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Recent advance

Applications of ultrasound elastography to hand and upper limb disorders

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ABSTRACT

Ultrasound elastography is a recently developed method for accurate measurement of soft tissue stiffness in addition to the clinician's subjective evaluation. The present review briefly describes the ultrasound elastography techniques and outlines clinical applications for tendon, muscle, nerve, skin and other soft tissues of the hand and upper limb. Strain elastography provides a qualitative evaluation of the stiffness, and shear-wave elastography generates quantitative elastograms superimposed on a B-mode image. The stiffness in degenerative tendinopathy and/or tendon injury was significantly lower than in a normal tendon in several studies. Elastography is also a reliable method to evaluate functional muscle activity, compared to conventional surface electromyography. The median nerve is consistently stiffer in patients with carpal tunnel syndrome than in healthy subjects, on whatever ultrasound elastography technique. Elastography distinguishes normal skin from scars and can be used to evaluate scar severity and treatment. Elastography has huge clinical applications in musculoskeletal tissues. Continued development of systems and increased training of clinicians will expand our knowledge of elastography and its clinical applications in the future.

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1. Ultrasound elastography

Ultrasound (US) elastography noninvasively measures tissue stiffness tissue by inducing and measuring tissue deformation [1]. Stiffness is the tendency of tissue to resist deformation induced by an applied force and is assessed by Young's elasticity modulus, defined as:

$$E = \sigma / \epsilon$$

where σ is the stress (Pa), corresponding to the normalized force, and ϵ is the strain (unitless), corresponding to the deformation of the tissue due to an applied force. This US technique was first introduced in the early 1990s with *in vitro* experiments [2], then gradually expanded into clinical practice for diagnostic and sometimes prognostic purposes in the fields of senology, hepatology, thyroid disease, prostate disease and musculoskeletal conditions [3,4].

Since 1990, different ultrasound elastography (UE) techniques have been used:

Strain imaging, which reveals physical tissue displacement, is estimated by axial deformation parallel to the externally applied force exerted on the body surface using the ultrasound probe (Fig. 1a). This method provides a qualitative evaluation of stiffness [5]. Two approaches for strain imaging using ultrasound techniques were developed: strain elastography (SE) and acoustic radiation force impulse (ARFI) strain imaging. For strain elastography, tissue displacement is generated by manual external compression with an ultrasound transducer [2] or by an internal physiologic (cardiovascular) motion to assess deeper organs [6]. For ARFI imaging, the force is produced by acoustic "pushing pulse". Different methods exist to measure displacement, such as radiofrequency echo correlation-based tracking or Doppler processing [7]. As the manual or physiological stresses are not quantifiable, the measured strain provides a qualitative assessment of the stiffness, or a pseudo-quantitative measure (strain ratio) represented on a color map called an elastogram.

Shear wave imaging uses dynamic stress to generate a shear wave inside the tissue, and measurement of shear wave speed allow determination of stiffness. Three approaches exist to obtain shear wave imaging. Firstly, 1D transient elastography, is

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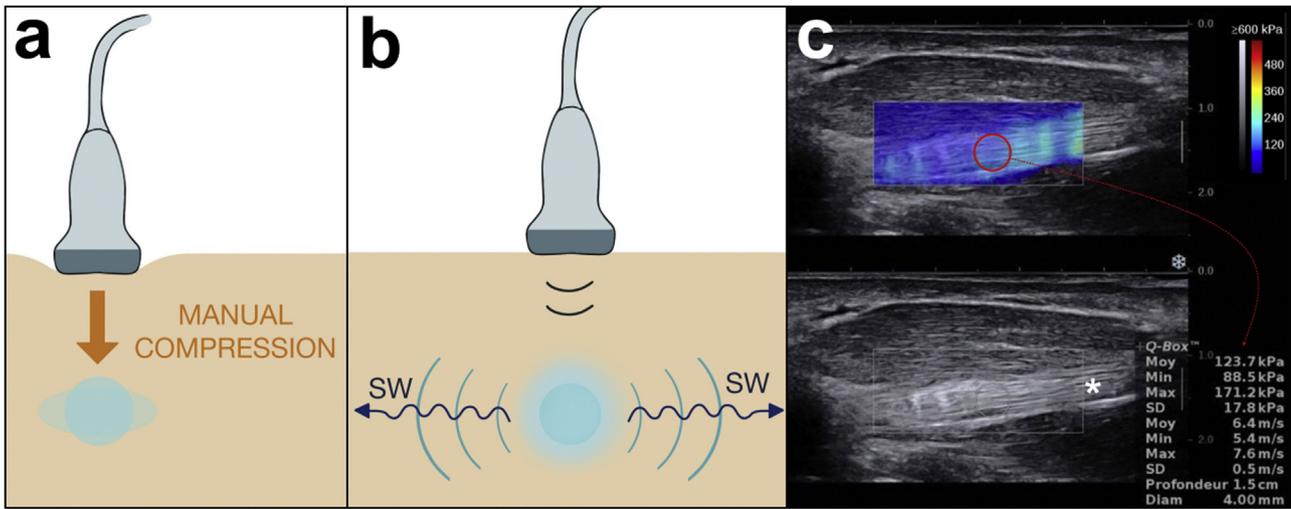


