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Healing of large dentofacial defects

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Dentofacial defects can be small or very large, consisting of defects in the craniomaxillofacial region with missing soft tissue, bony and other hard tissue components. Such combined mucosal, osseous and even cartilaginous defects can be reconstructed using flaps and bone grafts, or hopefully, in the future with bone graft substitutes or even tissue engineered constructs. The healing of such wounds always relies on the vascularity of the surrounding tissues. This chapter seeks to provide a physiological basis for the mechanisms involved in the healing of such large complex defects. The reconstruction of specific defects must follow sound and logical surgical principles. The authors employ the concept of the reconstructive surgical ladder, in which techniques of step-wise increasing complexity are used with a strong preference for the simplest possible procedure at the outset. A number of techniques are presented along with the principles of tissue engineering and the basis for bone regeneration using adipose derived stem cells, growth factors and resorbable scaffolds.

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Introduction

Dentofacial defects are defined as missing areas of tissue including defects of either or both the jaws, cranium, face and neck with missing adjacent soft tissue and bony components. There are numerous causes of dentofacial defects. Congenital bony defects in the craniofacial and maxillofacial skeleton arise as a result of areas of failed development such as in cleft lip and palate patients (1) (Fig. 1). Ablative surgery may produce bony defects (2) when segments of bones are resected to treat tumors (Fig. 2). Trauma may result in large bony defects when tissue may have been traumatically avulsed (3). Such combined mucosal, osseous and even cartilaginous defects can be reconstructed using flaps and bone grafts, or hopefully in the future with bone graft substitutes or even tissue engineered constructs (4). The healing of such wounds always relies on the vascularity of the surrounding tissues (5).

The reconstruction of a specific defect must follow sound and logical surgical principles. The authors employ the concept of the reconstructive surgical ladder (6), in which techniques of step-wise increasing complexity are used with a strong preference for the simplest possible procedure at the outset. The missing tissues are identified including mucosa, muscle, bone, cartilage, nerve, blood vessels and skin. Then plans are made to replace missing tissue elements with similar or like tissue. In the mouth, for example, one would always aim to replace missing palatal mucosa with attached mucosa rather than unattached alveolar mucosa.

Then flaps containing the missing tissue elements are planned with the following hierarchy, using the simplest reconstructive ladder technique first:

1. Local soft tissue grafts (free gingival grafts)
2. Local flaps (buccal advancement flaps)
3. Regional flaps (tongue flaps)
4. Intra-oral harvested bone grafts (chin, ramus, zygoma)
5. Extra-oral harvested bone grafts (iliac crest, tibia)
6. Distant pedicled flaps (deltopectoral, sternocleidomastoid, pectoralis flaps)
7. Distant microvascular flaps (fibula, iliac crest, latissimus dorsi, rectus abdominis).

The need for bone

Reconstruction of osseous defects in the oral and maxillofacial region represents one of the most challenging

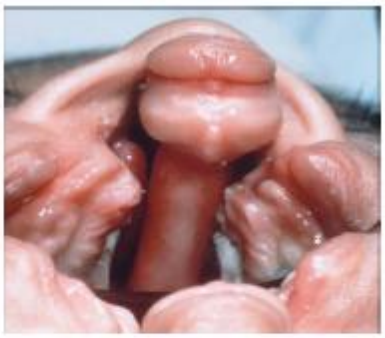

Fig. 1. Bilateral complete cleft lip and palate deformity with missing bone, cartilage, mucosa and skin.

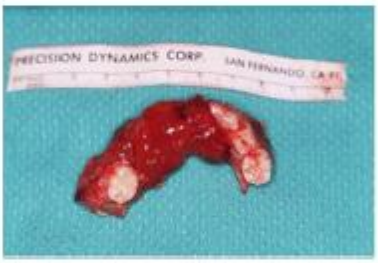

Fig. 2. Tumor resection specimen encompassing 11 tooth segments leaving a large mandibular dentofacial defect.

tasks to the reconstructive surgeon and encompasses the model of tissue engineering (Fig. 3). While significant advances have been made with bone substitutes, autogenous bone remains the gold standard in the reconstruction of bone defects (7). To understand bone reconstruction, the surgeon must first understand bone healing (7) and the healing of the surrounding soft tissues.

Bone healing

Inflammation, wound healing, vasculogenesis and bone healing are all delicately intertwined. Three types

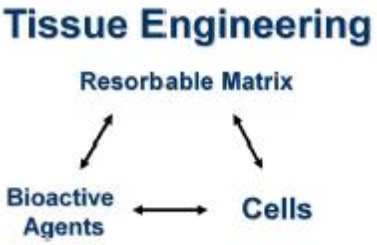

Fig. 3. The tissue engineering triad representing the interplay between scaffolds or biomaterials, stem cells and signaling molecules or growth factors.

of bone healing are described: primary, secondary and gap healing. The difference between the three is dependent on the size of the osseous defect and the rigidity of fixation. The three bone healing models give information about the differences between bone regeneration within non-grafted as well as grafted defects.

Primary bone healing

Primary bone healing without callus formation occurs when the bone ends are in direct contact and rigidly fixated, or anatomically reduced and are compressed together by bone plates (7). This process was initially described in 1949 after studying long bone fractures that were treated by rigid fixation with plating (8). These fractures failed to show callus formation. Osteoclasts were seen to begin cutting away cores on either side in the area of compression, progressing towards the fracture at a rate of 50–80 μm per day. Cutting cores were 200 μm wide which provided space for vessel ingrowth, osteoblastic proliferation and new bone formation (9).

Secondary bone healing

Fractures treated without rigid fixation heal with secondary bone healing. A good example of non-rigid fixation is the wiring of fractured jaws together in maxillomandibular or intermaxillary fixation. The initial injury elicits an inflammatory response and activation of the complement cascade. Damage to surrounding blood vessels initiates cellular extravasation

and cell signaling. Chemotactic factors (C5a, leukotriene B4) attract monocytes and macrophages (10). Activated macrophages release fibroblast growth factor (FGF) which stimulates endothelial cells to release plasminogen activator and procollagenase. Growth factors such as platelet derived growth factor (PDGF), transforming growth factor—β1 (TGF-β1) and—β2 are released from the alpha granules of degranulating platelets early in wound healing and are chemotactic stimulants for PMNs, lymphocytes, monocytes and macrophages. The blood clot acts as a hemostatic plug and contains the growth factors at the injured site and provides an environment for cell signaling. The injured tissue is normally hypoxic with oxygen partial pressures of 5–10 mmHg as well as being acidotic (pH 4–6). Acidosis and hypoxia are required for PMN and macrophage stimulation (10). A proliferation phase begins with the healing by day 3 and can last up to 40 days after fracture occurrence. A reparative phase follows with the appearance of new blood vessels, collagen and cells. Osteoprogenitor cells are then stimulated to proliferate and differentiate into active chondroblasts and osteoblasts, laying down large amounts of extracellular matrices forming a bridging callus. Chondroblasts lay down amorphous chondroitin sulfate matrices, then become chondrocytes, which eventually hypertrophy and die, leaving empty lacunae in a calcified matrix. These empty spaces (lacunae) allow for vascular ingrowth resulting in a higher oxygen tension and normalized pH, which in turn favor differentiation of osteoblasts. The cartilage is then removed by osteoclasts while osteoblasts lay down immature woven bone. Mobility at the regenerate site will disrupt the blood supply and result in cartilage and fibrous tissue predominance.

Gap osseous healing and bone grafts

Larger defects heal by gap healing and may require bone grafts to allow the bony wound to regenerate bone rather than produce a fibrous union. Three processes are involved in the healing of bone grafts: osteogenesis, osteoinduction and osteoconduction (11).

1. Osteogenesis is defined as the formation of new bone from osteocompetent cells contained within the bone graft.
2. Osteoinduction is defined as bone formation from primitive mesenchymal cells in the recipient bed, which have been stimulated to differentiate into bone forming cells by inductive proteins within the graft.
3. Osteoconduction is defined as ingrowth of capillaries and osteoprogenitor cells from the recipient bed into and around the grafted material.

Growth factors

Growth factors important in bone healing include the bone morphogenetic proteins (BMPs). The BMP subfamily of TGF-β is made of seven conserved cysteine residues at the mature carboxy terminal (12). BMPs are low molecular weight proteins (19–30 kDa) with a pH of 4.9–5.1 (13). BMPs stimulate mesenchymal stem cells to differentiate into osteoblasts during development and bone healing (14,15). BMPs are present in most tissues and play an important role in remodeling of the adult skeleton. When osteoclasts resorb bone matrix, BMP is released (16), initiating recruitment and differentiation of stem cell precursors to form osteoblasts and ultimately new bone (17).

BMP-7, also known as osteogenic protein 1 (OP-1), was first used to treat a mandibular segmental defect by Moghadam and colleagues in 2001 (13). BMP-7 was used to aid the healing of a maxillary Lefort I osteotomy by Warnke in 2003 (18). It is now approved for human use in maxillary sinus elevation procedures as well as in extraction socket preservation techniques. The recombinant human form is derived from a Chinese hamster ovary cell line. Both laboratory and human studies show data with superior results in regenerating critical-sized defects (13,19). Clokie and Sándor were first to report the use of OP-1 in human post-resection defects. They documented 10 cases of post-resection mandibular defects successfully reconstructed with BMP-7 (OP-1) in demineralized bone matrix (DBM) suspended in a reverse phase copolymer medium. Uneventful postoperative courses were reported with dental rehabilitation achieved 1 year post reconstruction (13,20).

Blood supply and the soft tissue envelope

Formation of a new blood supply is critical to wound healing (21). This is demonstrated most clearly in pathologic states where healing is compromised by diabetes, poor vascular supply, radiation, bisphosphonate exposure and where the normal healing process

becomes pathologic, such as in instances of heterotopic bone formation in response to surgery or trauma (22). The need for the re-establishment of nutrient and oxygen supply to support regeneration and repair of the wound exceeds the maintenance needs of the tissue that will ultimately form. Vascular endothelial growth factor (VEGF) is involved in the recruitment, survival and activity of endothelial cells, osteoblasts and osteoclasts in wound healing (21,23–28).

