Dynamic Functional Imaging of the Healthy and Cancerous Breast by Optical Tomography

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Abstract: Results from dynamic functional imaging studies of the breast are presented illustrating altered states of perfusion and an imbalance in tissue oxygen supply/demand in solid tumors.
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1. Introduction

Recently we have put forward the hypothesis that optical imaging techniques that explore the temporal dynamics of the vascular response might provide a sensitive means for the detection of solid tumors and monitor their response to therapeutic intervention [1]. The biological basis supporting this idea is the finding that solid tumors in general have sluggish perfusion that can lead to, among other things, an imbalance in tissue oxygen supply/demand. In this report we have explored the ability to detect such disturbances by imposing simple respiratory maneuvers that serve to alter tissue perfusion or limit oxygen delivery in healthy individuals and subjects diagnosed with Stage II breast cancer. The evidence obtained indicates that time series imaging studies provide a simple means to detect disturbances in the vascular bed without the use of contrast agents.

2. Methods

The measuring system used for dynamic imaging studies is described in the accompanying report by Schmitz et al. [2]. Measurements were performed on subjects lying prone with the breast hanging pendent through a hole in the examination table. An adjustable hemispheric measuring head containing a 17 source × 17 detector array was used to provide direct tissue contact between the breast and the sensing fibers without the need for compression. Time series dual wavelength measurements (760, 830 nm) were performed following a contiguous four step protocol; rest, deep breathing, breath-hold, recovery. A typical study involved the collection of ~1000 images over an 8 minute time period. Image recovery was accomplished based on the recently described normalized difference method [3], and employed the modifications described in the accompanying report by Pei et al. [4]. Where appropriate, standard time series analysis techniques such as computations involving the frequency structure and time correlation measures of the time dependent pixel data were computed.

Result and Discussion:

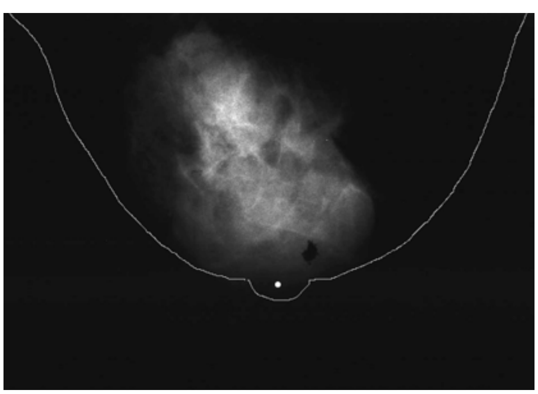

Figure 1: X–ray mammogram of the right (tumor–bearing) breast with indicated boundary (craniocaudal view).

i. Imaging of Altered Perfusion States in Solid Tumors.

To enhance possible differences in tumor perfusion from the surrounding tissue, subjects were asked to perform a series of deep breathing maneuvers all the while time series image data were being collected. This maneuver was selected as a means to modulate venous return. The expected finding is that the presence of disorganized vascular bed associated with the tumor will cause local delays in tissue perfusion and can be revealed by a spatial map of the phase of the respiratory signal. Figure 1 shows an x-ray mammogram of the subject's breast. Present is a large infiltrating carcinoma measuring 4 × 7 cm oriented from the lower media to the upper lateral regions of the breast. Figure 2 shows the corresponding phase image recovered from analysis of the Fourier spectrum of the time-series image pixel data. For comparison purposes, we also show the corresponding image derived from the healthy breast.

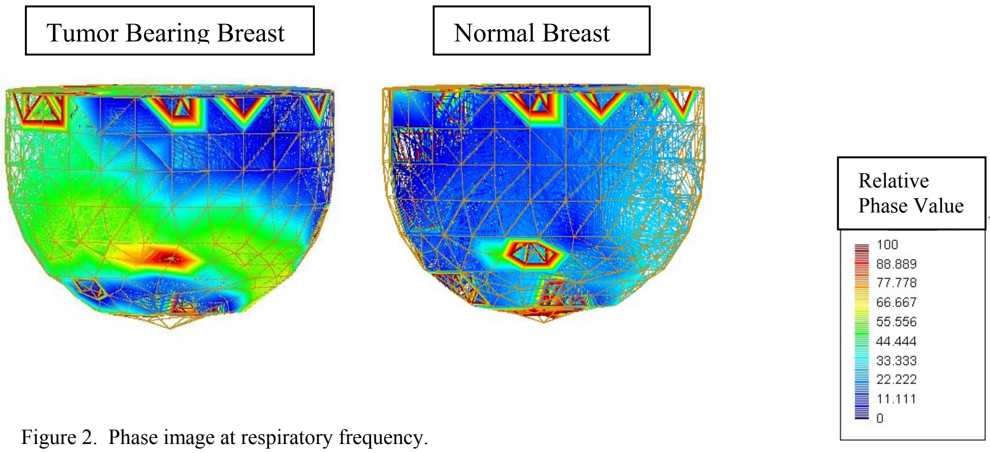

Figure 2. Phase image at respiratory frequency.

ii. Imaging of Disturbances in Tumor Tissue Oxygen Supply/Demand.

