Multi-parametric MRI assessment of cartilage repair with correlation to histology

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INTRODUCTION

Several quantitative MRI techniques have been proposed for probing the macromolecular composition and structure of articular cartilage. The present study aimed to characterize the repair tissue following osteochondral defects and surgical osteochondral allograft transfer in minipigs using T_2, T_1, dGEMRIC and the diffusion coefficient (D) with reference to qualitative histology.

METHODS

The lateral trochlear facets in the knees of two immature Yucatan minipigs were operated to produce 5- or 6-mm osteochondral defects that were left empty. A third pig underwent osteochondral transfer surgery, in which an osteochondral plug was transplanted from the medial to the lateral facet and the donor site was left empty. The opposite non-operated knees served as controls. The animals were sacrificed approximately 2 months post-operatively, and both facets of the operated and control knees were removed for further MRI and histological analyses.

Samples were equilibrated in saline, followed by measurements of T_2 (multi-echo sequence with TR=3s and 11 TEs between 9-99ms) and T_1 relaxation times (saturation recovery sequence with TE=9ms and six TRs between 200-4500ms) at 8.45T and room temperature. This was followed by equilibration in 1mM Gd-DTPA^{2-} solution for a minimum of two hours, and consequent determinations of T_1 relaxation time i.e. dGEMRIC (TE=9ms, six TRs between 50-2000ms) and D (diffusion-weighted stimulated-echo sequence with TE/TR=15/1000ms, Δ=14ms, δ=2ms and four B-values between 300-1200s/mm^2). The in-plane resolution was 100µm for T_2 and dGEMRIC measurements and 200µm for T_1 and ADC maps, with a 2-mm slice thickness.

Following the MRI measurements, both facets of the operated and control knees of two pigs (one with chondral lesion and one with osteochondral transfer) were processed for safranin-O-staining of glycosaminoglycans (GAGs), H&E-staining, immunostaining for type II collagen, and polarized light microscopy (PLM) of the collagen network.

RESULTS

The spontaneous repair tissue developed into the osteochondral lesion and the empty donor site of the osteochondral transfer showed (i) low GAG levels in histology, with a parallel low dGEMRIC index, and (ii) a non-hyaline-like fibrous appearance deficient in type II collagen, with a concomitant low T_2 relaxation time (Fig. 1). The cartilage of the osteochondral transfer appeared normal both in histology and quantitative MRI as compared to control tissue, however, qualitative MRI images (data not shown) demonstrated the cartilage-graft interface and histology revealed poor integration to adjacent cartilage. Spontaneous repair tissue in the osteochondral defects showed a trend toward lower T_2 and dGEMRIC values when compared to control, while the mean values of T_1 relaxation time and D were similar to control tissue (Fig. 2).

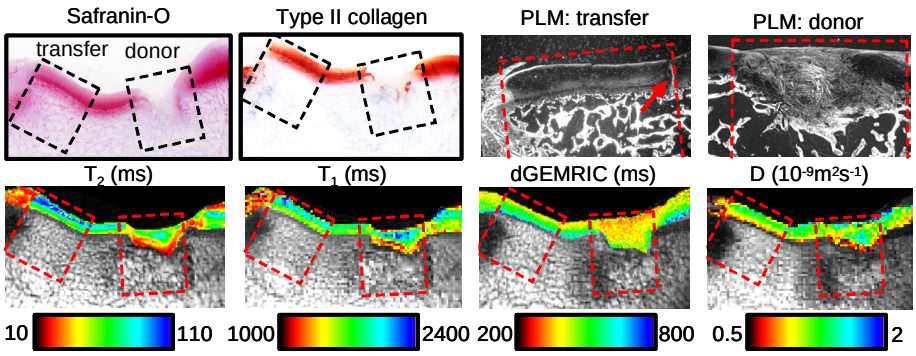

Fig.1: The donor and recipient sites of minipig trochlear facets two months after osteochondral autograft transfer surgery. The donor site reveals low GAG, type II collagen deficient fibrous repair tissue with non-hyaline-like appearance in PLM. Parallel to this, the donor site showed both low dGEMRIC values i.e. low GAG, and short T_2 relaxation times anticipated to relate to a different collagen content, organization, collagen type or fibrous nature of the repair tissue. The recipient site shows hyaline repair tissue comparable to control tissue, however, poor integration of the transfer into surrounding cartilage is evident (arrow).

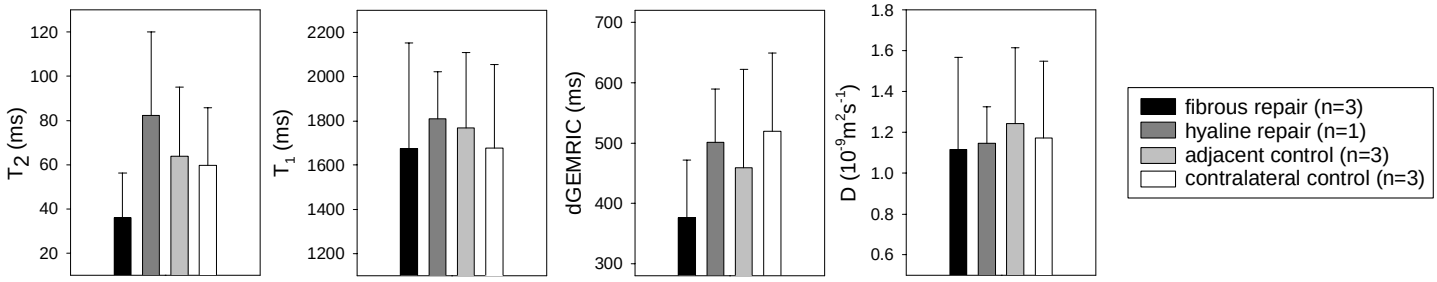

Fig. 2: MRI parameters in region-of-interests (full-thickness and width of defect/transfer) of repair and control cartilage in three minipigs. Fibrous repair tissue in the osteochondral defects show a trend toward lower T_2 and dGEMRIC values as compared to the control sites and hyaline repair in the surgical transfer site.

DISCUSSION

These preliminary results show the potential of quantitative MRI techniques to sensitively reveal the properties of repair tissue produced by different surgical procedures. dGEMRIC, developed for the indirect estimation of cartilage GAG concentration [1], reliably showed the differences in GAG between different tissues and was in agreement with histology of stained GAGs. T_2 relaxation time is sensitive to the collagen organization [2], concentration [3], and possibly also to the type of collagen or fibrous nature of tissue. While dGEMRIC and T_2 relaxation time appeared as the most sensitive MRI parameters to identify cartilage repair and fibrous repair tissue, T_1 and D also showed potential utility in differentiation of the tissues.

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