Measurement of magnetic resonance T2 for physiological experiments

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Hardy, Peter A., and Guang Yue. Measurement of magnetic resonance T2 for physiological experiments. J. Appl. Physiol. 83(3): 904–911, 1997.—The proton transverse relaxation time (T2) of human skeletal muscles has been increasingly used in magnetic resonance imaging experiments to examine muscle physiology and neuromuscular control. However, little attention has been paid to the experimental factors affecting the accuracy or sensitivity of the T2 measurement. We have explored theoretically and experimentally the structure of several magnetic resonance pulse sequences for measuring T2 of the first dorsal interosseous muscle and found that a multiecho imaging technique using non-slice-selective refocusing pulses (MENSS) produces more accurate T2 estimates than multiecho slice-selective (MESS) imaging methods that are commonly used. Using either technique we acquired four 5-mm-thick transverse images of the first dorsal interosseous muscle with a spatial resolution of 0.6 mm within 5 min. The T2 measured by the MENSS method was closer to the true T2 than was the T2 estimated by the MESS method. After a given amount of exercise, the MENSS technique revealed an average 28% increase in T2 compared with a 13 ± 3% increase measured with an equivalent MESS technique. We conclude that the MENSS method is a more accurate and sensitive procedure for studying neuromuscular physiology compared with the more commonly used MESS method.

Methods

Theory

The constraints on measuring T2 of muscle are established partly by the physiology of the process of muscle activation and recovery from exercise and partly by the physics and engineering of making MR images. Physiological constraints are imposed by the rate of recovery of a muscle once it is activated. This rate has been measured for various muscles and appears to have a half-life of ~14 min. Thus, to ensure that a T2 measurement captures the state of an activated muscle after exercise, the measurement must be completed as fast as possible before significant recovery has occurred. On the other hand, to follow the decay of the signal requires imaging with multiple echo times (TE). Ideally, each acquisition would have a different TE, but the time to acquire even four separate images would be nearly equal to the recovery time for the muscle to return to normal after exercise. Because of the need to obtain the measurements quickly, researchers have chosen the less accurate but faster multiple spin-echo pulse sequences for T2 measurements. In this technique, one 90° pulse excites the magnetization, which is then refocused into echoes by equally spaced 180° pulses. An image formed from each echo will track the decaying magnetization.
Muscle at rest has a $T_2$ of ~30 ms, which can increase to ~40 ms after vigorous exercise (2). With a typical spacing of multiecho images of 20 ms (i.e., 20, 40, 60...), the signal decays to the level of noise before many images can be acquired. Thus careful consideration must be given to the spacing of the echoes and the receiver bandwidth to maximize the received signal-to-noise ratio and to minimize the error in the calculated $T_2$.

Two multiecho pulse sequences were developed to image the FDI muscle. A schematic diagram of the multiecho spin-echo method for acquiring multiple images is shown in Fig. 1. The first sequence used slice-selective 90° excitation and 180° refocusing pulses (cf. bottom 2 traces in Fig. 1). This sequence was called the multiecho-slice-selective (MESS) technique, and it is similar to sequences used in many physiological experiments. The MESS sequence was thus capable of imaging multiple slices simultaneously, although in this study only four slices were imaged. The slice-selective 180° pulse used in the MESS technique was designed by the manufacturer to produce spin-echo images with minimum slice-to-slice interference. The second sequence used the identical 90° excitation pulse as in the MESS sequence but non-slice-selective 180° refocusing pulses (cf. top 2 traces of Fig. 1). The exact refocusing pulse used was the "version s" pulse designed by Poon and Henkelman (20) to refocus magnetization with immunity to inhomogeneities in both the main magnetic and the radio-frequency magnetic fields. This sequence was called the multiecho non-slice-selective (MENSS) technique (19). We adapted the MENSS technique to image four 5-mm-thick slices of the FDI muscle by incorporating a 750-ms delay between the end of one echo train and the start of the next echo train. With a repetition time (TR) = 3,000 ms, an echo train length of 145 ms, and a 750-ms delay, four slices could be imaged in a total acquisition time of under 5 min. In this way, data from each slice were acquired simultaneously. Both sequences used identical timing of the echoes generated. The major difference between the sequences was the absence of slice-selective gradients during the application of the 180° pulses and the use of a special radio-frequency pulse to refocus the maximum amount of transverse magnetization in the MENSS sequence. Both the MESS and MENSS sequences incorporated spoiler gradients paired about the 180° pulses. The purpose of these gradient pulses was to eliminate the unwanted refocusing of longitudinal magnetization created by imperfect 180° pulses. Imaging was done on a Siemens 1.5-T Vision imager. This instrument had a field strength of 1.5 T and magnetic field gradients capable of rising to 25 mT/m in 600 µs. Both the MESS and MENSS sequences were designed to image a minimum field of view of 150 mm with a slice thickness of 5 mm. Eight echoes were acquired with $TE = 17, 34, 51, \ldots, 136$ ms.

