Segmental long bone defects resulting from injury or surgical intervention are difficult problems to manage. Amputation, external fixators, vascularized fibular grafts, acute limb shortening, and various quantities of allograft and autograft have historically been the mainstays of treatment. Recently, the use of osteoinductive substances such as recombinant bone morphogenic proteins, and osteoconductive scaffolds such as calcium phosphate have found use in the treatment of these clinical situations. More recently, Masquelet described the use of a cement spacer placed within the osseous void followed by staged bone grafting within the induced biomembrane formed around the spacer as a potential treatment strategy to manage these large defects.

This article describes a series of 11 patients for which we used this technique of staged bone grafting following placement of an antibiotic spacer to successfully manage osseous long bone defects ranging from 4 to 15 cm. The limbs were stabilized and aligned at the time of initial spacer placement with a plate and screw construct, intramedullary nail, or fine wire fixator. Osteoinductive substances including bone morphogenic protein-2 and platelet rich concentrate were used in addition to allograft to improve bony healing. In our series, osseous consolidation and full weight bearing was achieved in 10 of 11 patients. Two patients developed heterotopic ossification. There was 1 non-union and 1 infection, which occurred in the same patient. Staged bone grafting within an induced biomembrane created after the use of a cement spacer is a reasonable option in the management of both acute and delayed segmental long bone defects.

Drs Donegan, Scolaro, Matuszewski, and Mehta are from the Department of Orthopaedic Surgery, University of Pennsylvania Health System, Philadelphia, Pennsylvania.

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Correspondence should be addressed to: Samir Mehta, MD, Department of Orthopaedic Surgery, Hospital of the University of Pennsylvania, 2 Silverstein, 3400 Spruce St, Philadelphia, PA 19104 (samir.mehta@uphs.upenn.edu).

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Segmental osseous defects from traumatic injury or surgical intervention (eg, infections or tumors) are complicated problems with significant long-term morbidity. Historically, due to the difficulty in managing segmental long bone defects, amputation was the preferred treatment. Alternatives to amputation allowing limb salvage have been developed over the last half century. During World War II, massive cancellous bone autograft had been the principle alternative. The use of the Ilizarov technique, vascularized fibular grafts, and acute limb shortening have been used previously to address defects of various lengths. Newer recombinant bone morphogenic proteins (BMPs) and calcium phosphate fillers have also been used to treat this complex problem. More recently, the staged use of an antibiotic cement spacer followed by grafting within this space under the induced biomembrane formed around the spacer has been described as a potential treatment strategy. This article describes a small series of patients at our institution successfully treated with this technique.

**Materials and Methods**

We performed a retrospective review between 2007 and 2010 of all patients at a single institution who had sustained a long-bone segmental defect managed by initial placement of an antibiotic spacer block with staged bone grafting (Table). The patients were evaluated for injury type, location, and mechanism; defect size; type of cement spacer; date of cement spacer placement; date of definitive treatment; type of definitive stabilization; material used to fill the void; date to union; date to full weight bearing; demographic data; and complications. Complications were considered nonunion, need for further surgery, infection, deep venous thrombosis (DVT), and/or pulmonary embolus. The review was carried out in accordance with the protocol approved by our Institutional Review Board.

**Surgical Technique**

The segmental bone defect (Figure 1) is approached in a staged fashion with the second stage performed approximately 4 to 5 weeks from the placement of the spacer. During the first stage, the operative extremity is prepped and draped in the usual sterile fashion. The area of bone loss is carefully debrided and irrigated, removing any gross debris and nonviable tissue. Material used to fill the void includes various donor sources such as cancellous allograft, iliac crest bone graft, platelet-rich concentrate, bone morphogenetic proteins, demineralized bone matrix, and autologous bone. The antibiotic cement spacer may be used to fill the void, and the area is allowed to heal for approximately 4 weeks before proceeding with the second stage.

