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A Pulse Sequence for Rapid In Vivo Spin-Locked MRI

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Abstract

Purpose—To develop a novel pulse sequence called spin-locked echo planar imaging (EPI), or (SLEPI), to perform rapid $T_{1\rho}$ -weighted MRI.

Materials and Methods—SLEPI images were used to calculate $T_{1\rho}$ maps in two healthy volunteers imaged on a 1.5-T Sonata Siemens MRI scanner. The head and extremity coils were used for imaging the brain and blood in the popliteal artery, respectively.

Results—SLEPI-measured $T_{1\rho}$ was 83 msec and 103 msec in white (WM) and gray matter (GM), respectively, 584 msec in cerebrospinal fluid (CSF), and was similar to values obtained with the less time-efficient sequence based on a turbo spin-echo readout. $T_{1\rho}$ was 183 msec in arterial blood at a spin-lock (SL) amplitude of 500 Hz.

Conclusion—We demonstrate the feasibility of the SLEPI pulse sequence to perform rapid $T_{1\rho}$ MRI. The sequence produced images of higher quality than a gradient-echo EPI sequence for the same contrast evolution times. We also discuss applications and limitations of the pulse sequence.

Keywords

$T_{1\rho}$; spin-lock imaging; EPI; echo planar imaging; SLEPI

$T_{1\rho}$ OR “SPIN-LOCKED” MRI produces contrast unlike conventional T_1 - or T_2 -weighted images. Spin-locking is achieved by the application of a low power on-resonance radiofrequency (RF) pulse to the magnetization in the transverse plane. The resulting MR signal decays with a time constant $T_{1\rho}$ and is dominated by processes that occur with a correlation time, τ_c , that is related to the amplitude of the spin-lock (SL) pulse ($\gamma B_1/2\pi$), which typically ranges from zero to a few kilohertz. $T_{1\rho}$ is commonly referred to as the longitudinal relaxation time constant in the rotating frame. In biological tissues, $T_{1\rho}$ increases with higher B_1 and approaches T_2 , the spin-spin relaxation time constant, as the amplitude of the SL pulse is reduced to zero. The sensitivity of $T_{1\rho}$ to low-frequency interactions facilitates the study of biological tissues in a manner that is unattainable by conventional T_1 - and T_2 -based MR methods. Consequently, $T_{1\rho}$ MRI has been used to investigate a variety of tissues such as breast, brain, and cartilage (1–3).

Recently, $T_{1\rho}$ imaging has been employed to measure blood flow and oxygen metabolism and the effect of tracers such as $H_2^{17}O$ (4,5). These studies were performed using standard spin-echo, turbo (fast) spin-echo, or gradient-echo-based pulse sequences. There is

substantial evidence demonstrating that the $T_{1\rho}$ relaxation time parameter is sensitive to the early detection of cerebral ischemia (6–8). Kettunen et al (9) revealed a linear dependence of $T_{1\rho}$ as a function of oxygen saturation in experiments performed in vitro. Dynamic studies such as these and others that involve imaging of flowing spins such as that of blood would benefit from a fast $T_{1\rho}$ imaging technique that is able to acquire images in the order of tens of milliseconds.

A method of rapid image acquisition is the echo planar imaging (EPI) technique (10,11). In its conventional form, the EPI pulse sequence consists of an excitation pulse that is followed by a train of gradient-echoes within a single pulse repetition time (TR), and is capable of generating images in tens of milliseconds. Here we present a method for acquiring $T_{1\rho}$ -weighted images in a time efficient manner by using SL pulses in a new pulse sequence called spin-locked EPI (SLEPI). This sequence is used to determine $T_{1\rho}$ values in the human brain. Further, for the first time, we report the $T_{1\rho}$ of blood obtained in vivo. These measurements were possible because of the short image acquisition window offered by the new sequence. It is shown that the SLEPI sequence can significantly reduce susceptibility-induced artifacts during EPI acquisition, while maintaining image contrast similar to long echo time (TE) images.

MATERIALS AND METHODS

The Institutional Review Board of our university granted approval for all human experiments. Two healthy volunteers were imaged on a 1.5-T Sonata Siemens MRI scanner using head and extremity coils for imaging the brain and blood in the knee joint, respectively. For this preliminary study, we studied healthy subjects without clinically apparent acute or chronic medical problems. Informed consent was acquired from both subjects in this study.

