dGEMRIC for Evaluation of Reparative Cartilage after Autologous Chondrocytes Implantation

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Synopsis

Evaluation of glycosaminoglycan (GAG) concentration in reparative cartilage after autologous chondrocyte implantation (ACI) was performed with delayed gadolinium-enhanced MR imaging of cartilage (dGEMRIC). R1 relaxation rate measurements were made before and 2 hours after intravenous administration of Gd-DTPA^{2-}. No correlation could be found between the GAG concentration of reparative cartilage evaluated by post-contrast imaging and that evaluated by High Performance Liquid Chromatography (HPLC). However, the GAG concentration of reparative cartilage evaluated by the difference between R1 before and after contrast administration is correlated with that evaluated by HPLC. Both pre-contrast and post-contrast images are indispensable for evaluation of the GAG concentration of reparative cartilage after ACI with dGEMRIC.

Introduction

In recent years, ACI has become a widely used technique for treating full-depth articular cartilage defects, and various groups have reported good to excellent results in clinical follow up. However, the histological appearance of the reparative cartilage has not been adequately documented in the literature, because only invasive techniques such as biopsy were used to evaluate it. A noninvasive technique for evaluating the detail of reparative cartilage has been needed. Recently, an MRI technique called dGEMRIC has been developed as a noninvasive method for monitoring GAG concentration, which is critical for the mechanical support function of cartilage[1)]. This method is based on the theory that both GAG and Gd-DTPA^{2-} are negatively charged, causing Gd-DTPA^{2-} to distribute in cartilage inversely to the concentration of GAG. The aim of this study is to use dGEMRIC to evaluate the relative GAG concentration of reparative cartilage after ACI.

Methods

Nine knees of nine patients (6 males and 3 females), on which ACI of the femoral condyle was performed, were studied 6 to 36 months postoperatively. The average age for the nine patients was 24.0±8.4 (15-35) years, and the average size of the defect was 2.9±0.8 (1.7-3.9) cm2. dGEMRIC was carried out according to the protocol described by Burstein et al2). MR imaging was performed with a 1.5T magnet before and 2 hours after intravenous administration of Gd-DTPA^{2-}. R1 (R1=1/T1) relaxation rate measurements were made with an inversion recovery sequence (TR 1800 ms, TE 28 ms, TI 50, 100, 200, 400, 800, 1600 ms, FOV 150×150mm, Slice thickness 3.0mm, Matrix 512×512, TSE factor 6). The Gd-DTPA^{2-} concentration in tissue is represented by ΔR1, that is, the difference between R1 before and after contrast administration. GAG concentration was estimated from Gd-DTPA^{2-} penetration into the cartilage. A second arthroscopy was performed about 12 months after the ACI, and biopsies were taken from the center of reparative cartilage. The concentration of chondroitin sulfate (major content of GAG) in reparative cartilage obtained from the biopsy was evaluated with HPLC.

Results

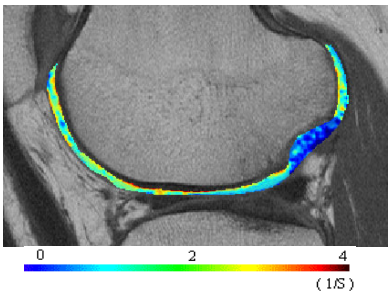
The pre-contrast and post-contrast R1 maps of cartilage are shown below (Figure 1, 2). The average pre-contrast R1 of the reparative cartilage was significantly higher than that of the native cartilage ($p<0.05$), whereas there was no significant difference between post-contrast R1 of the reparative cartilage and of the native cartilage (Table 1). The average ΔR1 of the reparative cartilage was significantly higher than that of the native cartilage ($p<0.05$), indicating that the GAG concentration of the reparative cartilage was lower than that of the native cartilage. The average chondroitin sulfate concentration of the reparative cartilage, obtained from the biopsy, was also significantly lower than that of the native cartilage ($p<0.05$) (Table 2).

Discussion

The original protocol for this method[2)], which estimates GAG concentration only from post-contrast T1, could not be applied to the reparative cartilage because pre-contrast T1 of reparative cartilage is not the same as that of normal cartilage. To monitor the GAG concentration of reparative cartilage after ACI, both pre-contrast and post-contrast images are necessary for evaluating the concentration of Gd-DTPA^{2-} penetration into cartilage.

References

1) A. Bashir, et al, Radiology. 1997, 205:551-8
2) D. Burstein et al, Magn. Reson. Med. 2001, 45:36-41



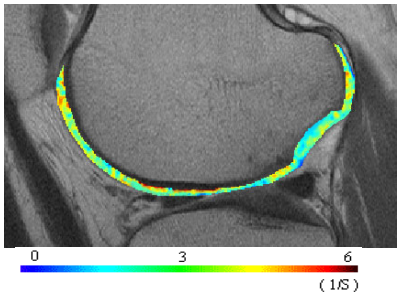


Figure 1(left): Pre-contrast *R*1 map of cartilage.
Figure 2(rt): Post-contrast *R*1 map of cartilage.

	pre-contrast		post-contrast	
	normal	reparative	normal	reparative
Case1	0.88	0.79	2.78	3.12
Case2	0.96	0.68	2.68	2.59
Case3	0.88	0.67	2.73	3.01
Case4	0.91	0.74	2.63	2.58
Case5	0.90	0.67	2.78	2.95
Case6	1.14	0.87	3.26	3.77
Case7	1.02	0.81	3.08	3.28
Case8	0.96	0.69	2.53	2.38
Case9	1.13	0.89	2.74	2.93
ave.	0.98±0.10*	0.76±0.08*	2.80±0.21**	2.96±0.40**

* P<0.05 **No significance

	ΔR1		CS concentration	
	normal	reparative	normal	reparative
Case1	1.90	2.33		131
Case2	1.72	1.91		162
Case3	1.85	2.34	238	153
Case4	1.72	1.84		160
Case5	1.88	2.28	187	156
Case6	2.12	2.90		116
Case7	2.06	2.47		132
Case8	1.57	1.69	211	145
Case9	1.61	2.04	191	137
ave.	1.83±0.18*	2.20±0.35*	207±20.2**	143±14.7**

* P<0.05 ** P<0.05

Table 1(left): Pre-contrast and post-contrast *R*1 value of normal and reparative cartilage (1/S).
Table 2(rt): Δ*R*1 value of normal and reparative cartilage (1/S), and chondroitin sulfate concentration of reparative cartilage which obtained from the biopsy (nmol/mg).