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Distributing synthetic focusing over multiple push-detect events enhances shear wave elasticity imaging performance

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Abstract

Plane wave imaging is a commonly used method for tracking waves during shear wave elasticity imaging (SWEI), but its unfocused transmission beam reduces tracking accuracy and precision. Coherent compounding minimizes this problem, but SWEI's stringent frame rate requirement and the coarse pitch of most clinical transducers limit its effectiveness. Synthetic aperture imaging (SAI) is an alternate ultrasound imaging approach with a much tighter focus than plane wave imaging, but its lower transmission power has deterred researchers from using SAI in SWEI. Hadamard-encoded multi-element SAI can overcome this limitation. However, only a limited number of sub-apertures (3 to 5) can be transmitted in a single push-detect event. We have developed methods to distribute more sub-apertures or more compounding angles over multiple push-detect events. In this paper, we report the results of experiments conducted on phantoms to assess SWEI's performance when using Hadamard-encoded distributed-multi-element synthetic aperture imaging (HDMSA) or distributed plane wave compounding (DPWC) to track shear waves. Tracking shear waves with HDMSA improved the elastographic signal-to-noise ratio (SNR_e) by 61.6% to 89.5% depending on the phantom employed. Similarly, DPWC tracking improved SNR_e by 56.2% to 93.3% for the same group of phantoms. Compared to focused ultrasound tracking (at the focus), SNR_e improved by 28.6% and 32.5% when tracking shear waves with HDMSA and DPWC, respectively. Long acquisitions could introduce decoding errors that decrease performance when performing HDMSA tracking within the clinical setting. Nevertheless, the results of studies performed on the bicep muscle of three healthy volunteers demonstrate that for stationary organs tracking shear waves with HDMSA yielded repeatable elastograms that offer better elastographic performance than those produced with current tracking methods.

I. INTRODUCTION

Shear wave elasticity imaging (SWEI) is an emerging ultrasound imaging method [1], [2], [3], [4], but the method used to track shear wave propagation can influence diagnostic performance. SWEI uses a four-step process to estimate the mechanical properties within soft tissues [5], [6], [7]. First, acoustic radiation force generates shear waves within the tissue. Second, a suitable ultrasound imaging technique tracks the propagating shear waves.

Third, differences in shear wave arrival times provide local estimates of shear wave speed (SWS). Fourth, knowledge of the local SWS and local tissue density (ρ) provides local estimates of shear modulus (μ). To improve SWEI's diagnostic performance, researchers are actively developing and evaluating different ultrasonic tracking methods [7], [6], [8].

Plane wave (PW) imaging provides high frame rate (>10 kHz) [6], [9], [10] that makes it a good technique for tracking shear waves, however the unfocused transmission beam creates high side-lobe levels [10]. Coherent compounding can reduce the side-lobe levels, but SWEI's stringent frame rate requirement and the coarse pitch of most clinically available transducers limit the effectiveness of compounding [11]. Synthetic aperture imaging (SAI), an alternate ultrasound imaging approach, employs dynamic focusing during transmission and reception that produces a tight focus at each point within the imaging field of view (FOV). We and others [12], [13] have demonstrated that SAI improves quasi-static elastography performance, but its low transmission power [14] has dissuaded researchers from utilizing SAI in SWEI. To increase SAI's transmission power, we have developed a diverging wave technique known as multi-element synthetic aperture (MSA) imaging that transmits with small sub-apertures rather than a single element [15]. Performing MSA imaging with more sub-apertures will enhance resolution and improve tracking performance, but only a limited number (3 to 5) of sub-apertures can be deployed in a single push-detect event [16], [17], a consequence of SWEI's stringent frame requirement.

In this paper, we will demonstrate that distributing Hadamard-encoded [14] sub-apertures over multiple pushdetect events overcomes the frame rate induced limitation; we will also show that distributing plane wave compounding over numerous push-detect events allows more compounding which also improves tracking.

To assess how different imaging parameters impact SWEI's performance when tracking shear waves with either Hadamard-encoded distributed MSA (HMDSA) or distributed compounded plane wave (DPWC) imaging, we performed studies on elastically homogeneous and inhomogeneous phantoms. We also performed studies to determine how the point spread function (PSF) of each approach behaved with different parameters, and with three healthy volunteers (on the bicep muscle) to gain insights regarding the clinical feasibility of using either approach to track shear waves.

II. METHODS

Hadamard-encoded distributed multi-element synthetic aperture (HDMSA) imaging

We developed a novel multi-element synthetic aperture approach that uses diverging waves to track propagating shear waves. This technique uses small sub-apertures to transmit diverging waves originating from virtual sources (focal points behind the transducer). Four virtual sources can produce diverging waves in a single push-detect event, the maximum number of virtual sources that can provide frame rates (>3 kHz) high enough for shear wave tracking. To use more virtual sources, we utilized multiple push-detect events (1, 2, 4, and 8) at the same location with different sets of four virtual sources for each push-detect event (Fig. 1(a)). Applying either phase encoding [14] or coded excitation techniques [18] will further boost transmission power. In this work, we used Hadamard matrices to encode the

phases of multiple virtual sources that we broadcast simultaneously. Hadamard matrices are square matrices with mutually orthogonal rows and columns composed of binary elements (+1 and -1). The number of rows and columns of a Hadamard matrix is 2^k , where k is a non-zero integer. We can define a Hadamard matrix H_{2^k} of order 2^k as follows:

$$H_{2^k} = \begin{bmatrix} H_{2^{k-1}} & H_{2^{k-1}} \\ H_{2^{k-1}} & -H_{2^{k-1}} \end{bmatrix}. \quad (1)$$

The base case H_2 is defined as follows:

$$H_2 = \begin{bmatrix} 1 & 1 \\ 1 & -1 \end{bmatrix}. \quad (2)$$

The mutually orthogonal rows and columns of a Hadamard matrix allow us to encode and decode multiple signals. To perform Hadamard encoding in DMSA, we select 2^k virtual sources with non-overlapping sub-apertures. Instead of transmitting ultrasound from these 2^k virtual sources sequentially, we activate all 2^k virtual sources simultaneously 2^k times, each time encoding the phases of the virtual sources with one of the 2^k rows of the Hadamard matrix.

