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A possible clinical tool for the muscle elasticity mapping with MRE

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Grant support : Picardie région, AFM

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Running title: Muscle elasticity mapping with MRE

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an 'Accepted Article', doi: 10.1002/mus.23678

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ABSTRACTS

Introduction: Characterization of muscle elasticity will improve the diagnosis and treatment of muscle disorders. The purpose is to compare the use of Magnetic Resonance Elastography (MRE) and ultrasound elastography (USE) techniques to elucidate the MRE cartography of thigh muscles.

Methods: Both elastography techniques were performed on 5 children and 7 adults. Quantitative (MRE) and qualitative (USE) cartographies of muscle elasticity, as a function of muscle state and age, were obtained with shear waves and manual compression of the ultrasound probe, respectively.

Results: Similar cartographies of muscle elasticity were obtained with the 2 methods. The combination of both imaging techniques results in an improved depiction of the physiological changes associated with muscle state and age.

Discussion: This study demonstrates the feasibility of MRE for use as a clinical tool in the characterization of neuromuscular pathologies and for assessing the efficacy of specific treatments for muscle related diseases.

Keywords: muscle elasticity, magnetic resonance elastography, ultrasound elastography, children, adults

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INTRODUCTION

Diseases that cause muscle degeneration, (e.g. sarcopenia, myopathy) are a major public healthcare problem. Thus, a better knowledge of muscle behavior, through analysis of its mechanical and morphological properties, will aid in the development of medical devices to improve the diagnosis and treatment of muscle disorders.

Previously, muscle disorders have been evaluated with functional examinations (e.g. the manual muscle test) or validated with clinical scales. However, these approaches are subjective and unreliable[1]. In addition to functional examinations, electromyography (EMG) or fine wire recordings have been used for research and clinical evaluation to determine the activity of specific muscles, but the process may be painful for the patient. Overall, there is no current gold standard examination to characterize muscle tissue.

For 20 years, medical tools have been developed to characterize the elastic properties of soft tissues[2]. Given that tumors or necrotic tissues are harder than the surrounding healthy tissues, technologies based on the propagation of shear waves were developed as a way to characterize soft tissues. Thus, ultrasound and magnetic resonance imaging techniques were further improved, with specific ultrasound probes or pneumatic drivers, to estimate the elasticity of soft tissue such as the liver[3] or skeletal muscle[4, 5].

Muscle characterization has previously been carried out on healthy and pathological muscles using the transient elastography technique, which assesses muscle hardness[6, 7, 8], and also with the magnetic resonance elastography (MRE) technique, which allows for shear modulus measurements[4, 9, 10, 11, 12]. Transient and MR elastography techniques provide local information of the muscle media, while the use of MRE allows one to obtain a global representation of the mechanical properties of larger muscle areas. MRE cartography of the muscle shear modulus identifies variations of muscle contractile properties from childhood

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through adulthood and accurately compares mechanical changes occurring during muscle growth and aging[12]. Moreover, Chen et al., (2007, 2008) used MRE to detect higher elasticity of taut muscle bands in patients with myofascial pain located in the upper region of the trapezius muscle[13, 14]. Similar to MRE, ultrasound elastography (USE) also provides a quantitative mapping of muscle hardness. It can reveal patterns of change after exercise[15, 16], as well as qualitative mapping of muscle elasticity for pathological muscles for such disorders as congenital myopathy[17].

The objective of this study was to compare 2 different elastography techniques (USE and MRE) to validate the use of MRE for muscle elasticity mapping as a possible clinical tool. Thus, qualitative comparisons were performed between USE and MRE mapping obtained in the thigh muscles of children and adults when the muscles were in both relaxed and contracted states.

2. MATERIALS AND METHODS

2.1 Participants

Five children (3 boys and 2 girls, mean age = 10.6 ± 0.9, range = 8-12, mean BMI = 16.44 ± 1.28 kg/m²) and 7 adults (3 men and 4 women, mean age = 30.6 ± 12.2, range = 23-58, mean BMI = 24.43 ± 1.84 kg/m²) with no muscle abnormality or history of muscle disease underwent magnetic resonance elatography (MRE) and ultrasound elastography (USE) tests. This study was approved by the institutional review board, and informed consent was obtained.

