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Fifth International Fascia Research-Congress Section: Fascia Research Review

Frontiers in fascia research

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ABSTRACT

Basic sciences are the backbone of every clear understanding of how the body is composed and how different structures and functions are connected with each other. It is obvious that there is a huge variability in human beings - not only in terms of the outer appearance such as measurements of height, weight, muscle mass and other physical properties, but also with respect to metabolic and functional parameters. This article highlights recent developments of research activities in the field of fascia sciences with a special emphasis on assessment strategies as the basis of further studies.

Anatomical and histological studies show that fascial tissue is highly variable in terms of density, stiffness, and other parameters such as metabolic and humoral activity. Moreover, it encompasses nerves and harbours a system of micro-channels, also known as the primo vascular system.

As ultrasound is a widely available method, its use is appealing not only for imaging of fascial structures, but also for thorough scientific analysis. Unlike most other imaging technologies, US has the advantage of real-time analysis of active or passive movements. In addition, other assessment methods for fascial tissue are discussed.

In conclusion, fascial tissue plays an important role not only in functional anatomy, but also in evolutionary and molecular biology, sport, and exercise science as well as in numerous therapeutic approaches. A high density of nerves is found in fascial tissue. Knowledge of individual characteristics, especially by visualizing with ultrasound, leads to personalized therapeutic approaches, such as in pain therapy.

1. Fascial anatomy

Over the last decade, numerous studies have focused on fascial anatomy such as the studies of fascia in the neck region (Kitamura, 2018), plantar fascia (Guo et al., 2018), the vasto-adductor fascia (Elazab, 2017), and on the infraspinatus fascia (Moccia et al., 2016). A new technique for studying fascial topography combining staining and plastination was described by Steinke et al. (Steinke et al., 2018). In an indication of the mainstreaming of fascial anatomy, a series of brief summaries of regional fascial anatomies was published as part of an online reference of biomedical knowledge at Statpearls.com, 2018. A robust and timely discussion of fascia nomenclature was engaged under the auspices of the Fascia Research Society, which convened a Fascial Nomenclature Committee in connection with its 2015 conference (Adstrum et al., 2017; Hedley, 2016; Stecco & Schleip, 2016; Stecco et al., 2018a). Carla Stecco continued to be a leading investigator of fascial anatomy. In one publication she suggested a distinction between two types of human abdominal fascia – that investing that encapsulates organs, and an insertional type that connects the organs to their larger

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biomechanical surroundings (Stecco et al., 2017). There is ongoing research into several receptors in fascial tissue, such as nociceptors and hormone receptors (Fede et al., 2016; Hoheisel et al., 2015).

The most dramatic developments during the last decade were actually anatomical – the discovery of telocytes in fascia (Dawidowicz et al., 2016), the discovery of cells devoted to the secretion of hyaluronic acid into the connective tissue matrix (Stecco et al., 2018b) and Theise's hypothesis of a network of micro channels – the primo vascular system.

2. Fascia and primo vascular channels: how important are they?

In the last decade evidence has emerged that a sophisticated channel system, also known as the primo vascular system, interpenetrates fascial tissue. The primo vascular system was described as early as 1961, first under the name Bonghan channels. However, because the detection methods described were very unclear and hard to replicate, interest in these channels was lost for several subsequent decades. Because their diameter is quite small (usually around 20–50 μm) and also because of their transparent nature, these channels are indeed easily missed.

Thanks to modern imaging systems these channels have been re-discovered and confirmed in recent years. The described channels have been shown to exist on the surface of most viscera, in adipose tissue, in blood vessels, and in lymph vessels. The channels carry a high concentration of hyaluronan, of nucleic acids and small adult embryonic like stem cells. They were renamed 'primo vascular system' in 2010 (Soh et al., 2012).

