# Spatially resolved relaxation analysis in bovine and human articular cartilage

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**Introduction:** Osteoarthritis (OA) as a degenerative disease of articular cartilage is well known to affect a number of parameters accessible by NMR methods, such as relaxation times, diffusion coefficient and its anisotropy, dipolar order and spectral properties. Among these, the rather large variation of relaxation times at low magnetic field strengths hold the best potential for a non-invasive early diagnosis of OA. We have found that $T_1$ not only varies significantly between the cartilage layers, but is also non-exponential on a microscopic scale due to multicomponent proton pools [1]. Earlier research has addressed the origin of this complex behavior by systematic drying [2] and deuteron replacement [3]. In this study, we extend these approaches towards frequency-dependent relaxation (NMRD) in order to develop models for the molecular reorientation dynamics of water and macromolecules in cartilage.

**Methods:** Low-field MR experiments employing the NMR-MOUSE with a one-dimensional spatial resolution of 100 µm or better were carried out to benefit from the enhanced contrast in relaxation times towards lower magnetic field strengths. Depth-dependent averaged $T_1$ and $T_2$ maps are obtained and are compared to different measures of the relaxation times distribution and their width. These data are complemented by volume-averaged $T_1$-$T_2$ correlation maps as well as relaxation times distributions as a function of magnetic field strength (field-cycling relaxometry). A particular focus was put on variation of relaxation properties under drying and rehydration using either $H_2O$ or $D_2O$ brine, comparing $T_1$ dispersion of residual protons with that of deuterons.

**Results and discussion:** Following proteoglycan depletion during OA, the water content in cartilage is known to increase locally, leading to longer $T_1$ of the main component while bound water and the contribution of macromolecules retain their shorter $T_1$ essentially unaltered, thus generating an increase of the width of the $T_1$ distribution function. Using spatially resolved averaged values, however, the spread of $T_1$ across the tissue tends to become smaller. Two-dimensional $T_1$-$T_2$ methods have been employed to elucidate this controversial behavior, and we have successfully detected the full range of water environments by combining FID and CPMG signal acquisition. The observed trend upon drying, and the finding that $^2$H relaxation in cartilage follows a field dependence similar to that of $^1$H, allows for an improved assignment of the individual relaxation components to different water environments.

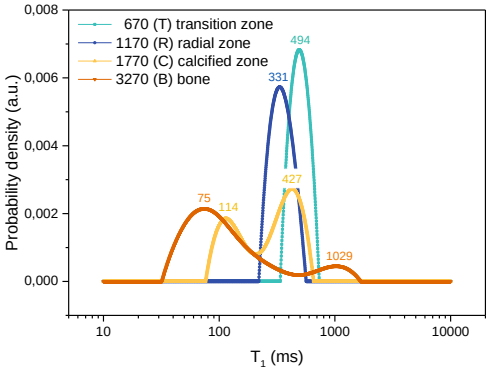


Fig. 1: $^1$H $T_1$ distributions within the four principal layers (670 to 3270 µm from the surface) of a healthy bovine articular cartilage sample obtained at 0.27 T.

**Conclusions:** Determining relaxation distributions at low field and variable field supports the development of models for molecular mobility in cartilage as a simple tissue model without vessels and low cell content. At the same time, methods have been developed to unambiguously quantify relaxation times distribution widths which can be correlated to the disease state in order to assess OA severity in low-field MRI scanners with insufficient spatial resolution.

**References:** [1] O.V.Petrov, S.Stapf, Magn. Reson Med. **81**, 2158 (2019). [2] R.A.Damion *et al.*, Osteoarthritis Cartilage **20**, 184 (2012). [3] S.Tadimalla, K.I.Momot, PLOS One **9**, e115288 (2014).