The Otto Aufranc Award

Demineralized Bone Matrix Around Porous Implants Promotes Rapid Gap Healing and Bone Ingrowth

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Abstract

Background Noncemented revision arthroplasty is often complicated by the presence of bone implant gaps that reduce initial stability and biologic fixation. Demineralized bone matrix has osteoinductive properties and therefore the potential to enhance gap healing and porous implant fixation.

Questions/purposes We determined at what times and to what extent demineralized bone matrix promotes gap healing and bone ingrowth around a porous implant.

Methods We inserted porous titanium implants into the proximal metaphyses of canine femora and humeri, with an initial 3-mm gap between host cancellous bone and implants. We left the gaps empty (control; $n = 12$) or filled them with either demineralized bone matrix ($n = 6$) or

devitalized demineralized bone matrix (negative control; $n = 6$) and left them in situ for 4 or 12 weeks. We quantified volume healing of the gap with new bone using three-dimensional micro-CT scanning and quantified apposition and ingrowth using backscattered scanning electron microscopy.

Results The density of bone inside gaps filled with demineralized bone matrix reached 64% and 93% of surrounding bone density by 4 and 12 weeks, respectively. Compared with empty controls and negative controls at 4 and 12 weeks, gap healing using demineralized bone matrix was two to three times greater and bone ingrowth and apposition were up to 15 times greater.

Conclusions Demineralized bone matrix promotes rapid bone ingrowth and gap healing around porous implants.

Clinical Relevance Demineralized bone matrix has potential for enhancing implant fixation in revision arthroplasty.

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Each author certifies that his or her institution approved the animal protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research. This work was performed at McGill University.

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Introduction

Total hip arthroplasty (THA) failure results in varying degrees of acetabular and femoral bone loss. Implant loosening, with subsequent motion of the prosthesis, osteolysis, and removal of the implants at the time of revision surgery, contributes to this loss of bone stock. The remaining deficient host bone can compromise initial implant stability and substantially diminish the contact between host bone and the ingrowth surface, both of which are required to reliably obtain bone growth into a porous-coated revision implant. Additionally, one of the most common types of femoral revisions involves obtaining distal fixation in the intact host bone, bypassing the bony-deficient proximal femur, using a monoblock or modular

extensively porous-coated cylindrical or tapered conical stem. However, distal fixation in the absence of proximal ingrowth can result in stem fracture [8, 25]. Therefore, one of the major challenges in revision THA remains the restoration of host bone stock and the promotion of bone ingrowth in deficient bone stock.

Gap filling of bony defects can be achieved with autogenous bone grafting; however, the limited availability of autogenous bone and the morbidity associated in graft harvesting has resulted in the search for alternatives, including allograft and bone graft substitutes [1, 4, 13, 14, 18, 22, 26, 35]. A bone graft substitute with potential benefit for addressing bone defects around cementless implants is demineralized bone matrix (DBM) [9, 20, 21]. DBM, produced by acid extraction of the mineralized phase of bone to create a composite of noncollagenous proteins, growth factors, and collagen [12], is capable of inducing osteogenesis by recruiting host mesenchymal stem cells [37]. Various commercial preparations of DBM are available, differing widely in their ability to induce bone formation due to different processing techniques and carriers [10, 11, 28, 30, 31, 36]. Evaluation of the potential for DBM to enhance bone ingrowth or promote gap healing around porous-coated implants is limited. Shen et al. [32] used a rabbit model with a noncritical implant gap size and reported bone growth into porous implants was comparable between DBM and autograft. Cook et al. [7] reported DBM gel did not enhance bone ingrowth in a canine transcortical implant model without bone-implant gaps. Shih et al. [33] demonstrated, in a canine gap implant model, DBM enhanced gap healing and bone ingrowth over empty controls but only at 6 months

postoperatively. However, after revision THA, patients are left nonweightbearing for no longer than 12 weeks to allow for implant stabilization by bone ingrowth; therefore, bone graft substitutes taking longer than 12 weeks to be effective are not practical. Also, no prior DBM studies utilized the new higher porosity implants now common in revision THA [5, 17, 24, 27, 29], even though implant surface topography influences bone ingrowth [6, 15, 16, 23, 38].

