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Simultaneous Axial Multifocal Imaging using a Single Acoustical Transmission: a Practical Implementation

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Abstract

Standard ultrasound imaging techniques rely on sweeping a focused beam across a field of view; however, outside the transmission focal depth, image resolution and contrast are degraded. High-quality deep tissue *in vivo* imaging requires focusing the emitted field at multiple depths, yielding high resolution and high contrast ultrasound images but at the expense of a loss in frame rate. Recent developments in ultrasound technologies have led to user-programmable systems, which enable real-time dynamic control over the phase and apodization of each individual element in the imaging array. In this paper, we present a practical implementation of a method to achieve simultaneous axial multifoci using a single acoustical transmission. Our practical approach relies on the superposition of axial multifoci waveforms in a single transmission. The delay in transmission between different elements is set such that pulses constructively interfere at multiple focal depths. The proposed method achieves lateral resolution similar to successive focusing, but with an enhanced frame rate. The proposed method uses standard dynamic receive beamforming, identical to two-way focusing, and does not require additional post-processing. Thus, the method can be implemented in real-time on programmable ultrasound systems that allow different excitation signals for each element. The proposed method is described analytically and validated by laboratory experiments in phantoms and *ex vivo* biological samples.

Graphical Abstract

Simulation result of the emitted acoustic pressure field of the SAMI method with three combined foci generated at 20, 40, and 60 mm.

Index Terms—

ultrasound imaging; multifoci; beamforming; frame rate

I. Introduction

Ultrasound offers a real-time, noninvasive and cost effective imaging modality with high penetration depth, and hence it is widely used in medical diagnostics [1]. Two-way focusing, typically applied in B-mode imaging, is a commonly used ultrasound imaging method in which the transmitted beam is focused to a specific depth to achieve constructive interference [2]. The beam is then steered in order to cover a region of interest within the sample under examination [3]. Focusing both the transmitted and received beam improves the lateral resolution, the signal to noise ratio (SNR) and the penetration depth compared to one-way focusing, where a planar wave illuminates the entire field and is focused only on reception [4]. With a single transmission focus, the signal diverges outside of the focal region thus, the lateral resolution and contrast of an object outside the depth of field (DOF) is significantly degraded. The term “standard two-way focusing” is used in this paper for protocols involving a single transmission focus with dynamic receive focusing.

To image a larger DOF, successive focusing is often used, where the transmission focal depth is updated successively with several transmissions [5]. A complete image is constructed by splicing together the focused area from each of the individual transmissions. While this method yields high resolution and contrast, and is widely used in the clinic, it comes at the expense of frame rate loss, which is degraded by a factor that equals the number of transmitted foci. Typically, up to four successive foci are used. An ultrasound method that can provide high lateral resolution over a large DOF with enhanced frame rate is desirable for important medical applications including the detection of anatomical landmarks, ultrasound-guided interventions, fetal surgeries [6], [7] and cardiovascular interventions [8]. Other possible applications are to map tumor borders and layers of peripheral vascular walls, and to detect changes in musculoskeletal tissues resulting from arthritis and other degenerative processes.

In this paper, temporal superposition of axial multifoci waveforms is used to achieve simultaneous axial multifoci imaging (SAMI) using a single transmission event. The proposed method aims to maximize the amplitude of the emitted signal, as well as the lateral and axial resolution. This is accomplished with a programmable ultrasound system (Verasonics Vantage, Kirkland, WA, USA) that can dynamically change the transmitted signal for each transducer element separately [9], [10]. A waveform that generates an axial multifoci pattern in a single transmission event is used and then incorporated in a standard two-way imaging sequence. The resulting image resolution is comparable to standard successive focusing but without the frame rate loss. The method is expected to be important for the increasing population of large patients for whom standard ultrasound imaging

techniques are insufficient and increased frame rate is desired. Further, the extended DOF achieved here can be applied in cardiac applications.

The idea of combining several waveforms into a single transmission event has previously been reported for the generation of lateral multifoci for higher frame rate in cardiac imaging [11], [12]. Similarly, the direct temporal summation of multiple waveforms was suggested in [13]. To our knowledge, these methods were previously implemented for lateral multifoci, but not for generating axial multifoci.

When generating lateral multifoci, only a single or a few central elements are common to all the transmitted waveforms, and overlap in the time domain. However, the axial multifoci waveforms temporal overlap is over a large number of elements and thus the multiline method cannot be directly implemented to generate axial multifoci, as will be further described in the following section. To our knowledge, the SAMI method is the first demonstrated implementation of axial multifoci in a single transmit event.

Extending the DOF is a well-known goal that was addressed by several reported methods but existing methods sacrifice lateral resolution, contrast, or frame rate. The first category of methods increases the DOF without compromising the lateral resolution, but at the expense of reduced contrast. Among these methods is the synthetic transmit aperture (SA) method. This method yields the highest DOF by sampling data corresponding to different transmission elements or sub apertures [14]–[16]. However, the uncoded SA transmission involves a single or small number of elements, and thus the SNR is significantly reduced compared to two-way focusing. Improved SA methods that are aimed to increase the signal intensity exist [17]–[21]; however they require substantial post processing, which can limit their use for real-time ultrasound imaging.

Beam shaping algorithms to generate axial multifoci, such as the conjugate field method [22], the pseudo-inverse method [23], and the Gerchberg–Saxton phase retrieval algorithm [24], can also extend the DOF with high lateral resolution. However, the intensity of each foci is reduced by a factor that equals to the number of foci, which degrades the contrast.

Frequency multiplexing enhances DOF by transmitting a multi-frequency single broadband pulse that is composed of higher frequency components focused at shallow depths, lower frequency components focused at deeper depths, and intermediate frequencies focused at intermediate depths [25], [26]. While this method yields a higher DOF, the signal amplitude is degraded both on transmit and on receive. Parallel transmit beamforming by orthogonal frequency division multiplexing [27], [28] can also be used for extending the DOF. However, orthogonal codes degrade the axial resolution, and require additional post processing on receive.

Coherent compounding of angled plane waves [29] is a method that yields a contrast comparable to successive focusing over a large region of interest, at the expense of reduced lateral resolution compared to successive focusing when full aperture is used to generate each foci. Additionally, the penetration depth is reduced compared to successive focusing. Further improvement to coherent compounding can be made using elaborate receive techniques [30]. Although useful, this method requires limited-diffraction array beam

weightings on receive and additional post processing, therefore increasing the computational complexity.

The DOF can also be enhanced using non-diffracting beams such as axicon beam [31], Bessel beam [32], and X waves [33]. However, in these methods the DOF enhancement is obtained at the expense of the lateral resolution that is degraded significantly, alongside with reduced focal energy. Consequently, these beams have received limited commercial application.

Successive focusing remains the dominant ultrasound imaging modality due to its compatibility with commercial systems, and high contrast and SNR. The SAMI method proposed here is aimed to enhance the frame rate by using a single transmission event to generate axial multifoci, with high lateral resolution. The paper is organized as follows; the design of the transmitted signal is presented first. Then, the method is validated using wire targets and cysts target, and its performance is characterized through contrast and resolution measurements. Finally, the method is validated in an *ex vivo* biological sample.

II. Design of the transmission signal

The proposed method is based on combining waveforms that correspond to different axial foci. An example of the time delays for a standard single focus transmission is presented in Fig. 1(a). Each element transmits a single cycle pulse at a specific time point. The delay in transmission between different elements is set such that all the pulses will interfere constructively at a predetermined location. The longest delay dictates the transmission duration. Since each element transmits only a single cycle, its signal is zero throughout most of the transmission duration, and therefore the time domain is not used efficiently.

