Biphasic Calcium Sulfate as an Alternative Grafting Material in Various Dental Applications

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Various grafting materials have been used in oral and periodontal surgeries to augment and rebuild bone intraorally. Calcium sulfate, a synthetic material, also known as an alloplast, has been used for decades in orthopedics, plastic surgery, and oncologic and maxillofacial surgeries for the treatment of osseous deficiencies caused by trauma or inflammation. Biphasic calcium sulfate provides benefits as a short-term space maintainer. Use of biphasic calcium sulfate as the sole material are limited to relatively small osseous defects surrounded by at least 3 bony walls (eg, extraction sockets). Thus, for augmenting large and more complex bone deficiencies Bond Apatite, a composite graft formulation, is indicated. This work will review the various clinical applications of Bond Apatite as an alternative to other graft materials.

Key Words: biphasic calcium sulfate, graft, sinus augmentation, socket preservation, ridge augmentation

INTRODUCTION

Literature supports that when performing socket preservations with grafting materials, the crestal bone levels are maintained at a higher level than those where socket grafting was not performed.[1,2] Alveolar resorption is a long-considered unavoidable consequence of tooth extraction and may be a significant problem in restorative and implant dentistry. It has been found that post–extraction maintenance of the socket minimizes residual ridge resorption whether or not an implant is planned. The use of osseous graft materials and guided bone regeneration have demonstrated enhancement of socket healing by potentially modifying the resorption process. Therefore, providing maintenance of the crestal bone and limiting bone width and height resorption during healing leads to improved socket preservation.[3] In uncomplicated extraction sockets, volumetric bone loss after 2 years may reach 60% in the absence of socket grafting; thus, compromising future implant placement.[4]

Various osseous graft materials are available today for dental applications. Included are those from human host origin (autografts), human cadaver origin (allografts), other species (equine, porcine, or bovine), and synthetic materials (alloplasts). They all require coverage by a membrane at the time of placement and for an extended portion of the healing period in order to prevent soft tissue ingrowth into the augmented site. Allografts are widely used but often involve a cumbersome placement technique, potential risk (albeit limited) of disease transmission, patient reluctance to have another individual's cadaver bone implanted, and financial cost, which can be a limiting factors for use. Autogenous bone is an alternative treatment option. The source can be intraoral or extraoral in origin. However, there may be limited available donor site bone with an inadequate volume for a large defect that needs to be grafted. Additionally, harvesting of donor bone may be associated with morbidity at the second surgical site (donor site) and may not be accepted by the patient.

The most common type of xenograft in the United States is bovine in origin. Xenograft use eliminates some negatives of allografts and autografts. However, xenografts are reported not to fully resorb and to be replaced by de novo bone over time. Residual particles are routinely found remaining 5 years or more following placement. Xenografts also require membrane coverage, and bovine materials have the potential risk of disease transmission.[5] This is of concern when placing an implant into the site which has been grafted with a xenograft as there is a decrease in the bone-to-implant contact due to the remaining residual xenograft particles at the implant bone interface.

To compensate for the various disadvantages mentioned for these graft types, some synthetic graft materials (alloplasts) offer a fully resorbable state and have no related disease transmission potential.

Calcium sulfate as a synthetic graft material has been used for decades in orthopedics, plastic surgery, and oncologic and maxillofacial surgeries in the treatment of osseous voids and traumatic or inflammatory bone deficiencies. Dreesman in 1892,[6] reported the osteogenic potential of calcium sulfate as a bone graft substitute, applying it orthopedically to treat traumatic and tuberous bone deficits. However, in 1961 Peltier[7] conducted a thorough literature review of osseous defects treated with calcium sulfate and reported only sporadic successful outcomes. According to Thomas and Puleo,[8] Thomas et al,[9] Pietrzak and Ronk,[10] Ricci et al,[11] Boden and Stevenson,[12] and Tay et al[13] calcium sulphate has been consistently found to be highly biocompatible, osteoconductive, and easy to use clinically. In the 1966 Bahn[14] review regarding the use of

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calcium sulfate, it was summarized that the material is simple to use, inexpensive, and offers many advantages as a grafting material for bone fill. These studies demonstrated that while acting as a space filler, calcium sulfate is resorbable and well tolerated by tissues. The material restores morphological contour and prevents soft tissue ingrowth into defects without the use of a membrane during the healing phase.[15] Peltier and Speer[16] confirmed the osteoconductive properties of calcium sulfate allowing ingrowth of both blood vessels and osteogenic cells. When implanted in the body, calcium sulfate completely resorbs over time, leaving behind calcium phosphate deposits that stimulate bone growth.

