Low-power Slice Selective Imaging of Broad Signals

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Imaging of solid

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Abstract

One of the major challenges in using magnetic resonance imaging (MRI) to study immobile samples, such as solid materials or rigid tissues like bone or ligaments, is that the images appear dark due to these samples short-lived signals. Although it is well known that narrowband signals can be excited in inhomogeneously-broadened lines, it is less well known that similar effects can be observed in dipolar-broadened systems. These long-lived signals have not been used much, mainly because their description frequently does not match intuition. While 3D imaging with these signals has previously been reported, here we focus on the demonstration of faster, 2D slice-selective imaging. The faster imaging provides more flexibility for visualizing these rigid objects, an approach that is not compatible with ultra-short echo time (UTE) techniques. We also focus on the frequently-encountered regime where the maximum power achievable for rf pulses is significantly weaker than the linewidth. This regime is typically encountered in clinical MRI scanning or large volume setups. When compared to UTE and conventional slice-selective spin echo, this technique provides better representations of the sample, and provides higher signal-to-noise ratios than spin-echo techniques in both the high and low power regimes for the eraser sample.

Introduction

Magnetic resonance imaging (MRI) has become a widely used technique providing exquisite images with excellent contrast detail of soft tissue and anatomic structures [1, 2] , and is increasingly used in materials science [3-7]. One of the major challenges in imaging solid materials or rigid tissues (such as bone and ligament) is that their signals

decay very quickly (within $\sim 1 \mu\text{s} - 1 \text{ ms}$), so they are mostly invisible in conventional MRI images [8-12]. Several advanced methods involving the use of specialized hardware have been developed for visualizing relatively short-lived signal components, but are frequently incompatible with *in vivo* constraints [8-14]. In solids or rigid tissues, the signals are short-lived, and the spectrum is 3-5 orders of magnitude broader than in liquids. Therefore, when the gradient strengths are limited, like in *in vivo* imaging, the linewidth becomes the limiting factor for resolution [15].

Two main processes contribute to the short signal lifetimes in rigid samples. First, the magnetic susceptibility of the tissues may vary in space, giving rise to considerable magnetic field inhomogeneity [16]. Second, the restricted molecular motion inside the tissues can leave dipolar couplings and chemical shift anisotropy in effect. These interactions can result in extremely strong signal dephasing and correspondingly broad resonance lines.

While it is well known that narrowband signals can be excited from inhomogeneously-broadened lines, it has also been demonstrated that long-lived signals can be excited from systems with homogeneously broadened dipolar spectra by using either a long and weak single rf irradiation or such irradiation in combination with a subsequent strong π pulse [17-20]. We have previously referred to the first method as the long-lived response (LLR) technique, and the second as the long-lived response echo (LLRE) technique. Our previous work indicated that dipolar coupling complexity may play an important role in producing the LLR and LLRE signals [21]. This effect was demonstrated by diluting the proton concentration in the sample, which showed a nonlinear effect on the LLR and LLRE signals. This observation was incompatible with a

description based solely on inhomogeneous broadening. The line narrowing afforded by this LLRE signal excitation is of great utility and could be used to enhance image resolution. Although these techniques have been implemented in 3D MRI [20, 21], showing improved resolution and power behavior, the implementation of direct slice selection is not obvious for signals arising in dipolar coupled systems.

Here, we demonstrate that the LLRE signal can be made slice-selective by applying a gradient during the π pulse, making the method compatible with fast 2D MRI applications. The approach is tested on samples of rubber materials, and their 2D images acquired with the slice-selective LLRE signals are compared to those from with conventional spin echo and UTE methods. We also include a description of the free induction decay obtained from the long-lived signals as a function of flip angle.

LLR and LLRE Formation Theory

To understand the origin of the long-lived signal, the collective evolution of all frequency components of the density operator has to be considered. Starting from equilibrium, where the magnetization is aligned with the magnetic field, a weak excitation pulse with duration t_p gives rise to the FID signal calculated by

$$M(t) = \text{Tr}\{S_+ \rho(t)\}, \rho(t) = \exp(-iHt) \rho(t_p) \exp(iHt), t > t_p. \quad (1)$$

$\rho(t)$ is the density operator, S_+ is an observable in a quadrature detection experiment, and H represents the full spin Hamiltonian, that describes free evolution of the system and includes internal spin interactions such as dipolar couplings and chemical shifts for all interacting spins.

