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Characterizing musculoskeletal tissue mechanics based on shear wave propagation - a systematic review of current methods and reported measurements

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Abstract

Developing methods for the non-invasive characterization of the mechanics of musculoskeletal tissues is an ongoing research focus in biomechanics. Often, these methods use the speed of shear wave propagation to characterize tissue mechanics (e.g., shear wave elastography and shear wave tensiometry). The primary purpose of this systematic review was to identify, compare, and contrast current methods for exciting and measuring shear wave propagation in musculoskeletal tissues. We conducted searches in the Web of Science, PubMed, and Scopus databases for studies published from January 1, 1900, to May 1, 2020. These searches targeted both shear wave excitation using acoustic pushes and mechanical taps, and shear wave speed measurement using ultrasound, magnetic resonance imaging, accelerometers, and laser Doppler vibrometers. Two reviewers independently screened and reviewed the articles, identifying 525 articles that met our search criteria. Regarding shear wave excitation, we found that acoustic pushes are useful for exciting shear waves through the thickness of the tissue of interest, and mechanical taps are useful for exciting shear waves in wearable applications. Regarding shear wave speed measurement, we found that ultrasound is used most broadly to measure shear waves due to its ability to study regional differences and target specific tissues of interest. The strengths of magnetic resonance imaging, accelerometers, and laser Doppler vibrometers make them advantageous to measure shear wave speed for high-resolution shear wave imaging, wearable measurements, and non-contact ex vivo measurements, respectively. The advantages that each method offers for exciting and measuring shear waves indicate that a variety of systems can be assembled using currently available technologies to determine musculoskeletal tissue material behavior across a range of innovative applications.

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Conflict of interest statement

One of the authors (JDR) is a co-inventor on a pending patent application related to one of the methods described herein. The other authors declare no conflict of interest.

Keywords

ultrasound elastography; magnetic resonance elastography; shear wave tensiometry; laser Doppler vibrometry; muscle; tendon; ligament; cartilage; bone

Introduction

Characterizing the mechanics of musculoskeletal tissues is crucial for understanding the etiology and progression of diseases, injuries, and disorders; as well as normal functioning. The mechanics of these tissues, particularly the tissue loads (e.g., axial stresses) and intrinsic material properties (e.g., elastic and shear moduli), are known to change in response to changes in loading,[411, 444] tissue health,[34, 221, 384] and morphology.[412] These changes occur both in the native tissue and following interventions such as orthopedic surgery[420] and rehabilitation.[452] Further, the material behavior of musculoskeletal tissues can change with aging[461, 516] and following changes in overall health.[303] While ex vivo mechanical tests such as axial, bending, and shear tests are valuable for characterizing tissue mechanics, they do not necessarily capture the complex loading environment of musculoskeletal tissues in vivo. Hence, the non-invasive evaluation of musculoskeletal tissue mechanics in vivo is fundamental to understanding the role of these tissues in human movement and the physiological processes that precede and follow disease or acute injury. Moreover, by characterizing these mechanics non-invasively, clinicians and researchers can evaluate tissue health without further disruption, enabling diagnostic monitoring and intervention planning.

Several methods for characterizing the mechanics of musculoskeletal tissues use the speed of shear wave propagation (i.e., shear wave speed) to non-invasively quantify tissue mechanics in vivo. These methods excite a shear wave in the tissue and then measure the speed with which the shear wave propagates along the tissue. The shear wave speed depends on both applied loads[112, 337] and material properties of the tissue.[132, 165, 337] To evaluate loading, a method often termed shear wave tensiometry can be used to measure the axial stress in a musculoskeletal tissue of interest across a broad range of tensile loads during functional activities.[337] To evaluate material properties, a method often called shear wave elastography (SWE) can be used to measure tissue moduli and is commonly performed in unloaded or passively stretched tissues using ultrasound (e.g., Bercoff et al. 2004[61]). This measurement can also be performed using magnetic resonance imaging (MRI), which is termed magnetic resonance elastography (MRE) (e.g., Debernard et al. 2011[141]). Despite the conceptual simplicity of these methods, the details of their implementation are highly dependent on the tissue type, loading state, boundary conditions, and mechanical parameters of interest (e.g., stress or shear modulus). This leads to challenges in identifying the most appropriate excitation and measurement methods to acquire meaningful data for a given application.

Systems to excite shear waves and measure the shear wave propagation speed are composed of two primary components: actuators and sensors. The fundamental requirement of an actuator is to transversely displace the tissue of interest to excite a shear wave. This may be accomplished using either non-contact or contact methods. An ultrasound transducer capable of generating an acoustic push (i.e., acoustic radiation force impulse (ARFI)) is the most commonly used non-contact method (e.g., Nightingale et al. 2002[381]) (Figure 1). Several contact actuators have been used to create a mechanical tap, with a few examples including a piezoelectric actuator (e.g., Martin et al. 2018[337]), an electromagnetic actuator (e.g., Cortes et al. 2015[132]), and a pneumatic actuator (e.g., Debernard et al. 2011[141]) (Figure 1). Equally as important as the actuators used to excite shear waves are the sensors used to track transverse motion of either the tissue of interest or the overlying tissue during shear wave propagation (Figure 2). For example, medical imaging modalities such as ultrasound and MRI are commonly used to measure shear wave propagation. In these systems, the transverse displacement of the tissue is measured via serial imaging in a region of interest (e.g., Bercoff et al. 2004[61] and Muthupillai et al. 1995[371]). Transverse accelerations and velocities of the tissue surface can also be measured using accelerometers (e.g., Cescon et al. 2008[94]) and laser Doppler vibrometers (e.g., Blank et al. 2020[70]), respectively. Given the multitude of actuators and sensors available, a prerequisite step to developing a system to non-invasively characterize the mechanics of musculoskeletal tissues is a thorough understanding of the technologies available for exciting shear waves and measuring shear wave speeds.

Accordingly, the primary objective of this systematic review is to identify, compare, and contrast commonly used methods for exciting shear waves and measuring shear wave speeds in musculoskeletal tissues. Our focus is on the application of these methods rather than their theoretical foundations, which have been reviewed previously (e.g., Sarvazyan et al. 2013[442]). With an understanding of the pros and cons of each method, researchers will be better prepared to develop novel measurement systems to assess the mechanics of musculoskeletal tissues in unique applications. A secondary objective is to compile shear wave speeds and measures of material properties in a broad range of musculoskeletal tissues and loading conditions. With these baseline datasets, researchers will be able to better evaluate whether the measurements of their novel systems are in the range of previous studies in similar tissues and/or loading conditions.

Methods

Literature Search Strategy

We conducted this systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[364] The Web of Science (Clarivate, Web of Science Core Collection), PubMed (National Institutes of Health, US National Library of Medicine), and Scopus (Elsevier B.V.) databases were used to perform a systematic search of primary research articles that used shear wave excitation and measurement methods in musculoskeletal tissues. The search was limited to peer-reviewed primary research articles published in English. Other document types, including review articles, pre-prints, dissertations, book chapters, conference proceedings, and conference abstracts, were excluded. Search methods were developed with advising from librarians at the University of Wisconsin-Madison Ebling Library for the Health Sciences.

The search terms (Table S1) were used to assemble a preliminary pool of candidate articles from each of the three databases. Each search included broad search terms specifying the tissue type, wave type, and description of propagation, as well as more specific search terms unique to the method of excitation or measurement, allowing search results to be categorized by method. The search terms for tissue type reflected the tissues of interest for this review, namely muscle, tendon, ligament, bone, and cartilaginous tissues (including menisci). The excitation methods were divided into two categories: ultrasound (i.e., acoustic push) and mechanical (i.e., mechanical tap) (Figure 1). The measurement methods were divided into four categories: ultrasound, MRI, accelerometers, and laser Doppler vibrometers (Figure 2).

For each Web of Science and PubMed search, at least one term from each of the broad categories (all rows in the left column in Table S1) and at least one term from the method categories (one row in the right column in Table S1) had to appear in any field for the article to be considered. For each Scopus search, the search domain was limited to article title, abstract, and keywords. This limited search domain was necessary because Scopus indexes the titles of all references listed within each journal article in the “all fields” setting, resulting in a large number of unrelated articles matching the search terms. Here is an example of the search for the mechanical tap excitation method: ([Tissue Type] ***AND*** [Wave Type] ***AND*** [Description of Propagation] ***AND*** [Mechanical Tap]) is: ([(musculoskeletal* AND tissue*) OR (orthopedic* OR orthopaedic* OR muscu* OR muscl* OR tendon OR tendons OR ligament* OR bone* OR bony* OR cartilag* or menisc*)] ***AND*** [“shear wave*” OR “transverse wave*” OR “s-wave*” OR “surface wave*”] ***AND*** [propagat* OR elastography* OR speed* OR veloc*] ***AND*** [actuator* OR stimulat* OR push* OR piezo* OR shaker*]). Refer to the supplementary material for a full description of the searches performed for each method-of-interest (Table S1).

