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Muscle shear elastic modulus is linearly related to muscle torque over the entire range of isometric contraction intensity

Filiz Ateş^{a,*}, François Hug^{a,b}, Killian Bouillard^a, Marc Jubeau^a, Thomas Frappart^c, Mathieu Couade^c, Jeremy Bercoff^c, Antoine Nordez^a

^a EA 4334 "Motricité, Interactions, Performance", UFR STAPS, University of Nantes, Nantes, France

^b The University of Queensland, NHMRC Centre of Clinical Research Excellence in Spinal Pain, Injury and Health, School of Health and Rehabilitation Sciences, Brisbane, Australia

^c Supersonic Imagine, Aix en Provence, France

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ABSTRACT

Muscle shear elastic modulus is linearly related to muscle torque during low-level contractions (<60% of Maximal Voluntary Contraction, MVC). This measurement can therefore be used to estimate changes in individual muscle force. However, it is not known if this relationship remains valid for higher intensities. The aim of this study was to determine: (i) the relationship between muscle shear elastic modulus and muscle torque over the entire range of isometric contraction and (ii) the influence of the size of the region of interest (ROI) used to average the shear modulus value. Ten healthy males performed two incremental isometric little finger abductions. The joint torque produced by Abductor Digiti Minimi was considered as an index of muscle torque and elastic modulus. A high coefficient of determination (R^2) (range: 0.86–0.98) indicated that the relationship between elastic modulus and torque can be accurately modeled by a linear regression over the entire range (0% to 100% of MVC). The changes in shear elastic modulus as a function of torque were highly repeatable. Lower R^2 values (0.89 ± 0.13 for 1/16 of ROI) and significantly increased absolute errors were observed when the shear elastic modulus was averaged over smaller ROI, half, 1/4 and 1/16 of the full ROI (mean size: $1.18 \pm 0.24 \text{ cm}^2$). It suggests that the ROI should be as large as possible for accurate measurement of muscle shear modulus.

1. Introduction

An accurate estimation of individual muscle force would provide crucial information for fields such as motor control, biomechanics, robotics and rehabilitation sciences. Biomechanical models to estimate muscle force have been proposed but in the absence of experimental methods to measure individual muscle force, these models cannot be validated. Consequently it remains one main challenge in biomechanics (Erdemir et al., 2007). The muscle shear elastic modulus (i.e. muscle stiffness) measured using the Supersonic Shear Imaging technique (SSI) is linearly related to muscle force during low-level isometric contraction (Bouillard et al., 2011, 2012) and passive stretching (Koo et al., 2014; Maisetti et al., 2012). In other words, more the muscle contracts or lengthens and more it becomes stiffer. Consequently, the

muscle shear elastic modulus can be easily used to estimate changes in muscle force (Bouillard et al., 2014; Hug et al., 2014).

Due to both hardware and software limitations, the saturation limit of the previous version of the SSI scanner (266 kPa) made impossible to measure accurately the elastic modulus of very stiff tissues such as muscles during high-intensity contractions. Consequently, previous studies were limited to low-intensity contractions, i.e. up to 50–60% of the maximal voluntary contraction (MVC) (Bouillard et al., 2011; Yoshitake et al., 2013). It is therefore unknown if muscle shear elastic modulus is linearly related to muscle force over the full range of contraction intensity (0–100% of MVC). In addition, the influence of the size of the region of interest (ROI) (i.e., the region of the muscle considered to average the shear elastic modulus), on the relationship between modulus and force has not been determined. It is unclear whether the muscle shear elastic modulus determined over relatively small ROIs accurately represents the modulus of the whole muscle.

Saturation of shear elastic modulus measurements is the main limitation of the software package previously developed. The new version used in the current study has been improved for the

* Corresponding author at: EA 4334 "Motricité, Interactions, Performance", Faculty of Sports Sciences, University of Nantes, 25 bis, Bld Guy Mollet, BP 7226, 44322 Nantes Cedex 3, France. Tel.: +33 02 51 83 72 08; fax: +33 02 51 83 70 45.

E-mail address: filiz.ates@boun.edu.tr (F. Ateş).

measurement of fast shear waves without a saturation limit for muscular tissues.