The residual calcium phosphate particles are identical to particles naturally occurring in the bone; therefore, they are nonimmunogenic and well tolerated. Adverse reactions or failures to heal have not been reported. Bioresorption studies of calcium sulfate and clinical experience have demonstrated consistent osteoconduction with complete resorption and subsequent replacement with de novo bone. When calcium sulfate is placed in direct contact with viable host bone, new bone growth occurs by apposition to the calcium of the graft material. Because of this, calcium sulfate is considered a short term space maintainer. The resorption period of calcium sulfate depends on graft volume, vascularity of the grafted site, and resorption model utilized.[17] This makes for varied reports on resorption time points in the literature. Graft materials in general need to remain for a suitable time period to facilitate the ingrowth of vascularity (angiogenesis) and conversion to host bone. Calcium sulfate's resorption rate is also dependent upon the crystalline structure and its impurities. The resorption rate that is consistent with new bone formation can be controlled by using a surgical grade calcium sulfate dihydrate possessing a rigid crystalline structure of specific size and shape.[18] As the material dissolves it promotes bone growth by (i) chemically activating the cycle of new bone formation, (ii) reacting with platelets to stimulate bone formation, and (iii) enhanced angiogenesis. Therefore, it is considered a bioactive graft material.

Calcium sulfate's porosity and hydroscopic properties promote absorption and infiltration of platelets and localized grow factors. The calcium ions activate platelets to release bone morphogenetic proteins and platelet derived growth factors that stimulate proliferation and osteogenic differentiation of mesenchymal stem cells.[19–21] After implantation, the graft's presence can easily be monitored radiographically due to its radiopacity. Initially calcium sulfate is radiopaque, then in 2–3 weeks, it appears radiolucent, and eventually the graft regains radiopacity in 12 weeks. This reflects the transformation of the material initially into newly formed uncalcified osteoid that gradually turns into calcified de novo bone.

Calcium sulfate is considered the bone graft material of choice in orthopedics due to its excellent osteoconductive capacity.[12–26] However, in maxillofacial applications, difficulties hardening calcium sulfate in the presence of saliva and bleeding have impeded its routine use. This obstacle to its use in oral surgery was overcome in 2010 by Dr Amos Yahav. Yahav modified the material's behavior by making it biphasic. This change to a biphasic form did not alter the chemical structure or behavior as a grafting material. However, the biphasic calcium sulfate form allows the calcium sulfate to harden in the presence of saliva and blood. Noting that calcium sulfate is a completely resorbable synthetic material with short-term space maintaining abilities, it is suggested that biphasic calcium sulfate be used as a composite graft when mixed with other slow resorbing bone grafts materials.[27] Bond Apatite (Augma Biomaterials Ltd, Monroe Township, NJ) is a ready-made composite bone graft material that meets these requirements. Bond Apatite is a biphasic calcium sulfate composite bone graft cement containing approximately 33% hydroxyapatite in a controlled particle distribution medium. The calcium sulfate component resorbs initially, then the hydroxyapatite particles provide maintenance of the deficit space for a much longer time-period.[28] Subsequently, there is a slower resorption of the hydroxyapatite component. Thus, the defect space is maintained while the host vascularizes the grafted area and de novo bone replaces the graft material. This sequence prevents the undesirable ingrowth of soft tissue into the defect. The hydroxyapatite particles are of various sizes (90–1000 μ) and shapes. The small and medium particles will resorb over 3–6 months, yielding fast bone regeneration of 90% of the grafted site.[29] The 10% larger particles of hydroxyapatite remain for a longer period of time.