We, therefore, determined whether DBM promotes healing of a critically sized bony defect or gap around a porous implant and increases bone ingrowth and apposition within a clinically relevant period of 12 weeks or less.

Materials and Methods

To address these questions, we developed a canine gap model using highly porous titanium implants. We analyzed the independent gap treatment variable; DBM, devitalized DBM, and empty controls, together with the independent time variables of 4 and 12 weeks, using three-dimensional (3D) micro-CT and scanning electron microscopy (SEM) to quantify the dependent variables of volumetric healing of gaps and the extent of bone ingrowth and apposition.

We fabricated gap-type intramedullary implants from commercially pure titanium (Fig. 1). Each implant was 4 cm in total length, had a 5-mm diameter porous core, and had 11-mm diameter solid end caps and central spacers. This resulted in two separate gap regions, 15 mm long and 3 mm wide, containing a volume of 1.13 cm³. We fabricated the implant core using a powder metallurgy

Fig. 1A–C (A) The photograph shows the titanium gap implant with porous core and solid end caps and middle spacer. End caps and spacers maintained the 3-mm gap between the reamed border of host bone and the porous implant core. (B) A SEM image illustrates the porous structure, which allows for bone ingrowth. (C) A radiograph illustrates a gap implant within the proximal humerus. Fixation in the proximal bone is preferable over fixation in the distal diaphyses as it avoids the occurrence of stem fracture and is associated with less stress shielding and bone pain.

approach. Pure titanium powder was mixed with a polymeric binder and a foaming agent. The resulting powder mixture was molded and heated up to foam the mixture. After foaming, the binder was removed and the part was sintered to consolidate the structure. The final structure had 55% volume porosity and an average pore size of 375 μm [38].

We custom-processed the DBM by exposing 100- to 500- μm canine cortical bone fibers to dilute HCl (Osteotech Inc, Eatontown, NJ). The content of the fibers was predominantly collagen matrix with embedded native bone morphogenetic proteins; the residual mineral content was less than 0.5%. We prepared the second graft material by exposing DBM to guanidine HCl to remove the matrix-embedded osteoinductive growth factors, creating a devitalized negative control. We combined both matrices with 100% glycerol as a carrier in a 1-to-4 ratio, producing graft materials with a putty-like consistency. By comparing total protein content using established protocols, we were able to compare growth factor content between the DBM and its devitalized form [2, 3, 30]. Protein extraction solution consisted of guanidine HCl 4 mol/L, Tris 50 mmol/L, and a protease inhibitor cocktail with EDTA 1 mmol/L (Sigma-Aldrich, Oakville, Canada). Samples of each material underwent extraction for 48 hours at 4°C, followed by centrifuging at 12,000 rpm for 30 minutes at 4°C. We dialyzed supernatant with a 3.5-kDa membrane against deionized distilled H₂O for another 48 hours at 4°C. Subsequently, the supernatant was assayed using Quick Start™ Bradford protein assay (BioRad, Mississauga, Canada) and read at 595 nm using a BioRad spectrophotometer. Using this method, the total protein content of the DBM was 48.3 $\mu\text{g/mL}$ compared with 3.2 $\mu\text{g/mL}$ for the devitalized DBM, confirming the effectiveness of the devitalization process. We did not include autograft material in the experiment because it is rarely utilized in revision THA and would not have provided a clinically meaningful comparison.

Before starting the experiment, a power analysis was performed to estimate the sample size required. Estimates for the analysis were based on previous studies using gap implants with and without bone morphogenetic protein [33, 34]. To show a twofold difference in percentage volume healing between gaps left empty or filled with DBM or devitalized DBM, combined with SDs of 50%, an alpha error level of 0.05, and a beta level error of 30%, the estimated (unpaired) sample size was six.

