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Flexible Integration of Both High Imaging Resolution and High Power Arrays for Ultrasound-Induced Thermal Strain Imaging (US-TSI)

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Abstract

Ultrasound-induced thermal strain imaging (US-TSI) for carotid artery plaque detection requires both high imaging resolution ($<100\ \mu\text{m}$) and sufficient US induced heating to elevate the tissue temperature ($\sim 1\text{-}3^\circ\text{C}$ within 1-3 cardiac cycles) in order to produce a noticeable change in sound speed in the targeted tissues. Since the optimization of both imaging and heating in a monolithic array design is particularly expensive and inflexible, a new integrated approach is presented that utilizes independent ultrasound arrays to meet the requirements for this particular application. This work demonstrates a new approach in dual-array construction. A 3D printed manifold was built to support both a high resolution 20 MHz commercial imaging array and 6 custom heating elements operating in the 3.5-4 MHz range. For the application of US-TSI on carotid plaque characterization, the tissue target site is 20 to 30 mm deep, with a typical target volume of 2 mm (elevation) $\times$ 8 mm (azimuthal) $\times$ 5 mm (depth). The custom heating array performance was fully characterized for two design variants (flat and spherical apertures), and can easily deliver 30 W of total acoustic power to produce intensities greater than $15\ \text{W}/\text{cm}^2$ in tissue target region.

I. Introduction

Atherosclerosis describes the formation of a pathological lesion in the inner lining of arteries. This lesion known as a plaque can have a range of features. Vulnerable plaques (VP) are those plaques prone to rupture which leads to stroke or myocardial infarction. VP are thought to consist of a lipid-rich core separated from the arterial bloodstream by a thin fibrous cap [1]. There is a need for early non-invasive identification of potential VP so that preventative treatment can be implemented [2].

Magnetic resonance imaging (MRI) has shown to be able to identify the lipid-rich necrotic core of plaques [3] and can help assess VP vulnerability [4]. However, it requires long

imaging times and the confined imaging enclosure can cause patient anxiety [5]. Ultrasound-induced thermal strain imaging (US-TSI) offers the potential for noninvasive lipid detection in atherosclerotic plaque [6] and temperature monitoring [7]. US-TSI exploits the fact that the dependence of sound speed on temperature is unique for lipid based tissues compared to water based tissues. Detection of lipids in carotid artery plaque using US-TSI requires both high imaging resolution and elevating tissue temperature by 3°C within 1-3 cardiac cycles to produce a detectable change in sound speed in tissues [8].

In addition to the need for combined imaging and heating for TSI, there are other modalities such as acoustic radiation force imaging (ARFI) [9], shear wave imaging (SWI) [10], and targeted drug delivery methods [11] which require a combination of high resolution imaging and high power delivery. However, there exists a tradeoff between high bandwidth imaging which usually requires a mechanically damped array, and high continuous power delivery which requires a minimally damped transmission. Although specialty multipurpose designs [12], [13] have been developed, there are limitations in US-based heat delivery due to both transducer heating and system power supply limits. As a practical example from earlier experiences with a custom designed heating array built alongside an imaging array, a standard commercial imaging system power supply could only provide a total of 17 W of total acoustic output power for 2 s before shutting down the entire imaging system. This is probably a typical performance for systems designed for pulse-echo imaging and, as we will report, this is generally inadequate even for modest heating over an intended X-Y region of 2×8 mm at a depth of 20 -30 mm.

Optimization of imaging and heating in a single array or set of arrays is challenging. Ideally, a single array could be used for this effort, but using the same array for imaging and heating can limit the effectiveness of the latter [14]. Our flexible approach utilizes independent US arrays which can be mechanically joined together in a low cost, high performance manner to suit the study application. In this work we show how a relatively inexpensive and flexible dual purpose imaging/heating system may permit high quality US-TSI for widespread use in the future.

The approach presented here is unique: it combines high resolution dedicated imaging array with a high power custom insonification array to produce a particular beam function. Low cost and rapid integration/adaptation are possible which permits high investigational flexibility. The prototype developed for US-TSI is designed to heat a 2×8 mm X-Y tissue region at a depth of 20-30 mm to achieve a 3°C temperature rise in 2 s and permits simultaneous imaging with a wide band array.

II. Methods

A prototype consisting of a custom array of elements mounted on a custom manifold was developed and validated to provide heating for US-TSI. This section includes a detailed description for the diverse spectrum of materials and methods employed in the prototype design process.