The initial search, which was performed by a single reviewer, was limited to articles published between the dates of January 1, 1900 and December 31, 2019. This yielded a total of 912, 766, and 906 results in the Web of Science, PubMed, and Scopus databases, respectively (Figure 3). After merging the results from all databases for each method category, a total of 1,277 out of 2,584 articles were identified as duplicates and removed. We divided the remaining 1,307 articles evenly amongst teams of two independent reviewers. Within each team, each reviewer screened the titles, abstracts, and keywords of their assigned articles to ensure that the article fit within the scope of the review. Common reasons for article exclusion were an emphasis on theory or simulation without experimental validation, as well as non-musculoskeletal applications. Articles studying adipose tissue (e.g., heel pad and patellar fat pad), aponeurosis, fascia, joint capsule, and tumors were excluded from this review. Phantom studies in which the phantom was not specifically musculoskeletal tissue-mimicking were also excluded. For each of the articles remaining after screening, full-text articles were acquired and critically assessed for eligibility by teams of two independent reviewers. If an article was disagreed upon during either the screening or eligibility phases, the opinion of a third independent reviewer was used to reach a consensus.

The last search was performed on articles published between January 1, 2020 and May 1, 2020 and yielded 77 additional articles that were subsequently screened and assessed for inclusion, as described previously. Ten articles were included from additional sources because they were known to the authors but did not appear in any of the searches. The final number of studies included in the systematic portion of this review after all screening, eligibility assessments, and additional searches were performed were 69, 11, 476, 36, 6, and 9 for the acoustic push, mechanical tap, ultrasound, MRI, accelerometers, and laser Doppler vibrometers, respectively.

Data Extraction and Risk of Bias

The outcomes of interest were descriptions of the experimental conditions, including the excitation and measurement methods, equipment, and subject/specimen information. Key results relevant to shear wave tensiometry and elastography were also extracted, particularly the shear wave speed, the shear moduli, and the elastic moduli. We emphasized the most representative results in studies where extensive conditions were studied. This involved prioritizing the presentation of in vivo results, common joint angles and tissues, and comparisons between the control and most extreme experimental groups (e.g., wave speed measurements under zero load and maximum load). Data from fibrocartilage (e.g., meniscus) and articular cartilage were grouped together for presentation of cartilaginous tissues. The articles were divided among each of the five reviewers for extraction of the pre-defined outcomes. A form was used to ensure consistency between reviewers, and the final extracted data was checked by one additional reviewer. No authors were contacted for additional information. After data extraction, we organized the papers by measurement modality and further by tissue type. To determine the effect of tissue load on measured shear wave speeds, we classified each paper as either “low” or “high” load according to the level of loading on the tissue reported in the paper. We classified load in in vivo studies as “low” if the tissue was stretched passively (e.g., during a passive range-of-motion task). We classified load in in vivo studies as “high” if the subject(s) actively contracted muscles at a minimum of 20% maximum voluntary contraction or the applied joint load was reported as high (e.g., during a laxity assessment). If the authors did not specify an activation percentage or applied load, then we classified the load level by approximating the amount of muscle activation given the nature of the task (e.g., holding a weight). In ex vivo studies, we classified the load as “high” when there was a reported load that was distinct from a reference or unloaded state. Otherwise, the load in ex vivo studies was classified as “low”. Tissue loads caused by ultrasound probe compression against the structure were also classified as “low”.

We minimized the risk of bias by reviewers by consulting a professional research librarian when developing the search terms and by having two independent reviewers perform article screening, eligibility assessments, and data extraction.[210] A source of bias at the study-level may be exclusion of articles published in languages other than English.

Results

The 525 papers included in this systematic review are summarized in the following sub-sections and in Tables S2-S5. These sub-sections are the same as those used during the search process (i.e., Methods Categories, Table S1) that included two excitation methods: ultrasound excitation (i.e., acoustic push) and mechanical excitation (i.e., mechanical tap) (Figure 1), and four measurement methods: ultrasound, MRI, accelerometers, and laser Doppler vibrometers (Figure 2). The supplemental tables that include all the extracted data (Tables S2-S5) are organized by measurement method but include both excitation and measurement methods for each study when specified.

Ultrasound Shear Wave Excitation

In this systematic review, 449 studies, or 86% of the total included studies, utilized ultrasound technology to excite shear waves in musculoskeletal tissues including muscle (n = 322), tendon (n = 100), ligament (n = 21), cartilage (n = 9), and bone (n = 21), as well as musculoskeletal tissue-mimicking phantoms (n = 11). Common strategies of shear wave excitation among acoustic pushes included acoustic radiation force impulse (ARFI)[381] and supersonic shear imaging excitation (SSI).[61] Studies using ultrasound excitation were conducted in musculoskeletal tissues ex vivo (n = 51), in situ (n = 11), and in vivo (n = 376). Shear waves excited by ultrasound were often measured using ultrasound as well.

Mechanical Shear Wave Excitation

In addition to the more common ultrasound wave generation technologies, 76 studies, or 14% of the total included studies, utilized a mechanical tapping device to excite shear waves in musculoskeletal tissues. Mechanically excited shear waves were used to study muscle (n = 41), tendon (n = 18), ligament (n = 1), cartilage (n = 4), bone (n = 4), and musculoskeletal tissue-mimicking phantoms (n = 9). These mechanical excitation technologies have included piezoelectric actuators (e.g., Martin et al. 2018[337]), electromagnetic actuators (e.g., Cortes et al. 2015[132]), and pneumatic actuators (e.g., Debernard et al. 2011[141]). These studies were conducted in musculoskeletal tissues ex vivo (n = 24), in situ (n = 3), and in vivo (n = 41).

Ultrasound Shear Wave Measurement

In addition to excitation, ultrasound is frequently used to measure the propagation of shear waves in musculoskeletal tissues. In this systematic review, we found 476 studies that used ultrasound technology to measure shear wave propagation (Figure 3). Most frequently (90% of all included studies), ultrasound was used to both excite and measure shear wave propagation (Table S2). The ranges of mean shear wave speeds measured using ultrasound were 0.7–16.9 m/s in muscle, 0.5–36.0 m/s in tendon, 1.7–29.7 m/s in ligament, 2.9–5.3 m/s in cartilage, 1074–3623 m/s in bone, and 1.2–7.0 m/s in phantoms (Table 3, Figure 4). Many of these studies also reported the shear or elastic moduli of the tissue. The ranges of mean shear moduli were 0.6–240.0 kPa in muscle, 8.4–563.5 kPa in tendon, 31.1–879.6 kPa in ligament, and 3.1–40.7 kPa in cartilage, $3.0–6.7 \times 10^6$ kPa in bone, and 3.8–64.6 kPa in phantoms (Table 4, Figure 5). The ranges of mean elastic moduli were 2.0–268.2 kPa in muscle, 22.6–722.4 kPa in tendon, 24.5–230.6 kPa in ligament, 17.1–50.3 kPa in cartilage, $6.5–25.8 \times 10^6$ kPa in bone, and 52.5–187.6 kPa in phantoms (Table 5, Figure 6).

Magnetic Resonance Imaging Shear Wave Measurement

There were 36 studies that used MRI measurements of shear wave propagation in conjunction with either ultrasound or mechanically excited shear waves to study muscle, cartilage, and tissue-mimicking phantoms (Table S3). The range of mean shear wave speeds was 1.0–4.7 m/s for muscle (Table 3, Figure 4). The mean shear wave speed was 2.9 m/s in phantoms (n = 1) (Table 3, Figure 4). The ranges of the mean shear moduli were 1.3–54.0

kPa in muscle, 1083–7714 kPa in cartilage, and 2.9–28.5 kPa in phantoms (Table 4, Figure 5). The range of mean elastic moduli was 11.4–71.0 kPa in muscle (Table 5, Figure 6).