Soft tissue wound healing is required to support bone healing. It has been well described and is characterized by four phases:

1. Coagulation (immediate to 1 hour)
2. Inflammatory (1 hour to 4 days)
3. Proliferative (3–21 days)
4. Remodeling (21 days onward).

Coagulation is characterized by endothelial damage and platelet activation resulting in a fibrin clot. Platelets release angiogenic cytokines including platelet-derived growth factor (PDGF) and TGF-β.

Vasculoendothelial growth factor (VEGF) effects

VEGF is also released by monocytes, damaged keratinocytes, endothelial cells and especially active macrophages in the wound (29,30). VEGF acts on nearby capillaries to induce vascular leakage, supporting inflammation in physiologic and pathologic conditions by enhancing vascular permeability (23). VEGF also attracts neutrophils and monocytes required for wound healing and likely also facilitates the formation of granulation tissue. The inflammatory phase is characterized by leukocyte migration, initially neutrophils to kill bacteria and then monocytes. VEGF release also increases local leukocyte rolling (a more than threefold increase) and adhesion (a > fourfold increase) in addition to increasing vascular permeability further facilitating inflammatory processes. Monocytes differentiate into macrophages and, in addition to their role in phagocytosis, become important in releasing cytokines important in subsequent healing and granulation tissue formation. VEGF is known to play a role in the regulation of initiation and growth of new vascular structures (23) as well as being necessary for endochondral ossification (23). Endothelial cells activated by VEGF initiate angiogenesis locally. Endothelial progenitors in bone marrow are also recruited to the wound for vasculogenesis. Together both processes supply the neovascularization required for granulation tissue formation (29), though angiogenesis dominates the process (21).

The absence of VEGF inhibits angiogenesis in wound healing, impairs the recruitment of cells necessary for normal bone development and interferes with necessary cell to cell cytokine cross-talk due to the absence of developing vasculature. VEGF is a key player in bone repair and regeneration for similar reasons (28). The potent angiogenic activity of the blood clot that forms immediately after fracture has been attributed to VEGF (28). The importance of VEGF in fracture healing has been demonstrated in mice and rabbits; when VEGF is inhibited it causes a reduction in blood flow and results in disruption of the fracture repair and non-union. While the role of VEGF remains to be completely understood, VEGF is clearly necessary for healing and bone repair through modulation of angiogenesis and new vessel formation (28).

In addition to stimulating and regulating angiogenesis, VEGF influences osteoblast differentiation and is involved in mineralization of fracture callus (31, 32). Different growth factors influence wound and bone healing in a manner that is both distinct and synergistically interconnected (32). VEGF is required in order for other factors to function, as is the case with BMP-2 and FGF-2 induced angiogenesis (33). Inhibition of VEGF blocks BMP-7 induction of osteoblast differentiation and BMP-4-induced bone formation (33).

Angiogenesis

Angiogenesis is important not only in soft tissue healing but also for bone tissue differentiation, bone formation, maintenance and remodeling. Bone repair follows four sequential steps:

1. Establishment of a thrombus
2. Formation of the soft callus
3. Formation of the hard callus, followed by
4. Bony remodeling.

The first step in angiogenesis involves the formation of a platelet—and leukocyte-rich blood clot around the site of fracture or bony defect. Activated platelets promote chemotaxis of leukocytes to assist in clearing debris. Both platelets and leukocytes release several growth factors which will ultimately favor the formation of granulation tissue rich in immature vessels which forms in and around the wound. These growth factors

include: tumor necrosis factors (TNF), BMPs, FGF, insulin-like growth factor (IGF), PDGF, TGF and VEGF (34,35). Neovessels (28) and fibroblasts proliferate, forming immature fibrous tissue that is responsible for forming the early soft callus. The callus undergoes further maturation to form the hard callus and is eventually replaced by lamellar bone. Immature woven bone formed by osteoprogenitor cells will eventually undergo remodeling. Bone remodeling follows the maturation of the newly formed bone, characterized by maturation and re-organization as the fracture or defect gains tensile strength. Each step in bone healing involves the migration, proliferation, differentiation and activation of local and distant cells, and this process is closely regulated (34,36). Osteoprogenitor cells respond to the presence of the growth factors including BMPs, FGF, IGF, PDGF, TGF and VEGF (34,36). Bone is an excellent source of most of these growth factors, which are released after remodeling or trauma, and this is responsible in part for the success of autogenous grafting compared to alternative sources of graft material (37). Growth factors modulate the healing response and mediate the remodeling process. VEGF increases angiogenesis at the graft or fracture site, providing greater oxygen and nutrient supply and thus enhancing differentiation of perivascular and mesenchymal stem cells into osteoblasts (32). BMPs are potent inducers of osteogenesis and are expressed during the bone deposition stage, though this is dependent on the formation of neovessels (37).

It has been reported that a process not unlike embryonic vasculogenesis may play a role in coalescence of vessel progenitors (38). VEGF-D, an isoform, and VEGFR-3 (VEGF receptor-3) are important in osteoblast maturation, with VEGF-D and VEGFR-3 acting downstream from VEGF in osteogenesis (38, 39). Rat studies have revealed VEGF splice variants VEGF121 and VEGF165, corresponding to human VEGF splice variants VEGF121 and VEGF165. These are expressed during fracture healing. VEGF is most strongly expressed in bone fracture callus at the early phase of healing, decreasing significantly by day 5 (39). The role of VEGF beyond 5 days in healing of the bony wound is not known. Angiogenic growth factors may mediate interaction between endothelial cells, osteoblasts and chondrocytes, all of which secrete endogenous VEGF (39). As healing progresses, the fibroblast dominates wound healing through the proliferative phase, forming collagen and scar tissue. Several factors assist in tipping the balance from repair to regeneration (39), favoring the formation of immature bone rather than fibrous tissue. For example, in a rabbit calvarial defect model, the addition of VEGF to DBM favors regeneration of the critical sized bony wounds compared to mainly repair in DBM or void controls (40). Moreover, treatment of rabbit mandibular defects with supraphysiologic doses of exogenous human recombinant VEGF165 results in increased angiogenesis and bone regeneration (41).

Bony wound healing, be it a fracture, a graft or a defect, requires stability and adequate blood supply. Bony wound healing relies on osteogenic progenitors from adjacent and distant bone marrow. Bone possesses limited potential for regeneration, yet this potential can be enhanced (5,42–44). The periosteum is a key source of blood supply and, when it remains intact, demonstrates the extensive microvasculature needed for bone healing and regeneration (45,46). Bone adjacent to a defect has limited capability for neovascularization and osteogenesis. The periosteum and, in the case of cranial defects even dura, stimulates bone formation and neovascularization (46).

Augmented angiogenesis in bony wounds and bone grafting application may improve graft survival, minimize resorption, hopefully reduce reliance on autogenous graft, reduce the amount of autogenous graft required for a given defect or ultimately enable entirely bio-engineered grafts. Moreover, the ability to promote neo-angiogenesis could potentially prove very useful in the treatment and prevention of osteoradionecrosis and bisphosphonate related necrosis.

Efforts to use angiogenic growth factors for treatment of chronic wounds have met with limited success. To date only PDGF has been approved by the US Food and Drug Administration (FDA) for use as a topical cytokine wound ointment. PDGF is active in all phases of the healing process and has been highly effective as an adjunct measure in the treatment of chronic wounds of the foot (21). Success is limited by the adequately perfused granulation tissue bed.

Attempts to improve bony and chronic wound healing have been the focus of much attention. Hyperbaric oxygen (HBO) improves the ability of macrophages to phagocytose bacteria, especially since hypoxic tissue impairs the oxidative function of macrophages (46). Moreover, macrophages release higher levels of angiogenic cytokines in response to HBO (46). Another approach under investigation is the adminis-

tration of VEGF gene therapy to locally increase neovacularization (39). However, results have been unpredictable, and disorganized vascular tissue and hematomas have resulted instead of normal angiogenesis or vasculogenesis due, in part, to overexpression of VEGF (39).

VEGF has been shown to increase blood vessel formation, mineral density and bone fill in rat calvarial defects (5) and rabbit mandibular defects. VEGF has also been shown to increase bone formation and improve demineralized bone allograft consolidation (41). Most studies using VEGF in bony wounds and fractures involve local infusions of VEGF (28,41), a technique that has proven effective but is not a practical or convenient long-term mode of delivery. Instead, delivery of VEGF incorporated into an implantable membrane or another allogenic scaffold material, possibly combined with other important growth factors, is a preferable and more viable mode of delivery which is directed at the target site with sustained exposure.

Since VEGF does not appear to drive osteoprogenitor cell differentiation, a combination therapy with BMPs may be ultimately required (4). Once combined with grafting materials, VEGF would be released initially to promote vascularization to the site followed by the release of BMP to promote osteoprogenitor cell differentiation and bone fill. This would exploit the synergy between bone formation and angiogenesis by the manufacturing bone grafting materials that promote angiogenesis in the early stages of injury, such as a tooth extraction, followed by treatment with bone growth factors, such as BMP, to stimulate osteoprogenitor cells to differentiate in the later stages. This type of combined treatment might lead to optimal wound healing.

