SIEMENS

Understanding ARFI and New Elastography Quantification Technologies

John Benson, BS, RDMS, RDCS
Director, Clinical Applications

Liexiang Fan, PhD
Senior Key Expert, Ultrasound Advanced Development

Answers for life.

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Ultrasound Elastography: New Thinking

Ultrasound imaging is a first-line imaging modality for a wide range of indications, playing a major role in screening, diagnosis, and therapeutic interventions for various diseases and pathologies. However, even with enormous improvements in recent years, conventional ultrasound is limited in its ability to differentiate between the mechanical properties of tissue, which can be important in assessing the morphology and physiology of focal or diffuse disease.

Compression elastography offered the promise of a new dimension of ultrasound. In addition to the anatomic detail visible in B-mode and the flow imaging offered by color Doppler, elastography was intended to enable visualization of tissue stiffness, long known as a harbinger of disease and malignancy (palpation searches for stiffness, after all). Early compression elastography could provide relative, qualitative visualization of tissue stiffness differences for assessing focal lesions, but lacked the ability to quantify stiffness differences of these lesions. It was also difficult to assess the degree of stiffness of homogeneous tissue, such as liver or spleen tissue.

ARFI (acoustic radiation force impulse) technology allows Siemens Healthcare to enable both qualitative and quantitative assessment of the mechanical stiffness (elasticity) differences in tissue. By offering a uniquely comprehensive "toolbox" of complementary tissue strain analytic applications, Siemens' HELX™ Evolution ultrasound systems can be configured with a wide range of elastography technologies and applications, helping physicians evaluate conditions of the liver, breast, thyroid and other organs.

Elastography and Tissue Strain: What Clinicians Need to Know

Compression Elastography

Acoustic Radiation Force Impulse (ARFI) Elastography

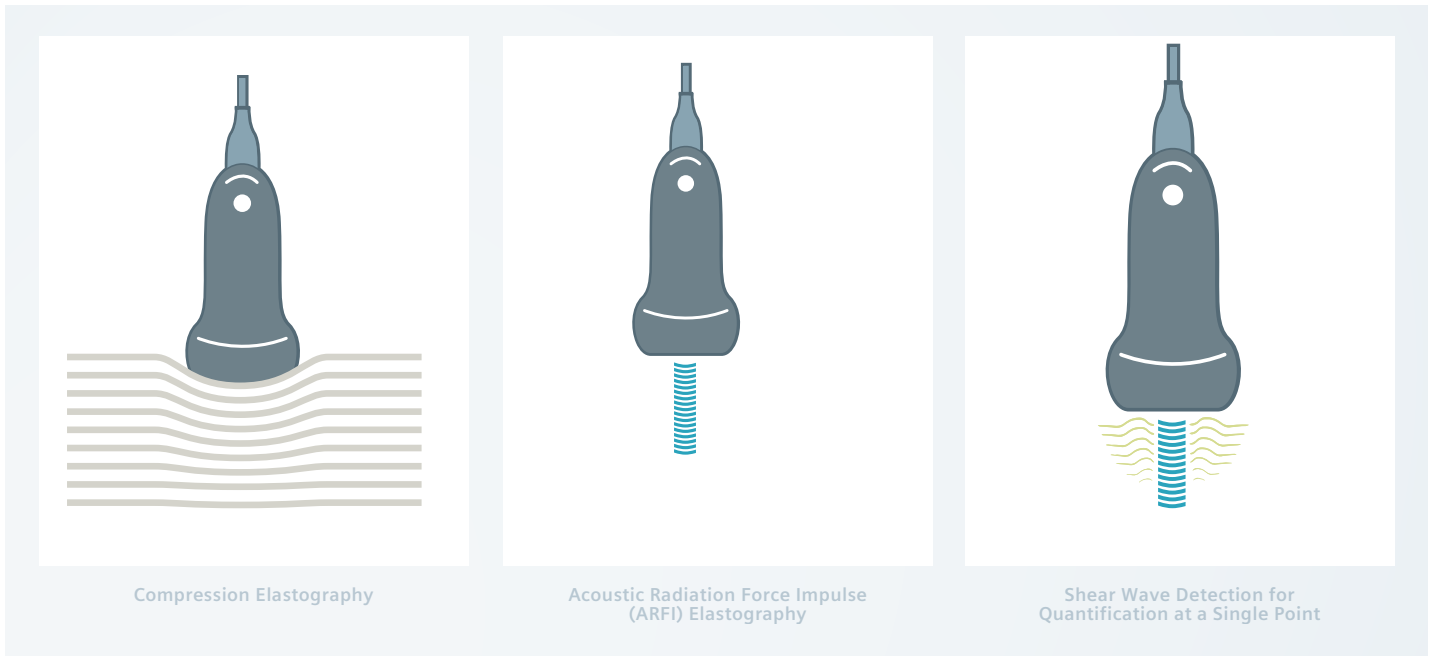Shear Wave Detection for Quantification at a Single Point

