Local and Microvascular Free Flaps in Patients with Medication-Related Osteonecrosis of the Jaw

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Abstract

Medication-and especially Bisphosphonate-related osteonecrosis of the jaw (MRONJ/BRONJ, also known as bisphosphonate-induced osteonecrosis and antiresorptive drug-induced osteonecrosis) is considered a therapy-resistant form of osteonecrosis. Despite this conservative and surgical treatment, regimens have been attempted and recommended in the years since it was first identified.

The key points after surgical debridement of the exposed bone sites are to close the wounds in a watertight manner to avoid exposure to the oral milieu and reinfection of the bone surface that has been rendered almost impossible to respond to challenges that require remodeling – essentially the purpose of the bisphosphonate and related drugs. While there are techniques described in the literature capable of achieving this aim, the relevance of patients' comorbidities and prognosis plays a very substantial part in planning logical individualized treatment. Many of these patients, often those worst affected, are suffering from malignant diseases with limited prognosis. Therefore, the choice of defect closure technique should also consider the individual situation of each patient; was the drug used for prophylaxis in osteoporosis or for advanced metastatic malignancy?

Therapeutic planning and treatment for MRONJ and BRONJ should be considered in two different ways. On the one hand, there is the need for removal of the exposed and necrotic bone, as described in the treatment chapter by Pautke [1]. On the other hand, there is a need for a watertight defect closure to minimize the risk of microbial contamination of the bone and ensure good healing of the bone. It is essential to realize this bone undergoes a different type of healing process due to the pathophysiology and the metabolism of the bisphosphonates (or other antiresorptives) [2, 3]. Additionally, these patients

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may be immunosuppressed or have carcinomatosis which also contributes to a prolonged and complicated healing of all wound defects. This is demonstrated by a very high relapse rate of patients after completion of therapy of MRONJ and BRONJ [4]. The relapse rate varies between 11 and 50 % in these patients observed mostly over a 2-year period. There are only a few studies with a close follow-up period [1, 4–12]. The impact of MRONJ and BRONJ for these patients in their daily quality of life is well known [13]. The need for further effective treatment which is acceptable in conjunction with their oncological treatments and does not further damage their remaining quality of life is challenging [13].

In view of this, there are several options for defect closure dependent on several factors which should be considered in the choice of treatment [7, 12, 14, 15]. If the bone can be completely debrided and there are enough soft tissues available, a simple technique should be favored [4]. Local tissue techniques in conjunction with a standardized routine conservative treatment (antibiotics, mouth rinse, omit dentures, soft diet, or in extended cases nasogastric tube) are of value [16, 17]. Large areas of exposed bone are more difficult to treat than small ones for self-evident reasons [4]. Patients with multiple relapses of BRONJ and exposed bone also require more extensive surgery, since the soft tissues around the damaged bone have been shown to undergo damaging change which reduces the effectiveness of local tissue for surgical wound closure [4, 10, 18]. The more recurrences are observed, the more likely the need for more extensive surgery due to the loss of surrounding healthy soft tissue [4, 10].

Early proactive treatment has a positive effect on the outcome [19, 20] and maximizes the chance to prevent further complications such as mandibular fractures, pain, extension of MRONJ and BRONJ, and the development of fistulas. This, in turn, reduces the demand for more extensive surgical procedures [4, 10, 20]. The primary concept is to remove all necrotic bone, retain vascularized apparently healthy bone, restore mucosal integrity to cover the underlying bone, prevent abnormal movement, and seal any abnormal communications. To achieve this, bearing in mind the extent of hard and soft tissue destruction and the comorbidity and prognosis of the patient, all approaches even microvascular free flaps should be considered if necessary [14, 15, 21]. Patients with reasonable life expectancy with regard to their malignant disease who are having significant life-altering symptoms should be considered for reconstruction by any appropriate means up to and including microvascular tissue transfer after aggressive resection of the affected region [14, 15, 21]. Only a very limited number of patients are likely to be in this category and are not sufficient to clarify a new standard treatment modality [14, 15, 21] but just as metastasectomy and hip replacement can improve quality of life in palliative oncology patients so can radical resection and reconstruction of painful, malodorous, or dysfunctional MRONJ and BRONJ. Individualized therapy seems to be appropriate for the patient in accordance to the stage of the oncological disease, the extension of MRONJ and BRONJ as well as the motivation and life expectancy of each individual [13].

