

# **15**

## **Lasers in Periodontal and Peri-implant Therapy: Challenges and Opportunities**

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## **Contents**



## <span id="page-0-0"></span>**15.1 Introduction**

Multiple nonsurgical and surgical approaches have been applied in the management and control of inflammatory periodontal and peri-implant diseases. The primary goal of treatment is to achieve periodontal and peri-implant health and to reduce risk of future disease recurrence and/or progression. A common clinical objective in the management of these inflammatory conditions is

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to reduce the burden of pathogenic bacteria and, presumably, risk for progressive inflammation and disease recurrence. Periodontal bacterial pathogens, such as *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, and *Aggregatibacter actinomycetemcomitans*, exhibit strong associations with periodontitis [\[1](#page-20-3)]. Evidence suggest that the microflora of the oral cavity prior to implant placement determines the composition of the microflora in the peri-implant area [\[2](#page-20-4)]. Consistent with the foregoing premise is the observation that the primary bacterial species implicated in the pathogenesis of peri-implantitis are recognized as periodontal pathogens [\[3](#page-20-5)]. In a recent systematic review, Perez-Chaparro et al. [\[3](#page-20-5)] concluded that there is moderate evidence to support an association of *P. gingivalis*, *T. denticola*, and *T. forsythia* in the etiology of peri-implantitis. Additionally, there is some evidence to implicate *P. intermedia* and *Campylobacter rectus* in the etiology of periimplantitis. Conventional active therapy has targeted the disruption and removal of dental plaque (biofilm) and calculus, root/implant surface decontamination and/or modification (e.g., root planing), with often a concomitant goal of reducing pocket depth. The management of contributing etiologic factors, such as cigarette smoking, inclusion of a conscientious regimen of daily oral hygiene, and regular professional supportive periodontal maintenance remain essential [[4\]](#page-20-6). Surgical treatment approaches are commonly applied to manage moderate and advanced periodontitis and peri-implantitis, often with the objective of achieving either periodontal or peri-implant bone regeneration, respectively [[5\]](#page-20-7). Longitudinal studies document the stability of clinical outcomes achieved with regenerative periodontal therapy; however, available data on long-term (>5 years) outcomes are insufficient to meaningfully compare clinical improvements and tooth or implant survival following various treatment approaches. Nevertheless, several factors consistently appear to increase risk of tooth or implant loss, including uncontrolled diabetes and pretreatment severity of bone loss [\[6](#page-20-8), [7\]](#page-20-9). Longitudinal studies suggest that the particular periodontal therapy is less important than thorough debridement of the diseased area, frequent professional care, and excellent oral hygiene practices by the patient [\[8](#page-20-10)]. Moreover, compliance with regular professional supportive care is associated with improved tooth retention [[6,](#page-20-8) [9](#page-20-11), [10](#page-20-12)] and implant survival [[7,](#page-20-9) [11\]](#page-20-13).

In general, the treatment of periodontal and peri-implant diseases targets the detoxification of root/implant surfaces alone or in combination with tissue regeneration and/or the elimination of periodontal/peri-implant pocketing as well as establishment of effective patient plaque-control regimens and regular professional supportive care [[12\]](#page-21-0). Conventional surgical approaches, such as open flap debridement, provide critical access to evaluate and detoxify root and implant surfaces as well as establish improved periodon-

tal form and architecture; however, these surgical techniques alone offer only limited potential in restoring or reconstituting bone or component periodontal tissues. Moreover, traditional therapeutic approaches are hampered by clinician-, patient-, and site-related factors. These factors include, among others, a clinician's surgical skills, patient habits such as smoking, defect configuration, and clinical access for effective debridement and disinfection.

The introduction of LASER (light amplification by stimulated emission of radiation) technology has ushered in new therapeutic strategies and approaches to the treatment of inflammatory periodontal and peri-implant diseases [\[13](#page-21-1)]. Laser radiation (beam) is characterized by high directionality (collimation), coherence (photons are emitted in-phase), monochromaticity (narrow spectral width), and intensity (brilliancy). When laser light strikes a tissue surface, it can be reflected and refracted, scattered, absorbed, or transmitted. The fractional intensity that goes into these different processes depends on the optical properties of the tissue as well as the laser parameters, such as wavelength, energy, and pulse duration. The wavelength of light is the primary parameter determining the extent of energy absorption by a target tissue (Fig. [15.1](#page-2-0)). Each wavelength of laser energy exhibits unique absorption characteristics by cellular chromophores—including keratin, melanin, collagen, lipids, and certain proteins, among others—hemoglobin, oxyhemoglobin, and water. Laser energy is similarly absorbed by bacterial chromophores. The laser wavelength defines the mechanism of interaction, depth of penetration (Fig. [15.2\)](#page-2-1), and absorption of photon energy which can include photothermal (i.e., heating), photodynamic (mediated by exogenous chromosphere molecules or photosensitizers), biostimulation, and photoablation (ablative decomposition) responses [\[15](#page-21-2)].

In a recent review of lasers and the treatment of periodontitis, Cobb succinctly summarized the key suppositions underlying the general rationale for laser periodontal therapy as well as evidence to support them. [[16\]](#page-21-3) The presumed clinical benefits of using lasers, or specific laser wavelengths, as a monotherapy or adjunct to traditional therapeutic

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**Fig. 15.1** Approximate net absorption curves of various tissue components, including water  $(H_2O)$ , tooth enamel, melanin, and hemoglobin (Hb).  $CO<sub>2</sub>$  carbon dioxide, *Er,Cr:YSGG* erbium, chromium-doped yttriumscandium-gallium-garnet, *Er:YAG* erbium-doped yttrium-aluminum-garnet, *KTP* potassium titanyl phosphate, *Nd:YAG* neodymium-doped yttrium-aluminum-

garnet, *Nd:YAP* neodymium-doped yttrium-aluminumperovskite. (Image courtesy of Dr. Donald J. Coluzzi, and adapted from D. J. Coluzzi, Fundamentals of lasers in dentistry: basic science, tissue interaction, and instrumentation. J Laser Dent 16 (Spec. Issue): 4–10, 2008; with permission<sup>®</sup> 2008 Academy of Laser Dentistry  $[14]$  $[14]$ 

<span id="page-2-1"></span>

**Fig. 15.2** Classification of lasers according to depth of light penetration in tissue—superficially absorbed type (shallow penetration and scatter) versus deeply penetrating type (deep penetration and scatter).  $CO<sub>2</sub>$  carbon dioxide, *CW* continuous wave, *Er,Cr:YSGG* erbium, chromium-doped yttrium-scandium-gallium-garnet, *Er:YAG* erbium-doped yttrium-aluminum-garnet, *Nd:YAG* neodymium-doped yttrium-aluminum-garnet. (Image reproduced from A. Aoki et al., Periodontal and peri-implant wound healing following laser therapy. Periodontol 2000 68: 217–269, 2015; with permission© 2015 John Wiley & Sons A/S [\[14](#page-21-4)])

strategies, include significant potential for root surface debridement and detoxification, reduced subgingival bacterial burden, targeted eradication of pigmented anaerobic gram-negative bacteria, effectual subgingival curettage, suppression of inflammation, biostimulation, and periodontal regeneration [[16\]](#page-21-3). Although peri-implant tissues differ from periodontal tissues in terms of composition and organization, these same suppositions apply and can be extrapolated to the application of lasers to peri-implant therapy.

This chapter provides an overview of laser science and clinical evidence on the therapeutic efficacy of lasers as a monotherapy or adjunct to traditional nonsurgical and surgical approaches in the treatment of periodontal and peri-implant diseases.

## <span id="page-3-0"></span>**15.2 Impact of Local Environmental Cues**

The ability of cells to sense and respond to their local environment is essential for normal cellular function and survival and provides an important therapeutic pathway to modulate wound healing. Bone grafts are intended to promote and/or accelerate natural regenerative processes at the site of the defect by providing architectural support and stability, serving as an osteoconductive scaffold for anchorage-dependent cells with osteogenic potential. Grafts containing growth factors or osteoblasts/osteoprogenitor cells also exhibit the ability to directly induce bone formation or promote osteogenesis, respectively. Evidence also points to the capacity for the graft, serving as a substratum, to function as an insoluble signal regulating the expression of the soluble osteogenic molecular signals of the TGF-β superfamily and initiating bone formation by induction [[17](#page-21-5)[–19](#page-21-6)].

