INTRACAVITARY ULTRASOUND PHASED ARRAYS FOR THERMAL THERAPIES

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Currently, the success of hyperthermia and thermal surgery treatments is limited by the technology used in the design and fabrication of clinical heating devices and the completeness of the thermometry systems used for guidance. For both hyperthermia and thermal surgery, electrically focused ultrasound generated by phased arrays provides a means of controlling localized energy deposition in body tissues. Intracavitary applicators can be used to bring the energy source close to a target volume, such as the prostate, thereby minimizing normal tissue damage. The work performed in this study was aimed at improving noninvasive prostate thermal therapies and utilized three research approaches: 1. Acoustic, thermal and optimization simulations, 2. Design and fabrication of multiple phased arrays, 3. Ex vivo and in vivo experimental testing of the heating capabilities of the phased arrays. As part of this study, a novel aperiodic phased array design was developed which resulted in a 30-45% reduction in grating lobe levels when compared to conventional phased arrays. Measured acoustic fields generated by the constructed aperiodic arrays agreed closely with the fields predicted by the theoretical simulations and covered anatomically appropriate ranges. The power capabilities of these arrays were demonstrated to be sufficient for the purposes of hyperthermia and thermal surgery. The advantage of using phased arrays in place of fixed focus transducers was shown by demonstrating the ability of electronic scanning to increase the size of the necrosed tissue volume while providing a more uniform thermal dose, which can ultimately reduce patient treatment times. A theoretical study on the feasibility of MRI (magnetic resonance imaging) thermometry for noninvasive temperature feedback control was investigated as a means to improve transient and steady state temperature distributions achieved in hyperthermia treatments. MRI guided ex vivo and in vivo experiments demonstrated that the heating capabilities of the constructed phased arrays were adequate for hyperthermia and thermal surgery treatments.

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1. INTRODUCTION

1.1 Prostate Diseases

The prevalence of benign prostatic hyperplasia (BPH) and prostate cancer and the high costs and complication rates currently associated with treating these diseases warrant the investigation of alternative treatments. Each year approximately 800,000 men receive treatment for BPH, and surgical treatment of BPH is the second most commonly performed surgery on men in the United States (Holtgrewe et al., 1989). In 1996, an estimated 317,000 U.S. men will be diagnosed with prostatic carcinoma and 41,400 will die from it, making it the most prevalent and the second most deadly form of cancer in U.S. men (American Cancer Society, 1996). Treatment modalities for BPH include transurethral resection, radical prostatectomy, hyperthermia, ablation, cryotherapy, pharmacological agents, stents and balloon dilatation. Treatment modalities for prostate cancer include radical prostatectomy, radiotherapy, pharmacological agents, hyperthermia and ablation. Although surgery is currently the treatment of choice for BPH, complications affect 15-25% of these BPH patients. (McCullough, 1993). While surgery is used as often as radiation therapy for treating prostate cancer, many of the men requiring treatment are of old age and may have health problems which rule out surgery as a viable option. The surgical complication rate for prostate cancer patients is 20-50% (Garnick, 1994). Complications which are common to both BPH and prostate cancer surgical patients include incontinence, impotence, retrograde ejaculation, urinary tract infection and hemorrhaging. The development of safe, effective and minimally invasive alternatives to surgery are potentially useful clinically for the treatment of BPH and prostate cancer.
1.2 Thermal Therapies

The thermal therapies discussed in this study are hyperthermia and thermal surgery. During a typical hyperthermia treatment, the objective is to heat a localized region of tissue to 42-45°C for 15-60 minutes. Hyperthermia, as a cancer treatment, has been shown to cause cell death directly (Dewey et al., 1977, and Stohbehn and Douple, 1984) and has also been shown to enhance the cytotoxicity of radiation therapy (Dewey et al., 1977, and Overgaard, 1989) and chemotherapy (Hahn, 1979). Direct hyperthermic cytotoxicity is most effective in acidic, hypoxic and poorly vascularized tissue (Suit and Gerweck, 1979 and Song et al., 1980), which is representative of a typical tumor environment. Hyperthermia enhances radiation therapy by preventing cellular repair mechanisms from repairing radiation induced injury (Overgaard, 1980) and is effective in killing hypoxic cells, which are resistant to radiation therapy (Overgaard and Overgaard, 1987). It has been shown that the synergistic effects of radiation combined with hyperthermia can be more than additive and are most effective when hyperthermia is administered simultaneously with, just prior to, or immediately following radiation treatment (Overgaard, 1989). Specifically for prostate hyperthermia purposes, the target treatment would be a 5-8°C (from 37°C to 42-45°C) temperature elevation over a volume approximating that of the prostate (approximately 4-5 x 4 x 2 cm), while tissue surrounding the prostate is kept below 42°C. Hyperthermia treatments have been studied clinically and have shown potential for the treatment of BPH (Stawarz et al., 1991) and prostate cancer (Strohmaier et al., 1991 and Fosmire et al., 1993).

Candidates for prostate hyperthermia cancer treatments include those patients which have the tumor localized within the prostate or those who have extraprostatic extension of the disease to surrounding tissue but not to those who have metastatic disease (unless for palliative purposes). The clinical stage for these patients is C1 to D0 as defined by the Whittmore-Jewett staging system for adenocarcinoma of the prostate (Jewett,
1975), or T2 to T4 as defined by the American Joint Commission on Cancer Staging System for adenocarcinoma of the prostate (Beahrs et al., 1996).

Thermal surgery, also referred to as tissue ablation or ultrasound surgery, is used clinically to necrose both malignant and nonmalignant tissue (e.g. benign tumors, benign prostate hyperplasia and aberrant cardiac conduction pathways). As early as the 1940’s and 1950's it was shown that well demarcated lesions could be created with focused ultrasound without injuring surrounding tissue (Lynn et al., 1942 and Fry et al., 1954). During ultrasound surgery, tissue is necrosed by elevating the temperature of a small region of tissue to 60°C-100°C for a short time (less than 1 minute). Specifically for BPH thermal surgery treatments, the target treatment would be to necrose a (4-6 x 0.5-1 x 0.5-1 cm) zone of tissue surrounding/constricting the urethra without heating tissue outside of the prostate to temperatures of 45°C or higher to prevent pain. Human prostate tissue has been successfully necrosed without rectal wall damage and has been studied as a treatment for BPH (Gelet et al., 1993 and Foster et al., 1993). Thermal surgery of the entire prostate may not be feasible as rectal wall damage may be sustained during ablation of adjacent tissue; however, ablation is potentially useful for treating localized cancer or for debulking portions of a large tumor (Madersbacher et al., 1995).

1.3 Motivation for Intracavitary Ultrasound Phased Arrays

Phased arrays developed for hyperthermia have used either electromagnetic energy in the form of microwaves and radio waves or acoustic energy in the form of ultrasound. For both electromagnetic and acoustical waves, higher frequencies and smaller wavelengths correspond to sharper focusing capabilities but also shallower penetration depths in tissue due to propagation losses. The following is a brief summary of some of the electromagnetic arrays that have been developed and their associated limitations. A
summary of previously developed ultrasound phased arrays will follow in an upcoming section.

1.3.1 Electromagnetic Phased Arrays

Microwave phased arrays for hyperthermia purposes were first studied by Short and Turner and shown to increase localized heating in vivo relative to unphased arrays (Short and Tuner, 1980). Microwave phased arrays have been shown to be able to shape the power deposition pattern produced by planar arrays (Diederich and Stauffer, 1993) and arrays that conform to the shape of the body (Lee et al., 1992). Previous studies have also investigated using phase and amplitude control to improve the penetration depth (Hand et al., 1986 and Lee et al., 1992). Annular radio wave phased arrays are known to increase the intensity of the electromagnetic energy at deep locations when compared to non-focused radio waves (Kato and Ishida, 1993). Even electromagnetic phased arrays consisting of only four elements have been shown to improve the control of steady state temperature distributions (Nikita et al., 1993).

Typically electromagnetic operating frequencies used for hyperthermia range from under 60 MHz to 2450 MHz. Frequencies near 100 MHz tend to have deep penetration but lack the ability to produce a significant focus. Operating frequencies near 2450 MHz have good focusing potential but very shallow penetration depths. Clinical microwave heating devices often operate at 915 MHz, as it represents a compromise between penetration depth and ability to focus. A previous study demonstrated that a 16 element planar phased array operating at 915 MHz was able to heat depths of only 3 cm or shallower (Fenn et al., 1993). An annular radio wave phased array operating at 100 MHz was studied for deep heating (> 10 cm), but due to substantial near field heating, adaptive nulling and focusing techniques were investigated to improve the heating of the target volume (Fenn, 1992). As further evidence of the problems associated with a lack of control of the electromagnetic field, a study concluded that an annular radio wave array
was not useful as a regional heating device for prostate cancer due to higher temperatures in the rectal wall than in the prostate (Anscher et al., 1992). Given the penetration and focusing limitations of electromagnetic hyperthermia, studies investigating limb heating with radio wave phased arrays have been performed (Charny and Levin, 1991), and limbs may prove to be among the most feasible of anatomical sites, other than superficial sites such as chest wall tumors.

Due to shorter wavelengths, ultrasound is able to produce much sharper (smaller), more controllable, and deeper foci than electromagnetic waves. For example, a 2450 MHz microwave has a wavelength of 1.8 cm in soft tissue and a penetration depth of 1.7 cm (Johnson and Guy, 1972) as compared to a 1.0 MHz ultrasound wave which has a 1.5 mm wavelength and a penetration depth of approximately 10 cm (Hynynen, 1990). As a result of the improved focusing capabilities, ultrasound is able to create a temperature rise in a deep tumor which is more uniform and controllable than that produced by microwaves (Lele, 1975). Typically therapeutic ultrasound frequencies range from 0.4 MHz to 10 MHz.

1.3.2 Focused Ultrasound

While nonfocused ultrasound has been used for therapeutic heating, both deeper heating and locally higher intensities can be achieved with focused ultrasound. By focusing the energy in a localized region, it is possible to selectively deliver more energy to a tumor than surrounding normal tissue. To achieve a geometric intensity gain, the radiating area of the transducer(s) must be larger than the cross-sectional area of the focal region. Several methods of focusing ultrasound have been used. Geometrically focused transducers, such as those that are sections of a sphere, produce a focus at a fixed location based on the radius of curvature of the transducer. Lenses and reflectors can be used to mechanically focus ultrasound produced by a planar transducer at a fixed focus. Variable
focal length liquid lenses have also been studied as means of changing the focus depth along the central axis (Yoon et al., 1990).

While techniques such as fixed focused radiators, lenses and reflectors are able to focus energy deposition, phased arrays have an advantage over these mechanical focusing methods in that with phased arrays the focal position can be varied by changing the phases of the array element driving signals. A phased array is constructed from an array of small independently driven transducer elements. A focus (i.e. an intensity maximum) can be created by driving all of the elements with signals having such a phase difference that the waves emitted by each element are in phase at the desired focal point. The focusing is caused by constructive interference of all of the waves at the focal point, whereas elsewhere the waves generally interfere destructively and thus, the resultant ultrasound field has the highest intensity at the focus. While fixed focus ultrasound transducers have been used most often for thermal surgery, phased arrays offer several advantages over fixed focus transducers. Phased arrays are able to electronically move the location of the focus, which is both faster and more reliable than mechanically moving a transducer and can eliminate mechanical positioning systems associated with fixed focus radiators. Also, phased arrays are able to change the dimensions of the focus and necrosed tissue volume by appropriately setting the phases of the driving signals (Fan and Hynynen, 1995, and Fan and Hynynen, 1996a).

1.3.3 Intracavitary Heating Devices

The use of intracavitary applicators to treat tumors close to body orifices (e.g. esophagus, rectum, trachea, and vagina) offers several advantages. Intracavitary applicators bring the energy source close to the target volume, thereby minimizing normal tissue exposure. Bringing the heating device closer to the target volume may facilitate the treatment of target volumes that are untreatable with external applicators for reasons such as excessive depth, proximity to air or bone (when using ultrasound), or patient movement
associated with respiration. An additional benefit of using intracavitary applicators is that it permits verification of the applicator location relative to the patient's anatomy. Located only millimeters away from the rectal wall, the prostate is easily accessible via intracavitary applicators. A disadvantage of intracavitary applicators is that they impose constraints on the applicator dimensions, which limits the total power emitting surface area, and in the case of phased arrays, limits the size and number of elements. For phased arrays, limiting the size and number of array elements, potentially limits power output and focusing capabilities. A limitation of linear (1-D) intracavitary arrays is that the power deposition can be controlled by electrical focusing in only two dimensions (parallel to the length of the array and in the depth dimension).

Microwave hyperthermia applicators have been proposed for transrectal treatment of prostate cancer (Strohmaier et al., 1991) and transrectal and transurethral BPH treatments (Stawarz et al., 1991), but as mentioned earlier, shallow penetration depth can be limiting with microwave applicators.

High intensity focused ultrasound has been shown to successfully ablate canine (Sanghvi et al., 1996) and human prostate tissue (Madersbacher et al., 1994); however each transrectal applicator used in these studies consisted of a single fixed focus transducer which produced a 10 mm lesion at the fixed focal length and were incapable of generating lesions at other depths.

Although nonfocused intracavitary ultrasound arrays have been shown to have clinical utility in the treatment of prostate cancer (Fosmire et al., 1993), previous attempts have been primarily limited by a lack of control of power in the depth dimension and limited thermometry information. In a nonfocused transrectal hyperthermia system it was found that for an applicator with cylindrical geometry (1.5 cm diameter) and frequency of 1.5 MHz, a minimum acoustic power output/applicator length of 12 W/cm was needed to produce therapeutic temperatures in the prostate (Hynynen, 1990). Transurethral nonfocused ultrasound arrays have recently been proposed for prostate thermal therapies
and initial in vivo studies indicate that this technique may be potentially useful (Diederich and Burdette, 1996).

In an effort to achieve power control in the depth dimension, as well as in the axial dimension, phased arrays have been investigated for intracavitary treatments. Often tumors corresponding to body cavities surround sectors of or even the entire circumference of the cavity wall, making an array of cylindrical elements favorable for treating these tumors. In one study, a series of simulations were performed which investigated the effects of element width ($\lambda/3$ to $5\lambda/3$ center-to-center), focus location (depth, center vs. off axis), frequency (0.5 MHz to 2.0 MHz), phased array length (3.75 cm to 10 cm), surface cooling (10°C to 40°C) and perfusion (0.5 - 5.0 kg/(m³s)) on the focus dimensions, absorbed power fields and steady temperature distributions (Diederich and Hynynen, 1991). Based on the simulations a 16 element array operating at 0.5 MHz was constructed from 180° cylindrical elements (0.85\(\lambda\) center to center spacing, 40 mm total length). While this array was not suitable for clinical use due to the presence of significant grating lobes (~40%) and its short length (small number of elements), it did demonstrate the feasibility of using electrical focusing in an intracavitary array to preferentially heat regions of tissue 2cm to 5cm from the array surface.

In a following study, a 64 channel amplifier system was built and a 64 element phased array was constructed with 0.58\(\lambda\) center-to-center spacing, 11.05 cm total length and an operating frequency of 0.5 MHz (Buchanan and Hynynen, 1994). This array did provide more focusing flexibility than the previous 16 element array; however, for a focus 4cm deep and shifted 2.5cm off axis (steering angle = 32°) grating lobes (~20%) did exist. This study also looked at the ability of this array to cause localized temperature elevations in an ex vivo perfused (2.9 kg/(m³s)) kidney for a variety of focusing techniques using scanning of a single focus and stationary fields of multiple foci. The peak temperature rise in the perfused phantom that this array was able to produce was 12°C, which was produced by a single stationary focus. The study concluded that this temperature rise was
marginal, and that the acoustical power capabilities of such an array would need to be improved before it would be able to heat larger target volumes to therapeutic temperatures. Another limitation of the arrays presented in these two studies is that they do not allow angular control of the power emitted from the array surface; however for some applications, such as prostate hyperthermia, this may not be necessary.

While cylindrical linear arrays are geometrically attractive for intracavitary applications, planar linear have also been proposed (Hand et al., 1993). The advantage of using planar elements is that they do not have 1/r losses associated cylindrical elements, which have a heating field that increases in cross-sectional area as the distance from the array increases. A disadvantage of planar linear arrays is that they will need to be mechanically scanned in order to heat in the angular direction, unless the tumor is not circular in geometry. The study mentioned above showed preliminary acoustic simulations for the proposed use of a linear planar array for thermal therapies of prostatic diseases. Based on the contour plots given in this study, 10% and 25% grating lobes covered very large regions of SAR field for off axis focusing. The array simulated in this study operated at 0.5 MHz and consisted from 25 planar elements (3 mm x 15 mm) (center-to-center spacing of λ) yielding a total array length of 7.5 cm. The performance of the simulated array in this study was not sufficient to be considered for use in prostate thermal therapies, although the design was relatively simple and did not utilize the full capabilities of linear planar phased arrays.

For hyperthermia purposes, ultrasound phased arrays provide both heating at greater depths and increased control over the power deposition field (Diederich and Hynynen, 1991) compared to nonfocused arrays. While the depth and control of power deposition has been demonstrated in intracavitary phased arrays, it has been suggested that high frequency ultrasound (greater than 500 kHz) is necessary for adequate power deposition (Buchanan and Hynynen, 1994).
1.3.4 High Frequency Ultrasound

High frequencies for therapeutic ultrasound is advantageous in that as the operating frequency increases, the beam becomes more sharply focused, thereby reducing near field and post-focus heating (Diederich and Hynynen, 1991). Also, at higher frequencies power absorption in tissue is higher, which leads to higher temperature elevations for a given power level. This increased power absorption is beneficial at the focal depth, but can also lead to increased temperature elevations in the near field. A disadvantage of using higher frequencies is that small element widths must be used, otherwise grating lobes (also referred to as secondary foci) will appear. It is not always clear how much of a problem grating lobes actually are to the resulting temperature distribution. Much of the impact of grating lobes have is dependent on the particular site being treated and the surrounding normal tissue. For example, a 20% grating lobe may be acceptable if the lobe falls in a region of soft tissue; however, this same lobe may be unacceptable if it hits bone, which has approximately ten times the absorption of soft tissue. Similarly, the reflections occurring at the bone surface or an air interface may accentuate the negative effects of grating lobes. Another problem with of grating lobes is that power is deposited in the grating lobe regions instead of the focal region, which can be problematic if the overall array power capabilities are marginal.

1.3.5 Grating Lobe Reduction

Linear array theory, developed for radar phased arrays, states that in order to avoid grating lobes, the following condition must be met for an array with uniformly sized, periodically spaced elements:

\[ \lambda/d \geq \Delta u \]

where \( \lambda/d \) is the lobe spacing (wavelength/element or center-center spacing) and \( \Delta u \) is the scan sector, also known as the visible region and is related to the steering angle (send and receive), \( \theta \), by the relation:
\[ u = \sin \theta \]

For symmetrical beamsteering capabilities:

\[ \Delta u = 2u = 2\sin \theta \]

For example, if it is desired to steer the beam from horizon to horizon without getting grating lobes, \( \theta = \pm \pi/2 \), \( u = \pm 1 \), \( \Delta u = 2 \) which leads to the condition: \( \lambda/2 \geq d \). In other words, it is required that element widths (center-center spacing) must be less than or equal to \( \lambda/2 \) in order to avoid grating lobes for any steering angle. For central axis focusing an element width (center-center spacing) of \( \lambda \) can be used and center-center spacing greater than \( \lambda/2 \) can be used if array periodicity is eliminated (Steinberg, 1976, and Skolnik, 1980).

Closely linked to the grating lobe problem in therapeutic phased arrays are the limitations of the driving electronics and the element size. As mentioned above, grating lobes form due to element sizes which are larger than ideal for optimal focusing and are arranged in a periodic manner. There are however problems with using \( \lambda/2 \) sized elements. Small elements, especially at high frequencies (e.g. \( \lambda/2 \) center-center spacing = 0.5 mm for 1.5 MHz), make array construction difficult, requiring more elements, amplifier channels and wiring for a given array length. As the element size is reduced, a larger number of these small elements is needed to cover the same surface area. Using a larger number of elements means that more amplifier channels and phase shifters are needed, which increases the complexity and cost of the driving electronics. Another disadvantage of small elements is that element efficiency decreases as element widths decrease (Hynynen et al., 1994a). To complicate matters regarding element width selection, an appropriate width to thickness ratio must be chosen to avoid reduced element efficiency in the thickness vibration mode due to increases in other modes of vibration (Challande, 1990). In array design, a balance between acoustical power output, grating lobes and element width must be achieved for successful phased array operation.
The reduction of grating lobes generated by phased arrays is of interest for applications including clinical heating devices, medical imaging and radar. Grating lobe suppression techniques were first developed for radar phased arrays, using methods such as wide band signals and thinned arrays with random element center spacing or spatial tapering (King et al., 1960, Sandler, 1960, and Wiley, 1962). Another design tool was the derivation of formulas which were used to calculate the peak sidelobe level for arrays of randomly located isotropic and anisotropic elements while varying the number and size of the elements, the wavelength, array length, beam steering angle, and signal bandwidth (Steinberg, 1972). In one study on radar phased arrays, randomly located and overlapping subarrays consisting of a random number of uniform elements ($\lambda/2$ width) was proposed as means of eliminating array periodicity and reducing grating lobes (Goffer et al., 1990).

In medical ultrasound imaging, sparse or thinned arrays of randomly distributed elements of width $\lambda/2$ have been used to reduce the number of elements without generating grating lobes, although sidelobes adjacent to the mainlobe did increase in amplitude (Davidsen and Smith, 1993, Turnbull and Foster, 1991, and Turnbull et al., 1992). Array apodization, which consists of unequal element excitation amplitude weighting, has also been used in ultrasound imaging arrays to reduce sidelobes at the expense of increasing the main lobe width, but was shown to be ineffective when used with sparse arrays (Turnbull and Foster, 1991).

For clinical heating systems, the use of broad band signals has been proposed to reduce the affects of grating lobes during ultrasound ablation (Dupenloup et al., 1994, and Dupenloup et al., 1996). Recently a study has investigated the random placement of array elements in a sparse configuration for therapeutical purposes (Goss et al., 1996). In this thesis, a new technique for reducing grating lobes by forming an aperiodic full (non-sparse) array of unequal element sizes is introduced (Hutchinson et al., 1996).
1.3.6 Other Ultrasound Phased Array Designs

Concentric-ring or annular arrays

The first attempts to use electrical focused ultrasound for hyperthermia were performed by Do-Huu and Hartemann (1981 and 1982). Using an annular phased array operating at 0.4 MHz and constructed from 15 concentric ring elements, the array was able to vary the depth of the focus and produce two foci simultaneously, heating regions up to 12 cm deep. Further theoretical studies of concentric ring applicators showed that by proper phase selection it was possible to generate an annular focal region which may be advantageous for heating some tumors; however, secondary foci (grating lobes) on the central axis both proximal and distal to the primary focal plane were also generated (Cain and Umemura, 1986). Another theoretical study investigated using electrical focusing to produce and scan single central focus, multiple central foci, and ring foci in conjunction with mechanical scanning to heat tumors of various volumes in three dimensions (Ibbini and Cain, 1990). The concentric-ring array has also been studied as a means to replace a mechanical axial positioning system and a single transducer for MRI guided ultrasound surgery (Fjeld et al., 1996a).

Sector-vortex arrays

In an attempt to increase the size of the focal volume, a design known as the sector-vortex array was developed (Cain and Umemura, 1986). The sector-vortex array combined electrical scanning with a fixed focused transducer by taking a spherically curved transducer (or a circular planar transducer with a lens) and dividing it into sectors, each of which was individually powered and phased. By appropriate phasing of the sectors, it was possible to reduce the intensity along the central axis and generate limited circularly asymmetric field patterns. Further theoretical studies showed that by driving the sectors of the array with phases that cycling from 0 to 360° multiple times in one revolution around the circular track, a larger diameter focal ring can be produced by
cycling around the track more times, which is aided by having more sectors and more than one track (Umemura and Cain, 1989). Testing of a 32-element 2-track sector-vortex array operating at 0.6 MHz to 0.8 MHz verified the ability of such an array to produce annular foci without generating large secondary foci (Ngo et al., 1989). While no limits were given, it appeared as if both the concentric-ring and sector-vortex arrays can only produce very limited off axis focusing before grating lobes (secondary foci) become large. More recently, a combined sector-vortex and concentric ring array design has been studied and shown to be capable of both moving the focus in the depth dimension and increasing the size of the focal volume (Fjield and Hynynen, 1996b).

