3

Ceramic Composites for Bone Graft Applications

Joel D. Bumgardner, Carlos M. Wells, and Warren O. Haggard

CONTENTS
3.1 Introduction .................................................................................................. 41
3.2 Collagraft ...................................................................................................... 42
3.3 PRO-DENSE .................................................................................................. 42
  3.3.1 General Information and Indications ..................................................... 42
  3.3.2 Physical/Mechanical/Degradation Properties ........................................ 43
  3.3.3 Biological/Preclinical Studies ................................................................... 47
  3.3.4 Clinical Studies ....................................................................................... 49
3.4 MASTERGRAFT Family of Products ............................................................ 49
  3.4.1 General Information and Indications ..................................................... 49
3.5 STRUCSURE CP Cement ............................................................................. 55
  3.5.1 General Information and Indications ..................................................... 55
  3.5.2 Physical/Mechanical/Degradation Properties ........................................ 56
  3.5.3 Biological/Preclinical Study ..................................................................... 59
3.6 Summary ........................................................................................................ 59
Acknowledgements ............................................................................................. 60
References ............................................................................................................ 60

3.1 Introduction

The repair of bone defects from trauma or disease continues to be an active clinical need. This need is intensified when dental/craniofacial applications are considered. As a result, new products are continuously being researched and developed. Approximately six million bone fractures with bone loss occur in the United States each year. This loss of bone in long bone fracture or dental procedures requires the use of some type of bone graft. Bone graft choices can be autograft, allograft, processed from natural materials, synthetic, or any combination of these with or without other biological agents or materials. Collagraft® bone graft substitute, PRO-DENSE®, the MASTERGRAFT® family of products, and STRUCSURE™ CP will be the products discussed herein. The chapter will address the reasons for the composite approach of
these bone graft materials to help highlight their advantages for clinical use. The chapter goal is to acquaint the reader with some background and engineering for these representative bone graft composites.

### 3.2 Collagraft

Collagraft bone graft substitute was an early bone graft composite of collagen and hydroxyapatite developed and commercialized by Zimmer and Collagen Corporation. Collagraft was developed to partially simulate the major components in bone: collagen and hydroxyapatite. Collagraft received approval to market in 1993 by the U.S. Food and Drug Administration (FDA) through a Premarket Approval application. Collagraft bone substitute is a composite of type 1 bovine dermal fibular collagen and a biphasic calcium phosphate ceramic, with each individual granule containing separate microdomains of hydroxyapatite (HA) and tricalcium phosphate (TCP) phases of a calcium phosphate ceramic. Collagraft created a combination of materials that were similar to bone and could have cells or other osteogenic materials/agents added to this synthetic graft. The combination of collagen with fast and slow degrading bioceramics presents a bone graft scaffold that allows for new bone formation. Multiple preclinical and clinical studies for bone graft repair reported the successful use of this bone graft composite with various biological agents and/or materials. Collagraft was the initial approved composite bone graft substitute and thus laid a developmental outline for subsequent bone graft substitute composites. It was the first composite bone grafting material containing both a calcium phosphate ceramic and a collagen binder. Previous bone-grafting products were just loose ceramic granules while Collagraft’s formulation provides a stable matrix for cells to attach to and deposit new bone within. Collagraft is no longer marketed/distributed through Zimmer; it is currently marketed/distributed through NeuColl, Inc. (Campbell, CA).

