Immediate Molar Implant Placement

AN ACCELERATED PROTOCOL FOR MOLAR TOOTH REPLACEMENT

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INTRODUCTION

Replacing the "hopeless prognosis" molar with an implant is one of the most predictable treatments in dentistry today. Nonetheless, there are some significant barriers to overcome in such a treatment plan. Some of these are the number of steps required, the duration of healing time, and the overall cost. Implant placement immediately post-extraction has the potential to minimize these particular factors, resulting in a much more positive experience for the patient and practitioner alike when replacing a tooth with an implant.

Conventional implant treatment for an acutely infected molar typically requires the following: extraction of the tooth; up to a three week delay for complete resolution of any remaining infection; surgical re-entry for ridge preservation with particulate bone grafting and collagen membrane placement; a three to six month healing period to allow for sufficient bone regeneration; implant placement; an additional three to six month healing period to allow for sufficient osseointegration of the implant; and final attachment of the prosthesis to the osseointegrated fixture.[1] If any of these steps can be reduced or eliminated, there is an opportunity to streamline the treatment for the patient's benefit. Specifically with regards to distress caused by treatment, number of surgeries, healing time, and cost.

Immediate post-extraction implant placement is not a new concept and has been proven effective, as evidenced in the literature.[2-4] Certainly, the placement of an implant in single rooted teeth sockets is predictable with what can be considered a fairly simple protocol in the hands of any experienced implant dentist. Immediate implant placement in multi-rooted sockets, on the other hand, has proven to be less predictable due to the amount of boney deficiency innate in this type of placement. Add to this bone loss from granulomas, radicular cysts, or frank infections and one can quickly see how challenging this type of procedure can be.

Predictable molar implant placement, as described in this article, relies on the principles of osteogenesis upregulation through the use of growth factors and particulate allografts. This particular method is comprised of the following steps: extraction of the tooth; immediate implant placement combined with a particulate bone graft as well as plasma rich in growth factors (PRGF); three to six months of healing; and finally, attachment of the prosthesis.[1]

By administering growth factors that promote the process of bone regeneration, it is reasonable to predict increased bone growth with the use of PRGF. It is not the physiological mechanism of bone regeneration itself that is being accelerated, but rather the treatment protocol that can be streamlined to allow for the implant to be placed immediately post-extraction. These growth factors activate osteoblast and osteoclast activity, allowing for de novo bone formation within bony deficiencies that in turn helps to anchor the implant in place.[5-8] By promoting

bone growth concurrently with implant placement, it would hypothetically no longer be necessary to have healing time between the bone graft and placement of the implant as prescribed by the conventional treatment protocol. The conventional approach results in treatment time of up to or beyond one year,[1] whereas the proposed immediate implant placement with particulate bone graft and PRGF can be completed in as little as three months. The predictable bone growth promoted by the administration of endogenous growth factors allows for this accelerated treatment to be carried out with confidence.

As mentioned above, the process of bone regeneration needs to be activated for this accelerated approach to be successful. As blood plasma contains many of the growth factors and elements responsible for this,[9] separating blood into its different components is integral to this process. First the blood must be drawn from the patient with a standard phlebotomy technique. Once spun in a centrifuge, the blood separates into three distinct parts from top to bottom: plasma, a buffy coat containing leukocytes, and erythrocytes.[5,9] The plasma is then further separated into three fractions from top to bottom: fraction 1 (F1), or the fibrin-rich layer; fraction 2 (F2), or the fibrin-poor layer; and fraction 3 (F3), or the growth factor rich layer.[9,10]

Key growth factors include bone-morphogenic protein (BMP), transforming growth factor beta (TGF-ß), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF).[5-10] Each of these growth factors plays a role in the activation of mechanisms involved with increasing bone growth quantity and quality. Such mechanisms include promoting the differentiation of osteoblasts and osteoclasts as well as their activity,[5-10] thereby increasing bone turnover and reducing the overall treatment time required to complete a case. The effects of these growth factors are explained below.

