Topical Administration of Raloxifene Does Not Significantly Improve Bone Toughness or Screw Pull-Out Strength in Multiple In Vitro Models

Michael R. Eby

University of Pennsylvania

Danielle M. Cristino

University of Pennsylvania

Matthew Counihan

University of Pennsylvania

Kendall M. Masada

University of Pennsylvania

Jaimo Ahn

University of Michigan–Ann Arbor

Michael W. Hast (✉ hast@pennmedicine.upenn.edu)

University of Pennsylvania

Research Article

Keywords: Raloxifene, fracture repair, proximal humerus, cadaveric, biomechanics

Posted Date: February 8th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-156190/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: A previous study has demonstrated an increase in mechanical properties of acellular canine bone after topical raloxifene exposure. The goal of this study was to determine if similar treatment yields the same results in bovine bone and whether this translates into a difference in screw pull-out strength in human cadaveric tissue.

Methods: Matched pairs of bone specimens were submerged in solutions of either raloxifene (20 μ M) or phosphate-buffered saline as a control for 7 days. In the first experiment, cancellous bone from fetal bovine distal femora underwent quasi-static four-point bending tests. In the second experiment, 3.5 mm unicortical cancellous screws were inserted to a 30 mm depth in human osteoporotic cadaveric humeral heads and quasi-static screw pull-out tests were performed.

Results: In the four-point bending tests, there were no significant differences between the raloxifene and control groups for any of the mechanical properties - including stiffness ($p = 0.326$) and toughness ($p = 0.850$). In the screw pull-out tests, the raloxifene soaked samples trended towards a higher load at failure, without statistical significance ($p = 0.099$). Failure loads were 122 ± 74.3 N and 89.5 ± 63.8 N for the raloxifene and control groups, respectively.

Conclusions: Biologic solutions that address the acute improvement of bone quality during the fracture healing timeframe are an important area of future research and untapped potential for reducing construct failure in osteoporotic fracture fixation. The bovine samples did not demonstrate an increase in toughness with raloxifene treatment, which is in contrast to previously published data. In vivo experiments are likely required to determine whether topical use of raloxifene will improve implant fixation.

Background

Osteoporotic fractures accounted for an estimated 9 million new fractures worldwide in the year 2000 and are projected to continue increasing in prevalence as our society ages and average lifespan lengthens.(1) In the United States alone, projections estimate upwards of 275,000 proximal humerus fractures by 2030.(2) Osteoporotic hip fractures are expected to reach 6.3 million worldwide by the year 2050.(1) The total population facility-related hospital cost of osteoporotic fractures in the United States from the year 2000–2011 averaged \$5.1 billion per year, higher than the respective facility-related costs of myocardial infarction (\$4.3 billion) or stroke (\$3.0 billion).(3) In addition to these costs, we must also consider morbidity from loss of function, mortality from associated complications, and the socioeconomic impact of lost work productivity and strain on caretakers among other downstream effects.(4)

Many of the challenges regarding successful reconstruction and repair of fractures in the elderly are associated with the decreased mechanical properties of osteoporotic bone. Complications are common and include implant failure, malunion, nonunion, collapse and screw cut out. (Fig. 1) One study

demonstrated that proximal humerus fracture reconstructions using internal fixation strategies had a 49% complication rate.(5) This included malunion, implant pull-out, and primary and secondary screw perforation of the shoulder joint. Similarly, a systematic review of osteoporotic hip fractures treated by all types of fixation found a failure rate of 14.8% in nondisplaced femoral neck fractures and 41% in displaced femoral neck fractures.(6) A separate implant-specific study showed failure rates greater than 50% in osteoporotic hip fractures.(7) Structural augments, such as allografts(8, 9) and bone substitute materials,(10, 11) are being utilized more frequently, but their long-term utility is not well understood and their complication rates remain unacceptably high.(12)

