Reproducibility of T1 and T2 Relaxation Times Calculated from Routine MR Imaging Sequences: Phantom Study

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Measurement of T1 and T2 relaxation times has been sought as one fundamental way to characterize tissue. Relaxation times can be calculated from routine spin-echo (SE) imaging sequences using two distinct repetition times (TRs), each with two SE samplings of signal intensity. Previous reports have quantified relaxation times without discussing the variation in their measurements. By imaging a phantom containing different samples with known T1 and T2 relaxation times on three separate occasions, the variation in relaxation time measurements inherent in different routine imaging sequences was studied. For the present study a more complete and accurate equation was used to calculate T1 values. The variation in T1 and T2 relaxation times for samples with relaxation times similar to solid tissue was 2%-4%. The amount of variability in calculated relaxation times was found to be dependent on the magnitude of the relaxation times themselves. However, the mean values were independent of the imaging sequences used to calculate the relaxation times. No significant differences were seen between left-to-right or section-to-section position within the same study or between studies performed on different occasions. The variability in the calculated T1 was dependent on the pair of TR sequences used to calculate T1. Samples with long T1 and T2 relaxation times, similar to many body fluids, had much larger variability. A computer simulation of measurement error was created to explain these results. This study indicates that properly performed routine imaging studies do yield reproducible T1 and T2 measurements.

In magnetic resonance (MR) imaging, signal intensity depends on both tissue and instrument parameters. In stationary solid tissue, signal intensity is mainly dependent on the T1 and T2 relaxation times and on the resonating hydrogen density. Alterations of these tissue parameters produce changes in signal intensity and thereby cause perceptible contrast changes on MR images. The signal intensity also depends on instrument parameters, including the selected imaging sequence and the receiver gain. The distinct intensity observed from any specific region, that is, image contrast, is clearly affected by these instrument settings. While the relative intensities of two regions in any imaged section will vary with different operator-selectable imaging sequences, the observable relaxation times and resonating proton density represent physical characteristics of the tissue that are independent of imaging sequences or other machine parameters. Therefore, the measurement of T1 and T2 relaxation times and resonating proton density has been sought as one of the fundamental ways of characterizing tissue using MR imaging.

Because of practical and physical constraints, measurement of T1 and T2 relaxation times using MR imagers is limited compared with in vitro spectrometers, which make more measurements on small samples of tissue. However, the imager-generated values are nevertheless important since clinical decisions might be made on the basis of this data. Studies at various field strengths have presented relaxation times of normal brain structures, but data concerning the variation in relaxation times in large series of patients are sparse [1, 2]. Previous reports on calculated T1 and T2 images of central nervous system (CNS) abnormalities have referred to
abnormalities in the relaxation times relative to normal brain, without giving the variability of T1 and T2 in normal brain and the amount that the relaxation times differed from normal [3]. Early reports on our prototype system suggested substantial variation in calculated values of normal and abnormal brain tissue [4]. Improved coil design and electronic hardware have been incorporated in the production model of our imager. This report discusses the reproducibility of T1 and T2 measurements made from routine imaging sequences using the clinical MR imager operating at 0.35 T. The methodology of such calculations is also addressed.

Materials and Methods

Both phantom and human-subject data were analyzed; the latter are discussed separately [5]. The phantom was imaged on an MR imager using a superconducting magnet operating at 0.35 T (Diasonic M7/S). A 2 cm head coil was used. Multiple-slice spin-echo (SE) sequences were performed with four separate repetition times (TRs) of 500, 1000, 1500, and 2000 msec, with five to 20 slices obtained simultaneously, two echoes (TEs) of 28 and 56 msec sampled in each slice. The matrix size was 128 × 128, yielding a voxel size of 1.7 × 1.7 × 7.0 mm. Four averages of the signal were obtained at each slice. The phantoms were imaged in this manner on three separate occasions so the variability between different studies could be determined. The imager and the pulse sequences have been described more completely [6-8].

