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Improved 3D Look-Locker Acquisition Scheme and Angle Map Filtering Procedure for T_1 Estimation

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Abstract

The 3D Look-Locker (LL) acquisition is a widely used fast and efficient T_1 mapping method. However, the multi-shot approach of 3D LL acquisition can introduce reconstruction artifacts that result in intensity distortions. Traditional 3D LL acquisition generally utilizes centric encoding scheme that is limited to a single phase encoding direction in the k-space. To optimize the k-space segmentation, an elliptical scheme with two phase encoding directions is implemented for the LL acquisition. This elliptical segmentation can reduce the intensity errors in the reconstructed images and improve the final T_1 estimation. One of the major sources of error in LL based T_1 estimation is lack of accurate knowledge of the actual flip angle. Multi-parameter curve fitting procedure can account for some of the variability in the flip angle. However, curve fitting can also introduce errors in the estimated flip angle that can result in incorrect T_1 values. A filtering procedure based on goodness of fit (GOF) is proposed to reduce the effect of false flip angle estimates. Filtering based on the GOF weighting can remove likely incorrect angles that result in bad curve fit. Simulation, phantom, and in-vivo studies have demonstrated that these techniques can improve the accuracy of 3D LL T_1 estimation.

Keywords

Look-Locker T_1 mapping; elliptical segmentation; goodness of fit weighted filtering

Introduction

Spin-lattice relaxation time (T_1) is one of the most basic parameters in MRI. Knowledge of T_1 value is also important in various quantitative MRI techniques, including arterial spin labeling for perfusion measurements and dynamic contrast enhanced-MRI for vascular permeability assessment.

Traditionally, T_1 maps are generated using the inversion recovery spin echo (IRSE) sequence that is considered to be the gold standard. However, IRSE-based T_1 measurements involve long scan times and are generally impractical for in vivo studies. Different methods have been proposed to accelerate the T_1 map acquisition. In general, rapid T_1 measurements fall into two categories: excitation using variable flip angles (1) and fast sampling of the inversion recovery curve (2).

In the variable flip angle (VFA) method T_1 is estimated from a set of at least two spoiled gradient recalled-echo (SPGR) data acquired with different flip angles. With short TR, the VFA method involves relatively short acquisition time. However, the uncertainty in the flip angle due to radiofrequency (RF) magnetic field (B_1) inhomogeneity results in significant

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errors to the T_1 estimation (3,4). As a result, separate B_1 mapping is required to correctly evaluate the T_1 values. In addition, the accuracy of T_1 measurement depends on the choice of flip angles (5,6) and the measurement can suffer from instability if the transverse magnetization is not sufficiently spoiled (7).

Fast sampling of inversion recovery can also be achieved with the Look-Locker (LL) acquisition scheme (8). The LL method monitors the magnetization recovery through T_1 relaxation by continuously acquiring series of images after spin inversion or saturation. The continuous data acquisition can decrease scan time compared to the traditional inversion recovery sequence. The LL T_1 mapping was originally designed for multi-slice 2D acquisition (9–12). Generally, 2D sequences have the time advantage over 3D sequences, but they suffer from low signal-to-noise ratio (SNR) and cross-talk. To reduce the 3D LL acquisition time, Henderson et al. (13) presented a 3D LL acquisition scheme by using multi-shot approach where multiple k-lines are sampled in each shot. Since then, many variants of the 3D LL methods have been proposed to improve the efficiency of T_1 measurements (14–16). However, since the k-lines for an image are acquired at different time points using the multi-shot approach, intensity artifacts can result due to evolving magnetization (17). Normally, the reconstruction artifacts are reduced by using a centric k-space encoding scheme. Conventionally, the 3D LL encoding scheme is linear and centric along a single phase encoding direction (13,15). However, the linear centric encoding scheme is not optimal and can also introduce intensity artifacts that compromise the accuracy of the reconstructed images (18).

Due to B_1 inhomogeneity (13,19), the actual RF angles varies spatially across the image. The accuracy of T_1 computation with the LL acquisition, however, depends on the knowledge of the actual RF flip angles in each voxel. Some published studies (11,19) proposed the application of a multi-step curve fitting procedure in which the flip angle map was initially estimated from multi-parameter curve fitting. The estimated flip angle was then smoothed and used as the actual flip angle map in the final curve fit to calculate T_1 . The flip angle estimated from the curve fitting however may be inaccurate because the additional parameter in curve fitting would increase fitting uncertainty. Unfortunately, simple smoothing methods cannot remove the incorrect flip angles that can still affect the accuracy of the T_1 values.

In this study, we propose elliptical k-space segmentation for the 3D LL sequence that is centrically encoded along both phase encoding directions. We also propose a filtering procedure for the flip angle map to improve the accuracy of T_1 measurements. This filter is based on the goodness of fit (GOF) and can remove incorrect angle estimates. These methods are applied to both digital and real phantoms as well as in-vivo animal brain and demonstrate improved results over the traditional 3D LL methods.

Experimental

3D Look-Locker Elliptical Segmentation

In the fast 3D LL sequence, an inversion pulse is first applied to invert the longitudinal magnetization, followed by a train of small flip angle pulses to sample the magnetization recovery. Because multiple k-lines within a group are acquired after each inversion pulse, it allows rapid acquisition of 3D images for T_1 estimation. However, since different k-lines are sampled at different magnetization states, the reconstructed image can suffer from intensity artifacts. Here we assume that x is the frequency encoding direction and the two phase encoding directions are along the y and z directions. Traditionally, the k_y lines for a single k_z are centrically acquired (13,15). However, such linear k-space segmentation is not truly centric. It was shown that the elliptical centric encoding segmentation can produce images

superior to those obtained from single direction centric encoding (18). Therefore, we implemented the elliptical centric encoding acquisition to minimize the reconstruction artifacts.

