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Realtime Control of Multiple-focus Phased Array Heating Patterns Based on Noninvasive Ultrasound Thermography

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Abstract

A system for the realtime generation and control of multiple-focus ultrasound phased-array heating patterns is presented. The system employs a 1-MHz, 64-element array and driving electronics capable of fine spatial and temporal control of the heating pattern. The driver is integrated with a realtime 2D temperature imaging system implemented on a commercial scanner. The coordinates of the temperature control points are defined on B-mode guidance images from the scanner, together with the temperature set points and controller parameters. The temperature at each point is controlled by an independent proportional, integral, and derivative (PID) controller that determines the focal intensity at that point. Optimal multiple-focus synthesis is applied to generate the desired heating pattern at the control points. The controller dynamically reallocates the power available among the foci from the shared power supply upon reaching the desired temperature at each control point. Furthermore, anti-windup compensation is implemented at each control point to improve the system dynamics. *In vitro* experiments in tissue-mimicking phantom demonstrate the robustness of the controllers for short (2 – 5 sec) and longer multiple-focus HIFU exposures. Thermocouple measurements in the vicinity of the control points confirm the dynamics of the temperature variations obtained through noninvasive feedback.

I. Introduction

High intensity focused ultrasound (HIFU) is a promising modality for the treatment of cancer and other tissue abnormalities [1]–[3]. It has proven to be effective in the treatment of prostate cancer [4], [5], uterine fibroids [6], and other tumors in accessible organs. While the benefits of HIFU are readily acknowledged by interventional radiologists and other clinicians (e.g. urologists), it suffers from limitations that still hinder a wider acceptance of this modality. One of the main limitations is the long treatment time compared to competing minimally invasive modalities. For example, a tumor may be treated in 15 minutes using RF ablation, but may require 2 – 3 hours using a conventional HIFU protocol (raster scan of small ablations within the focal region of the HIFU application). Another limitation is the possible obstruction of the HIFU beam by structures resulting in inadequate therapy at the target and/or treatment-limiting pain or damage to normal tissues in the path of the beam (e.g. ribs when targeting liver tumors). These limitations are likely to be overcome by advances in two enabling technologies for noninvasive application of therapeutic HIFU. Specifically, piezocomposite array transducer technology [7] and noninvasive thermometry and feedback control [8]–[13]. In addition, new protocols utilizing, for example, bubble generation for accelerating treatment are being investigated [14], [15].

Phased array applicators offer unparalleled level of spatial and temporal control over the heating pattern, including simultaneous heating at multiple-focus locations [16], [17]. This has many potential advantages in thermal therapy, including reduction in treatment time,

improved localization of therapeutic effects to the target volume, compensating for heterogeneous blood perfusion, etc. Modern phased array drivers are capable of dynamic control of heating patterns using a variety of man-machine interfaces with millisecond resolution [18], [19]. Realtime temperature control algorithms with spatial and temporal resolutions matching those of the drivers are needed to realize the full potential of phased array technology in thermal therapy. Furthermore, to preserve the noninvasive nature of the treatment, the algorithm must utilize a noninvasive method for measuring temperature change within the treatment volume.

Temperature imaging using MRI is now available on clinical MR-guided HIFU systems (MRgFUS) and can be credited in the increased awareness and acceptance of this form of noninvasive surgery [11], [12]. Feedback control algorithms of HIFU fields based on noninvasive temperature imaging using MRI is now becoming more available [11], [20]–[24]. Despite limitations [10], [25], [26], ultrasound thermography holds the promise of providing temperature feedback with high spatial and temporal resolution (sum-millimeter and sub-millisecond). Other related methods (e.g. photoacoustic-based approach described in [27]) are being developed. These efforts provide hope that ultrasound thermography will lead to a robust method for monitoring and guidance of HIFU-based thermal therapy.

