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Mechanical interaction between neighboring muscles in human upper limb: Evidence for epimuscular myofascial force transmission in humans

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Abstract

To confirm the existence of epimuscular myofascial force transmission in humans, this study examined if manipulating joint angle to stretch the muscle can alter the shear modulus of a resting adjacent muscle, and whether there are regional differences in this response. The biceps brachii (BB: manipulated muscle) and the brachialis (BRA: resting adjacent muscle) were deemed suitable for this study because they are neighboring, yet have independent tendons that insert onto different bones. In order to manipulate the muscle length of BB only, the forearm was passively set at supination, neutral, and pronation positions. For thirteen healthy young adult men, the shear modulus of BB and BRA was measured with shear-wave elastography at proximal and distal muscle regions for each forearm position and with the elbow joint angle at either 100° or 160°. At both muscle regions and both elbow positions, BB shear modulus increased as the forearm was rotated from a supinated to pronated position. Conversely, BRA shear modulus decreased as function of forearm position. The effect of forearm position on shear modulus was most pronounced in the distal muscle region when the elbow was at 160°. The observed alteration of shear modulus of the resting adjacent muscle indicates that epimuscular myofascial force transmission is present in the human upper limb. Consistent with this

assertion, we found that the effect of muscle length on shear modulus in both muscles was region-dependent. Our results also suggest that epimuscular myofascial force transmission may be facilitated at stretched muscle lengths.

1. Introduction

The force produced by individual muscle fibers is transmitted not only serially, but also laterally to other muscles by intermuscular mechanical interactions. Such interaction is the result of collagen linkages between epimysia of adjacent muscles, neurovascular tracts, or compartmental boundaries. Force transmission of this nature is referred to as “epimuscular myofascial force transmission (EMFT)” (see for a review (Huijing, 1999; Yucesoy, 2010). EMFT has until now been mainly demonstrated in invasive animal models. For example, direct evidence of EMFT has been illustrated by studying the changes in proximo-distal tendon forces of the adjacent muscle when the synergist (Maas et al., 2001; Yucesoy et al., 2003) or antagonist (Huijing et al., 2007; Meijer et al., 2007; Rijkelijkhuizen et al., 2007; Yucesoy et al., 2010b) muscle are either passively (artificially) lengthened or actively contracting in response to electrical stimulation. Differences in force between proximal and distal tendons in the adjacent muscle during passive lengthening of the neighboring distal tendon (see for a review (Maas and Sandercock, 2010)) suggests that the degree of EMFT may be partly influenced by heterogeneity of pre-strained epimuscular connections or muscle tissue strain (Yucesoy et al. 2005).

In living human models, EMFT has also been investigated and demonstrated by measuring muscle force (Kaya et al., 2018; Yucesoy et al., 2010a), but the force measurements were conducted under surgical operations and, therefore, the data have been reported only by limited research group. As a noninvasive approach, many studies have developed imaging methodologies (ultrasonography or MRI) and attempted to demonstrate EMFT when a limb is passively rotated to stretch a muscle that crosses the joint (Bojsen-Moller et al., 2010; Finni et al., 2017; Tian et al., 2012; Yaman et al., 2013). In studies that have implemented ultrasound imaging, EMFT was studied by quantifying the deformation of fascicles in the adjacent muscle (Bojsen-Moller et al., 2010; Finni et al., 2017; Tian et al., 2012). A limitation pointed out in these studies was that the deformation of the adjacent muscle-tendon complex cannot be completely attributable to EMFT because the targeted muscles anatomically share a common tendon. In addition, measurements of muscle deformation determined from ultrasound imaging are susceptible to errors associated with the imaging plane and, therefore, may lead to incorrect estimations of EMFT. Among the studies using MRI imaging, Yucesoy and colleagues (Karakuzu et al., 2017; Pamuk et al., 2016; Yaman et al., 2013) combined diffusion tensor imaging analyses and demonstrated strain heterogeneity along the fascicles of the medial gastrocnemius muscle when, for example, the knee was passively extended to stretch the proximal end of the medial gastrocnemius muscle. Although this finding is indicative of EMFT with heterogeneity, proximo-distal force differences confirmed in animal models have not been tested using this technique. Accordingly, to further confirm the occurrence of EMFT in living human muscles, it would be more appropriate to study proximo-distal force differences in neighboring muscles that do not share a tendon, and to examine if there are proximo-distal force differences by means of an alternative methodology.

Ultrasound shear wave elastography can quantify tissue stiffness by using an ultrafast imaging modality combined with a transient and remote mechanical vibration generated by a radiation force induced by a focused ultrasonic beam (Bercoff et al., 2004; Gennisson et al., 2013). Ultrasound shear-wave elastography enables a simple and highly reproducible noninvasive measurement of shear modulus (stiffness) for an individual muscle (Hirata et al., 2017; Hug et al., 2015; Yoshitake et al., 2014). A series of studies have revealed that there is a strong, linear relationship between muscle shear modulus measured by shear-wave elastography and both active and passive muscle force (see for a review (Hug et al., 2015)). On this basis, if the intermuscular mechanical interactions that have been linked to EMFT are present in humans, the shear modulus of the resting adjacent muscle should be altered when a muscle is passively stretched by extension of the joint.