Improvement of the implant-bone interface is central to the advancement of osteoporotic fracture care. Implant advances such as intramedullary nailing, locked plating, variable angle screws and pegs have all contributed to decreased failure of constructs in osteoporotic bone by tailoring their design to weaker bone.(13) A longstanding goal in orthopaedics has been to identify a therapeutic agent to improve the mechanical quality of the weaker bone for fracture fixation. This agent would be administered at the time of fixation and act rapidly enough to improve the bone as it heals, preventing implant failure. Several medications, including bisphosphonates and teriparatide, have successfully increased bone mineral density in osteoporotic bone.(14–16) However, orthopaedic surgeons use these drugs to prevent additional fragility fractures, so their role in acute fracture care is less clear. The use of bisphosphonates for acute fracture care is controversial, with some suggesting it delays fracture healing.(17) Others have found that bisphosphonate therapy has no appreciable effect on fracture healing(18, 19) and may even negatively influence fracture healing(20, 21) A meta-analysis of teriparatide in acute fracture care showed no significant improvements in fracture healing rates or time to radiographic healing.(22)

Raloxifene is a selective estrogen receptor modulator that is previously known to improve bone quality when taken systemically over a prolonged period of time.(23) Its primary mechanism of action involves modification of gene expression, as well as a decrease in the quantity and activity of osteoclasts.(24) A recent in vitro study of raloxifene investigated a potential secondary mechanism for improving bone quality.(25) Interestingly, canine bones soaked in raloxifene showed improved toughness, which challenges the assumption that a cellular response is required to improve bone properties with raloxifene. From an engineering standpoint, toughness is the ability of a material to deform and absorb energy without fracturing, and this mechanical property is quantified by calculating the area under the stress strain curve.

It is unknown whether this potential acellular effect is substantial enough to produce a clinically relevant improvements in bone toughness and screw pull-out strength, both of which play an important role in fragility fracture repair. The purpose of this study was twofold: First, to recapitulate the findings of Gallant et. al in a new (bovine) animal model; and second, to test the utility of raloxifene application with human cadaveric tissue in a clinically relevant application (proximal humerus fracture repair). We hypothesized that topical application of raloxifene on osteoporotic bone would increase toughness and screw pull-out resistance.

Methods

This study included deidentified cadaveric human and bovine specimens. All institutional guidelines regarding the use of these specimens were strictly followed. Approvals from the Institutional Animal Care and Use Committee (IACUC) and the Institutional Review Board (IRB) were not required by our institution for this study. Donors provided informed consent for use of their bodies for medical research (Source: ScienceCare, Phoenix, AZ, USA).

The first portion of this study involved four-point bending tests of cancellous bone beams harvested from the distal femora of fetal bovine specimens. Cancellous bone was tested because it is representative of bone in the head of the humerus and fetal specimens were selected because the underdeveloped cancellous bone more closely mimics the osteoporotic condition. Using a reciprocating saw with a 1 mm blade, a total of 20 specimens were harvested from the distal metaphysis of a single fetal bovine femora (~ 33 weeks gestation). Individual specimens were carefully hand sanded into 25 x 4 x 1.5 mm (+/- 0.05 mm) blocks and digital calipers were used to verify dimensions. The specimens were thoroughly cleaned of soft tissue, sonicated for 30 seconds at room temperature, and frozen until day 1 of the soak (-20°C). Specimens were submerged in one of two solutions in a sterile container: control (600 µL of dimethylsulfoxide (DMSO), 1% penicillin-streptomycin and phosphate-buffered saline (PBS)) or raloxifene (20µM of raloxifene suspended in 600 µL of DMSO and 1% penicillin-streptomycin in PBS). The bone beams and solutions were placed on a plate shaker for 7 consecutive days and held at 4°C.