The aim of the present study was to determine the relationship between muscle shear elastic modulus and joint torque over the full range of contraction intensity using the new version of the SSI scanner. For that purpose, the Abductor Digiti Minimi (ADM), which is the only muscle producing little finger abduction torque (Lebreton, 2010) was investigated. Therefore, the measurement of joint torque using a simple force sensor provides a good estimate of changes in the force produced by this muscle (Bouillard et al., 2011). The influence of the size of the ROI on this relationship was also investigated.

2. Methods

2.1. Participants

Ten healthy males participated in this experiment (age: 27.8 ± 2.9 years, height: 178.4 ± 5.9 cm, weight: 71.8 ± 8.6 kg). They were informed of the purpose and the methods used before providing written consent. The local ethical committee approved the study and all procedures conformed to the Declaration of Helsinki.

2.2. Ergometer

A homemade ergometer was used to measure the abduction torque produced by the little finger. The ergometer used in the present study was previously described in details (Fig. 1, Bouillard et al., 2011). The participants were seated with right elbow flexed at 130° with the pronated forearm supported by a platform. All fingers were extended with the palm facing down. The wrist and fingers #2 to #4 of the right hand were immobilized to prevent any motion (see Fig. 1, Bouillard et al., 2011). The lateral side of the little finger was in contact with a rigid interface, with the proximal interphalangeal joint aligned with the force sensor (SML-50, Interface, Arizona, USA). Data were sampled at 10 kHz (ADInstruments, Powerlab 16/35, NZ).

2.3. Elastography

An Aixplorer ultrasonic scanner (Supersonic Imagine, Aix-en-Provence, France), coupled with a linear transducer array (4–15 MHz, SuperLinear 15–4; Vermon, Tours, France), was used in Shear Wave Elastography (SWE) mode (musculoskeletal preset). This elastographic technique consisted of a radiation force induced by a focused ultrasonic beam (Bercoff et al., 2004). Each ultrasonic beam generated a transient and remote mechanical vibration resulting in the propagation of a transient shear wave. Then, an ultrafast echographic imaging sequence was performed to acquire successive raw radio-frequency data at a very high frame rate. A one-dimensional cross correlation of successive radio-frequency signals was used to determine the shear wave velocity (V_s) along the principle axis of the probe using a time-of-flight estimation. Then, assuming a linear (Bercoff et al., 2004; Catheline et al., 2004; Gennisson et al., 2003) and elastic (Deffieux et al., 2009; Gennisson et al., 2003; Nordez et al., 2008) behavior, the shear elastic modulus (μ) was calculated using V_s as follows:

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

where ρ is the density of muscle (1000 kg/m^3). Maps of shear elastic modulus (Fig. 2) were obtained with a spatial resolution of $1 \times 1 \text{ mm}$. The ultrasound transducer was aligned with the fiber direction. All the measurements were performed by the same experimenter. During data acquisition, minimal pressure was applied with the probe on the skin.

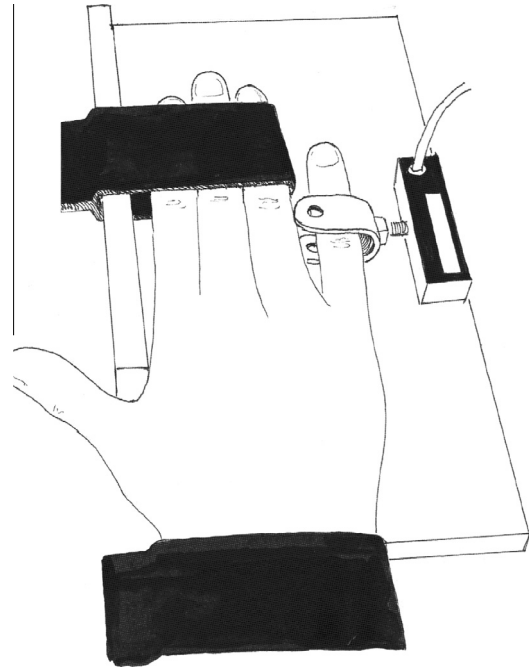


Fig. 1. The right pronated forearm was supported on a platform and all fingers were extended with the palm facing down. The hand and fingers 2–4 were immobilized with velcro straps to prevent any movement and compensation during contractions. The little finger was in contact with a rigid interface, with the proximal interphalangeal joint aligned with the force sensor. Adapted with permission from Bouillard et al. (2011).