### 3.3 PRO-DENSE

#### 3.3.1 General Information and Indications

Calcium sulfate (CS) has been used successfully as a bone void filler for over 120 years, but there have been reports of sterile effusion theorized to be due to the rapid dissolution of CS in vivo. The osteogenic activity of each component combined with the crystalline phase-dependent dissolution rates (calcium sulfate > brushite > β-tricalcium phosphate) produce a novel resorbable...
bolus for the encouragement of a material-assisted therapy aimed at “creeping-substitution” bone healing. In comparison, products based on various calcium phosphate minerals have been shown to be osteoconductive and biocompatible, but often exhibit extremely slow in vivo dissolution profiles that prevent complete regeneration of bone. The injectable, in situ curing PRO-DENSE Bone Graft Substitute (Wright Medical Technology, Inc., Memphis, TN) cement has been engineered such that the physiochemical and osteoconductive properties of calcium sulfate and calcium phosphates are utilized in a complementary manner which results in notable rates of osteogenesis within bone voids. The bone graft composite material is marketed in sterile kits which contain two vials (a precursor powder/β-tricalcium phosphate granule blend component and an aqueous liquid component), a vacuum mixing apparatus, and a syringe/Jamshidi® needle for minimally invasive delivery to a bone defect site.8 By mixing the liquid and powder/granule components, two cement reactions are initiated and allowed to proceed in unison, forming a calcium sulfate dihydrate (gypsum) and calcium hydrogen phosphate dihydrate (brushite) matrix encompassing a distributed phase of β-tricalcium phosphate granules (see reaction formulas at the end of this section).9,10 While in the preset paste form, the material can be syringe-loaded and injection-delivered via a large gauge needle; here, it can conform to defect site boundaries and harden in situ. Ultimately, after placement, the cured cement is a triphasic blend of calcium salts formed to the shape of a bone void. The cured product is a composite cement blend on a microscopic scale, largely consisting of gypsum with a lesser brushite component incorporating β-tricalcium phosphate granules (see Figure 3.1a).10 Granules are mechanically incorporated chemically through the involvement of surface reactions with the brushite system, locking them into the phosphate matrix. An underlying dogma of composite science is to utilize the beneficial properties of multiple materials in a concerted effort such that in combination the resultant exhibits multifunctional and improved properties over those of the individual constituents, and such synergistic effects have been exhibited by PRO-DENSE as a bone void filler medical device.

Calcium sulfate hemihydrate to calcium sulfate dihydrate (gypsum) reaction:

\[ 2\text{CaSO}_4 \cdot \frac{1}{2} \text{H}_2\text{O} + 3\text{H}_2\text{O} \rightarrow 2\text{CaSO}_4 \cdot 2\text{H}_2\text{O} \]

Monocalcium phosphate monohydrate and beta-tricalcium phosphate to calcium hydrogen phosphate dihydrate (brushite) reaction:

\[ \text{Ca(H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O} + 3\text{Ca}_3(\text{PO}_4)_2 + 7\text{H}_2\text{O} \rightarrow 4\text{CaHPO}_4 \cdot 2\text{H}_2\text{O} \]

3.3.2 Physical/Mechanical/Degradation Properties

The dissolution profile of PRO-DENSE’s components combined with their microscopic structural integration appears to result in a mechanically supported dynamic structure in vivo, resulting in a resorption profile
that greatly accommodates the multiple phases of osteogenesis across fractures, voids, and surgically created gaps. The fundamental steps associated with bridging such a defect have been generally described as overlapping stages of inflammation, repair, and remodeling. The triphasic composition of PRO-DENSE has been shown to demonstrate tiered dissolution kinetics in vitro as faster dissolving calcium sulfate is released leaving behind a highly porous, slower resorbing calcium phosphate structure, which largely retains the original overall geometry of the initial set cement. Figures 3.1 and 3.2 show the results of an accelerated dissolution study in distilled water.