We used 15 skeletally mature male and female mongrel dogs, weighing between 35 and 40 kg, for all experiments. The primary implant protocol consisted of initial bilateral surgery, during which we inserted gap implants into the proximal femora, followed 8 weeks later by secondary bilateral surgery, when we inserted implants into the proximal humeri. Harvest of the bones 4 weeks after the second surgeries provided implant-bone constructs from each animal at 4 weeks and 12 weeks. An additional (control) protocol consisted only of humeral surgery; we inserted gap implants into the proximal humeri and left them empty in situ for 12 weeks before bone harvest. This study had institutional approval of surgical and animal care protocols.

In the primary implant protocol including nine dogs, we filled the proximal gap of each implant with either DBM or devitalized DBM (negative control), while leaving the distal gap empty (control), for both femora and humeri. In three dogs, we used DBM on one side and used devitalized DBM on the contralateral side in both femora and humeri. In a second group of three dogs, we used DBM on one side without implanting devitalized DBM on the contralateral side. In a third group of three dogs, we used devitalized DBM on one side without implanting DBM on the contralateral side. This protocol resulted in six data points for each material at 4 weeks (proximal humerus) and 12 weeks (proximal femur) (Table 1). The secondary implant protocol, designed to assess healing within proximal empty gaps as further verification of the critical gap

Table 1. Allocation of 15 adult mongrel dogs into the various experimental groups

Time (weeks)	Gap treatment	First protocol*			Second protocol†	Sample size (n)
		3 dogs	3 dogs	3 dogs		
4	DBM	3	3			6
	Devitalized DBM	3		3		6
	Distal empty	6	3	3		12
12	DBM	3	3			6
	Devitalized DBM	3		3		6
	Distal empty	6	3	3		12
	Proximal empty				6	6

* In the first protocol, nine dogs underwent implantation in the femora and humeri to obtain the data points shown in the table; † in the second protocol, six dogs underwent humeral implantation to obtain the data points shown in the table; DBM = demineralized bone matrix.

size, consisted of six dogs with six empty gaps in the humeri at 12 weeks (Table 1).

We induced anesthesia using sodium pentobarbital and maintained it with 3% isoflurane and oxygen. We administered intravenous cefazolin in two 0.5-g doses in sterile water, once before and after surgery. The left hindlegs (or forelegs) were shaved and prepared in standard fashion. After making a small incision over the proximal end of the femur (or humerus) and splitting the gluteus medius (or rotator cuff), we drilled a 5-mm pilot hole into the intramedullary canal of the femur (or humerus), a procedure much like a blind intramedullary rodding. We progressively enlarged the hole in 0.5-mm increments to 11 mm using reamers. After filling an implant gap with 1.8 g ($\pm 10\%$) of DBM or devitalized DBM using manual pressure to ensure dense and uniform filling, we inserted the implant into a hollow, thin-walled stainless steel tube with an inner diameter of 11.3 mm. Then, we inserted the tube at the proximal opening of the reamed hole, placed an inserter rod into the other tube end, and gently tapped the implant down the intramedullary canal of the bone until it was positioned within metaphyseal cancellous bone. This insertion technique ensured containment of graft material within the implant gap and controlled placement of each implant. The surgical wound was closed in layers using Vicryl® (Ethicon, Inc, Somerville, NJ) sutures. Analgesia consisted of a 100-mg fentanyl patch placed before surgery and intramuscular buprenorphine (0.02 mg/kg) immediately after surgery and twice over the following 16 hours. We repeated the procedure on the contralateral femur (or humerus) for the primary implant protocol. All dogs returned to normal weightbearing activities 1 to 2 days after surgery; there were no infections or postoperative complications. Postoperative management included environmental enrichment and daily exercise for 1 hour. At the end of each experiment, euthanasia was induced with an overdose of intravenous pentobarbital (120 mg/kg).