**Cylindrical-section arrays**

Another type of proposed array geometry is that of the cylindrical-section phased array which consists of rectangular elements surrounding the surface of the patient's body to form a section of a cylinder (Ebbini et al., 1988). A theoretical study of this array configuration was investigated as a means of treating abdominal tumors for which acoustical windows (regions void of bone and gas) existed. Without electrical phasing of the rectangular elements, the beams converge and produce a geometric focus at the center of the cylinder. By appropriately varying the phases of the elements, the focus was scanned in the depth and in the azimuthal directions, and stationary fields of multiple foci were also synthesized.

A series of simulations were conducted for 75° cylindrical section array operating at 0.5 MHz, with a geometric focal depth of 20 cm. In general the simulations demonstrated that these arrays were able to produce a single focus near the geometric focus without high intensity grating lobes, but when the focus was shifted off axis, double foci were generated, or a single focus was scanned, significant grating lobes and near field heating became limiting. For an array consisting of 80 elements of 3 mm width (center-to-center spacing = 1.1λ), a grating lobe level of 25% (-12 dB) formed when the array was
focused at its natural depth (20 cm) but shifted off axis 3 cm (steering angle = 8.5°). For an array consisting of 40 elements of 6 mm width (center-to-center spacing = 2.2λ), a grating lobe level of 33% (-9.5 dB) formed when the array was focused at its natural depth (20 cm) but shifted off axis 3 cm (steering angle = 8.5°). When this array was then used to scan a simulated tumor 5 cm in diameter centered at 17 cm depth and 3 cm off axis, a very large grating lobe region appeared with a maximum of 65% (-3.7 dB) occurring at approximately 5 cm deep. Proposed solutions to reduce the effects of near field heating that could be caused by this grating lobe region include surface (skin) cooling and using fewer scanning points to reduce the summation effects of near field heating. An interesting comparison simulation was performed with a linear phased array consisting of 40 6 mm elements focused 20 cm deep and 3 cm off axis. The grating lobe peak was 55% (-5.2 dB) as compared to the comparable cylindrical section array which generated a peak grating lobe of only 33% (-9.5 dB).

This study concluded that based on steady state temperature distributions simulated with the bio-heat transfer equation, the large grating lobe regions would not produce secondary hot spots. However, for the temperature distributions given in the paper the peak grating lobe intensity was not mentioned, and judging from corresponding acoustic simulations, the temperature distributions given were not for the worst case. Another point worth noting is that the peak grating lobes and temperature distributions given in this study assumed a water bolus that extended 5 cm from the array surface, which corresponds to a geometric focus at 15 cm from the patient’s skin, rather than 20 cm. Using a water bolus between the array surface and the patient's skin is beneficial for two reasons. First, it allows for surface cooling of the skin which can prevent superficial burns. Second, it lowers the risk of near field heating in healthy tissue since large grating lobes and near field hot spots often occur relatively close to the transducer surface.

Although it was concluded that the cylindrical section array could produce better heat localization, comparisons of linear and cylindrical section array foci at depths other
than that of the geometric focus of the cylindrical section array were not given. It seems likely that as the distance between the focus location and the geometric focus location becomes larger (both in depth and in moving off axis), that the advantage of the cylindrical section array over the linear array may be reduced or even reversed if the distance is large enough. In a later study, a 64 element, 75° cylindrical section phased array prototype was constructed, which operated at 0.5 MHz and showed good agreement with the previously presented theoretical model (Ebbini and Cain, 1991).

Spherical section 2-D arrays with rectangular elements

A design that is similar to both a flat 2-D array and the sector vortex array is the spherical-section phased array, whose elements form a rectangular lattice (Ebbini and Cain, 1991). In many respects the spherical section 2-D array is similar to a planar 2-D array in much the same way that a cylindrical section 1-D array is similar to a linear 1-D array. This theoretical study examined how phasing could be used to produce foci at positions other than the geometric focus of the transducer. If all the array elements were driven in phase, this array would produce a focus at the geometric focus of the spherical section from which the array was constructed. In this theoretical study, the array was found to be capable of scanning a single focus, and using a direct pattern synthesis method the array was able to generate a field pattern based on a specified tumor geometry. This type of array showed promising results for focal patterns that were symmetric about the centerline, near the geometric focus and were relatively simple patterns; however for a focus at the geometric focal depth, but shifted off the central axis, significant grating lobes appeared (40% of main focus, i.e. -8db). As the depth of the focal pattern was moved away from the geometric focal depth or the complexity of the desired field pattern increased (e.g. making a smoother ring focus), undesirable power deposition in the near field also increased. The advantages of this array are that it has more flexibility in heating patterns than a single geometrically focused spherical transducer, and in some instances
may eliminate the need for mechanical scanning. The limitations of this type of array arise mainly due to grating lobes or secondary foci, which increase as the desired focal pattern deviates from the geometric focus. In addition to hyperthermia, spherical section ultrasound phased arrays have been investigated as means of necrosing tumors (Fan and Hynynen, 1995). In this study, simulations and a constructed 16 element spherical section array were used to investigate the utility of various multiple foci patterns for inducing high temperature elevations in tumors.

**Planar 2-D arrays**

The two-dimensional planar phased array offers the most flexibility in electrical focusing, with the ability to focus in three-dimensions and without a bias towards a specific focus location. The disadvantage of 2-D planar arrays is that they require a large number of small elements each with their own amplifier and phase shifter, making the electronic driving circuitry complex and costly. Previous studies have attempted to reduce the complexity of the electronic driving circuitry associated with two-dimensional planar arrays. One method investigated using a two-dimensional planar array of rectangular elements, but only powered three rows of elements at any one time (Ocheltree et al., 1984). In this manner, the focus could be scanned in the direction perpendicular to the rows of elements by sequentially switching the three excited rows such that the currently excited group included two of the three previous rows. The focus can be scanned both in depth and in the direction parallel to the rows by appropriately setting the phases of the elements within the three rows.

Another interesting approach to reduce the number of required amplifiers and phase shifters while still allowing the 3-D focusing associated with 2-D planar arrays, was to construct an apparently one-dimensional array made from long elements of tapered thickness (Benkeser, 1987). By driving an element with a given frequency, the element would generate the strongest ultrasound field at the position along the element length at
which the thickness is equivalent to the resonant thickness (i.e. one half of the wavelength). By varying the excitation frequency, the focus can be scanned in the direction parallel to the element length. The focus can be scanned both in depth and in the direction perpendicular to the array elements by appropriately setting the phases for each element at the current resonant frequency. While this technique reduces the number of amplifiers and phase shifters, it does require more complex phase settings as they will change with frequency. In this study, a 64 element tapered array was constructed with elements 15.2 cm in length and a thickness of 4.3 mm-5.8 mm which corresponded to a frequency range of 0.7 MHz to 0.5 MHz. An interesting point to note is that the element center-to-center spacing remained constant at 1.97 mm (1.79 mm elements with 0.19 mm spacers). For the range of frequencies used 1.97 mm corresponds to a center-to-center spacing of 0.60λ to 0.85λ. The tapered array would therefore have its best focusing capabilities at the thick end (5.8 mm) operating at the lowest frequency (0.5 MHz) and would generate its largest grating lobes at the 4.3 mm thick or 0.7 MHz end.

Recently, a new type of design known as the flat panel array has been introduced (McGough et al., 1995). The flat panel array seeks to approximate a spherical section array by appropriate geometrical placement of 5, 8, or 21 modular 2-D planar N x N arrays. Spherical section arrays can be difficult to fabricate, especially as the number of elements becomes large. The advantage of the flat panel array is that it is easier to construct and the N x N panels are interchangeable allowing for significant flexibility. The geometric gain of the flat panel array is not as high as that of a spherical section transducer, but is higher than that of flat 2-D arrays (assuming elements sizes > λ/2 in width and length) which lack any geometric gain. A 192 element array was constructed with 8 5 x 5 panels, each of which had the center element removed for mounting purposes. A 512 element 9 panel array configuration was also studied and built which had 5 square panels and 4 triangular panels placed in each corner. A 512 channel amplifier system was built to be used with the flat panel arrays. Initial results from these arrays show relatively
close agreement with the simulations. The initial results also showed some regions of grating lobes (~10%) for an acoustic focus located at the geometric focus.

1.4 MRI-Guided Ultrasound Thermal Therapies

Minimally invasive therapies are becoming increasingly popular as replacements for conventional surgery. The reasons for this include: faster recovery/shorter hospital stays, reduced chance of infection, reduced anesthesia requirements, and lower overall cost. Because thermal surgery and hyperthermia treatments can be delivered non-invasively with external or intracavitary ultrasound applicators, these treatments could become entirely non-invasive when monitored and guided by non-invasive imaging systems instead of invasive temperature sensing probes.

Diagnostic ultrasound imaging has been used to guide ultrasound surgery treatments (Coleman et al., 1985 and ter Harr et al., 1989), including those for treating prostatic diseases (Foster et al., 1993 and Gelet et al., 1993). Diagnostic ultrasound has also been proposed as a non-invasive guidance system for hyperthermia treatments (Seip and Ebbini, 1995); however this technique currently has several limitations: it requires invasive probes for calibration, the accuracy and robustness of the temperature estimation algorithms need to be addressed, 2D temperature imaging and in vivo testing has yet to be demonstrated.

Magnetic resonance imaging (MRI) is a promising imaging modality for non-invasive monitoring, guidance and control of ultrasound therapies. The advantages of using MRI are that it provides adequate spatial localization, temperature sensitivity and tissue contrast allowing for target and lesion identification. Tissue properties with temperature dependence that have been used for non-invasive temperature estimation include: proton density (Kato et al., 1983 and Kuroda et al., 1990a), spin-lattice relaxation time (T1) (Parker et al., 1983 and Dickenson et al., 1986), spin-spin relaxation time (T2)
(Kato et al., 1983, Dickenson et al., 1986 and Kuroda et al., 1990a), the molecular diffusion of water molecules (LeBihan et al., 1989, Hall et al., 1990 and Zhang et al., 1992), and the proton resonant frequency (chemical shift) of water molecules (Arus et al., 1985, Hall and Talagala, 1985, Kuroda et al., 1990b, Kuroda et al., 1993 and DePoorter et al., 1994).

MRI guidance has the potential to be incorporated into both hyperthermia and ultrasound surgery treatments. Implementation of MRI guidance for hyperthermia is more difficult than for ultrasound surgery as longer sonication times and smaller temperature elevations allow heat-induced physiologic changes (e.g. vasodilation/perfusion, edema) more time to influence a smaller signal. A clinical MRI-guided ultrasound system utilizing geometrically focused transducers and a mechanical positioning system has been developed, tested extensively in vivo and has recently begun use for clinical treatment of breast fibroadenoma (Hynynen et al., 1996a). Recently, in vivo studies using phased arrays with MRI guidance have been performed with concentric-ring and square element spherical section phased arrays (Hynynen et al., 1996b). Previously it was demonstrated with this system that MRI can detect non-damaging temperature elevations for use in target localization and that contrast agent can be used to improve delineation of necrosed tissue lesions (Hynynen et al., 1994b). For MRI guided hyperthermia treatments, the ultrasound system can be the same or similar to those used for ultrasound surgery, but the MRI temperature estimation techniques need to be more sensitive to small temperature changes and more robust in the presence of larger physiologic changes. Of the tissue properties used for non-invasive MRI thermometry, the proton chemical shift method has shown the most promise as it is determined by the frequency of the resonant signal, whereas the other methods are determined by signal amplitude (Kuroda and Tsutsumi, 1996).
1.5 Temperature Feedback Control

Using an ultrasound phased array, it is possible to focus the ultrasound and vary the location of the focus by applying different power field patterns. By applying multiple power patterns it possible to tailor the size of the heated region and temperature elevation achieved within the region. By using invasive temperature sensing probes or non-invasive methods, it is possible to monitor the temperature during the heating process, making the process a potential candidate for feedback control. Feedback control systems for ultrasound hyperthermia treatments have been investigated for mechanically scanned, focused ultrasound systems (Johnson et al., 1990, Lin et al., 1990 and Potocki and Tharp, 1992), non-focused arrays (Hartov, 1991 and Hartov, 1993) and phased arrays (VanBaren et al., 1995 and Seip et al., 1996).

The heating process is characterized by unknown and immeasurable physiologic parameters such as spatially and temporally varying blood perfusion. Due to the unknown physiologic parameters which can change both spatially and temporally, the heating process is well suited for an adaptive controller which is capable of estimating these parameters and adapting to changes in these parameters on-line (Hartov, 1991, Hartov, 1993, and VanBaren et al., 1995). In designing a control system for hyperthermia treatments, several issues will need to be addressed. In addition to the uncertainty in modeling the physiological heating process, the relatively large time constants associated with conduction and perfusion add significant delays. The fact that power can be generated but not removed by changing the input parameters must also be considered. Due to these issues, the finite limit on input power, and the fact that heat naturally tends to be dissipated, it is unlikely that the system will become unstable. Since the control system is multi-input, multi-output there is a potentially large number of unknown parameters which need to be estimated. To simplify the system identification computations, reduced
order modeling and reduced order controller designs have been proposed (Potocki and Tharp, 1992).

Clinically, an adaptive controller could be useful for determining the relationship between the input power patterns and the temperature increases produced at the sensors for two reasons: 1). The exact location of the ultrasound transducer relative to the sensors is not always known; and 2). The locations of the transducer relative to the sensors may change during the treatment due to patient motion. With an adaptive controller, the exact location of the transducer relative to the sensors is not necessary, as this relationship is implicitly identified during adaptation, and the inputs are appropriately weighted so as to result in the desired temperature increases at the sensors. Although an adaptive model based controller could be suitable for this application, other non-model based controllers using fuzzy logic (Mendel, 1995) may also be appropriate and less complicated. While most currently used clinical heating systems are open-loop (operator) controlled, computer control will enable faster and more complete evaluation of multi-sensor temperature information and more fully utilize the flexibility associated with the focusing capabilities of phased arrays.

As discussed in the previous section, MRI thermometry is a potentially useful approach to achieving temperature feedback non-invasively. The simulation study performed in this thesis investigated the use of MRI thermometry for feedback control of prostate hyperthermia treatments. Pertinent issues for using MRI thermometry feedback include the spatial resolution, sampling rate and noise in the temperature signal. Due to potential noise associated with MRI thermometry, an adaptive controller was not selected as adaptive algorithms can amplify the effects of modeling errors in the presence of noise. Instead an optimal control algorithm was investigated using a Linear Quadratic Regulator (LQR) (Hutchinson et al., 1996).
1.6 Scope of This Thesis

Currently, one of the major limitations associated with the application of prostate thermal therapies is the technology associated with the clinical heating devices. The goal of this project was to design, develop and experimentally test ultrasound phased arrays for both hyperthermia and thermal surgery treatments.

As part of this thesis a new technique for reducing grating lobes was developed (Hutchinson et al., 1996a). As with the grating lobe reduction techniques used in radar and ultrasound imaging, the technique presented here derives its utility from removing the periodicity associated with a uniform phased array. Unlike imaging, clinical heating devices demand high acoustical power output, thereby reducing the utility of sparse arrays or array apodization as means of reducing grating lobe levels. The proposed technique uses optimized random distributions of elements of nonuniform width to eliminate array periodicity and form a dense array. This is advantageous in that the benefit associated with the aperiodicity of random arrays is achieved, while maintaining the same power emitting surface area associated with dense uniform arrays.

Using ex vivo perfused and non-perfused organ phantoms and in vivo models, the heating capabilities of intracavitary ultrasound arrays were investigated for both hyperthermia and ultrasound surgery (Hutchinson et al., 1995). The feasibility of using a phased array for ultrasound surgery was investigated by creating lesions of necrosed tissue in fresh liver/meat at predictable and physiologically appropriate locations during short sonication times. A parametric simulation study was performed investigating the effects of focus location, frequency, perfusion, sonication time, and maximum temperature on lesion size. An optimization study investigating foci spacing and nonuniform temporal weighting of foci was performed to study single focus electronic scanning. It was hypothesized that using a stationary single focus will overheat the center of the target volume, while under heating the boundaries of the target volume, whereas electronically
scanning a single focus with appropriate temporal weighting would produce a larger and more uniform necrosed volume (Hutchinson and Hynynen, 1996b).

Using desired and measured temperatures as controller inputs and element driving signal phases as controller outputs, feedback control was investigated as a means to improve the temperature distributions used for thermal therapies. On-line and off-line parameter estimation algorithms and control algorithms were designed for hyperthermia treatments in which parameter uncertainties existed. This study investigated parameter estimation and control algorithms suitable for use with non-invasive temperature feedback from MRI, as this technology is expected to be available soon (Hutchinson et al., 1996c).

To facilitate future MRI feedback control experimentation, a 62 element phased array was designed and tested for MRI-compatibility. This array was tested in an MRI magnet in both ex vivo and in vivo heating experiments. The element widths used in the design of this array used the aperiodic design technique to reduce grating lobes and used empirical width-to-thickness versus efficiency data to achieve maximum element efficiency. In addition to being MRI compatible, this array was constructed in an intracavitary (transrectal) applicator (Hutchinson and Hynynen, 1997).
2. Design and Evaluation of a 57 Element Aperiodic Phased Array

2.1 Methods

In this study a new technique for reducing the grating lobes is introduced (Hutchinson et al., 1996a). As with the grating lobe reduction techniques used in radar and ultrasound imaging, the technique presented here derives its utility from removing the periodicity associated with uniform phased arrays having element widths larger than $\lambda/2$. Unlike imaging, clinical heating devices demand high acoustical power output, thereby reducing the utility of sparse arrays or array apodization as means of reducing grating lobe levels. The proposed technique uses optimized random distributions of elements of nonuniform width to eliminate array periodicity and form a dense array. This is advantageous in that the benefit associated with the aperiodicity of random arrays is achieved, while maintaining the same power emitting surface area associated with dense uniform arrays.

2.1.1 Acoustic Simulations

Using theoretical models for the ultrasound field, numerical simulations were performed on personal computers (Pentium 60 - 166 MHz CPUs). The majority of the simulation code for acoustic fields was written in FORTRAN, but C++ was also used. The acoustic pressure field generated by a linear array of ultrasound planar transducers was simulated as follows. The array was modeled as a series of rectangular elements of equal length (15 mm) and specified widths (0.7 to 2.0 mm), separated by non-emitting spacers of specified widths (0 to 0.3 mm). Figure 2.1 shows the 57 element aperiodic linear phased array designed and constructed in this study.
The power amplitude and phase of each element were independently controllable. The phases were discretized to the nearest 22.5° to match the resolution of the phase shifting circuits of the driving hardware. The 22.5° phase shift resolution has been shown to be sufficient for the purposes of this study (Diederich, 1990 and Wang et al., 1991). The acoustic pressure field was calculated using Huygen's principle, by modeling each element surface as a grid of simple hemispherical sources and then summing the contribution from each source to each point in the field (Zemanek, 1971). A grid spacing of \( \lambda/8 \) was found to be sufficient to accurately model the rectangular elements. The magnitude of the pressure generated from each simple source was calculated using the complex surface velocity of the element which is based on the specified total acoustical output power from the array (O'Neil, 1949). The pressure at any field point in the tissue, \( p_i(x,y,z) \), due to one simple source, was calculated using the following expression:

\[
p_i(x,y,z) = \sqrt{\frac{2WP}{cA}} \left( \frac{fS}{d} \right) e^{i \left( \frac{2\pi f}{\lambda} \right) x} e^{-2i \pi \frac{y}{d}}
\]  

(2.1)
where $W =$ total acoustical power output from the array, $\rho =$ density (998 kg/m$^3$), $c =$ the speed of sound (1500 m/s), $A =$ total array surface area, $f =$ frequency, $S =$ area represented by each simple source, $d =$ distance from the simple source to the field point, $\phi =$ phase of the simple source, $\lambda =$ wavelength, and $\alpha =$ attenuation. For most calculations, soft tissue was the simulated medium ($\alpha =$10 Np/m/MHz), but for comparisons with the ultrasound fields generated by the actual array and measured in water, water was the simulated medium ($\alpha =$ 0 in water). The pressure at any field point was calculated by summing the contributions from $n$ simple sources:

$$P(x,y,z) = \sum_{i=1}^{n} p_i(x,y,z) \tag{2.2}$$

Then using the calculated pressure, the power deposition $q(x,y,z)$ was calculated using the following expression (Nyborg, 1981):

$$q(x,y,z) = \frac{\alpha P^2(x,y,z)}{\rho c} \tag{2.3}$$

### 2.1.2 Optimization of Aperiodic Arrays for Grating Lobe Reduction

For an array consisting of randomly sized elements with an infinite number of possible element widths within a given range, both the complexity of array construction and computation time required for simulations become limiting. To reduce array construction complexity and computation time, primarily random distributions of two discrete element widths were studied. Limited simulations with three different element sizes suggested that combinations of three different element sizes, would not yield better results than combinations of two different element sizes. Furthermore, three element sizes would add significantly more random combination possibilities, leading to a large increase
in computation time. Even by limiting the array to just two different element widths, it was not computationally feasible to do an exhaustive search of all the different distributions for a given pair of element widths (e.g. for an array composed of 30 elements of width, and 30 elements of width\textsubscript{2} approximately \(10^{49}\) possibilities exist). It was believed that common optimization techniques such as gradient search methods would not work well due to the presence of a very large number of local minima for this discrete system. The optimization technique used here involved the calculation of a cost function for different random distributions of two element widths. For each pair of element widths, a sufficient number of random distributions were simulated to evaluate the utility of the element pair, and the distribution with the lowest cost function was selected.

A cost function was used to quantitatively rank the acoustic power field for each array of uniform element width and each array consisting of random combinations of nonuniform element widths. The cost function, CF, was calculated by dividing the maximum power in a grating lobe by the maximum power at the focus for several different focus locations and then choosing the maximum, or worst case, since this will be limiting.

\[
CF = \text{MAX} \left\{ \frac{q_{\text{lobe}_1}}{q_{\text{focus}_1}}, \frac{q_{\text{lobe}_2}}{q_{\text{focus}_2}}, \frac{q_{\text{lobe}_3}}{q_{\text{focus}_3}}, \ldots, \frac{q_{\text{lobe}_n}}{q_{\text{focus}_n}} \right\} \quad (2.4)
\]

where \(n\) = number of different focus positions. In other words, the cost function is a measure of the highest absorbed power in a grating lobe relative to the power absorbed at the focus. In comparing different random combinations of element widths, the cost function was calculated for three focus positions: a center focus and foci shifted ± 2 cm off axis, all at a 5 cm depth. Using three different foci was found to be sufficient to predict how well a specific random combination of element sizes would work for other focal positions. This was determined by simulating more focal positions for selected combinations of element widths.
approximately the anatomical range over which a focus would be scanned to heat the prostate. Element sizes ranging from 0.7 mm ($\lambda/2$ center-center spacing at 1 MHz) to 2.0 mm ($1.4\lambda$ center-center spacing at 1 MHz) in 0.1 mm increments were used in the simulations for both uniform and aperiodic arrays. As previously mentioned, the majority of the results presented in this study are for arrays composed of uniform elements or random combinations of two different element sizes.

For comparing different random distributions of two element widths, 200 random distributions for each pair of element widths were simulated. Of the 200 trials for each pair of element widths, the distribution which produced the lowest cost function was considered an optimized random distribution and was used as a measure of the performance of that particular pair of element widths. Based on histograms for the sets of 200 trials and one 5000 trial histogram, the probability densities of these random element distributions were found to be approximately normal distributions. A normal curve was fit to the histogram for 5000 combinations of two element widths, as shown in Figure 2.2. From this histogram and statistical theory of normal distributions (Bethea et al., 1985), it was determined that selecting the best of the 200 trials would ensure selection of a distribution within the top 20% of all possible distributions with 99% confidence. Based on the 5000 trial distribution, it was determined with 98% confidence that the lowest cost function of the 200 trials would be within 15% of the lowest cost function achieved with the 5000 trials. With regard to the two confidence measures, the former ranks the selected distribution relative to other distributions, whereas the latter ranks the selected distribution’s cost function relative to the best cost function achievable. While this optimization strategy does not find the absolute best element distribution, it finds a distribution that is sufficiently close to the best to allow evaluation of the array parameters. Another imposed constraint was that equal numbers of each of the two element sizes be used. The effect of using different ratios of one element size to the other was also studied.
The cost function was based on acoustic power for two reasons. First, the computation time required to calculate 2-D power fields is approximately 100 times shorter than the time required to calculate 3-D power, steady state temperature and transient temperature fields, which would be needed for a temperature and/or thermal dose based cost function. The large difference in computation time becomes critical when it is considered that 200 cost functions were calculated for each combination of two element widths. Second, acoustic models allow for more direct array evaluation since thermal models introduce new physiological parameter uncertainties which, especially in hyperthermia, could mask array performance.

