nahai F. Clinical application for muscle and musculocutaneous flaps. St. Louis: Mosby; 1982. p. 3.
5. Gottlieb LJ, Krieger LM. From the reconstructive ladder to the reconstructive elevator. Plast Reconstr Surg. 1994;93(7):1503–4.
6. Knobloch K, Vogt PM. The reconstructive sequence of the 21st century – the reconstructive clockwork. Chirurg. 2010;81:441–6.
7. Titscher A, Lumenta DB, Kamolz LP, et al. Emotional associations with skin: differences between burned and non-burned individuals. Burns. 2010;36(6):759–63.
8. Borges AF. Improvement of antitension line scar by the "W-plastic" operation. Br J Plast Surg. 1959;6:12–29.
9. McCarthy JG. Introsuction to plastic surgery. In: Plastic surgery. Philadelphia, PA: WB Saunders; 1990. p. 1–68.
10. Webster RD, Davidson TM, Smith RC. Broken line scar revision. Clin Plast Surg. 1977;4:263–74.
11. Tardy ME, Thomas RJ, Pashow MS. The camouflage of cutaneous scars. Ear Nose Throat J. 1981;60:61–70.
12. Alsarraf R, Murakami CS. Geometric broken line closure. Facial Plast Surg Clin North Am. 1998;6:163–6.
13. Thomas JR. Geometric broken-line closure. In: Thomas JR, Holt GR, editors. Facial scars: incision, revision and camouflage. St. Louis: CV Mosby; 1989. p. 160–7.
14. Pallua N, von Heimburg D. Pre-expanded ultrathin supraclavicular flaps for (full-) face reconstruction with reduced donor-site morbidity and without the need for microsurgery. Plast Reconstr Surg. 2005;115(7):1837–44.
15. Bozkurt A, Groger A, O'Dey D, et al. Retrospective analysis of tissue expansion in reconstructive burn surgery: evaluation of complication rates. Burns. 2008;34(8):1113–8.
16. Mittermayr R, Wassermann E, Thurnher M, et al. Skin graft fixation by slow clotting fibrin sealant applied as a thin layer. Burns. 2006;32(3):305–11.
17. Pallua N, Wolter T, Markowicz M. Platelet-rich plasma in burns. Burns. 2010;36(1):4–8.

18. Roka J, Karle B, Andel H, et al. Use of V. A. C. Therapy in the surgical treatment of severe burns: the Viennese concept. Handchir Mikrochir Plast Chir. 2007;39(5):322–7.
19. Nguyen DQ, Potokar TS, Price P. An objective long-term evaluation of Integra (a dermal skin substitute) and split thickness skin grafts, in acute burns and reconstructive surgery. Burns. 2010;36(1):23–8.
20. Haslik W, Kamolz LP, Nathschläger G, et al. First experiences with the collagen-elastin matrix Matriderm as a dermal substitute in severe burn injuries of the hand. Burns. 2007;33(3):364–8.
21. Haslik W, Kamolz LP, Manna F, et al. Management of full-thickness skin defects in the hand and wrist region: first long-term experiences with the dermal matrix Matriderm. J Plast Reconstr Aesthet Surg. 2010;63(2):360–4.
22. Bloemen MC, van Leeuwen MC, van Vucht NE, et al. Dermal substitution in acute burns and reconstructive surgery: a 12-year follow-up. Plast Reconstr Surg. 2010;125(5):1450–9.
23. Huang T, Larson DL, Lewis SR. Burned hands. Plast Reconstr Surg. 1975;56:21–8.
24. Song YG, Chen GZ, Song YL. The free thigh flap: a new free flap concept based on the septocutaneous artery. Br J Plast Surg. 1984;37(2):149–59.
25. Saint-Cyr M, Wong C, Schaverien M, Mojallal A, Rohrich RJ. The perforasome theory: vascular anatomy and clinical implications. Plast Reconstr Surg. 2009;124(5):1529–44159.
26. Brandacher G, Ninkovic M, Piza-Katzer H, et al. The Innsbruck hand transplant program: update at 8 years after the first transplant. Transplant Proc. 2009;41(2):491–4.
27. Siemionow MZ, Zor F, Gordon CR. Face, upper extremity, and concomitant transplantation: potential concerns and challenges ahead. Plast Reconstr Surg. 2010;126(1):308–15.
28. Gordon CR, Siemionow M, Zins J. Composite tissue allotransplantation: a proposed classification system based on relative complexity. Transplant Proc. 2009;41(2):481–4.
29. Siemionow M, Gordon CR. Overview of guidelines for establishing a face transplant program: a work in progress. Am J Transplant. 2010;10(5):1290–6.
30. Kamolz LP, Lumenta DB, Kitzinger HB, Frey M. Tissue engineering for cutaneous wounds: an overview of current standards and possibilities. Eur Surg. 2008;40(1):19–26.
31. Beier JP, Boos AM, Kamolz L, et al. Skin tissue engineering – from split skin to engineered skin grafts? Handchir Mikrochir Plast Chir. 2010;42:342–53.
32. Mansbridge JN. Tissue-engineered skin substitutes in regenerative medicine. Curr Opin Biotechnol. 2009;20(5):563–7.
33. Dragoo JL, Carlson G, McCormick F, et al. Healing full-thickness cartilage defects using adipose-derived stem cells. Tissue Eng. 2007;13(7):1615–21.
34. Klinger M, Marazzi M, Vigo D, Torre M. Fat injection for cases of severe burn outcomes: a new perspective of scar remodeling and reduction. Aesthet Plast Surg. 2008;32(3):465–9.
35. Mojallal A, Lequeux C, Shipkov C, et al. Improvement of skin quality after fat grafting: clinical observation and an animal study. Plast Reconstr Surg. 2009;124(3):765–74.
36. Rennekampff HO, Reimers K, Gabka CJ, et al. Current perspective and limitations of autologous fat transplantation – "consensus meeting" of the German Society of Plastic, reconstructive and aesthetic surgeons. Handchir Mikrochir Plast Chir. 2010;42(2):137–42.
37. Aszmann OC, Dietl H, Frey M. Selective nerve transfers to improve the control of myoelectrical arm prostheses. Handchir Mikrochir Plast Chir. 2008;40(1):60–5.
38. Hijjawi JB, Kuiken TA, Lipschutz RD, Miller LA, Stubblefield KA, Dumanian GA. Improved myoelectric prosthesis control accomplished using multiple nerve transfers. Plast Reconstr Surg. 2006;118:1573–7.

Tissue Expanders in Burn Surgery

15

Norbert Pallua and Erhan Demir

Part I

15.1 Introduction

Tissue expansion is based on a dynamic process of nature in which vital tissue responds to continuous mechanical stress load. The capability to gain or lose weight during pregnancy for instance demonstrates the skin ability to develop independently. Tissue expansion has a significant implication in different ethnic societies throughout the world. Enlarged lips of Ethiopian Mursi women or elongated necks of Padauang women attest the exotic esthetics associated with tissue expansion [1]. Tissue expansion represents the medical application of this normal physiologic process for reconstructive purposes and has already provided to be a reliable principle in plastic and reconstructive surgery [2, 3].

15.2 Historical Aspects

In 1905 the clinical use of tissue expansion gained significance when bone lengthening by distraction resulted in skin expansion [4]. However, the first clinical concept of tissue expansion was reported by Neumann in 1957 for the reconstruction of a traumatic ear defect with a post-auricular expanded skin flap to cover the cartilage framework of the ear [5]. Twenty years later, skin expansion was re-introduced independently by Radovan and Austad [6, 7]. Radovan became the first surgeon to gain extensive experience in the use of silicone expanders, whereas Austad was the first to report his laboratory scientific experience prior to the subsequent clinical application. Primarily established for breast reconstruction, skin expansion represents one of the major developments in reconstructive surgery in recent years, particularly as a valuable approach for many problems in reconstructive burn surgery [8]. More recent surgical modifications advanced the basic concept of tissue expansion to pre-expand flap donor regions or to prefabricate regional or microsurgical free flaps [9–15].

15.3 Biology of Expanded Tissue

Tissue expansion places an inflatable device beneath the skin flap, which is then expanded over a period of time. Basic studies confirmed that the increased surface area is the result of newly regenerated tissue [16]. Experimental data on the biology of expanded skin in animal and human studies showed that the epidermis underwent significant thickening after 5 weeks to 5 months of expansion. The dermis and subcutaneous tissues, on the other hand, were significantly thinner after expansion. They found the greatest thinning over the dome of the expander and a gradually decrease toward the periphery [17–20]. Histologically, the most significant thinning occurred in the reticular dermis. These observed changes persisted 2 years. Expanded tissues 2 years after cessation of expansion had the same thickness as control tissues and had no remnant fibrous capsule [6, 21]. Additional increase in dermal collagen content with disruption of elastic fibers has been noted. The noticed dermal and subcutaneous collagen increase occurs with a constant ratio between collagen type I and III. Skin appendages are not affected by the expansion procedure [1].

Therefore, some believe that much of the expanded skin represents stretch and reorganization of dermal collagen fibers rather than new skin created by mitosis. Austad postulated that tissue expansion causes a decrease in cell density in the basal layer of the skin and that cell density may regulate skin mitotic activity. A greater cell proliferation is a consequence of lower cell density, resulting in growth of additional skin [1]. The physiology of expansion by prolonged tissue expansion (PTE) is therefore considered not to

N. Pallua (✉) · E. Demir
Private Clinic Pallua & Grašys, Düsseldorf, Germany

Aachen University of Technology, Aachen, Germany
e-mail: info@pallua.de

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_15

be just a matter of skin stretching, but the formation of additional new skin, which has all the characteristics of the original tissue.

A significant increase in vascularity has been associated with soft tissue expansion. Experimental studies observed proliferation of blood vessels and numerous neovascular branches in expanded flaps [20, 22]. The measured blood flow after flap expansion was higher than contralateral non-expanded controls.

The ability of soft tissue to expand is based on several aspects. The skin has the constant ability to adapt, depending on the amount and distribution of structural proteins and tissue fluids. Collagen fibers become parallel with the stretching of tissue. Although elastin fibers are important for recoil after stretching, collagen fibers lengthen permanently [1].

Any expansion-related muscle damage with fiber atrophy or degeneration dissolves after pressure relief with expander removal.

The process of tissue expansion affects not only the adjacent tissue but also a number of cell types. On the molecular level, a key function in the mechanical intercellular signal transduction has been attributed to the protein kinase C. In this context, some growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), angiotensin II, and transforming growth factor beta (TGF-ß) have been reported to have important influence on cell proliferation and extracellular matrix production. TGF-ß can also enhance fibroblast proliferation [1, 22, 23].

In summary, prolonged dynamic tissue expansion is a passive physical process with a metabolically active component [8].

15.4 Basic Principles and Techniques

15.4.1 Indications, Patient Selection, and Compliance

The appropriate patient selected for burn reconstructions with tissue expanders faces a difficult reconstructive challenge. The patients must be willing to subject themselves to a prolonged treatment concept. The patient must be able to emotionally deal with the temporary extreme deformity and the somewhat bizarre appearance of the expanded anatomic regions. This may require a thorough dialog with the patient and high individual compliance and motivation.

Indications for the use of expanders in burn reconstructions are instances where there is not enough adjacent tissue to resurface or close a defect primarily or with a local flap. The same criteria used to select a suitable patient for a regional skin flap are applicable in the selection for tissue expanded skin or flap reconstruction. Ideally the patient should have no serious medical problems (e.g., diabetes, hypertension) and should not be a heavy smoker.

Tissue expansion allows large areas of burn scar to be resurfaced and provides tissue of similar texture and color to the defect to be covered combined with the advantage of reduced donor site morbidity. It is therefore indicated whenever defect repair by an alternative method such as a local, regional, or free flap may result in an unacceptable donor region or recipient site deformity [2, 11, 24, 25].

Issues and disadvantages that need to be addressed are that the technique of pre-expansion requires additional office visits for serial expansion and at least one extra surgical procedure with potential for additional complications. A significant time period between 9 and 12 weeks for progressive tissue expansion is required.

15.4.2 Expanders

Tissue expanders belong to the most frequently used implants in plastic and reconstructive surgery [26–28]. The most commonly used expanders are the different types and variations of Radovan expanders. Elliptical, rectangular, round, crescent type, or custom-made shapes with integrated or separate port systems are available. The various volumes range between 1 and 1000 cc. Expanders can be over inflated at least two times the stated maximum volume.

Expanders with an incorporated filling valve are designed in a way that the expander and injection port form a single unit. The port has a self-sealing membrane and is lined with metal or a thick polymer to prevent accidental puncture of the dome during injection of saline. The shapes include hemispheric, rectangular, crescent, and teardrop. Limitations are the size ranges between 50 and 1000 cc, as this type of expander are not available as mini-expanders. The stiffness of the injection port causes an increased risk of skin erosion.

The third relevant expander groups are the self-inflating systems. They consist of a semipermeable silicone membrane that surrounds a hydrogel core (co-polymer based on methylmetacrylate and N-vinylpyrolidon) to create an osmotic gradient across the expander wall. The interior core of the expander is hypertonic relative to the extracellular water, causing a net influx of water into the expander. In burn reconstructions, this type of expander is somewhat experimental [29].

15.4.3 Aspects in Expander Volume and Shape Selection

The three-dimensional expander geometry needs to match the expansion site and the design of the planned flap. The shape of the expander depends primarily on the site of expansion and the reconstruction needs. The use of a rectangular expander provides the most effective surface area gained when compared to the round or crescent types [30].

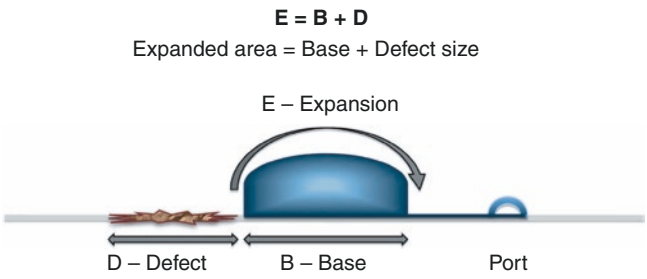


Fig. 15.1 Estimation of the expanded area, according to the base size and defect width

The selected expander size must be large enough to provide desired expansive forces necessary to achieve the sufficient tissue augmentation. One method of selecting the appropriate expander is based on the size of the expander base. The expander base and the defect width are helpful parameters to estimate the required expansion (Fig. 15.1) [31]. While using a rectangular or crescent expander, the appropriate size expander would be one in which the surface area of the expander base is 2.5 times as large as the defect to be closed. With round expanders, the diameter of the expander base should be 2.5 times as large as the defect [17]. Another method of expander selection is based on the circumference of the balloon portion of the expander. The expander must be of sufficient volume that the apical circumference of the dome of skin overlying the fully inflated expander is 2–3 times the defect width.

It is best to select the largest expander that can reasonably be placed beneath the donor region of expansion or to consider the use of two or more expanders to gain the needed tissue. Still, the proven safety of limited over inflation allows a margin of error in the initial choice of implant volume and later permits to continue expansion if more tissue is required. The disadvantage of over inflation is the increased leakage from the injection port dome.

15.4.4 Surgical Expander Placement and Expansion

The donor site is selected where tissues are most suitable (e.g., thickness, color, texture) to those of the anatomic region to be resurfaced with close proximity to the defect. The use of local tissue with the advantage of color and texture match with the recipient region is sometimes difficult or impossible to achieve in burned patients.

The incision for expander placement should be in a site well hidden or ideally perpendicular to the desired vector of expansion, to keep the forces of scar tension as low as possible. The incision can be incorporated into the scar area planned for reconstruction after expander removal but should not potentially compromise the viability of advancement flaps during reconstruction. However, while using more than one expander, it is crucial to respect appropriate distances between the expander pockets to prevent expander displacements with inefficient skin expansions.

The correct anatomic position while placing the expander is critical. In the face and neck, it is usually beneath the subcutaneous fat or below the platysma in the neck. In the scalp, expander placement is in a subgaleal plane. While performing pre-expanded muscular flaps such as the pre-expanded trapezius flap, the correct level of dissection while creating the expander pocket is submuscular. The dissected pocket needs to be large enough to fit the expander without any folding. The surgeon should make sure the implant is intact and functioning prior placement. The port system is placed subcutaneously in a more distant position approximately 5 cm away from the expander. Meticulous hemostasis is essential; suctions drains are placed to drain the wound. The implanted expander is inflated with 10% of the end-volume to obliterate dead space and to aid with the hemostasis.

The procedure of serial ambulatory expansion is begun after completion of wound healing about 2–3 weeks postoperatively. During inflation, aqua ad iniectabilia is instilled till tension of the overlying skin is noted or patients report about discomfort. In a clinical observation, the skin may blanch with pressure from the expander, but capillary refill should return to normal after pressure is withdrawn.

The process of expander inflation is continued on a weekly basis until the desired amount of volume and tissue needed is obtained (usually between 8 and 12 weeks). Meticulous documentation of instilled volumes is important.

15.4.5 Expander Explantation and Management of the Capsule

The second reconstructive step consists of removal of the expander and local, regional, or free flap reconstruction. Total capsule excision may create ultrathin and flexible flaps as desired in facial reconstructions [9, 32]. As an alternative, it is useful to incise the capsule or to remove the inner layers of the capsule to allow further lengthening of the expanded flap. Leaving the superficial layers of the capsule may prevent the compromise of the flap vasculature as the reported vascular proliferation occurs primarily at the junction of the capsule and the host tissue. Any surgical maneuver should be limited to the expander capsule [8].

15.4.6 Pre-expanded Flaps

Since their introduction, several pre-expanded flaps have been used in burn reconstructions. These include the lateral arm fasciocutaneous flap, the scapular/parascapular fasciocutaneous flap, radial forearm fasciocutaneous flap, the groin flap, the latissimus dorsi musculocutaneous flap, the trapezius muscle flap, the serratus anterior musculocutaneous

flap, the tensor fascia lata flap or the supraclavicular island flap to name a few [9, 12, 13, 15, 33–35]. More recently, methods of perforator-based tissue expansion for pre-expanded free cutaneous perforator flaps such as the anterior lateral thigh flap are becoming more common [36, 37].

15.5 Complications

Although the expansion related reconstructive procedure is based on a simple concept, this technique is associated with complications [38–43]. In studies providing data of all anatomical regions, failure rates ranged up to 24% [1, 44]. Appropriate patient selection and surgical experience may reduce the complication rates below 20%.

Major complications are usually defined as those requiring expander removals. These complications may include tissue loss caused by overexpansion and induced ischemia, inadvertent flap thinning, fat necrosis, expander infection, expander exposure, implant failure, and interference of the flap design due to incorrect incisions used to place the tissue expanders. This may occur secondary to trauma, flap erosion due to folds in the expander, aggressive expansion methods, or port placement over a bony prominence. If implant folding or flap ischemia secondary to over-filling of the expander is suspected, in an early stage, expander deflation and skin observation should be performed. If skin viability returns, the device can be slowly re-inflated in a later stage. In cases with skin necrosis or expander extrusion, the implant needs to be removed. After surgical debridement, the wound can be managed by conservative measures with broad-spectrum antibiotics and frequent wound dressings. Infections of the expander pocket may respond in some cases to antibiotics and partial implant deflation to minimize vascular compromise. If these procedures fail, the implant should be removed, the pocket irrigated, drained, and allowed to heal.

Minor complications are defined as seroma and drainage after expansion, poor compliance, intolerance of the injections to fill the expanders or alterations in the early preoperative plans secondary to incomplete coverage following expansion. Rates range between 17% and 40%, with a mean in the range of 20% [1, 44].

Part: II

15.6 Clinical Applications of Tissue Expanders

15.6.1 Head and Neck Reconstruction

15.6.1.1 Alopecia Reconstruction of the Burned Scalp

Deep scalp burns result in cicatricial alopecia in the long term [1]. The treatment of these problems depends on the size, the particular location, and the status of the remaining hair-bearing scalp. Burn alopecia is frequently noted in up to 32% of the patient population. In addition, a 2.2% incidence of complications including scar alopecia is due secondary to the use of the scalp donor site in burn patients [45, 46]. The reconstruction of scalp defects with serial excisions and rotational flaps may in some cases be not sufficient enough [25]; therefore, skin expansion and correction of alopecia using scalp rotational flaps have become the gold standard treatment.

McCauley classified burn alopecia in four types based on the pattern and the extent [1].

Patients with type IA and IB alopecia can be corrected with a single expansion. Patients with type I-C and ID may achieve complete defect coverage with sequential expansion. Type II can be corrected with a single pre-expanded scalp flap. Patients classified as IIB, IIC, or IID may respond well to multiple expanders. Unfortunately type III and IV patients are not good candidates for tissue expander procedures [1] (Table 15.1).

Multiple expanders (average volumes 200–400 cc) with distant injection ports are placed beneath the galea aponeurotica. Inflation of the expander begins 2 weeks postoperatively on a weekly basis. After an initial 3-week period with slow proceeding of the expansion due to galeal resistance or deformation of the external tabula in young patients, adequate expansion can be accomplished in 8–10 weeks. The endpoint of expansion is until the distance across the expanded scalp is equal to the starting distance, plus the scalp width to be replaced. The second stage involves incision at the margin of the alopecia and expander removal. The bald scalp is excised only after advancing or transposing the expanded scalp to be sure that sufficient tissue is available to close the proposed resection. If there is insufficient tissue to allow removal of the alopecia, tissue expanders can be replaced for further expansion. If there is adequate tissue, the capsule surrounding the expander is usually not excised. The wounds are closed in two layers, and suction drains are used.

Case sample: An 11-year-old boy with type II burn alopecia. Same patient with three implanted expanders and 2 years after scalp expansion and alopecia reconstruction (Figs. 15.2, 15.3, and 15.4).

Table 15.1 McCauley RL Classification of burn alopecia

Type I	Single alopecia segment
IA	Less than 25% of hair-bearing scalp
IB	20–50% of the hair-bearing scalp
IC	50–75% of the hair-bearing scalp
ID	75% of the hair bearing scalp
Type II	Multiple alopecia segments amendable to tissue expansion placement
Type III	Patchy burn alopecia not amendable to tissue expansion
Type IV	Total alopecia

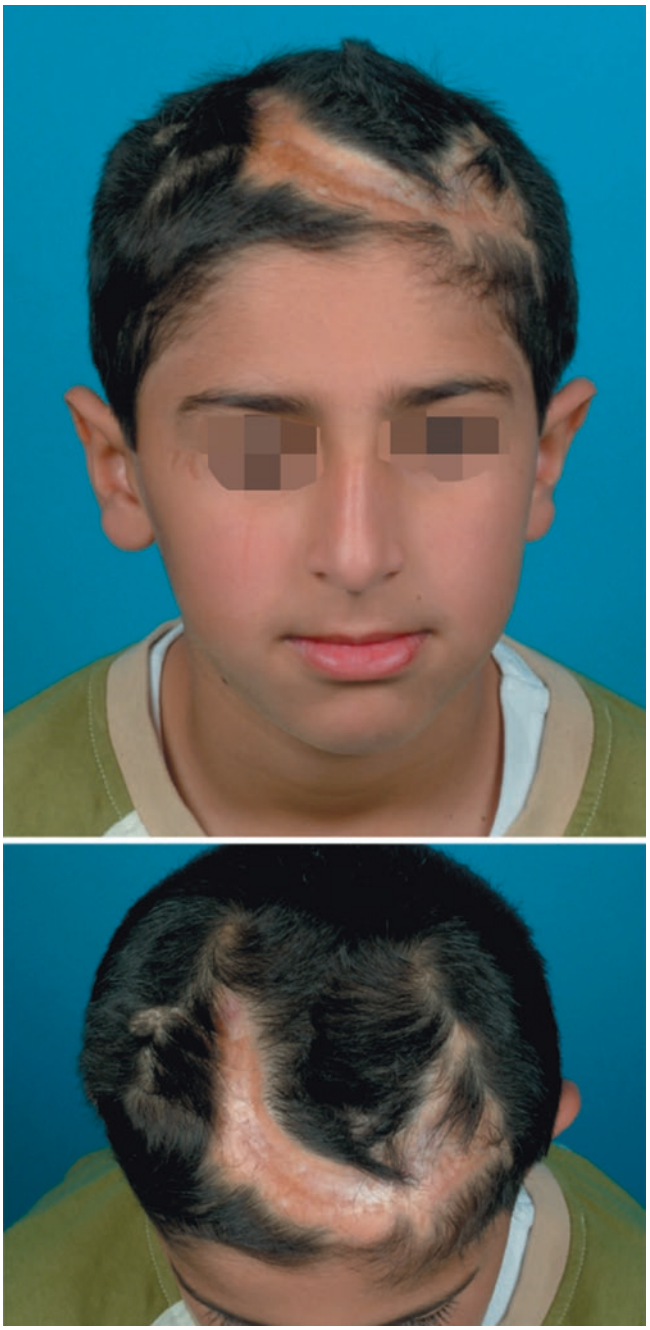


Fig. 15.2 An 11-year-old boy with type II alopecia, multiple segments

15.6.1.2 Eyelid Reconstruction

The skin of the eyelids is best replaced by adjacent eyelid tissue, rather than skin grafts. In rare indications, the ideal implant is a cigar-shaped, 1.2 cc silicone expander with an expansible anterior and rigid back wall to prevent expansion and pressure on the globe. An oblique skin incision is made in the crow's feet lateral to the canthal region. The implant is placed in a subcutaneous pocket that extends from the medial to lateral canthus. The reservoir dome is placed in a remote pocket over the temporal region. After sufficient expansion, the expanded skin will cover the lower lid defect.

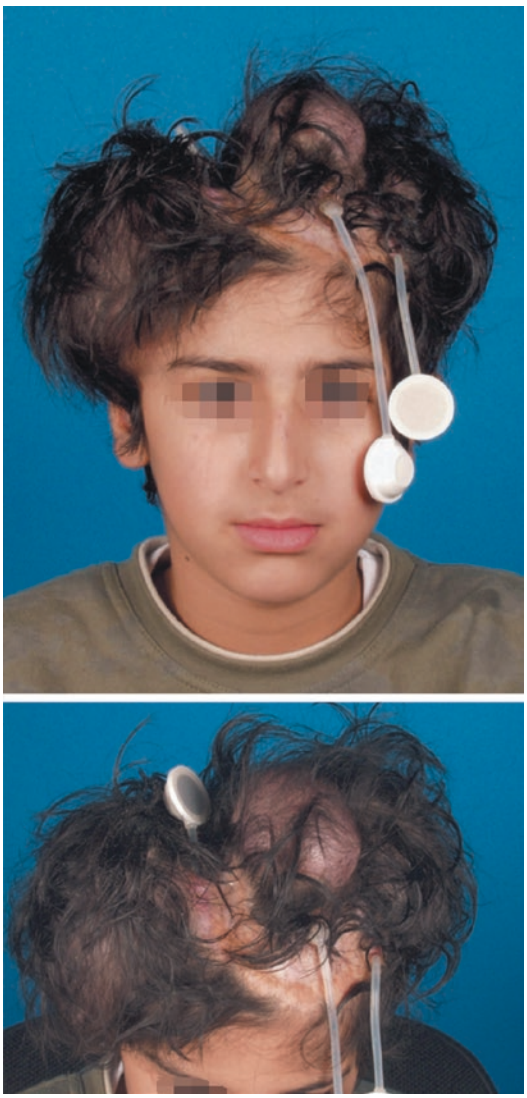


Fig. 15.3 Implantation of three tissue expanders with external ports

15.6.1.3 Nose Reconstruction

The total or partial reconstruction of the nose may require pre-expanded paramedian forehead flaps including the formation of the vestibular lining and columella. A careful staged plan with flap pre-lamination and pre-fabrication with previous placement of the cartilage framework prior reconstruction are the key to successful nose reconstruction with pre-expanded forehead flaps. A rectangular expander of 100–250 cc volume is placed through an incision behind the hairline in the subgaleal plane. The expansion of the forehead skin causes a desired thinning of the tissue to facilitate contouring to reconstruct the ala region.

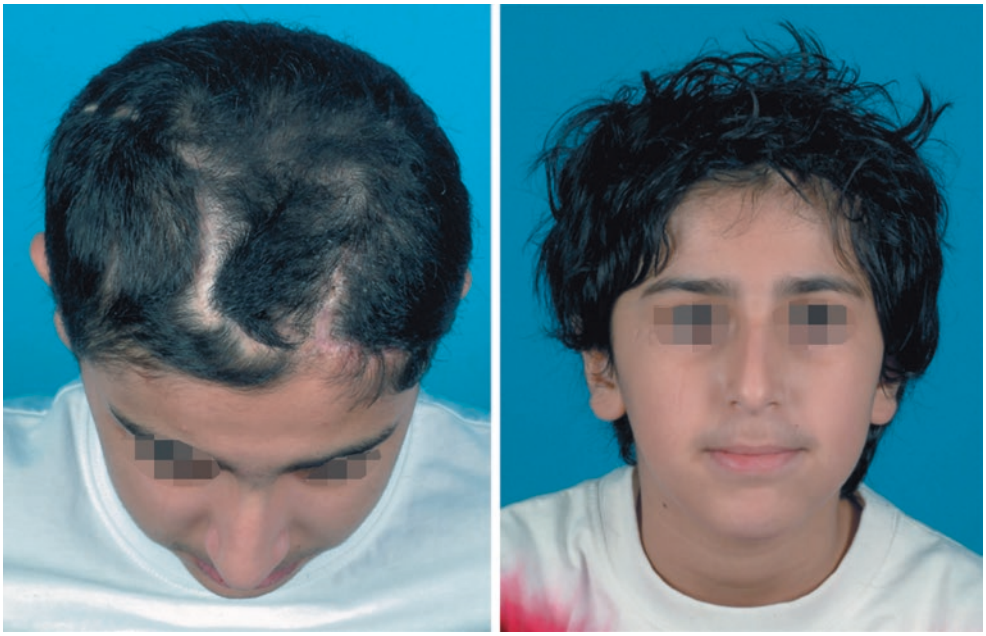


Fig. 15.4 Final result, 2 years post OP with short and long hair after burn scar excision and reconstruction with pre-expanded scalp flaps

15.6.1.4 Facial Reconstruction

The implantation of expanders into the head and neck region to use randomized loco-regional flaps is an elegant procedure. Still, loco-regional flaps may have their limitations in facial reconstruction depending on the defect size. The pre-expanded ultra-thin supraclavicular island flap is a useful option in facial resurfacing of hemifacial defects.

Generally to achieve satisfactory functional and esthetic results, the texture, color, and thickness of the flap need to be similar to those of the head and neck regions. The primary indication for facial reconstruction after burns is scar reduction or improvement [8, 9, 47]. Preferable donor sites in facial reconstruction are the supraclavicular area or the retroauricular area. As the retroauricular area is too small for large defects, the cervicohumeral shoulder region is well suited [9, 47–49]. Controlled tissue expansion with expanders prior transfer to modify the donor site and to increase the size of sensate thin pliable skin with good texture match creates flaps to cover the whole esthetic unit after complete scar resection [9, 35].

15.6.1.5 Supraclavicular Island Flap (SIF-Flap)

A random pattern flap of the supraclavicular region first described by Mutter in 1842 was modified after closer anatomic examination of the arterial blood supply of the shoulder region by Lamberty. The supraclavicular axial patterned flap was based on the supraclavicular artery arising from the superficial transverse cervical artery, beneath or lateral to the posterior part of the omohyoid muscle. The supraclavicular island flap, after having identified the venous drainage of the angiosome, was first introduced to reconstruct mentosternal contractures and has been further optimized to expand the indications in facial reconstruction [49]. The technique of SIF flap pre-expansion with expanders in the anterior shoulder region increased the size of ultra-thin pliable skin with good texture match to cover the whole esthetic unit of the face [9, 32].

Adequate planning and flap design needs to respect the esthetic units of the facial area. In *hemifacial reconstruction*, the entire scar area needs to be excised ranging from the nasolabial fold to the preauricular region and from the inferior orbital rim and the temporal region to the mandibular rim. The defect sizes range between 12 × 16 and 15 × 19 cm after complete excision with respect to the esthetic unit [32].

The expander, previously inserted into the supraclavicular artery angiosome, will be carefully removed. After complete flap dissection, the SIF flap is mobile on its vascular pedicle, allowing up to 180° angle of rotation on the vascular axis as required. To create an ultra-thin flap the expander, the capsule is partially removed taking care not to damage the flap vasculature. In facial reconstruction, a lesser degree of flap rotation is required to reach the facial defect. The donor side defect of the anterior shoulder region will be closed directly in a double layer fashion after extensive undermining and preparation of two advancement flaps. A secondary procedure 3 weeks later to divide the pedicle will utilize the spare skin to perform small local flaps of the mental and cervical region.

Case sample: An 18-year-old patient recovering from 25% TBSA full-thickness flame injury in a house presented with heavy facial scarring following primary burn reconstruction with eschar excision and multiple skin grafting procedures (Fig. 15.5). A multi-staged plan with bilateral pre-expanded SIF reconstructions was scheduled.

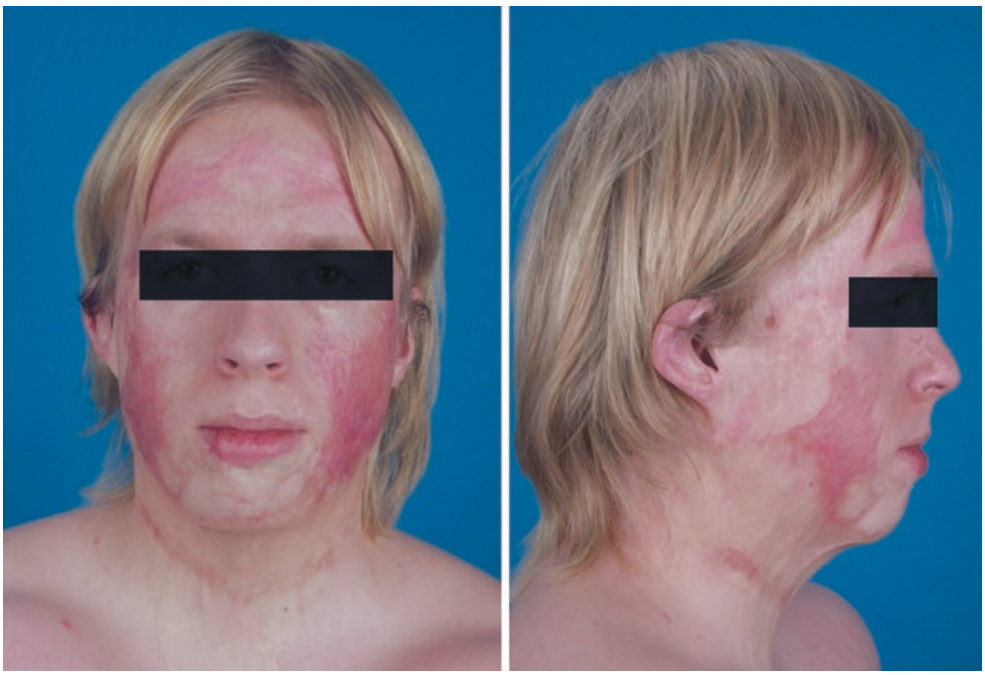


Fig. 15.5 Severe facial scarring following housefire

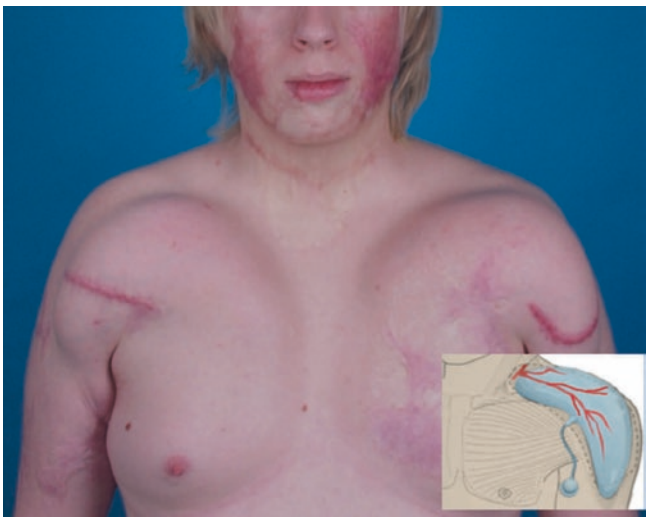


Fig. 15.6 Bilateral inflated crescent expanders in the angiosome of the supraclavicular island flap

Consecutive bilateral expansion with two crescent-type tissue expanders (Mentor Corporation, Irving, Texas, USA) of 700 cc each placed in the ventral shoulder regions has been carried out for 10 weeks (Fig. 15.6). The flap procedures were carried out 11 weeks after expander inflation with pre-expanded SIF-flaps on both sides. After bilateral pedicle division, a pleasant color and texture match has been achieved. The final outcome 6 years after reconstruction is shown (Fig. 15.7).

15.7 Reconstruction of the Trunk and Extremities

All previously mentioned random pattern lipo- and fasciocutaneous flaps or musculocutaneous flaps are useful in tissue expansion and reconstruction of the trunk and extremities [8, 34, 47, 50, 51].

Case sample: Severe shoulder scars have been resurfaced following local skin expansion with two 400 cc crescent type expanders. The final outcome illustrates acceptable scar reduction at the 2 year follow-up (Figs. 15.8, 15.9, and 15.10).

Musculocutaneous flaps require expander placement below the dorsal muscle surface, whereas fasciocutaneous flaps should be placed directly underneath the deep fascia. The angiosomes of the body and their clinical use have been studied in detail. Most recent developments have increased the interest in perforator-based expansion of angiosomes to create pre-expanded perforator flaps as needed. Vascularity and surface area resulting from tissue expansion allow the harvest of more healthy tissue beyond the anatomical angiosomes of local or regional flaps. The observed enhancements of perfusion rates in these flaps are attributed to a “delay phenomenon” in the distal parts of the flap. The meticulous preservation of the axial or segmental flap vasculature during expander implantation is critical [8].

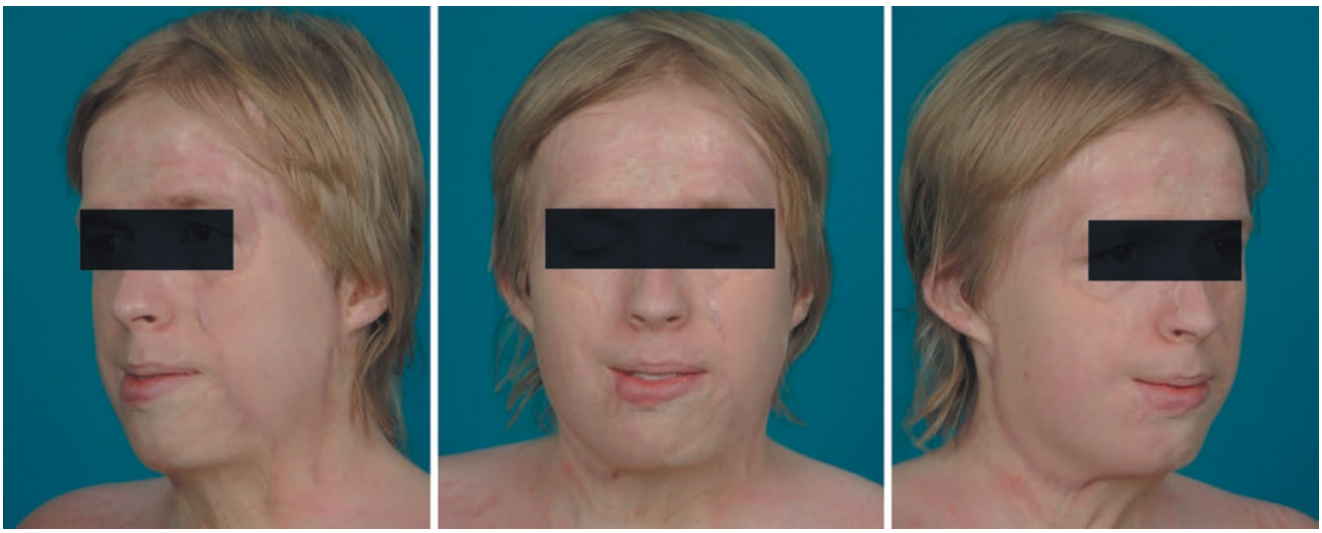


Fig. 15.7 Final outcome of facial reconstruction 6 years after bilateral pre-expanded supraclavicular island flaps

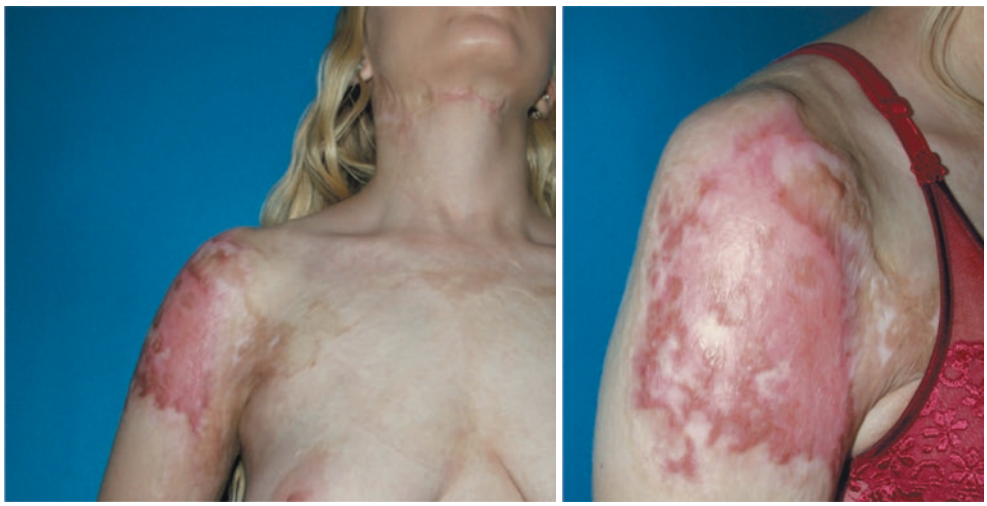


Fig. 15.8 Severe shoulder scars

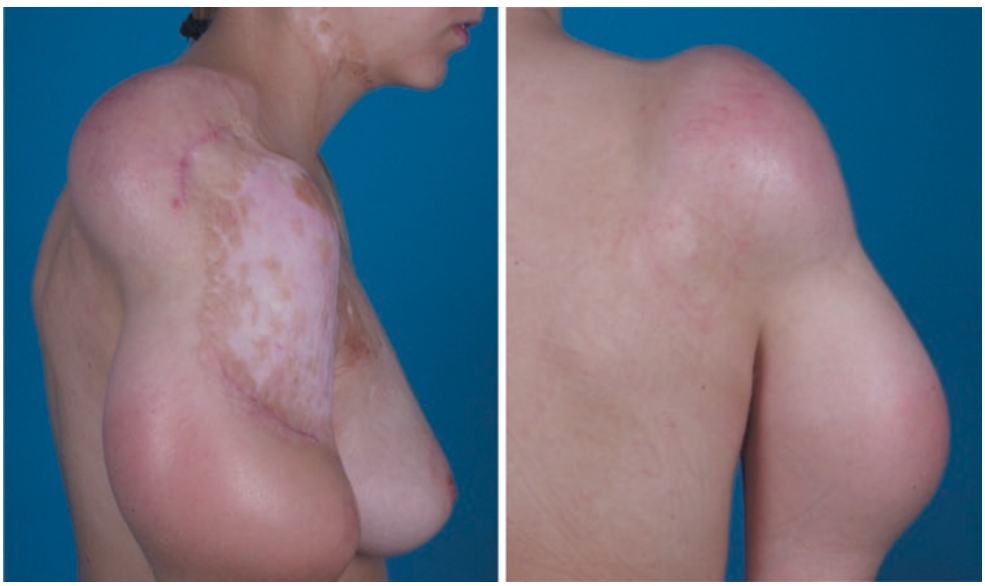


Fig. 15.9 Two implanted and inflated crescent expanders in the shoulder and upper arm region (400 cc)

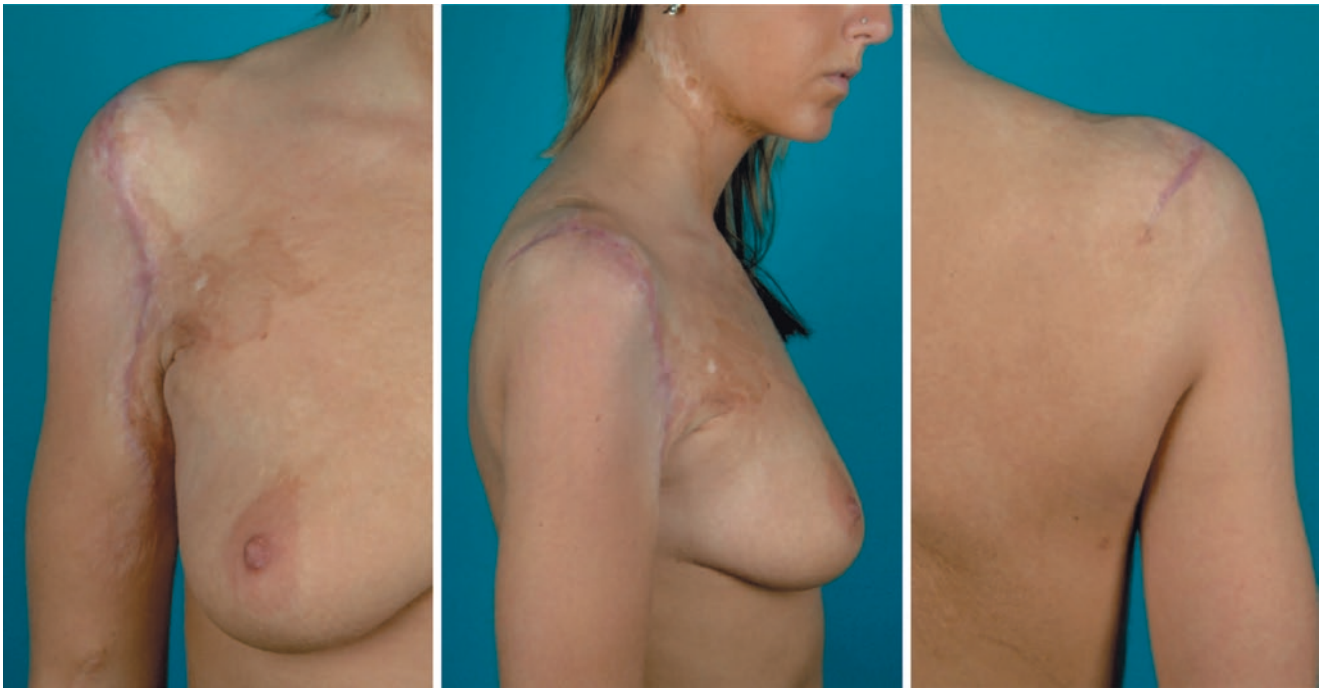


Fig. 15.10 Final outcome with pre-expanded locoregional flaps

Case sample: A pre-expanded parascapular flap has been worked out for a 25-year-old patient with severe hypertrophic scarring of the left lower arm region following burns (Fig. 15.11). Ten weeks after implantation of a 700 cc rectangular expander of the left donor region, a microsurgical free pre-expanded parascapular flap has been performed. The final outcome demonstrates sufficient defect coverage after scar excision (Figs. 15.12 and 15.13).

15.8 Summary

Tissue expanders are very versatile tools in reconstructive burn surgery. Still, careful patient selection, correct indications, realistic treatment concepts, large experience, well-selected surgical techniques, precise instruction of the medical staff, as well as detailed and continuous education of the patients are essential. However, although afflicted with a broad range of possible complications, tissue expansion procedures remain a valuable and reliable technique for the reconstruction of burn patients suffering from extensive scarring.

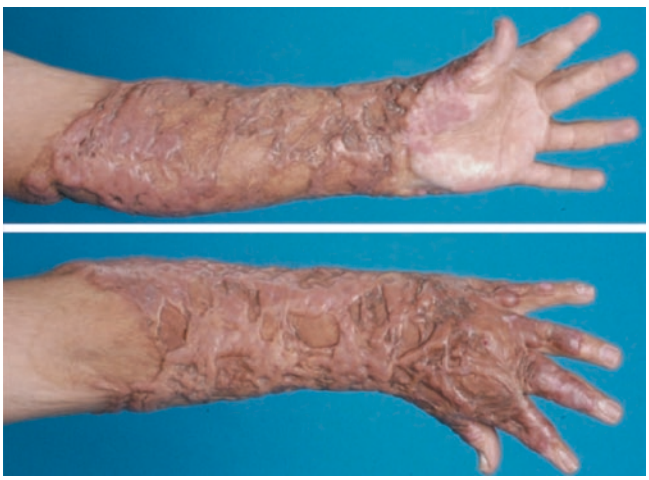


Fig. 15.11 Severe scarring of the left lower arm region

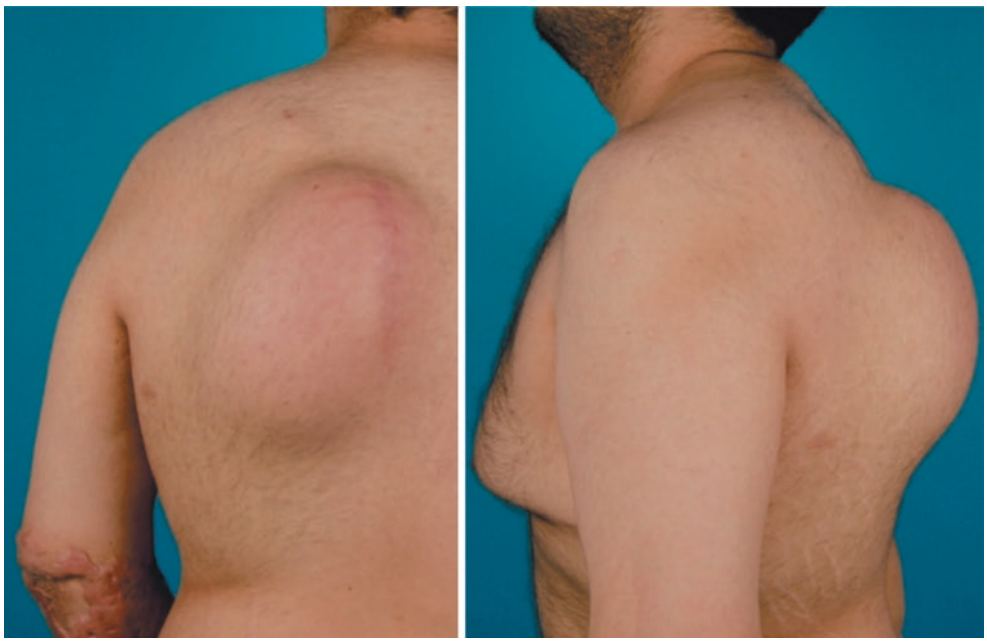


Fig. 15.12 Implanted rectangular expander for a microsurgical free pre-expanded parascapular flap

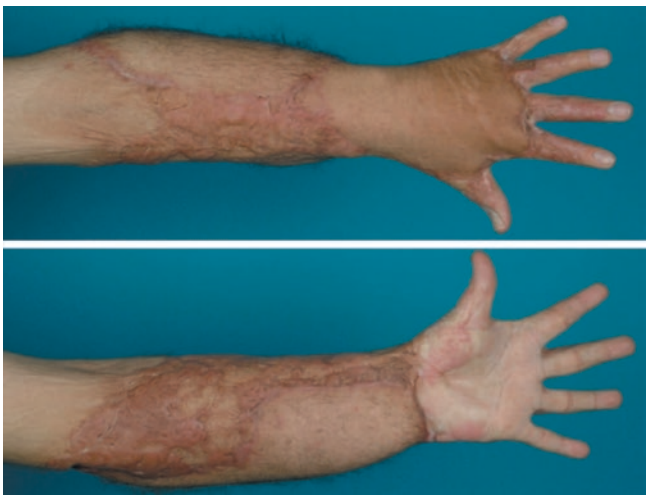


Fig. 15.13 Final outcome with pre-expanded parascapular flap

References

1. McCauley RL. Correction of burn alopecia. In: Herndon DN, editor. Total burn care. 3rd ed. London: Saunders; 2007. p. 690–4.
2. Argenta LC. Controlled tissue expansion in reconstructive surgery. Controlled tissue expansion in reconstructive surgery. Br J Plast Surg. 1984;37:520–9.
3. Hudson DA, Grob M. Optimising results with tissue expansion: 10 simple rules for successful tissue expander insertion. Burns. 2005;31(1):1–4.
4. Codivilla A. On the means of lengthening, in the lower limbs, the muscles and tissues which are shortened through deformity. Am J Orthop Surg. 1905;2:353–69.
5. Neumann CG. The expansion of skin by progressive distension of a subcutaneous balloon. Plast Reconstr Surg. 1957;19:124–30.
6. Austad ED. Evolution of the concept of tissue expansion. Facial Plast Surg. 1988;5:277–9.
7. Radovan C. Tissue expansion in soft-tissue reconstruction. Plast Reconstr Surg. 1984;74:482–92.
8. Pallua N, O'Dey D. II-7.1 Gewebeexpansion – Grundprinzipien und Funktion. In: Krupp S, Renne-Kampff S, Pallua N, editors. Plastische chirurgie. Landsberg: Ecomed; 2006. p. 1–14.
9. Pallua N, von Heimburg D. Pre-expanded ultra-thin supraclavicular flaps for (full-) face reconstruction with reduced donor-site morbidity and without the need for microsurgery. Plast Reconstr Surg. 2005;115(7):1837–44.. [discussion 1837–1845]
10. Acartürk TO, Glaser DP, Newton ED. Reconstruction of difficult wounds with tissue-expanded free flaps. Ann Plast Surg. 2004;52:493–9.
11. Teot L, Cherenfant E, Otman S, Giovannini UM. Prefabricated vascularised supraclavicular flaps for face resurfacing after postburn scarring. Lancet. 2000;355:1695–6.
12. Hallock GG. Preexpansion of free flap donor sites used in reconstruction after burn injury. J Burn Care Rehabil. 1995;16:646–53.
13. Ninkovic M, Moser-Rumer A, Ninkovic M, Ninkovic M, Spanio S, Rainer C, et al. Anterior neck reconstruction with pre-expanded free groin and scapular flaps. Plast Reconstr Surg. 2004;113:61–8.
14. Abramson DL, Pribaz JJ, Orgill DP. The use of free tissue transfer in burn reconstruction. J Burn Care Rehabil. 1996;17:402–8.
15. Pribaz JJ, Fine N, Orgill DP. Flap prefabrication in the head and neck: a 10 year-experience. Plast Reconstr Surg. 1999;103:808–8020.
16. De Filippo RE, Atala A. Stretch and growth. The molecular and physiologic influences of tissue expansion. Plast Reconstr Surg. 2002;109:2450–62.
17. Van Rappard JH, Sonnevald GJ, Borghouts JM. Histologic changes in soft tissues due to tissue expansion (in animal studies and humans). Facial Plast Surg. 1988;5:280–6.
18. LeightonWD RRC, Marcus DE, Eriksson E, Suchy H, Zook EG. Experimental pre-transfer expansion of free-flap donor sides: I. Flap viability and expansion characteristics. Plast Reconstr Surg. 1988;82:69–75.

19. Leighton WD, Russel RC, Feller AM, Eriksson E, Mathur A, Zook EG. Experimental pretransfer expansion of free flap donor sides: II physiology, histology, and clinical correlation. Plast Reconstr Surg. 1988;82:76–87.
20. Cherry GW, Austad E, Pasyk K, McClatchey K, Rohrich RJ. Increased survivial and vascularity of random pattern skin flaps elevated in controlled, expanded skin. Plast Reconstr Surg. 1983;72:680–7.
21. Pasyk KA, Argenta LC, Hassett C. Quantitative analysis of the thickness of human skin and subcutaneous tissue following controlled expansion with a silicone implant. Plast Reconstr Surg. 1988;81:516–23.
22. Lantieri LA, Martin-Garcia N, Wechsler J, et al. Vascular endothelial growth factor expression in expanded tissue: a possible mechanism of angiogenesis in tissue expansion. Plast Reconstr Surg. 1998;101:392–8.
23. Takei T, Mills I, Katsuyuki A, et al. Molecular basis for tissue expansion: clinical implementation for the surgeon. Plast Reconstr Surg. 1998;102:247–58.
24. Prasad JK, Bowden ML, Thomson PD. A review of the reconstructive surgery needs of 3167 survivors of burn injury. Burns. 1991;17:302–5.
25. Huang TT, Larson DL, Lewis SR. Burn alopecia. Plast Reconstr Surg. 1977;60:763–7.
26. Neligan PC, Peters WJ. Advances in burn scar reconstruction: the use of tissue expansion. Ann Plast Surg. 1989;22(3):203–10.
27. Cohen M, Marschall MA, Schafer ME. Tissue expansion for the reconstruction of burn defects. J Trauma. 1988;28(2):158–63.
28. Youm T, Margiotta M, Kasabian A, Karp N. Complications of tissue expansion in a public hospital. Ann Plast Surg. 1999;42(4):396–401; discussion 392–401.
29. Ronert MA, Hofheinz H, Manassa E, Asgarouladhi H, Olbrisch RR. The beginning of a new area in tissue expansion: self-filling osmotic tissue expander: four year clinical experience. Plast Reconstr Surg. 2004;14:1025–31.
30. Hudson DA. Maximising the use of tissue expanded flaps. Br J Plast Surg. 2003;56:784–90.
31. Aachauer BM. Burn reconstruction. New York, NY: Thieme; 1991.
32. Pallua N, Demir E. Postburn head and neck reconstruction in children with the fasciocutaneous supraclavicular artery island flap. Ann Plast Surg. 2008;60:276–82.
33. Shenaq SM. Pretransfer expansion of a sensate lateral arm free flap. Ann Plast Surg. 1987;19:558–62.
34. Santanelli F, Grippaudo FR, Ziccardi P, Onesti MG. The role of pre-expanded free flaps in revision of burn scarring. Burns. 1997;23:620–5.
35. Furukawa H, Yamamoto Y, Kimura C, Igawa HH, Sugihara T. Clinical application of expanded free flaps based on primary or secondary vascularization. Plast Reconstr Surg. 1998;102:1532–6.
36. Tsai FC. A new method: perforator based tissue expansion for a preexpanded free cutaneous perforator flap. Burns. 2003;29:845–8.
37. Tsai FC, Mardini S, Chen DJ, Yang JY, Hsieh MS. The classification and treatment algorithm for postburn cervical contractures reconstructed with free flaps. Burns. 2006;32:626–33.
38. Casanova D, Bali D, Bardot J, Legre R, Magalon G. Tissue expansion of the lower limb: complications in a cohort of 103 cases. Br J Plast Surg. 2001;54(4):310–6.
39. Cunha MS, Nakamoto HA, Herson MR, Faes JC, Gemperli R, Ferreira MC. Tissue expander complications in plastic surgery: a 10-year experience. Rev Hosp Clin Fac Med Sao Paulo. 2002;57(3):93–7.
40. Friedman RMIAJ, Rohrich RJ, Byrd HS, Hodges PL, Burns AJ, Hobar PC. Risk factors for complications in pediatric tissue expansion. Plast Reconstr Surg. 1996;98(7):1242–6.
41. Gibstein LA, Abramson DL, Bartlett RA, Orgill DP, Upton J, Mulliken JB. Tissue expansion in children: a retrospective study of complications. Ann Plast Surg. 1997;38(4):358–64.
42. Governa M, Bonolani A, Beghini D, Barisoni D. Skin expansion in burn sequelae: results and complications. Acta Chir Plast. 1996;38(4):147–53.
43. Pisarski GP, Mertens D, Warden GD, Neale HW. Tissue expander complications in the pediatric burn patient. Plast Reconstr Surg. 1998;102(4):1008–12.
44. Bozkurt A, Groger A, O'Dey D, Vogeler F, Piatkowski A, Fuchs PC, Pallua N. Retrospective analysis of tissue expansion in reconstructive burn surgery: evaluation of complication rates. Burns. 2008;34:1113–8.
45. Brou JA, Vu T, McCauley RL, Herndon DN, Desai MH, Rutan RL, et al. The scalp as a donor site: revisited. J Trauma. 1990;30:579–81.
46. Barret JP, Dziewulski P, Wolf SE, Desai MH, Herndon DN. Outcome of scalp donor sites in 450 consecutive pediatric burn patients. Plast Reconstr Surg. 1999;103:1139–42.
47. Achauer BM, VanderKam VM. Burn reconstruction. In: Achauer BM, Eriksson E, editors. Plastic surgery indications operations outcomes. St. Louis, MO: Mosby; 2000. p. 425–46.
48. Aranmolate S, Atah AA. Bilobed flap in the release of postburn mentosternal contracture. Plast Reconstr Surg. 1989;83:356–61.
49. Pallua N, Machens HG, Rennekampff O, Becker M, Berger A. The fasciocutaneous supraclavicular artery island flap for releasing postburn mentosternal contractures. Plast Reconstr Surg. 1997;99(7):1878–84; discussion 1876–85.
50. Manders EK, Oaks TE, Au VK, Wong RK, Furrey JA, Davis TS, et al. Soft-tissue expansion in the lower extremities. Plast Reconstr Surg. 1988;81(2):208–19.
51. Vogelin E, de Roche R, Luscher NJ. Is soft tissue expansion in lower limb reconstruction a legitimate option? Br J Plast Surg. 1995;48(8):579–82.

Burn Reconstruction: Skin Substitutes and Tissue Engineering

16

Raymund E. Horch, Volker J. Schmidt, and Andreas Arkudas

16.1 Introduction

Skin, also known as the integument, is not only the largest laminar organ but also the appropriate interface between the human organism and its environment. Besides other functions, the skin represents the primary barrier of the immune system. Thus, an extensive skin loss due to thermal trauma represents in the majority of cases a life-threatening situation and demands particular requirements from the plastic and burn surgery to provide a sufficient skin substitution. Development and improvement of innovative strategies concerning skin expansion and tissue engineering have contributed to the fact that burns affecting more than 80% of the body surface (TBS) are survivable today [1]. Although the application of cultured epidermis and compound cultured skin analogues is approved as a life-saving method today, the indications for this novel approach have become more differentiated. Besides historical aspects, the present chapter gives insights into both the conventional techniques and the application forms of current cultured skin substitutes.

16.2 History of Skin Transplantation

Skin replacement by means of transplantation is one of the earliest approaches in the history of reconstructive surgery. Following Baronios early sheep skin experiments (1804), it was Bünger who reported for the first time about the transplantation of a full-thickness human skin graft [2]. In 1869 Reverdin has set the gold standard for skin replacement with his landmark publication about the transplantation of the patient's own skin [3]. Nevertheless, Reverdin noticed a frequent loss of the small transplanted islands related to a strong wound secretion. During the following decades, the full-thickness skin graft practice according to Krause has become the most established technique. Meanwhile, insufficient integration into the healing wound and too little skin resources of the patients own body have driven investigators to find other approaches. In 1895 it was the German surgeon Mangoldt who described the clinical application scraped endothelial cells, which are considered to be the precursors of the recent keratinocyte suspensions [4]. The so-called epithelial cell seeding was epithelial cells or cell clusters harvested by scraping off superficial epithelium from a patient's forearm with a surgical blade, which were grafted together with the exudated serum to various wounds. Based on this technique, an additional approach was established later on whereby mechanical hackled skin particles were plunged into the granulation tissue [5]. Up to the present day, this modified technique is still useful for the therapy of chronic or problematic wounds and for the treatment of perianal burns [6].

Large-scale skin transplantation was first mentioned by Ollier [7] and subsequently improved by Thiersch [8]. In this context, he also designed the so-called Thiersch knife, which allows to gain split-thickness skin grafts in a reliable manner via a tangential excision. Although the Thiersch knife enabled the release of large skin surfaces, it was still a challenge to provide an equal thickness for the entire skin graft, even for experienced surgeons. Especially at the edge regions, grafts exhibited often less homogenous and less aesthetic appearance. Encouraged by this disadvantage, the search for new technologies led to the development of the dermatome in 1939 according to Padgett-Hood [9]. The dermatome is nowadays usually driven by an electrical motor that represents down to present day the standard tool to gain skin grafts with the possibility to select the depth of the tissue to be excised.

R. E. Horch (✉) · A. Arkudas
Department of Plastic and Hand Surgery, University Hospital Erlangen, Friedrich-Alexander-University Erlangen-Nuernberg FAU, Erlangen, Germany
e-mail: raymund.horch@uk-erlangen.de

V. J. Schmidt
Department for Plastic and Breast Surgery, Zealand University Hospital Roskilde, Roskilde, Denmark

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_16

16.3 Indications for Skin Grafting

In case of deep second-degree and third-degree burns, a solitary conservative management fails to achieve an adequate functional and aesthetic result. Thus, surgical interventions are required, whereby the early eschar debridement followed by a split-skin grafting (see below) is considered to be the gold standard [10, 11]. The choice of a respective skin substitute is also based upon the surgical procedure according to the depth of the eschar excision. For that reason, a brief introduction to wound preparation before transplantation is outlined in the following.

16.4 Necrotomy

Since necrotic tissue after deep second-degree and third-degree burns represents a principal nidus for bacterial infection and a source for toxic cytokines, excision of necrotic areas improves the general state of the patient rapidly [12] and exposes a viable bed for skin grafting (Fig. 16.1a, b).

Until recently, the most prevalent opinion concerning the ideal point of time for a necrotomy was to do the procedure at the second to third day of therapy associated with a decline of interstitial oedema and a more stable patient state. However, today there is broad consensus that the eschar or necrosis debridement should start as soon as possible after stabilization and that all the necrotic tissue should be excised during the following days in order to minimize vital threats due to toxins or bacterial infection [13]. Early tangential or epifascial excision of the burn eschar [14] is followed by a transplantation of either a split-thickness or a full-thickness skin graft during the same intervention [10, 15]. This early approach has been shown to reduce inflammation, as well as the risks of infection, wound sepsis, and multiorgan failure [16]. Furthermore the length of hospitalization is reduced among patients who underwent early excision.

16.5 Methods of Skin Grafting

As a current standard, wound surfaces are covered by means of full thickness or expanded or non-expanded split skin autografts after necrotomy [10, 15]. Although tangential excision induces usually a well-bleeding wound basis due to opening of the capillary bed, it is especially this environment that maintains a rapid and secure nutritive junction between the graft and the subsurface [17, 18]. Responsible for a solid adhesion of the transplant is the formation of a strong interplanar fibrin bridge which is fixed between the elastin parts of the skin graft and the wound ground elastin [19]. This modest linkage allows the sprouting of capillaries and bridges the time until more differentiated adhesion structures arise.

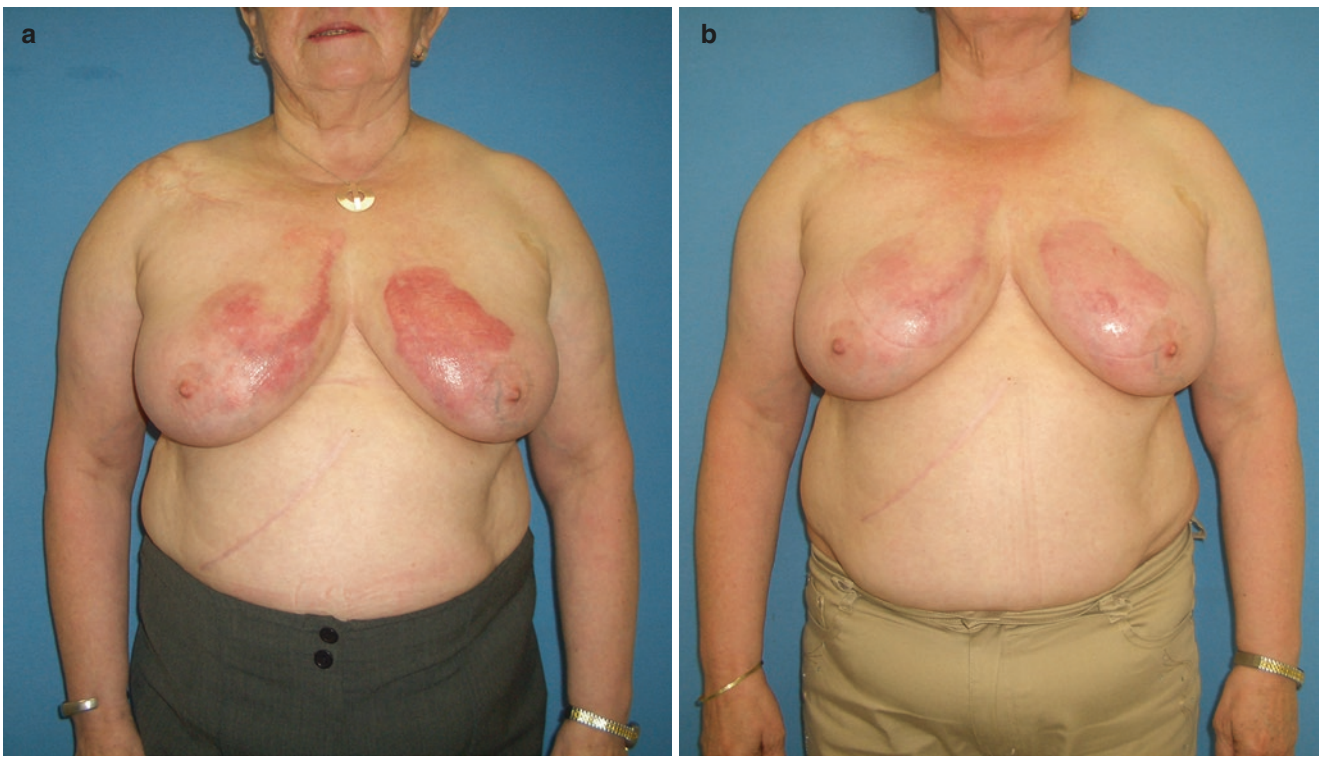


Fig. 16.1 Superficially burned skin (level IIa) depicted shortly after injury (**a**) and two months later (**b**). Up to a burn level of IIa a restitutio ad integrum take place without the need of surgical interventions

16.6 Split- and Full-Thickness Skin Grafts

Skin grafts are distinguishable according to their dermal proportion into split-thickness or split skin grafts and into full-thickness skin grafts. The latter occurs when the skin is excised under the preservation of the complete dermis [20].

The typical split skin graft has a thickness between 0.20 and 0.45 mm (Fig. 16.2). The sectional plane is located in a manner that not only the avascular tissue but also parts of the microcirluation are cut and thus transferred to the lesion. The dermal appendage which is located in deeper cutaneous layers remains at the excision site after transplantation and serves as a source for the reepithelization of the extraction site. An impressive reepithelization occurs when the skull is used as a donor, because the high density of hair follicles accelerates the regeneration, thus leading to an early restitutio ad integrum. Due to this shortened period of recovery, the skull represents an area, which can be used immediately up to six times as a donor [21]. However, full-thickness skin explanation sites are lacking for recovering dermal structures. Wound healing initiated from migrating keratinocytes of the surrounding intact tissue is only of limited extend, whereby it is obligatory to close the extraction defect primarily.

16.7 Standard Methods

16.7.1 Autologous Full-Thickness Skin Grafts

The autologous full-thickness skin graft is still considered to be the gold standard [22] and is most commonly used for areas, which do not bleed extensively after excision and provide an opportunity for compression. As the strong dermal component prevents an excessive scare formation, the full-thickness graft represents the best choice for aesthetic and functional demands, especially for grafting of burned areas that involve the face, the hands, or regions of large joints. Due to the limited amount, solitary full-thickness skin grafting is only suitable for burns which affect a minor percentage of the body surface.

16.7.2 Autologous Meshed Split-Thickness Skin Grafts

Reduction in the size of the skin graft donor site can be realized by turning the split-thickness skin graft into a "mesh graft". Due to a specific parallel arrangement of scissors on a role multiple small slits can be placed in the graft, allowing it to expand up to six times of the original area. The method

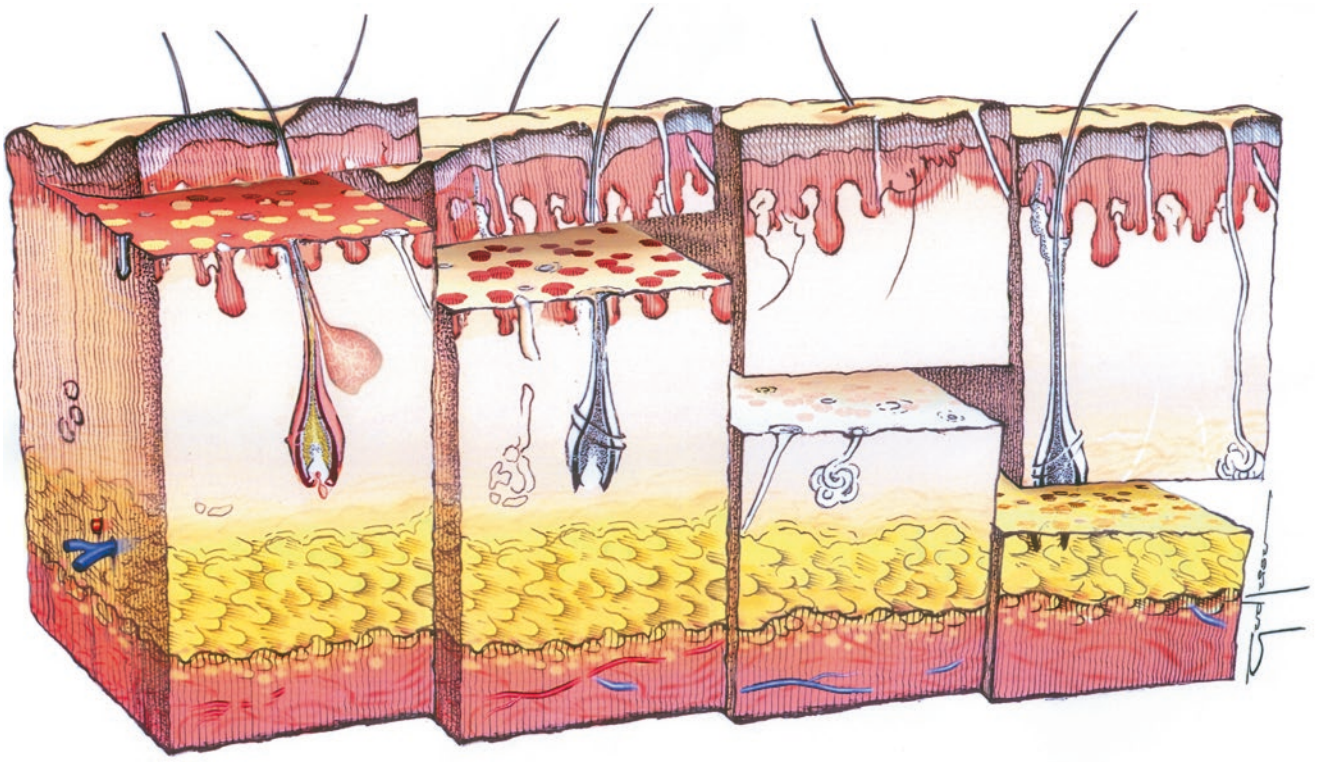


Fig. 16.2 Different skin grafts depicted according their thickness during excision. Graft thickness increases from thin split skin (0.2 mm, left-hand) to the full thickness skin grafts, which contain all skin layers (right-hand)

is based on the tendency of keratinocytes to migrate into the intermediate spaces. In addition, these so-called mesh slits provide a drain for wound secretions, thus preventing the appearance of hematoma and seroma. Mesh grafts are of special importance if the burn is so extensive that the surface of donor sites is limited. The most common expansion ratios are 1:1.5–1:3 [17, 18, 23] (Fig. 16.3a–g).

16.7.3 Meek Technique

In 1958, Meek invented a dermatome which was able to cut harvested split skin into small squares of equal size [24]. Meanwhile, the mesh technique was founded which was mostly preferred to Meek's invention because of its simpler handling. Besides rarely published Chinese

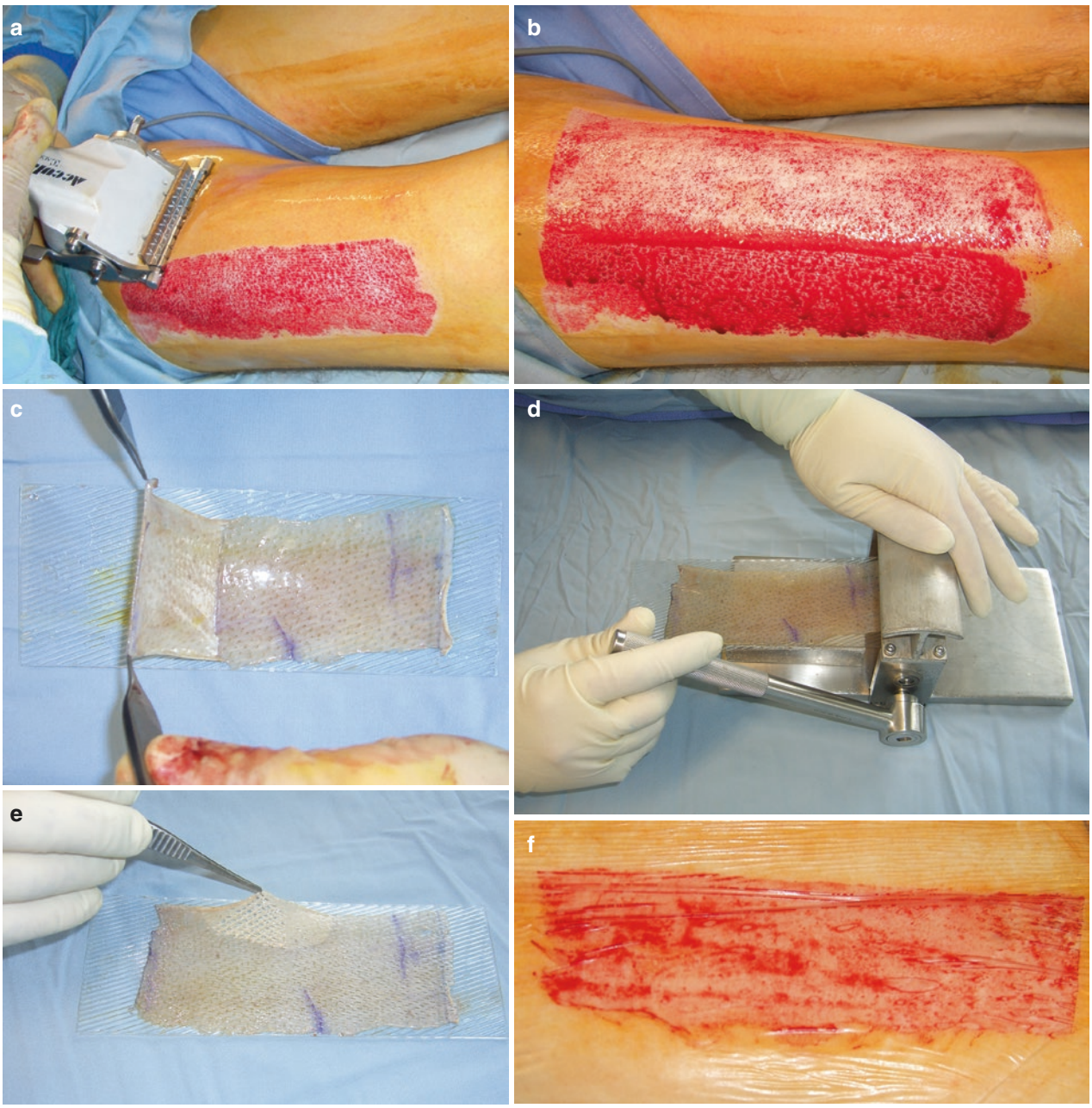


Fig. 16.3 (**a**) Excision of "thin" split skin (0.2 mm) using a battery driven dermatome. (**b**) Punctual bleedings of the superficial dermis after split skin removal. (**c**) Transfer of the split skin graft on a synthetic carrier with the dermis on top. (**d**) Split skin during meshing by means of a special dermatome. (**e**) Split skin graft after meshing (expansion ratio 1.5:1) with the visible mesh net grid structure. (**f**) Foil bandage of the graft removal area guarantees an adequate wound milieu for the reepitheliasation. (**g**) Split skin shortly after transplantation. Through the meshes wound secret can drain, thus preventing a diffusion barrier below the graft

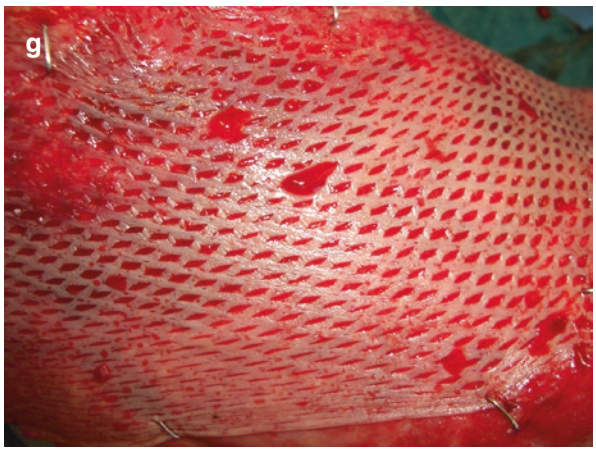


Fig. 16.3 (continued)

reports, it was Kreis and his colleagues who modified the Meek technique to a simple method that allows to cut off split skin as well as to expand it up to a ratio of 1:6 on a special cork and silk carrier in one step [25]. Due to its practicability and attractive magnification factor, this modified approach is currently well established in many burn centres and in case of extensive burns often favoured towards mesh grafts (Fig. 16.4a–g).

16.7.4 Stamp Technique

The stamp technique has a higher prevalence in Asia and is based on split skin cut into large squares. Afterwards the quadratic skin pieces are positioned in an appropriate manner over the debrided area. Through the variation of the square size and the distance between the islands, it is also possible to achieve an expansion ratio up to 1:6 [26, 27]. The stamp technique was no longer of practical importance in Europe after the microskin technique combined with allogenic or xenogenic skin as a carrier was implemented.

16.8 Alternative Methods

The surgical procedures discussed above are dependent upon the availability of intact donor skin. If the burn is so extensive (>70% of TBS) that there are only few viable areas of donor skin left over for harvesting, alternative methods should be used to enable a chance of survival. Insights into research and experiences with these alternative methods are discussed in the following.

16.9 Temporary Allogenic and Xenogenic Skin Grafts

16.9.1 Allogenic Skin Grafts

When there is a lack of sufficient donor skin, allogenic skin transplants can be used as a temporary skin graft. Usually this skin is submitted to a rejection process. Due to the burn injury of the mainly immunocompetent organ skin, the rejection starting from the recipient occurs usually with a delay of 1–2 weeks after application.

First experiences were collected with cryo-conserved skin, which was used to cover deep second-degree burns [28] or areas, where autologous grafts had not been grown in [29]. An advantage of the cryo-conservation is a partially loss of the antigenicity [30].

Burns treated with cryo-conserved allogenic skin become germ-free and exhibit an epithelial migration tendency starting from the wound edge [31]. Hence, it is a useful tool to bridge the time to the autologous transplantation. Cryo-conserved allogenic grafts were also used for the so-called sandwich technique (see below), where largely meshed autologous transplants were covered with less-expansive meshed allogenic skin. Although this approach did not represent a durable solution, it was able to prolong the period of the rejection occurrence up to 3 weeks [29]. To minimize the allogenic skin antigenicity among others, a graft conservation with 98% glycerine was developed [29], whereby the cellular plasma was replaced by glycerine without affecting the tissue structure. Glycerinized allografts are well suited for the sandwich technique expressed by a high epithelialization rate [32, 33].

Allogenic grafts mostly serve as a temporary cover when there is insufficient donor skin available. These grafts are usually attached with sutures or staples to the surrounding tissue after slitting at stated intervals with a scalpel to guarantee a draining of the secretions.

Until the rejection occurs, allogenic grafts have the same beneficial properties as autologous ones including the ability to reduce inflammation, fluid loss as well as the risk of infection, wound sepsis, and multiorgan failure.

Up to the present day, there are just a few cases known, whereby selected immunosuppression has achieved a durable integration of the allogenic graft into the wound ground [34, 35]. Usually the antigenic potency of the epidermis is responsible for the rejection. In theory the dermal elements might survive; however, selective y-chromosome methods for detection cannot prove the appearance of allogenic cells in all cases [34, 35]. Exposure to UV-light and the use of glucocorticoids can induce an inactivation of Langerhans

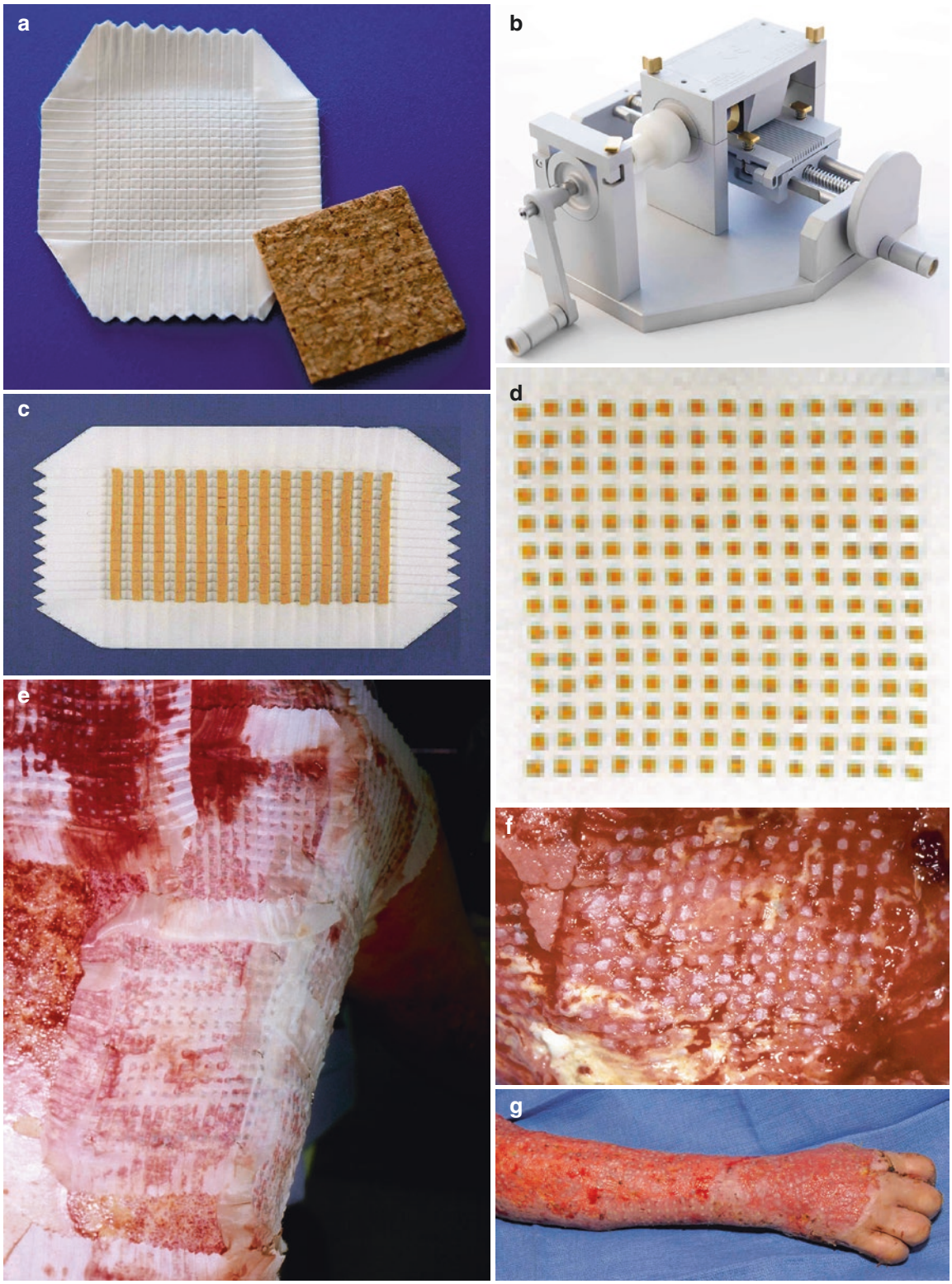


Fig. 16.4 Equipment and application of the modified Meek technique. (**a**) Special cork and silk carriers for the autologous skin graft. (**b**) Hand driven Meek dermatome. (**c**, **d**) Skin graft after cutting and expanding through the Meek dermatome. Noticeable is the characteristic quadratic arrangement of the skin at end of the process (**d**). (**e**) Square skin grafts shortly after application onto a burned shoulder. (**f**) Wound ground after Removal of the silk carrier (gauze) with remaining skin grafts. (**g**) Burned Arm a few days after Meek technique grafting. (Asterisk) Displayed pictures were kindly provided by Humeca BV (Enschede, The Netherlands)

cells within the graft in order to delay the duration up to the allograft rejection [36]. Due to immunosuppression, the interaction between Langerhans cells and class-II antigens of graft keratinocytes is diminished [37–40]. In this case, cyclosporine is a suitable agent because of its sufficient inhibition of the keratinocyte DNA synthesis without adverse effects for the vitality of the transplant [34, 41, 42].

16.9.2 Xenogenic Skin Grafts

Since the mid-1950s, the use of pig skin has become famous for temporary grafting of large burns especially in china. There it was used particularly in combination with the so-called intermingled technique.

The nutritive maintenance of the xenogenic grafts occurs mainly due to diffusion [43] because an initial revascularisation disappears after a short period and is rapidly replaced by collagen structures [44]. In countries that do not perform allogenic grafting because of ethical concerns, xenogenic transplants are still an important tool for temporary wound covering. From South America, comparable good results are also reported with frog or snake skin used as transplants.

16.10 Mixed Skin Grafts

16.10.1 The Chinese Method: Intermingled Grafting

The intermingled grafting method is based on the migrative properties of epidermal cells. On a large sheet of homo- or heterologous skin, islands of autologous skin are inserted into prepunched holes at certain distances. The expansion ratio is dependent upon the distance and the size of the skin islands. Yang and colleagues selected a distance of 1 cm between their 0.25 qcm sized autologous islands which correlates with an expansion ratio of 1:4 [45, 46]. Bäumer and his group modified this method by raising the island size up to 1 qcm and by inserting the islands 3.5 cm away from each other, thus enhancing the expansion ratio up to 1:20 [47]. Despite its effectiveness, the method is mostly restricted to the Far East primarily because of high personnel and manual requirements.

16.10.2 Autologous Allogenic Intermingled Grafts

The autologous allogenic intermingled graft technique was performed for the first time in the mid/end-1950s to minimize the loss of blood during the allograft removal [48].

After transplantation, the autologous epithelium grows concomitant to the recipient rejection from the placed islands rapidly in-between the allogenic dermis and the allogenic epidermis. This histopathomorphologic behaviour is called "sandwich phenomena" [46]. At the end of the process, the desquaming alloepidermis is replaced completely by the confluating neoepidermis. The allogenic dermis beneath the intact autoepidermis degenerates and is reabsorbed due to the immunogenic response [33, 46].

16.10.3 Autologous Xenogenic Intermingled Grafts

Intermingled grafts using xenogenic pig skin as a heterogenic donor show a similar outcome compared to autologous allogenic intermingled grafts. After transplantation, the xenogenic graft exhibits a vital character due to the plasma and tissue fluids of the underlying tissue that provide a nutritive environment [43]. Neocapillaries appear 2–4 days after transplantation within the heterogenic graft followed by an ingrowth of capillaries from the granulating wound ground on days 7–10 [49, 50]. The internal autologous transplants start to grow immediately leading to an undermining of the xenoepidermis. The rejection of the pig skin dermis occurs as either an external or an internal process [44]. The external rejection is associated with an infiltration of fibroblasts and inflammatory cells that degrade the heterogenic skin. The internal rejection describes the confluent and expansive growth of the autologous epithelium into the xenogenic corium. Rejection of the corium induces furthermore the desquamation of the xenogenic epidermis. During these processes, the heterogenic connective tissue is infiltrated by a large number of capillaries, fibroblasts, and lymphocytes. Finally the dermal collagen is degraded and partially reabsorbed.

16.10.4 "Sandwich" Technique

The term "sandwich" describes the application of a wide meshed autologous split skin graft, which is covered by a sparsely meshed (1:1.5), slit, or untreated allogenic transplant. Knowing that the integration into the healing wound of wide meshed autologous skin grafts with expansion ratio up to 1:6 is rather weak because of the adverse relation between the gaps and the cell carrying grid like skin, this method improves the rate of the integration into the healing wound by means of a temporary coverage with allogenic skin. Thus, it is well suited for the treatment of severe burns with limited skin donor sites [12, 51–53] (Fig. 16.5a, b).

16.10.5 Microskin Grafts

According to microskin grafts. thin split is harvested and mechanically reduced to small particles <1 qmm (microskin grafts), which are placed onto the wound followed by a cov-

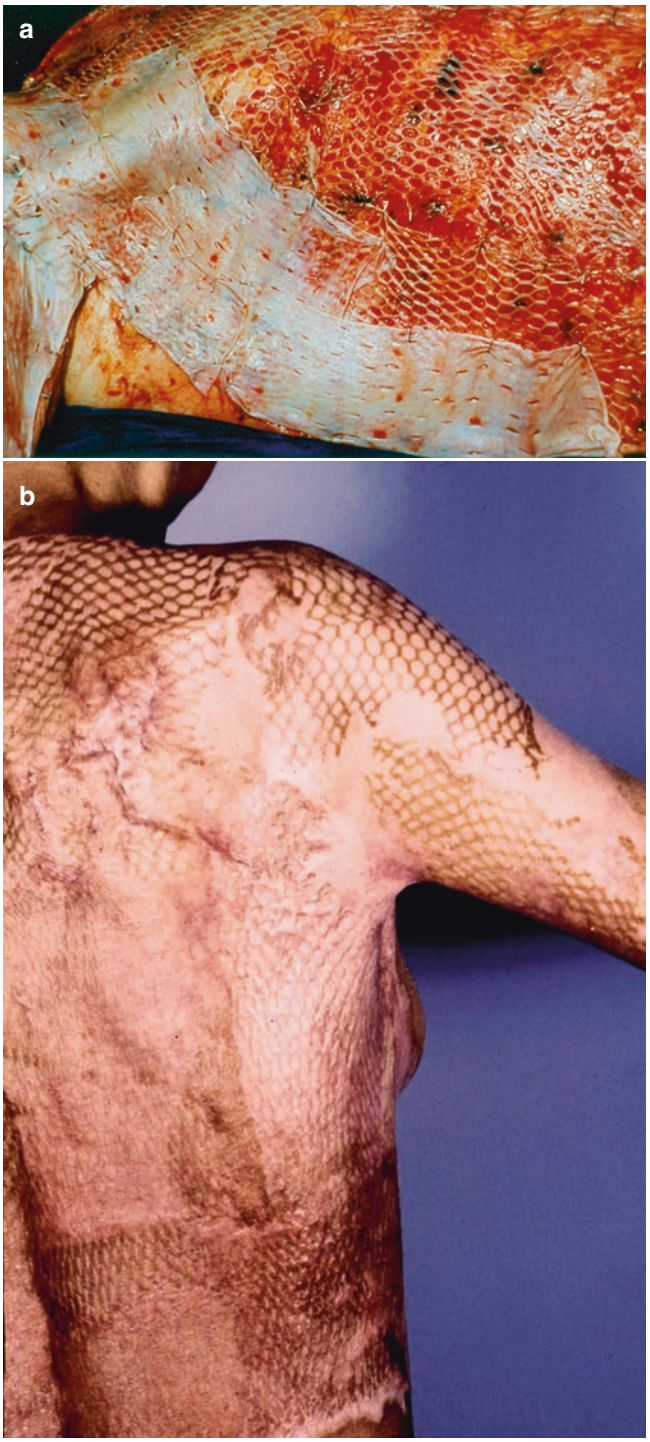


Fig. 16.5 Over transplantation of conservative external slit skin serves as a biological protector and enables the integration and healing of meshed skin grafts with large expansion ratios (e.g. 6:1 or 9:1). (**a**) Coverage of 3:1 and 6:1 mesh grafts with slit and glycerine-conserved allogenic skin. (**b**) Dark pigmented 6:1 and 3:1 expanded autologous split skin areas with the typical grid-like pattern after complete healing and rejection of the allograft

erage with a homo- or heterologous graft [54–57]. For this purpose, the skin particles are distributed equally on a fat gauze using a NaCl water bath. The resulting pulp is topically applied to the wound ground. The microskin technique was developed and perfected in China, where it is today the first choice for the treatment of large burns in combination with an allogenic coverage instead of the transplantation of cultured keratinocytes. Besides the relatively easy handling, the attainable expansion ratio up to 1:100 is one of the major benefits. Thereby, unburned areas are used economically, offering satisfying results [55].

16.10.6 Buried Chip Graft Technique

The effectiveness of conventional, meshed split skin is rather low in the critical perianal and perineal area because of the complex location und the usually heavily contaminated sore ground [58–60]. Therefore, in these areas, the buried chip graft technique is particularly useful.

Within this method, split skin taken from an unburned area is mechanically chopped into small pieces (1–2 qmm). Afterwards the particles are inserted obliquely (depth ~3–4 mm) and in rows (distance ~1 cm) into the wound ground, thus the gluteal skin's surface closes itself after a few weeks above the "seedlings" [5]. Usually a particle-free area is left within a radius of 5–6 cm around the anus. Due to their inoculation, the small transplants are well protected against faecal contamination and mechanical cleaning activities. Even in the case of infection, the risk for destruction and a complete loss of the transplants is rather low [1, 59].

Five to nine days after insertion, first epithelial islands appear at the surface. Starting from their edges, the epithelialization runs concentrically leading to a closed epidermis. Histomorphologically noticeable is a characteristic bell-shaped growth from the deep to the wound surface, which exhibits a regular epidermal layering [5].

Hand burns represent another sensitive field for skin grafting because of the particular anatomy. To preserve as much functional structures as possible (e.g., the sliding tissue) a spare and careful necrotomy is of special importance. The additional use of a vacuum-assisted closure (VAC) therapy has proved to be very effective in a lot of cases. Due to the negative pressure, not only oedema reduction but also increased perfusion and formation of granulation tissue can be observed. Meanwhile, it provides an adequate contact pressure for skin grafts, which is crucial because of the inconstant hand skin surface. Furthermore, the VAC therapy prevents the greatly feared dehydration of the tendon and its sliding tissue (Fig. 16.6a–g).

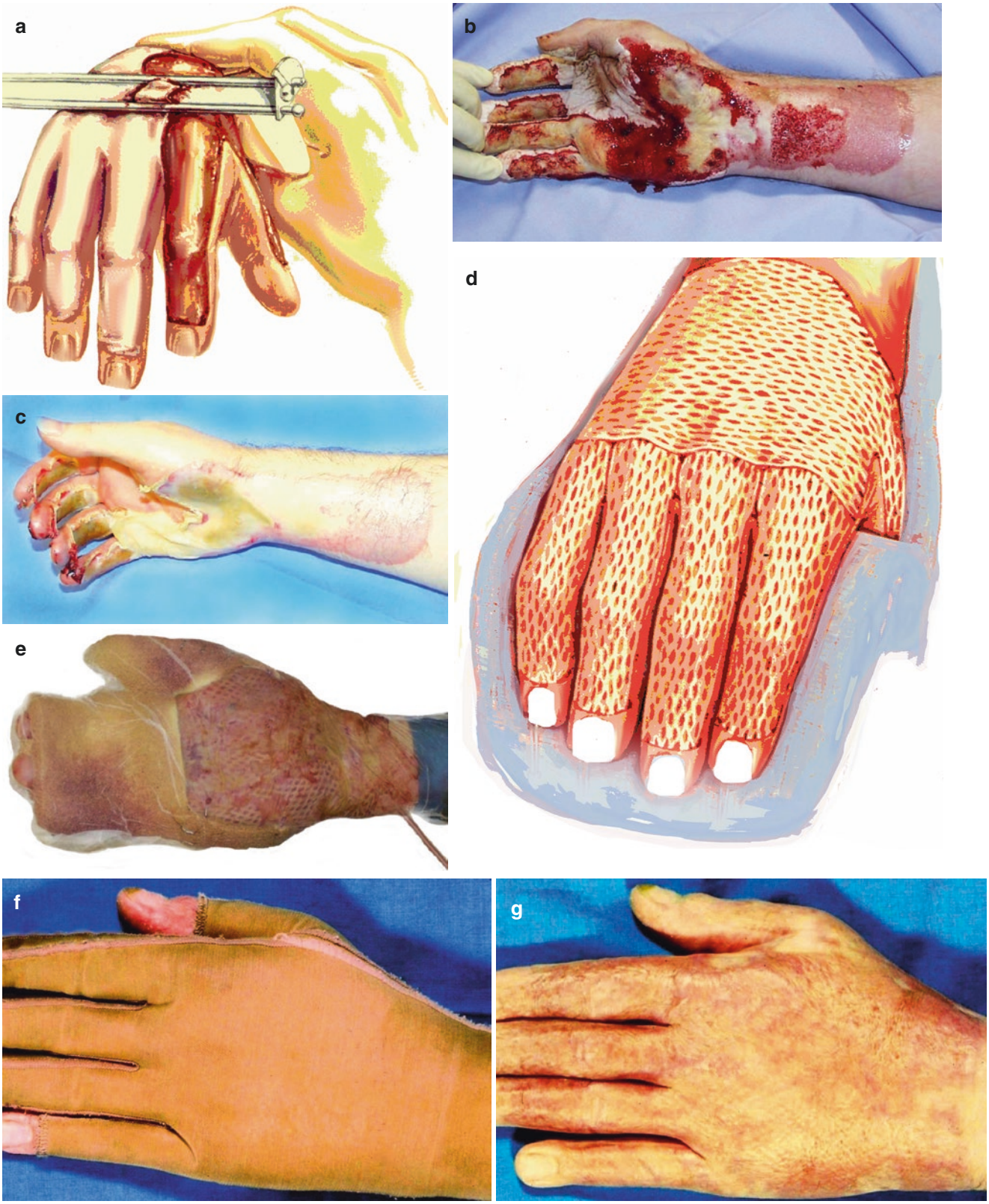


Fig. 16.6 (**a**) Depicted is a hand during tangential necrotomy after burn injury (modified from [61]). (**b**) Deep second- and third-degree burn of the hand. (**c**) Oedema reduction and beginning of granulation after tangential necrotomy and vacuum therapy. (**d**, **e**) Scheme (modified from [61]) and photography of split skin transplantation at the hand. (**f**) After the integration of the split skin a continuous compression with a specially-designed glove is of special importance. (**g**) Final result after split skin grafting and compression therapy

16.10.7 Purely Epithelial Skin Grafts

A method that has been known for diagnostic purposes in skin diseases treated by dermatologists and for repigmentation in vitiligo has recently been developed to serve as a potential source of transplantable skin cells. By applying shear stress to the epidermis by producing blisters merely, epithelial grafts can be harvested. These thin grafts consist of a layer of epithelial cells including a number of vital basal keratinocytes. A commercially available product has been launched that allows harvesting of a defined number of circular epidermal grafts utilizing gentle continuous suction to the skin. These grafts are then transferred to a carrier and can be used to transport epidermal cells to wounds. Although the 5 × 5 cm^2 template with cells can only be used for smaller areas in burns, it may well serve to optimize treatment of localized burns, such as in the face. The donor site is almost invisible, because only the superficial epidermal layer is removed, and no surgical excision is necessary to harvest these grafts. It has been shown in a standardized split-thickness skin donor site study that such grafts do help resurface the superficial wound at an early time point. In addition, it can be concluded from preliminary studies that wound healing and scarring are positively influenced [62].This method can lend itself as an adjunct for repigmentation and can be seen as another new option to influence the final healing process in burns and in paediatric scalds [63]. Studies that utilize the power of mesenchymal stem cells [64, 65] to accelerate epithelial growth are also promising and might further improve this new tool (Fig. 16.7) [66, 67].

