DEVELOPMENT OF PROTOTYPE PHASED ARRAY ULTRASOUND SYSTEMS FOR HYPERTHERMIA AND TARGETED DRUG DELIVERY

Don Chorman and Robert J. McGough
Dept. of Electrical and Computer Engineering, Michigan State University, East Lansing, Michigan, USA, 48824

1. INTRODUCTION

Thermal therapy utilizes heat to kill malignant cancer cells. Thermal therapies generally fit into one of two general categories, namely 1) moderate temperature hyperthermia or 2) high temperature thermal ablation [1]. Moderate temperature hyperthermia is characterized by the use of elevated temperatures in the range of 42-45 degrees Celsius, with treatment times of 15-60 minutes [1]. Moderate temperature hyperthermia produces cytotoxic effects in malignant tissue when used in multiple treatments. High temperature thermal ablation is characterized by the use of temperatures greater than 60 degrees Celsius, with treatment times of 4-6 minutes [1].

Two modalities that can be utilized to noninvasively generate moderate temperature hyperthermia in malignant tissue are ultrasound (US) and radiofrequency (RF) electromagnetic radiation. High power phased array ultrasound systems can be used to generate and direct both moderate temperature hyperthermia and high temperature thermal ablation.

In addition to creating hyperthermic effects, high intensity US can also generate cavitation induced cellular lysis that is useful for destroying malignant tissue [2, 3]. The effects of hyperthermia and cavitation can also be utilized as activation mechanisms in targeted drug delivery [4, 5]. Targeted drug delivery is a noninvasive form of treatment, which results in drug activation that is limited to a prescribed region of the body for a controlled amount of time.

The phased array ultrasound systems described in this research usually consist of five components: (1) an array of ultrasound transducers, (2) electrical interconnects (3) resonant filters, (4) driving electronics, and (5) computer control software. The ultrasound prototype applicators described in this paper are 1D arrays constructed from Lead Zirconate Titanate (PZT) elements. The electrical interconnect serves as the electrical connection for the filtered output of the power electronics. The resonant filters pass only the fundamental frequency component in the square-wave output of the power electronics. The resonant filters also provide a voltage gain 3-10 times the input voltage. The driving electronics consist of a digital signal generator and Class-D power amplifiers. The digital signal generator boards utilize field programmable gate arrays to generate low-level (0-3.3V) frequency and phasing signals. Class-D power amplifiers amplify these low-level signals. A personal computer is interfaced with the power electronics to control the frequency, phase, and mode of operation. Through software control, either continous-wave (CW) or pulsed output signals are produced by the driving electronics.

Commercially available, custom built high power ultrasound arrays and the associated power electronics for use with hyperthermia are expensive and inflexible when considering operational characteristics such as the number of transducers, number of electrical channels, frequency of operation, modes of operation, and phasing. These issues motivate this research, which generates robust and operationally flexible phased array ultrasound systems that are cost-effective for thermal therapy applications.

2. METHODS

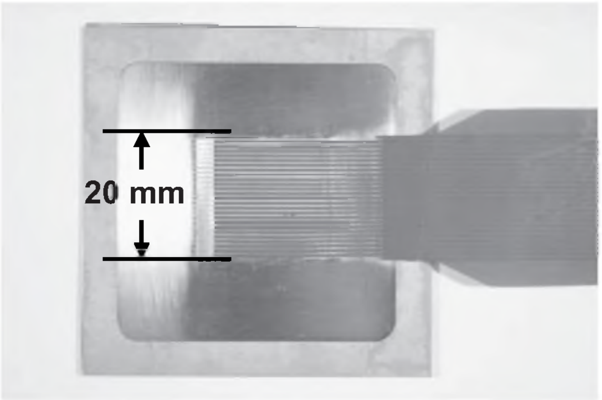

Fig. 1: 1D ultrasound array with a flex circuit interconnect.

2.1 Ultrasound Array and Electrical Interconnect

The one-dimensional prototype ultrasound arrays were constructed from PZT (Navy Type III) and double-sided copper-clad Pyralux baffles. For a single array, a PZT plate was bonded to a baffle and a flexible interconnect circuit was bonded to the top of the PZT plate. A completed array is shown below in Figure 1.

The adhesive used for bonding was Cho-Bond 584 silver electrically conductive epoxy. After curing the epoxy bonds, a wafer-dicing saw was used to cut the PZT plate into individual elements, forming a 1D ultrasound phased array with an attached electrical interconnect. The flex circuit interconnect was made of single-sided copper-clad Pyralux. The interconnect circuit was designed using Orcad Capture and Layout software.

2.2 Resonant Filters

The resonant filters were comprised of capacitors and hand-wound toroidal inductors. These form a low-pass filter that has the same electrical resonant frequency as the elements in the array.

