

Bound Pool Fractions Correlate with Proteoglycan and Collagen Content in Articular Cartilage

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Introduction: Cartilage damage in osteoarthritis is associated with loss of proteoglycan (PG) and degeneration of the collagen matrix [1–3]. Therefore, biomarkers specific to macromolecular content (collagen or proteoglycan) may serve as an early indicator of osteoarthritis. In this work we introduce quantitative magnetization transfer (qMT) to cartilage imaging. In particular, we look at how the bound pool fraction (BPF), defined as the fraction of exchanging protons that are bound to macromolecules, relates to collagen and proteoglycan concentrations in *ex vivo* cartilage specimens.

Methods: We obtained BPF maps of four fresh frozen human knee specimens (one tibia and three patellae) imaged at 1.5T. We used cross-relaxation imaging to map the BPF *in vivo* [4]. First, T_1 mapping was performed using four variable flip-angle SPGR scans (TR = 20ms, $\alpha = 4^\circ, 10^\circ, 20^\circ, 30^\circ$), followed by four magnetization transfer SPGR scans with variable offset frequencies (TR = 32ms, $\alpha = 10^\circ, \Delta = 3, 9, 15, 21$ kHz) and a reference image S_0 which gives the signal intensity in the absence of MT pulses. The offset frequencies were chosen to sample the z-spectrum of cartilage [5], and the data was fitted to an MT model based on a Superlorentzian lineshape [4,6]. Figure 1 shows that our model closely matches the z-spectrum of cartilage. The BPF values were compared against biochemistry measurements of sGAG (a measure of PG content) and hydroxyproline (a measure of collagen content) in cartilage plugs pulled from the specimens. Each plug was cut in half to produce top and bottom half samples in each ROI, resulting in 14 data points in each patella, and 10 data points in the tibia.

Results: Figure 2 shows the BPF, MTR, T_1 , and k map for a single slice of the tibia specimen. The T_1 and the k map in cartilage have a smooth gradient from top to bottom. The MTR is relatively flat in comparison, and the BPF map shows a nodular structure, which cannot be seen in any of the other qMT maps. For all four specimens the BPF is moderately correlated with sGAG content ($0.5 < r < 0.8$). The correlation decreases when it is computed across specimens ($r = 0.4$), but remains statistically significant ($p = .003$). The BPF values are negatively correlated with hydroxyproline content, and the correlation across specimens is slightly higher than for proteoglycans ($r = -0.57, p = 1.6e - 5$)

Discussion: The bound pool fraction is an indicator of macromolecular content in cartilage. It is positively correlated with proteoglycan content, and negatively correlated with collagen content. Going from the top of the cartilage to the bone surface, the bound pool fraction increases. This increase from the cartilage surface to the bone surface is consistent with the distribution of proteoglycan in cartilage, and opposite of the collagen distribution [7]. The method remains to be explored *in vivo*, but it is a promising new way of imaging cartilage that could be useful in early diagnosis of osteoarthritis.

References: [1] Le Roux, A.B., *et al.*, J Orthop Res, 2000. **18**: p. 383-392. [2] Rivers, P.A., *et al*, J Hand Surg Am, 2000. **25**: p. 889-898. [3] Kojima, T., Arthritis Rheum, 2001; **44**: p. 120-127. [4] Yarnykh, V.L. and C. Yuan, Neuroimage, 2004. **23**: p. 409-424. [5] Stanisz, G.J., *et al.*, Magn Reson Med, 2005. **54**: p. 507-512. [6] Morrison, C., *et al.*, J Magn Reson B, 1995. **108**: p. 103-113. [7] Muir, H., *et al.*, J Bone Joint Surg Br, 1970. **52**: p. 554-563.

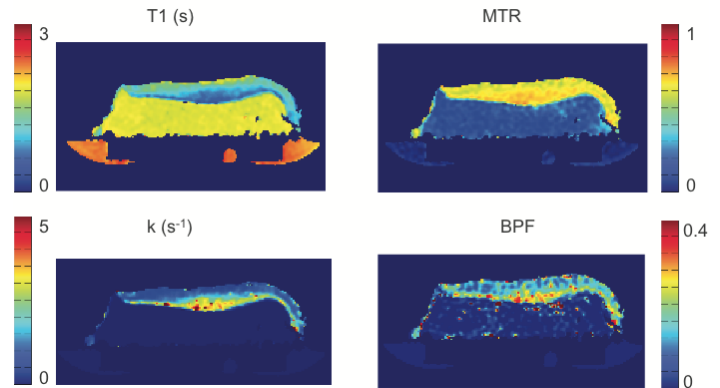
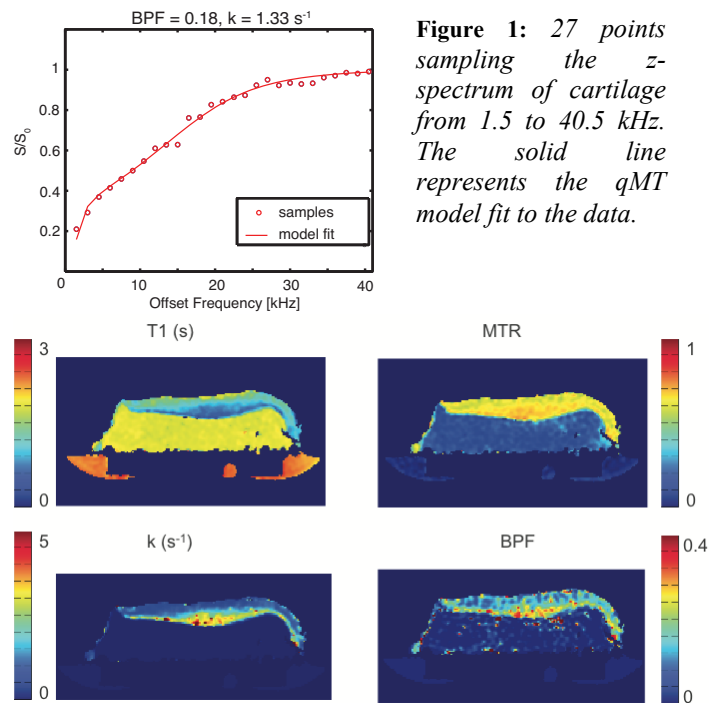


Figure 2: A single slice from a tibia specimen, imaged using the qMT protocol. Shown are a T_1 map (top left), MTR map (top right), k map (bottom left) and BPF map (bottom right). Resolution is $0.78 \times 0.78 \times 3$ mm.

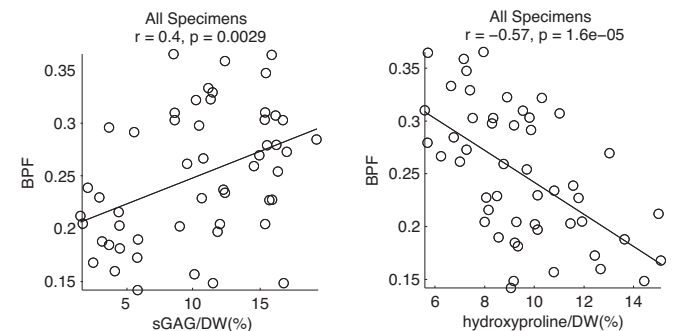


Figure 3: Scatter plots showing the correlations between BPF and sGAG (left) and hydroxyproline (right) across all four cartilage specimens. The biochemistry measurements are presented as percent of dry weight.