Pixel T2 distribution in functional magnetic resonance images of muscle

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Prior, Barry M., Jeanne M. Foley, Roop C. Jayaraman, and Ronald A. Meyer. Pixel T2 distribution in functional magnetic resonance images of muscle. J. Appl. Physiol. 87(6): 2107–2114, 1999.—Increases in skeletal muscle 1H-NMR transverse relaxation time (T2) observed by magnetic resonance imaging have been used to map whole muscle activity during exercise. Some studies further suggest that intramuscular variations in T2 after exercise can be used to map activity on a pixel-by-pixel basis by defining an active T2 threshold and counting pixels that exceed the threshold as “active muscle.” This implies that motor units are nonrandomly distributed across the muscle and, therefore, that the distribution of pixel T2 values ought to be substantially broader after moderate exercise than at rest or after more intense exercise, since moderate-intensity exercise should recruit some motor units, and hence some pixels, but not others. This study examined the distribution of pixel T2 values in three muscles (quadriceps, anterior tibialis, and biceps brachialis) of healthy subjects (5 men and 2 women, 18–46 yr old) at rest, after exercise to fatigue (50% 1 repetition maximum at 20/min to failure = Max), and at ½Max (25% 1 repetition maximum, same number of repetitions as Max). Although for each muscle there was a linear relationship between exercise intensity and mean pixel T2, there was no significant difference in the variance of pixel T2 between ½Max and Max exercise. There was a modest (10–43%) increase in variance of pixel T2 after both exercises compared with rest, but this was consistent with a Monte Carlo simulation of muscle activity that assumed a random distribution of motor unit territories across the muscle and a random distribution of muscle cells within each motor unit’s territory. In addition, 40% of the pixel-to-pixel muscle T2 variations were shown to be due to imaging noise. The results indicate that magnetic resonance imaging T2 cannot reliably map active muscle on a pixel-by-pixel basis in normal subjects.

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the macroscopic flow of current from the EMS electrodes. In contrast, recruitment during voluntary exercise depends on motor unit activation. Therefore, if active and inactive areas of muscle can be distinguished on a pixel-by-pixel basis by MR imaging during voluntary exercise, then the muscle fibers from different motor units must be nonrandomly distributed among the pixels, such that individual pixels contain a preponderance of fibers from a subset of the total motor unit pool. Although “clustering” of motor unit fibers is a well-known feature of motoneuron disease (19) and the location of motor unit territories is correlated with recruitment order in some animal muscles (4), there is little anatomic evidence for either of these fiber distribution patterns in muscles of healthy human subjects (5).

The primary purpose of this study was to test the validity of the above threshold method for estimating active muscle area by examining the distribution of pixel T2 in muscles at rest and after moderate vs. intense voluntary exercise. We reasoned that if the implicit assumption of the threshold method is correct, then the pixel-to-pixel distribution of T2 should be broadest after moderate exercise, ideally approaching a bimodal distribution, because in that case some motor units (and, therefore, some pixels) would be active while others would not. At the opposite extreme, if the muscle cells of all motor units were more randomly distributed across the muscle, then the T2 increase would be spread across the muscle at all exercise intensities. In that case, the pixel-by-pixel variation in T2 might largely reflect the noise inherent in the T2 measurement and could not be used to reliably map active vs. “inactive” pixels with a fixed threshold. The experimental results are more similar to the latter extreme and, moreover, are quantitatively consistent with a Monte Carlo simulation that assumed a random distribution of motor unit territories across muscles and a random distribution of motor unit cells within those territories. However, the simulation does suggest that pixel T2 variation after exercise could be substantially greater in patients with motoneuron disease.

**METHODS**

Subjects. Seven adult subjects [5 men and 2 women, mean age 34 (range 20–47) yr] were recruited from the university community. Subjects gave informed, written consent, and the study was approved by the University’s Committee on Research Involving Human Subjects.

Exercise protocols. Three single-limb weight-lifting exercises [biceps curl (5 subjects), ankle dorsiflexion (5 subjects), and knee extension (6 subjects)] were studied at two intensities: Max and ½Max. In each case, the Max exercise consisted of a single repetitive bout of lifting a weight equal to 50% of the previously determined one repetition maximum (1 RM) at a rate of 20 repetitions per minute until failure (Table 1). The ½Max exercise consisted of a single bout with the same number of repetitions performed at the same rate, but with the weight reduced to 25% of 1 RM. Each subject first performed the Max exercise, and the number of repetitions to failure was recorded. Approximately 30 min later the subject performed the ½Max exercise using the contralateral limb. In each case, two to three of the subjects used the dominant limb for the 1-RM testing and Max exercise, the other subjects used the nondominant limb.