The four-point bending protocol was adapted from ASTM standard C1161–18. (ASTM International, West Conshohocken, PA) All specimens were brought to room temperature prior to testing. Specimens were blotted with a paper towel and placed on a universal test frame (Instron 5542; Norwood, MA) equipped with a 50 N load cell (Fig. 2). The beams were quasi-statically loaded to failure at a rate of 0.1 mm/sec. The following mechanical properties were calculated: stiffness (N/mm), ultimate force (N), bending rigidity (Nm²), modulus of elasticity (MPa), ultimate stress (MPa), and toughness (J/m³). We were particularly interested in the stiffness and toughness results because they are representative of bone quality and fracture resistance.

The second portion of this study utilized 5 matched pairs (right and left) of cadaveric proximal humeri from donors that were confirmed osteoporotic by dual energy X-ray absorptiometry (DEXA) scan. (4 female, 1 male, average age 81.8 years, average T-score of the most osteoporotic vertebral body – 3.02) Specimens were skeletonized with standard gross dissection techniques and the proximal humeri were isolated from the rest of the shoulder joint with an oscillating saw. Except for the lateral wall, the humeri were decorticated. Pilot holes for 5 screws were drilled into each specimen with a 2.5 mm drill bit (Trajectories demonstrated in Fig. 3) using a LCP Proximal Humerus locking plate and corresponding drill guide (DePuy Synthes, West Chester, PA). Prepared specimens were soaked in solution after drilling to allow for permeation into the bone-screw interface. Each matched pair had one randomized side soaked in 20µM raloxifene solution and the contralateral side soaked in control solution for one week, following the same protocol as the first portion of the study.

Screw pull-out testing was performed in accordance with ASTM F543-17 (ASTM International, West Conshohocken, PA). Prior to testing, randomized frozen samples were brought to room temperature. A 3.5 mm cortical screw (DePuy Synthes, Warsaw, IN) was inserted unicortically (without the plate) into each of the randomly selected 5 pre-drilled trajectories to a depth of 30 mm. The screw was removed quasi-statically at a rate of 0.03 mm/sec on a universal testing frame (TA Electro-Force 3550; Eden Prairie, Minnesota) equipped with a 1,110 N load cell. Recorded force-displacement data was used to determine ultimate pull-out force.

Statistical analysis was performed in R Studio Version 3.6.0 (RStudio, Inc., Boston, MA). Shapiro-Wilk tests were used to test for normality. If the data were normal, two-tailed, two-sample, equal variance Student t-tests were used to assess unknown responses across groups. For non-Gaussian data, a Mann-Whitney-Wilcoxon test was performed to identify potential differences between groups. The significance level was set at $\alpha = 0.05$ for all tests and post-hoc Bonferroni corrections were made when necessary.

Results

In the fetal bovine experiment, there were no significant differences between the raloxifene and control groups for any of the mechanical properties determined from four-point bending. The stiffness values for the control and raloxifene groups were 1.4 ± 0.5 N/mm and 1.2 ± 0.5 N/mm, respectively ($p = 0.326$). The toughness values were 0.16 ± 0.05 J/m³ and 0.15 ± 0.07 J/m³ ($p = 0.850$) for the control and raloxifene groups, respectively (Figure 4). Other comparisons of mechanical properties did not show significant differences: ultimate force ($p = 0.560$), bending rigidity ($p = 0.422$), modulus of elasticity ($p = 0.303$), and ultimate stress ($p = 0.569$) (Table 1).

For the osteoporotic cadaveric tests, ultimate screw pull-out loads were 89.5 ± 63.8 N and 122 ± 74.3 N ($p = 0.099$) for the pooled control and raloxifene groups, respectively (Figure 5). Although a 36% increase in average pull-out strength was observed for the bone treated with raloxifene, the results were not statistically significant. Because the mechanical properties of bone itself likely changes at the different screw insertion points, we made paired comparisons of pull-out strength at each location (Table 2). Although a p-value of 0.021 was found for location 4, this was not significant after Bonferroni corrections were made. There were no other significant differences between groups.

