A COMPARISON OF TWO SEQUENCES FOR SPECTRAL IMAGING OF ^{19}F-CONTAINING EMULSIONS

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Introduction. ^{19}F MRI is a powerful technique for molecular imaging, which benefits from the absence of background signal and the ability of direct detection. Many perfluorocarbon (PFC) compounds have multiple resonance peaks, which necessitates the use of spectral imaging. Standard Chemical Shift Imaging (CSI) is inherently slow because it relies on phase encoding for all spatial directions. The **aim** of this study was to compare two accelerated ^{19}F MRI sequences: Fluorine ultrafast Turbo Spectroscopic Imaging (FuTSI) and Multi Chemical Shift Selective RARE (MCSS-RARE). A major advantage of the accelerated spectral sequences is that they allow for more signal averages within the same total acquisition time and allow for summation of different ^{19}F resonances for improved SNR and detection sensitivity. The sequences were compared in phantoms containing PFOB and PFCE emulsions, as well as in liver and spleen of living mice 24h after intravenous injection of PFOB emulsion. In view of future applications, in vivo experiments were performed in an ApoE-/- mouse model to assess uptake in atherosclerotic plaque.

Previously, targeted molecular imaging of atherosclerotic plaque biomarkers with ^{19}F MRI in vivo in rabbits and ex vivo in human and mice was demonstrated [1]. Recently PFC based nanoparticles were applied in vivo for passive macrophage labeling and ^{19}F MRI has enabled detection of various inflammatory processes, including myocardial infarction, cerebral ischemia, graft rejection [2].

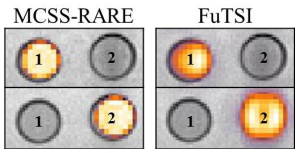

Figure 1 ^{19}F MCSS-RARE and FuTSI overlaid on ^{1}H MRI of a phantom with two vials containing emulsions of PFOB (1) and PFCE (2). Both sequences yielded two images in one acquisition.

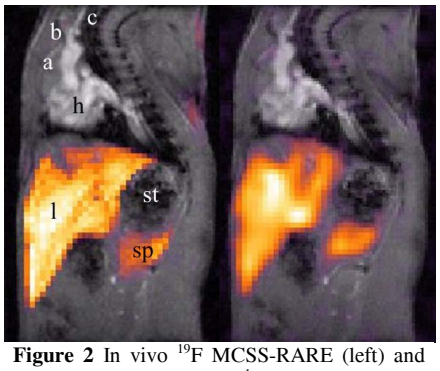

Figure 2 In vivo ^{19}F MCSS-RARE (left) and FuTSI (right) overlaid on ^{1}H MRI. a) aorta, b) brachiocephalic artery, c) right carotid, h) heart, l) liver, sp) spleen, st) stomach.

Materials & methods. FuTSI is a spectral imaging sequence based on spin echo CSI accelerated by turbo spin echo [3]. The use of a pseudo-radial trajectory with 64 spokes of length 16 resulted in a 31x31 matrix. A RARE factor of 16 was used, which means that one echo train covered one spoke. In vivo 50 averages (88min) and in phantoms 5 averages (8m50s) were acquired. MCSS-RARE is a spectrally selective turbo spin echo technique, which exploits the repetition time to do interleaved excitation of multiple spectral peaks without increasing scan time. In the phantom experiments the CF_3 peak of the PFOB and the PFCE peak were used for imaging, whereas the PFOB CF_3 and $BrCF_2$ peaks were used for in vivo imaging. The RARE factor was 64 and matrix size 64x64. In vivo 1500 averages (26.5min) and in phantoms 5 averages (9.9s) were acquired.