The multiline transmit method uses the time domain more efficiently by transmitting multiple waveforms that correspond to lateral multifoci in a single transmit event. An example of this method is presented in Fig. 1(b), where three lateral foci are transmitted simultaneously. The arched waveform shapes that correspond to lateral multifoci yield an overlap between the waveforms that is limited to only one or few central elements.

Trying to implement the multiline method for axial multifoci results in a significant overlapping area, indicated by the purple rectangle in Fig. 1(c). The overlap between the different waveforms is defined as the area where the minimal distance between adjacent waveforms is less than a single pulse length. One drawback of this overlap is a reduced signal compared to successive focusing transmission. The transmitted signal for the overlapping elements is equal to the sum of the waveforms. The overlapping area will influence the maximal transmitted intensity and the other parts of the waveforms will be scaled down by a factor that equals to the number of foci so that the sum of the waveforms will not exceed the piezoelectric maximal element response. Additionally, the overlapping area will contain high frequencies that cannot be transmitted by the transducer, and thus will not be transmitted.

The proposed SAMI method overcomes these problems through the super-position of waveforms such that there is no overlap between the various waveforms and thus eliminating

aliasing while assuring that the waveform can be transmitted by the transducer (Fig. 1(d)). In this example, the deepest desired focal point is inserted first (marked in green) and is transmitted with all elements of the array. An intermediate focal point is then inserted (marked in blue). This waveform will not use the elements that overlap with the previous waveform. As the overlap is in the central elements, it will transmit with the outer transducer elements. The proximal focal point is then inserted (marked in red). Similarly, this waveform is transmitted with the outer elements, where it does not overlap with the previous waveforms. The transmission is the sum of these three waveforms. A constant maximal amplitude is used for all elements in all waveforms to maximize the transmitted energy.

As opposed to successively updating the transmission focus (which requires three separate transmissions), here the three focal points are generated in a single transmission. This transmitted signal is inserted into a regular two-way imaging routine, where it is steered by adding linear delays. Here, a phased array transducer is used to demonstrate the method, and in order to avoid asymmetry during the steering process the center of the transducer is set as the angle steering origin. This process can be repeated for more than three foci, and the design can be optimized for the application and the imaging scene.

A geometrical approach was implemented to generate the focused waveforms. The geometrical focus delay equation is given by:

$$\tau(x, z) = \frac{z - \sqrt{z^2 + x^2}}{c} \quad (1)$$

where τ is the negatively signed delay time, z is the focal point depth, x is the lateral distance from the transducer origin (i.e. transducer center), and c is the sound velocity (see Fig. 1(a)).

The element location at which the second waveform transmission begins is denoted by $\pm\alpha/2$ ($0 < \alpha < D$), where D is the transmitting aperture width. For example, if a specific waveform uses 64 elements out of 128 total elements, then $\alpha=D/2$, i.e. the two outer quarters of the transducer elements are transmitting. It is desirable to relate the minimal axial distance between the generated foci to the system parameters. In order to make sure that there will be no overlap between the waveforms, the minimum delay difference between two waveforms at $x=\pm\alpha/2$ is $\lambda N/c$, where λ is the wavelength, and N is the number of transmitted cycles. This delay difference can be written as:

$$\tau\left(\pm\frac{\alpha}{2}, z_{n+1}\right) - \tau\left(\pm\frac{\alpha}{2}, z_n\right) = \frac{\lambda N}{c} \quad (2)$$

Substituting (1) in (2) yields:

$$\sqrt{z_{n+1}^2 + \left(\frac{\alpha}{2}\right)^2} - z_{n+1} - \sqrt{z_n^2 + \left(\frac{\alpha}{2}\right)^2} + z_n = \lambda N \quad (3)$$

This can be rewritten as:

$$z_{n+1} \sqrt{1 + \frac{\alpha^2}{4z_{n+1}^2}} - z_{n+1} - z_n \sqrt{1 + \frac{\alpha^2}{4z_n^2}} + z_n = \lambda N \quad (4)$$

While this equation can be solved numerically, using the Taylor approximation $(1+x) \approx 1+x/2$, it can be simplified to an analytic form, which provides a useful tool:

$$z_{n+1} \cong z_n \left(1 + \frac{8\lambda N z_n}{\alpha^2} \right)^{-1} \quad (5)$$

In order to demonstrate this, the following parameters were chosen (to fit what was later used in the experiments): $\lambda=0.345$ mm, $N=1$, $z_1=100$ mm, and $D=27.9$ mm (The transducer parameters match the phased array sector transducer P6-3 (Philips, Bothell, WA, USA) used in the experiments). For this example, it is assumed that 50% of the transducer elements are used to generate each additional focus, which means $\alpha=D/2$. The waveform for depth z_1 is presented in Fig. 2(a). The arched waveform is composed of two black and white lines, where the black is the negative half cycle of the pulse and the white is the positive half cycle of the pulse. The next focus is calculated using (5) to be at $z_2=41.3$ mm. The waveform combining foci at z_2 and z_1 is shown in Fig. 2(b), where the waveform for z_2 is created with half of the elements. The third focus is calculated similarly to be at $z_3=26$ mm, and the combined waveform is shown in Fig. 2(c). Finally, the fourth focus is calculated to be at $z_4=19$ mm, and the combination shown in Fig. 2(d). The process can be repeated, to yield $z_5=14.9$ mm, $z_6=12.4$ mm etc. The minimum delay distance λ was chosen such that the transmitted waveforms do not overlap. However, it is possible to optimize the signal further by transmitting half cycles in the remaining gaps. This is illustrated in Fig. 2(e), where the waveforms corresponding to the focal depths z_2 , z_3 , and z_4 also transmit half cycles (i.e. $N=0.5$). During the experimental section, two values of α are presented: α_1 , which correspond to the value of α that was used to send a single cycle, and $\alpha_{1/2}$ which correspond to the α value that was used to send a half-cycle.

Fig. 2(f) presents the waveform that corresponds to the multiline transmission method. The center overlapping elements appear brighter due to a relative higher intensity. In addition, the high frequencies in the overlapping area are filtered by the transducer.

The design of the waveforms was performed using MATLAB (version 2017a, MathWorks, Natick, MA, USA), while the acoustical simulation was implemented with Field II software [34].

III. Simulation results

The two-way point spread function (PSF) is the product of the transmit and receive responses [35]. During transmit, the SAMI method waveform is transmitted, hence the deepest waveform uses the entire aperture (all the elements) and the other waveforms are

transmitted with the outer elements. For receive, the entire aperture is used for all depths. The lateral resolution and the DOF are determined by the total aperture size [36], [37]. Since the SAMI method uses the same total aperture width both on transmit and on receive, the lateral resolution and the DOF remain similar to that achieved using standard two-way focusing. However, the transmission of waveforms with only the outer elements yields a transmit PSF with elevated side lobes compared to standard two-way focusing. Fig. 3(a–d) presents the two-way PSF at 20 mm using $\alpha=0$, $D/3$, $D/2$, $2D/3$ respectively for transmit, and full aperture for receive. The lateral and axial profiles (for $x = 0$ mm, and $z = 20$ mm) are presented in Fig. 3(e) and Fig. 3(f) respectively. The main lobe width that corresponds to the lateral resolution remains similar for all cases, and equal to 0.25 ± 0.02 mm. However, the side lobe increases as the number of transmitting elements reduces, with peak to side lobe ratio (PSLR) values of 25.6, 7.6, 6.4, 6.2 for $\alpha=0$, $D/3$, $D/2$, $2D/3$ respectively. The axial profiles (Fig. 3(f)), which correspond to the DOF also remain similar for all α values, and equal to 1.40 ± 0.14 mm.

