Relationships among Articular Cartilage Biomechanical Properties and Biomarkers Produced by Subchondral Bone from Osteoarthritic Knees

Orthopaedic Surgery
School of Medicine
University of Missouri Health

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Thompson Laboratory for Regenerative Orthopaedics

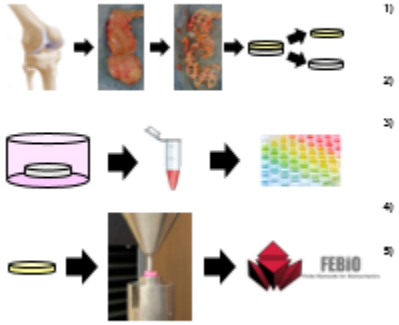
Introduction and Purpose

- Osteoarthritis (OA) is a multifactorial disease progressing from an initial injury to whole-joint inflammation and degeneration causing pain and dysfunction
- This study was designed to determine the relationship between biomechanical properties of the articular cartilage and production of biomarkers from the underlying bone

Hypothesis

There would be significant changes in subchondral bone biomarker production associated with changes in the biomechanical properties of the overlying articular cartilage from osteoarthritic knees.

Methods



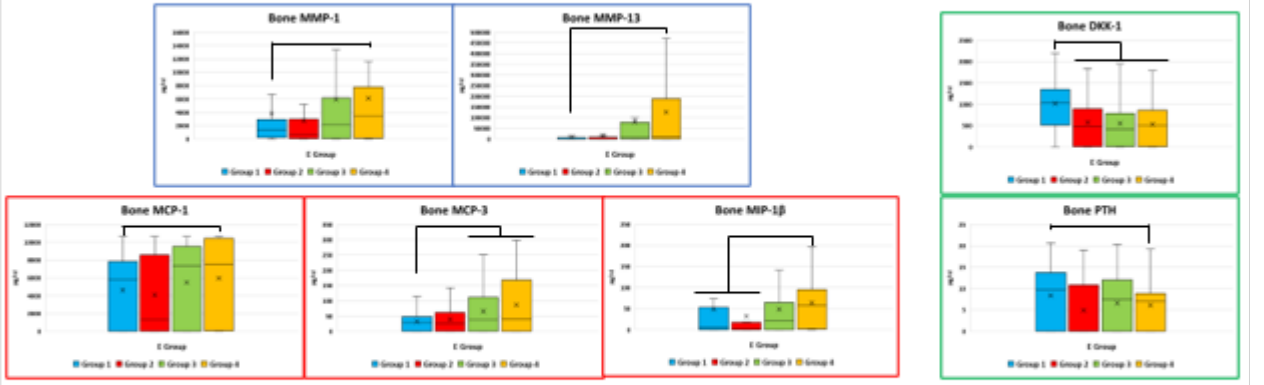
1) With IRB approval (IRB #1208302) and informed patient consent, tissues of bone and cartilage normally discarded after surgery were obtained from TKA patients (n=6). Osteochondral explants (6mm diameter, n=350) were created from across each articular surface and cartilage was separated from bone.
2) Bone and cartilage explants were cultured for 3 days in DMEM at 37°C and 5% CO2 and then media were collected for biomarker analyses.
3) Media were tested for MMP-1,-2,-3,-13, TIMP-1,-2,-3,-4, PDGF-AA, IL-6,-8,-10,-12,-16A,-18, FRACTALKINE, GRO-α, MCP-1,-3, MIP-1α,-1β, INF-α, VEGF, DKK1, OPG, OC, OPN, SOST, and PTH using commercially available assays. The media biomarker data were standardized to the weight of the explant for analyses.
4) Articular cartilage explants were tested in compression, then analyzed using FEBio to determine the modulus (E), KSI and permeability.
5) The cartilage biomechanical data were sorted from lowest to highest and placed into four quartiles with approximately 25% of all samples in each quartile. Kruskal-Wallis tests with post-hoc analyses and Bonferroni corrections were used to determine significant ($p<0.05$) differences in bone biomarker production between groups.

Conclusions

- The data indicates that as cartilage modulus increases and KSI decreases, the production of degradative and pro-inflammatory biomarkers by the bone increases significantly.
- Additionally, the data indicates that as cartilage modulus and KSI decrease, there is a potential decrease in bone formation
- Characterizing of the relationships among subchondral bone metabolic responses and the biomechanical properties of the articular cartilage may expand our understanding of the development and progression of OA.
- The outcome of the study reveals complex relationships in OA that expands knowledge on how to better delineate and developments of effective interventions for OA.

