

# Load-dependent low-field profiling and relaxometry of osteoarthritic articular cartilage

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At low magnetic fields,  $T_1$  variation within cartilage represents a robust parameter that is employed to quantify the layered structure in the tissue and is sensitive to factors such as enzymatic degradation, external load, and diseases such as osteoarthritis. Variable-field relaxometry provides access to the quadrupolar dips that probe proton-nitrogen interaction and thus the content and local order of glycosaminoglycans and collagen. In this study on 20 human cartilage samples, low-field and variable-field techniques were combined for the first time to correlate NMR parameters and response to load with the severity of osteoarthritis.

While low-field MRI significantly enhances the  $T_1$  contrast in cartilage tissue, variable-field relaxometry identifies the properties of cartilage and glycosaminoglycan (GAG) as well as overall molecular mobility. In particular, the  $^{14}\text{N}$  content of both collagen and GAG give rise to so-called quadrupolar dips, i.e. enhanced relaxation rates of  $^1\text{H}$  particularly at field strengths between 50 and 70 mT. In this study, both methods are combined for the first time with the purpose of quantifying correlations with the degree of osteoarthritic degeneration in human cartilage, and to establish cross-correlations between low-field and variable-field NMR.

The dependence of magnetic resonance relaxation times  $T_2$  and  $T_1$  in bovine and human articular cartilage is investigated by portable, single-sided scanners at magnetic field strengths of 0.27 T and 0.44 T, respectively. One-dimensional, depth-dependent scans (profiles) were carried out with spatial resolutions between 20 and 50  $\mu\text{m}$ . The well-known triple layer structure of cartilage was assigned with the relaxation weighted profiles for bovine as well as human samples. Bovine samples were measured before and after soaking for 24 h in either trypsin or collagenase. Twenty human samples with different degrees of osteoarthritis, covering Mankin grades 0-12, were compared with respect to their average and maximum vs. minimum values of relaxation times. In addition, the variation of these values under unidirectional compression at 0.6 MPa were recorded.

Employing field-cycling relaxometry, the dispersion of  $T_1$  in the  $^1\text{H}$  Larmor frequency range of 10 kHz to 30 MHz was monitored, and results were analysed in terms of power-law relations  $T_1 \sim \omega^\gamma$  and total area of the  $^1\text{H}$ - $^{14}\text{N}$  cross-relaxation quadrupolar dips for the set of human samples.

The layered structure of mammalian articular cartilage, which is a consequence of different degrees of order of the collagen fibers but also of a gradient of water and glycosaminoglycan (GAG) concentration, results in a pronounced  $T_2$  variation at all magnetic field strengths [1]. A similar variation of  $T_1$ , typically covering a ratio of 3-5 between maximum and minimum values inside the tissue, was identified at a field strength of 0.27 T, while it has been reported as minimal at high magnetic field strengths [2].  $T_1$  thus has thus been identified as a suitable parameter to follow changes in cartilage properties by low-field NMR. While previously the  $T_1$  relaxation rate at 400 MHz has been associated with water content of articular cartilage [3],  $T_1$  at lower field strength is anticipated to relate more directly to cartilage constituents.

Average  $T_1$ , as well as cartilage thickness obtained from  $T_1$  measurements of human samples, is found to correlate negatively with Mankin grade. At the same time, a significant correlation was identified for relaxation time reduction before and after uniaxial compression at 0.6 MPa, a typical value for forces appearing in the human knee and hip joint. This finding is of importance since the spatial resolution of 50  $\mu\text{m}$  obtained with the single-sided scanner is about one order of magnitude better than the one in clinical high-field or low-field scanners [4], thus allowing a much more reliable definition of thickness change which even includes resolution of the three main cartilage layers.

At  $^1\text{H}$  Larmor frequencies of 2-3 MHz, the so-called quadrupolar dips are superimposed onto a frequency-dependent signature of  $T_1$  that can be approximated by power-laws. Varying the composition, water content or structural integrity of cartilage affects both the general frequency dependence of  $T_1$  and the shape of the quadrupolar dips, providing a possible diagnostic access to arthropathies such as osteoarthritis (OA) [5]. In this study, a statistically significant correlation of the area of the quadrupolar dips with Mankin grade is demonstrated: diseased tissue contains less GAG but more water. This observation is confirmed by artificially altered tissue using trypsin or collagenase [6]. Furthermore, the exponent  $\gamma$  in the relation  $T_1 \sim \omega^\gamma$  correlates with the thickness of the tissue, providing a further approach to relating the molecular mobility to the macroscopic properties of cartilage. These results allow for an improved diagnostic interpretation of low-resolution clinical MRI particularly at dedicated extremity scanners.

## References

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