RARE Sequence Optimization Parameters for 19F MRI studies of Labeled Neuronal Stem Cells at 11.7 T

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Target Audience

This work is useful for radiologists, physicists, engineers and biologists that are involved in ^{19}F MRI studies in molecular imaging.

Background and Purpose

^{19}F MRI is a useful technique to perform *in vivo* cell tracking non-invasively and it is gaining an important role in molecular imaging. Fluorinated compounds were recently used to label dendritic cells, T cells, hematopoietic stem cells and neuronal stem cells (NSCs). Most ^{19}F MRI studies are performed using Fast Spin Echo or RARE sequences. Usually, ^{19}F MRI sequences are not fully optimized to obtain the best performance in terms of SNR. In order to increase the sequence sensitivity, actual relaxation times (T_1, T_2) are needed to correctly set the TR and Echo Train Length (ETL) parameters. In this work a simple though innovative strategy to optimize RARE parameters for ^{19}F labeled NSCs is proposed, which is based on relaxation times estimation and optimization of TR and ETL using numerical simulations. This approach was evaluated in different biological environments.

Methods

^{19}F-MRI acquisitions were performed on Cell Sense CS-1000 (Celsense, Pittsburgh, USA) in different biological environments: 1) ^{19}F labeled NSCs: A phantom containing $3*10^6$ NSCs labeled cells fixed with 4% PFA was used. Murine NSCs were labeled using a concentration of 25 µl/ml of CS-1000 and incubated for 42h at 37°; 2) CS-1000 phantom: The phantom was built filling an NMR tube of CS-1000 embedded in gelatin; 3) Fixed brain: $3*10^5$ NSCs were injected in the right striatum of a nude mouse brain, the animal was deeply anesthetized, the brain was removed and fixed in 4% PFA. Numerical simulations were performed to assess the dynamic of the SNR in RARE sequences with and without driven equilibrium pulse (Flip Back, FB) as previously reported[1]. MRI experiments were carried out on a Biospec 11.7 Tesla (16 cm diameter, horizontal bore) preclinical scanner system (Bruker BioSpin, Ettlingen, Germany). A single loop transceiver surface coil of 20 mm or 9 mm diameter was used. In order to compare experimental SNR variations with simulated values ^{19}F MRI was performed using RARE with and without FB pulses in 3 different SNR ranges (High >90%, Medium >75%, Low >50% compared to maximum SNR). ^{19}F labeled NSCs: Matrix= 32*32 pixels; FOV= 20*20 mm2; slice thickness= 3mm; slices=1; BW=15000 Hz; TE= 8ms; TA=2m40s. In case FB ON, TR and ETL were set to 500 ms and 8 for high SNR, 1000 ms and 16 for medium SNR and 2500 ms and 32 for low SNR level. CS-1000 phantom: Matrix= 48*32 pixels; FOV= 20*20 mm^2; slice thickness= 4mm; slices=1; BW=15,000 Hz; TE= 9ms; TA=1h. In case of FB ON TRs were set to 600, 2,000, 4,500 ms (high, medium, low SNR). ETL was fixed to 8. Fixed brain: Matrix= 32*32 pixels; FOV= 19.2*19.2 mm^2; slice thickness= 3mm; slices=1; BW=15000 Hz; TE= 8ms; TA=1h. In case of activated FB TRs were set to 500, 1700, 4000 ms (high, medium, low SNR). ETL was fixed to 8. TR and ETL parameters are displayed in figure 1. For T_1 estimation a RARE with variable TR was used. The following parameters were set: TR=16000, 8000, 4000, 2000, 1000, 500, 250, 120, 60, 30 ms; TE=10 ms. For T_2 calculation a MSME sequence was used. The following parameters were set: TR=15000 ms for NSCs, 10,000ms for CS-1000 and fixed brain; 40 TE from 20 to 800 ms. The experimental SNR was considered as the figure of merit in the whole study.

