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Characterization of Three Dimensional Volumetric Strain Distribution during Passive Tension of the Human Tibialis Anterior using Cine Phase Contrast MRI

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Abstract

Intramuscular pressure correlates strongly with muscle tension and is a promising tool for quantifying individual muscle force. However, clinical application is impeded by measurement variability that is not fully understood. Previous studies point to regional differences in IMP, specifically increasing pressure with muscle depth. Based on conservation of mass, intramuscular pressure and volumetric strain distributions may be inversely related. Therefore, we hypothesized volumetric strain would decrease with muscle depth. To test this we quantified 3D volumetric strain in the tibialis anterior of 12 healthy subjects using cine Phase Contrast Magnetic Resonance Imaging. Cine Phase Contrast data were collected while a custom apparatus rotated the subjects' ankle continuously between neutral and plantarflexion. A T2-weighted image stack was used to define the resting tibialis anterior position. Custom and commercial post-processing software were used to quantify the volumetric strain distribution. To characterize regional strain changes, the muscle was divided into superior-inferior sections and either medial-lateral or anterior-posterior slices. Mean volumetric strain was compared across the sections and slices. As hypothesized, volumetric strain demonstrated regional differences with a decreasing trend from the anterior (superficial) to the posterior (deep) muscle regions. Statistical tests showed significant main effects and interactions of superior-inferior and anterior-posterior position as well as superior-inferior and medial-lateral position on regional strain. These data support our hypothesis and imply a potential relationship between regional volumetric strain and intramuscular pressure. This finding may

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Conflict of interest statement

The authors report no conflict of interest.

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advance our understanding of intramuscular pressure variability sources and lead to more reliable measurement solutions in the future.

Keywords

Cine phase contrast; volumetric strain; intramuscular pressure; tibialis anterior

Introduction

An individual muscle's contribution to joint kinetics is clinically quantified using electromyography (EMG). This measurement provides reliable information on muscle electrical activation timing, but inference of force timing or magnitude from EMG remains tenuous (De Luca, 1997). Among other factors, EMG measurement amplitude varies unpredictably with the number, type, and specific selection of motor units within the electrode sensing region (De Luca, 1997). EMG is also insensitive to force output changes due to sarcomere length changes during dynamic tasks (Aratow et al., 1993; Masuda et al., 2001) as well as to passive tension (Baumann et al., 1979). In contrast, intramuscular pressure (IMP) has been established as a strong correlate with muscle tension during both passive lengthening and activation (Aratow et al., 1993; Davis et al., 2003; Sejersted et al., 1984; Winters et al., 2009), including dynamic activation (Aratow et al., 1993). Similar to fine-wire EMG, IMP measurement is now minimally invasive thanks to advances in the development of fiber optic pressure micro-sensors (Cottler et al., 2009; Kaufman et al., 2003).

A current challenge in advancing the clinical translation of IMP measurements is identifying the reasons for previously observed high variability in the correlation between IMP and force (Aratow et al., 1993; Ballard et al., 1998; Sadamoto et al., 1983; Styf et al., 1995). There is evidence for physiological differences in regional pressure, which may be a major factor in the measurement variability. Previous studies have found that IMP increases with depth, increases near stiffer structures such as tendon and bone, and may be related to fiber curvature (Ameredes and Provenzano, 1997; Nakhostine et al., 1993; Sejersted et al., 1984). This pressure distribution, while physiologically relevant, creates a technical challenge in quantifying the generated muscle tension. Regional pressure gradients in combination with sensor motion during muscle activation (Ward et al., 2007) and inconsistent sensor placement (Jenkyn et al., 2002) may contribute to within-trial and between-trial IMP measurement variability, respectively. One way to address this challenge is to characterize IMP distribution and identify strategic sensor placement in regions with low pressure gradients (Jenkyn et al., 2002). Unfortunately, detailed IMP characterization is impractical to accomplish experimentally due to the limited number of pressure sensors that can be inserted into a muscle simultaneously. However, volumetric strain quantification may provide a useful solution.