Beyond the conservative treatment options, there are a broad variety of surgical options. As the bone is debrided, several versions of wound closure are available dependent on the area of exposure, presence or absence of intact healthy bone as well as the available soft tissue. We outline some of the more suitable and common techniques.

Local Flaps

Mucosal Flap

The mucosal flap is a local flap providing tissue close to the area of the exposed bone. The incision should be minimal and aim for tensionless defect coverage and a broad supply of the minimally mobilized mucosa. The rationale for minimizing the flaps is that subperiosteal dissection will also require osteoclast activation – the essential underlying defect in MRONJ and BRONJ. For this reason, the ideal socket closure is achieved by reducing the intrasocket alveolar bone by bur and allowing the surrounding mucosa to “collapse” over the socket and sutured to create a watertight seal. Larger local mucosal flaps are necessary for mucosal dehiscences, and fistulas should be included in the surgical planning of the incision line. The surrounding mucosal parts of the exposed bone should be excised since they are chronically inflamed and unlikely to heal [18]. The mucosal flap should be inserted into

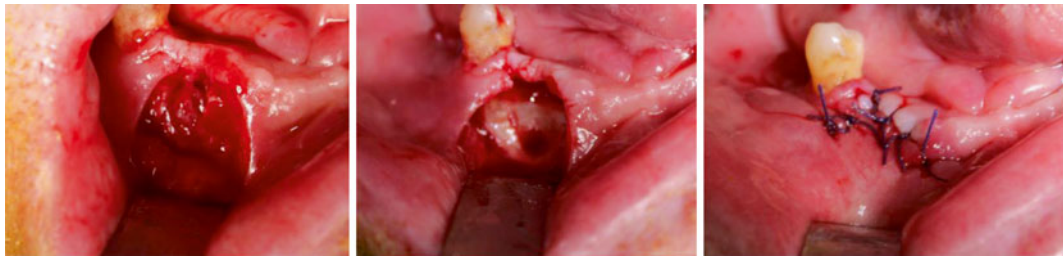

Fig. 8.1 Example of a BRONJ defect in the lower right jaw with a persistent exposed alveolus (*left*). The mucosal flap is designed in a trapezoid manner, and the decortication and debridement are performed (*middle*). After periosteal incision, the mucosal flap is sutured into the defect (*right*)

the defect area in a watertight manner by circular suturing. With the help of marionette sutures and circular careful mobilization of the mucosa, a watertight wound closure can be achieved (Fig. 8.1).

Buccal Mucosal Flap

The buccal mucosal flap is also a very versatile axial- or random-pattern flap with a much greater and better flexibility than the palatal flap [22–24]. Palatal bone is exposed in the palatal flap technique which is counterproductive in a patient with MRONJ and BRONJ. Therefore, the palatal flap is not indicated, but the buccal mucosal flap can be useful in small defects [24].

This flap can be based on the anterior or posterior part of the buccal mucosa, incorporating the buccal branch of the facial artery with some parts of the buccinator muscle if necessary [22–24]. The mucosa is incised including underlying glandular tissue, but the parotid duct should be preserved [22]. As mentioned above, parts of the buccinator muscle can be integrated as an axial-pattern flap if necessary [22, 23]. We prefer anteriorly based buccal mucosal flaps for defects in the incisional area of the alveolar crest and posteriorly based flaps for defects in the premolar or molar area.

Buccal Fat Pad Flap

The buccal fat pad flap is one of the most reliable flaps in the management of BRONJ in the upper jaw, as this flap offers additional tissue to cover mucosal defects [25, 26]. The exposed fat rapidly mucosalizes by epithelial seeding. The buccal fat pad is located in the cheek and surrounded by a thin capsule [27, 28]. The fat pad consists of four parts in the buccal, temporal, pterygoidal, and pterygopalatine area. The central and buccal parts are the most reliable and can easily be used for additional coverage especially in the upper but also in the lower jaw if necessary [27, 28]. The vascular supply of this flap is provided by small branches arising from the maxillary, facial, and superficial temporal artery [27, 28] entering the deep surface of the fat pad. This flap can be exposed and mobilized easily by incising the periosteum underlying a buccal mucoperiosteal flap [27, 28]. This flap can be combined with a standard mucosal flap (Fig. 8.2).