Pulse Sequence Design

In the SLEPI pulse sequence (Fig. 1), a nonselective $\pi/2$ pulse excites spins that are then spin-locked in the transverse plane by the application of two phase-alternating SL pulses ($\pm 90^\circ$ phase-shifted from the phase of the first $\pi/2$ pulse). Phase-alternating SL pulses have been previously demonstrated to reduce image artifacts in $T_{1\rho}$ MRI resulting from B_1 inhomogeneity (12). The duration of the SL pulses is denoted as TSL. A delay of 20 μ sec was maintained between the SL pulse segments for necessary electronic dead time between RF instructions. The second nonselective $\pi/2$ pulse restores the spin-locked magnetization to the longitudinal axis. A high amplitude gradient (indicated as a filled square block) is applied to destroy residual transverse magnetization. The “ $T_{1\rho}$ -prepared” longitudinal magnetization at the end of the crusher gradient is described by the equation:

$$M(TSL) = M_0 e^{-\frac{TSL}{T_{1\rho}}} \quad (1)$$

where M_0 is the thermal equilibrium magnetization.

For imaging the $T_{1\rho}$ -prepared signal, a gradient-echo EPI readout (10) was appended in which an excitation pulse is followed by a train of gradient-echoes. Spatial encoding of the echoes was accomplished by a gradient that began phase encoding at the positive end of k-space. K-space was traversed by negative gradients “blips” at the beginning of each echo while the echoes were frequency encoded by alternating gradients.

Estimation of $T_{1\rho}$ in the Brain

The utility of the SLEPI sequence to generate meaningful and accurate $T_{1\rho}$ maps in vivo was evaluated. A series of $T_{1\rho}$ -weighted images were acquired with SLEPI at four TSLs from 10–70 msec. Other imaging parameters were TR = 1000 msec, field of view (FOV) = 240 mm, 64×64 matrix size, with 3 mm-thick sections, and an SL amplitude fixed at 500 Hz. These images were used to generate $T_{1\rho}$ “maps” by fitting voxel signal intensities as a function of TSL by linear regression to Eq. [1] while keeping TE constant at 20 msec. This implies that although image intensity is a combination of $T_{1\rho}$ and T_2^* -weighting, the calculated maps generate only $T_{1\rho}$ values since the fitting program will treat this contrast as a baseline and not a relaxation time constant in the exponential function. In the fitting routine, pixels whose intensities correlated poorly with the equation (i.e., $R^2 < 0.95$) were set to zero. The calculated $T_{1\rho}$ values from these maps were verified by comparing them to $T_{1\rho}$ maps of the same slice in the brain obtained with a turbo spin-echo (TSE)-based $T_{1\rho}$ pulse sequence (3). These images were acquired with the same FOV and slice thickness as the SLEPI images but with image dimensions of 128×128 and total imaging time was one minute/image by acquiring seven echoes per TR. For comparison, T_2^* maps of the same slice location were calculated with a standard single-shot EPI sequence and same pixel size as the SLEPI by varying TE from 30 to 90 msec in four even increments.

Estimation of $T_{1\rho}$ in Blood

An eight-channel extremity knee coil (MRI Devices Corporation, Gainesville, FL, USA) was used to obtain $T_{1\rho}$ -weighted MR images of the knee joint to visualize blood in the popliteal artery on one healthy subject (male, age 35 years). A two-dimensional gradient-echo localizer image was acquired for slice positioning and to facilitate location of arteries and veins during data processing. The imaging parameters were TE/TR = 3.5/10 msec, flip angle = 90° , these values were chosen to enhance the signal from flowing blood, with an FOV of $180 \times 180 \text{ mm}^2$, and a slice thickness of 3 mm. $T_{1\rho}$ -weighted images were acquired using SLEPI at eight different TSL times (10, 20, 30, 40, 50, 60, 80, and 100 msec) of the same slice location, FOV, and thickness as the localizer image. The TE/TR = 20/200 msec, with a 64×64 matrix size, and the SL frequency fixed at 500 Hz for each image. We employed a pulse oximeter, attached to the volunteer’s index finger tip, to gate the image acquisition. The acquisition window for the pulse trigger was one second, i.e., each SLEPI image was acquired in effective TR = 1 second. This was done in order to reduce variations in signal intensity from pulsatile flow of blood. Subsequently, the beginning of the SLEPI sequence was set at 600 msec after the peak of the subject’s heart pulse. While the peak of the heart pulse cycle may occur at a different time in the popliteal artery than in the finger, the real purpose of pulse-gating was to acquire data consistently in the same 200 msec (window) of the pulse cycle.