The phantom in our study was a Lucite cylinder containing 12 axial compartments in which sample tubes containing different substances could be placed (fig. 1). The volume surrounding these sample tubes was filled with a dilute solution of copper sulfate. The sample tubes within the phantom are readily interchangeable. For our study, eight distinct samples with different T1 and T2 relaxation times were used in the 12 different locations. These samples were solutions of different concentrations of gadolinium diethylene triaminepentaacetic acid (Gd-DTPA). Four different samples were used in the four midline locations. Two identical sample tubes of each of the other four different solutions were placed in the four pairs of sample locations positioned symmetrically about the midline. In this manner, any variation between left and right in the imaging field for identical samples could be ascertained. The solutions were chosen to have T1 and T2 values similar to those of gray matter, white matter, fat, muscle, and cerebrospinal fluid based on measurements using a Praxis NMR spectrometer operating at 10 MHz. The T1 relaxation rates of our samples were about 5-10% faster when measured by our spectrometer operating at 10 MHz than the relaxation rates of the same samples measured on our imager operating at 15 MHz. This expected relaxation time dispersion was considered when choosing samples to be measured in the imaging instrument in this study.

Regions of interest (ROIs) were obtained for every one of the 12 samples in each of three adjacent sections for each of the three studies performed on separate occasions. Eight ROIs were also obtained in different locations within the surrounding copper sulfate matrix of the phantom. The sample ROIs contained 80 to 124 pixels, while the background ROIs contained 48 to 64 pixels. For each ROI, the mean intensity and standard deviation (SD) of the intensity was measured for the eight images of each section based on the four standard TR and two TE settings available on our imager. Using these mean intensity values, the T1 and T2 values were calculated using the SE equation for two SEs:

\[
I = k(N[H])(1 - 2e^{-(T1/T2)/(T1) + 2e^{-(T1/T2)/(T1) - exp^{-T6/2}}}),
\]

where the meaning of the symbols is explained (fig. 2). The absolute intensity measurements are meaningful only within the context of a single study, since the absolute intensities are not corrected for the receiver gain, which is variable for different studies. This variability is reflected in equation 1 by the unknown term, k, which varies from study to study depending on instrument settings. The T1 values of the ROIs were calculated using an iterative technique based on the intensities of the first echo samplings (28 msec TE) of two different TRs. Four different pairs of TR sequences were used for calculating T1 relaxation times: 500/2000, 500/1500, 500/1000, and 1000/2000 msec. T2 values were calculated directly for each of the four TR sequences by using the intensities of both echo samplings for each TR. Thus for each ROI, four different T1 values and four different T2 values were calculated.

The method described above is a refinement of a previously described method for calculation of relaxation times. Previous reports from our institution have used a simplified form of equation 1 based on

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Fig. 1.—MR image of phantom viewed at narrow windows. Twelve cylindrical sample tubes containing different solutions of Gd-DTPA are imaged in cross section. Background matrix is cupric sulfate solution. Higher intensity of upper and lower parts of background solution, secondary to receiver coil geometry.
on the saturation recovery model for the SE experiment [3, 4, 6–8]:

\[ I = k(N[H]) \left( 1 - e^{-TR/T1} \right) \left( e^{-TR/T2} \right). \] (2)

This simplified equation does not consider the effect of the dual 180°
sampling pulses on the longitudinal component of magnetization. This
is graphically illustrated in figure 3. The result is a systematic error in
the calculated T1 value, which becomes larger as the inversion time
(TI) in equation 1 becomes significant, such as for short TR sequences
and for longer T1 values. The discrepancy between the two equations
is the subject of a separate communication [9].

Both the 90° and 180° excitation pulses are slice-selective radio-
frequency pulses with a sin (bt)/t envelope resulting in an approxi-
mately rectangular slice-selection profile. This sin(bt)/t envelope gives
both more uniform slice widths for various TR settings and also
significantly more uniform slice excitation than a gaussian envelope
[10–12]. There will still be some flip angle inhomogeneity within the
slice, especially at the edges of the slice. This may contribute to the
variation of relaxation time measurement that we observed.

The variations of the calculated T1 and T2 relaxation times for
each of the different samples were evaluated in three different ways.

First, the overall mean T1 and T2 relaxation times for each sample
and the SDs of these means were calculated. The individual ROIs
from studies from the three separate occasions were subdivided by
sample type, and the mean and SD of the calculated T1 and T2
relaxation value for each sample were measured. This was done for
all eight distinct samples and for the background-matrix ROIs.

Second, the variation in the T1 and T2 relaxation times between
left and right within the same slice and within the same study was
measured for each of the four pairs of comparable left-right regions
containing identical sample types. The percentage difference and the
SD of the percentage difference was measured. This was also done
on four pairs of background-matrix ROIs located symmetrically about
the vertical midline.

Third, the variation in the T1 and T2 relaxation times of each
sample from slice to slice within the same study was measured. The
percentage difference in the calculated T1 and T2 value between the
center slice and two different off-center slices was measured as well
as the SD of this percentage difference. This was done for each of
the 12 sample locations and the eight background locations.

