Clinical Feasibility Study of Combined Optoacoustic and Ultrasonic Imaging Modality Providing Coregistered Functional and Anatomical Maps of Breast Tumors

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ABSTRACT

Two-dimensional optoacoustic imaging with a hand-held probe operated in backward mode is being developed for diagnostic imaging of breast cancer to evaluate the feasibility of a dual-modality optoacoustic plus ultrasonic system that maps functional information of anatomical tissue structures with ultrasonic resolution. Tissue is illuminated at 757nm and 1064nm for optical contrast between hypoxic blood of breast carcinomas and normally oxygenated blood in benign masses. The system is optimized and calibrated in phantoms for a pilot clinical study of patients with breast masses suspected for malignancy. Capability of the non-invasive system to improve detection and diagnosis of breast tumors is discussed.

Keywords: optoacoustic, breast cancer diagnosis, in-vivo functional imaging

1. INTRODUCTION

There are several different breast-cancer imaging systems currently in clinical use. These include ultrasound, MRI, X-ray mammography, PET and diffuse optical tomography. Unfortunately, these systems will often provide ambiguous diagnostic information about a tumor or lesion suspected of being cancerous.[1,2] When this is the case, a surgical or needle biopsy is required for determining a final prognosis, and this can be painful or expensive.[3] Typically, ultrasonography is used following an abnormal mammogram to provide additional anatomical information to help determine the need for a biopsy. However, there are still many classes of lesions detected by ultrasound that remain inconclusive, and in approximately 80% of cases, this biopsy result turns out negative.[3] There is a fundamental need for new imaging modality that is highly specific for malignant tumors and sufficiently sensitive to detect early in-situ tumors located deep inside dense breast tissue and further reduce unnecessarily performed biopsies.

Optoacoustic imaging represents a breakthrough in imaging technology. Unlike most imaging modalities, it can provide functional information in addition to anatomical information. Optoacoustic imaging combines light and sound to produce high-resolution, high-contrast images to indicate the presence of angiogenesis – the increased blood supply and vascular structure that surround and feed a tumor. The Imagio™ system is a functional imaging system designed to distinguish benign from malignant lesions. As cancer cells grow, they develop a dense micro-vascular network,[4] which serves as a marker that a breast tumor is growing aggressively and subject to metastasis.[5] In malignant tumors, the amount of blood will be substantially higher than in normal breast tissue. In addition, the blood in the tumor tends to be much less oxygenated than the blood in normal tissue.[6–10]

These differences between malignant and benign tumors are well suited for detection by optoacoustic imaging. First, optoacoustic images endogenously show natural high-contrast of blood against surrounding tissue. This is because the optical absorption (and hence the optoacoustic signal strength) from blood is much greater than in the surrounding tissue. This optical contrast is a significant advantage over standard pulse-echo ultrasound imaging, where blood vessels would generally have low contrast against the surrounding tissue. Secondly, since

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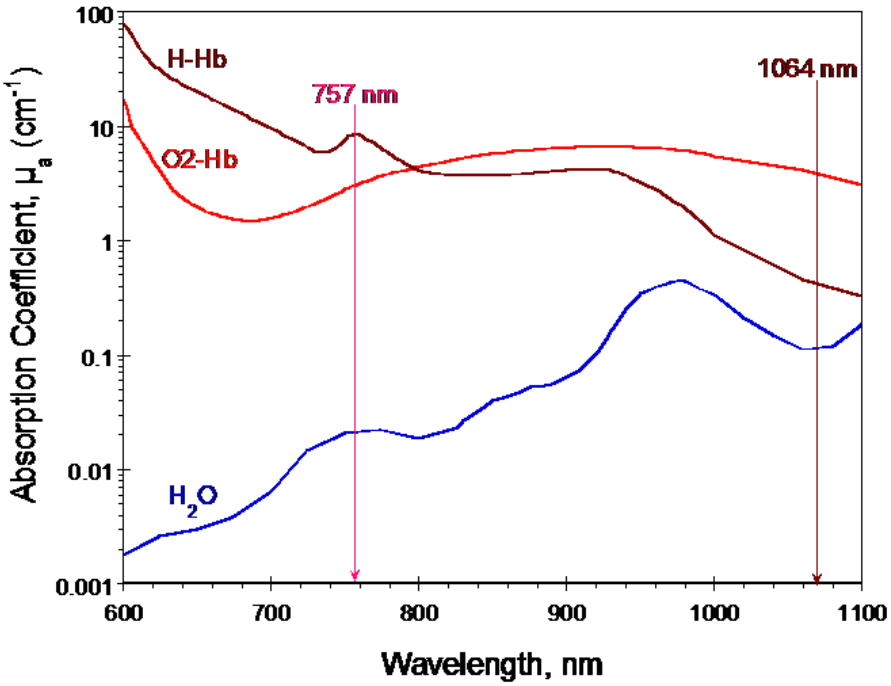


