Comparison of MRI (dGEMRIC) and CT (DICE-CT) for Molecular Imaging of Cartilage Glycosaminoglycan

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Introduction

delayed Gadolinium enhanced MRI of cartilage (dGEMRIC) was designed to image the glycosaminoglycan (GAG) distribution in articular cartilage utilizing the concept that a charged MRI contrast agent (Gd-DTPA^{2-}; Berlex, NJ) will distribute in inverse relationship to the negatively charged GAG molecules. A number of in vitro, animal, and clinical studies have been conducted utilizing T1(Gd) as the "dGEMRIC Index". However, the correspondence of the measured of T1 to Gd-DTPA^{2-} concentration requires assumptions regarding pre-contrast T1 and Gd-DTPA^{2-} relaxivity. Recently micro-computed tomography (CT) has been used to investigate GAG concentrations in cartilage using the ionic CT contrast agent Hexabrix (Mallincrodt Imaging Hazelwood, MO) (Palmer et al, Proc Orthop Res Society, 2005), and Gd-DTPA^{2-} at very high concentration (Cockman et al, Osteoarthritis Cartilage, 24:210, 2006). Iothalamate Meglumine (Conray, Mallincrodt Imaging Hazelwood, MO) is an ionic monomer (charge -1) CT contrast agent available for clinical use. This study compares dGEMRIC with Delayed Ionic Contrast Enhanced CT (DICE-CT) for evaluation of GAG distribution in cartilage.

Methods

Human tibial plateaus were imaged intact by standard dGEMRIC techniques at 4.7T (Bruker Instruments) after equilibration in 1mM Magnevist (Berlex, NJ) and by CT on a Toshiba Aquilion 64 system after equilibration in 74 mM (1/10 full strength) Conray. Clinical imaging was done by dGEMRIC on a 1.5T GE Signa HDx utilizing a standard dGEMRIC protocol. For DICE-CT, an intra-articular injection of 30 ml of contrast solution composed of a 1:5 dilution of Conray in normal saline and 0.3ml epinephrine (1:1000) was performed, and the patients were then imaged 4 hours after injection on a Toshiba Aquilion 64 system. All studies were approved by the institutional review board, and all subjects gave their informed consent. Both Gd-DTPA^{2-} and Conray are negatively charged and therefore will distribute in higher concentration in GAG depleted cartilage; however, in terms of measured metrics, high Gd-DTPA^{2-} will result in lower T1, and higher Conray will result in higher Hounsfield Units (HU). Therefore low-high T1 and high-low HU were plotted on a color scale of red-green.

Results

In the excised plateaus, spatial variations in GAG as visualized by dGEMRIC corresponded to those of DICE-CT (Figure 1a). In the clinical studies, the intra-articular injections were well tolerated, and the DICE-CT images after 4 hours clearly demonstrated penetration of contrast into cartilage. However, the contrast level in the joint at that time point was low, indicating a fast wash-out from the joint which might limit effective transport. General areas of high / low variations were apparent in both clinical dGEMRIC and DICE-CT of 3 individuals, although there were also possible lesions that were more apparent on one modality than the other (Figure 1b,c,d, for examples).

Discussion

In vitro, the correspondence of dGEMRIC and DICE-CT was readily apparent. *In vivo*, many of the observed patterns correlated between MRI and CT, although there were also areas of poor correlation between the two modalities, the cause of which requires further study. Differences are likely due to the different conditions of transport of contrast to the tissue in the two cases, and/or factors which impact the relationship between T1 and Gd-DTPA^{2-} concentration.

Both techniques have advantages and disadvantages (Table below). The current results demonstrate the concept of the CT approach, and provide a means of comparison to MRI dGEMRIC studies. Work is underway both on the bench and clinically to be able to provide a reliable technique for quantitative analysis of DICE-CT and to better understand the differences between the two modalities for imaging of charge distribution.

	dGEMRIC	DICE-CT
Image basis	No ionizing radiation	Ionizing radiation
Contrast injection	Intravenous	Intra-articular
Delay period	90 min	To be determined
Image acquisition	Requires special pulse sequence; long acquisition	Standard protocol; fast acquisition
Image analysis	T1 mapping routine needed	Signal intensity is measure of contrast concentration
Image interpretation	Requires understanding of T1o, relaxivity, transport	Requires understanding of transport
Additional soft tissue information	High soft tissue contrast	Limited soft tissue contrast
Cartilage segmentation	Available with additional sequence	Difficult, may require immediate post-injection scan

Figure 1

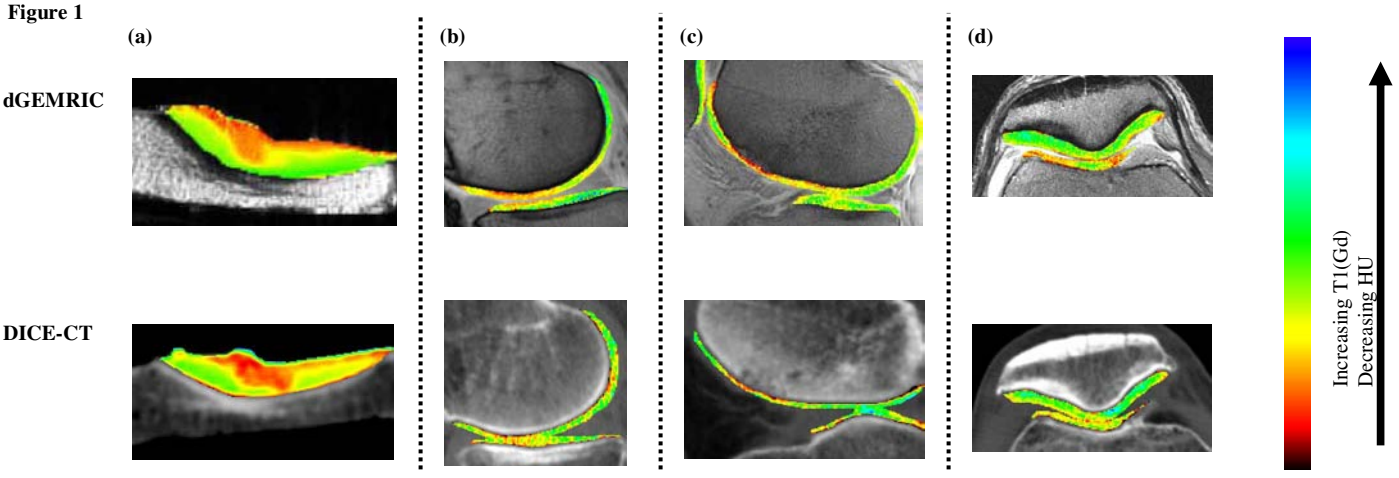

Figure 1a: Excised cartilage/bone section from tibial plateau imaged by dGEMRIC (top) and DICE-CT (bottom)
Figure 1b, 1c, 1d: Examples of dGEMRIC (top) and DICE-CT (bottom) from three individuals