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Discrepancies in Reporting Tissue Material Properties

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Over the last two decades, the field of ultrasound elastography has offered several noninvasive techniques to measure elasticity of various tissues with the aim of producing a clinical tool that would identify pathology based on variation in tissue elasticity¹. The potential of this rapidly evolving field is evidenced by the numerous clinical studies reporting alterations in liver, breast, kidney, prostate and thyroid elasticity due to various disease processes such as fibrosis and cancer¹.

We read with interest the article entitled “Evaluation of liver tumors using acoustic radiation force impulse elastography and correlation with histologic data” by Frulio, *et al*². However, throughout this article we noted a substantial error in the reporting of the elastography results. The authors used an elastography method called acoustic radiation force impulse (ARFI) elastography which uses focused ultrasound to produce shear waves in the tissue. (This method should be distinguished from the ARFI imaging method that maps the displacement from radiation force-based excitations³). The shear wave motion is then tracked with pulse-echo ultrasound and Doppler processing. The shear wave speed, c_s , is related to the shear modulus, μ , of the tissue by the relationship, $c_s = \sqrt{\mu/\rho}$, where ρ is the mass density of the tissue. While the paper presents important clinical findings on the use of this elastography mode for examining liver tumors, we have also noticed several physical misconceptions and nomenclatorial inaccuracies that, with the future of the development of the field in mind, we feel are necessary to address.

The device used in this study was the Siemens Acuson S2000 (Siemens AG, Berlin, Germany) which reports the shear wave speed in m/s⁴. Frulio and colleagues have made a fundamental error in their reporting of tissue stiffness in units of m/s, which are units of speed not stiffness, and this error is consistently applied throughout the paper.

Briefly, we review the different quantities that are measured using elasticity imaging techniques to understand this error. The shear modulus is the ratio of shear stress to shear strain which has units of Pascals (Pa) or Newtons per square meter (N/m²) and is a fundamental material property of the tissue. The modulus measures the resistance to shear elastic deformation. In significant numbers of papers in the literature, the term stiffness is used instead of modulus. Stiffness, defined as the force over displacement and having units of N/m, is a measure of rigidity of an object and is influenced by its structure. For example, if two cylinders of the same material (i.e., modulus) with equal height but different diameters are pushed with the same force along the height direction, the one with the larger diameter will deform less than the one with the smaller diameter, and the cylinder with the larger diameter will appear stiffer even though both cylinders are made with material having the same modulus. In cases that include materials of the same size and shape, then the material with the higher elastic modulus will feel stiffer than the one with lower modulus.

Unfortunately, this discrepancy of reporting tissue stiffness in units of shear wave speed is not isolated to a single article using the Siemens machine with the Virtual Touch Quantification. In fact, a literature review found 12 other articles with a similar error in

calling the shear wave velocity in units of m/s tissue stiffness⁵⁻¹⁶. In most of these cited articles, the description in the text is sometimes correct, but the graphs may have inappropriate labels. These types of errors range from minor occurrences such as labeling a plot with “liver stiffness measurement by ARFI elastography (m/s)” or something similar^{5, 6, 13, 15} to outright labeling as “Stiffness (m/s)”^{2, 14, 16}, mean liver stiffness (LS) in m/s,⁷⁻¹⁰ tissue elasticity in m/s¹¹, ARFI liver elastography¹². Although, the authors consistently use the values associated with the shear wave speeds throughout their respective papers for statistical analysis and discrimination of advanced pathology versus normal tissue or early pathology, the confusion of the terms remains.

Other devices that provide a quantitative measure of the tissue stiffness include the FibroScan device (Echosens, Paris, France) and the Aixplorer ultrasound scanner (SuperSonic Imagine, Aix-en-Provence, France). The FibroScan device employs a method called transient elastography¹⁷ and the Aixplorer utilizes a method called supersonic shear imaging¹⁸. Both of these devices report the Young's modulus values in units of kilopascals (kPa = kN/m²). However, the Aixplorer has recently been approved by the United States Food and Drug Administration (FDA) for reporting of an adjustable numerical speed scale for the shear wave speeds measured¹⁹. Therefore, users may be susceptible to making a similar type of error if the shear wave speed is used for reporting “stiffness”.