The responsiveness of mesenchymal stem cells, osteoprogenitor cells, and osteoblasts to certain environmental cues, such as pulsed electromagnetic fields and nanovibrational fields, forms the basis for clinical practice of biophysical stimulation to increase and enhance reparative anabolic activity of the bone [[20\]](#page-21-7). The molecular basis of bone mechanotransduction is complex and reflects

a diverse interplay of ion channels, integrins, cell membrane, cytoskeleton, and other systems [\[21\]](#page-21-8). Recent studies suggest that laser energy can also modify the molecular dynamics of the membrane [\[22](#page-21-9), [23\]](#page-21-10). These membrane alterations may be attributable in part to induction of free radical generation and to change in enzymatic and antioxidative activities of cellular components [\[23\]](#page-21-10). Laser energy has the potential to modulate a wide array of cellular and molecular pathways.

Hosseinpour et al. [[24](#page-21-11)], for example, comprehensively reviewed in vitro and in vivo studies evaluating the effects of laser radiation on cellular and molecular activities, including osteogenic markers, angiogenic markers, growth factors, and inflammatory mediators, with the potential to impact bone regeneration. Photobiomodulation was found to significantly enhance expression of osteocalcin, collagen, RUNX-2, vascular endothelial growth factor (VEG-F), bone morphogenetic proteins (BMPs), and COX-2. Given the heterogeneity of the studies, Hosseinpour et al. [[24\]](#page-21-11) concluded that the effects of laser irradiation depend on multiple laser parameters; however, the most important parameter appears to be energy density. Furthermore, the authors concluded that there is insufficient evidence to guide the clinical therapeutic application of photobiomodulation. Emelyanov and Kiryanova [[25\]](#page-21-12), in contrast, concluded that cell type, rather than wavelength, was most important in choosing laser parameters. These authors also concluded that the highest increases in proliferation or differentiation were obtained using high power density, low energy density, and short exposure time. Bayat et al. [\[26](#page-21-13)] also concluded that low-level laser therapy causes a stimulatory effect on osteoblasts and osteocytes and enhances osteoblast proliferation and differentiation of different bone cell lines used in in vitro studies. Escudero et al. [\[27](#page-21-14)] similarly concluded that low-level laser therapy has positive photobiostimulatory effects on bone regeneration, accelerating its process regardless of parameters and the use of biomaterials. The results of these studies are consistent with other evidence that laser radiation has the ability to stimulate gingival fibroblast proliferation,

collagen synthesis, and wound healing [\[28–](#page-21-15)[30\]](#page-21-16). Cell stimulatory effects have been demonstrated in response to irradiation by low-level lasers, including Ga-Al-As (805 or 650 nm), diode (810 nm, 870, or 940 nm), pulsed Nd:YAG, and Er:YAG lasers. [[31–](#page-21-17)[33](#page-21-18)] [[34\]](#page-21-19)

Preclinical investigations provide evidence for the potential of laser energy to influence bone metabolism and wound healing. Kim et al. [[35\]](#page-21-20), for example, examined bone repair following the application of a pulsed Nd:YAG laser, using a noncritical-sized calvarial defect model in rats and rabbits. The defects were left empty or filled with a collagen membrane prior to wound clo-sure (Fig. [15.3](#page-4-0)). Starting the day after surgery, one defect in each animal was irradiated with a Nd:YAG laser once every 2 days for 2 weeks at a constant total fluence rate (344 J/cm<sup>2</sup>), output power (0.75 W), pulse repetition rate (15 pps), and wavelength (1064 nm) holding the laser source 1–2 cm from the calvarial skin surface. Microcomputed tomography was performed after 4 weeks of defect healing. Laser irradiation resulted in significantly greater new bone area and percentage bone normalized to total defect area compared to nonirradiated control defects with and without scaffold in both animal models (Fig. [15.4](#page-5-1)).

Laser irradiation is absorbed by intracellular chromophores, presumably altering cellular activity, and is an important mechanism of action of low-level laser radiation. However, high-intensity pulsed laser irradiation can produce acoustic waves in the target tissue. Ninomiya et al.  $[36]$  examined the potential for high-intensity pulsed laser irradiation to accelerate bone formation using a femur model in rats. A Q-switched Nd:YAG laser was used to irradiate femurs either once a day, with the average fluence rate set at 100 mW/cm<sup>2</sup>, or twice daily, with the average fluence rate set at 50 mW/cm2 . The mean bone volume and mineral apposition rate in the metaphysis was significantly higher following laser irradiation than the nonirradiated control group; however, the increase was highest for the lower fluence and higher-frequency condition, suggesting an important role for pulse frequency in bone formation. Ninomiya et al. [[36](#page-21-21)] concluded that the formation of the bone induced by highintensity pulsed laser irradiation might be due to laser-induced pressure waves. In a subsequent study, Ninomiya et al. [[29\]](#page-21-22) demonstrated that nanosecond pulsed laser irradiation of the rat femur, using a Q-switched Nd:YAG laser, resulted in an increased bone volume and min-

<span id="page-4-0"></span>

**Fig. 15.3** Study of bone repair following application of a pulsed Nd:YAG laser, using a noncritical-sized calvarial defect model in rats and rabbits (**a**). In rats, a 5-mm-diameter bilateral calvarial bone defects were created and left empty or implanted with a collagen sponge. Starting the day after surgery, one defect in each animal was irradiated with a Nd:YAG laser once every 2 days for 2 weeks at a constant total fluence rate

(344 J/cm2 ), output power (0.75 W), and pulse repetition rate (15 pps), holding the laser source and adapted 1–2 cm from the calvarial skin surface (**b**). (Images courtesy of Dr. Soon Jung Hwang, and adapted from K. Kim et al., High-intensity Nd:YAG laser accelerates bone regeneration in calvarial defect models. J Tissue Eng Regen Med 9: 943–951, 2013; with permission© 2013 John Wiley & Sons [[35](#page-21-20)])

<span id="page-5-1"></span>

**Fig. 15.4** Histomorphometry based on microcomputed tomography-based analysis of calvarial defect after 4 weeks of healing (**a**–**b**). Dotted circles in blue (nonirradiated control group) and red (irradiated laser group) indicate the position and dimensions of the 5 mm original defect size. (**c**) Histomorphometric analysis revealed significantly  $(p < 0.05)$  greater new bone area (mm<sup>2</sup>; left axis) and percentage (%) normalized to total defect area (right axis) for

eral density based on morphometric analysis. Importantly, the histologic analysis revealed a decrease in number of osteoclasts, suggesting that the laser-induced increase in bone volume was partially attributable to a decrease in osteoclastic activity. Other preclinical studies, however, using different laser wavelengths, protocols, and experimental models, have provided varying results with respect to bone healing [[37](#page-21-23), [38\]](#page-21-24).

laser-irradiated defects (dark bar) compared to nonirradiated control defects (light bar) with and without scaffold. Similar results were shown using an 8 mm calvarial defect model in the rabbit. (Images courtesy of Dr. Soon Jung Hwang, and adapted from K. Kim et al., High-intensity Nd:YAG laser accelerates bone regeneration in calvarial defect models. J Tissue Eng Regen Med 9: 943–951, 2013; with permission<sup>®</sup> 2013 John Wiley & Sons  $[35]$  $[35]$  $[35]$ )

## <span id="page-5-0"></span>**15.3 Wound Healing: Windows of Opportunity**

Lasers have the potential to affect each of the four highly integrated and overlapping phases of the wound-healing process: hemostasis, inflammation, proliferation, and tissue remodeling or resolution [\[39,](#page-21-25) [40](#page-21-26)]. High-intensity lasers, for example, have been shown to induce photothermal and hemodynamic responses that

lead to swelling and rupture of erythrocytes, ultrastructural perturbation of the endothelial cell membrane and denudation of the endothelial monolayer triggering primary and secondary hemostasis, and coagulation secondary to protein denaturation, conformational rearrangement, and cross-linking and aggregation (reviewed by [\[41](#page-22-0)]).