It is clear that endogenous VEGF is required for normal bone fracture healing, remodeling, and osteoblast and osteoclast activity (28). In addition, the autocrine activity of VEGF in osteoblasts adjacent to cortical defects has been demonstrated. Exogenous VEGF given by a pump over 48 hours until day 7 increases early vascularization and bone healing in bone fracture healing and bone defect healing (28,41). The angiogenic role of VEGF has been studied separately in soft tissue porcine bladder models, and VEGF has been shown to improve neovascularization of porcine bladder constructs at VEGF doses of up to 1000 times less than in studies which demonstrate effects on bone fracture and bone defect healing. This may be largely explained by the fact that most studies on bone have used recombinant human VEGF165 (rhVEGF165), whereas recombinant human VEGF121 (rhVEGF121) has been used in many of the soft tissue studies. It is difficult to compare studies as the dose and mode of delivery of VEGF varies. Furthermore, it is not known if bone healing and angiogenesis have differing VEGF requirements. It is safe to say, however, that VEGF seems to be important in the paradigm of bone healing (5,47,48).

Surgical maneuvers to induce and promote healing of large defects

Periosteal healing

Manipulating the periosteum is one method that surgeons have learned which induces bone regeneration. Periosteal stretching occurs naturally in periosteal new bone formation under pathologically stretched periosteum, in osteomyelitis for example. The periosteum is a key source of blood supply and when it remains intact it demonstrates an extensive microvasculature which is necessary for bone healing and regeneration (45,46). Bone adjacent to a defect has a limited capability for neovascularization and osteogenesis. The periosteum and, in the case of cranial defects even dura, stimulates bone formation and neovascularization (46).

There are sites where periosteal bone regeneration can occur predictably in young children. The fibula or ribs are examples that may totally regenerate when a graft has been harvested in a child and the periosteum is maintained. The mandible has also been known to regenerate in a child when it has been resected and the periosteal sleeve was left intact. These same principles of periosteal stretching and defect maintenance are important in sinus lifting, guided bone regeneration with membranes (49) and distraction osteogenesis. Defects that are not maintained result in a periosteum that sags or collapses and there alveolar ridges become non-ideal in form.

Tent pole procedures

The value of re-establishing the continuity of a mandibular defect in tumor reconstruction with a bone graft and rigid fixation hardware is undeniable, but

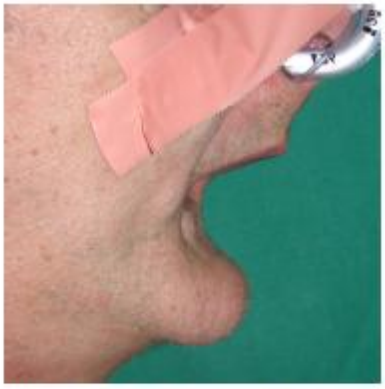

Fig. 4a. Edentulous male with severe mandibular alveolar atrophy and limited lower lip support.

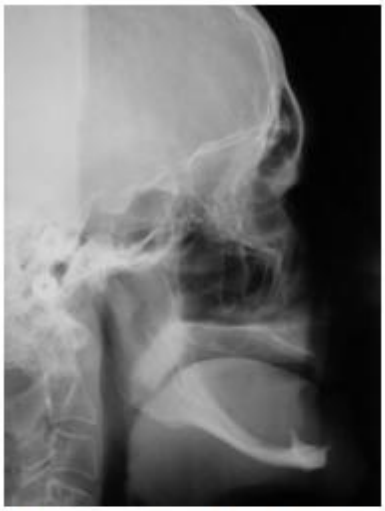

Fig. 4b. Lateral cephalogram showing 4 mm of mandibular ridge height.

reconstructions like these should be considered interim if they are not functionally loaded. If they do not restore chewing function, the bone grafts tend to undergo progressive disuse atrophy, and the absence of teeth permits overeruption of the opposing dentition. The authors have observed atrophy of non-vascularized grafts and, surprisingly, vascularized fibular reconstructions of the mandible as well. Atrophy of vascularized grafts has been documented in growing children (50) and has been observed in adult patients by these authors.

The soft tissue matrix expansion (STME) or tent pole procedure was originally described to manage severe alveolar atrophy secondary to long-standing mandibular edentulism (Figs. 4a–4i) by stretching the periosteum surrounding the part of the atrophic mandible to be reconstructed with dental implants (2, 51–55). The technique was adapted to arrest atrophy of a vascularized fibula used to reconstruct an ablative defect resulting from resection of a malignant tumor of the parasymphysis of the mandible in a growing child (50). The authors have further adapted the STME technique to treat an ablative defect of the lateral aspect of the mandible reconstructed initially with a vascularized fibular graft. The following reconstruction of a large mandibular dentofacial defect illustrates the principles of this technique (Figs. 5a–5s).

Sinus lifting/lateral ridge augmentation

Acute periosteal stretching

Sinus-augmentation procedures are well-accepted techniques to treat the loss of vertical bone height (VBH) in the posterior maxilla and are performed in two ways: an osteotome sinus floor elevation technique (56) (Figs. 6a–6e) and a lateral window technique (57) (Figs. 6f–j). Implants can be placed with an osteotome technique if there is at least 5 mm of bone height present (56). If the alveolar ridge has a VBH less than 5 mm, then primary stability of implants may not be achieved. Instead, implants could be placed in a delayed or second-stage surgery after graft remodeling is completed (56,57). While these techniques have been used to regenerate lost bone, the factors that contribute to the survival rate of sinus augmentation and dental implant placement are still the subject of discussion. The recent literature concerning sinus grafts showed differing long-term results depending on which type of bone graft material was used (58). Moreover, it has been documented that there are no

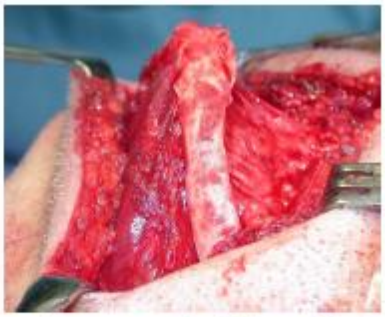

Fig. 4c. Anterior aspect of mandible exposed through an extraoral submental skin incision. There is no intraoral incision and the periosteum overlying the superior aspect of the mandibular ridge is peeled off and kept intact.

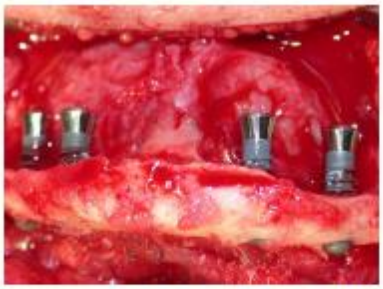

Fig. 4e. Anterior view of the mandibular implants with healing screws attached. The exposed parts of the implants will tent up the overlying periosteum like tent poles. The exposed parts of the implants will be covered with cancellous bone obtained from the posterior iliac crest.

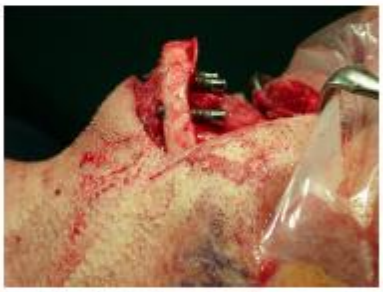

Fig. 4d. Implants have been inserted into the basal bone of the mandible with the apical one third of each implant engaging the mandibular bone.

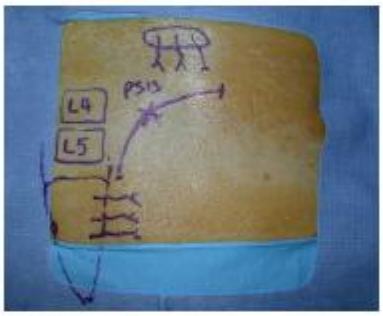

Fig. 4f. Posterior iliac crest donor site.

differences in implant survival rates if either osteotome or lateral window technique with synchronous implant placement were performed (59–61).

Lateral ridge augmentation is the most commonly used method to augment a deficient mandibular alveolus in preparation for dental implant treatment today (Figs. 7a–7d). Alveolar ridges in the maxilla which are deficient in the transverse dimension are augmented predictably with the placement of a bone graft and covered laterally with a resorbable membrane (62). Lateral ridge augmentation is stable with both block cortical and particulate bone grafts, whereas the results of vertical ridge augmentation tend to be unpredictable. Both non-resorbable membranes such as titanium reinforced polytetrafluoroethylene (PTFE) membranes and resorbable collagen membranes have been used (63).

Hyperbaric oxygen therapy (HBOT)

One maneuver surgeons have learned is to amplify the oxygen tension in a poorly vascularized wound to help

Fig. 4g. Cancellous bone harvested from posterior iliac crest.

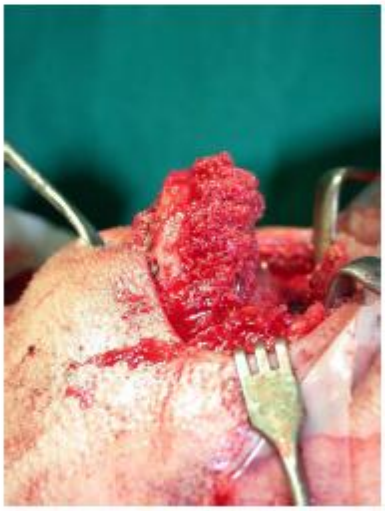

Fig. 4h. Exposed parts of dental implants covered by cancellous bone graft. Periosteum closed overtop will act like a natural membrane allowing bone graft healing beneath with no exposure of grafted material to oral environment.

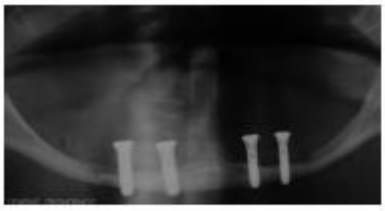

Fig. 4i. Post-operative orthopantomogram showing recently placed dental implants in atrophic mandibular ridge with healing bone graft.

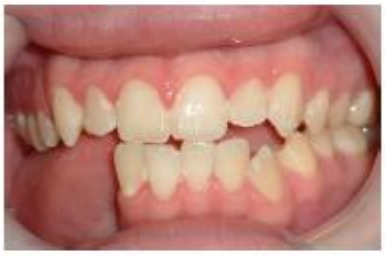

Fig. 5a. Anterior view of teeth on presentation. Note pre-existing class III malocclusion and anterior edge-to-edge relationship.

