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Real-time Implementation of a Dual-Mode Ultrasound Array System: *In Vivo* Results

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Abstract

A real-time dual-mode ultrasound array (DMUA) system for imaging and therapy is described. The system utilizes a concave (40-mm radius of curvature) 3.5 MHz, 32 element array and modular multi-channel transmitter/receiver. It is capable of operating in a variety of imaging and therapy modes (on transmit) and continuous receive on all array elements even during high-power operation. A signal chain consisting of field-programmable gate arrays (FPGA) and graphical processing units (GPU) is used to enable real-time, software-defined beamforming and image formation. Imaging data, from quality assurance phantoms as well as *in vivo* small and large animal models, are presented and discussed. Corresponding images obtained using a temporally-synchronized and spatially-aligned diagnostic probe confirm the DMUA's ability to form anatomically-correct images with sufficient contrast in an extended field of view (FOV) around its geometric center. In addition, high frame rate DMUA data also demonstrate the feasibility of detection and localization of echo changes indicative of cavitation and/or tissue boiling during HIFU exposures with 45 – 50 dB dynamic range. The results also show that the axial and lateral resolution of the DMUA are consistent with its f_{number} and bandwidth with well behaved speckle cell characteristics. These results point the way to a theranostic DMUA system capable of quantitative imaging of tissue property changes with high specificity to lesion formation using focused ultrasound.

I. Introduction

Image-guided high intensity focused ultrasound (IgHIFU) surgery is an active area of research in many academic and industrial labs worldwide [1]–[7]. Innovations and advances in technology have led to several clinical uses of IgHIFU [8], [9]. Currently, the two most common techniques of providing image guidance for focused ultrasound (FUS) are magnetic resonance imaging (MRgFUS) and diagnostic ultrasound (USgFUS). MRg-FUS is the most widely used image-guidance modality in the clinical setting. At present, it is the only FDA approved guidance method for the treatment of uterine fibroids in the US. The ability to create high-contrast anatomical images, as well as monitor HIFU induced temperature rise to 100°C are distinct advantages of MR [10], [11]. The impact of MRgFUS on the field of

IgHIFU surgery has been significant, but MR guidance has limitations. Specifically, the overall cost as well as the relatively long image-acquisition times. Ultrasound continues to be a promising image-guidance modality. While current diagnostic ultrasound scanners do not provide the same levels of soft-tissue contrast achievable by MRI, ultrasound has qualities that make it attractive as a guidance modality. Low cost ultrasound systems are capable of providing high-frame rate imaging that can provide quantitative information on the state tissue undergoing HIFU treatment. Specifically, ultrasound can provide fast tissue property measurements, highly localized and sensitive temperature maps, as well as information on the presence and spatial distribution of cavitation activity [12]–[15].

The targeted tissues of currently approved clinical systems (e.g. uterine fibroids and prostate cancer) share common characteristics of relative target immobility and largely nondistorting soft tissue access. To move beyond these targets will require guidance that can account for tissue motion and heterogeneity. Guidance systems will need to have the ability to interrogate the treatment volume with high spatial and temporal resolutions to capture the lesion formation dynamics both at the target location and throughout the path of the HIFU beam. The ability to monitor and control HIFU therapy in mobile organs will be a major step towards the widespread acceptance of noninvasive IgHIFU in applications like liver cancer [16]. Efficient noninvasive targeting of liver tumors requires optimal refocusing of therapeutic HIFU beam to account for tissue motion and to avoid the collateral damage to any ribs in its path, a problem that has received increased interest in recent years [4], [6], [17]–[19]. In addition, numerous therapeutic arrays have been recently proposed for IgHIFU operations [7], [20]–[23].

The increased interest in therapeutic arrays, together with the availability of new transducer technologies allowing larger bandwidth and reduced cross coupling, have allowed for the introduction of dual-mode ultrasound arrays (DMUA) for imaging and therapy [3], [24]–[28]. Real-time DMUA operation has the major advantage of precise interrogation of the tissue response to the HIFU beam [3] due to the inherent registration between the therapeutic and imaging coordinate systems. This becomes particularly important with the increased interest in the use of cavitation in the enhancement of the therapeutic effects due to heat [29], [30] or due to drugs [31]. A real-time imaging system capable of detecting, localizing, and characterizing the nature of cavitation activity will be essential to achieve controlled lesion formation with high levels of safety and precision. Real-time imaging with DMUAs offers the potential of providing this kind of feedback.

