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Journal of Magnetic Resonance 171 (2004) 90–96
JMR Journal of Magnetic Resonance
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# Spatially selective T2 and T2* measurement with line-scan echo-planar spectroscopic imaging

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Received 14 May 2004; revised 28 July 2004
Available online 28 August 2004

**Abstract**

Line-scan echo planar spectroscopic imaging (LSEPSI) is applied to quickly measure the T2 and T2* relaxation time constants in pre-selected 2D or 3D regions. Results from brain imaging studies at 3 T suggest that the proposed method may prove valuable for both basic research (e.g., quantifying the changes of T2/T2* values in functional MRI with blood oxygenation level-dependent contrast) and clinical studies (e.g., measuring the T2′ shortening due to iron deposition). The proposed spatially selective T2 and T2* mapping technique is especially well suited for studies, where T2/T2* quantification needs to be performed dynamically in a pre-selected 2D or 3D region.


*Keywords:* fMRI; Line-scan; Echo-planar spectroscopic imaging; T2 mapping

## 1. Introduction

Simultaneous measurement of both T2 and T2* relaxation time constants is important for both basic neuroscience research and clinical studies. For example, the basic mechanism of blood oxygenation level dependent (BOLD) contrast can be quantitatively studied by measuring the changes of brain tissue T2 and T2* values in response to a functional challenge [1–6]; Clinically, T2, T2*, and the derived T2′ measurements are valuable in quantifying the iron deposition due to neurological diseases [7–11].

Mapping for both T2 and T2* time constants using conventional spin-warp imaging, however, is time consuming and may not be practical for clinical scans. Recently, it has been shown that T2 and T2* mapping time can be greatly reduced when using EPI techniques [12]. However, EPI based measurements are generally prone to various artifacts (such as geometric distortions, [13–18]). In addition, because of EPI's long acquisition window, the minimal echo time available in EPI scans is usually long [19]. Therefore, in brain regions with pronounced susceptibility artifact or with short T2* values, it is difficult to acquire EPI data with satisfactory quality or signal-to-noise ratio [20,21].

To address the limitations in conventional relaxation time mapping protocols based on either spin-warp imaging or EPI, we propose to use a spatially selective line-scan echo-planar spectroscopic imaging (LSEPSI) technique [22] for T2 and T2* mapping. After identifying two-dimensional (2D) or three-dimensional (3D) regions of interest (ROIs) from whole brain images obtained from a reference structural or functional scan, local T2 and T2* values can be quickly characterized using LSEPSI. The spatially selective T2 and T2*

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doi:10.1016/j.jmr.2004.08.004

mapping technique is especially well suited for two classes of studies: (1) asymmetric in-plane field of view (FOV) imaging the selected ROIs, for example imaging the spinal cord [8,23], (2) T2/T2* mapping performed locally within a short time frame (or dynamically), for example quantifying the BOLD induced T2/T2* changes in fMRI studies [1–4,6].

## 2. Methods

The LSEPSI pulse sequence (Fig. 1) has been described previously [22]. Briefly, a 1D column is first selected with a pair of slice selective pulses tilted to each other to solicit a spin echo from the intersection of the two slices. Spatial information along the column is then frequency encoded with a series of gradient echoes using a rapidly switching, asymmetric, Gx readout gradient. Following acquisition of one column, the sequence is repeated to image other 1D columns in the selected 2D (or 3D) brain regions, so that a 2D (or 3D) spin-echo, and multiple 2D (or 3D) gradient-echo images can be reconstructed. To minimize the crosstalk between two columns, odd and even columns in the selected region are acquired in an interleaved manner (analogous to the interleaved slice ordering scheme used in conventional multi-slice imaging). The procedure is then repeated with different echo time ($TE_{SE}$ in Fig. 1), so that multiple 2D (or 3D) spin-echo images with different T2-weighting can also be obtained. In a protocol with $N_L$ image columns, inter-column sampling time $T_s$, and number of the reconstructed 2D (or 3D) spin-echo images $N_{SE}$, the total imaging time is $N_L \times N_{SE} \times T_S$.