In addition, if there is a different trend between proximal and distal tendon forces of the adjacent muscle, as shown in animal models, the degree of change in shear modulus of the resting adjacent muscle when the neighboring muscle is passively stretched will differ between proximal and distal muscle regions in humans.

The purpose of this study was to examine if the shear modulus of a resting muscle is altered when joint angle is manipulated to passively stretch a neighboring muscle in the distal direction and if the effect of passive muscle stretch on shear modulus shows regional differences. The findings of the present study indicate the presence of epimuscular myofascial force transmission between upper extremity muscles in humans.

2. Methods

2.1. Subjects

Thirteen healthy men (aged 21.6 ± 2.7 years, 173.2 ± 6.4 cm in height, 67.0 ± 7.7 kg in body mass; mean ± SD) voluntarily participated in the study. All participants gave informed consent according to the procedures approved by the Ethics committee of the National Institute of Fitness and Sports in Kanoya.

2.2. Procedures

The experimental setup is shown in Fig. 1A. In this study, the biceps brachii longus (BB) was selected as the muscle to be passively lengthened by manipulation of forearm position. The brachialis (BRA) was selected as the adjacent muscle that, in the absence of EMFT, would be predicted to be unaffected by BB muscle length. Indeed, these are neighboring muscles with distinct tendons that are connected to different bones such that changing the forearm position stretches BB without stretching the resting BRA. The right forearm was set at supinated (shorter BB muscle length), neutral, and pronated (longer BB muscle length) positions. Subjects were seated upright in a chair (attached backrest) with the right upper arm abducted to an angle of 90º, the forearm in a horizontal position, and the elbow joint flexed to either 160º or 100º (full elbow extension: 180º). The shoulder angle between the upper arm and back was also fixed at 180º with Velcro straps throughout the measurements. The right hand was fixed to the dynamometer’s attachment with Velcro straps (Fig. 1A). Special care was taken to keep the subjects in a relaxed condition throughout the measurements, as to avoid unwanted muscle activity. Muscle inactivity was confirmed by monitoring electromyographic (EMG) activity during measurements (see below).

2.3. Ultrasound shear-wave elastography

Shear modulus of BB (long head of the biceps brachii) and BRA during rest was measured with an Aixplorer ultrasound scanner (Ver.8.5; Supersonic Image, Aix-en-Provence, France) at each forearm position (Fig. 1). Shear modulus was calculated from the shear-wave propagation velocity in the direction of the longitudinal axis of a probe (4-15 MHz, SL15-4, linear-array, 50-mm wide, Supersonic Imagine, Aix-en-Provence, France) and displayed on the computer monitor as a color map. To examine the regional differences within a muscle, the location of the probe was set at distal and proximal segments for each muscle. We defined the regions to place the probe as follows; 1) aligned with the shortening direction of the muscle to measure shear modulus in the fiber direction, 2) not mainly overlying the tendon or aponeurosis, 3) causing minimal loss of the color map for accurate calculation of shear modulus, and 4) having maximal separation of proximal and distal regions. Images for the probe position are shown in Fig. 1B. In this study, the measureable area for muscle shear modulus in BRA, particularly in the proximal region, was limited because of the desired conditions outlined above. In addition, the relative positions of the origin and insertion of the BRA to the upper arm differed among individuals. Therefore, we have not reported a specific value that represents the place of measurement relative to the upper arm length in the current study.

Prior to the experiments, we performed preliminary measurements of muscle shear modulus from BB and BRA under the current experimental procedures and confirmed the repeatability of the measurements by performing additional measurements and calculating intraclass correlation coefficients (BB, $ICC_{(1:1)}$ = 0.992; BRA, $ICC_{(1:1)}$ = 0.958; number of data points = 42). The probe placement and ROI were consistent across trials. Care was taken not to deform the muscle with the probe during measurements. Shear modulus of the muscles was measured at each forearm position in a random order for each elbow joint angle. The order of elbow joint angles was also randomized.

2.4. Electromyography

To confirm the absence of background muscle activity during measurements, we monitored EMGs of BB and BRA throughout. The locations of the electrodes on the targeted muscle belly were carefully determined using an ultrasound echograph (B-mode, Aixplorer ultrasound scanner; Supersonic Imagine, France) for each joint angle. After lightly abrading the skin surface with sand particles and cleaning the skin surface with alcohol, EMG electrodes (3 mm diameter, 6 mm inter-electrode distance, FWS-SWMG1, 4Assist Inc., Japan) were placed on the skin along the fascicle direction for each muscle and connected to an amplifier (×1,000) with a bandwidth of 5 Hz to 500 Hz (FWS-8ABX, 4Assist Inc., Japan). Note that the electrodes for EMG, as well as the probe for shear-wave elastography, were positioned in the same orientation as the fascicles as much as possible to observe the same muscle fibers between these measurements. For this reason, the area where the electrodes were able to be placed was limited, particularly for BRA. Additionally, as the involvement of cross talk from neighboring muscles should be avoided, we employed small electrodes with a relatively small inter-electrode distance in the current study. We made preliminary measurements of EMG from BRA during isometric elbow flexion with a gradually increasing force exertion from rest under the current experimental procedures. As a consequence, we confirmed the electro-mechanical delay, indicating that small muscle activation in BRA could be monitored during the experiments even if unwanted muscle activations which affect the shear modulus were occurred.