Analysis

As shown in the APPENDIX, the best estimate of $T_2$ from a series of images with intensity $S(TE)$ after the decay of the transverse magnetization is

$$T_2 = \frac{\Delta}{\sum \omega_n \sum X_n Y_n - \sum \omega_n X_n \sum \omega_n Y_n}$$

where $X = -TE$ and $Y = \ln[S(TE)]$ and $\Delta$ is given by Eq. A4, and $n$ is the index running from 1 to the number of echoes collected. The weighting factor ($\omega_n$) is given by Eq. A2. The image data $S(TE)$ must first be corrected for the effect of the presentation of MR images as the magnitude of the complex received signal. This correction is outlined in the APPENDIX, and a suitable correction factor is shown in Fig. 2. A computer program was developed to take in multiecho images and calculate $T_2$ according to Eq. A3 after the correction of Fig. 2 was applied. All analysis was made from the calculated $T_2$ images.

Experimental Procedures

Studies with phantoms. The accuracy of the two imaging methods was established by imaging a phantom consisting of eight 50-ml vials of distilled water doped with varying concentrations of the paramagnetic agent gadopentetate dimegulmine (Gd). The phantom was imaged in a 20-cm-diameter extremity coil by using both the MENSS and MESS techniques. The TR was 1,500 ms for both sequences. Calculated $T_2$ images were derived from the multiecho images produced by each imaging sequence. A second estimate of the $T_2$ of each vial was made by repeated application of the single-echo spin-echo sequence (SESS) with a $TR = 1,250$ ms and multiple values of $TE$ (14,
were 5 mm thick. The imaging matrix was 256 × 256. The pollicis muscles. In both cases, TR was 30 ms, and typically 1 wk, were thus required to complete the study. For each imaging technique, four transverse slices were acquired through the FDI and adductor muscles. The time between the completion of exercise and the start of imaging was 1 min. Because the image acquisition took 4:50 sec the images correspond to the state of the muscle 3 min after the end of exercise. Two imaging sessions, separated by a minimum of 30 min, and typically 1 wk, were thus required to complete the study. For each imaging technique, four transverse slices were acquired through the FDI and adductor pollicis muscles. In both cases, TR = 3,000 ms and the slices were 5 mm thick. The imaging matrix was 256 × 96, which produced a 150 × 75-mm rectangular field-of-view image.