Fig. 1. Ultrasound elastography: strain elastography (a) and shear wave elastography (b). The colored region represents the 2D quantitative elastogram superimposed on a B-mode image with a color scale (see top right). The software allowed us to measure the mean stiffness (Young’s modulus, in kPa) value and the shear wave velocity ($\text{m}\cdot\text{s}^{-1}$) of the flexor pollicis longus (asterisk) inside a circular region of interest (ROI), (c).

performed with the FibroScan[®] machine (Echosens, Paris, France), composed of a vibration-controlled probe [8]. Secondly, ARFI (Acuson S2000; Siemens Medical Solutions, Berlin, Germany) can be used, a portion of its longitudinal waves being converted to

shear waves perpendicular to the longitudinal waves [9]. On the hypothesis of an isotropic, homogeneous, incompressible medium, shear wave velocity (SWV) is measured and converted to Young’s modulus (E) using the equation: $E = 3 \rho c^2$ where ρ is the density

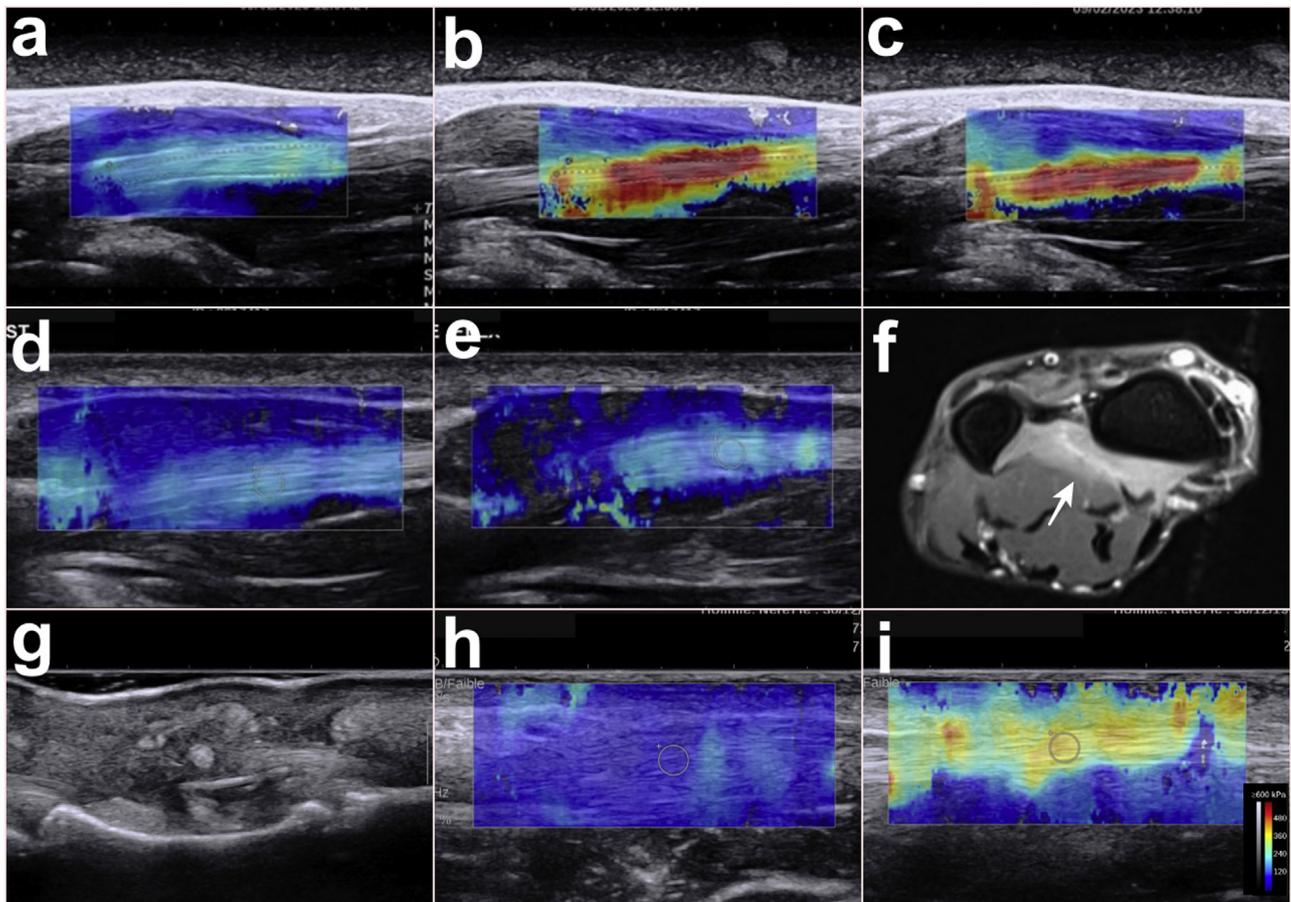


Fig. 2. Shear wave elastography of human flexor pollicis longus tendon in physiological conditions at rest (210.1 kPa , $8.4 \text{ m}\cdot\text{s}^{-1}$) (a) and active flexion (490 kPa , $12.7 \text{ m}\cdot\text{s}^{-1}$) (b) and passive extension (486.6 kPa , $12.7 \text{ m}\cdot\text{s}^{-1}$) (c). Patient with anterior interosseous nerve palsy (second row). Shear wave velocity (SWV) and stiffness does not increase between the rest position (175.7 kPa , $7.7 \text{ m}\cdot\text{s}^{-1}$) (d) and active flexion (172.5 kPa , $7.6 \text{ m}\cdot\text{s}^{-1}$) (e). Hyperintensity in flexor pollicis longus and pronator quadratus muscles (arrow) are revealed on 3 T MRI (f). Patient with tendon rupture after repair of the flexor digitorum profundus of the index (third row). Re-tear is difficult to identify in B-mode image (g) proximal to the tear. Stiffness maps show lower values for the flexor digitorum profundus of the index (66.1 kPa , $4.7 \text{ m}\cdot\text{s}^{-1}$) (h) compared to the flexor digitorum superficialis of the index (378.5 kPa , $11.2 \text{ m}\cdot\text{s}^{-1}$) (i).

and c the shear wave velocity. Thirdly, in 2D shear wave elastography, acoustic radiation force is also used (Fig. 1b), with the Aixplorer ultrasound system (Supersonic Imagine, Aix-en-Provence, France): multiple focal zones are stimulated and this creates a nearly cylindrical shear wave cone [10], enabling real-time 2D monitoring of shear waves and generating quantitative elastograms superimposed on a B-mode image (Fig. 1c).

2. Elastography and tendons