Clinical Cases

Treatment protocols

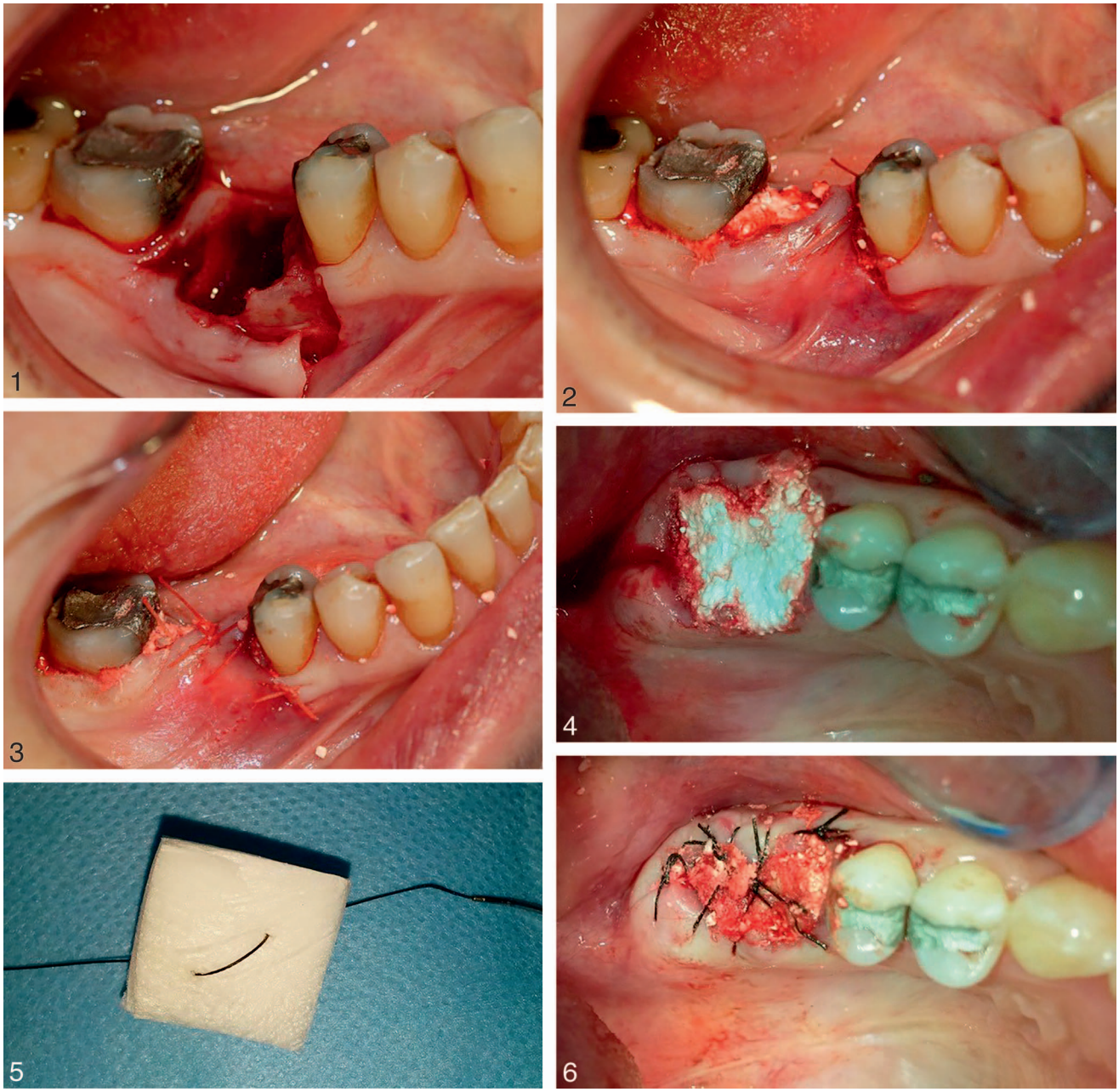
The protocols for treatment with Bond Apatite are as follows.

Protocol 1: Extraction Socket Grafting With Missing One Socket Wall

Following extraction of the tooth, an oblique vertical releasing incision is made at the mesial of the alveolus with the incision extending 2–3 mm past the mucogingival line. A full thickness flap is elevated to visualize the site and allow mobilization to cover the site following graft placement (Figure 1). Following curettage of the socket, the Bond Apatite is mixed and injected via the syringe into the osseous deficit. Sterile dry gauze is applied and firm pressure applied for 3 seconds. The flap is repositioned over the socket by stretching and attempting to achieve maximal closure of the flap margins, but 3 mm of graft exposure is acceptable. Sutures are placed to fixate the soft tissue in a tension manner starting with the mesial corner of the flap (Figure 2), continuing with the distal corner, and then the crestal aspect (Figure 3). A predictability test is performed by stretching the vestibule to ensure that the muscle movements will not influence graft stability during the healing phase. When no movement of the sutures is observed, it guarantees that the muscles will not influence the expected results, and a favorable clinical outcome can be expected with higher predictability. Following this predictability test, suturing is completed for maximum soft tissue closure. As previously mentioned, a small area of 3 mm of graft exposure does not require the use of a protective barrier membrane.