Following the analysis proposed by Khitrin [18], we introduce the spectral components

$$S_\omega: \exp(-iHt) S_\omega(t) \exp(iHt) = \exp(-i\omega S_z t) S_\omega(t) \exp(i\omega S_z t). \quad (2)$$

A spectral component S_ω is a part of the density operator that oscillates with frequency ω and in general is a linear combination of all possible single-quantum coherences for the spin system. Here, ω can take values from the set of spectral frequencies of the full spin Hamiltonian, H . Let us calculate the spectral components for an inhomogeneously broadened line, e.g., the signal of water in the presence of magnetic field gradient. A homogeneously broadened line can be analyzed in the same way, except that the linear response regime would have to be used[18]. The rotating frame Hamiltonian during the weak excitation pulse is given by[18]

$$H_1(\mathbf{r}) = \omega_1 S_y + \omega(\mathbf{r}) S_z. \quad (3)$$

The term $\omega(\mathbf{r})$ is a function of the spatial coordinates and describes the nonuniformity of the local static magnetic field, B_0 . The pulse applied to the initial z-magnetization leads to its rotation around the tilted effective field, $\omega_{eff} = \sqrt{\omega_1^2 + \omega^2}$, whose direction is specified by a unit vector $\mathbf{u} = \{u_x, u_y, u_z\}$, leading to

$$\exp(-iH_1 t_p) S_z \exp(iH_1 t_p) = u_y \sin \theta S_x + u_y u_z (1 - \cos \theta) S_y + (\cos \theta + u_z^2 (1 - \cos \theta)) S_z, \quad (4)$$

where $\theta = \omega_{eff} t_p$ is the effective flip angle. Taking into account that the z component of magnetization does not contribute to the FID signal, we obtain the expression for the frequency components,

$$S_\omega = \left[\frac{\sin(\omega_1 t_p \sqrt{k^2 + 1})}{\sqrt{k^2 + 1}} + ik \frac{1 - \cos(\omega_1 t_p \sqrt{k^2 + 1})}{k^2 + 1} \right] S_+, \quad (5)$$

where $k(\mathbf{r}) = \omega(\mathbf{r})/\omega_1$. The conjugated term proportional to the operator S_- is ignored in Eq. (5). The FID can be calculated from the inverse Fourier transform of the S_ω distribution function [22],

$$M(t) = \int_{-\infty}^{\infty} S_\omega e^{i\omega t} d\omega. \quad (6)$$

while the spectrum is obtained from the Fourier transform of the FID signal, assuming that the acquisition starts at $t = 0$,

$$I(\omega) = \int_0^{\infty} M(t) e^{-i\omega t} dt. \quad (7)$$

We note that the amplitudes of the individual spectral components S_ω are not equivalent to the spectral intensities $I(\omega)$ at a given frequency ω , due to the different integration limits in Eq. (6) and (7).

The appearance of the FID calculated from Eq. (6) is shown in Fig. 1(a). Following Eq. (7), the spectrum for the LLR signal is calculated from the Fourier transform of the positive ($t > 0$) part of this signal, and is shown in Fig. 1(c). The effect of the hard 180° pulse that follows the initial excitation pulse in the LLRE sequence is equivalent to changing the sign of the linear terms in the Hamiltonian (or time reversal in Eq. (6)) [7]. In this case, the calculated spectrum is the Fourier transform of the negative part of the FID in Fig. 1(a), yielding the characteristic lineshape in Fig. 1(b). These spectra match the published long-lived response lineshapes for inhomogeneously broadened water proton signals. [18]

Fig.1 Numerical simulation of the long lived signals in water in the presence of a static field gradient corresponding to a variation in the Larmor frequency of 100 kHz over the characteristic sample size. $B_1 = 10$ Hz, and on-resonance flip angle $\omega_1 t_p = \pi/2$. (a) The FID calculated as the reverse Fourier transform of Eq.(4) for LLR and LLRE experiments. A π pulse in LLRE sequence virtually reverses the direction of the arrow of time. (b) and (c): Spectra of LLRE and LLR signals, respectively.

