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Evaluate muscle tension using intramuscular pressure device in rabbit tibialis anterior model for improved tendon transfer surgery

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Abstract

Quantitative evaluation of passive tension in a muscle is important in tendon transfer surgeries, however, currently appropriate intraoperative measurement techniques are lacking.

Objective: Intramuscular pressure (IMP) is explored as an application to access force.

Approach: The tibialis anterior (TA) in New Zealand white rabbits ($n = 9$) was used to test the hypothesis of a strong correlation between the IMP, muscle force, and length. This study also helped to develop intraoperative techniques for future human studies evaluating various insertion techniques (parallel versus perpendicular).

Main results: The Pearson correlation between IMP and force for all trials was 0.74 ± 0.30 . Separating out the parallel insertion from the perpendicular insertion revealed a significantly higher correlation for parallel, 0.91 ± 0.13 versus 0.56 ± 0.32 .

Significance: These data indicate IMP sensors can be used to assess force in a single muscle and the parallel insertion method should be used.

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Author contributions

The animal related work for this study was carried out in the laboratory space of AYS and surgery was performed by LFB and LQE. Raw data was acquired by LFB and LQE. LQE, LFB, AYS, and KRK all contributed to the concept and design of the experiment. While LQE was responsible for the data analysis carried out in KRK's laboratory LFB was primary surgeon in AYS's operative laboratory space and assisted with the interpretation of the data. LQE drafted the manuscript and all authors contributed to the revising and critiquing the intellectual content, therefore approving the final version. All authors agree to be accountable for the work herein and will help to resolve any inaccuracies. Lastly, all those listed as authors meet the requirements for authorship and no one has been left off the author list.

Additional information

The authors report no conflict of interest.

Keywords

passive force; surgical tool; technology translation

Introduction

Force production in an individual muscle is of great interest to muscle physiologists and clinicians as it is often used as a standard of medical evaluation and diagnosis of disease progression (Barry *et al* 1990, Ali *et al* 2008). Present and past investigations of intramuscular pressure (IMP) have revealed a near linear relationship with muscle force (Sejersted *et al* 1984, Aratow *et al* 1993, Davis *et al* 2003, Winters *et al* 2009). Assuming the muscle is isovolumetric, movement of the fibers causes an increase in hydrostatic pressure and thus fluid movement in the muscle. This relationship is seen with passive muscle lengthening creating interstitial fluid flow in the rat tibialis anterior (TA) muscle (Evertz *et al* 2016). Recent studies have focused on using fiber optic sensors to assess hydrostatic changes in pressure during isometric muscle activation. For example, Davis *et al* and Winters *et al* illustrate a moderate force-pressure relationship in their New Zealand White rabbit studies, but observe poor pressure readings due to motion artifacts (Davis *et al* 2003, Winters *et al* 2009). Go *et al* expanded on these investigators' work using recent technological improvements in fiber optics and investigation of a protective housing unit to mitigate the effects of sensor motion (Go *et al* 2017).

Orthopedic surgical procedures often cause changes to the original physiological length of a muscle (Lieber *et al* 1996, Fridén and Lieber 1998). Tendon transfer is one such procedure which attempts to reestablish function in limbs where range of motion has been lost, for example due to nerve damage (Waters *et al* 1985) or arthritis (Clayton and Ferlic 1974). The optimal outcome of surgery is determined by maximum force production for joint torque. Several factors are considered during surgical planning: route to attachment, muscle synergy and—of most interest for this study—length of donor muscle (Lieber *et al* 1996). Muscle force production is directly related to its length and there is a point of optimal performance. Currently, there is not a quantifiable intraoperative method to guide surgeons to the optimal muscle length resulting in maximum force production. The absence of this methodology often results in the loss of one grade of muscle strength compared to the original donor muscle (Lieber *et al* 1996). In order to facilitate optimal surgical outcomes, the IMP sensor demonstrates to be a promising intraoperative tool that allows minimally invasive assessment of muscle force (Davis *et al* 2003, Winters *et al* 2009, Go *et al* 2017). Therefore, we believe this technique can quantify muscle passive tension and better identify optimal muscle length.