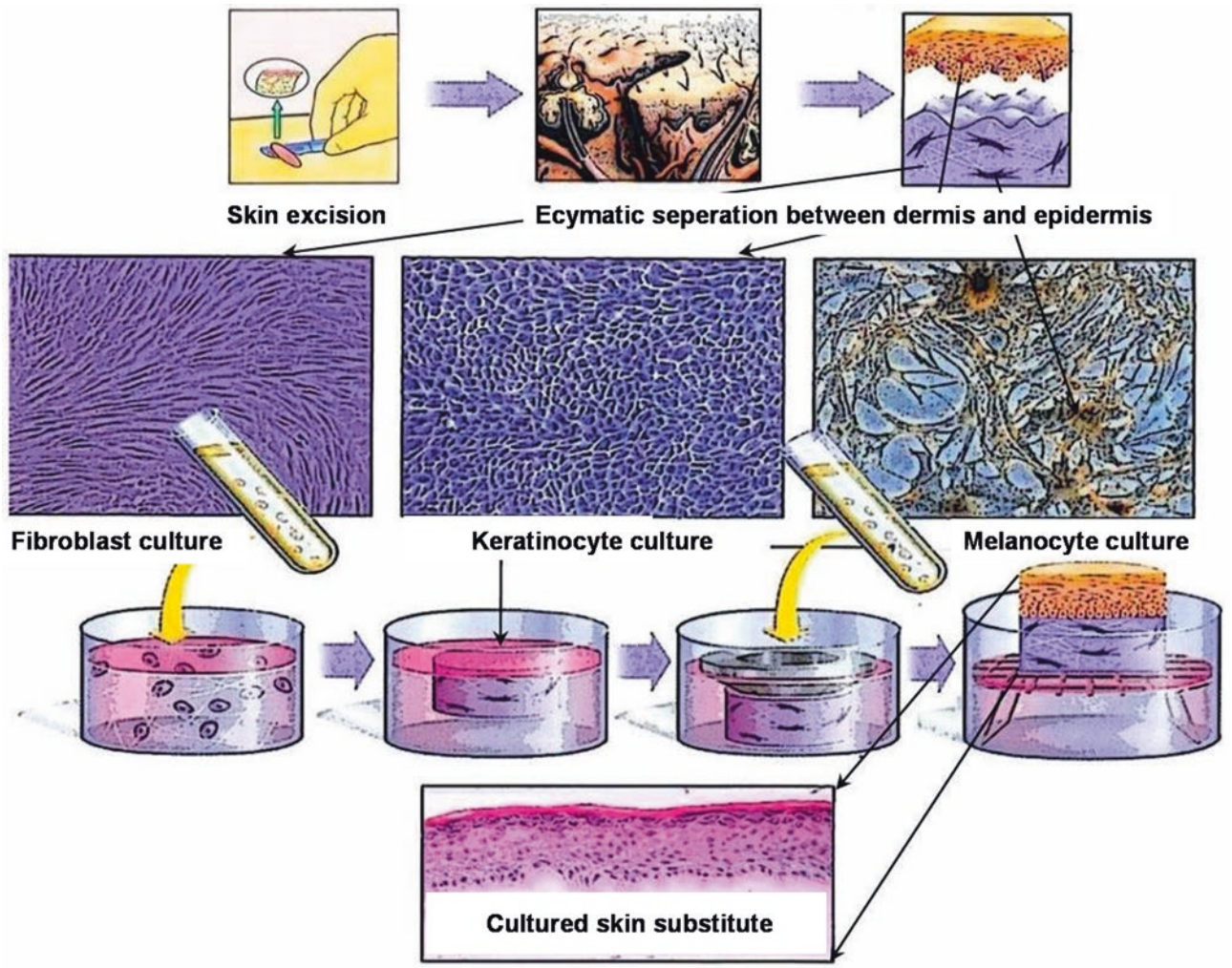


Fig. 16.7 Scheme of an ideal production process of tissue engineered skin substitutes. Subcultures of fibroblasts, keratinocytes and melanocytes are mixed and transplanted as a skin substitute. The depicted technique, which merges several components after subculturing to a skin like substitute, has since yet failed to prevail in the clinical practice due to several technical barriers.

16.11 Cultured Epithelia and Tissue Engineering

In case of extensive burns, the surgical standard methods described above are limited when the unburned skin is reduced to a minimum extent. A potential way out of this dilemma is the development and improvement of cultured skin substitutes as well as the integration of transplantable and resorbable biomaterials into the healing wound by means of tissue engineering. Aim of the former and recent efforts is the in vitro generation of tissues, which exhibit similar biomechanical and biochemical properties compared to the lost tissue and guaranty a permanent functional substitution. The first organ or layer of an organ that was ever generated in vitro and successfully transplanted in vivo was the epidermis. This ground-breaking success paved the way for the treatment of extensive burns with an affected TBS > 80% during the last 30 years. Today cultured autologous and allogenic skin substitutes are commercially available and used around the world (Fig. 16.7) [68–75].

16.11.1 Requirements

Demanded requirements to modern cultured skin grafts:

- Shortening of the culturing period for accelerated availability.
- Sufficient quantity to decrease lethality after extensive burns.
- Easy handling to reduce the operation time.
- Reduction and prevention of bacterial infection due to an early restitutio ad integrum of large-scaled wound surfaces.
- Economic consumption: Large amounts of transplants should be gained from a few autologous substrates.
- Application of biomaterials should improve both the adhesion between cells and the wound ground and the functional and aesthetic results.
- Time reduction of wound healing in order to decrease the period of therapy.

16.11.2 Historical Review

The beginnings of cell culturing go back to the nineteenth century. Since that time, the culturing of skin has been an object of interest not at least because the therapeutic potential due to the substitution of destructed skin has been identified very soon. It was recognized that explanted skin embedded into a culture medium exhibited an expansive growth starting from the peripheral edges.

According to the cell biology, the cell culture can be distinguished into two forms: the explant and the dissociated culture assay.

16.11.3 Explant Cultures

In 1899, Ljunggren for the first time kept human skin in a culture. He harvested small pieces of patient skin, transferred them for a longer time period into a special medium containing ascites and replanted them successfully to the donor [76]. Later on different investigators have observed that skin embedded into a suited medium exhibits a sprouting of epithelial and connective tissue cells [77–79]. The culture mediums used for these early assays were composed of physiological saline with or without glucose that were enriched with serum or ascites. The much later following additives of amino acids and peptides paved the way for the development of standardized mediums, which made it possible to compare the results from different work groups [80].

Börnstein [81] and Pinkus [82] revealed in their experiments that the epithelial sprouting is mainly based on the migration of keratinocytes within the explanted skin. A further landmark was the work of Medawar in 1941, who achieved an enzymatic separation between dermis and epidermis due to the addition of trypsin. Furthermore, he revealed by means of clinical and microscopical studies that elastic fibres from the basal membrane play an important role for the anchorage between the epidermis and the underlying tissue. In 1948 Medawar added fractionated explants to a continuously shaken culture and observed an overgrowth of the epidermal parts, which covered the dermal components after a few days [83]. Although the cell proliferation was abundant, this approach was still limited because the growth stopped while the dermis coverage was finished. Following investigators were able to circumvent this contact inhibition by modifying the breeding medium and adding a particular agent. However, they also failed to suppress the fibroblastic overgrowth, which was the limiting factor for a therapeutic use of explant cultures [84].

In 1949 Lewis and colleagues figured out by means of cell dynamic studies using a time-controlled film technique that keratinocytes own a peripheral lamellae-like membrane, which allows them to migrate [85].

In the 1960s culture techniques were perfected, so that it was possible to gain epidermal growth without the limiting connective tissue factor which is associated with fibroblastic activity. It was shown that the sprouting neoepidermis in explant cultures exhibits a similar cell formation compared to the in vivo epidermis [86]. However, one failed to submit them into a subculture. These high-density epithelial cell formations were primarily used for the dermatological research [87].

Several early investigators had recognized the therapeutic benefit of cultured skin for the treatment of burns and chronic wounds [79, 88, 89]. In 1948, it was the aforementioned anatomist Medawar, who was able to replant autologous cultured epidermis to the donor [90]. Moscana succeeded 1961 in transplanting a mixed dermal and epidermal cell suspension onto a wound surface [91].

The merit of the first well-documented transplantation of keratinocytes is due to efforts of Karasek, who succeeded in 1968 in transplanting primarily cultured autologous keratinocytes to rabbits [92]. Besides the evidence for a complete ingrowth of the cells, he observed a histomorphological reformation of the cells to a fully functional epidermis. However, the neoepidermis degraded after a period of 6 weeks due to unknown circumstances. Several years later, Freeman and his group continued Karasek's approach of generating transplantable epidermis from explant cultures [93]. They were able to increase the mitotic rate of isolated keratinocytes, thus achieving a considerable augmentation of the cell mass [94]. In contrast to Freeman's work, Rheinwald and Green presented in 1975 another approach to generate large amounts of keratinocytes based on a well-engineered system of subculturing [95, 96]. Their findings were a milestone on the way to therapeutically used keratinocytes cultures.

16.11.4 Dissociated Cultures

After Medawar's invention of an enzymatic separation between dermis and epidermis using trypsin [97], Billingham and Reynolds revealed in 1952 that trypsinized keratinocytes remain vital and are suitable for cell culturing [98].

In 1960, Cruickshank demonstrated the mitotic activity of cultured epithelial cells, thus enabling in vitro proliferation [99]. A further important step in the history of dissociated cultures was the development of fibroblast-free cultures due to Prunieras [100]. However, keratinocytes in his setting exhibited a rapid differentiation with a tendency to polystratifications [101]; hence, a sufficient augmentation via replication was still impossible at this stage. A significant improvement in this context was the additional use of acid-precipitated collagen gel [102]. This setting increased the proliferation rate of keratinocytes in a remarkable manner, plus enabling confluent growth and sub-culturing. Although the extraction rate has still been too small for a broad clinical use, it indicated the importance of the so-called feeder layer that contains connective tissue elements, for a large production of keratinocytes. Especially the presence of radiated embryonic 3T3-fibroblasts achieved good results due to their ability to inhibit normal fibroblast growth while not affecting the keratinocyte growth.

Finally the discovery of epidermal growth factor (EGF) paved the way for the clinical implementation of cultured epidermis. By means of EGF epidermal proliferation could be induced without hormonal influence, leading to a rapid and extensive growth of epidermal cell associations [103]. Thereby a transplantation of dissociated culture-gained epidermis became possible [70, 104, 105].

Since the crucial studies of Green and others, who brought the therapeutic use of cultured epidermis into clinical praxis, several innovations improved the culturing technique. Among others it has been shown that low potassium concentrations [106, 107] and the addition of trace elements [108, 109] have a positive impact upon the culture medium. Beneficial effects were also described after treatment with hydrocortisone, transferrin, and insulin. Due to these modifications, well-matched mediums arose over time, which enabled a proper proliferation of keratinocytes in the absence of a feeder layer [110, 111]. These keratinocytes remained undifferentiated, grew in a monolayer-like manner, and were suited for subculturing. By transferring these cells into a "normal" culture medium, enriched with foetal calf serum (FCS), differentiation as well as poly layer formation could be induced at a definite time.

16.12 Cultured Skin Substitutes

Although a large number of skin constructs is commercially available today (Table 16.1), only three techniques match the former mentioned requirements for the treatment of extensive burns. The majority of available skin substitutes are not qualified for the acute therapy of severely burned patient according to their complex and prolonged production. However, these substitutes are rather aiming at the market of chronic wound therapy (Table 16.1).

16.12.1 Cultured Epidermal Autografts (CEA)

The transplantation of a cultured epidermal cuticle derived from autologous keratinocytes was the first clinical application of a bioartificial organ component with a lifesaving effect. Since then, thousands of severely burned patients were treated and rescued by means of CEA worldwide. Nevertheless, the clinical use of CEAs is still discussed controversially. A major concern is the combination of high costs with uncertain healing rates, which may result in repeated transplantations [112, 113]. The estimated costs for 1% successfully treated body surface with CEAs were approximately 13,000 US$. The main reason for the transplant loss, which occurs usually within the first days after transplantation (critical period) starting from the sensitive dermo–epidermal

Table 16.1 Currently commercially available or marketed matrices and products for tissue engineered skin substitutes

Material	Brand name	Manufacturer
collagen gel + cult. Allog. HuK + allog. HuFi	Apligraf™ (earlier name: Graftskin™)	Organogenesis, Inc., Canton, MA
cult. Autol HuK	Epicell™	Genzyme Biosurgery, Cambridge, MA
PGA/PLA + ECMP DAHF	Transcyte™	Advanced Tissue Sciences, LaJolla, CA
Collagen GAG-polymer + silicone foil	Integra™	Integra LifeScience, Plainsborough, NJ
Acellular dermis	AlloDerm™	Lifecell Corporation, Branchberg, NJ
Acellular xenogenic dermis	Strattice™	KCI-Lifecell Corporation, Branchberg, NJ
HAM + cult. HuK	Laserskin™	Fidia Advanced Biopolymers, Padua, Italy
PGA/PLA + allog. HuFi	Dermagraft™	Advanced Tissue Sciences, LaJolla, CA
Collagen + allog HuFi + allog HuK	Orcel™	Ortec International, Inc., New York, NY
Fibrin sealant + cult. autol HuK	Bioseed™	BioTissue Technologies, Freiburg, Germany
PEO/PBT + autol. HuFi + cult autol HuK	Polyactive™	HC Implants
HAM + HuFi	Hyalograft 3D™	Fidia Advanced Biopolymers, Padua, Italy
Silicone + nylon mesh + collagen	Biobrane™	Dow Hickham/ Bertek Pharmac., Sugar Land, Tx

ECMP extracellular matrixproteins, *DAHF* derived from allog. HuFi, *GAG* glycosaminoglycan, *PGA* polyglycolic acid (Dexon™), *PLA* polylactic acid (Vicryl™), *PEO* polyethylen oxide, *PBT* polybutyliterephthalate, *cult.* cultured, *autol.* autologous, *allog.* allogeneic, *HuFi* human fibroblasts, *HuK* human keratinocytes, *HAM* microperforated hyaluronic acid membrane (benzilic esters of hyaluronic acid = HYAFF-11®)

Table 16.2 Summary of possible skin substitute techniques utilizing cultured human keratinocytes with regard to the various possible designs that are currently used or experimentally developed

I. Autologous cultured human keratinocytes
1. *Autologous epidermal sheet transplants* ("sheet grafts" = gold standard)
2. *In-vitro cultured and constructed dermo-epidermal autologous transplants*:
2.1. Keratinocytes on a collagen gel + fibroblasts
2.2. Keratinocyte sheets + Kollagen-Glycosaminoglycane-Membrane + Fibroblasts
2.3. Keratinocyte sheets on a layer of fibrin-gel
2.4. Keratinocyte sheets on cell free pig dermis
2.5. Keratinocyte sheets on cell free human dermis
2.6. Keratinocytes on bovine or equine collagen matrices
2.7. Keratinocyte sheets on micro-perforated hyaluronic acid membranes
2.8. Keratinocyte sheets on collagen + Chondroitin-6-sulfate with silicon membrane coverage (living skin equivalent)
3. Combination of allogenic dermis (in vivo) with epidermal sheets
4. Non-confluent keratinocyte suspensions
As a spray suspended in saline solutions
As spray or clots suspended in a fibrin matrix
4.1. Exclusively
4.2. In clinical combination with fresh or preserved allogenic skin
4.4. As non confluent keratinocyte monolayers on equine or bovine collagen matrices or on top of hyaluronic acid membranes
4.6. In combination with collagen coated nylon on silicone backing
4.7. Dissociated keratinocytes without cell culture
4.8. Outer root sheath cells (from plucked hair follicles) cultured or without culture
5. Three dimensional cell cluster cultures (spherocytes)
5.1. Cultured on microspheres as carrier systems (experimentally on: dextrane, collagen, hyaluronic acid)
5.2. Cell seeded microspheres + allografts/biomaterials
II. Allogeneic keratinocytes
6. Allogeneic Keratinocytes
6.1. Keratinocyte-sheets (as a temporary wound cover)
6.2. Allogeneic keratinocyte suspensions (experimentally)
6.3. Syngenic-allogeneic keratinocytes
In-vitro constructed dermo-epidermal composites/analogues
6.4. Keratinocytes and Fibroblasts (collagen matrices)

junction zone, is the liability of CEAs towards wound-ground-associated germs. Meta-analysis revealed that almost 50% of the transplanted CEAs do not integrate into the wound ground, thus requiring further operations [114].

Applied cultured epidermal autografts usually contain 3–5 cell layers; hence, not only the wound transfer but also the wound care within the first days after transplantation is rather difficult.

Until today, a serious problem of CEAs is the insufficient adherence to the wound bed often combined with blistering due to shear stress. An explanation for this phenomenon might be an incomplete formation of anchoring fibrils during culturing as well as an enzymatic separation within the culturing bottles before transplantation [115]. In addition, the lacking dermal component contributes to the development of bullae especially in case of third-degree burns. To solve this problem, much effort was put into the development of dermal substitutes with varying compositions (Table 16.2) during the last years. Some of these substitutes are already used in the clinical praxis.

Until an adequate amount of cultured epidermal autografts is available, the temporary coverage with allogenic and xenogenic skin (see above) represents a lifesaving and well established opportunity [1, 6, 33, 53, 116, 117].

16.12.2 Cell Suspensions

As mentioned introductorily, in 1985 von Mangold performed a successful transplantation of scraped keratinocytes suspended in autologous wound serum [4]. However, even after the invention of the cell amplification via culturing, this technique failed to prevail because of a lacking carrier substance.

Hunyadi et al. have been the first, who used fibrin glue as a suspension for trypsinized, non-cultured keratinocytes. By this means, they succeeded in the therapy of chronic wounds [118]. As a member of the coagulation cascade, fibrin is of special importance for the wound healing process. Besides its role as a carrier substance for keratinocyte suspensions, fibrin is also useful to improve the adherence and healing of split skin grafts [119]. It was also shown that fibrin glue does not affect the clonogenic properties as well as the growth and proliferation rate of epidermal cells. Especially in case of hardly manageable third-degree burns, suspended keratinocytes embedded into fibrin glue exhibit good healing and take rates. In addition, simultaneous covering with meshed allogenic skin grafts can be useful to increase the biostability by preventing a washing away effect of the cells after lysis of the fibrin clot. Moreover, this "biologic bandage" protects the cells against dehydration. After a brief initial revascularisation, the allogenic skin is rejected 12–14 days after transplantation.

Compared to CEAs, the usage of cell suspensions is not only cheaper but also easier to handle and more quickly available (Table 16.2).

16.12.3 Membrane Cell Transplants

The usage of bio-compatible membranes as a carrier for cultured cells for the coverage of burn wounds failed to prevail in the clinical practice. Although several constructs have shown good experimental results in vitro as well as in vivo, a further development remains questionable [52, 53, 120]. However, a potential advantage of this method is especially an improved mechanical handling, thus simplifying the application of cultured cells.

16.12.4 Alloplastic and Synthetic Biological Carriers for Cultured Cells

The combination of cultured autologous keratinocytes with different alloplastic materials as dermal regeneration matrices has been investigated by different groups [86]. In 1989 Yannas and Burke developed a skin equivalent by centrifuging trypsinized keratinocytes and fibroblasts in a collagen–glycosaminoglycan matrix (C-GAG). This mixture was completely integrated into the healing wound after transplantation onto guinea pigs. Despite these promising results, the technique failed to prevail among others due to the complex generating process.

A noticeable alternative is the usage of a bilaminare membrane (Integra®) containing a dermal component, which is covered by a silicone membrane as a temporary epidermal substitute [86]. Due to its porosity, the dermal component allows the in-growing of wound-grounded fibroblasts as well as the recapillarization through sprouting vessels out of the wound, which has to be covered. During these processes, there is a transformation of the substitute matrix through the incoming fibroblasts [106, 111] with consecutive reconstitution of a vital dermal compound in vivo, which can be covered with thin split skin grafts or CEAs [86] after removal of the temporary artificial epidermis. Recent studies show that the additional use of a vacuum sealing (VAC®) can shorten the time period until the healing of the dermal component is finished and improves significantly the intake rate.

Another approach is the transplantation of pre-confluent non-contact-inhibited keratinocyte monolayers embedded onto polymer membranes or polyurethane (membrane cell constructs). These constructs are available after a short culture period and reconstitute the epidermis in vivo after application onto the excised burn wound (Fig. 16.8).

16.12.4.1 Bioprinting and Biofabrication

A new field of research has been termed "biofabrication" and utilizes latest 3D printing technologies. This aims at hierarchically and spatially incorporating different cells, biomaterials, and molecules into a matrix to alleviate a directed maturation of artificial tissue. Various different printing techniques are momentarily under research, such as stereolithography, extrusion-based printing, laser-assisted printing, inkjet-based printing, and nano-bioprinting [121, 122].

It has also been preliminary applied to the generation of artificial skin but is not yet available for clinical use. It seems possible that using so-called bioinks to print cells into a special 3D scaffold, some of the problems of reconstituting replacement skin in the laboratory can be optimized. Nevertheless, future developments might also influence skin replacement in burns.

16.13 Summary

Cultured skin substitutes are nowadays a glimmer of hope for the recent and future treatment especially of large scaled burns. They can so far save lives, but have to be improved to completely reach the quality of split-thickness or full-thickness skin grafts in the future. Until this goal is reached, mixed techniques, like temporary allogenic skin grafting combined with a one- or second-stage transplantation of

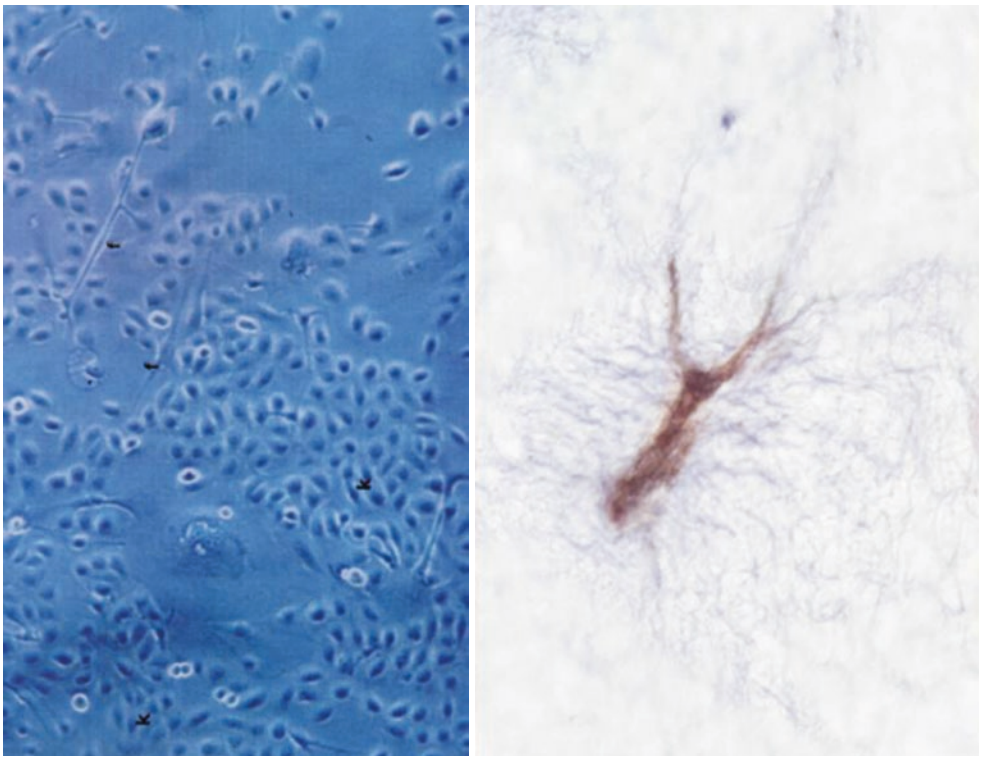


Fig. 16.8 Depicted is a subconfluent keratinocyte culture (left image) containing a few isolated fibroblasts. The right image displays melanocytes in a cell culture. (Asterisk) These images are friendly provided by PD Dr. Jürgen Kopp (Hannover)

autologous cultured skin substitutes, which already have achieved good clinical results, will be improved and used for the acute treatment of severe burned patients. In summary, cell culture and tissue engineering support and improve the conventional techniques of burn therapy and might have the potential to replace them in the future.

References[1]

1. Horch RE, Corbei O, Formanek-Corbei B, Brand-Saberi B, Vanscheidt W, Stark G. Reconstitution of basement membrane after 'sandwich-technique' skin grafting for severe burns demonstrated by immunohistochemistry. J Burn Care Rehabil. 1998;19:189–202.
2. Bünger C. Gelungener Versuch einer Nasenbildung aus einem völlig getrennten Hautstück aus dem Beine. J Chir Augenheilkd. 1823;4:569–73.
3. Reverdin JL. Greffe epidermique. Bull Soc Imperial Chirurg Paris. 1869;10:511–4.
4. Mangoldt F. Die Epithelsaat zum Verschluß einer großen Wundfläche. Med Wochenschr. 1895;21:798–803.
5. Braun W. Zur Technik der Hautpfropfung. Zentralb Chir. 1920;47:1355–61.
6. Horch RE, Stark G, Spilker G. Treatment of perianal burns with submerged skin particles. Zentralbl Chir. 1994;119:722–5.
7. Ollier L. Sur le greffes cutanees ou autoplatiques. Bull Acad Med. 1872;1:243–56.
8. Thiersch C. Ueber die feineren anatomischen Veränderungen bei Aufheilung von Haut auf Granulationen. Langenbecks Arch Klin Chir. 1874;17:318–24.
9. Mir Y, Mir L. The gauze technique in skin grafting; a quick method in applying dermatome grafts. Plast Reconstr Surg. 1950;5(1):91–6.
10. Janzekovic Z. A new concept in the early excision and immediate grafting of burns. J Trauma. 1970;10(12):1103–8.
11. Fisher JC. Skin—the ultimate solution for the burn wound. N Engl J Med. 1984;311(7):466–7.
12. Alexander JW, MacMillan BG, Law E, Kittur DS. Treatment of severe burns with widely meshed skin autograft and meshed skin allograft overlay. J Trauma. 1981;21(6):433–8.
13. Pallua N, Machens HG, Becker M, Berger A. Surgical prevention of post-traumatic infection by immediate necrectomy of burn wounds. Langenbecks Arch Chir Suppl Kongressbd. 1996;113:1144–8.
14. Gabarro P. A new method of grafting. Brit Med J. 1943;1:723.
15. Mac Millan B, Altemeier W. Massive excision of the extensive burn. Research in burns. Am Inst Biol Siences. 1962;9:331.
16. Ong YS, Samuel M, Song C. Metaanalysis of early excision of burns. Burns. 2006;32:145–50.
17. Tanner JC Jr, Vandeput J, Olley JF. The mesh skin graft. Plast Reconstr Surg. 1964;34:287–92.
18. Tanner JC Jr, Shea PC Jr, Bradley WH, Vandeput JJ. Large-mesh skin grafts. Plast Reconstr Surg. 1969;44(5):504–6.
19. Burleson R, Eiseman B. Nature of the bond between partial-thickness skin and wound granulations. Surgery. 1972;72(2):315–22.
20. Adams DC, Ramsey ML. Grafts in dermatologic surgery: review and update on full- and split-thickness skin grafts, free cartilage grafts, and composite grafts. Dermatol Surg. 2005;31(8 Pt 2):1055–67.
21. Brou J, Vu T, McCauley RL, Herndon DN, Desai MH, Rutan RL, et al. The scalp as a donor site: revisited. J Trauma. 1990;30(5):579–81.

[1]Sample references. In case of doubt, kindly consult Springer to obtain detailed guidelines for accurate reference entries for particular subject fields.

22. Corps BV. The effect of graft thickness, donor site and graft bed on graft shrinkage in the hooded rat. Br J Plast Surg. 1969;22(2):125–33.
23. Smahel J, Ganzoni N. The take of mesh graft in experiment. Acta Chir Plast. 1972;14(2):90–100.
24. Meek CP. Successful microdermagrafting using the Meek-Wall microdermatome. Am J Surg. 1958;96(4):557–8.
25. Kreis RW, Mackie DP, Vloemans AW, Hermans RP, Hoekstra MJ. Widely expanded postage stamp skin grafts using a modified Meek technique in combination with an allograft overlay. Burns. 1993;19(2):142–5.
26. Vandeput J, Tanner JC Jr, Carlisle JD. The ultra postage stamp skin graft. Plast Reconstr Surg. 1966;38(3):252–4.
27. Chang LY, Yang JY. Clinical experience of postage stamp autograft with porcine skin onlay dressing in extensive burns. Burns. 1998;24(3):264–9.
28. Bondoc CC, Burke JF. Clinical experience with viable frozen human skin and a frozen skin bank. Ann Surg. 1971;174(3):371–82.
29. Kreis RW, Hoekstra MJ, Mackie DP, Vloemans AF, Hermans RP. Historical appraisal of the use of skin allografts in the treatment of extensive full skin thickness burns at the Red Cross Hospital Burns Centre, Beverwijk, The Netherlands. Burns. 1992;18(Suppl 2):S19–22.
30. Abbott WM, Hembree JS. Absence of antigenicity in freeze-dried skin allografts. Cryobiology. 1970;6(5):416–8.
31. Hermans RP. The use of human allografts in the treatment of scalds in children. Panminerva Med. 1983;25(3):155–6.
32. Kreis RW, Vloemans AF, Hoekstra MJ, Mackie DP, Hermans RP. The use of non-viable glycerol-preserved cadaver skin combined with widely expanded autografts in the treatment of extensive third-degree burns. J Trauma. 1989;29(1):51–4.
33. Horch RE, Jeschke MG, Spilker G, Herndon DN, Kopp J. Treatment of second degree facial burns with allografts—preliminary results. Burns. 2005;31(5):597–602.
34. Achauer BM, Hewitt CW, Black KS, Martinez SE, Waxman KS, Ott RA, et al. Long-term skin allograft survival after short-term cyclosporin treatment in a patient with massive burns. Lancet. 1986;1(8471):14–5.
35. Takiuchi I, Higuchi D, Sei Y, Nakajima T. Histological identification of prolonged survival of a skin allograft on an extensively burned patient. Burns Incl Therm Inj. 1982;8(3):164–7.
36. Alsbjörn B, SÝrensen B. Grafting with epidermal Langerhans cell depressed cadaver split skin. Burns. 1985;11:259.
37. Burke JF, May JW Jr, Albright N, Quinby WC, Russell PS. Temporary skin transplantation and immunosuppression for extensive burns. N Engl J Med. 1974;290(5):269–71.
38. Burke JF, Quinby WC, Bondoc CC, Cosimi AB, Russell PS, Szyfelbein SK. Immunosuppression and temporary skin transplantation in the treatment of massive third degree burns. Ann Surg. 1975;182(3):183–97.
39. Hewitt CW, Black KS, Stenger JA, Go C, Achauer BM, Martin DC. Comparison of kidney, composite tissue, and skin allograft survival in rats prolonged by donor blood and concomitant limited cyclosporine. Transplant Proc. 1988;20(3 Suppl 3):1110–3.
40. Hewitt CW, Black KS, Harman JC, Beko KR, Lee HS, Patel AP, et al. Partial tolerance in rat renal allograft recipients following multiple blood transfusions and concomitant cyclosporine. Transplantation. 1990;49(1):194–8.
41. Frame JD, Sanders R, Goodacre TE, Morgan BD. The fate of meshed allograft skin in burned patients using cyclosporin immunosuppression. Br J Plast Surg. 1989;42(1):27–34.
42. Kanitakis J, Ramirez-Bosca A, Haftek M, Thivolet J. Histological and ultrastructural effects of cyclosporin A on normal human skin xenografted on to nude mice. Virchows Arch A Pathol Anat Histopathol. 1990;416(6):505–11.
43. Bromberg BE, Song IC, Mohn MP. The use of pig skin as a temporary biological dressing. Plast Reconstr Surg. 1965;36:80–90.
44. Ding YL, Pu SS, Wu DZ, Ma C, Pan ZL, Lu X, et al. Clinical and histological observations on the application of intermingled auto- and porcine-skin heterografts in third degree burns. Burns Incl Therm Inj. 1983;9(6):381–6.
45. Min J, Yang GF. Clinical and histological observations on intermingled pig skin and auto-skin transplantation in burns (author's transl). Zhonghua Wai Ke Za Zhi. 1981;19(1):43–5.
46. Yang ZJ. Treatment of extensive third degree burns. A Chinese concept. Rev Med Chir Soc Med Nat Iasi. 1981;85(1):69–74.
47. Baumer F, Henrich HA, Bonfig R, Kossen DJ, Romen W. Surgical treatment of 3d degree burns with mixed homologous/autologous and heterologous/autologous full-thickness skin grafts. Comparison of results with native and frozen homologous and heterologous tissues in animal experiments. Zentralbl Chir. 1986;111(7):426–30.
48. Jackson D. A clinical study of the use of skin homografts for burns. Br J Plast Surg. 1954;7(1):26–43.
49. Converse JM, Rapaport FT. The vascularization of skin autografts and homografts; an experimental study in man. Ann Surg. 1956;143(3):306–15.
50. Toranto IR, Sayler KE, Myers MB. Vascularization of porcine skin heterografts. Plast Reconstr Surg. 1974;54(2):195–200.
51. Phillips A, Clarke J. The use of intermingled autograft and parental allograft skin in the treatment of major burns in children. Br J Plast Surg. 1991;44:608.
52. Herndon DN, Rutan RL. Comparison of cultured epidermal autograft and massive excision with serial autografting plus homograft overlay. J Burn Care Rehabil. 1992;13(1):154–7.
53. Horch R, Stark GB, Kopp J, Spilker G. Cologne Burn Centre experiences with glycerol-preserved allogeneic skin: Part I: clinical experiences and histological findings (overgraft and sandwich technique). Burns. 1994;20(Suppl 1):S23–6.
54. Zhang ML, Chang ZD, Han X, Zhu M. Microskin grafting. I. Animal experiments. Burns Incl Therm Inj. 1986;12(8):540–3.
55. Zhang ML, Wang CY, Chang ZD, Cao DX, Han X. Microskin grafting. II. Clinical report. Burns Incl Therm Inj. 1986;12(8):544–8.
56. Lin SD, Lai CS, Chou CK, Tsai CW. Microskin grafting of rabbit skin wounds with biobrane overlay. Burns. 1992;18(5):390–4.
57. Lin SD, Lai CS, Chou CK, Tsai CW, Wu KF, Chang CW. Microskin autograft with pigskin xenograft overlay: a preliminary report of studies on patients. Burns. 1992;18(4):321–5.
58. Sawada Y. Survival of an extensively burned child following use of fragments of autograft skin overlain with meshed allograft skin. Burns Incl Therm Inj. 1985;11(6):429–33.
59. Sawada Y. Buried chip skin grafting for treatment of perianal burns. Burns Incl Therm Inj. 1989;15(1):36–8.
60. Ming-Liang Z, Chang-Yeh W, Zhi-De C. Microskin grafting II. Clinical report. Burns. 1986;12:544.
61. Achauer BM, editor. Burn reconstruction. New York, NY: Thieme Medical Publishers; 1991.
62. Buehrer G, Arkudas A, Horch RE. Treatment of standardised wounds with pure epidermal micrografts generated with an automated device. Int Wound J. 2017;
63. Buhrer G, Beier JP, Horch RE, et al. Surgical treatment of burns: special aspects of pediatric burns. Hautarzt. 2017;68(5):385–92.
64. Weigand A, Boos AM, Tasbihi K, et al. Selective isolation and characterization of primary cells from normal breast and tumors reveal plasticity of adipose derived stem cells. Breast Cancer Res. 2016;18(1):32.
65. Witt R, Weigand A, Boos AM, et al. Mesenchymal stem cells and myoblast differentiation under HGF and IGF-1 stimulation for 3D skeletal muscle tissue engineering. BMC Cell Biol. 2017;18:1–15.

66. Hafemann B, Frese C, Kistler D, Hettich R. Intermingled skin grafts with in vitro cultured keratinocytes—experiments with rats. Burns. 1989;15(4):233–8.
67. Wheeler CE, Canby CM, Cawley EP. Long-term tissue culture of epithelial-like cells from human skin. J Invest Dermatol. 1957;29(5):383–91; discussion 91–2.
68. O'Conner N, Mulliken J, Banks-Schlegel S, Kehinde O, Green H. Grafting of burns with cultured epithelium prepared from autologous epidermal cells. Lancet. 1981;1:75–8.
69. Hefton JM, Madden MR, Finkelstein JL, Shires GT. Grafting of burn patients with allografts of cultured epidermal cells. Lancet. 1983;2(8347):428–30.
70. Gallico GG III, O'Connor NE, Compton CC, Kehinde O, Green H. Permanent coverage of large burn wounds with autologous cultured human epithelium. N Engl J Med. 1984;311(7):448–51.
71. Madden MR, Finkelstein JL, Staiano-Coico L, Goodwin CW, Shires GT, Nolan EE, et al. Grafting of cultured allogeneic epidermis on second- and third-degree burn wounds on 26 patients. J Trauma. 1986;26(11):955–62.
72. Eldad A, Burt A, Clarke JA, Gusterson B. Cultured epithelium as a skin substitute. Burns Incl Therm Inj. 1987;13(3):173–80.
73. Teepe RG, Kreis RW, Hoekstra MJ, Ponec M. Permanent wound cover using cultured autologous epidermis transplants: a new treatment method for patients with severe burns. Ned Tijdschr Geneeskd. 1987;131(22):946–51.
74. Aubock J. Skin replacement with cultured keratinocytes. Z Hautkr. 1988;63(7):565–7.
75. Aubock J, Irschick E, Romani N, Kompatscher P, Hopfl R, Herold M, et al. Rejection, after a slightly prolonged survival time, of Langerhans cell-free allogeneic cultured epidermis used for wound coverage in humans. Transplantation. 1988;45(4):730–7.
76. Von der Ljunggren C. Fähigkeit des Hautepithels ausserhalb des Organismus sein Leben zu behalten, mit Berücksichtigung der Transplantation. Dtsch Chir. 1898;47:608–15.
77. Carrel A, Burrows M. Cultivation of adult tissues and organs outside of the body. JAMA. 1910;55:1379–81.
78. Hadda S. Aus der chirurg. Abteilung des israelitischen Krankenhauses zu Breslau: Die Kultur lebender Körperzellen. Berl Klin Wschr. 1912;49:11.
79. Kreibich K. Aus der deutschen dermatologischen Klinik in Prag: Kultur erwachsener Haut auf festem Nährboden. Arch Dermatol Syph. 1914;120:168–76.
80. Waymouth C. Construction and use of synthetic media. In: Willmer E, editor. Cells and tissues in culture. London: Academic; 1965. p. 99.
81. Börnstein K. Über Gewebezüchtung menschlicher Haut. Klin Wschr. 1930;9:1119.
82. Pinkus H. Über Gewebekulturen menschlicher Epidermis. Arch Dermatol Syph. 1932;165:53–85.
83. Medawar P. The cultivation of adult mammalian skin epithelium in vitro. Q J Microsc Sci. 1948;89:187.
84. Parshley MS, Simms HS. Cultivation of adult skin epithelial cells (chicken and human) in vitro. Am J Anat. 1950;86(2):163–89.
85. Lewis S, Pomerat C, Ezell D. Human epidermal cell observed in tissue culture phase-contrast microscope. Anat Rec. 1949;104:487.
86. Flaxman B, Harper R. Primary cell culture for biochemical studies of human keratinocytes. Br J Dermatol. 1975;92:305.
87. Flaxman BA, Harper RA. Primary cell culture for biochemical studies of human keratinocytes. A method for production of very large numbers of cells without the necessity of subculturing techniques. Br J Dermatol. 1975;92(3):305–9.
88. Blocker TG Jr, Pomerat CM, Lewis SR. Research opportunities with the use of cultures of living skin. Plast Reconstr Surg. 1950;5(4):283–8.
89. Bassett CA, Evans VJ, Earle WR. Characteristics and potentials of long term cultures of human skin. Plast Reconstr Surg. 1956;17(6):421–9.
90. Medawar P. Tests by tissue culture methods on the nature and immunity to transplanted skin. Q J Microsc Sci. 1948;89:239.
91. Moscona A. Rotation-mediated histogenetic aggregation of dissociated cells. A quantifiable approach to cell interactions in vitro. Exp Cell Res. 1961;22:455–75.
92. Karasek MA. Growth and differentiation of transplanted epithelial cell cultures. J Invest Dermatol. 1968;51(4):247–52.
93. Igel HJ, Freeman AE, Boeckman CR, Kleinfeld KL. A new method for covering large surface area wounds with autografts. II. Surgical application of tissue culture expanded rabbit-skin autografts. Arch Surg. 1974;108(5):724–9.
94. Freeman AE, Igel HJ, Herrman BJ, Kleinfeld KL. Growth and characterization of human skin epithelial cell cultures. In Vitro. 1976;12(5):352–62.
95. Rheinwald JG, Green H. Serial cultivation of strains of human epidermal keratinocytes: the formation of keratinizing colonies from single cells. Cell. 1975;6(3):331–43.
96. Rheinwald JG, Green H. Formation of a keratinizing epithelium in culture by a cloned cell line derived from a teratoma. Cell. 1975;6(3):317–30.
97. Medawar P. Sheets of pure epidermal epithelium from human skin. Nature. 1941;148:783.
98. Billingham RE, Reynolds J. Transplantation studies on sheets of pure epidermal epithelium and on epidermal cell suspensions. Br J Plast Surg. 1952;5(1):25–36.
99. Cruickshank CN, Cooper JR, Hooper C. The cultivation of cells from adult epidermis. J Invest Dermatol. 1960;34:339–42.
100. Prunieras M, Mathivon MF, Leung TK, Gazzolo L. Euploid culture of adult epidermal cells in monocellular layers. Ann Inst Pasteur (Paris). 1965;108:149–65.
101. Constable H, Cooper JR, Cruickshank CN, Mann PR. Keratinization in dispersed cell cultures of adult guinea-pig ear skin. Br J Dermatol. 1974;91(1):39–48.
102. Karasek MA, Charlton ME. Growth of postembryonic skin epithelial cells on collagen gels. J Invest Dermatol. 1971;56(3):205–10.
103. Cohen S. The stimulation of epidermal proliferation by a specific protein (EGF). Dev Biol. 1965;12(3):394–407.
104. Green H, Kehinde O, Thomas J. Growth of cultured human epidermal cells into multiple epithelia suitable for grafting. Proc Natl Acad Sci U S A. 1979;76(11):5665–8.
105. Cuono C, Langdon R, McGuire J. Use of cultured epidermal autografts and dermal allografts as skin replacement after burn injury. Lancet. 1986;1(8490):1123–4.
106. Hennings H, Michael D, Cheng C, Steinert P, Holbrook K, Yuspa SH. Calcium regulation of growth and differentiation of mouse epidermal cells in culture. Cell. 1980;19(1):245–54.
107. Yuspa SH, Koehler B, Kulesz-Martin M, Hennings H. Clonal growth of mouse epidermal cells in medium with reduced calcium concentration. J Invest Dermatol. 1981;76(2):144–6.
108. Barnes D, Sato G. Methods for growth of cultured cells in serum-free medium. Anal Biochem. 1980;102(2):255–70.
109. Shipley GD, Ham RG. Improved medium and culture conditions for clonal growth with minimal serum protein and for enhanced serum-free survival of Swiss 3T3 cells. In Vitro. 1981;17(8):656–70.
110. Tsao MC, Walthall BJ, Ham RG. Clonal growth of normal human epidermal keratinocytes in a defined medium. J Cell Physiol. 1982;110(2):219–29.
111. Wille JJ Jr, Pittelkow MR, Shipley GD, Scott RE. Integrated control of growth and differentiation of normal human prokeratinocytes cultured in serum-free medium: clonal analyses, growth kinetics, and cell cycle studies. J Cell Physiol. 1984;121(1):31–44.

112. Kopp J, Jeschke MG, Bach AD, Kneser U, Horch RE. Applied tissue engineering in the closure of severe burns and chronic wounds using cultured human autologous keratinocytes in a natural fibrin matrix. Cell Tissue Bank. 2004;5(2):89–96.
113. Yasushi F, Koichi U, Yuka O, Kentaro K, Hiromichi M, Yoshimitsu K. Treatment with autologous cultured dermal substitutes (CDS) for burn scar contracture in children. Wound Repair Regen. 2004;12:A11.
114. Freising C, Horch R. Clinical results of cultivated keratinocyzes to treat burn injuries – a metaanalysis. In: Achauer B, editor. Cultured human keratinocytes and tissue engineered skin substitutes. Stuttgart: Thieme; 2001. p. 220–6.
115. Woodley DT, Peterson HD, Herzog SR, Stricklin GP, Burgeson RE, Briggaman RA, et al. Burn wounds resurfaced by cultured epidermal autografts show abnormal reconstitution of anchoring fibrils. JAMA. 1988;259(17):2566–71.
116. Munster AM, Smith-Meek M, Shalom A. Acellular allograft dermal matrix: immediate or delayed epidermal coverage? Burns. 2001;27(2):150–3.
117. Ronfard V, Rives JM, Neveux Y, Carsin H, Barrandon Y. Long-term regeneration of human epidermis on third degree burns transplanted with autologous cultured epithelium grown on a fibrin matrix. Transplantation. 2000;70(11):1588–98.
118. Hunyadi J, Farkas B, Bertenyi C, Olah J, Dobozy A. Keratinocyte grafting: covering of skin defects by separated autologous keratinocytes in a fibrin net. J Invest Dermatol. 1987;89(1):119–20.
119. Altmeppen J, Hansen E, Bonnlander GL, Horch RE, Jeschke MG. Composition and characteristics of an autologous thrombocyte gel. J Surg Res. 2004;117(2):202–7.
120. Perry VP, Evans VJ, Earle WR, Hyatt GW, Bedell WC. Long-term tissue culture of human skin. Am J Hyg. 1956;63(1):52–8.
121. Groll J, Boland T, Blunk T, et al. Biofabrication: reappraising the definition of an evolving field. Biofabrication. 2016;8(1):013001.
122. Malda J, Groll J. A step towards clinical translation of biofabrication. Trends Biotechnol. 2016;34(5):356–7.

Twelve-Year Follow-Up: A Clinical Study on Dermal Regeneration

17

Monica C. T. Bloemen, Paul P. M. van Zuijlen, and Esther Middelkoop

17.1 Introduction

Improved wound care has increased life expectancy in both patients with chronic and acute wounds. Nowadays, treatment is not only focused on patient survival; eventual patient outcome has also become more important. The long-term consequences of skin loss, e.g. scars that remain after burns or other trauma can be severe and cause physical and cosmetic problems. Therefore, therapies for improvement of scar quality is mandatory. The standard therapy for extensive full-thickness wounds is the application of an autologous skin graft. However, this treatment leads to poor skin quality and scar contractures. One of the causes of this poor skin quality is the lack of dermis in the remaining scar. The dermal layer of the skin is responsible for pliability and mechanical resistance. Consequently, the lack of dermis predisposes to severe scarring.

In 1981, Yannas and Burke were the first to report on the development of an artificial dermis derived from bovine collagen [1]. Since then, research has focused on the use of dermal substitutes to improve the functional and cosmetic outcome. Dermal substitution in acute and reconstructive wounds is thought to lead to a better scar elasticity, mechanical stability, and appearance. This could be due to the fact that the use of a dermal substitute results in the formation of a neodermis that is comparable with the normal dermis. It is hypothesized that dermal substitution serves as a support structure for the in-growth of vessels and autologous fibroblasts [2–5].

Multiple studies have investigated the use of dermal substitutes, such as Integra®, Apligraf®, Matriderm®, and Alloderm®, in acute and reconstructive wounds [4, 6–17]. Good results have been demonstrated, e.g., an increased scar elasticity and an improved cosmetic appearance [4, 6–10, 12, 14, 16, 17]. The majority of these studies, however, only reported short-term follow-up. To our knowledge, one study reported on the results of a study on dermal substitution with a follow-up longer than 1 or 2 years [14]. Sheridan et al. described a study on the use of Integra® in acute burns with a follow-up of up to 10 years [14]. Good results were found for scar function and appearance in substituted scars. Unfortunately, only patients in whom the artificial skin was successfully grafted were evaluated in follow-up, thus a selection bias might probably have occurred. In addition, the quality of substituted scars was only evaluated subjectively. Besides the above described study, little information is available on the long-term effectiveness of dermal substitutes. A clinical trial with a long-term follow-up can investigate long-term effectiveness of dermal substitution and show a long-lasting functional and cosmetic scar improvement. In addition, the need for reconstructive surgery and patient's quality of life can be investigated in long-term studies. This chapter will focus on a study that was performed on the long-term effectiveness of a dermal substitute using objective and subjective criteria [18].

From 1996 to 1998, a controlled clinical trial was performed at the Burn Centre Beverwijk, The Netherlands, in which effectiveness of a dermal substitute was investigated. Publications of this study reported on the graft survival and scar aspects 3 and 12 months postoperatively [19, 20]. First, it was shown that this dermal substitute could be successfully applied in a one-stage procedure. Second, in scar assessment 3 months postoperatively, the clinical effectiveness of this

M. C. T. Bloemen
Association of Dutch Burn Centers, Beverwijk, The Netherlands
Burn Center, Red Cross Hospital, Beverwijk, The Netherlands
P. P. M. van Zuijlen
Association of Dutch Burn Centers, Beverwijk, The Netherlands
Burn Center, Red Cross Hospital, Beverwijk, The Netherlands
Department of Plastic, Reconstructive and Hand Surgery, Red Cross Hospital, Beverwijk, The Netherlands
Department of Plastic, Reconstructive and Hand Surgery, Academic Medical Center, Amsterdam, The Netherlands
E. Middelkoop (✉)
Association of Dutch Burn Centers, Beverwijk, The Netherlands
Burn Center, Red Cross Hospital, Beverwijk, The Netherlands
Department of Plastic, Reconstructive and Hand Surgery, VU University Medical Center, Amsterdam, The Netherlands
e-mail: e.middelkoop@vumc.nl

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_17

substitute was established by demonstrating a statistically significant increase of elasticity for reconstructive wounds [19]. Twelve months postoperatively, elasticity had improved in both scars, and although the substituted scar was more elastic, the difference did not reach the level of statistical significance. Also, in a separate analysis of acute burn scars, it was seen that elasticity was higher in substituted scars treated with a large expansion graft [20]. Finally, in the follow-up 12 months postoperatively, substituted scars seemed smoother compared with reference scars [20].

The Vancouver Scar Scale (VSS) and the Cutometer were used to assess the scars at 3 and 12 months postoperatively. Since then, several additional measuring tools have been developed. First of all, an improved subjective assessment scale was developed, the Patient and Observer Scar Assessment Scale (POSAS), which was used in the follow-up 12 years post-surgery, instead of the VSS [21]. In addition, scar color and pigmentation were quantified with objective measuring tools, and for the first time, the effect of dermal substitution on scar roughness was objectified [22–25]. Summarizing, more scar aspects were investigated subjectively and objectively 12 years after the application of the substitute.

17.2 Clinical Trial

From 1996 to 1998, 62 burn patients were included in the controlled clinical trial. The use of a collagen–elastin matrix as dermal substitute was investigated in both reconstructive and acute burn wounds [19, 20, 26]. Patients were included if they were admitted to the Burn Centre and needed surgical treatment for their reconstructive and acute burn wounds. In all patients, a paired intra-individual comparison was made; one (part of the) wound was treated with the conventional split skin graft (SSG) and the other (part of the) wound was treated with the precursor of the dermal substitute, Matriderm® (Dr. Otto Suwelack Skin & Health Care AG, Biller-beck, Germany) and an SSG (Fig. 17.1). This substi-

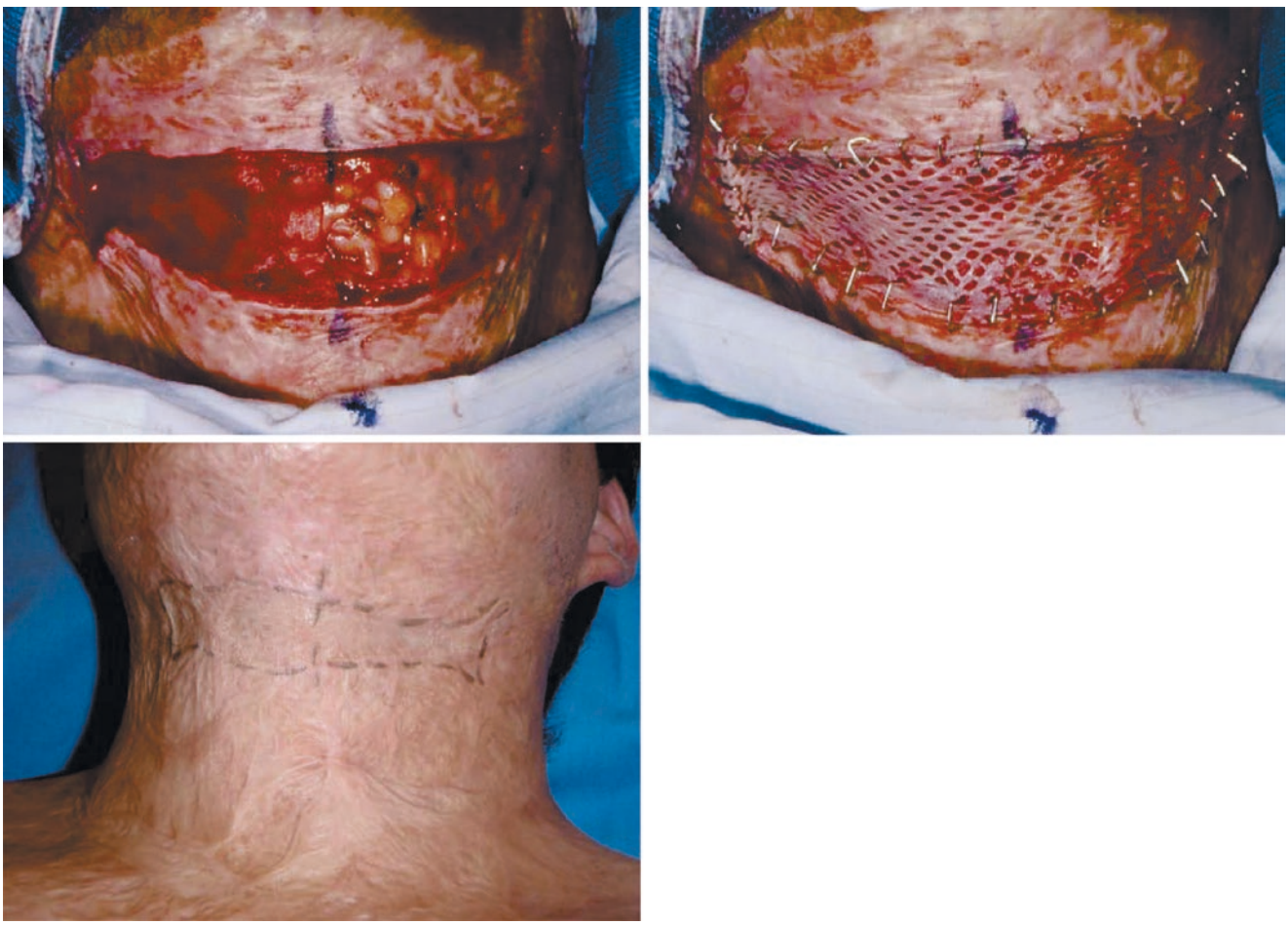


Fig. 17.1 Patient example of clinical application of the dermal substitute in a reconstructive burn wound and scar appearance 12 years postoperatively. Upper left: Reconstructive wound in the neck with the substitute applied on the right side of the patient's wound (in the picture left). Upper right: Reconstructive wound in the neck with an SSG applied on top of the substitute (patient's right side) and the wound (patient's left side). Below: Scar appearance 11.6 years postoperatively is presented; substituted scar in the picture left, reference scar in the picture right

tute is a 1-mm-thick, highly porous membrane, composed of a native bovine type I, III, and V collagen fiber template. The collagen fibers are coated with α-elastin hydrolysate derived from the bovine nuchal ligament in a concentration of 3% weight-to-weight ratio (GfN-Herstellung von Naturextrakten GmbH, Wald-Michelbach, Germany). The substitute was treated with low-dosed γ-irradiation (approximately 1000 Gy) and stored at room temperature. Matrices were applied in a single-stage grafting procedure. During the operation, the experimental and reference treatments were allocated to anatomically related areas; therefore, a right/left, superior/inferior, or medial/lateral comparison was made to exclude any bias caused by the selection of the surgeon.

After 12 years, all patients were addressed for a third follow-up. In total 46 of the initial 62 patients participated in this follow-up, consisting of patients with acute (26) and reconstructive burn wounds (26). Six patients were also included in the reconstructive group after being included in the burn wound category previously. The category of acute burn wounds consisted of 35 scar pairs which could be evaluated; in the reconstructive burn group, 34 scar pairs were included in the follow-up. Table 17.1 demonstrates several patient characteristics of the study group. In each patient, the experimental scar (treated with the dermal substitute and an SSG) and the reference scar (treated with an SSG alone) was located with the use of a well-documented photographic archive and precise wound descriptions (Fig. 17.2). Consequently, scar elasticity, erythema, melanin, and surface roughness were examined by means of different objective scar evaluation tools, and the scars were also evaluated subjectively.

17.2.1 Scar Elasticity

Scar elasticity was measured with the Cutometer Skin Elasticity Meter (Courage and Khazaka GmbH, Germany)

Table 17.1 Patient characteristics

Acute	
Number of patients (*n*)	26
Number of scar pairs (*n*)	35
Male sex	15 (58%)
TBSA (%)	24.3 ± 14.7
Follow-up period in years	11.8 ± 0.4
Reconstructive	
Number of patients (*n*)	26
Number of scar pairs (*n*)	34
Male sex	16 (62%)
TBSA (%)	30.5 ± 17.6
Follow-up period in years	11.8 ± 2.1

TBSA total body surface area

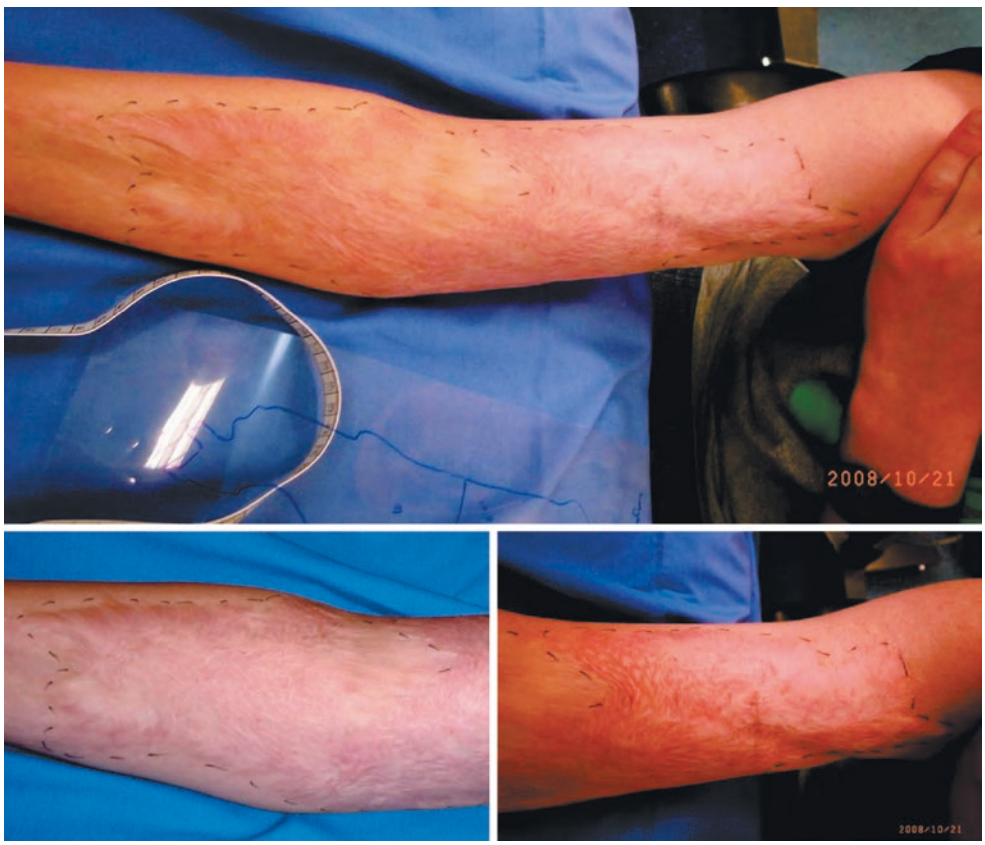


Fig. 17.2 Patient example of substituted and reference scar on arm with tracings of the previous assessment. Substituted scar in picture left (distal scar of arm). Reference scar in picture right (proximal scar of arm)

which has been established as a reliable and valid instrument for the evaluation of this scar aspect [27]. The Cutometer measures the vertical deformation of skin in millimeters during a controlled vacuum. The following elasticity parameters are provided (in mm): maximal skin extension, pliability, elasticity, retraction, and viscoelasticity. In the analysis of all acute and reconstructive scars together, elasticity parameters in the substituted scars were similar to or higher than elasticity data in reference scars, although not statistically different. In the separate analysis of scars in the acute burn category, no differences in elasticity were seen between the substituted and reference areas. In the reconstructive scars, all elasticity parameters were higher in substituted scars, although not statistically significant. Figure 17.3 shows the elasticity data 12 years post-operatively (student *t*-test). Figure 17.4 illustrates the improvement of elasticity of substituted areas compared to reference areas, on the short and long term.

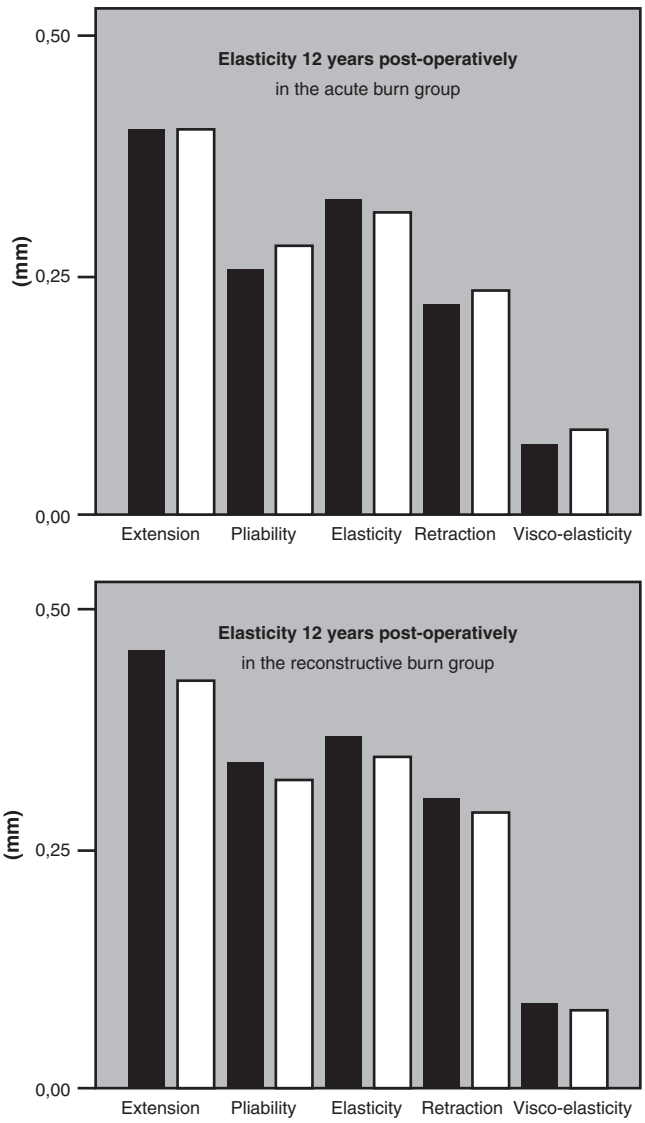


Fig. 17.3 Elasticity 12 years postoperatively . Different parameters of skin elasticity measured by the Cutometer in both the scar groups. Black: substituted scar. White: reference scar

17.2.2 Scar Erythema and Melanin

Scar erythema and melanin were measured with the DermaSpectrometer (Cortex Technology, Denmark). This is a validated assessment tool, which emits light by means of diodes at two defined wavelengths: green light (568 nm) and red light (655 nm) [28]. Photodetectors measure the light reflected by the skin. As green light is absorbed by hemoglobin and red light is absorbed by melanin, an erythema and melanin index can be computed, based on the intensity of absorbed and reflected light. In the analysis of acute and reconstructive scars together and in the analysis of the acute burn group alone, no statistically significant differences in erythema and melanin were found between the substituted and reference scars (Student's *t*-test, data not shown). In the reconstructive scars, a statistically significant difference was found between melanin of the substituted and reference scars. In substituted scars, melanin differed more from patient's normal skin compared to reference scars. However, this difference was only 5% (substitute versus normal skin 1.05; reference versus normal skin 1.00, $p < 0.010$).

17.2.3 Scar Surface Roughness

In this study, the relevant parameter scar surface roughness was assessed objectively. Scar surface roughness was evaluated with the PRIMOS (GFMesstechnik GmbH, Germany). This imaging system produces a three-dimensional image of the micro-topography of the skin and is proven to be reliable and valid in the assessment of surface roughness in scars [22–24, 29]. The system projects a parallel stripe pattern onto the skin and by means of elevation differences on the skin surface, a 3D image is achieved. Accordingly, images are digitized and the software reconstructs the data into several surface roughness parameters. In this study the parameters Sa, Sz, and PC were used and are described as follows. Sa is the arithmetic mean of the surface roughness (μm), Sz is the mean of the five highest peaks and five deepest valleys from the measuring field (mm), and PC (peak count) demonstrates the number of peaks per unit length. In Fig. 17.5 the use of the PRIMOS is demonstrated in one of the patients. In the analysis of the acute and reconstructive scars together, Sa, Sz, and PC were significantly lower (better) in substituted scars, indicating a smoother surface. In the scars of the acute burn category, the three roughness parameters were lower in substituted scars compared to the reference scars, although no statistically significant difference was seen. In the reconstructive scars, all roughness parameters showed

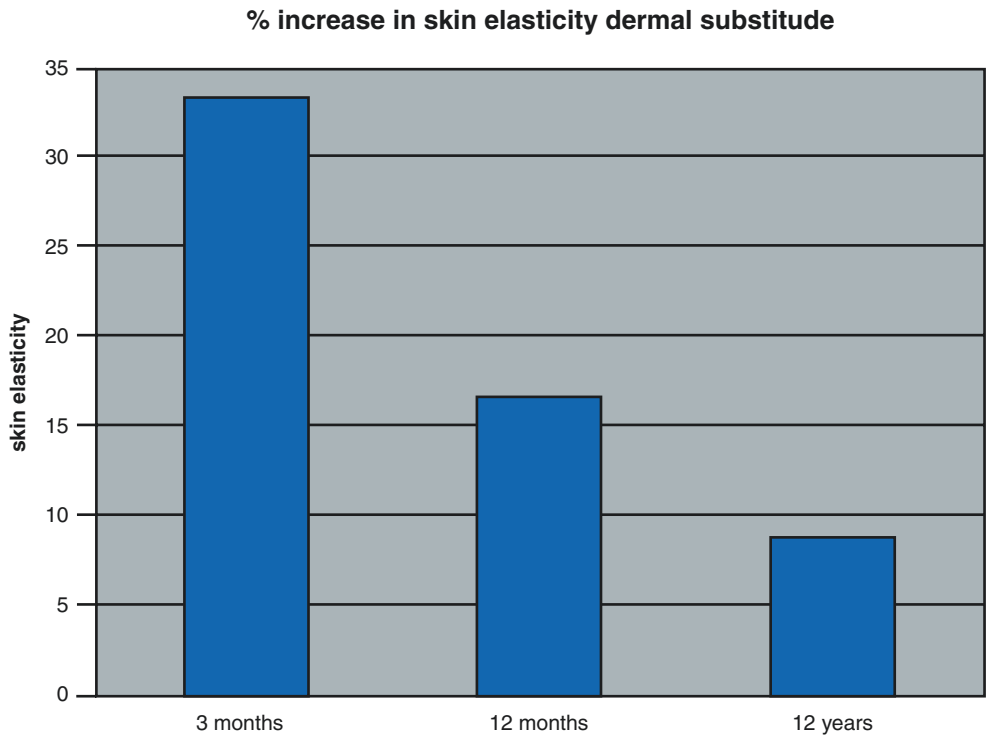


Fig. 17.4 Improvement in scar elasticity. Increase in elasticity of the substituted scar compared to the reference scar measured by the Cutometer in the reconstructive scar group (3 and 12 months, 12 years)

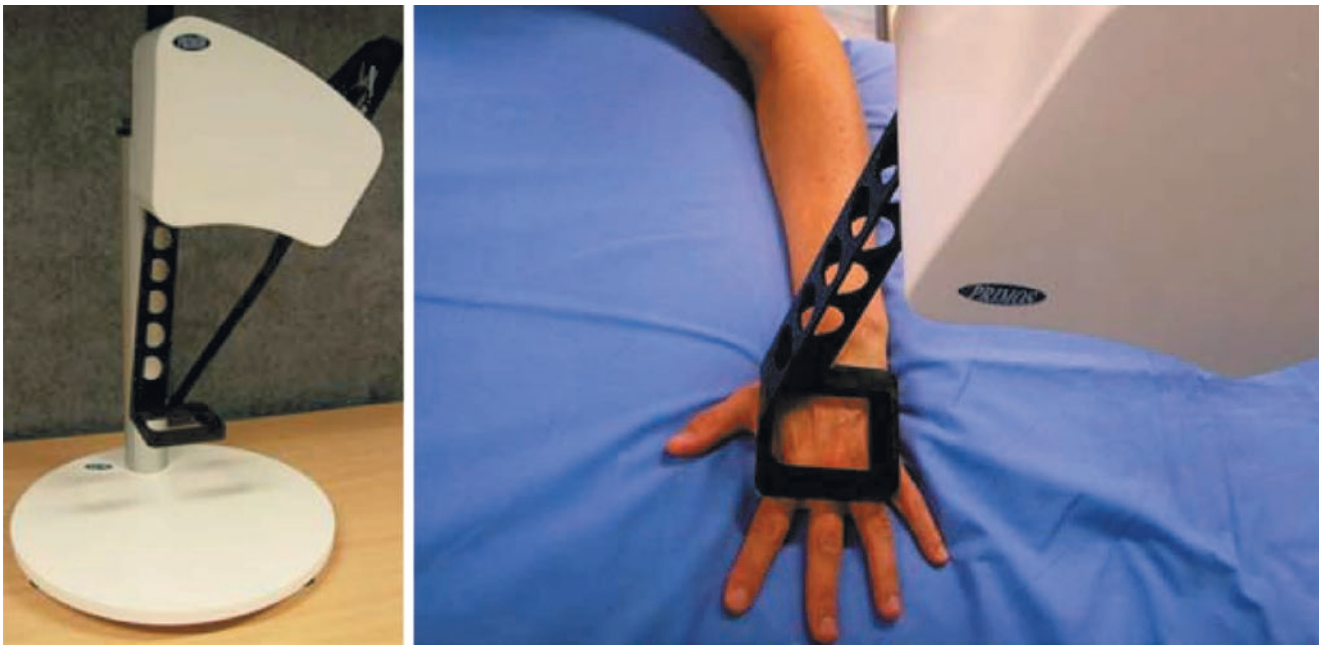


Fig. 17.5 Use of the PRIMOS in study patient. Upper left: The PRIMOS as objective measurement tool of scar surface roughness. Upper right: Use of the PRIMOS in the measurement of a scar on a hand. Middle left: PRIMOS live picture of scar treated with a substitute and a split-skin graft (substitute). Middle center: PRIMOS live picture of scar treated with split-skin graft alone (reference). Middle right: PRIMOS live picture of normal skin. Lower left: PRIMOS picture after filtering of scar treated with a substitute and a split-skin graft (substitute). Lower middle: PRIMOS picture after filtering of scar treated with split-skin graft alone (reference). Lower right: PRIMOS picture after filtering of normal skin

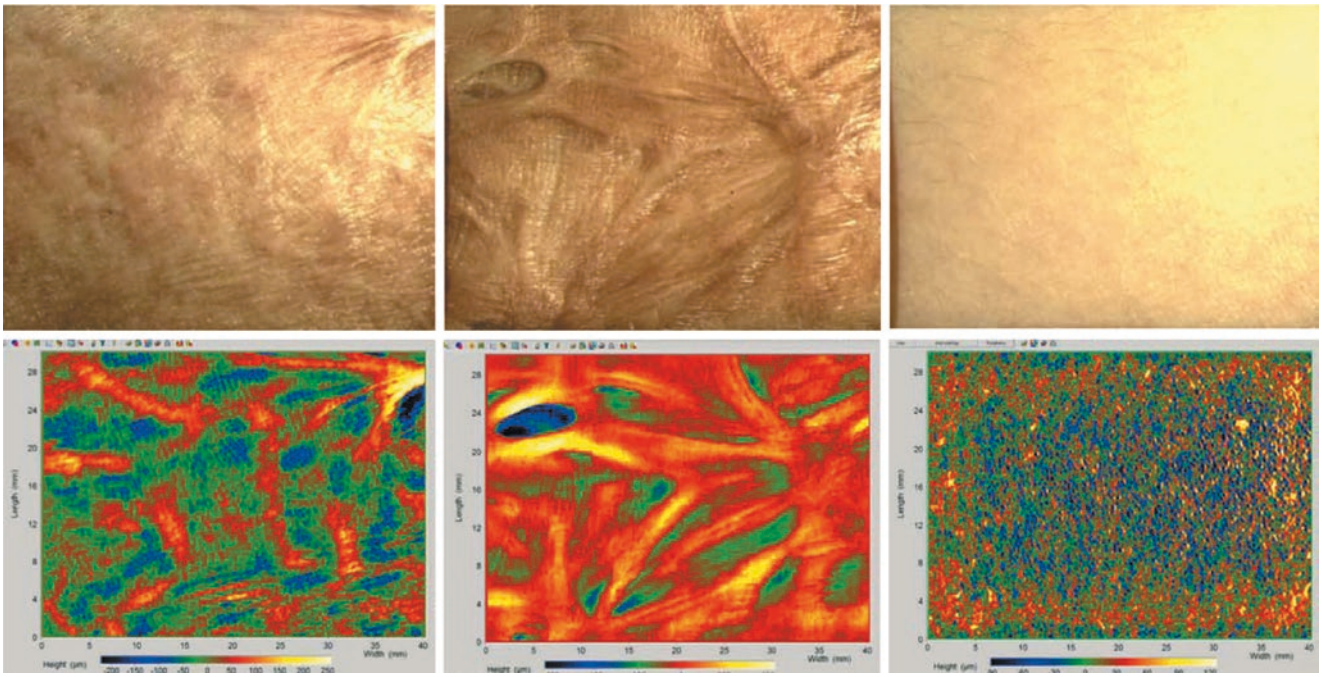


Fig. 17.5 (continued)

lower scores in substituted areas compared to conventionally treated areas, of which Sz differed statistically significantly (Wilcoxon signed-rank test, Fig. 17.6 and Table 17.2).

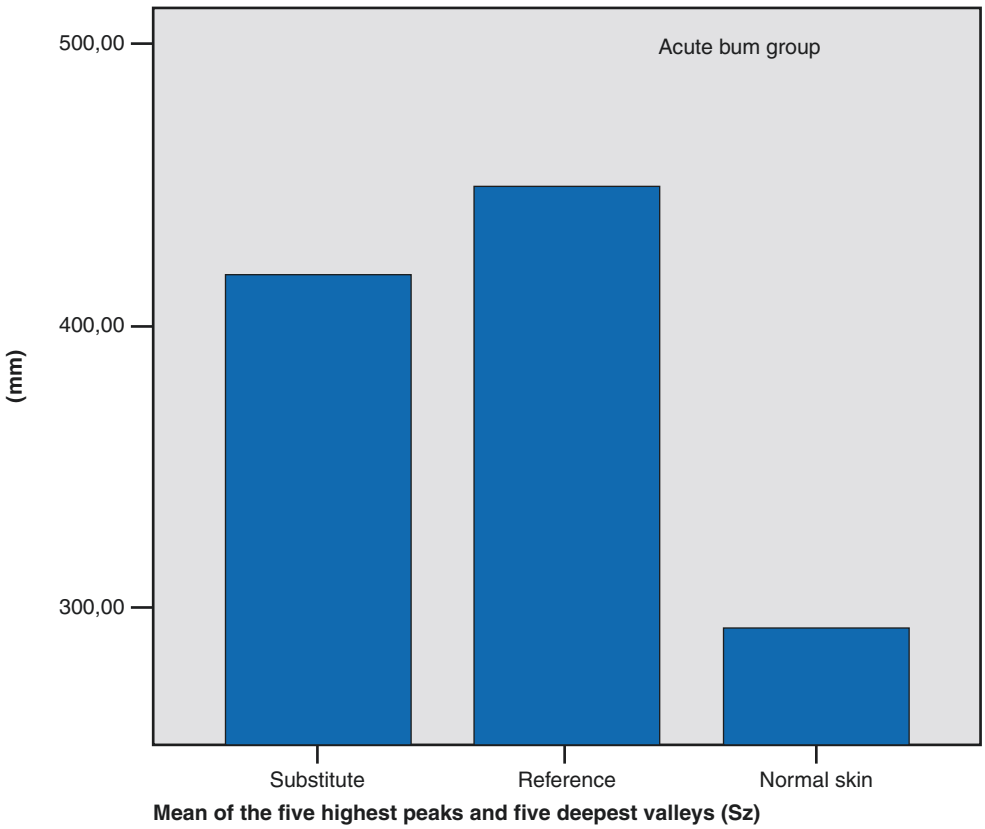
17.2.4 Subjective Scar Evaluation

Lastly, all scars were evaluated subjectively with the POSAS. This is a validated tool which consists of two subscales: the patient and the observer scales [21, 30]. On a 10-point scale, the patient gives his or her opinion on the parameters: color, thickness, surface roughness, pliability, itching, and pain. The observer scale was first validated for the use in burn scars and contained five items: vascularization, pliability, pigmentation, thickness, and relief [21]. Subsequently, the scale was validated for the use in linear scars as well, and therefore, the item surface area was added to include aspects of contraction and scar widening [30]. The total observer score and the total patient score consist of adding the scores of the six items (range 6–60). A low score means a better scar quality: 1 is comparable to normal skin and a score of 10 reflects the worst imaginable scar or sensation. In addition to these items, the observer and the patient give a general opinion on the scar appearance (score 1–10, in which a score of 10 corresponds with the worst possible scar). The observer assessment was performed by three experienced researchers.

Twelve years postoperatively, subjective scores were low (good) for all evaluated scars; a mean score of 3.6 was the highest (worst) observer score. In the acute and reconstructive scars together, a significant difference in favor of the substituted scars was seen for the items pliability, pigmentation, thickness, relief, general score, and the total score (data not shown). Substituted scars received lower (better) observer scores than the reference scars. In the separate analysis of scars in the acute burn group, a statistically significant difference was seen in favor of the substituted areas in all POSAS items, except for vascularization. In scars of the reconstructive category, observer scores for pliability, relief, and the general score were significantly lower (better) for substituted areas (Table 17.3). Assessment by the patient demonstrated that substituted scars in the acute group received a lower (better) total score than the reference scars (substitute 3.2, reference 4.0, $p = 0.034$). In both the groups, other POSAS items did not show significant differences (data not shown).

17.2.5 Substitution in Combination with Different Graft Expansions

All acute burn wounds in this study were treated with a split-skin graft, with or without a dermal substitute. For the skin grafts, different mesh expansions were used in each wound pair; small expansions (mesh 1:1.5 and 1:2) were applied in 20 wound pairs, and larger expansions (mesh 1:3 and 1:4) were used in 15 pairs. Twelve months postoperatively, an analysis was performed to investigate differences between these two groups. At that time, differences in elasticity



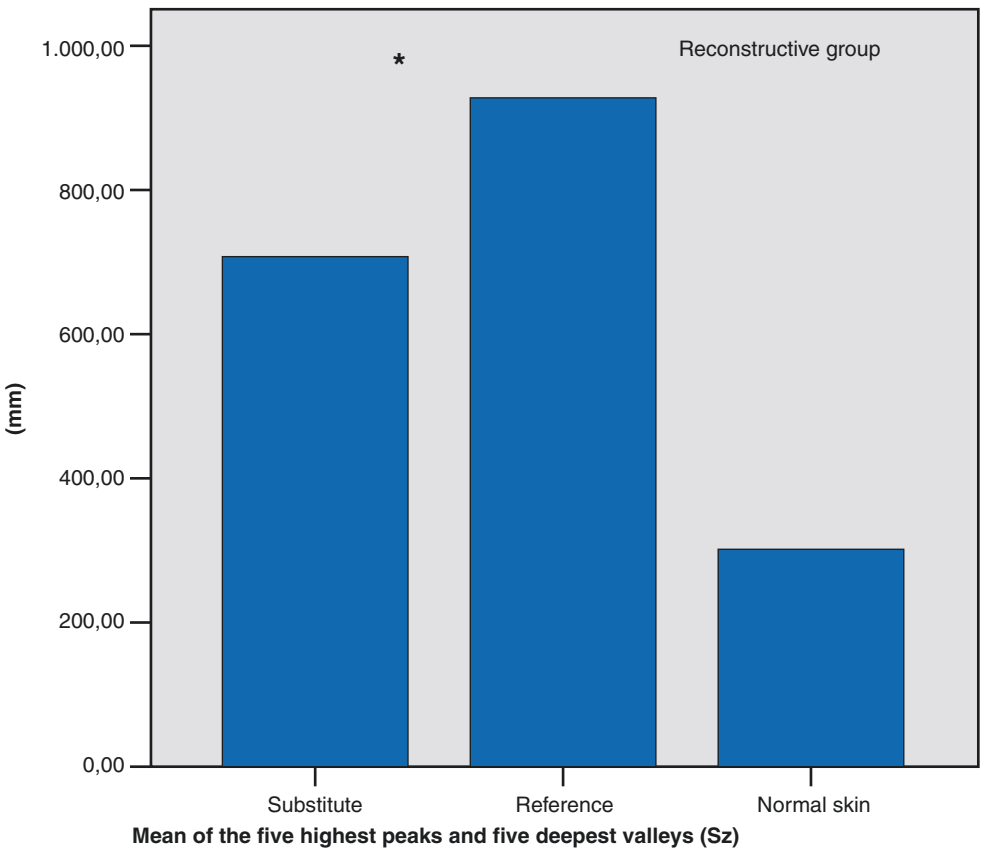


Fig. 17.6 Scar surface roughness in the acute and reconstructive group

Table 17.2 Results of surface roughness measurements

	Substitute	Reference	Normal skin	*p*-value
All scars ($n_{scar\ pairs}$ = 69)				
Sa	42.9	47.1	21.3	0.038*
Sz	558.8	682.0	297.5	0.015*
PC	30.0	39.4	15.2	0.022*
Acute ($n_{scar\ pairs}$ = 35)				
Sa	32.6	36.4	19.6	0.061
Sz	417.6	448.5	291.8	0.604
PC	25.3	34.1	16.3	0.083
Reconstructive ($n_{scar\ pairs}$ = 34)				
Sa	53.9	58.7	23.1	0.275
Sz	709.7	931.7	303.6	0.014*
PC	41.2	52.0	14.0	0.172

Substitute: wound sites treated with the dermal substitute and a split-skin graft
Reference: wound sites treated with a split-skin graft alone (control treatment)
CI confidence interval, *Sa* arithmetic mean of the surface roughness (μm), *Sz* mean of five highest peaks and five deepest valleys from the measuring field (mm), *PC* peak count, number of peaks, *p-value* substitute vs. reference
*$p < 0.038$

Table 17.3 Results of observer scar assessment 12 years postoperatively

	Acute burn group			Reconstructive group		
	Substitute	Reference	*p*-value	Substitute	Reference	*p*-value
Vascularization	2.0	2.2	0.206	2.2	2.2	0.768
Pliability	2.5	3.0	0.023*	3.0	3.6	0.038*
Pigmentation	2.3	2.7	0.002*	2.6	2.6	0.661
Thickness	2.0	2.4	0.001*	2.3	2.5	0.129
Relief	2.3	3.1	<0.001*	2.7	3.2	0.038*
Surface area	1.7	1.9	0.008*	2.4	2.5	0.496
Total score	12.8	15.0	<0.001*	15.2	16.6	0.087

The mean scores of three experienced researchers of the observer scar assessment scale (O-SAS) are shown. In this scale, 1 is comparable to normal skin, and a score of 10 reflects the worst imaginable scar
*$p < 0.038$

between the large and small mesh expansion groups were found.

In the analysis performed at 12 years postoperatively, significant differences were found for several elasticity parameters as well. The parameters pliability, retraction, and viscoelasticity were significantly lower (indicating less pliable scars) in substituted scars compared to the reference scars, in the small expansion group. In the category treated with the larger expansions, significant differences for the elasticity parameters maximal skin extension, elasticity, and retraction were found. Scars treated with the substitute showed higher scores of elasticity (i.e., more pliable) than the reference scars (Fig. 17.7). In this analysis, vascularization, pigmentation, and surface roughness were not significantly different between the substituted and reference scars. The subjective evaluation showed significantly lower (better) scores for relief, surface area, and the total score in the substituted scars with a small expansion. In scars treated with a larger expansion, all POSAS items received significantly lower (better) scores in the substituted scars, except for the item surface area (data not shown).

17.3 Discussion

In this chapter, the results of a long-term follow-up study on dermal substitution are presented. First, long-term subjective and objective data are described in which the clinical effectiveness of a collagen–elastin matrix is shown 12 years after application. In contrast to the scar evaluation at 3 and 12 months postoperatively, an objective evaluation tool for surface roughness was used 12 years postoperatively. Short-term scar assessment had shown a smoother surface in substituted scars compared to reference scars (subjectively), for that reason, we expected a difference in roughness between the substituted and reference scars [20]. In the analysis of the acute burn and reconstructive group together, all three surface roughness parameters were significantly better in the substituted scars, which implies a smoother surface of these scars (Fig. 17.6 and Table 17.2). In reconstructive scars, roughness parameter Sz was significantly lower in scars treated with the substitute. The larger number of patients in the analysis of all scars could have resulted in statistically significant differences.

Results of the objective scar surface roughness support the clinical observation, as numerous substituted scars showed a reduced visibility of the mesh pattern. In addition, in the acute and the reconstructive substituted scars, a better score for relief was found, measured with the POSAS. This positive effect of dermal substitution could be of great value as an irregular scar surface can be cosmetically disturbing and long-lasting, despite scar maturation (Fig. 17.2). How can this effect of dermal substitution be explained? One hypothesis is that the dermal substitute replaces the dermis and bridges the interstices of the autograft. As a consequence, the hypertrophy, which appears in the interstices of the autograft, is less when a dermal substitute is applied. This could explain the smoother surface of the scar.

In several studies, an improvement of elasticity (often evaluated subjectively) was reported in scars treated with a dermal substitute, such as Matriderm® or Integra® [9, 12, 31, 32]. In preceding studies, Van Zuijlen et al. had reported a significantly higher elasticity in substituted areas compared to reference areas in the reconstructive group, 3 months postoperatively [19]. In the scar assessment 12 months postoperatively, the absolute difference in elasticity between the

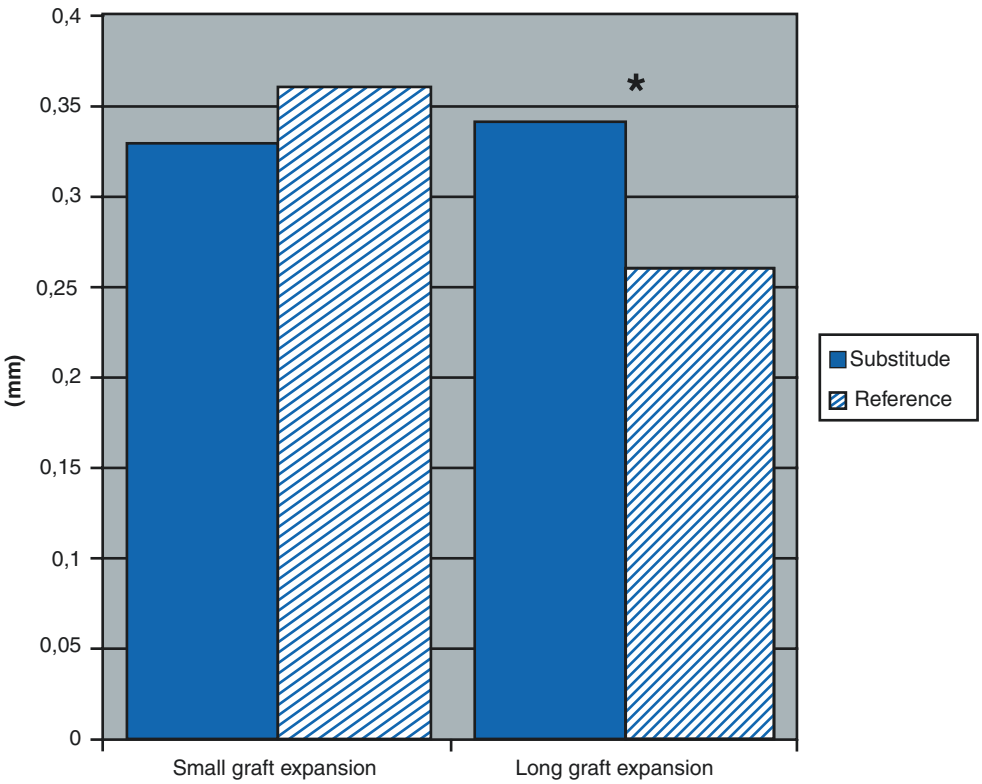


Fig. 17.7 Elasticity and graft expansion. Elasticity of the acute burn scars measured by the Cutometer. The acute burn scars were divided into scars treated with a small graft expansion (mesh 1:1.5 and 1:2) and scars treated with a large graft expansion (mesh 1:3 and 1:4). Substitute: wound sites treated with the dermal substitute and a split-skin graft. Reference: wound sites treated with a split-skin graft alone (control treatment). *$p < 0.009$

substituted and reference scars was the same; however, as both scars had improved, no statistically significant difference was found [20]. For this reason, no significant difference in elasticity was expected 12 years after the application of the substitute. Nevertheless, similar to the results of 12 months postoperatively, the scores were higher in the reconstructive scars treated with the substitute compared to reference scars. In addition, in the acute and the reconstructive substituted scars, a better score for pliability was found, measured with the POSAS. It appears that the application of a substitute in the early phase of wound healing contributed to a lasting higher elasticity. This gain in elasticity in the substituted scars is highest shortly after surgery and remains present, even after 12 years (Fig. 17.4).

Wounds treated with a smaller skin graft expansion generally develop into scars with a higher scar quality compared to scars treated with a larger mesh expansion. Van Zuijlen et al. reported that the effectiveness of the dermal substitute seemed to have a relation with the expansion of the overlying mesh graft [20]; a higher elasticity was found in acute burn scars treated with the substitute in combination with a largely expanded mesh graft (1:3 or 1:4) compared to the reference scars, after 1 year. Twelve years post-surgery, a higher elasticity was seen in the reference scars treated with a smaller expansion compared to the scars treated with the larger expansion. The substituted scars, however, showed almost the same elasticity when treated with large and small expansions (Fig. 17.7). Additionally, the elasticity of substituted scars treated with a larger expansion graft was significantly higher than non-substituted scars with the same expansion. In contrast to these results, the elasticity of substituted scars treated with a small graft expansion was lower than the reference scars. Dermal substitution appears to contribute to a higher elasticity, mainly in combination with a larger mesh expansion.

Besides the objective measurement tools, a subjective scar assessment tool was also used. The subjective scar data from this study are comparable with the results of other clinical studies on the use of dermal substitutes [6, 9, 12, 20, 32]. Three and 12 months after surgery, the subjective scar assessment using the VSS showed no significant differences between scars treated with and without the dermal substitute. Twelve years after application, the POSAS was used for subjective scar evaluation, as this tool was found to be more reliable than the VSS. It was remarkable that subjective scores were relatively low (good) for all scars, probably due to prolonged scar maturation. Despite the results seen shortly after surgery, the appearance of substituted scars, 12 years post-surgery, was found to be better than the reference scars; in both the reconstructive and the acute burn scars, significantly lower (better) scores were reported for the substituted scars in several POSAS items (Table 17.3). A shortcoming of the study was the impossibility to blind the observers, because no randomization procedure was applied, and in each patient the substitute was applied on the right, superior, or medial (side of the) wound. Therefore, a bias might have occurred.

Another disadvantage of this treatment allocation is that in patients with only one wound, two different therapies were used within the same wound. It is possible that treatments could have affected each other. Furthermore, after 12 years, some study areas were difficult to trace due to improvement of these areas. In several patients, it was therefore complicated to distinguish the substituted scar from the reference scar or even the surrounding skin or scar, especially when repeated corrective procedures were applied in that area. The scars were excluded if the original study areas could not be retraced or measured. Another limitation of the study was the difficulty for some patients to assess their own scars. Patients with a high percentage total body surface area (TBSA) burned found it complicated to give their opinion on a relatively small study area. Despite this, in the analysis of all scars, the total subjective patient score of substituted scars was lower compared to the reference scars, but not significantly different (substitute 18.2; reference 19.7; $p = 0.089$).

17.4 Conclusion

This chapter describes the first study that objectifies scar outcome after 12 years with the use of a collagen–elastin matrix in acute and reconstructive burn surgery. This dermal substitute showed clinical effectiveness by a significant increase of scar elasticity in the short term. Even after a period of 12 years, improved scar parameters in both acute and reconstructive substituted wounds were found. For the first time, scar surface roughness was objectified, and it was shown that substituted areas were significantly smoother than areas treated with an SSG only. Another important finding was the increased elasticity in substituted scars treated with a largely expanded autograft. The results of this study indicate a long-lasting effect of dermal substitution on scar quality, and it can be concluded that dermal substitutes play an important role in the treatment of full-thickness skin defects.

Acknowledgments The original clinical trial was financially supported by grants from the Technology Foundation and the Dutch Organization for Scientific Research. The follow-up study was financially supported by the Dutch Burns Foundation.

References

1. Burke JF, Yannas IV, Quinby WC Jr, Bondoc CC, Jung WK. Successful use of a physiologically acceptable artificial skin in the treatment of extensive burn injury. Ann Surg. 1981;194(4):413–28.
2. De Vries HJ, Mekkes JR, Middelkoop E, Hinrichs WL, Wildevuur CR, Westerhof W. Dermal substitutes for full-thickness wounds in a one-stage grafting model. Wound Repair Regen. 1993;1(4):244–52.
3. De Vries HJ, Middelkoop E, Mekkes JR, Dutrieux RP, Wildevuur CH, Westerhof H. Dermal regeneration in native non-cross-linked collagen sponges with different extracellular matrix molecules. Wound Repair Regen. 1994;2(1):37–47.
4. Haslik W, Kamolz LP, Nathschlager G, Andel H, Meissl G, Frey M. First experiences with the collagenelastin matrix Matriderm as a dermal substitute in severe burn injuries of the hand. Burns. 2007;33(3):364–8.
5. Lamme EN, de Vries HJ, van Veen H, Gabbiani G, Westerhof W, Middelkoop E. Extracellular matrix characterization during healing of full-thickness wounds treated with a collagen/elastin dermal substitute shows improved skin regeneration in pigs. J Histochem Cytochem. 1996;44(11):1311–22.
6. Branski LK, Herndon DN, Pereira C, Mlcak RP, Celis MM, Lee JO, Sanford AP, Norbury WB, Zhang XJ, Jeschke MG. Longitudinal assessment of Integra in primary burn management: a randomized pediatric clinical trial. Crit Care Med. 2007;35(11):2615–23.
7. Eaglstein WH, Alvarez OM, Auletta M, Leffel D, Rogers GS, Zitelli JA, Norris JE, Thomas I, Irondo M, Fewkes J, Hardin-Young J, Duff RG, Sabolinski ML. Acute excisional wounds treated with a tissue-engineered skin (Apligraf). Dermatol Surg. 1999;25(3):195–201.
8. Hansbrough JF, Dore C, Hansbrough WB. Clinical trials of a living dermal tissue replacement placed beneath meshed, split-thickness skin grafts on excised burn wounds. J Burn Care Rehabil. 1992;13(5):519–29.
9. Haslik W, Kamolz LP, Manna F, Hladik M, Rath T, Frey M. Management of full-thickness skin defects in the hand and wrist region: first long-term experiences with the dermal matrix Matriderm. J Plast Reconstr Aesthet Surg. 2010;63(2):360–4.
10. Heimbach D, Luterman A, Burke J, Cram A, Herndon D, Hunt J, Jordan M, McManus W, Solem L, Warden G, et al. Artificial dermis for major burns. A multicenter randomized clinical trial. Ann Surg. 1988;208(3):313–20.
11. Heimbach DM, Warden GD, Luterman A, Jordan MH, Ozobia N, Ryan CM, Voigt DW, Hickerson WL, Saffle JR, DeClement FA, Sheridan RL, Dimick AR. Multicenter postapproval clinical trial of Integra dermal regeneration template for burn treatment. J Burn Care Rehabil. 2003;24(1):42–8.
12. Ryssel H, Gazyakan E, Germann G, Ohlbauer M. The use of MatriDerm in early excision and simultaneous autologous skin grafting in burns—a pilot study. Burns. 2008;34(1):93–7.
13. Sheridan R, Choucair R, Donelan M, Lydon M, Petras L, Tompkins R. Acellular allodermis in burns surgery: 1-year results of a pilot trial. J Burn Care Rehabil. 1998;19(6):528–30.
14. Sheridan RL, Hegarty M, Tompkins RG, Burke JF. Artificial skin in massive burns—results to ten years. Eur J Plast Surg. 1994;17:91–3.
15. Wainwright D, Madden M, Luterman A, Hunt J, Monafo W, Heimbach D, Kagan R, Sittig K, Dimick A, Herndon D. Clinical evaluation of an acellular allograft dermal matrix in full-thickness burns. J Burn Care Rehabil. 1996;17(2):124–36.
16. Wainwright DJ. Use of an acellular allograft dermal matrix (AlloDerm) in the management of full-thickness burns. Burns. 1995;21(4):243–8.
17. Waymack P, Duff RG, Sabolinski M. The effect of a tissue engineered bilayered living skin analog, over meshed split-thickness autografts on the healing of excised burn wounds. The Apligraf Burn Study Group. Burns. 2000;26(7):609–19.
18. Bloemen MC, van Leeuwen MC, van Vucht NE, van Zuijlen PP, Middelkoop E. Dermal substitution in acute burns and reconstructive surgery: a 12-year follow-up. Plast Reconstr Surg. 2010;125(5):1450–9.
19. van Zuijlen PP, van Trier AJ, Vloemans JF, Groenevelt F, Kreis RW, Middelkoop E. Graft survival and effectiveness of dermal substitution in burns and reconstructive surgery in a one-stage grafting model. Plast Reconstr Surg. 2000;106(3):615–23.

