Optoacoustic imaging of HIFU-induced thermal lesions in tissue

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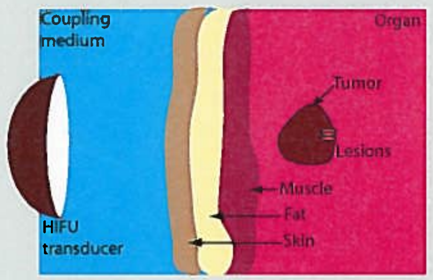
Motivation: High-intensity focused ultrasound (HIFU) provides noninvasive and nonionizing treatment of tumors. HIFU relies on absorption of ultrasonic energy at the focus to induce temperature elevation, which can lead to thermal necrosis when the temperature exceeds 56°C for a duration of 2 s [1]. High precision, noninvasive implementation and the ability to treat deeply seated diseased sites make HIFU a particularly attractive hyperthermia modality. Economical methods for reliably and noninvasively guiding and monitoring HIFU therapy are essential to develop HIFU into a clinically viable modality.

Figure 1



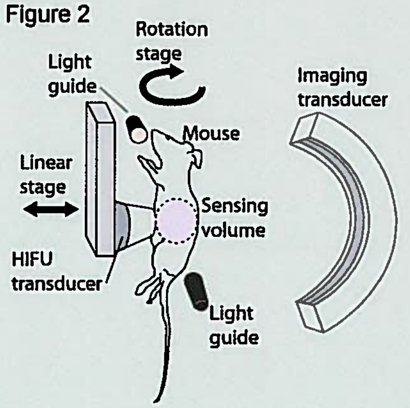
Experimental concept: The present study investigates the feasibility of exploiting the optoacoustic (OA) effect for noninvasively detecting thermal damage induced by HIFU. The OA effect relies on local absorption of a brief monochromatic light pulse; optical absorption induces rapid thermoelastic expansion resulting in the generation of broadband ultrasonic waves [2]. The OA pressure at the absorption site is estimated from the following expression:

$$P = \left(\frac{\beta c^2}{C_p}\right)\mu_a F$$

P : local OA pressure
c: sound speed
β : coefficient of thermal expansion
C_p : specific heat
μ_a : local absorption coefficient
F : incident laser fluence

The optical absorption coefficient of the tissue that undergoes thermal necrosis changes irreversibly [3,4,5] and can be distinguished from the surrounding tissue using optoacoustic imaging (OAI). This study used OA-based 3-D tomography system to image lesions created in excised chicken liver and live nude mice. Specimens were subjected to HIFU exposures and 3-D OA scans were acquired before and after the HIFU exposure. The system was capable of generating 3-D images with a cubic voxel size of 0.5 mm. The key components of the experimental setup are shown in Fig. 2.

Figure 2

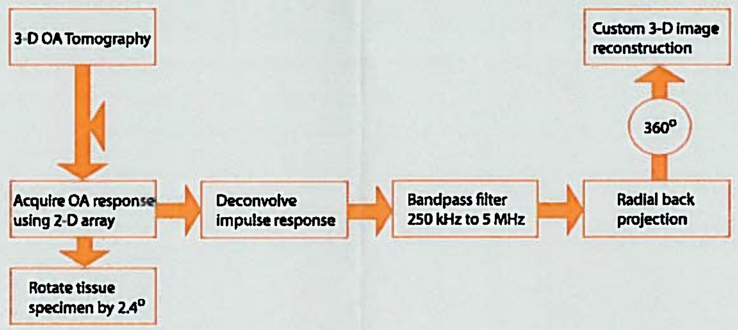


HIFU transducer
Center frequency: 7.5 MHz
Focal distance: 35 mm
Aperture: 30 mm
Focal intensity: 5.5kW/cm^2
Exposure time: 30 s or 60 s

Imaging transducer
# of elements: 64 (curved array)
Element: 2mm X 2 mm
Center frequency: 3.1 MHz
Focal length: 65 mm
-6dB bandwidth: 80%