Figure 1. Absorption spectra of the three main breast tissue chromophores, oxy-hemoglobin, deoxy-hemoglobin and water.

blood has a wavelength-selective optical absorption in the near infrared (NIR) region, optoacoustics can be used to distinguish oxygenated from deoxygenated blood.[7,11]

Third, optoacoustics can penetrate deep into breast tissue at high resolution because of the relatively low optical attenuation of normal breast tissues and the low acoustic distortion and attenuation.[12,13] In other optical methods, blurring occurs at depth because photons cannot penetrate deeply in tissue without optical scattering. In optoacoustics this is not a problem because the image resolution arises mainly from the acoustic process where ultrasonic scattering is much less than its optical counterpart. Consequently, optoacoustics takes advantage of optical contrast for functional imaging but with ultrasonic resolution and depth penetration.

2. PHYSICS OF OPTOACOUSTICS

In optoacoustics, a several nanosecond laser pulse is used to illuminate a volume of tissue. This causes the light absorbing structures in tissue to rapidly heat up, expand and then contract. When this occurs, the tissue structures emit ultrasonic waves that propagate to the surface of the tissue.[14] To measure the waveforms, a probe consisting of ultrasonically sensitive elements is positioned at the tissue surface. The ultrasound waveforms reaching each sensory element are recorded simultaneously. The recorded waveforms are then used topographically to compute a two-dimensional image map related to the optical absorption of the tissue.

In breast tissue, the major tissue chromophores (light absorbing molecules) in the near-infrared spectral range are deoxy-hemoglobin, oxy-hemoglobin and water.[9,10,15] The absorption spectra of these molecules is shown in Figure 1. Optoacoustic imaging offers the capability to differentiate deoxy-hemoglobin from oxy-hemoglobin using their specific absorption spectra. Since blood contains hemoglobin, it has a much higher absorption than non-vascularized breast tissue which has properties similar to water.[6] Arterial blood typically has an oxygen saturation of around 95%-99%, while venous blood has an oxygen saturation of around 60%-80%.[9,16–18]

It should be noted that the optical energy that penetrates into the tissue decreases with depth. This introduces a limit on how deep an absorber can be detected in tissue. Furthermore, the attenuation of an acoustic wave increases at high frequencies so this places a further limit on the depth penetration, with the resolution being inversely related to depth. In Figure 2, the observed brightness for the cross-section of an absorbing cylindrical