Results

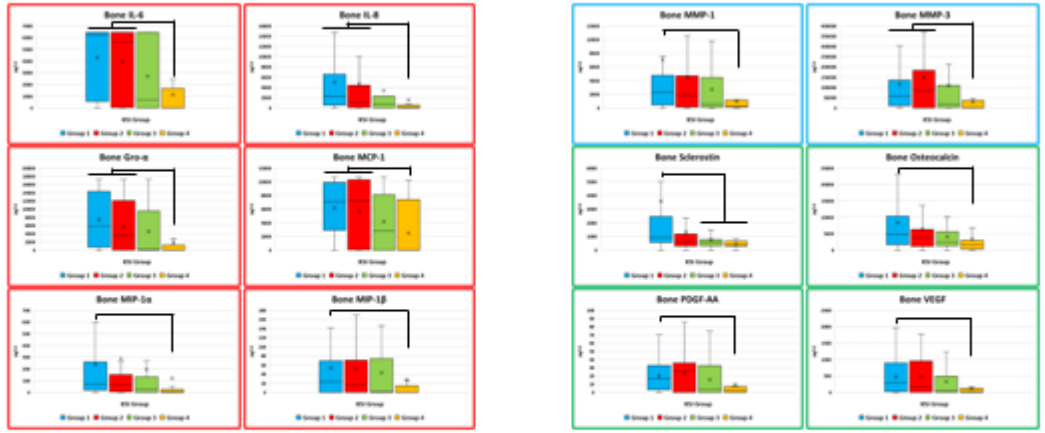
Cartilage Modulus



- As the modulus of the articular cartilage decreased, the production of the degradative enzymes (blue boxes) and pro-inflammatory chemokines (red boxes) decreased, with subchondral bone samples underlying cartilage with the lowest modulus (group 1) producing significantly lower levels than sample with the highest modulus (group 4).
- As the modulus of the articular cartilage decreased, there appears to be a decrease in bone formation (green boxes) as indicated by the significant increase in subchondral bone DKK-1 and Parathyroid Hormone (PTH) production in group 1 compared to group 4.

Results

KSI



- As the fiber strength (KSI) modulus of the articular cartilage decreased, the production of the inflammatory biomarkers by the subchondral bone (red boxes) increased as indicated by the significantly higher production in groups 1 and 2 compared to group 4.
- The production of degradative enzymes (blue boxes) by the subchondral bone also increased as the KSI of the cartilage decreased, as indicated by the significantly higher production in groups 1 and 2 compared to group 4.
- Further as KSI decreased there appears to be a dysregulation in bone formation (green boxes) with increased SOST production, which inhibits bone formation. However, the increased osteocalcin production indicates an attempt to increase bone density, and the increased PDGF-AA and VEGF indicates an increase in bone vascularization potentially associated with increased bone formation.

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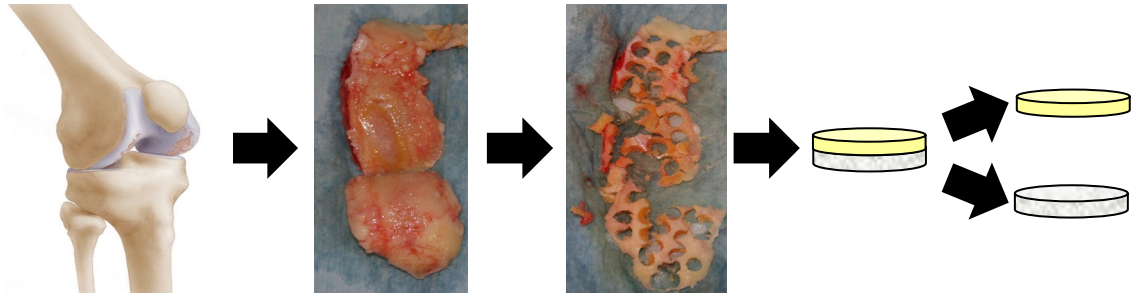

