A Novel Multi-modality Image-guided US-NIR Scanner for Breast Cancer Diagnosis

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Abstract— **Near infrared (NIR) spectroscopy and ultrasound (US) are noninvasive modalities extensively investigated for cancer diagnosis. NIR is sensitive to changes in blood oxygen saturation, which is well suited to the study of tumor angiogenesis and hypoxia. Due to properties of photon transport in tissue, the region of NIR interrogation cannot be well localized. On the other hand, focused US has been shown to produce reversible blood stasis in the focal region, which can be accurately localized. We have previously demonstrated that changes in NIR signal due to the onset of focused US may be used as a powerful discriminator of tumor vs. normal tissue in a murine model. In the present work, we present a clinical scanning system for breast cancer diagnosis based on the same principle, which additionally incorporates a standard US probe for image guidance.**

A five degrees-of-freedom (DOF) clinical device was designed for acquiring correlated US and NIR images of the breast under focused US induction. It consists of a fully revolving multi-modality scanhead mounted on a ring frame and sliding radially to achieve optimal contact with the skin surface with minimal need for tissue compression. The ring frame slides along a linear base guide for optimal positioning on the breast in a sitting position. The scanhead consists of two focused US transducers angled at 90 degrees to define a known focal spot, and a commercial US probe directed at the focal spot. All elements within the scanhead have fixed mutual positions, but as a group can move with two DOF. An array of optical fibers, both sources and receivers, are incorporated in the scanhead. While transducers and probes are moveable within the scanhead, the optical fiber array maintains fixed position and stable contact with the skin surface. All elements of the scanhead are enclosed in an oil-filled, hermetically sealed box (i.e., a "dry" system).

The focused US subsystem is designed to be activated under computer control and below diagnostic limits. The scanner design minimizes discomfort for the patient and maximizes image correlation over time, while maintaining normal tissue and blood flow properties. After initial positioning, image acquisition does not affect tissue in a mechanical way, since no movable part of the scanhead is in contact with the breast surface. These characteristics have been shown to be critical in our prior work on demonstrating the feasibility of US-induced NIR tissue typing.

Keywords—**Near-Infrared, Focused Ultrasound, Breast Cancer.**

I. Introduction

The use of ultrasound for breast cancer detection and diagnosis is a common technique. Ultrasound is widely used due to its relatively inexpensive costs and noninvasive, nonionizing image acquisition. In general, ultrasound is sensitive to tissue density properties, although blood flow can be measured in larger vessels using Doppler techniques.

It is limited, however, to resolutions of microns in the high frequency range and millimeters in the more common frequency range of 1-10 MHz. The high frequency probes have a depth limited of several millimeters, depending on the power of the acoustic field. Common ultrasound probes can generate images of tissue several centimeters from the surface.

Near infrared (NIR) spectroscopy is another noninvasive technique being investigated for breast cancer detection and diagnosis. Like ultrasound, it is nonionizing, relying instead upon molecular and atomic absorption for contrast and image creation. Hemoglobin, both oxy and deoxy, are well documented primary absorbers in the NIR wavelength range, resulting in images most sensitive to blood volume and blood oxygen saturation.

The primary limit of NIR spectroscopy as a deep tissue imaging technique is the intense scattering of the light in this wavelength range. The large amount of scattering gives rise to deep image capabilities in the range of centimeters but also destroys the resolution, with the resolution of diffuse optical imaging (DOI) approximately one centimeter. Different configurations can generate images with resolutions on the order of a micron but such images have a depth of around 10 microns and deeper only when the scattering and absorption are reduced, i.e. the eye.

Our work has recently demonstrated another use of ultrasound, specifically stationary acoustic fields, of great potential for breast cancer diagnosis [3]. The stationary acoustic field causes blood stasis in the stationary region of the field which can be focused to a size of one centimeter. Changes in blood velocity affect the blood oxygenation level which is measured with NIR spectroscopy, providing a localized noninvasive contrast element.

This present work details a novel multi-modality delivery and image acquisition system, combining the three (two ultrasound and one NIR) aforementioned techniques. There are several groups working on dual-modality, ultra-

sound/NIR probes for breast cancer detection and diagnosis [1-2]. The probes employ different delivery mechanisms, some compress the breast between two plates and others use a specially designed dual modality probe.