A number of different ultrasound thermography methods [8], [28], [29] have been proposed. The speckle tracking based method described in [10] was recently implemented in realtime using a commercially-available diagnostic scanner and general -purpose graphics processing unit (GPGPU) [30]. In addition, we have also demonstrated realtime control of a 64-element dual-mode ultrasound array (DMUA) system [18], [19]. The temperature imaging system was integrated with the DMUA driver allowing for the selection of multiple temperature control points within the treatment volume (as seen on the B-mode realtime images). The spatially distributed feedback available through noninvasive realtime ultrasound thermography allows for realtime control of spatially distributed multiple-focus phased-array heating patterns [16]. In this paper, we give a description of an ultrasound phased array system for image-guided thermal therapy applications with illustrative examples of multiple-focus heating patterns. We also describe our multi-point (multiple-focus) control algorithm that with emphasis on special requirements for multiple-focus heating patterns. In particular, we describe our implementation of dynamic power reallocation among different focal points upon reaching each set point. Examples of long-exposure (used in hyperthermia) and short-exposure (used in ablative therapy) multiple-focus patterns are given and their potential applications are discussed.

II. Materials and Methods

A. Experiment Setup

The setup shown in Figure 1 was used to generate the results presented in this paper. A 1-MHz, 64-element ultrasound phased array was used for generating single and multiple-focus heating patterns (Imasonic, Inc., Voray sur l'Ognon, France). A tissue mimicking phantom fabricated according to the procedure described in [31] was used as a target. A linear array imaging probe (LA14-5) was used to acquire ultrasound images for guidance and noninvasive thermography.

A needle thermocouple (TMQSS-020U-6) was used to monitor the temperature rise in the phantom in response to the array heating patterns as shown in the figure. The needle shaft was carefully positioned at the boundary of the imaging slice to minimize distortion of the RF data collected using the imaging probe.

1) Array Driver and Control System—The therapeutic array driver employs a 1000 W programmable DC power supply (Agilent 6030A). The supply is capable of providing DC voltage, V_{DC} of up to 200 V and a maximum current up to 17 A (within the 1000 W limit). The DC supply feeds the 64-channel amplifier driving the array elements through series matching inductors (an improved version of the system described in [17]). The supply voltage, together with the matching circuit and the power factor of a given array element, determine the maximum particle velocity achieved on the surface of that element, U_{max} .

The current drawn from the supply is determined by the amplitude distribution of the active array channels. This is subject to the maximum current limitation, a user-specified value up to 17 A for the DC supply used in these experiments. The instantaneous current value supplied by the Agilent 6030A was interrogated during each heating experiment at a sampling rate of 12.5 Hz with time stamp information.

For the experiments shown in this paper, V_{DC} was set to achieve a desired heating rate at a given control point in the heating pattern, e.g. 1°C/s for typical long exposure experiment. This may be adjusted up or down to meet certain requirements on the heating rate as may be dictated by the application, e.g. slower values in drug activation and larger values in high-temperature applications.

2) Multiple-focus Synthesis—Phase and amplitude control is achieved through a 200-MHz FPGA-based digital control circuit [18] allowing for 0.01 V_{DC} and 1.8° amplitude and phase resolution, respectively. The phase and amplitude distributions are obtained using the optimal pattern synthesis method we introduced in [32]. The weighted minimum-norm solution described in [32] was used to obtain an equal-magnitude distribution, which achieves the highest driving efficiency from the DC supply. Mathematically, the pressures at a set of M control points are specified as the vector $p = [p_1 p_2 \dots p_M]'$, where $[\cdot]'$ indicates matrix (vector) transpose. For an N -element array, an $M \times N$ matrix propagation operator, H , is defined with the mn th element defining the directivity of the n th array element at the m th control point. The N -element array excitation vector is obtained through a weighted minimum-norm solution,

$$\hat{u} = W H^H (H W H^H)^\dagger p \quad (1)$$

where W is a positive definite weighting matrix with $[\cdot]^H$ and $[\cdot]^\dagger$ representing, respectively, the Hermitian transpose and the regularized pseudoinverse.

B. Temperature Measurements

1) Direct Measurements—A needle thermocouple (Omega, Stamford, Connecticut) connected to a GPIB-controlled data acquisition system (Agilent 34970A) was used to directly measure the temperature at one of the control points for verification purposes. The needle shaft was inserted into the phantom in parallel to both the imaging and therapeutic array faces. It was carefully placed at the edge of the imaging slice of the diagnostic system with the junction just past the (geometric) focal plane of the therapeutic array. The raw thermocouple readings were acquired at a rate of 100 Hz and stored in the Agilent 34970A buffer. The sampled data was uploaded to the controlling workstation at the conclusion of each heating experiment. The thermocouple data shown in the Results Section below are filtered using an 8-point moving average.

