Characterization of Perfluorocarbon Relaxation Times and Optimization of Fluorine-19 MRI at 3 Tesla

Roberto Colotti[1,2], Christine Gonzales[3], Juerg Schwitter[3], and Ruud B. van Heeswijk[1,2]

[1]Department of Radiology, University Hospital (CHUV) and University of Lausanne (UNIL), Lausanne, Switzerland, [2]Center for Biomedical Imaging (CIBM), Lausanne, Switzerland, [3]Division of Cardiology and Cardiac MR Center, Department of Internal Medicine, University Hospital of Lausanne (CHUV), Lausanne, Switzerland

Introduction: Fluorine-19 (^{19}F) MRI of perfluorocarbon emulsions (PFCs) has recently been increasingly used in studies of inflammation due to its high specificity and chemical inertness [1]. One of the primary translational goals of this technique is to apply inflammation imaging in patients in a clinical setting. Since the obtained signal-to-noise ratio (SNR) per unit time is the main limiting factor of ^{19}F MRI at these lower magnetic field strengths, it is essential that ^{19}F MR pulse sequences are executed with optimal parameter settings. Such a pulse sequence parameter optimization mainly depends on the ^{19}F relaxation times, which have been demonstrated to depend on temperature [2], magnetic field strength [2] and oxygenation level [3, 4]. The goal of this study was therefore to characterize the ^{19}F relaxation times at 3T in different physiological conditions and to characterize the impact of relaxation time differences on the acquisition efficiency.

Methods: A 2% agar phantom with perfluoropolyether (PFPE; V-sense, Celsense Inc) was constructed and considered as a reference standard. All experiments were performed on a 3T clinical system (Magnetom Prisma, Siemens). A 35-mm-diameter ^{19}F volume transmit/receive coil (Rapid Biomedical) was used for ^{19}F excitation and detection. An unlocalized inversion recovery (IR) spin echo (SE) sequence with 11 geometrically increasing inversion times (TI=5 to 4000ms; TR=5s) was used to ascertain the T_1 relaxation time. An unlocalized SE sequence with geometrically increasing echo times (TE=9.3 to 350 ms; TR=5s) was used to measure the T_2 relaxation time. Adiabatic pulses were used to compensate for B_1 inhomogeneity (BIR-4 for the 90° excitation pulse, hyperbolic secants for the 180° pulses). In order to compare the PFC phantom ^{19}F relaxation times to those of PFCs taken up by immune cells, bone-marrow-derived macrophages were isolated from C57BL/6 mice and incubated with PFPE for 24h for in-vitro labeling. After washing of the cells and collection in 2ml tubes (n=2 samples), the T_1 and T_2 relaxation time were measured as described above. To determine the stability of the relaxation times over time, two-year-old *ex-vivo* livers from mice that were intravenously injected with the abovementioned PFC-incubated macrophages one day prior to euthanasia (n=5) were also scanned with the same sequences. All experiments were repeated at both room temperature (24°) and body temperature (37°). All animal studies were approved by the local animal ethics committee. The obtained relaxation times were used in Matlab (The MathWorks, Inc) in Bloch equation simulations of a turbo spin echo (TSE) pulse sequence (TE= 9ms) in order to determine the TR and echo train length (ETL) that resulted in the highest signal per unit of time (i.e. signal normalized by $\sqrt{TR \cdot ETL}$) for each physiological and temperature condition. For each condition, the acquisition efficiency η was calculated using the condition-optimized parameters (TR_{cond} and ETL_{cond}) versus the phantom-optimized parameters (TR_{phan} and ETL_{phan}) as the reference, yielding:

$$\eta = \frac{[S/\sqrt{TR \cdot ETL}]_{phan}}{[S/\sqrt{TR \cdot ETL}]_{cond}} \quad (1)$$

where S stands for the simulated signal for a given parameter set, while *phan* and *cond* indicate values calculated with phantom and the various cellular condition's relaxation times, respectively.