To decode the response of the i^{th} virtual source, where i is an integer between 1 to 2^k , we multiply each of the acquisitions with the i^{th} row of the Hadamard matrix. Summing 2^k acquisitions multiplied with the respective weight provides the decoded response amplified by a factor of 2^k . The frame rate of Hadamard encoded MSA, and regular MSA is similar because both approaches employ an identical number of transmissions. Figure 2 illustrates the Hadamard encoding and decoding process. For a single push-detect event, we used a H_4 Hadamard matrix to encode four virtual sources. However, we used a higher order matrix in case of multiple push-detect events. For example, to perform SWEI with 2 push-detect events, each push-detect event uses four unique virtual sources (Fig. 1(b)). We encode the 8 virtual sources (4 sources per push-detect event) with an H_8 matrix. After decoding, we coherently added acquired frames to form a single frame.

Hadamard matrices only support discrete numbers of transmissions (2, 4, 8, 16, 32, . . .). Therefore, we evaluated configurations consisting of 4, 8, 16, and 32 sub-apertures. To maximize the sonographic signal-to-noise ratio (SNR_s), we chose sub-apertures that activate most of the transducer's elements (in our case 120 to 128) simultaneously. Table I provides the transmit parameters which the array configurations employed in this study. The decoding process is less error-prone for configurations with fewer sub-apertures than arrangements with more sub-apertures. Nevertheless, configurations with more sub-apertures (16–32) produce better sonograms (higher sonographic SNR_s and better resolution) than arrangements with fewer sub-apertures (4–8). To minimize the impact of physiological motion on the decoding process for configurations employing more than eight sub-apertures, we divide the set of sub-apertures into groups and encode each group separately. To

illustrate, let us consider a configuration with 16 sub-apertures. To minimize the impact of physiological motion, we first select a group of eight non-overlapping sub-apertures (each containing 15 elements) encoded with an H_8 matrix and distribute the eight encoded transmissions over two push-detect events. This would allow us to excite 120 elements simultaneously. To produce 16 unique sub-apertures, we repeat the process by selecting another group in which we shift the sub-apertures' center laterally by 8 elements (see Fig. 1(c)). Similarly, for a configuration consisting of 32 sub-apertures, we divide the sub-apertures into four groups of eight non-overlapping sub-apertures (each containing 15 elements) that are also encoded with an H_8 matrix and distributed over two push-detect events. Shifting the center of each sub-aperture by two elements would yield 32 unique sub-apertures.

Plane wave based SWEI with distributed compounding

To test the hypothesis that increased compounding improves SWEI performance, we distributed several plane waves (4, 8, 16, and 32) over multiple push-detect events (Fig. 3). We made four unique transmissions for each push-detect event (Fig. 3(a)), dictated by the ultrasonic pulse-repetition-frequency (12 kHz) and the desired frame rate (3 kHz). During the post-processing stage, we compounded sets of four images from all push-detect events (1,2,3 or 4) corresponding to the same phase of the shear wave (Fig. 3(b)). We did not perform DPWC with very large angular increments ($> 15.5^\circ$) because doing so would produce transmission delays within the imaging FOV ($> 5\text{mm}$).

Focused ultrasound tracking based SWEI

To determine if tracking shear waves with either HDMSA or DPWC produces better elastograms than focused ultrasound (FUS) tracking, we also implemented SWEI with FUS [7]. Like HDMSA and DPWC, we transmitted repeated push beams at the same location. After each push beam, we used focused ultrasound beams to track the propagating shear waves. To sweep the FOV, we translated the tracking beam after each push beam by a distance equivalent to the pitch of the ultrasound transducer.

Elastographic data acquisition and processing

Data acquisition: We implemented three shear wave tracking methods (HDMSA, DPWC, and FUS) on a research scanner (Vantage 256, Verasonics Inc., Kirkland, WA, USA) with an L11-5v transducer (Verasonics Inc., Kirkland, WA, USA). To generate shear waves, we used 200 micro-second push beams (5 MHz) with transmission focal (F-number = 2.0) zone centered 20 mm from the tissue or phantom surface. To reduce jitter and bias, we used a higher frequency (10 MHz) beam to track shear waves [8]. In all cases, push beams were delivered at 10.3 mm to left of the center of the imaging plane.

- *Multiple push-detect acquisitions (HDMSA and DPWC):* We transmitted push beams at a rate of 1 push per second, unless otherwise specified. In all cases, we placed the push beam 10.3 mm to the left of the center of the transducer.
- *Tracking shear waves with FUS:* We configured the scanner to track shear waves with a PRF of 12 kHz using a focused tracking beam with transmission focal zone centered 20 mm below the surface of the tissue or phantom. A narrow

tracking transmit focus (F-number = 1.0) compared to push excitation was used to reduce the effect of lateral speckle shearing [8]. To cover a lateral distance of 12 mm, we configured the scanner to transmit 40 tracking beams at 40 different lateral locations.

For all acquisitions, we stored the channel data to disk for off-line processing in MATLAB (version 2017b, MathWorks Inc, Natick, MA, USA) programming environment.

Beamforming: Before applying the delay-and-sum (DAS) beamforming method, we decoded the HDMSA data set using the same Hadamard matrix used to encode the data. To accelerate the beamforming process, we implemented the delay-and-sum method on a graphics processing unit (GPU) [19]. We applied no apodization during transmission or reception. Dynamic received beamforming was performed on a uniform grid (grid spacing of 0.5λ). We have demonstrated in a previous study that this grid density produced reliable SWS estimates [20]. Smaller axial sampling intervals will improve the precision of the axial motion, but the lateral grid spacing will impact the estimated motion negligibly because the displacements incurred during SWEI are mainly axial. For all methods (HDMSA, HDPWC, and FUS) the dynamic receive F-number was set to 1.5 [8]. For both HDMSA and DPWC, we beamformed low resolution images corresponding to each transmission. During HDMSA, each virtual source insonified a conical area with an opening angle (θ) given by

$$\theta = 2\tan^{-1} \frac{D_s}{2L_z}, \quad (3)$$

where D_s is the length of the sub-aperture and L_z is the axial distance of the virtual source from the transducer. We applied a horizontally Hanning-windowed conical mask, centered around the corresponding low resolution virtual source HDMSA images [21] before combining them to form high resolution radio-frequency (RF) echo frames. For data acquired with FUS imaging, we synthesized a single A-line along the center axis of the focused beam. Combining four successive tracking pulses produced PRF and averaging that was comparable to that achieved with the other imaging approaches.