Identification of optimum muscle length and proper tendon placement may avoid degradation of muscle function. So that effective assessment of passive muscle tension can be performed, the IMP device needs to be translated to patient use. This study evaluates the combination of intraoperative experimental techniques with the IMP sensor to assess passive tension in a rabbit model. We hypothesize IMP will be correlated to the passive force. Second, we hypothesize the best sensor insertion will be perpendicular to the muscle fibers compared to parallel. It is believed the perpendicular insertion of the sensor will have

superior anchoring compared to parallel and thus increase the overall correlation to force production.

Methods

Animals

Ethical approval.—All protocols were approved by the Institutional Animal Care and Use Committee at the Mayo Clinic, in compliance with National Institute of Health guidelines. The investigators in this study understand the ethical principles and this work complies with the journal's animal ethics checklist.

Changes in IMP were evaluated in the TA muscle of skeletally mature male New Zealand White rabbits ($n = 5$) obtained from Harlan Laboratories Inc., Indianapolis, IN.

In total, 9 rabbit TA muscles were used to assess the passive force-IMP-length relationship. Animals were kept housed on a 12h light/dark cycle and given a daily ration of food and free choice of water except for food fast on the day of surgery.

Surgical anesthesia

Animals were anesthetized using 35mg kg^{-1} of ketamine (Ketaset®, Fort Dodge Animal Health, Fort Dodge, IA), and 5mg kg^{-1} Xylazine® (Vettek, Bluesprings, MO) via an intramuscular injection into the lumbar muscles. An initial bolus of Propofol (1.5 mg kg^{-1}) was given via intravenous (IV) delivery and a rate between $0.2\text{—}0.6\text{mg/kg/min}$ was used to maintain anesthesia during the surgical procedure. Propofol is selected over isoflurane as it has been shown it does not interfere with skeletal muscle contraction (Bouhemad *et al* 2002). The animal was intubated and mechanically ventilated while monitoring temperature with a rectal thermometer and maintaining the animal's temperature with a heating pad at 37°C (K®-module Model K-20, American Pharmaseal Company, Valencia, CA). Corneal reflex, respiration and heart rate were monitored so the infusion rate of Propofol could be adjusted accordingly. To reduce muscle fatigue, an infusion of 5% dextrose was administered via an IV drip. With the distal tendon of the TA transected, isometric muscle force testing and IMP measurements were performed. Once testing was complete the rabbit was euthanized with an overdose of Pentobarbital IV.

Experimental setup

The sciatic nerve and its peroneal branch extending into the TA muscle were exposed with a 10cm longitudinal incision on the posterolateral aspect of the thigh. A skin incision was made anterior to the ankle to expose the TA tendon. The anterior fascia was released and the tendon was cut distally while the TA muscle was kept in place without injuring the neurovascular pedicle or muscle fibers. The examined muscle was prevented from drying with a constant warm saline drip. The knee and ankle joints were rigidly secured to a platform by transfixation using Kirschner wires 5 min after a localized injection of lidocaine was given.

With the TA muscle exposed and the knee and ankle secured on a custom made platform, a force transducer (MDB-50, Transducer Techniques, Temecula, CA) was attached to the

distal end of the TA tendon, as depicted in figure 1(A). Two fiber optic pressure sensors with nitinol protective housing of diameter 457 μm calibrated for ± 300 mmHg (model FOP-M260, FISO Technologies, Inc.) were inserted into the mid-belly of the TA within 2mm of each other. Insertion technique was varied in relation to the muscle fibers' force generating axis: (i) parallel (i.e. in the direction of fiber shortening)—right limb (figure 1(B), and (ii) perpendicular (i.e. perpendicular to the direction of fiber shortening)—left limb (figure 1(C)). The IMP sensors were placed using a 22G catheter which was removed once the sensors were in place. IMP measurements were taken simultaneous to the isometric force testing described in detail below.

