ESTIMATION OF MUSCLE FORCE DERIVED FROM IN VIVO MR ELASTOGRAPHY TESTS: A PRELIMINARY STUDY

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ABSTRACT
The objective is to estimate the vastus medialis (VM) muscle force from multifrequency magnetic resonance elastography MMRE tests and two different rheological models (Voigt and springpot). Healthy participants (N = 13) underwent multifrequency (70, 90 and 110 Hz) magnetic resonance elastography MMRE tests. Thus, in vivo experimental elastic (µ) properties of the VM in passive and active (20% MVC) conditions were characterized. Moreover, the muscle viscosity (µ) was determined with Voigt and springpot rheological models, in both muscle states. Subsequently, the VM muscle forces were calculated with a generic musculoskeletal model (OpenSIM) where the active and passive shear moduli (µ) were implemented. The viscosity measured with the two rheological models increased when the muscle is contracted. During the stance and the swing phases, the VM tensile forces decrease and the VM force was lower with the springpot model. It can be noted that during the swing phase, the muscle forces estimated from springpot model showed a higher standard deviation compared to the Voigt model. This last result may indicate a strong sensitivity of the muscle force to the change of active and passive contractile components in the swing phase of gait. This study provides for the first time an estimation of the muscle tensile forces for lower limb, during human motion, from in vivo experimental muscle mechanical properties. The assessment of individualized muscle forces during motion is valuable for finite element models, increasing the patient specific parameters. This

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novel muscle database will be of use for the clinician to better elucidate the muscle pathophysiology and to better monitor the effects of the muscle disease.

Keywords: In vivo muscle force; In vivo muscle viscoelastic properties; Musculoskeletal model; Multifrequency MR elastography.

INTRODUCTION

A better knowledge of the normal and abnormal muscle behaviors of musculoskeletal disorders, such as children with cerebral palsy or patients with post-polio residual paralysis, will allow for the establishment of appropriate muscle diagnosis leading to more appropriate treatment plans. Inverse and forward dynamic models in biomechanics represent the bones as rigid bodies, and are used to describe the behavior of muscles and joints, and to diagnose the pathologies of the musculoskeletal system. The objectives of these rigid multi-bodies models are to estimate the muscle forces, based on an optimization approach, through musculoskeletal modeling and simulation.

The specific gap of the musculoskeletal model is to use rheological properties instead of in vivo mechanical properties of isolated muscles. Indeed, Hill-based model, which is the most commonly employed phenomenological model, revealing the passive and active muscle components through the representation of the muscle force as a function of the muscle length and velocity, respectively. Moreover, the musculotendinous properties were also characterized with the force-length relationship. Recently, a quantification of the sarcomere contractile dynamics, using invasive advanced optical microendoscopy technique or in situ laser diffraction technique, improved the musculoskeletal models. In addition to the rheological properties, the anthropometrical properties, such as segment body mass, inertial moments and muscle sectional areas, were also commonly used in the musculoskeletal models from the literature. Medical images such as MRI and CT Scans have been used to improve the morphological data and the geometrical properties of the musculoskeletal model.

Different types of techniques, such as ergometer, ultrasound and magnetic resonance elastography (MRE) techniques were used to determine the in vivo behavior of soft tissues such as the muscle mechanical properties. However, the ergometric technique can assess the mechanical properties of the entire musculo-articular system, but these data cannot be used in musculoskeletal models where only the functional properties of the muscle are used. The use of ultrasound was able to provide the viscoelastic properties of passive and active muscles, using the Voigt model. However, a large range of viscoelastic values are found in the literature, and their use should be made with caution in musculoskeletal model. It can be noted that ultrasound methods applied a unique frequency and therefore did not demonstrate the viscous muscle behavior. Moreover, ultrasound techniques have a limited field of view and cannot provide the characterization of different muscles simultaneously. In addition, comparison between MRE and US elastography techniques demonstrated differences between elastic properties due to local versus global assessments. It must be noted that a recent experimental study has demonstrated a correlation between the finger muscle torque and the shear modulus, obtained with the supersonic shear imaging technique, and also the electromyography signal. MRE technique was further developed with new experimental...
protocols such as multifrequency MR elastography\textsuperscript{3-26} and advanced inversion algorithms\textsuperscript{13} providing a complex modulus, in which the imaginary part corresponds to the loss modulus and reflects the viscosity of the tissue. Thus, this study aims to estimate the VM muscle force from the quantification of the viscoelastic properties using MMRE tests and rheological models (Voigt and springpot).