We scanned the femora and humeri with a high-voltage, high-resolution X-Tek micro-CT scanner (Model XTH 225; Nikon Metrology, Leuven, Belgium) [19]. We imaged the bone samples in water at 135 kV and 65 μ A, with a 0.5-mm copper filter and 1000-ms exposure time to obtain 18- μ m-thick serial images of the complete bone-implant construct. Using CT Pro 2.0 (Metris, Derby, UK), we were able to reconstruct raw images and used the resulting 3000 serial CT images of each specimen to quantify gap healing using image analysis software ORSVisual v1.5.1.1371 (Objects Research Systems, Montreal, Canada). Bone that formed within the 3-mm implant gaps was measured and expressed as a volume percentage of the gap. In similar fashion, we measured the density of host cancellous bone immediately adjacent to each implant gap (proximal and distal) to compare with and normalize the gap healing data.

We subsequently embedded specimens in acrylic and imaged undecalcified transverse serial sections through the gap regions using backscattered SEM (three sections/images per gap). Using ImageJ software v.1.6.0_12 (National Institutes of Health, Bethesda, MD) and Bone Ingrowth Macro (SA Hacking, ImageJ Macro PTBI v1.0), we analyzed digital images for quantitative measurements of the mean percentage of filling of the implant pores with new bone and the mean percentage of bone apposition to the perimeter of the implant. We estimated the effect of empty controls compared to devitalized DBM controls and DBM on gap healing, bone ingrowth, and apposition using a Bayesian hierarchical (random effects) linear model. Differences between outcomes were expressed with 95% credible intervals (95% CrIs). Independent variables in the model included host bone, number of weeks, and treatment. We ran models both with and without an interaction term between weeks and treatment. A random intercept term was used to account for possible baseline differences between dogs. All analyses were conducted using WinBUGS v.1.4.3 (MRC Biostatistics Unit, Cambridge, UK).

Results

Whereas post-harvest radiographs revealed no differences in gap filling between the experimental and control groups, the 3D micro-CT scans provided clear visualization of the bone-implant gaps and differences between treatments (Fig. 2). Qualitatively, the micro-CT scans revealed only small amounts of gap healing in the empty and devitalized DBM-filled gaps, which formed mainly at the borders of the peri-implant host bone (Fig. 3). The gaps filled with DBM showed substantial bone healing compared with the controls, more so at 12 weeks than 4 weeks, apparent on both cross-sectional (Fig. 4) and longitudinal micro-CT sections. However, the trabecular thickness and connectivity of new bone in the gaps were generally less than those of peri-implant native bone (Fig. 2B). At 4 and 12 weeks, only 33% of the implant gaps filled with devitalized DBM showed any bridging between native host bone and the implant. In contrast, the DBM-filled gaps typically had islands of newly formed bone that could be visualized throughout the width and depth of the entire gap (Fig. 3), with 67% of the implant gaps showing such bony bridging at 4 weeks and 100% by 12 weeks. Also apparent from the micro-CT images were more bone ingrowth and bone-implant apposition with DBM-filled gaps compared with controls (Fig. 4).

Quantification of volumetric gap healing at 4 weeks using micro-CT showed absolute mean values of 5.3%, 4.3%, and 10.2% for the distal empty gap, the devitalized DBM, and the DBM groups, respectively (Fig. 5).

Fig. 2A–B (A) A 3D micro-CT image shows a gap implant within the proximal femur at 12 weeks that was filled with devitalized DBM. Only a small amount of bone is present within the gap, with little bridging to the surrounding host bone. (B) A 3D micro-CT image shows a gap implant within the proximal femur at 12 weeks that was filled with DBM. The gap is substantially filled with new bone and there is extensive connectivity between the implant and host bone.