MR Imaging and analysis. Immediately before and within 3 min after each exercise, the exercised muscles were imaged on a 1.5-T GE Signa MR imaging machine (GE Medical Systems, Milwaukee, WI). For leg muscles, axial fast spin-echo images (256 × 128 matrix zero-filled to 256 × 256, repetition time = 2,000 ms, echo time = 30 and 60 ms, 9 or 10 1-cm-thick slices, echo-train length = 4) were acquired via the body coil (knee extensors, 40 cm FOV) or via a standard 25-cm-diameter extremity coil (ankle dorsiflexors, 16–20 cm FOV). For arm muscles, spin-echo images (repetition time = 1,500, 16-cm FOV, other parameters as described above) were acquired via the extremity coil. T2 images were computed on a pixel-by-pixel basis from the two magnitude images with the assumption of a single-exponential decay and after subtraction of the mean magnitude of the background noise measured in a large region of interest (ROI) outside the imaged limb. T2 images were analyzed by tracing an ROI around the muscle group of interest with a custom-written image analysis program. The T2 values (mean ± SD), the total number of pixels in the ROI, and a histogram of the pixel T2 distribution were determined for the ROI in each slice. Results for the whole muscle were computed by summing the results from the 9–10 images of each set. Active muscle area was estimated by the threshold method, as described by Ploutz-Snyder et al. (22), except no correction was made for “nonmuscle pixels” within the ROI of the muscle at rest. Instead, visible nonmuscle areas, such as fat and vascular structures, were manually excluded during tracing of the ROIs.

Monte Carlo simulation of T2 variance. The dependence of pixel T2 variance on motor unit size and cell distribution was simulated using the model of muscle cell distribution and recruitment developed by Fuglevand and Segal (16). The model assumed a 200 × 200 grid of 50 × 50 µm square muscle fibers (total 1-cm² area, 4 × 10⁶ cells) innervated by 100 motor units. Motor units ranged in size and number according to an exponential function, such that there were many small units and few large units (mean 400 fibers/unit, median 164 fibers/unit, smallest 14 fibers, largest 1,853 fibers). As in the original model (16), motor unit territories were assumed to be square, with cell densities a linear function of motor unit size ranging from 10 to 40 unit fibers/mm², resulting in a mean territory area of 15.1 mm². For each trial, the territory of each motor unit was randomly assigned a location on the grid, and the cells of this unit were randomly selected from cells in the assigned territory (see Fig. 2 in Ref. 16). These random assignments were made in order from the first (smallest) unit to the 99th (second largest) unit. If a unit’s territory exceeded the boundaries of the grid, its territory was wrapped around to the opposite side. The remaining cells were then assigned to the largest unit, which was not recruited in the simulations. Recruitment was assumed to be an “off-on” phenomenon in fixed order from the smallest to the largest unit as a function of force (proportional to total cells recruited) for four force levels: 10, 25, 50, and 75% of maximum force. This

**Table 1. Maximal weight lifted for each exercise and number of repetitions completed**

<table>
<thead>
<tr>
<th></th>
<th>1 RM, kg</th>
<th>No. of Repetitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbow flexion</td>
<td>15.9 ± 3.6</td>
<td>25.8 ± 4.3</td>
</tr>
<tr>
<td>Ankle dorsiflexion</td>
<td>20.0 ± 1.8</td>
<td>48.0 ± 4.9</td>
</tr>
<tr>
<td>Knee extension</td>
<td>54.9 ± 5.8</td>
<td>35.5 ± 3.3</td>
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</table>

Values are means ± SE. RM, repetition maximum.
corresponded to recruitment of 55, 73, 87, and 97 of the motor units, respectively. MR image pixels were modeled as a 20 × 20 pixel grid overlying the muscle grid; i.e., each pixel was 0.5 × 0.5 mm and contained 100 muscle fibers. Pixel T2 was assumed to be proportional to the fraction of “on” fibers in the pixel and to range from 30 ms (no fibers on) to 40 ms (all fibers on). Finally, random Gaussian noise (mean = 0, SD = 1, 2, or 3 ms) was added to the pixel T2 values. The effect of this noise on the accuracy of threshold classification of individual pixels as active vs. inactive was computed by assuming a threshold at 1 SD greater than 30 ms (e.g., for noise SD = 2, the active threshold was 32 ms or 20% of the fibers in a pixel active) and computing the percentage of correctly classified pixels. Twenty-five trials of each of these “normal” muscle simulations were computed, and the results were averaged.

