Broadband Dual-Mode HIFU Array for Therapy Monitoring and 3D Target Motion Estimation

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***Abstract*—This project implements previously developed techniques for guiding and monitoring thermal HIFU therapy using imaging arrays with a spherically shaped therapeutic array for dual-mode operation. Three-dimensional motion tracking, thermal strain measurement, and radiation force rebound measurement within the HIFU steering volume are performed using only the therapy array. The techniques have typically been studied for conventional ultrasound imaging using linear, curvilinear, or phased arrays which are usually placed coaxially in the center of the HIFU array. While the dual-mode approach does not provide the image quality and wide field of view of an imaging array, the perfect co-registration of the therapy array, and its 3D view of the region of interest present a valuable opportunity for ultrasound-guided focused ultrasound (USgFUS) therapy systems. A family of Sonic Concepts broadband spherically-focused HIFU array transducers, driven with the Verasonics HIFU-configured ultrasound system, is used to assess real-time performance of the dual-mode approach, in simulation and experiment. Simulations using the Verasonics acquisition software with a set of point scatterers produce the RF backscatter data used by the monitoring algorithms. The particles are displaced in time using motions that mimic the true or apparent displacements of tissue-like media either in translation, heated by a HIFU focus, or deformed by a radiation force beam. Preliminary experiments using a 128-element HIFU array and a scattering hydrogel phantom indicate that the simulations are effective for studying a range of tradeoffs in transducer design and therapy monitoring approaches.**

Keywords—HIFU, FUS, ultrasound therapy, therapy monitoring, dual-mode array, motion detection, ultrasound thermometry, acoustic radiation force

I. INTRODUCTION

High Intensity Focused Ultrasound (HIFU) therapy is no longer a new therapeutic modality. It has been well studied as a thermal and mechanical method of ablating tissue, as well as targeted drug delivery mediated by microbubbles or moderate heating (hyperthermia), and is beginning to enter ever more widespread clinical use. Though initially guided by ultrasound, the intensive development of MRgFUS (Magnetic Resonance [imaging] guided Focused Ultrasound) systems has rapidly advanced clinical adoption, and exciting trials are underway for many pathological indications.

As with any noninvasive therapy, the need for accurate and reliable guidance and monitoring is essential. Simulation for detailed therapy planning and delivery is not currently practical for ultrasound therapy because of extremely large set of unknowns in the acoustic and biological model; thus, real-time feedback is essential. MRgFUS provides excellent 3D imaging, even in the presence of bone, and is also capable of providing quantitative 3D maps of relevant tissue change parameters, including temperature rise and change in elasticity. Though MR is the current gold standard for guidance, monitoring and assessment, it is expensive (compared to ultrasound) and the medical physicist must still tradeoff frame rate for resolution and accuracy in measurement. Ultrasound guidance remains of great importance to the broader adoption of focused ultrasound therapy.

Several tissue change properties can be exploited for monitoring with ultrasound: change in sound speed, change in shear stiffness, and others (change in local attenuation, change in tissue nonlinearity parameters, appearance of cavitation microbubbles and boiling bubbles, etc.). Unfortunately, many of these properties are weakly dependent on the measurable parameters, and other clinical realities compound the ultrasound guidance and monitoring problem. Tissue motion is inevitable, and very large natural displacements from breathing or cardiac pulsatility can disrupt therapy as well as monitoring efforts. Therefore, any proposed method should be capable of compensating for tissue motion, and heterogeneity through high frame rate and accurate feedback. Ultrasound can address many of these challenges.

Ultrasound imaging using conventional approaches is good for targeting and visualization of the region of interest, but the large apertures and long focal distance typical of extracorporeal HIFU applicators require imaging with a long standoff distance. Furthermore, the need to fit mechanically within space subtracted from the HIFU array's active area usually limits the aperture available for imaging, thus reducing image quality compared to radiological expectations. Finally, 3D imaging is not practical for now except for very expensive arrays, or with mechanically swept "4D" arrays, which are difficult to use for many monitoring approaches that require very highly correlated sequences of acquisitions. This challenge presents an opportunity for motion detection and therapy monitoring using the HIFU array itself. Though HIFU arrays are not able to image outside a relatively small steering range, they are capable of accurately registered sensing in 3D, and many of the monitoring techniques developed for conventional arrays can be implemented with the therapeutic array.

