Measurement of spin-lattice relaxation times with FLASH for dynamic MRI of the breast

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Abstract

Using a variable flip angle gradient refocused imaging technique, dynamic quantitative $T_1$ relaxation maps acquired before and after the administration of a gadolinium contrast bolus enable the concentration–time curve of the paramagnetic agent in breast tissue to be calculated. This imaging technique has the aim of improving the diagnostic accuracy of MR mammography. Measurements with phantoms of calibrated $T_1$ values have been carried out to investigate the accuracy of the method, with particular reference to errors caused by incomplete spoiling of residual transverse magnetization and inaccurate radio frequency (RF) flip-angle settings. A clinical example is presented. The method has potential use for any patient study which necessitates rapid quantitation of changing $in vivo$ $T_1$ values as a result of contrast agent injection.

In contrast enhanced magnetic resonance mammography (MRM), the amount and rate of enhancement of a lesion are often used for diagnostic evaluation, with malignant lesions generally showing greatest and most rapid enhancement [1-10]. However, benign lesions such as fibroadenoma and sclerosing adenosis are often difficult to distinguish from malignant lesions on the basis of signal enhancement characteristics alone, since their signal enhancement curves may also demonstrate rapid and/or high uptake of contrast agent [3, 5, 6-8, 10].

To improve the specificity of dynamic contrast enhanced MRM, a protocol derived from the variable flip-angle method [11-13] of measuring spin-lattice relaxation times ($T_1$) has been developed. The protocol is able to produce a $T_1$ map of the entire breast, from two three-dimensional (3D) image data sets obtained at different radiofrequency (RF) flip-angles, prior to injection of the contrast agent gadolinium (Gd-DTPA). It is able to do this in a time much faster than would be possible with conventional saturation recovery/inversion recovery (SR/IR) methods of measuring $T_1$. Post-contrast changes in $T_1$ are monitored by acquiring images at one RF flip-angle only. Obtaining pre- and post-contrast values of $T_1$ enables the corresponding change in relaxation rate, $R_1$, to be calculated, by virtue of the fact that $R_1$ is simply the inverse of $T_1$. Since the change in $R_1$ of any particular tissue is directly proportional to the amount of contrast agent absorbed by that tissue [10, 14], the protocol enables a Gd-DTPA concentration–time curve to be drawn which, it has been argued [10], may improve the specificity of contrast enhanced MRM.

This protocol represents a new method of measuring $T_1$ (and hence $R_1$) in the breast. The means by which post-contrast changes in $T_1$ are monitored has not previously been reported. In this paper, the theory behind the protocol is outlined and experiments aimed at validating the protocol as a practical clinical procedure described. Sources of error such as reference RF power calibration and incomplete spoiling of transverse coherence are explored. Finally, a clinical example is presented.

Note that whereas $T_1$ is a well understood quantity in MRI, the concept of $R_1$ is less widely used. For clarity, therefore, we refer to $T_1$ in the text where possible. However, as we are ultimately interested in changes of Gd-DTPA concentration in tissue, and since these are proportional to changes in $R_1$, some interchange between $R_1$ and $T_1$ in the text cannot be entirely avoided.

Theory

The contrast agent Gd-DTPA shortens the $T_1$ of tissue into which it is absorbed, leading to a greater signal intensity in fast low angle shot (FLASH) images. Signal enhancement curves have been used to aid differentiation of tissues [1-10]. However, because a particular quantity of contrast agent causes a variable degree of signal enhancement depending on the initial $T_1$ of the tissue into which it is absorbed [10, 14], a bias is introduced. The computer simulation in Figure 1 demonstrates how a given quantity of contrast agent absorbed by a tissue of high initial $T_1$ will lead to a greater change in signal ($AS_b$) than if the same quantity had been absorbed by a tissue of lower initial $T_1$ ($AS_a$). Figures indicate values for $T_1$ at 1.0 T of the order of 1000 ms for fibroadenoma and anywhere in the range 700-1000 ms for various types...
T1 measurement in breast MRI

Figure 1. Simulation of signal intensity curve for FLASH (S/kp plotted using Equation (1) for $T_R = 8.4$ ms and $\alpha = 30^\circ$) demonstrating non-linearity of signal response to a given uptake of paramagnetic contrast-agent. $\Delta$(Gd-DTPA) represents the change in tissue concentration of Gd-DTPA.