The above normal simulation was modified to explore the effect of the fiber clustering associated with partial muscle denervation due to motoneuron disease. Fifty motor units were randomly selected for elimination from the total population of 100 units assigned as described above. The cells previously assigned to these units were randomly reassigned to a motor unit innervating one of the eight adjacent fibers or, if no such unit was available, to a random unit innervating one of the 24 fibers within two squares. After this reassignment of fibers, pixel T2 was recomputed for the four levels of activity, again by averaging the results of 25 trials.

Statistics. Data were analyzed using SPSS version 6.1 (SPSS, Chicago, IL). A one-way ANOVA was used to test for significant differences between the whole muscle ROI mean and the active muscle mean T2 values. Paired t-tests with a Bonferroni adjustment were used to test for significant differences between mean T2 values across exercise intensities. The Brown-Forsyth procedure was used to test the homogeneity of whole muscle group T2 variance (18). All tests were at the \( P < 0.05 \) level.

RESULTS

Experimental results. Figure 1 shows representative axial images of the three muscle groups after the Max exercises. There was an obvious increase in intensity of the muscles expected to be recruited after each of these exercises (i.e., biceps/brachialis, tibialis anterior, and quadriceps for curl, ankle dorsiflexion, and knee extension, respectively). As expected from previous studies, within each recruited muscle group there was a roughly linear increase in mean muscle T2 with increasing exercise intensity (Fig. 2, Table 2). In contrast to previous studies (22), the mean T2 at “rest” was significantly higher for the knee extensors and ankle dorsiflexors than for the elbow flexors. Because spin-echo and fast spin-echo T2 pulse sequences are subject to errors caused by imperfections in the refocusing pulses (8), these differences in absolute T2 of the muscles before exercise may arise in part from instrument errors. However, despite the differences in initial T2, the changes in T2 with exercise were similar in the three muscles, e.g., an 8- to 10-ms increase after the Max exercise.

Figure 3 shows sample histograms of the distribution of pixel T2 values summed across the whole muscles of individuals at rest and after the two exercise intensities. Although in each case the mean T2 increased with exercise, in no case was there a distinct bimodal distribution. Thus there was no significant difference in the pixel-to-pixel variance between the \( \frac{1}{2}\text{Max} \) and the Max exercise (Table 3). There were trends toward increased variance after the exercises compared with rest, although these trends were not significant according to the Brown-Forsyth procedure.

Figure 4 shows the percent active muscle area and the mean T2 of the active muscle, computed as described in METHODS, for the three muscles. As expected from previous studies (20, 22), the percent active muscle also increased with exercise intensity. The mean T2 of the active muscle also increased slightly with exercise intensity, but the magnitude of this increase was small compared with the T2 change averaged across the whole muscle.

The variation of the pixel-by-pixel T2 calculation depends on the inherent signal-to-noise ratio (S/N) of the images, which in turn is a complex function of the
ratio of echo time to T2, the receiver coil’s properties, the pixel size and slice thickness, the receiver bandwidth, and other factors. The contribution of this image noise to the variation in pixel T2 can be estimated from images of a homogeneous sample with similar T2 acquired at the same instrument settings. For example, as shown in Fig. 5, image noise alone accounts for 1.43 ms (46%) of the SD of pixel T2 in the resting anterior tibialis images of this study. Similar measurements showed that noise accounts for 1.0 ms (43%) and 1.6 ms (39%) of the SD of pixel T2 in the resting biceps and quadriceps muscles, respectively.

