

# Calcium phosphate cement and locked plate augmentation of distal femoral defects: A biomechanical analysis

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## ABSTRACT

**Purpose:** Bone tumors are common in the distal femur and often treated with intralesional curettage. The optimal method of stabilization of large distal femoral defects after curettage remains unclear. The goal of this study is to compare stabilization techniques for large distal femoral defects.

**Methods:** Large defects (60 cm<sup>3</sup>) were milled in the distal lateral metaphysis of 45 adult composite sawbone femurs. The defect was either (1) left untreated or reconstructed with (2) locked plate fixation, (3) calcium phosphate cement packing, or (4) locked plate fixation with calcium phosphate cement packing, or (5) polymethylmethacrylate packing. Each specimen then underwent axial and torsional stiffness testing followed by torsional loading to failure. The data were analyzed using ANOVA with Tukey–Kramer post-hoc analysis.

**Results:** The calcium phosphate cement filled defect with a locked plate was the stiffest construct in axial and torsional loading as well as the strongest in torque to failure. However, this difference only reached significance with respect to all other groups in torque to failure testing. The calcium phosphate cement filled defect with a locked plate was significantly stiffer than three of the four other groups in both axial and torsional stiffness testing.

**Conclusions:** These results indicate that calcium phosphate cement, with or without the addition of locked plate fixation, may provide improved construct stability under time zero testing conditions. This result warrants further testing under cyclic loading condition and consideration for fixation of large femoral metaphyseal defects in future clinical trials.

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## 1. Background

Bone tumors are relatively common in the distal femur and are often treated with intralesional curettage. Small metaphyseal defects do not require stabilization and typically heal without consequence. Larger metaphyseal defects, however, are associated

Abbreviation: CaPO<sub>4</sub>, Calcium Phosphate Cement.

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with pathologic fractures and early onset osteoarthritis [1]. Although this risk is reduced with stabilization, the optimal method of stabilization of large defects after curettage of the distal femur remains unclear [2–4].

Conventional materials used to fill the void left by tumor curettage include bone graft, polymethylmethacrylate, and a variety of bone graft substitutes. Autograft is an excellent source of bone graft, but is often associated with donor site morbidity and is limited in quantity [5]. Allograft bone sources typically include corticocancellous bone chips or demineralized bone matrix. Allograft is widely available; however, it possesses limited remodeling potential, significant cost, and the potential for disease transmission [6]. Additionally, both autograft and allograft provide very limited structural support.

Packing with polymethylmethacrylate cement is likely the most commonly utilized method of stabilization following curettage [7]. Although polymethylmethacrylate cement is extremely resistant to compressive loading, it does not permit bone remodeling. Also, polymethylmethacrylate is prone to fractures and may not be suitable in cases where adjunctive plate fixation is desired.

Commonly used bone graft substitutes include coralline hydroxyapatite granules, calcium sulfate cement, bioactive glass, and calcium phosphate cement [8]. Calcium phosphate cements have shown favorable osteoconductive properties in lapine models as well as increased donor site strength during split cranial bone grafting [9–10]. Biomechanical analysis of split-depression tibial plateau fractures has also shown significantly higher fatigue strength and ultimate load in cadaver models treated with calcium phosphate cement versus autogenous bone graft [11].

Clinically, calcium phosphate cement is frequently used for subchondral support in periarticular fractures in order to prevent articular surface subsidence. Clinical studies of the tibial plateau and proximal humerus have also shown excellent results with short to intermediate term follow-up [12–14]. Although results in fracture surgery are encouraging, little is known about the role of calcium phosphate cements following tumor curettage.

