Simultaneous $^{19}F/^{1}H$ imaging for Quantification : Calibration and Sensitivity Assessment

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Introduction

^{19}F MR imaging allows the direct quantification of fluorinated molecular probes or nanoparticles [1] for imaging of diagnostic agents or labeled drugs [2]. Despite the high signal per ^{19}F nucleus and the absence of physiological background signal, low concentrations of externally administered probes complicate quantitative ^{19}F MRI. This study presents a thorough assessment of the sensitivity and detection limits for ^{19}F signals made at 3 T. The results were reproduced with perfluoro-carbon (PFC) imaging probes and PFC nanoparticles [6] using various measurement approaches and can be compared to results [3] based on Gadolinium loaded nanoparticles and proton T_1 relaxation studies.

Materials and Methods

The imaging study was performed on a 3T clinical whole-body scanner (Achieva, Philips Medical Systems) equipped for simultaneous transmission/reception of $^{19}F/^{1}H$ signals (120 & 128 MHz) [4] using a dual-tuned volume coil (∅7cm) [5]. For simultaneous acquisition of weak ^{19}F signals from imaging probes and strong ^{1}H signals from the anatomy, the system allows individual gain settings for the ^{19}F and ^{1}H channels. The fluorine gain was set to maximum in the study. The imaging probes - perfluoro-crown-ether (PFCE; $C_{10}F_{20}O_5$) and PFCE nanoparticle emulsions (mean ∅205±2 nm) [6] - were filled in 1.5 ml tubes and mounted in a water bottle phantom. A series with different voxel volumes was recorded on pure PFCE probes with 3D gradient-echo sequences (GRE) or 3D SSFP sequences using the following parameters: matrix 176^2, FOV 100 to 250 mm (voxel volume 1-6 mm^3), 3 mm slices, TR/TE = 7.4/3.7 ms, pixel-BW 300 Hz, flip angle $\alpha = 15°$ (GRE) and $\alpha = 35°/60°$ (SSFP), scan time 24 s. In a FOV of 100 mm, but otherwise identical parameters, a series of different concentrations (2 to 20 $nM_{PFCE-NP}$) of diluted nanoparticle emulsions was imaged. In both different approaches, the detection limit was extrapolated for SNR = 5 (10 min averaging) by linear regression of signal values found in a fixed ROI. Noise was determined on the complex images using $N=\sqrt{(\sigma_{Re}^2+\sigma_{Im}^2)}$. For the spatial calibration of the coil sensitivity, a simultaneous $^{19}F/^{1}H$-GRE sequence was used: matrix 176^2, FOV 90 mm, voxel 0.5×0.5×3 mm^3, 19 slices, TR/TE = 16.8/8.4 ms, pixel-BW 90 Hz, $\alpha = 20°$.

Results and Discussion

Selected results for the signal levels for different voxel volumes are shown in Figure 1. Noise values were found to be constant for low voxel volumes. The SNR measurements for different PFCE nanoparticle concentrations are shown in Figure 2. The following detection limits (SNR = 5 in 10 minutes) were found: 0.3 μmol_{19F}/voxel (GRE), 0.14 μmol_{19F}/voxel (SSFP 35°), 0.22 μmol_{19F}/voxel (SSFP 60°) – independent from voxel size. The obtained detection limits (in terms of ^{19}F atom concentrations) are found to be equal for the different probes and methods. The signal gain, obtained by the SSFP technique, depends on the actual T_1/T_2 relaxation properties of the probe, but is similar for pure PFCE and for PFCE-loaded nanoparticles. The influence of coil loading (imperfect tuning/matching) was shown to result in a signal decrease of a factor of 2 in the worst case. Figure 3 shows an example for a calibration of the spatial sensitivity pattern based on the simultaneously recorded proton signal. With a single scaling factor, the coil offers an equal sensitivity on both ^{19}F /^{1}H frequencies. Thus, a sparse ^{19}F signal can be precisely calibrated in each location using the ^{1}H morphology picture.

