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Applications of ultrasound elastography to hand and upper limb disorders.

Applications de l'élastographie ultrasonore dans les pathologies de la main et du membre supérieur.

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Abstract

Ultrasound elastography is a recently developed method for accurate measurements of soft tissue stiffness in addition to the subjective clinician's evaluation. The present review briefly describes the ultrasound elastography techniques and outlines clinical applications for tendon, muscle, nerve, skin and others soft tissues of the hand and upper limb.

Résumé

L'élastographie ultrasonore est une méthode récemment développée pour déterminer la rigidité des tissus mous en complément de l'appréciation subjective du clinicien. Cet article de synthèse décrit brièvement les techniques d'élastographie par ultrasons et leurs applications cliniques pour les tendons, muscles, nerfs, peau et autres tissus mous de la main et du membre supérieur.

Mots-clés : Elastographie; Ultrason; Main; Chirurgie; tendon; muscle; nerf; peau.

Keywords: Elastography; Ultrasound; Hand; Surgery; tendon; muscle; nerve; skin.

1. Ultrasound Elastography

Ultrasound (US) elastography method noninvasively measures the stiffness of the tissue by producing and measuring tissue deformation [1]. Indeed, the stiffness represents the tendency of the tissue to resist at a deformation induced by an applied force and is characterized by the modulus of elasticity (Young's modulus; Pa) defined as follows:

$$E = \sigma/\epsilon$$

where σ is the stress (Pa), corresponding to the normalized force, and ϵ is the strain (unitless) which represents 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 diseases, prostatic diseases, and musculoskeletal conditions [3, 4].

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

The strain imaging of the tissue, which revealed the physical tissue displacement, is estimated by its axial deformation parallel to the externally applied force exerted on body surface using the ultrasound probe (Fig. 1a). This method provides a qualitative evaluation of the stiffness [5]. Two approaches for strain imaging using ultrasound techniques were developed: the strain elastography (SE) and the acoustic radiation force impulse (ARFI) strain imaging. For the strain elastography, tissue displacement is generated by manual external compression with ultrasound transducer [2] or by an internal physiologic motion (cardiovascular) to assess more deeper located organ [6]. For ARFI technique, 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 with a color map called an elastogram.

The Shear wave imaging uses a dynamic stress to generate shear wave inside the tissue and the measurement of shear wave speed allow the determination of the stiffness. Three approaches exist to obtain shear wave imaging. Firstly, 1D transient elastography 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 and a portion of its longitudinal waves is converted to shear waves perpendicular to the longitudinal waves [9]. With 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 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) but multiple focal zones are stimulated and this creates a near cylindrical shear wave cone [10], permitting real-time monitoring of shear waves in 2D and generating quantitative elastograms superimposed on a B-mode image (Fig. 1c).

2. Elastography and tendon

Tendon rupture 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 conventional ultrasonography (US) [12]. Decreased mechanical properties (stiffness values) in degenerative tendinopathy and/or tendon injury compared to healthy tendon have been demonstrated in several studies [12-16] but in some cases of tendinopathy (long-head biceps tendon), UE analysis provides conflicting results [17]. Despite the different data, shear wave elastography (SWE) seems to be a reproducible technique to evaluate tendon elasticity with low inter-observer differences [21,22].

SWV of human hand tendons in physiologic in vivo conditions (Figs. 2a, 2b, 2c) has been analyzed in various studies [23]. Experimental studies using flexor tendons of porcine demonstrated that the stiffness of a partially teared tendon is lower in the vicinity of the injury and is dependent on the size of the tear [21]. Moreover, the stiffness of a damaged tendon induced by collagenase solution is significantly lower than a normal tendon [24]. Fluids accumulation and hematoma associated with acute ruptures appear as signal void areas on SWE [13,15]. After flexor tendon repair, re-rupture can be much more difficult to assess in B-

mode. SWE of the flexor tendon proximally to the lesion demonstrated systematically a significant decrease of SWV compared to healthy side (figs. 2g, 2h, 2i). Injured flexor hand tendons after surgical repair showed altered regional mechanical elastic properties and appeared locally stiffer compared to the healthy side using SWE. The clinical significance of these findings was that the tendon would glide less on rigid local zone and authors propose to focus rehabilitation on these stiffer zones, aiming at improving gliding [24].