This paper presents DMUA-based real-time *in vivo* demonstration of image-guided lesion formation and target tracking in small and large-animal models. In particular, the use of single-transmit focus (STF) imaging [3] at high frame rates to monitor the dynamics of lesion formation, including sporadic cavitation activity. In addition, speckle tracking of DMUA data is also shown to produce displacement fields suitable to characterize the motion/deformation patterns of the target tissue, e.g. pulsating artery. The *in vivo* images (and associated multimedia) demonstrate the DMUA's ability to provide anatomically correct images with sufficient dynamic range and spatial resolution to localize and capture the large variation in echogenicity associated with cavitation and/or tissue boiling. Results from imaging the same targets using an integrated diagnostic probe are also given to provide a reference for the evaluation of the performance of the DMUA imaging as a means of image guidance.

II. Materials and Methods

A. Transducer Assembly

We describe a fenestrated DMUA transducer shown in Figure 1 with a diagnostic probe positioned such that DMUA and diagnostic images are in the same plane. The diagnostic system is fully synchronized with the DMUA driver and is capable of producing real-time M2D-mode imaging of temperature and strain as described in [15]. Briefly, M2D is a generalization of M-mode imaging on the Sonix RP where we collected image frames with reduced number of A-lines to improve the frame rates in a region of interest, e.g. near a pulsating blood vessel. M2D imaging improves the correlation of the frame-to-frame ultrasound data in tissues undergoing significant deformations. M2D strain imaging has been used for monitoring thermal and mechanical tissue responses to pulsed HIFU beams *in vivo* [32].

1) DMUA Prototype Characterization—Piezocompos-ite transducer technology (Imasonic, Voray sur l'Ognon, France) was used for manufacturing a custom-designed DMUA for use in small-animal experiments as well as peripheral vascular applications. The array consists of two rows of 32, $1.2 \times 6.8 \text{ mm}^2$ elements spaced 1.5 mm apart on a concave, spherical section with a radius of 40 mm and an f_{number} of 0.86.

The therapeutic and imaging performance of a DMUA can be characterized by its therapeutic operating field ($ThxOF$) and imaging field of view ($IxFOV$) [3], [25]. The $ThxOF$ can be determined using CW or pulsed simulations of the array geometry as shown in [3] and is defined from the profile of the intensity focusing gain. For this prototype, the focusing gain drops gradually with a -6 dB isocontour approximately a circle with a radius of 4 mm centered around the geometric center. Steering beyond the boundaries of the $ThxOF$ results in unacceptable reduction in focusing gain at the target. The $IxFOV$ can be estimated using pulsed field simulations taking the transmit-receive impulse response of the array elements and the concave low f_{number} into account [25]. For this prototype, the manufacturer reported an average pulse length of 1288 nsec (56 nsec standard deviation) and an average fractional bandwidth of 51% (1% standard deviation). These values were confirmed in our laboratory using wire targets and steel block measurements. The $IxFOV$ for this array was estimated to cover an elliptical region extending by $\pm 12 \text{ mm}$ and $\pm 5 \text{ mm}$ in the axial and lateral directions (from the geometric center).

2) Diagnostic Probe—The DMUA probe shown in figure Figure 1a) has a fenestration allowing for the use of a diagnostic probe as shown. The use of a diagnostic probe allows us to take advantage of M2D-imaging capabilities described in [15]. It was critical that the diagnostic probe used be small to minimize the loss in active transducer surface area in therapeutic mode. A HST15-8/20 imaging probe connected to a Sonix RP scanner (Ultrasonix Medical Corporation, Richmond, British Columbia, Canada) was used to provide the diagnostic images. According to the manufacturer data sheets, the HST is a linear array with a mechanical focus at 16 mm and a bandwidth of 6 MHz. The HST probe was driven at a center frequency of 10 MHz.