Two studies performed at 3 T (General Electric, Milwaukee, WI) illustrate the LSEPSI technique. Approval from the institutional Human Research Committee was obtained, as was written informed consent for each subject. In the first study, brain tissue T2 and T2* values were measured from three healthy subjects. Structural reference images were first obtained with multi-slice 2D fast spin-echo imaging with TR 2000 ms, effective TE 60 ms, FOV $26 \times 26$ cm$^2$, matrix size $256 \times 256$, and slice thickness 5 mm. An axial slice was then chosen for LSEPSI based T2 and T2* mapping.

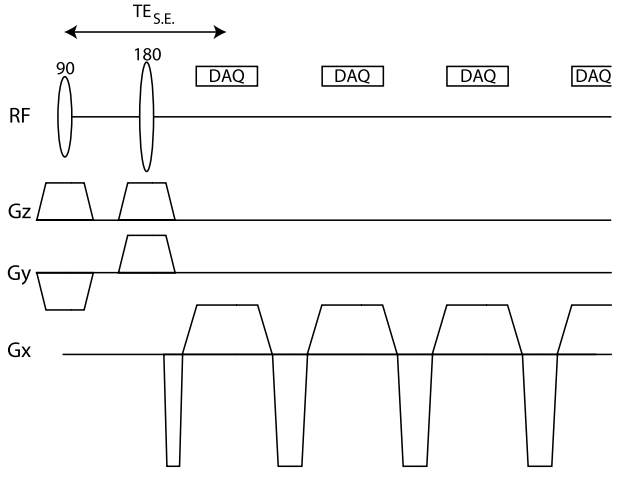


Fig. 1. Line-scan echo-planar spectroscopic imaging (LSEPSI) pulse sequence.

Parameters for LSEPSI scans included: FOV along the readout direction 26 cm, matrix size along the readout direction 128, cross-sectional area for each column $4 \times 6$ mm$^2$, number of columns 64, inter-column sampling time 500 ms, EPSI inter-echo spacing time 2.3 ms, and number of EPSI echo trains 32. The scan time for each EPSI data set (128 readout matrix size $\times$ 64 columns $\times$ 32 echo trains) was 32 s (i.e., inter-column time 0.5 s $\times$ 64 columns). Ten LSEPSI data sets, corresponding to different echo times ($TE_{SE}$ in Fig. 1) ranging from 10 to 100 ms, were acquired from each subject, and the scan time was 5 min 20 s per subject. In our preliminary studies, all of the columns in the selected slice were imaged, so that the quality of the reconstructed 2D image could be evaluated. In future LSEPSI studies, the temporal resolution may be further improved if only the columns inside the pre-selected ROI are imaged.

The acquired LSEPSI data sets were analyzed with Matlab (Mathworks, Natick, MA, USA). The Fourier transformation was first performed along the readout direction to reconstruct 1D image profiles for each column for each gradient echo acquired. Columns of profiles were combined to form 2D spin-echo and gradient-echo images with different T2/T2* weightings. Signal intensities of the reconstructed spin-echo and gradient-echo images were fitted with exponential curves, on a pixel-by-pixel basis, and thus T2 and T2* maps of the imaged regions were derived.

In the second study, we used the LSEPSI technique to characterize the TE-dependent BOLD induced signal changes in spin-echo and gradient-echo images in two healthy subjects. Reference fMRI data were first acquired with a conventional 2D EPI method, with the subjects performing a finger-tapping motor task [6]. The fMRI block-design paradigm consisted of four 30 s rest periods, interleaved with four 30 s finger-tapping periods. In finger-tapping periods, the subjects tapped the fingers of their right hands at a rate of approximately 1 Hz. EPI scan parameters included TR 2.5 s, TE 40 ms, FOV $24 \times 24$ cm$^2$, in-plane matrix size $64 \times 64$, and slice thickness 5 mm. The acquired data were processed with the near real-time fMRI analysis tool developed in house [24], and the activation maps were displayed on a Linux-workstation to identify an appropriate imaging region that included sensori-motor areas for subsequent LSEPSI scans.