Magnetic resonance elastography is another method that uses mechanical vibration to create shear waves in different organs and then uses magnetic resonance imaging methods to measure the shear wave propagation²⁰. In a number of studies, the shear modulus, μ , also referred to in many papers as the shear stiffness, is reported²¹⁻²³. The shear modulus in an elastic, homogeneous, isotropic, and incompressible tissue is related to the Young's modulus, E , by $E \approx 3\mu$.

It should be noted that reporting the shear wave speed along with the frequency characteristics of the shear wave is the most appropriate so that results may be interpreted fairly between different studies. The frequency information is important because of the influence of the viscosity and geometry of soft tissues which causes the shear wave speed to vary with frequency²⁴⁻²⁷.

The scientific fallacy stemming from not discerning stiffness, shear modulus and shear wave speed as distinct physical phenomena does not obscure the clinical relevance and statistical analysis of the changes in shear wave velocity through various disease states. However, neglecting the relationship between the quantities speed, stiffness and the modulus and the importance of reporting the frequency makes it difficult to compare the results of a study with others conducted with the same device or studies performed with other devices in the field.

These errors have been reported in numerous clinically-oriented journals with 2011 impact factors that range from 1.25-3.82²⁸. The field of clinical quantitative ultrasound-based elasticity imaging has been growing over the past few years. This is evidenced that just in the Journal of Ultrasound in Medicine for issues ranging from January 2012-January 2013 there were 11 articles or letters addressing this field. The number of articles will only grow as the field expands so it is important to recognize these errors now so that the integrity of the field is maintained.

Finally, we need to address how to avoid these types of errors in the literature in the future. There are five groups or institutions that need to be involved in this process including the authors, the device manufacturers, basic scientists, journal reviewers, and journal editorial staff. First, the authors of an article should take responsibility to accurately report their results which requires a basic knowledge of what the ultrasound device is actually

measuring and reporting. It was observed that in the articles cited for containing these aforementioned discrepancies generally came from authors with M.D. degrees that identify with clinical departments. It may be the case that these clinicians may not have a strong foundation in the physics involved in the measurement techniques so the nuances of reporting shear wave speed versus tissue stiffness may be missed.

Second, the device manufacturers that have elastography modes may need to offer more education on the different elastography modes that are employed on their systems. In addition, a consensus within the industry on what to report would help to alleviate these discrepancies. Recently, the Radiological Society of North America (RSNA) Quantitative Imaging Biomarkers Alliance (QIBA) established the Ultrasound Shear Wave Speed Technical Committee to work on the standardization of quantitative elasticity measurements for clinical use²⁹. As these elastography modes are introduced more prevalently into clinical practice the sonographers and physicians need to understand what the machine is reporting.

Third, basic scientists that work in the elastography field need to provide the clearest descriptions of their methods within the engineering and basic science community as well as when they interact with clinicians who will use these devices on a daily basis.

Lastly, the final gatekeepers for publication and dissemination of research results are journal reviewers and the editorial staff of the journal, including the associate editors as well as the editor-in-chief. The reviewers and editors need to be sensitive to this type of error, particularly for a method that is now emerging into clinical studies.

Elasticity measurement and imaging have strong potential to make an impact in clinical care, particularly as the devices for making these types of measurements become more prevalent. The integrity of the measurement must be maintained to have sufficient meaning for use in diagnosis and that means having a more complete understanding of the fundamental properties that are being measured. This responsibility is shared by many within the scientific community, particularly basic scientists and engineers, device manufacturers, clinical scientists and reviewers and editors associated with the reporting and dissemination of biomedical study results.

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