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On System Dependent Sources of Uncertainty and Bias in Ultrasonic Quantitative Shear Wave Imaging

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Abstract

Ultrasonic quantitative shear wave imaging methods have been developed over the last decade to estimate tissue elasticity by measuring the speed of propagating shear waves following acoustic radiation force excitation. This work discusses eight sources of uncertainty and bias arising from ultrasound system dependent parameters in ultrasound shear wave speed (SWS) measurements. Each of the eight sources of error are discussed in the context of a linear, isotropic, elastic, homogeneous medium, combining previously reported analyses with Field II simulations, full-wave 2D acoustic propagation simulations and experimental studies. Errors arising from both spatial and temporal sources lead to errors in SWS measurements. Arrival time estimation noise, speckle bias, hardware fluctuations, and phase aberration cause uncertainties (variance) in SWS measurements, while pulse repetition frequency and beamforming errors, as well as coupling medium sound speed mismatch, cause biases in SWS measurements (accuracy errors). Calibration of the sources of bias is an important step in the development of shear wave imaging systems. In a well-calibrated system, where the sources of bias are minimized, and averaging over an ROI is employed to reduce the sources of uncertainty, a SWS error < 3% can be expected.

I. INTRODUCTION

Acoustic radiation force impulse (ARFI) based elasticity imaging methods have been under investigation since the early 2000's. Tissue elasticity is known to be associated with underlying pathological conditions, and ultrasound elasticity imaging methods are able to image these features non-invasively to provide diagnostic information. A number of quantitative shear wave imaging techniques have been proposed in recent years, such as shear wave elasticity imaging (SWEI) [1], supersonic shear imaging (SSI) [2], shear wave spectroscopy [3], and shear wave dispersion ultrasound vibrometry (SDUV) [4]. All of these methods use long duration focused ultrasound waves to generate ARFI excitations to induce tissue motion, and use standard ultrasound imaging techniques to track the shear wave to measure the speed of propagation. The shear wave speed (SWS) measured is related to the material's shear modulus. For an elastic isotropic material, SWS is proportional to the square root of the shear modulus μ divided by the density ρ :

$$\text{SWS} = \sqrt{\frac{\mu}{\rho}}. \quad (1)$$

SWS typically has units of m/s, shear modulus (μ) of soft tissue typically has units of kPa, and ρ is usually assumed to be 1 g/cm³ for soft tissue. Shear wave spectroscopy and SDUV also evaluate the frequency dependence of SWS to assess tissue dispersion. Many clinical

applications of these techniques in various organs and diseases have been reported in the literature [5], [6], such as liver fibrosis staging [7], bladder dysfunction [8], kidney monitoring [9], thyroid gland [10], breast [11], and prostate cancer detection [12].

In addition, shear wave imaging methods have been translated into clinical practice. They have been adopted in clinics in Europe since 2008 [13], [14], [15]. Recently, the Food and Drug Administration (FDA) approved commercial shear wave imaging products from several leading ultrasound manufacturers for clinical use in the U.S, such as Siemens Virtual Touch Imaging™ [16], Philips ElastPQ™ [17], GE Logiq E9 Elastography™ [18], Toshiba Shear Wave Elastography™ [19], and SuperSonic Imagine™ ShearWave Elastography [20]. Several clinical applications, such as liver fibrosis staging [21], require accurate SWS estimation to guide diagnostics. The Radiology Society of North America (RSNA) / Quantitative Imaging Biomarkers Alliance (QIBA) Ultrasound SWS technical committee was established in 2011 to advance and standardize quantitative shear wave imaging [22], [23].

The quality of ultrasonic quantitative shear wave imaging systems largely depends on the ability to induce detectable shear waves in soft tissue and accurately monitor tissue motion and the propagation of the shear waves. The data processing pipeline of such a system typically involves the following steps: (1) Beamforming radio frequency (RF) or demodulated analytic (commonly known as IQ) data acquired before and after the ARFI excitation; (2) tissue motion estimation using cross-correlation or phase shift algorithms from the data in (1) [24]; and (3) SWS reconstruction from temporal-spatial tissue motion data using time-of-flight (TOF) or wave equation based methods. Uncertainties and biases can arise from each processing step that propagate through the data processing pipeline resulting in errors in the reconstructed SWS. This paper focuses on the sources of uncertainty and bias arising from ultrasound system dependent parameters, including arrival time estimation noise, speckle bias, hardware fluctuations, pulse repetition frequency error, beamforming errors, and coupling medium sound speed mismatch. We discuss each error source and analyze its impact in a typical SWS measurement, using simulation, analytic tools, literature references, and experiments.

II. BACKGROUND

The estimation of SWS can be accomplished by a variety of methods. Magnetic resonance elastography acquires 3D sets of tissue motion data and uses direct inversion of the Helmholtz equation [25], [26]; however, most ultrasonically-tracked tissue motion data is acquired in a single axial-lateral imaging plane, so that additional assumptions are required for the inversion of the Helmholtz equation. In addition, the jitter present in ultrasonically-tracked tissue motion data are amplified from calculating second-order spatial and temporal derivatives using this approach [2], [27], resulting in noise and artifacts in the estimated SWS.

Instead, TOF methods have been shown to be effective in ultrasonic SWS quantification. TOF methods take advantage of *a priori* information about the shear wave propagation direction to estimate wave speed [28], [29]. In 2D shear wave imaging, the ARFI push

displaces tissue in the axial direction, and the shear wave is assumed to travel in the lateral direction. The first step of TOF methods is to determine the shear wave arrival time at each lateral position, which can be accomplished by a variety of metrics, such as time of peak displacement [29], time of peak particle velocity [30], and cross-correlation of tissue motion profile at adjacent spatial locations [28]. Then SWS can be reconstructed from the wave arrival time profile using several approaches, such as linear regression, RANdom Sample Consensus (RANSAC) [31], Radon sum transformation [32], and level-set methods [33]. The analysis in this paper assumes that a TOF method is used for SWS reconstruction.

