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## Elastosonography – General overview of technical and clinical applications

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Elastosonography is a comparatively new technique that can evaluate the viscoelastic properties of tissue by ultrasound (US) imaging. To understand the advantages and limitations of elastography and to use elastography effectively, it is necessary to know the basic principle of elastography. The main principle of the elastography method is palpation that one of the oldest medical time-tested diagnostic tools and was defined in BC 1552. Tissue hardness considerably changes among different physiological states of normal and pathologic tissues. However, pathological tissues can be locally like tumors, which are often stiffer than their surrounding healthy tissues or diffusely like a liver fibrosis.

Elastosonography brought a new dimension to US imaging by means of providing information about of the viscoelastic properties of tissue. Nowadays, viscoelastic properties of tissues could be identified by different elastosonography technical approaches that can rely on the same basis and provide different data.

First, sonoelastography began as a method to assess the mechanical properties of soft tissue proposed by Krouskop et al., in 1987 [1]. The term elastography was used, and potentially useful application of elastography (breast and prostate tumors, focal and diffuse liver disease, and muscle disease, etc.) was discussed by Ophir et al., in 1991 [2]. In the early 1990s, Sugimoto was the first person to assess the tissue mechanical properties by monitoring of the response to the acoustic radiation force of tissue. A technique known as shear wave elasticity imaging was termed by Sarvazyan et al. In 1998, they used to quantify tissue stiffness, a high intensity focused US piston to induce shear waves and monitored using magnet resonance imaging. In the method of Nightingale et al., shear wave (SW) in tissue is generated using acoustic radiation force impulse (ARFI), and the tissue response was evaluated using US correlation-based technique.

Another method for elasticity imaging that is transient elastography (TE) was first performed using the FibroScan (Echosens, Paris, France). A single transient shear wave into tissue was induced via a special transducer.

Sonoelastographic technique approaches differ according to external excitation application to the tissue (static [or quasistatic] or dynamic), measurement of the tissue response to this excitation, and calculate parameters provided from this response that reflected the mechanical properties [3,4]. The common base of all elastography techniques is to assess the elastic modulus, which is the property assessed by palpation. The elastic modulus is denoted as Young modulus or the Shear modulus, according to different technical approaches. Young modulus is ratio of the longitudinal stress to the longitudinal strain and represents the tendency of the medium to deform axially when forces opposite and parallel to this axis are applied. On the other hand, shear modulus is ratio of the shear stress to the shear strain and represents the tendency of the medium to change its shape to keep a constant volume.

In quasistatic methods, the response of tissues to internal endogenous forces resulting from physiological movements (such as cardiac motion) can be measured. Furthermore, the tissues can excite mechanically using one transducer by applying repetitive manual pressure. For optimal evaluation, at least three consecutive cycles of compression and decompression have been proposed, but the tissue elasticity may vary over a large number of cycle repetitions, resulting in misinterpretations [5]. When a tissue is compressed, owing to the applied force (stress) is unknown, only occurring longitudinal strain (displacement) is displayed.

These displays exist irrespective of the technology used in most machines. The easy application of this technique is also a great advantage. However, the lack of knowledge of the applied force distribution hinders any quantitative assessment. In real time imaging, occurred images by compression and relaxation of the scan area can be monitored on the US monitor as two separate windows, B-mode and colored elastogram.

At the same time, the applied compression and decompression waves can be monitored in the form of a sinusoidal wave on an ultrasonic device monitor. It is preferable to measure from the decompression wave watched on the monitor while measuring the strain value, because of the force is not exerted on tissue during decompression wave phase. This phase shows the response which the tissue with its internal dynamics to the applied force. The color represented the relative stiffness of the tissues within the region of interest (ROI) and ranged from blue (stiff) to red (soft) in the spectrum. Green and yellow indicated medium stiffness.

Dynamic elastography methods also obtain data by measuring tissue movement, but the difference between these two methods is the way of application of force and measuring technique of the response of the tissue. In dynamic sonoelastography techniques, the tissue is stimulated by acoustic waves from the probe without the need for a second force. The frequency range of both approaches is very different: 0 Hz in static elastography and 50-500 Hz in dynamic elastography. The main advantage of transient excitation is to naturally separate shear waves from compression waves since shear waves are 3 times slower than compression waves.

Transient elastosonography that is the first commercial elastography technique to assess the elasticity of depth tissues has two parts: A piston that produces a vibration of mild amplitude and low frequency, and a single channel sonography transducer which is located at the end of this piston.