Cell culture and experimental animal models of inflammation provide evidence that low-level laser irradiation reduces inflammatory mediators and markers of inflammation. Lee et al. [\[42\]](#page-22-1), for example, examined the anti-inflammatory effect of laser irradiation on human periodontal ligament cells cultured with or without lipopolysaccharide (LPS) from *P. gingivalis* or *Escherichia coli*, followed by irradiation with a gallium-aluminum-arsenide (GaAlAs) laser (660 nm) at an energy density of 8 J/ cm2 . Laser irradiation was shown to inhibit the LPS-induced pro-inflammatory cytokine gene expression, including tumor necrosis factor- $\alpha$ (TNF-α), interleukin 1-ß (IL-ß), interleukin 6 (IL-6), and interleukin 8 (IL-8), decrease nuclear factor-κB (NF-κB) transcriptional activity, and elevate intracellular levels of cyclic adenosine monophosphate (cAMP) relative to the unexposed control cells. The results suggest that low-level laser irradiation might inhibit LPS-induced inflammation through the cAMP/ NF-κB pathway. Wu et al. [[43\]](#page-22-2) investigated the anti-inflammatory effect of low-power laser irradiation using a GaAlAs laser (660 nm) on LPStreated human adipose-derived stem cells. LPS exposure significantly induced the production of pro-inflammatory cytokines (cyclooxygenase-2, IL-1ß, IL-6, and IL-8). Laser irradiation markedly inhibited LPS-induced, pro-inflammatory cytokine expression at an optimal dose of 8 J/ cm2 . Giannelli et al. [\[44](#page-22-3)] reported that lowintensity Nd:YAG laser irradiation significantly reduced *P. gingivalis* LPS-induced nitric oxide production and cell activation by macrophages and strongly attenuated intercellular adhesion molecule-1 and vascular cell adhesion molecule expression, as well as interleukin-8 production, by endothelial cells, thereby blunting the LPSinduced inflammatory response. These culture studies highlight the ability to modulate the inflammatory response through laser irradiation,

presumably through common or overlapping cellular pathways.

Bortone et al. [\[45](#page-22-4)] examined the effect of lowlevel laser irradiation on kinin receptor messenger ribonucleic acid (mRNA) expression in the carrageenan-induced rat paw model of edema. The results demonstrated that laser irradiation (660 or 684 nm wavelength) significantly decreased Kinin B1 receptor mRNA expression and modestly decreased Kinin B2 receptor mRNA expression. Using an LPS-induced peritonitis model in mice, Correa et al. [[46\]](#page-22-5) examined the effect of an infrared low-level laser (GaAs; 904 nm, 4 mW) on the migration of inflammatory cells. Laser irradiation was found to diminish inflammatory cell migration in a dose-dependent manner, with the strongest effect on migration with the 3-J/ cm2 exposure, with reductions of 77% in neutrophil counts and 49% in leukocyte counts. Pires et al. [[47\]](#page-22-6) reported that low-level laser irradiation decreased IL-6 and cyclooxygenase-2 (COX-2) expression in both acute and chronic phases in collagenase-induced tendinitis in rats.

Boschi et al. [\[48](#page-22-7)] reported that low-level laser irradiation (660 nm) induced an antiinflammatory effect characterized by inhibition of either total or differential leukocyte influx, exudation, total protein, nitric oxide (NO), IL-6, monocyte chemoattractant protein-1 (MCP-1), interleukin 10 (IL-10), and TNF- $\alpha$ , in a dosedependent manner in carrageenan-induced pleurisy in a rodent model. Collectively, the results of these studies and others [[49–](#page-22-8)[51\]](#page-22-9) document the potential for low-level laser (e.g., Nd:YAG, diode) to suppress mediators of inflammation and that this effect likely involves modulation of the NF-κB transcriptional pathway [\[52](#page-22-10)].

Of particular importance to regenerative wound healing is evidence that low-level laser (e.g., Nd:YAG, diode,  $CO<sub>2</sub>$ ) irradiation has the capacity to promote the proliferation and differentiation of mesenchymal stem cells as well as the proliferation of gingival fibroblasts, osteoblasts, and other cell types [[25,](#page-21-12) [26,](#page-21-13) [30,](#page-21-16) [53–](#page-22-11)[60\]](#page-22-12). Studies also document the potential for laser irradiation to augment the immune response, including lymphocyte stimulation, mast cell function, and dendritic cell mobilization [\[61](#page-22-13), [62](#page-22-14)].

Recent systematic reviews generally conclude that laser irradiation promotes wound healing in experimental animal models [\[63–](#page-22-15)[65](#page-23-0)]. Gál et al. [\[66](#page-23-1)], for example, concluded that low-level laser irradiation, when applied to wounded animals, was associated with superior results for tensile strength (8 studies) and wound contraction analysis (11 studies) based on controlled studies. Posten et al. [\[67](#page-23-2)], however, noted that improvements in surgical wound healing in rodent models have not been duplicated in larger animals, such as pigs, which have skin more closely resembling that of humans. Nevertheless, other reviewers have concluded the results of cell studies and animal experiments show strong evidence to substantiate conducting large clinical trials to evaluate the efficacy of lowlevel laser in promoting wound healing. [[68](#page-23-3)]

The unequivocal interpretation of available evidence is hampered by multiple factors, including heterogeneity of experimental models, protocols, and irradiation parameters, such as wavelength, irradiance, and pulse structure as well as the energy, energy density, irradiation time, and treatment interval [\[69\]](#page-23-4). The studies provide little insight into the mechanism of laser action, whether photothermal, photochemical, or photomechanical. Similar concerns have arisen with studies evaluating the efficacy of irradiation with different laser types, including carbon dioxide  $(CO<sub>2</sub>)$ , Nd:YAG, and diode, on wound healing following tooth extraction in animal models and humans. Systematic reviews generally conclude that there is limited evidence that certain lasers and protocols appear to improve bone and soft tissue wound healing [\[70\]](#page-23-5); however, there are insufficient well-designed and randomized controlled clinical trials with comparable study design to conclude that laser therapy enhances wound healing following tooth extraction [\[71\]](#page-23-6). The availability of such data is necessary for the development of evidence-based recommendations and clinical guidelines.

## <span id="page-7-0"></span>**15.4 Therapy: Setting the Stage**

A major challenge in treating periodontal and peri-implant diseases, such periodontitis and peri-implantitis, is the effective removal of bacterial toxins and disruption of tooth/implantassociated biofilms.

## **15.4.1 Decontamination and Detoxification**

## **15.4.1.1 Root Surface**

The effective decontamination and disinfection of root and dental implant surfaces by mechanical instrumentation, whether using hand instruments or powered devices, is often clinically challenging to achieve. The rationale for selecting laser therapy generally includes the expectation that lasers, whether used as a monotherapy or adjunctive to scaling and root planing (SRP), are effective in detoxifying root surfaces, in producing a significant reduction in subgingival bacterial load, and in reducing inflammation [\[16](#page-21-3)]. Another rationale for the selection of lasers is the premise that lasers can access deep periodontal pockets, furcation defects, and complex root topography, including grooves and concavities, better than scalers [[72\]](#page-23-7).

Lasers provide the ability to deliver large amounts of energy into relatively small, targeted regions of soft or hard tissue. Achieving a desired tissue or material modification is dependent on the proper selection of laser wavelength and parameters. The unique interaction of laser light with a tissue or material can lead to permanent changes in the tissue or material properties.

Early in vitro studies provided important information on the behavior of different laser parameters, such as wavelength and pulse duration, directed at root surfaces for the purpose of disrupting and removing calculus. The studies sought to characterize the efficiency and effectiveness of calculus removal as well as potential alterations in root surface topography and structure. The diode laser is one such laser that alters the root surface and has been shown to result in severe surface modifications, such as crater formation [[73\]](#page-23-8). Additionally, the application of  $CO<sub>2</sub>$  and Nd:YAG laser resulted in morphologic changes in the root surfaces concordant with energy density, with or without air/water surface cooling [[74\]](#page-23-9). Descriptions of laser-induced surface changes include, among others, cavitation, globules of melted and resolidified mineral, surface crazing, and production of a superficial char layer. The significance and impact of root surface

modifications on periodontal regeneration are unknown; however, there is evidence that such morphologic surface changes may hinder cell attachment [[75–](#page-23-10)[77\]](#page-23-11).

More specifically, the Nd:YAG laser wavelength is minimally absorbed in water and exhibits minimal absorption by the tooth, bone, calculus, or enamel. As a result, it is not effective for the removal of calculus, and the energy density necessary to ablate the calculus has significant collateral thermal effects [[78\]](#page-23-12). Similarly, the thermal effects of the  $CO<sub>2</sub>$  laser will lead to carbonization and root damage [\[78](#page-23-12)]. Schwarz et al. [\[73](#page-23-8)] reported diode lasers are overall ineffective at calculus removal and cause undesirable root surface alterations, such as grooves and cratering.

