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Augmentation of a Locking Plate System Using Bioactive Bone Cement—Experiment in a Proximal Humeral Fracture Model

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Abstract

Introduction: The purpose of this study was to test whether local *filling* of a novel strontium-containing hydroxyapatite (Sr-HA) bone cement can augment the fixation of a locking plate system in a cadaveric proximal humeral facture model. **Materials and Methods:** Twelve pairs of formalin-treated cadaveric humeri were used. One side in each pair was for cemented group, while the other side was for the control group. The bone mineral density (BMD) of the samples was tested. A 3-part facture model was created and then reduced and fixed by a locking plate system. In the cemented group, the most proximal 4 screw holes were filled with 0.5 mL bone cement. In the control group, the screw holes were not filled by cement. Locking screws were inserted in a standard manner before the cement hardened. X-ray was taken before all the specimens being subjected to mechanical study, in which 6 pairs were used for axial loading (varus bending) test, while other 6 pairs were used for axial rotational test. **Results:** There is no difference in BMD between the cemented side and the control side. The X-ray shows that the implant is in position. Cement filling was noted in the most proximal 4 screws in the cemented group. Better mechanical outcome was seen in the cemented groups, in terms of less maximal displacement per cycle and higher failure point and stiffness in varus bending test. However, *no* difference was found between the cemented group and the control group in the axial rotation test. **Discussion:** In similarity with the previous studies, our results showed better mechanical results in the cemented group. However, due to the limitations (e.g. sample size, fracture model, testing protocol, etc), we still cannot directly extrapolate current mechanical results to clinical practice at the present moment. Furthermore, it is still unknown whether better primary outcome may lead to better long-term results, even though the local release of strontium may enhance the local bone formation. **Conclusion:** The local filling of Sr-HA bone cement augments the fixation of the locking plate system in current proximal humeral fracture model.

Keywords

osteoporosis, fracture fixation, proximal humerus, cement augmentation, strontium-containing hydroxyapatite (Sr-HA) bone cement

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Introduction

Proximal humeral fractures are common in elderly patients with osteoporosis. The incidence is approximately 4% to 5% of all fractures, with rising frequency because of the increase of osteoporosis in elderly population in recent years.[1,2]

It is a challenge for orthopedic surgeons to fix osteoporotic proximal humeral fractures. The bone quality is poor, unable to provide adequate screw anchorage to the bone.[3-7] The post-operative implant *loosening* rate was reported in the range 14% to 22.2%, and the reoperation rate is up to 29%.[3-5,8,9]

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In recent years, efforts have been made to improve the fixation of proximal humeral fractures. Endeavors include the techniques of using a valgus construct, tuberosity suturing, and calcar screw placements.[10,11] Cement augmentation, with either polymethylmethacrylate (PMMA) bone cements[12-15] or calcium phosphate cements (CPCs),[1,2,16,17] is one method to enhance fixation in the humeral head and has higher relevance in osteoporotic bone. By local filling of bone cement, the anchorage of screws in the humeral head is enhanced in terms of higher pullout strength, less interfragmentary motions, and more load cycles to failure.[12,17] However, PMMA has shortcomings such as exothermic polymerization, nonbiocompatability, and nonbiodegradability. On the other hand, CPCs has drawbacks including inferior mechanical properties and injectability as compared to PMMA, delayed degradation, and nonosteoinductivity which unable to induce new bone formation.[18-20]

A strontium-containing hydroxyapatite (Sr-HA) bioactive bone cement has been developed.[21-24] In a porcine spine burst fracture model, filling of this bioactive cement resulted in restoration of original stiffness and strength of the vertebra.[23] Similar results were also reported in a study using a fresh frozen cadaveric vertebral fracture model.[24] Thus, we hypothesize that local use of Sr-HA cement may have the potential effect of augmentation for implant fixation in osteoporotic proximal humeral fractures. In this study, a cadaveric proximal humeral fracture model was adopted and fixed with a proximal humeral locking plate system (PHILOS; Synthes Holding AG, Solothurn, Switzerland). The Sr-HA cement was used to fill the screw–bone interface in the augmented group. The differences in the mechanical properties of Sr-HA augmented fixation and nonaugmented fixation were compared.

