ARTICLE

Elastography for Muscle Biomechanics: Toward the Estimation of Individual Muscle Force

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[1]University of Nantes, Laboratory "Movement, Interactions, Performance" (EA 4334), UFR STAPS, Nantes, France; [2]The University of Queensland, NHMRC Centre of Clinical Research Excellence in Spinal Pain, Injury and Health, School of Health and Rehabilitation Sciences, Brisbane, Australia; [3]The University of Queensland, School of Biomedical Sciences, Brisbane, Australia; and [4]Institut Langevin-Ondes et images, ESPCI ParisTech, PSL Research University, CNRS UMR7587, INSERM U979, Université Paris VII, Paris, France

HUG, F., K. TUCKER, J-L. GENNISSON, M. TANTER, and A. NORDEZ. Elastography for muscle biomechanics: toward the estimation of individual muscle force. *Exerc. Sport Sci. Rev.*, Vol. 43, No. 3, pp. 125–133, 2015. *Estimation of individual muscle force remains one of the main challenges in biomechanics. This review presents a series of experiments that used ultrasound shear wave elastography to support the hypothesis that muscle stiffness is linearly related to both active and passive muscle forces. Examples of studies that used measurement of muscle stiffness to estimate changes in muscle force are presented.* **Key Words:** stiffness, elasticity, shear modulus, supersonic shear imaging, shear wave elastography, force sharing, muscle coordination

INTRODUCTION

Because of muscle redundancy, even single-joint motor tasks can be produced theoretically by an infinite number of muscle force combinations. Understanding how the central nervous system manages force sharing between muscles will provide fundamental information for fields such as motor control, biomechanics, and robotics. To this end, accurate quantification of the force produced by individual muscles is necessary.

Several methodologies using electromyography (EMG) and/or musculoskeletal models (15) have been proposed to quantify individual muscle force. Although EMG can be used to quantify neural drive to muscles, and, thus, to study the neural control of muscle coordination during both isometric and dynamic contractions, many factors limit its utility to accurately predict muscle force. First, change in muscle length distorts the relationship between muscle activation and muscle force because of the well-known force-length relationship. Consequently, different muscle forces can be produced for the same activation levels if the muscle operates at different lengths. Second, EMG does not provide any information about passive force. Furthermore, the presence of neuromuscular fatigue alters the relationship between EMG amplitude and force (14). Even if musculoskeletal models have also been used to estimate individual muscle force, their validity cannot be established in the absence of experimental techniques to quantify muscle force (15). Consequently, estimation of individual muscle force remains one of the main challenges in biomechanics.

Within this article, we aim to demonstrate that the measurement of localized muscle stiffness through the application of shear wave elastography (SWE) has provided, and is likely to continue to provide, new insights in the estimation of muscle force, with important applications for both basic and clinical sciences. More precisely, we present a series of experiments that support the hypothesis that *muscle stiffness is linearly related to both active and passive muscle forces*. This work has provided the foundation for studies that use measurement of muscle stiffness (using elastography) to estimate changes in muscle force. For example, the ability to accurately quantify muscle stiffness *in vivo* has led to a deeper understanding of force-sharing strategies during nonfatiguing and fatiguing isometric contractions (5,6), motor adaptations during experimental pain (38), and muscle behavior during passive stretching (33). SWE is also beginning to be used to quantify changes in muscle stiffness (or muscle tension) associated with progression and treatment of

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musculoskeletal and neurological conditions (27). Beyond these applications of elastography, we contend that measurements of muscle stiffness are likely soon to be used to reliably estimate the force/torque (in N or Nm, respectively) produced by an individual muscle. Current limitations and perspectives related to this goal will be discussed.

ACCURATE MEASUREMENT OF MUSCLE STIFFNESS USING ELASTOGRAPHY

In vivo muscle biomechanical (*i.e.*, contractile and viscoelastic) properties have been classically inferred from inverse dynamics or measurements of joint torque performed using ergometers. However, these measures provide information about the combined behavior of several structures (*e.g.*, muscles, tendons, nerves, skin) acting around a given joint and cannot isolate the behavior of an individual muscle. Since the introduction of elastography in the 1990s, many techniques have been developed with the aim to assess localized muscle stiffness noninvasively. It is beyond the scope of this review to detail each of these techniques; however, comprehensive summaries can be found elsewhere (8,18,23,40). Among these techniques, qualitative elastography techniques (*e.g.* quasi-static methods, also called *strain elastography*, whereby displacement/strain associated with the application of a constant (and unknown) stress is estimated) have a limited application in muscle biomechanics. This is because they do not provide a precise quantification of muscle stiffness that is required to test the effect of an intervention and/or to make comparisons between muscles/individuals. In contrast, quantitative elastography techniques measure muscle elasticity by calculating the velocity of the shear waves that result from mechanical perturbations applied on the tissue. This propagation velocity is directly related to the shear modulus of the tissue, that is, the stiffer the tissue, the faster the shear wave propagation (Eq. 1).

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

where μ is the shear modulus of the tissue, ρ is the density of muscle (1000 kg m^{-3}), and V_s is the shear wave velocity.

The relevance of the shear modulus measurement for the study of muscle biomechanics requires some considerations. The Young's modulus (E) is the most relevant measure of stiffness of a given material. For isotropic locally homogeneous and quasi-incompressible biological tissues (*e.g.*, breast, liver), the shear modulus is directly linked to the Young's modulus:

$$E \approx 3\mu \quad (2)$$

However, because of its anisotropy (*i.e.*, the mechanical properties are not the same in all directions), this equation cannot be theoretically applied to skeletal muscles. Interestingly, using an *in vitro* muscle preparation (swine), Eby *et al.* (13) demonstrated that, when the ultrasound probe is parallel to muscle fibers, muscle shear modulus is strongly linearly related to the Young's modulus measured using traditional material testing. This demonstrates that, despite the anisotropy of skeletal muscle, the measurement of muscle shear modulus provides an accurate characterization of muscle stiffness.

Among SWE techniques, magnetic resonance elastography offers an excellent spatial resolution; however, the acquisition time is relatively long (from ≈35 s for one-dimensional measurements to several minutes for two-dimensional measurements (2)), which limits its use for muscle loading conditions (contraction or stretching). For example, long acquisition times preclude the assessment of contraction intensities that cannot be maintained for long periods and, if changes across time are being assessed (*e.g.*, passive stretching, ramping contractions), a much higher temporal resolution is needed. In contrast, using ultrasound SWE, measurement of shear modulus is almost instantaneous and therefore opens interesting perspectives for muscle biomechanics.