For a system of many coupled spins, S_ω is proportional not only to the operator S_+ but a combination of all single-quantum operators. In this case, the operator part of S_ω may be calculated from the following commutation equation

$$[H - \omega S_z, S_\omega] = 0. \quad (8)$$

A quantitative description of the spectral components generation mechanism in a many-spin system with a homonuclear dipolar interaction network is not yet developed, mainly due to the difficulty in simulating systems with a sufficient number of coupled spins. A possible qualitative explanation, however, has been suggested and the similarity of the signals obtained in inhomogeneous and homogeneous systems have been demonstrated [17, 18]. It has been suggested that a non-vanishing chemical shift difference between dipolar coupled spins is essential to the visibility of the effect.

As long as the spin Hamiltonian commutes with the operator I_z and the condition in Eq. (8) is fulfilled, additional offset terms imposed by the applied gradients lead to the same frequency shift for all spectral components S_ω at a given spatial position. This observation means that despite the nature of the broadening, once a long-lived signal is excited by LLR, the static field gradients may be used in the same manner as is done in conventional MRI.

Materials and Methods

Sample preparation

From a piece of eraser (AXP96318, M&G eraser, China), a large hollow cylinder (outer radius $R = 4.30$ mm, inner radius $r_1 = 1.05$ mm, height = 10 mm) and a smaller and shorter cylinder (radius $r_2 = 0.75$ mm) were prepared, and placed in a 10 mm NMR tube. Four different slices images were acquired using the spin echo method, LLRE3D and the slice selective LLRE methods.

NMR and MRI Measurements

All the MRI and NMR experiments were performed on a Bruker Avance I spectrometer (Bruker, MA, USA) operating at 400.13 MHz for ^1H , equipped with a microimaging accessory. Images were collected with a Bruker Micro2.5 gradient assembly and imaging probe in combination with a 15 mm i.d. coil (Bruker Biospin GmbH, Germany). The coil has a uniform excitation profile over a length of 15 mm, with a total profile extending to 23 mm. The samples were carefully aligned at the center of the coil to ensure full and uniform signal excitations across their full volumes. For conventional UTE and spin echo MRI experiments, the pulse sequences of Ultrashort TE(UTE) [23], UTE3D [24] and Multi-Slice Multi-Echo (MSME) [25] provided in Paravision 5.1 (Bruker, Biospin, Germany) were used. For LLRE experiments, the imaging was implemented in Topspin 2.1 (Bruker, Germany).

UTE method

The 2D UTE sequence consisted of a slice-selective RF pulse followed by 2D radial ramp sampling. The size of the data matrix was 128×128 , the pixel size $102 \times 102 \mu\text{m}^2$, and the slice thickness 1 mm. TE and TR were 0.424 ms and 5 s, respectively. For the signal excitation, a 0.5950 ms long Gaussian pulse with a flip angle of 90° was applied. We also performed a scan in which the maximum rf amplitude ($\gamma B_1/2\pi$) of the Gaussian pulse was limited to 1000 Hz in order to test constraints that would be found on a clinical MRI system. The duration and flip angle of the Gaussian pulse were 0.6073 ms and 90° in this case. The size of the data matrix, the pixel size, and the slice

thickness were kept the same as above. TE and TR were 0.43 ms and 5 s, respectively. The maximum gradient strength was 38.4 G/cm along the slice-selective direction and 95.9 G/cm along the x and y encoding directions. The number of projections was 402. The 3D UTE imaging was performed by a 3D radial FID sampling sequence using a square pulse of duration 0.02 ms with a flip angle of 5°. The size of the data matrix was $128 \times 128 \times 128$, the voxel size $102 \times 102 \times 234 \mu\text{m}^3$, TE 0.02 ms, and TR 8.0 ms. Only one scan was taken per k -space readout in all experiments. The number of projections was 51360.