A. System

The US-TSI system presented in this paper is comprised of four parts (Fig. 1): the imaging array of choice (P), the US heating array elements (e), the single output power source (RF), and the splitter electronics (Split). A key contribution of this work is combining a 3D printed manifold designed to support and align the heating elements with a high efficiency RF power splitter which simplifies the power source requirements for this application. This heating manifold can be easily adapted to a chosen system. In this work, we demonstrate this flexible integration using a commercial high-frequency ultrasound imaging system (Vevo

2100, FUJIFILM VisualSonics Inc., Toronto, Canada). Ideally a linear heating array could be used, but prior to that development we use a collection of single elements, all driven with the same phase with overlapping beam foci. We chose the frequency band of 3-4 MHz in order to conservatively optimize power delivery for a total beam path length of 35 to 40 mm and element sizes of 6-10 mm in order present a 50 Ohm load to the RF driving source. These choices are explained in detail in the following sections.

B. Heating Transducer Design and Construction

The heating transducer was designed to provide a 3°C temperature rise in 2 seconds in a tissue volume (at depth of 20-30mm) of approximately 2 mm by 8 mm in a X-Y footprint, with 5 mm or more in Z, while providing approximately a 50 Ohm electrical load to the RF source. The best operational frequency was first determined, then the size of the elements was selected, and, finally, the number and position of heating array elements were established.

1) Optimal Heating Frequency and Element Size—It is assumed for simplicity the absorption coefficient, α , is linear with frequency, the flat circular aperture with diameter D produces a natural focus at a depth $z = D^2/4\lambda$, where z is the total beam path to target from heating element, and λ is the wavelength. The heating function is directly proportional to the product of beam intensity and absorption coefficient; however, an acoustic frequency change affects the magnitudes of absorption coefficient and intensity with opposing trends at a given depth. An estimate for an optimalinsonification frequency can be found by solving $d[2\alpha I]/df=0$. The relative intensity at the focus, I , is $4\exp(-2\alpha' Cfz)$. The frequency dependent expression $\alpha' Cf$ replaces the absorption coefficient, α (Np/m). Thusly, the absorption coefficient, α' is in units of dB/cm/MHz, constant C is $(20\log(e))^{-1}$, and f is in units of MHz. The estimate for the optimal frequency is:

$$f_{flat} = \frac{10 \log(e)}{\alpha' z}, \quad (1)$$

where z is in units of cm. Early assessments were made for this best frequency, but some corrections were made using the average beam path absorption (e.g. $\alpha' = 0.33$ dB/cm/MHz) which took into account a near field water stand-off path and a (total beam path) target depth of 37 mm from heating element. We found the optimal frequency to be 3.56 MHz using these calculations. We observed that the maximum frequency (or depth) calculation does not depend on the absorption coefficient at the heating depth, but rather the average absorption along the beam path before reaching the intended site at the heating depth.

After constraining the operating frequency to 3.5 MHz, the electrical impedance to 50 Ohms, and the total focus path length of 35 to 40 mm, an aperture diameter of 8.8 mm was chosen for a first set of flat aperture heating elements. To achieve an appropriate temperature rise, the intensity should be 15 W/cm² in a 2×8 mm target region. Approximately 2/3 of the power is lost due to path loss and 3/4 of the remaining power is lost due to beam diffraction. Using these assumptions (with detailed rationale described later), an estimated upper bound for total power from the entire transducer set was determined to be ~ 30 W total acoustic power for 2 second periods. As a result, we chose to construct a heating transducer set with six elements that each provided an acoustic power of 5 W.

We extended the above analysis for the spherical aperture case. By combining the geometry of a spherical aperture [15] and previously described optimal depth calculations [16], [17] the optimal operating frequency for a spherical aperture can be found. We examined the highly curved spherical aperture with $kh > 4$. Here k is the wave number and h is the depth

of the spherical aperture, or $z(1 - \cos\theta)$. In this highly focused case, it can be shown that relative intensity at a focus depth z is $(kz)^2(F(1-\cos\theta))^2\exp(-2\alpha' C_f z)$ where F is the fraction of the active spherical surface and θ is the angle formed with a vertex at the geometric focus depth subtended by the spherical aperture centerline and a line from focus to aperture edge. The optimal frequency for delivering heat to a given depth z for a highly curved spherical aperture is:

$$f_{\text{spherical}} = \frac{30\log(e)}{\alpha' z}, \quad (2)$$

which is a very similar to (1) above. From (2), it is evident that the optimal frequency is three times the frequency predicted for a flat aperture, and (as shown in more detail later) this seems reasonable since the beam produced by the spherical aperture considered produces a beam energy density near its central axis which is a significant multiple of the flat beam.

