Complications in the quantification of GAG in cartilage with $T_{1\rho}$ imaging

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INTRODUCTION

Glycosaminoglycans (GAGs) are long, unbranched polysaccharides that are largely responsible for the viscoelastic properties of articular cartilage. In osteoarthritis (OA), the GAG content in cartilage is diminished, and the cartilage becomes hard. The resulting inflammation is the root of the pain associated with OA. Reddy et al.[1] have used the contributions to $T_{1\rho}$ from chemical exchange of bulk water with various functional groups on GAGs, to quantify GAG content in enzymatically-treated cartilage. Although excellent correlation of $T_{1\rho}$ with GAG content has been obtained ex vivo, corresponding in vivo correlations have not been demonstrated to the same degree.

One possible reason for this apparent lack of agreement might be due to the trypsin-induced degradation that is employed to produce a variation of GAGs in the ex vivo studies. It has recently been shown by others[2] that the enzyme used to degrade GAG, trypsin-2, will also cleave collagen-II. Collagen-II constitutes a greater fraction of articular cartilage than GAGs[3], and may have a greater variability in its constitution of normal cartilage. Additionally, collagen-II has many functional groups that are expected to have water exchange rates similar to those on the target GAG components.

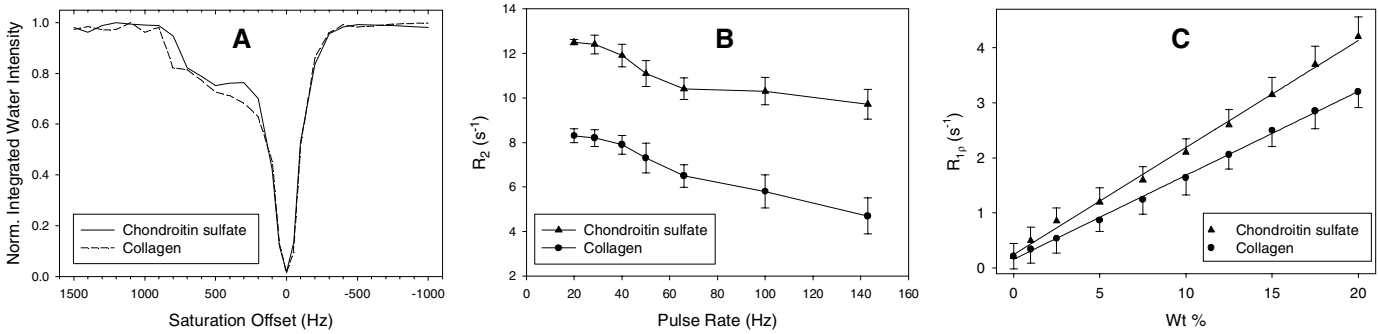
These facts might confound and obscure the ability to directly correlate $1/T_{1\rho}$ with GAG content in articular cartilage. Data are presented here to demonstrate that collagen has $T_{1\rho}$ dispersion similar to other GAG components over the critical spin-lock power levels. In addition, we present CPMG-type T_2 dispersions and Chemical Exchange Saturation Transfer (CEST) Z-spectra for these specimens.

MATERIALS AND METHODS

Chondroitin sulfate (CS) from bovine trachea and collagen were purchased from Sigma Chemical (St. Louis, MO), and phosphate-buffered saline (PBS) was purchased from Fisher Scientific (Pittsburgh, PA). All chemicals were used without additional purification. Ten phantoms each of CS and collagen (0, 1, 2.5, 5, 7.5, 10, 12.5, 15, 17.5, and 20% wt/wt) in PBS were prepared and placed in polypropylene tubes (17mm O.D.) from BD Biosciences (Bedford, MA). The phantoms were imaged at 4.7T in a small animal MR scanner with a 63 mm quadrature birdcage coil (both from Varian Inc., Palo Alto, CA). The phantoms were held by a Teflon plug machined to the inner diameter of the coil with seven holes drilled to the diameter of the sample tubes. $T_{1\rho}$-weighted images and CEST Z-spectra were acquired by adding appropriate spin-lock and saturation preparations to standard Varian fast spin-echo and gradient echo pulse sequences. CPMG data were acquired by adding time-varying gradient spoilers before and after composite refocusing pulses in a standard multi-echo sequence. All scans were performed at room temperature.

RESULTS

Panel A is a representative Z-spectrum of CS and collagen (5% wt/wt). Saturation transfer for the two GAG components is very similar over the range of saturation offsets used. Panel B shows the R_2 dispersion of the same tubes from panel A. Although the R_2 dispersion profiles have different offsets, they do have strikingly similar features. Panel C shows the response of $R_{1\rho}$ (ω_1=343Hz) with concentration of each component. The relaxivity of CS under these conditions was calculated to be 0.194 1/s·%, and collagen was 0.152 1/s·%. The difference in relaxivity probably largely reflects the large molecular weight difference between the two macromolecules.



DISCUSSION

The contributions to $R_{1\rho}$ from chemical exchange as described by Chopra[4] are sensitive to the spin-lock power used, the frequency difference between the exchanging groups, their exchange rates, and the relative pool sizes. Each macromolecule has a large number of different functional groups that exchange with bulk water. The transfer of saturation seen in the Z-spectra suggest that the effective exchange pathways have similar rates and involve groups at similar chemical shifts. The R_2 dispersion curves do not show obvious gross feature differences. Since a CPMG experiment with very small interecho spacing approaches a spin-lock, it is not surprising that there is little difference in $R_{1\rho}$ dispersion (not shown), and the relaxivity difference at physiological concentrations is not large. In consideration of these facts, it is reasonable to assume that there are other components in cartilage that may significantly affect $R_{1\rho}$. Whether or not collagen alone explains the difference between the enzymatically-degraded ex vivo studies and the in vivo measurements cannot be answered with these experiments. One group[3] has measured collagen content at 53±13%. If that variation is representative of normal cartilage, more work needs to be done to enhance the specificity of $R_{1\rho}$ to GAG content.

REFERENCES

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