Figure 2.2 Histogram of cost functions for 5000 random distributions of 29 1.2 mm and 28 1.6 mm elements. Normal curve fit to distributions.

2.1.3 Other Array Designs for Grating Lobe Reduction

In addition to the aperiodic array design described above, other means of reducing grating lobes were also investigated. As mentioned previously, sparse arrays and spatially tapered arrays have been used to reduce grating lobe levels in radar and imaging arrays.
Simulations were performed to evaluate the potential of sparse arrays and spatially tapered arrays to reduce grating lobes in intracavitary ultrasound arrays for thermal therapies.

The sparse array designs used in imaging and radar remove up to 90% of the elements (of λ/2 width) at random from a dense array. The remaining randomly located 10% of the elements are able to produce a main beam with low grating lobe levels. For intracavitary therapeutic heating devices, high output power requirements and small available space prevent a 10% element usage ratio from being feasible. For this reason, element usage ratios of 25%, 50% and 100% (dense array) were simulated (acoustic fields) to determine if the reduction in grating lobes achieved by using sparse arrays warranted the reduction in power emitting surface areas. The simulated arrays operated at 1 MHz and had 64, 96, and 128 elements of width 0.75 mm. Like the imaging and radar designs, elements (of width λ/2) were removed at random until the desired number of elements remained.

Spatially tapered arrays, which have thinner element widths at the array ends than at the array center, were also simulated. The underlying principle governing tapered array design is that elements at the array ends will be at sharper steering angles than the elements in the center of the array. For this reason element widths at the array ends should be thinner than element widths at the array center to prevent destructive interference at the focus caused by waveforms emitted by one end of the element against waveforms emitted by the other end of the element. In the design of the tapered arrays, a focal range and a focusing criterion were chosen, which specify the maximum phase difference that could arise at the focus from waves emitted by the same element. The focal range used included foci shifted ±2 cm off axis, at a 5 cm depth. The focusing criterion used was λ/2 (i.e. 180°), which maximizes the width of each element with the constraint that the path length difference (to the focus, for any focus in the focal range) from opposite edges of an element can be at most λ/2. Using a smaller focusing criterion (e.g. λ/4) would result in a sharper focus, but smaller element widths. A focusing criterion such as this can be used with a non-tapered array by turning off elements at the ends of an array when focusing at sharp
steering angles to reduce grating lobe levels. Testing of this method for reducing grating lobes by turning off end elements was tested with the 57 element phased array.

2.1.4 Construction of 16 Element Test Phased Arrays

Two 16 element test arrays were constructed prior to construction of the full size 57 element array. With these two 16 element arrays, the power capabilities of two materials were evaluated during electrical focusing. The second of the 16 element phased arrays also served as a preliminary test of the aperiodic array design technique. Construction of these two arrays prior to constructing a full length array was useful in evaluating supplementary materials such as silicone and coaxial cable, and aided in improving construction techniques such as element cutting, soldering vs. pin connections, and grounding of the front sides of the elements.

The first 16 element phased array was constructed from 1.5 MHz lithium niobate (LiNbO₃) crystal (Crystal Technologies, Palo Alto, CA). Each of the sixteen elements were cut to 1.0 mm in width with a diamond wire saw. Between each of these elements, 0.13 mm of double-sided tape (Chomerics, Woburn, MA) was used for electrical and mechanical insulation; however, this tape provided a poor seal and required silicone on the front surface of the array which prevented water leakage but reduced efficiency as power is absorbed and reflected by the silicone. The overall array dimensions were 18 mm by 15 mm (element length), and the array was mounted in acrylic frame. The (hot) connections to the back of the elements were made by soldering the wires to the gold electrode; however, the electrode had a tendency to lift off the crystal. The wires were then connected to coaxial cable (Belden Wire, Alexandria, VA, 32 Ω mini-coax, 161 pF/m) to reduce the cross-talk between wires; however, the high capacitance of this coaxial cable made impedance matching difficult and limited the maximum length of the coaxial cable to approximately 0.6 meter. Electrical (inductive and capacitive) impedance matching networks were used to match each element to a 50-Ω, 0° phase load. The front surface of
the elements shared a common ground, which was achieved using silver conductive epoxy and a braided wire; however, the silver epoxy connections had a tendency to break during sonication. An additional problem which was encountered with this array was an uneven (non-flat) array surface which led to the need for significant phase corrections due to elevation errors (discussed in section 2.1.6). A 16 channel amplifier (Labthermics, Champaign, IL) was used to power this array.

The second 16 element phased array was constructed to test the power capabilities of PZT-EC69 ceramic (EDO, Salt Lake City, UT) and the new aperiodic array design technique. This array consisted of an optimized random distribution of 8 1.1 mm elements and 8 1.5 mm elements (26 mm total length, 15 mm array width), and was operated at 850 kHz. Low viscosity silicone rubber adhesive (Rhone-Poulenc Silicones VSI, Troy, NY, V-1022 A and B) of 0.13 mm width (interelement spacing) was used to glue the elements together and provide mechanical and electrical isolation. The array was then mounted in an acrylic frame. The elements were connected to coaxial cable (Belden Wire, Alexandria, VA, RG-178, 95 pF/m) on the air-backed side by soldering. The elements on the front face of the array were grounded by soldering them to silver foil. Each element was electrically matched to 50-Ω using L-C matching networks. The flatness of the array was maintained by mounting the elements on tape prior to gluing the array together; however, after cutting the elements the polarity of some of the elements was reversed which resulted in the need for phase correction.

2.1.5 Construction of a 57 Element Aperiodic Phased Array

Based on the promise shown by the 16 element aperiodic array made from PZT-EC69, a 57 element array was constructed to test the acoustic and heating capabilities of this material when used in a full length aperiodic array. The 57 element linear array was constructed with 29 1.6 mm wide elements and 28 1.2 mm elements (15 mm array width, 87 mm total array length, 0.85λ average center-center spacing), using an optimized random
distribution of two element widths based on the computer simulations. The elements were cut from PZT-EC69 ceramic with a wafer dicing saw (Boston Piezo-optics, Medway, MA) and operated in their thickness mode at a resonant frequency of 0.83 MHz. Silicone rubber adhesive of 0.13 mm width (interelement spacing) was used to glue the elements together and provide mechanical and electrical isolation. The array was then mounted in an acrylic frame. The elements were connected to coaxial cable (RG-178, 95 pF/m) on the air-backed side using conductive pogo pins; however, the sum force from all 57 springs in the pogo pins visibly deflected the array surface and made it difficult to keep all 57 pins in contact with their respective elements. The front face of each element was grounded using conductive silver epoxy and soldered to silver foil. Unfortunately, the best conducting and bonding silver epoxies tend to require heat curing, which can cause depolarization of the elements if too high a temperature (i.e. the Curie point) is reached. Each element was electrically matched to 50-Ω load using L-C matching networks. Fifty seven channels were used of a 64 channel computer controlled amplifier system that consisted of phase shifters, duty cycle controllers, amplifiers, and RF power meters (Buchanan and Hynynen, 1994). Phase error correction was again needed; this time due to the deflection of the array surface by the pogo pins.

2.1.6 Acoustic Measurements

Measurement of Element Efficiency and Power Output

Prior to array construction, the efficiency of elements cut to a range of different widths were measured using a radiation force technique, which consisted of sonicating into an ultrasound absorber and measuring the resultant force (Stewart, 1982 and Hynynen, 1993). The element efficiency is the quotient of total acoustic output power divided by total electrical input power. The resonant frequency was also measured for each of the element sizes, and each element was powered at its resonant frequency to achieve maximum element efficiency (Hunt, 1987). By measuring the element efficiency at a given
The array was placed in a tank of degassed, deionized water, and the ultrasound field was measured by mechanically scanning a needlepoint (0.6 mm diameter) hydrophone (NTR, Seattle, WA). The grid spacing for the measurements varied from 0.25 mm to 1 mm, depending on the scan. Prior to scanning a full 2-D field, 1-D scans were performed to gauge the required field length and width so as not exclude significant portions of the field near the scan boundaries (i.e. grating lobes).

Electrical Focusing and Phase Error Correction

Single and double foci were produced with the phased arrays by setting the phases of each element so that constructive interference of the pressure waves from each element occurred at the desired focal position(s). The required phase for each element was calculated using the differences in path length from the center of each element to the focus:
\[ \phi_i = \frac{360^\circ}{\lambda} (d_i - d_o) - 360^\circ n \]  
(2.5)

where \( \phi_i \) = phase of element i in degrees, \( d_i \) = distance from the center element i to the focus, \( d_o \) = reference distance (e.g. focus depth), \( n \) = an integer used to maintain \( 360^\circ \geq \phi_i \geq 0^\circ \). Two foci were generated with the 57 element array by using half the array to focus at one location and the other half of the array to focus at a second location.

Due to construction techniques, the arrays were not perfectly flat, and due to slight elevation variations between elements, a correction factor was needed to improve the sharpness of the focus. An additional factor that necessitated phase correction was the fact that the polarity of the elements was not all the same (i.e. the front surface of each element was not necessarily the front surface of the original, larger ceramic/crystal from which the elements were cut), resulting in a \( 180^\circ \) phase difference for elements with opposite polarity.

The arrays were placed in a tank of degassed, deionized water, and a needlepoint hydrophone was used to measure the phases of each element individually so that pressure wave from each element would be in phase at the location of the hydrophone. Using the phases measured with the hydrophone and those calculated with (2.5), an elevation error was calculated for each element. Using the elevation error for each element, \( \varepsilon_i \), a corrected equation was used to calculate the phases for any focal position:

\[ \phi_i = \frac{360^\circ}{\lambda} (d_i - d_o + \varepsilon_i) - 360^\circ n \]  
(2.6)

For the 57 element phased array, the phase corrections were based on the error between the calculated-uncorrected and hydrophone measured phases for a 4 cm deep center focus. To verify the validity of the phase corrections, ultrasound fields generated using corrected phases were compared to fields generated by hydrophone measured phases for other focal positions.
2.1.7 Hyperthermia Experiment: Ex Vivo Perfused Kidney

The hyperthermia capabilities of the 57 element aperiodic phased array were investigated by performing a heating experiment with an ex vivo perfused kidney. The preserved canine kidney weighed approximately 50 g and was perfused at flow rates between 0 and 5 ml/min. As shown in Figure 2.3, the array and kidney were submerged in a tank of degassed water at 23°C, with the kidney approximately 1.5 cm away from the array surface, which is a reasonably approximation of the water bolus used for transrectal ultrasound treatments. Temperature sensing thermocouple probes were used to record temperatures for 10 minute sonications followed by 5 minutes of cool down time for both single focus sonications and electronic scanning of a single focus.

![Figure 2.3 Setup for hyperthermia ex vivo canine perfused kidney experiment.]

2.2 Results

First simulation results will be presented for the three techniques investigated for grating lobe reduction: sparse arrays, spatially tapered arrays, and aperiodic arrays. Next,
acoustic performance of two materials, EC69 and LiNbO$_3$, will be presented, including their performance in 16 element test arrays. Phase correction measurements will be presented, followed by comparisons of simulated and measured fields for the 57 element aperiodic array and reduction of grating lobes by deactivating array elements at sharp steering angles. Lastly, results of the ex vivo kidney experiment will be shown.

**Sparse Array Simulations**

Figure 2.4 shows simulated ultrasound fields with the corresponding relative maximum power (at the focus) for sparse arrays of 64 and 96 randomly selected elements as well as for a full array of 128 elements (each had an overall array length of 9.6 cm).
Figure 2.4 Simulated power field for sparse arrays, 5 cm deep center focus, 1 MHz, $\lambda/2$ element width (0.65 mm + .1 mm dead spacing).
Tapered Array Simulations

Phased arrays with tapered element widths were designed such that one side of any element (front surface) would never be more than 180° (λ/2 focusing criterion) out of phase relative to the other side of the element (front surface) for focal positions at 5 cm deep over the range ±2 cm off axis. Ideal arrays were simulated in which the element widths were not limited in resolution and no interelement dead spacing was used. Practical arrays were also simulated in which element width resolution was limited to 0.1 mm and 0.1 mm interelement dead spaces was used. Figure 2.5 shows the element distributions that were used in the simulations for the ideal and practical tapered phased arrays. The end elements are thinner than the center elements as they are at sharper steering angles. The simulated beam plots associated with these tapered arrays are shown in Figure 2.6, which shows foci over the design range (up to 2 cm off axis) as well as outside the design range (3 cm off axis), all at the design depth (5 cm).

![Element Width Distribution](image)

Figure 2.5 64 element phased arrays with tapered element width distributions, 1 MHz, λ/2 focusing criterion for a 5 cm deep focus -2 to +2 cm off axis, ideal array: 1.24 mm average element width, 79 mm total array length, practical array: 1.17 mm average element width, 83 mm total array length.
Figure 2.6 Comparisons of ideal (no dead spacing, infinite resolution in element width, array length = 79 mm) and practical (0.1 mm dead spacing, 0.1 mm resolution in element width, array length = 83 mm) tapered phased arrays. Frequency: 1 MHz.
Aperiodic Array Simulations

The results of the random element distribution optimization study are summarized in Tables 2.1 and 2.2 and Figures 2.7, 2.8, and 2.9. The best random distributions of two element widths as determined by 200 trials with three focal positions per trial were compared to arrays of uniform elements. By comparing cost functions, it was discovered that aperiodic arrays allow for smaller grating lobes and/or larger element widths than uniform arrays. As shown in Table 2.1, for average element widths of 1.1 mm to 1.6 mm, the cost function was reduced by an average of 0.034 (or 34%) by using aperiodic arrays rather than uniform arrays. If the grating lobe levels are acceptable using uniform arrays, but larger elements are desired, it was found that aperiodic arrays could be used to increase the average element width by 0.34 mm (or 27% or $\lambda/4.4$) as shown in Table 2.2. Figure 2.7 shows the ability of combinations of different element sizes to reduce the grating lobe level while maintaining a constant average element width. There is a general trend that as the two element widths begin to deviate from their average width, the grating lobes first decrease and then begin to increase as the size difference between the two widths becomes larger.

Table 2.1 Grating lobe reduction for a constant average element width. A comparison of cost functions for arrays with uniform element widths and aperiodic arrays with optimized random distributions of two element widths.

<table>
<thead>
<tr>
<th>Uniform Element Width</th>
<th>Cost</th>
<th>Random Element Sizes</th>
<th>Cost</th>
<th>ΔCost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 mm (0.73λ)</td>
<td>.072</td>
<td>0.9 &amp; 1.3 mm</td>
<td>.049</td>
<td>-.023 (32%)</td>
</tr>
<tr>
<td>1.2 mm (0.8λ)</td>
<td>.090</td>
<td>1.0 &amp; 1.4 mm</td>
<td>.053</td>
<td>-.037 (41%)</td>
</tr>
<tr>
<td>1.3 mm (0.87λ)</td>
<td>.097</td>
<td>1.1 &amp; 1.5 mm</td>
<td>.054</td>
<td>-.043 (44%)</td>
</tr>
<tr>
<td>1.4 mm (0.93λ)</td>
<td>.101</td>
<td>1.2 &amp; 1.6 mm</td>
<td>.071</td>
<td>-.030 (30%)</td>
</tr>
<tr>
<td>1.5 mm (λ)</td>
<td>.111</td>
<td>1.1 &amp; 1.8 mm</td>
<td>.076</td>
<td>-.035 (32%)</td>
</tr>
<tr>
<td>1.6 mm (1.07λ)</td>
<td>.118</td>
<td>1.3 &amp; 1.9 mm</td>
<td>.081</td>
<td>-.037 (31%)</td>
</tr>
</tbody>
</table>
Table 2.2  Average element width increases for a constant grating lobe level achieved by using aperiodic arrays with optimized random distributions of two element widths instead of arrays with uniform element widths.

<table>
<thead>
<tr>
<th>Uniform Element Width</th>
<th>Cost</th>
<th>Random Element Sizes</th>
<th>Cost</th>
<th>ΔElement Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 mm (0.73λ)</td>
<td>.072</td>
<td>1.2 &amp; 1.6 mm (0.93λ)</td>
<td>.071</td>
<td>+0.30 mm (27%)</td>
</tr>
<tr>
<td>1.2 mm (0.8λ)</td>
<td>.090</td>
<td>1.3 &amp; 1.9 mm (1.07λ)</td>
<td>.086</td>
<td>+0.40 mm (33%)</td>
</tr>
<tr>
<td>1.3 mm (0.87λ)</td>
<td>.097</td>
<td>1.5 &amp; 1.8 mm (1.10λ)</td>
<td>.093</td>
<td>+0.35 mm (27%)</td>
</tr>
<tr>
<td>1.4 mm (0.93λ)</td>
<td>.101</td>
<td>1.5 &amp; 1.9 mm (1.13λ)</td>
<td>.101</td>
<td>+0.30 mm (21%)</td>
</tr>
</tbody>
</table>

Figure 2.7  The effect of random distributions of two element widths on grating lobes for a constant average element width. Element widths are expressed in difference from the average element width. Frequency: 1 MHz. Array length ≥ 8.7 cm.
Figure 2.8 The effect of using different ratios of two unequal element widths on grating lobes. Frequency: 1 MHz. Array length = 8.7 cm.

Until now, all of the aperiodic array results have been for arrays consisting of half of one element size and half of a second element size, with the lowest cost function arising from a selected distribution of 50% 0.9 mm and 50% 1.3 mm elements. Ratios other than 50%/50% were investigated to determine if lower cost functions could be achieved. Figure 2.8 shows cost functions for ratios ranging from 100% 0.9 mm and 0% 1.3 mm to 0% 0.9 mm and 100% 1.3 mm. The results of this figure indicate that a 50%/50% ratio provided the lowest cost function, although all ratios that included nonzero numbers of both element sizes produced lower cost functions than did uniform arrays consisting of either all 0.9 mm or all 1.3 mm elements. While a thorough simulation study was not conducted using combinations of elements different element sizes, using 33% 0.9 mm, 33% 1.1 mm and 33% 1.3 mm elements corresponded to the same average element width as using 50% 0.9 mm elements and 50% 1.3 mm elements but lead to a cost of 0.054 as opposed to 0.049.
A comparison of the relative power profiles for a uniform and an aperiodic array with the same average element width (1.5 mm) is shown in Figure 2.9. The main beam for each of the two arrays were virtually identical to each other, however visible differences existed in the grating lobe region. The peak grating lobe magnitude generated by the aperiodic array was only about half of the peak grating lobe magnitude generated by the uniform array, but the grating lobe width was larger for the aperiodic array than the uniform array.

![Graph of relative power profiles](image)

**Figure 2.9** Simulated power profiles for uniform (54 1.5 mm wide elements) and aperiodic (27 1.1 mm wide and 27 1.9 mm wide elements) arrays with a blow-up of the grating lobe region. Frequency: 1 MHz, 5 cm deep focus shifted 2 cm off the center axis.

**Material Characteristics**

As shown in Table 2.3, the efficiency of the elements tended to decrease as the element width decreased with the exception of the 2 mm element width. Figure 2.10 shows the power capabilities of the 16 element lithium niobate phased array and the 16 element PZT-EC69 aperiodic array. The power measurements were performed with the PZT-EC69 16 element aperiodic array, prior to construction of the 57 element array to determine if sufficient acoustical power output was attainable with this material and design. The array was able to generate 28 W of acoustical power per cm of array length.
while focusing at 3 cm deep. The power limitations of this array were never realized as it performed robustly for the duration of the power measurements without any noticeable losses in efficiency or damage to the array. The 16 element lithium niobate array was only able to output 14 W of acoustical power before the array failed (e.g. electrical arcing, electrode detachment, water leakage).

<table>
<thead>
<tr>
<th>Element Width</th>
<th>Efficiency</th>
<th>Resonance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 mm</td>
<td>38%</td>
<td>0.89 MHz</td>
</tr>
<tr>
<td>1.5 mm</td>
<td>46%</td>
<td>0.82 MHz</td>
</tr>
<tr>
<td>2.0 mm</td>
<td>29%</td>
<td>0.91 MHz</td>
</tr>
<tr>
<td>5.0 mm</td>
<td>62%</td>
<td>1.02 MHz</td>
</tr>
<tr>
<td>15.0 mm</td>
<td>83%</td>
<td>1.05 MHz</td>
</tr>
</tbody>
</table>

Table 2.3 PZT-EC69 material properties for different element widths. Original frequency prior to cutting material: 1.05 MHz.

Figure 2.10 Acoustical power output normalized to array length for the two 16 element phased arrays, focused at 3 cm deep and centered.
**Measured Fields for 16 Element Arrays**

Figure 2.11 shows measured ultrasound fields for the 16 element LiNbO₃ phased array for a 2 cm deep center focus and a focus 2.5 cm deep shifted 2 mm off axis. Measured ultrasound fields for the 16 element aperiodic phased array made from PZT-EC69 are shown in Figure 2.12. The focal positions are as follows: 3 cm deep axially centered, 2 cm deep shifted 0.5 mm off axis, and 2 cm deep shifted 1.3 cm off axis to the end of the array.

![Figure 2.11 Measured ultrasound fields in water. 16 element aperiodic phased array made from LiNbO₃. Freq: 1.5 MHz, Array length: 1.8 cm.](image-url)
Figure 2.12 Measured ultrasound fields in water. 16 element aperiodic phased array made from PZT-EC69. Freq: 0.85 MHz, Array length: 2.6 cm.

*Phase Corrections*

The 57 element array was able to focus at different specified locations using the uncorrected calculated phases given by Equation (2.5). The corrected phases given by Equation (2.6) generated a sharper focus than that produced by the uncorrected phases.
The best focus however was produced by phases measured with a hydrophone. Figure 2.13 shows a comparison of power profiles generated by uncorrected, corrected and measured phases for a 3 cm deep focus shifted 2 cm off axis.

![Graph showing power profiles comparison](image)

Figure 2.13 Comparison of axial power profiles generated by calculated-uncorrected, calculated-corrected, and hydrophone measured phases for the 57 element aperiodic phased array. Frequency: 0.83 MHz, 3 cm deep focus shifted 2 cm off the center axis.

**Comparison of Field Measurements and Simulations for the 57 Element Array**

The 57 element aperiodic array was able to produce a single focus at the following focal positions while keeping the grating lobe peak intensity below 10% of the focus intensity: 5 cm deep center (Figure 2.14), 4 cm deep center (Figure 2.15), and 3 cm deep center (Figure 2.16), 5 cm deep and 2 cm off axis (Figure 2.17), and 4 cm deep and 2 cm off axis (Figure 2.18). The 4 cm deep focus, shifted 2 cm off axis corresponds to a...
steering angle of 26.5° with all grating lobes less than 10%. Grating lobes greater than 10% were present for foci at the following locations: 3 cm deep 2 cm off axis (Figure 2.19), and 5 cm deep 2.5 and 3 cm off axis (not shown). Double foci were produced at 5 cm deep, each 2 cm off axis, by splitting the array in half and using each half to produce its own focus (Figure 2.20). The half peak power beam width and length in a plane parallel to the array was measured to be 5 mm x 2 mm for a 5 cm deep center focus (Figure 2.21). As a means of validating the model, measured and simulated ultrasound fields were compared and found to be in close agreement for all focal positions tested as shown in Figures 2.14-2.21.

Figure 2.14 Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, 5 cm deep center focus.
Figure 2.15  Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, 4 cm deep center focus.

Figure 2.16  Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, 3 cm deep center focus.
Figure 2.17 Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, focus: 5 cm deep 2 cm off axis.

Figure 2.18 Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, focus: 4 cm deep 2 cm off axis.
Figure 2.19 Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, focus: 3 cm deep 2 cm off axis.

Figure 2.20 Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, foci: 5 cm deep ±2 cm off axis.
Figure 2.21.a Measured and simulated ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, 5 cm deep center focus.

Figure 2.21.b Measured and simulated ultrasound fields in water in a plane parallel to the 57 element aperiodic phased array surface. Frequency: 0.83 MHz, 5 cm deep center focus. The wide beams are in the transverse dimension, and the narrow beams are in the axial dimension. The solid lines are simulated and the dotted lines are measured.
**Measured Fields for End Elements Turned Off**

In a manner similar to the focusing criterion of the spatially tapered array, the end array elements of the 57 element array were not powered when the array was focused off axis towards the other end of the array. As shown in Figure 2.22, the grating lobes are significantly reduced by not powering the elements which are at sharp steering angles. By using 80% of the array surface, the maximum power at the focus fell to 80% while the grating lobes dropped from 20% to 10%. In this case the focus was 5 cm deep and shifted 3 cm off axis, and elements for which the $\lambda/2$ focusing criterion was not satisfied were turned off.