Discussion

The high rate of fixation failure in osteoporotic fractures poses a significant challenge to surgeons and their patients, warranting exploration of novel approaches to improving fixation strength. Few treatments have shown promise in addressing the underlying issue of poor bone quality within the timeframe of fracture healing. We determined that topical application of raloxifene did not improve bone material properties in bovine bone and screw pull-out strength in osteoporotic human cadaveric bone. Unlike the results of previous research(25), toughness in 4-point bending was not increased by soaking the

specimens in raloxifene. A trend towards a higher screw pull-out strength in osteoporotic cadaveric bone was observed for bone treated with raloxifene, however the results were not statistically significant.

Raloxifene is a commonly used drug in the treatment of osteoporosis, but the traditional belief was that it required a cellular response to improve bone density and that this response took longer than fracture healing timeframes(24). Based on this premise, orthopaedic surgeons typically begin treatment with raloxifene or similar medications to prevent additional osteoporotic fractures (instead of treating the current fracture acutely). To the authors' best knowledge, this is the first investigation to determine whether an acellular effect of raloxifene is significant enough to produce a clinically relevant improvement in acute osteoporotic fracture fixation.

This experiment only examined the in vitro response of tissue to direct exposure to raloxifene, and an in vivo animal model would provide a clearer understanding of the mechanisms at play. For example, we could measure the cellular uptake locally within a fracture as well as gauge the cytotoxicity of local administration of raloxifene. The classical mechanism of action is based on the general premise that it must enter the nucleus and bind to an estrogen receptor to effect changes in gene expression. Because it is a selective estrogen receptor modulator, raloxifene does not share all effects with estrogen. While estrogen has a myriad of effects depending on the type of tissue it is exposed to(24), the full mechanism of action of raloxifene is still uncertain. Further, raloxifene has been shown to decrease the number and activity level of osteoclasts.(26) These cell-mediated mechanisms explain the clinical effect of prolonged raloxifene treatment systemically, in which bone mineral density is increased.

Recent success with an in vitro model suggests that acellular mechanisms may influence the mechanical properties of bone. Gallant et al. suggested that hydroxyl groups on the molecular structure of raloxifene may be the key to a short-term, acellular effect of raloxifene on the mechanical properties of bone – these groups affect the interface between mineral bone and collagen and may increase hydration of the bone. (25) Multiple studies have demonstrated improved mechanical properties of bone that is more hydrated. (27,28) This potential mechanism would allow for a much faster effect than the steroid based effect on gene expression. This would theoretically allow raloxifene to be utilized locally in an acute perioperative setting to lower the likelihood of implant failure by acutely increasing mechanical quality of osteoporotic bone. It remains unclear why an increase in toughness of acellular bone was observed after a short period of exposure to raloxifene in the study by Gallant et al.(25), but similar results were not seen in the current experiment.

The high rate of fixation failure in osteoporotic fractures poses a significant challenge to surgeons and their patients. There were several differences between this study and the previous study. The current study included cancellous bone from fetal bovine femora and human cadaveric humeri, whereas the previous study was performed with cortical bone harvested from adult canine femora and adult human tibiae. The architecture of cancellous bone introduces more structural variability into the specimens, which may have made it more difficult to detect a subtle effect of raloxifene on the mechanical properties of bone. We also increased the concentration of raloxifene tenfold (20 μ M vs. 2 μ M). Although it was

expected that increasing the concentration would have a stronger effect on outcome, pilot testing did not demonstrate a concentration-dependent relationship to mechanical properties (data not shown).

Our analysis did not demonstrate significant results for screw pull-out, which limits the clinical translation of this experiment. A post hoc power analysis demonstrated the sample size would need to be increased to 72 for 80% power (sample size of 118 for 95% power). For toughness in four point bending a sample size of 2,113 specimens would be required for 80% power (sample size of 3,498 for 95% power). An important next step in this line of investigation would involve increasing sample size, however increasing sample size to achieve adequate power may not be practical. Further work should also include testing constructs with more clinical applicability. Rather than using individual screw pull-out testing as a proxy for failure of a fracture fixation construct, an entire locking plate-screw construct could be tested. While significantly more costly, testing a locking plate-screw construct would provide additional clinical relevance to the experiment. Furthermore, a plate-screw construct may make the detection of a smaller clinical effect possible due to the summative effect of increasing pull-out strength of all the screws in the construct. Additionally, in vivo experiments are likely required to determine whether topical use of raloxifene will improve implant fixation. Other research could focus on osteoporotic fracture care that does not involve fixation, such as the prevention of progressive loss of height in vertebral body compression fractures.