In a second patient we have perform a similar study except, following the deep breathing maneuver, the subject was asked to perform a breath-hold for a period lasting approximately one minute. The rationale for this maneuver is that the enhanced metabolic activity associated with a growing tumor, combined with a possible compromised vascular supply, could push the tumor tissue into oxygen debt causing a decline in the level of oxyhemoglobin together with a rise in the level of deoxyhemoglobin. As a measure of these trends we first computed the time series of 3D images for oxy– and deoxy–hemoglobin levels separately and from this we derived a single 3D image for each breast that reveals the time correlation value between the two hemoglobin states. A value of + 1 indicates that the two time trends are rising in-step with each other. A value of –1 indicates that one level is rising with the other is falling. The former case would suggest that accompanying the expected increase in blood volume due to pressure changes, oxygen supply/demand remains in balance. The latter case would indicate that an imbalance is occurring. Results of this study are shown in Figure 3. Note, whereas a true 3D image was computed, to better reveal interior values, the data is presented as a stacked set of slices in two different orientations. The color scale reflects the computed correlation value varying from –1 (deep blue) to +1 (dark red). The left-hand images shows the result from the non-tumor bearing breast, the

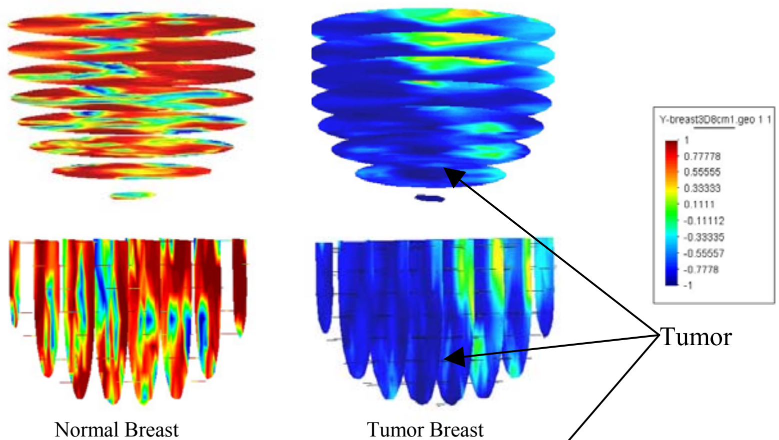

Figure 3. Time correlation image of hemoglobin states.

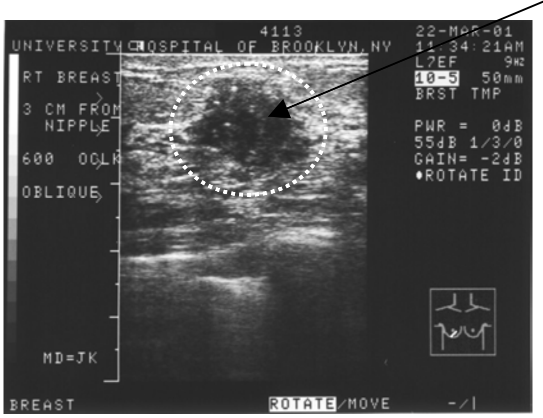

Figure 4. Sonographic image of tumor

right-hand images, the result obtained from the contralateral breast containing a 2 cm diameter tumor located behind the nipple as revealed by sonography (see Figure 4). Inspection shows that whereas most of the volume of the normal breast exhibits strong positively correlated values, the opposite is seen throughout much of the tumor-bearing breast. In addition, careful inspection of the latter figure also reveals possible evidence of features that have an arborizing structure. Although the image resolution is rather low, we interpret this as suggestive of the presence of engorged vessels, possible due to the expected changes in blood pressure upon a breath hold.

4. References

[1] R. L. Barbour, H. L. Graber, Y. Pei, S. Zhong, C. H. Schmitz, "Optical tomographic imaging of dynamic features of dense–scattering media," J. Opt. Soc. Am. A **18**, 3018–3036 (2001).

[2] C. H. Schmitz, H. L. Graber, R. L. Barbour, J. M. Lasker, A. H. Hielscher, and Y. Pei , "A real-time system for dynamic optical tomography," accompanying report.

[3] Y. Pei, H. L. Graber, and R. L. Barbour, "Influence of systematic errors in reference states on image quality and on stability of derived information for DC optical imaging," Appl. Opt. **40** 5755–5769 (2001).

[4] Y. Pei, H. L. Graber, and R. L. Barbour, "SVD–based normalized–transformed scheme for real–time DC optical tomography," accompanying report.