Not only was the variation in the relaxation rates measured in
different ways, the dependence of this variation on the machine
parameters and on the relaxation rates themselves was investigated.
The variation in the calculated T1 value was compared for samples
with different T1 relaxation times. More specifically, the percentage
SD of the T1 measurement was related to the T1 relaxation value
itself. The variation in the calculated T1 values was also compared
for the different TR pairs used to calculate T1 relaxation times. A
similar analysis was performed for the calculated T2 values. The T2
values obtained from different TR sequences for the same ROI were
compared. The SD of the T2 values was related to the magnitude of
the T2 relaxation times.

The variation in the intensity of the background-matrix ROIs was
measured for the eight images of each section and compared with
the variation in the calculated T1 and T2 relaxation times of the
background ROIs.

Finally, a computer model was created to determine optimal im-
ageing sequences for measurement of T1 and T2 relaxation times by
simulating the effect of errors in intensity measurement on the cal-
culated T1 and T2 values. As mentioned, the ratio of the intensities
obtained from the first echoes of any two TR sequences is used to
calculate T1 relaxation with the above equation. If the intensity
variation in any measurement is, say 1%, the maximum effect on the
calculated T1 value will occur when the intensity error of the first
echo from one TR sequence is increased by 1%, while the intensity
of the first echo from the other TR sequence is decreased by 1%.
For this simulation, a 1% intensity change was defined as a 1% change
in the maximum possible intensity, that is, the intensity expected with TR = infinity and TE = 0. The expected maximum and
minimum T1 relaxation time changes were subsequently simulated
for 0.5%, 1%, and 2% variations in the intensity measurements. The
effect of these errors in intensity measurement on the calculated T1
was determined for five different TR pairs. These results were com-
pared with our experimental data.

A calculation was also performed to determine the range of T2
values best measured by a TE pair of 28 and 56 msec. In calculating
T2 relaxation times, the ratio of intensities of the first and second
echoes within one TR sequence is used. For a 1% intensity variation,
the maximum change in the calculated T2 value will occur when the
intensity of the first echo increases by 1%, the intensity of the second
echo decreases by 1%, and vice versa. The maximum effects of
0.5%, 1%, and 2% intensity measurement errors on the calculated
T2 values were determined for substances with different T2 relaxation
times.

Results

Variation

The variation of calculated T1 and T2 relaxation times for
the different samples in the phantom was measured in several
ways and is shown in table 1. For reasons discussed below,
T1 values obtained from the 500/2000 and the 500/1500 TR
sequence pairs were used in the final evaluation of the T1
relaxation time variation. The T2 values obtained from all four
TR sequences were used in evaluating T2 relaxation-time
variation. A measure of overall variation for each sample was
obtained by comparing all of the ROIs from the phantom
studies done on three separate occasions (table 1). The
variation within a study from one slice to another is shown as well as the variation between comparable regions within the same slice on the left and right of midline. The variation in T1 and T2 values between the different studies was not greater than the left-to-right variation or the slice-to-slice variation within the same study. For the samples with T1 values similar to normal solid tissues (280–720 msec), the SD of the T1 values was 2.5%–4%. For samples with T2 values similar to normal solid tissues (40–62 msec), the SD of the T2 values was 2%–3.5%.

Worth noting is the fact that the amount of variability of T1 and T2 relaxation times depended on the magnitude of the T1 and T2 values themselves. Figures 4 and 5 demonstrate the SD of T1 and T2 measurements relative to the magnitude of the T1 and T2 values, respectively. The T1 relaxation measurements demonstrate the lowest SD for the samples with a T1 relaxation time of 431–632 msec. Also, the SD of T2 measurements is smaller for the samples with T2 relaxation times of 40–62 msec.