Five C57bl6 ApoE-/- mice received a Western-type diet for 15 weeks and developed plaque in the aortic root and arch, the brachiocephalic artery and the carotid bifurcation. Emulsions were prepared with 55% w/v perfluorooctylbromide (PFOB) and 4% egg yolk phospholipids. Mice were intravenously injected with 250µl of emulsion 24h before in vivo imaging. For the phantoms additionally a 34% w/v perfluoro-15-crown ether (PFCE) emulsion and a dilution series of PFOB emulsion were prepared. All phantom and in vivo imaging was performed with a 7T Bruker MR scanner using a dual tunable ^{19}F/^{1}H volume coil. Ex vivo imaging of the excised and flushed aortic arch was performed at 7T (5mm loop-gap coil) and 9.4T (5mm solenoid coil) using a MCSS-RARE acquisition with 22000 averages (607min).

Results and discussion. The phantom experiment (Fig 1) demonstrated the ability of both sequences to generate images of multiple PFC compounds in a single acquisition. In vivo imaging using both sequences (Fig 2) revealed PFOB uptake in liver and spleen. This is in accordance with the known blood clearance pathway for these emulsions. In the aorta and carotid arteries ^{19}F signal in vivo remained below the detection sensitivity. Ex vivo MCSS-RARE imaging with long acquisition times (Fig 3), however, did reveal ^{19}F resonances at major plaque sites, proving passive uptake of PFOB emulsion by plaque. In vivo detection sensitivity might be further improved by the use of local surface coils or coil arrays and by respiratory and heart motion synchronization.

Comparing the sequences, the shorter echo spacing of MCSS-RARE (8.9 vs 26.7ms) enabled the use of a longer echo train (64 vs. 16) and in contrast to FuTSI or traditional CSI the sequence does not need a second spatial phase encoding. Combined this makes MCSS-RARE the faster method, allowing for a higher resolution and superior SNR in a shorter total acquisition time. Concerning ^{19}F signal linearity with concentration, both sequences performed equally well with linear SNR versus PFOB concentration curves of R^2>0.95 (FuTSI) and R^2>0.98 (MCSS-RARE). Both sequences were not matched for total acquisition time or spatial resolution. Even though, it was clear that MCSS-RARE provided far superior SNR. In the phantoms, the >50x faster MCSS-RARE acquisition resulted in a 3.7x higher SNR as compared to FuTSI (SNR= 31.9 vs. 8.7). In vivo, SNR of MCSS-RARE was 2.8x higher in a third of the scan time (SNR=15 vs. 5.4), while also the acquired spatial resolution was higher for MCSS-RARE.

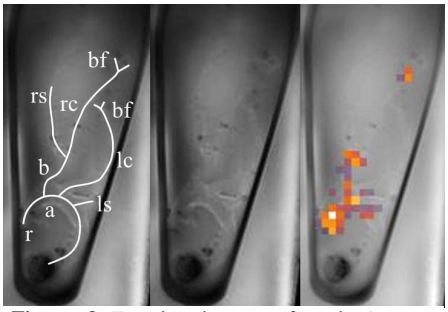

Figure 3 Ex vivo images of excised aorta: centerlines of the arteries (left), ^{1}H MRI (middle), ^{19}F MCSS-RARE overlay (right). a) aorta, b) brachiocephalic artery, lc/rc) left/right carotid, bf) carotid bifurcation, ls/rs) left/right subclavian artery, r) aortic root.

Conclusion. In this study we compared FuTSI and MCCS-RARE sequences for imaging multiple ^{19}F PFC resonances in phantoms and in a mouse model of atherosclerosis. The MCSS-RARE sequence proved superior in terms of scan time and SNR. Both sequences enabled spectral imaging of ^{19}F resonances in liver and spleen of ApoE-/- mice injected with PFOB emulsion, but failed to visualize PFOB accumulation in plaques in vivo. Ex vivo MCSS-RARE imaging, however, did reveal ^{19}F resonances at major plaque sites, providing proof for passive uptake of PFOB emulsion by plaque.

References. [1] Winter, JCMR(2010)12:62; [2] Temme, Nanomed.Nanobiotech.(2012)4:329-43; [3] Yildirim, Proc.ISMRM(2007)15:1249

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