The In Vivo Transport of Anionic Contrast Agent into Human Femoral Knee cartilage

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INTRODUCTION

Delayed gadolinium enhanced MRI of cartilage (dGEMRIC) is a quantitative MRI method utilizing anionic contrast agent Gd-DTPA^{2-}. The suggested mechanism is that the fixed charge density (FCD) of cartilage, induced by glycosaminoglycans (GAG), dictates the contrast agent distribution in cartilage via electrostatic repulsion [1]. However, this assumption has not been thoroughly examined and confirmed. Furthermore, very little is known about temporal and spatial transport patterns. This knowledge would be important for interpreting dGEMRIC results with respect to cartilage molecular structure. Previously, transport of Gd-DTPA^{2-} has been investigated using an interval of one hour between measurements, showing different transport patterns into deep and superficial cartilage [2]. The aim of the present study was to investigate the transport of Gd-DTPA^{2-} into human knee cartilage in vivo.

METHODS

Asymptomatic volunteers (n=5, age 20-45 years) were examined by MRI using a 1.5 T clinical scanner (Siemens Sonata, Siemens AG, Erlangen, Germany) with a dedicated knee coil. T_1 relaxation time was measured using inversion recovery fast spin echo sequence (TR=2000 ms, 6 TI's between 50 and 1600 ms, FOV 12 cm, matrix 256*256, in-plane resolution 0.5mm, slice thickness 3 mm). Single sagittal slice was localized into the middle part of lateral femoral condyle of the left knee. Before contrast agent injection, T_1 value of cartilage was measured. Triple dose (0.3 ml/kg) of Gd-DTPA^{2-} (Magnevist, Bayer Schering Pharma AG, Berlin, Germany) was injected. Subsequently, the volunteers walked up and down stairs (96 steps) twice, which took approximately 10 minutes. After this, T_1 relaxation time was measured, and the measurement was repeated every 12 minutes until two hours after contrast agent injection. Between the measurements the volunteers walked the stairs up and down once.

Regions of interest (ROI) were segmented manually into anterior, central and posterior femoral cartilage and central tibial cartilage (Figure 1). Mean T_1 values of the deep and superficial 50% of articular cartilage, respectively were calculated for each volunteer at each time point. The change of relaxation rate (ΔR_1), reflecting the contrast agent concentration, was calculated for each time point.

RESULTS

ΔR_1 increased faster in the superficial than the deep cartilage layer at all regions (Figure 2). The ratio of superficial and deep ΔR_1 2 hours after injection varied between regions, from 4 at central tibia to nearly 1 at posterior femur. At the two first measurements after injection (12 and 24 min), there was no or negligible amount of contrast agent in the deep cartilage layer at central femur, and for tibia, the ΔR_1 of deep cartilage did not start to increase until 50-60 minutes after injection. For anterior and especially posterior femur, the ΔR_1 of deep cartilage increased quite fast right after injection, but increase was even faster in the superficial cartilage. ΔR_1 kept increasing at all regions throughout the entire measurement period. The patterns were similar for all five individuals. There was a significant difference between deep and superficial ΔR_1 at all time points, except for anterior femur (Kruskal-Wallis test).

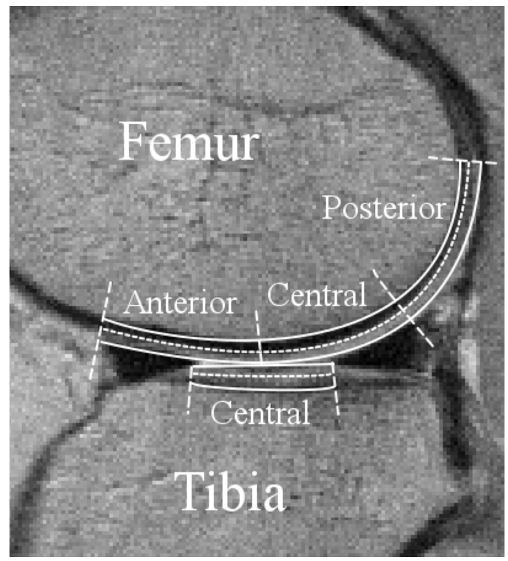

Figure 1. The regions of interest segmented into femoral and tibial cartilage.

DISCUSSION

This study consists of a limited number of volunteers, but their results are in very good agreement. In contrast to previous assumptions, results strongly indicate that no transport of Gd-DTPA^{2-} into cartilage occurs from the subchondral bone, because in the deep cartilage regions of central femur and tibia at the earliest time points ΔR_1 could be considered to be zero in the limits of the reproducibility of dGEMRIC [3]. The amount of contrast agent and the speed of the transport vary considerably between different regions, with lower amounts and slower transport with more weight bearing regions, which is in agreement with previous results about the relation between loading conditions and dGEMRIC [4]. With transport only from the synovial side, a T_1 analysis of bulk cartilage regions will be influenced by cartilage thickness. If full thickness cartilage is analyzed as a single ROI, some depth-wise changes may be undetectable. We therefore suggest analyzing T_1 by dividing cartilage into two or more ROIs in depth-wise direction in future dGEMRIC studies.

REFERENCES

[1] Bashir et al., Magn Reson Med 1999;41:857-865; [2] Hawezi et al., ISMRM 2009:3963; [3] Multanen et al., Osteoarthritis Cartilage 2009;17:559-564; [4] Tiderius et al., Magn Reson Med 2004;51:286-290

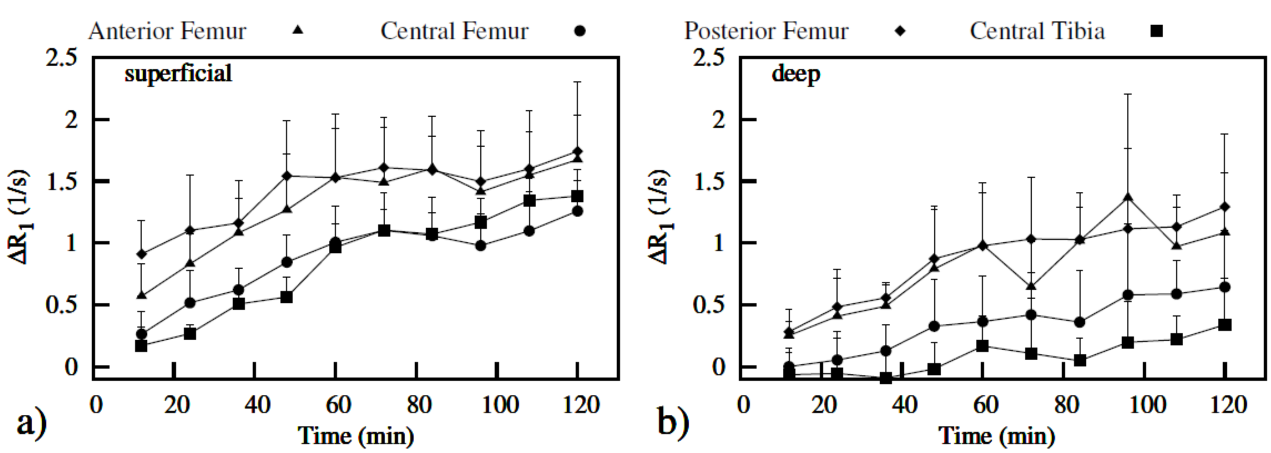

Figure 2. The change of relaxation rate (ΔR_1) representing the contrast agent concentration as a function of time after Gd-DTPA^{2-} injection in different cartilage regions for a) superficial and b) deep regions.