RESULTS

Results From Experiments on Phantoms

Figure 3A presents the comparison of the T2 measured by using the MESS (open squares) and the MENSS (filled circles) techniques with the true value of T2 calculated from the SESS data. The line of identity between the y-axis and x-axis is drawn to facilitate comparison of the accuracy of the two techniques. It is apparent that the T2 values calculated by using the MENSS technique are far more accurate than the values determined by the MESS procedure. The third set of data (filled squares) on Fig. 3A shows the estimates of T2 derived from the MESS data after a correction was applied in an attempt to compensate for the effects of signal loss due to the slice-selective 180° pulse. After the correction, the data were closer in agreement with the true values. An estimate was made of the fraction (f) of signal lost by each refocusing pulse to correct for this effect. The data of signal decay from the vial with the longest relaxation time was used to estimate f. The decay data were fit to Eq. A7, where the value of T2 used in the fitting was the true value obtained from the SESS data. From this procedure, f = 0.873 was estimated, and this value was used to correct the data presented in Fig. 3A as the open squares. The corrected values of T2 appear in Fig. 3A as the filled squares.
Figure 3B plots the comparison of the estimate of T2 derived from the multiecho data obtained from the GE Signa images against the true value of T2. A fit of Eq. A7 to the data of Fig. 3B was made, and the dotted line in Fig. 3B shows the results of this fit. From the least squares fit, a value of \( f = 0.908 \) was estimated.

The additional signal lost to the MESS images from the use of slice-selective 180° pulses is demonstrated in Fig. 4. Figure 4 presents the profile of the excitation power of the slice-selective 180° refocusing pulse used in the MESS imaging sequence. The profile was measured as the image intensity across the slice measured in a large, homogeneous bottle of water. This profile represents the variation of refocusing power across a nominal slice of 50 mm, which is drawn as the dotted rectangle on Fig. 4. A perfect refocusing pulse would have the profile as shown by the dotted line. The area between the rectangle and the actual profile represents signal lost to the image made from the spin echo formed by this refocusing pulse.

Results From Human Experiments

With use of a region-of-interest tool on the imager, individual measurements of image intensity in images tracking the decay of the signal from the FDI muscle in one subject measured before exercise by using the MENSS technique were recorded. These decay values are plotted in Fig. 5 as the open circles. Equation A3 was used to derive a \( T_2 = 41.9 \pm 3.0 \) (SD) ms. The data were then corrected by using the factor shown in Fig. 2. The corrected data are shown in Fig. 5 as the filled circles. The best fit to the corrected data was \( T_2 = 30.3 \pm 2.4 \) ms. The lines drawn on Fig. 5 are derived from the fitting to the data. Weighing each data point equally instead of according to Eq. A2 gave a fit of \( T_2 = 44 \pm 9.3 \) ms.

The T2 of the FDI muscle measured in one volunteer as a function of the time after exercise showed a linear decrease with time. Immediately after exercise, the T2 was elevated 35%, from 29.8, to 40.2 ms. Over the next 10 min the T2 decayed \(~12\%\) from its highest value. The decay rate was \( 9.0 \times 10^{-3} \) ms/s postexercise. Thus, for an acquisition lasting \(~5\) min, we would expect a 2.7-ms decrease in the T2 during the acquisition time. There was no significant variation in the T2 of the adductor pollicis muscle during the 10-min observation time.

A typical calculated T2 image from one volunteer obtained before exercise is shown in Fig. 6A, and the corresponding image taken after exercise is shown in Fig. 6B. From these images, hand-drawn regions of interest were outlined in the FDI and adductor pollicis muscles to measure their T2. The oval bright object appearing in both figures was a small vial of water doped with Gd-labeled diethylenetriamine pentaacetic acid, which was taped to the hand of each volunteer and used as a reference. The increased T2 in the FDI muscle after exercise is clear in Fig. 6B.

The results of T2 measurements made by using the two techniques in each of the six volunteers are shown in Fig. 7. Figure 7 presents the change in T2 after exercise compared with that measured before. The results have been averaged over the four slices imaged, and the error bars represent the SD among the measurements from the four slices. A paired t-test showed that the increase in T2 measured from the MENSS technique was significantly different from that measured by using the MESS technique at the \( P = 0.0001 \) level. There was a small \((6 \pm 5\%\)) increase in the T2 of the adductor pollicis muscle with exercise. This increase was not significantly different from zero, and the two imaging techniques measured equivalent increases. The difference in T2 of the reference vial measured before and after exercise was not significantly different from zero.
DISCUSSION

