Eight channel Tx/Rx RF coil array for $^{1}H/^{19}F$ MR of the Human Knee and Fluorinated Drugs at 7.0 T

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Target audience: For MR imaging researchers, scientists and radiologists interested in RF coil technology, non-invasive *in vivo* drug tracking and theranostics at 7.0 T.

Purpose: The virtual absence of fluorine (^{19}F) in biological tissues encourages the use of ^{19}F MR for *in vivo* tracking and quantification of fluorine containing exogenous agents. However, the sensitivity limit for ^{19}F detection constitutes an impediment for translational research and clinical applications of *in vivo* ^{19}F MR [1], illustrated by the limited number of reports referring to ^{19}F MR in humans [2]. Realizing these limitations and the intrinsic sensitivity gain at higher magnetic field strengths, it is appealing to pursue *in vivo* ^{19}F MR at UHF strengths ($B_0 \geq 7.0$ T). This work proposes a modular, double-tuned $^{1}H/^{19}F$ eight channel Tx/Rx RF coil array tailored for knee imaging to examine the feasibility of human $^{1}H/^{19}F$ MR at 7.0 T. The suitability of the proposed approach for ^{19}F MR, following topical application of an ointment containing flufenamic acid (FA), a ^{19}F-containing non-steroidal anti-inflammatory drug, is demonstrated.

Methods: The RF coil consists of three modules (**Figure 1a**): a posterior module with two ^{1}H loop elements (size: (18.0 × 9.5) cm^2) and two identical anterior modules, each with two ^{19}F and one ^{1}H loop elements (size: (5.0 × 5.0) cm^2). The modules fit each other and accommodate an average sized knee (**Figure 1b**). Decoupling between adjacent elements was achieved by a common conductor with a sharing decoupling capacitor. The elements of the anterior modules were arranged into a triangle to facilitate decoupling of nearby elements [3]. The Electromagnetic field (EMF) and specific absorption rate (SAR) simulations were computed using SEMCAD X (SPEAG, Zurich, Switzerland) with the human voxel model "Duke" (IT'IS, Zurich, Switzerland). B_1^+ phase shimming was performed based on the EMF simulation data using MATLAB (MathWorks, Natick, Massachusetts, USA); the mean phase within a ROI in the knee of each channel was compensated in a way that all channels were in phase for a constructive interference. MR experiments were conducted using a 7.0 T whole-body scanner (Siemens Healthcare, Erlangen, Germany). ^{19}F single voxel spectroscopy (SVS) using the SPECIAL technique [4] was performed to determine T_1 and T_2 relaxation times for two concentrations of FA (47 and 101 mmol/L) contained in NMR tubes. ^{19}F signal-to-dose relationship was determined for increasing amounts of FA (15.3 to 76.5 µmol) by increasing the voxel size of SVS placed around the NMR tube of 101 mmol/L sample. ^{1}H GRE (TR = 10 ms, TE = 2.7 ms, spatial resolution = (0.8 × 0.8 × 5.0) mm^3, scan time = 10.8 s) and ^{19}F GRE images (TR = 90 ms, TE = 1.3 ms, spatial resolution = (1.5 × 1.5 × 5.0) mm^3, scan time = 3.06 min) were performed on knee following topical application of FA.

Results: At ^{19}F and ^{1}H frequencies, the reflection coefficients (S_{ii}) of each channel were below -26 dB. The transmission coefficients (S_{ij}) were lower than -14 dB (**Figure 1c-d**). The Q_L/Q_U was found to be below 0.5 for all channels. 10 g averaged SAR evaluation showed a maximum local SAR of 0.65 W/Kg for the ^{1}H channels and 1.76 W/kg for ^{19}F channels for the calculated B_1^+ shimming phase settings and 1 W of input power. The RF power used for *in vivo* studies was adjusted to stay within the SAR limits specified by the IEC guidelines [5]. To determine the reproducibility of the ^{19}F SVS signal, ten acquisitions were performed using a calibrated reference transmitter voltage (**Figure 2a**). It yielded a mean signal intensity of 3.94 ± 0.04 (a. u.), which translated into a signal variation of 1%. The slope of the signal-to-dose curve shows a relationship of 0.05 arbitrary signal per µmol FA with a linear regression coefficient of 0.99 (**Figure 2b**). T_1 and T_2 relaxation times changed with different concentrations of FA. For 101 mmol/L FA, it was found that T_1 = 673 ms and T_2 = 31 ms, and for 47 mmol/L FA, T_1 = 616 ms and T_2 = 26 ms. The proposed RF coil supported ^{1}H GRE imaging providing uniform signal and contrast across the patella by applying the phase settings derived from the B_1^+ shimming procedure (**Figure 2c**). The topically applied FA ointment was well depicted in ^{19}F GRE (**Figure 2d**). The overlay of ^{19}F image (red) and ^{1}H anatomical image (gray scale) provides visualization of the FA ointment at the site of application (**Figure 2e**).

