

## Editorial

# Editorial on the Special Issue of Applied Sciences on the Topic of Elastography

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Received: 20 June 2018; Accepted: 17 July 2018; Published: 26 July 2018



**Keywords:** guideline; EFSUMB; WFUMB; elastography; contrast enhanced ultrasound; point of care ultrasound; health care

Elastography is the science of creating noninvasive images of the mechanical characteristics of tissues. The basic principles of elastography have been described some years ago and have remained unchanged since they were outlined in the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines [1,2]. The first elastography guidelines worldwide were introduced and published by EFSUMB in April 2013 [1,2], were updated in 2017 for the liver [3,4], and were followed by the Japanese Society of Ultrasound in Medicine (JSUM) [5] and the World Federation for Ultrasound in Medicine and Biology (WFUMB) guidelines on basic principles [6] and applications in various organs [7–14]. The mentioned guidelines provide an introduction to the physical principles and technology on which all forms of current commercially available ultrasound elastography are based. The practical advantages and disadvantages that are associated with each of the techniques are described, and guidance is provided on the optimisation of scanning technique, image display, image interpretation, and some of the known image artefacts. The EFSUMB and the WFUMB guideline articles can be freely downloaded from the EFSUMB website ([www.efsumb.org](http://www.efsumb.org)) [15] and the WFUMB website ([www.wfumb.org](http://www.wfumb.org)).

As described in [1], ultrasound elastography uses ultrasonic echoes to observe tissue displacement as a function of time and space after applying a force that is either dynamic (e.g., by thumping or vibrating) or varying it so slowly that it is considered “quasi-static” (e.g., by probe palpation). The commercially available technologies can be classified according to whether this tissue displacement is (a) displayed directly as the imaged quantity, as in the method that is known as acoustic radiation force impulse (ARFI) imaging; (b) used to calculate and display strain, producing what is termed strain elastography (SE); or (c) used to calculate and display an image of shear wave speed. The last of these is an image that is, in principle, quantitative for a tissue property and is the only one that requires the creation of a shear wave, which in turn requires the use of a dynamic force. The others may use a dynamic force but can also work with a static or nearly static force [1]. However, even the measurement of shear wave speed is dependent on system parameters such as the applied shear force and the frequency of the shear wave. Elastography may be considered as a type of remote palpation that allows the measurement and display of biomechanical properties that are associated with the elastic restoring forces in the tissue that act against shear deformation. This view unifies the different

types of elastography, namely SE, ARFI imaging, and SWE, and explains why they all display images with contrast for the same underlying information, which is associated with the shear elastic modulus.

A variety of methods that measure shear wave speed should be grouped under the term shear wave elastography (SWE). These include systems that calculate either the regional values of shear wave speed (without making images) using methods referred to as transient elastography (TE, including vibration-controlled transient elastography, VCTE) and point shear-wave elastography (pSWE), or images of shear wave speed using methods referred to as 2D (or 3D) shear-wave elastography (SWE). The type of elastography that is most suited to the assessment of diffuse liver disease is SWE, which measures the speed of a shear wave in the liver. In the 2017 update of the European guidelines [3,4], VCTE is regarded as a type of SWE, although it differs from other SWE methods because it uses a body-surface vibration to create a shear wave which then travels to the liver, whereas the other methods use acoustic radiation force to create the shear wave within the liver. Recently, normal values of quantities that were measured by SWE of the liver have been summarized [16] and the official American Gastroenterological Association Institute (AGAI) Guidelines on the Role of Elastography in the Evaluation of Liver Fibrosis have been published [17]. Unfortunately, despite the title of the AGAI guidelines paper, it focuses only on the role of VCTE in the evaluation of liver fibrosis, ignoring the fact that the term elastography covers all of the technologies mentioned above. This approach might indicate to the reader that elastography equates only to one commercially available equipment, the Fibroscan<sup>®</sup>, manufactured only by Echosens, which implements VCTE. This is not true. The review also classifies VCTE as an imaging-based fibrosis assessment, which it is not. VCTE as implemented on the Fibroscan<sup>®</sup> does not display an anatomical image, although, interestingly, General Electric has recently announced that the Echosens technology has been integrated into its conventional ultrasound system.

Guidelines were introduced in part because of the extremely rapid spread of the use of elastography systems in the clinic once the technology had become commercially available. It is worth mentioning that new methods can be clinically valid and yet are not always (or are rarely) supported by the highest ranking scientific evidence, namely by randomized trials. Often these innovations are so obviously of benefit that randomized controlled trials comparing them with older, less safe or less effective techniques could be deemed unethical.

Elastography can be applied to examine almost all organs in the human body. We refer to a variety of clinical papers with practical applications in the thyroid [9,18–22], pancreas [13], prostate [10,23,24], and endoscopic (endorectal) ultrasound applications [25–27] including the endobronchial use of elastography [28].

The current special issue of Applied Sciences deals with a wide range of elastography methods from many different points of view including open issues of the liver, thyroid, and magnetic resonance elastography (MRE), as well as applications in selected patient groups, e.g., pediatric patients.