The 3D LL pulse sequence is depicted in Fig. 1. After applying an inversion pulse with angle α , N_{TL} k-lines at all the time points, N_{time} , are acquired. An RF pulse of small flip angle β is applied to sample the recovering magnetization. The repetition time between each pulse is $TR = t_d + (N_{time}N_{TL} - 1) \cdot t_r$, where t_d is the initial delay between the inversion pulse and the first β pulse, t_r is the time between each β pulse and t_r is the undisturbed delay after the final β pulse for magnetization recovery prior to the next inversion pulse. The acquisition is elliptically encoded so that the order of k-space data acquisition goes from center k-space to outer k-space. The elliptical segmentation scheme ensures that the most centric part of the k-space is acquired after the same β pulse and thus has the same magnetization. Since the central k-space contributes more to the signal intensity, the elliptical segmentation can reduce intensity artifacts in the reconstructed images. An illustration of the elliptical centric scheme is shown in Fig. 2.

Assuming perfect spoiling of the transverse magnetization and that the magnetization has reached steady state, the transverse magnetization after the n^{th} pulse can be expressed as follows:

$$M_{\perp}(n) = \sin\alpha \cdot M_0 \left\{ \frac{F_E(1-F_1)}{F_0} + \frac{F_1}{(1-\cos\gamma \cos\alpha \cdot EdErF_2)} \left[1 - (1-\cos\gamma)Ed - \cos\gamma \cdot EdEr + \frac{\cos\gamma \cos\alpha \cdot EdErF_E(1-F_2)}{F_0} \right] \right\} \quad [1]$$

where

$$\begin{aligned} E\tau &= \exp(-\tau/T_1) \\ Ed &= \exp(-t_d/T_1) \\ Er &= \exp(-t_r/T_1) \\ F_0 &= 1 - \cos\alpha \cdot E\tau \\ F_1 &= (\cos\alpha \cdot E\tau)^{n-1} \\ F_2 &= (\cos\alpha \cdot E\tau)^{N_{tot}-1} \\ F_E &= 1 - E\tau \end{aligned}$$

and M_0 is the equilibrium magnetization. The derivation of Eq. 1 is presented in the Appendix. As suggested by Henderson et al (13), n in which the center of k-space is sampled should be assigned as the effective n of the reconstructed image. Using the elliptical segmentation scheme, the most centric part of k-space is acquired following the first β pulse and thus should optimize the proper association between the reconstructed image and its effective n . Therefore, the final reconstructed images would be associated with $n = \{1, N_{TL}+1, 2N_{TL}+1, \dots, (N_{time}-1)N_{TL}+1\}$. This optimization would improve the accuracy of the subsequent curve fitting.

Goodness of Fit Weighted Angle Filtering

In principle, the T_1 value can be obtained by fitting the LL data in Eq. 1 with two parameters (M_0 and T_1), provided that the actual RF pulse angles are known. Although the inversion angle of an adiabatic pulse is considered to be sufficiently accurate, the actual flip angle of the RF pulse is not necessarily the same as the nominally prescribed one and shows spatial dependence because of the B_1 inhomogeneity. Using incorrect angles in the curve fitting procedure will lead to inaccurate T_1 values. Curve fitting using three parameters (M_0 , α , and T_1) on a voxel-by-voxel basis can take into account the variation in the actual α . However,

with the additional parameter, α , the curve fitting becomes less robust and could also produce spurious α and T_1 values. To reduce the effect of incorrect α estimates, Deichmann spatially smoothed the estimated α map (19). The smoothed α map was considered to be the actual α map and was used in the subsequent two-parameter curve fit. This approach is analogous to the method suggested by Clare et al (20), in which the inversion angle map is smoothed with a Gaussian kernel. Although the smoothing parameters were not mentioned in these publications, these techniques likely employed a spatially weighted averaging to smooth the respective angle maps. However, weighted spatial averaging still cannot remove the incorrect angles from the calculation that can affect the final T_1 estimates.

In this study, we propose a filtering approach weighted by the GOF to produce reliable estimates. This is a hierarchal multi-step approach in which Eq. 1 is first fitted with three parameters (M_0 , α , and T_1) to the coarse resolution image for generating the preliminary map. The coarse resolution was used to reduce processing time and to improve the effective SNR and hence the consistency of the estimated α map. Since α is expected to vary smoothly, the use of coarse resolution is justified. The inversion angle α , which is generated by the adiabatic pulse, is considered to be constant across the image. Assuming that the correct α estimate can produce better curve fit to the data, α that yields large deviation from the data is likely to be incorrect and should be removed; whereas α that yields small deviation is likely to be a correct estimate and should be weighted more. The preliminary map is therefore filtered based on the GOF of the three-parameter fit. The preliminary coarse α map is interpolated back to the original resolution and α in each voxel is filtered with a user defined spatial kernel using the following equation:

$$\alpha = \left\{ \frac{\sum_i \alpha_i (E_{\text{thre}} - E_i)}{\sum_i (E_{\text{thre}} - E_i)} \mid E_i < E_{\text{thre}} \right\} \quad [2]$$

where

$$E_i = \sqrt{\sum_t (I(i, t) - \hat{I}(i, t))^2} \quad [3]$$

In the above equation, index i represents all the voxels within the spatial kernel in which $E_i < E_{\text{thre}}$, and the time index t includes all the acquired time points. In the above equation, $I(i, t)$ represents the signal intensity at time point t of the coarse voxel in which voxel i belongs to, and $\hat{I}(i, t)$ is the signal intensity of the fitted curve. Instead of using the more common σ^2 value as a weighting factor, Eq. 3 is used because the σ^2 weighting includes intensity variance within the coarse voxel. The variance within the coarse voxel is mostly the result of different tissue types in biological samples. It has relatively small influence on the curve fitting but can affect the σ^2 value greatly. Therefore, Eq. 3 is preferred to the σ^2 value. The summation in Eq. 2 only includes α within the kernel that has its corresponding E_i below a threshold E_{thre} and therefore removes α 's with high fitting error. The weighting factor depends on the difference $(E_{\text{thre}} - E_i)$, so the smaller the E_i , the more the corresponding α_i weight is. The optimal E_{thre} would be determined in this study using simulations. The filtered α map is used in the final full resolution T_1 map calculation using the two-parameter curve fit.