Mylohyoid Flap

The mylohyoid flap can be used if the lingual part of the mandible is affected. In such cases mucosal flaps are not best suited due to the tension of the floor of the mouth as well as the alveolar crest and the vestibular mucosa [29]. Especially in cases of relapsing BRONJ at this site, the mylohyoid muscle flap can be used for defect coverage in the same manner as the buccal fat pad flap for additional coverage of the bone [4]. The mylohyoid flap is a myofascial flap which is accessible at the lingual border of the mandible, inserting at the mylohyoid line. The muscle is detached from here, mobilized and placed over the decorticated mandible with interrupted and tensionless sutures [29]. A mucosal flap should also be used, but is not essential due to the capacity of intraoral exposed muscle flaps to rapidly mucosalize albeit with fibrosis and scarring [30] (Fig. 8.3).

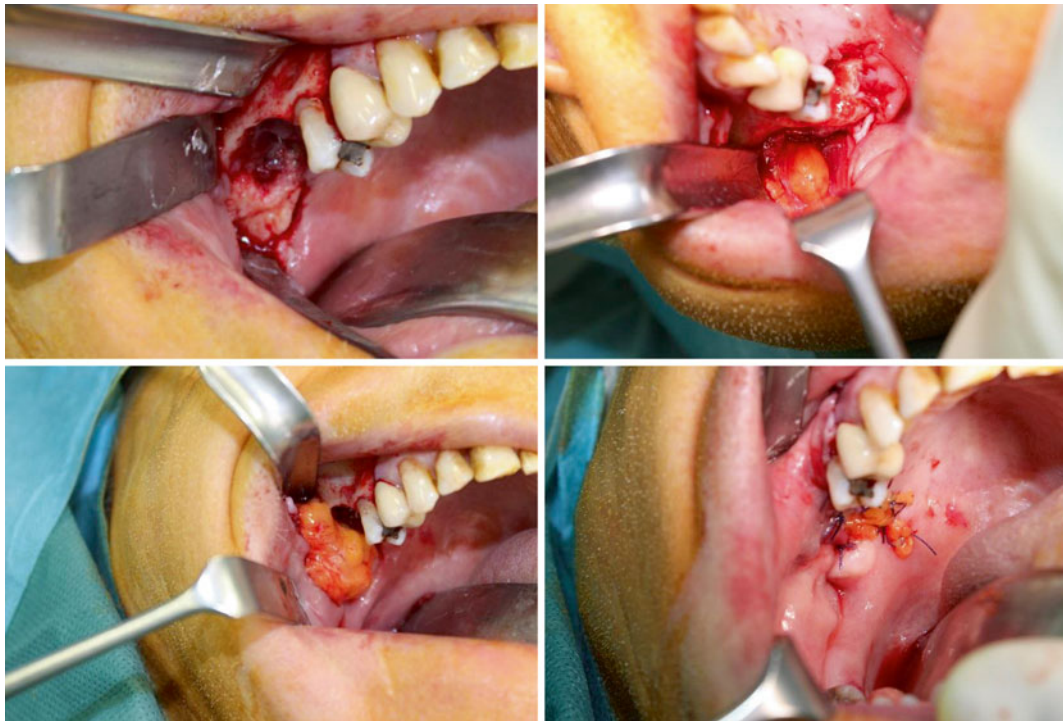

Fig. 8.2 Example of a BRONJ defect in the upper right jaw with exposure of the maxillary sinus (*upper left*). The buccal fat pad flap can be exposed at the pterygopalatine line (*upper right*). After careful mobilization (*lower left*), the buccal fat pad flap is sutured into the defect and covered by an additional mucosal flap (*lower right*)