Data Processing

The images were transferred to a G4 PowerBook computer (Apple, Cupertino, CA, USA) and processed in custom-written software in the IDL programming language (RSI, Boulder, CO, USA). The 64×64 matrix-sized images were interpolated to 128×128 images to facilitate image processing. Average ($\pm$ SD) of $T_{1\rho}$ values were recorded in three 5×5 pixel regions of interest (ROIs) that were manually selected by a single user (A.B.). For signal-to-noise ratio (SNR) measurements, the mean signal from two ROIs located in the frontal and occipital regions of the brain was expressed as a ratio of the mean signal from the background for a given contrast evolution time (TSL + TE for SLEPI and TE for EPI). Measurements of relaxation times ($T_{1\rho}$ and T_2^*) were performed in cortical gray matter (GM), superficial white matter (WM), and cerebrospinal fluid (CSF) in SLEPI- and TSE-generated $T_{1\rho}$ maps as well as in EPI-generated T_2^* maps. Statistical analysis (Student’s *t*-test) was performed in MS Excel to detect significant differences of $T_{1\rho}$ values obtained by

the SLEPI and $T_{1\rho}$ -TSE sequences. Finally, $T_{1\rho}$ measurements were recorded from an ROI located entirely inside the popliteal artery from a SLEPI-generated $T_{1\rho}$ map of the knee joint by determining the location of the center and diameter of the popliteal artery in the localizer image.

RESULTS

Figure 2 displays MR images (in grayscale) and relaxation time maps (in color) of an axial slice through the brain obtained by SLEPI (top), T_2^* -weighted EPI (middle), and $T_{1\rho}$ -prepared turbo spin-echo (bottom) pulse sequences. The SLEPI and EPI images were acquired in one second each with identical imaging parameters, except TSL and TE were varied. At longer echo times, EPI images experience signal loss from susceptibility artifacts that arise from the air-tissue interface in the ventral frontal region of the brain. These images are corrupted and unusable for most quantitative analyses as demonstrated by the “hole” indicated by the arrow in the T_2^* map. The SLEPI images, however, were acquired at the equivalent contrast times (TSL + TE) but are free from signal drop-off and facilitate the calculation of a quantitative $T_{1\rho}$ relaxation map. The SNR in the frontal (ROI 1) and occipital (ROI 2) lobes were measured as a function of TE for the T_2^* -weighted EPI images and TSL + TE for the $T_{1\rho}$ -weighted SLEPI images and is illustrated in Fig. 3. In equivalent evolution times, the SNR from $T_{1\rho}$ images was always larger than corresponding T_2^* images. Further, in the T_2^* images, ROI 1 exhibits a substantial reduction in SNR compared to ROI 2 even at an early TE of 50 msec. The $T_{1\rho}$ -weighted images, however, maintain similar SNR in both ROIs for all values of TSL + TE.