When α increases and fewer elements are used for transmission, the intensity of the PSF is reduced. Fig. 3(g) presents the relative focal peak intensity as a function of α/D for foci at $z = 5, 10, 15, 20$ mm. At a shallow depth of 5 mm, the intensity reduces exponentially as a function of the transmitting elements size, since the directivity of the elements reduces the intensity that arrives to the focus from the outer elements. As the depth increases, the intensity reduction becomes linearly dependent to the number of transmitted elements. Fig. 3(h) presents the PSLR as a function of α/D , and it can be seen that the PSLR follows the intensity trend and decreases more steeply at closer distances.

The number of foci that can be generated increases as a function of α . This can be seen from (5), when α increases, the successive focal position z_{n+1} becomes closer to the previous focal position z_n . The focal position z_{n+1} is illustrated as a function of the previous focus z_n and α in Fig. 4.

For $\alpha=D/2$ it is possible to generate four foci between 15–100 mm (the red line in Fig. 4). By increasing α to $2D/3$, eight foci can be generated in the same depth range (the green line in Fig. 4). Alternatively, by reducing α to $D/3$, two foci can be generated in this range (the blue line in Fig. 4).

The DOF, which is the axial dimension surrounding an ideal focus where the magnitude is within 3 dB of the maximal value [38] also increases quadratically as a function of depth, according to:

$$DOF = 7.1\lambda(F\#)^2 \quad (6)$$

where $F\#$ is defined as z_0/D , and z_0 is the focus position.

Deeper foci have a larger DOF, which compensates for the larger axial spacing between foci in the SAMI method. The DOF for each focal position in Fig. 4 is presented as a horizontal black bar. At $\alpha=2D/3$, a waveform satisfying the -3 dB criterion in (6) reaches most axial locations, and an almost continuous DOF is achieved for the range from 15 to 100 mm. If

$\alpha=D/2$ is desirable, and continuous DOF is required, this can be achieved by transmitting a second set of foci that will cover gaps, and then splicing the two images together (similarly to conventional successive focusing). Alternatively, it is possible to achieve uniform coverage by changing the parameter α between waveforms so that the DOF of the waveforms will overlap.

In a practical scenario, the user defines the focal depths according to the sample that is imaged, similar to standard successive focusing. In this case, by determining z_n and z_{n+1} , the parameter α can be calculated using:

$$\alpha = \pm \sqrt{8\lambda N \left(\frac{1}{z_{n+1}} - \frac{1}{z_n} \right)^{-1}} \quad (7)$$

This value of α can be used for generating the combined transmitted signals. Let us consider the case where three foci located at 20, 40, and 60 mm are desired. The three single focus pressure fields corresponding to 20, 40, and 60 mm are presented in Fig. 5(a–c) respectively. The acoustic pressure fields were simulated using Field II software [34]. The simulated transducer parameters match the phased array sector transducer P6–3 used in our experiments. The transducer elevation focus is located at a depth of 60 mm, thus the pressure of the focus at 60 mm is enhanced (Fig. 5(c)). The SAMI's pressure field demonstrating the generated three foci (Fig. 5(d)) was simulated with the following α parameters; for the focus at 20 mm $\alpha_1=0.38D$ and $\alpha_{1/2}=0.27D$; for the focus at 40 mm $\alpha_1=0.65D$ and $\alpha_{1/2}=0.46D$; and for the focus at 60 mm all the elements transmit ($\alpha=0$). Fig. 5(e) is the magnification of the SAMI's three foci area in Fig. 5(d). Validation of the simulation was performed by measuring the emitted pressure field using a needle hydrophone (HNP-0400, Onda, Sunnyvale, CA, USA) (Fig. 5(f)).

IV. Experimental results

Imaging was performed using the Verasonics ultrasound system (Vantage 256, Verasonics Inc., Kirkland, WA, USA), with a phased array sector transducer P6–3. The array has 128 elements with a 0.22 mm pitch, elevation focus at 60 mm and imaging was performed at a center frequency of 4.46 MHz. The resolution experiments in the water tank were performed with 512 angles over a 45° field of view, resulting in an angular precision of 0.09°. The field of view was selected to fit the phantom's physical dimensions. The high angular precision was selected for fine sampling of the PSF [39]. All other experiments used 128 angles over the same field of view, resulting in an angular precision of 0.35°. Beamforming was implemented using the Verasonics software, with its build-in scripts in Matlab. The experiments were performed in real-time in a water tank, in a tissue mimicking phantom, and in an *ex vivo* cow liver.

A. Resolution measurements

Each SAMI transmission is a combination of multiple waveforms. Therefore, the PSF should also be a combination of the multiple PSFs. For a specific depth, the focused PSF's contribution to the local wavefront is the greatest. Hence, the main lobe is similar to that

resulting from a single focused pulse. However, the multifoci transmitted energy that is not focused contribute to the side lobes. To validate this and estimate the SAMI method's PSF, a wire target experiment was conducted in a water tank. The target contained five 50 μm nylon wires that were evenly distributed at depths ranging from 20 to 60 mm, with 10 mm axial spacing.

The SAMI method was compared to SA using 128 acquisitions where in each acquisition single channel is active for transmission and 128 channels are active on receive. Since the SAMI method was developed to achieve maximal lateral resolution, SA transmission was performed using a single element in order to achieve the maximal possible lateral resolution. The SAMI method was also compared to two-way focusing with a single focus at different depths, and to successive focusing using multiple transmissions.

Fig. 6(a) presents the SA image, Fig. 6(b)–(d) present images obtained by transmitting waveforms focused at 20 mm ($F\#=0.7$), 40 mm ($F\#=1.4$) and 60 mm ($F\#=2.1$), respectively. In each of these images, the wires that are not in focus appear blurry. With successive focusing at 20, 40, and 60 mm, the three corresponding wires are in focus (Fig. 6(e)). Applying the SAMI method with three combined foci at 20 (using $\alpha_1=0.38D$ and $\alpha_{1/2}=0.27D$), 40 ($\alpha_1=0.65D$ and $\alpha_{1/2}=0.46D$), and 60 mm in a single transmission (Fig. 6(f)), achieves a lateral resolution that is similar to that of the successive focusing image (Fig. 6(e)). However, with the three combined foci, the contribution of the multifoci transmitted energy, which is not focused, increased side lobes and creates an artifact at the deepest focus. However, the artifact is 40 dB below the main lobe, hence it does not degrade image quality substantially. Obviously, the unfocused PSFs at 30 and 50 mm are degraded. However, using the SAMI method additional waveforms can be added to the single transmission without a time penalty and thus further improvement of the lateral resolution is possible. By combining five foci at 20 ($\alpha_1=0.46D$ and $\alpha_{1/2}=0.33D$), 30 ($\alpha_1=0.65D$ and $\alpha_{1/2}=0.46D$), 40 ($\alpha_1=0.84D$ and $\alpha_{1/2}=0.6D$), 50 ($\alpha_1>D$ and was not transmitted, and $\alpha_{1/2}=0.73D$), and 60 mm using the SAMI method, high resolution imaging is maintained for each wire target (Fig. 6(g)).