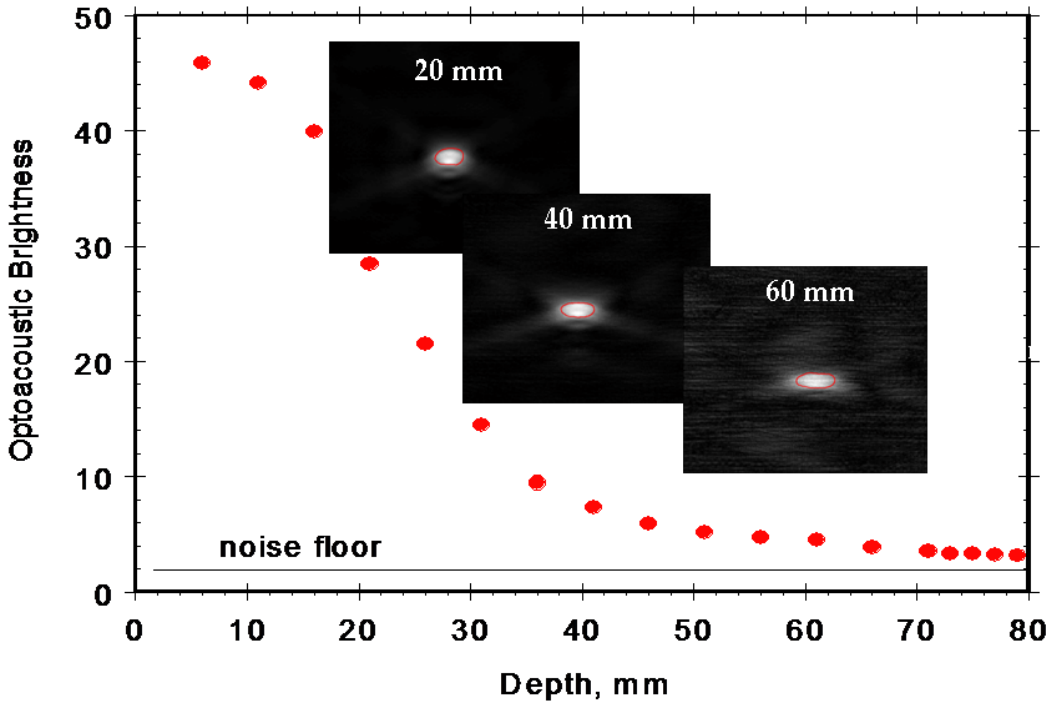


Figure 2. Optoacoustic brigtness and depth. When an object is located deeper in a scattering medium, the measured optoacoustic signal will attenuate with depth. At greater depths it becomes more difficult to separate an object from other sources of noise.

object is shown. As the depth of the object becomes greater, its signal approaches the noise floor of the system. These details depend on the characteristics and geometry of the system and object being imaged.

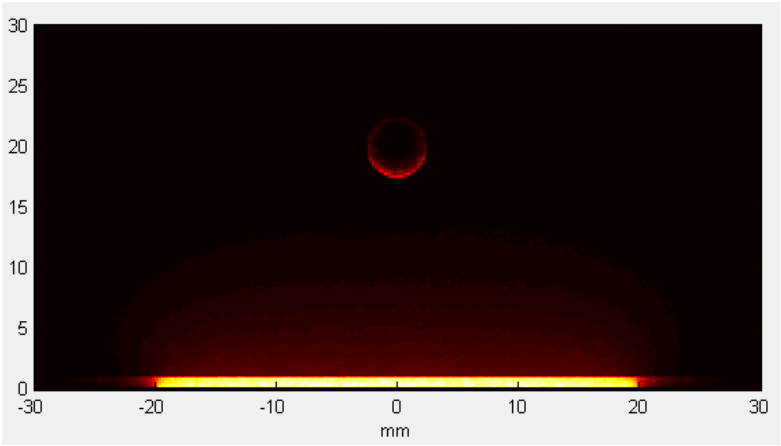
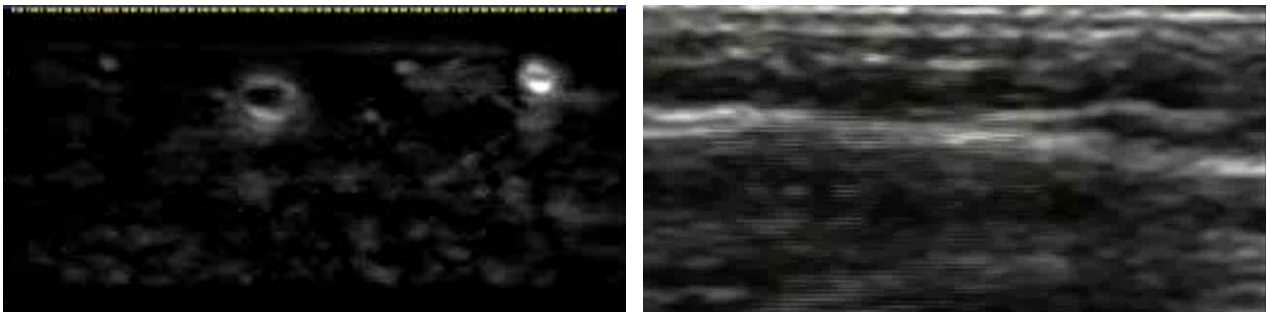


