Technical Note

NMR Properties of Human Median Nerve at 3 T: Proton Density, T1, T2, and Magnetization Transfer

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Purpose: To measure the proton density (PD), the T1 and T2 relaxation time, and magnetization transfer (MT) effects in human median nerve at 3 T and to compare them with the corresponding values in muscle.

Materials and Methods: Measurements of the T1 and T2 relaxation time were performed with an inversion recovery and a Carr-Purcell-Meiboom-Gill (CPMG) imaging sequence, respectively. The MT ratio was measured by acquiring two sets of 3D spoiled gradient-echo images, with and without a Gaussian saturation pulse.

Results: The median nerve T1 was 1410 ± 70 msec. The T2 decay consisted of two components, with average T2 values of 26 ± 2 msec and 96 ± 3 msec and normalized amplitudes of 78 ± 4% and 22 ± 4%, respectively. The dominant component is likely to reflect myelin water and connective tissue, and the less abundant component originates possibly from intra-axonal water protons. The value of proton density of MRI-visible protons in median nerve was 81 ± 3% that of muscle. The MT ratio in median nerve (40.3 ± 2.0%) was smaller than in muscle (45.4 ± 0.5%).

Conclusion: MRI-relevant properties, such as PD, T1 and T2 relaxation time, and MT ratio were measured in human median nerve at 3 T and were in many respects similar to those of muscle.

Key Words: median nerve; T2 relaxation time; T1 relaxation time; magnetization transfer; magnetic resonance imaging; 3.0 T
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WITH ITS EXCELLENT soft-tissue contrast, MRI could be of great benefit for investigations of the peripheral nervous system (PNS) in humans, in particular for diagnosis of neurodegenerative diseases, detection of compressive/inflammatory neuropathies, and monitoring of postoperative nerve regeneration (1–3). However, very little is known about the intrinsic NMR properties, such as proton density (PD), T1, T2 relaxation time, and magnetization transfer (MT) effects in human PNS.

In each tissue the MR signal is primarily dependent on PD, T1, and T2 of water protons. These parameters determine the signal intensity and contrast in MR images that are routinely acquired in clinical settings. Hence, for optimized clinical MRI protocols and to enhance visibility of pathophysiological changes in tissues, it is of particular importance to assess PD and relaxation times of the tissue of interest. Currently, MR contrast has been optimized for most tissues, such as brain, muscle, pelvic and abdominal tissue, breast tissue, and cartilage at 1.5 T and 3 T. In human PNS, and specifically in median nerve, T2 relaxation measurements have been performed at 1.5 T and 7 T (4,5). However, no measurements of PD, T1, and T2 have been reported at 3 T.

The PD, T1, and T2 are NMR properties representative of water protons that belong to the pool of relatively mobile water molecules. On the other hand, protons associated with macromolecules or bound water are characterized by a much slower rotational correlation time and thus do not contribute to the MRI signal intensity, because of their very short T2 (<1 msec). Nevertheless, it was observed that these protons can still substantially affect the MRI signal intensity (6). Specifically, when selectively saturated the bound proton pool can transfer its magnetization—through exchange or dipolar mechanisms (so-called MT effects)—to the more mobile water proton pool. As a result, MT sequences provide a contrast which is also sensitive to properties of the less mobile (or bound) protons associated with macromolecules. Thus, for a more complete MR tissue characterization, in addition to the PD, T1, and T2, MT effects need to be assessed as well.

As 3 T scanners are becoming more common in clinical settings it is of interest to investigate NMR proper-

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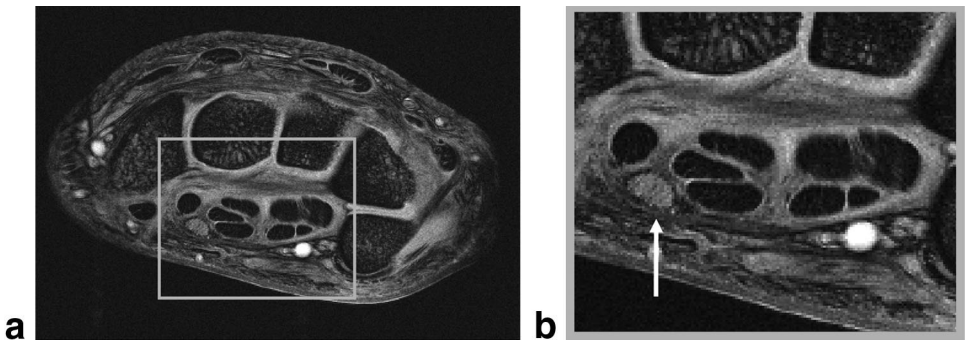