2) Transducer Modeling and Construction—The heating elements should be both capable of relatively high continuous acoustic power output with minimal internal heating and high heat capacity. Some other alternate materials could be used, however since a substantial increase of the transducer temperature ($> 60^\circ\text{C}$) is not anticipated for this particular application, high dielectric constant (and high figure of merit [18]) PZT-5H material was selected with silver (Ag)-epoxy as the electrical contacts to circuit wiring. An air backing is desired, but with an adequate front layer matching to assure front port transmission efficiency. Although narrow band operation is acceptable, a narrower bandwidth increases the difficulty in matching element output at a specific frequency; therefore a modest bandwidth was chosen to assure that all elements are within a 3 dB range.

The transducer material (PZT-5H, Boston PiezoOptics, Bellingham, MA) was used with a thin Ag-Epoxy front matching layer (8331, MG Chemicals, Surrey, B.C., Canada) and a very thin insulation epoxy layer for protection (EpoTek 301, Epoxy Technology, Inc., Billerica, MA). A small thermistor (R805-103J-3518B, Redfish Sensors, Meridian, ID) was mounted on the rear side of the piezoceramic to monitor the core temperature of each transducer element. A KLM model served as a design tool and provided a means to verify the front layer thickness of each device by comparing the model (Fig. 2) to the spectral impedance (4396B, Agilent Technologies, Santa Clara, CA) during device bench testing.

The Butterworth-Van Dyke (BVD) circuit model was useful to assist in transducer characterization. Figure 3 shows the model used which was refined further with the aid of the more complete KLM model. Attention was made to the spherical elements which were made after the earlier flat aperture prototypes with matching layer thicknesses in the 120 to 135 micron thick range to permit operation at a slightly higher frequency (at 4 MHz as determined earlier). With the values in Table I, the complex transducer impedance Z_{xd} was calculated to be $30.5 - j24$ Ohms at 4 MHz and the transmit sensitivity, S_{xd} , was determined to be approximately 17.5 kPa/V. For these values, R_a and R_d values in the model (Fig. 3) are 45 and 73 Ohms, respectively. The voltage V_s necessary to produce a desired acoustic output power magnitude (P_a in Watts) can be found using equation (3)

$$P_a = \frac{(V_s S_{xd})^2}{2} \left| \left(\frac{Z_{xd}}{R_{out} + Z_{xd}} \right) \right|^2 \frac{A_{xd}}{Z_w} 10^{-4}, \quad (3)$$

where R_{out} is the generator output impedance, and V_s the peak voltage inside the generator which is equal to twice the peak voltage across a R_{out} dummy load (i.e. 50 Ohms) used to calibrate the source. Z_w is the acoustic impedance of water and A_{xd} is the area of the single

element transducer. The effect of the cable was not considered in the calculation for reasons discussed below.

This acoustic power can now be used to find the dissipative power from the total electrical power and the expected reactive power component. First, the total electrical (i.e. apparent) power delivered to the transducer element is the product of the voltage and current magnitudes with its complex plane operators using the radian angle difference between voltage and current as $\theta_v - \theta_i$. This total power is

$$P_e = \frac{V_s^2}{2} \left| \frac{Z_{xd}}{(R_{out} + Z_{xd})^2} \right| e^{j(\theta_v - \theta_i)}, \quad (4)$$

and the dissipative power is the real part of this total electrical power minus the acoustic power found in (3). The reactive power is the imaginary part of the apparent power. The power factor, which is ideally unity, is the ratio of the real power and the apparent power. Since the power factor in this design is approximately 0.78 with an element impedance magnitude close to 39 Ohms, there is relatively little use for inductor tuning to remove the effect of the cable capacitance. The only issue with a longer cable is the minor impact of the increased effective series cable resistance.

C. Heating Array Manifold Design and Construction

The 3D printed array manifold (Fig. 4) was constructed at the UC Davis Department of Biomedical Engineering TEAM prototyping facility using a 3D printer (Objet 260v, Objet Inc., MN). A 3D software casting of the imaging probe (MS250, FUJIFILM VisualSonics Inc., Toronto, Canada) was acquired by laser scanning (3D Scanner HD, NextEngine, CA). Based upon the 3D acoustic beam performance from simulations, the aperture positions of the heating elements were determined and a CAD design of the manifold was created with cavities to accommodate the imaging probe and heating array elements (Fig. 5). This CAD output is exported as a stereo lithography (STL) file in point mesh format for use by the 3D printer. The part was printed, water jet cleaned, and ready for immediate use.

