CHEMICAL EXCHANGE AND IN VIVO INTERVERTEBRAL DISC R1-RHO DISPERSION IMAGING: A FEASIBILITY STUDY

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Introduction:

Chemical exchange (CE) between water protons and exchangeble protons such as hydroxyl, amide, and amine may provide valuable biochemical information. $R_1\rho$ (= $1/T_1\rho$) dispersion has been investigated to study CE [1]: under different spin-lock powers $R_1\rho$ value changes as a result from varying contributions from CE. Intervertebral disc (IVD) is a structure rich in glycosaminoglycan (GAG). IVD degeneration is associated with discogenic pain, a disease with high incidence and huge burden. $T_1\rho$ imaging has been employed to study IVD degeneration [2-3], yet no effort has been made to link IVD $R_1\rho$ dispersion with CE, nor to demonstrate the feasibility to image IVD $R_1\rho$ dispersion *in vivo*. In this study we 1) developed a novel pulse sequence for IVD $R_1\rho$ dispersion imaging *in vivo*, 2) explored the relationship between $R_1\rho$ dispersion and pH and concentration in a GAG phantom that mimics IVD composition, and 3) demonstrated the feasibility of the above method on healthy volunteers. Results indicate the proposed method is a promising technique, and has the potential to image important disease biomarkers such as GAG concentration and pH value.

Methods:

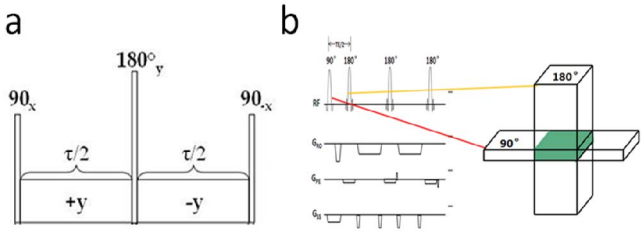

Fig 1. Pulse sequence. a: spin-lock preparation. b: rFOV TSE imaging.

Pulse Sequence & Imaging: A rFOV spin-lock TSE sequence (Fig. 1) is impletmented on a 3.0T system (Verio, Siemens) by using a spin-lock preparation that is insensitive to B_0 and B_1 inhomogeneity, and by applying the gradients for the imaging 180° refocusing pulses in the phase-encoding direction. Using this rFOV technique and centric-encoding, all k-space lines were acquired within a few excitations, thus minimize breathing and bowel movement artifacts. To calculate $R_1\rho$ map, six images with varying spin-lock durations (100, 80, 60, 40, 20, 10 ms) were acquired under each spin-lock power. To obtain the dispersion curve, four measurements with varying spin-lock magnitudes (0, 100/50, 200, 300/400 Hz) were run for each volunteer/phantom. Phantom studies: To explore the association between GAG properties and $R_1\rho$ dispersion, four samples with GAG concentrations of 50, 100, 150, and 300mM were prepared from chondroitin sulphate A (Aldrich-Sigma, St Louis) in a standard solution of phosphate-buffered saline and subsequently titrated to a pH of 7.0. Four samples with the same concentration of 150mM were also prepared in phosphate-buffered saline, and subsequently titrated to pHs of 6.2, 6.48, 6.7, and 7.1, respectively. Volunteer studies: Three healthy volunteers (31Y/F, 46Y/M, 45Y/M) were recruited. The study was approved by our Institutional Review Board and informed consent was obtained from all volunteers. For each volunteer one sagittal slice covering the lower spine was used. Parameters were: slice thickness= 8 mm, FOV= 73×220 mm^2, in-plane resolution= 1.56×1.15 mm^2, TE/TR= 9/3750 ms, 8 averages, bandwidth=300Hz/pixel, TA =10mins. In order to demonstrate the accuracy of $R_1\rho$ imaging, in one volunteer (31Y/F) the acquisition was repeated three times. Data analysis: $R_1\rho$ (= $1/T_1\rho$) was calculate by fitting images with varying spin-lock durations to a mono-exponential decay model. In phantom study, linear regression was used to exam the association between concentrations and pH values, and $R_1\rho$ difference between low (50Hz) and high (400Hz) spin-lock magnitude. In volunteer studies, ROIs containing nucleus pulposus were manually drawn in the center of the following IVDs: L5/S1, L4/L5, L3/L4 and L2/L3. R1ρ values were subsequently averaged within the ROI.

