10 MHz Catheter-based Annular Array for Thermal Strain Guided Intramural Cardiac Ablations

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Abstract — A yearly global population of well over 100,000 ventricular tachycardia patients could benefit from guided cardiac ablation of otherwise untreatable intramural arrhythmogenic substrates. A guided catheter-based HIFU device used epicardially with a subxiphoid approach is proposed which is placed with electroanatomical mapping. After the HIFU device is positioned, the thermal strain feedback at low intensities can confirm myocardial contact and establish a projected power titration guideline for full HIFU ablation. This PZT based spherical array design is an early adjunct prototype of a fully beam steerable CMUT array design in development at Stanford.

The multifunctional catheter is designed to direct an axially steerable 10 MHz HIFU beam into the myocardium without damaging the epicardium itself and the vitally important coronary vessels. The spherical array is 7 mm in diameter with a radius of curvature of 7 mm; it is housed in a custom 3D printed tip housing (see figure) which is 10 mm in total diameter and 4 mm in profile and joined to a 7 Fr (2.3 mm) catheter shaft. The prototype array is water cooled and has a built-in thermistor to monitor transducer temperature. The ablation axial steering addresses the 4 to 10 mm depth range, while 10 MHz can produce a high focus gain to produce a 23 C rise in temperature with bursts of 200 msec durations. A unique feature of this work is the use of the Verasonics Vantage 256 system as both the HIFU power source and thermal strain echo data receiver; a custom 32 channel power combiner/splitter (4 annuli x 8:1) interface was built to permit this development.

Two 10 MHz 7 mm prototype spherical devices have been built and tested. Both are made from PZT-5A with no backing material and only a 100 micron EPOTEK-301 epoxy front matching/insulation layer. The first device is a 9.6 MHz single element spherical HIFU transducer which was driven with an ENI amplifier and produced heating intensities sufficient to visibly ablate (0.5 mm ablation diameter by 1.5 mm length, or 0.3 mm3) beef tissue in a room temperature bath in less than 0.5 sec. The second device is a spherical four element annular array which has been used to collect thermal strain echo data from a laboratory phantom. Continued development is underway to demonstrate both heating and thermal strain data from in-vivo animal experiments.

Keywords – thermal strain, array, acoustic heating, dual mode transducers, RF

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INTRODUCTION

This device in development is designed to address the unmet need for transmural cardiac ablation in the treatment of patients with ventricular tachycardia and arrhythmias. The prevalence of sudden cardiac death (SCD) cases in the USA is in the range of 0.1 to 0.2% (i.e. 300,000 to 600,000 per year) [1]. More than 75% of sudden cardiac death is due to ventricular tachycardia (VT) or ventricular fibrillation (VF) [2]; this is an annual death rate in the USA of approximately 240,000 to 480,000. As many as 50% patients experience recurrent VT despite standard epicardial and endocardial ablation methods, particularly, patients with non-ischemic cardiomyopathy [3]. Therefore, over 100,000 patients per year in the USA alone could benefit directly from our proposed precision guided, minimally invasive high intensity focused US (HIFU) ablation of VT.

Conventional VT ablations using RF ablation (RFA) can not a) create a deep-focused E-field, b) heat tissue uniformly, and c) produce consistent transmural lesions. Therefore, a great unmet need exists for a therapy which can direct focused energy to deep tissue, e.g. HIFU. Recently a Japanese group [4] demonstrated with in-vitro testing that conventional RFA produces a very large ablation zone which is likely to be 10 times the volume necessary for a VT ablation.

Further goals of this project are to offer a) a means of interventional guidance such as electroanatomical mapping (EAM), and b) ultrasound induced thermal strain imaging (US-TSI) temperature feedback to help determine the depth of the epicardial fat and to titrate low intensity heating feedback prior to a full power ablation. Additionally, it is desirable to use the Verasonics Vantage 256 system as both the HIFU power source as well as the US-TSI processing engine. The expected TSI display is expected to be an M-mode like display which shows A-mode echo data in depth and heating duration in time in a similar way shown by [5].

