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

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Estimation of muscle force derived from in vivo MR elastography tests: a preliminary study

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Running title: *in vivo* muscle force estimation from MRE

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ABSTRACT

The purpose of this study is to estimate the *in vivo* vastus medialis muscle tensile forces, during human motion, from *in vivo* experimental mechanical properties.

Thirteen healthy subjects underwent multifrequency (70Hz, 90Hz and 110Hz) magnetic resonance elastography (MMRE) tests. Thus, experimental elastic (μ) properties of the *in vivo* vastus medialis (VM) muscle in passive and active (20% MVC) conditions were characterized. Moreover, the muscle viscosity (η) was determined with two different rheological models (Voigt and springpot) in both muscle states. Then, the estimation of the *in vivo* VM muscle forces was performed with a generic musculoskeletal model (OpenSIM) parameterized with the *in vivo* passive and active elastic properties obtained through MMRE tests.

Both rheological models showed an increase of the viscosity with the level of contraction. The results of the VM tensile forces, during the different phases of gait, estimated with springpot model were less than those computed with Voigt model. Muscle forces decrease during both the stance phase and the swing phase of gait for Voigt and springpot model. Furthermore, muscle forces estimated from springpot model seem to be more sensitive to the changes of active and passive contractile components in the swing phase of gait.

To conclude, this study opens a new direction to simulate muscle force by introducing *in vivo* muscle elastic properties, leading to future simulation of abnormal muscles.

Key words: *in vivo* muscle force; *in vivo* muscle viscoelastic properties; musculoskeletal model; multifrequency MR elastography.

1. INTRODUCTION

A better knowledge of the normal and abnormal muscle behaviors of musculoskeletal disorders, such as children with cerebral palsy[1] or patients with post-polio residual paralysis[10], will allow for the establishment of appropriate muscle diagnosis leading to more appropriate treatment plans. Models used in Biomechanics are based on rigid bodies in order to understand the mechanism of bone and joint, and to diagnose the pathologies of the musculoskeletal system. The objectives of these models are to estimate the muscle forces, based on an optimization approach, through musculoskeletal modeling and simulation[17,35].

These musculoskeletal models used Hill-based model[19], which is the most commonly employed phenomenal rheological 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 musculo-tendinous properties were also characterized with the Force-Length relationship. Concerning the morphological data, anthropometrical properties, such as segment body mass, inertial moments and muscle sectional areas, which were provided by the literature, are commonly used[13,36].

Recently, improvements of musculoskeletal models were performed with the quantification of the sarcomere contractile dynamics using invasive advanced optical microendoscopy technique[25,26]. In addition, medical images such as MRI and CT Scans have been used to improve the geometrical properties of the musculoskeletal model[7,10].

According to our knowledge no in vivo mechanical properties of isolated muscles and tendon tissues have been used in musculoskeletal models.

Different types of techniques, such as ergometer[14,15], ultrasound[18,21,27] and magnetic resonance (MR) elastography[5,6,22] techniques were used to determine in vivo 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. The use of ultrasound was able to provide the viscoelastic properties of passive and active muscles, using the Voigt model. However, these results cannot be used in musculoskeletal models due to the variation of the viscoelastic values, presented in the literature[18,21], for passive and active muscles. It can be noticed 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[5,6]. It must be noted that a recent experimental study[8] 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.

In the present study, we propose to determine the mechanical properties of isolated muscle in passive and active conditions using magnetic resonance elastography (MRE). The muscle functional properties, which were mainly quantified by the tissue elasticity, was also characterized by the viscosity (η) parameter revealing the impact of the micro structural changes occurring during the friction of the different components within soft tissues. Thus, the MR elastography technique was further developed with new experimental protocols such as multifrequency MR elastography and advanced inversion algorithms[30,31] providing a complex modulus, which the imaginary part corresponds to the loss modulus and reflects the viscosity of the tissue. Few biological tissues such as brain[23] and liver[2] were investigated with multifrequency MR elastography technique. To quantitatively measure the viscoelasticity (μ, η) parameters, different rheological models[32], composed of spring and dashpot were used. In the literature, the main rheological model used for the biological soft tissues, was Voigt's model due to its simple composition. To our knowledge, the muscle viscosity was presented by a unique study[22] which combined multifrequency MR elastography test and rheological model (springpot) to analyze the viscosity of a group of femoral muscles. It must be noted that Klatt’s study has fixed the viscosity parameter to η = 1 Pa.s or η = 10Pa.s in order to characterize the muscles elastic properties.