2.2 Magnetic Resonance Elastography (MRE) tests

A. Experimental Setup

A diagram of the MRE set-up was previously published by Bensamoun et al. (2006) and is summarized here. MRE tests were performed with a phase-contrast MRI technique[2]. The subject lay supine within a 1.5T General Electric HDxt MRI machine on an adult leg press, which was adapted to account for the size of children. The knee was flexed to 30° with the right foot placed on a footplate in which a load cell (SCAIME, Annemasse, France) was fixed to record the developed force. Visual feedback (LABVIEW program) of the applied load was given to the volunteers in the MR room. A pneumatic driver consisting of a remote pressure driver was connected to a long hose. A smaller silicone tube was wrapped and clamped around the subject's thigh one third of the distance from the patellar tendon to the greater trochanter, and a custom-made Helmholtz surface coil was placed around the thigh. Shear waves were induced through the thigh muscles at 90Hz (*f*), which is the optimal frequency to characterize muscle elasticity with the tube driver using the MRE technique[4, 11, 12, 18].

B. MRE cartography of muscle elasticity

Anatomical images of MRE as well as phase images of the propagation of shear waves within the soft tissue are shown in Figure 1a. This allows for the measurement of muscle elasticity. Thus, MRE images were collected in the sagittal plane, using a gradient echo technique, a 256x64 acquisition matrix (interpolated to 256 x 256), a flip angle of 45°, a 24cm field of view and a 5mm slice thickness[4, 12]. Two slices were prescribed through the vastus medialis (VM), and four offsets were recorded with the VM muscle in relaxed and contracted [10%, 20%, maximum voluntary contraction (MVC)] states. Subsequently, the slice revealing the best muscle architecture, as previously defined by Bensamoun et al. (2006), was selected for analysis. For each offset, a phase image was recorded, and the muscle elasticity was represented by the mean values of the shear modulus (μ) with its corresponding standard deviations using the following equation[12]:

$$\mu=\rho\lambda^2 f^2$$

where λ is the wavelength, ρ is the muscle density (1000 kg/m^3) and f is the frequency. It is assumed that the muscle is linearly elastic, locally homogeneous, isotropic, and incompressible. The scan time was 52 seconds using a TR/TE of 100 ms/23 ms.

In addition to the anatomical and phase images, MRE can also provide a map of muscle elasticity (Figure 1b), with a quantitative elasticity color-code reflecting the spatial distribution of the shear modulus. This cartography was generated from the phase images using a local frequency estimation (LFE) algorithm[19] (Fig 1b) and quantified within a region of interest (ROI$_{_MRE}$). The prescribed ROI$_{_MRE}$ was placed in a homogeneous region of the muscle represented by a uniform color and located near the tube attachment site, which is used as a reference mark for the ultrasound acquisition[18]. In addition to the shear modulus measurement, a histogram representing the color distribution of each ROI was generated using Image J software (Image J 1.37v, Wayne Rasband National Institute of Health, USA) (Fig 2a). A quantification of the Standard Deviation (SD) of the pixel intensities representing the variation of color within the ROI was measured. Subsequently, the same ROI was repeated for the other recorded cartographies in the same muscle area when the muscle was in a contracted state. This allowed for the comparison of the shear modulus as a function of the muscle state.

Repeatability of MRE cartographies was performed on a few children and adults with the same MRE set up at different times when the muscle was relaxed and contracted.

2.3 Ultrasound elastography (USE) tests

A. Experimental Setup

The USE tests were performed a few days after the MRE tests using a Logic E9 ultrasound machine (GE Healthcare, Velezy, France). Each subject lay in a supine position on the same leg press with the same leg position (knee flexed to 30°) as used during the MRE test. The indentation left by the fixation of the silicone tube was used as a reference to record the ultrasound image in the same muscle area as was investigated using MRE[18]. The ultrasound transducer (Linear probe ML 6-15, 13 MHz) was placed perpendicular to the tube, and the vastus medialis (VM) muscle was located visually.