This study included several limitations. There were several parameters within this experimental protocol, including type of bone (animal vs. human), bone type (cancellous vs. cortical), raloxifene concentration, duration of bone exposure to raloxifene, and conditions of raloxifene treatment (temperature, solution, antibiotics) that remain untested and may confound the effectiveness of raloxifene. While the variables used in this study did not yield the expected result, there may be other conditions in which bone material properties may be enhanced.

Conclusions

Fixation of osteoporotic fractures represents a major clinical challenge. Surgical repair is often not considered as an option due to the high likelihood of failure - even with the most advanced implants and construct designs.(29–31) Current research overwhelmingly focuses on the design of new implants and modification of current implants and construct designs. However, it is important to explore biologic treatments that can address the fundamental, underlying problem of bone quality. This will allow improved outcomes in all aspects of osteoporotic fracture care, from improving surgical outcomes to increasing the number of patients who can be treated with surgery. It is also important to appreciate the context of a biological solution and the potential to be immediately applicable to everything from proximal humerus fractures to osteoporotic vertebral compression fractures to hip fractures. An intervention to rapidly improve the mechanical properties of osteoporotic bone in the acute fracture setting could significantly decrease the burden of osteoporotic fractures in aging populations around the world.

Abbreviations

IACUC: Institutional Animal Care and Use Committee

IRB: Institutional Review Board

DMSO: dimethylsulfoxide

PBS: Phosphate Buffered Saline

DEXA: dual energy X-ray absorptiometry

Declarations

Ethics approval and consent to participate

Deidentified human cadaveric tissue was used in this study. This study was approved by the University of Pennsylvania Cadaveric Body Part Operational Committee. The University of Pennsylvania does not require Institutional Review Board approval for cadaveric studies. Written consent was obtained from donors for anatomical donation for the purposes of medical research.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

This project was funded with a grant from AO Trauma North America (PD# 10065960). This money was used to pay for cadaveric specimens and materials used during testing.

Authors' contributions

MRE: Contributed to research design, acquisition, analysis, and interpretation of data. Drafted and revised the paper. Read and approved the final submitted manuscript.

DMC: Contributed to research design and interpretation of data. Provided revisions of the paper. Read and approved the final submitted manuscript.

MC: Contributed to acquisition, analysis and interpretation of data. Provided revisions of the paper. Read and approved the final submitted manuscript.

KMM: Contributed to acquisition, analysis and interpretation of data. Provided revisions of the paper. Read and approved the final submitted manuscript.

JA: Contributed to research design, analysis and interpretation of data. Provided revisions of the paper. Read and approved the final submitted manuscript.

MWH: Contributed to research design, acquisition, analysis and interpretation of data. Drafted and revised the paper. Read and approved the final submitted manuscript.

Acknowledgements

Not applicable.