To our knowledge, the ultrasound SWE technique called Supersonic Shear wave Imaging ((SSI) Imagine, Aix en Provence, France) is the current *state of the art* in ultrasound elastography because it provides real-time, quantitative, and accurate imaging of tissue stiffness. Measurements are made with an ultrasound probe placed over the tissue under consideration (as for conventional ultrasound measurements). This technique uses an ultrafast imaging modality combined with a transient and remote mechanical vibration generated by radiation force induced by a focused ultrasonic beam (*i.e.*, "pushing beam") (for more details, see (3,18)). Each pushing beam generates a remote vibration in the target tissue that results in the propagation of a transient shear wave. Then, an ultrafast ultrasound imaging sequence is performed to acquire successive raw radio frequency data at a very high frame rate (up to 20 kHz). A one-dimensional cross correlation of successive radio frequency signals is used to calculate the shear wave velocity along the principal axis of the probe using a time-of-flight estimation. Two-dimensional maps of the shear elastic modulus (Fig. 1) are obtained in real time using equation 1. More precisely, the measurement of shear wave propagation velocity is performed in less than 15 ms, and the current version of the SSI scanner (Aixplorer V8; Supersonic Imagine, Aix-en-Provence, France) provides a measurement at one sample per second. Currently, this technique is limited to shear modulus measurement of 266 kPa (corresponding to a shear wave speed of 16.3 m s^{-1}), which corresponds to about 40% to 70% of maximal voluntary contraction torque (MVC) (depending on the muscle studied). However, recent improvements of the SSI scanner allow a higher shear modulus measurement, that is, higher than the modulus measured during a typical MVC (this is further discussed in the Perspectives section).

Very good to excellent accuracy of the SSI technique to quantify the shear modulus has been demonstrated in tissue-mimicking phantoms (24,39) with moderate stiffness (up to 100 kPa in (39)). In addition to this accuracy, very good reliability (*i.e.*, intrasession, intersession, and/or inter-rater) of the SSI technique to measure muscle shear modulus has been reported at rest (26) and during passive stretching (24,33) and contractions (5,7). However, it should be kept in mind that, as with all ultrasound measurements, the measure is operator dependent (mainly dependent on pressure applied through the transducer on the underlying tissues) and therefore practice is required by the operators to obtain high reliability. Taken together, these results suggest that SSI provides an accurate and reliable measurement of muscle shear modulus and thus provides a reliable characterization of muscle stiffness.

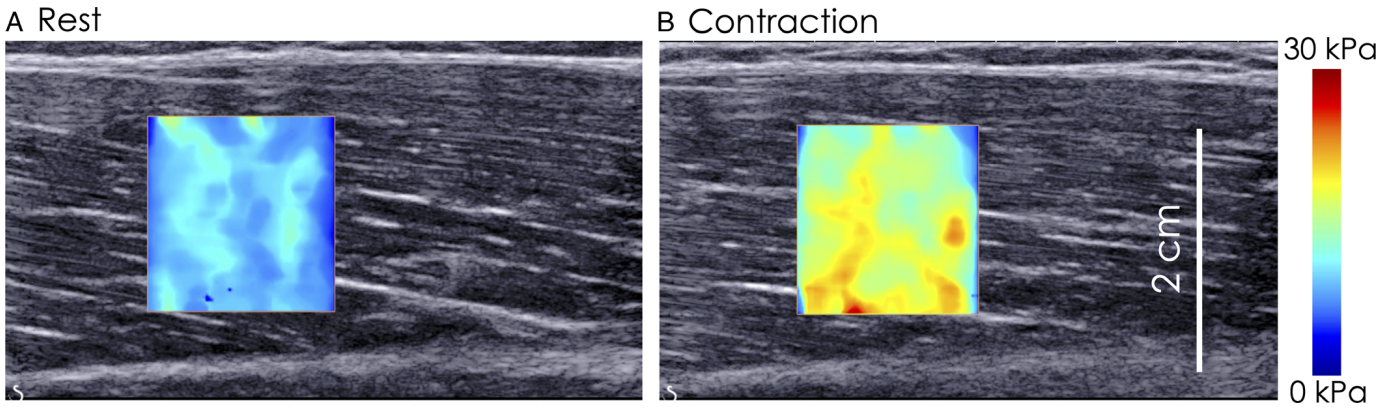

Figure 1. Representative example of the shear modulus maps obtained in vastus lateralis at rest (A) and during 5% of maximal voluntary isometric contraction (B). The map of shear elastic modulus is superposed onto a B-mode image, with the scale depicting gradation of shear modulus. To obtain a representative value, the shear modulus is classically averaged over the whole map.

To date, most of the studies on muscle contraction/stretching used SSI and, therefore, this technique is highly cited within this article. However, it is important to note that any SWE technique able to provide an accurate quantitative value of shear modulus at a relatively high temporal resolution could be used in the same way. This is likely the case of the combo-push ultrasound shear elastography (CUSE (37)) that is similar to SSI; however, its reliability for measuring muscle stiffness remains to be determined.

CAN MUSCLE SHEAR MODULUS BE USED TO ESTIMATE MUSCLE FORCE?

Theoretical Considerations and Hypothesis

Young's modulus is defined as the slope of the relationship between stress (force per unit area) and strain. Because the stress-strain relationship of biological tissues is *nonlinear*, Young's modulus varies as a function of stress (Fig. 2). However, until recently, the nature of the relationship between muscle Young's