Most likely the primo vascular channels are identical with the newly described 'conduits' by Weigelin et al., (2012). Based on third harmonic generation microscopy a system of small channels has been described, which migrating cells use via their movements through the extracellular matrix. Similar to animals using the paths of least resistance by migrating through a jungle, these cells seem to widen and to 'create' these pathways through the fibrous matrix. It will be exciting to learn to what extent these pathways will have beneficial health aspects (e.g. by allowing immune cells to migrate) and possibly also detrimental aspects (e.g. for the spreading of cancer cells). Neal Theise recently proposed that the aforementioned extended network of micro channels should be recognized as a fundamental organ (Benias et al., 2018).

3. Pathomechanical significance of fascial dysfunctions

A landmark 2015 conference on Fascia, Acupuncture and Oncology was summarized in a white paper which suggested areas ripe for further investigation (Langevin et al., 2016). In relation to this, one of that conference's most widely acclaimed presenters, Melody Swartz, continued her innovative investigations of cancer tumor interactions with lymphatic and fascial systems (Procopio et al., 2015). A detailed study of cellular components of fascia using light, electron and confocal microscopy, including the identification of telocytes, was published by Szotek et al. (Szotek et al., 2016). Studies of disease and injury related fascial dysfunction focused on lumbar paraspinals (Ranger et al., 2016), the tensor fascia lata and gluteus maximus (Cibulka Mt Pt and Bennett J Pt, 2018), and the mediastinum (Bordoni et al., 2018). The contribution of disorders of the lumbodorsal fascia to low back pain continues to attract a number of investigators. A narrative review was provided by Wilke et al., (2017). Hypotheses of the pathomechanical significance of fascial disorder were not however, without their critics (Thalhamer, 2018).

4. Manipulation and stretching of fascia as therapeutic interventions

Langevin and associates continued to investigate the effects of soft tissue stretching on inflammation, wound healing and restoration of mobility (Berrueta et al., 2018; Langevin et al., 2018; Xiong et al., 2017). A review of associated biological changes by manual therapy emphasizes the modification of pro and anti-inflammatory mechanisms (Parravicini and Bergna, 2017). Leon Chaitow provided a narrative review of hypotheses of mechanotransduction as a therapeutic mechanism (Chaitow, 2018). Geoffrey Bove continued a groundbreaking line of studies using rat models of connective tissue fibroticization, adhesion, and manual intervention (Bove et al., 2017a, b; Bove et al. 2016).

Clinical investigations of fascial stretching and manipulation in humans included several studies of low back pain (Bae et al., 2017). Studies of intervention in biomechanical properties of thoracolumbar fascia included randomized controlled trials by Griefahn et al., (2017), and Tom Findley's lab (Sanjana et al., 2017). The latter used the MyotonPro, an innovative handheld device for measuring biomechanical properties of soft tissues, to assess change in the biomechanical properties of thoracolumbar tissue. Evidence for its reliability had been presented earlier (Orner et al., 2018).

In addition, one of the deans of human biomechanics, Serge Gracovetsky, contributed two provocative theoretical discussions (Gracovetsky, 2016, 2018).

5. Biomechanical modeling of force transmissions in fascial structures in the human lower back

Over the last decade, many advancements in measurement and diagnostic tools have acted as catalysts towards new research methods and findings of high clinical value. These advancements can be driven by two motivating factors. Firstly, the need to take specific measurements leads to the development of new tools. Secondly, the converse, as new tools become available and thus enable new measurements, they then create a need for clinical interpretations. Lately, the ability to qualitatively and quantitatively interpret clinical images at high frequencies has led to interpretations of innervation of fascial tissues and relative analyses of tissue stiffness, amongst others. In parallel, reliable measurement of tissue mechanical properties, such as fascia, has long been desired by way of non-invasive techniques. While ultrasound methods are making strides in this direction, direct mechanical manipulations, such as indentometry, also appear promising for clinical applications. For example, an application of high clinical focus lies in the lower back where the thoracolumbar fascia's involvement continues to gain attention.