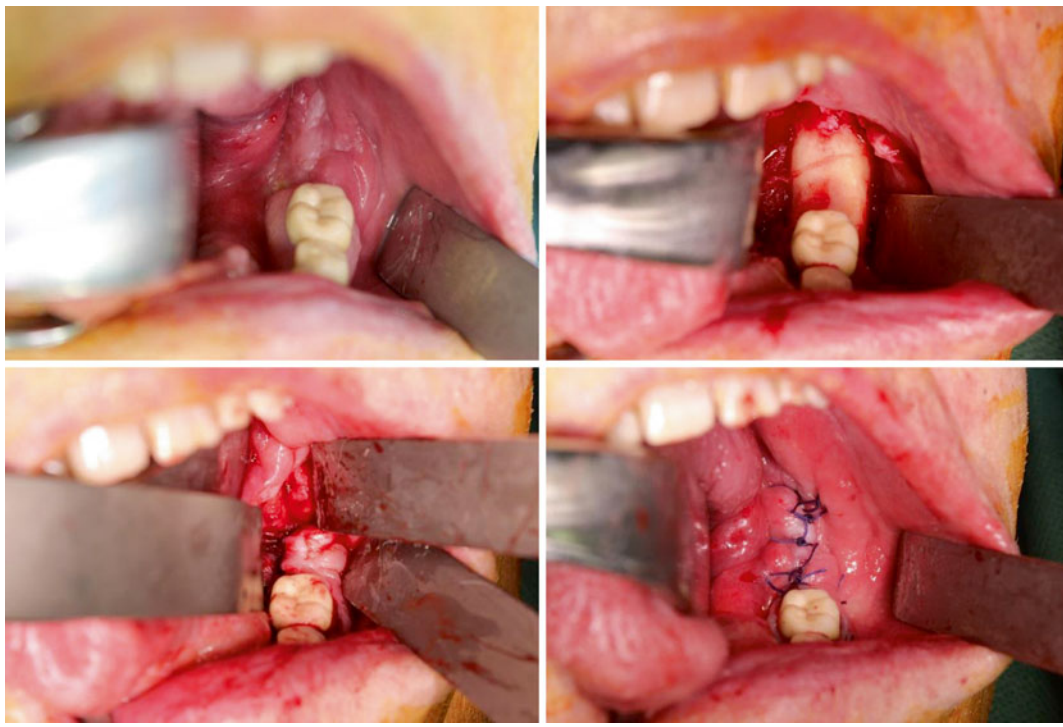

Fig. 8.3 Example of a BRONJ defect in the lower left jaw with exposure of the lingual part of the mandible (*upper left*). The mylohyoid muscle flap can be exposed at the mylohyoid line and mobilized (*upper right*). After careful fixation over the debrided mandible (*lower left*), this flap is covered by an additional mucosal flap (*lower right*)

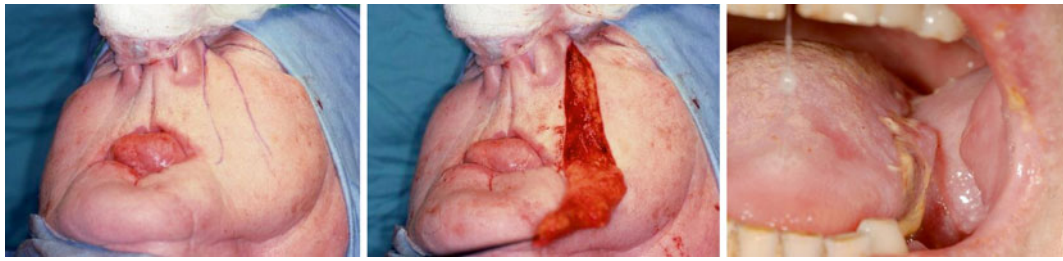

Fig. 8.4 Example of a nasolabial flap after planning (*left*). The flap is prepared (*middle*). After intraoral transposition, the flap is sutured into the defect (*right*)

Nasolabial Flap

The nasolabial flap is a random-pattern flap relying on the subdermal plexus of vessels arising from small branches of the facial artery and accompanying veins. While it can be raised on the facial vessels, this by definition disrupts the muscles of facial expression and is entirely unnecessary. This flap can be based on a cranial or caudal pedicle, although the caudally based type of this flap is more valuable for intraoral reconstruction [31]. The incision is outlined in the nasolabial fold and as far lateral as needed. The incision is through skin and subcutaneous fat [31, 32]. The distal part of the flap includes thin lower eyelid skin and the proximal thicker subcutaneous flap. The facial vessels are often seen in the deeper fat of the face and are not included in the flap itself. A tunnel is created just above this point through into the mouth. This is widened by blunt dissection and the distal end of the flap passed into the mouth for inset. Parrafin gauze is wrapped around the base of the pedicle to prevent it healing into the tunnel [31, 32]. The flap is limited by its axis of rotation and is not a good choice in the dentate patient. The donor site defect in the nasolabial fold is surprisingly easily closed directly in two layers [31, 32]. The singular disadvantage to this technique is the need to divide and inset the pedicle at 3 weeks necessitating a second operation, although the second stage can be performed under local anesthesia. With this type of flap, both defects of the upper and lower jaw can be covered [32, 33] (Fig. 8.4).