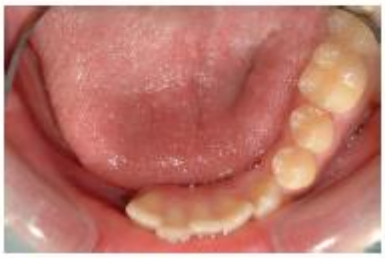

Fig. 5b. Occlusal view of mandibular arch. Note absence of right lateral segment of mandible.

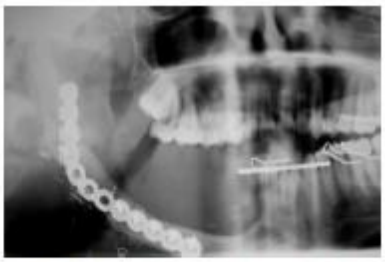

Fig. 5c. Panoramic tomograph on presentation showing right side of mandible reconstructed with vascularized fibular graft. Note the lack of vertical height of the graft and the potential crown-implant ratio.

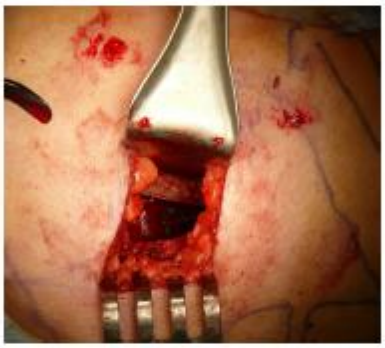

Fig. 5d. Posterior iliac crest exposed.

Fig. 5e. Posterior iliac crest graft stored in saline on ice.

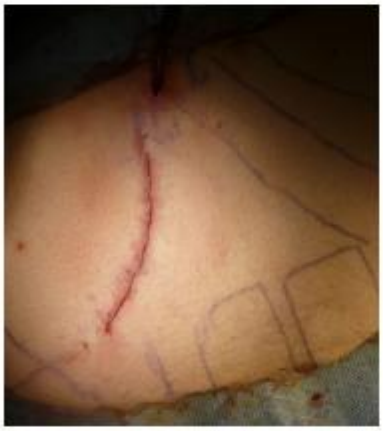

Fig. 5f. Closure of donor site incision.

promote healing. Some wounds are poorly vascularized due to excessive scarring or from repeated failed surgical attempts (6). Radiation therapy also causes tissues in the irradiated field to become hypovascular. HBO can help in the healing of problem wounds in the dentofacial skeleton (5).

HBOT is defined as intermittent exposure to 100% oxygen under pressures greater than 1 absolute atmosphere (ATA). The concentration of oxygen in the atmosphere is 21%. At 1 ATA, the oxygen in blood is almost entirely carried by hemoglobin. Ninety five percent of oxygen carried in the arterial blood is chemically bound to hemoglobin while only 3% is dissolved in plasma. One gram of hemoglobin carries a maximum of 1.34 ml of oxygen. Fully saturated hemoglobin (100%) in 100 ml of blood carries approximately 20 ml of oxygen. Ninety seven percent saturated hemoglobin in 100 ml of blood carries 19.5 ml of oxygen. This amount is reduced to 5 ml of

Fig. 5g. Right submandibular incision through the pre-existing scar.

Fig. 5i. Implants are inserted into basal bone up to junction of apical and middle thirds.

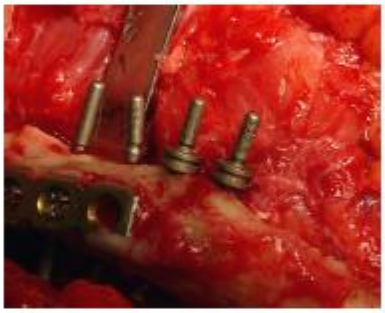

Fig. 5h. Implant osteotomy preparation with submandibular soft tissue retracted upwards over the mandible. Note suctioning of bone particles from drilling site under irrigation.

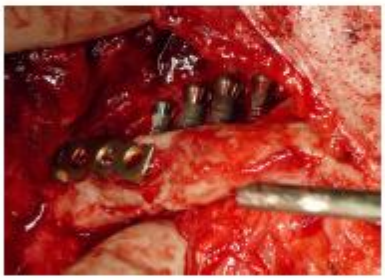

Fig. 5j. Periosteum propped up by implants and healing caps.

oxygen while passing through capillaries. Increasing the oxygen-carrying capacity of blood by increasing hemoglobin saturation is not possible (42).

At sea level, gas pressure is 760 mmHg or 1 ATA. Arterial hemoglobin saturation is 97%, while venous hemoglobin saturation is 70%. Inhalation of HBO increases the quantity of oxygen dissolved in plasma. At 1 ATA, the amount of dissolved oxygen in 100 ml of plasma is 0.449 ml. When inhaling 100% oxygen at 1 ATA, oxygen concentration increases to 1.5 ml/100 ml of plasma. When inhaling 100% oxygen at 3 ATA, the amount of dissolved oxygen in 100 ml of plasma increases to 6.422 ml/100 ml of plasma, which is enough to meet the basic metabolic needs of healing tissues in the human body (5,42–44).

The driving force for oxygen diffusion from the capillaries to tissues can be estimated by the difference between the partial pressure of oxygen on the arterial side and the venous side of the capillaries. The difference in the partial pressure of oxygen from the arterial side to the venous side of the capillary system is

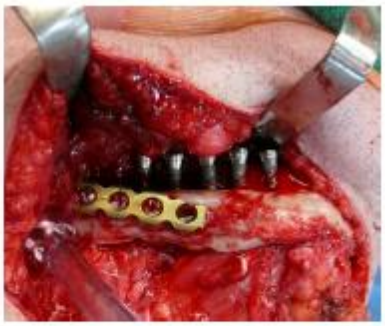

Fig. 5k. Five standard SLA RN (Straumann Sand-Blasted Large Grit Acid Etched Regular Neck) dental implants with healing caps in fibular reconstruction.

Fig. 5l. Cancellous bone particles from the posterior iliac crest and implant osteotomies packed around dental implants in space created under propped up periosteum.

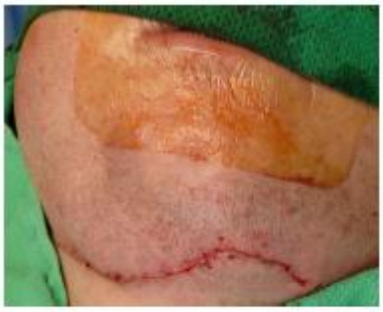

Fig. 5m. Closure of the submandibular incision.

Fig. 5n. Immediate post-operative panoramic tomograph showing implants and bone graft.

approximately 37 times greater when breathing 100% oxygen at 3 ATA than air at 1 ATA (5,42–44).

Distraction osteogenesis

Gradual periosteal stretching

Distraction osteogenesis involves osteotomy of a bone with minimal periosteal disruption and slow continuous traction on the ends of the osteotomized bone to produce a lengthening that is unsurpassed by standard osteotomy techniques. There is evidence that during this process bone and other tissues are formed to compensate for this lengthening. Some refer to this process as histiogenesis. Distraction osteogenesis actually recapitulates all the processes of embryonic bone formation to produce new bone without requiring a bone graft. The levels of growth factors such as BMPs, PDGF and VEGF are markedly elevated in the distraction regenerate.

The treatment of alveolar defects includes guided bone regeneration using a variety of membranes, onlay grafting of autogenous bone, connective tissue grafting and alloplastic augmentation. Vertical alveolar defects are difficult to overcome in a predictable manner using autogenous bone grafts and often lead to esthetic shortcomings (64,65). Distraction osteo-

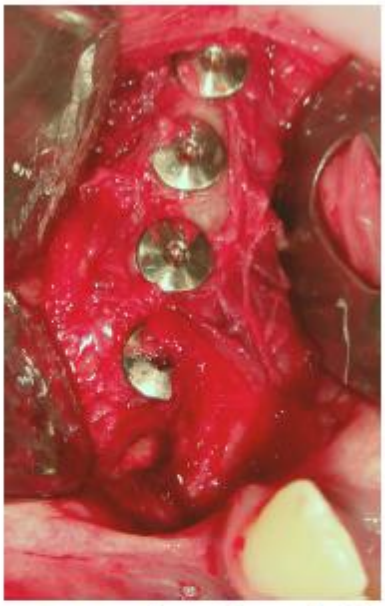

Fig. 8o. Exposure of 2-mm healing caps through a crestal incision of the mucoperiosteum.

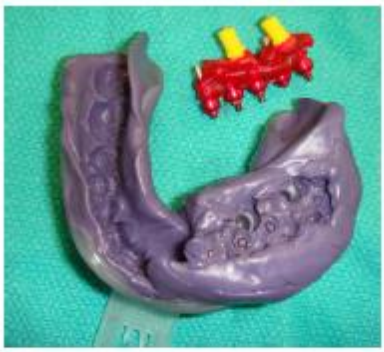

Fig. 8p. Polyether impression and components assembly removed from mouth. Note the plastic impression caps embedded in impression.

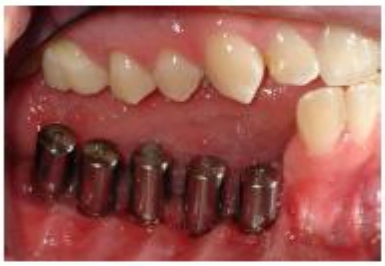

Fig. 8q. Implants are sealed with 15-mm healing caps.

genesis of the maxillary alveolus permits correction of alveolar defects oftentimes without the use of a bone graft.

