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Longitudinal and Multi-Echo Transverse Relaxation Times of Normal Breast Tissue at 3 Tesla

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Abstract

Purpose—To measure longitudinal (T_1) and multi-echo transverse (T_2) relaxation times of healthy breast tissue at 3 Tesla (T).

Materials and Methods—High-resolution relaxation time measurements were made in six healthy female subjects. Inversion recovery images were acquired at 10 inversion times between 100 ms and 4000 ms, and multiple spin echo images were acquired at 16 echo times between 10 ms and 160 ms.

Results—Longitudinal relaxation times T_1 were measured as 423 ± 12 ms for adipose tissue and 1680 ± 180 ms for fibroglandular tissue. Multi-echo transverse relaxation times T_2 were measured as 154 ± 9 ms for adipose tissue and 71 ± 6 ms for fibroglandular tissue. Histograms of the voxel-wise relaxation times and quantitative relaxation time maps are also presented.

Conclusion— T_1 and multi-echo T_2 relaxation times in normal human breast tissue are reported. These values are useful for pulse sequence design and optimization for 3T breast MRI. Compared with the literature, T_1 values are significantly longer at 3T, suggesting that longer repetition time and inversion time values should be used for similar image contrast.

Keywords

breast; magnetic resonance imaging; relaxation times

MRI of the breast is becoming increasingly used for several clinical indications, including screening of women known to be of high risk for developing breast cancer, identifying and characterizing lesions not seen on conventional X-ray mammography, staging of breast cancers, guiding biopsies, as well as following the response of breast tumors to neoadjuvant chemotherapy (1–6).

Traditionally, clinical MRI of the breast has been performed at the widely available field strength of 1.5 Tesla (T). However, with the increasing prevalence of 3T scanners and the development and optimization of body imaging methods at high field (7), 3T is gradually becoming more accepted for clinical breast MRI (8,9). One of the most important features of high field breast MRI is the increased signal-to-noise ratio compared with lower fields, which allows images to be performed at better spatial and/or temporal resolution with the latter being paramount for dynamic contrast enhanced studies. For optimal MR sequence

design (i.e., best signal- and/or contrast-to-noise ratio) it is important to know the longitudinal (T_1) and transverse (T_2) relaxation times of normal fibroglandular and adipose tissue. Knowledge of water and lipid relaxation times in the breast is also useful for designing lipid suppression saturation schemes (such as short inversion time inversion recovery [STIR]) and water suppression schemes for MR spectroscopy. However, currently there is only a single paper (10) describing normative breast relaxation times at 3T which used a limited number of echo and inversion times. The purpose of this study therefore was to provide additional normative relaxation time data for 3T breast MRI, in particular by sampling relaxation curves more extensively.

MATERIALS AND METHODS

Six premenopausal female volunteers (age 34 ± 6 years; range, 28 to 49 years) with no personal history of breast disease participated in the study, which was approved by the local institutional review board. Written informed consent was obtained before examination. All scans were performed on a Philips Intera 3T (Philips Healthcare, Best, The Netherlands) MRI system with body coil excitation and a four-channel phased-array (with left-right, anterior-posterior arrangement, InVivo, Gainesville, FL) breast coil for reception. All scans were performed on the right breast. After initial localizer and reference images were acquired, the quantitative T_1 and multi-echo T_2 measurements were made (see below). Additional imaging data (not presented here) were also collected so that the total exam time was 50 min.