Figure 1. a: Gradient-echo axial MR image of the wrist at 3 T. **b:** Zoom-in of carpal tunnel region. The median nerve is indicated by the arrow. Three tendons, which appear as low signal intensity oval-shape structures, are adjacent to the median nerve.

ties of tissues at 3 T. The purpose of this study was to measure PD, T1, T2, and the MT ratio (MTR) in human median nerve, chosen as a representative model of peripheral nervous tissue, to pave the way for exploring new sources of contrast for PNS at 3 T.

MATERIALS AND METHODS

Magnetic Resonance Imaging

MRI experiments were performed on a clinical 3 T Tim Trio Siemens scanner (Siemens Medical Solutions, Erlangen, Germany) using a dedicated transmitter/receiver circularly polarized (CP) wrist coil. Vendor-supplied sequences were used for all measurements in six healthy volunteers (four males and two females, mean age 38 ± 4 years). Each NMR property was measured in five subjects. Gradient-echo images were acquired for anatomical identification of the median nerve in order to properly plan the T1, T2, and MT measurements. The imaging parameters were: repetition time (TR) 500 msec, echo time (TE) 9 msec, flip angle 45°, field of view (FOV) 100 × 100 mm, slice thickness (SLT) 2 mm, image matrix size 512 × 512, 20 slices, number of averages (NA) = 1. T1 and T2 measurements were performed on a single slice. T1 relaxation was measured with an inversion recovery turbo spin-echo imaging sequence. A slice-selective hyperbolic secant pulse of 10.24 msec duration was used for magnetization inversion. Imaging parameters were: TR/TE = 6000/15 msec, six inversion times TI = 36, 200, 1000, 2000, 4800, 5800 msec, FOV 75 × 100 mm, SLT 3 mm, image matrix size 240 × 320, NA = 1, turbo factor = 7. T2 relaxation time was measured with a Carr-Purcell-Meiboom-Gill (CPMG) imaging sequence (32 echoes, TR/TE = 3000/11 msec, FOV 75 × 100 mm, SLT 3 mm, and image matrix size 192 × 256). Optimized 180° sinc pulses of 2.56 msec duration were used for refocusing of the magnetization. Spoiler gradients of constant amplitude were applied around each refocusing pulse along the frequency-encoding direction. Preliminary CPMG experiments performed with 20 echoes revealed that the relaxation decay curve of nerve displayed a biexponential behavior. Therefore, the final protocol of T2 measurements consisted of a CPMG with the extended number of 32 echoes, for a more detailed coverage of the T2 relaxation decay curve. Fat saturation was applied in both T1 and T2 measurements.

To assess the MTR in median nerve, two sets of 3D spoiled gradient-echo images were acquired with the following parameters: TR/TE = 33/7 msec, flip angle 10°, FOV 75 × 100 mm, SLT 2 mm, image matrix size 288 × 384, 32 slices, NA = 1. One set was acquired with an additional saturation pulse (8 msec Gaussian pulse, 500° effective flip angle, applied 1.5 kHz off-resonance) prior to excitation to generate magnetization transfer contrast.

Data Analysis

T1, T2, PD, and MTR were calculated within a manually segmented region of interest (ROI) of the median nerve. The ROI was carefully chosen to include only voxels well within the median nerve. T2 relaxation data were first analyzed with the nonnegative least square (NNLS) technique of Lawson and Hanson (7). The NNLS algorithm provides the number of relaxation components and the distribution of T2s in a given decay curve. Following NNLS analysis, the T2 relaxation time and amplitude of each component were obtained from fitting the CPMG signal decay. The relative proton density was obtained from the signal amplitude at TE = 0 of the fit of the signal decay. T1 values were obtained from a three-parameter nonlinear least squares fit of the image intensities according to the equation $S = A + B\,exp(-TI/T1)$ where TI is the inversion time. For each dataset the coefficient of determination (R^2), which is a measure of the goodness of the fit, was also computed. Pixel-by-pixel MTR maps were calculated according to the standard equation $MTR = 100*(So - Ss)/So$, with So and Ss being the signal without and with off-resonance saturation pulse, respectively. In order to compare the NMR properties of the median nerve with those of muscle, the same data analysis was performed on a manually segmented ROI within muscle adjacent to the median nerve. All algorithms were implemented in MatLab (MathWorks, Natick, MA). Results were expressed as mean value ± standard deviation (SD, across subjects).