Laser
Wavelength: 755 nm or 1064 nm
Pulse energy: 100 mJ
Pulse duration: 10 ns
Spot diameter: 4 cm
Repetition rate: 10 Hz

3-D OA tomography: Custom 3-D image reconstruction algorithm was implemented after post-processing the OA data



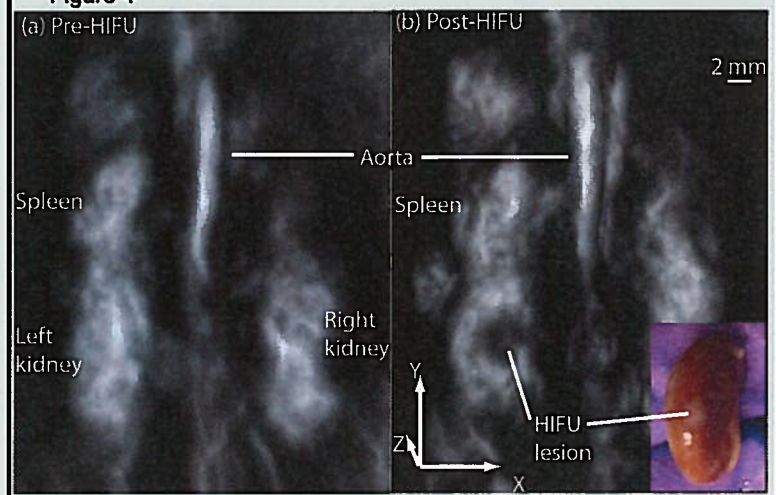
Results: Figure 3 shows the 3-D OA images of an excised chicken liver before and after HIFU exposures. The exterior surface of the tissue specimen was imaged using 755 nm light. The HIFU-induced lesion was visible in the 1064 nm OAI. Thermal damage resulted in an enahanced optical absorption (positive contrast) at 1064 nm which is consistent with prior works.

Figure 3

Lesion size
OA measurment: 6 mm X 4 mm
Dissection: 8 mm X 4 mm

Figure 4 shows *in vivo* OA images of nude mice acquired before and after HIFU exposures. The precise location of the HIFU transducer's focus was not known a priori but the post-HIFU dissection revealed that the thermal dose was delivered to the left kidney resulting in a soft lesion (diameter 2 mm). The diameter of the lesion estimated from OA slices along the HIFU focus was between 1.5 and 2 mm. The OA image provided indication to the location and the extent of the lesion. The lesion resulted in a reduction in optical absorption (negative contrast) compared to the OA signal from the surrounding tissue, which was inconsistent with results obtained from *ex vivo* experiments.

Figure 4



Discussion: OAI was performed at both 755 nm and 1064 nm but the HIFU-induced lesions were visible only in the 1064 nm OAI. The 1064 nm wavelength is sensitive to water and hemoglobin. Localized changes in these chromophores likely contribute to a change in the OA signal from the thermally damaged tissue, which is apparent in two possible ways: a positive contrast or a negative contrast.

Positive contrast	Negative contrast
Ex vivo	*In vivo*
Aggressive thermal deposition	Moderate thermal dose (blood perfusion and attenuation limits energy deposition)
Hard lesion with a hemorrhagic ring	Soft lesion, no hemorrhagic ring
Thermo-chemical reactions (formation of methaemoglobin)	Loss of optically absorbing chromophores (hemoglobin and water)
Increase in optical scattering at the lesion	

Conclusions: The feasibility of imaging HIFU-induced lesions using OAI was demonstrated both *ex vivo* and *in vivo*. OAI can noninvasively and reliably guide and monitor thermal ablation therapies.

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[1] G. T. Clement. *Ultrasonics.*, 42: 1087-1093, 2004.
[2] A. A. Oraevsky et al. *SPIE*, 1882:86-101, 1993.
[3] T. D. Khokhlova et al. *Quantum Electronics*, 36(12):1097-1102, 2006.