2) Noninvasive Thermography—We used the LA14-5 linear array probe on the Sonix RP to acquire 2D RF data in realtime. The system described in [30] was used to obtain 2D

temperature change images at 99 fps. The estimated temperature values were determined based on the measured material properties of the tissue-mimicking phantom used according to the algorithm described in [10], [30]. The temperature imaging equation used:

$$\Delta T(z) = \frac{c(T_0)}{2} \left[\frac{1}{\beta - \alpha} \right] \frac{\partial}{\partial z} (\delta t(z)), \quad (2)$$

where $\alpha = (\partial d(T)/\partial T)/d(T)$ and $\beta = (\partial c(T)/\partial T)/c(T)$. For the phantom material used to obtain the experimental results shown in this paper, Figure 2 shows the speed of sound vs temperature curves used to determine the material constant suggested in [10]. This result shows that the temperature dependence of the speed of sound in the phantom material is consistent with many *in vitro* tissues as reported by Nasoni [33].

C. Realtime Feedback Control

For the experiment setup described in Figure 1, the coordinates of the control points were placed on the line of intersection between the imaging (xz) and therapeutic (xy) planes. Two control points or foci were defined for each heating experiment to illustrate the operation of realtime temperature control, but the methods described herein apply to larger number of foci. A proportional integral (PI) controller represented by the block diagram shown in Figure 3 was used to determine the power level at each control point. Anti-windup compensation was implemented digitally using a limiter in the integral component path as shown in Figure 3. It functions by preventing the integral term from accumulating above or below pre-determined bounds [34]. This technique is widely used in conjunction with PI control applications where the control output (CO) values are subject to upper or lower limits, or both. In this case, the CO cannot be negative, which sets a lower limit of zero. In addition, the power delivered to any control point is limited by a maximum value determined by the available power at the supply and/or power allocation scheme to the individual control points. The setpoint temperatures at the control points can be defined independently as long as the control points are sufficiently spaced. There are two factors guiding the judicious choice of control points: 1) The conditioning of the propagation operator in (1) [16], and 2) The thermal properties of the medium, together with the duration of the heating. It should be noted that the multipoint control algorithm described herein is fundamentally different from the realtime control algorithm described in [9]. In [9], we have described an algorithm for multipoint temperature control by changing the *dwell times* of precomputed single- or multiple-focus patterns, i.e. no modification of the driving signal distributions. In this paper, we describe the realtime control of multiple-focus heating patterns by resynthesizing the heating patterns according the demand of the PID controllers associated with the control points. This mode is well-suited for the relatively short exposures used in ablative thermal therapies.

1) Efficient Generation of Multiple-Focus Heating Patterns: As discussed in [32], the pseudoinverse solution to the pattern synthesis problem often results in driving signal vectors with variable amplitude distribution. This may limit the power deposition at the focal spots when the voltage across some of the array elements is at or near the maximum value determined by V_{DC} and the matching circuit topology [17]. The weighting algorithm described in [32] allows for compressing the dynamic range of the magnitude distribution to improve the array driving efficiency defined by

$$\eta_A = \frac{\sum_{n=1}^N |u_n|^2}{NU_{max}^2} \times 100\%, \quad (3)$$

where U_{max} is the maximum achievable value of the driving signal on the surface of the array. A maximum efficiency of 100% indicates equal-amplitude (or phase-only) synthesis, which is highly desirable provided the phase distribution does not result in evanescent modes on the surface of the array. We have shown in [32] that the improved efficiency achieved using the iterative weighting algorithm results in corresponding improvement in power deposition at the foci.

2) Dynamic Power Reallocation—The multiple-focus synthesis problem, as given in (1), gives the complex particle velocities at the surface of the array elements in terms of the specified complex pressures at the control points. The complex pressures at the control points can be determined from the desired initial heating rate at the m th point,

$$\frac{dT_m}{dt} = \frac{1}{\rho C} Q_m = \frac{\alpha}{\rho^2 c C} |p_{md}|^2, \quad (4)$$

where ρ , c , C and α are the density, speed of sound, specific heat, and absorption, respectively. The complex particle velocity distribution obtained using (1) is directly related to the terminal voltage, which determines the current supplied by the DC supply to the amplifier circuits driving the array elements. The maximum particle velocity, U_{max} may be determined by the transducer technology. For example, the therapeutic array described in this paper is designed to provide a maximum surface intensity of 5 W/cm^2 . The driving circuitry may limit the maximum achievable particle velocity, e.g. saturation current in matching inductors or current limitation of the amplifier transistors. Finally, the DC supply may limit the total current supplied to the array driver. For these reasons, U_{max} must be predetermined based on the requirements of the therapy and the capabilities/limitations of the driving circuitry.

