Localization of Articular Cartilage Damage in the Rat Medial Meniscus Tear Model for Osteoarthritis Using Contrast Based Micro-CT Imaging

INTRODUCTION

Osteoarthritis (OA) is the most common degenerative joint disease in humans. Development and characterization of small animal models of osteoarthritis is important to provide a platform for better understanding OA pathogenesis and evaluating disease modifying therapies. A common surgical method of inducing OA for testing therapeutics involves transecting the medial meniscus (MMT). A full cut is made at the narrowest point of the meniscus simulating a meniscal tear which leads to fibrillation, proteoglycan loss and eventual degradation of the cartilage. The traditional method to detect these changes is histology which is destructive, time consuming and qualitative in nature.

**Objective:** Assess differences in articular cartilage of control and MMT-injured knee joints by quantifying microstructural changes via localized analyses using μ-CT imaging.

**Hypothesis:** Contrast-based μ-CT can detect articular cartilage damage in the rat MMT model

**METHODS**

**Animal model:** Weight matched male Lewis rats (275-300g, n=4) underwent meniscal transection on the left leg (right leg = unoperated control) and were sacrificed at 3 weeks. **μ-CT Imaging:** Joints were dissected and scanned using the EPIC-μCT technique. Axial cross-sectional images were resectioned sagittally, and cartilage was segmented by global thresholding combined with semi-automatic contouring. **μ-CT Image Analysis:** Images were evaluated for 4 volumes of interest (VOIs): (1) Full articular cartilage in the proximal tibia (2) Only the medial plateau (3) Medial 1/3 of the medial tibial plateau (4) Only focal lesions on the medial plateau (Fig 1). Two outcome measures were defined for evaluation of focal defects: fibrillation (defect < 50% of cartilage thickness) and lesion (defect > 50% of cartilage thickness). To calculate lesion volume, cartilage volume was subtracted from total evaluated volume. (All experiments were approved by the Institutional Animal Care and Use Committee protocol at Georgia Tech)

**RESULTS**

For evaluation VOI 1, no difference in cartilage thickness was detected between control and MMT samples but there was a trend towards higher attenuation (Fig 2).

**DISCUSSION**

This study successfully demonstrated the ability of contrast-based μ-CT to detect and quantify cartilage changes on the micron level. Fibrillation/lesions were defined as measures to examine the cartilage surface, and μ-CT evaluations were used to assess differences in attenuation and lesion volume. The MMT samples displayed higher attenuation and presence of lesions and fibrillations compared to contraartal controles. These changes were not detected in full cartilage, therefore localized regions of interest were defined for a more focused analysis. Histology allows for visualization and 2D analysis lesions but is destructive and cannot provide quantitative 3D measurements of focal defects. This study showed that contrast-based μ-CT has the sensitivity to detect focal degeneration in articular cartilage morphology and composition and may therefore be a valuable tool for the assessment of therapeutic efficacy in small animal models of OA.

**SIGNIFICANCE**

There is a need for quantitative tools to test the efficacy of OA drugs in small animal models. This study demonstrates the ability of μ-CT to detect local changes and quantify them in the MMT model for OA.

**ACKNOWLEDGEMENTS**

This work is supported by the NIH grant R21 AR053716.

**REFERENCES**

1. Palmer et al. PNAS, Dec 2006. 103 (51). P19255-60