FIGURE 3.1
Exemplary micrographs of PRO-DENSE’s staged dissolution profile are shown. Cast cylinders (3.3 x 4.8 mm OD) were exposed to an accelerated in vitro dissolution protocol using distilled water. Representative specimens at time points 0, 4, 8, and 12 days (frames a, b, c, and d, respectively) were withheld from further treatment for electron microscopy and electron dispersive spectroscopy processing (plastic embedded, polished, and cross-sections scanned). High-density β-tricalcium phosphate granules (white aggregate) can be seen throughout the continuous, composite matrix of gypsum (CaSO4·H2O) and brushite (CaHPO4·2(H2O)) (light grey) in frame a. Consecutive frames (b-d) demonstrate the phosphate- and sulfate-staged dissolution of the composite. Note that as the faster dissolving sulfate component is dissolved, a highly porous yet structural osteoconductive brushite cement/β-tricalcium phosphate granule scaffold is left behind. Complete resorption of the material can be inferred through observation that the slowest dissolving granule/brushite components demonstrate an ever-reducing cross-sectional area with treatment time (a through d).
Mass loss was measured as a function of time in vitro for cast pellets of PRO-DENSE, pure calcium sulfate, and pure calcium phosphate materials. At selected time points, pellets were embedded in plastic, cross-sectioned, and polished to assess the morphology. The early, more rapid dissolution kinetics of the calcium sulfate may harness the early stages of repair in which neovascularization penetrates and high-collagen-level woven bone is throughout a defect site in an inward-working fashion. The later, slower dissolution kinetics of the remaining phosphate compounds may support biomaterial-assisted remodeling of the immature bone through both osteoblast-assisted mineralization of woven bone to a high mechanical integrity state. Also, osteoclast-assisted resorption and dissolution of the final implant material will occur later. This theory of assisting in staged healing is supported by preclinical in vivo canine studies using critically sized defects, where histology identified bone cells and tissue types incorporated within the partially resorbed material. PRO-DENSE has resulted in a statistically significant increased healing rate over that of autograft and pure calcium sulfate in critical defects based on biomechanical and histological findings (see Table 3.1 and Figures 3.3 and 3.4).
### TABLE 3.1
Biomechanical Tensile Test Data of Cored Trabecular Bone Specimens Are Presented.

<table>
<thead>
<tr>
<th>Implant Material</th>
<th>In-Life Time (weeks)</th>
<th>Ultimate Compressive Strength ± SD (MPa); n</th>
<th>Modulus of Elasticity ± SD (MPa); n</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRO-DENSE®</td>
<td>13</td>
<td>5.29 ± 2.61; n = 5</td>
<td>283 ± 217; n = 5</td>
</tr>
<tr>
<td>PRO-DENSE®</td>
<td>26</td>
<td>2.19 ± 0.41; n = 5</td>
<td>150 ± 73.5; n = 5</td>
</tr>
<tr>
<td>Autograft</td>
<td>13</td>
<td>0.71 ± 0.31; n = 8</td>
<td>40.41 ± 21.72; n = 10</td>
</tr>
<tr>
<td>Normal healthy bone</td>
<td>NA</td>
<td>1.38 ± 0.66; n = 8</td>
<td>117 ± 71.5; n = 8</td>
</tr>
</tbody>
</table>


**Note:** Cored regions were from critically sized defects sites treated with either injectable PRO-DENSE® or autograft. Additionally, results of normal trabecular bone cores harvested from the same anatomical region are shown for comparison.

**FIGURE 3.3**
Ultimate compressive strength values associated with graft-assisted healing at the 13-week time point of a critically sized osseous canine proximal humerus in vivo preclinical model are shown. Additionally, values found for normal trabecular bone harvested from the same anatomical location is the comparison. Averages and standard deviations are shown. At 13 weeks, defects treated with PRO-DENSE demonstrated advanced healing over the autograft group based on a significant increase in ultimate compressive strength over the autograft group ($p = 0.004$). The increase in strength over that of normal bone seen for the PRO-DENSE groups decreased with time after 13 weeks, and biomechanical properties approached that of normal bone at a later 26-week time point.12
Such defects model highly compromised nonunion fractures, where treatment can be very challenging. These studies, in combination with the known healing cascade, are suggestive of the potential benefit PRO-DENSE offers over more traditional, single-component bone graft substitutes which resorb through linear kinetics via an “outside-in” fashion, such as that of Wright Medical’s comparatively faster resorbing pure calcium sulfate bone graft substitutes. The bulk materials of the composite PRO-DENSE demonstrate comparatively slower resorption, such as found in commercially available hydroxyapatite cements. Clinical complications have been associated with the faster resorbing materials; sterile exudates and delayed mineralization have been noted within the literature.