Protocol Number 2: Extraction Socket Grafting, Intact Socket

Following extraction, Bond Apatite is activated in its syringe and injected into the socket; gauze compression is performed for 3 seconds (Figure 4). A collagen sponge that can be

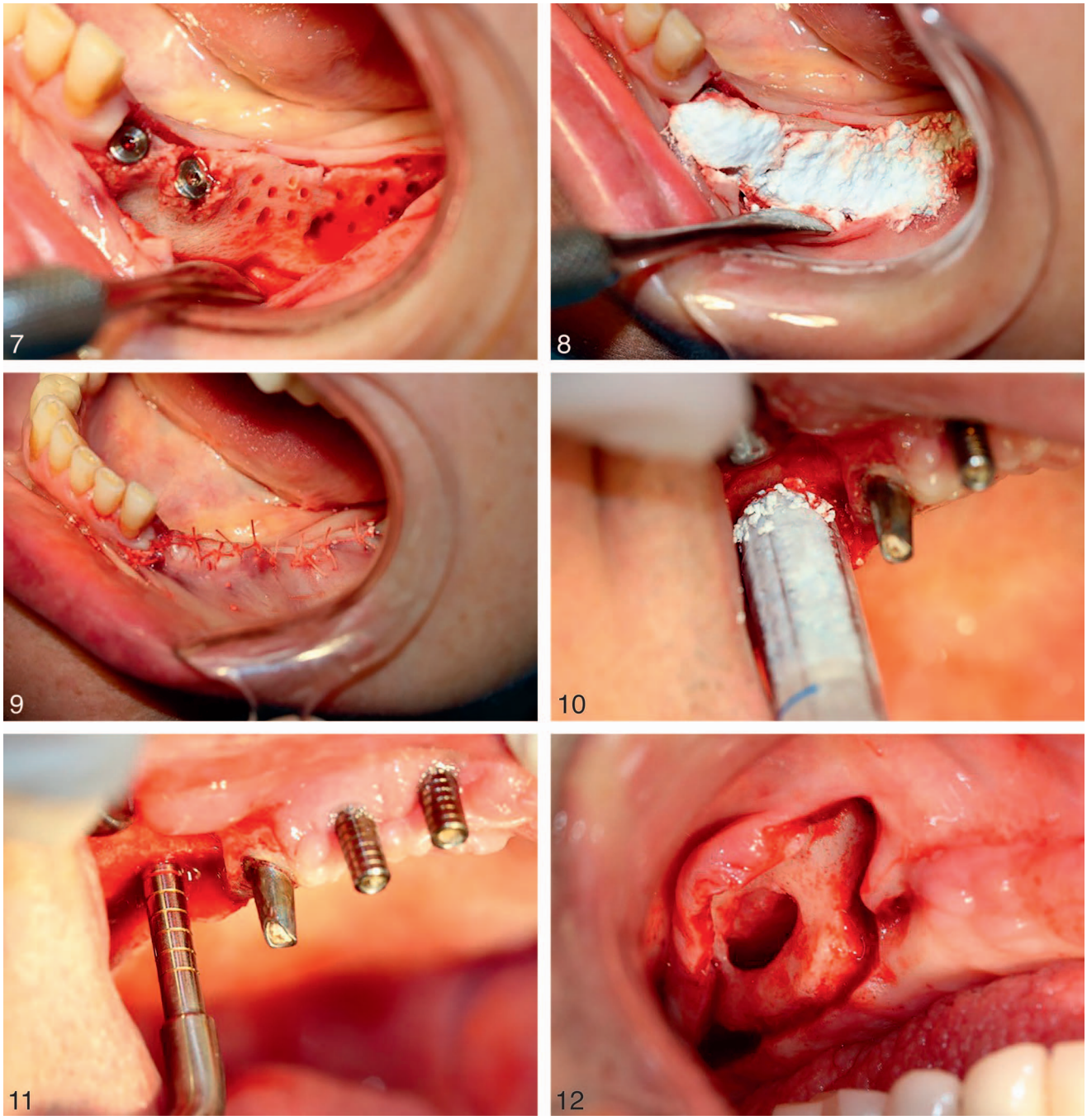


Figures 1–6. Figure 1. Following extraction, an oblique vertical releasing incision is made at the mesial aspect and a full thickness flap elevated. **Figure 2.** The papilla is sutured in a tension manner by stretching the flap to place for closure. **Figure 3.** The crestal aspect of the flap is closed with maximum closure in a tension manner. **Figure 4.** The socket is filled with Bond Apatite following extraction of the tooth. **Figure 5** A suture is placed through the collagen sponge prior to placement intraorally in order to secure the sponge in place. **Figure 6**. Sutures are placed within and over the collagen sponge covering the large area of exposed Bond Apatite.

maintained for 7–14 days (Figure 5) is placed over the exposed graft. A suture is then placed, securing the collagen sponge in place with the surrounding soft tissue. Then, a cross suture is placed to fix the sponge above the extraction socket (Figure 6).