Pressure is generated by an interaction between changes in tissue volume and fluid influx to efflux ratio. Therefore, the regional IMP may be affected by regional volumetric strain. Pertinently, muscle tissue strain demonstrates regional differences during passive tension

and activation of skeletal muscle (Finni et al., 2003; Huijing et al., 2011; Kinugasa et al., 2008; Pappas et al., 2002; Silder et al., 2010; Yaman et al., 2013; Zhong et al., 2008). The distribution has been successfully modelled and found to be a function not only of muscle tension, but also of fiber architecture, boundary conditions, and material properties (Blemker et al., 2005) – factors which also affect IMP distribution (Ameredes and Provenzano, 1997; Nakhostine et al., 1993; Sejersted et al., 1984). Furthermore, strain –like IMP – varies with muscle depth and near stiffer structures (Blemker et al., 2005), supporting the possibility that a relationship may exist between these measures. Therefore, we expect that strain distribution data may play an important role in the development of a generalizable computational model relating tension and pressure distribution. This model may ultimately allow us to quantify muscle force from IMP measurements.

Cine Phase Contrast (CPC) Magnetic Resonance Imaging (MRI), which measures 3D velocity distribution at finite time segments throughout a motion cycle, can be used to quantify both actively and passively generated strain. To date, CPC MRI-based strain measures in skeletal muscle have been constrained to a single 2D cross section (Blemker and Delp, 2005; Finni et al., 2003; Kinugasa et al., 2008; Pappas et al., 2002; Silder et al., 2010; Zhong et al., 2008), restricting the output to planar tensile, compressive, and shear strain. However, volumetric strain is more likely to play a prominent role in the generation of IMP. Three-dimensional muscle strain has been quantified previously using high-resolution 3D MRI image sets and Demons nonrigid registration algorithm (Huijing et al., 2011; Yaman et al., 2013). While these data provide evidence for regional differences in volumetric strain, the nature of the distribution was not described. CPC MRI technology also lends itself to 3D volumetric strain measurements through multiple slice acquisition and tracking in three dimensions.

The aim of this study was to characterize the *in vivo* volumetric strain distribution of the human TA during passive tension using CPC. We hypothesized that there would be regional differences in 3D volumetric muscle strain. We further hypothesized that volumetric strain would decrease with muscle depth because IMP increases with muscle depth (Nakhostine et al., 1993; Sejersted et al., 1984) and the two are inversely related according to the principal of mass conservation.

Methods

Subjects

Twelve subjects (9F, 26±2 y.o., 22.6±2.7 BMI) with good neuromuscular health volunteered for this study. All twelve participated in at least one two hour visit. Five of the subjects (4 F, 25±1 y.o., 22.0±2.0 BMI) also participated in three additional visits (same protocol) within a one week time span to establish measurement repeatability. The study was approved by the Mayo Clinic Institutional Review Board (IRB #13-002825) and all subjects provided written, informed consent.

Data collection

Subjects were positioned supine on the MRI table, oriented feet first into the bore. A custom MRI-compatible apparatus continually rotated the right ankle between neutral (0 degrees) and 26 degrees of plantarflexion on a two second cycle. A rectangular two-channel, receive-only MRI coil was positioned over the right lower leg and remained undisturbed during the passive ankle motion.

A commercially available Fast 2D Phase Contrast sequence on a 1.5T MRI scanner (Signa HDX 16.0, GE Medical Systems, Waukesha, WI) was used to measure velocity distribution in the tibialis anterior (TA) during the passive ankle rotation. Eight sagittal slices were positioned to image the entire TA (Table 1) and velocity was encoded in the frequency (superior/inferior), phase (anterior/posterior), and through plane (medial/lateral) directions successively. Before the CPC data were collected, T2-weighted image stacks (Table 2) covering the length of the TA were collected with the ankle in the neutral position to provide 3D anatomical data for muscle segmentation.

Data processing

Data processing methods have been described in detail previously (Jensen et al., 2015a). Briefly, the TA muscle was manually segmented from all T2-weighted images (Mimics, Materialise, Leuven, Belgium). The segmented boundary was eroded by 1.5 to 2.5 mm around the edges to alleviate misalignment-associated tracking errors. The segmented surface was then used to manually generate a 3D hexahedral mesh (TrueGrid, XYZ Scientific, Livermore, CA). The mesh was designed to match the muscle curvature while maintaining optimally uniform element shape and volume, resulting in 11808 elements (164 elements per axial layer and 72 layers) with a mean volume of 6.7 mm³ (4.2 to 9.8 mm³ IQR). The mesh was also carefully matched to the muscle features to ensure that each element corresponded with approximately the same muscle position across subject meshes. The mean±SD volume of the twelve subjects' final mesh was 86.5±18.7 cm³.

