Water-selective 3D bSSFP imaging of biomaterials promoting bone repair in rats; Comparison with micro-CT

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TARGET AUDIENCE: This study would benefit to scientists studying bone tissue engineering who need a non-invasive technique to evaluate bone regeneration.

PURPOSE: Large bone defects still represent a challenge for orthopaedic and reconstructive surgeons. The conventional imaging method for bone repair is based on X-ray, because the tissue is dense and injuries and disease often change the bone density. Its disadvantage is the presence of ionizing radiations which can prevent longitudinal monitoring of bone repair in patients. On the other hand, MRI appears as a non-invasive and non-ionizing technique well suited to in vivo longitudinal evaluation of tissue repair following grafting procedure. This technique is a good candidate to visualize biomaterials degradation, because cortical bone is a tissue with well-know very short T2 relaxation time, whereas biomaterials during early period after implantation posses very long T2 [1]. However, adipose tissue, main component of the bone marrow, induce hyper-intense signal due to short T1, that could hamper the detection of the biomaterials. To visualize the biomaterial degradation, the balanced Steady-State Free Precession (bSSFP) sequence was employed as it can be used in 3D in short acquisition time and induces high SNR. However, inherent banding artifacts are problematic, but can be suppressed by using the "Sum-Of-Square" method for example [2]. To avoid exciting fat protons a frequency-selective radiofrequency pulse was inserted [3]. The objective of this project was to develop a non-invasive MR imaging method to repetitively survey integration of biomaterials in bone sites at high magnetic field.

METHODS: For orthotopic rat model (female WISTAR rats, 250g, Charles River Laboratories, France), a cylinder of 3 mm diameter and 5 mm depth was used for implantation in the femoral condyles. Longitudinal MRI was performed once every week during 5 weeks after biomaterials implantation. After each time point, rats were euthanized and bones were extracted to perform CT scans.

The MR images were acquired on a horizontal 4.7T magnet (Bruker, Biospec, Germany). The system was equipped with a 12cm gradient insert capable of 660mT/m maximum strength and 110us rise time. The rats were imaged using an emission 4-phase array surface rat brain coil. Rats were anesthetized with isoflurane (1.5% in air). The respiration rate was monitored using an air balloon place on top of the lungs (SA Instruments Inc., NY, USA). A 3D bSSFP sequence was used in which the usual radiofrequency pulse was replaced by a water frequency-selective binomial pulse (containing 5 hermite sub-pulses). Each pulse lasted 150µs, the interpulse delay was set to 200µs, the intensities of the pulses followed the schematic 1-2-3-2-1. The slice selection gradient was removed. The other sequence parameters were as follow: TE/TR=1.9/5.1ms; reception bandwidth =75kHz; FOV=30x35x25; matrix=192x192x128; 4 phase offsets; FA=27°; 2 averages; acquisition time=4min15s. The 3D images were reconstructed after a "Sum-Of-Square" of the 4 offsets.

For 3D micro-CT scans (General Electric, Milwaukee/WI, USA), the following parameters were used: 15 µm resolution; 900 X-ray radiographs, source voltage=80 kV, current=80 mA, exposure time=3000 ms.

RESULTS: The binomial pulse induced a drop in fat signal contained subcutaneously and also within the bone marrow in the entire 3D FOV. The SOS reconstruction allowed to suppress all the banding artifacts caused by inhomogeneities in the magnetic field. Thus, the biomaterials were easily detected as hyper-intense areas within the bone marrow (arrow in Figure). The degradation of the biomaterials was followed over time. While the biomaterial hyper-intense signal disappeared slowly over time, bone regeneration took place as demonstrated by the hypo-intense signal appearing within the bone defect. This degradation has been correlated with cortical bone formation observed with micro-CT (Figure). Indeed, the volume of the biomaterials measured by MRI corresponded to the volume of the bone defect.

DISCUSSION: The 3D water-selective bSSFP sequence allowed to obtain high-resolution images without ionizing radiations. The degradation of the implanted biomaterials could be followed longitudinally. The volume of the biomaterials was accurately measured.

CONCLUSION: This study confirms the efficiency of MRI to monitor integration of a biomaterial in a bone site. The 3D sequence used here can be useful in fundamental research for new biomaterial developments and in clinical to follow bone repair with biomaterials.

REFERENCES: [1] Schlaubitz S, et al. Pullulan/dextran/nHA Macroporous Composite Beads for Bone Repair in a Femoral Condyle Defect in Rats. PLoS ONE 2014;9(10):e110251. [2] Bangerter NK, et al. Analysis of multiple-acquisition SSFP. Magn Reson Med 2004;51:1038–1047. [3] Yuan J, et al. Fat–water selective excitation in balanced steady-state free precession using short spatial–spectral RF pulses. J Magn Reson 2011;208:219–224

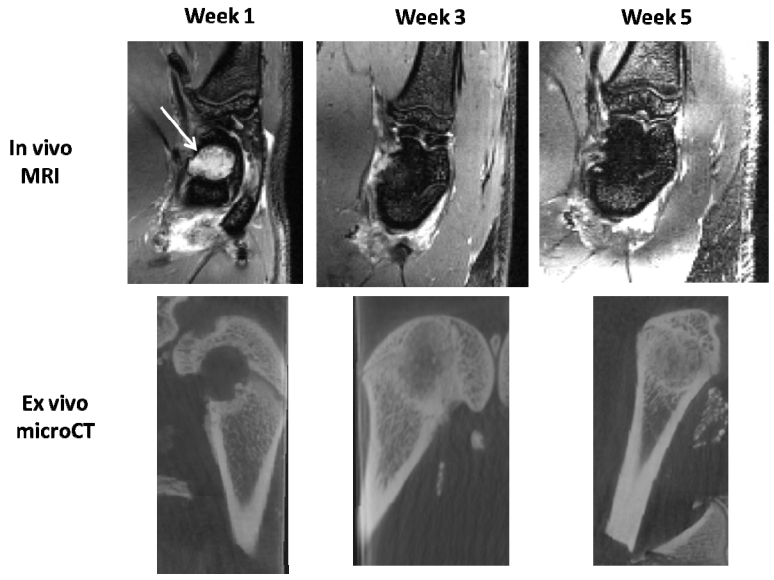

Figure : In vivo 3D MR imaging and ex vivo 3D micro-CT of a representative rat 1, 3 and 5 weeks after a biomaterial implantation into a femoral condyle bone defect.