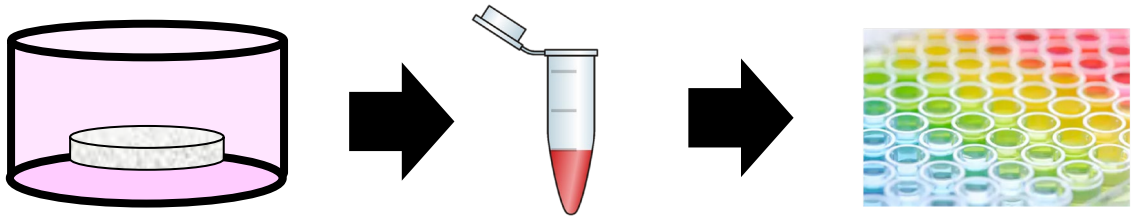

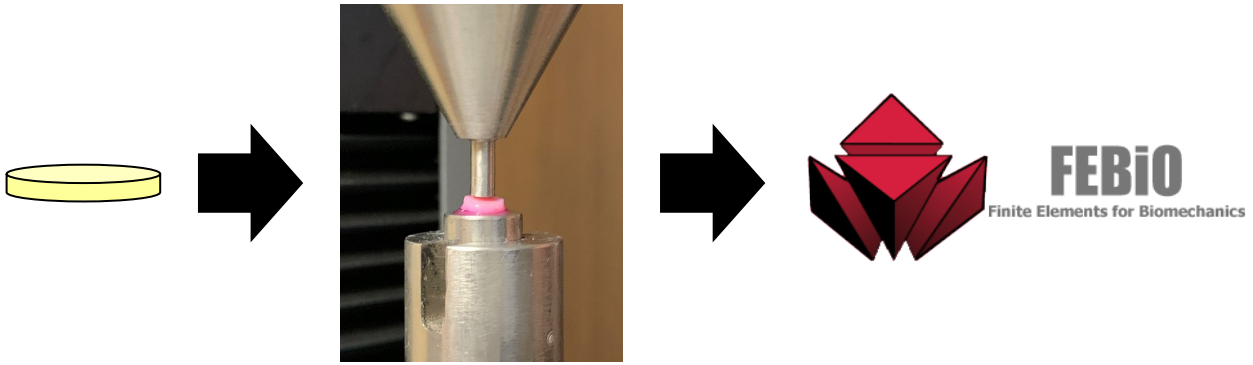

1) With IRB approval (IRB #1208392) and informed patient consent, tissues of bone and cartilage normally discarded after surgery were obtained from TKA patients (n=8). Osteochondral explants (6mm diameter, n=359) were created from across each articular surface and cartilage was separated from bone.
2) Bone and cartilage explants were cultured for 3 days in DMEM at 37˚C and 5% CO_2 and then media were collected for biomarker analyses.
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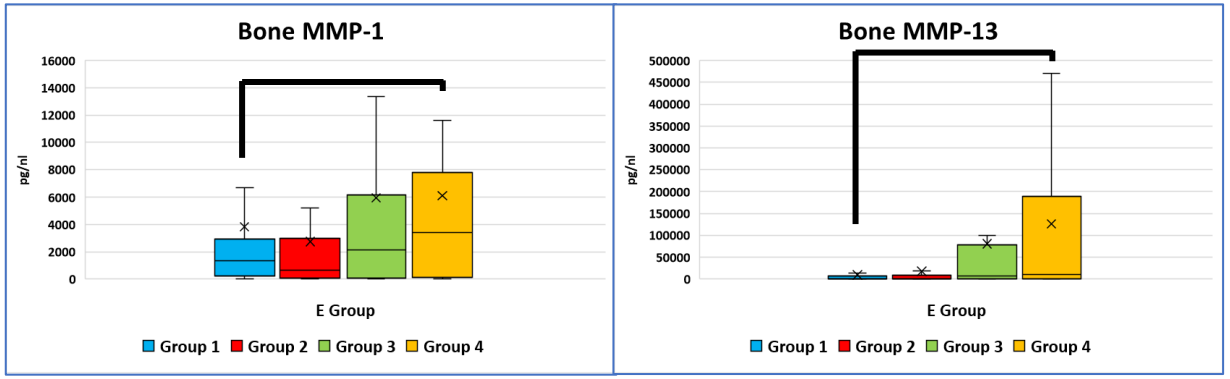