Figure 1. The design of the 3D printed headshell of the spherical annular array is shown with the catheter mockup at far right. An atrumatic tip (with water cooling under a TPX cover) and EAM electrodes permit epicardial use via a subxiphoid introduction of the catheter through the chest wall.

Finally, the effort here is to show feasibility and not the final design. There are insights gained here which will help steer future development. It is likely that the ultimate device

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will be a 2D array (which is also in development) which has the advantage of enabling full US imaging as well as HIFU beam steering from one anchored position on the epicardium.

The acknowledged general frequency range for HIFU is in the 0.5 to 3 MHz range. The 10 MHz frequency was chosen for the production of very fast and strongly focused HIFU ablation sequences at depths of 3 to 20 mm. As an interventional device the HIFU device aperture is small, thus its focusing ability is much greater at high frequency compared to low. For the same spherical aperture size and intensity the focus intensity will go as the square of the frequency. Therefore, neglecting higher tissue path attenuation, for the same focus intensity the aperture intensity of a 10 MHz device can be (10/1.5)^2, or ~ 44 times that of a 1.5 MHz device; the heat function developed at the focus is higher in proportion to the frequency ratio which also helps this argument.

Threshold lesions in brain tissue at 9 MHz were first measured in 1975 [6]. This early work developed the relationship between minimum exposure time, t, and focus intensity as \( I = 489 t^{-0.512} \) in units of W/cm². For a 0.2 second insonation the calculated required minimum intensity is 1115 W/cm². This calculation agrees with an Arrhenius equation calculation. If a rapid 23°C focal temperature rise (i.e. 60°C if starting from 37°C) is possible, the 240CEM requirement is satisfied in approximately 0.22 seconds. Since it is anticipated that half the intensity in the beam path is lost to tissue attenuation, it is necessary to produce a focal intensity of about 2000 W/cm² neglecting attenuation. The intensity gain for the spherical aperture is \((kh)^2\), where \( k \) is the wave number and \( h \) is the depth of the aperture, or \( h = \text{ROC}(1 - \cos(\text{asin}(0.5))) \). The \( kh \) product (the focal pressure gain for a spherical aperture) is 35.97; the intensity gain is then approximately \((kh)^2\) or 1294. This indicates an aperture intensity of 2000/1294 = 1.55 W/cm² is needed to produce an adequate focal intensity in the tissue with tissue attenuation considered. For the 7 mm diameter spherical array with a total aperture area of 0.41 cm², an aperture acoustic power of at least 635 mW is required. The Verasonics Vantage 256 system and cable have been configured to address this power requirement.

### I. METHODS

#### A. Transducer Construction and Modeling

Since it is desired to allow only moderate transducer temperature elevation, PZT-5H was selected (Boston PiezoOptics, Bellingham, MA). The elements were defined by cutting though the metal surface on the spherical aperture backside with a 10 micron CO₂ laser. No backing material was used; the front layer is only a 50 micron thick EPOTEK 301 epoxy layer for nominal coupling and front-face ground electrode isolation. Since this is a bench testing device at this time the 42 AWG interconnection wires are only about 25 cm long. The spherical elements sizes were designed to be equal areas. A very small thermistor was glued to the back-side of the array to monitor array temperature during HIFU.

A simple Van Dyke circuit model was developed for the array elements based on the electrical impedance spectrum for each on an Agilent 4396B impedance analyzer. The transmit sensitivity was measured on an acoustic radiation force balance (Ultrasound Power Meter, Model UPM-DT-1E, Ohmic Instruments Co., Easton, MD).