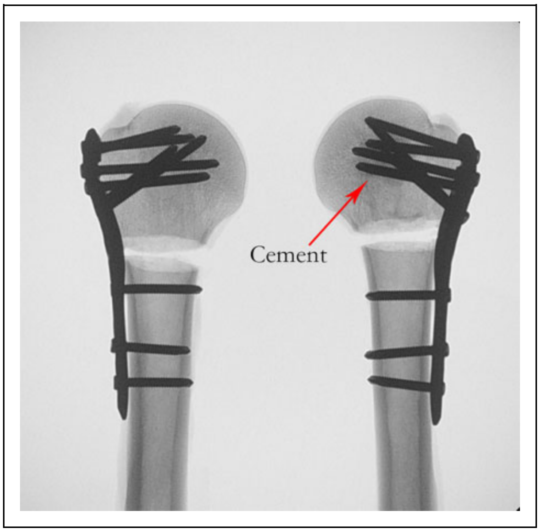

Figure 1. X-rays of a representative paired humeri. The osteotomies on the greater tuberosity and beneath the surgical neck are shown. The gap between the humeral head and the distal shaft is shown. The left nonaugmented specimen with the fracture lines of the simulated 3-part fracture and the right one is the augmented specimen. The arrow shows the cement around the screw.

Materials and Methods

Study Design

The study was approved by the institutional ethics committee of our hospital. Twelve-pair formalin-treated cadaveric humeri were used. The age at the time of death was over 65 years old. The soft tissues were removed. The bone mineral density (BMD) of the humeral head was assessed with dual energy X-ray absorptiometry (Hologic Discovery-A, Bedford, Massachusetts). The specimens were stored frozen at −20°C and thawed overnight at 4°C before preparation. The left side of each pair was selected to be the control group (without cement augmentation), while the right side was selected to be the cemented group (with Sr-HA cement augmentation). For the mechanical test, 6 pairs were selected for varus bending test, while the other 6 pairs for axial rotation test. Accordingly, 24 proximal humerus locking plates with screws (PHILOS; Synthes Holding AG) were used to fix the fracture model.

Cement Preparation

Strontium-containing hydroxyapatite bone cement was prepared according to the literature.[21] The composition includes a filler blend of Sr-HA (97.0 wt%), fumed silica (2.5 wt%), and benzoyl peroxide (0.5 wt%) and a resin blend of bisphenol A diglycidylethermethacrylate (50 wt%), triethylene glycol dimethacrylate (40 wt%), poly(ethylene glycol) methacrylate (9.75 wt%), and N, N-dimethyl-p-toluidine (0.25 wt%). After mixing the powders and the liquids, the mixture was then stirred for 2 minutes. The setting time for the cement ranges 8 to 12 minutes after mixing. Thus, there are 6 to 10 minutes for the surgeons to inject the cement and reinsert the screws into the humeral head.

Fracture Model and Osteosynthesis

A modified 3-part fracture model was created according to the literature (Figure 1).[12,17] Osteotomy was performed utilizing a power microsagittal saw. Two osteotomies were created: one horizontal gap osteotomy of 10 mm was done just beneath the surgical neck, while the other one was an osteotomy of the greater tuberosity. The osteotomy and the size of the fragments of each specimen were kept as similar as possible to ensure the homogeneousness of each fracture model.