Regardless of the specific algorithm used, TOF methods ultimately extract the shear wave trajectory in the spatial-temporal tissue motion data, and SWS is calculated simply as the slope of this trajectory:

$$\text{SWS} = \frac{ds}{dt} \quad (2)$$

where s is the distance traveled by the shear wave, and t is the time elapsed. Figure 1 shows experimental data from SWS estimation using TOF methods. The displacement versus time profiles for 6 lateral locations at the focal depth are plotted in Figure 1(a). Wave arrival times were calculated from the time of peak displacement in each displacement trace, and plotted in Figure 1(b). A linear regression was performed between arrival time and lateral distance, and the linear fit with least square error is shown. SWS is equal to the inverse of the slope of the linear fit in Figure 1(b), under the assumption of uniform wave propagation in the lateral direction. Higher SWS spatial resolution can be achieved using the time lag between the adjacent displacement pairs, as shown in Figure 1(c). The time lag was estimated from the position of maximum correlation coefficient between adjacent displacement pairs. SWS is equal to the distance between lateral locations divided by the time lag, which can be averaged across multiple pairs to decrease variance at the expense of spatial resolution.

Errors arising from either space (s) or time (t) calculation would lead to errors in the estimated SWS. Spatial positions are determined by the lateral beam positions in the ultrasound image, as tissue motion is in the axial direction and the shear waves travel in the lateral direction. Temporal measurements are determined by the system timing. Assuming lateral position and time are independent Gaussian distributed variables on a typical system, the percent SWS error (δ_{SWS}) can be approximated by the summation of the percent errors in space (δ_s) and time (δ_t) by the uncertainty propagation principle [34], [35]:

$$\frac{\delta_{\text{SWS}}}{\text{SWS}} \approx \frac{\delta_s}{s} + \frac{\delta_t}{t}. \quad (3)$$

Table I lists the temporal and spatial error sources that are discussed in this paper. Four temporal and four spatial error sources are considered herein. (1) Arrival time estimation noise and (2) speckle bias have been previously discussed in the literature, and are reviewed in this paper. (3) Hardware fluctuations and (4) pulse repetition frequency (PRF) errors are higher order errors, which are described briefly in this work. (5) Phase aberration, (6) and (7) beamforming errors, and (8) coupling medium sound speed mismatch are evaluated with

simulation and experimental validation herein. Section III introduces the simulation and experimental methods. Each error source is discussed in succession in section IV. Finally, the relative magnitude between the errors is discussed in section V, for a typical liver imaging configuration.

III. METHODS

The temporal error sources are discussed using literature references and descriptive analysis. The spatial error sources are investigated with the aid of Field II simulations [38], full-wave acoustic propagation simulations [39] and experiments on tissue mimicking phantoms using a Verasonics™ research scanner.

A. Field II simulations

Field II simulations were employed to demonstrate beam-forming errors (Table I items (6) and (7)) with realistic transducer parameters. An ATL™ L7-4 linear array was simulated to demonstrate pitch errors in linear and phased arrays. Walking aperture beamforming was used in this simulation. For each A-line, a subperture of 41 elements centered around that A-line was used for beamforming with lateral F-number = 2, and 20 elements on each side of the A-line. A Philips™ C5-2 curvilinear array was simulated in Field II to demonstrate radius of curvature (ROC) and sector angle errors in curvilinear arrays. Table II lists the Field II input parameters for both arrays. The pitch error, ROC error, and sector angle error were arbitrarily chosen to be 5%, to generate quantifiable lateral position errors but minimal distortion to the point spread functions in the simulation results. The 5% level is generally higher than the industrial tolerance level of transducer variance. However, if a research system is used and the transducer specifications are not available or are empirically determined, 5% errors are realistic.

B. Full wave simulations

Full wave 2D acoustic propagation simulations were employed to demonstrate the effect of phase aberration (Table I item (5)) using previously validated simulation tools and abdominal wall models [39]. The simulations were designed to image a point target behind an abdominal layer to mimic typical abdominal imaging. The transmit pulse had an amplitude of 0.1 MPa, and had a center frequency of 2 MHz with 50% fractional bandwidth. The transmit pulse was focused on the point target, which was located at 60 mm axially, with an F-number of 2 to simulate typical liver imaging configurations. The control simulation was performed with a uniform background speed of sound of 1540 m/s. Six different abdominal wall models derived from healthy subjects were simulated. The tissue representation was obtained from histologically stained samples of human abdominal wall [40], [41], and the structures in the tissue were correlated with their measured properties. Table III shows the speed of sound, attenuation, and nonlinearity of the components in the abdominal wall model [39].

C. Experimental studies

SWS was measured on a CIRS Zerdine™ homogeneous elastic phantom with the Verasonics™ Vantage Scanner and the Philips™ C5-2 curvilinear array transducer to

demonstrate coupling medium sound speed mismatch (Table I item (8)). The phantom has a speed of sound of 1540 m/s and the beamforming process assumes a speed of sound of 1540 m/s. The SWS measurements were performed with two coupling media, room temperature water (speed of sound: 1485 m/s) and an alcohol solution (9.6% by volume) that has a speed of sound of 1540 m/s [42]. SWS was measured at 60 mm axially, and the transducer was controlled by a translation stage to move it away from the phantom to measure SWS with various distances through the coupling fluid. Eight repeated measurements were made at each distance using different speckle patterns.

D. Spatial error analysis terminology

In the investigation of beamforming errors and coupling medium sound speed mismatch (Table I items (6), (7) and (8), and Figures 5, 10(a)), points P and P' are used to represent intended points of interest in the ultrasound Bmode images (P) as compared to their corresponding true physical locations (P'). In the absence of spatial errors, P and P' are co-located. In the Field II simulations, the receive delays were computed to focus at a fixed point P with correct and erroneous transducer input parameters. Given a set of erroneous transducer parameters, the receive delays are inaccurate, and lead to a shift of the actual receive focus to the physical location at P'; i.e., the system attempts to focus at P, but in reality is imaging at P' due to the erroneous transducer parameters. Point P in the image reflects the information at point P' in the physical field. The resultant images and the point spread functions (Figure 6, 8 and 9) are shown with respect to physical spatial coordinates (P') to illustrate the lateral location errors. The blue curves in the point spread function (PSF) plots in these figures (all references to color refer to the online version of this paper) represent the cases with correct input parameters (no spatial error), where P and P' overlap with each other.