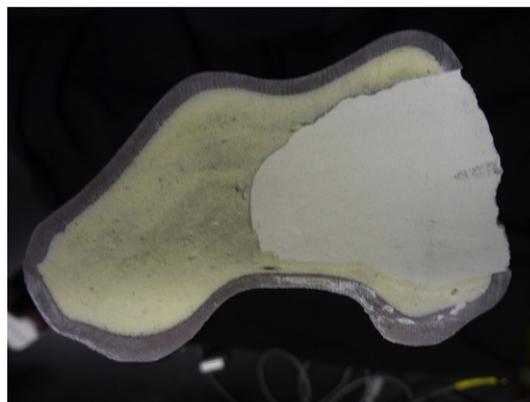
The goal of this study is to compare the initial biomechanics of commonly used techniques to treat large distal femoral defects. We hypothesized that: 1) defects packed with calcium phosphate cement would be stiffer and more resistant to torsional failure than an unpacked defect and 2) the addition of a locked plate would further increase the stiffness and torsional strength.

## 2. Methods

### 2.1. Specimen

Forty-five fourth generation composite large adult femurs (Sawbones, Pacific Research Laboratories, Vashon, WA) were evenly divided into five groups ( $n = 9$  per group). Sawbones were used instead of cadaveric specimens because of their consistent biomechanical properties. Defects to simulate tumor resection with pathologic fracture risk ( $60 \text{ cm}^3$ ) were precision milled in the distal lateral metaphysis (three-centimeter diameter cortical window) of each specimen using a preprogrammed computer numerical controlled machine (Figure 1) [1]. Care was taken to leave smooth edges and to avoid the generation of any artificial stress risers as a result of the machining process.

In the first group of femurs, the defects were left untreated in order to simulate packing with harvested autograft bone or allograft bone chips. No plating was performed. In the second group of femurs, the defects were left empty, but a customized (precontoured to the lateral face of the femur) stainless steel distal femoral lateral large fragment locking plate and screw construct (three screws in the metaphysis and three screws in the diaphysis with the plate) was applied (Acumed, Hillsboro, OR). In the third group of femurs, defects were packed with calcium phosphate cement (Callos Impact Cement, Acumed, Hillsboro, OR) and left unplated. In the fourth group of femurs, defects were packed with calcium phosphate cement and then a customized lateral locking large frag plate and screw construct (three screws in the cement three screws filled proximally) was applied. In the fifth group of femurs, defects were packed with polymethylmethacrylate cement (COE Tray Plastic, GC America, Alsip, IL) and left unplated.



**Figure 1.** Cross section of the femur taken through the apex of the calcium phosphate cement ( $\text{CaPO}_4$ ) filled defect, approximately at the level of the epicondylar axis. At least 2 mm of cancellous bone was left between the defect and the cortex at all points.

## 2.2. Biomechanical testing

The proximal and distal aspects of each femur were fixed into a custom jig that applied axial load and torque. The same servohydraulic axial/torsion material testing machine was used for each specimen (Model 809, Axial-torsional Load Transducer, Model 662.20C-04, Multipurpose Testware in the FlexTest GT controller, MTS Systems Corporation, Eden Prairie, MN). Each femur underwent axial and torsional stiffness testing followed by clockwise torsional loading of the proximal femur to failure. All tests were performed along the long axis of the femur to simplify the interpretation and extrapolation of data with respect to each defect.

For axial stiffness testing, each specimen was loaded from 20 N to 200 N for three cycles at 10 N/s. For torsional stiffness testing, each specimen was axially loaded to 200 N followed by the application of an external rotation moment along the long axis of the femur from 0.5 Nm to 12 Nm for three cycles at one Newton meter per second [15]. Axial and torsional stiffness was calculated from the linear portion of the load–displacement and torque–angle curves, respectively. All values were calculated for the entire construct in a grip-to-grip fashion.

Following stiffness testing, each specimen was failed in torsion at a rate of one Newton meter per second with axial preload held at 200 N. The failure load was defined as the maximum torque attained on the torque–angle graph (Figure 2).

## 2.3. Statistics

Continuous variables are reported as mean and standard deviation. All resultant data was analyzed using an ANOVA test with Tukey–Kramer post-hoc analysis (JMP 9, SAS, Cary, NC). A *p*-value of less than 0.05 was considered to be statistically significant. A power analysis based on pilot data revealed that a sample size of 9 would offer the ability to detect a difference of 0.9 Nm from an effect size of seven Newton meter with a standard deviation of 0.7 Nm between samples with 95% confidence and a statistical power greater than 80%.