Accelerometer Shear Wave Measurement

Six studies used accelerometer measurements of shear wave propagation in conjunction with mechanically excited shear waves to study muscle and tendon (Table S4). The mean shear wave speed was 2.4 m/s in muscle (n = 1) (Table 3, Figure 4). The range of mean shear wave speeds was 34.1–85.6 m/s in tendon (Table 3, Figure 4).

Laser Doppler Vibrometer Shear Wave Measurement

Nine studies used laser Doppler vibrometers to measure shear wave propagation (Table S5). Laser Doppler vibrometers were most commonly used with mechanically excited shear waves to measure the mechanics of muscle, tendon, ligament, cartilage, and bone tissues, as well as tissue-mimicking phantoms. The ranges of mean shear wave speeds were 4.0–12.4 m/s in muscle and 24.2–165.0 m/s in phantoms (Table 3, Figure 4). The mean shear wave speed was 128.0 m/s in ligament (n = 1). The ranges of mean shear moduli were 700–1000 kPa in cartilage and 0.8–0.9 kPa in phantoms (Table 4, Figure 5).

Discussion

The primary purpose of this systematic review was to identify the broad range of technologies and methods for exciting shear waves and measuring shear wave speeds in musculoskeletal tissues, then compare and contrast them to provide insight into building novel excitation and measurerments systems for future clinical and biomechanical investigations. Our secondary purpose was to summarize the range of shear wave speeds, shear moduli, and/or elastic moduli in the 525 papers by tissue and measurement type. We further sub-divided these summaries by the sensor used to measure shear wave speeds.

Ultrasound Shear Wave Excitation

The most common technique used to excite shear waves includes methods that use an acoustic push applied transversely to the tissue of interest (Figure 1). Acoustic pushes using an ultrasound transducer are viable for non-invasively characterizing material properties of human tissue in vivo and are particularly useful because they provide a stimulus that can extend through the depth of a tissue of interest; hence, acoustic pushes are useful for studying deep tissues (e.g., multifidus[22] and tibialis posterior[387]). In an acoustic push, the ultrasound transducer emits an acoustic radiation force impulse (ARFI) capable of exciting shear waves at a prescribed focal depth using one or a sequence of pushing beams.[381] Another implementation of an acoustic push commonly used in musculoskeletal tissues is supersonic shear imaging (SSI), in which successive focused pushing beams are used to build fast, two-plane shear waves through constructive interference of each sequential shear wave excited at locations through the depth of the tissue.[61] Another method a series of unfocused pushing beams across the tissue width to generate a 2D elasticity map using shear waves generated in one experimental collection (comb-push ultrasound shear elastography (CUSE)).[458] However, the unfocused pushing method limits this technique to surface level tissues like tendon and muscle, and this method has yet to be used widely across musculoskeletal tissues.

There are distinct advantages and disadvantages to exciting shear waves using an acoustic push (Table 1). For example, acoustic pushes can excite a shear wave uniformly through the entire tissue thickness (i.e., a plane wave). Additionally, it is easier to excite a particular tissue or tissue region with the image guidance provided by ultrasonography. A disadvantage of ultrasonic excitation is that it may be burdensome to measure shear wave speeds in musculoskeletal tissues during movement. Additionally, the structure of the tissue of interest (e.g., muscle fiber pennation[482]) can cause scattering of the acoustic push and variable acoustic attenuation, which can lead to a reduction in displacement amplitude near the focal location.[390] This is especially true of anisotropic tissues,[188] where users may need to know the primary direction of anisotropy prior to shear wave excitation. However, acoustic pushes are the most feasible form of excitation in methods that use ultrasound to measure shear waves because it limits the components necessary to excite and measure in the system.

Mechanical Shear Wave Excitation

The second most common technique used to excite shear waves includes methods that use mechanical excitation to generate a shear wave in the tissue of interest. This method of excitation has most frequently been used in vivo. For instance, mechanical taps are the primary method of excitation for shear wave tensiometry, where shear waves are excited using a wearable piezoelectric tapper mounted superficial to the skin over the tissue of interest.[162, 262, 337] Additionally, piezoelectric tappers have been used to excite shear waves in tissues ex vivo, such as tendon, ligament, and muscle.[70, 314, 339] Mechanical excitation methods have also been used when monitoring shear waves using ultrasonic imaging. For example, shear waves excited by piezoelectric elements have been used to study the material properties of cancellous bone.[35] Handheld mechanical shakers have also been used to excite shear waves in the Achilles and semitendinosus tendons, with the resulting shear wave speeds being measured using ultrasound.[132, 465] Finally, mechanical excitation is a prominent method of shear wave excitation used during MRE.[50, 58, 380, 391]

There are distinct advantages and disadvantages to exciting shear waves using a mechanical excitation (Table 1). When measuring shear wave speeds during human movement, it may be more feasible to excite shear waves using a mechanical actuator[162, 262, 337] than an acoustic push due to the smaller size and profile of a piezoelectric actuator compared to that of an ultrasound probe. Additionally, mechanical actuators provide a method of excitation that generates a 3D displacement field,[199] can be high in amplitude and untethered, and is typically easier to adapt for compatibility with MRI,[488] which is why they are used more frequently than ultrasound-generated acoustic pushes in MRE. A final advantage of mechanical actuators is their capacity to generate a greater magnitude of input motion/ force, which increases the amplitude of the shear wave and thus the signal-to-noise ratio of the measurement. A disadvantage of using a mechanical actuator is that it generates a complex excitation that contains both compressive and shear wave components.[132] Hence, mechanical actuators may not excite a uniform shear wave through the depth of the tissue, which is why they are infrequently used in studies exploring spatial variations in shear wave propagation measured using ultrasound. Additionally, noninvasive mechanical actuators are limited to applications of superficial tissues because the induced motion must pass through overlying tissue before exciting a shear wave in the tissue of interest. In conclusion, mechanical actuators are most feasible for exciting high-amplitude shear waves in superficial tissues, such as in wearable applications.

Ultrasound Shear Wave Measurement

Ultrasound is the most common clinical tool used to measure shear wave speeds in musculoskeletal tissues. To our knowledge, one of the first applications using this method for measuring shear wave propagation on musculoskeletal tissue was employed in animal tissue ex vivo. This study by Ramana et al. showed that shear wave speed measurements could be used to characterize material properties in striated leg muscle.[418] Since then, shear wave elastography has seen widespread use in other applications and has emerged as the primary method for measuring shear wave speeds in vivo, where muscles are the most common musculoskeletal tissue studied. Using ultrasound, shear wave speeds can be measured in parallel and pennate muscles, such as the biceps brachii,[4, 102, 170] biceps femoris,[18, 71, 122] and soleus,[287] in healthy skeletal muscle with unique functions (e.g., masseter[45]), and in skeletal muscles with unique fiber patterns (e.g., pectoralis major[306]). Hence, the versatility of ultrasound measurement of shear wave speed often makes it the best candidate for research groups interested in more than one type of muscle.

A likely source of variation in ultrasound-measured shear wave speeds (Figure 4) is the variability in the specific joint pose, subject demographics, and tissue health. This can easily be seen in studies focused on the Achilles tendon, which is a tissue widely studied with elastography because it is a large, superficial tendon. Ruan et al. noted that shear wave speeds can differ by 0.5–1.5 m/s between the relaxed and tensioned Achilles tendon, and that measured shear wave speeds can be greater in older groups of subjects.[425] DeWall et al. reported shear wave speeds of 7.2 m/s in the plantarflexed and 12.0 m/s in the neutral Achilles tendon,[147] while Karatekin et al. reported shear wave speeds of 6.5 m/s in the plantarflexed and 7.4 m/s in the neutral Achilles tendon, albeit in an ankle orthosis.[259] Dewall et al. also showed that tear thickness may alter measured shear wave speeds in an ex vivo tendon model.[146] Finally, shear wave speeds in the unloaded Achilles, and thus material properties, are known to vary for subjects with tendinopathy.[126, 151, 555] Together, these studies indicate that even tissues of the same type can have different shear wave speeds during different loading conditions and across different age groups, and that these differences are further exacerbated by tissue pathology, which can also alter the shear wave speed measured in the tissue.[151] Thus, when comparing measured shear wave speeds to those from prior studies, it is important to identify a study with similar specific joint poses, subject demographics, and tissue health.