In contrast, the Er:YAG laser affects calculus removal without gross morphologic alterations in the cementum surface. Eberhard et al. [[79\]](#page-23-13) compared the non-surgical effectiveness of Er:YAG laser and conventional SRP in achieving calculusfree subgingival root surfaces on single-rooted teeth with untreated periodontitis. When residual calculus was measured by digitized planimetry following extraction and both treatments were performed for the same time duration, SRP produced a significantly greater area free of residual calcified deposits than with Er:YAG laser irradiation (93.9  $\pm$  3.7% versus 68.4  $\pm$  14.4%, respectively). When laser irradiation was performed for twice the time utilized for hand instrumentation, the mean area of root surface devoid of calculus increased but remained significantly less than with SRP (83.3  $\pm$  5.7% versus 96.3  $\pm$  3.5%, respectively). The effectiveness of both treatments in subgingival calculus removal was not related to the initial probing depth. Notable, too, was that laser-treated tooth surfaces exhibited no dentin exposure and minimal reduction of cementum, whereas hand instrumentation was associated with denudation of dentin.

In a similar study, Schwarz et al. [[80\]](#page-23-14) evaluated the effectiveness of an Er:YAG laser for subgingival calculus removal from root surfaces of singlerooted teeth treatment planned for extraction due to severe periodontitis. In this study, subgingival laser irradiation was performed using a fluorescent

calculus detection system. Histologic evaluation revealed that Er:YAG laser application provided subgingival calculus removal comparable to that provided by SRP. Again, no detectable surface alterations were noted. Additionally, Crespi et al. [\[81](#page-23-15)] found smooth root surfaces and an absence of debris following Er:YAG laser application. In sum, Er:YAG laser can be effective in calculus removal without root surface alteration or major thermal side effects to adjacent tissue [[82–](#page-23-16)[84\]](#page-23-17). Furthermore, the resultant smooth root surface morphology was attained even at higher energy settings [\[80](#page-23-14), [81](#page-23-15), [85](#page-23-18)].

Similar results for calculus removal have been reported for the Er,Cr:YSGG laser [[86\]](#page-23-19). Etemadi et al. [\[87](#page-23-20)], however, reported that the Er:YAG laser appears to have an advantage in terms of time and efficiency of calculus removal compared to the Er,Cr:YSGG laser. Stereomicroscopic examination revealed no carbonization or residual calculus in either treatment group; however, root surfaces exhibited craters, with significantly higher number of craters in the Er,Cr:YSGG laser group than the Er:YAG laser group. Ting et al. [\[88](#page-23-21)] found Er,Cr:YSGG laser irradiation produced root surface alterations without thermal alterations, such as carbonization and melting [\[88](#page-23-21)]. As summarized in a recent review by Lavu et al. [\[89](#page-23-22)], erbium lasers are suitable for calculus removal with minimal root surface alteration or thermal damage, providing a favorable surface for cell attachment.

#### **15.4.1.2 Dental Implant Surface**

Laser application to dental implant surfaces has significant potential to induce thermal alterations on the implant surface and impact to surrounding tissue. The  $CO<sub>2</sub>$  laser, diode laser, Er:YAG laser, and Nd:YAG laser have all been used clinically in the treatment of peri-implant diseases. With respect to surface implant decontamination, the Nd:YAG laser is not recommended for implant decontamination, since it alters and ablates the titanium surface at any applied energy level [\[90\]](#page-23-23). However, it has been used successfully for treatment of the surrounding peri-implant tissues. The  $CO<sub>2</sub>$ , diode, and Er:YAG lasers all have been effective at decontamination in vitro [[91](#page-24-0)]. The diode laser does not damage the titanium surface and is also capable of decontamination of rough surface implants [\[92\]](#page-24-1).  $CO<sub>2</sub>$  lasers can be used without implant surface damage if appropriate power output is selected. Implant decontamination has been reported when applying a  $CO<sub>2</sub>$  laser at an energy density of 286 and  $245$  J/cm<sup>2</sup> in vitro  $[93]$  $[93]$ .

The Er:YAG laser can effectively remove calculus and plaque from a variety of contaminated titanium surfaces of different characteristics [\[94](#page-24-3), [95\]](#page-24-4). Schwarz et al. [\[94](#page-24-3)] reported that irradiation with an Er:YAG laser resulted in greater plaque biofilm removal on sandblasted and acid-etched titanium surfaces prepared in the oral cavity than with ultrasonic instrumentation or plastic curettes with chlorhexidine rinsing. In another clinical trial, Er,Cr:YSGG laser application to contaminated sandblasted and acid-etched surfaces resulted in effective biofilm removal [[96\]](#page-24-5). Both Er:YAG and Er,Cr:YSGG lasers cause no visible changes to the implant surfaces, and the addition of a water spray minimizes the potential temperature changes at the implant material surface [\[97\]](#page-24-6). Overall,  $CO<sub>2</sub>$ , diode, and erbium lasers appear effective for decontamination of implant surfaces. What remains to be defined is the biocompatibility of titanium surfaces and their potential to support re-integration after the laser decontamination.

#### **15.4.2 Microbial Disinfection**

In clinical practice, antimicrobial chemotherapeutic agents are widely used in an effort to reduce or change the quality of microbial pathogens in biofilms through local or systemic delivery. Laser radiation exhibits the ability to disrupt biofilms and exert broad-spectrum antimicrobial activity, although the effect and action appear dependent on laser beam parameters, dose, and bacterial species [\[98](#page-24-7)[–102](#page-24-8)]. The antimicrobial properties of lasers and laser-activated photosensitizers have received considerable attention in the management of periodontal and peri-implant diseases.

#### **15.4.2.1 Photodynamic Therapy**

One means of disinfection is the use of low-level light energy and chemical photosensitizers. The photodynamic process is based on converting

light energy to chemical, which requires an additional agent to transform the light energy, called a photosensitizer. This process has been termed antimicrobial photodisinfection or photodynamic therapy. The stimulation of a photosensitizer by an appropriate light wavelength produces highly reactive oxygen species, such as reactive singlet oxygen  $(^{1}O_{2})$  [[103,](#page-24-9) [104\]](#page-24-10). The singlet oxygen  $(^{1}O_{2})$  and free radicals generated are highly reactive with extremely short lifespans (measured in μ seconds) due to their unstable electronic configuration.

A variety of exogenous compounds have been used that can be photoactivated in the ultraviolet and visible regions of the electromagnetic spectrum [[105\]](#page-24-11). Multiple photosensitizing compounds, including phenothiazine chloride, toluidine blue, methylene blue, and tolonium chloride, have been used in photodynamic therapy for periodontal and peri-implant disease [[106\]](#page-24-12). Photosensitizing molecules when delivered in a pocket may interact with different cellular constituents based on their affinities for these components, while the binding sites determine the localization of the photodynamic damage effect in situ due to the generation of reactive oxygen species [[105\]](#page-24-11).

Bactericidal efficacy of photodynamic therapy was explored by Akram et al. [\[106](#page-24-12)] in a systematic review of clinical trials that assessed bactericidal efficacy of photodynamic therapy when combined as an adjunct to SRP in patients with periodontitis. Seventeen prospective, randomized controlled clinical trials examining antimicrobial photodynamic therapy (aPDT) for the treatment of periodontitis met the inclusion criteria. Additionally, study inclusion required pre- and posttreatment microbial counts for any of the following periodontal bacteria: *P. gingivalis*, *T. forsythia*, *T. denticola*, and *A. actinomycetemcomitans*. Of the 17 studies, 13 clinical trials showed similar reduction in the selected periodontal pathogens for SRP and SRP plus aPDT. All studies utilized diode lasers but with differences in protocols that included irradiation wavelength (470 and 810 nm), exposure duration (60–300 sec), photosensitizing agent, and followup period, limiting the interpretation of outcomes regarding the effectiveness of aPDT as an adjunct to SRP to reduce periodontal pathogens. In sum, only 24% of the clinical studies reported bacterial count reductions of key periodontal pathogens beyond that accomplished by SRP alone. Of note, in one study, *T. denticola* was actually significantly increased at 24 weeks following SRP plus aPDT [[107\]](#page-24-13). Gandhi et al. [[108\]](#page-24-14) recently reported a 9-month clinical trial demonstrating significant reductions in *A. actinomycetemcomitans* and *P. gingivalis* counts using low-level laser therapy and aPDT as an adjunct to SRP in the treatment of periodontitis.