E. Common parameters for quantitative comparison

In order to compare the relative contribution between different sources of errors in an ultrasound shear wave imaging system, a common set of parameters for the medium and imaging sequences were selected. Table IV summarizes the parameters, which were selected based on typical values used in a liver fibrosis shear wave imaging system. The shear modulus of human liver is rarely greater than 20 kPa, including cirrhotic livers [7]. The shear wave center frequency and track beam acoustic center frequency are typical values assuming an abdominal ultrasound transducer. The region of interest (ROI) was chosen to be a 8×2 mm box, which is typically used in liver fibrosis point measurements [43]. This ROI covers 10 lateral beams and 4 independent speckles axially given the other imaging parameters. The ROI for each pixel is typically smaller for 2D SWS image computation [43].

IV. ANALYSIS OF ERRORS

A. Arrival time estimation noise

Errors in the arrival time profile of the shear waves result in errors in the estimated SWS. The expected variance of the arrival times as computed by TOF algorithms has been estimated from the Cramér-Rao lower bound (CRLB) [36]. The CRLB gives the minimum

variance of a time-delay estimator from the signal properties. Deffieux *et al.* extended the CRLB to predict the lower bound of the variance of the arrival time measured between two shear waveforms at two lateral positions using correlation approaches ($\sigma_{dT}^2(z, x)$, as Equation 15 of [36]):

$$\sigma_{dT}^2(z, x) \geq \frac{1}{8\pi^2 \cdot F_{sw}^2 BWT} \times \left(\left(1 + \frac{1}{\text{SNR}_{V_z}(z, x - \frac{dr}{2})} \right) \times \left(1 + \frac{1}{\text{SNR}_{V_z}(z, x + \frac{dr}{2})} \right) - 1 \right). \quad (4)$$

where SNR is the signal-to-noise ratio of the shear wave, defined as the ratio of the shear wave energy to the tissue motion variance, F_{sw} is the shear wave frequency, T is the ensemble length, BW is the shear wave bandwidth, and dr is the distance between lateral beams. Figure 2(a) shows the standard deviation of the arrival time (σ_{dT}) as a function of shear wave SNR calculated from Equation 4. High frequency, broadband, and high SNR shear waves result in more accurate arrival time estimation. Deffieux *et al.* also estimated the variance of the shear modulus (σ_{μ}^2) based on the variance of the arrival time profile (σ_{dT}^2) for high SNR tissue motion data (Equation 20 of [36]):

$$\sigma_{\mu}^2 \approx \frac{4\mu_0^3 \sigma_{dT}^2}{dr^2 \rho}. \quad (5)$$

where μ_0 is the shear modulus of the material, and ρ is acoustic density. Figure 2(b) shows the standard deviation of the shear modulus (σ_{μ}) as a function of shear wave SNR calculated from Equation 5, estimated with a typical liver fibrosis shear wave imaging system. Softer materials and larger distances between lateral beams result in smaller variance and more accurate shear modulus estimation.

Arrival time estimation noise is a source of uncertainty, which can be reduced through averaging. Deffieux *et al.* developed Equation 4 using cross-correlation of the tissue motion profiles between adjacent spatial locations to calculate wave arrival time. The time lag between multiple pairs of spatial locations in an imaging sequence can be calculated, and taking the average value of the time lags effectively reduces the arrival time estimation noise. The time lag was calculated in 5 available pairs of adjacent lateral locations in Figure 1(c), and SWS was estimated from the average time lag. On the other hand, the absolute wave arrival time at each spatial location can also be estimated using time of peak displacement or time of peak particle velocity, and SWS can be calculated from the slope of the linear regression between arrival time profiles at multiple lateral locations, as illustrated in Figure 1(b). The step of linear regression incorporates information from multiple wave arrival time data points, and the linear fit with least square errors effectively averages out the uncertainties present in each data point, which is analogous to averaging the time lags in Figure 1(c). In a linear homogeneous medium, both SWS estimation approaches result in similar levels of RMS errors [30].

B. Speckle bias

Speckle bias was originally described by McAleavey *et al.* [44]. Speckle bias is a source of arrival time estimation noise that is not captured by the CRLB model. As described by

McAleavey *et al.*, scatterers within the resolution cell of an ultrasound system scatter the transmitted pulses and generate echoes that constructively and destructively interfere. Such interference results in the speckle pattern in ultrasonic images. When tissue motion is tracked, the system is more sensitive to the areas of constructive interference. Therefore, the wave arrival times for a particular beam location are biased towards the bright speckle [44]. The magnitude of this bias is determined by the size of the point spread function (PSF) of the system, as speckle size is correlated with PSF size. Elegbe and McAleavey simulated the variation in arrival time estimation in a homogeneous phantom (Top right panel in Figure 6 of [37]). They measured the shear wave arrival time 2 mm away from the ARFI push, and repeated these measurements at various locations within the phantom to perform a statistical analysis. The arrival time profile had a Gaussian distribution centered at 1.4 ms, with Full Width Half Maximum (FWHM) ranging from 1.2 ms to 1.7 ms, which corresponded to the time for the shear wave to travel across the size of the PSF in their experiments. This distribution of wave arrival time results in a Gaussian distribution of reconstructed shear moduli centered at 2 kPa, with FWHM ranging from 1.7 – 2.3 kPa (Bottom right panel in Figure 6 of [37]). Although named as “bias”, speckle bias is a source of uncertainty, which is a random error on different lateral tracking beams as well as across axial speckle regions in multiple-track-location (MTL) SWEI.

C. Hardware fluctuations

The ARFI push pulses in shear wave imaging sequences typically have high intensity and long duration. A large amount of current is drawn through the scanner hardware to deliver the push pulses to the transmitters, which can introduce hardware fluctuations. Therefore, shear wave imaging sequences can suffer from higher hardware fluctuations than standard Bmode or Doppler sequences. Hardware fluctuations can result in jitter in the scanner timing. The magnitude of timing jitter due to hardware fluctuations is typically on the order of nanoseconds.