B. Signal Transmission

The multiple-focus synthesis method, described in [33], is used to calculate the phases and amplitudes required to generate a desired pressure field. This synthesis technique, which requires the multiplication and inversion of several low order matrices, is carried out on a core i7 processor with Intel's Math Kernel Library and requires less than 1 msec processing time. Update rates of this magnitude provide the ability for extremely precise spatiotemporal control of the therapy process [34].

The calculated amplitudes and phases are conveyed to the array through a 32 channel, FPGA based, arbitrary waveform generator. Commands and data are transmitted to the waveform generators through a gigabit ether-net connection ensuring a low latency, high-bandwidth communication link. Each channel has a dedicated 10-bit DAC (DAC5652, Texas Instruments, Dallas, Texas) which generates a signal that is fed through a custom-built 10 Watt linear amplifier, a high power matching network, and delivered to the array through a micro-coaxial cable. This setup allows the array to produce focal intensities in the range of 5,000 – 12,000 W/cm² (in water), which is suitable for lesion formation in tissues at depths 0.6 – 2.3 cm.

The transmitter circuitry is also capable of supporting pulsed operation for imaging applications using the same amplifiers and matching networks used for therapy. This is due to the use of wideband amplifiers (0.5 – 10 MHz flat gain operation) and relatively wideband matching circuit topology allowing the use of the transducer bandwidth (2.6 – 4.6 MHz).

C. Signal Receive Chain

Each element on the array has an independent receiver and signal processing chain. Echo data from each element is passed through a software controllable analog front end (AFE) before being digitized by a 12 bit, 50 MSPS ADC (AFE5801, Texas Instruments, Dallas, Texas). The AFE allows dynamic control over the filtering and scaling of the analog signal to ensure the full dynamic range of the ADC is utilized without causing saturation. This control is crucial for monitoring tissue during HIFU therapies where dramatic changes in echogenicity can cause the strength of the received echo signal to vary by orders of magnitude. The 32 channels of digitized echo data are processed by two FPGAs (Virtex 5, Xilinx, San Jose, CA). The FPGAs work in parallel to pass the data through a reconfigurable 208 tap FIR filter and an optional 4x decimator before buffering the data in on-chip memory.

D. Image-based Monitoring Methods

The data received from the FPGAs through the gigabit ethernet is transferred to a GPU (GTX 285, NVIDIA, Santa Clara, CA) where massively parallel processing allows for additional filtering, beamforming, envelope detection, and log compression to take place in real-time. The processing times for the individual steps is shown in Table II for both STF and synthetic aperture (SA) imaging. With the high-performance computing (HPC) capabilities of our DMUA system, real-time implementation of SA and STF allows for monitoring the lesion formation process with high temporal and spatial resolutions. SA is used to image the media at the highest spatial and contrast resolutions within the *IxFOV* (based on traditional delay and sum beamforming). STF imaging is used primarily during therapy to provide high frame rate imaging for monitoring the dynamics of the lesion formation at the treatment site (with high specificity within and in the immediate vicinity of the HIFU focal spot). This property, together with the high temporal resolution of STF, allow for immediate and precision identification of tissue change in response to HIFU and/or other abnormal events in the treatment region. For the DMUA system described in this paper, the GPU allows for the collection and processing of full SA and STF imaging data at over 30 and 1000 frames per second, respectively.

E. Imaging Targets

1) Quality Assurance Phantom—A wire target quality assurance phantom (Model 040, CIRS, Norfolk, VA) was used for the characterization of the image quality of both DMUA and the diagnostic imaging probe when used in conjunction with the DMUA (in the configuration shown in Figure 1a). The phantom contains an array of wires as well as low and high contrast targets embedded in a speckle generating material. For purposes of this

paper, we have focused on the wire targets to establish the registration between the DMUA and the diagnostic imaging probe. To achieve this, the position of the HST probe within the transducer assembly was adjusted manually to: 1) maximize the brightness of the wire targets, and 2) maximize the alignment between the wire locations on both DMUA and HST images.

2) Femoral Artery and Vein in Adult Swine—The femoral arteries and veins of adult familial hypercholesterolemic (FH) swine (100–200 Kg) were imaged using the transducer assembly shown in Figure 1. A water filled bolus was used to couple the DMUA and diagnostic transducer to the animal (in a supine posture). The animals were anesthetized and mechanically ventilated during the imaging and therapy procedure in accordance with approved animal care protocol VSP001 (American Preclinical Services, Coon Rapids, MN.) SA DMUA imaging was performed in the course of image-guided lesion formation using HIFU for purposes of target identification and tracking.