Table 2. T2 values for muscle groups

<table>
<thead>
<tr>
<th></th>
<th>ROI Mean T2, ms</th>
<th>Active Muscle Mean T2, ms</th>
</tr>
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<tbody>
<tr>
<td><strong>Biceps</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>27.1 ± 0.2</td>
<td>32.4 ± 0.4†</td>
</tr>
<tr>
<td>½ Max</td>
<td>32.7 ± 1.4*</td>
<td>33.7 ± 1.1*‡</td>
</tr>
<tr>
<td>Max</td>
<td>36.5 ± 0.5†</td>
<td>36.8 ± 0.5‡</td>
</tr>
<tr>
<td><strong>Tibialis anterior</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>33.0 ± 0.7</td>
<td>41.9 ± 0.9†</td>
</tr>
<tr>
<td>½ Max</td>
<td>37.8 ± 0.7*</td>
<td>41.6 ± 0.6‡</td>
</tr>
<tr>
<td>Max</td>
<td>41.0 ± 0.3†</td>
<td>42.8 ± 0.8‡</td>
</tr>
<tr>
<td><strong>Quadriceps</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>36.7 ± 0.3</td>
<td>48.0 ± 0.5‡</td>
</tr>
<tr>
<td>½ Max</td>
<td>41.2 ± 0.7*</td>
<td>47.7 ± 0.7‡</td>
</tr>
<tr>
<td>Max</td>
<td>46.6 ± 0.4*†</td>
<td>48.7 ± 0.5‡</td>
</tr>
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Values are means ± SE. Rest is from Max exercise (single repetitive bout of lifting a weight equal to 50% of previously determined 1 RM at 20 min until failure). ½ Max, single bout with same number of repetitions performed at same rate as Max, but with weight reduced to 25% of 1 RM. *Significantly different from rest. †Significantly different from ½ Max exercise. ‡Significantly different from region of interest (ROI) value.

Simulation results. Figure 6 illustrates the distribution pattern of recruited fibers in single trials of the simulation of normal and partially denervated muscle with 50% of the fibers active. Figure 7 shows the summed pixel T2 histograms computed from 25 trials of these simulations at four fiber activity levels. In the normal simulation, there is a modest increase in T2 variance (Table 4) with activity compared with rest, but there is little change in variance between 25 and 75% activity and only slight divergence of the histogram shape from a Gaussian distribution at the highest activity. On the other hand, in the denervation model

Table 3. Variance (standard deviation) of ROI pixel T2 distribution for each exercise at each exercise intensity

<table>
<thead>
<tr>
<th></th>
<th>Elbow Flexion</th>
<th>Ankle Dorsiflexion</th>
<th>Knee Extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>2.3 ± 0.1</td>
<td>3.1 ± 0.1</td>
<td>4.1 ± 0.1</td>
</tr>
<tr>
<td>½ Max</td>
<td>2.9 ± 0.2</td>
<td>3.6 ± 0.2</td>
<td>4.5 ± 0.2</td>
</tr>
<tr>
<td>Max</td>
<td>3.3 ± 0.2</td>
<td>3.8 ± 0.2</td>
<td>4.3 ± 0.4</td>
</tr>
</tbody>
</table>

Values are means ± SE. Rest is from Max exercise condition.
the variance of pixel T2 increases more dramatically with exercise and depends more strongly on total fiber activity level, and there is clear distortion of the histogram shape at the higher activities.

Finally, the simulation shows that the addition of Gaussian noise profoundly degrades the accuracy of the threshold method for individually classifying pixels as active vs. inactive. For example, at the 25% fiber activity level, the percentage of correctly classified pixels at noise SD = 1, 2, and 3 ms was 88, 65, and 59%, respectively. Thus, with noise SD > 1 ms, the accuracy of the threshold method for identifying individual active pixels is little better than a purely random classification (i.e., 50% correctly classified). On the other hand, the accuracy of threshold pixel classification is somewhat better in the noisy denervation simulations (87, 71, and 65% for SD = 1, 2, and 3 ms, respectively), as would be expected from the greater dispersion of pixel values during exercise in this model.

DISCUSSION

Pixel threshold mapping of active muscle by MR imaging. Application of an absolute threshold criterion to map active pixels within an MR image of muscle after voluntary exercise depends on two implicit assumptions. First, the method assumes that the distribution of motor unit cells among pixels is not random, such that, at intermediate recruitment intensities, some pixels are substantially more active than other pixels. Second, the method assumes that the variance of the pixel T2 measurement is low compared with the expected variance due to pixel recruitment. Our results indicate that neither of these assumptions is correct for studies of normal subjects with standard imaging techniques.