Discussion: The sensitivity of the proposed RF coil array and its use at UHF enabled ^{19}F imaging following epicutaneous administration of FA ointment to the human knee with an in-plane spatial resolution of (1.5 × 1.5) mm^2 in a total scan time of three minutes. This setup is very well suited for translational human studies and for clinical applications. T_1 and T_2 relaxation times were found to change as a function of FA concentration. Therefore, T_1 and T_2 mapping techniques can be considered as tools for investigating the profile of ^{19}F containing compounds along with drug quantification.

Conclusion: The proposed RF coil contributes to the technological basis for the clinical assessment of biodistribution and bioavailability of ^{19}F drugs. The results underscore that the challenges of ^{19}F MR in humans can be offset by using tailored RF coil hardware. The benefits of such improvements would be in positive alignment with the needs of explorations that are designed to examine the potential of ^{19}F MR to trace and quantify ^{19}F contained drugs.

References: [1] Chen, J., et al., WIREs Nanomed Nanobiotechnol, 2010; [2] Ahrens, E.T., et al., MRM, 2014; [3] Graessl, A., et al., MRM, 2014; [4] Mekle, R., et al., MRM, 2009; [5] IEC Guidelines, Edition: 3.0. PP. 36-40, 2010.

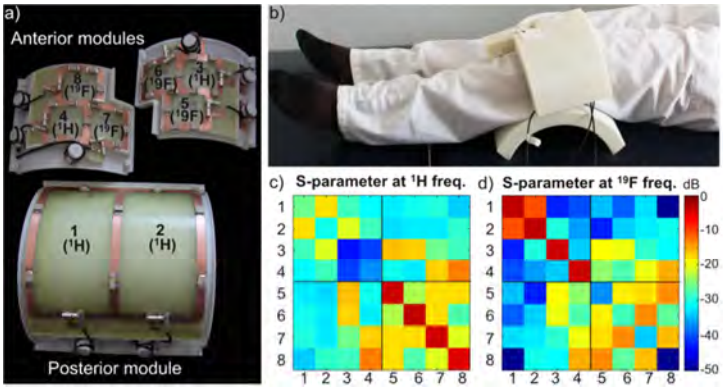

Figure 2: a) Photograph of the proposed RF coil with the top casing being removed, showing the numbering of the elements (1-8) and nuclei identification ($^{1}H/^{19}F$). **b)** The RF coil positioned on a volunteer. S-parameters matrix of an exemplary subject **c)** at ^{1}H frequency and **d)** at ^{19}F frequency. Please note: elements 1-4 are tuned to ^{1}H frequency and 5-8 to ^{19}F frequency

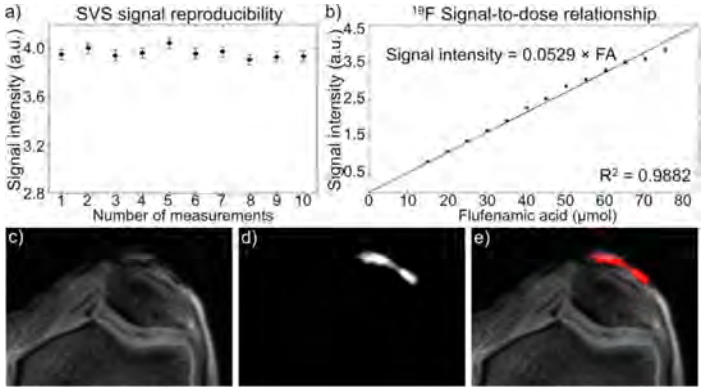

Figure 1: a) Ten consecutive measurements for determination of SVS signal reproducibility. **b)** Signal-to-dose relationship curve of FA. Axial view of **c)** high resolution ^{1}H GRE image ((0.8 × 0.8 × 5.0) mm^3, matrix 256 × 256), **d)** corresponding threshold filtered ^{19}F GRE image of topically applied FA ((1.5 × 1.5 × 5.0) mm^3, matrix 128 × 128) and **e)** the overlay of the ^{1}H (grey scale) and ^{19}F (red)