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SPECIAL ISSUE ON ROTATOR CUFF BIOLOGY AND HEALING

Measurement of in vivo tendon function

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Chronic tendon pathologies (eg, rotator cuff tears, Achilles tendon ruptures) are common, painful, debilitating, and a significant source of medical expense. Treatment strategies for managing tendon pathologies vary widely in invasiveness and cost, with little scientific basis on which to base treatment selection. Conventional techniques for assessing the outcomes of physical therapy or surgical repair typically rely on patient-based assessments of pain and function, physical measures (eg, strength, range of motion, or stability), and qualitative assessments using magnetic resonance imaging or ultrasound. Unfortunately, these conventional techniques provide only an indirect assessment of tendon function. The inability to make a direct quantitative assessment of the tendon's mechanical capabilities may help to explain the relatively high rate of failed tendon repairs and has led to an interest in the development of tools for directly assessing in vivo tendon function. The purpose of this article is to review methods for assessing tendon function (ie, mechanical properties and capabilities) during in vivo activities. This review will describe the general principles behind the experimental techniques and provide examples of previous applications of these techniques. In addition, this review will characterize the advantages and limitations of each technique, along with its potential clinical utility. Future efforts should focus on developing broadly translatable technologies for quantitatively assessing in vivo tendon function. The ability to accurately characterize the in vivo mechanical properties of tendons would improve patient care by allowing for the systematic development and assessment of new techniques for treating tendon pathologies.
Level of evidence: Review Article.

Keywords: Tendon; rotator cuff; in vivo; biomechanics; stress; strain; stiffness

Rotator cuff tears are a common condition, affecting up to 50% or more of the population aged older than 60 years.[4,56,99] This condition is estimated to account for approximately \$3 to \$5 billion per year in medical costs, workers compensations, and decreased productivity in the United States alone.[81,92] In addition, rotator cuff tears have a far-reaching impact on function, comfort, general health, and quality of life.[28,86]

Treatment strategies for managing rotator cuff tears vary widely in invasiveness and cost, with little scientific basis on which to base treatment selection. Patients with rotator cuff tears are typically prescribed 6 to 12 weeks of physical therapy, and surgical repair is indicated when physical therapy fails to improve patients' symptoms.[54] Despite improvements in the understanding of rotator cuff pathology and advances in treatment options, the relative effectiveness of physical therapy and surgical repair is not known.[75,76] Furthermore, although surgical repair of a rotator cuff tear may provide short-term to medium-term pain relief, long-term function is often poor. Normal shoulder strength is rarely restored after rotator cuff repair,[7,13,42,59,62,70,93] and

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repairs of large, chronic rotator cuff tears fail to heal in 20% to 95% of cases.[27,29,35] Borgmästars et al[8] studied long-term outcomes (16-25 years) of rotator cuff repair and found that only 37% of patients had persistent pain relief, while 43% had impaired activities of daily living due to shoulder complaints.

Currently, physicians and therapists must make a subjective judgment about the timing and nature of postoperative activity after rotator cuff repair without knowing the mechanical capabilities of the healing tendon. Conventional techniques for assessing the outcomes of therapy or surgical repair typically rely on patient-based assessments of pain and function, physical measures of joint function (eg, strength, range of motion, or stability), and qualitative assessments using magnetic resonance imaging or ultrasound scans. Although these conventional techniques may provide an indication of joint function, they provide only an indirect assessment of tendon function. The inability to make a direct quantitative assessment of the tendon's mechanical capabilities may help to explain the relatively high rate of failed rotator cuff repairs and has led to an interest in the development of more direct tools for assessing in vivo tendon function.

Tendons function to transmit muscle forces to bone, thereby facilitating movement and contributing to joint stability. The mechanical properties of the tendon and its insertion to bone contribute to its ability to perform its mechanical function and may serve as indictors of normal or compromised tendon function. Thus, physicians could use methods to directly quantify the mechanical loads, displacements, stresses, and strains in tendon to critically evaluate the efficacy of specific physical therapy protocols or surgical techniques for improving tendon healing. From a basic science perspective, the ability to accurately characterize the mechanical properties of tendons in vivo is necessary for the systematic development and assessment of new techniques (eg, tissue-engineered scaffolds) for treating tendon pathologies. Without such tools, advancements in the treatment of tendon injuries will continue to occur incrementally and will be based largely on indirect measures or qualitative assessments of tendon function.