If the effect of pixel variance is ignored for a moment, the first of the above assumptions suggests that, after moderate-intensity exercise, when a muscle is not fully active, the pixel T2 histogram should substantially broaden, ideally approaching a bimodal distribution. As illustrated in Fig. 3, we found no evidence for such bimodal behavior in the muscles of normal human subjects after voluntary exercise. On the contrary, there was no significant difference in pixel-to-pixel variance in any of the muscle groups after moderate exercise compared with after exercise to exhaustion and, therefore, no evidence that different pixels within the muscles behaved differently at these two intensities. Although there was a trend toward increased variance after exercise compared with rest, similar behavior was evident in the simulation of normal muscle, which assumed random distributions of motor unit cells among pixels, and of motor unit territories across the muscle. Unfortunately, it is not possible to position a subject's limb so precisely (i.e., within <1 pixel dimension) that the pixel locations exactly correspond in images acquired before and after the exercises and, thereby, demonstrate that the change in T2 is similar in every pixel. Nonetheless, neither our data nor previously published T2 histograms (22) can exclude the hypothesis that the change in T2 occurs...
throughout the recruited muscles in normal subjects at different exercise intensities.

The application of an absolute threshold to map active pixels also ignores the inherent variance of the pixel-by-pixel T2 calculation. These variations in pixel T2 arise from two sources: 1) from the noise associated with the imaging process and 2) from true biological variation in the composition of the pixels. On the basis of relationships similar to that shown in Fig. 5, it appears that in this study the imaging noise per se contributed 1.0–1.6 ms to the total variation in resting intramuscular T2. The results of the simulations demonstrate that this noise can profoundly degrade the accuracy of the threshold method. For example, at image S/N level one-half of that achieved in this study (as might easily occur if slice thickness or FOV were decreased to obtain increased spatial resolution), the threshold classification of individual pixels as active or inactive after moderate exercise would be little better than random, even with the assumption that the T2 of the muscles at rest was perfectly homogeneous.

The remaining biological variation in pixel T2 must arise in part from random inclusion of unresolved nonmuscle tissues (e.g., fat, small blood vessels, and connective tissue) in the pixels. This inference is supported by the observation that, in this study, imaging noise accounted for the smallest fraction of the T2 variance in the quadriceps muscle, which had the highest total T2 variance but the lowest spatial resolution. In the presence of such variations in pixel composition, application of a single absolute threshold criterion for “activity” is clearly not appropriate, even in the absence of imaging noise. This is nicely illustrated on a macroscopic scale by comparing our results across the three muscles. Although the change in T2 during the exercises was comparable in the three muscles, the initial “resting” T2 was higher in the leg muscles than in the arm muscle. Clearly, no single active threshold would be appropriate to the three cases. Similarly, no

Table 4. Computed pixel T2 in simulations of normal and denervated muscle at rest and at 4 activity levels, with Gaussian noise added

<table>
<thead>
<tr>
<th>Activity Level</th>
<th>Normal Simulation (ms)</th>
<th>Denervation Simulation (ms)</th>
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<tbody>
<tr>
<td>Rest</td>
<td>30.0 ± 1.0</td>
<td>30.0 ± 1.0</td>
</tr>
<tr>
<td>10% Active</td>
<td>31.0 ± 1.1</td>
<td>31.1 ± 1.4</td>
</tr>
<tr>
<td>25% Active</td>
<td>32.6 ± 1.3</td>
<td>32.7 ± 1.9</td>
</tr>
<tr>
<td>50% Active</td>
<td>35.2 ± 1.4</td>
<td>35.4 ± 2.2</td>
</tr>
<tr>
<td>75% Active</td>
<td>37.8 ± 1.4</td>
<td>38.0 ± 1.9</td>
</tr>
</tbody>
</table>

Values are means ± SD. SD = 1 for Gaussian noise.
single threshold can be applied to all the pixels within a muscle, because there is also a broad distribution of intramuscular pixel T2 at rest.

On the basis of the findings described above, we conclude that, given the image resolution, S/N, and T2 variance presently achievable in standard clinical MR imaging machines, the computation of active muscle area on a pixel-by-pixel basis in normal subjects with use of a single threshold T2 is not justified. Why then does the total active area calculated by this method consistently correlate with exercise intensity in this study (Fig. 4) and in previous studies (20, 22)? Furthermore, why is it that the T2 of the "active area" is relatively independent of exercise intensity, a result that seems superficially consistent with the idea that active motor units fire at a relatively constant rate once recruited (10), analogous to what occurs during fixed-rate EMS? In fact, these two results are just mathematical consequences of the threshold method for defining active area in the presence of noise. First, with the assumption of a Gaussian distribution of pixel T2 values at rest