References

1. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporosis International*. 2006;
2. Kim SH, Szabo RM, Marder RA. Epidemiology of humerus fractures in the United States: Nationwide emergency department sample, 2008. *Arthritis Care and Research*. 2012;
3. Singer A, Exuzides A, Spangler L, O'Malley C, Colby C, Johnston K, et al. Burden of illness for osteoporotic fractures compared with other serious diseases among postmenopausal women in the United States. *Mayo Clinic Proceedings*. 2015;
4. Sabesan VJ, Valikodath T, Childs A, Sharma VK. Economic and social impact of upper extremity fragility fractures in elderly patients. *Aging Clinical and Experimental Research*. 2015;
5. Sproul RC, Iyengar JJ, Devic Z, Feeley BT. A systematic review of locking plate fixation of proximal humerus fractures. *Injury*. 2011;
6. Broderick JM, Bruce-Brand R, Stanley E, Mulhall KJ. Osteoporotic Hip fractures: The burden of fixation failure. *The Scientific World Journal*. 2013.
7. Kim WY, Han CH, Park JI, Kim JY. Failure of intertrochanteric fracture fixation with a dynamic hip screw in relation to pre-operative fracture stability and osteoporosis. *International Orthopaedics*. 2001;
8. Bae JH, Oh JK, Chon CS, Oh CW, Hwang JH, Yoon YC. The biomechanical performance of locking plate fixation with intramedullary fibular strut graft augmentation in the treatment of unstable fractures of the proximal humerus. *Journal of Bone and Joint Surgery - Series B*. 2011;
9. Cha H, Park KB, Oh S, Jeong J. Treatment of comminuted proximal humeral fractures using locking plate with strut allograft. *Journal of Shoulder and Elbow Surgery*. 2017;

10. Hast MW, Chin M, Schmidt EC, Sanville J, Van Osten GK, Mehta S. Mechanical Effects of Bone Substitute and Far-Cortical Locking Techniques in 2-Part Proximal Humerus Fracture Reconstruction. *Journal of Orthopaedic Trauma*. 2020 Apr 1;34(4):199–205.
11. Mattsson P, Alberts A, Dahlberg G, Sohlman M, Hyldahl HC, Larsson S. Resorbable cement for the augmentation of internally-fixed unstable trochanteric fractures. A prospective, randomized multicentre study. *Journal of Bone and Joint Surgery - Series B*. 2005;
12. Namdari S, Voleti PB, Mehta S. Evaluation of the osteoporotic proximal humeral fracture and strategies for structural augmentation during surgical treatment. *Journal of Shoulder and Elbow Surgery*. 2012.
13. Cornell CN. Internal fracture fixation in patients with osteoporosis. *The Journal of the American Academy of Orthopaedic Surgeons*. 2003.
14. Xie Y, Zhang L, Xiong Q, Gao Y, Ge W, Tang P. Bench-to-bedside strategies for osteoporotic fracture: From osteoimmunology to mechanosensation. *Bone Research*. 2019.
15. Crandall CJ, Newberry SJ, Diamant A, Lim YW, Gellad WF, Booth MJ, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: An updated systematic review. *Annals of Internal Medicine*. 2014.
16. Barrionuevo P, Kapoor E, Asi N, Alahdab F, Mohammed K, Benkhadra K, et al. Efficacy of pharmacological therapies for the prevention of fractures in postmenopausal women: A network meta-analysis. *Journal of Clinical Endocrinology and Metabolism*. 2019;
17. Molvik H, Khan W. Bisphosphonates and their influence on fracture healing: a systematic review. *Osteoporosis International*. 2015.
18. Seebach C, Kurth A, Marzi I. The influence of bisphosphonates on fracture healing. *Orthopade*. 2007;
19. Hak DJ. The biology of fracture healing in osteoporosis and in the presence of anti-osteoporotic drugs. *Injury*. 2018;
20. Kates SL, Ackert-Bicknell CL. How do bisphosphonates affect fracture healing? *Injury*. 2016;
21. Xue D, Li F, Chen G, Yan S, Pan Z. Do bisphosphonates affect bone healing? A meta-analysis of randomized controlled trials. *Journal of Orthopaedic Surgery and Research*. 2014;
22. Shi Z, Zhou H, Pan B, Lu L, Liu J, Kang Y, et al. Effectiveness of teriparatide on fracture healing: A systematic review and meta-analysis. *PLoS ONE*. 2016.
23. Delmas PD, Bjarnason NH, Mitlak BH, Ravoux AC, Shah AS, Huster WJ, et al. Effects of raloxifene on bone mineral density, serum cholesterol concentrations, and uterine endometrium in postmenopausal women. *New England Journal of Medicine*. 1997;
24. Rey JRC, Cervino EV, Rentero ML, Crespo EC, Álvaro AO, Casillas M. Raloxifene: Mechanism of Action, Effects on Bone Tissue, and Applicability in Clinical Traumatology Practice. *The Open Orthopaedics Journal*. 2009;
25. Gallant MA, Brown DM, Hammond M, Wallace JM, Du J, Deymier-Black AC, et al. Bone cell-independent benefits of raloxifene on the skeleton: A novel mechanism for improving bone material