The new software package used in the present study combines three new features compared to the previous version: (1) adjustment of the sequence and in particular increase of the ultrafast frame rate to allow shear wave velocity of stiff tissues to be measured; (2) ability to increase the SWE frame rate from 1 to 4 Hz during a limited time (4 s); and (3) increase of the size of the 2-D map of shear elastic modulus (up to 5 cm^2).

2.4. Protocol

First, preconditioning was performed to avoid interference in the measurements of early changes in mechanical properties of musculo-tendinous structures (Maganaris et al., 2002). To this end, participants performed three maximal isometric little finger abductions lasting 4 s separated by 2 min of recovery. Then, they performed additional 3 maximal contractions (lasting 4 s and separated by 2 min of recovery) during which the maximal force (MVC) was measured. Finally, each participant performed 2 tasks.

Task 1. Isometric ramp contraction from 0% to 70% of MVC in 16 s. This task was performed to determine the effects of region of interest (ROI, i.e., the region of the muscle considered to average the shear elastic modulus) size on the shear elastic modulus (at 1 Hz of data acquisition).

Task 2. Isometric ramp contraction from 0% to 100% of MVC in 4 s. This task was performed to test the relationship between the shear elastic modulus and torque over the full range of contraction intensities with a data acquisition rate of 4 Hz.

For each task, ramps were repeated 2 times to assess the repeatability of the measurements. 16 data points were obtained for each ramp contraction in both tasks. Recovery time between each ramp was 2 min. To control the ramp contractions, a real-time visual feedback was displayed on a monitor.

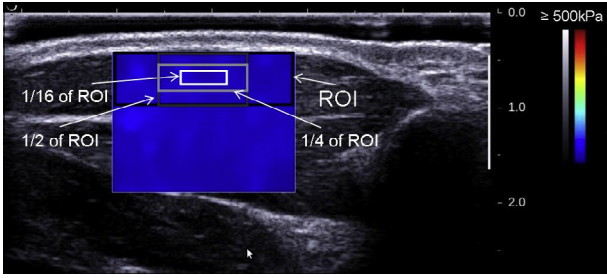


Fig. 2. Typical example of shear elastic modulus measurement from ADM. Black outlined box shows ROI (the greatest muscular region avoiding aponeurosis). Dark grey, light grey, and white outlined boxes show 1/2, 1/4, and 1/16 of ROI (the smaller areas tested to examine the effects of ROI size on the relationship between shear elastic modulus and torque).

2.5. Data analysis

Videos of shear wave elastography recordings were exported in “mp4” format and sequenced into images (“jpeg” compression) for task 1. Data processing was performed using MATLAB scripts (The Mathworks, Natick, USA). A rectangular area as large as possible with exclusion of aponeurosis was chosen as the ROI from the shear elasticity map (Fig. 2). The colored map was converted into shear elastic modulus values. An average value of the shear elastic modulus over the ROI was calculated for each image. For task 2, the average shear elastic modulus was obtained from the software of the ultrasound device (Q-box function). These modulus values were synchronized with the torque using the trigger signal sent at the time of each shear elastic modulus measurement during data acquisition. Force values (in N) were normalized to MVC for each participant. Assuming a constant moment arm during the

