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Experimental Analysis of T_1 Imaging with a Single-Scan, Multiple-Point, Inversion–Recovery Technique

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Look and Locker's single-scan, multiple-point, T_1 determination technique modified for imaging applications was evaluated experimentally for its accuracy and reliability with respect to the pulse sequence parameters, in particular, to the interpulse delay, t_D, and the tip angle, α. T_1 imaging experiments were performed with a 0.5-T imaging system on a phantom which consisted of an array of vials containing 2% agarose gels doped with various amount of Mn^{2+} using different combinations of the parameter set $\{t_D, \alpha\}$. T_1 results obtained with this technique were compared with those measured by a conventional inversion–recovery procedure using the same spectrometer. Strategic choice of pulse sequence parameters to minimize experimental errors and the criteria for these choices will be discussed.

INTRODUCTION

Inversion recovery (IR) is well recognized as the most reliable way of measuring T_1 in conventional NMR (*1*). The main drawback of this technique is the long dead time required for the longitudinal recovery which, when coupled with the need for acquisition of multiple data points, makes the whole measuring process time consuming. To make the data acquisition time for T_1 measurements more tolerable for imaging applications, the common practice is to abridge it by acquiring only two data points in the relaxation curve. While this practice, if used carefully, can produce fairly good measurements within a narrow target T_1 range (*2, 3*), its usage is still limited because the degree of accuracy achievable, even under optimal conditions, is not very high. The method is especially inaccurate for those nuclei whose T_1 does not fall into the target range of the experiment.

To improve accuracy as well as widen the measurable T_1 range in imaging experiments, schemes to acquire multiple data points in a single scan (*4–6*) have been proposed. A detailed analysis of the relative merits of these techniques was given by Crawley and Henkelman (*7*). Our objective here is to provide an empirical verification of one of the more promising schemes in this category, namely the imaging version (*6*) of the Look and Locker (ILL) experiment (*8*). We analyzed the accuracy of this technique using phantom results for illustration. We also examined the issues of what parameters to use in order to have the best accuracy of the measurement over a chosen range of T_1 values.

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METHOD

The pulse sequence of the ILL technique is shown in Fig. 1. The image intensity $M(j)\sin\alpha$ after the jth ($j = 1, 2, \ldots, N$) α pulse can be shown (*1*) to be (here we ignore the effect of t_0 which is small)

$$M(j) = A + Be^{-Ct_j}; \qquad t_j = t_0 + (j-1)t_D, \qquad C = \frac{1}{T_{1e}}, \tag{1}$$

with

$$A \equiv M_z(\infty); \qquad M_z(\infty) = M_0 \frac{1 - e^{-t_D/T_1}}{1 - e^{-t_D/T_1}\cos\alpha}; \tag{2a}$$

$$-B \equiv [M_z(\infty) - M_z(1)] = \text{Dynamic Range}$$

$$= \frac{M_z(\infty)(1 + e^{-D/T_1}) + M_0(1 - e^{-D/T_1})}{1 + e^{-TR/T_1}\cos^N\alpha}; \tag{2b}$$

$$M_z(1) = -M_0 + \{M_0 - M_z(N)\}e^{-D/T_1},$$

and

$$\frac{1}{T_{1e}} = \frac{1}{T_1} - \frac{\ln(\cos\alpha)}{t_D}, \tag{2c}$$

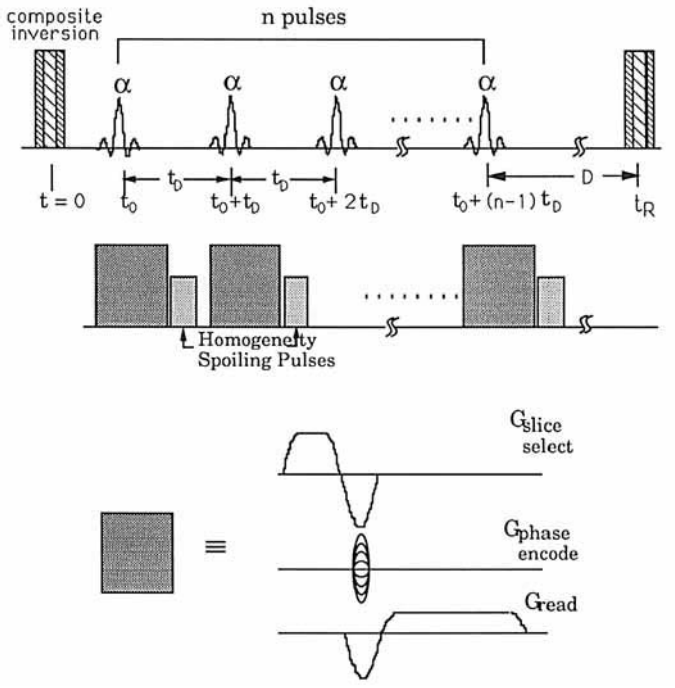

FIG. 1. Schematic diagram of the ILL pulse sequence.

where $A \equiv M_z(\infty)$ is the steady-state longitudinal magnetization one would have obtained after a large number of α pulses, $-B$ the dynamic range, D the dead time ($D = \mathrm{TR} - Nt_D$), and T_{1e} the effective relaxation time. By least-square fitting $M(j)$ to the three parameters, A, B, and T_{1e}, T_1 can be evaluated from [2c].

