Longitudinal Characterization of Inflammatory Biomarkers concurrent with the progression of an injury-induced model of Osteoarthritis

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Introduction

- Osteoarthritis (OA) is a chronic and progressive degenerative joint disease.

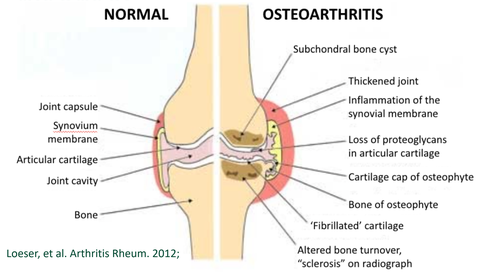

Figure 1. **A joint with OA vs. a Normal joint.** This disease is characterized by many morphological changes in the joint space.

- Currently, no curative therapeutics are available for the disease, only ones to help manage the pain.
- Early pilot studies demonstrated feasibility of longitudinal monitoring of immune responses in the MMT model of OA.
- We aim to identify early immune biomarkers that may be indicative of disease status.

Analysis:
Microcomputed Tomography (MicroCT):

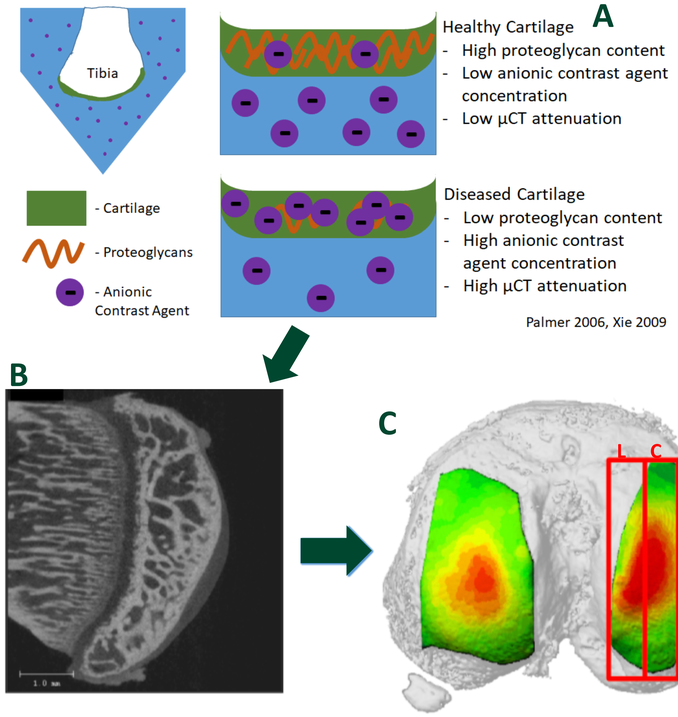

Figure 3. **MicroCT Analysis.** (A) Contrast enhancing in healthy and diseased cartilage. (B) 2D greyscale image of a medial Left section in a Y sagittal view. (C) 3D representations of the cartilage in medial and lateral tibial plateau. The medial tibial plateau can then be sectioned into thirds: lateral, central and medial. This allows for more localized evaluations.

