

Sodium MRI: A Reproducibility Study in Subjects with Osteoarthritis of the Knee

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Introduction: Cartilage degeneration in osteoarthritis (OA) is characterised by loss of collagen and proteoglycans (PGs). PGs contain negatively charged sulphate and carboxylate groups, which constitute a fixed charge density (FCD). The Donnan equilibrium dictates that positively charged mobile ions distribute into cartilage in proportion to this FCD and in synovial fluid and cartilage the majority of positively charged ions are Sodium (Na). Measuring Na in cartilage may be a sensitive marker for PG loss and cartilage degeneration [1-3]. In this study we sought to assess the reproducibility of sodium MRI scanning of articular cartilage using knee osteoarthritis as a model.

Materials and Methods: 17 subjects were scanned using a Siemens 3T Tim Trio (Siemens Healthcare, Erlangen, Germany) and a dual tuned 1H/23Na quadrature volume coil (Rapid Biomedical GmbH, Rimpar, Germany). High resolution 3D structural dual-echo steady state (DESS) and Na scans were acquired during the same scanning session without repositioning the subject. Sodium scanning used an 8ms 3D cones readout (FOV=18cm, res=2.5mm³, TE=0.27ms, TR=15ms, NEX=118, TA=21mins) [4]. The scans were performed twice during the same visit, with a short break for the subject to walk between scans. Two small phantoms of sodium chloride (NaCl) with sodium concentrations of 150mM and 250mM were attached to the scanned knee within the coil for signal normalisation. The knee cartilage was manually delineated using the DESS images. The derived cartilage ROIs were then overlaid on the sodium MRI and the sodium concentration within the cartilage ROIs was quantified based on a single value of T1 for Na in cartilage normalised to the NaCl (with Na of known T1 and concentration). Hence for each patient we calculated one value of knee cartilage Na for each of the two scans.

Results: 11 subjects had complete scan pairs (8 of the 34 scans in 6 subjects were not usable due to poor alignment). 6 of the 11 subjects had a confirmed diagnosis of OA by ACR criteria [5] and 5 were healthy age and sex matched controls (mean age 64 +/- 10 yrs, 73% female). OA patients represented a wide range of disease severity. The interclass correlation coefficient was 0.88 (0.6 – 0.97), the percent coefficient of variation was 4.2% (2.9%-7.3%) and the limits of agreement (scan 2-1) were -7.7% to 14%. A Bland Altman plot showing repeatability of the measurement is shown in figure Fig 1.

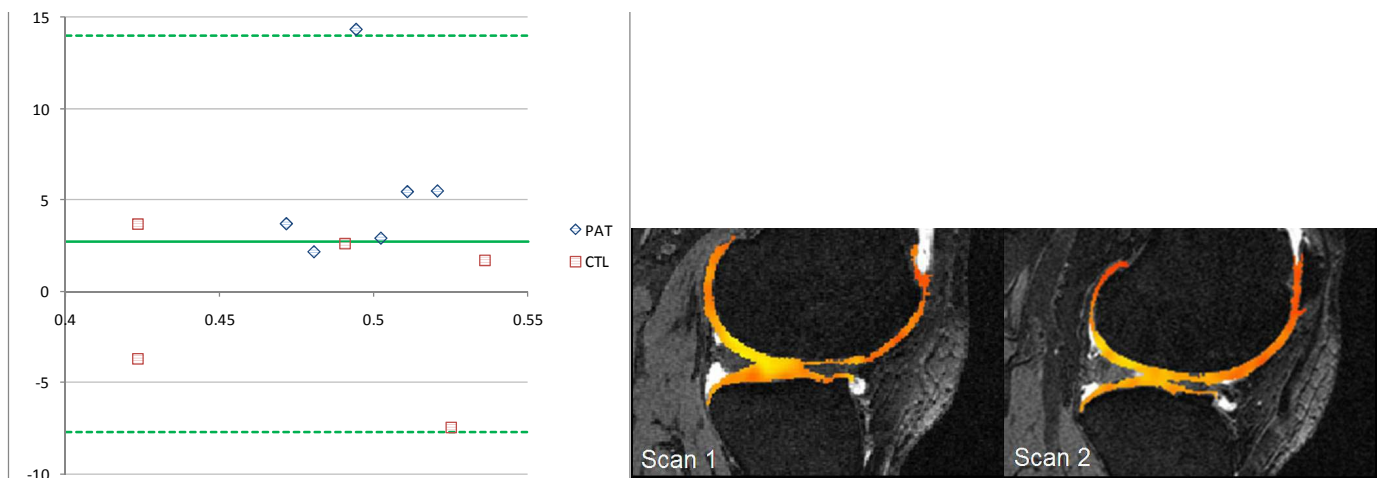


Figure 1- Bland Altman Plot, showing difference in percent (Scan2-1) against mean sodium concentration (in arbitrary units), with lines showing bias (solid) and 95% limits of agreement (dashed)

Figure 2- An example of 2 DESS images of the same OA subject knee overlaid with false colour sodium concentration in the articular cartilage.

Discussion: In this study we have observed differences in sodium concentration of up to 50% amongst subjects suffering from various stages of OA. The inter-scan coefficient of variation of 4.2% seems promising. This implies that a study with 30 subjects would have 90% power with 5% type-I error to detect a mean within-group change over time of 3.6%. Within an individual subject test-retest differences due to measurement error will rarely be more than 12%, so an observed change of this magnitude may be considered as reflecting genuine change in the underlying disease. One potential confound to our current method is not measuring a sodium T1 map in each subject, but rather assuming a literature value of the T1. Should the sodium T1 lengthen with cartilage degradation, the sodium value will be underestimated, increasing the separation between patients and controls. However, this does not affect the test-retest results, which would be identical in absolute or arbitrary units. Having a robust and repeatable methodology is the first step in developing Na MRI as a tool for detecting cartilage changes over time and hence ultimately for use as a marker for OA drug development; we are currently using this technique in a cross sectional and longitudinal study of 30 OA subjects and 30 healthy controls.

References: [1] Borthakur OA Cartilage 2000;8:288-293. [2] Shapiro MRM 2002;47: 284-291. [3] Reddy MRM,1998;39;697-701 [4] Gurney MRM,2006;55(3):575-582. [5] Altman R et al Arthritis and Rheumatism 1986;29 1039-1049 2