METHODS
Participants
Thirteen healthy subjects (11 males and 2 females, mean age = 36.6 ± 4.6 years, mean body mass index (BMI) = 24.2 ± 1.5 kg/m\textsuperscript{2}) without muscle pathology and no prior muscle disease underwent MMRE. This study was approved by the ethical committee and consent was signed by the participants before the MMRE test.

MMRE tests performed on the vastus medialis muscle
MMRE tests allowed for the determination of the functional properties revealed by the viscoelastic (\(\mu, \eta\)) properties composed of elastic (\(\mu\)) and viscous (\(\eta\)) parameters of the \textit{in vivo} vastus medialis (VM) muscle in passive and active conditions.

Experimental setup for \textit{in vivo} MMRE tests
The present MMRE experimental protocol was described in a recent study\textsuperscript{13} and is briefly summarized here. The subject is lying on his back, inside a MRI machine (1.5 T General Electric HDxt). The right leg is flexed with an angle about 30° and the foot rests on a support where a load cell (SCAIME, Annemasse, France) was placed to measure the VM force. The participant sees a color code that allows it to maintain the level of force required.

A pneumatic driver, which is a silicone tube, is wrapped twice around the thigh and is connected to a long hose where different pressures will be applied. A specific coil will also be placed around the thigh.

Shear waves were applied to the thigh muscles at three different frequencies (\(f\)) (70, 90 and 110 Hz) to measure the viscoelastic (\(\mu, \eta\)) properties of the VM muscle in passive and active (20% MVC of the maximum voluntary contraction) states. A break (5 min) is provided to the participant between each test. The three frequencies (70, 90 and 110 Hz) were close because the reference frequency is 90 Hz, and is mainly applied with MRE technique using pneumatic driver for muscle elasticity characterization.\textsuperscript{4,6,12,19,33}

All the muscles of the thigh were obtained through an axial acquisition from a gradient echo sequence. Then, an oblique scan plan was oriented in the medial region of the thigh in order to analyze the VM muscle.\textsuperscript{5-7} Subsequently, MMRE acquisitions were recorded with a 256 × 64 acquisition matrix (interpolated to 256 × 256), a flip angle of 45°, a 24 cm field of view and a slice thickness of 5 mm. Four offsets were performed for each MMRE test performed at each frequency. The scan times at 70, 90 and 110 Hz were 38 s (TR/TE of 54 ms/24.6 ms), 32 s (TR/TE of 56 ms/23.2 ms) and 33 s (TR/TE of 50 ms/32.1 ms), respectively.

Image processing and data analysis for \textit{in vivo} MMRE tests
MMRE technique provides phase images, showing the displacement of the shear wave within the VM muscle for the three different applied frequencies [see Figs. 1(a)-(c)]. A red profile, manually placed for each frequency in the same muscle area, was prescribed along the wave’s displacement as explained by Debernard \textit{et al.}\textsuperscript{12}
The measurement of the wavelength ($\lambda$) allowed the calculation of the shear modulus ($\mu$) for each frequency ($\mu$, 70 Hz, $\mu$, 90 Hz, $\mu$, 110 Hz), assuming that the muscle tissue was linearly elastic, locally homogeneous, isotropic and incompressible. Then the shear modulus corresponding to the relaxed and contracted VM muscle, calculated at the frequency reference 90 Hz, was compared to those computed with Voigt and springpot models.