Knowledge of the initial heating rate and approximate tissue properties in the treatment region, together with the propagation model allow for the computation of the needed power deposition at each focal spot. Assuming an initial power distribution among the control points (e.g. equal distribution), the total acoustic power requirement can be determined. The DC supply power can be determined from the acoustic power and the efficiency of the driving circuitry. For the system used in this paper, V_{DC} and I_{DCmax} are set on the DC supply at the outset of the heating experiment. This defines the available DC power, which will not be exceeded during the experiment.

The above considerations, coupled with the PID control strategy at the individual control points, necessitate a dynamic power reallocation strategy for minimizing the time to reach the *setpoint* temperatures. Simply stated, the controller needs to be aware of the power requirement for each focus to *maximize* the heating rate at the points that have not yet reached the setpoint temperatures. Once a setpoint temperature has been reached, the power delivered to the focus controlling it can be significantly reduced, leaving a larger fraction of the supply power to be directed to the remaining foci controlling points below their setpoint temperatures.

The logic driving the dynamic power reallocation while the PID controllers are active relies on testing the truth of the statement “*All setpoint temperatures have been reached.*” This determines the output of the PID controllers according to the flowchart shown in Figure 4. If yes, only a fraction of the available power is needed to maintain control ($u_{max} < U_{max}$); each focus will receive its requested power as specified by the PIDs. If no, the algorithm attempts to use 100% of the available power ($u_{max} = U_{max}$) by shifting excess power from points which are not using their full share, to points which are requesting more than their share.

This can be performed adaptively (based on online measurement of temperature response) or in a prespecified manner (e.g. equal fractions of the available power).

In order to share power between multiple focal points there must exist a function that relates the maximum complex pressure for any set of focal points, given the pressures at the remaining focal points, such that $u_{max} = U_{max}$. Figure 4 b) shows such a function for a double-focus pattern where power has initially been split evenly between the foci. The hatched region under the curve represents all realizable combinations of pressures. The diagonally hatched region represents the pressures achievable without power reallocation, i.e. each PID receives its requested power. The horizontally and vertically hatched regions represent the additional pressures made available by power reallocation. As an example, assume the two focal points were being heated to the same temperature, but focal point 1 were to heat faster than focal point 2. Once focal point 1 reached its setpoint temperature and its controller asked for less power, the function in Figure 4 b) would be used to determine how much the pressure at focal point 2 could increase. In this way, an array that utilizes power reallocation is able to adaptively compensate for tissue inhomogeneities and tissue changes during therapy without any user input. In addition, the algorithm guarantees the use of maximum array efficiency as long as any of the control points is below its setpoint temperature. This minimizes the time to reach all setpoint temperatures and, consequently, minimize the treatment time when multiple-focus patterns are used.

For the purposes of this paper, we have developed a table-lookup approach for determining the magnitude of the complex pressure at the m th control point as a function of the desired values at the remaining control points. Briefly, assuming equal power sharing for points below their setpoint temperatures, the desired value at the m th control point, p_{md} , can be raised to a higher value based on the available power fraction. As an example, assume a two-focus pattern initialized with 50% of the available supply power delivered to each focus ($p_{1d} = p_{2d} = p_{max}$, where p_{max} is the pressure magnitude achievable using 50% of the available power.) Once one of the two control points (say Point 1) has reached its temperature setpoint, $PID1$ requests $p_{1d} < p_{max}$ leaving a larger fraction for $PID2$ to request $p_{2d} > p_{max}$. This accelerates the heating rate at Point 2 to minimize the time to reach its temperature setpoint. This control approach with dynamic power reallocation is summarized in Figure 4. The hatched regions in Figure 4 b) show when the lookup table is used (horizontal and vertical lines) and when direct calculation is used (diagonal lines). As illustrated by the figure, the lookup table is used whenever the desired pressure on any of the control points exceeds the maximum pressure preallocated to that point.