The percentage error of T_1 using the ILL technique can be shown to be

$$\frac{\delta T_1}{T_1} = \frac{T_1}{t_D}\{\tan \alpha \delta\alpha - t_D \delta C\}, \qquad [3]$$

with $\delta\alpha$ and δC being the estimated errors of the tip-angle and apparent rate constant measured by the experimental fit, respectively. It is clear from [3] that the two most important parameters in determining the T_1 accuracy using this technique are the interpulse timing t_D and the tip-angle of the sampling pulses α. In the analysis of the optimal parameters of this technique, Crawley and Henkelman (*7*) recommended the use of a smallest possible D and an optimized set of $\{\alpha, t_D\}$ based on N and a single target T_1. For pure samples and RF coils the tip-angle of which can be accurately controlled, this appears to be the strategy of choice. However, for imaging experiments where we assume the target is a T_1 range rather than a single value and that one has to confront the problem of RF inhomogeneity, it may be more appropriate to follow a different strategy. For timing considerations, we follow a scheme similar to that of Weiss and Ferretti (WF) (*9a*) who used a lower and upper time limit, T_A and T_B, which were estimated to bracket the target range of T_1 values as a basis for optimization. The timing parameter t_D is then chosen to minimize the error for a given signal-to-noise. However, because of the special manner in which the spin magnetization in an LL experiment approaches the steady-state, two important differences must be kept in mind before the WF results can be applied to the optimization of the LL experiments.

First, as shown in [1] and [2c], the apparent relaxation rate in an LL experiment is $1/T_{1e}$, which nearly equals $1/T_1$ only if α is small. Second, the optimum dead time D in an IR experiment, according to the WF scheme (*9a*), is often quite long ($\sim 10T_A$). In the LL experiment, D should be chosen to maximize, within the constraint of a scan time appropriate for *in vivo* applications, the dynamic range $-B = M(\infty) - M(1)$, which according to [2b] depends also on α, t_D, T_1, and, to a lesser extent, N. It is not difficult to show that the optimum choice of D (in maximizing the quantity $|\mathrm{B}|/\sqrt{\mathrm{TR}}$) is 0 or the smallest value possible in all cases except when α is large. There is, however, another reason to keep α small (see below), but even in those cases when α is not small, a small D would still correspond very closely to the optimum point.

The choice of α is dictated by the compromise of two opposing factors. The first factor, which favors a small α, is to keep the dynamic range large and the effect of tip-angle and its error on the T_1 accuracy small. The second factor, which favors a large α, is to increase signal sensitivity. A good compromise is an α ranging from 15° to 30°. The effect of the choice of α on T_1 will be evaluated empirically using the phantom results presented below.

What remains to be optimized is the time spacing parameter t_D. The optimization process of t_D, following the WF scheme (*9a*), is an iterative one. To illustrate by example, nine data points were used in the relaxation curve ($N = 9$) in our experiments. We picked time limits T_A and T_B which bracket T_1 values of most tissues: $T_B/T_A = 6$, $T_A = 150$ ms. Assuming an $\alpha \sim 20°$, T_{1eB}/T_{1eA} is approximately 4 for t_D between

50 to 100 ms. For this ratio, the recommended pulse spacing is ζT_A; where ζ is a number obtained by optimization. For the LL experiment, one can then solve t_D from the following equation:

$$t_D = \zeta T_{1e}(\alpha, T_A) = \zeta \frac{T_A t_D}{t_D - T_A \ln(\cos \alpha)} = T_A(\zeta + \ln \cos \alpha). \quad [4]$$

