Multinuclear (^{19}F + ^{1}H) MRI at 3T using an internal probe

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Audience: MR Interventionalists interested in monitoring therapeutic delivery of fluorinated drugs and cells.

Purpose: Fluorine (^{19}F) MRI combined with anatomic proton (^{1}H) MRI provides an effective method for tracking therapeutically labeled cells post-delivery[1] or fluorinated chemotherapeutics. Conventionally, surface and/or volume radiofrequency coils have been utilized for ^{19}F/^{1}H MRI, but internal probes can yield higher local signal-to-noise ratios (SNR)[2,3]. Preliminary results from a 3T intravascular (IV) MRI probe designed for interchangeable ^{1}H and ^{19}F use have been previously reported[4]. Here, the signal-to-noise ratio (SNR) of the probe was studied, ^{19}F MRI of a chemotherapeutic drug (5-fluorouracil: 5-FU, $C_4H_3FN_2O_2$, 50mg/mL) was investigated, and multinuclear MRI of prototype perfluorooctyl bromide (PFOB)-labeled microcapsules was performed in tissue samples *ex vivo* and in a rabbit thigh *in vivo*.

Methods: Experiments were conducted on a Siemens 3T (Tim Trio) system. A multinuclear IVMRI probe was designed using a 2.2mm outer-diameter 3T loopless antenna[5] with a 40mm resonant whip. The whip length was the same at ^{19}F/^{1}H frequencies (123,116MHz)[3], affording interchangeable operation (Fig. 1). The performance of the internal probe was compared with a conventional ^{19}F surface coil by measuring the SNR in a test tube of trifluoro-acetic acid (TFA). The sensitivity of the IVMRI probe for 5-FU was performed by imaging serial dilutions, i.e., 25mg/mL (1:2) and 5mg/mL (1:10) dilutions. Microcapsules were produced using a modified alginate encapsulation method, with the addition of 12% (v/v) PFOB[1] and used for *ex vivo* and *in vivo* studies. *Ex vivo* studies were performed by inserting the IVMRI probe in the brachiocephalic trunk of an excised pig heart immersed in 3.5g/L saline, after injection of PFOB-impregnated microcapsules in the vessel adventitia. The IVMRI probe was inserted percutaneously in an anesthetized New Zealand White rabbit and the probe was alternately used for ^{1}H and ^{19}F MRI (Fig. 1) to detect percutaneously injected PFOB microcapsules. The proton and fluorine images were overlaid to form a composite image. MRI was followed by cone beam CT (CBCT) imaging (Artis Zee, Siemens) to confirm the deposition of the radiopaque microcapsules.

Results: The internal probe demonstrated increased SNR with respect to the surface coil for structures deeper than 2cm from the surface. Imaging of 10 fold dilutions of5-FU was possible in two minutes, which were undetectable by a conventional surface coil. High-resolution (in-plane, up to 0.2mm ^{1}H, 0.8mm ^{19}F) MRI of PFOB capsules was possible *ex vivo*[4]. *In vivo*, anatomical detail was provided by ^{1}H MRI (Fig. 2a; 2D GRE; 0.9×0.7×6 mm^3; TR/TE 7.8/3.69 ms; FA 20°). Using ^{19}F MR spectroscopy, PFOB capsules could be detected followed by high resolution imaging(Figs. 2b, c. ^{19}F MRS: STEAM; BW 20kHz; 40 avg; vector 512; amplitude 60 V. ^{19}F MRI: 3D TruFISP; TR/TE= 12.5/6.2ms; FA =11°; voxel =2×2×5mm^3; 32 avg.). A composite overlay shows capsule injection with respect to the anatomy (Fig. 2d, magenta). The injection location was confirmed by CBCT (Fig. 2e, arrows) and by visual inspection *post mortem* (Fig. 2f).

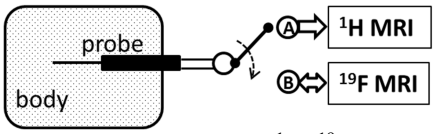

Figure 1: Schematic of a ^{1}H/ ^{19}F MRI switchable device.

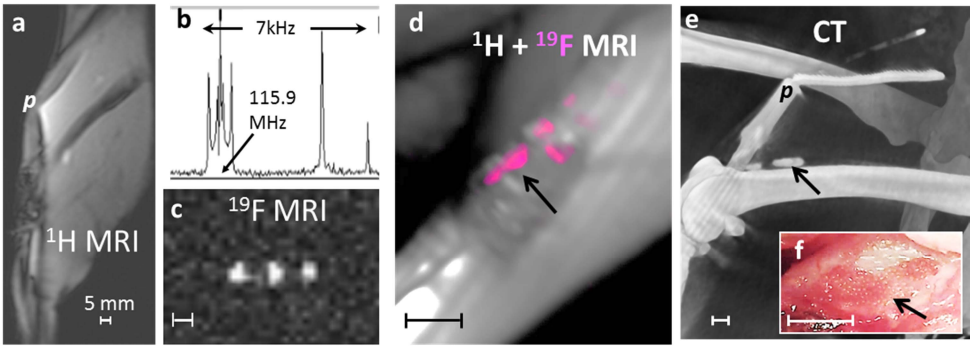

Figure 2: **(a)** *In vivo* ^{1}H MRI with internal probe *p* reveals muscle tissue. **(b)** An injection of PFOB capsules is detected by the probe via MR spectroscopy. **(c)** ^{19}F IVMRI reveals the capsules. **(d)** A composite overlay of ^{1}H and ^{19}F MRI (magenta) reveals both anatomy and capsule location (arrows), as confirmed by **(e)** CT in the same location. Probe *p* is annotated. **(f)** A photograph of the tissue reveals the injected capsules. Scale bar :5mm.

Conclusions: A single 3T IV MRI detector was used for both ^{1}H and ^{19}F detection in phantoms, *ex vivo* and *in vivo,* using three ^{19}F formulations: TFA, 5-FU, and PFOB-laden microcapsules. Such multi-nuclear IVMRI probes can be used to image/monitor ^{19}F-labeled cells or drugs in deep structures *in vivo* that would be signal starved using surface coil imaging.

Referencess: **(1)** Barnett BP, et al. Radiology. 2011;258(1):182-91 **(2)** Sathyanarayana S, et. al., JACC Card Im. 2010; 3:1158-1165. **(3)** El-Sharkawy AM et al. Med Phys 2008; 35:1995-2006. **(4)** Hegde S.S. et. al., Proc. ISMRM 22 (2014), 3698**. (5)** Ocali O, Atalar E. Magn. Reson. Med., 1997;37(1):112-118. *Support: 2011-MSCRFII-0043, Siemens Corporation*