Figure 1: Elastography Technologies

The perfect diagnostic tool would have 100% sensitivity (a positive result when disease is present) and 100% specificity (a negative result in the absence of disease) in all cases. Such a technology does not exist, of course. However, the use of more than one imaging tool can provide overall higher diagnostic accuracy than one imaging modality alone. This is true when adding elastography to conventional ultrasound and when using multiple elastography technologies in cooperation.

Modern **elastography** can refer to multiple technologies. Some depend upon heavy user-generated manual pressure. More advanced elasticity imaging, enabled by sophisticated architecture, can detect extremely small changes in tissue displacements (on the order of 1 to 10

microns). These advanced elastography tools rely less on manual pressure and can detect tissue stiffness based on native tissue motion, induced by the patient's cardiac pulsations and respiration.

Using **Acoustic Radiation Force Impulse (ARFI) technology**, rather than manual compression techniques, tissue is compressed by an acoustic beam. One advantage of this approach is that the acoustic beam is focused at the region of interest (ROI) to maximize the local displacement of tissue, rather than just at the skin surface with uncontrollable stress being applied in deeper tissues. This more controllable application of stress improves the uniformity of the resulting elastogram.

ARFI technology also induces and tracks the propagation of **shear waves (transverse

waves) for quantification of tissue stiffness**. An increase in shear wave velocity correlates closely with increasing tissue stiffness, providing a more precise indication of true tissue elasticity at a point location. This ability to quantify tissue stiffness, rather than qualitatively evaluating stiffness compared to surrounding tissue with focal lesions, expands the clinical utility of elastography to homogeneous tissue, such as liver and spleen.

In addition, compared to manual compression, ARFI offers a reduction in user technique dependence. The user simply initiates the acquisition of the elastogram or quantitative measurement with the push of a button, further improving inter-operator reproducibility, which is an important aspect of clinical utility.

How Elastography Works: The Physics of Tissue Strain

Many studies have characterized the normal range of elasticity values of various tissue types and that certain disease processes can change the viscoelastic properties of tissue [1, 2]. Elastography tools work by measuring how much strain tissues exhibit in response to stress. The relationship between stress and strain provides information about the mechanical stiffness of the tissue in question.

Stress and strain are not the same. Stress is the force exerted and strain is what happens to the tissue in response to the pressure. Two kinds of strain exist, longitudinal and shear. Longitudinal, or normal strain, occurs when tissue is either stretched or compressed. Shear strain occurs as a result of angular forces, such as twisting or bending.
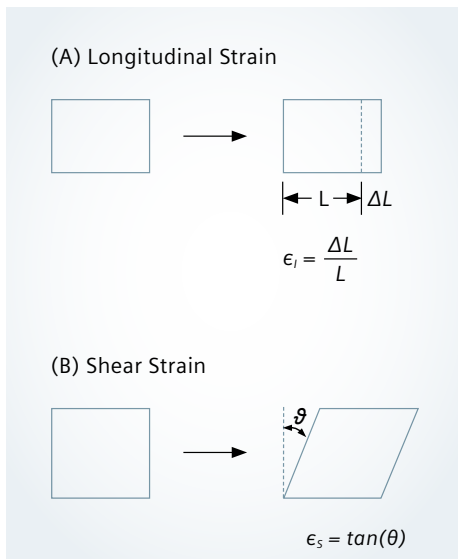
In tissue, both longitudinal and shear strains are usually present when manual compression force or radiation force is used. In fluid, pressure is the same in all directions, therefore, shear strain and shear waves do not exist in fluids.

