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Effect of Fatigue on Muscle Elasticity in the Human Forearm Using Ultrasound Strain Imaging

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Abstract— **The etiology of skeletal muscle fatigue is not well understood partly because techniques portraying muscle performance *in vivo* are limited by either their invasiveness (e.g., needle electrodes) or poor spatial resolution (e.g., surface EMG). To better characterize effects of FES and muscle fatigue, we captured real-time high resolution dynamics of the human forearm before and after a fatigue exercise using ultrasound strain imaging. A 10 MHz linear ultrasound probe aligned with the fiber axis of the 3rd flexor digitorum superficialis (FDS) provided scans at 3-msec intervals during isometric twitch and tetanic contractions evoked by low and high frequency electrical stimuli (ES). Ultrasound images synchronized with traditional force and EMG were obtained for 5 healthy adults before and after a fatiguing exercise, induced by sustained maximal exertion of the middle finger pressed against a restraint until the initial force decreased by 75%. Immediately after fatigue, twitch and tetanic stimuli generated 55.1% and 19.5% less force, respectively, implying that low frequency fatigue dominated. The force deficit was associated with a decrease in several mechanical properties of the fatigued muscle during twitch contractions, such as transverse peak strain (34±15%) and half peak strain duration (32.3±12.5 msec). Changes were not uniform across the imaged section of the muscle, suggesting that boundary conditions or fiber heterogeneity affected the strain profile. Indeed, high stress zones appeared closer to the muscle-tendon junction during isometric contractions. This study provided new insight on the elastic behavior of muscle and potential mechanisms of injury, especially directed at prolonged stimulation and control of a neuromuscular prosthesis.**

I. Introduction

Several commercial devices, such as ActiGrip® and foot drop, use functional electrical stimulation (FES) to elicit peripheral muscle contractions in limbs paralyzed by primarily a stroke or spinal cord injury. Although these devices can improve function and reduce muscle atrophy by enhancing local circulation, stimulated muscles fatigue rapidly, severely limiting FES for prolonged use. The actual mechanism leading to reduced contractile force during exercise is not fully understood, but believed to be a consequence of a decreased myoplasmic free Ca^{2+} concentration or decreased sensitivity to Ca^{2+} [1]. Depressed conduction of the action potential along the sarcolemma or into the transverse tubules has also been proposed for high frequency fatigue [2].

Direct effects of muscle fatigue at the scale of muscle fibers and milliseconds, however, are difficult to capture *in vivo*. Cutting-edge methods to monitor dynamics inside contracting skeletal muscle, such as multichannel EMG and phase contrast MRI, are generally limited in spatial or temporal resolution [3];[4];[5]. Ultrasound has also been used to determine skeletal muscle thickness, fiber length and pennation angle [6];[7];[8]; In addition, we have previously reported strain dynamics and fatigue effects in excised rat and mouse extensor digitalis longus using 1D ultrasound speckle tracking [9]. Electrically-induced muscle fatigue was correlated with decreased peak normal strain (defined perpendicular to the long axis of the muscle) and increased onset latency of strain development in response to a twitch stimulus. In this study, as an extension of that work, we used a high frame rate commercial ultrasound scanner and phase-sensitive speckle tracking to generate high resolution 2D displacement and strain maps during electrically-induced isometric contractions of the human forearm *in vivo*. Force and EMG were simultaneously recorded with ultrasound images. Deformation maps were compared before and after a fatigue exercise that affected primarily the FDS muscle compartment of the third finger. Effects of muscle fatigue were assessed using both fast and slow rates of ES.

II. Methods And Apparatus

A. Force, Electrical Recording and Stimulation

Bipolar surface EMG electrodes (AgCl) were placed approximately 12 cm proximal to the wrist joint on the right forearm over the FDS muscle compartment that controls the middle finger. To ensure that the primary source of the EMG signal was, indeed, the third FDS, electrode position was optimized during voluntary flexions of the third finger with minimal contribution due to neighboring finger or wrist motion. A differential amplifier (SR560, Stanford Research Systems) was used to amplify the EMG signal. ES was passed to an AgCl electrode, positioned ~4 cm proximal to the EMG electrodes with a reference placed near the elbow. Precise electrode positioning was obtained by monitoring movement and twitch force of the third finger during sub-

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maximal twitch stimuli. Both twitch (square pulse, 100-μs duration, ~30 mA, 2 Hz) and tetanic stimuli (train of twitches at 50 Hz, 550-msec duration) were used to induce low and high frequency muscle contractions, respectively. Monopolar stimulation level was controlled so that activation of neighboring structures was minimized. A constant current source driven by a programmable voltage generator (S88 Grass, Inc) delivered ES. A metal plate placed over the palm of the hand helped maintain a supine position. A force transducer (Interface, Inc) positioned over the middle of the second phalanx of the third finger measured the strength of each contraction. Amplified force and EMG signals were digitized and recorded using a 12-bit PC-based data acquisition card (Signatec, Inc). Twitch force was recorded following 2 to 3 minutes of potentiation [10].