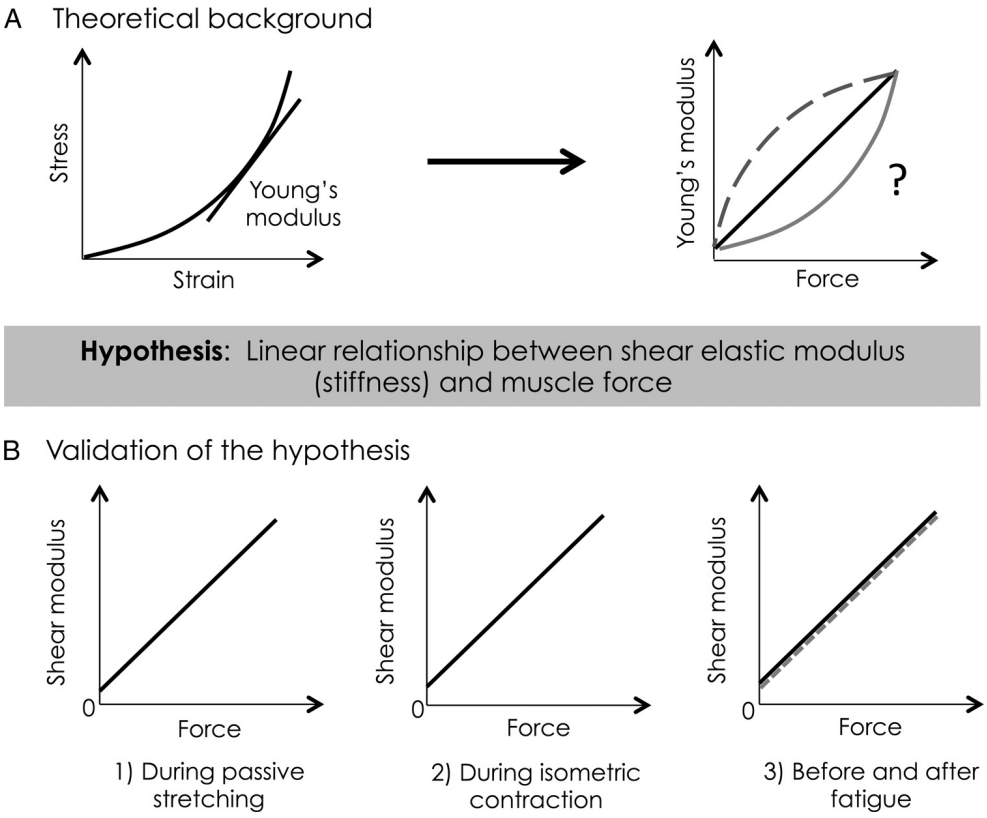

Figure 2. Synopsis. A. *Young's modulus* is defined as the slope of the relationship between stress (*i.e.,* force per unit area) and strain. Because a *nonlinear* relationship exists between muscle stress and muscle strain, the muscle Young's modulus varies as a function of stress. Based on previous works, we hypothesized that there is a linear relationship between muscle shear modulus (an index of Young's modulus, as further detailed in the article) and both active and passive muscle force. B. Using elastography, recent experimental works demonstrated that the relationship between muscle shear modulus and muscle force is linear during passive stretching and isometric contractions. Furthermore, neuromuscular fatigue does not impair this relationship.

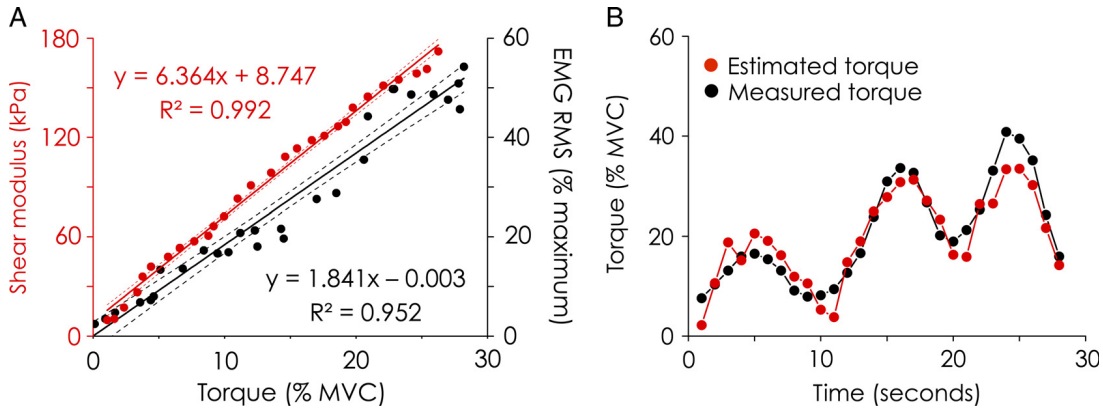

Figure 3. Typical example of the relationship between electromyography amplitude or muscle shear modulus and torque (A) and torque estimation using muscle shear modulus (B). A. Linear regressions (and their 95% of confidence interval in *dashed lines*) between little finger abduction torque and normalized EMG RMS (*black dots/lines*) or shear modulus (*gray dots/lines*) of the *abductor digiti minimi* muscle are depicted. B. Shear modulus and torque (*black dots/lines*) measurements were obtained during a 30-s contraction where participants were asked to freely vary the torque produced. Torque estimation (*gray dots/lines*) was performed using the linear regression obtained from the ramp contraction depicted in A. MVC, maximal voluntary contraction torque. [Adapted from (7). Copyright © 2011 the authors. Used with permission.]

modulus and muscle stress remained unclear. Experimental and simulation data from isolated frog muscles suggested a linear relationship between muscle stiffness and the number of attached cross bridges (*i.e.*, force (17)). Consistent with these observations, human experiments that used magnetic resonance elastography (12) reported a linear relationship between muscle shear modulus and joint torque. However, this relationship between the shear modulus of an individual muscle and joint torque was established within a redundant system (*i.e.*, elbow flexion). Therefore, it could not provide conclusive evidence of a linear relationship between muscle shear modulus and individual muscle force. This is because of possible torque-dependent changes in force-sharing strategies, that is, the relationship between individual muscle force and joint torque may be nonlinear (6). In addition, because of a limitation in the temporal resolution of magnetic resonance elastography, the aforementioned study was limited to a few contraction intensities (12). Taking advantage of recent developments of ultrasound SWE, recent works have tested the hypothesis that *muscle shear modulus is linearly related to both passive and active muscle forces* (Fig. 2).

The Relationship Between Muscle Shear Modulus and Passive Muscle Force Is Linear

Muscle shear modulus has been measured during passive stretching in humans (dorsiflexion (33) and plantarflexion (25)). Maïsetti *et al.* (33) showed that the relationship between muscle shear modulus and muscle length (determined from passive stretching performed at 2 degrees per second) is linearly related to the passive force predicted by musculoskeletalmodeling (Hoang's model (19)), that is, R^2 values ranging from 0.964 to 0.992. This suggested that muscle shear modulus measured using elastography could be used to estimate the passive tension. This result now has been confirmed *in vitro* on chicken muscles (24), where a strong linear relationship (R^2 values ranging from 0.971 to 0.999) between shear modulus (measured using SSI) and passive muscle force was reported.