The number ζ depends heavily on whether the fitting is a two- or three-parameter one (*9a*, *9b*). For $T_B/T_A = 4$, $\zeta \sim 0.39$ for a two-, and $\zeta \sim 2.71$, for a three-parameter fit. The reason for this large difference in choice of timing is that in the two-parameter case (here one presumably has precise knowledge of the tip-angle(s)), $M_z(\infty)$ can be estimated from data of short recovery times. In the case of a three-parameter fit, because of the uncertainty of the tip-angle, one must estimate $M_z(\infty)$ exclusively from longer times in the relaxation curve. The LL experiment is a hybrid case since the model Eq. [1] is certainly three-parameter. Yet fundamentally the only parameters to be determined from [2] are two, M_0 and T_1 (assuming that α is known, though not necessarily precisely). Our strategy is then to compromise by using a t_D twice as long as the one recommended by the two-parameter model, bearing in mind the finding (*9b*) that too long a t_D does not significantly (while one that is too short does) affect the T_1 accuracy. On this basis, our t_D of choice is $2T_A(\zeta + \ln \cos \alpha) \sim 70 - 100$ ms for $\alpha = 15°$–$30°$.

EXPERIMENTAL PROCEDURE

A T_1 phantom was built consisting of an array of sample vials filled with 2% agarose gels doped with Mn^{2+}. The sample vials were placed in a holder that consists of three parallel acrylic plates. It provides a uniform distribution of samples within the head coil of the scanner. The Mn^{2+} concentrations in these vials were 0.05, 0.10, 0.30, 0.40, and 1.0 m*M*, respectively. The samples were prepared by mixing proper amounts of stock $MnCl_2$ solutions and agarose powder at elevated temperature to form a gel. Detailed steps for the gel preparation can be found in Ref. (*10*). This sample set provides very stable T_1 values which have not changed over a period of over 1 year (in contrast to the sample set of $CuSO_4$ solutions, the T_1 of which was found to increase substantially as solid particles precipitated in a matter of days).

The ILL technique was implemented in a 0.5-T Picker (Cleveland, Ohio) MRI whole-body scanner. The phantom was placed inside a receive head coil, while RF was transmitted from the body coil which yielded good RF homogeneity over the volume of the phantom. Sixteen sets of T_1 data were collected comprised of the combinations of four t_D values: 44.4, 64.4, 84.4, and 104.4 ms, and four tip-angle values: 15°, 20°, 25°, and 30°. Since from Eq. [3] the T_1 error can be substantial for long T_1 samples for $\alpha > 15°$ even if $\delta\alpha$ is small (1° to 2°), it is important to assess the effect of $\delta\alpha$ on T_1 with tip-angles determined routinely using software supplied by the manufacturer for normal imaging experiments. In each of these data sets, 192 phase-encoding steps, 4 signal accumulations per scan, and $t_0 = 8.3$ ms were used. To serve as reference standards, T_1 determinations of these phantom vials by a nine-point IR technique were also conducted in the Picker scanner using a very long TR.

RESULTS

Figure 2 shows the results of the T_1 measurements performed on the phantom with the ILL technique using the 16 combinations of α and t_D plotted against the T_1 of the same substances measured with the conventional IR technique in the same spectrometer. The results shown in the plots on the left-hand side of Fig. 2 can be fully explained