The spine is a very intricate system that is balanced or stabilized via active and passive contributions from our musculoskeletal system. It is the passive system which benefits primarily from fascial involvement, particularly via the thoracolumbar fascia (TLF). While the morphology and anatomy of this tissue is well described (Benjamin, 2009; Goss, 1973; Hafferl, 1953; Hollinshead, 1982; Standring, 2004; Vleeming et al., 1995), its mechanical role is less evident. Experimental studies have exemplified however that the TLF contributes towards force transmission to the spine which likely plays a considerable role in spinal stability (Vleeming et al., 2014). Clinical studies utilizing imaging showed increased thickness of the posterior region of the TLF and decreased shear strain in low back pain patients (Langevin et al., 2011). Phenomenological observations often link intra-abdominal pressure (IAP), whose force is conveyed to the spine via the TLF, to spinal stability as well. Thus, a number of complementary analytical methods have separately, yet correspondingly, indicated the role of TLF in spine stability.

Another analysis method, named *in silico,* finite element, or numerical, is growing in its application towards musculoskeletal biomechanics. Notably, in spine biomechanics, several active engineering research groups are striving to solve the puzzle that is spinal stability by way of numerical analyses. Carl-Eric Aubin, of Ecole Polytechnique, focuses on spinal deformities such as scoliosis and their treatment. Another group from the same institution under Saeed A. Shirazi-Adl explores spine stability. Hendrik Schmidt's group at the Berlin Julius Wolff Institute focuses on spinal motion and loads as causes for back pain. The McGill Musculoskeletal Biomechanics Research Lab focuses on the role of IAP on spine biomechanics and stability as well as muscle activation strategies (Fig. 1). Hans-Joachim Wilke's group at Ulm University is also leveraging *in silico* analyses and merging clinical studies. These and other groups utilize the numerical platform to make objective and quantitative interpretations while leveraging clinical data for direct or indirect validation.

Despite the improvement of the aforementioned methods of imaging and indentology, which allow one to gauge mechanical properties of tissues, the majority of biomechanical analyses by way of numerical modeling relies on bench data. This is when tissues are resected, isolated, and then stretched until failure. Absolute properties derived from such studies give a baseline upon which to build numerical models. Nevertheless, imaging and indentology methods provide good relative distributions of mechanical behaviors and can often identify certain phenotypes which serve clinical users well. Engineers, with clinical collaborators, are now leveraging these new measurements to run “what if” scenarios with the numerical models to more objectively evaluate the biomechanical impact of such phenotypical range of properties. For example, with imaging, measurement, and diverse experimental platforms at our disposal, many interdisciplinary teams are now able and starting to critically assess fascia in musculoskeletal biomechanics. This will take time, and will likely be both fueled and propelled by new measurement techniques but, without a doubt, it will improve our biomechanical understanding of the role of fascia in the spine and throughout the never-ending complexity that is our body.

6. Ultrasound - widely available moving images

Ultrasound has continued to develop as a favored technology for imaging and measuring fascia and its response to manual interventions, often with a focus on the thoracolumbar region (Bishop et al., 2016; De Coninck et al., 2018; Engell et al., 2016; Salavati et al., 2017). Advances have also been reported in imaging soft tissue in plantar fasciitis (Draghi et al., 2017). Interrater reliability was assessed by Bisi-Baolgun et al. (Bisi-Balogun and Rector, 2017).