Tendon tear and histological modifications (e.g., disintegration of collagen fibers or mucoid degeneration) in degenerative tendinopathy are expected to lead to a localized decrease in tendon stiffness [11] and can be detected by UE earlier than by conventional ultrasonography (US) [12]. Decreased stiffness in degenerative tendinopathy and/or tendon injury compared to healthy tendon were demonstrated in several studies [12–16] but, in some cases of tendinopathy (long head of the biceps tendon), UE analysis provided conflicting results [17]. Despite the differing data, shear wave elastography (SWE) seems to be a reproducible technique to evaluate tendon elasticity, with low inter-observer differences [18,19].

SWV in human hand tendons in physiologic in vivo conditions (Figs. 2a, 2b, 2c) was analyzed in various studies [20]. Experimental studies using porcine flexor tendons demonstrated that the stiffness of a partially torn tendon is lower in the vicinity of the injury and is dependent on the size of the tear [21]. Moreover, the stiffness of a tendon damaged by collagenase solution was significantly lower than in a normal tendon [22]. Fluid accumulation and hematoma associated with acute tear appear as signal

void areas on SWE [13,15]. After flexor tendon repair, re-tear can be much more difficult to assess in B-mode. SWE of the flexor tendon proximal to the lesion systematically demonstrated a significant lower SWV compared to the healthy side (Figs. 2g, 2h, 2i). Injured flexor hand tendons after surgical repair showed impaired regional elasticity and appeared locally stiffer than the healthy side on SWE. The clinical significance of these findings was that the tendon would glide less in the rigid local zone, and authors advocated focusing rehabilitation on these stiffer zones, to improve gliding [20].

Turkey et al. [13] compared SWE acquisitions performed on 40 patients suffering from De Quervain tenosynovitis, versus 40 healthy volunteers. Young’s modulus values in healthy tendons of the first extensor compartment were 69.17 ± 22.45 kPa whereas pathologic tendons showed lower values of 29.75 ± 8.02 kPa.

Medial and lateral epicondylitis were analyzed in several studies, all suggesting that pathological tendons are softer than healthy tendons [14,16,23–25]. Park et al. [25] concluded that UE was more accurate than US by 7.1% for epicondylitis diagnosis, sensitivity and specificity being 96% and 89%, respectively. Moreover, SWV increased after conservative treatment in patients with lateral epicondylitis [14]. The combined modalities of UE and B-mode ultrasonography showed significant improvement in agreement between imaging and histologic results compared with each modality alone [16] in common flexor tendinopathy at the medial side of the elbow.

In a recent systematic review of rotator cuff tears [26], SWE was successfully used to identify the location and degree of supraspinatus tendon tear, improving the value of ultrasound. Patients with rotator cuff tears had a lower mean SWV values in muscle and