Findings

- Possible Sex Differences with OA treatment

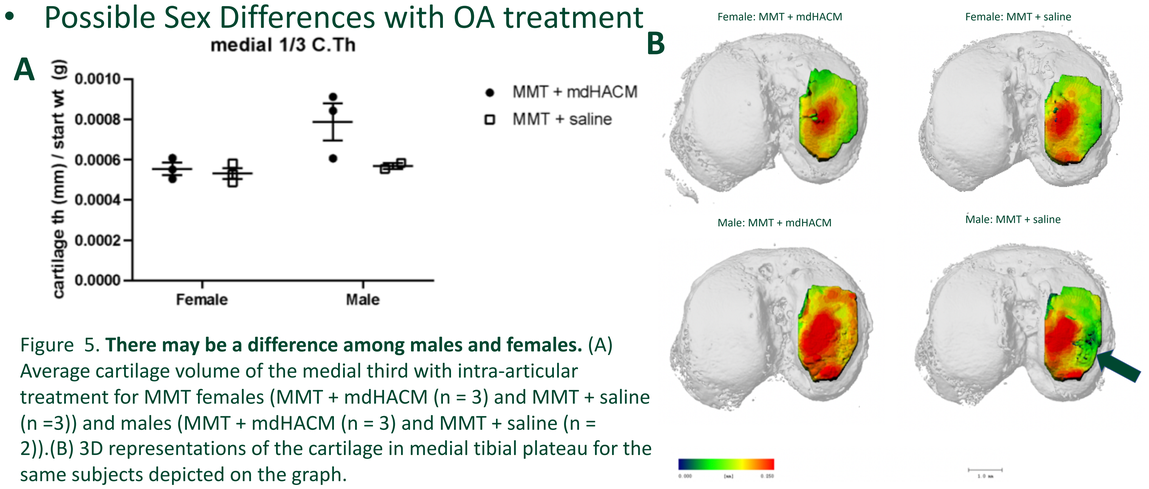

Figure 5. **There may be a difference among males and females.** (A) Average cartilage volume of the medial third with intra-articular treatment for MMT females (MMT + mdHACM (n = 3) and MMT + saline (n =3)) and males (MMT + mdHACM (n = 3) and MMT + saline (n = 2)).(B) 3D representations of the cartilage in medial tibial plateau for the same subjects depicted on the graph.

Next Steps:

- Calculate cartilage surface roughness

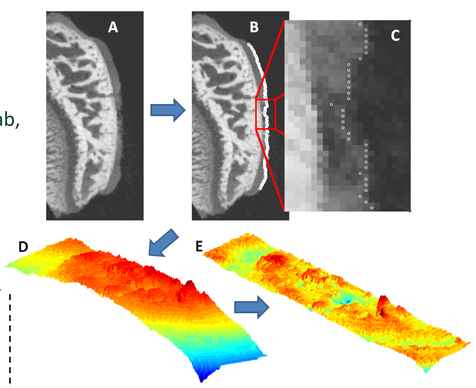

Figure 6. **Surface Roughness**. Using a MATLAB program developed by our lab, we will calculate cartilage surface roughness.

- Complete microCT cartilage evaluations:
  - ➢ n=7-8 per group for 3 week treatment study (with females & males)
  - ➢ n=9-10 per group for 6 week MMT only study (with females & males)
- Linear and nonlinear multivariate regression techniques to identify **immune biomarkers** that are correlated with the **cartilage surface roughness, volume, thickness, and X-ray attenuation** of the articular cartilage at the end point.

Methods

Surgical preparation of subjects:

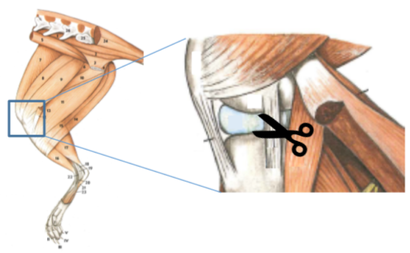

Figure 2. **MMT Model in the rat.** We expose the joint space and meniscus on the medial side and transect it. This creates a mechanical instability that doesn't get repaired.

Blood Draw: *Synovial Fluid (SF):*

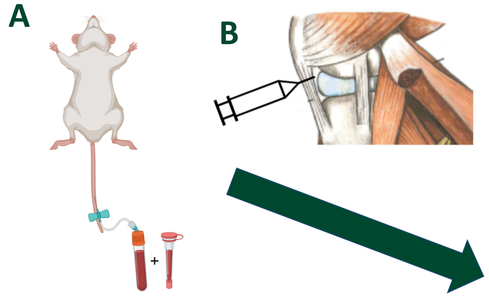

Figure 4. **Immune Response Analysis.** (A) Blood collection schematic. (B) Synovial fluid aspiration schematic. (C) Using flow cytometry blood samples are ran and circulating immune cell levels are measured. (D) Luminex allows us to measure circulating inflammatory cytokine levels in both the blood and the SF.

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