Low-Field (0.55 T) $T_1\rho$ MRI for Dispersion and Voxel-Wise Mapping Analysis of PG-compromised Cartilage

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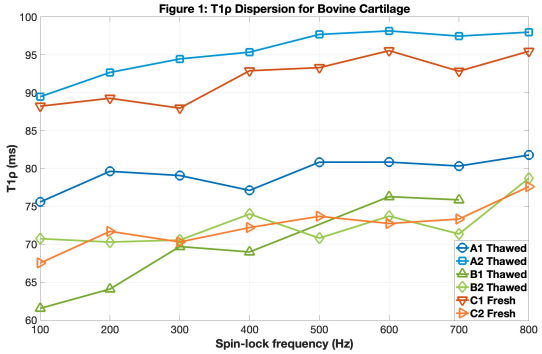
INTRODUCTION: Osteoarthritis (OA) is a degenerative joint disease and a leading cause of pain and disability. Early in the disease, subtle biochemical changes, such as proteoglycan (PG) loss in cartilage, occur before visible joint damage. Understanding these early changes is critical for developing interventions that can slow disease progression and preserve joint function. Quantitative magnetic resonance imaging (qMRI), particularly $T_1\rho$ mapping, enables spatially resolved assessment of cartilage PG content. Recent developments in low-field 0.55 T MRI offer several advantages for cartilage imaging, including reduced susceptibility and magic-angle artifacts, longer T_2* for better signal preservation, improved B_1 homogeneity, and lower specific absorption rate, enabling more uniform, artifact-free visualization of cartilage. These improvements may facilitate the detection of early cartilage degeneration and biochemical changes, supporting more accurate diagnosis and monitoring in both clinical and preclinical studies. However, sequence parameters for low-field (0.55 T) $T_1\rho$ MRI that provide optimal contrast between healthy and damaged cartilage have not yet been established. The objective of this study was to apply low-field $T_1\rho$ MRI to bovine cartilage to capture the expected dispersion behavior, namely an increase of $T_1\rho$ (and corresponding decrease of $R_1\rho = 1/T_1\rho$) with spin-lock frequency, and to assess whether sufficient contrast between healthy and damaged tissue can be achieved, providing a foundation for future preclinical studies of early PG-related changes in OA.

METHODS: Cartilage plugs (8 mm diameter, 3–5 mm deep) were harvested from 4 bovine patellofemoral joints (24–28 weeks old; 3 frozen, 1 fresh). Frozen joints were thawed for 24 hours prior to harvest, while the fresh joint was harvested within 24 hours of slaughter. From Animals A, B, and C, 2 plugs per joint (n = 2 per animal) were collected, rinsed with phosphate-buffered saline (PBS), and imaged, with all samples maintained in PBS while awaiting imaging. Five plugs were collected from Animal D. Three were assigned to damaging conditions: chemical extraction using 4 M guanidine hydrochloride (GuHCL; n=1) with 50 mM Tris and 10 mM EDTA (pH 7.7) at 4 °C with rotation (n = 1), enzymatic digestion in 0.1 M Tris (pH 7.5) at room temperature for 24 h with either 30 mg trypsin (n = 1) or 1 mL chondroitinase ABC plus 15 mg hyaluronidase (cABC/HA; n = 1). Two controls were maintained in PBS (n = 2). PG release was quantified using the dimethylmethylene blue assay. All samples were imaged in vitro on a 0.55 T tabletop MRI system (Pure Devices, Germany). Voxel-wise $T_1\rho$ relaxation times were obtained by fitting signals across multiple spin-lock times (TSL; 0–50 ms) to an exponential model at each spin-lock frequency (FSL; 100–800 Hz for initial scans of healthy plugs [Fig. 1], 100–450 Hz for second experiment of healthy vs damaged plugs), with repetition time (~3600 ms, ~3×T_1) allowing near-complete recovery. T_2 relaxation times were measured in parallel across echo times (0–50 ms; 5 ms intervals) to account for water–matrix interactions and guide selection of spin-lock parameters with minimal T_2 influence. $T_1\rho$ maps were analyzed in cartilage regions of interest (ROIs) encompassing the entire plug for all samples. SNR was calculated as the mean ROI signal divided by background noise standard deviation (SD_, using magnitude data corrected for Rician bias (× 0.655). Mean ± spatial SD values of $T_1\rho$, T_2, and the $T_1\rho/T_2$ ratio were quantified within each ROI for each FSL. CNR was estimated as the mean signal difference between damaged and control plugs divided by SD of background noise at each FSL (100–450 Hz). Typically, CNR is calculated within a single image; here it was approximated across separate plugs, with future studies planned for within-image measurements.