Microvascular Free Flaps

Radial Forearm Flap

This reliable, common flap provides thin, pliable, and reliable skin from the forearm. The skin is hair bearing in many men. The flap design was first described in 1981 [34]. Before this flap can be raised, an Allen test should be performed to ensure the perfusion of the hand [35]. The flap raising is straightforward, but the microvascular anastomoses of the accompanying venae comitans might be more challenging in some patients due to their small diameter. Flap harvesting normally starts at the ulnar site of the forearm, raising a fasciocutaneous portion of the forearm being careful to leave the paratenon which creates a donor site of muscle and paratenon which readily accepts a split- or full-thickness skin graft. The radial artery and accompanying venae are identified at the most distal point of the flap, usually 2 cm proximal to the flexor crease (minimizing the tension on the repairing skin graft). These vessels should be ligated and then dissected after identifying the superficial branch of the radial nerve, which should be preserved. The flap can be raised with the cephalic vein and the lateral antebrachial cutaneous nerve of the forearm [34]. Neither is essential for success of the flap. The vascular pedicle lies between the flexor carpi radialis muscle and the brachioradialis muscle. The vascular bundle should be dissected from the deep septum (which carries perforating vessels to the radius in 40 % of which can be included creating an osteocutaneous flap) followed by ligation or even bipolar coagulation of the muscular perforators arising from the

radial artery and its concomitant veins. The pedicle length can be dissected to the length dictated by the site of reconstruction and microvascular anastomosis. If necessary, the microanastomoses can also be performed at the contralateral neck of reconstruction if needed. The donor site should be closed by a full-thickness skin graft or a split-thickness skin graft [36].

Osteocutaneous Fibular Flap

Reconstruction with the fibular bone flap was first described by Taylor et al. in 1975 [37] and was modified by Chen and coworkers with an integrated skin paddle [38]. The skin paddle allows good defect coverage of the affected mucosa and makes this type of flap suitable in patients with extensive MRONJ. This flap is especially beneficial in cases with pathological fractures of the mandible requiring continuity resections and additional mucosal reconstruction [14, 15, 21].

The vessels of the lower leg should be assessed by magnetic resonance imaging or computed tomography combined with an angiographic visualization [39]. While it is extremely unlikely that the fibula will be a site of metastases of the primary disease, this should be excluded. It may be helpful to assess the perforator inserted into the skin paddle by a Doppler examination. The dissection starts with an incision along the fibular bone on the peroneus longus muscle 2 cm anterior to the intermuscular lateral septum. In the area of the anticipated perforator, the incision should be curved anterior to the line of the fibula. The subcutaneous tissue is dissected down to the muscular fascia and intermuscular septum to the peroneal muscles. The perforator vessels become visible in most cases. The lateral part of the fibular bone should be dissected, and the flexor hallucis muscle is dissected from the soleus muscle. The peroneal artery can be palpated behind the fibular bone and is carefully dissected. The distal osteotomy of the fibular bone should be performed 6–8 cm above the lateral malleolus. The proximal osteotomy should preserve a similar amount of fibular bone below the fibular head. The fibular bone is then mobilized by dissection of the intermuscular fascia and interosseous membrane. The guide to this part of the preparation is the tibialis posterior muscle with its v-shaped muscle bundles. The pedicle should be cut after ligation at the most distal part of the fibular bone. The skin paddle is then incised, but the intermuscular septum should be left intact as the perforators are located in this area. The pedicle is further dissected and the flap raised completely, then either detached and shaped on a side table or osteotomized to a preformed template on the leg while still perfused to allow reconstruction of the mandible and the soft tissue defect. The anastomosis can be performed to the standard vessels of the neck as they are of good diameter and the pedicle length is long.

The shaping of the fibula is one of the advantages described in the literature but also prolongs overall operation time [40, 41]. The flexibility of the skin paddle is another advantage of the fibular free flap but also is time consuming due to the handling of the skin paddles containing small perforators [42]. The cutaneous component of the flap provides additional soft tissue for reconstruction of resected fistulas as in the presented cases and helps to establish tension-free wounds in the oral cavity as well [14].

The fibula flap is associated with significantly fewer complications such as infections at the recipient site and free flap loss compared to the iliac crest flap [41]. Debate continues as to whether the ileum or the fibula leave the more significant donor site defect although a majority would agree the ileum is more morbid. The DCIA composite flap has an unreliable skin component although the bulky internal oblique muscle can be used as a well-vascularized space filler which subsequently scars down into fibrous neomucosa.

