COMPARISON OF 3T AND 14T MRI IN A RAT ANTIGEN-INDUCED ARTHRITIS MODEL.

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Introduction: The purpose of this study is to compare super paramagnetic iron oxide nanoparticle (SPION) uptake at 3T and 14T in a clinically relevant model of antigen-induced arthritis (AIA) in rat. SPION uptake is assessed after intra venous or intra-articular injection.

Methods: All particles described in this work are amino-PVA-SPIONs (SPION) provided by EPFL (Lausanne) (1).

Animal handling and model: Female Lewis rats (Janvier, France), weighing 150-175g and aged two months on reception, were used in this study. Ethical committee approval was obtained for the protocol and animals were kept in the institutions animal facility with free access to food and water. Rats with antigen-induced arthritis in the right knee were given intra-articular or intra-venous injection of 6μg-7mg (respectively) SPION on day 5 after disease induction.

Magnetic resonance imaging: Scanning used a Siemens Magnetom Trio 3T clinical scanner and the manufacturers 4cm loop coil and a Varian/Magnex 14T preclinical scanner and a homemade 2cm loop coil. The protocol at 3T consisted: 3D T1 gradient echo (VIBE) with parameters: TR/TE 14.3/5.9ms, flip angle 12°, fat suppression, isotropic resolution 0.16mm, and FOV 100mm with a total scan time of 1 hour. At 14T 3D gradient echo images were acquired with parameters: TR/TE 15/6ms, flip angle 20°, isotropic resolution 0.0625 mm, 4 averages, 1 hour scan time.

Image analysis: Images were compared with respect to visibility of SPION signal and anatomical structures and took into account relative scan time between the two fields. SNR and CNR with respect to SPION bone and muscle was calculated and is given for the intra-articular case.

Results

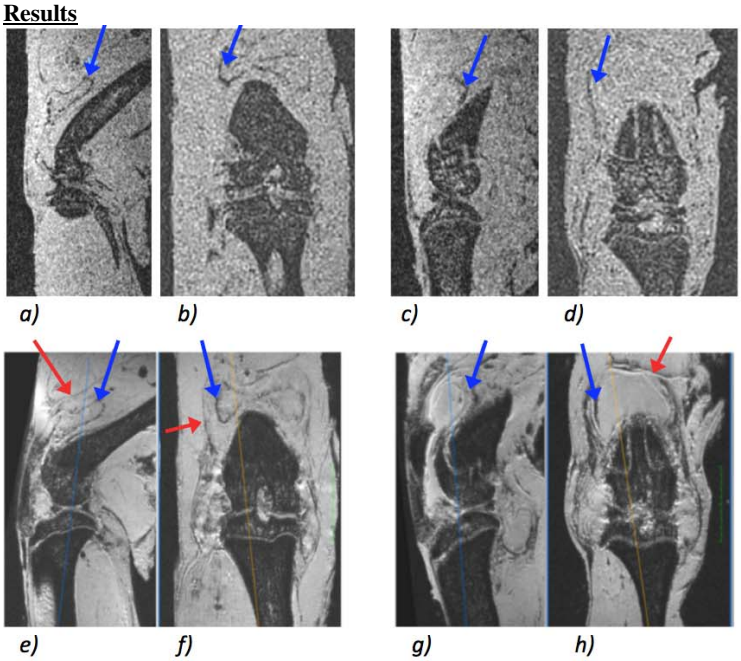

Figure 1. *3T, sagittal and coronal, 140µm resolution, SPION injected on day 5 of AIA imaging ex-vivo at 2 hours (a, b) and 5 days (c, d) after SPION injection (n=4 iv). 14T, sagittal and coronal, 62.5µm resolution, corresponding images (e-f). SPION shown around the synovial lining indicated by blue arrows and the red arrows indicate structures not well visualized at 3T*

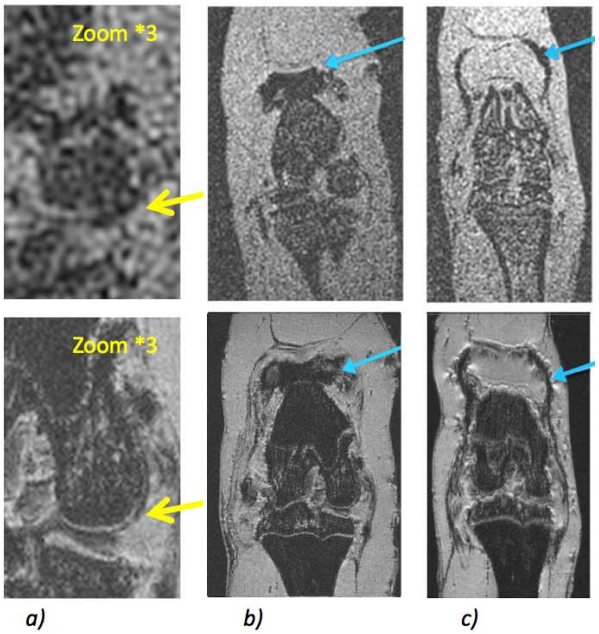

Figure 2. *Intra-articular SPION (n=12, 12ug on day 2 of AIA) MRI is 2 hrs (a, zoom x3, and b) and 5 days (c) after SPION at 3T (upper) and 14T (lower). Yellow arrows indicate improved visualization of cartilage structure at 14T. SPION is indicated by blue arrows and shows the distribution change with time at both fields.*

	SNR (mean/sd) **	CNR muscle to bone (mean/sd) ***	CNR muscle to SPION (mean/sd) *
3T	10.6 /1.8	6.2 /1.6	9.2 /2.3
14T	22.6 /4.6	17.5 /2.3	18.5 /3.0

Statistically improved SNR (**$p<5x10^{-6}$) is obtained at 14T, as well as enhanced contrast with muscle and bone/SPION (***$p<5x10^{-7}$ *$p<5x10^{-5}$). SPION (amino-PVA, G1, MB4) shown as signal loss in a high-resolution image at 3T that takes 1 hour (140μm), compared to a 14T image acquired in 1 hour with 62.5μm resolution. The previously published in vivo 3T images (ISMRM, 2012) acquired in 20 minutes (lower resolution) show only presence or absence of SPION and the contour line for its localization. The ex vivo scans, at three times the in vivo scan time, give better visualization of the SPION location with respect to bone and ligaments. The further improvement in resolution and visualization of SPION, bone micro-structure, erosion, cartilage, muscle ligament and synovium structure at 14T is clearly seen (e.g. yellow arrows, fig 2a) and allows an accurate localization of the SPION in the different compartments of the knee. In particular, a clear differentiation of the synovial uptake of SPION from the bone cortex and cartilage is possible at 14T that is not feasible at 3T. Comparison with histology and no SPION AIA (n=7) confirms the signal loss is due to the presence of SPION in the synovial macrophages. At the timepoints studied, the SPION distribution is in good agreement with this robust and predictable AIA model.

Discussion and Conclusions: In a comparable scan time, the bulk magnetization gain at 14T and the use of a dedicated RF coil resulted in a net improvement of image resolution and SNR, despite the shortening of T2*, while going to higher magnetic field. 14T clearly distinguish itself when looking at the bone erosion with a hyperintense signal when compared to healthy bone. At 3T, the noise contamination as well as the reduced resolution made differentiation less clear. In contrast 3T has the added advantage of a larger coil with homogeneous signal that can be used to scan up to 3 samples at the same time. Nevertheless, both magnetic fields provided an accurate localization of the SPION particles, and with more detailed anatomical information at higher field strength.

1. Chastellain M, et al. J Colloid Interface Sci 2004; 278(2):353-360.