B. US elastogram of muscle

Ultrasound images were acquired with B-mode after slight manual compression was applied perpendicular to the skin surface, leading to longitudinal ultrasonic images (resolution 960 x 720 mm). These images showed the muscle architecture (Fig. 3a) with the corresponding muscle elasticity elastogram (Fig 3b). This technique applied a post-processing of the US signals obtained before and after slight compression of the tissue, resulting in a color-coded map of the elastic properties of the media called “elastograms”. Visual feedback in the form of a color scale on the ultrasound screen quantified the applied manual compression. Thus, ultrasound images were recorded only when the entire color scale was green, insuring the repeatability of the applied load for each subject. Acquisitions were performed when the muscle was at relaxed and contracted (10% and 20% MVC) states, and a qualitative assessment of muscle tissue elasticity was represented by another color scale indicating soft and hard tissues. It must be noted that the USE color scale was spectrally opposite to that of the MRE color scale.

In addition, a quantitative measurement of the color distribution was performed using the Image J software with the entire elastogram considered as the region of interest (ROI_{USE}) (Fig. 2b). This region of interest was nearly identical to that of the ROI used for MRE analysis. As previously stated, the Standard Deviation (SD) of the pixel intensities, representing the variation of color within the ROI as a function of the muscle state, was measured.

Repeatability of ultrasound elastographic acquisitions was conducted on each child and adult on the same day but at different times when the muscle was relaxed and contracted.

3. RESULTS

3.1 Comparison of MRE and USE muscle elasticity cartographies on children

At rest, USE and MRE muscle elasticity mapping exhibited a quasi-homogeneous color: green for the USE mapping (Fig. 4b) and purple for the MRE cartography (Fig. 4c). These results demonstrate the homogeneity of the mechanical properties in a passive muscle condition confirmed with the relatively low standard deviation (SD) measurement obtained for both histograms ($SD_{\_USE}$ = 22.7±1.9 vs. $SD_{\_MRE}$ = 9±1.6) (table 1).

When the muscle was in a contracted state, MRE cartographies revealed a diffuse distribution of colors (Fig. 4f,i) indicating an increase of the shear modulus with the level of contraction ($SD_{\_10\%MVC}$= 27.1±3.8 vs. $SD_{\_20\%MVC}$= 33.2±1.5). This result was also confirmed by the increase in mean stiffness measured within the prescribed MRE region of interest (ROI) (Fig. 4c,f,i). The corresponding ultrasound elastogram (Fig. 4e,h) also revealed an increase in the color distribution from the relaxed to the contracted state ($SD_{\_10\%MVC}$= 37.4±0.7 vs. $SD_{\_20\%MVC}$= 41.3±2.7). Indeed, the presence of blue bands reflecting harder areas within the muscle during contraction (10% and 20% MVC) could be seen. Moreover, US elastograms demonstrated that these areas followed the direction of the fascicle path that is only visible on the B-mode ultrasonic image (Fig. 4d,g).

3.2 Comparison of MRE and USE muscle elasticity cartographies on adults

At rest, ultrasound elasticity mapping depicted a non-homogeneous area with a mixture of blue and green colors within the vastus medialis muscle ($SD_{\_Rest}$ = 26.1±1.9). The presence of local blue areas (Fig. 5b), located along the muscle fascicles, revealed the pre-stretch state of muscle fibers in the passive state. A similar result was found for MRE mapping ($SD_{\_Rest}$= 10.3±1.6) with locally high values of the shear modulus (4.6kPa) within the vastus medialis, also represented by a range of blue colors.

In a contracted state, MRE cartographies revealed a slight distribution of colors (Fig. 5f) ($SD_{\_10\%MVC}$= 15.1±2.4 $SD_{\_20\%MVC}$= 21.3±1.7) which contrasts with the important distribution of colors found on the MRE cartographies for children, revealing higher mechanical properties. Similarly, the ultrasound elastogram showed few blue areas at 10% (Fig. 5e) ($SD_{\_10\%MVC}$= 38.6±1.5), and 20% MVC (Fig. 5f) ($SD_{\_10\%MVC}$= 39.3±1.6), reflecting locally hard regions due to the contraction of muscle fibers.