Alveolar distraction osteogenesis (ADO) may offer several advantages over bone grafting alone in the treatment of vertical alveolar defects: no donor site is required; distraction of bone and surrounding soft tissue occurs simultaneously; the transport segment is a form of pedicled graft which is never separated from its blood supply, thus maximizing vitality and minimizing resorption; and it has the potential for better control of vertical height, esthetics and biomechanical loading (66,67).

Alveolar distraction devices have three basic components: an upper member, a distraction rod and a lower member/base plate supporting the vertical force of distraction. These devices can be classified as intra-osseous or extra-osseous; uni-, bi- or multi-directional; non-resorbable or resorbable (not requiring a second surgery to remove distracter components); and prosthetic (can remain in place to be used to support the dental prosthesis) or non-prosthetic (must be removed following distraction and replaced with a dental implant) (68,69).

ADO is indicated for the treatment of alveolar defects where the alveolar processes are atrophic and deficient. ADO can also be used to correct vertical defects caused by ankylosis and submergence of primary teeth retained in the absence of succedaneous teeth (Fig. 1). ADO is contraindicated in severe

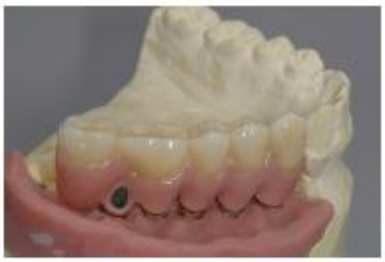

Fig. 5a. Completed bridge on master cast, buccal view.

Fig. 5b. Completed bridge in mouth, frontal view.

atrophy where there is insufficient bone to allow safe hardware placement between tooth roots and the floor of the nose, the maxillary sinus or the inferior alveolar nerve. It may also be contraindicated in cases of severe osteoporosis where bone quality is poor, or in patients who are unlikely to demonstrate compliance with the rigors of the distraction process. This latter requirement in an adolescent patient may be the most important. ADO is a labor intensive technique with a significant transitional morbidity. Bone grafts may greatly simplify treatment and should always be considered as an alternative in young patients.

The first step in ADO is to plan the vector of distraction. A distractor is chosen that is capable of delivering a force in the direction of the chosen vector. If teeth are available to anchor a distraction device then an external tooth-borne device can be chosen (Figs. 8a and 8b); otherwise, an internal bone-borne device must be selected. The effect of the rigid palatal tissues

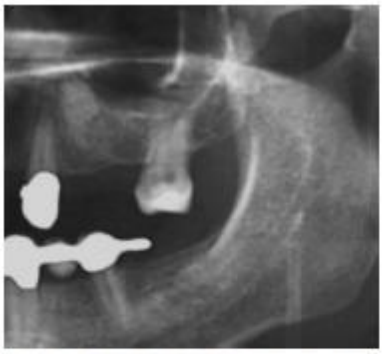

Fig. 6a. Radiographic appearance of left maxillary sinus before implant placement using osteotome technique.

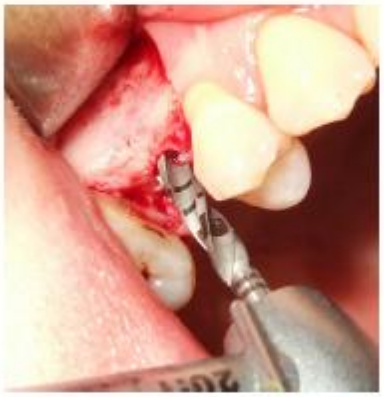

Fig. 6b. Implant osteotomy site prepared to allow entry of sinus elevator.

and the lingual tissues on the vector of distraction should be kept in mind when distracting the maxilla or mandible. Palatal tissues tend to exert pull on the distracting segment causing it to tilt lingually away from the desired vector.

An incision is made either in the vestibule or at the crest of the alveolar process, and a mucoperiosteal flap

Fig. 6c. Selection of sinus floor elevation instruments.

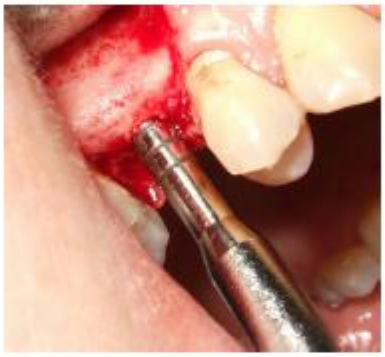

Fig. 6d. Sinus elevator inserted into implant osteotomy site. Manual pressure or malleting can be used to fracture the maxillary sinus floor.

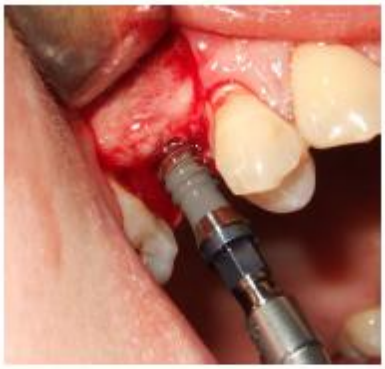

Fig. 6e. Implant inserted into elevated sinus floor site.

Fig. 6f. Lateral approach outlining window for open sinus floor augmentation.

is elevated. Vertical and horizontal osteotomies are performed through the labial or buccal cortical bone of the alveolus using a saw or a fine fissure bur (Figs. 8c–8e). The device is then attached to the teeth flanking the partially osteotomized segment (Figs. 8d and e). The osteotomies are then completed by extending the cuts through the palatal cortical bone using osteotomes, and the segment is mobilized (Fig. 8e) to ensure that there are no bony or dental interferences to unrestricted transport along the selected vector of distraction. The wound is then closed.

After a 5- to 7-day latency period the segment is distracted once or twice daily at a rate of 0.5–1.0 mm per day until the desired bony position is attained. Overdistraction of the segment by 1–2 mm may minimize relapse. A consolidation phase of 6–12 weeks with the distractor in place allows undisturbed healing of the distracted bone to occur. If teeth are present in a configuration which, when united by fixed orthodontic appliances, can facilitate stabilization of the segment, then the distractor can be removed. Fixed orthodontic appliances should be worn for the duration of the consolidation phase (Figs. 8f–8h). At some point following the consolidation phase, all metal distractors must be removed, unless they are resorbable.

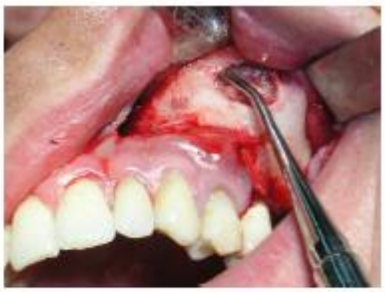

Fig. 6g. Lateral maxillary infracture to allow access for open sinus floor augmentation.

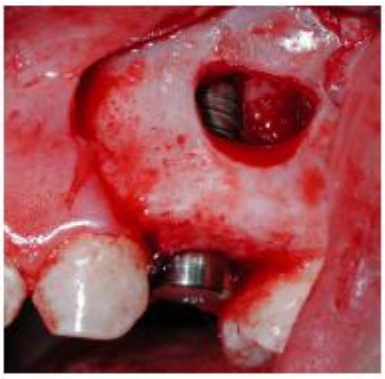

Fig. 6h. Insertion of a dental implant fixture at same surgery as sinus floor augmentation.

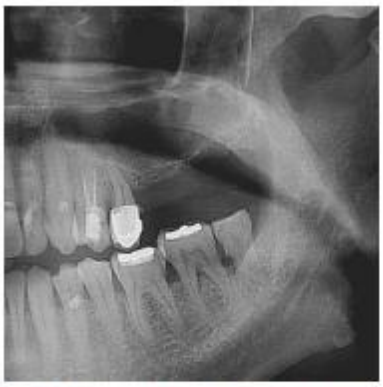

Fig. 6i. Preoperative orthopantomogram showing well pneumatized sinus where there was too little bone to allow closed sinus floor elevation.

If ankylosed teeth were used for anchorage of the distraction segment, they are extracted following the removal of the distraction hardware (Fig. 8h). Dental implants can then be placed into the distracted alveolar segment and restored in their new ideal position (Figs. 8i and j).

The distracting dental implant

There are clear advantages to having a device that can be used to correct a vertical bony defect by distraction osteogenesis and which can also serve as the anchor for a prosthesis following completion of the distraction. Such an intra-osseous, prosthetic distraction device with completely internalized components is presently in the preclinical stage of development (Figs. 8k and l). The distracting implant comprising a fixture connected to a footing by means of a retaining screw is placed within the bone. When the assembly is completely installed, the proximal surface of the footing bears against the bottom of the osteotomy. Following the completion of the distraction process, the distracting dental implant is used to support a dental prosthesis.

Guidance of implant placement

Although the distracting dental implant is a unidirectional distraction device, its trajectory can be guided to a certain extent using orthodontic forces or a prosthodontic docking station. A further consequence of the unidirectional nature of the distracting dental implant is that the vector of distraction will be defined primarily by the implant's longitudinal axis. To a certain extent, the geometry of the corticotomy can be designed to counter-pull from the lingual or palatal mucoperiosteum. As the trajectory of the distracting

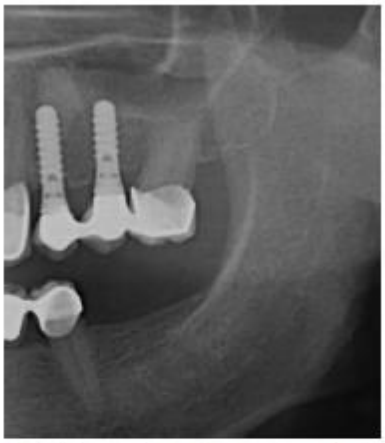

Fig. 6j. Post-operative orthopantomogram showing two implants inserted with a concurrent open sinus floor elevation and bone grafting.