The CPC velocity data were smoothed and corrected according to Jensen et al (Jensen et al., 2015b). Mesh node trajectories were tracked according to the forward-backward method (Pelc et al., 1995; Zhou and Novotny, 2007) and smoothed by averaging across the nearest neighbors. Volumetric strain distribution was calculated in Abaqus (Dassault Systemes Simulia Corp., Providence, RI) using custom software (Abaqus Python; Python v2.7). First, the 3D node trajectories were applied as boundary conditions to the hexahedral mesh to generate the deformed mesh. Next, both the undeformed and deformed element volumes were calculated as the sum of the tetrahedral shapes generated using Python's Delaunay triangulation function. Finally, the normalized change in element volume was calculated.

Data analysis

The mesh was divided into finite regions along all three anatomical directions in order to reduce the spatial degrees of freedom and enable statistical analysis of regional volumetric strain trends. First, the mesh elements were partitioned into five equal length sections along the superior/inferior (S/I) direction (Figure 1a). Next, elements were partitioned into ten equal width medial/lateral (M/L) and ten equal width anterior/posterior (A/P) slices (Figure

1b,c). Due to muscle curvature, the volume was not equally distributed in these regions (Figure 1d,e). For each subject and visit, volumetric strain was averaged across the elements within each of these regions.

To test whether there were statistically significant regional changes in volumetric strain, the mean and between-subject standard deviation were calculated for each section and slice from a single trial of each of the twelve subjects. The main effects and interactions of S/I and A/P (or S/I and M/L) position on regional volumetric strain were assessed using a full factorial repeated measures ANOVA (JMP, the SAS Institute Inc. Cary, NC). Post-hoc comparisons were made with a Tukey-Kramer HSD adjustment. The significance level was set at $p < 0.05$.

Finally, the repeatability trial data (from the sub-group of five subjects) was used to assess regional strain measure reliability. Reliability was quantified using the Bland and Altman coefficient of repeatability (CR) (Bland and Altman, 1999). CR was quantified for each S/I section and A/P slice and for all subjects and trials.

Results

Regional differences in volumetric strain were found on both the individual and group level. A representative individual subject demonstrated trends of low magnitude volumetric strain in the posterior and superior regions of the muscle, with increasingly positive volumetric strain in the anterior and inferior muscle regions (Figure 2). The region with the highest positive volumetric strain was at the inferior end of the muscle on the anterior surface (Figure 2).

Both the whole group of twelve subjects and the sub-group of five subjects (tested independently) demonstrated trends of increasingly positive volumetric strain from the superior to inferior sections, from the posterior to anterior slices, and from the lateral to medial slices (Figure 3). Mean $\pm$ SD volumetric strain in the most superior muscle slice was $0.018 \pm 0.026 \text{ mm}^3/\text{mm}^3$ while volumetric strain in the most medial, inferior region was $0.26 \pm 0.13 \text{ mm}^3/\text{mm}^3$ (Figure 3). Statistical tests showed significant main effects and interactions of S/I and A/P position as well as S/I and M/L position on regional volumetric strain ($p < 0.001$; Figure 3). Tukey post hoc analysis revealed significantly higher volumetric strain in the extreme medial, anterior, and inferior regions of the muscle (Figure 3).

The median(IQR) CR of the volumetric strain across all fifty muscle regions was $0.056(0.045, 0.084) \text{ mm}^3/\text{mm}^3$. This was quantified using the three data collections of the five subject sub-group.

Discussion

This study characterized the volumetric strain distribution in the human tibialis anterior during passive lengthening using Cine Phase Contrast MRI. Intramuscular pressure, which is inversely related to volume according to conservation of mass, has been found to increase with muscle depth (Ameredes and Provenzano, 1997; Nakhostine et al., 1993; Sejersted et al., 1984). In concordance with our hypothesis, this study has demonstrated that volumetric

strain distribution is also characterized by regional differences with a decreasing trend from the anterior (superficial) to the posterior (deep) muscle regions. This qualitative evidence of distribution pattern similarity supports the possibility that regional volumetric strain differences may play a role in skeletal muscle's pressure distribution and encourages further investigation into this relationship. Furthermore, the volumetric strain distribution trends quantified from independent repeatability measurements on a subject subset were visually consistent with the data collected on the full subject set, establishing confidence in the final outcome measures.

