Dual Resolution Simultaneous $^{19}F/^{1}H$ *In Vivo* Imaging of Targeted Nanoparticles

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Introduction

^{19}F-labeled diagnostic or therapeutic agents [1], like targeted perfluorocarbon nanoparticles, offer a high potential for quantified molecular MRI [2] with excellent specificity. For anatomical co-registration of the fluorine signal, a proton image of the morphology is needed, because there is no ^{19}F signal from biological tissue and only exogenous contrast agents are visible. Simultaneous $^{19}F/^{1}H$ imaging was shown [3] to be an ideal approach to time-efficient recording of molecular information and morphology, including the possibility of motion tracking and correction [4]. An unmet need of truly simultaneous imaging approaches so far is to satisfy the substantially different requirements on sensitivity and resolution between the ^{19}F and ^{1}H acquisition, while being constrained to a single choice of spatial encoding gradient strengths. This work presents in vivo results of angiogenesis-targeted imaging of Vx-2 tumors in rabbits, demonstrating that 3D radial simultaneous acquisition offers an SNR-efficient way to acquire ^{19}F and ^{1}H images at different resolutions at the same time. The basic principle is to modify the weight applied to samples in the gridding reconstruction, such that in the ^{19}F image, the balance between SNR and resolution can be optimized *a posteriori* according to the different signal levels found for ^{19}F and ^{1}H in *in vivo* targeted imaging experiments.

Methods

The study was performed on a 3.0 T clinical whole-body scanner (Achieva, Philips Healthcare, The Netherlands) using a dual-tuned transmit/receive surface RF coil (7×12 cm) and a dual $^{19}F/^{1}H$ spectrometer system [3]. A 3D radial gradient-echo sequence with concurrent dual-frequency RF and acquisition [5] for ^{19}F and ^{1}H was used with a 3D isotropic k-space trajectory [6]. Imaging parameters were: FOV 140 mm, matrix 96^3, ^{1}H-resolution 1.46 mm^3, α_{19F}/α_{1H} = 40°/10°, pixel bandwidth 400 Hz, TR/TE = 6.8/2.4 ms, 230400 radial readouts, scanning time 26 min. For the ^{19}F image reconstruction, the radius of a sphere in *k*-space is determined, in which sampling is dense enough to satisfy the Nyquist criterion. For *k* values inside this sphere, standard k^2 weighting of samples is applied [7], whereas outside, uniform weighting is applied. A factor *n* was introduced to modify the radius of the sphere, thereby changing the range of k^2 weighting, as shown in Fig. 1.

Male New Zealand White rabbits (~2 kg) were implanted in one of their hind legs with Vx-2 adenocarcinomas (National Cancer Institute, MD), which grew to about 15 mm within 2 weeks. Imaging was performed 3h post-injection of 1.0 ml/kg of $\alpha_v\beta_3$-targeted paramagnetic NP (15-5 perfluorocrownether, 20 vol%, Gd-DTPA bis-oleate labeled). All animal care and protocols were in accordance with institutional guidelines.

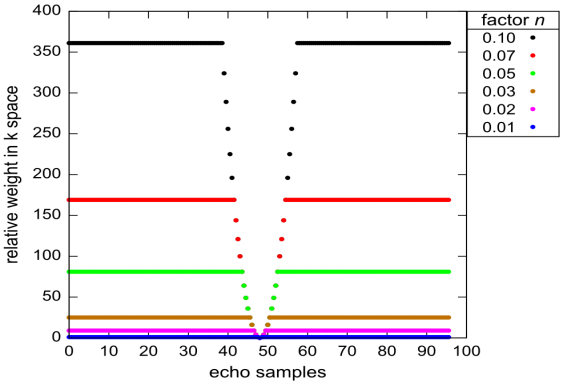

***Figure 1**: Relative weight applied to samples of a 3D radial echo readout in k-space. Smaller factors n reduce the range of k^2 weighting and thus suppress higher k values.*

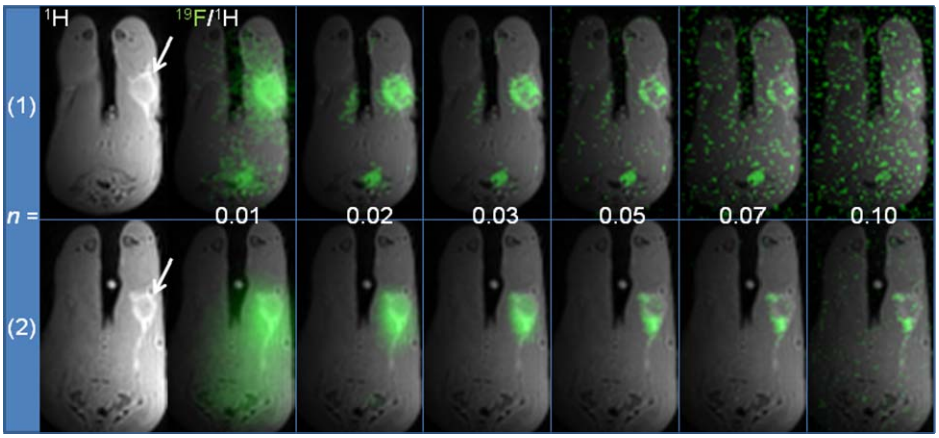

***Figure 2**: 3D radial dual-resolution ^{19}F / ^{1}H imaging with reconstruction at different resolutions for the fluorine image (k-space weighting factor n=0.01…0.10). The selected slices show the signal of angiogenesis-targeted perfluorocrownether nanoparticles (^{19}F: overlay in green) in Vx-2 tumor-bearing rabbits (hind leg). An appropriate resolution can be chosen a posteriori for a given in vivo ^{19}F signal level.*

Results and Discussion

Figure 2 shows two series of slices selected from 3D isotropic $^{19}F/^{1}H$ data measured on the hind legs of two rabbits. Gd-contrast enhancement from the NP at the target leads to bright signal around the implanted tumor in the proton image (arrows). The green overlays represent the simultaneously measured ^{19}F signal from the PFC core of the NP. The series of images correspond to reconstructions with varying factor *n*. While the proton image resolution is kept constant, a different *n* changes the fluorine image resolution in all three spatial directions. For low *n* (Figure 2 on the left) SNR is increased at the cost of resolution, whereas for larger *n*, resolution is improved at lower SNR (to the right). While the high SNR images are suitable to localize (weak) ^{19}F signal spots, the medium SNR images are well suited to extract the detailed vascularization (indicating targeted NP density) around the tumor. The optimal balance between SNR and resolution is different for the two rabbit experiments, which is caused by different ^{19}F signal levels at the tumors corresponding to different NP density at the target.

Conclusion

Variable *k*-space weighting in the reconstruction of simultaneously acquired $^{19}F/^{1}H$ 3D radial data allows optimizing the balance between SNR and resolution in the ^{19}F image retrospectively, while maintaining high resolution for the ^{1}H image for anatomical co-registration. An *a posteriori* approach for the choice of ^{19}F image resolution is powerful, because the degree of angiogenesis and corresponding signal levels are unknown before the diagnostic measurement.

References

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