Spin echo method

A slice-selective, 2D spin echo sequence was implemented using the multi-slice multi-echo (MSME) method with 128 averages. The size of the data matrix was 128×128 , the pixel size $102 \times 102 \mu\text{m}^2$, and the slice thickness 1 mm. TE and TR were 8.01 ms and 1 s, respectively. We also performed a scan with the rf amplitude ($\gamma B_1/2\pi$) of the refocusing pulse limited to 1000 Hz to test power-limited conditions. Here, data matrix, the pixel size, and the slice thickness were kept the same as above, but TE and TR were 14 ms and 1 s respectively, and 128 averages were used. The RF pulse shape was a normalized sinc function on the $[-\pi - \pi]$ interval. The maximum gradient strength was 54.7 G/cm along the slice selection direction, 24.0 G/cm along the readout direction, and 13.4 G/cm along the phase-encoding direction.

LLRE method

The excitation of a LLRE signal was performed by a long and weak rf irradiation followed by a strong π pulse, which was phase-shifted by $\pi/2$ relative to the weak rf irradiation (Fig. 2(a)). The weak pulse was optimized to give the maximum signal. Its duration and rf amplitude ($\gamma B_1/2\pi$) were 6 ms and 27 Hz, respectively. The rf amplitude ($\gamma B_1/2\pi$) of the π pulse was 14 KHz.

The 3D LLRE sequence consisted of the excitation of the LLRE signal followed by a 3D gradient-echo 3D acquisition. The $128 \times 128 \times 128$ data matrix covered a FOV of $13 \times 13 \times 16 \text{ mm}^3$ with $TR = 5 \text{ s}$ and a slice thickness of $132 \text{ }\mu\text{m}$. The maximum strength of the applied gradients was 29.8 G/cm for the read-out gradient and 18.8 G/cm for the phase-encoding gradient. The echo time of 3.90 ms for the LLRE method is defined as the time between the middle of the soft rf excitation pulse and the peak of the signal induced in the coil.

The slice-selective 2D LLRE imaging sequence consisted of the excitation of the LLRE signal, a slice selection gradient, and a 2D gradient echo readout (Fig. 3(b)). The slice selection is achieved using a slice selection gradient during the second pulse that is now a soft π pulse to refocus the spins in the selected plane only. The same sinc-shaped pulse of 1 ms duration was used for the soft π pulse. For the eraser sample (maximum excitation power of π pulse= 2800 Hz, Fig. 3 (c)), the 128×128 data matrix covers a FOV of $13 \times 13 \text{ mm}^3$. A 0.283 mm slice was used. The strengths of the applied gradients were 38.7 G/cm for the read-out gradient, 28.4 G/cm for the phase-encoding gradient, and 29.8 G/cm for the slice selection gradient. The image was obtained with $TR = 5 \text{ s}$ and $TE = 7 \text{ ms}$. For a quantitative evaluation of the LLRE method, the 128×128 data matrix covers a FOV of $13 \times 13 \text{ mm}^3$. A 1 mm slice was used. The strength of

applied gradients is 35.7 G/cm for the read-out gradient, 28.9 G/cm for the phase-encoding gradient and 3.6 G/cm for the slice selection gradient. The image was obtained with a TR of 1 s and TE of 5.0 ms. We also performed a scan in which the maximum rf amplitude ($\gamma B_1/2\pi$) of the π pulse was limited to 1000 Hz, the image was obtained with a TR of 1 s and TE of 6.8 ms.

Results and Discussion

The Fourier-transformed spectrum of a LLRE signal from the eraser sample is shown in Fig. 2(b), together with the conventional ^1H NMR spectrum acquired with a 90° hard pulse. With the LLRE excitation, a single peak generally appears on the LLRE spectrum at the same frequency offset as the weak rf irradiation, and its linewidth is significantly narrower than that of the conventional ^1H spectrum. For example, the linewidths of the spectra shown in Fig. 2(b) are 176 Hz and 856 Hz, respectively for the LLRE and conventional spectra. The signal intensity ratio between the LLRE and conventional spectra is 1:2.3. Although LLRE signals are weaker than the signals excited by a hard pulse, the decreased signal intensity can be compensated for by their slower decay in time.