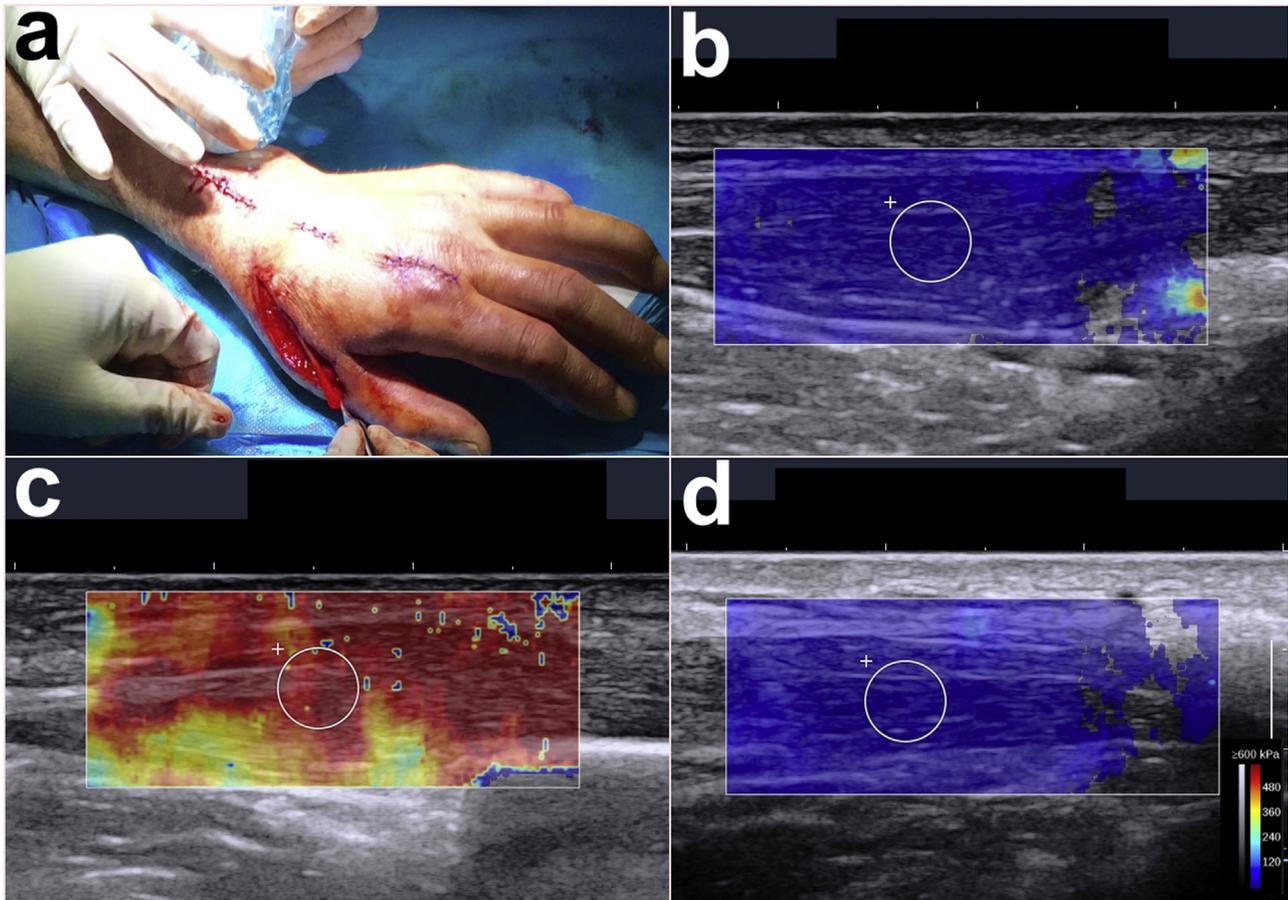


Fig. 3. Intraoperative photographs of transfer of the extensor indicis proprius to the extensor pollicis longus using ultrasound shear wave elastography (a). Differences in stiffness values at the various stages of surgery were obtained from rest (b) to active extension during the tendon transfer (c) and at rest after tendon transfer (d).

tendon under active conditions. The intraclass correlation coefficient was excellent (0.96). Supraspinatus tendon stiffness increased between 8 days and 24 weeks after repair [26].

3. Elastography and muscles

With Young's modulus ranging from 5 to 40 kPa at rest and up to 300 kPa during passive stretching or active contraction, SWE is a validated method to assess muscle stiffness [27,28]. Reliability for measuring muscle stiffness was demonstrated for several muscle groups, including lower limb, trunk and upper limb muscles, including the intrinsic muscles of the hand [29,30]. Furthermore, studies suggested using SWE to monitor muscle activity or muscle force and to demonstrate contraction of accessory muscles [29,31]. SWE was also found to be a reliable method to evaluate functional muscle activity compared to the physiological activity recorded with conventional surface electromyography [32]. SWV in muscle seems to be influenced by gender, age and dominance [32,33]. Moreover, studies highlighted the importance of probe orientation, as stiffness is lower with a perpendicular than a parallel orientation to the muscle fibers [34,35]. This result shows the anisotropic behavior of the skeletal muscle. Parallel probe orientation is more valid and reliable for SWV measurement.

Increased stiffness values, related to muscle spasticity, were shown in patients with neuromuscular diseases such as cerebral palsy [36], Duchenne muscular dystrophy [37] in passive state, Parkinson's disease or neonatal brachial plexus palsy [38]. SWE provides an additional objective tool for spasticity evaluation, targeting the right skeletal muscle in a spastic upper limb [39], and

could be helpful to assess results of botulinum toxin injection [40] or surgery.

Li et al. performed SWE of the thenar muscle in hemiplegic patients. The plegic side showed lower stiffness than the healthy side. Changes in muscle stiffness over follow-up could be used as an objective assessment of rehabilitation [41].

In 2017, Lamouille et al. reported assessment of in vivo muscle tension during transfer of the extensor indicis proprius to the extensor pollicis longus (Fig. 3). SWE measurements were obtained at different stages of surgery, including at rest before tendon transfer, during active extension and at rest after transfer. Results showed differences in stiffness values at the various stages of the procedure, providing new insights to improve treatment [42].

