Rapid in vivo quantification of oxygen concentration in blood flow with a fluorine nanoparticle reporter and a novel blood enhanced saturation recovery (BESR) sequence

L. Hu[1], J. Chen[1], S. D. Caruthers[1], G. M. Lanza[1], and S. A. Wickline[1]
[1]Washington University, St. Louis, MO, United States

Introduction: Blood oxygen levels in heart chambers and major blood vessels are typically measured with invasive methods for quantification of cardiovascular disorders, e.g. shunt detection and oxygen consumption, etc. [1]. We propose that perfluorocarbon (PFC) nanoemulsion might offer a molecular imaging probe for non-invasive assessment of blood oxygenation in vivo, because ^{19}F longitudinal relaxation rate of PFC linearly correlates with local concentration of paramagnetic oxygen [2]. To optimize such applications in blood flow, we introduce a new rapid blood flow ^{19}F T1 measurement sequence, i.e. blood enhanced saturation recovery (BESR) sequence, for quantitative assessment of blood oxygenation using PFC emulsion administered intravenously and ^{19}F MRI.

Method-pulse sequence: BESR sequence has the same time efficiency as classic Look-Locker sequence [3]. Compared to Look-Locker technique, the BESR sequence (Fig.1) was implemented by: (1) replacing the typical 180° inversion RF pulse with five non-selective 90° saturation RF pulses in the same phase to achieve homogenous spin preparation in the whole body; (2) replacing the small flip angle gradient echo with 90° flip angle gradient echo, with imaging slices perpendicular to the flow direction to take advantage of time-of-flight refreshment with new sets of recovering ^{19}F spins; (3) gated with electrocardiography (ECG), at both pre-saturation and gradient echo imaging. With each repetition time, spin saturation (< 10 ms) is triggered by the first QRS complex of ECG followed by gradient crushers. Each of the following N QRS complex triggers one gradient echo at the same phase of cardiac cycle (T), i.e., corresponding to saturation recovery time TS=N*T. Due to the time-of-flight effect of the blood flow, each gradient echo is acquired from refreshed spins that are not excited by the previous imaging pulse. Thus, the BESR sequence directly measures the real ^{19}F T1 correlating with blood oxygenation.

Method-experiment: All the experiments were carried out on Varian 4.7 T small animal scanner. The pulse sequence was first tested by measuring the ^{1}H T1 of arterial blood. To confirm that BESR sequence can realize homogenous magnetization pre-preparation for blood flow all over the imaging object, two volume transmission coils, i.e., a birdcage coil (15 cm in diameter and 15 cm in length) and an actively-decoupled saddle coil (7 cm in diameter and 15 cm in length), were used for different trials; an actively-decoupled surface coil was positioned close to the ROI for signal receiving. Two Swiss Webster mice were anesthetized with isofluorine, and ^{1}H T1 measurement was carried out in carotid arteries (CA) and left ventricle (LV). For the ^{19}F imaging, Swiss Webster mice (n=3) were anesthetized with ketamine/xylazine followed by intravenous injection of 40% v/v perfluoro-15crown-5-ether (CE) emulsion (4ml/kg). ^{1}H images were first acquired to position the slices that cover both left and right ventricle. Blood ^{19}F T1 measurements were carried out when mice were breathing room air and then pure oxygen. Aforementioned saddle coil and surface coil was re-tuned to proper frequency for ^{1}H and ^{19}F imaging respectively. T1 measurement parameters: pulse sequence, BESR; TR, 4 s; TE, 2.2 ms; rf band width; 3000 Hz; N, 5; rf band width, 3000 Hz; nt, 4; in plane resolution: 1 mm * 0.5 mm; slice thickness: 2 mm; total acquisition time, 8.5 min. In order to minimize the partial volume effect, average intensity of pixels in left and right ventricle was used for T1 data fitting. According to the oxygen pressure calibration curve of CE emulsion [4], the absolute oxygen pressure can be estimated from ^{19}F T1, i.e., $PO_2 = (1/T1-0.51)/0.0031$ mmHg.

Table 1. Arterial ^{1}H T1measurement results.

Number of trial	^{1}H T1	Average heart period	Region of Interest	(N, nt)	Transmission coil
Trial 1	1.40 s	175 ms	LV	(9, 1)	Birdcage
Trial 2	1.45 s	360 ms	LV	(8, 1)	Birdcage
Trial 3	1.64 s	250 ms	LCA	(10, 1)	Saddle
Trial 4	1.61 s	250 ms	RCA	(10, 4)	Saddle
Trial 5	1.60 s	255 ms	LCA	(10, 4)	Saddle

*LV: left ventricle, LCA: left carotid artery, RCA: right carotid artery.