The purpose of this article is to review methods for assessing tendon function (ie, mechanical properties and mechanical capabilities) during in vivo activities. This review will describe the general principles behind the experimental techniques and provide examples of previous applications of these techniques and will also characterize the advantages and limitations of each technique, along with its potential clinical utility.

Implanted sensors

Previous research aimed at understanding in vivo tendon function has relied extensively on sensors that are physically attached to or implanted within tendons. This category of sensors includes strain gauges, buckle transducers, implantable force transducers, and fiber optic transducers (Table I). These devices often rely on strain gauges that deform as the tendon elongates under load (Fig. 1). The deformation causes a change in an electrical signal/voltage that is recorded by data acquisition equipment. Calibration of these devices involves recording the electrical signal/voltage while imposing a known level of force or deformation. Fiber optic transducers work in a similar manner but are based on the variation in light flow that occurs when the transducer is bent or compressed as the tendon is loaded. A brief review of the application of these devices is presented here.

Liquid metal strain gauges have been used frequently in veterinary applications to measure strains and forces of tendons in the forelimb and hind limb of horses during various gait activities.[39,49,67-69,91] Brown et al[9] also used these devices to measure Achilles tendon strain in rabbits during slow hopping.

Buckle transducers have been used for estimating forces in the Achilles tendon of humans during walking and running,[44,45] cycling,[33] and vertical jumping[26] (Fig. 1). Schuind et al[74] used a buckle transducer to measure forces in the flexor tendons of the wrist. Buckle transducers have been used for characterizing medial gastrocnemius tendon force in the cat during treadmill walking.[79] This approach has also been used extensively to characterize in vivo muscle/tendon mechanics in various animal models.[6,14,66]

Implantable force transducers have been used to estimate tendon forces in a variety of animal models. For example, these devices have been used to measure forces in the flexor tendons of horses during gait,[63,89] Achilles tendons[96] and patellar tendons[40] of rabbits during treadmill activity, and patellar tendon of goats[47] and cats.[36] For human applications, Bull, Reilly, and colleagues recently described the use of an arthroscopically implanted force probe for measuring force in the subscapularis tendon during maximum internal rotation.[10,65]

Fiber optic transducers have been used to measure Achilles tendon force in humans during gait[23] and in the Achilles and patellar tendons during vertical jumping.[22] These devices have also been used to measure Achilles tendon forces during a realistic cadaveric simulation of walking.[19,20]

Meyer et al[55] recently described an alternative approach for measuring tendon force that used a surgically *implanted load cell*. This device was implanted in the humerus of a sheep at the insertion site of the infraspinatus tendon and thus recorded tensile forces during elongation of the infraspinatus tendon.[55]

Muscle pressure transducers have also been used in various animal models[15,94,98] and may have future application for assessing tendon function.

The use of implanted sensors has provided considerable insight into the understanding of in vivo tendon function.

Table I Techniques for measuring in vivo tendon function

Approach	Device or technique	Advantages	Limitations	Clinical utility
Implanted sensors	• Liquid metal strain gauges • Force (eg, buckle) transducer • Fiber optic transducer • Implanted load cell • Muscle pressure transducer	• Direct measurement • Readily available	• Invasive • Not designed for prolonged implantation • May alter tendon function • Difficult calibration	• Limited, due to surgical implantation
Medical imaging	• Radiographic measurement of implanted markers: plain radiographs	• Readily available	• 2D • Static • X-ray exposure • Marker implantation/ attachment	• Limited clinical application due to marker implantation and x-ray exposure
	• Radiographic measurement of implanted markers: static RSA or CT imaging	• High accuracy • 3D	• Static • X-ray exposure • Marker implantation/ attachment	
	• Radiographic measurement of implanted markers: dynamic RSA	• High accuracy • 3D • Dynamic	• Limited availability • X-ray exposure • Marker implantation/ attachment	
	• Conventional ultrasound imaging to estimate tissue deformation with anatomical landmark tracking, image correlation, speckle tracking, etc.	• Readily available	• Accuracy not well characterized • 2D	• Potentially high, pending rigorous accuracy assessment
	• Sonoelastography or shear wave elastography	• Potential for direct measure of tendon tissue stiffness	• Not yet used extensively for musculoskeletal applications • Limited availability	• Unknown

2D, 2-dimensional; *3D,* 3-dimensional; *RSA,* radiostereometric analysis.