The PSFs from Fig. 6 for the various methods are presented in Fig. 7 as a line profile at the focal depth. The SAMI result with five foci (Fig. 6(g)) is compared to the SA method (Fig. 6(a)), and to the three single focus acquisitions (Fig. 6(b–d)). In Fig. 7(a), (c), (e) the SAMI PSF with five foci has a similar main lobe width, compared to the corresponding single focus images (focused at 20, 40, 60 mm). In Fig. 7(b), (d) the SAMI PSF main lobe is narrower than the other single focus images, as it is focused on all five wires simultaneously. The side lobes of the SAMI PSF are reduced compared to the unfocused images, with a reduction of 8, 4, 6, 1, 13 dB for Fig. 7(a)–(e), respectively. Compared to the focused transmissions, the SAMI PSF side lobes are similar except in Fig. 7(c), where the side lobes are elevated by 6 dB, and reach a maximal value of -25 dB. The SA result has the lowest side lobes compared to the other methods. However, from Fig. 6(a), the background is noisier for SA due to its reduced signal. The lateral resolution of each wire in Fig. 6 was measured using the full width at half maximum (FWHM) [40]. The results are summarized in Table I in mm (the results of the focused wires are marked in bold). SA (Fig. 6(a)) achieves high lateral resolution across all depths. For the three single focus images (Fig.

6(b–d)), the spot's width is narrowest at the focal point. For successive focusing (Fig. 6(e)), and SAMI transmission with three foci (Fig. 6(f)), the FWHM of the three foci is similar to that of the individual focused two-way focusing transmissions. The FWHM of the two wires positioned at 30 and 50 mm is larger since they are out of focus. The FWHM of these two wires is improved in Fig. 6(g), using the SAMI transmission with five foci. The axial resolution is governed by the transmitted pulse duration [41], hence it was similar for all the wires in Fig. 6 and measured to be 0.31 ± 0.02 mm.

The wire target experiment was repeated in a commercial tissue-mimicking phantom (CIRS 040GSE, Virginia, USA), consisting of a Zerdine[®] hydrogel polymer [42], with attenuation of 0.5 dB/cm/MHz. The phantom contains wires and cysts with calibrated attenuation and spacing and homogenous specular reflectors in the background. Unlike the water background in Fig. 6, these reflectors form speckle in the ultrasound image that obscures side lobes that are apparent in Fig. 6. This provides the opportunity to compare the methods in a more realistic scenario.

Similar to the water tank experiment, five wires spaced by 10 mm were imaged and the SA image is provided in Fig. 8(a). Single focus images, focused at 20, 40 and 60 mm, respectively, are provided in Fig. 8(b)–(d), and images resulting from successive focusing at 20, 40 and 60 mm in Fig. 8(e). Images obtained with the SAMI method with three foci and five foci are provided in Fig. 8(f) and Fig. 8(g), respectively. The lateral resolution for each wire in Fig. 8 was estimated by the FWHM and the results were similar to the values in Table I.

B. Contrast measurements

The same phantom was used to measure the contrast, and a set of three cyst mimicking targets were imaged at depths of 45, 70, and 100 mm. An illustration of the cyst phantom is presented in Fig. 9(a). The green and blue squares mark the cysts and speckle positions respectively. The SAMI method was compared to SA image, to two-way focusing, and to successive focusing. Fig. 9(b) presents the SA method. The unfocused cysts are not easily visualized with standard single focus imaging with focal points at 45 mm ($F\#=1.6$), 70 mm ($F\#=2.5$) and 100 mm ($F\#=3.6$), respectively (Fig. 9 (c)–(e)). Successive focusing at 45, 70, and 100 mm enhances the visualization of the three cysts (Fig. 9(f)). The SAMI method with three combined foci at 45 ($\alpha_1=0.67D$ and $\alpha_{1/2}=0.47D$), 70 ($\alpha_1=0.91D$ and $\alpha_{1/2}=0.64D$), and 100 mm, also enhances visualization of the cystic regions (Fig. 9(g)). The uniformity and contrast of the speckle area between the first two cysts can be further improved by adding another focal point to this area, thus transmitting four foci at 45 ($\alpha_1=0.94D$ and $\alpha_{1/2}=0.66D$), 55 ($\alpha_1=0.95D$ and $\alpha_{1/2}=0.67D$), 70 ($\alpha_1=0.91D$ and $\alpha_{1/2}=0.64D$), and 100 mm simultaneously (Fig. 9(h)), which achieves image quality similar to successive focusing.

For each of the cysts in Fig. 9(b)–(h), the contrast and the contrast to noise ratio (CNR) were calculated [43]. The contrast is defined as the difference in brightness between the cyst and the surrounding region as:

$$\text{Contrast[dB]} = 20\log_{10}\left(\frac{\mu_i}{\mu_o}\right), \quad (8)$$

where μ_i is the mean of a region inside the cyst, and μ_o is the mean of the background speckle region outside the cyst.

The CNR provides a metric for cyst detection compared to the surrounding background. It is defined by:

$$\text{CNR[dB]} = 20\log_{10}\left(\frac{\mu_o - \mu_i}{\sqrt{\sigma_o^2 + \sigma_i^2}}\right) \quad (9)$$

where σ_i is the standard deviation of a region inside the cyst, and σ_o is the standard deviation of the background speckle region outside the cyst [44].

The contrast results are summarized in Table II, where the contrast in the cysts that are in focus are indicated in bold. In the three single focus images, the focused cysts have a higher contrast compared to the other two unfocused cysts. With the successive focusing approach, all three cysts have contrast values similar to the corresponding focused result for the individual single focus images. The average contrast of the three cysts in the SAMI method using 4 foci is -22.8 dB, which is higher than the average contrast in the three single focus images, and higher than the SA method by 8.4 dB. The contrast in the SAMI method using 4 foci is lower than that in the successive focusing method by 0.8 – 6.8 dB. This is expected, since four foci are transmitted simultaneously, and the unfocused waveforms increase the background signal and thus lower the contrast. The CNR results are summarized in Table III, where the results for the cysts in the focal regions are indicated in bold.

The SA method yields lower CNR compared to the other methods. In the three single focus images, the cyst that is in focus has a larger CNR compared to the unfocused cysts. With the successive focusing approach, all three cysts have CNR values that are similar to the corresponding focused result in the individual single focus images. The average CNR value from the SAMI method using 4 foci is 0.7 dB lower than the successive focusing, and 2.8 dB higher than the SA method. Thus, the detectability of the cysts is not significantly impaired compared to successive focusing.

The speckle resolution cell size, which corresponds to the lateral resolution at each cyst depth, was calculated using the speckle's autocorrelation FWHM value [45]. The results are summarized in Table IV, where the results for the focal regions are indicated in bold.

C. Ex vivo experiments

Further validation of the method was performed by imaging an *ex vivo* cow liver (Fig. 10). Fig. 10(a)–(c) presents standard single focus imaging, where the focal depth was 20 mm ($F\#=0.7$), 35 mm ($F\#=1.3$) and 45 mm ($F\#=1.6$), respectively. The foci positions were

selected based on features detected in the *ex vivo* sample. In these images, the contrast and resolution are improved at the focal depth and degraded outside this region.

Images were also obtained with successive focusing to 20, 35 and 45 mm (Fig. 10(d)) and SAMI transmission (Fig. 10(e)) combining these three focal points at 20 ($\alpha_1=0.41D$ and $\alpha_{1/2}=0.29D$), 35 ($\alpha_1=0.75D$ and $\alpha_{1/2}=0.53D$) and 45 mm. The SAMI method yields a similar image quality. As expected, the lateral resolution for successive focusing and SAMI are similar and are superior to single focus imaging. Further, the SAMI frame rate is three-fold higher than the successive focusing.

D. Safety of SAMI

The acoustic safety of an ultrasound sequence is typically regulated by the mechanical index (MI) and the thermal index (TI) [46]. The MI is related to the mechanical effects such as cavitation, and the TI relates to undesired thermal heating effects in the human body.