Muscle testing force-IMP-length relationship

To test the hypothesis, we utilized the IMP sensor to assess force by evaluation of isometric force and pressure at positions above and below optimal length (L_o).

Identification of L_o .—A preload was placed on the muscle in increments of 50 g, from 0 to 300 g, by changing the length of the muscle, e.g. larger lengths resulted in larger passive tension or preload. The muscle was stimulated at each preload/length via the peroneal nerve with a bipolar stimulator (Grass SD9; Grass Instrument Co, Quincy, MA) at a frequency of 100 Hz (2 V, 0.4ms). L_o was defined one length increment below which the output force was not able to overcome the 50 g preload.

Muscle testing.—While recording IMP and force, the muscle was passively lengthened from of $\pm 30\%$ of L_o at 5% increments at a rate of no more than 2cm s^{-1} . For isometric activation, the peroneal nerve was stimulated with a bipolar stimulator at a frequency of 100 Hz (10 V, 0.4ms) for a duration of 2–5s. To avoid muscle fatigue, the muscle was allowed to relax for 5 min with zero preload between each increment of length.

Data collection and processing

Data was collected using a custom LabVIEW program (NI USB-6009 DAQ) to simultaneously record input from the force transducer and IMP sensors. The gauge pressure in each passive trial was adjusted so baseline was at zero for the length of L_o and normalized by the maximum pressure for each sensor, referred to as relative pressure as a percentage of maximum. Similarly, force was adjusted at L_o and normalized by the maximum force. Similarly, force was shifted to zero at L_o and normalized by the maximum force. The peak force was identified and corresponding pressures from the two sensors were found at each muscle length. Active force/IMP data was not the focus of data processing, as the study goal was to mimic tendon transfer surgeries in humans, where only passive force is evaluated and no muscle activation occurs. The effects of muscle activation have been reported previously by Davis *et al* (2003) and Winters *et al* (2009).

Statistical analysis

Pearson correlations for IMP and force were evaluated using MatLAB (The MathWorks Inc., Natick, MA). The Fisher's Z transformation was used to compare the two correlation coefficients using a two-tailed test with $\alpha = 0.05$ (Kleinbaum and Kupper 1978). First the

combined relationship of the successful trials ($n = 18$) was evaluated, followed by separate analysis for parallel and perpendicular insertion techniques.

Results

One set of trials was defined as unsuccessful and discarded due to a tear in the muscle during activation and improper sensor placement. This yielded a total of $n = 9$ muscles evaluated.

Force/pressure relationship

The visual trend in the passive IMP measurements reflects that of the force measurements; the force and IMP increase as the length increases past L_o (figure 2(a)). These trends were quantified using Pearson correlations and coefficients of determination are reported. For the combined trials the correlation was 0.74 ± 0.30 . The parallel insertion method (i.e. in the direction of fiber shortening) had significantly higher correlations at 0.91 ± 0.13 compared to the perpendicular insertion at 0.56 ± 0.32 (table 1). Using the Fisher's Z transformation to compare the two correlation coefficients, a statistically significant difference is observed ($p < 0.05$). The measurements for parallel insertion are clustered tightly ($R^2 = 0.91$), whereas, for the perpendicular insertion, data points have a larger spread illustrating a lower correlation ($R^2 = 0.53$). These correlations can be visualized in the scatter plots for both insertions (figure 2(b)).

Discussion

This study demonstrated IMP can be used as a surrogate for passive force assessment. This application is ready to be translated into human application and promises to be a useful tool for orthopedic surgeons during tendon transfer surgeries.