According to the current data, the muscle regions with the least uniform volumetric strain were anterior, medial, and inferior. Regional volumetric strain differences may be associated with high regional pressure gradients (not expressly quantified in this study), which can lead to pressure measurement uncertainty. Therefore, IMP sensor placement in non-uniform strain regions should likely be avoided. Conversely, the region with the most consistent volumetric strain, which likely corresponds to the most ideal pressure sensor placement region, was the posterior-lateral quartile of the second and third S/I sections. This corresponds anatomically with the deep muscle, away from the tibia, between midbelly and just proximal of midbelly and is consistent with IMP sensor placement methods used previously in the human TA (Crenshaw et al., 1992). Therefore, the sensor placement recommendations of the current study data align with sensor placement based on an experimental trial-and-error approach.

Several important factors that likely contribute to volumetric strain distribution include muscle geometry, architecture, material properties, and boundary conditions (Blemker et al., 2005). These factors can be used to generate a muscle model to help explain the nature of both volumetric strain and IMP distribution, as well as their relationship to muscle force. Implementing such models in the future could allow the IMP distribution to be established theoretically for any muscle of interest, reducing the need for extensive MRI and IMP experimental work. Consider the following basic modelling example. The tibialis anterior has a relatively simple, bipennate structure (Figure 4). Passive tension, which acts functionally on the internal aponeurosis, causes fiber pennation angle changes and lengthening. The net neutral volumetric strain in the deep TA region indicates that along fiber lengthening is counterbalanced by compression perpendicular to the fibers. This compression likely occurs as a result of the extensor retinaculum (ER), which straps the TA tendon tightly against the tibia (Varghese and Bianchi, 2014). The ER also causes the TA tendon to generate perpendicular tension on the superficial muscle fibers, which, in combination with the simultaneous muscle fiber lengthening, could explain the observed volume increase in the superficial TA region. Extensive computational modelling is needed to explain the more complex details of the volumetric strain distribution – taking into consideration non-uniform deformation both transversely between muscle fibers and longitudinally along the muscle fiber direction (Pappas et al., 2002), for example – and to determine how the pressure is affected accordingly.

In addition to the growing evidence for regional differences in both IMP and strain throughout a muscle, there is also evidence for differences in regional force. Our previous finite element modelling study, which defined IMP as the hydrostatic component of the

Cauchy stress tensor, suggests that both pressure and stress are characterized by regional differences in muscle (Jenkyn et al., 2002). Related modeling work has more directly demonstrated region differences in fiber-direction muscle stress and sarcomere length (recently confirmed experimentally (O'Connor et al., 2016)), concluding that intramuscular force transmission is also non-uniform (Yucesoy et al., 2003a). This and similar studies further found that muscle force at the proximal and distal muscle ends were unequal, providing evidence for inter- and extramuscular myofascial force transmission (Huijing and Baan, 2001; Maas et al., 2001). These findings complement the current study and may provide useful insight into the physiological basis of regional pressure and volumetric strain differences.

An interesting finding of this work was that the vast majority of the volumetric strain was positive, indicating a volume increase. This prompts questions about the manner in which IMP is generated. Previous studies have demonstrated muscle fiber volume reduction during passive muscle stretch (Mazzoni et al., 1990), where a fiber diameter is on the order of 50 μm (Maier and Bornemann, 1999). These volume changes are presumed to be maintained at the fascicle level (Causey et al., 2012; Mazzoni et al., 1990). Both the muscle fiber and fascicle are substantially smaller than the imaging resolution and their volumetric changes would, therefore, not be observable using the current CPC MRI methods. Indeed, increases in IMP, as measured using a fiber optic pressure microsensor, are likely induced by reduced fascicle volume during passive stretch. However, these fascicle-level volume changes may be moderated by larger scale positive volumetric strain in superficial muscle regions and neutral volumetric strain deep muscle regions, leading to the previously described regional pressure differences (Ameredes and Provenzano, 1997; Nakhostine et al., 1993; Sejersted et al., 1984).

Passive tibialis anterior tension was selected for this study because it is an ideal model for beginning the investigation into the relationship between IMP and strain distribution. Passive tension was strategically selected instead of active tension for method development purposes. Three-dimensional acquisition of CPC MRI requires sustained repeatable cyclic motion over an extended period and passive tension is more readily controlled than active tension. With successful method development using passive tension, the technique can more easily be modified for active tension application. Possible strategies include applying accelerated CPC imaging sequences with higher RF coil channel counts to reduce the total data collection time and using low level muscle activation with breaks. For example, a high-speed 3D radial cine phase contrast acquisition method has enabled acceleration factors of up to 11 with adequate SNR for angiography applications (Johnson et al., 2008). Additionally, muscle activation studies have been successfully performed previously involving multiple scans of several minute repeated muscle activations at 40% of maximal voluntary contraction (Sinha et al., 2012).