20. van Zuijlen PP, Vloemans JF, van Trier AJ, Suijker MH, van Unen E, Groenevelt F, Kreis RW, Middelkoop E. Dermal substitution in acute burns and reconstructive surgery: a subjective and objective long-term follow-up. Plast Reconstr Surg. 2001;108(7):1938–46.
21. Draaijers LJ, Tempelman FR, Botman YA, Tuinebreijer WE, Middelkoop E, Kreis RW, van Zuijlen PP. The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation. Plast Reconstr Surg. 2004;113(7):1960–5; discussion 6–7.
22. Bloemen MCT, van Gerven MS, van der Wal MBA, Verhaegen PDHM, Middelkoop E. An objective measuring device for surface roughness in skin and scars. J Am Acad Dermatol. 2011;64(4):706–15.
23. Friedman PM, Skover GR, Payonk G, Geronemus RG. Quantitative evaluation of nonablative laser technology. Semin Cutan Med Surg. 2002;21(4):266–73.
24. Friedman PM, Skover GR, Payonk G, Kauvar AN, Geronemus RG. 3D in-vivo optical skin imaging for topographical quantitative assessment of non-ablative laser technology. Dermatol Surg. 2002;28(3):199–204.
25. Oliveira GV, Chinkes D, Mitchell C, Oliveras G, Hawkins HK, Herndon DN. Objective assessment of burn scar vascularity, erythema, pliability, thickness, and planimetry. Dermatol Surg. 2005;31(1):48–58.
26. van Zuijlen PP, Lamme EN, van Galen MJ, van Marle J, Kreis RW, Middelkoop E. Long-term results of a clinical trial on dermal substitution. A light microscopy and Fourier analysis based evaluation. Burns. 2002;28(2):151–60.
27. Draaijers LJ, Botman YA, Tempelman FR, Kreis RW, Middelkoop E, van Zuijlen PP. Skin elasticity meter or subjective evaluation in scars: a reliability assessment. Burns. 2004;30(2):109–14.
28. Draaijers LJ, Tempelman FR, Botman YA, Kreis RW, Middelkoop E, van Zuijlen PP. Colour evaluation in scars: tristimulus colorimeter, narrow-band simple reflectance meter or subjective evaluation? Burns. 2004;30(2):103–7.
29. Jacobi U, Chen M, Frankowski G, Sinkgraven R, Hund M, Rzany B, Sterry W, Lademann J. In vivo determination of skin surface topography using an optical 3D device. Skin Res Technol. 2004;10(4):207–14.
30. van de Kar AL, Corion LU, Smeulders MJ, Draaijers LJ, van der Horst CM, van Zuijlen PP. Reliable and feasible evaluation of linear scars by the patient and observer scar assessment scale. Plast Reconstr Surg. 2005;116(2):514–22.
31. Clayman MA, Clayman SM, Mozingo DW. The use of collagen-glycosaminoglycan copolymer (Integra) for the repair of hypertrophic scars and keloids. J Burn Care Res. 2006;27(3):404–9.
32. Dantzer E, Queruel P, Salinier L, Palmier B, Quinot JF. Dermal regeneration template for deep hand burns: clinical utility for both early grafting and reconstructive surgery. Br J Plast Surg. 2003;56(8):764–74.

Part V

Burn Reconstruction: Special Body Regions

Burn Reconstruction: Neck Region

18

Norbert Pallua and Erhan Demir

18.1 Part I: Basic Principles

18.1.1 Introduction

The cervical region with its functional and anatomical design to achieve a maximum range of motion is of eminent importance. The anatomic prone interposition of the neck between the corpus and the head represents great challenges and opportunities. Therefore, the reconstructive surgeon is confronted with a unique set of problems compared with the rest of the body. The thin pliable neck is prone to contracture formation. It is important to emphasize that burn scar contractures of the neck region have an impact on facial deformities and may cause considerable problems especially in the developing period of young burn victims [1, 2].

The success in treatment requires sound surgical judgment, technical expertise in combination with a thorough understanding of the pathophysiology of the burn wound, scarring, neck contracture formation, and alteration of skin texture and pigmentation. Realistic expectations of both patients and surgeons are crucial to achieve and value successful treatment outcomes. Still, profound functional and aesthetic improvement of the neck region for this large group of challenging patients is possible [3].

The requirement of a well-functioning and extensive team in the approach to reconstructive head and neck surgery cannot be overemphasized [4]. Therefore, in addition to the plastic surgeon, many disciplines such as skilled burn nursing, experienced occupational and physical therapy, and psychological and social support systems are required to successfully treat and care for patients with burns of the neck. The care of a patient from the onset of a major burn involving the head and neck to a successful reconstructive outcome requires skill, patience, determination, and enthusiasm from all who are involved [1].

N. Pallua (✉) · E. Demir
Private Clinic Pallua & Grašys, Düsseldorf, Germany

Aachen University of Technology, Aachen, Germany
e-mail: info@pallua.de

18.1.2 Pathogenesis and Associated Problems of Neck Contractures

The skin of the neck is thin and pliable and highly flexible; it is prone to contracture formation following deep burns with tissue damage and scarring. While superficial second-degree burns usually heal without scars or pigment changes, still some completely epithelialized "medium-thickness" superficial burns may demonstrate long-term changes in skin texture and pigmentation. Deep second-degree burns in the neck region usually require surgical intervention with tangential excision and skin grafting or the use of biological membranes (Biobrane® or Suprathel®). After the initial healing with wound closure and complete epithelialization these patients require careful management and monitoring, as they have the potential to develop severe late hypertrophic scars and contractures. Additional preventive perioperative measures after surgery include the immediate application of neck extension casts.

The pathologic process of wound contracture involves contraction of tissue by myofibroblasts until the limits of neck motion are reached. Wound contracture occurs during scar remodeling as collagen undergoes reorganization. The resulting distortion may be either extrinsic or intrinsic. Extrinsic contractures result from shrinking of adjacent tissues, whereas intrinsic contractures result from direct contracture of the affected region. Extrinsic contractures require release; intrinsic contractures require replacement of tissue.

Full-thickness injuries are usually excised and skin grafted. Any tension on the neck region may promote early hypertrophic scarring. Relief of neck tension requires either focal release with Z-plasties or extensive adhesiolysis and defect coverage with flaps [1, 5].

At first signs or any tendency towards hypertrophic scarring and contracture formation of skin grafts, ancillary

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_18

modalities such as compression garments or silicon pressure treatment need to be carried out.

Patients with neck contractures are confronted with several problems. Burn scar contractures not only affect neck movements but also face function as traction forces may pull the chin, cheeks, and lower lip caudally or by tension through either normal or scarred cheek skin pulling down the lower eyelids. Increased tension in facial scars caused by burn contractures of the neck can create increases in the size, thickness, and contracture of hypertrophic scars of the face.

In the developing child considerable problems, including flexion deformity with restricted extension, lateral flexion and rotation, aching of muscle and vertebral joints eventually with compensatory kyphosis posture, growth disturbances of the spine, incomplete oral occlusion with drooling of saliva, airway problems, and dental imbalance with severe permanent damage due to neck contractures are well-documented [5, 6].

In addition to pure physical problems, studies clearly indicate that children with extensive head and neck scarring from burns may have temporary or permanent alterations in their process of psychological growth and development [7].

Table 18.1 Achauer classification of anterior neck contractures

Achauer classification of anterior neck contractures	
I—Mild defect	Scar band which involves less than 1/3 of the anterior surface of the neck
II—Moderate defect	More than 1/3 but less than 2/3 of the anterior surface involved
III—Severe defect	Greater than 2/3 of the anterior surface of the neck
IV—Extensive defect	A mentosternal adhesion

Table 18.2 Classification of cervical burn contractures by Remensnyder und Donelan (2002)

1. Severe neck contractures	
a.	Labiosternal
b.	Mentosternal
2. Moderate neck contractures	
a.	Cervicosternal
b.	Heavy multiple bands
c.	Upper neck involvement exclusively
3. Mild neck contractures	
a.	Discrete linear bands
b.	Isolated cervical scars

18.1.3 Evaluation and Classification of Burn-Related Neck Deformities

In 1958 Kirschbaum reported about Spina's classification of neck contractures into central, lateral, or complete [8]. Later Achauer classified anterior neck contractures into mild, moderate, extensive, and severe depending on the fraction of the anterior part of the neck involved in the contracting band [9].

A classification in three main groups of neck contractures (severe, moderate, and mild) defined by the degree of involvement and functional deformity has been described by Remensnyder und Donelan in 2002 [5].

The classification proposed by Remensnyder und Donelan is very useful while reviewing and analyzing patients, as the degree of involvement and functional deformity, are described very precisely by the abnormal joining up of various anatomical areas. During the assembly of an individual surgical treatment plan for mentosternal contractures, the Achauer classification describes the extent of the anterior neck defect after surgical release very well and is therefore of eminent practical use (Tables 18.1 and 18.2).

18.1.4 Case Samples

Especially in the group with *severe neck contractures*, the functional impairment is a very distressing problem, with the burn scar extending directly from the lower lip down to the sternum. The head is uncomfortably fixed in a caudal position to the chest with the mandible involved in all cases. The severe flexed position limits any head and neck movements to a certain degree. You may notice that these patients tend to walk around with their mouths constantly open to reduce the tension of the contracture (Fig. 18.1).

Moderate neck contractures cause discomfort and reduced neck movements with some degree of limitations in the lower facial features (Fig. 18.2).

Mild contractures with isolated scars create discomfort with a minor degree of tension on the lower face.

18.1.5 Prevention, Nonsurgical Treatment Modalities, and Adjunct Surgical Procedures

In the treatment of burn patients, the development of hypertrophic scarring and contractures belong to the most common and frustrating problems. In the neck region, due to the fact that the knowledge of the pathogenesis is still limited to some extent, different techniques are used.

Nonsurgical management options include massage, hydrotherapy, ultrasound therapy, or adhesive tapes. However, the two most commonly accepted noninvasive therapies without major side effects are topical silicone gel application and pressure therapy. Different studies have demonstrated that the silicone gel sheeting is a safe and effective option in the management of hypertrophic scars. Pressure therapy is essential in the treatment of neck burns and is recommended as a "first-line therapy" even if scientific evidence of its efficacy is limited.

Useful *invasive strategies* such as laser therapy, radiotherapy, cryotherapy, high pressure steroid injections, and

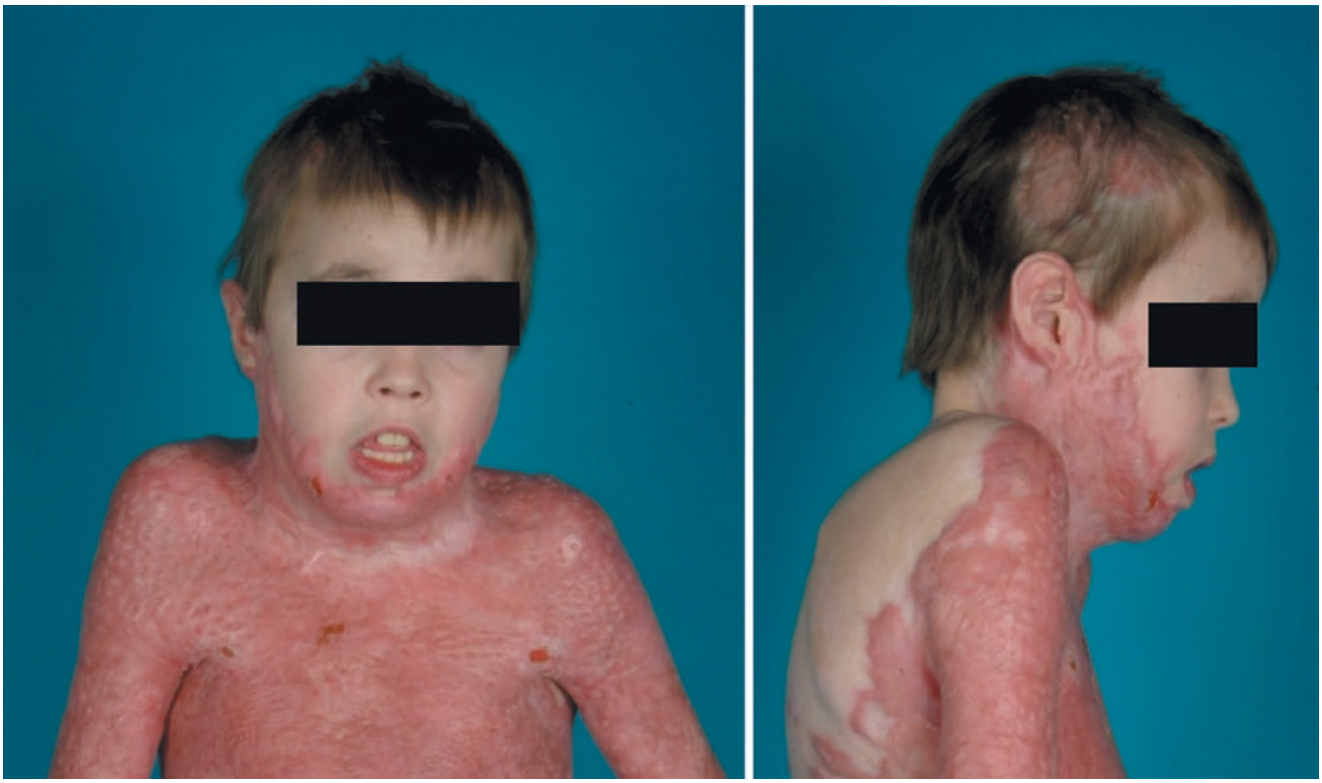


Fig. 18.1 Severe neck contracture

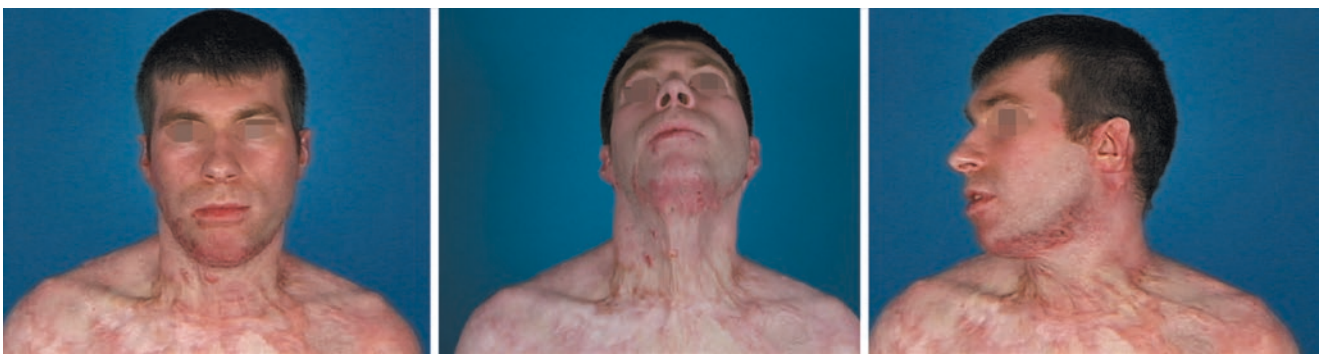


Fig. 18.2 Moderate neck contracture with multiple bands

application of cytokines such as TGF-ß or interferon-α2b are most commonly used [10].

18.2 Part II: Surgical Reconstruction of Neck Contractures

18.2.1 Indications

Neck contractures with functional and aesthetic deficits, drooling, dental deterioration, folliculitis, significant deformity, and obstacle for intubation for general anesthesia are indications to reconstruct the neck region [11]. Severe neck flexion contractures on the acute phase often require early reconstruction to aid in airway management. Neck contractures should usually be managed prior to carrying out facial burn reconstruction. Due to the extrinsic contractile forces from the neck, any facial deformity may adversely affect the maturation of facial scars [1].

18.2.2 Reconstructive Options and Guidelines

In comparison to burn injuries of the face with distorting features, proportions, and expression, thermal injuries of the neck region result rather in functional impairments than aesthetic alterations. They require careful strategic planning in which different reconstructive options are analyzed, and

areas with distortion of neck features, displaced mobile structures, and compression of soft tissue contours requiring reconstructive surgery are carefully prioritized [9]. However, major deformities of patients with various forms of neck contractures caused by burns may limit both neck and jaw mobility and may also influence and increase facial deformities. In order to achieve optimal correction of burned facial deformities of patients who have scarring of both the face and neck, it is necessary to correct the neck contracture first in order to attain the best possible result of successful facial reconstruction [5].

Ignoring these principles may result in iatrogenic failures and catastrophes during the process of reconstructive surgery of the head and neck following thermal injuries.

Many surgical approaches with varying success for the treatment of neck contractures or facial resurfacing following burns are favored including skin grafting, Z-plasties, a variety of local skin flaps with or without expansion, transferred regional flaps, and microsurgical free flaps [11–14]. Generally, to achieve satisfactory functional and aesthetic results, the texture, color, and thickness of the flap need to be similar to those of the original tissue [15]. Therefore, the technically most feasible operation is favored if functional and aesthetic results are good, and postoperative risks for recurrence remain low.

18.2.2.1 Mild Defects

Mild scar bands can generally be corrected by the use of local flaps or Z-plasties. As vertical scars of the neck are likely to produce contractures, the vertical scar is converted to a transverse orientation.

18.2.2.2 Moderate Defects

Local flaps are not useful to correct moderate neck contractures. One option is to consider tissue expansion: unscarred lateral aspects of the neck are expanded, and afterwards the adjacent pre-expanded skin is brought into the area of contracture. The lateral skin can be stretched and transposed medially. The lack of hard tissue immediately underneath the expanded skin limits efficiency of expansion procedures in the neck region.

Skin grafting should be avoided if possible. There is a tendency for the transplanted skin to contract as the neck angle does not oppose shrinkage.

18.2.2.3 Severe and Extensive Defects

Severe contractures require regional flaps, any types of local flaps are not adequate.

Extensive (mentosternal adhesion) contractures require an extensive surgical release and flap coverage. The importance of an extensive, complete release cannot be overemphasized. The most common error is to do an inadequate release. All contracting bands regardless of the depth require release. This procedure may include strap muscles in depth and the midlateral neck in width. Defect coverage options include regional flaps such as the supraclavicular island flap (SIF-flap) or the trapezius flap as primary options; free flaps remain as second options [2, 16–20].

18.2.3 Skin Grafts

Skin grafts after scar release are suitable, but there is a tendency for recurrence of contracture. Therefore, after extensive scar release and thorough hemostasis, split-thickness skin graft sheets (non-meshed) are placed in transversely oriented fashion. A pressure dressing with foam rubber sponges is applied. It is critical to immobilize the neck for 14 days with a custom-made splint [9, 11]. A recurrence rate of 89% without splinting in comparison to 17% after splinting is reported [21]. However, skin grafts may work well, but they require the prolonged period of neck immobilization and pressure application and are often not aesthetically pleasing.

18.2.4 Dermal Regenerative Templates

For the past several years, artificial dermal substitutes have been developed from alloplastic or xenographic materials, e.g., AlloDerm®, Integra®, or Matriderm® [3, 22, 23].

Following full-thickness excision of scars and the release of contractures utilization of dermal substitutes or dermal regenerative templates such as Integra® or Matriderm® in combination with skin grafts demonstrated some promising results [22, 23].

Yannis and Burke initially described in 1980 the two-layered template composed of semipermeable silicone membrane and biodegradable collagen–glycosaminoglycan matrix [24]. The implanted material has been found to form a layer of parenchymal structures resembling dermis. In the second stage, after skin grafting, acceptable results of the neck region are possible [25, 26] (Figs. 18.3, 18.4, 18.5 and 18.6).

Another template is Matriderm® which contains non-crosslinked bovine collagen types I, III, V, and elastine. It is available as 1 mm or 2 mm thick sheets. Good outcomes are recently reported after early excision and Matriderm® application with simultaneous autologous skin grafting in facial burns [23]. However, early experimental results revealed no major differences in engraftment rates or vascularization between Matriderm® and Integra® [22].

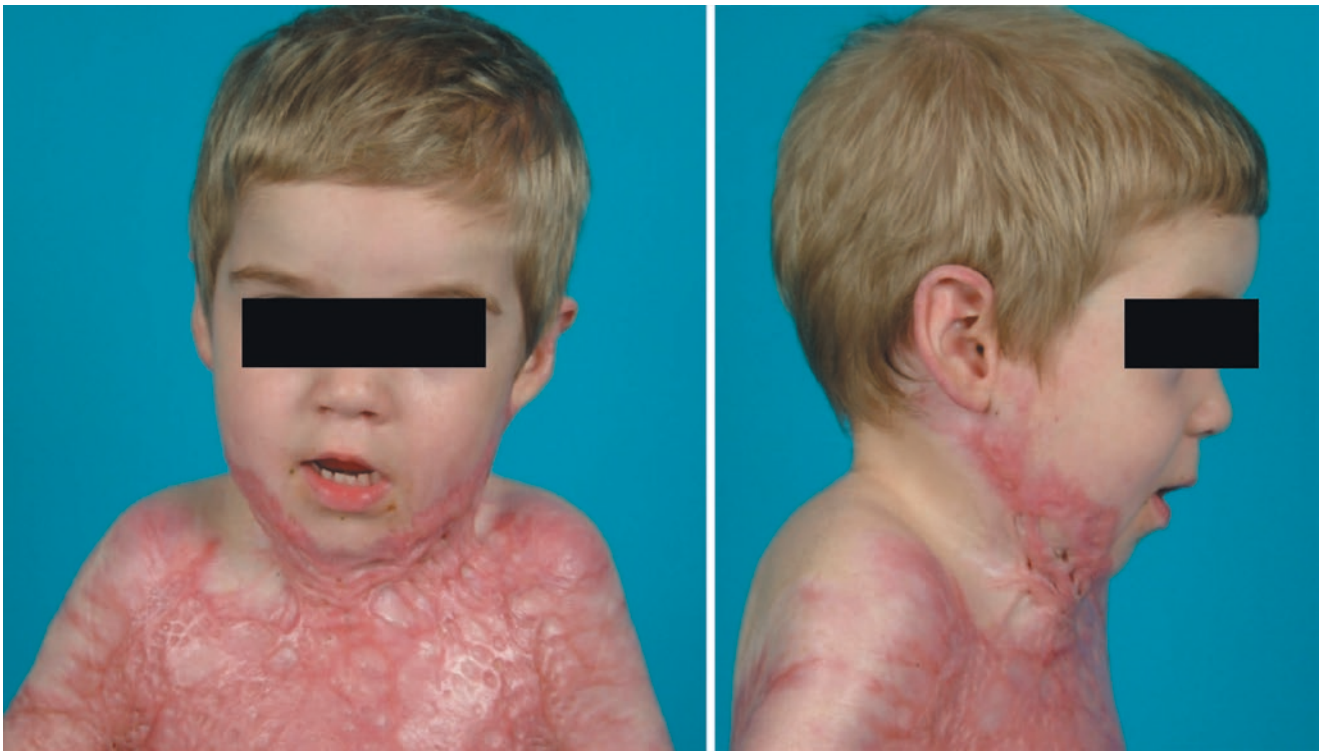


Fig. 18.3 Severe neck contracture, scheduled for scar release and Integra® transplantation

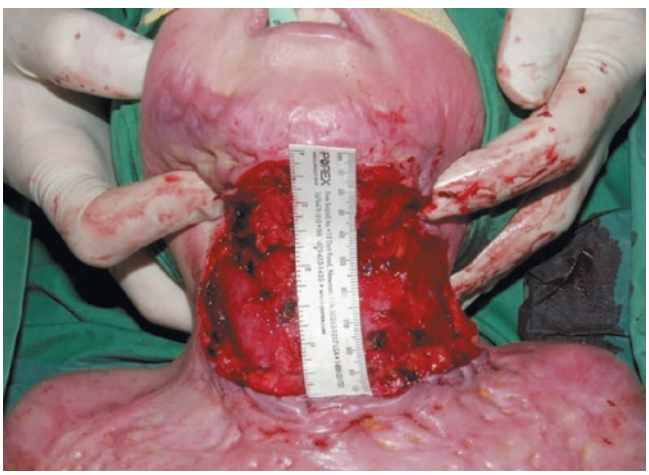


Fig. 18.4 Scar excision and release

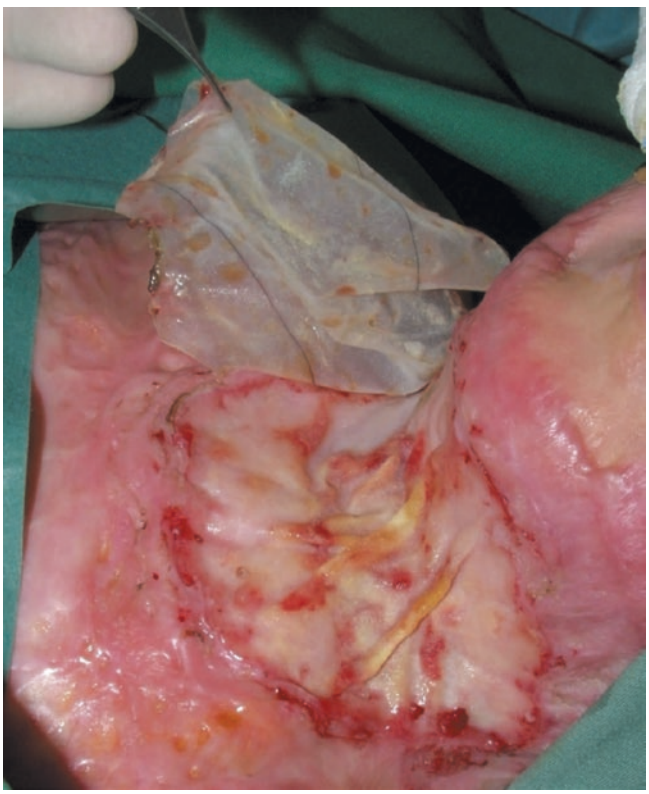


Fig. 18.5 Integra® transplantation

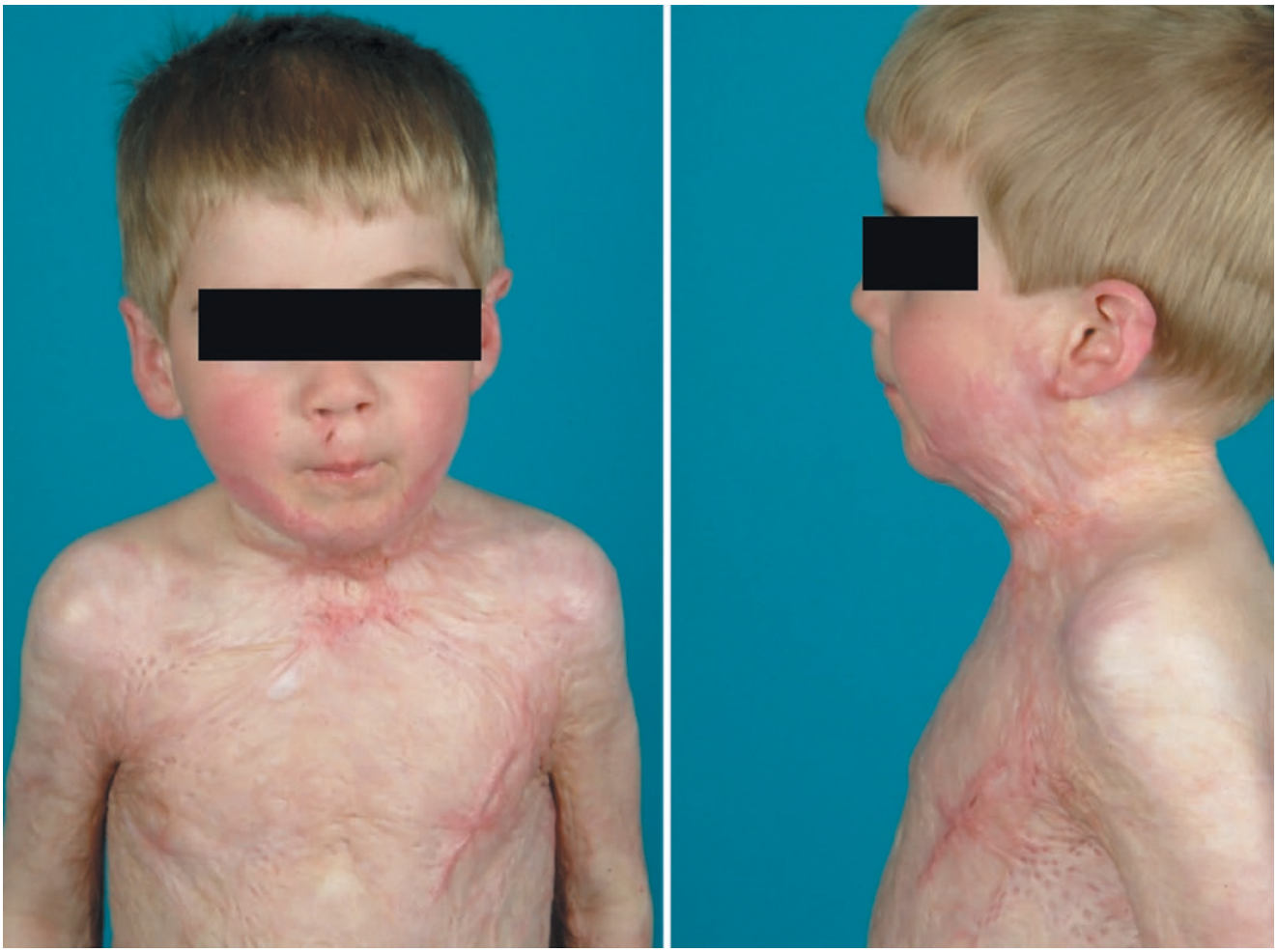


Fig. 18.6 Temporary sufficient outcome after full-thickness skin graft transplantation on Integra®

18.2.5 Local Flaps

Any type of local tissue without scars might become useful to restore smaller scar bands or contracture of the neck area after mobilization. Unfortunately, nearby tissue is often burnt and unavailable [27].

Any axial skin flap, Z-plasty, or W-plasty technique is based on the principle of mobilizing a full segment of skin without disturbance of their vascular supplies from an area adjacent to the region to be resurfaced. After scar excision and contracture release the local flaps are interposed in an opposite direction to release the vector of tension [3]. It might be very useful to include the platysma or cervical fascia underneath the transposed flap to secure vascular blood supply. Especially in severe cases with deep burns when Z-plasties are performed to release tension bands without the possibility to resurface the neck region with uninjured skin, this technical modification of including muscle or fascia will enhance local flap survival rates.

18.2.6 Tissue Expansion

The technique of tissue expansion is based on the dynamic nature in which the integument responds to constant mechanical stress load using an inflatable device system, such as an expander. The neck region is not the primary region for direct application of expanders, in comparison to pre-expanded regional or free flaps, which have a permanent place in the armamentarium of reconstructive burn surgery of the neck region. Tissue expanders should be used with caution in the head and neck region [1]. Stretching adjacent tissue in order to carry out scar excision may result in an increase in tension and can lead to iatrogenic contour changes. However, expansion of the skin and local flap coverage might be useful in smaller defects as tissue expansion offers the chance to replace unstable neck tissue with uninjured normal adjacent tissue. Larger defects usually require regional flaps from distant sites [1, 28–30].

18.2.7 Regional Flaps

Extensive and often recurrent neck flexion contracture with defects larger than two thirds of the anterior neck require distant tissue and are usually not amenable to local flaps [9]. Regional flaps are the primary choice as they provide full-thickness skin and subcutaneous tissue, with improved aesthetics and superior resurfacing options compared to skin grafts without the need for microsurgery. Fasciocutaneous flaps are preferred as they are thin, elastic, and easily contoured, leading to decreased bulk [2, 31]. Therefore, the first choice is the thin supraclavicular island flap with its good color and texture match of the anterior neck region followed by the myocutaneous trapezius flap or the dorsal scapular island flap if the angiosome of the SIF-flaps is scarred and unavailable [16, 32]. The pre-expansion of flaps allows their thinning and delay prior to transfer will enhance the safety in terms of tissue perfusion [33].

18.2.7.1 Supraclavicular Island Flap (SIF)

A random pattern flap of the supraclavicular region first described by Mutter in 1842 was further modified after closer anatomic examination of the shoulder region angiosome by Lamberty [34, 35]. Anatomically, this supraclavicular axial patterned flap was based on the supraclavicular artery. In 1997 Pallua introduced the supraclavicular artery island flap (SIF) for the release of postburn mentosternal contractures [16]. Modifications have been added to optimize and expand indications in head and neck reconstruction [17]. Further modifications such as flap pre-expansion through tissue expansion resulted in ultra-thin SIF flaps [33].

Adequate planning and flap design need to respect the aesthetic units of the neck. Mentosternal contractures require dissection up to the borders of the aesthetic units, until the neck is fully released. Deep scars such as collagen tension bands and plates of scar require special attention to create an optimal bed for the flaps and to release facial tensions. Due to the skin laxity, a much larger defect than expected will occur after resection and release of severe neck contractures. The defect sizes after mentosternal scar excisions may reach dimensions of 12 cm × 21 cm up to 15 cm × 26 cm.

The supraclavicular vessels arise from the superficial transverse cervical artery, beneath or lateral to the posterior part of the omohyoid muscle. During the flap elevation from its lateral to its medial portion, skin and subcutaneous tissue are elevated en bloc with the axially running supraclavicular pedicle. In prefabricated flaps, the tissue expander will be removed prior to flap preparation. After dissection of the medial portion, the complete flap is mobile on its vascular pedicle, allowing up to a 180° angle of rotation on the vascular axis as required. In mentosternal contractures, it is recommended to subcutaneously tunnel the isolated pedicles into the anterior cervical defect. The flap tissue will efficiently cover the entire surface of the anterior neck region. The donor site defect will be closed directly in a double layer fashion after extensive undermining and preparation of two advancement flaps. A sterile soft dressing is placed on the wound together with a suited Philadelphia collar for 2 weeks [2, 16, 17, 33] (Figs. 18.7, 18.8 and 18.9).

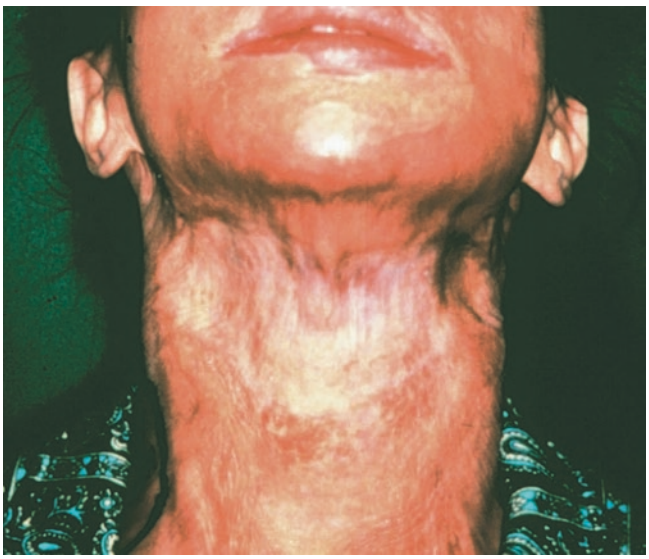


Fig. 18.7 Severe scarring with disfigured cervical and mental region. Scheduled for a supraclavicular island flap from the right donor region to restore the anterior neck region

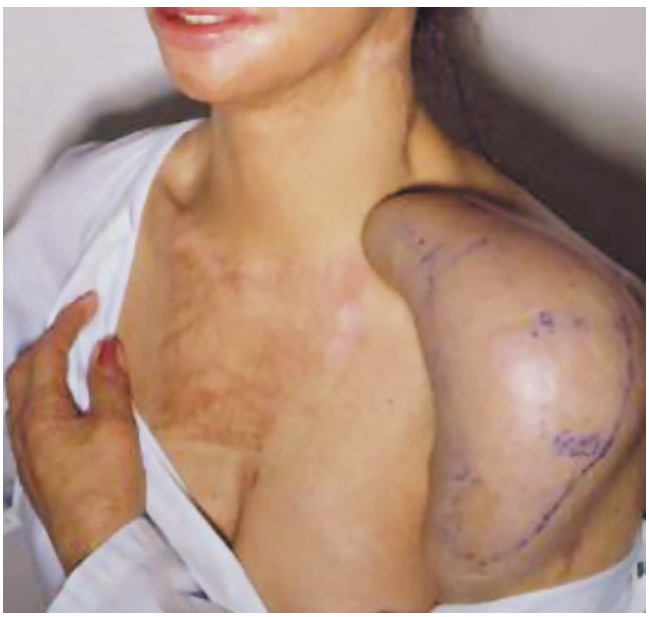


Fig. 18.8 Five years after successful mentosternal restoration with a supraclavicular island flap from the right shoulder region. She has been scheduled for a pre-expanded SIF flap from the left side to resurface the mental region. Inflated crescent-type expander with 700 cc

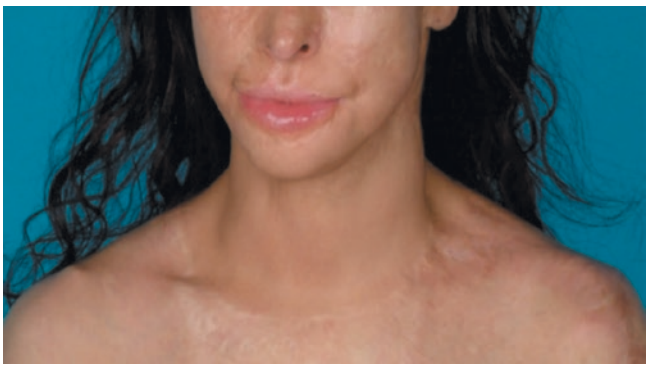


Fig. 18.9 Final outcome with good restoration of the anterior neck and mental region with bilateral pre-expanded supraclavicular island flaps

18.2.7.2 Trapezius Muscle Flap

The trapezius muscle flap is a useful myocutaneous flap to release contractures of the anterior and lateral neck. The trapezius muscle originates from the external occipital protuberance and the spinous processes of C7–T12. Fibers insert on the clavicle, the acromion, and the scapular spine. Motor innervation is done by means of the spinal accessory nerve and ventral rami of the third and fourth cervical nerves. The trapezius muscle is vascularized through the trapezial branch of the occipital artery and the transverse cervical artery and its extension through the dorsal scapular artery. Based on these vessels, superior, lateral, and lower trapezius myocutaneous flaps can be developed. The skin and subcutaneous tissue are supplied through cutaneous and musculocutaneous perforators [36, 37].

The boundaries of the flap are the midline, the lateral muscle border of the trapezius, and a keypoint approximately 5 cm to 10 cm below the scapula tip. After mentosternal contracture release, the flap dissection is carried out to the level of the facial investment of the muscle including the fascia. The clavicle is the limit of the superior mobilization. The superior medial aspect of the flap with the vascular pedicles, the dorsal scapular, and the transverse cervical arteries need to be handled with care to avoid injury to the vessels. The mobile longitudinal flap is transposed anterior into the defect of the neck region and secured in two layers over two suction drains [37].

Further modifications with flap pre-expansion are possible to provide thin, large, and pliable tissue for the neck reconstruction [36]. The pre-expanded trapezius flap requires the insertion of a tissue expander below the trapezius muscle via a lateral incision in the first reconstructive stage. Two months later, after serial ambulatory expansion of the expander, the neck scar can be excised and the pre-expanded flap harvested and rotated anterior into the defect. Primary donor site closure is possible.

This procedure cannot be carried out without causing morbidity, even with muscle-preserving techniques with skeletonization and tedious dissections of the proximal vascular pedicle. The muscle-sparing flap or its perforator alternative is the dorsal scapular island flap utilizing the dorsal scapular arteries [32]. The trapezius flap or the dorsal scapular island flap in anterior and lateral neck resurfacing belongs to the most distant areas the flap can be harvested from, still we believe that mentosternal contracture release and defect closure with a trapezius muscle flap or the dorsal scapular island flap should remain in the armamentarium of reconstructive options for this anatomic region (Figs. 18.10, 18.11 and 18.12).

18.2.8 Free Flaps

Microsurgical transfer of free flaps is indicated whenever local or regional options are not available—it is usually not considered a first-line option in neck reconstruction. Published reports and series underline that the use of free flaps in the neck region is reserved for cases in which more conventional methods were considered to be less feasible. Still, the number of reports of successful utilization of free flaps in reconstruction of burns in the head and neck region has increased in the last years due to advances in free tissue transfer and microsurgical techniques [12, 13, 38, 39]. Additional modifications such as flap prefabrication, prelamination, pre-expansion, chimeric flaps, and super-thin flaps have increased the quality of preexisting well-established free flaps [15, 40–45]. These advances allow the use of thinner, customized flaps with better color and texture match of the head and neck region combined with low donor site morbidity [41]. Therefore, free flaps belong to the essential tools used in burn reconstruction of the neck region. Microsurgical free tissue transfer requires proper patient selection, long, complex-staged operations with the need for revision procedures. Therefore, the surgeon and the patient must be flexible with realistic goals and expectations. Whenever regional options are unavailable, free flap reconstruction can be successfully applied.

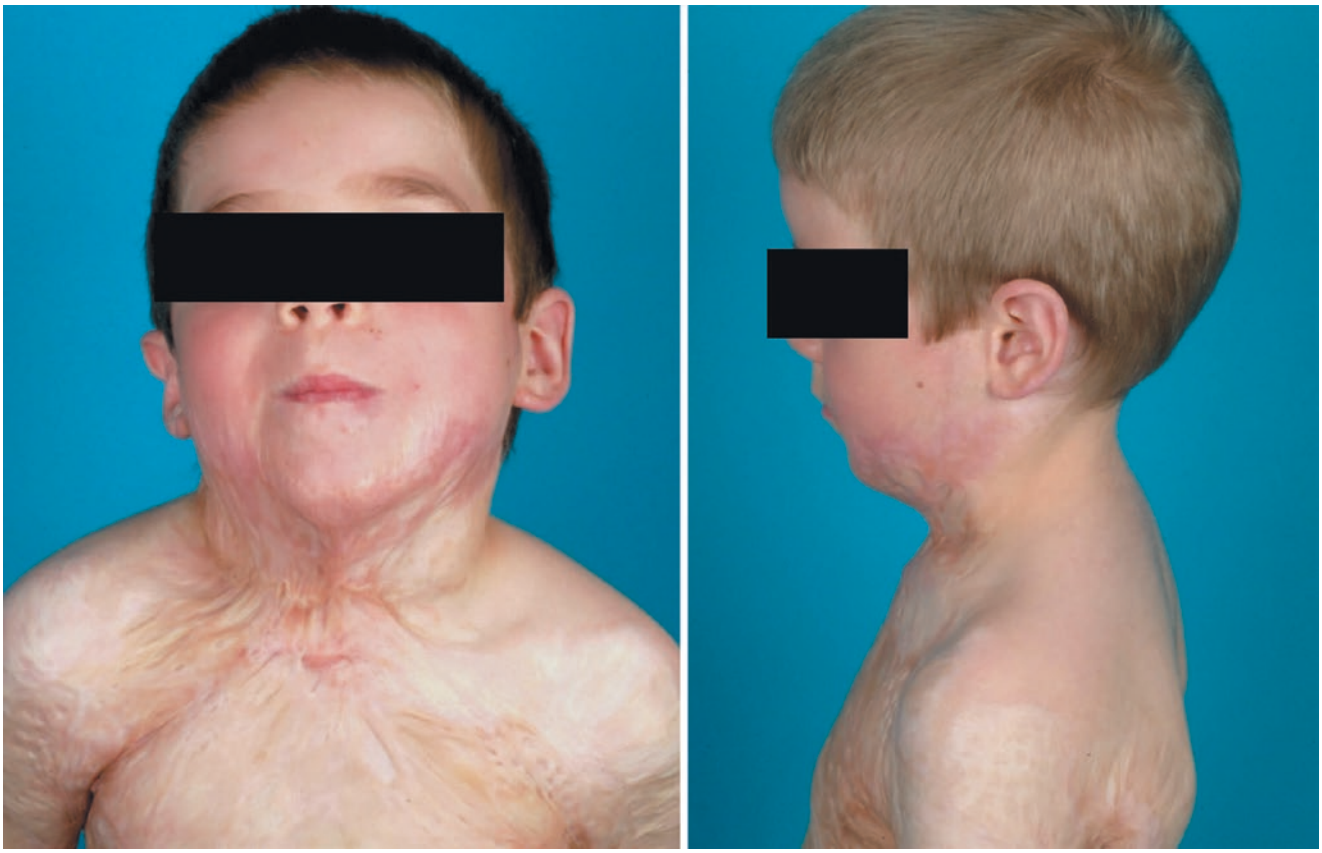


Fig. 18.10 Recurrence of mentosternal bands 2 years after initial surgery

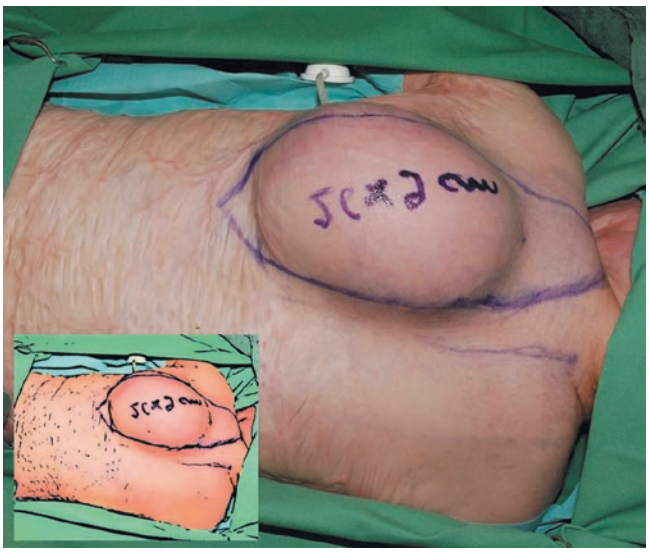


Fig. 18.11 Reoperative surgery with pre-expanded musculocutaneous trapezius flap. Inflated submuscular expander of the left donor region

In complex cases, free flaps may be preferred to pedicled flaps to achieve the optimal functional and aesthetic result for the patient. The principle of the reconstructive ladder of Gillies may be transposed into a reconstructive elevator [15].

Among the well-established flaps, the free fasciocutaneous scapular-parascapular flap and the groin flap are very versatile in the reconstruction of the anterior neck region [12, 13].

Perforator-based free flaps are suitable as they provide thin, supple, large, and well-vascularized tissue with low donor site morbidity. The anterolateral thigh perforator flap (ALT) and the thoracodorsal artery perforator flap (TDAP) are most commonly used [46, 47]. Especially the suprafascial dissection technique of ALT flaps provides a thin flap to improve the cervical contour.

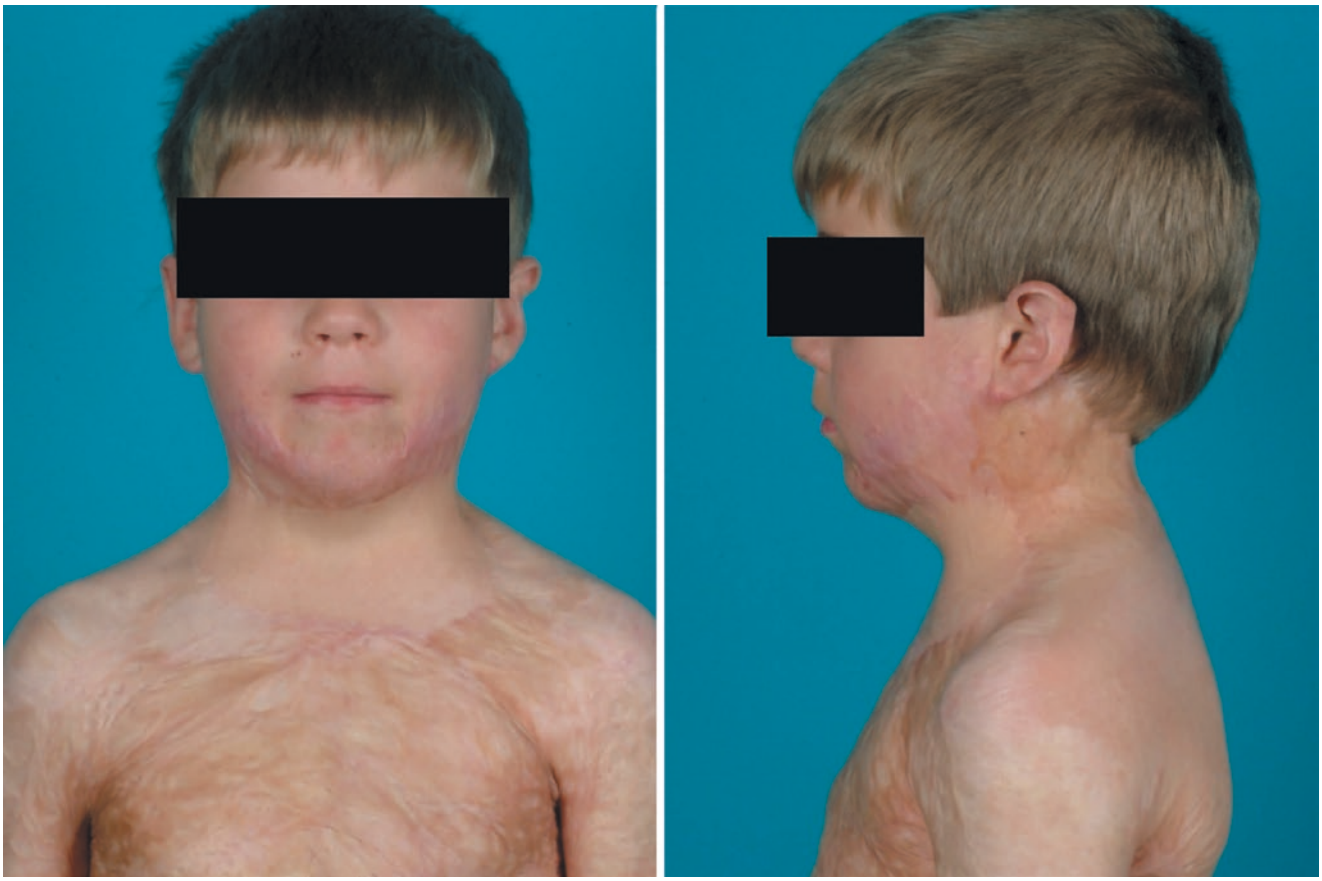


Fig. 18.12 Final outcome with good mentosternal release

18.2.9 Summary

The reconstruction of neck deformities is a difficult task. Careful selection of reconstructive tools and adequate timing of reconstructive procedures may achieve a functional and aesthetic restoration of the burn victim. Most recent technical innovations of pre-expanded, pre-fabricated, or perforator flaps, to name a few, may overcome difficulties with the high functional and aesthetic requirements of the neck region. The pre-expanded ultrathin supraclavicular artery island flap for instance is a reliable and safe tool to resurface defects of the neck region after the release of cervical contractures following burns.

References

1. Donelan MB. Reconstruction of the head and neck. In: Herndon DN, editor. Total burn care. 3rd ed. London: Saunders; 2007. p. 701–18.
2. Pallua N, Demir E. Postburn head and neck reconstruction in children with the fasciocutaneous supraclavicular artery island flap. Ann Plast Surg. 2008;60:276–82.
3. Huang T. Overview of burn reconstruction. In: Herndon DN, editor. Total burn care. 3rd ed. London: Saunders; 2007. p. 674–86.
4. Engrav L, Donelan MB. Face burns: acute care and reconstruction. Oper Tech Plast Reconstr Surg. 1997;4:53–85.
5. Remensnyder JP, Donelan MB. Reconstruction of the head and neck. In: Herndon DN, editor. Total burn care. 3rd ed. London: Saunders; 2002. p. 656–89.
6. Fricke NB, Omnell L, Dutcher KD, et al. Skeletal and dental disturbances after facial burns and pressure garment use: a 4-year follow-up. J Burn Care Rehabil. 1999;20:239–49.
7. Abdullah A, Blakeney P, Hunt R, et al. Visible scars and self-esteem in pediatric patients with burns. J Burn Care Rehabil. 1994;15:164–8.
8. Kirschbaum S. Mentosternal contracture: preferred treatment by acromial (charretera) flap. Plast Reconstr Surg. 1958;21:131–8.
9. Achauer BM. Reconstructing the burned face. Clin Plast Surg. 1992;19:623–36.
10. Mustoe TA, Cooter TD, Gold MH, Hobbs FD, Ramelet AA, Shakespeare PG, et al. International clinical recommendations on scar management. Plast Reconstr Surg. 2002;100:560.
11. Achauer BM, VanderKam VM. Burn reconstruction. In: Achauer BM, Eriksson E, editors. Plastic surgery indications operations outcomes. St. Louis, MO: Mosby; 2000. p. 425–46.
12. Angrigiani C. Aesthetic microsurgical reconstruction of anterior neck burn deformities. Plast Reconstr Surg. 1994;93:507–18.
13. Ninkovic M, Moser-Rumer A, Ninkovic M, et al. Anterior neck reconstruction with pre-expanded free groin and scapular flaps. Plast Reconstr Surg. 2004;113:61–8.

14. Cronin TD, Barrera A. Deformities of the cervical region. In: McCarthy JG, editor. Plastic surgery, vol. 3. Philadelphia: Saunders; 1990. p. 2057–93.
15. Gillies HD. The tubed pedicle in plastic surgery. N Y Med J. 1920;111:1.
16. Pallua N, Machens HG, Rennekampff O, et al. The fasciocutaneous supraclavicular artery island flap for releasing postburn mentosternal contractures. Plast Reconstr Surg. 1997;99:1878–86.
17. Pallua N, Noah M. The tunneled supraclavicular island flap: an optimized technique for head and neck reconstruction. Plast Reconstr Surg. 2000;105:842–51.
18. Abramson DL, Pribaz JJ, Orgill DP. The use of free tissue transfer in burn reconstruction. J Burn Care Rehabil. 1996;17:402–8.
19. Aranmolate S, Atah AA. Bilobed flap in the release of postburn mentosternal contracture. Plast Reconstr Surg. 1989;83:356–61.
20. Motamed S, Davami B, Daghagheleh H. Trapezius musculocutaneous flap in severe shoulder and neck burn. Burns. 2004;30(5):476–80.
21. Waymack JP, Law E, Park R, et al. Acute upper airway obstruction in the postburn period. Arch Surg. 1985;120:1042–4.
22. Schneider J, Biedermann T, Widmer D, Montano I, Meuli M, Reichmann E, Schiestl C. Matriderm versus Integra: a comparative experimental study. Burns. 2009;35:51–7.
23. Atherton DD, Tang R, Jones I, Jawad M. Early excision and application of matriderm with simultaneous autologous skin grafting in facial burns. Plast Reconstr Surg. 2010;125:60e–1e.
24. Yannas IV, Burke JF. Design of an artificial skin. I. Basic design principles. J Biomed Mater Res. 1980;14:65–81.
25. Heimbach D, Luterman A, Burke J, Cram A, Herndon D, Hunt J, Jordan M, McManus W, Solem L, Warden G, et al. Artificial dermis for major burns. A multi-center randomized clinical trial. Ann Surg. 1988;208:313–20.
26. Berger A, Tanzella U, Machens HG, Liebau J. Administration of Integra on primary burn wounds and unstable secondary scars. Chirurg. 2000;71:558–63.
27. Gahhos FN, Ariyan S, Cuono CB, et al. Burn wound excision and local flap closure. Ann Plast Surg. 1985;14:535.
28. Neale HW, Kurtzmann LC, Goh KB, et al. Tissue expanders in the lower face and anterior neck in pediatric burn patients: limitations and pitfalls. Plast Reconstr Surg. 1993;91:624–31.
29. LoGiudice J, Gosain AK. Pediatric tissue expansion: indications and complications. J Craniofac Surg. 2003;14:866–72.
30. Gibstein LA, Abramson DL, Bartlett RA, et al. Tissue expansion in children: a retrospective study of complications. Ann Plast Surg. 1997;38:358–64.
31. Hallock GG. The role of local faciocutaneous flaps in total burn wound management. Plast Reconstr Surg. 1992;90:629–35.
32. Angrigiani C, Grilli D, Karanas YL, Longaker MT, Sharma S. The dorsal scapular island flap: an alternative for head, neck and chest reconstruction. Plast Reconstr Surg. 2003;111:67–78.
33. Pallua N, von Heimburg D. Pre-expanded ultrathin supraclavicular flaps for (full-) face reconstruction with reduced donor-site morbidity and without the need for microsurgery. Plast Reconstr Surg. 2005;115:1837–44.
34. Mutter TD. Cases of deformity from burns, relieved by operation. Am J Med Sci. 1842;4:66.
35. Lamberty BG. The supra-clavicular axial patterned flap. Br J Plast Surg. 1979;32:207–12.
36. Ulrich D, Fuchs P, Pallua N. Preexpanded vertical trapezius musculocutaneous flap for reconstruction of a severe neck contracture after burn injury. J Burn Care Res. 2008;29:386–9.
37. Isenberg JS, Price G. Longitudinal trapezius fasciocutaneous flap for the treatment of mentosternal burn scar contractures. Burns. 1996;22:76–9.
38. Ohkubo E, Kobayashi S, Sekiguchi J, et al. Restoration of the anterior neck surface in the patient by free groin flap. Plast Reconstr Surg. 1991;87:276–84.
39. Bootz F, Preyer S. Microvascular tissue transplantation in plastic reconstruction of the external head-neck area. Laryngorhinootologie. 1994;73:538–42.
40. Teot L, Cherenfant E, Otman S, et al. Prefabricated vascularised supraclavicular flaps for face resurfacing after postburn scarring. Lancet. 2000;355:1695–6.
41. Parrett BM, Pomahac B, Orgill DP, Pribaz JJ. The role of free-tissue transfer for head and neck burn reconstruction. Plast Reconstr Surg. 2007;120:1871–8.
42. Pribaz JJ, Fine NA, Orgil DP. Flap prefabrication in the head and neck: a 10 year experience. Plast Reconstr Surg. 1999;103:808.
43. Hallock GG. Preexpansion of free flap donor sites used in reconstruction after burn injury. J Burn Care Rehabil. 1995;16:646.
44. Koshima I, Yamamoto H, Hosoda M, et al. Free combined composite flaps using the lateral circumflex femoral system for repair of massive defects of the head and neck regions: an introduction to the chimeric flap principle. Plast Reconstr Surg. 2005;58:550.
45. Chin T, Ogawa R, Murakami M, et al. An anatomical study and clinical cases of “super-thin flaps” with transverse cervical perforator. Br J Plast Surg. 2005;58:550.
46. Mun GH, Jeon BJ, Lim SY, Hyon WS, Bang SI, Oh KS. Reconstruction of postburn neck contractures using free thin thoracodorsal artery perforator flaps with cervicoplasty. Plast Reconstr Surg. 2007;120:1524–32.
47. Yang JY, Tsai FC, Chana JS, Chuang SS, Chang SY, Huang WC. Use of free thin anterolateral thigh flaps combined with cervicoplasty for reconstruction of postburn anterior cervical contractures. Plast Reconstr Surg. 2002;110:39–46.

Burn Reconstruction: Eye Region

19

Andreas Heckmann and Peter M. Vogt

19.1 Introduction

Facial burns occur in up to 30% of thermal trauma patients admitted to burn units [1]. Eyelid and ocular involvement is relatively common [2], but the loss of an eye primarily from a thermal injury is rather rare [3]. Reasons therefore are mechanisms like protective movements of the head and arms to avoid the source of a burn, the blink reflex with the closure of the eye, and the Bell phenomenon of the eyeball.

The lid is built-on of skin, the orbicularis muscle, the tarsus, lashes, meibomian glands, lid retractors, and tarsal conjunctiva. The lower eyelid is commonly described as a series of tissue layers (Figs. 19.1 and 19.2):

- The anterior lamella is composed of the outer skin and orbicularis oculi muscle.
- The middle lamella consists of the orbital septum.
- The posterior lamella consists of the tarsus, the lower lid retractors, and the conjunctiva.

The goals of eyelid reconstruction are restoration of the lid lamellae, reconstitution of facial symmetry and provision of corneal protection. Inadequate reconstruction techniques may produce corneal exposure and sight-threatening keratopathy. Visual deprivation and amblyopia are rare but may also follow. Periocular skin is thin with no subcutaneous fat, resulting in deeper burns than a similar exposure to skin elsewhere. Eyelid burns (50–85%) and eyelid contractures (30–65%) in burned people are more frequent than injuries to eyeball like conjunctival burns (3–11%), corneal abrasions (7–22%), corneal burns (5%), corneal perforations (1–2%), and cataracts (2%) [1, 4]. A series of 143 burn patients with ocular injuries reported that two were left blind, two had impaired vision, and three underwent enucleation [5]. Mandatory in burns involving the eyelids is immediate consultation of the ophthalmologist and prophylactic ocular lubrication. Early surgical intervention is indicated if eyelid retraction causing corneal exposure occurs. But this often requires repeated procedures due to eyelid contraction.

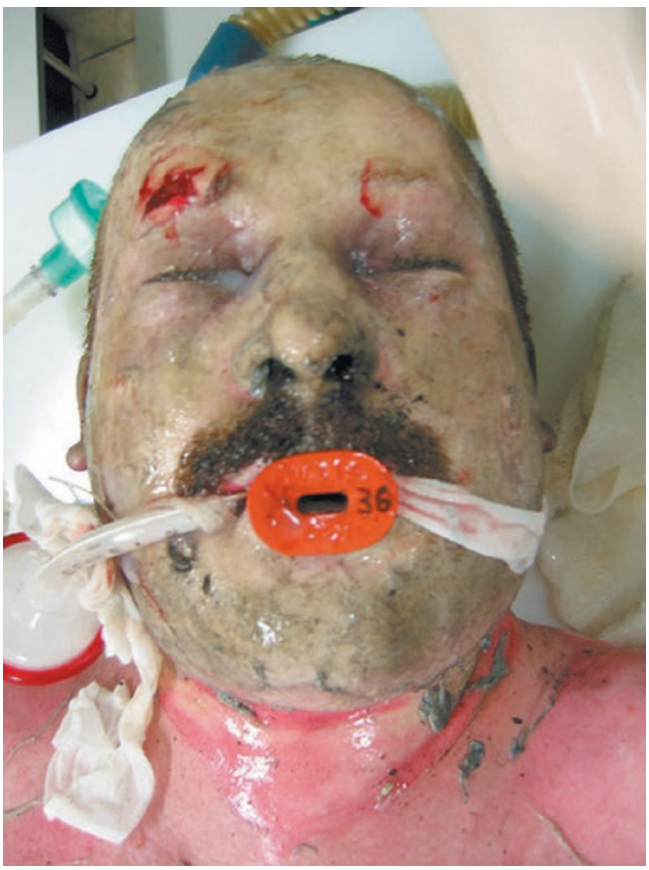


Fig. 19.1 Third-degree burned face involving the eyelid region, directly after the damage, 45-year-old male patient with burned 50% of body surface area degree 2–3

A. Heckmann · P. M. Vogt (✉)
Department of Plastic, Hand, and Reconstructive Surgery, Medizinische Hochschule Hannover, Hannover, Germany
e-mail: vogt.peter@mh-hannover.de

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_19

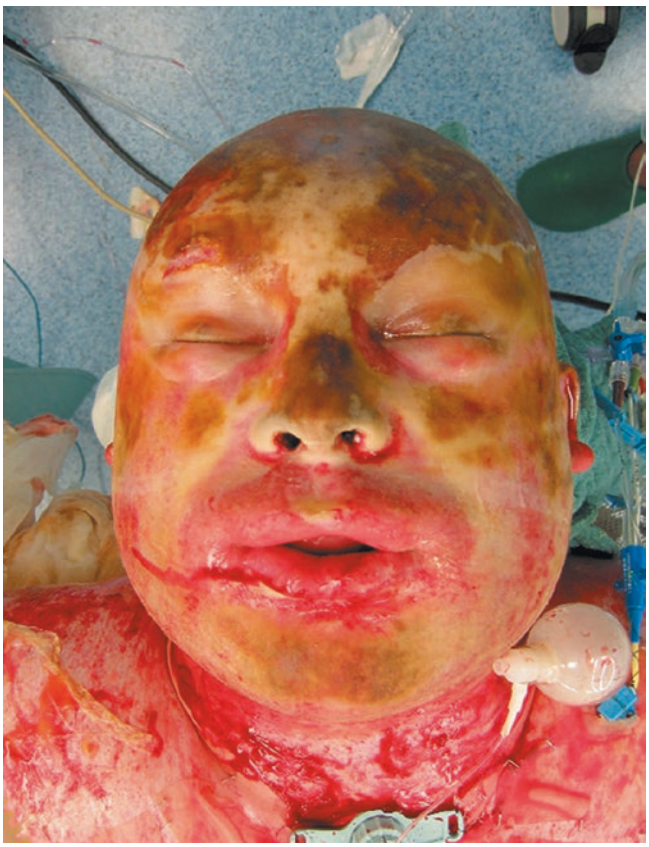


Fig. 19.2 Third-degree burned face involving the eyelid region, 7 days after damage

Secondary complications such as corneal ulceration, exposure keratopathy, secondary infection, and orbital compartment syndrome are potentially preventable by appropriate early and sustained management and are thought to be preventable. In further readings, controversial meanings exist regarding the role of prophylactic ocular lubrication, excision and debridement of eschar, temporary suture and surgical tarsorrhaphy, timing of surgery for eyelid contraction, and the role of full- and split-thickness skin grafts in eyelid reconstruction. For eyelid reconstruction, each case needs an individual approach based on what defect exists and what skin is available. The lid surgeon needs a wide knowledge of the reconstructive principles and possibilities. The reconstruction of anterior lamellar has a significant risk of developing ectropion. Large defects may require different transposition flaps to achieve a good skin texture and color reconstruction. New autogenous and cadaveric materials for posterior lid reconstruction are known well meantime. They reduce donor site morbidity and surgical time, but they undergo contraction significantly after surgery. A new approach for entropion and symblepharon caused by conjunctival cicatricial changes is reached by amniotic membrane transplantation and may enhance the prognosis for patients.

19.2 Reconstruction of the Eyelid Region

19.2.1 Upper Eyelid and Anterior Lamella of Lower Eyelid

Reconstruction of the anterior lamella of the upper eyelid can be done by:

1. Skin grafting
2. Local flaps
3. Free flaps (often used in combined damage of anterior and posterior lamella)

19.2.2 Reconstructive Skin Grafting (Split-Thickness or Full-Thickness Skin Graft) in the Eyelid Region

Both full-thickness skin grafts (FTSG) (most suitable harvested from post-auricular, supra-clavicular or from the unburned contra lateral upper eyelid) and split-thickness skin grafts (STSG) (mostly harvested from the upper leg) are not ideal for eyelid burn reconstruction. In literature, there are different reports concerning which method (FTSG or STSG) is the best for upper and lower eyelid reconstruction. Most authors use STSG (more mobility) for the upper eyelid and FTSG (less contraction tendency) for lower eyelid reconstruction. Some others prefer FTSG for both. Very thin but full-thickness skin grafts are often-used grafts for reconstruction of both upper and lower eyelid. Both kinds of skin grafts have disadvantages and advantages in color-match, tendency to contraction, range of mobility, transplantation of root of hairs, developing ectropion, and hyperpigmentation.

Wound contraction tendency is indirectly proportional to the amount of structurally dermal collagen. For this, FTSG (more dermis) should have fewer tendencies for contraction than STSG. In cases of extensive burn damage with limited viable skin, FTSG is often reserved for later repair, and STSG is used for first reconstruction [6, 7] (Figs. 19.3, 19.4 and 19.5). Also STSG is used when FTSG areas are not available. FTSG contracts less than STSG and does not compromise mobility or appearance too much. For a good color-match, FTSG should be harvested from post-auricular, supra-clavicular, or the unburned contralateral upper eyelid and should be taken oversized because of contraction over time. If upper and lower eyelids require grafting, it is best to perform grafting at separate sessions. This is to avoid insufficient skin being introduced to each and to maximize the stretched graft-bed for each eyelid. Some authors prefer first the upper and others the lower eyelid reconstruction. Maybe it should depend on the extent of the damage of the particular eyelid. The skin should be placed under tractioned wound-bed and padded for 5 days.

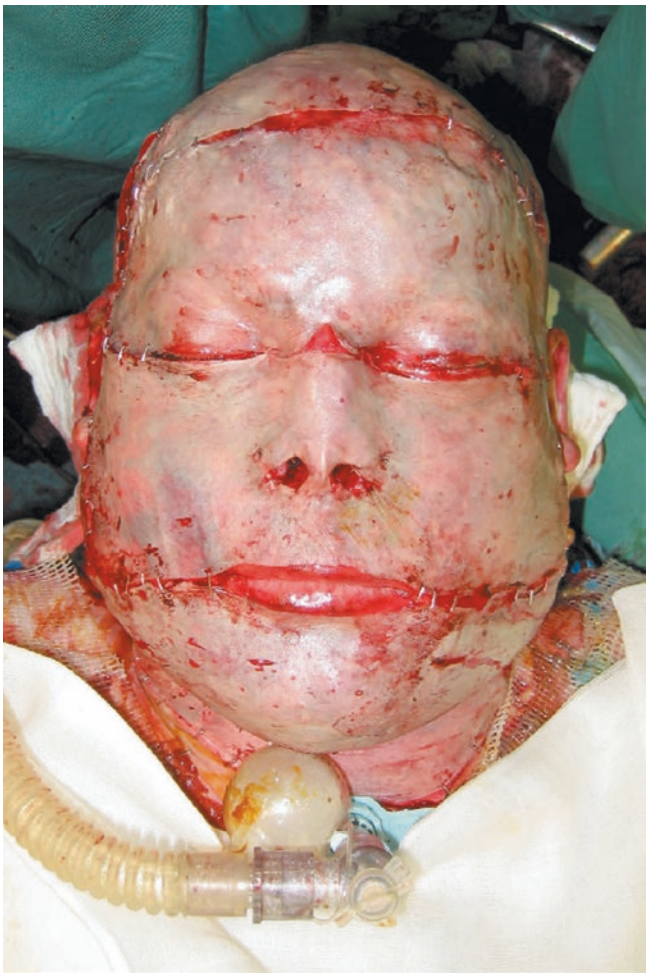


Fig. 19.3 Postoperative view 3 days after split thickness skin grafting of the face region, first step in reconstruction of the face and eyelid region

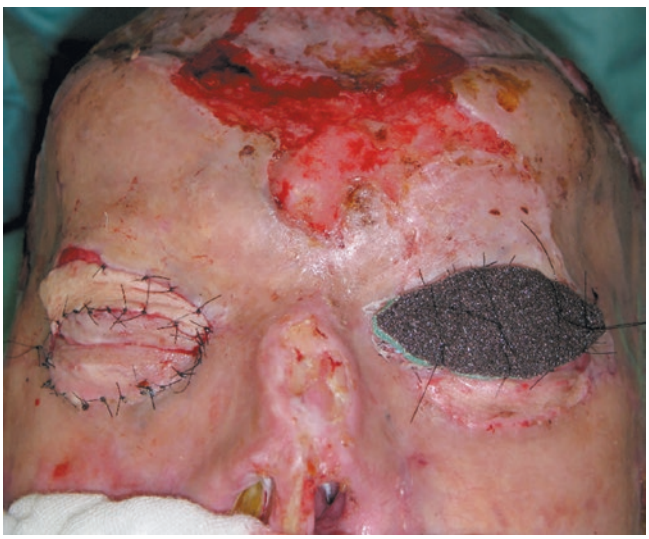


Fig. 19.4 Postoperative view after full-thickness skin grafting of lower and upper eyelid because of skin contraction, left eye still covered with a bolster

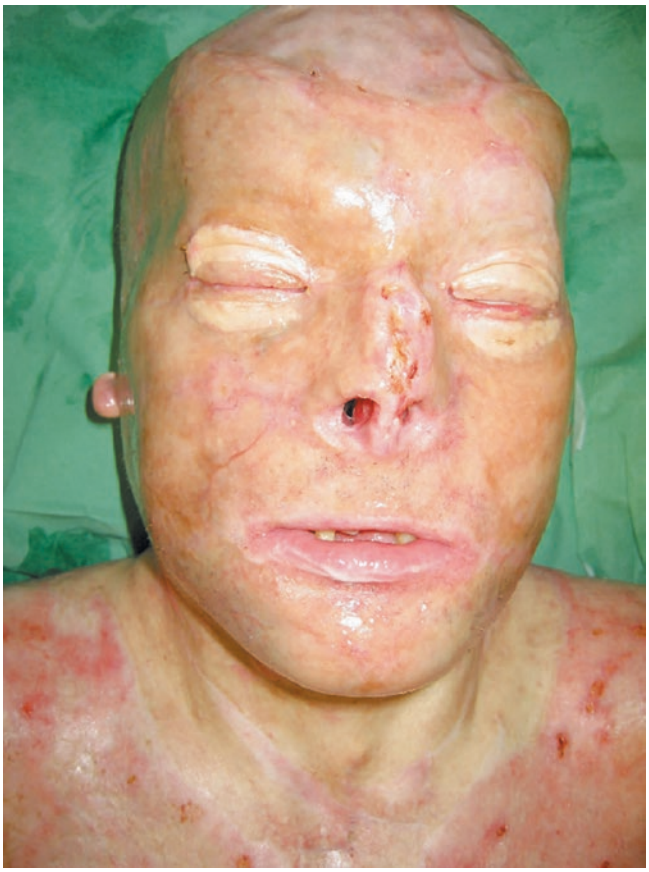


Fig. 19.5 Postoperative view 3 weeks after full-thickness skin grafting of lower and upper eyelid

The other eyelid can be reconstructed after sufficient skin grafting and healing 7 days later. Before skin transplantation to upper eyelid, a skin crease incision is used at the lower border of the graft. For the lower eyelid, a subciliary incision is preferred. For both upper and lower eyelids, the way of dissection should be canthus-to-canthus [8] and extend up to 2 cm beyond the lateral canthus, very slightly angulated upwards for lower eyelid incisions and well into the nose at the medial canthus [9, 10]. Dissection should be layered with a wide release and resection of all scar tissue because of later shrinking. Special attention should be placed to the preservation of Müllers muscle (if still present) and the levator aponeurosis. After this a thinned full-thickness graft could be fashioned to fit the recipient wound, and a petrolatum gauze is placed over the graft and a bolster is tied in place for 5–7 days.

19.2.3 Reconstructive Local Flaps in the Eyelid Region

Local tissue flaps in the eyelid region include the skin pedicle flap with subcutaneous base, anterior and posterior lamel-

lar advancement flaps, and more complex interpositional flaps for combined lid and cheek defects.

The possibilities of reconstructive flaps in the eyelid region in the treatment of burns and contracture are limited. Mostly the reason therefore is the lack of normal adjacent skin [7, 11]. Orbicularis oculi myocutaneous flaps are obviously indicated only in the rare circumstance where the upper eyelid is unaffected and available for harvesting. They have the advantage of additional support and possible lower eyelid suspension in the repair of lower eyelid burn-ectropion [12]. A destroyed tarsus because of severe burn damage complicates reconstruction possibilities because it normally stabilizes skin grafts and flaps in their new position. The simple skin grafting of the posterior lamella is not a successful long-lasting tool in reconstruction. This damage better needs a vascularized flap for reconstruction of the eyelid. Some possibilities are a tarsoconjuctival Hughes flap, a forehead periosteal flap, or an island pedicle flap. If ambient skin is not damaged, a local subcutaneously based pedicled flap can be transposed into the defect after debridement. For this Tei et al. [13] described the advantage of using a subcutaneously based flap in lower lid reconstruction. They used for reconstructing of a lower lid defect a Hughes tarsoconjunctival flap in combination with a nasolabial skin transposition flap, with a deep subcutaneous base. A nasolabial flap results in an acceptable scar and provides a good color and texture match for the lower lid, and the advantages of this approach over a cheek rotation flap, which also maintains its good blood supply, is a lower risk of ectropion, entropion, or inadvertent facial nerve damage, and that hair-bearing skin from the upper cheek is not brought medially. Large defects of the anterior lamella of the lower lid combined with burned cheek skin have a high risk for developing ectropion after reconstruction. They can be closed with a heteropalpebral skin flap from the unburned upper to the lower lid and a temporomandibular and retroauricular transposition flap for closure of the cheek defect. This approach enables optimal color and texture matches [14].

Medial and Lateral Canthal Deformities after burn injury often result in displacement of the punctum and causing epiphora because of hypertrophic scars and vertical contracture [6, 8, 15]. Multiple Z-plasties or Mustarde's Jumping Man plasty may be good possibilities for the correction of mild linear contractions on the medial canthus. Otherwise local transposition flaps or transplantation of skin after releasing the canthus is viable [15, 16]. Lateral epicanthal folds and scar bands can be corrected by a local transposition flap.

Spherical contraction due to full-thickness skin-burned eyelids (scar contracture, adhesion of eyelid margin) will lead to a minor function of the palpebral opening. The typical "round eye deformity" particularly resulting of skin contracture leads to lagophthalmos. The first step in reconstruction is the correction of the skin deficit of the eyelids. By incisional release including the whole horizontal opening length, a reposition of the medial canthus is possible [9].

19.2.4 Reconstructive Free Flaps in the Eyelid Region

Myocutaneous free flaps are often indicated in full thermal damages of both eyelids and are combined with other reconstructive procedures when both the anterior and posterior lamella of the lower lid are burned. Thai et al. [17] report a patient with a unilateral complete defect of both upper and lower eyelids from a deep thermal injury with partial sclera burn (damage of anterior and posterior lamella). Local tissues were unavailable for donor sites due to the severe burn of the head and neck areas. They used a free-tissue transfer of the unburned dorsalis pedis flap (anastomosing with the superficial temporal vessels) as soft tissue coverage for the outer lamella. The partially burned inner lamella was reconstructed by releasing and advancing the upper and lower conjunctiva. To preserve the natural inner lamella lining, this can be achieved by advancing the conjunctival tissues from the conjunctival cul-de-sacs. Furthermore, it also serves as a vascularized bed for cartilage grafts for replacing a missing tarsal plate and providing support for the new eyelids. A conjunctivodacryocystorhinostomy was performed for lacrimal drainage. The dorsalis pedis flap's advantage as donor tissue is the thin and pliable nature of this flap. This coverage will only provide static support without active mobility of the reconstructed eyelids.

19.3 Posterior Lamella

Reconstruction of the posterior lamella can be done by:

1. Nasal septal-, auricular-, and hard palate cartilage
2. Bovine-preserved sclera
3. Amniotic membrane transplants (AMT)
4. Dermis skin grafts
5. Conjunctival release

Posterior lamella can be reconstructed by using nasal septal-, auricular-, and hard palate cartilage, bovine-preserved sclera, amniotic membrane transplants, and dermis skin grafts. In particular, when more than 50% of the lid has full-thickness burn damage, a graft of stabilizing material is necessary. An allograft of preserved bovine sclera has the advantages of avoiding donor site morbidity and reducing surgical time. Fortunately allogeneic grafts for reconstruction of the posterior lamella of the lower lid are well toler-

ated without appearance of keratopathy in the interval between surgery and re-epithelialization at 3 months. Unfortunately, in several countries, the use of preserved sclera has fallen from favor due to the association with transmission of prion disease [18].

The use of autogenous dermis skin grafts has no risk of prion disease but leaves a little donor site defect. Therefore, dermabrasion of preferably posterior auricular skin for complete absence of epidermal structures and keratin is performed and is used similar to a full-thickness skin graft [19]. Conjunctival epithelialization of the graft occurred within a month. Because of its tendency to contract, the graft should be taken oversized. The advantage of autogenous dermis skin grafting includes low donor site morbidity and the availability of a material sufficiently supple to conform to the shape of the globe. Split-thickness dermal grafts or tenonplasty are procedures in large corneal and scleral defects without the possibility of reconstruction with conjunctival flaps [20]. After raising a superiorly hinged, thin epidermal flap, the split-thickness dermal graft could be harvested from the thigh. A thin dermal graft may then be taken from the exposed dermal bed. The epidermis flap is then closed after being perforated. The graft is placed on the defect following a limbal peritomy, depending on the site of the defect with or without undermining of close-by conjunctiva. Postoperative thinning of the grafts may be needful.

An alternative material to autogenous dermis without donor site morbidity is acellular allogenic human or porcine cadaveric dermis. This material has unfortunately a high tendency of contraction and shrinking (up to more than 70% in comparison to hard palate mucosal cartilage grafts with only 15%) and high costs [10, 21]. Because of this, its application should be reconsidered well and should be used rather as a temporary spacer.

The structural arrangement of collagens and laminin in amniotic membrane transplants (AMT) is similar to that in conjunctiva. AMT acts as a scaffold for conjunctival re-epithelialization and restores the integrity of the corneal and conjunctival surfaces. Its advantages compared with buccal and labial mucous membrane grafting include no donor site morbidity, and no need for adjunctive irradiation or antimetabolite treatment for reducing shrinkage of an autogenous graft. AMT is an acellular nonimmunogenic material with stromal epithelial growth factors, antiangiogenic proteins, and anti-inflammatory proteins.

19.4 Scar Management

Controlling burn scar contraction is a difficult task as usual in face burns. Compression with custom-made splints which are fitted inside a face mask or custom-fitted conformers is a common treatment. The patients have to be followed closely to see if the splint works effectively in preventing ectropion. If the eyeball is effectually covered, it is acceptable to wait for scar maturation for definitive correction. Ectropion of the lower eyelid is the most appearing and feared problem after burn lid damage and unfortunately cannot been eliminated totally.

19.4.1 Retraction of Upper Eyelid and Ectropion of Lower Eyelid

After early eyelid reconstruction combined with skin graft appearance of progressive upper eyelid contraction and lower eyelid ectropion could be estimated (Figs. 19.6 and 19.7).

In general, opposing forces in ectropion are levator function and scar contraction against gravity, edema, elasticity, and orbicularis function in upper eye lid. In the lower eye lid tissue pliability, age (loss of elasticity), paralysis, gravity, and lid scar contraction work against orbicularis function, tissue elasticity, and tarsal rigidity [22].

The operative correction of entropion and retraction is one of the most important operations in the entire surgical

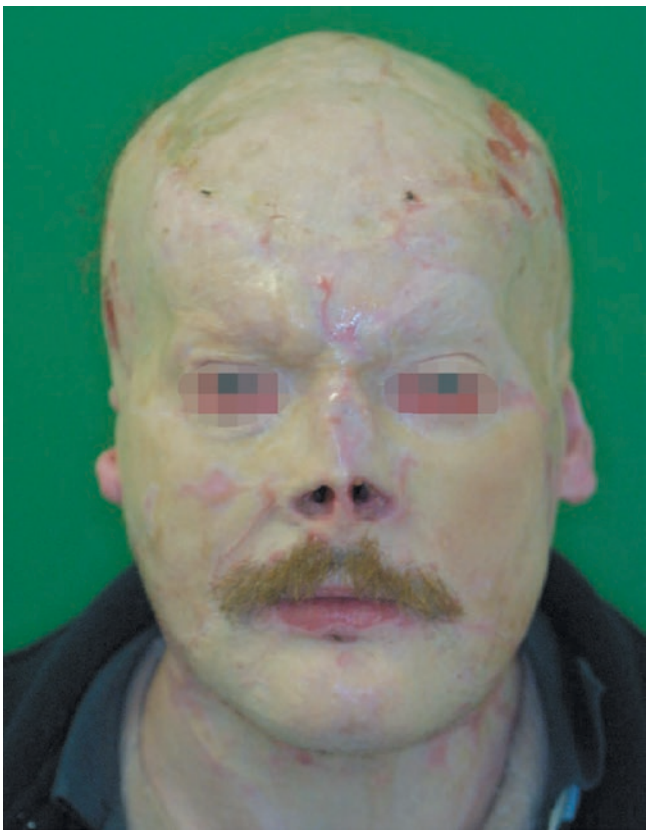


Fig. 19.6 Fourteen months after reconstruction face with split-thickness skin grafts and upper and lower eyelid regions with full-thickness skin grafts with scleral show and ectropion

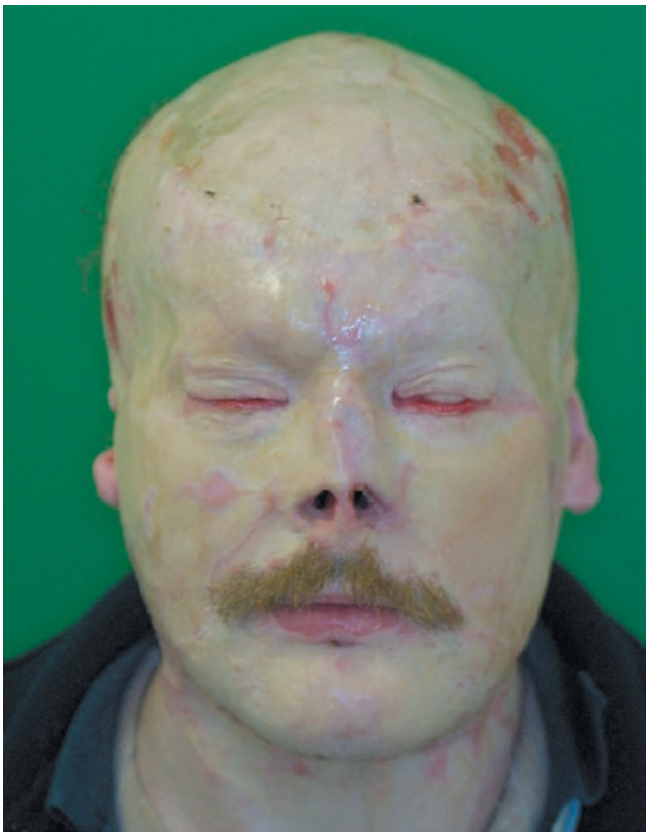


Fig. 19.7 Fourteen months after reconstruction face with split-thickness skin grafts and upper and lower eyelid regions with full-thickness skin grafts. Nearly fully eyelid closure

rehabilitation of the facial burn and should be carried out before any other facial surgery [23], but early surgery has no evidence-based advantage to reduce further reconstructive procedures required in the long term. It has only been shown to help reduce the risk of exposure keratopathy. Controversial is the time of debridement in deep eyelid burns. In general, eyelid burn debridement is performed later compared to burns elsewhere [6, 8]. Time of surgery is often at 2–3 weeks post injury. Then tissue destruction has become demarcated, and eyelid contracture and lagophthalmos are present. Therefore, fully, wide and overcorrecting releasing of the eyelids is essential. It is recommended that either the upper or lower eyelid should be reconstructed at one setting. The reason for this is the difficulty of doing an adequate and fully overcorrection of upper and lower eyelid release simultaneously. There is a big controversy in literature if the upper or the lower eyelid should be released first. It should be always individually decided due to the amount of damage of the particular lid and fear for the globe.

To avoid damage to the M. orbicularis oculi, Huang [9] only excises the eschar. However, most of the authors consider a full debridement to receive a wound bed with a good blood supply and to prevent further wound contracture [24, 25]. If there are repeated problems with irritation of the eye and damage to the cornea, the ectropion is released early in the post burn period. If there is no risk for the eye, one can await scar maturation [26]. An important consideration is to eliminate extrinsic forces which cause entropion before correcting the eyelids. There could be a tight contraction over the face or neck which pulls on the eyelids and causes ectropion or retraction.

In summary generally the surgical release and skin grafting should be done delayed. If there is early appearing of lagophthalmos, corneal exposure, conjunctival injection, or chemosis, the eyelids could be closed and secured with drawstring tarsorrhaphy sutures.

19.4.2 Surgical Tarsorrhaphy

Surgical tarsorrhaphy is discussed as very controversial in facial burns and has largely been abandoned as routine practice. Tarsorrhaphy does not prevent wound contraction when there is cicatricial ectropion present. Furthermore the basic principle of tissue replacement should be the better procedure [6, 23, 27]. This procedure seems to be ideal 2 weeks after burn accident when eyelid contracture occurs, overcoming any temporary suture tarsorrhaphy and producing ectropion. Suturing of the eyelids together may be indicated in certain situations like following destruction of the eyelid margins if there is sufficient tissue remaining instead of the masquerade procedure [15]; also in case of combined grafting of upper and lower eyelid in cases where the tarsus is missing. A tarsorrhaphy combined with skin grafting may help reduce the need for further skin grafting or recurrent ectropion. As the risk for ectropion persists for months due to persistent eyelid shrinkage, a tarsorrhaphy would need to remain in place until facial scars mature [28].

19.4.3 Masquerade Procedure

This is a temporary procedure of closing the eye for further reconstruction of the eyelids. It is used if there is severe damage of the eyelid, and no viable or adjacent tissue is available. All necrotic tissues including muscle and eyelid margins get excised, then mobilizing and suturing together of a conjunctival flap from the remaining upper and lower eyelid to cover the anterior surface of the globe with the epithelial surface of conjunctiva. This is covered usually with a split-thickness skin graft. Because of the poor vascularity of the wound bed, a full-thickness graft will undergo necrosis. After 3 months, the reconstructed lids get divided to create new eyelid margins. The globe has nearly normal coverage, and the eyelid function is very good [7]. But we could also

have appearance of slight eyelid eversion, followed by ptosis, stiffness, and lagophthalmos.

If the upper and only the upper part of the lower eyelid need full reconstruction, advancing the muscle levator palpebrae and covering with a full-thickness skin graft show good results after flap dividing with good function of the new eyelids [6].

19.4.4 Tenonplasty

In the absence of nearby conjunctival flaps, this alternative globe-preserving procedure involves dissection of the Tenon's layer and anterior advancement of Tenon's in a flap-like fashion and suturing to the globe at the limbus in order to provide a vascular supply and promote corneal epithelialization [29]. The results nearly complete epithelialization of advanced Tenon's within 21–54 days [30] with the prevention and healing of scleral ulceration.

19.5 Deformities of the Eyebrows

A loss of the eyebrows is noticeable and defacing. A good cosmetic result could be achieved by temporal pedicle flaps of hair-bearing skin [8, 9]. The flap is outlined above an appropriate branch of the superficial temporal artery. Hair direction should correspond similar to the brow hair. The flap is then pedicled subcutaneous on the temporal artery and vein and transposed a little more medially than the normal eyebrow position because of the tendency of contraction to the lateral side.

Hair transplantation is another good tool for correction after burn damage. Full-thickness composite skin graft of hair-bearing skin from the temporoparietal region (because of the thinness of this regional skin) could be transplanted. A portion of the scalp should be taken that has the same general angle of hair follicles exiting the skin as the remainder of the eyebrow or the opposite eyebrow. While excising care must be taken to cut parallel to the hair follicles. Then they are positioned in the way that the hair can grow in the correct direction [23]. Due to the minor satisfactory vascularized wound bed, they should be taken as 1 mm strips up to 5 mm grafts [8, 9]. Unfortunately there is loss of hair within 3 weeks, but hair returns in the following 3 months with up to 70% of surviving follicles [23]. Re-grafting is here often required.

The micrograft technique in hair transplantation shows good natural and long-lasting results in eyebrow reconstruction. But this technique depends on a not too much scared wound bed and is very time consuming and may be repeated for a complete new eyebrow [31–33]. Using this technique or small grafts is useful in producing the correct angle of the eyebrow. McConnell and Neale prefer a pedicle island flap based on the superficial temporal artery especially for reconstruction in bushy male eyebrows. The vascular pedicle is tunneled beneath the skin to the eyebrow. They recommend that free hair transplantation has marginal results due to the scarred recipient site [34].

The gender of the patient plays a big role in the choice of reconstruction. Male patients need more thick and bushy eyebrows, and the flap procedure is more capable. In female patients, permanent make up or eyebrow pencils can be an alternative method to surgery [8, 9].

19.6 Horizontal Eyelid Shortening

Horizontal eyelid tightening is a possible procedure in ectropion after skin transplantation for eyelid reconstruction. The reconstructed eyelid does not have the luxury blood supply like in normal circumstances, so this is not a safe procedure in the presence of severe burn-induced progressive ischemic scarring.

Danger of necrosis if eyelid shortening is really required is less in the lower eyelid. To avoid central infarction, the release should be at the lateral canthus maybe with a lateral tarsorrhaphy for a safer blood supply via an upper eyelid transconjunctival flap [7]. Normally an additional skin transplantation is essential.

19.6.1 Lower Eyelid Sling

For recurrent lower eyelid ectropion, the use of lower eyelid fascial slings (fascia temporalis or fascia lata) have been reported [35]. It provides a vertical support and does not overcome contraction or tissue deficit, which requires release and tissue replacement. It is secured to the medial canthal tendon and to the lateral orbital rim and braces the lower lid margin [36].

19.6.2 Obstruction of Canaliculi

A burn damage involving the puncta and canaliculi is infrequent. Meyer et al. recommend early punctal evaluation and daily dilatation if necessary during the first 10 days [37]. This may be a good opportunity to prevent early stenosis but is not practical for longer prophylaxis or for reconstruction.

References

1. Stern JD, Goldfarb IW, Slater H. Ophthalmological complications as a manifestation of burn injury. Burns. 1996;22(2):135–6.

2. Bouchard CS, Morno K, Jeffrey P, et al. Ocular complications of thermal injury: a 3-year retrospective. J Trauma. 2001;50(1):79–82.
3. Spencer T, Hall HJA, Stawell RJ. Ophthalmological sequelae of thermal burns over ten years at the Alfred Hospital. Ophthal Plast Reconstr Surg. 2001;18(3):196–201.
4. Linhart GW. Burn of the eyes and eyelids. Ann Ophthalmol. 1978;10:999–1001.
5. Still JM, Law EJ, Belcher KE, Moses KC, et al. Experience with burns of the eyes and lids in a regional burn unit. J Burn Care Rehabil. 1995;16:248–52.
6. Marrone AC. Thermal eyelid burns. In: Hornblass A, Haing CJ, editors. Oculoplastics, orbital and reconstructive surgery. Baltimore, MD: Williams & Wilkins; 1988. p. 433–7.
7. Mauriello JA Jr, Hollsten DA. Cicatricial ectropion due to thermal burns of the eyelids. In: Mauriello JA, editor. Unfavourable results of eyelid and lacrimal surgery, prevention and management. Boston: Butterworth-Heinemann; 2000. p. 219–26, Chap 9.
8. Tsur H. Eyelid burns. A general plastic surgeons's approach. In: Hornblass A, Haing CJ, editors. Oculoplastics, orbital and reconstructive surgery. Baltimore, MD: Williams & Wilkins; 1988. p. 448–54.
9. Huang TT, Blackwell SJ, Lewis S. Burn injuries of the eyelids. Clin Plast Surg. 1978;5(4):571–81.
10. Sloan DF, Huang TT, Larson DL, et al. Reconstruction of eyelids and eyebrows in burned patients. Plast Reconstr Surg. 1976;58:340–6.
11. Jackson DM, Roper-Hall MJ. Preservation of sight after complete destruction of the eyelids by burning. Burns. 1983;7:221–6.
12. Kostakoglu N, Ozcan G. Orbicularis oculi myocutaneous flap in reconstruction of postburn lower eyelid ectropion. Burns. 1999;25:553–7.
13. Tei TM, Larsen J. Use of the subcutaneously based nasolabial flap in lower eyelid reconstruction. Br J Plast Surg. 2003;56:420–3.
14. Zaccagna A, Raiteri E, Picciotto F. Repair of a large surgical defect involving the lower lid, cheek, and temporal region. Dermatol Surg. 2003;29:182–4.
15. Achauer BM, Adair SR. Acute and reconstructive management of the burned eyelid. Clin Plast Surg. 2000;7:87–95.
16. Tajima S, Aoyagi F. Correcting post-traumatic lateral epicanthic folds. J Br Plast Surg. 1977;30:200–1.
17. Thai KN, Billmire DA, Yakuboff Kevin P. Total eyelid reconstruction with free dorsalis pedis flap after deep facial burn. Plast Reconstr Surg. 1999;104(4):1048–51.
18. Mehta JS, Franks WA. The sclera, the prion and the ophthalmologist. Br J Ophthalmol. 2002;86:587–92.
19. Brock WD, Bearden W, Tann T III, et al. Autogenous dermis skin grafts in lower eyelid reconstruction. Ophthal Plast Reconstr Surg. 2003;19:394–7.
20. Mauriello JA, Pokorny K. Use of split-thickness dermal grafts to repair corneal and scleral defects—a study of 10 patients. Br J Ophthalmol. 1993;77:327–31.
21. Sullivan SA, Dailey RA. Graft contraction: a comparison of acellular dermis versus hard palate mucosa in lower eyelid surgery. Ophthal Plast Reconstr Surg. 2003;19:14–24.
22. Bowers DG Jr. In: Tessier P, editor. Burn trauma of eyelids: late reconstruction. Symposium on plastic surgery in the orbital region. St. Louis: C. V. Mosby; 1976. p. 31–8.
23. McIndoe AH. Total reconstruction of the burned face. Br J Plast Surg. 1983;36:410–20.
24. Hollsten DA, White WL. Management of periorbital burns. Semin Ophthalmol. 1994;9:152–64.
25. Lille ST, Engrave LH, Caps MT, et al. Full-thickness grafting of acute eyelid burns should not be considered taboo. Plast Reconstr Surg. 1999;104(3):637–45.
26. Achauer BM. Burn reconstruction. New York: Thieme Medical; 1991. p. 40–51, ISBN 0-86577-341-6.
27. Frank DH, Wachtel T, Frank HA. The early treatment and reconstruction of eyelid burns. J Trauma. 1983;23:874–7.
28. Malhotra R, Sheikh I, Dheansa B. The management of eyelid burns. Surv Ophthalmol. 2009;54(3):356–71.
29. White WL, Hollsten DA. Burns of the ocular adenexa. Curr Opin Ophthalmol. 1994;5(5):74–7.
30. Kuckelkorn R, Redbrake C, Reim M. Tenonplasty, a new surgical approach for the treatment of severe eye burns. Ophthalmic Surg Lasers. 1997;28(2):105–10.
31. Choi YC. Single-hair transplantation by Choi's procedure. Int J Cosmetic Surg Aesth Dermatol. 2000;2(3):187–94.
32. Goldman GD. Eyebrow transplantation. Dermatol Surg. 2001;27(4):352–4.
33. Wang J, Fan J. Cicatricial eyebrow reconstruction with a dense-packing one to two hair grafting technique. Plast Reconstr Surg. 2004;114(6):1420–6.
34. McConnel CM, Neale HW. Eyebrow reconstruction in the burn patient. J Trauma. 1977;17:362–6.
35. De la Torre J, Simpson RL, Tenenhaus M, et al. Using lower eyelid fascial slings for recalcitrant burn ectropion. Ann Plast Surg. 2001;46:621–4.
36. Tyres AG, Collins JRO. Colour atlas of ophthalmic plastic surgery. 2nd ed. Edinburgh: Butterworth Heinemann; 2001. p. 118–21.
37. Meyer DR, Kersten RC, Kulwin DR, et al. Management of canalicular injury associated with eyelid burns. Arch Ophthalmol. 1995;113(7):900–3.

Ear Reconstruction in Post-burn Ear Deformity

20

Andrew Burd, Paul Wurzer, and Thomas Rappl

20.1 Introduction

Post-burn ear reconstruction is a challenge for reconstructive and burn surgeons. Depending on the damage, the ear requires a total or partial reconstruction. The anatomy of the external ear is quite simple but still unique. The ear consists of a sandwich of skin, cartilage and skin, and all three layers have to be reconstructed in order to achieve a natural and aesthetically pleasing outcome. In addition to the layered reconstruction, the three-dimensional shape including helix, anti-helix, triangular fossa, concha, tragus and lobule have to be formed. In this chapter, we describe the basic anatomy, history of the ear reconstruction, initial post-burn treatment and principal methods.

20.2 Basic Anatomy and the Appearance of a Natural Ear

The anterior border is defined by the tragus, whereas the caudal border is defined by the lobule, which is directly connected to the helix. The posterior and superior borders are determined by the most prominent structure of the ear, the helix. The centre is formed by the concha (derived from Latin meaning spiral shell), which is surrounded by the anti-helix and triangular fossa (Fig. 20.1). The avascular cartilage is covered by the vascular perichondrium, which is in turn covered by a thin and almost hairless skin. The blood supply to the external ear comes from the anterior auricular artery, a branch of the superficial temporal artery, and the posterior auricular artery, a branch of the external carotid. The auricular temporal branches of the mandibular nerve provide sensory innervation of the external ear.

20.3 The Position of the External Ear

The outer ear is located in the middle third of the face and is roughly the length of the nose; some say that the length is directly proportional to the length of the nose. On average, it is 6 cm, from the top of the helix to the lowest part of the lobe. The distance of the helical rim from the scalp is commonly 2 cm, but can be larger in protruding ears (Fig. 20.2). For reconstructive purposes, if there is unliteral damage, it is important to consider the shape of the unharmed contralateral ear. In cases where both outer ears are deformed or even not available, the surgeon needs to focus on the established surgical landmarks (Fig. 20.3).

Studies have looked at variations of ear positioning in different racial groups [1, 2]. There are no distinct racial features as far as the external structure of the ear is concerned, and the relative position of the external ear is another global feature. The vertical position of the ear is shown in Fig. 20.4a. It is the same height as the nose and when looking at the lateral aspect of the face, the lower edge of the ear is at the level of the lateral ala base, and the upper level of the pinna typically lies on the same level as the lateral extent of the eyebrow. The ear can be considered to pivot around the external auditory meatus, and the horizontal position of the central point of the upper margin of the external auditory meatus, the porion, lies in the same vertical axis as the vertex of the skull (Fig. 20.4b). The long axis of the ear is not vertical, and the normal ear inclines backwards and the axis of recline is parallel to that of the line from the tip to the nasion of the nose (Fig. 20.4c).