III. Results

We demonstrate the performance of the multiple-focus control algorithm with two sets of experiments referred to as *long exposure* and *short exposure* with heating durations of 15 seconds and 5 seconds, respectively. The latter is an example of typical exposure duration in high-temperature surgery using HIFU. The former is long enough to demonstrate the workings of the algorithm in lower temperature applications such as drug delivery and hyperthermia. While heating durations in these applications may be much longer than 15 seconds, this duration is long enough to demonstrate the well-behaved nature algorithm in reaching the specified setpoint temperatures with typical settings of the PID parameters.

A. Long Exposure Temperature Control

A two-focus pattern similar to that shown in Figure 1 b) was used. The timing of the control experiment was as follows:

- Five seconds of baseline data was collected before the application of the heating pattern.
- The two-focus pattern was applied at 5 seconds with equal power applied to both foci. The setpoint temperatures were 3°C for the primary focus (on the left) and 2, 3, 4, 5, and 6°C at the secondary focus. The supply voltage, V_{DC} , was arbitrarily set to achieve approximately 1°C/s heating rate at the primary focus. The PID constants were selected to achieve a short settling time and minimum overshoot for the selected initial heating rate and given the values $k_p = 2$, $k_i = 4$, and $k_d = 0$. While the power was on (15-second duration):
  - Both PIDs were active according to the flowchart shown in Figure 4.
  - For all setpoint combinations, equal power was allocated to each of the two foci at the start. While the temperatures at the primary and secondary focus remained below the setpoint temperatures, each PID requested the maximum available, which was 50% of the available DC power for the two-focus heating pattern used.
  - Once a setpoint temperature has been reached, the corresponding PID requested less power to maintain the temperature, which left some fraction of the DC power to be reallocated to the other focus.
  - The dynamic power reallocation algorithm recalculated the fraction of power delivered to each focus. This resulted in an increase in the heating rate at the focal point with temperature below the setpoint temperature.
  - Once all setpoint temperatures have been reached, all the PIDs requested only the necessary power to maintain the temperature. This typically resulted in reducing the total power required from the DC supply.
- Temperature imaging continued for another 12 seconds after the array was turned off to monitor the temperature decay in the target plane.

Note that the thermocouple was carefully placed so that it was barely visible in the imaging plane (at the edge of the imaging slice). At the same time, it was also placed within the focal spot of the secondary focus, but below the focal point. This ensured that the thermocouple junction was directly heated by the secondary focus, but with minimum distortion to the therapy and imaging beams. The direct heating of the thermocouple produced a self-heating artifact that served as an indicator of the change in acoustic intensity at the thermocouple junction, which allowed us to observe the dynamic power reallocation.

The results of this set of long-exposure experiments are shown in Figure 5. The estimated temperature profiles at the primary and secondary control points are shown in Figure 5 a) – e) for $T_{sec} = 2, 3, 4, 5, 7^\circ\text{C}$, respectively. Figure 5 f) shows the corresponding thermocouple measurements recorded near the secondary control point. For the cases where T_{sec} was set equal to 4, 5, and 7°C, it is easy to see the change in the heating rate at the secondary control point upon reaching the set point at the primary control point in Figure 5 c) – e) and the corresponding thermocouple measurement. Additionally, the thermocouple measurements exhibit self-heating artifacts that appear as overshoot before decaying to the control temperature at the thermocouple junction location. These dynamics reflect the sudden increase of power delivered to the secondary focus upon reaching the setpoint temperature at the primary control point. It is also interesting to note that, for $T_{sec} = 2^\circ\text{C}$, a small but measurable change in the heating rate can be observed at the primary control point upon reaching the setpoint temperature at the secondary control point.