Due to the frequency of degenerative rotator cuff lesions, shoulder muscles are the most widely analyzed structures in the upper limb. In non-pathologic shoulders, SWE supraspinatus muscle values gradually decreased with increasing passive abduction of the shoulder. In large to massive tears, supraspinatus stiffness did not vary from adduction to abduction [43]. After surgical rotator cuff repair, the contractile behavior of the supraspinatus muscle increased from 6 weeks to 3 months after surgery and stiffness reached a steady state after 3 months. Opposite variation was found for deltoid muscle activity, which reached the same level as healthy muscle after 6 months [44]. This phenomenon is explained by a compensatory role of the deltoid in rotator cuff injury. In addition to human muscles, SWE was used to characterize muscle stiffness in small rodents to monitor the effect of treatment [45].

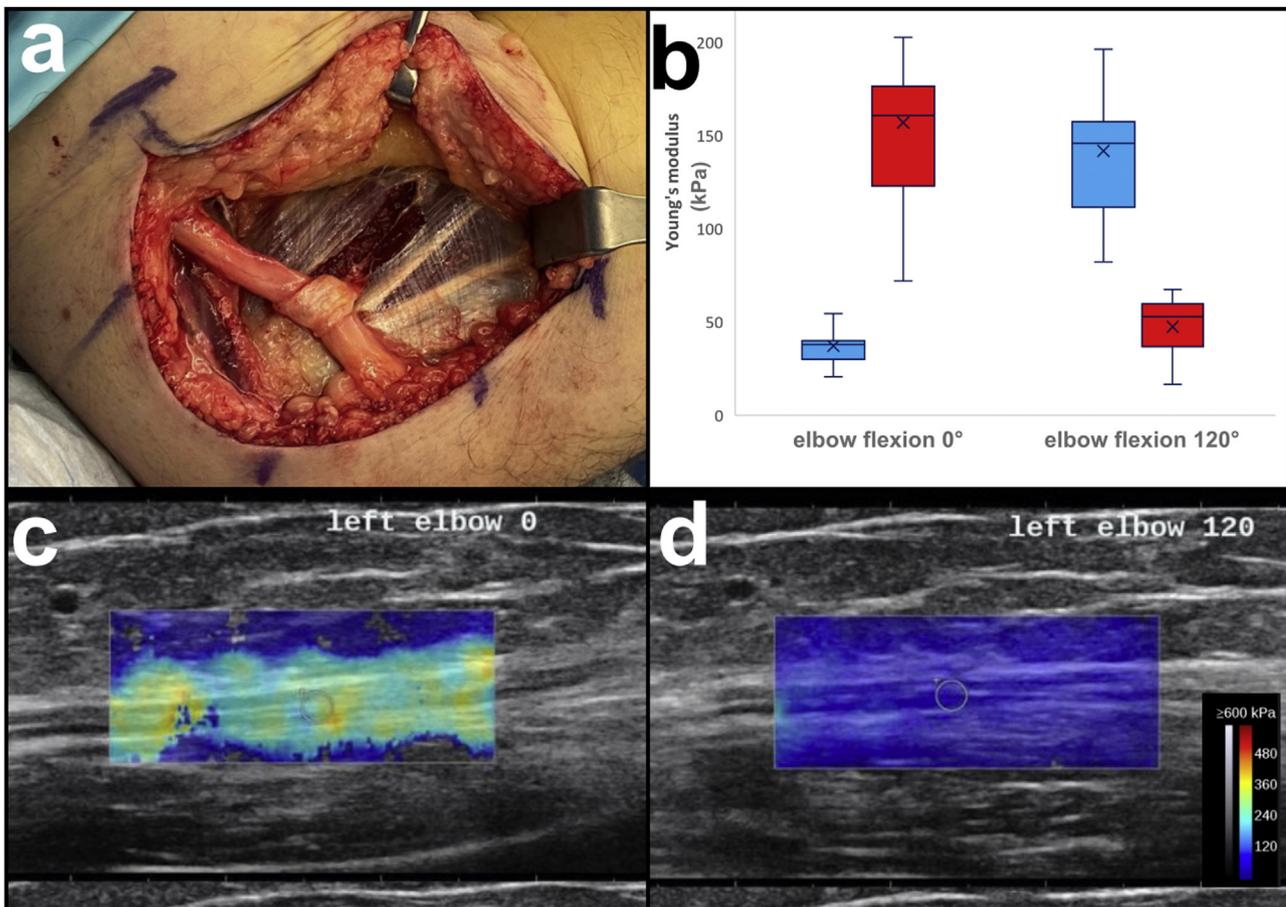


Fig. 4. Decompression of the ulnar nerve at the elbow with subcutaneous transposition and anterior stabilization with a fascial sling (a). Boxplot of ulnar nerve stiffness (kPa) in 0° and 120° elbow flexion on the operated (red) and non-operated side (blue) (b). Elastogram of the ulnar nerve after anterior transposition at rest (c) and in 120° elbow flexion (d).