Bone-Morphogenic Protein

Bone-morphogenic protein (BMP) is a growth factor that plays a key role in the differentiation of mesenchymal stem cells into osteoblasts.[6,11] Mesenchymal stem cells have the ability to differentiate into a variety of cell types, including osteogenic, myogenic, adipogenic and chondrogenic cell lineages.[12] Based on the presence of specific transcription factors and morphogenetic signals, mesenchymal stem cells will proceed to differentiate into one of the above mentioned cell types.[12] BMP's promote differentiation from mesenchymal stem cells into the osteoblastic lineage.[6,7,11,12] These growth factors are a part of the transforming growth factor-beta (TGF-ß) superfamily of proteins, with both sharing osteoinductive properties.[6,13] BMP's rely on the SMAD signaling pathway to encourage the differentiation of mesenchymal stem cells.[7,14] Through phosphorylation, BMP's activate SMAD proteins, which then regulate the expression of transcription factors and co-activators responsible for osteoblast differentiation.[6,7,13,14] One such transcription factor is core-binding factor subunit alpha-1 (Cbfa-1),[11,15] otherwise known as runt-related transcription factor 2 (RUNX2); this transcription factor has been found to be crucial in the downstream activation of osteoblast differentiation.[16,17] Cbfa-1/RUNX2 induces mesenchymal stem cells to differentiate into osteoprogenitor cells and further to immature osteoblasts, while also inhibiting differentiation into adipogenic or chondrogenic lineages;[16] Cbfa-1/RUNX2 alone cannot yield fully functional and mature osteoblasts. Other growth factors are believed to then induce the maturation of these osteoblasts.[18]

Although a viable option, the use of RH-BMP is an extreme technique and practitioner-sensitive treatment protocol

Recombinant human-BMP (RH-BMP) has been found to help promote desirable bone regeneration in implant surgery post-placement, and has been used adjunctively with PRGF.[12] RH-BMP targets the osteogenic process at a higher level than PRGF; as mentioned above, it helps undifferentiated mesenchymal stem cells to differentiate into osteoprogenitor cells and then further into osteoblasts.[12,13] In contrast, PRGF targets this process further downstream, by activating osteoblastic and osteoclastic activity.[5] In theory, RH-BMP is a more desirable activator, but the difficulty of its use clinically remains a hindrance. Although a viable option, the use of RH-BMP is an extreme technique and practitioner-sensitive treatment protocol. RH-BMP is administered via an absorbable collagen sponge that gradually releases the growth factor into the surgical site.[19] The

key complication of this method is the requirement of a space maintenance mechanism, which is necessary to uphold the integrity of the sponge and to prevent the outflow of the RH-BMP stored within it. The RH-BMP soaked sponge is thus secured via a titanium mesh that must be molded and fastened over the surgical site by the clinician.[19] The surrounding tissue is then stretched over the titanium mesh and sutured overtop.[19] This proves to provide difficulty in healing, as routine patient activity results in stress on the surgical site, causing dehiscence and harmful disruption of the area. This, along with the complexity of the construction of the titanium mesh mechanism onto the surgical site, causes PRGF to be preferred to RH-BMP in practice. In comparison, the xenograft membrane that comprises the buccal-most component of the bone graft in the proposed treatment provides innate space maintenance,[1] eliminating the need for further surgical intervention as is required by the RH-BMP soaked sponge to uphold its integrity.

Insulin-like Growth Factor

Insulin-like Growth Factor (IGF), like BMP, has also been found to promote the late-stage differentiation of osteoblasts from osteoprogenitor cells.[6,20] IGF has also been found to stimulate type I collagen synthesis and inhibit collagen degradation;[20,21] type I collagen is the primary component of osteoid, the unmineralized, organic compound released by osteoblasts prior to the maturation of osseous tissue.[20,21] Once mineralized, osteoid becomes new bone tissue. Therefore, IGFs key a key role in the regulation of the ossification process and in turn, the osseointegration of an implant. By promoting osteogenic properties in cases with significant bone loss, it is possible for an immediate implant placement treatment to be successfully performed.

Vascular Endothelial Growth Factor

Vascular Endothelial Growth Factor (VEGF) plays a large role in the survival of osteoblasts during ossification. VEGF is responsible for initiating angiogenesis via endothelial cell proliferation and recruitment.[22,23] In this process, endothelial cells are stimulated to proliferate and develop capillaries in newly formed osteoblasts by infiltrating the extracellular matrix.[22] These capillaries provide blood supply to the osteoblasts, and thus oxygen and nutrients for bone cells. VEGF is therefore crucial to the survival and ossification activity of osteoblasts. VEGF is a subfamily of growth factors belonging to a larger subset called platelet-derived growth factors (PDGF).[8] PDGF also plays a large role in angiogenesis and blood vessel formation, while also being responsible for the proliferation and migration of other cells involved in wound healing.[8,23] One such cell type is osteoblasts,[8] and thus PDGF also promotes ossification and plays a role in initiating substantial bone tissue formation immediately post-implant placement in the proposed treatment protocol.