Protocol Number 3: Lateral Ridge Grafting (Osseous Deficiency With No Bony Frame)

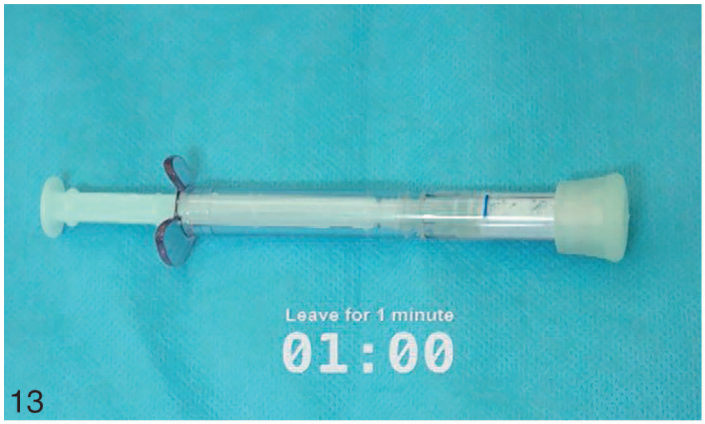
A full thickness flap extended 2–3 mm past the mucogingival line is reflected to visualize the site. If the crestal incision is long enough in the mesial distal direction, a vertical releasing incision may not be necessary (in cases when the clinician prefers to perform the envelope technique). Decortication is initiated in the buccal bone to provide stem cells to the graft to be placed (Figure 7). Bond Apatite is activated and placed over the buccal lateral aspect of the ridge and compressed with gauze for 3 seconds (Figure 8). The flap is repositioned directly on the graft with tension by stretching it for maximal closure over the graft (3 mm of graft exposure is acceptable). Sutures are placed to fix the soft tissue (Figure 9).

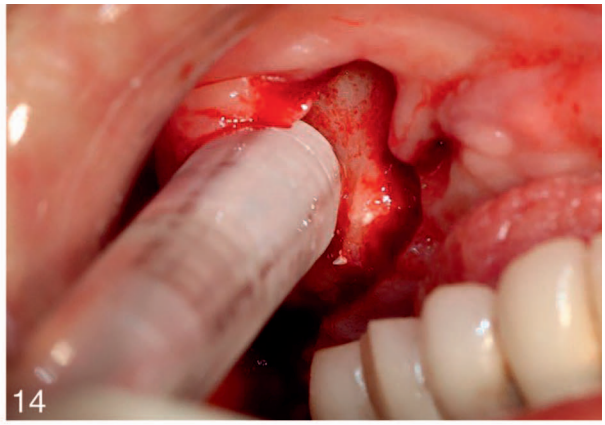


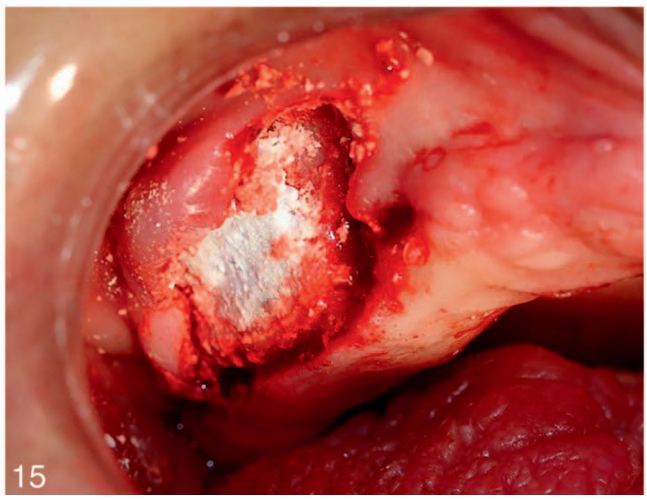
Figures 7–12. Figure 7. Following a full thickness flap, elevation bleeding points are created in the buccal lateral aspect of the ridge. **Figure 8.** Bond Apatite is placed over the area to be grafted to widen the ridge. **Figure 9.** The flap is stretched for closure and secured with sutures in a tension manner to gain maximal closure (3 mm graft exposure is acceptable). **Figure 10.** After being reloaded into the syringe, Bond Apatite is introduced via the syringe into the site receiving the crestal sinus elevation. **Figure 11.** An osteotome is utilized to place the Bond Apatite superiorly into the elevated sinus area. **Figure 12.** Conventional window created for lateral sinus elevation.