The Relationship Between Muscle Shear Modulus and Active Muscle Force Is Linear

Bouillard *et al.* (7) investigated the relationship between muscle shear modulus and force during isometric contractions of two human finger muscles with different architectures. For this study, two tasks were used: i) isometric index finger abduction (at 0 to 5 degrees of abduction), which mainly involves the *first dorsal interosseous* (bipennate muscle); and ii) isometric little finger abduction (at 0 to 5 degrees of abduction), which mainly involves the *abductor digiti minimi* (fusiform muscle). Assuming a negligible change in moment arm during the isometric contractions, the torque measured during these tasks was assumed to be directly related to force produced by the investigated muscle. During contractions with ramped torque (up to 30% and 60% of MVC for *abductor digiti minimi* and *first dorsal interosseous*, respectively), muscle shear modulus measured using SSI was strongly linearly related to muscle force (R^2 values ranged from 0.951 to 0.997 (7)). Note that, although the relationship between EMG amplitude and torque was also linear, R^2 values were lower (Fig. 3). Furthermore, participants then performed isometric contractions where they were asked to freely vary the torque produced. Using the previously determined linear relationship between muscle shear modulus and torque, Bouillard *et al.* (7) demonstrated the ability to estimate the torque accurately (RMS_{error} < 6% of MVC) from muscle shear modulus measured (Fig. 3), regardless of the pennation of muscle fibers (*i.e.*, bipennate vs fusiform muscle). Further to this, Sasaki *et al.* (36) reported a linear relationship between force and shear modulus of *tibialis anterior* during maximal isometric dorsiflexion performed at different ankle joint angles (from −15 degrees of dorsiflexion to +25 degrees of plantarflexion, 0 degree being the neutral position). This work provides solid evidence that an individual

muscle force-length relationship can be estimated by measuring muscle shear modulus.

Fatigue Does Not Alter the Relationship Between Muscle Shear Modulus and Force

As neuromuscular fatigue dramatically alters the relationship between EMG amplitude and force, there is a paucity of data that describe changes in muscle force during fatiguing contractions. In contrast to EMG measurements that are influenced by several electrophysiological parameters (*e.g.*, motor unit action potential propagation velocity), the shear modulus is a mechanical property. As such, it is less likely to be influenced by neuromuscular fatigue. To test this hypothesis, Bouillard *et al.* (4) asked participants to perform linear isometric torque ramps (little finger abduction) before and after a fatiguing protocol. They demonstrated that the relationship between muscle shear modulus and force is not affected by fatigue. Then, by using the linear regression of the relationship obtained before fatigue, they estimated with good accuracy the change in little finger abduction torque during a submaximal isomeric fatiguing task performed until task failure (Fig. 4). This experiment provides evidence that fatigue does not influence the ability to estimate the changes in muscle force using the shear modulus measurement.

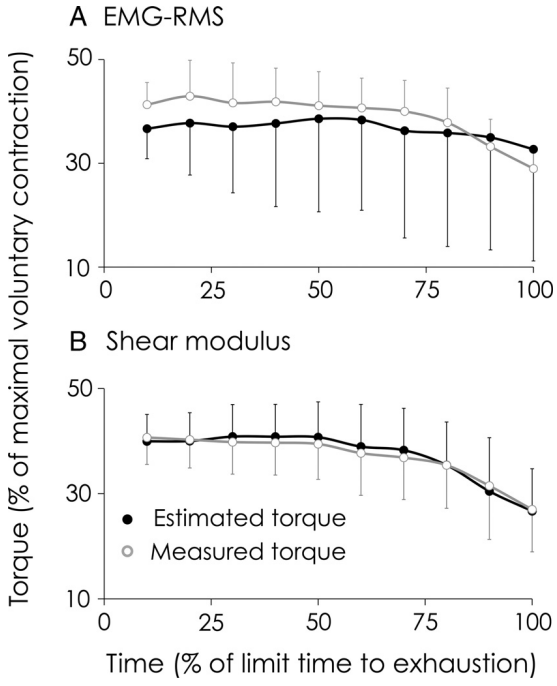

Figure 4. Measured and estimated torque from electromyography (A) and shear modulus (B) throughout an isometric fatiguing contraction. Participants performed an isomeric fatiguing task (little finger abduction) until task failure. Both surface electromyography (EMG) and shear modulus were measured. Using the linear regression of the relationship between EMG-RMS or shear modulus and torque obtained before fatigue, little finger abduction torque was estimated. [Adapted from (4). Copyright © 2014 The American Physiological Society. Used with permission.]

Conclusions and Current Limitations

Taken together, the results presented in the previous section support the hypothesis that *muscle stiffness is linearly related to both active and passive muscle forces*. Although measurement of muscle shear modulus alone cannot be used to estimate muscle force (in N) or torque (in Nm) (discussed in Perspectives section), it can be used to estimate relative changes in muscle force. Concurrent measurements of shear modulus of multiple agonist muscles will provide information about force-sharing strategies and thus provide valuable insight into how the neural system chooses to generate force in different muscles that cross the same joint. It is important to note that, in the absence of normalization of the shear modulus to that recorded during MVC (which until very recently has not been possible because of the saturation limit), a change in force-sharing strategies could only be determined when different muscles demonstrate an opposite or a different profile of change in the shear modulus. In contrast, if the changes in shear modulus of two muscles were in the same direction (*i.e.*, both increased or both decreased), a change in force sharing between these muscles could not be determined, even if different amplitudes of absolute change were noted. This is because the slope of the relationship between the modulus and force may differ between muscles, so the same absolute change in shear modulus could relate to very different changes in force between muscles.