D. Power Distribution Electronics

Although driving all the heating elements in equal phase will produce a fine grating lobe structure in the beam field, this will not result in major disadvantages in the production of mild hyperthermia. Thus, we chose to design a high efficiency power splitter driven by a single RF source. An RF power splitter design was chosen which offers relative simple construction, high efficiency, and the ability to be cascaded to create any 2^N outputs. The design is shown in Fig. 6 using ferrite toroids (FT-114-61, Amidon, Costa Mesa, CA) with trifilar and bifilar winding. The key attribute is that the output impedance of each power splitter port is the same as the driving source impedance which makes this design easily cascable. This splitter has better than 99% efficiency, 1 dB bandwidth of approximately 150 kHz to 8 MHz, and can accept over 100 W as an input with minimal signal compression. By creating an N=3 cascaded splitter arrangement, 8 outputs are available. The two unused outputs were terminated in 50 Ohm power resistors to maintain a balanced output for the other 6 splitter ports. The 1:8 power splitter is driven by a single RF source (Model 100A250A, Amplifier Research) which is capable to deliver over 100 W of RF output with less than 1 dB compression distortion.

E. Acoustic Heating Analysis (Flat vs. Spherical elements)

A heating array comprised of 6 elements with 2 mm nominal focal beam diameters is expected to adequately heat a 2×8 mm XY region at a tissue depth of 20-30mm with a total

beam path length of approximately 35-40mm. For this reason, beam steering was not needed in this early design. If the elements are spaced at a distance d in a particular dimension, the expected grating lobes will appear at intervals of $\lambda z/d$ for a given depth z and assuming $d \gg \lambda$. At 3.5 MHz with a z depth of 41 mm (i.e. long beam path length utilizing the recessed heating element position), the grating lobes are expected at intervals of approximately 0.5 mm and 1.0 mm in elevational and azimuthal directions, respectively.

Rather than a “diffraction loss” calculation, which describes the effective power loss in a “pitch-catch” transducer set as a function of separation, we define a similar normalized beam power integration which we use to find the relative beam focusing capability of an aperture at a particular depth of interest, z_i . The beam power fraction (BPF) at the target depth z_i can be defined for a circular aperture as the normalized fraction of the total power in the axial symmetrical beam from zero at the centerline to a lateral dimension of x_0 by

$$BPF(x_0, z_i) = \frac{\int_0^{x_0} p(r, z_i) p^*(r, z_i) dr}{\int_0^{r_0} p(r, 0) p^*(r, 0) dr}, \quad (5)$$

where r is the radius in the x-y plane at some particular depth z_i , r_0 is the radius of the aperture, $p()$ is the pressure field, and $p^*()$ is its complex conjugate. The BPF approaches unity as the lateral dimension x_0 becomes large. The BPF is computed for both the flat and spherical aperture cases using the Rayleigh-Sommerfeld equation to calculate the pressure. The flat aperture BPF (at $z_i = 41$ mm) and the spherical BPF (at $z_i = 30$ and 41 mm) are shown in Fig. 7d.

Flat and spherical apertures were compared. There are advantages and disadvantages to both: the flat aperture device is easier to construct and has a broader beam profile with less phase deviation. The spherical aperture device has a higher energy density as compared to the flat aperture and shows a comparable beam shape at a depth past the element focus depth (i.e. 41 mm, Fig. 7c, d). The “long path” (recessed elements in the manifold) was used for both aperture cases.

Using previously described methods [17], [19], the Rayleigh-Sommerfeld (RS) equation was used to obtain a combined volumetric pressure field for the 6 elements. With regards to the flat aperture beam modeling, it is expected that a single beam focus will occur at depth $z = D^2/4\lambda$ with a focal intensity of four times the aperture surface pressure and a full width half power beam (FWHP) angle of approximately λ/D . For the spherical aperture, RS simulations show that a focus depth of about 28 mm is expected for an 8.8 mm diameter spherical aperture at 3.5 MHz with a radius of curvature (ROC) of 50 mm (Fig. 7). Since the ratio λ/D is small, the estimate for the FWHP beam width at the focus distance and beyond is $\lambda z/D$. At a depth of 41 mm, the -3 dB beam diameter is approximately 2 mm for both flat and spherical aperture beams, however the BPF profiles are quite different.

F. 3D Thermal Modeling

It is desirable to find the power input necessary to achieve a 3°C temperature increase in 2 s with uniform insonification over an 8×5 mm region in the Y-Z plane. A 3D, general heating simulation (COMSOL Multiphysics, v3.2, Comsol Inc., Burlington, MA) has been constructed to accept both 3D acoustic simulation data as well as laboratory data. Unless otherwise specified, the initial temperature for all simulation results was assumed to be 37°C. The 3D bio-heat transfer equation (BHTE) simulation was able to accept input data as volumetric heat flux points either from RS acoustic models or from laboratory pressure measurements. Beam data from both flat and spherical aperture element sets were examined.