To further illustrate the dynamic power reallocation for the multiple-focus patterns pattern, we show the profiles of the various parameters of the two-focus pattern used similar to the control experiments shown in Figure 5 for the case $T_{sec} = 7^\circ\text{C}$. Figure 6 shows the estimated temperatures at the primary and secondary control points and the corresponding thermocouple measurement near the secondary control point. The changes in the heating rate at the secondary point are clearly visible in both the estimated and directly measured temperature profiles. These occur at 5 sec (POWER ON time), ≈ 7 sec (primary setpoint temperature reached), and ≈ 10 sec (secondary setpoint temperature reached). These changes in the heating rate reflect the changes in power deposition at the secondary control point in response to the request of *PID2* controller subjects to the constraints on the power supply and the dynamic power reallocation described in Figure 4. Figure 7 a) shows the relative pressure magnitudes at the primary and secondary points during the experiment. The profiles show both the synthesized (solid) and actually achieved pressure values (dashed, taking the discretization in the driver into account). It is clear that the amplitude control with $< 0.01 U_{max}$ precision allows for excellent realization of the theoretically specified (desired) pressure values at the control points. Figure 7 b) shows a mapping of the control weights on the decision regions described in Figure 4 b) starting at POWER ON time with $(p_{1d}, p_{2d}) = (1, 1)$. For $5 < t < 7$ sec (both control points below setpoint temperatures), $p_{1d} = p_{2d} = 1$ and no power reallocation occurs. When one or more of the setpoint temperature is reached, p_{1d} and p_{2d} will be increasing (indicated by $\uparrow$), decreasing (indicated by $\downarrow$), or fluctuating (indicated by $\uparrow\downarrow$). For $7 < t < 7.5$ s (just after reaching setpoint temperature at primary control point), $p_{1d} < 1 \downarrow$ and $p_{2d} > 1 \uparrow$ with p_{2d} maximum allowable for a given value of p_{1d} as determined by the lookup table. For $7.5 < t < 10$ sec (*PID1* actively controlling primary set point temperature), $p_{1d} < 1 \uparrow\downarrow$ and $p_{2d} > 1 \uparrow\downarrow$ excess power reallocated to the secondary point, but limited by the fluctuation in p_{1d} values to maintain control of the primary control point. For $10 < t < 11$ (just after reaching secondary setpoint temperature), $p_{1d} < 1 \uparrow\downarrow$ and $p_{2d} > 1 \downarrow$ *PID2* requesting less than the maximum allowable as it moves toward maintaining the temperature at the secondary control point. Finally, for $t > 11$ sec, $p_{1d} < 1 \uparrow\downarrow$ and $p_{2d} < 1 \uparrow\downarrow$ both *PID1* and *PID2* are actively controlling the primary and secondary control points around their respective setpoint temperatures. This is an important result that clearly illustrates the fast, but well-behaved, response of the *PID* controllers to reaching the various setpoint temperatures.

To confirm the dynamics of power reallocation, we computed the power delivered in the vicinity of each control point for each set of weights shown in Figure 7. The result is shown in Figure 8. One can see three distinct intervals in terms of power sharing and total power delivered to the focal plane. These can be described as follows:

- 1) $0 < t < 2$ s after POWER ON: Equal power was delivered to each focus before the setpoint temperature at the primary control point was reached. In this case, both *PIDs* were asking for the maximum available power since the error was negative. The power sharing was set at 50%, but other ratios could have been set to satisfy specific treatment considerations. The relative weights of the pressure at both control points was set to 1 as can be seen in Figure 7.
- 2) $2.5 < t < 5$ s after POWER ON: Setpoint temperature at the primary control point is reached and *PID1* requested less power. The relative weight at the primary control point dropped while that at the secondary increased. Correspondingly, the power allocated to the focus at the primary control point was approximately 20% of the total power in the focal plane while the power delivered to the secondary was 80%.
- 3) $6 < t < 15$ s after POWER ON: Setpoint temperatures were reached at both control points and both *PIDs* requested less power to maintain the temperature.

The supply power was reduced and the power share at each focus was determined by the relative weight requirement (both < 1 , but not necessarily equal).

Figure 9 a) shows the normalized DC supply power and the array efficiency predicted by Equation 3 for the $T_{sec} = 7^{\circ}\text{C}$ experiment. The DC supply power is determined by the set voltage on the Agilent 6030A and the actual current measured during operation using the GPIB interface. Figure 9 b) shows the normalized DC supply power and the normalized power deposition in the focal plane for the same experiment. This result serves to demonstrate that the synthesis process results in well-behaved multiple-focus patterns where the power delivered to the focal points is proportional to the input (DC supply) power. This would not have been the case, for example, if the multiple-focus patterns required high spatial frequencies at the array surface resulting in evanescent waves. This serves to demonstrate the robustness of the synthesis process in response to dynamic changes dictated by the PID requirements at the different control points.