The bone fragments were reduced anatomically and fixed using PHILOS. Three bicortical locking screws were used to fix the plate to the shaft, while 6 locking screws were inserted into the head fragment via the most proximal 6 screw holes of the plate (Figure 1).[12]

A gauge provided by the manufacturer was used to measure the maximum possible length of the screws for head fixation. In the nonaugmented group, screw length was determined as the maximum measured length subtracted by 6 mm as recommend by the manufacturer. In the cemented group, the 4 most proximal head screws were augmented (Figure 1).[12] The screws

Figure 2. The setting of the varus bending test.

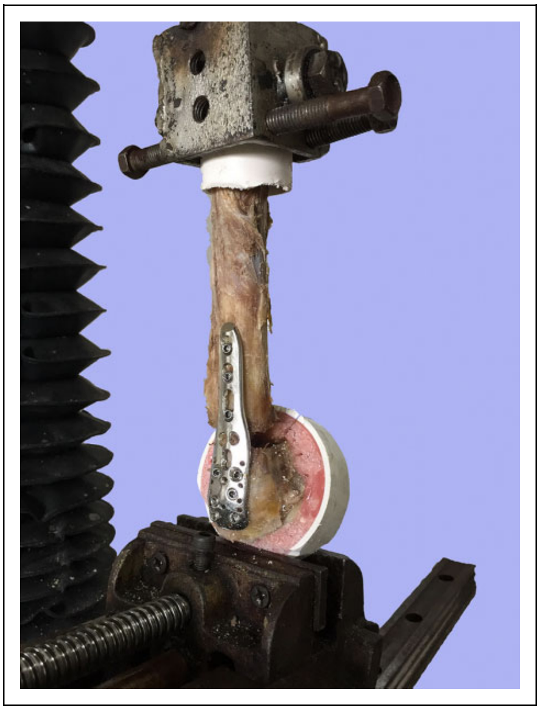

Figure 3. The setting of the axial rotation test.

were first inserted into the humeral head and then removed. To each screw hole, 0.5 mL of cement[12] was injected and then the screws were reinserted into the screw holes before the cement was set. The remaining 2 head screws were inserted as what had been done in the nonaugmented group.

Biomechanical Study

All specimens were prepared to be 250 mm in length by cutting the distal end of the humerus and embedded in PMMA in a specially made device for mechanical test. The tests were conducted using a biaxial servo hydraulic material testing machine (Bose, 3510-AT, Eden Prairie, Minnesota). Two testing protocols were used: varus bending cyclic loading test and axial rotational cyclic loading test. There were in total 12 pairs of specimens. Six pairs ($n = 6$) of specimens were used for the varus bending test, while the other 6 pairs were used for the axial rotational test ($n = 6$).

For the varus bending test, the humeral head was attached to a device which applied compressive load to the head, simulating varus deforming action on the humeral head (Figure 2). The specimens were cyclically loaded in a sinusoidal pattern with the initial range from 2 to 15 N preload for 20 cycles in a frequency of 2 Hz. Then the lower load magnitude was set constantly to be 50 N. The upper load magnitude was set constantly to 150 N. The frequency was 2 Hz. Four thousand cycles were completed. Data were collected at an interval of every 10 load cycles and the maximal displacement (mm) per cycle of the humeral head was determined. Then compression load in a displacement-controlled mode was applied at a speed of 0.08 mm/s to the specimen until failure. The failure load and stiffness were analyzed.

For the axial rotation test, the specimen was placed in the mechanical testing machine with the axis of the humeral shaft being aligned with the axis of the rotational road cell. The axial rotation of the humeral head was permitted via torque applied along the axis of humeral shaft (Figure 3). With an axial preload of -1 to $+1$ N·m torque being applied for 20 cycles, rotation cycle load was continually applied to the specimens with the torque being -6 to $+6$ N·m for the first 2000 cycles at a frequency of 2 Hz, followed by -8 to $+8$ N·m for the second 2000 cycles, -10 to $+10$ N·m for the third 2000 cycles, and -12 to $+12$ N·m for the fourth 2000 cycles, with total 8000 cycles being completed. Data were collected at an interval of every 10 load cycles, and the maximum rotation angle (degree) per cycle of the humerus head with respect to the distal shaft was determined. Then, axial rotation in a displacement-controlled mode was applied at a speed of $0.1°/0.1$ second to the specimen until failure. The failure load and stiffness were analyzed.