By homeostatically regulating osteoblast and osteoclast activity, RANKL, IL-1 and IL-6 promote osseous tissue turnover and necessary bone regeneration

Cytokines

Ossification and osseous tissue turnover is a homeostatic mechanism; osteoblasts help to build new osseous tissue while osteoclasts resorb it, allowing for new tissue to be built up again.[24] This process is regulated by parathyroid hormone (PTH) in response to low serum calcium levels.[24] Osteoblasts and osteoclasts also secrete homeostatic elements that aid in the maintenance of a consistent blood calcium concentration. When bone metabolism is initiated to begin turnover, the cytokine known as receptor activator of nuclear factor kappa-B ligand (RANKL) is secreted by osteoblasts;[25,26] RANKL is an osteoclast differentiation factor, and thus encourages osteoclastogensis and helps initiate osteoclast activity.[25,26] Via a similar mechanism, interleukin-6 (IL-6) is another cytokine secreted by osteoblasts to promote osteoclast differentiation and activity.[27,28] Interleukin-1 (IL-1) also has similar osteoclast differentiation and activation effects.[29,30] By homeostatically regulating osteoblast and osteoclast activity, RANKL, IL-1 and IL-6 promote osseous tissue turnover and necessary bone regeneration.

Fibrin

Fibrin is important in relation to immediate molar implant placement surgery as it plays a key role processes such as wound healing and maintenance of the healing area.[31] In this treatment, a fibrin membrane is created by activating the F1 plasma layer with calcium chloride.[1] This membrane acts as a matrix for progenitor cells and upholds a regenerative boundary to ensure tissue turnover does not undesirably spread to areas beyond

the surgical site.[1,31] Secondly, the fibrin scaffold also contains activated platelets that further promote the release of growth factors involved in increasing bone regeneration.[32] Due to its osteoconductive and wound-healing properties,[9] fibrin has been used to seal surgical sites in a variety of medical fields, including oral surgery. It promotes the epithelialization of the affected area and thus encourages successful healing of surgical sites.

As can be seen, all the above elements play a crucial role in promoting bone regeneration, and subsequently implant osseointegration. By activating osteogenic mechanisms, it is possible to stimulate bone regeneration around the placed implant and effectively reduce the number of surgical procedures required to successfully complete an implant case. In turn, the overall impact on the patient is favourable, as both cost and treatment time are reduced.

Bone Grafts

There are three types of bone grafts that are used in dentoalveolar surgery to stimulate de novo bone turnover.[33] The first is an autograft, which is a graft of bone taken from the patient to whom the graft will be given.[34] This type of graft often originates from non-essential areas, and in conventional implant surgery is often taken from the chin, hip or sternum.[35] This can be a painful and invasive method of obtaining an autograft; in the proposed immediate placement protocol, the autograft is often taken from the interseptal bone remaining in the empty socket post-extraction. This prevents the need for a second surgical site, and can thus be seen as favourable for the patient. Autografts are found to be osteoconductive, osteoinductive and osteogenic, meaning they can contribute to de novo bone growth via osteoblast activity.[34] The second type of bone graft is an allograft, which although still originates from human bone, is collected from an individual other than the patient to whom the graft will be given.[33] The type of allograft used in the proposed protocol is freeze-dried bone allograft (FDBA).[1] Allografts are osteoconductive and lack osteogenic properties, and their osteoinductive ability is currently under debate.[36] Finally, the third type of bone graft is a xenograft. Xenografts are harvested from non-human species; in this case, the most common type of xenograft is bovine.[37,38] Xenografts are osteoconductive, and simply provide a scaffold for bone growth.[38]

CASE REPORT

History and Initial Presentation:

A 58-year-old healthy female presented to the office with dislodged #16 post, core and crown. Upon radiographic evaluation, it was noted that #16 had been previously root canal treated with mesial root apical surgery. After examination, it was determined that #16 was non-restorable for long-term predictability.

