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TITLE: High Resolution X-ray Phase Contrast Imaging With Acoustic Tissue-Selective Contrast Enhancement

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We show that ultrasound can be used for contrast enhancement in high-resolution x-ray imaging of tissue and soft materials. Interfacial features of objects are highlighted as a result of both the displacement introduced by the ultrasound and the inherent sensitivity of x-ray phase contrast imaging to density variations. Experimental results are reported for tumor phantoms. The method produces a directional image that is equivalent to the first space derivative of the phase contrast image along the propagation coordinate of the ultrasound.
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Introduction

Acoustically Modulated X-ray Phase Contrast Imaging

The method of modifying a phase contrast image using acoustic radiation pressure $^{21,22}$ consists of two steps: first, an x-ray image is made with a sound beam directed into a body to displace an object through acoustic radiation force and the image stored in a computer, second, another x-ray image is of the object is taken, this time without the presence of the sound beam. Both images are recorded in the compute and then subtracted pixel by pixel to give a subtracted phase contrast image, the component of the image from absorption contrast being largely eliminated, leaving a nearly pure phase contrast image, inherently background and flatfield corrected. Figure 1 gives a diagram of the experimental apparatus.

![Figure 1: Diagram of the experimental apparatus. X-radiation generated by a microfocus tube penetrates a sample and is detected by a CCD camera that views a scintillation plate. The CCD camera is read by the computer which stores the images and performs the subtractions.](image)

Body

Figure 2 shows the results of a set of experiments involving a simulated breast. The phantom (purchased from CIR, Inc.) was designed to simulate both the physical density and attenuation characteristics of breast tissue under x-ray and ultrasound exposure. The interior of the phantom contains two types of masses; one with the density and elasticity of malignant tumors and the other with the density of fluid-filled cysts. The results show that the “tumors” respond to the applied 1.14 MHz, 300W sound field whereas the “cysts” do not. This is a significant development since it would give clinicians the ability to differentiate common and benign cysts from malignant tumors.
Figure 2 (a) Phase contrast image of a phantom cystic mass; (b) subtracted phase contrast image of (a); (c) phase contrast image of a phantom malignant tumor; (d) subtracted phase contrast image of (c); (e) phase contrast image of the intersection of the cystic and malignant masses placed to the left and right of center, respectively. Note that the image of the cyst is not visible after subtraction, yet the image of the tumor remains.

Figure 3 shows the results of an experiment designed to test the ability of the ultrasonic beam to penetrate biological tissue and produce differential motion. A Teflon bead was embedded in the center of a piece of chicken muscle and exposed to a 1.14 MHz, 300W ultrasonic beam. The Teflon bead was clearly moved despite being tightly embedded in the tissue. The additional objects seen in the image are fat bubbles and would not be expected to be a source of background in breast tissue.

Figure 3. (a) Phase contrast image of a Teflon bead embedded in muscle tissue; (b) subtracted image of (a). The additional round objects are fat bubbles.

We have also tested the ability of our technique to manipulate mouse skin tumors given to us by our collaborators at Brown University Medical School. Figure 4 shows the results of an experiment with one of the skin tumors; the image on the left is a phase contrast image of the tumor and surrounding skin, the image on the right shows the subtracted image. Note that the tumor appearance is enhanced while the background is essentially flat.
We have also explored the response of ultrasonic contrast agents to the combination of both x-rays and ultrasonic pressure in an effort to gauge their potential for use as x-ray contrast agents. The bubbles shown in Figure 5 are gas-filled protein shells dispersed in an agarose matrix. The images show that these bubbles respond to the ultrasonic field differently than do solid or fluid-filled spheres. Instead of being pushed by the acoustic pressure, they expand and contract radially.
Reportable Outcomes

“Acoustically Modulated X-Ray Phase Contrast and Vibration Potential Imaging” with a.
C. Beverideg, C. J. Bailat, T. J. Hamilton, S. Wang, C. Rose-Petruck, and V. E. Gusev
(Proc. SPIE 2005) selected as the best conference paper

C. J. Bailat, T. J. Hamilton, C. Rose-Petruck, G. J. Diebold, Acoustic radiation pressure:
19, Nov. 2004, 4517-4519.

“Ultrasonically modulated x-ray phase contrast and vibration potential imaging
methods”, with Theron J. Hamilton, Guohua Cao, Shougang Wang, Claude J. Bailat,
Cuong K. Nguyen, Shengqiong Li, Stephan Gehring, Jack Wands, Vitaliy Gusev,
Christoph Rose-Petruck, Proc. SPIE Vol. 6086, Photons Plus Ultrasound: Imaging and
Sensing (2006)

“Ultrasonically Modulated X-ray Phase Contrast Imaging”, with Theron J. Hamilton,
Guohua Cao, Claude J. Bailat, Jack Wands, Stephan Gehring, Christoph Rose-Petruck
(2006)

“X-ray Phase Contrast Imaging: Transmission Functions Separable in Cartesian
Coordinates”, with Guohua Cao, Theron Hamilton, and Christoph Rose-Petruck
(submitted for publication)

“X-ray Phase Contrast Imaging: Experiments and Calculations with Objects having
Transmission Functions Separable in Cartesian Coordinates”, with Theron J. Hamilton,
Guohua Cao, Phillip Wintemeyer, Jack Wands, and Cristoph Rose-Petruck (submitted
for publication)

Conclusions

We have completed all the necessary construction of experimental apparatus and proven
the concept of ultrasonically modified x-ray phase contrast imaging. We have shown the
method has the ability to select objects within a body for imaging and have demonstrated
the feasibility of the technique with phantoms and biological samples.
References