Data Analysis/Statistics

Statistical analysis was performed using SPSS 12.0 (SPSS Inc, Chicago, Illinois). The results of BMD of the humerus head were expressed as median (minimal-maximal). In the varus bending test, the maximal displacement (mm) per cycle of the humerus in the first 1000 cycles, second 1000 cycles, third 1000 cycles, and fourth 1000 cycles was analyzed. In the rotational test, the maximal angle (degrees) per cycle of the humerus head in the first 2000 cycles, second 2000 cycles, third

Table 1. Results of the BMD Test.

	Bone Mineral Density (BMD)		
	Left (g/cm^3)[a]	Right (g/cm^3)[a]	*P* Value[b]
All specimens (12 pairs)	0.529 (0.343-0.770)	0.526 (0.354-0.729)	.469
Varus bending (6 pairs)	0.540 (0.343-0.592)	0.524 (0.390-0.578)	.312
Axial rotation (6 pairs)	0.516 (0.397-0.770)	0.536 (0.354-0.729)	.687

[a]Values are expressed as median (minimal-maximal) of bone mineral density (BMD).
[b]Mann-Whitney *U* test.

Table 2. Results of the Varus Bending Test.

	Groups		
	Control (mm)[a]	Cemented (mm)[a]	*P* Value[b]
1st 1000 cycles	10.15 (9.33-13.56)	9.20 (8.92-10.15)	.016[c]
2nd 1000 cycles	10.37 (9.60-13.91)	9.34 (8.93-10.28)	.010[c]
3rd 1000 cycles	10.41 (9.65-14.07)	9.37 (8.94-10.32)	.010[c]
4th 1000 cycles	10.43 (9.67-14.15)	9.39 (8.94-10.33)	.010[c]

[a]Values are expressed as median (minimal-maximal) of the maximal displacement (mm) per cycle.
[b]Mann-Whitney *U* test.
[c]Significant difference.

2000 cycles, and fourth 2000 cycles was analyzed. A Mann-Whitney *U* test was used to compare the results between the control group and the cemented group. Differences were considered statistically significant if $P < .05$.

Results

The results of BMD are shown in Table 1. The median (minimal-maximal) of the BMD of all specimens is 0.528 (0.343-0.770) g/cm^3, with 0.529 (0.343-0.770) g/cm^3 on the left side and 0.526 (0.354-0.729) g/cm^3 on the right side. The difference of the BMD between the left and the right side was not statistically significant ($P = .469$). Also, there was no statistically significant difference in the BMD between both sides in either of the varus bending test group or the axial rotation test group ($P = .312$ for the varus bending test group and $P = .687$ for the axial rotation test group).

During the varus bending test, interfragmentary motions were observed between the head and the distal shaft in both cemented group and the control group. However, no interfragmentary motions between the head and the tuberosity were observed in both groups. In the first 1000 cycles, the maximal displacement per cycle of the humerus head was 10.15 mm (9.33-13.56 mm), median (minimal-maximal), on the control side while 9.20 mm (8.92-10.15 mm), median (minimal-maximal), on the cemented side ($P = .016$; Table 2). With cycles increased, the maximal displacement per cycle of the humerus head increases accordingly (Figure 4 and Table 2). In addition, the maximal displacement per cycle in the cemented side was less as compared with that in the collateral side ($P = .010$; Table 2). In the load-to-failure test, the failure point of the cemented group was 958.59 N (652.56-1248.13 N), median (minimal-maximal), while 468.94 N (321.36-904.24 N), median (minimal-maximal), for the control group ($P = .025$; Table 3 and Figure 5). Also, higher stiffness was in the cemented group (Figure 5, Table 3).

