Evaluation of sensitivity increase by T1 and T2 contrast agents in 19F MRI of PF15C

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Introduction:

Perfluoro-15-crown-5-ether (PF15C) emulsions have proven their applicability to face different medical questions [1,2]. It was also shown that PF15C labeled cells can be used to visualize cells *in-vitro* and *in-vivo* [3,4]. However, the relative long T_1 relaxation time constant of PF15C seems to make the usage of short repetition times for MR experiments not optimal. The T_1 constant of perfluoro-octyl-bromide (PFOB) can be shorten effectively by using fluorinated gadolinium (Gd) complexes [5]. The present study faces the question whether the T_1 shortening is advantageous for PF15C emulsions by yielding a higher SNR per unit time for Turbo Spin Echo (RARE) and Fast Gradient Echo (FLASH) sequences. Furthermore it was investigated how the addition of very small iron oxide particles (VSOPs®) added to a PF15C emulsion influences the ^{19}F signal. This question is of interest regarding double-labeling methods for combined contrast enhanced ^{1}H MRI using VSOPs and ^{19}F MRI [6].

Material and Methods:

For T_1 shortening experiments three samples were prepared with 50 µl of a 15% PF15C emulsion* to which 2.2 ml Earle`s minimum essential medium (MEM) were added and supplemented with 10% FCS, 100 U/ml penicillin and 100 µg/ml streptomycin. To obtain T_1 shortening different amounts of H_2O_2 were added.

Furthermore, in four separate samples 50 µl of a 40% PF15C customized emulsion were mixed with different amounts of VSOPs. All MR experiments were performed on a 7T Bruker Biospec Spectrometer using a homebuilt $^{1}H/^{19}F$ double-resonant Birdcage resonator. For MRI standard RARE and FLASH experiments were made with different imaging parameters.

Results:

Regarding our T_1 experiments, the highest SNR per measurement time was achieved for RARE sequences with relatively long repetition times and high RARE factors for untreated emulsion (c.f. Fig. 1B). Regarding short repetition times, RARE as well as FLASH sequences resulted in a higher SNR per measurement time for the treated emulsions compared to the untreated emulsion (c.f. Fig. 1C). For low RARE factors (4), the treated emulsions show a higher SNR per measurement time at short repetition times (100 ms / 250 ms) compared to higher repetition times (1000 ms / 2500 ms).

For the VSOP treated emulsions, a significantly higher SNR per measurement time for the untreated emulsions was observed for all RARE factors and repetition times (c.f. Fig. 1D-E). Nevertheless, for low RARE factors, the ratio of the SNRs per measurement time for the VSOP supplemented emulsions compared to the untreated emulsion increases (c.f. Fig. 1D-E). Furthermore, the FLASH experiments showed similar signal intensities for the untreated PF15C emulsions and the VSOP treated emulsions, but the signal intensities was still significantly lower than in the case of the RARE experiments yielding the best SNR per measurement time (c.f. Fig. 1F).

Discussion and Conclusion:

Our results indicate that in general it is not necessary to shorten the T_1 relaxation time constant of PF15C in order to obtain the highest SNR per measurement time. This is due to the fact that with the T_1 shortening also T_2 is reduced. In this case high RARE factors are not useful. Nevertheless, when only short acquisition windows are available (e.g. tissue movement) T_1 shortening of the PF15C emulsion increases the SNR per measurement time regarding short repetition times.

Applying VSOPs to a PF15C emulsion leads to a lower SNR per measurement time for the used sequences due to the shortened T_2 constant of the VSOP treated emulsions. For short acquisition windows, corresponding to low RARE factors, the difference in the SNR per measurement time is significantly smaller compared to the untreated emulsion.

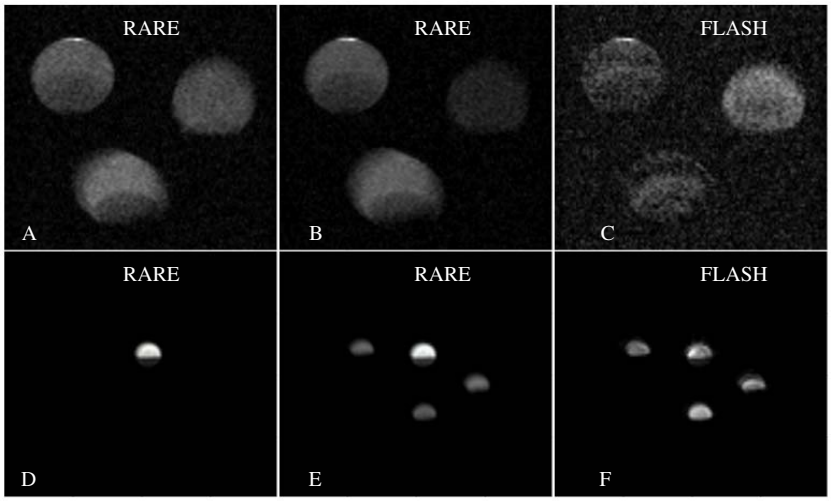

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Figure 1:

A)–C) Samples for T_1 shortening experiments (50 µl 15 % PF15C with upper left: 30 µl, upper right 340 µl 30% H_2O_2 added, lower: control). A) RARE image with TR = 500ms, RARE factor (Rf) = 8, B) RARE image with TR = 1000ms Rf = 16, C) FLASH image with TR = 10ms, TE = 3 ms.

D)-F) Samples for PF15C emulsions supplemented with VSOPs (50 µl 40% PF15C with upper left: 0.2 µmol Fe, upper middle: control, upper right: 0.05 µmol Fe and lower: 0.1 µmol Fe) D) RARE image with TR = 2500ms, Rf = 96, E) RARE image with TR = 500ms Rf = 2, F) FLASH image with TR = 400ms, TE = 3 ms.