RESULTS

The median nerve and other tissue structures such as tendons, connective tissue, and bone marrow were clearly visualized in the gradient echo images (Fig. 1a). The zoom-in of the carpal tunnel is illustrated in Fig. 1b. In median nerve, NNLS analysis of T2 decay curves revealed two relaxation components: a fast component with T2 ≈30 msec and a slow component with T2 ≈100 msec (Fig. 2). On the contrary, the T2 spectrum of

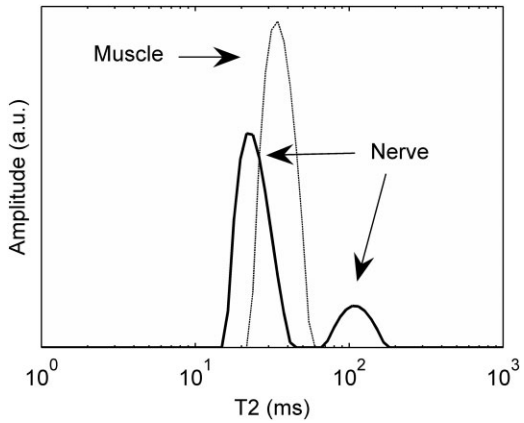

Figure 2. The T2-NNLS spectrum of muscle and median nerve, shown on a logarithmic scale with T2 values equally spaced between 1 and 1000 msec. The NNLS analysis reveals a two-component T2 spectrum with peaks at ≈30 and 100 msec in nerve. A single relaxation peak is observed in muscle, at ≈30 msec.

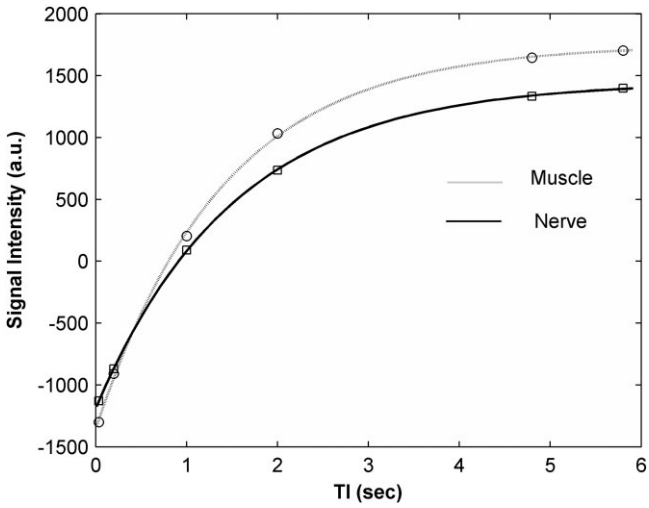

Figure 4. Inversion-recovery of magnetization in muscle and median nerve. The lines indicate the exponential fit.

muscle showed a single relaxation peak at ≈30 msec. As a result, the T2 decay data of nerve and muscle were fitted to a bi- and monoexponential function, respectively. An example of the T2 decay data with the biexponential fit of the nerve and monoexponential fit of muscle is shown in Fig. 3. The coefficient of determination R^2 was 0.989 and 0.991 for the fit of nerve and muscle data, respectively, in Fig. 3. In the median nerve the average T2 and normalized amplitudes of the two components were 26 ± 2 msec and 96 ± 3 msec and 78 ± 4% and 22 ± 4%, respectively. The average T2 value for muscle was 33 ± 2 msec. The T2 biexponential decay was observed in all subjects. The value of proton density of MRI-visible protons in nerve was 81 ± 3% that of muscle. The average T1 relaxation time of the median nerve was 1410 ± 70 msec (Fig. 4). In all subjects, for both the T1 and T2 data, R^2 was always greater than 0.980. The MT ratio (Fig. 5) observed in median nerve was 40.3 ± 2.0%, while in muscle it was 45.4 ± 0.5%.