## 3. Results

### 3.1. Fracture pattern

All experimental specimens failed with a spiral fracture pattern that originated within the defect and exited superiorly toward the diaphysis.

### 3.2. Axial stiffness

Axial stiffness testing revealed that the calcium phosphate cement filled defect with a locked plate was the stiffest construct ( $3.5 \pm 0.4$  N/m, Figure 3). This construct was 11% stiffer than the calcium phosphate cement filled defect ( $3.1 \pm 0.5$  N/m), 14% stiffer than the unfilled defect with a locked plate ( $3.0 \pm 0.4$  N/m), and 17% stiffer than the unfilled defect ( $2.9 \pm 0.3$  N/m). The increase in stiffness for the calcium phosphate cement filled defect with a locked plate was statistically significant when compared with the three aforementioned groups ( $p < 0.03$ ). Although the calcium phosphate cement filled defect with a locked plate was stiffer than the polymethylmethacrylate cement filled defect ( $3.1 \pm 0.8$  N/m), this difference did not reach statistical significance ( $p = 0.15$ ).

### 3.3. Torsional stiffness

Torsional stiffness testing revealed that the calcium phosphate cement filled defect with a locked plate was the stiffest construct ( $15.6 \pm 0.4$  Nm/degree, Figure 4). This construct was significantly ( $p < 0.01$ ) six percent stiffer than the unfilled defect

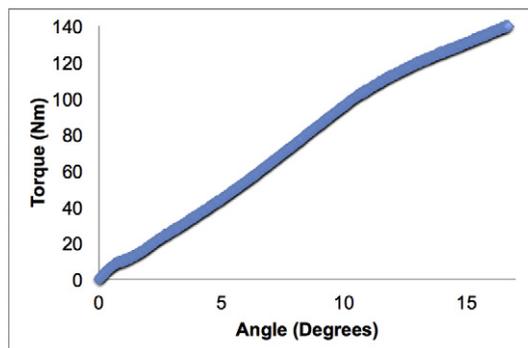
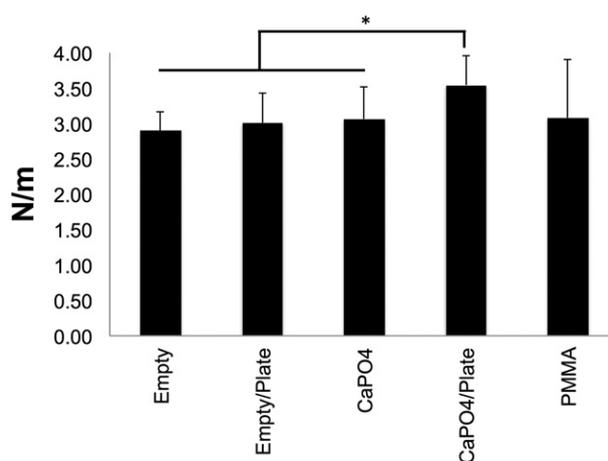


Figure 2. Example torque–angle curve.



**Figure 3.** Axial stiffness of empty, locked plate (Empty/Plate), calcium phosphate cement (CaPO<sub>4</sub>), calcium phosphate cement and locked plate (CaPO<sub>4</sub>/Plate), and polymethylmethacrylate cement (PMMA) constructs. \* is p-value <0.05 when compared to calcium phosphate cement and locked plate fixation.