In each case studied the aggregate echo path attenuation was assumed to be 2/3 of the initial transmitted power (net attenuation considering both gel and tissue lengths).

Heat loss through perfusion was ignored due to short heating durations. In addition, diffusion will also be limited over the brief heating duration because the diffusion distance in 2 s will be ~0.75 mm [20]. The nominal diffusion distance can be estimated as the square root of tissue diffusivity ($\sim 1.4 \times 10^{-7} \text{ m}^2/\text{s}$) multiplied by time. A 3D BHTE simulation volume of $10 \times 10 \times 8 \text{ mm}$ in X-Y-Z dimensions was used and the volume boundary conditions were assumed to be at 37°C . The simulation mesh density was set such that the separation between points was less than 0.5 mm throughout the entire 800 mm^3 volume. The tissue heating simulation input is a 3D pressure magnitude field result of all 6 elements. The 3D pressure data are converted into volumetric flux density, Q_{3D} , by

$$Q_{3D} = \alpha |P_{3D}|^2 (Z_w)^{-1}. \quad (6)$$

With a single iteration, the simulation aperture pressure could be scaled to achieve the criterion of a 40°C maximum in the simulated tissue volume. In this manner, the YZ plane heating region characteristics as well as the required input power could both be determined for each test case. The 3D BHTE simulation computes the temperature elevation of tissue by assuming the form of the heat equation [21]

$$Q + \nabla \cdot (\kappa \nabla T) = C_v \frac{\partial T}{\partial t}, \quad (7)$$

where Q is the volumetric heat flux (W/m^3) derived from the acoustic input data set and κ is the thermal conductivity. This expression however can be simplified to enable an estimate for the acoustic intensity required for the first few seconds (by ignoring conductive loss during these first few seconds), as

$$2\alpha I = C_v \frac{\Delta T}{\Delta t}, \quad (8)$$

where α is the absorption coefficient (Np/m), and is assumed to be $25 \text{ Np}/\text{m}$ at 3.5 MHz with an arbitrary frequency dependent tissue characteristic of $0.62 \text{ dB}/\text{cm}/\text{MHz}$. Using (8), an intensity of $12 \text{ W}/\text{cm}^2$ was necessary given $C_v = 4.07 \times 10^6 \text{ J}/\text{m}^3/^\circ\text{C}$ and assuming a 3°C rise over 2 s.

G. Thermal Strain Imaging with a Phantom

An *in vitro* validation study of the US-TSI system was conducted by first assembling an imaging phantom of gelatin with a rubber inclusion as the TSI target. To make an approximately 6 mm diameter cylindrical rubber target for the phantom, scatterers (0.5% by weight Amberlite, I6641, Sigma Aldrich Corp, St. Louis, MO) were added to a hot (450°C) liquid 80:1 mixture of plastic hardener/softener (M-F Manufacturing, Ft. Worth, TX) and allowed to cool. The cooled rubber cylinder was introduced to the liquid gelatin matrix. The gelatin matrix was made by combining gelatin (G-2500, Sigma Aldrich Corp., St. Louis, MO), water, and ultrasound scatterers (1% cellulose by wt, S3504, Sigma Aldrich Corp., St. Louis, MO). The physical properties of the test phantom are listed in Table II. The properties for the rubber target were measured while those of gelatin matrix were estimated from the literature.

The TSI imaging/heating sequence consists of standard B-mode imaging sequences interleaved with heating sequences. The phantom was imaged with the MS250 transducer on

the Vevo 2100 system. The heating transducer was excited using parameters listed in Table III. Two-dimensional speckle tracking [22] was applied on RF data to estimate displacement between a reference image and an image taken after heating. The apparent thermal strain is the derivative of displacement along short-time echo beams and was estimated using a 2nd order Savitzky-Golay filter. TSI was applied to the same phantom using both the spherical and flat elements.

III. Results and Discussion

RS derived axial and lateral responses for both flat and spherical aperture elements exhibited good agreement with laboratory acoustic measurements. The flat element had a spectrum similar to the spectrum for the KLM model with a 100 μm matching layer.

Using the elements' spatial positions and simulated beam characteristics, the theoretical heating profiles for the two array types (Fig 8 a and c) were examined to determine a reasonable set of element target foci. It was found that a staggered arrangement (Figs. 8 b and d) provided a good acoustic beam power coverage in the target plane.

The parameters necessary to achieve a 3°C temperature rise in 2 s for the flat and spherical elements are summarized in Table IV. The modest peak pressures and MI indicate little concern for acoustically driven mechanical cavitation effects. The simulation derived average intensities in the heating region agree well with the calculation using (8).