3) Hind Limb in Copenhagen Rat Model—Lesion formation experiments were conducted on healthy rats (≈ 250 g in weight) as approved by the University of Minnesota IACUC protocol # 0802A26282. The rats were anesthetized using Ketamine and Xylazine before being placed in a temperature-controlled water bath at 33°C for the duration of the experiment. The setup was described in [32]. The imaging results described herein are intended to illustrate the different modes of monitoring and their potential advantages in image-guided lesion formation. In one experiment, high frame rate STF imaging is used to capture the spatiotemporal changes in echogenicity due to cavitation activity. In another case, STF and M2D imaging frames are synchronously acquired to illustrate the feasibility of DMUA operation in conjunction with other diagnostic image guidance. In each experiment, an anesthetized rat was placed in a holder attached to a 3D position system and immersed in a 33°C water bath. DMUA and diagnostic imaging were used to guide the rat such that the geometric focus of the array was located in the thigh, approximately 7–10 millimeters from the previously depilated surface.

III. Results

Imaging results are presented to demonstrate the capabilities of this DMUA prototype in identifying target locations and tracking the spatiotemporal characteristics of lesion formation dynamics. In most cases, DMUA images are provided together with images obtained using the HST15-8/20 probe positioned as shown in Figure 1. The images from both transducers are provided without post-beamforming image processing, each with its own dynamic range (based on intensity distribution).

A. Quality Assurance Phantom

Figure 2 shows images of the CIRS Model 40 QA phantom obtained using the HST15-8/20 probe (a) and the DMUA (b). Three of four wires placed within the displayed range are visible in both images. The fourth wire at -5 mm lateral and 50 mm axial is visible on the DMUA image, but not on the HST image. This is due to both the attenuation and the loss of focusing gain, especially due to elevation focusing of the HST probe. The visible wires common to both images were used to establish the spatial registration between the two coordinate systems. This is necessary due to the fact that the diagnostic array position within the DMUA fenestration, while secure, is not locked and is subject to small shifts and rotations. Registration between the two coordinate systems is necessary for comparison of results. This adjustment was performed as described in Sec. II-E1 to produce maximum visibility of the wires on the HST image.

The QA phantom images shown demonstrate the capabilities and relative merits of DMUA and diagnostic US transducers in the context of image guidance. For example, the HST probe provides superior axial resolution consistent with its larger bandwidth while the DMUA offers superior lateral resolution consistent with its low f_{number} . One can also observe the limited $IxFOV$ of the DMUA compared with the HST probe, which is predicted from the two-way focusing gain results [25]. One can observe the effects of the grating lobes at the edges of the $IxFOV$ of the DMUA in Figure 2b) (35 – 42 mm axial and 7 – 9 mm lateral), which result from the strong wire target reflectors near the geometric center. The visibility of the grating lobes can be controlled by including the element directivity in the beamforming equations [25] at the expense of the $IxFOV$.

A speckle cell size measurement [25], [35] was made by imaging a uniform speckle region in the CIRS Model 40 phantom (i.e. no wires and no contrast targets). Figure 3a) shows a 50-dB image of a uniform speckle region obtained using the DMUA prototype. Figure 3b) shows the speckle autocovariance function for the region defined by the $10 \times 5 \text{ mm}^2$ rectangular region shown in Figure 3a). The 6-dB speckle cell size for the DMUA was determined to be 0.25 mm and 1.60 mm in the lateral and axial directions respectively. These values are consistent with the appearance of the wire targets in Figure 2b). Similar measurements for the HST probe resulted in a 6-dB speckle cell size of 2.4 mm and 0.3 mm in the lateral and axial directions, respectively (consistent with the wire target appearance in Figure 2a). Based on imaging results from the QA phantom, we can summarize the imaging characteristics of the DMUA and HST transducers in the following table: The speckle statistics in a region near the geometric center were determined to be approximately Rayleigh with a signal-to-noise ratio of 1.85. These statistics, together with well-defined speckle cell dimensions, suggest that the beamformed RF data obtained using the DMUA transducer can be used in the estimation of tissue motion using speckle tracking. They also suggest that DMUA data will be suitable for quantitative imaging.