D. Pulse repetition frequency (PRF) error

The PRF defines the maximum shear wave speed that can be tracked due to the sampling criterion. Specifying PRF on the scanner can be subject to systematic errors, which is more likely at high PRFs. It is useful to measure the actual PRF after setting it to avoid these errors. If a systematic error is present in the PRF setting, this percent error will directly translate to the percent error in the estimated SWS.

E. Phase aberration

Most ultrasonic imaging systems assume a constant acoustic velocity of 1540 m/s in tissue. This assumption is utilized in the computation of electronic delay profiles for array transducers to focus both transmitted and received acoustic energies. However, the *in vivo* speed of sound varies from 1470 m/s in fat to 3700 m/s in bone [45]. As an ultrasound wavefront propagates through tissue, parts of the wavefront encounter regions with different acoustic velocities and are shifted with respect to the rest of the wavefront. This shift is known as phase aberration [46]. Phase aberration introduces delay errors that degrade image quality. When the different parts of the received wavefront in each element of the array are summed during the beamforming process, the shifted portions of the wavefront cause

mainlobe energy spreading and higher sidelobe amplitudes. In addition, the shape of the PSF is distorted, which can lead to shifts of the object appearing in the image. Trahey *et al.* measured phase aberrations across the breasts of 22 patients using a 4.2 MHz phased array [46]. The lateral shift of the beams caused by phase aberration in the breasts introduced an average steering error of 1.4° . Freiburger *et al.* measured phase aberrations across the breasts of 7 patients using a 4.3 MHz matrix array, and measured azimuth steering error to be $0.8^\circ \pm 0.7^\circ$ [47]. Kramer and Hassler found in vitro that normal livers introduced minor phase distortions while the abdominal wall introduced time-of-flight differences of up to 1 μsec across 20 mm of tissue [48].

Figure 3 shows the results of full wave simulations with abdominal layers. Figure 3(a) shows the speed of sound profile of one of the 6 abdominal layers. The point target was located below the abdominal wall at 60 mm axially and 0 mm laterally. Figure 3(b) and 3(c) show the images of the point target without and with an abdominal wall. The point target appears less bright and less prominent in (c). Figure 3(d) plots the lateral PSFs from (b) and (c) as computed by the peak pressure amplitudes from each axial line in the images. As expected, in the presence of the aberrating abdominal wall, the PSF of the point target is distorted. The mainlobe has lower energy and the sidelobes have increased amplitudes. The center of the lateral PSF is shifted to the left by 0.12 mm, which corresponds to a steering error of 0.1° . The lateral shifts of the point target in the 6 simulations range from -0.33 mm to 0.17 mm, corresponding to steer errors between -0.2° and 0.1° .

In summary, phase aberration can lead to a lateral shift of the beams in an image, and this shift causes lateral position errors and therefore SWS errors. Phase aberration occurs randomly across a field of view in in vivo imaging, and is generally not present in phantom characterizations.

F. Pitch error in linear and phased arrays

Delay-and-sum (DAS) beamforming is used to focus received channel data and produce each beam line or amplitude line (A-line) in most ultrasound scanners. DAS beamforming calculates the time for ultrasound waves to travel from the point of interest to each element of the transducer array, then delays and aligns the channel data according to the relative differences in that time. The aligned channel data is then summed to produce a beam line in the ultrasound Bmode image. Incorrect transducer parameters lead to delay computation errors in the beamforming process. Incorrect delays in turn result in beam position errors, as well as a de-focused ultrasound image. Errors in lateral beam position result in errors in SWS estimation as discussed below.

In linear and phased arrays, element positions are determined by the pitch of the transducer. The pitch is the distance between the elements of the array. An incorrect pitch input would lead to incorrect element positions, resulting in incorrect focal delay computations. Figure 4 shows the receive delays of a 64-element linear array transducer focused at a point target at 60 mm axially and 0 mm laterally. The physical pitch of this transducer was 0.3 mm. The solid line shows the correct receive delay of each element, which was the time for the back-scattered ultrasound wave to travel from the point target to each element. It was calculated as the distance between the point and each element divided by the speed of sound (assumed to

be 1540 m/s). The point target was located at the center relative to the transducer laterally (0 mm), so that the delay profile is a symmetrical parabolic arc. The dashed line shows the wrong delay, computed with a pitch that is 20% larger than the physical pitch, i.e., a +20% pitch error. The wrong delay profile had an elliptical shape with a steeper slope, because the elements were perceived to be further apart, so that the relative path differences between the elements were higher. If this wrong delay was used in the DAS beamforming process, the channel data would not be properly aligned, and the point target would be de-focused and shifted axially. There is no lateral shift of the point in this case because both the correct and wrong delay profiles are symmetrical.

Linear Arrays—In linear array beamforming, a walking aperture technique is usually employed given the large size of the array. A sub-aperture is used to beamform a certain A-line in the image, and this sub-aperture is centered around the A-line laterally. This sub-aperture is then translated (or walked) across the array to beamform adjacent A-lines to form a Bmode image. In this case, a pitch error would lead to both an axial position error as described in Figure 4, and a lateral beam position error due to the center element shift effect, as described in Figure 5. Figure 5 demonstrates the center element shift effect with a pitch error of 100%, which is an exaggeration for demonstration purposes. In Figure 5, the solid squares represent the physical elements of a linear array with a pitch of d , and the dashed squares are perceived erroneous element positions with a pitch of $2d$. The perceived pitch is twice as large as the physical pitch, i.e. +100% pitch error. In order to focus at a point P, which is directly below element e1, a sub-aperture symmetrical about e1 was used to compute the delay profile. Element e1 is the perceived center element of this sub-aperture. However, given that the perceived pitch is larger than the physical pitch, the delay profile computed around element e1 was applied to the physical aperture centered around position E1. Therefore, element E1 was the physical center element of this sub-aperture, and this sub-aperture would focus at a point P', instead of P. Point P in the Bmode image corresponds to P' physically due to the center element shift from e1 to E1. The physical position of the beam is closer to the center (Lat = 0 mm) than the perceived beam in the image, because P' is closer to the center than P. A pitch error leads to a lateral beam position error of the same percentage, which in turn leads to a SWS error of the same percentage.