In their study, Turkey et al. [13] compared SWE acquisitions performed on 40 patients suffering from De Quervain tenosynovitis, with 40 healthy volunteers. They have demonstrated that the Young's modulus values of healthy tendons of the first extensor compartment were 69.17 ± 22.45 kPa whereas pathologic tendons showed lower values (29.75 ± 8.02 kPa).

Medial and lateral epicondylitis have also been 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 accuracy was better than US by 7.1% for epicondylitis diagnosis, sensibility and specificity being of 96% and 89%, respectively. Moreover, it has been demonstrated that SWV increases after conservative treatment in patients with lateral epicondylitis [14]. The combined modalities of UE and B-mode ultrasonography provided a statistically significant improvement in the 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 concerning rotator cuff tears [26], SWE has been successfully used to identify the localization and degree of supraspinatus tendon tear, improving the value of ultrasound. Indeed, patients with rotator cuff tears had a lower mean SWV of muscle and tendon under active conditions. Intraclass correlation coefficient was excellent (0.96). Supraspinatus tendon Stiffness increased between 8 days and 24 weeks after repair [26].

3. Elastography and muscle

With a Young's modulus ranging from 5-40 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]. The reliability of the SWE for measuring muscle stiffness has been proven for several muscle groups including lower limb, trunk, upper limbs muscles including the intrinsic muscles of the hand [29,30]. Furthermore, studies suggested using SWE to monitor the 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 the functional muscle activity compared to the physiological activity recorded with conventional surface electromyography [32]. SWV of muscle seems to be influenced by sex, age, and dominance of the patient [32, 33]. Moreover, studies have highlighted the importance of the probe orientation, as the stiffness may decrease in a perpendicular position compared to the parallel orientation to the muscle fibers [34,35]. This result showed the anisotropic behavior of the skeletal muscle. The parallel orientation of the probe with the main direction of the muscle fiber is more valid and reliable for SWV measurements.

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 in 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.

In the study of Li et al., SWE of thenar muscle in hemiplegic patients was performed. The plegic side showed decreased stiffness compared to the healthy side. Changes in muscle stiffness in the follow-up could be used as an objective assessment of rehabilitation degree [41].

In 2017, Lamouille et al. reported the 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 transferring, during active extension, and after tendon transfer at rest. The investigators showed differences in stiffness

values at the various stages of the tendon transfer procedure, providing new insights to improve therapeutic treatments of tendon transfers [42].

Due to the frequency of rotator cuff degenerative lesion, shoulder muscles are of interest, and the most analyzed structures in the upper limb. In non-pathologic shoulders, SWE supraspinatus muscle values gradually decreased with increased passive abduction of the shoulder. In case of large to massive tears, the stiffness of supraspinatus muscle did not vary from adduction to abduction conditions [43]. After rotator cuff surgical repair, the contractile behavior of the supraspinatus muscle increased from 6 weeks to 3 months after surgery and the 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 during rotator cuff injury. In addition to human muscle, SWE technique is developed to characterize the muscle stiffness of small rodents to follow the effect of treatment [45].