**Table**

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Type of Injury</th>
<th>Injury Mechanism</th>
<th>Defect Size, cm</th>
<th>Acute Injury</th>
<th>Spacer</th>
<th>Bone Graft/Osteoinduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/31</td>
<td>Chronic infected tibial plateau &amp; shaft</td>
<td>Hit by car</td>
<td>5</td>
<td>N</td>
<td>Antibiotic block &amp; antibiotic nail</td>
<td>ICBG</td>
</tr>
<tr>
<td>2/F/34</td>
<td>Open supracondylar femur (type IIIa)</td>
<td>MVC</td>
<td>10</td>
<td>Y</td>
<td>Antibiotic block</td>
<td>DBM, PRC, BMP-2, ICBG, cancellous allograft</td>
</tr>
<tr>
<td>3/M/35</td>
<td>Chronic infected femoral allograft &amp; nail</td>
<td>Sarcoma resection</td>
<td>15</td>
<td>N</td>
<td>Antibiotic block &amp; antibiotic nail</td>
<td>DBM, PRC, BMP-2, cancellous allograft</td>
</tr>
<tr>
<td>4/F/84</td>
<td>Chronic infected proximal tibia nonunion</td>
<td>MVC</td>
<td>4</td>
<td>N</td>
<td>Antibiotic block</td>
<td>DBM, BMP-2</td>
</tr>
<tr>
<td>5/M/34</td>
<td>Open distal third tibia fracture (type IIIb)</td>
<td>MVC</td>
<td>5.5</td>
<td>Y</td>
<td>Antibiotic block</td>
<td>DBM, BMP-2, PRC, cancellous allograft</td>
</tr>
<tr>
<td>6/M/58</td>
<td>Open supracondylar femur (type IIIa)</td>
<td>MVC</td>
<td>10</td>
<td>Y</td>
<td>Antibiotic block</td>
<td>DBM, PRC, autograft (hip HO)</td>
</tr>
<tr>
<td>7/M/15</td>
<td>Open supracondylar femur (type IIIa)</td>
<td>Hit by train</td>
<td>15</td>
<td>Y</td>
<td>Antibiotic block</td>
<td>DBM, BMP-2, PRC, cancellous allograft</td>
</tr>
<tr>
<td>8/F/52</td>
<td>Nonunion s/p open supracondylar femur (type IIIa)</td>
<td>Fall</td>
<td>6</td>
<td>N</td>
<td>Antibiotic block</td>
<td>DBM, BMP-2, PRC, cancellous allograft</td>
</tr>
<tr>
<td>9/M/40</td>
<td>Chronic proximal third tibia nonunion</td>
<td>Crush</td>
<td>7</td>
<td>N</td>
<td>Antibiotic block</td>
<td>DBM, BMP-2, autograft (RIA)</td>
</tr>
<tr>
<td>10/M/67</td>
<td>Open tibia fracture (type IIIb)</td>
<td>Fall</td>
<td>8</td>
<td>Y</td>
<td>Antibiotic block</td>
<td>DBM, BMP-2, cancellous allograft</td>
</tr>
<tr>
<td>11/M/50</td>
<td>Chronic infected pilon fracture</td>
<td>Fall</td>
<td>8</td>
<td>N</td>
<td>Antibiotic block</td>
<td>DBM, BMP-2, cancellous allograft</td>
</tr>
</tbody>
</table>

Abbreviations: BMP-2, bone morphogenetic protein 2; DBM, demineralized bone matrix; HO, heterotopic ossification; ICBG, iliac crest bone graft; MVC, motor vehicle collision; PRC, platelet-rich concentrate; RIA, reamer–irrigator–aspirator; s/p, status post.
pieces of bone or soft tissue. We prefer gravity lavage to reduce the insult to the soft tissues. Careful dissection is then performed down to the fracture site and the fracture ends are identified and debrided again. Based on preoperative templating, the length, alignment, and rotation of the injured limb is obtained. Fracture type and location determine the appropriate implant (ie, plate and screw device vs intramedullary nail) for fixation. Once acceptable fracture reduction is achieved (ensuring anatomic length, alignment, and rotation), fixation is undertaken.

Once fixation has been achieved, attention is then turned to the bone defect. The defect is measured and filled with a spacer made from polymethylmethacrylate (PMMA) bone cement (Simplex; Stryker, Mahwah, New Jersey). The amount of PMMA necessary to fill the void is based on the size of the defect. If concern exists for infection or the fracture is open, the cement may be mixed with vancomycin and/or tobramycin. We prefer to use 2 g vancomycin and 2.4 g of tobramycin per 40 g of cement prepared. It is essential to fill the entire defect with the antibiotic spacer, from bone end to bone end (Figure 2). Cement polymerization is an exothermic reaction that results in a slight amount of expansion in the initial volume of cement placed. For this reason, if too much cement is placed, it can be difficult to remove when the defect is later revisited for grafting. Therefore, we prefer to slightly undersize the cement block to allow for easier retrieval. The wound is then closed in a layered fashion with a watertight fascial closure, followed by skin closure using the Donati-Allgöwer technique. This reduces the chance of wound drainage and/or compromise to the soft tissue envelope.