Figure 3. A three dimensional optical simulation of a blood vessel in tissue. Light enters the system from the bottom and penetrates a 1mm thick skin layer into homogeneous tissue. The vessel has a radius of 2.5mm and depth of 20mm. The light is primarily absorbed in a crescent-shaped ring around the vessel.

Figure 3 shows an optical simulation involving a large blood vessel in tissue. When light travels through breast tissue, it first passes through a layer of skin which has different optical properties than the typical breast parenchyma. The scattering and absorption properties of light may also vary by the patient skin type and tissue density.[8,12,15] Light attenuates more when travelling through blood than tissue. The simulation shows that most of the optical energy reaching the vessel is absorbed in a crescent-shaped ring around the vessel. For a smaller sized vessel, the absorption profile is more homogeneous with the crescent-shape effect being less pronounced.



(a) (b)

Figure 4. Ulnar artery and a vein in human arm. An optoacoustic image (a) provides high contrast of structures containig blood. An utrasonic image (b) provides high contrast of tissue morphology.

3. IMAGIO SYSTEM

The Imagio™ breast imaging system involves a hand-held linear probe and co-registration of optoacoustic (functional) and ultrasound (anatomical) images. For our feasibility study, we have selected two optical wavelengths, 757 nm that is absorbed preferentially in deoxygenated blood and 1064 nm that is absorbed preferentially in oxygenated blood. An illustration of the system is shown in Figure 5.