### 3.3.3 Biological/Preclinical Studies

Supplementing the passive, yet favorable, nature of PRO-DENSE’s multiphase dissolution in vivo is the bioactive phenomenon of a well-orchestrated relationship between protein adsorption and desorption on
the material’s surface and the beneficial cellular activities that emanate on and are adjacent to the composite cement as a result of these dynamic processes. In vitro protein adsorption/desorption studies have demonstrated that osteogenesis-related chemotactic agents, angiogenic factors, and differentiation factors exhibit a higher affinity for PRO-DENSE versus pure calcium sulfate. Bone morphogenetic protein-2 (BMP-2) and vascular endothelial growth factor (VEGF) have demonstrated preferential absorption onto the surface of PRO-DENSE over pure calcium sulfate. Preservation of protein functionality has been demonstrated through release of absorbed VEGF from PRO-DENSE’s surface. PRO-DENSE specimens exposed to VEGF-containing buffer solutions for various times passively desorbed protein into fresh solutions where chemotactic bioactivity was shown to be retained in vascular endothelial cells (see Figure 3.5). The novel addition of calcium phosphate cement and granules with calcium sulfate cement results in a more bioactive composite over calcium sulfate alone and may explain the enhanced tissue healing response associated with PRO-DENSE over that of pure calcium sulfate and autograft treatment seen in preclinical canine models.12

![FIGURE 3.5](image-url)

Chemotaxis results (average cell count and standard deviation) from an in vitro study in which human umbilical vein endothelial cells (HUVECs) migrated through transwell plate filters are shown, demonstrating PRO-DENSE’s angiogenic potential. PRO-DENSE demonstrated the ability to sustain release of VEGF over a 72-hour period in vitro, inferring absorption of the protein as well. VEGF-containing eluates, derived from a protein absorption/desorption protocol from PRO-DENSE surface, were used for the experimental conditions shown. Desorption was allowed for the times shown (24, 48, and 72 hours). The positive and negative controls were 40 ng/mL VEGF in phosphate buffer and buffer alone, respectively.17
3.3.4 Clinical Studies

This composite bone graft substitute has been used with large success in U.S. clinics since its FDA marketing approvals in 2007 as a bone void filler and a core decompression material for the osteonecrotic femoral head. Clinical studies have largely reported positive findings with use of the injectable graft. In retrospective studies, a 24 patient population with benign primary bone tumors was successfully treated with PRO-DENSE. In 21 of 24 patients bone void repair was achieved with early return to load bearing activity. There were two tumor recurrences and one infection in this small series after wound break-down events. Another large retrospective study on PRO-DENSE’s treatment of benign tumors was conducted by Fillingham, et al. where 56 patients’ records were reviewed with a high degree of treatment benefit. In this study, the following adverse events were observed: three recurrences (successfully treated through an additional administration of PRO-DENSE or curettage), two post-op fractures (treated through closed technique), and two cases of wound complications that did not require graft retrieval. Backfilling of the surgical site and replacement of the necrotic bone space in hip core decompression surgeries was prospectively evaluated by Civinini et al. The treatment of 37 enrolled patients’ hips revealed the following clinical observations: a statistically significant increase in average Harris hip score (68 to 86), either radiographic improvement or the absence of further collapse in 29 (78.4%) of these hips, and disease progression to the stage that arthroplasty was required in three hips. These mostly successful clinical experiences with the use of PRO-DENSE reflect positive effects that can be achieved with the innovative design of this composite bone graft substitute.

Collectively, the aforementioned work illustrates PRO-DENSE to be a novel composite from material and biologic perspectives, and a biomaterial with a unique blend of physiochemical and bioactive functionality that has proven efficacious in the treatment of clinically demanding bone voids.

3.4 MASTERGRAFT Family of Products

3.4.1 General Information and Indications

In the United States, the MASTERGRAFT family of products includes MASTERGRAFT Granules, MASTERGRAFT Mini Granules, MASTERGRAFT Putty, MASTERGRAFT Strip, and MASTERGRAFT Matrix EXT. The Granules (diameter 1.6–3.2 mm) and Mini Granules (diameter 0.5–1.6 mm) are biphasic calcium phosphate (BCP) ceramic bone void fillers composed of 85% beta-tricalcium phosphate (β-TCP) and 15% hydroxyapatite (HA) by mass. This ratio falls within the range described in the literature as an optimal ratio for use in vivo. These ceramic granules have an interconnected porous structure that facilitates bone ingrowth.
products are composite materials that combine the BCP ceramic granules with bovine type I collagen.

