Tumor detection by simultaneous bilateral diffuse optical tomography (DOT) breast imaging


Physiological Insight → Clinical Study Design (cont.)

- Three categories of diagnostic metrics (cont.)
  - Group 3: Measures of pressure-induced blood volume and oxygenation shifts
  - Computes from data collected during Validation maneuver
  - Awa re sensitive to venous congestion and release functional imaging in venous
  - In the TBB, relative to the contralateral TFB, one would expect to see:
    - Increased oxygenation and decreased perfusion
    - Increased blood volume change
    - Time-lagged responses

- Essential strategy for image time series analysis: Figure 1
- Differences between metric values, for each subject’s two breasts, are calculated as:
  - Tumor minus non-tumor for training-set cancer subjects
  - Left minus right for training-set non-cancer subjects, and for validation-set subjects
  - Each metric is converted into six candidate diagnostic parameters, by normalizing the inter-breast difference in a variety of ways:
    - Difference divided by larger, smaller, or average value of the two individual-breast values
    - Difference multiplied by larger, smaller, or average of the individual-breast values
    - Assessment of sensitivity (SH), specificity (SP), positive and negative predictive values (PPV, NPV)
  - Univariate: variability-sensitive test for difference between means of CA and non-CA-subgroups of the training set
  - Spots-check with non-parametric Mann-Whitney test, to ensure that small sample sizes do not bias the test

- Multivariate: regression-sensitive (LR)
  - Initial model is a linear combination of all univariate predictors that yield statistically significant differences between the sub-group means
  - Use a LR algorithm to find the optimal coefficients for the model
  - Remove redundant metrics (i.e., eliminate least significant metric from the model and repeat LR computation)
  - Use leave-one-out cross-validation (LOOCV) to determine sensitivity to differences in the test set

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Clinical Study Results

- Patient population: 37 volunteers
- 14 with breast cancer and 23 healthy controls
- Groups are matched in terms of age and body-mass index
- Heterogeneous control group: includes healthy subjects and subjects having non-cancer breast pathologies
- Data are processed [4,5] to produce time series of volumetric images for each state parameter: [Box-Cox, Hanning, Hanning, and Hanning Bar]

- Univariate Analysis
  - SH, SP, PPV, NPV (range: minimum, maximum, mean) are summarized in Table 1
  - Range includes all univariate metrics
  - Whether or not they show a statistically significant sub-group mean difference
  - For the metrics that are statistically significant predictors, predictive values range from 57% to 91%
  - Mean predictive values range from 60% to 86%, when each metric Group is considered separately
  - Taking all Metric Groups collectively, mean PPV is 69% and mean NPV is 81%

- Multivariate Analysis
  - SH, SP, PPV, NPV (range: minimum, maximum, mean) are summarized in Table 2
  - Predictive models including Group 3 metrics can consider only 21 subjects
  - Models including only Group 1 and/or 2 metrics include all 37 subjects
  - Composite clinical predictive values can increase markedly, relative to the constituent univariate predictors (UPs)
  - Range is from 82% to 100%
  - Best-case composite having minimum values >95% for each of SH, SP, PPV, and NPV

- Validation Study
  - Compute values UPs, for the subjects in the validation set
  - Combine new UP values with multivariate-predictor coefficients derived from the training-test subjects
  - Compute a probability of CA for each validation-subset (event) subject

Table 1. Diagnostic Measures for Group 1 - 3 Data  Minimum – Maximum (Mean)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbOxy</td>
<td>42.9-78.6 (59.8)</td>
<td>56.5-95.7 (82.6)</td>
<td>44.4-88.9 (69.8)</td>
</tr>
<tr>
<td>Hbdeoxy</td>
<td>42.9-78.6 (59.8)</td>
<td>56.5-95.7 (82.6)</td>
<td>44.4-88.9 (69.8)</td>
</tr>
<tr>
<td>HbTotal</td>
<td>42.9-78.6 (59.8)</td>
<td>56.5-95.7 (82.6)</td>
<td>44.4-88.9 (69.8)</td>
</tr>
</tbody>
</table>

Table 2. Summary of Multivariate Analysis Results

<table>
<thead>
<tr>
<th>Model</th>
<th>n</th>
<th>PPV</th>
<th>NPV</th>
<th>Sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>21</td>
<td>70.6%</td>
<td>97.5%</td>
<td>82%</td>
<td>92%</td>
</tr>
<tr>
<td>Group 2</td>
<td>21</td>
<td>70.6%</td>
<td>97.5%</td>
<td>82%</td>
<td>92%</td>
</tr>
<tr>
<td>Group 3</td>
<td>21</td>
<td>70.6%</td>
<td>97.5%</td>
<td>82%</td>
<td>92%</td>
</tr>
<tr>
<td>Group 4</td>
<td>21</td>
<td>70.6%</td>
<td>97.5%</td>
<td>82%</td>
<td>92%</td>
</tr>
</tbody>
</table>

References


Acknowledgments

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