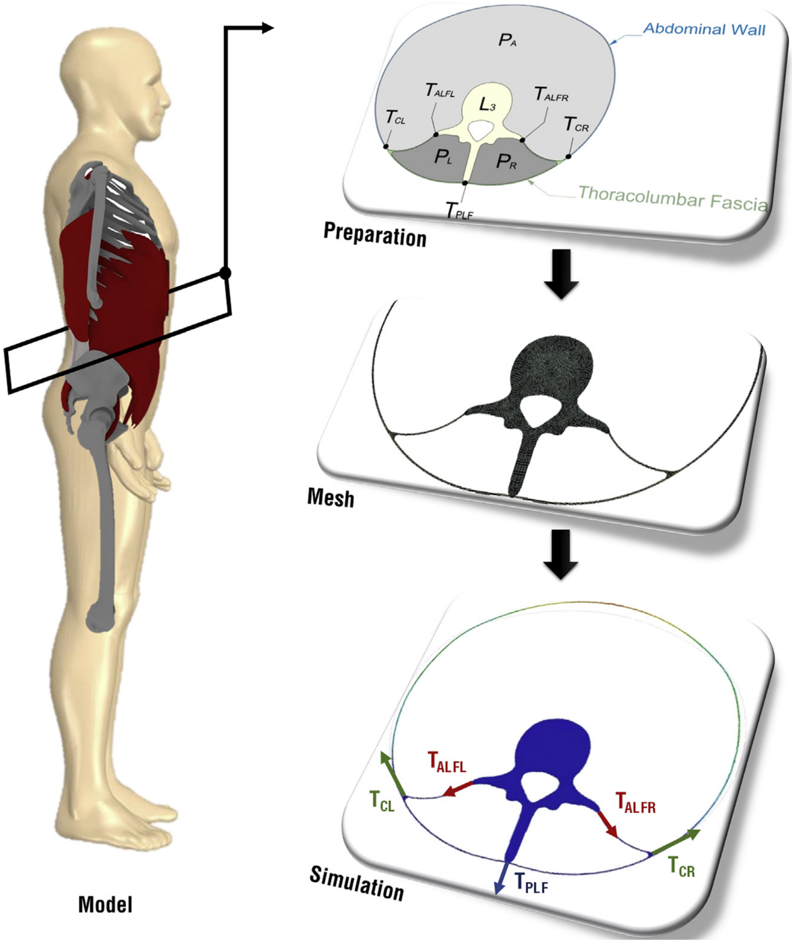

Fig. 1. Cross section exemplifying in part the fascial envelope of the spine explored via finite element numerical analysis – courtesy of Khaled El-Monajjed of the McGill Musculoskeletal Biomechanics Research Lab.

The great majority of publications on fascia research continue to be concerned with surgical strategy and recovery. Modern imaging allows us to estimate the percentages of anatomical variability, which has a tremendous impact on anaesthesiological or surgical procedures (Marhofer et al., 2010).

Imaging technologies have taken big steps ahead over recent decades, not least because of more sophisticated methods and computer algorithms. Several technologies are in use, such as X-ray, computed tomography (CT), magnetic resonance imaging (MRI), Positron emission tomography (PET) and many others.

Unlike the aforementioned technologies, ultrasound has the great advantage of being widely available and not based on X-ray technology. Most notably, ultrasound produces dynamic pictures and shows the different structures as they move. For the fascia thoracolumbalis, it has been shown that ultrasound imaging can detect pathological changes in the gliding function and anatomical properties of patients with chronic low back pain (Langevin et al., 2011).

In brief, ultrasound is technically generated by piezoelectric activation. In the body, the different effects occurring when using ultrasound are transmission, absorption, reflection, dispersion and refraction. The strength of ultrasound is in penetrating soft tissues. Basically, the greyscale image seen on the screen is the summary of waves “mirroring back” from the tissue.

In the following examples, different strategies of ultrasound imaging are displayed and adapted to fascial tissue.

7. Ultrasound in B-mode

Modern high resolution systems are able to work with frequencies of up to 70 Mhz (Cartwright et al., 2017). With such frequencies, axial and spatial resolutions of less than 0.1 mm are possible, allowing for the depiction of the network of fascia layers (Fig. 2). However, due to the physics of ultrasound, the best images may be achieved at a distance of up to 2–3 cm from the skin. As mentioned above, ultrasound waves traveling to tissues are attenuated with travel distance (Fig. 3). For the imaging of deeper structures, e.g. in obese individuals (Fig. 4), lower frequencies have to be used for deeper penetration. The lower the frequency, the higher the penetration depth, but unfortunately resolution decreases with decreasing frequencies. For example, a frequency of 10 MHz allows imaging to a depth of 4–5 cm while a frequency of 30 MHz travels only about 1 cm. Therefore, very small structures are best imaged with high frequencies but unfortunately only in the near field (Fig. 2).