High power array elements are usually narrow band for the sake of efficiency; self-heating can be a significant limitation when tens of Watts are delivered continuously from each element that may have an active area on the order of a square centimeter. Imaging typically requires broad band

performance: there is likely a benefit to building a HIFU element that is *both* (relatively) broadband and efficient.

Furthermore, for monitoring to be practical using the therapy array, the electronic drive system must also be capable of both high energy delivery and pulse-echo imaging, and be capable of rapidly switch between those modes.

II. Background — HIFU Arrays

Many clinical and acoustic performance constraints force engineering tradeoffs when designing therapeutic transducer arrays for tissue ablation, mechanical cavitation, histotripsy and radiation force applications. Key performance parameters include acoustic power density, steering range, operating band and conversion efficiency. Prior work describes a family of transducer designs over a range of configurations with an emphasis on reducing grating lobes within and outside the steering range using an Archimedean spiral geometry.[1] Such transducer elements have been built with high efficiency (over 80 %) over a wide relative bandwidth (over 40 %) in the 1 – 10 MHz range of center frequencies.

Additionally, the steering range (targetable volume boundary) achievable with such arrays can be very well approximated by taking the intersection of all of the individual beams from each element. Consequently, it is easy to see that the steering range scales inversely with element diameter and frequency. Prior experimental work characterized a 128-element array, with a *f*-1 focal characteristic with both radius of curvature and aperture of 150 mm. For that 2 MHz array, the steering range centered on the geometrical focus was about 3 cm wide, and provided on the order of 30 x 30 independent pixels in the X-Y plane, and on the order of 5 - 7 ablative pixels in depth, but on the order of 30 pixels for imaging in the axial dimension due to the temporal resolution of an imaging pulse, for a total imaging volume with about 30,000 voxels.

Array elements must be paired with other system components such as cables, connectors, circuit board and matching networks; ideally, these are designed to maximize the efficiency and bandwidth of the transducer while also matching each individual driving channel to a 75 Ohm / 0 degree load impedance. The matching circuit network enclosure is designed to plug directly into the Verasonics system connectors.

Although the HIFU-configured Vantage System is able to deliver high energy ultrasound signals over a wide band, it is able to deliver on the order of a thousand Watts of continuous power indefinitely, at up to 5 MHz. This investigation considers a family of transducer designs operating within that band, at center frequencies of 1.1, 2.0 and 4.0 MHz, and element counts of 128, 256, 512 and 2048, for a total of 11 different configurations (2,048 elements x 1.1 MHz is not available) See Figure 1.

The elements and associated tuning networks can always be designed and built with cost / performance tradeoffs. For a given geometrical configuration and element count, the tradeoff is usually between bandwidth and efficiency. The following curves illustrate the frequency dependence of efficiency and bandwidth for a set of 2 MHz transducer designs suitable for use in this application.

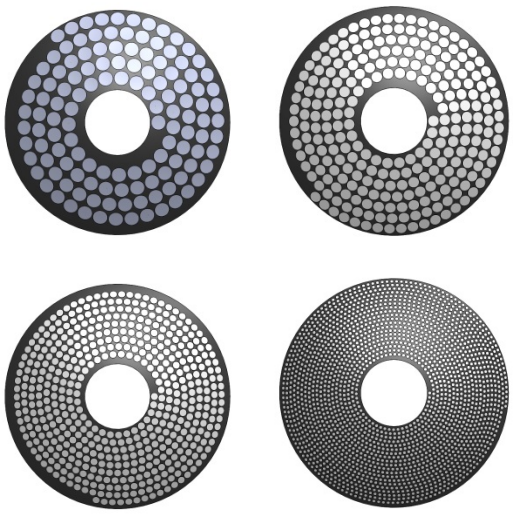

Figure 1. 128 element (upper left), 256 element (upper right), 512 (lower left) & 2,048 element (lower right) configurations.