SWEI processing: To compute the particle velocity wavefield, we applied the 2D auto-correlation method [22] to the IQ data. We used a 3D (axial, lateral, and time) directional filter [23] to remove reflection artifacts from the measured wavefield; applied a 2nd order Butterworth bandpass filter (band limited between 50 Hz and 1 kHz) to the slow time data at each pixel [24] and used a GPU accelerated cross-correlation based tracking method (with a 3 mm kernel) to compute the time-of-flight (TOF) from the filtered data [25]. We computed local estimates of SWS from the ratio of kernel length and TOF time-delay.

Sonographic SNR evaluation: To evaluate the sonographic signal-to-noise-ratio (SNR_s), we executed SWEI sequences without active push beams [26]. For these acquisitions, we analyzed the beamformed and compounded RF echo data.

Performance metrics

We used the elastographic signal-to-noise ratio (SNR_e) performance metric to evaluate SWS elastograms, defined as follows [27]:

$$SNR_e = \frac{\mu}{\sigma}, \quad (4)$$

where μ represents the mean SWS in an elastically homogeneous region of the tissue, and σ represents the variance of SWS values within the region. We computed SNR_e from the central 1 cm of the imaging plane. The left edge of the ROI was 5.3 mm from the push beam center. We chose a larger ROI offset than previously reported (1.5mm in [28], <3mm in [29], ~1.3 mm in [27]) to reduce the impact of near field artifacts in the resulting computations.

We used the elastographic contrast-to-noise ratio (CNR_e) performance metric to assess lesion detectability, defined as follows [30]:

$$CNR_e = \frac{|\mu_L - \mu_B|}{\sqrt{\sigma_L^2 + \sigma_B^2}}, \quad (5)$$

where μ_L and μ_B represent the mean SWS in the lesion and background material respectively; and σ_L and σ_B represent the variance of SWS in the lesion and background material respectively.

We also assessed sonographic signal-to-noise (SNR_s) from sonographic data (beamformed and compounded) acquired from a fixed FOV over time defined as follows [14].

$$SNR_s = \frac{\langle b(t) \rangle}{\sigma_{b(t)}}, \quad (6)$$

where $\langle b(t) \rangle$ represents the mean (temporal) intensity, and $\sigma_{b(t)}$ represents the variance of (temporal) intensity.

III. PHANTOM STUDY

The goal of these studies was three-fold. First, to characterize the point spread function of different tracking methods (HDMSA and DPWC) under varied conditions. Second, to assess how HDMSA and DPWC imaging parameters (number of transmissions, angular increments, and depths of virtual sources) affect SNR_s . Third, to evaluate the performance (SNR_e , CNR_e) of HDMSA and DPWC elastograms relative to those produced with FUS.

Phantoms

1. *Homogeneous*: We used four commercially available elastic phantoms (homogeneous with attenuation coefficient of 0.5 dB/cm/MHz; CIRS Inc.,

Norfolk, VA, USA) of varying stiffness to evaluate HDMSA, DPWC, and FUS elastograms.

2. *Heterogeneous phantoms:* We used the highly controlled and repeatable fabrication described in [31] to manufacture two heterogeneous phantoms from a suspension consisting of gelatin (300 bloom, Type A, Sigma-Aldrich Corporation, St. Louis, MO, USA), corn starch (Argo Cornstarch, ACH Food Companies Inc., IL, USA), and degassed distilled water (18 M Ω). Table II provides the composition of the materials used in each phantom. One heterogeneous phantom contained a high contrast spherical inclusion (5.6 mm diameter) manufactured from 15% by weight gelatin, which we embedded in homogeneous background gel. The other heterogeneous phantom contained a lower contrast spherical inclusion (5.2 mm diameter) that we manufactured from 12.5% by weight gelatin and embedded in a background gel. In both phantoms, we manufactured the surrounding background gel from 10% by weight gelatin.

Quantifying the levels of grating lobes incurred during HDMSA and DPWC imaging

Grating lobes are image artifacts that appear when the transducers pitch is larger than half wavelength [11]. The elements of such a transducer generate wavefronts that interfere constructively along undesired directions to produce grating lobes and corrupt images. To evaluate the impact of grating lobes, we measured the PSFs incurred during HDMSA and DPWC imaging. We measured the PSF by suspending a wire target (6–0 surgical suture, Surgipro 2, Medtronic Plc, MN) in degassed water at the center of the imaging FOV. In these studies, we performed HDMSA imaging with virtual source distances (VS_z) of -5 mm, -7.5 mm, -10 mm, -12.5 mm, -15 mm, and -20 mm. DPWC imaging was conducted with angular increments (α) of 0° , 0.06° , 0.13° , 0.25° , 0.5° and 1° . The PSF was also characterized as a function of number of transmissions (4, 8, 16, and 32) using the parameters that yielded the optimum SWEI performance (HDMSA ($VS_z = -15$ mm) and DPWC ($\alpha = 0.25^\circ$)). To quantify the grating lobe level, we computed the magnitude of the logarithmically compressed sonograms outside the central 1 cm of the image.

Assessing how imaging parameters impact the quality of HDMSA and DPWC sonograms

We used the 50.4 kPa phantom to study how SNR_s varied with different imaging parameters (number of transmissions, angular increments, virtual source depths). We computed SNR_s in the central 1 cm of the imaging FOV between 10 mm and 20 mm depth. We choose this region to match SWEI's FOV. During HDMSA imaging, we evaluated SNR_s as a function of virtual source depth (-5 mm, -7.5 mm, -10 mm, -12.5 mm, -15 mm, -17.5 mm, and -20 mm). For DPWC imaging, we computed SNR_s as a function of angular increments (0° , 0.06° , 0.13° , 0.25° , 0.50° , 1° , 2° , and 3°) and transmission frequency (6 MHz to 10 MHz, in increments of 1 MHz). Sonograms were acquired with increasing transmissions (4, 8, 16, and 32) during HDMSA and DPWC imaging. We also assessed the SNR_s of images acquired at individual transmission angles during DPWC.

Evaluating the performance of elastograms created with different ultrasound tracking methods.

