32nd URSI GASS, Montreal, 19-26 August 2017

Numerical Study of Contrast-Enhanced Focused Microwave Thermal Therapy

John P. Stang*(1), Susan Love (2), and Mahta Moghaddam(1)
(1) University of Southern California, Los Angeles, CA, 90089, mixil.usc.edu
(2) Dr. Susan Love Research Foundation, Encino, CA, 91436, www.drsusanloveresearch.org

Abstract
A numerical study of contrast-enhanced focused microwave thermal therapy has been undertaken. Using a numerical breast phantom in a focused microwave therapy cavity containing a 24 antenna array, targeted heating using time-reversal focusing [1] was applied to a region surrounding a tumor-cell-containing branch of the breast duct network. The specific absorption rate throughout the volume was calculated and compared for two cases: (1) microwave focusing alone and (2) microwave focusing with saline contrast agent. Results from this test showed greater than an order of magnitude improvement in microwave absorption and improved selectivity in thermal dose between tumor and healthy tissue.

1. Introduction
Thermal therapies–which include thermal ablation, hyperthermia, and heat activated drug delivery–have seen increasing clinical use in the treatment of cancer and other diseases. In the various ablation methods, which include microwave, RF, cryoablation, and high intensity focused ultrasound (HIFU), either significantly elevated temperatures (typically above 50 °C) or freezing temperatures generated by liquid nitrogen are used to cause very rapid and localized tissue destruction. In the case of hyperthermia, moderately elevated temperatures (typically between 40–45°C and delivered regionally) have been shown to achieve cytotoxic effects that render cancer cells more vulnerable to radiotherapy [2] and chemotherapy [3], as well as inducing both apoptotic and necrotic cell death given a sufficient thermal dose [4-6].

For the methods that use elevated temperatures to achieve therapeutic effect, the primary difference between the electromagnetic (RF and microwave) and ultrasound (HIFU) systems is in the size of the treatment zone. In the case of RF and microwave, the controllable heating zone is on the order of centimeters, while the focal spot size for HIFU is typically in millimeters. While this leads to HIFU offering finer targeting, treatment times are often much longer as the focal spot must be swept over the region until full coverage is achieved. In addition, whereas HIFU systems are able to deliver heat transcutaneously, current microwave systems used clinically to deliver targeted therapy rely on the use of invasive probes placed at the treatment location.

With the goal of combining the advantages of invasive microwave probe ablation and noninvasive HIFU, researchers have been investigating focused microwave systems capable of noninvasively delivering localized thermal therapy. Clinical studies of a 2-element adaptive phased array that used an invasive electric-field probe to guide focusing within a compressed breast have been reported by Dooley et al. [7] and Vargas et al. [8]. In addition, Stauffer et al. [9-10], and Dewhirst et al. [11] have demonstrated MR-guided phased arrays for the treatment of locally advanced breast cancer, chest wall recurrence, and osteosarcomas. Stang et al. [1] reported a preclinical phased array system that used full-wave forward modeling based on prior imaging studies to compute the relative phases necessary to focus at the target location.

While each of the systems above have made strides towards the goal of a noninvasive focused microwave therapy system, challenges still remain in achieving sufficient focusing resolution, monitoring and guidance, and targeting accuracy.

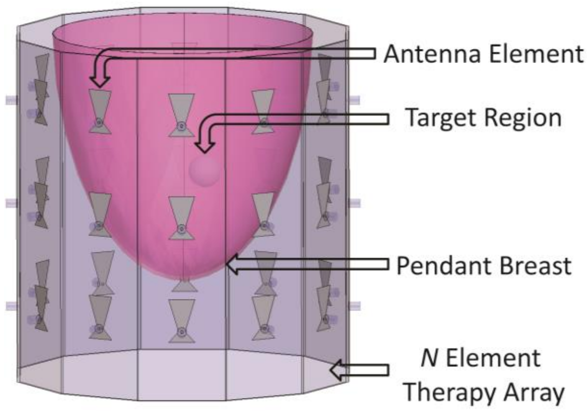
2. Methods


Figure 1. Focused Microwave Therapy Cavity in [1].