Pediatric and adult muscle elasticity mappings obtained with US and MR elastography were in accordance with one another both in passive and active states.

DISCUSSION

This study represents a continuation of our previous work performed using magnetic resonance elastography (MRE) and has demonstrated a relationship between the shear modulus map and the muscle states as a function of age[12]. The issue with our previous findings was with regard to the validity of the results. Thus, the goal of this study was to verify the capability of the MRE technique to provide a quantitative cartography revealing passive and active muscle mechanical properties.

This study compared the MR and ultrasound (US) elastography techniques on the same muscle in children and adults and compared the muscle elasticity properties between these 2 populations. These cartographies represent the physiological activity of pediatric and adult muscle for which the neuromuscular (muscle fiber stretching and recruitment) and the structural (fiber orientation) properties are different. MR and US techniques are complementary methods which enable a large field of view and a superficial analysis of the tissue of interest, respectively. In the literature, MR and US elastography measurements are usually compared to biopsy results[20], biological tests[20, 21], electromyography analysis[7, 22, 23], and ergometric[7, 8, 23] techniques. The comparison of MRE and ultrasound elastometry (Fibroscan) techniques has previously been performed only on liver tissue to show why MRE should be investigated beyond the Fibroscan[24].

The qualitative comparison of the US and MR muscle elasticity mapping confirms the sensitivity of the MRE technique to detect changes in muscle shear modulus in children and adults[12, 18]. Indeed, the visualization of the adult ultrasound elastograms, which showed locally blue colors located partially along the muscle fibers, may reflect a pre-stretch condition of the muscle in its passive state and could explain the variation of 1kPa previously measured between the upper (close to the subcutaneous tissue) and lower (close to the aponeurosis) regions of the passive muscle[19]. Moreover, ultrasound elastograms acquired on passive pediatric muscle, which revealed a homogeneous green color corresponding to the uniform purple color obtained using MRE, supports the homogeneity of its elastic properties. In addition, ultrasound elastograms allow for the confirmation of differences in mechanical properties between children and adults[19]. Indeed, in active conditions, the adult muscle showed a slight distribution of color compared to the larger one obtained for pediatric muscle. This may be attributed to the structural organization of the muscle[12]. The similar spatial distribution of colors through the US elastograms of pediatric and adult muscles validates the feasibility of the MRE technique and the potential of US elastography to determine the mechanical properties of muscle for patients suffering from neuromuscular disorders, particularly during therapeutic trials. Thus, Drakonaki et al. (2010) acquired US elastographic patterns on Bethlem myopathy and successfully identified abnormal muscle represented by harder muscle areas (blue color) that were confirmed with MRI anatomical images. Degenerative myopathies were reported to induce structural disorganization of muscle[25] which should be easier to monitor with the use of an US device compared to the MRE technique. However, the US elastography technique can only characterize superficial muscles to a limited depth, compared to the MRE technique, which provides a larger field of view and is not limited by the thickness of subcutaneous adipose tissue or muscle depth.

In conclusion, MRE cartography of muscle elasticity was qualitatively compared to ultrasound elastography (USE). The combination of both imaging techniques enables the correlation of the muscle mechanical properties (shear modulus) with the muscle physiological properties associated with the muscle state and age. This study demonstrates that MRE can provide an elasticity map of passive and active muscle, and it can become a

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clinical tool for the characterization of the muscle mechanical properties which will be of interest for the follow-up of healthy and diseased muscle.

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Figure legends

Figure 1: MR elastographic images of the vastus medialis (VM) muscle at rest in an adult subject. A: Representation of shear wave displacement within the VM muscle. B: Corresponding cartography of the muscle shear modulus with a color scale quantifying the VM shear modulus.