MRE is an alternative to ultrasound elastography which has been described in a number of reviews, including [29–31]. The modern method was originated by the Mayo Clinic in 1995 [32] and, like ultrasound elastography, the technique has evolved with a number of technical variations. As with ultrasound elastography, MRE begins by measuring tissue displacement as a function of time and space. Variations exist both in terms of the motion encoding and displacement readout strategies [33] and with respect to algorithms that are used to reconstruct the viscoelastic properties from the measured displacements [34]. As with ultrasound elastography, considerable technical development continues to take place in a research context. One difference to ultrasound elastography is that although quasistatic MRE has long existed (based on a technique known as MR tagging [35]), and it provides cardiac strain assessment [36,37], it is dynamic methods that emerged into widespread clinical use, and 3D-SWE is the ultrasound elastography method that is the closest equivalent of most MRE. However, although acoustic radiation force has been tried as a method of generating displacement, MRE routinely employs harmonic vibrations that are generated by a relatively complex external MR-compatible mechanical device. The clinical use of MRE is less widespread than that of ultrasound elastography,

which is likely to be due to a combination of factors, including the high entry-cost, the more limited regulatory approval, the relatively few manufacturers, the relative difficulty of patient set-up, the lack of system portability, and the relatively long examination time. Nevertheless, MRE offers a number of advantages over ultrasound elastography, such as the ability to make elastograms of parts of the body which ultrasound cannot reach (the brain transcranially and the lungs), as well as its intrinsic: controlled-frequency of vibration, 3D imaging, ability to image both elastic and viscous moduli, and capability to provide elastic anisotropy information (i.e., as a function of the direction of shear wave propagation). Commercial ultrasound elastography has yet to evolve some of these technical capabilities which arguably makes current MRE potentially more accurate and precise than current ultrasound elastography. This may explain why recent comparisons suggest that, although ultrasound and MR elastography both have good accuracy for identifying and staging liver fibrosis, MRE is the more accurate of the two [31,38–41]. Nevertheless, they each have technical strengths and limitations; ultrasound elastography may be unreliable in obese patients or where intercostal access is limited, and MRE quality may be poor in patients with substantial iron deposition [41].

The paper on the “Effect of HCV Core Antigen and RNA Clearance during Therapy with Direct Acting Antivirals on Hepatic Stiffness Measured with Shear Wave Elastography in Patients with Chronic Viral Hepatitis” C showed that liver stiffness significantly declined during and after successful antiviral treatment [42]. So far, liver stiffness monitoring during antiviral therapy has been mostly published using TE. Published data on patients who were treated with direct antiviral agents (DAAs) suggest that liver stiffness declines during treatment in patients with advanced fibrosis [43–49]. The decline in liver stiffness reflects more the reduction of inflammatory changes of the liver than it does in true fibrosis.

The paper “Interpretation US Elastography in Chronic Hepatitis B with or without Anti-HBV Therapy” concludes that 2D-SWE (regrettably referred to as ARFI) is a reliable tool for the measurement of liver fibrosis in chronic hepatitis B patients with alanine aminotransferase  $<5\times$  the upper limit of normal. For those patients under anti-HBV therapy, the optimal timing for SWE analysis will be over 1 to 2.5 years of nucleos(t)ide analogue therapy [50].

The paper “Shear Wave Elastography Combining with Conventional Grey Scale Ultrasound Improves the Diagnostic Accuracy in Differentiating Benign and Malignant Thyroid Nodules” tackles the issue of the differential diagnosis of thyroid nodules. In patients with normal thyroid parenchyma, elastography can rule out malignancy with a high level of certainty if the lesion is displayed as soft. A stiff lesion can be either benign or malignant [51]. The same is true for other parenchymatous organs, e.g., the pancreas [52].

“Non-Invasive Assessment of Hepatic Fibrosis by Elastic Measurement of Liver Using Magnetic Resonance Tagging Images” is a paper that aims to overcome the disadvantage of MRE mentioned above, i.e., that it normally requires an MR-compatible mechanical vibrator which complicates patient set-up. Multiple locations covering a grid in the liver were tracked using MR tagging during liver displacement that was caused by forced exhalation. Two features were then extracted from the resulting time-varying grid patterns, bending energy and the difference between the spatial Fourier transforms of the grid from one moment to another. These features summarize the overall non-rigid deformation in the liver, both normal and shear strain. The more rigid the liver, the lower the values for both of these types of features. In preliminary testing on 17 normal and 17 abnormal liver cases (6 chronic hepatitis cases and 11 liver cirrhosis cases), with manual intervention in setting grid landmarks for tracking, only one abnormal liver was misclassified as normal by a bivariate linear classifier. Although the method does not result in a quantitative tissue property value such as an elastic modulus, its simplicity makes it worthy of further evaluation after development to improve its automated landmark setting.

The paper “Current knowledge in ultrasound based elastography of pediatric patients” reviews the current available literature on the use of SWE in children. Shear wave elastography techniques can be applied in children for the evaluation of liver fibrosis in several etiologies. However, for most

pathologies, the evidence is still limited. The confounding factors are similar in adults, including the degree of inflammation and necrosis, iron and copper deposits, cholestasis, and congestions [53].

**Funding:** For J.C.B. and C.F.D., this research received no external funding.

**Conflicts of Interest:** J.C.B. declares membership of the advisory board of Supersonic Imagine and Michelson Diagnostics, and collaboration agreements with Phoenix Solutions, Zonare, iThera Medical and Delphinus. C.F.D. declares membership of the advisory board of Hitachi Medical Systems, Siemens Healthineers, Mindray and collaboration agreements with Supersonic Imagine, Olympus and GE. In addition honoraria are also reported for Bracco and Pentax.

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