The influence of the position of the external ear on the overall aesthetics of the lateral view of the head and neck is illustrated by this patient who has sustained a unilateral facial burn (Fig. 20.5). The scarring on the ear has caused the pinna to curl forwards losing the grace and 'flow' of the

A. Burd (✉)
Division of Plastic, Reconstructive and Aesthetic Surgery, Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong

P. Wurzer · T. Rappl
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_20

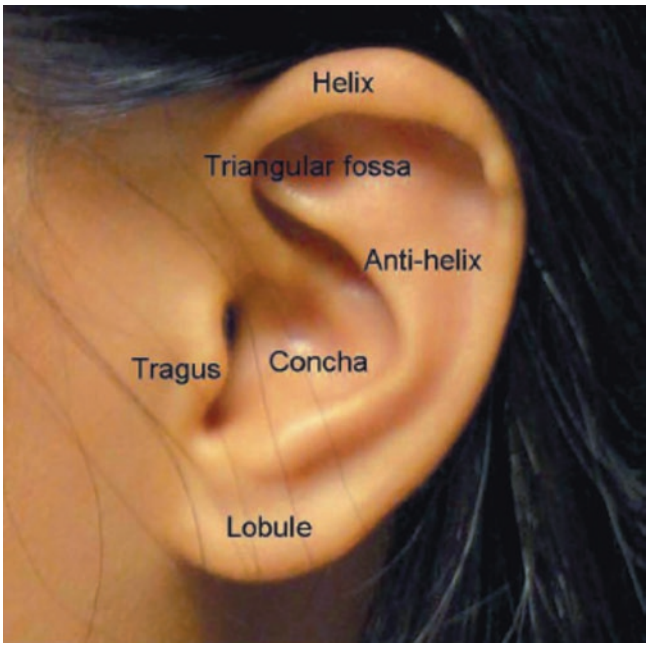


Fig. 20.1 The elegance of the human ear—anatomy

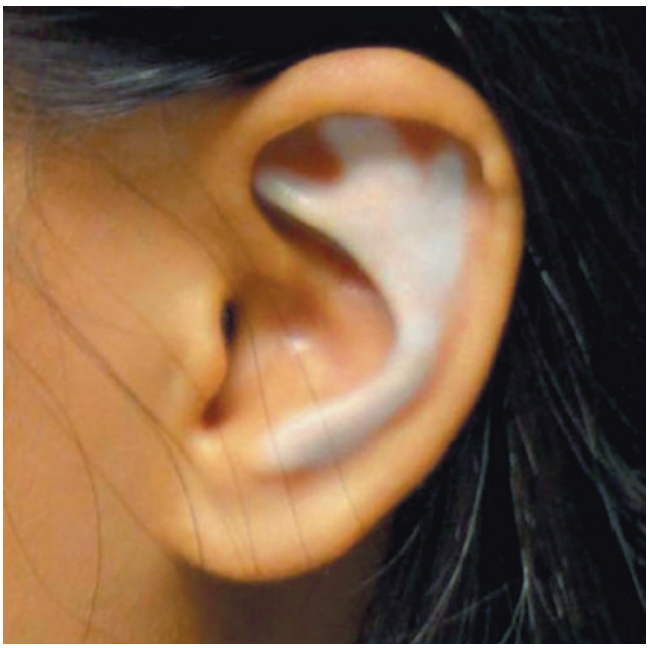


Fig. 20.2 The elegance of the human ear—imagery

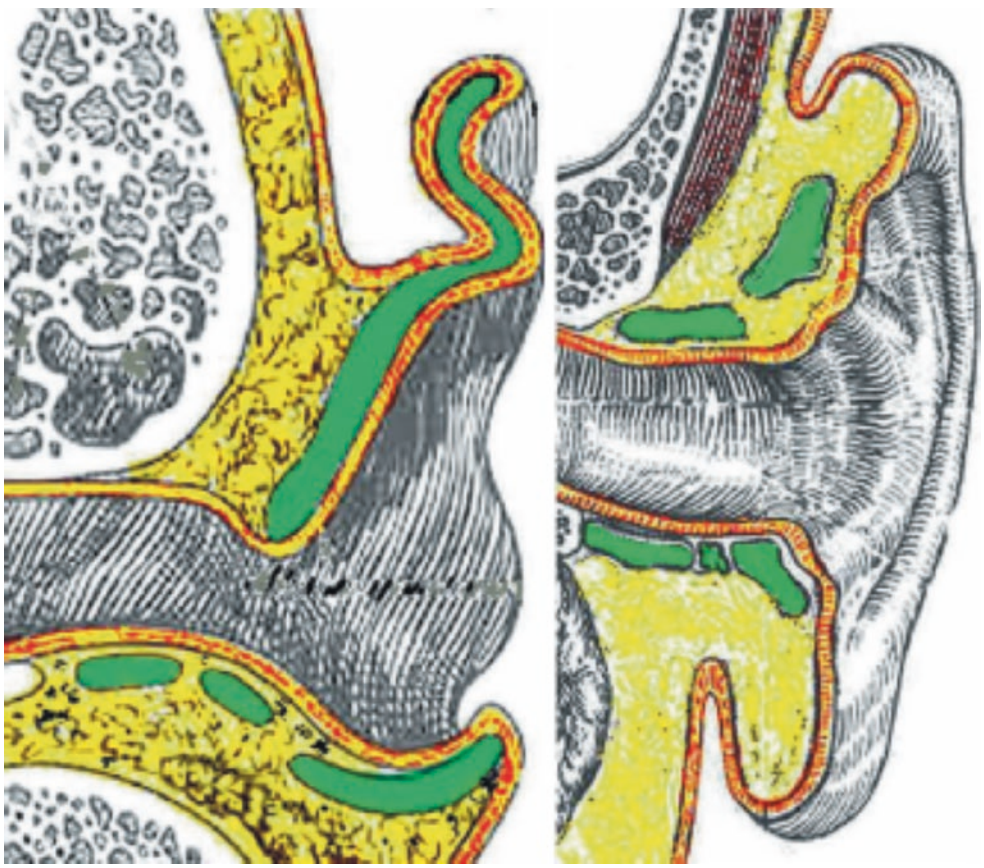


Fig. 20.3 The 'sandwich' with cartilage in green and fibrous connective tissue (yellow)

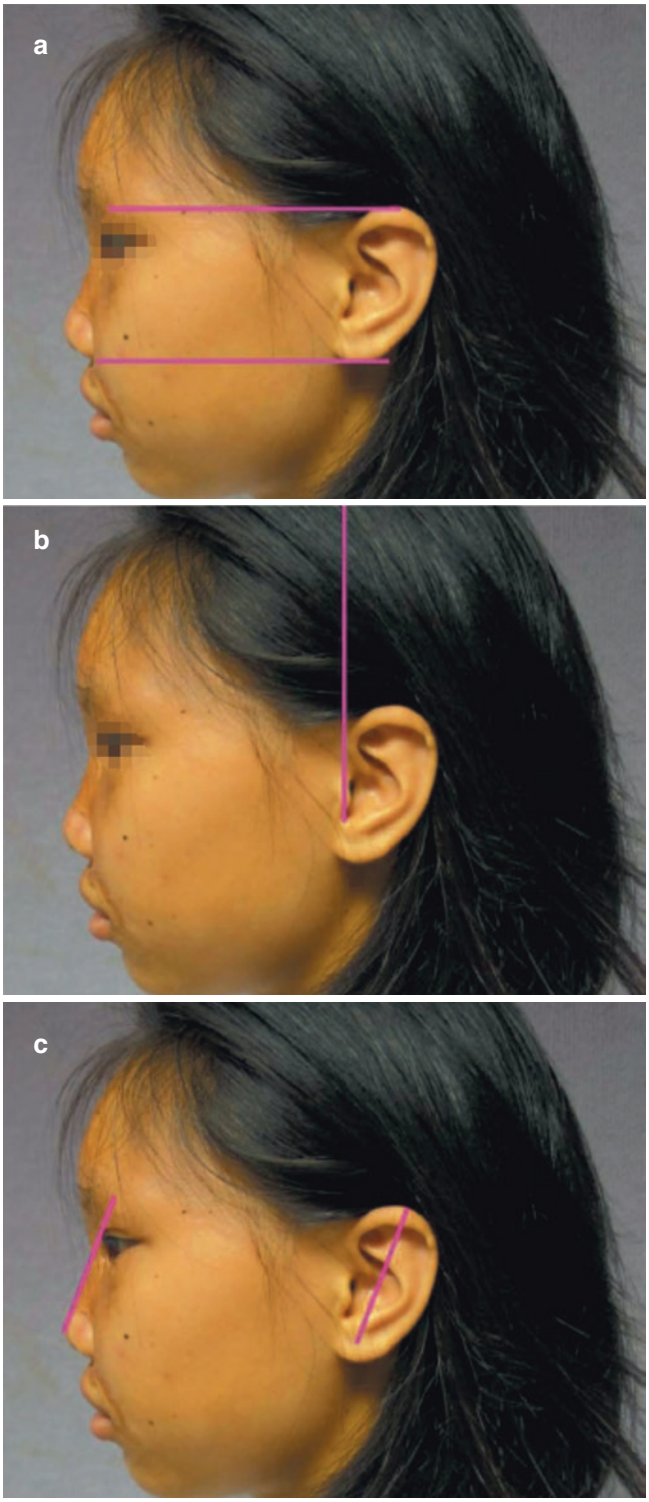


Fig. 20.4 (**a**–**c**) The position of the normal ear

contralateral (normal) ear. In addition, the right side of the face is scarred, and there has been a contracture of the right cheek and neck which is distorting the position of the ear. The entire ear is pulled forwards and also downwards. This is possible due to the mobility of the external auditory canal. Figure 20.6 shows a computer-generated overlay of the right and left sides of the face which puts into perspective the two contrasting ear positions.

20.4 Initial Management of the Burned Ear

Burns involving the head and neck commonly affect the ears. Depending on the temperature as well as exposure time, the burn can cause superficial up to full-thickness burns. However, the structures of the external ear including skin and cartilage are very vulnerable, and hence, a short time exposure to a thermal source can cause a severe damage to the ear. Besides the external structures, the internal ear, especially the tympanic membrane, can be damaged. If there is concern about deep damage, a physical examination by an ENT physician of a burn to an ear is recommended, to avoid misdiagnosis and prevent further damage to inner structures of the ear. This must be done acutely before swelling of the auditory meatus precludes examination.

Initial care of the burned ear includes a well-padded cover with antimicrobial dressings. The priority is to maintain the shape of the ear and to prevent local infection and in particular a perichondritis. The dressing has to be moulded to the shape of the ear It is important to cover every part of the ear, including the postauricular fold. Padding and correct positioning of the ear is crucial to prevent folding, pressure effects and preserve vital tissue. Initial treatment of the burned ear is conservative, and attempts at surgical interventions should be delayed. If topical antimicrobial creams are used a cotton wool pledget can prevent blocking of the external auditory meatus. Determination of the burn depth can be difficult after using some agents such as silver sulphadizine; however, this is still a popular product due to simplicity of use and patient comfort.

20.5 History of Ear Reconstruction

The first records of rear reconstruction are going back to sixth century BC, where an Indian advancement flap was performed to address partial ear reconstruction by the Sushruta Samhita [3]. In Europe, the first description of partial rear reconstruction was described in the sixteenth century by the Branca family in Sicily, who used skin from the arm. Later, Gaspare Tagliacozzi, an Italian surgeon, described in his book, De Curtorum Chirurgia per Insitionem Libri Duo, the reconstruction of the helical rim as well as lower auricle. Later in 1845 Dieffenbach spoke against a total ear reconstruction due to the high rates for complications and the poor aesthetic outcome [4]. In 1970, the ‘Gavello flap’, a bilobed flap for lower auricle reconstruction was described by Szymanowski [3]. Ear reconstruction underwent a new

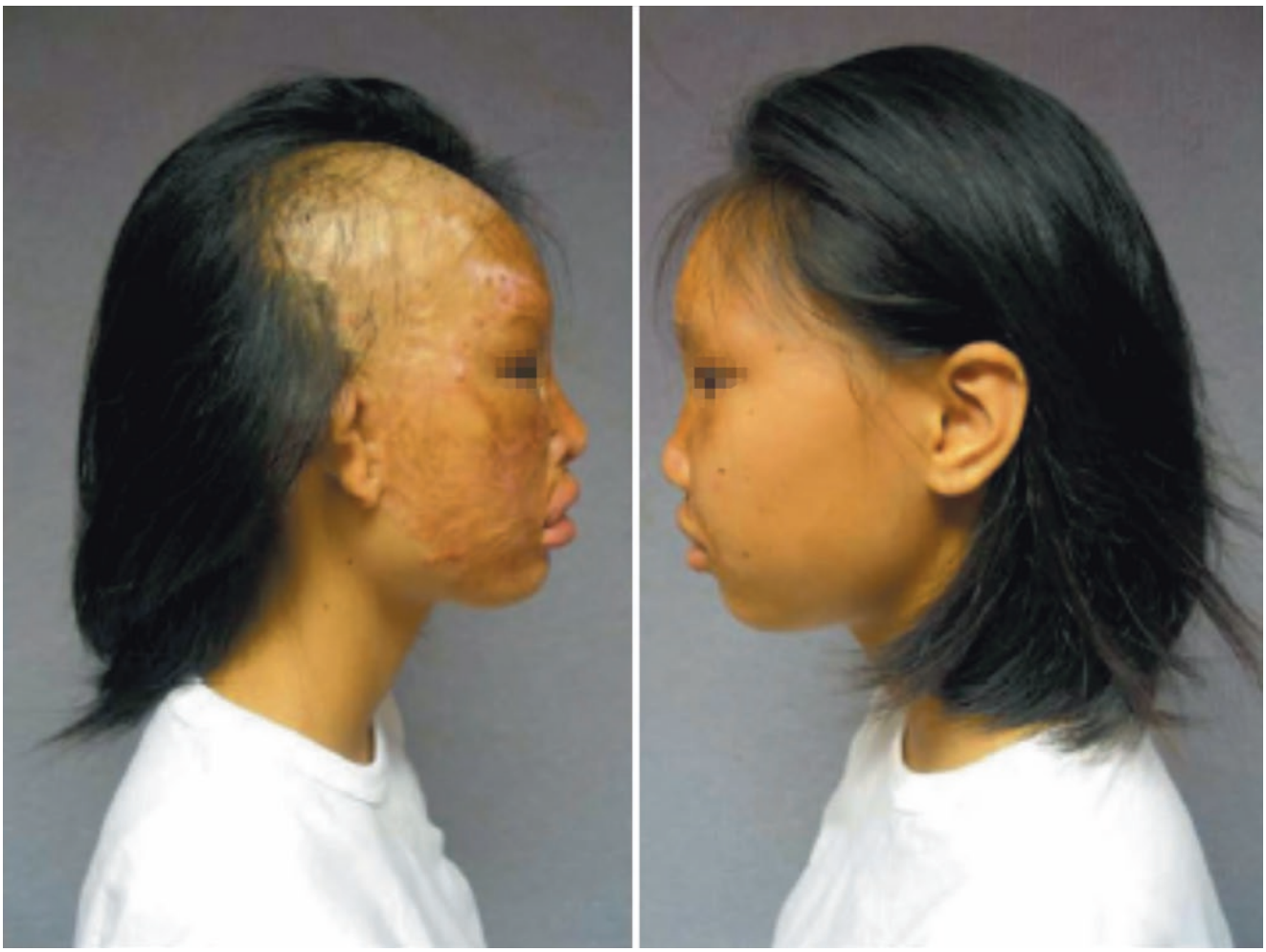


Fig. 20.5 A unilateral facial burn resulting in malpositioning of the right ear

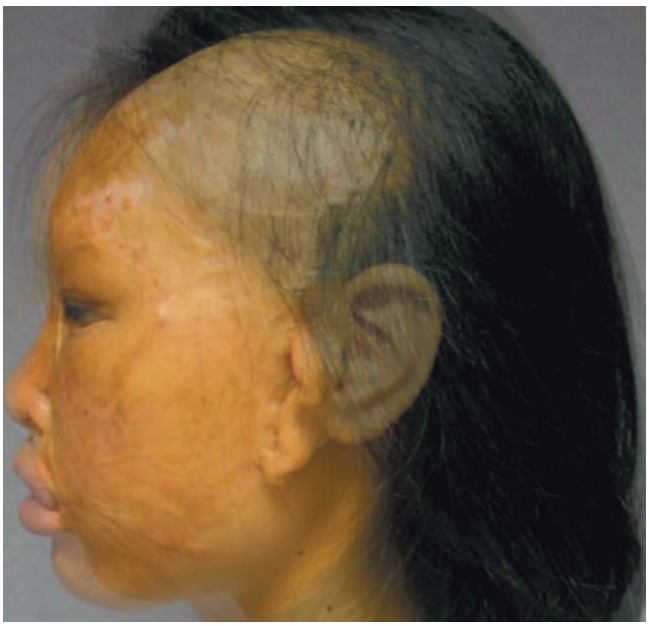


Fig. 20.6 An overlay of right and left lateral views to emphasis malposition

phase in the early twentieth century, where regional superiorly based retroauricular skin flaps were described by Smith and later by Ombredanne. Meanwhile, Gilles described, for the first time, an inferiorly based island flap for the lower third auricle reconstruction [5]. Another surgical approach for ear reconstruction, a tubed cervical and supraclavicular pedicled flap, was described by Pierce [3]. With further time, new surgical improvements in reconstruction of the cartilage framework using xenografts or ivory, silicone, metal, Teflon or porous polyethylene were described. Nevertheless, most surgeons in the early twentieth century were still unhappy with the aesthetic outcomes [6].

20.6 Post-burn Reconstruction

In 1944, Suraci [7] defined seven important criteria for ear reconstruction: symmetrical size, similarity of outline and height, correct cephalo-auricular angle, permanency of size and shape, rigidity of the ear and matching colour (Fig. 20.7).

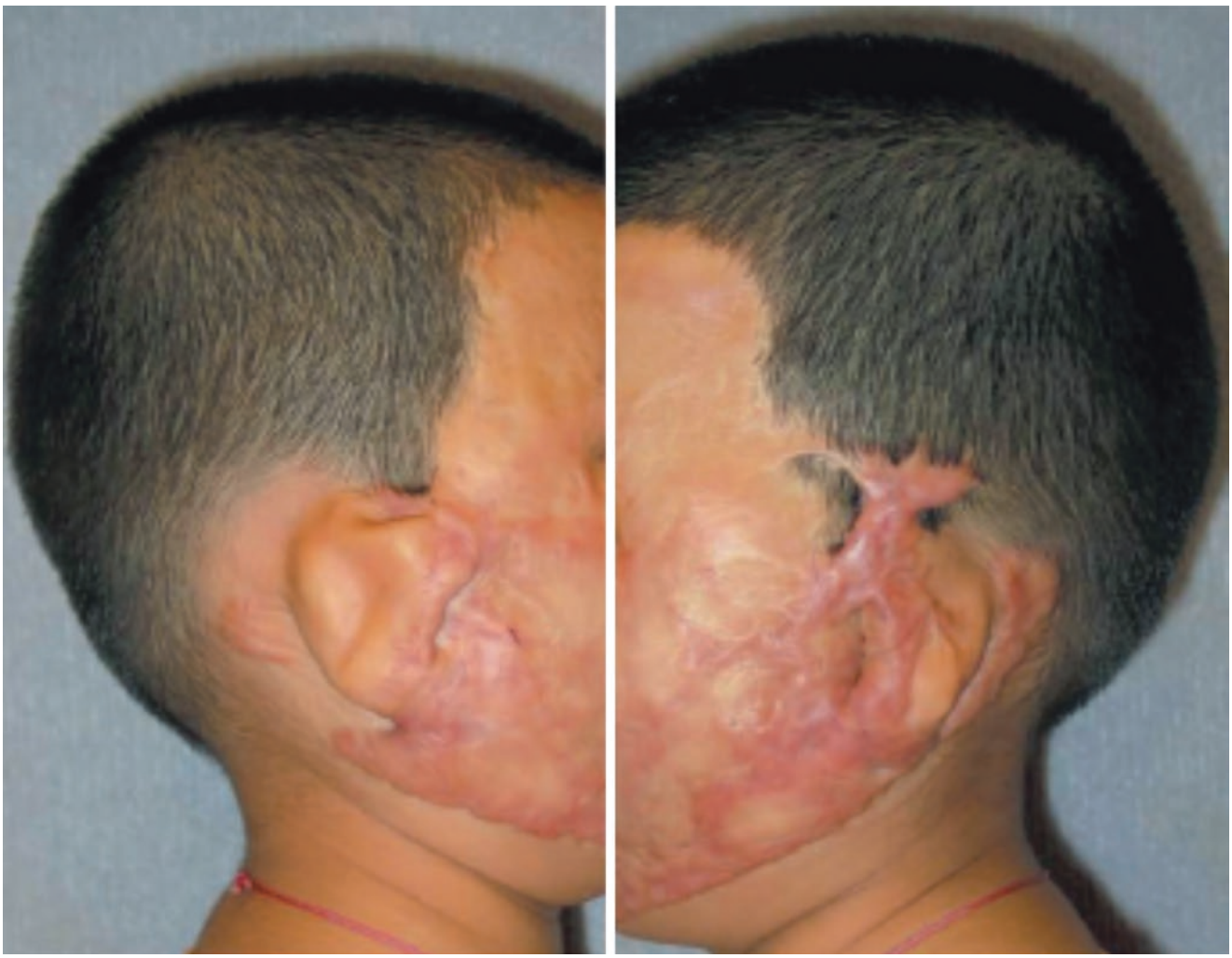


Fig. 20.7 The unfortunate consequences of suboptimal acute care

When a patient is being reviewed regarding problems related to the ear after a burn, the patient will focus on one, or a combination, of the following problems:

1. Impaired hearing
2. Abnormal scarring
3. Loss of function
   (a) Retention of glasses
   (b) Inability to adorn with jewellery
4. Deformity of the ear (without loss of tissue)
5. Displacement of the ear due to surrounding scarring
6. Loss of part or whole of the extend ear

20.6.1 Impaired Hearing

Whilst this may be due to meatal stenosis, there are other causes of unilateral or bilateral hearing impairment that could be completely unrelated to the burn injury. In view of this, it is important to arrange for a baseline audiometric assessment to be made when the patient presents with such a concern. Other causes need to be excluded.

Hearing impairment can be attributed to a physical blockage or distortion of the external auditory meatus, and direct involvement of the skin by the original burn injury can result in scarring and a cicatricial stenosis.

If the deformity is more like a slit due to a traction force, then release of this force will be needed. The case illustrated shows a typical example of how this can be achieved by insetting a flap into an incisional (or excisional) defect created by the surgical release of the deforming scar tensions. The patient illustrated had been the victim of an acid assault and had developed extensive scarring of the mouth, nostrils, chin, neck and left ear. She was referred having had the acute burn treated elsewhere, and some initial reconstruction had been commenced, but her specific concerns were the ectropion of the lower lip and the deformity of the left neck and impaired hearing. A splint had been made to try and

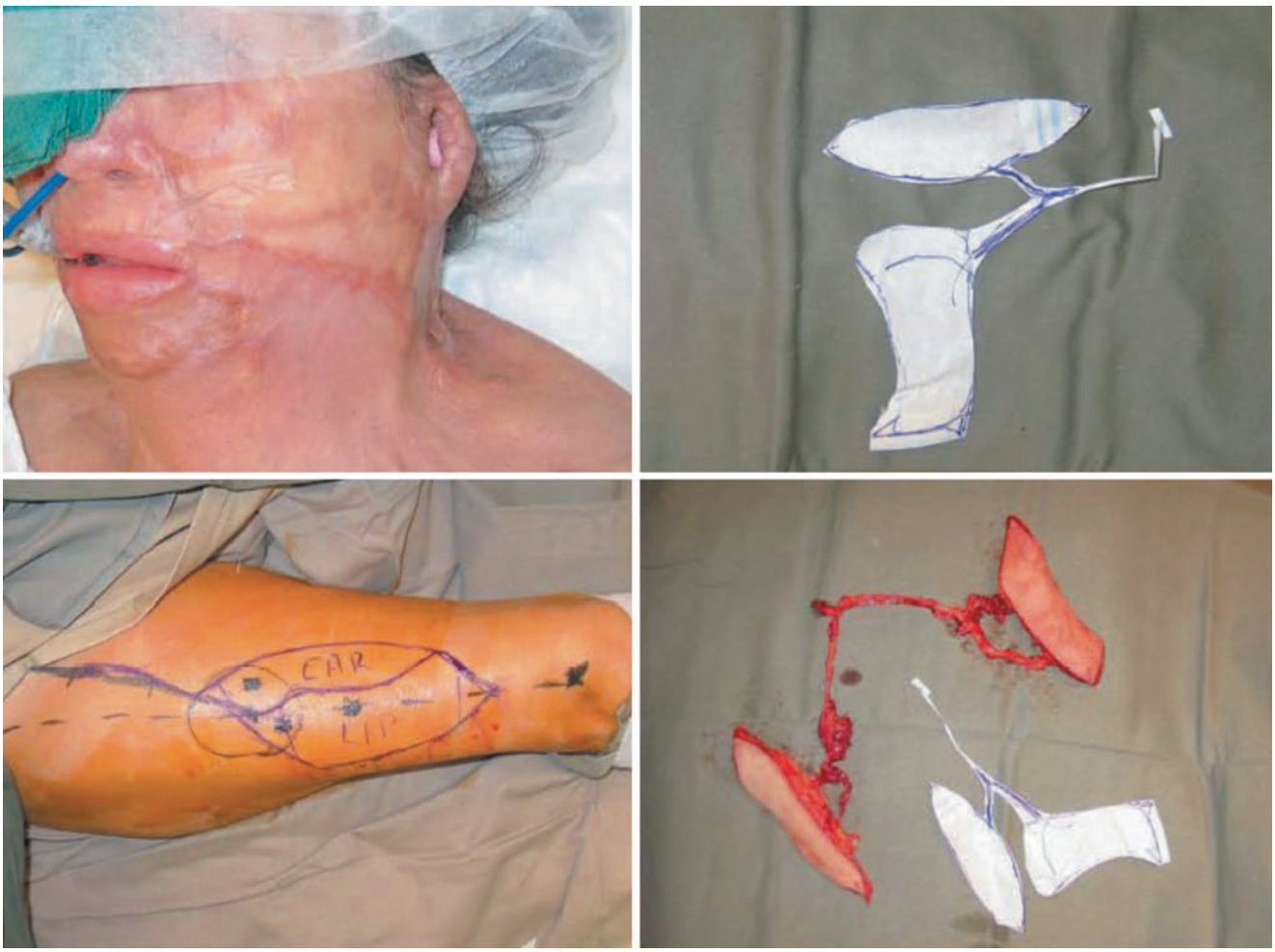


Fig. 20.8 An intra-operative series indicating the two flaps

counteract the 'stenosis' of the EAM, but on inspection it was the scarring in the neck that was causing the problem. To address both the problems, a bi-paddled anterolateral thigh flap was raised. This actually proved to be anatomically interesting as the perforators came from two completely separate systems allowing the flaps to be placed some distance from each other whilst there was only one anastamosis to the recipient vessels (Fig. 20.8).

The two flaps were inset with the anterior paddle oriented horizontally to correct the lower lip ectropion. The posterior paddle was oriented vertically and was inset into the lateral neck defect left after an incisional scar release. The upper tip of the flap was inset into the external audiotory meatal canal to release the cicatricial stenosis (Fig. 20.9).

20.6.2 Abnormal Scarring

In certain patients, there is an accumulation of excessive connective tissue which forms an abnormal scar. The two principle forms of abnormal scar are hypertrophic and keloid scars. These do appear to be two very different forms of scar [5]. A major clinical difference is that the hypertrophic scar appears to be associated with active tissue remodelling, and the effect is that tensions are created within the skin surrounding the scar tending to cause a contracture of the scar area. This can be seen by the effects of the scar on the surrounding soft tissues, for example, the mouth or eyelids. When the hypertrophic scar is excised, the resulting defect is always much larger than the area of excised scar. The keloid scar behaves very differently and is characterized more by an accumulation of connective tissue matrix which appears to grow into the surrounding tissues. The edge of the scar is often raised and rolled, and when the scar is excised, the resulting defect is usually the same size as the excised scar. There is another very important clinical difference between the keloid scar and the hypertrophic scar and that relates to the duration of the abnormal scarring. Typically a keloid scar will grow to a certain size and then remain at that size for a prolonged period of time. Indeed the keloid scar is generally

thought not to involute. The hypertrophic scar in contrast is a self-limiting form of abnormal scarring and will mature albeit over the course of several years.

The two forms of scarring are rarely seen together in any patient group other than in post-burn patients and particularly children. The reason for this is not clear, and it is also clear that the pathology as well as the pathogenesis of the keloid scar, in particular, is different in the burns patient when compared to keloid arising from other stimuli, such as acne or ear piercing. Our understanding of the nature of the evolution of the post-burn keloid scar remains rudimentary, and it is possible that it does have a tendency to be more self-limiting than other types of keloid.

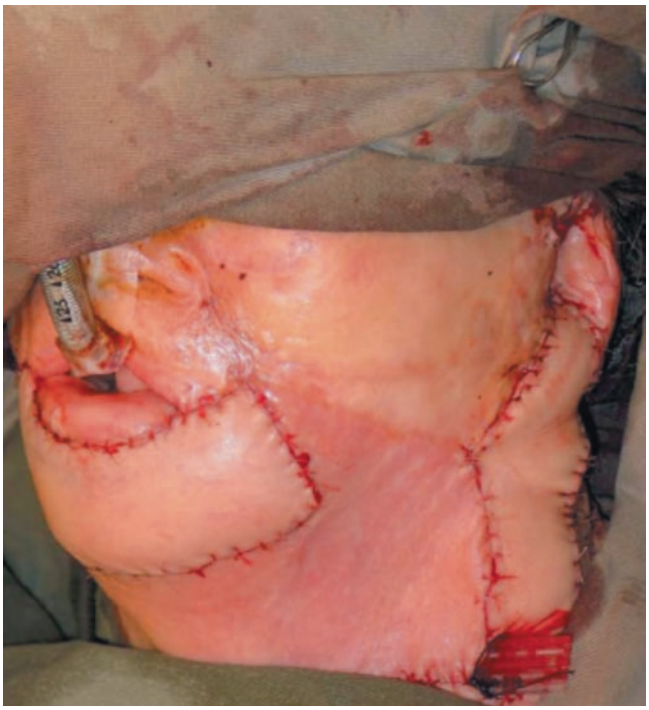


Fig. 20.9 Two flaps inset

Figure 20.10a shows both right and left lateral views of a young boy who developed classical keloid-type scarring of the upper helical ruin. The close-up view shows the massive raised, rolled accumulations of scar tissue (Fig. 20.10b). The standard teaching is that if a keloid scar is excised, then it always recurs and also tends to be more aggressive. To prevent or reduce the incidence of recurrence, it is always necessary to apply some adjuvant treatment in combination with the surgery. This may involve the application of cytotoxic agents to the post-excisional wound, the injection of steroids or exposure to irradiation or even cryotherapy. These approaches reduce the cellular response to further wounding and appear to have an immunosuppressive effect.

Our approach to the post-burn keloid is rather different, and the first case was detailed in a case report involving a large buttock and posterior thigh keloid [4]. Basically, the keloid was shaved flesh with the normal skin, and cells cultured from a biopsy taken from a site of normal skin were applied as suspension with a concentration of 8.3×10^4 cells per cm^2. The cells were pipetted onto the excisional defect and 'fixed' in place by the subsequent application of Tisseel® fibrin glue. The glue was sprayed on gently taking care not to blow the liquid suspension off the wound. The wound was then allowed to dry, and Mepitel was then applied. The healing of the wound is depicted in Fig. 20.11.

The upper two pictures show the post excisional wound at 1 week post cell spray. Of note as the 'excision' of the keloid was flesh with the surface of the surrounding skin, there is still keloid tissue in the wound bed. The lower two pictures show the wound dressed with gentian violet and complete healing occurred in 3 weeks. Figure 20.12 shows the appear-

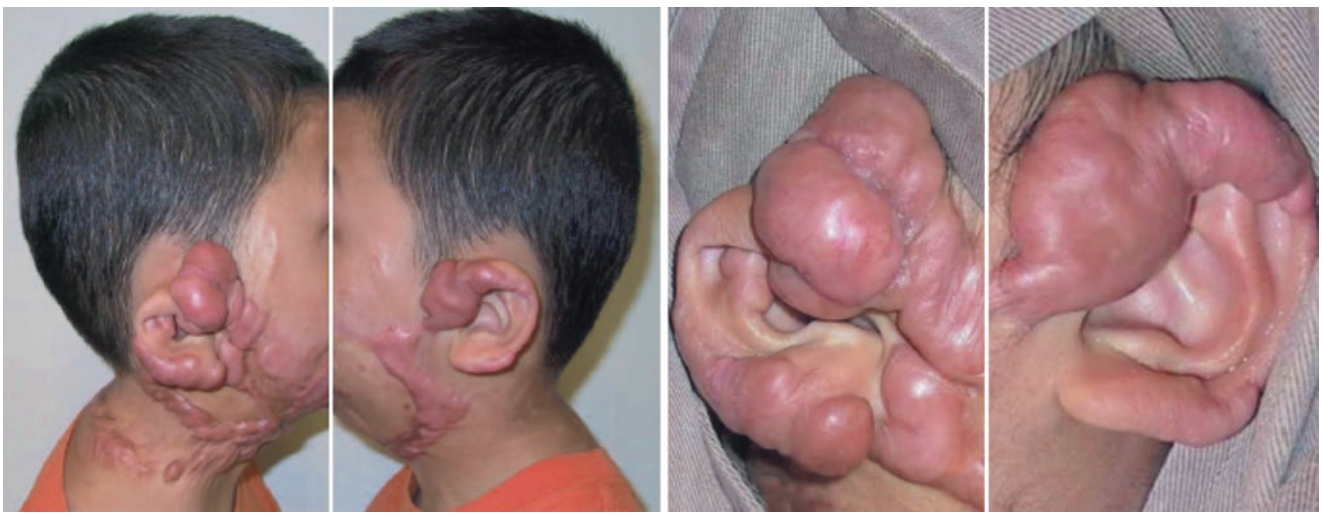


Fig. 20.10 (**a**, **b**) Abnormal scarring with close-up view

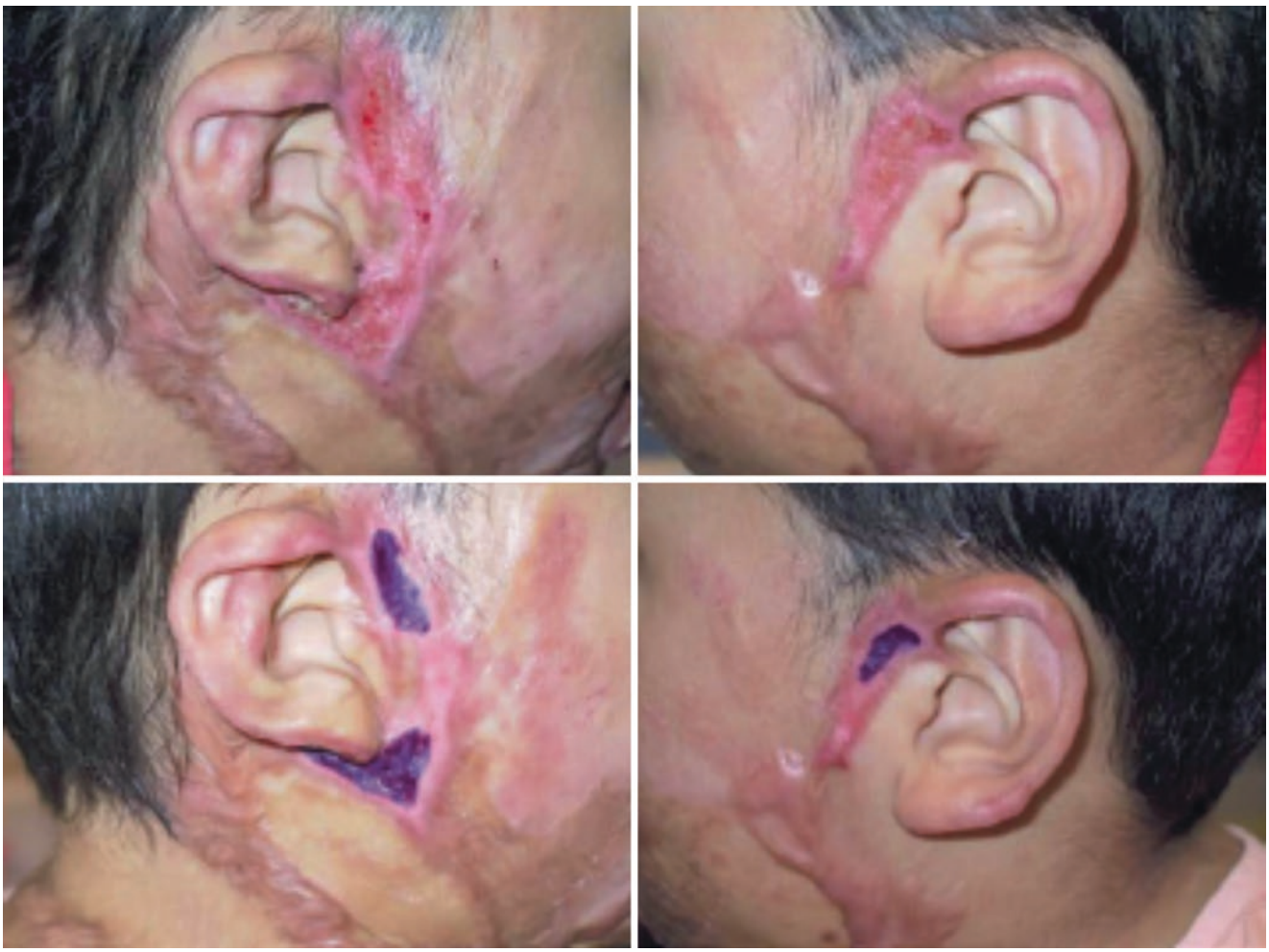


Fig. 20.11 Early post-operative views

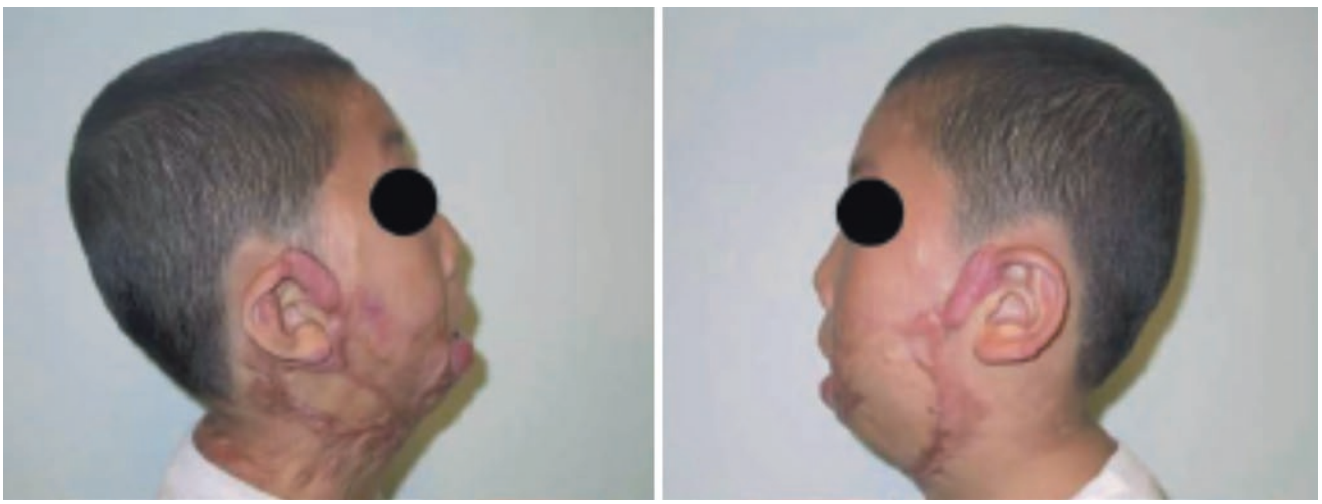


Fig. 20.12 Lateral views. It appears as if the scar trajectory has changed, and whilst initially there is obvious scar growth, this does resolve in 12 months

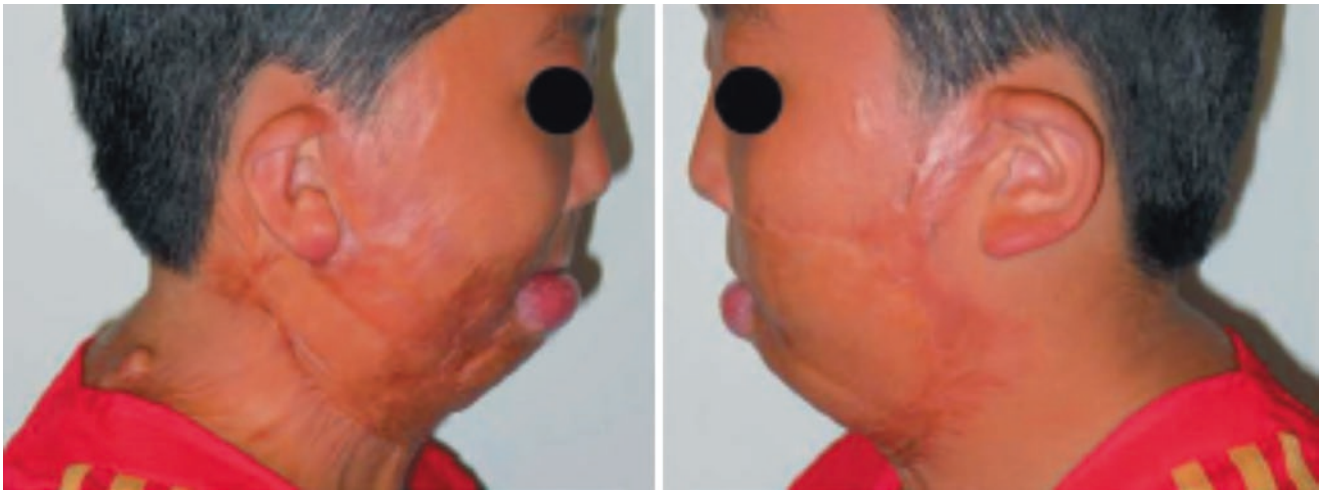


Fig. 20.12 (continued)

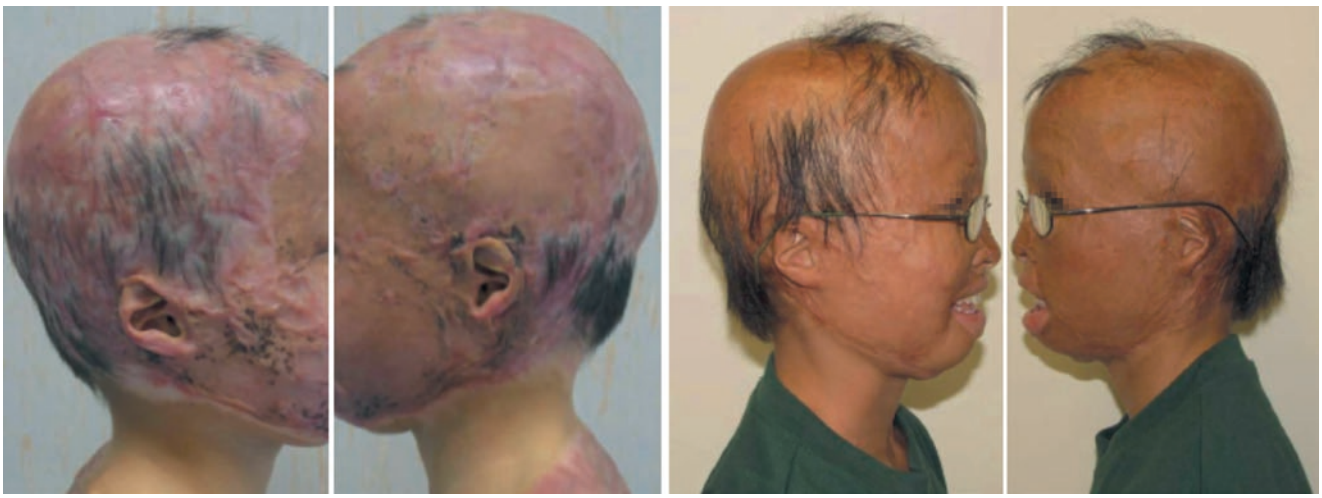


Fig. 20.13 (**a**, **b**) Early and late views of bilateral ear burns which caused deformity but retained the function of supporting eyeglasses

ance at 6 months post cell spray. The scar is raised and red but subsides and when viewed 3 years post cell spray (the lower two pictures of Fig. 20.12). The scarring is all flat and mature. Again, the underlying biological mechanisms at work remain unknown, but in a series of five cases, the response has been similar and persistent.

20.6.3 Loss of Function

Apart from the function in association with the middle and inner ear for hearing, the external ear has a function for retaining ear-mounted devices. These may simply be spectacles although there is an increasing range of wireless free devices that can be attached to the ears. This retention function depends more upon the well-defined upper pole of the ear with a retroauricular sulcus. The other function is for the adornment of jewellery, and this is typically applied to the lobe of the ear. Thus loss of the lobe can be a concern for some patients.

Figure 20.13a shows a patient who sustained 65% TBSA burns in an injury involving a mosquito net [3]. The scalp was severely damaged and the external ears were deformed, but the patient was not concerned about the ears as they retained their function of stabilizing his eye glasses (Fig. 20.13b).

The interval between Figs. 20.4c and 20.13b was 3 years, and in that time, the patient had received multiple surgeries to improve the function of his hands. Another case shows the creation of a retroauricular sulcus by elevating the cartilage together with a rim of scar approximately 8 mm wide and then inserting a split thickness graft secured with a tie over dressing (Fig. 20.14).

The appearance is shown 2 years later, and the sulcus has been maintained although some graft contracture has dis-

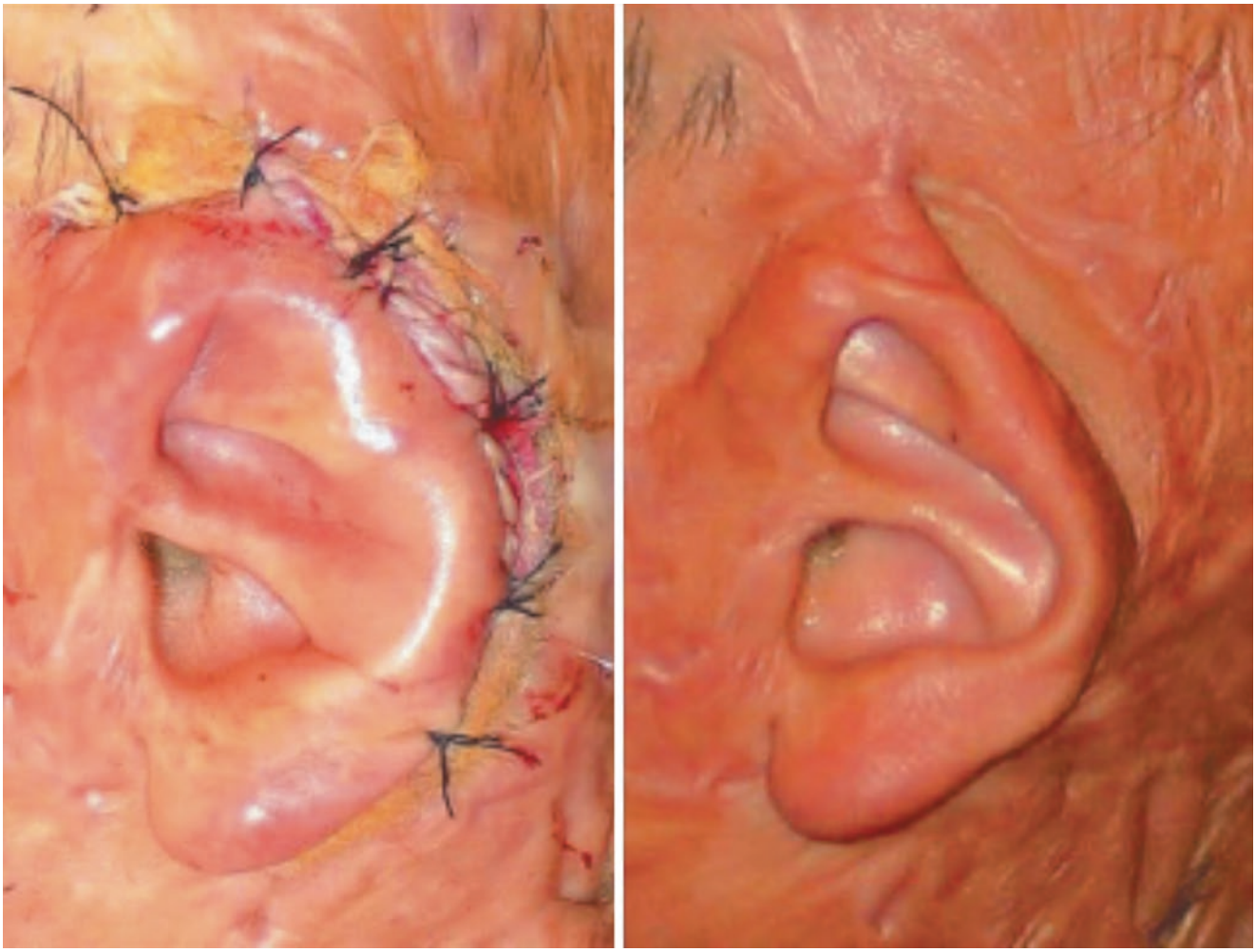


Fig. 20.14 Both this and the previous patient suffered from mosquito net-related burns. These cause deep burns of head, neck and hands. The patient was happy with a very limited procedure

torted the upper pole of the ear, and the superior sulcus has not been satisfactorily defined.

20.6.4 Deformity of the Ear Without Loss of Tissue

This is a preventable but unfortunately all too common complication of inadequate primary treatment of ear burns. The deformity is a consequence of dressings that are either inappropriately applied or not checked. The ear becomes folded forwards and the helical rim becomes attached to the pre-auricular skin or scar tissue. Where the attachment occurs, there will inevitably be an accumulation of scar tissue, and when releasing the anteriorly displaced ear, the helical rim will appear as a secondary deformity.

There will also be a defect in the pre-auricular region that was the site of the attachment. This defect can often be conveniently closed using a superiorly based flap of post-auricular skin. The ear thus formed lacks the helical definition of the normal ear but is acceptable to most patients.

Examples of this type of reconstruction are shown in Figs. 20.7, 20.15 and 20.16. Figure 20.7 is the deformity at presentation. The entire cartilaginous framework is present, but the ear has been folded anteriorly, and scarring is maintaining the deformity. When the scar is released, there is a significant loss of skin that prevents a direct closure of the defect in the pre-auricular area and on the helical rim. A superiorly based post-auricular flap can be used to close the defect. Although the resulting ear does not have the aesthetic impact of the natural ear, the return to a normal position and a grossly normal ear has produced a result that is acceptable to the patient.

Of interest in this case is the keloid-like scar nodule that is arising from the anterior aspect of the ear. The follow-up 2 years after the surgery shows a result that is acceptable to the patient. Of interest is that the keloid-like scar has matured and is no longer visible suggesting atypical keloid behaviour.

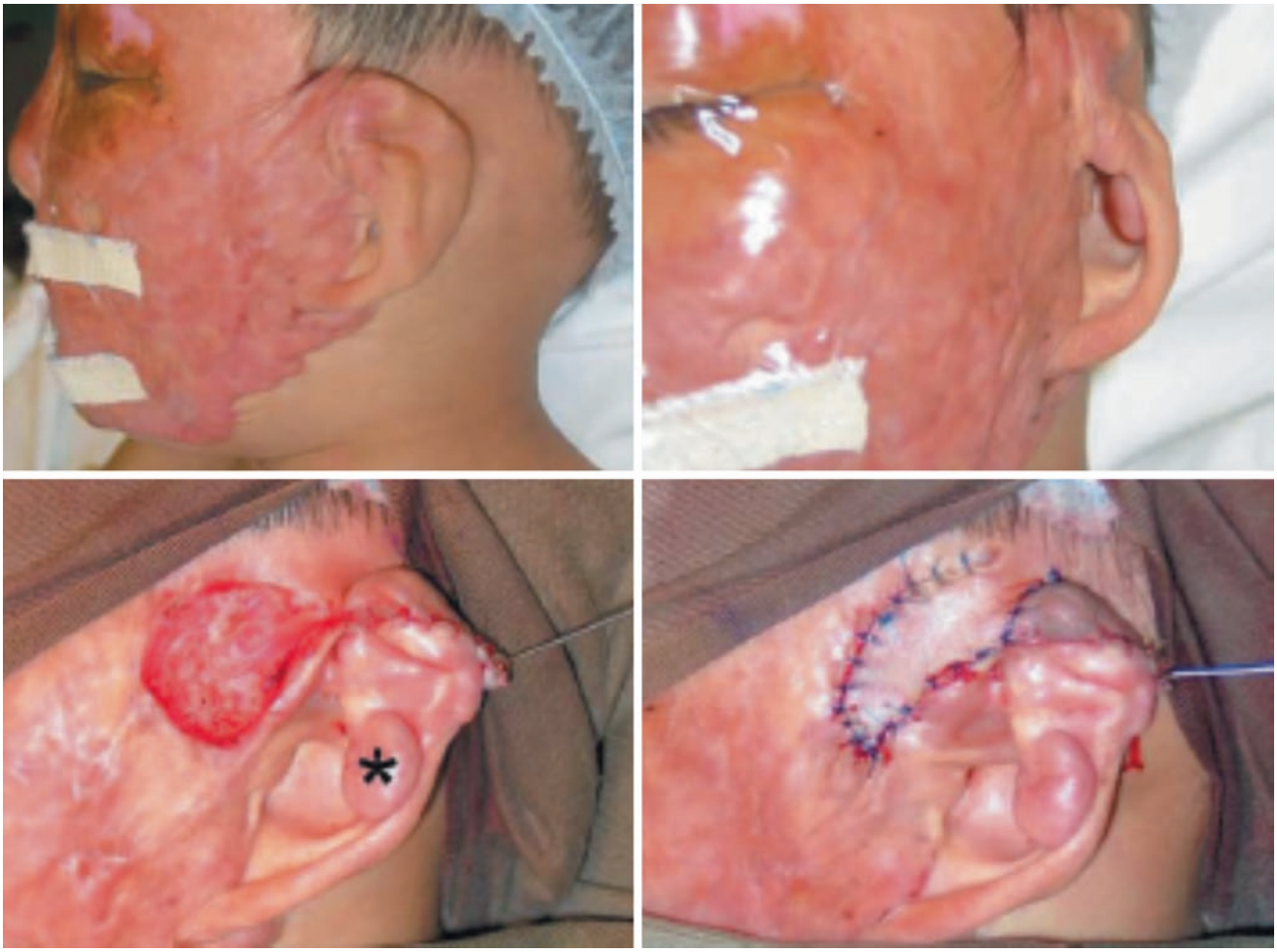


Fig. 20.15 Another case using the superiorly based post-aurical flap. A 'keloid' nodule is present on the anterior surface of the ear (*)

20.6.5 Displacement of the Ear Due to Surrounding Scarring

It is quite fascinating how the human brain processes information with regard to facial features. With regard to the ear, the extent and nature of a deformity of shape are secondary to an appreciation of an abnormal position. The external ear is joined to the skull by a deformable cartilaginous tube lined by skin and surrounded by fibro-fatty tissue. Scarring of the neck and/or the cheek can cause the ear to be pulled down and/or anteriorly. The extent and nature of the scarring will determine the extent and nature of the deformity, and in turn the extent of the defect created as the ear is returned to its original position.

In the neck which is a highly flexible part of the body, a substantial and permanent release is most often achieved by the use of flaps. These have the shared advantages of requiring no post-operative immobilization or splinting, and there will be no subsequent contracture.

The cheek is not so dynamic in its movement, and full-thickness or thick split-thickness grafts or the use of tissue engineered material specifically Integra dermal regeneration template can achieve satisfactory closure of the defect left after excision of the scar causing the positional deformity.

The series of pictures in Fig. 20.17 show the excision of the right facial scar of the patient with unilateral facial scarring shown in Fig. 20.5. The defect is resurfaced with a sheet of full-thickness skin graft. The three pictures at the bottom of Fig. 20.17 show the situation before the surgery and the immediate and 4-year post-reconstruction appearance. Figure 20.18 shows computer composites of the pre- and post-surgery to show the change in ear position and also a composite of the right and left sides which underlines the importance of ear position in the overall aesthetics of the face.

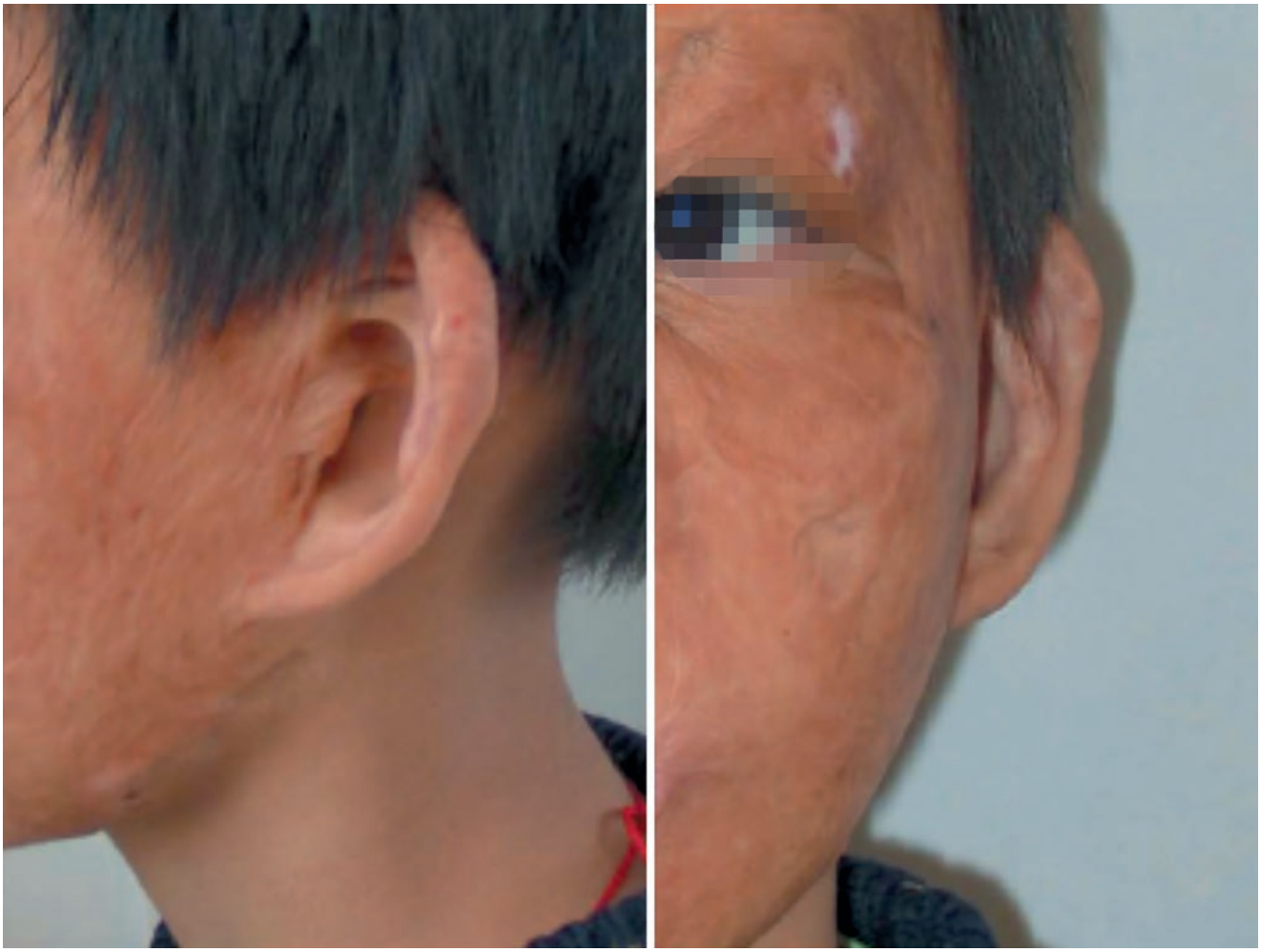


Fig. 20.16 Two years later, the ear shape is acceptable, and the 'keloid' nodule has gone

20.6.6 Loss of Part or Whole of the External Ear

There is a major difference in reconstructing the ear after congenital absence and reconstructing an ear after traumatic loss and in particular burns. The difference relates to working with skin on the one hand and scar tissue on the other. Skin is a much more versatile reconstructive medium, and the quantity can always be increased by tissue expansion. It is interesting to note that the first reported case of medical skin expansion was performed by Neumann in 1956. He used a rubber balloon which he inflated by air. And the patient? The patient had sustained traumatic amputation of the upper two thirds of his right ear many years before. Neumann introduced the balloon under the skin in the temporoparietal region. He subsequently removed this and inserted a C-shaped costal cartilage graft. Neumann conceded that much work needed to be done before such a reconstruction could become accepted by the plastic surgical community at large, but a concept had been born [8].

Even in busy specialized units, taking trauma and congenital cases, there is little call for tissue expansion. The details are however very clearly explained by the Mount Vernon team. They expanded the available skin and then when removing the expander, also performing a capsulectomy. This very thin skin was drawn over the preformed framework and a close attachment was created using prolonged mini-suction drains [9].

Looking at the literature regarding ear reconstruction, it would be misleading to think that they will be equally useful using skin flaps compared to scar flaps. Scarred skin can be used in other parts of the body because the subdermal capillary plexus is still present if the burn was of partial thickness. It is the movement that is the problem so skin can be tubed but scar cannot, or at least cannot be tubed so easily [10].

Tubing can be useful for loss of the helical rim and the lobule, but when more extensive loss involving a significant cartilage deficiency occurs, then the reconstruction requires a framework.

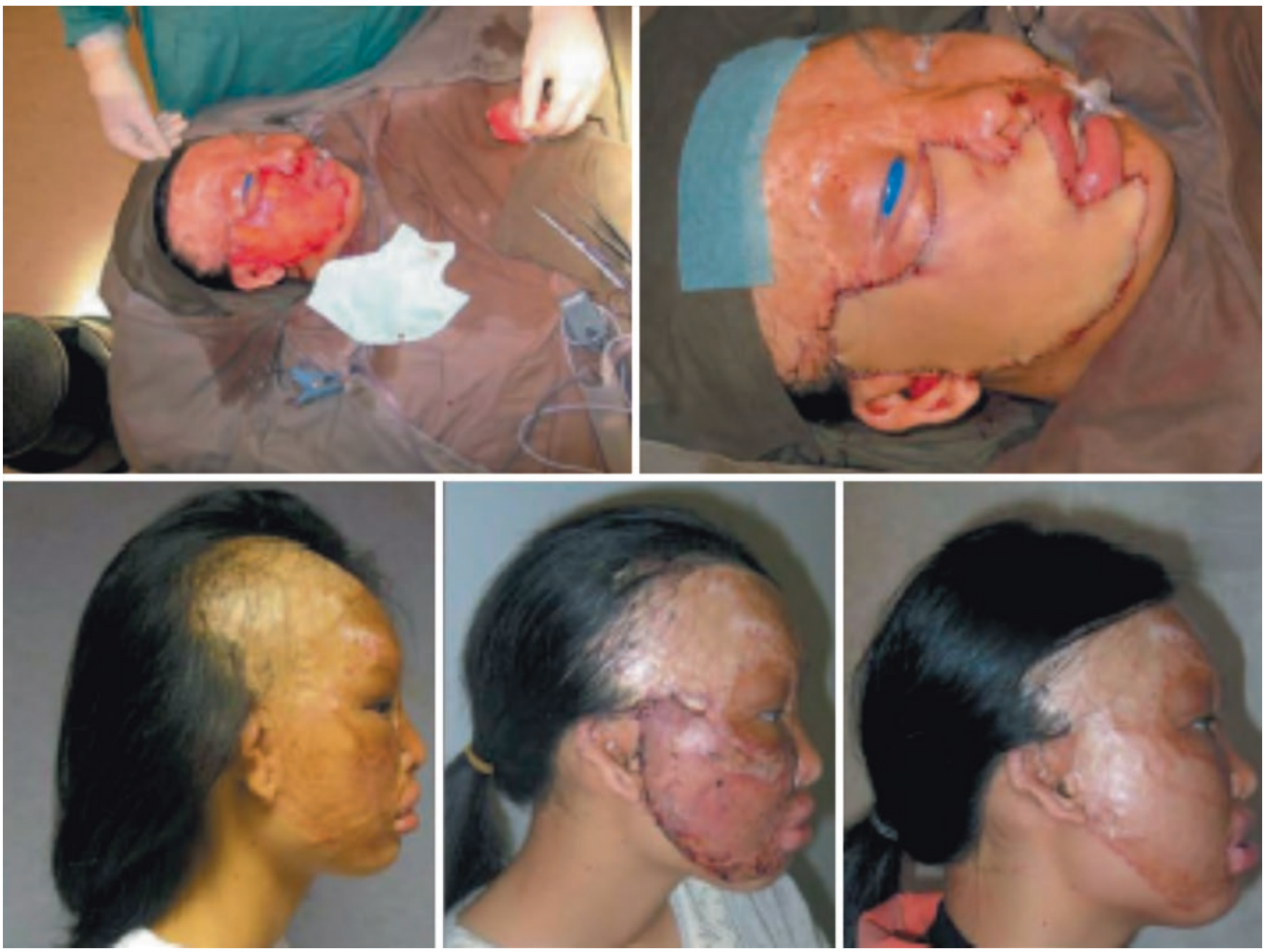


Fig. 20.17 The malposition of the right ear shown in Fig. 20.5 is corrected with a full-thickness graft to resurface the right face. A post-auricular flap has also been used to 'open' up the ear. The follow-up picture is 4 years after the operation

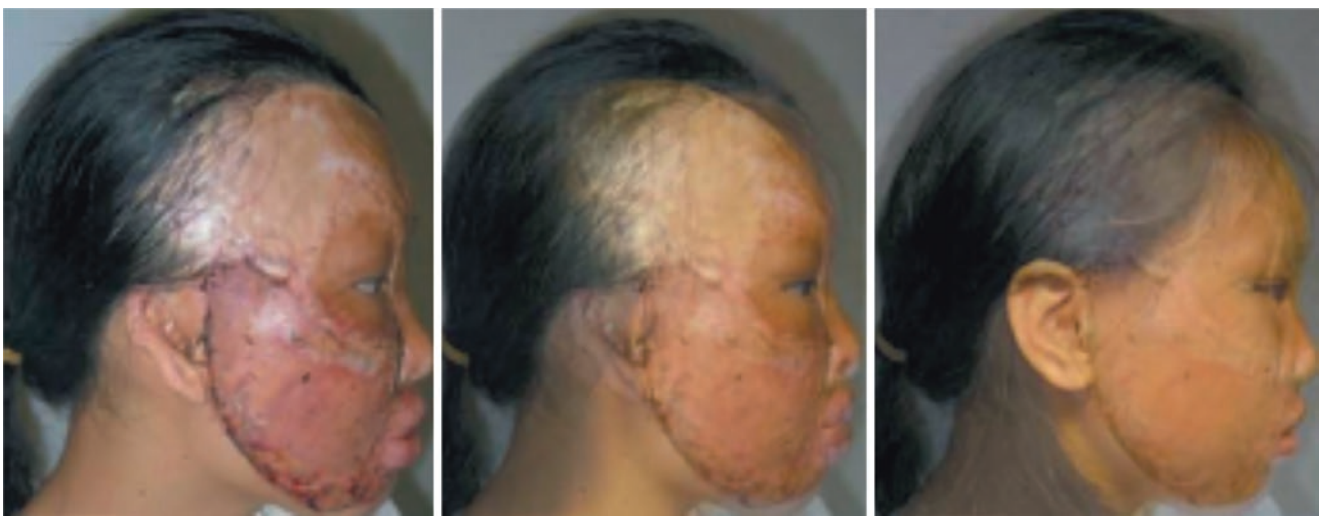


Fig. 20.18 Computer-generated overlays to demonstrate the change in position and appearance of the right side of the face

The Mount Vernon team published their experience in 1999 [11] looking at partial ear defects. In a series of 27 cases, they dealt with four ears from three patients. Three involved upper defects and one a lower pole defect. This group used autologous costal cartilage, covering it with local skin with and without prior tissue expansion. In three cases where there was a significant scarring of the local tissues, the framework was covered with temporoparietal fascia flaps.

A more burn specific review of a case series was presented by the group from Qatar who reported a series of 22 patients who underwent subtotal reconstruction of the auricles after burns [12]. All patients had autogenous cartilage used for the framework, but different techniques to cover this were used:

1. Temporoparietal flap
2. Subcutaneous pocket technique
3. The pre-auricular skin flap
4. The post-auricular skin flap

These papers introduce new concepts of reconstruction with specific relation to the ear.

Figure 20.19 shows a case of unilateral loss of the upper pole of the ear together with tethering and distortion of the lower pole (lobule). Both can be addressed with local procedures, the upper pole requiring cartilage support.

20.6.6.1 The Temporoparietal Flap

This flap was first described in 1898 but remained primarily overlooked until 1983 when Brent and his colleagues reported the flap as:

1. An axial-pattern fascial flap
2. A random-pattern fascial flap
3. A free fascial flap

This flap is highly versatile and is unique in being the only flap consisting of a single, vascularized, fascial layer in the head and neck region. It can readily drape over the convexities and concavities of the cartilagineous framework but also

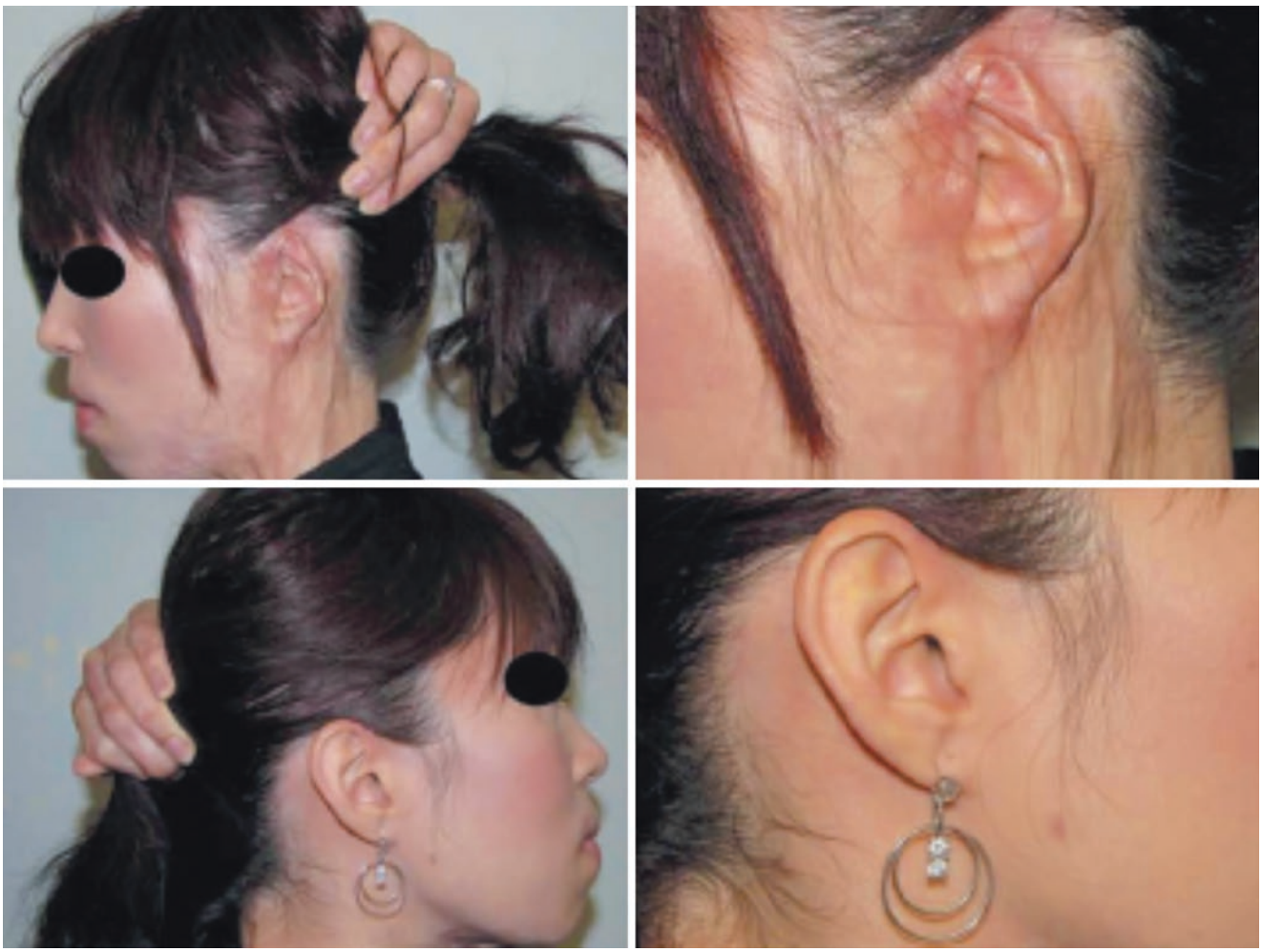


Fig. 20.19 Distortion of both upper and lower poles in a unilateral burn

is able to take a thin skin graft providing reliable vascularized cover. Because of the rich vascularity of the flap, it is sturdy and resists infection. The flap comprises the superficial temporal fascia and the superficial temporal artery and vein.

Figure 20.20 shows a pre-operative slide of the course of the posterior branch of the superficial temporal artery which has been mapped with the Doppler. Although the patient does not have an upper pole of the right ear, he has elected for a reconstruction of the right eyebrow instead. This is an important point to consider before using the temporoparietal flap for ear reconstruction: what are the patient's priorities for repair.

Figure 20.21 shows another case where there is obviously some surviving ear cartilage, but the side of the scalp has been grafted. In such cases, it is not possible to harvest the flap safely and replace the overlying skin.

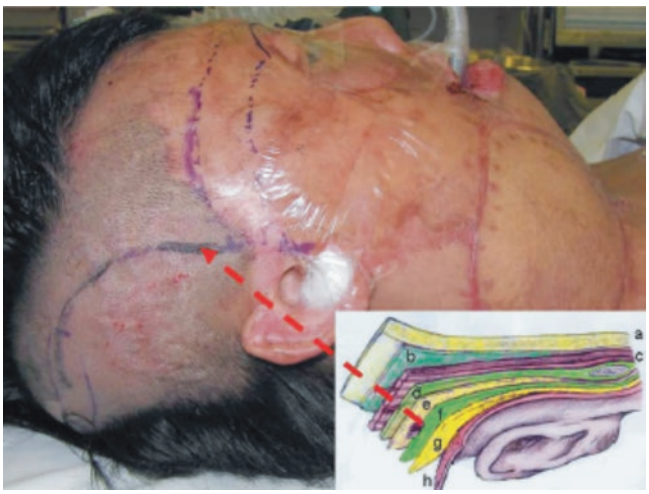


Fig. 20.20 The temporoparietal layer of the scalp is a multilayered complex comprising (**a**) bone, (**b**) pericranium, (**c**) temporalis muscle, (**d**) temporalis muscle fascia, (**e**) loose areola tissue, (**f**) temporoparietal fascia, (**g**) subcutaneous tissue, (**h**) skin. The posterior branch of the superficial temporal artery runs in the temporoparietal fascia and is marked out before raising a pedicled flap for eyebrow reconstruction

20.6.6.2 The Subcutaneous Pocket Technique

The subcutaneous pocket technique has a number of applications in reconstructive and trauma surgery. Essentially it means burying something in a pocket, so that viability can be

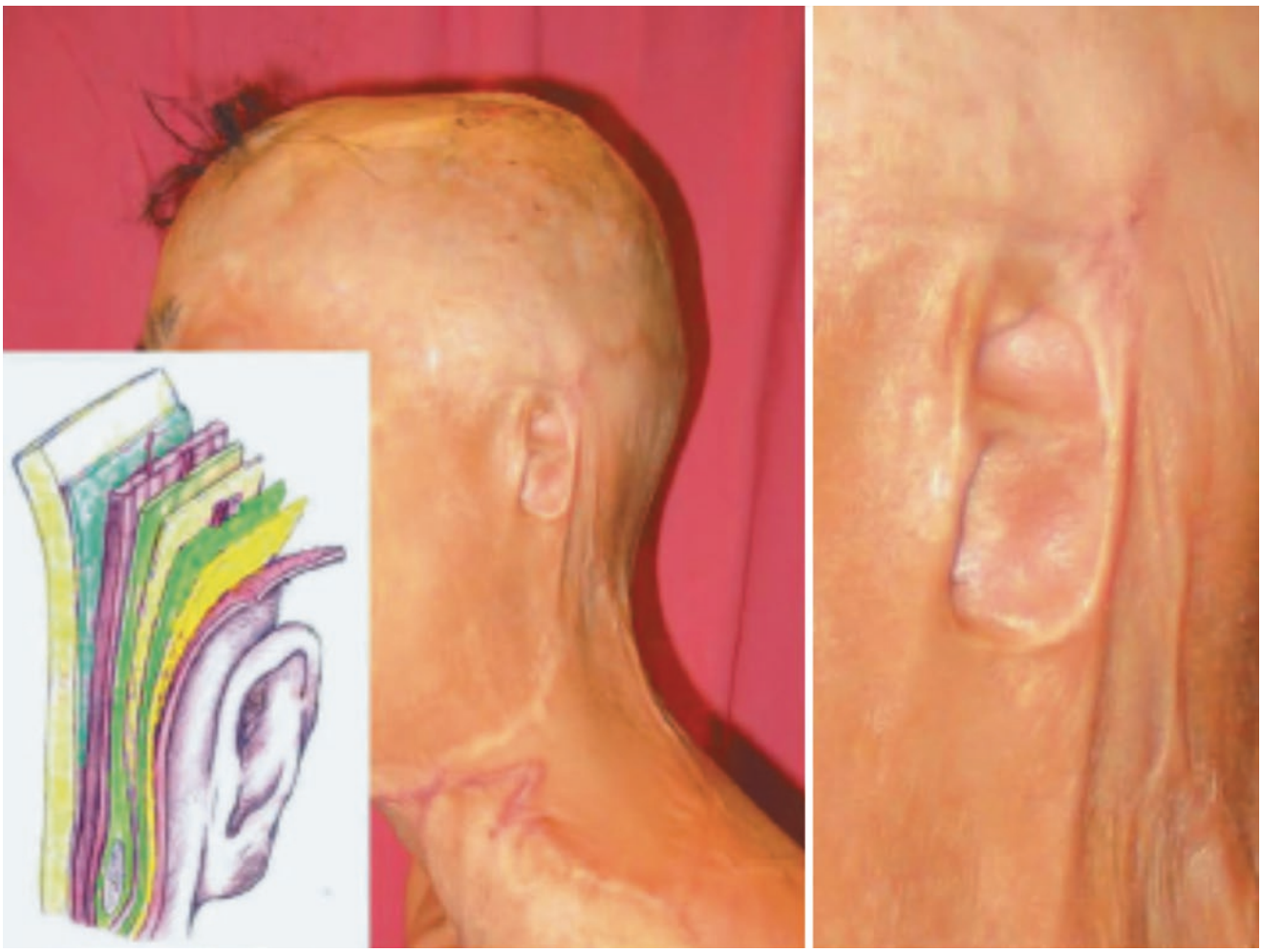


Fig. 20.21 In this patient, the left side of the scalp has been grafted, and it will not be possible to raise a temporoparietal flap

achieved immediately via diffusion and subsequently by neovascularization. The group from Qatar described harvesting cartilage from the seventh and eighth costal cartilages and, after carving them, inserting them into a subcutaneous pocket. This pocket was dissected at a level that kept the subdermal plexus intact and was large enough to drape easily over the cartilaginous framework. Suction drains were used to maintain a closed space, and creation of the posterior auricular groove was undertaken 3–4 months later.

This case demonstrates another burn injury where there has been a loss of the helix and a significant loss of hair-bearing skin of the scalp surrounding the posterior ear. A precise analysis of the defect told us that the posterior wall of the concha, anti-helix and anti-tragus were all preserved, and so a partial reconstruction of the helix and scaphoid fossa was possible (Fig. 20.22). The skin of the retroauricular region has been preserved and used as subcutaneous pocket to cover the cartilage in the first stage. An expander was used to expand the hair-bearing area and allow a further resection of the retroauricular scar to create a more natural hair border (Fig. 20.23).

20.6.6.3 Pre- and Post-auricular Skin Healing Flaps

The anteriorly based post-auricular flap has already been illustrated in the context of repositioning displaced ears whilst a caudally based pre-auricular skin flap can be used for lower pole/lobe, defects.

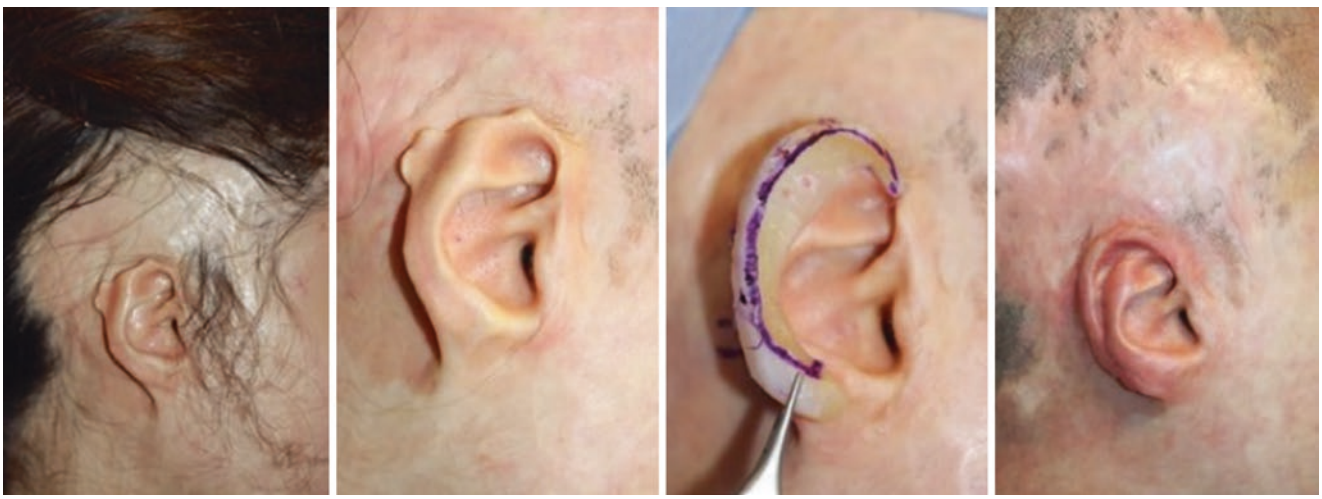


Fig. 20.22 In this patient presented with a loss of the helix and hair-bearing post-auricular skin, the ear has been reconstructed with the subcutaneous pocket technique using autologous rib cartilage (Photos with the courtesy of Dr. Francoise Firmin)

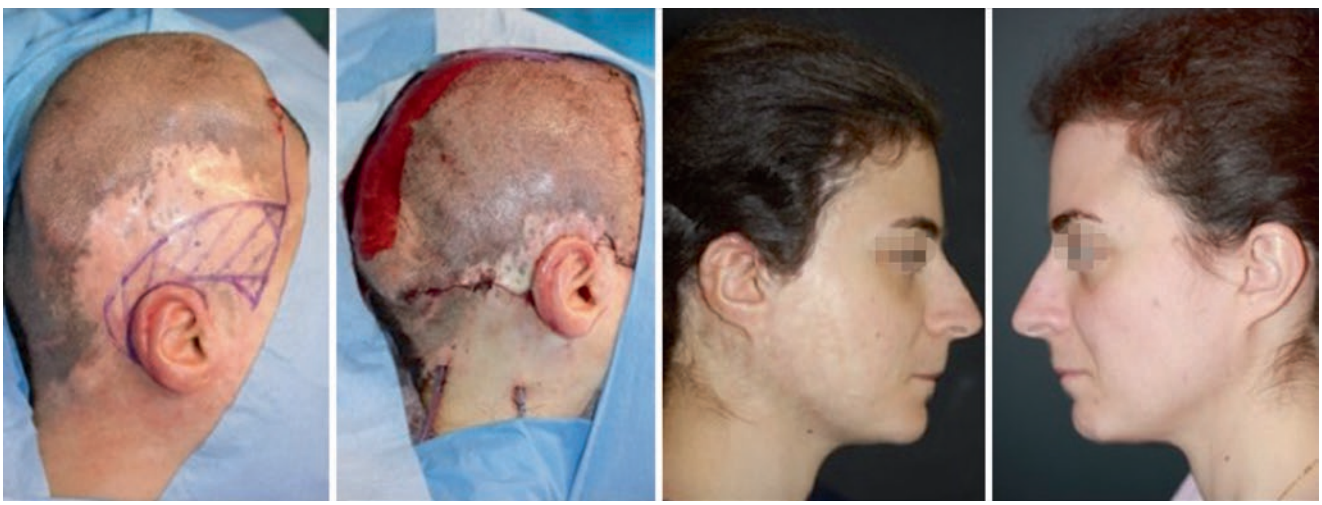


Fig. 20.23 The retroauricular hair defect was reconstructed using an expander; both the pictures on the right show a post-operative comparison of burned and reconstructed ear to non-burned ear (Photos with the courtesy of Dr. Francoise Firmin)

20.7 Total Ear Reconstruction

Total ear reconstruction following burns is a considerable challenge. Indeed there are few reported cases worldwide and even fewer where the results are aesthetically pleasing. The problem relates to the specific nature of the burn injury in that in many patients the total loss of the pinna is associated with very severe burns involving other parts of the body. The priority in these cases is to address the areas of greater functional significance first, and ear reconstruction comes low in the list of priorities. It is not just that prioritization is an issue, but also with extensive scarring, the possibility of reconstructing an ear that is aesthetically acceptable is realistically limited. Although having counselled over 20 patients who did have complete loss of the ear, when considering the risk–benefit analysis, all patients have opted not to have reconstruction. This decision is not affected by sex or culture.

Bhandari [13] describes the challenge in terms of (a) the framework fabrication and (b) the quality and quantity of the skin available for covering the framework. On the basis of skin availability, they recognize five groups of patients.

Group I	Patients with healthy skin in the auricular region
Group II	Patients in whom the surrounding skin is either scarred or grafted but is supple
Group III	Patients with no local skin but a pedicled temporoparietal flap can be used for draping over the cartilage framework
Group IV	Patients with neither local skin nor fascial flap available but who have potential donor fascial flaps available for free microvascular transfer
Group V	Patients with no donor sites for free fascial flaps or having other problems such as high anaesthetic risk. In this group, ear reconstruction is not possible

In Bhandari's paper, the framework is made of cartilage, but synthetic materials have been used such as Teflon, polyethylene and silicone. This is strong and flexible, but also being porous, it encourages both vascular and soft tissue ingrowth. The design of the cartilaginous framework has been well described in the chapter in Mathes written by Brent. He describes an evolution in technique beginning first with sculpting a framework from an 'en -bloc' resection of cartilage from the ipsilateral ribs and progressing to subsequent refinements adding a tragal strut and helical run. Figure 20.23 is an adaptation from Brent's chapter and shows the 'en bloc' creation of the cartilage scaffold. More recent publications have focused more on a reconstruction of the framework from several rib cartilages [14], and increasing attention is being paid to reconstituting the cartilage donor site to avoid both unpleasant scar and contour defects [15].

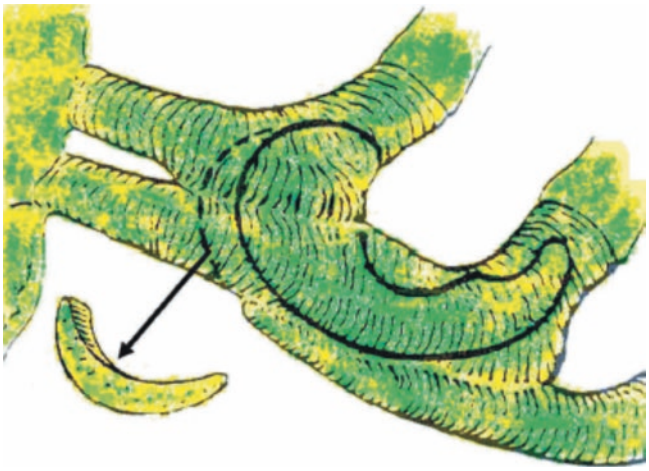


Fig. 20.24 The composite cartilage harvest

Nevertheless, no matter how sophisticated the technique, the results of total ear reconstruction in the post-burn patient still leave much to be desired in terms of the aesthetics [16]. Ultimately the reality of the Group V classification according to Bhandari has to be faced. Even ectopic reconstruction using the pre-laminated ear reconstruction under an expanded radial forearm flap as illustrated by Wikstrom [17] is an unlikely possibility in a major burn where fascial excision of burns of the limbs may have been undertaken (Fig. 20.24).

An option remains and that is to use an external prosthesis attached either with adhesive or better still using osteointegration. In a review of nearly 1500 ear reconstruction cases, the Auricular Centre of the Plastic Surgery hospital of the Chinese Medical Sciences reported 24 cases using titanium dowel-retained prosthesis and described favourable clinical outcomes [18].

20.8 Summary

Reconstruction of the burned ear remains a challenge. It ranges from simple plastic surgical techniques to complex reconstructive procedures. Simple procedures which involve repositioning and/or unfolding a deformed ear have to be kept in mind and may lead to good aesthetic and functional results.

The total reconstruction of the ear in a patient with an extensive burn is a completely different issue, and good results can hardly ever be obtained. In some cases, an external prosthesis may overcome the aesthetic appearance of surgical reconstructed ears and should hence be offered the patient as another option.

References

1. Farkas LG, Hreczko TA, Kolar JC, Munro IR. Vertical and horizontal proportions of the face in young adult North American Caucasians: revision of neoclassical canons. Plast Reconstr Surg. 1985;75:328–38.
2. Posnick JC, al-Qattan MM, Whitaker LA. Assessment of the preferred vertical position of the ear. Plast Reconstr Surg. 1993;91:1198–207.
3. Berghaus A, Nicoló MS. Milestones in the history of ear reconstruction. Facial Plast Surg. 2015;31:563–6. https://doi.org/10.1055/s-0035-1567886.
4. Dieffenbach J, Dieffenbach J. Die Plastische Chirurgie in ihrem-weitesten Umfang dargestellt und durch Abbildungen erläutert von Dr. H. E. Fritze u. Dr. C. F. G. Reich. Berlin: Hirschwald; 1945.
5. Gilles H. Plastic surgery of the face. London: Oxford Univerity Press; 1920.
6. Madjidi A. Historic aspects of ear reconstruction. Semin Plast Surg. 2011;25:247–8. https://doi.org/10.1055/s-0031-1288915.
7. Suraci A. Plastic reconstruction of acquired defects of the ear. Am J Surg. 1944;66:196–202.
8. Neumann CG. The expansion of an area of skin by progressive distention of a subcutaneous balloon; use of the method for securing skin for subtotal reconstruction of the ear. Plast Reconstr Surg. 1957;19:124–30.
9. Chana JS, Grobbelaar AO, Gault DT. Tissue expansion as an adjunct to reconstruction of congenital and acquired auricular deformities. Br J Plast Surg. 1997;50:456–62.
10. Ellabban MG, Maamoun MI, Elsharkawi M. The bi-pedicle post-auricular tube flap for reconstruction of partial ear defects. Br J Plast Surg. 2003;56:593–8.
11. Harris PA, Ladhani K, Das-Gupta R, Gault DT. Reconstruction of acquired sub-total ear defects with autologous costal cartilage. Br J Plast Surg. 1999;52:268–75. https://doi.org/10.1054/bjps.1998.3053.
12. El-Khatib HA, Al-Basti HB, Al-Ghoul A, Al-Gaber H, Al-Hetmi T. Subtotal reconstruction of the burned auricle. Burns J Int Soc Burn Inj. 2005;31:230–5. https://doi.org/10.1016/j.burns.2004.09.022.
13. Bhandari PS. Total ear reconstruction in post burn deformity. Burns J Int Soc Burn Inj. 1998;24:661–70.
14. Jiang H, Pan B, Lin L, Zhao Y, Guo D, Zhuang H. Fabrication of three-dimensional cartilaginous framework in auricular reconstruction. J Plast Reconstr Aesthetic Surg. 2008;61(Suppl 1):S77–85. https://doi.org/10.1016/j.bjps.2008.07.007.
15. Fattah A, Sebire NJ, Bulstrode NW. Donor site reconstitution for ear reconstruction. J Plast Reconstr Aesthetic Surg. 2010;63:1459–65. https://doi.org/10.1016/j.bjps.2009.07.036.
16. Ibrahim SMS, Salem IL. Burned ear: the use of a staged Nagata technique for ear reconstruction. J Plast Reconstr Aesthetic Surg. 2008;61(Suppl 1):S52–8. https://doi.org/10.1016/j.bjps.2008.03.029.
17. Stewart K, Wikström S-O. Autologous ear reconstruction—celebrating 50 years. J Plast Reconstr Aesthetic Surg. 2008;61(Suppl 1):S2–4. https://doi.org/10.1016/j.bjps.2008.09.014.
18. Zhao Y, Wang Y, Zhuang H, Jiang H, Jiang W, Hu X, et al. Clinical evaluation of three total ear reconstruction methods. J Plast Reconstr Aesthetic Surg. 2009;62:1550–4. https://doi.org/10.1016/j.bjps.2008.07.009.

Reconstruction of the Perioral Region After Facial Burns

21

Timo Alexander Spanholtz and Riccardo E. Giunta

21.1 Introduction

21.1.1 Aetiology and Pathophysiology

Deep facial burns occur for different reasons and often affect patients' outcome and life quality in a dramatic fashion. Although they are present in a minority of burned patients, they pose a greater challenge in surgical and non-surgical treatment. Chemical, electrical and thermal burns can lead to disfiguring scar formations and restrain sufficient mouth opening (impaired temporomandibular joint range of motion). The average physiological mouth opening measures 40–50 mm. An opening of 25–35 mm is still functional while an opening of less than 24 mm is severely limiting in daily life [1]. In the literature, 3.7–10.8% of thermal burn admissions are complicated by reduced size of the oral aperture, generally called microstomia. In infants, perioral burns often occur when a child bites into or sucks on an electrical cord or the improperly connected junction of two electrical cords.

In case of electrical accidents, both the enoral mucosa and the lip are damaged more extensively than the surrounding skin, as the high electrical resistance of skin tissue reduces injury to the skin while the saliva-coated lip and enoral surfaces conduct electricity very well. The soft tissue injury caused by electricity is often more extensive than initially estimated, because the current may follow the low-resistance paths of nerves, vessels and facial muscles. Coagulation necrosis with inflammation of adjacent vital tissues results in crippling scars causing hypotonicity of the circumoral muscles.

As, in fact, thermal burns of 95% total body surface area (TBSA) are today associated with a 50% chance of survival in children [2], the treatment of deep facial thermal burns becomes more important to improve the quality of life in these patients. The scar contracture caused by deep facial thermal burns or electrical accidents results in several problems such as tongue cicatrization, disturbance in facial expression and microstomia. Nowhere in the body are scars more apparent than in the face.

21.1.2 Relevant Anatomy

No cartilage or any other rigid frame supports the oral orifice nor the lips. The vermillion border flanks the oral aperture and extends to facial skin tissue to all sides. The upper lip is subdivided in three subunits: the philtrum and two lateral subunits that extend from the philtral columns to the nasolabial folds. At the oral commissure, upper and lower lips meet. Not subdivided, the lower lip stretches out to the labiomental fold inferiorly and to the nasolabial folds laterally (Figs. 21.1 and 21.2).

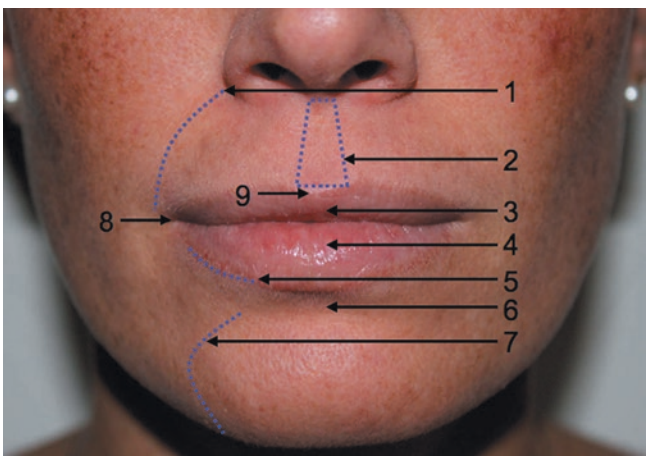


Fig. 21.1 Surface anatomy of the lip: (1) Nasolabial fold; (2) Philtrum; (3) Tubercle; (4) Vermilion of the lower lip; (5) Vermilion border; (6) Horizontal fold of mentum; (7) Mental fold; (8) Oral commissure; (9) Cupid's bow

T. A. Spanholtz (✉) · R. E. Giunta
Department of Hand Surgery, Plastic and Aesthetic Surgery, Universitätsklinik, Ludwig-Maximilians Universität München, Munich, Germany
e-mail: timo@spanholtz.net; Riccardo.giunta@med.uni-muenchen.de

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_21

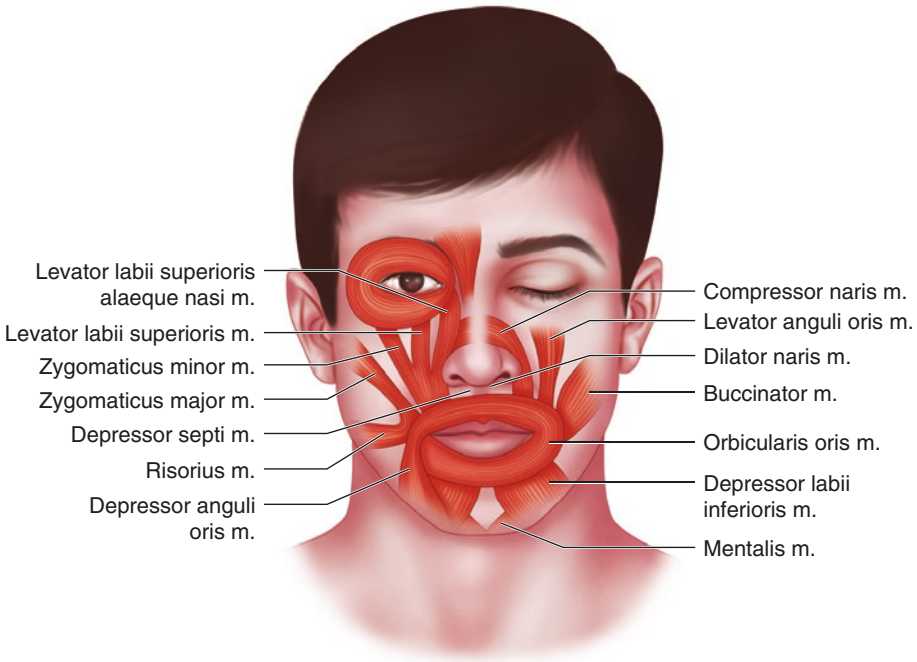


Fig. 21.2 Facial muscles in the perioral region

Fig. 21.3 Arterial and nervous supply of the perioral region

The infraorbital nerve (V2) and the mandibular nerve (V3) assure the sensory innervation to the upper and lower lips. Oral commissures are innervated mainly through the buccal branch of the mandibular nerve. The main arterial supply is from the labial arteries (branches from the facial artery, Fig. 21.3). This arterial frame forms a 360° loop, which allows for various flap designs. The arteries provide perforators through the orbicularis muscle to the overlying skin of the lip. Theoretically flaps in the lip area should contain one labial artery, although blood supply is so numerous in the perioral region that survival of local flaps can be secured by including one single segment of mucosa. Lymph nodes of the submandibular and submental area drain the lymph of the lower, preauricular and infraparotid nodes and the lymph of the upper lip.

The orbicularis oris muscles consist of two portions: the deep portion is oriented horizontally and acts to compress the upper and lower lips and to provide sphincter function. The superficial portion is in control of finer movements for facial expression. The depressors of the lip include four muscles: the depressor anguli oris, mentalis, depressor labii inferioris, and the platysma muscle. Elevation of the lips is secured by the levator anguli oris, zygomaticus, and risorius muscle. Many of these muscles stretch out to the oral commissures (Fig. 21.2).

21.1.3 Presentation and Classification

Dependent on the degree of tissue damage, individuals with perioral burns may experience a large variety of functional symptoms such as nutritional needs with limited oral intake, articulation abnormalities with impaired communication, dental hygiene, dental treatments, and abnormal development of the definition and dental arches in childhood. Restriction of mandibular motion can be hazardous when attempting to administer general anaesthesia [3]. Apart from these functional restrictions, patients suffer from their facial asymmetry, disfigurement and noticeable facial expression deficits.

Ortiz-Monasterio offered a classification based on the percentage of upper and lower lip involvement [4], while Al-Qattan classified electrical commissural burns in a three-stage grading system [5] (Table 21.1). A more general classification according to the involved structures is presented by Hashem and colleagues [6]: type I includes isolated anterior oral contractures, type II isolated posterior oral contractures and type III total contractures (anterior and posterior).

Table 21.1 Classification of electrical burns to the perioral region [5]

Degree	Description	Treatment	Prognosis
Minor	Second-degree burn of the red lip only	Nil	Excellent
Moderate	Full-thickness burn at the commissure involving the red lip	Early splinting plus commissuroplasty if needed	Good
Severe	Extensive tissue destruction	Flap surgery is required	Poor, with aesthetic and functional problems

21.1.4 General Considerations and Indications

Rose outlined five general principles for the treatment of facial burns [7]: an undistracted "normal" look at conversational distance, facial balance and symmetry, distinct aesthetic units fused by inconspicuous scars, a doughy skin texture appropriate for corrective makeup and a dynamic facial expression. The subunits of the face as described by Gonzalez-Ulloa [8], which are of certain interest in perioral burns, are the following:

- Cheek unit (medial subunit, zygomatic subunit, lateral subunit, buccal subunit)
- Upper lip unit (with the philtral columns and the Cupid's bow which is the concave or dipped portion of the vermillion border in the centre of the upper lip)
- Lower lip unit (central subunit, mucosal subunit)
- Mental unit

Crossing these units will always lead to disfiguring scars for the patient. Scars should always be positioned into the lines connecting these units, what will make them most unimpressive.

Focusing on perioral burn injuries, the commissures should form an acute angle at a vertical perpendicular dropped from the patient's pupil and need to be positioned symmetric with the opposite side. The ratio of the height of the upper lip to that of the lower one is ideally 1:1.4. These principles should guide the surgeon when planning both conservative therapy and reconstructive surgery.

In accordance to any deep burn injury, facial burns are treated by excision and soft tissue reconstruction. Aesthetic subunits are excised in their entity. Mesh grafting should always be avoided to gain satisfying aesthetic results. Fraulin et al. provide the largest study on this issue, finding that patients with extensive deep facial burns fared best with tangential excision and split-thickness skin grafting [9]. Unlike the rest of the face, where excision and grafting can avoid poor skin texture, primary (or early) excision of perioral burns is generally not recommended, as it may result in overresection of indispensable tissue or underresection of necrotic skin and muscle [2, 10].

A wide veriety of techniques have been described for the the reconstruction of the upper and lower lips. Most important in addressing reconstruction are two basic principles: reconstruct lost tissues with tissues of the same kind ("like-with-like") and respect aesthetic units of the face.