In the system reported in [1], an array of antennas operating at 915 MHz is used to focus continuous-wave microwave energy transcutaneously into the pendent breast suspended in a coupling medium (shown in Figure 1). Prior imaging studies are used to ascertain the material properties of the breast tissue, and this data is incorporated into a multiphysics model. Time-reversal techniques are employed to find a solution (relative amplitudes and phase) for focusing, resulting in maximal thermal dose at the tumor location. Using this system, focal spot sizes of approximately 1.5 cm in diameter were achieved with targeting accuracy better than 1 cm.

While this is sufficient for treating large tumors, sub-centimeter diameter treatment zones would allow for improved control and the treatment of a wider variety of cancers, including ductal carcinoma in situ (DCIS). One potential method of improving the spatial resolution of the focused microwave heating zone is to introduce contrast agent at the site of the tumor location. Further, if the contrast agent were injected in the duct where the cancer originated (in the case of invasive ductal carcinoma) or were contained (in the case of of DCIS), highly precise targeting could be achieved through the combination of focused microwaves and localized contrast agent.

To investigate the potential of this approach, a numerical study of the specific absorption rate (SAR) for contrast-enhanced focused microwave thermal therapy was undertaken. Using the numerical model shown in Figure 2, the time-reversal method described above was performed using a 24 antenna array (two rows of twelve antennas) to focus microwave heating in a region at the center of the array surrounding one branch of the breast duct network (targeted branch shown dark red, other branches in pink). Incident power of 1 watt per channel was applied to each antenna, and the specific absorption rate throughout the volume was calculated for two cases:

1. Microwave focusing alone without contrast agent.
2. Microwave focusing with saline contrast agent added to the targeted branch of the duct network.

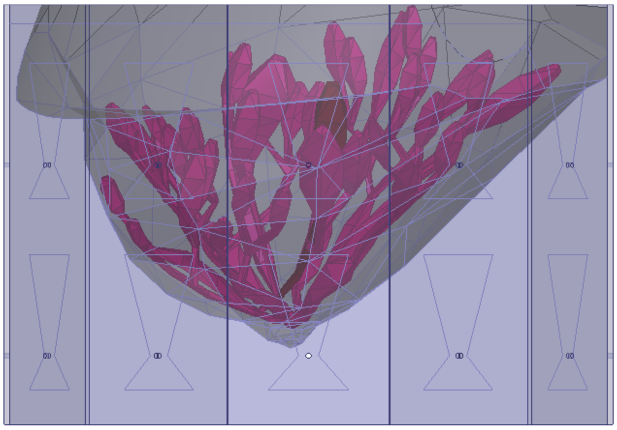


Figure 2. Numerical Model of Breast with Duct Network (Healthy Branches Shown in Pink, Targeted Branch Shown in Dark Red)

In the numerical model above, the following electrical properties were used:

Table 1. Tissue Dielectric Properties (Breast Phantom)

Material	*Relative Permittivity*	*Conductivity*
Coupling Fluid	23	0.05 S/m
Bulk Breast Tissue	20	0.25 S/m
Healthy Breast Ducts	10	0.10 S/m
Duct with Tumor Cells	50	0.45 S/m
Saline Injected Duct	60	0.94 S/m

3. Results and Discussion

As shown in Figure 3 (microwave focusing alone) and Figure 4 (focusing plus saline contrast agent) below, the addition of saline contrast agent increases the power absorbed in the target region by greater than an order of magnitude. Furthermore, the introduction of contrast agent improved the targeting selectivity (in terms of relative microwave power absorption) between tumor and surrounding healthy tissue to greater than an order of magnitude as well.