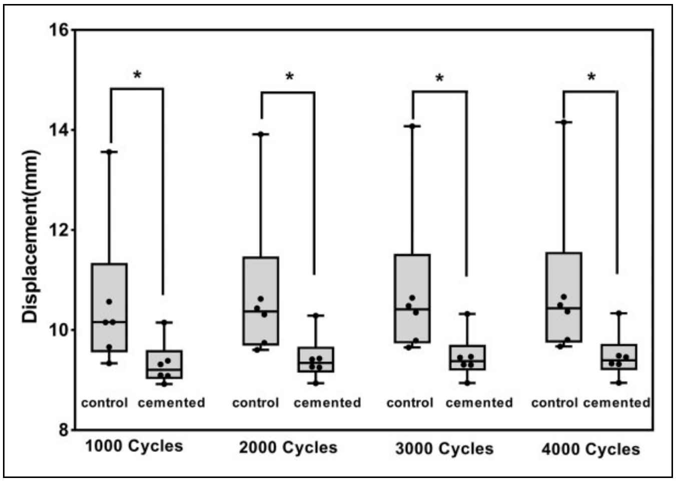

Figure 4. Results of the varus bending test. *$P < .05$.

During the axial rotational test, there were interfragmentary motions between the head and the distal shaft. On the other hand, no interfragmentary motions between the head and the greater tuberosity were observed. In the first 2000 cycles, the maximal per cycle rotational angle of the control group was 2.25° (1.80°-2.72°), median (minimal-maximal), while 2.10° (1.80°-2.10°), median (minimal-maximal), for the cemented group (Table 4). The difference between both groups was not statistically significant. With the increase in the rotational torque, the rotation degree of the humerus head increased accordingly (Table 4 and Figure 6). However, no statistical difference was observed in the second, third, and fourth 2000 cycles between both groups (Table 4). In the failure test, the rotation failure point was 7.82 N·m (3.28-20.92 N·m), median (minimal-maximal), for the cemented group, while 9.08 N·m(7.29-17.37 N·m), median (minimal-maximal), for the control group ($P = .522$, Table 3 and Figure 7). The stiffness was 11.50 N·m/rad (4.40-25.41 N·m/rad), median (minimal-maximal), for the cemented group, while 15.92 N·m/rad (9.71-26.70 N·m/rad), median (minimal-maximal), for the control group ($P = .337$, Table 3 and Figure 7). No statistical difference was found between both groups in the rotation failure test.

Discussions

It has been reported that local cement filling offers additional stability to the humerus head in proximal humerus fracture fixed with locking screws systems. In the study of Unger et al, local injection of 0.5 mL PMMA cement per screw in

Table 3. Results of Failure Test.

	Groups		
	Control[a]	Cemented[a]	*P* Value[b]
Compression failure point (N)	468.94 (321.36-904.24)	958.59 (652.56-1248.13)	.025[c]
Compression stiffness (N/m)	1.66×10^5 (1.23×10^4-2.07×10^5)	2.34×10^5 (1.93×10^5-3.54×10^5)	.010[c]
Rotation failure point (N·m)	9.08 (7.29-17.37)	7.82 (3.28-20.92)	.522
Rotation stiffness (N·m/rad)	15.92 (9.71-26.70)	11.50 (4.40-25.41)	.337

[a]Values are expressed as median (minimal-maximal) of the maximal rotation (degrees) per cycle.
[b]Mann-Whitney *U* test.
[c]Significant difference.