Protocol Number 4: Sinus Elevation Via Crestal Approach

The osteotomy is prepared in anticipation for a crestal sinus elevation. The sinus is elevated using a Summer's technique.[30] Bond Apatite is activated in the syringe and then injected into a sterile dish and left to harden for 3 minutes. Then, the semi-hard material is reloaded back into the Bond Apatite syringe barrel, or another bone graft carrier, and introduced into the osteotomy (Figure 10). An osteotome is utilized to gently place the graft material into the elevated sinus area (Figure 11). If the implant can be placed at that appointment it is introduced into the site and a cover screw placed and the site closed with a suture across it. If an implant cannot be placed at that appointment the entire osteotomy is filled with additional Bond







Figures 13–15. Figure 13. Following mixing of the Bond Apatite it is allowed to sit in the syringe for 1 minute before applying into the sinus. **Figure 14.** The Bond Apatite is applied into the sinus via the syringe. **Figure 15.** The sinus is filled with Bone Apatite to be level with the exterior lateral osseous surface.

Apatite and compressed with gauze, and the site is closed with a suture over the socket.

Protocol Number 5: Sinus Elevation Via Lateral Approach

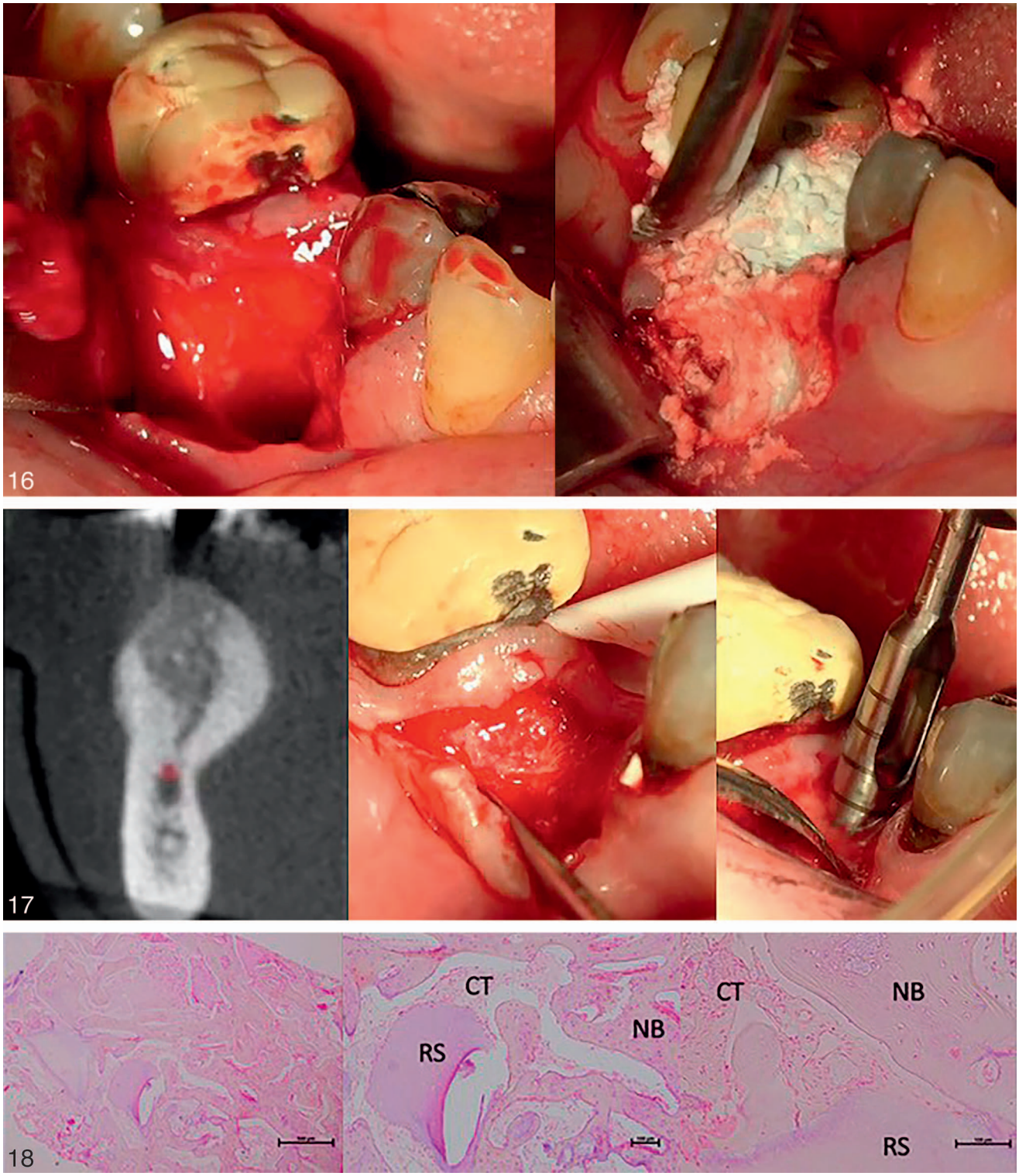
Conventional preparation of the lateral window for sinus elevation is performed following flap elevation, and the sinus membrane is elevated (Figure 12). Bond Apatite is mixed and after a 1 minute waiting time (Figure 13) is injected into the sinus area that has been created by elevation of the membrane (Figure 14). The graft is dispersed in the sinus cavity first mesially, then distally, and finally in the center until two-thirds of the sinus is filled. During graft dispersion, the graft material should be compressed against the sinus walls and, if needed, dry sterile gauze is used to tap gently over the graft surface to absorb excess fluids and blood. When filling the last third of the sinus and closing the sinus window the last syringe of Bond Apatite is activated and immediately injected into the sinus, followed by pressing firmly for 3 seconds with dry sterile gauze. The augmentation is finished with graft material level with the buccal aspect of the bony window that had been created (Figure 15). The flap is repositioned and sutures placed.