There are distinct advantages and disadvantages to measuring shear waves using ultrasound (Table 2). A distinct advantage of using this modality is the ability to measure shear wave speeds in deep tissues and in tissues with material properties that vary regionally.[147] Further, the corresponding image is useful for guiding handheld measurements and can be used to verify measurement location relative to the tissue of interest and the direction of tissue anisotropy in fibrous tissues. However, as stated previously, ultrasound systems that excite shear waves may have variable excitation patterns due to the structure of the tissue of interest.[390, 482] Additionally, shear wave speeds and material properties measured using ultrasound elastography are dependent on tissue anisotropy,[38,40,82,91,297] so users must make an educated assumption about tissue anisotropy with respect to transducer orientation prior to measurement to avoid misinterpretation of experimental results.[32] Finally, when using ultrasound elastography on tissues undergoing high loads, especially in stiff, transversely isotropic tissues like the Achilles tendon, one must consider the tradeoff between spatial and temporal resolution within a set ultrasound system. A key example of this is a study by Martin et al., who found that shear wave speeds exceeding 12–14 m/s can saturate the ultrasound signal using a Supersonic Imagine Aixplorer system.[336] These effects should be accounted for when designing an experimental setup using a clinical ultrasound system. In conclusion, measuring shear wave propagation using ultrasound is most feasible under experimental conditions that do not require both high spatial and temporal resolution (e.g., detailed measurements in static tissue, or low-resolution measurements in a dynamically loaded tissue).

Magnetic Resonance Imaging Shear Wave Measurement

In addition to ultrasound, MRI is an imaging modality commonly used to measure shear wave propagation in musculoskeletal applications. MRI offers an additional dimension to image, as well as improved resolution relative to ultrasound. To our knowledge, the first in vivo musculoskeletal application of MRE was performed by Dresner et al. on the biceps brachii, where they measured an increase in muscle stiffness with increasing muscle contraction.[158] These results agreed with previously published stiffnesses determined via sonoelastography,[311] suggesting that MRE is a viable method for determining material properties of muscle in vivo. The majority of studies using MRE in vivo have focused on lower extremity muscles, and several studies have reported a shear modulus of 2.1–4.6 kPa in the vastus medialis at rest.[59, 141, 142] However, this may change with pathology and contraction.[57, 58] Basford et al. noted that the shear modulus was much higher for muscles in the shank;[50] however, more recent studies in the soleus, gastrocnemius, and tibialis anterior have quantified a shear modulus lower than the quadriceps group (1.9–2.0 kPa).[203] Differences in measured material properties like these across studies could be due to experimental setups that have changed over time.

There are distinct advantages and disadvantages to measuring shear waves using MRE (Table 2). The first advantage is that MRE has a higher processing resolution than ultrasound elastography, which can provide a more detailed description of local shear wave speeds and thus material properties. Second, like ultrasound, MRE analysis can image deep tissues in the extremity of interest. A final advantage of MRE is that the tissue's mechanical information obtained from MRE can be combined with structural information from 3D images reconstructed using MRI. Despite these numerous advantages, MRE is not used to measure fast longitudinal waves that have a frequency exceeding the maximum vibration frequencies observable in MRE (1 kHz).[462] This disadvantage is why MRE is commonly used in unloaded muscle instead of loaded tendon or ligament. A second disadvantage is that with higher resolution comes longer collection and processing times,[61] which is the reason that the tissue of interest remains stationary during the collection time in most studies. In conclusion, MRE is most feasible for acquiring high resolution, local shear wave speed measurements in tissues under quasi-static loading.

Accelerometer Shear Wave Measurement

The recent use of accelerometers to measure shear wave speeds has enabled the characterization of tendon loading during dynamic human movement in vivo (i.e., shear wave tensiometry). Martin et al. used two accelerometers to measure the speeds of mechanically excited shear waves to track physiological loads in the Achilles, patellar, and biceps femoris tendons.[337] Interestingly, they found that loading patterns observed in ex vivo porcine digital flexor tendons and in vivo human Achilles tendons (20–80 m/s) could be predicted similarly using an analytical tensioned beam model. Such a development has enabled additional investigations into the aging Achilles tendon (e.g., Ebrahimi et al. 2020[162]) and the calibration of a subject-specific shear wave speed-stress relationship during walking or isometric loading (e.g., Keuler et al. 2019[262] and Martin et al. 2020[338]). Accelerometry has also been used to investigate shear waves produced by muscle contractions in the tibialis anterior muscle in vivo. Cescon et al. showed in healthy adults that shear waves propagating along muscle fibers were an order of magnitude slower than those in tendon (2.4 ± 1.1 m/s),[94] which may be due to the relationship between the shear wave speed and axial tissue stress.[337]

There are several advantages and disadvantages to measuring shear wave propagation using accelerometers (Table 2). The primary advantage is that the small size of accelerometers make it simple to obtain wearable measurements. The small size together with the higher dynamic range of these sensors compared to the imaging modalities makes it possible to measure higher shear wave speeds that arise during functional activities (Figure 4). For example, accelerometers have been used to track shear waves in tendons loaded up to 48 MPa.[262] The primary disadvantage of accelerometers is that shear wave speed measurements can only be performed in superficial tissues. Additionally, it is more challenging to perform regional measurements with accelerometers than with one of the imaging measurement methods. This is because accelerometers do not have image-guidance, thus it is challenging to relate the position of accelerometers to a precise location on the tissue, or in a direction of principal tissue anisotropy if not otherwise known. In conclusion, the use of accelerometers is most feasible for global measurements of shear wave propagation on superficial tissues.

Laser Doppler Vibrometer Shear Wave Measurement

Laser Doppler vibrometry is an established non-contact measurement method for monitoring the transverse motion of elastic materials.[424] This method provides non-contact measurements at specific locations and has primarily been used in quasi-static ex vivo applications. Previous studies have used this method to measure shear wave speeds in collateral ligaments and flexor tendons ex vivo (ranges = 40–130 and 30–100 m/s, respectively).[70, 339] Both studies concluded that the relationship between shear wave speed and stress is consistent with an analytical beam model.[337] Laser Doppler vibrometers have also been used to investigate muscle contractions in vivo. Salman et al. demonstrated that mechanically excited shear waves, with speeds between 4 and 12 m/s, can be measured using laser Doppler vibrometers in the human bicep during isometric contractions up to 60% of maximum voluntary contraction.[438, 439] Salman and colleagues went on to perform the same measurement on Achilles tendons in vivo, reporting shear wave speeds ranging from 10 to 40 m/s for varying ankle flexion.[437] Together, these studies demonstrate the utility of using laser Doppler vibrometers to monitor tissue motion and track shear waves using non-contact measurements directly on the tissue or skin surface.

There are several advantages and disadvantages to measuring shear wave propagation using laser Doppler vibrometers (Table 2). Like accelerometers, laser Doppler vibrometers have a higher dynamic range than ultrasound and MRI, which allow shear waves to be measured during functional tissue loading and in tissues with high moduli.[70, 155, 156, 337, 437–439] Additionally, laser Doppler vibrometers are a non-contact measurement method, which enables users to measure shear wave speeds without regard for contact dynamics or inertial effects between the sensor and the tissue surface. The primary disadvantage of laser Doppler vibrometers is that they are sensitive to focal distance, which limits their use to tissues that primarily move in a single plane (e.g., axial loading ex vivo). Additionally, laser vibrometers require a sufficient intensity of light to reflect back to the laser origin,[424] meaning that users may be limited by signal-to-noise ratio in applications where retro-reflective tape cannot be used. Finally, like when using ultrasound or accelerometers, users must understand the material anisotropy prior to aligning lasers to avoid misinterpretation of shear wave speeds. In conclusion, using laser Doppler vibrometers to measure shear wave propagation is most feasible in ex vivo, single plane loading experimental conditions.

