In vivo transport of Gd-DTPA^{2-} after intravenous and intra-articular injection

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INTRODUCTION

Delayed gadolinium enhanced MRI of cartilage (dGEMRIC) is used to assess GAG content in articular cartilage [1]. When applied in vitro, the concentration of the equilibrating Gd-DTPA^{2-} bath is precisely known allowing the estimation of absolute contrast agent concentration. For in vivo applications, the transport of Gd-DTPA^{2-} into articular cartilage is not fully understood [2]. Typically Gd-DTPA^{2-} is administrated intravenously, but the concentration actually present in the synovial fluid is very difficult to determine, limiting the technique to relative measures. The transport of Gd-DTPA^{2-} to articular cartilage in vivo has not been adequately studied. The aim of the current study was to investigate the effect of transport route by comparing dGEMRIC after intravenous and intra-articular administration.

METHODS

Six patients, with knee pain and scheduled for knee arthroscopy were recruited for this study. First, T_1 relaxation time without any contrast agent was measured. Sunsequently, double dose (0.2 mmol/kg) of Gd-DTPA^{2-} (Magnevist, Schering, Germany) was injected intravenously. After injection, the patients walked for approximately 10 minutes, and the T_1 measurement was repeated 90 minutes after injection. Two weeks later, the patients returned for intra-articular injection of 2.5 mM Gd-DTPA^{2-} solution, the concentration typically used in MR arthrography. The joint was flexed without loading for ten minutes after injection, and T_1 was measured once more 90 minutes after the injection.

All T_1 measurements were performed using a clinical 3T scanner (Siemens Skyra, Siemens Healthcare, Erlangen, Germany) with 15ch transmit/receive knee coil. T_1 was measured using IR-FSE sequence (TR 4060 ms, TE 11 ms, eight TI's between 50 and 3900 ms, FOV 12 cm, matrix 256x256, yielding in-plane resolution of 0.47 mm, slice thickness 3 mm). A sagittal slice was positioned to cover the center part of lateral femoral condyle.

T_1 relaxation times for all the three time points were calculated using an in-house Matlab application. The change in relaxation rate for the both administration methods were calculated using the formula: $\Delta R_1 = (1/T_{1Gd} - 1/T_{1pre})$, where T_{1pre} and T_{1Gd} are the T_1 relaxation times before and after the Gd-DTPA^{2-} injection, respectively.

Three regions of interest (ROI) were manually segmented: the central, weight bearing area of femoral cartilage, and regions anterior and posterior to that (Figure 1a). The regions were further divided into 50% deep and 50% superficial sub-ROIs. Mean relaxation times and relaxation rate changes were calculated for each ROI. Wilcoxon signed rank test was used to examine the difference between the administration methods.

RESULTS

The results are presented in Table 1. For superficial regions, there were significant differences between intravenous and intra-articular administration at all regions. Representative images of one patient are shown in Figures 1b) - 1d).For bulk (full thickness) region, differences were significant for all regions except for posterior femur. For deep regions, there were no significant differences.

DISCUSSION

The present results suggest that the transport of Gd-DTPA^{2-} into articular cartilage is more complete after intravenous injection. This may be due to longer exposure to contrast agent concentration. The solution is assumed to distribute evenly into exctracellular water after injection, and total amount of Gd-DTPA^{2-} injected intravenously is considerably higher. While the effective equilibrating concentration between the intra-articular and intravenous setup may be different, the lack of significant differences in deep cartilage suggests that most of the contrast agent enters cartilage from the synovial fluid also after intravenous injection, supporting recent study [3]. In the current study, T_1 was measured only for a single time point. Further studies, systematically investigating different timings after Gd-DTPA^{2-} administration, are warranted to determine the dynamics of Gd transport more accurately.

REFERENCES

[1] Bashir et al, Magn Reson Med, 36:665, 1996. [2] Bashir et al,. Radiology, 205:551, 1997. [3] Hawezi et al., J Magn Reson Imaging, doi: 10.1002/jmri.22750; 2011.

Figure 1. a) Segmented regions of interest. b)-d) T1 relaxation time (ms) of single patient b) before, c) 90min after intravenous injection, and d) 90 min after intra-articular injection.

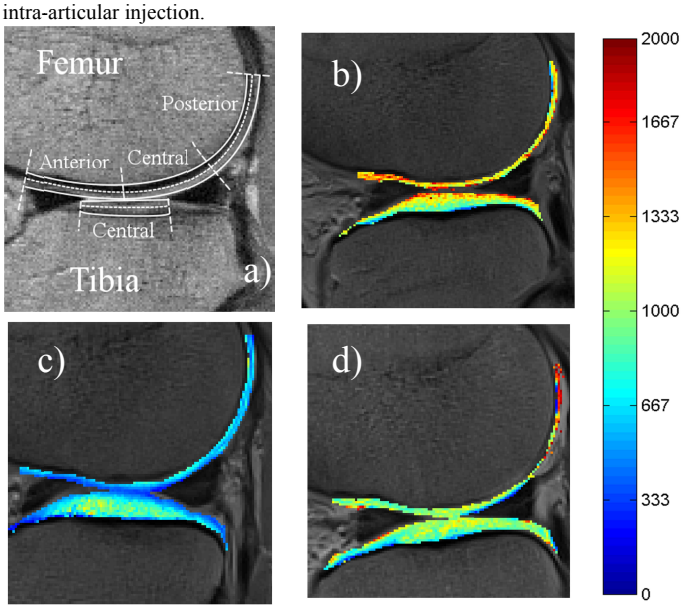

Table 1. Mean and SD values for ΔR1 after intravenous and intra-articular Gd-DTPA administration, and p-values for their difference (Wilcoxon signed rank test).

		intravenous		intra-articular		
		mean	SD	mean	SD	p-value
Femur	bulk anterior	1.040	0.100	0.616	0.267	0.015*
	bulk central	0.901	0.304	0.581	0.165	0.041*
	bulk posterior	1.111	0.388	0.649	0.335	0.132
	superficial anterior	1.427	0.226	0.721	0.241	0.002**
	superficial central	1.257	0.384	0.731	0.191	0.004**
	superficial posterior	1.127	0.299	0.643	0.292	0.026*
	deep anterior	0.769	0.115	0.567	0.350	0.065
	deep central	0.645	0.264	0.501	0.229	0.589
	deep posterior	1.179	0.683	0.660	0.403	0.240
Tibia	bulk tibia	0.659	0.361	0.308	0.104	0.009**
	superficial tibia	1.041	0.374	0.513	0.183	0.009**
	deep tibia	0.190	0.289	0.003	0.183	0.485