![Graph showing signal intensity vs. time](image)

The equation predicting signal intensity $S$ for the FLASH imaging sequence, assuming a homogeneous voxel and $T_E \ll T_2^*$, is [14]

$$S = \frac{k \rho (1 - \exp[-T_R R_1]) \sin \alpha}{(1 - \exp[-T_R R_1]) \cos \alpha}$$  \hspace{1cm} (1)

where $k$ is the system gain; $\rho$ is the proton density; $\alpha$ is the RF excitation flip-angle; $T_R$ is the RF pulse repetition time; $T_E$ is the echo delay time; $R_1$ is the spin-lattice relaxation rate and $T_2^*$ is the spin-spin relaxation time modified to include the effects of magnetic field inhomogeneity and variations in tissue magnetic susceptibility.

If two images are obtained with flip-angles $\alpha_1$ and $\alpha_2$, then the signal intensity ratio, $\beta$, of the two images at each corresponding voxel location is given by

$$\beta = \frac{S_1}{S_2} = \frac{\frac{\sin \alpha_1 (1 - \exp[-T_R R_1]) \sin \alpha_1}{(1 - \exp[-T_R R_1]) \cos \alpha_1}}{\frac{\sin \alpha_2 (1 - \exp[-T_R R_1]) \sin \alpha_2}{(1 - \exp[-T_R R_1]) \cos \alpha_2}}$$

so that, re-arranging for $R_1$ gives

$$R_1 = \frac{1}{T_R} \ln \left( \frac{\beta \sin \alpha_2 \cos \alpha_1 - \sin \alpha_1 \cos \alpha_2}{\beta \sin \alpha_2 - \sin \alpha_1} \right)$$  \hspace{1cm} (2)

Re-arranging Equation (1) to make the product $k \rho$ the subject of the equation, we obtain

$$k \rho = \frac{S_1 \sin \alpha_1 (1 - \exp[-T_R R_1]) \sin \alpha_1}{(1 - \exp[-T_R R_1]) \sin \alpha_1}$$

Having estimated a value for $R_1$ from two image signal intensities (Equation (2)), this value can be substituted into Equation (3) to obtain an estimate for the product $k \rho$. If it can then be assumed that absorption of Gd-DTPA into a tissue does not affect its proton density or $T_2$, and taking care to keep the imaging system gain characteristics constant, post-contrast injection changes in $R_1$ can be monitored simply by acquiring images at a third RF flip-angle, $\alpha_3$, and using the consequent value for $S_3$, along with the estimate for $k \rho$, in Equation (1), giving (after re-arranging)

$$R_1 = \frac{1}{T_R} \ln \left( \frac{k \rho \sin \alpha_3 - S_3 \cos \alpha_3}{k \rho \sin \alpha_3 - S_3} \right)$$  \hspace{1cm} (4)

RF flip-angle optimization

Due to thermal noise in the imaging system, random errors are introduced into $S_1$ and $S_2$. As a result, the image intensities at any given voxel will be $S_1 \pm \Delta S_1$, $S_2 \pm \Delta S_2$. Consequently, the $R_1$ of a voxel calculated by this method will be in error. Optimization on the combination of flip-angles ($\alpha_1, \alpha_2, \alpha_3$) that gives least error in $R_1$ and $R_1_{\text{new}}$ is necessary. From Equation (1),

...
\[ R_1 = f_1(T_R, \alpha_1, \alpha_2, \beta) \]  
Assuming that: \( \Delta T_R = \Delta \alpha_1 = \Delta \alpha_2 = 0 \), then

\[ \Delta R_1 = \frac{\partial R_1}{\partial \beta} \Delta \beta \]

Now, \( \beta = f_2(\alpha_1, \alpha_2) = S_1/S_2 \), so that

\[ \Delta \beta = \frac{\partial \beta}{\partial S_1} \frac{\Delta S_1}{S_1} + \frac{\partial \beta}{\partial S_2} \frac{\Delta S_2}{S_2} \]