The external lip consists of four layers: skin and subcutaneous tissue, the underlying orbicularis oris muscles, the lip mucosa and the vermilion (visible portion of the lip), which is distinct from the mucosa in its colour, texture and appearance. All techniques of vermilion reconstruction by using other tissues will lead to unsatisfying results. Whenever planning reconstructive surgery to the lip, the most important factor is therefore the amount of residual lip vermilion as it shows a unique light reflection and can hardly be replaced.

If either upper or lower lip is not injured, healthy tissue can be transferred from one unit to the other. The planning should always prefer to reconstruct lip tissue with lip tissue ("like-with-like"). Two techniques available to achieve like-with-like reconstruction are the Abbe flap and the reverse Abbe flap. Both are lip-switch flaps with two advantages: they have no impact on the oral commissure, and they tighten the donor lip and thereby redress the balance with the (also tightened) reconstructed lip. Another approach to reconstruction is to slide parts of the uninjured lip through the commissure to the recipient side: flaps that follow this concept are for example Estlander-flaps, Gilles-flaps and Karapandzic-flaps. Not pedicled, they do not need any secondary flap division, but always affect the oral commissure and therefore often need secondary corrective procedures to restore normal lip architecture.

In presurgical decision-making, it is important to know that defects of >40% of the total available upper- and lower-lip surface (or >80% of either lip) cannot be reconstructed with local flaps but need other techniques. For these cases different authors described pedicled and free flaps for soft tissue reconstruction, such as DIEP flaps [11], bilateral pedicled forehead flaps [12] and free gracilis flaps [13].

Particular attention should be drawn to deep burns of the oral commissure that may result in microstomia—the most challenging complication from perioral burn injuries. Apart from early non-surgical therapies, reconstruction of the oral commissure can become necessary. Principles for commissuroplasty are based on the idea of reconstructing a symmetrical appearance and a decent function. Therapy is composed of non-surgical and surgical approaches. Anyway, as the skin is relatively mobile in the perioral region, scar maturation can take from 6 months to over a year [2]. Early and effective conservative (non-surgical) treatment is important and can prevent microstomia and the need of delayed reconstructive surgery. If microstomia developed, the surgical procedure must be fitted to the patient's need and performed by a plastic surgeon experienced in burn surgery. One important principle for surgery

is that the commissure needs to be in a symmetrical position with the opposite member. This requires optimal measurement to determine this location and some overcorrection to prevent relapse. Another important detail is the fact that the oral commissure is not triangular. The short vertical component of the lateral margin needs consideration. Again, when planning surgery, local tissues are primarily used, and lost tissues are replaced by tissues of the same kind ("like-with-like").

21.2 Treatment of Facial Burns

21.2.1 Microstomia: Acute and Non-surgical Treatment

Early therapy of perioral burns includes some sort of appliances to prevent microstomia and is non-surgical at first. Moreover, conservative treatments for the prevention and management of microstomia include compression therapy [3, 14], mouth splinting [3, 5, 15, 16], scar massage [17], contact media [15], exercise [3, 16], patient education and neck splinting [3, 15].

Devices used in burn patients having circumoral burns need vertical, horizontal and oblique stretch vectors in order to prevent contracture in more than one plane [18]. While adults find putting on these devices tolerable, it can be challenging to satisfy children and toddlers, in particular over the extended period of time necessary for obtaining satisfying results. There are many appliances available, categorized as intraoral vs. extraoral and removable vs. fix and to provide force in a vertical, horizontal or circumferential direction [3] (Fig. 21.4a–c).

The efficacy of many different types was reported [2, 3, 5, 6, 15, 16]. Obviously, neither perfect tool nor generally accepted protocol has been agreed upon. In general, the device should be simple to fabricate, easy to handle and well tolerated by the patient, as the compliance is known to be the

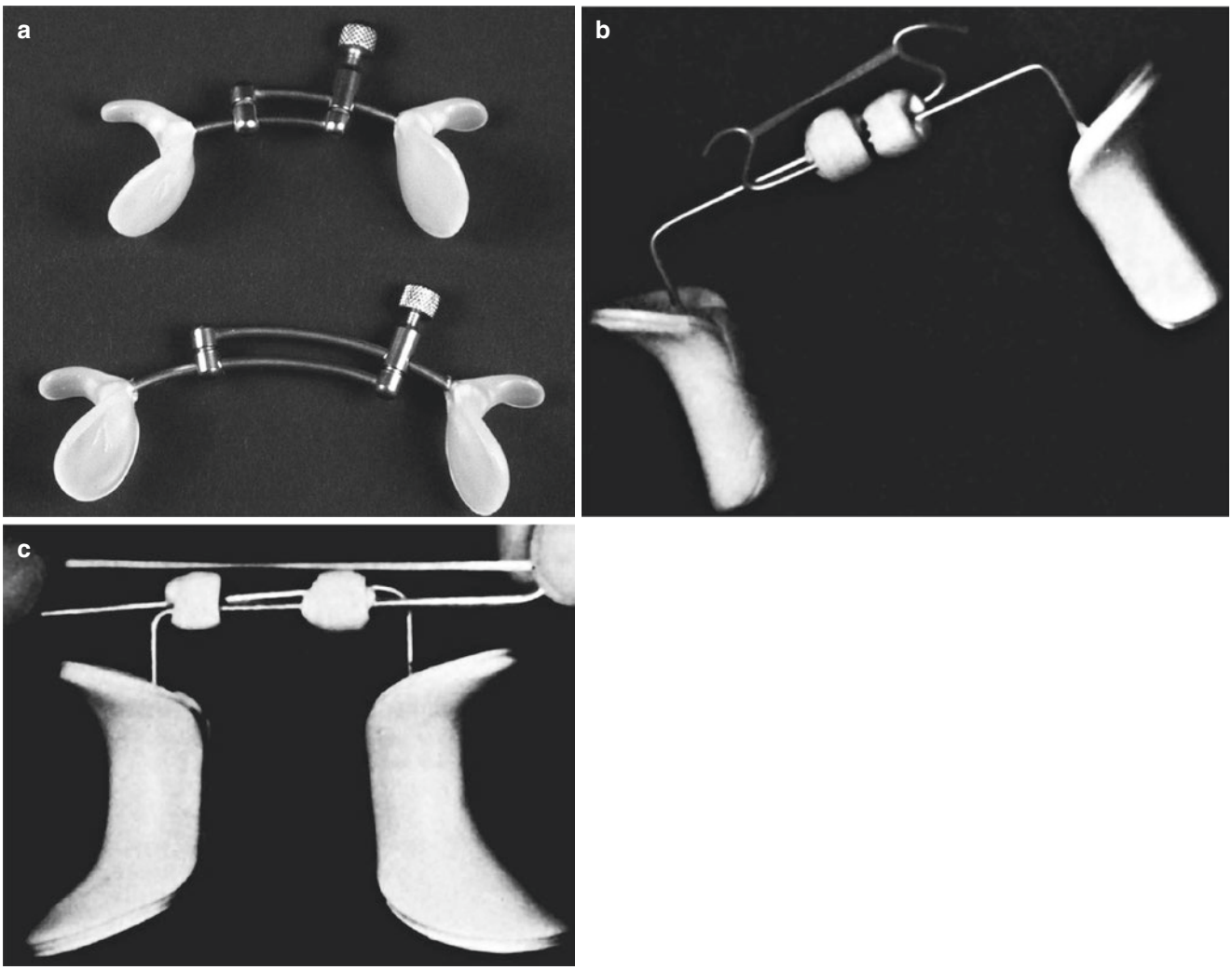


Fig. 21.4 Different microstomia prevention devices

most limiting factor [3]. It is generally recommended to use the splints continuously over a period of 6 months even after scar maturation [2, 3].

Stretching devices are but one aspect of the treatment: exercise, local pressure and massage are mandatory and must be implied early as well for optimal outcome [3]. Scar contracture can be very forceful, and early splinting alone may not prevent contracture of the oral commissures [1].

21.2.2 Microstomia: Reconstruction of the Oral Commissure

Aim of the surgical procedure (named "commissuroplasty" or "commissurotomy") is the restoration of the oral commissure by correction of the oral commissure contracture. Indication for commissuroplasty is found in patients with manifest microstomia, impairment of function and aesthetic appearance as those described above. There are no contraindications for the correction of microstomia. Depending on the technique, all scarred contractures are either released or excised, and the apex of the oral commissure is redefined. The emerging soft tissue defect is then covered with local adjacent tissues. Mucosal flaps taken from the enoral cheek proved to be more reliable and successful than advancement of the remaining vermilion towards the defect for closure. This last procedure usually resulted in shortening of the oral orifice on the affected side.

Landmarks to plan the new position of the commissure can be determined by examining the contralateral anatomy or—if both sides are affected—according to the general anatomical landmarks. In this case, a slight overcorrection is sensible, so that the commissural apex is positioned between the medial limbus and the midpupillary perpendicular of the eye (Fig. 21.5), allowing a slight overcorrection of 1–2 mm but taking care to avoid macrostomia.

Numerous technical variants of surgical procedures have been put forth in the literature, but none has proven ideally

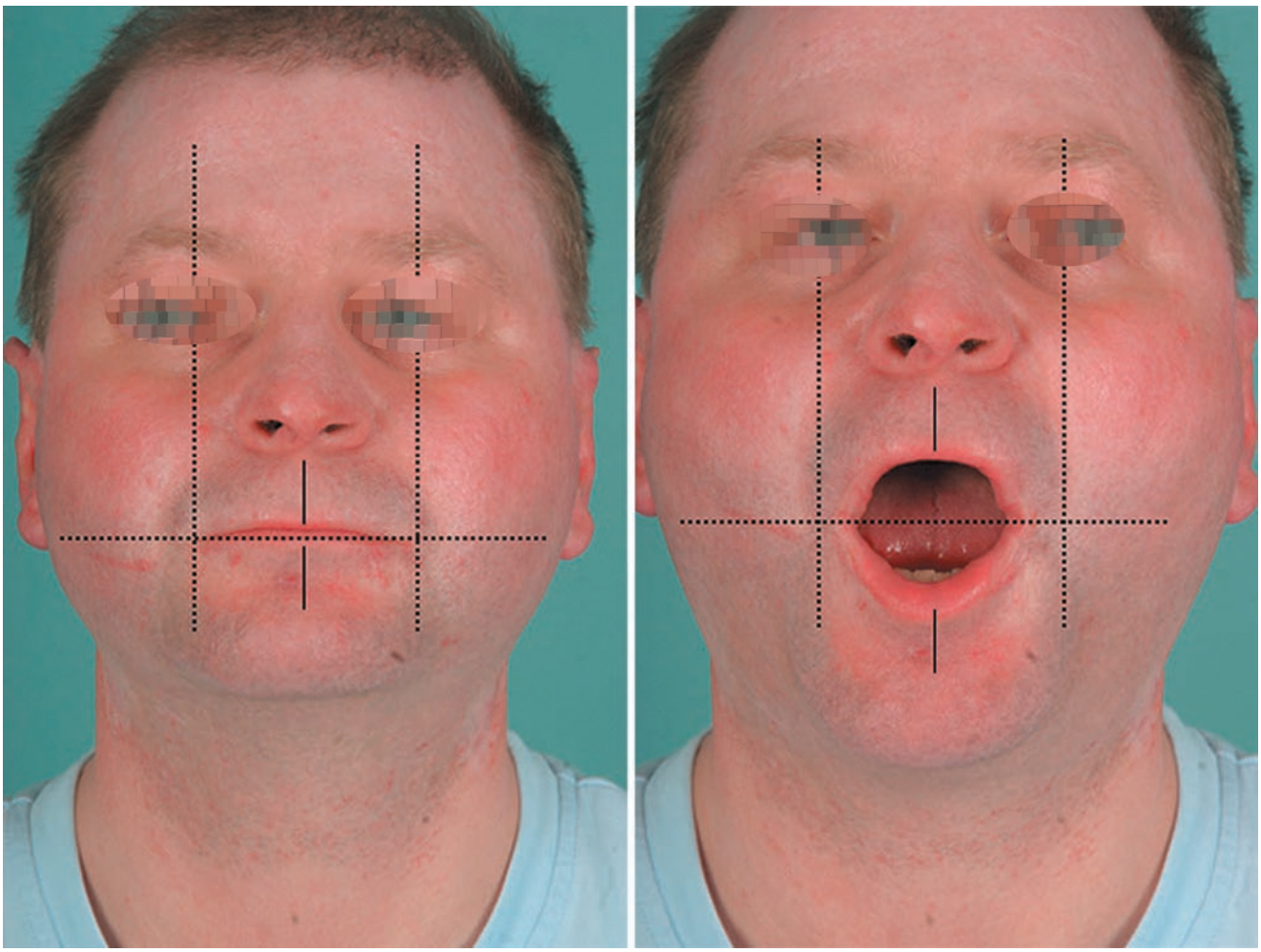


Fig. 21.5 Patient with microstomia and oral commissure medial to the perpendicular of the pupil; left: mouth closed; right: maximum opening of the mouth with significant microstomia

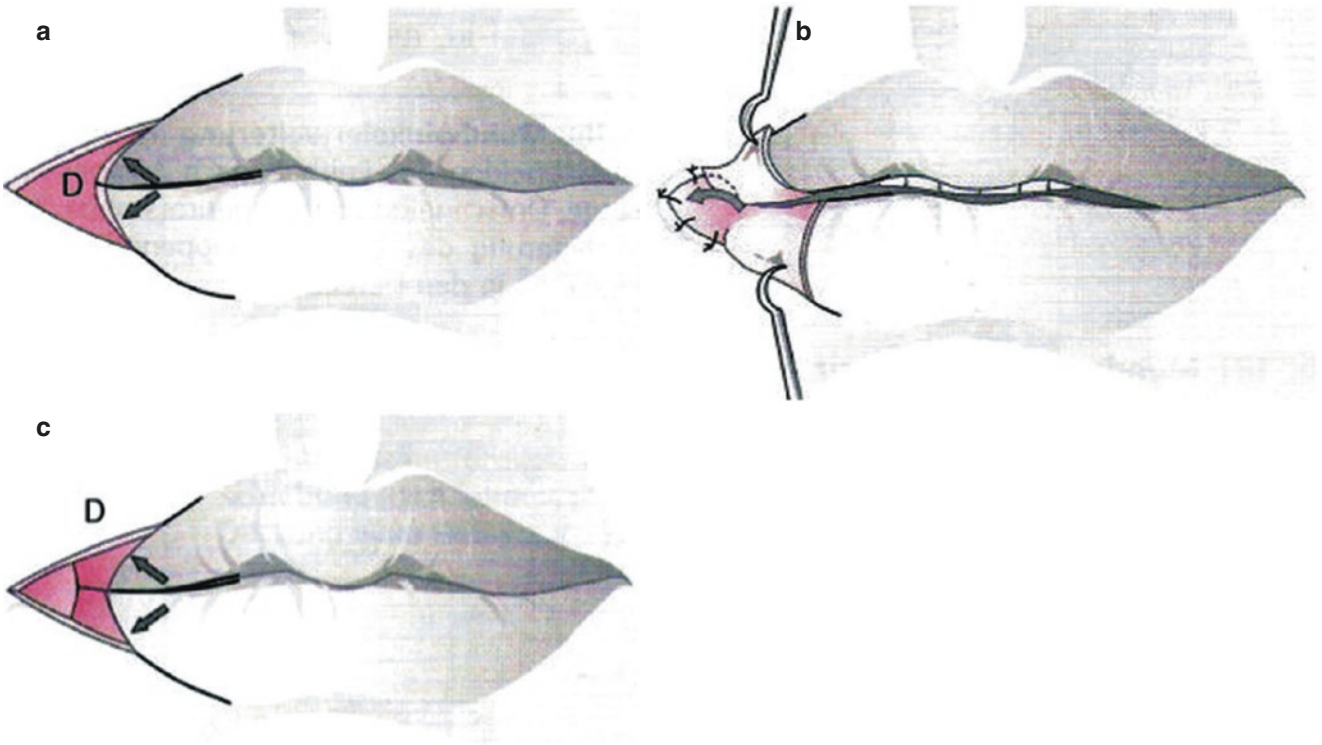


Fig. 21.6 Converse technique to correct microstomia: (**a**) pink zone to be deepithelialized; (**b**) full-thickness horizontal Y-shaped dissection of the deepithelialized zone; (**c**) advancement of the intraoral portion of mucosa to replace the vermilion

suited to address all problems associated with commissural contractures. Although Dieffenbach was the first author to present a surgical technique in 1831 [19], today's common procedures were initially described by Converse [20] and Fairbanks [21] in 1972. Converse described a commissuroplasty whereby a dermal triangle was excised at the contracted commissures which was then deepened by full-thickness incision to the new apex position. Buccal mucosa flaps were then wrapped out to meet the skin edges (Fig. 21.6a–c). The small flap in the commissure is crucial to the success of this technique. Several authors presented a modification of this technique that pays respect to the vertical component of the lateral margin. Brent Egeland introduced a modified technique without resection of any tissue. Instead he releases all intrinsic and extrinsic contractures and used a "Y to V" musculomucosal advancement flap to cover the soft tissue defect [2].

Fairbanks and Dingman used two small triangular mucosal flaps, one with a superior base and one with an inferior base [21]. After dissection, these flaps were transposed for a lengthening effect while the buccal mucosa was advanced to the commissure to cover the soft tissue defect (Fig. 21.7a). Spanholtz et al. modified this technique and covered the soft tissue defect of the lateral lip with an additional rotation flap raised from the mucosa of the enoral lower lip. Resulting scars were thereby shifted to the enoral side of the lower lip, which caused less contracture in the region of the oral commissure [22] (Fig. 21.7).

Some others presented more experimental ideas using composite grafts harvested and reshaped from the ear lobule [23]. A major shortcoming of all techniques is the difficulty of precisely reconstructing the vermillion border.

It can be useful to combine surgical correction with splinting devices as described by Koymen and colleagues, who found an increase of the interincisal opening by an average of 5 mm when Converse' technique was combined with postoperative splinting for 3 months [24].

On some occasions, one procedure may not be sufficient to manage large deformities, and numerous surgical procedures are necessary over the years to eliminate functional and aesthetic impairment. In these cases, it is advisable to delay reconstruction until scar contracture is complete, and the scar and surrounding tissue are adequately softened. Between reconstructive procedures, months may elapse before considering a result final, requiring great patience for all parties involved.

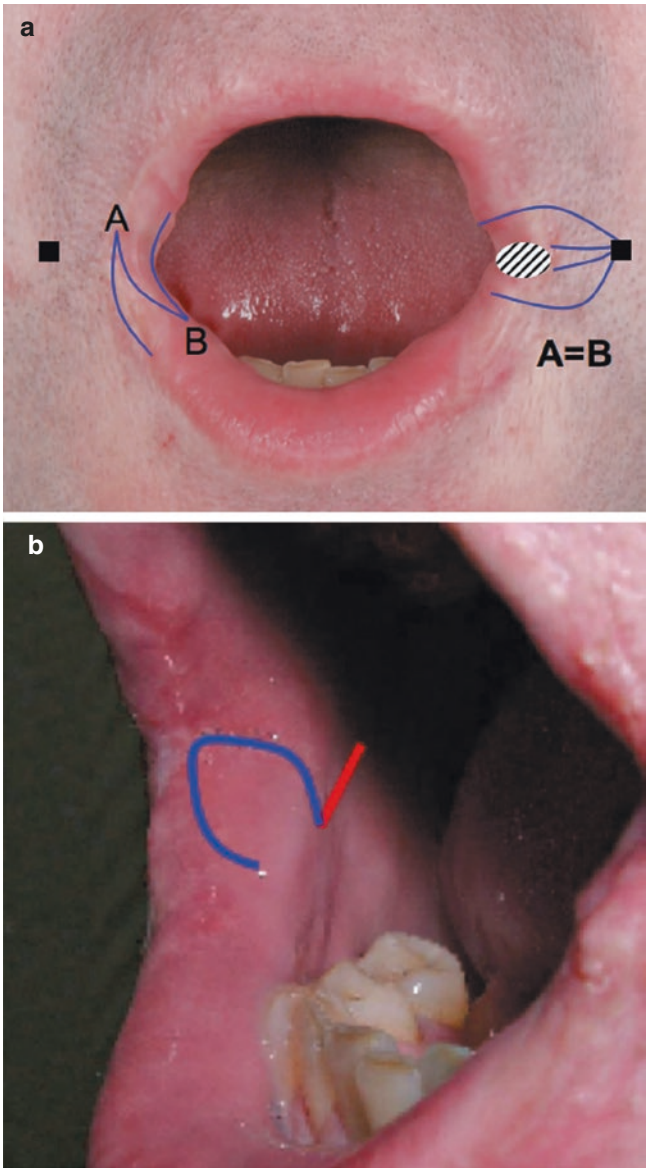


Fig. 21.7 (**a**) Left part of the picture: Fairbanks technique to correct microstomia with two flaps facing each other on the oral commissure; right part of the picture: expected soft tissue defect of the donor site after lateral rotation of the flaps; (**b**) intraoral mucosa rotation flap to cover the donor site defect of the vermillion and to shift the scar contracture away from the commissural zone

Complications of surgical correction include flap failure with partial or complete flap necrosis. Bleeding and infection can be considered as general risks of any surgical procedure.

The most important complication is represented by the recurrent contracture with subsequent microstomia. Also unfavourable cosmetic results may occur at the mouth or donor site. Seldom one can see cases of postoperative incomplete mouth closure with leakage of fluids when swallowing increases intraoral pressure (macrostomia). This can result from overcorrection or false technique and needs surgical correction after an adequate period of time.

21.2.3 Reconstruction on the Upper and Lower Lips

21.2.3.1 Flowchart for Surgical Planning (Table 21.2)

The goal when using healthy adjacent lip tissue for reconstruction is to evenly distribute the remaining lip tissue between the upper and lower lips.

21.2.3.2 The Upper Lip

With regard to the subunits of the upper lip, defects are classified as central defects and lateral defects. Superficial central defects of the philtrum need wedge resection if they involve less than half of the central segment. If the defect exceeds the philtral borders, the whole subunit can be replaced by (haired) skin from retro- or preauricular full-thickness skin grafts.

If the orbicularis muscles are involved, and the surgeon is facing a full-thickness defect, damaged structures need to be

Table 21.2 Flowchart for surgical planning

Defect size	Tissue quality/ defect localization	Involvement of lip tissue	Technique
Lower lip			
<1/3	Primary closure		
1/3–2/3	Sufficient lip tissue	Commissure involved	Karapandzic (first choice) Estlander
		Commissure not involved	Abbe (first choice) Karapandzic
	Insufficient lip tissue		Bernard–Burrow's
>2/3	Sufficient cheek tissue		Karapandzic
	Insufficient cheek tissue		Distal flap or free flap
Upper lip			
<1/3	Central		Perialar crescentic closure
	Vermillion intact		Local flap from nasolabial fold
	Lateral		Primary closure
1/3–2/3	Central		Abbe (first choice) Karapandzic
	Lateral	Commissure and philtrum intact	Abbe
		Commissure and/or philtrum involved	Estlander with/ without perialar crescentic excision
>2/3	Sufficient cheek tissue	Central	Bernard–Burrow's
		Lateral	Bernard–Burrow's plus contralateral perialar crescentic excision
	Insufficient cheek tissue		Distal flap or free flap

fixed layer by layer. Defects up to 30% can be managed by primary closure via advancement of adjacent tissue. Full-thickness defects within the philtrum and affecting up to half of the philtrum width can be managed by direct closure. For wide defects, Abbe flap gives best results, although bridging of one column will result in asymmetry. Described in 1898 by Robert Abbe who was plastic surgeon and radiologist in New York City, the flap was initially used as a complete reconstruction technique for the relief of the bilateral cleft lip deformity. It can be raised from upper and lower lips, and its size and shape are dependent on the corresponding defect (Fig. 21.8). The flap can be based on the labial artery. A por-

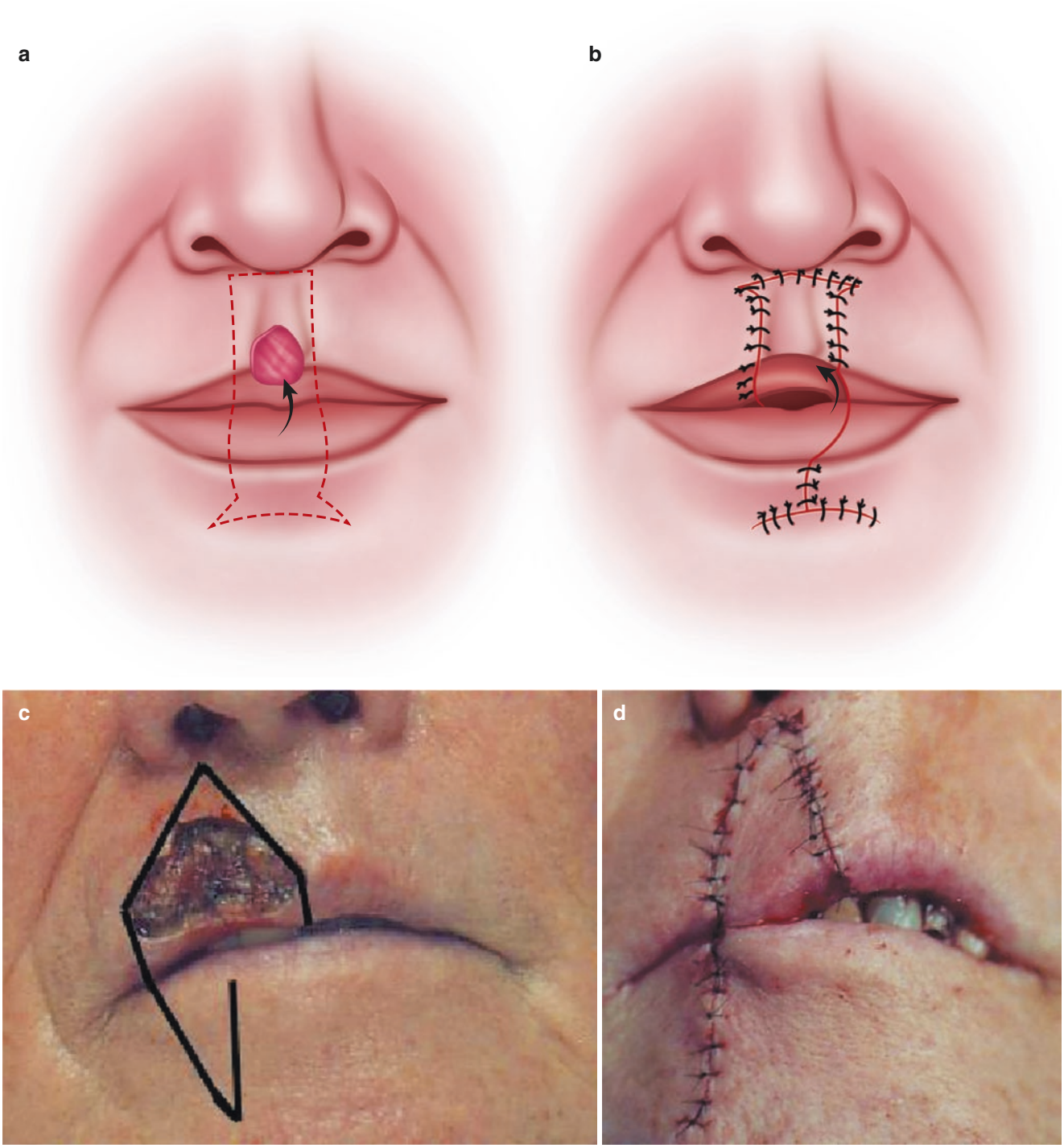


Fig. 21.8 The Abbe flap (lip-switch procedure) for defects of the upper and lower lips; it can either be raised to cover central or lateral defects; (**a**) defect and planning of the flap; (**b**) after 180° rotation of the flap with left-sided pedicle; (**c**) clinical example of soft tissue defect of the upper lip; (**d**) clinical picture after soft tissue coverage with Abbe flap

tion of the uninjured lip is rotated across the oral orifice and into the defect of the burned lip. An accurate closure of all three layers at the recipient site is standard. A second stage is required to ligate the pedicle and inset at around 2–3 weeks after the initial procedure. From our experience, this flap has an excellent cosmetic result when it is used to replace the entire philtrum of the upper lip.

If the defect is located on the lateral site of the upper lip and involves the oral commissure, the Estlander flap is a reasonable procedure (Fig. 21.9). This flap, too, is a lip-switch flap but designed at the lateral part of the lip. It uses a medially based full-thickness portion of the upper lip. Upon realignment of the vermillion border, the mucosa needs to be advanced to match the thickness of the recipient site. This technique may result in a typical rounding of the oral commissure and therefore often needs corrective procedures at earliest 12 weeks after the initial operation. A triangular part of the flap can be incised, and the oral commissure can be reconstructed based on available techniques (see above).

The Gillies flap allows for subtotal or total lip reconstruction and is an extension of the Estlander flap. Tissues lateral to the commissures are advanced, and the flap is rotated to create new commissures while tissue is advanced medially to fill the defect (Fig. 21.10). This technique surely has the disadvantage of sensory loss of the flap caused by surgical denervation as well as vermillion deficiency.

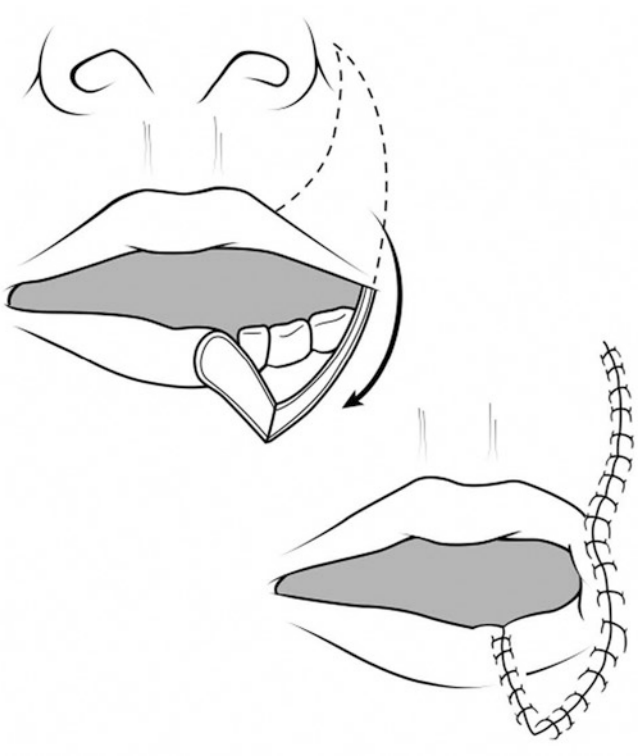


Fig. 21.9 The Estlander flap (rotation flap procedure) for defects of the upper and lower lips; it is rotated through the commissure and thereby shifts the commissure and thereby reduces the oral orifice

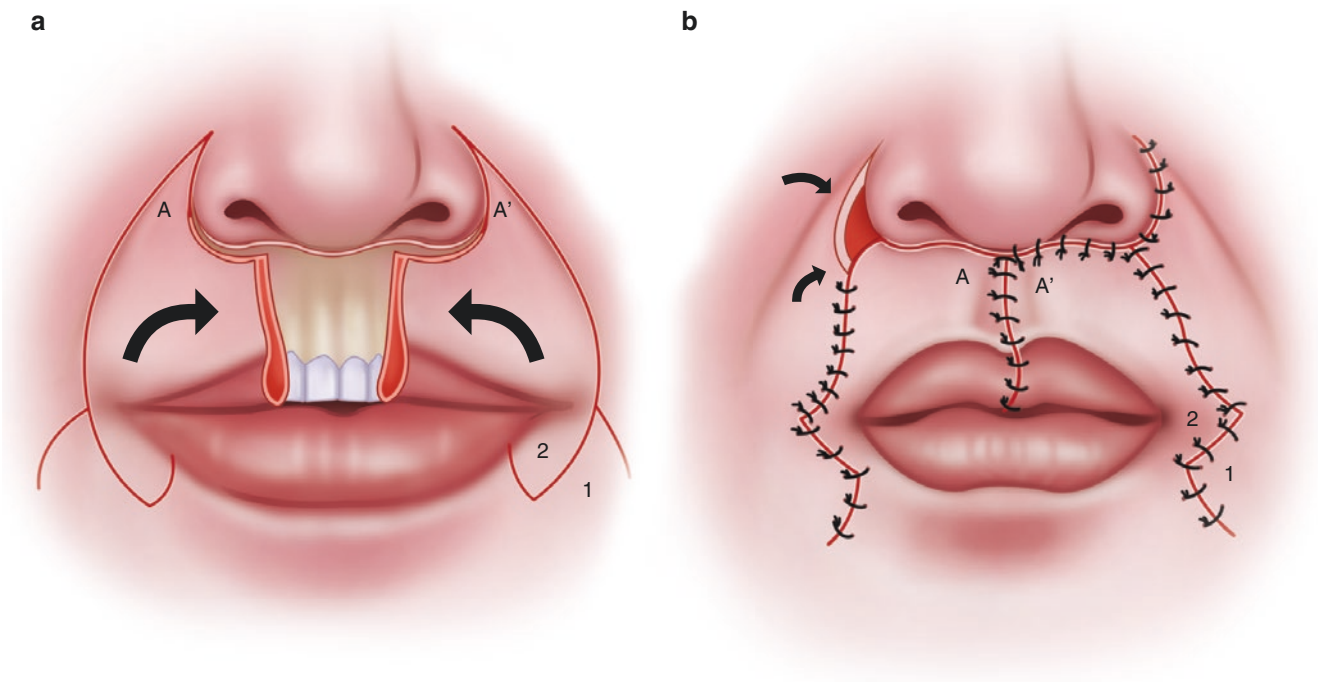


Fig. 21.10 Gillies flap to cover hugh central defects of the upper lip. Philtrum is sacrificed by this procedure. To spare out the paranasal skin, a sickle-shaped piece can be excised lateral to the alae nasi

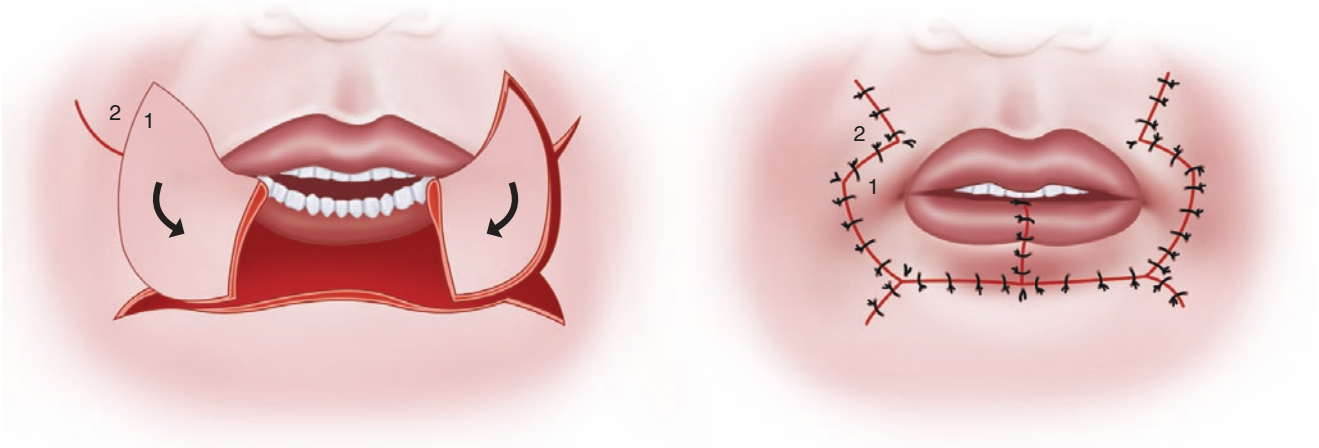


Fig. 21.11 Karapandzic flap to cover hugh soft tissue defects of the lower lip; musculocutaneous flaps raised bilaterally and slid forward each other and stitched up in the midline

Large defects that need functional reconstruction can instead be addressed with the Karapandzic flap, which takes the disadvantages of the Gillies flap into account. It was described in 1974 and is based on the idea of reconstructing the lost lip tissues with tissues from the adjacent lip and cheek. Two flaps are raised from the neighbourhood skin with a width equal to the height of the defect. These full-thickness musculocutaneous flaps are then slid towards each other and stitched to one another (Fig. 21.11). The neurovascular supply (facial artery and facial nerve branches) are dissected out and spared. For advancement, it can be necessary to gradually cut the peripheral muscle fibres without the need to dissect the mucosa. Philtrum relief will commonly be lost and needs second-stage reconstruction. Perialar crescentic cheek excision is applied in large defects of the upper lip that need extensive advancement from the cheek. Because simple advancement would result in bunching at the perialar folds, a perialar elliptical skin excision is carried out with the upper part shifted laterally to avoid the nostril.

Defects affecting more than 80% of the upper lip can only be covered with the help of non-lip tissues (local flaps from surrounding skin or free flaps [25, 26], e.g., free gracilis [27] or free radial forearm flap folded to also reconstruct the inner lining of the mouth [28]) and seldom appear naturally, especially when the lip if moving.

The distinct contour of the upper lip is difficult to create and maintain for correction. Diligent study of the surface anatomy of the upper lip is required. The sophisticated realignment of the vermillion is paramount. If vermillion is lost, it can be reconstructed with tattooing or buccal mucosa grafting. If relevant parts of the philtrum are affected, resurfacing of the entire aesthetic subunit should be considered [29]. Philtrum can be reconstructed with ear composite cartilage grafts. It must be located centrally in relation to the nasal columella.

21.2.3.3 The Lower Lip

The reconstruction of the lower lip is not as complicated as the upper lip as it tolerates wedge resection in the majority of cases. Moreover, Abbe and Estlander flaps can be used in a reverse manner to cover defects of the lower lip with tissues from the upper lip.

In most of the cases, wedge resection and direct closure leads to satisfying results. If more than 50% of the central portion are deeply burned and need reconstruction, Schuchard's technique or Karapandzic flap is to use. Schuchard's technique utilizes the tissue from the lower lip/cheek region to close central defects by advancement with bilateral inferior incisions along the labiomental folds the mandibular border (Fig. 21.12a). This sliding-lip procedure has the advantage of minimal scarring most of which lie in between the aesthetic units. The Karapandzic techniques preserve the nerves to the orbicularis muscle, and the lip stays innervated. Bilateral flaps can be used to cover defects with up to 80% of tissue loss. Disadvantage is the risk of microstomia and the rounding of the commissure that might need corrective procedures afterwards (Fig. 21.12b).

For larger or paramedian defects, the (bilateral) reverse Abbe flap allows like-with-like reconstruction with primary closure of the upper lip, which serves as donor site (Fig. 21.13). This technique gives best results, when the flap is harvested from the lateral aspect of the upper lip and thereby does not include the philtrum. The calculated width of the flap should account for half of the defect width. It must not affect more than one third of the upper lip, so the donor defect can be closed primarily. Literature differentiates between a central and a lateral reverse Abbe flap. The central reverse Abbe flap is primarily used for median tissue loss of the lower lip and differs from the lateral flap in that it does

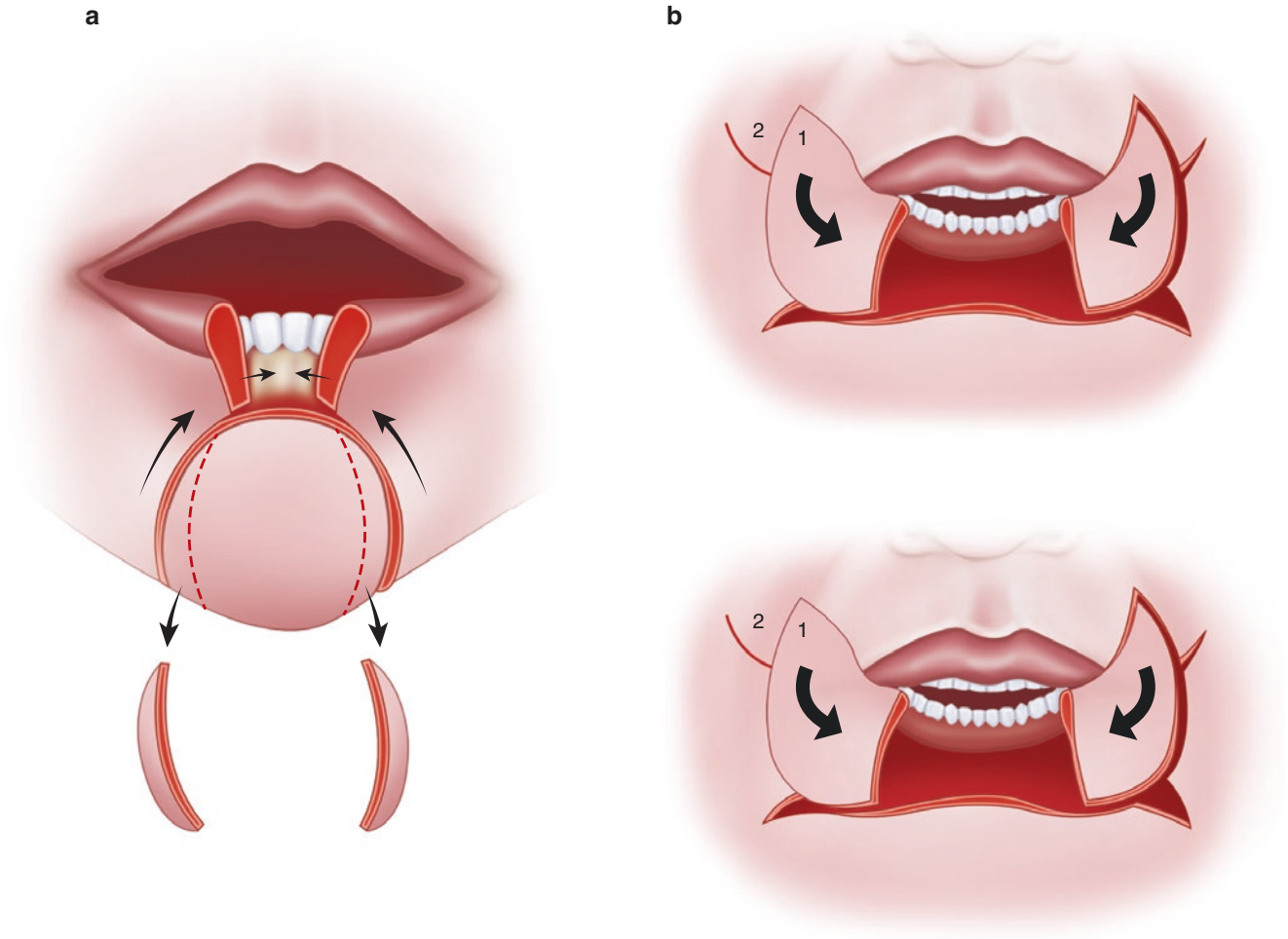


Fig. 21.12 Schuchard flap to cover hugh defects of the lower lip by rotating skin from the lower cheek around the chin

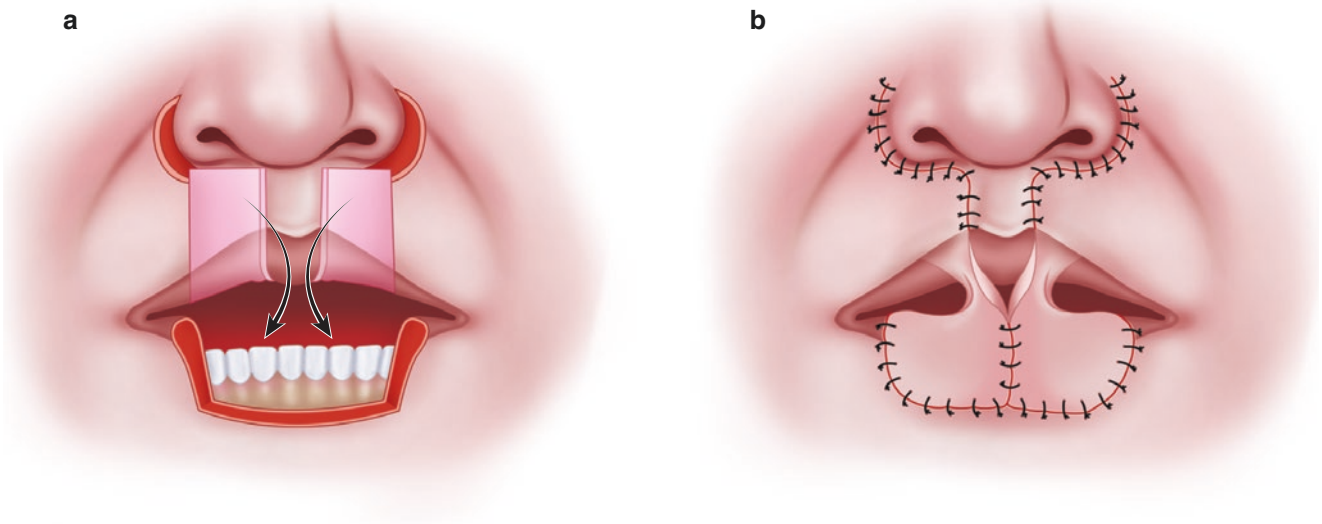


Fig. 21.13 Bilateral (reverse) Abbe flap to cover hugh defects of the lower lip by replacing vermillion with vermillion from the upper lip; sickle-shaped parts of surplus tissues; (**a**) two medial pedicled Abbe flaps are raised from the upper lip; (**b**) after 180° rotation, the flaps are stitched to the defect in the lower lip

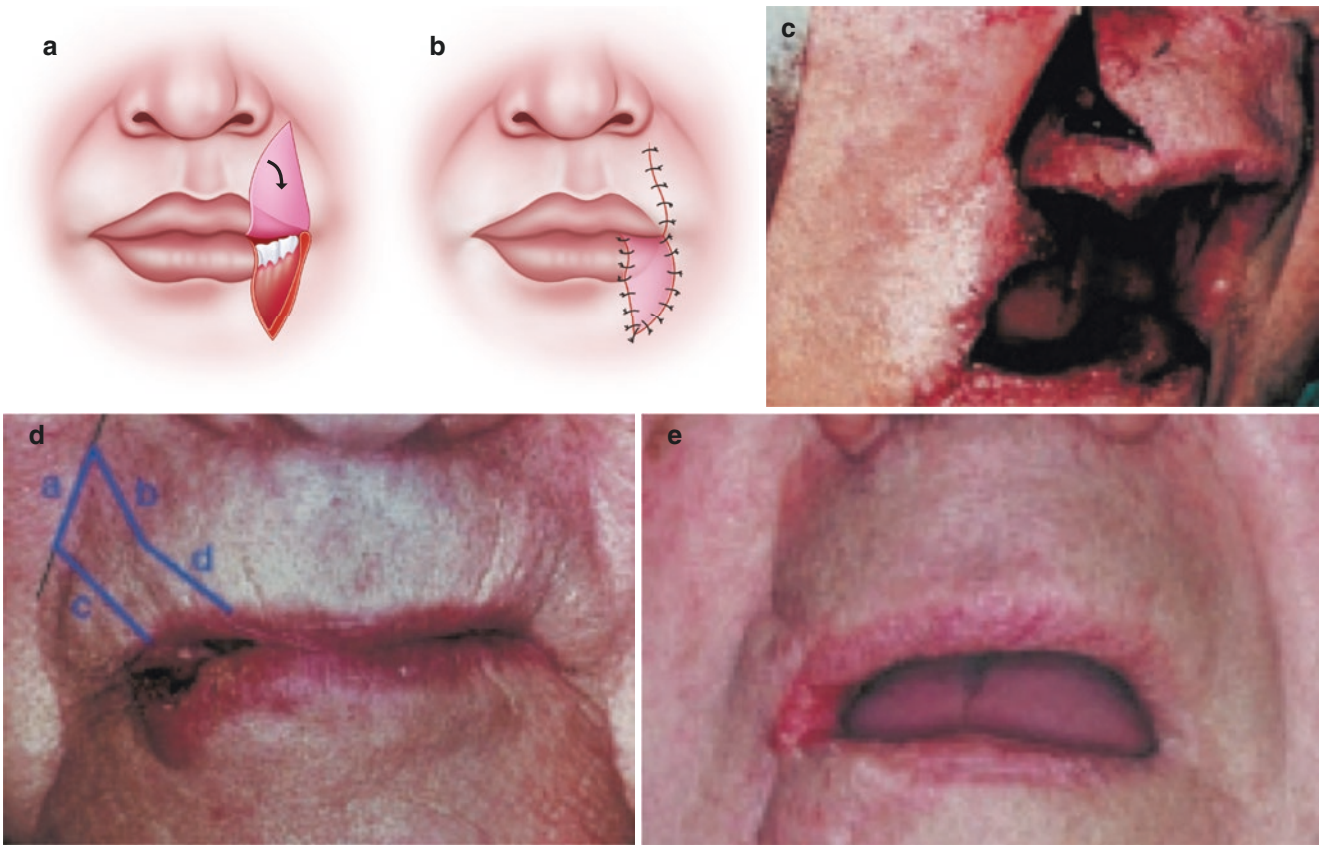


Fig. 21.14 (**a**, **b**) Classic Estlander flap; (**c**–**e**) Balch flap raised from the nasolabial fold to reduce donor defect of the upper lip by placing the donor site more laterally

not involve the perialar crescents and is based on a medial vascular pedicle.

There are also two sliding procedures available for the reconstruction of the lower lip. The Estlander flap as described above for reconstruction of the upper lip provides good amounts of mucosa for reconstruction of the vestibulum oris and also matches with rectangular defects in the lower lip. Like the Abbe flap, the Estlander technique can be combined with the step technique in defects involving more than two thirds of the lip and in cases with involvement of the commissure. Estlander full-thickness flap matches well with the remaining lower lip tissue but has a tendency to produce microstomia especially when performed bilaterally. A reasonable modification was provided by Balch [30], minimizing the resulting deformity in the donor (upper) lip. He positioned the lateral aspect of the flap into the nasolabial fold and thereby preserved the natural course of the fold which prevents philtrum disturbance. Moreover, this procedure pays respect to the oral commissure more than the classic Estlander technique (Fig. 21.14).

Based on the procedure described by Gillis, Karapandzic modified this technique by preserving the nerve supply to the lower lip and thereby replaced the technique of Gillis completely. The flap pivots at the commissure and upper lip and slides along the nasolabial fold. It must be classified a rotation-advancement flap and is the most useful flap for large defects.

Also described for large defects of the lower lip, the Bernard–Burrow flap allows reconstruction with the advancement of adjacent cheek tissue (Fig. 21.15). Lateral triangular flaps based at the level of the commissures are flipped over to reconstruct defects of the central portion of the lower lip. Webster modified this technique and described incision through skin and subcutaneous tissue to preserve underlying neuromuscular structures.

Large defects of the lower lip that make the use of local solutions impossible can be challenging and demanding for the treating surgeon [31]. Distant flaps include submandibular, anterior cervical, deltopectoral, sternocleidomastoidal, as well as forehead flaps. Also free tissue transfer [26] (e.g. radial forearm flap [28, 32] or gracilis flap [27]) has been described [26].

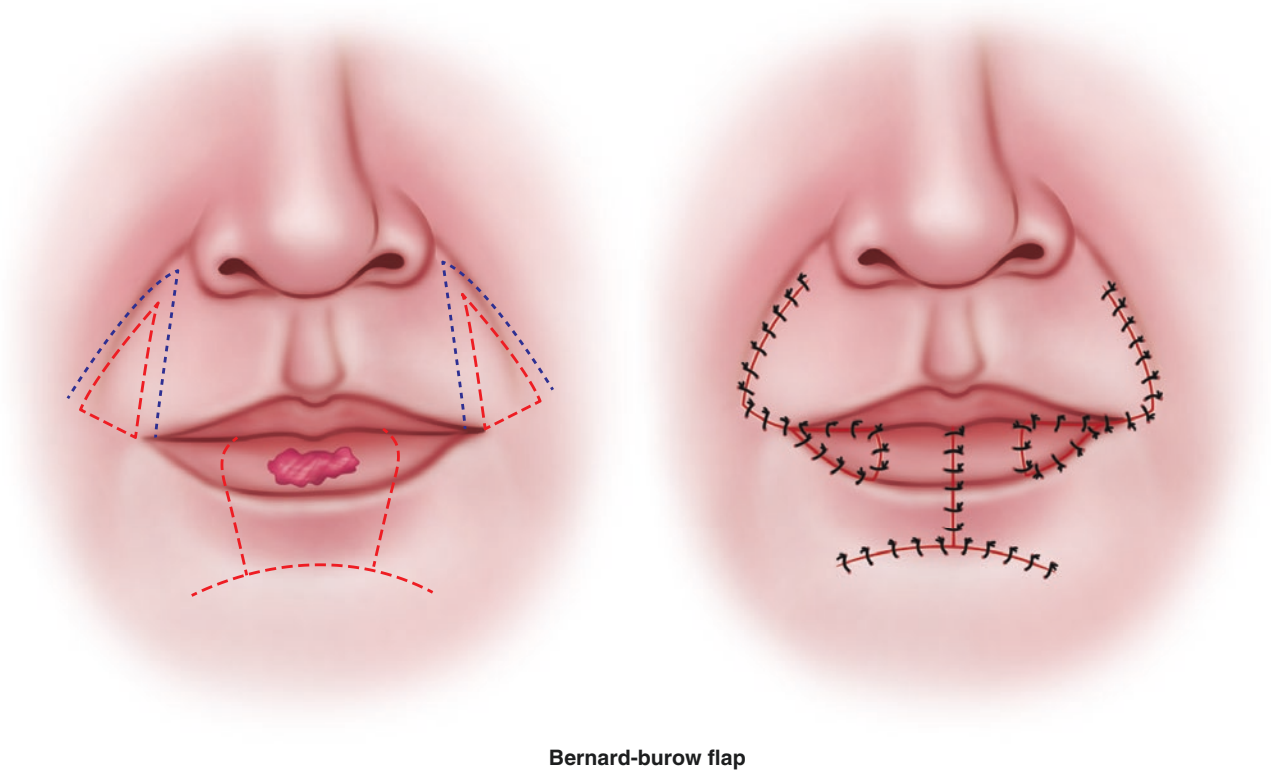


Fig. 21.15 Bernard–Burrow flap to cover defects of the lower lip with the use of adjacent cheek tissue rotated from the nasolabial fold into the defect

21.3 Summary and Conclusion

Patients with facial burns often suffer from perioral loss of tissue with subsequent facial scarring. Some individuals present with nutritional needs with limited oral intake, articulation abnormalities with impaired communication, dental hygiene, dental treatments and abnormal development of the definition and dental arches in childhood. Early treatment options are different stretching devices that positively influence contract scarring in the perioral region. The treating physician must not forget to apply such a device even in mechanically ventilated patients. Externally placed devices may not be able to be used too early because of open wounds or recently transplanted skin grafts. Important: early splinting decreases the need for surgical reconstruction.

In general, surgical treatment is not indicated directly after injury, because the extent of necrotic tissue cannot be defined accurately. If microstomia develops and surgery is needed, different techniques are available for the reconstruction of the oral commissure. A detailed preoperative planning according the opposite (uninjured) side or to typical established landmarks should be carried out. Most techniques are based on the idea of recruiting a mucosal flap from the cheek and transferring it to the commissure. Aesthetic and functional results are sometimes not optimal and make subsequent surgery necessary.

When analysing lip defects and planning reconstructive procedure, the amount of remaining vermillion is the most important assessment. It is distinct in colour and texture and can hardly be replaced. Reconstruction of the function is more critical in the lower lip, whereas it can generally tolerate wedge resection in the majority of defects.

Aim of all reconstructive procedures is a well-balanced length of upper and lower lips. The two lips should generally share the remaining tissue. Lip switch procedures are accompanied by lip sliding procedures. Most of the techniques are single-step procedures but might need corrective surgery in some cases. All techniques show advantages and disadvantages. To pick the appropriate procedure for specific defects and the individual needs of patients ensure best functional and aesthetic outcomes.

References

1. Zweifel CJ, Guggenheim M, Jandali AR, Altintas MA, Kunzi W, Giovanoli P. Management of microstomia in adult burn patients revisited. J Plast Reconstr Aesthet Surg. 2010;63(4):e351–7. Epub 2009 Nov 25.

2. Egeland B, More S, Buchman SR, Cederna PS. Management of difficult pediatric facial burns: reconstruction of burn-related lower eyelid ectropion and perioral contractures. J Craniofac Surg. 2008;19(4):960–9.
3. Dougherty ME, Warden GD. A thirty-year review of oral appliances used to manage microstomia, 1972 to 2002. J Burn Care Rehabil. 2003;24(6):418–31; discussion 410.
4. Ortiz-Monasterio F, Factor R. Early definitive treatment of electric burns of the mouth. Plast Reconstr Surg. 1980;65(2):169–76.
5. al-Qattan MM, Gillett D, Thomson HG. Electrical burns to the oral commissure: does splinting obviate the need for commissuroplasty? Burns. 1996;22(7):555–6.
6. Hashem FK, Al Khayal Z. Oral burn contractures in children. Ann Plast Surg. 2003;51(5):468–71.
7. Rose EH. Aesthetic restoration of the severely disfigured face in burn victims: a comprehensive strategy. Plast Reconstr Surg. 1995;96(7):1573–85; discussion 1586–1577.
8. Gonzalez-Ulloa M. Regional aesthetic units of the face. Plast Reconstr Surg. 1987;79(3):489–90.
9. Fraulin FO, Illmayer SJ, Tredget EE. Assessment of cosmetic and functional results of conservative versus surgical management of facial burns. J Burn Care Rehabil. 1996;17(1):19–29.
10. Pitts W, Pickrell K, Quinn G, Massengill R. Electrical burns of lips and mouth in infants and children. Plast Reconstr Surg. 1969;44(5):471–9.
11. Jin X, Teng L, Zhao M, et al. Reconstruction of cicatricial microstomia and lower facial deformity by windowed, bipedicled deep inferior epigastric perforator flap. Ann Plast Surg. 2009;63(6):616–20.
12. Fan J, Liu L, Tian J, Gan C, Lei M. Aesthetic full-perioral reconstruction of burn scar by using a bilater-al-pedicled expanded forehead flap. Ann Plast Surg. 2009;63(6):640–4.
13. Ninkovic M, Spanio di Spilimbergo S. Lower lip reconstruction: introduction of a new procedure using a functioning gracilis muscle free flap. Plast Reconstr Surg. 2007;119(5):1472–80.
14. Stewart R, Bhagwanjee AM, Mbakaza Y, Binase T. Pressure garment adherence in adult patients with burn injuries: an analysis of patient and clinician perceptions. Am J Occup Ther. 2000;54(6):598–606.
15. Neale HW, Billmire DA, Carey JP. Reconstruction following head and neck burns. Clin Plast Surg. 1986;13(1):119–36.
16. Ward RS. Pressure therapy for the control of hypertrophic scar formation after burn injury. A history and review. J Burn Care Rehabil. 1991;12(3):257–62.
17. Gallagher J, Goldfarb IW, Slater H, Rogosky-Grassi M. Survey of treatment modalities for the prevention of hypertrophic facial scars. J Burn Care Rehabil. 1990;11(2):118–20.
18. Gay WD. Prostheses for oral burn patients. J Prosthet Dent. 1984;52(4):564–6.
19. Berlet AC, Ablaza VJ, Servidio P. A refined technique for oral commissurotomy. J Oral Maxillofac Surg. 1993;51(12):1400–3.
20. Converse JM. Orbicularis advancement flap for restoration of angle of the mouth. Plast Reconstr Surg. 1972;49(1):99–100.
21. Fairbanks GR, Dingman RO. Restoration of the oral commissure. Plast Reconstr Surg. 1972;49(4):411–3.
22. Spanholtz TA, Theodorou P, Phan V, Perbix W, Spilker G. Reconstruction of the oral commissure in microstomia patients with deep dermal facial burns: a modified technique. Handchir Mikrochir Plast Chir. 2007;39(5):350–5.
23. Ayhan M, Aytug Z, Deren O, Karantinaci B, Gorgu M. An alternative treatment for postburn microstomia treatment: composite auricular lobule graft for oral commissure reconstruction. Burns. 2006;32(3):380–4.
24. Koymen R, Gulses A, Karacayli U, Aydintug YS. Treatment of microstomia with commissuroplasties and semidynamic acrylic splints. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;107(4):503–7.
25. Bozikov K, Arnez ZM. Reconstruction of large upper lip defects by free tissue transfer. Acta Chir Plast. 2008;50(2):51–3.
26. Ueda K, Oba S, Nakai K, Okada M, Kurokawa N, Nuri T. Functional reconstruction of the upper and lower lips and commissure with a forearm flap combined with a free gracilis muscle transfer. J Plast Reconstr Aesthet Surg. 2009;62(10):e337–40.
27. Cordova A, D'Arpa S, Moschella F. Gracilis free muscle transfer for morpho-functional reconstruction of the lower lip. Head Neck. 2008;30(5):684–9.
28. Daya M, Nair V. Free radial forearm flap lip reconstruction: a clinical series and case reports of technical refinements. Ann Plast Surg. 2009;62(4):361–7.
29. Neale HW, Billmire DA, Gregory RO. Management of perioral burn scarring in the child and adolescent. Ann Plast Surg. 1985;15(3):212–7.
30. Balch CR. Modification of cross-lip flap. Plast Reconstr Surg. 1978;61(3):457–8.
31. Rifaat MA. Lower lip reconstruction after tumor resection; a single author's experience with various methods. J Egypt Natl Canc Inst. 2006;18(4):323–33.
32. Daya M. Simultaneous total upper and lower lip reconstruction with a free radial forearm-palmaris longus tendon and brachioradialis chimeric flap. J Plast Reconstr Aesthet Surg. 2010;63(1):e75–6. Epub 2009 Apr 3.

Nasal Reconstruction

22

Lars-Peter Kamolz, Maike Keck, Harald Selig, and David B. Lumenta

The nose has a central position in the face and serves as the key anatomic area for aesthetic and facial balance. Due to its central position, the nose is very often involved in facial burns. Due to its importance, nose reconstruction plays a major role in regaining quality of life, but besides its aesthetic impact, the nose also plays a major role as a functional organ in the upper airway.

Advances in the philosophy, approach, and techniques for nasal reconstruction have resulted in increasingly refined aesthetic and functional results. This has been achieved by adhering to the paradigm of replacing missing tissue with like tissue.

The tenets include replacing the:

- Lining
- Framework
- Cover of the nose with material that matches the deficient tissues as close as possible

Achauer has described a nasal deformity according to the following schema [1]:

- Burn scar deformity without major tissue loss (hypertrophic scars, hypo- and hyperpigmentation, asymmetry)
- Ectropium (e.g., due to the loss of the alar rim)
- Subtotal tissue loss
- Extensive tissue loss
- Nostril stenosis

22.1 Principles of Nasal Reconstruction

Nasal reconstruction in patients suffering from burns is similar to nasal reconstruction in patients suffering from cancer. The most important factors are soft tissue coverage, lining, and skeletal support. Therefore, an exact analysis of the missing tissue has to be performed prior to surgery in order to understand the tissue needs.

If there is only a need for skin coverage, an unmeshed split-thickness or full-thickness skin graft is required. Don't forget to take the aesthetic subunits of the nose into account (Fig. 22.1) [2, 3]. In case of small defects and good quality of the surrounding tissue, a local flap can be used to solve the problem (Figs. 22.2 and 22.3).

In case of extensive or subtotal tissue loss, autologous material and alloplastic material can be used for bony augmentation or bony reconstruction. With reference to the literature, autologous material seems to be superior than

L.-P. Kamolz (✉)
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

COREMED - Cooperative Centre for Regenerative Medicine, JOANNEUM RESEARCH Forschungsgesellschaft mbH, Graz, Austria
e-mail: lars.kamolz@medunigraz.at, Lars-Peter.Kamolz@joanneum.at

M. Keck · D. B. Lumenta
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

H. Selig
COREMED - Cooperative Centre for Regenerative Medicine, JOANNEUM RESEARCH Forschungsgesellschaft mbH, Graz, Austria

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_22

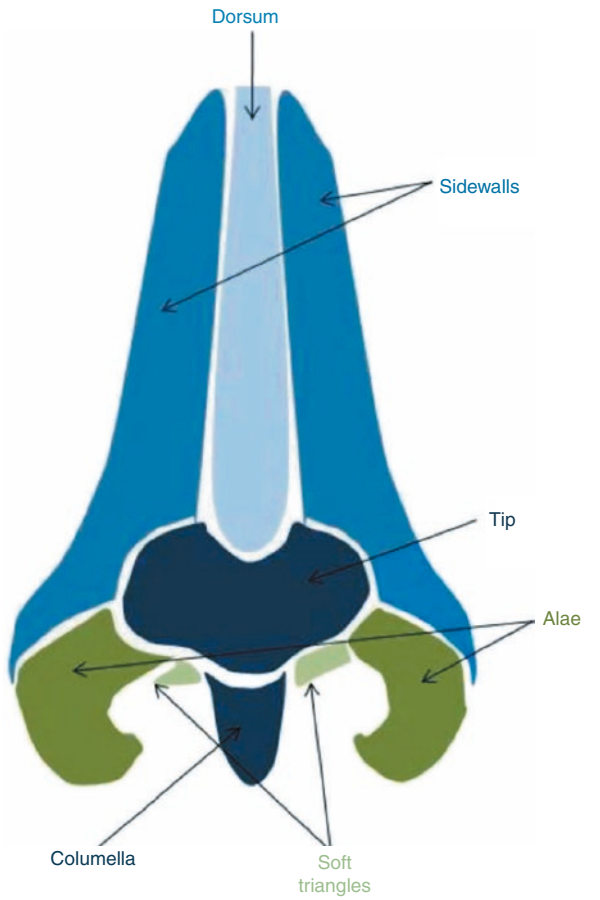


Fig. 22.1 Aesthetic subunits of the nose

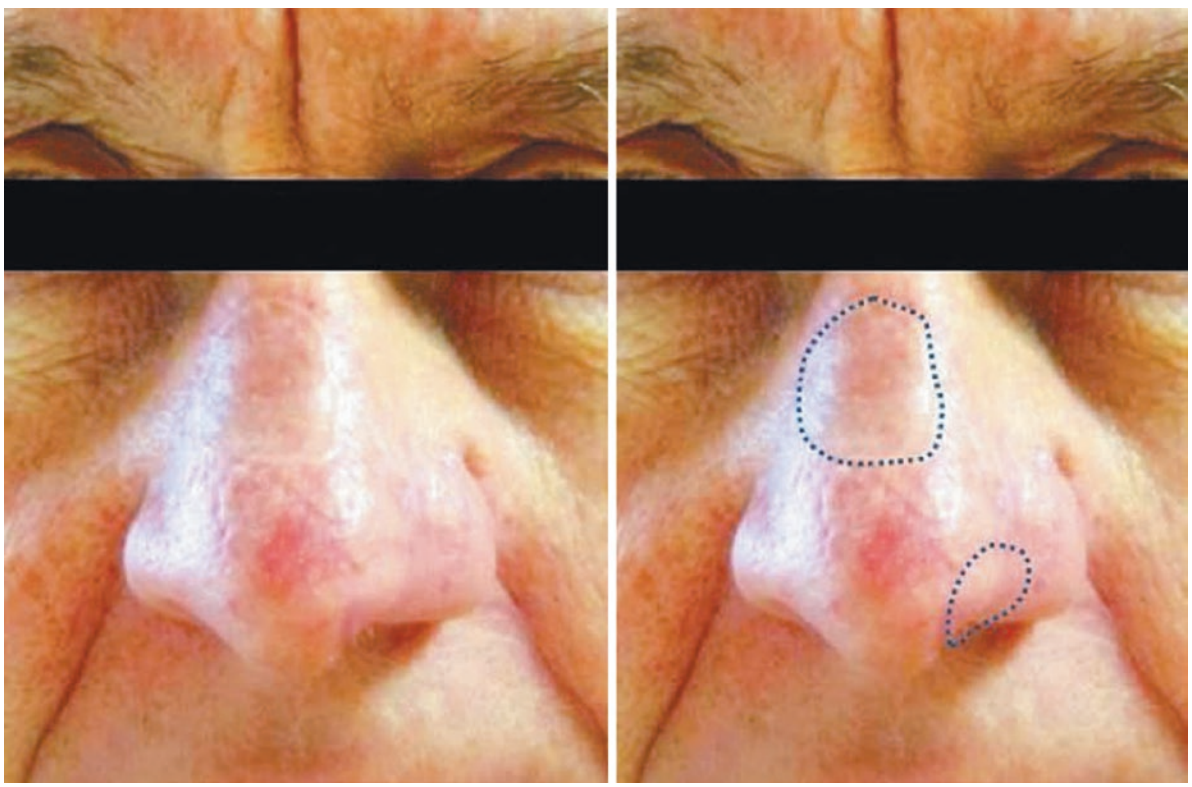


Fig. 22.2 Late results after defect coverage (frontal view): Dorsum: full-thickness graft. Tip—Alar Region: tunneled nasolabial island flap

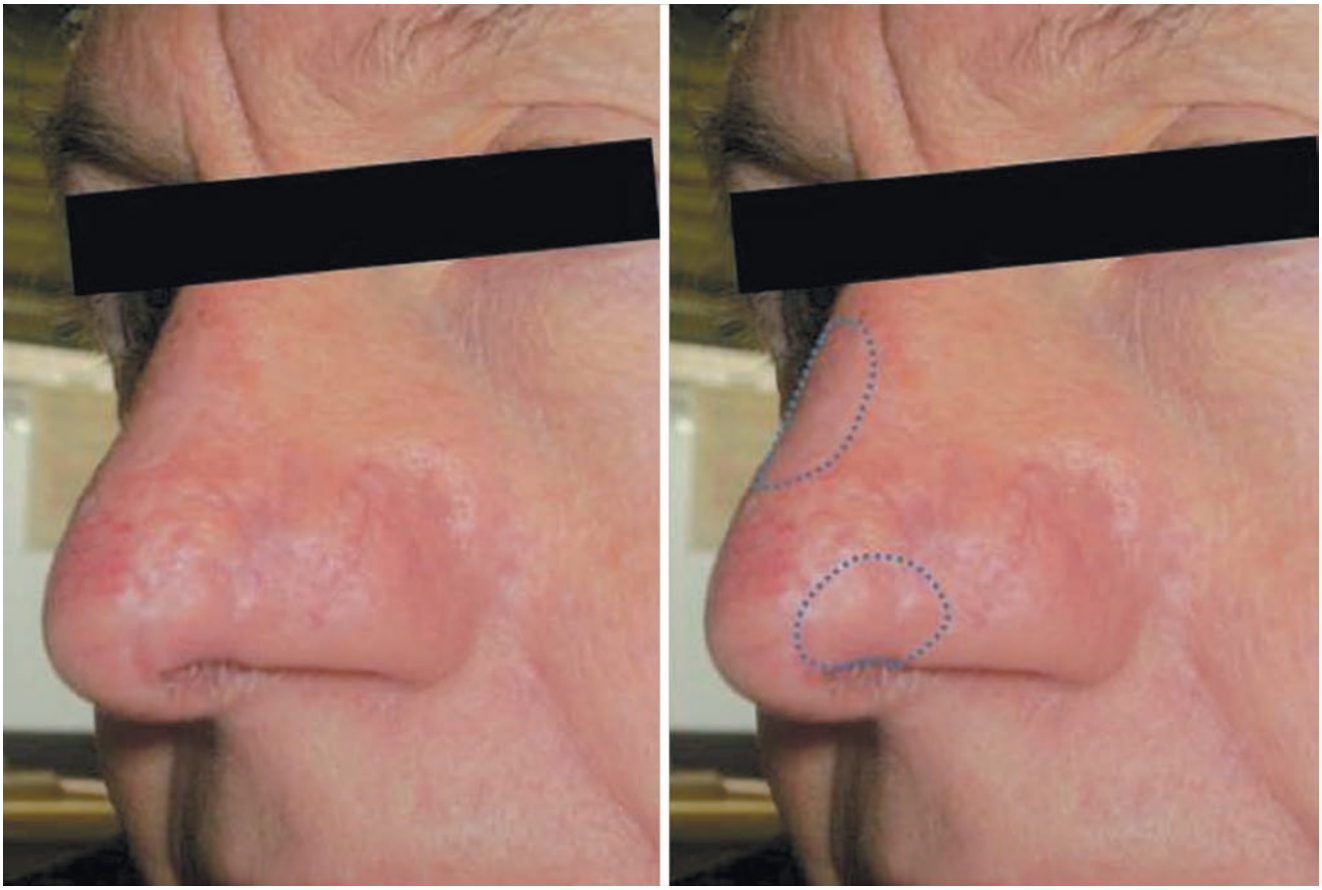


Fig. 22.3 Late results after defect coverage (lateral view): Dorsum: full-thickness graft. Tip—Alar Region: tunneled nasolabial island flap

alloplastic material due to their possible complications, which are associated with the use of alloplastic materials [4–10], but in both cases, an adequate soft tissue coverage is of utmost importance. Bone and cartilage are really optimal for replacing the framework of the nose. Generally free grafts harvested from the rib, calvarium, nasal, septum, or ear can provide the foundation for the internal lining and external coverage. Occasionally, composite grafts from the ear can serve as a replacement for full-thickness defects of the lower nose [11], but also free composite auricular flaps have been used to cover larger defects in the lower part of the nose [12].

The workhorse for nasal reconstruction in case of larger defects is the forehead flap [13, 14] (Figs. 22.4, 22.5 and 22.6) and for inner lining the septal mucoperichondrium [15].

A total nasal defect including all layers of tissue, from skin to bone, might be reconstructed with a prelaminated free flap. Prelamination includes additional tissues into a flap in a multistage fashion. The forearm has been cited as a common donor site. Skin, mucosa, and cartilage grafts are inserted prior to flap raising. After lining, support, and coverage have formed a stable unit, they are raised and a microvascular anastomosis performed [16].

In future allotransplantation might gain importance for large and complex defects of the face [17–19]. Moreover, the use of tissue engineering and engineered products like cartilage will improve future possibilities for nasal reconstruction [20, 21].

22.2 Summary

Reconstruction of the nose continues to progress to new level that allows plastic surgeons to restore near normal form and function to the majority of nasal defects. These advances are based on the concepts of respecting the borders of the aesthetic units (Fig. 22.1) and replacing missing tissue with like tissue. In future allotransplantation and tissue engineering will gain importance for nasal reconstruction.

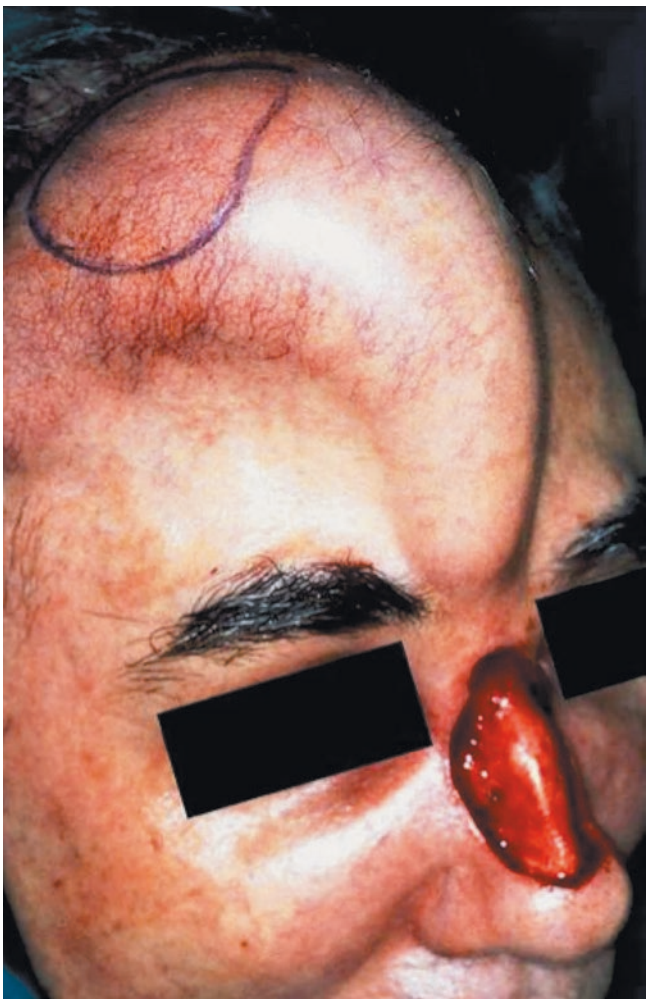


Fig. 22.4 Preexpanded forehead flap

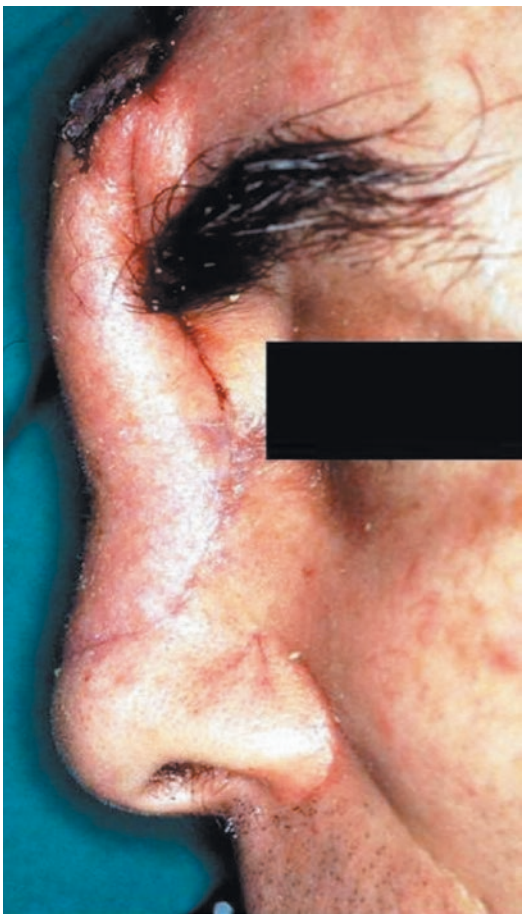


Fig. 22.5 Forehead flap in position

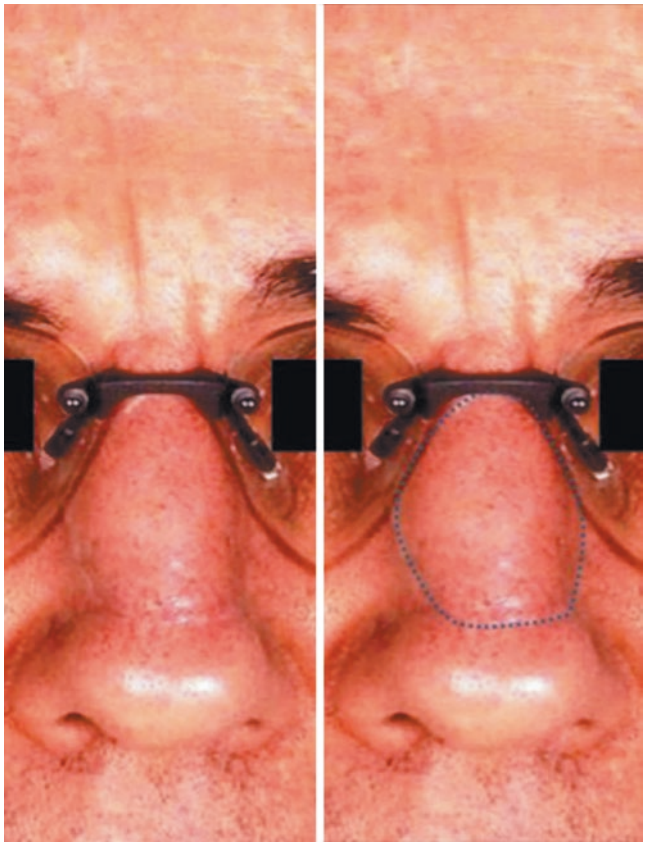


Fig. 22.6 Final result after forehead flap procedure

References

1. Achauer BM. Burn reconstruction. New York: Thieme Medical; 1991.
2. Manson PM, Hoopes JE, Chambers REG, et al. Algorithm for nasal reconstruction. Am J Surg. 1979;138:528.
3. Gonzales-Uloa M. Regional aesthetic units of the face. Plast Reconstr Surg. 1987;79:489.
4. Adams JS. Grafts and implants in nasal augmentation: a rational approach to material selection. Otolaryngol Clin North Am. 1987;29:913–30.
5. Schuller D, Bardach J, Krause D. Irradiated homogenous costal cartilage for facial contour restoration. Arch Otolaryngol. 1997;103:12–5.
6. McCollough EG, Weol C. Augmentation of facial defects using Mersilene mesh implants. Otolaryngol Head Neck Surg. 1979;87:515–21.
7. Brown BL, Neel HB, Kern E. Implants of supramid, proplast, plasti-pore, and silastic. Arch Otolaryngol. 1979;104:605–9.
8. Berman M, Pearce W, Tinnin M. Theo sue of Gore-Tex E-PTFE bonded to silicone rubber as an alloplastic implant. Laryngoscope. 1986;96:480–3.
9. Chou TD, Lee WT, Chen SL, et al. Split calavarial bone graft for chemical burn associated nasal augmentation. Burns. 2004;20:380–5.
10. Neel HB. Implants of Gore-Tex. Arch Otolaryngol. 1983;109:427–33.
11. Haug MD, Rieger UM, Witt P, Gubisch W. Managing the ear as a donor site for composite graft in nasal reconstruction: update on technical refinements and donor site morbidity in 110 cases. Ann Plast Surg. 2009;63:171–5.
12. Pribas JJ, Falco N. Nasal reconstruction with auricular microvascular transplant. Ann Plast Surg. 1993;31:289–97.
13. Mennick FJ. Nasal reconstruction. Forehead flap. Plast Reconstr Surg. 2004;113:100–11.
14. McCarthy JG, Lorenc ZP, Cutting C, et al. The median forehead flap: the blood supply. Plast Reconstr Surg. 1989;84:189.
15. Burget GC, Menick FJ. Nasal support and lining: the marriage of beauty and blood supply. Plast Reconstr Surg. 1989;84:189.
16. Taghina AH, Pribas JJ. Complex nasal reconstruction. Plast Reconstr Surg. 2008;121:15e–27e.
17. Decauchell B, Badet L, Lengele B, et al. First human face allograft: early report. Lancet. 2006;368:203–9.
18. Alam DS, Papay FP, Djohan R. The technical and anatomical aspects of the world's first near-total human face and maxilla transplant. Arch Facial Plast Surg. 2009;11:369–77.
19. Semionow M, Papy F, Alam D, et al. Near total human face transplantation for a severely disfigured patient in the USA. Lancet. 2009;374:203–9.
20. Watson D. Tissue engineering for rhinoplasty. Facial Plast Surg N Am. 2009;17:157–65.
21. Sage A, Chang AA, Schumacher B, et al. Cartilage outgrowth in fibrin scaffolds. Am J Rhinol Allergy. 2009;23:486–91.

Reconstruction/Correction of Burn Alopecia

23

Christian Smolle, Lars-Peter Kamolz, Maike Keck, Harald Selig, and David B. Lumenta

Burn alopecia is a significant disfigurement, and its sequela includes not only physical problems but also psychological problems, such as low self-esteem, unhappiness, and dissatisfaction. Therefore, burn alopecia is a significant challenge for plastic surgeons concerning reconstruction and rehabilitation. The primary goal of reconstruction for burn alopecia is to recreate a natural hair-bearing appearance on the reconstructed scalp.

Generally, there are two basic principles available to achieve this:

- First, scalp tissue should be replaced by scalp tissue, if possible.
- Second, the reconstructive procedure must restore and preserve hair growth patterns and hairlines for a cosmetically appealing result [1].

Based on these principles, numerous reconstructive methods, including hair grafting, serial excision, local scalp flaps, as well as scalp extension and expansion procedures have been described in literature [2–12].

To facilitate an easy and good assessment of the burn alopecia and formulation of a reconstructive algorithm, burn alopecia was classified by Seong-HO et al. based on the area, scar quality, and location [13].

They classified burn alopecia as small (50 cm^2), medium (50–100 cm^2), and large (>100 cm^2) based on the surface area involved.

Second, they classified burn alopecia as good, moderate, and poor based on its scar quality, mainly based on its pliability and elasticity. Good quality referred to a burn scar that was pliable and had adequate elasticity. Moderate quality indicated pliability, but reduced elasticity. Poor quality signified that the scar was not pliable, but fibrotic and hard.

Finally, they classified the scars as frontal and parietal scars (including temporal, occipital, and vertex scars) based on their location (Fig. 23.1).

23.1 Hair Grafting

Hair grafting is a simple technique that redistributes the patient's existing hair, but having a densely populated donor area is essential to the procedure. Due to the fact that in case of burn alopecia available donor area is often limited, the reconstruction of burn alopecia using hair grafting may be impossible, if the alopecic area is too large.

Therefore, hair grafting is mainly used for reconstruction of small or medium burn alopecia, in case of the fact that scar quality is good, and the burn alopecia location is frontal or parietal. Hair grafting is a safe procedure, and reasonably good results can be obtained in a single session (Fig. 23.2) [14].

The recently introduced partial longitudinal follicular unit transplantation is a promising method to overcome limited donor area. The principle is simple and comparable to that of split-thickness skin grafting: during harvesting hair follicles are split longitudinally in situ with a specific extraction needle. Thus part of the hair follicle remains at the donor site while the explanted part can be used for hair grafting. After sometime, almost all split follicles both at the recipient site and at the donor site reproduce adequate hair (Fig. 23.3) [15].

For the reconstruction of the anterior hairline in the frontal or parietal areas, hair grafting is the best option because the hairs can be easily grafted into the desired position. Even though it is a very tedious process for the surgeon, we consider hair grafting as an optimal reconstructive option in patients with small, good-quality burn alopecia (Fig. 23.4).

C. Smolle (✉) · L.-P. Kamolz · D. B. Lumenta
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria
e-mail: christian.smolle@medunigraz.at; lars.kamolz@medunigraz.at; david.lumenta@medunigraz.at

M. Keck · H. Selig
Division of Plastic and Reconstructive Surgery, Department of Surgery, Medical University of Vienna, Vienna, Austria
e-mail: maike.keck@meduniwien.ac.at

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_23

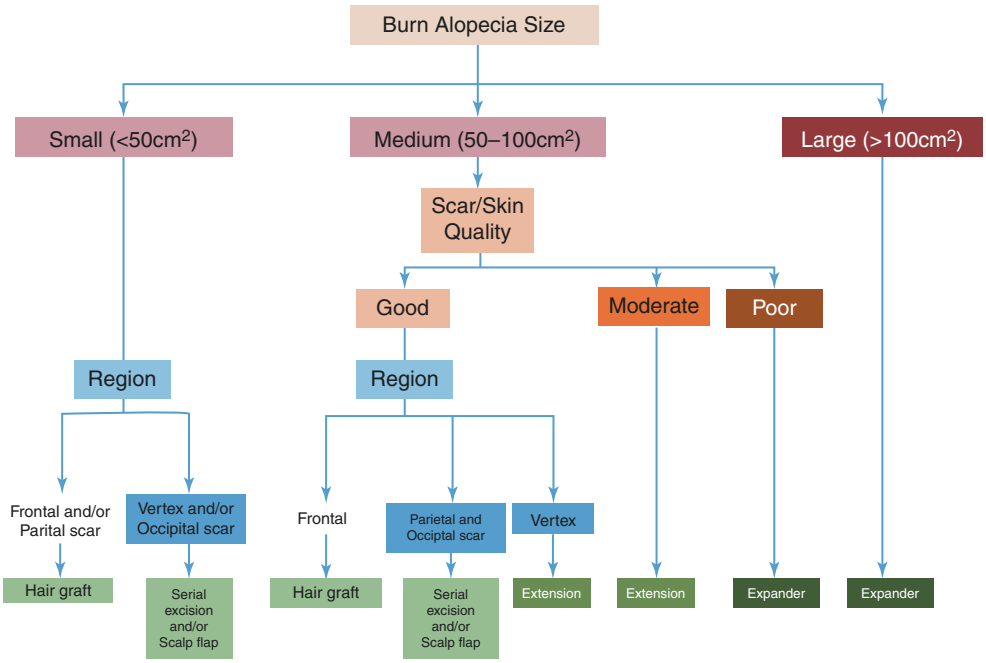


Fig. 23.1 Algorithm for the reconstruction of postburn alopecia depending on size, scar quality, and location

Fig. 23.2 Hair micrografts

23.2 Scalp Reduction (Serial Excision and Local Scalp Flap)

Scalp reduction in this study includes serial excision and the local scalp flap. This method is mainly performed for reconstruction, if the area of burn alopecia is small or medium, and if the scar quality is good. Serial excision is an easy and effective method to remove the burn scar within the alopecic area.

Although the scalp is not very elastic, its mobility can be increased by the surrounding scalp, and if necessary, criss-cross incisions can be made in the underlying galea to further increase the elasticity [6].

Therefore, small burn alopecia can be totally excised, and moderate burn alopecia can be diminished to an inconspicuous size by repeated excisions, if the scar quality is good. However, this method cannot be used for large burn alopecia of poor quality [7]. It has been reported that burn alopecic areas up to 15% of the total scalp can be surgically removed by serial excisions. Generally, the resulting minimized scar is easily hidden with the hair. Local scalp flaps are useful for the reconstruction of relatively small burn alopecia [16]. Generally, successful local flap mobilization requires a well-vascularized donor site, which is free of scars and contractures. In burn alopecia, neighboring scalp tissue is often fibrotic as a result of burn damage, thereby severely limiting the use of local flaps. Moreover, local scalp flaps can be accompanied by some aesthetic problems, including incisional scars, iatrogenic alopecia, and unnatural hair growth patterns.

23.3 Scalp Extension

Scalp extension surgery was first introduced by Frechet [17]. This technique uses a stretchable device that consists of an elastic silicone band with several hooks on the distal ends. With time, the memory of the silastic band pulls the hair-bearing tissues closer together via the property of biologic creep [18]. The most useful component of scalp extension is that it eliminates the stretch-back phenomenon postoperatively and can reduce the number of repetitions [19]. In addition, this method proves more socially presentable and minimizes social limitations. Moreover, this method reduces the length of hospitalization and total treatment time, as well as the number of checkups required to perform periodic pumping [8]. Nevertheless, this proce-

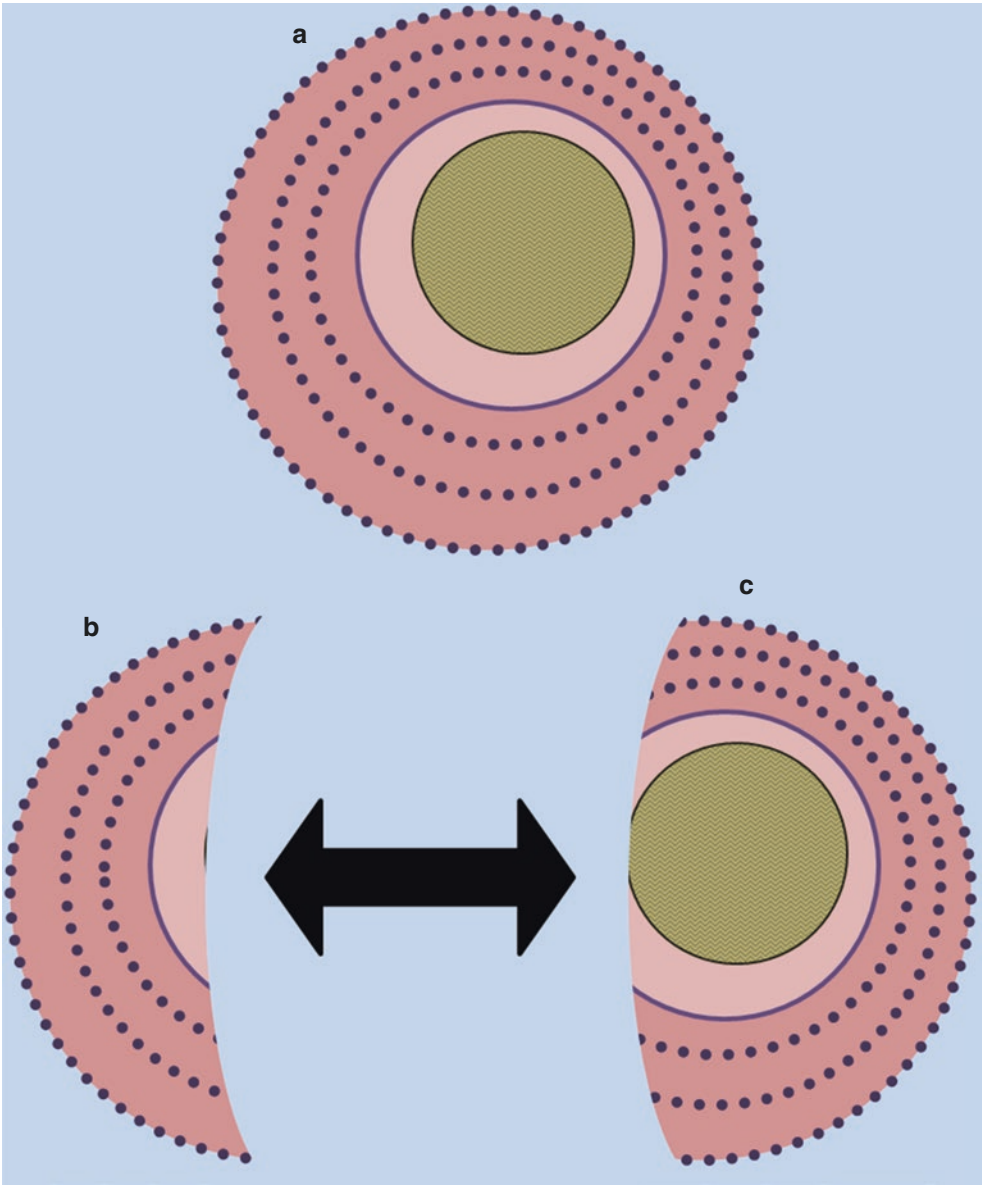


Fig. 23.3 Partial longitudinal follicular unit transplantation. Scheme of follicular unit under the microscope (**a**). After harvest, an appreciable amount of the follicle remains at the donor site (**b**) and regenerates to reproduce hair while graft follicles (**c**) can be transplanted as usual

dure is associated with more complications than scalp reduction or hair grafting.

An alternative method of scalp extension involves the use of microporous tape instead of the hooked silastic band. With this technique, the hair-bearing scalp surrounding the alopecic area is shaved and pre-stretched in the desired direction manually. The skin is then held in position with multiple strips of microporous tape. Taping is repeated weekly until skin laxity is appropriate to remove and cover part or all of the alopecic area. Usually between 5 and 10 taping sessions are needed before surgery can be performed. Small to medium alopecic areas can be treated effectively with this technique. Generally this noninvasive technique is relatively complication-poor and well tolerated by patients. However, poor scar quality and adherence of the alopecic area to underlying tissues may hinder the extension process. Very compliant patients can also perform the taping by themselves which further reduces the need for regular checkups [20].

23.4 Scalp Expansion

Scalp expansion surgery is mainly used when the area of burn alopecia is large, and the scar quality is poor (Figs. 23.5, 23.6 and 23.7). Scalp expansion is the most popular way to reconstruct the burned scalp, and it has produced satisfactory results in most patients [9–12]. It provides hair-bearing scalp to the alopecic region with minimal donor site morbidity, and huge alopecic regions of up to 50% of the scalp can be reconstructed using this method without an appreciable change in hair density [21, 22]. However, scalp expansion places a foreign body beneath the skin over a long period of time.

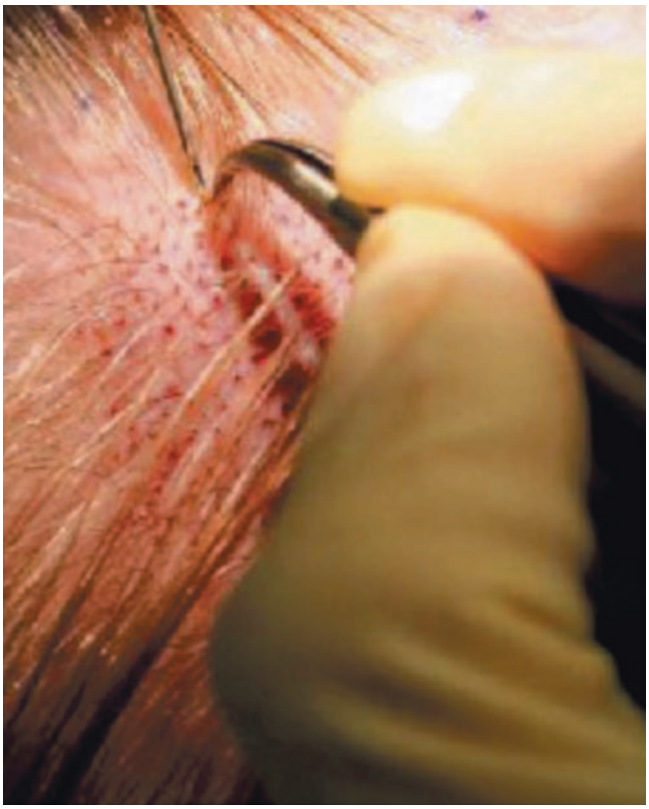


Fig. 23.4 Technique of hair grafting in a small frontal area

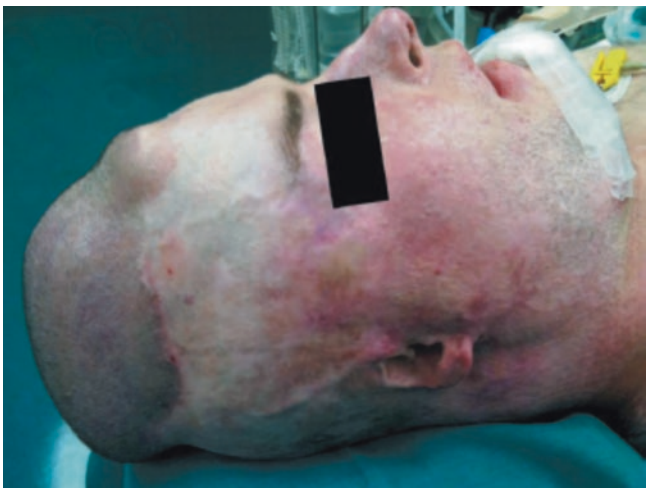


Fig. 23.5 Large area with moderate to poor scar/skin quality

Inevitably, this technique has a greater chance of complications than other techniques, including infections, implant exposure, and seromas. Although the majority of these complications are manageable and do not automatically necessitate abruption of therapy, they may impair the end result. Moreover, tissue expansion does have the disadvantage of requiring multiple hospital visits and the accompanying "bubble head-like" appearance (Fig. 23.5).

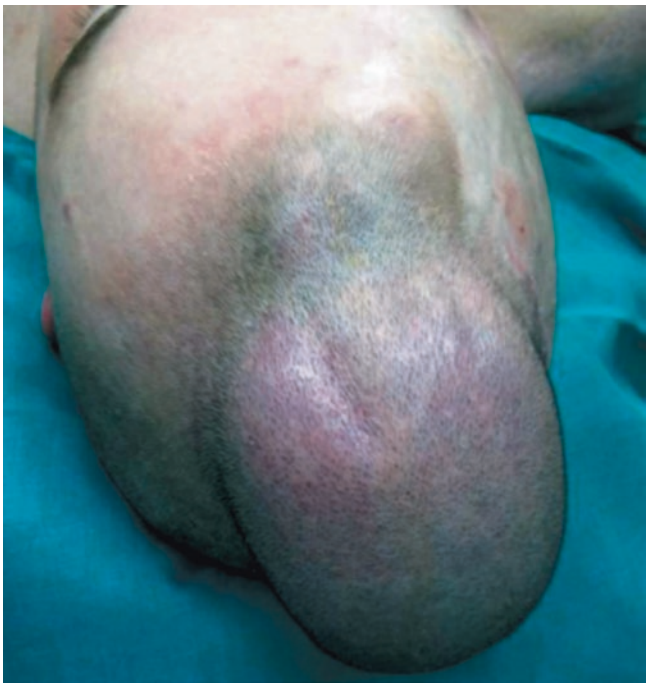


Fig. 23.6 "Bubble head-like" appearance of the expanded scalp

The osmotic expander is a self-filling tissue expander built of a semipermeable envelope filled with hypertonic solution. After implantation, the expander draws fluid from its surrounding and gradually inflates. The main advantage lies in the reduced need for repeated hospital visits and absence of painful refilling procedures. This makes the technique especially attractive for the use in children. On the downside, the speed of the filling process cannot be controlled and adapted to the amount of tissue tension [23].

In summary, size of alopecia, scar quality, and location of the burn alopecia are important determinants for choosing a reconstructive method for burn alopecia. Generally, it takes a long time to correct burn alopecia because it usually requires repetitive procedures. Therefore, it is very important to discuss the advantages and disadvantages of each of the reconstructive methods with the patients and select an appropriate method after considering patient's needs and desires.

23.5 Conclusions

The method for reconstruction of burn alopecia should be tailored to the conditions of the alopecic lesion and the patient's preference. We suggest an algorithm based on the conditions of burn alopecia, including the size, scar quality, and location of the burn alopecia. The algorithm may not be perfect, but this approach can offer a reliable guideline to achieve satisfactory results.