- properties. Bone. 2014;
26. Kumar V, Green S, Stack G, Berry M, Jin JR, Chambon P. Functional domains of the human estrogen receptor. Cell. 1987;
 27. Cattani-Lorente M, Rizzoli R, Ammann P. In vitro bone exposure to strontium improves bone material level properties. Acta Biomaterialia. 2013;
 28. Nyman JS, Roy A, Shen X, Acuna RL, Tyler JH, Wang X. The influence of water removal on the strength and toughness of cortical bone. Journal of Biomechanics. 2006;
 29. Von Rüden C, Augat P. Failure of fracture fixation in osteoporotic bone. Injury. 2016;
 30. Marongiu G, Mastio M, Capone A. Current options to surgical treatment in osteoporotic fractures. In: Aging Clinical and Experimental Research. 2013.
 31. Konstantinidis L, Helwig P, Hirschmüller A, Langenmair E, Südkamp NP, Augat P. When is the stability of a fracture fixation limited by osteoporotic bone? Injury. 2016;

Tables

Table 1. Mechanical Properties derived from four-point bending of Control group and Raloxifene treatment group (metaphyseal fetal bovine femora)

Mechanical Property	Control	Treatment	P-Value
Stiffness (N/mm)	1.4 ± 0.5	1.2 ± 0.5	0.326
Ultimate Force (N)	1.69 ± 0.423	1.56 ± 0.527	0.560
Bending Rigidity (Nm ²)	0.0004 ± 0.0002	0.00038 ± 0.000162	0.422
Modulus (MPa)	226 ± 86.5	190 ± 62.2	0.303
Ultimate Stress (MPa)	4.05 ± 1.08	3.77 ± 1.08	0.569
Toughness (J/m ³)	0.16 ± 0.05	0.15 ± 0.07	0.850

Table 2. Pull-out strength of 3.5 mm screws from 5 different locations on matched pairs of cadaveric humeri from control (CTRL) and raloxifene (RALOX) groups. All units are Newtons.

	Location 1		Location 2		Location 3		Location 4		Location 5	
	CTRL	RALOX	CTRL	RALOX	CTRL	RALOX	CTRL	RALOX	CTRL	RALOX
Pair 1	58.9	223.6	42.7	97.9	120.3	75.6	26.1	202.0	76.8	42.2
Pair 2	39.3	45.5	25.5	70.8	221.0	114.2	28.9	72.0	62.1	19.6
Pair 3	167.0	292.9	108.9	154.4	138.7	163.3	67.8	134.4	146.7	0.3
Pair 4	172.8	105.8	86.6	28.2	124.4	91.0	206.7	322.1	84.3	184.2
Pair 5	121.9	119.6	71.5	60.7	87.9	125.8	32.6	141.9	32.1	42.4
Average	112.0	157.5	67.0	82.4	138.5	114.0	72.4	174.5	80.4	57.7
Standard Dev.	61.1	99.2	33.4	47.3	49.7	33.8	76.9	94.5	42.1	72.8
p-value	0.321		0.26		0.2		0.021		0.301	

Figures

Figure 1

Proximal humerus fractures (A) preoperatively (B) status post open reduction, internal fixation (C) status post failure of fixation

Figure 2

4 point bending test setup

Figure 3

Locations of screw placement for pull-out testing for locations 1 – 5. Note: plate and drill tower were utilized for trajectory but removed prior to screw insertion and pull-out testing.

Figure 4

Toughness results

Figure 5

Screw pull-out results