Results: The measured ^{1}H T1 of arterial blood (Table. 1) are consistent with previously published result (1400 to 1600 ms) [5], suggesting BESR can achieve an accurate readout of blood T1. The measured ^{19}F T1 (Fig. 2) showed that blood oxygen pressure in the left ventricle (LV) was substantially higher than that in the right ventricle (RV) (Fig. 3). Hyperoxia resulted in increased blood oxygen pressure in both LV and RV.

Discussion and Conclusion: We demonstrate the application of PFC emulsion as a blood oxygen pressure probe with use of a novel BESR pulse sequence. Compared to the traditional inversion recovery and Look-Locker sequence, the BESR sequence maintains high time-efficiency and is insensitive to B1 and B0 field inhomogeneity and pulsatile in-flow effects [6]. Because of the high blood volume in the ventricle and time of flight effect, only 8 minutes was needed to acquire all ^{19}F images with sufficiently high SNR (>5) for T1 measurement. Compared to the traditional invasive measurement using cardiac catheter, the BESR sequence may provide a simple and rapid method for non-invasive assessment blood oxygenation in vivo. In addition to ^{19}F imaging, this sequence might also be useful for other in vivo blood flow ^{1}H T1 measurement applications, including perfusion studies, temperature monitoring, and dynamic contrast enhanced MRI [7-8]. With slower heart rates, e.g. human imaging, where sampling once per cardiac cycle is too slow, the sequence could be easily modified to image more than once per cardiac cycle.

References: [1] W. Grossman., Cardiac Catheterization and Angiography, 3rd Edition; [2] R. P. Mason, el al., IJRO, Bi: 93 (1994); [3] I. Kay, et al., MRM, 22: 414 (1991); [4] L. Hu, et al., ISMRM proceeding, 2010; [5] D. L. Thomas, et al, ISMRM proceeding, 2006; [6] H. L. Margaret, el al., JMRI, 25: 1073 (2007); [7] J. Zheng, et al, JMRI, 10: 576 (1999); [8] C. L. Dumoulin, MRM, 32: 370 (1994).

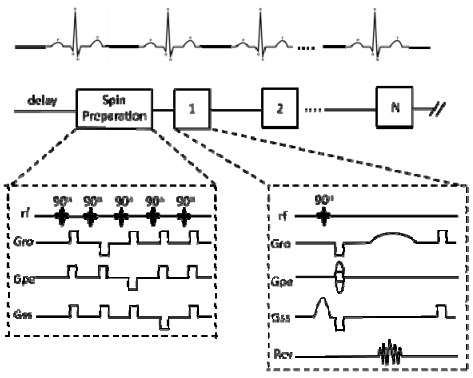

Figure 1. Scheme of the BESR sequence. Spin preparation is achieved with non-selective saturation pulses and image acquisition is realized with gradient echo.

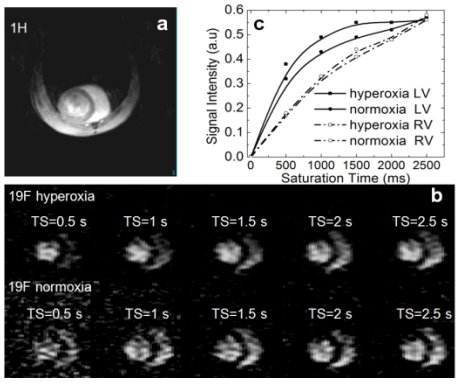

Figure 2. (a) ^{1}H image shows the location of ROI. (b) ^{19}F BESR images in hyperoxia and normoxia scenarios. (c) ^{19}F saturation recovery curve in LV and RV.

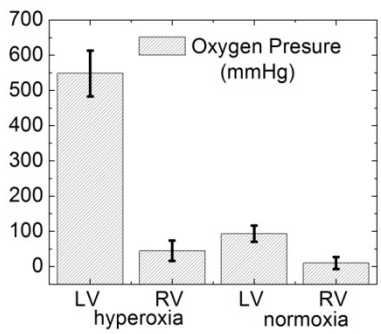

Figure 3. Blood oxygen pressure calculated from T1 of PFC emulsion.