In particular, small nerves cross fascia layers on their pathway to muscles or to the skin (Figs. 2 and 5). Ultrasound technology allows for the depiction of such nerves during their course through fascia layers. These small nerves may be affected after any trauma such as surgery or even contusions leading to pain perception. High resolution ultrasound enables the visualization of these nerves in the near field and can help to detect the causes for nerve affection and

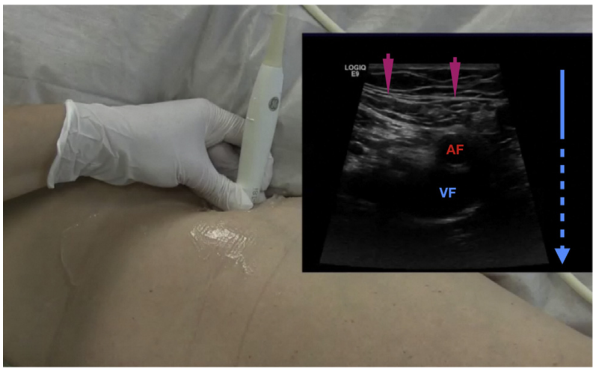

Fig. 3. An 18 MHz sonogram of the thigh shows the attenuation of the ultrasound waves with increasing depth as a loss of brightness in the inferior part. The different layers of the fascia lata can be clearly depicted. Magenta arrows: fascia lata, AF: femoral artery, VF: femoral vein. The blue arrow exemplifies the attenuation of the ultrasound beam.

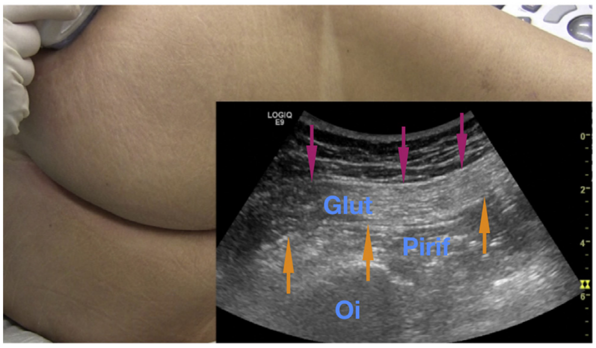

Fig. 4. A 6 MHz sonogram of the gluteal region. The muscle layers, but not the respective fascia layers can be clearly differentiated. Magenta arrows: gluteal fascia with fascia of gluteus maximus muscle (Glut), golden arrows: fascias of piriformis (Pirif) and gluteus maximus muscles (Glut).

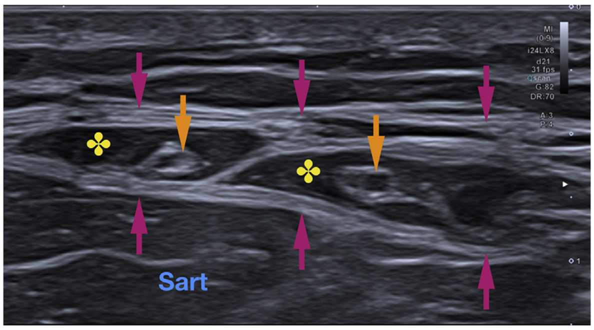

Fig. 2. A 24 MHz sonogram of the thigh clearly shows branches of the lateral femoral cutaneous nerve (golden arrows) within fat-filled fascial tunnels (yellow asterisks) in-between different layers of the fascia lata (magenta arrows). Sart: sartorius muscle.

