**IN VIVO COMPARISON OF INTRA-ARTICULAR AND INTRA-ARTICULAR DGMERIC AND DELAYED QUANTITATIVE CT ARTHROGRAPHY**

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Target audience: Scientists and clinicians aiming to apply quantitative MRI techniques for assessing cartilage.

**Purpose:** Loss of glycosaminoglycan (GAG) side chains of proteoglycans is one of the earliest signs of degeneration of articular cartilage. Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) and contrast-enhanced CT, or delayed quantitative CT arthrography (dQCTA), were initially designed to probe GAG content of the cartilage¹,². These methods assume that negatively charged contrast agent distributes into cartilage in an inverse relation to GAG content of the cartilage¹. Diffusion and distribution of contrast agent are influenced also by other factors, e.g., water and collagen content and contrast-enhanced CT has not been thoroughly validated in this clinical setting. Furthermore, dGEMRIC and dQCTA have not been systematically compared in vivo in a knee joint of a same patient. Thus, the aim of the study was to compare dGEMRIC with intravenous (dGEMRICIV) and intra-articular contrast agent injection (dGEMRICIA) and dQCTA to each other.

**Methods:** Ten patients with knee pain were scanned at 3T MRI (Siemens Skyra, Siemens Healthcare, Germany) and using a clinical 64-slice CT (Discovery PET/CT 690, GE Medical Systems, USA). The study protocol was approved by the local ethics committee and informed consent was obtained from all subjects.

Prior to contrast agent injection in MRI, single-slice T1-mapping was performed at the center of medial and lateral condyles using an IR-FSE sequence (TR/TE/TI=4060/8.6/50-3900 ms; FOV=120*120 mm², matrix=256*256, slice thickness=3 mm). Subsequently, 0.2 mM/kg of Gd-DTPA2 was injected intravenously and T1 measurements were repeated after 2 hours. Two weeks later, dGEMRICIV was performed at 90 minutes after intra-articular injection of ioxaglate - Gd-DTPA2 mixture (see below). T1 maps were generated using MATLAB (MathWorks inc., USA). Mean T1 relaxation time (i.e., dGEMRIC index) was separately calculated for dGEMRICIV and dGEMRICIA (T1IV and T1IA respectively) from the same regions as in dQCTA (medial and lateral trochlear grooves and condyles of femur and tibia). Change in relaxation rate was calculated for cartilage and synovial fluid (ΔR1IV, ΔR1IA, and AR1SF) as follows: ΔR1 = (1/T1IV -1/T1IA), where T1IV and T1IA are relaxation time values with and without Gd-DTPA2 respectively. Additionally, AR1SF was normalized by AR1SF = (AR1IV/AR1IA).

In CT (tube voltage=100 kV; tube current=160 mA, focal spot size=0.7 mm; pitch=0.53), ioxaglate - Gd-DTPA2 contrast agent mixture (20 ml; 105 mM Hexabrix 320, Guerbet, France) and 2.5 mM Magnevist, Bayer Healthcare Pharmaceuticals, Germany) was injected intra-articularly. The knee joint was scanned at 5 and 45 minutes after the injection and mean X-ray attenuation values were measured from the same cartilage regions as in dGEMRIC and from synovial fluid. Cartilage parameters were normalized by the contrast agent concentration in synovial fluid (C/CSF, C/CSFIV). Analyze 10.0 software (AnalyseDirect, Inc., USA) was used for CT analyses.

Either Pearson (r) or Spearman (rS) correlation analysis (with 95% CI) was applied using SPSS 19 software (SPSS Inc., USA).

**Results:** T1 relaxation time map of cartilage overlaid on top of a MR image and illustrated normalized X-ray attenuation map of cartilage overlaid on top of a CT image of a patient with cartilage lesion are shown in Figure 1. dGEMRICIV showed the strongest correlation to normalized dQCTA parameters, while dGEMRICIA correlated strongest with dQCTA at 45 minutes after both the parameters were normalized with contrast agent concentration in synovial fluid (Table 1). There was no relation between dGEMRICIV and dGEMRICIA when correlating either T1 (r=0.12 [-0.38–0.16], n=53, p=0.39) or AR1SF values (r=0.01 [-0.29–0.27], n=50, p=0.95). When ΔR1IA was normalized by the AR1SF, a significant correlation to ΔR1IV was established (r=0.52 [0.28–0.70], n=50, p<0.01).

**Discussion:** These results suggest that dQCTA is in best agreement with dGEMRICIV at 45 minutes after ioxaglate injection. If judged only by visual evaluation, CT conducted at 5 minutes after the contrast agent injection had the best diagnostic quality for evaluation of cartilage lesions. dGEMRICIV and dGEMRICIA were related with the AR1SF was taken into account in dGEMRICIA analyses. The results indicate the importance to take into account the contrast agent concentration in synovial fluid in dQCTA and dGEMRIC with intra-articular contrast agent injection. Normalization is justified because the contrast agent is diluted in synovial fluid and the volume of the synovial fluid in a joint varies among the patients. Limitations of the study include small sample size and the difference in time delay between contrast agent injection and imaging as well as differences in segmentation procedures in dGEMRIC and dQCTA.

**Conclusion:** dGEMRICIV and normalized dGEMRICIA correlated strongly with dQCTA. dGEMRICIV and dGEMRICIA were not correlated without taking into account the synovial fluid in dGEMRICIA. The findings of this study indicate the importance to normalize contrast agent concentration in cartilage with the contrast agent concentration in synovial fluid in dQCTA and dGEMRIC with intra-articular contrast agent injection.


**Figure 1.** MR (A-C) and CT (D-F) images of a patient with cartilage lesion (arrow). (A) Anatomical DESS (TE/TR=5/14.1ms) and (B) IR-FSE images (TI/TE/TR=2008/6.4060ms) without contrast agent. (C) T1 relaxation time map of cartilage after intra-articular contrast agent injection. (D) CT at 5 min and (E) CT at 45 min after injection. (F) Illustrative normalized X-ray attenuation map of cartilage at 45 minutes after injection (C/CSF). Contrast of the images has been adjusted to enhance visibility of the lesion.