\[
f(x) = \left( \frac{\sigma}{\sqrt{2\pi}} \right) \exp \left[ -\frac{1}{2} \frac{(x - \mu)^2}{\sigma^2} \right]
\]

where \( f(x) \) is the number of pixels with \( T2 = x \), \( \mu \) is the mean T2, and \( \sigma \) is the SD, the active muscle area is just

\[
y = \int_{t}^{\infty} f(x) \, dx
\]

where \( t \) is the threshold T2. As illustrated in Fig. 8A, if the mean of the distribution increases but the noise level is relatively high, such that the SD does not change with exercise, then over a considerable range the computed active area is just directly proportional to the mean T2 of the distribution. Thus, in the presence of noise, the observed correlation between total active area and exercise intensity just reiterates the fact that the mean muscle T2 increases with exercise intensity and does not demonstrate that the activity has been mapped to specific pixel locations. Second, the mean T2 of the active muscle area, computed as described above, is

\[
y = \frac{\int_{t}^{\infty} xf(x) \, dx}{\int_{t}^{\infty} f(x) \, dx}
\]

As shown in Fig. 8B, this parameter does not scale linearly with the overall mean T2, which can be easily understood from the fact that the mean of the active area cannot be less than the threshold T2. Thus the observation that the T2 of active muscle is relatively invariant compared with the whole muscle T2 is just a mathematical consequence of the threshold method for demarcating active muscle in noisy images and does not provide any additional information about the firing rate or other behavior of active motor units.

Justified applications of muscle functional MR imaging. Although we observed no gross regional variations in T2 within muscles in this study, our results do not exclude the possibility that functional compartmentation of activity might be observed by MR imaging in other muscles (9) or within these same muscles during different types of exercises. On the contrary, our results confirm that the muscle T2 averaged over whole muscles or fairly large ROIs (17) increases linearly with exercise intensity (Fig. 2) and, therefore, support the use of T2 as an index of muscle activity. In fact, as a practical matter, the computation of total active muscle area as performed by others (22) can also be used as an index of global muscle activity, because, as shown above, this global index is roughly proportional to mean muscle T2. However, we see no advantage to this more complicated calculation, and the terminology, active area, is not justified, because it falsely implies that activity has been localized on a pixel-by-pixel level.

Despite the inability to resolve activity of single fibers or motor units by MR imaging, comparison of the summed pixel T2 histograms with those predicted by the Monte Carlo simulation suggests that MR imaging could nevertheless yield information about the overall
state of the motor unit pool in human muscles. The simulation of normal muscle predicts that the variance of pixel $T_2$ should increase modestly after exercise compared with rest but should be relatively constant across intensities that recruit 25–75% of the total fibers (Fig. 7, Table 4). This is remarkably similar to the observed behavior in our healthy, relatively young subjects (Fig. 3). Of course, it cannot be argued that the $\frac{1}{2}$Max and Max exercises in this study (performed at 25 and 50% of 1 RM) recruited 25 and 50% of the total fiber populations, and it is probable that the number of recruited units increased during the Max exercises as fatigue was approached. Furthermore, the muscle simulation does not consider the effect of rate modulation of force or the possibility that the $T_2$ change in a muscle fiber depends on unit firing rate or on fiber type. Nonetheless, the agreement between the simulation and the results tends to confirm that the basic assumptions of the simulation are correct, e.g., that the distribution of motor unit territories and of fibers within those territories is random in healthy human muscle (16). In contrast, loss of $\geq$50% of the total motoneuron pool is common in patients with motoneuron disease (19), and decreases up to 50% in motor unit number have been measured in elderly subjects (23). In both cases, these changes are known to be accompanied by increased motor unit size and fiber clumping. The simulation of these processes indicates that the muscle $T_2$ distribution acquired after moderate exercise ought to be substantially broadened in these patients compared with normal young subjects and also that the accuracy of $T_2$ threshold maps of activity in these subjects would be greater. Therefore, if this simulation is correct, then it may be possible to monitor the pathological changes accompanying motor unit disease noninvasively by using a simple MR imaging exercise test.

In summary, the results of this study show that the variance of MR imaging pixel $T_2$ in the recruited muscles of healthy subjects does not substantially vary between different exercise intensities. Although MR imaging does provide an empirical index of whole muscle recruitment and may yield additional information on the overall state of the motor unit pool, the use of MR imaging data to calculate active muscle area on a pixel-by-pixel basis in normal subjects is not justified.

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