T1-rho dispersion in human OA cartilage specimens using HRMAS Spectroscopy at 11.7T

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Introduction

Osteoarthritis (OA) is a disease characterized by articular cartilage degeneration. Proteoglycan loss and alteration in cartilage has been considered an important marker for understanding OA and monitoring the disease. NMR spectroscopy is useful to providing direct measurement of biochemical changes in tissues. Furthermore, High-resolution magic angle spinning (HR-MAS) NMR spectroscopy provides attenuation of the dipolar coupling and chemical shift anisotropy effects in intact tissues, such as cartilage, that result in broad resonances. T_1-rho is the longitudinal relaxation time T_1 measured in the rotating frame under the influence of a low RF field (B_1) which translates to an on-resonance spin locking frequency in the low frequency range (500 Hz for example) according to $\omega = \gamma B_1$. As a result the T_1-rho parameter is sensitive to relaxation mechanisms in the low frequency range corresponding to inverse correlation times of macromolecular processes in cartilage. T_1-rho dispersion which is the variation of the T_1-rho with increase in B_1 RF field has shown to be sensitive to macromolecular changes in cartilage matrix and may serve as a differentiating parameter between control and OA cartilage [1,2]. The goal of this study was to use HRMAS NMR spectroscopy to quantify T_1-rho and T_2 relaxation times and examine the T_1-rho dispersion characteristics of human OA cartilage specimens.

Materials and methods

Three OA cartilage samples were harvested from 3 patients who underwent Total Knee Arthroplasty (TKA) surgeries due to severe OA; and 3 healthy (control) samples were extracted from NDRI cadaver knees using 3.5 mm biopsy punches from the lateral inferior femoral condyle. The samples were flash-frozen at -80˚C for storage. The samples were scanned in a 500MHz Varian INOVA spectrometer in a 30μL zirconium rotor which was spun at a rate of 2.25 kHz. T_2 measurements were measured using a rotor synchronized CPMG pulse sequence where TE ranged from (5 - 300) ms with an increment of 6.7 ms. The T_1-rho pulse sequence was developed in house. All spectra were acquired at a temperature of 1˚C. The T_1-rho measurement was repeated for increasing spin-locking frequencies namely 50, 150, 250, 340, 500, 1500, 3500, 8000 Hz. Time of spin-lock ranged from 5 ms to 353 ms, with an increment of 12 ms. A spectral bandwidth of 20 kHz was used in the above experiments. The NMR spectra were processed using the Varian software on the console computer. A two-tailed t-test was performed to determine whether there was a statistically significant difference between the relaxation parameters of OA and healthy cartilage.

Result and Discussion

T_2 of water in cartilage showed a bi-exponential decay as shown in Figure 1. The shorter component was found to be significantly higher in OA cartilage when compared to control healthy cartilage ($p<0.05$). An ultra short component (approximately 2.3ms) associated with the water molecules in contact with collagen [3] was not observed in this study as it was outside the T_2 measurement range. A mono-exponential decay was a better fit to T_1-rho of control cartilage as against a bi-exponential decay for OA cartilage. The longer T_1-rho component of OA cartilage was found to be significantly higher than the T_1-rho of healthy cartilage (Figure 2). The mono-exponential decay of control cartilage can be due to a well organized and intact collagen and proteoglycan framework in healthy cartilage. Whereas, a breakdown of collagen and proteoglycan molecules in OA may lead to the existence of water molecules in multiple compartments and hence the bi-exponential nature of the T_1-rho decay in OA specimens. HRMAS NMR spectrometer can be a powerful tool to investigate relaxation mechanisms associated with cartilage matrix degeneration, and to identify useful diagnostic imaging markers for OA that can be translated into in vivo imaging for clinical applications.

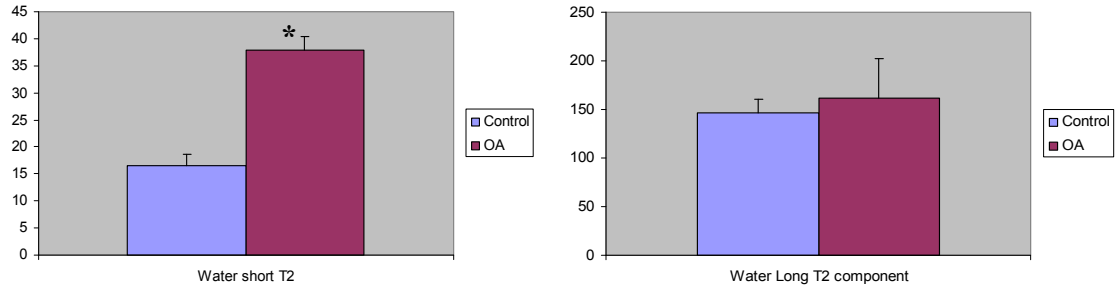

Figure 1. Short (left) and long (right) T_2 relaxation components (in ms) of cartilage water (* $p<0.05$)

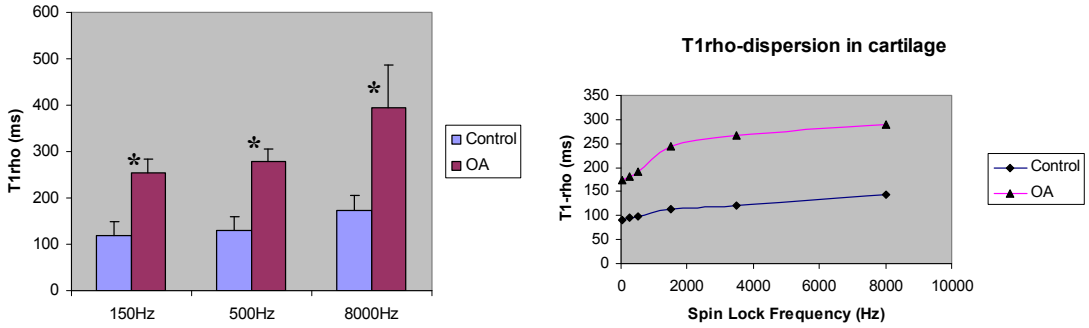

Figure 2. T_1-rho at 150, 500 and 8000 Hz (left) and T_1-rho dispersion characteristics of OA and control cartilage (right) (* $p<0.05$)

References:
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Acknowledgement: NIH/NIAMS R21AR056773-01A1