Thus, the purpose of this study was to quantify the viscoelastic properties of the vastus medialis muscle from multifrequency MR elastography tests and two different rheological models (Voigt and springpot). Then, the originality will be to use the experimental elastic properties to estimate the in vivo muscle force of the vastus medialis muscle.

2. METHODS

2.1 Participants

Thirteen healthy subjects (11 males and 2 females, mean age = 36.6 ± 4.6 yrs, mean Body Mass Index: BMI = 24.2 ± 1.5 kg/m²) without muscle abnormality and no history of muscle disease underwent multifrequency magnetic resonance elastography (MMRE). This study was approved by the institutional review board and informed consents were obtained from adult participants.

2.2 Multifrequency Magnetic Resonance Elastography (MMRE) tests performed on the vastus medialis (VM) muscle

Multifrequency MR elastography tests allowed for the characterization of the functional properties revealed by the viscoelastic (μ, η) properties composed of elastic (μ) and viscous (η) parameters of the *in vivo* vastus medialis (VM) muscle in passive and active conditions.

Experimental setup for *in vivo* MMRE tests

The present MRE experimental protocol was described in previous studies[4,5] and is briefly summarized here.

The subject lays supine, inside a 1.5T General Electric HDxt MRI machine, on an adult leg press. 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 and a visual feedback (LABVIEW program) of the applied load is given to the volunteers inside the magnetic resonance room. A pneumatic driver consisting of a remote pressure driver connected to a long hose was wrapped and clamped around the subject's thigh. Then, a custom-made Helmholtz surface coil was placed around the thigh.

Shear waves were applied to the thigh muscles at three different frequencies (*f*) (70Hz, 90Hz and 110Hz) to quantify the viscoelastic (μ, η) properties of the vastus medialis muscle in relaxed and contracted (20% of the maximum voluntary contraction: MVC) states. A delay (five minutes) between individual experiments was given to the volunteers in order to avoid exhaustion effects. The three frequencies (70Hz, 90Hz and 110Hz) were chosen in the same range as the reference frequency (90Hz) mainly applied with MRE technique using pneumatic driver for muscle elasticity characterization[3,4,5,11,16,28,29].

Anatomical axial image of the thigh muscle was first acquired with a gradient echo sequence in order to place an oblique scan plan on the medial side of the thigh to visualize the vastus medialis muscle[4,5]. Then, MMRE images were collected with a 256 x 64 acquisition matrix (interpolated to 256 x 256), a flip angle of 45°, a 24 cm field of view and a slice thickness of 5 mm. Four offsets were recorded for each MMRE test performed at each frequency. The scan times at 70Hz, 90Hz and 110Hz were 38s (TR/TE of 54 ms/24.6 ms), 32s (TR/TE of 56 ms/23.2 ms) and 33s (TR/TE of 50 ms/32.1 ms), respectively.

Image processing and data analysis for *in vivo* MMRE tests

MMRE technique provides phase images, showing the propagation of the shear wave within the vastus medialis muscle for the three different applied frequencies (Fig. 1a, Fig. 1b, Fig. 1c). A red profile, manually placed for each frequency in the same muscle area, was prescribed in the direction of the shear wave propagation, which follows the orientation of the muscle fascicle paths, as previously demonstrated by Debernard et al. 2011[11].

The quantification of the wavelength (λ) leads to the measurement of the shear modulus ($\mu = \rho\lambda^2 f^2$, with ρ = 1000 kg/m^3: muscle density) for each frequency (μ_{70Hz}, μ_{90Hz}, μ_{110Hz}), assuming that the muscle tissue was linearly elastic, locally homogeneous, isotropic and incompressible. Then the passive and active shear modulus of the vastus medialis muscle, calculated at the frequency reference 90Hz[4,5], was compared to those computed with Voigt and springpot models.

