Cross-Validation of Magnetic Resonance Elastography and Ultrasound-based Transient Elastography in Phantom Materials

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Introductions:

Two non-invasive quantitative techniques, **Magnetic resonance Elastography** (MRE) and **Ultrasound-based Transient Elastography** (UTE) have emerged into clinical practice for diagnosing hepatic fibrosis and are now undergoing clinical investigations around the world [1-10] . A study with 35 normal volunteers and 50 patients with chronic liver diseases showed that MRE had a specificity of 99% and sensitivity of 98% to detect all grades of liver fibrosis using a *shear modulus* threshold of 2.9 kPa, and a specificity of 85% and sensitivity of 86% to detect significant fibrosis (>F2) using a *shear modulus* threshold of 4.89kPa [2]. A study of 327 patients with chronic hepatitis C (CHC) concluded that a *Young's modulus* threshold of 8.7 kPa (*shear modulus*--2.9 kPa) allowed correct diagnosis of significant fibrosis (>F2) with an area under ROC of 0.79 [9]. Motivated by the usefulness of both techniques in liver disease diagnosis, comparisons between the two were also performed in terms of specificity and sensitivity, as well as the advantages and disadvantages of each technique such as performance on obese patients and those with ascites [5, 6, 10]. The focus of these previous studies has centered on comparing the performance of these two techniques when imaging *in vivo*, which lacks the control necessary to assess the agreement of the fundamental mechanical properties measured by the two techniques. The goal of this study was to directly compare the stiffness values measured by MRE and UTE on a set of standardized phantoms made and used in the lab.

Methods and Materials:

Elasticity properties such as the *shear modulus* (μ) and *Young's modulus* (E) describe the mechanical response of medium under shear stress and longitudinal stress respectively. *Young's modulus* is the ratio between longitudinal stress and longitudinal strain, and *shear modulus* is the ratio between shear stress and shear strain. As the Poisson's ratio (ν) of most soft tissue is very close to that of uncompressible liquid ($\nu = 0.500$), the *shear modulus* and *Young's modulus* differ only by a scaling factor of 3 (E=3μ). For a homogeneous, isotropic and linearly elastic medium, the shear modulus is a simple function of the speed of shear wave propagation in the medium: $\mu = \rho V_S^2$, where V_s is the speed of shear wave, ρ is the density of the material (assumed to be 1.0 g/cm^3 for soft tissue). Both MRE and TE measure shear wave speed to calculate the *shear modulus* and *Young's modulus* of an object [4, 7]. MRE uses a phase-contrast based MRI sequence to acquire the images of steady-state shear waves propagation in an object induced by an external mechanical driver, and the local shear wave speed is typically calculated base on local frequency estimation (LFE) or other algorithms like direct inversion [8]. UTE uses an ultrasound transducer in A-mode to detect the shear wave propagation of a transient mechanical vibration produced at the same location as the ultrasound transducer. In the direction of the axis of the ultrasound transducer, the distance of the shear wave propagation and time are measured and a spatial-temporal strain map is recorded, and the shear wave speed is calculated based on the slope of the wave front[4]. MRE acquisitions were performed on a 1.5 T MRI scanner (GE, Milwaukee, Wisconsin, USA) using gradient echo MRE protocol similar to [2], and a continuous 60Hz mechanical motion was applied. UTE acquisitions were performed using a Fibroscan system (Echosens, Paris, France), using a measurement protocol similar to [4] and a duration of 20ms (one cycle of 50Hz sinusoid wave) transient mechanical vibration was applied. 17 MRI and Ultrasound compatible B-gel and polymer standardized homogeneous phantoms with a range of stiffnesses were made and used in the lab for this study. One of the authors (J. C.) performed the MRE exams while another author performed the UTE exams (J. O.). Both operators were blinded to the results from the other technique during the measurements.

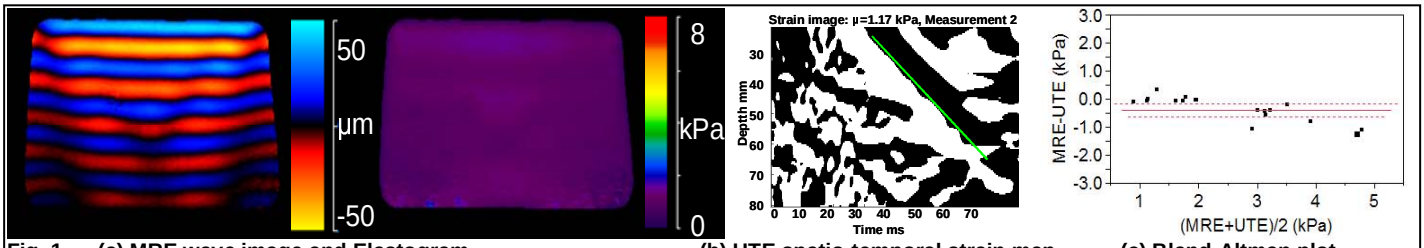

Fig. 1 (a) MRE wave image and Elastogram (b) UTE spatio-temporal strain map (c) Bland-Altman plot

MRE: FOV=14cm,Matrix=256X64,TR/TE=50/26.5ms, flip angle=30˚, thickness=10cm, BW=±16kHz, continues vibration=60Hz, average stiffness of ROI drawn on the elastogram was measured as the stiffness of the phantom. UTE: center frequency of transducer=3.5 MHz, transient vibration=20ms (1 cycle of 50 Hz sinusoid wave), mean value of 10 valid measurements (the slope of the wavefront in the spatio-temporal strain map) was reported as the stiffness of the phantom. Bland-Altman plot: the x-axis is the average value of the MRE and TE measurements, and the y-axis is the difference between them (MRE-UTE).

Results and Discussions:

MRE and UTE measures in 17 standard phantoms were obtained successfully. Fig. 1 (a) and (b) show an example of the measurements of a 1.1kPa (average of MRE and UTE) phantom by MRE and UTE. The results of a Bland-Altman analysis [11] are shown in Fig. 1 (c). The mean difference (MRE-UTE) value was -0.39 kPa, and the standard error was 0.11kPa.

Conclusions:

Detailed *in vitro* cross validation of MRE and UTE in well-characterized phantom materials has demonstrated excellent correlation in measurement of shear stiffness, and no evidence of systemic differences. The most significant differences between the two techniques are that MRE provides a spatial map of stiffness at different locations within the liver, while TUE is very portable. As potential alternatives to liver biopsy, these two non-invasive methods provide clinicians with important new options for improving patient care in liver disease.

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