EMG signals were collected at a sampling rate of 2 kHz by a 16-bit analog-to-digital converter (Power-Lab/16sp, ADInstruments, Sydney, Australia). After the measurements of shear modulus, all subjects performed isometric elbow flexion at the 100º elbow position, and isometric forearm supination at the neutral forearm position with maximal effort (MVC task) twice to detect maximal amplitudes of EMG for subsequent normalization.

2.5. Data and statistical analysis

The spatial average of shear modulus in the selected circular areas, which were at least 9.0 mm in diameter, was calculated using the software (Q-BoxTM) in the ultrasound system. Shear modulus values of three images were averaged for each condition. To make sure if the degree of change in shear modulus during forearm supination/pronation in both muscles was region-dependent, we calculated the relative changes in muscle shear modulus of BRA and BB for both regions from supination to pronation and at each elbow joint angle.

In the MVC tasks, the root mean square amplitude value of EMG was calculated over a 0.5-s window for each trial and the maximal value, EMGmax, was determined for each muscle. To calculate the muscle activation level during the measurements of shear modulus, the root mean square amplitude of EMG (AEMG) for each muscle was calculated over a 4-s window. The AEMG values were normalized using the corresponding values obtained during the MVC tasks (% EMGmax).

For comparisons of muscle shear modulus as a function of forearm position, elbow position, and muscle region, a three-way ANOVA (two elbow joint angles × three forearm positions × two regions) was implemented for each muscle. When appropriate, post-hoc comparisons were performed with the Tukey HSD test. Statistical significance was set at $P < 0.05$. All data were analyzed using STATISTICA software (version 10; Statistica, Oklahoma, USA). Normality tests (Shapiro-Wilk test) were consistently passed ($W \geq 0.888$, $P > 0.05$). Descriptive data in the text are reported as mean ± SD and data in figures are expressed as means ± SE as preferred in our previous studies (Yoshitake et al., 2017; Yoshitake et al., 2016; Yoshitake et al., 2014).

3. Results

EMG activity during measurements was small, being 0.21 ± 0.10% EMGmax for BB and 0.56 ± 0.46% EMGmax for BRA when collapsed across elbow joint angles and forearm positions.

With respect to BB, there was a main effect of forearm position ($F = 119$, $P <$

0.01) and elbow position on shear modulus (Fig. 3, $F = 44.4$, $P < 0.01$). There was also a significant interaction between these two factors (Fig. 3, $F = 16.5$, $P < 0.01$). Specifically, BB shear modulus increased as the forearm was rotated and was greatest when the elbow was at 160° ($P < 0.05$), and changes in BB shear modulus as a function of forearm position were more pronounced when the elbow was at 160° (Fig. 4).

Main effects of forearm position ($F = 46.93$, $P < 0.01$) and elbow position ($F = 73.21$, $P < 0.01$) were also found for BRA shear modulus, however, BRA shear modulus decreased as the forearm was rotated from a supinated to forearm position (Fig. 3). BRA shear modulus was also greatest when the elbow was at 160° ($P < 0.05$). BRA shear modulus exhibited a significant interaction between all three factors ($F = 3.85$, $P < 0.05$). Changes in shear modulus as function of forearm position were also more pronounced when the elbow was at 160°, and were more pronounced for the distal muscle region when the elbow was at 160° (Fig. 4).

4. Discussion

The main findings of the current study were that 1) shear modulus of the resting adjacent BRA was altered by stretching BB resulting from manipulations of forearm position, and 2) the magnitude of this change was greater in the distal muscle region when the elbow was in an extended position (160°). The current results support the presence of epimuscular myofascial force transmission (EMFT) between muscles of the human upper limb, and suggest that there may be regional differences in the mechanical interaction between muscles when the muscles are already largely stretched.

Whereas BB crosses the elbow joint and inserts onto the radius in the forearm, BRA crosses the elbow joint and inserts onto the ulna. As the radius rotates around the ulna during pronation and supination, we can say that muscle length of only BB was manipulated when the forearm was set at different positions. In this study, manipulating forearm position produced significant changes in the shear modulus of both BRA and BB in the absence of EMG activity in either muscle. Since changes in muscle shear modulus in relaxed muscle reflect changes in muscle passive tension (Koo et al., 2013; Maisetti et al., 2012), the observed changes in muscle shear modulus in the current study indicate that forearm position alters the mechanical state of the passive BRA even though this muscle does not contribute to forearm rotation. This finding suggests that EMFT is present in humans. In previous studies on EMFT in humans (Bojsen-Moller et al., 2010; Finni et al., 2017; Tian et al., 2012; Yaman et al., 2013), evidence of intermuscular mechanical interaction was also found. However, in these studies, the muscles investigated shared a common tendon, which may also facilitate mechanical interactions between adjacent muscles. Accordingly, it was not entirely clear whether EMFT was responsible. In contrast, there are no shared tendons between BB and BRA, thus, the current results provided stronger of the presence of EMFT in humans.