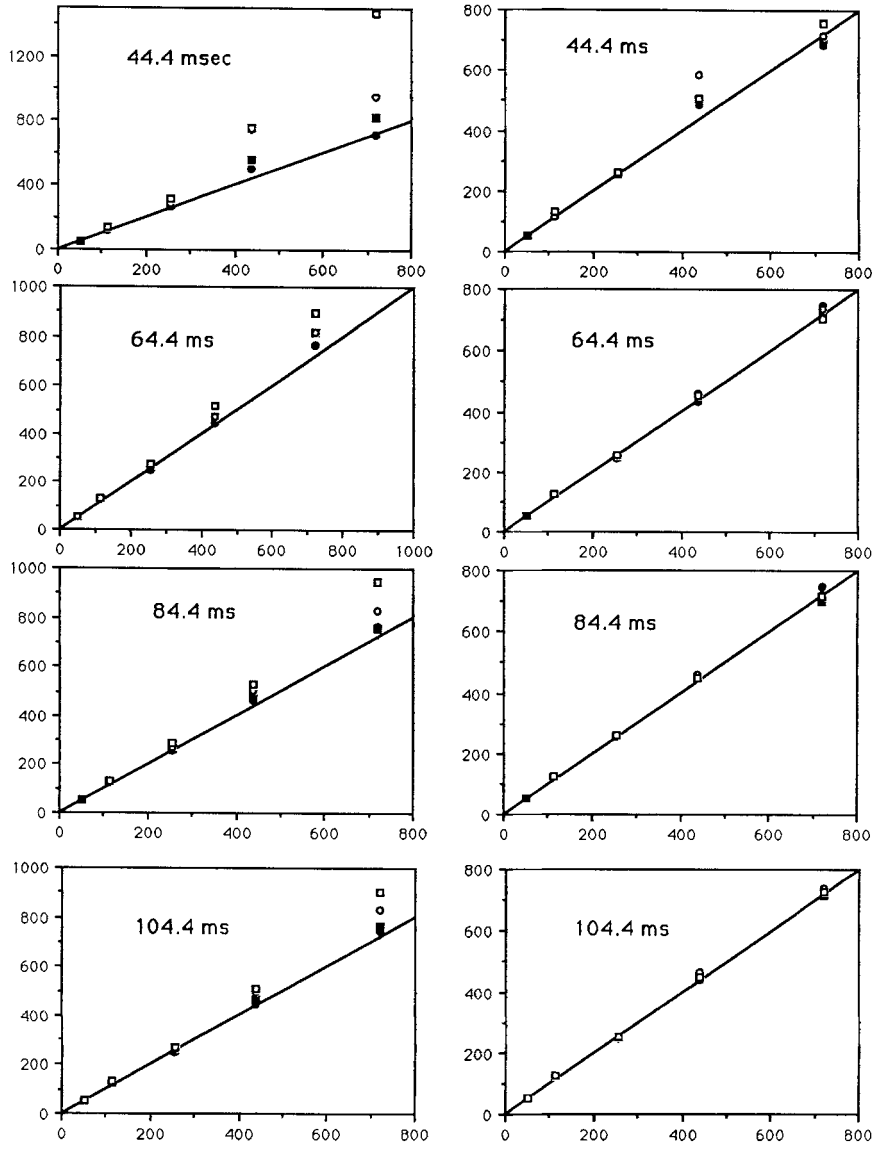

FIG. 2. Experimental results of the Mn^{2+}-doped agarose gel comparing T_1 measured by the ILL technique (in the ordinate) with T_1 results measured by conventional IR technique (abscissa): left—before tip-angle correction; right—after tip-angle correction. □, 30°; ○, 25°; ■, 20°; ●, 15°.

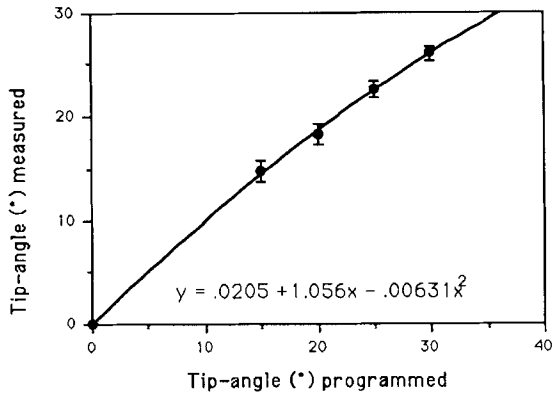

FIG. 3. Tip-angle calibration curve.

in terms of Eq. [3]. For samples with short T_1 (<500 ms), the errors are small in almost all cases. For samples of longer T_1, the T_1 values are progressively overestimated as α becomes larger and t_D shorter. This arises from a systematic underestimation of the α employed by the system software. For small tip angles, this underestimation is slight; it is caused by simply (and incorrectly) taking the Ernst angle, $\alpha_E = \cos^{-1}(e^{-TR/T_1})$ as the 90° tip-angle when TR (1 s) is insufficiently long. To verify this point, we filled the phantom holder with vials containing doubly distilled water (T_1 was independently determined to be 2.93 s) and measured the tip-angles by taking the intensity ratio of two gradient echo images, one with a TR of 300 ms and the other, a virtually infinite TR (15 s). The result, shown in Fig. 3, fits a quadratic equation between the mean actual tip-angle measured and its programmed value (the error bars are measures of degree of RF homogeneity rather than measurement accuracy which is significantly smaller). As the programming value reached 90°, $\bar{\alpha}$ evaluated from the fitted equation is 44° which is very nearly equal to the Ernst angle when TR = 1 s. Based on this relation, one can calibrate the amplitude of the RF transmitted by the body-coil in terms of the averaged tip-angles used in the T_1 experiments. The T_1 results after the tip-angle error correction are shown in the right side in Fig. 2.

CONCLUSION

To conclude, we have demonstrated the feasibility, and established the conditions, of a method of accurately measuring T_1 *in vivo* using an imaging version of the Look and Locker technique. Our phantom results indicated that this technique is very sensitive to tip-angle error for substances with long (compared to t_D) T_1 if a tip-angle greater than 20° is used. With this stipulation, it is reasonable to say that ILL is an efficient, reliable, and accurate technique. Our preliminary experiences of applying this technique, at 0.5 T, for T_1 determination of liver, kidney, and spleen of normal human volunteers (all yielding results comparable to published values (*3*) at comparable field strength) strengthened this assessment.

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