T_1 Measurement

An inversion recovery-prepared multi-shot spin-echo EPI sequence was acquired at nine inversion times: 100; 300; 500; 700; 900; 1200; 1500; 2000; 3000; and 4000 ms. A single 3-mm coronal slice was acquired at a location midway between the nipple and the chest wall, with in-plane resolution of $1.8 \times 1.8 \text{ mm}^2$, reconstructed to $0.7 \times 0.7 \text{ mm}^2$ (100×100 acquired matrix zero-filled to 256×256), imaging bandwidth in the direction of the fat-water shift of 102 Hz/pixel (acquired) or 40 Hz/pixel (reconstructed), giving an 11 pixel fat-water shift in reconstructed images. Other sequence parameters were: repetition time (TR) = 5 s; echo time (TE) = 14.1 ms; EPI factor 9. The longitudinal relaxation time, T_1 , was calculated from a “magnitude monoexponential” fit (Eq. [1]) to the signal recovery data for each voxel using the nonlinear fitting routine *lsqcurvefit* supplied in Matlab (The Mathworks, Natick, MA). A three-parameter model was used, with T_1 , the equilibrium magnetization S_0 and the inversion efficiency α included as variable fitting parameters:

$$S(TI) = |S_0(1 - 2\alpha \exp(-TI/T_1) + \exp(-TR/T_1))| \quad [1]$$

Multi-echo T_2 Measurement

To measure the multi-echo transverse relaxation time T_2 , a 16-echo spin echo sequence was acquired with echo times from 10 ms to 160 ms in 10-ms steps and a TR of 3 s. As with the T_1 measurement, the same 3-mm-thick slice was acquired with in-plane resolution of $1.8 \times 1.8 \text{ mm}^2$, reconstructed to $0.7 \times 0.7 \text{ mm}^2$ (100×100 acquired matrix zero-filled to 256×256), and imaging bandwidth in the direction of the fat-water shift of 102 Hz/pixel (acquired) or 40 Hz/pixel (reconstructed), giving an 11-pixel fat-water shift in reconstructed images. Single-slice imaging avoids substantial magnetization transfer effects. A mono-exponential fit in Matlab was applied to the even echo data only, to account for imperfections in the 180° refocusing pulse, off-resonance effects, and to eliminate possible stimulated echo contributions (11). A three-parameter model (Eq. [2]) was used, allowing T_2 , the equilibrium magnetization S_0 and the y-offset C to vary:

$$S(TE)=S_0\exp(-TE/T_2)+C. \quad [2]$$

Data Analysis

All fitting was done on a voxelwise basis, thus deriving relaxation time constants independently for each voxel. After fitting models to the individual voxel data, histograms were plotted showing the distribution of fitted relaxation time values across the whole image. Modal values were identified in each histogram to determine the T_1 and multi-echo T_2 relaxation times of fibroglandular and adipose tissues. The mean and standard deviations of these values were calculated across all volunteers. Using histogram analysis and modal values, there is no need to identify representative regions of interest (ROIs) for each tissue type in the images and a major source of human variability is removed from the analysis.

RESULTS

Good quality coronal plane images were acquired at all inversion times and echo times for the T_1 and multi-echo T_2 experiments. Model curves for individual voxels (representative of adipose tissue [upper] and fibroglandular tissue [lower]) are shown in Figure 1 (inversion recovery data on the right and multiple echo time data on the left), along with the quantitative T_1 and multi-echo T_2 maps for one of the six volunteers. Visual inspection of curve-fitting results demonstrated excellent agreement between the models (Eqs. [1] and [2]) and the acquired data.

Quantitative T_1 and multi-echo T_2 maps for all volunteers are shown in Figure 2; both differentiate adipose and fibroglandular tissue. Histograms of the maps, as have previously been used to analyze relaxation properties of brain tissue (12), underline differences of tissue composition between individuals and reveal modal values for populations representing tissue types (adipose: $T_1 = 423 \pm 12$ ms; multi-echo $T_2 = 154 \pm 9$ ms. fibroglandular: $T_1 = 1680 \pm 180$ ms; multi-echo $T_2 = 71 \pm 6$ ms). The envelope of the T_1 and T_2 histograms for all six volunteers are shown below the maps in Figure 2. Figure 3 shows a voxel-wise plot of T_1 against T_2 and a two-dimensional histogram of the same data, showing distinct populations that are spatially localized to the adipose tissue and fibroglandular tissue.