As mentioned in Methods section, we assessed the repeatability of the shear modulus measurements by calculating intraclass correlation coefficients. This analysis confirmed that the influence of time on muscle shear modulus is negligible. The current study showed that both the absolute and relative changes in shear modulus in response to forearm rotation from supination to pronation were larger with the elbow at the more extended position of 160°. In both animal and human models, the magnitude of EMFT is influenced by the mechanical states of the interacting muscles. For example, EMFT is greater when a muscle is actively generating force (i.e. electrically-induced contraction) than when a muscle is being passively lengthened (Finni et al., 2017). These findings imply that transverse bulging of the muscle, as a result of muscle activation and dynamic fascicle behavior, could potentially stiffen connective tissue structures. Changes in the relative positions of the adjacent muscles has also been proposed to be primarily responsible for EMFT (Bernabei et al., 2015; Huijing and Baan, 2003; Maas et al., 2004). For example, in animal models, it has been shown that applying a force to the distal tendon as to lengthen the same muscle causes the adjacent muscle to be pulled distally, thereby decreasing the force in the distal tendon of the adjacent muscle (Huijing and Baan, 2001). As a result, the position of the two muscles relative to one another is altered (Maas et al., 2001, 2004; Maas and Sandercock, 2010). In the current study, the effect of forearm position on shear modulus differed markedly for the two muscles investigated (Fig. 3 & 4). When the forearm position was changed from supination to pronation, shear modulus increased in BB and decreased in BRA with a stronger effect in the distal region at the 160° of elbow joint angle (Fig. 4). The mechanism responsible for the current results may be changes in relative position between BB and BRA as drawn in Fig. 5. Stretching of BB in the distal direction in response to rotation of the forearm from a supinated to pronated position, which was associated with an increase in shear modulus in BB (Fig. 3), may cause epimuscular connections between the muscles to be stretched distally and subsequently result in distally directed myofascial loads act, at the very least, on distal parts of the BRA. Hence, the decrease in shear modulus in BRA in the distal region when the forearm was rotated from supination to pronation indicates that there were mechanical interactions between BRA and BB and, consequently, supports the presence of epimuscular myofascial force transmission in humans.

In the current study, shear modulus of BRA decreased from forearm supination to pronation for the proximal region as well, albeit to a lesser degree (Fig. 3). In animal models, distal lengthening of a muscle increases the force in the proximal tendon of the adjacent muscle (Maas et al., 2001, 2004; Maas and Sandercock, 2010). As stated before, muscle shear modulus measured by shear-wave elastography in resting muscle corresponds well to passive muscle force (Hug et al., 2015). On this basis, we expected that the shear modulus of the adjacent BRA at the proximal region would increase when forearm position was changed from supination to pronation, however, this was not the case. The reasons for this result are not clear, although the relative position of the adjacent muscles might be partly responsible (Fig. 5). If there were mechanical interactions between the adjacent muscles along the entire length of the BRA muscle belly, the whole BRA would be pulled toward the distal direction upon lengthening of BB, resulting in a decrease in muscle tension not only in the distal region, but also the proximal region (i.e., pronation position). Moreover, from Fig. 5, it is predicted that the changes in passive muscle force due to changes in the position of the muscle relative to one another should be larger when muscle passive force is initially large (i.e. at an extended elbow position). In the current study, the distal tendon would be manipulated by changing forearm position. Therefore, the larger changes in shear modulus of the BRA in the distal region would be owing to larger changes in the position of the muscles (relative to one another) in the distal region compared to the proximal region. In addition, as demonstrated in a study by Yucessoy and colleagues (2005), pre-strain in the structures connecting muscles, as well tissue heterogeneity, could lead to local differences muscle shear modulus. If the degree of pre-strain in the structures connecting muscles was relatively small in the distal region compared to proximal region, the greater relative position changes in the distal region, owing to forearm rotation, would not necessarily induce larger changes in muscle shear modulus in the distal region. Hence, the combined effect of changes in relative muscle position and pre-strain in the interconnecting tissues may best explain EMFT. These assumptions support the current result that the degree of relative change in muscle shear modulus was larger in the distal region at the elbow joint angle of 160° (Fig. 4), although further studies are needed to clarify these assertions.

A limitation of the current study is that we cannot exclude the possibility that the alternations in muscle shear modulus of BRA were owing to changes in muscle length of