Multiecho spin-echo techniques are time-efficient methods of collecting data for calculating T2. However, careful attention must be paid to the methods of image acquisition and image analysis to estimate T2 accurately. The need to correct the distortion created by the magnitude reconstruction of MR images is clearly demonstrated by the data in Fig. 5. Without this correction, later echo (long TE) images of the muscle will have little signal, and including them in the analysis will exaggerate the calculated T2. After correction of the magnitude signal and weighting of the fitting procedure appropriately, the contribution of data with low signal amplitude to T2 is small. The images with short TE and the largest signal will contribute the most to T2. Ignoring the weighting factor of Eq. A2 will significantly exaggerate T2. Our method of calculating T2 thus differs from that used by others in three important aspects. First, a larger number of points (8 in this case) were used to follow the decay of the signal from muscle. Second, the points were corrected for the effect of the magnitude reconstruction, and, third, the points were weighted proportional to their amplitude.

The comparison of the accuracy of T2 derived from the two imaging techniques and presented in Fig. 3, A and B, demonstrates the inaccurate T2 derived from the MESS sequence. The primary reason for the reduced T2 is the progressive loss in signal through the use of slice-selective refocusing 180° pulses. Each pulse refocuses a constant fraction of the magnetization and leaves a fraction in the longitudinal direction. The profile of the refocusing 180° pulse used in the MESS sequences shown in Fig. 4 shows the imperfect nature of the refocusing profile. Although relatively rectangular, the profile does show regions at the edges of the nominal 50-mm cut that do not experience the full 180°
refocusing, and hence their contribution to the image is lost. The correction of Eq. A7 to the data of Fig. 3A only moderately improved the accuracy of the MESS results, as shown by the scatter of the corrected values of T2 about the line of identity in Fig. 3A.

The greater sensitivity of the MENSS technique to detecting muscle activation is demonstrated in Fig. 7. The results of Fig. 7 show that, for a given exercise, the MENSS images revealed a larger increase in T2 than revealed by the MESS images. Detecting lower levels of activation or differentiating different patterns of muscle recruitment should thus be possible by using the MENSS technique. The major disadvantage of the MENSS imaging technique is the relatively long time required to image each slice. Because of the use of non-slice-selective 180° pulses, a delay after each echo train is required to allow signal recovery. The sequence is thus less efficient at acquiring data than is the MESS technique. Nevertheless, by using the MENSS technique, an adequate number of slices to image the entire FDI muscle can be acquired in 5 min.

Although the multiecho technique described in this paper produces accurate T2 values, alternative imaging strategies may be adequate for describing simple features of muscle activation, even if it is not possible to derive a T2 value or if the value is in error. With the advent of faster imaging methods, such as echo planar imaging, it has become possible to record multiecho images rapidly (6). However, with echo planar imaging it is not possible to image small muscles such as FDI with sufficient resolution to differentiate different muscle groups. The accurate estimates of T2 provided by the MENSS technique will still be of great value in comparing the effects of different exercise on muscle recruitment patterns or other physiological experiments that demand an accurate and reproducible index of muscle activation. Additionally, the data provided by MENSS techniques with smaller interecho spacing may enable the estimation of multiple components in the signal decay. The nuclear magnetic resonance (NMR) signal from muscle has been observed to decay with multiple exponential rates that may be related to the distribution of water in the muscle (7, 11). Detecting the different rates requires sampling the decay with many echoes and analyzing the data with suitable mathematical techniques (21). Thus, while the MENSS imaging technique provides information about the spatial variation of muscle activation in a few locations, it may provide other information that can answer important questions about neuromuscular physiology.