Simulations

The software for data processing and simulations was written in IDL 8.1 (ITT Visual Information Solutions, Boulder, CO). All curve fitting procedures were performed using the MPFIT curve fitting routine (21).

A 3D Shepp-Logan phantom was used to investigate the quality of image reconstruction using the elliptical LL segmentation as well as the effectiveness of the GOF filter. The matrix size of the phantom was $128 \times 128 \times 128$ and composed of ten ellipsoidal segments with eight combinations of M_0 and T_1 (T_1 ranged from 750 msec to 3000 msec). To create the effect of partial volume and reduce the sharpness of the edges, the phantom was then downsampled to $64 \times 64 \times 64$ by simple averaging. Fig. 3a shows the T_1 map of the $64 \times 64 \times 64$ Shepp-Logan phantom. The following parameters were used to simulate the LL acquired images: ($\tau = 8$ msec, $t_d = 10$ msec, $t_r = 1000$ msec, $\alpha = 8^\circ$, $\beta = 180^\circ$, $N_{\text{time}} = 10$, $N_{\text{TL}} = 16$). These parameters are similar to those used in the phantom studies described below.

To simulate the B_1 inhomogeneity, a synthetic B_1 field was created with the following smoothly varying function:

$$B_1(i, j, k) = (1.32 - 0.011(i-21)^2) \times (1.14 - 0.016(j-32)^2) \times (0.77 + 0.014(k-32)^4) \quad [4]$$

where i, j, k are the pixel indices of the simulated volume. The spatially varying B_1 was calculated by multiplying Eq. 4 with the nominal 8° flip angle. This B_1 variation produced flip angle ranged between 7.4° and 9.7° with an average value of 8.8° within the phantom. The range of B_1 field produced by Eq. 4 is in reasonable agreement with a real B_1 field (22). The mean B_1 was chosen to be different from the nominal B_1 so that correct estimation of B_1 was not a result of its value being close to the nominal value.

Two types of noise were added to the images: intensity based Gaussian noise and uniformly distributed white noise. The Gaussian noise depends on the inherent image intensity. In this experiment, we applied different level of Gaussian noise with standard deviations of 2%, 4%, 6%, 8% and 10% of the intensity. The white noise is independent of the intensity and was generated with a mean of zero. The standard deviation of white noise was chosen to be 1% of the mean intensity of the image at the first time point, which has the highest intensity among all time points. All images and noise were created in the image space and the phase information was ignored. The k-space data were then computed and segmentation of the k-space was performed using both linear segmentation and the proposed elliptical segmentation. For each noise level, four sets of data were created by generating the random noise four times, to ensure that the results were not affected by the randomness. Images were reconstructed and the magnitude of the signal was used to compute T_1 . T_1 was computed with the multi-step curve fitting procedure where the preliminary T_1 map was first obtained with three-parameter curve fit. The proposed GOF filter was used to smooth the preliminary T_1 estimates. For comparison, the preliminary T_1 map was also smoothed with the Gaussian weighted spatial averaging method.

Phantom Study

All MRI measurements were performed on a USR70/30 horizontal bore 7T MR scanner (Bruker BioSpin, Karlsruhe, Germany). The 3D LL acquisition with elliptical segmentation and linear segmentation were both implemented for this study. In the phantom study, a 71 mm diameter birdcage resonator was used for both RF transmission and signal reception. Four 12 mm diameter cylindrical glass vials, filled with water doped with different concentration of NiCl_2 (1.2 mM, 0.93 mM, 0.85 mM, 0.66 mM), served as our phantoms of different T_1 values. Since T_1 within each vial was homogenous, artifacts caused by k-space segmentation scheme are expected to be minimal. Therefore, only the elliptical segmentation was used in the phantom study. Different combinations of LL parameters were used to examine the consistency of the LL method. Specifically, the effects of different train length, N_{TL} , and number of time points, N_{time} , were investigated (See Fig. 7 caption). The common acquisition parameters for all the scans were: (TE = 2.2 msec, $t_d = 10$ msec, $t_r = 1000$ msec,

$= 8^\circ$, $N_{\text{dummy}} = 5$, matrix size = $96 \times 96 \times 48$, field-of-view (FOV) = $35 \times 35 \times 60 \text{ mm}^3$. The scan time for each of the LL acquisitions was 12.5 min except for the scan described in Fig. 7b, for which the scan time was 21 min. All the parameters were chosen such that the span over which the inversion recovery being sampled was similar in each scan. A multi-step procedure was employed to compute T_1 with the use of the GOF filtering as well as the Gaussian weighted spatial averaging for comparison. T_1 was also computed using the IRSE acquisition as the reference standard. T_1 measurements using IRSE were performed only on a single slice to reduce the total acquisition time. The acquisition parameters for the IRSE sequence were: (TE/TR = 7.5/10,000 msec, TI = 50, 100, 200, 300, 450, 600, 800, 1000, 1250, 1500, 2000, 2500, 3000 msec, matrix size = 96×96 , in-plane FOV = $35 \times 35 \text{ mm}^2$, slice thickness = 2.5 mm, total scan time = 3.5 hr).

