Age dependent modulation of Aggrecan in human knee cartilage measured via sodium MRI at 7T

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Objective: To determine the age dependent variation of molecular changes in human knee cartilage via sodium MRI at ultrahigh fields.

Background: While OA is a disease of diverse etiologies cartilage tissue is primarily affected. Aggrecan (a large aggregating proteoglycan) along with Type-II collagen forms a major structural component of cartilage, particularly articular cartilage. Aggrecan has been shown to undergo predominant change in early OA [1]. More than 80% of population over 65 years of age experience pain due to knee OA [2-4]. Currently there is no cure for the disease and therapeutic interventions are primarily targeted to symptomatic relief. Before quantifying the OA changes with any noninvasive method, it is critical to estimate the natural course of molecular degeneration in cartilage matrix. In the present study, using sodium MRI at ultrahigh field, we investigated the natural, age dependent molecular changes in the healthy human knee cartilage in vivo.

Methods: All human studies were approved by the Institutional Review Board. The knees of three healthy young male (20-24 years) and three aged (43-59 years) male volunteers were imaged on 7T Siemens MRI scanner. We used a custom built birdcage coil tuned to sodium frequency with optimal SNR. Sodium MRI was performed using an Ultra short Echo (UTE) (Siemens medical solutions, Erlangen) 3D radial sequence with a mean SNR of 24 (TR=75ms, TE = 0.07ms, FOV=16cm, Matrix =128×128×128 and 600 radial spokes for total scan time of 45 sec per image) [5]. 16 individual acquisitions (12 min total acquisition time) were co-added offline to further improve SNR for more accurate concentration measurements. The same parameters were maintained in all experiments for all subjects for direct comparison. For B_1 field variation and concentration corrections, a phantom with 250 mM Nacl and 5% agarose was imaged and appropriate calibrations were computed. The images obtained using UTE sequence have higher SNR compared to 3D FLASH sequence (approximately by a factor of 20) for comparable scan time of 12 - 15min.

Results and Discussion: The sodium concentration maps (Fig.1) show differences in sodium concentration in human knee cartilage between a young male volunteer (24 years) and an aged male volunteer (59 years). The same trend is observed in the other subjects as well. The B_1 field variations were found to be ~10% in the knee and concentration corrections have been computed for sodium concentration in the human cartilage and the agarose phantom. The sodium concentration measured in younger group is in the range of 242mM - 253mM (mean of 247.5 mM) and in aged group is 209mM - 220 mM (mean of 214.5mM), which shows 15% variation of sodium concentration in both the age groups. As described previously [3], these sodium maps can be used to calculate the tissue's fixed charge density (FCD), which is a map of Aggrecan distribution. These preliminary results demonstrate that it is feasible to obtain sodium maps of human knee in-vivo at 7T with reasonable acquisition times and quantify age dependent molecular changes in knee cartilage of healthy human subjects. Further work is in progress to quantify age dependent Aggrecan changes in larger groups of subjects to quantitatively establish the natural course of degenerative changes in cartilage.
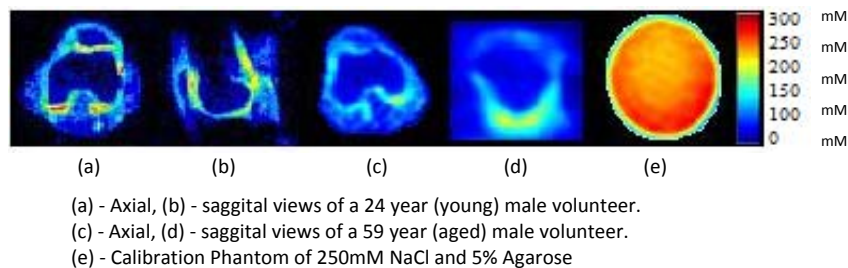

(a) - Axial, (b) - saggital views of a 24 year (young) male volunteer.
(c) - Axial, (d) - saggital views of a 59 year (aged) male volunteer.
(e) - Calibration Phantom of 250mM NaCl and 5% Agarose

Figure 1. Comparison of sodium concentration in young (24 years) and aged (59 years) human subjects.

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