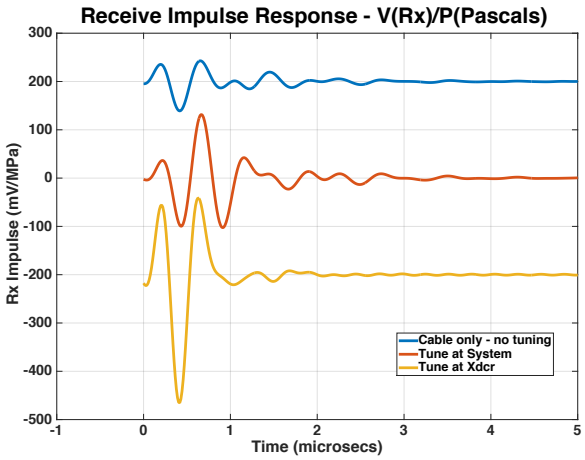

Figure 2. Impulse responses for different electrical tuning approaches (offset for clarity, but to the same scale): cable only, tuning at the system end of the cable, and tuning at the transducer before connecting the cable. Tuning at the transducer is always best, because of the large impedance mismatch between cable and large elements. This comparison also illustrates how poorly an un-tuned transducer performs at the end of a (3 m) cable, in terms of efficiency, impulse duration and bandwidth.

The frequency dependent transmit efficiency curves for the designs in Figure 2 are presented in Figure 3. While the cost of efficiency can be evaluated by the transducer manufacturer, the benefits of bandwidth require consideration of the ultrasound application, the scattering properties of the target, and the signal processing algorithms to assess. This work examines the role bandwidth plays in the accuracy of the monitoring and motion estimation algorithms explored here for thermal ablative therapy in scattering media with saturated speckle, and with a small number of relatively strong point scatterers in addition to the speckle.

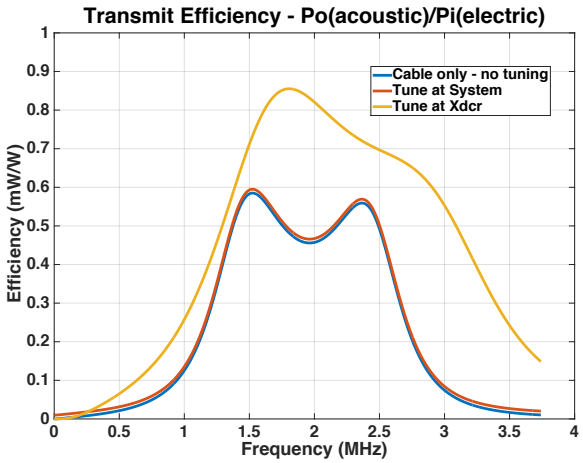

Figure 3. Efficiency versus frequency for the same transducers as in Figure 2. Curves for the Cable-only and system side tuning are identical, but separated for visualization.

III. Background – HIFU Ultrasound System

The Verasonics Vantage ultrasound system, configured with HIFU drive capability, can alternate rapidly between high-energy ultrasound delivery into a HIFU array and imaging acquisition and processing. In these experiments, the 256-channel Vantage is used with the H-302 128-element HIFU array, operating at 2 MHz, and an IP-104 128-element phased array imaging transducer with passband centered at 3.5 MHz.

The HIFU-configured transmitters are capable of delivering 8W into 50 Ohms continuously, easily reaching ablative intensities in the array's focal zone. The IP-104 phased array is capable of imaging to 20 cm depth through tissue. When located in the center of the HIFU array, a significant portion of the acoustic path is usually water, or another low attenuation coupling medium. The array may be inserted part way into the HIFU "bowl" before it will interfere with the HIFU beam.