To establish whether aPDT can substitute for the incorporation of a systemic antibiotic during SRP, another comparative review of aPDT by Akram et al. [[109](#page-24-15)] identified five clinical trials comparing aPDT to systemic antibiotics as an adjunct to SRP. These studies provided outcome data following irradiation of periodontal pockets with diode laser wavelengths with follow-up from 12 to 48 weeks. When compared to adjunctive antibiotics, aPDT did not produce any additional benefit in clinical outcomes. Therefore, it remains equivocal whether aPDT can substitute for systemic administration of antibiotics in the nonsurgical therapy of periodontitis, particularly in patients with more aggressive rates of disease progression. Overall, consistency is lacking with respect to the adjunctive impact of aPDT on microbial counts.

#### **15.4.2.2 Dental Implant Surface Disinfection**

Decontamination of dental implants was the focus of a recent review by Alasqah et al. [[110\]](#page-24-16). This review of in vitro studies examined the effects of aPDT on bacterial colonization and dental implant surface topography, including titanium implants, zirconia implants, and titanium discs. All included studies used diode laser energy, ranging in wavelength from 625 to 810 nm. Photosensitizers applied included methylene blue, toluidine blue, indocyanine green, and phenothiazine chloride, and a variety of bacterial species were evaluated, including *P. intermedia*, *A. actinomycetemcomitans*, *P. gingivalis*, *Streptococcus gordonii*, *Actinomyces naeslundii*, *Fusobacterium nucleatum*, *Campylobacter rectus*, *Filifactor alocis*, *Eikenella corrodens*,

*Parvimonas micra*, *T. forsythia*, *T. denticola*, and *Staphylococcus aureus*. All studies showed a significant but incomplete reduction in the bacterial load. Implicated in other studies is the suggestion that the implant surface type may influence the effectiveness of photodynamic therapy, presumably due to differences in biofilm or biofilm access [[111\]](#page-24-17). Regardless, most studies addressing different implant surfaces generally demonstrate some reduction of bacterial load following photodynamic therapy [[112–](#page-24-18)[116\]](#page-24-19). It has been suggested that, dependent on the implant surface, the combination of titanium brush application with aPDT might be more efficient for the reduction of bacteria [\[111](#page-24-17)]; however, this remains to be tested in vivo since the assessment with the combined application was in vitro and with only one seeded pathogen, *S. aureus*, over a short-incubation period. It is important to note that aPDT did not eliminate the bacteria; therefore, an important consequence is the persistence of residual LPS, which was not evaluated in these studies.

Huang et al. [\[117](#page-24-20)] evaluated osteoblast-like MG63 cell attachment, proliferation, differentiation, and mineralization on contaminated SLA (sandblasting, large grit, and acid-etching) titanium alloy surfaces after photodynamic therapy using different concentrations of methylene blue and the application of a 660 nm diode laser. The titanium alloy surfaces were first contaminated with *A. actinomycetemcomitans* or *Streptococcus mutans*. aPDT resulted in significant reductions in bacterial colonies. Importantly, the disinfected disc surfaces were found to support osteoblast-like MG63 cell attachment, proliferation, differentiation, and mineralization. The highest methylene blue concentrations (350 and 400 μg/mL) resulted in the lowest lipopolysaccharide (LPS) remaining quantity on the *A. actinomycetemcomitans*-contaminated surfaces. Notably, osteoblasts cultured on disinfected surfaces with the application of the higher methylene blue concentration photodynamic therapy achieved comparable osteoblast culture to that of the control without contamination. Thus, aPDT offers the potential to sufficiently reduce bacterial and LPS contamination to allow for bone growth or reintegration of the bone along the previously diseased dental implant. Clinical studies,

however, are necessary to extrapolate these and other experimental results with titanium and titanium alloy surfaces to patient care.

### **15.4.3 Implant Particulate and Debris**

Orthopedic implant materials can undergo corrosion, degradation, and wear, releasing particles and debris into the surrounding tissues that can elicit inflammatory and immune responses [\[118](#page-25-0)]. Titanium dioxide  $(TiO<sub>2</sub>)$  nanoparticles, for example, exhibit the potential to induce oxidative stress, cellular apoptosis, and inflammation [\[119](#page-25-1)]. Titanium particles and degradation products have been detected in oral tissues associated with dental implants (reviewed in [\[120](#page-25-2)]). Of growing concern is the potential for titanium particles to elicit an inflammatory response in oral tissues [\[120](#page-25-2)[–122](#page-25-3)]. Although there is no direct evidence of a causal relationship between particulate titanium debris and inflammation in oral tissues, a growing number of reports have documented the presence of particulate debris in the soft tissues surrounding dental implants with peri-implantitis. One recent report describes two cases of peri-implantitis that initially responded poorly to regenerative therapy; however, when the sites were subsequently irradiated with either an Nd:YAG or  $CO<sub>2</sub>$  laser, demonstrable improvements emerged in clinical parameters and radiographic bone fill [[123\]](#page-25-4). The authors suggested that the successful treatment of periimplantitis may need to also incorporate decontamination of the soft tissues in addition to the implant surface. Particulate debris may also provide insight into the etiology of certain cases of refractory peri-implant mucositis. Future investigations appear warranted.

## <span id="page-11-0"></span>**15.5 Periodontal Therapy**

#### **15.5.1 Nonsurgical**

In a recent systematic review, Chambrone et al. [\[124](#page-25-5)] examined the use of infrared lasers (i.e.,

Diode, Er:YAG, and Nd:YAG) alone or as an adjunct to SRP for the nonsurgical treatment of chronic periodontitis. The clinical application of SRP plus infrared lasers as part of debridement procedures was found to promote significant improvements in bleeding on probing, clinical attachment level, and probing depth. Nonetheless, it was concluded that infrared laser (Er:YAG and Nd:YAG) alone did not show additional gains to those accomplished by SRP alone. Moreover, no overall differences were identified when comparing clinical outcomes between infrared laser alone and SRP alone (Diode, Er:YAG, or Nd:YAG); however, the results of studies evaluating SRP plus infrared laser (Diode, Er:YAG, or Nd:YAG) suggest modest additional clinical benefits in clinical attachment level gains (<1 mm) and probing depth reduction  $\left(\langle 1 \rangle \right)$  to those achieved by SRP alone. Consistent with the clinical outcomes, Chambrone et al. [\[124](#page-25-5)] found the application of SRP alone, laser alone, and SRP plus laser was essentially comparable in reducing total colony-forming units and levels of different bacterial pathogens (e.g., *A. actinomycetemcomitans*, *T. forsythia*, *C. rectus*, *E. corrodens*, *F. nucleatum*, *P. gingivalis*, *P. intermedia*, *T. denticola*) within 4–12 weeks after treatment. Consistent with studies following mechanical instrumentation, levels of the bacterial pathogens generally returned to levels comparable to base-line 6 months after treatment [[125–](#page-25-6)[127\]](#page-25-7); however, sustained superior reductions in selected periodontal pathogens after Er:YAG laser or SRP plus laser treatment have been reported at 12 months [[128\]](#page-25-8).

Zhao et al. [\[129](#page-25-9)] conducted a systematic review to evaluate the Er:YAG laser versus SRP as alternative or adjunctive treatment for chronic periodontitis. The meta-analysis, which included data from eight studies, showed that Er:YAG laser resulted in comparable short-term (3 months) improvements in clinical attachment level gain and probing depth reduction to those obtained with SRP. At 12-month follow-up, the comparison of the two treatment modalities (three studies) demonstrated no statistically significant difference in clinical attachment level gain or probing depth reduction.

Recent systematic reviews generally conclude that compared to SRP alone, the ER:YAG laser results in similar or improved short-term clinical outcomes; however, no significant treatment differences remained with respect to outcomes at the 6- and 12-month follow-up periods [\[72,](#page-23-7) [130\]](#page-25-10). Er:YAG laser and Er,Cr:YSGG laser result in modestly more surface roughness when compared with ultrasonic and hand instru-mentation [\[86](#page-23-19)]. Interpretation of the results, however, was limited by heterogeneity and risk of bias [\[72\]](#page-23-7). The level of evidence for the nonsurgical application of lasers for the treatment of periodontitis was critically appraised in a more recent systematic review and metaanalysis [\[131\]](#page-25-11). The authors concluded that SRP plus aPDT will attain a 0.53 mm mean gain in clinical attachment level with moderate certainty. However, when compared to SRP alone, the adjunctive use of a diode laser (non-aPDT), Nd:YAG laser, or erbium laser had a low level of evidence or certainty of effect on clinical attachment level gain (0.21–0.41 mm benefit) in the reported critical appraisal [[131](#page-25-11), [132\]](#page-25-12).

