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Quantifying changes in material properties of stroke-impaired muscle

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ABSTRACT

Background: Material properties of muscles are clinically important parameters for evaluating altered muscle function. Stroke survivors display motor impairments almost immediately after the vascular event, and then gradually develop altered muscle properties. Little is known about the magnitude of these changes in muscle material properties, specifically stiffness. Previous measures of stiffness are limited to estimates of joint stiffness or groups of muscles. Thus, our aim was to determine changes in passive muscle stiffness and composition by measuring: (1) shear wave speed using shear wave ultrasound elastography and (2) echo intensity of the B-mode ultrasound images of the biceps brachii muscle in individuals who have had a stroke.
Methods: Shear wave ultrasound elastography and B-mode ultrasound images of the biceps brachii muscle of the paretic and non-paretic limbs of sixteen stroke survivors were captured at rest.
Findings: Our main results show that shear wave speed and echo intensity of the paretic side were on average 69.5% and 15.5% significantly greater than those of the non-paretic side, respectively. Differences in shear wave speed between the non-paretic and the paretic muscles were strongly correlated with differences in echo intensity, time since stroke, and with Fugl–Meyer scores.
Interpretation: Muscle stiffness and muscle composition, as indicated by SW speed and echo intensity, may be altered in stroke-impaired muscle at rest. These findings highlight the potential for SW elastography as a tool for both investigating the fundamental mechanisms behind changes in stroke-impaired muscle, and for evaluation of muscle mechanical properties as part of clinical examination.

1. Introduction

Stroke is one of the leading causes of long-term disability in the United States, with an annual incidence of approximately 800,000 persons (Lloyd-Jones et al., 2010). Stroke survivors routinely experience long-term motor and sensory impairments, especially in the upper extremity (Gray et al., 1990; Nakayama et al., 1994). These motor impairments include weakness for voluntary movement, spasticity, and impaired coordination, and they emerge almost immediately after the vascular event. Over time, material properties of muscles in the impaired limbs can also change gradually, further disrupting motor function, and adversely impacting the stroke survivor's quality of life. These material changes appear to be associated with the increasing accumulation of collagenous connective tissue (Lieber and Ward, 2013) and are accompanied by a progressive loss of skeletal muscle fibers (McLachlan and Chua, 1983; Tabary et al., 1972) and ultimately, with contractures, that potentially limit range of joint motion. Currently, the origins of these changes in material properties remain unclear. It is our objective in this study to compare material properties in spastic-paretic muscles with contralateral muscles of stroke survivors, using shear wave (SW) speed measurements as a surrogate measure of stiffness changes.

There have been a number of prior descriptions of muscle material properties in stroke survivors. Muscle stiffness has been shown to be different in individuals after a stroke (Katz and Rymer, 1989) in both lower (de Vlugt et al., 2010; Roy et al., 2011; Sinkjær and Magnussen, 1994) and upper extremity musculature (Chardon et al., 2010). However, these earlier stiffness estimates were made indirectly, such as by using kinematic protocols while recording muscle electrical activity, by calculating limb dynamics (Sinkjær and Magnussen, 1994), or by measuring the force generated during tendon indentation (Chardon et al., 2010).

Historically, the accurate quantification of passive muscle stiffness has only been possible through such approaches as cadaveric biomechanical studies, animal *in situ* experiments, muscle biopsies, and intra-operative force and torque measures. Obtaining non-invasive

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measurements that can quickly quantify changes in muscle stiffness of specific muscles in a clinical setting remains a challenge.

Recently, ultrasound imaging techniques appear to offer promising alternative approaches. Building upon traditional elastography (Brandenburg et al., 2014; Ophir et al., 1991), shear wave (SW) elastography, allows measurement of SW speed using either magnetic resonance imaging or ultrasound imaging, which is related to stiffness, specifically the shear modulus:

$$\mu = \rho V_s^2$$

where μ is the elastic shear modulus, ρ is the muscle mass density ($\rho \approx 1000$ kg m^{-3}), and V_s is the SW speed (Bercoff et al., 2004; Brandenburg et al., 2014; Muthupillai et al., 1995). The stiffer the tissue, the faster the SWs will travel. Here we use supersonic shear imaging (SSI) (Bercoff et al., 2004), a method that uses acoustic radiation forces to induce the SWs and subsequently measure the SW speed in muscle.

Several studies have investigated the stiffness of muscles using SSI in muscles of intact subjects, including the biceps brachii (Bouillard et al., 2012; Lacourpaille et al., 2012; Nordez and Hug, 2010; Yoshitake et al., 2014), gastrocnemius (Chernak et al., 2013; Lacourpaille et al., 2012; Maïsetti et al., 2012), and vastus lateralis muscles (Lacourpaille et al., 2012). SW speed has been reported to be higher in spastic muscles of children with cerebral palsy and in individuals with Duchenne muscular dystrophy compared to muscles of typically developing children (Kwon et al., 2012; Park and Kwon, 2012) and individuals without muscle disorders (Lacourpaille et al., 2015), respectively. By measuring the SW speed in muscle, we can indirectly estimate stiffness of muscle.