Table V shows the summary of simulation results on expected heating effectiveness. Approximate planimetry (Fig. 8) was used to assess the YZ plane area between 39°C and 40°C. The “efficiency ratio” is a metric indicator showing the ratio of this YZ plane area and the total aperture power (Power_{ap}) required to heat the desired target region. This metric shows that the spherical aperture design uses 56% less power to heat a similarly sized region as compared to the flat aperture design.

For every 1 W delivered to the transducer, the transducer converts 0.78 W into real power and 0.62 W into reactive power. The real power is divided into 0.48 W of acoustic power and the remaining of 0.3 W is lost to heat. These values were calculated using the modified BVD model (Fig. 2), and confirmed with both KLM and COMSOL modeling as well as lab measurements. The thermistor mounted on the back of every PZT element provided laboratory readings to confirm the heat dissipation magnitudes predicted with an axisymmetric 3D thermal model of the transducer itself. Typical single element self-heating performance showed a PZT temperature elevation from 22 °C to 50 °C in 13 s at 2.5 W of dissipation and an output of 4 W acoustic power.

Using simulations and laboratory measurements for confirmation, a power flow link budget (Fig. 9) was assembled for both flat and spherical apertures to account for the translation efficiencies at each point in the transmission pathway. The laboratory pressure field data revealed a ~two-fold difference in overall power requirements between the two designs which agrees with the difference shown in Fig. 9. The numbered pathways in Fig. 9 have explanatory narratives which are presented here.

1. The 3 stage cascaded RF power splitter produces 8 outputs of which we only use 6.
2. This acoustic power is estimated from 3D BHTE modeling with 6 apertures. Individual beam estimates were computed using a 3D RS acoustic model. A single recursion approach with the BHTE model produces the estimated aperture pressure necessary to produce 3°C temperature rise in 2 s.

3. The previously discussed transducer efficiency analysis has revealed that 48% of the input electrical power is converted to acoustic output, while 30% is dissipated as heat.
4. Reactive (imaginary) electrical power is approximately 62% of the total input power.
5. The fractional loss of acoustic power due to tissue absorption is calculated as $1 - \exp(-2\alpha z)$ where α is an arbitrary 25 Np/m (0.62 dB/cm/MHz and 3.5 MHz) and a tissue path length of 22 mm is used.
6. The quantity of tissue heating power is derived both from a) the 3D BHTE simulation where the average acoustic intensity in the 2×8 mm X-Y target region is $\sim 12 \text{ W/cm}^2$ and, b) the hand calculation of intensity neglecting perfusion and diffusion as in equation (8).
7. The beam loss is the acoustic power which is far enough from the heating target area such that it does not significantly contribute to heating. The beam loss fractional estimates are the result of total input acoustic power minus the power needed in the target region heating, and match reasonably well the beam characteristics shown in Fig 7.

Several early array manifolds were built with the 3D printer. Testing was completed with combined imaging and heating using a single RF power source and 1-input 6-output custom RF power splitter. The custom heating array acoustic and electrical performance was compared against KLM modeling and can easily deliver 30 W of total acoustic power which produces intensities beyond 12 W/cm^2 in the 2 mm by 8 mm target region. For tissue this would result in a 3°C rise in temperature in 2 s. Custom beam modeling software was used to determine arbitrarily the beam target points for the custom arrays, and then implemented in the desired array manifold configuration. The flat and spherical aperture elements with the staggered manifold design were evaluated for their ability to produce effective and uniform heating in the desired target volume. The 39°C 3D heating contour comparison of the flat and spherical elements is shown in Fig 10. The equivalent 2D heating planes are shown in Fig. 11. The manifold design fixes the position of the element such that only the rotation can be adjusted. Element rotation helped ameliorate beam skew errors but was unable to adequately compensate for all 6 beam positions as is evident from the undesirable beam skew in the right side of Fig 11d. In addition, it is apparent that the defocused flat aperture beam has a greater tolerance for beam skew as compared to the focused spherical beam despite the fact that the spherical beam is focused at 41 mm which is 37% greater than the individual focus of each spherical element (29 mm).

