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## Bio-integration assessment of rat knee cartilage repair using in vivo MRI at 7T

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## Introduction

## ● Background:

High-field Magnetic Resonance systems allowing high-resolution Magnetic Resonance Imaging (HR-MRI) is a powerful research tool to visualize and examine hyaline cartilage of small joints non-invasively. Different studies have shown that qualitative assessment of degenerative joint disease, derived from MR images, was reliable (1). The capability to show pathologic changes throughout the time course of the disease from three-dimensional (3D) datasets has also been demonstrated. However, *in vivo* quantitative imaging for an accurate determination of cartilage thickness and volume is challenging due to small size of rodent joints and dedicated coils are mandatory (2-3). Surgical articular cartilage repair therapies for cartilage defects such as osteochondral autograft transfer, autologous chondrocyte implantation or matrix associated autologous cell transplantation require non-invasive technique to evaluate longitudinally the biointegration of the graft.

## ● Objectives:

The aim of this study was to follow using 7T MRI the biointegration of biomaterials colonized by mesenchymal stem cells or not after implantation in a calibrated full thickness focal lesion in the rat knee.

## Material and method

## ● Animal Protocol:

Ethics guidelines for experimental investigations in animals were strictly followed after acceptance by the animal experimentation ethics committee from Université de Lyon. The knee joint were exposed by medial parapatellar incision, and the trochlear groove were exposed by lateral dislocation of the patella. A 1.8 mm outer diameter drill was used to create osteochondral defects (1.8 - 2.0 mm). 24 adult male lewis rats (7-week-old animals) et 12 adult male nude rats underwent surgically a focal calibrated defect of their right femoral articular cartilage on the medial side according to a validated procedure:

- 12 Lewis rats underwent a parapatellar incision without defect
- 12 Lewis rats underwent a full-thickness cartilage defect
- 12 nude rats underwent a full-thickness cartilage defect treated by collagen sponges seeded with human mesenchymal stem cells.

MR exploration of rat knee was performed at D7, D14, D28 and D120. After MR exploration, 3 rats were sacrificed at each time course and knees were fixed for further histological confrontation.

## ● MRI acquisition:

A four-channel surface coil designed for the simultaneous acquisition of both knee of a rat on a Bruker 7T Biospec MR system was used (Fig.1). HR-MR images of the rat knees were obtained using a 3D FLASH sequence with the following parameters:

30° flip angle, 50 ms TR, 3.6 ms TE, 27.8 kHz receiver bandwidth.

Fat suppression was used to enhance the bone/cartilage contrast and help in the segmentation process

A FOV of 1.25 x 1.88 x 1.25 cm<sup>3</sup> per leg was acquired with a spatial resolution of 49 x 49 x 98 μm<sup>3</sup>. The scan time for the FLASH sequence was 1h22 to cover both knee.



Fig. 1: Four-channels array coil designed for simultaneously image both knees\*



Fig. 2: Sagittal HR-MR image

## Material and Method

## ● Data processing

Due to the simultaneous signal acquisition of large matrices (256x384x128 voxels) on each of the four channels, the amount of data for a single reconstruction (400Mo) was not handled by the proprietary Bruker Paravision 5.1 software; consequently, the raw datas were sent to the lab cluster where a home-made Matlab® program was used to reconstruct the volumes.

The 3D-MRI data sets (Fig. 2) were used to compute the femoral condylar groove as well as medial and lateral tibial plateaus cartilage volumes. The knee cartilage compartments were drawn directly on an interactive pen-sensitive screen. Manual contouring and pixel counting were done using AMIRA® software.

## Results

On Sham group, volumes for femoral, medial and lateral tibial cartilages (Fig. 3) were comparable between the right (9.2±0.5; 1.7±0.5; 2.5±0.4 mm<sup>3</sup> respectively) and left (9.1±0.7; 1.9±0.2; 2.1±0.6 mm<sup>3</sup> respectively) rat knee joint (Fig. 4), and these volumes are constant over the time. Segmentation of rat cartilages with defect (with or without biomaterial) was more difficult to achieve. Rats with calibrated defect on the right knee showed a lower femoral cartilage volume at D7 compared to sham group. The femoral cartilage volume of the right knee was significantly lower compared to the left knee. The growth rate of the right femoral knee is also significantly increased between the 14th and 28th day.

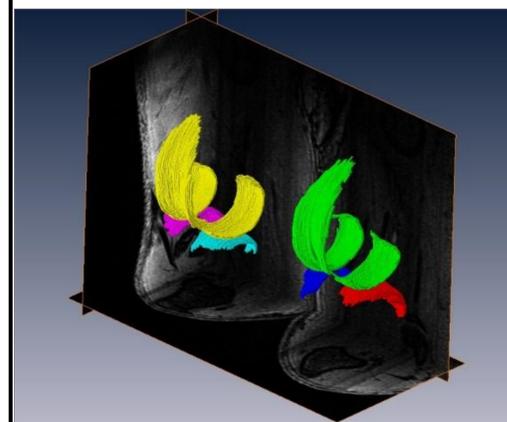


Fig. 3: Segmented cartilage compartments of both knees in control rat.

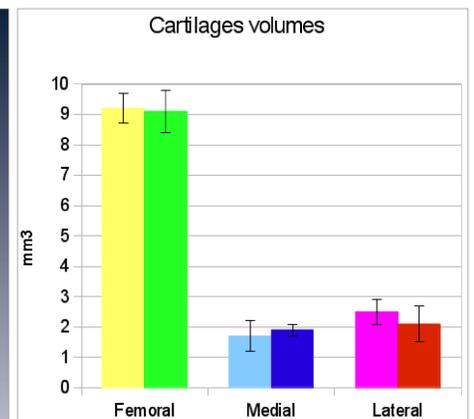


Fig. 4: volumes for femoral, medial and lateral tibial cartilages for the right and left knees.

## Conclusion

Quality of HR-MR images obtained with the developed array coils allowed the segmentation of cartilage compartments and measurements of cartilage thickness and volumes. HR-MRI allowed the follow up of cartilage to evaluate *in vivo* therapeutical responses after chondrogenic biomaterial grafting and cartilage regrowth seems to be helped by the implant but additional information is required to estimate the real biofunctionality of the result.

## References

1. J. Tessier et al., Osteoarthritis Cartilage 11:845-53 (2003).
2. R. Bolbos et al., Osteoarthritis Cartilage 15:656-65 (2007).
3. J.C. Goebel et al., Rheumatology 49:1654-1664 (2010).

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\* More information about the array coil can be find at poster # 1833 entitled : "Design of a four-channel array coil for dual high-resolution rat knee MR Imaging"