These parameters were evaluated for the same configuration presented in Fig. 6, with 5 foci located at 20, 30, 40, 50 and 60 mm. The SAMI method's safety parameters were compared to that of standard single focus at these multiple depths. The acoustic pressure was measured using a needle hydrophone (HNP-0400, Onda, Sunnyvale, CA, USA) with an active aperture of 0.4 mm. The hydrophone probe was mounted on a three-dimensional positioning system (Newport motion controller ESP 300, Newport 443 series). The pressure signals received by the hydrophone were first displayed on a digital oscilloscope (DPO4034, Tektronix, OR, USA), and further recorded and converted to pressure via post processing. The MI was calculated using:

$$MI = \frac{p_-}{\sqrt{f_c}} \quad (10)$$

where p_- is the peak negative pressure, and f_c is the central frequency measured in MHz.

Measurements were performed with a transmitted voltage of 20 Vpp (corresponds to a pressure of 1 MPa at the deepest foci (60 mm)), and the MI results are summarized in Table V. The MI for all tested methods was below 1.9 [47]. In addition, the SAMI MI was lower than the single focus at all depths. This is expected in SAMI as a fraction of the aperture is used for transmission and the peak intensity is lower.

The TI for soft tissue was calculated according to [48]:

$$TIS = \frac{W_{01}f_c}{210} \quad (11)$$

where TIS is the TI for soft tissue, and W_{01} is the maximum value of the time-averaged acoustic output power emitted from the most active 1 cm length of the radiating aperture [46].

For scanned mode imaging, such as SAMI, the TI model assumes that the greatest temperature increase happens near the ultrasound source [49], [50]. Hence this value is calculated near the transducer's surface. The TIS for SAMI with five foci and for single focus was measured using the same setup as the MI. The hydrophone was placed 5 mm from the transducer, and the full height of the transducer was scanned along a 1 cm line in the lateral direction. As the SAMI transmits the highest signal from the outer elements of the transducer, the 1 cm scan was performed in that area. In order to maximize the potential thermal effect, the transmitted voltage was set to 100 Vpp. The TI was 0.036 for the single focus case and was 0.048 for the SAMI method. This increase of 33% is due to the longer signals that are being transmitted in SAMI. Nevertheless, the measured TI is well below the safety limit [47].

V. Discussion and conclusions

The SAMI method is a real-time method for achieving simultaneous axial multifocal imaging using a single transmission. The method relies on the superposition of axial multifoci waveforms in a single transmission while eliminating overlap between the multiple waveforms. The SAMI method is intended to facilitate the imaging of an extended depth of interest without compromising the frame rate while maximizing the lateral resolution, hence the entire aperture is used for both transmit and receive. The SAMI method should be particularly useful in ultrasound applications that require high spatial resolution of high dynamic range targets over an extended depth.

Implementation of the method was achieved using an arbitrary waveform generator in a programmable ultrasound system, by programming a different transmission waveform for each of the transducer elements. The arbitrary waveform generator, combined with programmable ultrasound systems, provides a unique platform to engineer the transmission waveform for each element. A central advantage of such programmable systems is the simplicity of implementation of tailored excitations. This adds a degree of freedom in transducer's waveform design and opens the door for implementing more complex ultrasound patterns. Here, this feature was used to practically implement axial multifoci for the first time.

The method can be incorporated in a regular imaging routine, by changing the transmitted signal based on the designed pattern. Imaging and image reconstruction can be performed by the programmable ultrasound system in real-time in a user-friendly manner.

To eliminate overlap in the axial multifoci waveform, only the deepest focus is transmitted with the entire aperture and the other foci are transmitted using only the outer aperture elements. As a result, the intensity and the PSLR of each of the foci are decreased compared to standard two-way focusing. The reduction in intensity and PSLR is dependent upon the fractional aperture distance α , which corresponds to the reduction in the number of transmitting elements. Improvement in the PSLR can be achieved using coherence receive beamforming, as in [51]. In order to maximize the emitted energy, apodization was not used during transmission. Adding an apodization window in order to reduce the transmit phase pattern is feasible. Although the SAMI method uses the outer elements for transmit, the

entire aperture is used for receive. Since the two-way PSF is the product of the two apertures, the side lobes or phase pattern are greatly reduced in the two-way PSF.

Since the method uses the outer elements to create the shallow depth foci, the intensity and PSLR of the foci that are closer than 10 mm is degraded while using the P6–3 phased array transducer. This is due to the limited directivity of the outer elements that cannot be steered to these shallow depths, and therefore reduces exponentially the intensity that arrives to the nearest foci. To overcome this, it is possible to use a higher frequency transducer with smaller aperture size that is intended for shallow depth imaging.

The SAMI method performance was initially compared to SA. In order to achieve the maximal possible lateral resolution, 128 acquisitions were used where in each acquisition a single channel was active for transmission and 128 channels were active on receive. The SAMI method yields similar lateral resolution, with improved contrast and CNR. While a SA sequence with multiple elements active for each transmit will increase the contrast and the SNR, the lateral resolution will be reduced, and the SAMI method will inherently yield better resolution. Next, the SAMI performance was compared to two-way focusing using a single focus at various depths. The imaging time is similar for both methods. For the in-focus targets, the SAMI and the single focus methods yield similar lateral resolution and CNR, with a reduction of 4.5 dB on average in the contrast. However, the SAMI lateral resolution, contrast and CNR are significantly better for targets that are far from the single focus. Thus, the SAMI method is preferable for applications that require high lateral resolution over a large depth of field. Lastly, the SAMI method was also compared to successive focusing at multiple depths with the full aperture used for transmitting all foci. This method yields the highest quality images in terms of lateral resolution, CNR and contrast, while compromising the frame rate by a factor that is proportional to the number of foci. The SAMI method yields similar lateral resolution and CNR, with an average contrast reduction of 4.5 dB. Nevertheless, the SAMI frame rate is that of a single focus, regardless of the number of axial multifoci generated. Hence, it is increased by a factor equal to the number of foci compared to successive focusing.

It should be noted that if a uniform resolution is desired in successive focusing, the $F\#$ is kept constant for all foci. Since it is not possible to improve the resolution of the deeper foci, it lowers the resolution of the shallow foci by not using the entire aperture [52], [53]. The SAMI method uses the outer parts of the aperture for each of the waveforms and thus it is not possible to reduce the aperture size in order to maintain a fixed $F\#$ and a fixed resolution.

To enhance the axial resolution and minimize post processing, single-cycle pulses were used in this paper. Therefore, the axial resolution for all the methods is comparable, since they all use single cycle transmission. Longer waveforms (that are required for example for pulsed wave Doppler or color flow) can also be considered, however they will require a larger separation between waveforms, and yield larger α values. The safety of the SAMI method was also assessed and compared to standard single two-way focusing. With SAMI, the MI was decreased by 6%–53%. This is expected since SAMI uses only the outer elements to transmit, and thus the intensity at the foci is reduced. The TI increases by 33% compared to two-way focusing (a value of 0.036 with single two way focusing compared to 0.048 with

SAMI). The increase in TI with SAMI is due to the longer signals that are transmitted at the outer edges of the transducer. The TI values comply with the safety regulations that require a TI value below 6.

In this paper, the demonstration of the SAMI method was done using a 1D transducer array. While the SAMI method increases the DOF and thus improves the lateral resolution as a function of depth, the elevation focus of such arrays is fixed, and significantly larger than the lateral resolution. Implementation of the SAMI method using a 2D matrix array is expected to enhance the performance of the method in the elevation axis. This is because 2D arrays allow for acoustic beam steering in any given direction, and enable controllable 3D beam formation.

In conclusion, we have presented a practical implementation of simultaneous axial multifoci imaging using a single acoustical transmission event, which yields high resolution over a large region of interest. The method was evaluated using wire targets, cyst mimicking phantoms, and an *ex vivo* cow liver biological sample.

