Determination of correlation time in articular cartilage by T1rho relaxation dispersion

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TARGET AUDIENCE: Researchers and clinicians curious to employ MRI parameters sensitive and specific to structural changes in articular cartilage.
PURPOSE: To employ spin-lock $T_{1\rho}$ dispersion measurements to obtain a constituent-specific MRI contrast, correlation time, in human and animal cartilage.
METHODS: ***Experimental:*** Human osteochondral specimens (diameter d = 6 mm, N = 14) from tibial plateau were obtained from patients who had undergone total knee replacement surgery. The local ethics committee approved the study. MRI was performed at 9.4 T (Oxford instruments Plc, Witney, UK) with a 19-mm quadrature RF volume transceiver (RAPID Biomedical GmbH, Rimpar, Germany), and Varian DirectDrive console (Varian Inc. Palo Alto, CA, USA). Prior to imaging, the specimens were thawed, placed inside a Teflon test tube and immersed in perfluoropolyether, with the cartilage surfaces perpendicular to B_0. A magnetization preparation block was modified for continuous wave (CW) $T_{1\rho}$ dispersion measurements, with spin-lock powers γB_1 = 125, 250, 500, and 1000 Hz, followed by a fast spin echo readout (TR = 5 s, ETL = 4, TE_{eff} = 5 ms, 256x128 matrix size, slice thickness 1 mm, FOV of 16 x 16 mm^2, 62.5 µm depth-wise resolution). From $T_{1\rho}$ maps, two regions of interest (ROIs) for each sample were used to calculate the mean values: superficial zone (SZ) (5% depth), and full-thickness (100%). Next, two groups were established based on their histological OARSI grading [1]: early osteoarthritis (OA) (grade <1.5, N = 5) and advanced OA (grade > 1.5, N = 9).
Bovine osteochondral cylinders (d = 25 mm, N = 6) were drilled from intact patellae, and cut to three separate sections. To induce specific collagen or proteoglycan (PG) depletion, one section was digested in 30 U/ml collagenase and the other in 0.1 U/ml chondroitinase ABC, respectively. The remaining section was used as an intact control. All sections were incubated at +37°C for 44 hours and subsequently frozen. Ultimately, a smaller osteochondral cylinder-shaped (d = 7.2 mm) sample was drilled from the center of each section for MRI. MRI was carried out with an identical setup, including same ROI specifications, as in the case of human samples. The MRI measurements for human and bovine data are detailed in Refs. [2] and [3], respectively.
Theory: The use of correlation time as an MRI contrast is validated in terms of direct fits to experimental relaxation dispersion data, both for collagen and PG within bovine digestion model, as well as for human cartilage specimens *in vitro*. To this end, we employ a mathematical model based on the measured on-resonance $R_{1\rho} = 1/T_{1\rho}$ relaxation dispersion. In this approach, dispersion of the $T_{1\rho}$ spin-lock relaxation time is described by a fit function [4], where A and B, and in particular τ_c, are fit parameters.