The TA muscle was specifically selected for this study for a number of reasons. IMP sensor insertion is relatively easy due to the muscle's superficial location and large belly: it is approximately 22 cm long, and 3.5 cm wide (Wolf and Kim, 1997). The muscle is also nearly isolated in action. Although it shares the role of ankle dorsiflexion, it is the only muscle to additionally generate foot inversion. This makes it an optimal choice for future

applications in which the actively generated tension must be quantified. The TA is also ideal for CPC measurements specifically because, unlike the knee and hip joints, the ankle can easily rotate through its full range of motion inside the 60 cm wide MRI magnet bore. Finally, the TA is a well-studied muscle, providing ample reference for method development and data (Aratow et al., 1993; Ballard et al., 1998; Nakhostine et al., 1993; Sejersted and Hargens, 1995).

There are a few limitations of this study. First, although statistically significant trends were identifiable on the group level, the reliability results spur caution in interpretation. The median Bland and Altman coefficient of repeatability, which can be interpreted as the minimum detectable difference, was $0.056 \text{ mm}^3/\text{mm}^3$. Given that the interesting volumetric strain differences seen in the data are between approximately 0.02 and $0.24 \text{ mm}^3/\text{mm}^3$ (Figure 3), a portion of the regional differences fall below the detectable difference. Still, the reliability of the observed regional distribution trend is supported by the visual consistency of whole group and the independently-collected sub-group results (Figure 3). A future strategy to increase the measurement precision and, therefore, the reliability will be to design a custom coil with a much higher signal-to-noise ratio.

A second limitation is that most previous studies describing IMP distribution have been performed under conditions of muscle activation. These descriptions are also restricted due to limitations on the number of sensors that can safely be placed in a muscle. However, we can draw inferences about the general IMP distribution from these data. In the future, local strain and IMP will be directly compared under conditions of both passive and active TA tension at a few strategic, representative muscle locations. By quantifying the correlation between these measures at multiple distinct muscle locations, we can directly test the hypothesis that they are inversely related.

Another limitation is the lack of physiological element orientation in the current model. This limitation constrained the current analysis to the primary output of volumetric strain, which is unaffected by orientation. Adapting element orientation to correspond with fiber orientation (Blemker and Delp, 2005) using techniques such as diffusion tensor imaging (Pamuk et al., 2016) would allow us to analyze various forms of strain – such as along fiber principle and shear strains – in the true physiological context. These types of analysis were not possible with previous 2D strain measurements. It may also provide insight into the manner in which volumetric strain is generated across the muscle. Furthermore, it would allow closer analysis of local sarcomere length changes and provide insight into regional fiber force – and hence IMP – output differences (Yucesoy et al., 2003b). Thus, closer analysis of 3D along fiber strains may provide further explanation for the mechanism of regional IMP differences.

This is the first study to thoroughly characterize 3D volumetric strain distribution in skeletal muscle. We have demonstrated regional differences in volumetric strain during passive tension of the human tibialis anterior, with the highest positive strains in the most anterior, medial, and inferior regions. Although some caution must be applied in the interpretation due to marginal reliability, these results align with previously observed trends of decreasing IMP near the muscle surface and may provide important insight into ideal sensor placement

regions to maximize measurement repeatability. These data advance our understanding of the tension-IMP relationship in muscle by providing insight into the mechanism behind the regional differences in IMP. For future application, methodological improvements are needed to lower total scan time and increase signal-to-noise ratio.