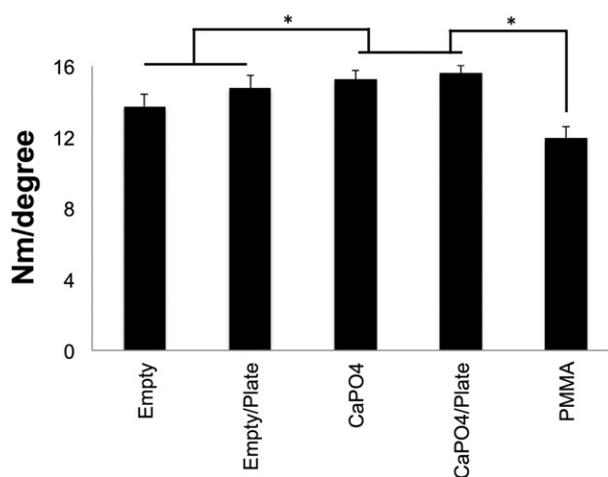
with a locked plate ( $14.7 \pm 0.7$  Nm/degree), 12% stiffer than the unfilled defect ( $13.7 \pm 0.7$  Nm/degree), and 31% stiffer than the polymethylmethacrylate group ( $11.9 \pm 0.6$  Nm/degree) but not significantly ( $p = 0.09$ ) stiffer than the calcium phosphate cement filled defect ( $15.3 \pm 0.5$  Nm/degree). The calcium phosphate cement filled defect group and calcium phosphate cement filled defect with a locked plate group had statistically significant increases in stiffness when compared with the unfilled defect and unfilled defect with locked plate groups ( $p < 0.01$ ).

### 3.4. Torque to failure

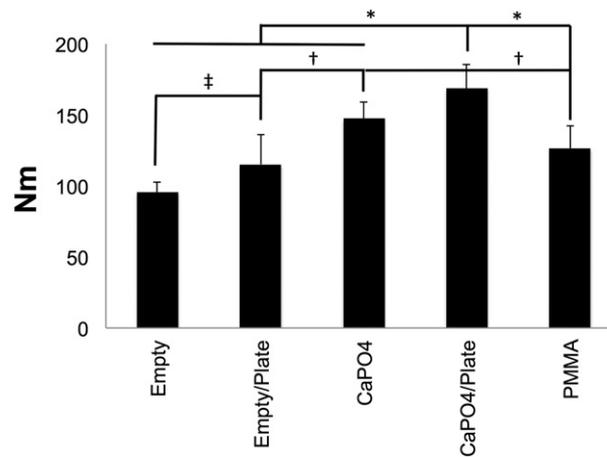
A calcium phosphate cement filled defect with a locked plate had the highest torque to failure ( $167 \pm 19$  Nm, Figure 5), which was statistically significant compared with the other four groups ( $p < 0.01$ ). This construct sustained 12% more torque than the calcium phosphate cement filled defect ( $147 \pm 18$  Nm), 31% more torque than the unfilled defect with a locked plate ( $115 \pm 14$  Nm), 33% more torque than polymethylmethacrylate ( $126 \pm 16$  Nm), and 43% more torque than the unfilled defect ( $96 \pm 13$  Nm). A calcium phosphate cement filled defect sustained 22% more torque than the unfilled defect with a locked plate and 35% more torque than the unfilled defect ( $p < 0.01$ ). Maximum torque for intact femurs was  $253 \pm 13$  Nm.

## 4. Discussion

The calcium phosphate cement filled defect with a locked plate was the stiffest construct in axial stiffness and torque to failure. However, in torsional stiffness calcium phosphate cement filled defect with or without a plate were indistinguishable. Several case series encourage curettage without defect filling or plating of benign bone tumors, but these series must be interpreted cautiously. Chigira et al. reported on seventeen patients with mixed diagnoses of benign tumors treated with curettage alone. In this series,



**Figure 4.** Torsional stiffness of empty, locked plate (Empty/Plate), calcium phosphate cement (CaPO<sub>4</sub>), calcium phosphate cement and locked plate (CaPO<sub>4</sub>/Plate), and polymethylmethacrylate cement (PMMA) constructs. \* is p-value <0.05 when compared to calcium phosphate cement and locked plate fixation.