Accordingly, we sought to determine whether there are differences in SW speed in the biceps brachii muscles by comparing the paretic and contralateral limbs in stroke survivors. We also assessed the echogenicity of these muscles (measured as echo intensity from the B-mode image) and correlated our estimates of material properties with major clinical assessments, including the Fugl–Meyer scale (Gladstone et al., 2002), the modified Ashworth (Pandyan et al., 1999), and the modified Tardieu tests (Singh et al., 2011). (The Ashworth and Tardieu each provide a clinical measure of the severity of spasticity.) Conveniently, the quantification of muscle echo intensity from ultrasound images can also provide information about the tissue composition of muscle (Strasser et al., 2013) in that increased amounts of fibrous tissue can result in higher ultrasound echo intensity (Pillen et al., 2009a). Higher echo intensity has been associated with aging (Arts et al., 2010; Fukumoto et al., 2012; Strasser et al., 2013) and arise in children with myopathic and neuromuscular disorders (Lamminen et al., 1988; Pillen et al., 2007).

2. Methods

2.1. Subjects

Sixteen subjects participated in this study (10 females and 6 males, mean (SD) age: 60.7 (8.0) years; height: 1.71 (0.15) m; body mass: 85.5 (18.2) kg; time post-stroke: range: 1.9–42.2, mean (SD) 11.6 (11.4) years; Fugl–Meyer: range: 4–48, mean (SD): 19 (15); modified Ashworth: range: 0–3; modified Tardieu: 1–3 muscle quality, 62°–145° catch angle for three speeds). All subjects gave informed consent prior to testing and Northwestern University's Institutional Review Board approved all procedures.

2.2. General setup

Participants were instructed to sit upright in a Biodex (Biodex Medical Systems, Inc., Shirley, NY) chair with their upper arm resting on a plastic support. To standardize the hand position and to minimize activity of unrecorded muscles, the forearm was secured in a fiberglass cast, with the wrist and forearm held in a neutral position (flexion–extension and supination–pronation) and placed in a ring-mount interface that was mounted to the table. The shoulder was positioned so that the humerus was abducted 45°, and the elbow positioned at 90°.

Surface EMG was recorded from the long and short heads of the biceps brachii and the triceps muscles using bipolar electrodes with the signal amplified by 1000 and band-pass filter of 20–450 Hz (Bagnoli, Delsys, Inc., Boston, MA). Visual inspection of the EMG signal during data collection was conducted to ensure there were no bursts of activity when the ultrasound image was captured.

2.3. Ultrasound

Ultrasound images were captured using an ultrasonography system (Aixplorer SuperSonic Imagine, Aix en Provence, France) with a linear transducer array (4–15 MHz, SuperLinear 15–4, Vermon, France) (Bercoff et al., 2004). We collected images of the paretic side and non-paretic side sequentially (five images per side, Fig. 1). Technical details of this technology have been described previously (Bercoff et al., 2004). The transducer was positioned at the mid-belly region of the biceps brachii and aligned with the fascicles as viewed from the B-mode image. A customized neoprene sleeve held the transducer in place to minimize undesired translation of the transducer. The SW speed map region of interest (12 mm by 12 mm, Fig. 1) was manually placed in middle section between the superficial and deep aponeuroses.

2.4. Data analysis

A custom software, written in Matlab (Mathworks, Natick, USA), was used to extract the SW speed and "quality factor" values from the region of interest (12 mm by 12 mm region) as given by the Supersonic Imaging software, Q Box. Each SW speed value is accompanied by a "quality factor" that indicates the reliability of the SW speed value. The software, Q Box, requires the experimenter to choose a circular region with a desired diameter from which the mean SW speed is calculated. Our custom software required the experimenter to verify that the region of interest did not include the superficial or deep aponeuroses and calculated the mean SW speed from the SW speed values in those boxes that had a quality factor greater than 0.8. Thus, the custom software ensured this step was systematic and objective.

The thickness of the muscle and adipose tissue was measured from the B-mode ultrasound image using a custom-written software in Matlab. To confirm that no contraction was generated while images were captured, EMG data were scanned, and signals with potential EMG activity were discarded. EMG data were fully-wave rectified and then low-pass filtered with a first-order Butterworth filter at 5 Hz.

To quantify the echo intensity of the B-mode images (Fig. 2), the parameters of the ultrasound system, gain and power, were kept the same for imaging the paretic and non-paretic muscles for all subjects. The mean echo intensity of the region of interest within the muscle, using the same region as for SW velocities, was calculated using the "impixel" function in Matlab, which determines the intensity values of each pixel. Only eleven subjects, out of the total sixteen subjects, were used for this analysis, as the ultrasound parameters (gain and power) were not kept the same when imaging the paretic and non-paretic for five subjects.

2.5. Repeatability and reliability

We have previously tested the repeatability and reliability of the SW speed and echo intensity measurements. In these analyses, three unimpaired subjects were tested twice on separate days; the results obtained were highly consistent. SW speed and echo intensity measurements were reliable and repeatable (SW speed: ICC = 0.932, CV = 4.5%; echo intensity: ICC = 0.882, CV = 4.2%). Inter-day reliability of the SSI technique has been previously reported (Lacourpaille et al., 2012; Yoshitake et al., 2014).