At the second stage, performed 4 to 5 weeks later if soft tissue permits, the patient is positioned in an identical manner as the first stage. If bone graft is to be harvested from the iliac crest, femoral canal, or other area, this should also be considered. The fracture is approached through the previous incision and careful dissection is performed down to the defect. If a plate and screw device was used, the pseudosynovial membrane will often form around the plate as well as the cement spacer. The plate, however, is palpable under the membrane. The biomembrane encapsulating the cement spacer is incised along the anterior border of the plate leaving enough tissue to reapproximate at the end of the case. Once exposed, the cement spacer is removed en bloc or in a piecemeal fashion. An osteotome can be used to longitudinally split the cement spacer into smaller pieces before removal. It is critical to be sure to remove all of the cement. It is tempting to lever on the plate to remove the spacer, but this should be avoided so as not to have unnecessary stress applied to the surgical construct. Once the cement spacer is removed, the biomembrane capsule is irrigated to remove any residual debris, being sure not to violate the membrane at any point.

With the defect open, bone graft and bone graft substitute is placed to fill the entire defect. A defect-filling osteoconductive material is necessary because these defects are often large enough that there is inadequate autograft available to fill the entire defect. In addition, osteoinductive and osteogenic agents can be used at the discretion of the surgeon. Our preference is to use crushed cancellous allograft, demineralized bone matrix (DBM...
Grafton; Osteotech Inc, Eatontown, New Jersey), bone morphogenic protein-2 (BMP-2) (Infuse; Medtronic, Memphis, Tennessee), and local or iliac crest bone graft. Platelet-rich concentrate (Caption; Smith & Nephew, Memphis, Tennessee) was also included in certain instances. The defect should be completely filled, but not overstuffed. Overfilling the defect will prevent closure of the biomembrane. Once the defect is filled, the biomembrane is closed with absorbable Vicryl suture (Ethicon, Inc, Somerville, New Jersey), followed by wound closure in a layered fashion. Again, it is important to obtain a watertight fascial closure, followed by skin closure using Donati-Allgöwer technique.23 Patients are allowed immediate passive motion and weight bearing is determined by fracture location and stability. Weight bearing is increased starting approximately 6 weeks after the second stage based on radiographic healing and formation of new bone (Figure 3).

RESULTS

A total of 11 consecutive patients were identified within the time period. All patients were treated by the senior author (S.M.) and deemed at the time of presentation to require staged management of their osseous defects. Eight men and 3 women had an average age of 45.4 years (range, 15-84 years). Five femurs and 6 tibias were treated with this technique. There were 5 cases of acute traumatic bone loss, 3 cases of an infected nonunion, 2 cases of sterile nonunions, and 1 case of delayed infection following femoral resection. Average time from spacer placement to definitive treatment was 58 days (range, 32-92 days).

Definitive stabilization included plating (8 patients), intramedullary nailing (2 patients), and revision from a plate construct to a fine-wire fixator at the time of staged bone grafting (1 patient). Type of fixation (plate or nail) was determined by location and morphology of the defect. In 2 cases, an antibiotic intramedullary nail was placed at the time of spacer placement because an infected intramedullary device had been removed. At the time of bone grafting, provisional fixation of the limb was achieved with an external fixator, the antibiotic nail and spacer were removed and an unreamed intramedullary device was then placed. The contralateral limb was used to determine overall length, alignment and rotation. Throughout the procedure, care was taken to avoid injury to the biomembrane.

The void left by the antibiotic spacer was filled with a combination of allograft, autograft (when available) BMP-2, de-mineralized bone matrix, and platelet-rich concentrate. The senior author made the determination of which biologics were used at the time of surgery. In almost all cases, cancellous allograft and demineralized bone matrix was used to provide the majority of the volume to the implanted graft. Bone morphogenic protein was also used in every case except for 2. In the first case, the treating surgeon did not want to use BMP-2 at the time of grafting, and in the second, there was adequate autograft available following resection of heterotopic bone from the patient’s ipsilateral hip as well as the predisposition of this specific patient to form heterotopic bone. In all cases, if an adequate quantity of autograft was not available, and the patient consented to the use of platelet rich concentrate, it was also used. A specific formula for which biologic substances are used at the time of grafting has not been standardized but is the focus of continued research.

Ten of the 11 patients (90%) demonstrated radiographic consolidation of the defect an average of 226 days after definitive fixation. Ten of the 11 (90%) were full weight bearing an average 133 days after definitive fixation. There was 1 nonunion (9%) and 1 infection (9%), both of which occurred in the same patient. Interestingly, this nonunion occurred in the only patient who had iliac crest bone graft alone added to the void at the time of secondary bone grafting. One patient required hardware removal (9%) and 2 (18%) developed heterotopic ossification. No DVTs or pulmonary emboli were reported.