## **15.5.2 Subgingival Curettage (Pocket De-epithelialization)**

Gingival curettage is a surgical procedure designed to remove the epithelial lining of the periodontal pocket, with the goal of denuding the subjacent gingival connective tissue. The original objective of the gingival curettage procedure was to remove the pocket lining and junctional epithelium, including any granulation tissue, thereby setting the stage for new connective tissue attachment to the tooth. Subgingival curettage has been performed using manual curettes, chemicals, and excisional gingival flap surgery [\[133,](#page-25-13) [134](#page-25-14)]. Clinical studies, however, have consistently failed to show any additional benefit of subgingival curettage, when compared to SRP alone, with respect to probing depth reduction, attachment level gain, or inflammation reduction [\[135,](#page-25-15) [136](#page-25-16)]. One of the limitations of mechanical curettage is the potential for epithelial remnants, such as at the gingival margin or near the

epithelial attachment, or due to epithelial rete extensions. Centty et al. [\[137](#page-25-17)] histologically compared periodontal flaps elevated using an inverse-beveled incision, extending from the free gingival margin to the alveolar crest, with the goal of surgically excising the pocket epithelium. The experimental periodontal sites were next irradiated using a carbon dioxide laser to remove any remaining pocket lining and gingival (oral) epithelium. Following the procedure, soft tissue biopsies were obtained and submitted for histologic examination. The results revealed the remnant pocket epithelium on all the specimens. The histologic results of available studies, therefore, suggest that gingival curettage, regardless of procedural method, does not completely remove pocket lining epithelium. Moreover, the results of clinical studies suggest minimal benefit of subgingival curettage performed with lasers either as a monotherapy or adjunctive to traditional periodontal therapy. [[124](#page-25-5)]

Lin et al. [\[138](#page-25-18)] compared gingival curettage performed with an 810 nm diode laser to curettage performed with hand instruments. Significant and comparable improvements in clinical measures were observed following curettage in both groups after 4 weeks. Notably, the investigators reported that laser curettage required less treatment time and was associated with less treatment discomfort than curettage with hand instruments.

Using a primate model, Rossman et al. [\[139](#page-25-19)] examined whether de-epithelialization with the  $CO<sub>2</sub>$  laser would increase the amount of connective tissue attachment to root surface. Elastics were used to create periodontal defects on the maxillary premolars and incisors of cynomolgus monkeys. Bilateral open flap debridement was performed. On the experimental side,  $CO<sub>2</sub>$ laser was used to remove the oral epithelium prior to flap replacement. Histologic examination revealed a delay in sulcular epithelialization (day 14 versus day 28, respectively) and a trend to less epithelium and more connective tissue attachment after 7 days on the experimental side than on the control side. The investigators concluded that the  $CO<sub>2</sub>$  laser may be a useful tool to retard epithelium and thereby enhance new connective tissue attachment.

Israel et al. [[140\]](#page-25-20) conducted a pilot study to evaluate whether pocket de-epithelialization with a  $CO<sub>2</sub>$  laser at the time of flap surgery and at 10-day intervals over the first 30 days of healing can enhance the formation of a connective tissue attachment. Six mandibular incisors in two patients were splinted prior to open flap debridement, when a notch was placed on the roots at the height of the crest of the alveolar bone, prior to flap closure. The experimental side received deepithelialization of the outer (oral) gingiva with the carbon dioxide laser and the inner gingival flap. The de-epithelialization was repeated on the test side at 10, 20, and 30 days postsurgically. Block sections were taken at 90 days and processed for histologic analysis. The results showed that for both patients, junctional epithelium (JE) was formed on both test and control teeth. In all control teeth, the JE extended the entire length of the root to the base of the reference notch. In one patient, on the experimental side, the notch was filled with connective tissue and limited new cementum [[140\]](#page-25-20).

In sum, laser curettage can be performed efficiently with the application of lasers, such as diode or  $CO<sub>2</sub>$ , but the supposition of complete de-epithelialization of the pocket lining remains elusive, and there is a lack of added benefit for surgical curettage beyond that attained with SRP.

#### **15.5.3 Surgical Periodontal Therapy**

#### **15.5.3.1 Surgical Flap Access with Laser Treatment**

A limited number of studies combine surgical flap access with laser treatment for the treatment of periodontitis. The majority of laser therapy clinical trials have focused on the inclusion of laser treatment in the nonsurgical management of the disease, where laser therapy is an adjunct to nonsurgical instrumentation of the teeth. Testimony to this clinical research focus is characterized in the comprehensive tabulation of studies in a recent review of lasers and the treatment of periodontitis [\[16](#page-21-3)]. Surgical flaps combined with adjunctive laser treatment have been reported for Er,Cr: YSGG, CO<sub>2</sub>, diode, Er:YAG, and Nd:YAG lasers. Er:YAG and diode lasers, when used with mechanical debridement, have been compared to mechanical debridement following access flap surgery of 5 mm or deeper pockets. [[141–](#page-25-21) [144\]](#page-26-0). The studies found comparable or superior improvements in clinical outcome measures after either 3 or 6 months [[142–](#page-25-22)[144\]](#page-26-0) or 6, 12, 24, and 36 months [\[141](#page-25-21)]. Gaspirc and Skaleric [\[141](#page-25-21)] reported significantly greater improvements in clinical attachment level and probing depth after flap access plus Er:YAG compared to conventional flap surgery.

Er:YAG studies, some of which also included guided tissue regeneration with enamel matrix protein, found minor differences favoring the laser treatment group when comparing probing depth reduction and clinical attachment level gain. However, the level of evidence is limited for the inclusion of laser treatment with regenerative surgical therapy and enamel matrix derivative, since no significant differences between the surgical therapies, with or without the laser treatment, were noted in a meta-analysis. [[145\]](#page-26-1) There is only one clinical trial with Er,Cr: YSGG laser, and the authors concluded that laser treatment resulted in significant reductions in probing depth and bleeding score but had similar gains in clinical attachment level [\[16](#page-21-3)]. Notable was one controlled clinical study with 15-year follow-up after coronally advanced flap surgery and  $CO<sub>2</sub>$  laser root treatment. The control group had modified Widman flap treatment. Significant reductions in probing depth and gains in clinical attachment level at initial sites with probing depth of 5 mm or greater were maintained over the 15-year period [\[146\]](#page-26-2) providing evidence for maintenance of the attained treatment results. Overall, there is modest benefit reported for the inclusion of laser treatment with periodontal flap surgery for the treatment of periodontitis. In a meta-analysis [\[145\]](#page-26-1) of laser application for surgical therapy, the weighted mean difference for probing depth was 0.56 mm and that of clinical attachment level was 1.34 mm favoring the laser treatment with flap surgery. However, this report found no statistical differences when comparing surgical outcomes with or without laser treatment. Thus, the benefit of the application of lasers to surgical periodontal therapy is surmised

but not clinically recognized in the limited number of available studies, reflecting, in part, the heterogeneity in study design and methodology.

Several suppositions underlie the rationale for incorporating lasers into periodontal surgery [\[16](#page-21-3)], including some evidence from preclinical studies. In addition to root surface decontamination and detoxification, as considered earlier, certain lasers and laser protocols are thought to contribute to more effective subgingival curettage, targeted and/or overall reduction in subgingival bacteria, reductions in inflammation, and rapid wound healing.

## **15.5.3.2 Regenerative Surgical Therapy with Laser Treatment**

Regenerative therapies are designed to support *regeneration* of the attachment apparatus, namely, the formation of new bone, cementum, and periodontal ligament (Figs. [15.5](#page-14-0), [15.6](#page-14-1), [15.7](#page-15-0), [15.8,](#page-15-1) [15.9](#page-15-2), [15.10](#page-15-3), [15.11,](#page-15-4) and [15.12](#page-16-0)). The biological goal of periodontal regeneration, therefore, is restoration of the lost periodontium. Conventional surgical approaches, such as open flap debridement, heal primarily through *repair*, characterized principally by the formation of a long junctional epithelial attachment to the previously diseased root surface. Repair is healing of the periodontal attachment apparatus by tissue, such as junctional epithelium, which does not fully restore architecture and function. Long junctional epithelium can be produced rapidly during wound healing, due to high proliferative activity of epithelial cells [\[148](#page-26-3)]. Limited evidence of formation of other component tissues, such as the bone, has been reported following open flap debridement surgery [[149\]](#page-26-4).