Diagnosis and Treatment Plan:

Tooth #16 was found to be beyond salvaging, and a decision was made based on the evidence provided to extract the tooth. As was outlined earlier, the conventional implant treatment was possible, but immediate molar implant placement was preferred due to its vast benefits. Taking into consideration the aggregate impact on the patient was a strong factor in proceeding with this preferred treatment. In this case, the following treatment plan was recommended:[1]

- Extraction of tooth #16; followed by
- Immediate implant placement; with
- A particulate bone graft as well as PRGF

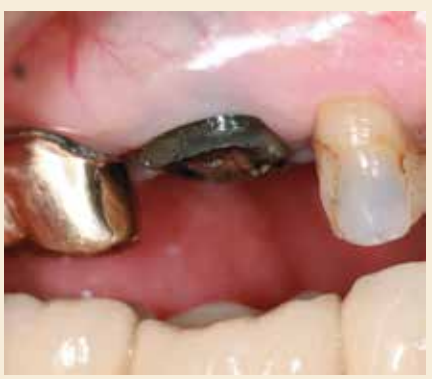

FIGURE 1—Initial presentation of patient with dislodged #16 post, core and crown.

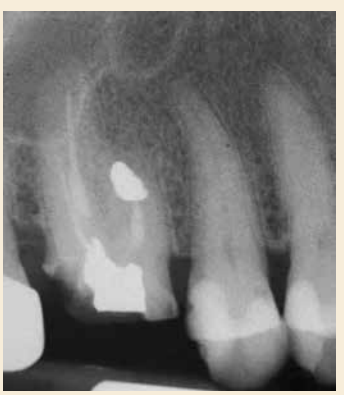

FIGURE 2—Radiograph of tooth #16 at initial presentation.

FIGURE 3—Standard phlebotomy kit used for blood draw.

This treatment plan would significantly reduce treatment time, the number of surgical procedures required, the distress caused to the patient's oral cavity and the overall cost to the patient. It should be noted that the case was completed within three months, compared to cases where the conventional treatment plan could be used that would require treatment time of up to or beyond one year.

Surgical and Restorative Procedure:
Immediate molar implant placement was determined to be the best clinical approach to resolve this case. In order to obtain the PRGF that would be used to upregulate osteoinductive processes, a phlebotomy kit was used for a blood draw. Once the autologous blood was drawn from the patient, it was placed in a centrifuge to be spun. The resul-

FIGURE 4—Centrifuge used to spin and separate blood into fractions.

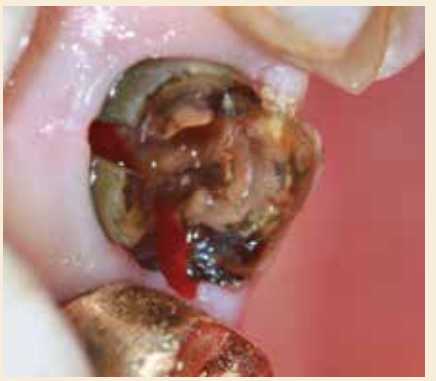

FIGURE 5—Sectioning of roots of tooth #16.

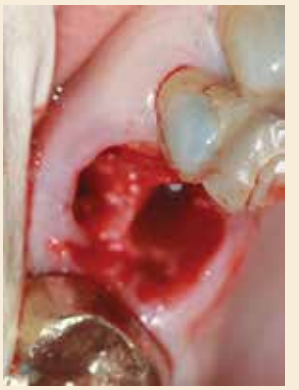

FIGURE 6—Interseptal bone reveal in empty socket post-extraction.

tant sample tube revealed three separated strata of blood, of which the uppermost was blood plasma. The autologous plasma was further separated into three fractions: F1 (fibrin-rich), F2 (fibrin-poor), F3 (growth-factor rich). The three resultant fractions of plasma were each delicately pipetted out of the sample tube and into individual, sterilized glass containers, as to separate and prepare the fractions for use. Special care was taken not to include the leukocyte-containing buffy coat when extracting F3 located right above.

The procedure began with sectioning the roots of tooth #16; this technique allowed for the least amount of disruption of the alveolar bone that houses the roots. Once tooth #16 was intricately removed, an empty socket remained revealing significant bone loss and large bony deficiencies on both buccal and palatal sides. An osteotomy was created in the exposed interseptal bone, and was consequently enlarged to prepare for implant placement. Once interseptal bone expansion was completed, the sinus floor was apically condensed with an osteotome to prevent sinus inva-

FIGURE 7—Osteotomy being created in interseptal bone.

