

In vivo follow-up of spontaneous repair of osteochondral defects in rabbit's patellar groove with quantitative MRI

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Introduction:

Magnetic resonance imaging (MRI) has been widely used in clinical settings to distinguish tissues, as it provides better contrast than plain radiography or computed tomography. The success of MRI has also increased due to its non-invasive nature and usability, as the images can be taken in any plane and from any part of the body needed. Quantitative MRI techniques, particularly techniques known as delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC) and T₂-relaxation time mapping are of great importance, as they are known to provide information on the proteoglycan content and collagen integrity in the cartilage tissue, respectively [1, 2], also in the clinical environment [3]. T₁-relaxation time mapping without contrast agent provides information on tissue hydration [4]. In this study we used T₂-weighted imaging, T₁-mapping, and dGEMRIC to follow the spontaneous repair of osteochondral defect in the patellar groove of the rabbit.

Methods:

Lesions of 4 mm in diameter and 3 mm in depth were made into the patellar groove of female New Zealand rabbits (n = 6). For MRI, rabbits were anaesthetized with subcutaneous administration of Domitor (Orion Ltd, Espoo, Finland, 0.4 ml/kg) and Ketaminol (Intervet International B.V., Boxmeer, Netherlands, 0.75 ml/kg), and the body temperature of the animals was maintained close to +37°C using a heated water blanket. O₂ was supplied while the animals were in the magnet. MRI was performed in a horizontal 4.7T magnet (Magnex Scientific Ltd) interfaced to Varian UNITY INOVA console. A quadrature surface coil (Highfield Imaging, Minneapolis, MN) was used in receive/transmit mode. MRI was taken 1 week, 2, 4, and 6 months after surgery. T₁-mapping was conducted before contrast agent administration (IR-FSE sequence, TIs = 10, 150, 300, 800, 1300, 2500 ms, slice thickness = 2 mm, TR = 4 s, FOV = 30x30 mm², matrix = 256x128, echo train length = 4), and for the dGEMRIC experiment 45 minutes after an i.v. bolus of anionic contrast agent (0.4 ml/kg Gd(DTPA)²⁻, Magnevist®, Schering, Berlin, Germany) [5]. T₂-weighted anatomical images from the site were taken while waiting for the uptake of contrast agent (multislice spin echo, TE = 50 ms, slice thickness = 1 mm, TR = 3 s, FOV = 30x30 mm², matrix = 512x256). For the analysis of the repair tissue, the defect area was divided into four sections: cartilage was divided into two equally thick halves in relation to the surface, and the same was done to the defect area affecting the bone (Figure 1). Regions of interest (ROIs) were drawn for every animal according to their defect area, and kept the same at latter time points. At six months, a similar set of images was acquired for the contralateral leg serving as a control. After six months animals were euthanized and histology from the repair tissue was made. Friedman's test for K related samples were used to study the changes in the T₁-values with time within each ROI.

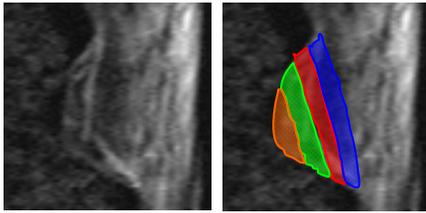


Figure 1. Example how the ROIs were selected: the blue ROI is referred to as Cartilage 1, red as Cartilage 2, green as Bone 1, and orange as Bone 2.

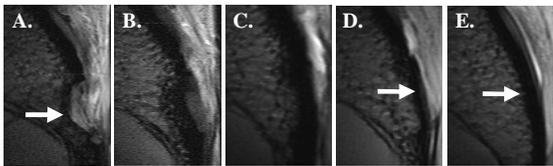


Figure 2. Sagittal T₂-weighted anatomical MR images at (A) 1 week, (B) 2 months, (C) 4 months, (D) 6 months after surgery, and (E) from the control joint. Arrows point to the lesion (A) and to the cartilage (D and E).

Results:

One week after operation, the lesions were clearly seen in the sagittal T₂-weighted anatomical images in the middle of the patellar groove. Four months after operation lesions were filled with repair tissue and seemed to be repaired. At six months an overgrowth of subchondral bone was seen in some of the animals (Figure 2). In this animal histology showed partial repair of the subchondral bone defect and the cartilage repair tissue stained with toluidine blue. The repair tissue had failed to integrate to the surrounding cartilage (Figure 3). Pre-contrast T₁-values shortened significantly (p=0.02-0.04) both for cartilage and bone repair, with cartilage repair T₁ approaching the value of intact tissue (Figure 4A). The dGEMRIC index, i.e. T₁-value after contrast agent, also showed a decreasing trend (Figure 4B).



Figure 3. Toluidine blue-stained histological section (transversal) of the repair tissue 6 months after surgery. Scale bar = 1 mm. Arrows point to the cartilage of the surrounding tissue.

Conclusion:

In this work we show the feasibility of MRI to follow the properties of repair tissue in osteochondral defects with time. With high resolution T₂-weighted anatomical imaging the changes in the size of the lesion could be easily seen, and also the overgrowth of the subchondral bone could be detected. The differences between the properties of the repair and control tissues are more detectable with pre-contrast T₁-mapping. Pre-contrast T₁-values show significant changes in the hydration status of the site of lesion while repair tissue is built, approaching the values of control tissue. dGEMRIC values are near to the control tissue already at four months, however, changes in hydration may affect contrast agent relaxivity and thus hinder the estimation of proteoglycan content.

In summary, we have used MRI successfully to follow the properties of spontaneous repair tissue of osteochondral defect in rabbit. In six months the repair tissue did not achieve the structure of intact cartilage, as shown with MRI and confirmed with histology.

Acknowledgments:

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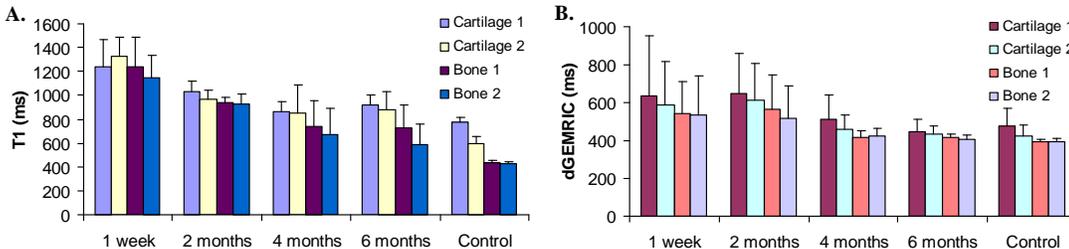


Figure 4. Pre contrast T₁-values (A) and dGEMRIC values (B) for the analyzed ROIs showing the changes in the properties of the repair tissue with time. Values are mean ± SD.

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