HIGH INTENSITY FOCUSED ULTRASOUND AND MICROBUBBLE INDUCED TISSUE ABLATION: EFFECT OF TREATMENT EXPOSURE ON THERMAL LESION VOLUME AND TEMPERATURE

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1. INTRODUCTION

High intensity focused ultrasound (HIFU) with microbubbles has demonstrated the enhancement of the therapeutic efficacy of HIFU [1, 2]. Acoustically stimulated microbubbles that consist of the perflurocarbon gas enclosed in lipid shell enhance the bioeffects induced through cavitation (mechanical effect) and thermal mechanisms [3, 4, 5]. Holt and Roy have experimentally demonstrated that ultrasonically induced cavitation bubbles locally enhance tissue heating in HIFU treatment [6]. The ultrasonic intensity for inducing cavitational bioeffects can be reduced by orders of magnitude with administration of such an agent externally. This is especially important for the treatment of deep-seated tumors, where the ultrasonic power high enough for the treatment is difficult to deliver. Current limitations are creating and controlling the cavitation microbubbles. This issue can be resolved, if the ultrasonic absorption of tissues can be significantly increased in a well-controlled manner with administration of microbubble agents externally.

The current study investigates the effects of ultrasound treatment parameters and microbubble concentration on the HIFU lesion volume and temperature.

2. METHODS

Figure 1 shows the HIFU system that consists of a therapeutic ultrasound unit and an imaging ultrasound unit. A therapeutic transducer made of a high-power PZT4 crystal (Boston Piezo-optics Inc., Boston, MA) with a diameter of 50 mm and a focal length of 75 mm was used. The imaging was done using the EC9-5/10 Endovaginal microconvex transducer (Ultrasonix Inc., Richmond, BC) that was aligned with the HIFU transducer. Artenga® microbubbles (MBs) (Artenga Inc, Ottawa, CA) with the mean bubble diameter of 2 μm and concentration of 10^9 microbubbles/ml were injected into the *ex vivo* chicken breast tissue. The *ex vivo* chicken breast tissue was treated with US (HIFU alone) and USMB (HIFU and microbubbles). Lesions were created using HIFU exposure of intensities ranging from approximately 600 to 2500 W/cm^2 for 5 seconds exposure duration. The lesion volume and peak temperature were measured at varying intensities (600 to 2500 W/cm$^{2)}$ and varying microbubble concentrations (0%, 10%, 25%, 50%, 75% and 100%). K-type thermocouple was used to measure the peak temperature. The lesion volume was approximated to be an ellipsoid. Volume of ellipsoid was used to calculate the lesion volumes.

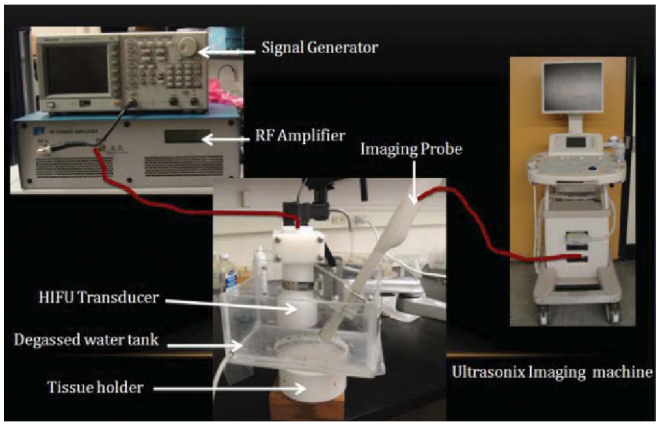

Figure 1. Experimental setup

3. RESULTS

The lesion volume and peak temperature for various intensities in absence and presence of microbubbles are shown in figures 2 and 3 respectively. The lesion volumes for both the groups (US and USMB) at intensities greater then 1200 W/cm^2 are stastically signifiant. There is no significant difference between the lesion volumes at intensities below 1200 W/cm^2. The peak temperature for the USMB treatment compared to the US treatment alone is stastically significant ($p<0.05$) (Figure 3).

Figure 4 shows the graph for lesion voume as a function of peak temperature. The lesion volume for US and USMB treatments increase constantly as same rate as the peak temperature rises to approximately 70 °C. However lesion volume increase more rapidly for the USMB treatment over 70 °C.