4. Elastography and nerve

For many years, electroneuromyography (ENMG) has been considered as the main diagnostic tool for peripheral neuropathies. Then, B-mode ultrasound image and doppler examination were found to be of interest in Carpal Tunnel Syndrome (CTS) diagnosis showing 1) an increase in nerve cross sectional area (CSA) proximal to the region where the nerve is compressed, 2) a reduced mobility of the nerve, 3) a modification of the structural properties through a variation in echogenicity, and 4) an increased vascularity of the nerve. SWE in adjunction to B-mode ultrasound seems to be reliable for entrapment neuropathy diagnosis, with the advantages of being a noninvasive test, accessible and fast for the surgeon. Most SWE studies related to the upper limb nerves were performed on the median nerve (MN) for CTS. Authors have demonstrated that long term edema or high carpal tunnel pressure could lead to increase median nerve stiffness [46]. Reliability and feasibility of the stiffness

measurements obtained with SWE realized in healthy MN (N = 40) subjects showed excellent interobserver and intra-observer agreement (0.852–0.930), with no difference between bilateral forearm measurements [47]. Attention must be paid to limb positioning during SWE measurements, as it directly affects nerve tension and the stiffness values [48]. A meta-analysis, composed of 17 studies, using sonoelastography to image the MN at wrist level (N = 1401 wrists) confirmed that the nerve is consistently stiffer in patients with CTS than healthy subjects regardless of the ultrasound elastography technique [49]. Moreover, studies have successively identified the severity of the nerve disease through different stages [50,51]. Thus, SWE allowed for a classification of CTS similar as the gold-standard electrodiagnostic, with cases stratified as mild, moderate or severe based on the stiffness of the MN. This was not achievable using B-mode US alone. Both median nerve CSA at the wrist and shear wave velocity were reduced one week after surgical carpal tunnel release, reflecting nerve recovery [52]. However, cut-off stiffness values proposed for CTS diagnosis are different according to authors, varying from 40.4 kPa to 79 kPa [46,53]. Also, Sugiyama et al. [54] proposed SWE technique as an objective, quantitative and noninvasive evaluation test for MN follow-up after volar locking plate osteosynthesis of distal radius fracture, helping to decide on material removal and MN neurolysis timing.

For ulnar nerve neuropathy at the elbow and at the Guyon's canal, SWE appears as a new reliable method to support this diagnosis [55,56]. Ulnar nerve stiffness with a Young's modulus over 61 kPa and the stiffnesses ratios of the cubital tunnel to distal arm and to mid-arm were 1.68 and 1.75, respectively, provided 100% specificity and sensitivity for the detection of ulnar neuropathy at the elbow [55]. Also, SWE can be used to differentiate ulnar neuropathy at the cubital tunnel from asymptomatic ulnar nerve with medial epicondylitis and healthy uncompressed ulnar nerve [57]. Patients with unilateral ulnar tunnel syndrome showed higher CSA and stiffness in the affected side for all positions, i.e., extension, 45° flexion, 90° flexion and at the maximum flexion of the elbow where the stiffness increased [58]. In patients with ulnar nerve decompression associated with anterior transposition, post-operative ulnar nerve stiffness increased with elbow joint extension (Fig. 4). However, on the non-operative 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 fractures [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 cancers, connective tissue diseases, chronic systemic inflammation, lipodermatosclerosis or patients at risk of ulceration [62] but it may also find applications in aesthetic 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, excellent intra-observer and inter-observer reliability was noted, even when the test is performed by a novice clinician versus an experienced sonographer. A direct linear relationship was established between scar thickness, scar pliability and SWV measurements [63]. In a similar way, SWE was also used to quantify keloid response to treatment after intralesional corticosteroid injection [64]. The results showed no statistical differences in thickness between normal skin and treated keloids. SWE values of treated keloids significantly decreased but the data were 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 the regenerated fingertips [65]. Compared to collateral uninjured finger, there were no difference in pulp thickness, but vascularization and stiffness were both significantly higher after fingertip regeneration.

SWE appears also as an objective tool to assess elasticity of the skin after flap reconstruction. In our clinic, we used the UE to measure the stiffness the skin of the hand after fascia superficialis flap surgery following a severe hand trauma (Fig. 5). To our knowledge, this is

the first case described. To date, a unique 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 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 hand and upper extremity.

