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● *Original Contribution*

MUSCLE SHEAR WAVE ELASTOGRAPHY IN INCLUSION BODY MYOSITIS: FEASIBILITY, RELIABILITY AND RELATIONSHIPS WITH MUSCLE IMPAIRMENTS

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Abstract—Degenerative muscle changes may be associated with changes in muscle mechanical properties. Shear wave elastography (SWE) allows direct quantification of muscle shear modulus (MSM). The aim of this study was to evaluate the feasibility and reliability of SWE in the severely disordered muscle as observed in inclusion body myositis. To explore the clinical relevance of SWE, potential relationships between MSM values and level muscle impairments (weakness and ultrasound-derived muscle thickness and echo intensity) were investigated. SWE was performed in the biceps brachii at 100°, 90°, 70° and 10° elbow flexion in 34 patients with inclusion body myositis. MSM was assessed before and after five passive stretch-shortening cycles at 4°/s from 70° to 10° elbow angle and after three maximal voluntary contractions to evaluate potential effects of muscle preconditioning. Intra-class correlation coefficients and standard errors of measurements were >0.83 and <1.74 kPa and >0.64 and <1.89 kPa for within- and between-day values, respectively. No significant effect of passive loading–unloading and maximal voluntary contractions was found (all *p* values >0.18). MSM correlated to predicted muscle strength (all Spearman correlation coefficients (ρ) > 0.36; all *p* values < 0.05). A significant correlation was found between muscle echo intensity and muscle shear modulus at 70° only (ρ = 0.38, *p* < 0.05). No correlation was found between muscle thickness and MSM (all ρ values > 0.23 and all *p* values > 0.25, respectively). Within- and between-day reliability of muscle SWE was satisfactory and moderate, respectively. SWE shows promise for assessing changes in mechanical properties of the severely disordered muscle. Further investigations are required to clarify these findings and to refine their clinical value. (E-mail: d.bachasson@institut-myologie.org)

Key Words: **Skeletal muscle, Shear wave elastography, Quantitative muscle ultrasound imaging, Myositis, Neuromuscular disorders, Muscle stiffness, Muscle elasticity, Passive muscle mechanics.**

INTRODUCTION

In the skeletal muscle, passive and active mechanical properties may be affected by structural alterations induced by disuse and pathological processes (Wisdom et al. 2015). Measuring these properties may help to assess and monitor disease-induced muscle changes (Bilston and Tan 2015; Brandenburg et al. 2014).

Ultrasound elastography techniques provide an opportunity for direct quantification of passive and active muscle elasticity in real time (Dubois et al. 2015; Eby et al. 2013; Gennisson et al. 2013). In comparison with previous ultrasound-based techniques for elastography, shear wave elastography (SWE) has been found to exhibit superior reliability (Bavu et al. 2011; Brandenburg et al. 2014). Assessments of muscle stiffness using SWE have been reported to be particularly relevant for investigating mechanisms underlying limitations in range of motion in conditions involving muscle/tendon retraction and/or spasticity, such as cerebral palsy (Brandenburg et al. 2016), stroke (Lee et al. 2015) and Duchenne muscular dystrophy (Lacourpaille et al. 2015). Good agreement between fibrosis staging using biopsy and elasticity assessed from SWE has been repeatedly reported in liver (Deffieux et al. 2015), highlighting the great potential of this technique to characterize tissue-level changes. However, studies that have investigated relationships between local muscle

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elasticity and the severity of degenerative muscle changes are particularly scarce (Bilston and Tan 2015). For instance, the muscle pathology in inclusion body myositis (IBM, *i.e.,* the most common acquired inflammatory myopathy after 50 y of age) combines inflammation and myofiber degeneration, leading to severe muscle atrophy, fatty infiltration, fibrosis and edema. It is unclear whether these changes affect passive mechanical muscle properties when they co-occur (Virgilio et al. 2015; Wisdom et al. 2015). In addition, data regarding within- and between-day reliability of measurements using SWE in the severely disordered muscle are scarce.