DISCUSSION

Accurate knowledge of relaxation times is the foundation for the development and optimization of MR imaging sequences. Optimal water-fat contrast and signal-to-noise in both T_1 - and T_2 -weighted images requires a knowledge of these relaxation times. In addition, in the context of breast MRI, the identification of small contrast-enhancing lesions at the fibroglandular–adipose boundary requires reliable, high quality fat suppression, and optimal design of fat saturation sequences requires a knowledge of fat T_1 values (13). Finally, for MR spectroscopy of the breast, design of water suppression techniques requires knowledge of breast water T_1 relaxation times (14). Therefore, the normative data presented here is expected to be of use in the development of multiple MR breast imaging methods (15). The design of this study has several limitations, such as the small number of subjects studied ($n = 6$), and the fact that imaging was performed without standardizing the menstrual phase of subjects.

There has been one previous report of normative breast relaxation values at 3T (10), also in a small group ($n = 5$) of women, with a similar age range (24 to 51 years) to the current study. This study significantly differed from the current in terms of the methods used. For T_1

measurements, four inversion times (3000 ms, 800 ms, 300 ms, and 150 ms) were used in combination with the “IDEAL” method for separating water and fat signals. T_2 measurements were made using two echo times only (20 and 100 ms). Table 1 shows the current study results compared with the results of Rakow-Penner et al (10). T_1 values are similar between studies for both adipose and fibroglandular tissues, with the current study showing ~15% higher T_1 ’s. There are greater differences in T_2 relaxation times, with fibroglandular T_2 31% longer, and an almost three-fold longer T_2 of adipose tissue resulting in much greater T_2 contrast between adipose and fibroglandular tissue in the current study. One likely source of the increased T_2 relaxation time in adipose tissue in the current study is the use of a 32-echo readout with a 5-ms interval between echoes, compared with the single spin-echo (at TEs of 20 and 100 ms) used by Rakow-Penner et al (10). Water T_2 values are probably longer in the current study because of the reduced effects of diffusion in the multi-echo sequence, while it has previously been shown that there is “anomalous” increase in apparent fat T_2 relaxation times in fast-spin echo (FSE) images because of removal of the effects of homonuclear scalar coupling between fat protons at short inter-echo spacing in Carr-Purcell-Meiboom-Gill type sequences (16). Because most clinical T_2 -weighted imaging is currently performed using FSE-based sequences, the longer fat T_2 values of the current study are, therefore, more relevant for sequence design considerations. In particular, residual fat signals in fat suppressed T_2 -weighted FSE sequences may be worse than expected because of the long apparent T_2 of fat using this read-out. One clear advantage of IDEAL experiments is the avoidance of artifactual signal overlap due to the fat–water shift. As seen in the images above, the 11-pixel fat–water shift in this study is significant and results in spatial separation particularly of the water and fat components of fibroglandular tissue.

As expected, and consistent with prior publications, the T_1 values of both water and fat in the breast were longer in the current study at 3T compared with literature 1.5T values (by approximately 20% and 40%, respectively). Previous literature measurements have been published at a range of field strengths from 0.3T to 3T (10,17–19) and the variability across field strengths has been modeled up to 100 MHz or 2.5T (20); these data are shown in Figure 4. Therefore, for similar contrast (and fat suppression) as at 1.5T, repetition time (TR) and inversion time (TI) need to be lengthened accordingly. While the longer TR lengthens the pulse sequence duration at 3T (keeping all other parameters the same), the improved SNR at higher field more than compensates for this disadvantage and thus would allow for parallel imaging to be used thereby reducing the scan time to that of 1.5T.