#### Table I. Spherical Annular Array Transducer Parameters

<table>
<thead>
<tr>
<th>Design Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Array Diameter</td>
<td>7 mm</td>
</tr>
<tr>
<td>Radius of Curvature</td>
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</tr>
<tr>
<td>Frequency</td>
<td>9 to 10 MHz</td>
</tr>
<tr>
<td>Elements</td>
<td>4</td>
</tr>
<tr>
<td>Intensity Gain at focus</td>
<td>1294</td>
</tr>
<tr>
<td>Tx Sensitivity</td>
<td>28 kPa/V</td>
</tr>
</tbody>
</table>

#### B. Acoustic Performance Modeling

Heating beam focusing simulations using the Rayleigh-Sommerfeld equation were performed to verify linear regime analytical estimates for focusing and to determine the ratio of the main lobe beam to grating lobes. As well, beam heating simulations were performed by using an axisymmetric finite-element analysis (FEA) field implementation of the bioheat equation (Comsol Multiphysics v4.4, Comsol Inc., Burlington, MA) based on imported acoustic intensity data from the beam focusing simulations.

![Figure 2](image)

**Figure 2.** The simulation analysis of the beam produced by the annular element spherical aperture. In panel (a) the spherical annular array beam (focus gain in dB) has been steered to a 5 mm depth focus, in (b) the steered beam is centered at its natural focus of 7 mm depth, and in (c) the focus is placed at a depth of 9 mm. In (c) the X-Z plane plot shows the natural focus produces a 0.2 mm wide (lateral) beam with an axial length of 1.1 mm. Panel (e) shows the expected heating pattern at a 1 s. burst, 10 mm depth.

#### C. Verasonics System Interface

With the aid of the 1200 W external DC supply (Aim-TTI QPX600DF) the Verasonics system is capable of 8 W per channel of electrical power output, although this is significantly derated for frequencies above 5 MHz. An ordinary L7-4 cable assembly without the array was used as the multi-coax trunk cable transmission line in this work. A custom PCB was designed to plug directly into the end of the L7-4 cable in place of the linear array.

The L7-4 cable used was modeled (Fig. 3a) in a piecewise manner; the coax input (Fig. 3b) and output (Fig. 3c) impedance were measured as well as the general magnitude transfer function for small impedance loads (Zload < 100 Ω).
Using an RL series source impedance as shown in Fig. 3b that represents the equivalent Verasonics transmitter output impedance, and the measured cable voltage output for various termination loads, a Thevenin equivalent source was devised for the cable output circuit as shown in Fig 3c. Since the single coax output impedance at 9.6 MHz is quite high at 276 Ω with an inductive phase angle of 76 degrees, eight cable outputs can be summed together which reduces the net cable output impedance greatly.

![Figure 3.](image)

**Figure 3.** Piecwise electrical modeling of the L7-4 cable at 9.6 MHz.

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![Figure 4.](image)

**Figure 4.** The Verasonics interface circuit used to sum 8 in-phase channels is shown for 1 of the 4 annular ring elements. The calculated apparent power (Wapp) is large at the cable inputs while the desirable real power (Wr) is comparatively small. The power factor (0.7) at the 2:1 (impedance) transformer is much better. For the prototype developed in this study, the Ctune is about 25 pF of RG174 coax with an additional 1000 pF, the Lwires is 0.4 μH due to a 42AWG connection wire for each element. A single element of the spherical array has 650 pF of bulk capacitance while the Rx is approximately 12 Ohms. The 2:1 impedance transformer is made using 3 turns (primary and secondary are bifilar) on an Amidon toroid FT-50A-61.

II. RESULTS

A. Assembly and Testing of the Verasonics Interface

A link study analysis was assembled to determine the minimum GUI voltage to be used by the Verasonics Vantage 256 system. To complete this analysis a detailed circuit model was attempted to emulate the L7-4 cable, but this was very problematic for several reasons. The 42 AWG coaxes making up the L7-4 cable produce a significant skin effect resistance which contributes to significant real power losses at 9.6 MHz. The skin effect will cause an increase in the resistance per meter [7], and will generally cause a decrease in the inductance per meter (this is due to the loss of magnetic flux lines inside the wire itself as the great majority of the current resides on the “skin” of the conductor). An additional and more prominent effect is observed though which contributes to a large decrease in the cable signal velocity which then makes transmission line effects even more significant. This effect is a large (in the range of a factor of 4 to 8) increase in the effective inductance per meter for the coax simply because the coax grounds are all coupled together which prevents the return current path for the center conductor of a particular coax from using the shield path for that particular coax. When this occurs (i.e., the return current is spread to other ground return paths) the magnetic flux is no longer limited (as in classic coax operation) to only the dielectric between the inner and outer conductors.