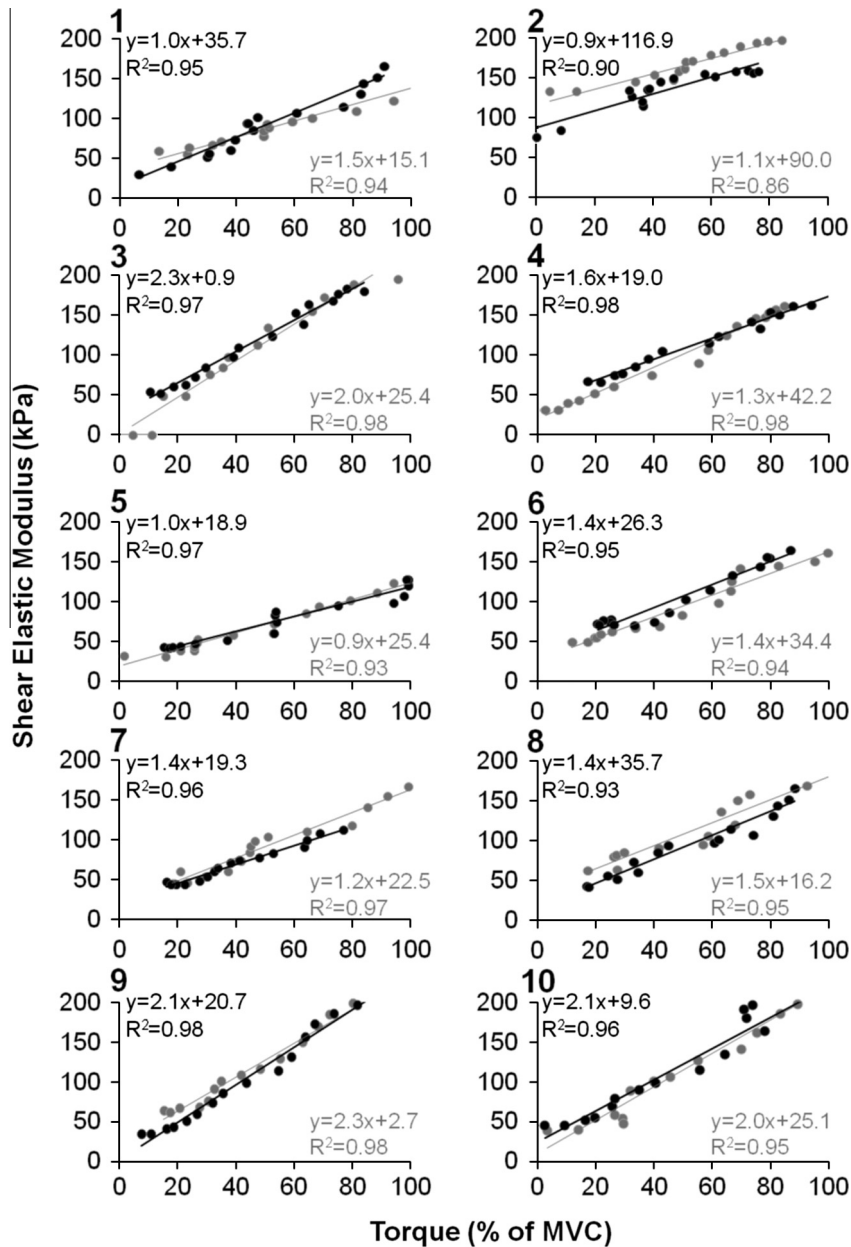


Fig. 3. Shear elastic modulus-force relationships obtained from the ten participants during two ramp contractions from 0% to 100% of MVC (task 2). Ramp 1 and 2 are depicted in black and grey, respectively.

isometric contractions, these relative force values corresponded to normalized torque values (in% of MVC; Bouillard et al., 2011, 2012). The shear elastic modulus (in kPa) and normalized torque values were fitted to a linear equation and the coefficient of determination (R^2) was calculated for all contractions as a measure of the goodness of the fit. For both tasks 1 and 2, the shear elastic modulus values corresponding to 20%, 40%, 60%, 80%, and 100% of MVC were calculated using the coefficients of the equation of these linear regressions.

To determine the effect of ROI size on shear elastic modulus measurements, data collected during task 1 were analyzed for full ($1.18 \pm 0.24 \text{ cm}^2$), half (the mid half of the area horizontally), 1/4 (mid half of the area both horizontally and vertically), and 1/16 (mid half of the 1/4 of ROI area both horizontally and vertically) of ROI (Fig. 2). The R^2 value of the linear regression between torque and shear elastic modulus was calculated for each ROI size. Absolute error between the shear elastic modulus of full ROI (modulus_{ROI}) and that of half (modulus_{half of ROI}), 1/4 (modulus_{1/4 of ROI}), and 1/16 (modulus_{1/16 of ROI}) of full ROI were calculated at 20%, 40%, 60%, 80%, and 100% of MVC. The ratio of absolute error to the modulus of full ROI (%Error) was calculated as

$$\%Error = \left(\frac{ABS(\text{modulus}_{ROI} - \text{modulus}_{\text{half,1/2,1/4,1/16 of ROI}})}{\text{modulus}_{ROI}} \right) * 100 \quad (2)$$

2.6. Statistical analysis

Coefficients of determination (R^2) were calculated using Excel (Microsoft, Redmond, WA, USA) to assess the quality of linear fits for the shear elastic modulus – torque relationships. For each of these torque values, the repeatability between the 2 contractions performed within each task was assessed using the standard error of measurement (SEM), coefficient of variation (CV), and intraclass correlation coefficient (ICC) (Hopkins, 2000).

