# Monitoring Tissue Volume Fraction and $T_1$ Changes During Brain Activation Using a Look-Locker EPI Sequence

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## Introduction

Physiological and biophysical changes accompanying brain activation are critical for understanding fMRI signals and for interpreting fMRI data. VASO (vascular space occupancy) technique [1], for example, requires an understanding of the signal changes in different tissue compartments. We present here a fast imaging method based on Look-Locker echo-planar imaging (LL-EPI) sequence [2] to measure tissue volume fraction ($f_v$) and spin-lattice relaxation time ($T_1$) during brain activation. Conventional Look-Locker sequence requires additional time for a full recovery of the longitudinal magnetization for the repeated measurements. In this study, a robust steady-state method to measure $f_v$ and $T_1$ was developed, and the feasibility of measuring these parameters during brain activation was demonstrated.

## Theory

***IR LL-EPI at Steady State (IR LL-EPI$_{SS}$):*** When a train of α° pulses is applied (with a time interval $T_s$) following the first inversion pulse, the inversion recovery (IR) procedure is expressed with the equilibrium longitudinal magnetization ($M_0$), the steady-state magnetization ($M_{ss}$), and the effective spin-lattice relaxation time constant ($T_1^*$): $S(t) = \left| M_{SS} - (M_0 + M_{SS})\exp(-t/T_1^*) \right|$, where $M_{ss} = M_0\cos\alpha(1-\exp(-Ts/T_1))/(1-\cos\alpha\exp(-Ts/T_1))$, and $1/T_1^* = 1/T_1 - \ln(\cos\alpha)/Ts$ [3]. After signal intensity approaches to the steady-state $M_{ss}$, a series of inversion pulses is applied, and the signal can be expressed as: $S(t) = M_{SS}\left|1 - 2\exp(-t/T_1^*)\right|$ (Fig. 1).

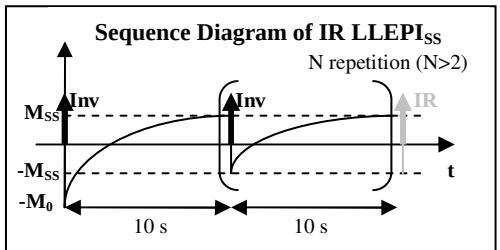


**Fig. 1**. Following the first inversion pulse, a set of LL-EPI data are acquired. When the longitudinal magnetization approaches to $M_{SS}$, a series of inversion pulses with an interval of 10 s is applied to collect a time series of LL-EPI data sets.

***$T_1$ Measurement:*** Since $Ts \ll T_1^*$, $T_1$ can be estimated from the ratio of the equilibrium magnetization to the steady-state magnetization (= $T_1^*$ ($M_0/M_{ss}$)) [3]. $M_0$ was obtained by fitting data in the first inversion repetition (10 s), and $M_{ss}$ in each repetition time was obtained by averaging last five data points at the end of each repetition. $T_1^*$ can be fitted from the measured data at each repetition to the above signal equation, thus $T_1$ values are measurable at each repetition.

***$f_v$ measurement:*** A three-compartment model, including gray matter (GM), white matter (WM), and cerebral spinal fluid (CSF), was used for $f_v$ measurement. The signal normalized by $M_0$ can be expressed as: $S(t)/M_0 = \sum_{i=1}^{3} f_{v,i}\left(M_{SS}/M_0\right)_i\left(1 - 2\exp(-t/T_{1,i}^*)\right)$, where subscript *i* represents each tissue type. $(M_{ss}/M_0)_i$ and $T^*_{1,i}$ are functions of *Ts*, α, and $T_{1,i}$ of each tissue type. The $T_1$ values of the human brain at 3.0T (699/1209/4300 ms for WM/GM/CSF respectively) [1] were used for data fitting.

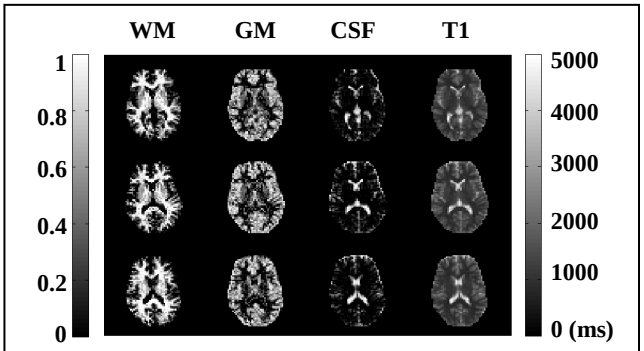


**Fig. 2**. Representative $f_v$, and $T_1$ maps of brain slices. Scales are 0-1 for $f_v$ maps, and 0-5000 for $T_1$ maps.

## Methods

***MR Imaging:*** Three healthy controls were scanned using a single-shot, multi-slices LL-EPI sequence on a Siemens 3.0T scanner (Allegra). The following MR imaging protocols were used: non-selective IR, Ts/TE=108/18 ms, α=10°, matrix=64x64, 3 slices, 30 inversion repetition with TR=10 s, and 92 α° pulses applied during each inversion recovery.

***Functional Study:*** A 5-minute block-design flashing checkerboard paradigm (3 "off" periods and 2 "on" periods) was presented during the IR LL-EPI$_{SS}$ scanning. This measurement was repeated two times. A separate set of BOLD fMRI data with similar visual stimulus was acquired to determine the region of interest (ROI) in the visual cortex ($p_{uncorrected} < 10^{-4}$, cluster size=16 voxels). Measured $M_{ss}$ and fitted $T_1$ and $f_v$ were analyzed in the same ROI.

## Results and Discussion

Fig.2 shows an example of $T_1$ and $f_v$ maps of WM, GM, and CSF (3 slices), calculated from the data acquired in one inversion recovery. The average $T_1$, $f_v$, and $M_{ss}$ values (n=3) in the visual ROI at rest and during the visual stimulation are shown in Tab.1. Following stimulation, apparent $T_1$ decreased ~1% probably due to increased flood flow elicited by the stimulus. During activation, GM and WM fractions increased and decreased respectively, while CSF fraction remained the same. The increase of GM fraction may attribute to blood volume increase coupled with blood flow elevation. The unchanged CSF volume fraction is consistent with a recent study [4]. The 1.7% increase of $M_{ss}$ during activation is likely due to increased $T_2^*$ if $M_0$ remains unchanged [5]. Blood was not considered as a separate compartment in the model, but can be taken into account in GM and WM assuming fast exchange with brain tissues.

| | *M*ss | $f_v$ | | | $T_1$ (ms) |
|---|---|---|---|---|---|
| | | WM | GM | CSF | |
| Rest | 117±18 | 0.22±0.02 | 0.65±0.03 | 0.13±0.02 | 1531±40 |
| Activation | 119±18 | 0.20±0.02 | 0.67±0.03 | 0.13±0.02 | 1516±40 |

**Tab. 1**. The $T_1$, $f_v$, and $M_{ss}$ in the visual cortex ROI at rest and during visual stimulation (n=3).

## Conclusions

We have developed an IR LL-EPI$_{SS}$ method that is able to acquire data for $T_1$ and $f_v$ maps in 10 seconds. Our initial results demonstrated the feasibility of this technique in monitoring the changes of $f_v$ and $T_1$ during brain activation.

## References

1. Lu et al., MRM, 2003. 2. Look & Locker, RSI, 1970. 3. Henderson et al, MRI, 1999. 4. Donahue et al., MRM, 2006. 5. Schulte et al., MRM, 2001.