Hooke's law describes the relationship between stress and strain for most materials, including viscoelastic tissue:

$$\sigma = Y\epsilon,$$

where Y is Young's Modulus or Modulus of Elasticity; and

σ is a deformation proportional to the force of ϵ

Young's Modulus or Modulus of Elasticity can be computed by examining the slope of the stress/strain diagram in the elastic portion of the curve, as shown in Figure 3.
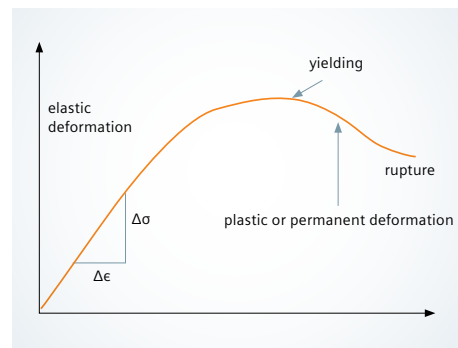
The shear modulus G, also known as the Modulus of Rigidity, can also be calculated through examination of a shear stress vs. shear strain curve.

In elastic materials, the relationship between the velocity of a shear wave and shear modulus is:

$$v_s = \sqrt{\frac{G}{\rho}}$$

where G is the tissue shear modulus; and

ρ is the solid tissue density

Tissues with a higher shear modulus, or modulus of rigidity (less compliant to shear forces), will have a higher shear wave velocity than tissues with a lower modulus of rigidity (more compliant to shear forces).

(A) Longitudinal Strain

$$\epsilon_l = \frac{\Delta L}{L}$$

(B) Shear Strain

$$\epsilon_s = tan(\theta)$$

Figure 2: (A) Longitudinal and (B) Shear Strain.

Figure 3: Relationship between strain and stress in any material

Elastography Offerings from Siemens Healthcare

Ultrasound-Based Elastography Tools

Siemens Healthcare offers four advanced elastography tools designed to help physicians to accelerate diagnostic understanding in various parts of the body:

- eSie Touch™ Elasticity Imaging
- Virtual Touch™ imaging
- Virtual Touch™ quantification
- Virtual Touch™ IQ

In addition, Siemens Healthcare offers an optimized Liver Analysis Package that includes the two technologies most useful for the liver (Virtual Touch imaging and Virtual Touch quantification). Clinical applications of the Virtual Touch™ Liver Analysis Package is covered in more detail later in this document, including an overview of published studies.

The advanced ultrasound-based elastography tools offered by Siemens Healthcare include:

eSie Touch Elasticity Imaging

With eSie Touch Elasticity Imaging, the elastogram is created using either minimal compression or physiologic tissue motion from cardiac pulsations or respiration as the stress force on tissue. Compressive strain of tissue is recorded in the image through continuous analysis of acquired ultrasonic detection signals.
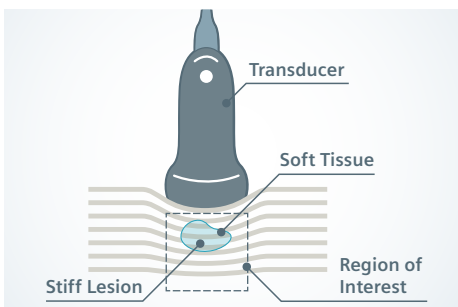

Figure 4: With eSie Touch Elasticity Imaging, tissue strain is induced by minimal mechanical compression with the transducer or cardiac pulsations and respiration. Detection pulses track displacement, which are used to derive a strain image in grayscale or color-coded display.