A repeated-measures ANOVA (within subject factors: muscle contraction intensity and ROI size) was performed to determine the effects of ROI size on absolute error (The Mathworks, Natick, USA). If significant effects were found, post hoc tests were performed using the Bonferroni procedure for multiple pair-wise comparisons. P values < 0.05 were considered significant.

3. Results

Fig. 3 depicts the shear elastic modulus – torque relationships obtained during tasks 2 for each participant. The R^2 values averaged across the 10 participants of the linear regression calculated from each of the two contractions during task 1 and 2 were high (averaged value between the 2 repetitions: 0.96 ± 0.02 and 0.95 ± 0.03

Table 1
Within-session repeatability of shear elastic modulus measurement between the two ramps for each task.

| Force (% MVC) | 20% | 40% | 60% | 80% | 100% |
|---------------|------|------|------|------|------|
| <i>Task 1</i> | | | | | |
| CV (%) | 16.3 | 11.6 | 11.0 | 11.1 | 11.2 |
| SEM (kPa) | 4.1 | 3.9 | 5.4 | 7.7 | 10.3 |
| ICC | 0.97 | 0.98 | 0.98 | 0.98 | 0.98 |
| <i>Task 2</i> | | | | | |
| CV (%) | 18.6 | 9.5 | 7.1 | 6.9 | 7.3 |
| SEM (kPa) | 5.1 | 4.9 | 5.6 | 6.8 | 8.3 |
| ICC | 0.73 | 0.86 | 0.90 | 0.90 | 0.89 |

Shear elastic modulus measured (Task 1) from 0% to 70% of MVC and (task 2) from 0% to 100% of MVC. MVC, Maximal Voluntary Contraction; CV, coefficient of variation; SEM, Standard Error of Measurement; ICC, Intraclass correlation coefficient.

from 0% to 70% – task 1 – and 0% to 100% of MVC – task 2, respectively). This indicates that the relationship between the joint torque and shear elastic modulus can be accurately modeled by a linear regression, over the entire range of contraction intensity (0% to 100% of MVC). The low SEM values and high ICC values shown in Table 1 indicate the high reproducibility of the shear elastic measurement, regardless the contraction intensity. Coefficient of variations between the 2 repetitions were lower (for task 2) or slightly higher (for task 1) than 10% for almost all estimated forces (Table 1).

The coefficients of determination of the relationship between muscle elastic modulus and torque were 0.96 ± 0.02 , 0.96 ± 0.03 , 0.94 ± 0.07 , and 0.89 ± 0.13 when the elastic modulus was calculated from full, half, 1/4, and 1/16 of full ROI, respectively. The %error between the shear elastic modulus of full ROI and that of half, 1/4, and 1/16 of full ROI increased with decreasing ROI size (Table 2). A significant main effect of both muscle contraction ($P = 0.000$) and ROI size ($P = 0.009$) was found. However, the muscle contraction x ROI size interaction was not significant ($P = 0.6$). Post-hoc test on size located the difference only for the absolute error between full and 1/16 of the full ROI ($P = 0.02$).

4. Discussion

The present study shows that the relationship between ADM shear elastic modulus and little finger abduction torque is linear from 0% to 100% of MVC. The repeatability reported in the present study is similar to that previously reported (i.e., standard errors were 4.5 kPa, 4.7 kPa and 8.3 kPa at 15%, 30% and 50% of MVC in Bouillard et al., 2012). These suggest that relative change in ADM muscle force can be estimated from changes in muscle shear elastic modulus within the full range of contraction intensity. This offers promising perspectives. For instance, the normalization of shear elastic modulus to that recorded at MVC is important to be able to compare stiffness between muscles and participants. In addition, if associated with other architectural parameters (physiological cross-sectional area and moment arms), muscle shear elastic modulus might be used to provide a more direct estimation of muscle force. Although the within-day reliability of the relationship between muscle shear elastic modulus and torque was good, the between-day reliability remains to be determined.