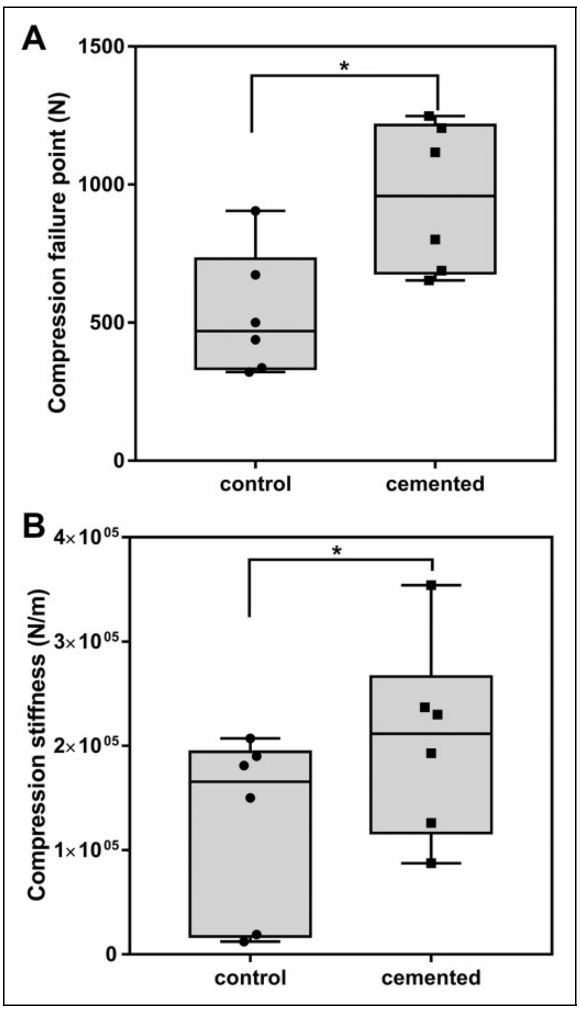

Figure 5. Results of the compression failure test. (A) Compression failure point, (B) compression stiffness.

Table 4. Results of the Rotation Test.

	Groups		
	Control (degrees)[a]	Cemented (degrees)[a]	*P* Value[b]
1st 2000 cycles	2.25 (1.80-2.72)	2.10 (1.80-2.10)	.087
2nd 2000 cycles	3.15 (2.50-3.82)	2.60 (2.90-3.41)	.194
3rd 2000 cycles	4.21 (3.50-4.91)	3.50 (3.22-3.91)	.056
4th 2000 cycles	4.90 (3.60-5.67)	4.39 (3.84-4.49)	.102

[a]Values are expressed as median (minimal-maximal) of the maximal rotation (degrees) per cycle.
[b]Mann-Whitney *U* test.

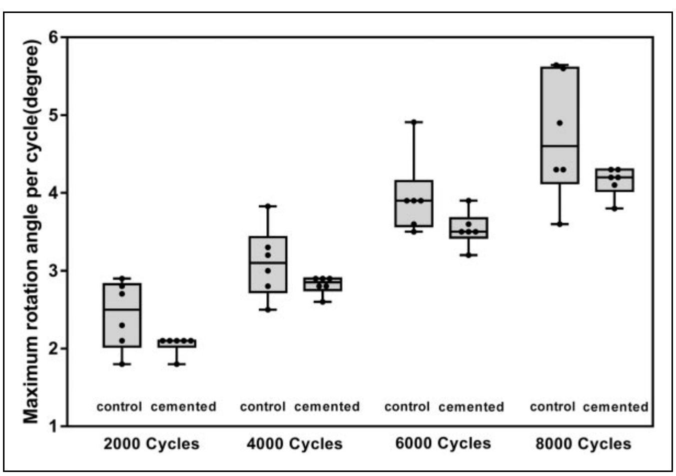

Figure 6. Results of the rotation test.