- *Image quality:* We used four homogeneous phantoms to evaluate the quality of SWS produced with HDMSA, PW, and DPWC imaging. In all cases, we performed imaging with 4, 8, 16, and 32 transmissions. HDMSA imaging was conducted with virtual source depths of -5 mm, -15 mm, and -20 mm. Compounding was performed with angular increments of 0° , 0.25° , and 1° . We obtained five independent acquisitions for each configuration. To observe the performance of HDMSA and DPWC over a wider parameter range, the 50.4 kPa phantom was imaged with a wider range of angular increments (0° , 0.06° , 0.13° , 0.25° , 0.50° , 1° , 2° , and 3°) and virtual source depths (-5 mm, -7.5 mm, -10 mm, -12.5 mm, -15 mm, -17.5 mm, and -20 mm).
- *Depth dependent SNR_e :* To assess how SNR_e varied with depth, we conducted studies to compare the quality of HDMSA and DPWC elastograms obtained with 32 transmissions to those acquired with focused ultrasound (FUS) imaging. Two-dimensional kernels (1.2 mm (height) by 1 cm (width)) that overlapped by 50% provided estimates SNR_e as a function of depth. We used the depth-of-field (DOF) of the focused imaging as the height of the kernel: $8(F\text{-number})^2\lambda$, where F-number is the focal configuration and λ is the wavelength [32].
- *Frame rates:* We computed the frame rates incurred when performing SWEI with HDMSA, DPWC, and FUS. SWEI frame rate depends on push repetition frequency which may vary from system to system; therefore, to simplify the evaluation, we used a relative scale to evaluate SWEI frame rate, which assumes a push repetition frequency of 1 Hz. Since tissue shear attenuation limits the ROI of SWEI, we evaluated frame rate with ROI widths of 1 cm and 2 cm.

Determining how well HDMSA and DPWC SWEI can detect localized increase in shear modulus

We used two heterogeneous phantoms to evaluate lesion detectability (CNR_e) of SWS elastograms acquired with HDMSA and DPWC imaging. We performed HDMSA imaging with virtual source depths of -5 mm, -15 mm, and -20 mm; DPWC imaging with angular increments of 0° , 0.25° , and 1° . To observe the performance of HDMSA and DPWC over a wider parameter range, the phantom with high contrast inclusion was imaged with a wider range of angular increments (0° , 0.06° , 0.13° , 0.25° , 0.50° , 1° , 2° , and 3°) and virtual source depths (-5 mm, -7.5 mm, -10 mm, -12.5 mm, -15 mm, -17.5 mm, and -20 mm). For both groups of elastograms (DPWC and HDMSA), we made five independent acquisitions with four different transmissions (4, 8, 16, and 32).

IV. *In vivo* STUDY

The goal of the *in vivo* study was to assess the quality of HDMSA and DPWC elastograms produced with 32 transmissions. One concern was that more transmissions could introduce decoding errors when performing HDMSA imaging in real tissues. As an initial test of performance we imaged bicep brachii muscle (right arm) of three healthy volunteers (male)

with age ranging from 23 to 30 y. Several researchers have used this organ to characterize SWEI's *in vivo* performance [33], [34], [35], [36].

Image Quality assessment:

We placed the right arm of each volunteer on a table with the elbow angled at 120°. The muscle fibers were aligned laterally to the imaging plane during HDMSA and DPWC imaging. We used identical transmission parameters as those used in the phantom studies, except the push beam repetition frequency was increased from 1 to 16 pushes per second. We used free-hand scanning to acquire SWE images from the subjects. We acquired three data sets from each subjects: HDMSA with 32 transmissions ($VS_z = -15\text{mm}$), DPWC with 4 transmissions ($\alpha = 0.25^\circ$), and DPWC with 32 transmissions ($\alpha = 0.25^\circ$). The DPWC with 4 transmission was the gold-standard against which the performance of HDMSA and DPWC elastograms were compared.

Reproducibility assessment:

We assessed the reproducibility of HDMSA (32 transmission) elastograms acquired *in vivo* by performing five repeated acquisitions from subject 3, each time removing and repositing the transducer. The goal of this repeatability study was to assess the variability of SWS estimates induced by motion due to free-hand scanning and physiological sources.

V. RESULTS

The imaging parameters influence the amount of grating lobes incurred during HDMSA or DPWC imaging.

Figure 4 shows PSFs incurred when performing HDMSA and DPWC imaging with different imaging parameters. More transmissions reduced the grating lobes incurred during HDMSA (Fig 4(a–d)) and DPWC (Fig 4(e–h)) imaging; however, HDMSA images generally had more grating lobes especially for lower transmissions. Grating lobes were less visible in HDMSA images obtained with deeper virtual sources than those acquired with shallower ones; however, we observed no visible reduction in grating lobes for virtual sources with depths greater than -10 mm (Fig. 4(j–o)). Increasing the angular increments from 0° to 0.25° reduced the grating lobes incurred during DPWC (Fig 4(p–s)); however, grating lobes increased noticeably when we performed DPWC imaging with larger angular increments ($> 0.25^\circ$) Fig 4(t–u). Fig 4 (v–x) shows the magnitude of grating lobes plotted as a function of transmissions (Fig. 4v), virtual source depth (Fig. 4w), and angular increment (Fig. 4x). Imaging with fewer transmissions (4–16) induced more grating lobes in HDMSA images than DPWC, which is consistent with our visual observations (Fig 4 (a–h)). The grating lobes incurred during HDMSA and DPWC were comparable when imaging with 32 transmissions (Fig. 4(v)). Grating lobe amplitude decreased by 5.6 dB when we increased the depth of the virtual sources from -5 mm to -10 mm during HDMSA imaging, but remained constant with further increase in depth (Fig. 4(w)). Performing DPWC with angular increments up to 0.25° produced lower grating lobe amplitude (10.6 dB) compared to PW (no compounding) (Fig. 4(x)). However, performing DPWC with larger angular increment (1°) produced higher grating lobe amplitude than standard plane wave imaging.

The number of transmission, angular increment, virtual source depth, and transmission frequency influence the signal-to-noise ratio of sonograms acquired during DPWC and HDMSA.