Figure 2: Color distributions of the region of interest (ROI) located on the muscle shear modulus cartography ($ROI_{\_MRE}$) (A) and on the muscle hardness elastogram ($ROI_{\_USE}$) (B). VM: vastus medialis, Sr: Sartorius

Figure 3: Ultrasound elastographic acquisition on an adult subject. A: Ultrasound image of the VM muscle architecture. B: Elastogram representing the muscle elasticity. A color-coded scale ranging from red to blue reflects the level of muscle hardness, and the green scale indicates the applied manual compression.

Figure 4: MR and ultrasound elastographic images recorded in the same VM muscle of a child in passive and active (10% and 20% of MVC) states. The mean shear modulus was measured within the $ROI_{\_MRE}$ (Debernard et al., 2011).

Figure 5: MR and ultrasound elastographic images recorded in the same VM muscle of an adult in passive and active (10% and 20% of MVC) states. The mean shear modulus was measured within the $ROI_{\_MRE}$ for adults aged between 23 and 58 years.

	USE			MRE		
	Rest	10%MVC	20%MVC	Rest	10%MVC	20%MVC
Children	22.7 ± 1.9	37.4 ± 0.7	41.3 ± 2.7	9 ± 1.6	27.1 ± 3.8	33.2 ± 1.5
Adults	26.1 ± 1.9	38.6 ± 1.5	39.3 ± 1.6	10.3 ± 1.6	15.1 ± 2.4	21.3 ± 1.7

Table 1: Standard deviation (SD) of the pixel intensities obtained by USE and MRE revealing the variation of colors within the specified regions of interest ($ROI_{\_MRE}$ and $ROI_{\_USE}$) for pediatric and adult muscles at relaxed and contracted (10% and 20% of MVC) states.