In-Vivo Animal Study

In-vivo LL data was acquired from the acquisition of a normal Sprague-Dawley rat. The protocol of this study was reviewed and approved by the Institutional Animal Welfare Committee. We followed strictly the National Institutes of Health Guide for the Care and Use of Laboratory Animals. During the MRI scan, the animal was anesthetized with 2.5% isoflurane, 30% oxygen and medical grade air. Respiration, rectal temperature and heart rate were monitored throughout the scan. The 71 mm diameter birdcage resonator was used for RF transmission and an in house built surface coil was used for RF reception. 3D LL acquisitions (both linear and elliptical segmentations) were acquired with the following parameters: (TE = 3.1 msec, $\alpha = 9^\circ$, $t_d = 11.5$ msec, $t_r = 1000$ msec, $\alpha = 8^\circ$, $N_{\text{TL}} = 16$, $N_{\text{time}} = 10$, $N_{\text{dummy}} = 5$, matrix size = $128 \times 128 \times 32$, FOV = $25 \times 25 \times 32 \text{ mm}^3$, total scan time = 10.5 min). T_1 maps were calculated using the multi-step procedure with the GOF filter and also with the Gaussian weighted spatial averaging for comparison. IRSE data was acquired on one slice for verification with the following parameters: (TE/TR = 7.6/6,000 msec, TI = 20, 200, 400, 600, 800, 1000, 1500, 2500 msec, matrix size = 128×128 , in-plane FOV = $25 \times 25 \text{ mm}^2$, slice thickness = 1 mm, total scan time = 1.7 hr).

Results

Simulation

The relative root mean square (RMS) error was used to quantify the overall error within an image. The relative RMS error of a given parameter, θ , in a particular region of interest (ROI) was calculated using:

$$\Delta\theta_{\text{RMS}} = \sqrt{\frac{1}{N} \sum_x \left(\frac{\theta(x) - \theta_0(x)}{\theta_0(x)} \right)^2} \quad [5]$$

where $\theta(x)$ and $\theta_0(x)$ are the estimated and the actual values of the parameter in the voxel x , respectively. The summation included all voxels within the ROI and N is the total number of voxels in the summation. The relative mean difference between the estimated and actual values was used to assess the error in the parameter value. The errors in the entire image were calculated for each data set. In addition, we also computed the errors at the edges between structures with different intensity since the reconstruction artifacts are expected to be more prominent at the edges. The edges are identified if the voxels within a $2 \times 2 \times 2$ region consisted of different combinations of M_0 and T_1 .

The original T_1 map of the Shepp-Logan phantom is shown in Fig. 3a. For comparison, the corresponding maps generated using the linear and elliptical LL segmentation are shown in Fig. 3b and c, respectively. The relative RMS errors in the image intensity and T_1 values in the reconstructed images using both linear and elliptical segmented LL acquisitions are

summarized in Table 1. This table shows data on noiseless images to emphasize the intensity artifacts inherent in the 3D LL acquisition. The errors in intensity were different at different acquisition time points. Larger errors were observed between the third and sixth images (associated with the 33th, 49th, 65th and 81st pulses). These images were located around the null points in the inversion recovery curves. Therefore, they had lower SNR and were more susceptible to reconstruction artifacts. Since the edges are characterized by high spatial frequencies, the RMS errors are expected to be more prominent at the edges. The results shown in Table 1 confirm this. As seen from this Table, an overall increase in the RMS errors was observed using the linear LL scheme relative to the elliptical segmented LL scheme. As listed in Table 1, using the elliptical segmentation reduced the RMS error in T_1 by 1.3% in the whole image and 1.9% at the edges. The superior performance of the elliptical segmented LL scheme can also be visually appreciated by comparing Fig. 3b with 3c. In this example, a ripple pattern artifact was seen in the central ellipse in the T_1 map generated using the linear segmentation LL scheme in Fig. 3b. This artifact was greatly reduced using the elliptical segmentation as shown in Fig. 3c. Fig. 4 shows a typical example of data obtained from a voxel outside of the ripple region in Fig. 3. In this example, the T_1 values generated with the elliptical segmentation are closer to the actual values.

The relative mean differences in the image intensity and T_1 values between the LL acquired images and the original images are summarized in Table 2. As can be seen from this Table, the elliptical segmentation also reduced the negative bias by about 0.7% in the whole image and 1.5% at the edges.

Without noise, the voxel-by-voxel three-parameter curve fit in the presence of B_1 inhomogeneity yielded T_1 errors comparable to those listed in Table 1. However, once noise was introduced, voxel-by-voxel curve fitting using three parameter fit resulted in T_1 error of 13% for elliptical segmented LL images with 6% Gaussian noise. We therefore applied the multi-step procedure to improve the T_1 estimation in the presence of B_1 inhomogeneity. In this study, we chose to downsample the images by a factor of 4 along each dimension for the initial three-parameter curve fit (64 times faster processing time). The parameters for the GOF filter and Gaussian weighted spatial averaging were determined by searching for the parameters that yielded the smallest RMS error in T_1 estimation. The optimal kernel size for the GOF filter was found to be 11 voxels in width. Additional Gaussian weighted spatial filter with optimal variance $\sigma^2 = 4.0$ was applied. The optimal threshold E_{thre} in Eq. 2 was found to be $2.0 \times \bar{E}_i$, where $\bar{E}_i$ is the mean E_i within the kernel. This particular E_{thre} removed on average about 6% to 18% values within the kernel, depending on the noise level. It was also found that the optimal width for the Gaussian weighted averaging kernel was 17 voxels in order to minimize the T_1 error. In this case, the optimal variance of the Gaussian weighted spatial filter was found to be $\sigma^2 = 2.0$.

All map smoothing procedures employed the optimal parameters mentioned above. In general, the map obtained from the three-parameter curve fitting followed by smoothing showed good consistency at all noise levels we tested. Using the Gaussian weighted spatial averaging, the estimated map yielded errors between 1.7% and 2.0%, whereas map smoothed by the GOF filter yielded errors between 0.9% and 1.1%. Application of the GOF filter improved the accuracy of T_1 estimation compared to the Gaussian weighted spatial averaging. For linear LL acquisition, the GOF filter reduced T_1 error from 7.2% to 6.8% at 10% Gaussian noise and from 5.5% to 4.7% at 2% Gaussian noise. For elliptical LL acquisition, the GOF filter reduced the errors in T_1 from 6.7% to 6.6% at 10% Gaussian noise and from 4.4% to 4.0% at 2% Gaussian noise. In addition, the GOF filter reduced the negative bias in T_1 estimation by about 2.0% in the linear LL acquisition and about 1.5% in the elliptical LL acquisition.