In LSEPSI based functional scans, the parameters included: FOV along the readout direction 32 cm, matrix size along the readout direction 128, cross-sectional

dimension for each column $5 \times 5$ mm, number of columns 64, inter-column spacing time 500 ms, EPSI inter-echo spacing time 2.3 ms, and number of EPSI echo trains 32. The scan time for each EPSI data set (128 readout matrix size $\times$ 64 columns $\times$ 32 echo trains) was 32 s. The functional paradigm consisted of four 32-s rest periods, interleaved with four 32-s finger-tapping periods. Eight EPSI data sets were acquired during those eight rest/motor periods. This procedure was repeated three times with different spin-echo echo times ($TE_{SE}$ in Fig. 1): 10, 30, and 50 ms.

Activated pixels in the LSEPSI based fMRI data sets were identified with the following procedures. First, by averaging 384 2D LSEPSI images acquired in the finger-tapping periods (32 echo trains $\times$ 4 finger-tapping periods $\times$ 3 repetitions with different $TE_{SE}$), a single 2D "ON" image was generated. Similarly, by averaging 384 LSEPSI images acquired in the rest periods, a single 2D "OFF" image was generated. Second, a 2D difference image was calculated by subtracting the averaged "OFF" image from the averaged "ON" image. Third, an appropriate threshold was chosen and applied to the calculated 2D difference images, so that the resultant activation map resembled the one derived from EPI based reference fMRI data. After identifying the activated pixels, the TE-dependent signal intensities, corresponding to rest and finger-tapping periods, were measured from those pixels.

The reconstructed complex multi-TE image data set was then Fourier transformed, along the gradient echo direction, to produce a spectral-domain image data set [25]. The spectral domain representation of the BOLD induced signal change was then evaluated, from the previously identified activated pixels. As demonstrated by Yang et al. [25] the spectral-domain analysis is an approach to improve the functional contrast-to-noise ratio of multi-TE fMRI data.

## 3. Results

Results of the first study are presented in Fig. 2. Fig. 2A compares a spin-echo (the first gradient echo acquired at $TE_{SE}$ of 10 ms) and three gradient-echo images (corresponding to $T2^*$ weighting times 11.5, 29.8, and 48.2 ms) of the first LSEPSI data set (with $TE_{SE} = 10$ ms). Because of susceptibility field gradients, signals in ROI 1 decrease rapidly with increasing $T2^*$-weighting, in comparison to signals in ROI 2. Fig. 2B compares four spin-echo images derived from LSEPSI data corresponding to $TE_{SE}$ 10, 20, 40, and 60 ms. Signals in ROI 1 and ROI 2 decrease at approximately the same rate with increasing T2-weighting.

Signal intensities from two ROIs of the acquired LSEPSI data sets (i.e., 10 data sets with different $TE_{SE}$ and 32 echo trains in each data set) are presented in Fig. 2C. The fitted T2 decay curves of ROI 1 and ROI 2 are shown by blue dashed lines and red dashed lines with two dots, respectively, indicating that both regions have similar T2 time constants (70.0 and 68.5 ms). On the other hand, as indicated by fitted $T2^*$ decay curves (blue dotted lines and red solid lines), ROI 1 and ROI 2 have significantly different $T2^*$ time constants (18.4 and 56.6 ms), because of the susceptibility effect in ROI 1 near the air-tissue interface. The left and right panels of Fig. 2D show T2 and $T2^*$ maps calculated, on a pixel-by-pixel basis, from LSEPSI data.

Results of the second study are presented in Fig. 3. The left panel of Fig. 3A shows the activation map calculated from EPI based fMRI data, using $t$ test with $P < 0.0001$. The right panel shows the activation map derived from LSEPSI data, using subtraction approach with an appropriate threshold (so that the derived activation map resembles the one obtained from EPI, as described in Section 2). Signals of 18 activated pixel in the left motor cortex (inside the yellow box) are averaged and their TE-dependent values corresponding to rest- and activation-periods are shown by upper blue dashed curves and red solid curves (with L label), respectively, in Fig. 3B. The left, middle, and right panels of Fig. 3B present the data of 32 echo trains obtained from three LSEPSI data sets (with $TE_{SE} = 10$, 30, and 50 ms), respectively. In data corresponding to $TE_{SE}$ 10 ms, the BOLD contrast (i.e., the difference between red and blue curves) generally increases with $T2^*$-weighting and reaches the maximum at a $T2^*$-weighting of 60 ms (which is actually close to the calculated tissue $T2^*$ value). In data corresponding to $TE_{SE}$ 30 ms, the BOLD contrast is generally smaller, and reaches its maximal value at a $T2^*$-weighting of 46 ms. In data corresponding to $TE_{SE}$ 50 ms, the BOLD contrast is more uniform over a wide range of $T2^*$-weighting. The TE-dependent signal intensities of the control ROI (18 pixels in right motor area) at rest- and activation-periods are presented by lower blue dashed and red solid curves (with R label), respectively, in Fig. 3B. No BOLD induced signal change is observed in the control ROI.

