Syllabus Outline Specialty area: Ultrasound James F. Greenleaf; jfg@mayo.edu

HIGHLIGHTS – There are two kinds of ultrasound waves commonly used in ultrasound, longitudinal and transverse, commonly called compressional and shear waves.

The propagation speed of shear waves provides a measure of the shear modulus of the tissue. Induction of shear waves can be done with external vibration as with MRE or with ultrasound radiation force produced with an intense ultrasound beam.

Multiple approaches have been devised to produce and measure shear waves in tissue. Ultrasound elastography is widely available, fast, and used in many regions of the body to measure tissue stiffness.

TARGET AUDIENCE – Radiologists interested in measuring the stiffness of tissues.

OUTCOME/OBJECTIVES – Attendees will understand the methods and applications of ultrasound for measurement of viscoelastic properties of tissue. The objective is to compare MR methods to ultrasound methods of measuring elastic properties of tissue and to attempt to describe when/whether ultrasound is optimal for such measurements.

PURPOSE – Tissue properties such as elasticity and viscosity have been shown to be related to such tissue conditions as contraction, edema, fibrosis, and fat content among others. MRE has shown outstanding ability to measure the elasticity and in some cases the viscosity of tissues and has been shown, especially in the liver, the ability to stage fibrosis similarly to biopsy. This talk will discuss the methods and applications of ultrasound for measuring elasticity and viscosity in tissues. Many of these methods are becoming widely available in the extant ultrasound machines available throughout the world. Some of the methods to be discussed are in the developmental stage. The advantages of the ultrasound methods are that the machines are widely available and that many of the viscoelastic measurements can be made as a short addition to the normal ultrasound examination time. In addition, the measurements can be made by ultrasound repetitively allowing the evaluation of dynamic physiologic function in circumstances such as muscle contraction or artery relaxation. Measurement of viscoelastic tissue mechanical properties will become a consistent part of the ultrasound examination in our opinion.

APPROACH – There are 2 kinds of waves in the world of ultrasound – compression waves and transverse waves. The compression or longitudinal waves are used widely for imaging in ultrasound and provide images in which the contrast is related to reflectivity or a function of density and compressibility of the tissue. Compressibility of tissue depends on the springiness of molecules themselves in relationship to each other and is a very short-range effect. On the other hand, transverse waves are waves that produce contrast depending on longer distance interactions among elastic strands or fibrous materials of the tissue such as fluid content, lipid content, or fibrous content of the tissue. Essential to ultrasound shearwave elastography is the ability to quickly and accurately measure mechanical properties of the tissue. In this method, shear waves are induced in the tissue either by external vibration such as used in MRE or with internal motion induced with the intensity of the ultrasound. The intensity of the ultrasound and its interaction with

attenuation and reflectivity of tissue causes radiation force, and this radiation force moves the tissue causing propagating shear waves. In a material that is incompressible, isotropic, linear, and purely elastic, the relationship for the modulus μ of soft tissue is shown in equation 1, $\mu = \rho c_s^2$, where c_s is the shear wave propagation speed, ρ is the density of the tissue which can be assumed to be about 1100 kg/cm³ for all soft tissues because they are saturated with water. Shear waves are often produced by pushing on the soft tissue with acoustic radiation force as was proposed by Sarvazyan et al (1). This imaging method is often called shear wave elastic imaging (SWEI). Sometime later Nightingale et al developed a radiation force imaging method which is termed ARFI and was used to push tissue. The magnitude of the resulting displacement was as an indication or surrogate of the stiffness of the tissue (4). Erkoff et al invented a method that is termed supersonic shear imaging (SSI) in which shear waves were generated by pushing at multiple places in the tissue very, very quickly (5). This method produces quite large motion and relatively flat or planar shear waves. Later, a method using spatially modulated acoustic radiation force was used to generate shea rwaves and motion measurements could be measured at a single spatial location resulting in speed measurements of a shear wave(6). These methods basically measured the shear wave speed at some known frequency or in some cases at unknown frequencies of the shear wave. However these methods did not take into account that the material properties of the tissue are different at different shear wave frequencies. This property is called dispersion and a dispersion ultrasound vibrometry technology using shear waves, termed SDUV, was invented by Chen et al in which shear waves at multiple frequencies were used to characterize tissue elasticity and viscosity(7). Many other methods were developed for measuring shear wave speed and improving methods of measuring shear wave speed over the years (9-11). A problem with elasticity imaging methods that use acoustic radiation force is that in the region where the force is exerted, there is no shear wave. The shear wave propagates in all directions away from that push, but there is no shear wave directly in the push region, therefore, speed of shear wave cannot be calculated in that region. Therefore, multiple pushes at various places in the tissue must be used so that each region of the tissue is exposed to a propagating shear wave that is then measured. Song et al recently proposed a method in which multiple push beams are produced within the tissue. The resulting shear waves going in many different directions are then filtered with a directional filter that produces a measurement of shear wave propagation in each of 8 directions of propagation. The method is called CUSE, comb-push ultrasound shear elastography(13). Because each imaging pixel has several beams nearby, even pixels under a push are exposed to shear waves from local pushes nearby. The entire region of interest (ROI) can be measured by ultrasound. The push beams for CUSE can either be focused or unfocused. In general, unfocused beams are used for making shear wave images near the surface of the probe and focused ultrasound radiation force pushes are used for making images further away from the ultrasound probe.

RESULTS – The use of multiple push beams and the decomposition of the resulting shear waves into individual directions with directional filtering produces fast, large region of interest elasticity images. Examples will be given of images in liver, thyroid, breast, heart, artery and kidney. Commercial instruments currently in use around the world require some hardware modification of the transmit electronics to produce the intensities required to push the tissue to the degree required to produce shear waves as deep as 10 cm in the tissue.

DISCUSSION -

Ultrasound methods of measuring viscoelasticity are fast, quantitative, inexpensive and widely available for application in socioeconomically stressed regions of the world. But disadvantages are that ultrasound is difficult to use, can only penetrate up to 10 cm in tissue, and cannot evaluate regions for which there is no ultrasonic window. Nevertheless addition of this capability to modern ultrasound instruments will add a new set of biomarkers to the ultrasound examination.

CONCLUSION –The availability of mechanical biomarkers to the ultrasound examination will enhance the diagnostic, staging, and detection capabilities of clinicians and technologists throughout the world.

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