Delayed Contrast Enhanced MRI of Cartilage: Comparison of Ionic and Non-ionic Contrast Agents

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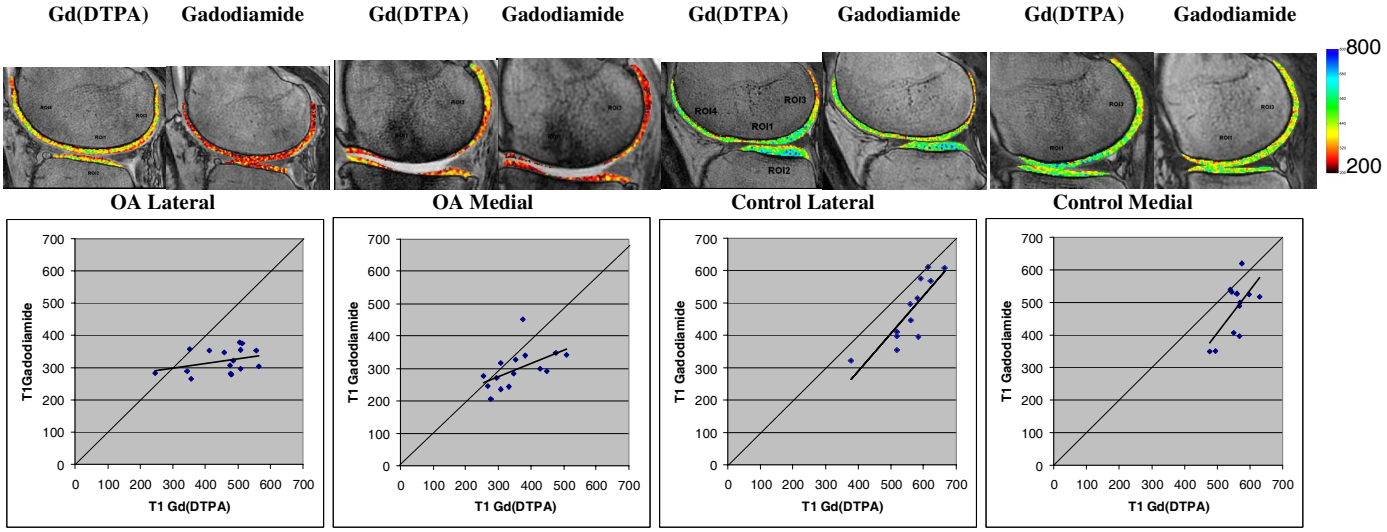
Hypothesis: Delayed Gd(DTPA)$^{2-}$ enhanced MRI of cartilage (dGEMRIC) is a method designed to image the distribution of fixed charge density in cartilage, based on the premise that mobile ions will distribute in cartilage in relation to the concentration of the charged glycosoaminoglycan (GAG) molecules. The hypothesis to be tested here is whether the variation of T_1 values post-Gd is a true reflection of charge distribution or if there may be other competing or synergistic effects that may influence the post-Gd T_1 within the cartilage. To accomplish this, T_1 maps were obtained in the same individuals after administration of Gd(DTPA)$^{2-}$ (Berlex, NJ) as an ionic contrast agent or gadodiamide (GE Healthcare, WI) as non-ionic contrast agent. The expectation would be that gadodiamide T_1 values would be uniformly low (as it would penetrate cartilage uniformly at higher concentration, irrelevant of charge), while Gd(DTPA)$^{2-}$ T_1s would have a distribution of values due to variations in its distribution due to the cartilage matrix fixed charge.

Materials & Methods:

