

PRESERVATION OF PERIARTICULAR CANCELLOUS MORPHOLOGY AND MECHANICAL STRENGTH IN POST-TRAUMATIC EXPERIMENTAL OSTEOARTHRITIS BY ANTIRESORPTIVE THERAPY

^{1,2} Josh MacNeil, ^{1,2,4} Steven Boyd, ³ Michael Doschak and ^{1,3,4} Ron Zernicke

¹Department of Mechanical and Manufacturing Engineering, University of Calgary, Alberta, Canada

²Calgary Center for Innovative Technology, Alberta, Canada

³Department of Surgery, University of Calgary, Alberta, Canada

⁴Faculty of Kinesiology, McCaig Centre for Joint Injury and Arthritis Research, University of Calgary, Alberta, Canada

email: skboyd@ucalgary.ca, web: <http://www.enme.ucalgary.ca/~skboyd/>

INTRODUCTION

Osteoarthritis (OA) is the most common joint disease in humans and results in a severe degradation of joint structures that ultimately leads to joint degradation and failure [1]. The onset of OA is joint dependent and its probability increases with age or joint injury [2]. An anterior cruciate ligament transection (ACLX) is a well established animal model for post-traumatic OA, and changes in the periarticular bone in experimental OA occur as early as 3 weeks after injury [3].

This project is aimed at investigating whether antiresorptive bisphosphate (BP) drug therapy conserves long term joint function and retards OA progression. The effectiveness of BP therapy was assessed in conserving bone mineral at the MCL entheses, periarticular cancellous bone architecture and the apparent mechanical properties of the periarticular bone in the distal femur and at the MCL insertion in an ACLX joint.

METHODS

Skeletally mature, female New Zealand White rabbits were used as an experimental OA model and were randomly assigned to three groups (N=10/group). ACLX was performed in two groups; the first group was dosed with BP (risedronate, 0.1 mg/kg s.c. daily for 6 wk), the second group was untreated. The third group was comprised unoperated normal controls. After 6 wk, all animals were sacrificed, and the femur-MCL-tibia complex was dissected free. The medial and lateral femoral condyles were separated with a band saw to reduce the size of the specimen to facilitate scanning of the entire condyle.

Micro computed tomography (μ CT) scans of the medial condyle of each cohort group were obtained (Skyscan 1072, Skyscan, Aartselaar, Belgium) at 100 kV through 180° with a rotation step of 0.9°, at an x12 magnification that produced serial cross sectional images of isotropic 19.4 μm^3 voxels. All data were filtered ($\sigma = 1.2$, support = 2) and a global threshold was applied to extract the mineral phase. The μ CT data were input for large-scale finite element (FE) models to determine differences between groups in their apparent mechanical properties using a direct mechanics approach [4]. The approach accounted for the variation in bone micro architectural geometry, but not variation in tissue modulus.

A morphological analysis for each group was also completed and provided a quantification of periarticular cancellous bone architecture by determining trabecular thickness (Tb.Th),

trabecular number (Tb.N), trabecular separation (Tb.S), bone surface to volume ratio (BS/BV), structural model index (SMI) and anisotropy (by mean intercept length, MIL).

RESULTS AND DISCUSSION

The experimental results revealed that BP therapy conserved medial collateral ligament (MCL) bone complex laxity and bone mineral at the MCL entheses [5]. It was previously shown by our group (Doschak et al. 2004) that BP therapy conserved periarticular cancellous bone mineral density, elastic modulus, and maximal energy to failure [6]. A qualitative assessment of the μ CT scans indicated that periarticular cancellous bone architecture was conserved. Full morphological and finite element results are proceeding.

Conservation of bone mineral density, bone mineral at the MCL entheses, elastic modulus and energy to failure in the cancellous bone indicated that primary and secondary joint structures were being maintained through BP therapy. A reduction in joint laxity may also have reduced the effect of an ACL injury on joint loading conditions. Those improvements in joint structure and function may have a long term effect on retarding the pathogenesis of OA.

CONCLUSIONS

Based on a qualitative assessment of the data and on the experimental results obtained, BP therapy appeared to have a positive effect on joint structure and function in the post-traumatic ACLX joint that may retard long term OA progression.

ACKNOWLEDGEMENTS

Supported in part by Canadian Institutes for Health Research and the Wood Professorship in Joint Injury Research.

REFERENCES

1. Kelsey JL. *Epidemiology of musculoskeletal disorders*. New York: Oxford University Press, 1982
2. Praemer A, Furner S, Rice DP. *Musculoskeletal conditions in the United States*. American Academy of Orthopaedic Surgeons, Park Ridge, IL, 1992.
3. Boyd SK, et al. *J Bone Miner Res.* **17**:687-694, 2002
4. van Rietbergen, et al. *J Biomech.* **12**:1653-1657, 1996
5. Doschak MR, et al. *Osteoarthritis Cartilage.* **11**:S85; P236, 2003
6. Doschak MR, et al. *J Orthop Res.* **22**:942-948, 2004