BRA associated with movement of the ulna, although this outcome is unlikely as forearm rotation anatomically corresponds to movement of the radius only. However, even if forearm rotation was accompanied by rotation of the ulna, the direction of the rotation of the ulna would be same as the radius, in which case, stretching would occur in the distal direction (changes in muscle length) of both BB and BRA and would give rise to the same response in both muscles. As shown in Fig. 3, forearm position had opposing effects on shear modulus in BB and BRA in the current study. It is possible that the effect of forearm position on shear modulus in BRA was underestimated and, therefore, the true mechanical interactions between the muscles might be larger. Another limitation is that we cannot confirm whether the bicipital aponeurosis of BB contributes to the shear modulus of BRA. From an anatomical viewpoint, rotation of the forearm from supination to pronation stretches the bicipital aponeurosis in the distal direction, which may potentially result in a further reduction of BRA shear modulus. Force measurements derived from cadaveric studies or gathered during surgical operation are likely necessary to solve this concern. Finally, muscle shear modulus in the supinated position was relatively low, suggesting that passive tension was also low in this position. Nonetheless, the changes in muscle shear modulus in the adjacent BRA muscle were still able to be clearly detected when BB was stretched by changing forearm position. The forces generated by muscles of the upper limb muscles are much smaller than those generated by lower limb muscles, and therefore, we believe that the changes in shear modulus in adjacent muscles are likely to have a real functional effect. This effect is likely to be strongest when the elbow joint is extended, a position where shear modulus values, and presumably muscle passive tension, are highest and are quantitatively similar to values measured in the medial gastrocnemius muscle when EMFT is observed in the soleus muscle (Ates et al. 2018).

In conclusion, this is the first study to provide strong evidence supporting the presence of EMFT in upper extremity muscles of humans using shear-wave elastography. When joint angle was manipulated, shear modulus of the resting adjacent muscle was altered in a region-dependent manner, especially in conditions where both muscles were initially lengthened. The measurement of muscle shear modulus under passive conditions might be a simple tool to objectively evaluate the effectiveness of interventions that aim to mechanically release the intermuscular mechanical interactions between muscles, such as the Graston Technique® and self-myofascial release techniques.

Conflict of interest

The authors acknowledge no conflict of interest.

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FIGURE LEGENDS

Figure 1: Experimental setup. A) Photographs illustrating the posture of subjects during measurements at two different elbow joint angles and three different forearm positions. B) Schematic representing the placement of the probe to record ultrasound images at the distal (solid rectangle) and proximal (dot rectangle) regions of the biceps brachii (BB) and the brachialis (BRA).

Figure 2: Representative images of color maps showing shear modulus of the biceps brachii (BB, *upper*) and the brachialis (BRA, *lower*) at supination (*left*), neutral (*middle*), and pronation (*right*) forearm positions with the elbow joint angle at 160°.

Figure 3: Shear modulus of the biceps brachii (BB) and the brachialis (BRA) at distal (*left*) and proximal (*right*) regions. Data were obtained at supination (S), neutral (N), and pronation (P) forearm positions with the elbow joint angle at 100° (A) and 160° (B). * $P < 0.05$ between forearm positions, † $P < 0.05$ between regions for supination position at 160° elbow joint angle.

Figure 4: Relative changes in shear modulus of the biceps brachii (BB, open bars) and the brachialis (BRA, filled bars) when forearm position was rotated from supination to pronation. Box and whisker plots show the results for all subjects; the middle line in each box plot represents the median value and the whiskers indicate the range. The lower and upper limits of each box represent the interquartile range. Note that the change in shear modulus of BRA is larger in the distal region at 160° of elbow joint angle.

Figure 5: Schematic illustrating how the shear modulus of the brachialis (BRA, grey ellipse) was theoretically altered by manipulating forearm position. When the forearm was changed from supination (*top*) to pronation (*bottom*) positions, BB (open ellipse) was passively stretched in the distal direction, causing the adjacent BRA to be mechanically pulled toward the distal direction. In this case, the shear modulus of BRA may have decreased entirely because of myofascial loads acting on the BRA. This effect would be larger in the distal region compared with the proximal region because of the larger change in position of the muscles relative to one another in the distal region, and may explain differences in the relative change of muscle shear modulus between regions (Fig. 4). Moreover, this effect would be predicted to be larger when the initial muscle passive

tension is larger (i.e. at an extended elbow position, Fig. 4).