Increasing the virtual source depth generally improved the SNR_s of HDMSA sonograms before it plateaued (Fig. 5(a)). At 16 and 32 transmissions, increasing the virtual source depth from -5 mm to -15 mm during HDMSA imaging improved SNR_s by 3.1 dB and 4.5 dB, respectively. Fig. 5(b) shows a plot of SNR_s as a function of angular increments at different transmissions for DPWC imaging. Conducting DPWC imaging with more transmissions with angular increments ranging from 0° to 0.25° increased SNR_s , but for all transmissions SNR_s rapidly decreased when employing larger angular increments (Fig 5b). SNR_s degraded more severely with increasing angular increments at larger transmissions. For example, with four transmissions, SNR_s dropped by 2.3 dB when performing DPWC imaging with angular increment of 3° rather than 0° ; whereas, with 32 transmissions, SNR_s dropped by 12.8 dB when conducting DPWC imaging with angular increment of 1° rather than 0° . Fig. 5c shows SNR_s of DPWC sonograms plotted as a function of transmissions at different angular increments. We acquired the data presented in this figure with a smaller transmission increment than that presented in Fig. 5b. Additionally, we restricted the maximum angular increment to 1° . For all angular increments, except 1° , SNR_s increased rapidly with more transmissions, then plateaued after a certain number of transmission. For example, performance plateaued after 16 and 11 transmissions when conducting DPWC with angular increments of 0.25° and 0.5° , respectively. The peak performance achieved using DPWC with the largest angular increment (1°) occurred when we performed imaging with six transmissions, but SNR_s dropped precipitously with more transmissions. The transducer's angular sensitivity could lower the SNR_s of sonograms acquired at large angular increments [11]. To investigate this, we plotted SNR_s of plane wave images obtained at different beam steered angles (Fig. 5d). Varying the transmission angle within $\pm 15.5^\circ$ influenced SNR_s negligibly. This SNR_s degradation as a function of number of transmissions only occurred with larger angular increments (Fig. 5(e-f)) and with transmission center frequencies that are close to the edges of the transducer bandwidth (Fig. 5f).

More transmissions improve HDMSA and DPWC elastograms.

Fig. 6 shows representative examples of HDMSA, DPWC, and PW elastograms obtained from a homogeneous phantom. The visual appearance of HDMSA elastograms improved with more transmissions (Fig. 6(a-l)), but deeper virtual sources (-10 mm and -20 mm) produced visually smoother images than the shallower ones (-5 mm). DPWC elastograms also improved with more transmissions especially when employing small angular increments ($\alpha=0.25$). The quality of DPWC elastograms deteriorated with more transmissions for larger angular increments (i.e., $\alpha=1^\circ$) (Fig 6(m-x)). Frame averaging visually improved the quality (less noise and less degradation as you move from the center to edges) of PW elastograms produced without angular compounding (Fig 6(m-p)). The gain of SNR_e achieved when performing SWEI with HDMSA rather than DPWC with conventional settings (4 transmits) ranged from 61.6 to 89.5%, depending on the shear modulus of the phantom (Fig 7(c-f)). Similarly, the gain in SNR_e when performing SWEI with DPWC using 32 transmissions rather than 4 transmissions varied from 56.2 to 93.3%, depending on

the shear modulus of the phantom used to evaluate image quality (Fig 7(c–f)). At higher transmissions (32), the SNR_e of HDMSA and DPWC elastograms were comparable (SNR_e ranging from 20 to 30.8 and 21 to 30.3 for DPWC and HDMSA, respectively). For HDMSA imaging, SNR_e increased with the deeper virtual sources (Fig 7a), however, SNR_e plateaued for virtual sources deeper than -15 mm. SNR_e performance of DPWC was highly sensitive to angular increment (Fig 7b). SNR_e degraded at larger angular increments and the degradation occurred more rapidly with larger number of transmissions. For example, with 32 transmissions, SNR_e of DPWC decreased precipitously when angular increment was higher than 0.25° .

HDMSA and DPWC tracking improved lesion detectability, but the parameters used during tracking determined the performance gain over the current gold standard.

Figure 8 shows representative examples of HDMSA and DPWC elastograms acquired from the low contrast heterogeneous elasticity phantoms. Performing SWEI with more transmissions improved the elastograms. We observed a similar trend in elastograms obtained from the high contrast elasticity phantom (not shown). When conducting HDMSA tracking with high transmissions (32) CNR_e grew rapidly with increasing virtual source depth (-5 mm to -15 mm), then plateaued. Performing HDMSA imaging with lower transmissions caused CNR_e to behave erratically when the virtual source depth was varied (Fig 9a). Figure 9(c,d) reveals that for both phantoms CNR_e acquired with deeper virtual sources were generally higher than those acquired with shallower ones especially at higher transmissions (16 and 32). CNR_e was 66.9% and 66.6% higher than that achieved when we performed DPWC with four transmissions for high and low contrast inclusions, respectively, when carrying out HDMSA tracking with 32 transmissions and a -15 mm deep virtual source (Fig. 9(c)–(d)). DPWC elastograms acquired with small angular increments (0° and 0.25°) had fewer artifacts than those obtained with larger angular increments (i.e., 1°) (Fig 8(m–x)). CNR_e was highest when employing an angular increment of 0.25° , but larger angular increments reduced CNR_e (Fig. 9b). The CNR_e of DPWC (32 transmissions, $\alpha=0.25^\circ$) elastograms was 76.3% and 94.4% higher than that achieved when we performed DPWC with four transmissions for high and low contrast inclusions, respectively (Fig. 9(c,d)).

Using synthetic aperture ultrasound imaging techniques (DPWC and HDMSA) to track shear wave propagation produces better (less noise, and higher depth dependent SNR_e) elastograms than those created when we used FUS for tracking.

Figure 10 (a–c) shows representative examples of DPWC (32 transmit, $\alpha=0.25^\circ$), HDMSA (32 transmits, $\text{VS}_z=-15\text{mm}$), and FUS (transmission focus of 20 mm) elastograms obtained from a homogeneous phantom (50.4 kPa). Tracking with HDMSA or DPWC produced more consistent elastograms than those obtained when we used FUS to track shear waves—FUS elastograms had good image quality only within transmit focal zone. Figure 10(d) shows SNR_e plotted as function of scan depth for the three imaging approaches (DPWC, HDMSA, and FUS). DPWC and HDMSA elastograms had higher SNR_e than FUS elastograms for all depths. Figure 10e summarizes the SWEI frame rate of three ultrasound imaging methods (DPWC, HDMSA, and FUS) to track shear waves within 1 cm (Fig. 10e) and 2 cm (Fig. 10f) wide ROIs.

Performing DPWC or HDMSA SWEI with 32 transmissions produced useful *in vivo* elastograms.

