Quantitative 11.7 T MRI and EPIC-µCT Assessment of Cartilage Repair in a Rabbit Glenohumeral Joint Model following Microfracture and Autologous Matrix Induced Chondrogenesis

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Target Audience: Clinicians and researchers investigating cartilage regeneration will find this information useful as it correlates cartilage repair of tissue following MFX and AMIC treatments with \(T_1p\) and \(T_2\) measurements.

Introduction: Microfracture (MFX) tissue stimulation is a first-line surgical treatment for cartilage defects [1]. Autologous matrix induced chondrogenesis (AMIC) is also under investigation for the repair of cartilage defects which combines MFX with a collagen membrane [2]. Here we present a comparison of X-ray and MR based imaging methods to compare the effectiveness of the MFX and AMIC treatments. MRI maps of \(T_1\) and \(T_2\) relaxation times are highly correlated with the proteoglycan (PG) and collagenous changes that occur in cartilage regeneration [3-4], while EPIC (Equilibrium Partitioning of an Ionic Contrast-agent)-µCT provides complementary data for cartilage morphology and PG content distribution [5-6]. To our knowledge, MRI and EPIC-µCT have not been used together to assess cartilage regeneration following MFX and AMIC. The purpose of the current study is to examine the regenerative potential of AMIC treatment in comparison to MFX in an in vivo rabbit glenohumeral joint repair model using \(T_1p\) and \(T_2\) and EPIC-µCT.

Methods: Fifteen adult New Zealand white rabbits (4-5 kg) randomized into 3 treatment groups, underwent unilateral shoulder surgery under IACUC approval. Full-thickness cartilage defects (6 mm diameter) were created on the left shoulder and treated with MFX alone, MFX augmented with a collagen I/III scaffold (AMIC), or left untreated (surgical control (SC)). Contralateral shoulders (intact) served as unjured controls. Rabbits were sacrificed at 8-9 months after surgery. MRI: Immediately after sacrifice, cartilage plugs (6 mm diameter) were harvested from the surgical and intact joints, and imaged using a vertical 54 mm diameter clear bore Bruker DRX-11.7 T AVANCE macro-imaging system. The data were acquired with an in-plane resolution of 62.5 \(\mu\)m and a slice thickness of 0.5 mm. The imaging plane was perpendicular to the \(B_0\) field in all cases. The \(T_1p\) data were acquired using a preparatory self-compensation pulse cluster followed by a FSE sequence (TE/TR: 8 ms/ 3 s, spin-lock duration: 10 - 160 ms, spin-lock strength: 100 \(\mu\)T) [7]. The \(T_2\) data were acquired using a modified CPMG sequence (TR: 10 s, TE: 6.2 - 100 ms, 16 echoes) [8]. Custom written MATLAB programs were used to calculate \(T_1p\) and \(T_2\) maps on a pixel-by-pixel basis. \(T_1p\) and \(T_2\) indices (defined as the ratio: repair tissue / normal cartilage) were calculated for each rabbit to standardize the absolute \(T_1p\) and \(T_2\) changes. The Mann-Whitney statistical test was used to compare the \(T_1p\) and \(T_2\) indices between the MFX and the AMIC groups. The significance level was set at \(p < 0.05\). EPIC-µCT: After MRI, cartilage plugs were fixed in formalin, incubated in Hexabrix contrast agent, and then scanned using a SCANCO µCT-40 scanner with a 12 \(\mu\)m resolution in all three spatial planes [6]. The scanner software was used to segment the cartilage, calculate its thickness and volume, and to create cartilage thickness maps. Repair site filling was quantified as the ratio of repair tissue volume to contralateral normal cartilage volume.

Results: Representative \(T_1p\) and \(T_2\) maps of normal cartilage (NC) and repaired tissue (RT) after MFX and AMIC are shown in Figs. 1a-d. No repaired tissue was observed in the SC group using MRI (images not shown). The \(T_1p\) index was 1.17 ± 0.08 and 1.03 ± 0.07 for MFX and AMIC groups, respectively. The \(T_2\) index was 0.84 ± 0.01 in the MFX group and 0.97 ± 0.03 in the AMIC group (Fig. 1e). Significant differences between the MF and the AMIC groups were observed for both \(T_1p\) and \(T_2\) indices (p < 0.01). Typical thickness maps for NC and RT after MFX and AMIC treatments are shown in Fig. 2. The RT volume fill grade results are provided in Table 1.

Discussion and conclusions: To the best of our knowledge, this work provides the first long-term MRI and EPIC-µCT data comparing in vivo glenohumeral joint cartilage repair following MFX and AMIC. After 9 months of healing there was a significant difference in both the \(T_1p\) and \(T_2\) indices when comparing MFX and AMIC treatments. \(T_1p\) is known to be inversely correlated with the PG content in cartilage [9]. Therefore, the lower \(T_1p\) index observed in the AMIC group relative to the MFX group indicates a higher PG content in RT following AMIC surgery. On the other hand, \(T_2\) has been demonstrated to be dependent on the integrity and concentration of collagen in cartilage [10]. The lower \(T_2\) index in the MFX group compared to the AMIC group indicates a higher fibrous tissue composition in RT after MFX treatment. Hence, our \(T_1p\) and \(T_2\) results suggest that the tissue growth observed in RT following AMIC is more biochemically similar to native hyaline cartilage. The morphological outcomes derived from EPIC-µCT show that an RT volume fill grade above 50% was seen in 4 out of 5 animals for both treatment groups. RT hypertrophy (above 100%) occurred in both groups. Thus, no superiority of AMIC over MFX could be determined on the basis of the volume filling grade results.

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