For example, previous research has used implanted sensors to report peak forces in the human Achilles tendon of 661 N during cycling,[33] 1430 N during gait,[23] 1305 to 2233 N during vertical jumping,[22,26] 3786 N during submaximal hopping,[26] and 9000 N during running.[44] Forces of similar magnitude have been quantified in the equine superficial digital flexor tendon, with Takahashi et al[89] reporting maximum forces of 3110 N during walking, 5652 N during trotting, and up to 7030 N during cantering.[89] In contrast to these high loads, forces of the wrist tendons (flexor pollicis longus, flexor digitorum superficialis and profundus) have been reported to be up to 118 N during a fingertip pinch,[74] and force of the subscapularis tendon during internal shoulder rotation has been reported to be 250 N.[10]

Several significant limitations are associated with the use of implanted sensors: First, the invasive nature of these devices limits the number of willing human participants and places volunteers at increased risk due to the surgical implantation procedure. Furthermore, these devices are not designed to remain implanted for extended periods of time, and therefore are not suitable for longitudinal studies that measure changes in tendon force or strain over intervals longer than several hours. In addition, the extent to which the physical size and presence of these devices alters normal in vivo function is unknown. Lastly, previous research has reported that sensor size, loading rate, cable migration, skin movement, repeated implantation, sensor location within the tendon, rotation of the sensor within the tendon, and rotations of neighboring bones are all capable of significantly affecting sensor output.[19,20,24,25,38,64]

Previous studies have concluded that these implanted sensors should be used with caution and have suggested that the devices are probably not well suited for estimating tissue forces or strains during unrestrained locomotion.[25,38] For additional information on specific technical aspects of these implantable devices, the reader is referred to the excellent reviews by Fleming and Beynnon[24] or Ravary et al.[64]

Medical imaging

Radiographic measurement of implanted markers

Radiographic techniques have been used with increasing frequency to characterize in vivo tendon function (Table I). In

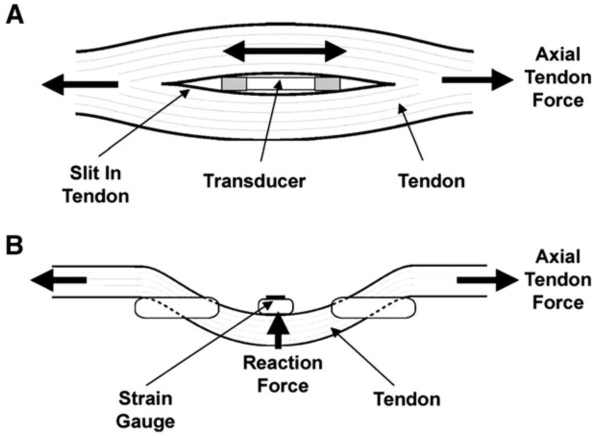

Figure 1 Schematic diagram showing representative examples of implantable sensors for measuring in vivo tendon deformation or strain. Devices that have been used previously include (**A**) liquid metal strain gauges and (**B**) buckle transducers. Figures adapted with permission from Ravary et al.[64]

general, markers are attached to or implanted within the tendon, radiographic images are acquired in various joint positions or loading conditions, and the position of the markers is determined from the images. Small tantalum beads are often used as markers because tantalum is biocompatible (allowing markers to remain implanted indefinitely) and has high radiographic density; also, the location of spherical objects can be determined with high accuracy.

Radiographic techniques that can be used for image acquisition include conventional plain x-ray films, single-plane or dual-plane fluoroscopy, dual-plane radiographic imaging, or computed tomography (CT) scanning. When plain films or single-plane fluoroscopy are used, the 2-dimensional (2D) position of the implanted markers can be determined. If multiple radiographic images can be obtained from different views, radiostereometric analysis (RSA) can be used to calculate the 3D position of implanted markers. CT scanning is also capable of quantifying 3D marker positions. By tracking the position of markers under different loading conditions or during dynamic activities, tendon deformation and strain can be determined.