If we assume \( \Delta S_1 = \Delta S_2 = \Delta S \), then

\[ \Delta \beta = \beta \Delta S \left( \frac{1}{S_1} \right)^2 + \frac{1}{S_2} \]

giving

\[ \frac{\Delta R_1}{\Delta S} = \beta \frac{\partial R_1}{\partial \beta} \sqrt{\left( \frac{1}{S_1} \right)^2 + \left( \frac{1}{S_2} \right)^2} \]

where

\[ \frac{\partial R_1}{\partial \beta} = \frac{\sin \alpha_1 \sin \alpha_2 (\cos \alpha_2 - \cos \alpha_1)}{2T_\phi \sin \alpha_2 \sin \alpha_1} \]

The partial derivative \( \frac{\partial R_1}{\partial \beta} \) is obtained by differentiation of Equation (2). By assuming values for \( T_1 \) and \( T_R \), Equation (5) can be computed for a complete range of RF flip-angles \( \alpha_1 \) and \( \alpha_2 \). It is then merely a matter of selecting the combination of \( \alpha_1 \) and \( \alpha_2 \) that gives the smallest value for \( \frac{\Delta R_1}{\Delta S} \).

In order that the temporal resolution of the protocol is as high as possible, a \( T_R \) of 8.4 ms was chosen, this being the minimum possible \( T_R \) on our imaging system for a 3D FLASH pulse sequence. With regard to the choice of values for \( T_1 \) on which to perform the computer simulation, the following data were taken into account. These data being the \( T_1 \)s of breast tissues at 1.0 T [15]: fat, 175 ms; fibrocystic tissue, 765 ms; parenchyma, 800 ms; malignant tissue, 900 ms; fibroadenoma, 1000 ms. In light of these figures, it was decided to optimize \( R_1 \) measurement accuracy over a \( T_1 \) range of 150–1100 ms. Figure 2 shows the contour maps produced by calculating \( \frac{\Delta R_1}{\Delta S} \) for different combinations of \( \alpha_1 \) and \( \alpha_2 \) at the outer limits of this range. At a \( T_1 \) of 150 ms, flip-angles \( (\alpha_1, \alpha_2)_{\text{opt}} = (8^\circ, 44^\circ) \) are suggested whilst at a \( T_1 \) of 1100 ms, flip-angles \( (\alpha_1, \alpha_2)_{\text{opt}} = (3^\circ, 17^\circ) \) appear to be the optimum choice. Taking the average of these two sets of flip-angles, the final choice of \( (\alpha_1, \alpha_2)_{\text{opt}} = (5.5^\circ, 30.5^\circ) \) is arrived at. Figure 3 plots \( \frac{\Delta R_1}{\Delta S} \) for each of these three sets of flip-angles over the whole range of 150 < \( T_1 < 1100 \) ms, from which it will be seen that the final choice of flip-angles does indeed give least error in \( R_1 \) over the range of tissue \( T_1 \)s that are expected to be present in the breast.

As a result of random errors in \( S_1, S_2 \) and \( S_3 \) being propagated into Equations (3) and (4), optimization on the third RF flip-angle, \( \alpha_3 \), is required in order to minimize the potential for error in the estimate for \( R_{1,\text{new}} \). This requires expressing \( R_{1,\text{new}} \) (Equation (4)) implicitly in terms of \( S_1, S_2 \) and \( S_3 \), using Equations (2) and (3) (see Appendix for the complete expression). Differentiation of \( R_{1,\text{new}} \) with respect to each of these variables then produces an expression for \( \frac{\Delta R_{1,\text{new}}}{\Delta S} \)

\[ \frac{\Delta R_{1,\text{new}}}{\Delta S} = \frac{\partial R_{1,\text{new}}}{\partial \alpha_3} \frac{\Delta \alpha_3}{\alpha_3} \]