EXAMPLES OF APPLICATION FOR BASIC AND CLINICAL SCIENCE

Force-Sharing Strategies During Nonfatiguing Isometric Contractions

To investigate force sharing during nonfatiguing contractions, Bouillard *et al.* (6) measured the shear modulus of elbow flexor (*brachialis*, *biceps brachii* (both heads), and *brachioradialis*) and extensor muscles (*triceps brachii*) during isometric elbow flexion with ramped torque (from rest to 40% of MVC). Each muscle exhibited a unique relationship between shear modulus and elbow flexion torque, which provided evidence of torque-dependent changes in force-sharing strategy. More precisely, the characteristic shape of the change in shear modulus of both heads of *biceps brachii* with increasing torque demonstrated little change initially but with increasingly large increments in modulus at higher torques (see Fig. 2 in 6). In contrast, the shear modulus of the *brachioradialis* and *brachialis* increased rapidly at low torques and then plateaued for *brachialis*. These data provide an alternative explanation for the nonlinear relationship reported between surface EMG and torque in large muscles such as *biceps brachii* (30) and contrasts the long-held hypothesis of altered motor unit recruitment strategies (30). Interestingly, the shear modulus of the antagonist muscle (*triceps brachii*) did not simultaneously increase, and indeed remained very low, throughout the ramp contraction. It provides evidence that the frequent reports of a systematic increase in surface EMG amplitude of antagonist muscles (*i.e.*, increased coactivation) at high force levels may relate more to cross talk than increased drive to the antagonist muscles. Overall, these observations suggest that elastography might provide a unique opportunity to reconsider our current understanding of muscle co-contraction.

Force-Sharing Strategies During Fatiguing Isometric Contractions

A change in force sharing between agonist muscles during a prolonged task is thought to limit the occurrence of neuromuscular fatigue and enhance the ability to sustain a contraction. A complete understanding of this adaptation, therefore, is crucial for sports scientists who aim to optimize human performance. Evidence of altered force-sharing strategies mainly comes from surface EMG studies (*e.g.*, alternate activation of the quadriceps muscles, albeit limited to compensations between the *rectus femoris* muscle and the *vastii*). However, because fatigue alters the relationship between EMG amplitude and force (14), it is difficult to dissociate the effects of neuromuscular fatigue from putative compensations of force between muscles. Subsequently, these results cannot be interpreted directly as changes in muscle force and thus in force-sharing strategies.

As the relationship between muscle shear modulus and force is not altered by neuromuscular fatigue (4), elastography can be used to assess relative change in force of individual muscles during isometric fatiguing contractions. In this way, some evidence for altered force sharing among the heads of the quadriceps muscle has been reported during a force-matched isometric knee extension task (4). Interestingly, a change in force sharing was not observed in all participants and, when it was observed, participants did not exhibit the same strategies, that is, compensations did not occur systematically between the same muscles. To investigate the origin of this variability in force sharing, Bouillard *et al.* (5) used electrical stimulation to fatigue the *vastus lateralis* muscle selectively. They observed a systematic decrease in the force produced by this muscle during a subsequent submaximal isometric force-matched task. However, the compensation strategy (*i.e.*, the muscle(s) that produced more force to compensate for the reduction in force of *vastus lateralis*) varied between individuals. This data further confirmed the absence of a consistent redistribution of force sharing among the heads of the quadriceps muscles between individuals during force-matched fatiguing contractions. We contend that it is particularly important to understand the origin and the consequence of this individual variation in force sharing, as specific force-sharing strategies have been suggested to contribute to the development of some musculoskeletal conditions. For instance, an imbalance of generation of force between *vastus medialis* and *lateralis* is speculated to be a main contributing factor to the development of anterior knee pain.

Do Motor Adaptations During Pain Aim to Alter Stress Within the Painful Tissue?

The effects of pain on movement control have been studied widely during acute experimental pain and in clinical populations (for review, see (20)). This work underpins the conclusion that the control of movement is altered during pain. It is hypothesized that the primary aim of altered motor control is to modify stress (*i.e.*, tension or force per unit area) on painful tissue to protect from further pain and/or injury (20). Although this hypothesis is logical and generally assumed to be correct, until recently, it has never been tested directly. Taking advantage of localized shear modulus measurement performed using elastography, recent experiments have demonstrated no systematic change in stress within a muscle (*vastus lateralis* (38), *vastus medialis* (21)) that is made painful by injection of hypertonic saline during force-matched isometric knee extension. At first glance, this questions the fundamental assumption that the adaptations during pain are associated with altering stress in the painful region. However, decreased stress within painful tissue has been reported during tasks with more degrees of freedom (isometric bilateral leg squat (21)), providing evidence that, when an obvious solution is available to decrease stress on painful tissue, this option is selected. Therefore, the lack of adaptation observed during force-matched tasks with fewer degrees of freedom might be explained by the limited potential to redistribute stress (*i.e.*, alter force sharing) or a high control cost associated with such compensation.

By taking advantage of elastography, this series of experiments provides evidence that, although reduced stress within the painful tissue likely is to be the goal motor adaptation during pain, it is not always an achievable goal. Taken together, these results show that the development of elastography to estimate change in muscle force (or stress) provides a unique opportunity to test long-lasting hypotheses on motor adaptations to pain. Ultimately, knowledge on change in tissue stress during pain will provide a framework for understanding the factors that determine the nature and extent of motor adaptation to pain.

Muscle Behavior During Passive Stretching

The slack length of the muscle-tendon unit is defined as the length beyond which the muscle-tendon unit begins to develop passive force. Although sensitivity analyses have shown that the slack length is the most important parameter for musculoskeletal modeling, until recently, the experimental methods used to estimate the slack length were limited. Traditionally, slack length was determined as the muscle-tendon length at which the passive joint torque (measured using an ergometer) first exceeds zero. However, passive torque is influenced by all structures crossing the joint (*e.g.*, all the agonist/antagonist muscles, skin, and tendons). Therefore, the first increase in passive joint torque cannot be definitively associated with the true slack length of an individual muscle-tendon unit. Based on the Hoang's model (19), the slack length of the *gastrocnemius* muscle-tendon unit can be estimated. However, this model can be used only for this specific muscle, and it remains to be validated. Taking advantage of the strong linear relationship between muscle stiffness and passive muscle force (discussed in detail above, *e.g.*, 24), the slack length of individual muscles (*e.g.*, *gastrocnemius medialis* (33); long and short head of *biceps brachii* (28)) has been recently determined using SSI. Using this new method, the slack length of *gastrocnemius medialis* was determined to be more plantarflexed (~20 degrees of plantarflexion; knee extended) than when using the Hoang's model (~29 degrees of plantarflexion; knee extended) (33). Using elastography to determine the slack length of individual muscle-tendon units provides a unique opportunity to improve the accuracy of musculoskeletal models and our understanding of passive muscle-tendon biomechanics.

