# Cartilage MR T1ρ and T2 quantifications: longitudinal reproducibility and variations using different coils and scanners at single and multi-sites

Xiaojuan Li[1], Valentina Pedoia[1], Deepak Kumar[1], Drew Lansdown[1], Cory Wyatt[1], Julien Rivorie[1], Narihiro Okazaki[1], Dragana Savic[1], Matthew F Koff[2], Joel Felmlee[3], Williams Steven[3], and Sharmila Majumdar[1]

[1]*University of California, San Francisco, CA, United States,* [2]*Hospital for Special Surgery, New York, NY, United States,* [3]*Mayo Clinic, Rochester, MN, United States*

**Introduction** Quantitative magnetic resonance imaging (MRI) of articular cartilage matrix composition, including $T_{1\rho}$ and $T_2$ mapping, are promising techniques that have potential as early markers of cartilage degeneration; these methods however also present significant challenges with a high threshold for quantification accuracy to make measurements in a thin curved structure. Currently, applications of cartilage $T_{1\rho}$ and $T_2$ imaging in multicenter clinical trials are very limited. One impeding factor is the lack of documentation of potential variations of $T_{1\rho}$ and $T_2$ introduced by different scanners, coils and sites. Further, previous studies on reproducibility of $T_{1\rho}$ and $T_2$ quantification were primarily limited to short-term measurements, except for a recent report on 8-year $T_2$ quantification as part of the Osteoarthritis Initiative (OAI) study quality control procedure (1). Currently, a multi-center feasibility study applying $T_{1\rho}$ and $T_2$ imaging in knees after acute ACL injury, which is a high risk-factor for post-traumatic OA, is being performed among three sites. In this report, we evaluate the longitudinal reproducibility of $T_{1\rho}$ and $T_2$, and the variation of $T_{1\rho}$ and $T_2$ by using different scanners and coils at one site, and the reproducibility and cross-validation of $T_{1\rho}$ and $T_2$ among the three sites.

**Methods** Single-Site study: Phantom data were collected monthly for up to 29 months on three GE 3T scanners (HDx Long Bore, MR750 and MR750 Wide Bore). Human subject data were collected on two scanners using the same type of coil; and were collected on one scanner using two types of coil. Multi-site study: Three participating sites used the same type of scanner (GE MR750) and coil, and identical imaging protocols. Phantom data were collected monthly. Human subjects were scanned and rescanned at each site. Two traveling human subjects were scanned at all three sites. Custom phantom sets with agarose concentrations varying from 2%-4% were scanned at isocenter, left 70mm and right 70mm positions. A 3D sequence that combines $T_{1\rho}$ and $T_2$ quantification in one acquisition was applied (2). The same phantom and *in vivo* imaging protocol were applied at all three sites with the same parameters (FOV = 14 cm, matrix size = 256 x 128, slice thickness = 4 mm, time of spin-lock (TSL) = 0/10/40/80 ms, frequency of spin-lock = 500 Hz; magnetization preparation TE = 0/12.8/25.7/51.4 ms). High-resolution 3D FSE images (CUBE, FOV = 14 cm, matrix size = 384 x 384 slice thickness = 1mm) were registered to $T_{1\rho}$ and $T_2$ maps and cartilage was segmented semi-automatically using in-house developed software (3) on the registered CUBE images. $T_{1\rho}$ and $T_2$ relaxation times were calculated in phantoms and in anatomically defined compartments *in vivo*. All data analysis was performed at one site. The reproducibility and differences were evaluated using Bland-Altman method, and calculation of root-mean-square coefficients of variation (RMS-CV, %), absolute difference (in ms) and intra-class correlation (ICC).

**Results** *Single-Site Study* **Long-term reproducibility**: The RMS-CV was 1.8%, 2.0% and 2.1% for $T_{1\rho}$ and 2.3%, 2.9% and 2.8% for $T_2$ for HDx Long Bore, MR750 and MR750 Wide Bore respectively. **Variations using different model of scanners:** $T_{1\rho}$ and $T_2$ values measured with the MR750 Wide Bore were significantly lower compared to using the HDx Long Bore. In phantoms: the mean CV was 2.7% and 1.0% and the mean absolute difference was 1.7 ± 1.3 ms and 0.4 ± 0.4 ms for $T_{1\rho}$ and $T_2$ respectively; In healthy volunteers (n=10), the absolute difference was 4.5 ± 2.4 ms for $T_{1\rho}$ and 2.2 ± 1.6 ms for $T_2$. **Variations using different coils:** Using the MR750 Wide Bore, $T_{1\rho}$ and $T_2$ values were significantly higher using the 16-channel coil than those using the 8-channel coil in healthy volunteers (n=5). The absolute difference was 3.5 ± 2.1 ms for $T_{1\rho}$ and 1.5 ± 1.4 ms for $T_2$. *Multi-Site Study* **Reproducibility in phantoms** (up to 8 months): The RMS-CV was 1.8%, 2.3% and 1.5% for $T_{1\rho}$ and 2.1%, 3.8% and 1.8% for $T_2$ for site 1, 2 and 3 respectively. **In vivo scan-rescan reproducibility:** Across all three sites (n=16), the scan-rescan RMS-CV was 3.1% and 4.0% and the mean absolute difference was 1.9 ms and 1.8 ms for $T_{1\rho}$ and $T_2$, respectively, Figure 1. The RMS-CV in each compartment ranged from 2.3% - 3.9% for $T_{1\rho}$, and ranged 3.2% - 5.3% for $T_2$. **Cross-validation among three sites:** Phantom $T_{1\rho}$ and $T_2$ values were significantly different among three sites but highly correlated (ICC > 0.99). The mean CV was 2.9% and 4.1% for $T_{1\rho}$ and $T_2$ quantification respectively, with the mean absolute difference as 0.9 ms and 1.2 ms respectively. No significance difference was found in $T_{1\rho}$ and $T_2$ values in the traveling controls who were scanned at all three sites. The RMS-CV was 4.9% and 4.4% with absolute difference as 1.5 ms and 1.0 ms for $T_{1\rho}$ and $T_2$, respectively.