Conclusions

We have demonstrated the superiori ty of a MENSS imaging technique for the measurement of T2 in physiological experiments. This technique provides more accurate estimates of muscle T2 than do MESS imaging methods. A valuable consequence of the accuracy of the MENSS method is that the technique is more sensitive to detecting muscle activation. By using the MENSS technique we found an average 28% increase in the T2 of the FDI muscle after exercise compared with a 13% increase measured by using a conventional MESS technique. The disadvantage of the technique is that fewer slices can be imaged at a time. We have also outlined the appropriate method for analyzing the multiecho data to calculate accurate T2 values. Correcting the image intensity data for the distortion of the magnitude presentation of the image and appropriate weighting of the data are important for achieving the most accurate results.

APPENDIX

In MR images made with high field-strength magnets, (i.e., >1T), the noise in the image arises primarily from the person being imaged and secondarily from the receiver coil. This noise is typically white and is normally distributed about zero (17). Most importantly for our considerations, the noise does not depend on the amplitude of the signal received. Assuming that the signal from the transverse magnetization decays at a monoexponential rate to zero, the signal recorded at echo time TE is

\[ S(TE) = S_0 \cdot e^{-TE/T2} \]  

where \( S_0 \) is the maximum signal receivable for a hypothetical echo time, \( TE = 0 \). Thus T2 can be determined as the reciprocal of the slope determined from a linear least squares regression of \( Y = \log[S(TE)] \) vs. \( X = -TE \). In this regression, it is important to weigh the fitting appropriately. Assuming that the noise in each image has a SD \( \sigma \) and that noise in different images is uncorrelated, the weight in the least squares solution is

\[ \omega_n = \frac{[S(TE_n)]^2}{\sigma^2} \]  

The best estimate of T2 is

\[ T2 = \frac{\Delta}{\sum \omega_n \Sigma \omega_n X_n Y_n - \Sigma \omega_n X_n \Sigma \omega_n Y_n} \]  

where

\[ \Delta = \Sigma \omega_n \Sigma \omega_n X_n^2 - \left( \Sigma \omega_n X_n \right)^2 \]  

Similarly, the error in measuring T2 can be estimated as

\[ \sigma_T^2 = \left( T2 \right)^2 \left( \Sigma \omega_n - \left( \Delta \right)^{-1} \right) \]  

Before the calculation of T2, the data \( S(TE_n) \) must be corrected for the image distortion arising from the presentation of the image data as the magnitude of a complex quantity. The NMR signal has real (\( SR \)) and imaginary (\( SI \)) components. Noise is present in both components, but the mean of each is zero. The reconstructed image is the magnitude of these signals as

\[ S = \sqrt{S_{R}^2 + S_{I}^2} \]
A series of images tracking a decaying signal will have the lowest value of $1.25\sigma$ instead of zero, where $\sigma$ is the SD of the noise in each of $S_a$ and $S_c$ (12). The magnitude distortion can be corrected by multiplying the normalized signal by a suitable correction factor (3). This correction is plotted in Fig. 2 as a function of the normalized image intensity $S(S_{\text{rms}})$, where $S_{\text{rms}}$ is the SD of the noise found in the background of the magnitude image. The SDs $\sigma_m$ and $\sigma$ are related as $\sigma_m = 0.655\sigma$. The correction only needs to be applied for image intensity $S/S_{\text{rms}} < 5$ because beyond this level the correction is insignificantly different from unity. The correction is crucial in preventing low signal levels collected in the later echo (long TE) images from biasing the T2 estimate.

Use of slice-selective $180^\circ$ pulses will result in T2 estimates below the true value of T2. The reason is that each refocusing pulse causes a constant loss of signal. This additional mechanism of signal loss masquerades as a T2 shorter than the true value. It is possible to correct for this effect if the amount of signal loss per radio-frequency pulse can be measured. If each pulse causes a constant fractional loss of signal, the decay of the signal in the MESS images can be expressed as

$$S(\text{TE}_n) = S_0 f^m e^{-\Delta \text{TE}/T2}$$  \hspace{1cm} (A7)

where $n$ is the index of the echo number, and $\Delta \text{TE}$ is the spacing of the echoes. The corrected value of T2 is related to $f$ and the value of T2 derived from the MESS images as $T2' = T2 + \ln(f)/\Delta \text{TE}$  \hspace{1cm} (A8)

In principle, the value of $f$ is independent of the relaxation times of the sample, and thus one value of $f$ can be used to correct the results from other samples.