RESULTS SECTION: Voxelwise mean $T_1\rho$ across FSLs (100–800 Hz) ranged: A1 75.6–81.8 ms; A5 89.5–98.2 ms; B5 61.5–76.3 ms; B6 70.3–78.7 ms; C1 88.0–95.5 ms; C2 67.5–77.6 ms (Fig. 1). Across animals A–C, magnitude SNR ranged from 19.6 to 35.6 (mean ± SD = 29.2 ± 6.6), indicating adequate signal for voxel-wise $T_1\rho$ mapping. For all samples, ROI and corresponding voxel-wise $T_1\rho$ distribution were visualized. T_2 decay fits showed strong agreement (R^2 > 0.97). $T_1\rho/T_2$ ratios decreased with increasing FSL, reflecting greater T_2 contributions, with relative changes from 100 Hz of 3.31% (200 Hz), 4.50% (300 Hz), 6.26% (400 Hz), 6.23% (500 Hz), 10.15% (600 Hz), 8.87% (700 Hz), and 10.43% (800 Hz). A FSL range of 100–450 Hz was used to assess damaged cartilage, guided by the 100–400 Hz range which showed lower T_2 contributions. Within this range, 250 Hz provided the highest SNR, and data are reported at this frequency (Table 1). ROI selection and voxel-wise $T_1\rho$ distribution at 250 Hz for healthy control are shown in Figure 2. Estimated CNR between damaged and control cartilage, calculated across separate samples rather than within the same sample, was highest at 400 Hz for trypsin (23.5), at 250 Hz for cABC/HA (17.5), and at 200 Hz for GuHCl (15.1).

DISCUSSION: This study shows that low-field (0.55 T) $T_1\rho$ MRI reproducibly generates dispersion curves with sufficient SNR, capturing both mean relaxation and spatial heterogeneity, with $T_1\rho$ increasing ($R_1\rho$ decreasing) across FSLs in bovine cartilage in vitro. T_2 increasingly influenced $T_1\rho$ at FSLs, but a 100–400 Hz range minimized T_2 effects while maintaining SNR. Over the range of 100–450 Hz applied to the damaged and healthy control samples, 250 Hz provided the highest SNR for most samples. Within damaged groups, GuHCl produced the longest $T_1\rho$, cABC/HA was shorter, and trypsin was the shortest. These findings highlight that both the mechanism and magnitude of matrix degradation influence $T_1\rho$ relaxation, although absolute values at 0.55 T may differ than those at high field. Estimated CNR varied across damaged samples, indicating that $T_1\rho$ sensitivity to cartilage damage depends on both the degradation mechanism and the spin-lock frequency, which does not always correspond to the setting with the highest SNR. Because damaged and control tissues were imaged in separate samples, these CNR values are approximate; nonetheless, they suggest that $T_1\rho$ MRI at optimized FSL may detect compositional changes in cartilage, supporting its potential for evaluating early degeneration and treatment effects. To fully capitalize on the advantages of low-field MRI, future studies should include paired pre- and post-damage imaging and T_2 mapping to enable mapping of damaged and control regions within the same sample, allowing optimization of spin-lock parameters to balance SNR and CNR while accounting for intra- and inter-joint variability.

SIGNIFICANCE/CLINICAL RELEVANCE: Low-field (0.55 T) $T_1\rho$ MRI provides a non-destructive, high-resolution method to detect early biochemical changes and spatial heterogeneity in cartilage, offering a powerful imaging tool for studies of OA. Defining reproducible and optimal imaging parameters and relaxation metrics may enable the reliable evaluation of preclinical studies that model early OA progression and test interventions.



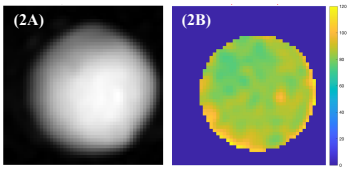


Figure 2. **(2A)** Grayscale image of healthy control (Animal D, D2) used for definition of the circular region of interest for voxel-wise analysis; intensity reflects relative $T_1\rho$ signal magnitude. **(2B)** Color-coded voxel-wise $T_1\rho$ map of healthy control (Animal D, D2) at 250 Hz spin-lock frequency, illustrating quantitative relaxation times (ms) and spatial heterogeneity of the cartilage matrix.

Group	$T_1\rho$ (ms)	SD $T_1\rho$ (ms)	SNR	PG (µg/uL)
GuHCl	68.6	29.5	32.7	228.4
Trypsin	51.4	21.9	23.7	191.9
cABC/HA	54.7	23.9	27.5	31.5
Control D1	89.4	16.5	28.9	119.5
Control D2	89.2	21.3	31.3	34.2

Table 1. Mean ± SD of $T_1\rho$ relaxation times, signal-to-noise ratio (SNR), and proteoglycan (PG) release (µg/µL) in Animal D cartilage. Damage groups: guanidine hydrochloride (GuHCl, broad PG removal), Trypsin (proteolytic digestion), chondroitinase ABC/hyaluronidase (cABC/HA, selective GAG degradation), and control (PBS immersion).