(assuming \( \Delta S_1 = \Delta S_2 = \Delta S_3 = \Delta S \)). By calculating \( \frac{\Delta R_{1,\text{new}}}{\Delta S} \) over a range of \( \alpha_3 \), the minimum value of \( \frac{\Delta R_{1,\text{new}}}{\Delta S} \) suggests the optimum value for \( \alpha_3 \). Computation of \( \frac{\Delta R_{1,\text{new}}}{\Delta S} \) obtained the same values regardless of whether \( (\alpha_1, S_1) \) or \( (\alpha_2, S_2) \) were used in Equation (6), suggesting \( \alpha_{3,\text{opt}} = 47^\circ \) for a \( T_1 \) of 150 ms and \( \alpha_{3,\text{opt}} = 20^\circ \) for a \( T_1 \) of 1100 ms, as shown in Figure 4. Note that these \( T_1 \) limits are still expected to cover the whole range of \( T_1 \)s that might be found in the breast, even after the injection of Gd-DTPA. (Figure 8(b), showing post-Gd-DTPA changes in \( T_1 \), retrospectively proves this assumption to be valid.) Taking the average of these two values for \( \alpha_{3,\text{opt}} \) suggests the optimum set of RF flip-angles \( (\alpha_1, \alpha_2, \alpha_3)_{\text{opt}} \) to be \( (5.5^\circ, 30.5^\circ, 33.5^\circ) \).

Sources of error

The protocol uses gradient refocused echoes to produce images, as a result the signal observed during these echoes will be reduced by a factor of \( \exp(-TE/T_\phi) \). In this protocol \( T_\phi \) is set to as small a value as possible in order to reduce this potential source of error. This will also reduce errors due to possible changes in tissue \( T_2 \) arising from the absorption of Gd-DTPA.

Several potential problems with regards to RF flip-angles may contribute to the errors observed in \( T_1 \) (and hence \( R_1 \)) estimations. These include deviation in the overall flip-angle, spatial variations in flip-angle across the plane of the slice as a result of inhomogeneities in the RF field power delivered across the field of the slice (B1 inhomogeneities) and spatial variations in flip-angle across the thickness of the slice [12]. Flip-angles are set by linear variation of the amplitude of the RF excitation pulse. This requires an initial calibration to determine the transmitter amplitude necessary in order to achieve a reference flip-angle, which is typically chosen as 90° or 180° (the transmitter amplitude used to provide a 90° excitation pulse would then be halved to obtain a 45° excitation pulse, for example). Deviation in the overall flip-angle might be caused either by non-linearity in the RF amplifier or by an error in the calibration of the amplitude of the RF excitation pulse required to achieve the reference flip-angle.

It is assumed in the above theory that no residual transverse magnetization remains at the time of the next sampling pulse. This condition is satisfied when \( T_K > T_\phi \), which is clearly not the case for the \( T_K \) of 8.4 ms used in this protocol. The coherence of transverse

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Figure 2. RF flip-angle optimization for the pre-contrast $T_1$ data; computer generated contour plots of $\Delta R_1/\Delta S$ for:
(a) $T_1 = 150$ ms and (b) $T_1 = 1100$ ms. Contour lines represent percentage increases (as indicated) of $\Delta R_1/\Delta S$ above its minimum value.

Figure 3. Computer generated plot of $\Delta R_1/\Delta S$ against $T_1$ for three possible combinations of RF flip-angle. The third combination ($5.5^\circ, 30.5^\circ$) was suggested by taking the mean of the two combinations suggested by Figures 2a and b.

magnetization is removed by RF spoiling [17]. If this RF spoiling was incomplete, one would expect to see $T_1$ estimations become increasingly inaccurate with either increasing $T_2$ or decreasing $T_K$ as a consequence of increased signal intensity above that predicted by Equation (1). Elimination of residual transverse magnetization by increasing $T_K$ to satisfy the above condition is not desirable because temporal resolution would be reduced, compromising the efficiency of the protocol as a tool for monitoring dynamic changes in $T_1$ over a large volume.

The protocol presented here excites a 3D slab and uses two phase-encoding gradients in addition to the readout gradient, in order to produce an image. Thus errors due to intravoxel slice profile effects can be ruled out. To investigate flip-angle errors, the commercial calibration of the reference (180° flip-angle) RF transmitter amplitude was checked against an independent flip-angle
calibration scheme. The possibility of transverse coherence effects was investigated by imaging sets of solutions with different $T_2/T_1$ ratios.

**Methods**

All imaging was carried out on a Siemens Magnetom Impact 0.95 T (40.5 MHz) system (Siemens AG, Erlangen, Germany), transmitting on the body coil and receiving on a dedicated double breast surface coil.

