Quantification of Cartilage and Subchondral Bone Microstructure in Glenohumeral Osteoarthritis using MRI and µCT
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INTRODUCTION: Primary glenohumeral osteoarthritis (GOA) accounts for up to 26% of patients with shoulder complaints and leads to debilitating loss of functionality in the shoulder. Treatment to slow early-stage GOA could improve outcomes and delay index arthroplasty, however, diagnosing GOA early with existing strategies is difficult as many patients are asymptomatic, and imaging to detect early abnormalities are not well defined. GOA is characterized by the degeneration of articular cartilage covering the humeral head and glenoid in the glenohumeral joint. Articular cartilage is primarily composed of type II collagen, proteoglycans, and water, and the onset of destruction of proteoglycan and collagen matrix is an early indicator of the presence of GOA. Furthermore, the structure and composition of the glenoid and humeral head subchondral bone is correlated to cartilage degeneration. Quantitative magnetic resonance imaging (MRI) using T1ρ and T2 relaxation mapping identifies changes in proteoglycan (T1ρ) and collagen content of cartilage (T2). Micro-computed tomography (µCT) is a translationally relevant technique that produces three-dimensional (3D) images at higher resolution than the clinically used computed tomography widely used to diagnose bone fractures and osteoporosis. Combined, these imaging techniques deliver a non-invasive assessment of cartilage and bone in GOA shoulders. The aims of the current study were to evaluate initial differences in MRI relaxation times and subchondral bone composition between mild and severe osteoarthritic humeral head and glenoid samples and to determine if these methods could distinguish differences in cartilage and subchondral bone between donors with rotator cuff tear or biceps tendon tear and those without rotator cuff or biceps tendon tear.

METHODS: Sample Collection: Paired humeral heads and glenoids were isolated from de-identified asymptomatic cadaveric human shoulders (IRB exempt, non-human subjects research) with prior screening to exclude donors (n=21) with a history of shoulder injury, pain, or surgery. Samples were graded using the Outerbridge classification system and separated by Outerbridge score (normal/mild, score of 0-2 and severe, score of 3-4) osteoarthritis and rotator cuff tendon condition (torn and intact). Quantitative MRI: Humeral heads and glenoids underwent T1ρ and T2 imaging using Bruker 7T MRI Scanner at 250μm in-plane resolution. For T1ρ, Echo time was minimized to 4.717ms to produce the greatest amount of cartilage signal and repetition time was set at 1500ms to allow full relaxation of excited protons in the cartilage. For T2, echo times between 4.717 – 37.736ms and repetition time of 1500ms were used. A custom MATLAB code was used to fit T1ρ and T2 relaxation times to exponential decay equations (Fig. 1) and calculate their respective goodness of fit, R². µCT Imaging: Humeral heads and glenoids were imaged using Perkin Elmer’s Quantum GX with an acquisition FOV of 72mm and high-resolution scan mode (148μm voxel size). A custom MATLAB code and BoneJ were used to calculate bone volume fraction (BV/TV), cortical bone density (CBD), trabecular bone density (TBD), trabecular spacing (Tb.Sp), cortical thickness (CTh), trabecular thickness (Tb.Th), and cartilage thickness (Car.Th). Statistics: Data were compared using the Kruskal-Wallis test followed by Wilcoxon Each-Pair post-hoc test to determine the differences between groups. Significance was reported at the 95% confidence level for all analyses.

RESULTS: A total of 21 (left/right) paired humeral head and glenoid samples (Female = 9, Male = 12, age 58-79) were evaluated: humeral heads (mild = 30, severe = 12), glenoids (mild = 32, severe = 10). MRI identified elevated T1ρ relaxation time between mild and severe GOA in humeral heads, but no significant difference in T2 relaxation times (Fig. 2A). T2 and T1ρ relaxation time were not different between mild and severe GOA in glenoids (Fig. 2B). µCT imaging demonstrated significant increase in Tb.Sp in humeral heads with increasing severity of GOA (Fig. 3). For glenoids, there was a significant decrease in CBD and increased Tb.Th and CTh between mild and severe GOA (Fig. 4). There was a trend to decrease in Car.Th between mild and severe GOA in humeral heads (p<0.1), and a trend to increase in Tb.Sp between mild and severe GOA in glenoids (p<0.1). There was no difference in BV/TV, or TBD between mild and severe GOA in humeral heads and glenoids, and the presence or absence of tendon tear did not influence MRI or µCT parameters in this cohort.

DISCUSSION: Prior studies observed associations between elevated T1ρ times with decreased proteoglycan content and increased T2 times with decreased collagen content. Our results suggest lower proteoglycan content in humeral heads and decreased collagen content in glenoids with severe compared to mild GOA. This result is in contrast with T1ρ and T2 relaxation times in patients with hip osteoarthritis. This suggests that these MRI sequences could differentiate the disruption of matrix cartilage components at different stages of GOA. The changes in subchondral bone microstructure identified using µCT also correlated with degree of GOA. In a prior hip study, the increase in Tb.Th was consistent, but the increase in BV/TV was not present in our findings. This suggests the possibility of subchondral bone remodeling due to persistent abnormal mechanical stresses which causes a cellular and biomolecular response to microfractures. Limitations of this study include the small sample size of severe GOA samples, the surprisingly limited number of normal shoulders in this cohort, and a number of confounding factors such as age, BMI, and gender. Additional regional analyses of humeral heads and glenoids combined with histology will provide further insight into the regional changes in GOA with increasing severity.

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Figure 1: Representative T1ρ and T2 maps of humeral head and glenoid cross section at 0 and 4 Outerbridge scores. Figure 2: Overall T1ρ and T2 relaxation times for A) humeral heads and B) glenoids. Figure 3: Humeral head subchondral bone microstructure quantified from µCT imaging. Figure 4: Glenoid subchondral bone microstructure quantified from µCT imaging. Individual data points are distinguished by torn or intact biceps or shoulder (rotator cuff) tendon.