Fig. 2 (a) The LLRE pulse sequence consisting of a weak pulse and a 180° pulse. For the weak pulse, $t_{LLR} = 6$ ms and $\gamma B_1/2\pi = 27$ Hz. For the 180° pulse, a 36.7 μ s-long hard pulse with $\gamma B_1/2\pi = 13624$ Hz was used for the LLRE spectrum shown in (b). (b) Conventional and LLRE ^1H NMR spectra of an eraser sample. The conventional spectrum was obtained with a 90° hard pulse ($\gamma B_1/2\pi = 13624$ Hz). The LLRE spectrum was acquired with the pulse sequence shown in (a).

The slice selection is achieved using a gradient during the π pulse, which thus acts on spins in the selected plane only (Fig. 3(b)). Four different slices were chosen to verify the slice selection and compare to the 3D LLRE and UTE imaging, as illustrated in Fig. 3(a). Slices A and D were chosen at 4.22 mm and -3.28 mm away from the isocenter, where only the outer hollow outer cylinder is present. Slices B and C were set at 2.34 mm from the isocenter and at the isocenter itself, respectively, hence both the inner and outer cylinders should show up. The images of the chosen slices acquired with 2D slice-selective LLRE, 3D LLRE, and 3D UTE sequences are shown in Fig. 3(b). The LLRE3D images appear superior to the UTE images of the same nominal resolution, showing more structural details and a clearer gap between the inner and outer material. The slice-selective LLRE images have lower signal-to-noise ratio than the other two, as expected considering that only spins on the selected plane contribute to the signal. This result proves that the slice selection is implemented successfully in the LLRE pulse sequence. Direct slice-selective excitation does not work with this and similar samples, because the gradient localization is convoluted with the inherent

broadening. By contrast, a slice-selective π pulse preserves the long-lived signal, while also providing the slice localization.

Fig. 3 Slice-selective LLRE imaging of an eraser sample. (a) Schematic and slices of the eraser sample used in the MRI experiments. ($R = 4.3$ mm, $r_1 = 2.1$ mm, $r_2 = 1.5$ mm) (b) Slice-selective imaging sequence using LLRE as the signal excitation method. For the first pulse, $t_{LLR} = 6$ ms and $\gamma B_1/2\pi = 27$ Hz. The 180° pulse was implemented by a 1 ms sinc pulse with $\gamma B_{1,(max)}/2\pi = 2816$ Hz. (c) Images obtained with slice-selective LLRE imaging, along with slices extracted from 3D LLRE and UTE scans.

For a quantitative evaluation of the LLRE method, the images for slice C were compared with a slice-selective spin echo sequence, and a 2D UTE sequence as well,

under the same nominal resolution and repetition time. As illustrated in Fig. 4, the LLRE image manifests the finer details and higher sensitivity than the other two images. The quality of the image was assessed via the signal-to-noise ratio (SNR) determined by

$$SNR = \frac{S_{ROI}}{SD_{air}}, \quad (9)$$

where S_{ROI} is the mean signal in the large circular region covering most of the test object and SD_{air} is the average of the standard deviations in two smaller regions placed over air [26]. The UTE image has the highest SNR (Table 1), however, it is blurry in details compared to the other two. This effect is also seen from the cut view of the images along the horizontal line located in the center of images (bottom of Figure 4). The LLRE image clearly shows the gap between the inner and the outer material, the signal of which is almost as low as the noise level outside, while the spin echo and UTE images show a blurry gap. This is expected, because during the readout, the gradient localization is convolved by the spectral width of the excited signal. While one could remedy this situation by applying a stronger gradient, such strong gradients are not always available on MRI scanners, and sensitivity would be degraded. The slice-selective LLRE image has a higher SNR than the spin echo image and represents the object's features more clearly than the UTE image, due to its narrower spectral width.