RSA has been used extensively to measure 3D joint kinematics by tracking the position of tantalum beads implanted into bone,[77] and this approach has been adapted for measuring soft-tissue function. For example, the research team of Hull and Howell et al[82-85] has used this approach to investigate changes in anterior cruciate ligament (ACL) grafts after surgical repair. For tendon applications, Schepull et al[71] have implanted tantalum beads into the Achilles tendon of patients who were undergoing surgical repair after rupture. The beads were injected into the tendon, and the insertion locations were closed with fibrin glue. Static RSA analyses were performed at 6, 12, and 18 weeks after surgical repair. The study reported decreased strain per force over time, increased modulus over time, and changes in tendon length at 1 year after surgery ranging from 9.3 mm of shortening to 11.2 mm of lengthening. The study reported no association between tendon elongation and mechanical properties at 1 year after surgery, and the authors believed that the changes in length did not represent bead migration within the tendon.

This research team has also used this experimental approach to compare operative and nonoperative treatment of Achilles tendon rupture[72] and the effects of platelet-rich plasma on Achilles tendon repair.[73] These studies reported high variability between patients in the reported outcome measures, and the studies failed to detect differences in mechanical parameters between operative and nonoperative treatment, or between platelet-rich plasma and control groups.

RSA has also been combined with more advanced imaging techniques to provide measures of tendon deformation under dynamic conditions. For example, Bey et al[5] used biplane x-ray imaging to measure dynamic, 3D deformation of tendon repair tissue during treadmill trotting in a canine model (Fig. 2). In this study, 1.6-mm diameter tantalum beads were attached to the infraspinatus tendon by passing suture through a 0.5-mm laser-drilled hole and tying the bead to the tendon fibers. This study demonstrated that deformation of the tendon repair tissue during treadmill activity decreased over time when the surgical repair remained intact but increased or failed to change over time in a failed repair.

In contrast to studies of joint kinematics where the beads are rigidly implanted into bone, the secure attachment of tantalum beads to tendons is challenging. As an alternative approach to implanted metal beads, Cashman et al[11] demonstrated the feasibility of using steel sutures for measuring soft-tissue migration after rotator cuff repair. This research team implanted 3 stainless steel suture markers into the supraspinatus tendon and 3 tantalum beads into the greater tuberosity of 10 patients undergoing rotator cuff repair.[3] RSA imaging was performed at 5 times points from 1 hour to 1 year after surgery. Ultrasound imaging at 1 year indicated 5 intact repairs, 3 partial retears, and 2 complete retears. The average increase in distance between the tendon and bone markers after surgery was 0.3 mm at 3 days, 1.2 mm at 3 to 4 weeks, 7.0 mm at 12 to 14 weeks, and 7.8 mm at 1 year. The findings suggest that "gap formation, tendon stretching, or failure of the repair occurred before the 3-month point and that healed intact repairs were then strong enough at this point to cope with the physiologic loading." Although this appears to be an excellent approach for documenting the timing of failed repairs, the authors reported that the steel suture markers failed in 3 of the 10 patients before the 1-year assessment, indicating that these markers are not suitable for longer-term follow-up.

These radiographic approaches have the potential to produce highly accurate measures of tendon deformation under in vivo conditions and provide significant insight into tendon function when combined with dynamic imaging