The center element shift effect is demonstrated with Field II simulation in Figure 6. The simulation was configured to focus at a point P located at -3 mm laterally and 60 mm axially in the image. The images were generated both with a correct pitch and a pitch error of +5%. The 5% pitch error had minimal impact on the appearance of the point target in the Bmode images (Figure 6(a), (b)). Figure 6(c) plots the lateral PSFs. P' was located at -3 mm laterally in (a), which agrees with the location of P on the image. However, P' in (b) was located at -2.85 mm laterally. The 5% pitch error results in the shift of receive focus to -2.85 mm, introducing 5% lateral position error, and a corresponding 5% error in tracking beam lateral spacing and eventually a 5% SWS error.

Phased Arrays—The beamforming process for a phased array is similar to that for a linear array. However, due to the limited aperture size of a phased array, the entire aperture is often used to focus every beam. Therefore, phased arrays do not have symmetrical sub-

apertures around the beam lines. Figure 7 plots the receive delay profile of the same aperture as in Figure 4, but for a point located at 60 mm axially and -3 mm laterally. The dotted curves show the delays computed with +20% pitch errors. The minimum delay point (marked by crosses) shifted closer to 0 mm laterally similar to the center element effect in linear arrays. This shifts the receive beam closer to the center laterally (as previously discussed in Figure 5). However, due to the asymmetrical aperture shape, there is an extra steering effect that has an opposing effect. In this case, there are more elements on the right of the minimum delay element than on the left. The arrows in Figure 7 show that by using the dashed delay profile instead of the solid one, this aperture is steered farther off-axis (away from 0 mm laterally). This steering effect works against the center element shift effect.

This steering effect was evaluated using Field II simulations. Figure 8(a) shows the results of similar simulations as used in Figure 6, but with 3 values of asymmetry ratio (AR), defined as the ratio of number of elements on the right side of the A-line over the number of elements on the left side. For example, when the asymmetry ratio was 2, the sub-aperture had 20 elements on the left and 40 elements on the right of the A-line. The simulation was again configured to focus at a point P at -3 mm laterally and 60 mm axially. The blue curve shows that with correct pitch, P' (physical location) is at -3 mm laterally, which is co-located with point P. The orange curve shows the same results as in Figure 6. P' is located at -2.85 mm laterally with 5% pitch error and AR = 1. The yellow and purple curves show different locations of P' with the same 5% pitch error but different ARs. Figure 8(b) shows the trend of P' location as a function of AR. The center element shift effect shifts the receive focus towards 0 mm laterally, while the steering effect shifts the focus farther off-axis. As the AR increases, the steering effect becomes more dominant. In this case, the steering effect neutralizes the center element shift effect when AR = 2 (yellow cross), and the steering effect becomes the dominant effect for larger ARs.

For typical phased array imaging systems, the asymmetry ratio varies at different steering angles. The steering effect is more dominant when the target points are farther away from the center of the array. For shear wave imaging targeted at regions close to the center of the array, a phased array would behave similarly to linear arrays in the presence of pitch errors, where the center element shift effect is the dominant artifact: a 5% pitch error used for delay calculation would lead to a 5% overestimation of SWS. However, for large steering angles, due to the competing effects of center element shift and steering angle, the same 5% pitch error would lead to a SWS error of less than 5%.

G. Radius of curvature (ROC) and sector angle error in curvilinear arrays

A curvilinear array transducer is defined through 2 parameters, radius of curvature (ROC), and sector angle (Figure 9(a)). The axial and lateral position of each element is calculated as $ROC \times \sin(\theta_n)$ and $ROC \times \cos(\theta_n)$ respectively, where θ_n is the angle of the n^{th} element, which is dependent on the sector angle and number of elements of the array. An error in either ROC or sector angle would lead to incorrect element positions, which in turn would lead to beam position errors. Similar to linear arrays, symmetrical walking sub-apertures are typically used in the beamforming process in curvilinear arrays, due to the large foot-print of

the transducer. Moreover, a higher F-number (smaller aperture) is usually used in curvilinear arrays than in linear arrays, because of the decreased sensitivity of side elements due to the curved transducer surface. Consequently, the steering effect from asymmetrical sub-apertures observed with phased arrays can be ignored for curvilinear arrays. The lateral beam position error is primarily caused by the center element shift effect in the presence of ROC or sector angle errors.

The same percentage error in ROC and in sector angle will result in different percentage errors in lateral beam positions (Figure 9). This is because the lateral position X of a point of interest in an image is calculated as

$$X = \text{ROC} \left(1 + \frac{r}{\text{ROC}}\right) \sin(\theta) \quad (6)$$

where r is the shortest distance between the point and the face of the transducer, and θ is angle of the radial line that connects the point of interest and the apex of the curvilinear array (Figure 9(a)). For small θ , where $\sin(\theta) \approx \theta$, a 5% θ error would lead to 5% error in X .

On the other hand, a 5% ROC error would lead to <5% error in X , due to the term $\frac{r}{\text{ROC}}$ in Equation 6. The magnitude of the error in X is dependent on the magnitude of r . As a result, the lateral beam position error decreases as the imaging window goes deeper, with the same magnitude of ROC error.

Field II simulations were used to quantify the effect of ROC and sector angle errors in lateral beam positions. Assume the target point P is located at 60 mm axially and -10 mm laterally. A +5% ROC error and sector angle error were simulated respectively. Figure 9(b) plots the lateral PSFs with respect to the corresponding physical locations (P). The point P' was located at -10 mm with correct imaging parameters, which agrees with the desired lateral location of P. With a 5% sector angle error, P' was located at -9.5 mm, corresponding to a 5% lateral position error. With a 5% ROC error, P' was located at -9.8 mm, corresponding to a 2% lateral position error. Figure 9(c) plots the lateral beam location error as a function of ROC and sector angle error. A sector angle error leads to a beam location error of the same percentage, while an ROC error results in a smaller lateral position error. Each percent lateral position error would lead to a corresponding matched percent error in SWS.