![Graph showing grating lobe reduction](image)

**Figure 2.12** Grating lobe reduction by turning off end elements at sharp steering angles. Measured ultrasound fields in water from the 57 element aperiodic phased array. Frequency: 0.83 MHz, 5 cm deep focus, shifted 3 cm off axis.
Hyperthermia Experiment: Ex Vivo Perfused Kidney

The hyperthermia capabilities of the 57 element aperiodic phased array as tested with an ex vivo canine kidney are shown in Figures 2.23 and 2.24. Figure 2.23 shows the measured temperatures in the ex vivo kidney at the end of a 10 minute sonication for a single stationary focus and an electronic scan -2 to +2 cm off the central axis, both with a 5 cm focus depth and both without perfusion. Figure 2.24 shows the temperature rise versus time for a 10 minute electronic scan at 5 cm depth, -2 to +2 cm off axis with a perfusion of 4 ml/(min-100 g tissue) (or approximately 0.7 kg/(m^3*sec)), and an approximate acoustical power output of 9 W. For the data shown in Figures 2.23 and 2.24, the 7 temperature sensors were located 5 cm deep, -1.5 to +1.5 cm off axis (5 mm spacing between sensors).

![Figure 2.23 Unperfused kidney after 10 min. sonication with the 57 element aperiodic array: single focus and 5 cm deep scan, -2 to +2 cm off axis, thermocouples: 5 cm deep, -1.5 to +1.5 cm off axis](image-url)
Figure 2.24 Perfused (4 ml/min-100g) kidney, temperatures rise vs. time, 10 min. sonication with aperiodic array: 5 cm deep scan -2 to +2 cm off axis, acoustic power ≥ 9W, thermocouples: 5 cm deep, center axis (thick shaded line), ±0.5 cm off axis (dashed lines), ±1.0 cm off axis (dotted lines), ±1.5 cm off axis (thin solid lines).

2.3 Discussion

A new technique of reducing grating lobes using optimized random distributions of unequal element widths has been introduced. The reduction in grating lobes can be attributed to the aperiodic nature of the arrays designed with this technique, in contrast to periodic arrays consisting of uniform elements. The technique presented in this study has two potentially useful applications: (1). Reduction of peak grating lobe levels while maintaining a constant average element width, and (2). Increasing both the average and minimum element width, while maintaining a constant peak grating lobe level. Reduction of grating lobes is desirable in that better control of the ultrasound field is achieved, which reduces the deposition of power outside of the target region. Clinically this is important, since it enables more power to be deposited in the tumor, allowing it to reach therapeutic temperatures without excessive heating of surrounding normal tissue.

If grating lobe levels are acceptable, it can be advantageous to use larger array
elements since fewer elements need to be used for an array of a given length. Using fewer elements and hence fewer amplifier channels, phase shifters and less wiring translates into simpler and less expensive array construction. An additional benefit of using larger element sizes is that element efficiency has been shown to increase with element width both in this study and in previous studies (Hynynen et al., 1994), given that the element width to thickness ratio does not become disadvantageous. An example of an unfavorable width to thickness ratio was the 2 mm wide element, which having a width to thickness ratio of 1.0, probably had sufficient secondary transverse modes of vibration to lower the efficiency of the primary thickness vibration mode. In addition, the changes in resonant frequency which accompanied changes in element width have been observed previously for elements in which two of the three dimension are comparable in size (Lerrch, 1988).

While grating lobe reduction techniques such as sparse random arrays can also reduce the number of required elements, amplifier channels and array periodicity, the technique presented here is better suited for therapeutic applications since the array is dense and its entire surface area can emit acoustical power.

The goal of the optimization routine used in this study was to select distributions of two element widths which provided acceptable field patterns for a range of focal positions. A sufficient number (200) of random element distributions were simulated to ensure that the selected distribution was within the top 20% of all existing distributions and within 15% of the best achievable cost function for three focal positions. This was considered to be a reasonable compromise between the optimal solution and computation time. A search for global minima would not have been possible with the available computer resources. While the optimization routine used in this study provided meaningful results, other optimization methods might be worth investigating. Traditional methods such as gradient search techniques would probably not work very well since the selection of random element distributions is a discrete process that is certain to have a large number of local maxima and minima. Other procedures such as dynamic programming, which has
been applied to sparse arrays in radar (Skolnik, 1964), or simulated annealing algorithms (Kirkpatrick et al., 1983) employ somewhat of a trial and error approach and may be appropriate.

As previously stated a 50%/50% ratio provided a lower cost function than other ratios of 0.9 mm and 1.3 mm elements. An interesting finding was that all ratios consisting of both 0.9 mm and 1.3 mm elements produced lower cost functions than did uniform arrays consisting of all 0.9 mm or all 1.3 mm elements. Of particular interest was the finding that replacing only 10% of the elements in a uniform 1.3 mm array with appropriately placed 0.9 mm elements could reduce the cost function from .097 to .057, a reduction of 41%. Even with this marked reduction in cost function, an even greater reduction can be achieved (.097 to .054) by using a 50%/50% combination of 1.1 & 1.5 mm elements, suggesting again that 50%/50% ratios of element widths will lead to the lowest cost functions. An additional point regarding this last comparison is that replacing 10% of the 1.3 mm elements with 0.9 mm elements will result in a average element width slightly less than the 1.3 mm average element width associated with an array composed of 50% 1.1 mm and 50% 1.5 mm elements.

The measured acoustic fields were in good agreement with the theoretical simulations. A slight discrepancy was apparent for the comparison of the 4 and 5 cm deep foci shifted 2 cm off axis. In these cases a small 10% grating lobe appeared in the simulations but not in the actual field measurements. This discrepancy may be explained by experimental uncertainty, and for example could have arisen from a slight directionality bias in measurements with the hydrophone. From the field measurements, the array demonstrated the ability to focus at depths up to 5 cm and 2 cm off axis with no 10% grating lobes present. By turning off end elements based on the $\lambda/2$ focusing criterion, the array was able to focus at 5 cm deep and 3 cm off axis, with small regions of 10% grating lobes. One disadvantage of turning off elements is that the overall array power output is reduced unless increased power is generated from the remaining elements.
which are on. The power at the focus dropped in proportion to the drop in power emitting surface area (100% to 80%), while the grating lobes dropped more than proportionately (20% to 10%). For hyperthermia this may be acceptable, but for thermal surgery, it is likely that full power output from all elements will be necessary. It is also likely that grating lobes 10% or larger may not be a problem during hyperthermia, due to the smoothing effects of conduction and perfusion, especially when scanning a focus, which tends to spread out the effects of grating lobes; however, for thermal surgery, smaller grating lobes may become more significant, especially if the grating lobes occur near bone. For this reason, this aperiodic array design may show greater improvements over uniform arrays in thermal surgery applications, rather than hyperthermia applications. Given the anatomical location and size of the prostate, the ability of this array to scan a single focus is potentially useful as a means of delivering power to the prostate.

Other than the aperiodic array design technique developed in this study, two other array design techniques were also investigated for reduction of grating lobes. The first was sparse array design like that used in imaging arrays. This technique is probably not useful for intracavitary therapeutic phased arrays, as these are typically limited in size due to anatomical constraints and require full use of the available surface area. It is possible that for therapeutic phased arrays which are located external to the body, sparse array design may be feasible as more space is available. Recently a study has investigated the random placement of array elements in a sparse configuration for therapeutical purposes (Goss et al., 1996).

The second design technique studied to reduce grating lobes was the development of spatially tapered phased arrays with larger elements in the center and smaller elements on the ends of the array based on a $\lambda/2$ focusing criterion. The simulation results achieved with this spatially tapered phased array were promising; however, construction of such array was not attempted as low efficiency for some of the elements was predicted. For the spatially tapered phased array, a wide range of element widths are needed which would
exceed the span of the favorable width-to-thickness range for the materials tested in this study. It may be possible to design a spatially tapered array with upper and lower limits on the element widths used to maintain high element efficiency. Another possibility is that certain materials, such as piezocomposites, may have wider favorable width-to-thickness ratio ranges and may be well suited for use in a spatially tapered phased array.

The power capabilities of using PZT-EC69 elements in this aperiodic array design technique were clearly demonstrated. For the purposes of prostate hyperthermia, 28 W of acoustical power per cm of array length should easily satisfy the power requirements (Hynynen et al., 1994). This was supported by the ex vivo perfused kidney experiment performed using the 57 element phased array. The acoustical power output measurements suggest that this array is capable of producing sufficient power for thermal surgery, and this was confirmed experimentally (ex vivo) in a subsequent study (see section 3.2).

The array developed in the study has improved upon past arrays (Diederich and Hynynen, 1991 and Buchanan and Hynynen, 1994) by providing better focusing with fewer elements and more acoustical power output. The reasons for improvement include using the aperiodic array design technique presented in this study and possibly the use of a piezoelectric with better material properties. Later in this thesis, the ability of this array to create necrosed tissue lesions in ex vivo beef will be demonstrated (Chapter 3) and an array designed using the aperiodic design technique and constructed in a transrectal applicator will be tested in vivo (Chapter 4). To be effective in treating the entire prostate, a method of mechanically tilting the array about its long axis could be implemented.

The technique of using random distributions of unequal element sizes to reduce array periodicity and lower grating lobes has the potential to be incorporated into phased array designs other than the linear planar array design described in this study. Previous studies have shown that sector-vortex (Cain and Umemura, 1986), cylindrical-section (Ebbini et al., 1988), and spherical-section array (Ebbini and Cain, 1991) phased arrays produce lower grating lobe levels than planar arrays with similar element sizes. It is
possible that by using an aperiodic design technique in conjunction with these array geometries, even further grating lobe reduction may be achievable. In addition, this aperiodic array design technique could be applied to arrays operating at other frequencies by appropriately scaling the element sizes based on the wavelength.

In conclusion, this study has introduced a new method of reducing grating lobes using optimized random distributions of unequal element widths. This technique allows for the reduction of peak grating lobe levels and/or increases in average element width. This array design was implemented in an experimental array and good agreement with theoretical field distributions was achieved. The array demonstrated adequate acoustical power output for the purposes of both hyperthermia and thermal surgery.
3. Intracavitary Phased Arrays for Noninvasive Prostate Ultrasound Surgery

3.1 Methods

Until now, ultrasound surgery studies have involved spherically curved single transducers and phased arrays in spherically curved geometries composed of square (Fan and Hynynen, 1995, Fan and Hynynen, 1996a, Fan and Hynynen, 1996b, Hynynen et al., 1996b, and Wan et al., 1996) and annular (Chapelon et al., 1993, and Hynynen et al., 1996b) elements. The purpose of this study was to investigate the feasibility of using linear (1-D) ultrasound phased arrays for non-invasive surgery of the prostate; the ability of these arrays to create necrosed tissue lesions has not been studied until now. A parametric study was performed to investigate the effects of frequency, sonication time, maximum temperature, perfusion and focus location on the necrosed tissue volume generated by a single focus. Also investigated was the ability of phased arrays to increase the necrosed tissue volume by uniform and optimized electronic scanning of a single focus. Previous studies have investigated optimized temperature distributions for hyperthermia treatments (Wust et al., 1991, Lin et al., 1992, and Nikita et al., 1992), but prior to this study optimization of necrosed tissue volumes has not been studied.

3.1.1 Thermal Field Simulations

The acoustic pressure field generated by a linear array of ultrasound planar transducers was simulated on a computer using the method described earlier (Section 2.1.1). The array was modeled as a series of rectangular elements of equal length and width. Ideal arrays were simulated in this study without non-emitting spacers between the elements, with infinite phase resolution and element widths equal to one-half wavelength ($\lambda/2$) to allow focusing at all steering angles without grating lobes (Steinberg, 1976 and
Skolnik, 1980). The array length remained constant at 9 cm due to anatomical constraints, which predetermined the number of elements needed for a given frequency (e.g. 0.5 MHz: 60 elements, 1.0 MHz: 120 elements, 1.5 MHz: 180 elements, 2.0 MHz: 240 elements). Figure 3.1 shows a representative linear phased array.

Figure 3.1 Representative 1 MHz phased array with 120 elements each 0.75 mm wide and 15 mm long, no spacing between elements. Array dimensions: 15 mm x 90 mm.

The three-dimensional thermal fields were simulated on a computer using the Pennes bioheat transfer equation (BHTE) (Pennes, 1948). The 3-D transient version of this equation in Cartesian coordinates with constant spatial and temporal thermal properties was used for the thermal surgery simulations:

\[
\rho c_t \frac{dT}{dt} = k \left( \frac{d^2T}{dx^2} + \frac{d^2T}{dy^2} + \frac{d^2T}{dz^2} \right) - wc_b(T - T_a) + q(x,y,z) \tag{3.1}
\]

where \( k \) = thermal conductivity (0.5 W/(m°C)), \( w \) = perfusion (in kg/(m³s)), \( c_b \) = specific heat of the blood (3770 J/(kg°C)), \( c_t \) = specific heat of the tissue (3770 J/(kg°C)), \( T_a \) = arterial blood temperature (37°C), and \( T \) is the temperature at time \( t \) at the location (x,y,z). The BHTE was solved using a numerical finite difference method with all boundary and initial conditions set to 37°C. A time step of 0.05 seconds and a grid spacing of 0.5 mm
(radial: perpendicular to the array surface) x 0.5 mm (transverse: parallel to the array surface and perpendicular the longest dimension) x 0.25 mm (axial: parallel to the array surface and along the longest dimension) were determined to be sufficient for calculation accuracy.

The thermal dose, or equivalent time at a reference temperature was used to estimate the necrosed tissue volume for thermal surgery simulations. The accumulated thermal dose was calculated numerically using the following expression (Sapereto and Dewey, 1990).

\[
Dose(t_{\text{ref}}) = \int_{t=0}^{t=t_{\text{final}}} R^{T_{\text{ref}} - T(t)} dt \approx \sum_{t=0}^{t=t_{\text{final}}} R^{T_{\text{ref}} - T_{\Delta t}} \Delta t (3.2)
\]

where \( T_{\text{ref}} \) is the reference temperature, \( t_{\text{final}} = t_{\text{heating}} + t_{\text{cooling}}, \Delta t \) is the time step, \( T_{\Delta t} \) is the average temperature during the current time step, and \( R \) is given by the following expression.

\[
R = \begin{cases} 
0.5, & \text{if } T(t) \geq 43^\circ C \\
0.25, & \text{if } T(t) < 43^\circ C 
\end{cases} (3.3)
\]

The necrosed tissue volume was estimated by the volume enclosed within an isothermal dose of 240 minutes at a reference temperature of 43°C. This technique was found to predict the necrosed tissue lesion size with reasonable accuracy (Damianou and Hynynen, 1994).

3.1.2 Necrosed Tissue Volume with Electronic Scanning
To simulate scanning of a focus, power fields from multiple focus locations were averaged and then the averaged field was used as an input to the temperature solver. For thermal surgery simulations, it was determined that an axial foci spacing of 0.5 mm was small enough to avoid drops in power, temperature and dose between the foci. The following weighted average expression allowed for unequal weighting (weighting can be either temporal or relative power) of each focus location.

\[ q_{\text{ave}}(x, y, z) = \frac{1}{n} \sum_{i=1}^{n} w_i q_i(x, y, z) \]  

(3.4)

It was hypothesized that unequal weighting of different focal locations, in particular weighting the end scan points more heavily, would result in a more uniform temperature and dose profile than that achieved by uniform weighting of each focus location. Due to the close foci spacing (0.5 mm), the system was not decoupled (i.e. changing the weighting factor of one focus affected the power at neighboring focal locations). For this reason, individually scaling the power at each point to produce a desired temperature was not possible, and an optimization technique was needed.

A simple direct search optimization algorithm (Reklaitis et al., 1983) was used to find foci weighting factors that would produce uniform temperature and dose profiles at the scan depth. The algorithm is outlined in Figure 3.2. Symmetry was used since the scan was chosen to be symmetric about the central axis. For example, for a scan from -5 mm to +5 mm with 0.5 mm foci spacing, there are 21 focal locations but only 11 independent weighting factors exist, each of which may be incremented or decremented yielding a total of 22 possible directions. The cost function (CF) that was used is given in the following expression:

\[ CF = \frac{1}{m} \sum_{j=1}^{m} (X_j - X_{\text{ave}})^4 \]  

(3.5)
where \( m \) is the number of field points along the width of the scan, \( X_j \) is the temperature (or dose) at position \( j \) of the scan, and \( X_{\text{ave}} \) is the average temperature (or dose) over the width of the scan.

**Figure 3.2** Direct search optimization algorithm used to adjust focus weighting factors to achieve uniform temperature or dose profiles.

This optimization algorithm can be used to achieve either uniform temperature or uniform dose profiles. The advantage of optimizing temperature is that it requires much
less computation time. For example, using temperature in the cost function requires calculating the temperature only during the sonication (5 seconds), but using dose in the cost function requires temperature and dose calculations during both the sonication and cool down period (often > 70 sec). Although uniform temperature profiles do improve dose uniformity, they do not ensure that the dose profile is as uniform as possible. For this reason, the temperature was first quickly optimized, and then the result was used as a starting point for more computationally intensive dose optimization.

3.1.3 Ultrasound Surgery Experiment: Ex Vivo Unperfused Liver

The 57 element aperiodic phased array was used to create necrosed tissue lesions in fresh beef liver; however, prior to ex vivo testing of the experimental array, the ability of this array to create necrosed tissue lesions was investigated using simulations. These simulations used the actual element widths, inter-element non-emitting spacers and phase discretization to more accurately model the parameters of the actual array and amplifier system.

The ability of the aperiodic phased array to create lesions in fresh beef liver was tested with a single stationary focus and uniform scans using a range of power levels and sonication times. As shown in Figure 3.3, the array and the liver were submerged in a tank of degassed water to reduce the effects of ultrasound reflections at gas-water interfaces. The water temperature was 23°C and separated the array and liver surfaces by 1.5 cm, which is a reasonably approximation of the water bolus used for transrectal ultrasound treatments. The water temperature was set to 23°C rather than 37°C to provide a conservative estimate of the array’s ability to generate necrosed tissue lesions.
3.2 Results

Single Focus Simulations

The focusing capabilities and the results of the parametric study involving necrosed tissue volumes generated by a single stationary focus are summarized in Table 3.1 and Figures 3.4 - 3.8. Separately generated lesions are superimposed in Figure 3.4, demonstrating the ability of a 1 MHz, 9 cm long phased array to produce lesions in the axial direction from one end of the array (-4.5 cm) to the other (+4.5 cm) while focusing at depths of 2 to 6 cm. Due to anatomical considerations, generation of lesions outside of the 2-6 cm depth and ±4.5 cm axial range was not attempted.

The effects of frequency, sonication time and maximum temperature on the necrosed tissue volume are demonstrated in Figure 3.5, where it can be seen that the ultrasound field is more sharply focused at higher frequencies, leading to a more compact lesion size. Figure 3.5 also shows that the lesion size increases when either the maximum temperature achieved in the tissue or the sonication time is increased. Table 3.1 demonstrates the effects of sonication time, maximum temperature, blood perfusion, frequency, and focus depth on the acoustic power output required from the array and the time required for the entire target volume to cool to less than 44°C. As

Table 3.1  Acoustic power output and cooling time for the entire target volume
temperature to drop below 44°C. Unless otherwise stated the sonication time was 10 seconds, the maximum temperature was 100°C, the frequency was 1 MHz, the blood perfusion was 5 kg/(m³s) and the focus was 4 cm deep and centered axially.

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<th>Cooling Time (s)</th>
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</tr>
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<td>6</td>
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sonication time increases, maximum temperature increases or perfusion decreases, the time required for the entire target volume to cool down below 44°C increases. The effect of sonication time on cool down time is shown graphically in Figure 3.6. The cool down time trend was not as predictable for changes in frequency or focus depth. The reason for this is that higher frequencies are more sharply focused, resulting in a smaller lesion size and a shorter cool down time; however, higher frequencies are also associated with higher
attenuation in tissue, which for a given focus depth, can result in more near field heating and a longer cool down time. These competing effects of frequency suggest that increasing frequency or decreasing focus depth will not always result in shorter cool down times.

Figure 3.4 Isothermal dose lines (240 minutes at 43°C) for single foci produced by a 1 MHz, 9 cm long phased array for 5 sec sonications, maximum temperature = 100°C, and perfusion = 5 kg/(m³s). Foci locations are at 2, 4 and 6 cm deep and 0.0, ± 1.5, ± 3.0, and ± 4.5 cm off the central axis. (a) shows a plane perpendicular to the array surface, parallel to the array length. (b) shows a plane parallel to the array surface, 4 cm deep.
Figure 3.5. For all figures: horizontal axis = axial direction and vertical axis = radial direction, both in (mm). Freq: 0.5 MHz: (a), (e), (i); 1.0 MHz: (b), (f), (j); 1.5 MHz: (c), (g), (k); 2.0 MHz: (d), (h), (l). (a), (b), (c) and (d) show ultrasound fields for 4 cm deep center foci generated by 9 cm long phased arrays. (e), (f), (g) and (h) show corresponding isothermal dose lines (240 min. at 43°C) for Tmax = 100°C, perfusion = 5 kg/(m³s) and varying sonication times: 1 sec (solid line), 5 sec (dotted line), 10 sec (dashed line), 20 sec (dashed-dotted line). (i), (j), (k) and (l) show corresponding isothermal dose lines (240 min. at 43°C) for 10 sec sonications, perfusion = 5 kg/(m³s), and varying Tmax: 70°C (solid line), 80°C (dotted line), 90°C (dashed line), 100°C (dashed-dotted line).
Figure 3.6  Peak temperature histories for varying sonication times, 4 cm deep center focus, 1 MHz, Tmax = 100°C, perfusion = 5 kg/(m²s).

Figure 3.7  Centerline temperature profile for varying sonication times, 4 cm deep center focus, 1 MHz, Tmax = 100°C, perfusion = 5 kg/(m²s).
Figure 3.8  Axial temperature profile at 4 cm depth for varying sonication times, 4 cm deep center focus, 1 MHz, Tmax = 100°C, perfusion = 5 kg/(m^3s).

The effects of sonication time on the centerline and axial temperature profiles are shown in Figures 3.7 and 3.8, respectively. Similar to the results shown for the necrosed tissue lesions shown in Figure 3.5, Figures 3.7 and 3.8 demonstrate that increases in sonication time, will result in increased length and width of the heated region due to conduction.

**Uniform Electronic Scan Simulations**

The results of the parametric study for uniform power scans are summarized in Table 3.2 and Figures 3.9 and 3.10. In Figure 3.9, the size of the necrosed tissue generated by a single focus is compared to those generated by electronic scans of varying
width (i.e. a single focus was electronically scanned across 1, 2 and 3 cm axial widths at a constant radial depth of 3.5 cm). As shown in Figure 3.10, the necrosed tissue volume increases as the maximum temperature is increased, but changes only slightly for changes in sonication time and perfusion. It can be seen in Table 3.2 that the required acoustic power increases for decreases in sonication time, increases in maximum temperature or increases in scan width, while the time required to cool the entire target volume to 44°C increases for increases in maximum temperature, decreases in perfusion or increases in scan width.

Figure 3.9 Isothermal dose lines (240 minutes at 43°C) for a single focus (solid line) and uniform power scans of 1 cm (dashed-dotted line), 2 cm (dotted line) and 3 cm (dashed line) axial widths produced by a 1 MHz 9 cm long array for 5 second sonications, maximum temperature = 60°C and perfusion = 5 kg/(m³s). (a) shows a plane perpendicular to the array surface and parallel to the array length. (b) shows a plane parallel to the array surface and 3.5 cm deep.
Figure 3.10 Isothermal dose lines (240 min at 43°C) for 1 cm wide uniform power scans 3.5 cm deep generated by a 1 MHz, 9 cm long phased array. (a) and (d) are for varying Tmax: 60°C (solid line), 65°C (dotted line), 70°C (dashed line), 75°C (dashed-dotted line) but constant perfusion (5 kg/(m³s)) and sonication time (5 s). (b) and (e) are for varying sonication times: 1 sec (solid line), 20 sec (dashed-dotted line) but constant perfusion (5 kg/(m³s)) and Tmax (60°C). (c) and (f) are for varying perfusion: 0 kg/(m³s) (solid line), 10 kg/(m³s) (dashed-dotted line) but constant Tmax (60°C) and sonication time (5 s). (a), (b) and (c) show planes perpendicular to the array surface and parallel to the array length. (d), (e) and (f) show planes parallel to the array surface and 4 cm deep.
Table 3.2. Acoustic power output and cooling time for the entire target volume temperature to drop below 44°C. Unless otherwise stated the sonication time was 5 seconds, the maximum temperature was 60°C, the frequency was 1 MHz, the blood perfusion was 5 kg/(m³s) and the focus was 3.5 cm deep and scanned axially from -0.5 to +0.5 cm off the central axis.