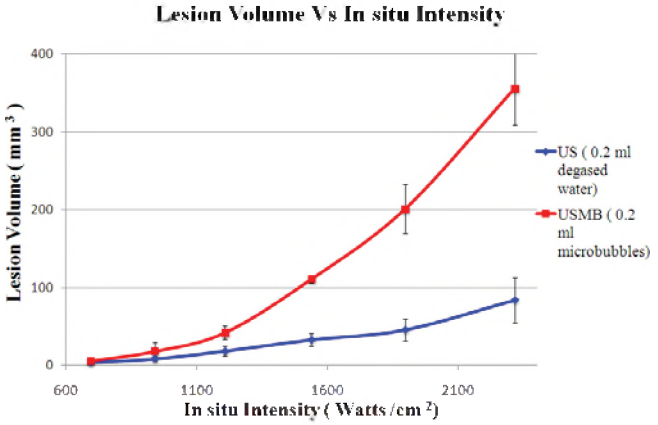

Figure 2. Lesion volume vs. *in situ* intensity at constant microbubble concentration (100% MBs)

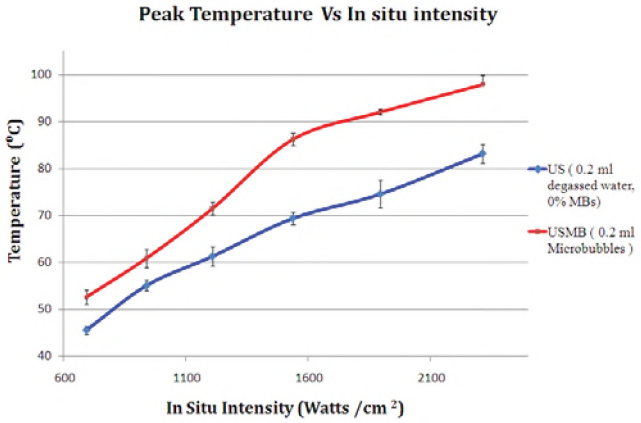

Figure 3. Peak Temperature vs. *in situ* intensity at constant microbubble concentration (100% MBs)

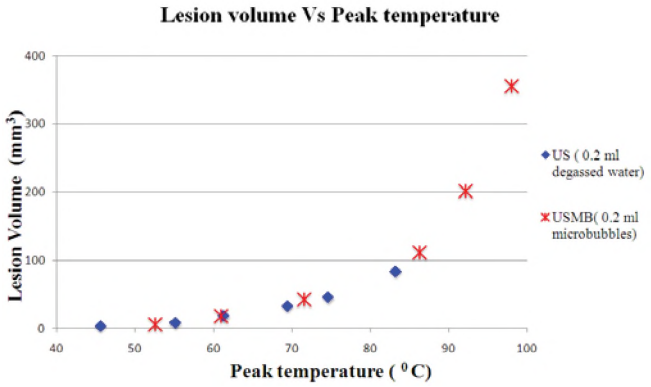

Figure 4. Lesion volume vs. Peak temperature

4. DISCUSSION AND CONCLUSIONS

In the active group, larger tissue volume was coagulated in the presence of MBs, despite equal exposure time. This shows that the MBs enhance the tissue ablation induced by HIFU. HIFU causes localized tissue temperature rise because ultrasound energy is converted to heat. As for the mechanisms by which the MBs in the ultrasound field cause enhanced heating, two factors are considered to be important: heating by oscillation or explosion of microbubble contrast agents exposed to HIFU, and cavitation bubbles generated by the HIFU exposure.

It was noted that the lesion volume for the US and USMB treatment was same for until upto 70 °C. This indicates that the thermal mechanism was the only prominent mechinism of the tissue damage. However, the lesion volume for the USMB treatment rose at higher rate then the US treatment. This indicates that the mechanisms other then thermal damage also play role in the tissue damage. Therotically these results can be explained by thermal damping, viscous damping and acoustical damping (explained eleswhere) [6].

In conclusion, enhancements in HIFU tissue ablation efficacy are achievable using controlled microbubble induced tissue ablation. Furture work includes measuring lesion volume and Peak temperature at various microbubble concentration to determine the appropriate treatment combination.

REFERENCES

1. He W, Wang W, Zhou P, Wang YX, Zhou P, Li RZ, Wang JS, Ahuja AT. (2010). Enhanced Ablation of High Intensity Focused Ultrasound with Microbubbles: An Experimental Study on Rabbit Hepatic VX2 Tumors. Cardiovasc Intervent Radiol. [Epub ahead of print].

2. Yu T, Fan X, Xiong S, Hu K, Wang Z. (2006). Microbubbles assist goat liver ablation by high intensity focused ultrasound. Eur Radiol. 16(7): 1557-63.

3.Hynynen K. (1991). "The threshold for thermally significant cavitation in dog's thigh muscle in vivo". Ultrasound Med Biol.17(2):157-69.

4.Sokka SD, King R, Hynynen K. (2003) MRI-guided gas bubble enhanced ultrasound heating in in vivo rabbit thigh. Phys Med Biol.48(2):223-41.

5.Umemura S, Kawabata K, Sasaki K. (2005). "In vivo acceleration of ultrasonic tissue heating by microbubble agent". IEEE Trans Ultrason Ferroelectr Freq Control.52 (10): 1690-8

6. Holt RG, Roy RA. (2001) Measurements of bubble-enhanced heating from focused, MHz-frequency ultrasound in a tissue-mimicking material. Ultrasound Med Biol.27 (10): 1399-412.

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