Results

^{19}F labeled NSCs displayed a T_1 of 504.09 ± 43.81 ms and a T_2 of 67.60 ± 10.12 ms; CS-1000 had a T_1 of 534 ± 49 ms and a T_2 of 103 ± 5 ms; the fixed brain showed a T_1 of 488 ± 95 ms and a T_2 of 43 ± 13ms. Numerical simulation can help choosing the correct TR and ETL parameters. For ^{19}F labeled NSCs, the maximum simulated SNR is achieved with TR=800 ms and ETL=9 in case of FB OFF and TR=400 ms and ETL=5 in case of FB ON. Regarding CS-1000, the maximum simulated SNR is achieved with TR=900 ms and ETL=12 in case of FB OFF and TR=500 ms and RF=7 in case of FB ON. Considering the fixed brain, the maximum simulated SNR is achieved with TR=700 ms and ETL=6 in case of FB OFF and TR=500 ms and ETL=4 in case of FB ON. In general, for NSCs labeled with CS-1000 at 11.7 T, in case of FB OFF an average TR of 800 ms and an ETL of 9 is the best setting to obtain an high SNR. While in case of FB ON, an average TR of 500 and an ETL of 5 is the best choice to achieve an high SNR. The SNR predicted by simulations has shown a maximum error of 21% for FB OFF and 19% of FB ON compared to experimental SNR. In general a mean error of 9.8% was observed for RARE sequence with FB ON and a mean error of 9.8% in case of FB OFF. The use of FB can improve SNR up to 50%.

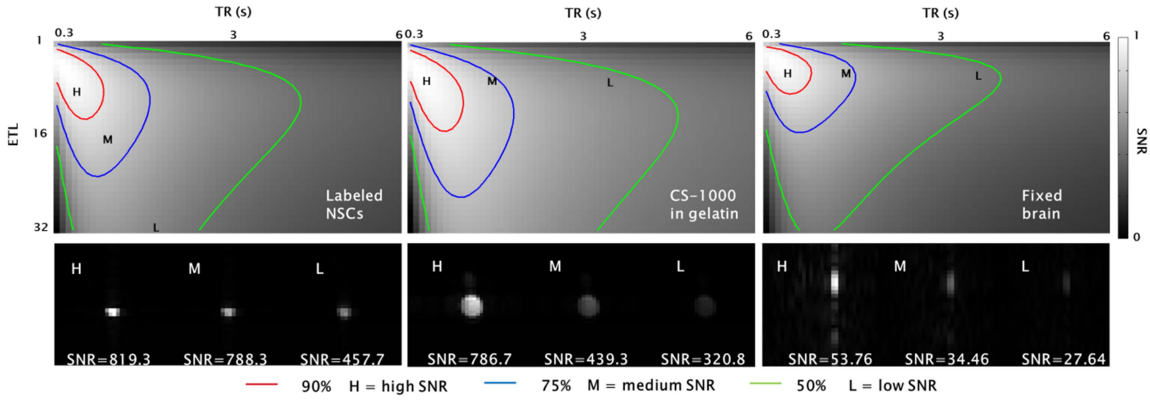

Figure 1. Upper Panels: Simulated SNR maps TR vs ETL evaluated at the actual relaxation times T_1 and T_2 with FB ON.
Lower Panels: ^{19}F MR images acquired in 3 different ranges of SNR (H, M ,L) in different biological environments. TR and ETL values are marked in the upper panels.

Discussion and Conclusion

In this work a promising method to optimize RARE sequence was validated for ^{19}F labeled NSCs. Numerical simulations were confirmed as a useful tool to choose the optimal parameters TR and ETL for a RARE sequence. The actual relaxation times were estimated and the results highlight a low variation in T_1 relaxation times (less than 10%) and an important variation of T_2 (about 50%). T_2 relaxation times are more sensitive to changes in different environments. RARE with and without driven equilibrium pulse was evaluated experimentally and in general a better performance was highlighted in RARE with FB ON. The use of driven equilibrium pulse was already suggested in a previous work[2] but a punctual parameter optimization was absent in the literature. The use of low TRs according to T_1 and T_2 can increase SNR in RARE sequence. Experimental analysis is in good agreement with simulations. In general this method can be exported to *in vivo* studies if the T_1 and T_2 are known. Further improvements are needed to evaluate the effect of different bandwidths, and a reliable method to estimate *in vivo* relaxation times should be developed and applied.

References

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