White Paper

VIBRATION-CONTROLLED Transient Elastography

VCTE™

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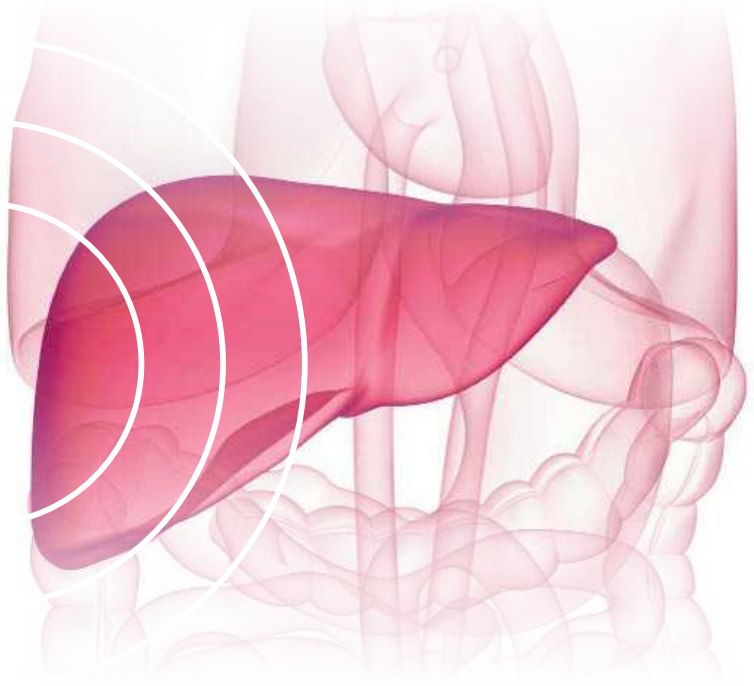
Elastography is a new modality recently introduced into routine clinical practice. Fibroscan® (Echosens®, Paris, France) is the first quantitative elastography device introduced on to the market. Since 2004, it is increasingly used to measure liver stiffness and to help assess the state of the liver.

The technological platform of Fibroscan® is Vibration-Controlled Transient Elastography (VCTE™), a technology covered by international patents.

POWERED BY VCTE™



I. TRANSIENT elastography

Transient Elastography [1-3] relies on the estimation of shear wave velocity as a means to assess tissue stiffness. Stiffness or Young's modulus is directly related to shear velocity by the following expression, $E=3pVs^2$, where p is the density, Vs the shear velocity and E the Young's modulus or stiffness expressed in kilopascals.

A very important feature of transient elastography is that the vibration be transient to avoid reflections and interferences occurring within the tissues. The transient shear wave travels through the tissues within tens of milliseconds which implies that the ultrasound-based imaging modality be ultrafast to follow its propagation. Within these constraints stiffness can be deduced from the strain rate images of the shear wave propagation.

II. VIBRATION-CONTROLLED transient elastography

Echosens® adapted transient elastography to medical application by introducing a variety of new features. The improved technique is called Vibration-Controlled Transient Elastography (VCTE™)[1-3].

→ The proper use of shear wave velocity analysis for clinical diagnosis requires the control of various physical parameters to ensure an accurate, reliable, and reproducible assessment of tissue stiffness. These include the control of vibration frequency, energy intensity, applied force and a standardized algorithm.

These important controls ensure that the shear wave, which is the ultimate source of stiffness information, is properly induced in the medium.

A. CONTROLLED VIBRATION

One of the most important components of VCTE™ is the control of the vibration. To ensure proper assessment of tissue stiffness the vibration is controlled in shape, frequency and amplitude. The vibration needs to satisfy several very important criteria.

→ First of all, as the stiffness value depends on the frequency of the shear wave, the frequency of the vibration is controlled to obtain a consistent measurement that can be used for diagnostic purposes whatever the mechanical properties of the organ under investigation, whatever the etiology of the patient.

→ Second, the amplitude of the vibration is adapted to the morphology of the patients: small amplitude in children, large amplitude in obese patients to increase the penetration depth of the shear wave.

→ Third, the shape of the vibration is servo controlled to ensure a correct shear wave generation whatever the examination conditions (fat thickness, soft and stiff livers, abdominal wall distortion, etc).

→ Fourth, the electro-mechanical system used to induce the vibration is calibrated to ensure standardized and optimized vibration

With a constant shape of the vibration, a reference frequency of the shear wave generated by a calibrated mechanical system (vibrator), VCTE™ allows comparison of shear wave propagation parameters independently of the organ conditions, etiology, patient and operator. All quantitative results given by a VCTE™-based device are comparable.

B. CONTROLLED ENERGY

→ VCTE™ uses low acoustic energy to follow the propagation of the shear wave inside the organ. The sensitivity of the single ultrasound transducer is controlled to ensure that the amount of acoustic energy sent into the patient is below the official levels for fetal imaging, abdominal, intraoperative, pediatric, small organ, etc. (see Table 1).

Table 1. Fibroscan acoustic output exposure levels comply with preamendments from FDA (source: guidance for industry and FDA staff, CDRH). ISPTA.3 = derated Spatial-Peak Temporal-Average Intensity, ISPPA.3 = derated Spatial-Peak Pulse-Average Intensity

$ISPTA_{.3}$	• < 94 mW/cm²
$ISPTA_{.3}$	• < 190 mW/cm²

→ VCTE™ is based on the transmission of mechanical energy through the patient. The mechanical vibration can be compared to a flick; the energy amount is very small compared to shear waves caused by organs such as the heart or respiratory motions. The vibration is controlled and monitored during the examination. The electro-mechanical system is calibrated periodically to ensure that these parameters key to performance and safety do not drift over time.