**Determination of VM elasticity ($\mu$) and viscosity ($\eta$) parameters using rheological models**

The characterization of in vivo viscoelastic ($\mu$, $\eta$) muscle properties was made with two different rheological models (Voigt and springpot), composed of spring and dashpot, revealing a complex shear modulus ($G^*$, kPa) related to the shear stiffness ($\mu$, kPa), the viscosity ($\eta$, Pa-s) and the excitation pulsation ($\omega$, Hz). Voigt model was chosen for its simple composition while springpot model, being a more complex model composed of three independent constitutive parameters (the elasticity: $\mu$, the viscosity: $\eta$ and the excitation pulsation: $\omega$), was chosen for its frequent usage in the publication to quantify the viscoelastic properties of biologically soft tissues. To measure the rheological parameters ($\mu$, $\eta$) an identification method was realized with a mean squared analysis with the Matlab software (The Matworks, Inc., Natick, MA) based on Helmholtz equation. Then, the experimental velocities calculated from the different in vivo MMRE tests were used to solve this equation.

**Estimations of in vivo muscle forces**

A generic musculoskeletal model was developed using OpenSIM software. The model (Gait2354_Symbody) was parameterized using the mean anthropometrical data of the present healthy subjects, which underwent the MMRE tests. The model includes seven segments composed of head, arms and trunk (HAT) segment, thighs, legs and feet. Moreover, the model has 23 degree-of-freedom (DOF) (6-DOF Ground-Model Joint, 3-DOF Lumbar Spine Joint, 3-DOF Hip Joint, 1-DOF Knee Joint, 3-DOF Ankle Joint) and 54 muscles actuated by Hill-based model. The muscle tensile force is estimated by using computed muscle control (CMC) strategy with normal gait kinematics data. The active and passive shear modulus ($\mu$) of the VM muscle, previously measured from Voigt and springpot models, were implemented to properly adjust the curves representing the active and passive muscle components through the force–length and force–velocity relationships. Other parameters (e.g. peak isometric muscle force, pennation...
angle, tendon slack length) were set up as default values provided by the OpenSIM software. Then, the model was simulated using inverse dynamic and static optimization with gait cycle from the stance phase to the swing phase. Data post-processing (standard deviation calculation) was performed using Matlab R2008b (The Matworks, Inc., Natick, MA).

Statistical Analysis

The software Statgraphics 5.0 (Sigma Plus, Maryland, USA) was used to perform the paired t-test analysis in order to compare the elasticity and viscosity parameters obtained experimentally (MMRE) and numerically (Voigt, springpot). This analysis was realized for the VM muscle at different conditions. \( p < 0.05 \) was the level of significance.

RESULTS

Mechanical Properties of Passive and Active Muscles

Determination of elastic (\( \mu \)) properties

The shear modulus (\( \mu \)), measured for the passive and active VM muscle, revealed an increase of the elastic properties, which is significant (\( p < 0.05 \)) as a function of the level of contraction for the different frequencies. The comparison between the experimental (MMRE tests at 90 Hz) and numerical (Voigt and springpot models) shear modulus calculated for the VM in different states, revealed closest shear modulus using the springpot model for the passive (\( \mu_{\text{MMRE,VM Passive}} = 3.90 \pm 0.26 \text{ kPa} \) versus, \( \mu_{\text{Springpot,VM Passive}} = 3.67 \pm 0.71 \text{ kPa} \)) as well as for the active condition (\( \mu_{\text{MMRE,VM Active}} = 11.03 \pm 1.21 \text{ kPa} \) versus, \( \mu_{\text{Springpot,VM Active}} = 11.29 \pm 1.04 \text{ kPa} \)) (see Table 1).