Conclusions

With the advent of new sensors and enhancements to existing imaging modalities, using shear wave propagation to investigate musculoskeletal tissue mechanics is more readily accessible. As such, the contents of this systematic review demonstrate that the use of shear waves to characterize the mechanics of musculoskeletal tissues has proliferated, with over half of the included studies being published in the last three years (Figure 7). Among excitation methods, acoustic pushes and mechanical taps are particularly useful in accessing deep tissues and superficial tissues during motion, respectively. Various setups that combine one of these excitation methods with ultrasound, MRI, accelerometers, or laser Doppler vibrometers can be used to determine shear wave speeds and thus material properties or loading for a wide variety of musculoskeletal tissues. Given the multitude of possible combinations of excitation and measurement technologies, researchers can use the advantages and disadvantages of different combinations presented in this review to identify the optimal method for a given application.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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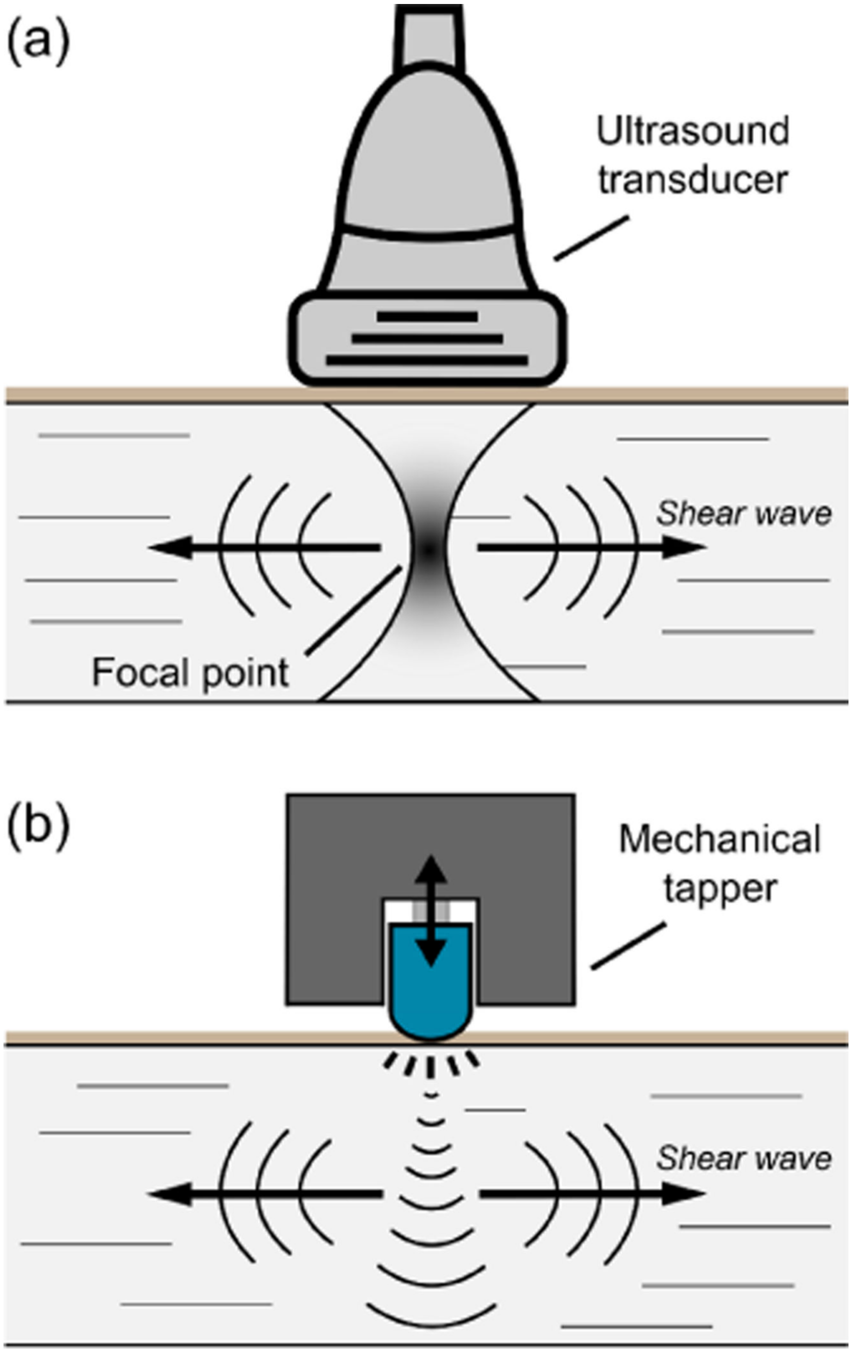

Figure 1:

The two primary methods used to excite shear waves in musculoskeletal tissues are (a) acoustic pushes, such as an acoustic radiation force impulse (ARFI) (shown), supersonic shear imaging (SSI), and comb-push ultrasound shear elastography (CUSE) based techniques, and (b) mechanical taps using electrodynamic, piezoelectric elements, or electromagnetic shakers (shown).

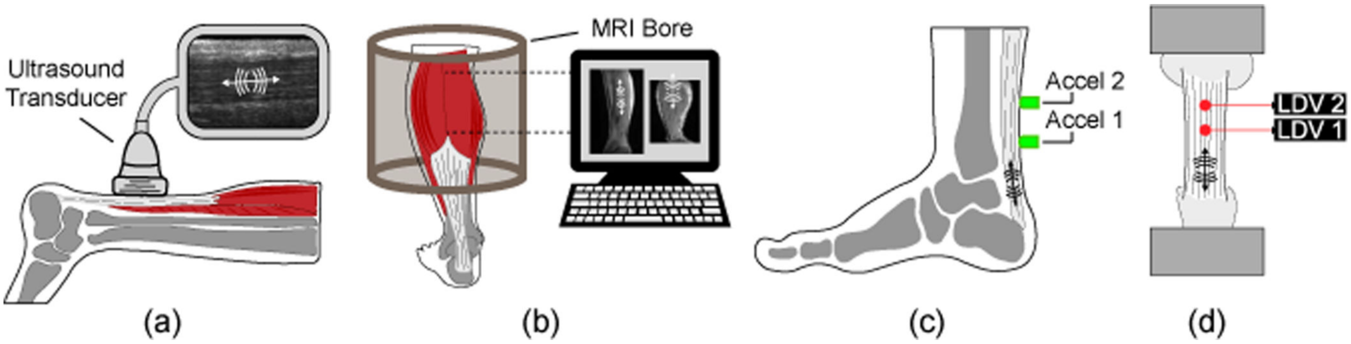

Figure 2:

The four primary methods used to measure shear waves are (a) ultrasound, (b) magnetic resonance imaging (MRI), (c) accelerometers (Accel), and (d) laser Doppler vibrometers (LDVs).

