Biomarkers for Breast Cancer Detection in the Resting-State Dynamics of the Hemoglobin Signal

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Introduction: Increased tissue stiffness, presence of structural malformations, and altered perfusion of the vascular bed are known phenotypic markers for the presence of breast cancer [1,2]. Awareness of these phenomena has motivated our development of instrumentation platforms that can explore the naturally occurring dynamics of the hemoglobin signal. The dimensionality of the information space that could be explored has prompted us to consider simplified data-collection conditions. An example is a simple resting-state measure, wherein time-series optical measures are obtained from both breasts simultaneously under defined conditions of optode contact [3]. As evidenced by the reported results, promising findings have been obtained based on examination of the resting-state responses.

Methods: Data were obtained during an fNIRS-based breast imaging study conducted primarily to evaluate the potential of applied-pressure and respiratory-gas maneuvers to enhance discovery and characterization of breast tumors. These maneuvers were preceded by a five-minute resting baseline scan. For analysis, a high-pass filter (frequencies > 0.01 Hz) was applied, followed by use of the Normalized Difference Method to reconstruct images of oxygenated and deoxygenated hemoglobin, tissue oxygen saturation, and blood volume [4]. The 4D image time series were reduced to scalar metrics by computing: first, the temporal standard deviation (TSD) in each image voxel ($4D \rightarrow 3D$) or the spatial mean (SM) or standard deviation (SSD) for each image time frame ($4D \rightarrow 1D$); second, the spatial mean and standard deviation of TSD, temporal mean of SSD, and temporal standard deviation of SM and SSD.

Results: In most unilateral breast cancer cases the TSD metric in is larger in the tumor-bearing breast, and the region of elevated TSD extends well beyond the known structural borders of the tumor. Corresponding results for cases of benign breast lesions, or no known breast pathology, do not show a comparable asymmetry. In group-level comparisons, all scalar metrics have larger values in the tumor-bearing breast, and show little inter-breast disparity in non-cancer subjects. Using the left-to-right-breast ratio of metric values for bilateral comparisons, there are highly significant group-mean differences between the non-cancer and breast-cancer groups. ROC analysis [5] yields area-under-curve values in the range of 74-86%, sensitivities in the range of 70-84%, and specificities in the range of 76-92%.

Discussion: While the elevated TSD metric extends into regions far from the structural borders of the tumor, imaging results derived from fNIRS data collected during response to either applied-pressure [3] or respiratory-gas [6] maneuvers have shown that tumor locations and sizes can be accurately extracted from the latter. This suggests that resting-baseline recordings are sensitive to dynamic vascular phenomena that do in fact extend over a large percentage of the breast volume. A potentially significant corollary is that it may be possible to conduct breast-cancer screening by means of a simplified bilateral measurement involving a small number of probes distributed over the surface of both breasts.

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