B. Ultrasound Imaging System

A commercial ultrasound scanner (iU22, Philips, Bothell, WA) captured RF signals (phase and magnitude) during electrically-induced muscle contractions. A 10 MHz linear probe was fixed and aligned along the fiber axis of the FDS muscle using a customized restraint placed around the subject's forearm. The transducer was placed parallel and just radial to the EMG electrodes. After identifying the third FDS muscle in the ultrasound image, a small region was selected (~1 cm lateral, 3 cm axial to the probe) to increase the machine's frame rate to nearly 320 Hz. An output pulse from the iU22 synchronized image collection with the ES and recording systems. Ultrasound data were typically collected for a three-second interval, which included pre, peri and post contraction time. Following capture by the iU22, RF data were transferred to a laptop via an Ethernet connection. A schematic of the entire setup is illustrated in Figure 1. All subjects were free from any muscle injury and neurological disorder.

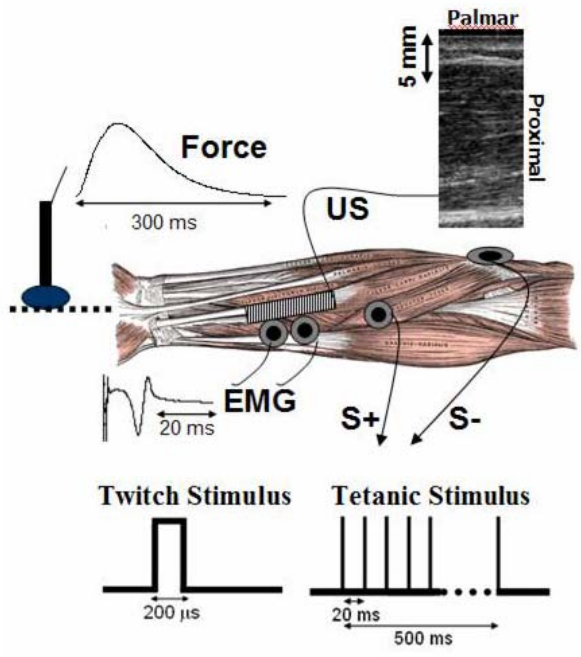

Fig. 1. Layout of apparatus used to collect ultrasound images, force and EMG during muscle contractions induced by electrical stimulation.

C. Subject Pool and Fatigue Protocol

Data were collected for the 5 adult human subjects immediately before and after a fatigue exercise, which required pressing the third finger against a restraint until the initial maximal voluntary contraction decreased by 75%. The exercise typically lasted for 5 to 10 minutes.

D. Data Analysis

A custom Unix-based speckle tracking algorithm used both phase and magnitude to estimate the interframe displacement at each position in the ultrasound image [11]. The complete 2D displacement map relative to the first frame of each contraction was obtained by accumulating the displacements across all frames. Muscle velocity, strain and strain rate images were then generated from appropriate space and time derivatives of the axial and lateral displacements. This paper examines several statistical properties of the axial normal strain (dv/dy, transverse to long axis of muscle), including peak and time to peak, half peak width, time constant of initial response and terminal relaxation, averaged over ≈300-μm^2 regions of the FDS. The median and absolute median deviations were computed for each subject before and after fatigue. Peak amplitude and latency were also extracted from the force and EMG signals using custom software developed in Matlab® (Mathworks, Inc). Significant changes in these parameters were determined across the subject pool using a paired Student's t-test.

III. Results and Discussion

A. Fatigue Effects on EMG and Force

Figure 2 summarizes the main effects of fatigue on EMG and force generation. There was no significant change due to fatigue in the EMG signal (peak magnitude or latent response) induced by a twitch stimulus, which suggests that the electrical conduction pathway, as manifested by the EMG, remains mostly unaltered. This is consistent with several other fatigue studies, in which the EMG signal was unaltered by fatigue [12]. Note that direct muscular stimulation decouples changes in the activated muscle from modifications of the peripheral and central nervous system.

The ability for the third FDS muscle to generate force, however, was severely altered by the fatigue. A substantial decrease in twitch force (55 ± 10%) and increase in latent response (3.5 ± 1.0 ms) suggests that muscle fatigue affected the mechanical properties and response distribution of activated muscle fibers. In contrast, the more modest reduction in peak tetanic force (19.5 ± 5.6%) further suggests that fatigability depends in part on the force-frequency relationship and fatigability of the underlying muscle fibers.

