Quantification of longitudinal changes in cartilage following viscosupplementation therapy via Tρ MRI

Matthew Fenty MBA1, Roshan Shah MD JD,2 Yinan Kuang3, Jeff Stanbrough MD, John Kelly MD, Ravinder Reddy PhD, and Fotios Tjoumakaris MD

1Center for Magnetic Resonance and Optical Imaging, University of Pennsylvania, Philadelphia, PA, United States, 2McKay Orthopaedic Research Laboratory, Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA, United States, 3School of Engineering and Applied Sciences, University of Pennsylvania, Philadelphia, PA, United States, 4Sports Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA, United States, 5Sports Medicine, Rothman Institute, Egg Harbor Township, NJ, United States

OBJECTIVE: To quantify changes to articular cartilage in patients following viscosupplementation therapy with mild to moderate osteoarthritis using Tρ MRI.

BACKGROUND: Osteoarthritis (OA) affects nearly 30 million Americans and comprises a significant burden to the healthcare system. Viscosupplementation (VS) is frequently used for the management of mild to moderate OA. VS purportedly increases the duration that VS remain within the joint space and is hypothesized that the treatment effects of the VS will be diminished by 3 months following injection. Additionally, we hypothesize that the treatment effects of the VS will be diminished by 3 months following injection.

METHODS: Following IRB guidelines, 10 subjects (mean age, 56 ± 10 yrs) with Kellgren-Lawrence Grades 1 and 2 OA, and who never had prior VS or knee surgery, were scanned at baseline, 6 weeks post-injection, and 3 months post-VS using a 3T MRI scanner. Tρ-weighted images were acquired for segmentation of cartilage, and Tρ-weighted 3D TrueFISP images were acquired to calculate spatial Tρ relaxation maps. Sixteen Tρ-weighted slices were acquired in each aspect to allow for volumetric analysis. Image acquisition parameters have been described previously [4]. Isotropic sagittal MPRAGE images were re-sliced along coronal and axial views and interpolated to match the resolution of Tρ-weighted images. Inter- and intra-scan motion was corrected using 3D rigid-body co-registration algorithms. Femoral and tibial images were co-registered separately due to discrepancies in flexion angle between imaging sessions. ROI analysis was performed on the same locations for three time points to accurately quantify changes in Tρ through mean compartmental analysis and percent change maps from baseline images. Cartilage was segmented using the SlicerOMatic (Tomovision, Quebec, CA) software package. Co-registered Tρ-weighted images were fit pixelwise to the linearized, mono-exponential signal decay equation ln(S) = -TSL/Tρ + ln(S0). Volumetric Tρ values were calculated by layer depth (superficial, middle, deep) as well as by region (medial and lateral patella, femoral condyles, and tibial plateau). Statistical analysis was performed using a one-tailed paired t-test between time points. Additional data to be analyzed but not presented for this abstract include the visual analog pain, WOMAC, and IKDC subjective scores before injection and at the time of follow-up MRI. WORMS scoring for each patient is currently being performed and will be correlated to quantitative findings. Statistical significance was accepted when p<0.05.

RESULTS:

There were significant differences in volumetric Tρ scores in both the medial and lateral compartments of the superficial patella (p<0.05) 6 weeks following treatment but not after three months (Med. - p<0.01, Lat. - p<0.006). Table 1 lists several regions with significant differences between individual or aggregated compartments (by depth level, all medial or all lateral or total joint) between various time point (1st and 2nd and 1st and 3rd). Visual inspection of the Tρ images and percent change maps demonstrate a varied physiological response to VS injection between individuals. The Tρ signal can change uniformly or regionally throughout joint as shown in Figure 1 and Figure 2. Figure 1 data demonstrates volumetric mean drop in Tρ > 20% across the entire patella while Figure 2 has no significant difference in average between two following time points. There is a large region across the middle of the lateral facet with an average Tρ score < 20% versus the volumetric mean. This trend of non-uniform spatial changes to Tρ following VS regimen is prevalent among all patients.

CONCLUSIONS: These data suggest that VS has a quantifiable physiological effect on knee articular cartilage. This effect is greater in the superficial layers than in the deep layers. Intuitively, direct contact between VS and cartilage occurs at the superficial layer, and there may be a subsequent physical mechanism of action for VS. Interestingly, the greatest effects were observed in the patella-femoral compartment which may be due to lower load-bearing activities and increased cartilage thickness. Future work will assess methods to predict homo- or heterogeneous changes within the articular cartilage through correlation analysis with WORMS, WOMAC, and other qualitative assessments. While some patients responded positively to the VS, as calculated through lower Tρ scores, there were some who did not or had higher Tρ values. There may be both placebo effects as well as anti-inflammatory mechanisms associated with the VS which allowed patients to push through pain more than before thereby causing increased damage to the cartilage tissue. We will follow this cohort to determine whether this improvement in cartilage Tρ is sustained and whether these changes continue to associate with improved patient reported outcomes. Tρ MRI is a feasible non-invasive method of studying human in vivo articular cartilage changes following this routine clinical intervention. This is the first in vivo human study to demonstrate a potentially disease modifying effect of VS on early stage knee OA. It further demonstrates the utility of Tρ MRI as a noninvasive technique for assessing changes in cartilage proteoglycan content in response to an intervention. This modality and protocol may have utility in studying the disease modifying effects of therapeutic agents used in the treatment of osteoarthritis.

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