We also performed a spectral-domain analysis of the acquired LSEPSI data, by Fourier transforming the time-domain signals corresponding to 32 echo trains [25]. For example, by taking the complex Fourier transformation of the upper red solid curve shown in the left panel of Fig. 3B, a spectrum corresponding to finger-tapping period (with $TE_{SE} = 10$ ms) was obtained, and its magnitude representation is shown in Fig. 3C. Similarly, by taking the complex Fourier transformation of the upper blue dashed curve in the left panel of Fig. 3B, a spectrum corresponding to rest period (with $TE_{SE} = 10$ ms) was obtained, and its magnitude representation is shown in Fig. 3D. Because of the BOLD effect, the spectrum corresponding to finger-tapping period has a larger magnitude (as indicated by dashed

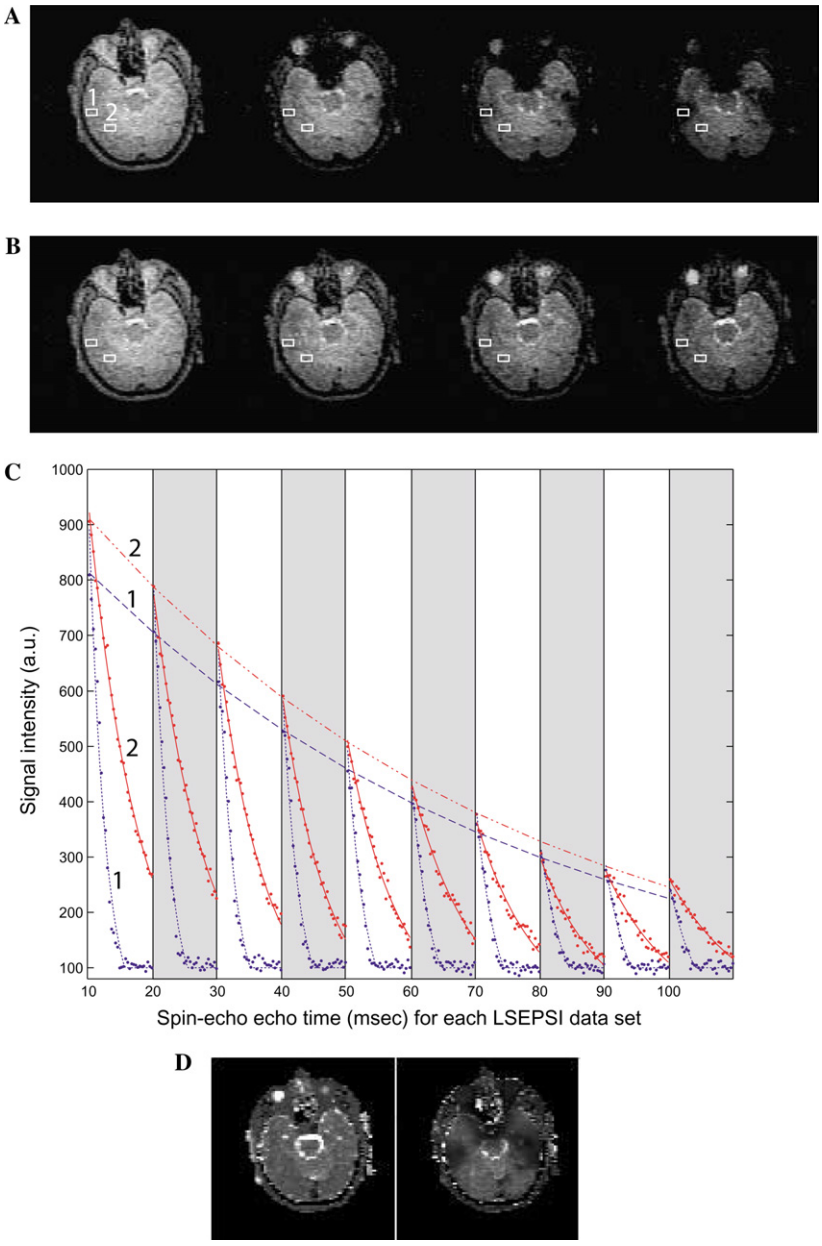


Fig. 2. Human brain T2 and T2* mapping with LSEPSI: (A) Comparison of a spin-echo and three gradient-echo images corresponding to different T2* weighting times (11.5, 29.8, and 48.2 ms), (B) Comparison of spin-echo images corresponding to different T2 weighting times (10, 20, 40, and 60 ms), (C) Echo time dependent signal intensities of two chosen ROIs. (T2* decay of ROI 1: blue dotted line; T2* decay of ROI 2: red solid line; T2 decay of ROI 1: blue dashed line; T2 decay of ROI 2: red dashed line with two dots) (D) The calculated T2 (left) and T2* (right) maps. (For interpretation of the references to colours in this figure legend, the reader is referred to the web version of this paper.)

lines in Figs. 3C and D). The BOLD induced signal change is about 5% (for $TE_{SE}$ = 10 ms). Our data show no frequency shift associated with the BOLD effect, in agreement with previous reports [26].

## 4. Discussion

The LSEPSI technique allows for a quick measurement of both T2 and T2* relaxation time constants in a pre-selected 2D rectangular or 3D cubic region. In comparison to conventional time-consuming T2/T2* mapping protocol based on 2D spin-warp imaging, the proposed method can acquire many more data points (for T2/T2* curve fitting) within the same amount of scan time. For example, in one of our studies (Fig. 2), 320 2D images with different T2 and T2*-weightings were acquired within just 5 min and 20 s (for 10 different spin-echo TEs) with one signal average. The acquisition time may be reduced, if a shorter inter-column delay