Therefore, this study was aimed at assessing the feasibility and reliability (within- and between-day) of use of SWE in the severely disordered muscle that may be observed in patients with neuromuscular diseases such as IBM. The acute effect of stretching and muscle contraction was also evaluated. To explore the clinical relevance of SWE, potential relationships between MSM values and level muscle impairment (weakness and ultrasound-derived muscle thickness and echo intensity) were investigated.

METHODS

Participants

A total of 34 patients diagnosed with IBM volunteered to participate in this study (18 men: age = 67.5 ± 7.6 y, height = 172 ± 6 cm, weight = 78 ± 12 kg; 16 women: age = 61.9 ± 8.5 y, height = 161 ± 6 cm, weight = 63 ± 11 kg). All patients had definite IBM; that is, pathological examination of their biopsies revealed fibers invaded by lymphocytes, vacuoles and amyloid deposits (Benveniste and Hilton-Jones 2010). Symptom onset was 7.6 ± 4.5 y, and time since diagnosis was 2.6 ± 2.6 y. The mean IBM weakness composite index (Benveniste et al. 2011) was 60 ± 18 (maximal score = 100). Patients had no history of traumatic event in their right upper limb. This study conformed to the Declaration of Helsinki and was approved by the local ethics committee. All patients gave written informed consent.

Muscle shear modulus assessment

Patient setup. Participants sat (85° hip flexion) on an ergometer (Biodex, Biodex Medical, Shirley, NY, USA) with the right upper limb positioned as follows: 90° shoulder flexion, 20° shoulder abduction, 0° shoulder rotation, 90° elbow flexion, 0° supination. The upper body was stabilized with straps across the thorax and the abdomen.

Muscle SWE. Measurements were performed in the short head of the right biceps brachii because of its longitudinal architecture (Lieber and Ward 2011) and because it is variably affected in patients with IBM (Cox et al. 2011). SWE measurements in biceps brachii have also been found to be feasible and reliable in healthy subjects (Lacourpaille et al. 2012). Muscle shear modulus (MSM) was assessed at different elbow joint angles. Measurements were performed using an Aixplorer Ultrasound scanner (V9.2, Supersonic Imagine, Aix-en-Provence, France) driving a 4- to 15-MHz linear transducer array (SL15-4, 256 elements, pitch = 0.2 mm). Settings were defined as follows: supersonic shear imaging mode enabled; musculoskeletal pre-set, penetration mode enabled; tissue tuner at 1540 m/s; gain at 40%; dynamic range at 80 dB. MSM was calculated assuming a linear elastic behavior in muscle tissue (Bercoff et al. 2004) as:

$$\mu = \rho V_s^2 \quad (1)$$

where ρ is the density of muscle (1000 kg/m^3), and V_s is the shear wave speed.

A generous amount of water-soluble transmission gel was used during scanning for optimal acoustic coupling, and minimal pressure was applied to the transducer to limit tissue deformation. The belly of the short head of the biceps brachii was identified during transverse scanning in B-mode at two-thirds of the distance between the acromion and antecubital fossa. Then the probe was rotated and carefully aligned with the direction of muscle fascicles as recommended by Gennisson et al. (2010). Appropriate transducer alignment was achieved when several fascicles were continuously visible. A > 5-s delay was used before capturing all clips to obtain stabilized acquisition. During all measurements, participants were asked to keep their whole upper limb as relaxed as possible, and elastograms and B-mode images were carefully monitored. Clips were discarded if subtle movement and/or contraction was detected. Typical recordings for one patient are illustrated in Figure 1.

Post-processing of SWE data. Each frame of the 10-s clips was processed using a custom software developed in MATLAB (The MathWorks, Natick, MA, USA) (Dubois et al. 2015; Vergari et al. 2014). A rectangular region of interest (ROI) was manually defined on the first frame as large as possible between the superficial and the deep aponeurosis in the muscle belly, and focal penetration defects or fibrous septa were carefully avoided. The ROI was tracked over other frames to evaluate the same region all over the measurement. MSM was computed as the mean of shear modulus values within whole ROIs. A normalized shear modulus was computed for each individual by dividing values at all tested joint angles by the value obtained at 100°.

Within- and between-day reliability

For all measurements, two clips were consecutively acquired after re-positioning the probe to assess within-