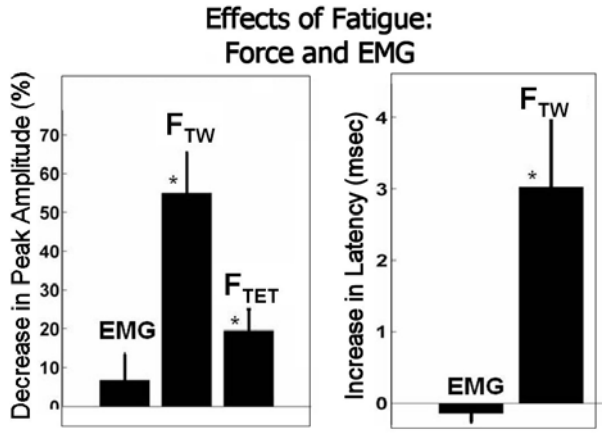

Fig. 2. Effects of fatiguing exercise on EMG and twitch (F_{TW}) and tetanic (F_{TET}) force signals, expressed as change in peak amplitude (%) and increase in response latency (msec). Bars represent a global average across subjects. An "*" denotes a significant change (p<0.05) from pre-fatigue values. Error bars represent standard error of the mean. Peak twitch force, an indicator of low frequency fatigue, decreased by more than 50%, whereas tetanic force, an indicator of both high and low frequency fatigue, reduced by almost 20%. An increase in latent force response suggests a delay in initiating contraction following stimulation, whereas no change in the EMG signal indicates the electrical conduction pathway (as manifested by the EMG signal to the ES) remains unaltered after fatigue.

B. Fatigue Effects on Muscle Elasticity

All five subjects experienced a decrease in maximum dv/dy (palmar-dorsal strain) following fatigue (-34±15%). This is consistent with the decrease in force generation of the muscle, which should impact the active stress-strain relationship in the muscle. This is consistent with the results from our previous study examining maximum dv/dy before and after electrically-induced fatigue in excised and isolated rat extensor digitalis longus muscle. The 15% standard error is close to the variability in twitch force following fatigue. It is also likely that other muscles (e.g., FDS, flexor digitalis profundus or flexor carpi radialis) contributed to the strain profile of the 3rd FDS. Nonethless, the high correlation between change in force and median dv/dy support the use of ultrasound strain imaging for portraying muscle dynamics. This approach provides 150-µm spatial and 3-ms temporal resolution over a segment of the muscle and neighboring structures, as illustrated in Figure 3. Note that at peak force axial normal strain is not uniform and increases at the distal segment. This pattern also emerges following fatigue, as the distal segment exhibits a larger change in peak strain rate (Figure 4). Although this trend was observed for multiple subjects, this was not always the case. Most likely muscle boundary conditions (e.g., muscle-tendon junction) affect the stress-strain relationship and contribute to the strain profile, although muscle fiber heterogeneity also likely enhances nonuniformity. Motion of neighboring muscles (e.g., other FDS, FDP or FCR) may also impact the strain profile. Electrode placement and anatomical differences may also enhance experimental variability.

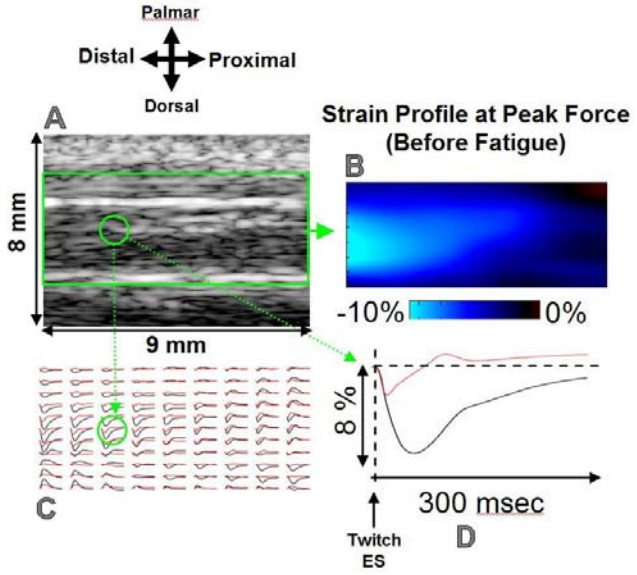

Fig. 3. A: Ultrasound B-mode image of the 3rd FDS (along muscle axis) , as well as adjacent superficial and deeper structures. B: Distribution of dv/dy (axial normal strain in palmar-dorsal direction) at peak force due to a twitch ES. Strain profile corresponds to boxed region in A. Whereas force decreased 43%, the median reduction in peak strain magnitude (3rd FDS) for this subject was 47.1 %. C: An overlay of the temporal profile of dv/dy before and after fatigue (averaged over 1-mm^2 regions) is also illustrated (scale: absolute peak -12%, 300 ms). D: A full scale overlay representing dv/dy before and after fatigue (red, dotted) at the encircled region.