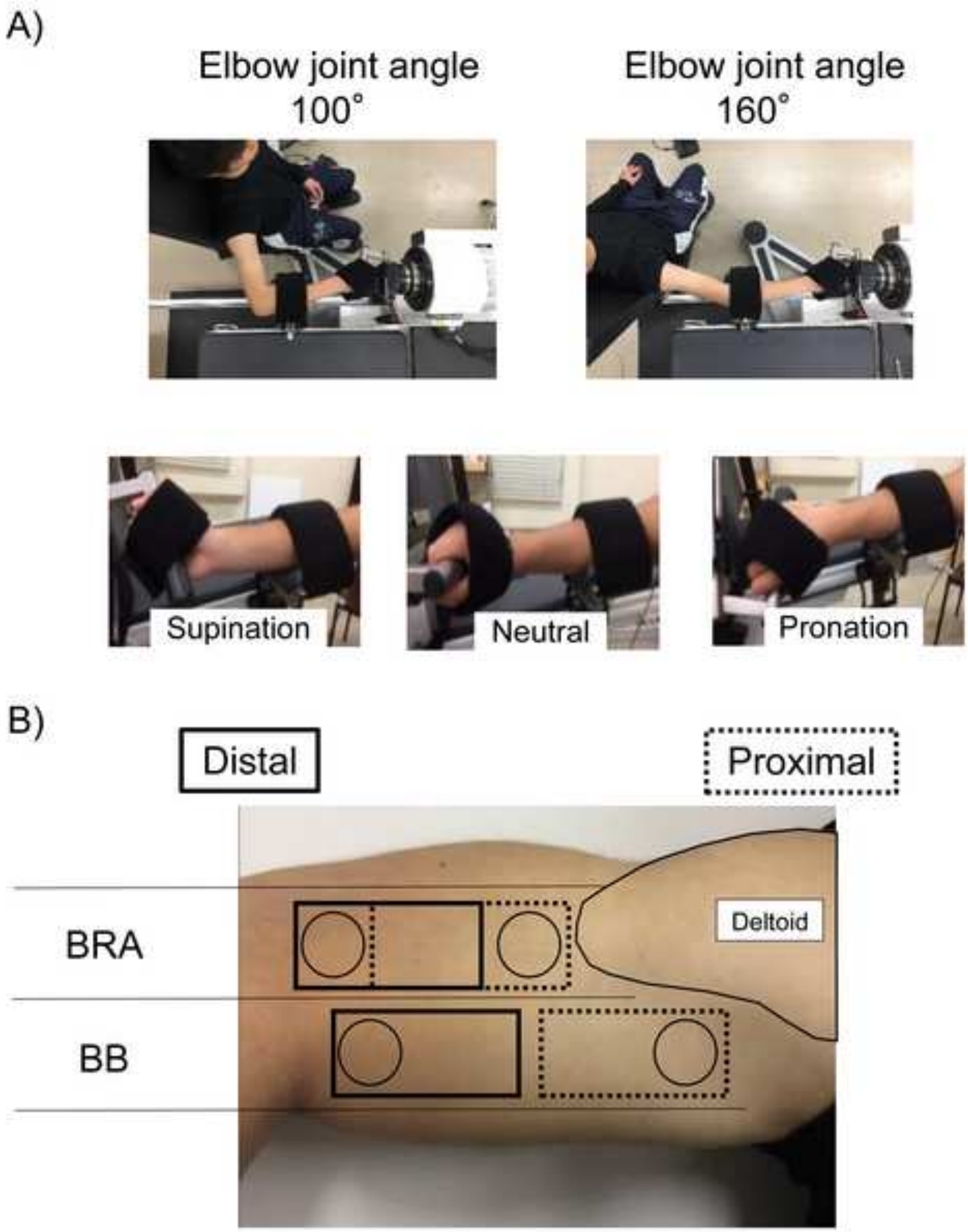

A)
Elbow joint angle 100°
Elbow joint angle 160°
Supination
Neutral
Pronation
B)
Distal
Proximal
BRA
BB
Deltoid