FIGURE 8—Successive enlargement of osteotomy.

FIGURE 9—Apically sinus floor being condensed with osteotome.

sion by the implant. The surgical site was then deemed primed for implant placement.

A BioHorizons Tapered Internal LaserLok 5.8 by 10.5mm implant (TLR5810) was prepared for placement through bioactivation of its surface with the previously obtained F3 growth factor rich layer. The implant was placed and a final torque value was tested to be greater than 40 Ncm. Mineross (BioHorizons) cortico-cancellous freeze-dried bone allograft (FDBA) was also placed in the F3 growth factor rich layer and employed to fill the bony deficiencies around the placed implant. Bio-oss (Geistlich) was subsequently added to the F2 plasma layer and activated with calcium chloride to form a mineralized xenograft in a biologically active carrier. This resultant xenograft was placed and comprised the buccal-most layer of the bone graft; this stimulated bone regeneration while preventing soft tissue invasion.[1]

Next, the F1 fibrin-rich layer was activated with calcium chloride to form an F1 plasma membrane. The healing abutment was then secured to the implant with the F1 plasma membrane placed over top, completing the "socket seal." As was previously mentioned, the F1 fibrin-rich layer encourages wound healing and recruitment of necessary clotting factors. F1 plasma components also encourage epithelial creep over top of the membrane, resulting in robust soft tissue growth and excellent implant emergence profile without soft tissue invasion of the composite graft. The tissue was then approximated and sutured with a 4.0 chrome gut suture. F3 growth factors were then injected into the surgical site to promote substantial osseointegration. Standard antibiotic and analgesic regimens were then prescribed for the patient.

Post-Operative Assessment and Result:
Radiograph was taken immediately post-surgery and showed successful placement of the implant. Patient was reexamined 10 days post-operatively; sutures were removed and the surgical site showed desirable soft tissue healing and preliminary epithelial creep over the socket was

FIGURE 10—Bioactivation of implant surface with F3 growth factor rich layer.

FIGURE 11—Final torque value of implant tested to be greater than 40Ncm.

FIGURE 12—Final placement showing parallelism and depth of implant.

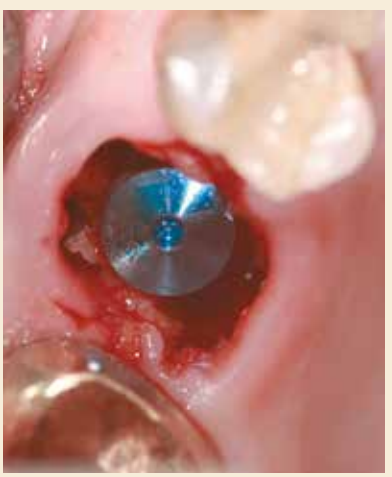

FIGURE 13—BioHorizons Tapered Internal LaserLok Implant 5.8mm x 10.5mm with large bony deficiencies on buccal and palatal sides.

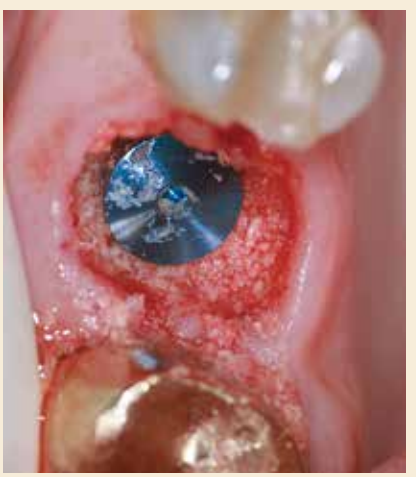

FIGURE 14—FDBA placed to fill bony deficiencies.

FIGURE 15—Activated F2 plasma portion with mineralized xenograft embedded.

recorded as well. Three months post-operatively, excellent soft tissue collar formation was noted following removal of the healing abutment. Complete soft tissue maturation was recorded, and the implant was torque tested to be greater than 40 Ncm, indicating strong osseointegration. It should be noted that after only three months, significant bone integration and soft tissue maturation was present, and the case was able to proceed. At this point, an impression was taken using polyvinyl siloxane (PVS) material and was sent to the laboratory for processing. One week post-impression, the final implant crown was inserted and desirable results were achieved. Furthermore, at one-year follow up appointment, results had been maintained and implant was optimally and successfully osseointegrated.