The examination is performed with the probe (A 3.5-MHz "M" probe, a 2.5 MHz "XL" probe for obese patients, or a 5.0 MHz probe for children) placed typically in the 9th-11th intercostal space overlying the liver when the patient is lying in the supine position. TE often referred to as liver ultrasonographic elastography. Applied force is mechanically induced rather than acoustic radiation force and it creates shear stress in the target tissue. This type of force is classified as a dynamic elastography technique but it has not been under the term SW elastography (SWE). The speed of a single transient shear wave is calculated using the Young modulus. The TE result is reported as the median value of at least 10 successful liver stiffness measurement (LSM), which is expressed in units of kilopascals (kPa).

This technique is well-defined and repeatable. TE results are generally recognized to be well correlated with liver fibrosis grades. It has been reported minimal intra- and inter-observer variation [6]. The disadvantage of TE is that it primarily does not provide a B-mode image and only evaluates a portion of the liver. Second, the results of TE LSM can be overestimated depend on etiology. LSM can be elevated due to hepatic inflammation (in elevated alanine aminotransferase), hepatic congestion in the right heart failure, increased stiffness from

biliary dilatation (in cholestasis). Third, it is not performed for the patient with ascites due to the high rate of unsuccessful LSM, because of the interruption of shear waves by ascites. Finally, TE supplies only local elasticity measurement in limited depth. Subsequent studies established that if a skin-liver capsule distance >2.6 cm as such in obesity, TE examinations using the M probe were more likely to have unsuccessful and the XL probe should be used for accurate measurement [7].

The acoustic radiation force is related to the propagation of acoustic waves in an environment. In ARFI imaging, an US probe creates a focused "push" pulse that is short-term (0.03-0.4 ms) and high-energy. The frequency and magnitude of the pusher pulses are automatically regulated to prevent overheating of the transducer during operation. This pulse can cause very small size displacement (1-20  $\mu \rm m$ ) that occurs as a result of shear waves. The distribution of displacement or its normalized values within the ROI is displayed. The ARFI technique measures the velocity of shear waves in a rectangular box measuring 1 cm  $\times$  0.5 cm. In the quantitative evaluation, the SW speed increases as the tissue stiffness increases. Shear wave velocities are expressed in m/s and are equivalent to the square root of the tissue elasticity.

Soft tissues are seen in bright color in black and white images, while hard tissues are observed in black color. ARFI images less user dependent than those in hand-induced strain imaging. ARFI supplies similar knowledge as the strain images. Both methods provide a quantitative estimate of the tissue elastic moduli due to they are both affected by tissue geometry [8]. Compared to the phantom and clinical investigations of strain elastography and ARFI, it has been observed that ARFI has a better resolution, exhibit improved signal-to-noise ratio at depth.

Supersonic shear wave imaging that is one of the dynamic elastography methods was developed 12 years ago. Unlike ultrasonic or compressive waves, the shear waves propagate in a direction perpendicular to the direction of the tissue displacement. During the propagation of high-frequency longitudinal p (primer or plane) waves used in ultrasonography, transverse (shear) waves are generated by various interactions and transformations. Transverse waves had a lower frequency and lower propagation velocity (1-10 m/s) than p-waves, and there was no its effect on B-mode sonography image formation.

For this reason, shear waves have been ignored initially, but nowadays the shear wave is the basis of the elastography. In shear wave elastography, mechanical vibrations are generated by acoustic radiation forces generated by focused high-frequency US bundles instead of external compression. These vibrations result in a "shear wave" depending on the viscoelastic properties of the target tissue. Quantitative values of shear waves are calculated as either a velocity in m/s or stiffness in kPa.

There are two methods for SWE: Point SWE (pSWE) and the two-dimensional color coded SWE (2D SWE). pSWE

also was known as ARFI quantification, provides only single point measurement. The ROI size is about 0.5-1.0 cm<sup>3</sup>. 2D SWE displays 2D color velocity maps of a larger field of view and allows for multiple measurements to be obtained. ROI size is about 20 cm<sup>3</sup>. Both methods can be used to assess liver fibrosis in chronic liver disease. Measurement location of two methods is also same; most often segment VII or VIII.

The shear wave elastography technique provides a good acoustic windowed real time imaging with the B-mode guidance advantages, when compared to TE. In contrast to transient elastography, SWE can be applied to patients with acid.

Compared to strain elastography, the SWE is more reproducible, quantitative, and provide good elasticity contrast. Unlike strain elastography techniques, achieving real numerical data with SWE is very important not only for diagnosis but also for follow-up. Shear waves can be produced at depths where manual compression in strain elastography is ineffective. However, very deep tissues (>9 cm deep) cannot be evaluated because the shear waves are attenuated at depth [5].

Consequently, sonoelastography is becoming part of the normal sonographic examination by integration into conventional US devices. Hence, to increase usage of sonoelastography in clinical medicine, clinicians from other disciplines should be informed and trained.

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