Overall, the shear modulus measurement provides a unique opportunity to measure localized muscle stiffness and thus to estimate the passive tension of individual muscles when being stretched. It can provide a deeper understanding of individual muscle mechanical behavior than more global measurements

(such as maximal range of motion or joint torque during passive stretching). For example, Le Sant *et al.* (31) measured the shear modulus of each hamstring muscle during passive knee extension at different hip angles. They found that the long head of the *biceps femoris* is stiffer than the *semimembranosus*, and the *semimembranosus* is stiffer than the *semitendinosus*. This is in accordance with the prevalence of strain injuries that occur in the *biceps femoris*. This example shows that elastography may be useful to determine the stiffer muscle such that stretching interventions may target it using an optimal joint configuration.

Clinical Applications

Estimation of individual muscle force and, more generally, quantification of stiffness of a localized area of muscle provide the opportunity for new insights into changes in muscle mechanical properties with musculoskeletal and neurological disease progression and rehabilitation. Although elastography is used widely for diagnosis of breast cancer, liver fibrosis, and thyroid nodules, the musculoskeletal applications are just beginning to be realized. The main advantages of the ultrasound SWE techniques (mainly SSI) for clinical assessment and rehabilitation purposes are that they provides noninvasive, quantitative, reliable, and fast measurements. In addition, localized areas of several muscles (rather than global stiffness of a given joint), including deep muscles, can be assessed independently.

Duchenne muscular dystrophy (DMD) is associated with increased muscle stiffness, leading to a high degree of joint contractures. Lacourpaille *et al.* (27) have quantified this increased muscle stiffness recently in a cross-sectional study that compared people with DMD and healthy controls. As the disease severity evolves mainly in a proximal-distal manner, not all muscles are affected similarly. This work demonstrated that SSI could be used to provide a localized and sensitive measure of early changes in stiffness of targeted muscles. Such information may in the future be used to direct physical interventions and, thus, slow joint deformities and prolong autonomy. Assessment of muscle stiffness might also be helpful to quantify the efficacy of new therapies. Although longitudinal studies with large sample sizes are needed to determine the sensitivity of elastography to detect changes in muscle stiffness throughout the course of the disease, it opens interesting perspectives for many neurological conditions associated with increased muscle stiffness (*e.g.*, DMD, cerebral palsy, Parkinson's disease).

Elastography may also be useful to quantify changes in muscle mechanical properties associated with musculoskeletal conditions. For example, using an animal (rabbit) model of muscle crush injury, Lv *et al.* (32) demonstrated that it is possible to detect an increase in muscle stiffness subsequent to the injury using elastography. Similarly, Lacourpaille *et al.* (29) reported increased muscle stiffness associated with more subtle muscle damage in humans, that is, exercise-induced muscle damage. This ability to accurately quantify the increase in passive stiffness associated with muscle injury and to isolate this objectively to the muscle that is damaged (and not its synergists) might help the clinician to target interventions to the most affected muscle or muscle region.

Finally, quantification of muscle stiffness also provides crucial insight into the mechanisms that may underlie treatments and rehabilitation programs and ultimately to assess their efficacy. Interventions that aim to alter muscle stiffness are common in physiotherapy/physical therapy practice (*e.g.*, massage, taping, dry needling, stretching). Because of the lack of techniques to assess stiffness of a localized area of muscle tissue, their mechanical effect has not been verified. Therefore, controversies exist regarding their mechanical and thus clinical efficacy. Taking advantage of SSI, Hug *et al.* (22) demonstrated that deloading tape applied to the skin directly over the *rectus femoris* muscle reduced tension in the underlying muscle region for the muscle conditions where the muscle was loaded (during moderate and high muscle stretch and contraction). These data provided a biomechanical explanation for the effect of deloading tape observed in clinical practice (reduce pain, restore function, and aid recovery). Massage is another controversial technique that may be used to reduce muscle stiffness. Eriksson Crommert *et al.* (16) provided the first direct evidence that 7 min of massage effectively decreases muscle stiffness. However, it also was demonstrated that this decrease in muscle stiffness did not persist after a short period of rest (3 min). It is important to note that the aforementioned studies have been performed on asymptomatic participants and do not confirm that the techniques are effective clinically. However, they do provide insight into the mechanisms through which these techniques may provide benefit in the clinical population.

PERPECTIVES

Toward a More Direct Estimation of Individual Muscle Force

As indicated in the previous section, recent improvements of the SSI technique allow a higher shear modulus measurement, that is, higher than the modulus measured during a typical MVC. In this way, Ates *et al.* (1) demonstrated that the relationship between muscle shear modulus and muscle force is linear over the entire range of contraction intensity during isometric little finger abduction with ramped torque. This ability to normalize muscle shear modulus to that recorded during MVC opens interesting perspectives for between-muscle comparisons and for more direct estimation of individual muscle forces.

Both physiological cross-sectional area (PCSA, *i.e.*, area of a muscle perpendicular to its fibers) and moment arms can be either estimated using anthropometric reference data or directly measured using imaging techniques (magnetic resonance elastography and/or ultrasonography). Assuming that all agonist muscles are at a similar relative muscle length (in relation to their optimal length), PCSA and moment arms may be used to estimate the relative contribution of each muscle ($\%T_{mvc}$) to maximal joint torque during MVC (T_{mvc}). Associated with the measurement of the shear modulus normalized to that measured at MVC ($\%\mu_{max}$), muscle torque (T_m) produced during an isometric submaximal contraction might be estimated for each individual muscle as follows:

$$T_m = \%\mu_{max} \times \%T_{mvc} \times T_{mvc} \quad (3)$$

It is important to note that this method is based on the hypothesis of a similar specific tension between muscles (and, thus, of a strong linear relationship between PCSA and

maximal force). However, this remains debatable. Specific tension has been shown to be similar among 25 different guinea pig hindlimb muscles with similar typology but was significantly lower in the soleus, which has greater slow-twitch muscle fibers (34). Consequently, the ability to estimate an accurate T_m likely will be impaired in the case whereby the agonist muscles exhibit very different muscle typologies. However, the comparison of T_m between two muscles of similar typology will remain valid. Alternatively, in case of a simple comparison of muscles with similar typology, the product of normalized muscle shear modulus and PCSA might be used as an index of muscle force. This method is simpler because it does not require the estimation of PCSA of all agonist muscles.