B. Short Exposure Temperature Control

A similar set of experiments were carried out to demonstrate the performance of the algorithm in the control of multiple-focus patterns with shorter exposure durations. As was done above, the setpoint temperature at the primary control point, T_{pri} was fixed at 3°C in all experiments. On the other hand, the temperature setpoint at the secondary control point, T_{sec} was set at 2, 3, 4, 5, and 6°C for the different experiments. The DC supply voltage was fixed at higher value (approximately $2\times$ to achieve a faster heating rate of $\approx 4^{\circ}\text{C}$ per second. The PID constants, k_p , k_i , k_d , were the same as in the long exposure experiments to give the reader an idea about the dynamic behavior of the controllers when faster heating rates are sought.

The estimated and measured temperature profiles for the short exposure experiments are shown in Figure 10. In this case, the heating rate at the control points is such that the temperature response exhibits an overshoot and oscillations as can be seen from both the noninvasive estimates and the thermocouple measurements. As before, the overshoot in the thermocouple measurement is more pronounced (compared to the noninvasive estimate) due to the direct heating at the thermocouple junction. It is clear from these results, however, that the thermocouple measurements reflects the dynamics of the control and dynamic power reallocation algorithm. It is also clear that both PIDs achieve control within a fraction of the POWER ON time for this short exposure protocol.

IV. Discussion

The results shown in this paper demonstrate, to the best of our knowledge, the first realtime demonstration of temperature control using multiple-focus phased array patterns based on noninvasive temperature feedback and with sub-second resolution. The configuration presented in this paper is an example of an ultrasound-guided focused ultrasound (USgFUS) employing phased array technology for generating single or multiple-focus patterns that may be tailored to achieve the treatment objectives, e.g. hyperthermia, drug activation, high-temperature ablative therapies, etc. This system is currently operational in realtime and is ready for deployment in realtime thermal therapy applications.

While control is a major focus of this paper, the specific controller used to achieve the control objective is not. Standard PID controllers were used for the individual control points as an example of a commonly used control algorithm familiar to most readers. More sophisticated control algorithms could have been used [9] and are currently being investigated in the context of the transient bioheat equation (tBHTE) as a distributed model of the treatment volume and possibly thermal dose calculations [35], [36]. A more important

aspect of the controller implementation, however, is the dynamic power reallocation algorithm, which was used to dynamically (adaptively) determine the power directed to the individual focal points (based on PID commands). This is fundamentally important to the successful use of multiple-focus pattern synthesis in achieving specific heating rates at the control points given the characteristics/limitations of the available power supply. The results shown demonstrate how the dynamic power reallocation algorithm achieves:

- 1) Maximize the array efficiency by compressing the dynamic range of the driving signal distribution resulting from the theoretical multiple-focus synthesis.
- 2) Distribute the available power among the individual foci to satisfy the PID requirements.

For the feedback control system described in this paper, this was achieved in realtime at 25 Hz update rate. It should be emphasized that the update rate could have been done at the full frame rate of the temperature feedback of 99 Hz. In fact, our GPU/FPGA beam synthesis/driver for our array allows update rates in the 400 – 600 Hz range. Therefore, with the advent of high frame rate ultrasound systems, this allows for exquisite control over the spatial and temporal dynamics of the heating/lesion formation process in ways that cannot be match by other guidance modalities, e.g. MRI. For example, [24] and [37] are examples of the most recent publications on MR thermometry for guidance of therapeutic ultrasound. The thermometry information is available at rates of 1.25 – 2.9 times per second and with relatively coarse spatial resolution (slice thickness of 4 – 7 mm and grid sampling of 0.7 – 2.4 mm within slices). Regardless of the method used for obtaining noninvasive temperature measurements at the control points, however, the dynamic power reallocation and optimal synthesis methods described in this paper may be the key to successful use of multiple-focus patterns in therapeutic applications.

