Phenotype-Motivated Strategies for Optical Detection of Breast Cancer

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Introduction: Blood delivery to tissue, and bulk fluid redistribution among tissue compartments, frequently are impacted by disease or trauma: for example, derangements in hemodynamic states, accompanied by increased tissue stiffness and local edema, in many breast cancer cases [1]. Accordingly, we have hypothesized that dynamic responses markedly different between diseased and healthy tissues can be induced via applied-pressure or respiratory-gas maneuvers [2,3], and that diagnostic image contrast can be thereby enhanced. Here we present results from pilot studies conducted to evaluate the hypothesis, using an instrumentation platform that facilitates the application of the considered maneuvers, while recording time-series optical measures are obtained from both breasts simultaneously [4].

Methods: Research participants were seated and the sensing heads, which contain the articulating elements used to execute the pressure maneuvers and monitor the resulting skin displacements, were adjusted to make good contact with both breasts. Following a five-minute baseline scan, the skin-optode contact pressure was alternately rapidly (~2 s) increased to a level of either 4.4 N or 7.1 N and lowered to its initial value, and data were continuously collected during the alternating periods (60-120 s duration) of stress relaxation and stress recovery. The preceding sequence was performed twice in succession, with the subject breathing room air in one cycle and a 98% O_2, 2% CO_2 in the other. The Normalized Difference Method was used to reconstruct images of oxygenated and deoxygenated hemoglobin (HbO, HbD), tissue oxygen saturation (HbSat), and blood volume (HbT) [5].

Results: Imaging results obtained from 61 subjects (17 breast cancer, 21 benign pathology, 23 healthy control) are consistent with the hypothesis that the articulation maneuvers enhance the contrast between tumor and healthy tissue. Image contrast is improved by transforming pairs of co-varying image-values to measures of the statistical extremeness for each image voxel [6], and the preceding effect is maximized by referencing the image-pixel data of one breast to the distribution of image values for the other breast. At the group level, paired differences between the numbers of image pixels identified as abnormal is greater for subjects with breast cancer than for either of the other sub-groups, for both types of maneuver. Depending on the Hb signal components and maneuver(s) considered, diagnostic accuracies for breast cancer of ranging from 85% to 97% were obtained (ROC analysis [7]).

Discussion: The controlled manipulations studied had the effect of enhancing detectability of cancer, by exploiting known tumor phenotypes. The impact of the maneuvers on reconstructed images is maximized when the image-voxel data of one breast are referenced to the distribution of image values for the contralateral breast, demonstrating the utility of the simultaneous dual-breast measurement approach.

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