T1ρ measurements in the intervertebral discs: Analysis of reproducibility and diurnal changes

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Target Audience: This presentation is intended for clinicians and researchers who study spinal disc degeneration.

Introduction: The majority of chronic back pain is associated with degeneration of the intervertebral discs (IVD). Johannessen et al showed that T1ρ images could be used to assess proteoglycan loss; therefore, it can be employed as a quantitative measure of disc degeneration. T1ρ could provide valuable information[1], especially in early stages of degeneration. In order to use T1ρ as a diagnostic or prognostic tool, however, one needs to assess the reproducibility of these measurements. Moreover, earlier reports showed diurnal changes in the IVDs during rest and loading conditions[2]. Therefore the goal of this work was to assess the reproducibility and diurnal changes in T1ρ measurements in the lumbar discs.

Methods: This study was approved by the IRB and written consents were obtained from 12 adults who took part in this study. Demographic details of study group are given in Table 1. Images were acquired using a 3T GE Discovery MR750 (Waukesha, WI USA) MRI system. All images were acquired with a CTL-spine coil, FOV=310mm and 16-sagittal slices with 3mm thickness. 3D MAPSS pulse sequence[3] with four spin-lock times (TSL) values = [0 20 40 60] ms, spin-lock amplitude=400Hz, and TR/TE=6.5/1.6ms were used for T1ρ. Pixel-by-pixel T1ρ values were calculated based on mono-exponential fitting: $S(TSL)=S_0 \cdot \exp(-TSL/T1\rho)$. Additionally, T_2 and T_1 weighted (T_2W, T_1W) images were acquired. For reproducibility analysis, the follow up scans were acquired with a median delay of 112 days and at a different time of day (ToD). For analysis, a trained operator manually drew regions of interest (ROI) on T1ρ images with TSL=0ms, which encompassed the Nucleus Pulposus (NP). To reduce variability in ROI drawings in repeated scans, a second operator compared the two ROIs in repeated scans and corrected them if they did not match. Then, average T1ρ values were calculated in each ROI. The data processing pipeline is illustrated in Fig. 1.

Table 1. Subjects' demographics

	Med.[Min-Max]
Age in years	28.5 [20-41]
Sex	F:5, M:7
Height in inches	69.5 [61-74]
Weight in lbs.	167.5 [130-200]
BMI in kg/m²	24.0 [20.1-30.7]

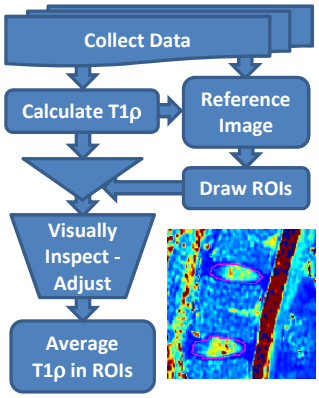

Fig.1. Flow diagram of data processing pipeline

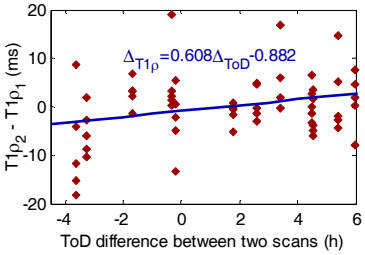

Fig.2. ΔT1ρ versus ΔToD

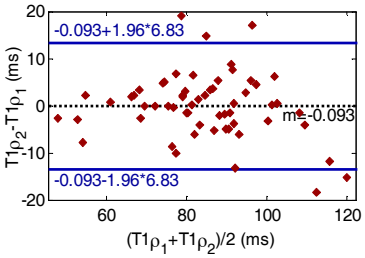

Fig.3. T1ρ Bland–Altman plot

Diurnal changes in T1ρ measurements in the IVDs were analyzed using IBM SPSS v21 (Armonk, NY USA). The statistical significance (alpha) level of 0.05 was used. Two variables were defined for analysis: 1) ToD difference between the two scans in hours (Med.[Min,Max]:2.2[-3.6,6.0]). 2) T1ρ difference between two scans in milisecond (mean±std:-0.093±6.83). Generalized Estimating Equations (GEE) procedure was employed to find linear scale response between these two variables. To account for the day difference between the repeated scans, it was included as a covariate in the model. Within-subject measurements were taken into account with the GEE procedure.

To investigate reproducibility: 1) Bland–Altman[4] plot was generated 2) repeatability coefficient, RC, $(1.96\sqrt{2\sigma^2})$; coefficient of variation, CV, (σ/μ); and intra-class correlation coefficient, ICC, $(\tau^2/(\tau^2+\sigma^2))$ were calculated. σ^2 is the variability attributed to measurement error, μ is the grand average of measurements, and τ^2 is the between disc variability.

Results: Data from 59 lumbar discs from 12 subjects were used for analysis (one L5/S1 disc from a subject was excluded due to a severe artifact in that region). GEE analysis revealed that the time of day was a significant factor (**p=0.035**) in T1ρ measurements. On the other hand, the number of days between the repeated scans was not found as a significant factor (p=0.852). Fig. 2 shows the difference between the repeated T1ρ measurements plotted against the number of days between the scans. Interestingly, T1ρ values in the NP increased during the day with sustained loading.

The Bland–Altman plot for reproducibility analysis of T1ρ (μ=84.5ms, σ=4.83ms, τ=15.2ms) is shown in Fig. 3. Calculated repeatability coefficients are RC=13.4ms, CV=0.057, and ICC=0.90.

Discussion and Conclusion: GEE analysis showed that diurnal changes were a small but significant factor in T1ρ measurements. Similar results were reported earlier for T2 changes[5]. On the other hand, there were no significant changes in T1ρ measurements in the repeated scans. This was expected since the intervals between the longitudinal scans were relatively short compared to the typical time scale of age-associated disc degeneration processes. Therefore, this finding confirms that there was no discernible bias in repeated measurements. The CV of Bland-Altman test showed that the standard deviation of repeated T1ρ measurements was about 6% of the average T1ρ value. Moreover, ICC parameter showed that the variation in repeated T1ρ measurements was small compared to between subject variations. In this study, we used a longitudinal design to analyze both reproducibility and diurnal changes. Diurnal effects alone could probably be measured more accurately if the scans were repeated on the same day.

Acknowledgement: This study is supported by AOSpine SRN and Advancing a Healthier Wisconsin research grants.

References: **1.** Johannessen W, *et al*, *Spine*, 31, 1253–57, 2006. **2.** Adams MA, *et al*, *J. Bone Joint Surg. Br.*, 72-B, 266–70, 1990. **3.** Li X, *et al*, *MRM*, 59, 298–307, 2008. **4.** Bland JM, *et al*, *Lancet*, 1, 307–10, 1986. **5.** Karakida O, *Clin. Radiol.*, 58, 389–92, 2003.