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Optimized Electronic Scan Simulations

Figure 3.11 shows the temperature (a) and dose (b) profiles at the focal depth (3.5 cm) for a single stationary focus, a uniform power scan, a scan optimized for uniform temperature and a scan optimized for uniform dose. The width of all scans was 1 cm (-5 mm to +5 mm). The uniform temperature scan was optimized from -5 mm to +5 mm.
(a), (b), and the uniform dose scan was optimized from -4.5 mm to +4.5 mm (a), (b), (c) and from -5 mm to +5 mm (c). Figure 3.11 (c) demonstrates that a smoother dose profile is achieved when the optimization width is narrower than the scan.

Figure 3.11 Temperature (a) and dose (b) profiles for a single stationary focus (dotted line), a uniform power scan (dashed-dotted line), a scan optimized for uniform temperature (dashed line) and a scan optimized for uniform dose (solid line). (c) shows dose profiles for dose optimized scans with constant scan width: -5 mm to +5 mm, but the optimized width varied: -5 mm to +5 mm and -4.5 mm to +4.5 mm. All cases are for a 5 sec sonication from a 9 cm 1 MHz array, Tmax = 58°C, perfusion = 10 kg/(m’s), focal depth = 3.5 cm (centered axially).
width. The optimization width refers to the width over which the cost function is calculated; however, weighting factors associated with foci outside of the optimization width but within the scan width can be adjusted during optimization. In comparison to the uniform power scan, all optimized scans produced less heating in the scan center and more heating near the scan endpoints, which resulted in a wider more evenly heated necrosed tissue volume, especially for the dose optimized scan. Again it can be seen that electronic scanning is capable of significantly enlarging the necrosed tissue volume in comparison to a single stationary focus.

Simulations for the Experimental Array

Simulated necrosed tissue lesions for the 0.83 MHz, 8.7 cm long, 57 element aperiodic phased array used in the ex vivo experiments are shown superimposed in Figure 3.12. These predicted lesions are for 5 second sonications, maximum temperature = 100°C, and perfusion = 5 kg/(m^3s) for single foci at 2, 4, and 6 cm deep and 0.0, ±1.5, ±3.0, and ±4.5 cm off the central axis. Significant secondary lesions are present for the 2 cm deep ±4.5 cm off axis foci, and the necrosed tissue volume is discontinuous for the 6 cm deep -4.5 cm off axis focus. The secondary lesions were associated with grating lobes that were 20-25% in magnitude and approximately the same size and shape as the secondary lesions. The maximum temperature elevations within the regions of the secondary necroses were approximately 59 to 75 °C.
Simulated necrosed tissue lesions generated by the 0.83 MHz, 8.7 cm long, 57 element aperiodic phased array used in the ex vivo experiments. Isothermal dose lines (240 min. at 43°C) for 5 sec sonifications, $T_{\text{max}} = 100^\circ\text{C}$, and perfusion $= 5$ kg/(m$^3$)s for single foci at 2, 4, and 6 cm deep and 0.0, ±1.5, ±3.0, and ±4.5 cm off the central axis. (a) shows a plane perpendicular to the array surface and parallel to the array length. (b) shows a plane parallel to the array surface and 4 cm deep.

**Ex Vivo Experimental Necroses**

The experimental aperiodic phased array was able to produce necrosed tissue lesions in fresh beef liver using both uniform scans and single stationary foci at different locations for sonication times ranging from 10 to 30 seconds. The lesion sizes listed in Table 3.3 represent approximate cross-sectional areas that were calculated using the product of the measured lesion width and length. Since the actual array acoustic power output could not be measured during the experiments, approximate acoustic power levels listed in Table 3.3 were estimated based on earlier acoustic power measurements. Figure
3.13. shows a photograph of one of the representative lesions (4 cm center focus, 10 second sonication). Figure 3.14 shows a photograph of a representative lesion created by an electronic scan (4 cm deep, 6 mm wide (± 3 mm) and centered axially, 20 second sonication).

Table 3.3 Beef liver lesions created by the 0.83 MHz, 57 element aperiodic phased array. Single foci were 4 cm deep and centered axially. The scan was 4 cm deep, 8 mm wide and centered axially.

<table>
<thead>
<tr>
<th>Sonication Time (s)</th>
<th>Estimated Acoustic Power (W)</th>
<th>Focus</th>
<th>Approximate Lesion Size (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>140</td>
<td>single</td>
<td>8</td>
</tr>
<tr>
<td>20</td>
<td>140</td>
<td>single</td>
<td>32</td>
</tr>
<tr>
<td>20</td>
<td>140</td>
<td>scan</td>
<td>64</td>
</tr>
<tr>
<td>20</td>
<td>110</td>
<td>single</td>
<td>21</td>
</tr>
</tbody>
</table>

Figure 3.13 Necrosed tissue lesion generated in beef liver with a 0.83 MHz, 8.7 cm long, 57 element aperiodic phased array. The sonication time was 10 seconds, the focus was 4 cm deep and on the central axis, and the approximated cross-sectional area of the lesion was 8 mm².
3.3 Discussion

This study investigated the feasibility of using linear intracavitary phased arrays for ultrasound surgery of the prostate. The advantage that linear intracavitary arrays have over previously proposed transducer designs is that 2-D electronic focusing is possible, which eliminates the need for multi-dimensional mechanical positioning systems or multiple applicators with varying focal depths. The simulation results indicate that linear intracavitary arrays are capable of focusing and producing necrosed tissue lesions over anatomically appropriate prostate target volumes. While capable of covering the entire prostate, the necrosed tissue lesions generated by a single focus are relatively small and would require many sonications to cover the large volumes. To avoid temperature build-up in the near field during multiple sonications, sufficient cool down time would be needed between sonications, which could lead to an excessively long treatment time (Damianou and Hynynen, 1993 and Fan and Hynynen, 1996b). As a means to reduce the number of sonications required and the treatment time, enlargement of the necrosed tissue volume is desirable.
Four methods of enlarging the necrosed tissue volume were presented in this study: increasing the maximum temperature elevation, increasing the sonication time, decreasing the operating frequency, and using electronic scanning. Increasing the maximum temperature achieved in the target volume will enlarge the necrosed tissue volume as a result of increased thermal conduction from the center of the target volume; however, this technique is limited in that maximum temperatures over 100°C will lead to cavitation (boiling) and unpredictable results. Increasing the sonication time also permits the necrosed tissue volume to be enlarged by increased effects from thermal conduction; however, longer sonications will lead to higher perfusion dependence and more near field heating which will result in longer cool down times between sonications and may not reduce the total treatment time. Decreasing the operating frequency also enlarges the necrosed tissue volume since the focus is not as sharp, although lower cavitation thresholds and decreased power absorption in tissue limit the utility of low frequencies.

Of the methods studied for enlarging the necrosed tissue volume, electronic scanning of a single focus was demonstrated to be the most effective. Relative to a single focus sonication, scan widths of 1 and 2 cm increased the calculated necrosed tissue volumes by factors of 100 and 300 respectively, while holding the maximum temperature and sonication time constant. However, as the scan width increased, the necrosed tissue volume moved towards the array surface as a result of increased near field heating. For a scan width of 3 cm, tissue at the focal depth (3.5 cm) was no longer necrosed over a major portion of the scan width. This can be explained by the decrease in geometric gain that accompanies increases in scan width for a fixed array length. Another observed trend was that the width of the necrosed tissue volume was always less than the scan width, particularly as the scan width increased.

While uniform scanning offered significant advantages over single stationary focus sonications, further improvement was realized with optimized scanning. For uniform scans, the center of the necrosed tissue volume received a dose much higher than the dose
received near the volume boundaries. This overheating of the center and under heating of the target volume edges was minimized by optimally setting the weighting parameter associated with each focus location along the width of the scan. For a scan optimized to produce a uniform dose profile at the focal depth, the corresponding temperature profile was characterized by higher temperatures near the scan endpoints, and the corresponding pressure profile was even more uneven, with the pressure being much higher near the scan endpoints.

Additionally, using a scan width one focal spacing wider than the optimization width resulted a smoother dose profile for the following reasons. When the entire width of the scan was optimized, a very steep gradient was needed at the scan endpoints to bring these points up to the desired dose. While increasing the power at the scan endpoints brought the endpoint doses up to the desired level, the points adjacent to the endpoints and towards the scan center received a higher dose due to conduction effects from the scan center. The dose at these adjacent points cannot be brought down to the desired level even when the power is decreased to zero at these points. Therefore, a more uniform dose can only be achieved by increasing the scan width relative to the optimization width. In other words, to achieve uniform dose across the target volume, it is necessary to heat a narrow margin of tissue on the edges of the target volume. Another method of enlarging the necrosed tissue volume, which was not investigated in this study, is the generation of multiple foci simultaneously (Ebbini and Cain, 1989) which can be stationary or electronically scanned to control the necrosed tissue volume (Fan and Hynynen, 1995 and Fan and Hynynen, 1996a). During multiple scan sonications, temperature build up in the near field is an important consideration in determining the required cooling time between sonications and the total treatment time.

For most of this study, ideal arrays were simulated to investigate the effects of various parameters on the necrosed tissue volume; however, the simulations based on the experimental array indicated that it was capable of generating lesions similar to those
generated by the ideal arrays over most of the range covered by the ideal arrays. In addition to the non-ideal attributes of the actual array, several other differences existed, which provide additional support for the observed differences between the simulated necrosed tissue volumes generated by the actual and ideal arrays. These differences include a shorter actual array length which will detract from off axis focusing capabilities, a lower operating frequency which will increase lesion size, and the aperiodic array design which will lead to asymmetric lesions.

For the cases in which secondary lesions were present in the simulations based on the experimental array, it was estimated that they were caused by large regions of grating lobes that were 20-25% in magnitude. These simulations were for 5 second sonications which resulted in maximum temperatures of 100°C and the secondary lesions were present for the foci 2 cm deep and ±4.5 cm off the central axis. The minimum grating lobe level required to form secondary lesions is dependent on many factors such as maximum temperature, sonication time, tissue attenuation, absorption, conductivity and perfusion, and the size and shape of the grating lobe. It may be that 20-25% grating lobes will create secondary lesions in some instances but not in others. A conservative approach would be to introduce a factor of safety. For example, a factor of safety of two, would keep grating lobe levels below 10% and increase the margin for error in pre-treatment simulations used to predict secondary lesions.

The ability for linear phased arrays to create necrosed tissue lesions was demonstrated by generating lesions in beef liver. As expected, the lesion generated by a 20 second sonication was larger than the lesion generated by a 10 second sonication, but smaller than the lesion generated by the 20 second electronic scan. Also expected was the smaller lesion size that was created using a lower electrical input power level, which likely corresponded to a lower maximum temperature.

The clinical applications for linear intracavitary phased arrays include treatments for BPH and prostate cancer. For BPH treatments, the treatment goal would be to reduce
urethral constriction by ablating the tissue surrounding the urethra. By using 5 second, 1 cm wide scans with adequate cooling time between sonications, the entire length of transurethral prostate tissue could be ablated using 5-8 consecutive sonications, yielding a total treatment time on the order of 10 minutes. Enlarging the necrosed tissue volume with electronic scanning may also be useful in the treatment of prostate cancer. However, since the inferior boundary of the prostate lies adjacent to the rectal wall, it may not be feasible to completely necrose this portion of the prostate without sustaining damage to the rectal wall. For this reason, ultrasound surgery as a treatment for prostate cancer may be more useful as a means to debulk portions of the tumor as opposed to ablating the entire gland. Due to the flat geometry of the array, a mechanism for rotation of the array about its long axis would need to be implemented prior to treating tumors with large transverse dimensions. Ultrasound surgery may also be a useful supplement to prostate hyperthermia treatments in that under heated tissue surrounding blood vessels could be necrosed.

In conclusion, this study has proposed the use of linear intracavitary ultrasound phased arrays for thermal surgery of the prostate. The ability of phased arrays to significantly enlarge the necrosed tissue volume by electronic scanning was established, as was the ability to produce more uniform temperature and dose distributions by optimizing scan weighting factors. The heating capabilities of linear phased arrays were verified experimentally by creating necrosed tissue lesions in ex vivo beef liver.
4. Design and Evaluation of a 62 Element MRI Compatible Intracavitary Aperiodic Phased Array

4.1 Methods

This study involves the feasibility of using an MRI compatible transrectal ultrasound phased array for treatment of prostate diseases with thermal therapies. In designing the 62 element phased array, a series of acoustic simulations were performed to evaluate aperiodic array designs and efficiency measurements were performed for a range of element sizes. Following construction of the array, beam plots produced by the array were compared to those predicted by the acoustic simulations and the array efficiency was tested. Following acoustic testing, the heating capabilities of the array were tested ex vivo and in vivo using MRI temperature monitoring.

4.1.1 Acoustic Simulations

The acoustic pressure field generated by a linear array of ultrasound planar transducers was simulated on a computer using the method described earlier (Section 2.1.1). A cost function (Section 2.1.2) was used to optimize random distributions of unequal element widths to result in reduced grating lobe levels. The acoustic simulations were also used for comparison with the measured ultrasound fields produced by the 62 element array.

4.1.2 Acoustic Measurements and Width-to-Thickness Ratios

Prior to array construction, the efficiency of elements cut to a range of different widths were measured using a radiation force technique (Stewart, 1982 and Hynynen, 1993). The element efficiency is the quotient of total acoustic output power divided by total electrical input power. The resonant frequency was also measured for each of the element sizes, and each element was powered at its resonant frequency to achieve maximum element efficiency (Hunt, 1987). Element efficiency and acoustic power
measurements were performed to determine element widths that resulted in favorable and unfavorable width to thickness ratios.

Following construction of the array, the efficiency the entire array was measured using the same radiation force technique. The efficiency of the array was measured while driving all of the elements in phase (unfocused) and while driving the elements to produce a 5 cm deep center focus. The ultrasound field generated by the array was measured by placing the array in a tank of degassed water and mechanically scanning a thermistor across the ultrasound field, using a grid spacing of 0.25 mm to 1.00 mm (Martin and Law, 1983).

4.1.3 Construction of a 62 Element Aperiodic Phased Array

Based on the aperiodic design simulations, the empirical width-to-thickness correlation with element efficiency, the acoustic power capabilities demonstrated by the 16 element arrays, and the acoustic and heating capabilities of the 57 element array, a 62 element aperiodic phased array was constructed using PZT-EC69. This array was constructed in an intracavitary applicator (see Figure 4.1) making it suitable for transrectal use. Due to anatomical constraints, the applicator was designed to be as small as possible, yet still large enough to house the array, 62 coaxial cables, two water tubes and two air tubes. The portion of the applicator which would be in the rectum has the following dimensions: 101 mm in length, 21 mm outer diameter which tapers to 15 mm where the anus is located and is rounded at the front to ease insertion. Slots for O-rings located at both ends of the array enable mounting of a latex membrane which can be used in conjunction with the water inflow and outflow to provide a temperature controlled water bolus. While the water tubes enable circulation of water on the front face of the array, air tubes allow for the circulation of air behind the array, which can be used to provide positive pressure to prevent water leakage and remove any moisture that could corrode the back electrode surface. In addition, all of the array components, including the applicator, electrodes, coaxial cable, wiring, water bolus
circulation system tubing, were constructed using non-ferromagnetic materials, enabling it to be experimentally tested in an MRI magnet.

![Diagram of Intracavitary applicator for 62 element aperiodic phased array.]

Figure 4.1 Intracavitary applicator for 62 element aperiodic phased array.

The 62 element linear array, shown in Figure 4.2, was constructed with 32 1.00 mm wide elements and 32 1.15 mm elements (15 mm array width, 77 mm total array length, 0.75λ average center-center spacing), using an optimized random distribution of two element widths based on the computer simulations. The elements, which had silver electrode plating, were cut from PZT-EC69 ceramic, using a silicon wafer dicing saw (Penn State Whitaker Center for Medical Ultrasonics, Transducer Characterization Laboratory, State College, PA). The elements were powered at a resonant frequency of 1.05 MHz in their thickness mode. Silicone rubber adhesive of 0.13 mm thickness was used to glue the elements together and provide mechanical and electrical isolation. The array was then mounted in the Delrin transrectal applicator. The elements were connected to coaxial cable (Tensolite, St. Augustine, FL, 30830/9E232X-1(LD), 79 pF/m) on the air-backed side using solder. This MRI-compatible coaxial cable was non-ferromagnetic and was low in capacitance, allowing 6 meter lengths of coaxial cable to run from the array elements to the amplifier system, which must be located outside of the magnet room. The elements on the front face of the array were grounded by soldering them to a strip of silver foil. Each element was electrically matched to 50-Ω using L-C matching networks. For the non-MRI testing of the 62 channel array, a 64 channel computer controlled amplifier system was used that consisted of phase shifters, duty
cycle controllers, amplifiers, and RF power meters (Buchanan and Hynynen, 1994). For the MRI testing, a newly developed amplifier system was used that produced less electrical noise, and had individual power control and phase locking capability for each channel (Daum et al., 1996). Flatness of the array was maintained by only cutting through 85% of the thickness of the elements, which also served as a common ground on the front surface of the array (herein referred to as array A). A second array was cut, which was identical to the first array, except that it was cut through the entire thickness (herein referred to as array B). For this array, wires soldered to the elements and a strip of silver foil were used to ground the front face of the array. Array A was used for the field measurements and the ex vivo beef experiments. Array B was used for the in vivo experiments.

Figure 4.2 The MRI compatible aperiodic 1.05 MHz intracavitary phased array.
4.1.4 MRI Guided Heating Experiment: Ex Vivo Beef

The MRI compatibility of the 62 element phased array was tested by sonicating fresh beef in a clinical 1.5 Tesla MRI system (Signa, General Electric Medical Systems, Milwaukee, WI). The water bolus was inflated with degassed water and placed adjacent to a piece of fresh beef (separated by a 0.09 mm mylar membrane) at a distance approximating that of a transrectal prostate treatment. The array was powered at 60-90 W of electrical power for 10 seconds while producing a focus 5 cm deep and 0 to 2 cm off axis. The setup was similar to that used in the ex vivo bovine liver ultrasound surgery experiment, except that the 62 element array was used with a water bolus, and this whole setup was inside an MRI magnet (see Figure 4.3). A surface coil was used to improve the signal to noise ratio. Baseline images were taken prior to sonication and images were taken during and immediately following sonication to allow for image subtraction, which results phase shifts proportional to temperature elevation (Chung et al., 1996). The following imaging parameters were used with a fast spoiled gradient echo imaging sequence: TR = 52.6 msec, TE = 12.8 msec, flip angle = 30°, resolution = 256 X 128, field of view = 16 X 16 cm, imaging time = 7 seconds, slice thickness = 5 mm.

Figure 4.3 Setup for MRI guided ex vivo beef heating experiment.
4.1.5 MRI Guided-Heating Experiments: In Vivo Muscle

The in vivo heating capabilities of the array were tested by heating rabbit thigh muscle in a 1.5 Tesla MRI system (Signa, General Electric Medical Systems, Milwaukee, WI). In each of the 4 experiments, New Zealand white rabbits were used, anesthetized with a mixture of sodium xylazine and ketamine, and the hair from the thighs was removed with an electric shaver and hair removing lotion. The array was placed adjacent to the shaved rabbit thigh, and the array water bolus was inflated with degassed water (see Figure 4.4). A thin mylar membrane (0.09 mm) separated the rabbit thigh and the water bolus and the bolus-mylar interface was covered with acoustic coupling gel. For rabbits 3 and 4, a layer of degassed water separated the rabbit thigh muscle and the bolus, allowing for deeper focal positions to be tested. A surface coil, placed either under or on top of the animal, was used to improve the signal to noise ratio. Prior to the sonications, baseline T1 weighted MRI images were taken, which were used to determine the distances from the array to the desired focal locations within the thigh muscle (see Figure 4.5). The following

![Diagram of MRI setup](image-url)
imaging parameters were used with a fast spoiled gradient echo imaging sequence: TR = 48.5 - 74.2 msec, TE = 23.9 - 36.9 msec, flip angle = 30°, resolution = 256 X 128, field of view = 16 X 16 cm, imaging time = 3.5 - 10 seconds, slice thickness = 3 - 5 mm. Using single focal spots and electronic scans, focal locations ranging from 3.0 to 6.0 cm deep, shifted off axis from 0.0 to 3.0 cm were used to position the focus within the thigh muscle while avoiding bone. Power levels up to 100 watts of electrical input power (~40 watts acoustical power) and sonication times from 10 seconds to 5 minutes and 22 seconds were used. Baseline images were taken prior to sonication and images were taken during and immediately following sonications to allow for image subtraction, which results phase shifts proportional to temperature elevation (Chung et al., 1996). After each in vivo heating experiment, the animal was sacrificed.

Figure 4.5 T2-weighted MRI image of the 62 element phased array with the water bolus inflated and placed adjacent to the rabbit thigh muscle, which rests in degassed water. Rabbit 3.
4.2 Results

Array Design

The array design was based on the aperiodic design technique for grating lobe reduction (Table 4.1) and width-to-thickness ratios which provided high element efficiency (Figure 4.6). Based on the aperiodic array simulations performed in this study and a previous study (Hutchinson et al., 1996a), it was determined that element widths ranging from 0.67λ to 1.33λ were useful for aperiodic array design. The empirical width-to-thickness versus efficiency data showed that width-to-thickness ratios of 0.65 to 0.85 resulted in high element efficiency. This data is comparable to a study which showed an optimal width-to-thickness ratio of approximately 0.6 for various other types of PZT ceramics used in diagnostic imaging (Sato et al., 1979). The combination of the aperiodic array data and the width-to-thickness data can be used to come up with a design criterion for selecting element widths in phased arrays (Figure 4.7). Figure 4.7 demonstrates that the width-to-thickness ratio is more constraining than the aperiodic array design widths, when selecting element widths.

Table 4.1 Grating lobe reduction achieved by the aperiodic array design technique. Cost function comparisons for arrays with uniform element widths and aperiodic arrays with optimized random distributions of two element widths. Constant average element width. Frequency = 1.05 MHz.

<table>
<thead>
<tr>
<th>Uniform Element Width</th>
<th>Cost</th>
<th>Random Element Widths</th>
<th>Cost</th>
<th>ΔCost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.05 mm (.73λ)</td>
<td>0.069</td>
<td>1.00 and 1.10 mm</td>
<td>0.065</td>
<td>-0.004 (6%)</td>
</tr>
<tr>
<td>1.075 mm (.75λ)</td>
<td>0.079</td>
<td>1.00 and 1.15 mm</td>
<td>0.064</td>
<td>-0.015 (19%)</td>
</tr>
<tr>
<td>1.10 mm (.77λ)</td>
<td>0.087</td>
<td>1.00 and 1.20 mm</td>
<td>0.062</td>
<td>-0.025 (29%)</td>
</tr>
<tr>
<td>1.125 mm (.79λ)</td>
<td>0.091</td>
<td>1.05 and 1.20 mm</td>
<td>0.064</td>
<td>-0.027 (30%)</td>
</tr>
</tbody>
</table>
Figure 4.6 Width-to-thickness versus acoustic efficiency measurements for PZT EC69. The favorable zone of 0.65 to 0.85 is marked.

Figure 4.7 Favorable width-to-thickness ratios and element sizes for aperiodic array design. The favorable width-to-thickness zone of 0.65 to 0.85 is marked, as is the favorable zone for aperiodic design of 0.67\(\lambda\) to 1.33\(\lambda\).
Acoustic Measurements

Comparisons of the measured ultrasound fields with the ultrasound fields predicted by the simulations are shown in Figures 4.8 through 4.15 for focal locations of: 3 cm deep center axis (Figure 4.8), 4 cm deep center axis (Figure 4.9), 5 cm deep center axis (Figure 4.10), 5 cm deep and shifted 1 cm towards the array handle (Figure 4.11), 5 cm deep shifted 2 cm towards array handle (Figure 4.12), 5 cm deep and shifted 1 cm towards array tip (Figure 4.13), 5 deep center axis transverse-radial plane (Figure 4.14), and 5 cm deep transverse-axial plane (Figure 4.15). The agreement between the simulations and the actual ultrasound fields was good for these focal locations. The contour plots in Figures 4.8, 4.9 and 4.10 show 10% incremental intensity contours scaled to the maximum intensity.