2.3 Determination of vastus medialis (VM) elasticity (μ) and viscosity (η) parameters using rheological models

The characterization of *in vivo* viscoelastic (μ, η) muscle properties was performed using two different rheological models (Voigt and springpot), composed of spring and dashpot[32], reflecting a complex shear modulus (G*, kPa) related to the shear stiffness (μ, kPa), the viscosity (η, Pa.s) and the excitation pulsation (ω, 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: μ , the viscosity: η and the excitation pulsation: ω), was chosen for its frequent used in the literature to quantify the viscoelastic properties of biological soft tissues. To quantify the rheological coefficients (μ, η) an identification method was performed using a mean squared analysis with the software Matlab R2008b (The Matworks, Inc., Natick, MA), based on Helmholtz equation[9], and using the velocities measurements from the calculated wavelengths obtained with the *in vivo* muscle MMRE tests.

2.4 Estimations of *in vivo* muscle forces

A generic musculoskeletal model was developed using OpenSIM software[12]. The model was parameterized using the mean anthropometrical data of the present healthy subjects, which underwent the MMRE tests. The model includes 7 segments composed of HAT (head, arms and trunk) segment, thighs, legs and feet. Moreover, the model has 23 degree-of-freedom and 54 muscles actuated by Hill-based model. The muscle tensile force is estimated by using computed muscle control strategy[33] with normal gait kinematics data. The active and passive shear modulus (μ) of the vastus medialis 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 muscle tensile forces were estimated with gait cycle from the stance phase to the swing phase. Data post-processing was performed using Matlab R2008b (The Matworks, Inc., Natick, MA).

2.5 Statistical analysis

The statistical analysis was performed with the software Statgraphics 5.0 (Sigma Plus, Maryland, USA) using paired *t*-test in order to compare the rheological methods on the elasticity and viscosity parameters. This analysis was realized for the vastus medialis muscle at different conditions. The significance was fixed to $P < 0.05$.

3. RESULTS

3.1 Mechanical properties of passive and active muscles

a) Determination of elastic (μ) properties

The passive and active shear modulus (μ) measured with MMRE tests showed a significant (*P*<0.05) increase of the elastic properties with the level of contraction for each frequency. The comparison of the passive and active experimental VM shear modulus, measured at 90Hz from MMRE tests, with those numerically calculated using the Voigt and springpot models, revealed closest shear modulus using the springpot model as well for the passive condition ($\mu_{MMRE\_VM\_Passive}$= 3.90 ± 0.26 kPa vs. $\mu_{Springpot\_VM\_Passive}$= 3.67 ± 0.71 kPa) as for the active condition ($\mu_{MMRE\_VM\_Active}$ = 11.03 ± 1.21 kPa vs. $\mu_{Springpot\_VM\_Active}$ = 11.29 ± 1.04 kPa) (Table 1).

b) Determination of the viscous (η) properties

MMRE tests revealed an increase of the passive and active elastic properties (μ) as a function of the frequency, demonstrated the qualitative viscous (η) behavior of the vastus medialis, which was quantified using rheological models (Table 1). Both rheological models showed an increase of the viscosity with the level of contraction. The comparison of the rheological models revealed a slight higher viscosity value for springpot model in passive condition ($\eta_{Springpot\_VM\_Passive}$ = 4.50 ± 1.64 Pa.s, $\eta_{Voigt\_VM\_Passive}$ = 3.27 ± 0.38 Pa.s) while this increase is emphasized in active state ($\eta_{Springpot\_VM\_Active}$ = 12.14 ± 1.47 Pa.s, $\eta_{Voigt\_VM\_Active}$ = 8.88 ± 1.35 Pa.s).

3.2 Estimation of *in vivo* muscle forces

Figures 2 and 3 illustrated the tensile forces of the vastus medialis muscle during different phases of gait. VM muscle forces estimated from springpot model were less than those computed with Voigt model. Moreover, tensile forces of vastus medialis muscle decrease during both the stance phase (from 791 ± 2 N to 170 ± 24 N) and the swing phase (from 511 ± 73 N to 93 ± 31 N) of gait for Voigt model (Table 2). 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. It can be noted that the muscle forces estimated from springpot model are more sensitive to the change of active and passive contractile components in the swing phase of gait.

4. DISCUSSION

According to our knowledge, the present study provides for the first time an estimation of the *in vivo* muscle tensile forces, during human motion, from *in vivo* experimental mechanical properties.

