Depth-wise relaxivity of Gd-DTPA^{2-} and Gd-DTPA-BMA in human femoral head cartilage

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INTRODUCTION

Delayed gadolinium enhanced MRI of cartilage (dGEMRIC) is used to assess GAG content in articular cartilage [1]. Measuring T1 relaxation time before contrast agent administration and when the contrast agent is assumed to have reached equilibrium state, it is possible to estimate the Gd concentration. However, to calculate precise Gd concentration, information about the relaxivity of cartilage is needed. Usually relaxivity is assumed constant across the cartilage depth but this has not been confirmed. Previously relaxivity has been investigated in full-thickness cartilage [2]. The aim of the current study was to investigate the depth-wise variation of relaxivity in human femoral head articular cartilage using anionic and nonionic contrast agent.

METHODS

Two MRI contrast agents, namely anionic Gd-DTPA^{2-} (Magnevist, Bayer Schering Pharma AG, Berlin, Germany), and nonionic Gd-DTPA-BMA (Omniscan, GE Healthcare, Milwaukee, WI, USA) were used. Human femoral heads (n=8, age: 79±7, range 65-88) were harvested from patients undergoing hip replacement surgery due to hip fracture. The cartilage was visually intact. Two adjacent osteochondral plugs (diameter=4mm) were detached from weight-bearing region, one plug to be investigated using each contrast agent. Third adjacent plug was harvested to measure the water content of the samples. A 200MHz (4.7T) spectrometer (Bruker Avance-II) was used to obtain profile images from the samples in depth-wise direction. First, T_1 relaxation time was measured without contrast agent (inversion recovery sequence, TR=5 s, 16 TI's between 1 and 1000 ms, depth-wise resolution of 20 μm). Subsequently, the samples were exposed to 2mM solution of contrast agent. Due to test tube geometry the contrast agent could transport into the cartilage through cartilage surface only. T_1 was measured again ten hours later. Subsequently, the samples were split in two halves, which were quickly frozen by inserting the test tube into dry ice. While being frozen, one half of the sample was cut across the cartilage depth into segments with a thickness of 100 μm. The Gd concentration of each segment was obtained by inductively coupled plasma-atomic emission spectroscopy (ICP-AES). T1 relaxation times for the both time points were calculated, and the depth-wise profiles were downsampled to match the thickness of the segments cut for ICP-AES. Depth-wise relaxivities for the both contrast agents were were calculated using the formula: $r_1 = (1/T_{1Gd} - 1/T_{1pre})/ [Gd]$, where T_{1Gd} is the T_1 value ten hours after the beginning of contrast agent exposure, T_{1pre} is the T_1 value before Gd-DTPA^{2-} exposure, and [Gd] is the calculated concentration of each contrast agent.

RESULTS

After ten hours, the samples exposed to Gd-DTPA^{2-} had reached constant T_1 values at all samples, while the samples exposed to Gd-DTPA-BMA displayed still decreasing T_1 values. Despite incomplete transport, the Gd concentration measured by ICP-AES was substantially higher for Gd-DTPA-BMA at all cartilage depths (Fig. !a). Both contrast agents displayed decreasing concentration towards the deep cartilage. The ΔR_1 values (defined as $1/T_{1Gd} - 1/T_{1pre}$) showed similar behavior (Fig. 1b). The relaxivities calculated from this data were nearly identical, with mean value of 3.8 1/mM/s for both contrast agents, showing similar values through the entire cartilage depth (Fig. 1c).

DISCUSSION

The current preliminary results suggest that the relaxivity of both Gd-DTPA^{2-} and Gd-DTPA-BMA remains constant across the cartilage depth. With the field strength of 4.7T, the numerical value is 3.8 1/mM/s. Even though Gd-DTPA-BMA had not reached the equilibrium concentration in ten hours, the relaxivity can be calculated because the samples were frozen immediately after the T_{1Gd} measurement and never thawed before cut into segments. The current results suggests that the ΔR_1 may provide sufficient estimate of cartilage quality, but based on the variation of Gd concentration across the cartilage depth, analyzing full-thickness regions of interest may not give the best possible estimate of the GAG content of articular cartilage.

REFERENCES

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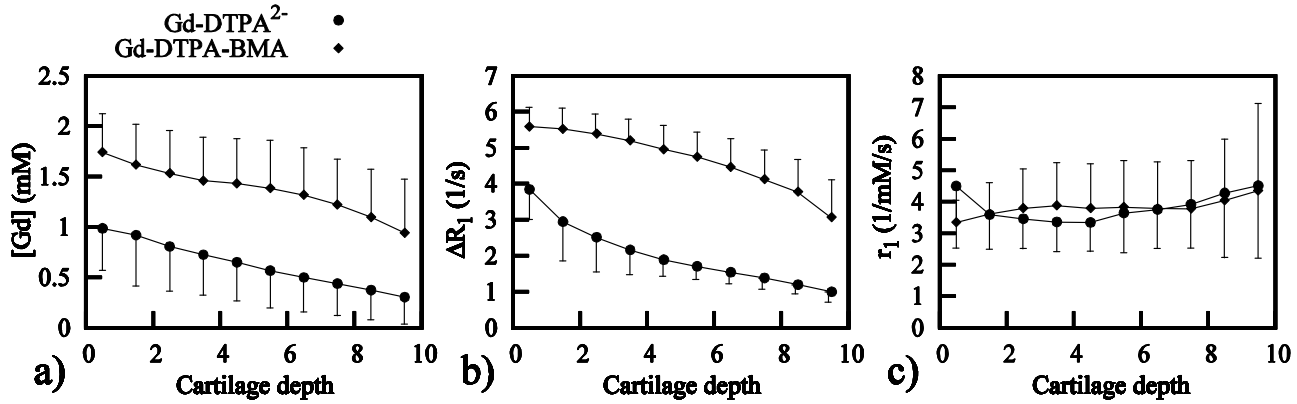

Figure 1. a) measured Gd concentration, b) measured change of R1 relaxation rate and c) calculated relaxivity for the two contrast agents across normalized cartilage depth.