Table 4.2 shows acoustic power and efficiency measurements for both unfocused and focused ultrasound fields generated by both 62 element arrays: array A (partially cut through 85% of its thickness) (Table 4.2.a) and array B (completely cut) (Table 4.2.b). The focused and unfocused efficiencies of the two arrays were relatively stable, averaging 51% and 42% unfocused and 40% and 41% for a 5 cm deep center focus for arrays A and B, respectively. In each case approximately 100 W of electrical power was the maximum tested power input to the array. The maximum acoustical power capability of this array was not tested, although a similar aperiodic array made from the same piezoelectric material, in a previous study was able to produce 28 W/cm of array length (Hutchinson et al., 1996a), which would roughly translate to 215 W of acoustical power for this array. A representative comparison of the ultrasound fields for the two arrays is shown in Figure 4.16. In this example and others (not shown) measured ultrasound fields for the two arrays were also in close agreement.
Table 4.2.a Acoustic power and efficiency measurements for the 62 element phased array cut 85% of the way through in the thickness dimension (array A). Measurements were made in degassed water using a radiation force technique.

<table>
<thead>
<tr>
<th>Electric Power (W)</th>
<th>Acoustic Power(W)</th>
<th>Efficiency(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unfocused: All elements in phase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.5</td>
<td>1.8</td>
<td>51</td>
</tr>
<tr>
<td>12.6</td>
<td>6.5</td>
<td>52</td>
</tr>
<tr>
<td>28.2</td>
<td>14.7</td>
<td>52</td>
</tr>
<tr>
<td>49.2</td>
<td>24.9</td>
<td>51</td>
</tr>
<tr>
<td>76.5</td>
<td>39.1</td>
<td>51</td>
</tr>
<tr>
<td>108</td>
<td>55.0</td>
<td>51</td>
</tr>
<tr>
<td><strong>Focused: 5 cm deep, center</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.9</td>
<td>1.9</td>
<td>39</td>
</tr>
<tr>
<td>18.0</td>
<td>7.1</td>
<td>39</td>
</tr>
<tr>
<td>39.6</td>
<td>16.0</td>
<td>40</td>
</tr>
<tr>
<td>69.2</td>
<td>28.4</td>
<td>41</td>
</tr>
<tr>
<td>106</td>
<td>42.7</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 4.2.b Acoustic power and efficiency measurements for the 62 element phased array cut 100% of the way through in the thickness dimension (array B). Measurements were made in degassed water using a radiation force technique.

<table>
<thead>
<tr>
<th>Electric Power (W)</th>
<th>Acoustic Power(W)</th>
<th>Efficiency(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unfocused: All elements in phase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.0</td>
<td>7.8</td>
<td>43</td>
</tr>
<tr>
<td>36.6</td>
<td>15.2</td>
<td>42</td>
</tr>
<tr>
<td>54.8</td>
<td>22.8</td>
<td>42</td>
</tr>
<tr>
<td>73.0</td>
<td>30.6</td>
<td>42</td>
</tr>
<tr>
<td>91.6</td>
<td>38.7</td>
<td>42</td>
</tr>
<tr>
<td><strong>Focused: 5 cm deep, center</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17.7</td>
<td>7.5</td>
<td>42</td>
</tr>
<tr>
<td>35.9</td>
<td>15.0</td>
<td>42</td>
</tr>
<tr>
<td>54.8</td>
<td>22.5</td>
<td>41</td>
</tr>
<tr>
<td>72.7</td>
<td>29.6</td>
<td>41</td>
</tr>
<tr>
<td>91.6</td>
<td>36.8</td>
<td>40</td>
</tr>
</tbody>
</table>
Figure 4.8 Measured and simulated ultrasound fields in water from the 62 element aperiodic phased array. Frequency: 1.05 MHz, 3 cm deep center focus.

Figure 4.9 Measured and simulated ultrasound fields in water from the 62 element aperiodic phased array. Frequency: 1.05 MHz, 4 cm deep center focus.
Figure 4.10 Measured and simulated ultrasound fields in water from the 62 element aperiodic phased array. Frequency: 1.05 MHz, 5 cm deep center focus.

Figure 4.11 Measured and simulated ultrasound fields in water from the 62 element aperiodic array. Frequency: 1.05 MHz, 5 cm deep focus shifted 1 cm towards handle.
Figure 4.12 Measured and simulated ultrasound fields in water from the 62 element aperiodic array. Frequency: 1.05 MHz, 5 cm deep focus shifted 2 cm towards handle.

Figure 4.13 Measured and simulated ultrasound fields in water from the 62 element aperiodic array. Frequency: 1.05 MHz, 5 cm deep focus shifted 1 cm towards tip.
Figure 4.14 Measured and simulated ultrasound fields in water from the 62 element aperiodic phased array. Frequency: 1.05 MHz, 5 cm deep center focus.

Figure 4.15 Measured and simulated ultrasound fields in water from the 62 element aperiodic phased array. Frequency: 1.05 MHz, 5 cm deep center focus.
Figure 4.16 Measured ultrasound fields in water from the partially cut and the completely cut (in the thickness dimension) 62 element aperiodic phased arrays. Frequency: 1.05 MHz, 4 cm deep center focus.
Figures 4.17 shows a result from the MRI ex vivo beef heating experiment for a 5 cm deep center axis focus. The dark spot on this subtracted image represents the temperature elevation in the beef in the region of the focus. Using the image information, the position of the foci relative to the transducer was verified to be 5 cm deep and center axis. Based on an MRI temperature elevation estimation algorithm (Chung et al., 1996), the approximate temperature rise at the focus was found to be 10.5 °C after the 10 second sonication at 60 W of electrical power.

Figure 4.17 Phase difference MRI image (axial-radial plane) of a temperature elevation in beef created with a 5 cm deep center focus using the 62 element phased array. The focal location appears as a dark spot located at (0,50) mm. Approximate temperature elevation = 10.5 °C. Image acquisition time = 3.5 seconds.
In Vivo MRI Heating Experiments: Rabbit Thigh Muscle

Since MRI temperature imaging uses a subtraction of a baseline image from an image taken after heating (Chung et al., 1996), any motion that occurs between the time that these two images are taken will result in noise, which could arise from respiratory motion, muscular contractions, or blood flow. Figure 4.18 shows phase difference MRI images in axial-radial planes (perpendicular to the array surface and parallel to the array length) of temperature elevations (dark spots) in rabbit thigh muscle produced by the 62 element phased array during an in vivo MRI experiment. These temperature elevations resulted from 20 second sonications at a power level of 45 W electrical (~18 W acoustical) while electronically focusing at depths of 3, 4, 5 and 6 cm and on the central axis.

Figure 4.18  Central axis focusing, varying depth. Phase difference MRI images (axial-radial plane) of temperature elevations in rabbit thigh muscle generated by the 62 element array. Focus depth: (a) 3, (b) 4, (c) 5, and (d) 6 cm. Approximate temperature elevations are: 9, 12, 19, and 17 °C, respectively. Image acquisition time = 6 seconds. Approximate location of array surface: -4.5 cm radially and -3 to 4.5 cm axially. Electrical input power = 45 W. Sonication time = 20 seconds. Rabbit 3.
While Figure 4.18 demonstrated the ability of the array to heat tissue in vivo at varying radial locations (depths), Figures 4.19 and 4.20 demonstrate the ability of the array to heat tissue at varying axial locations. Figure 4.19 shows phase difference MRI images in transverse-axial planes (parallel to the array surface and 5 cm deep) of temperature elevations in rabbit thigh muscle produced by the 62 element phased array during an in vivo MRI experiment. These temperature elevations resulted from 20 second sonications at a power level of 45 W electrical (~18 W acoustical) while electronically focusing at 5 cm deep and -1, 0, +1, and +2 cm off the central axis. Figure 4.20 shows phase difference MRI images in axial-radial planes (perpendicular to the array surface and parallel to the array length) of temperature elevations in rabbit thigh muscle produced by the 62 element phased array during an in vivo MRI experiment. These temperature elevations...

![Figure 4.19 Off axis focusing, 5 cm depth. Phase difference MRI images (5 cm deep transverse-axial plane - parallel to array surface) of temperature elevations in rabbit thigh muscle generated by the 62 element array. Axial position relative to the central axis: (a) -1, (b) 0, (c) +1, and (d) +2 cm. Approximate temperature elevations are: 8, 18, 12, and 10 °C, respectively. Image acquisition time = 6 seconds. Electrical input power = 45 W. Sonication time = 20 seconds. Rabbit 3.](image-url)
elevations resulted from 20 second sonications with 45 W electrical (~18 W acoustical) while electronically focusing at 5 cm deep and +1, 0, -1, and -3 cm off the central axis. The small heated areas in Figures (a) at (-1.5,-1.5) and (d) at (-2.5,-1), are likely due to air bubbles in the path of the main or grating lobe.

Figure 4.20 Off axis focusing. Phase difference MRI images (axial-radial plane, 5 cm deep) of temperature elevations in rabbit thigh muscle generated by the 62 element array. Axial position: (a) +2, (b) 0, (c) -1, and (d) -3 cm off the center axis. Approximate temperature elevations are: 10, 19, 13, and 5 °C, respectively. Image acquisition time = 6 seconds. Approximate location of array surface: -4.5 cm radially and -3 to 4.5 cm axially. Electrical input power = 45 W. Sonication time = 20 seconds. Rabbit 3.
Figure 4.21 demonstrates the ability of the 62 element phased array to increase the size (axially) of the heated volume by utilizing electronic scanning. This figure shows transverse-axial plane (parallel to the array surface, 5 cm deep) phase difference MRI images of temperature elevations in rabbit thigh muscle for a single focus, a 6 mm wide axial electronic scan (-3 to +3 mm), and a 10 mm wide axial electronic scan (-5 to +5 mm) generated by the 62 element phased array. Because the power level remained constant, the temperature elevation decreased as the scan width increased.

Figure 4.21 Axial electronic scanning of a single focus, 5 cm depth. Phase difference MRI images (5 cm deep transverse-axial plane - parallel to array surface) of temperature elevations in rabbit thigh muscle generated by the 62 element array. (a) single center focus, (b) scan: -3 to +3 mm axially, (c) scan: -5 to +5 mm axially. Approximate temperature elevations are: 18, 10, and 8 °C, respectively. Image acquisition time = 6 seconds. Electrical input power = 45 W. Sonication time = 20 seconds. Rabbit 3.
Figures 4.22 (transverse-axial plane) and 4.23 (axial-radial plane) show 2-D temperature mapping based on phase difference MRI images in the region of the focus. This was for a 5 cm deep center focus and an electrical input power level of 45 W, with sonication occurring from t= 0 to 20 seconds. Images were taken at 6 second intervals.

Figure 4.22 Temporal temperature mapping based on MRI phase difference images (transverse-axial plane) of a temperature elevation in rabbit thigh muscle created with a 5 cm deep center focus using the 62 element array. The temperature contours are 3, 6, 9, 12, and 15 °C. Electrical input power = 45 W. Sonication time = 20 seconds. Rabbit 3.
Figure 4.23 Temporal temperature mapping based on MRI phase difference images (axial-radial plane) of a temperature elevation in rabbit thigh muscle created with a 5 cm deep center focus using the 62 element array. The temperature contours are 3, 6, 9, 12, and 15 °C. Electrical input power = 45 W. Sonication time = 20 seconds. Rabbit 3.
Figure 4.24  Phase difference MRI image (3 cm deep transverse-axial plane - parallel to the array surface) of a temperature elevation in rabbit thigh muscle created with a 3 cm deep center focus using the 62 element array. The focal location appears as a dark spot located at (0,0) mm. Approximate temperature elevation = 12°C. Image acquisition time = 10 seconds. Electrical input power 31 W. Sonication time = 5 minutes 22 seconds. Rabbit 2.

Figures 4.24 and 4.25 show transverse-axial plane phase difference MRI images (planes parallel to the array surface and 3 cm deep) of temperature elevations in rabbit thigh muscle produced by the 62 element phased array during in vivo MRI experiments with longer sonication times to simulate hyperthermia treatments. Figure 4.24 shows a 12°C temperature elevation occurring at 3 minutes during a 5 minute 22 second sonication with 6 minutes and 32 seconds of data collection (40 images, each with 10 second acquisition time) at a power level of 31 W electrical (~12 W acoustical) at a focal location of 3 cm deep and center axis. Figure 4.25 shows a 9°C temperature elevation occurring at 3 minutes during a 5 minute 22 second sonication, with 6 minutes and 32 seconds of data collection (40 images, each with 10 seconds acquisition).
second acquisition time) at a power level of 65 W electrical (~26 W acoustical) for an
electronic scan of the focus at 3 cm deep and -1 to +1 cm off the center axis.

Figure 4.25 Phase difference MRI image (3 cm deep transverse-axial plane parallel to the
array surface) of a temperature elevation in rabbit thigh muscle created with a 3 cm deep
2 cm wide electronic scan (± 1 cm axially) using the 62 element array. The focal location
appears as a dark spot located at (0,0) mm. Approximate temperature elevation = 9 °C.
Image acquisition time = 10 seconds. Electrical input power = 65 W. Sonication time =
5 minutes 22 seconds. Rabbit 2

Figures 4.26 and 4.27 show temperature histories for the maximum temperature and
an additional point outside the focal volume, as determined by MRI thermometry, during in
vivo rabbit thigh muscle heating experiments with longer sonication times to simulate
hyperthermia treatments. Figure 4.26 shows the temperature history for a 4 cm deep center
focus shifted 1 cm off the center axis with a power level of 44 W electrical (~18 W
acoustical). Figure 4.27 shows the temperature history for a 3 cm deep center focus scanned
axially from +1 to -1 cm off the center axis with a power level of 65 W electrical (~26 W
acoustical). In these figures (4.26 and 4.27) the sonication started 10 seconds after the
baseline image, lasted 5 minutes and 22 seconds and was followed by 1 minute of data.
collection for a total data collection time of 6 minutes and 32 seconds (40 images, each with 10 second acquisition time).

Figure 4.26 Temperature vs. time for a 4 cm deep focus shifted 1 cm off the center axis produced in rabbit thigh muscle using the 62 element phased array with MRI guidance and thermometry. Temperatures profiles shown are for the focus (4 cm deep, 1 cm off axis) and for a point off the focus (4 cm deep, 2.5 cm off axis). Image acquisition time = 10 seconds. Rabbit 2.
Figure 4.27 Temperature vs. time for a 3 cm deep focus electronically scanned from +1 to -1 cm off the center axis in rabbit thigh muscle using the 62 element phased array with MRI guidance and thermometry. Temperatures profiles shown are for the scan center (3 cm deep, center axis) and for a point outside the scan volume (3 cm deep, 2 cm off axis). Image acquisition time = 10 seconds. Rabbit 2.

Figures 4.28 and 4.29 show lesions created in rabbit thigh muscle as a result of 20 second sonications at a focal location of 5 cm deep and center axis generated by the 62 element phased array with 96 W (~24 W acoustical) and 109 (~27 W acoustical), respectively. A small second lesion is apparent in Figure 4.29 (b) due to a 5 cm deep 1 cm off axis sonication (20 second, 136 W, ~34 W acoustical). These T2-weighted images were taken approximately 15 minutes after the sonication. The applicator and water bolus can be seen in Figures 4.28 (b) and 4.29 (b). In these experiments (Rabbits 3 and 4) an additional water bag between the water bolus and rabbit thigh was used to act as a spacer (without sacrificing acoustic coupling) so that deep focal positions (up to 6 cm) could be tested.
Figure 4.28 T2 weighted images (a) transverse-axial, (b) radial-axial of a lesion (arrow) created in rabbit thigh muscle with a 5 cm deep center focus generated by the 62 element array. Sonication time = 20 seconds. Electrical input power = 91 W. Approximate temperature elevation = 25°C. Lesion dimensions: 8 x 6 x 4 mm. Rabbit 3.

Figure 4.29 T2 weighted images (a) transverse-axial, (b) radial-axial of a lesion (upper arrow) created in rabbit thigh muscle with a 5 cm deep center focus generated by the 62 element array. Sonication time = 20 seconds. Electrical input power = 109 W. Approximate temperature elevation = 22°C. Lesion dimensions: 7 x 4 x 4 mm. A second small lesion was beginning to form (lower arrow, (b) only) due to another sonication: 5 cm deep, 1 cm off axis, sonication time = 20 second, electrical input power = 136 W. Approximate temperature elevation = 22°C. Rabbit 4.
4.3 Discussion

This study investigated the feasibility of using linear intracavitary ultrasound phased arrays to deliver thermal therapies to the prostate using MRI guidance. Using the grating lobe reduction technique developed earlier (Section 2.1.2) in combination with empirical data which correlated element width-to-thickness ratios and element efficiencies, a 62 element MRI compatible phased array was designed and fabricated. The acoustical performance, MRI compatibility and heating capabilities of the array were tested with both ex vivo and in vivo MRI guided experiments. Using MRI guidance for the ex vivo experiment, it was possible to localize the position of the focus and estimate the temperature elevations achieved during the heating experiments. During the in vivo heating experiments, MRI imaging was used to position the array and applicator correctly relative to anatomical landmarks, to inflate the water bolus to the desired size, to select appropriate focal locations to heat within the rabbit thigh muscle and estimate the resulting temperature elevations.

Based on an aperiodic array design technique developed previously (Section 2.1.2), simulations were performed to yield a range of element widths suitable for array design based on grating lobe levels. A series of acoustic power and efficiency measurements were performed, which resulted in an acceptable range of element widths relative to element thickness. Combination of these two design considerations demonstrated that element width-to-thickness design criterion was more constraining than the aperiodic array design criterion when selecting element widths for phased array design. It should be noted that while the aperiodic array design technique is based theoretical simulation and is material independent, the width-to-thickness design criterion is based on empirical data for the material used in this study and would most likely need to be verified experimentally if other piezoelectrics were to be used.

Measured ultrasound fields generated by the 62 element phased array were in close
agreement with the ultrasound fields predicted by the simulations, verifying the theoretical model used in the numerical simulations. The agreement for the ultrasound fields produced by the completely and partially cut arrays was good. Minor differences in the fields can be explained by the fact that for the partially cut array a previously developed amplifier system (Buchanan and Hynynen, 1994) was used to drive the array and the fields were measured with a thermistor, while for the completely cut array, a newer amplifier system (Daum et al., 1996) was used in conjunction with a hydrophone.

The acoustic efficiency measurements made with the arrays were very consistent over a large range (0 to over 100 W electrical) of power levels, allowing for a relatively high degree of confidence when estimating acoustical power output based on the electrical power input. The slight reduction in array efficiency seen in the focused case relative to the unfocused case (for the partially cut array) can be explained by electrical or mechanical cross coupling which occurs when elements are driven with different phases. It is also possible that post-focus beam divergence may contribute to the reduced efficiency measured for the focused case.

The focused efficiencies were in close agreement for the array cut all the way through and the array cut 85% through, indicating that cutting 85% through the piezoelectric may be sufficient for eliminating mechanical coupling between adjacent elements. The unfocused efficiency was slightly higher (51% as compared to 42%) for the array cut 85% through. One explanation for this may be that the additional 15% of the thickness which remains on the front surface of the array may vibrate synchronously with the two adjacent elements when they are driven in phase.

The array which was cut only 85% of the way through its thickness worked well at low power levels, providing a common ground plane and ensuring flatness of the array. At high power levels, however, the mechanical coupling between adjacent elements resulted in cracking of the remaining 15% of the element thickness. As a result the elements no longer shared a common ground plane and in some instances, the cracks were
uneven. Cracking did not occur until the array was driven at an electrical power of 300 W (about 5 W per channel). Prior to cracking, the maximum power at which the array had been driven was 150 W (about 2.5 W per channel). For arrays which are intended to only be used for hyperthermia, the partially cut design may be worthwhile, but for ultrasound surgery which requires driving the array at high power levels, partially cut arrays may be less reliable. Experimentally, a lesion was created in vivo with an electrical power level of only 91 W, which could have been produced without damaging the partially cut array; however, clinically it may be necessary to use more power especially if electronic scanning is used or lesions at sharp steering are desired, both of which increase the power requirements.

In experiments using the water bolus, problems were occasionally encountered due to formation (cavitation) and trapping of air bubbles within the water bolus. This can occur if the water is not adequately degassed, or if air in the water lines is not completely flushed out during filling of the bolus. The problem that air causes is related to reflection of ultrasound at air-water and air-bolus interfaces which will detract from the focusing capabilities of the array and can result in surface heating adjacent to these interfaces.

Using MRI guidance, it was possible to localize the position of the focus and estimate the temperature elevations achieved during the ex vivo beef heating experiment and the in vivo rabbit thigh muscle heating experiments. Accurate temperature measurement will be necessary if MRI thermometry is to be used for hyperthermia, where temperature measurements to within 1°C are needed; however, for thermal surgery accurate temperature measurement is not as essential, as the therapeutic temperature range is much larger (60-100°C). MRI guidance proved useful during the heating experiments as a means to position the array correctly relative to the rabbit/phantom, to inflate the water bolus to the desired size, and to measure distances from the array to desired focal locations within the rabbit/phantom.

The 62 element aperiodic array was able to produce therapeutic temperature
elevations in vivo over a wide range of focal locations using electronic phase shifting. Therapeutic heating was achieved at focal locations from 3 to 6 cm deep and up to 3 cm off axis. For a given power level, the maximum temperature decreased as the focus was shifted further off axis. This occurs since off axis focusing results in increased grating lobes, and hence less power is deposited in the focal region. The focal region also tends to be larger and not as sharply focused for side focusing which would also contribute to the lower maximum temperature. The maximum temperature was largest for the 5 cm deep focus and decreased for shallower or deeper focal depths. This can be explained by the following reasoning: For an ideal array with $\lambda/2$ element widths, a given power level will result in decreasing temperature elevations as focal depth is increased (see Table 3.1). For a non-ideal array, shallow focal depths will result in end array elements that are at sharp steering angles and hence grating lobes will increase, resulting in lower temperature elevations at shallow focal depths. This second effect, in combination with the fact that sharp steering angles will result in more wave reflection at water-bolus-mylar-tissue interfaces may explain the lower temperature elevations achieved at the 3 and 4 cm focal depths. Axial electronic scanning was shown to increase the axial width of the heated volume and as expected resulted in a lower maximum temperature than the single focus case for a given power level.

The array was capable of generating and maintaining temperature elevations sufficient for the purposes of hyperthermia (>8°C generated, >5°C needed for hyperthermia) in vivo for center axis focusing, off axis focusing and electronic scans at different radial depths. Using MRI thermometry, it was shown that the temperatures in the focal regions were elevated to therapeutic temperatures while points outside of the focal volumes remained at baseline or had non-damaging temperature elevations (<3°C).

In combination with the ex vivo liver lesions created with 57 element array (Chapter 3), the ability of the 62 element array to create lesions in vivo demonstrates the potential of aperiodic linear intracavitary phased arrays to be used for ultrasound surgery.
Using MRI guidance it is possible to use non-damaging temperature elevations to localize appropriate focal locations within a target volume and then use high power sonications to necrose tissue within the target volume.

In conclusion, this work demonstrated the heating capabilities of a transrectal ultrasound phased array for MRI guided prostate thermal therapies. The array designed and constructed in this study demonstrated predictable and sufficient acoustical performance, MRI compatibility, and adequate heating abilities for delivering thermal therapies. These heating capabilities were demonstrated ex vivo and in vivo in an MRI magnet.
5. MRI Feedback Control for Prostate Hyperthermia Treatments with Phased Arrays

5.1 Methods

This study investigated control algorithms designed to be used with non-invasive MRI thermometry. Using batch and on-line methods system parameters were identified in state space form. Control issues relevant to MRI were investigated, including spatial resolution, sampling time, and noise. Acoustic pressure fields used in the parameter estimation and control algorithms were calculated for different focal positions for an ideal linear phased array operating at 1.0 MHz: 120 elements of width 0.75 mm (λ/2 element width), no dead space between elements, with surface dimensions of 90 mm x 15 mm. The numerical simulations used to generate pressure fields and temperature distributions (based on the bio-heat transfer equation) were similar to those described earlier (Sections 2.1.1 and 3.1.1). The acoustic and thermal simulation code was written in FORTRAN and Matlab (Mathworks, Inc., Natick, MA) was used to program the parameter estimation and control algorithms.