The updated version of SSI technique used in the present study does not have any saturation limit. However, it is expected that the measurements is not reliable above a given shear wave velocity (and thus above a given elastic modulus value). This limit has not yet been determined since phantoms stiff enough does not exist. Nevertheless, this limit is likely achieved for much stiffer tissue than the muscle in contraction (e.g., tendon). In this way, the present study indicates that this version is able to measure repeatable muscle elastic modulus values up to MVC.

Another challenging issue in estimation of muscle force using muscle shear modulus is the size of the ROI. It is classically assumed that the shear elastic modulus is representative of the whole muscle (Nordez and Hug, 2010), but this has never been demonstrated. In the present study the average shear elastic modulus was calculated from the greatest region possible (depending

Table 2
The ratio of absolute error (%Error) between the shear elastic modulus measured over the full ROI and that measured over smaller ROI.

| Force (% MVC) | %Error | | |
|---------------|--------|-----|------|
| | 1/2 | 1/4 | 1/16 |
| 20 | 2.0 | 3.8 | 6.6 |
| 40 | 4.2 | 5.4 | 6.1 |
| 60 | 5.8 | 7.4 | 8.9 |
| 80 | 6.7 | 8.6 | 10.5 |
| 100 | 7.3 | 9.3 | 11.5 |

on muscle size and shape). If the ROI size decreased to 1/16 of the full ROI, not only the R^2 value was lower but also the absolute error (compared to full ROI) increased significantly.

In the passive condition, Kot et al. (2012) tested the effects of ROI size on the resting shear modulus values for the rectus femoris muscle. They reported significant differences only for the maximal modulus value over the 2-D map but not for the averaged value. Previous electromyography studies reported spatial variability in activation level of the biceps brachii (Holtermann et al., 2005) and the upper trapezius (Farina et al., 2008) muscles. Furthermore, using magnetic resonance imaging, Finni et al. (2003) determined the spatial variability of intramuscular strain distributions within soleus muscle during isometric contractions. It was shown on dorsiflexor muscles that this spatial strain variability increases with the level of contraction (Damon et al., 2008). This spatial variability could be related to a spatial variability of muscle stiffness, that requires further consideration. It is not possible to assume that our findings on ADM directly translate to other muscles however, considering the heterogeneity of various human muscles, it is reasonable to consider that the error is high for larger muscles if very small ROI are analyzed. Our results indicate that only very small ROIs affect significantly the quantification of shear elastic modulus (i.e. 1/16 of the full ROI that corresponds to about 2% of the transverse area of muscle). Based on these results, it should be recommended to (i) calculate the shear elastic modulus over the greatest possible ROI and (ii) average the modulus over multiple ROIs in order to get value as representative as possible of the whole muscle if the ROI is too small compared to the muscle investigated.

In conclusion, our study showed that the relationship between shear elastic modulus and torque is linear over the full range of contraction intensity (0 to 100% of MVC). Therefore, regardless of the contraction intensity, muscle force index can be estimated from shear elastic modulus measured. However, to improve the accuracy of the measurements, the present findings suggest to use measure shear elastic modulus over a ROI as large as possible.

Conflict of interest

Thomas Frappart, Mathieu Couade, and Jeremy Bercoff are employed by the company Supersonic Imagine (Aix-en-Provence, France), which commercializes the Aixplorer device used in this experiment. This did not influence any aspect of this work.

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Filiz Ates received her B.Sc. degree from the Electronics Engineering Department of Istanbul University, and M.Sc. degree from the Institute of Biomedical Engineering of Bogazici University in Istanbul. Her M.Sc. studies were on light-tissue interactions. In 2013, she received her Ph.D. degree from the same institution in the field of biomechanics and with the focus on skeletal muscle mechanics. She is working as a post doctoral researcher in the laboratory “Motricite, Interactions, Performance”, Faculty of Sports Sciences, University of Nantes, France. Her active research areas include soft tissue mechanics, muscle force estimation with ultrasound elastography, mechanical interactions of skeletal

muscle, assessment of the effects and implications of orthopaedic surgery as well as other treatment methods, and management of rehabilitation techniques in neuro-muscular diseases.