PHILOS resulted in an increase of 50% of the numbers of load cycles to failure under varus loading test as compared with the uncemented group.[12] Similarly, in the study of Kathrein et al, using a 2-part fracture model, the per cycle interfragmentary motion under adduction cyclic loading test is significantly diminished by the local use of 0.5 mL PMMA cement per screw hole.[13] More interestingly, in a 3-part fracture model, local filling of 0.5-mm PMMA per screw hole to 2 screws, which were at region of the lowest bone quality, resulted in more load cycles to failure, showing almost as effective as 4 screws with twice the amount of bone cement.[14]

The rationale for cement augmentation in primary stage is that the load-bearing surface is enlarged by local filling of cement which is surrounding the screw surfaces, thus the stress on the local trabecular bone is diminished accordingly.[13,25] However, the long-term stability need an integrated bonding between bone and cement.[26] Traditional PMMA bone cement does not favor local bone formation, as it is exothermic and not biocompatible. The long-term bone-cement bonding of PMMA is still questionable as aseptic implant loosening has been reported in arthroplasty using cemented prosthesis.[27] Though

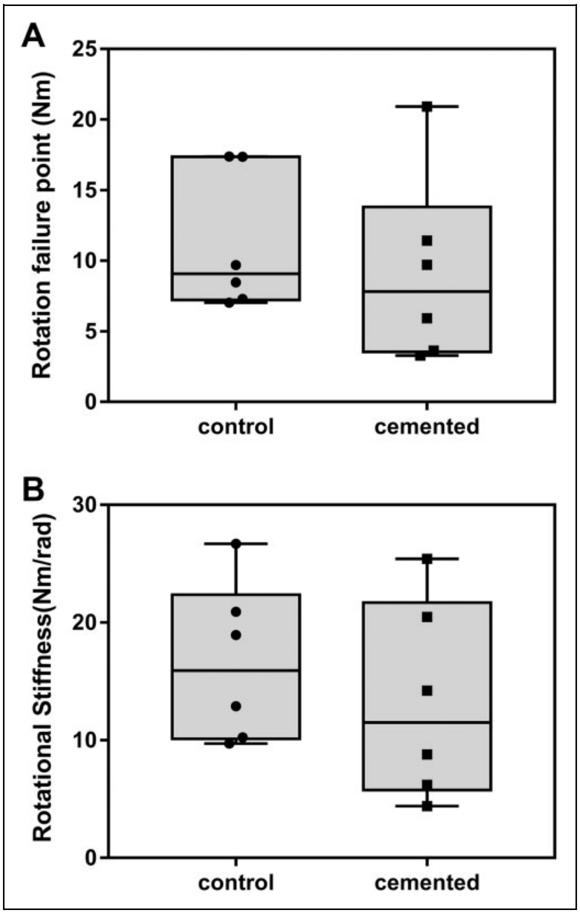

Figure 7. Results of the rotation failure test. (A) Rotational failure point; (B) rotational stiffness.

CPC is bioactive and osteoconductive, the mechanical properties of CPCs are inferior to those of PMMA. In this study, the Sr-HA bone cement is biocompatible and osteoconductive. Animal studies have shown that active peri-cement new bone formation and remodeling was observable at 1 month and osteointegration into the cement was noted at 3 months in the rabbit.[26,28] In a mechanical study and a clinical study, it has also shown that Sr-HA has acceptable biomechanical properties for spinal fractures fixture.[23,24] It has also been shown that oral administration of strontium ranelate induces new bone formation and reduces fracture risk in patients with osteoporosis. In this study, the Sr-HA allows local delivery of strontium ions. The local strontium may have the same effect on the osteoporotic proximal humerus bone, in form of enhancing local new bone formation. The bone-screw bonding surface is increased and thus the fixation of the screws is expected to be augmented in the long-term.

In similarity with the previous studies, our results showed that the local injection of Sr-HA results in a significant decrease in per cycle motion between the head and shaft fragment. Also, higher failure load and higher stiffness under varus bending test were observed in the cemented group. Varus collapse is one of the common complications after proximal humeral fracture surgery.[7,29,30] Lack of medial support and insufficient fixation are reasons leading to such a complication.[31] Though the use of medial calcar screws, bone block grafting, or the technique of impaction of the humerus shaft to the head fragment have been reported, establishment of sufficient medial support still lacks of clinical evidence.[10,13] The results of this study may provide and alternative way to reduce the risk of varus collapse.