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Biographies

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Tali Ilovitsh received her B.Sc. (2010), M.Sc. in a direct track (2011), and Ph.D. (2016) degrees in electrical engineering from Bar Ilan University, Israel. Her Ph.D. research in the

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Josquin Foiret was born in 1985 in Paris, France. He received his B.Sc. degree in Physics and his M.Sc. degree in Acoustics from the Paris VII University in 2008 and 2009, respectively. In 2013, he received the Ph.D. degree from the Paris VI University for his work on ultrasonic characterization of cortical bone. From 2013 to 2016, he joined the department of Biomedical Engineering of the University of California, Davis as a postdoctoral researcher where he worked on enhancing drug delivery in tumor using sonoporation and temperature sensitive liposomes and ultrasound monitoring of thermal therapy. He later became Assistant Project Scientist continuing his research on enhancing drug/gene delivery to solid tumor, as well as blood brain barrier opening for the delivery of small molecules and viruses and ultrasound localization microscopy. Since July 2018, he is working for Stanford University as an Instructor for the department of Radiology. His current research interest includes the characterization and use of contrast agents for imaging and therapeutic applications, the design of novel imaging techniques, and the design of next generation 2D imaging arrays.

Douglas N. Stephens (M'82) received the B.S. degree in physiology from the University of California, Davis in 1976, and the B.S. and M.S. degrees in electrical and electronic engineering and biomedical engineering in 1981 and 1983, respectively, from California State University, Sacramento. In early 1985 he joined the pioneering technical group at EndoSonics Corporation. As a key contributor at EndoSonics in solid state intravascular ultrasound (IVUS) technology, he was responsible for all catheter electronics and analog signal processing. In 1990 Mr. Stephens led the technical effort in the creation of the world's first commercial 3.5 F solid-state ultrasound imaging catheter and was awarded the first EndoSonics Fellowship Award in that year. That IVUS catheter is still in production and has been used in over 1 million interventional procedures worldwide. As vice president of strategic technology at EndoSonics he was responsible for new designs of IVUS solid state

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Katherine W. Ferrara is a Professor of Radiology at Stanford University. She is a member of the National Academy of Engineering and a fellow of the IEEE, American Association for the Advancement of Science, the Biomedical Engineering Society, the Acoustical Society of America and the American Institute of Medical and Biological Engineering. Dr. Ferrara received her Ph.D. in 1989 from the University of California, Davis. Prior to her PhD, Dr. Ferrara was a project engineer for General Electric Medical Systems, involved in the development of early magnetic resonance imaging and ultrasound systems. Following an appointment as an Associate Professor in the Department of Biomedical Engineering at the University of Virginia, Charlottesville, Dr. Ferrara served as the founding chair of the Department of Biomedical Engineering at UC Davis. Her laboratory is known for early work in aspects of ultrasonics and has more recently expanded their focus to broadly investigate molecular imaging and drug delivery.

References

- [1]. Carson PL, Meyer CR, Scherzinger AL, and V Oughton T, "Breast imaging in coronal planes with simultaneous pulse echo and transmission ultrasound," *Science*, vol. 214, no. 4525, pp. 1141–1143, Dec. 1981. [PubMed: 7302585]
- [2]. Vogel J, Bom N, Ridder J, and Lancee C, "Transducer design considerations in dynamic focusing," *Ultrasound Med. Biol.*, vol. 5, no. 2, pp. 187–193, Jan. 1979. [PubMed: 505618]
- [3]. Szabo TL, *Diagnostic Ultrasound Imaging*. Elsevier, 2004.
- [4]. Ilovitsh T, Ilovitsh A, Foiret J, Fite BZ, and Ferrara KW, "Acoustical structured illumination for super-resolution ultrasound imaging," *Commun. Biol.*, vol. 1, no. 1, p. 3, Jan. 2018. [PubMed: 29888748]
- [5]. Maslak SH, "Computed sonography," *Ultrasound Annu.* 1985, pp. 1–16, 1985.
- [6]. Barbachowska A, Balis M, Krzanik K, Zamlynski M, Bodzek P, and Olejek A, "Intrauterine fetal surgery," *World Sci. News*, vol. 76, pp. 5–15, 2017.
- [7]. Luks FI, "New and/or improved aspects of fetal surgery," *Prenat. Diagn.*, vol. 26, no. 10, pp. 980–984, 2006. [PubMed: 16941719]
- [8]. Light ED, Lieu V, and Smith SW, "Progress in ring array transducers for real-time 3D ultrasound guidance of cardiac interventional devices," *Ultrason. Imaging*, vol. 33, no. 3, pp. 197–204, 2011. [PubMed: 21842583]
- [9]. "Verasonics." [Online]. Available: <http://verasonics.com>. Accessed date is June 01, 2018.
- [10]. Flynn J, Daigle R, Pflugrath L, Linkhart K, and Kaczowski P, "Estimation and display for vector Doppler imaging using planewave transmissions," *IEEE Int. Ultrason. Symp. IUS*, pp. 413–418, 2011.
- [11]. Mallart R and Fink M, "Improved imaging rate through simultaneous transmission of several ultrasound beams," in *SPIE New Developments in Ultrasonic Transducers and Transducer Systems*, 1992, vol. 1733, pp. 120–130.

- [12]. Matrone G, Ramalli A, Savoia AS, Tortoli P, and Magenes G, "High frame-rate, high resolution ultrasound imaging with multi-line transmission and filtered-delay multiply and sum beamforming," *IEEE Trans. Med. Imaging*, vol. 36, no. 2, pp. 478–486, 2017. [PubMed: 28113492]
- [13]. Bolorforosh MS, Chou CH, Ustuner KF, and Gee A, "Medical diagnostic ultrasound imaging method and system using simultaneously transmitted ultrasound beams," U.S. Patent 6,277,073, 2001.
- [14]. Ylitalo JT and Ermert H, "Ultrasound Synthetic Aperture Imaging: Monostatic Approach," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 41, no. 3, pp. 333–339, 1994.
- [15]. Holm S and Yao H, "Improved framerate with synthetic transmit aperture imaging using \nprefocused subapertures," 1997 *IEEE Ultrason. Symp. Proceedings*, vol. 2, pp. 1535–1538, 1997.
- [16]. Matrone G, Savoia AS, Caliano G, and Magenes G, "Depth-of-field enhancement in Filtered-Delay Multiply and Sum beamformed images using Synthetic Aperture Focusing," *Ultrasonics*, vol. 75, pp. 216–225, Mar. 2017. [PubMed: 28011340]
- [17]. Chiao RY, Thomas LJ, and Silverstein SD, "Sparse array imaging with spatially-encoded transmits," 1997 *IEEE Ultrason. Symp. Proceedings. An Int. Symp. (Cat. No.97CH36118)*, vol. 2, no. c, pp. 1679–1682, 1997.
- [18]. Gong P, Kolios MC, and Xu Y, "Delay-encoded transmission and image reconstruction method in synthetic transmit aperture imaging," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 62, no. 10, pp. 1745–1756, Oct. 2015. [PubMed: 26470037]
- [19]. Harrison T, Sampaleanu A, and Zemp R, "S-sequence spatially-encoded synthetic aperture ultrasound imaging," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 61, no. 5, pp. 886–890, 2014. [PubMed: 24801516]
- [20]. Misaridis TX and Jensen JA, "Space-time encoding for high frame rate ultrasound imaging," *Ultrasonics*, vol. 40, no. 1–8, pp. 593–597, 2002. [PubMed: 12160007]
- [21]. Bottenus N, "Recovery of the Complete Data Set From Focused Transmit Beams," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 65, no. 1, pp. 30–38, Jan. 2018. [PubMed: 29283345]
- [22]. Ibbini MS and Cain CA, "A Field Conjugation Method for Direct Synthesis of Hyperthermia Phased-Array Heating Patterns," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 36, no. 1, pp. 3–9, 1989. [PubMed: 18284943]
- [23]. Ebbini ES and Cain CA, "Multiple-focus ultrasound phased-array pattern synthesis: optimal driving-signal distributions for hyperthermia," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 36, no. 5, pp. 540–548, Sep. 1989. [PubMed: 18290231]
- [24]. Gerchberg WR and Saxton WO, "A practical algorithm for the determination of phase from image and diffraction plane pictures," *Optik (Stuttg.)*, vol. 35, pp. 237–246, 1972.
- [25]. Hossack JA, "Extended focal depth imaging for medical ultrasound," in 1996 *IEEE Ultrasonics Symposium. Proceedings*, vol. 2, pp. 1535–1540.
- [26]. Zhou S and Hossack JA, "Dynamic-transmit focusing using time-dependent focal zone and center frequency," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 50, no. 2, pp. 142–152, 2003. [PubMed: 12625587]
- [27]. Demi L, Verweij MD, and Van Dongen KWA, "Parallel transmit beamforming using orthogonal frequency division multiplexing applied to harmonic Imaging-A feasibility study," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 59, no. 11, pp. 2439–2447, Nov. 2012. [PubMed: 23192807]
- [28]. Demi L, Ramalli A, Giannini G, and Mischi M, "In Vitro and in Vivo tissue harmonic images obtained with parallel transmit beamforming by means of orthogonal frequency division multiplexing," *IEEE Ultrason. Symp. Proc*, vol. 62, no. March 2016, pp. 230–5, 2015.
- [29]. Montaldo G, Tanter M, Bercoff J, Benech N, and Fink M, "Coherent plane-wave compounding for very high frame rate ultrasonography and transient elastography," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 56, no. 3, pp. 489–506, 2009. [PubMed: 19411209]
- [30]. Cheng J and Lu JY, "Extended high-frame rate imaging method with limited-diffraction beams," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 53, no. 5, pp. 880–899, 2006. [PubMed: 16764444]