4. Elastography and nerves

For many years, electroneuromyography (ENMG) was the main diagnostic tool for peripheral neuropathy. The, B-mode ultrasound image and doppler examination were found to be of interest in carpal tunnel syndrome (CTS) diagnosis showing 1) greater nerve cross-sectional area proximal to the region where the nerve is compressed, 2) reduced nerve mobility, 3) modified structural properties with variation in echogenicity, and 4) increased vascularity of nerve. SWE in addition to B-mode ultrasound is reliable for diagnosing entrapment neuropathy, with the advantages of being noninvasive, accessible and fast. Most upper-limb nerve SWE studies were performed on the median nerve for CTS. Authors demonstrated that long-term edema or high carpal tunnel pressure could lead to increase median nerve stiffness [46]. The reliability and feasibility of stiffness measurement on SWE in subjects with healthy median nerve (N = 40) showed excellent inter- and intra-observer agreement (0.852–0.930), and no difference between bilateral forearm measurements [47]. Attention must be paid to limb positioning during SWE measurement, as it directly affects nerve tension and stiffness [48]. A meta-analysis of 17 studies using sonoelastography to image the median nerve at the wrist (N = 1401 wrists) confirmed that the nerve is consistently stiffer in patients with CTS than healthy subjects, whatever the ultrasound elastography technique [49]. Moreover, studies successively identified nerve disease severity through different stages [50,51]. Thus, SWE enabled classification of CTS as effectively as gold-standard electrodiagnosis, with cases stratified as mild, moderate or severe based on median nerve stiffness. This was not achievable using B-mode US alone. Both median nerve cross-sectional area at the wrist and shear wave velocity were reduced 1 week after surgical carpal tunnel release, reflecting nerve recovery [52]. However, cut-off values for CTS diagnosis differ between authors, varying from 40.4 kPa to 79 kPa [46,53]. Also, Sugiyama et al. [54] proposed SWE as a noninvasive objective quantitative evaluation test for median nerve follow-up after volar locking plate osteosynthesis of distal radius fracture, helping to decide on timing for material removal and neurolysis.

For ulnar neuropathy at the elbow and in Guyon's canal, SWE is a new reliable method to support diagnosis [55,56]. Ulnar nerve stiffness Young's modulus >61 kPa and stiffness ratios of the ulnar tunnel to the distal arm and to the mid-arm of 1.68 and 1.75, respectively, provided 100% specificity and sensitivity for detection of ulnar neuropathy at the elbow [55]. Also, SWE can be used to differentiate ulnar neuropathy in the ulnar tunnel from asymptomatic ulnar nerve with medial epicondylitis and healthy uncompressed ulnar nerve [57]. Patients with unilateral ulnar tunnel syndrome showed greater cross-sectional area and stiffness in the affected side for all positions: 45° extension, 90° flexion and in maximum flexion of the elbow [58]. In patients with ulnar nerve decompression associated with anterior transposition, postoperative ulnar nerve stiffness increased with elbow joint extension (Fig. 4). However, on the non-operated side, ulnar nerve stiffness increased with elbow flexion [59].

Recently, SWE was used before ultrasound-guided perineural hydrodissection to identify the level of stiffness of the scar surrounding the radial nerve in two cases of radial nerve palsy after humeral shaft fracture [60].

5. Elastography and skin

The use of high-frequency ultrasonographic transducers has made elastographic assessment of the skin possible [61]. Most of the previous studies using elastography for skin evaluation included patients with cancer, connective tissue disease, chronic

systemic inflammation, lipodermatosclerosis or risk of ulceration [62], but it may also find applications in esthetic medicine.

SWE distinguishes normal skin from scars and could be used to evaluate scar severity, which could be important for patient care and treatment. Additionally, intra- and inter-observer reliability were excellent, even when performed by a novice clinician versus an experienced sonographer. A direct linear relationship was established between scar thickness, scar pliability and SWV [63]. Likewise, SWE was used to quantify keloid response to treatment after intralesional corticosteroid injection [64], with no significant difference in thickness between normal skin and treated keloids. SWE values of treated keloids were significantly lower but still higher than normal skin.

Conservative treatment of fingertip amputation using occlusive dressings can lead to soft tissue regeneration. Ultrasonography and SWE were performed on regenerated fingertips [65]. Compared to uninjured fingers, there were no differences in pulp thickness, but vascularization and stiffness were both significantly greater after fingertip regeneration.

SWE is also an objective tool to assess skin elasticity after flap reconstruction. In our clinic, we used UE to measure the stiffness of the skin of the hand after fascia superficialis flap surgery following a severe hand trauma (Fig. 5). To our knowledge, this is the first reported case. To date, a single study conducted by a team of plastic surgeons focused on elastography applied to this field [66]. They used SWE on subcutaneous fat after deep inferior epigastric perforator (DIEP) flap and found a positive correlation between flap