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ABBREVIATIONS

BMI: Body mass Index

LFE: Local frequency Estimate

MR: Magnetic Resonance

MRE: Magnetic Resonance Elastography

MVC: Maximun Voluntary Contraction

ROI: Region of Interest

SD: Standard Deviation

US: Ultrasound

USE: Ultrasound Elastography

VM: Vastus Medialis

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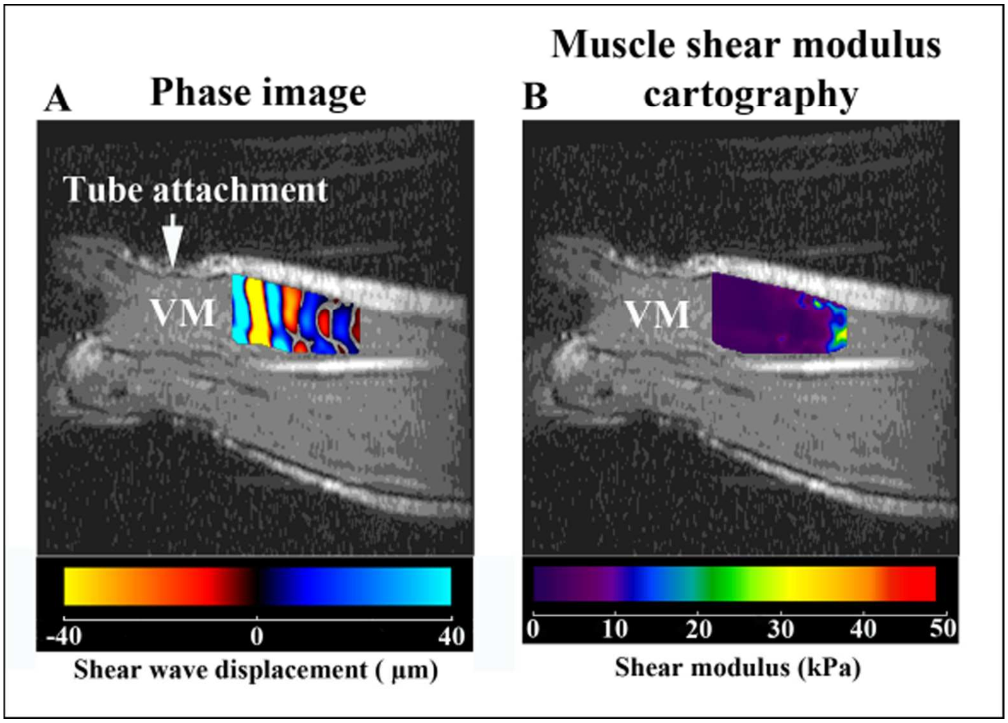
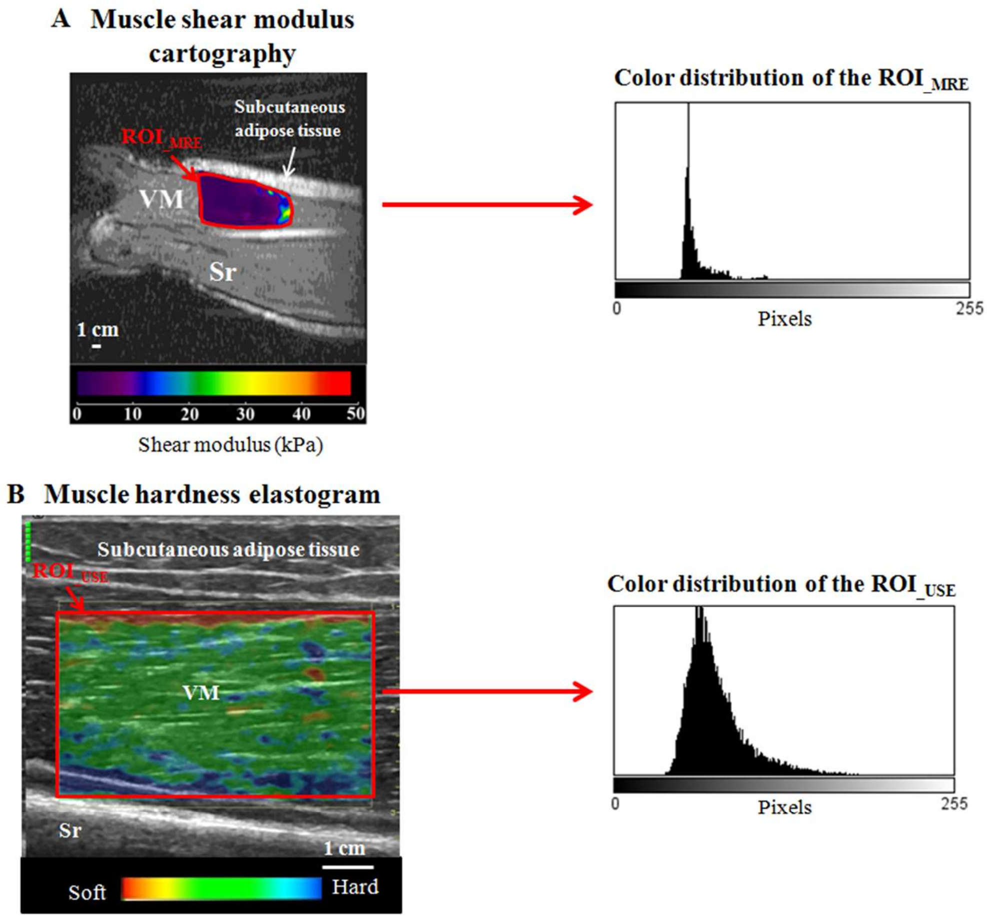
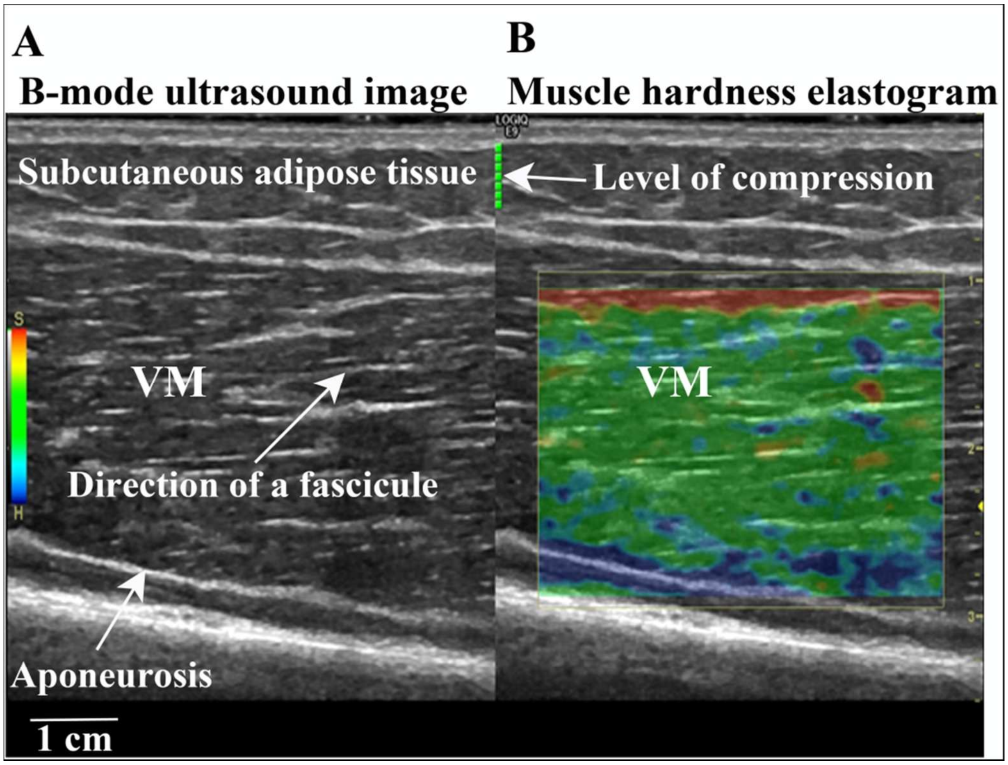