The MASTERGRAFT Granules and Mini Granules (Figures 3.6 through 3.8) are indicated for filling of bony voids or gaps not intrinsic to the

![MASTERGRAFT Granules SEM Image](image.png)

**FIGURE 3.6**
Top: Scanning electron microscopy (SEM) image of MASTERGRAFT Granules. The porous structure of the ceramic granule can be seen. Middle: Energy Dispersive X-ray Spectroscopy (EDS) spectrum of Region 1 in the SEM. Peaks representing calcium and phosphorus are seen. Bottom: EDS spectrum of Region 2 in the SEM. Peaks representing calcium and phosphorus are seen.
FIGURE 3.7
X-ray diffractograms (XRD). Top: XRD showing the crystal structure of MASTERGRAFT Granules. Bottom: XRD showing the crystal structure of MASTERGRAFT Strip. Note that the same peaks are present for both materials.

FIGURE 3.8
MASTERGRAFT Granules. Left: Photograph of Granules. Right: Schematic showing bone voids filled with Granules.
stability of the bony structure including the extremities, pelvis, ilium, and posterolateral spine. They are also indicated for use in oral/maxillofacial applications including filling of dental extraction sockets and cystic defects. The smaller size of the Mini Granules allows them to be used for the filling of periodontal defects, sinus lifts, and alveolar ridge augmentation. The ability of MASTERGRAFT Granules to promote osseous filling of alveolar extraction sockets and backfilling of iliac crest defects has been demonstrated.

MASTERGRAFT Putty (Figures 3.9 and 3.10) is a composite material indicated for filling of bony voids or gaps not intrinsic to the stability of the bony structure and also for oral/maxillofacial applications. MASTERGRAFT Putty contains BCP particles (diameter 0.5–1.6 mm) uniformly distributed throughout bovine type I collagen for enhanced handling characteristics. The collagen is a combination of 70% insoluble fibrous collagen and 30% soluble collagen. Putty is supplied dry and becomes moldable when hydrated with autogenous bone marrow aspirate or sterile water.

FIGURE 3.9
MASTERGRAFT Putty. Left: MASTERGRAFT Putty being hydrated with sterile water. Middle: The Putty is malleable after being hydrated. Right: Putty being manipulated after hydration.

FIGURE 3.10
MASTERGRAFT Putty. Left: Example of Putty being placed into a bone void. Right: Close-up of Putty in bone void demonstrating the ability of Putty to conform to geometry of defect space.
MASTERGRAFT Strip (Figures 3.11 through 3.14) and Matrix EXT must be combined with autogenous bone marrow aspirate and are indicated for filling of bony voids or gaps not intrinsic to the stability of the bony structure. Strip and Matrix EXT are similar to Putty in that they contain BCP ceramic particles (diameter 0.5–1.6 mm) dispersed throughout bovine type I collagen; however, all of the collagen is insoluble and the mineral:collagen ratio is increased compared to that of Putty.\(^{34,35}\) This formulation allows the products to be both flexible and compression-resistant. The ability to resist compression by the surrounding tissue and muscles maintains space at the defect site, facilitating complete bone healing in challenging applications such as posterolateral spine arthrodesis. Additionally, the geometry (2.0 cm wide, 0.6 cm thickness, and 10 cm or 36 cm lengths) and flexible nature of Strip allows a single implant to span multiple spinal levels. For instance, the 36-cm-long Strip can be used to fill the bony voids associated with scoliosis reconstructions.

**FIGURE 3.11**

(a and b) SEM images of MASTERGRAFT Strip. The collagen and ceramic components of the composite can be seen. (Continued)
FIGURE 3.11 (Continued)
(c) Energy dispersive x-ray spectroscopy (EDS) spectrum of Region 1 in the SEM on the left. Peaks representing high levels of calcium and phosphorus indicative of ceramic are seen. (d) EDS spectrum of Region 4 in the SEM on the left. Peaks corresponding to high levels of carbon, nitrogen, and oxygen indicative of collagen are present.

FIGURE 3.12
MASTERGRAFT Strip. Left: Strip in plastic tray. Middle: The flexibility of Strip is being demonstrated. Right: The compression resistance of Strip is shown.