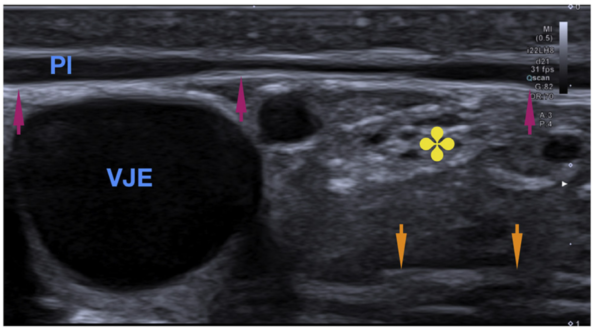

Fig. 5. A 22 MHz sonogram of the neck: the different fascia layers as well as the supraclavicular nerves (yellow asterisk) coursing between the superficial (magenta arrows) and prevertebral (golden arrows) fascias are clearly visible. VJE: external jugular vein, Pl: platysma.

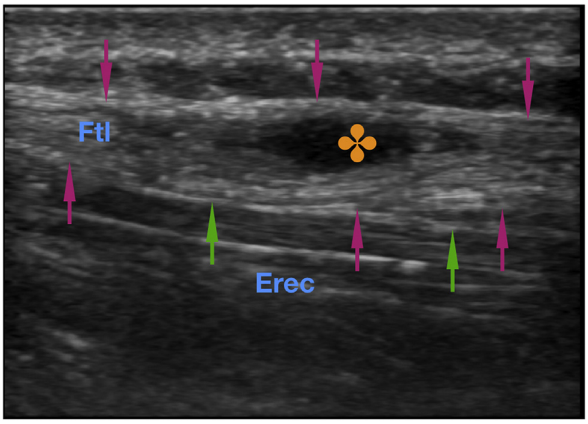

Fig. 6. A 15 MHz sonogram of a lipoma (golden asterisk) located between the posterior layer of the thoracolumbar fascia (Ftl, magenta arrows) and the fascia of the erector spinae (Erec, green arrows) in a 13-y-old girl. Only during movement does the girl suffer from pain caused by movement of the lipoma between both fascia layers.

pain. In deeper layers a specific visualization of the nerves is challenging and sometimes not possible due to the aforementioned physical limitations of ultrasound. However, the understanding and interpretation of the sonoanatomy can help to explain complaints even if the affected nerves cannot be visualized (Fig. 6). In clinical practice, nerve blocks are performed for diagnostics as well as a therapeutic tool. To achieve a specific diagnostic or therapeutic effect it is crucial to place the injection needle at or in the right compartment (Video 1, 2). For this purpose, sonography has an obvious advantage over surface landmark based injection techniques because it allows one to position the needle tip even in the small space between fascia layers (Video 1, 2). The spread of the injectate can and should be traced in real time in order to achieve the desired effects and avoid side effects. For example, it is possible to visualize the spread of injected local anesthetics to adjacent nerves coursing within the same compartment (Video 3).

A supplementary video related to this article can be found at https://doi.org/10.1016/j.jbmt.2018.09.077.

In summary, ultrasound is a valuable tool for the treatment of patients with pain in the immediate vicinity of fascial compartments. However, its accurate application requires a thorough understanding of the specific sonoanatomy, its physical characteristics and limitations.

8. Transmission-mode ultrasound

In contrast to classic B-mode ultrasound imaging, which is predicated on an assumed speed of ultrasound in all soft tissue of 1540 m/s, transmission-mode ultrasound makes no such assumption but rather involves the direct measurement of the propagation velocity of ultrasound in the target tissue. Transmission-mode ultrasound has been widely used to assess ultrasound propagation in both hard and soft connective tissues, including those of bone (≈4000 m/s), skin (≈1760 m/s), cartilage (≈1600 m/s), and tendon and ligament (≈2000 m/s) (Langton et al., 1984; Ling et al., 2007; Miles et al., 1996; Pan et al., 1998; Wearing et al., 2016). Although studies evaluating bone have typically focused on the attenuation of ultrasound waves as an indicator of osteoporosis, bone mineral density and fracture risk (Kauppi et al., 2014), studies evaluating soft tissues have typically evaluated the velocity of ultrasound waves as a measure of the mechanical properties (material stiffness) of the tissue.