Fig. 5 illustrates the relative RMS errors in T_1 estimation in the presence of B_1 inhomogeneity at different Gaussian noise levels. The proposed LL modifications with elliptical segmentation and GOF filter were compared against the traditional LL method with linear segmentation and Gaussian weighted spatial averaging. T_1 computation using the proposed modifications showed smaller errors than the traditional methods and greater improvement was observed at the edges in the Shepp-Logan phantom. The proposed methods also reduced the negative bias of T_1 values calculated from LL data. On average, the relative mean difference in T_1 using linear segmentation and Gaussian weighted spatial averaging was about -3.2% for the whole image and -4.9% at the edges for all noise levels. The relative mean difference in T_1 using the proposed LL modifications was about -0.6% for the whole image and -1.7% at the edges.

Phantom Study

The T_1 maps of the Ni-doped water phantoms using the elliptical LL acquisition with the GOF filter are shown in Fig. 6a. The T_1 maps show rather homogenous T_1 within each of the four tubes. As an example, the LL data along with the fitted curves obtained from the center voxel in each tube is shown in Fig. 6b. The values of T_1 obtained from the curve fitting are: 817 msec, 962 msec, 1056 msec, and 1259 msec for the four NiCl_2 concentrations (highest to lowest concentration). Fig. 7 shows four representative T_1 distributions in the phantoms using the GOF filtering and Gaussian weighted spatial averaging methods. These distributions were generated using different acquisition parameters. The parameters were chosen such that much of the inversion recovery was covered in each case. The T_1 values computed from the IRSE acquisition were considered to be the real T_1 values and are shown as vertical lines in Fig. 7. These distributions show that the calculated T_1 value from the LL acquisition was on average lower than the real T_1 values. Out of all the cases except for one, the GOF filtered map yielded T_1 estimates closer to the real T_1 compared to the Gaussian weighted averaging map. The GOF filtered map yielded T_1 values that were within one standard deviation of the real T_1 values 83% of the time and within two standard deviations 100% of the time. The Gaussian weighted averaging map yielded T_1 values within one standard deviation of the real T_1 values only 21% of the time but 96% of the time they were within two standard deviations.

The standard deviations of T_1 generated from both smoothing methods were within 3% of their respective mean T_1 values except in one case where the standard deviation of one phantom was 5% of its mean T_1 value. In general, using smaller N_{TL} and larger N_{time} yielded narrower T_1 distribution or smaller standard deviation. In most cases, the standard deviations in T_1 values between the two smoothing methods were within 0.1% of each other. However, as shown in Fig. 7a and b, the Gaussian weighted spatial averaging method occasionally yielded distributions that were noticeably boarder. In three cases (third peak in b and fourth peak in a and d), the T_1 distribution was observed to be non-Gaussian. In almost all these cases, the GOF filter was able to eliminate this non-Gaussian behavior.

Fig. 8 shows the T_1 maps of the phantoms that have non-Gaussian distribution. From these examples, it appears that the non-Gaussian part of the distribution is mainly the result of T_1 overestimation at the water-glass boundary. The hyper-intense ring is likely an artifact as the phantoms were homogenous and the ring was not present in the T_1 maps obtained from other parameters. While the Gaussian weighted averaging method smeared the over-estimated T_1 as a diffuse hyper-intense ring in Fig. 8a and c, the GOF filtered map removed much of the hyper-intensity in Fig. 8b. The GOF filter also appears to be more immune to incorrect angle estimation (Fig. 8d).

In-Vivo Animal Study

Fig. 9a-c show the brain T_1 maps acquired using the linear and elliptically segmented LL sequences and the corresponding slice acquired using the IRSE sequence. In general, the T_1 maps based on the GOF filter were less noisy compared to those with Gaussian weighted averaged map. Otherwise, there were no other obvious differences in the T_1 maps acquired with the LL acquisitions. Fig. 9d and e show the T_1 distributions of the cortical gray matter (GM) and corpus callosum (CC) white matter (WM) of the three T_1 maps. We assumed that the T_1 values obtained using the IRSE acquisition were the actual T_1 values. The T_1 distributions with elliptical segmentation and GOF filter were sharper and closer to the actual T_1 distributions compared to the linear segmentation. Table 3 summarizes the average T_1 values in the cortical region and CC of the rat brain. Similar to the simulation and phantom studies described above, the average T_1 values obtained with LL acquisitions were lower than the actual values. The average T_1 values based on IRSE were within one standard deviation calculated from the LL acquisitions, with the exception of the T_1 values in the CC region using linear segmentation. GOF filtered map generally reduced the standard deviation compared to Gaussian weighted averaged map. On the other hand, the elliptical segmentation produced T_1 values closer to the actual values compared to the linear segmentation. Table 4 shows the RMS differences between the LL and the IRSE T_1 maps. In the regions with high SNR such as the cortex and CC, the RMS differences were below 200 msec. However, due to the physical limitation of the surface coil, parts of the entire T_1 maps included regions with lower SNR. The overall RMS difference, including these low SNR regions, increased to about 350 msec. In general, combination of the elliptical segmentation and GOF filter reduced the RMS differences by about 1 to 5%, even when the comparison included the low SNR regions. The one noticeable exception was the RMS difference in the CC, which was reduced by about 20% using the elliptical segmentation compared to the linear segmentation.

Discussion

In this study, we presented a modification to the LL acquisition scheme and introduced the GOF filtering of the flip angle map to improve the quality of 3D T_1 mapping using the Look-Locker sequence. We performed computer simulations, phantom studies and in-vivo animal brain study to evaluate the performance of these modifications.

The limitation of the 3D LL technique arises from the acquisition of each image at different states of magnetization. This introduces intensity artifacts in the images and a negative bias in the T_1 estimation. We demonstrated, based on the simulations, phantom and in-vivo studies, that the elliptical LL segmentation can reduce the errors in T_1 measurements compared to the linear segmentation. Application of the GOF filter to smooth the flip angle map can further reduce errors in the T_1 estimation. Combination of both elliptical segmentation and GOF filter is shown to improve the accuracy of T_1 estimation. Larger improvements are seen at lower noise level. At higher noise levels, however, the proposed methods yielded smaller improvement because the noise overshadows the artifacts. It is also worth noting that the elliptical segmentation appeared to greatly reduce errors in smaller regions such as the CC in rat brain as shown in our in-vivo study.

