Phenotype-Motivated Strategies for Optical Detection of Breast Cancer

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Abstract: Optical breast imaging studies show that controlled pressure maneuvers enhance contrast between tumors and both the surrounding healthy tissue and the contralateral breast. Our ability to detect tumors, and to distinguish them from non-cancer breast pathologies, is further improved by performing inter-breast comparisons of the reconstructed images of hemodynamic states.

Introduction: Blood delivery to tissue, and bulk fluid redistribution among tissue compartments, are frequently impaired by disease or trauma: for example, derangements in hemodynamic states, accompanied by increased tissue anoxia and local ischemia, may burden breast cancer cases [1]. Accordingly, we have hypothesized that dynamic responses markedly differ between diseased and healthy tissues, and can be induced by applied-pressure or respiratory-gas maneuvers [2,3], and that diagnostic image contrast can be thereby enhanced. (See Figure 1.)

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: Measurement data were obtained during an fNIRS-based breast imaging study that was conducted to evaluate the potential of applied pressure and respiratory-gas maneuvers to enhance discovery and characterization of breast tumors (see Figure 1). After research participants gave informed consent and provided a brief medical history (for subject population demographics, see Biomarkers for Breast Cancer Detection in the Resting-State Dynamics of the Hemoglobin Signal, this conference), they were seated and the sensing heads were adjusted to make good contact with both breasts. Following a five-minute resting baseline scan, the sequence of applied pressure and carbogen-inspiration maneuvers depicted in Figure 2 was performed.

Results: Figure 3 (Left) A representative force-vs.-time function obtained during an fNIRS recording session, with the nomenclature adopted for the time series parameterization (for articulation maneuver indicated, Right) An enlargement of the corresponding displacement-vs.-time function during the Force Relaxation expression to the articulation maneuver indicated. (At a timescale of 0.01 s between data points). A comparison of hemodynamic states changes that occurred during the articulation maneuver indicated. (See Figure 1.)

Figure 4. (a) Different degrees of spreading of image values (each colored dot represents one image voxel), indicates that the effect of applied pressure is different in the tumor-bearing (blue dots) and healthy (red dots) breasts. Strong correlation between HbSat and HbTot further supports the utility of considering this pair (among others) of hemodynamic states simultaneously. (b) A scaled value called the Mahalanobis distance (MD) (9) is a measure of association between the image values in each voxel. By introducing the novel element of referencing the data for one breast to the mean and covariance for either, the different applied force responses are presented in the result (c), whereas a conventional MD computation would tend to suppress them. For subsequent analysis of breast-cancer diagnosis potential, the MDs were computed by referencing each breast to the other. In this way, we avoid the use of any prior knowledge regarding the presence or absence of breast cancer, or of which was the affected breast.

Figure 5. MD-computation results, employing the technique (see Figure 4) of referencing data values for each breast to the mean and covariance of the other. Images of the fNIRS and HiDesoxy hemodynamic states, during the first compression maneuver, are used as input. Plotted are histograms of the MD probability density function, for selected subsets with a right-breast tumor (a), a left-breast tumor (b), and with no diagnosed pathologies in either breast (c). In each plot, the largest MD value for either breast is plotted for a value of 100, and all other MDs are adjusted accordingly.

Discussion: A wide range of differential responses, many of which serve to discriminate healthy from cancerous breasts, can be derived from hemodynamic responses during mechanical provocations (Fig 5), or from adjusting the composition of the respiratory gas (Fig 5), or from both types of maneuver performed in concert (Fig 2).

However, the large number of maneuvers employed (different pressure levels, full vs. partial compression, gas composition during the pressure application) gives rise to a large, multidimensional data mining problem. Initial tests for breast cancer diagnostic power, considering all study participants, typically yield sensitivity and specificity values of ~75% and ~80%, respectively.

Future efforts will focus on the choice of measurement time interval (Fig 3) and on the choice of breast-difference metric derived from the modified MD computations (Fig 5), as ways of improving the diagnostic sensitivity and specificity.

References:

Acknowledgements: This research was supported by the National Institutes of Health, NIH grant R24CA168102, the U.S. Army Grant DAMD1703-C-0018, the Susan G. Koman Foundation, the New York State Technology Foundation, the Research Investigator Program, the New York State Foundation for Science, Technology and Innovation, Optical Imaging for Cancer Detection Program (NYSTAR contract C402044), and NIRx Medical Technologies.