In axial transmission-mode ultrasound, an emitter(s) and receivers are placed in series along the long-axis of the target tissue, and the transmission velocity of the ultrasound wave is determined from the known position of the receivers and the measured time-of-flight of the first-arriving ultrasound signal (Fig. 7). Although ultrasound waves propagate in several modes in various types of connective tissue, in tendon ultrasound compression waves propagate at ≈ 2000 m/s with a wavelength λ of ≈2 mm, and as such the first arriving signal typically corresponds to a lateral wave (Camus et al., 2000) guided by the interface between tendon and surrounding soft tissue, emitted from the surface of the tendon at the critical angle and propagating at the bulk wave velocity (Wulf et al., 2016).

The axial transmission velocity of ultrasound waves (V) is known to be dependent on the instantaneous material stiffness (Elastic modulus, E) and density (ρ) of the material through which it propagates, and in tendon is governed by the Newtonian–Laplace equation with adjustment for Poisson's effects (ν) (Vergari et al., 2012c).

$$V = \sqrt{\frac{E}{\rho}\frac{(1-\nu)}{(1+\nu)(1-2\nu)}}$$

Equine studies have also confirmed that the axial transmission speed of ultrasound in tendon is related to the applied load and can be effectively modelled as an exponential function (Crevier-Denoix et al., 2009; Pourcelot et al., 2005a; Vergari et al., 2012b). The error in predicting applied tensile force from direct measures of TSOU in animal tendon has been shown to be <2% (Crevier-Denoix et al., 2009). *In vivo* experiments in human Achilles tendon have also shown that the mean within-subject coefficient of variation for peak ultrasound velocity during walking ranges between 0.2% and 1.7% (Wearing et al., 2014). Hence, while the variation in the transmission speed of ultrasound with the application of mechanical load represents a limitation of most elastographic approaches (Ooi et al., 2014), ultrasound transmission techniques take advantage of this relationship, to afford a direct non–invasive method of quantifying the change in instantaneous material

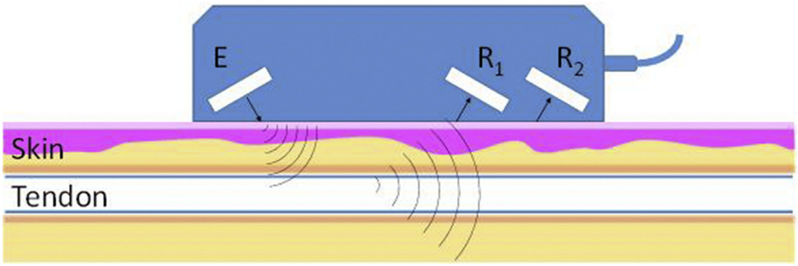

Fig. 7. Illustration of the basic measurement principle of transmission-mode ultrasound in characterising the instantaneous material stiffness of tendon.

stiffness of human tissues under dynamic conditions.

Recently, measures of axial transmission velocity of ultrasound have been shown to be sensitive to changes in tendon loading with footwear (Wearing et al., 2014), orthotic intervention (Wulf et al., 2016), changes in gait speed (Brauner et al., 2017), and with tendon injury and repair (Vergari et al., 2012a; Wearing et al., 2016). While the technique has also shown early promise for the characterisation of muscle properties (Fig. 8), to date its application has been largely limited to evaluating the properties of relatively superficial tendons and ligaments (Pourcelot et al., 2005b; Wearing et al 2014, 2016). Moreover, in its current form, the technique is unable to isolate the properties of the various component structures of tissues, such as tendon fascicles; however, signal processing methods such as transit time spectroscopy (Alomari et al., 2018) may in future provide greater insight into the structural of component tissues.

9. Assessment methods for mechanical properties

Quantitative ultrasound techniques such as elastography have recently emerged as a potentially useful non-invasive measurement tool for characterizing the mechanical properties of tendon *in vivo*. These approaches typically characterise the relative deformation or strain of the tissue midsubstance to provide semi-quantitative or quantitative indices of tendon hardness or stiffness (Gennisson et al., 2013).

However, all elastographic techniques, with the potential exception of shear wave elastography, are predicated on an assumed transmission speed of ultrasound in the target tissue (Gennisson et al., 2013).