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References

- Ameredes BT, Provenzano MA. Regional intramuscular pressure development and fatigue in the canine gastrocnemius muscle in situ. *J Appl Physiol* (1985). 1997; 83:1867–1876. [PubMed: 9390957]
- Aratow M, Ballard RE, Crenshaw AG, Styf J, Watenpaugh DE, Kahan NJ, Hargens AR. Intramuscular pressure and electromyography as indexes of force during isokinetic exercise. *J Appl Physiol* (1985). 1993; 74:2634–2640. [PubMed: 8365963]
- Ballard RE, Watenpaugh DE, Breit GA, Murthy G, Holley DC, Hargens AR. Leg intramuscular pressures during locomotion in humans. *J Appl Physiol* (1985). 1998; 84:1976–1981. [PubMed: 9609792]
- Baumann JU, Sutherland DH, Hanggi A. Intramuscular pressure during walking: an experimental study using the wick catheter technique. *Clin Orthop Relat Res*. 1979:292–299. [PubMed: 535286]
- Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res*. 1999; 8:135–160. [PubMed: 10501650]
- Blemker SS, Delp SL. Three-dimensional representation of complex muscle architectures and geometries. *Ann Biomed Eng*. 2005; 33:661–673. [PubMed: 15981866]
- Blemker SS, Pinsky PM, Delp SL. A 3D model of muscle reveals the causes of nonuniform strains in the biceps brachii. *J Biomech*. 2005; 38:657–665. [PubMed: 15713285]
- Causey L, Cowin SC, Weinbaum S. Quantitative model for predicting lymph formation and muscle compressibility in skeletal muscle during contraction and stretch. *Proc Natl Acad Sci U S A*. 2012; 109:9185–9190. [PubMed: 22615376]
- Cottler PS, Karpen WR, Morrow DA, Kaufman KR. Performance characteristics of a new generation pressure microsensor for physiologic applications. *Ann Biomed Eng*. 2009; 37:1638–1645. [PubMed: 19495983]
- Crenshaw AG, Styf JR, Hargens AR. Intramuscular pressures during exercise: an evaluation of a fiber optic transducer-tipped catheter system. *Eur J Appl Physiol Occup Physiol*. 1992; 65:178–182. [PubMed: 1396642]
- Davis J, Kaufman KR, Lieber RL. Correlation between active and passive isometric force and intramuscular pressure in the isolated rabbit tibialis anterior muscle. *J Biomech*. 2003; 36:505–512. [PubMed: 12600341]
- De Luca CJ. The use of surface electromyography in biomechanics. *J Appl Biomech*. 1997; 13:135–163.
- Finni T, Hodgson JA, Lai AM, Edgerton VR, Sinha S. Nonuniform strain of human soleus aponeurosis-tendon complex during submaximal voluntary contractions in vivo. *J Appl Physiol* (1985). 2003; 95:829–837. [PubMed: 12716873]
- Huijing PA, Baan GC. Extramuscular myofascial force transmission within the rat anterior tibial compartment: proximo-distal differences in muscle force. *Acta Physiol Scand*. 2001; 173:297–311. [PubMed: 11736692]