A sequence based on the method of Perman et al [18] was implemented to check the Siemens RF flip-angle calibration. This consisted of a train of three single side-lobed sinc RF pulses ($\alpha - \alpha - \alpha$) in the presence of a constant slice selection gradient of 1.8 mT m$^{-1}$. Each RF pulse had a duration of 5120 $\mu$s and was apodised using a Hanning window. Interpulse timings were $\tau_1 = 20$ ms and $\tau_2 = 60$ ms. Such a sequence produces three free induction decay (FID) signals, one primary spin-echo, one stimulated spin-echo and three secondary spin-echoes, the second of which occurs at time $t_2$ after the final RF pulse with amplitude proportional to $|\cos(\alpha) \sin(\alpha) \sin^2(\alpha/2)|$, and exhibiting a sharp minimum when $\alpha = 90^\circ$. This spin-echo was used to create a 10 mm slice profile (field of view (FOV) 400 mm, 128 x 128 acquisition matrix; the selection gradient also provided frequency encoding) through the centre of two 500 ml polythene bottles filled with paramagnetically doped water and placed in each half of the breast coil. Region of interest (ROI) analysis obtained an average signal over each half of the breast coil. This value was then obtained across a wide range of flip-angles in order to locate the relative position of the minimum signal.

The accuracy of the technique was investigated using three sets of solutions, each set containing eight samples with $T_1$ in the range 150 to 1100 ms. The compounds used to prepare the solutions: CuSO$_4$, Cr$_2$(SO$_4$)$_3$ and MnSO$_4$ were intended to give high (~1.0), intermediate (~0.6) and low (~0.2) values of $T_2/T_1$, respectively. If any transverse coherence remained in spite of RF spoiling, the solutions with highest $T_2$ would deviate most from the signal intensities predicted by Equation (1), giving poorer estimates for the $T_1$ of the sample. The solutions were calibrated at 25°C on a Bruker CXP100 spectrometer (Bruker Analytische Messtechnik GMBH, Rheinstetten, Germany) operating at 40.5 MHz. The solutions were imaged at 23°C with a 3D FLASH sequence of 32 slices (4 mm slice thickness) and a sampling matrix of 214 x 256 (350 x 350 mm$^2$ FOV), $T_R = 8.4$ ms, $T_E = 3$ ms. Each image data set took 60 s to acquire. Nominal RF flip-angles of 6° and 30° were used, these having been chosen following computational simulation (described earlier) of the noise error associated with a whole range of possible combinations of flip-angles.

Clinical data were obtained from a patient who was imaged as part of a separate clinical trial to evaluate dynamic Gd-DTPA enhanced MRI of both breasts. Patients with clinical or mammographic suspicion of tumour recurrence following wide local excision and radiotherapy for breast cancer were included in the clinical trial. Ethical committee approval was obtained, and informed consent obtained. Imaging was carried out with the patient positioned prone in the imager. Prior to patient positioning a 21 G intravenous cannula with long line flushed with saline was inserted into an antecubital vein. Images were acquired before injection of contrast agent using nominal RF flip-angles of 6° and 30°. After injection of a rapid bolus of Gd-DTPA (0.1 mmol kg$^{-1}$ patient–mass; “Magnevist”, Schering AG, Berlin, Germany), images were acquired with a nominal RF flip-angle of 30°, at 1 min intervals. No check was made on the Siemens RF flip-angle calibration, as was the case prior to imaging the copper, chromium and manganese sulphate solutions. The pulse sequence FOV, timing and sampling parameters used were the same as reported in the previous paragraph.

**Results**

A clear minimum at 104° in Figure 5 suggests that the actual RF flip-angle being delivered is 13.5% less than...
that requested. Figure 6 predicts the inaccuracy in $T_1$ as a result of a given systematic error in the calibration of the reference RF transmitter amplitude.

The solutions were imaged with nominal RF flip-angle combinations of $6^\circ$, $30^\circ$ and $7^\circ$, $35^\circ$. The latter pair of excitations are equivalent to actual $6^\circ$ and $30^\circ$ excitations, once the error in the calibration of the reference RF transmitter amplitude suggested by Figure 5 has been taken into account. The results are plotted in Figures 7a and b.