When viewing our images of the phantom at narrow windows, the intensity of the background matrix is not homogeneous. Because of receiver-coil proximity the anterior and posterior parts are more intense than a horizontally oriented less intense band through the middle of the phantom (fig. 1). The variation of intensity within a single study was measured in the background matrix in eight different locations. In this homogeneous material in three different sections, the SD in the intensity of the first echoes (28 msec TE) of the 2000/500 m sec TR sequences was 7.2% and 6.4%, respectively, while the SD of the corresponding calculated T1 relaxation time was only 3.7%. The first and second echoes of the 2000 msec TR sequence used in calculating T2 had SDs in intensity of 7.2% and 8.2%, respectively, while the SD in the calculated T2 value was only 6.7%. For the background matrix with a T1 relaxation time of 275 msec and a T2 relaxation time of 95.2 msec, when imaged with a TR sequence pair of 2000/500 msec, a +1% error in the measurement of the intensity of the first echo of the 2000 msec TR will cause a 2.5% error in the calculated T1 value and a ~3.3% error in the calculated T2 value. Thus, the variation in the T1 and T2 values for the background material is much less than expected if the variation of the measured intensity of the different section is independent of location. In this case, however, the band of low intensity is present on all of the four images of a section obtained with two TR sequences and two TEs each. This intensity variation is largely canceled out in the relaxation-time calculations. Thus, the calculated T1 and T2 relaxation times may be more reproducible than direct intensity measurements in differentiating tissue types.

**Dependence on Machine Parameters**

As mentioned in Materials and Methods, the T1 value of the different regions was calculated using four different TR sequence pairs: 500/2000, 500/1500, 500/1000, and 1000/2000 msec. These TR sequence pairs correspond to those often used in the past in clinical imaging at our institution. The mean T1 values and SDs for the different samples calculated using these four TR pairs is shown in table 2. No significant differences were present between the mean T1 values obtained from the four different TR sequence pairs. This would not be the case if the simplified equation (equation 2) were used [7]. Although the mean T1 values did not vary significantly when different TR sequence pairs were used for the calcula-
TABLE 2: T1 Values and Standard Deviations Using Different TR Sequence Pairs

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean T1 (SD) per TR Pair (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>500/2000</td>
</tr>
<tr>
<td>A</td>
<td>1252 (4.7)</td>
</tr>
<tr>
<td>B</td>
<td>711 (3.6)</td>
</tr>
<tr>
<td>C</td>
<td>631 (3.3)</td>
</tr>
<tr>
<td>D</td>
<td>433 (2.4)</td>
</tr>
<tr>
<td>E</td>
<td>281 (3.8)</td>
</tr>
<tr>
<td>Background</td>
<td>277 (3.4)</td>
</tr>
</tbody>
</table>

TABLE 3: T2 Values and Standard Deviations Using Different TR Sequences

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean T2 (SD) per TR Sequence (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2000</td>
</tr>
<tr>
<td>A</td>
<td>138.4 (8.1)</td>
</tr>
<tr>
<td>B</td>
<td>118.6 (7.8)</td>
</tr>
<tr>
<td>C</td>
<td>123.6 (5.5)</td>
</tr>
<tr>
<td>D</td>
<td>106.0 (4.6)</td>
</tr>
<tr>
<td>E</td>
<td>98.3 (6.7)</td>
</tr>
<tr>
<td>F</td>
<td>61.8 (1.3)</td>
</tr>
<tr>
<td>G</td>
<td>51.1 (3.6)</td>
</tr>
<tr>
<td>H</td>
<td>39.8 (4.0)</td>
</tr>
<tr>
<td>Background</td>
<td>97.8 (5.6)</td>
</tr>
</tbody>
</table>

Computer Simulation

The results of the computer simulation confirm the experimental results, showing larger T1 calculation errors for substances with T1 relaxation times less than 300 msec or greater than 900 msec, as well as the results showing larger error for calculations based on the 1000/2000 msec TR sequence pair. Figure 6 demonstrates the maximum effect of a 1% error in intensity measurement on the T1 calculation using three different TR sequence pairs. We see that effect of an error in intensity measurement using a TR sequence pair of 500/2000 msec becomes significantly greater for substances with a T1 of less than 300 or greater than 900 msec. Of note, this TR sequence pair yielded the smallest errors in T1 relaxation measurements of all of the TR pairs for equal-intensity errors. The 500/1500 msec TR sequence pair and the 1000/2000 TR sequence pairs are often clinically used in T1 calculations, but as is seen in figure 7 similar-intensity errors will produce larger T1 relaxation time errors using these TR sequence pairs than the 500/2000 msec pair. This computer simulation confirms our experimental measurements that for the T1 range of most tissues the variation in T1 relaxation is very similar for the 500/2000 msec and the 500/1500 msec TR sequence pairs. Also both the simulation and experimental data indicate that both of these TR pairs showed less variation in the T1 values than the 1000/2000 msec TR sequence pair.

