The GAG quantification in articular cartilage depends on the mechanical strain and gadolinium concentration - A microscopic MRI study

Nian Wang[1], and Yang Xia[1]
[1]*Dept of Physics and Center for Biomedical Research, Oakland University, Rochester, Michigan, United States*

INTRODUCTION

The concentration of glycosaminoglycans (GAG) in articular cartilage determines the load-bearing properties of the tissue. To investigate the strain dependency of the GAG calculation by the MRI T1 method (dGEMRIC), quantitative MRI T1 experiments were carried out on cartilage under different compression (up to ~ 40% strains) before/after the tissue was immersed in various concentration of gadolinium contrast agent (up to 1 mM), at a spatial resolution of 17.6 μm across the depth of the tissue.

MATERIALS AND METHODS

Canine cartilage-bone blocks (each about 3.5 × 2.5 × 6 mm) were harvested from the central part of the humeral head, soaked in a commercially available $Gd(DTPA)^{2-}$ contrast agent (Magnevist, Berlex, NJ) with different concentration (0 mM, 0.05 mM, 0.1 mM, 0.2 mM, 0.4 mM, 0.7 mM, and 1 mM), and T1-imaged under the 0, 20, and 40% static compressions. MRI experiments were conducted on a Bruker AVANCE II NMR spectrometer equipped with a 7-T/89-mm vertical-bore superconducting magnet and micro-imaging accessory (Billerica, MA). A homemade 5 mm solenoid coil was used for imaging, where the orientation of the cartilage block with respect to B_0 was at 55° (the magic angle) since T1 in articular cartilage was homogeneous over the tissue depth and isotropic with respect to the specimen orientation. The echo time (TE) of the imaging sequence was 7.2 ms; and the repetition time (TR) of the imaging experiment decreased steadily from 1.5 s without Gd to 0.5 s with 1 mM Gd immersion respectively. The 1 mm thick imaging slice was transversely located in the middle of the 6 mm long specimen. The 2D in-plane pixel size was 17.6 μm. The measurement of 2D T1 images used the inversion-recovery pulse sequence with 5 inversion points (steadily reduced from 0, 0.4, 1.1, 2.2, 4.0 s for tissue without Gd to 0, 0.1, 0.3, 0.5, 1 s for tissue soaked in 1 mM Gd), which allowed the calculation of T1 in the tissue through a single exponential equation on a pixel-by-pixel basis.

RESULTS

Fig 1 showed the T1 images for three specimens (0 strain, ~ 20% strain, and ~ 40% strain) immersed in different concentrations of the $Gd(DTPA)^{2-}$ solution. The depth-dependent profiles of all T1 images were plotted on the relative tissue depth in Fig 2 (0 = articular surface, 1 = cartilage-bone interface). The T1 images and profiles of the tissue before/after immersed in 1 mM Gd solution were highly consistent with several previous reports in the literature. A number of additional features were clearly visible. First, T1 profiles decreased when the Gd concentration in the soaking solution increased, no matter whether the tissue was loaded or not; but there were less changes at higher strains. Second, for the tissue block without compression, T1 profiles of the surface tissue (the superficial zone and the transition zone) reduced more rapidly compared to the deep tissue (the radial zone). The T1 values of SZ and TZ were higher than that of RZ without Gd, but became lower when the Gd concentration increased to 0.4 mM or higher. Third, T1 profiles showed less clear depth-dependent features when the tissue bock was compressed, even at a modest compression with the 20 % overall strain. Based on the Donnan equilibrium equations, the profiles of the GAG in cartilage were calculated and shown in Fig 3. It is clear that the measured GAG concentration for the uncompressed cartilage increases with the strains, which was consistent with the assumption that the total GAG in the tissue should be conserved regardless of the amount of compression. In addition, higher the Gd concentration in the solution, better the determination of the GAG profiles in the tissue. The concentration profiles of the Gd ions and GAG in the tissue were averaged, as the function of the Gd concentration in the solution. The dependency of the Gd in the tissue was clearly linearly with the solution concentration. It could be shown that when the Gd concentration in the solution was higher than 0.4 mM, the calculated GAG in the tissue was constant, which was consistent with the conservation of the GAG in cartilage during the compression. When the Gd concentration was lower than 0.4 mM, the calculation of the GAG in cartilage became noisy, worse for the compressed tissue. The dependency of the averaged GAG in cartilage on the total strain of the tissue could be fitted with a linear function, with a correlation coefficient of the linear fitting as 0.99885.