H. Coupling medium sound speed mismatch

In phantom imaging, the coupling between the transducer and the phantom is a potential source of error for SWS measurement with curvilinear arrays. Due to the curved surface of curvilinear arrays, there is a gap between the outer elements of the array and the phantom surface when the transducer is in contact with the phantom, which is generally not a problem when imaging patients due to the compliant nature of the skin. Tissue-mimicking phantoms are usually made to have a speed of sound of 1540 m/s to match the average sound speed in tissue. The speed of sound in water, which is commonly used as the coupling medium, is between 1480 m/s and 1490 m/s at room temperature [45]. The sound speed mismatch between water and phantom causes refraction at the boundary, as shown in Figure 10(a). When the system attempts to focus at a point P in the phantom, it computes the delay assuming the sound travels in a straight path (blue solid line in Figure 10(a)) from point P to

the transducer. However, in reality, the sound wave is refracted at the boundary and travels according to the red dotted path. This refraction phenomenon can cause lateral beam position errors, especially with large d , where d is the shortest distance between the transducer surface and the phantom surface.

To investigate the lateral beam position errors arising from refraction in phantom experiments, we used a least square delay error model to locate the physical position of the beams. For a particular point of interest P in the Bmode image, the delay profile computed by the ultrasound scanner assuming no refraction, *Delay Scanner*, is calculated. Then, a search region is formed around this point. For each point in the search region, the correct delay profile considering refraction at the water/phantom boundary, *DelayRefraction*, is calculated. The difference between *DelayScanner* and *Delay Refraction* is calculated for each point in the search region. The physical location of the point P' that corresponds in the image to point P, is determined from the location within the search region that has the minimum delay error between *Delay Refraction* and *DelayScanner*.

$$P'(r, \theta) = \min_i \left(\text{Delay Refraction}(P'(r, \theta), i) - \text{DelayScanner}(P, i) \right)^2. \quad (7)$$

The summation over i integrates the delay errors over all the elements of the aperture. The search region is a 2D search region in both r and θ , where r and θ are defined in the same way as in Equation 6 and Figure 9(a). The step size of the search region was arbitrarily chosen to be 0.01 mm in the r dimension and 0.001 radians in the θ dimension.

Figure 10 shows the calculation for a Philips™ C5-2 curvilinear array model with the shortest path from the transducer to the phantom surface $d = 20$ mm. The line color and style are consistent between the sound travel path in Figure 10(a) and the delay curves in the top panel of (b). The blue solid line in (b) shows *DelayScanner* of a point P located at 60 mm axially and 17 mm laterally in the image, corresponding to the straight solid path between P and the transducer in (a). The red dotted line in (b) shows *Delay Refraction* of this point P. The offset between the blue solid curve and the red dotted curve is a result of the path difference arising from refraction at the phantom/water boundary. The speed of sound in the phantom is assumed to be 1540 m/s, and the speed of sound in water is assumed to be 1485 m/s. The yellow dashed line shows *Delay Refraction* of the point P' in the search region that corresponds to the *DelayScanner* of P. The solid and dashed lines in (b) almost overlap with each other. This means that the total delay for P' with consideration of refraction is almost identical to the total delay for P assuming straight travel path. Therefore, the system attempts to focus at P, but actually focuses at P' due to refraction. The bottom panel of Figure 10(b) shows the delay error of each point in the search region. The cross marks the position of P' that has minimum least square delay error.

The least square delay error model was compared with experimental SWS measurements. Figure 11 shows the results. The data was normalized to the mean SWS measured with the alcohol solution at $d = 0$ mm. As d increases, the SWS measured through the alcohol solution does not change because the sound speed in the alcohol solution and the phantom are the same. The SWS measured in water increased with increasing d , and this

observation agrees with the least square delay error model. Figure 11 shows that using water as the coupling medium leads to over-estimation of the SWS measurements. The percent errors increase with increasing d , up to about 5% when $d = 30$ mm.

V. DISCUSSION

We have presented 8 system dependent sources of error that contribute to uncertainty and bias in the measurement of SWS following ARFI excitation. Four of them: arrival time estimation noise, speckle bias, hardware fluctuations, and phase aberration cause uncertainties (variance) in SWS measurements. As presented by Deffieux *et al.* [36], arrival time estimation noise decreases with increasing shear wave SNR. The impact of arrival time estimation noise on estimated SWS depends on several factors, such as shear wave frequency, lateral beam spacing, as well as material stiffness. Given the parameters typical for hepatic SWS measurements in Table IV, arrival time estimation noise results in an uncertainty of $\pm 6\%$ in SWS measurements. However, speckle bias and phase aberration are the dominant sources of uncertainty. Speckle bias leads to lateral position errors up to half the beam width, resulting in an uncertainty of $\pm 15\%$ in SWS estimation in the context of Figure 6 in [44]. Phase aberration was shown to cause lateral shifts of 0.12 mm in the beam locations in Figure 3. This level of phase aberration could cause an average of $\pm 16\%$ error on the lateral position of each beam. The abdominal wall models used in this study were derived from healthy subjects. Obese patients with thicker fat layers typically cause higher phase aberration and higher lateral position errors. On the other hand, the effect of phase aberration can be reduced by using harmonic tracking methods [49]. The scanner timing uncertainty caused by hardware fluctuations can be on the order of several nanoseconds. This error is generally negligible compared to the pulse repetition interval, which is usually on the order of hundreds of microseconds.

Each of these four sources of uncertainty can be reduced by averaging over multiple lateral beams, with improvements of up to a factor of $\sqrt{N}$, where N is the number of lateral beam positions in the ROI, assuming that the noise in each of the N lateral beams is constant, independent and uncorrelated to the signal. However, averaging across lateral beams results in a corresponding decrease in the spatial resolution of the SWS estimate by a factor equal to the number of beams averaged. Speckle bias and phase aberration can be further reduced by averaging over an axial range covering several speckle regions, up to a factor of $\sqrt{M}$, where M is the number of speckles axially covered by the ROI. Therefore, in a homogeneous medium, it is preferable to have a large ROI in both lateral and axial dimensions for SWS measurements in order to allow more averaging to reduce the impact of these sources of uncertainty. However, the ROI should only include areas where there is sufficient shear wave signal. Thus, the lateral extent of the ROI is limited by shear wave attenuation and dispersion in biological tissues. The axial extent of the ROI is limited by the size of the region of excitation. Boundary conditions sometimes further limit the size of the possible ROI. Given a homogeneous ROI that has 10 lateral beams and an axial extent of 4 independent speckles as shown in Table IV, the uncertainties can be reduced by a factor of $\sqrt{40}$ ($N = 10$, $M = 4$, $N \times M = 40$). Therefore, the SWS errors caused by the sources of

uncertainty mentioned above from a typical liver fibrosis SWS measurement are expected to be $< 3\%$ [32].