Fig. 7a. Harvesting of a cortical strut of bone from the left lateral ramus of the mandible.

implant depends substantially on the vector of distraction, it is of critical importance to have control over the spatial location and axial inclination of the implant. An implant positioning device with the capability to control spatial location and axial inclination is currently under development.

Fig. 7b. Cortical bone graft perfect for lateral augmentation.

Fig. 7c. Cortical bone graft secured with two intraosseous screws. The graft will be covered by a resorbable membrane before flap closure.

Tissue engineering with growth factors BMPs and VEGF

With the constraints of both autogenous bone and allogeneic bone, scientists have focused on the fabrication of completely synthetic bioimplants. By the late 1980s the active factor responsible for the induction of bone was identified, bone morphogenetic protein (BMP). BMP is regarded as a morphogen, a protein that replicates the embryonic induction of bone formation (70). BMP can induce pluripotent mesenchymal stem cells to differentiate into bone-forming

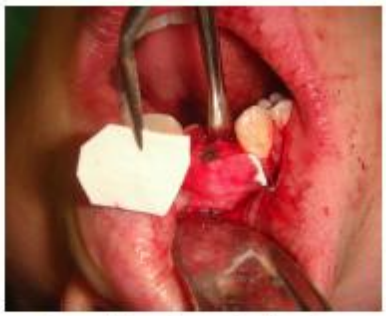

Fig. 7d. Resorbable membranes placed in two layers to cover particulate bone graft in lateral augmentation procedure.

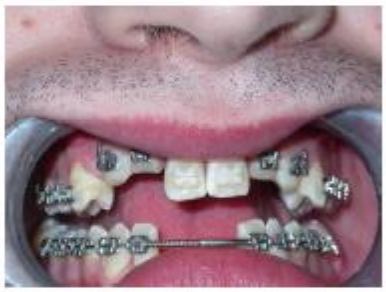

Fig. 8a. Oligodontia patient with ankylosed deciduous maxillary lateral incisors and canine teeth. Note the vertical hypodevelopment of the maxillary alveolus due to the ankylosed teeth.

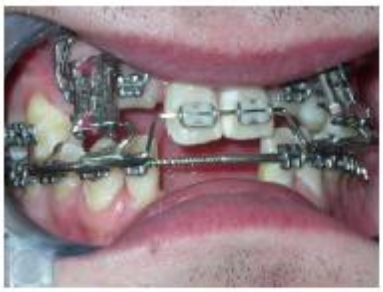

Fig. 8b. Distraction hardware attached to the ankylosed deciduous teeth bilaterally.

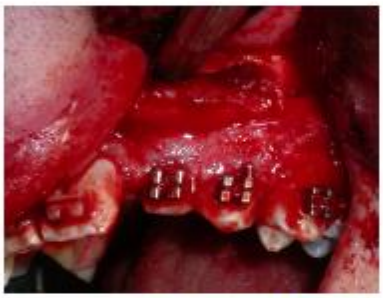

Fig. 8c. Hardware removed and segmental osteotomy performed bilaterally to enable a two tooth segment with the deciduous teeth to move downwards vertically.

osteoblasts. BMP-2, 4 and 7 have been shown to stimulate *de novo*, *in vitro* and *in vivo* bone formation in various animal models. Currently, there are many BMPs that have been isolated, and with the exception of BMP-1, they are all members of the TGF-β superfamily (71). In the early 1990s the ability to fabricate these proteins synthetically using recombinant technology was developed, and in 2006 this lead finally to the development products OP-1 (BMP-7; Stryker, Allendale, New Jersey, USA) and Infuse (BMP-2; Medtronic, Fridley, Minnesota, USA), both of which are now available for clinical use (19).

It has become apparent that one of the greatest challenges to the clinical application of BMP has been the identification of an acceptable carrier. Investigations of various delivery agents have identified certain ones as being more effective for the optimal clinical application of BMP. Over the past decade our group has explored the use of a reverse phase block medium as a carrier for BMP, and while others have struggled to achieve acceptable clinical results, our first BMP bioimplant was successfully made in 1999. Since that time our group has reconstructed ten human mandibular defects using bioimplants consisting of OP-1 (BMP-7; Stryker Biotech, Allendale, New Jersey,

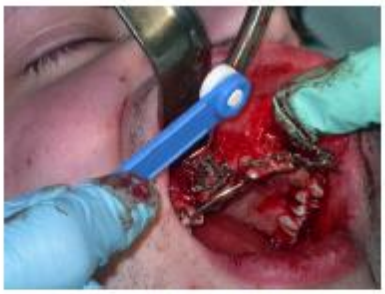

Fig. 8d. Hardware reattached and device is activated.

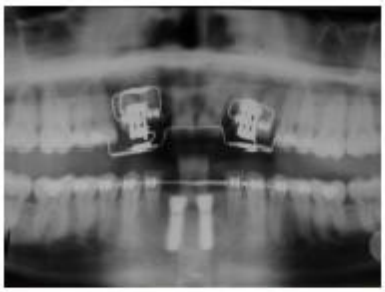

Fig. 8f. Immediate post-operative orthopantomogram.

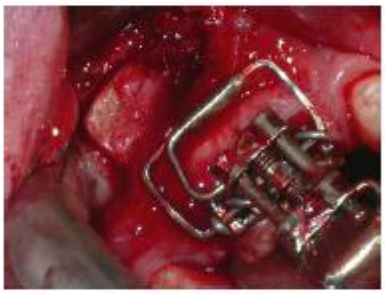

Fig. 8e. Note the gap between the distracted segment and the superior aspect of the maxilla.

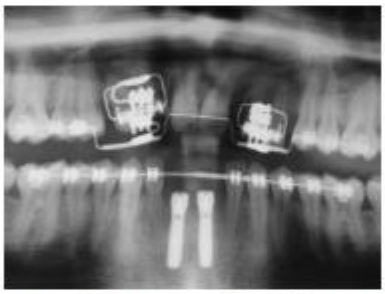

Fig. 8g. Orthopantomogram at the end of distraction.

USA) and DynaGraft Putty (DBM in a reverse phased medium; IsoTis, Irvine, California, USA) (20).

The BMP bioimplant was created by manually mixing BMP-7 (OP-1; Stryker Biotech, Allendale, New Jersey, USA) with 10 cc of DBM in a reverse phased medium (DynaGRaft Putty, IsoTis, Irvine, California, USA) and then molding it to form the shape of the resected segment of mandible (Figs. 9a–e). This was then inserted into the defect in the mandible and the muscular sling surrounding the mandible was re-approximated to ensure complete coverage of the bioimplant (Fig. 9e). The superficial tissues were then closed in a traditional fashion. Patients were carefully followed both clinically and radiographically to ensure proper integration of the bioimplant with the mandible (Fig. 9f).

Tissue engineering with stem cells and growth factors

Interdependency exists between adipogenesis, the formation of fat tissue from stem cells, and osteogenesis, the formation of bone from its stem cell precursors. Adipose-derived adult mesenchymal stem cells may be useful in future bone regeneration and tissue engineering efforts. We will now discusses possible future relationships between autogenous adipose-derived stem

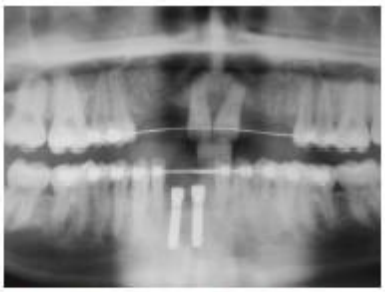

Fig. 8h. Orthopantomogram in retention phase following extraction of the expendable ankylosed deciduous teeth.

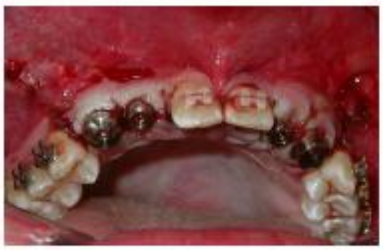

Fig. 8j. Implants placed at correct vertical level. Distraction osteogenesis offers a method to correct vertical alveolar discrepancies but in a labor intensive manner.

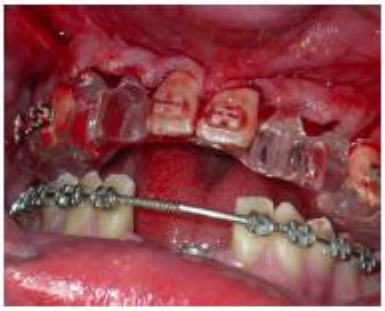

Fig. 8i. Stents to guide implant placement.

Fig. 8k. Distracting dental implant.

cells, growth factors and resorbable scaffolds in the context of future tissue engineering efforts.

The field of tissue engineering

Tissue engineering efforts include the vital collaboration between cell biologists, biochemists, material scientists, engineers and clinicians. In order to understand the complex role of the various components of tissue engineering, one can consider an equilateral triangle where stem cells, resorbable scaffolds and bioactive molecules such as growth factors continuously interact with each other (Fig. 3). It is the understanding of the nature of the interactions between these three key components that tissue engineering is built upon.

Sources of stem cells

The source of cells for tissue engineering depends on the structure that is to be replaced. Human embryonic stem cells (hESC) are pluripotent stem cells isolated from the inner mass of human blastocysts. While these cells have great potential due to their differentiation capacity, there are problems that must be solved prior

Fig. 8l. Distracting dental implant in series as it distracts.

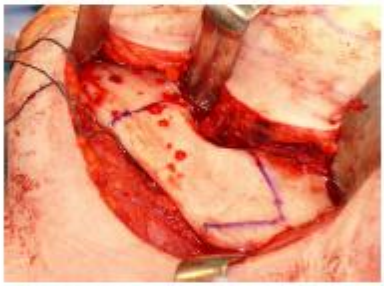

Fig. 9a. Mandibular resection to treat ameloblastoma.