Extrapolating results from the pre-mentioned tissues, it was felt that UE may be a useful way to assess ligament health and integrity. Decreased SWV in the ulnar collateral ligament of the elbow in the dominant side was observed in baseball pitchers at midseason [67]. This functional decline of the ulnar collateral ligament was probably associated with structural modification. Another study described the use of SWE to quantify the central band stiffness of interosseous membrane located in the forearm placed in different positions of pronosupination [68]. The results demonstrated that the stiffness measurements were reproducible between examiners. Authors raised that elastography could help guiding diagnostic and therapy in the management of interosseous membrane lesions.

B-mode US image for trigger finger diagnosis shows A1 pulley thickening. Additional UE acquisitions showed A1 pulley stiffness. These two parameters tend to alleviate after corticosteroid injection, being a valid asset for treatment follow-up [69].

To date, measurement methods of acute compartment syndrome are invasive and clinical diagnosis may be challenging. According to Zhang et al. [70], muscle stiffness indirectly reflects intra-compartmental pressure revealing that SWE may be a noninvasive quantitative diagnostic tool for compartment syndrome diagnosis. In a short study [70], muscle stiffness was found to be significantly higher than the unaffected side in four patients with actual 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, higher stiffness values are noted for malignant lesions (breast, thyroid, prostate, skin, lymph node) compared to benign masses [71-74]. SWE shows higher sensitivity and specificity than traditional B-mode US image to identify malignant lesion [72] and could avoid invasive risky procedures such as biopsies. Musculoskeletal tumors encompass a vast array of distinct tumor types, the majority of which are usually benign. Malignant musculoskeletal tumors may express a wider range of stiffness values due to its more heterogeneous structure compared to benign lesions [75]. With only a few studies on this topic [75-79], no evident correlation was found between stiffness and malignancy detection of musculoskeletal tumors [75-77].

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

Finally, elastography could be also used for vessels 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 of stiffness in brachial arteries was statistically inferior in patients with known cardiovascular disease when compared to the healthy control group. 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 biological tissue. With the growing interest in developing new elastography applications in hand and upper extremity, one should keep in mind technical limitations concerning reproducibility and repeatability. This technique has a promising future but a significant amount of work remains to be done. Indeed, protocol must be standardized as positioning of the joint affects SWV measurement of the surrounding soft tissues. In addition, the selection of region of interest (ROI) is operator dependent and may introduce

variability. Also, several commercial systems exist leading to the use of different probes with different ranges of frequencies which can impact SWV values.

SE provides only qualitative values of stiffness and the external force is difficult to reproduce, or is variable through time, and can generate artifacts. SWE takes a simplistic view on the soft tissues mechanical properties (isotropic, homogeneous, linear elastic, incompressible) to facilitate the process of imaging, but tissues are anisotropic, heterogeneous, viscoelastic and skeletal muscle, for example, accounting for the associated vascular and lymphatic components, is compressible.

Despite the above cited limitations, UE has demonstrated important correlation to diffuse and focal disease states in multiple soft tissues of the upper limb. UE holds huge clinical applications in MSK tissues. Continued development of systems and increased formation of clinicians to UE will lead to expand our knowledge of Elastography and its clinical applications in the future.

Authors declare no conflicts of interest.

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Figures legends

Fig. 1: Ultrasound elastography represented by 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).

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), 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 the 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

using 3T MRI acquisitions (f). Patient with tendon rupture after flexor digitorum profundus of the index repair (third row). Re-rupture is difficult to identify in B-mode (g) proximally to the rupture. The cartographies of stiffness show lower values for the flexor digitorum profundus of the index (66.1 kPa, 4.7 m.s⁻¹) (h) compared to the flexor digitorum superficialis of the index (378.5 kPa, 11.2 m.s⁻¹) (i).

Fig. 3: Intra operative photographs of the 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 the rest (b) to the transferring active extension (c) and after tendon transfer at rest (d).