- [31]. Burckhardt CB, Hoffmann H, and Grandchamp PA, "Ultrasound Axicon: a device for focusing over a large depth," J. Acoust. Soc. Am, vol. 54, no. 6, pp. 1628–1630, Dec. 1973.
- [32]. Hsu DK, Margetan FJ, and Thompson DO, "Bessel beam ultrasonic transducer: Fabrication method and experimental results," Appl. Phys. Lett, vol. 55, no. 20, pp. 2066–2068, 1989.
- [33]. Lu JY and Greenleaf JF, "Experimental Verification of Nondiffracting X Waves," IEEE Trans. Ultrason. Ferroelectr. Freq. Control, vol. 39, no. 3, pp. 441–446, 1992. [PubMed: 18267654]
- [34]. Jensen JA, "Field: A Program for Simulating Ultrasound Systems," Med. Biol. Eng, vol. 34, pp. 351–353, 1996.
- [35]. Ranganathan K and Walker WF, "A novel beamformer design method for medical ultrasound. Part I: Theory," IEEE Trans. Ultrason. Ferroelectr. Freq. Control, vol. 50, no. 1, pp. 15–24, 2003. [PubMed: 12578133]
- [36]. Robert J-L, Erkamp R, Korukonda S, Vignon F, and Radulescu E, "Using redundancy of round-trip ultrasound signal for non-continuous arrays: Application to gap and blockage compensation," J. Acoust. Soc. Am, vol. 138, no. 5, pp. 3375–3382, 2015. [PubMed: 26627809]
- [37]. Ilovitsh T, Ilovitsh A, Foiret J, and Ferrara KW, "Imaging beyond ultrasonically-impenetrable objects," Sci. Rep, vol. 8, no. 1, p. 5759, Dec. 2018. [PubMed: 29636513]
- [38]. Kino S, Gordon, Acoustic Waves: Devices, Imaging, and Analog Signal Processing. Prentice Hall Englewood Cliffs, New York, 1987.
- [39]. Garcia D, Le Tarnec L, Muth S, Montagnon E, Poree J, and Cloutier G, "Stolt's f-k migration for plane wave ultrasound imaging," IEEE Trans. Ultrason. Ferroelectr. Freq. Control, vol. 60, no. 9, pp. 1853–1867, Sep. 2013. [PubMed: 24626107]
- [40]. Alasaarela E and Koivukangas J, "Evaluation of image quality of ultrasound scanners in medical diagnostics," J. Ultrasound Med, vol. 9, no. 1, pp. 23–34, Jan. 1990. [PubMed: 2404131]
- [41]. Kremkau FW and Taylor J, "Artifacts in ultrasound imaging," Journal of ultrasound in medicine, vol. 5, no. 4 American Institute of Ultrasound in Medicine, pp. 227–237, 4-1986. [PubMed: 3514956]
- [42]. Culjat MO, Goldenberg D, Tewari P, and Singh RS, "A Review of Tissue Substitutes for Ultrasound Imaging," Ultrasound Med. Biol, vol. 36, no. 6, pp. 861–873, Jun. 2010. [PubMed: 20510184]
- [43]. Deng Y, Palmeri ML, Rouze NC, Trahey GE, Haystead CM, and Nightingale KR, "Quantifying Image Quality Improvement Using Elevated Acoustic Output in B-Mode Harmonic Imaging," Ultrasound Med. Biol, vol. 43, no. 10, pp. 2416–2425, Oct. 2017. [PubMed: 28755792]
- [44]. Bottenus N and Üstüner KF, "Acoustic reciprocity of spatial coherence in ultrasound imaging," IEEE Trans. Ultrason. Ferroelectr. Freq. Control, vol. 62, no. 5, pp. 852–861, 2015. [PubMed: 25965679]
- [45]. Wagner RF, Smith SW, Sandrik JM, and Lopez H, "Statistics of Speckle in Ultrasound B-Scans," IEEE Trans. Sonics Ultrason, vol. 30, no. 3, pp. 156–163, 5 1983.
- [46]. Abbott JG, "Rationale and derivation of MI and TI—a review," Ultrasound Med. Biol, vol. 25, no. 3, pp. 431–441, Mar. 1999. [PubMed: 10374986]
- [47]. Acoustic Output Measurement Standard for Diagnostic Ultrasound Equipment, Revision 3. NEMA, 2009.
- [48]. Bigelow TA et al., "The Thermal Index," J. Ultrasound Med, vol. 30, no. 5, pp. 714–734, 2011. [PubMed: 21527623]
- [49]. Curley MG, "Soft tissue temperature rise caused by scanned, diagnostic ultrasound," IEEE Trans. Ultrason. Ferroelectr. Freq. Control, vol. 40, no. 1, pp. 59–66, Jan. 1993. [PubMed: 18263157]
- [50]. O'Brien WD et al., "The Risk of Exposure to Diagnostic Ultrasound in Postnatal Subjects," J. Ultrasound Med, vol. 27, no. 4, pp. 517–535, Apr. 2008. [PubMed: 18359907]
- [51]. Dahl JJ et al., "Coherence beamforming and its applications to the difficult-to-image patient," Ultrason. Symp. (IUS), 2017 IEEE Int., pp. 1–10, 2017.
- [52]. Robinson B and Cooley C, "Synthetic dynamic transmit focus," Proc. IEEE Ultrason. Symp, vol. 2, no. i, pp. 1209–1214, 2000.