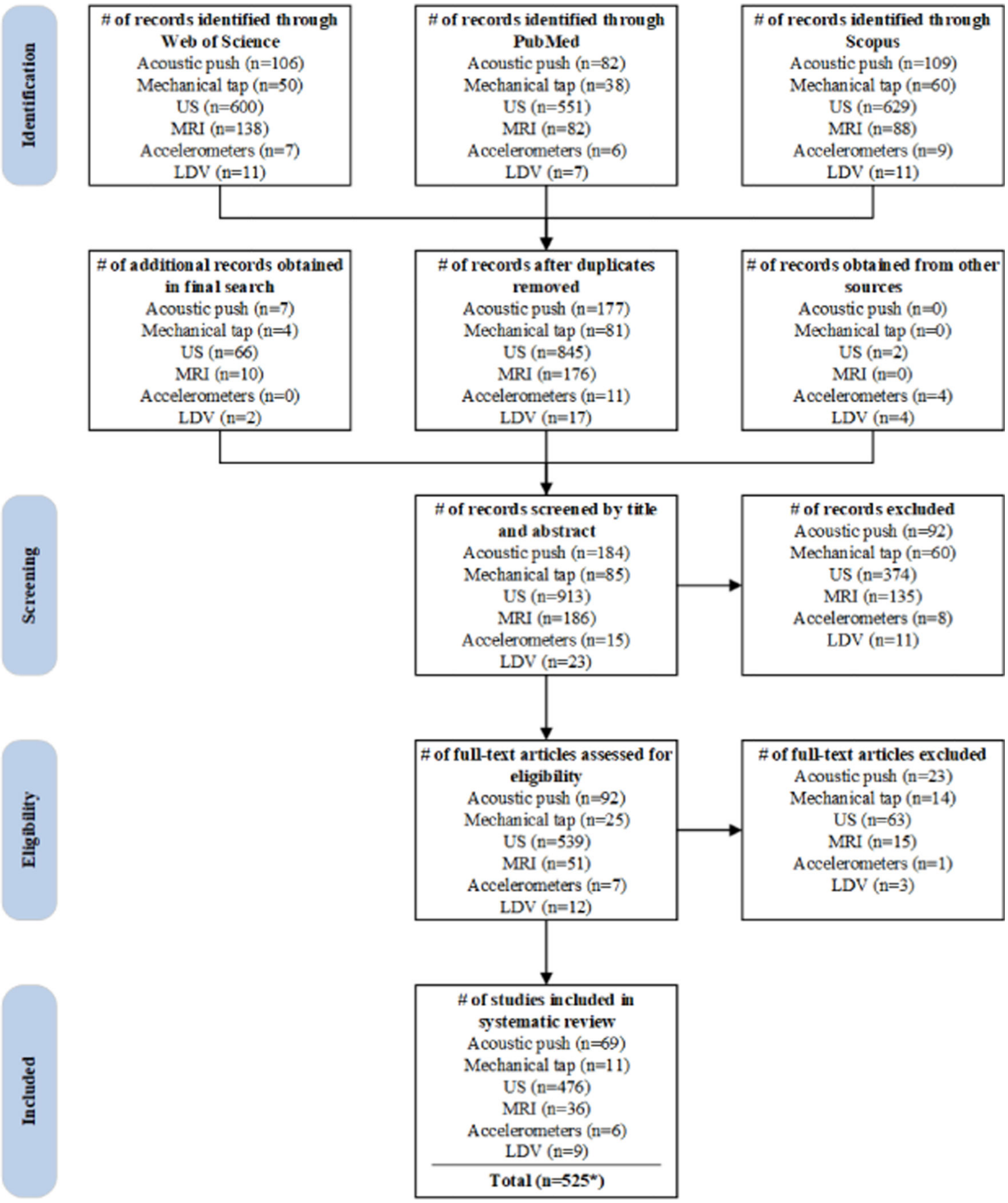

Figure 3.

PRISMA flow chart showing the number of articles included and removed at each stage of the search process (US = Ultrasound, MRI = Magnetic Resonance Imaging, and LDV = Laser Doppler Vibrometers). Note that the numbers may differ from the sum from each excitation and measurement category because some papers: 1) used more than one excitation or measurement method, 2) do not state which excitation or measurement method was used, and/or 3) appear in both excitation and measurement categories.

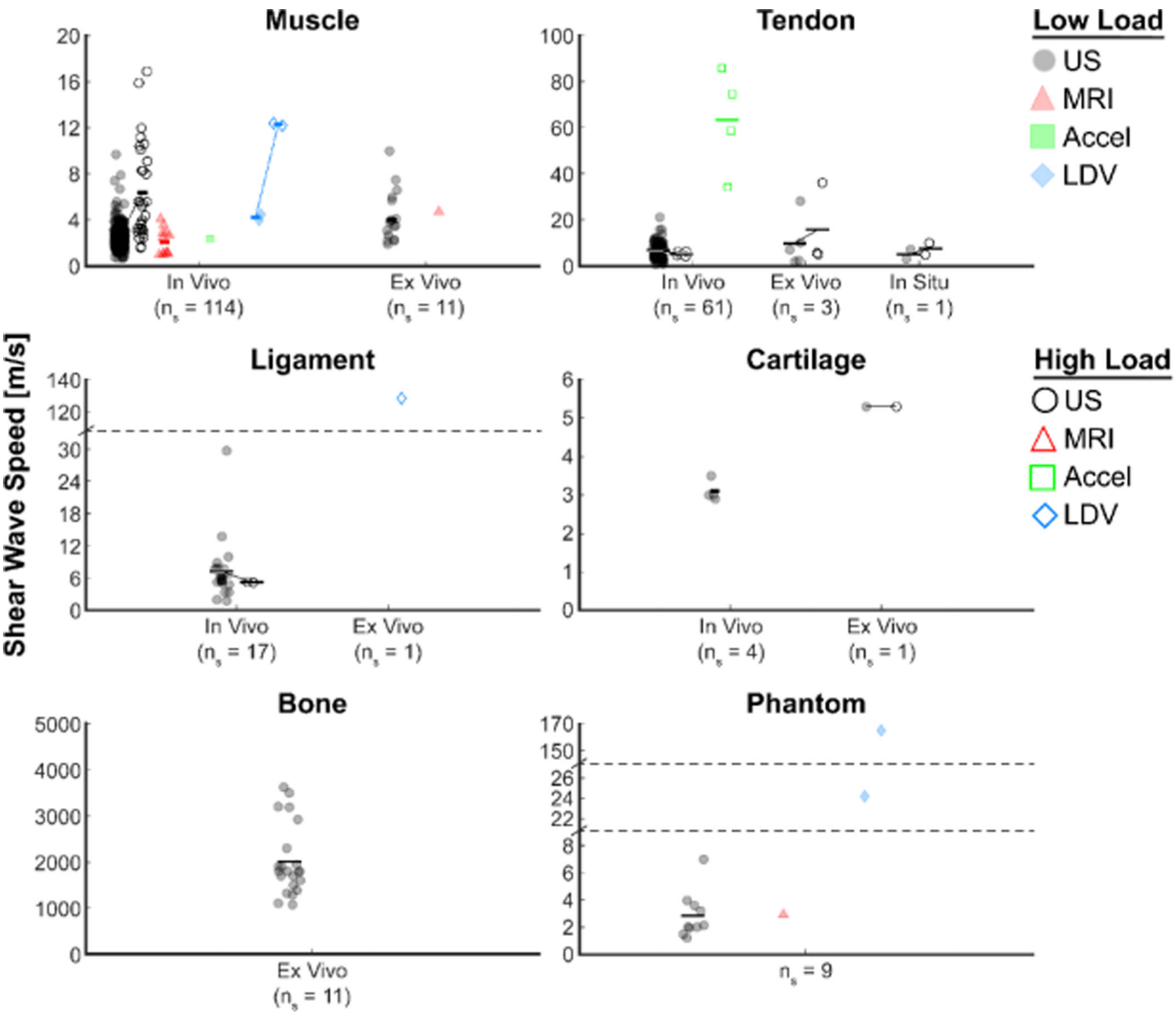

Figure 4.

Scatter plots show the mean shear wave speeds reported in muscle, tendon, ligament, cartilage (including both articular and fibrocartilage), bone, and tissue-mimicking phantoms. These reported values are further divided by the measurement method used (i.e., ultrasound (US), magnetic resonance imaging (MRI), accelerometers (Accel), and laser Doppler vibrometers (LDV)) and the experimental condition (i.e., in vivo, ex vivo, in situ). Solid horizontal lines indicate the mean of all measurements within a condition. The number of conditions/subgroups across all studies (n_S) is indicated in the x-axis label. Mean values exceeding measurements from other studies by over two orders of magnitude were excluded from the scatter but can be found in Tables S2-5.

