

## Sodium concentration reduction in human knee cartilage with healthy aging

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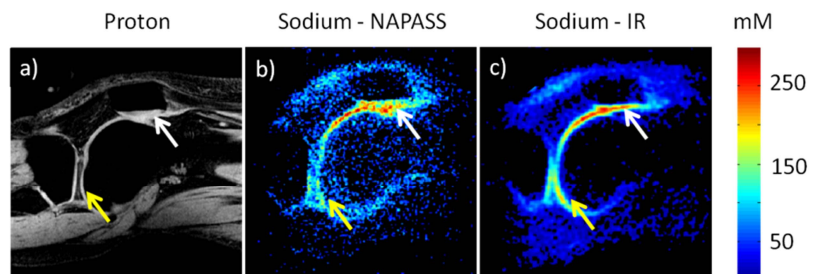
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**Introduction:** Osteoarthritis (OA) is a disease associated with aging and is characterized by cartilage deterioration. However, in early stages of the disease cartilage volume can remain unaffected while biochemical change occurs and this makes it difficult to track the progression of OA *in-vivo*. A reduction in cartilage glycosaminoglycan (GAG) content is associated with early OA and can be correlated to a reduction in sodium (<sup>23</sup>Na) ion concentration<sup>1</sup>. This makes <sup>23</sup>Na-MRI a promising tool for tracking cartilage health *in-vivo*. Substantial reductions of GAG have also been noted as a function of age over the lifespan in autopsy specimens<sup>2</sup>, but it is not known if sodium concentration changes with age. The purpose of this study is to investigate alterations of sodium concentration in adult human cartilage *in-vivo* during healthy aging.

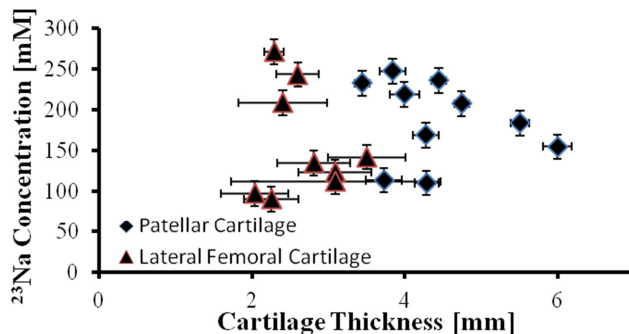
**Method:** The right knee of 10 male subjects (age 19-58 years), with no knee injury, was imaged on a 4.7T MRI (Varian) with a custom <sup>23</sup>Na/<sup>1</sup>H birdcage coil. Sagittal images were acquired using: (i) a higher resolution steady state sodium sequence using 3D twisted projection imaging (TPI) acquisition (NAPASS:  $\alpha = 74^\circ$ , TR = 30 ms, TE = 0.186 ms, FOV = 120 mm, readout = 15 ms, matrix = 150x150x30,  $N_{avg} = 2$ , time = 9.36 min), (ii) a soft inversion recovery sodium sequence with TPI acquisition that nulled sodium signal from synovial fluid (IR: TR = 51 ms,  $P_{inv} = 24$  ms, TI = 15 ms, TE = 0.186 ms, FOV = 120 mm, readout = 12.95 ms, matrix = 80x80x20,  $N_{avg} = 4$ , time = 10 min), and (iii) a gradient echo proton acquisition (TR = 1200 ms, TE = 7.5 ms, FOV = 255 x 127 mm<sup>2</sup>, matrix = 512x256, slice thickness = 2 mm, 25 slices). Average sodium concentrations for each subject were measured in patellar and lateral femoral cartilage over two slices (**Figure 1**) using 3 “beside the knee” agar phantoms (100, 250, 500 mM) for reference, and accommodating for cartilage relaxation using a sequence simulation. Cartilage thickness was measured on the proton images in the same regions of interest. Finally, sodium concentration was measured in the popliteal artery for the steady state sodium acquisition.

**Results/Discussion:** Patellar cartilage (3.5-6 mm) was thicker than the lateral femoral cartilage (2-3.5 mm), but overall sodium concentration did not correlate with cartilage thickness in either region (**Figure 2**). Sodium concentration in the blood (measured on the steady-state images) was found to be between 130-150 mM and was not correlated with age. However, sodium concentration in the cartilage was negatively correlated with age (**Figure 3 for IR data**). This trend was evident in the patellar cartilage (PASS: R=-0.57, p=0.07; IR: R=-0.59, p=0.06) and significant in the femoral cartilage (PASS: R=-0.59, p=0.08; IR: R=-0.70, p=0.04). Sodium concentration in patellar cartilage decreased from a maximum value ~230-250 mM in younger subjects to ~110-150 mM in older subjects. Similarly, sodium concentration in the lateral femoral cartilage declined from ~230-280 mM to 100-150 mM. The sodium concentration was reduced by a factor of 1.5-2.5 times at the older ages relative to the young adults. This agrees with literature that shows that GAG content of cartilage decreases by a factor of ~2.1 in post-mortem samples from humans aged 20 to 70 years<sup>2</sup>, and is similarly decreased with age in bovine cartilage samples<sup>4</sup>.

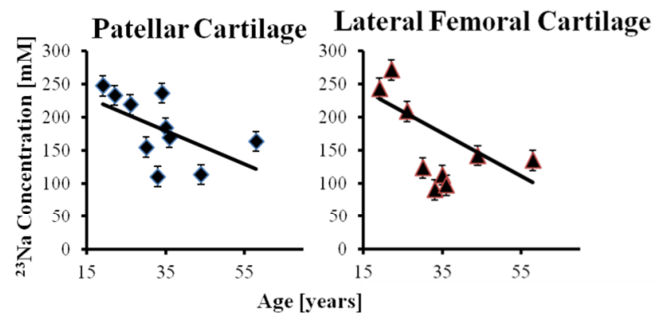
In the absence of thinning cartilage or other physical symptoms of osteoarthritis, the concentration of sodium in knee cartilage declines with age. Sodium MRI can measure these internal biochemical composition changes of cartilage even during normal aging. These results can serve as a baseline to future studies of osteoarthritis and other conditions. Therefore, age should be considered in all sodium MRI studies of cartilage.



**Figure 1:** Sagittal slices of the human knee. (a) Proton images were used to determine the cartilage thickness. [<sup>23</sup>Na] in the patellar (white arrow) and lateral femoral (yellow arrow) cartilage was obtained using both (b) a steady state and (c) an inversion recovery technique to suppress the synovial fluid.



**Figure 2:** Cartilage thickness vs. [<sup>23</sup>Na]. No relationship was found between [<sup>23</sup>Na] (from the inversion recovery <sup>23</sup>Na image) plotted against the cartilage thickness (<sup>1</sup>H image) for the same region.



**Figure 3:** <sup>23</sup>Na vs. age. [<sup>23</sup>Na] (calculated from inversion recovery) is shown to decrease with increasing age in cartilage.

**References:** [1] Borthakur et al. Osteoarthr Cartilage 2000;8. [2] Elliott et al. ARD. 1979; 38. [3] Newbould et al. Osteoarthr Cartilage. 2012; 20. [4] Thonar et al. J Biol Chem. 1986; 261.