4. Conclusion and Ongoing Work

Based on the encouraging results of the initial study, more clinically accurate numerical studies using MRI derived phantoms are planned. In addition, parametric studies of the effect of using saline solutions of varying concentration will be performed. Last, multiphysics modeling will be performed to couple the predicted microwave absorption to the Penne's bioheat equation in order to estimate the effect of contrast agent on the thermal dose delivered in the treatment region over time.

5. Acknowledgements

This research was supported in part by DoD/BCRP award number BC095397.

6. References

1. Stang J, Haynes M, Carson P, Moghaddam M. A preclinical system prototype for focused microwave thermal therapy of the breast. IEEE Trans. Biomedical Engineering. 2012; 59(9):2431–2438.

2. Vernon CC, et al. Radiotherapy with or without hyperthermia in the treatment of superficial localized breast cancer: results from five randomized controlled trials. Int J Radiat Oncol Biol Phys. 1996;35: 731–744.

3. Vujaskovic Z, et al. A Phase I/II Study of Neoadjuvant Liposomal Doxorubicin, Paclitaxel, and Hyperthermia in Locally Advanced Breast Cancer. Int J Hyperthermia. 2010; 26(5): 514–521.

4. Hildebrandt B, Wust P, Ahlers O, Dieing A, Sreenivasa G, Kerner T, Felix R, Riess H. The cellular and molecular basis of hyperthermia. Critical Reviews in Oncology/Hematology. 2002 Jul; 43(1):33–56.

5. Dewhirst MW, Viglianti BL, Lora-Michiels M, Hansen M, Hoopes PJ. Basic principles of thermal dosimetry and thermal thresholds for tissue damage from hyperthermia. Int J Hyperthermia. 2003; 19:267–294.

6. Jones E, Thrall D, Dewhirst MW, Vujaskovic Z. Prospective thermal dosimetry: the key to hyperthermias future. Int J Hyperthermia. 2006; 22:247–253.

7. Dooley WC, Vargas HI, Fenn AJ, Tomaselli MB, Harness JK. Focused microwave thermotherapy for

preoperative treatment of invasive breast cancer: a review of clinical studies. Ann Surg Oncol. 2010; 17:1076–1093.

8. Vargas HI, Dooley WC, Gardner RA, Gonzalez KD, Venegas R, Heywang-Kobrunner SH, Fenn AJ. Focused microwave phased array thermotherapy for ablation of early-stage breast cancer: results of thermal dose escalation. Ann Surg Oncol. 2004; 11:139–146.

9. Li Z, Vogel M, Maccarini PF, Stakhursky V, Soher BJ, Das S, Arabe OA, Joines WT, Stauffer PR. Improved Hyperthermia Treatment Control using SAR/Temperature Simulation and PRFS Magnetic Resonance Thermal Imaging. Int J Hyperthermia. 2011; 27(1):86–99.

10. Stauffer PR, et al. Conformal Microwave Array (CMA) Applicators for Hyperthermia of Diffuse Chestwall Recurrence. Int J Hyperthermia. 2010; 26(7):686–698.

11. Cheng KS, Dewhirst MW, Stauffer PR, Das S. Effective learning strategies for real-time image-guided adaptive control of multiple source hyperthermia applicators. Medical Physics. 2010; 37(3):1285–1297.