François Hug (PhD) is a Principal Research Fellow in the NHMRC Centre of Clinical Research Excellence in Spinal Pain, Injury and Health (CCRE SPINE), at the University of Queensland (Australia). He has a background in Human Movement Sciences (PhD in 2003 at the University of Aix-Marseille II, France). After a post-doctoral period at the University of Paris VI, he was employed as research fellow at the French National Institute of Sports (France). He continued his research at the University of Nantes (France) from 2006 to 2012. Particular research interests lie within the areas of muscle coordination and muscle biomechanics. Taking advantage of elastography to estimate individual muscle force, his recent works

aim to understand motor adaptations during experimental pain and muscle fatigue. François has published over 85 peer-reviewed articles in the fields of muscle biomechanics and neurophysiology. He serves on the editorial board of *Journal of Electromyography and Kinesiology* and as an academic editor for *PLoS ONE*.



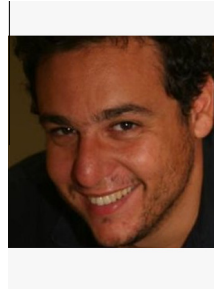
Killian Bouillard received his MSc. in Sport Sciences from the University of Nantes, France, in 2010. Then he received his Ph.D. in muscle biomechanics at the university of Nantes, in 2014. His primary research interest focuses on the estimation of individual muscle force using and innovative elastographic technique named Supersonic Shear Imaging. Through this technique his research investigates the muscle fatigue and the load sharing phenomenon.



Mathieu Couade received the Diplôme d'ingénieur in physics from the Ecole Supérieure de Physique et de Chimie Industrielles de Paris (ESPCI), and an M.S. degree and a Ph.D. degree in acoustics from Paris VII University in 2007 and 2011, respectively. He is currently in charge of the R&D of shear wave elastography for the company Supersonic Imagine in Aix en Provence, France. His research interests are in the medical applications of ultrasound. His main current research activities are focused on shear wave elastography and cardiovascular imaging.



Marc Jubeau received his Ph.D in Exercise Physiology from the Faculty of Sports Sciences of the University of Burgundy, Dijon, France in 2006. He is currently an Assistant Professor at the Faculty of Sports Sciences (UFR STAPS), University of Nantes, France. His major research interests include the study of neuromuscular function (e.g. fatigue, muscle damage).



Jeremy Bercoff. Co-founder of Supersonic Imagine and R&D Director of Ultrasound, Jeremy Bercoff graduated from the School of Physics and Chemistry of Paris (ESPCI). He obtained in 2004 a PhD in Physics at the University of Paris VII for his work on ultrafast ultrasound imaging. After his PhD, Jeremy Bercoff achieved the technological transfer of his thesis work at SuperSonic Imagine introducing to the medical community a new generation of ultrafast ultrasound scanners and a new tissue elasticity imaging mode, ShearWave Elastography. His area of expertise includes medical ultrasound imaging, tissue rheology, and blood flow analysis. He is the author of over 20 scientific publications and holds 10 patents in the

field of medical imaging.



Thomas Flappart graduated from School of Industrial Physics and Chemistry (Ecole Supérieure de Physique et de Chimie Industrielles) in 2010. After several internships in Research and development departments of Institut Langevin and Phillips Research North America, he worked as an Engineering contractor in Samsung. Later on, he specialized on Physics of Acoustics and Fluids and obtained a Masters degree from Université Paris 7 Denis Diderot. Currently he is working as an Ultrasound Engineer and an expert on Supersonic Imaging.



Antoine Nordez is an associate professor at the University of Nantes. He has a background in mechanical engineering (Msc in 2003 at the Ecole Centrale de Nantes) and biomechanics (PhD in 2006 at the University of Nantes, France). After a post-doctoral period at the Biomechanics Lab (2006-2007, Arts et Metiers ParisTech), he continued his research at the University of Nantes (France) from 2008. Particular research interests lie within the areas of muscle biomechanics. Antoine has published over 52 peer-reviewed articles in this field.