Figure 12 shows B-mode and the corresponding US-TSI of the custom phantom with the 6 mm rubber inclusion for both flat and spherical aperture cases. Rubber is known to produce a large, positive thermal strain when heated, whereas gelatin produces small negative thermal strain [26]. This is evident in the US-TSI image with the rubber inclusion appearing red and the gelatin background appearing to be very slightly blue. The maximum thermal strain generated in the inclusion using the flat and spherical arrays was 0.66% for 6.8 s, and 0.59% for 0.5 s, respectively. Considering the ratio of thermal strain per unit time, the spherical aperture array generated about 12 times more thermal strain per second in comparison to the flat aperture array. This is a considerable difference and can be explained by a number of factors. First, the same electrical power, the flat elements deliver approximately half as much power to the target region. Second, the actual alignment of individual elements may be different between the water tank experiments used to generate the simulation data and the phantom experiments. Finally, the total time in which heating was applied to the flat elements is approximately five times as long as that used for the

spherical elements. Over the course of 6.8 s the temperature rise with respect to time was probably no longer linear and that there were thermal diffusion losses. This illustrates two points: first, less efficient power delivery to the target region forces a longer heating time in order to obtain a robust and detectable signal and, second, as the length of time required to heat an object increases, the heating process becomes less efficient due to conductive loss of heat which is described by the BHTE.

The use of only 6 heating elements appears to provide enough power and beam uniformity to be useful for tissue heating and is still simple with respect to cost and complexity. Spherical heating elements can reduce the diffraction loss of a flat aperture beam and reduce the system power requirements, but this comes at the cost of a more precise beam alignment procedure. The main drawbacks with this heating array implementation are in element matching and beam alignment; the former can be addressed with robust manufacturing procedures, while the latter can be either solved through the use of more monolithic arrays, or by using custom beam alignment tooling.

Tissue temperature tolerance is a significant concern, however this has been well studied over the last 20 years with guidance adopted by the American Institute of Ultrasound in Medicine (AIUM) [27]. For non-fetal tissue heating with 2 s of expected exposure, the AIUM standards predict the highest safe temperature rise to be 10.9°C. The safety margin of 7.9°C is reasonable for this application.

One important reason to enable a US heating system with substantial power is to counter the substantial cooling effects of arterial blood flow close to the intended site of TSI. These effects have been studied [28], [29], [30] which show very high heat transfer loss to blood. A short time, uniform, high intensity heating regime may be the proper means to permitting good TSI. This will be a major topic of interest as development of TSI for the carotid artery progresses.

IV. Conclusions

This work demonstrated the feasibility to construct a low cost, highly flexible integrated solution in cases where typical commercial imaging systems cannot deliver enough continuous power into tissue for US-TSI. A small number of heating elements may be sufficient to achieve uniform heating in small regions. The application of spherically focused beams may provide higher efficiency heating compared to flat beams and 3D printing of custom transducer manifolds may be a highly efficient means of developing a new “dual-mode” array paradigm. This approach for combining very different array functions demonstrates a pathway for rapid growth in this research area as designs are continuously refined.

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Fig. 1.

The dual-mode US system for US-TSI of carotid arteries. The left panel (a) shows the long axis imaging transducer, (b) shows the short axis with the principal system components. Artery orientation is arbitrary here.

Fig. 2. KLM simulations showing spectral power band shapes for thickness ranges of Ag-Epoxy matching layer. The flat devices (3.5 MHz) targeted 100 μm thick and spherical devices (4 MHz) targeted 130 μm thick matching layers.

Fig. 3. Simplified tank circuit model near resonance used to calculate the heating element electrical to acoustic efficiency. The cable is 3 m, but had little effect as the transducer impedance magnitude was close to 50 Ohms (39 Ohms), and thus no tuning inductors were needed.

Fig. 4.

The 3D printed manifold. Panel (a) shows an individual circular element recessed in its alignment tube. View (b) shows the manifold from the top showing the precision formed bay for the MS250 imaging probe body; view (c) shows the bottom with a plaster probe dummy where the imaging probe resides.

Fig. 5.

Each of the 6 individual heating elements (1a) is inserted into the manifold (1b) to permit insonation of a heated region (X-Z heating plane is shown) in the tissue while allowing clear visualization with the imaging transducer. Each heating element positioned in a recessed location 16 mm deep at the rear of the gelfilled metal tube (i.e. “deep aperture,” in 2a). The dark rectangular “target volume” (2b, 2c) describes the 2 mm by 8 mm by 5 mm heating target site.

Fig. 6.

The core 1:2 power splitter design is shown which is cascaded in three stages to provide a 1:8 overall power split. A two stage design offers the 50 Ohm impedance as both input and output impedances; this assures efficiency.

Fig. 7.

Simulation comparisons of flat and spherical beam characteristics. With the same aperture diameter of 8.8 mm, the flat beam (a) and spherical beam (b) profiles show peaks at 44mm and 30mm respectively (fine dots), with dashed line depth indicating the approximate target depth of interest, or 41mm. The lateral beam patterns are shown in (c). The BPF near the aperture centerline is plotted in (d). The black and gray dots in the lower panels are the -3 dB lateral distances for the flat and spherical beams respectively.

Fig. 8.