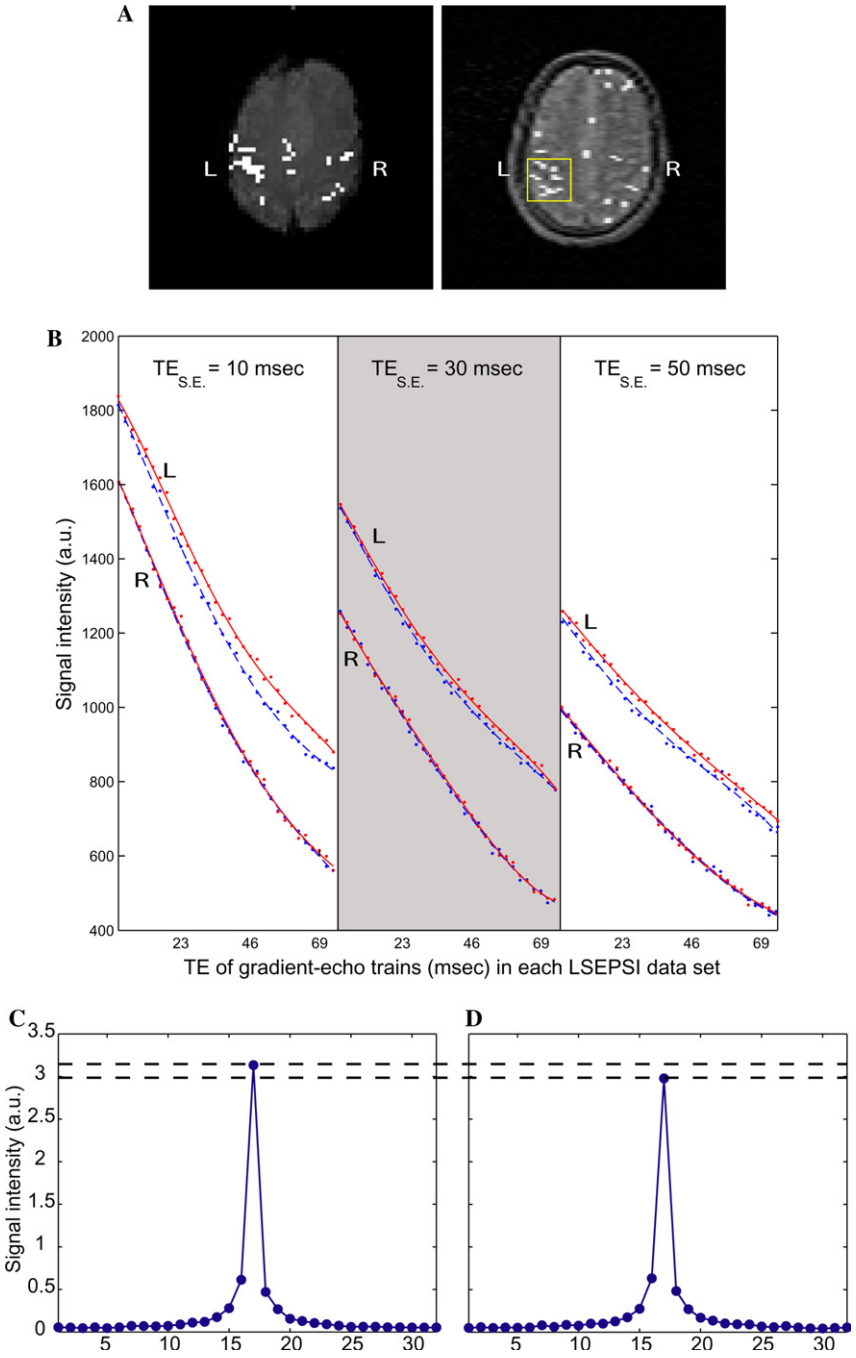


Fig. 3. Characterization of TE-dependent fMRI responses with LSEPSI: (A) Activation maps calculated from EPI based fMRI data (left) and LSEPSI data (right), (B) TE-dependent LSEPSI signals of left and right motor cortex corresponding to rest (blue dashed lines) and finger-tapping (red solid lines) periods, for different spin-echo echo-time (10, 30, and 50 ms). Spectral-domain representation of LSEPSI based BOLD signals ($TE_{SE}$ = 10 ms): (C) The magnitude spectrum measured from left motor cortex during finger-tapping periods, (D) The magnitude spectrum measured from left motor cortex during rest periods. (For interpretation of the references to colours in this figure legend, the reader is referred to the web version of this paper.)

time is chosen. The number of image columns, and thus the total scan time, can be further reduced, if the ROI for T2/T2* mapping is smaller, thus requiring fewer columns.

In studies that require T2/T2* mapping only in a pre-selected 2D or 3D region, the proposed LSEPSI method is superior to EPI based mapping protocol in two ways. First, EPI images are always geometrically distorted by the field inhomogeneity [13–17]. On the other hand, as suggested by our preliminary data, LSEPSI is less susceptible to field inhomogeneity. Second, high-quality spin-echo and gradient-echo images with short echo