5.1.1 System Representation

Prior to parameter identification, the system was represented in state space form. Both batch methods and on-line methods were used to estimate the system parameters, which consisted of two n x n matrices for a total of 2n² unknown parameters. The system had n states: temperature as measured by n sensors (which were also the n system outputs) and n inputs: the power applied to each of n ultrasound power field patterns, each of which was a field focused at the location of one of the n temperature sensors. For most of this study the number of power patterns and sensors were taken to be the same, n, and co-located. For the purposes of parameter identification, data from previous numerical temperature field
simulations were used. The temperature sensors (and foci locations) were located at depths of 2 to 5 cm depth from the array surface and were located axially up to 2 cm from the centerline.

A continuous time representation of the system is as follows:

\[ y = \dot{x} = Ax + Bu \]

where:
- \( x \) is the \((n \times 1)\) state vector, consisting of the \(n\) temperature elevations (i.e. temperature - 37°C, assuming a uniform initial temperature of 37°C) as measured by the sensors;
- \( u \) is the \((n \times 1)\) input vector, consisting of the \(n\) power levels applied to each of the \(n\) input patterns;
- \( A \) is the \((n \times n)\) system response matrix, representing both conduction (coupling) and perfusion terms;
- \( B \) is the \((n \times n)\) system input matrix, representing the amount of power applied by each of the \(n\) power patterns at each of the \(n\) sensors.

The corresponding estimator is:

\[ \hat{y} = \hat{A}x + \hat{B}u \]

### 5.1.2 Off-line Parameter Identification

Because the actual system consists of temperatures which are sampled at discrete, evenly spaced intervals in time, a discrete representation of the system is appropriate. The first approach for system identification was to use the entire time history to estimate the system parameters off-line (assumed time invariant) using a least squares batch method. The discrete time system can be represented in the following form.
\[ y(k) = Fy(k - 1) + Gu(k - 1) \]

where: \( y(k) = \begin{bmatrix} y_1(k) & y_2(k) & \cdots & y_n(k) \end{bmatrix}^T \in \mathbb{R}^{7 \times 1} \) and \( u(k) = \begin{bmatrix} u_1(k) & u_2(k) & \cdots & u_n(k) \end{bmatrix}^T \in \mathbb{R}^{7 \times 1} \)

or

\[ y(k) = \hat{\Theta}^T \phi(k - 1) \]

where \( \hat{\Theta} = \begin{bmatrix} F & G \end{bmatrix}^T \in \mathbb{R}^{2 \times n} \)

and

\[ \phi(k - 1) = \begin{bmatrix} y_1(k - 1) & y_2(k - 1) & \cdots & y_n(k - 1) & u_1(k - 1) & u_2(k - 1) & \cdots & u_n(k - 1) \end{bmatrix}^T \in \mathbb{R}^{2 \times n} \]

The rows of \( \hat{\Theta} \) (i.e. \( \hat{\Theta}_i \)) can be identified individually using a least squares approximation for all \( n \) \((k = 1, \ldots, n)\) data points.

\[ y_i(1) = \hat{\Theta}_i \phi(0) \]

\[ \vdots \]

\[ y_i(k) = \hat{\Theta}_i \phi(k - 1) \]

\[ \vdots \]

\[ y_i(n) = \hat{\Theta}_i \phi(n - 1) \]

which can be rewritten as:

\[ \mathbf{Y}_i = \Phi^T \hat{\Theta}_i \]

where \( \mathbf{Y}_i = \begin{bmatrix} y_i(0) & y_i(1) & \cdots & y_i(n) \end{bmatrix} \)

and \( \Phi^T = \begin{bmatrix} y^T(0); & \cdots; & y^T(n); & u^T(0); & \cdots; & u^T(n) \end{bmatrix} \)

and solving for \( \hat{\Theta}_i \) using a pseudoinverse:

\[ \hat{\Theta}_i = \left( \Phi \Phi^T \right)^{-1} \Phi \mathbf{Y}_i \]

Once all \( \hat{\Theta}_i \) are known, the discrete time system matrix \( \hat{\Theta} \) is determined. After determining the discrete time parameters, the system and input matrices can be converted to continuous time (\( \mathbf{A} \) and \( \mathbf{B} \)) matrices, simulated and compared to the original temperature time history data.
The discrete time system matrix ($\hat{\Theta}$) was converted to the continuous time system and input matrices ($A$ and $B$) using the “[A,B]=d2c(F,G)” command in Matlab. A comparison between the built-in Matlab “d2c” conversion and standard first (and forward first) difference approximations showed similar results.

For both the off-line and on-line parameter estimation algorithms, persistently exciting inputs were used to achieve quick parameter convergence and avoid matrix singularities which would result in non-invertible matrices. The basic idea behind persistent excitation is that if each input is sufficiently different, the relationships between the system outputs and inputs (i.e. the system parameters) are more readily identifiable (Narendra and Annaswamy, 1989). For the simulations performed here, sinusoidal fluctuations in the power level applied to each focus location were used, with each sinusoid having a unique amplitude and frequency. Because the sinusoidal power level at each focal location is different, the effect of each actuator (input focal pattern) on each sensor (temperature sensor) can be determined over time as heating is occurring.

5.1.3 On-line Parameter Identification

A potentially more useful approach for system identification is on-line parameter estimation, which updates the parameter estimates each sampling period, and can potentially be incorporated into on-line control algorithms. Two such recursive on-line algorithms are the recursive least squares algorithm and the projection algorithm, which can be used for systems represented in the Discrete Auto-Regressive Moving Average (DARMA) model form (Goodwin and Sin, 1984). For the purposes of this study, a recursive multivariable least squares algorithm was used as it results in faster convergence than the multi-output projection algorithm. The discrete time system can be represented in the following form (identical to the form used for the off line parameter estimation).
\[ y(k) = Fy(k - 1) + Gu(k - 1) \]

where: \( y(k) = [y_1(k) \ y_2(k) \ldots y_n(k)]^T \in \mathbb{R}^{7 \times 1} \) and \( u(k) = [u_1(k) \ u_2(k) \ldots u_n(k)]^T \in \mathbb{R}^{7 \times 1} \)

or

\[ y(k) = \Phi^T(k - 1) \]

where \( \Phi = [F \ G]^T \in \mathbb{R}^{2 \times n} \)

and

\[ \Phi(k - 1) = [y_1(k - 1) \ y_2(k - 1) \ldots y_n(k - 1) \ u_1(k - 1) \ u_2(k - 1) \ldots u_n(k - 1)]^T \in \mathbb{R}^{2 \times n} \]

The estimated parameter matrix \( \hat{\Theta} \) is updated with a simplified version of the multivariable recursive least squares algorithm (Goodwin and Sin, 1984):

\[
\hat{\Theta}(k) = \hat{\Theta}(k - 1) + \frac{P(k - 2)\Phi(k - 1)}{1 + \Phi(k - 1)^T P(k - 2) \Phi(k - 1)} [y(k)^T - \Phi(k - 1)^T \hat{\Theta}(k - 1)]
\]

\[
P(k - 1) = P(k - 2) - \frac{P(k - 2)\Phi(k - 1)\Phi(k - 1)^T P(k - 2)}{1 + \Phi(k - 1)^T P(k - 2) \Phi(k - 1)}
\]

where \( \hat{\Theta}(0) \) and \( P(-1) \) are given (\( P \in \mathbb{R}^{14 \times 14} \)).

Once \( \hat{\Theta} \) is known, this discrete time system matrix can be converted to continuous time (A and B) matrices, simulated and compared to the original temperature time history data.

5.1.4 Linear Quadratic Regulator Control

A multi-input, multi-output (MIMO) Linear Quadratic Regulator (LQR) controller was implemented using the parameter estimates for the A and B matrices. Matlab was used to implement the control algorithms such that it called temperature simulation code written in FORTRAN. The LQR controller is a form of optimal control which consists of minimizing a quadratic cost function (Kwakernaak and Sivan, 1972):

\[
J = \int_{0}^{\infty} [x'(t)Qx(t) + u'(t)Ru(t)]dt
\]

where \( Q, R \) are selected to be positive semi-definite matrices. Solution of the LQR control problem to find the control input vector, \( u \), requires solving the Riccati equation
\[ u(t) = -Gx(t) \]
\[ G = R^{-1}B'K \]
\[ 0 = -KA - KA'Q + KBR^{-1}B'K \]

where \( K \) is the solution to the Riccati equation. An integrator was used to eliminate steady state error, such that tracking was achieved.

The reference inputs to be tracked consisted of step, ramp and exponential inputs, taking the temperatures from 37 to 42-45°C, with varying rise times.

Originally an adaptive control algorithm with an on-line parameter estimation was considered; however, prior to implementation of an adaptive controller, implementation of the above (LQR) controller was performed to determine whether or not adaptation was
necessary. As will be shown in the results that follow, the LQR controller performed adequately without adaptation. An additional reason for not pursuing an adaptive control algorithm was the fact that often adaptation in the presence of noise can lead to poorer controller performance or even instability.

5.1.5 MRI Control Issues

Because hyperthermia treatments can be delivered non-invasively with intracavitary ultrasound applicators, these treatments could become entirely non-invasive with the use of non-invasive thermometry. MRI is a promising modality for non-invasive monitoring, guidance and control of ultrasound therapies, as it provides good spatial localization, temperature sensitivity in two or three dimensions. MRI offers several advantages over the standard hyperthermia thermometry system of invasive probes on which thermocouples are mounted. MRI is non-invasive, provides 2-D or 3-D temperature information, is more likely not to miss the focus/hot spot, and does not cause artifacts in the ultrasound field (see Figure 5.3).

However, with MRI there are issues which make the feedback control problem an interesting one. With MRI, a large number of temperature measurements in 3-dimensions are available; however, a compromise exists as a larger averaging volume size (decreased spatial resolution) and longer sampling periods result in reduced noise. In this simulation study, resolution for feedback sensors (averaging volume size) and foci was varied from 2 to 10 mm, sampling periods (image acquisition times) ranged from 10 to 120 seconds, and a random error of up to ±1°C was introduced into the feedback temperatures to simulate noise associated with MRI thermometry. For hyperthermia a typical image acquisition time might be 60 seconds (20 seconds per plane X 3 imaging planes), with 5 x 5 x 5 mm averaging volume and ±1°C noise. A recent study indicates that for a 16 mm³ volume, in vivo temperatures can be resolved to within 0.6°C within 10 seconds (MacFall et al., 1996), which is consistent with the MRI temperature monitoring used in this study for ultrasound
surgery (Chapter 4). MRI thermometry for hyperthermia is more difficult than for ultrasound surgery as longer sonication times and smaller temperature elevations allow heat-induced physiologic changes (e.g. vasodilation, edema) more time to influence a smaller signal (i.e. a smaller temperature elevation).

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Non-invasive</td>
<td>Noise, Uncertainty</td>
</tr>
<tr>
<td>No Positioning Errors</td>
<td>Sampling Time</td>
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<tr>
<td>2 &amp; 3-D Temp. Mapping</td>
<td>Averaging Volume</td>
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<tr>
<td>Fast sampling</td>
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<tr>
<td>High Resolution</td>
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<td>Stable</td>
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<tr>
<td>Reliable</td>
<td>Positioning Errors</td>
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<td></td>
<td>1-D Temp. Info.</td>
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</table>

Figure 5.3 Advantages and disadvantages of MRI as a replacement for thermometry involving thermocouples mounted on invasive probes.

It has been shown that the induction of hyperthermic temperature elevations in vivo result in increases in blood perfusion, which has a strong influence on temperature distributions (Song, 1984, Dewhirst, 1988, and Bowman et al., 1991). The magnitude of the perfusion changes, and the time over which these changes occur is quite variable and is likely to depend on many factors such as tissue type, local vasculature, the magnitude and duration of the temperature elevation. In this simulation study, step changes in perfusion resulting in increases by a factor of 2 to 16 or decreases resulting in complete cessation of perfusion, as well as more physiologic responses (based on the above references) such as a tripling of perfusion occurring over the first 10 minutes of heating.
5.2 Results

Sample results from parameter estimation trials are shown in Figures 5.4, 5.5, and 5.6. Figure 5.4 shows a comparison of simulated temperature histories based on the system parameters estimated with the least squares batch method and the original data of temperature histories. The wave-like fluctuations apparent in these temperature histories are reflective of the sinusoidal power variations used to persistently excite the system. The agreement between the original and simulation data is within 0.5°C and is a measure of the accuracy with which the least squares batch method can predict the system parameters and represent the system in state-space form.

Sample results of the on-line parameter estimation are given in Figure 5.5, which shows the estimates of the A and B matrices as a function of time. Each plot in Figure 5.5 shows a row of the A or B matrix (7 parameters per row in this example). In a typical plot, there is one fairly dominant parameter, two smaller but significant parameters and five relatively insignificant parameters. Intuitively this makes sense, as it corresponds to the focus co-located with the sensor being dominant, with the two neighboring foci being significant but smaller, and the remaining 5 foci having relatively little effect as they are further away. In the most cases the dominant parameter can be identified by 10 minutes into the trial. The accuracy of the model obtained with the on-line parameter estimation is represented in Figure 5.6, where the simulated data is compared with the original data. In this case there is a brief instant in the beginning of the trial in which the error is larger than 1°C, followed by errors of less than 1°C. The error is not driven to zero over time as the parameter estimates are updated and improved since a controller is not implemented here which forces the error to zero.
Figure 5.4 Comparison of simulated data based on the parameter estimates obtained with the least squares batch method and the original data for a 7 focus - 7 sensor system.
Figure 5.5 On-line parameter estimates, obtained using the recursive multi-variable least squares method, for the system response matrix (A) and the system input matrix (B) for a 7 focus - 7 sensor system.
Figure 5.6 Comparison of simulated data based on the parameter estimates obtained with the recursive multi-variable squares method and the original data for a 7 focus - 7 sensor system.
The results of a parametric study investigating the effects of focus/sensor (control point) spatial resolution, perfusion variations, thermometry noise, controller sampling time, reference input trajectory structure, focus/sensor (control point) depth, electronic scan (control) width and frequency on the transient and/or steady state temperature responses achieved using 1-D LQR + integral control are shown in Figures 5.7 - 5.19. Unless otherwise stated, the bold contour on the temperature distributions represents the 43°C isothermal line, the outermost contour represents the 38°C isothermal line, and the other contours are incremental 1°C isothermal lines. Unless otherwise stated, the temperature histories are for the points that are being controlled.

Figure 5.7 Comparison of temperature histories for different reference input trajectories. (a). step, (b). ramp to step over 6 minutes, (c). exponential 4*time constant = 6 minutes. Scan parameters: 4 cm deep, 4 cm wide, 9 point control. 60 sec sampling period, perfusion = 1 kg/(m³*sec).

The comparison of different input trajectories shown in Figure 5.7, reveals that the step input resulted in the shortest rise time to 43°C, but the highest overshoot. The exponential input resulted in the smallest overshoot and had shorter rise and settling times than the step input. More data is shown later, which confirms these findings that the exponential reference input resulted in the best overall controller performance for this system.
Figure 5.8  The effects of spatial resolution on transient and steady state temperatures. (a),(e),(i): 2 mm resolution (21 point control). (b),(f),(j): 5 mm resolution (9 point control). (c),(g),(k): 8 mm resolution (6 point control). (d),(h),(l): 10 mm resolution (5 point control). (a)-(d): temperature histories for the control points. (e)-(h): final temperature distributions axial-radial plane - parallel to array length, perpendicular to array surface. (i)-(l): final temperature distributions transverse-radial plane - perpendicular to array length and surface. Scan parameters: 4 cm deep, 4 cm wide. 60 sec sampling period, perfusion: 1 kg/(m^3*sec) doubles at 2500 sec. Reference input: ramp 37 to 43°C over 6 min, then maintenance of 43°C.
Figure 5.8 shows the effects of spatial resolution on the transient and steady state temperature responses. Spatial resolution refers to the distance between foci/sensors/control points, which in MRI could correspond to the averaging volume over which temperatures are estimated. For finer spatial resolution (i.e. more foci/temperature measurements), the temperature was more uniform at the control depth, however there was also more near field heating. For example using 10 mm resolution (5 points over 4 cm width) resulted in a maximum temperature elevation contour of 44°C, while 2 mm resolution resulted in a maximum temperature contour of 46°C.

![Figure 5.8](image)

Figure 5.9 Temperature histories for varying random noise levels simulating noise associated with MRI thermometry. (a). no noise, (b). random noise: ±0.5°C, (c). random noise: ±1.0°C. Scan parameters: 4 cm deep, 4 cm wide, 9 point control. 60 sec sampling period, perfusion = 1 kg/(m^3*sec), reference input: exponential, 4*time constant = 6 minutes.

Often with MRI thermometry, noise is present which increases as the sampling time decreases and the averaging volume decreases (i.e. spatial resolution is increased). To simulate the effects of this noise in the feedback signal, a random noise error was introduced into the temperature feedback. Figure 5.9 shows a comparison of no noise, ±0.5°C noise, and ±1.0°C noise. In each case, the temperatures are controlled to within the noise level (e.g. for ±0.5°C noise, the temperatures track to 43 ± 0.5°C and for ±1.0°C noise, the temperatures
track to $43 \pm 1.0^\circ C$), which is as good as can be expected. The $\pm 1.0^\circ C$ noise case, which has a 60 second sampling time is representative of the noise levels which could be encountered when 3 2-D planes ($16 \times 16$ cm, $256 \times 256$ pixels, $\sim 32 \times 32$ averaging volumes or control points) of data are collected. It is likely that the actual noise levels will not be this high, or alternatively the sampling time will be shorter, especially if 2-D control is used as opposed to 3-D control.

Figure 5.10 Temperature histories for conditions of varying perfusion. (a). perfusion $= 1$ kg/(m$^3$*sec) at $t = 0$ sec, step change to 0 kg/(m$^3$*sec) at $t = 1000$ sec, (b) perfusion $= 1$ kg/(m$^3$*sec) at $t = 0$ sec, step change to 2 kg/(m$^3$*sec) at $t = 500$ sec, step change to 4 kg/(m$^3$*sec) at $t = 1000$ sec, step change to 8 kg/(m$^3$*sec) at $t = 1500$ sec, step change to 16 kg/(m$^3$*sec) at $t = 2000$ sec,(c). perfusion $= 1$ kg/(m$^3$*sec) at $t = 0$ sec, ramp change to 3 kg/(m$^3$*sec) over 0 to 600 sec. Scan parameters: 4 cm deep, 4 cm wide, 9 point control. 30 sec sampling period, reference input: exponential, 4*time constant $= 6$ minutes.

As was mentioned earlier, an adaptive controller was initially considered in the design of an appropriate control algorithm. Figure 5.10 shows the effects of various perfusion changes on the system transient response. Whether the perfusion was abruptly stopped, increased by a factor of as much as 16, or tripled during a ten minute period, the LQR controller was able to compensate for these changes and retrack without adaptation. In addition, it was found that changing the values of the $A$ and $B$ matrix parameter estimates by
as much as a factor of ±1/3, resulted in negligible changes in the system response, providing further evidence that adaptation is unnecessary. The effects of perfusion on temperature overshoot are shown in Figure 5.11. As perfusion increased from 0 to 10 kg/(m³*s) (constant perfusion during each simulation), temperature overshoot decreased from 0.63°C to 0.01°C.

![Figure 5.11](image)

Figure 5.11 Temperature overshoot for various rates of perfusion. Scan parameters: 4 cm deep, 4 cm wide, 9 point control. 30 sec sampling period, reference input: exponential, 4*time constant = 6 minutes.

The effects of sampling time on the transient temperature response are shown graphically in Figure 5.12. As can be seen from these three cases, overshoot and settling time both increase as sampling time increases. The expected sampling times to be used with MRI thermometry may be approximately 20 seconds for a plane of 2D data and 60 seconds for 3D data (3 2D planes). As shown earlier in Chapter 4, image acquisition times of 3.5 to 10 seconds can provide useful temperature information.
Figure 5.12 Temperature histories for varying sampling time. (a). sampling time = 10 sec, (b) sampling time = 60 sec (c). sampling time = 120 sec. Scan parameters: 4 cm deep, 4 cm wide, 9 point control. Reference input: exponential, 4*time constant = 6 minutes. Perfusion = 1 kg/(m³*sec).

Figure 5.13 shows the effects of focal depth on the transient and steady state temperatures. The transient temperature responses indicate that overshoot and settling time both increase with focal depth. The steady state temperature distributions show that near field heating increases as the focal depth is increased. For the 3, 4, and 5 cm focal depths, the respective maximum temperature contours are 43, 44, and 45°C.
Figure 5.13 The effect of focal (control) depth on transient and steady state temperatures. 
(a),(d),(g): 30 mm focal depth (b),(e),(h): 40 mm focal depth. (c),(f),(i): 50 mm focal depth. 
(a)-(c): temperature histories for the control points. (d)-(f): final temperature distributions 
al axial-radial plane - parallel to array length, perpendicular to array surface. 
(g)-(i): final temperature distributions transverse-radial plane - perpendicular to array 
length and surface. Scan parameters: 4 cm wide, 5 mm spatial resolution (9 point 
control), 60 sec sampling period, perfusion: 1 kg/(m^3*sec). Reference input: 
exponential, 4*time constant = 6 minutes.
Figure 5.14 The effect of control (scan) width on transient and steady state temperatures. (a),(f),(k): 1 cm width (b),(g),(l): 2 cm width, (c),(h),(m): 3 cm width, (d),(i),(n): 4 cm width, (e),(j),(o): 5 cm width. (a)-(e): temperature histories for the control points. (f)-(j): final temperature distributions axial-radial plane - parallel to array length, perpendicular to array surface. (k)-(o): final temperature distributions transverse-axial plane - perpendicular to array length and surface. Scan parameters: 4 cm deep, 5 mm spatial resolution (3, 5, 7, 9, 11 point control, respectively), 60 sec sampling period, perfusion: 1 kg/(m^3*sec). Reference input: exponential, 4*time constant = 6 minutes.
The effects of varying the control (scan) axial width are shown in Figure 5.14. As the scan width is increased near field heating increases. For scan widths of 1, 2, 3, 4, and 5 cm, the corresponding maximum temperature contours were 43, 44 (small volume), 44 (larger volume), 45, and 46 °C. As the scan width increased, both the transverse and radial dimensions of the 43°C isothermal contour increased in addition to the axial width. For scan widths of 1, 2, 3, 4, and 5 cm, the approximate maximum dimensions (in mm) of the 43°C isothermal contour were (10 x 6 x12), (20 x 11 x 19), (30 x 14 x 23), (40 x 18 x 25), and (50 x 23 x 26) respectively in the axial (width), transverse, and radial dimensions.

Figure 5.15 The effects of operating frequency on transient and steady state temperatures. (a),(c),(e): 0.5 MHz (b),(d),(f): 1.0 MHz. (a),(b): temperature histories for the control points. (c),(d): final temperature distributions axial-radial plane - parallel to array length, perpendicular to array surface. (e),(f): final temperature distributions transverse-radial plane - perpendicular to array length and surface. Scan parameters: 4 cm deep, 4 cm wide, 5 mm spatial resolution (9 point control), 60 sec sampling period, perfusion: 1 kg/(m^2*sec) doubles at 2500 sec. Reference input: ramp 37 to 43°C over 6 min, then maintenance of 43°C. Note: the 0.5 MHz array consisted of 60 1.5 mm elements for a total length of 9 cm.
While a thorough study investigating the effects of array operating frequency was not conducted, Figure 5.15 shows a comparison between an array operating at 0.5 MHz versus an array operating at 1.0 MHz. The reason for selecting 0.5 MHz was that previous studies proposing the use of intracavitary phased arrays (Buchanan and Hynynen, 1994) have constructed arrays which operated at 0.5 MHz, in contrast to the arrays constructed as part of this thesis which operated closer to 1.0 MHz. From Figure 5.14, it can be seen that lower frequencies will result in smoother transient temperature profiles and steady state temperature distributions than higher frequencies, but also more near field heating.

The previous Figures (5.7 - 5.15) have shown comparisons of individual simulations in a graphical format. These type of figures are intended to qualitatively show trends associated with the parametric study, as well as, provide some quantitative data. The following figures (5.16 - 5.19) provide a more quantitative representation of how various control parameters affect controller performance measures such as overshoot and settling time.

Figure 5.16 shows temperature overshoot as a function of sampling time for step, ramp to step, and exponential reference inputs. As was shown for one example in Figure 5.7, exponential reference inputs resulted in the smallest overshoot, followed by ramps, and then steps. Generally for all three reference inputs, as the sampling time increases the overshoot increases. The exceptions to this observed trend will be discussed in the following section (Section 5.3).