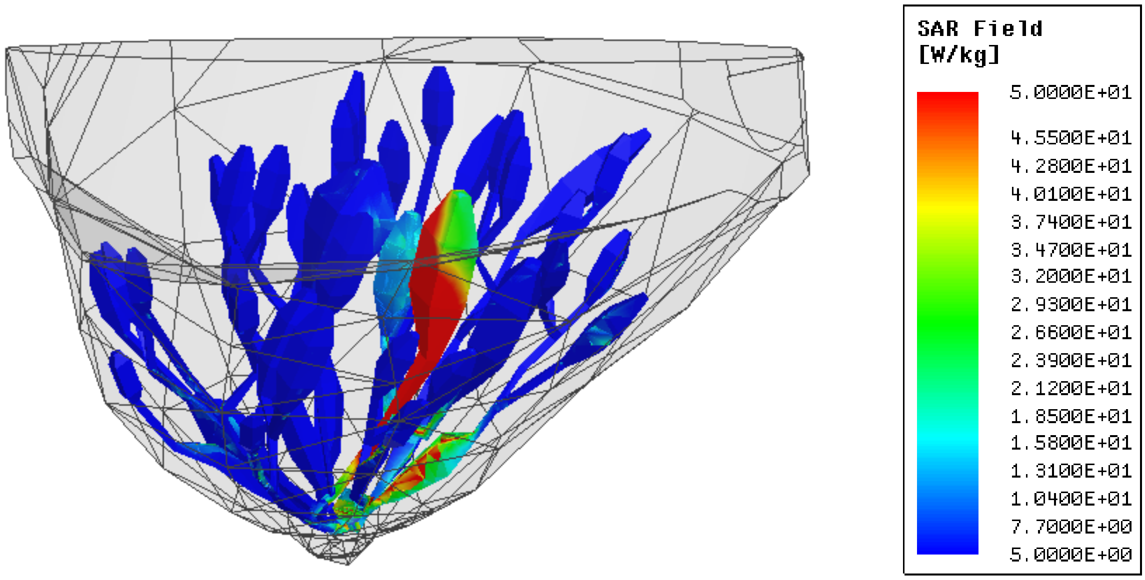


Figure 3. Specific Absorption Rate (measure of microwave energy absorbed and converted to thermal energy) on surface of breast ducts due to microwave focusing alone (1 watt per channel, 24 total antennas).

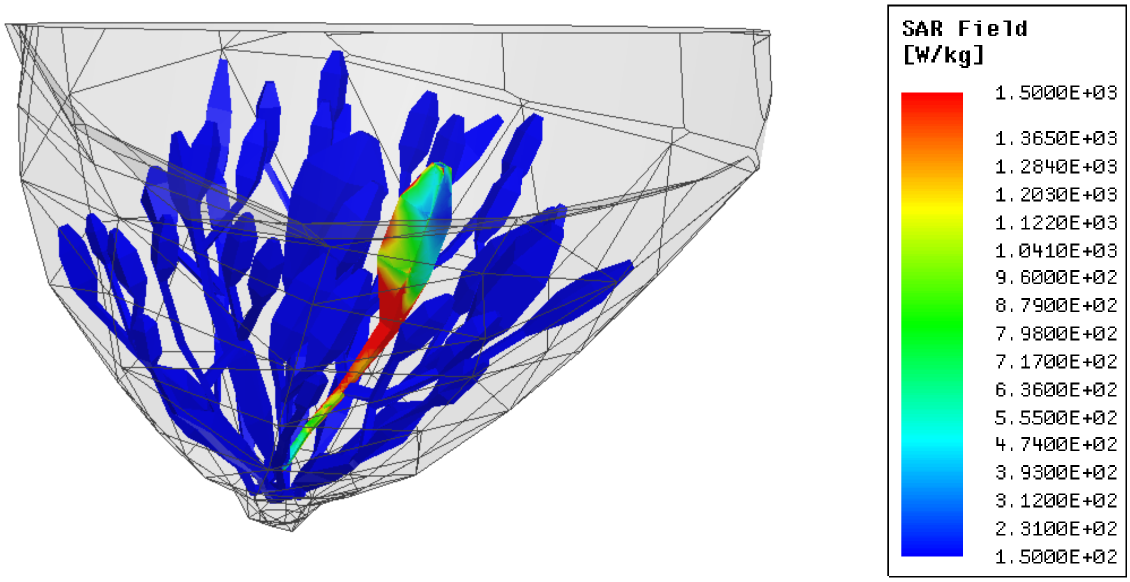


Figure 4. Specific Absorption Rate on surface of breast ducts with saline added to target duct. Focusing combined with contrast enhancement provides greater than an order of magnitude larger thermal dose at target location, and improved selectivity relative to surrounding healthy tissue. (1 watt per channel, 24 total antennas).