Figures 8b and c show $T_1$ and $R_1$ data calculated from signal intensities (Figure 8a) obtained by ROI software over three areas of interest within the breast of a 52-year-old patient with tumour recurrence in her left breast at the scar site of previous surgery. This was subsequently diagnosed as invasive ductal carcinoma.

Discussion

The calibration method used to check that the correct RF transmitter amplitude was being delivered suggested nominal RF flip-angles of $7^\circ$ and $35^\circ$ were necessary in order to deliver actual excitations of $6^\circ$ and $30^\circ$. In Figure 7b, the data lie much closer to the line of identity, at least up to 900 ms, than in Figure 7. This retrospectively verifies the accuracy of Perman et al's calibration method over which is automatically performed by Siemens software. The Siemens method of calibrating the reference RF transmitter amplitude involves applying three RF pulses ($a/2 - a/2$), measuring the ratio of the amplitudes of the spin-echo occurring after the second RF pulse, and the stimulated-echo occurring after the third RF pulse. This ratio is proportional to $|\cos(a/2)|$ and tends to a sharp minimum when $a = 180^\circ$. Plotting the functions $|\cos(a/2)|$ and $|\cos(a) \sin(a) \sin^2(a/2)|$ out, only a marginal difference in change of gradient at the minima (located at $a = 180^\circ$ and $a = 90^\circ$, respectively) is seen. This suggests that both methods should be equally accurate. However, the Siemens method requires the collection of two signals rather than one (as is the case for the method of Perman et al). Thus the subsequent calculation of a ratio may render the Siemens method more susceptible to error. Further work will be necessary to evaluate the relative accuracy of the two techniques.

Figure 6 suggests that a $T_1$ of 750 ms will be estimated as approximately 605 ms for a $-10\%$ error and 540 ms for a $-15\%$ error in calibration of the RF transmitter amplitude. The data in Figure 7a, certainly for the copper and manganese solutions, show that a $T_1$ of 750 ms would be estimated as approximately 550 ms. This implies an error in RF flip-angle calibration in the range of $-15\%$ to $-10\%$, concurring with the prediction obtained from Figures 5 and 6. From this, it can be concluded that the errors in the $T_1$ estimations (for $T_1$s less than 900 ms) are understood and correctable.

The $T_1$ estimated for the copper sulphate (high $T_2/T_1$...
Figure 8. (a) Signal intensity, (b) $T_1$ and (c) $R_1$ are plotted against time (post-injection of Gd-DTPA) for ROIs drawn over a patient's heart, around the site of a suspicious lesion, and over adjacent fatty tissue.

The ratio solutions proved to be no more inaccurate than those for the manganese sulphate (low $T_2/T_1$ ratio) solutions (see Figure 7). There is, in general, some reduction in accuracy at $T_1$ above 900 ms. Long $T_1$ are difficult to measure accurately, due to the fact that at high $T_1$, large changes in $T_1$ result in only small changes in signal intensity. Had the $T_1$ of the copper sulphate solutions proved to be more difficult to estimate correctly, this would have pointed strongly to the possibility that the Siemens FLASH sequence was not completely spoiling residual transverse magnetisation that remained at the end of a $T_R$ interval. Transverse coherence effects can thus be ruled out as a possible source of error in the $T_1$ estimations.

Clinical data were acquired using nominal RF flip-angle settings ($\alpha_1, \alpha_2, \alpha_3$) = (6°, 30°, 30°). The final flip-angle is different to that suggested by the optimization procedure described earlier by 3.5°. The angle $\alpha_3$ was set to the same value as $\alpha_2$ in order that the conventional method used by the examining clinicians, which involves subtracting pre- and post-contrast images so that non-enhancing tissue disappears in the subtracted image data set, was not changed. As Figure 4 shows, the rate of change of $dR_{1\text{new}}/dS$ with respect to $\alpha_2$ is relatively low for $25^{\circ} < \alpha_2 < 35^{\circ}$. This discrepancy is not expected to compromise the accuracy of the estimations of post Gd-DTPA $T_1$ (and hence $R_1$) values.