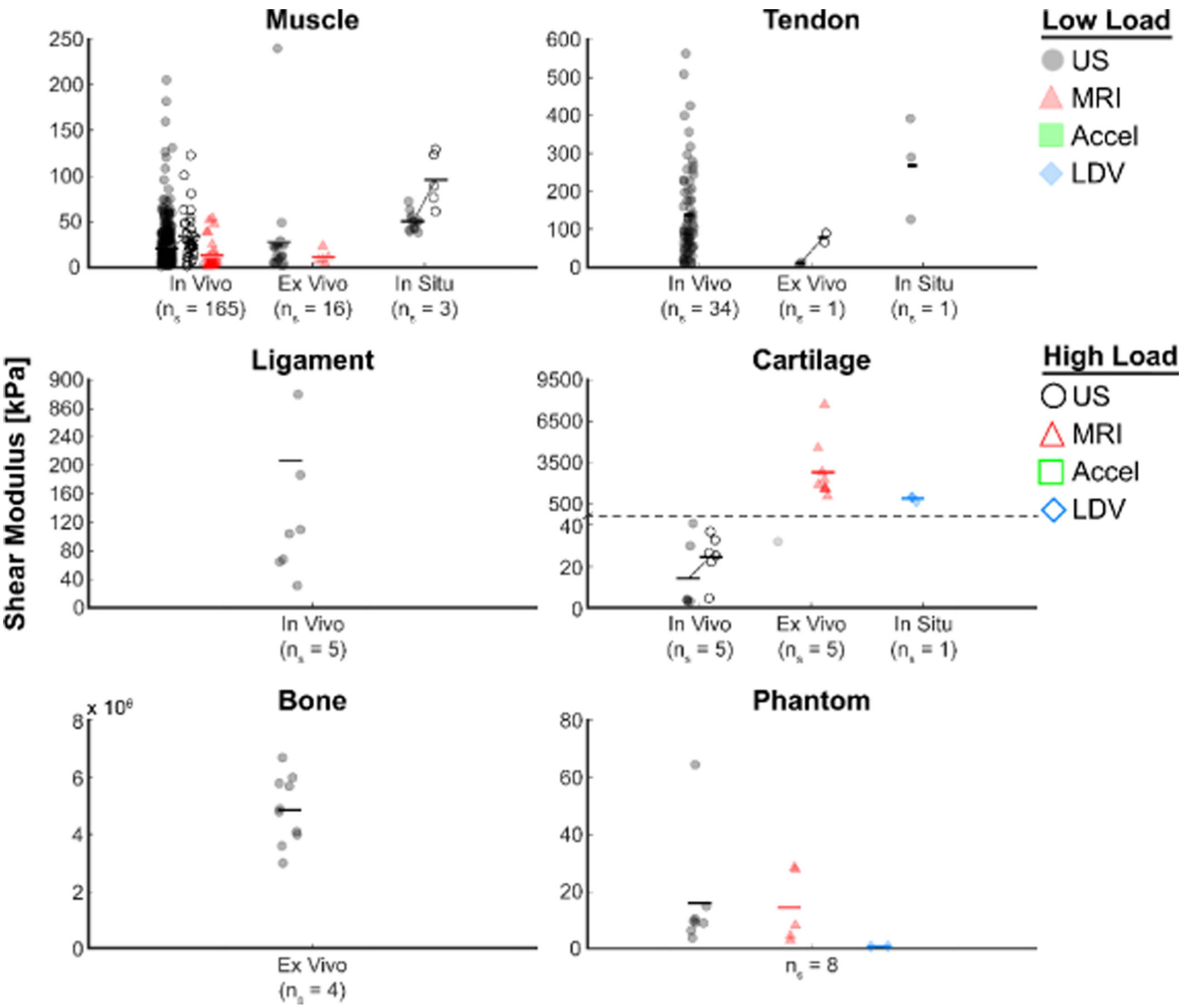

Figure 5.

Scatter plots show the mean shear moduli reported in muscle, tendon, ligament, cartilage (including both articular and fibrocartilage), bone, and tissue-mimicking phantoms. These reported values are further divided by the measurement method used (i.e., ultrasound (US), magnetic resonance imaging (MRI), accelerometers (Accel), and laser Doppler vibrometers (LDV)) and the experimental condition (i.e., in vivo, ex vivo, in situ). Solid horizontal lines indicate the mean of all measurements within a condition. The number of conditions/subgroups across all studies (n_S) is indicated in the x-axis label. Mean values exceeding measurements from other studies by over two orders of magnitude were excluded from the scatter but can be found in Tables S2-5. Note that Accel was left in the legend for consistency, but there were no papers that reported shear modulus measured with accelerometers.

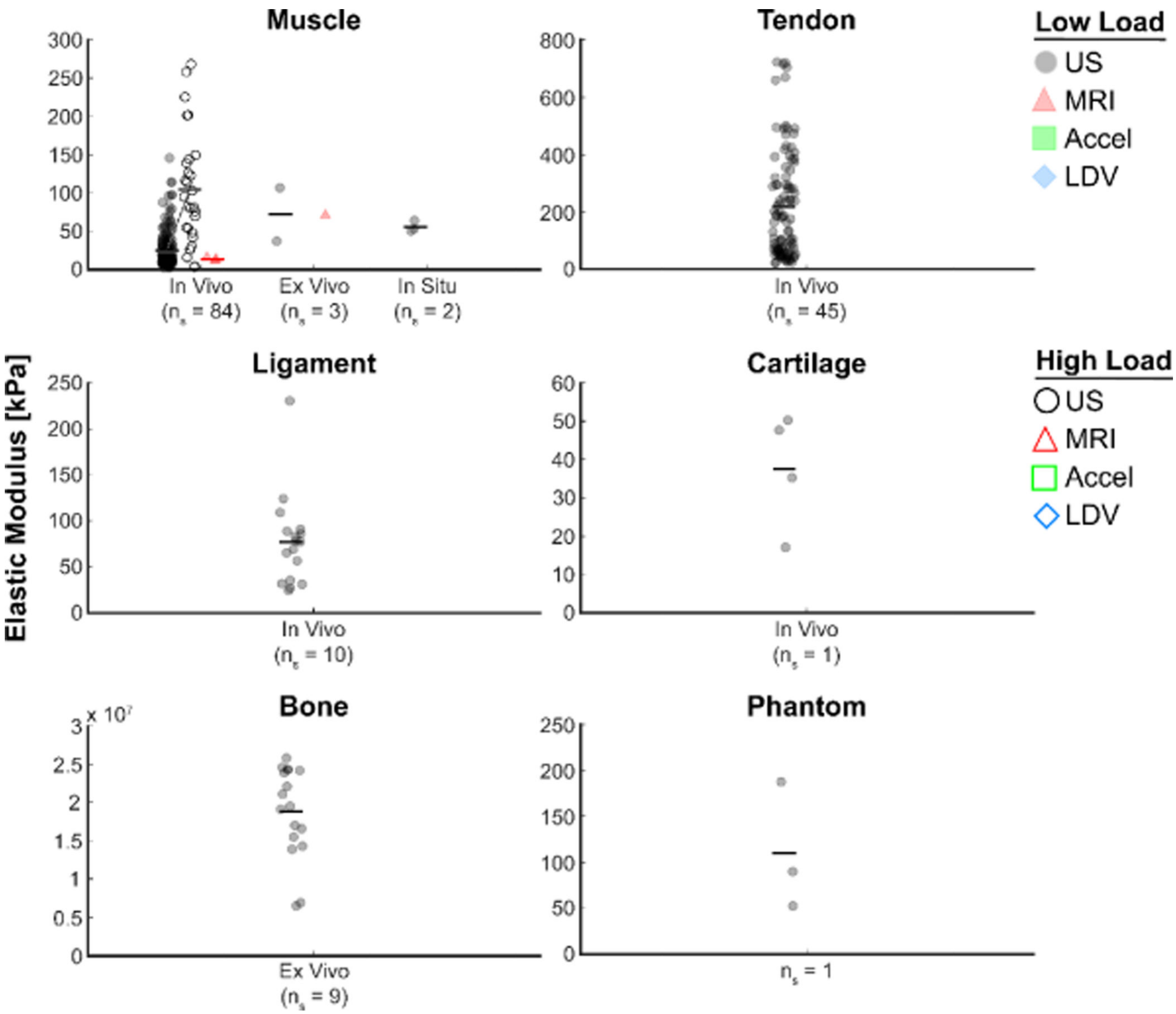

Figure 6.

Scatter plots show the mean elastic moduli reported in muscle, tendon, ligament, cartilage (including both articular and fibrocartilage), bone, and tissue-mimicking phantoms. These reported values are further divided by the measurement method used (i.e., ultrasound (US) and magnetic resonance imaging (MRI)) and the experimental condition (i.e., in vivo, ex vivo, in situ). Solid horizontal lines indicate the mean of all measurements within a condition. The number of conditions/subgroups across all studies (n_S) is indicated in the x-axis label. Mean values exceeding measurements from other studies by over two orders of magnitude were excluded from the scatter but can be found in Tables S2-5. Note that Accel and LDV were left in the legend for consistency, but there were no papers that reported elastic modulus measured with either modality.