Although bisphosphonates are also integrated into the transferred fibular flap, as they are systemic and present in all bones, the evidence to date is that this kind of bone with a direct blood supply and minimal demand on osteoclasts in integrating into the neomandible by internal fixation and prevention of contamination by a watertight mucosal seal has little risk of developing osteonecrosis related to bisphosphonates [14, 15, 21]. This is a high-risk strategy as

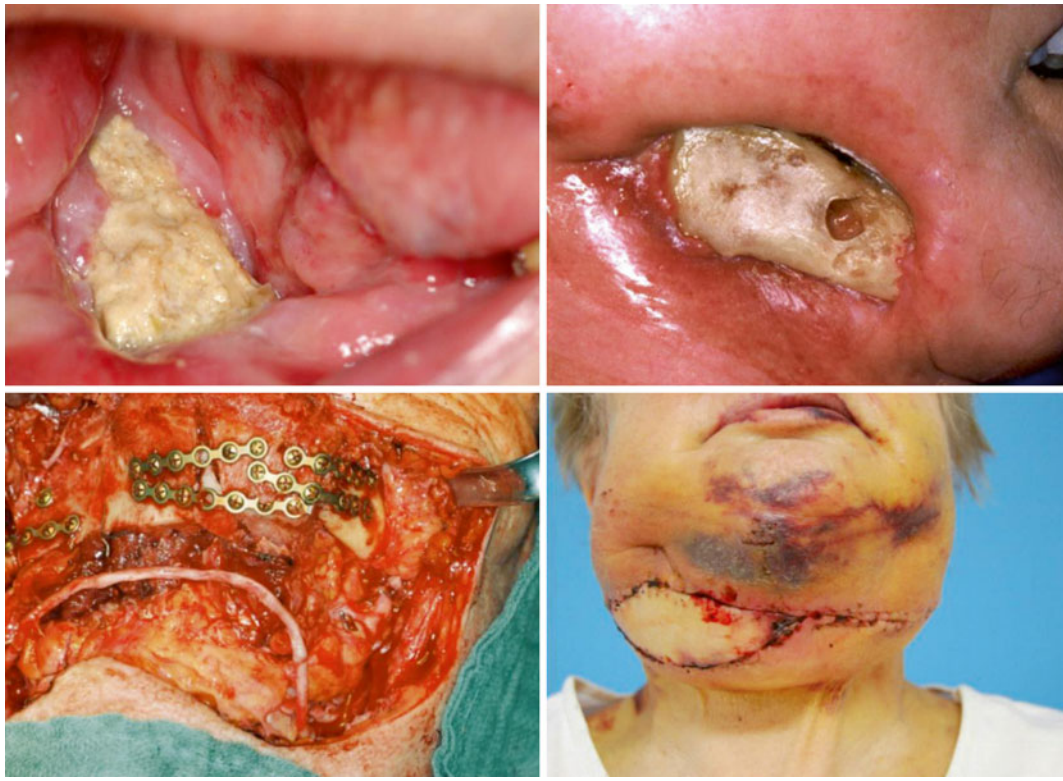

Fig. 8.5 Example of a patient with an extensive BRONJ at the intra- and extraoral part of the mandible (*upper row*). After continuity resection, the fibular osteocutaneous free flap was inserted (*lower left*) containing a skin paddle for the extraoral defect site (*lower right*)

if the fibula flap is not well perfused, the risk of flap failure and total necrosis of the transferred flap and surrounding bone would be increased [14, 15, 21]. The risk of occurrence of BRONJ within the flap should be critically observed, although just one report can be found in the literature [43]. While this may be due to technical failure, management of this risk should be kept in focus if a microvascular free flap is considered. The surgeon's objective should always be to "do no net harm."

Therapeutic options for treating established MRONJ range from comparatively simple to the much more complex and require intensive communication between the patient, contributing professionals, and an experienced surgeon. An interdisciplinary approach should be favored to provide best possible outcome for the patient. The limitations of each therapeutic concept have to be considered in accordance with the general condition of the patient, their needs, wants and aspirations, life expectancy, or other significant prognosis due to the stage and nature of the underlying disease. Thus, a microvascular free flap reconstruction containing bone might be an option in the treatment of extended MRONJ cases, but it is not recommended as the first step in the therapy. It should, however, be critically appraised for special cases (Fig. 8.5).

Conclusion

Several conservative and surgical options are available to treat patients with established MRONJ. Prevention will always be better than cure. Each patient's demands require an individualized therapy approach integrating an interdisciplinary decision making process including all of the available treatment options. Depending on the prognosis of the underlying

disease, the patients' symptoms, and their individual needs and wants, a cautious therapeutic plan is recommended. Extensive surgery should only be applied in special cases respecting the surgeons´ experience and extent of MRONJ of the patient.

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