Fig. 3A–F (A) A longitudinal micro-CT image at 4 weeks shows an empty gap in the humerus. (B) A longitudinal micro-CT image at 12 weeks shows an empty gap in the femur. (C) A longitudinal micro-CT image at 4 weeks shows a gap in the humerus filled with devitalized DBM. (D) A longitudinal micro-CT image at 12 weeks shows a femoral gap filled with devitalized DBM. (E) A longitudinal micro-CT image at 4 weeks shows a gap in the humerus filled with DBM. (F) A longitudinal micro-CT image at 12 weeks shows a femoral gap filled with DBM. The images further depict greater bone healing inside gaps filled with DBM compared to the other treatment groups.

At 4 weeks, the mean absolute increase in gap filling using DBM was 5.1% (95% CrI, 1.6%–8.5%). By 12 weeks after surgery (Fig. 5), the absolute mean gap healing using DBM was 18.7%, with an absolute mean of 12.3% greater gap

Fig. 4A–F (A) A 12-week micro-CT image shows an empty gap region in the femur. (B) A 12-week SEM image shows the corresponding empty gap region depicted in (A). (C) A 12-week micro-CT image shows a gap region in the femur that was filled with devitalized DBM. (D) A 12-week SEM image shows the corresponding gap region depicted in (C). (E) A 12-week micro-CT image shows a gap region in the femur that was filled with DBM. (F) A 12-week SEM image shows the corresponding gap region depicted in (E). New bone is present deep within the pores of the implant. The images illustrate the additional bone healing, bone apposition to the implant, and bone ingrowth using DBM.

filling (95% CrI, 8.8%–15.9%) than the distal empty gap (3.6%), proximal empty gap (6.5%), and the devitalized DBM (8.6%) control groups. None of the control groups

Fig. 5 A graph shows the mean and SD of the absolute percent volumetric filling of the implant gaps for each of the treatment groups at 4 weeks and 12 weeks quantified using micro-CT scans. At 4 weeks, the mean absolute increase of 5% gap filling using DBM (95% CrI, 1.6%–8.5%) is equivalent to approximately twice as much bone compared to empty and negative control groups. The amount of bone in the gap increased by an absolute mean of 8.5% by 12 weeks (95% CrI, 5.2%–10.2%), and this increase led to a greater absolute difference of 12.3% gap filling when compared to the empty and negative controls (95% CrI, 8.8%–15.9%). The micro-CT scans generated data that were volumetric and quantified the complete gap, instead of the usual two-dimensional analysis of histologic sections as a sampling of the whole experimental region.

substantially differed from each other or increased with time (all 95% CrIs included negative values and overlapped with a zero difference). Between 4 and 12 weeks (Fig. 5), there was an absolute increase in gap filling of 8.5% (95% CrI, 5.2%–10.2%).

The average ($\pm$ SD) peri-implant bone density for the humeri was 17.1% ($\pm$ 4.5%) adjacent to proximal implant gaps and 13.8% ($\pm$ 3.4%) adjacent to distal implant gaps. For the femora, the mean host bone density was 19.1% ($\pm$ 7.7%) adjacent to proximal gaps and 10.0% ($\pm$ 3.8%) adjacent to distal gaps. Peri-implant bone densities were used to normalize the gap healing data for each implant at each time period (Fig. 6). On average, gap healing using DBM reached 64% and 93% of the density of peri-implant bone by 4 and 12 weeks, respectively. The normalized data showed DBM-filled gaps contained more bone (Fig. 6) than either the empty gaps or gaps filled with devitalized DBM by an absolute mean of 28.3% at 4 weeks (95% CrI, 8.7%–47.8%) and 67.5% at 12 weeks (95% CrI, 47.9%–87.1%). Between 4 and 12 weeks, there was an absolute increase of 29.2% (95% CrI, 18.3%–41.5%).