The orthogonal heating plane simulations for the flat aperture (a, b) and the spherical aperture (c, d) studies with planimetry. Blue dots represent the center focus target for a particular heating element. The entire temperature range plotted is 37°C to 40°C with planimetry borders defining the 39 – 40°C regions.

Fig. 9.

Power flow link budget for the flat and spherical aperture set of 6 transducers. Efficiency at each stage (in parentheses) is defined as $\text{power}_{\text{out}} / \text{power}_{\text{in}}$.

Fig. 10.

The target depth region BHTe *volumetric heating* results using the 3D acoustic data set in each case; the heating array is above the plots with X and Y at a 10mm span and Z is 8mm centered at 37mm depth. The temperature range in this plot is 37°C to 40°C. For each set, the peak temperature was limited to 40°C in 2 s of insonation. The red isothermal surface in each is 39°C with YZ imaging plane at center. (a) and (b) are the simulation and lab for the flat aperture array set; (c) and (d) are the simulation and lab for the spherical aperture array set.

Fig. 11.

The target depth region BHTe *planar heating* results for the same two designs, conditions, and dimensions as shown in Fig. 10 a-d. The heating planes are Y-Z (left column), X-Z (middle), and X-Y (right). Panels (a) and (b) are the simulation and lab results for the flat aperture array set; (c) and (d) are the simulation and lab results for the spherical aperture array set, respectively.

Fig. 12. Both B-mode (left) and TSI images (right) of cylindrical rubber inclusion embedded in gelatin. The flat aperture array was used in (a) and (b); the spherical aperture array for (c) and (d).

TABLE I

Transducer Model Parameters

Transducer (PZT - 5H)		Matching Layer (Ag-Epoxy)	
diameter	8.8 mm	thickness	100 10^{-6} m (nominal)
frequency	3.5 (flat) – 4.1 (spher) MHz	Z_{acous}	5.14 10^6 kg s $^{-1}$ m $^{-2}$
thickness	0.57 mm	velocity	1900 m/s
rel. dielectric	1413	absorption	322 Np/m at 3.5 MHz
Z_{acous}	34.9 10^6 kg s $^{-1}$ m $^{-2}$		
velocity	4650 m/s	Insulator (EpoTek 301)	
k_T	0.54	thickness	25 - 40 10^{-6} m (nominal)
$\tan \delta$	0.017	Z_{acous}	2.85 10^6 kg s $^{-1}$ m $^{-2}$
absorption	36 Np/m at 3.5 MHz	velocity	2680 m/s
Au thickness	0.6 10^{-6} m	absorption	150 Np/m at 3.5 MHz
Transducer Tank Model Parameters		RF Source Parameters	
C_0	1335 pF	R_{out}	50 Ohms
C_x	445 pF	Z_{cable}	50 Ohms (RG174)
L_x	4.5 μ H	$\text{Length}_{\text{cable}}$	3.0 m
Z_{xd}	30.5 – j24 Ohms at 4 MHz	R_{cable}	0.4 Ohms/m (at 3.5MHz)
S_{xd}	17.5 kPa/V	L_{cable}	252 nH/m
Z_w	1.5 10^6 kg s $^{-1}$ m $^{-2}$	C_{cable}	102 pF/m
A_{xd}	0.61 cm 2		

Table II

Physical Properties of the Test Phantom

Properties	Units	Gelatin Matrix	Rubber Target
Density	kg/m ³	1050 [23]	880
Acoustic Speed	m/s	1510 [23], [24]	1387+/- 30
Acoustic Attenuation	dB/cm/MHz	0.3 [24]	1.68 +/- 0.11
Thermal Conductivity	W/mK	0.6 [24], [25]	0.04
Heat Capacity	J/kgK	4180 [25]	600

Table III

In Vitro US-TSI Study Heating Array Excitation Parameters

Parameter	Units	Flat Element Array	Spherical Element Array
Excitation Freq.	MHz	3.55	4.0
Duty Cycle	%	56	56
System Input Power	W	25	25
TSI Sequence Duration	s	6.8	0.5

Table IV

Metrics to produce 3C Tissue Rise in 2 s

Aperture Type	At Aperture		At Target Plane Depth			
	P _{pk}		P _{pk}	MI	I _{pk}	I _{avg}
	kPa	MPa	MPa		W/cm ²	W/cm ²
Flat	445	1.3	1.3	0.7	56	12.4
Spherical	334	1.1	1.1	0.6	40	11.8

Table V

Heating Effectiveness for the Flat and Spherical Apertures

Aperture	Focus Length	Beam Path	Power _{ap}	YZ Area	Efficiency Ratio
	mm	mm	W	mm ²	
Flat	44	41	24.1	35	1.45
Spherical	30	41	13.7	31	2.26