Subjects: Twenty seven subjects, including 15 patients with self reported OA (5 men and 10 women, aged 40-86, average age of 60.1 years) and 12 volunteers without OA symptoms (controls, 4 men and 8 women, aged 18-40, average age of 29.9 years), participated in this study. **Imaging:** Data were acquired on 1.5T GE Signa short bore Twin speed system (GE Healthcare, Milwaukee, WI) using a commercial transmit/receive extremity coil. Each subject had two imaging sessions, using 0.2 mmol/kg Gd(DTPA)$^{2-}$ (Magnevist, Berlex, NJ) or gadodiamide (Omniscan, GE Healthcare, WI) respectively. The time interval between the two imaging sessions was no less than 3 days. Sagittal images were acquired with a 3D look locker (3DLL) sequence, started at 90 (n=4), 120 (n=12), or135 min (n=11) post contrast injection. For each subject, the acquisition start time in the 2 imaging sessions were identical. Parameters for the sequence included: slices prescribed=32, flip angle =5°, TR=2.2 s, τ=5.693 ms, bandwidth = +/-62.5 kHz, Matrix = 256x256. Eleven echoes with TIs ranged from 20 to 1839 ms were obtained. The acquisition time was 9 min 24 sec.
Data analysis: T_1 mapping was performed for both medial and lateral condyles of the femur, with a custom software analysis routine written in MATLAB (The Mathworks; Natick, MA). ROIs were placed at the central region of the cartilage between the outer edges of the meniscus horns in central slices of the condyles.

Results:



Top Row: Shown are cartilage T_1 maps obtained in one representative subject in each OA and control group with Gd(DTPA)$^{2-}$ and gadodiamide (0.2 mmol/kg) on two separate days. Note one central slice for each lateral and medial condyle are shown. In the OA subject, note the difference in T_1 maps obtained with either agent, especially in the lateral slice. With ionic Gd(DTPA)$^{2-}$, there is a distribution of T_1 values and generally higher than what is seen with gadodiamide in the same slice.
Bottom Row: Summary plots showing the T_1 measured by gadodiamide *vs.* Gd(DTPA)$^{2-}$ in each slice in the lateral and medial condyles in OA and control group. Only ROIs in the weight bearing central femoral compartment were used. In the OA group the gadodiamide T_1 were generally low and consistent across subjects in the lateral compartment, while GdDTPA T_1 values covered a wide range of values. In the medial compartment, there was a slightly larger range of gadodiamide T_1s, although the medial compartments frequently had very little cartilage. Control subjects showed a much larger range of T_1 values with gadodiamide. While the correlation coefficients are low in OA (0.12 (lateral) and 0.3 (medial)), they are relatively higher (0.7 (lateral) and 0.41 (medial)) with a negative bias in the control subjects.

Discussion & Conclusion:

- The lateral (generally "uninvolved") section of OA knees showed the expected results, in which T_1 with gadodiamide was relatively constant while there was a range of Gd(DTPA)$^{2-}$ T_1s across individuals. A similar trend is also apparent in the medial slice; however, many of the subjects had little or no cartilage in this condyle. The consistency of gadodiamide T_1 supports the hypothesis that T_1 distributions with Gd(DTPA)$^{2-}$ reflect cartilage fixed charge in this population.
- In control subjects, there was a range of T_1 values with gadodiamide, which correlated to the T_1 values with Gd(DTPA)$^{2-}$. While the reason for these observations is not yet clear, they may be related to other factors influencing the transport of gadolinium in to the cartilage not based on charge that were not apparent in the OA knees (with higher diffusivity of small molecules).

In summary, Gd(DTPA)$^{2-}$ demonstrated a range of values in cartilage from individuals with OA; this variation has previously been shown to correlate to the radiographic stage of disease (*AJR* 2004;182:167; *Knee Surg Sports Traumatol Arthrosc.* 2006;14:718). In contrast, gadodiamide showed no variation in those compartments. In asymptomatic individuals, both contrast agents resulted in relatively high T_1 values. While the high Gd(DTPA)$^{2-}$ T_1 is presumably at least in part due to high cartilage fixed charge (*Magn Reson Med.* 1996; 36:665), the high T_1 with gadodiamide may be reflective of either impeded transport of this agent in normal cartilage and/or altered relaxivity of the agent in normal cartilage. If the Gd(DTPA)$^{2-}$ T_1 is due to both cartilage fixed charge and transport issues, these effects would be synergistic, as degenerated cartilage would have both increased transport and increased contrast agent concentration. These results support the continued use of the ionic contrast agent to reflect cartilage fixed charge in degenerated cartilage, as well as further studies to investigate the transport and/or relaxivity component of the contrast enhanced T_1 values.

Acknowledgement: Study supported in part by Berlex Inc. (NJ, USA).