Figure 5.17 shows the settling time to within 5% (0.3°C) of the steady state temperature (43°C) as a function of the controller sampling time for ramp and exponential reference inputs. Ramp inputs resulted in longer settling times than exponential inputs. Increasing sampling time increased settling time for both types of reference inputs.
Figure 5.16  Temperature overshoot as a function of sampling time for step (37 to 43°C at time = 0), ramp to step (37 to 43°C over 6 minutes), and exponential reference inputs (4*time constant = 6 minutes). Scan parameters: 4 cm deep, 4 cm wide, 5 mm spatial resolution (9 point control), 60 sec sampling period, perfusion: 1 kg/(m^3*sec)

Figure 5.17  Settling time to within 0.3°C (5%) of steady state (43°C) as a function of sampling time for ramp to step (37 to 43°C over 6 minutes), and exponential reference inputs (4*time constant = 6 minutes). Scan parameters: 4 cm deep, 4 cm wide, 5 mm spatial resolution (9 point control), 60 sec sampling period, perfusion: 1 kg/(m^3*sec)
Figures 5.18 and 5.19 show that as the time that is taken to heat the control points from the baseline temperature (37°C) to the target temperature (43°C) is increased, the temperature overshoot will decrease, both for ramp to step (Figure 5.18) and exponential (Figure 5.19) reference inputs. This observed trend held true for both the nominal system (no noise, perfusion constant at 1 kg/(m³·sec)) and the robust system (±1°C noise, perfusion = 1 to 3 kg/(m³·sec) over the first 10 minutes). For both ramp and exponential reference inputs, the robust system always had a larger overshoot than the nominal system.

Figure 5.18 Temperature overshoot as a function of ramp time for ramp to step (37 to 43°C) reference inputs, for the nominal (no noise, perfusion = 1 kg/(m³·sec)) and the robust (±1°C noise, perfusion = 1 to 3 kg/(m³·sec) over the first 10 minutes) systems. Scan parameters: 4 cm deep, 4 cm wide, 5 mm spatial resolution (9 point control), 60 sec sampling period.
Figure 5.19 Temperature overshoot as a function of ramp time for exponential (37 to 43°C) reference inputs, for the nominal (no noise, perfusion = 1 kg/(m³*sec)) and the robust (±1°C noise, perfusion = 1 to 3 kg/(m³*sec) over the first 10 minutes) systems. Scan parameters: 4 cm deep, 4 cm wide, 5 mm spatial resolution (9 point control), 60 sec sampling period.

Until this point, all the presented results have dealt with 1-dimensional control, which could be used in conjunction with MRI or a linear invasive probe with multiple thermocouples. The results of Figures 5.20 - 5.22 and Table 5.1 are for 2-dimensional control such as that which can utilize MRI thermometry.

Figure 5.20 shows a comparison of the temperature histories and steady state temperature distributions for a 3 cm wide (axially) electronic scan (1-D, 7 point control, 7 foci/sensors/control points located at 4 cm deep: 0, ±5 mm, ±10 mm, ±15 mm off axis) and a 3 cm wide (axially) by 2 cm deep (radially) electronic scan (2-D, 21 point control, 21 sensors located at 2 cm , 3 cm, and 4 cm deep: 0, ±5 mm, ±10 mm, ±15 mm off axis, 7 foci located at 4 cm deep: 0, ±5 mm, ±10 mm, ±15 mm off axis). For the 1D temperature history, the 2 cm and 3 cm deep temperatures are shown for the purpose of comparison even though they are not being controlled. For the 2D control case, all 21 sensors were used to generate the control inputs for the 7 focal locations. While it would have been relatively straightforward
to utilize 21 foci to match all 21 sensors, the way the figure is currently shown (7 foci, 21 sensors) demonstrates the improvement that can be gained in some instances by simply increasing the number of sensors without changing the number of foci. The maximum temperature (on the temperature histories) was 44.4°C for the 2D control case and 45.5°C for the 1D control case. The maximum temperature contour (on the steady state temperature distributions) was 44°C for the 2D control case and 45°C for the 1D control case. In the 1D control case, both the transient and steady state peak temperatures occurred at depths that were not being controlled.

Figure 5.21 shows a comparison of the temperature histories and steady state temperature distributions for a 1 cm wide (axially) electronic scan (1-D, 3 point control, 3 foci/control points located at 4 cm deep: 0 and ±5 mm off axis) and a 1 cm wide (axially) by 2 cm deep (radially) electronic scan (2-D, 15 point control, 15 foci/sensors/control points located at 2, 2.5, 3, 3.5, and 4 cm deep: 0 and ±5 mm off axis). For the 1D temperature history, the 2, 2.5, 3, and 3.5 cm deep temperatures are shown for the purpose of comparison even though they are not being controlled. For the 2D control case, having the sensors located on a grid with 5 mm between each sensor in both the axial and radial dimensions approximated a 5 x 5 x 5 mm MRI averaging volume which is a reasonable resolution for the MRI thermometry. In contrast to Figure 5.20, which shows the ability of 2D control to reduce potentially undesirable near field heating, Figure 5.21 shows the ability of 2D control to increase potentially desirable near field heating. Using 1D control with a 1 cm scan width, the 43°C contour is small and irregularly shaped, but with 2D control, the size of the 43°C contour can be enlarged and the shape can be made more uniform in two dimensions.
Figure 5.20 Comparison of 2D (21 point) control versus 1D (7 point) control. (a),(b): 2D control, 21 sensors/control points: 2, 3, and 4 cm deep, 0, ±5, ±10, and ±15 mm off axis, 7 foci: 4 cm deep, 0, ±5, ±10, and ±15 mm off axis. (c),(d): 1 D control, 7 sensors/foci/control points: 4 cm deep, 0, ±5, ±10, and ±15 mm off axis. Note in (c), temperatures are also shown at 2 and 3 cm deep, 0, ±5, ±10, and ±15 mm off axis for comparison purposes. (a),(c): temperature histories. (b),(d): final temperature distributions axial-radial plane - parallel to array length, perpendicular to array surface. Scan parameters: 60 sec sampling period, perfusion = 1 to 3 kg/(m³·sec) over the first 10 minutes. Reference input: exponential, 4*time constant = 6 minutes.
Figure 5.21 Comparison of 2D (15 point) versus 1D (3 point) control. (a),(b): 2D control, 15 foci/sensors/control points: 2, 2.5, 3, 3.5, and 4 cm deep, 0, ±5 mm off axis. (c),(d): 1D control, 3 sensors/foci/control points: 4 cm deep, 0, ±5 mm off axis. Note in (c), temperatures are also shown at 2, 2.5, 3, and 3.5 cm deep, 0, ±5 mm off axis for comparison purposes. (a),(c): temperature histories. (b),(d): final temperature distributions axial-radial plane - parallel to array length, perpendicular to array surface. Scan parameters: 60 sec sampling period, perfusion = 1 to 3 kg/ (m²*sec) over the first 10 minutes. Reference input: exponential, 4*time constant = 6 minutes.
Figure 5.22. High temperature hyperthermia. 2D control: 15 foci/sensors/control points: 2, 2.5, 3, 3.5, and 4 cm deep, 0, ±5 mm off axis. (a): temperature history. (b): final temperature distribution axial-radial plane - parallel to array length, perpendicular to array surface. Scan parameters: 60 sec sampling period, perfusion = 1 to 3 kg/(m^3*sec) over the first 10 minutes. Reference input: exponential, 4*time constant = 6 minutes. The bold contour is 46 °C isothermal line.

Figure 5.22 shows a high temperature hyperthermia simulation in which, the target steady state temperature is set to 46 °C instead of 43 °C. Two dimensional control was used, with control points spaced every 5 mm in the axial and radial dimensions, approximating an MRI 5 x 5 x 5 mm averaging volume.

Table 5.1 shows a summary of 1 and 2 cm wide (axially) by 2 cm deep (radially) 2-D electronic scans. Control points (foci/sensors) were located on a grid from 2 to 4 cm radial depth, and from -1 to +1 cm off the center axis, with a spacing of 5 mm axially and 5 or 10 mm radially. Depending on the spacing between foci (control points), the desired temperature trajectories and the perfusion rate, in some cases, the steady state power levels (weighting factors) selected by the controller were set to zero for some of the focal locations. In general, the temperature gradients in the axial dimension were larger than in the radial dimension, allowing for closer spaced foci axially with non-zero power levels. As shown in
Figure 5.20, 2-D control can yield better results than 1-D control even when some control points are used only as sensors, but not as foci.

Table 5.1 2-D controlled electronic scans. Radial heating depth: 2 to 4 cm.

<table>
<thead>
<tr>
<th>Scan Width (mm)</th>
<th>Axial Spacing (mm)</th>
<th>Radial Spacing (mm)</th>
<th>Perfusion (kg/m^3*s)</th>
<th>Desired Temperature</th>
<th># foci powered of total # foci</th>
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5.3 Discussion

This study investigated the use of an LQR control algorithm for simulated prostate hyperthermia treatments in which MRI is used to provide non-invasive temperature feedback. On-line and off-line parameter identification algorithms were used to estimate unknown system parameters, while representing the system in state space form. A parametric study investigating the effects of control point spatial resolution, control width, control depth, perfusion variations, feedback noise, sampling time, reference input trajectory structure, and array operating frequency on the transient responses and steady state temperature
distributions. Although this parametric study was performed for 1-D control and could be applicable to either MRI or invasive probe thermometry systems, issues most relevant to MRI thermometry such as sampling time, feedback thermometry noise and spatial resolution were investigated. The benefits of using 2-D control information, such as that which is available with MRI thermometry, were demonstrated when compared with similar 1-D control cases. With 2-D control it is possible to either reduce or increase near field heating such that the size and shape of the heated volume is controlled in both the radial and axial dimensions.

Previous hyperthermia controls studies have proposed an initial parameter identification phase, in which one at a time, each focal pattern is powered while the effects of each pattern on each sensor are determined (Hartov, 1993, and VanBaren et al., 1995). This method is used to identify the system input matrix (B), but cannot identify the system response matrix (A) and furthermore assumes the system is decoupled (i.e. the system response matrix is diagonal). The validity of this method is questionable, especially if this system is not decoupled (e.g. when the control points are relatively close together), but may serve as a useful initial estimate for the system input matrix (B). Using persistent excitation to identify the system parameters is advantageous in that the system is not assumed to be decoupled and the identification can be performed during the actual heating process, which lends itself to adaptive parameter estimation algorithms. The experimental or clinical use of persistently exciting inputs, such as sinusoidal power levels with an independent amplitude and frequency (of oscillation of the power level) for each focal location, demands a more sophisticated amplifier system (such as the one currently used: Daum et al., 1996) and controlling software than would be needed for simply shutting on and off individual power patterns in an initial parameter identification trial.

The controller performed robustly in the presence of large physiologic parameter changes (e.g. perfusion increases by a factor of 16) and errors in parameter estimation (e.g. ± 33%) without adaptation. Hence, implementation of the on-line (adaptive) parameter
estimation algorithm is probably not necessary and could even result in instability due to noise. Instead, a treatment could include a ten minute pre-treatment parameter identification phase, during which a batch (off-line) algorithm could be used to get parameter estimates. After this initial identification phase, the controller could be used throughout the treatment, and only if tracking was lost would it be necessary to update parameter estimates.

Using hyperthermia feedback control simulations, it was possible to evaluate the effects of both control parameters (e.g. sampling time, spatial resolution, feedback noise, reference input structure) and parameters associated with the heating process (e.g. perfusion, scan width, scan depth, frequency). Using exponential reference inputs resulted in the smallest overshoot and settling time, when compared to ramp and step reference inputs. For both ramp and exponential reference inputs, as more time was taken to rise from baseline to 43°C, overshoot decreased, and with addition of noise overshoot increased by approximately the noise level. Increased sampling time (i.e. decrease sampling frequency) resulted in increased overshoot, although at large sampling times, this trend was not as predictable for ramp and exponential inputs since it is possible to have a longer sampling time, yet sample such that it coincides more appropriately with power on/power off times. This up and down shape on the ramp and exponential sampling time curves, is a function of the rise time used for the ramp and step inputs. For the step input, there is an inherent amount of overshoot that will occur by trying to instantaneously bring the system from baseline to 43°C, and this explains the flatness of the step overshoot curve for short sampling times. The linear shape to the step overshoot versus sampling time curve, for long sampling times, is due to the power being on and temperature rising until the second sample (first controller update) is performed.

As perfusion increased, temperature overshoot decreased since perfusion acts as a heat sink. Because negative power or actively controlled cooling is not physically possible, increased perfusion can actually be advantageous in that shutting off power will have a greater cooling effect.
Both increasing the width or increasing the depth of the electronic scan (and the corresponding control width or depth), resulted in increased near field heating. More near field heating was expected when the scan width increased since the geometric gain of the array relative to the target volume is decreased. Increased near field heating was also expected to accompany increased scan depth, since the ultrasound must pass through more tissue to reach the focal depth, resulting in more attenuation, which requires more total power deposition to achieve the target temperatures at the target depth, and hence will result in more near field heating.

The effects of varying spatial resolution show that the 5 mm spacing between temperature measurements, which would be a typical averaging volume for MRI thermometry, did not produce inferior temperature distributions relative to 2 mm spacing and actually slightly reduced near field heating. Further increasing the spacing resulted in less near field heating, although temperature uniformity at the control depth was sacrificed.

The smoother profiles and distributions associated with the lower frequency is due to the fact that lower frequencies are not as sharply focused. Because lower frequency foci are not as sharply focused and the absorption of power is halved when using 0.5 MHz instead of 1.0 MHz, more power must be used to achieve the same temperature elevations, which explains why more near field heating is seen with lower frequencies. To verify that more power was actually required for the lower frequency case, the total acoustic power at steady state was compared. For the 0.5 MHz and 1.0 MHz arrays, the respective total acoustic power levels were: 12.7 and 5.7 W respectively, both of which are easily achievable given the acoustic power measurements presented earlier (Section 4.3).

The benefits of using 2-D control information, such as that which is available with MRI thermometry, were shown by comparing the transient responses and steady state fields for similar 1-D control and 2-D control cases. For a relatively wide scan (control) width (3 cm), it was possible to reduce near field heating both transiently and in the steady state by using sensor information from multiple depths, without using additional input power patterns
at these focal depths. This additional control which resulted in less near field heating could be the difference between a patient having pain or not having pain. For a narrower scan (control) width (1 cm), it was possible to tailor the size and shape of the heated volume in both the radial and axial dimensions by using additional foci (sensors) at multiple depths, located on a grid with 5 mm in both directions, as would be available with MRI thermometry. Based on the information in Table 5.1, it was shown that for 1 cm wide electronic scans, complete 2-D control could be achieved with grid spacing of 5 mm axially and 10 mm radially. By “complete” control, it is meant that non-zero power was deposited at every focal location regardless of perfusion levels. It should be noted that in any 2-D control case where the number of foci powered is greater than the number of foci that would be used for 1-D control (e.g. 3 foci for 1 cm, 5 foci for 2 cm, and 7 foci for 3 cm), it is advantageous to use 2-D rather than 1-D control. For every 2-D case presented, more than the minimum (1-D) number of foci were powered, indicating that 2-D control was always able to make use of additional information and use it to improve the temperature distributions with additional power patterns.

High temperature hyperthermia simulations results were shown for the 1 cm wide scans, which consisted of heating the target volume to 46 - 47°C instead of 43 - 44°C. Delivering 30 equivalent minutes at 43°C is a good treatment goal, as recent clinical hyperthermia treatments have set goals of > 42°C for 45 minutes (Formenti et al., 1996). To achieve 30 equivalent minutes at 43°C, it is only necessary to heat at 46°C for 3.75 minutes or at 47°C for 1.9 minutes, based on the Sapareto and Dewey thermal dose equation (Sapareto and Dewey, 1990). One factor which is relevant to the success of the proposed high temperature hyperthermia is patient pain. Typically pain sensors are activated near 45°C, however, the prostate is poorly innervated and clinical studies suggest that temperatures above 45°C may be tolerated by some patients (Fosmire et al., 1993). With the use of appropriate anesthesia, it may be possible to use high temperature hyperthermia on all patients.
High temperature hyperthermia may be the most promising method for heating the prostate in a reasonable amount of time. An approximate volume for a cancerous prostate is 40 cm³, although larger volume are possible (Kimura et al., 1986 reported 28 cm³, n=51, stage B (n=21), C (n=7) or D (n=21); Fosmire et al., 1993 reported 44 cm³, n=14, stage C or D). Based on the simulations, it appears that by using a phased array with feedback control it is possible to deliver an acceptable therapeutic dose to a relatively small volume (~1 x 1 x 2 cm) in a relatively short period of time (~5 minutes at 46°C or ~3 minutes at 47°C, including warm-up time), while controlling the entire heating process in two dimensions. Assuming a prostate volume of 40 cm³ and a target volume of 2 cm³ per sonication, it would take 20 sonications to heat the entire gland. If the target volume was controlled to 46°C, the entire treatment would take approximately (5 minutes/sonication)*(20 sonications) = 100 minutes. If the target volume was controlled to 47°C, the entire treatment would take approximately (3 minutes /sonication)*(20 sonications) = 60 minutes.

The alternative to multiple high temperature hyperthermia sonications, is heating of a larger volume by using a single (or a few) axial scan(s) of larger width. With a wider scan, active heating at all focal locations would not be used by the controller; however, 2-D control could still be used to minimize near field heating. For the purposes of comparison, a 4 cm wide axial (1-D control) scan controlled to 43°C delivers a therapeutic treatment to an 8 cm³ target volume in 30 minutes (+~5 minutes warm up), yielding a total treatment time (for a 40 cm³ prostate) of (35 minutes/sonication)*(5 sonications) = 175 minutes. It may be possible to use temperatures higher than 43°C with a 4 cm wide axial scan; however, the wider the scan, the less 2-D control can be utilized, which could potentially lead to uneven heating of the treatment volume, with transient or steady state temperature spikes in the near field.

Using sampling times (20 - 60 seconds) and noise levels (up to ±1°C) representative of those which would be encountered using an appropriate MRI averaging volume (about 5 x 5 x 5 mm), the performance of the LQR + integral control algorithm performed acceptably.
both in the transient response (in terms of overshoot and settling time) and in the steady state
temperature distributions by using 2-D control, such as that which would be available while
using MRI thermometry. In combination with the 62 element MRI compatible phased array
(Chapter 4), the control algorithms presented here show promise for use with MRI controlled
prostate hyperthermia treatments.
6. Conclusions and Recommendations for Further Study

6.1 Conclusions

There are two major limitations associated with the current clinical heating devices used for prostate thermal therapies. The first is that nonfocused ultrasound arrays allow for power control in the axial and angular dimension but not in the radial (or depth) dimension. The second limitation is associated with the current clinical thermometry systems used to monitor the heating process, which typically use thermocouples mounted on probes. These thermometry systems are invasive and do not provide enough information on the complete temperature field. By using phased arrays in combination with MRI guidance and thermometry, it is possible to achieve increased power control in the radial dimension while obtaining complete 2-D or 3-D temperature information. It is this reasoning that justified the work performed in this thesis.

This study has been concerned with the investigation of ultrasound intracavitary phased arrays for thermal therapies. In particular, the use of transrectal phased arrays for delivering thermal therapies to the prostate was studied. In this study, acoustic and thermal numerical simulations were performed, and based on these simulations, experimental phased arrays were constructed. The MRI compatibility, acoustic and heating capabilities of these arrays were tested using acoustic power and efficiency measurements, ultrasound field measurements and MRI monitored ex vivo and in vivo heating experiments.

This study introduced a new method of reducing grating lobes using optimized random distributions of unequal element widths. This technique allows for the reduction of peak grating lobe levels and/or increases in average element width, without sacrificing power emitting surface area. This array design was implemented in a 16 element test array, a 57 element experimental array, and a 62 element intracavitary experimental array. Each
of these arrays performed as predicted, in that good agreement with theoretical field distributions was achieved and adequate acoustic power output for thermal therapies was realized.

A theoretical study was performed which proposed the use of linear intracavitary ultrasound phased arrays for thermal surgery of the prostate. The ability of phased arrays to significantly enlarge the necrosed tissue volume by electronic scanning was established, as was the ability to produce more uniform temperature and dose distributions by optimizing scan weighting factors. The ability of phased arrays to enlarge the size of the necrosed tissue volume is potentially a means to reduce total treatment time by reducing the number of required sonications to necrose a given volume of tissue.

The heating capabilities of aperiodic linear phased arrays were verified experimentally for the purposes of hyperthermia and ultrasound surgery. Ex vivo perfused kidney and in vivo muscle experiments were performed demonstrating the ability of these arrays to produce sufficient temperature elevations for hyperthermia for both single focus cases and electronic scanning. A likely hyperthermia treatment strategy to treat the entire prostate gland would be to use 2 - 3 electronic scans each with an axial width 2 - 4 cm depending on the anterior-posterior dimension of the prostate being treated, and then repeat this process once after rotating the array in the angular dimension to cover the entire lateral expanse of the prostate. This rotation would be necessary due to the flat geometry of the array. The potential for these arrays to be used for ultrasound surgery was demonstrated by creating necrosed tissue lesions in ex vivo beef liver using a single focus and electronic scans and by creating lesions in in vivo muscle using a single focus. In vivo lesions created with electronic scans may be achievable; however, to avoid risking array damage this was not attempted. Ultrasound surgery could be used to treat a very localized tumor within the prostate, to debulk portions of a large prostatic tumor, or to remove urethral constriction in BPH by necrosing the tissue surrounding the urethra. Multiple sonications with a single focus could be used for these treatments, although if the
clinical array is capable of necrosing tissue with electronic scans, this could potentially reduce the treatment times.

Using the 62 element phased array, MRI compatibility was demonstrated with both ex vivo and in vivo experiments. Using MRI thermometry, the array was shown to be capable of producing therapeutic temperature elevations for varying axial and radial locations and with electronic scans. This demonstrates the advantage that phased arrays have over nonfocused arrays, in that they are capable of controlling heating in two dimensions.

To further improve the transient and steady state temperature distributions achieved during hyperthermia treatments, noninvasive MRI thermometry for temperature feedback control was investigated using simulations. Using worst case estimates for sampling times and noise representative of those which could be encountered using a MRI, the LQR control algorithm performed acceptably both in the transient response (in terms of overshoot and settling time) and in the steady state temperature distributions. By using 2-D control, such as that which would be available while using a single plane of MRI thermometry data, it was shown that both the transient and steady state temperatures could be improved relative to those achievable with 1-D control, such as that which could be available with invasive probe thermometry. In combination with the 62 element MRI compatible phased array, the control algorithms presented here show promise for use with MRI controlled prostate hyperthermia treatments.

6.2 Recommendations for Further Study

It may be possible to further improve the power and focusing capabilities of intracavitary phased arrays with the development of piezoelectrics with improved acoustic properties. Recently developed piezocomposites have shown promising acoustic power potential for therapeutic purposes (Imasonic, Inc., France). By using piezocomposites, the secondary (longitudinal and transverse) modes of vibration are greatly reduced, eliminating
the concern of certain width-to-thickness ratios yielding poor efficiencies. Since width-to-thickness ratios would no longer be a concern it might be possible to use smaller elements (e.g. \(\lambda/2\) width) with adequate power capabilities to achieve superior focusing performance. Using smaller elements is not without disadvantages, as it would be necessary to use more elements to cover the same surface area, which would require more amplifier channels. With smaller elements, making soldered connections to the elements would become more difficult and it is likely that a new method for making electrical connections would be needed. Another disadvantage of having more elements is that more wiring would be required, which could require using a flexible circuit board, and a custom made coaxial cable bundle, since the 62 element array currently uses all of the available space within the lumen of the applicator.

While this study has investigated and suggested methods for treatment of prostatic diseases with thermal therapies, the optimal way to treat the prostate has not been studied. Using methods similar to those done for other treatment volumes (Fan and Hynynen, 1996, Fan and Hynynen, 1996b, and Wan et al., 1996), the ideal method of treating the prostate could be investigated using intracavitary phased arrays. Methods such as single focusing with multiple sonications, electronic scans (single or multiple, possibly with feedback control), or simultaneous multiple foci (single or electronically switched) may yield significantly different thermal dose distributions and required cooling times between sonications could make some methods more time intensive than others.

As MRI temperature calibration continues to improve, practical implementation of the LQR control algorithms with intracavitary phased arrays is becoming feasible. This will require appropriate interfacing the phased array, MRI scanner, and a controlling computer. While the LQR control algorithms worked well in the simulations presented in this study, these will need to be verified or potentially modified experimentally in MRI controlled ex vivo and in vivo experimentation.
References