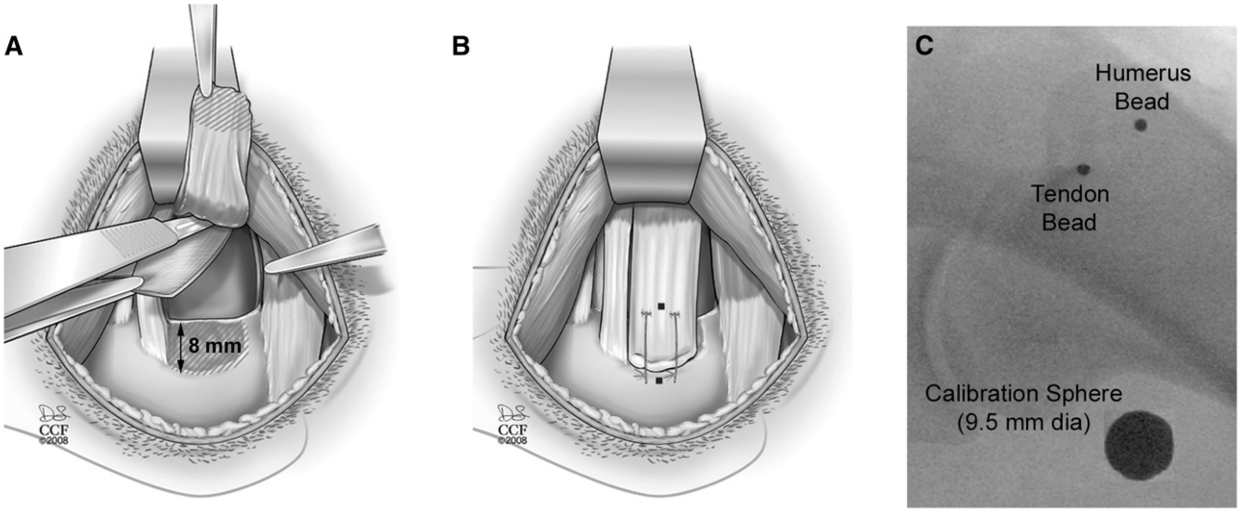

Figure 2 Radiographic methods for assessing in-vivo tendon function measure the 2-dimensional or 3-dimensional position of markers that are attached to or embedded within a tendon. In this example: (**A**) a tendon injury was created in the canine infraspinatus tendon. (**B**) Tantalum beads (shown as *black circles* •) were sewn on the surface of the infraspinatus tendon and implanted into the humerus at the repair site. (**C**) Intraoperative x-ray image shows the tendon bead, bone bead, and calibration sphere (*large circle*). Figure used with permission from Bey et al.[5]

techniques; however, the need for surgical implantation of markers is a significant limitation of this approach. Specifically, it will be difficult to document normal in vivo tendon function if the markers must be inserted under surgical conditions. Additional limitations that will limit the widespread application of this approach include the exposure to ionizing radiation, limited availability of dynamic RSA imaging systems, and the lack of a simple and reliable method for attaching markers to the tendon.

Ultrasound imaging

In recent years, the use of ultrasound imaging for quantifying in vivo tendon deformation or strain has increased. The basic principle is that anatomic landmarks (eg, tendon insertion site or myotendinous junction) can be reliably identified in successive frames of a dynamic ultrasound imaging sequence, the 2D position of these landmarks can be determined, and the time-series of landmark positions can be used to estimate in vivo tendon deformation and strain (Fig. 3). The position of these anatomic landmarks in the ultrasound image is often determined manually, but some researchers have used advanced pattern-matching algorithms to automatically or semiautomatically track the location of unique grayscale patterns within the tendon.

This experimental approach is conceptually attractive for several reasons: no physical sensors are implanted, images can be acquired dynamically, ultrasound imaging has no known side effects, and ultrasound systems are relatively inexpensive and readily available. Furthermore, the ultrasound-based estimates of tendon deformation or strain are frequently combined with estimates of tendon force and stress to provide in vivo estimates of force, deformation, and stiffness, or stress, strain, and modulus.

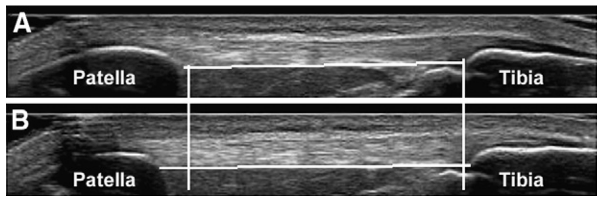

Figure 3 Ultrasound-based approaches for measuring tendon deformation or strain involve acquire images of the tendon under 2 or more loading conditions, and then manually or automatically tracking the position of anatomic landmarks. In this example, ultrasound images of the patellar tendon are shown (**A**) at rest and (**B**) during isometric contraction. The *horizontal lines* indicate the tendon's length and the *vertical lines* indicate the tendon's rest length to indicate the change in length with muscle contraction. Figure adapted with permission from O'Brien et al.[60]