Fig. 11 shows representative examples of sonograms and SWS maps obtained with DPWC and HDMSA from the right biceps of three healthy volunteers. Shear wave attenuation corrupted the right side of the SWS maps; however, using more transmissions during SWEI minimized this problem. DPWC elastograms acquired from subject 2 had more erroneous SWS estimates (right-side) than those obtained from the other subjects (Fig. 11(g)). This degradation in image quality occurred because for this subject, low echo intensity (low SNR_s) in this region (Fig. 11(e)) produced higher tracking error. However, performing DPWC with more transmissions (32 instead of 4) minimized this problem (Fig. 11h). HDMSA displayed a similar behavior, more transmissions produced more reliable SWS estimates (Fig. 11f). Fig. 11(m–p) shows the similarity of statistically independent HDMSA elastograms acquired with 32 transmissions from subject 3. The mean SWS values for the three subjects ranged within 2.3 to 2.73 m/s when SWEI (DPWC and HDMSA) with 32 transmissions (Fig. 11(q)) was performed, which is consistent with previously reported results for relaxed bicep [33], [37].

VI. DISCUSSION

To evaluate the effectiveness of HDMSA and DPWC tracking, we performed studies on phantoms and healthy volunteers. These studies revealed important observations. The parameters employed during HDMSA or DPWC tracking dictate the magnitude of grating lobes incurred during imaging (Fig. 4). Tracking shear waves with either HDMSA or DPWC produces elastograms with higher SNR_e compared to those created with FUS tracking (Fig. 10). Performing tracking with more transmissions increases SNR_e and CNR_e dramatically (Figs. 7 & 9). Increasing virtual source depths from -5 mm to -15 mm improves the HDMSA elastogram performance (SNR_e and CNR_e), but performance plateaus for deeper virtual source (Figs. 7 & 9). Similarly, DPWC elastogram performance (SNR_e and CNR_e) improved with increasing angular increment up to 0.25° then decreased rapidly (Figs. 7 & 9). HDMSA and DPWC produced highly repeatable and useful elastograms *in vivo* (Fig. 11).

Increasing SNR_s reduces tracking error but this doesn't improve the transmission focus, which has a profound impact on SWS maps. Researchers have previously demonstrated that harmonic imaging [38], [39] and coded excitations [40] improves SNR_s and SWEI tracking. Tiran *et al.* used multiple phase-encoded plane waves in quick successions to enhance the SNR_s [16]. Although evidence that multi-acquisition averaging improves SNR_s is overwhelming, this does not improve the transmit focus, which also impacts tracking performance. The HDMSA and DPWC tracking methods were designed to exploit the benefits of averaging and using synthetic focusing techniques to improve the transmission focus. Figures 7 and 9 demonstrate that HDMSA and DPWC elastograms have higher SNR_e (Fig 7) and CNR_e (Fig 9) than those produced with either standard PWC-SWEI (four compounding angles) or PW-SWEI with multi-frame averaging.

Improving the tracking performance of HDMSA and DPWC tracking represents a tradeoff in tightening the PSF and eliminating grating lobes. Montaldo *et al.* demonstrated that in

mediums with high echogenic contrasts, unwanted PSF components corrupt the estimated wave motion [10]. They also demonstrated that side-lobes from a hyperechoic area induced artificial motion in anechoic regions, and suppressing the sidelobe levels minimized this phenomena. Figures 4 and 7 demonstrated that this occurs for an homogeneous scattering medium, PSF impacts tracking performance. Figure 7 demonstrate that performing DPWC imaging with large angular increments (2° or 4°) as recommended [9], [16] degrades elastographic performance. Compounding with large angular increments does indeed reduce the PSF's main lobe width, but doing so also increases grating lobes, which is consistent with the results reported in [41]. HDMSA tracking performance also displayed a similar behavior. Placing the virtual source at shallower depths can reduce the PSF's main lobe width and increases the grating lobe. For a given aperture size, placing the virtual source closer to the transducer produces a diverging beam with a larger opening angle and more grating lobes (Fig 4(w)) than those created by deeper ones. Ponnle *et al.* also observed an increase in grating lobes when performing diverging wave ultrasound imaging with large opening angles [42], [43]. Increasing the distance between the virtual source and the transducer reduces the grating lobe; however, doing this broadens the main-lobe (Fig 4y). Deeper virtual sources produce broader main lobes because the resulting wavefront is a plane wave which is known to have a wide mainlobe [44]. However, grating lobe level had more dramatic impact on the elastographic performance than the main lobe width. Elastographic performance improved when we placed the virtual source at depths ranging from -5 mm to -10 mm. Elastograms produced with deeper virtual sources (-10 mm to -20 mm) are similar because the grating lobe levels are virtually similar in those cases. We predict that placing virtual sources at deeper depths will cause performance to fall precipitously when the transmit beam approximates a plane wave.

High grating lobe levels correlated with reductions in SNR_s which degraded tracking performance [26], [44]. Researchers have demonstrated that the angular directivity of transducer elements in large plane wave transmission angles can reduce SNR_s of individual and compounded sonograms [11]. However, Fig 5(d) demonstrates that for our study this was not the case. A better reason why SNR_s decreased when conducting PWC with large angular increments ($> 0.25^\circ$) is that grating lobe components produced sums incoherently with the main lobe that reduces echo amplitude and lower SNR_s . We plan to perform further studies to confirm this expectation. Figure 9(e,f) demonstrates that SNR_s decrease typically occurs when the transducer's operation frequency is close to its bandwidth edge because in these spectral regions, the transducer's bandwidth truncates the bandwidth of the transmitted pulses, consistent with the behavior of grating lobes [45]. This observation is important because in order to reduce phase jitter and bias during SWEI, researchers recommend performing shear wave tracking at higher frequencies than the push (near the upper edge of the bandwidth) [8]).

Performing SWEI with repeated transmission reduces the frame rate of SWEI, but the frame rate achieved during HDMSA and DPWC is comparable to that obtained with clinical SWEI systems. Song *et al.* used a multi-transmission scheme to measure SWS over a wide FOV [46], an approach that is routinely used in the clinic. They used seven repeated push beams to reconstruct the SWS map, which is similar to our 32 transmission based methods (eight push). However, they did not implement coherent compounding and thus the resulting SWS

quality is likely much lower than that achieved when performing SWEI with either HDMSA or DPWC. Using focused ultrasound to track shear wave will also lower SWEI frame rate [7]. Figure 10(e)–(f) demonstrates that the frame rate achieved with HDMSA and DPWC is up to eight times faster than that obtained with FUS imaging. Parallel beamforming (4 parallel lines) will improve FUS's frame rate [47]. However, misalignment between transmit and receive beams will degrade image quality [48], which restricts the amount of parallelization (i.e., lines) that one can perform during FUS imaging. Besides lower frame rates, tracking shear waves with FUS produced reliable SWS estimates only within the vicinity of the focal zone (Fig 10(d)), which is not the case when performing HDMSA or DPWC tracking: both approaches produce reliable SWS estimates over more considerable depths than FUS. This observation is consistent with previously reported results [10], which demonstrates that plane wave compounding has higher SNR_s than focus ultrasound imaging at all depths including the focal zone.