DISCUSSION

Despite the great clinical potential of MRI to investigate the human PNS, only a few quantitative measurements of the MR properties of peripheral nerves have been performed to date. With regard to T2 relaxometry, two studies have reported T2 relaxation measurements in median nerve, at 1.5 T (T2 ≈50 msec, (4)) and 7 T (T2 ≈20 msec, (5)). The T2 value of the dominant component observed in the current study falls between the values measured at 1.5 T and at 7 T. This is in agreement with the expected functional dependence of the T2

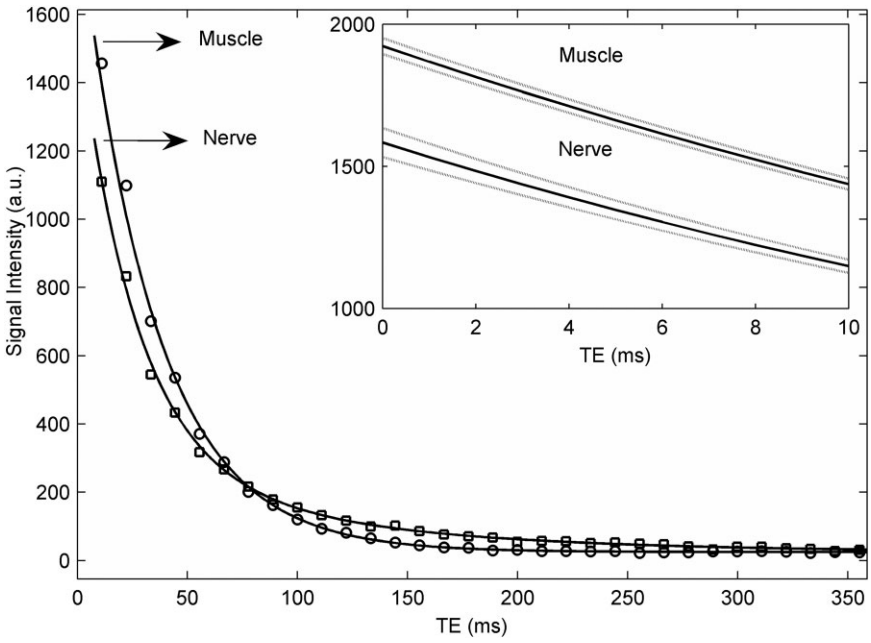

Figure 3. Plot of the CPMG echo signal amplitudes of muscle (circles) and median nerve (squares). The lines indicate the mono- and biexponential fit for muscle and nerve, respectively. In the inset, the extrapolation of the fit to the TE = 0 msec intercept, which is proportional to the proton density is shown. The thin lines represent the 95% confidence bounds.

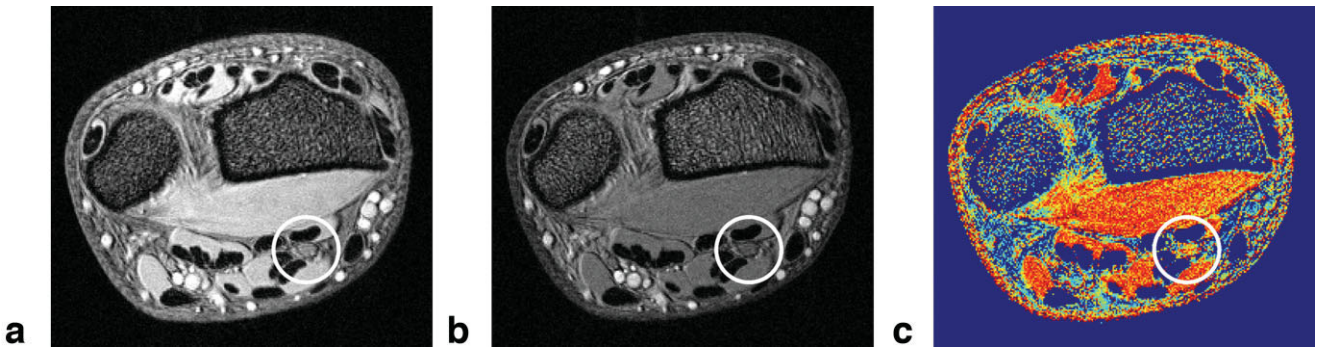

Figure 5. Gradient-echo axial MR image of the wrist without (**a**) and with (**b**) MT saturation pulse and MT ratio map (**c**). The median nerve is at the center of the white circle.

relaxation time on the magnetic field strength B0, i.e., a decrease of T2 with increasing B0, as observed in other tissues, due to dynamic dephasing induced by microscopic susceptibility gradients (8). In the two previous studies, a single T2 component was observed. In contrast to the current study, where the CPMG sequence was used, T2 relaxation was measured using a single spin-echo approach in the previous studies. Due to diffusion signal losses, the latter yields faster signal decay, which makes detection of a small second component difficult.