The ultrasound thermography algorithm described in this paper has some limitations that must be overcome in order to become a viable clinical tool in USgFUS. In [30] we have introduced M2D imaging mode as an important tool in capturing the full range of thermal and mechanical strains in 2D spatial coordinates with high temporal resolution (100s of fps with limited FOV). This will be the key in removing tissue motion/deformation artifacts through new formulations dealing with the temperature imaging as an image reconstruction problem [38]. We have recently applied these techniques on *in vivo* RF data acquired during sub-therapeutic FUS heating in tumors implanted in the hind limb of nude mice. The results demonstrate clearly that strain components due to temperature change can be reliably separated from strain components resulting from natural deformations, e.g. due to breathing [39].

V. Conclusions

We have experimentally demonstrated the realtime control of multiple-focus phased array heating patterns for thermal therapy based on noninvasive ultrasound thermography. We have shown results relevant to the control of short-exposure multiple-focus patterns suitable for ablative therapy as well as longer exposure patterns suitable for hyperthermia, drug delivery and other thermal therapy applications. We have also demonstrated the use of dynamic power reallocation method designed to maintain maximum array driving efficiency with multiple-focus patterns, an important factor in the practical implementation in real clinical situations. In fact, dynamic power reallocation is essential to the successful use of multiple-focus patterns in reducing the treatment time. Even for the simple, double-focus, patterns shown in this paper, the driver would have failed to provide adequate heating at the primary and secondary foci if we did not employ the weighting and dynamic power reallocation algorithms. The results also demonstrate the fact that dynamic power

reallocation is observed through changes in the heating rate at the control points, which can be reliably computed from noninvasive temperature estimation. Thermocouple measurements in the vicinity of the HIFU focus confirm the dynamics of temperature variation in response to the control algorithm, including the effects of power reallocation method. The results presented in this paper clearly demonstrate the feasibility of using multiple-focus heating patterns to achieve treatment objectives without compromising the driving efficiency of the phased array.

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Fig. 1. Experiment Setup: a) Imaging and therapy probes with needle thermocouple shown. b) Imaging slice with temperature overlay together with the intensity profile of a double-focus pattern generated using the therapeutic array.

Fig. 2. Measured speed of sound in water and in phantom material used in the control experiments in the range of 23 – 50°C. Measurements were made using the pulse transmission technique described in [33].

Fig. 3.

Multi-point PI controller with anti-windup compensation. Noninvasive temperature data at a given control point is used to compute the error signal, which drives the PI controller for that control point. The limiter inside the integrator loop prevents the integrator from going deep into saturation. Control outputs from all the PIDs are handled by the power reallocation algorithm described in Sec. II-C.2.

Fig. 4.

a) Flowchart of Dynamic Power Reallocation and, b) regions for p_{md} , $m = 1, 2$ calculations for a two-focus heating pattern.

Fig. 5.

Long Exposure Experiments: a) – e) Estimated temperature rise at the primary (Blue) and secondary control points. In all cases, setpoint temperature at primary control point $T_{pri} = 3^{\circ}\text{C}$. Setpoint temperatures at secondary control point $T_{sec} = 2, 3, 4, 5, 7^{\circ}\text{C}$ for the different experiments. f) Thermocouple measurements near the secondary control point for the different experiments.

Fig. 6. Illustration of dynamic power reallocation: a) Primary control point at 3°C. Secondary control point at 7°C. b) Corresponding thermocouple measurement at secondary point.

Fig. 7.

a) Desired pressures at control point as requested by the PIDs (solid) and as actually realized by the controller (dashed), including discretization in the digital implementation. b) Mapping of requested control weights by PIDs on the decision regions described in Figure 4 b).

Fig. 8.
Relative power at each control point as a fraction of the power delivered to the focal plane for the $T_{sec} = 7^{\circ}\text{C}$ experiment.

Fig. 9.

a) Relative DC supply power (from measured current) and η_A (Equation 3). b) Relative DC supply power (from measured current) and relative power deposition in the focal plane for the $T_{sec} = 7^\circ\text{C}$ experiment.

Fig. 10.

Short Exposure Experiments: a) – e) Estimated temperature rise at the primary (Blue) and secondary control points. In all cases, setpoint temperature at primary control point $T_{pri} = 3^{\circ}\text{C}$. Setpoint temperatures at secondary control point $T_{sec} = 2, 3, 4, 5,$ and 6°C for the different experiments. f) Thermocouple measurements near the secondary control point for the different experiments.