On the other hand, no statistically significant difference is found between the augmented group and the control group in the rotational test in this study. In the study by Kwon et al, the head rotation degrees were significantly decreased by local filling of 10 mL CPC into the screw holes and the head void.[17] However, the cement volume, the implant and the testing protocol is different from the presented study and thereafter we cannot compare the findings of both studies directly. In the study of Kathrein et al, though 0.5 mL PMMA per screw could significantly reduce the per cycle motion under adduction and abduction cyclic test, however, the rotational cyclic test was not performed.[13] In our study, during the rotational test, we observed that the rotation motion occurred at the interface between the plate and the distal shaft of the humerus in both of the cemented and control groups, suggesting the weak point is at the distal construct but not the head construct during the rotation test. Although 3 bicortical locking screws were used to fix the distal shaft of humerus, these 3 locking screws aligned at a same plane, which was perpendicular to the direction of the rotational torque during the test, and thus considered to be a weak point during the test. Increase the length of the plate and the more distal screws may help to increase the stability.

This study has a few limitations. First, only 6 samples ($n = 6$) were used in each group, the sample size may be considered relatively small. Moreover, the specimens were formalin-treated but not fresh frozen cadaveric bone. Formalin fix may have effect on stability. However, this study is for comparative purpose. The pair compared study allows us to make a direct comparison of the difference between the cemented and non-cemented group.

Secondly, a modified 3-part fracture model was used. Although the simple osteotomy is unable to represent the real fractures, however, it allows all fracture models being equivalent for comparison. Also, the soft tissues were removed and therefore additional stability by adjacent soft tissues to the implant was neglected.

Thirdly, since there were no standard methods to calculate the T score of the specimens, we cannot define these specimens being osteoporotic. Moreover, other variations such as no soft tissues covering the cadaveric bones, unknown structures of the bones (the percentage of trabecular bone and cortical bone), and variation in the shape of the bones could also affect the results of BMD.

In this study, either the varus bending test or the axial rotational test might not completely mimic the physiological loads exerting on the proximal humerus. For example, both of the varus stress and the rotational stress were exerted on the humeral heads but not on the greater tuberosities, which is the attachment of the rotator cuff. In addition, the shoulder is not weight bearing, a pure axial load may be difficult to simulate the natural motion of a shoulder. Moreover, the tests of forward bending and adduction/abduction were not performed, thus we are unable to known whether cement augmentation may have effects on such motions that the rehabilitating shoulder is subject to. On the other hand, the unavoidable technical errors, for example, nonparalleled locking screw placement, may also have effects on the stability. Although better mechanical results obtained in the augmented group, we still cannot directly extrapolate current mechanical results to clinical practice at the present moment. In addition, we did not take post-failure X-rays for the samples, thus we do not know whether the anchorage between the proximal 4 locking screws and the surrounding bone was maintained better in Sr-HA bone cement augmentation.

Our study only showed the biomechanical results of Sr-HA cement augmentation in primary stage. However, it is still unknown whether better primary outcome may lead to better long-term results, even though the local release of strontium may enhance the local bone formation. More studies are needed to answer this question.

Finally, though the local use of cement augmentation is one of the optimizing techniques improving the surgical outcomes in proximal humeral fractures, we should not neglect that there are multiple factors contributing to the success of surgery, including optimal soft tissue handling, minimal periosteal stripping, satisfactory fracture reduction and fixation, and optimal postoperative rehabilitation.

Conclusion

This study showed that local injection of Sr-HA cement augments proximal humeral fracture fixation in cadaveric models, in terms of less maximal displacement per cycle, higher failure point, and stiffness in the humerus head construct in varus bending test. However, no significant difference was found between cemented group and control group in axial rotational test.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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