19F Signal Amplification by Heteronuclear Polarization Transfer

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Introduction: 19F MRI is highly specific since MR-visible fluorine is not present in biological systems. However, this technique suffers from the low SNR due to the small amounts of fluorinated substances that can be administered to living organisms.
The MR signal can be increased by saturating heteronuclei using RF pulses, which leads to a transfer of longitudinal magnetization (Nuclear Overhauser Effect, NOE). In 19F MRI a maximum amplification of 53% can theoretically be achieved when saturating protons. From spectroscopic experiments with 5-FU and FBAL, an increase in 19F MR signal has previously been reported [1].

Methods: 19F signal enhancement was determined in model solutions of 2-Fluoro-2-deoxy-D-glucose (FDG) and 2,2,2-Trifluoroethanol (TFE) (Sigma-Aldrich Inc., St. Louis, MO, USA) by comparing signal-to-noise ratio (SNR) of identical experiments with and without 1H-prepulses. All measurements were made on a 3T clinical whole-body MRI scanner (Intera Quasar Dual, Philips Medical Systems B.V., Best, The Netherlands) equipped with a double resonant 19F/1H rat coil. Steady-state NOE was measured using 19F spectroscopy as well as gradient-echo and spin-echo imaging sequences with a 5ms 180° block pulse on the water proton frequency prior to each 19F excitation pulse without prolonging TR.
Novel potential carriers of contrast agents, zeolite L crystal nanocontainers [2] with pores of 7.5 Å inner diameter, were loaded with TFE and sealed with a silica coating. 10 mg of the washed and dried nanocontainers were dispersed in 5 ml of water; 1H and 19F MR RARE images were acquired. The 19F imaging parameters were: TR/TE 1300/4.5 ms, acquisition matrix 60x48, resolution 2x2 mm^2, slice thickness 10mm, number of averages 11000, delay between 1H and 19F pulse 100 ms, resulting measurement time 8 h.
Radioactive 18F-FDG is commonly used as a marker in PET scans, as it targets metabolic activity and accumulates in tumors or metabolically active muscles like the heart. Mice (C57BL/6, male) were given either 400 µl of 10 % FDG in physiological saline intravenously over two hours or else two bolus injections of 200µl of the same solution were applied retroorbitally in intervals of 60 minutes. After transcardial perfusion with formalin, the hearts were extracted, embedded in agarose gel and 1H and 19F RARE images were acquired.

Results: For both TFE and FDG, the signal increased in measurements with long TR times (> 1s). In fast gradient-echo imaging, stable signal amplification could not be observed, but was found to depend on TR and the delay of the 1H saturation pulse. Signal enhancements achieved in TFE and FDG solutions are shown in Fig. 1. Magnetization was effectively transferred from water protons; shifting the frequency of the 1H saturation pulse off the water frequency reduced the 19F MR signal. When using dimethyl sulfoxide (DMSO) as solvent, no signal amplification was observed. Compared to a fast gradient echo-image (TR/TE 5.7/2.7 ms, α=10°), 19F-RARE-images of FDG solution with steady-state NOE preparation resulted in approx. 230 % more SNR efficiency. An image of the dispersion containing TFE-filled zeolite nanocontainers is shown in Fig. 2. An image of a fixed mouse heart is shown in Fig. 3. For the first time, TFE in zeolite nanocontainers has been measured with 19F MRI and TFE seems to remain in aqueous solution in the pores.

Conclusion: 19F NMR signal was considerably increased by a steady-state NOE preparation which can be easily applied to RARE and spectroscopy measurements. Improvement can be expected by going to higher B0 field strengths and using suitable coil sizes, as the signal available from the small amounts of 19F is close to the detection limit for imaging at 3T. TFE in zeolite nanocontainers appears to be a promising probe for 19F-MRI.

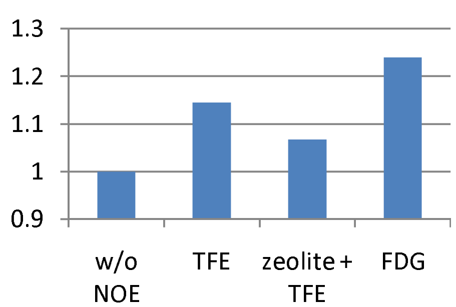

Fig 1: relative change of 19F signal by steady-state NOE preparation

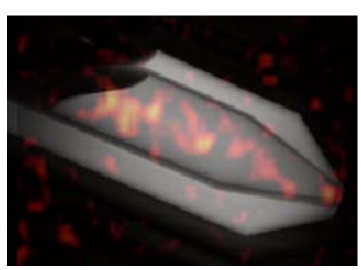

Fig. 2: 1H-image of a dispersion containing TFE-filled zeolite nano-containers (grayscale), 19F-image of TFE (red - yellow)

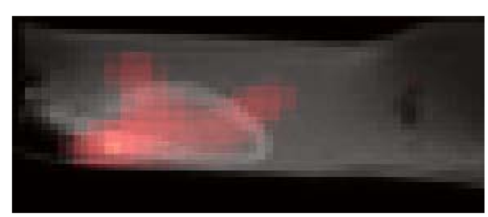

Fig 3: 1H-image of a fixed mouse heart (grayscale), 19F-image of FDG (red)

[1] JMR 1995, **108**, 155-164
[2] Chem. Mater. 2008, **20**, 5888-5893