In this work, we have demonstrated that the tracking SNR can be substantially enhanced by increasing the number of push-detect events which may be consequential in viscoelastic characterization. In real tissue, attenuation of shear waves due to viscoelastic effects degrades the SNR of tracked shear wave. This situation is further exacerbated in viscoelastic estimators where researchers often attempt to estimate phase speed of individual shear wave spectral components [49]. Since the energy of a frequency component is much lower than that of the broadband signal, large variances are reported in the literature while estimating viscous attenuation (>50 Np/m in [50]). A common technique to tackle this issue is to use a larger shear wave propagation ROI [49], [51]. However, at larger distances, shear wave severely attenuates and thus there is a limit on estimation variance that can be achieved [51], [49]. Also, higher frequencies of shear waves are more severely attenuated, which limits the bandwidth of shear wave available for viscoelastic characterization [49]. It is evident from the phantom (Fig. 6 & 8) and *in-vivo* (Fig. 11) experiments that the proposed method can increase the lateral range of shear wave tracking which may be used to improve the estimation variance of viscoelastic estimators. We also speculate that, by increasing echo SNR, the proposed distributed focusing based methods will allow better tracking of low amplitude shear waves at high frequencies, thereby increasing the frequency bandwidth of viscoelastic characterization. We plan to conduct a future study to investigate these issues.

In this work, we used SNR_e as the performance metric to evaluate the quality of elastograms obtained from homogeneous phantoms. The visual appearance of elastograms produced by averaging 0° PW elastograms were comparable to those produced with either HDMSA or DPWC (see Fig. 6p&t); however, differences in SWS variance caused SNR_e to vary noticeably (Fig 7).

A limitation of tracking shear waves with HDMSA is that tissue motion can degrade performance. Figure 11 demonstrated the feasibility of using HDMSA to perform SWEI in the bicep; however, the technique could prove difficult to image organs such as heart where tissue motion is more significant. Tissue motion is more of a problem in HDMSA imaging than DPWC because tissue motion could produce inaccurate phase cancellation during HDMSA decoding. To minimize this problem, we plan to use coded excitation techniques and a motion correction scheme [44], [52] when tracking shear waves with our MSA

approaches. We also plan to perform further *in vivo* studies to investigate the performance of HDMSA and DPWC based SWEI relative to simple PWC based SWEI (0° PW averaging). Another potential limitation is that we assume that shear waves generated with multiple excitations are identical, which is reasonable for stationary tissue. However, this will not necessarily be the case for moving organs, and thus it could prove more difficult to track shear waves. Tissue harmonics will also produce inaccurate phase cancellation during Hadamard decoding; however, delay-encoding scheme can minimize this problem [53].

VII. CONCLUSIONS

Synthetic focusing techniques (HDMSA or DPWC) improve shear wave tracking performance especially when performed with more transmissions. They produce tighter focus for greater depths than focused ultrasound tracking. However, grating lobes prevent synthetic focusing techniques from tracking shear wave precisely. Transmission frequency and the size of the angular increments dictates the magnitude of grating lobes incurred during plane wave compounding; while the virtual source depth controls the amount of grating lobes incurred during multi-element sparse array imaging. Hadamard encoding boosts MSA transmission power that increases SNR_e and CNR_e of SWS elastograms. Although HDMSA imaging produces useful and repeatable *in vivo* elastograms, long acquisitions times could introduce decoding errors and decrease performance when using HDMSA to track shear waves in mobile organs such as the heart. Consequently, we plan to perform a more detail evaluation of HDMSA based SWEI under different clinical scenarios.

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Fig. 1:

Illustrates how MSA and HDMSA imaging was performed during SWEI. (a) shows MSA with 8 virtual sources ($V_1, V_2, V_3, \dots, V_8$) at 8 different lateral locations. These virtual sources were distributed over two push-detect events. (b) shows the Hadamard-encoded version of the MSA technique from (a). The 8 virtual sources shown in (a) were phase encoded with the rows a Hadamard H_8 matrix. (c) shows H-MSA with 16 phase-encoded virtual sources distributed over 4 push-detect events. Just like the case (b), (c) uses a H_8 matrix with the phase encoding distributed over two push-detect events. Using 15 element sub-apertures, in this case, and translating the entire sequence to the right, effectively generated 16 unique virtual sources.

Fig. 2:

Hadamard encoding and decoding process illustrated with 4 virtual source transmits. (a) First, the transmit phases of 4 virtual sources with non-overlapping sub-apertures are encoded using a row of the Hadamard matrix, H and transmitted simultaneously. (b) The combined acoustic response (pre-beamformed aperture domain data) is acquired. The process is repeated four times and in each case, the transmit phase encoding is performed with a different row of H . (c) During the decoding stage, the aperture data is multiplied by a row of H and then summed (d) to obtain individual contribution of virtual sources (e). Each decoded virtual source becomes amplified by four.

Fig. 3:

Illustrates how DPWC imaging was performed during SWEI. (a) shows the commonly used plane wave compounding imaging following the push pulse, where 4 unique angular transmissions are repeatedly used to track shear waves. (b) shows the approach to increase the number of angular transmissions. Two push beams are transmitted at the same location and the shear wave from each push beam was tracked with a different set of four angular plane waves. Eight plane waves distributed over two push beams (dotted box) roughly corresponding to the same phase of the shear wave are coherently added to achieve better imaging resolution than (a).

Fig. 4:

Point spread function incurred when HDMSA and DPWC imaging was performed with different imaging parameters (number of transmissions, angular increment, and depth of virtual source). First (a-d) and second (e-h) rows show the PSF incurred when HDMSA ($VS_z = -15$ mm) and DPWC ($\Delta\alpha = 0.25^\circ$), respectively, were performed with transmissions of 4, 8, 16, and 32. (i) Shows the ROIs used to evaluate the grating lobes. The mean amplitudes within the dotted boxes outside the central 1 cm region was computed. The third (j-o) and fourth (p-u) rows show the PSFs obtained when HDMSA and DPWC imaging was performed with 32 transmissions and varying virtual source depths and angular increments. (v-x) show grating lobe magnitude in (v) DPWC and HDMSA sonograms, (w) when HDMSA imaging was performed with different virtual source depths, and (x) when DPWC was performed with different angular increments. (y) Lateral profiles of PSF obtained with HDMSA at 32 transmissions with different VS_z .