B. Transducer Tissue Heating

Early tissue (beef) heating tests have been performed to show the rapid heating capability of the small spherical aperture (Figs. 5, 6). These early tests used a 50 W ENI to directly drive the spherical device to show capability prior to full Verasonics interface functionality.

![Figure 5.](image)

**Figure 5.** Lab data with a calculated focus intensity in a beef tissue sample of 1000 W/cm². HIFU ablation site temperature is shown with 23 C rise in 0.2 sec with the 7 mm device. The thermocouple used was large here, which suppresses max. heating ability.

![Figure 6.](image)

**Figure 6.** The HIFU ablation of beef tissue in 22°C bath water; (a, b) shows (pre/post) effect from a single HIFU burst of 0.5 sec from a 7 mm single element prototype transducer; multiple burst HIFU in (c, d) show white ablation regions. Audible steam pops were heard during HIFU burst heating.
C. Ultrasound Induced – Thermal Strain Imaging

Early efforts to obtain US-TSI data with the Verasonics system have been undertaken with single focus heating in phantoms. One of these results is shown in Fig. 7 as the M-mode map of the displacement following the correlation step. Subsequent to this is the spatial filtering needed before applying the axial derivative and the final filtering. These early data were gathered with a non-optimized cable and element functionality so it represents early feasibility results. We expect very good capability for M-mode TSI when the lab set up is finalized.

Figure 7. An M-mode-format is shown of an US-TSI echo displacement map following the correlation processing step of very mild heating of an agarose phantom at about 4 mm from the spherical array face. Heating was started at 3 seconds and was stopped at 13 seconds. The color coded scale is the correlator output sample point shift (peak here is -0.1 of 1/4 lambda shift).

III. DISCUSSION AND CONCLUSIONS

A spherical shaped aperture can develop a substantial focus for heating tissue, but certain practical improvements are needed before in vivo success can be fully realized. It is certainly acknowledged that we may find that a slightly lower frequency (6 to 8 MHz) with a slightly larger aperture may be needed. Our anticipated next steps are discussed here.

Firstly, the power factor at the ZIF connector must be improved to prevent too great of a power demand on the Verasonics system. Ideally, if only real power is required of the host system, a total of 12 Watts of power is needed. This ignores anticipated improvements in the acoustic coupling of the transducer itself. At 12 Watts and 32 system channels, this means the average channel power needed is only 0.375 W per channel, a very safe power draw from the Verasonics. The optimal cable characteristic impedance would be an 85 Ohm real value; otherwise, tuning this system/cable interface with reactive components can increase power transfer but unfortunately not improve on the power factor which is paramount. Additionally, the catheter cabling electronics (Fig. 8) must be optimized to allow power coupling; this is a reasonably tractable problem though with several options to explore.

Secondly, catheter transmission line shielding and array connection wire RF shielding will be needed to achieve a high SNR echo signal data pathway. EAM electrodes and their wire connections will be incorporated into the final design as well.

Finally, we anticipate the challenges of using the EAM electrodes to correctly position the HIFU aperture near the suspected lesion site; this may require additional or better positioned electrodes to properly enable this function. Additionally, there is the issue of maximizing the HIFU heating region in the tissue. We anticipate the possible need for mechanically steering the HIFU beam by “rocking” the transducer slightly at angles of about 4 degrees off its center axis to better distribute HIFU ablation energy (to create a lateral HIFU lesion width of 3 to 5 mm wide rather than only 2 mm wide). This mechanical motion of the array alone would be implemented while the catheter ablation tip is stationary on the surface of the epicardium. Various design options to implement this scheme are in consideration for the in vivo application version of the device.

REFERENCES