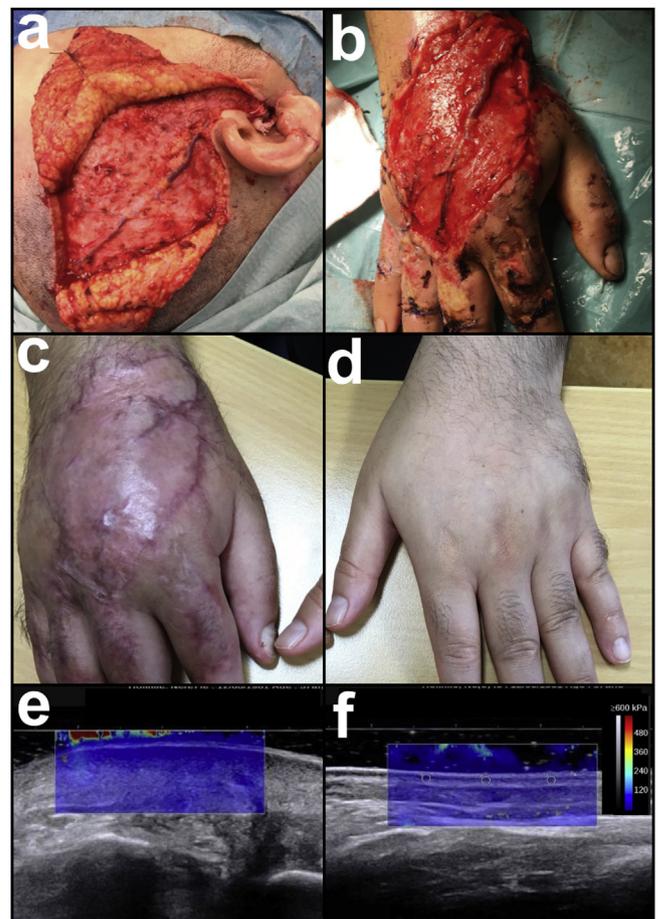


Fig. 5. Temporoparietal fascial free flap (a) for coverage of a large defect in the dorsal aspect of the hand (b). Combination of Matrigel[®] and skin graft. Clinical outcome at 6 months postoperatively (c, d). Similar skin shear wave velocity and elasticity observed in the pathologic (e) and contralateral sides (f): respectively, 17.3 kPa, 2.4 m.s⁻¹, and 16.8 kPa, 2.4 m.s⁻¹.