While both ultrasound based elastography and magnetic imaging based elastography are promising technologies for the assessment of stiffness alterations, they are associated with high costs and other methodological challenges. A promising alternative involves mechanical tissue indentation devices. Pathological changes in myofascial tissues are often associated with alterations in their mechanical properties (Wilke et al., 2018).

A cost effective new tool is the semi-electric Tissue Compliance meter (STCM), which can be basically described as a upgrade of the original mechanical Tissue Compliance Meter by Fischer, (1987). A high test-retest reliability and day-to-day reliability, and sufficient to good inter-rater reliability was shown for this new tool, together with a high validity for stiffness changes (Wilke et al., 2018). An advantage of this tool is that the indentation depth can be adjusted to between 1 mm and 15 mm. Accordingly, a differentiated assessment of the stiffness changes at different depths of skin are possible with this tool.

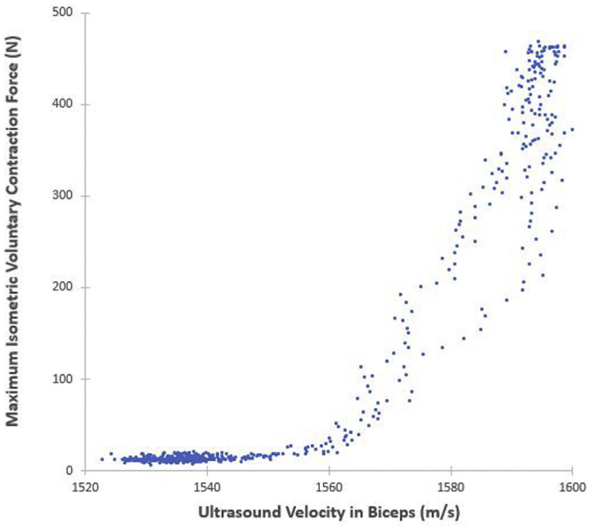

Fig. 8. Axial transmission velocity of ultrasound measured in the biceps of a young adult male during a maximum voluntary isometric contraction in which the elbow was flexed at 90°.

Another portable option is the MyotonPRO. Here a small automated indentation of 0.4 N is made in the skin for 15 ms with a quick release afterwards. This can be repeated up to 10 times at short intervals on the same spot. Intratester and intertester reliability has been shown to range from good to very good, and also demonstrates a high validity with other muscle tonus assessment modalities (lo et al., 2017). A disadvantage is that the indentation depth is constant, based on the fixed force impulse, ranging between 1 mm and 2 mm only. Therefore, no clear differentiation can be made regarding stiffness changes at different depths under the skin. An advantage is the additional assessment option for viscoelastic properties, based on the time-dependent measurement changes during repeated indentations. Thanks to their portability, reliability and validity, both tools appear to be promising developments for clinical practice. It can be predicted that most likely similar tools will become available for quick and easy assessment of mechanical tissue properties associated with pathologies such as delayed muscle soreness, iliotibial band syndrome, plantar fasciosis, etc. (Wilke et al., 2018).

10. Conclusion

This article summarizes recent highlights of fascia research. Most notably, fascia is essential for physiological and metabolic homeostasis, as well as for healing and repair mechanisms. The primo vascular network has been shown to interpenetrate fascial tissue. However, the evolutionary background and function of the hypothesized “novel” organ is still unclear. Many studies focus on fascial properties and impact on pathological conditions and potential therapeutic options.

This article presents evidence that imaging of fascia by ultrasound is a promising approach. Fascial layers and interpenetrating nerves can be identified in real-time by ultrasound imaging. While innocent fascial layers are separable by e.g. hydrodissection, this is not the case in fascial disorders. Further analysis is described by transmission ultrasound; a novel method for analysing tissue properties and discovering pathologies related to disorders of the fascial system.

Fascia research can deliver a link between functional anatomy, metabolic parameters and therapeutic approaches. We are looking forward to novel ideas and strategies in fascia research.

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