When utilized in socket preservation procedures, the resorption time allows bone regeneration without volumetric loss while limiting soft tissue ingrowth into the site. As calcium sulfate is very biocompatible, connective tissue cells of the soft tissues proliferate on the surface of the material. As a graft material, calcium sulfate facilitates cell attachment and fibroblast migration, contributing to its osteoconductive properties. A greater potential is thus offered for guided tissue regeneration in surgical sites where primary wound closure cannot be obtained.[31,32] It has been reported that the gene expression profile of cells on the calcium sulfate surface involved in new bone formation were expressed with an increased ratio and an increase in alkaline phosphatase activity.[33–35]

Results

Bond Apatite was utilized in 454 clinical cases, with the clinical cases separated into as follows:

1. Site grafting at time of tooth extraction in (a) the maxilla, (b) the anterior mandible, and (c) the mandibular posterior areas
2. Lateral ridge augmentation in the maxilla and mandible



Figures 16–18. Figure 16. Large defect with missing buccal wall following extraction of the tooth 30 (a) and socket filled with Bond Apatite prior to flap closure (b). **Figure 17.** Following 3 months of healing a cone beam computerized tomography was taken to verify osseous fill of the socket (a), the site was flapped and bone was noted filling the grafted socket (b), and a trephine core sample of healed bone was taken for histological analysis (c). **Figure 18.** Histology of the core sample taken at the 3 months healed site demonstrating new bone (NB), residual scaffold (RS) particles of Bond Apatite, and connective tissue surrounding the graft particles (CT) at ×4 (a), ×10 (b), and ×20 (c) magnification.

Table

Statistical results over 2 years of 454 cases treated with Bond Apatite with failures shown in parentheses

	Sector				
	Anterior Maxillary	Posterior Maxillary	Anterior Mandibular	Posterior Mandibular	Total
Surgery					
Socket preservation	38	53 (3)	6	86 (1)	183
Preservation					
Implant dehiscence	44 (3)	61	19	34	158
Crestal sinus augmentation		62			62
Lateral sinus augmentation		12			12
Lateral ridge augmentation	12 (1)	5	2	8	27
Canines included	3				3
Other: periapical defects and crestal implant grafting		7	1	1	9
Total	97	200	28	129	454

3. Fill of osseous defects around implants during implant placement
4. Sinus elevation by crestal approach
5. Sinus elevation by lateral approach
6. Apical surgery defect fill
7. Periodontal lesion fill

Following the protocols for the 454 cases treated, a failure rate of less than 2% was noted (Table). Based on this, the author found Bond Apatite appears to be a stable and predictable bone graft material. In addition, due to the biological qualities of the material, bone fill of nearly 90% has been routinely noted. The biocompatibility and bacteriostatic properties also note the grafts are generally incorporated without pain, and an absence of inflammatory reaction is routinely observed.

