

T1rho Imaging of Mechanically Stressed Human Cartilage

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Introduction

Magnetic resonance imaging (MRI) has long been recognized as the gold standard for assessing cartilage morphology and visualizing defects. The many contrast mechanisms available in MRI permit rapid acquisition of images with exquisite detail and clarity. However, cartilage changes associated with the early stages of OA occur at the tissue level and are not seen as changes in morphology. The early stages of OA are associated with the loss of proteoglycans, subsequently making the cartilage susceptible to mechanical injury. Routine contrast mechanisms are not sensitive enough to reliably detect and display these biochemical changes.

T1 ρ relaxation is a promising marker for assessing proteoglycan content [1-3]. In cartilage, the T1 ρ relaxation time is sensitive to the low-frequency interactions between water and proteoglycans. In particular, decreased proteoglycan content reduces the relaxation rate of water molecules, increasing the T1 ρ time constant. Previous studies demonstrate the sensitivity of this method both in vitro and in vivo [4-5], but additional insight into the disease process and its progression can be gained with imaging in controlled experiments applying accurately calibrated mechanical loading on human cartilage. The purpose of this study was to investigate the feasibility of T1 ρ imaging to detect proteoglycan changes in human cartilage subjected to rigidly controlled and realistic mechanical stresses.

Methods

Mechanical stresses representative of normal human gait in vivo were reproduced in load-controlled triaxial compression chamber (TRIAX). Twelve 4-mm diameter full-thickness (1.8-3.2 mm) cylindrical plugs were created from continuous sheets of fresh human articular cartilage derived from the tibial plateau of an amputee with no known history of osteoarthritis. These plugs received a loading regimen of either 2 MPa or 5 MPa (six plugs each) lasting one hour (3600 1Hz loading cycles) followed by placement back within the cartilage sheet between TRIAX episodes. This was repeated on days 1, 5, and 9. Additionally, half of the plugs at each loading were treated with N-Acetylcysteine (NAC) to inhibit proteoglycan loss. In this single-specimen forum, the sheet acts as a common carrier for the explants and as the unloaded control.

Upon completion of the mechanical loading, T1 ρ imaging was performed on a Varian INOVA 4.7-T research system (Varian Medical Systems, Palo Alto, CA) equipped with a 4-cm diameter quadrature RF coil. The pulse sequence applied a T1 ρ preparation block consisting of 90 $^\circ$ square pulse, 500 Hz spin lock pulse of seven different durations (5 to 80 ms), a 90 $^\circ$ tip-up and a final crusher gradient. The magnetization preparation was applied to a fast spin echo pulse sequence with TR/TE=4000/11 ms, echo train length of 4, 512 x 128 matrix over a 50 x 25 mm field of view, and a 4 mm thick slice aligned to pass through the loaded plugs. Pixel-by-pixel regressions estimated the T1 ρ parameter at each location. The plug locations within the slices were determined from localizer images, and mean T1 ρ values were computed over manually selected regions of 1.5 x 1.5 mm² interest centered within the imaged plugs to assure that the region was completely within the plug, along with a region of intact and unloaded cartilage for use as an internal control.

Results and Discussion

Figure 1 below shows the location and corresponding T1 ρ maps for one plug from each of the four loading and NAC combinations, along with the regions of interest used for T1 ρ assessment. Table 1 shows the regional measures of T1 ρ acquired for each of the loading and NAC combinations as well as an intact section of unloaded cartilage. The measured T1 ρ time increased considerably for the highest mechanical loading without NAC treatment, indicating the greatest proteoglycan loss. This was subsequently confirmed by biochemical assay. The treated samples showed a lesser increase in T1 ρ and loss of proteoglycan.

T1 ρ values for cartilage loaded at 2 MPa showed no qualitative difference compared to intact and unloaded segments of cartilage in either treated or untreated plugs, reflecting a level of proteoglycan change that was undetected by imaging. This feasibility study suggests that T1 ρ imaging can detect regional changes in proteoglycan content resulting directly from mechanical loading effects. The ability to follow the time course of proteoglycan depletion in cartilage under controlled loading conditions will help lay necessary groundwork for sensitive and accurate assessment of cartilage degradation in vivo.

References

- [1] Duvvuri U et al., *Magn Reson Med* **38**:863, 1997.
[2] Akella SVS et al., *Magn Reson Med* **46**:419, 2001.
[3] Wheaton AJ et al., *Magn Reson Med* **54**:1087, 2005.

- [4] Regatte RR et al., *Radiology* **229**:269, 2003.
[5] Duvvuri U et al., *Osteoarthritis Cartilage*, **10**:838, 2002.

Table 1:

Measured T1 ρ (mean \pm s.d., ms) of sample regions

| <u>Loading</u> | <u>Untreated</u> | <u>NAC Treated</u> |
|----------------|------------------|--------------------|
| None | 21.2 \pm 2.7 | 22.6 \pm 3.8 |
| 2 MPa | 21.4 \pm 3.2 | 22.0 \pm 2.5 |
| 5 MPa | 27.6 \pm 2.7 | 25.8 \pm 6.7 |

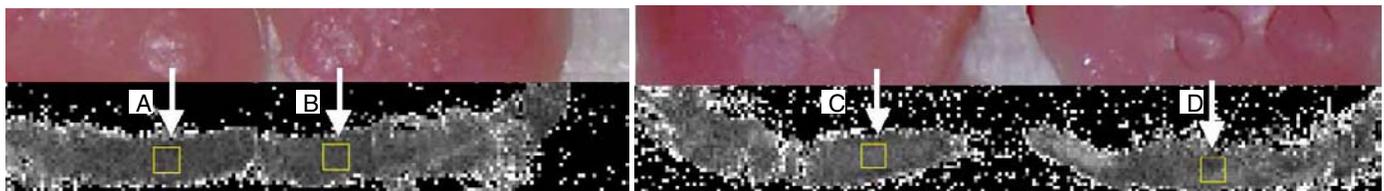


Figure 1: Coronal photographic view (top) of embedded cartilage plugs taken for loading and corresponding sagittal T1 ρ maps through the plug (bottom), showing matching region of interest for T1 ρ measurement. The regions shown correspond to plugs with (A) 2 MPa loading, no NAC, (B) 2 MPa loading with NAC (C) 5 MPa loading, no NAC, (D) 5 MPa loading with NAC.