Virtual Touch imaging

Virtual Touch imaging, similar to eSie Touch elasticity imaging, provides a qualitative elastogram. However, Virtual Touch imaging uses ARFI instead of traditional compression or tissue motion to induce tissue displacement. Virtual Touch imaging provides a grayscale or color-coded display of relative tissue stiffness in a user-defined region of interest. This information is computed by examining the displacements of tissue elements in response to an acoustic push pulse. Detection and computation of relative elasticity is similar to eSie Touch elasticity imaging.
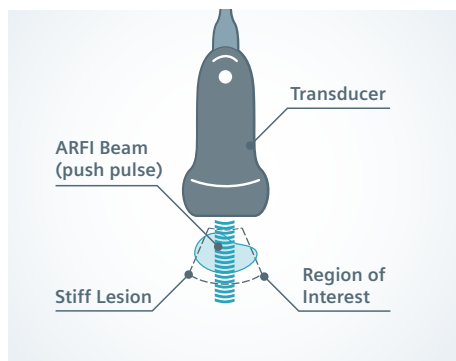

Figure 5: Virtual Touch imaging utilizes acoustic push pulses (blue) and detection echo (not shown), sequenced across a user-defined region of interest, to generate a displacement map depicting the relative stiffness of tissue.

In contrast to conventional ultrasound imaging pulsing strategy, Virtual Touch imaging uses a three-step pulsing method. First, a conventional ultrasound signal is acquired as a baseline in a narrow region of interest. Second, a push pulse is applied along the center of this region of interest. Third, another conventional ultrasound signal is acquired and is compared to the baseline to obtain tissue displacement. The more elastic a given tissue element, the more displacement it experiences. This process is repeated for each axial line within the region of interest, as with a conventional B-mode image.

Virtual Touch quantification

By combining shear wave velocity measurement with ARFI push pulses, Virtual Touch quantification measures tissue stiffness directly rather than only relative to surrounding tissues.

When an acoustic push pulse displaces the tissue residing in its path, shear waves are generated. These shear waves propagate perpendicular to the push pulse. In tissue, shear waves travel at a velocity of around 1–10 m/s, which is slow enough to be well sampled by detection beams. As described above, there is a close correlation between tissue elasticity and its associated shear wave velocity. By observing the shear wavefront arrival at multiple locations and correlating these locations with the arrival time, shear wave speed within the region of interest is calculated.
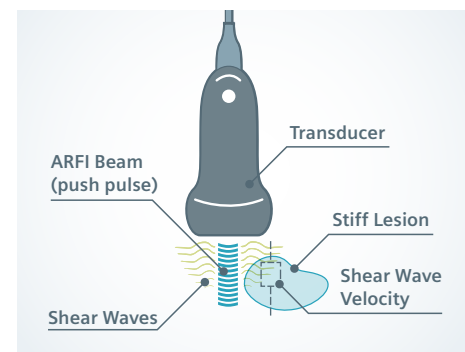

Figure 6: Virtual Touch quantification utilizes an acoustic push pulse (blue) to generate shear waves (green) through a user-defined region of interest. Detection pulses are applied in multiple locations and reveal arrival time, allowing quantification of shear wave propagation speed and therefore correlation of tissue stiffness.