At the present time, the optimization technique has been accepted as a unique solution to estimate healthy muscle forces[17,35] but abnormal behavior of the musculoskeletal system, due to muscle diseases[30], cannot be modeled and simulated. Generic parameterized musculoskeletal models are mainly composed of Hill-based model, which is the most used rheological model to estimate the muscle tensile forces. Some authors investigated the sensitivity study of abnormal behavior of muscle due to ageing-affect[34] or paralyzed effect[24] 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[25] or the characterization of the muscles mechanical properties[6,7].

The elastic properties (μ) found for the vastus medialis muscle are in the same range as the literature, which had demonstrated a variation of the shear modulus as a function of the muscle condition[6]. These results attest the suitability of the applied multifrequency MRE tests. Interestingly, the viscous properties of the VM muscle, in relaxed or contracted states, follow the same mechanical behavior as their own elastic properties. This result revealed the sensibility of the viscous parameter to reflect the muscle architecture changes, and therefore justify the interest to develop specific viscoelastic (μ, η) muscle database in order to better characterize the muscle functional properties, in case of muscle pathology[28] or during the muscle ageing process[16]. 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.

To our knowledge, the present study is the first to quantitatively measure the muscle viscous (η, Pa.s) component with MMRE technique. Klatt et al 2010 was the only study to also use MMRE technique in order to assess the femoral viscoelastic property, with the viscous parameter fixed to 1 or 10Pa.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. It can also be assumed that the viscous properties may depend to the type of muscle, as previously demonstrated for the elastic properties[5,6].

Muscle micro structural information should also be taken into account by computing the *in vivo* viscoelatic properties and 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.

Developments of bone and joints finite element models with individualized geometrical and mechanical properties derived from medical images were performed for almost a decade[20]. The present study allows the assessment of individualized *in vivo* muscle forces during motion which are valuable for finite element models, increasing the patient specific parameters.

To conclude, this study opens a new direction to estimate muscle forces by introducing *in vivo* muscle elastic properties, leading to future simulation of abnormal muscles. The MR-elastography technique could provide a full database of active and passive elastic properties of different types of muscle allowing for the measurement of 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.

CONFLICT OF INTEREST

All authors have no conflict of interest to disclose.

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TABLE

			Vastus Medialis (VM)	
			Passive condition	**Active condition**
MMRE tests	**Shear modulus (kPa)**	70Hz	μ = 3.28 ± 0.18	μ = 9.57 ± 0.96
		90Hz	μ = 3.90 ± 0.26	μ = 11.03 ± 1.21
		110Hz	μ = 4.34 ± 1.20	μ = 12.92 ± 1.65
Rheological models	**Voigt**		μ = 2.64 ± 0.20 kPa η = 3.27 ± 0.38 Pa.s	μ = 7.92 ± 1.60 kPa η = 8.88 ± 1.35 Pa.s
	Springpot		μ = 3.67 ± 0.71 kPa α = 0.34 ± 0.07 η = 4.50 ± 1.64 Pa.s	μ = 11.29 ± 1.04 kPa α = 0.68 ± 0.12 η = 12.14 ± 1.47 Pa.s

Table 1: Elastic properties (shear modulus : μ) obtained with MMRE tests and viscoelastic (μ, η) properties obtained with Voigt and springpot models for the active and passive vastus medialis muscle.

Model	**Tensile VM force during the Stance Phase (0 – 60 %)**			**Tensile VM force during the Swing Phase (60 - 100 %)**		
	Heel Strike (0-2%)	Midstance (10-30%)	Toe-off (50-60%)	Initial Swing (60-73%)	Midswing (73-87%)	Terminal Swing (87-100%)
Voigt	791 ± 2	220 ± 25	170 ± 24	511 ± 73	294 ± 61	93 ± 31
Springpot	793 ± 1	157 ± 22	108 ± 21	272 ± 106	104 ± 81	14 ± 24

Table 2: Tensile forces (mean ± SD in Newton) of vastus medialis muscle at different phases during gait.