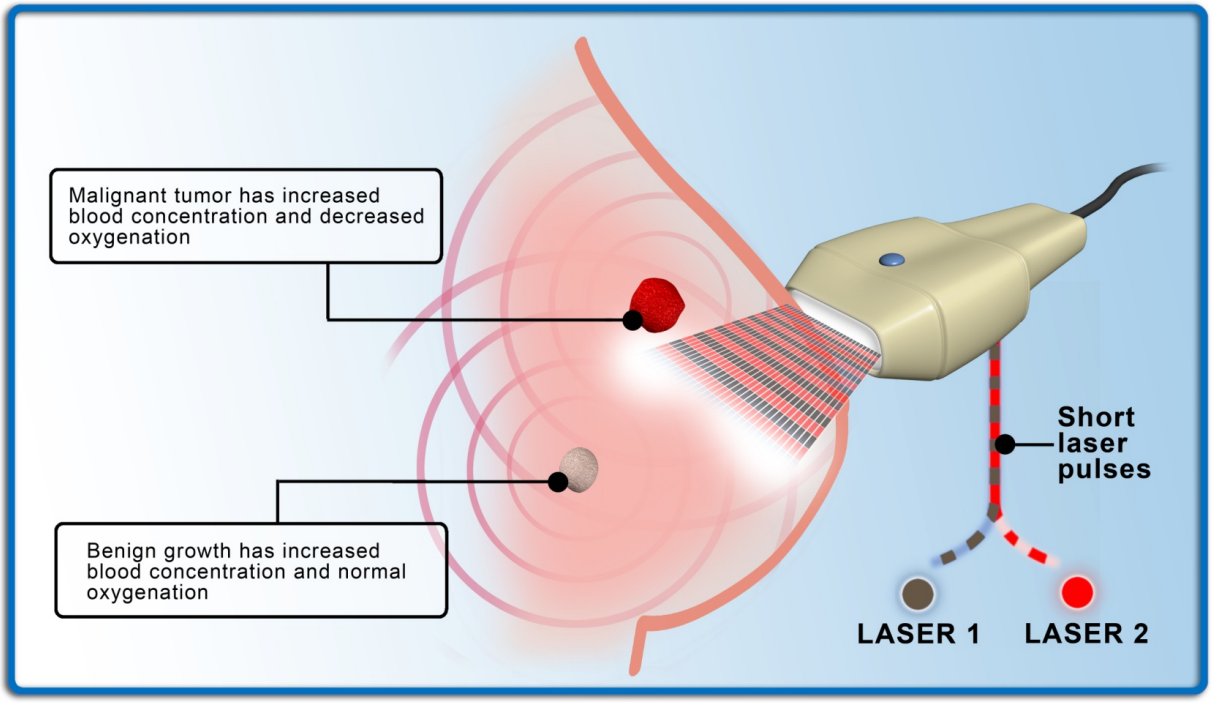
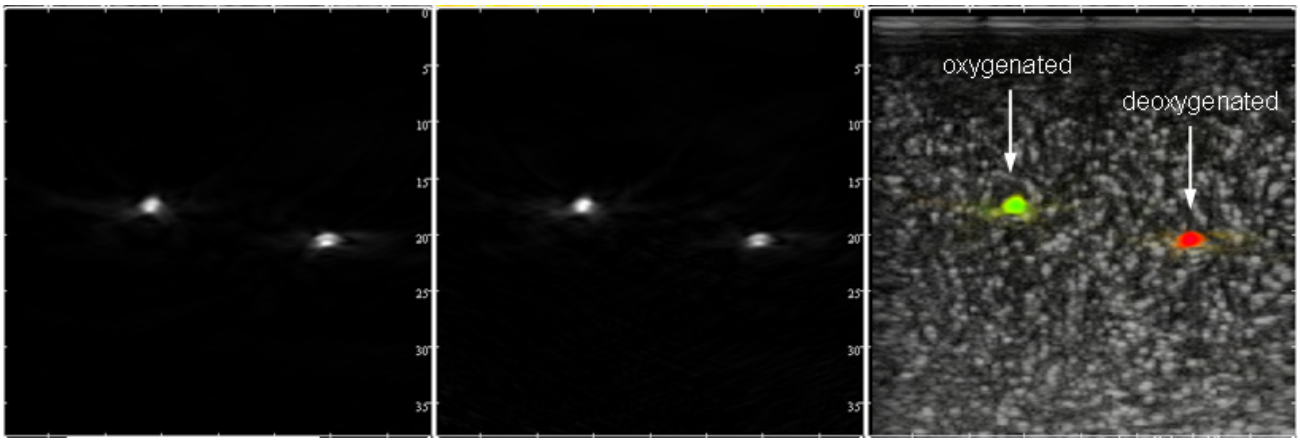


Figure 5. The Imagio™ functional breast imaging system.

4. RESULTS AND VALIDATION

We demonstrate our system performance on an phantom designed to simulate the optoacoustic properties of blood and tissue. Tubes filled with liquid simulating the absorption of an oxygenated and de-oxygenated blood

are embedded in a background medium representing biological tissue. Figure 6a shows the reconstructed image at 757nm. Figure 6b show the image at 1064nm. At 757nm the tube representing a deoxygenated vessel is brightest and at 1064nm the tube representing the oxygenated vessel is brightest. Figure 6c shows a functional overlay co-registered with ultrasound. Green is used to represent oxygenation and red shows areas of hypoxia.



(a) 757nm (b) 1064nm (c) functional overlay

Figure 6. Calibration Phantom. Tubes of liquid simulating the absorption of an oxygenated and a de-oxygenated blood are embedded in a medium. The reconstructed images are shown at (a) 757nm and (b) 1064nm. The functional overlay co-registered with ultrasound (c) reveals the oxygenated vessel (green) and the de-oxygenated vessel (red).

5. DISCUSSION AND CONCLUSION

Optoacoustic tomography draws on both optical and ultrasound methods resulting in a higher-resolution functional imaging technique with substantial advantages over anatomic and functional imaging modalities currently in use. A short laser pulse illuminates a large region of tissue creating thermo elastic expansion and resultant acoustic waves propagate to the surface of the tissue where they are detected by wideband ultrasonic receivers. Reconstruction algorithms can determine the spatial location of optical absorbers from the time-domain data. By using dual wavelength illumination, the image contrast is related to hemoglobin concentration and oxygen saturation, both of which have direct relevance to tumor pathophysiology.

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