**Figure 5.** Torque to failure of empty, locked plate (Empty/Plate), calcium phosphate cement (CaPO<sub>4</sub>), calcium phosphate cement and locked plate (CaPO<sub>4</sub>/Plate), and polymethylmethacrylate cement (PMMA) constructs. \* is p-value <0.05 when compared to calcium phosphate cement and locked plate fixation. † is p-value <0.05 when compared to calcium phosphate cement fixation. ‡ is p-value <0.05 when compared to locked plate fixation.

there were no adverse sequelae and the authors advocated that the implantation of “biomaterials” is unnecessary [16]. Similarly, Waldram et al. reported 20 cases of giant cell tumor of bone treated by curettage without defect filling or plating and reported no postoperative fractures [17]. However, half of the patients in the Chigira et al. series were skeletally immature, and accordingly, had tremendous remodeling capacity. Furthermore, several patients in this series had protected weight bearing for up to 24 months [16]. In the Waldram et al. series, there was no mention of lesion size and 30% of patients had recurrence that required endoprosthetic replacement [17]. A larger case series of 78 varied benign bone tumors treated with curettage alone reported only three (four percent) post-operative fractures [18]. This series, however, had a mean tumor volume of only 35 cm<sup>3</sup>. This is well under the metaphyseal defect volume reported to significantly increase the risk of post-operative fracture and joint degeneration [1]. The incidence of post-operative fracture in the Hirn et al. series for defects less than 60 cm<sup>3</sup> was only five percent, while it was 17% for defects larger than 60 cm<sup>3</sup>. The risk of post-operative joint degeneration for defects less than 60 cm<sup>3</sup> was only three percent, but it was 59% for defects larger than 60 cm<sup>3</sup>. These risks are sufficiently high in defects greater than 60 cm<sup>3</sup> to warrant consideration of adjunctive fixation. Given that the two most common adverse sequelae following benign tumor curettage in this region are fracture and joint subsidence leading to arthritis, the use of calcium phosphate with or without supplemental locked plate fixation is encouraging. Previous studies evaluating the failure of femoral defects focus on torsion as the most likely failure mechanism of the femur [15,19–21]. We note an improvement in axial stiffness and torque to failure with a locked plate in addition to calcium phosphate cement, but this needs to be assessed in cyclic loading prior to making an assessment on weight bearing. However, our data suggests that the combination would be superior at resisting a catastrophic torsional event, whether this is a clinically relevant improvement is hard to predict without additional study as well.

This study is not without limitations. The remodeling potential of calcium phosphate is well described in smaller defects; however, we are not aware of any studies describing the remodeling potential of calcium phosphate cement when used in the volume described in this study [22–23]. There is some evidence that defect size may influence the remodeling rate of the calcium phosphate mass [24]. Another limitation of this study is the use of synthetic bone. Fourth generation sawbones were chosen over cadaveric bones because they have been shown to replicate the biomechanical properties of natural bone and are validated for use in the femur [25]. The use of a uniform testing material removes the confounding variations in bone size and quality that hinder biomechanical studies utilizing cadaveric bone. Further, any stability conferred by morselized allograft bone chips was negated as we used an empty defect to simulate this technique. Perhaps most importantly, this study does not consider changes due to loading. Postoperative fractures and joint subsidence may occur many months following the initial postoperative period, making time-zero biomechanical data less relevant to a clinical scenario. Hence, cyclic testing and clinical validation of these results is warranted. It is also notable to consider that previous studies have demonstrated improved construct stability with incorporation of screw fixation into the cement reconstruction [26–27]. Future studies could compare plate/screw constructs with cement versus bone substitute augmentation. We also did not consider the difference between a medial or lateral cortical gap as an independent variable in this study nor collect data to determine the curve of torque-to-failure.

In conclusion, given the risk of fracture and high rate of postoperative arthritis following treatment of defects greater than 60 cm<sup>3</sup>, resorbable bone cement, like calcium phosphate, remains a viable choice. The biomechanical properties, remodeling capability, and compatibility with adjunctive plate fixation make calcium phosphate cement an attractive option in the repair of large distal femoral defects.

## Ethics

This is a biomechanical study and exempt from ethics committee approval.

## Declaration of Competing Interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. However, all saw bones, calcium phosphate cement (Callos Impact Cement), and custom stainless steel distal femoral plate constructs were generously supplied by Acumed (Hillsboro, OR).

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