An alternative approach would be to estimate the specific tension (F_{spe}) and, thus, muscle torque in Nm of each muscle using a calibration task (*i.e.*, isometric linear ramp) where the joint torque would be measured using a dynamometer or estimated using inverse dynamics. This task should be repeated such that measurements of shear modulus are performed for each muscle. The torque produced by each muscle "i" can be written as:

$$Tm^i = \%\mu_{max}{}^i \times F_{spe}{}^i \times PCSA^i \times MA^i \qquad (4)$$

Assuming that the measured torque is the sum of the torque produced by all agonist muscles and a minimal contribution of antagonist muscles (6), F_{spe} may be estimated for each muscle using optimization. After this estimation of F_{spe}, individual muscle force might be easily estimated during isometric tasks using shear modulus measurement. Compared with EMG-driven models (10), this approach has two advantages: i) it does not require the use of muscle models (*e.g.*, Hill-type model) and ii) only one parameter per muscle has to be estimated in the optimization process.

Future Developments in Elastography and Perspectives for Muscle Biomechanics

To date, the ultrasound SWE techniques provide maps of shear modulus at a relatively low sampling rate (*e.g.*, up to one sample per second for the commercialized version of the SSI scanner, *i.e.*, Version 8), which limit to the study of isometric contractions and slow passive stretching tasks (<10 degrees per second). Because the measure of shear wave propagation velocity is performed in less than 15 ms with the SSI technique, this limitation can be overcome by improving hardware and software capabilities. In this way, a beta version of the SSI scanner with a temporal resolution up to four samples per second has been used recently for measurements during ramped isometric muscle contraction (1). In addition, a recent study measured the shear modulus of the heart through the cardiac cycle at more than 30 samples per second (11). This development is likely to provide the opportunity to measure muscle shear modulus during dynamic contractions (*e.g.*, walking) in the near future.

Beyond the measurement of muscle stiffness, measurements of tendon stiffness may provide important insights into musculoskeletal biomechanics. However, the application of SWE technique for tendons requires some consideration. Because tendons are both very stiff and thin, shear wavelengths are greater than the tendon thickness, leading to guided wave propagation (9). As a consequence, measurements are biased if no correction is applied (and no correction has been applied within the current commercialized SSI scanners, *i.e.*, Version 8). For instance, two tendons with the same stiffness but with different thickness will exhibit different shear modulus values. This problem can be resolved by using shear wave spectroscopy, which involves additional dispersion analysis (*i.e.*, spectral analysis) of the shear wave propagation. Combined with a simple viscoelastic model, this technique has been shown to provide accurate tendon elasticity and viscosity values (9). This technique, therefore, is recommended for future elastography studies on the tendon. Alternatively, a method that takes into account tendon thickness to correct measurements performed using conventional SWE should be developed in the future.

Currently, ultrasound SWE measures the shear wave velocity in two dimensions; however, the wave propagation occurs in three dimensions. New developments in ultrasound devices enable the measurements to be performed in three dimensions in real time (35). This pilot study demonstrated that it is possible to perform ultrafast ultrasound acquisition and SWE measurements in three dimensions using a two-dimensional matrix array probe. This technique will provide a unique opportunity to assess spatial variability of muscle stiffness. In addition to information on muscle stiffness, three-dimensional elastography will provide crucial information on muscle anisotropy (*i.e.*, changes in muscle stiffness across directions) and shear viscosity (*i.e.*, attenuation of shear waves). As both anisotropy and shear viscosity are thought to be related to the structural organization of the muscle, three-dimensional elastography is promising for the evaluation of muscle neuromuscular conditions where muscle structure is affected.

CONCLUSIONS

A series of experiments support the hypothesis that *muscle stiffness is linearly related to both active and passive muscle forces*. This work has provided the foundation for studies that use measurement of muscle stiffness to estimate changes in muscle force during isometric actions and passive stretching, therefore providing new insights into force-sharing strategies. Elastography is also beginning to be used to quantify changes in muscle stiffness (or muscle tension) associated with progression and treatment of musculoskeletal and neurological conditions. Beyond these applications of elastography, we contend that measurements of muscle stiffness is likely to soon be used to reliably estimate the force/torque (in N or Nm, respectively) produced by an individual muscle.

Disclosure

Michael Tanter is cofounder and shareholder of the company Supersonic Imagine, which commercializes the elastography technique "Supersonic Shear wave Elastography." Jean-Luc Gennisson is a scientific consultant for the company Supersonic Imagine. This did not influence any aspect of this work.

References

1. Ates F, Hug F, Bouillard K, *et al.* Muscle shear elastic modulus is linearly related to muscle torque over the entire range of isometric contraction intensity. Proceedings of the ISEK, Rome, Italy; 2014.