B. Targeting of Peripheral Vessels in Adult Swine Model

Figure 4 shows an example result (from hundreds of similar images taken) where both the DMUA and the HST probes were used to image the femoral artery and vein through a water bolus before, during, and after lesion formation. SA DMUA imaging is performed before and after each HIFU shot while STF imaging was used during the shot (at a PRF of 0.1 – 1 kHz). The upper left image in Figure 4 shows the B-Mode image of the artery and vein at 50 dB. The artery lies superficial to the vein and at an approximate depth of 15 mm below the skin. The specular reflector along the posterior wall of the vessel helps to highlight the boundaries of the artery. The DMUA image is shown in the upper right of Figure 4 and corresponds the region outlined in red on the diagnostic B-mode image. The DMUA image allows for clear identification of both vessels and the surrounding tissue. The specular reflector along the posterior wall of the artery is also present in the DMUA image. The fast acquisition rate of the SA images allows for tracking of the vessel dynamics. The bottom plot in Figure 4 shows the axial displacement in time along the white line in the DMUA image. The vessel pulsation is clear with an approximate frequency of 1.6 beats per second. The displacement on the proximal side of the vessel is 180° out of phase with the displacement along the distal side of the vessel, indicative of radial expansion of the artery. This high resolution spatiotemporal map of tissue motion could provide a key feedback component in accurate targeting and tracking of the vessel wall during HIFU exposure.

C. Image-guided Lesion Formation

1) Lesion Formation with STF Monitoring—The first experiment consisted of a 500 millisecond exposure at an *in situ* intensity of approximately $5,100 \text{ W/cm}^2$. The images in Figure 5a) & b) show the rat leg prior to and immediately following the HIFU shot acquired

using the HST (left) and DMUA (right). The DMUA images show a clear echogenic change in the focal region. The B-Mode images show some changes in the focal region, but the difference is muted compared to the DMUA. Changes in tissue echogenicity have been suggested as a means of monitoring tissue damage and therapy progression. These hyperechoic changes are associated with HIFU induced bubble activity. The DMUA STF imaging is ideally suited for monitoring these echogenic changes. This is primarily due to the match between the lateral dimensions of the induced lesions and the lateral extent of the imaging point spread function (psf). Figure 6 displays M-mode echo data from a 6 mm axial segment centered at 0 mm laterally and 40 mm axially. Baseline data was collected for 1 second before the therapy shot was delivered between 1 and 1.5 seconds. The first echogenic change appeared 161 milliseconds into the therapy followed by sporadic echoes within the HIFU focus indicative of cavitation activity. The video included in the multimedia section shows the progression of the echogenic changes throughout the treatment and clearly illustrates the sporadic nature of the bubble dynamics in space and time. This is also illustrated by the close up M-mode (1100 – 1400 msec) shown in Figure 6. One can see five transient events starting at ≈ 1161 msec each resulting in a sudden change in echogenicity followed by a drop in echogenicity with highly dynamic (but more correlated) changes in the echo location and/or amplitude. This behavior is consistent with the creation and depletion of cavitation bubbles in the focal region. The high frame rate STF captured both the fast and slow dynamics of this process with high spatial resolution as can be seen from both the M-mode and the multimedia results shown.

This case illustrates another noteworthy issue where continuous monitoring using DMUA may prove essential. The animal twitched its leg approximately 400 msec into the therapy introducing a large global shift resulting in loss of echo at 1400 msec as can be seen on the M-mode image as well as the video. It also illustrates that the DMUA image has sufficient dynamic range to capture the large variation in backscatter energy due to cavitation activity and motion. In this case, the echo intensity at a depth of 38.6 mm and $t = 1.362$ sec was 34.5 dB higher than the base line intensity at the same location before HIFU. The intensity dropped by 13 dB below baseline during the twitch.