Prior demonstrations using this arrangement have demonstrated that acoustic travel time is the dominant limitation on frame rate, though the software beamformer has many more pixels to reconstruct when the imaging sector extends to 20 cm. To minimize the number of transmit receive acquisitions, broad unfocussed beams have been used to ensonify the region. For example, on the order of 10 phase-tilted and apodized spherically expanding beams are effective in a phantom; realistic tissue environments may require 40 to 60 broadly focused beams to provide higher image quality. If the HIFU array can be used for monitoring therapy and quantifying motion of the target region, the requirements for fast imaging frame rate are significantly reduced, because the number of transmit/receive acquisitions using the HIFU elements can be as few as three per frame for motion detection and HIFU thermometry, and on the order of a Doppler ensemble (10 – 30 pulses) for radiation force measurements.

IV. Motion Tracking Using Directed Beams

Motion detection of the target region is essential in HIFU therapy because the HIFU focal region is typically very small compared to typical target tissue motion, and delivery of a well-controlled dose depends on reliable registration of the HIFU beam with the desired target. To mitigate targeting risk, many clinical studies have been conducted by tracking respiration and then gating therapy delivery with phases in the respiratory cycle where motion is slow, typically corresponding to a displacement extreme. Alternatively, breath holds can be used, often under anesthesia, for well controlled therapy delivery periods with little movement. Ideally, to minimize treatment time and minimize risks of under and overtreatment, it is desirable to compensate for the motion by steering the focal spot either electronically or mechanically. Motion quantification in three dimensions is necessary in such motion compensation schemes. [2] [3]

Pioneering work in this application using HIFU arrays was performed by Pernot et al. [4], in which four subarrays were formed from within the HIFU array, and used to interrogate the medium using an RF correlation tracking approach. Because the subarrays provide linearly independent vectorial motion measurements, the results can be combined to estimate the motion anywhere in the steering volume of the array. Several experiments were undertaken by the group in phantoms and *in vivo* [5], confirming the efficacy of the approach. A similar method is implemented here, with the goal of providing a pre-packaged solution for this application, using cross-correlation of the RF data from one or several elements within a subarray to obtain vectorial components of motion along the axial direction. The magnitude and phase of the analytic signal obtained from the RF backscatter data are also used in estimating motion given a time series of frames, to compare approaches.

Three subarrays were chosen in regions 120 azimuthal degrees apart, as illustrated in Figure 4. The beams emanating from these element groups are simply drawn as cones to depict how the different view angles will be sufficient, in principle, to compute vector motion in the reference coordinate system.

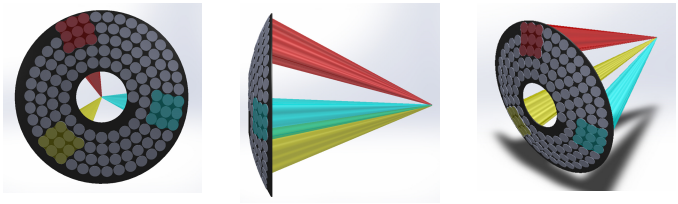

Figure 4. Three sub-array "clusters" of elements in the 128-element HIFU were used to transmit and receive imaging ultrasound pulses for motion measurement. These clusters have acoustic directions that are sufficiently linearly independence to provide 3D displacement information.

Steered and collimated ultrasound beams can be used to obtain the motion of a rigid region of interest along the beam direction using frame-to-frame correlation of the RF waveforms, or of image speckle (RF magnitude). Such techniques can detect small displacements using medium speckle, but rapidly decorrelate with displacement, requiring a very fast pulse repetition frequency (PRF) and phase-based methods for high sensitivity, such as those used in Pulse Wave Doppler methods. [6] In our experiments, 20 mm/s velocities are readily measured at a frame rate of 20 Hz. The presence of strong separated scatters in the ROI relaxes requirements on PRF, because the scattering from these targets remains coherent over large displacements and dominates the rapidly decorrelating speckle background. If the motion is small enough between frames, the phase can be used to measure displacements of a small fraction of the wavelength.