**Discussion** This is the first report on longitudinal reproducibility of $T_{1\rho}$ quantification in phantoms, and $T_{1\rho}$ and $T_2$ quantification on the same phantoms and volunteers across multiple-sites. *Single-site study* The CV of repeated $T_{1\rho}$ and $T_2$ measurements up to 29 months were all less than 3%, indicating excellent longitudinal reproducibility. The differences of system hardware (e.g. peak gradient amplitude, gradient slew rate, and bore size) among the three scanners used in the single-site study could produce different pulse widths and minimal TRs/TEs resulting in the observed differences of $T_{1\rho}$ and $T_2$ values among the scanners. In addition, different RF coil transmit uniformity and load, flip angle accuracy, and signal-to-noise ratio can also introduce variations in the relaxation time quantification (4). *Multi-site study* The overall scan/re-scans reproducibility CV was comparable to single site CVs and was better compared to previously reported multi-site studies (5), which can be attributed to the stringent study design requiring the same hardware (scanner and coil) and scanning software at all sites and the centralized data analysis with stringent quality control. Although significant differences were observed in phantom $T_{1\rho}$ and $T_2$ values, the values between sites were highly correlated (ICC > 0.99), suggesting the bias might be readily correctable during data analysis. No significant differences of $T_{1\rho}$ and $T_2$ values were observed in cartilage of traveling controls, suggesting that the variation introduced by different sites (as observed in phantoms) were smaller in magnitude compared to scan/re-scan measurement errors. In conclusion, the results from this study suggest that with careful quality control and cross-calibration, quantitative MRI can be readily applied in multi-site studies and clinical trials for evaluating cartilage degeneration. Future studies will expand the multi-site study to include scanners from multiple manufacturers.

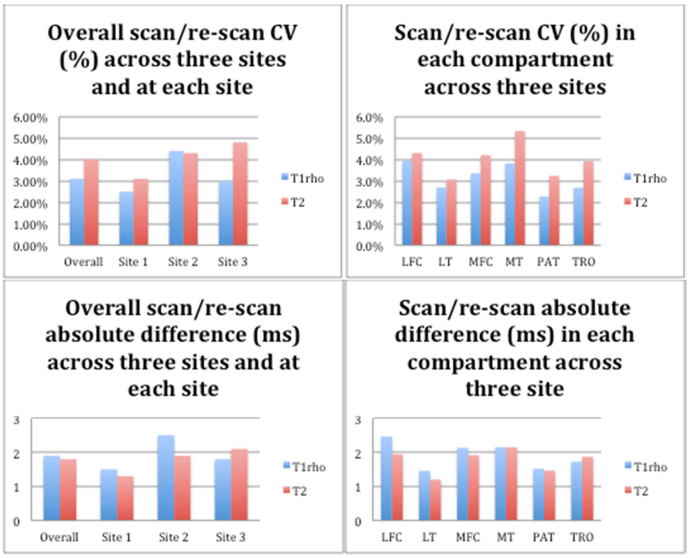


Figure 1. Scan-rescan reproducibility of $T_{1\rho}$ and $T_2$ values in healthy controls in a three site study. LFC: lateral femoral condyle; LT: lateral tibia; MFC: medial femoral condyle; MT: medial tibia; PAT: patella; TRO: trochlea.

**Acknowledgements** The study was supported by NIH/NIAMS P50 AR060752 and Arthritis Foundation (AF), and the authors would like to thank the AF multi-site ACL study team.

**References** 1. Schneider et al Osteoarthritis Cartilage 2012; 2. Li et al, J Magn Reson Imag 2014; 3. Carballido-gamio et al, Med Image Anal 2008; 4. Dardzinski et al Osteoarthritis Cartilage 2013; 5. Mosher et al, Radiology 2011.