- Huijing PA, Yaman A, Ozturk C, Yucesoy CA. Effects of knee joint angle on global and local strains within human triceps surae muscle: MRI analysis indicating in vivo myofascial force transmission between synergistic muscles. *Surg Radiol Anat.* 2011; 33:869–879. [PubMed: 21912991]
- Jenkyn TR, Koopman B, Huijing P, Lieber RL, Kaufman KR. Finite element model of intramuscular pressure during isometric contraction of skeletal muscle. *Phys Med Biol.* 2002; 47:4043–4061. [PubMed: 12476981]
- Jensen ER, Morrow DA, Felmlee JP, Murthy NS, Kaufman KR. Method of quantifying 3D strain distribution in skeletal muscle using cine phase contrast MRI. *Physiol Meas.* 2015a; 36:N135–N146. [PubMed: 26595686]
- Jensen ER, Morrow DA, Felmlee JP, Odegard GM, Kaufman KR. Error analysis of cine phase contrast MRI velocity measurements used for strain calculation. *J Biomech.* 2015b; 48:95–103. [PubMed: 25433567]
- Johnson KM, Lum DP, Turski PA, Block WF, Mistretta CA, Wieben O. Improved 3D phase contrast MRI with off-resonance corrected dual echo VIPR. *Magn Reson Med.* 2008; 60:1329–1336. [PubMed: 19025882]
- Kaufman KR, Wavering T, Morrow D, Davis J, Lieber RL. Performance characteristics of a pressure microsensor. *J Biomech.* 2003; 36:283–287. [PubMed: 12547368]
- Kinugasa R, Shin D, Yamauchi J, Mishra C, Hodgson JA, Edgerton VR, Sinha S. Phase-contrast MRI reveals mechanical behavior of superficial and deep aponeuroses in human medial gastrocnemius during isometric contraction. *J Appl Physiol* (1985). 2008; 105:1312–1320. [PubMed: 18703759]
- Maas H, Baan GC, Huijing PA. Intermuscular interaction via myofascial force transmission: effects of tibialis anterior and extensor hallucis longus length on force transmission from rat extensor digitorum longus muscle. *J Biomech.* 2001; 34:927–940. [PubMed: 11410176]
- Maier F, Bornemann A. Comparison of the muscle fiber diameter and satellite cell frequency in human muscle biopsies. *Muscle Nerve.* 1999; 22:578–583. [PubMed: 10331356]
- Masuda T, Kizuka T, Zhe JY, Yamada H, Saitou K, Sadoyama T, Okada M. Influence of contraction force and speed on muscle fiber conduction velocity during dynamic voluntary exercise. *J Electromyogr Kinesiol.* 2001; 11:85–94. [PubMed: 11228422]
- Mazzoni MC, Skalak TC, Schmid-Schonbein GW. Effects of skeletal muscle fiber deformation on lymphatic volumes. *Am J Physiol.* 1990; 259:H1860–1868. [PubMed: 2260710]
- Nakhostine M, Styf JR, van Leuven S, Hargens AR, Gershuni DH. Intramuscular pressure varies with depth. The tibialis anterior muscle studied in 12 volunteers. *Acta Orthop Scand.* 1993; 64:377–381. [PubMed: 8322604]
- O'Connor SM, Cheng EJ, Young KW, Ward SR, Lieber RL. Sarcomere length distribution quantification in whole muscle frozen sections. *J Exp Biol.* 2016
- Pamuk U, Karakuzu A, Ozturk C, Acar B, Yucesoy CA. Combined magnetic resonance and diffusion tensor imaging analyses provide a powerful tool for in vivo assessment of deformation along human muscle fibers. *J Mech Behav Biomed Mater.* 2016; 63:207–219. [PubMed: 27429070]
- Pappas GP, Asakawa DS, Delp SL, Zajac FE, Drace JE. Nonuniform shortening in the biceps brachii during elbow flexion. *J Appl Physiol* (1985). 2002; 92:2381–2389. [PubMed: 12015351]
- Pelc NJ, Drangova M, Pelc LR, Zhu Y, Noll DC, Bowman BS, Herfkens RJ. Tracking of cyclic motion with phase-contrast cine MR velocity data. *J Magn Reson Imaging.* 1995; 5:339–345. [PubMed: 7633112]
- Sadamoto T, Bonde-Petersen F, Suzuki Y. Skeletal muscle tension, flow, pressure, and EMG during sustained isometric contractions in humans. *Eur J Appl Physiol Occup Physiol.* 1983; 51:395–408. [PubMed: 6685038]
- Sejersted OM, Hargens AR. Intramuscular pressures for monitoring different tasks and muscle conditions. *Adv Exp Med Biol.* 1995; 384:339–350. [PubMed: 8585463]
- Sejersted OM, Hargens AR, Kardel KR, Blom P, Jensen O, Hermansen L. Intramuscular fluid pressure during isometric contraction of human skeletal muscle. *J Appl Physiol Respir Environ Exerc Physiol.* 1984; 56:287–295. [PubMed: 6706739]
- Silder A, Reeder SB, Thelen DG. The influence of prior hamstring injury on lengthening muscle tissue mechanics. *J Biomech.* 2010; 43:2254–2260. [PubMed: 20472238]