On the other hand, PRF error, beamforming error, and coupling medium sound speed mismatch cause biases in SWS measurements (accuracy errors). For prototype and research scanners, PRF error is more likely to be present at high PRFs, especially when the desired PRF approaches the scanner's limit. Beamforming errors include pitch errors in linear and phased arrays, as well as ROC and sector angle errors in curvilinear arrays. A 5% pitch error would lead to biases in SWS measurements of 5% in linear arrays and 5% in phased arrays. The steering effect and the center element shift effect in phased arrays lead to biases in SWS measurements in opposite directions. For curvilinear arrays, a 5% error of sector angle would lead to 5% errors in SWS measurements, while a 5% error of ROC would lead to $< 5\%$ errors depending on the imaging depth. Coupling medium sound speed mismatch is specific to phantom imaging with curvilinear arrays, as well as imaging through standoffs. Figure 11 shows that the error is $< 1\%$ when $d = 0$ mm, i.e., the phantom is in contact with the transducer for realistic ROC values. The error increases with increasing d , up to 5% at $d = 30$ mm. In clinical imaging, the skin is usually in contact with the entire surface of the transducer, since skin is likely to wrap around the transducer under pressure, and thus this source of bias is not likely to be present in clinical settings.

In our experience, the calibration of transducer parameters in research systems is likely to be less rigorous than in commercial systems. Calibration of these sources of error is an important step in the development of shear wave imaging systems. Spatial errors can be characterized by calibrating the lateral beam positions, which can be accomplished by imaging point targets with known lateral translations. Temporal errors can be characterized by monitoring the timing of the scanner with an oscilloscope. In a well-calibrated system, where the sources of bias are minimized through calibration, the SWS measurement errors result from sources of uncertainty, where speckle bias and phase aberration are likely to be the dominant sources of error.

This work assumed an elastic, isotropic, homogeneous medium, in order to estimate a minimum expected error. Clinical SWS measurements are likely to have higher errors due to complex material properties, including viscosity, anisotropy, and boundary conditions. Viscosity introduces frequency dispersion which leads to changes in shear wave shape as the wave propagates. Shear wave dispersion and attenuation, as well as boundary conditions, limit the lateral and axial extent of the shear wave signal, therefore limiting the size of the ROI for averaging. Anisotropic tissues result in different SWS measured at different angles. Dispersive materials may also cause different SWS measurements between systems, as the shear wave excitation frequency may be variable across transducers and scanners. However, most manufacturers use similar transducer and focal configurations for abdominal imaging, which serves to mitigate the impact of that effect. The scope of this study was limited to the simplest material model in order to quantify errors arising from system dependent sources of uncertainty and bias, with the goal of determining a lower bound on what could ultimately be achievable in a more complex imaging scenario.

There are other factors that could contribute to SWS estimation errors in addition to the system dependent sources discussed so far. The choice of post-processing algorithms could result in discrepancies in SWS measurements across systems. Certain shear wave arrival time estimation algorithms are more sensitive to errors than others. The time of peak displacement algorithm is more sensitive to wave shape changes introduced by reflections at the boundaries compared to the time of peak particle velocity [30]. It is also noted that this study assumed plane shear wave propagation. Data taken within the excitation beamwidth laterally would introduce bias to SWS estimates due to shear wave diffraction effects within this region [31]. In addition, the speckle decorrelation resulting from speckle shearing within the track PSF leads to underestimation of the tracked tissue displacement [36], [50], [51]. Although quantitative shear wave imaging is less susceptible to displacement bias, this speckle correlation effect can result in lower shear wave SNR and higher arrival time estimation noise, particularly in soft materials and/or under strong excitations. Moreover, it has been shown that shear wave measurements at depths away from the elevational focus of the transducer can lead to over-estimation of SWS, which has been attributed to out-of-plane shear wave sources [52]. In summary, we have analyzed the minimum error from system dependent sources in ultrasound shear wave imaging, providing a lower bound of SWS measurement uncertainties in a properly calibrated system.

VI. CONCLUSIONS

This paper discussed the system dependent sources of uncertainty and bias in ultrasonic quantitative shear wave imaging, assuming a linear, elastic, isotropic, homogeneous medium. Arrival time estimation noise, speckle bias, hardware fluctuations, and phase aberration cause uncertainties (variance) in SWS measurements. These errors are decreased through averaging when including multiple lateral locations in a SWS regression. PRF error, beamforming error, and coupling medium sound speed mismatch cause biases in SWS measurements (accuracy errors). In our experience, the calibration of transducer parameters, such as pitch, ROC and sector angle in research systems can be less rigorous than in commercial systems. Calibration of these sources of error is an important step in the development of shear wave imaging systems. In a well-calibrated system, where the sources of bias are minimized, speckle bias and phase aberration are likely to be the dominant sources of error. In the typical liver imaging parameters explored in this study, system dependent sources lead to < 3% errors in SWS measurements.

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Fig. 1.

Experimental data measured on a CIRSTM tissue mimicking phantom. (a) Displacement versus time profiles at the focal depth at several lateral locations resulting from an ARFI excitation at lateral position of 0 mm. d denotes the distances between the track and push location. (b) Shear wave arrival time versus lateral distance from excitation. Arrival time was estimated from the time of peak displacement. The dotted line shows the linear regression fit for the data. SWS is calculated as the inverse of the slope of the line. (c) Time lag between the adjacent displacement pairs. The dotted line shows the average time lag of the 5 displacement pairs, which is 0.82 ms. S refers to the distance between each displacement pair, which is 0.83 mm.

Fig. 2.

