MRI Study of the Repair Tissue Following ACI in the Defect of the Human Cartilage Specimens

Z. Majdisova[1,2], P. Szomolanyi[1,2], V. Juras[1,2], and S. Trattnig[1]

[1]Department of Radiology, MR Centre - Highfield MR, Vienna, Austria, [2]Department of Imaging Methods, Institute of Measurement Science, Slovak Academy of Sciences, Bratislava, Slovakia

Purpose/Introduction: Articular cartilage injury can result in degeneration of the entire joint. If cartilage pathology is localised in early state, an operative reconstruction of cartilage can be done using tissue engineering techniques [1].The goal of our study was to investigate the in vivo regenerative ability of human chondrocytes in human cartilage by using MRI. An Autologous Chondrocyte Implantation (ACI) procedure was applied to treat focal defect in cartilagous samples in a model environment under the skin of nude mice. ACI procedure has the potential to produce the hyaline-like tissue. Magnetic resonance T1, T2 and diffusion measurements are able to assess chemical composition and morphology of cartilage and to evaluate the maturation of the repair tissue [2]. We observed global T1precontrast, T1postcontrast ($\Delta R1 = R1post - R1pre$; $R1=1/T1$), T2, and ADC (Apparent Diffusion Coefficient) values for normal cartilage and repair tissue.

Subjects and Methods: A partial thickness chondral defect was induced in the middle of each cartilage-bone human specimen. Isolated viable chondrocyte cells were treated with enzymes and then cultured with growth medium. Specimen defects were covered with human periosteum and completely filled with cell suspension. Such discs were implanted subcutaneously on the back of nude mice, with the bone side facing the body. The first set of discs was explanted from this environment after five weeks and the second set was explanted after eight weeks. MRI studies of both groups were performed on the 3 Tesla MEDSPEC whole body scanner (Bruker, Ettlingen, Germany), while using a microimaging gradient system and a 35 mm inner diameter resonator. T1-weighted images were acquired using an inversion recovery sequence with the following parameters: repetition time TR of 4000 ms; and inversion times TI of 15, 30, 60, 160, 400, and 2000 ms. T2-weighted, multi-slice, multi-echo measurements were carried out. Six series of images with constant TR of 4000 ms; and six different echo times TE of 15, 30, 45, 60, 75, and 90 ms were acquired. Diffusion-weighted sequences were applied with five different diffusion gradient strengths (5, 80, 120, 155, 180 mT/m). Timing parameters included TR of 4000 ms, TE of 35.2 ms, and a large delta of 16.26 ms. T1, T2, and ADC maps were calculated from series of the particular weighted images by using nonlinear least-squares curve fitting on a pixel-by-pixel basis. After MR measurements, specimens were histologically analyzed.

Results: Five-week T1 values (Tab.1) are similar for repair tissue and normal cartilage. Eight-week T1 values for repair tissue decreased and are lower than that for normal cartilage. After contrast enhancement ($Gd\text{-}DTPA^{2-}$), the intensity of normal cartilage on the T1 map (Fig.1) is nearly constant in the whole volume, but higher than the intensity of repair tissue volume, which is also nearly constant. Global T2 values (Tab.1) of the defect filling are higher than global T2 values of the surrounding normal tissue in both groups. An internal laminar appearance of repair tissue is not visible. Intensity on the ADC map (Fig.2) across the normal cartilage layers is lower than the intensity of the repair tissue. Pseudocolor T2 map (Fig.3) shows an anisotropy of the repair tissue.

	T1pre [ms]		**T1post [ms]**		**relative ΔR1**	**T2 [ms]**		**ADC [x10^{-4} mm^2/s]**	
	RT	*N*	*RT*	*N*	($\Delta R1_{RT}$/ $\Delta R1_N$)	*RT*	*N*	*RT*	*N*
5 w	562 ± 66	579 ± 69	191 ± 31	300 ± 31	2,15	99 ± 32	37 ± 10	13,7 ± 0,5	8,5 ± 0,5
8 w	515 ± 41	551 ± 59	142 ± 6	209 ± 17	1,71	126 ± 21	41 ± 4	11,6 ± 2,2	8,5 ± 0,5

Table 1 Global T1precontrast, T2 postcontrast and ADC values for repair tissue (RT) and normal cartilage (N) at five and eight weeks

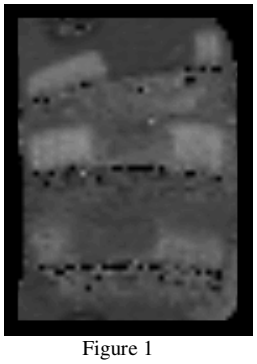

Figure 1

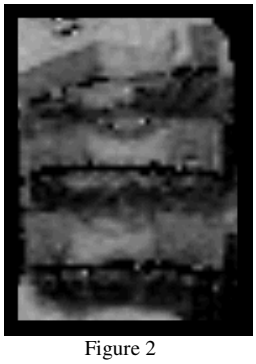

Figure 2

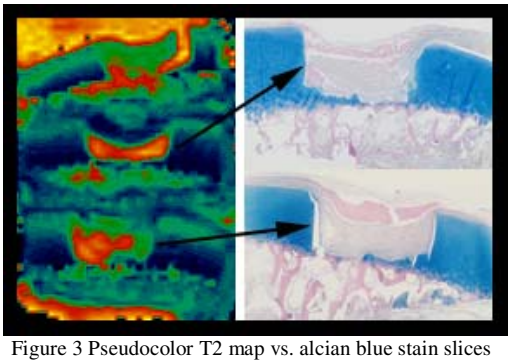

Figure 3 Pseudocolor T2 map vs. alcian blue stain slices

Discussion/Conclusions: The relative ΔR1 was lower after eight weeks than that after five weeks. In another study [3], autors found a significant correlation between relative ΔR1 and relative proteoglycans (PGs) concentration. In case of our specimens it means, that lower relative ΔR1 after longer maturation relates to higher amount of PGs in repair tissue. ADC increasing detects cartilaginous tissue from which some components have been removed [4]. We can deduce that the decrease in ADC values after the eight-week maturation reflects an improvement in tissue quality and growth of cartilage matrix components. A zonal variation in T2 values, like that in normal hyaline cartilage, should be present in repair tissue when there is a collagen network organization.
An increase in collagen staining and in PG staining was observed after the eight-week maturation, which is indicative of more cartilage-specific matrix components in the repair tissue. We can conclude that chondrocyte cells contribute to the repair response and MR imaging is suitable for evaluation of reparative cartilage after ACI.

References

1. Nesic D, et al. Cartilage tissue engineering for degenerative joint disease. Adv Drug Deliv Rev 2006;58(2):300-322.
2. Trattnig S, et al. MR imaging of osteochondral grafts and autologous chondrocyte implantation. Eur Radiol 2007;17(1):103-118.
3. Watanabe A, Wada Y, Obata T, et al. Delayed gadolinium-enhanced MR to determine glycosaminoglycan concentration in reparative cartilage after autologous chondrocyte implantation: Preliminary results. Radiology 2006;239(1):201-208.
4. Mlynarik V, et al. Investigation of apparent diffusion constant as an indicator of early degenerative disease in articular cartilage. JMRI 2003;17(4):440-444.