Contemporary therapeutic approaches to periodontal regeneration include bone replacement grafts, guided tissue regeneration (GTR), and biologics [\[150](#page-26-5), [151](#page-26-6)]. These regenerative therapies have been used in combination and in conjunction with agents to modify and promote wound healing [[149\]](#page-26-4). Evidence-based systematic reviews and meta-analyses support the efficacy of commercially marketed mammalian-derived bone grafts, guided tissue regeneration, and biologics for periodontal regeneration, as reflected in clinical improvements evidenced by probing depth reduction, clinical attachment gain, and reentry/radiographic defect fill. Histologic evidence of periodontal regeneration—new bone, cementum, and periodontal ligament on a previously diseased root surface—is available for each regenerative therapy. However, the most thoroughly and extensively characterized histologic outcome evidence in humans is for alloge-

<span id="page-14-0"></span>

**Fig. 15.5** Pretreatment clinical view of 44-year-old Caucasian man with a medical history of multiple drug allergies, including antibiotics (penicillin) and sulfa medications (treatment was provided by PSR). Periodontal examination revealed generalized bleeding upon probing and periodontal pocketing, with probing depths of 5–7 mm involving the maxillary molars

<span id="page-14-1"></span>

**Fig. 15.6** The preoperative radiograph is consistent with stage III periodontitis, with evidence of calculus deposits on the roots. An angular osseous deformity is suggested on the distal of tooth # 2; note the close root proximity of the molars

<span id="page-15-0"></span>

**Fig. 15.7** Clinical presentation after second pass using the laser-assisted new attachment procedure with the Nd:YAG laser (3.8 W for each pass) prior to occlusal adjustment. A modification to postoperative protocol management was necessary because of patient concerns about his drug allergies; consequently, he was not placed on antibiotics, and a botanical rinse (PeriActive, Izun Oral Care) was prescribed for infection and plaque control. Supportive periodontal maintenance was performed on a 3-month interval

<span id="page-15-1"></span>

Fig. 15.8 Clinical presentation 1 year after treatment. Highly effective oral hygiene was consistently maintained during this period. Note the reduction in gingival volume and healthy tissue appearance. Probing depths range from 2 to 4 mm without bleeding

neic demineralized freeze-dried bone [[152,](#page-26-7) [153\]](#page-26-8). Despite the histologic evidence, wound healing is characterized by a combination of periodontal regeneration and repair. Consequently, there currently exists a need for more robust and costeffective regenerative strategies. Considerable interest in regenerative periodontics and medicine has focused on emerging technologies, including scaffolds and cell-based grafts [\[154](#page-26-9), [155](#page-26-10)], biologics [[156\]](#page-26-11), and lasers [[124\]](#page-25-5).

<span id="page-15-2"></span>

Fig. 15.9 Radiograph 1 year after treatment suggests osseous fill of the intrabony lesion on the distal of the second molar. The crestal lamina dura is well defined elsewhere

<span id="page-15-3"></span>

Fig. 15.10 Clinical improvements remain stable 5 years after treatment, excellent oral hygiene, and regular professional care

<span id="page-15-4"></span>

Fig. 15.11 Radiographic findings 5 years after treatment are consistent with the clinical findings of periodontal stability

<span id="page-16-0"></span>

**Fig. 15.12** (**a**) Panoramic histologic view showing bone fill and periodontal regeneration of an intrabony defect 9 months after treatment with laser-assisted new attachment procedure (LANAP). The arrow confirms the 9-mm notch (base of calculus) measurement from cementoenamel junction made at time of surgery. (**b**) Higher-magnification view of box 1 shows inserting Sharpey fibers into the new cementum (NC) and presence of cementoblasts. D (dentin). (**c**) Higher-magnification view of box 2 shows supracrestal collagen fibers inserting into the new cementum

The exploration of laser irradiation for periodontal regeneration has been reported within clinical case series and, infrequently, within controlled clinical trials. Nevertheless, histologic evidence provides proof of principle that laser therapy, particularly the proprietary laser-assisted new attachment procedure (LANAP®), supports periodontal regeneration, including new bone,

(NC) just apical to the junctional epithelium (JEP). The layer of new cementum extends to the coronal extent of the defect with adjacent new periodontal ligament (N-PDL). [Images courtesy of Dr. Marc L. Nevins. Reproduced and adapted from M. L. Nevins et al., Human clinical and histologic evaluation of laser-assisted new attachment procedure. Int J Periodontics and Restorative Dent 32: 497-507, 2012; with permission© 2012 By Quintessence Publishing Co, Inc. [[147](#page-26-12)])

cementum, and periodontal ligament [[140,](#page-25-20) [147](#page-26-12), [157\]](#page-26-13). One such case series applied LANAP®, utilizing a Nd:YAG laser, for the surgical management of periodontitis and was pivotal in providing histologic evidence of periodontal regeneration following a laser surgical procedure on teeth that were determined to be hopeless in their prognoses [\[147](#page-26-12)] (Fig. [15.12](#page-16-0)). Clinical outcomes reported for this series yielded a mean probing depth reduction of  $5.4 \pm 2.64$  mm and mean clinical attachment level gain of  $3.8 \pm 2.38$  mm after 9 months of follow-up. Another case series incorporated the Er:YAG laser into traditional regenerative periodontal surgery [\[158](#page-26-14)]. In this study, nine intrabony defects were surgically debrided via curettes and included the adjunctive use of the Er:YAG laser to complete degranulation; then the Er:YAG laser was applied to the root surfaces. After the application of enamel matrix derivative and bone graft, the laser was applied to establish a coagulated blood clot over the graft. At 12 months, the mean defect depth was reduced from a baseline of 6 mm to 1 mm, the mean probing depth was reduced from 6.2 mm to 2.0 mm, and the mean clinical attachment level improved from 7.5 mm to 3.4 mm [[158\]](#page-26-14) at 12 months. An assessment of the comparative efficacy of laser treatment was not possible in this study.

A meta-analysis of controlled clinical studies which included Nd:YAG or Er:YAG laser treatment groups and guided tissue regeneration with enamel matrix protein found only minor differences between the laser and non-laser treatment groups when comparing probing depth reduction and clinical attachment level gain favoring the laser group, weighted mean differences of 0.01 mm and 0.10 mm, respectively. No significant differences between the surgical therapies, with or without the laser treatment, were noted in this meta-analysis, and the authors concluded the level of evidence was limited for the inclusion of laser treatment in regenerative surgical therapy. [[145](#page-26-1)]

#### <span id="page-17-0"></span>**15.6 Implant Therapy**

#### **15.6.1 Peri-implant Mucositis**

Nonsurgical mechanical therapy, good oral hygiene, and regular professional care are only modestly beneficial in treating peri-implant mucositis [[159\]](#page-26-15). A growing concern is that periimplant mucositis may not be completely reversible with treatment [[160\]](#page-26-16). Only three laser studies were identified in a recent review of laser treatment of peri-implant mucositis [[161\]](#page-26-17), and the

authors conclude there was no evidence of added benefit of laser therapy for mucositis. Future clinical trials, therefore, are necessary to evaluate the potential benefit of this approach.

#### **15.6.2 Peri-implantitis**

## **15.6.2.1 Nonsurgical Treatment Outcomes for Peri-implantitis**

Application of lasers for the treatment and decontamination of dental implants has been considered to improve nonsurgical outcomes and overcome the shortcomings of traditional mechanical debridement. Inclusion of local delivery of antimicrobials has not overcome the limitations of the surface topography of the infected dental implant surface. Two recent systematic reviews explored nonsurgical treatment of peri-implantitis with lasers. Chambrone et al. [[162\]](#page-26-18) focused on antimicrobial photodynamic therapy (aPDT) as a treatment modality. Overall, aPDT provides similar results to conventional nonsurgical therapy. One randomized controlled study, however, reported that the adjunctive use of aPDT resulted in about a 1 mm greater reduction in mean probing depth than debridement alone at implant sites with initial probing depth  $\geq 4$  mm [[163\]](#page-26-19). While clinical improvement occurs following aPDT, when compared to scaling alone, it was concluded that no additional benefit was manifest. The authors noted that additional conclusions were not possible due to the restricted base of evidence for some treatment approaches and conditions [\[162](#page-26-18)].