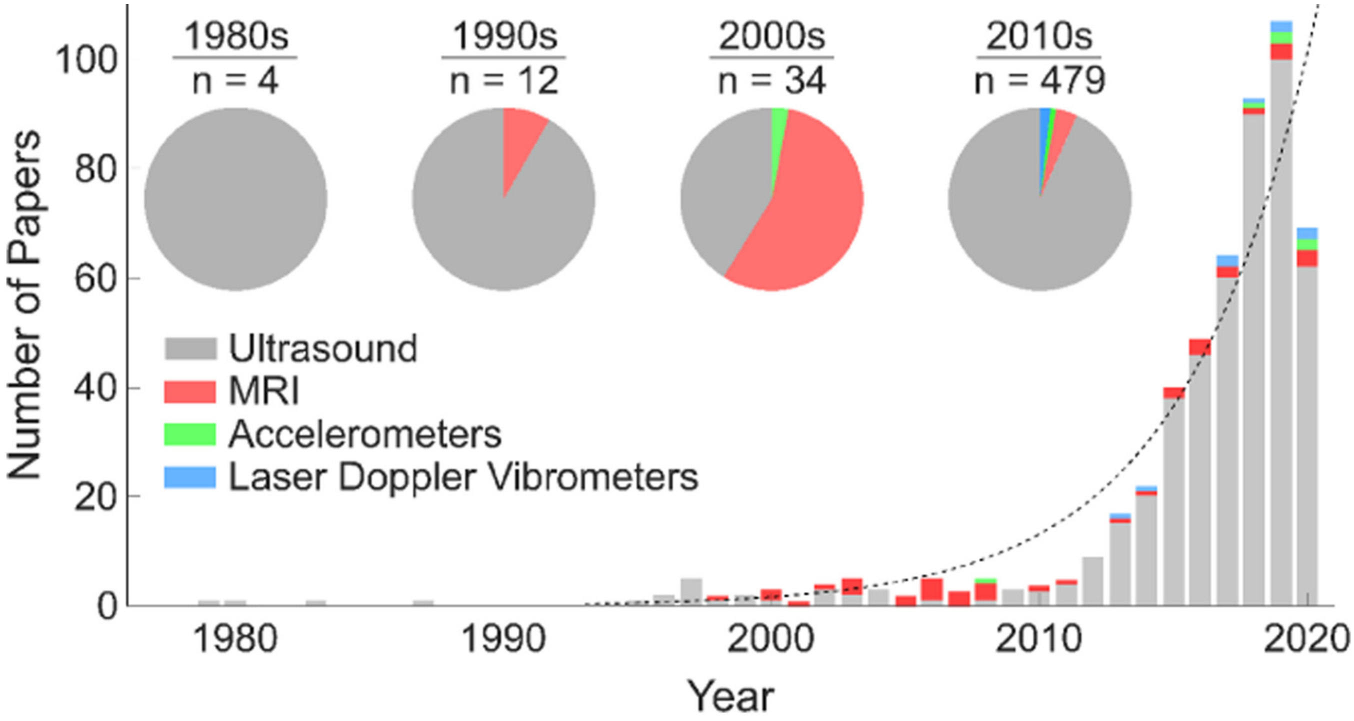

Figure 7.

Pie charts and bar graphs show the rapidly increasing number of papers that met our search criteria, especially within the last decade. Overall, ultrasound was the most widely used among measurement techniques, with MRI being the second most widely used. Laser Doppler vibrometers have emerged as a measurement technique only within the last decade (2010s).

Table 1:

Advantages and disadvantages of shear wave excitation methods

	Advantages	Disadvantages
Ultrasound Excitation	•Can excite a shear wave through the entire thickness •Can excite deep tissues •Easily compatible with ultrasound elastography	•Acoustic scattering due to tissue geometries (e.g., pennation) •Difficult to perform during movement
Mechanical Excitation	•Easy to use during movement •Compatible with all measurement methods •Can excite large-amplitude shear waves	•Generates multiple types of waves (e.g., shear, compressional) •Cannot excite deep tissues

Table 2:

Advantages and disadvantages of shear wave measurement methods

	Advantages	Disadvantages
Ultrasound	•Permits shear wave speed measurements across entire tissue depth •Can measure in deep tissue	•Limited temporal resolution on most systems •Burdensome to use during functional tasks •Need to know tissue anisotropy relative to transducer orientation
Magnetic Resonance Imaging	•Easy to pair shear wave speed measurements with 3D geometry acquisition •Non-contact •Can measure in deep tissues	•Burdensome to use during functional tasks •Long processing time
Accelerometers	•Works well during movement •High dynamic range	•Must be in contact with tissue surface or on skin over tissue •Limited to superficial tissues •Sensitive to design of sensor holder
Laser Doppler Vibrometers	•Non-contact •Point-and-shoot •High dynamic range	•Difficult to perform in vivo measurements, especially during movement •Sensitive to focal distance and light scatter

Table 3:

Ranges of mean values of reported shear wave speeds. Values reported can be visualized in Figure 4. Mean values from two studies[143,418] were excluded as the reported shear wave speeds in muscle occur on the scale of mm/s and km/s, respectively (results from all studies can be found in Tables S2-5).

		Shear Wave Speed [m/s]							
		In Vivo		**Ex Vivo**		**In Situ**		**Phantom**	
		Low	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Muscle	**US**	0.7–9.7	1.6–16.9	1.9–10.0	–	–	–	–	–
	MRI	1.0–4.1	–	4.7–4.7	–	–	–	–	–
	Accel	2.4	–	–	–	–	–	–	–
	LDV	4.0–4.5	12.2–12.4	–	–	–	–	–	–
Tendon	**US**	0.5–21.0	4.0–6.1	1.8–28.0	5.0–36.0	2.9–7.1	4.9–9.9	–	–
	MRI	–	–	–	–	–	–	–	–
	Accel	–	34.1–85.6	–	–	–	–	–	–
	LDV	–	–	–	–	–	–	–	–
Ligament	**US**	1.7–29.7	5.1–5.2	–	–	–	–	–	–
	MRI	–	–	–	–	–	–	–	–
	Accel	–	–	–	–	–	–	–	–
	LDV	–	–	–	128.0	–	–	–	–
Cartilage	**US**	2.9–3.5	–	5.3	5.3	–	–	–	–
	MRI	–	–	–	–	–	–	–	–
	Accel	–	–	–	–	–	–	–	–
	LDV	–	–	–	–	–	–	–	–
Bone	**US**	–	–	1074–3623	–	–	–	–	–
	MRI	–	–	–	–	–	–	–	–
	Accel	–	–	–	–	–	–	–	–
	LDV	–	–	–	–	–	–	–	–
Phantom	**US**	–	–	–	–	–	–	1.2–7.0	–
	MRI	–	–	–	–	–	–	2.9	–
	Accel	–	–	–	–	–	–	–	–
	LDV	–	–	–	–	–	–	24.2–165.0	–

Abbreviations used: US = Ultrasound, MRI = Magnetic Resonance Imaging, Accel = Accelerometers, and LDV = Laser Doppler Vibrometers.

Table 4:

Ranges of mean values of reported shear moduli. Values reported can be visualized in Figure 5. Mean values from one study[418] were excluded as the reported shear moduli in muscle occur on the scale of GPa (results from all studies can be found in Tables S2-5).

		Shear Modulus [kPa]							
		In Vivo		**Ex Vivo**		**In Situ**		**Phantom**	
		Low	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Muscle	**US**	0.6–205.5	1.1–122.8	1.6–240.0	−	38.2–72.4	61.3–129.3	−	−
	MRI	1.3–54.0	−	4.2–23.5	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Tendon	**US**	9.5–563.5	−	8.4–14.6	67.1–89.9	126.7–392.0	−	−	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Ligament	**US**	31.1–879.6	−	−	−	−	−	−	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Cartilage	**US**	3.1–40.7	4.5–36.7	31.9	−	−	−	−	−
	MRI	−	−	1083–7714	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	700–1000	−	−	−
Bone	**US**	−	−	3×10^6–6.7×10^6	−	−	−	−	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Phantom	**US**	−	−	−	−	−	−	3.8–64.6	−
	MRI	−	−	−	−	−	−	2.9–28.5	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	0.8–0.9	−

Abbreviations used: US = Ultrasound, MRI = Magnetic Resonance Imaging, Accel = Accelerometers, and LDV = Laser Doppler Vibrometers.

Table 5:

Ranges of mean values of reported elastic moduli. Values reported can be visualized in Figure 6. Mean values from one study[418] were excluded as the reported elastic moduli in muscle occur on the scale of GPa (results from all studies can be found in Tables S2-5).

		Elastic Modulus [kPa]							
		In Vivo		**Ex Vivo**		**In Situ**		**Phantom**	
		Low	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Muscle	**US**	2.0–145.6	3.3–268.2	37.0–106.8	−	50.5–63.9	−	−	−
	MRI	11.4–16.0	−	71.0	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Tendon	**US**	22.6–722.4	−	−	−	−	−	−	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Ligament	**US**	24.5–230.6	−	−	−	−	−	−	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Cartilage	**US**	17.1–50.3	−	−	−	−	−	−	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Bone	**US**	−	−	6.5×10^6–25.8×10^6	−	−	−	−	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−
Phantom	**US**	−	−	−	−	−	−	52.5–187.6	−
	MRI	−	−	−	−	−	−	−	−
	Accel	−	−	−	−	−	−	−	−
	LDV	−	−	−	−	−	−	−	−

Abbreviations used: US = Ultrasound, MRI = Magnetic Resonance Imaging, Accel = Accelerometers, and LDV = Laser Doppler Vibrometers.