Various technical aspects of this study merit discussion; although several methods have been proposed for the measurement of T_1 in an time-efficient manner (21), the gold-standard method remains the acquisition of inversion-recovery data over a range of inversion times. In acquiring inversion recovery images at 10 separate inversion times (and transverse relaxation data using eight time points), it was possible to perform accurate curve-fitting of the relaxation time data on a voxel-by-voxel basis. The data presented in Figure 1 are representative of the whole sample and the fitted models show very good agreement with the data, showing mono-exponential behavior. Although a significant range of TE and TI values were sampled, the curves reveal that a wider range would improve measurements for both long- T_1 and long- T_2 regions. Neither the fibroglandular T_1 curve (bottom left) nor the adipose T_2 curve (top right) are close to asymptote by the last measurement—i.e., at long inversion times and long echo times respectively. Approaching the asymptote improves fitting of exponential data, especially when the zero time point (that is, TI = 0 ms or TE = 0 ms) is not experimentally accessible (as is the case in both measurements). In the case of T_1 measurements, the maximum inversion time of 4 s arises from the trade-off between experiment time and measurement quality, resolved by choosing ten inversion times and a TR of 5 s.

Even though relaxation mapping was performed at high spatial resolution ($3 \times 1.8 \times 1.8$ mm), many voxels contained partial volume of adipose and fibroglandular tissue. Inspection of the histograms in Figure 2 indicates that only two volunteers show a clear bimodal distribution (corresponding to the two tissue types), whereas in the others at least one (i.e., the minor) component is significantly smeared by partial voluming. Comparison with the images shows that the subjects with clearly bimodal distributions are those with the most extensive and densest fibroglandular tissue.

Close inspection of the multi-echo T_2 relaxation curves shows that the first point ($TE = 20$ ms) of both decay curves is often high relative to the fit line (Fig. 1). When observed across many voxels, this is suggestive of an additional pool of short- T_2 spins. Attempts were made to fit the data with bi-exponential models, using five-parameter models allowing an additional relaxation time and volume-fraction to vary. However, only marginal improvements in the fit quality resulted, insufficient to justify the change from three-parameter to five-parameter fits as judged by the Akaike information criterion (22).

In conclusion, normative longitudinal and multi-echo transverse relaxation times for healthy breast tissue have been measured at 3T, and quantitative relaxation time maps clearly distinguish between adipose and fibroglandular tissue. Further studies will be required to determine if relaxation times change as a function of age, breast density, menstrual cycle, menopausal status, lactation, or other factors.

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Figure 1.

T_1 (left) and multi-echo T_2 (right) relaxation measurements of a single volunteer. Images show the quantitative relaxation time maps, and selected voxels from adipose and fibroglandular tissue are selected to display signal as a function of TI (left) and TE (right). To measure T_1 , magnitude-exponential curves are fit to inversion-recovery data from single representative voxels in the adipose (above) and fibroglandular (below) tissue data. To measure multi-echo T_2 , exponential decay curves are fit to multiple-echo data from the same voxels. It can be seen that these models fit the experimental data well.

Figure 2.

T₁ (upper) and multi-echo T₂ (lower) maps of all six volunteers. Adipose and fibroglandular tissue are well differentiated in both sets of images. Colored spots are included to link the images to histogram envelopes plotted below. T₁ is longer in fibroglandular tissue than adipose, whereas T₂ is longer in adipose than fibroglandular tissue.

Figure 3. Voxelwise scatter plot (a) and two-dimensional histogram (b) of T_1 against multi-echo T_2 relaxation times across all subjects. Larger open circles mark the values in Table 1, identified from analysis of the individual histograms.

Figure 4.

T_1 relaxation times as a function of field strength up to 3T. The continuous data shows the parametrized function proposed by Bottomley et al (as mean $\pm$ standard deviation) with dotted lines denoting extrapolation beyond the original range (20). Other individual studies (10,17–19) are represented by individual points with error bars denoting $\pm$ standard deviation (except *for which error bars represent $\pm$ range/3) and marked with reference numbers. Points at 1.5T and 3T are displaced slightly along the x-axis to differentiate overlapping error bars (which are displayed asymmetrically for the same reason).

Table 1Comparison of T₁ and T₂ Values of the Current Study With Those Given by Rakow-Penner et al (10)

	T1 (ms)		T2 (ms)	
	Adipose	Fibroglandular	Adipose	Fibroglandular
Current study	423 ± 12	1680 ± 180	154 ± 9	71 ± 6
Ref. (10)	367 ± 8	1445 ± 93	53 ± 2	54 ± 9