VCTE™ is a non-invasive method which quantifies tissue stiffness with only small mechanical and acoustic energies with no tissue heating. These amounts of energy only depend on the probe model; they do not vary between stiff or soft livers.

III. CONTROLLED static force

In VCTE™ the static force applied by the operator is monitored with a force sensor. The force must be sufficient to ensure a proper transmission of the vibration from the subcutaneous tissues to the liver parenchyma. The force should not be excessive to prevent vibration distortion and modification of the tissues characteristics. Furthermore the stiffness of soft tissue may vary when stress is applied on it. Controlling the static force is crucial in quantitative elastography.

IV. CONTROLLED algorithm

The stiffness computation algorithm is the heart of VCTE™. Highly sophisticated algorithms have been developed for tissue stiffness assessment. Data and image processing technologies are used to measure tissue stiffness in kilopascals and to automatically reject invalid measurements. In practice, shear wave propagation can be very complex in some conditions or some organs such as lungs or intestines. These may yield poor strain rate images. These images are automatically invalidated by a specific and standardized algorithm to ensure consistent, reproducible and high quality results.

V. ELASTOGRAPHIC techniques

Elastography techniques may be separated into two groups: qualitative elastography and quantitative elastography.

A. QUALITATIVE ELASTOGRAPHY

Qualitative elastography as a modality is now offered in some ultrasound scanners. Based on the work of Ophir's group [4], these techniques give a color image of the relative stiffness within tissues. These techniques are qualitative because the mechanical impulse is not controlled. Indeed they do not use shear waves.

B. QUANTITATIVE ELASTOGRAPHY

Shortly after the VCTE-based Fibroscan® was commercialized in 2004, other elastographic techniques were proposed to assess liver stiffness (LS). These techniques (see Table 2) rely on the use of shear waves.

Table 2. Quantitative elastography techniques.

	IMAGING MODALITY	VIBRATION MODE	FREQUENCY
ACOUSTIC RADIATION FORCE IMPULSE	• Ultrasound	• Transient Radiation force	• Wideband
VIBRATION-CONTROLLED TRANSIENT ELASTOGRAPHY	• Ultrasound	• Transient Mechanical actuator	• 50 Hz
MAGNETIC RESONANCE ELASTOGRAPHY	• Magnetic resonance imaging	• Continuous Mechanical actuator	• 50 – 60 Hz

1) Magnetic resonance elastography

Magnetic resonance elastography (MRE) was introduced in 1995 by Muthupillai [5] from the Mayo clinic (Rochester, USA). A few groups reported liver stiffness measurements using MRE [6] [7] [8-10]. Liver shear stiffness is often chosen as the output stiffness parameter. The shear stiffness μ can be deduced from Young's modulus E using the simple relationship: μ=E/3.

2) Radiation force

More recently, several techniques [11-14] based on radiation force [15, 16] such as ARFI (Acoustic Radiation Force Impulse) have been proposed for liver stiffness measurement. These techniques use high intensity ultrasound beams to induce displacements and tissue heating inside the liver remotely. Other techniques such as those developed at the Mayo clinic [17] or at the Institut Langevin (Paris, France) [18] are currently investigated.

VI. STANDARDIZATION

The standardization of elastography procedures is a challenging aspect of the emergence of new elastographic technologies in the medical field. Preliminary studies performed on tissue-mimicking materials showed a good correlation between stiffness measured using MRE and VCTE™[19] [20]. Both techniques are based on the use of external mechanical vibrators. Thus they are using a controlled 50 Hz frequency which is favourable to standardization.

In radiation force-based ARFI technique, shear waves are induced remotely using a high intensity and focused ultrasound beam. While shear waves frequency is controlled in MRE and VCTE™, ARFI shear wave frequency can not be controlled and depends on elements such as the etiology-dependent mechanical properties of the organ and on the depth of the region of interest, etc.

A direct conversion of liver stiffness obtained using VCTE™ and ARFI is tempting. Indeed, theoretically Young's modulus as provided by VCTE™ could be deduced from the shear velocity as measured by ARFI. However, this relationship is only valid at a given frequency, f: $E(f)=3\ Vs(f)^2$. Shear wave frequencies in VCTE™ and ARFI are 50 Hz and several hundreds hertz respectively.

Furthermore, in ARFI the frequency of the shear wave is wide ranging and depends on the mechanical properties of the organ. The stiffer the tissues are, the higher the frequency is. As a consequence, the frequency of the shear wave in a cirrhotic liver can be much higher than the frequency of the shear wave in a healthy liver.

As ARFI and VCTE™ (or MRE) frequencies are significantly different, the classical relationship $E=3\ Vs^2$ is invalid. A direct conversion of ARFI shear velocity to VCTE™ Young's modulus is not possible.

CONCLUSION

Elastography techniques such as VCTE™ opened a new domain of support to clinical diagnosis. More elastography techniques are now being developed to offer new diagnostic tools to physicians. Although they measure stiffness, all techniques do not provide comparable numbers and identical performance. This emphasizes the need for standardization of elastography techniques.

VCTE™-based Fibroscan® is the first medical device dedicated to clinicians for tissue stiffness measurement. It has been extensively validated clinically in a large number of liver diseases. Easy to perform, safe, reproducible and simple, liver stiffness measurement using Fibroscan® is a standardized procedure.

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