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2D and 3D MOCART scoring systems assessed by 9.4 T high-field MRI correlate with elementary and complex histological scoring systems in a translational model of osteochondral repair

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SUMMARY

Objective: To compare the 2D and 3D MOCART system obtained with 9.4 T high-field magnetic resonance imaging (MRI) for the *ex vivo* analysis of osteochondral repair in a translational model and to correlate the data with semiquantitative histological analysis.

Methods: Osteochondral samples representing all levels of repair (sheep medial femoral condyles; $n = 38$) were scanned in a 9.4 T high-field MRI. The 2D and adapted 3D MOCART systems were used for grading after point allocation to each category. Each score was correlated with corresponding reconstructions between both MOCART systems. Data were next correlated with corresponding categories of an elementary (Wakitani) and a complex (Sellers) histological scoring system as gold standards.

Results: Correlations between most 2D and 3D MOCART score categories were high, while mean total point values of 3D MOCART scores tended to be 15.8–16.1 points higher compared to the 2D MOCART scores based on a Bland–Altman analysis. "Defect fill" and "total points" of both MOCART scores correlated with corresponding categories of Wakitani and Sellers scores (all $P \leq 0.05$). "Subchondral bone plate" also correlated between 3D MOCART and Sellers scores ($P < 0.001$).

Conclusions: Most categories of the 2D and 3D MOCART systems correlate, while total scores were generally higher using the 3D MOCART system. Structural categories "total points" and "defect fill" can reliably be assessed by 9.4 T MRI evaluation using either system, "subchondral bone plate" using the 3D MOCART score. High-field MRI is valuable to objectively evaluate osteochondral repair in translational settings.

Introduction

Magnetic resonance imaging (MRI) is of great value for translational studies of osteochondral repair[1–3]. MRI is the major noninvasive tool to assess the structure of normal and osteoarthritic articular cartilage and cartilaginous repair tissues[4–10]. Particularly the development of the 2D and 3D MOCART system has greatly influenced and advanced non-destructive investigations of cartilage repair[11–14]. Clinical scanners with field strengths of 1.5 and 3.0 T (T) are also applied to assess cartilage repair in translational models *in vivo*[15,16]. Using indirect arthrography at 1.5 T *in vivo*, ovine osteochondral repair was shown to correlate with histological findings[16]. This ability to provide information on the structure of the repair tissue is of great value because histological evaluation – the main pillar to reliably and reproducibly investigate articular cartilage repair – is more time-depending[16,17]. Recently, a higher degree of spatial resolution and image quality has been achieved by greatly enhancing the field strength of the applied systems[15]. Particularly the development of high-field MRI scanners at 9.4 T allows for a detailed assessment of experimental cartilage

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repair, especially when dedicated transmit/receive coils for small samples are employed[18]. An increase in field strength directly correlates with a better signal-to-noise ratio (SNR) and higher resolutions, a main pillar when morphological MRI analysis are performed, while high-field MRI offers a vast range of possible applications[15,19–21]. Moreover, it has been already shown that semiquantitative macroscopic analysis of articular cartilage repair correlates with the 2D MOCART score using high-field MRI[18].

However, it remains unknown whether histological repair of articular cartilage defects in a large animal model correlates with the MOCART scores assessed by a high-field MRI at 9.4 T. Therefore, the first aim of this study was to compare the 2D and 3D MOCART systems obtained at 9.4 T for the *ex vivo* analysis of osteochondral repair in a sheep model. The rationale was based on the fact that the 3D MOCART score permits a more accurate and detailed assessment of cartilage repair compared with the 2D system[12,13]. Second, we tested the hypothesis that the structural data from the 2D and 3D MOCART scoring systems significantly correlate with the respective categories from semiquantitative histological analysis using the elementary Wakitani[22] and complex Sellers[23] score as gold standards.

Materials and methods

Study design

Adult Merino sheep received standardized full-thickness cartilage defects in the weight-bearing area of the medial femoral condyle of their stifle joints that were treated by Pridie drilling. After 6 months, the animals were sacrificed and the explanted osteochondral units containing the defects were scanned in a 9.4 T high-field MRI. The 2D and adapted 3D MOCART scores were applied independently by two different observers (A and B), and additionally a second time by observer A. By keeping a time interval of 19 months between both evaluations of observer A, a bias by recognition was ruled out. Data of both MOCART systems were compared between each other and correlated with the categories of a semiquantitative elementary and a complex histological scoring system (Fig. 1).