time and short echo spacing time can be readily obtained with LSEPSI. Furthermore, because of EPI's long acquisition window, it is difficult to acquire full k-space EPI data at short echo times [19].

The proposed LSEPSI protocol is inherently a 1D imaging technique. Therefore, the signal-to-noise ratio (SNR) is expected to be lower than that in either 2D spin-warp imaging, or turbo-PEPSI [5]. Fortunately, the SNR can be improved by simply averaging the data acquired from repeated scans. This approach is feasible, especially since the scan time for acquiring one LSEPSI data set is short. It should be noted that, since many data points can be obtained with LSEPSI for T2 and $T2^*$ curve fitting, the derived T2 and $T2^*$ map is reliable and the quality is not too much offset by the noise in each LSEPSI data point (e.g., Fig. 2D). In the proposed line-scan method, one may choose to either (1) acquire many signal averages to improve the SNR, or (2) achieve higher temporal resolution, if the SNR achieved with one or two averages is sufficient to detect the desired information. On the other hand, in conventional phase-encoded imaging protocol (including spin-warp imaging, EPI and turbo-PEPSI etc), the option of improving the dynamic scan temporal resolution through reducing the phase-encoding steps is not straightforward and requires more complex reconstructions [28,29]. In comparison to conventional 2D spin-warp or EPI, the full power and feasibility of reduced FOV imaging can be achieved much more easily using the line-scan technique [22,27].