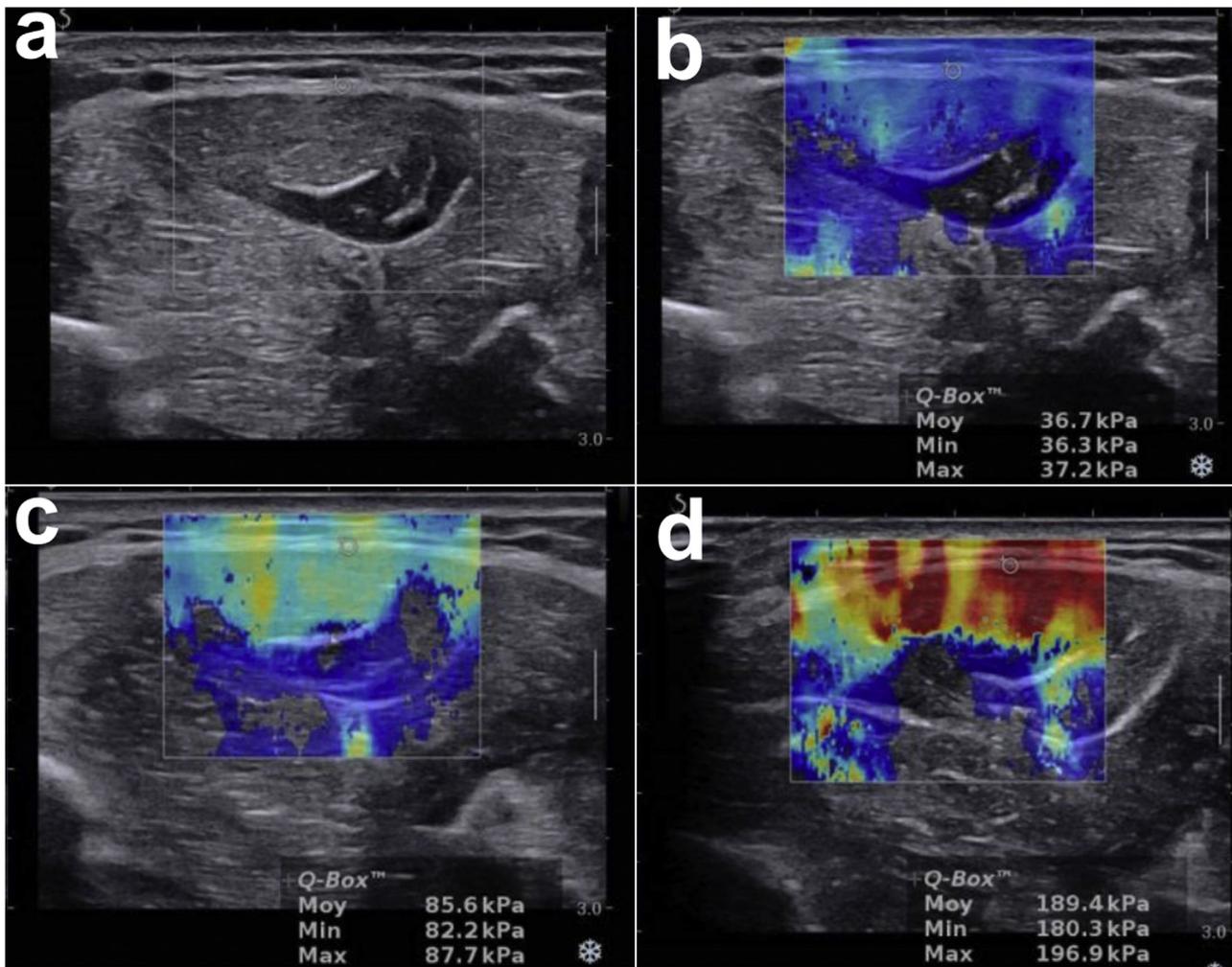


Fig. 6. Patient with chronic compartmental syndrome of the right forearm confirmed on intracompartmental pressure monitoring (Compass[®]). B-mode of the transverse/axial image of the right forearm (a). Shear wave elastography measurement of the antebrachial fascia showed stiffness of 36.7 kPa at rest (b), increasing to 85.6 kPa (b) and 189.4 kPa (c) after 10 min and 20 minutes' muscle contraction exercise, respectively. Then, the patient stopped, because of pain and tingling in the fingers (d).

weight and fat tissue stiffness. This result is particularly relevant because fat induration and necrosis are common complications after breast reconstruction with DIEP flaps but are currently only evaluated clinically.

6. Elastography and other indications in the hand and upper extremity

Extrapolating results from the above-mentioned tissues suggested that UE could be a useful way to assess ligament health and integrity. SWV in the ulnar collateral ligament of the elbow on the dominant side was lower in baseball pitchers at midseason [67]. This functional decline in the ulnar collateral ligament was probably associated with structural modification. Another study used SWE to quantify the central band stiffness of the interosseous membrane in forearms placed in different positions of pronation-supination [68]. Stiffness measurements were reproducible between examiners. The authors concluded that elastography could help guide diagnosis and therapy in interosseous membrane lesions.

B-mode US imaging for diagnosis of trigger finger showed A1 pulley thickening. Additional UE acquisitions showed A1 pulley stiffness. These two parameters tend to be alleviated by corticosteroid injection, and are thus contributive for treatment follow-up [69].

To date, measurement methods for acute compartment syndrome are invasive and clinical diagnosis may be challenging. According to Zhang et al. [70], muscle stiffness indirectly reflects intra-compartmental pressure, and SWE may be a noninvasive quantitative diagnostic tool in compartment syndrome. In a short study [70], muscle stiffness was significantly greater than on the unaffected side in 4 patients with acute compartment syndrome, but more data are needed before a quantitative cut-off can be established. Chronic compartment syndrome can also be explored using SWE (Fig. 6).

In the oncological field, stiffness values are greater for malignant lesions (breast, thyroid, prostate, skin, lymph node) than for benign masses [71–74]. SWE shows higher sensitivity and specificity than traditional B-mode US imaging to identify malignant lesions [72] and can avoid risky invasive procedures such as biopsies. Musculoskeletal tumors encompass a vast array of distinct tumor types, the majority of which are benign. Malignant musculoskeletal tumors may express a wider range of stiffness values, due to their more heterogeneous structure compared to benign lesions [75]. However, with only a few studies on this topic [75–79], no clear correlation emerged between stiffness and malignancy in musculoskeletal tumors [75–77].

In a recent retrospective study [80], the combination of elastography with 2D imaging and color flow imaging achieved excellent diagnostic accuracy for schwannoma in patients with soft-tissue masses in the limb.

Finally, elastography can be also used for vessel stiffness evaluation. For example, SWE can distinguish between acute and chronic clots by characterizing tissue stiffness in deep vein thrombosis. It was also demonstrated that variation in stiffness in brachial arteries was significantly less in patients with known cardiovascular disease than in healthy controls. This could be an early sign of atherosclerosis [81].

7. Conclusion

Ultrasound elastography is an accessible non-invasive imaging modality that can be used to measure stiffness in a variety of soft tissues. With the growing interest in developing new elastography applications in the hand and upper extremity, technical limitations concerning reproducibility and repeatability should be kept in mind. This technique has a promising future, but a significant amount of work remains to be done. Protocols must be standardized, as joint positioning affects SWV measurement in the surrounding soft tissue. In addition, the selection of regions of interest (ROI) is operator-dependent and may introduce variability. Also, several commercial systems exist, using different probes with different frequency ranges, which can impact SWV values.

Strain elastography provides only qualitative values of stiffness and the external force is difficult to reproduce or is variable over time, and artifacts are liable to be generated. SWE takes a simplistic view of soft-tissue mechanical properties as being isotropic, homogeneous, linear elastic and incompressible, to facilitate the process of imaging, whereas tissues are in fact anisotropic, heterogeneous, viscoelastic, and skeletal muscle, for example, is compressible when associated vascular and lymphatic components are taken into account.

Despite these limitations, UE demonstrated important correlations with diffuse and focal disease states in multiple soft tissues of the upper limb. UE should have huge clinical applications in musculoskeletal tissues. Continued development of systems and increased training in UE will expand our knowledge of elastography and its clinical applications in the future.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article and that this report does not contain any personal information that could lead to their identification.

Disclosure of interest

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Author contributions

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