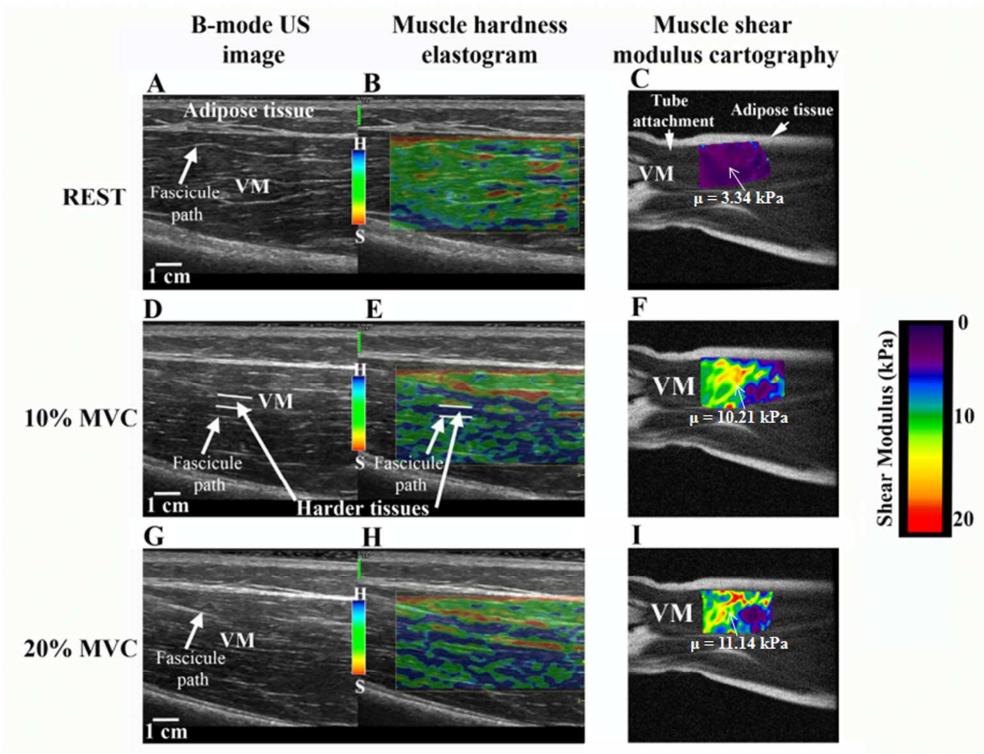
MR elastographic images of the vastus medialis (VM) muscle at rest on adult subjet. A: Representation of the shear wave’s displacement within the VM muscle. B: Corresponding cartography of the muscle shear modulus with a color scale quantifying the VM shear modulus.
155x110mm (300 x 300 DPI)