- [53]. Zemp RJ, Abbey CK, and Insana MF, "Linear System Models for Ultrasonic Imaging: Application to Signal Statistics," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 50, no. 6, pp. 642–654, 2003. [PubMed: 12839176]

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Fig. 1.

Schematic illustration of the proposed method. (a) A standard single focused beam with corresponding delays applied to the array elements. (b) The multiline transmit method, generating three lateral foci. The overlap between the waveforms is limited to the central elements. (c) Attempt to generate three axial foci using the multiline transmit, resulting in an overlapping area that is marked in a purple rectangle (d) Combination of three foci in a single transmit using the SAMI method.

Fig. 2.

Steps in generating the transmitted SAMI waveform. Axes are common to all subfigures (a) Waveform for $z_1=100$ mm. (b) Combined waveforms for $z_1=100$ mm, and $z_2=41.3$ mm. (c) Combined waveforms for $z_1=100$ mm, $z_2=41.3$ mm, and $z_3=26$ mm. (d) Combined waveforms for $z_1=100$ mm, $z_2=41.3$ mm, $z_3=26$ mm, and $z_4=19$ mm. (e) Optimized waveforms by allowing half-cycle transmissions. (f) Combining the same waveforms using the multiline transmit method; the total energy is lower, and the signal in the overlapping area is distorted.

Fig. 3.

Two-way focusing PSFs at 20 mm using different α values for transmit, and full aperture for receive. Axes are common to subfigures (a)-(d). Result using (a) $\alpha=0$. (b) $\alpha=D/3$. (c) $\alpha=D/2$, (d) $\alpha=2D/3$, (e) Lateral profile of (a)-(d). (f) Axial profile of (a)-(d). (g) Relative focal intensity versus α/D for different focal depths. (h) Relative PSLR versus α/D for different focal depths.

Fig. 4.

Focal depths and the depth of field are illustrated for varied α . The horizontal black bars represent the depth of field for each focal location. The red line corresponds to the example in Fig. 2(e), with foci at 100, 41.3, 26 and 19 mm.

Fig. 5.

Emitted acoustic pressure fields. Axes are common to (a-d), (e-f). Simulation results for (a) single focus at 20 mm, (b) single focus at 40 mm, and (c) single focus at 60 mm. (d) Simulation of SAMI with three foci generated at 20, 40, and 60 mm. (e) Magnification of the simulated SAMI's three foci area. (f) Hydrophone measurements - SAMI with three foci generated at 20, 40 and 60 mm.

Fig. 6.

Experimental results: wire targets imaged in water. All subfigures are presented with a 60 dB dynamic range. Axes are common to all subfigures. The red triangles mark the foci positions. (a) SA. (b) Single focus at 20 mm. (c) Single focus at 40 mm. (d) Single focus at 60 mm. (e) Successive focusing at 20, 40, and 60 mm. (f) SAMI using three foci at 20, 40, and 60 mm. (g) SAMI using five foci at 20, 30, 40, 50, and 60 mm.

Fig. 7.

Experimental results: wire target lateral PSFs. Comparisons of SAMI to SA and to three single focus transmissions at different depths. Axes are common to all subfigures. Wire at (a) 20 mm, (b) 30 mm, (c) 40 mm, (d) 50 mm, (e) 60 mm.

Fig. 8.

Experimental results: wire targets in a calibrated tissue mimicking phantom. All subfigures are presented with a 60 dB dynamic range. Axes are common to all subfigures. The red triangles mark the focal positions. (a) SA (b) Single focus at 20 mm. (c) Single focus at 40 mm. (d) Single focus at 60 mm. (e) Successive focusing at 20, 40, and 60 mm. (f) SAMI method with three foci at 20, 40, and 60 mm. (g) SAMI method with five foci at 20, 30, 40, 50, and 60 mm.

Fig. 9.

Experimental results: cysts target in a tissue mimicking phantom. All subfigures are presented with a 50 dB dynamic range. Axes are common to all subfigures. The red triangles mark the foci positions. (a) Phantom cysts illustration, where the green and blue squares mark the cysts and speckle positions respectively. (b) SA. (c) Single focus at 45 mm. (d) Single focus at 70 mm. (e) Single focus at 100 mm. (f) Successive focusing at 45, 70, and 100 mm. (g) SAMI method with three foci at 45, 70, and 100 mm. (h) SAMI method with four foci at 45, 55, 70, and 100 mm.

Fig. 10.

Experimental results – *ex vivo* cow liver. All subfigures are presented with a 60 dB dynamic range. Axes are common to all subfigures. The red triangles mark the focal positions. (a) Single focus at 20 mm. (b) Single focus at 35 mm. (c) Single focus at 45 mm. (d) Successive focusing at 20, 35 and 45 mm. (e) SAMI method with three foci at 20, 35, and 45 mm.

Table I

Lateral Resolution Comparison (FWHM in mm)

Depth \ Method	Synthetic aperture	Single focus at 20 mm	Single focus at 40 mm	Single focus at 60 mm	Successive focusing	SAMI 3 foci	SAMI 5 foci
20 mm	0.31	0.32	0.43	0.42	0.35	0.31	0.30
30 mm	0.34	0.54	0.52	0.53	0.54	1.05	0.34
40 mm	0.47	0.68	0.48	0.65	0.48	0.49	0.47
50 mm	0.58	0.76	0.68	0.80	0.67	0.68	0.62
60 mm	0.64	0.96	0.96	0.69	0.69	0.70	0.69

Table II

Cyst Contrast [dB]

Depth \ Method	Synthetic aperture	Single focus at 45 mm	Single focus at 70 mm	Single focus at 100 mm	Successive focusing	SAMI 3 foci	SAMI 4 foci
45 mm	-16.4	-24.0	-12.7	-10.9	-24.1	-17.4	-17.3
70 mm	-15.0	-16.3	-30.8	-21.5	-30.7	-22.9	-24.8
100 mm	-11.8	-13.6	-13.7	-27.2	-27.1	-25.8	-26.3
Average	-14.4	-18.0	-19.1	-19.9	-27.3	-22.0	-22.8

Table III

Cysts CNR [dB]

Depth \ Method	Synthetic aperture	Single focus at 45 mm	Single focus at 70 mm	Single focus at 100 mm	Successive focusing	SAMI 3 foci	SAMI 4 foci
45 mm	7.5	9.9	5.3	5.4	9.8	8.3	8.6
70 mm	4.8	6.0	7.6	6.5	7.7	6.8	6.8
100 mm	4.9	8.0	7.0	10.2	10.2	10.1	10.1
Average	5.7	8.0	6.6	7.4	9.2	8.4	8.5

Table IV

Speckle Lateral Resolution Comparison (FWHM in mm)

Depth \ Method	Synthetic aperture	Single focus at 45 mm	Single focus at 70 mm	Single focus at 100 mm	Successive focusing	SAMI 3 foci	SAMI 4 foci
45 mm	0.72	0.72	0.94	0.93	0.72	0.72	0.73
70 mm	1.13	1.35	1.14	1.34	1.14	1.15	1.14
100 mm	1.80	1.97	1.98	1.76	1.76	1.77	1.76

Table V**Mechanical Index**

Method	Measured at	Pressure [MPa]	Mechanical index
Single focus at 20 mm	20 mm	0.88	0.42
SAMI 5 foci		0.55	0.26
Single focus at 30 mm	30 mm	1.05	0.50
SAMI 5 foci		0.55	0.26
Single focus at 40 mm	40 mm	1.16	0.55
SAMI 5 foci		0.54	0.25
Single focus at 50 mm	50 mm	1.25	0.59
SAMI 5 foci		0.80	0.38
Single focus at 60 mm	60 mm	1.18	0.56
SAMI 5 foci		1.13	0.53
Safety limit	-	-	1.9