Our research has observed that pressure and changes in pressure between optical probes and tissue can result in greatly distorted and constantly varying measurements of blood volume and oxygenation. This paper demonstrates a mechanized five degree of freedom (DOF) multi-modality delivery system which uses a scanhead pressed gently against the breast tissue surface in an area approximately above the questionable tissue sample (mass). The initial use of this device will be for tissue diagnosis, instead of imaging, but the design can be easily changed to accommodate imaging techniques.

II. Methods And Materials

A. Scanhead

We have designed a scanhead (Fig. 1) capable of delivering focused acoustic stationary fields up to 4 cm deep in the tissue. The two 1 MHz focused transducers are aligned in a single plane at 90 degs. The focal zone is approximately 1 cm in diameter and, with a 5 second exposure, can be shown to successfully stop blood flow. The field intensity is within the FDA diagnostic limit and generates less than 1 C local temperature increase.

The scanhead also incorporated a fiber array (not shown) similar to that proposed in Ref. 2. The fiber array is connected to a dual wavelength diode light source (680 and 830 nm) which is split into 9 fibers placed on the surface of the tissue with the scanhead. The collection fibers are combined into a single fiber which terminates at a room temperature spectroscope. The collection fibers can be separated and the sources intensity modulated for DOI.

The final component of the scanhead is a commercial ultrasound probe. The ultrasound probe is located in the same plane as the focused transducers and is used for image co-registration with the NIR spectroscopy information, tissue density information and blood flow information.

The scanhead is designed to be gently placed upon the surface of the skin, above the tumor or questionable tissue. This information is gathered with a pre-scan ultrasound or mammogram. After the scanhead is placed on the surface of the skin, the optical data collection is begun. From this point to the conclusion of the exam, the scanhead is not moved. Any motion of the tissue or the scanhead will destroy image correlation.

In order to minimize motion of the scanhead, the ultrasound probe and focused transducers are given two DOF within the scanhead in order for the focal zone to be positioned at various depths and lateral locations with respect to the tumor. This will generate a two dimensional map of the tissue surrounding and including the questionable tissue sample.

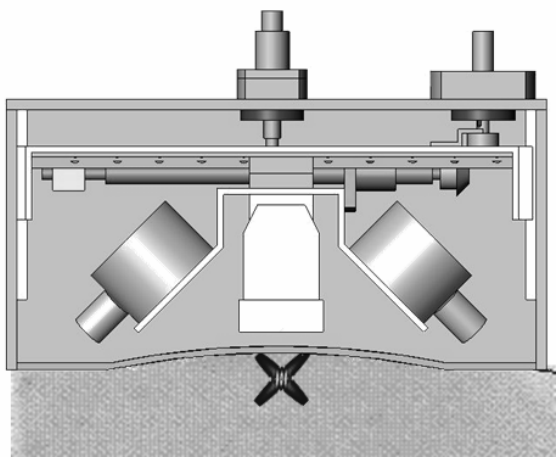

Fig. 1. The scanhead placed upon the surface of the skin. The blue and red cross is a simulated focal zone produced by the dual focused transducers aligned at 90 degrees.

B. Delivery mechanism

The delivery mechanism (Fig. 2) is capable of positioning the scanhead at any angle, depth and height. We employ a 360 degree ring assembly to rotate the scanhead around the breast. The delivery mechanism can translate the scanhead along a radial path to place the scanhead on the surface of the skin with only minor compression. Additionally, the mechanism can position the entire radial and angular elements along the lateral dimension of the breast.

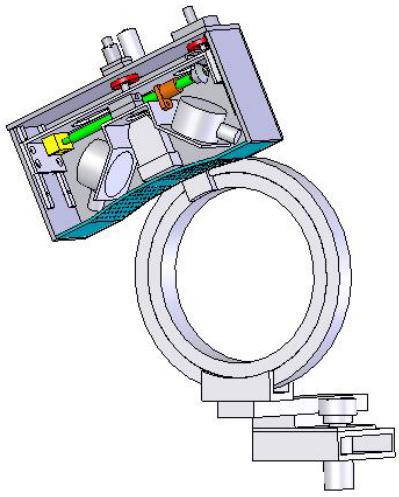

Fig. 2. The five DOF delivery mechanism including the 2 DOF within the scanhead.