Mean bone ingrowth values associated with empty gaps and those filled with devitalized DBM were small, ranging between 1.5% and 3.2% at 4 and 12 weeks, with no substantial increases between these time periods (Fig. 7). In contrast, the mean extent of bone ingrowth using DBM reached 10.7% at 4 weeks, greater than the control groups by an absolute mean of 7.9% (95% CrI, 3.6%–12.2%), and

Fig. 6 A graph shows the mean and SD of the percent volumetric filling of the implant gaps for each of the treatment groups at 4 weeks and 12 weeks after being individually normalized according to the density of adjacent cancellous bone obtained from the same micro-CT scans. Similar to the absolute values, there was more bone in gaps filled with DBM compared to the other treatment groups at 4 weeks (absolute mean of 28.3% more bone; 95% CrI, 8.7%–47.8%) and even more so at 12 weeks (absolute mean of 67.5% more bone; 95% CrI, 47.9%–87.1%), an absolute increase of 29.2% (95% CrI, 18.3%–41.5%). Normalizing the data not only overcame the issue of individual variance of bone density, regeneration, and implant placement but also gave context to the absolute values. The 19% filling of gaps packed with DBM at 12 weeks actually had bone healing that reached 93% of the peri-implant host cancellous bone density.

Fig. 7 A graph shows the mean and SD of the percent bone ingrowth for each of the treatment groups at 4 weeks and 12 weeks obtained from analysis of backscattered SEM images of histologic sections. Bone-implant ingrowth forms the mechanical interlock required for biologic fixation. There is an absolute mean of 7.9% more bone ingrowth in implants filled with DBM compared to the empty or negative controls at 4 weeks (95% CrI, 3.6%–12.2%) and an absolute mean of 22.7% greater at 12 weeks (95% CrI, 18.5%–27.0%).

25.6% at 12 weeks, an even larger absolute increase of 22.7% compared with controls (95% CrI, 18.5%–27.0%). In five of the six cases using DBM, histology sections showed extensive new bone deep within the center of the porous implants (Fig. 4E).

Fig. 8 A graph shows the mean and SD of the percent bone apposition for each of the treatment groups at 4 weeks and 12 weeks obtained from SEM. Bone-implant apposition also contributes to the mechanical link that is the basis of biologic fixation. As with the ingrowth data, implants filled with DBM had an absolute mean of 8.0% more bone-implant apposition compared to the empty and negative controls at 4 weeks (95% CrI, 4.2%–11.8%) and 10.2% at 12 weeks (95% CrI, 6.4%–13.9%).

The mean apposition of new bone to the perimeter of the porous implants was also limited for empty and devitalized DBM-filled gaps, ranging from 0.8% to 2.5% between 4 and 12 weeks (Fig. 8). Implants with DBM-filled gaps had mean bone apposition of 10.6% at 4 weeks, an absolute mean of 8.0% more apposition than the controls (95% CrI, 4.2%–11.8%), and 12.8% at 12 weeks, an absolute mean of 10.2% more apposition than the controls (95% CrI, 6.4%–13.9%).

Discussion

DBM is widely studied for use in diverse applications, such as fracture healing and spine fusion, but surprisingly very little in the context of revision arthroplasty, where it could have utility for gap healing and enhancement of porous implant fixation. An ideal bone graft substitute material would promote relatively fast and substantial healing of critically sized bone-implant gaps, in addition to mechanical connectivity with the porous implant by bone ingrowth. We assessed the extent to which DBM induced peri-implant bone formation, bone ingrowth, and bone apposition using porous titanium implants in a canine gap model.