Because of the T1 saturation effect in conventional 2D spin-warp imaging, the SNR generally decreases by shortening the TR, even after the flip angles are appropriately adjusted for different TRs. On the other hand, in the LSEPSI technique, the impact of inter-column TR on the image SNR is much less significant. For example, in our preliminary studies, the LSEPSI images obtained with different inter-column TR values (500 and 100 ms) have very similar image quality (Figs. 4A and B), and SNR (15.6 and 15.3). Therefore, it is feasible to improve the temporal resolution of LSEPSI scans by shortening inter-column spacing time, without compromising the image quality.

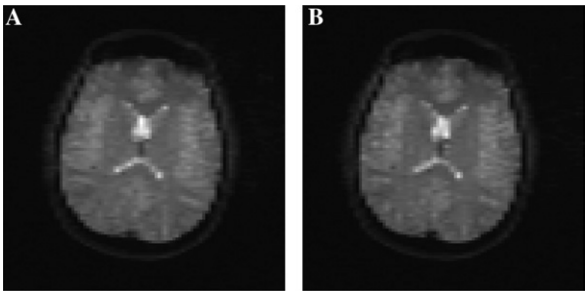


Fig. 4. Comparison of LSEPSI images obtained with different inter-column TR values: (A) 500 ms, (B) 100 ms. The SNR values measured from these two images are 15.6 and 15.3.

Although not seen in our data, the line-scan based imaging technique is potentially susceptible to two types of artifacts. First, in the presence of a significant susceptibility field gradient, the shape of the excited columns and therefore the reconstructed 2D/3D image may be distorted. Second, if the implementation of the RF pulses is less than optimal, there may exist some residual signals from outside the excited columns. Impact of these potential artifacts on the accuracy of LSEPSI based T2 and $T2^*$ measurement remains to be investigated. In general, line-scan MRI is less susceptible to subject movement, due to the "snapshot" nature of individual column acquisition [22,27], in comparison to conventional spin-wrap imaging. However, the proposed LSEPSI based T2/$T2^*$ measurement may still be affected by subject movement, especially when the subject moves between measurements for different spin-echo TEs.

We have shown that the TE-dependent BOLD contrast for spin-echo and gradient-echo images can be measured with the proposed technique. This measured information may be useful for (1) determining the scan parameters for an optimal BOLD contrast [2,4,20,30,31], (2) separating the stimulation-induced changes in blood inflow from the true BOLD signal changes [1], and (3) understanding the basic mechanism of BOLD, such as the relative contribution from large and small vessels [3,32]. In addition, detection of functional activation through $T2^*$ mapping is expected to be more robust than a fixed-TE fMRI protocol, since the echo time for an optimal BOLD contrast may vary from session to session, depending on the subject positions and shim settings. In brain regions affected by pronounced susceptibility effects (e.g., near air-tissue interfaces), the $T2^*$ decay may not be mono-exponential, and thus it is difficult to choose a fixed TE to optimize the functional sensitivity in conventional fMRI protocols [5,6]. On the other hand, with the proposed multi-TE fMRI protocol, the functional sensitivity in brain regions with pronounced susceptibility effect may be improved when data corresponding to different TEs are appropriately combined (e.g., weighted summation or spectral domain analysis) [5,6,25].

We have demonstrated that the LSEPSI technique can quickly measure the T2/$T2^*$ time constants in pre-selected 2D or 3D regions. The proposed spatially selective imaging technique is complementary to conventional whole-brain structural imaging, and may prove valuable for addressing specific questions in both basic neuroscience research (e.g., measuring the TE-dependent BOLD contrast in fMRI) and clinical studies (e.g., measuring the T2′ shortening due to iron deposition). Though we have focused on rapid $T2^*$ and T2 mapping, it should also be noted that LSEPSI has also been shown capable of rapidly measuring temperature

related water frequency shifts relative to the temperature insensitive fat resonance, a capability which may prove useful for tissue temperature monitoring in thermal therapy procedures within the breast [33].

## Acknowledgment

This work was funded in part through NIH Grant R21CA087806.

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