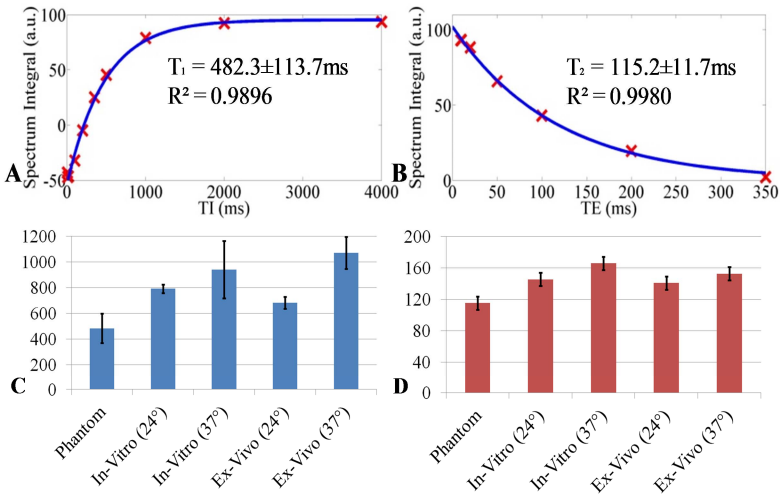

Figure 1. Fluorine-19 relaxation times. **A)** and **B)** T_1 and T_2 relaxation times for the PFC phantom. The high R^2 value for both T_1 and T_2 relaxation curves confirms the fit quality. **C)** T_1 and **D)** T_2 values in different physiological and temperature conditions. Relaxation times consistently increase in the cellular environments, and more so at the higher temperature. Bars: mean±standard deviation.

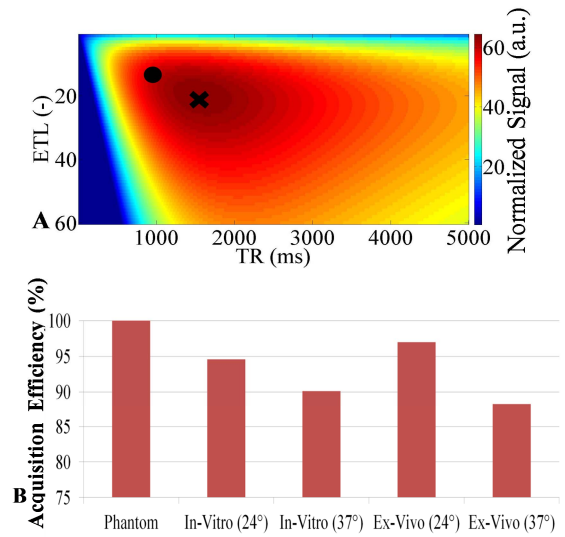

Figure 2. Results of the Bloch equation simulations. A) Normalized signal for PFC *in-vitro* at 37°. The cross indicates the maximum normalized signal for PFC *in-vitro* at 37°, while the dot indicates the normalized signal at the optimal TR and ETL obtained from the PFC phantom simulation (considered as reference). **B)** Comparison of the relative acquisition efficiency η. The loss of η is small at room temperature (<6%), both *in-vitro* and *ex-vivo*, while it is slightly larger but still moderate at physiological temperature (<12%).

Results: The PFC phantom ^{19}F relaxation times at room temperature were T_1 = 482.3 ± 113.7 ms and T_2= 115.2± 11.7 ms (Fig. 1A, B). T_1 values increased significantly with both temperature and physiological condition (41-123%, Fig.1C), while the increase of T_2 is smaller (21-43%, Fig. 1D). The PFC phantom relaxation times resulted in an optimal TR=841ms and ETL=13 in the Bloch equation simulations. A small decrease in pulse sequence acquisition efficiency η was observed at 24° for both the *in-vitro* and *ex-vivo* cellular environments (3 and 6%, respectively, Fig. 2), while a slightly larger decrease in η was observed at 37° for both cellular environments (9 and 12%, respectively).

Discussion and Conclusions: PFC relaxation times were characterized under different conditions and the acquisition efficiency of a TSE pulse sequence was evaluated for incorrectly assumed relaxation times. As expected [2], the temperature had a significant influence. However, the resulting loss of acquisition efficiency is fortunately moderate and indicates that using a TSE pulse sequence with parameters optimized for a room-temperature phantom would result in a signal loss of less than 12% in the body.

References: [1] Floegel et al., Circulation 2008 [2] Kadayakarra et al., J Magn Reson 2014 [3] Duong et al., Magn Reson Med 2000, [4] Zhong et al., PLoS ONE 2013