It is worth noting that linear segmentation generally produces excessive errors along the k_y direction and relatively modest errors along the k_z direction. Compared to linear segmentation, elliptical segmentation reduces errors along the k_y direction; however the errors along the k_z direction increases slightly. In the case where T_1 does not change along one direction, linear segmentation might perform better by setting k_y parallel to this direction. In all other cases, elliptical segmentation has the advantage because it reduces the overall error and artifacts as shown in our study.

We observed that the choice of parameters used in the LL acquisition can introduce artifacts that can be seen on the T_1 maps. The presence of these artifacts appears to depend on the combination of T_1 values and the acquisition parameters. For example in Fig. 3, the ripple artifact only occurred in one part of the image. Similarly, the ring artifact in the phantom studies only appeared in several tubes with selected LL acquisition parameters. One possible reason for the ring artifact could be the result of higher susceptibility at the interface of the glass wall and water. This artifact could not be eliminated by simple averaging alone. Conversely, the GOF filter significantly reduced/removed the artifacts by eliminating the incorrect angles in the preliminary map. In addition to reducing the ring artifact, the GOF filter was also shown to decrease the negative bias in the T_1 estimation in the phantom studies.

In this study, we assumed that the inversion angle, α , did not deviate from the prescribed angle. The use of an adiabatic pulse for the inversion pulse perhaps justifies this assumption. As demonstrated by Kingsley et al (23), the adiabatic pulse could deliver spin inversion with at least 99% efficiency, which corresponds to α above 172° , in almost all cases. As suggested by Clare et al (20), we also attempted to include α in the curve fitting in our T_1 calculation using the IRSE acquisition (results not shown). The fitted α was 175.5° on average and the resulting phantom T_1 values increased between 0.2% and 0.4%. Since the LL sequence utilized the same adiabatic pulse, similar variation in α could be expected. In theory, fitting for α can also be included in the analysis of LL data. Unfortunately, we found that in most cases, there were large number of combinations of T_1 , α , and N_{time} that would yield the same χ^2 fitting if all three parameters were allowed to vary. Acquiring more time points might ameliorate this problem. However, it would take longer scan time that may not be appropriate for in vivo studies and even then the resolution of this problem is not guaranteed. Since the difference is expected to be less than 0.5%, we fixed α at 180° .

Several factors could affect the T_1 mapping using the LL acquisition scheme. Published literature has shown that the choice of TI can affect the accuracy of T_1 estimation using an IRSE sequence (24). Similarly, different selections of α and N_{time} in a LL acquisition were shown to impact the results of T_1 computation (see Fig. 7). With all the parameter combinations we tested, results obtained from different parameters were all within 3% of each other when using the GOF filter.

The use of Eq. 1 relies on two conditions: the transverse magnetization is completely spoiled before each RF pulse and the magnetization is in steady state. In this study, we used both the RF and gradient spoiling methods. A standard RF spoiler with 117° increment from pulse to pulse was applied (25). The strength of the gradient spoiler was determined by increasing the gradient amplitude and/or duration in the SPGR sequence until the signal reached an asymptotic value. Based on our study, it appears that a gradient amplitude of 150 mT/m applied for 4 msec is sufficient. The two spoiling methods should create sufficient incoherence in the transverse magnetization. Additionally, adequate number of dummy scans is necessary to drive the magnetization into steady state. Using a Bloch simulator (26), we found that $N_{\text{dummy}} = 5$ is needed to reach the steady state if T_1 is below 1800 msec. If the T_1 value is 3000 msec, a value of 7 is required for N_{dummy} .

In conclusion, the proposed elliptical segmentation scheme, in combination with the GOF map filtering, is shown to improve the accuracy and reduce the artifacts in the T_1 map using 3D LL acquisition.

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Abbreviations

B₁	RF field
FOV	field-of-view
GOF	goodness of fit
IRSE	inversion recovery spin echo
LL	Look-Locker
RF	radiofrequency
RMS	root mean square
ROI	region of interest
SNR	signal-to-noise ratio
SPGR	spoiled gradient recalled-echo
VFA	variable flip angle

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Appendix

Derivation of the Transverse Magnetization in a Look-Locker Acquisition

The LL sequence is composed of an inversion pulse followed by a series of small flip angle pulses, α , to acquire the SPGR images. Let M_n^- and M_n^+ be the longitudinal magnetization right before and after the n^{th} pulse following the inversion. Then:

$$M_n^+(0) = M_n^- \cos \alpha \quad [\text{A1}]$$

The $(n + 1)^{\text{th}}$ pulse is applied at time τ after the n^{th} pulse, so:

$$M_n^+(\tau) = M_0(1 - e^{-\tau/T_1}) + M_n^- \cos \alpha e^{-\tau/T_1} = M_{n+1}^- \quad [\text{A2}]$$

Let N_{tot} be the total number of pulses applied after each inversion, and M_{γ}^- be the longitudinal magnetization right before the γ pulse. The γ pulse is applied at time t_{γ} after the last pulse (N_{tot}). Therefore, the magnetization just prior to the application of the γ pulse is given by

$$M_{\gamma}^{-} = M_{N_{\text{tot}}}^{+}(t_r) = M_0(1 - e^{-t_r/T_1}) + M_{N_{\text{tot}}}^{-} \cos \alpha e^{-t_r/T_1} \quad [\text{A3}]$$

The magnetization after the pulse is:

$$M_{\gamma}^{+}(0) = M_{\gamma}^{-} \cos \gamma = [M_0(1 - e^{-t_r/T_1}) + M_{N_{\text{tot}}}^{-} \cos \alpha e^{-t_r/T_1}] \cos \gamma \quad [\text{A4}]$$