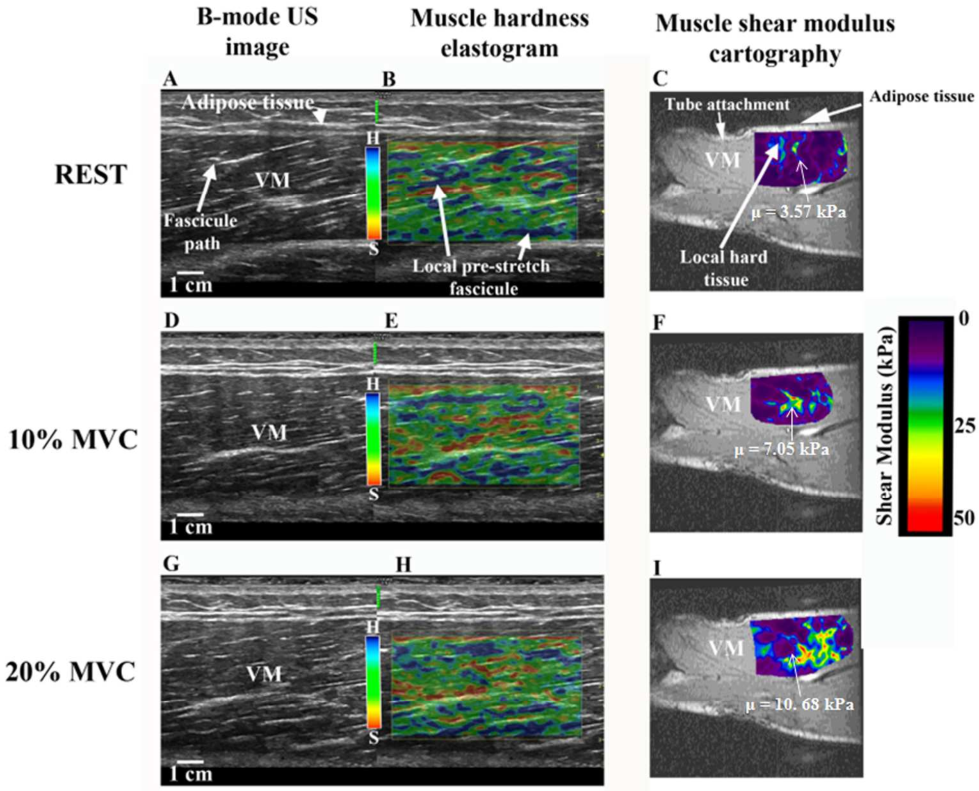
Color distributions of the region of interest (ROI) located on the muscle shear modulus cartography (ROI_MRE) (A) and on the muscle hardness elastogram (ROI_USE) (B). VM: vastus medialis, Sr: Sartorius
227x210mm (96 x 96 DPI)



Ultrasound elastographic acquisition on an adult subject. A: Ultrasound image of the VM muscle architecture. B: Elastogram representing the muscle elasticity. A color-coded scale ranging from red to blue reflects the level of muscle hardness, and the green scale indicates the applied manual compression.
252x190mm (106 x 106 DPI)



MR and ultrasound elastographic images recorded for the same VM muscle of a child in passive and active (10% and 20% of MVC) conditions. The mean shear modulus was measured within the ROI_MRE (Debernard et al., 2011).
247x190mm (300 x 300 DPI)



MR and ultrasound elastographic images recorded for the same VM muscle of an adult in passive and active (10% and 20% of MVC) conditions. The mean shear modulus was measured within the ROI_MRE for adults aged between 23 and 58 years.
235x190mm (300 x 300 DPI)