Plots computed using Equations 4 and 5 (Equations 15 and 20 of [36]). (a) Standard deviation of the arrival time (σ_{AT}) as a function of shear wave SNR, using different shear wave frequencies and bandwidth. (b) Standard deviation of the shear modulus versus shear wave SNR using a typical shear wave imaging system, for materials of different shear stiffness. Curves are given for a shear wave center frequency $F_{SW} = 400$ Hz, and 100% BW. Common parameters: inter-beam distance $dr = 0.4$ mm, ensemble length $T = 10$ ms, and acoustic density $\rho = 1000$ kg·m⁻³.

Fig. 3.

(a) A graphical representation of the variation in the sound speed for one of the abdominal layers. There is a point scatterer at 23 mm axially and 0 mm laterally. (b) and (c) Images of the point target without (b) and with (c) the abdominal layer shown in (a), with the same dynamic range of 50 dB. (d) Lateral PSFs of the point targets as computed by the peak pressure amplitudes from each beam line between 21 and 25 mm axially in (b) and (c).

Fig. 4.

Receive delays for a 64-element linear array transducer focused at a point that is at 60 mm away from the transducer and centered laterally. The physical pitch of this transducer is 0.3 mm. The dashed line shows the delays computed assuming a pitch that is 20% bigger than the physical pitch.

Fig. 5.

Demonstration of the center element shift effect from a pitch error in linear arrays. A pitch error of 100% is drawn here, which is an exaggeration for demonstration purposes. The solid squares represent the physical elements of a linear array with a pitch of d , and the dashed squares below are perceived elements with a pitch of $2d$. P is the point of interest on the Bmode image. Point P' is the physical location of P , and the distance between P and P' is the lateral position error of the beam.

Fig. 6.

Field II simulations results for a pitch error in L7-4 linear array. Images of point target beamformed with correct (a) and wrong (b) pitches, the wrong pitch is 5% larger than the correct pitch. (c) shows lateral PSFs of the point targets; the horizontal axis shows the physical lateral position of the point targets. The center of the point targets are located at -3 mm and -2.85 mm physically for the solid and dashed line respectively. For linear arrays, a pitch error is linearly related to the corresponding SWS error.

Fig. 7.

Receive delays for a 64-element phased array transducer focused at a point target at 25 mm axially and -3 mm laterally. The dashed line shows the delays computed with a pitch that is 20% bigger than the physical pitch. The arrows illustrate the direction of steering of the correct and wrong delays.

Fig. 8.

Field II simulations results for a pitch error in phased arrays. (a) Lateral PSFs of the point targets imaged with correct and +5% error pitches with values of the asymmetry ratio (AR) of 1, 2 and 4. (b) Lateral position of P' imaged with 5% pitch error, with different element asymmetry ratios. The asymmetry ratio is defined as the number of elements on the right side of the A-line to the number of elements on the left side in the aperture. Note that the position converges to that for a linear array (Figure 6) when $AR = 1$ (i.e., symmetric aperture).

Fig. 9.

(a) Schematic of a curvilinear array. (b) Field II simulations results for ROC and sector angle errors in C5-2 curvilinear array. The ROC and sector angle error resulted in the location of Point P' at -9.8 mm and -9.5 mm respectively. (c) Lateral beam location error as a function of ROC and sector angle error.

Fig. 10.

(a) Sound wave travel path from a point of interest in the phantom to the transducer. The typical sound speed in phantom is 1540 m/s, whereas the sound speed in water is 1485 m/s at room temperature. Per Snell's law, θ_2 is greater than θ_1 because sound speed is higher in the phantom. The distance d is the shortest distance between the transducer surface and the phantom surface. (b) Top: delays for a point target at 60 mm axially and 17 mm laterally in the image, the solid line shows the *DelayScanner* of P, assuming a straight path. The dotted line shows the *Delay Refraction* of P, which incorporates refraction at the water/phantom boundary. The dashed line shows the *Delay Refraction* of P' close to P. The dashed and solid line almost overlap with each other. The line color and style match with the paths shown in (a). Bottom: delay error for each point in the search region. The cross marks the point with least delay error, which was shown as the dashed line in the top panel.

Fig. 11.

Experimentally acquired normalized SWS measured with various d in water (speed of sound: 1485 m/s), and alcohol solution (speed of sound: 1540 m/s), and from least square delay error calculations (Equation 7). The errorbars represent the standard deviation from the 8 repeated measurements at each d for the experimental measurements.

TABLE I

System dependent sources of uncertainty and bias with the methods used to explore each parameter.

Error source	Time/Space	Uncertainty/Bias	Method (Reference)
(1) Arrival time estimation noise	Time	Uncertainty	Literature references ([36])
(2) Speckle bias	Time	Uncertainty	Literature references ([37])
(3) Hardware fluctuations	Time	Uncertainty	Descriptive analysis
(4) Pulse repetition frequency (PRF) error	Time	Bias	Descriptive analysis
(5) Phase aberration	Space	Uncertainty	Full wave simulations
(6) Pitch error in linear and phased arrays	Space	Bias	Field II simulations
(7) Radius of curvature (ROC) and sector angle error in curvilinear arrays	Space	Bias	Field II simulations
(8) Coupling medium sound speed mismatch	Space	Bias	Experimental studies

TABLE II

Field II simulation parameters for a linear array and a curvilinear array

Transducer	L7-4	C5-2
Center frequency	5 MHz	3 MHz
Bandwidth	70%	70%
Sampling frequency	100 MHz	100 MHz
Pitch	0.3 mm	NA
Pitch error	5%	NA
ROC	NA	40 mm
ROC error	NA	5%
Sector angle	NA	75°
Sector angle error	NA	5%
Number of elements	128	128
Focal depth	25 mm	60 mm

TABLE III

Acoustic parameters utilized in the abdominal wal models [39]

Tissue	B/A	α (dB/cm/MHz)	c_0 (m/s)
Fat	9.6	0.40	1479
Muscle	8.0	0.15	1550
Connective	8.0	0.68	1613

TABLE IV

A common set of parameters of medium and imaging sequence for the comparison of different sources of errors

Name	Value
Shear modulus	20 kPa
Shear wave center frequency	200 Hz
Shear wave bandwidth	100%
Shear wave SNR	40 dB
Track beam acoustic center frequency	3 MHz
lateral beam spacing	0.4 mm
Region of interest (ROI)	8 mm $\times$ 2 mm
Frame rate	5 kHz