FIGURE 3.13
MASTERGRAFT Strip. Left: Strip is being hydrated with BMA. Middle and right: The Strip is extremely flexible after hydration.
Since the MASTERGRAFT materials do not possess sufficient mechanical strength to support reduction of a defect site prior to soft and hard tissue ingrowth, rigid fixation methods are recommended as needed to ensure stabilization of the defect. If desired, autograft bone can be used in conjunction with the MASTERGRAFT products. In rabbit posterolateral fusion studies, MASTERGRAFT Strip and Putty were successfully used as autograft extenders. The advantage of these composites is that the addition of collagen to the BCP granules yields products with improved handling characteristics and reduces the possibility of granule migration from the defect site. The MASTERGRAFT family of products provides options for surgeons when selecting the proper bone void filler (Table 3.2).

3.5 STRUCSURE CP Cement

3.5.1 General Information and Indications

STRUCSURE CP cement from Smith & Nephew Inc. (Memphis, TN) is an injectable, self-setting bone graft substitute that incorporates hydroxypropyl methylcellulose (HPMC) into the formulation. This polymer/ceramic formulation allows greatly improved mixing and handling characteristics.
The addition of the polymer provides multiple benefits including enhanced viscosity during curing, improved cohesion, and permeability of the cement. This improved rheological behavior allows the cement to be mixed and delivered from the syringe. The addition of a gun to hold the syringe allows a simple, one-handed delivery system.

### 3.5.2 Physical/Mechanical/Degradation Properties

Calcium phosphate cements are useful materials to replace or augment bone loss in orthopedic surgery.\textsuperscript{38} Traditionally, these materials have required the materials engineer to balance a range of competing properties in the formulation selection. For example, increasing the viscosity of the cement to improve its injectability would also significantly decrease the set time of the final product. Early injectable cement systems had a viscosity that was initially very low and would increase with time as the setting reaction progressed. This would make the injection inconsistent throughout the delivery of the product. Early injectable cement systems had a viscosity that was initially very low and would increase with time as the setting reaction progressed. This would make the injection inconsistent throughout the delivery of the product. The initial, low viscosity of the product (similar to water) would make it difficult for the injected material to stay in place when injected. As the curing reaction progresses, the viscosity of the cement increases allowing the cement to be used; eventually, the viscosity becomes too high and the cement is no longer injectable. In some cases, this can result in the material setting before it can be injected. Another common issue with early products was a phenomenon called “filter press,” which is a form of phase separation of the liquid and powder ingredients during mixing.\textsuperscript{39} This can prematurely plug the tip of the syringe, thus preventing full use of the product.

By moving to a composite system, the trade-offs of a simple powder-liquid system were greatly changed, allowing for improved products to be developed. The components of the STRUCSURE CP cement system are

<table>
<thead>
<tr>
<th>Product</th>
<th>Composition</th>
<th>Description of Composite</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASTERGRAFT Granules and Mini Granules</td>
<td>Biphasic calcium phosphate (BCP) granules</td>
<td>N/A</td>
<td>Oral/maxillofacial bony tissue + bony voids or gaps of the skeletal system</td>
</tr>
<tr>
<td>MASTERGRAFT Putty</td>
<td>BCP granules + collagen (70% insoluble, 30% soluble)</td>
<td>Malleable</td>
<td>Oral/maxillofacial bony tissue + bony voids or gaps of the skeletal system</td>
</tr>
<tr>
<td>MASTERGRAFT Strip and Matrix EXT</td>
<td>BCP granules + insoluble collagen</td>
<td>Flexible and compression resistant</td>
<td>Bony voids or gaps of the skeletal system</td>
</tr>
</tbody>
</table>

The addition of the polymer provides multiple benefits including enhanced viscosity during curing, improved cohesion, and permeability of the cement. This improved rheological behavior allows the cement to be mixed and delivered from the syringe. The addition of a gun to hold the syringe allows a simple, one-handed delivery system.