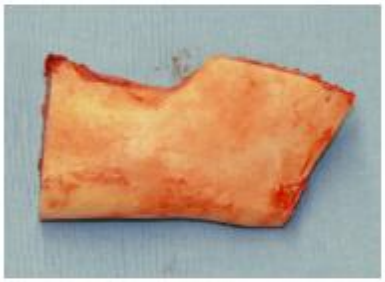

Fig. 9b. Resected mandibular fragment.

to their clinical use in tissue engineering. The problems with hESC include culturing hESC without exposure to animal proteins, avoidance of teratoma development and immune rejection by the recipient host (72). For the present time it is adult stem cells that are used clinically. Those cells with the lowest morbidity in harvesting and those that still retain a degree of pluripotentiality would be the most advantageous in the tissue engineering of bone, for example.

One source of mesenchymal stem cells (MSC) for bone regeneration is adipose tissue to provide adipose-derived stem cells (ASC). This should not be surprising as there is interdependency between adipogenesis and osteogenesis (73). Certainly the harvesting of adipose tissue is not morbid and may even be advantageous for some if liposuction were used as the harvesting method (Figs. 10a and b).

Stimulating stem cells

Using the tissue engineering model, autogenous ASCs could be harvested from a patient having a liposuction

Fig. 9c. Gap caused by resection is larger than a critical-sized defect and will not heal without some osteogenic intervention.

Fig. 9d. Demineralized bone matrix mixed with BMP-7 to form osteogenic bioimplants.

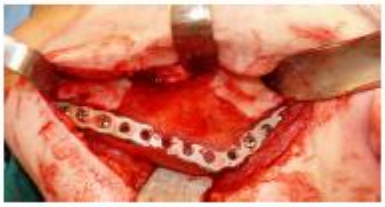

Fig. 9e. Construct placed into wound and surrounded by muscle tissue in the closure of the wound.

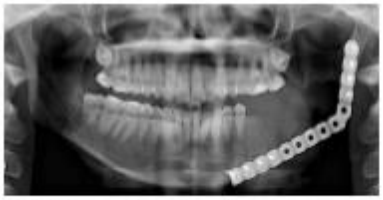

Fig. 9f. Post resection radiograph.

Fig. 10a. Liposuction is one convenient and minimally morbid way of harvesting adipose-derived stem cells for cell culturing and tissue engineering purposes.

procedure and used to seed a resorbable scaffold (74) which was made using CAD/CAM technology to the precise dimensions of a missing segment of bone, for example. The seeded cells could be stimulated by physical means using magnetic or galvanic stimulation, ultrasound, hypoxic or hyperoxic gradients (7) or growth factors such as TGF-β1 (75) or the BMPs (76) to guide the differentiation and growth of the cells. In some cases the surface configuration of a particular scaffold may stimulate stem cells to differentiate in a certain direction. Bioactive glasses, for example, are known to cause mesenchymal stem cells to differentiate into osteoblasts.

Manipulating the construct

Once the cells have populated the scaffold (Figs. 10c and d), the resulting bioimplant or construct could be transplanted into the patient to restore the defect. This *ex vivo* derived reconstruction has one major obstacle. The vitality of the bioimplant is entirely dependent upon the vascularity of the recipient bed. To this end,

Fig. 10b. Fat cells are isolated in the laboratory and mesenchymal stem cells are grown out in culture.

Fig. 10c. The appearance of adipose-derived stem cells grown in cell culture. These cells can be frozen for storage and later usage.

growth factors such as VEGF could be used to stimulate angiogenesis (10) to help vascularize the construct.

Future directions

Another source of stem cells could be from suction trap aspirates of bone during mandibular third molar removal (77,78). This technique would allow stem cell harvesting during one of the most common oral surgical procedures performed today. Third molar removal also presents some new opportunities. The removed developing third molar follicle can yield follicular cells, cementoblast-like cells and dental pulp

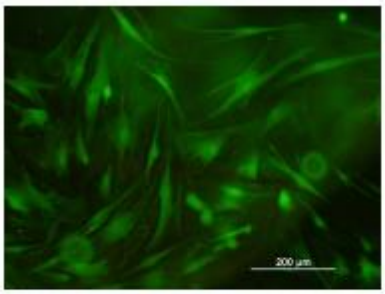

Fig. 10d. Live/dead staining of adipose stem cells attached onto a scaffold of resorbable biomaterial fibers (3 hour time point). Scale 200 µM. Green cells are viable.

stem cells which can also be cultured and studied. The receptors of these cells can be characterized and this is an important first step in the understanding of these cells and their possible future utilization.

Specifically difficult wounds

Maxillectomy cavities

The incidence of oral cancer increases with age in all parts of the world. In Western countries 98% of the patients are over 40 years of age (79). In high prevalence areas of the world many of the patients are less than 35 years of age owing to heavy usage of various forms of tobacco. There has been an alarming rise in the incidence of oral cancer during the last three decades particularly among younger men, and the trend appears to be continuing (79).

Squamous cell carcinoma of the oral cavity is rare in pediatric patients. The tongue and lower lip are the most frequently reported sites (80). In this chapter we illustrate a rare case of a squamous cell carcinoma of the maxillary gingiva in a 10-year-old female who was treated and reconstructed by a multidisciplinary team.

Such malignant tumors require clear surgical margins for survival. Maxillectomy defects often involve multiple missing teeth, alveolar bone, and attached and alveolar mucosa and may have large openings or fistulae connecting the mouth with the nasal cavity or maxillary sinus. Such wounds are challenging to manage.

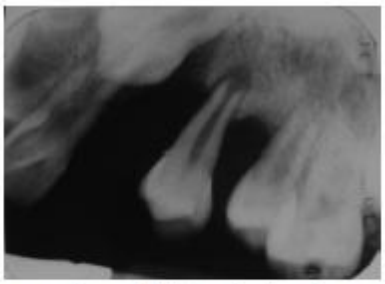

Fig. 11a. Ten-year-old female with radiographic image of aggressive bone destruction due to a squamous cell carcinoma of the maxillary alveolus.

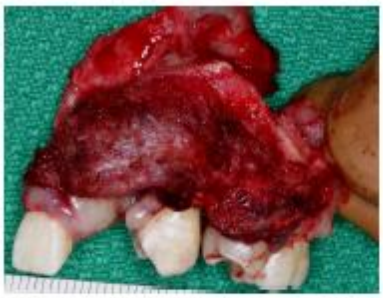

Fig. 11c. Maxillary resection specimen with clear margins resulting in large dentofacial defect with significant oral antral fistula.

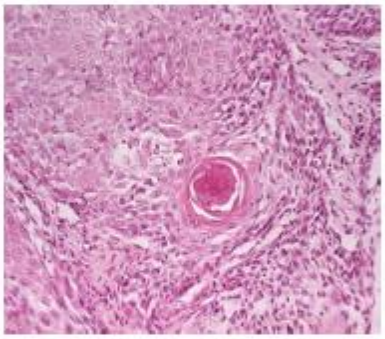

Fig. 11b. Histologic appearance of well differentiated squamous cell carcinoma.

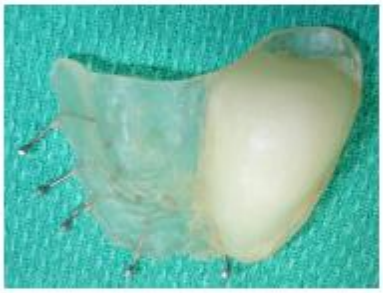

Fig. 11d. Temporary obturator made pre-operatively.

The management of a maxillectomy defect is illustrated in the following case of a 10-year-old female (Figs. 11a–g) who underwent a left partial maxillectomy via an intraoral approach with a left elective supraomohyoid neck dissection. 1 here > The intraoral defect was packed with iodine-impregnated gauze and immediately reconstructed with a prefabricated obturator which was secured in position using palatal screws (Fig. 11). The goal of the obturator was to allow healing of the tissues remaining in the maxillectomy defect by granulation or secondary intention. The obturator also minimizes the impact of large oronasal and oral antral fistulae by separating the oral and nasal cavities. This makes speech much more intelligible and aids in swallowing as well.

The surgical specimen demonstrated an invasive squamous cell carcinoma with negative margins. None of the lymph nodes from the neck dissection specimen showed any evidence of metastatic disease. The obturator and packing were removed 2 weeks post surgery and a hallow obturator ultimately bearing prosthetic teeth was inserted. Such obturators form the backbone of prosthetic reconstruction. Future options for the patient include prosthetic reconstruction versus a vascularized tissue transfer with dental implants. In the

Fig. 11e. Obturator inserted with iodine-impregnated gauze packing to obdurate oral antral fistula and encourage healing by secondary intention.

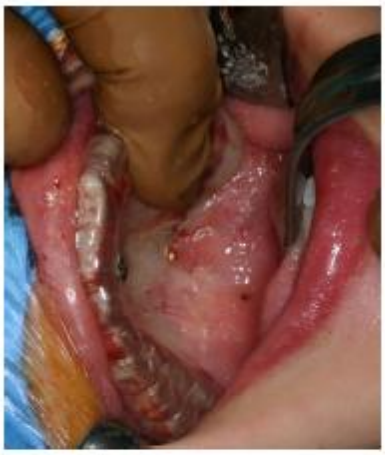

Fig. 11f. Obturator secured with palatal transosseous screw to retain obturator, facilitating swallowing without nasal regurgitation of food and making speech more intelligible.

long term the teeth adjacent to the borders of the resection are prone to periodontal tissue loss and failure.

Wound infections necrotizing fasciitis

Necrotizing fasciitis (NF) is a rapidly spreading life threatening infection involving the superficial fat and fascial layers with necrosis of the overlying skin. The lesion was first described during the American Civil War (81) and has been reported extensively in the general surgery literature. It is most common in the perineum, abdominal wall and extremities. It is most often seen in the elderly and immunocompromised patients (82). NF is less common in the head and neck, especially in the face. This rare infection (83) can result from dental (84–86), sinus (87), peritonsillar (88,89) and salivary gland (90) infections or secondary to surgery (91) or trauma (83). The causative agents have classically been described as group A beta-hemolytic streptococci and staphylococci, and also include obligate anaerobic bacteria (85,92). If not promptly recognized and treated the infection may spread into the deep spaces of the neck and compromise the airway, as well as spreading into the mediastinum, producing life-threatening sepsis. Such wounds require extreme measures.