It should be emphasized that for the TR sequence pairs we use (2000 msec TR or less), the effect of an intensity error in measuring substances with long T1 relaxation values above 1500 msec is large (such as for cerebrospinal or other fluids) (fig. 7). Using a simulated TR sequence pair of 2000/5000 msec (fig. 6) the effect on intensity variation would be much smaller in such substances. While this TR sequence pair would yield more accurate and reproducible T1 relaxation times for such fluids, this sequence would require a very long imaging time and it would be unsuitable for measuring the T1 relaxation times of solid normal tissues with T1 relaxation times of less than 1000 msec. As seen in figure 8, for a substance with a T1 of 500 msec, a 1% intensity measurement error will lead to a −50% to +30% error in the calculated T1 when a 2000/5000 msec TR sequence pair is used.

Figure 8 shows the maximum effect of a 1% intensity error on the calculated T2 values for substances of different T2 relaxation times. From this figure, it is clear that substances with T2 relaxation times of 30–90 msec are least susceptible to significant variations in the calculation of T2 relaxation from intensity-measurement error. This graph is similar to our experimental results (fig. 5). As is seen in both our experimental data and in our computer model, the relaxation times
of fluids with long T2 values are not well evaluated with SEs obtained only at 28 and 56 msec.

Discussion

There are inherent limitations in accurate measurements of T1 and T2 relaxation values during routine imaging sequences when compared with in vitro measurements. Potential sources of error include inhomogeneous radiofrequency irradiation, gradient nonlinearity, tissue bulk magnetic susceptibility, diffusion, motion, and a lower signal-to-noise ratio. Nevertheless, given such limitations, reproducibility of those measurements that are obtained is desirable. Our clinical imaging system was able to calculate the T1 values by routinely imaging with two different TR sequences. However, two TRs are the minimum for this calculation, and the inherent problems in attempting to plot an exponential curve that represents a given relaxation function from two points is obvious. Similarly, the two SEs we use are the minimum number necessary to calculate T2. If multiple points are used to measure longitudinal or transverse relaxation, the accuracy of the measurement can be evaluated easily with goodness-of-fit parameters. Because only two points are used for both the T1 and T2 calculations, there is no way to determine the validity of the calculated values other than to test them with known standards and/or to measure the reproducibility of such measurements. Even if the calculated values contain a systematic error, the values may nevertheless be very useful in evaluating pathology if they are reproducible. Again, an imager measures the signal intensity of a region, and the relaxation times are calculated from these intensities. The errors or variations in these intensity measurements are responsible for the variation in the calculated T1 and T2 values. This dependence is not simple and linear but reflects the complex relation between the relaxation times of the substance and the imaging sequences used. The SD in the calculated T1 and T2 relaxation times for our known samples was only 2%–4%. In addition, the calculated relaxation values of a given sample was independent of left-to-right and section-to-section positioning, and was stable on separate occasions.

An important consideration in imager-based T1 and T2 measurements is the choice of imaging sequences. The TR and TE settings of the imager must be appropriate for the T1 and T2 relaxation values of the tissue. With our instrument, using a short TR of 500 msec and a long TR of either 1500 or 2000 msec achieves the most reproducible results for substances with T1 relaxation values similar to most tissues—about 300–800 msec (at 0.35 T). A TR sequence pair of 1000/2000 msec produced less reproducible results, especially for samples with a T1 relaxation time of less than 300 msec. This is because most of the longitudinal relaxation (T1) in tissue where the T1 relaxation time is less than 1000 msec has already occurred before the first measurement at 1000 msec takes place. While we do not have control over the TE setting of our imager, a similar analysis on samples with different T2 relaxation times reveals that for the TE pair of 28 and 56 msec, substances with T2 values of 40–60 msec demonstrate the smallest variation. Again, this corresponds to the values at 0.35 T in most tissues. These conclusions were confirmed in our computer simulation of the effect of intensity-error measurement on calculated T1 and T2 values.
The results reported herein document the relative lack of instrument-related variability in relaxation-time calculations of samples with relaxation times similar to most tissues. Other sources of variability exist when analyzing living subjects. One difficulty in measuring phantoms is the lack of physiologic and geometric variation inherent to biologic systems. For this reason, similar analyses of measurement of reproducibility are needed in human subjects. These also have been performed and are reported in another communication [5].

REFERENCES

2. Wehrli FW, MacFall JR, Glover GH, Grisby N. The dependence of NMR image contrast on intrinsic and pulse sequence timing parameters. Magnetic Resonance Imaging 1984;2:3–16