Determination of the viscous (\( \eta \)) properties

MMRE tests revealed an increase in the passive and active elastic properties (\( \mu \)) as a function of the frequency, demonstrated the qualitative viscous (\( \eta \)) behavior of the VM, which was quantified using rheological models (see Table 1). The viscosity increased as a function of the level of contraction and according to the used rheological models. The comparison of the rheological models revealed similar range of values with a slight higher viscosity value for springpot model in passive condition (\( \eta_{\text{Springpot,VM Passive}} = 4.50 \pm 1.64 \text{ Pa-s} \), \( \eta_{\text{Voigt,VM Passive}} = 3.27 \pm 0.38 \text{ Pa-s} \)) while this increase is emphasized in active state (\( \eta_{\text{Springpot,VM Active}} = 12.14 \pm 1.47 \text{ Pa-s} \), \( \eta_{\text{Voigt,VM Active}} = 8.88 \pm 1.35 \text{ Pa-s} \)).

Table 1 Elastic Properties (Shear Modulus: \( \mu \)) Obtained with MMRE Tests and Viscoelastic (\( \mu, \eta \)) Properties Obtained with Voigt and Springpot Models for the Active and Passive VM Muscle.

<table>
<thead>
<tr>
<th>Vastus Medialis</th>
<th>Passive Condition</th>
<th>Active Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMRE tests</td>
<td>70 Hz</td>
<td>90 Hz</td>
</tr>
<tr>
<td>Shear modulus (kPa)</td>
<td>( \mu = 3.28 \pm 0.18 \text{ kPa} )</td>
<td>( \mu = 9.57 \pm 0.96 \text{ kPa} )</td>
</tr>
<tr>
<td>Rheological models</td>
<td>Voigt</td>
<td></td>
</tr>
<tr>
<td>( \mu = 2.64 \pm 0.20 \text{ kPa} )</td>
<td>( \mu = 7.92 \pm 1.60 \text{ kPa} )</td>
<td>( \mu = 3.27 \pm 0.38 \text{ Pa-s} )</td>
</tr>
<tr>
<td>( \eta = 3.67 \pm 0.71 \text{ kPa} )</td>
<td>( \mu = 11.29 \pm 1.04 \text{ kPa} )</td>
<td>( \alpha = 0.34 \pm 0.07 )</td>
</tr>
<tr>
<td>Springpot</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \eta = 4.50 \pm 1.64 \text{ Pa-s} )</td>
<td>( \eta = 12.14 \pm 1.47 \text{ Pa-s} )</td>
<td></td>
</tr>
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</table>
Estimation of in vivo muscle forces

Figures 2 and 3 illustrated the tensile forces of the VM muscle during the swing and the stance phases. The comparison of the muscle force behavior showed lower values calculated with springpot model compared to Voigt model. Moreover, tensile forces of VM muscle decrease during both the stance phase (from 791 ± 2 N to **Fig. 2** VM tensile forces from Voigt and springpot models during the stance phase of gait.

**Fig. 3** VM tensile forces from Voigt and springpot models during the swing phase of gait.
were obtained with lower force values.

The same remark was noted for the springpot model with a decrease of the tensile forces, from 793 ± 1 N to 108 ± 21 N, during the stance phase, and from 272 ± 106 N to 14 ± 24 N, for the swing phase. Similar muscle forces were obtained for both legs. It can be noted that during the swing phase, the muscle forces estimated from springpot model showed a higher standard deviation compared to the Voigt model. This last result may indicate a strong sensitivity of the muscle force to the change of active and passive contractile components in the swing phase of gait. Moreover, OpenSIM model was simulated with the default muscle properties, and the same muscle force behaviors during the stance and the swing phases were obtained with lower force values.

**DISCUSSION**

This study estimates the muscle tensile forces for lower limb, during the stance and the swing phases, from the VM viscoelastic properties obtained in vivo with MRE technique. The assessment of individualized muscle forces during motion is valuable for the definition of boundary loading condition in musculoskeletal finite element models, increasing the patient specific parameters. Moreover, this novel muscle database will be of use for the clinician to better elucidate the muscle pathophysiology and to better monitor the effects of the muscle disease.