$$R_{1\rho} = \frac{A}{1+4\omega_{SL}^2\tau_c^2} + B$$

RESULTS: The fitted correlation time, based on the mean relaxation dispersion values, increases in PG depletion as compared to the control, at the superficial zone of bovine cartilage (see Table 1, and Fig. 1). At the same time, the collagen digestion appears to involve shortened τ_c in comparison to the control group. For full-thickness analysis, both the two digested and control group yield similar τ_c. The fitted human MRI correlation time also increases both at the SZ and full-thickness in the advanced OA cartilage, as compared to the early OA specimens, although standard errors are generally slightly larger.
DISCUSSION: The difference between the spin-lock and external field Larmor frequency is very large, so that the use of the above fitting function is justified. The fitting function is purely based on dipolar relaxation, which may be a possible limitation at high magnetic fields, as chemical exchange is dependent on B_0. At clinically relevant magnetic fields, the role of chemical exchange should be smaller than at 9.4 T [5], which should improve the current results. It should be noted, that there are reports providing different views on the importance of chemical exchange amongst relaxation mechanisms occurring in articular cartilage [5,6], which might affect the fitting procedure as well. The proposed contrast is obtained from direct fit to the experimental relaxation dispersion data, and is indicative of the dynamics of the water molecules close to the macromolecular constituents of the tissue. However, due to the novelty of the approach, together with controversial role of chemical exchange relaxation in articular cartilage, the results need to be validated with a larger range of spin-lock frequencies, and a larger number of samples. Nonetheless, we propose that the correlation time τ_c can be directly fitted from the relaxation time maps of cartilage, and used as a macromolecule-specific indicator of structural changes observed in early stages of OA.
CONCLUSION: The proposed tissue inherent contrast for cartilage is based on the fitted correlation time values for bovine and human articular cartilage. The correlation time may develop into a fundamental biophysical MRI contrast. Further experimental and theoretical validation, preferably at clinically relevant magnetic fields, is still required. This is crucial so as to assess the feasibility of the proposed parameter, and to estimate the various technical aspects of the relaxation dispersion fitting protocol.

Table 1: The correlation times and standard errors, based on direct fits of the different mean $T_{1\rho}$ relaxation dispersion profiles.

Data set	Group	ROI (%)	Correlation time τ_c (10^-4 s)	Standard error (10^-4 s)
Bovine cartilage samples	Control (N=6)	5	3.76	0.20
		100	3.10	0.31
	Collagen digested (N=6)	5	2.46	0.11
		100	3.50	0.78
	PG digested (N=6)	5	5.21	0.80
		100	3.74	1.25
Human cartilage samples	Early OA (N=5)	5	4.68	0.86
		100	4.32	0.78
	Advanced OA (N=9)	5	7.13	3.34
		100	6.34	1.00

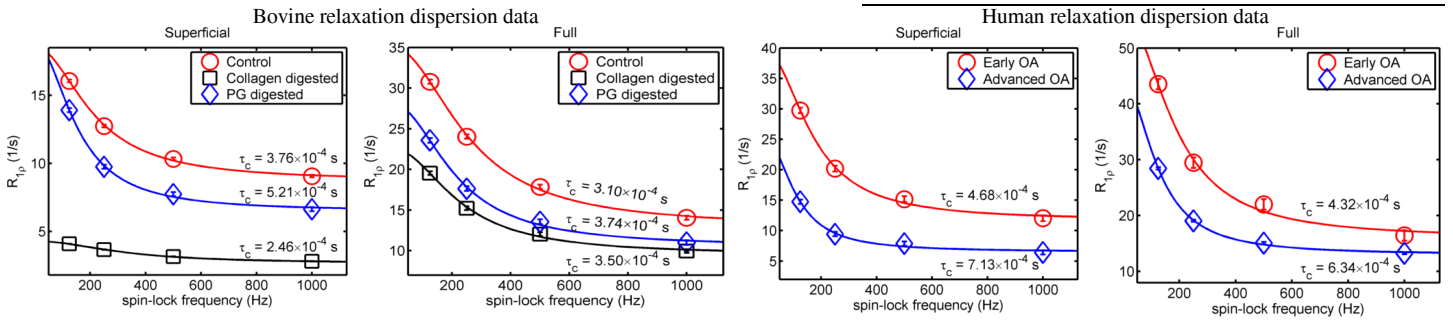

Figure 1. Mean spin-lock CW-$T_{1\rho}$ relaxation dispersion profiles, and the corresponding fitted correlation times in the superficial zone (5 % of depth) and full-thickness (100 %) of bovine (left, N = 6) and human (right, N = 5 (early OA), N = 9 (advanced OA)) articular cartilage samples.

REFERENCES. 1. Saarakkala S et al Osteoarthritis Cartilage 18:73-81, 2010 2. Rautiainen J et al MRM in press, 2014. 3. Salo E-N et al Proc. ISMRM 20:51, 2012. 4. Blicharska B et al J Magn Reson 207:287-93, 2010. 5. Mlynárik V et al J Magn Reson 169:300-7, 2004. 6. Duvvuri U et al PNAS 98:12479-84, 2001.