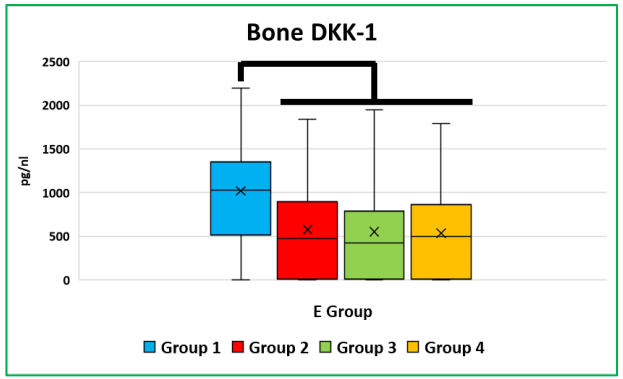

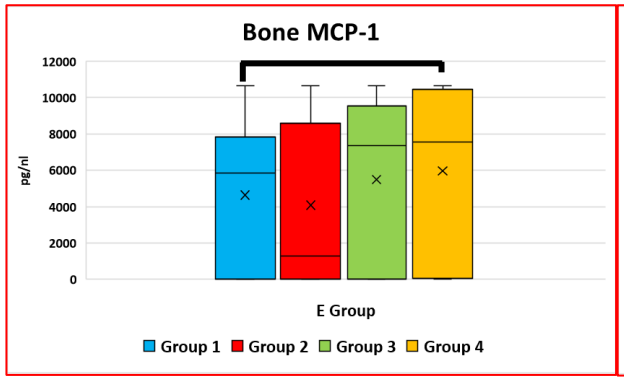

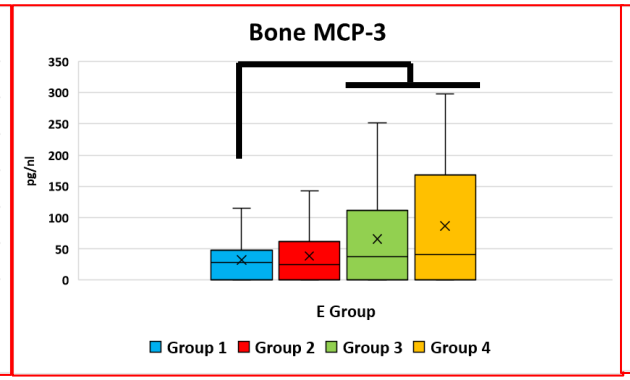

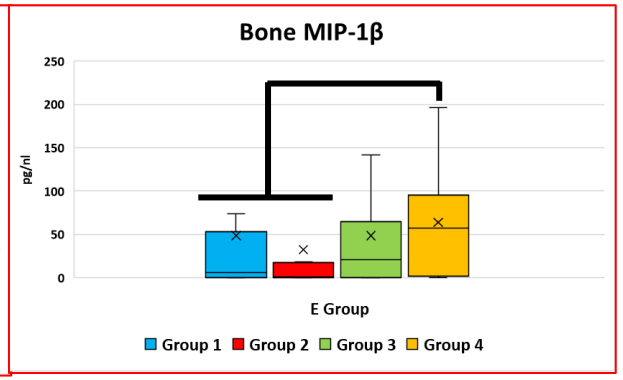

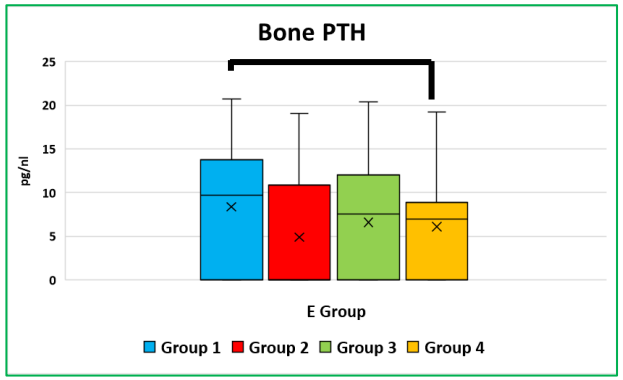