Conclusion

The quantitative results show a promising ^{19}F sensitivity for in vivo targeted imaging, in particular for fluorine nanoparticles. As an example, the detection limit for the PFCE nanoparticles corresponds to 2 $pmol_{NP}$/liter in a voxel of $1cm^3$. The sensitivity results are specific for the MR system, but are expected to be typical for 3T whole-body scanners.

References

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6. *We thank G. Lanza, S. Wickline, R. Fuhrhop and S. Caruthers (St. Louis, USA) for providing samples of PFC nanoparticle emulsions.*

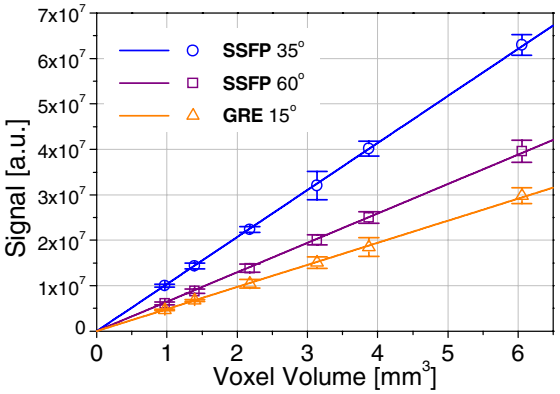

Figure 1: Extrapolation of signal strength for low probe quantities using GRE and SSFP acquisitions with variable voxel volume (Perfluoro-Crown-Ether). For ^{19}F MR of a homogeneous probe fluid, the probe quantity per voxel is directly given by the voxel volume.

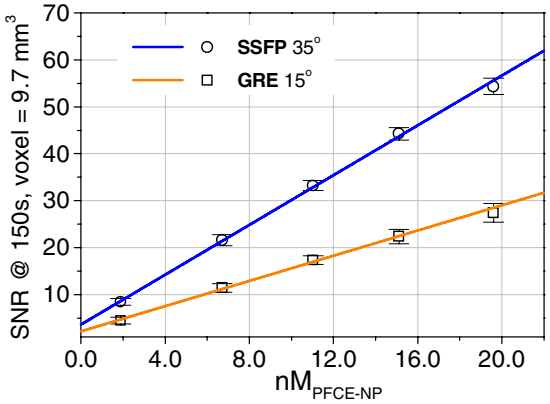

Figure 2: SNR measurement for a series of nano-molar concentrations of nanoparticles loaded with Perfluoro-Crown-Ether. The nanoparticles are readily detected at 2½ min averaging and a voxel of 0.6×0.6×3 mm^3 in gradient echo or SSFP sequences.

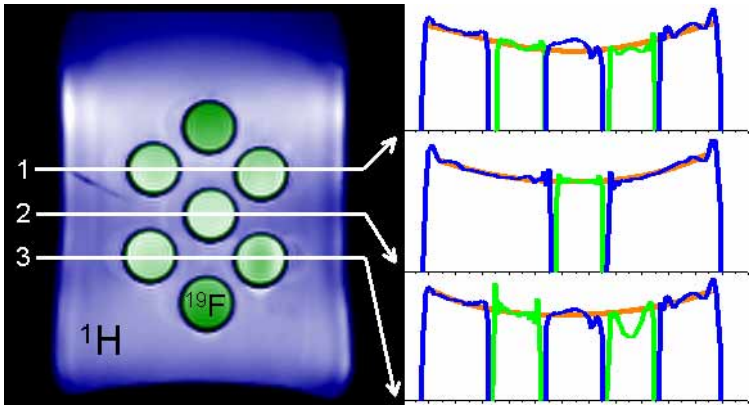

Figure 3: A slice from a simultaneous $^{19}F/^{1}H$ 3D phantom image illustrates calibration of the spatial coil sensitivity pattern based on the ^{1}H signal. Spatial patterns on the ^{19}F and ^{1}H channel are equal – as shown in 3 cross sections. A polynomial fit is added, which extrapolates the pattern recorded with the ^{1}H signal.