### TABLE 3.2

The MASTERGRAFT Family of Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Composition</th>
<th>Description of Composite</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASTERGRAFT Granules and Mini Granules</td>
<td>Biphasic calcium phosphate (BCP) granules</td>
<td>N/A</td>
<td>Oral/maxillofacial bony tissue + bony voids or gaps of the skeletal system</td>
</tr>
<tr>
<td>MASTERGRAFT Putty</td>
<td>BCP granules + collagen (70% insoluble, 30% soluble)</td>
<td>Malleable</td>
<td>Oral/maxillofacial bony tissue + bony voids or gaps of the skeletal system</td>
</tr>
<tr>
<td>MASTERGRAFT Strip and Matrix EXT</td>
<td>BCP granules + insoluble collagen</td>
<td>Flexible and compression resistant</td>
<td>Bony voids or gaps of the skeletal system</td>
</tr>
</tbody>
</table>
shown in Figure 3.15. The inclusion of the polymer provides a more consistent viscosity throughout the injection of the cement. This is shown in Figure 3.16, which illustrates the force required to deliver STRUCSURE from a 10 mL syringe as a function of displacement. The test was conducted at a rate of 1 mm/min.

**FIGURE 3.15**
Components of the STRUCSURE CP delivery system. Top: Cannula. Middle: Mixing syringe pre-loaded with the powder and liquid components. Bottom: Delivery gun into which the syringe is placed after mixing. This allows a one-handed delivery of the mixed cement.

**FIGURE 3.16**
Injection force vs. displacement for the STRUCSURE CP cement. The force required to inject the cement is almost constant until the end of the syringe is reached at ~25mm displacement.
The graph in Figure 3.16 shows an almost constant injection force for the cement, even though the setting reaction is ongoing. The cohesion of the material is also improved as the polymer acts to hold together the powder as it reacts and cures. These improved rheological and cohesive properties also allow the cement to stay in place, allowing the surgeon to have great control over the location of the material. This also allows the cement to be drilled and hardware (e.g., screws) to be inserted into the cement before it is fully cured. The improved cohesion of the cement means it will not fracture or sag when a hole is drilled into the material (Figure 3.17). Figure 3.18 shows a cross-section of the cement after placement of hardware through the cement.

Finally, the water-soluble polymer will dissolve out of the cement in the first few days after implantation; this space vacated by the polymer will be replaced with the patient’s extracellular fluids (interstitial fluid and blood plasma). This inclusion of extracellular fluids improves the biocompatibility and osteoconductivity of the implanted cement.

FIGURE 3.17
Photograph of STRUCSURE cement which was drilled 8 minutes after injection.

FIGURE 3.18
Sectioned Sawbone after insertion of hardware through cement.
3.5.3 Biological/Preclinical Study

STRUCSURE CP cement was evaluated in an in vivo model for its biocompatibility and osteoconductivity. The cement was placed into 2 cm segmental defects made in the distal radius of New Zealand white rabbits. The performance of the STRUCSURE material was evaluated through radiological scoring and histological analysis, including measuring the percentage of bone in the defect at 4 and 8 weeks post-operatively. In all of these measures, the performance of the tested cement was compared to morselized autograft, the gold standard in scaffolds for bone regeneration. In this study, the STRUCSURE CP material behaved similarly to the autograft group. The STRUCSURE CP material was statistically equivalent to autograft in all measures at all time points apart from the amount of bone formed at 4 weeks as measured from the radiographs. No inflammatory response was seen in any of the animals. A micro-CT image of the treated defect, at 8 weeks, is shown in Figure 3.19.

3.6 Summary

With this chapter, several bone graft composites were discussed, while outlining the reasons for their composite approach. The clinical need for bone graft in musculoskeletal and dental/craniofacial applications continues to expand. Composite approaches to bone grafting, while currently clinically successful, may offer improved bone restoration outcomes in the future with further scientific and technical refinements.
Acknowledgements

The authors would like to thank Jonathan McCanless, Jon Moseley, John Rose, Ben Reeves, and Cheyenne Rhodes for their support and assistance with this book chapter.

References

2. FDA, COLLAGRAFT(TM) BONE GRAFT SUBSTITUTE, Docket # 93M-0210, PMA # P900039. NEUCOLL, INC, 05/28/1993.
3. FDA, COLLAGRAFT(TM) BONE GRAFT SUBSTITUTE, PMA # P900039, Supplement # S002. COLLAGEN CORP., 08/05/1993.


24. MASTERGRAFT® Granules IFU-0381438 Rev. C.

25. MASTERGRAFT® Granules IFU-0381416 Rev. C.