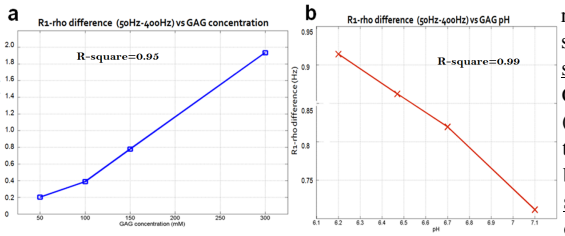

Fig 2. Dependence of $R_1\rho$ difference (between 50Hz and 400Hz spin-lock magnitude) on a) concentration, and b) pH, in a GAG phantom.

Results:

Phantom study demonstrated a linear relationship between $R_1\rho$ dispersion (calculated as the difference between 50Hz and 400Hz spin-lock magnitude) and GAG concentration with R^2=0.95, and between R1ρ dispersion and pH value with R^2=0.99 (Fig 2). This could be explained by the exchangeable –OH protons and also possibly –NH protons in GAG molecules, and is in line with the theoretical equation [1]. Images of one volunteer are shown in Fig 3. Remarkably $R_1\rho$ difference between 100Hz and 300Hz can be identified on the image. Quantitative results from three volunteers are shown in Fig 4 (a-c): $R_1\rho$ dispersion curves showed obvious decrease as spin-lock magnitude increases. This dispersion varied from disc to disc, indicating different disc may have different GAG concentrations and pHs. To assess the reliability of the proposed method, in one volunteer acquisition was repeated three times to investigate the repeatability of measurement. In Fig 4(d), the standard deviation between repetitions is generally smaller than the dispersion between low and high spin-lock magnitude, meaning the proposed method has good power to image $R_1\rho$ dispersion in vivo.

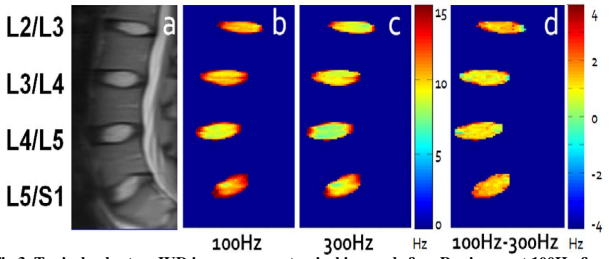

Fig 3. Typical volunteer IVD images. a: anatomical image. b & c: $R_1\rho$ image at 100Hz & 300Hz spin-lock magnitude, respectively. c: Difference between b and c.

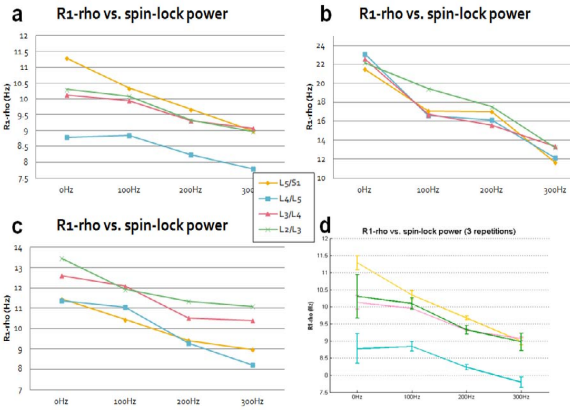

Fig 4. a, b, and c :$R_1\rho$ dispersion curve for three healthy volunteers. a: 31Y/F, b: 46Y/M, c: 45Y/M. d: $R_1\rho$ dispersion curve with mean and standard deviation calculated from three repetitions for the volunteer (a-c). Bars show standard deviation.

Discussion and Conclusions:

We have demonstrated that both pH and concentration could affect $R_1\rho$ dispersion via chemical exchange, and with a newly proposed rFOV spin-lock TSE technique we were able to successfully detect $R_1\rho$ dispersion *in vivo* with high accuracy. Both pH and concentration are important biomarkers for IVD degeneration and lower back pain. Further work is needed to separate contributions from these two factors, in the hope to obtain pH value and GAG concentration maps separately.

References: [1] Neuroimage. 2012 Jan 16;59(2):1218-27. [2] Magn Reson Med. 2010 May; 63(5): 1193–1200. [3] Spine (Phila Pa 1976). 2006 May 15; 31(11): 1253–1257.