Force/pressure relationship

In our hypothesis, we predicted the perpendicular insertion of the sensor would better anchor the sensor and result in the best force-IMP correlation. We assumed the nitinol housing protects the sensor diaphragm from any mechanical force on the sensor, which are likely from the lateral direction. Opposing the original hypothesis, the study revealed the parallel insertion technique outperformed the perpendicular. The parallel insertion allows the sensor to be oriented in the direction of fiber shortening. We assume this orientation results in lower shear forces compared to the perpendicular insertion. Parallel insertion allows the barbs on the sensor to engage in the interstitial tissue. This secures the sensor and prevents it from being ejected when pressure changes due to fiber shortening and lengthening. The pressure value increases greatly at 20% L_o in the case of perpendicular insertion (figure 2(a)). We theorize shear forces due to the muscle fibers push the sensor out of the muscle. This can cause a suctioning effect on the diaphragm resulting in lower than expected pressure values at lengths 5%-15% of L_o . However, at muscle lengths greater than 20% L_o , the large passive force is likely attributed to connective tissue and the outward force diminishes. If this is the case, it explains the increase in pressure with force at muscle lengths greater than 20% L_o . These findings are similar to those found by Go *et al* who evaluated the performance of the

sensor at isometric tetanic activation at optimal length (Go *et al* 2017). This study expands on that work and further evaluates the performance of the sensor at muscle lengths above and below optimal length. The correlation of force and IMP holds at all muscle lengths.

Comparison to past studies

Results from this study are similar to investigations done previously by Davis *et al*, Winters *et al* and Go *et al*, further confirming the relationship between IMP and force production in the TA muscle (Davis *et al* 2003, Winters *et al* 2009, Go *et al* 2017). Although a relationship was observed in previous studies, this work reports the highest force-IMP correlation (table 1). The same sensor design was first evaluated with isometric muscle activation at optimal length (Go *et al* 2017). The other studies evaluated the isolated TA compartments (Davis *et al* 2003) and intact myofascial compartment (Davis *et al* 2003), however, Winters *et al* concluded the nature of the muscle does not affect the production of pressure (Winters *et al* 2009). Therefore we also conclude, the use of an isolated compartment had little effect on the results in this study. Go *et al* point out that the superior performance of the sensors is likely due to the advances in technology and the introduction of an anchoring device to keep the sensor in place when the muscle fibers are shortening (Go *et al* 2017).

Studies investigating the effects of sensor insertion location have revealed pressure may be a localized effect with increased pressure near aponeurosis, bone and tendon (Sejersted *et al* 1984, Nakhostine *et al* 1993). Jensen *et al* developed a technique to evaluate strain with cine phase contrast MRI (Jensen *et al* 2015a, 2015b) in order to investigate the relationship between strain and IMP. Early findings using these techniques reveal the mid-belly of the human TA had the most uniform strain and will result in the most reliable pressure recordings (Jensen *et al* 2016). Therefore we suggest inserting the sensor in the muscle mid-belly to half depth and avoid tendon insertions.

Clinical relevance

Proper tensioning on the tendons is crucial for successful functional outcome after tendon or muscle transfers. Currently, the tension of the transferred tendon is estimated by the surgeon during the operation, mainly based on past clinical experience. There are some rules of thumb that are commonly used; however, estimating which tension will provide sufficient function of the transferred tendon remains a surgical challenge (Ratner *et al* 2010). For less extensive procedures such as single tendon transfers in the hand, it is possible to use a wide-awake approach (Lalonde 2014). This way the patient can already practice the new function during surgery and proper function can be confirmed. However, it is still not possible to confirm if the tendon is at optimal tension and this approach is not suitable for more extensive procedures such as free functioning muscle transfers. We have shown that this improved technique to measure IMP is a suitable way to indirectly measure optimal tendon tension in a relatively non-invasive way. We believe this technique can be easily implemented into daily surgical practice. Especially for free functioning muscle transfers or more extensive injuries where the muscle belly is already exposed. Transcutaneous placement of the sensors is also possible but some more research is recommended to determine the optimal insertion techniques.