Fig.4 Top: 2D slices from an eraser sample acquired with the spin echo, UTE2D, and slice-selective LLRE imaging sequences. The same nominal resolution, data matrix, FOV, and repetitions time were used. The maximum RF amplitude for each method is around 2800 Hz. (For both spin-echo sequence and LLRE sequence, the amplitude of second pulse (the π pulse) is set as the maximum.) Bottom: A cut view of images for each method along the horizontal line.

Table 1. Signal-to-noise ratio calculation for MRI methods

	Spin echo	UTE	LLRE
S/N ratio (maximum RF amplitude = 2800 Hz)	1.13	13.46	4.46
S/N ratio (maximum RF amplitude = 1000 Hz)	0.57	8.97	1.7

On clinical scanners, the power of rf pulses power is significantly restricted for safety reasons. On instruments designed for materials imaging, rf pulse power may also be restricted, especially when large volume coils are used. For the purposes of testing

this situation, we repeated the experiments with the maximum rf amplitude ($\gamma B_1/2\pi$) limited to 1000 Hz. The images are shown in Fig. 5. Compared to the images acquired with the 2D UTE and spin echo with slice selection, the slice-selective LLRE method clearly results in higher resolution and higher sensitivity than the spin-echo method (Table 1). The cut view in Fig. 5 also indicates better signal to noise ratio and detail representation of LLRE signal when compared with the other two methods.

The same sequence as well as the spin echo and UTE3D sequences were applied to a hollow eraser sample containing water, the result of which is shown in Fig. 6. As expected, the spin echo image exhibited only the water compartment. The UTE image showed both the solid compartment as well as the water compartment. By contrast, the LLRE image displayed the solid compartment exclusively with the water compartment remaining invisible. This technique, therefore, shows potential for slice-selective imaging of objects with broad resonance lines in both the high- and low-power limits. Certain distortions and modifications of image contrast can be expected due to B_0 inhomogeneities, although the frequency of the LLRE signal is determined by the frequency of the weak pulse, not by the local Larmor frequency [27]. Such effects can be mitigated by using an excitation pulse well within the center of the broad resonance, especially in the presence of a line with broad linewidth. In the samples considered here, the intrinsic lineshape was much larger than typical inhomogeneities expected from susceptibility differences.

When power and gradient strength are unlimited, UTE, ZTE, and single-point imaging (SPI) currently remain the methods of choice, however.

Fig.5 Top: 2D slices from an eraser sample acquired with the spin echo, UTE2D, and slice-selective LLRE imaging sequences. The same nominal resolution, data matrix, FOV, and repetitions time were used. The maximum RF amplitude for each method is 1000 Hz. (For both spin-echo sequence and LLRE sequence, the second pulse (π pulse) is set as the maximum.) Bottom: A cut view of images for each method along the horizontal line.

Fig. 6. Top: 2D slices from a hollow eraser cylinder containing un-doped water acquired with the slice-selective spin echo, UTE3D and slice-selective LLRE imaging sequence. Bottom: A cut view through the images for each method along the horizontal line.

Conclusions

We have examined here the possibility of low-power excitations for slice-selective imaging in samples with strong line broadening due to either inhomogeneous or dipolar broadening mechanisms. We demonstrate that long-lived signals in rigid samples can be excited, which can subsequently be inverted by slice-selective rf pulses. This procedure is implemented for an imaging method where we compare its performance with the 3D UTE, 2D UTE, and slice-selective spin-echo sequences. In addition, we examine here the power-limited case, which is important for MRI scanners or large volume and materials applications. It is seen that the slice-selective LLRE method clearly demonstrates better images with higher sensitivity under both the high and low power regimes. These results show that the slice-selective LLRE method may have potential for imaging semi-solids or biological rigid tissues containing water, especially under power-limited conditions. The method may not be applicable to all solid-like materials, however, for certain conditions should be met to excite the LLRE signal. At present the understanding about the origin and mechanism of LLR excitation is incomplete, and further efforts in this area could help clarifying the nature of the obtained image contrast. The 2D method itself could be further improved by the use of a multiple-slice acquisition scheme.

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