An Experimental Feasibility Study of Microbubbles as a Contrast Agent for Microwave-Induced Thermoacoustic Imaging of Breast Cancer

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Microwave-induced thermoacoustic tomography (MI-TAT) is a hybrid imaging modality that exploits dielectric-properties contrasts at microwave frequencies while creating images with ultrasound-quality resolution. In MI-TAT, the tissue is irradiated with a sub-microsecond electromagnetic pulse. This electromagnetic energy is selectively absorbed by the higher-conductivity tissues and induces acoustic waves that are detected by ultrasound transducers and processed for image reconstruction. As with other microwave imaging techniques, one promising application for MI-TAT is early-stage breast cancer detection. Earlier studies on breast tissue dielectric properties suggested that there exists a significant microwave contrast between normal and malignant breast tissues. However, a recently published large-scale dielectric spectroscopy study conducted by the Universities of Wisconsin-Madison and Calgary (Lazebnik *et al*, *Phys. Med. Bio.*, vol. 52, pp. 2637-2656 and 6093-6115, 2007) has shown that the contrast in the microwave-frequency dielectric properties between malignant tissues and healthy adipose-dominated tissues in the breast is as large as 10:1, while the contrast between malignant and normal glandular/fibroconnective tissues in the breast is no more than about 10%.

Intravenously injected contrast agents that are systemically delivered to the site of a malignancy are commonly used in medical imaging to enhance the intrinsic tissue-properties contrast. Here, we propose microbubbles as a contrast agent in MI-TAT. Instead of increasing microwave absorption in the tumor, tumors infused with microbubbles have the potential to be more easily detected because of their predicted low microwave absorption relative to surrounding normal glandular tissue.

As an initial step towards evaluating the feasibility of microbubble contrast agents for MI-TAT, we tested the extent to which the microwave-induced thermoacoustic (TA) response of a dielectric target is modified by the presence of microbubbles. First, we created mixtures of ethylene glycol (EG) with varying concentrations of 18-μm-diameter air-filled glass microbubbles and characterized their dielectric properties using a precision open-ended coaxial probe technique (Popovic et al, *IEEE Trans. Microwave Theory Tech.*, vol. 53, pp. 1713-1722, 2005). For an estimated microbubble concentration of 20% by weight, the mixture's average relative permittivity at 3 GHz was reduced from approximately 14 to 9.8; the average conductivity was reduced from approximately 2.3 S/m to 1.3 S/m. Second, we characterized the TA response of simple targets containing the mixtures. Specifically, we poured solutions of varying concentrations into plastic tubes, immersed each tube in an oil tank, illuminated the target with a 3-GHz microwave signal, and recorded the time-varying acoustic wave received at a nearby transducer. We observed that the average peak amplitude of the TA response of the target containing the 20%-microbubble mixture was diminished by approximately 15% and the average temporal width was reduced by 29% relative to the response of the pure EG target. These promising preliminary results suggest that microbubble contrast agents have the potential to enhance the sensitivity of MI-TAT for breast imaging.