DISCUSSION

As outlined above, this case was positively influenced by the use of PRGF. The growth factors harvested from the autologous blood of the patient activate mechanisms that allow for immediate molar implant placement to be a viable treatment option in cases with extensive bone loss. Based on thoroughly examined effects of specific growth factors and their upregulation of already present processes, it is now possible to place implants immediately post-extraction in such cases. The key desirable result in administering the growth factors is increased bone tissue formation; as the prescribed protocol is based on the activation of osteoblastic and osteoclastic activity, the result is osteogenesis and de novo bone formation. This allows for the treatment plan to be streamlined, as osteogenesis is stimulated immediately post-placement. As was mentioned above, this eliminates the necessity of a healing period between the transplantation of the bone graft and placement of the implant. Naturally, this would be in the best interest of the patient as cost and treatment

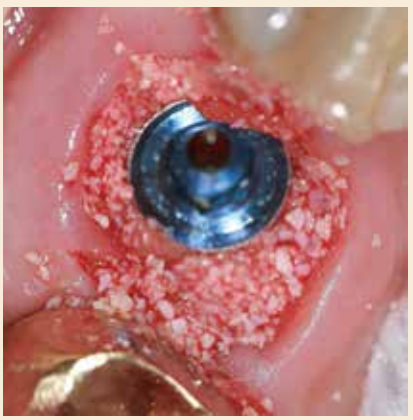

FIGURE 16—F2-xenograft layer placed most buccally.

FIGURE 17—Activated F1 fibrin membrane "skewered" on the end of the healing abutment.

FIGURE 18—Healing abutment secured to implant with F1 membrane in place, completing "socket seal".

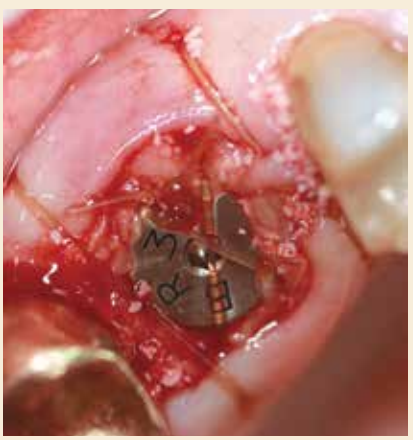

FIGURE 19—Soft tissue approximated and sutured with 4.0 chrome gut suture.

FIGURE 20—F3 growth factors to be injected into surgical site.

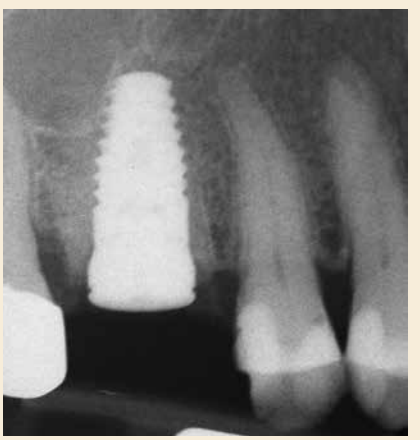

FIGURE 21—Radiograph taken immediately post-surgery.

FIGURE 22—Healing of surgical site 10 days post-operatively.

FIGURE 23—Healing of surgical site three months post-operatively. Note excellent soft-tissue collar formation.

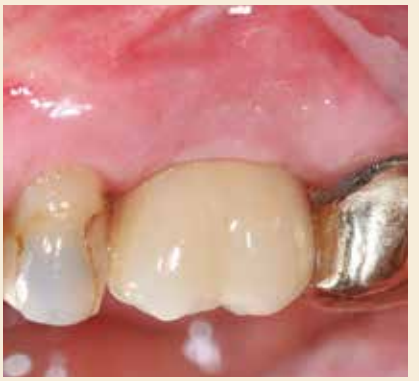

FIGURE 24—Final crown placement.

time can both be reduced without increasing morbidity or risk. This treatment protocol can be carried out with confidence, as the processes being promoted are already initiated during the healing period post-intervention. Based on this, the proposed treatment is much more predictable in practice compared to the RH-BMP method mentioned earlier that is based on driving undifferentiated mesenchymal stem cells into specific cell lineages. Although RH-BMP promotes bone formation at a higher level than PRGF, PRGF yields superior and more consistent clinical results.