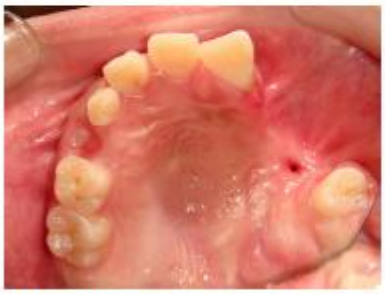

Fig. 11g. Maxillectomy defect in healed state with pinhole oral antral fistula.

The management of NF is illustrated by the following case: a 57-year-old female with a moderate right buccal space infection with right submandibular involvement secondary to grossly decayed tooth numbers 46 and 47. The parapharyngeal spaces were

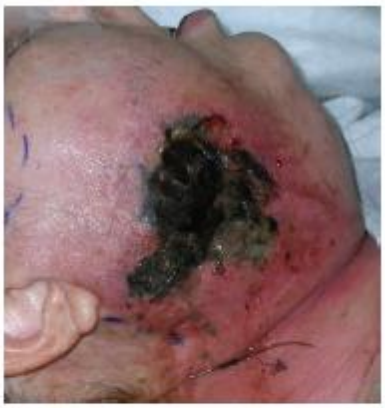

Fig. 12a. Patient with full-thickness necrosis of the cheek and initial extensive bullae and erythema from the zygomatic arch to the inferior border of the mandible.

clear and there was no airway compromise. The patient was admitted for intravenous antibiotics, observation and analgesia. Unfortunately on the night of her admission, she pulled out her intravenous catheter and discharged herself from the hospital against medical advice (AMA). Multiple attempts at contacting her were unsuccessful.

Five days later, she returned to the emergency department with marked deterioration. She appeared toxic, was febrile and tachycardic. There was a large necrotic region on the right cheek extending from the zygomatic arch superiorly to below the mandible inferiorly (Fig. 12a). There was severe right temporal, bilateral submandibular, cervical and floor of the mouth swelling.

The skin appeared grossly abnormal, with a spectrum of findings ranging from erythema, patchy areas of bullae to frank necrosis. There was marked crepitus noted from the zygomatic region to the laryngeal cartilages in the neck. The patient was taken to the operating room for immediate endotracheal intubation which was performed uneventfully. An emergent CT scan was obtained after the airway was secure and revealed the presence of severe subcutaneous gas formation and marked generalized head and neck edema (Fig. 12b).

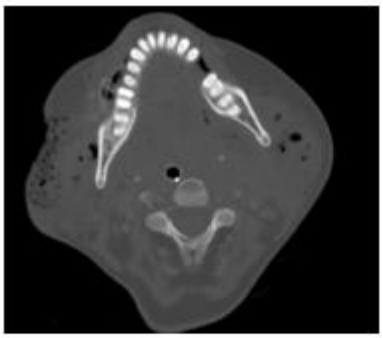

Fig. 12b. Pre-operative CT scan showing marked edema and extensive subcutaneous gas formation which is also present in the parotid gland bilaterally.

The patient was taken to the operating room where immediate complete debridement of all necrotic tissue was performed until bleeding tissue was encountered. The areas of debridement needed to be extended throughout the operation as the zones of involvement and necrosis were seen to extend and increase during the surgery (Figs. 12c and d). Clindamycin 900 mg iv q 8 h was started following an intra-operative infectious disease consultation. Exploration and decompression of all involved fascial spaces was also completed, and tooth numbers 46 and 47 were extracted. Multiple tissue samples were sent for culture, which later revealed the presence of a mixed infection, including *Streptococcus milleri*, coagulase negative *Staphylococcus* and anaerobic gram negative bacilli. The wound was packed with iodine gauze (Fig. 12e). Intra-operatively, the patient exhibited signs of septic shock with hemodynamic instability requiring inotropic agents to maintain her blood pressure. She was transferred to the intensive care unit (ICU) and remained intubated.

The patient stayed in the ICU for approximately 2 weeks. A total of six sessions of hyperbaric oxygen treatment (HBOT) were administered during the initial period in the ICU. Wound care in the form of frequent poviodine-soaked gauze changes and debridements of further necrotic tissue were performed. The patient was also taken to the operating room on one occasion for further debridement and partial

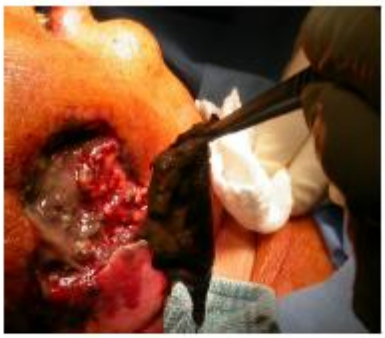

Fig. 12c. Necrotic tissue excised from the wound. The margins of the excision had to be extended several times at surgery as the lesion continued to spread intra-operatively.

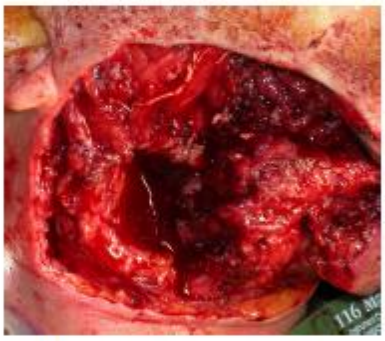

Fig. 12d. Post-operative defect after extensive resection of all necrotic tissues.

decortication of the now exposed surfaces of the mandible and zygoma. The mandible was covered using a split sternocleidomastoid muscle flap, and all teeth with questionable prognosis were extracted.

At a later date, when the wound bed was judged to be adequate (Fig. 12f), multiple strips of split thickness skin grafts were taken from the lateral thigh and grafted to the exposed areas to provide primary cutaneous coverage over the large exposed area left by the surgical debridements (Fig. 12g).

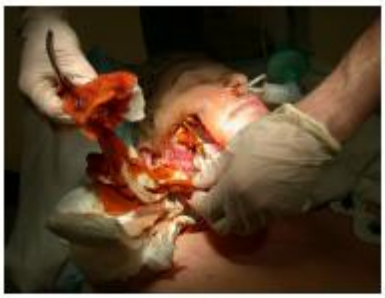

Fig. 12e. Wound managed using iodine-soaked gauze dressings.

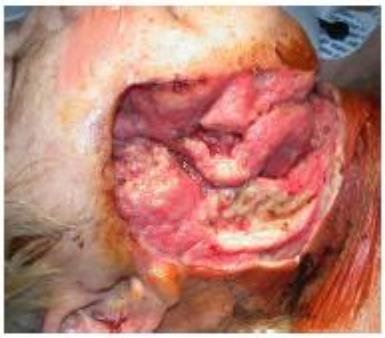

Fig. 12f. The appearance of fresh granulation tissue signals the improvement of the wound and its readiness for skin grafting.

At 6 weeks of follow-up, she remained asymptomatic with excellent skin coverage over her large wound (Figs. 12h–j) and good oral food intake. Definitive treatment to provide bulk and improved cosmesis in the form of further rotational or free vascularized flaps could be considered in the future.

Conclusions

Large dentoalveolar wounds can be difficult to manage. Surgeons have a number of reconstructive

Fig. 12g. Split thickness skin grafts with perforations placed over the resection defect.

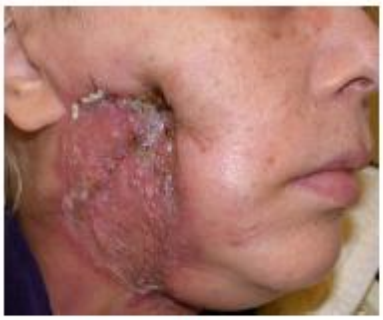

Fig. 12i. Healed skin grafts 4 weeks after resection.

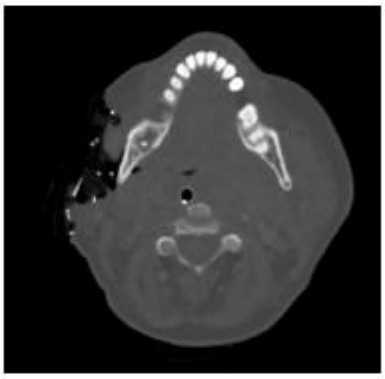

Fig. 12h. Post-operative CT scan showing resolution of the infection and the defect of the right face due to the resection of the necrotic tissue.

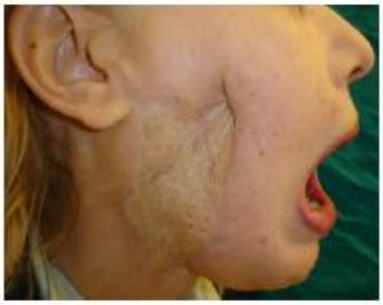

Fig. 12j. Healed skin grafts 12 months after placement. The loss of a great volume of tissue makes the defect more pronounced though the surrounding soft tissues have healed well despite the life-threatening infection.

choices such as autogenous bone grafts, vascularized bone grafts and alloplastic materials which depend on the condition of the wound and surrounding soft tissues. Surgeons can also augment the healing potential of large wounds by acute and chronic periosteal stretching, using growth factors and stem cells and by augmenting angiogenesis indirectly by the use of hyperbaric oxygen therapy.

While all these modalities are of interest, costs, access to the various treatment modalities and practicality are issues. Future surgeons will likely combine the useful features of all these modalities to simplify reconstructive, measures with the goal of making the reconstruction of dentofacial defects more predictable with less morbidity.

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