Histological Findings

The question is, "What remains of the Bond Apatite following healing, and is it replaced by native bone?" Following the extraction of a tooth (mandibular right 1st molar) leaving a 3 walled osseous defect, socket grafting was planned for site development in anticipation of eventual implant placement (Figure 16a). Bond Apatite was placed in the extraction socket (Figure 16b) and flap closure was accomplished with sutures. A cone beam computerized tomography was taken at 3 months postgrafting to evaluate the socket-fill, and it was noted that the site was an estimated 90% filled with a material similar in density to medullary bone (Figure 17a). A full thickness flap was raised and the socket was clinically noted to be filled with new bone similar to the surrounding bone (Figure 17b). A trephine bur (3.0 mm internal diameter) was used to obtain a bone-core sample (Figure 17c). Histological analysis of the sample confirmed new host bone with some remaining residual particles consisting of the Bond Apatite (24%), new bone (42%), and connective tissue (24%) (Figure 18). Histomorphological evaluation revealed hydroxyapatite particles were initially surrounded by connective tissue. Then during hydroxyapatite particle degradation, the remnant of the connective tissue around the particles underwent ossification as it was replaced by host bone. Three months post–graft placement there was typically 10% residual graft remaining in the single core sample taken from the site.

Discussion

Frequently, there is a cumbersome surgical technique requiring membrane coverage of autograft, allograft, and xenograft graft material. The ease of use of biphasic calcium sulfate cement as an alternative graft material make it an attractive option for the clinician. The biphasic calcium sulfate's cement properties enable for easy, rapid graft placement with stabilization due to the bonding properties and hardening of the cement intraorally, while excluding the need for membrane coverage.[36,37]

Biphasic calcium sulfate sets quickly and therefore prevents infiltration of epithelio-conjunctive cells into the graft. Thus, it acts not just as a grafting material, but also as a barrier membrane. Connective tissue cells are able to proliferate over the material's surface; which promotes soft tissue healing. This attribute allows for a simpler surgical protocol compared to use of other grafting materials that require a tension primary flap closure. The biphasic calcium sulfate sets with a firm shape-retaining quality that allows for its use without a membrane or other intermediary barriers when exposure is minimal. Because of this characteristic, biphasic calcium sulfate offers: (i) minimal flap reflection, and (ii) flap closure can be performed under tension. This closure quality offers the benefit of no releasing incisions as normally found with a tension-free flap closure technique used with nonfirm grafting materials. This allows the clinician to stretch mobile mucosa into place for closure, netting a resulting pressure on the graft that does not lead to the adverse effects normally observed with other graft materials that tend to collapse when under the pressure of tissue closed with tension. This relates to the hard-set nature of the biphasic calcium sulfate and its ability to tent the site without the tissue pressure leading to volumetric shrinkage of the graft during the healing phase that is often encountered with particulate graft materials. Additionally, with less extensive flap elevation, the flap and graft are not influenced by muscle movements during the healing phase and are less likely to open during healing, compromising the graft placed. Due to the nature of the material and its properties, the lack of primary

closure with graft exposure of 3 mm is acceptable. Soft tissue cells at the flap margins proliferate over the exposed set graft material, closing the flap margin over a few days to a week.[38]

Additionally, bacteriostatic properties are imparted due to (i) the material being a salt and (ii) creating an environment that is inhospitable to bacteria, yet there are no noted negative effects on host cells.[39] Additionally, the presence of sodium chloride in the physiological saline (used to mix the biphasic calcium sulfate powder) adds to the bonding qualities when coming into contact with the native bone prior to setting. Following mixing, the material is applied to the osseous deficit. Any residual liquid is removed by compression of the placed graft with sterile gauze for 3 seconds. The resulting dehydrated crystallized form hardens and adheres to the walls of the osseous defect, resulting in a stable block. This stable firm block is unlike other grafts that are supplied in granule or paste form.

As a short-term space maintainer, biphasic calcium sulfate is indicated for use when small osseous defects are surrounded by at least 3 bony walls (eg, extraction sockets). Thus, when augmenting large and more complex osseous deficiencies, Bond Apatite is a composite graft material that can be used as a solo agent or mixed with other graft materials for use in larger defects. The composite cement is provided in a dual-compartment syringe, with one side of the syringe containing the composite mixture of biphasic calcium sulfate powder with hydroxyapatite, and the second compartment containing sterile physiologic saline. Depressing the syringe plunger to the provided blue line marked on the syringe tube activates the material. The syringe cap is removed and the mixed graft is then ready for placement directly into the osseous defect. Soft tissue is then re-approximated (by stretching) with sutures placed to stabilize the flap margins.

Conclusion

Biphasic calcium sulfate, and in particular biphasic calcium sulfate combined with hydroxyapatite (Bond Apatite), are different from granular type bone graft materials in both its properties and handling. The protocols were specifically adapted to this new type of material allowing results of up to a 98% of success under various clinical applications. Due to its less invasive surgical protocols, ease of use, and a predictable regenerative outcome and cost effectiveness compared to comparable graft materials appears to make Bond Apetite an alternative to other grafting material.

Note

The author reports no conflicts of interest regarding this article.

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