Notice that Eq. A4 also holds for saturation recovery sequence where is 90° instead of 180° . The first pulse is applied at time t_d after the pulse, therefore the longitudinal magnetization right before the first pulse is:

$$M_1^{-} = M_0(1 - e^{-t_d/T_1}) + M_{\gamma}^{-} \cos \gamma e^{-t_d/T_1} \quad [\text{A5}]$$

The following simplified notation is used:

$$\begin{aligned} E\tau &= \exp(-\tau/T_1) \\ Ed &= \exp(-t_d/T_1) \\ Er &= \exp(-t_r/T_1) \end{aligned}$$

So, the magnetization right before the n^{th} pulse is:

$$M_n^{-} = M_0(1 - E\tau) [1 + \cos \alpha E\tau + (\cos \alpha E\tau)^2 + \dots + (\cos \alpha E\tau)^{n-2}] + [M_0(1 - Ed) + M_{\gamma}^{-} \cos \gamma Ed] (\cos \alpha E\tau)^{n-1} \quad [\text{A6}]$$

The series in the first term can be summed and Eq. A6 yields:

$$M_n^{-} = M_0(1 - E\tau) \left[\frac{1 - (\cos \alpha E\tau)^{n-1}}{1 - \cos \alpha E\tau} \right] + [M_0(1 - Ed) + M_{\gamma}^{-} \cos \gamma Ed] (\cos \alpha E\tau)^{n-1} \quad [\text{A7}]$$

Combining Eq. A3 with Eq. A6, M_{γ}^{-} under steady state condition can be calculated:

$$\begin{aligned} & M_{\gamma}^{-} = M_0(1 - Er) \\ & + \left\{ M_0(1 - E\tau) \left[\frac{1 - (\cos \alpha E\tau)^{N_{\text{tot}}-1}}{1 - \cos \alpha E\tau} \right] + [M_0(1 - Ed) + M_{\gamma}^{-} \cos \gamma Ed] (\cos \alpha E\tau)^{N_{\text{tot}}-1} \right\} \cos \alpha Er \\ & \Rightarrow (1 - \cos \gamma Ed \cos \alpha Er (\cos \alpha E\tau)^{N_{\text{tot}}-1}) M_{\gamma}^{-} \\ & = M_0 \left\{ (1 - Er) + (1 - E\tau) \left[\frac{1 - (\cos \alpha E\tau)^{N_{\text{tot}}-1}}{1 - \cos \alpha E\tau} \right] + (1 - Ed) (\cos \alpha E\tau)^{N_{\text{tot}}-1} \cos \alpha Er \right\} \end{aligned}$$

which leads to

$$M_{\gamma}^{-} = \frac{M_0}{1 - \cos \gamma Ed \cos \alpha Er (\cos \alpha E\tau)^{N_{\text{tot}}-1}} \left\{ (1 - Er) + (1 - E\tau) \left[\frac{1 - (\cos \alpha E\tau)^{N_{\text{tot}}-1}}{1 - \cos \alpha E\tau} \right] + (1 - Ed) (\cos \alpha E\tau)^{N_{\text{tot}}-1} \cos \alpha Er \right\} \quad [\text{A8}]$$

Substituting M_{γ}^{-} in Eq. A8 into Eq. A7 yields:

$$\begin{aligned}
 M_n^- = M_0 \left\{ \frac{1-E\tau}{1-\cos\alpha E\tau} (1-(\cos\alpha E\tau)^{n-1}) \right. \\
 \left. + \frac{(\cos\alpha E\tau)^{n-1}}{1-\cos\gamma E d \cos\alpha E r (\cos\alpha E\tau)^{N_{\text{tot}}-1}} \left[1 - (1-\cos\gamma) E d \right. \right. \\
 \left. \left. - \cos\gamma E d E r + (1-E\tau) \cos\gamma E d \cos\alpha E r \left(\frac{1-(\cos\alpha E\tau)^{N_{\text{tot}}-1}}{1-\cos\alpha E\tau} \right) \right] \right\} \quad [\text{A9}]
 \end{aligned}$$

The transverse magnetization $M^-(n)$ is equal to M_n^- , which is represented in Eq. 1.

Figure 1.

Schematic diagram of the proposed elliptical segmented 3D LL sequence. After an inversion pulse, $N_{\text{time}} \times N_{\text{TL}}$ k-lines are acquired. Within each shot (external bracket), N_{TL} of k lines are acquired at each time point (internal bracket). In this implementation, both G_y and G_z increase with increasing number of pulse; while a fixed G_z is employed within each shot in the traditional linear segmented LL acquisition.

Figure 2.

Examples of different k space segmentation schemes with $N_{TL} = 4$ in the 3D LL sequence. k_y and k_z are the two phase encoding directions whereas k_x is the fully sampled frequency encoding direction. Regions with different colors in the k-space are acquired with different pulses. Intensity artifact may occur because different k space is sampled at different magnetization. a) The traditional LL scheme is linearly segmented with fixed k_z . b) The proposed elliptical segmentation scheme ensures that acquisition is centered in both phase encoding directions and should provide images with less intensity artifact.

Figure 3. T1 maps of the 3D Shepp Logan phantom shown in the x-y plane: a) original, b) generated using the LL acquisition with linear segmentation, and c) elliptical segmentation. A ripple like artifact (arrow) is visible in b, but is considerably reduced in c.

Figure 4.

The LL data of a representative voxel outside of the ripple area in the Shepp Logan phantom shown in Fig. 3. In this example, there was an underestimation in intensity before and overestimation after the null point in the LL acquisition. The elliptical segmented LL acquisition generally yielded data closer to the original data. In the original image, $T_1 = 1600$ msec; the linear segmented LL acquisition yielded $T_1 = 1514$ msec and the elliptical LL acquisition yielded $T_1 = 1568$ msec. This figure represents data without any noise.

Figure 5.