DISCUSSION

Treatment of large segmental bone defects can be challenging for orthopedic surgeons. Bone grafting of these defects is often delayed after primary fixation to allow soft tissue healing, decrease the risk of infection, and prevent graft resorption during the early inflammatory healing phase.23 In traumatic wounds, antibiotic impregnated cement beads or spacers are often used for local antibiotic administra-
tion to the soft tissue bed or within an osseous defect. In addition, the advantages of inserting such a spacer include maintaining the void to allow for later placement of graft, providing structural support, offloading the implant, and inducing the formation of a biomembrane, which can function to contain secondary grafting.

Masquelet and Masquelet et al first described this technique of formation of a pseudosynovial membrane around a cement spacer with later bone grafting of the defect, proposing that this membrane prevents graft resorption and improves vascularity and corticalization. It has been described that after the initial placement of the antibiotic impregnated spacer, 4 to 5 weeks is needed for development and maturation of a biologically active membrane suitable for grafting. The spacer also maintains the defect and inhibits fibrous growth. Recent literature has shown that this biomembrane can be 0.5 to 1 mm thick and has been described as both hypervascular and impermeable. Pelissier et al studied the properties of this membrane in a rabbit model and found that it secreted several growth factors including BMP-2, vascular endothelial growth factor, and transforming growth factor β-1 (TGF-β1). Their research revealed that levels of BMP-2 were highest at 4 weeks. Finally, Viateau et al studied this technique in a sheep model and found that the membrane alone was inadequate to heal a large defect, but when autologous bone graft was placed within the membrane, all of the defects studied went on to heal.

The technique of inducing a biomembrane at the site of an osseous defect with staged grafting has been described in multiple case reports for defects of various sizes and in various locations throughout the skeletal system. Biua et al described the management of a 16-cm defect in the femur of a 12-year-old child who had been diagnosed with Ewing’s sarcoma and required resection of a large segment of his femur. The segmental defect was stabilized with an intramedullary nail, then maintained with an antibiotic spacer until later grafting and eventual healing.

As mentioned, the technique has been used to address bone loss in areas other than long bones. Huffman et al reported use of the technique in a significant area of bone loss in the midfoot of a patient who had sustained multiple gunshot injuries. They obtained medullary autograft with the reamer-irrigator-aspirator from the ipsilateral femur for placement within the defect area, which was then stabilized with a plate and screw construct.

The original description of this technique described stabilization of the bone with an external fixator, but as noted, other means of fracture fixation have been used with success. Aparid et al reported a series of 12 patients who presented with segmental defects in the tibia >6 cm, all of whom were initially fixed with an intramedullary nail. They reported healing following the second-stage procedure in 11 of 12 patients at an average of 4 months. Our series included patients who had fracture fixation with both intramedullary implants and locked plate constructs. To our knowledge, no study has evaluated the optimal biomechanical environment for such a technique, rather each fracture is “bridged” according to the treating surgeon’s assessment of the fracture. A potential effect of a construct that is too rigid may be stress shielding near the plate, reducing integration of the bone graft near the implant. This does not preclude bony union but may increase time to osseous consolidation and affect the radiographic appearance of the defect.

The technique as described by Masquelet and Begue relies on the placement of morselized cancellous autograft harvested from the iliac crests within the biomembrane lined defect. If this amount is not sufficient, demineralized allograft is added to the autograft in a ratio that does not exceed 1:3. No studies have compared the use of different auto- or allograft compositions used with this technique. Biua et al used both iliac crest corticocancellous autograft as well as a medial tibial cortical strut autograft to fill their large defect. Use of cancellous autograft from the femoral canal has also been described, and evidence exists to show that levels of many growth factors (fibroblast growth factor-α, platelet-derived growth factor, insulin-like growth factor 1, TGF-β1, and BMP-2) in femoral cancellous bone are present in higher concentrations than they are in iliac crest and platelet preparations.

In our series, we used a nonstandardized grafting technique that was determined by the individual defect size, patient profile, and senior author’s discretion. We used combinations of iliac crest bone graft, reamed femoral cancellous autograft, free fibula allograft, recombinant BMP, platelet-rich concentrate preparations, demineralized bone matrix allograft, and crushed cancellous allograft to fill the residual defects. Further research and clinical series will hopefully elucidate the grafting components necessary to optimize healing in these patients.

**CONCLUSION**

The technique of delayed bone grafting after initial placement of a cement spacer provides a reasonable alternative for the challenging problem of significant bone loss in extremity reconstruction. This technique can be used in either an acute or delayed fashion with equally promising results. The bioactivity of the membrane created by filling large bony defects with cement leads to a favorable environment for bone formation and osseous consolidation of a large void. As this technique becomes more widely applied, the answer to which graft substances to place in the void may become clearer. Increasing clinical evidence will also help support the use of this technique in treating segmental bone loss.

**REFERENCES**

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