2.3 Driving Electronics

The digital signal generator boards use XILINX Spartan field programmable gate arrays to generate low-level (0-3.3V) frequency and phasing signals. These boards were programmed using the XILINX ISE Webpack software. The digital signal generator operates in continuous-wave or pulsed mode with a frequency Range of 50kHz-20MHz. The phase resolution at 1MHz is 0.6 degrees. This design can be expanded to synthesize 1024 channel signals. The Class-D power amplifiers are from a previous research project. The amplifiers are capable of driving 20 watts per channel, with a frequency range of 500-1000 kHz.

2.4 Computer Control

A personal computer controls the digital signal generator through a Matlab interface. A simple script adjusts the frequency, phase, and mode (CW or pulsed) of operation.

3. RESULTS

The system was tested after the ultrasound phased array was mounted in a water tank. The computer-controlled power electronics steer a focus at specified locations within the tank. The resulting focal patterns were mapped using a computer controlled positioning system and a hydrophone. The hydrophone was traced through a rectilinear grid, measuring the pressure generated by the ultrasound. Figures 2 and 3 show two experimentally measured pressure fields.

4. DISCUSSION

The experimentally measured pressure fields demonstrate that the 1D ultrasound phased array is capable of generating and steering a focus within a water tank. The shape of the measured field in the direction of the array sampling is similar to the results obtained from computer simulations; however, measurements and simulations are dissimilar along the long axis of the array elements. This suggests that the particle velocity is not uniform across each active element, so more detailed computer models are required. This is confirmed in comparisons of simulations and measurements of single element pressure fields.

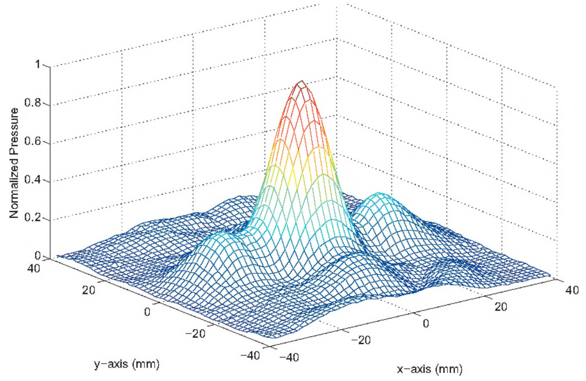

Fig. 2: Normalized pressure field generated by the 22-element 1D array shown in Figure 1. This array, which operates at 971.5kHz, is focused on-axis at [0, 0, 304.8] (mm).

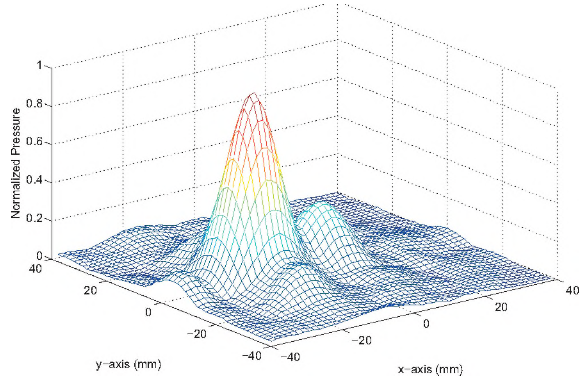

Fig. 3. Normalized pressure fields generated by the 22-element 1D array shown in Figure 1. This array, which operates at 971.5kHz, is steered off-axis with a focus located at [-15, 0, 304.8] (mm).

5. REFERENCES

1) P.R. Stauffer, S.N. Goldberg. Introduction: Thermal Ablation Therapy, *International Journal of Hyperthermia*, 2004; 20(7): 671-677

2) B.C. Tran, Seo Jongbum, T.L. Hall, J.B. Fowlkes, and C.A. Cain. Microbubble enhanced cavitation for noninvasive ultrasound surgery. *IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control*, October 2003; 50(10): 1296-1304

3) F.J. Fry, N.T. Sanghvi, R.S. Foster, R. Bihrle, and C. Hennige. Ultrasound and microbubbles – Their generation, detection, and potential utilization. *Ultrasound in Medicine and Biology*, 1995; 21(5): 1227-1237

4) Neru Munshia, Natalya Rapoportb and William G. Pitt. Ultrasonic activated drug delivery from Pluronic P-105 micelles. *Cancer Letters*, September 1997; 118(1):13-19

5) Jared L. Nelson, Beverly L. Roeder, John C. Carmen, Friederike Roloff and William G. Pitt, Ultrasonically Activated Chemotherapeutic Drug Delivery in a Rat Model. *Cancer Research*, December 2002; 62: 7280–7283

ACKNOWLEDGEMENTS

The authors would like to thank F. Foust from the Department of Electrical and Computer Engineering at Michigan State University. This work was supported in part by NIH R01CA093669.