III. Results

The ultrasound elements of the system have been tested using various gelatin and PVC phantoms to simulate ultra-

sound propagation in breast tissue. We have demonstrated, both with computer simulations (Fig. 3) and phantom Doppler ultrasound experiments (Fig. 4), the creation of small stationary waves zones in deep tissue with two 7 cm focused 1 MHz transducers placed at 90degs. relative to each other.

The computer simulations were conducted with Matlab, using acoustic wave characteristics [wavelength (λ = 0.15 cm), intensity (I_{SPTA} = 1 W/cm^2), focal zone dimensions, for – 6 dB, l = 1.5 cm, r = 0.3 cm)] obtained from measurements of the physical experimental setup. The computer simulation demonstrated the appearance of a stationary acoustic wave with three bands of high intensity ultrasound at distances of 0.5 λ and separated by regions of zero acoustic pressure. The bands are cylindrically symmetric, with a radius of ~ 0.3 cm.

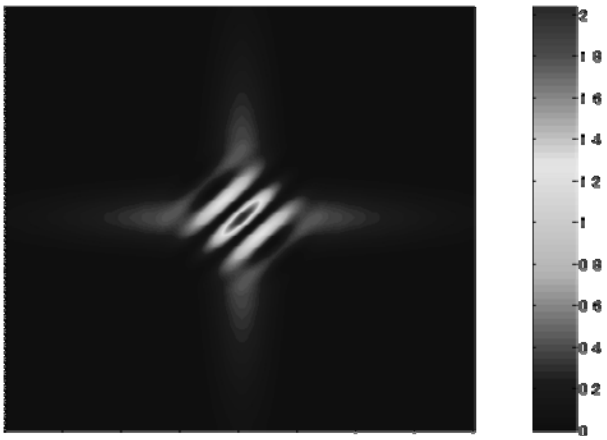

Fig. 3. Computer simulation of the variance of the overlap region of two transducers at 90 degs., calculated for two complete cycles. The diameter of the overlap region is 3λ.

The phantom measurements seen in Fig. 4 were obtained with a specially programmed GE Logiq 9, capable of producing variance Doppler images. The size of the stationary acoustic wave zone is 0.5 cm x 0.3 cm, with a dark area in the middle corresponding to the region of zero acoustic pressure. Being obtained with a Doppler probe, which is direction sensitive, it is only capable of capturing half of the stationary acoustic wave, corresponding to a single transducer. Similar images were obtained when pointing the probe along the other transducer path.

To date the optical system has been tested with computer simulations only. The wavelengths have been selected for their sensitivity to changes in hemoglobin oxygen saturation and long mean free path, which is the distance, on average, a photon travels before absorption or scattering. The simulations employed a simple multi-layer Monte Carlo

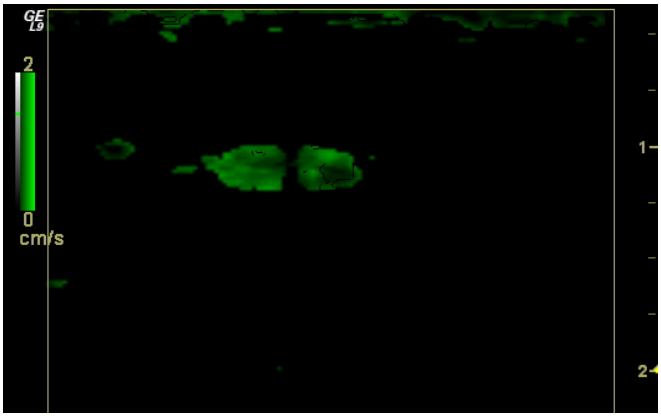

Fig. 4. A variance Doppler image of the stationary acoustic field generated by two focused 1 MHz transducers at a depth of 7 cm. The units of the labels on the right-hand side are centimeters. Notice that the size of the focal region is less than 0.5 cm x 0.3 cm. The intensity units are relative.

photon tissue migration algorithm [4]. The simple algorithm allows for various tissue layers, layer thicknesses, and user defined scattering and absorption properties for the various layers.

The reduced scattering spectra were derived with the assumption that they obey the following equation:

$$\mu_s' = b\lambda^{-a} \qquad (1)$$

where a is the scattering exponent and is generally close to 1 and b is the scattering coefficient. The absorption spectra were assumed to obey the following equation:

$$\mu_a(\lambda) = a_1\, \mu_{aHbO}(\lambda) + a_2\, \mu_{aHb}(\lambda) \qquad (2)$$

with a_1 and a_2 being the concentrations of oxy and deoxy hemoglobin, respectively, and μ_{aHbO} and μ_{aHb} being the absorption coefficient of oxy and deoxy hemoglobin at wavelength, λ. Oxy and deoxy hemoglobin absorption coefficients were compiled by Prahl [5].