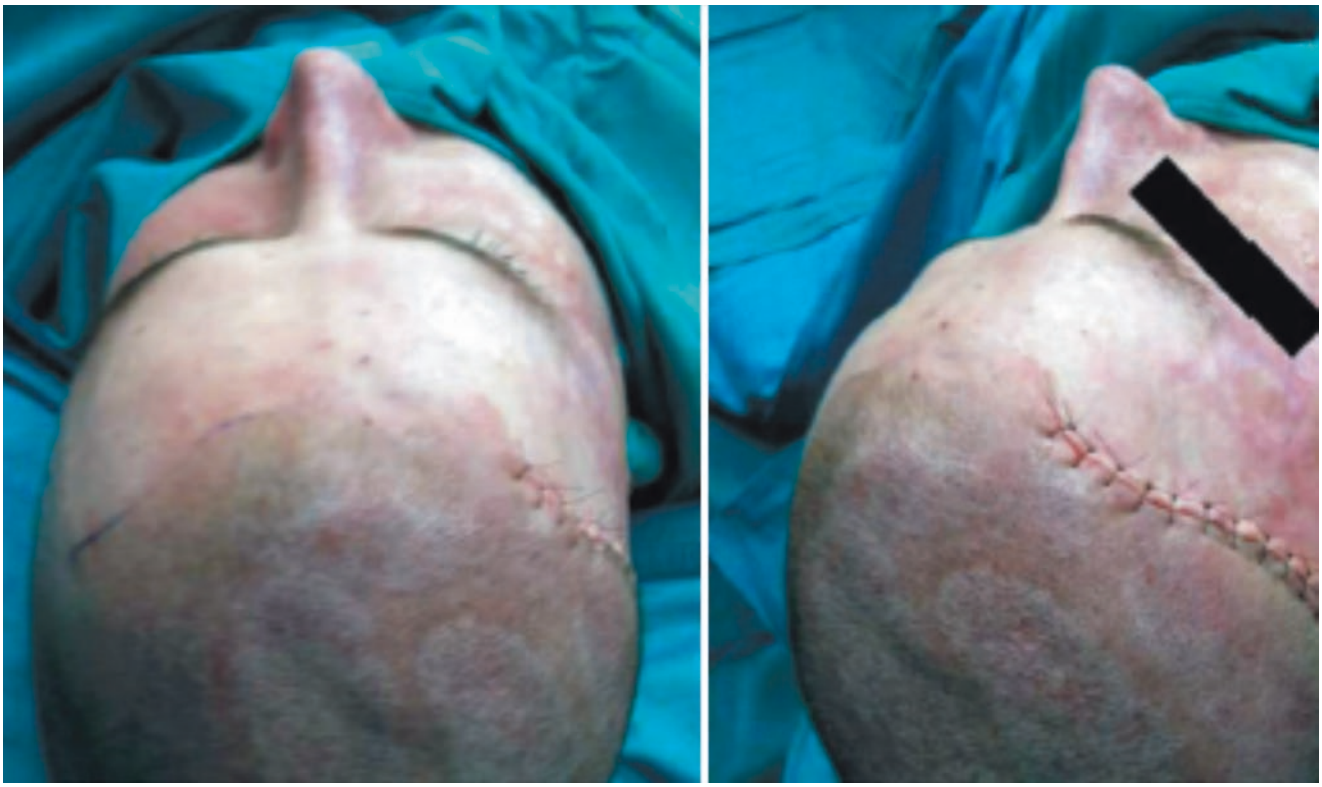


Fig. 23.7 Reconstruction of large alopecia area including frontoparietal hairline

References

1. Leedy JE, Janis JE, Rohrich RJ. Reconstruction of acquired scalp defects: an algorithmic approach. Plast Reconstr Surg. 2005;116:54e–72e.
2. Barrera A. The use of micrografts and minigrafts in the aesthetic reconstruction of the face and scalp. Plast Reconstr Surg. 2003;112:883–90.
3. Barrera A. The use of micrografts and minigrafts for the treatment of burn alopecia. Plast Reconstr Surg. 1999;103:581–4.
4. Moreno-Arias GA, Camps-Fresneda A. Hair grafting in postburn alopecia. Dermatol Surg. 1999;25:412–4.
5. Emsen IM. The use of micrografts and minigrafts together with advancement of temporalis fascia and its periosteum on the treatment of burn alopecia. J Craniofac Surg. 2008;19:907–9.
6. Vallis CP. Surgical treatment of cicatricial alopecia of the scalp. Clin Plast Surg. 1982;9:179–96.
7. Huang TT, Larson DL, Lewis SR. Burn alopecia. Plast Reconstr Surg. 1977;60:763–7.
8. Rosati P. Extensive head burns corrected by scalp extension. Dermatol Surg. 1995;21:728–30.
9. Voulliaume D, Chichery A, Chekaroua K, Comparin J-P, Foyatier J-L. Tissue expansion in surgical treatment of burn scars of the scalp. Ann Chir Plast Esthet. 2007;52:590–9.
10. Fan J, Yang P. Aesthetic reconstruction of burn alopecia by using expanded hair-bearing scalp flaps. Aesthetic Plast Surg. 1997;21:440–4.
11. Silfen R, Hudson DA, Soldin MG, Skoll PJ. Tissue expansion for frontal hairline restoration in severe alopecia in a child. Burns. 2000;26:294–7.
12. Buhrer DP, Huang TT, Yee HW, Blackwell SJ. Treatment of burn alopecia with tissue expanders in children. Plast Reconstr Surg. 1988;81:512–5.
13. Jeong S-H, Koo S-H, Han S-K, Kim W-K. An algorithmic approach for reconstruction of burn alopecia. Ann Plast Surg. 2010;65:330–7.
14. Barrera A. The use of micrografts and minigrafts for the correction of the postrhytidectomy lost sideburn. Plast Reconstr Surg. 1998;102:2237–40.
15. Gho CG, Neumann HAM. Improved hair restoration method for burns. Burns. 2011;37:427–33.
16. Baker SR, editor. Local flaps in facial reconstruction. St. Louis: Mosby-Year Book; 1995.
17. Frechet P. Scalp extension. J Dermatol Surg Oncol. 1993;19:616–22.
18. Dzubow LM. Hair today, gone tomorrow. J Dermatol Surg Oncol. 1993;19:602.
19. Brandy DA. Circumferential scalp reduction with a suture-in-place Silastic-Dacron extender. Dermatol Surg. 1996;22:137–47.
20. Daya M, Nair V. Traction-assisted dermatogenesis by serial intermittent skin tape application. Plast Reconstr Surg. 2008;122:1047–54.
21. Mathes SJ, editor. The head and neck: part 2. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2006.
22. Sharony Z, Rissin Y, Ullmann Y. Postburn scalp reconstruction using a self-filling osmotic tissue expander. J Burn Care Res. 2009;30:744–6.
23. Böttcher-Haberzeth S, Kapoor S, Meuli M, Neuhaus K, Biedermann T, Reichmann E, et al. Osmotic expanders in children: no filling—no control—no problem? Eur J Pediatr Surg. 2011;21:163–7.

Burn Reconstruction: Breast

24

Eva Koellensperger and Guenter Germann

24.1 Introduction

Thermal injuries to the anterior chest wall with affection of the breast can cause major functional and aesthetic problems, especially when burns are full thickness and happen early in childhood.

Thermal burns can result in damage of overlying skin, glandular breast tissue itself, and postburn scar contractures that may lead to asymmetries and functional growth disturbances.

Reconstructive procedures encompass the entire spectrum of reconstructive breast surgery, including scar release, split- and full-thickness skin grafting—potentially combined with dermal templates, the use of local flaps, pedicled flaps and free flaps with or without a prostheses, tissue expanders, nipple areola reconstruction, balancing reduction or augmentation mammaplasty, and various techniques of mastopexy.

24.1.1 Reconstructive Principles

The trunk is the second most frequently injured body area in burn injuries [1]. The breast is the part of the trunk, where complex reconstructive procedures are often required. Breast reconstruction begins with preserving as much breast tissue as possible during the acute phase of burn treatment. Excision of eschar should be handled carefully. In general, today early excision in acute burn care is considered to be the procedure of choice. However, when the breast is involved in the burned areas, especially during adolescence, a more delayed and conservative approach with regard to the nipple areola complex (NAC) has been shown to be beneficial for the later breast development [2]. The extent of breast tissue in young children is often underestimated while the depth of the burn injury is easily overestimated. The rudimentary breast lies directly underneath the NAC in the subcutis, is 4–8 mm of size, and should be preserved during eschar excision whenever possible. Even if the NAC is lost due to the burn injury, the immature breast is often not damaged and should be carefully preserved. The regeneration of nipple-like structures from proliferating epithelium of the milk ducts in children with third-degree burns of the NAC has also been documented [2–6]. When general deep fascial excision of the anterior chest wall needs to be performed in children, a complete or partial lack of breast development has to be expected.

Compared to patients with congenital pediatric breast anomalies, patients with burn injuries to the breast usually need more procedures to reach a satisfactory reconstructive outcome [7]. Kunert et al. propose the differentiation between scald and burn injuries regarding the surgical procedures in patients with thermal injuries in childhood. They state that scalds result in a deep second-degree to superficial third-degree burn which does not harm the underlying subcutaneously located mammary gland tissue [6].

Consequences of burns of the anterior chest wall with involvement of the breast in all ages are asymmetry, deformity, lack of any breast, lack of projection, lack of NAC, inhibition of normal breast development, unpleasant skin texture, and psychological problems. Problems associated with thermal breast injury are related to direct damage of breast tissue and the overlying skin as well as contracture of scar tissue and development of a restrictive skin envelope. The aim of reconstructive surgery should be:

- To release scar contractions
- To re-establish breast volume and shape
- To reposition and recreate the NAC
- To restore the self-image and confidence of the patient

E. Koellensperger · G. Germann (✉)
ETHIANUM, Clinic for Plastic, Aesthetic and Preventive Medicine at Heidelberg University Hospital, Heidelberg, Germany
e-mail: guenter.germann@urz-uni-heidelberg.de

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_24

Reconstructive procedures depend on:

- The severity of the trauma
- The type and amount of tissue lacking
- The quality of the surrounding soft tissue
- The distribution and amount of burned surface area
- In particular, the age and demands of the patient

However, reconstructive procedures should not be performed until wounds are fully healed and scars are stable and mature.

Simultaneous combined procedures bear the advantage of a high immediate benefit with limited downtime, hospital stay, and anesthesia. However, one needs to address the fact that the definitive outcome of one procedure needs to be anticipated if the following operative step is planned to be processed simultaneously. This implicates a high level of experience with those kinds of procedures. One such example would be NAC reconstruction and contralateral reduction mammaplasty, two procedures that—at least in our opinion—should be planned with a minimum of 6 month in between to allow the opposite breast to reach a stable situation with only minor upcoming changes in shape and position of NAC. Otherwise, the long-term outcome is at risk to be unsatisfactory (Figs. 24.1 and 24.2).

24.2 Scar Release

Scar release is often the first step of breast reconstruction after a burn injury. It should be performed as early as breast development is inhibited in adolescent girls, especially when surrounding healthy tissue is beginning to bulge. Release is also indicated when a significant limitation in the range of motion, unstable wound situations, and functional or subjective discomfort is present. In most pediatric patients, scar release is undertaken between 14 and 16 years. It is recommended to excise all scarred tissue completely and cover the resulting defect with a thick split-thickness skin graft or full-thickness skin graft. If scaring is very severe, it is often necessary to incise scarred skin down to the deep fascia of the chest or abdomen to fully release all inhibiting contractures. When the whole breast is affected from scars, it is recommended to incise 5/8 of the total circumference and to proceed with the incision into unburned areas. An inframammary incision is the most common location for a scar release. However, if scarring involves the whole breast and contractures are located around the breast, supra-, intra-, or intermammary release might be necessary [5, 6, 8, 9].

Depending on the location of the contractures, local or distant flaps may be required to reconstruct the resulting soft tissue deficit in order to achieve the best possible aesthetic outcome.

24.3 Split-Thickness Skin Graft

Split-thickness skin grafts (STSG) have been used not only in primary wound care after excision of burned tissue but also for secondary procedures in combination with scar release.

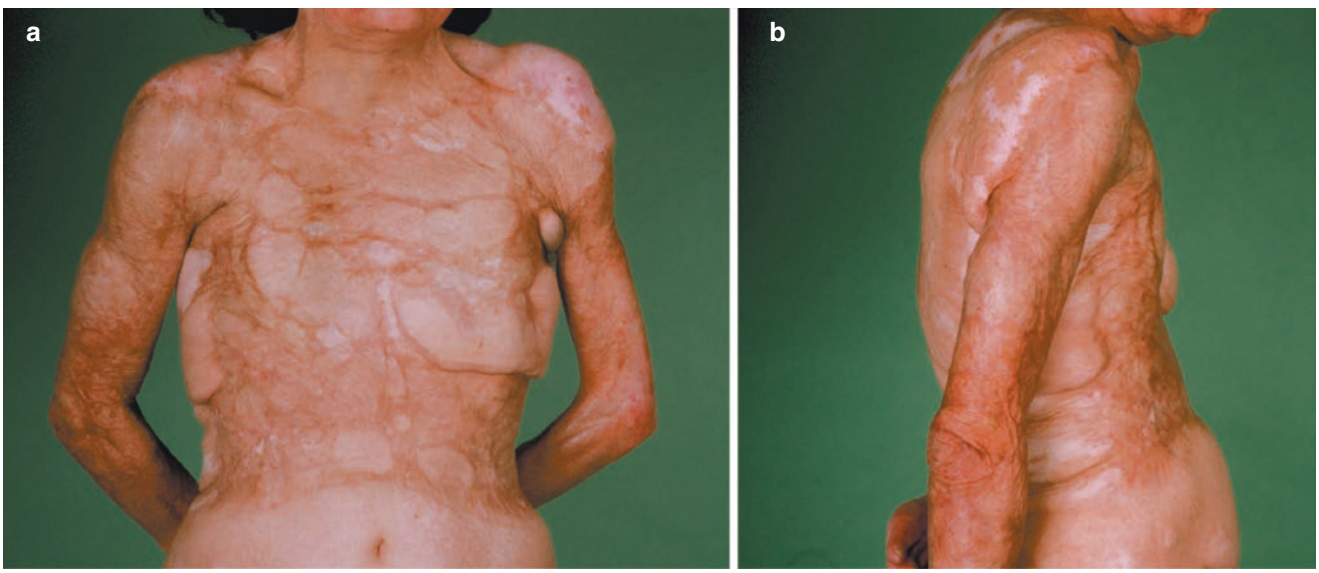


Fig. 24.1 A 35-year-old woman with a deep burn injury of 80% total body surface including total fascial excision of both breasts at the age of 17 (**a** and **b**). Twelve years after the injury, breast volume was reconstructed with a bilateral TRAM flap. Eight months later, the inframammary fold on the left side was lifted with fixing sutures to the chest wall. Nipple reconstruction was performed simultaneously on both sides using a skate flap and inguinal FTSG. In the same procedure, liposuction was performed on the lateral chest wall on both sides. (**a/b**) Patient before breast reconstruction with bilateral TRAM flap. (**c/d**) Patient 7 months after breast reconstruction with bilateral TRAM flap. (**e/f**) Patient 7 days after NAC reconstruction with skate flap, FTSG, and bilateral liposuction on the lateral chest walls

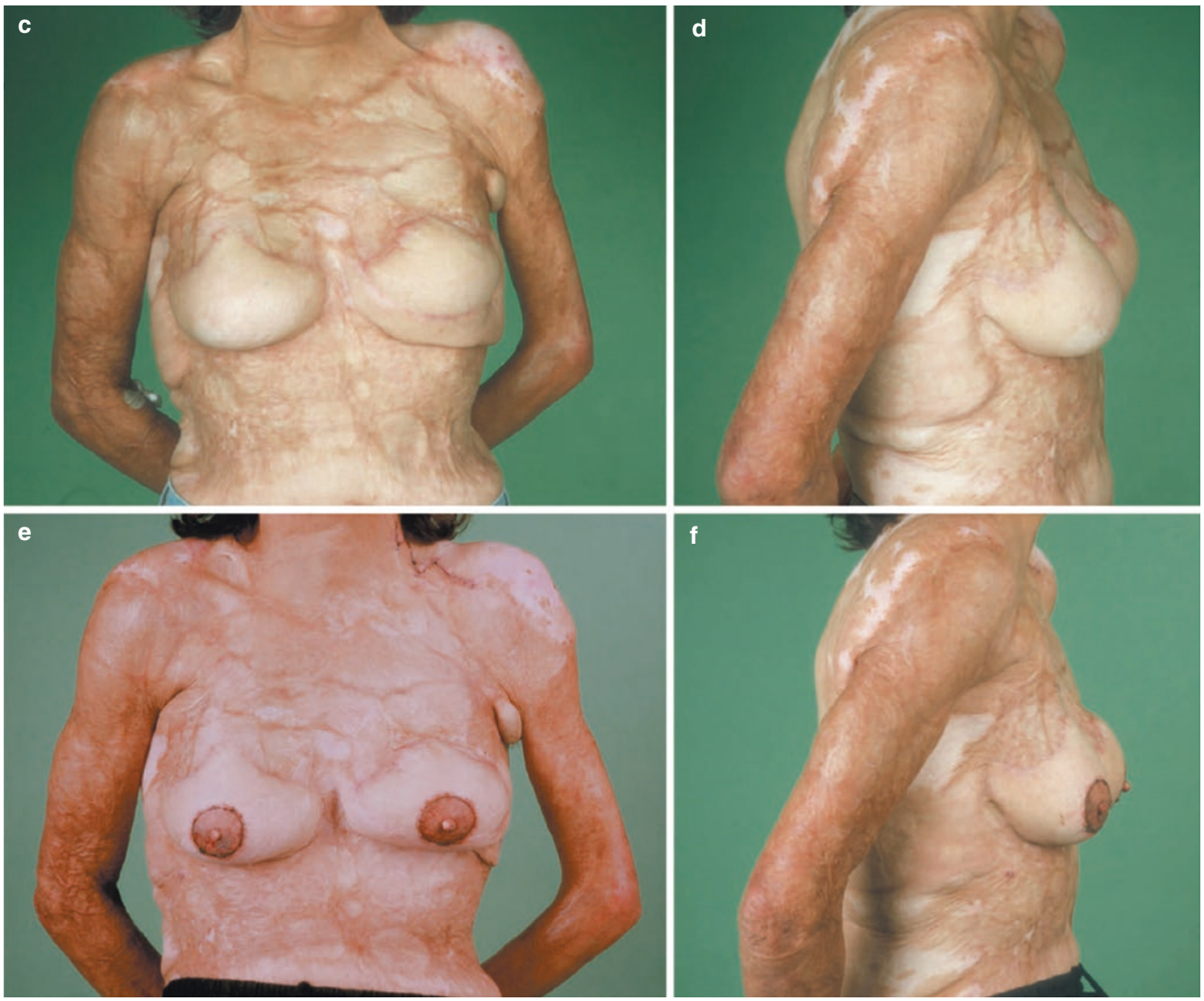


Fig. 24.1 (continued)

Unfortunately STSG have a tendency to contract. If the total burn surface is small enough, non-meshed STSG sheets should be used preferably for coverage of breast and décolleté regions with regard to aesthetic issues. In comparison to STSG mesh grafts, sheets have a better aesthetic outcome creating a more homogenous surface and no visible mesh pattern. Most authors use and recommend STSG with a thickness of 0.016–0.02 mm for best results in burned breasts [9].

24.4 Full-Thickness Skin Grafts

Full-thickness skin grafts (FTSG) are used for the reconstruction of NAC, reconstruction of the inframammary fold after scar release, and resurfacing of burned breast soft tissue [10]. Skin grafts have a tendency to shrink and contract; however, FTSG have a comparatively lower tendency than STSG. Shelley et al. have proposed the use of FTSG from aesthetic procedures, such as abdominoplasty or reduction mammaplasty, for reconstructive purposes in burn patients. Thus donor site morbidity of skin harvesting for FTSG could be minimized with a dual benefit of improved functional and aesthetic outcomes [11]. Mueller et al. have shown a case of breast resurfacing with a full-thickness abdominal skin graft with good results in a patient with no loss of glandular tissue. They propose abdominal skin as a good donor site for breast resurfacing procedures because of similar skin color and texture [12].

24.5 Combination of Split- or Full-Thickness Grafts with Dermal Substitutes (Matriderm®, Integra®)

Integra® is a dermal regeneration template consisting of collagen and chondroitin-6-sulfate. It has been shown to gain a stable vascularization from the wound bed within 28 days if

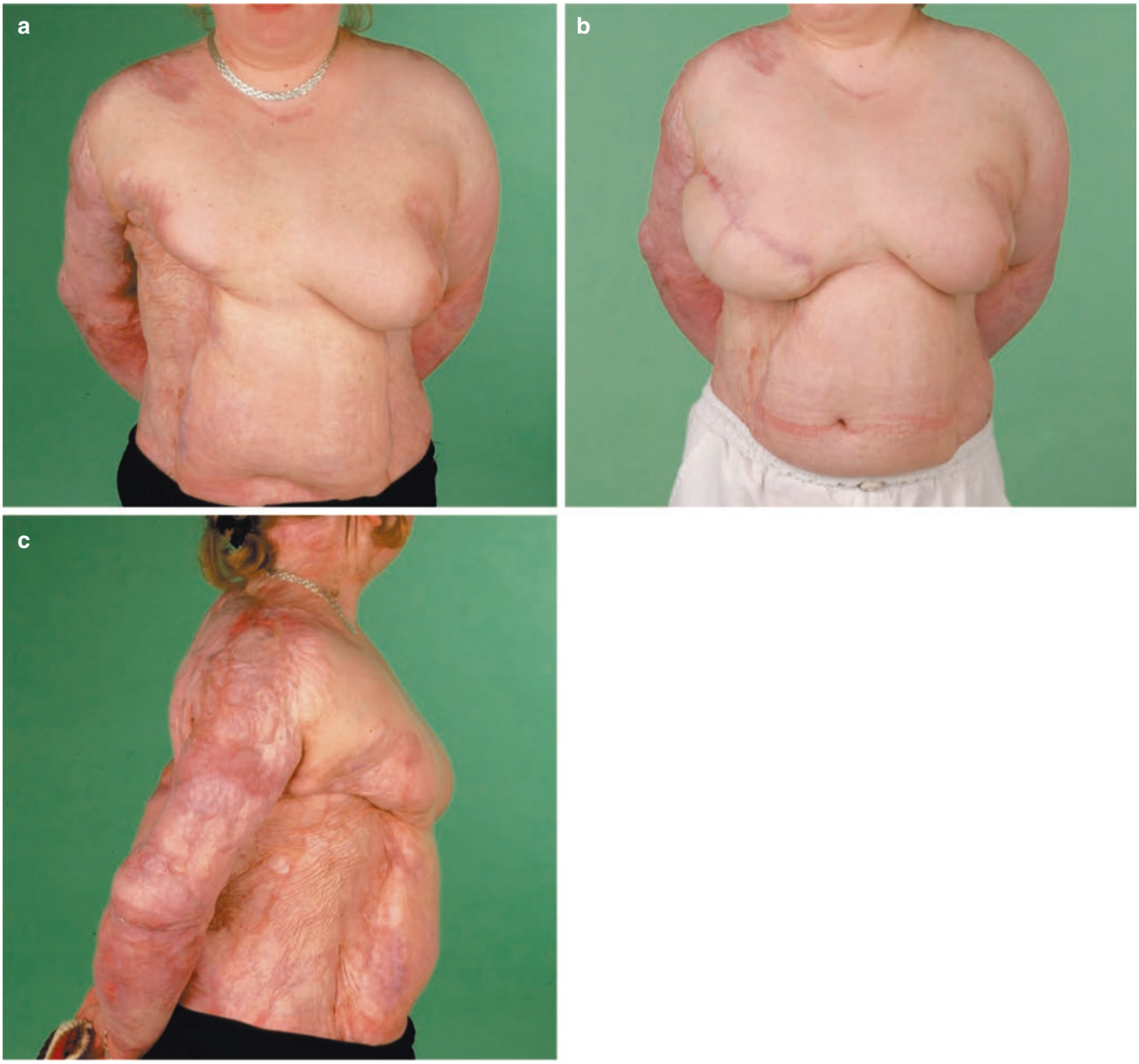


Fig. 24.2 A 22-year-old female presented with a 78% full-thickness burn. Deep fascial excision was performed on the right chest wall with ablatio mammae and coverage with STSG. A free DIEP flap was performed for reconstruction of her right breast 4 years after the injury. The patient was satisfied with the result and did not show up for further reconstructive procedures, such as nipple-areola complex reconstruction. (**a/b**) Patient before breast reconstruction with DIEP flap on the right side. (**c**) Patient 6 weeks after breast reconstruction with DIEP flap on the right side

placed in a well-vascularized environment after meticulous hemostasis. Integra® has been used successfully for the management of breast postburn contractures in combination with split-thickness grafts [13, 14]. The clinical and functional outcome was convincing. When used by Palao et al. for thermal breast injuries in combination with overlying STSG, a statistically significant improvement in the Vancouver scar scale score after 1 year and a high level of satisfaction in treated patients with lasting improvements in breast contour and shape could be demonstrated. No contracture of the skin grafts overlaying Integra® was seen. Integra® was completely replaced by host collagen and elastic fibers within 1 year [15]. Groos et al. have used Integra® in 10 children with a medium of 45% TBSA including breast burns, preferably with unmeshed skin grafts. After 12–45 days, the initially placed Integra® was covered with a 0.15–0.2 mm thin STSG. The final outcome was described as functionally and cosmetically improved [16]. Tsoutsos et al. expanded non-

meshed Integra® combined with a STSG for the coverage of a soft tissue breast defect after excising scars and releasing contractures with insertion of a subpectorally placed expander. After 17 months, no re-contracture or distortion was seen [14]. Clinically, it has been shown that Integra® needs at least 3 weeks to produce a stable neodermis suitable for skin grafting [17].

Integra® and Matriderm®, a non-cross-linked collagen–elastin matrix with bovine collagen type I, III, and V, have been compared in a recent animal study. It has been shown that there is no difference regarding vascularization, building of a neodermis, and graft take between the two matrices. The combined use of both with skin grafts leads to a significantly more and better structured neodermis in comparison to skin grafting alone [17].

To our knowledge, the use of Matriderm® for the reconstruction of burns in the breast area has not yet been published. However, we think that it could be a worthwhile option, as its use in burns demonstrated significant advantages in other delicate regions of the body, such as burned hands and face. Combining split-thickness grafts with Matriderm® leads to a significant improvement of skin elasticity, measured with Vancouver Burn Skin Score, with a consistent survival of applied skin grafts [14, 18–22]. We could show that a one-stage procedure combining Matriderm® and split-thickness skin grafts simultaneously, can be performed safely in regard to skin take [20].

24.6 Local Flaps

24.6.1 Z-plasties

When breast development is normal, and only breast shape or position is disturbed by local band-like contractures, single or multiple Z-plasties are a useful option for scar release [6, 23].

24.6.2 Transposition Flaps

Local flaps are especially used for the reconstruction of the inframammary fold in combination with scar-releasing procedures. Payne et al. have used a Ryan-type thoracic advancement flap. McCauley demonstrated longitudinal abdominal transposition flaps [2, 24]. Hsiao et al. have used a lateral chest rotation flap to reconstruct breast tissue insufficiency [25].

Compared with split-thickness skin grafts, local flaps possess the advantage of a lower tendency for contracture and no need for postoperative splinting to maintain the correction of breast deformity [2, 26].

24.7 Pedicled Flaps

24.7.1 Transverse Rectus Abdominis Muscle (TRAM)

TRAM flaps have been used by several authors for the reconstruction of lacking breast volume not only in burned patients. By using a TRAM flap for breast reconstruction, one gains enough volume and skin to rebuild a totally destroyed breast. However, the known disadvantages and risks, such as instable abdominal walls, herniation, and prolonged postoperative pain, need to be addressed carefully. Furthermore, most young patients lack a sufficient abdominal laxity to easily and safely perform a TRAM flap, and often the abdominal area is also affected by the burn injury and thus not available. Patients of child-bearing age should also not be considered for a TRAM flap as pregnancy can enhance the risk of unwanted abdominal wall side effects [9, 23, 27].

24.7.2 Myocutaneous Latissimus Dorsi Flap (LD)

The pedicled myocutaneous LD flap can be used for the reconstruction of the breasts soft tissue envelope or for mid-size volume deficits. Especially when most of the breast tissue has been destroyed and the opposite breast is rather large, LD flaps almost always lack enough volume to reconstruct a breast size equal to the non-injured normal breast. Therefore, they often need to be combined with a permanent implant [5, 9, 10, 23, 28].

24.8 Free Flaps

24.8.1 Deep Inferior Epigastric Artery Perforator Flap (DIEP)/Superior (SGAP)/Inferior (IGAP) Gluteal Artery Perforator Flap

The use of the free TRAM flap has decreased in recent years. However, in selected cases, it is still a valuable option (case 1); DIEP or SGAP/IGAP flaps in general provide enough volume to restore full breast size in patients who experienced total breast loss. To our knowledge their use for the reconstruction of burned breast has not been published before. Here we show for the first time one case (see case 2) of breast reconstruction with a free DIEP flap. We think that the use of these free flaps for this indication will become more and more popular, regarding their excellent outcome in other patients with total loss of breast volume.

24.8.2 Anterior Lateral Thigh Flap

Tsai et al. have published the use of a free ALT flap, split in to two equal skin paddles for the reconstruction of breast volume in one patient [8]. It could also be a possible option to use super-thin cutaneous ALT flaps to restore a soft tissue envelope over adequate existing breast tissue.

24.9 Nipple-Areola Complex Reconstruction

Nipple-areola complex (NAC) reconstruction is the final step of breast reconstruction and a very important issue to restore patients' self-confidence and feeling of femininity. It includes restoration of the nipple and the surrounding areola with adequate projection and pigmentation. There are multiple different methods for NAC reconstruction; however, they all have in common that they should not be performed unless the newly formed breast has fully settled to its final shape and position. Such prior procedures mandating an adequate waiting time, usually 6–12 months, may include scar release, reconstruction of the inframammary fold, and augmentation or reduction mammaplasty.

Skin for NAC reconstruction can be obtained from the opposite NAC, by excising the outer half circumferentially as full-thickness skin graft or full nipple and areola sharing, or from the inner upper portion of the thigh or the labia majores. Best match in texture and pigmentation is achieved by transplanting parts of the opposite NAC. Further options are local flaps or transplants from the toe pulps, ear lobes, or rib cartilage. The latter can be used especially when free flaps are used for the reconstruction of the breast mound, and the anastomosis is performed at the internal mammary artery which includes partial resection of rib cartilage. After trimming, it can be banked near the wound borders underneath the flap for approximately 6 months until tissue settling is finished, and NAC reconstruction is performed with the banked cartilage [5, 9, 28, 29].

AlloDerm® has been used in non-burned patients to improve long-term nipple projection in nipple reconstruction with local flaps with promising results. AlloDerm® was rolled together and placed in the center of the new nipple [30–32]. Nipple reconstruction in burns with AlloDerm® has not yet been published to our knowledge. However, it could be a useful and supportive alternative.

For simple repositioning of a distorted but existing NAC in breast burn injuries, Mohmand et al. have shown a double U-plasty technique with good results [33]. The ductal system is thought to be preserved with this technique.

24.9.1 Tattoo

Tattooing for aesthetic medical purposes is also named "micropigmentation" or "dermatography." The micropigments are placed between superficial and middle dermal layers and are initially fixed intracellular and gradually become extracellular [34]. After NAC reconstruction with local skin or skin transplants, tattooing is often required to achieve a satisfactory pigmentation matching the opposite NAC. It should be performed with a delay of at least 8 weeks after nipple reconstruction [9, 35].

24.9.2 Local Flaps

Local flaps for nipple restoration usually work well in breast reconstruction patients without previous burn injury. With scared burned skin, however, dermal blood supply is restricted, making local flaps more unreliable and difficult.

Bunchman et al. proposed the double-bubble technique in 1974, using two concentric incisional circles within the scared skin, each one sutured with the base to the surface of the outer one, followed by epithelializing and tattooing [35]. Pensler et al. compared a local flap (quadropod flap) with earlobe grafts, the double-bubble technique, split-thickness skin grafts, and tattooing from the opposite areola. They found that the quadropod flap and the earlobe grafts give comparable results concerning projection; however, the quadropod flap had a lower donor-site morbidity. Tattooing gave poor long-term results with fading pigments. With split-thickness grafts from the contralateral areola, severe hypopigmentation or hyperpigmentation associated with asymmetry was observed. The authors recommend employing local flaps for nipple reconstruction if there is adequate vascularity of the surrounding soft tissue and full-thickness skin grafts for areola reconstruction [36].

Motamed and Davami have used a variation of the modified star flap for the reconstruction of the NAC in seven females with breast burns in childhood [37]. Besides the central portion of the new nipple, all flap parts are deepithelialized and buried to increase central nipple projection. This reduces the risk of skin necrosis and the amount of necessary sutures, which itself can compromise skin blood supply. With this technique, a medium nipple projection of 5 ± 1 mm after a medium follow-up period of 10 ± 3 month is achieved. Complications such as hematoma, necrosis, or discolorations have not been reported.

24.10 Tissue Expanders

In breast reconstruction after a burn injury with the loss or lack of glandular tissue, expanders are often placed under the pectoralis muscle to pre-expand the overlying soft tissue before insertion of permanent implants [7, 10]. Tissue expanders can also be inserted in a submammary position and prior to scar and contracture release with split-thickness skin grafting. The expander is exchanged for a permanent implant 1–3 month after being fully inflated. Approximately 200 cc of overexpansion is recommended [23, 38, 39]. Tissue expanders have also been used underneath STSG prior to insertion of a permanent prosthesis [26] and with an overlying Integra® dermal template with good results, as mentioned above [14].

Care needs to be taken when implanting expanders underneath previously burned or scarred tissue [25]. Following such procedures, general complications include skin necrosis or ulceration, exposure of the expander or injection port, wound healing problems, infections and capsule formation, or even chest wall deformations [9, 10]. However, in a breast-specific study, Levi et al. showed that tissue expanders used to reconstruct burned breasts do not have a higher complication rate than those used to reconstruct congenital breast deformities. Furthermore, endoscopic placement of tissue expanders resulted in a significantly lower operative time, significantly less complications, and a significantly decreased time needed for full expansion [40].

Internal pressure due to tissue expanders or prostheses together with external pressure due to custom-made compression garment can sufficiently soften existing scars and prevent further hypertrophic scarring in the breast area [25, 38].

24.11 Reduction and Augmentation Mammaplasty/Mastopexy

Due to loss of breast volume or lack of elasticity of the skin envelope in the burned breast, asymmetry compared to the opposite breast can result. To achieve breast symmetry, reduction mammaplasty or mastopexy at the burned or contralateral breast may be indicated. Furthermore, women with burned breast can also suffer from hyperplastic breasts or macromastia requesting reduction mammaplasty.

Prior to reduction mammaplasty, full scar release should be performed and full development of the breast should be allowed. The ideal reduction mammaplasty technique addresses volume and shape asymmetries, scar areas, and skin contractures as well as a possible NAC distortion.

Payne et al. demonstrated the use of a Lejour-type reduction technique with a nearly vertical skin resection pattern in a burned breast with severe ptosis, contracting inferior scars, and inferiorly dislocated NAC. The NAC was transposed superiorly with a superior parenchymal pedicle [24]. Hunter et al. favored a one-stage procedure for the correction of a post-burn superior pole scar contracture and simultaneous reduction mammaplasty in a patient with hyperplastic breasts [41]. They used a combination of a rotational glanduloplasty with NAC transposition and a contralateral superior pedicle-based reduction mammaplasty. In this case, however, a positive aesthetic outcome of the resulting scars is questionable, especially regarding possible alternative treatment options, such as a conventional reduction mammaplasty.

El-Khatib showed the reliability of an inferior pedicle in reduction mammaplasty in hyperplastic burned breasts [42]. The inferior dermal pedicle was placed in scar tissue but nevertheless showed good blood supply. The author concludes that the use of an inferior pedicle is the best technique for the reduction of hyperplastic burned breasts with a very low NAC.

Thai et al. have documented a series of six patients with burns to the breast in early childhood and consecutive split-thickness skin grafting. Ten reduction mammaplasties were safely performed in these patients with hyperplastic or asymmetric breasts after breast burn. An inferior pedicle technique with limited undermining is recommended by the authors to avoid problems with skin blood supply [43].

Hsiao et al. and Ozgur et al. propose the simultaneous correction of functional postburn scar release procedures and aesthetically indicated augmentation mammaplasty by using the excess skin as FTSG for scar release [23, 25]. Hsiao et al. state that implants should be placed under the pectoralis muscle to reduce the risk of capsular contraction and decrease palpability and visibility of the implant.

Ozgur et al. experience skin necrosis after insertion of subglandular and submuscular placed permanent inplants [23]. He recommends the solitary use of inplants only if suitable skin coverage is available.

Burned breasts in which the soft tissue envelope has not been fully restored often lack the natural developing ptosis. Therefore, mastopexy of the contralateral breast might be necessary in unilateral breast burn injuries when the contralateral breast is at least moderately ptotic [1].

24.12 Conclusion

Burn injury to the anterior chest wall can cause contracting and hypertrophic scarring, breast deformity and asymmetry, lack of breast tissue, distortion or lack of nipple areola com-

plex, and thus functional, aesthetic, and psychosocial problems. Long-term follow-up and surveillance of patients with breast burns is required to achieve the best possible outcome and address all rising problems at an adequate point in time. Correction of these problems in general requires multiple serial procedures that have to be cautiously fitted into a reliable timetable.

Take Home Message

1. Breast reconstruction starts with breast saving in acute burn care. Precaution should be taken with excision of eschar in the area of the breast and the NAC in children and adolescents.
2. Wounds should be closed and scars be allowed to mature before further reconstructive procedures are undertaken.
3. Wearing a custom-made compression garment until scars are mature is essential for optimal outcome and can, in part, prevent invasive procedures.
4. Scar release should be performed extensively and as soon as breast development is inhibited or breast deformity is induced.
5. Reconstruction of breast volume can be achieved with local, pedicled, or free flaps as well as with permanent implants, depending on the amount of lacking volume, the quality of the surrounding tissue, available donor sites, and patients' desires.
6. Contralateral and ipsilateral reduction or augmentation mammaplasty, contralateral mastopexy, and balancing procedures may be necessary to achieve aesthetically pleasing results.
7. Reconstruction of the nipple-areola complex should not be performed until the breast has fully developed and prior reconstructive steps have achieved a stable long-term result.
8. Long-term follow-up is necessary with all burn patients, especially in females with breast burns, due to life-long changes in breast shape.

References

1. McCauley RL. Reconstruction of the trunk and genitalia. In: Herndon DN, editor. Total burn care. 2nd ed. Philadelphia: W. B. Saunders; 2002. p. 707–10.
2. McCauley RL, et al. Longitudinal assessment of breast development in adolescent female patients with burns involving the nipple-areolar complex. Plast Reconstr Surg. 1989;83(4):676–80.
3. al-Qattan MM, Zuker RM. Management of acute burns of the female pediatric breast: delayed tangential excision versus spontaneous eschar separation. Ann Plast Surg. 1994;33(1):66–7.
4. Foley P, et al. Breast burns are not benign: long-term outcomes of burns to the breast in pre-pubertal girls. Burns. 2008;34(3):412–7.
5. Neale HW, et al. Breast reconstruction in the burned adolescent female (an 11-year, 157 patient experience). Plast Reconstr Surg. 1982;70(6):718–24.
6. Kunert P, Schneider W, Flory J. Principles and procedures in female breast reconstruction in the young child's burn injury. Aesthetic Plast Surg. 1988;12(2):101–6.
7. Sadove AM, van Aalst JA. Congenital and acquired pediatric breast anomalies: a review of 20 years' experience. Plast Reconstr Surg. 2005;115(4):1039–50.
8. Tsai FC, et al. Free split-cutaneous perforator flaps procured using a three-dimensional harvest technique for the reconstruction of post-burn contracture defects. Plast Reconstr Surg. 2004;113(1):185–93; discussion 194–195.
9. Ogilvie MP, Panthaki ZJ. Burns of the developing breast. J Craniofac Surg. 2008;19(4):1030–3.
10. Loss M, et al. The burned female breast: a report on four cases. Burns. 2002;28(6):601–5.
11. Shelley OP, et al. Dual benefit procedures: combining aesthetic surgery with burn reconstruction. Burns. 2006;32(8):1022–7.
12. Mueller M, Boorman JG. Post-burn breast resurfacing using an abdominal full-thickness skin graft. Br J Plast Surg. 2002;55(2):148–50.
13. Shariff Z, Rawlins JM, Austin O. Burned breast reconstruction by expanded artificial dermal substitute. J Burn Care Res. 2007;28(6):929.
14. Tsoutsos D, et al. Burned breast reconstruction by expanded artificial dermal substitute. J Burn Care Res. 2007;28(3):530–2.
15. Palao R, Gomez P, Huguet P. Burned breast reconstructive surgery with Integra dermal regeneration template. Br J Plast Surg. 2003;56(3):252–9.
16. Groos N, et al. Use of an artificial dermis (Integra) for the reconstruction of extensive burn scars in children. About 22 grafts. Eur J Pediatr Surg. 2005;15(3):187–92.
17. Schneider J, et al. Matriderm versus Integra: a comparative experimental study. Burns. 2009;35(1):51–7.
18. Haslik W, et al. Management of full-thickness skin defects in the hand and wrist region: first long-term experiences with the dermal matrix Matriderm. J Plast Reconstr Aesthet Surg. 2010;63(2):360–4.
19. Kolokythas P, et al. Dermal substitute with the collagen-elastin matrix Matriderm in burn injuries: a comprehensive review. Handchir Mikrochir Plast Chir. 2008;40(6):367–71.
20. Ryssel H, et al. The use of MatriDerm in early excision and simultaneous autologous skin grafting in burns—a pilot study. Burns. 2008;34(1):93–7.
21. Boyce A, et al. The use of Matriderm in the management of an exposed Achilles tendon secondary to a burns injury. J Plast Reconstr Aesthet Surg. 2010;63(2):e206–7.
22. Atherton DD, et al. Early excision and application of matriderm with simultaneous autologous skin grafting in facial burns. Plast Reconstr Surg. 2010;125(2):60e–1e.
23. Ozgur F, et al. Reconstruction of postburn breast deformities. Burns. 1992;18(6):504–9.
24. Payne CE, Malata CM. Correction of postburn breast asymmetry using the LeJour-type mammaplasty technique. Plast Reconstr Surg. 2003;111(2):805–9.
25. Hsiao YC, et al. Are augmentation mammaplasty and reconstruction of the burned breast collateral lines? Experience in performing simultaneous reconstructive and aesthetic surgery. Burns. 2009;35(1):130–6.
26. Guan WX, Jin YT, Cao HP. Reconstruction of post-burn female breast deformity. Ann Plast Surg. 1988;21(1):65–9.
27. Psillakis JM, Woisky R. Burned breast: treatment with a transverse rectus abdominis island musculocutaneous flap. Ann Plast Surg. 1985;14(5):437–42.

28. Bishop JB, Fisher J, Bostwick J III. The burned female breast. Ann Plast Surg. 1980;4(1):25–30.
29. Heitland A, Markowicz M, Koellensperger E. Long-term nipple shrinkage following augmentation by an autologous rib cartilage transplant in free DIEP-flaps. J Plast Reconstr Aesthet Surg. 2006;59(10):1063–7.
30. Chen WF, Barounis D, Kalimuthu R. A novel cost-saving approach to the use of acellular dermal matrix (AlloDerm) in postmastectomy breast and nipple reconstructions. Plast Reconstr Surg. 2010;125(2):479–81.
31. Holton LH, et al. Improving long-term projection in nipple reconstruction using human acellular dermal matrix—an animal model. Ann Plast Surg. 2005;55(3):304–9.
32. Garramone CE, Lam B. Use of AlloDerm in primary nipple reconstruction to improve long-term nipple projection. Plast Reconstr Surg. 2007;119(6):1663–8.
33. Mohmand H, Naasan A. Double U-plasty for correction of geometric malposition of the nipple-areola complex. Plast Reconstr Surg. 2002;109(6):2019–22.
34. Garg G, Thami GP. Micropigmentation: tattooing for medical purposes. Dermatol Surg. 2005;31(8 Pt 1):928–31; discussion 931.
35. Bunchman HH II, et al. Nipple and areola reconstruction in the burned breast. The “double bubble” technique. Plast Reconstr Surg. 1974;54(5):531–6.
36. Pensler JM, Haab RL, Parry SW. Reconstruction of the burned nipple-areola complex. Plast Reconstr Surg. 1986;78(4):480–5.
37. Motamed S, Davami B. Postburn reconstruction of nipple-areola complex. Burns. 2005;31(8):1020–4.
38. Versaci AD, Balkovich ME, Goldstein SA. Breast reconstruction by tissue expansion for congenital and burn deformities. Ann Plast Surg. 1986;16(1):20–31.
39. Slator RC, Wilson GR, Sharpe DT. Postburn breast reconstruction: tissue expansion prior to contracture release. Plast Reconstr Surg. 1992;90(4):668–71; discussion 672–674.
40. Levi B, Brown DL, Cederna PS. A comparative analysis of tissue expander reconstruction of burned and unburned chest and breast using endoscopic and open techniques. Plast Reconstr Surg. 2010;125(2):547–56.
41. Hunter JE, Gilbert PM, Dheansa BS. Correction of postburn superior pole breast deformity and macro-mastia—a novel approach. Burns. 2009;35(5):746–9.
42. El-Khatib HA. Reliability of inferior pedicle reduction mammaplasty in burned oversized breasts. Plast Reconstr Surg. 1999;103(3):869–73.
43. Thai KN, et al. Reduction mammaplasty in postburn breasts. Plast Reconstr Surg. 1999;103(7):1882–6.

Reconstruction of Burn Deformities of the Lower Extremity

25

Christian Ottomann and Bernd Hartmann

25.1 Introduction

In addition to reconstructive surgery to restore form, the main goal of reconstructive burn surgery is to reintegrate the patient into professional and social life [1]. Although the stigmatizing scars which result from burns to the lower extremities can be covered by clothing, functional restrictions are particularly noticeable due to changes in the patient's gait [2]. As a result, the goal of reconstructive surgery on patients who have suffered burn trauma is to both restore the skin's surrounding soft tissue in order to improve form and to restore function. Acute treatment applied to the lower extremity is similar to that applied to the body's remaining surface, with the exception that the exposed tendons and bones in the area of the tibia and foot are only protected by extremely thin soft skin tissue. Problems in reconstructing the skin's soft tissue often already arise during acute treatment, and they often result in secondary healing and subsequent scarring [3]. As a result, post-burn contractures and unstable scars occur with some frequency on the lower extremities [4]. Unfortunately, a post-burn contracture still does not only result from the trauma which causes the tissue damage but also—particularly in elderly patients—as a result of immobilizing the area within the scope of providing initial treatment. As is the case in the entire field of plastic reconstructive surgery, reconstruction of the burned extremity should be oriented along the reconstructive ladder.

C. Ottomann (✉)
Plastische Chirurgie, Handchirurgie, Intensiveinheit für Schwerbrandverletzte, Universitätsklinikum Schleswig-Holstein Campus Lübeck, Lübeck, Germany
e-mail: Christian.Ottomann@uk-sh.de

B. Hartmann
Zentrum für Schwerbrandverletzte mit Plastischer Chirurgie, Unfallkrankenhaus Berlin, Berlin, Germany

25.2 Reconstructive Ladder Stage 1: Z-Plasty

The Z-plasty technique represents a form of plastic surgery in which two triangular skin flaps across from each other are mobilized. By rotating these flaps, tension is reduced along the central limb. This technique makes use of the area's width, which means that sufficient tissue must be available on each side of the scar. If more length is needed, or if the available tissue elasticity in the lateral skin areas is not sufficient for a single Z-plasty, several small z-shaped incisions can be strung together (Figs. 25.1 and 25.2). Necrosis in the tips of the flaps, which occurs in small flaps whose angles are too acute, and old scars running perpendicular to the base of the flap, which have a negative effect on blood circulation, represent the primary complications in this case. In addition to the actual Z-plasty technique, there are also other modified versions of the flap triangles which can be selected in special cases, for example incisions with the opposite alignment (such as the butterfly or jumping man) [5].

25.3 Reconstructive Ladder Stage 2: Skin Graft Transplantation

Reconstruction of an excision scar is carried out using a skin graft transplantation. Healthy subcutaneous fatty tissue, uninjured peritendineum, healthy muscle fascia, or healthy muscle tissue are suitable for receiving a skin graft (Fig. 25.3). Debrided granulation tissue or tissue conditioned with an artificial dermal substitute can also serve as the recipient site. Free skin grafts differ in their thickness, and thick split-skin or full-thickness skin is suitable for scar reconstruction (Fig. 25.4). The individual grafts all have advantages and disadvantages, both as they pertain to the donor site and their characteristics at the recipient site. With thick split-skin grafts, one must take factors into consideration ranging from poor reepithelialization of the donor site with the possibility of subsequent scarring to the possibility of keloid scarring. In

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_25

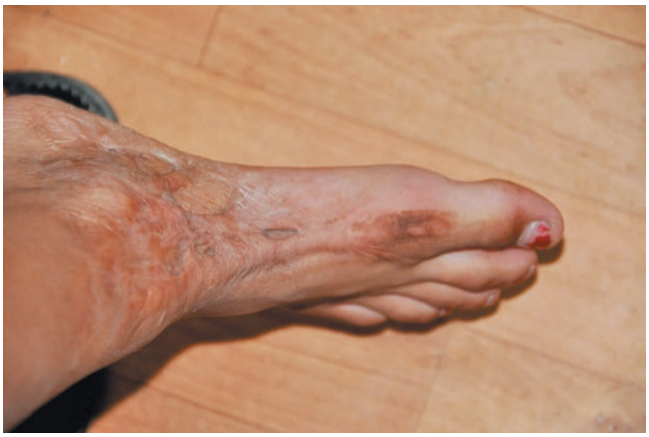


Fig. 25.1 Post-burn contracture on the dorsum of the right foot with consecutive restrictions to mobility

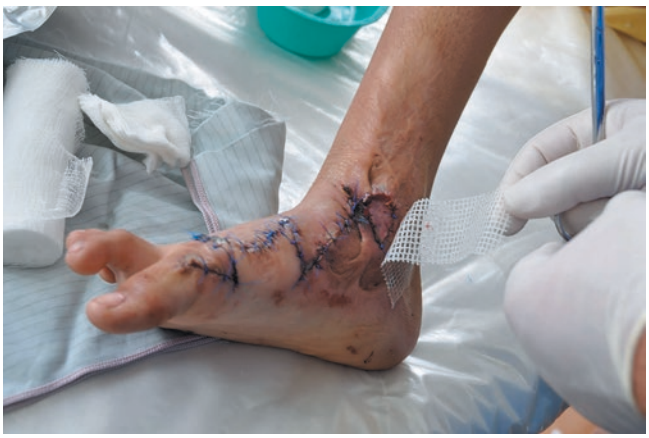


Fig. 25.2 Result after scar adhesiolysis and Z-plasty

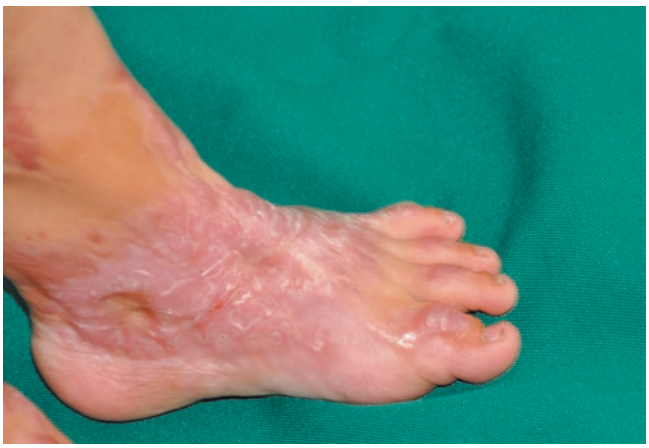


Fig. 25.3 Scarring on the dorsum of the left foot after a scald

addition, the area of full-thickness skin which can be used as donor tissue is limited. At the recipient site, free skin grafts heal better the thinner they are; however the thickness of the layer of skin used corresponds with the desired result. A sufficient dermal layer must be used, particularly when grafting on the soles of the feet, since a three-dimensional network of

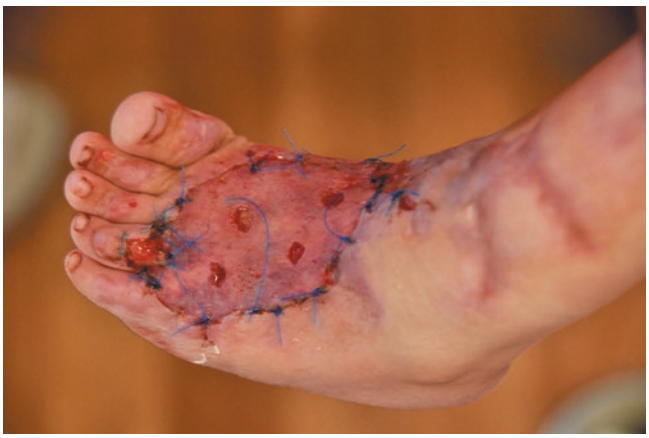


Fig. 25.4 Result after scar excision and full-thickness skin graft

fine fibroelastic tendons, which form a multitude of small cushioning elements, pervades the plantar fat pad. This unique anatomical configuration makes the sole of the foot the perfect shock absorber while walking. Preserving this tissue—particularly since this area of the foot often exhibits repeated bruising after suffering a burn—represents an important reconstructive goal. In this case, one must always consider the use of skin grafts. Another factor which must be noted is the tendency of free skin grafts to shrink. For example, thick split-skin grafts can shrink by up to 30%. In addition, artificial dermal substitutes are available for use in modern reconstructive treatment. The advantages lie in the reduction in donor morbidity from full-thickness skin grafts and the benefits from their wide availability in comparison with full-thickness skin grafts. As a result of the graft, improved dermal regeneration is achieved, which reduces the formation of new scar tissue [6]. Dermal substitutes promote the formation of a vascularized neodermis, which can be covered with an extremely thin autologous epidermal split-skin graft or with cultivated keratinocytes after 14–21 days [7].

25.4 Reconstructive Ladder Stage 3: Pedicle Flaps

Selecting the skin flap to use in reconstructive surgery on the lower extremities is done according to different principles than for the upper extremities. In the upper extremities, a large portion of all muscles are needed to ensure that the arms and hands can function sufficiently, and removing a single muscle can cause a significant loss of function in this area. In contrast, the lower extremities have a number of different muscles which all have the same function. For example, the four individual muscles which form the quadriceps femoris are responsible for extending the knee joint. Using one of these individual muscles as a graft will not affect the active extension of the knee joint. Based on the same principle, the individual muscles which form the hamstring or those used for dorsiflexion or plantar flexion can also be used. The following is a list of flaps which are used most often.

25.4.1 Tensor Fascia Lata Flap (TFL)

The tensor fascia lata flap is located in the area of the lateral circumflex femoral artery. It is comprised of a muscular and fascial portion. It can measure up to 15 cm wide and up to 40 cm long. Vascularization of the distal portion can sometimes be problematic but can be improved through bilateral elevation. This flap is particularly suited to reconstructive procedures in the upper third of the thigh. The TFL flap can also be used as a free microsurgical flap or as a perforator flap [8].

25.4.2 Anterolateral Thigh Flap (ALT)

The ALT is a flap with a relatively constant vascular supply. It can be harvested as a myocutaneous or perforator flap. It is mainly indicated for use with defects in the upper and middle third of the thigh. In addition, the ALT can also see application as a free microsurgical flap, and in this case can also be used as a myocutaneous or perforator flap [9].

25.4.3 Gracilis Flap

The myocutaneous gracilis flap is a thin flap for defects in the upper third of the thigh. It can be up 24 cm long, and this length can be extended to 32 cm by including the tendon. Its width is limited to 6–8 cm. This graft exhibits very constant and secure vascularization. A further benefit is that with this graft, primary closure is usually feasible [10].

25.4.4 Vastus Lateralis Flap

The vastus lateralis flap, as part of the quadriceps femoris, is supplied by numerous vascular pedicles which primarily stem from the profunda femoris artery. It is vascularized proximally by one or two branches of the lateral circumflex femoral artery, the middle third is supplied by the perforating arteries of the profunda femoris, and the distal third receives branches from the popliteal artery. The two branches of the lateral circumflex femoral artery are sufficient to supply the entire muscle. Defects in the proximal section of the thigh, particularly with unstable scars in the area of the trochanter, are an indication for the use of the vastus lateralis flap in reconstructive surgery for burns to the lower extremity [11].

25.4.5 Soleus Muscle Flap

Soleus muscle flaps are particularly suited for use in the reconstruction of lower leg defects. This muscle is located in the superficial posterior compartment of the leg. The muscle is triangular, and its length differs from person to person, which is an important factor as it pertains to the potential radius of rotation. Secure proximal vascularization is supplied by a main branch of the tibialis posterior artery, which allows it to be mobilized at its isolated proximal vascular pedicles. An indication for its use in the scope of reconstruction of a burned lower extremity is soft tissue reconstruction in the middle third of the lower leg, especially if the tibial ridge is exposed [12].

25.4.6 Gastrocnemius Muscle Flap

The gastrocnemius muscle has a medial and a lateral head and is supplied by the sural arteries, which arise from the popliteal artery. Each head can be harvested individually at its proximal vascular pedicle (Figs. 25.5 and 25.6). This flap is particularly suited to reconstruction of the knee joint and the proximal third of the lower leg [13].

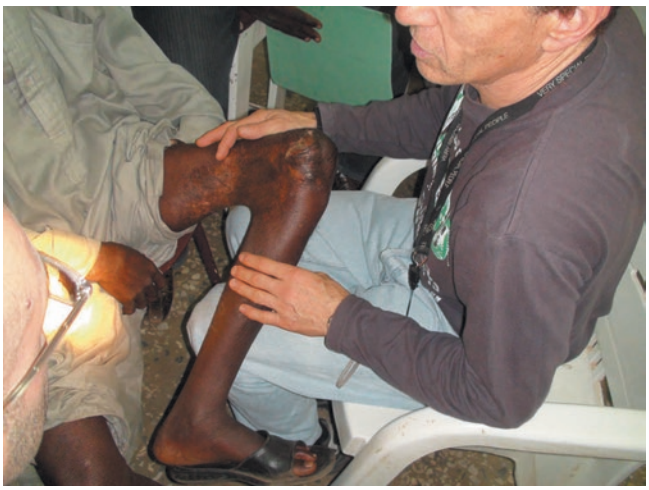


Fig. 25.5 Severe contracture on the inside of left knee after III° burn trauma

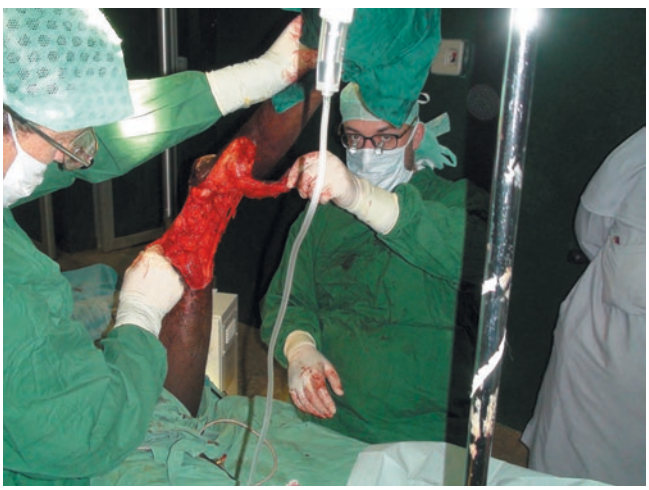


Fig. 25.6 Intraoperative contracture release and reconstruction with a rotation flap

25.4.7 Saphenous Flap

The saphenous flap is a fasciocutaneous flap that is harvested from the medial area of the calf. The skin of the calf is supplied by branches of the great saphenous vein, which runs along the saphenous nerve [14].

25.4.8 Sural Flap

The distal sural pedicle flap is supplied by the sural arteries. It is a relatively thin flap and is primarily used in the area around the ankle, Achilles tendon, and heel. The donor site defect usually needs to be covered with a split-skin graft. In certain cases, a bilateral approach is required which calls for modifying the primary flap by cutting it in advance [15].

25.4.9 Dorsalis Pedis Flap

The dorsalis pedis flap is a neurovascular flap, which can also be used as a free flap. It is mainly supplied by the dorsalis pedis artery, which is a continuation of the anterior tibial artery. The tendons of the extensor hallucis longus muscle serve as a point of reference and run medial to the artery, while the tendons of the extensor digitorum muscle run lateral to the artery. In the proximal area, the artery perforates plantar, anastomosing with the plantar arch. Harvesting the flap is extremely difficult. An indication for the use of this flap is if reconstruction is necessary in the area of the distal third of the lower leg as well as the foot [16].

25.5 Reconstructive Ladder Stage 4: Free Flaps

Free microsurgical flaps are indicated especially for use in reconstruction of burned extremities, since due to the subsequent scarring after a burn trauma, adequate local or pedicle flaps are not available in this area [17].

25.5.1 Latissimus Dorsi Flap

Due to its flap volume and the fact that it can be used anywhere, the latissimus dorsi flap is one of the most important. It can be elevated as a myocutaneous or osteocutaneous flap. In addition, a functional reconstruction can also be carried out at the same time, for example using a muscle transposition flap from the posterior tibialis muscle. At the same time, the muscle flap can also serve as a free neurovascular flap for restoring motor function. This allows it to be used to cover defects and to restore the function of the quadriceps femoris [18].

25.5.2 Scapular and Parascapular Flap

The scapular flap is adipocutaneous flap which is fed by the circumflex scapular artery. Primary closure can usually be used on the donor site defect. The flap is indicated for large defects in the entire lower leg and ankle region. In case of extremely large defects, it can be combined with a latissimus dorsi flap [19].

25.5.3 Lateral Arm Flap

The lateral upper arm flap is a septocutaneous flap. It is supplied by the posterior radial collateral artery and the deep brachial artery. Its benefit lies in the consistent neurovascular pedicle, which allows it to be transplanted as a sensitive flap [20].

25.5.4 Radial Artery Flap

The fasciocutaneous radial artery flap is particularly well suited to reconstruction in the area of the ankle and/or Achilles tendon, as well as the heel and dorsum of the foot (Fig. 25.7). In addition, the flap can also be used for limited defects in the area of the patella. The preoperative Allen Test is obligatory. A significant drawback to this flap is the obvious donor site [21].

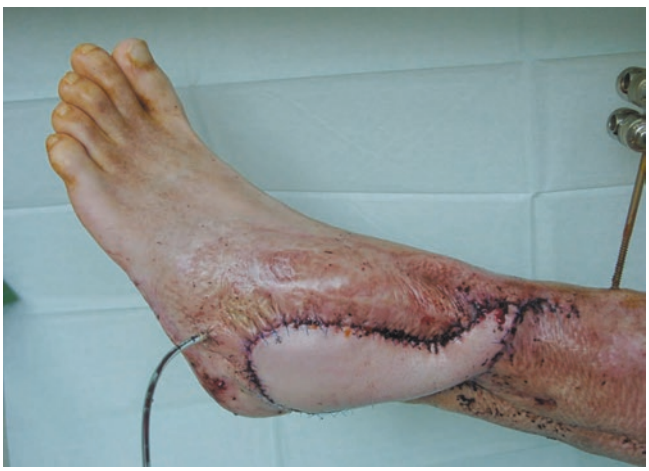


Fig. 25.7 Result after free flap reconstruction with an unstable scar on the left upper ankle joint

25.6 Reconstructive Ladder Stage 5: Perforator Flap

As a modern variation of free microsurgical reconstruction, all musculocutaneous and adipocutaneous flaps can be elevated as perforator flaps. In primary patients with severe burn wounds, a healthy island of skin is often not available, which means the ability to harvest a flap is limited. Using this technique, however, defects in all areas of the body can be reconstructed with particularly flexible and thin flaps. Perforator flaps are an important advancement in reconstructive surgery for patients with severe burn injuries, especially from an aesthetic standpoint [22].

25.7 Discussion

Platt et al. report that 3.6% of all their burn victims who receive acute treatment in an inpatient setting require a free flap reconstruction. Figures on the percentage of patients requiring free flaps solely in the scope of reconstructive surgery on the lower extremity are not available. Reconstruction of burned extremities represents a particular challenge to reconstructive surgeons, since they must cover defects of various sizes and depths. Correction of burn scar contractures for the purpose of restoring function is the primary indication for secondary reconstructive surgery, as well as treating unstable scars and scar carcinoma resulting in lesions of different sizes. In addition, amputation stumps often need to be stabilized. Soft tissue reconstruction is carried out based on principles set forth in the reconstructive ladder which are adapted to the individual situation, from simple to complex free flap surgery [23]. The skin tissue which borders the defect is often scarred, however, which means that a local or rotation flap often cannot be used within the reconstructive ladder. In order to achieve the goal of restoring form, function, and aesthetics in the best way possible, a number of indications require mastery of the entire microsurgical spectrum. The selection of a free microsurgical flap can also be limited by a scarred donor site, however, which requires the surgeon to use their second or third choice. As a result, when performing reconstructive surgery on a burned lower extremity, the entire spectrum of plastic surgical methods must be considered when selecting the operative procedure, which means that procedures must also be considered which appear obsolete in reconstructive surgery on patients who have not suffered burn injuries. Cross leg flaps and the use of Kirschner wire in the case of an exposed tibial ridge are often successful when other reconstructive procedures have been ruled out [24, 25]. In primary reconstruction of a burned extremity, the distal extremity is the most often affected anatomical area, since the tibial ridge and the foot are only protected by a thin subcutaneous layer, which means tendons and bones are affected and/or are exposed after debridement at above-average rates. In contrast, the proximal extremity of the thigh offers better protection thanks to the soft tissue pad found in this area, which means that reconstructive flap surgery is carried out on the thigh less often. Due to its thin layer of soft tissue, the foot presents significant challenges to reconstruction as it pertains to restoring a sufficient level of function, especially when plantar structures are involved. Flaps used on the foot must be thin, yet still offer a secure sheath for the tendons. A number of authors prefer to use thin fascia flaps, which are then covered with split-skin grafts. These can be wrapped around the extensor tendons using the sandwich technique to create a layer of connective tissue [26]. As an alternative to a thin flap, De Lorenzi et al. describe arterialized venous flaps, which are harvested from along the great saphenous vein [27]. Their reliability as a standard procedure is still open to debate, however, but they represent a viable alternative with a small harvesting defect. Furthermore, adipocutaneous flaps are suitable for use in reconstructive surgery, especially for thin patients, since they offer excellent skin elasticity. As a classical microsurgical flap, the radial or lateral upper arm flaps can be used for small areas, and the scapular and parascapular flaps can be used for larger defects. In reconstructive procedures on the foot, one must generally differentiate between stress-bearing and non-stress-bearing areas. When operating on a stress-bearing area, muscular flaps should be preferred, since these flaps offer stable coverage that can withstand shear stress [28].

Within the scope of primary reconstruction carried out after suffering a burn, flap surgery is conducted earlier on in patients with electrical injuries than those with thermal trauma. In addition to superficial burns, injuries from high-voltage current also cause electricity to flow through deep tissue. The current flows through the path of least resistance, primarily through the body's vasculature, nerves, and muscles (Fig. 25.8). Concealed deep tissue lesions

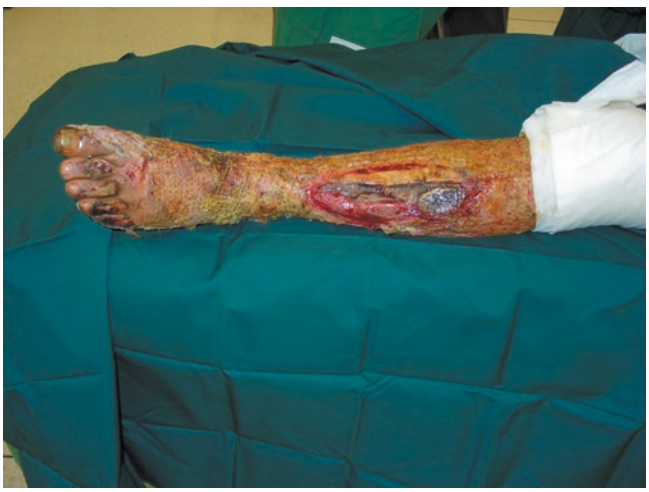


Fig. 25.8 Primary reconstruction necessary after III° high-voltage burn

occur as a result, particularly periosteal lesions in the muscles [29–31]. Radical debridement after an electrical injury also leads to exposure of deeper structures. When dealing with lesions from electrical injuries that require the use of free flaps, the assumption of progressive necrosis exists, meaning that the extent of the tissue damage is first demarcated after several debridements (principle of progressive awareness) [32, 33]. In this context, there is always the danger that even when performing radical debridement, if the reconstructive procedure is carried out too early, necrosis could persist. In these cases, large-size muscular flaps are indicated, as they are better at terminating infections thanks to their vascularization [34]. The latissimus dorsi flap is particularly suited for this purpose, since it can be harvested with a size of up to 26 cm in women and 33 cm in men [35]. For smaller defects which require sufficient vascularization from a muscle, we recommend the microsurgical gracilis flap, which can be harvested with close to zero donor morbidity [36]. If needed, the serratus anterior flap can also be harvested for even smaller defects [37]. When covering defects which involve bone, in some cases a vascularized bone transplant may be required [38]. In particularly severe contractures as a result of a burn to the lower extremity, Bar-Meir et al. describe the combination of using an Ilizarov apparatus and a free flap [39].

Concrete data comparing the complication rate of local, pedicle, or microsurgical flaps used in the scope of secondary reconstruction to those used in reconstruction in the primary stage is not available. Baumeister et al. were able to detect a relationship between the time reconstructive surgery was carried out and the complication rate, however [40]. In their study on reconstruction of burned extremities through transplantation of free flaps in primary reconstructive surgery, they report that 80% of flap losses occurred when the flap surgery was conducted between the fifth and twenty-first day post-trauma. In contrast, flap losses did not occur in elective secondary reconstruction.

25.8 Summary

As a result of the specific anatomical conditions found in the knee, lower leg, and foot (which exhibit a thin soft tissue covering), a thermal trauma to the lower extremity often results in scarred contractures which affect the patient's gait and necessitate secondary reconstruction. When treating a patient with a severely burned lower extremity, functional structures often become exposed in the initial stages after radical debridement, which then require early stage primary reconstruction. Regardless of when reconstructive surgery on the lower extremity is carried out, the reconstructive ladder should be followed. Due to changes to the local area caused by scarring, it is often impossible to use treatment methods which are used on unburned tissue as a standard procedure, which means that modified operative procedures can be successful, as well as operative techniques which would otherwise be viewed as obsolete. Due to these reasons, a reconstructive surgeon should possess knowledge of the entire range of plastic surgical methods, since treating high-grade burn contractures of the lower extremity poses a significant challenge to even the most experienced surgeons.

References

1. Wrigley M, et al. Factors relating to return to work after burn injury. J Burn Care Rehabil. 1995;16(4):444–50.
2. Silverberg R, Lomardo G, Gorga D, et al. Gait variables of patients after lower extremity burn injuries. J Burn Care Rehabil. 2006;21(3):259–67.
3. Barbour JR, Schweppe M. Lower extremity burn reconstruction in the child. J Craniofac Surg. 2008;19(4):976–88.
4. Ezoe K, Yotsuyanagi T, Saito T, et al. A circumferential incision technique to release wide scar contracture. JPRAS. 2009;61(9):1059–64.
5. Ulkur E, Acikel C, et al. Use of rhomboid flap and double z plasty technique in the treatment of chronic postburn contractures. Burns. 2006;32(6):765–9.
6. Wainwright D, et al. Clinical evaluation of an acellular allograft dermal matrix in full-thickness burns. J Burn Care Rehabil. 1996;17(2):124–36.
7. Stern R, Pherson M, Longaker MT. Histologic study of artificial skin used in the treatment of full-thickness thermal injury. J Burn Care Rehabil. 1990;11:7–13.
8. Kimura N, Satoh K, Hosaka Y. Tensor fasciae latae flap. Clin Plast Surg. 2004;30(3):439–46.
9. Wong CH, Wie FC. Anterolateral thigh flap. Head Neck. 1967;32(4):529–40.
10. Redett RJ, Robertson BC, Chang B, et al. Limb salvage of lower extremity wounds using gracilis muscle reconstruction. Plast Reconstr Surg. 2006;106(7):1507–13.
11. Mathes SJ, Nahai F, editors. Clinical application for muscle and musculocutaneous flaps. St. Louis: Mosby; 1982. p. 482–3.
12. Rios-Luna A, Fahandezh-Saddi H, et al. Pearls and tips in coverage of the tibia after a high energy trauma. Int J Orthod. 2009;42(4):387–94.
13. Withney T, Heckler F, White M. Gastrocnemius muscle transposition to the femur: how high can you go? Ann Plast Surg. 1995;34:415.
14. Thatte MR, Thatte RL. Venous flaps. Plast Reconstr Surg. 1993;91:747.
15. Loonen MP, Kon M, Schuurman AH. Distally based sural flap modifications. Ann Plast Surg. 2009;64(1):128.
16. Ritz M, Mahendru S, Somia N, et al. The dorsalis pedis fascial flap. J Reconstr Microsurg. 2009;25(5):313–7.
17. Yücel A, Senyuva C, Aydin Y, et al. Soft tissue reconstruction of sole and heel defects with free tissue transfers. Ann Plast Surg. 2004;44(3):268.
18. Segev E, Wientroub S, Kollender Y, et al. A combined use of a free vascularised flap and an external fixator for reconstruction of lower extremity defects. J Orth Surg. 2007;15(2):207–10.
19. German G, Bickert B, Steinau HU, Sauerbier M. Versatility and reliability of combined flaps of the sub-scapular system. Plast Reconstr Surg. 2000;103:1386–99.

20. Song R, Song Y, Yu Y, Song Y. The upper arm free flap. Clin Plast Surg. 1982;9:27.
21. Steinau HU, Clasbrummel B, Josten C, et al. The interdisciplinary approach in reconstructive surgery of the extremities. Chirurg. 2004;5(4):390–8.
22. Feng CH, Yang JY, Chuang SS, et al. Free medial thigh perforator flap for reconstruction of the dynamic and static complex burn scar contracture. Burns. 2010;36(4):565–71.
23. Platt AJ, McKiernan MV, McLean NR. Free tissue transfer in the management of burns. Burns. 1996;22:474–6.
24. Ruano-Ravina A, Jato Díaz M. Autologous chondrocyte implantation: a systematic review. Osteoarthritis Cartilage. 2003;14(1):47–51.
25. Zao L, Wan L, Wang S. Clinical studies on maintenance of cross-leg position through internal fixation with Kirschner wire after cross leg flap procedure. Chin J Rep Reconstr Surg. 2006;20(12):1211–3.
26. Upton J, Rogers C, Durham-Smith G, Swartz WM. Clinical applications of free flaps in reconstruction. J Hand Surg [Am]. 1986;11:475–83.
27. De Lorenzi F, Boeck W, et al. Free flaps in burn reconstruction. Burns. 2001;27:603–12.
28. Baumeister S, Germann G. Soft tissue coverage of the extremely traumatized foot and ankle. Foot Ankle Clin. 2001;6:867–903.
29. Luce EA, Dowden WL, Hoopes JE. High tension electrical injury of the extremity. Surg Gynecol Obstet. 1978;147:38–42.
30. Lewis GK. Electrical burns of the upper extremities. J Bone Joint Surg. 1958;40:27–32.
31. Mann RJ, Wallquist JM. Early decompression fasciotomy in the treatment of high-voltage electrical burns of the extremities. South Med J. 1975;68:1103–8.
32. Robson MC, Murphy RC, Heggers JP. A new explanation for the progressive tissue loss in electrical injuries. Plast Reconstr Surg. 1984;73:431–7.
33. Zelt RG, Daniel RK, Brisette Y, et al. High-voltage electrical injury: chronic wound evolution. Plast Reconstr Surg. 1988;82:1027–41.
34. Chang N, Mathes SJ. Comparison of the effect of bacterial inoculation in musculocutaneous and random-pattern flaps. Plast Reconstr Surg. 1982;70:1–10.
35. Serafin D. Atlas of microsurgical composite tissue transplantation. 1st ed. Philadelphia: WB Saunders; 1996.
36. Menktelow RT. Microvascular reconstruction. New York: Springer; 1986. p. 37–44.
37. Gordon L, Levinsohn DG, Finkemeier C, et al. The serratus anterior free-muscle transplant for reconstruction. An analysis of the donor and recipient sites. Plast Reconstr Surg. 1993;92:97–101.
38. Tu YK, Yen CY. Role of vascularized bone grafts in lower extremity reconstruction. Orthop Clin North Am. 2007;38(1):37–49.
39. Bar-Meir E, Yaffe B, Winkler E, et al. Combined Ilizarov and free flap for severe recurrent flexion—contracture release. J Burn Care Res. 2006;8:529–34.
40. Baumeister S, German G, Gielser G, et al. Wiederherstellung der verbrannten Extremität durch Transplantation freier Lappenplastiken. Chirurg. 2004;75:568–78.

Thermal Injuries to the Foot

26

Thilo Schenck and Riccardo E. Giunta

26.1 Introduction

Thermal injuries to the foot, in particular isolated burns, are less common than burn injuries to other body parts such as the face or the hand. One reason for this low number of injuries is due to the fact that most of the time our feet are protected by shoes. Despite the foot's relatively small percentage of the total body surface area (TBSA) of approximately 3.5%, special attention should be paid on foot burns because the sequelae of these injuries can dramatically reduce the patients' quality of life [1]. The significance of foot injuries becomes obvious when we consider how much of our daily life depends on the main function of our feet, i.e., to statically and dynamically carry body weight. The long-term impairments of thermal foot injuries can include anything from problems with shoe fit to recurrent ulcerations, and from gait disturbances to inability of standing and walking.

Many different causes can lead to thermal injuries of the feet. Especially children, the elderly, and disabled persons are at risk [2] (Fig. 26.1). Burns of the feet in children are often caused by scalds [1]. Neuropathy due to diabetes puts the elderly at risk for burn injuries [3]. Burns of the feet are also common in electrical injuries because the electric current exits the body through the feet. The risk factors for thermal foot injuries also depend on geographical and cultural factors. In tropical or subtropical geographic areas, walking on hot road surfaces or sand without adequate footwear can lead to severe injuries, especially in children [4]. Fire walking rituals, as being performed particularly in India, are a frequent cause of isolated foot burns as well [5]. The aim of acute therapy and reconstruction is to allow patients to return to normal gait and ambulation. Additionally, follow-up care of patients with burn wounds of the feet is necessary. Long-term consequences like foot deformities, scarring, and contractures can lead to impaired walking, ulceration, chronic problems in wearing shoes, and secondary injuries after falls. Compared to burn injuries of other body areas, injuries of the feet can lead to rather long hospital stays as pressure on the injured areas has to be avoided.

26.2 Anatomy

Knowing the anatomy and understanding the function of the foot is essential for the surgeon to perform reconstruction of the foot. Similar to the hand, the plantar and dorsal soft tissues of the foot have different functions and therefore have different anatomic structures. The dorsum of the foot has tendons and veins lying superficially under the skin. Since the skin of the dorsum is not prone to mechanical stress, it is relatively thin. In contrast, the plantar side of the foot has to carry the weight of the body and serves as a shock absorbing cushion. Carrying the body weight without developing pressure sores highly depends on intact sensibility.

Vulnerable structures such as blood vessels, nerves, and the plantar fascia are protected by strong layers of subcutaneous fat with fibrous septa, which provide adherence to the deep structures. Special emphasis should be put on the weight-bearing surfaces of the foot which include the heel, the metatarsal heads, the lateral arch, and parts of the medial arch. Vascularization and skin coverage above the Achilles tendon make the ankle region a challenge for reconstruction.

Three major arteries provide blood supply to the foot. Similar to the vascular anatomy of the hand, the major arteries of the foot communicate with each other through numerous anastomoses [6]. The three main arteries of the foot divide the foot and ankle region into six angiosomes [7]. The peroneal artery has two major branches that supply the anterolateral portion of the ankle and the rear foot. The ante-

T. Schenck
Klinik und Poliklinik für Plastische Chirurgie und Handchirurgie, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

R. E. Giunta (✉)
Handchirurgie, Plastische Chirurgie und Ästhetische Chirurgie, Klinikum der Ludwig-Maximilians Universität München, Munich, Germany
e-mail: r.giunta@med.uni-muenchen.de

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_26

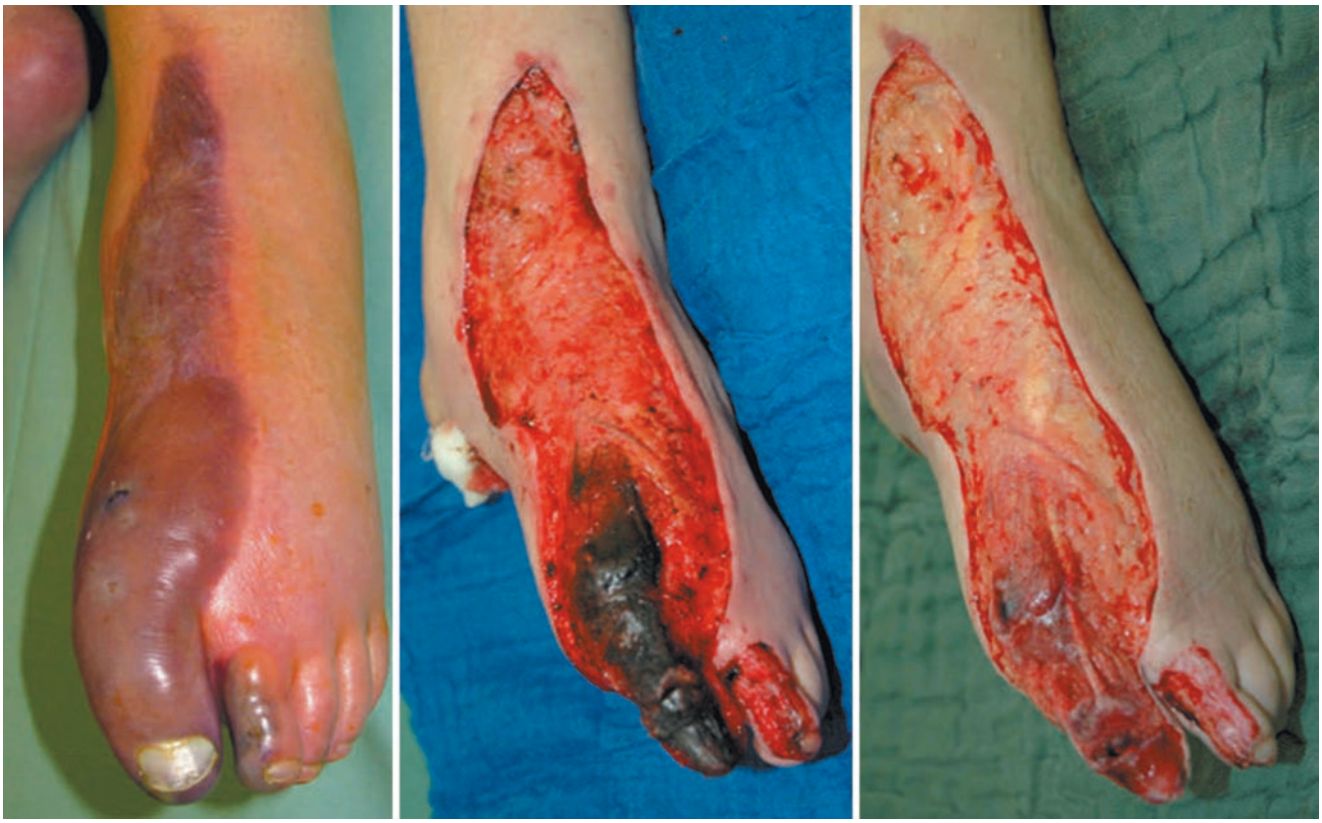


Fig. 26.1 Third degree burn of the forefoot including the toes in a paraplegic patient who burned herself with a power supply pack of her computer. This case demonstrates how lack of protective sensibility leads to increased risk for thermal injuries of disabled patients. Exact debridement with careful preservation of the paratendon of the extensor hallucis longus tendon could achieve a wound bed, which was suitable for skin graft transplantation

rior tibial artery continues into the dorsalis pedis artery and then builds up the dorsal system, which supplies blood to the dorsum of the foot and later on breaks up into the dorsal metatarsal arteries. The posterior tibial artery is responsible for the plantar system, which consists of the medial and the lateral plantar artery.

Venous drainage of the lower extremities including the feet is provided by a deep and a superficial venous system, which are connected to each other by perforator veins [8]. Due to our upright body position, the hydrostatic pressure is highest in the veins of the lower extremities, which are therefore vulnerable for venous insufficiency. The veins of the deep system accompany the arteries and are named accordingly. The course of the superficial venous system is independent of the arteries and consists of the great and the small saphenous vein and their branches.

Lymphatic vessels of the lower extremity and foot run with the veins and share the principle of a deep and superficial system. The superficial lymphatic vessels of the foot are divided into a small dorsolateral bundle, which accompanies the small saphenous vein, and a ventromedial bundle that accompanies the great saphenous vein [9]. While the dorsolateral bundle is responsible for the lateral border of the foot, the ventromedial bundle is responsible for the rest of the foot.

Innervation of the foot is provided exclusively by branches of the sciatic nerve except for the medial malleolus which is innervated by the saphenous nerve, the continuation of the femoral nerve [10]. The tibial nerve follows the course of the posterior tibial artery and correspondingly breaks up into a medial and lateral plantar nerve to innervate the sole of the foot. Dorsal innervation of the foot is mainly provided by branches of the superficial peroneal nerve. Sensation to the first interdigital web space is provided by the deep peroneal nerve. The lateral side of the foot, from the lateral malleolus to the little toe, is innervated by the sural nerve. Compared to the nerves of the sole, the branches of the superficial peroneal nerve, the sural nerve, and the saphenous nerve are located relatively superficially that puts them at higher risk for injury.

26.3 Burn Therapy

26.3.1 General Assessment

The long-time result of burn therapy is mostly influenced by the extent and severity of the burn wound, the involvement of certain specialized areas, and the quality of the initial ther-

apy. Except for minor injuries, treatment should be managed by specialized burn care facilities [11]. In combination with further burn injuries, burns of the feet are sometimes not given enough attention from the beginning, as they are thought to have less severe consequences compared to burns of the face and the hands for instance.

Similar to burns of other locations, wound conditions including size and depth of the wound and type of damaged or exposed structures must be evaluated before selecting therapy. Special focus should be put on possible involvement of weight-bearing surfaces, damaged bones, tendons, vessels, and nerves. In the later phase of treatment, weight-bearing patterns by Harris mat prints and mapping of plantar sensation can be required [12].

Prior to treatment, the general situation of the patient and the relevance of the burn injury to the foot have to be evaluated thoroughly. This information is required to choose the right reconstructive strategy. In addition to accurate evaluation of all injuries, including the burned proportion of total body surface area, the patient's medical history plays an important role as well. To assess the possible goals of therapy, general risk factors like diabetes, obesity, smoking, and age and specific risk factors for the lower extremities like, e.g., peripheral artery disease, chronic venous insufficiency, and peripheral polyneuropathy should be taken into account. Additional diagnostic efforts such as arteriography and Doppler sonography might be required when preparing complex reconstructive approaches. In spite of the benefits of these convenient and quantifiable methods, the fast, simple, and cheap method of examining the pedal pulses should not be disregarded. When considering flaps with defined blood supply such as free, pedicled, or axial flaps, existence and patency of the chosen vessels should be evaluated in advance. It should be always kept in mind that vessels could be unavailable due to trauma or anatomic variations. One example is the congenital absence of the dorsalis pedis artery which occurs in 2% of the population, leading to unavailability of the numerous standardized dorsalis pedis artery flaps [13]. For proximally based flaps, arteries of the plantar and dorsal systems have to be uninterrupted and communicating anastomoses open. Clinical examination of the vessels, angiography, and Doppler sonography are crucial. Especially in the preparation of perforator flaps, the Doppler sonography plays an important role [14]. Although the possibilities of reconstruction and microsurgery have tremendously increased in the last decades, considerations in primary burn care should not exclude amputation as an option in some injuries [15]. The basic principle of "life before limb" remains a pillar of any reconstructive procedure.

26.3.2 Goal of Therapy

The main goal in the treatment of thermal feet injuries is to restore the function of the foot, which is to carry body weight and the ability to stand and walk. The functional outcome of reconstruction can be estimated by the parameters ulceration, pain, and footwear [16, 17]. The patient's daily activities, capability to return to work, and quality of life are highly affected by pain, which therefore serves as an appropriate parameter for the outcome of the reconstruction [18]. Incidence of ulcers is a suitable parameter as well, because it indicates durability of soft tissue coverage. Ulcers are also a measure of quality of life because repetitive changes of dressings interfere with daily activities. Although aesthetic goals are of minor importance in extensive injuries to the feet, an adequate contour should be aimed at to allow the patient to use normal footwear. Hence the ability to use normal footwear acts as an indicator of a good flap shape [18]. Another goal is to maintain sensation at the sole of the foot. Without sensibility, especially to pressure, in the reconstructed foot the patient has similar risks for secondary injuries as known from patients suffering from neuropathic feet [18]. In the early phase of therapy, fast skin coverage should be achieved to protect the subjacent structures and to prevent infections. The long-term outcome of skin coverage can be rated by occurrence of contractions and hypertrophic scars.

26.3.3 Primary Treatment

The first steps of acute treatment of thermal feet injuries should not differ from other burn injuries. At first, the vital threat of the injury and the overall situation of the patient have to be evaluated. The goal of acute treatment of the wound is cleaning, debridement, necrosectomy, and if possible early closure of the wound (Figs. 26.1 and 26.2). Besides, management of foot burns in the acute phase should consist of pain control, foot elevation to prevent swelling, wound dressings with antiseptic agents, frequent observations, and depending on the extent of the wound prophylactic systemic antibiotics [1, 19, 20]. Superficial partial thickness burns are often underestimated. Treating them aggressively is often a worthwhile procedure to prevent the progression from a superficial to a deep partial thickness burn injury [2]. However, necrosectomy has to be performed very carefully so that vulnerable structures like peritendineums, superficial veins, and lymphatic vessels which are crucial to defect coverage remain intact. Hospital treatment should be rigorously indicated to avoid infections. In some cases early skin grafting as temporary or final defect coverage can be considered (Fig. 26.2). In the acute treatment of foot burns, the use of splints should be

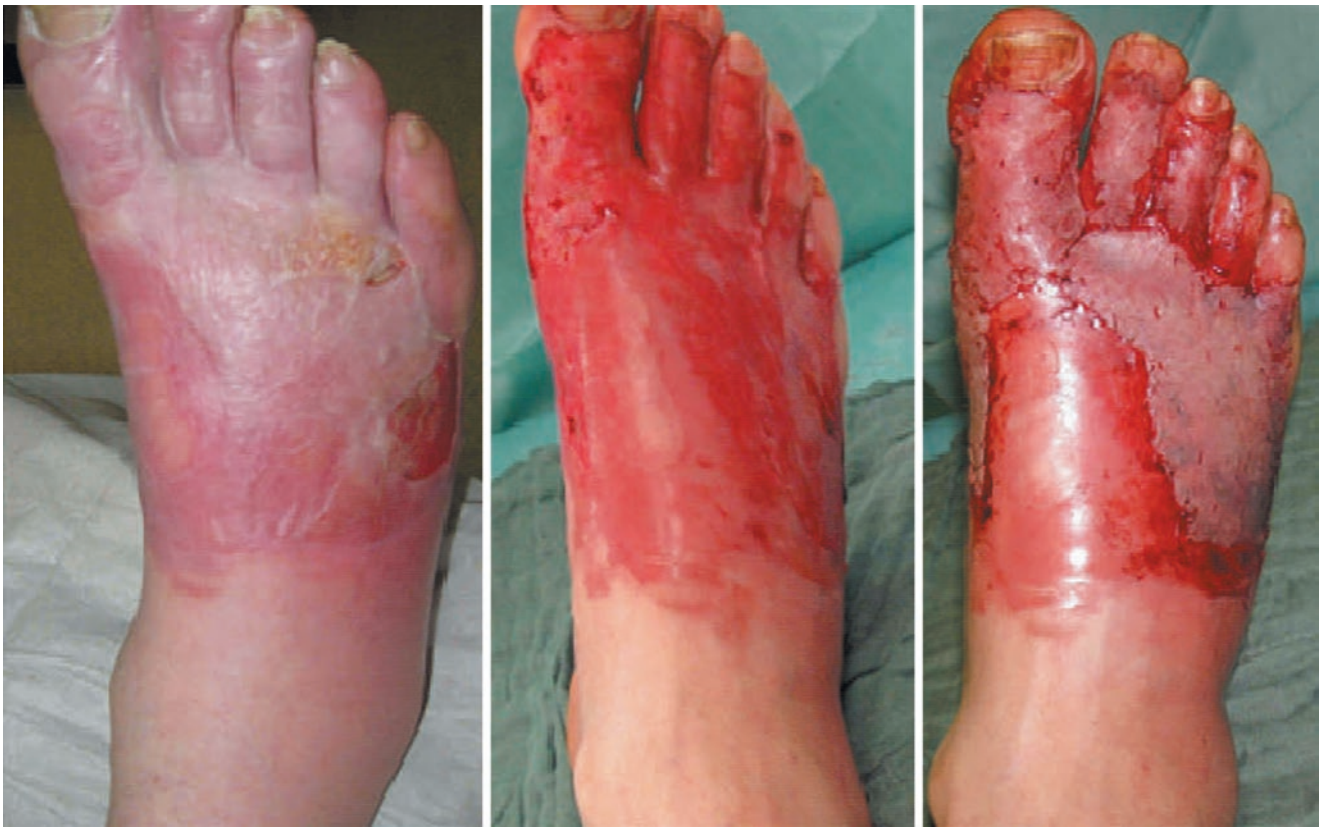


Fig. 26.2 This second degree burn injury of the foot resulted from spilling hot water in the kitchen. The patient came to the emergency department with a delay of 5 days. Debridement revealed a combination of deep and superficial dermal injury. For injuries without exposure of vulnerable structures, bones or tendons, such as this deep dermal injury, skin grafting is the best treatment option. Before skin transplantation, the wound needs careful cleaning and debridement. Skin grafting is a fast and easy method with very limited harvesting defects. If applied on larger defects contractions can occur

considered to prevent deformities due to contractions. Although the aim of the treatment is to rescue as much structures of the foot as possible, indications for amputation should be checked already in the beginning. Delay of amputation in cases where it is unavoidable often leads to unnecessary operations and more psychological stress. It has to be evaluated if the patient might have a higher benefit from a good prosthesis than from an insufficiently reconstructed foot [21]. In addition, amputation often allows faster return to ambulation than complex reconstruction. In the decision process for or against amputation, the extent of the injury, the presence and severity of wound infections, and the situation of the patient as a whole have to be considered. If one or more toes are severely damaged, amputation is often indicated because the loss of function is relatively negligible. An exception to this is the great toe, which is of higher importance to gait stability. If the forefoot or midfoot is severely damaged or severe proximal injury of the lower extremity is present, Chopart, Lisfranc, or even more proximal amputation can be indicated. Even though amputation is a destructive procedure, it has to be performed accurately and can only be considered successful if the resulting stump has a stable, well-cushioned soft tissue coverage, is free from pain, and allows good ambulation.

26.3.4 Bridging the Time to Final Reconstruction

Fast and definitive closure of wounds should be the goal of treatment. But if defects are more complex, reconstruction of the injured foot often becomes a more than one stage approach. In cases of foot injuries occurring as a concomitant injury, its treatment is often postponed until the patient is out of vital danger and co-existing injuries of higher importance such as injuries of the face or hand have been treated. Reconstructing at a later point gives time for thorough evaluation—and accurate repetitive debridement, but also bears the risk of developing complications. Attention should be paid to the development of soft tissue infections. Sample collection for microbiological analysis should be performed to allow specific antibiotic treatment. Microbiological analysis should be generously indicated

as the foot is a very susceptible region for infections. In cases where bone structures are not covered, osteomyelitis is a feared complication, which can be ruled out by plain radiographs. In cases of osteomyelitis or wound infection, the use of muscle flaps can be advantageous [22, 23]. During the time span until final defect coverage is achieved, wound treatment aims at preserving stable wound conditions, preventing infections, and limiting fluid and protein loss. Infections of the wounds have to be ruled out or treated successfully before the final defect coverage. For skin defects, skin grafts can be helpful in this phase but synthetic or biologic wound coverage has gained popularity as well. Especially in cases when donor skin is unavailable due to extensive burn injury or when the wounds are not ready for autografting, temporary skin substitutes are valuable [24]. Many temporary artificial skin replacement products such as collagen-glycosaminoglycan matrix, acellular allogenic dermis, or collagen/elastin matrix are available on the market and their number is constantly growing [25]. If deeper structures are exposed vacuum-assisted closure devices can help to temporarily close the wound. Similar to burns to the hand, the complex anatomic structure of the foot makes the application of temporary wound dressings a challenge. For the hand a temporary wound dressing in the shape of a glove has been developed [26]. So far, no analog for feet is available on the market, but in some cases the existing glove can be used for the foot as well.

26.4 Skin Grafting

Skin grafts are a good and frequently applied option for burn injuries if the extent of the injury is limited (Fig. 26.2). Split skin grafts are fast and easily applicable and leave only very limited harvesting defects [27]. Full skin grafts are thought to have better mechanical properties but are limited in availability. If skin grafts serve the demands of the defect, it has to be evaluated if the defect serves the demands of the skin graft as well. For successful graft take, the area to be covered must be able to supply the skin graft with nutrition and oxygen. This can be successfully provided in most soft tissue defects. Exposed bones and tendons without peritendineum cannot sufficiently meet the needs of skin grafts; hence a different approach should be chosen. If vulnerable structures like vessels or nerves are exposed, skin grafts will usually not provide enough mechanical protection. Even though bare bones are generally considered a contraindication for skin grafts, they can be tolerated if their contribution to the whole defect is just minor. In these cases debridement of the wound bed should include decortication of the exposed bones to stimulate the formation of granulation tissue before skin graft transplantation can be carried out as a next step [21]. Prior to grafting, infections of the recipient site should be ruled out or sufficiently treated surgically and with antimicrobial agents. Preparation of the recipient site should include sufficient debridement to achieve good perfusion. In the early phase after transplantation, nutrition and oxygen are provided by diffusion. To allow diffusion the graft must be well attached to the wound ground. Because the hydrostatic pressure is highest in the feet, leaking of arterioles, venous capillaries, and lymphatic vessels brings the risk of fluid accumulation under the graft. For this reason, constant pressure should be applied to the graft for the first days after transplantation and the wounded foot should be elevated at all times. The use of vacuum-assisted closure (V. A. C.® therapy) devices to fix split-thickness skin grafts and to withdraw fluid from the transplanted area has risen steadily in the last decade [28]. Thin split skin grafts and mesh grafts should be avoided on the foot because they show higher risks for contraction and the aesthetic outcome is lower than in unmeshed grafts [29]. However, it is advantageous to make some incisions in the graft to avoid accumulation of wound fluid under the transplant.

Even though skin grafts often need corrections including re-grafting, skin grafting is an effective method to cover defects fast and easily or at least to reduce them significantly in size. Skin grafting can also help to bridge the time from acute treatment to further complex reconstructive approaches. Frequent problems seen with skin grafts on the foot are hyperkeratosis at the borders of the grafts, ulcerations, and contractions. Although skin grafting remains the gold standard for skin lesions, the development of bioartificial skin is proceeding constantly and dermal replacement products based on collagen already show satisfying results in burn patients [30].

26.5 Postoperative Care

Successful treatment of thermal foot injuries highly depends on postoperative care. Most of the surgical efforts take place in the first couple of weeks after the accident, but the postoperative care may be necessary for a much longer time. Postoperative care should therefore be accurately planned and multidisciplinarily approached. Its extent depends on the extent of the injury and the complexity of the reconstructive efforts.

In the early phase after reconstruction, the focus lays on monitoring, appropriate wound dressings, medication, and bed rest with elevation of the operated foot. For sufficient monitoring frequent changes of wound dressings combined with accurate cleaning are necessary. Maximum attention has to be paid to signs of infections and delayed wound healing. If free flaps are applied perfusion has to be monitored frequently. Monitoring devices such as external and laser

Doppler are increasing but most frequent visual controls including recapillarization time remain the gold standard.

Medication should address antibiotic coverage, pain medication, fluid management, and anticoagulation until full ambulation. Systemic comorbidities like diabetes, peripheral artery disease, chronic venous insufficiency, and malnutrition should be treated as well. Time of bed rest, leg elevation, and time until weight-bearing depend on the chosen defect coverage. When patients return to ambulation, pressure treatment and orthopedic footwear, such as thermoplastic boot splints, become necessary. In case of split skin transplantation accumulation of fluid under the graft and shear forces have to be avoided. This works best by applying pressure on split skin grafts with elastic bandages for at least 5 days. Pressure should not be applied on skin grafts which are used on top of free flaps. In this case dressings with pressure would impair perfusion and make monitoring difficult.

Hydrostatic pressure as in a standing position sets free flaps of the lower extremity at risk for venous and lymphatic congestion. Three to five days after free flap transfer, the strict elevation can be started to be periodically interrupted. In order to protect the foot from fluid congestion, elastic bandages have to be applied. This procedure is started for a duration of 15 min per day and is increased within approximately 1 week to three times 3 h per day. As soon as wounds are stable and postoperative swelling has decreased, an orthopedic pressure stocking is customized which replaces the elastic bandages in the following months. Intensive physical therapy is of great importance to return to ambulation and to regain or maintain joint flexibility. Besides selection of an adequate reconstructive approach, detailed education about foot care and frequent follow-up visits play an important role in maintaining reconstructed feet healthy and the flap intact [31]. The patient has to learn that a loss of sensation has to be replaced by frequent self-examinations [32]. Treatment of scars with silicone sheets, compression garment, and scar reduction creams can be started when defect coverage is accomplished and wounds have reached a stable level.

26.5.1 Secondary Reconstruction

Defects of the foot and the lower one third of the leg are challenging subjects for reconstruction. Since thermal injuries to the feet occur in a countless number of variations, each defect has to be evaluated individually. Depending on the extent of the injury, treatment can reach from conservative treatment with wound dressings to multi-step operational approaches [33]. A multidisciplinary team and accurate planning of all reconstructive efforts are crucial for success and can only be managed if the medical team is capable of the full surgical armamentarium [34].