Fig. 1

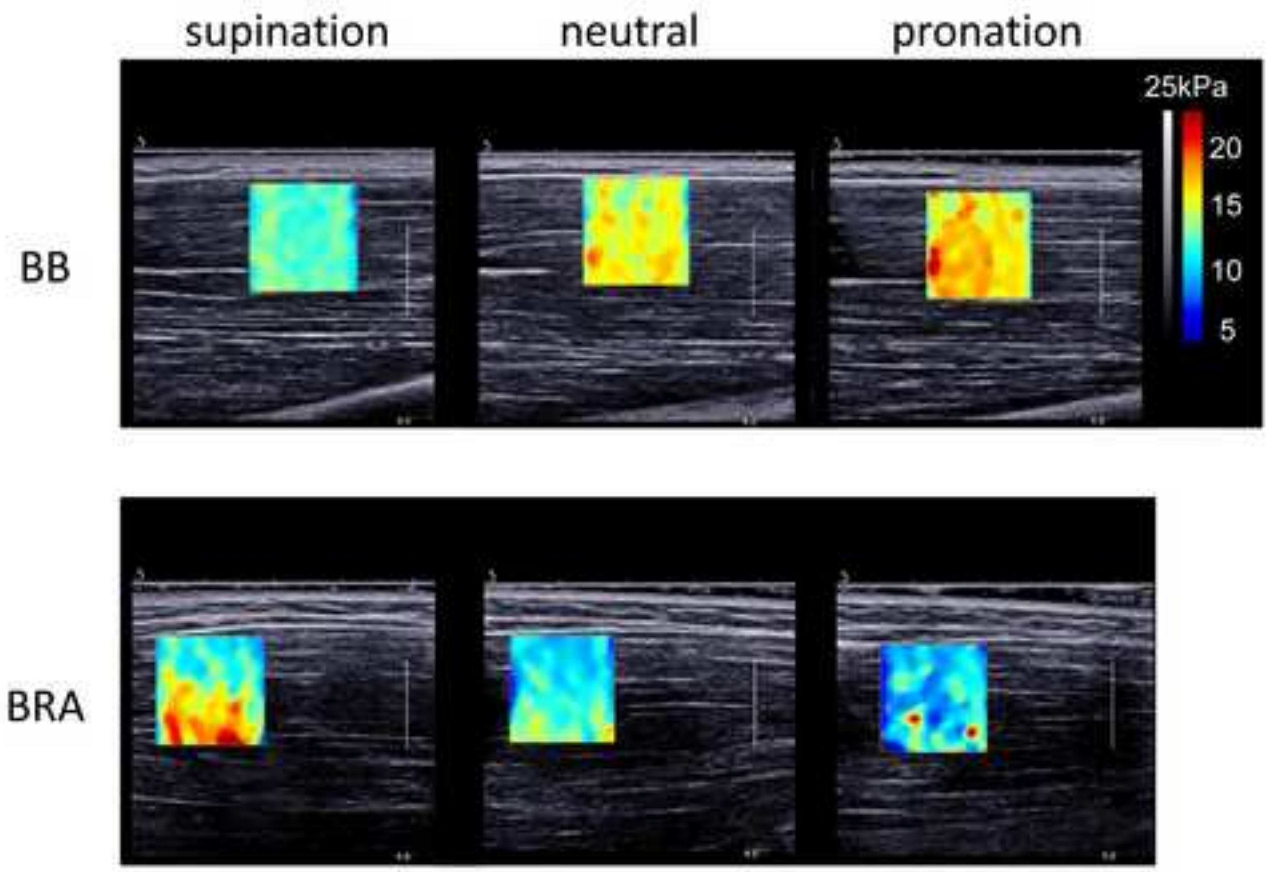


Fig. 2

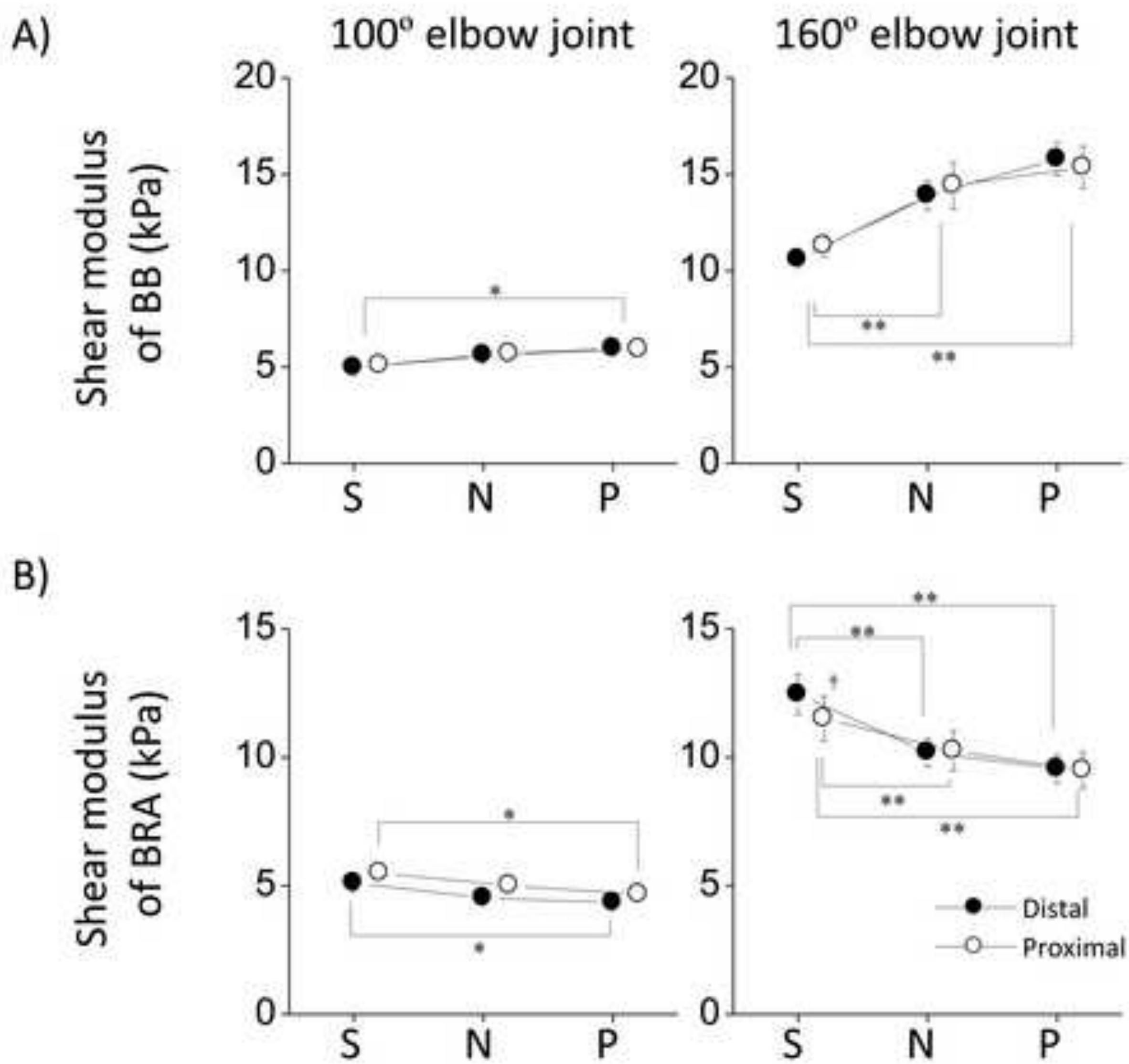
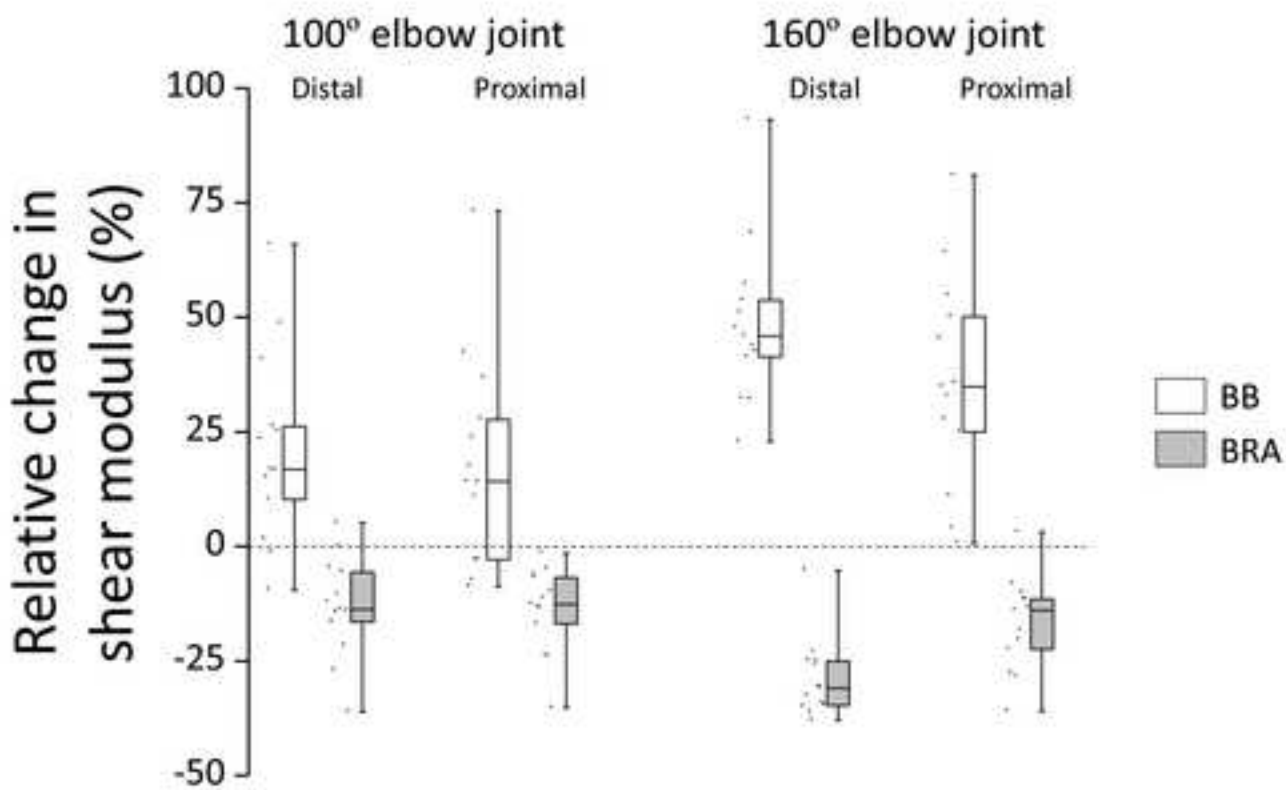

