

**Introduction**

Automated segmentation of the brain structure in MR images has been widely utilized in quantitative tissue volumetric measurement. MR images weighted by spin-lattice relaxation time constant ( $T_1$ ) are usually employed for tissue segmentation. However, the signal intensity of a  $T_1$ -weighted image is sensitive to hardware settings such as RF coil uniformity and gradient-induced eddy currents [1]. Furthermore, the segmentation algorithms used for  $T_1$ -weighted images usually rely on statistical models for a general population, but may not account for individual variation. Recently, we proposed a new brain segmentation method using quantitative  $T_1$ , named FRASIER [2]. Information on tissue fractions in each voxel can be incorporated into functional MRI (fMRI) studies for improving data interpretation. At a spatial resolution typically used in fMRI (3-4 mm), FRASIER can obtain  $T_1$  and fractional volume ( $f_v$ ) maps in every 10 seconds. In this study, we test the reproducibility of  $T_1$  and  $f_v$  mapping, and demonstrate the application of FRASIER in fMRI settings.

**Methods**

**FRASIER: Fractional Signal mapping from Inversion Recovery** (FRASIER): FRASIER is based on a recently developed fast  $T_1$  mapping method using inversion recovery Look-Locker echo-planar-imaging at a steady state (IR LL-EPI SS) [3]. Using a single-shot IR LL-EPI SS, the effective relaxation time constant ( $T_1^*$ ) can be expressed as  $1/T_1^* = 1/T_1 - \ln(\cos\alpha)/TR$ , where  $\alpha$  is a flip angle, and TR is a time gap between two consecutive EPI acquisitions of the same slice. The signal recovery during the time of duration (TD, see Fig. 1) is described as  $S(t) = M_{SS}[1 - 2\exp(-t/T_1^*)]$ . The measured voxel-wise signal during IR procedure is fitted into a three-compartment (WM, GM, and CSF) exponential recovery model:

$signal = \sum f_{s_i} \times (1 - 2\exp(-t/T_{1,i}^*))$ , where subscript  $i$  represents each tissue.  $f_v$  can be derived from the measured fractional signal ( $f_s$ ) by considering the each tissue density and the steady state signal [2]. Note that  $T_1^*$  and  $T_1$  in WM, GM, and CSF need to be determined prior to fitting. Considering individual variations in  $T_1$ ,  $T_1^*$  and  $T_1$  in WM and GM are obtained individually from the whole brain  $T_1$  histogram and  $T_1$  value in CSF was set to 4500 ms.

**MR imaging:** Nine healthy subjects were scanned using a single-shot IR LL-EPI SS sequence. The following MR imaging protocols were used: non-selective IR, TR/TE=400/13 ms,  $\alpha=16^\circ$ , matrix=64x64, bandwidth=4112Hz/voxel, 15 slices, no gap between slices, and TD=10s (Fig.1B). A series of five IR LL-EPI SS measurements were acquired in 1 min including the preparation (prep.) time of 10 s. After 20 min of fMRI experiments, another series of five IR LL-EPI SS scans were repeated to test the reproducibility of  $T_1$  and  $f_v$  mapping using FRASIER. For convenience, we referred to the first scan series as “Test”, and the latter one as “Re-test” in the following content.

**Data analysis:** A total of 10  $T_1$  and  $f_v$  maps were acquired for each subject (5 in Test and 5 in Re-test). Registration parameters were obtained by registering each IR LL-EPI SS image to the average IR LL-EPI SS images over 10 measurements and then were applied to the fitted  $T_1$  and  $f_v$  maps to correct for head motion. Voxel-wise standard deviation (SD) of  $T_1$  and of  $f_{v,GM}$  were calculated to test reproducibility of FRASIER among the i) Test scan (within the first 5 measurements), ii) Re-test scan (within the last 5), and iii) Test and Re-test scans (all 10)

**Results and Discussion**

FRASIER was incorporated into an fMRI protocol, taking 1 min each before and after the fMRI experiment. Ten  $T_1$  and  $f_v$  maps were reliably obtained from the FRASIER measurements (5 before and 5 after the fMRI scan). Figure 2 demonstrates the representative 3 slices of  $T_1$  and  $f_v$  maps in WM, GM and CSF (from 15 slices). Over five consecutive measurements, voxel-wise average SD of  $T_1$  and  $f_{v,GM}$  were 37 ms and 3.5% in Test and 40 ms and 3.7% in Re-test. Reproducibility considering both Test and Re-test was reduced (59 ms and 5.6%), as shown in Tab 1 and Fig 3., probably due to the head motion between the two FRASIER runs separated by 20 min. Note that each of the  $T_1$  and  $f_{v,GM}$  maps were measured within 10 seconds. When applying 1 min FRASIER, averaging over 5 measurements improves the signal-to-noise ratio by a factor of 2.2 times, the voxel-wise SDs of  $T_1$  and  $f_{v,GM}$  would be improved to approximately 18 ms and 1.7 %