The fiber array is designed to gather maximum amounts of diffuse reflected light at maximum depths. The array has various source detector separations, with the capability of sampling tissue at nearly continuous depths of < 1 cm to more than 4 cm in the region of the stationary acoustic field. The intensity of the light emitted by the source fibers at both wavelengths is 2 mW which is bright enough to travel several cm's into the tissue. The source fibers are 600 microns in diameter while the detector fibers are bundles of 600 micron multimode fibers, with a bundle diameter of ~ 0.5 cm.

Image guidance was considered a key component of the scanhead design for targeting the focused ultrasound pulse at the point of interrogation. Figure 5 shows a typical breast mass on ultrasound requiring further diagnostic work-up, for which the present system is designed. A minimally inhomogeneously hypoechoic mass was seen on ultrasound in the right breast at the 10 o'clock location, with a lobulated appearance and ill defined margin. It was a clinically occult

mass, later proven by tissue diagnosis to be a malignant breast cancer via an ultrasound-guided biopsy.

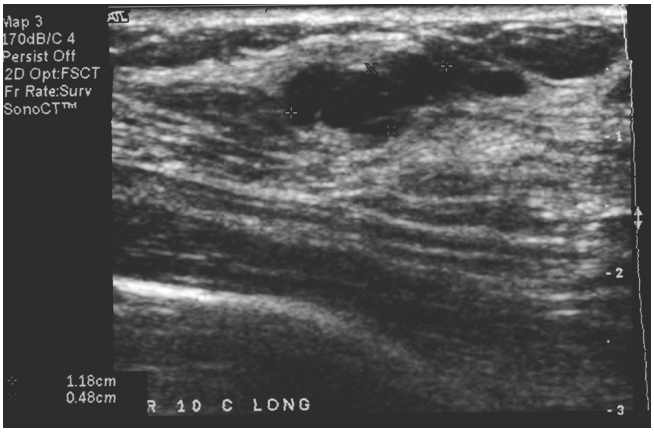

Fig. 5. Appearance of suspicious mass in breast tissue on diagnostic ultrasound, which was designed to be part of the scanhead of the present system for image guidance and precise targeting.

IV. Discussion

In current diagnosis of breast cancer and prognostic characterization during therapeutic work-up, vascular morphology, density distribution, and oxygenation status play an increasingly important role, especially in conjunction with high resolution functional imaging. In dynamic contrast-enhanced breast MRI, for example, the uptake and wash-out of contrast injection as a function of time within the first 4 – 10 min are now being widely used as diagnostic indicators to discriminate between malignant and benign breast tissues.

The rationale for discrimination on the basis of blood flow distribution and dynamics is related to vascular proliferation, the relatively chaotic network of angiogenic vessels, and extravasation in the tumor environment, and the subsequent occurrence of hypoxic regions in more advanced stages of tumor development. The clinical multi-modality scanning system reported in this paper employs focused ultrasound at a level below the FDA diagnostic ultrasound limits to manipulate blood flow and oxy-hemoglobin concentrations at the time and location of detection, causing a measurable difference in the dynamic behavior of the tissue blood supply environment as interrogated by optical spectroscopy. Although optical spectroscopy alone can in principle report relative concentrations of oxy- and deoxy-hemoglobin in vivo, it is very difficult to infer the specific location at which such information is obtained. This is because photon transport at this energy regime is dominated by scattering. We overcome this problem in the present design by measuring and imaging the *changes* in the reflectance spectrum before, during and after the activation of the ultrasound pulse; thus, the spatial resolution of the system is defined by the "focal spot" of the focused ultrasound that intersect the photon paths. This technique was demonstrated to be highly diagnostic in a murine tumor model [6,7].

V. Conclusions

Design rationale, performance specification and experimental characteristics for a novel multi-modality scanning system for breast cancer diagnosis were presented in this paper. Additional performance and safety characteristics will be documented before the system undergoes clinical studies as approved by the IRB, which will assess its diagnostic value in patients who require subsequent ultrasound-guided biopsies and tissue diagnosis for suspicion of breast cancer.

Acknowledgment

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