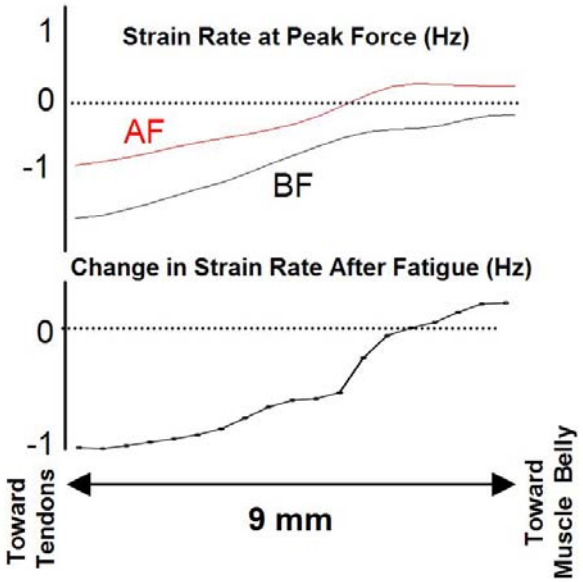

Fig. 4. Decrease in (dv/dy)/dt leading to peak force after fatigue along the muscle fiber axis for subject represented in Fig 3. In this case, high frequency fatigue had a larger impact on the distal segment of the muscle closer to the tendon. It is possible that the fixed muscle boundary conditions enhanced effects at one side of the muscle during the fatiguing isometric contractions. Although this trend was observed for multiple subjects, this was not always the case (see text).

There were also several changes in the temporal profile of dv/dy strain generation and relaxation immediately after fatigue. Most notable, the time constant of half relaxation

after time to half strain (τ_f) decreased from 50.0 ms to 34.5 ms, as well as half peak strain duration ($t_{1/2}$), from 116 ms to 84.0 ms. These changes (-16.0 ± 5.9 ms and -32±12.5, respectively) were significant among subjects ($p<0.05$). This is consistent with what others have reported in the force profile following various types of fatigue [1];[2];[13]. Interestingly, there was no significant change in the early stage (first 20 ms) of strain development, as measured by peak strain rate, time constant of ½ growth (1.9±1.8 ms) and onset latency following ES (1.7±5.3 ms). It is possible that early development of strain after fatigue does not convert directly to force generation, especially since the significant increase in latent response of force generation (3.50±1.0 ms) was matched with a delay in the latent response to dv/dy strain. This suggests that early muscle displacements and strain development do not completely convert to force generation of the 3rd FDS following fatigue. Because our previous study in isolated rat EDL muscle revealed an increase in dv/dy strain response latency, the early strain development may be due to a passive deformation from other structures that may also be stimulated but not as affected by the fatiguing process. It is also possible that additional changes in the temporal profile of strain generation occurred outside of the imaged section of the muscle and closer to either the point of stimulation (proximal) or muscle-tendon junction (distal).

C. Implications for FES, Muscle Injury and Recovery

Results suggest that the origin of the isometric fatiguing exercise was located within the 3rd FDS muscle. Whereas there was no remarkable alteration in the ES-evoked EMG signal after fatigue, the peak magnitude and rate of relaxation of the normal strain was consistent with the deficit in force. A combination of mechanisms likely contributes to fatigue, especially since the overall effects depend on the type of muscle (e.g., fatigable), nature and duration of the exercise (e.g., isometric, voluntary), and category of electrical stimulation (twitch verse tetanic). One possible explanation for the reduction in twitch force and strain generation is depletion of Ca^{2+} in the sarcoplasmic reticulum [14]; [15]; [16]. Whether fatigue arises from a change in muscle metabolic content, transport capability or transmitter release, a fatigued muscle likely undergoes elastic and viscoelastic modifications. We also observed an increased strain near the muscle-tendon junction during an isometric contraction (Figure 3 and 4), further indicating that stress also increased distal to the muscle belly. Because muscle injury usually occurs from a stretch during contraction, ultrasound strain imaging might be used to probe the mechanical integrity of soft tissue and predict when and where a muscle injury might occur.

IV. Conclusions and Future Direction

Whether fatigue arises from a change in muscle metabolic content, transport capability or transmitter release, a fatigued muscle likely undergoes elastic and viscoelastic modifications. Ultrasound elastography depicted strain and strain rates at the scale of a fiber bundle with millisecond precision and revealed effects of a sustained maximal contraction dominated by low frequency fatigue. Higher strains occurred near the muscle-tendon junction during an isometric contraction, perhaps highlighting high stress zones of the muscle profile. Ultrasound strain imaging could also be readily extended to assess muscle elasticity during FES in normal, diseased and deficient subjects and provide valuable real-time feedback during muscle activation.

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