There are several limitations to this study. First, the gap implant was nonfunctional and essentially unloaded, in contrast to the clinical scenario. Utilizing a functional implant introduces a second, uncontrolled variable into the experiment; it was thought more scientifically rigorous to eliminate load as a potential confounding factor. Furthermore, in complex revision surgery, patients are often kept

minimally or nonweightbearing for up to 12 weeks post-operatively. Second, the metaphyseal cancellous bone bed within the proximal femur and humerus is not homogeneous in density, with a tendency toward lower density distally. This had the effect of placing distal empty implant gaps in host bone of less density than the proximal gaps filled with DBM. Related to this was that not all implants were placed in the exact same position in the proximal femur or humerus, resulting in further differences in peri-implant bone density. This limitation was addressed in two ways: the data were normalized relative to adjacent host bone density and a separate, 12-week experiment was conducted in the humerus with the empty gaps in the proximal position to definitively establish the 3-mm gap was of at least critical size. Third, the amount of DBM varied somewhat within each gap ($\pm 10\%$) due to the nature with which it was manually packed around each implant. However, the differences in bone healing between regular and devitalized DBM were much greater than the variation in the amount of material used between implants. We only evaluated one formulation of DBM with recognition that there are wide variations among commercially available formulations, differing in percentage content, carrier material, and osteoinductive index. We elected to custom-fabricate DBM made from canine cortical bone allograft using an established commercially available process with a documented history of high osteoinductive index and proven clinical results. This was coupled with fabrication of devitalized DBM as a negative control to enable a definitive answer to the question regarding osteoinductivity in an orthotopic implant site. Finally, the study was conducted in healthy animal bone, unlike a revision scenario where the bone bed may be partially absent, sclerotic, or deficient in osteoprogenitor cells. DBM has been shown to be effective, however, in a variety of clinical scenarios in patients of different ages and bone healing potential [21].

The finding of greater amounts of bone formation and bone ingrowth in gap regions filled with regular DBM definitively answered the question about whether the material possesses osteoinductive potential in an orthotopic bone site. This information has particular importance because devitalized DBM has never before been utilized as a negative control in any type of gap or fracture healing or joint reconstruction study. New bone formation within empty gaps only reached mean absolute values of approximately 5% at 4 and 12 weeks. This was consistent with the data of Sumner et al. [34] who reported gap healing of 5.3% in a canine humerus 3-mm gap implant model at 4 weeks. There was no substantial difference in empty gap healing between 4 and 12 weeks; this enabled meaningful evaluation of the relative effectiveness of DBM for promoting bone formation inside a gap that showed

little spontaneous healing. The only prior study that can be somewhat compared with our study is that of Shih et al. [33], which measured healing within 3-mm gaps using porous-coated implants placed within the canine distal femur. Compared with our study, they found the formulation of partially DBM had much higher residual mineral content (~2% versus < 0.5%), the host cancellous bone in the distal femur had a much higher mean native density than in the proximal femur or humerus (33.7% versus 18.7%), and the implantation period was much longer (26 weeks versus 4 and 12 weeks). Empty control gaps and gaps filled with the partially DBM showed 16.6% and 22.6% volume filling, or approximately 50% and 67% of the density of adjacent host bone, respectively. This difference was not statistically significant. In contrast, our study of DBM demonstrated a mean normalized gap filling of 64% by 4 weeks, essentially the same as reported by Shih et al. [33] at 26 weeks, and 93% or almost complete healing by 12 weeks. Both normalized values were greater than those occurring in control gaps or those filled with devitalized DBM. From a clinical perspective, this is valuable information, demonstrating the additional bone healing derived from using DBM occurs to a relatively great extent within a relatively short time period.

Revision of loose total hip components remains a challenge for the surgeon as the reconstruction must encompass both restoring bone stock and obtaining fixation. This study clearly demonstrated these two goals can be effectively and reproducibly achieved with the use of DBM to fill the bony gaps around porous implants. Furthermore, gap healing closely approaching peri-implant bone density and excellent mechanical connectivity of the implant by bone ingrowth and apposition occurred within 12 weeks of surgery. This is a clinically relevant time period by which a patient would be expected to safely begin full weightbearing. Failure to identify these advantageous features in the past has resulted in DBM being almost completely ignored as a viable bone graft substitute material in revision THA.

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