Equation A5 can be used to derive the optimal method of measuring a given relaxation time (16). It is known from previous experiments that the T2 of skeletal muscle is $30\text{ ms}$ and can increase to $40\text{ ms}$ with exercise. The calculation is straightforward with the exception that the weight applied in the fitting now depends on $\Delta \text{TE}$ as well as $S$ because $\Delta \text{TE}$ will influence the duration of the readout window for the analog-to-digital converter to sample the spin echo. Larger $\Delta \text{TE}$ can be used to have a longer readout time and, as a consequence, a reduced image bandwidth (BW) which reduces the amount of noise in the image. Because the signal-to-noise ratio (SNR) of the image varies as $1/\sqrt{\text{BW}}$, the image SNR can be improved at the rate of $\sqrt{\Delta \text{TE}}$ by reducing the image BW at larger $\Delta \text{TE}$. The BW cannot be reduced arbitrarily because below a value of $\sim 130\text{ Hz}$ per image pixel the image distortion resulting from fat protons having a chemical shift with respect to water protons becomes unacceptable. There is a value of $\Delta \text{TE} = \Delta \text{TE}'$ where the receiver bandwidth has reached its lower limit consistent with the restriction on the chemical shift artifact. The lowest value $\Delta \text{TE}$ is restricted to a minimum of $\Delta \text{TE}_{\text{min}}$ established by the duration of the radio-frequency pulses and necessary imaging gradients. At $\Delta \text{TE} = \Delta \text{TE}_{\text{min}}$ the duration of the readout window would be zero. With these considerations the complete weighting function ($\Psi$) becomes

$$\Psi(S, \Delta \text{TE}) = \omega(S) \left[ \frac{\Delta \text{TE} - \Delta \text{TE}_{\text{min}}}{\Delta \text{TE}' - \Delta \text{TE}_{\text{min}}} \right]$$  \hspace{1cm} (A9)

where the upper factor applies if $\Delta \text{TE}_{\text{min}} < \Delta \text{TE} < \Delta \text{TE}'$ and the lower factor applies if $\Delta \text{TE} > \Delta \text{TE}'$ and $\omega$ is given by Eq. A2. Equations A5 and A7 were used to predict the variation in the error in calculated values of T2 for different numbers of echoes (4, 8, and 12) and different echo spacing. The calculation was performed for a hypothetical image SNR = 100:1 and a range of $\Delta \text{TE}$ between 10 and 25 ms. For the imager used to develop the MESS and MENS$\text{S}$ sequences $\Delta \text{TE}_{\text{min}} = 4.5\text{ ms}$ and $\Delta \text{TE}' = 17\text{ ms}$. The results of this prediction are shown in Fig. 8 as the SD in a calculated T2 for the three different numbers of echoes and various echo spacing. The break in the curves comes where the weighting shifts as in Eq. A7. The error in $T2$ increases as $\Delta \text{TE}$ decreases because receiver BW must increase, allowing more noise into the images. The error rises as $\Delta \text{TE}$ increases because the signal decays, resulting in less signal received at large TE. The optimal value of $\Delta \text{TE}$ appeared to be $17\text{ ms}$, and the error in T2 was not reduced significantly by acquiring more than eight echoes. For these reasons the MESS and MENS$\text{S}$ sequences were developed to acquire 8 echoes at an echo spacing of $17\text{ ms}$. Keeping the number of echoes to a relatively small number reduced the total acquisition time. A constant delay of $750\text{ ms}$ after the last echo was required in the MENS$\text{S}$ technique to allow for adequate signal recovery before the next echo train was generated.

This work was supported partially by National Institute of Arthritis and Musculoskeletal and Skin Diseases Grant AG-090000.

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Received 23 December 1996; accepted in final form 14 May 1997.

REFERENCES