Fig. 5:

Sonographic signal-to-noise ratio incurred when the 50.4 kPa phantom was imaged ultrasonically with HDMSA and DPWC imaging. Showing SNR_s incurred when (a) HDMSA imaging was performed with virtual sources with focal depths ranging from -5 mm to -20 mm and transmissions ranging from 4 to 32; (b) DPWC was performed with angular increments ranging from 0° to 3° and transmissions ranging from 4 to 32; (c) DPWC was performed with transmissions ranging from 0 to 32. (d) SNR_s of the individual sonograms obtained with transmission angles in the range of $\pm 15.5^\circ$. SNR_s of DPWC imaging as a function of number of transmissions at different transmission frequencies with (e) $\alpha = 0.25^\circ$ and (f) $\alpha = 1^\circ$.

Fig. 6:

Elastograms obtained from the 50.4 kPa homogeneous phantom using HDMSA imaging with (a-d) $V S_z = -5$ mm, (e-h) $V S_z = -15$ mm, and (i-l) $V S_z = -20$ mm. Showing elastograms obtained using (m-p) standard PW imaging (with different levels of frame averaging), (q-t) DPWC with $\alpha=0.25^\circ$, and (u-x) DPWC with $\alpha=1^\circ$. The first, second, third and fourth columns represents acquisitions with 4, 8, 16, and 32 tracking transmits distributed over 1, 2, 4 and 8 push-detects respectively. In each of these images, the push beam was located at -10 mm horizontal location (region not shown on the image). The black dotted rectangle is the ROI over which the results presented in Fig. 7 were computed.

Fig. 7:

SNR_e analysis of the homogeneous phantom experiments. Impact of (a) virtual source depths and (b) angular increments on the SNR_e of HDMSA and DPWC elastograms, respectively, obtained from the 50.4 kPa phantom. (c-f) showing comparative SNR_e evaluation of PW with frame averaging, DPWC with $\alpha=0.25^\circ$ and 1° , HDMSA with $VS_z=-5, -15$ and -20 mm. Evaluations were performed on (a) 3.4 kPa, (b) 13.9 kPa, (c) 27.1 kPa and (d) 50.4 kPa phantoms. Results on each phantoms are grouped for 4, 8, 16 and 32 transmits. Errorbars represent ± 1 STDEV of five independent acquisitions at same location.

Fig. 8:

Elastograms obtained from the low contrast inclusion phantom using HDMSA imaging with (a-d) $VS_z = -5$ mm, (e-h) $VS_z = -15$ mm, and (i-l) $VS_z = -20$ mm. Showing elastograms obtained using (m-p) standard PW imaging (with different levels of frame averaging), (q-t) DPWC with $\alpha = 0.25^\circ$, and (u-x) DPWC with $\alpha = 1^\circ$. The first, second, third and fourth columns represents acquisitions with 4, 8, 16, and 32 tracking transmits distributed over 1, 2, 4 and 8 push-detects respectively. In each of these images, the push beam was located at -10 mm horizontal location (region not shown on the image). The dotted circles and semi-circles represent the ROIs used to compute the CNR_e values reported in Fig.9.

Fig. 9:

Quantitative analysis of the inclusion phantom experiments. Impact of (a) virtual source depths and (b) angular increments on the CNR_e of HDMSA and DPWC elastograms, respectively, obtained from the high contrast inclusion phantom. (c-d) showing comparative CNR_e evaluation of PW with frame averaging, DPWC with $\alpha=0.25^\circ$ and 1° , HDMSA with $VS_z=-5, -15$ and -20 mm. Evaluations were performed on the (c) high contrast and (d) low contrast inclusion phantoms. Results on each phantoms are grouped for 4, 8, 16 and 32 transmits. Errorbars represent ± 1 STDEV of five independent acquisitions at same location.

Fig. 10:

Comparison of the proposed techniques against the FUS tracking. Elastograms of the 50.4 kPa homogeneous phantom obtained using (a) HDMSA with 32 transmits, (b) DPWC with 32 transmits and (c) focused tracking with 40 tracking lines. (d) Depth dependent SNR_e of (a)-(c) obtained with a sliding kernel. Errorbars represent ± 1 STDEV of five independent acquisitions at same location. The relative SWEI frame rate of different techniques for a 1 cm wide ROI (e) and a 2 cm wide ROI (f). Although parallel beamforming was not implemented for FUS imaging, it is included in the frame rate analysis.

Fig. 11:

Analysis of elastograms obtained from the bicep of three healthy volunteers. Showing (a,e,i) sonograms, (b,f,j) HDMSA elastograms with 32 transmissions, and DPWC elastograms obtained with (c,g,k) 4 and (d,h,l) 32 transmissions. For each of the subjects, free-hand scanning was used to obtain these images from the same spatial location without displacing the transducer noticeably. (m-p) HDMSA elastograms obtained when subject 3 was imaged repeatedly with 32 transmissions. Mean SWS computed from dotted rectangular ROIs of the first three rows are shown in (q). Errorbars represent ± 1 STDEV of the SWS within the ROI. (r) mean and ± 1 STDEV of SWS for the five independent HDMSA acquisitions (32 transmissions) obtained from subject 3.

TABLE I:

Transmit parameters of HDMSA-based SWEI sequences

# of push-detect events	# of virtual sources	Sub-aperture size	Hamdard matrix
1	4	32	H_4
2	8	16	H_8
4	16	15	H_8
8	32	15	H_8

TABLE II:

List of phantoms used in experimental studies.

Type	Nominal Stiffness (kPa)	Source
Homogeneous	3.4	CIRS - Model 039
Homogeneous	13.9	CIRS - Model 039
Homogeneous	27.1	CIRS - Model 039
Homogeneous	50.4	CIRS - Model 039
High contrast inclusion	-	Gelatin-based (Inclusion:Background = 15%:10%)
Low contrast inclusion	-	Gelatin-based (Inclusion:Background = 12.5%:10%)