Figure 8b plots the $T_1$ of several tissue types as a function of time post-Gd-DTPA injection. ROIs were drawn on the patient images around a suspected lesion located originally from pre- and post-contrast subtraction images, over an area of adjacent fatty tissue and over the heart. Signal intensities from these ROIs were then used to calculate the $T_1$ plotted in Figure 8b, using Equations (2)-(4) and values of ($\alpha_1, \alpha_2, \alpha_3$) = (6°, 30°, 30°). The graph shows the $T_1$ of fat remaining constant at approximately 260 ms, while the lesion $T_1$ decreases from a pre-contrast value of 1100 ms to 300 ms 3 min after injection of Gd-DTPA. The value for fat falls within the range 240 ms ± 28% predicted by Bottomley et al [16] (at 40.5 MHz), whilst the initial value for the lesion is only 5% outside the range predicted (again by Bottomley et al [16]) for "miscellaneous" tumours; 816 ms ± 28%.

Figure 8b shows that post-Gd-DTPA $T_1$ do not fall below 150 ms, the lower limit of the $T_1$ range over which
optimization on the RF flip-angles was carried out. It is not expected, then, that this optimization would be rendered invalid as a result of Gd-DTPA shortened $T_1$.

Finally, in Figures 8a and c, signal intensity and $R_2$ values generated from the same ROIs that produced the curves in Figure 8b are shown, demonstrating the typical peak enhancement of signal for the heart within the first minute, the lesion enhancement curve, and non-enhancement of the fatty tissue.

The temporal resolution of the protocol was 60 s. This could have been made faster (say 15 s) by reducing to eight the number of slices interrogated (rather than 32), or by reducing the in-phase resolution. Greater temporal resolution is attractive because it would allow more detailed characterization (i.e. a greater number of data samples) of the first 3–5 min post-Gd-DTPA injection. It is this period that is most important in differentiating between benign and malignant disease [2,4,8,9]. However, a trade off has to be made between speed of scan and area covered by the scan, as Kerslake et al [9] have pointed out. Their protocol has a temporal resolution of 12 s, but they are only able to image four slice locations, thus covering only a small region of the breast. This is not desirable for routine MRM, since a clinically or mammographically observed lesion may be difficult to locate once the patient is in the MRI scanner, and because detection of multifocal and/or secondary tumours outside the covered region would not be possible. One possible way around this problem would be to bring the patient back for a second imaging session, with a higher temporal resolution limited to a specific region of the breast, after the whole breast had been imaged using the protocol described earlier.

Conclusions

It has been shown that it is possible to estimate $T_1$ accurately up to 900 ms, over a large 3D volume, in a time much less than would be possible with conventional SR/IR methods. Several possible sources of error have been either quantitated or ruled out, and the method has been shown to produce clinically realistic data. It is a method that is potentially applicable to any dynamic study of a 3D volume where quantitation of the uptake of paramagnetic contrast agent might prove to be of diagnostic value. Future work will require a broad spectrum of clinical cases to be examined, to evaluate the diagnostic value and specificity of the technique. Image registration would improve the accuracy with which $T_1$ values are estimated and would also allow more accurate comparisons of data obtained from subsequent imaging sessions of a particular patient (e.g. with a higher temporal resolution over a smaller volume, once areas of enhancement had been identified). Finally, it may be possible to incorporate a physiological model into the calculations that would enable other physiological parameters such as capillary permeability and leakage space to be measured [19].

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References

Appendix

Quantitation of post-contrast relaxation rate, $R_{1,\text{new}}$

The full expression for $R_{1,\text{new}}$ in terms of $S_1$, $S_2$ and $S_3$ is

$$R_{1,\text{new}} = \frac{1}{T_R} \ln \left( \frac{\cos(\chi_{1,\text{or}2})}{S_1 \sin(\chi_2) \cos(\chi_1) - \sin(\chi_1) \cos(\chi_2)} - \frac{S_2 \sin(\chi_2) - \sin(\chi_1)}{S_3 \cos(\chi_1)} \right)$$

This expression was differentiated with respect to $S_1$, $S_2$ and $S_3$ using the PC software package "Mathcad" (Mathsoft Inc., 1986–1992) to obtain analytical expressions for $\partial R_{1,\text{new}}/\partial S_1$, $\partial R_{1,\text{new}}/\partial S_2$ and $\partial R_{1,\text{new}}/\partial S_3$, which were subsequently used to calculate $\Delta R_{1,\text{new}}/\Delta S$. 

References