2) Lesion Formation with STF/M2D Monitoring—The second rat experiment consisted of a 750 millisecond exposure at an *in situ* intensity 5,500 of W/cm². Figure 7 show the DMUA SA (40 dB) and M2D grayscale images (50 dB) before and after therapy. In this case, both the DMUA and the diagnostic B-Mode captured an echogenic change at the focus. The video attached in the multimedia section offers a frame by frame comparison of the DMUA STF image and the diagnostic B-Mode image taken during therapy. Both imaging modalities show clear changes in the speckle pattern prior to the large echogenic change.

The STF M-Mode image in Figure 8 corresponds to a 6 millimeter axial line segment centered at 0 mm laterally and 40 mm axially. As before, baseline data was collected for 1 second before therapy began. The M-mode data shows a small displacement due to the acoustic radiation force as well as a strong echogenic change approximately 600 msec into the therapy (typically indicative of tissue boiling). In this case, the echogenic changes due to lesion formation exhibited less sporadic behavior than the previous case even though the exposure is higher, both in terms of focal intensity and shot duration. This experiment represents a situation often encountered in practice where the change in echogenicity is very subtle before the strong change observed upon tissue boiling. The boiling event often indicates *overexposure* where the excessive HIFU energy is used for forming the lesion. In fact, we have run numerous experiments where thermal lesions were formed without reaching the boiling event seen here. In these cases, temperature imaging or other tissue

characterization imaging methods may provide better indicators of lesion formation that avoids *overexposure*.

IV. Discussion

The major goal of this paper is to introduce the DMUA approach to IgHIFU as a platform technology, which allows high resolution spatiotemporal visualization of HIFU-tissue interactions in real time. To the best of our knowledge, the results shown in this paper represent the first real-time demonstration of DMUA use in monitoring the lesion formation dynamics (including cavitation activity) using grayscale and RF data *in vivo*. We have also presented results that demonstrate the feasibility of using DMUA image data in the identification and tracking of peripheral vessels *in vivo* in a large animal model, with significant practical implications in IgHIFU.

We emphasize that neither the DMUA nor the HST images shown in this paper are of diagnostic quality. This is primarily due to imaging through the water bolus which, together with the large aperture of the DMUA, cause reverberations to interfere with the imaging data in the region of interest. For example, a standard linear array probe in direct contact with the swine skin, produces images of the femoral artery and vein far superior to those shown in Figure 4. Despite these limitations, the results shown in this paper illustrate two opportunities for real-time feedback possible with DMUA imaging. First, the feasibility of speckle tracking using beam-formed DMUA echo data as illustrated in Figure 4b). This will open the door for the implementation of real-time US thermography [15] and elastography [36] using DMUA data allowing for tissue property measurements at the lesion formation site with specificity unmatched by any other image guidance mechanism. Figure 5 is one illustration of this point where one can see the change in echogenicity at the HIFU focus location is visible on the DMUA images, while hardly seen on those obtained using the diagnostic probe. In addition to the inherent registration between the imaging and therapy beams, the high focusing gain and lateral resolution of the DMUA maximize the sensitivity and specificity to localized bubble activity within the therapeutic HIFU focus. Second, the feasibility of detection and localization of abrupt changes in echo signals from the treatment site is illustrated by Figure 6 and 8.

The real-time imaging results from *in vivo* lesion formation experiments shown in this paper illustrate the need for continuous monitoring of lesion dynamics. For example, even though the intensity levels were comparable in both experiments, the nature of the cavitation activity appeared to be markedly different. In one case, sporadic activity was observed with what appears to be generation and depletion of bubbles. In the other, a gradual structural change was observed for the first 600 msec before tissue boiling occurred resulting in a significant increase in echogenicity as observed on both DMUA and HST imaging. The high frame rate STF imaging ensures anomalous events are recognized before they can lead to unintended damage. In addition, high frame rate STF could also provide the spatial and temporal feedback for the initiation and control of bubble clouds to improve the heating rate as suggested in [30]. High frame rate STF imaging can also be used in adaptive refocusing in the presence of strongly scattering objects. For example, the image-based refocusing approach described in [18] can now be implemented in real time where hundreds of refocusing vectors can be safely tested in a fraction of a second before choosing the optimal vector.