V. ARFI Monitoring of Viscoelastic Changes

HIFU therapy induces many tissue property changes which can be measured using ultrasound tissue characterization methods. Ablated tissue is much stiffer than untreated tissue, and elastographic methods using acoustic radiation force are particularly well suited to monitoring therapy progress. Here we describe the fundamentals of Acoustic Radiation Force Imaging (ARFI), [7] which is very practical for dual-use array applications since the therapeutic focus is by definition ideally registered with interrogation beams emanating from the same array. A high intensity focused ultrasound beam is able to transfer some of its momentum into an attenuating medium. The radiation force resulting from a long pulse, typically lasting a few hundred microseconds, can be used to "push" on the medium remotely, primarily at the beam focus. The resulting displacement can be measured using strain imaging methods. These are again based on correlating the ultrasound backscattered signal between successive interrogation pulses, typically short imaging pulses. The parameters characterizing the displacement and restoration of the medium to its original position provide local information on stiffness, attenuation, reflectivity, and viscoelastic properties, many of which change as tissue is thermally ablated using HIFU therapy. [8], [9]

VI. Thermal Monitoring via Strain Imaging

Thermal ablative HIFU therapy typically destroys tissue by raising its temperature sufficiently to denature tissue proteins. This "cooking" of tissue occurs within milliseconds once the temperature has exceeded about 60 degrees C. To ensure necrosis in the desired target regions while maintaining non-targeted tissue at relatively safe temperatures, remote monitoring of medium temperature for real-time feedback is highly desired.

Acoustic strain measuring techniques have been used to detect the very small changes in apparent position of scatterers within a medium whose temperature is changing. Water-like tissue expands as it warms, moving scatterers apart as the medium becomes less dense. Compressibility decreases (stiffness increases) up to a given temperature, beyond which compressibility does not change very much. These two effects result in a small and multivalued dependence of the sound speed on temperature, and consequently on the apparent position of scatterers as the medium changes temperature throughout the therapeutic range. Nevertheless, these changes can be detected and mapped using RF speckle correlation methods to produce thermal strain images that resemble the acoustic intensity beam pattern of the HIFU beam. [10]-[12]

VII. Notes on Implementation

The ultrasound sequence for alternating between therapy delivery and monitoring depends on th eapplication. Sequence diagrams for the three methods considered here are presented in Figure 5.

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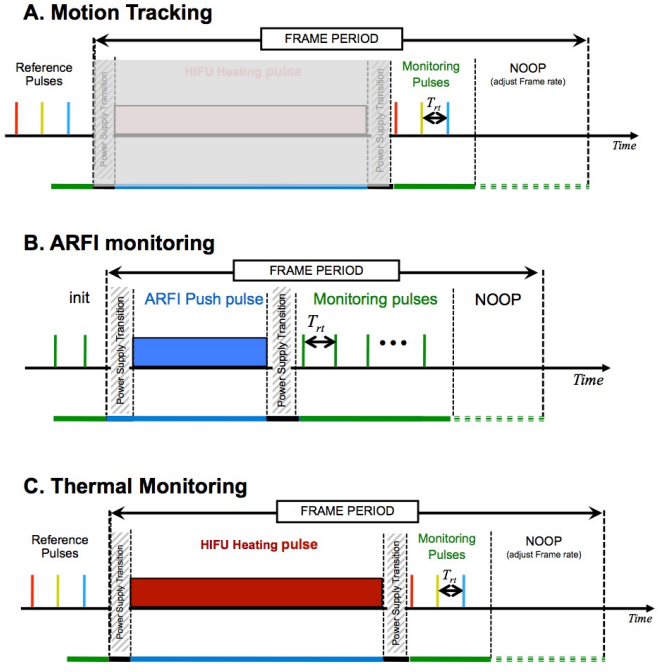

Figure 5. Three sequences are diagrammed for A. motion tracking, B. ARFI monitoring for change in stiffness, and C. temperature change monitoring using the apparent strain induced by heating-induced changes in sound speed.