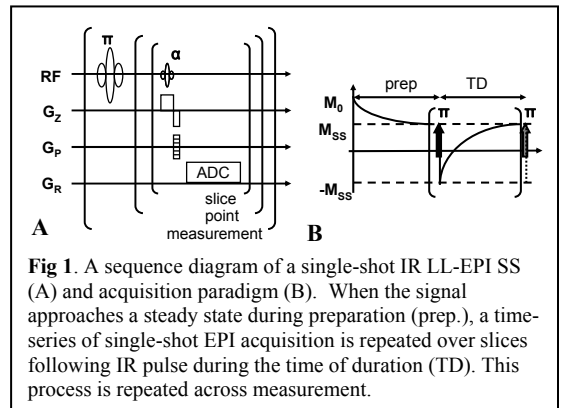
This work demonstrates that FRASIER can be used to measure  $T_1$  and  $f_v$  in the brain within 10 seconds with high reproducibility. When FRASIER sequence is incorporated into an fMRI protocol, it provides  $T_1$  and  $f_v$  maps with similar geometric distortion as fMRI images (e.g. BOLD) because the gradient-echo EPI kernel with the same configuring parameters as fMRI acquisition were used in FRASIER sequence. Therefore, additional image registration between fMRI and  $f_v$  maps is not required, while most of automated brain tissue segmentation need normalization and smoothing due to the dependence of a prior image template. This advantage would allow the proposed method to be easily used in patient populations with severe neurological disorders and age-dependent populations.

**Acknowledgements**

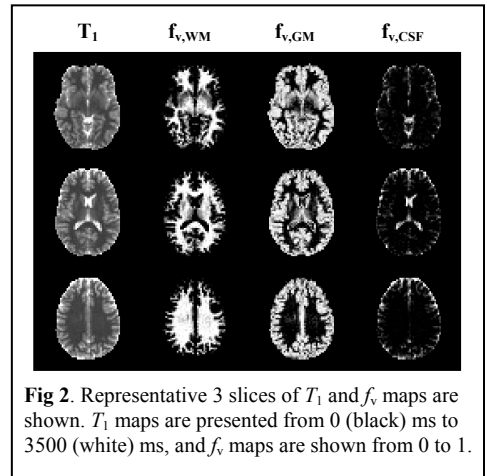
This work was supported by the Intramural Research Program of the National Institute on Drug Abuse (NIDA), National Institute of Health (NIH)

**Reference**

1. Sled et al, IEEE,1998;17(1):87-97.
2. Shin et al., ISMRM, 2009.
3. Shin et al., MRM, 2009;61(4):899-906.



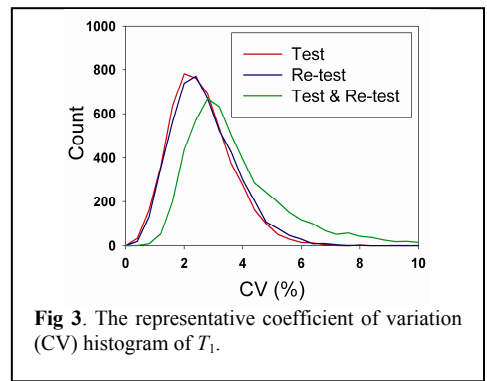
**Fig 1.** A sequence diagram of a single-shot IR LL-EPI SS (A) and acquisition paradigm (B). When the signal approaches a steady state during preparation (prep.), a time-series of single-shot EPI acquisition is repeated over slices following IR pulse during the time of duration (TD). This process is repeated across measurement.



**Fig 2.** Representative 3 slices of  $T_1$  and  $f_v$  maps are shown.  $T_1$  maps are presented from 0 (black) ms to 3500 (white) ms, and  $f_v$  maps are shown from 0 to 1.

	SD of $T_1$ (ms)	SD of $f_{v,GM}$ (%)
Test	37±8	3.5±0.3
Re-test	40±9	3.7±0.5
Test & Re-test	59±9	5.6±1.2

**Tab 1.** Voxel-wise average SDs of  $T_1$  and  $f_{v,GM}$  over 9 subjects



**Fig 3.** The representative coefficient of variation (CV) histogram of  $T_1$ .