FIGURE

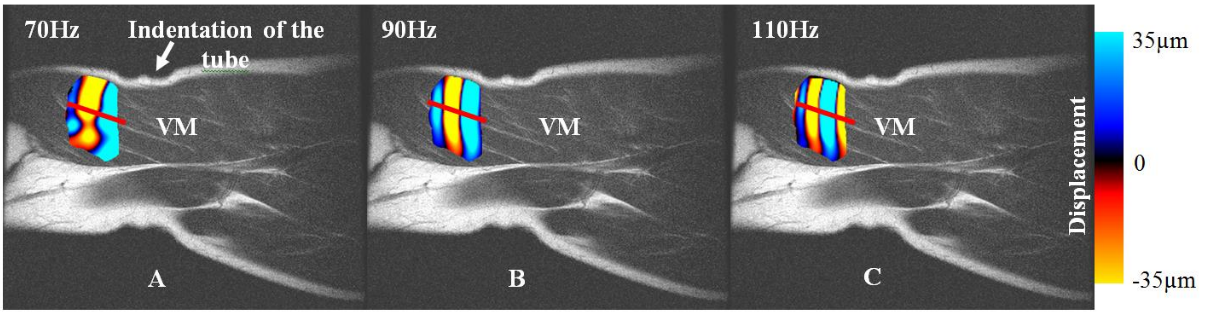

FIGURE 1. Phase images illustrating the shear wave propagation within the vastus medialis (VM) at 70Hz (A), 90Hz (B) and 110Hz (C). The wavelength (λ) was measured along the red profiles.