At the present time, the optimization technique has been accepted as a unique solution to estimate healthy muscle forces but abnormal behavior of the musculoskeletal system, due to muscle diseases, cannot be modeled and simulated. Generic parameterized musculoskeletal models are mainly composed of Hill-based model, which is the most used rheological model to assess the muscle tensile forces. Some authors investigated the sensitivity study of abnormal behavior of muscle due to ageing effect or paralyzed effect by adjusting the contractile properties of the Hill-based model. However, there is no way to validate such parameters adjustment strategies. In fact, the quantification of these forces requires more intrinsic properties of muscles which can be determined in vivo with the determination of the sarcomere contractile dynamics properties or the characterization of the muscles mechanical properties. Heintz’s study has compared the muscle forces estimated by static optimization and by electromyography approach. The comparison of the present VM force with Heintz’s study revealed the same muscle force behavior during the stance phase while the behavior is different during the swing phase. Moreover, these comparisons revealed quantitative differences in the force values which may be explained by the implementation of in vivo mechanical properties. Another reason could be the methodological difference such as the used technique (MRE versus EMG) and muscle force control algorithms.

**Table 2** Tensile Forces (Mean ± SD in Newton) of VM Muscle at Different Phases During Gait.

<table>
<thead>
<tr>
<th>Model</th>
<th>Tensile VM Force During the Stance Phase (0-60%)</th>
<th>Tensile VM Force During the Swing Phase (60-100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heel Strike (0-2%)</td>
<td>Midstance (10-30%)</td>
</tr>
<tr>
<td>Voigt</td>
<td>791 ± 2</td>
<td>220 ± 25</td>
</tr>
<tr>
<td>Springpot</td>
<td>793 ± 1</td>
<td>157 ± 22</td>
</tr>
</tbody>
</table>
The elastic properties ($\mu$) found for the VM muscle are in agreement with other studies, which had demonstrated a variation of the elastic properties as a function of the muscle condition.\(^6,7\) These results attest the suitability of the applied MMRE tests. Interestingly, the viscous properties of the VM, in passive and active conditions, follow the same mechanical behavior as their own elastic properties, revealing an increase of the viscosity as a function of the muscle condition. The elasticity parameter showed the global behavior of the muscle while the viscosity parameter may show the microstructural changes occurring during the friction of the muscle fibers.

This result revealed the sensibility of both parameters to reflect the muscle architecture changes, and therefore justify the interest to develop specific viscoelastic ($\mu$, $\eta$) muscle database for a better characterization of the muscle functional properties, during pathology\(^33\) or muscle ageing process.\(^19\) The present study also revealed that the two applied rheological models (Voigt and springpot) can be used for the assessment of the viscous properties for the VM muscle.

The present study showed a quantification of the viscous ($\eta$, Pa·s) component for the lower limb muscle, using the MMRE technique. Klatt \textit{et al.}\(^25\) was the only study to also use MMRE technique in order to assess the viscoelastic properties of the femoral muscle, with the viscous parameter fixed to 1 or 10 Pa·s using the springpot model. It can be noted that Klatt’s study measured the viscous properties for a group of femoral muscle, while the present study succeeded to measure the viscous properties of the isolated VM muscle. The present viscosity data found for the VM muscle were in the range of viscosity fixed by Klatt. It can also be assumed that the viscous properties may depend to the type of muscle, as previously demonstrated for the elastic properties.\(^6,7\)

The main limitation of the present study is the lack of validation of the forces estimated with OpenSim model. In a future study, gait data from patients who the MMRE measurement were collected from should be used to validate the muscle forces. However, this study opens a new direction to estimate lower limb muscle forces by introducing \textit{in vivo} muscle elastic properties, leading to future simulation of abnormal muscles. The MRE technique could provide a full database of active and passive elastic properties of different types of muscle allowing for the measurement of \textit{in vivo} muscle forces, corresponding to each muscle, in order to better understand abnormal muscle behavior or to characterize the effect of age and growing processes on the musculoskeletal system.

\textbf{CONFLICT OF INTEREST}

All authors have no conflict of interest to disclose.

\textbf{References}

In Vivo Muscle Force Estimation from MRE