The case outlined in this article is an example of just one of the many cases that have been resolved using this treatment plan. Placement of an implant immediately post-extraction is not a novel procedure, but being able to do so with large-scale bone recession is very promising. This procedure can be viewed as a discernable improvement on the conventional treatment as it brings several tangible benefits without carrying any drawbacks in comparison. By exposing the surgical site to increased amounts of IGF, VEGF, cytokines and fibrin in conjunction with the osteoinductive nature of the particulate allograft, it is possible to jumpstart the osseous tissue turnover that is necessary to yield success in cases such as these. IGF stimulates the formation of the building blocks of osseous tissue in the form of collagen,[20,21] while VEGF cause endothelial cell proliferation resulting the formation of capillaries in osteoblasts.[22,23] These two processes are integral to bone tissue survival and regeneration, and are both activated when PRGF is administered. Prior to final placement, the implant is also coated with PRGF to bioactivate its surface;[9] it is surmised that this has a positive effect on the osseointegration of the implant. Although the exclusive impact of this particular step cannot be isolated, final torque values taken three and six months post-placement demonstrate clear and robust osseointegration of the implant.

Placement of an implant immediately post-extraction is not a novel procedure, but being able to do so with large-scale bone recession is very promising

This accelerated treatment plan should be fairly straightforward for experienced implant specialists to master and implement. Although some aspects of the methodology may be unfamiliar, it is a logical and systematic treatment protocol to follow. Benefits are wide-ranging and impact both the clinician and patient. Results have shown this to be the most superior tooth replacement treatment protocol, compared to conventional implant placement techniques and other growth factor based treatments. One such novel technique has been branded the "platinum standard" of care; the crux of this treatment protocol is harvesting and grafting autogenous bone marrow aspirate as an alternative to a conventional autograft sites.[39] Autogenous bone marrow aspirate provides an abundance of adult stem cells and growth factors involved in osteogenesis.[39] It can be harvested with minimal morbidity from one of three areas: anterior iliac crest, posterior ilium and the sternum.[39] Although excit-

ing, this treatment protocol has not been sufficiently examined but does appear to be exciting. Further examination would be necessary to determine the true efficacy of this procedure as well as its clinical consequence in comparison to the use of PRGF.

CONCLUSION

Overall, this case was a success from both a clinician and patient standpoint. From a clinician's perspective, the use of PRGF upregulated osteogenesis and promoted robust bone regeneration in a socket with extensive bony deficiencies. This allowed for the implant to immediately placed with the predictable knowledge that there would be sufficient osseous tissue turnover to further anchor implant. At three, six and 12 month post-operative appointments, implant was examined and torque tested to reveal desirable healing and osseointegration. With regards to the patient, the healing time for this case was substantially reduced to three months, with both cost and the number of procedures required to complete the case being reduced. The final result was an aesthetically pleasing and well-integrated implant with a completely healed surgical site with no complications. The use of PRGF along with the particulate allograft yielded clear benefits compared to the conventional treatment.

Aiming to minimize the impact such a procedure would have on a patient is the true crux of this proposed treatment protocol. Having a patient-centered approach is important in clinical dentistry, and being able to recognize the opportunity to provide the absolute highest standard of care to patients is crucial to being a successful clinician. As was discussed in this article, there are other treatment options available to replace a tooth with a hopeless prognosis. The use of RH-BMP to stimulate osteoblast differentiation from mesenchymal stem cells is highly technique sensitive and therefore may yield inconsistent results in a clinical setting. Secondly, introduction of autogenous bone marrow aspirate into the surgical site provides an exciting avenue to research but needs to be more extensively investigated as to determine its efficacy in practice. Overall, the use of PRGF with a particulate allograft yields the most consistent and desirable results while requiring a more reasonable level of expertise. The key mark that this treatment protocol can be carried out with confidence lies in its activation of

already occurring processes, due to the osteoconductive, osteoinductive and osteogenic properties of the different bone grafts used throughout the procedure. The future is bright in this field of research, and is well on the path to absolute regeneration of teeth. Until complete tooth regeneration comes to fruition, this treatment protocol provides the best opportunity for success when immediately placing an implant in cases with significant bone regression. **OH**

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Oral Health welcomes this original article.

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