The ultrasound transducer both generates the focused ARFI beam and receives echo signal. The ARFI beam is most intense at a selected depth within the tissue. The magnitude of tissue displacement decreases when distance from the ARFI beam increases, and the magnitude in the same spatial location changes over time.
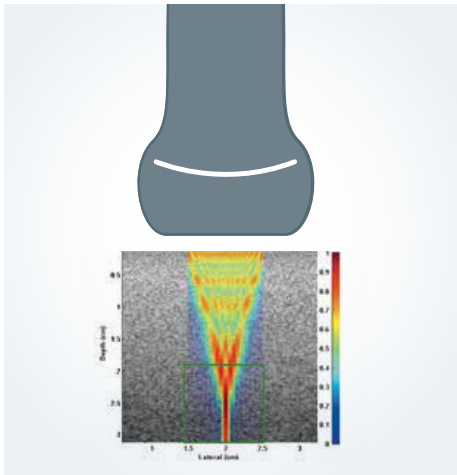
Figure 7: ARFI beam with color representation of acoustic intensity: red represents highest intensity, lighter colors represent lower intensity.
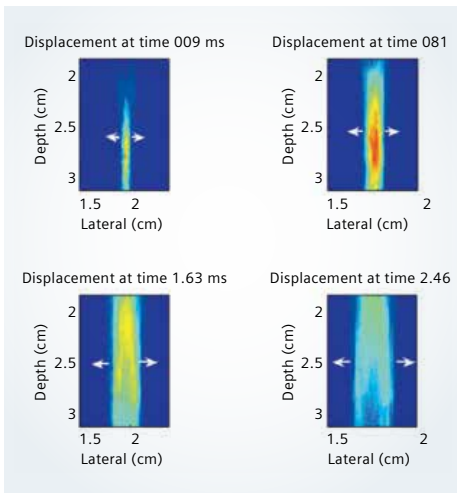

Figure 8: Illustration of tissue displacement information (both its spatial location and magnitude) after ARFI application. The four images show the displacement information at four observation times 0.09, 0.81, 1.63 and 2.63 milliseconds after the cessation of ARFI. The spatial scale in the four images are identical and the arrows in each image indicate that the spatial location of the displaced tissue moves outwards perpendicular to the ARFI beam application direction.

Virtual Touch IQ

Virtual Touch IQ provides the advantage of both quantitative and relative stiffness imaging combined in one display. The user defines a two-dimensional region of interest, which represents shear wave velocities at many point locations. The image is formed by a pulse sequence that is comprised of up to 256 acquisition beam lines. For each beam line, the system is instructed to sequentially acquire a noise level estimate, a number of reference vectors, application of ARFI excitation, and then a relative large number of tracking vectors.

This sequencing takes place for one single location and gives the estimation of shear wave propagation time for each depth along the beam direction. By taking a similar data acquisition after moving the spatial location of the detection vectors to a location different than the first acquisition, a new line of shear velocity estimates is obtained. This line is in between the detection locations.
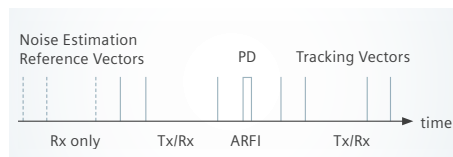

Figure 9: Data acquisition sequencing for a pair of ARFI excitation and detection locations. In the noise estimation segment there is no transmit (Tx), and the received echo signal (Rx) is used to estimate the noise level. In both reference vectors and tracking vectors, wide band transmit and receive is used to obtain the echo signals, and these signals are used to estimate the tissue displacement.

Courtesy of: Prof. Wu Chang Jun. Affiliated #1 Hospital of Harbin Medical University, China

To generate an image of shear wave velocities, the above sequencing is repeated for all the lines in a region of interest.
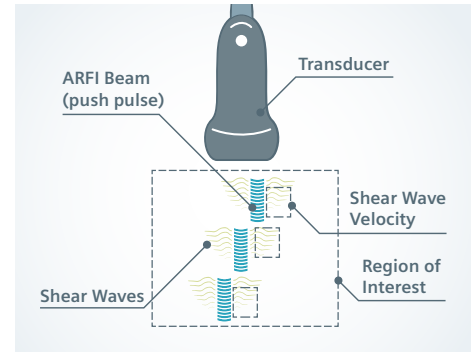

Figure 10: Virtual Touch IQ utilizes multiple acoustic push pulses (blue) and multiple detection pulses to provide tissue stiffness quantification throughout a region of interest, rather than in a single location.