The $T_{1\rho}$ map generated from the SLEPI images is in good agreement with that obtained by the $T_{1\rho}$ -TSE sequence computed from images that each required one minute to acquire. Average relaxation times were calculated in the brain. $T_{1\rho}$ values are significantly greater (83 ± 8 msec in WM, 103 ± 6 msec in GM, and 584 ± 58 msec in CSF) than the corresponding T_2^* values (67 ± 9 msec, 72 ± 11 msec, and 432 ± 69 msec) in the same locations. This is expected since the $T_{1\rho}$ -weighted signal is less predisposed to loss by susceptibility and diffusion-related processes than the T_2^* -weighted signal. The effect of the SL pulse on the transverse magnetization is essentially similar to a series of 180° pulses in a Carr-Purcell train (13) in which the pulses are separated by the inverse of the B_1 frequency, which in our case would be 1/500 Hz or 2 msec. $T_{1\rho}$ calculated from SLEPI images are in good agreement with those calculated by the $T_{1\rho}$ -TSE sequence (85 ± 3 msec in WM, 102 ± 2 msec in GM, and 614 ± 45 msec in CSF) and none of the measurements were statistically different between the two pulse sequences. $T_{1\rho}$ in brain parenchyma was consistent with previous measurements (3). The lower SNR of the SLEPI images produced larger variations in $T_{1\rho}$ in all three ROIs. $T_{1\rho}$ of CSF was lower in the SLEPI sequence (584 msec) compared to the $T_{1\rho}$ -TSE value (614 msec) but not significantly. This could be due to the volume averaging of periventricular tissue with CSF as the large SDs would indicate.

SLEPI-acquired images of the knee joint of a healthy volunteer are shown in Fig. 4. The location of $T_{1\rho}$ measurements in the artery is indicated in the short TSL time image (10 msec). A substantial signal was also observed from the articular cartilage located in the patellar-femoral joint due to its long $T_{1\rho}$ relaxation times (14). The frequency of the SL pulse was centered on the water resonance, consequently the MR signal from fatty marrow inside the femur and patella bone was substantially reduced. While the signal from surrounding tissues is nonexistent at TSL of 80 msec and higher, a very robust signal was observed from blood in the artery. From the localizer image in Fig. 5, the diameter of the artery was determined to be ~10 mm, corresponding to 7 pixels in the 128×128 -pixel $T_{1\rho}$ map. A plot of the profile through the artery along the dotted arrow in the localizer image is illustrated in the graph. The middle seven pixels indicated that $T_{1\rho}$ ranged from 100 to 225

msec inside the artery. The average $T_{1\rho}$ was determined from a ROI analysis to be 183 ± 21 msec (mean $\pm$ SD). Incidentally, T_2^* was previously measured in vivo in human blood and ranged from 83 to 200 msec (15).

DISCUSSION

Application of SLEPI to measure $T_{1\rho}$ in the brain and in flowing blood was demonstrated in this work. The SLEPI sequence has the advantage of rapid acquisition of $T_{1\rho}$ data compared to a $T_{1\rho}$ -prepared TSE sequence. This new sequence should allow studies that determine the dependence of $T_{1\rho}$ on blood oxygenation levels in vitro (9) to be performed in vivo in a clinical setting. As an example, $T_{1\rho}$ mapping could be used to detect ischemia in regions in the brain with some basic modifications, such as the use of an appropriate RF coil to SL flowing blood, for example, in the carotids.

The SLEPI sequence is currently limited to acquiring only one slice per TR since the SL pulse is not slice-selective. Moreover, there are limits on the duration of the SL pulse based on the maximum RF energy permitted during clinical imaging (16). This energy is reported as the specific absorption rate (SAR), and was calculated a priori according to Collins et al (17) and monitored by the scanner during the experiments as part of a routine protocol (18). Another variation of the SLEPI sequence that is currently under development reduces SAR by eliminating both $\pi/2$ pulses. $T_{1\rho}$ -weighting is achieved by placing only SL pulses between the excitation pulse and encoding gradients of the EPI sequence. Additionally, a 180° refocusing pulse could follow excitation and SL pulses to generate a $T_{1\rho}$ -weighted spin-echo EPI signal.

We deliberately chose a slice located near the center of the knee coil for the measurement of $T_{1\rho}$ in blood. This was necessary to assure that all the blood flowing into the imaged slice was $T_{1\rho}$ -prepared by the nonselective pulses in the SLEPI sequence. The femoral artery was also a convenient choice since it is nearly orthogonal to the imaged slice. The length of the column of blood flowing into the imaged slice was calculated by knowing the duration of the SLEPI sequence (~ 100 msec) and the velocity of blood in the femoral artery (30 cm/second). Therefore, a 3-cm-long column of blood was spin-locked by the $T_{1\rho}$ -preparatory sequence. It is reasonable to assume that the body coil on a clinical scanner has a large region of homogenous B_1 along its long axis and therefore all the flowing spins were $T_{1\rho}$ -prepared and, for a $TE = 3.5$ msec, remained in the 3-mm-thick imaged slice. Triggering the start of the SLEPI sequence with the subject's pulse rate was necessary for eliminating signal fluctuations from pulsatile flow. The choice for timing the trigger was 600 msec after the peak of the pulse, as at this time blood flow should be relatively slow. The choice of this delay time was not crucial, as long as $T_{1\rho}$ -preparation of the flowing spins occurred at the same moment in each blood flow cycle.