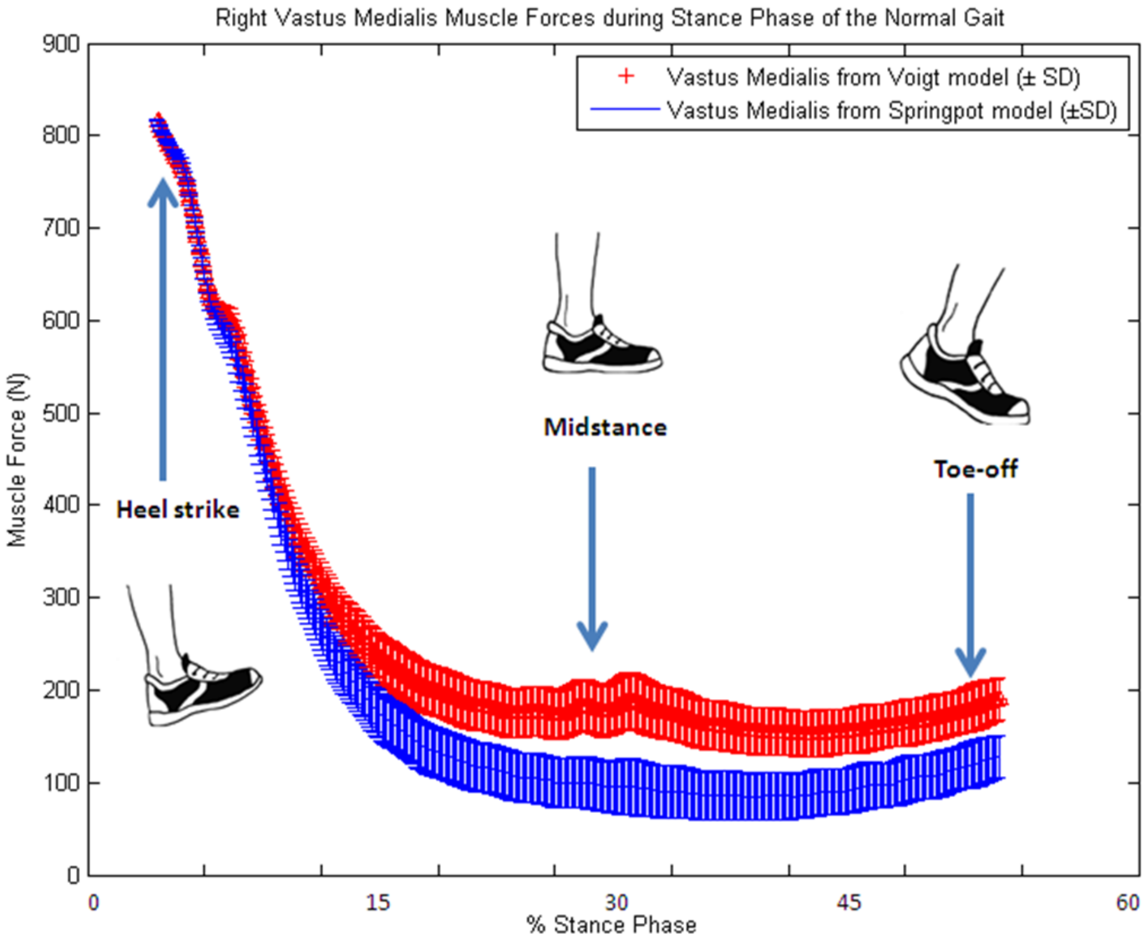

FIGURE 2. Vatus medialis tensile forces from Voigt and springpot models during the stance phase of gait.

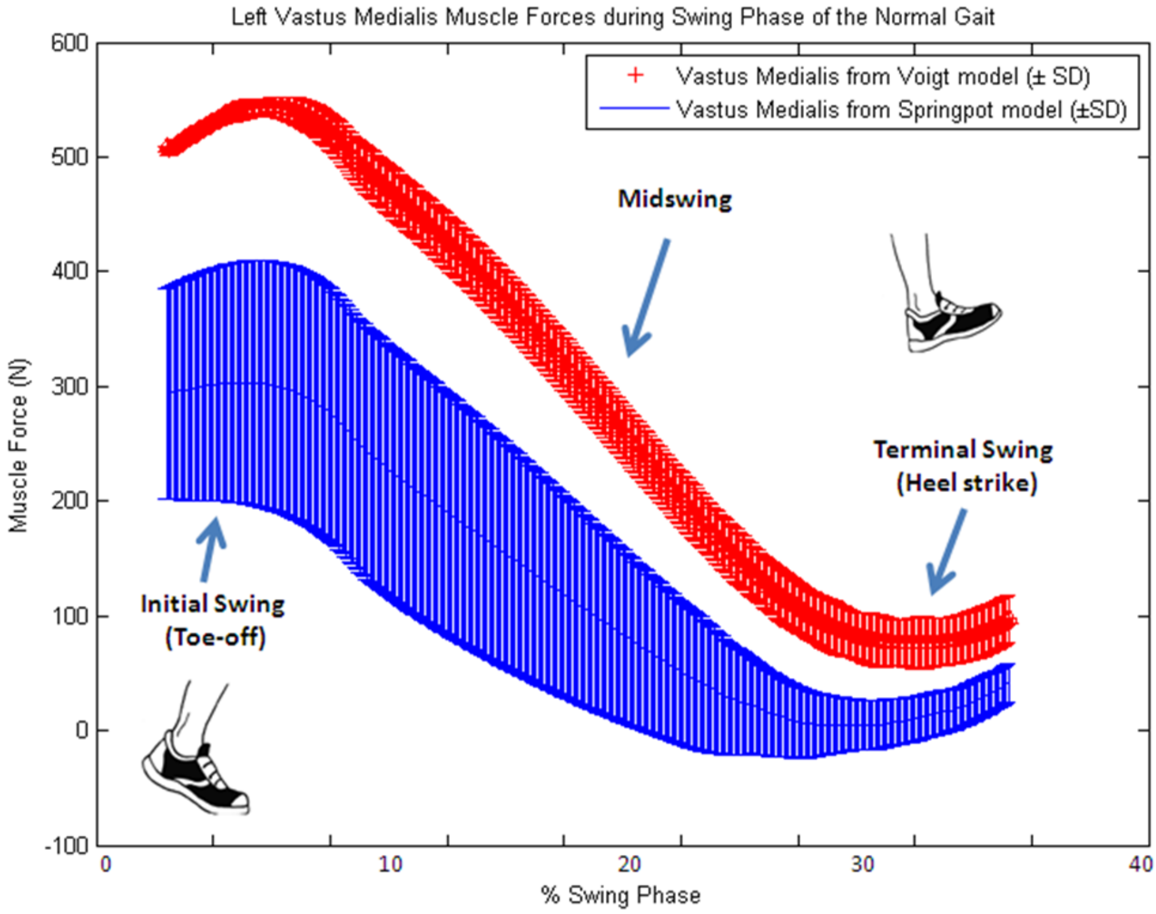

FIGURE 3. Vatus medialis tensile forces from Voigt and springpot models during the swing phase of gait.