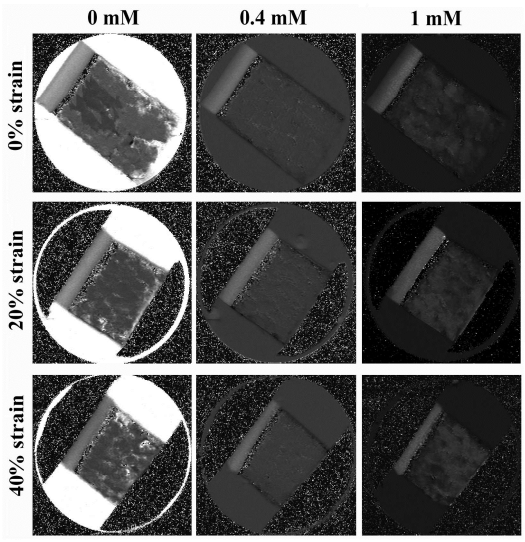

Fig 1 T1 images at different strains and in different Gd solutions.

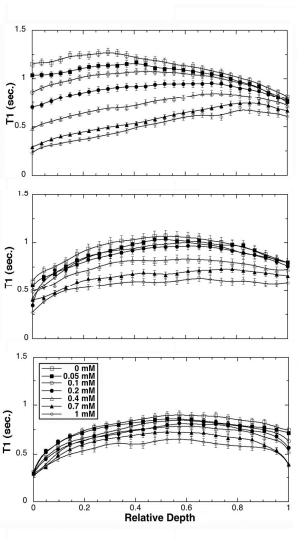

Fig 2 T1 profiles of compressed tissue

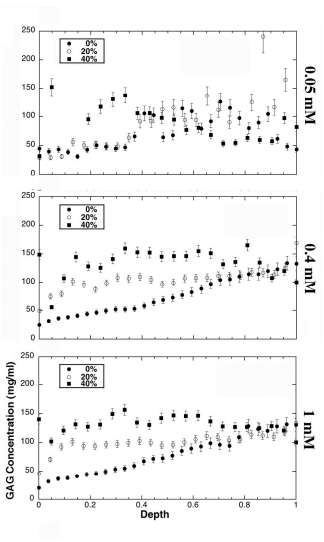

Fig 3 GAG profiles in compressed tissue

DISCUSSION

Articular cartilage is known to have a depth-dependent GAG concentration, which governs its depth-dependent mechanical properties. The strain-dependent T1 profiles in this study are due precisely to this depth-dependent mechanical property of cartilage. Tissue compression could cause a significant reduction of T1 values when the Gd concentration was low (less than 0.4 mM), or an increase of T1 values when the Gd concentration was high. This project demonstrates that the loading or loading history of the patients should be considered for the use of gadolinium contrast agent in clinical MRI of cartilage (the dGEMRIC) if a quantitative determination is desired, since loading is an inevitable consequence of human daily activities and a lesioned cartilage is softer than healthy cartilage hence easier to be compressed.

REFERENCES

(1) Bashir A, Gray ML and Burstein D. MRM 1996; 36: 665-673. (2) Burstein D, Velyvis J, Scott KT, Stock KW, Kim YJ, Jaramillo D, Boutin RD, and Gray ML. MRM 2001; 45: 36-41. (3) Chen S, Falcovitz Y, Schneiderman R, Maroudas A, & Sah R Osteoarthritis and Cartilage 2001; 9: 561-569. (4) Xia Y, Zheng SK and Bidthanapally A. JMRI 2008; 28: 151-157. (5) Zheng SK and Xia Y. MRM 2010; 63: 25-32. (6) Xia Y, Wang N, Lee J and Badar F. MRM 2011; 65: 1733-1737.

ACKNOWLEDEMENTS

This project was supported by two R01 grants from the NIH (NIAMS).