Studies using this ultrasound-based approach have focused primarily on characterizing in vivo function of the Achilles tendon,[1,2,31,37,46,50,58,61,88,90] quadriceps/patellar tendons,[34,60,78,87,97] and tibialis anterior tendons.[21,51-53] Several studies, for example, have focused on characterizing strains, estimated forces, or mechanical properties in the Achilles tendon during maximum isometric contractions.[1,2,31,46,50,58,88] The effects of low-strain vs high-strain exercise protocols,[1] an 8-week strengthening program,[90] a warm-up protocol,[37] and a comparison of static stretching vs warm-up[61] on Achilles tendon mechanical properties have also been evaluated using this experimental technique. Kongsgaard et al[46] reported maximum in vivo Achilles tendon deformations ranged from 2.2 to 2.4 mm during maximum isometric plantarflexion,[46] whereas Muramatsu et al[58] reported maximum Achilles tendon displacements of 4 to 16 mm, depending on torque level. In general, maximum Achilles tendon strains have been reported to be 2% to 9%.[37,58,61,90]

Recently, Kim et al[41] used an ultrasound-based approach to document strains in the rotator cuff supraspinatus tendon. Ultrasound images were collected during isometric and isotonic abduction, and longitudinal strains were calculated in the superficial, middle, and deep regions of the supraspinatus tendon with an automated tracking technique. During isometric contraction, the study reported peak strains of 17%, 9.1%, and 3.4% in the superficial, middle, and deep regions of the supraspinatus tendon, respectively. Peak strains in the superficial region were reported to range from 10.9% to 35.3% across shoulders.

An ultrasound-based approach for measuring in vivo tendon function shows great promise and overcomes many of the limitations associated with previously reported techniques. However, this approach is not without limitations. Perhaps the most significant limitation is that the in vivo accuracy of this technique is largely unknown. In vitro assessments of accuracy typically show that the technique performs well under very well controlled conditions where deformation occurs parallel to the imaging plane. However, the extent to which the ultrasound 2D imaging plane can be aligned and maintained parallel to the direction of in vivo tendon deformation is unknown. Several studies have acknowledged this issue,[34,97] For example, Hansen et al[34] acknowledged that ‘‘an inherent limitation…is the 2-D nature of the technique’’ and that a ‘‘slightly altered angle of the transducer relative to the sagittal plane may induce small changes in the US picture, thereby causing artefactual length changes in the subsequent analysis.’’ How orientation of the ultrasound-imaging plane can be maintained parallel to the direction of tendon deformation is unclear, particularly when the activity being tested involves a maximal contraction. Consequently, the extent to which out-of-plane deformations affect accuracy remains unknown.

Although not as informative as a rigorous assessment of accuracy, several studies have reported repeatability of the ultrasound-imaging technique. For example, Kongsgaard et al[46] assessed between-day reproducibility and reported a ‘‘typical error’’ of 11.8% in maximum Achilles tendon deformation and 8.8% in Achilles tendon stiffness. Similarly, Muramatsu et al[57,58] characterized between-day reproducibility and reported that coefficients of variation were approximately 5% to 14%. However, measures of repeatability, reproducibility, or reliability are not synonymous with accuracy, because it is possible to have high repeatability with low accuracy (ie, to be consistently wrong). As a consequence, it remains unclear if ultrasound-imaging techniques have sufficient accuracy to detect differences in in vivo tendon mechanical function due to clinical interventions such as physical therapy or surgical repair.

Sonoelastography (also referred to as ultrasound shear wave elastography) is a relatively new ultrasound-based technique that has been used to directly estimate in vivo tissue stiffness. This technique has been validated for assessing the mechanical properties of muscle and breast tissue,[12,30,32,80,95] and there are preliminary reports of the application of this technique in the Achilles tendons of rabbits[48] and humans.[16-18,43] The accuracy and reliability of this technique for quantifying in vivo tendon function has not been rigorously evaluated., however, and the long-term clinical utility of this technique is largely unknown.

Conclusion

Chronic tendon conditions are common, painful, debilitating, and a source of significant medical expense. Conventional techniques for assessing the outcomes of treatment provide only an indirect assessment of tendon function and are therefore not designed to rigorously characterize the mechanical characteristics of the tendons themselves. The techniques for directly measuring the mechanical properties of tendons under in vivo conditions that currently exist have limited use due to invasiveness, lack of widespread availability, and uncertain accuracy. Future efforts should focus on developing broadly translatable technologies for quantitatively assessing in vivo tendon function. The ability to accurately characterize the in vivo mechanical properties of tendons would improve patient care by allowing for the systematic development and assessment of new techniques for treating tendon pathologies.

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