While the DMUA system described herein is being used in pre-clinical real-time IgHIFU applications, there continue to be active areas of research to move closer to clinical use. One area of research is in how to further refine the DMUA imaging capability. The low f_{number} array combined with the transmit/receive capability of this DMUA system provide an ideal

platform for reconstructive imaging. The ability to obtain high resolution images would greatly enhance targeting as well as provide additional information on pre- and post-treatment lesion site analysis. With the availability of HPC FPGA/GPU platforms for post-beamforming processing of DMUA data, it will be possible to employ quantitative imaging methods such as those described in [36] for mechanical property measurements, in [15] for thermal property measurement, and in [37] for nonlinearity imaging. Of course, traditional and modern quantitative imaging techniques [38]–[41] can still be used to characterize structural changes due to lesion formation. With these quantitative imaging methods, it will be possible to use the DMUA as a *theranostic* system providing *diagnostic* quality imaging of the tissue response to *therapeutic* HIFU.

V. Conclusions

Real-time imaging of *in vivo* targets in small and large animal models demonstrate the potential advantages and unique features of the DMUA approach to IgHIFU applications. First, DMUA images capture anatomically-correct features consistent with predicted and measured psf. These results are further corroborated using a diagnostic imaging probe with a co-registered imaging slice in a synchronous manner. Images from QA phantoms provide quantitative support for this conclusion. Second, high frame rate STF imaging during lesion formation capture the spatiotemporal changes in echogenicity associated cavitation activity during therapeutic HIFU exposure. Examining the M-mode data and associated multi-media files from the experiment described in Sec. III-C1 shows how DMUA imaging captures the spatial (axial and lateral) and temporal changes in the echoes around the focal region with over 45 dB dynamic range. This form of feedback can be used to achieve fine control of the lesion formation process with mm precision and with minimal collateral damage. The latter is an inherent advantage of STF imaging as we have described in [3]. Combining the spatial localization of HIFU-tissue interactions with the high temporal resolution of the image-based feedback will allow for the real-time implementation of feedback control strategies [34] providing high levels of safety and efficacy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

a) DMUA-diagnostic transducer assembly. The diagnostic probe is positioned within fenestration with its imaging slice shown. b) The active elements of the DMUA and a coarse grid centered at the geometric center demonstrating the DMUA imaging slice.

Fig. 2.

Images of the CIRS Model 40 phantom: (a) 65 dB image using the HST15-8/20 and (b) 45 dB SA image using the DMUA.

Fig. 3. Speckle cell size measurement for 3.5 MHz DMUA prototype. (a) 50 dB from a uniform region in the QA phantom and (b) speckle autocovariance function with the 6-dB contour shown.

Fig. 4.

Real-time imaging of peripheral vessels in adult swine: a) B-mode image of artery and vein (left) and DMUA synthetic aperture image of area highlighted in red. b) Axial displacement (in μm) of vessel along white line on DMUA image.

Fig. 5.

B-mode (HST) and SA DMUA images: a) prior to therapy b) immediately following therapy for the STF only monitoring case. Note the pronounced change in echogenicity on DMUA image while the change is muted on the HST image.

Fig. 6.

M-mode STF data (1 kHz PRF) from the lesion location (40 dB). Top: Full acquisition over 2500 msec with HIFU turned on at 1000 msec and animal twitch at ≈ 1400 msec. Bottom: Two close ups showing 300 msec during shot starting at 1100 msec (left) and 50 msec starting at 1140 msec, which shows the first cavitation event.

Fig. 7. M2D grayscale (HST) and SA DMUA images: a) prior to therapy b) immediately following therapy for the STF/M2D monitoring case. Both systems show pronounced change in echogenicity at the lesion location.

Fig. 8.
M-mode STF data (91 Hz PRF) from the lesion location.

TABLE I

Time (in msec) for each processing step on GPU.

Processing Step	STF	SA
Memory Transfer	0.2	3.2
64 Tap FIR Filter	0.3	8.1
Beamforming	0.5	11.8
Envelope Detection	0.04	
Log Compression	0.02	

TABLE II

Imaging characteristics of DMUA and HST Transducers.

Transducer	DMUA	HST
Center Freq (MHz)	3.5	10
Bandwidth (MHz)	2	6
Lateral PSF (mm)	0.25	2.4
Axial PSF (mm)	1.6	0.3