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

Fig. 5: Temporoparietal fascia free flap (a) for coverage of a large defect of dorsal aspect of the hand (b). Combination of Matriderm® and skin graft. Clinical outcomes at 6 months post operative (c, d). Similar skin shear wave velocity and elasticity observed in the pathologic (e) and contralateral side (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 using intra compartmental pressure monitor (Compass®). B-mode of the transversal / axial image of the right forearm (a). Shear wave elastography measurement of the antebrachial fascia showed a stiffness at 36.7 kPa at rest (b) which increase after 10 min and 20 min muscle contraction exercise at 85.6 kPa (b) and 189.4 kPa (c), respectively. Then, patient stopped because of pain and tingling in the fingers (d).

Fig.1

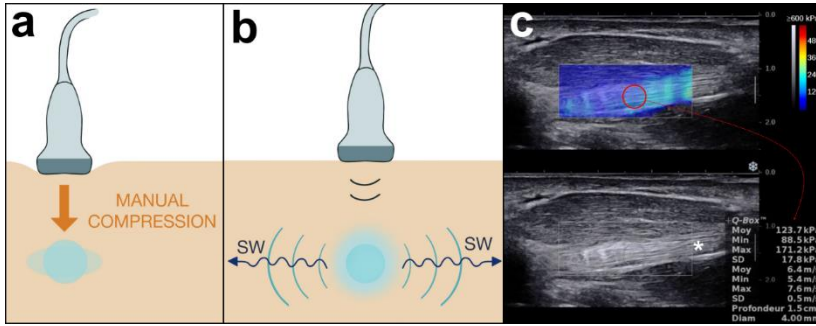


Fig.2

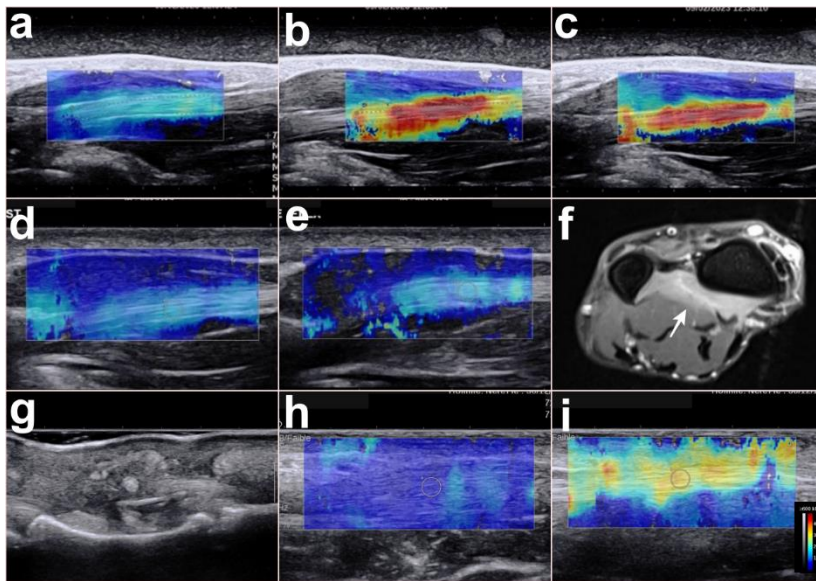


Fig.3

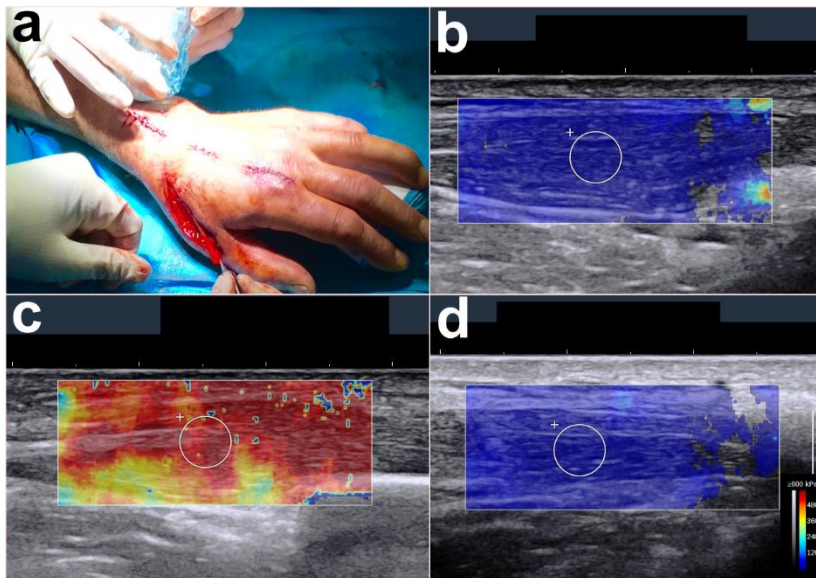


Fig.4

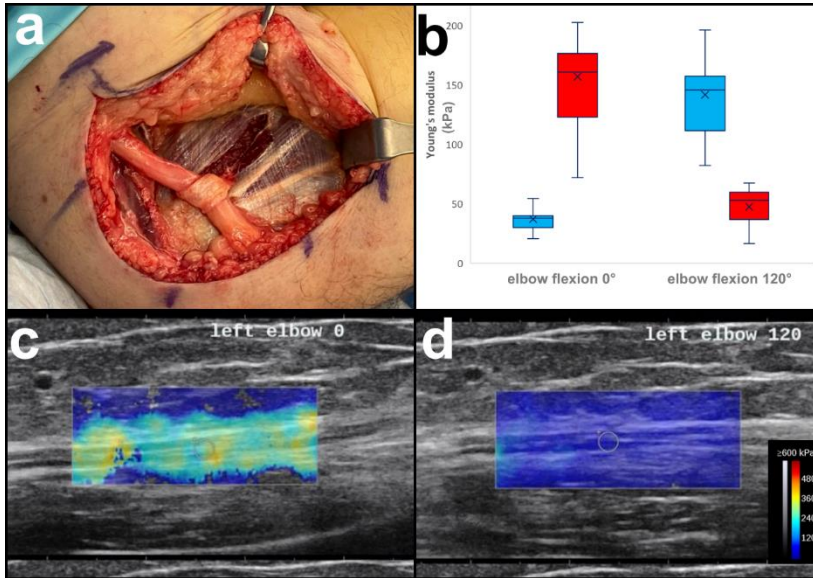


Fig.5

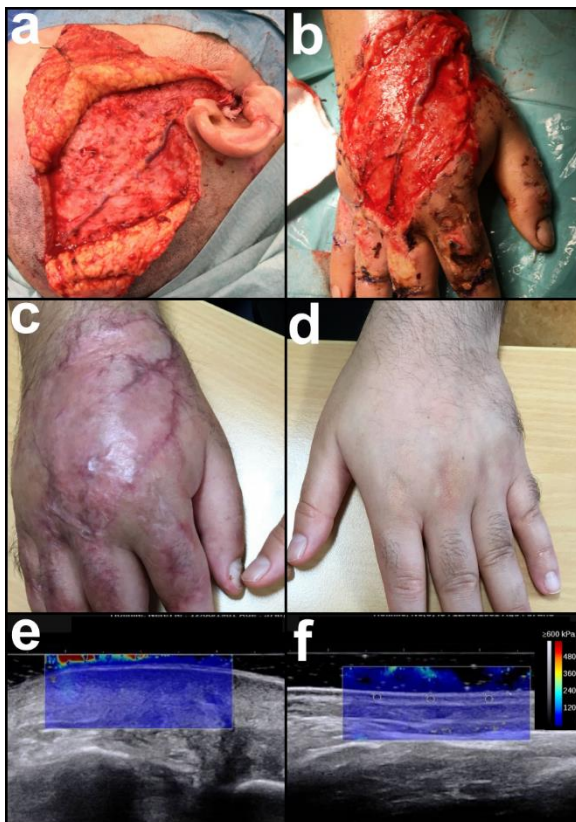


Fig.6