2. Bensamoun SF, Glaser KJ, Ringleb SI, Chen Q, Ehman RL, An KN. Rapid magnetic resonance elastography of muscle using one-dimensional projection. *J. Magn. Reson. Imaging.* 2008; 27(5):1083–8.
3. Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.* 2004; 51(4):396–409.
4. Bouillard K, Hug F, Guével A, Nordez A. Shear elastic modulus can be used to estimate an index of individual muscle force during a submaximal isometric fatiguing contraction. *J. Appl. Physiol. (1985).* 2012; 113(9): 1353–61.
5. Bouillard K, Jubeau M, Nordez A, Hug F. Effect of vastus lateralis fatigue on load sharing between quadriceps femoris muscles during isometric knee extensions. *J. Neurophysiol.* 2014; 111(4):768–76.
6. Bouillard K, Nordez A, Hodges PW, Cornu C, Hug F. Evidence of changes in load sharing during isometric elbow flexion with ramped torque. *J. Biomech.* 2012; 45(8):1424–9.
7. Bouillard K, Nordez A, Hug F. Estimation of individual muscle force using elastography. *PLoS One.* 2011; 6(12):e29261.
8. Brandenburg JE, Eby SF, Song P, *et al.* Ultrasound elastography: the new frontier in direct measurement of muscle stiffness. *Arch. Phys. Med. Rehabil.* 2014; 95(11):2207–19.
9. Brum J, Bernal M, Gennisson JL, Tanter M. *In vivo* evaluation of the elastic anisotropy of the human Achilles tendon using shear wave dispersion analysis. *Phys. Med. Biol.* 2014; 59(3):505–23.
10. Buchanan TS, Lloyd DG, Manal K, Besier TF. Neuromusculoskeletal modeling: estimation of muscle forces and joint moments and movements from measurements of neural command. *J. Appl. Biomech.* 2004; 20(4): 367–95.
11. Couade M, Pernot M, Messas E, *et al. In vivo* quantitative mapping of myocardial stiffening and transmural anisotropy during the cardiac cycle. *IEEE Trans. Med. Imaging.* 2011; 30(2):295–305.
12. Dresner MA, Rose GH, Rossman PJ, Muthupillai R, Manduca A, Ehman RL. Magnetic resonance elastography of skeletal muscle. *J. Magn. Reson. Imaging.* 2001; 13(2):269–76.
13. Eby SF, Song P, Chen S, Chen Q, Greenleaf JF, An KN. Validation of shear wave elastography in skeletal muscle. *J. Biomech.* 2013; 46 (14): 2381–7.
14. Edwards RG, Lippold OC. The relation between force and integrated electrical activity in fatigued muscle. *J. Physiol.* 1956; 132(3):677–81.
15. Erdemir A, McLean S, Herzog W, van den Bogert AJ. Model-based estimation of muscle forces exerted during movements. *Clin. Biomech. (Bristol, Avon).* 2007; 22(2):131–54.
16. Eriksson Crommert M, Lacourpaille L, Heales L, Tucker K, Hug F. Massage induces an immediate, albeit short-term, reduction in muscle stiffness. *Scand. J. Med. Sci. Sports.* 2014; (In press).
17. Ford LE, Huxley AF, Simmons RM. The relation between stiffness and filament overlap in stimulated frog muscle fibres. *J. Physiol.* 1981; 311:219–49.
18. Gennisson JL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: principles and techniques. *Diagn. Interv. Imaging.* 2013; 94(5):487–95.
19. Hoang PD, Gorman RB, Todd G, Gandevia SC, Herbert RD. A new method for measuring passive length-tension properties of human gastrocnemius muscle *in vivo*. *J. Biomech.* 2005; 38(6):1333–41.
20. Hodges PW, Tucker K. Moving differently in pain: a new theory to explain the adaptation to pain. *Pain.* 2011; 152(3 Suppl):S90–S8.
21. Hug F, Hodges PW, Tucker K. Task dependency of motor adaptations to an acute noxious stimulation. *J. Neurophysiol.* 2014; 111(11):2298–306.
22. Hug F, Ouellette A, Vicenzino B, Hodges PW, Tucker K. Deloading tape reduces muscle stress at rest and during contraction. *Med. Sci. Sports Exerc.* 2014; 46(12):2317–25.
23. Klauser AS, Miyamoto H, Bellmann-Weiler R, Feuchtner GM, Wick MC, Jaschke WR. Sonoelastography: musculoskeletal applications. *Radiology.* 2014; 272(3):622–33.
24. Koo TK, Guo J, Cohen JH, Parker JP. Relationship between shear elastic modulus and passive muscle force: an *ex-vivo* study. *J. Biomech.* 2013; 46(12):2053–9.
25. Koo TK, Guo JY, Cohen JH, Parker KJ. Quantifying the passive stretching response of human tibialis anterior muscle using shear wave elastography. *Clin. Biomech. (Bristol, Avon).* 2014; 29(1):33–9.
26. Lacourpaille L, Hug F, Bouillard K, Hogrel JY, Nordez A. Supersonic shear imaging provides a reliable measurement of resting muscle shear elastic modulus. *Physiol. Measure.* 2012; 33(3):N19–28.
27. Lacourpaille L, Hug F, Guével A, *et al.* Non-invasive assessment of muscle stiffness in patients with Duchenne muscular dystrophy. *Muscle Nerve.* 2014; (2):51–6.
28. Lacourpaille L, Hug F, Nordez A. Influence of passive muscle tension on electromechanical delay in humans. *PLoS One.* 2013; 8(1):e53159.
29. Lacourpaille L, Nordez A, Hug F, Couturier A, Dibie C, Guilhem G. Time-course effect of exercise-induced muscle damage on localized muscle mechanical properties assessed using elastography. *Acta Physiol.* 2014; 211(1):135–46.
30. Lawrence JH, De Luca CJ. Myoelectric signal versus force relationship in different human muscles. *J. Appl. Physiol. Respir. Environ. Exerc. Physiol.* 1983; 54(6):1653–9.
31. Le Sant G, Ates F, Brasseur JL, Nordez A. Individual behaviors of hamstrings during passive knee extensions performed in various hip positions. *JFK2015, Paris, France*; 2015.
32. Lv F, Tang J, Luo Y, *et al.* Muscle crush injury of extremity: quantitative elastography with supersonic shear imaging. *Ultrasound Med. Biol.* 2012; 38(5):795–802.
33. Maïsetti O, Hug F, Bouillard K, Nordez A. Characterization of passive elastic properties of the human medial gastrocnemius muscle belly using supersonic shear imaging. *J. Biomech.* 2012; 45(6):978–84.
34. Powell PL, Roy RR, Kanim P, Bello MA, Edgerton VR. Predictability of skeletal muscle tension from architectural determinations in guinea pig hindlimbs. *J. Appl. Physiol. Respir. Environ. Exerc. Physiol.* 1984; 57(6): 1715–21.
35. Provost J, Papadacci C, Arango JE, *et al.* 3D ultrafast ultrasound imaging *in vivo*. *Phys. Med. Biol.* 2014; 59(19):L1–13.
36. Sasaki K, Toyama S, Ishii N. Length-force characteristics of *in vivo* human muscle reflected by supersonic shear imaging. *J. Appl. Physiol. (1985).* 2014; 117(2):153–62.
37. Song P, Urban MW, Manduca A, Zhao H, Greenleaf JF, Chen S. Comb-push ultrasound shear elastography (CUSE) with various ultrasound push beams. *IEEE Trans. Med. Imaging.* 2013; 32(8):1435–47.
38. Tucker K, Hodges PW, Van den Hoorn W, Nordez A, Hug F. Does stress within a muscle change in response to an acute noxious stimulus? *PLoS One.* 2014; 9(3):e91899.
39. Yoshitake Y, Takai Y, Kanehisa H, Shinohara M. Muscle shear modulus measured with ultrasound shear-wave elastography across a wide range of contraction intensity. *Muscle Nerve.* 2013; 50(1):103–13.
40. Zaleska-Dorobisz U, Kaczorowski K, Pawlus A, Puchalska A, Inglot M. Ultrasound elastography — review of techniques and its clinical applications. *Adv. Clin. Exp. Med.* 2014; 23(4):645–55.