For the thermally injured foot a broad spectrum of methods has been described that includes almost all options of defect coverage. It spans from skin graft, skin and muscle flaps to free flaps. The challenge for the plastic surgeon is to choose the most adequate strategy according to general principles for reconstruction. Form and function of injured structures should be restored by replacing them with structures of similar properties. When doing so, the gain of function at the recipient site must outweigh the loss of function at the donor site. If different options remain, the least complicated and traumatizing should be applied. Accurate planning of flap contour in the beginning can reduce the amount and extent of later flap debulking procedures, which become necessary in many cases [32].

To achieve a reconstruction providing the proper weight-bearing surfaces, reconstruction efforts should aim at re-establishing the bone architecture including its longitudinal and transverse arches. In the long term, bony prominences are a high-risk factor for the development of ulcers and should be removed if possible [32]. According to the different needs of the anatomic regions, different reconstructive approaches should be chosen.

26.6 Defects of the Dorsum of the Foot and Ankle

The dorsum of the foot and ankle is more frequently involved in burn injuries than the sole. In the majority of cases, burns are superficial and the extensor tendons and the bones remain covered with subcutaneous tissue. In these cases, split skin grafts are suitable. If the peritendineum of the extensor tendons is destroyed or even deeper structures are involved, flap coverage becomes necessary. In the region of the Achilles tendon and the dorsum of the foot, the skin is thin and mobile. Any form of coverage of these areas must maintain or restore the unrestricted motion of the underlying structures. Flap coverage can be managed by local, regional, and free flaps (Figs. 26.3, 26.4, 26.5 and 26.6). Local fasciocutaneous and muscle flaps from the dorsalis pedis artery are useful for medium size defects of the complete dorsum, the ankle, and malleoli (Table 26.1). Small defects of the proximal dorsum and the proximal sides of the foot can also be covered with local muscle flaps from the posterior tibial artery (Table 26.1). Fasciocutaneous flaps from the posterior tibial artery have been described for the posterior aspect of the heel and the insertion of the Achilles tendon. For large defects or if defects are too proximal for local flaps of the foot, regional flaps from the lower leg and individual flaps (“freestyle flaps,” “propeller flaps”) can serve as coverage. Large and complex defects usually require the application of free flaps (Table 26.2).

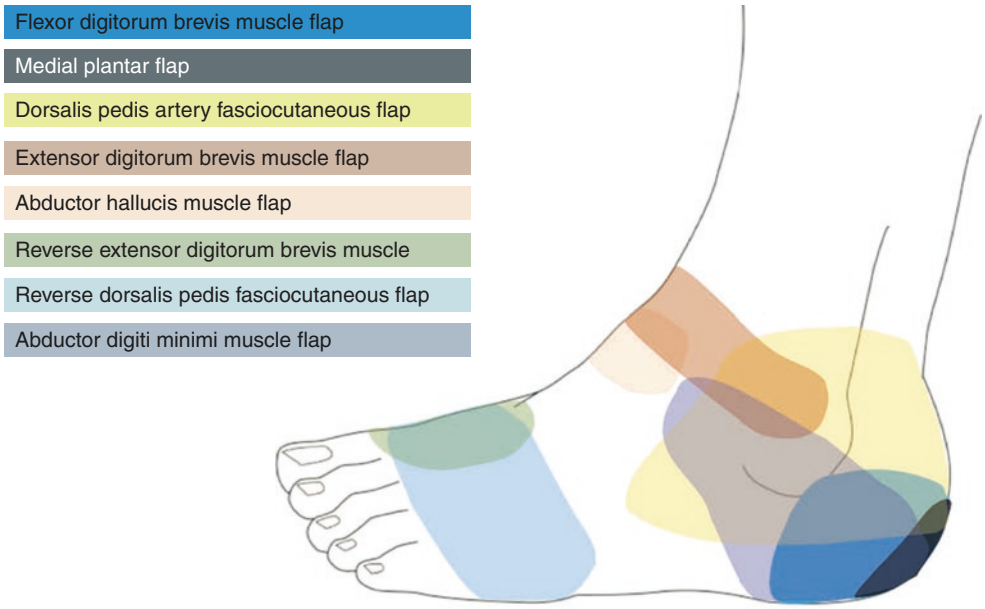


Fig. 26.3 Local fasciocutaneous and muscle flaps for the dorsum and the lateral ankle region. If defects are too extensive for local solutions, regional or free flaps have to be considered

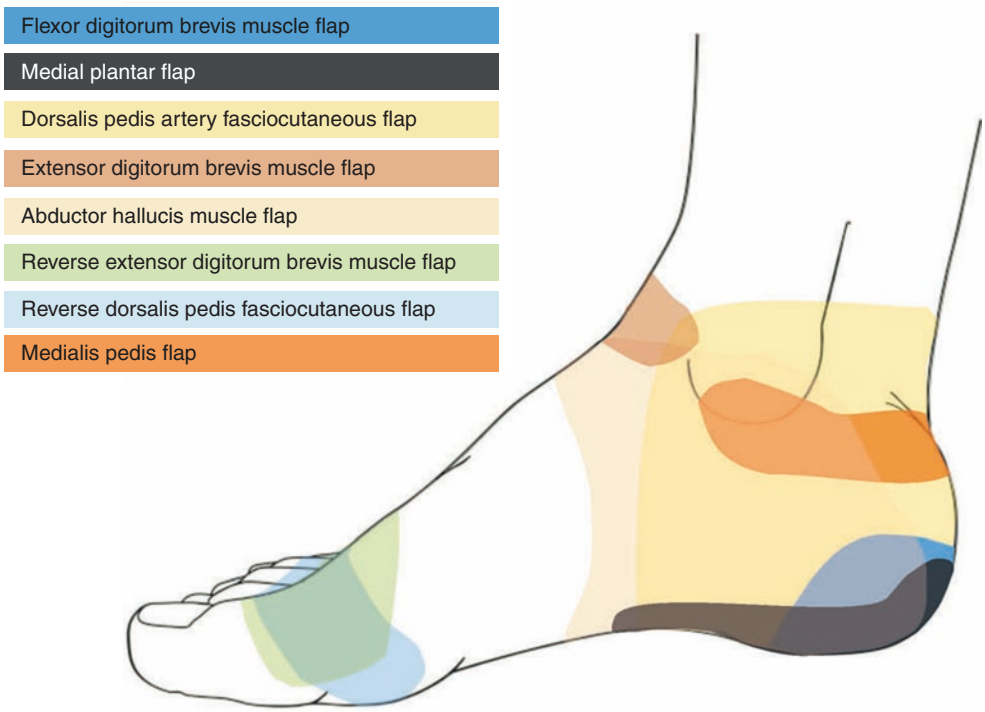


Fig. 26.4 Local fasciocutaneous and muscle flaps for the dorsum and the medial ankle region. If defects are too extensive for local solutions, regional or free flaps have to be considered

26.7 Defects of the Sole

Injuries of the sole are not as frequent as injuries of the dorsum of the foot. One reason is that shoe soles offer some protection to our feet. Another reason is that in burns due to spilling of hot liquids, the liquids usually damage the dorsum and rinse off the feet without getting in contact with the sole. Thermal injuries to the sole are seen more frequently in patients with neuropathies, e.g., due to diabetes and as exit wounds in patients that suffer from high-voltage injuries. The reconstruction of the sole is challenging because the reconstructed site must be very durable and able to bear weight load. If wounds do not involve deeper structures, skin grafts can achieve stable wound conditions. For defects of the proximal sole and the heel, a group of local muscle flaps from the posterior tibial artery has been described (Fig. 26.7). The distal half of the foot, including the weight-bearing areas, is a difficult place to reach with local flaps. For these defects, just like any other sole defects that expose deeper structures, free flaps covered with split skin grafts are used (Table 26.2).

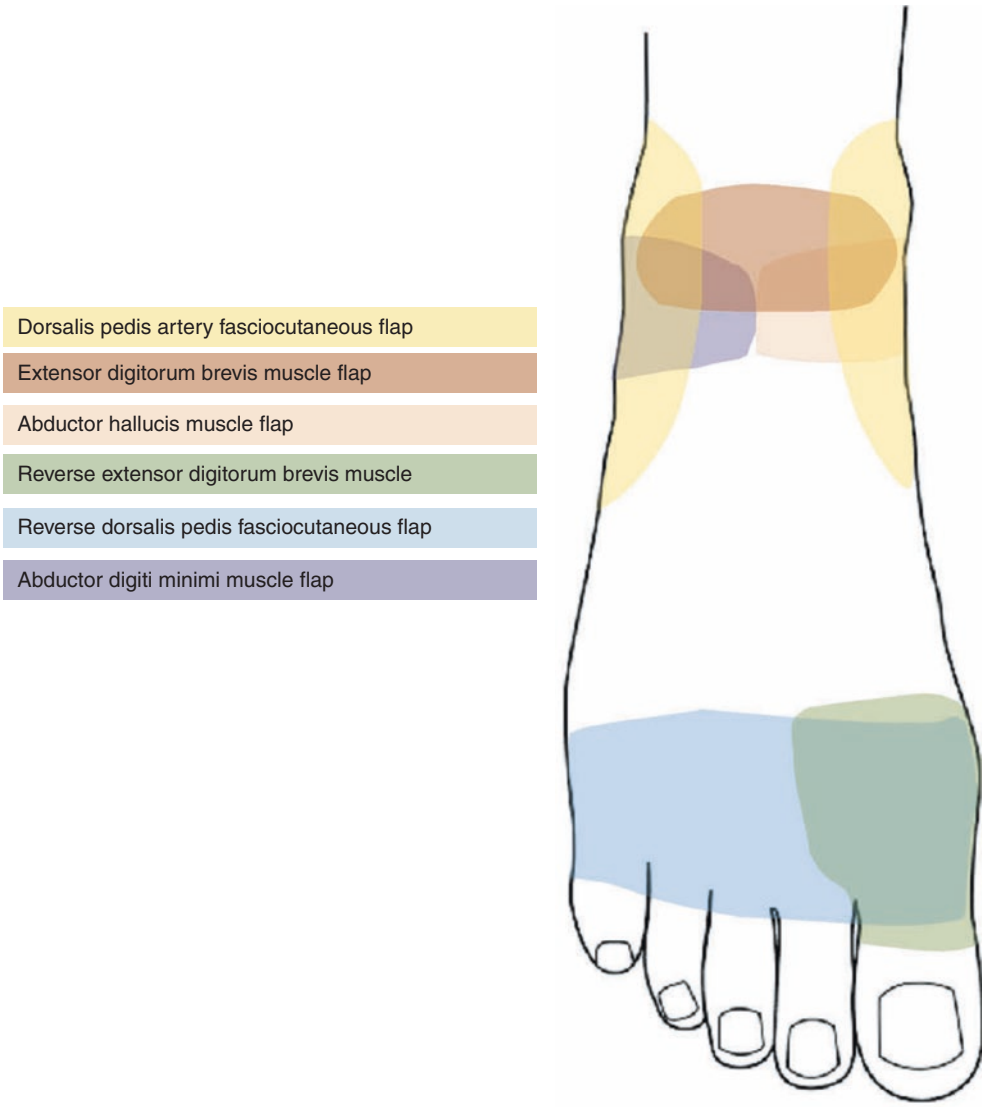


Fig. 26.5 Local fasciocutaneous and muscle flaps for the dorsum of the foot. If defects in this area are superficial and the peritendineum of the extensor tendons is uninjured, split skin coverage brings good results

26.8 Local Flaps

For small and moderate defects coverage with local tissue transfer is a recommendable option if involvement of bones, joints, or tendons is absent or of limited extent. Availability of local tissue on the foot which is suitable for transfer is limited due to relatively tight skin and poor vascularity. If local flap coverage is possible, it has the advantage of being a simple, safe, and economical solution with shorter operation and hospitalization time than free flaps [57]. Since many patients with foot burns have additional injuries, local coverage of defects has the advantage of avoiding additional trauma by flap harvesting [57]. Small defects of the foot can be covered with transposition flaps, advancement flaps, rotation flaps, or Z-plasties. Z-plasties and W-plasties play also an important role in the correction of postburn contractions (Fig. 26.8). If small skin flaps are not sufficient for defect coverage, local fasciocutaneous and muscle flaps are applied. These flaps can be classified according to their vascular origin into the groups of dorsalis pedis artery flaps and posterior tibial artery flaps (Table 26.1).

26.9 Local Flaps from the Dorsalis Pedis Artery

The dorsalis pedis artery is used for the dorsalis pedis artery fasciocutaneous flap, which can be applied in defects of the malleoli and the ankle region [35]. By including the superficial or deep peroneal nerve a sensory flap can be created. Even burn injuries of the distal foot and toes including the web spaces can be covered with flaps of the dorsalis pedis artery. For this purpose, the dorsalis pedis artery fasciocutaneous flap can be harvested as a reverse dorsalis pedis flap [36, 37] or its continuation, the first dorsal metatarsal artery, can be included in a flap [38].

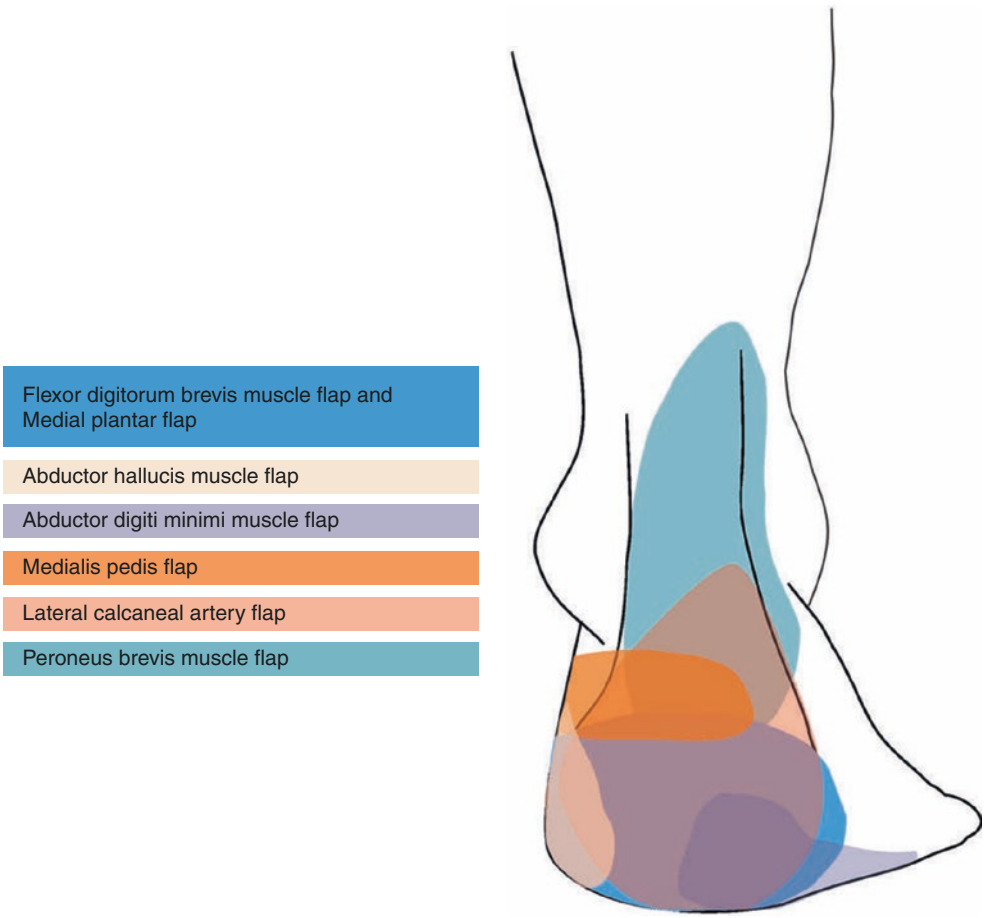


Fig. 26.6 The posterior aspect of the foot can often be covered by local muscle and fasciocutaneous flaps. These flaps do not reach the height of the malleoli. In cases of more proximal or larger defects, regional flaps from the lower leg or free flaps are used

Table 26.1 Summary of the local and regional flaps classified by vascular supply and type of flap

Local fasciocutaneous flaps		Region	General literature	Burn-specific literature
Dorsalis pedis artery fasciocutaneous flaps				
	Dorsalis pedis artery fasciocutaneous flap	Malleoli and ankle region	McCraw and Furlow (1975) [35]	Shah (2002) [2]
	Reverse dorsalis pedis fasciocutaneous flap	Distal foot and web spaces	Ishikawa et al. (1987) [36]	Schwabegger and Wechselberger (1996) [37]
	First dorsal metatarsal artery fasciocutaneous flap	Distal foot and web spaces	Hayashi et al. (1993) [38]	Goldberg et al. (2000) [39]
Posterior Tibial artery fasciocutaneous flaps				
Medial plantar artery	Medial plantar flap	Weight-bearing and posterior aspect of the heel	Shanahan and Gingrass (1979) [40]	Uygur et al. (2008) [41]
	Medialis pedis flap	Medial malleolus, Achilles tendon insertion	Masquelet and Romana (1990) [42]	
Local muscle flaps		Region	General literature	Burn-specific literature
Dorsalis pedis artery muscle flaps				
	Extensor digitorum brevis muscle flap	Proximal dorsum, malleoli, and ankle region	Landi (1985) [43]	Goldberg (2000)
	Reverse extensor digitorum brevis muscle flap	Distal forefoot	Kurata (1992) [44]	Shah (2002) [2]
Posterior tibial artery muscle flaps				
Medial plantar artery	Abductor hallucis muscle flap	Heel, medial malleolus proximal dorsum and medial side of the midfoot	Ger (1986) [45]	Goldberg (2000)

(continued)

Table 26.1 (continued)

Local muscle flaps		Region	General literature	Burn-specific literature
Medial and lateral plantar artery	Flexor digitorum brevis muscle flap	Heel defects, both malleoli, Achilles tendon insertion	Bostwick (1976) [46]	Goldberg (2000)
Lateral plantar artery	Abductor digiti minimi muscle flap	Heel, lateral malleolus, and proximal dorsum	Ger (1976) [47]	Goldberg (2000)
Regional flaps from the lower leg		Region	General literature	Burn specific literature
Peroneal artery	Lateral supramalleolar flap	Complete dorsum and lateral aspect of the foot, distal Achilles tendon	Masquelet et al. (1988) [48]	Goldberg (2000)
	Distally based sural island flap	Ankle, heel, distal Achilles tendon	Jeng and Wei (1977) [49]	Sood (2006) [50]
	Lateral calcaneal artery flap	Dorsal aspect of the heel	Grabb and Argenta (1981) [51]	Goldberg (2000)
	Peroneus brevis muscle flap	Achilles tendon insertion	Jackson and Scheker (1982) [52]	
Anterior tibial artery	Tibialis anterior muscle flap	Distal third of tibial crest	Ger (1970) [53]	Sood (2006) [54]
	Distally based anterior tibial fasciocutaneous flap	Complete dorsum and sides of the foot	Morrison and Shen (1987) [55]	Sood (2006)
Posterior tibial artery	Distally based posterior tibial fasciocutaneous flap	Complete dorsum, sides and sole of the foot	Hong et al. (1989) [56]	Goldberg (2000)
	Distally based posterior tibial fasciocutaneous flap	Complete dorsum, sides and sole of the foot	Hong et al. (1989) [56]	Goldberg (2000)

Table 26.2 Summary of free flaps which have been described for use in reconstruction of severe burn injuries to the foot and ankle [21]

Free flaps		Region
Frequently used free flaps	Latissimus dorsi muscle flap	Sole, complete dorsum, and sides of the foot
	Rectus abdominis muscle flap	Complete dorsum, sides of the foot, and ankle region
	Anterolateral thigh flap	Heel, dorsum, sides of the foot, and ankle region
	Radial forearm flap	Heel, dorsum, sides of the foot, and ankle region
	Gracilis muscle flap	Sides of the foot and ankle region
Less frequently used free flaps	Lateral arm flap	Heel, dorsum, sides of the foot, and ankle region
	Medial arm flap	Heel, dorsum, sides of the foot, and ankle region
	Temporalis fascia flap	Dorsum, sides of the foot, and ankle region
	Scapular flap	Dorsum, sides of the foot, and ankle region
	Deltoid flap	Heel, complete dorsum, sides of the foot, and ankle region
	Serratus anterior muscle flap	Sole, complete dorsum, sides of the foot, and ankle region

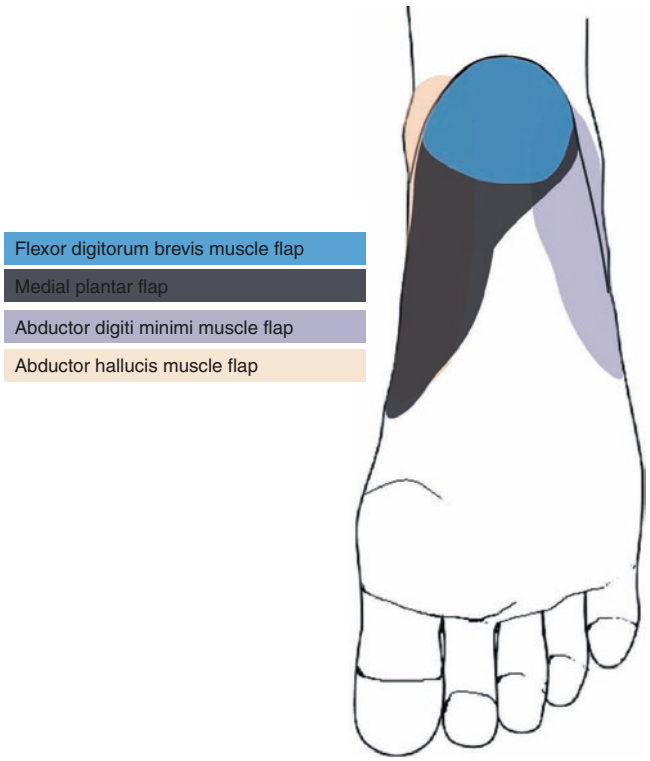


Fig. 26.7 The sole of the foot, especially the weight-bearing parts, is a delicate area for coverage. Only few local muscle flaps are available. In many cases split skin covered free flaps have to be used

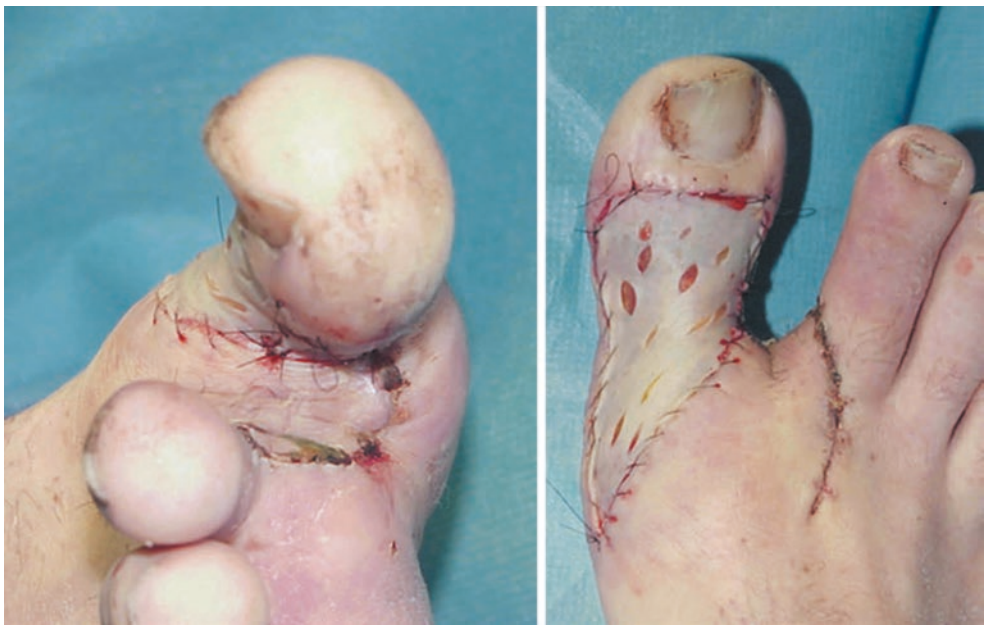


Fig. 26.8 Reconstruction of first web space by rotation flap and skin grafting

A variant of the dorsalis pedis flap for defects, which require muscle for coverage, is the extensor digitorum brevis muscle flap [43]. It can be used distally or proximally based on defects of the forefoot and the ankle region including the distal tibia [44, 58].

26.10 Local Flaps from the Posterior Tibial Artery

The posterior tibial artery divides into two major branches below the medial malleolus, the medial and the lateral plantar artery. Both arteries or one of their branches can be used in a number of fasciocutaneous, musculocutaneous, or muscle flaps.

The medial plantar artery can be used for flaps that have their origin at the medial border of the foot including the non-weight-bearing portion of the plantar arch. They can be used to cover defects of the weight-bearing plantar skin of the heel with tissue from the non-weight-bearing parts of the foot. The medial plantar flap and the medialis pedis flap are both fasciocutaneous flaps from the medial plantar artery. The medial plantar flap can also be used as a musculocutaneous or as a muscle flap with skin graft coverage [59, 60]. For treatment of burn defects it has been described as both an antegrade or retrograde flap [41]. The medial plantar artery is accompanied by the medial plantar nerve, which makes harvesting of a sensory flap possible [40]. Plantar flaps can be raised in a level below or above the plantar fascia. Including the plantar fascia makes flaps very suitable for heel defects because the fascia adheres well to the calcaneus [61]. Planning of medial plantar artery flaps should include angiography because the artery can have alterations in their course or even be completely missing. The medialis pedis flap has a cutaneous branch of the medial plantar artery as a pedicle. It is a small and thin fasciocutaneous flap, which has not been described for use in burns but can be used for the cranial part of the medial malleolus and for the area superficial to the insertion of the Achilles tendon [42].

For heel and malleolar defects a group of local muscle flaps originating from the posterior tibial artery has been described [62].

The posterior tibial artery provides blood support for three local muscle flaps, the abductor hallucis muscle flap, the flexor digitorum brevis muscle flap, and the abductor digiti minimi muscle flap. They are used for defects of the heel pad and the malleoli but also for the proximal dorsum. They are frequently covered with skin grafts and in some cases it is indicated to use them in combination. The abductor hallucis muscle flap and the abductor digiti minimi muscle flap have their pedicles arising from the lateral and medial side of the hindfoot, so that their arc of rotation allows using these flaps for dorsal and plantar defects. The blood supply of the abductor hallucis muscle is derived from several branches from the medial plantar artery [45]. The abductor hallucis flap can be harvested with the medial plantar artery or with one of its branches [63]. In this way a proximal pedicle is created that arises below the medial malleolus. The flap can be rotated in an upward direction to cover proximal dorsal defects or even the medial malleolus. It can be also rotated downward to the sole in order to cover defects of the medial aspects of the midfoot and the heel.

The abductor digiti minimi muscle flap is quite similar to the abductor hallucis muscle flap but located at the lateral border of the foot [47]. It is based on the lateral plantar artery and can be used for defects of the proximal dorsum and the

lateral malleolus. If rotated downward to the sole, the lateral aspects of the midfoot and the heel can be reached. For distal foot coverage a distally based abductor digiti minimi muscle flap has been described [64]. The largest local muscle flap in this group is the flexor digitorum brevis muscle flap. Its blood support is provided by branches of the lateral and medial plantar artery, and it can be used as a muscle or musculocutaneous flap [65]. It is not used for dorsal defects but serves for covering the posterior aspect of the heel, the medial and lateral malleoli, and the lower part of the Achilles tendon [66].

26.10.1 Regional Flaps from the Lower Leg

If the extent of injury makes local flaps not suitable for defect coverage, flaps from the lower leg, especially reverse flow flaps, have to be considered. The three arteries of the lower leg, the anterior tibial, the posterior tibial, and the peroneal artery, can serve as base for flaps if left intact by the trauma and can also serve for classification of the flaps. Most of the proximally based flaps from the lower leg do not reach the foot and ankle region. Hence, only the most relevant flaps from the lower leg are presented. The proximally based flaps serve as a good addition to the local flaps from the foot. In the challenging region of the malleoli and the Achilles tendon, most of the local flaps do not reach much higher than to the level of the malleoli. Above that level the proximally based flaps can be valuable. The distally based flaps can cover relatively large defects of almost any part of the foot but it has to be evaluated very thoroughly whether scarifying one of the three arteries of the lower leg is justified. Preoperatively, the blood flow through the anastomosis has to be assured.

26.10.2 Regional Flaps from the Peroneal Artery

For the dorsum of the foot a group of flaps originating from the peroneal artery can provide defect coverage. The lateral supramalleolar flap has become the most commonly used flap of this group [67, 68]. This large cutaneous perforator flap is based on a branch of a perforator of the peroneal artery [48]. The perforator is found proximal to the superior extensor retinaculum, where it perforates the interosseous membrane and from thereon has a cranial and a caudal branch. The cranial branch supplies a large area of skin on the lateral aspect of the lower leg and therefore is ideal for flap harvesting. Because of the anastomosis of the caudal branch with the anterior lateral malleolar artery, which originates from the anterior tibial artery, the flap can be used as a distally based flap. Its axis of rotation is centered at the midtarsal joint. With its rather long pedicle, it can be used as a pedicled flap and as an island flap. In this way its range of coverage reaches to the distal dorsum of the foot, the Achilles tendon, and the whole lateral side of the foot. Even though the flap can reach the weight-bearing areas it is not indicated for those areas because, since it originates from the lower leg, it is composed of relatively thin skin.

The distally based sural island flap is an adaptation of the lateral supramalleolar flap. It has the same pedicle but includes the lateral sural cutaneous nerve, making it a sensory flap [49]. The lateral calcaneal artery flap is a reliable flap for coverage of the dorsal aspect of the heel. It is designed with a neurovascular pedicle consisting of the continuation of the peroneal artery, the lesser saphenous vein, and the sural nerve for sensation. Its axis for rotation lies dorsal to the lateral malleolus [51]. Defects over the insertion of the Achilles tendon into the calcaneus can be covered by a peroneus brevis flap, which has not been described in the context of burn injuries to the foot. It gets its blood supply from small branches of the peroneal artery [52].

26.10.3 Regional Flaps from the Tibialis Anterior Artery

The tibialis anterior muscle supplied by branches of the anterior tibialis artery can be used for the middle third of the tibial crest [53]. A distally based anterior tibial fasciocutaneous flap was described to reach the complete dorsum and the sides of the foot [55].

26.10.4 Regional Flaps from the Tibialis Posterior Artery

Based on the posterior tibial artery, the reverse posterior tibial fasciocutaneous and myofasciocutaneous flap have been described [56, 69].

The reverse posterior tibial flaps have their axis of rotation at the height of the medial malleolus and can reach the complete dorsum, the lateral and medial aspects, and the sole of the foot [70].

26.10.5 Cross-Leg Flaps

Since the introduction of microsurgical free flap transplantation, the use of cross-leg flaps has become more or less outdated. In rare occasions, such as complete unavailability of recipient vessels, cross-leg flaps could be indicated [71]. For coverage of the weight-bearing areas, a cross-foot skin flap of the sole has also been described [72].

26.10.6 Free Flaps

Large or complicated defects with exposure of bones or other deep structures require free tissue transfer for defect coverage [73]. Since burn injuries of the foot are very variable, using a free flap gives the surgeon maximum flexibility in defect coverage. The advantage of free flaps is that they are independent of uninjured vascular anatomy because they can be connected to further proximal vessels. When free flaps are indicated, the broad majority of defects can be covered by standard free flaps, such as the latissimus dorsi or rectus abdominis flap [21] (Table 26.2). Many more free flaps have been described and may be indicated in special situations but for the choice of flap it is also legitimate to take into account which flap the individual surgeon is familiar with and has the most experience with. With the trend to perforator flaps and better understanding of the anatomy of the septocutaneous vessels of the lower leg, the popularity of fasciocutaneous flaps has risen [74]. Free flaps can be used in the weight-bearing areas but the ulceration rate is three times higher and the time to full ambulation is significantly longer when the flap is used in the weight-bearing areas compared to non-weight-bearing areas [75]. For the weight-bearing areas flaps with a broad and flat shape like, e.g., the latissimus dorsi muscle flap, the serratus anterior muscle flap, the rectus abdominis muscle flap, or the gracilis muscle flap plus split skin graft are most commonly used in sole reconstruction. Choice of free flap should also include considerations of the required length of the pedicle to reach uninjured and suitable recipient vessels.

Two strategies for reconstruction with free flaps have been discussed thoroughly in literature and can be used successfully for foot reconstruction in weight-bearing areas: split skin grafted muscle flaps and innervated fasciocutaneous flaps [31, 76]. Many authors state that flap insensitivity is a risk factor for ulcer development [77, 78]. To avoid insensitivity, many neurosensory flaps have been described which are thought to prevent ulceration and injuries to the flap similar to the injuries known to occur in patients with neuropathic feet [79, 80]. Long-term sensory evaluation shows that almost all of the sensory and nonsensory flaps develop sensitivity for deep pressure [75]. Sensation to light touch occurs much less frequently in both groups [75]. Ulceration rate as a measure of flap quality could not show superiority of sensory flaps [32]. Successful reconstruction correlates only with restored deep pressure sensibility, while light touch sensation does not correlate with successful reconstruction [32, 79]. Skin graft covered muscle flaps show the advantage of being more adjustable to the demand of contours and lessen the necessity of debulking procedures [81, 82]. This is mainly due to the lack of excessive subcutaneous fat, which also leads to unstable gait [32]. Despite the discussed benefits of neurosensory flaps, the split-thickness skin graft covered muscle flaps remain the most successful method for defects of the sole [21, 75] (Fig. 26.9).

For many large defects of the foot, the latissimus dorsi flap with its broad and flat shape provides excellent coverage [83] (Fig. 26.9). Due to its size it can be adjusted to fit almost any shape of defect. If defects are smaller, rectus abdominis muscle flaps, radial forearm flaps, anterolateral thigh flaps, and gracilis muscle flaps are frequently used [21]. The final shape of the flap becomes visible months after reconstruction, when muscle atrophy due to denervation is complete.

26.10.7 Long-Time Sequelae

The success of foot burn treatment has to be evaluated in the long run. Inadequate sensitive protections, poorly shaped contours, or bony prominences can lead to recur-

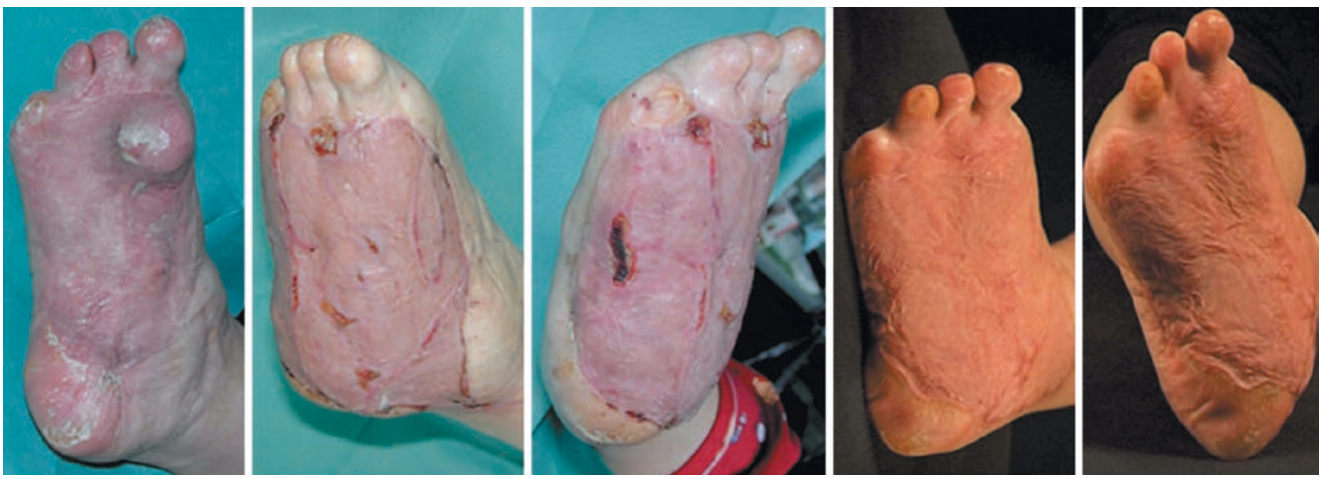


Fig. 26.9 Free rectus abdominis flap with split skin graft for reconstruction of the sole. Instable wound as a sequela of a burn injury (left) made this reconstruction necessary. High effort was put into good cushioning of the prominent first metatarsal bone

rent ulcerations and pain. Due to lymphatic destruction edema can occur as long-term consequences affecting especially the dorsum of the foot. Return to pain-free, unimpaired ambulation is the goal. Especially contracture deformities of the soles of the feet can make this goal harder to achieve [84]. Wound contraction, a physiologic process to lessen the size of the wound, leads to contractures in the wounded area, which is accompanied by severe static and dynamic problems in the long run. Without prevention and treatment of contractures, the success of a good reconstruction can easily be diminished, leading to a prolonged convalescence [46]. Splints and physical therapy are very useful in preventing contractures. If foot burn contractures are mild, basic plastic techniques like single or multiple Z-plasties or W-plasties can be used to release tension of the scar [85]. Dorsal scar contractures can be successfully treated by a transverse and/or longitudinal burn scar release in combination with a skin graft [29, 86] (Fig. 26.10). Dorsal foot burn contractures are often accompanied by syndactyly of the toes which can be treated with Z- or W-plasties, V-Y Advancement flaps, or skin grafts [87]. The most common sequelae of dorsal foot burn scar contractures are hyperextension and metatarsophalangeal subluxation of the toes leading to the rocker bottom deformity [85, 88]. It can be corrected by closed capsulotomies and K-wire fixation [86]. In the treatment of hyperextension or hyperflexion a moderate hypercorrection is recommended to achieve an enduring result [84]. In the treatment of chronic burn deformities, especially dorsiflexion deformities, the Ilizarov fixateur is frequently used [89]. If postburn contractures are very severe, free flaps must be considered [90].

26.10.8 Thermal Injuries of Feet in Children

Infants and children are a special risk group for foot burns [1]. Due to their thinner skin especially infants are at increased risk to suffer from full-thickness thermal injuries [2]. Again, the success of treatment has to be evaluated by the return to normal gait and ambulation but also by the incidence of contractures and other late sequelae [84]. Treatment of burns in children is different due to higher regeneration potential, lack of cooperation, and different risk profile for long-time consequences including psychological factors [91, 92].

Especially plantar burns in children show unique characteristics and their treatment, particularly the decision between conservative and surgical treatment, is subject to controversial debate. Skin grafts are often used and it has been shown that in children even deep burns of the weight-bearing parts of the sole can be sufficiently covered by split-thickness skin grafts [93]. It has been stated that early excision and grafting results in a reduction of reconstructive needs [94]. Then again it has been reported that there is no difference in outcome between early excision followed by autografting and conservative treatment [95]. A widely accepted treatment protocol for plantar burns proposes conservative treatment together with progressive weight-bearing rehabilitation, active physiotherapy, and stretching of the burned skin [92]. It also includes that wounds which do not heal within 3 weeks should be excised and covered by skin grafts. This protocol shows a negligible complication rate and significantly reduced incidence of contractures and late sequelae. Children are exceptionally at risk for contractures because growth brings additional tension to the scarred areas. If contractures in children are not corrected in time, they can lead to defor-

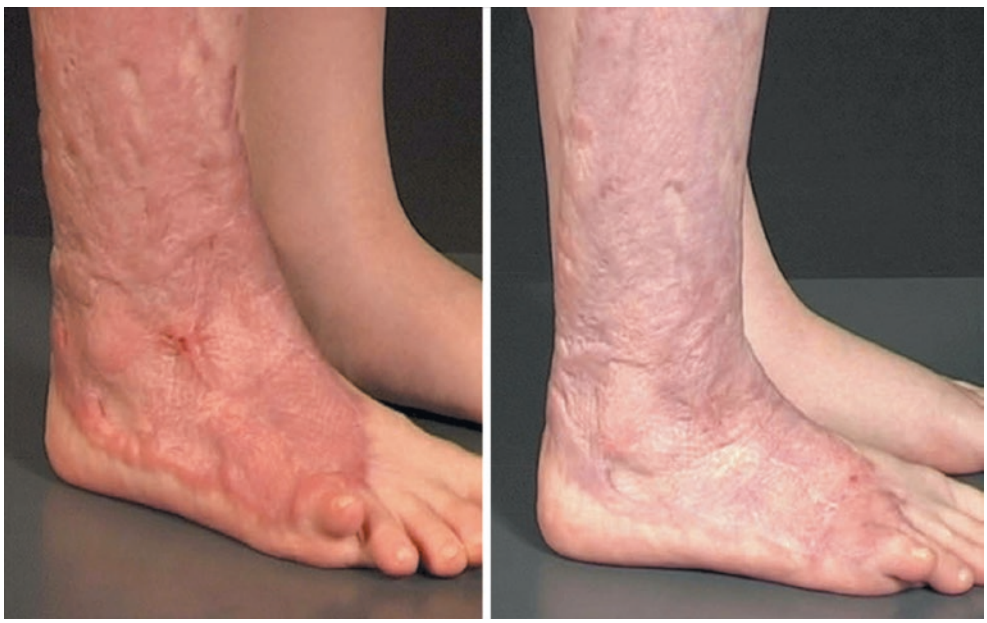


Fig. 26.10 A burn injury of the dorsum of the foot and the lateral lower leg was initially treated by transplantation of meshed split skin grafts. Several months after defect coverage, the patient suffered from problems with plantar flexion of the foot and hyperextension deformity of the fifth toe. Since hyperextension was mild and metatarsophalangeal luxation was absent, treatment of the toe consisted of scar release and transplantation of a full skin graft. The plantar flexion of the foot could be improved by scar release by a Z-plasty on the proximal dorsum

mities of bones and joints, such as equinus or equinovarus deformity [84, 96]. In these cases, scar release and skin grafting are insufficient. Osteotomy, tendon lengthening, and soft tissue flaps must be considered. The contracture recurrence rate in children's feet, unlike other parts of their body, does not differ between full-thickness skin grafts, unmeshed split-thickness skin grafts, or meshed split-thickness skin grafts [73, 97].

26.11 Summary and Conclusion

Thermal injuries to the feet may not be underestimated because a lack of their function can dramatically reduce the patients' quality of life. The importance of adequate treatment becomes obvious when we think of how many of our daily activities depend on ambulation. Thermal wounds can occur in a wide range of variations. This makes individual evaluation of each case necessary. Accurate assessment of the wounds and of the overall situation of the patient is important to choose the right treatment. For the choice of reconstruction the location of the defect on the foot plays an important role. Especially weight-bearing areas are challenging fields. Profound knowledge of the foot's complex anatomy and availability of the full armamentarium of therapeutic options are prerequisites for a successful treatment. Hence, treatment should be managed by specialized burn care facilities. Long-term pain-free ambulation is the goal of therapy. Depending on the extent of the injury, treatment can reach from conservative approaches with wound dressings to multi-step operational approaches. In the acute phase of treatment, cleaning of the wounds and fast coverage with skin or dermal replacements are intended. Similar to other burn wounds, skin grafts play an important role in covering defects, which do not expose deeper structures. If defects are deeper or more complicated, the surgeon can choose between different options of local, regional, and free flaps. Treating burn wounds of children's feet is different not only because the regenerative potential is higher but also because special attention must be paid to the prevention of long-time sequelae such as contraction deformities.

References

1. Hemington-Gorse S, Pellard S, Wilson-Jones N, Potokar T. Foot burns: epidemiology and management. Burns. 2006;33:1041–5.
2. Shah BR. Burns of the feet. Clin Podiatr Med Surg. 2002;19(1):109–23.
3. Djikstra S, vd Bent MJ, vd Brand HJ, Bakker JJ, Boxma H, Tjong Joe Wai R, Berghout A. Diabetic patients with foot burns. Diabet Med. 1997;14:1080–3.
4. Winfield RD, Chen MK, Langham MR Jr, Kays DW, Beierle EA. Ashes, embers, and coals: significant sources of burn-related morbidity in children. J Burn Care Res. 2008;29(1):109–13.
5. Sayampanathan SR, Ngim RC, Foo CL. Fire walking in Singapore: a profile of the burn patient. J R Coll Surg Edinb. 1997;42(2):131–4.
6. Harold E. Clinical anatomy. 11th ed. Maiden, Oxford, Carlton: Blackwell; 2006. p. 247.
7. Attinger CE, Evans KK, Bulan E, Blume P, Cooper P. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions and revascularization. Plast Reconstr Surg. 2006;117(7):261–93.
8. Harold E. Clinical anatomy. 11th ed. Maiden, Oxford, Carlton: Blackwell; 2006. p. 248.
9. Schünke M, Schulte E, Schumacher U. Prometheus Lernatlas der Anatomie. Allgemeine Anatomie und Bewegungssystem. Stuttgart, New York: Georg Thieme; 2005. p. 468.
10. Schünke M, Schulte E, Schumacher U. Prometheus Lernatlas der Anatomie.Allgemeine Anatomie und Bewegungssystem. Stuttgart, New York: Georg Thieme; 2005. p. 421.
11. Giunta RE, Kamholz LP, Mailander P. Management of burn injuries. Handchir Mikrochir Plast Chir. 2007;39(5):301.
12. Hidalgo DA, Shaw WW. Reconstruction of foot injuries. Clin Plast Surg. 1986;13(4):663–80.
13. Harold E. Clinical anatomy. 11th ed. Maiden, Oxford, Carlton: Blackwell; 2006. p. 213.
14. Giunta RE, Geisweid A, Feller AM. The value of preoperative Doppler sonography for planning free perforator flaps. Plast Reconstr Surg. 2000;105(7):2381–6.
15. Hallock GG. Severe lower extremity injury. The rationale for micro-surgical reconstruction. Orthop Rev. 1986;15:465.
16. Gidumal R, Carl A, Evanski P, Shaw W, Waugh TR. Functional evaluation of nonsensate free flaps to the sole of the foot. Foot Ankle. 1986;7:118.
17. Durham JW, Saltzman CL, Steyers CM, Miller BA. Outcome after free flap reconstruction of the heel. Foot Ankle. 1994;15:250.
18. Sonmez A, Bayramicli M, Sonmez B, Numanoglu A. Reconstruction of the weight-bearing surface of the foot with nonneurosensory free flaps. Plast Reconstr Surg. 2003;111:2230–6.
19. Daeschlein G, Assadian O, Bruck JC, Meinl C, Kramer A, Koch S. Feasibility and clinical applicability of polihexanide for treatment of second-degree burn wounds. Skin Pharmacol Physiol. 2007;20:292–6.
20. Zachary LS, Heggers JP, Robson MC, Smith DJ Jr, Maniker AA, Sachs RJ. Burns of the feet. J Burn Care Rehabil. 1987;8(3):192–4.
21. Goldberg DP, Kucan JO, Bash D. Reconstruction of the burned foot. Clin Plast Surg. 2000;27(1):145–61.
22. Mathes SJ, Alpert BS, Chang N. Use of the muscle flap in chronic osteomyelitis: experimental and clinical correlation. Plast Reconstr Surg. 1982;69(5):815–29.
23. Mathes SJ, Feng LJ, Hunt TK. Coverage of the infected wound. Ann Surg. 1983;198(4):420–9.
24. Saffle JR. Closure of the excised burn wound: temporary skin substitutes. Clin Plast Surg. 2009;36(4):627–41.
25. Rennekampff HO. Skin graft procedures in burn surgery. Unfallchirurg. 2009;112(6):543–9.
26. Busche MN, Herold C, Schedler A, Knobloch K, Vogt PM, Rennekampff HO. The Biobrane glove in burn wounds of the hand. Evaluation of the functional and aesthetic outcome and comparison of costs with those of conventional wound management. Handchir Mikrochir Plast Chir. 2009;41(6):348–54.
27. Grube BJ, Engrav LH, Heimbach DM. Early ambulation and discharge in 100 patients with burns of the foot treated by grafts. J Trauma. 1992;33(5):662–4.
28. Roka J, Karle B, Andel H, Kamolz L, Frey M. Use of V. A C therapy in the surgical treatment of severe burns: the Viennese concept. Handchir Mikrochir Plast Chir. 2007;39(5):322–7.

29. Alison WE Jr, Moore ML, Reilly DA, Phillips LG, McCauley RL, Robson MC. Reconstruction of foot burn contractures in children. J Burn Care Rehabil. 1993;14(l):34–8.
30. Machens HG, Berger AC, Mailander P. Bioartificial skin. Cells Tissues Organs. 2000;167(2–3):88–94.
31. Potparic Z, Rajacic N. Long-term results of weight-bearing foot reconstruction with non-innervated and reinnervated flaps. Br J Plast Surg. 1997;50(3):176–81.
32. May JW Jr, Halls MJ, Simon SR. Free microvascular muscle flaps with skin graft reconstruction of extensive defects of the foot: a clinical and gait analysis study. Plast Reconstr Surg. 1985;75(5):627–41.
33. Haug MD, Valderrabano V, Rieger UM, Pierer G, Schaefer DJ. Anatomically and biomechanically based treatment algorithm for foot and ankle soft tissue reconstruction. Handchir Mikrochir Plast Chir. 2008;40(6):377–85.
34. Machens HG, Kaun M, Lange T, Egbers HJ, Wenzl M, Paech A, Reichert B, Mailander P. Clinical impact of operative multidisciplinarity for severe defect injuries of the lower extremity. Handchir Mikrochir Plast Chir. 2006;38(6):403–16.
35. McCraw JB, Furlow LT Jr. The dorsalis pedis arterialized flap. A clinical study. Plast Reconstr Surg. 1975;55(2):177–85.
36. Ishikawa K, Isshiki N, Suzuki S, Shimamura S. Distally based dorsalis pedis island flap for coverage of the distal portion of the foot. Br J Plast Surg. 1987;40(5):521–5.
37. Schwabegger A, Wechselberger G. Distally based dorsalis pedis island flap for distal lateral electrical burn of the big toe. Burns. 1997;23(5):459.
38. Hayashi A, Maruyama Y. Reverse first dorsal metatarsal artery flap for reconstruction of the distal foot. Ann Plast Surg. 1993;31(2):117–22.
39. Goldberg DP, Kucan JO, Bash D. Reconstruction of the burned foot. Clin Plast Surg. 2000;27(1):145–161.
40. Shanahan RE, Gingrass RP. Medial plantar sensory flap for coverage of heel defects. Plast Reconstr Surg. 1979;64(3):295–8.
41. Uygur F, Duman H, Ulkiir E, Noyan N, Celikoz B. Reconstruction of distal forefoot burn defect with retrograde medial plantar flap. Burns. 2008;34(2):262–7.
42. Masquelet AC, Romana MC. The medialis pedis flap: a new fasciocutaneous flap. Plast Reconstr Surg. 1990;85(5):765–72.
43. Landi A, Soragni O, Monteleone M. The extensor digitorum brevis muscle island flap for soft-tissue loss around the ankle. Plast Reconstr Surg. 1985;75(6):892–7.
44. Kurata S, Hashimoto H, Terashi H, Honda T, Takayasu S. Reconstruction of the distal foot dorsum with a distally based extensor digitorum brevis muscle flap. Ann Plast Surg. 1992;29(l):76–9.
45. Ger R. The clinical anatomy of the intrinsic muscles of the sole of the foot. Am Surg. 1986;52(5):284–5.
46. Pap GS. Hot metal burns of the feet in foundry workers. J Occup Med. 1966;8(10):537–9.
47. Ger R. The management of chronic ulcers of the dorsum of the foot by muscle transposition and free skin grafting. Br J Plast Surg. 1976;29(2):199–204.
48. Masquelet AC, Beveridge J, Romana C, Gerber C. The lateral supramalleolar flap. Plast Reconstr Surg. 1988;81(1):74–81.
49. Jeng SF, Wei FC. Distally based sural island flap for foot and ankle reconstruction. Plast Reconstr Surg. 1997;99(3):744–50.
50. Sood R, Achauer BM. Achauer and Sood's burn surgery, reconstruction and rehabilitation. New York: Elsevier Health Sciences; 2006. p. 349–50.
51. Grabb WC, Argenta LC. The lateral calcaneal artery skin flap. Plast Reconstr Surg. 1981;68:723.
52. Jackson IT, Scheker L. Muscle and myocutaneous flaps on the lower limb. Injury. 1982;13(4):324–30.
53. Ger R. The management of open fracture of the tibia with skin loss. J Trauma. 1970;10(2):112–21.
54. Sood R, Achauer BM. Achauer and Sood's burn surgery, reconstruction and rehabilitation, vol. 330. New York: Elsevier Health Sciences; 2006.
55. Morrison WA, Shen TY. Anterior tibial artery flap: anatomy and case report. Br J Plast Surg. 1987;40(3):230–5.
56. Hong G, Steffens K, Wang FB. Reconstruction of the lower leg and foot with the reverse pedicle posterior tibial fasciocutaneous flap. Br J Plast Surg. 1989;42:512.
57. Mozafari N, Moosavizadeh SM, Rasti M. The distally based neurocutaneous sural flap: a good choice for reconstruction of soft tissue defects of lower leg, foot and ankle due to fourth degree burn injury. Burns. 2008;34:406–11.
58. Koul AR, Patil RK, Philip V. Extensor digitorum brevis muscle flap: modified approach preserving extensor retinaculum. J Trauma. 2009;66(3):835–9.
59. Hidalgo DA, Shaw WW. Anatomic basis of plantar flap design. Plast Reconstr Surg. 1986;78(5):627–36.
60. Harrison DH, Morgan BD. The instep island flap to resurface plantar defects. Br J Plast Surg. 1981;34(3):315–8.
61. Morrison WA, Crabb DM, O'Brien BM, Jenkins A. The instep of the foot as a fasciocutaneous island and as a free flap for heel defects. Plast Reconstr Surg. 1983;72(l):56–65.
62. Bostwick J III. Reconstruction of the heel pad by muscle transposition and split skin graft. Surg Gynecol Obstet. 1976;143(6):973–4.
63. Scheflan M, Nahai F, Hartrampf CR. Surgical management of heel ulcers—a comprehensive approach. Ann Plast Surg. 1981;7(5):385–406.
64. Yoshimura Y, Nakajima T, Kami T. Distally based abductor digiti minimi muscle flap. Ann Plast Surg. 1985;14(4):375–7.
65. Hartrampf CR Jr, Scheflan M, Bostwick J III. The flexor digitorum brevis muscle island pedicle flap: a new dimension in heel reconstruction. Plast Reconstr Surg. 1980;66(2):264–70.
66. Ikuta Y, Murakami T, Yoshioka K, Tsuge K. Reconstruction of the heel pad by flexor digitorum brevis musculocutaneous flap transfer. Plast Reconstr Surg. 1984;74(1):86–96.
67. Beveridge J, Masquelet AC, Romana MC, Vinh TS. Anatomic basis of a fascio-cutaneous flap supplied by the perforating branch of the peroneal artery. Surg Radiol Anat. 1988;10(3):195–9.
68. Okazaki M, Ueda K, Kuriki K. Lateral supramalleolar flap for heel coverage in a patient with Werner's syndrome. Ann Plast Surg. 1998;41(3):307–10.
69. Costa H, Malheiro E, Silva A. The distally based tibial myofasciocutaneous island flap for foot reconstruction. Br J Plast Surg. 1996;49:111.
70. Emsen IM. An alternative and new approach to free flap in treatment of calcaneal region and lower third of the lower extremity reconstruction: reverse flow posterior tibial fasciocutaneous skin island flaps. J Trauma. 2008;64(3):780–5.
71. Agarwal P, Raza H. Cross-leg flap: its role in limb salvage. Indian J Orthop. 2008;42(4):439–43.
72. Mir y Mir L. Functional graft of the heel. Plast Reconstr Surg. 1954;14(6):444–50.
73. Waymack JP, Fidler J, Warden GD. Surgical correction of burn scar contractures of the foot in children. Burns Incl Therm Inj. 1988;14(2):156–60.
74. Carriquiry C, Costa MA, Vasconez LO. An anatomic study for the septocutaneous vessels of the leg. Plast Reconstr Surg. 1985;76:354–63.
75. Goldberg JA, Adkins P, Tsai TM. Microvascular reconstruction of the foot: weight-bearing patterns, gait analysis, and long-term follow-up. Plast Reconstr Surg. 1993;92(5):904–11.
76. Sinha AK, Wood MB, Irons GB. Free tissue transfer for reconstruction of the weight-bearing portion of the foot. Clin Orthop. 1989;242:269–71.

77. Lister GD. Use of an innervated skin graft to provide sensation to the reconstructed heel. Plast Reconstr Surg. 1978;62(2):157–61.
78. Wood MB, Irons GB, Cooney WP. Foot reconstruction by free flap transfer. Foot Ankle. 1983;4(1):2–7.
79. Sommerlad BC, McGrouther DA. Resurfacing the sole: long-term follow-up and comparison of techniques. Br J Plast Surg. 1978;31(2):107–16.
80. Rautio J. Patterns of recovery of sensibility in free flaps transferred to the foot: a prospective study. J Reconstr Microsurg. 1990;6(1):37–41.
81. May JW Jr, Lukash FN, Gallico GG III. Latissimus dorsi free muscle flap in lower-extremity reconstruction. Plast Reconstr Surg. 1981;68(4):603–7.
82. Gordon L, Buncke HJ, Alpert BS. Free latissimus dorsi muscle flap with split-thickness skin graft cover: a report of 16 cases. Plast Reconstr Surg. 1982;70(2):173–8.
83. Clark N, Sherman R. Soft-tissue reconstruction of the foot and ankle. Orthop Clin North Am. 1993;24(3):489–503.
84. Shakirov BM, Tursunov BS. Treatment of severe foot burns in children. Burns. 2005;31(7):901–5.
85. Leung PC, Cheng JC. Burn contractures of the foot. Foot Ankle. 1986;6(6):289–94.
86. Dhanraj P, Owiesy F, Phillips LG, McCauley RL. Burn scar contractures of the feet: efficacy of bilateral simultaneous surgical correction. Burns. 2002;28(8):814–9.
87. Krizek TJ, Robson MC, Flagg SV. Management of burn syndactyly. J Trauma. 1974;14(7):587–93.
88. Kucan JO, Bash D. Reconstruction of the burned foot. Clin Plast Surg. 1992;19(3):705–19.
89. Shen YM, Huang L, Hu XH, Li M, Zhang GA. Treatment of burn cicatricial foot drop with Ilizarov fixator. Chin J Burns. 2008;24(4):287–9.
90. Uygur F, Duman H, Ulkur E, Celikoz B. Are reverse flow fasciocutaneous flaps an appropriate option for the reconstruction of severe postburn lower extremity contractures? Ann Plast Surg. 2008;61(3):319–24.
91. Lohmeyer JA, Eich U, Siemers F, Lange T, Mailander P. Psychological and behavioural impairment following thermal injury in childhood. Handchir Mikrochir Plast Chir. 2007;39(5):333–7.
92. Barret JP, Herndon DN. Plantar burns in children: epidemiology and sequelae. Ann Plast Surg. 2004;53(5):462–4.
93. Heimburger RA, Marten E, Larson DL, Abston S, Lewis SR. Burned feet in children. Acute and reconstructive care. Am J Surg. 1973;125(5):575–9.
94. Singh K, Prasanna M. Tangential excision and skin grafting for ash burns of the foot in children: a preliminary report. J Trauma. 1995;39(3):560–2.
95. Gore D, Desai M, Herndon DN. Comparison of complications during rehabilitation between conservative and early surgical management in thermal burns involving the feet of children and adolescents. J Burn Care Rehabil. 1988;9:92–5.
96. Steinwender G, Saraph V, Zwick EB, Uitz C, Linhart W. Complex foot deformities associated with soft-tissue scarring in children. J Foot Ankle Surg. 2001;40(l):42–9.
97. Waymack JP. Release of burn scar contractures of the neck in paediatric patients. Burns Incl Therm Inj. 1986;12(6):422–6.

Burn Reconstruction: Hand

27

Hugo Benito Kitzinger

27.1 Introduction

Although hand burns affect less than 3% of the total body surface area (per hand), they are classified to be severe injuries, which will require the treatment in a specialized burn center. In more than 80% of severely burned patients, the hand is involved [1]. Even if hand burns do not play a major role concerning mortality, they are important factors for a successful reintegration into society and professional life after discharge from hospital [2]. An adequate treatment of the hands is often neglected in the acute phase in favor of the treatment of other body parts or intensive care, but already in this acute phase the course for a successful restoration of hand function is set. Already at the end of the 1940s, surgeons pointed out that failing to mobilize fingers will lead to early stiffening of the fingers and therefore to a loss of hand function [3]. Apart from functional rehabilitation, the aesthetic outcome is also essential since hands cannot, similar to the face, be hidden by clothes so easily.

An optimal hand burn management demands a number of major decisions concerning: necessity of a escharo- or fasciotomy in the early posttraumatic phase, time and type of surgical debridement, type of wound coverage, as well as immobilization and rehabilitation. These efforts primarily aim to restore hand function or as Peacock et al. [4] stated it, the preservation and not the restoration of finger and hand function. Sheridan et al. [5] succeeded in regaining normal hand function in 97% of the patients with superficial dermal burns, whereas in patients with deep dermal and full-thickness burns the success rate was only 81%.

27.2 Mechanisms of the Injury and Anatomic Characteristics

Most of the deep dermal and full-thickness hand burns affect the dorsum of the hand. Full-thickness palmar burns occur relatively rarely, mostly infants, who have just started grabbing things. The low incidence of palmar involvement in adults is due to the fact that hands are used to protect the face against a severe burn trauma and thereby only the dorsal parts of the hands are exposed. Moreover the skin of the palm has a higher tolerance for thermal energy due to its thickness and its well-developed stratum corneum.

There are some special characteristics in the hand's anatomy. Its physical sturdiness, the sensory qualities, and the high capillary density in the stratum papillare are making this skin unique. The proportion between skin surface and tissue volume is extraordinary: there is a disproportional shift in favor of the hand. A volume of 1 cm^3 correlates with a skin surface of 2.5 cm^2, whereas this value decreases already in the forearm to 0.5 cm^2 [6].

There are distinctive differences between the dorsum of the hand and the palm. The skin at the extensor side of the hand is thin and pliable, thus facilitating the flexion of the finger joints. The palmar skin is sturdy and resistant against pressure, contains essential sensory end organs, and adheres strongly to the palmar aponeurosis. A density of Merkel's tactile disks, Meissner's tactile corpuscles, Vater-Pacini's lamellated corpuscles, and free nerve ends are found in the skin. That is the reason why hand burns may cause severe sensory deficits [7]. In contrast to other body parts, blood vessels, tendons, and joints are located very close to the skin surface. This circumstance makes these structures extremely vulnerable when exposed to high thermal energy.

H. B. Kitzinger (✉)
Hand Center Vienna, Vienna, Austria
e-mail: hugo@kitzinger.de

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_27

27.3 Aims and Principles of Treatment

An optimal treatment of a hand burn can only be provided by a close interdisciplinary co-operation among surgeons, physiotherapists, occupational therapists, psychologists, and motivated health care personnel. A wound healing within 2 weeks must be the primary aim in order to achieve a well-functioning hand, which will facilitate a rapid reintegration of the burn patient into society and normal life. According to Robson et al. [8], treatment of hand burn trauma can be divided into aims and principles.

The key aims are:
- Prevention of additional or deeper injuries
- Rapid wound closure
- Preservation of active and passive motion
- Prevention of infection or loss of functional structures
- Early functional rehabilitation

The following aims should be gained by applying basic treatment principles:

- Determination of dimension and depth of the burn
- Escharotomy (if indicated)
- Application of adequate wound dressings
- Decision upon conservative or surgical treatment
- Surgical management (necrosectomy, skin grafts, skin substitutes, free flaps, etc.)
- Early hand therapy with splinting
- Functional rehabilitation by early active and passive motion due to physiotherapy
- Secondary and tertiary corrections (if indicated)

27.4 Determination of Burn Depth

After stabilizing the burn patient's vital functions, a clinical examination should provide exact information about the severity of trauma (e.g., burn depth, secondary injuries). Clinical assessment remains the most frequent technique to measure the depth of a burn wound although this has been shown to be accurate in only 60–75% of the cases, even when carried out by an experienced burn surgeon. But there are more and more modalities available, which are useful to provide an objective assessment of burn wound depth. These modalities range from simple clinical evaluation to punch biopsy and histology and to various perfusion measurement techniques such as thermography, vital dyes, video angiography, video microscopy, and laser Doppler techniques [9–12].

27.5 Escharotomy

27.5.1 Indication for Escharotomy

The maintenance of perfusion is the first and foremost aim in the acute treatment of hand burns. After cleaning of the affected sites assessment for circumferential deep partial-thickness or full-thickness injuries is performed as they can act as a tourniquet and compromise distal perfusion of the extremities. When determining the need for escharotomy, it should be noted that edema can increase for up to 36 h after injury due to fluid resuscitation and the increased vascular permeability. Thus the risk for the development of a compartment syndrome in massive burns is much higher. In such cases a prophylactic escharotomy might be indicated. The evaluation of a burned hand must always be carried out in the context of the other burned areas [5]. In case fingers are circumferentially firmly strained regardless of burn depth, the dorsum of the hand appears pale white, the recapillarization of the nail bed is deregulated, and a loss of sensibility can be observed, an escharotomy will be inevitable [13] (Fig. 27.1). Missing pulse of the radial or ulnar artery under adequate resuscitation is a sign of a progressed ischemia and requires immediate escharotomy. The escharotomy will lead to a decrease of the compartment pressure and the tissue perfusion will increase. Delayed decompression may cause circulatory disorders, nerve damage, extensive muscle necrosis, and a consecutive loss of hand function.

In urgent cases, an escharotomy can be carried out bedside under sterile conditions, but it is recommended to do it in the operating room. An incision on arm and hand is best

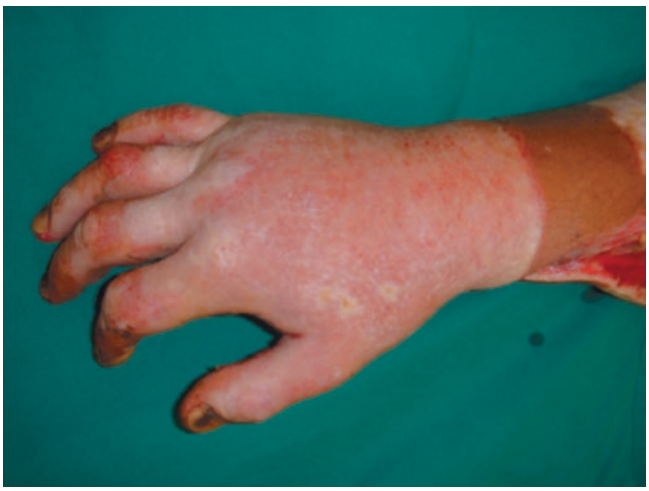


Fig. 27.1 Full-thickness hand burn: fingers are firmly strained and appear pale white

carried out by electrocautery in order to reduce bleeding. During incision attention should be paid to the ulnar nerve at the medial epicondyle, to the superficial branch of the radial nerve and to the tendon of the flexor carpi radialis muscle at the distal forearm due to their superficial location. At the wrist it is obligatory to decompress the carpal tunnel. In the finger area the monopolar needle or a No. 15 blade can be used to split the necrosis completely without injuring the extensor tendons or the lateropalmar neurovascular bundle [14]. In order to achieve as few motion-limiting scars as possible, the line of incision is radial on thumb and little finger and ulnar on the other fingers [15]. This line can be defined well by putting the fingers in maximum flexion, marking the lateral extensions of the finger joint flexor crease, and completing them to a continuous line. Salisbury and Levine [16] have shown that the number of finger amputations could be significantly reduced by carrying out an adequate digital escharotomy.

An ischemic necrosis of the intrinsic muscles is accompanied by a significant functional impairment because the fingers will develop an intrinsic minus position [17]. In deep hand burns and in case of an intrinsic tightness, the intrinsic compartment should always be decompressed. An intrinsic tightness is diagnosed by fixing the metacarpophalangeal joint in a 0° position and flexing the finger passively in the proximal or distal inter-phalangeal joints. Resistance is an indication for intrinsic tightness, which requires an additional fasciotomy of the intrinsic muscles. For that purpose the area between the metacarpals II/III and IV/V is incised longitudinally whereby the extensor tendons remain covered. From there a fasciotomy of the intrinsic compartments can be carried out easily. To prevent desiccation of the uncovered structures, wounds are covered temporarily by skin substitutes.

Formally, fasciotomy has to be distinguished from escharotomy. In an escharotomy, burn eschar is incised to the subcutaneous fat tissue, whereas in case of a fasciotomy the muscle fascia is also released. This intervention is indicated in case an escharotomy did not provide the desired increase in perfusion or if the patient suffers from electrical burn injuries [15].

27.6 Treatment of Edema

Immediately after a burn trauma it is reasonable to cool the hand by applying cold water in order to eliminate the high thermal energy and to reduce pain. In most favorable cases cooling also reduces the edema formation and thereby burn wound progression [18]. Massive burns should not be cooled in order to avoid a massive decrease of body temperature, which will lead consecutively to burn wound progression. An effective and simple way to prevent or to decrease the development of edema is a continuous elevation of the hand above heart level.

27.7 Splinting

Positioning of the burned hand is critical prior to definitive treatment but is often neglected in the acute setting of severely injured patients. As edema and inflammation ensue, fibrosis and scarring will occur over time and will result in joint contractures. This is extremely evident in the characteristic burn claw deformity. Especially in patients with severe burns the incidence of edema is significantly increased. The reason for the intrinsic minus position of the hand is an increased fluid accumulation in the joints with distension of the joint capsule and imbibition of the collateral ligaments and subsequent ligament contraction. The intrinsic minus position is a wrist flexion with a simultaneous hyperextension of the metacarpophalangeal joints (MCP), a flexion of the proximal and distal interphalangeal joints [19], and a thumb adduction. This defective position emanates in the MCP joints. If the MCP joints are extended, joint capsule and collateral ligaments shrink [20]. The joint is relatively unstable with a high degree of freedom for rotation, abduction, and adduction. The contact areas of the corresponding joint surfaces are minimized. The combination of these factors will provide the biggest volume capacity for interstitial fluid accumulation. In flexion, the collateral ligaments are tightened with maximum contact of joint surfaces, which reduces the possibility of fluid accumulation in the joint. In the presence of the burn edema, the intra-articular fluid increase causes an extension of the MCP joint, similar to a hydraulic pump. In this position, the tension of the flexors increases whereas the tension of the extensors decreases. This causes a flexion in the proximal as well as in the distal IP joints. In contrast to the MCP joints, the volumetric capacity of the IP joints in flexion and extension is nearly identical, so that there is no hydraulic effect. Thus the flexion of the IP joints is the immediate consequence of the extension of the MCP joints (Fig. 27.2).

So, the therapeutic principle must be an optimal positioning of the hand in order to avoid permanent contractures and deformities [21]. Ideally, a customized thermoplastic splint should be applied in intrinsic plus position already on the day of injury. The hand should be slightly extended in the wrist with 20°–30°, flexed in the MCP joint with approximately 80° and completely extended in the IP joints. This position maintains tension across the collateral ligaments, decreasing the likelihood of contractures. The thumb is placed in maximum abduction to prevent an adduction contracture.

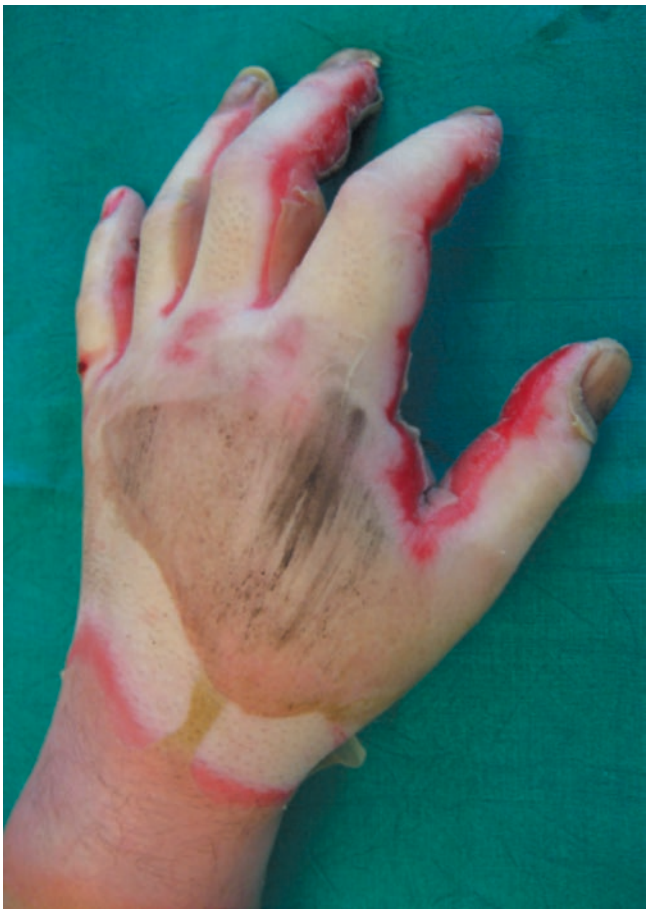


Fig. 27.2 Edema with hyperextension of the MCP joints and flexion in the IP joints

In awake and cooperative patients a nighttime orthosis is often sufficient. Active and passive exercises with the hand should be carried out twice a day. Only in deep partial-thickness or full-thickness burns, in which there is suspicion of an injured central extensor slip over the PIP joint, an aggressive early hand therapy should be avoided to prevent a rupture of the central slip and thus a Boutonnière deformity.

27.8 Wound Management

The acute burn wound has to be cleaned and debrided. Until some years ago, blisters were not removed because it was believed that they serve as a biological wound dressing. Recent studies showed though that the blister's secretion contains prostaglandins and other pro-inflammatory cytokines as for example interleukin-6 and interleukin-8 [22]. Therefore, it is recommended to remove the blisters or at least the fluids [23].

First degree hand burns are treated with a topical agent for a few days. It is important to familiarize the patient with the immediate active mobilization of the hand.

Superficial partial-thickness burns require dressings, which protect the wound against infection and reduce pain at the same time. In the first days after trauma and until final assessment of the burn depth, paraffin gauze in combination with a moist antiseptic dressing (e.g., biguanide) provides maximum mobilization of the hand and avoids painful adherence to the wound. If nonsurgical treatment is possible modern local agents, like Mepilex-Ag®, Mepitel®, or Acticoat®, are applied [24]. These dressings have better healing properties, cause less pain because of less dressing changes, and therefore increase patient satisfaction compared to silver sulfadiazine. Goodwin et al. [25] showed that a hypertrophic scar formation is very rare in these cases and that the functional outcome is generally very good. Accordingly silver sulfadiazine is no longer the first choice in treating burn wounds [26].

It is particularly important to keep hand dressings as thin as possible in order to allow mobilization. This also includes the supply of thumbs and fingers with tube dressings.

27.9 Surgical Treatment

As soon as the burn depth can be determined—usually on the second or third day post trauma—the wounds should be excised and covered [15]. During the first 5 days, the burn wound is defined as "sterile" and thus optimal for surgery. After these 5 days there is a higher risk for infection and graft failure [27]. In case of the fact that a surgical intervention is not possible in the initial phase, it is recommended to postpone the coverage until the infection has been treated sufficiently. Adequate splinting and physical therapy should be provided in order to achieve results nearly as good as after early surgical debridement and coverage [28].

The surgical therapy that is most often applied on hand burns with deep dermal burns is tangential excision: the necrotic skin is abraded in layers until capillary hemorrhage occurs. In isolated hand burns the blood loss can be reduced significantly by use of a tourniquet. In these cases, the surgeon cannot rely on the capillary bleeding but has to pay attention to other characteristics as the whitish color of vital dermis and the yellow color of vital fat tissue. If thrombosis of the subdermal vessels is evident, the plane of excision has to be deeper at the fascial level.

27.10 Methods of Coverage

27.10.1 Skin Grafting

The most performed coverage technique of the hand is autologous split-thickness skin grafting applied as unmeshed sheet graft [29]. Fluid retention underneath the graft with the risk of graft loss can be avoided by scarifying with a No. 11 blade (Fig. 27.3a–c). Alternatively, split-thickness skin grafts can be processed into mesh grafts with various expansion levels or used in Meek technique [30]. These techniques

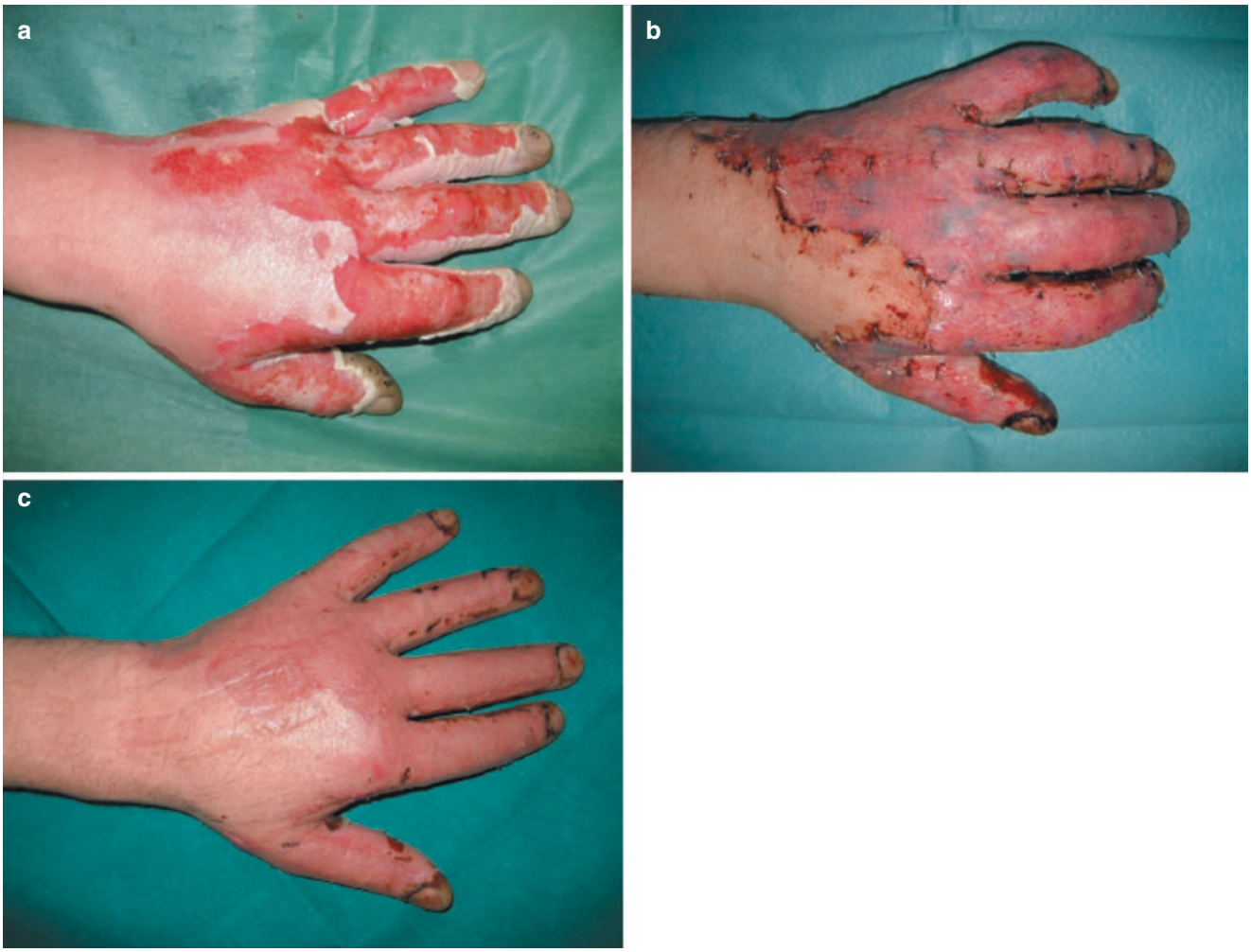


Fig. 27.3 (**a**) Deep dermal hand burn prior to surgery. (**b**) After debridement and split-thickness skin graft. (**c**) Early result three weeks after surgery

should only be applied in case that there are not enough autologous donor sites available. In comparison with mesh grafts, sheet grafts show a lower tendency to shrink and provide better aesthetic outcome. In the postoperative stage the hands are put in intrinsic plus position by a palmar forearm splint; hand therapy will be determined as early as possible dependent on the wound condition.

27.10.2 Skin Substitutes

In recent years dermal skin substitutes have been used as an alternative to conventional skin grafting in partial-thickness burn wounds and became first choice. Most of the superficial partial-thickness and deep partial-thickness hand burns are treated nowadays with biosynthetic wound dressings like Biobrane® or Suprathel® after tangential excision. In full-thickness burn wounds and when soft tissue donor sites are limited or tendons are left without coverage, the use of dermal matrices is a valuable alternative. Because they serve only to replace the dermal layer, epidermal coverage in the form of thin split-thickness skin grafts is still required (which results in faster donor site healing). They provide stable coverage with minimal scarring, good mobility, and acceptable appearance [31].

27.10.3 Skin Substitutes for Superficial Burn Injuries

Biobrane® is one of the most widely used biosynthetic wound dressing used in the treatment of superficial partial-thickness burns. It is constructed of a semipermeable silicone film with a nylon fabric partially embedded into the film. Porcine collagen type I is also incorporated. Ready-made Biobrane® gloves facilitate the application once the hand is debrided. Benefits of Biobrane® are pain reduction, avoiding dressing changes, possibility of immediate active and passive mobilization of the hand, and continuous observation of the wound due to the transparent material. After complete epithelialization, the film can be easily removed [32]. Downsides of this

material are the relatively high costs and the fact that fluid accumulations underneath the membrane should be drained in order to avoid infection [33].

Suprathel® is a copolymer consisting of polylactide, trimethylene carbonate, and caprolactone. It is supplied as a membrane, whose properties are similar to those of Biobrane®. Benefits of Suprathel® are painless dressing changes, faster epithelialization, and the possibility of an early hand therapy [34]. Studies have demonstrated that Suprathel® provides good healing not only to superficial partial-thickness wounds but also to deep partial-thickness wound with small areas of full-thickness burns [35]. After healing Suprathel® will degrade.

27.10.4 Acellular Dermal Substitutes for Deep Burn Injuries

Integra® has been the most popular dermal equivalent in the field of permanent dermal replacements. Integra® is a bilaminate membrane consisting of bovine collagen and glycosaminoglycans. Integra® must be applied in a two-step procedure with a split-thickness skin grafting after incorporation of Integra® after 2–3 weeks. The prolonged immobilization of the hand and the elevated risk of infection are the reasons why today Integra® is used primarily in the field of postburn reconstruction than in the management of the acutely burned hand [36].

Matriderm® is a 1 mm thick membrane consisting of native bovine collagen and elastin. A distinctive advantage of Matriderm® is that it can be applied in a one-stage procedure simultaneously with thin split-thickness autografts. This quality expedites wound healing, improves functional outcome by minimizing the need for immobilization, and decreases costs [31]. Long-term results show excellent appearance, pliability, and hand function with similar elasticity and protective properties compared with normal skin (Fig. 27.4a–d) [37, 38].

27.10.5 Allografts

Allogeneic skin is applied in those cases where the period between trauma and definite coverage has to be bridged. The

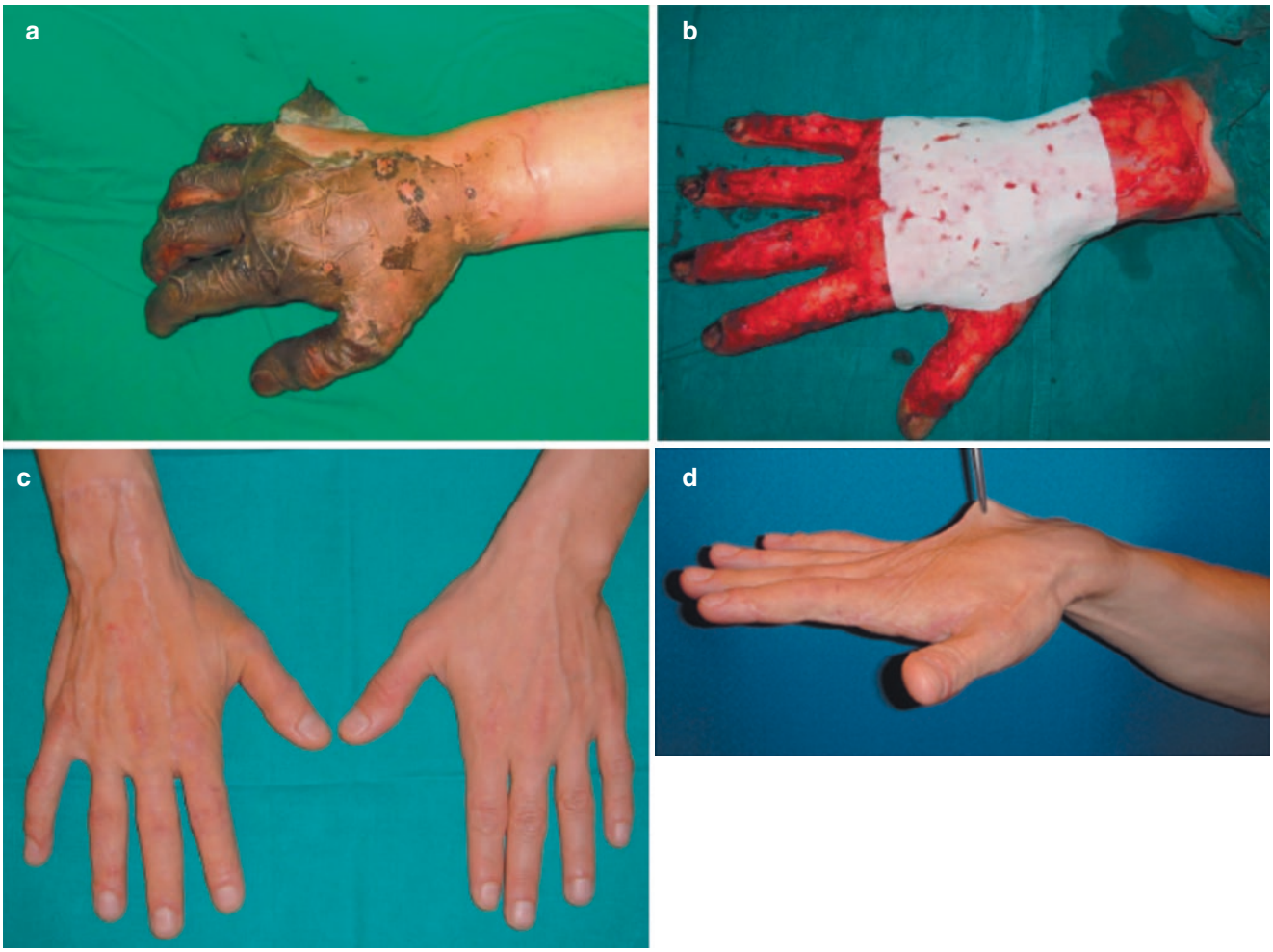


Fig. 27.4 (**a**) Full-thickness burn of the hand. (**b**) After debridement and application of Matriderm®. (**c**) Long-term result (1 year after surgery) after single step reconstruction and compression therapy. (**d**) Skin elasticity

advantage of allogeneic skin is the fact that it is a biological scaffold which supports wound bed preparation. Moreover it reduces the risk of infection and protects the wound from water loss [19].

27.11 Palm Burns

Burns to the palm usually result from direct contact with a hot surface such as a radiator or iron especially in toddlers. Surgical intervention is very rarely indicated because the epidermis is thick and the dermis rich in adnexal elements. A surgical debridement is difficult to carry out due to the palm's distinct anatomy and the tight coherence to the palmar aponeurosis. A substitution is only applicable to a limited degree. These factors justify a conservative treatment for 3–4 weeks. In case of the fact that a necrosectomy is required, a sparing debridement is important. Since the palm is used excessively in daily life, thick split-thickness in adults or full-thickness skin grafts in children should be used [39]. After surgical treatment and complete wound healing a compression hand glove has to be worn for at least 6 months. Post-burn contractures of the growing hand remain a challenging problem and often require further reconstructive surgery. Especially deformities of the web space (web space contracture, syndactylism, and adduction contracture) are common following deep palmar burns.

27.12 Exposed Joints

The areas above the extensor-sided PIP joints must be particularly well observed. Boutonnière deformities are often seen at the PIP joints in deeper burns. The central extensor slip denaturizes due to the direct heat damage or desiccates following a longer period of exposition. That makes the lateral bands move into palmar direction below the axis of rotation of the PIP joint, which makes them to PIP joint flexors instead of extensors. So, an attempted extension causes a flexion of the PIP joint. Therefore in the acute setting all attempts are made at preserving the paratenon of the extensor surface and the areolar tissue surrounding the joint capsule to allow for acceptance of a skin graft. In case of skin graft breakdown the risk of a secondary Boutonnière deformity can be reduced with stable flap coverage like a dorsal metacarpal artery flap (DMCA-flap), which is even possible in dorsally grafted hands [40]. Whereas there are numerous treatments for Boutonnière deformity in a non-burned hand, attempts to reconstruct this deformity in a burned hand with scarred tissue and tendons are often not promising. A good alternative is the arthrodesis of the joint in functional position [41]. Functionally inhibiting defective positions of the DIP joints are rare but can be corrected by arthrodesis if necessary.

In case tendons, joints, and bones are also affected by the burn trauma, these structures must be debrided, regardless of their function. A reconstruction which adheres to the principle of the reconstructive ladder is justified in these situations. When choosing flaps, it should be kept in mind that more reconstructive interventions will become necessary later on (Fig. 27.5a–c). Larger defects on the dorsum of the hand with exposed tendons and bones are treated in the acute phase with a reverse radial forearm flap or groin flap, even today. The temporary immobilization of the shoulder joint is well tolerated and the donor site of the flap is cosmetically inconspicuous. In case that the trauma is an isolated severe hand burn or the patient's general condition is stable, free microvascular tissue transfer is an excellent means of coverage [42, 43]. A very pleasing cosmetic outcome is achieved by using lateral upper arm flaps or gracilis muscle flaps (Fig. 27.6a–c). If there is also a peritendineum necessary due to an injured paratenon, solutions can be found by use of serratus anterior fascia or temporoparietal fascia flaps [44].

27.13 Reconstruction

An adequate treatment of the hand burn in the acute phase determines the functional outcome. Due to the complex trauma accompanied by the destruction of highly specific soft tissue, deformities sometimes cannot be avoided even under an optimal therapy. The deformities after hand burn trauma were outlined by Achauer (1987) [1, 45]:

- claw deformity
- palmar contracture
- web space deformity
- hypertrophic scars
- amputation deformity
- nail bed deformity

Numerous surgical techniques have been described for the treatment of these deformities. Generally, the patient suffers from a combination of various deformities. The most frequent problems following hand burns are scar and soft tissue contractures, as they might appear following spontaneously healed deep burns, split-thickness skin grafting of inadequate size and thickness, with missing and/or not correctly positioned splints or inadequate physical therapy.

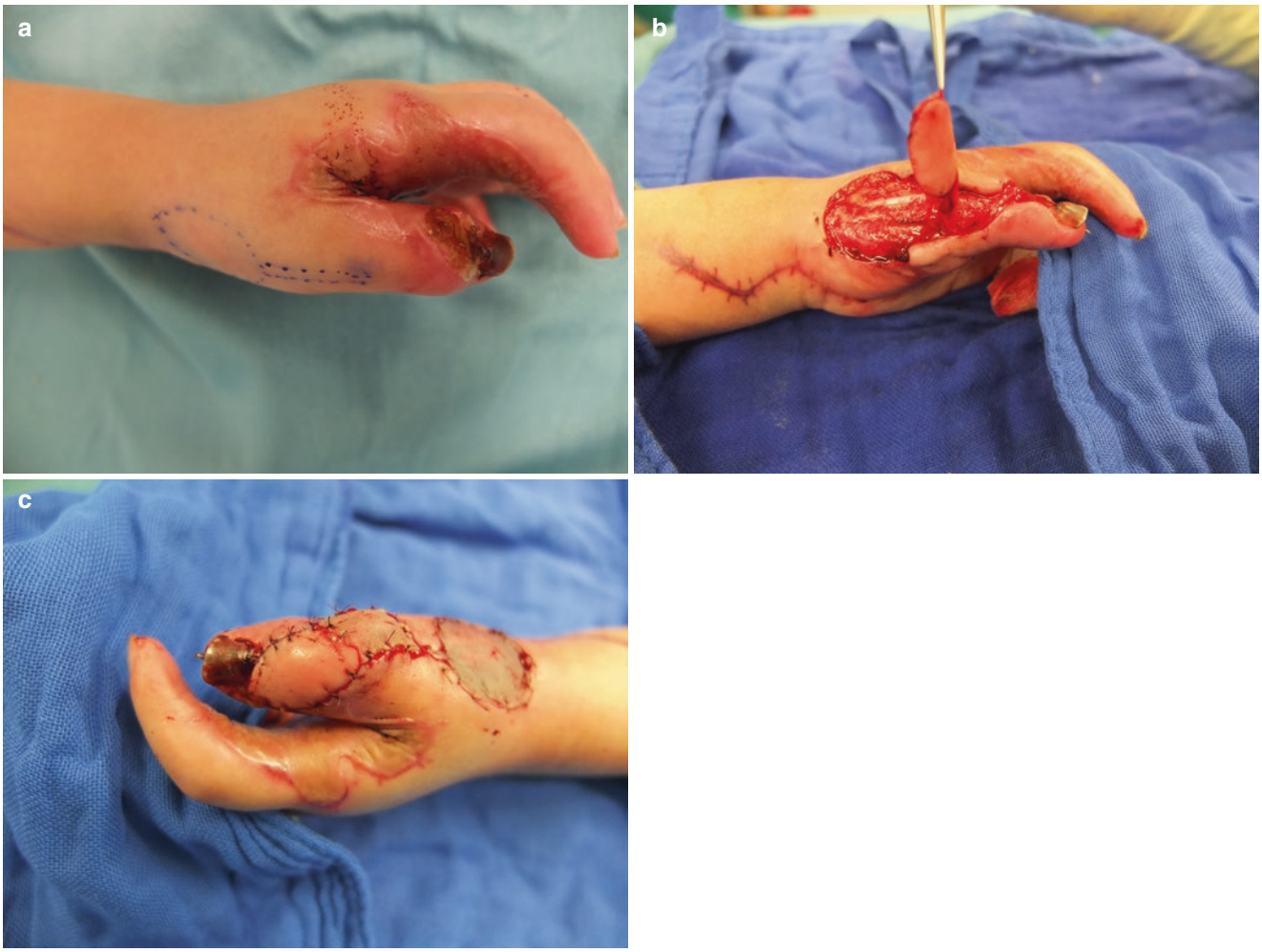


Fig. 27.5 (**a**) Skin breakdown and exposed IP joint of the thumb in a 5-year-old boy after electrical burn injury. (**b**) After debridement the IP joint and extensor tendon are covered with a reverse homodigital dorsal radial flap. (**c**) After inset of the pedicled flap

27.13.1 Claw Deformity

Claw deformities represent some of the most challenging problems to correct after development. Hypertrophic scars on the dorsum of the hand can lead to a hyperextension in the MCP joints, in severe cases to a dorsal dislocation of the joints, and secondary flexion contracture of the PIP joints. The PIP joint deformity in these cases originates from MCP joint hyperextension and not from direct injury to the central slip over the PIP joint.

The surgical management is aimed to reconstruct a rudimentary grasp and consists of wide excision of scar contracture followed by soft tissue coverage for the resultant defect. For this purpose there are numerous options available: split-thickness skin grafts or the combination of a dermal skin substitute like Matriderm® with split-thickness skin grafts showed good results as well as local or microvascular flaps [46]. In case of long-standing fixed deformities with ligament shrinkage of the joints, an arthrolysis of the MCP joints is required. Temporary fixation with Kirschner wires at near 90° is indicated if significant residual tension remains in the longitudinal contraction of the extensor tendons.

27.13.2 Palmar Contractures

Posttraumatic contractures of the palm can develop due to secondary healing or due to inadequate positioning of the hand. They might also occur after a successful primary surgical treatment. There is a high tendency to develop a flexion contracture in the wrist and fingers as well as an adduction contracture in the thumb. These deformities require splinting with slight wrist extension and 80° flexion of the MCP joints with extended PIP and DIP joints (intrinsic plus position) and maximum abduction of the thumb. In case contractures develop, a surgical incision or excision of the scar followed by full-thickness grafting is still the method of choice [47]. Isolated, linear scars with sufficient tissue in the vicinity can

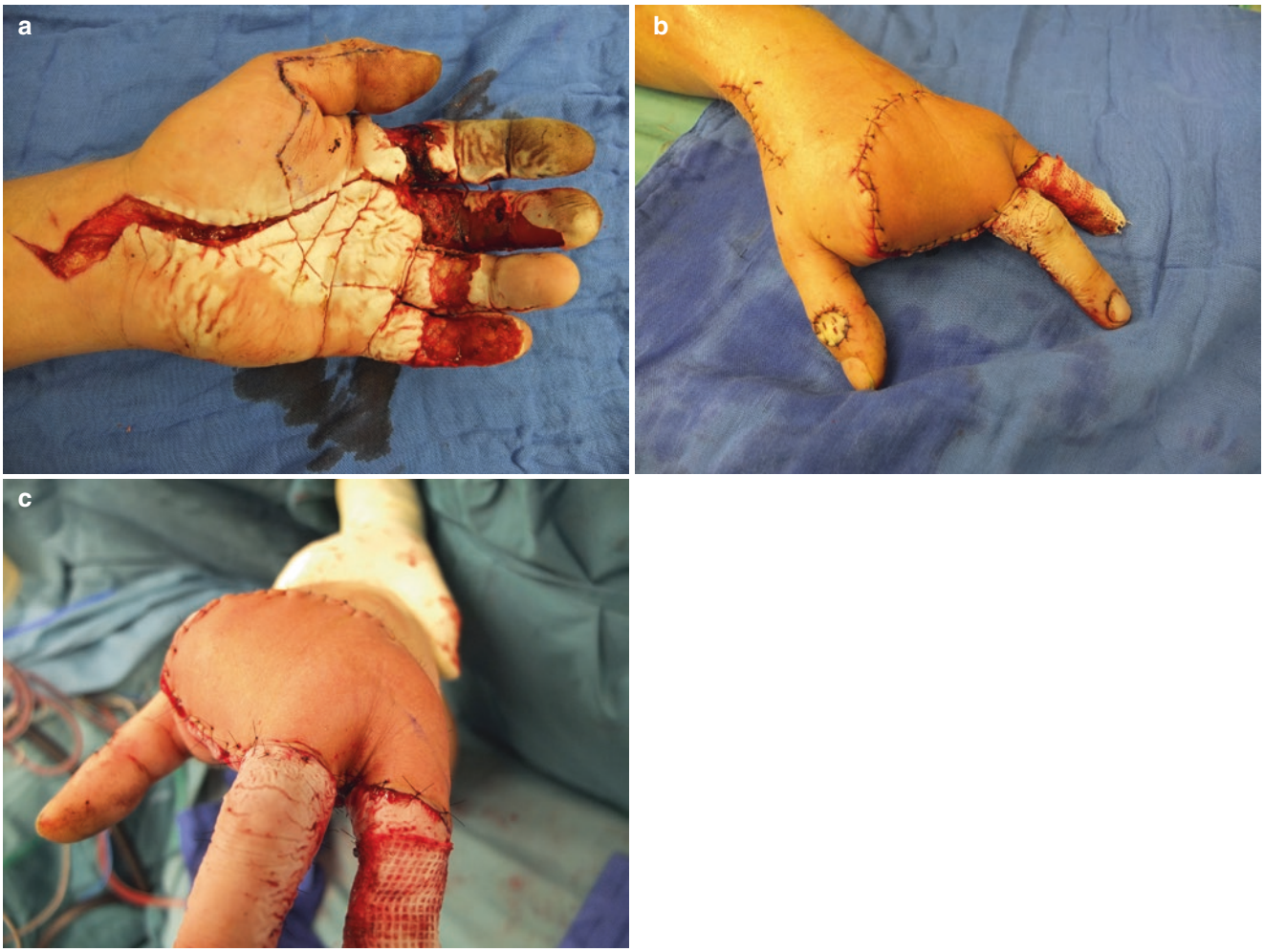


Fig. 27.6 (**a**) Electrical burn injury to the left hand with tissue necrosis at the index and middle finger (after escharotomy). (**b**) After debridement coverage of the exposed tendons and MCP joints with a microvascular lateral arm flap. (**c**) With the thin and pliable fasciocutaneous lateral arm flap, it is possible to reconstruct the fourth web space

be dissolved by one or multiple Z-flap plasties. In the presence of a longer existing scar contracture of the MCP or PIP joint, a release of the periarticular structures, as for example the articular capsule, the collateral tendons, and the palmar plate, is often required to achieve a complete extension of the joint [48]. In these cases a digital ischemia distal of the mobilized joint might occur due to traction of the lateropalmar vessels. For a definitive arthrodesis of the joint, the phalanges have to be shortened in this situation in favor of a functionally beneficial arthrodesis angle with still good perfusion.

An early physiotherapy and particularly a consequent nightly splinting over a period of at least 1 year are the decisive factors in avoiding a contracture relapse.

27.13.3 Web Space Deformities

Syndactylia or web space deformities are commonly observed following conservative treatment of deep burns, but also after surgery. In an intact hand, the web space goes in a 45° angle from the extensor-sided MCP joints in the palmar direction until the center of the basic phalanx. This anatomy can change considerably in burned web spaces. A palmar scar contracture can be distinguished from a dorsal scar contracture, which stretches—like a roof—over the commissure (syndactylia). A correction by using local flaps, which usually consist of variations of Z-plasty, is generally successful [49]. In very severe cases the combination of local flaps and full-thickness grafts is the method of choice [50].

The span of the first web space is of particular importance for the grip function of the hand. In addition to scar contracture, a possible cause for a limited grip function might be adduction contracture of the thumb. Such a contracture is caused by a secondary fibrosis of the adductor pollicis and the first dorsal interosseous muscles. In case of a slight scar contracture, a Z-plasty or butterfly plasty is sufficient. In more distinct contractures, full-thickness grafts are used. Depending on the intraoperative findings an additional

release of the adductor pollicis muscle may be required. In rare and intense cases, a reconstruction of the first web space supported by a flap is necessary.