Animal experiments

Animal experiments were in accordance with the German legislation on protection of animals and the NIH Guidelines for the Care and Use of Laboratory Animals [NIH Publication 85-23, Rev. 1985] and were approved by the local governmental animal care committee (see Fig. 2). Osteochondral units were obtained from a previous study focusing on the development of a macroscopic scoring system for cartilage repair and its correlation with 9.4 T MRI[18]. The animal model has been reported before[24]. Briefly, standardized full-thickness chondral defects (4 × 8 mm, rectangular) were created in the weight-bearing area of the medial femoral condyle in each stifle joint ($n = 44$) in healthy, skeletally mature female Merino sheep ($n = 22$; age between 2 years and 4 years; average weight 70 ± 20 kg) after entering the stifle joint through a medial parapatellar approach. The articular cartilage, including the calcified cartilage, was meticulously removed down to the cement line. Based on an *ex vivo* 9.4 T MRI analysis of two medial femoral condyles of a non-operated, age-matched, healthy, skeletally mature female Merino sheep, cartilage thickness ranged between 1.0 and 1.1 mm on either edge of the created cartilage defects. No bleeding from the subchondral bone was observed. Six subchondral drill holes (diameter: 1.0 mm) were introduced into each defect using a Kirschner wire to a depth of 10 mm in a standardized manner (2 × 3 parallel drill holes per defect). Animals were allowed fully weight-bearing *post operationem*. Preoperative, osteoarthritis has been excluded by X-ray examination. Three sheep ($n = 3/22$) were excluded due to infection. After 6 months, the sheep ($n = 19/22$) were sacrificed, the medial femoral condyles were explanted ($n = 38$), fixated in 4% formalin, transferred to 70% ethanol and prepared for further investigation.

Evaluation by 2D and 3D MOCART score with 9.4 T high-field MRI

Explanted medial condyles were examined in a 9.4 T high-field MRI scanner developed for imaging of small animals (Biospec Avance III 9.4/20, Bruker Biospin, Ettlingen, Germany) as previously described[18]. A circular polarized volume coil (inner diameter: 40 mm) adapted for imaging experiments of rat brain, in receive/transmit configuration was used. A three-dimensional (3D) spoiled gradient echo (GE) sequence was chosen to perform isovolumetric scans of the osteochondral samples. Optimized imaging categories were evaluated as: repetition time (TR): 10 ms, time echo (TE): 3 ms, flip angle (FA): 10°, number of excitations (NEX): 10 and bandwidth (BW): 98,684.2 kHz. To minimize acquisition time and warming of the samples and the employed coil system, readout direction was placed in alignment with the longest dimension of the scanned objects, adapting the matrix size to completely cover the samples (typically consisting of a set of 256 × 128 × 128 voxels).

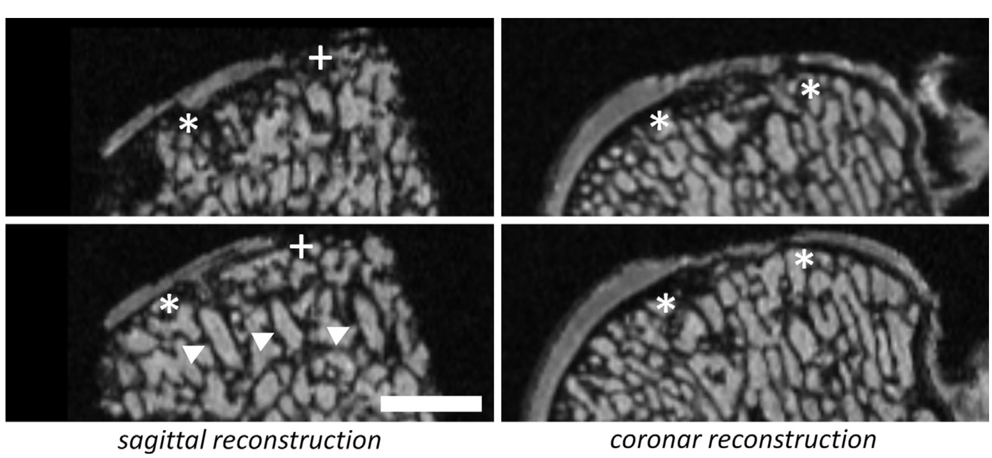

Fig. 1. Example of coronar and sagittal reconstructions of an osteochondral sample in a 9.4 T high-field MRI. Isometric voxel size (edge length = 120 μm) allows to virtually reconstruct MRI evaluations in any plane in space without losing steric information. Asterisks indicate the integration zone of the repair tissue with the adjacent normal articular cartilage, in the sagittal plane crosses demarcate artifacts caused by sample preparation, arrowheads point at drill holes. Scale bar, 4 mm.