A)
100º elbow joint
160º elbow joint
Shear modulus of BB (kPa)
20
15
10
5
0
S
N
P
*
**
B)
Shear modulus of BRA (kPa)
Distal
Proximal
†

Fig. 3



100° elbow joint
160° elbow joint
Distal
Proximal
Distal
Proximal
Relative change in shear modulus (%)
100
75
50
25
0
-25
-50
BB
BRA

Fig. 4

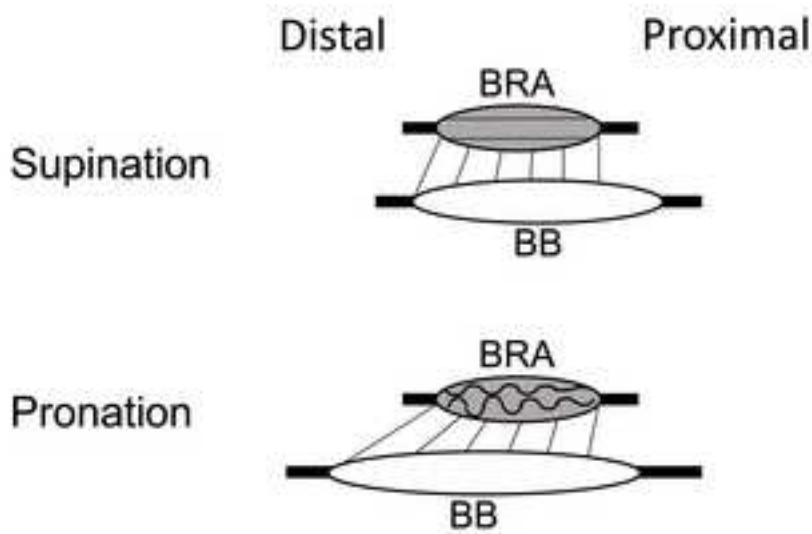


Fig. 5