27.13.4 Hypertrophic Scars

In burn injuries it takes the scars at least 1 year until they are healed and mature. Thus, corrections of scars should be carried out ideally after that period. In case of scar-related, functional constraints, e.g., in the finger joints, an early correction is necessary. Isolated scars with extensive surrounding soft tissue can be dissolved by small, local flaps, e.g., Z-plasty. Alternatively, numerous other flaps, as for example a cross-finger or reversed cross-finger flap or full-thickness grafts, can be used [51, 52]. The application of a tailor-made compression glove, possibly with silicone inlets, can reduce hypertrophic scarring and scar contractures significantly [53, 54].

27.13.5 Amputation Deformity

In severe burns, e.g., caused by high voltage, a loss of thumbs or fingers might be possible. The numerous techniques for a reconstruction of the trauma-related isolated amputation injury can be adopted only to a limited extent for a burned hand. The desired functional outcome is limited due to a combined defect of essential structures. Generally, hand function can be improved by a phalangization with deepening of the web space [55], by a distraction osteogenesis of the metacarpalia [56], by a pollicization [57], or by a toe transfer [45]. The precondition for these interventions is a high quality soft tissue coverage. For this purpose free tissue transfer is often necessary to create a good soft tissue surrounding.

27.13.6 Nail Bed Deformity

A defective nail growth following burn trauma of the hand is frequently observed. In very few cases the reason for that is a direct impairment of the nail bed or the germinative matrix. More often the reason is a secondary contracture of the soft tissue proximal to the nail bed. This leads to an eversion of the nail bed with proximal dislocation and to a loss of contact between dorsal nail matrix and nail and/or eponychium and nail. This causes coarse nails with longitudinal furrows. Injuries of the nail bed occur very often even after slight trauma. The extent of the nail bed eversion and the defective growth are proportional. A defect in the germinative matrix causes a cleft nail and/or a completely missing nail.

Various techniques have been published for the treatment of nail bed eversion, including dissolution of the underlying contractures by wrapping local flaps or skin grafts with subsequent reposition of the nail bed. Bilateral and proximal pedicled skin flaps are often used to create sufficient tissue at the extensor side [58]. Though this causes an unnatural diminution at the donor site, it usually evens out over time.

27.14 Rehabilitation

The best treatment of burn scars is their prevention: an appropriate timing and burn depth specific surgery, and well-fitting pressure garments worn as soon as the skin grafts are stable. Silicone sheets have been useful on the dorsum of fingers and webspaces, placed under the pressure garment glove [59]. Pressure garments are worn 24 h a day at least for an initial period of approximately 6 months in burns with prolonged healing time or burns that have required skin grafting [53]. Subsequent pressure garment use is individualized depending on scar quality and response. The exact mechanism by which pressure garments alter scar formation is not clear but they do improve the quality of scars in both texture and color in the long term [60]. Other scar manipulation techniques, such as steroid injection, can be used as indicated but also laser is used to improve scar quality [61, 62]. Heat and ultrasound are used to assist with joint mobilization. Physical and occupational therapy progress from the acute phase to rehabilitation. Hand therapy continues until function returns to normal or treatment is no longer providing improvement. A maintenance hand therapy program is then continued.

27.15 Summary

Burn injuries very often affect the hands. Small burns can already cause severe deformities accompanied by loss of function. A fast wound closure is of utmost importance because the risk of infection, of hypertrophic scar formation, and contractures increases with a prolonged healing time. Important parts of the treatment include early excision and early coverage within the first few days post trauma. The success of the treatment also depends heavily on infection control and the preservation of the active and passive motion of the hand as well as on an early splinting and functional rehabilitation. The interdisciplinary teamwork of surgeons, physiotherapists and occupational therapists, psychologists, motivated health care personnel, and consequent treatment strategies can contribute to regaining normal hand function.

References

1. Luce EA. The acute and subacute management of the burned hand. Clin Plast Surg. 2000;27(1):49–63.
2. Harvey KD, Barillo DJ, Hobbs CL, Mozingo DW, Fitzpatrick JC, Cioffi WG, et al. Computer-assisted evaluation of hand and arm function after thermal injury. J Burn Care Rehabil. 1996;17(2):176–80; discussion 5.
3. Braithwaite F, Watson J. Some observations on the treatment of the dorsal burn of the hand. Br J Plast Surg. 1949;2(1):21–31.
4. Peacock EE. Management of conditions of the hand requiring immobilization. Surg Clin North Am. 1953;33:1297–309.
5. Sheridan RL, Hurley J, Smith MA, Ryan CM, Bondoc CC, Quinby WC Jr, et al. The acutely burned hand: management and outcome based on a ten-year experience with 1047 acute hand burns. J Trauma. 1995;38(3):406–11.
6. Morel FD. Surgery of the skin. In: Tubiana R, editor. The hand. Philadelphia: WB Saunders; 1961. p. 224–5.
7. Schmidt H-M, Lanz U. Chirurgische Anatomie der Hand. 2., überarb. und aktualisierte Aufl. ed. Stuttgart: G. Thieme; 2003.
8. Robson MC, Smith DJ Jr, VanderZee AJ, Roberts L. Making the burned hand functional. Clin Plast Surg. 1992;19(3):663–71.
9. Jan SN, Khan FA, Bashir MM, Nasir M, Ansari HH, Shami HB, et al. Comparison of Laser Doppler Imaging (LDI) and clinical assessment in differentiating between superficial and deep partial thickness burn wounds. Burns. 2018;44(2):405–13.
10. Heimbach DM, Afromowitz MA, Engrav LH, Marvin JA, Perry B. Burn depth estimation—man or machine. J Trauma. 1984;24(5):373–8.
11. Kamolz LP, Andel H, Haslik W, Donner A, Winter W, Meissl G, et al. Indocyanine green video angiographies help to identify burns requiring operation. Burns. 2003;29(8):785–91.
12. Monstrey S, Hoeksema H, Verbelen J, Pirayesh A, Blondeel P. Assessment of burn depth and burn wound healing potential. Burns. 2008;34(6):761–9.
13. Wong L, Spence RJ. Escharotomy and fasciotomy of the burned upper extremity. Hand Clin. 2000;16(2):165–74, vii.
14. Weinzweig J, Weinzweig N. Burns of the hand and upper extremity. In: Berger RA, Weiss APC, editors. Hand surgery. 2. Philadelphia: LWW; 2004. p. 1073–84.
15. Smith MA, Munster AM, Spence RJ. Burns of the hand and upper limb—a review. Burns. 1998;24(6):493–505.
16. Salisbury RE, Levine NS. The early management of upper extremity thermal injury. In: Salisbury RE, Priutt BA, editors. Burns of the upper extremity. Philadelphia: WB Saunders; 1976. p. 36–46.
17. Salisbury RE, McKeel DW, Mason AD Jr. Ischemic necrosis of the intrinsic muscles of the hand after thermal injuries. J Bone Joint Surg Am. 1974;56(8):1701–7.
18. Raine TJ, Heggers JP, Robson MC, London MD, Johns L. Cooling the burn wound to maintain microcirculation. J Trauma. 1981;21(5):394–7.
19. Philipp K, Giessler GA, Germann G, Sauerbier M. Die akzidentelle thermische Verletzung der Hand. Unfallchirurg. 2005;108(3):179–88.
20. Kitzinger HB, Lanz U. Die Anatomie der Fingergelenke. DAHTH. 2004;6(1):3–11.
21. Prasad JK, Bowden ML, Thomson PD. A review of the reconstructive surgery needs of 3167 survivors of burn injury. Burns. 1991;17(4):302–5.
22. Ono I, Gunji H, Zhang JZ, Maruyama K, Kaneko F. A study of cytokines in burn blister fluid related to wound healing. Burns. 1995;21(5):352–5.
23. Sargent RL. Management of blisters in the partial-thickness burn: an integrative research review. J Burn Care Res. 2006;27(1):66–81.
24. Norman G, Christie J, Liu Z, Westby MJ, Jefferies JM, Hudson T, et al. Antiseptics for burns. Cochrane Database Syst Rev. 2017;7:CD011821.
25. Goodwin CW, Maguire MS, McManus WF, Pruitt BA Jr. Prospective study of burn wound excision of the hands. J Trauma. 1983;23(6):510–7.
26. Heyneman A, Hoeksema H, Vandekerckhove D, Pirayesh A, Monstrey S. The role of silver sulphadiazine in the conservative treatment of partial thickness burn wounds: a systematic review. Burns. 2016;42(7):1377–86.
27. Germann G, Steinau HU. Aktuelle Aspekte der Verbrennungsbehandlung. Zentralbl Chir. 1993;118(5):290–302.
28. Levine BA, Sirinek KR, Peterson HD, Pruitt BA Jr. Efficacy of tangential excision and immediate autografting of deep second-degree burns of the hand. J Trauma. 1979;19(9):670–3.
29. Logsetty S, Heimbach DM. Modern techniques for wound coverage of the thermally injured upper extremity. Hand Clin. 2000;16(2):205–14.
30. Raff T, Hartmann B, Wagner H, Germann G. Experience with the modified Meek technique. Acta Chir Plast. 1996;38(4):142–6.
31. Sando IC, Chung KC. The use of dermal skin substitutes for the treatment of the burned hand. Hand Clin. 2017;33(2):269–76.
32. Lou RB, Hickerson WL. The use of skin substitutes in hand burns. Hand Clin. 2009;25(4):497–509.
33. Weinzweig J, Gottlieb LJ, Krizek TJ. Toxic shock syndrome associated with use of Biobrane in a scald burn victim. Burns. 1994;20(2):180–1.
34. Schwarze H, Kuntscher M, Uhlig C, Hierlemann H, Prantl L, Noack N, et al. Suprathel, a new skin substitute, in the management of donor sites of split-thickness skin grafts: results of a clinical study. Burns. 2007;33(7):850–4.
35. Uhlig C, Rapp M, Hartmann B, Hierlemann H, Planck H, Dittel KK. Suprathel-an innovative, resorbable skin substitute for the treatment of burn victims. Burns. 2007;33(2):221–9.
36. Heitland A, Piatkowski A, Noah EM, Pallua N. Update on the use of collagen/glycosaminoglycate skin substitute-six years of experiences with artificial skin in 15 German burn centers. Burns. 2004;30(5):471–5.
37. Haslik W, Kamolz LP, Manna F, Hladik M, Rath T, Frey M. Management of full-thickness skin defects in the hand and wrist region: first long-term experiences with the dermal matrix Matriderm. J Plast Reconstr Aesthet Surg. 2010;63(2):360–4.
38. Min JH, Yun IS, Lew DH, Roh TS, Lee WJ. The use of matriderm and autologous skin graft in the treatment of full thickness skin defects. Arch Plast Surg. 2014;41(4):330–6.
39. Prasetyono TO, Sadikin PM, Saputra DK. The use of split-thickness versus full-thickness skin graft to resurface volar aspect of pediatric burned hands: a systematic review. Burns. 2015;41(5):890–906.
40. Gregory H, Heitmann C, Germann G. The evolution and refinements of the distally based dorsal metacarpal artery (DMCA) flaps. J Plast Reconstr Aesthet Surg. 2007;60(7):731–9.
41. Souter WA. The problem of boutonniere deformity. Clin Orthop Relat Res. 1974;104:116–33.
42. Sauerbier M, Ofer N, Germann G, Baumeister S. Microvascular reconstruction in burn and electrical burn injuries of the severely traumatized upper extremity. Plast Reconstr Surg. 2007;119(2):605–15.
43. De la Garza M, Sauerbier M, Gunter G, Cetrulo CL Jr, Bueno RA Jr, Russell RC, et al. Microsurgical reconstruction of the burned hand and upper extremity. Hand Clin. 2017;33(2):347–61.
44. Flugel A, Kehrer A, Heitmann C, Germann G, Sauerbier M. Coverage of soft-tissue defects of the hand with free fascial flaps. Microsurgery. 2005;25(1):47–53.
45. Achauer BM. The burned hand. In: Green DP, Hotchkiss RN, Pederson WC, editors. Operative hand surgery. 2. 4th ed. Philadelphia: Churchill Livingstone; 1999.

46. Haslik W, Kamolz LP, Nathschlager G, Andel H, Meissl G, Frey M. First experiences with the collagen-elastin matrix Matriderm as a dermal substitute in severe burn injuries of the hand. Burns. 2007;33(3):364–8.
47. Iwuagwu FC, Wilson D, Bailie F. The use of skin grafts in post-burn contracture release: a 10-year review. Plast Reconstr Surg. 1999;103(4):1198–204.
48. Hintringer W. Arthrotenolyse der Mittelgelenke (PIP). Technik und Ergebnisse. Handchir Mikrochir Plast Chir. 2002;34(6):345–54.
49. Hirshowitz B, Karev A, Rousso M. Combined double Z-plasty and Y-V advancement for thumb web contracture. Hand. 1975;7(3):291–3.
50. Gulgonen A, Ozer K. The correction of postburn contractures of the second through fourth web spaces. J Hand Surg [Am]. 2007;32(4):556–64.
51. Groenevelt F, Schoorl R. Cross-finger flaps from scarred skin in burned hands. Br J Plast Surg. 1985;38(2):187–9.
52. Ulkur E, Uygur F, Karagoz H, Celikoz B. Flap choices to treat complex severe postburn hand contracture. Ann Plast Surg. 2007;58(5):479–83.
53. Kealey GP, Jensen KL, Laubenthal KN, Lewis RW. Prospective randomized comparison of two types of pressure therapy garments. J Burn Care Rehabil. 1990;11(4):334–6.
54. Perkins K, Davey RB, Wallis KA. Silicone gel: a new treatment for burn scars and contractures. Burns Incl Therm Inj. 1983;9(3):201–4.
55. Tubiana R, Roux JP. Phalangization of the first and fifth metacarpals. Indications, operative technique, and results. J Bone Joint Surg Am. 1974;56(3):447–57.
56. Matev IB. Thumb reconstruction through metacarpal bone lengthening. J Hand Surg [Am]. 1980;5(5):482–7.
57. Ward JW, Pensler JM, Parry SW. Pollicization for thumb reconstruction in severe pediatric hand burns. Plast Reconstr Surg. 1985;76(6):927–32.
58. Achauer BM, Welk RA. One-stage reconstruction of the postburn nailfold contracture. Plast Reconstr Surg. 1990;85(6):937–40; discussion 41.
59. Hsu KC, Luan CW, Tsai YW. Review of silicone gel sheeting and silicone gel for the prevention of hypertrophic scars and keloids. Wounds. 2017;29(5):154–8.
60. Tredget EE, Shupp JW, Schneider JC. Scar management following burn injury. J Burn Care Res. 2017;38(3):146–7.
61. Tang YW. Intra- and postoperative steroid injections for keloids and hypertrophic scars. Br J Plast Surg. 1992;45(5):371–3.
62. Willows BM, Ilyas M, Sharma A. Laser in the management of burn scars. Burns. 2017;43(7):1379–89.

Burn Reconstruction: Future Perspectives—Facial Transplantation

28

Maria Siemionow and Fatih Zor

28.1 Introduction

Extensive burn patients may have severe facial mutilations, and only a few fields in burn care are a greater challenge than the management of the burned face. These people have a poor quality of life, functional deformities, and aesthetic problems. The final aesthetic and functional outcome of a facial burn injury depends on many variables, including the extent and depth of the injury, and preservation of critical areas, such as the oral commissure, mental crease, and canthal region. Many techniques have been described thus far for the reconstruction of these deformities. However, especially for severe injuries affecting the central facial region (perioral, nasal, and orbital), the final outcome is not always satisfying. Based on this there is a high demand for new techniques to obtain optimal results. This chapter aims to provide general information about vascularized composite allotransplantation (VCA), its role in post-burn facial reconstruction, and identification of main clinical and immunological problems.

28.2 Burn Injury in the Twenty-First Century

According to American Burn Association, there are around 500,000 burn victims requiring medical treatment each year in the United States, accounting for 40,000 hospitalizations per year [1]. Acute burn care, rehabilitation, and reconstruction remain a major problem worldwide. Today, due to advancement in resuscitation, early coverage of burn wound, intensive care management, support for hypermetabolic response, infection control, new drug protocols, and a better understanding of the pathophysiology of the burn wound, there is a significant increase in survival. Especially, in developed countries, this rate is as high as 96.8%. Patients with severe burn injuries, which were fatal in the past, now survive, but with more sevre deformities. This is leads to a new reconstructive challenge and demand. The anatomical regions most commonly involved in burn injuries are: upper extremities (70%) and head and neck region (50%), which frequently result in long-term morbidity [2]. There are many patients who, despite the best efforts in burn resuscitation, treatment, and rehabilitation, are not able to return to their normal social life and activities.

The face is an extremely important medium through which one interacts with the rest of the world. The unique characters of the facial skin and close anatomical and functional association with the underlying muscles allow for facial expression of emotions, which is critical to social interactions. Since a person's identity is bound to the appearance of the face, sustaining major facial deformity is thus one of the most devastating injuries one can suffer from in terms of social interaction and quality of life [3].

Successful treatment of burn patients requires surgical judgment and technical expertise, as well as understanding of burn wound pathophysiology and development of wound contractures. Burn injuries not only cause tissue defect but also constrict and deform the face, distort its features, proportions, and expression. Burns also alter the surface of the facial mask due to scarring as well as due to alteration of facial skin texture and pigmentation. These changes of the skin surface need reconstruction; however the real challenge is created by the changes in facial proportion and functional expression [4].

28.3 Evaluation of Facial Burn Deformities

Facial burn reconstruction should be based on an overall strategy and clear understanding of the underlying functional deformity. Following a deep second- and third-degree burn injury of the face, the wound healing process involves epithelialization and wound contraction. The degree of contraction depends on

M. Siemionow (✉)
Department of Orthopaedics, University of Illinois at Chicago, Chicago, IL, USA
e-mail: siemiom@uic.edu

F. Zor
Department of Plastic Surgery, Private Life Hospital, Antalya, Turkey

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_28

Table 28.2 Facial burn categories

Type I	Essentially normal faces with local burn scarring with or without contractures
Type II	Pan-facial burn deformities with some or all stigmata of facial burns

Table 28.1 Stigmata of facial burn injury

• Ectropion of lower eyelid
• Short nose
• Alar flaring of the nose
• Short and retruded upper lip
• Eversion and inferior displacement of lower lip
• Flat and stiff facial features
• Loss of jawline

the severity of the injury and treatment modalities. Due to the effect of contracting forces, facial structures are gradually deformed resulting in the characteristic appearance of a burned face. These severe deformities are to a variable degree similar for all facial burns and constitute the stigmata of facial burn injury (Table 28.1). The eyelids are distorted by ectropion, the nose is shortened with flaring of the ala, the upper lip is shortened and retruded with loss of the philtral contour, the lower lip is everted and inferiorly displaced, and the lower lip is wider than the upper lip on the anterior view. The tissues of the face and neck appear in the same plane with loss of jawline definition. The severity of these changes is proportional to the severity of the burn trauma. Fortunately, the majority of facial burn injuries are not severe and do not involve the entire face. Patients with facial burn injuries can be divided into two different categories according to the severity of the injury as described in Table 28.2. Type I deformities consist of essentially normal facial features with localized scarring with or without contractures. Type II deformities are found in a much smaller number of patients and represent "pan-facial" burn deformities presenting some or all characteristics of facial burn stigmata [5]. There are many techniques, which have been described for the reconstruction of facial subunits such as nose [6, 7], ears [8, 9], eyelids [10], scalp [11], mouth [12], and neck [13, 14]. However, only a few articles report a total reconstruction of the burned face [15, 16]. Whole full-thickness skin grafting or monoblock flap usage for full face resurfacing has been described recently [17–19]. However, the functional and aesthetic outcomes of these conventional techniques are less than optimal, and the management of most severe injuries is challenging and outcomes are often questionable.

28.4 Conventional Reconstructive Methods

The human face is a demanding structure to reconstruct because it represents unique subunits, texture, and functions. The face also plays a central role in our daily interactions through its expression of feelings, beauty, and identity. Therefore, it is essential in social interaction. As a result, face trauma and disfigurement caused by burns, tumor resection, and congenital malformations have deleterious effects on a person's life. Reconstruction of severe facial deformities following deep burns is a challenge for surgeons, who wish to reliably restore facial function and appearance. Current reconstructive procedures for facial deformity include combinations of standard skin grafting, application of local flaps, tissue expansion, prefabrication (including tissue engineering and stem cell applications), and free tissue transfers (Table 28.3) [12, 20–26]. Although these severely injured patients are subjected to multiple surgical interventions, the functional and aesthetic outcomes of currently available conventional reconstructive procedures are less than optimal. Long-term follow-ups quite often result in a tight, mask-like face with a lack of facial expression and an unsatisfactory cosmetic outcome [16]. In cases involving large and wide areas of the burned face including scarring of the adjacent tissue there are only limited options to provide reconstruction with soft, thin, and pliable tissue. The best result of facial reconstruction was reported following replantation of the avulsed scalp and face where normal animation and facial expression were achieved as well as adequate hair growth on the scalp [27]. Current methods of face reconstruction fail when tissue loss is considerable, because the body does not provide tissue possessing the texture, pliability, and complexity of the human face. For this reason, in severely burned faces, particularly with injuries in the perioral, nasal, and periocular regions, face transplantation becomes a real therapeutic option for restoring facial features and functions.

Table 28.3 Techniques available for burn reconstruction

1. Without tissue deficiency	Excision and primary closure
	Z-plasty
2. With tissue deficiency	
Simple reconstruction	– Skin graft
	– Transposition flaps (Z-plasty and modifications)
Reconstruction of skin and underlying tissues	– Axial and random flaps
	– Myocutaneous flaps
	– Tissue expansion
	– Free flaps

28.5 Vascularized Composite Allotransplantation and Face Transplantation

Vascularized composite allotransplantation (VCA) involves transplantation of tissue, derived from ectoderm and mesoderm. It typically contains skin, fat, muscle, nerves, lymph nodes, bone, cartilage, ligaments, and bone marrow as

opposed to a single tissue organ, which is the case in conventional solid organ transplantation (SOT). An example of VCA is limb transplantation, in which the transplanted graft includes skin, muscle, nerve, blood vessels, bone, and bone marrow. The function and the immunologic properties of the composite tissue transplant are more difficult to define, because each individual component has its own unique characteristics that ultimately affect the successful outcome of the transplantation. Most applications of VCA predominantly improve the quality of life for non-life-threatening conditions and aim to restore anatomic, cosmetic, and functional integrity. The benefits gathered by such procedures have to be balanced against the morbidity of the surgical procedure itself and a long-term immunosuppression therapy [28].

Following years of experimental studies, after report on the first successful hand transplantation in France, the field of VCA has further developed opening new alternatives for facial reconstruction [29]. On 27 November 2005, in Amiens, France, a surgical team led by Dr. Bernard Devauchelle and Jean-Michel Dubernard announced that they had performed a partial face transplant on a 38-year-old female, whose face had been disfigured by a dog bite [30]. Up to now, nearly 40 face transplantations have been performed all over the world. According to International Registry on Hand and Composite Tissue Transplantation, in 7 cases the cause of disfiguration was a burn injury (electrical or thermal) [28, 31–33]. The world's first near total face transplantation was performed in Cleveland in December, 2008, by a team led by Dr. Maria Siemionow [32, 33]. The patient was a 45-year-old woman who suffered from severe facial trauma to her midface from a close-range shotgun blast in September 2004. Her facial deformities included absence of nose, nasal lining, and underlying bone; contracted remnants of the upper lip; loss of orbicularis oris and orbicularis oculi muscle functions; distorted and scarred lower eyelids with ectropion; right-eye enucleation supported by eye prosthesis; and facial nerve deficit manifested by the lack of midface function. Before face transplantation, the patient had undergone 23 major autologous reconstructive operations that included correction of bone defect by free fibula and split-calvaria/rib grafts, soft-tissue defect by anterolateral free flap, temporalis muscle flap, paramedian forehead flap, and radial forearm free flap and skin defect by multiple split-thickness skin grafts. The donor was a brain-dead woman who matched the patient in age, race, and skin complexion. The allograft was designed to cover the recipient's anterior craniofacial skeleton, and it included about 80% of the surface area of the anterior face. It was based on a Le Fort III composite tissue allograft containing total nose, lower eyelids, upper lip, total infraorbital floor, bilateral zygomas, and anterior maxilla with incisors, and included total alveolus, anterior hard palate, and bilateral parotid glands [3, 32, 33] (Fig. 28.1). The allotransplant inset to the recipient started with the adjustments of a Le Fort III composite allograft to the recipient's skeletal defect. Once bone components of the facial allograft were secured and stable, bilateral microvascular anastomoses of both arteries and veins were performed. Once craniofacial skeleton was intact, the bilateral facial nerves were connected using standard epineural repair. First, the donor's vagus nerve, taken as an interpositional graft, was attached to the upper division of the trunk of the right side of the recipient's facial nerve. On the left side, the donor's hypoglossal nerve, used as an interpositional graft, was attached to the upper division of the trunk on the recipient's facial nerve. Both grafts were connected to the main trunk of the donor nerve. Then, porous polyethylene implants were used to reconstruct orbital floors. Finally, the lower eyelids, including the recipient's conjunc-

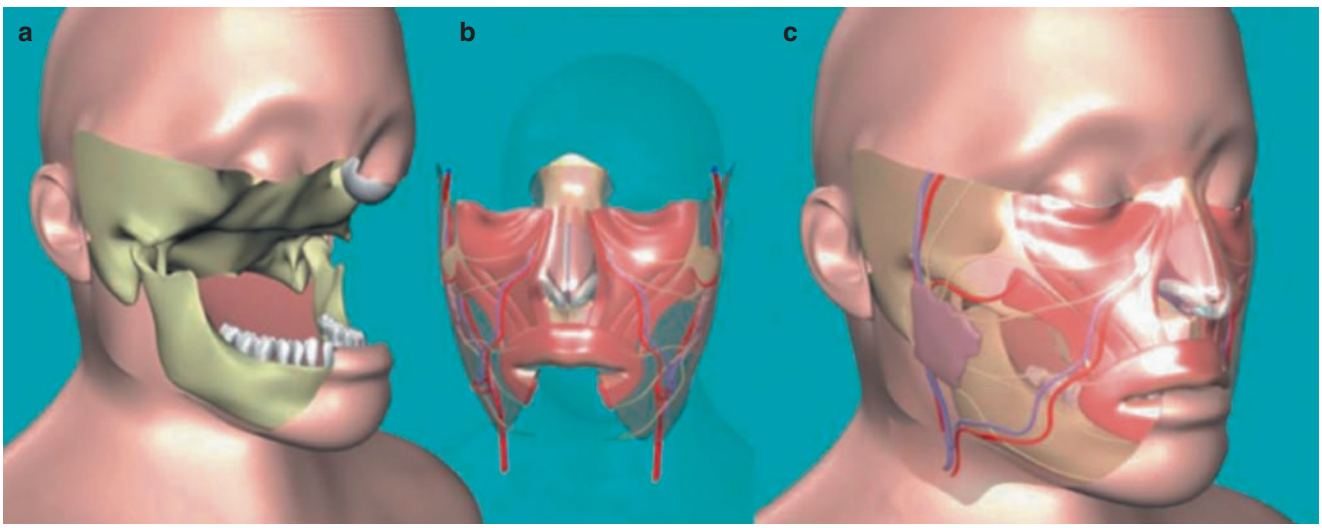


Fig. 28.1 Illustration of the first US near-total human face transplantation. (**a**) Facial defect following resection of the scars. (**b**) Composite tissue allograft including nose, lower eyelids, and upper lip. (**c**) Reconstruction of the facial defect

tiva and lash lines, were reconstructed bilaterally using donor eyelid skin. The composite facial allograft inset was completed after skin closure. Induction of immunosuppression was carried out with rabbit anti-thymocyte globulin (1 × 2 mg/kg intravenously once a day for 9 days) in combination with methylprednisolone 1000 mg bolus intravenously on the day of transplant, and rapidly tapered thereafter. The immunosuppressive regimen was maintained with tacrolimus, mycophenolate mofetil, and low-dose oral prednisone.

During the long-term follow-up, sensory discrimination returned to the entire facial skin, as measured by pressure-specified sensory device presence of two-point sensory discrimination at the area under the lower eyelids, upper lip, and the tip of the nose on both sides of the graft. Motor recovery included improved facial mimetics with asymmetric smile and upper lip occlusion.

Functional recovery of this three-dimensional facial defect is excellent, with restoration of major missing functions such as eating solid food without the need of a gastric tube, drinking from a cup, and restoration of intelligible speech after hard palate reconstruction with composite allograft and palatal obturator support. At 1 year post-transplant, aesthetic outcome is improved by excision of the redundant skin and subcutaneous tissues. Psychologically, the patient is doing well without symptoms of depression or post-traumatic stress disorder. Finally, her pain level was significantly reduced since scarred and contracted tissue within the face was removed during face transplantation.

The first application of face transplantation in burn patient was reported by Dr. Lantieri in April 2009 in Paris. The entire upper face including nose, eyelids, forehead, scalp, and ears as well as bilateral hands were transplanted to a burn victim from a male donor [34]. Unfortunately, nearly 2 months after transplantation, the patient died due to complications including severe infection and heart failure [35]. Following this patient, more concern was paid to burned patients with regard to VCA application. Since then a total of 7 facial VCA have been reported for burn face reconstruction. Although the first case was discouraging, following cases were successful with good long-term results.

28.6 Face Transplantation in Facial Burn Reconstruction

Based on current reports on successful face transplantation, it is obvious that face transplantation meets all criteria needed for an excellent reconstruction of a burned face. However, both the face transplantation and facial burn reconstruction bring about very unique challenges and issues: facial transplantation involves immunological, psychological, and ethical issues, which may interfere with burn reconstruction. On the other hand, the conventional reconstruction of a burned face is limited by timing of the reconstruction, by development of scar tissue and skin contracture, and by the need for reconstruction of specific functional units, which may interfere with facial transplantation.

28.6.1 Indications for Burned Face Reconstruction

It is helpful to categorize facial plastic surgery procedures in burned patients as urgent, essential, and desirable. Urgent procedures are commonly performed during the acute phase. These include flap reconstruction to cover exposed bones and vital organs or to allow for mouth opening to facilitate feeding. Essential procedures are carried out to restore function such as neck release and ectropion repair. Desirable procedures are performed to restore the normal facial appearance. Examples are nasal reconstruction, ear reconstruction, and scalp reconstruction. Today, face transplantation is still considered an experimental procedure and may be indicated as the last therapeutic option for severely disfigured patients to restore major functional deficits of the burned face. For this reason, currently, face transplantation cannot be considered as an emergency procedure neither in trauma nor in the burn patient.

28.6.2 Timing of Burned Face Reconstruction

The timing of reconstructive plastic surgery following facial burn injuries falls into three separate phases: acute, intermediate, and late phase. Acute reconstructive surgery takes place during the first months after burn injury and includes urgent procedures, which are required to facilitate patient care or to prevent the development of contractures, which could lead to permanent functional damage. Acute reconstructive intervention is most frequently indicated in the eyelid, perioral, and cervical regions. Intermediate reconstructive surgery is performed months or years after burn injury when wounds are closed and scar maturation process is completed. Finally, late phase reconstruction is performed many years after burn injury. Considering reconstructive ladder in burn patient, face transplantation seems to be appropriate for late phase reconstruction in cases where conventional options have failed. With current advances in VCA, indications for face transplantation in burn patients may be considered during intermediate or even acute phase of treatment in the near future.

28.6.3 Reconstruction of Specific Facial Regions

Facial deformity can be divided into three categories: peripheral only, central only, or combined peripheral and central [36]. Although many techniques are described for reconstruction of peripheral and central deformities, no satisfying method for whole facial reconstruction after burn injury is available today. This is even more challenging when considering burn injury in the central face which includes the most important aesthetic units as the lower lip and chin, upper lip, nose, and bilateral upper and lower eyelids. These facial units have both aesthetic and functional features, and the surgical outcome is directly related to the number and function of the units, which are involved.

Large facial burn deformities are almost always a combined type of deformities affecting both the peripheral and central areas of the face. Usually, following burn injury, there is a limited access to the normal facial skin, which is left for potential reconstruction. Currently, tissue expansion and microsurgical tissue transfer are the only reconstructive options in these complex cases. However, these techniques are useful for the coverage of skin defect and are far from meeting the actual need for functional reconstruction of the facial burn. Functional units such as nose, periorbital, and perioral areas are hard to reconstruct by means of tissue expansion and microsurgical tissue transfer because of the limited availability of donor tissue and texture mismatch.

Facial transplantation provides a unique opportunity to reconstruct the structures of a burned face with the same structures coming from a human donor. Mathes et al. performed a survey on North American burn and plastic surgeons on their attitudes toward facial transplantation. The survey report concluded that VCA should be supported in reconstruction of complex facial deformities [37]. The first face transplant for face reconstruction included the entire upper face, nose, eyelids, forehead, scalp, and ears. In addition due to amputation of both hands during burn accident, this patient received simultaneously bilateral hand transplantation from the same donor. Unfortunately, the patient died at 2 months post-transplant due to severe infection and cardiac arrest [34, 35]. Following this patient, total face transplantations have neen transformed. Although outcomes of these patients were satisfying, it is clear that more clinical cases are needed to address the long-term outcomes of facial transplantation in burn patients.

28.7 Burned Patient and Immunology

Face transplantation is a very good option for severely disfigured burn patients. However, as an allotransplantation, the major concern in face transplantation is to prevent rejection of the transplanted allograft. Although there are different immunosuppressive protocols used to overcome rejection, the ultimate goal is to develop a donor-specific tolerance to avoid the need for life-long immunosuppression. The immunologic status of the patient is quite important for the success of the VCA. In this context, burn patients are different from other trauma patients since extensive burn injury affects all organs including the immune system. During the acute period following burn injury, a systemic immunosuppression develops. During this early period skin allograft take without additional immunosuppression was reported [20, 38]. There is, however, a lack of studies describing immunological changes throughout the acute burn care. So far, there is only one study reporting delayed immunosuppression up to 3.5 months following major burn injury. So, more research and clinical studies are needed to further evaluate immunological sequel of severe burn injury [39]. Thus, if the VCA is planning to be performed in the acute period, immunosuppressive regime following VCA may be different from standard immunosuppression protocols.

Patients with major burns are often subjected to transfusion of blood and blood products such as fresh frozen plasma. The long-term effect of these therapies on immunological responses in case of face transplantation is still unknown. The same is true for early wound coverage with cadaver skin allograft, which may result in patient presensitization and have potential impact on the outcome of VCA.

Burn patients are likely to be a candidate for VCA; however, they may be sensitized during their early burn management. Recently, Chandraker et al. reported antibody-mediated rejection of facial allograft within 5 days after transplantation in a burn patient [40]. Garza et al. investigated the immunological effect of skin allograft in burn treatment and its impact on future vascularized composite allotransplantation [41]. In this study, they showed that burn patients who receive skin allografts as a method of acute burn wound closure demonstrated significantly increased immunological sensitization, which is measured by cPRA levels. Interestingly, detection of HLA antibody in the acute burn period is lower that antibody detection in the long-term follow-up. Duhamel et al. similarly reported that extensively burned patients become highly sensitized during burn care. They think that skin allografts (cryopreserved but not glycerol preserved) and the number of transfused packed red blood cells are mainly responsible for this [42]. Klein et al.

reported an excellent review about sensitization and desensitization of burn patients as potential candidates for VCA [43]. They stated that pregnancy, blood transfusions, previous transplants, allogeneic skin transplants, assist devices as well as HLA-unrelated immune stimulation (such as infections and sepsis) are all causes of HLA sensitization.

In order to prevent sensitization-related problems following transplantation, various treatment options are developed for the presensitized patient. Of those, immunoadsorption and plasma exchanges, anti-B cell agent (rituximab), proteasomal inhibitor (bortezomib), intravenous immunoglobulins (IVIG), and splenectomy may be used. However, desensitization protocols have some additional side effects such as desensitized patients are at higher risk of severe infections and malignancy [44].

In addition to desensitization procedures, some modifications can be made in acute care of the burned patient in order to prevent presensitization. Phenotyped packed red blood cells and platelets can be used during the acute care and may aid in reducing allosensitization. If possible, coverage of burn wound may be performed with artificial or biosynthetic dermal grafts in patients with extensive face and hand burns. If allograft will be used, glycerol-preserved allografts can be preferred to cryopreserved allografts as they cause less allosensitization [15].

28.8 Conclusions

Severe burn injuries at the head and neck region often result in deep tissue damage with development of scarring, contracture, and functional loss. Thus, the primary goal of facial burn reconstruction should be functional restoration and optimal aesthetic outcome. Currently available techniques are limited in providing complex tridimensional craniofacial reconstruction due to the lack of facial-like tissues and lack of facial subunits in our own body.

Facial transplantation would provide such a unique reconstructive option; however life-long immunosuppression is required afterwards.

With the advancements in transplant immunology and development of donor-specific tolerance, face transplantation may replace most of conventional reconstructive methods and may be considered as an alternative reconstructive option for severely burned patients.

References

1. American Burn Association. Burn incidence fact sheet. http://www.ameriburn.org/resources_factsheet.php. Accessed 5 Apr 2017.
2. Prasad JK, Bowden ML, Thomson PD. A review of the reconstructive surgery needs of 3167 survivors of burn injury. Burns. 1991;17:302–5.
3. Siemionow M, Sonmez E. Face as an organ. Ann Plast Surg. 2008;61:345–52.
4. Engrav L, Donelan MB. Face burns: acute care and reconstruction. Oper Tech Plast Reconstr Surg. 1997;4:53–85.
5. Donelan MB. Reconstruction of head and neck. In: Herndon D, editor. Total burn care. 3rd ed. Amsterdam: Elsevier; 2007. p. 701–18, ISBN: 978-1-4160-3274-8.
6. Benmeir P, Neuman A, Weinberg A, Rotem M, Eldad A, Lusthaus S, Kaplan H, Wexler MR. Reconstruction of a completely burned nose by a free dorsalis pedis flap. Br J Plast Surg. 1991;44:570–1.
7. Bernard SL. Reconstruction of the burned nose and ear. Clin Plast Surg. 2000;27:97–112.
8. Bhandari PS. Total ear reconstruction in postburn deformity. Burns. 1998;24:661–70.
9. Rosenthal JS. The thermally injured ear: a systematic approach to reconstruction. Vogt PM Clin Plast Surg. 1992;19:645–61.
10. Sassoon EM, Codner MA. Eyelid reconstruction. Oper Tech Plast Reconstr Surg. 1999;6(2):50–264.
11. Mangubat EA. Scalp reconstruction and repair. Facial Plast Surg. 2008;24:428–45.
12. Pribaz JJ, Weiss DD, Mulliken JB, Eriksson E. Prelaminated free flap reconstruction of complex central facial defects. Plast Reconstr Surg. 1999;104:357–65.
13. Ninkovic M, Moser-Rumer A, Ninkovic M, Spanio S, Rainer C, Gurunluoglu R. Anterior neck reconstruction with pre-expanded free groin and scapular flaps. Plast Reconstr Surg. 2004;113:61–8.
14. Parrett BM, Pomahac B, Orgill DP, Pribaz JJ. The role of free-tissue transfer for head and neck burn reconstruction. Plast Reconstr Surg. 2007;120:1871–8.
15. Angrigiani C, Grilli D. Total face reconstruction with one free flap. Plast Reconstr Surg. 1997;99:1566–75.
16. Birgfeld CB, Low DW. Total face reconstruction using a preexpanded, bilateral, extended, parascapular free flap. Ann Plast Surg. 2006;56:565–8.
17. Li Q, Zan T, Li H, Zhou S, Gu B, Liu K, Xie F, Xie Y. Flap prefabrication and stem cell-assisted tissue expansion: how we acquire a monoblock flap for full face resurfacing. J Craniofac Surg. 2014;25:21–5.
18. Zan T, Gao Y, Li H, Gu B, Xie F, Li Q. Pre-expanded, prefabricated monoblock perforator flap for total facial resurfacing. Clin Plast Surg. 2017;44:163–70.
19. Zhao JH, Diao JS, Xia WS, Pan Y, Han Y. Clinical application of full-face, whole, full-thickness skin grafting: a case report. J Plast Reconstr Aesthet Surg. 2012;65:1576–9.
20. Achauer BM. Reconstructing the burned face. Clin Plast Surg. 1992;19:623–36.
21. Baumeister S, Koller M, Dragu A, Germann G, Sauerbier M. Principles of microvascular reconstruction in burn and electrical burn injuries. Burns. 2005;31:92–8.
22. Celikoz B, Deveci M, Duman H, Nisanci M. Reconstruction of facial defects and burn scars using large size freehand full-thickness skin graft from lateral thoracic region. Burns. 2001;27:174–8.
23. Feldman JJ. Facial burns. In: McCarthy JG, editor. Plastic surgery, vol. 3. Philadelphia, PA: Saunders; 1990. p. 2153–236.
24. Latifoglu O, Ayhan S, Atabay K. Total face reconstruction: skin graft versus free flap. Plast Reconstr Surg. 1999;103:1076–8.
25. Santanelli F, Grippaudo FR, Ziccardi P, Onesti MG. The role of pre-expanded free flaps in revision of burn scarring. Burns. 1997;23:620–5.
26. Teot L, Cherenfant E, Otman S, Giovannini UM. Prefabricated vascularised supraclavicular flaps for face resurfacing after postburns scarring. Lancet. 2000;355:1695–6.
27. Wilhelmi BJ, Kang RH, Movassaghi K, Ganchi PA, Lee WP. First successful replantation of face and scalp with single-artery repair: model for face and scalp transplantation. Ann Plast Surg. 2003;50:535–40.

28. Siemionow M, Ozturk C. Face transplantation: outcomes, concerns, controversies, and future directions. J Craniofac Surg. 2012;23(1):254–9.
29. Dubernard JM, Owen E, Herzberg G, Lanzetta M, Martin X, Kapila H, Dawahra M, Hakim NS. Human hand allograft: report on first 6 months. Lancet. 1999;353:1315–20.
30. Devauchelle N, Badet L, Lengele B, Morelon E, Testelin S, Michallet M, D'Hauthuille C, Dubernard JM. First human face allograft: early report. Lancet. 2006;368:203–9.
31. Guo S, Han Y, Zhnag XLB, Yi C, Zhang H, Ma X, Wang D, Yang L, Fan X, Liu Y, Lu K, Li H. Human facial allotransplantation: a 2 year follow-up study. Lancet. 2008;372:631–8.
32. Siemionow M, Papay F, Alam D, Bernard S, Djohan R, Gordon C, Hendrickson M, Lohman R, Eghtesad B, Coffman K, Kodish E, Paradis C, Avery R, Fung J. Near-total human face transplantation for a severely disfigured patient in the USA. Lancet. 2009;374:203–9.
33. Siemionow M, Papay F, Djohan R, Bernard S, Gordon CR, Alam D, Hendrickson M, Lohman R, Eghtesad B, Fung J. First U.S near-total human face transplantation—a paradigm shift for massive complex injuries. Plast Reconstr Surg. 2009. [Epub ahead of print].
34. Lantieri L, Meningaud JP, Grimbert P, Bellivier F, Lefaucheur JP, Ortonne N, Benjoar MD, Lang P, Wolkenstein P. Repair of the lower and middle parts of the face by composite tissue allotransplantation in a patient with massive plexiform neurofibroma: a 1-year follow-up study. Lancet. 2008;372:639–45.
35. Carty MJ, Hivelin M, Dumontier C, Talbot SG, Benjoar MD, Pribaz JJ, Lantieri L, Pomahac B. Lessons learned from simultaneous face and bilateral hand allotransplantation. Plast Reconstr Surg. 2013;132:423–32.
36. Spence RJC. The challenge of reconstruction for severe facial burn deformity. Plast Surg Nurs. 2008;28:71–6.
37. Mathes DW, Kumar N, Ploplys E. A survey of north American burn and plastic surgeons on their current attitudes toward facial transplantation. J Am Coll Surg. 2009;208:1051–8.
38. Achauer BM, Hewitt CW, Black KS, Martinez SE, Waxman KS, Ott RA, Furnas DW. Long-term skin allograft survival after short-term cyclosporin treatment in a patient with massive burns. Lancet. 1986;1(8471):14–5.
39. Parment K, Zetterberg A, Ernerudh J, Bakteman K, Steinwall I, Sjoberg F. Long-term immunosuppression in burned patients assessed by in vitro neutrophil oxidative burst (Phagoburst). Burns. 2007;33:865–71.
40. Chandraker A, Arscott R, Murphy G, et al. Face transplantation in a highly sensitized recipient. Mil Med. 2016;181:221.
41. Garza RM, Press BH, Tyan DB, Karanas YL, Lee GK. Immunological effect of skin allograft in burn treatment: impact on future vascularized composite allotransplantation. J Burn Care Res. 2017;38(3):169–73.
42. Duhamel P, Suberbielle C, Grimbert P, Leclerc T, Jacquelinet C, Audry B, Bargues L, Charron D, Bey E, Lantieri L, Hivelin M. Anti-HLA sensitization in extensively burned patients: extent, associated factors, and reduction in potential access to vascularized composite allotransplantation. Transpl Int. 2015;28:582–93.
43. Klein HJ, Schanz U, Hivelin M, Waldner M, Koljonen V, Guggenheim M, Giovanoli P, Gorantla VS, Fehr T, Plock JA. Sensitization and desensitization of burn patients as potential candidates for vascularized composite allotransplantation. Burns. 2016;42:246–57.
44. Marfo K, Lu A, Ling M, Akalin E. Desensitization protocols and their outcome. Clin J Am Soc Nephrol. 2011;6:922–36.

Modern Myoprostheses in Electric Burn Injuries of the Upper Extremity

29

Agnes Sturma, Stefan Salminger, Clemens Gstoettner, and Oskar C. Aszmann

29.1 Introduction

Electrical high-voltage burn injuries occur predominantly in young men due to work-related trauma [1]. However, in the last years, train surfing became a non-negligible share among burn admissions [2]. High-voltage injuries have several unique characteristics that differ from other thermal or chemical injuries. Their treatment requires expertise in surgical and anaesthesiologic management [3], which is described elsewhere in this book. The most momentous fact, however, is that they are the most frequent cause of extremity amputations in a burn service. These injuries affect the upper and the lower extremity alike, depending what route the electric current travelled through the body [4]. Current will flow through tissues exhibiting less electrical resistance more readily. Since deep tissues, such as nerves, vessels and muscle, have less resistance than skin, the surface markings in electrical burn injuries are only the tip of the iceberg and do not reveal the possibly immense damage hidden beneath [5]. If a fasciotomy is deemed necessary, all compartments of the affected extremity need to be opened. In the hand all intrinsic compartments, the carpal tunnel, superficial and the deep forearm as well as the dorsal compartment need to be opened through separate incisions. These injuries all require a second and third look until one can be sure that the climax of tissue damage is overcome. Even at this stage of treatment one must have both the biological and technical reconstructive options in mind. If an amputation of the upper extremity at any level is necessary, one must be aware that every joint preserved adds several degrees of freedom and every inch of length adds stability to a given prosthetic device. These are not diabetic patients with recurrent ulcerations where an amputation is almost an inevitable consequence, but a sudden massive assault to an extremity of an otherwise healthy and most often young individual. One should therefore tap the entire spectrum of reconstructive surgery to maintain length and definitely think twice before resecting a joint. Since often both upper extremities are affected, a preserved limb, even if without any function, can at a later stage be used as a biological spare part donor site for the contralateral extremity (Fig. 29.1a–g). Additionally, amputation can also be considered at a later time, if the patient is not satisfied with biological hand function [6] as presented in Fig. 29.2.

29.2 Standard Myoelectric Fittings

If all biological reconstructive measures for the upper extremity fail, myoelectric prostheses present a promising resort to go to. The movement of standard myoelectrical arm prostheses is controlled via two transcutaneous electrodes that are activated by two separately innervated muscle groups. In a transradial amputee one electrode might be placed on the extensor muscles and one on the flexor muscles of the wrist. This allows the patient to control opening of the prosthetic hand by thinking about wrist extension and closing by thinking of wrist flexion. While this provides an easy and robust way of controlling a simple hand with two functions, prostheses with multiple degrees of freedom require switching between the different grips/joints. Usually, this change of control levels is performed by voluntary co-contractions of the two muscle groups and the respective level then is linearly controlled by the same muscles. Especially in above-elbow amputees, where prosthetic

A. Sturma
Clinical Laboratory for Bionic Extremity Reconstruction, Department of Surgery, Medical University of Vienna, Vienna, Austria

Department of Bioengineering, Imperial College London, London, UK

S. Salminger · O. C. Aszmann (✉)
Clinical Laboratory for Bionic Extremity Reconstruction, Department of Surgery, Medical University of Vienna, Vienna, Austria

Division of Plastic and Reconstructive Surgery, Department of Surgery Medical University of Vienna, Vienna, Austria
e-mail: oskar.aszmann@meduniwien.ac.at

C. Gstoettner
Clinical Laboratory for Bionic Extremity Reconstruction, Department of Surgery, Medical University of Vienna, Vienna, Austria

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_29

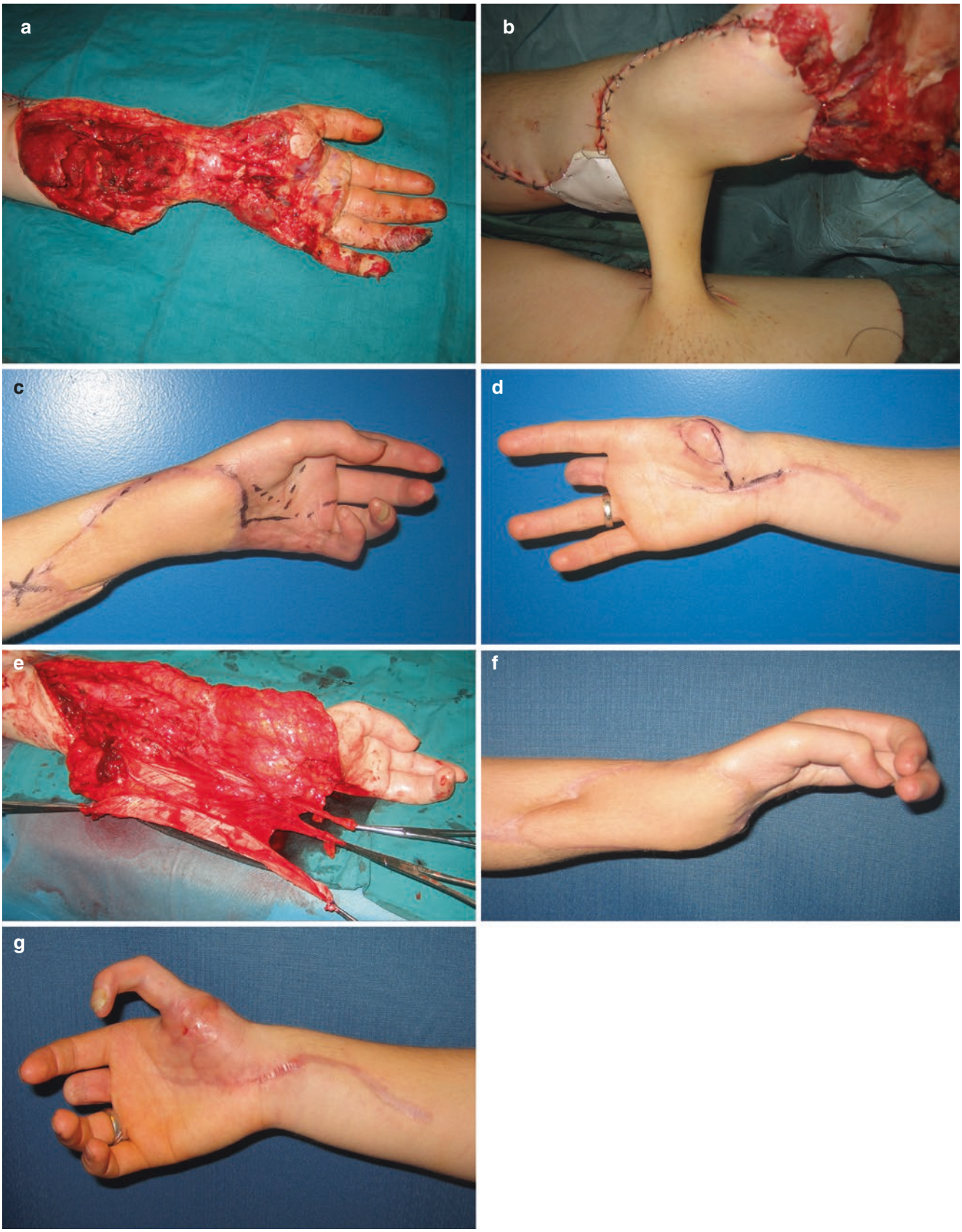


Fig. 29.1 (**a**–**g**) Work-related electrical burn injury of both hands of a 20 years old young man. All four extremities were affected with loss of the thumb and III finger of the right hand and loss of all internal structures of the left forearm. To preserve the left hand a groin flap was invested after final debridement. At a later stage the IV finger of the left hand was used as a free graft to reconstruct the thumb of the right hand. Six months later an ALT flap was invested at the left hand to augment soft tissue coverage and reconstruct tendons to the I–III finger with vascularized fascia lata strips. Furthermore, the ulnar nerve was used to reconstruct the median nerve in the same session

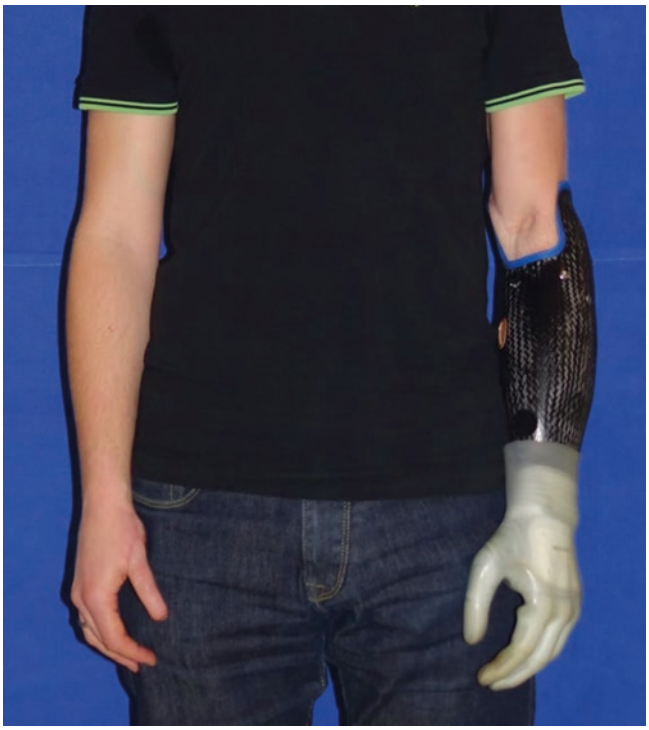


Fig. 29.2 As biological reconstruction left the patient with a functionless and aesthetically not appealing left hand, it was replaced with a myoelectric prosthesis that allowed good grip function

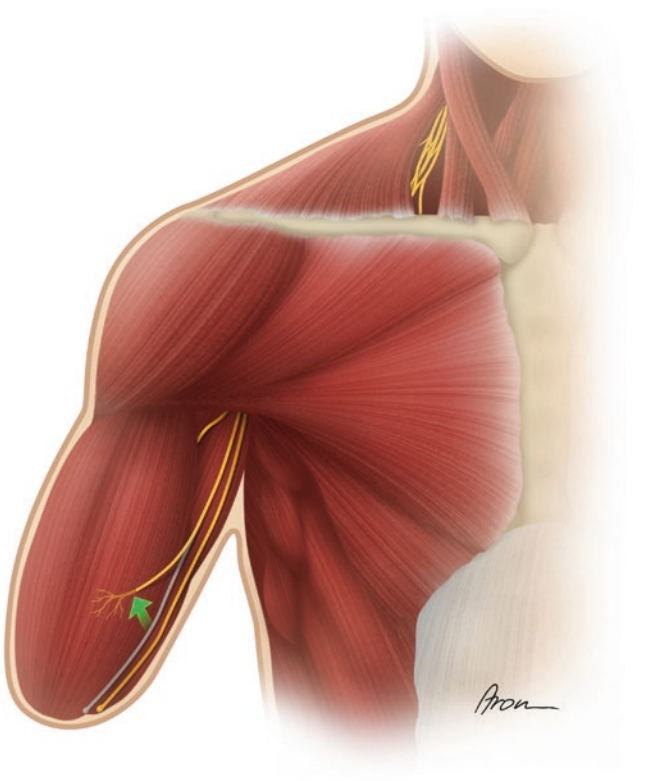


Fig. 29.3 Targeted muscle reinnervation (TMR) in a transhumeral amputee: The ulnar nerve, which would otherwise end in scar tissues, is transferred to the short head of the biceps. This creates a new neuromuscular target that can be used to control closing the prosthetic hand intuitively

functions include not only hand and wrist movements but also elbow flexion and extension, the patient frequently needs to switch between joint movements by using this approach. A harmonious course of movement as in the corresponding natural pattern of motion is not possible this way. This limits perceived prosthetic function and is one of the reasons for a relatively high rejection rate in above-elbow prosthetic fittings [7]. An appreciable improvement would be given if the individual movement levels could be governed by signals that correspond to the natural pattern of motion.

29.3 Targeted Muscle Reinnervation

One approach to achieve a more natural prosthetic control for proximal amputations are selective nerve transfers. The aim of "Targeted Muscle Reinnervation" (TMR) is to create a higher number of functional neuromuscular units for picking up myoelectric signals [8, 9]. During surgery, the major arm nerves, such as the musculocutaneous nerve, radial nerve, median nerve and ulnar nerve, are separated from the proximal arm plexus and transferred to the residual nerve branches of remaining muscles in the stump. This allows to create meaningful neuromuscular units, which can serve as impulse generators for the myoelectrical prosthesis [10]. In a transhumeral amputee expendable muscles are the short head of the biceps and the brachial muscle on the ventral surface as well as the lateral head of the triceps on the dorsal aspect of the arm. Depending on the level of amputation possibly the brachioradialis muscle is still present and can also be used as target muscle. A common approach includes transferring the ulnar nerve to the short head of the biceps [11], as shown in Fig. 29.3. As this nerve usually controls muscles responsible for "hand closing", patients should at a later stage be able to activate this part of the biceps by thinking about closing the hand. If the long head of the biceps still has its original innervation, it is activated by thinking about elbow flexion. In this way, TMR creates an additional signal for prosthetic control. By transferring the other hand nerves as well (as shown in Table 29.1), up to six different signals can be created for more intuitive and dexterous prosthetic control [11, 12]. The advantage of this protocol is that the individual signals can be separately picked up with electrodes embedded in the socket of the prosthesis, which allows direct, independent and intuitive control of all relevant prosthetic functions. Since these nerve transfers are all done very proximally, they are generally feasible for all transhumeral amputees without the need of nerve grafts.

Table 29.1 A standard nerve transfer matrix of a transhumeral amputee

Source nerve	Target muscle	Target function	Innervation
Musculocutaneous nerve	M. biceps caput longum	Elbow flexion	Original
Ulnar nerve	M. biceps caput breve	Hand close	Transferred
Median nerve	M. brachialis	Pronation	Transferred
Radialis nerve	M. triceps caput longum/mediale	Elbow extension	Original
Split of ramus profundus n. radialis	M. triceps caput laterale	Hand open/ supination	Transferred
Split of ramus profundus n. radialis	M. brachioradialis	Supination/ hand open	Transferred

Table 29.2 A standard nerve transfer matrix of a glenohumeral amputee

Source nerve	Target muscle	Target function	Innervation
Musculocutaneous nerve	Pars clavicularis M. pectoralis major	Elbow flexion	Transferred
Split of median nerve	Pars sternocostalis M. pectoralis major	Pronation	Transferred
Split of median nerve	Pars sternocostalis M. pectoralis major	Wrist flexion/ pronation (might be later used for prosthetic supination)	Transferred
Ulnar nerve	M. pectoralis minor	Hand close	Transferred
Radialis nerve	M. latissimus dorsi	Elbow extension	Transferred
Ramus profundus n. radialis	M. infraspinatus	Hand open	Transferred

In patients with shoulder exarticulation TMR can be used as well to enhance the neuromuscular interface for prosthetic control. Here, the different parts of the major and minor pectoral muscles at the ventral body surface and the latissimus dorsi at the posterior body surface are accessible. As the clavicular, the sternocostal and the abdominal head of the pectoralis major, as well as the pectoralis minor have their distinct motor branches [13, 14], they can be used as individual targets for selective nerve transfers to provide a new neurological landscape for blindly ending the axons of the brachial plexus. Similar to the nerve transfers of the transhumeral amputee, all major nerves can and should be transferred to new targets as described in Table 29.2. Before performing the surgery, one must carefully evaluate the remaining function of these muscles, the presence and whereabouts of the proximal nerve stumps (MRI/high resolution ultrasound) and rule out more proximal nerve lesions (i.e. root avulsions or supraclavicular nerve damage).

After these selective nerve transfers and the subsequent phase of reinnervation, cognitively demanding motor learning is needed to enable the amputee to activate the reinnervated muscles selectively and thereby control the prosthesis. This process of TechNeuroRehabilitation after Targeted Muscle Reinnervation takes between 1 and 2 years [15]. During nerve regeneration after surgery, muscles cannot be activated for 3–6 months. During this time, therapy might include treatment of post-surgical pain, conservation of range of motion and strength of the remaining joints, as well as facilitation of cortical representation of the hand area. The latter can include mirror therapy, motor imagery and left-right discrimination training. In above-elbow amputees, patients can control conventional two-signal myoprosthesis during the phase of nerve regeneration, as the original innervated muscles can be used. As soon as the muscles are reinnervated, motor training is initiated. To gain selective and precise motor control, the use of surface EMG biofeedback is recommended [16]. Once the distinct muscle signals are stable and can be clearly and individually addressed by the patient, a diagnostic fitting will be provided to start the early prosthetic rehabilitation programme [17]. At the beginning the focus is set on simple movements, while manipulating objects within activities of daily living should be possible by the end of rehabilitation. Finally, the prosthesis can be used at home. With time, the patient will learn how to incorporate this technical device in his new body image and it will feel natural and intuitive to use it. At this stage, regular follow-up examinations ascertain continued prosthetic functionality [15].

29.4 Pattern Recognition for Prosthetic Control

While the limiting factor in prosthetic control after proximal amputations is the low number of available muscles, in the transradial amputee an array of functional muscles is usually still present in the forearm. Standard fittings only use one electrode on the flexor and extensor muscle groups, whereas more recent approaches aim to record and process more information from the extrinsic hand muscles. These pattern recognition algorithms provide a means for multifunctional control by classifying different muscle activation patterns instead of only interpreting the amplitude of one electrode for one prosthetic movement. Fundamentally, the raw EMG signal is first measured by an array of electrodes. The EMG data is then windowed; features (such as amplitude or signal frequency of all activated electrodes) are extracted and classified before they are used as control inputs [18]. The clas-

sification is basically comparing the extracted features of the EMG data with the features for predefined prosthetic movements (hand open/close, pronation/supination, etc.). The algorithm defines the most likely prosthetic movement intended by the user which the prosthesis is then going to perform. This process is displayed in Fig. 29.4. To allow this comparison of EMG features, the prosthesis needs to be trained in advance. Usually, this involves calibration of the device where the patient is asked to think of a given hand movement while the corresponding raw EMG data is recorded and saved. When the patient is using the prosthesis, each pattern of muscle activation is then compared with the stored EMG data and the most appropriate movement is chosen. While this approach has been successfully tested in lab conditions, its robustness in daily life situations is yet to be proven [18]. Additionally, standard pattern recognition has the disadvantage of lacking simultaneous multifunction control as well as proportional control [19]. This means that different movements (e.g. hand close and pronation) cannot be performed at the same time and that they will always be performed with the same predefined speed.

To overcome these limitations, different strategies of EMG signal interpretation have been applied, including regression algorithms. In contrast to standard pattern recognition, regression algorithms are able to continuously estimate multiple control signals directly from the EMG signal [18]. If a patient therefore tries to close and pronate the prosthetic hand, this results in one control signal for the rotation angle of the wrist and a second estimate for closing the hand. Therefore, this approach provides greater flexibility for the user leading to more intuitive and natural prosthetic control [20]. So far, it has provided promising performance and is under continuous development to further increase its robustness.

29.5 Osseointegration

The recent years have brought new solutions not only for prosthetic control but also for the mechanical interface between the user and prosthesis. In many patients, the stable attachment of a prosthesis using a socket is not possible because of insufficient stump length. In transhumeral amputees for example, anything proximal to the deltoid tuberosity will present a considerable challenge to the prosthetist and may benefit from a stump lengthening protocol. The goal must be unrestricted shoulder movement with sufficient active stability of the prosthesis. If this goal is not achievable, the socket of the prosthesis needs to enclose the entire shoulder for reasons of stability. This fitting, however, restricts independent movement of the joint. To preserve shoulder movement in cases with high transhumeral amputations, osseointegration has shown to be a viable solution [21]. Additionally, especially in high-voltage burn injuries, patients may end up with a skin-grafted stump. In these cases, skin irritations and chronic wounds are an issue due to the stump-socket interface. Here, osseointegration allows a stable fitting without loading on skin-grafted areas. Direct anchorage of the prosthetic limb to the humeral bone thereby produces a stable connection and allows the patient to have unrestricted range of motion in the shoulder joint. A titanium implant is surgically placed into the residual humerus with an extension that penetrates the skin. This abutment is then used as an anchor for the attachment of the prosthetic limb (see Figs. 29.5 and 29.6). Depending on the implant system used, the surgical procedure is performed in one [22] or two stages [23, 24]. Although there is yet a limited numbers of patients with amputation of the upper extremity treated with osseointegration, the complication rate for the procedure in general is low [23, 24] and good clinical outcomes have been

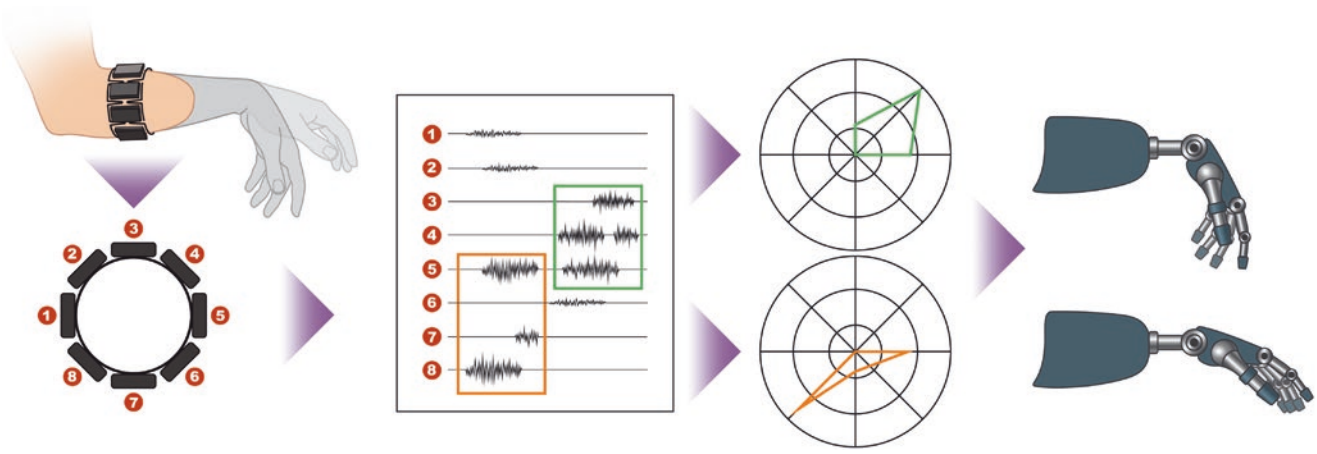


Fig. 29.4 Schematic drawing of a pattern recognition system used by a transradial amputee: Muscular activity on the forearm is measured by an array of electrodes. The raw signals of all channels are processed and compared to predefined activation patterns. If an activation pattern (marked in orange and green) is recognized, the prosthesis gets the control input to perform the intended movement (here flexion or neutral position of the wrist)

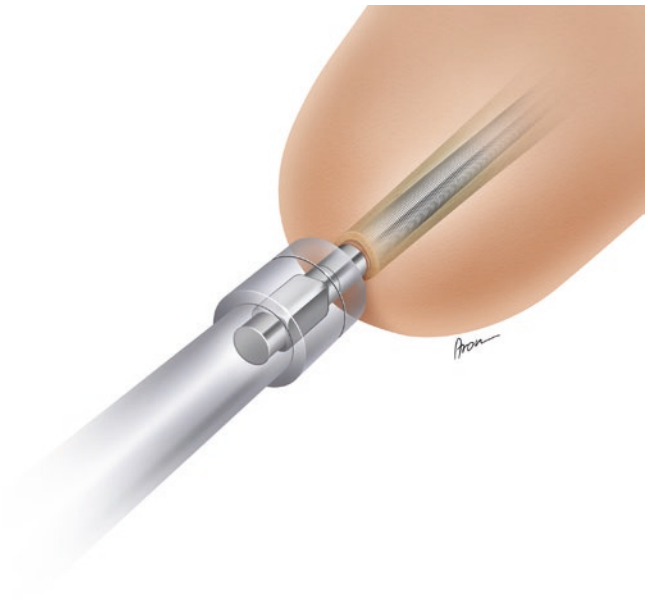


Fig. 29.5 Schematic drawing of an osseointegration system: The implant is surgically placed into the residual bone with an extension that penetrates the skin and is used as an anchor for the attachment of the prosthesis

reported [24]. Nevertheless, most post-surgical protocols after osseointegration require well-monitored rehabilitation by an interdisciplinary team, and the patient's long-term motivation and commitment must be ascertained prior to treatment [21].

29.6 Bionic Reconstruction in Patients Left with a Functionless Hand

In some patients after electrical burn injury, preservation of the upper extremity might be primarily successful, but still leave the patient with a functionless hand. As shown in Fig. 29.1f these patients are often confronted with a useless and aesthetically unappealing limb. This might not only limit them in activities of daily life but can also have a huge impact on psychological well-being, body image and self-worth [25]. Considering the functional and psychological impact on patients' lives, it is clearly evident that they cannot be left untreated after failure of standard reconstructive techniques. In these cases, where biological reconstruction cannot provide an acceptable outcome, bionic reconstruction should be considered. As proposed by our group [6], elective amputa-

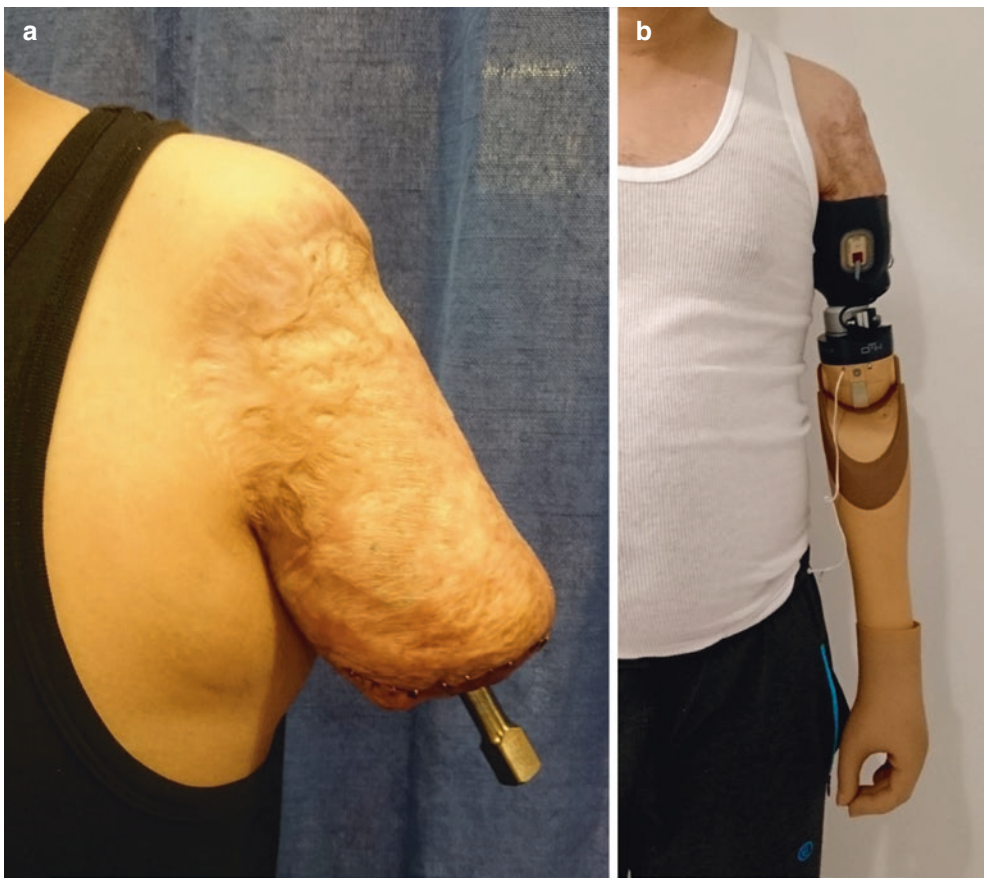


Fig. 29.6 (**a** and **b**) Patient with a skin-grafted transhumeral stump and osseointegration without (**a**) and with (**b**) his prosthetic fitting

tion of the functionless limb alongside prosthetic reconstruction of the hand can be a good solution for these patients. After amputation, rehabilitation and prosthetic fitting (see Fig. 29.2), we observed a clear improvement not only in hand function and perceived disability but also in quality of life, mental health and self-confidence. Considering the promising results of this approach, we encourage every clinician to discuss this option with patients where biological reconstruction has failed to provide a functional hand. Nevertheless, as this is an irreversible and elective procedure, patient selection and psychological evaluation are crucial before considering amputation, and performing a structured psychological assessment is therefore highly recommended [26].

29.7 Outlook

Extremity reconstruction in the twenty-first century will see many new avenues to replace the loss of a limb and reconstruct the loss of function. Both biological and technical advances will provide possibilities that may well open up therapies that have been unthinkable only a few years ago. Targeted muscle reinnervation, pattern recognition algorithms and improved skeletal attachments such as osseointegration together with the provision of various myoelectric prostheses with several degrees of freedom are definitely a solid stepping stone leading to new strategies in extremity rehabilitation. Technologies that are currently tested in the research setting, such as implantable electrodes for prosthetic control [27], systems for tactile feedback [28] or the innovative use of the postural synergies of the human hand [29], will further increase function, intuitivity and embodiment of biomimetic hands and thereby enable amputees to live a full life without restrictions.

References

1. Vierhapper MF, Lumenta DB, Beck H, Keck M, Kamolz LP, Frey M. Electrical injury: a long-term analysis with review of regional differences. Ann Plast Surg. 2011;66(1):43–6.
2. Lumenta DB, Vierhapper MF, Kamolz LP, Keck M, Frey M. Train surfing and other high voltage trauma: differences in injury-related mechanisms and operative outcomes after fasciotomy, amputation and soft-tissue coverage. Burns. 2011;37(8):1427–34.
3. Cheema SA. Pattern and profile of electric burn injury cases at a Burn Centre. J Ayub Med Coll. 2016;28(4):702–5.
4. Hunt JL, Mason AD Jr, Masterson TS, Pruitt BA Jr. The pathophysiology of acute electric injuries. J Trauma. 1976;16(5):335–40.
5. Sharma K, Bichanich M, Moore AM. A 3-phase approach for the management of upper extremity electrical injuries. Hand Clin. 2017;33(2):243–56.
6. Aszmann OC, Vujaklija I, Roche AD, Salminger S, Herceg M, Sturma A, et al. Elective amputation and bionic substitution restore functional hand use after critical soft tissue injuries. Sci Rep. 2016;6:34960.
7. Fitzgibbons P, Medvedev G. Functional and clinical outcomes of upper extremity amputation. J Am Acad Orthop Surg. 2015;23(12):751–60.
8. Kuiken TADG, Lipschutz RD, Miller LA, Stubblefield KA. The use of targeted muscle reinnervation for improved myoelectric prosthesis control in a bilateral shoulder disarticulation amputee. Prosthet Orthot Int. 2004;28(3):245–53.
9. Kuiken TA, Li G, Lock BA, Lipschutz RD, Miller LA, Stubblefield KA, et al. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. JAMA. 2009;301(6):619–28.
10. Aszmann OC, Dietl H, Frey M. Selective nerve transfers to improve the control of myoelectrical arm prostheses. Handchir Mikrochir Plast Chir. 2008;40(1):60–5.
11. Salminger S, Sturma A, Herceg M, Riedl O, Bergmeister K, Aszmann OC. Prosthetic reconstruction in high amputations of the upper extremity. Orthopade. 2015;44(6):413–8.
12. Salminger S, Mayer JA, Sturma A, Riedl O, Bergmeister KD, Aszmann OC. Prosthetic reconstruction of the upper extremity. Unfallchirurg. 2016;119(5):408–13.
13. Aszmann OC, Rab M, Kamolz L, Frey M. The anatomy of the pectoral nerves and their significance in brachial plexus reconstruction. J Hand Surg Am. 2000;25(5):942–7.
14. Stockinger T, Aszmann OC, Frey M. Clinical application of pectoral nerve transfers in the treatment of traumatic brachial plexus injuries. J Hand Surg Am. 2008;33(7):1100–7.
15. Sturma A, Bischof B, Herceg M, Stamm T, Fialka-Moser V, Wakolbinger R, et al. Recommendation for therapy after targeted muscle Reinnervation. University of new Brunswick's myoelectric controls/powered prosthetics symposium; 2014. New Brunswick: Institute of Biomedical Engineering, University of New Brunswick; 2014.
16. Sturma A, Roche AD, Gobel P, Herceg M, Ge N, Fialka-Moser V, et al. A surface EMG test tool to measure proportional prosthetic control. Biomed Tech. 2015;60(3):207–13.
17. Stubblefield KAML, Lipschutz RD, Kuiken TA. Occupational therapy protocol for amputees with targeted muscle reinnervation. J Rehabil Res Dev. 2009;46(4):481–8.
18. Roche AD, Rehbaum H, Farina D, Aszmann OC. Prosthetic myoelectric control strategies: a clinical perspective. Curr Surg Rep. 2014;2(3).
19. Englehart K, Hudgins B. A robust, real-time control scheme for multifunction myoelectric control. IEEE Trans Biomed Eng. 2003;50(7):848–54.
20. Roche AD, Vujaklija I, Amsuss S, Sturma A, Gobel P, Farina D, et al. A structured rehabilitation protocol for improved multifunctional prosthetic control: a case study. J Vis Exp. 2015;(105):e52968.
21. Jonsson S, Caine-Winterberger K, Branemark R. Osseointegration amputation prostheses on the upper limbs: methods, prosthetics and rehabilitation. Prosthet Orthot Int. 2011;35(2):190–200.
22. Al Muderis M, Lu W, Tetsworth K, Bosley B, Li JJ. Single-stage osseointegrated reconstruction and rehabilitation of lower limb amputees: the Osseointegration Group of Australia Accelerated Protocol-2 (OGAAP-2) for a prospective cohort study. BMJ Open. 2017;7(3):e013508.
23. Tsikandylakis G, Berlin O, Branemark R. Implant survival, adverse events, and bone remodeling of osseointegrated percutaneous implants for transhumeral amputees. Clin Orthop Relat Res. 2014;472(10):2947–56.
24. Hoffmeister T, Schwarze F, Aschoff HH. The endo-exo prosthesis treatment concept: improvement in quality of life after limb amputation. Unfallchirurg. 2017;120(5):371–7.
25. Kovacs L, Grob M, Zimmermann A, Eder M, Herschbach P, Henrich G, et al. Quality of life after severe hand injury. J Plast Reconstr Aesthet Surg. 2011;64(11):1495–502.

26. Hruby LA, Pittermann A, Sturma A, Aszmann OC. The Vienna psychosocial assessment procedure for bionic reconstruction in patients with global brachial plexus injuries. PLoS One. 2018;13(1):e0189592.
27. Weir RF, Troyk PR, DeMichele GA, Kerns DA, Schorsch JF, Maas H. Implantable myoelectric sensors (IMESs) for intramuscular electromyogram recording. IEEE Trans Biomed Eng. 2009;56(1):159–71.
28. Nghiem BT, Sando IC, Gillespie RB, McLaughlin BL, Gerling GJ, Langhals NB, et al. Providing a sense of touch to prosthetic hands. Plast Reconstr Surg. 2015;135(6):1652–63.
29. Fu Q, Santello M. Improving fine control of grasping force during hand-object interactions for a soft synergy-inspired myoelectric prosthetic hand. Front Neurorobot. 2017;11:71.

Part VI

Simulation and Training

Simulation and Training

30

Raimund Winter and Thomas Wegscheider

30.1 Introduction

Simulation is an important tool in teaching and increasingly used in medical education [1]. It provides the ability to improve teamwork, leadership, and technical skills [2]. In fact, simulation-based medical education (SBME) with deliberate practice appears to be superior to traditional medical education, especially in teaching practical skills [3]. Moreover, SBME can improve patient outcome [4] and has even shown to enhance the effectiveness of clinical day-to-day routines (e.g., surgical ward rounds) as well as burn care management algorithms. Research shows that medical staff that underwent training in Emergency Management of Severe Burns (EMSB) have better knowledge and improved practical skills. Nevertheless, SBME has not been widely used in EMSB training so far [5].

This chapter aims to give an introduction to SBME and its importance in the field of the management of severe burns.

30.2 Different Levels of Simulation

Simulation facilities all over the world face the same questions: Is it really all about realistic and true-to-life simulation (high fidelity)? Can training objectives be better achieved by less expensive and less complex simulation-based training modalities?

30.2.1 Low-Fidelity Training

The level of "fidelity" describes how realistic the training environment or training scenarios appear to the trainees [6]. "Low-fidelity training" (LFT) does not aim to mimic true-to-life scenarios and could take place in seminar rooms or lecture halls. There is no need for high-tech infrastructure or high-tech simulators. Part-task training (see Sect. 30.4.1) is commonly run as "low-fidelity training" by using mannequins designed for a limited set of tasks in a simple training environment. These so-called part-task trainers are often sturdy, resistant, and free of inbuilt electronics. They offer ideal conditions for efficient, repetitive task training, which is key in effective learning with simulation [7].

30.2.2 Mid-Fidelity Training

"Mid-fidelity training" (MFT) provides a higher level of realism. It takes place in more realistic environments (e.g., emergency-room-like settings) and/or uses more sophisticated mannequins. These mannequins or patient simulators commonly provide the possibility of simulating and exercising standard airway management procedures, cardiopulmonary resuscitation, defibrillation, cardioversion, etc. They are often equipped with central and peripheral pulses, lung, heart, and abdominal sounds.

30.2.3 High-Fidelity Training

"High-fidelity training" (HFT) emulates a true-to-life situation and often takes place in real care environments (in situ simulation) or virtual environments (virtual reality). HFT combines patient simulators, standardized patients (actors), and specific simulation software that provides realistic training in the assessment and management of patients. All vital parameters are simulated and displayed via a software-based virtual monitoring system. Trainees are encouraged to make

R. Winter (✉)
Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria
e-mail: r.winter@medunigraz.at

T. Wegscheider
Division of Special Anesthesiology, Pain and Intensive Care Medicine, Department of Anesthesiology and Intensive Care Medicine, Graz, Austria

Clinical Skills Center, Medical University of Graz, Graz, Austria
e-mail: thomas.wegscheider@medunigraz.at

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2_30

decisions and respond as though they are in a real medical care or emergency situation. Therefore, high-fidelity mannequins provide palpable central and peripheral pulses, speech transmission, chest raise, and lung, heart, and abdominal sounds. In addition, a wide range of invasive procedures can be performed [8].

If a scenario uses real actors, specific simulation suits designed to protect against invasive procedures are provided in order to prevent any injuries.

Another important part of HFT includes virtual reality training, which is of growing significance in simulation-based medical education. It allows the recreation of care situations in almost any environment at a remarkably high level of realism [9, 10].

30.2.4 It Is All About the Right Blend

Simulation-based training programs should consist of a variety of different fidelity levels, although the fidelity level has no significant impact on learning specific algorithms like advanced cardiac life support [11]. The right blend of LFT, MFT, and HFT modalities is important in enhancing trainees' knowledge, technical and communicative skills [12].

30.3 Training Modalities in Simulation-Based Medical Education

Training success in simulation-based medical education depends on not only the level of fidelity but also an understanding of the training objectives and the use of appropriate training modalities [13]. Each training module should provide an introductive briefing in procedures, skills, simulation equipment, and training environment and should conclude with a professional and structured debriefing. Research shows that feedback is the most important feature in SBME for efficient learning [7]. Audio-visual records can assist in a debriefing in all fidelity levels, not only in high-fidelity scenario training [14]. Trainees are provided with comprehensive feedback to enhance their learning experience.

30.3.1 Part-Task Training

Part-task training (PTT) is a low-cost, but highly effective modality in simulation-based medical education. Almost every medical skill can be practiced by PTT, dividing complex procedures into single, clear tasks. During PTT, trainees should be encouraged to concentrate on performing a specific task, aiming to master a particular technical skill. PTT is commonly used for learning airway management skills, such as bag-mask-ventilation, endotracheal intubation, or cricothyrotomy [15].

30.3.2 Algorithm Training (AT)

Medical societies have created general and specific algorithms for many care situations. These algorithms set the standard of care that health care professionals must adhere to; therefore training is essential. Algorithms help to break up complex procedures into consecutive single tasks. In AT, trainees are coached to work through all relevant tasks in a structured and accurate way. It requires teamwork and training of communication skills. These soft skills are essential in learning how to handle unplanned disruptions ("distractors") in real-life situations, which are simulated in this training. In health care, algorithms aim to facilitate decision-making in complex, potentially time-sensitive situations [15].

30.3.3 Scenario Training

Scenario training (ST) aims to consolidate a trainee's knowledge, technical and communication skills in a specific situation. Thus, ST combines different care processes and algorithms with a "story." Various scenarios are used, mixing different care processes and algorithms to simulate a real-life situation for the trainee. Distractors play an important part in this type of training. Experienced simulation professionals gradually incorporate distractions during scenarios, taking into consideration the participants' performance [15].

30.3.4 Full-Scale Care Process Simulation Training

Full-scale care process simulation training (FSCPST) provides high-fidelity training of the entire process of patient care. This begins with the initial assessment and management at the emergency department and includes all diagnostic, therapeutic, logistic, and transfer decisions. It continues with critical care transfer to the OR or ICU as well as surgical care in the OR and ends with the postoperative management on the ward. This training modality uses mannequins, actors as well as virtual reality elements to create a maximum of realism. It is also vital that this training includes multidisciplinary decision-making, triage and disaster management, communication with patients and their relatives as well as end-of-life decisions. This not only fosters improvement of soft skills but also instills a comprehensive understanding of trainee's performance expectations in critical care management [15].

30.4 SBME in the Emergency Management of Burns

SBME became an important tool for education in the last years, especially for residency training [16]. Simulation can improve patient safety and medical care by optimizing clinical skills, management, leadership, and decision-making abilities [2, 17]. However, only few reports of comprehensive burn care simulation can be found in the literature [18–21]. FSCPSTs containing a simulation pathway including all steps of treatment (from the arrival at the Emergency Room to discharge from the hospital) have not been reported so far, to the best of our knowledge.

Complex burn injuries require cooperation between different departments in order to successfully manage potential complications including complex fluid and electrolyte lapse, cardiac complications from high-voltage current, smoke inhalation injury, and carbon monoxide (CO) and cyanide (CN) intoxication. As a consequence, proficient communication skills are necessary for optimal coordination between participating departments. Simulation provides an effective tool for training and can help large interdisciplinary teams avoid medical errors and maximize care efficacy. It can lead to an improvement in communication, teamwork, and consequently the overall efficiency of patient care [22, 23]. Moreover, trainees can practice in an environment where mistakes are acceptable and expected in the learning process [24], whereas in medicine learning from errors is generally considered a notorious teaching method [25–27].

In a trauma room, total-care algorithms should run as smoothly as possible. The physician in charge of the initial management of a burn patient has to be confident in his ability to diagnose and treat thermal burns, smoke inhalations, and possible intoxication.

However, given the relatively low number of severe burn injuries, a resident in training is not likely to have witnessed enough cases of severe burn injuries and thus gain enough hands-on experience to be able to confidently manage these cases by the time he or she is the physician in charge. Trained physicians who begin working at a hospital with a burn center can improve their knowledge and skills with simulation training in order to provide the standard quality of care required. Severe burns have an approximate incidence of 0.2 to 2.9/10.000 inhabitants in Europe with a mortality between 1.4 and 34% [28]. Considering the low incidence, SMBE allows residents to acquire skills and learn specific procedures to optimize management of these rare cases [16]. By identifying sources of error, knowledge gaps, resource shortages, and weaknesses in teamwork, simulation is an important tool to further improve the outcome of severely burned patients.

30.4.1 Burn Care-Specific Technical Skills and Tools

On one hand, burn care requires the collaboration of different specialties. As a consequence, FSCPST with critical care transfer and intensive care simulation is an important part of the training. It improves the coordination between different departments and the trainees' communicative skills. Role-playing and computer-based scenario simulation sharpen the participants' awareness of the importance of effective communication strategies and the principles of crisis resource management (CRM) in emergency situations.

On the other hand, part-task training as a component of SBME is necessary to practice specific surgical skills and become familiar with the handling of medical instruments and tools. These skills acquired in simulation training can be directly applied in the operating theater [29]. As an example, trainees can practice escharotomy [30] on mannequins as well as the tangential excision of predefined areas in foam wound suture pads (Limbs&Things.com, Savannah, GA) [31]. Furthermore, skin grafting with simulators using Microfoam™ tape (3M Health Care) [32], porcine skin [33], or even lasagne [34] to imitate skin can be practiced.

In addition to the surgical treatment, patients in a critical state need accurate therapy of airway problems and fluid loss. Again, simulation-based training allows the development and practicing of specific skills such as surgical airway installation, bronchoscopy, chest tube insertion, fiberoptic endotracheal intubation, central venous access, and intraosseous access to the vascular system. Moreover, central and peripheral pulses, chest X-rays, and lung, heart, and abdominal sounds can be evaluated. A transurethral catheterization for fluid management, central and peripheral punctures, as well as vital sign evaluation with a virtual monitoring software can also be simulated.

In EMSB, the assessment of a patients' total body surface area (TBSA) plays a central role for fluid resuscitation. Inaccurate estimations result in high variations of initial fluid resuscitation volumes [35]. To improve these estimations, burned areas can easily be simulated by photographs, films, or with "burned" mannequins.

Generally, emergency management and the management of severe burn injuries follow specific algorithms. In mid- and high-fidelity simulation-based algorithm training sessions, participants can learn how to apply their technical and soft skills in critical situations and to follow common and special algorithms in Advanced Burn Life Support. Debriefing using audio-visual recordings, focusing on leadership, and effective communication in medical teams can further improve the outcome.

In the simulated environment, all these skills can be perfected not only for adult patients but also for children without

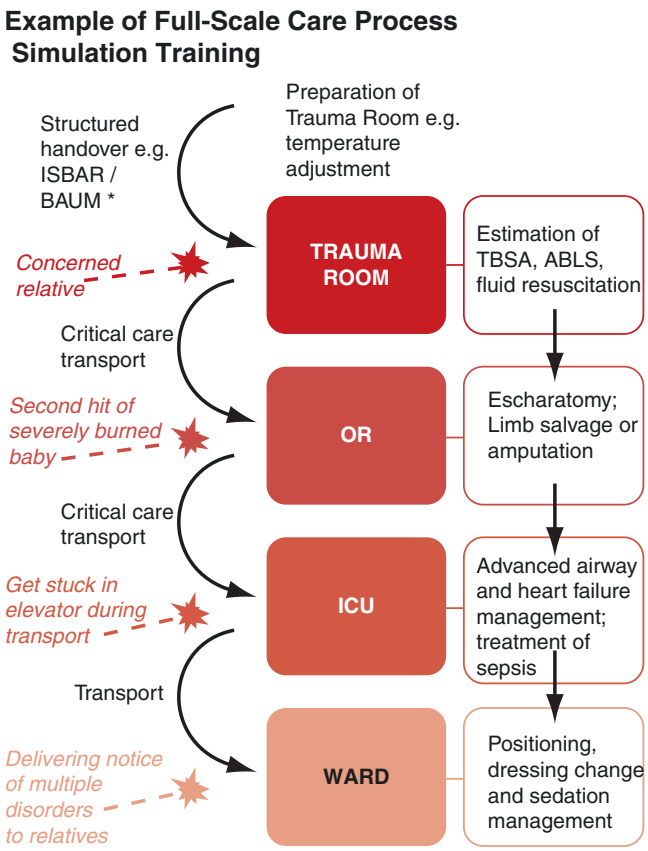


Fig. 30.1 Example 1 of FSCPS for the management of severely burned patients. *ISBAR/BAUM/SAFE: handover performance tools/algorithm for structured medical handovers

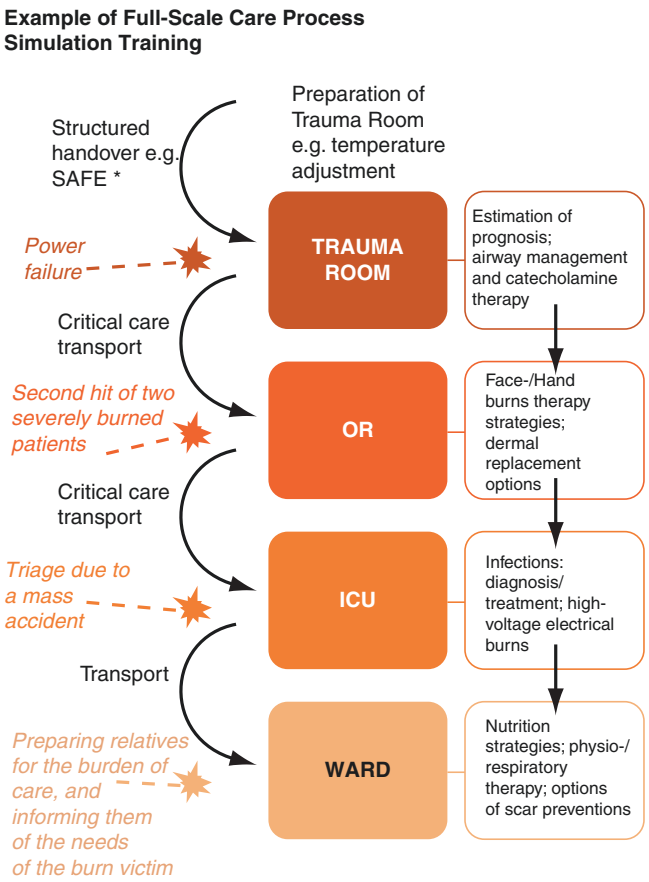


Fig. 30.2 Example 2 of FSCPS for the management of severely burned patients. *ISBAR/BAUM/SAFE: handover performance tools/algorithm for structured medical handover

time constraints, helping medical staff to gain competence and confidence in emergency situations.

Figures 30.1 and 30.2 demonstrate two examples of the structure of full-scale care process simulation training.

References

1. McLaughlin S, Fitch MT, Goyal DG, Hayden E, Kauh CY, Laack TA, et al. Simulation in graduate medical education 2008: a review for emergency medicine. Acad Emerg Med. 2008;15(11):1117–29.
2. McMahon GT. What do I need to learn today?—the evolution of CME. N Engl J Med. 2016;374(15):1403–6. https://doi.org/10.1056/NEJMp1002530.
3. McGaghie WC, Issenberg SB, Cohen ER, Barsuk JH, Wayne DB. Does simulation-based medical education with deliberate practice yield better results than traditional clinical education? A meta-analytic comparative review of the evidence. Acad Med. 2011;86(6):706–11. http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00001888-201106000-00018.
4. Brydges R, Hatala R, Zendejas B, Erwin PJ, Cook DA. Linking simulation-based educational assessments and patient-related outcomes. Acad Med. 2015;90(2):246–56. http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00001888-201502000-00032.
5. Breederveld RS, Nieuwenhuis MK, Tuinebreijer WE, Aardenburg B. Effect of training in the Emergency Management of Severe Burns on the knowledge and performance of emergency care workers as measured by an online simulated burn incident. Burns. 2011;37(2):281–7. https://doi.org/10.1016/j.burns.2010.08.011.
6. Alessi SM. Simulation design for training and assessment. Aircrew training and assessment. Mahwah, NJ: Lawrence Erlbaum Associates; 2000. p. 197–222.
7. Barry Issenberg S, Mcgaghie WC, Petrusa ER, Lee Gordon D, Scalese RJ. Features and uses of high-fidelity medical simulations that lead to effective learning: a BEME systematic review. Med Teach. 2005;27(1):10–28.
8. Laerdal [Internet]. http://www.laerdal.com/de/doc/86/SimMan.
9. Székely G, Satava RM. Virtual reality in medicine. Br Med J. 1999;319(7220):1305.
10. Kneebone R. Simulation in surgical training: educational issues and practical implications. Med Educ Wiley Online Library. 2003;37(3):267–77.
11. Conlon LW, Rodgers DL, Shofer FS, Lipschik GY. Impact of levels of simulation fidelity on training of interns in ACLS. Hosp Pract. 2014;42(4):135–41.
12. Scerbo MW, Dawson S. High fidelity, high performance? Simul Healthc LWW. 2007;2(4):224–30.
13. Maran NJ, Glavin RJ. Low-to high-fidelity simulation—a continuum of medical education? Med Educ. 2003;37(s1):22–8.
14. Motola I, Devine LA, Chung HS, Sullivan JE, Issenberg SB. Simulation in healthcare education: a best evidence practical

guide. AMEE Guide No. 82. Med Teach. 2013;35(10):e1511–30. https://doi.org/10.3109/0142159X.2013.818632.
15. Kyle R, Murray WB. Clinical simulation. New York: Academic Press; 2010.
16. Okuda Y, Bond W, Bonfante G, McLaughlin S, Spillane L, Wang E, et al. National growth in simulation training within emergency medicine residency programs, 2003-2008. Acad Emerg Med. 2008;15(11):1113–6.
17. Ziv A, Ben-David S, Ziv M. Simulation based medical education: an opportunity to learn from errors. Med Teach. 2005;27(3):193–9.
18. Parsons M, Murphy J, Alani S, Dubrowski A. Thermal burns and smoke inhalation: a simulation session. Cureus. 2015;7(10):e360. http://www.cureus.com/articles/3367-thermal-burns-and-smoke-inhalation-a-simulation-session.
19. Nilsson H, Jonson CO, Vikström T, Bengtsson E, Thorfinn J, Huss F, et al. Simulation-assisted burn disaster planning. Burns. 2013;39(6):1122–30.
20. Kearns RD, Hubble MW, Holmes JH IV, Lord GC, Helminiak RAC, Cairns BA. Advanced burn life support for day-to-day burn injury management and disaster preparedness: stakeholder experiences and student perceptions following 56 advanced burn life support courses. J Burn Care Res LWW. 2015;36(4):455–64.
21. Stone CA, Pape SA. Evolution of the emergency management of severe burns (EMSB) course in the UK. Burns. 1999;25(3):262–4.
22. Capella J, Smith S, Philp A, Putnam T, Gilbert C, Fry W, et al. Teamwork training improves the clinical care of trauma patients. J Surg Educ. 2010;67(6):439–43. https://doi.org/10.1016/j.jsurg.2010.06.006.
23. Steinemann S, Berg B, Skinner A, Ditulio A, Anzelon K, Terada K, et al. In situ, multidisciplinary, simulation-based teamwork training improves early trauma care. J Surg Educ. 2011;68(6):472–7.
24. Ziv A, Wolpe PR, Small SD, Glick S. Simulation-based medical education: an ethical imperative. Acad Med. 2003;78(8):783–8. http://www.ncbi.nlm.nih.gov/pubmed/12915366.
25. Blumenthal D. Making medical errors into medical treasures. JAMA. 1994;272(23):1867–8.
26. Rasmussen J. The role of error in organizing behaviour. Ergonomics. 1990;33(10–11):1185–99.
27. Senders JW, Moray NP. Human error: cause, prediction, and reduction. Hillsdale, NJ: Lawrence Erlbaum; 1991.
28. Brusselaers N, Monstrey S, Vogelaers D, Hoste E, Blot S. Severe burn injury in Europe: a systematic review of the incidence, etiology, morbidity, and mortality. Crit Care. 2010;14(5):R188. http://ccforum.com/content/14/5/R188.
29. Sturm LP, Windsor JA, Cosman PH, Cregan P, Hewett PJ, Maddern GJ. A systematic review of skills transfer after surgical simulation training. Ann Surg LWW. 2008;248(2):166–79.
30. Foot C, Host D, Campher D, Tomczak L, Ziegenfuss M, Cohen J, et al. Moulage in high-fidelity simulation—a chest wall burn escharotomy model for visual realism and as an educational tool. Simul Healthc LWW. 2008;3(3):1–5.
31. Gallagher JJ, Goldin IM, Sullivan GMO, Silverman EL, Mitchell KB, Yurt RW. Simulation of tangential excision: a test for construct validity. J Burn Care Res. 2004;36:558–64.
32. Watt DA, Majumder S, Southern SJ. Simulating split-skin graft harvest. Br J Plast Surg. 1999;52(4):329.
33. Wilson PA, Rhodes ND, Southern SJ. Surgical simulation in plastic surgery. Br J Plast Surg. 2001;54(6):560–1.
34. Bennett SPH, Velander P, McArthur PA, McPhail J, Alvi R, Graham KE. A novel model for skin graft harvesting. Plast Reconstr Surg LWW. 2004;114(6):1660–1.
35. Parvizi D, Kamolz L-P, Giretzlehner M, Haller HL, Trop M, Selig H, et al. The potential impact of wrong TBSA estimations on fluid resuscitation in patients suffering from burns: things to keep in mind. Burns. 2014;40(2):241–5.

Index

L.-P. Kamolz et al. (eds.), *Handbook of Burns Volume 2*, https://doi.org/10.1007/978-3-030-34511-2