Towards Theranostics of Rheumatoid Arthritis: 1H/19F Imaging of Non-Steroidal Anti-Inflammatory Drugs in Hand and Wrist at 7 Tesla

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Introduction: Rheumatoid arthritis (RA) is a chronic and systemic inflammatory condition of the skeletal system that also affects adults within the prime of their work productivity. By targeting synovial tissue, cartilage and bone, RA is a debilitating condition since it significantly hinders the physical functioning and working capacity of an individual [1]. While the therapeutic armamentarium for RA is extensive, a comprehensive diagnosis of the disease (particularly knowledge of the exact location of inflammation) during early stages of disease is central for preventing and delaying further disease progression. New emerging MRI technologies to study cartilage composition include gadolinium enhanced cartilage imaging, 23Na-MRI and T2 relaxation mapping [2]. 19F-MRI has become increasingly important for small animal imaging in multiple fields of pre-clinical research including cell tracking and detection of inflammation [3]. Since 19F-containing molecules are scarce in the human body, administration of exogenous fluorine containing compounds such as non-steroidal anti-inflammatory drugs (NSAIDs) will give a background free signal in 19F MRI. This study involves the development of a double-tuned 1H/19F birdcage resonator and examines its applicability for hand and wrist 19F imaging at 7 T following topical application of the NSAID 2-[[3-(Trifluoromethyl) phenyl]amino]benzoic acid.

Methods: Electromagnetic field (EMF) simulations with CST MWS (CST AG, Darmstadt, Germany) (Fig. 1A) were performed using the right arm of the voxel model “Billie” of the Virtual Family (Fig. 1C) were performed to assess SAR (Fig 1C) and B1+ (Fig. 1D) distribution. The coil was built using a design derived from initial simulations. Extended simulations were then performed for the final coil geometry. The 8-leg high-pass birdcage has a diameter of 10 cm and a length of 16 cm, one port was tuned to 279 MHz for 19F and the other one to 297 MHz for 1H (Fig 1B). Phantom and in vivo measurements were performed on a 7 T Siemens Magnetom using a 3D gradient-echo sequence modified for 19F application. (GRE 3D TR/TE=15/1.0ms, Matrix 48x48, FOV 100x100, Slab 80mm, 16 slices 5mm, 64 averages, TA 12:20min). Proton images were acquired using a T1 weighted turbo spin-echo sequence (TSE TR/TE=400/9ms, Matrix 384x384, FOV 100x100, 16 slices 5mm, TA 1min).

Results: SAR calculations from the EMF Simulation show that the maximum 10g local SAR of 16.2W/kg (@4W stimulated power) lies well below IEC 60601-2-33 limits (Fig 1C). Simulated B1+ gives a maximum of 114μT/sqrt(kW) in the center of the voxel model (Fig 1D) and 116μT/sqrt(kW) in a phantom with a relative permittivity of ε = 78 and conductivity of σ = 0.3S/m (Fig 1E). The measured B1+ on the proton channel is 97μT/sqrt(kW) in the center of a cylindrical phantom with similar properties as used in the EMF-Simulation (Fig 1F). Figure 2 shows first in vivo images acquired with the present dual-tunable 1H/19F birdcage at 7 T. Twenty minutes prior to imaging, the wrist of the volunteer received a 10g topical application of a cream containing the active compound 2-[[3-(Trifluoromethyl) phenyl]amino]benzoic acid at a concentration of 1mmol/l. Fig 2A shows the original 19F GRE image and Fig 2B the masked and threshold filtered image of the same slice. Fig 2C shows the overlay of a T1W TSE proton image with the filtered 19F image (red). The dotted line in the reference image (Fig 2D) depicts the position of the transversal slice in Fig 2A-C.

Discussion and Conclusions: The preliminary in vivo images acquired by the double-tuned 1H/19F birdcage resonator demonstrate the feasibility of hand- and wrist-imaging at 7 T. While the diagnostic quality of the acquired proton images still needs to be assessed in patients with inflammatory rheumatoid disease of the hands and wrist, first 19F images of fluorine-containing NSAIDs such as 2-[[3-(Trifluoromethyl) phenyl]amino]benzoic acid are encouraging, and point towards the prospect of applying 19F-MRI and NSAID therapy to the field of theranostics, for visualizing and measuring the concentration of the therapeutically-active compound reaching the inflammatory site in RA patients.