The distance between ARFI excitation and detection locations is set as constant when repeating the sequencing across the region of interest; therefore, estimating for shear velocity is a function of the travel time and the difference of travel times between detection locations.

Virtual Touch IQ (VTIQ) is capable of four discrete Shear Wave (SW) display modes:

1) Velocity
2) Quality
3) Time
4) Displacement

These display modes assist the user in understanding the complex nature of shear waves that may confound image interpretation in the standard SW Velocity display.

The SW Quality display in particular is useful for interpreting whether the shear wave was of sufficient magnitude with adequate signal to noise ratio (SNR) to accurately estimate shear wave velocity in the SW Velocity display. SW Displacement indicates the regions in tissue of low elasticity that may also be associated with higher shear wave velocity. The combination of these display modes provides additional information that when correlated create a better understanding of the shear wave displacement profile.

Clinical Report:
Virtual Touch Liver Elastography Suite

New non-invasive techniques have been a research priority for the diagnosis and follow-up of chronic liver disease in recent years. The gold standard for diagnosing and monitoring the progression of liver fibrosis is a liver biopsy. Yet there are known limitations of liver biopsy that make it less than ideal for ongoing assessment of disease progression. Percutaneous biopsy underestimates or overestimates fibrosis stage or grade in up to 33% of cases [3], and is not representative of the distribution of fibrosis throughout the liver. Histologic analysis is also prone to inter-observer variability [3].

Virtual Touch quantification has been extensively studied in chronic liver disease [4–13]. These studies have examined the diagnostic accuracy of Virtual Touch quantification in multiple etiologies, including chronic hepatitis (HBV, HCV), non-alcoholic fatty liver disease (NAFLD) and nonalcoholic steato-hepatitis (NASH).

Table 1 (below) summarizes the results of several studies conducted to determine the diagnostic accuracy of Virtual Touch quantification in helping physicians evaluate conditions of the liver. As reported in these

studies, Virtual Touch quantification has proven to be rapid, reliable and reproducible in the measurement of shear wave velocity in the liver. Because Virtual Touch quantification is a software option on some Siemens' HELX™ Evolution ACUSON S Family™ ultrasound systems, it is easy and convenient to use in conjunction with a standard abdominal sonogram.

ARFI AUROC F0-2 vs F3, 4 only	Disease	N	AUROC	Optimal Vs Cutoff	Sensitivity	Specificity	PPV	NPV	Technical Adequacy Rate
Fierbinteanu-Braticevici, et al	HCV	74	0.993	1.54 m/s	97%	100%	100%	97%	100.0%
Lupsor, et al	HCV	112	0.869	1.61 m/s	97%	95%	92%	86%	91.1%
Goertz, et al	HCV, HBV	77	0.920		Not reported				96.7%
Friedrich-Rust, et al	HCV, HBV	81	0.930	1.55 m/s	82%	82%	88%	97%	100.0%
Takahashi, et al	CLD	80	0.940	1.44 m/s	96%	96%	81%	96%	100.0%
Yoneda, et al	NAFLD	64	0.973	1.77 m/s	100%	100%	71%	100%	100.0%
Palmeri, et al	NAFLD	135	0.900	N/A	90%	90%	NR	NR	88.5%
Rizzo, et al	HCV	139	0.940	1.70 m/s	91%	86%	80%	94%	100.0%

Table 1: Results of multiple independent studies in the diagnosis of advanced liver fibrosis (Metavir > F2)

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Global Siemens Headquarters
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

**Global Siemens Healthcare
Headquarters**
Siemens AG
Healthcare Sector
Henkestrasse 127
91052 Erlangen
Telephone: +49 9131 84-0
Germany
www.siemens.com/healthcare

Legal Manufacturer
Siemens Medical Solutions USA, Inc.
Ultrasound
685 E. Middlefield Road
Mountain View, CA 94043 USA
Phone: 1-888-826-9702
www.siemens.com/ultrasound

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