Significant improvement in attachment level can occur when aPDT is combined with mechanical scaling, but probing depths, bleeding, and plaque levels did not reach significance in a network meta-analysis [[164\]](#page-26-20). A network meta-analysis was conducted to compare across interventions, namely, a comparison of photodynamic therapy with mechanical debridement to local drug delivery with mechanical debridement, since no direct comparisons are available in existing clinical trials. The analysis allowed for indirect comparisons of pooled existing studies where no direct comparison was available by study treatment groups using common outcome measures: probing depth, clinical attachment level, bleeding, and plaque scores. The quality of the evidence was still considered low in this reported network analysis, concordant with the conclusions of Chambrone et al. [[124\]](#page-25-5) in their report on the best-evidence consensus [\[164](#page-26-20)].

Nonsurgical adjunctive use of laser irradiation for the treatment of peri-implantitis with diode or erbium lasers results in a significant reduction in bleeding on probing  $[161]$  $[161]$  when compared to non-laser treatment. However, given the lack of long-term clinical studies for this comparison, the bleeding reduction should be considered short term (a year or less). Even with long-term followup, it can be difficult to discern treatment effects from other factors, such as level of oral hygiene. Furthermore, no statistical difference relative to probing depth reduction was attained for metaanalysis of adjunctive use of lasers when treating peri-implantitis. Of note, in the same review and meta-analysis, a significant but slight mean bone level loss with nonsurgical laser treatment was reported [\[161](#page-26-17)]. Thus, other than bleeding on probing and mean bone level, adjunctive nonsurgical laser treatment results in a nonsignificant change in the clinical outcomes of probing depth, plaque levels, and recession relative to the net changes of mechanical debridement alone.

## **15.6.2.2 Surgical Treatment Outcomes for Peri-implantitis**

The surgical treatment of peri-implantitis has shown potential for clinical benefit; however, the predictability of treatment approaches remains unclear [\[165\]](#page-26-21). In a meta-analysis of nonsurgical and surgical treatment, it was concluded that regenerative surgical treatment of peri-implantitis was most effective when compared to nonsurgical and resective surgical techniques [\[166\]](#page-26-22). Recent comparative summative reviews have not included the evaluation of laser surgery as a modality for peri-implantitis treatment.

Early application of laser therapy by Romanos et al. [[167\]](#page-26-23) reported that decontamination of implant surfaces with a  $CO<sub>2</sub>$  laser, in combination with augmentative techniques, was effective

for establishing radiographic bone fill. The  $CO<sub>2</sub>$ laser did not harm the implant surface and presumptively aided in clot formation. Interestingly, a surgical flap was elevated and then the implant surface laser treated in this report. As such, there are currently no controlled clinical trials with the use of lasers as a monotherapy  $[161]$  $[161]$ . In a best-evidence review of laser therapy for periimplantitis [\[161](#page-26-17)], nine studies were identified with lasers as a surgical intervention. Analysis of only Er: YAG,  $CO<sub>2</sub>$ , and diode lasers was possible since no controlled studies were available for other laser types. When compared with debridement by hand with curettes and antiseptics in combination with a surgical flap access, the addition of laser treatment showed only minimal to no benefit in reduction of probing depth and bleeding on probing or gain in clinical attachment level. Meta-analysis of long-term (greater than 48 months) outcomes following surgical treatment, with and without the addition of laser treatment, yielded weighted mean differences of 7.26% for bleeding on probing reduction, 0.22 mm for clinical attachment level gain, and 0.45 mm of probing depth reduction.

Although minimal additive benefit may be realized with the addition of laser treatment to surgical treatment of peri-implantitis, in a report that factored analysis of cost-effectiveness of combinations of therapy for peri-implantitis into the assessment of varied treatment modalities, it was concluded the most effective treatment combination includes bone grafts, barrier, and laser treatment [\[168\]](#page-26-24).

The incorporation of lasers remains an effective application for peri-implantitis treatment, including regenerative therapies (Figs. [15.13](#page-19-0), [15.14](#page-19-1), [15.15](#page-19-2), [15.16,](#page-19-3) [15.17](#page-19-4), and [15.18\)](#page-19-5). Systematic reviews indicate that although peri-implantitis treatments can produce successful outcomes, no strong evidence is available to suggest the most effective treatment intervention [[7\]](#page-20-9). A more recent case series [\[169](#page-26-25)] utilized an Er: YAG laser for implant surface and defect debridement of the granulomatous tissue prior to grafting the peri-implant defects. Probing depths of 6 mm or greater were reduced on average to 3.5 mm and presented with radiographic defect fill 1 year following treatment. Unfortunately, this report did not have standard-

<span id="page-19-0"></span>

**Fig. 15.13** Pretreatment clinical presentation of a 59-year-old Caucasian man (treatment was provided by PSR). Medical history includes cigarette smoking (approximately one pack of cigarettes per day) and arthritis. Dental implants were placed in another office 7 years prior, with cemented restorations. Purulence and bleeding upon probing are present. Significant swelling and erythema of the soft tissues are evident posteriorly

<span id="page-19-1"></span>

Fig. 15.14 Pretreatment radiograph suggests early to moderate bone loss around the dental implants. A gap appears in the crown-abutment interface of the posterior implant

<span id="page-19-2"></span>

**Fig. 15.15** The dental implants can be seen after the second pass using the laser-assisted peri-implantitis procedure with the Nd:YAG laser (3.8 W for each pass). Postoperative management included amoxicillin (500 mg t.i.d.) for 1 week and a botanical rinse twice daily (PeriActive, Izun Pharma) for 2 weeks

<span id="page-19-3"></span>

**Fig. 15.16** Buccal view of the implants 6 weeks following the laser treatment. Note the significant clinical resolution of inflammation, with minimal soft tissue recession. Bleeding on light probing is absent

<span id="page-19-4"></span>

**Fig. 15.17** Buccal view of the implants 1 year following the laser treatment. Initial improvements in soft tissue appearance remain stable. Supportive maintenance care was performed on a 3-month interval

<span id="page-19-5"></span>

**Fig. 15.18** Radiographic appearance at 1 year suggests no change in crestal bone levels or possible improvement (distal of implant #15)

ized repeatable measurements or a control group to ascertain the impact of laser versus curettes for bone debridement. Currently, in the absence of histologic data, the effect of lasers on the re-osseointegration of dental implants remains unclear.

#### <span id="page-20-0"></span>**15.7 Patient Preferences**

Patient preferences in treatment decisions are an important consideration in the overall assessment of laser therapies, especially given the factors commonly influencing treatment selection, such as cost, convenience, comfort, and clinical outcomes, among others. Laser therapies often achieve clinical improvements comparable to conventional periodontal/peri-implant treatment, as reviewed earlier, and can be associated with less discomfort and pain [\[170](#page-27-0), [171](#page-27-1)]. The adoption of lasers into clinical practice continues to rapidly increase, and practitioners incorporating lasers into clinical care continue to report high levels of satisfaction [\[171](#page-27-1)]. Patient preferences, therefore, must be taken into consideration when reviewing treatment options.

#### <span id="page-20-1"></span>**15.8 Conclusions**

Lasers have the capacity to stimulate cellular activity, reduce inflammation, and promote wound healing. Surgical treatment with lasers is generally associated with less pain than conventional therapy. Lasers have been shown to provide an effective and safe alternative to conventional therapeutic approaches for biofilm disruption and calculus removal. Laser treatment as a monotherapy or adjunct to conventional therapy has been generally associated with improvements in clinical attachment level and probing depth comparable or marginally superior to conventional therapy. Nevertheless, systematic reviews conclude that clinical outcomes of laser treatment are similar or slightly better than reference nonsurgical or surgical therapies; however, any differential benefits remain short term. Moreover, there is limited human histologic

evidence that is consistent with the potential for periodontal regeneration following laser-assisted therapy in patients with moderate to severe periodontitis. The ability of lasers to interact with the periodontium and surrounding peri-implant tissues warrants the continued development and evaluation of laser treatment protocols that capture the cellular, biochemical, and molecular potential of laser energy.

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