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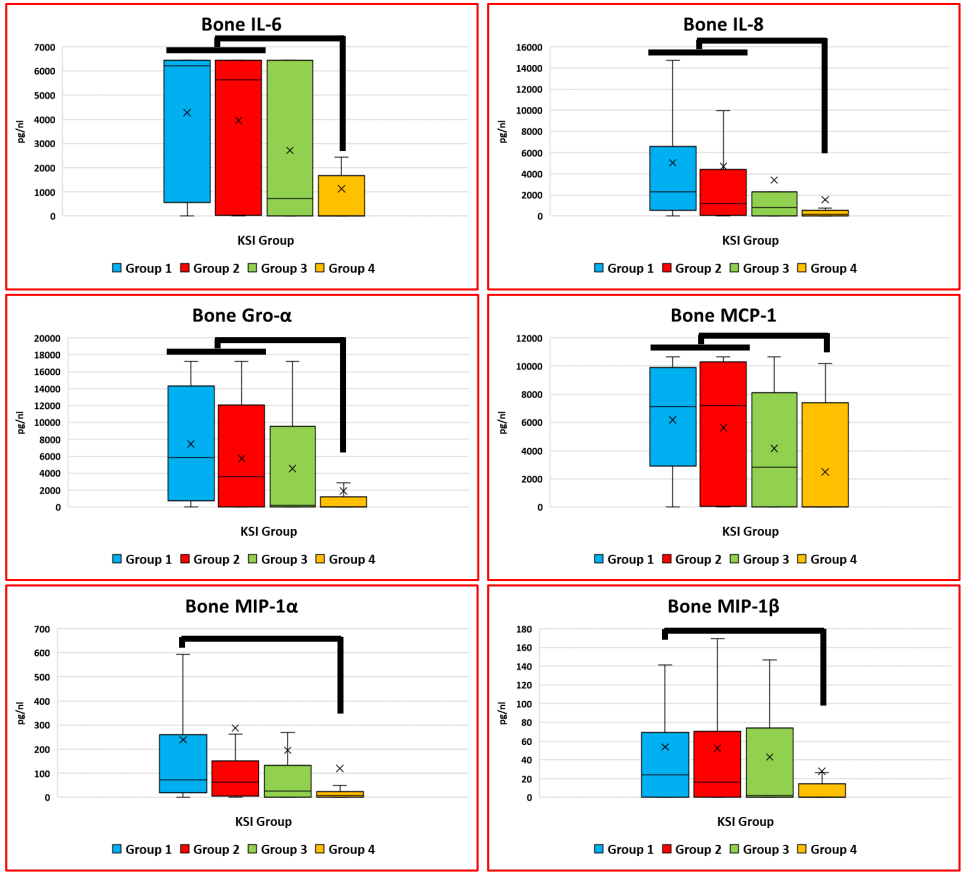

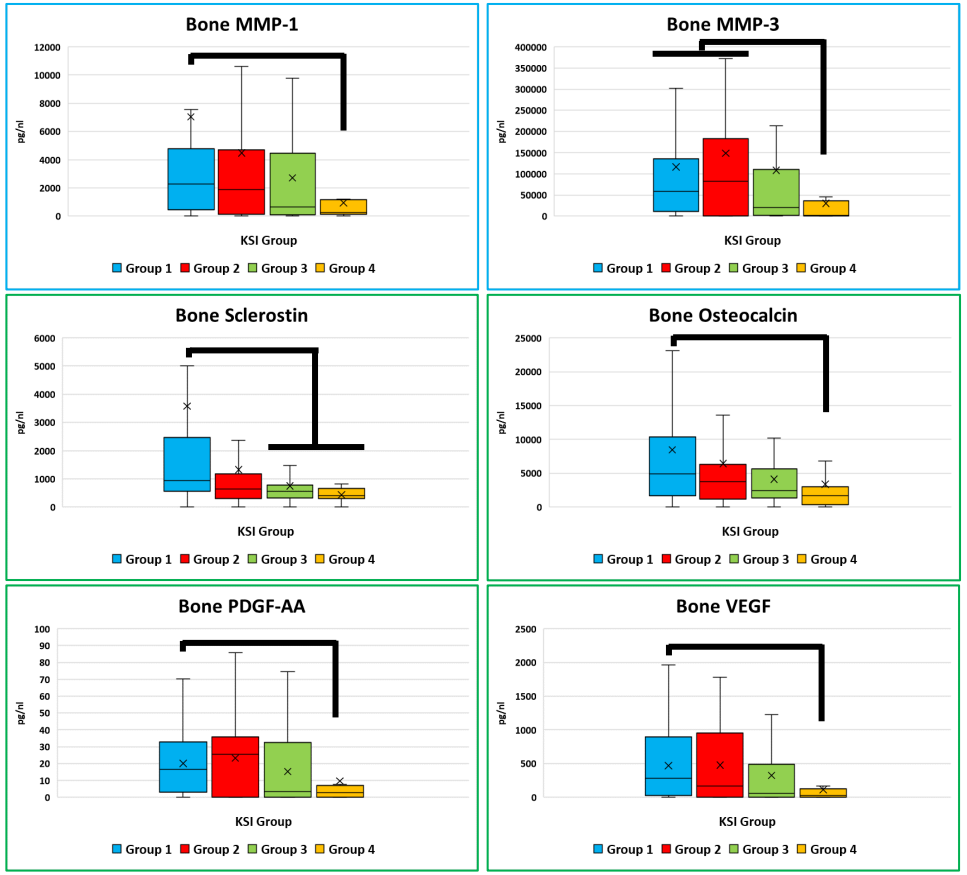

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