The T2 relaxation measurements yielded two components, a short-T2 component, which accounts for 80% of the signal intensity, and a smaller long-T2 component. The dominant component likely contains signal from myelin water (9) and connective tissue (10), since both are characterized by a short T2 value. In particular, it should be noted that the median nerve connective tissue consists largely of collagen fibers running mostly along the nerve axis. In a previous study the T2 relaxation time of collagen at 3 T was found to be ≈30–36 msec (10), which is similar to the T2 of the dominant component observed in the present study. The assignment of the dominant component to the collagen and myelin water protons is also in agreement with the findings of another study (4), where a significant proportion of the signal intensity in median nerve was observed to originate from collagen. The long-T2 component, which accounts for ≈20% of the MRI-visible water protons, is characterized by a T2 value close to the T2 of white matter at 3 T (T2 ≈80 msec (11)). Thus, the signal intensity of the less abundant component might originate from the intra-axonal water protons of the median nerve.

In animal models, multiexponential T2 relaxation decays in PNS have been previously observed in a number of studies (12,13). On the other hand, in human studies monoexponential decays are generally observed in tissues. A high signal-to-noise ratio and the acquisition of many echoes—with a short echo spacing—are among the requirements for observing multicomponent T2 relaxation decays with CPMG sequences. In the current study the acquisition of 32 echoes, with a relatively short echo spacing of 11 msec, and the use of a dedicated wrist coil allowed for the detection of a T2 biexponential behavior in the median nerve. The ability to assess microanatomical compartments within PNS in humans, as shown here, provides a method for studying in vivo biophysical properties of nerves and offers a means to investigate neurodegenerative diseases.

For MRI protocol optimization, it is of interest to compare the PD, T1, and T2 relaxation time of median nerve with that of muscle, since the median nerve is typically surrounded by muscle tissue. The T2 of muscle measured in the current study is in good agreement with the value measured by Gold et al. at 3 T (14). Since the T2 of the major component in median nerve is similar to that of muscle, it is difficult to enhance the image contrast between nerve and muscle with T2-weighted imaging at 3 T. The same argument applies to T1-weighted imaging. On the other hand, the nerve PD is somewhat smaller than that of muscle. All these factors should then be taken into account for adjusting PNS imaging protocols at 3 T for a specific contrast.

For a more complete MR tissue characterization, in addition to the PD, T1, and T2, the MTR in median nerve was measured as well. MT effects provide a means to study the microenvironment of those protons that are virtually MRI-invisible because of their short T2. For most tissues the MTR values—although dependent on sequence parameters and saturation schemes—are well established, with muscle, cartilage, and white matter having higher MTR values than gray matter and liver, for instance (15). The MT ratio observed in muscle is in the range of muscle MTR measured in another study (50 ± 2%), where a similar sequence and MT saturation pulse were used (15). The MTR observed in the median nerve is probably dominated by the collagen component, since a large part of the signal intensity of median nerve originates from connective tissues within the median nerve (4). At this stage, it is not clear in which proportion the water protons within myelin sheets would contribute to the overall MT effect and further studies are needed to elucidate this aspect. Regardless of the role of myelin water protons in the overall MTR, MT measurements can be an attractive alternative to T2-weighted images in detecting and investigating diseases of PNS in humans, since the MTR can provide information on nerve damage, in particular on assessment of collagen integrity.

One limitation of the current study is the relatively small sample size. Further studies will be required to

address this issue as well as the reproducibility over time or between scanners. Nevertheless, the results obtained in the current study serve as baseline values in normal subjects at 3 T. This could be useful for future comparison, for instance, in subjects with carpal tunnel syndrome, provided that the same experimental conditions and parameters of this study are used.

In conclusion, MR relevant properties—such as PD, T1, and T2 relaxation time and MT ratio—were measured in human median nerve at 3 T and were in many respects similar to those of muscle. Knowledge of these properties offers valuable information for optimization of clinical MRI protocols and for enhancing visibility of pathophysiological changes.

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