Derivation and validation of metrics for breast cancer screening from diffuse optical tomography imaging data


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Introduction

- Dynamic Near-Infrared Optical Tomography (DYNOT)
- Provides measures of relative concentrations of hemoglobin (Hb)
- Oxygenated, deoxygenated, total
- Non-invasive functional imaging in vivo
- Exogenous contrast agents not required
- Growth of solid tumors frequently accompanied by:
  - Marked changes in the vascular supply sustaining tumor growth
  - Marked relative hypoxic environment

To image the preceding, we developed:
- A dual-bread diffuse optical tomography (DOT) imaging system
- Capable of simultaneous distance measurement

Measuring Head (1st-Generation) for Simultaneous Dual-Bread Imaging

- DYNOT simultaneous dual-bread imaging
  - Each optical fiber (2 in each) in both sources and detectors for full light path
  - Data collected from 124 channels (22 pairs, 3 wavelengths) in parallel
  - Sources location is time multiplexed
  - Measurement rate: 2 complete image frames (< 1 ms) data (peak) per second

Clinical Study Design

1. Subject population
   - Resting state—subjects whose data are used for derivation of breast-cancer diagnostic metrics
   - Prophylactic—subjects whose data are used for testing and validation

2. Analysis of dual-bread DOT image time series (continued)
   - Assessment of sensitivity, specificity, and negative predictive values
   - Univariate, parametric, and non-parametric tests for difference between mass/CA and non-CA subgroups of the training set
   - Multivariate: linear regression (LR)
     - Use leave-one-subject-out cross-validation (LOOCV) to determine sensitivity to subject variability
   - Validate the procedures that are most successful with respect to the retrospective group, comparing data to the data for the prospective group
   - Aggregates (averages) for 2 or more multivariate predictors
     - The total number of aggregates is 2 + W, where W = number of predictors
   - For each subject, the aggregate breast-cancer probability is the average of the separate probabilities according to the n multivariate predictors
   - For sensitivity and specificity calculations, a breast-cancer probability of 0.5 is taken as the diagnostic threshold

Physiological Hypotheses

- There are mechanisms by which a cancerous tumor’s "volume of influence" may be appreciably larger than the tumor itself
- This is the consequence of widespread differences between vascularity in cancerous solid tumors, healthy tissue, and/or non-cancerous pathologies
- Regional hypoxia
  - Reduced blood delivery to the tumor
  - Oxygenation levels are a function of the distance from the tumor
- Increased blood flow
  - Increased oxygen desaturation of Hb

Conclusions

1. Prognosis group results show that the derived multivariate metrics do
   - Detect increases in the image data that are related to breast cancer status, and not just to any dysmorphic properties of the retrospective group
2. The observation that the inter-bread differences have the predicted directly implies that our assumptions, regarding the effects of tumor hypoxia and increased growth on the dynamic properties of the vasculature, are largely correct
3. The successful application of metrics derived by spatial integration of DOT image data implies that the vascular correlates of tumor growth and development are present over a volume that extends a substantial distance beyond the histological margins of the tumor
4. The prospective conclusion, plus the suggestive sugggests that results from preliminary assessment of the visualization of the DOT data (Hb, H-boxy) can give a functional view of inter-observer fluctuations of breast types (diagnostic, histology, tumor-refuser findings) should be more fully explored (NH17-114)