The advantage of SLEPI over conventional EPI in reducing image artifacts resulting from static field inhomogeneities has potential applications in functional MRI (fMRI) experiments. Consequently, we are currently pursuing studies that compare results from T_2 , T_2^* , and $T_{1\rho}$ -weighted fMRI experiments to elucidate mechanisms of Blood Oxygenation Level Dependent (BOLD) contrast as the relative contribution of susceptibility to the relaxation times will differ between sequences (9). Further, the magnetic susceptibility of blood affects the MR signal in brain parenchyma differently depending on the size of the vessel. Designing appropriate interleaved SLEPI-EPI experiments may differentiate the relative contributions to the BOLD effect from blood flow and saturation changes in the arterial, capillary, and venous pools. As development of this pulse sequence continues, it will be of interest to compare the SLEPI sequence to a spin-echo-based EPI sequence (19), in order to compare artifact reduction and contrast in different tissues in the brain.

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Figure 1.

The SLEPI pulse sequence. For $T_{1\rho}$ -weighted MRI, a four-pulse cluster followed by a crusher gradient (filled square block) preencodes a $T_{1\rho}$ -weighted magnetization that is read out by a gradient-echo EPI sequence with the shortest possible echo time (TE) to minimize T_2^* -weighting.

Figure 2.

$T_{1\rho}$ mapping with SLEPI (top row) EPI (middle row) and $T_{1\rho}$ -TSE (bottom row). The $T_{1\rho}$ -TSE sequence was assumed as the “gold-standard” $T_{1\rho}$ mapping sequence. Data was obtained at 1.5 Tesla. $T_{1\rho}$ and T_2^* values are reported in milliseconds. Each column contains images that are acquired at the same “effective echo time”, i.e., TSL + TE for the $T_{1\rho}$ -weighted images and TE for the T_2^* -weighted images. The arrow in the T_2^* map indicates a region of reduced T_2^* resulting from a susceptibility artifact-induced signal void in the EPI images.

Figure 3.

Plot of signal-to-noise ratio (SNR) as a function of TE for the T₂*-weighted EPI images and TSL + TE for the T_{1ρ}-weighted SLEPI images. Measurements were performed in the frontal (ROI 1) and occipital (ROI 2) lobes as indicated in the inset image of the brain. T_{1ρ} images consistently have a greater SNR than corresponding T₂* images. ROI 1 shows a susceptibility-induced reduction in SNR in T₂* images, a trend that was not observed in the T_{1ρ}-weighted images.

Figure 4.

$T_{1\rho}$ -weighted images of the knee joint of a healthy volunteer acquired with SLEPI. The anatomy of the knee joint is clearly visible in the short TSL time images, while the signal from blood in the artery persists even at long TSL times. The bright signal between the patella and femur is from articular cartilage with relatively long $T_{1\rho}$ values. As the SL pulse was centered on the water resonance, the fat signal from the marrow inside the femur and patella bone was substantially reduced. These images were used to calculate the $T_{1\rho}$ map in Fig. 5.

Figure 5.

A localizer image (top left) was used to prescribe the SLEPI scans on a volunteer's knee. The resulting $T_{1\rho}$ map (top right) was calculated from the images shown in Fig. 4 and clearly shows substantially elevated $T_{1\rho}$ in blood in the artery compared to other tissues. The dotted arrow in the localizer image shows the location where the profile plot of $T_{1\rho}$ values (below) was obtained in the $T_{1\rho}$ map. On average, the $T_{1\rho}$ of blood was measured to be 183 ± 21 msec (mean $\pm$ SD). The large variations in blood $T_{1\rho}$ could result from partial-volume effects from tissue surrounding the artery.