The relative RMS error of the T_1 values using different LL methods in the presence of noise and B_1 affected flip angle in the Shepp-Logan phantom. Traditionally, the LL method utilizes a linear segmentation scheme and Gaussian weighted spatial averaging map. We propose to modify the acquisition scheme with elliptical segmentation and use the GOF filter on the map. Each data point in the graph represents the average error over the four data sets. The standard deviation at all points is below 0.03% and therefore is not shown in this figure. In general, the RMS error is lower using the proposed techniques (Elliptical + GOF), and the improvement is particularly noticeable at the edges.

Figure 6.

a) The T1 map of the Ni-doped water phantoms using the elliptical LL acquisition with the GOF filter (parameters listed as in Fig. 7c). The T1 maps show rather homogenous T1 within all the four tubes. b) The LL data and the fitted curves obtained from the center voxel in each tube. The four T1's obtained from the curve fits are: 817 msec (circle), 962 msec (square), 1056 msec (rhombus), and 1259 msec (triangle).

Figure 7.

The T_1 histograms of the Ni-doped water phantoms using different methods and parameters. Data acquired with a) $\tau = 10$ msec, $N_{\text{time}} = 10$, $N_{\text{TL}} = 16$, b) $\tau = 15$ msec, $N_{\text{time}} = 10$, $N_{\text{TL}} = 8$, c) $\tau = 12.5$ msec, $N_{\text{time}} = 8$, $N_{\text{TL}} = 16$, and d) $\tau = 16.7$ msec, $N_{\text{time}} = 6$, $N_{\text{TL}} = 16$. The vertical lines are the T_1 values acquired using the IRSE acquisition and are considered to be the true T_1 values. In most cases, the distributions using the two angle smoothing techniques produced T_1 with very similar width. The GOF filtered map generally produced T_1 values that are closer to the true values. In three cases (third peak in b and fourth peak in a and d), the T_1 distribution is non-Gaussian and is likely the result of incorrect estimation. The GOF filter is able to remove some of these possible false angle estimations.

Figure 8.

T_1 maps of the Ni-doped phantoms. a and b correspond to the third peak in Fig. 7b; c and d correspond to the fourth peak in Fig. 7d. The window and level of the images are set to $\pm 15\%$ of the actual T_1 . In these images, the hyper-intense ring surrounding the water-glass interface is likely the result of incorrect angle estimation. The Gaussian weighted averaging map appears to smear the hyper-intense ring through the images as shown in a and c. The GOF filtering map on the other hand removes much of the rings seen in b and d.

Figure 9.

T1 maps of rat brain using a) LL acquisition with linear segmentation and Gaussian weighted averaged map, b) LL acquisition with elliptical segmentation and GOF filtered map, and c) IRSE acquisition from the corresponding slice. A small surface coil superior to the brain was used in acquisition. As a result, lower SNR was observed at the bottom part of the image. In general, a and b appeared very similar, with image a appearing noisier. IRSE has higher SNR due to long TR, but its total scan time was too to be of practical use. Figures d and e show the T1 histograms of the cortical gray matter and corpus callosum (CC) white matter. LL acquisition with elliptical segmentation and GOF filter produced distributions that were sharper and closer to (IRSE) values compared to the traditional LL methods. Numerical comparisons are summarized in Table 3.

Table 1

Relative RMS error of the image intensity and T_1 value of the reconstructed images from the LL acquisition using linear segmentation (Linear LL), and from the elliptical segmented LL sequence (Elliptical LL). Noiseless images were used to emphasize the intensity artifacts as a result of the 3D LL acquisition. Errors of the whole phantom as well as at the edges are presented.

img (n^{th})	Linear LL		Elliptical LL	
	whole	edges	whole	edges
1	2.5%	3.8%	1.9%	2.9%
17	4.4%	6.6%	3.9%	5.8%
33	152.8%	228.1%	149.1%	222.4%
49	82.1%	122.5%	65.6%	98.0%
65	265.8%	394.7%	193.1%	287.8%
81	16.8%	23.2%	14.7%	21.4%
97	1.1%	1.7%	0.7%	1.1%
113	0.7%	1.0%	0.4%	0.7%
129	0.5%	0.7%	0.3%	0.5%
145	0.3%	0.5%	0.2%	0.3%
T1 Error	4.5%	6.7%	3.2%	4.8%

Table 2

The relative mean difference of the image intensity and T_1 values between the LL acquired images and the original images.

img (n^{th})	Linear LL		Elliptical LL	
	whole	edges	whole	edges
1	-0.4%	-1.1%	-0.2%	-0.4%
17	-1.0%	-2.4%	-0.7%	-1.5%
33	13.3%	29.6%	13.4%	29.9%
49	14.6%	32.6%	11.2%	24.9%
65	35.8%	76.4%	23.3%	50.5%
81	-0.5%	0.5%	0.0%	-0.2%
97	0.3%	0.7%	0.1%	0.2%
113	0.2%	0.4%	0.0%	0.1%
129	0.1%	0.3%	0.0%	0.1%
145	0.1%	0.2%	0.0%	0.1%
T1 Error	-1.6%	-3.5%	-0.9%	-2.0%

The T₁ values (in msec) of the cortical gray matter (GM) and white matter (WM) at the corpus callosum of the rat brain obtained from T₁ map as shown in Fig. 9.

Table 3

	IRSE	LL linear w/spatial avg	LL linear w/GOF filter	LL ellip w/spatial avg	LL ellip w/GOF filter
GM	1416 ± 126	1344 ± 164	1332 ± 136	1358 ± 158	1342 ± 130
WM	1157 ± 66	1066 ± 75	1068 ± 74	1091 ± 75	1090 ± 75

The RMS differences in the T_1 values (in msec) between the LL and the IRSE acquisition schemes using the T_1 maps shown in Fig. 9. The differences in the overall T_1 values were calculated for the cortical gray matter, and the corpus callosum.

Table 4

	LL linear w/spatial avg	LL linear w/GOF filter	LL ellip w/spatial avg	LL ellip w/GOF filter
GM	178	171	174	164
WM	104	102	83	84
overall	370	361	337	333