Limitations

The lengthening rate of the muscle can affect the force production and thus observed pressure changes in the muscle. Other studies use a motor with a lever arm to achieve constant rates of lengthening. However, in order to mimic conditions in the operating room the muscle was lengthened manually. The authors recognize the study does not reflect the muscle's true physiological state since the tendon is transected and connected to the force transducer. This is not seen as a strong limitation as the proposed application of this technique is to improve tendon transfer surgeries in which the tendon is transected and reattached at a new sight.

Ideally, IMP measurements would be taken during muscle activation in addition to those during passive motion. The combination of the active and passive pressure-length curves would best help to identify the optimal length of the muscle. None the less, performing muscle activation during surgery would add unwanted time and require restricting the use of muscle relaxants; therefore, the focus of this study was on passive measurements. Additional experiments would further support the findings by increasing the overall sample size. However, to avoid delay in translating this research to clinical applications, the important findings are reported.

Conclusion

Tendon transfers can be used to restore function to a muscle paralyzed due to nerve injury or other tendon/muscle injury. For optimal functional outcome, it is crucial to reconstruct the transferred tendon at optimal tension. The tension can be roughly estimated by the surgeon and function can be roughly tested using a wide-awake approach, however this is not very accurate and not possible in more extensive surgical cases or free functioning muscle transfers. Currently appropriate quantitative intra-operative measurement techniques are lacking. The findings in this study illustrate the IMP sensor can be used to assess changes in passive tension and experimental techniques can be implemented in the operating room. The next step in the translation of this research is to assess passive tension during tendon or muscle transfer surgeries.

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New findings

- What is the central question of this study?

Successful outcomes of tendon and muscle transfers depend on proper muscle tension. A near linear relationship has been seen between muscle force and intramuscular pressure. This study aims to develop an intraoperative technique for assessing passive muscle tension using intramuscular pressure.
- What is the main finding and its importance?

The findings from this study reveal a high correlation between pressure and passive tension in a single muscle. The techniques developed in this study will allow the translation to a human model. The work will help to improve surgical outcomes and aim to retain muscle strength in the patient following procedures such as tendon and muscle transfers.

Figure 1.

(A) Experimental setup with Kirschner wires securing the knee and ankle (a), force transducer connected to the distal tendon of the TA (b), bi-polar stimulator on the peroneal nerve (c), and electrical ground (d). IMP sensors (e) inserted in the mid-belly with different orientations to the muscle fiber shortening direction: (B) parallel and (C) perpendicular.

Figure 2.

Summary of passive IMP measurements reflects the same force measurement trends within the TA of New Zealand White rabbits ($n = 18$). The trends were separated into parallel and perpendicular insertion. Each trial was normalized to the maximum IMP and force and averaged. (a) The increasing trend of IMP and force are seen when plotted versus length. Error bars display SEM. (b) The parallel insertion method (i.e. in the direction of fiber shortening) had significantly higher correlations at 0.91 ± 0.13 compared to the perpendicular insertion at 0.56 ± 0.32 .

Table 1.

Comparison of force-IMP correlation across studies.

Coefficient of determination (mean $\pm$ SD)	Range		Study
	Min	Max	
0.91 $\pm$ 0.13 (parallel)	0.64	0.99	Current
0.56 $\pm$ 0.32 (perpendicular)	0.02	0.87	Current
0.74 $\pm$ 0.30 (combined)	0.02	0.99	Current
0.96	0.86	0.99	Go <i>et al</i> (2017)
0.77 $\pm$ 0.05	0.51	0.93	Winters <i>et al</i> (2009)
0.53 $\pm$ 0.36 (ascend. limb)	0.045	0.84	Davis <i>et al</i> (2003)
0.86 $\pm$ 0.11 (desc. limb)	0.672	0.98	Davis <i>et al</i> (2003)