- Sinha S, Shin DD, Hodgson JA, Kinugasa R, Edgerton VR. Computer-controlled, MR-compatible foot-pedal device to study dynamics of the muscle tendon complex under isometric, concentric, and eccentric contractions. *J Magn Reson Imaging*. 2012; 36:498–504. [PubMed: 22392816]
- Styf J, Ballard R, Aratow M, Crenshaw A, Watenpaugh D, Hargens AR. Intramuscular pressure and torque during isometric, concentric and eccentric muscular activity. *Scand J Med Sci Sports*. 1995; 5:291–296. [PubMed: 8581572]
- Varghese A, Bianchi S. Ultrasound of tibialis anterior muscle and tendon: anatomy, technique of examination, normal and pathologic appearance. *J Ultrasound*. 2014; 17:113–123. [PubMed: 24883132]
- Ward SR, Davis J, Kaufman KR, Lieber RL. Relationship between muscle stress and intramuscular pressure during dynamic muscle contractions. *Muscle Nerve*. 2007; 36:313–319. [PubMed: 17554796]
- Winters TM, Sepulveda GS, Cottler PS, Kaufman KR, Lieber RL, Ward SR. Correlation between isometric force and intramuscular pressure in rabbit tibialis anterior muscle with an intact anterior compartment. *Muscle Nerve*. 2009; 40:79–85. [PubMed: 19533654]
- Wolf SL, Kim JH. Morphological analysis of the human tibialis anterior and medial gastrocnemius muscles. *Acta Anat (Basel)*. 1997; 158:287–295. [PubMed: 9416360]
- Yaman A, Ozturk C, Huijing PA, Yucesoy CA. Magnetic resonance imaging assessment of mechanical interactions between human lower leg muscles in vivo. *J Biomech Eng*. 2013; 135:91003. [PubMed: 23722229]
- Yucesoy CA, Koopman BH, Baan GC, Grootenboer HJ, Huijing PA. Effects of inter- and extramuscular myofascial force transmission on adjacent synergistic muscles: assessment by experiments and finite-element modeling. *J Biomech*. 2003a; 36:1797–1811. [PubMed: 14614933]
- Yucesoy CA, Koopman BH, Baan GC, Grootenboer HJ, Huijing PA. Extramuscular myofascial force transmission: experiments and finite element modeling. *Arch Physiol Biochem*. 2003b; 111:377–388. [PubMed: 15764078]
- Zhong X, Epstein FH, Spottiswoode BS, Helm PA, Blemker SS. Imaging two-dimensional displacements and strains in skeletal muscle during joint motion by cine DENSE MR. *J Biomech*. 2008; 41:532–540. [PubMed: 18177655]
- Zhou H, Novotny JE. Cine phase contrast MRI to measure continuum Lagrangian finite strain fields in contracting skeletal muscle. *J Magn Reson Imaging*. 2007; 25:175–184. [PubMed: 17152055]

Figure 1.

a) The TA muscle mesh was sectioned into five superior/inferior sections. Within each section, the mesh elements were grouped into ten posterior/anterior (b) and ten medial/lateral (c) slices for analysis. Due to muscle curvature, the mean(SD) volume is unequal across posterior/anterior (d) and medial/lateral (e) slices and superior/inferior sections.

Figure 2. Sagittal, frontal, and axial mid-belly cross sections of a representative subject's volumetric strain distribution across the right TA muscle, demonstrating non-uniform distribution.

Figure 3.

The regional volumetric strain is reported across each A/P (a,b,c) or M/L (d,e,f) slice (x-axis) and each S/I section (color, as defined in (g)) for the sub-group (b,e) and the full group of twelve (c,f). Reported means were calculated as average volumetric strain across elements in region, subjects, and data collections. Error bars are reported as within-subject SD (sub-group data) and between-subject SD (full group data). A/P (or M/L) slice means with different letters and S/I section means with different symbols are statistically different ($p < 0.05$).

Figure 4.

Diagram of an axial TA cross-section (right mid-belly viewed from above) depicting the muscle structure and boundary conditions. The muscle is bi-pennate with fibers originating either at the tibia, the interosseous membrane, or the superficial fascia (origin regions highlighted in thick dark grey), extending a length of ~7cm at a five degree pennation angle to the long axis (Friedrich and Brand, 1990), and inserting at the internal aponeurosis. The muscle is flanked on the medial side by the tibia, the deep side by the interosseous membrane, the lateral side by the extensor digitorum longus (and, more distally, the extensor hallucis longus), and on the superficial side by the skin. It is part of the anterior compartment of the leg, which is encased by fascia.

Table 1

Cine Phase Contrast MRI imaging parameters

Pulse sequence	Vasc PC
Imaging options	Gat, Seq, Fast
Mode	2D
Orientation	Feet-First Supine
Imaging plane	Sagittal
Frequency direction	S/I
Gradient	Whole
X/Y resolution	192 × 192
Phase FOV	240 mm
Slice thickness	5.0 mm
# Slices	8
Encoding velocity (v_{enc})	50 mm/s
Views per segment	4
# Time segments	12
Data collection duration	40 min (1:40 per slice and encoding direction)

Table 2

T2-weighted MRI imaging parameters

Pulse sequence	Fast Spin-Echo
Imaging plane	Axial
X/Y resolution	320 × 320
Phase FOV	200 mm
Slice thickness	5.0 mm
Slice spacing	0 mm
TE	41.1 ms