Intraoperative Optical Breast Tissue Characterization Device for Tumor Margin Assessment

J. Quincy Brown, Ph.D.¹, Torre M. Bydlon, B.S.¹, Stephanie A. Kennedy, B.S.¹, Lisa Richards, B.S.¹, Marlee S. Junker, M.S.¹, Gregory M. Palmer, Ph.D.², Joseph Geradts, M.D.³, Lee G. Wilke, M.D.⁴ and Nirmala Ramanujam, Ph.D.¹

¹ Dept. of Biomedical Engineering, Duke University
² Dept. of Radiation Oncology, Duke University Medical Center
³ Dept. of Pathology, Duke University Medical Center
⁴ Dept. of Surgery, Duke University Medical Center

San Antonio Breast Cancer Symposium
Poster Discussion Session 8
December 13, 2008
**Problem:** Cancer is not Always Completely Removed during Surgery

**US Breast Cancer Incidence**
- 250,000 Women

**Stage 0, I, II Breast Cancer**
- 215,000 Women

**BCS Instead of Mastectomy**
- 180,000 Women

**Surgery (lumpectomy)**
- 20-70% require a 2nd surgery!\(^1\)

Optical contrast in the breast

**Oxygenation/ Metabolism**
- Hemoglobin oxygenation
- Total hemoglobin content
- Redox ratio
- Porphyrins

**Cellular proliferation / death**
- Size, density of cellular components

**Extracellular matrix**
- Collagen (stroma)
- β-carotene (adipose tissue)

info.med.yale.edu/intmed/cardio/imaging/anatomy/breast_anatomy/
Our Solution: Handheld Optical Spectral Imaging Probe

I. Tumor margins imaged with probe array
II. Informative margin maps
III. Margin Classification & Feedback to Surgeon

Study endpoint: *In 150 patient study, estimate the reduction in missed positive margins, and unnecessary tissue removal, that intra-operative use of the probe would provide.*
## Current Methods for Intra-operative Margin Assessment

<table>
<thead>
<tr>
<th>Method / Technology</th>
<th>Touch-Prep</th>
<th>Frozen Section</th>
<th>Optical Imaging Probe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologist required in OR?</td>
<td>Yes</td>
<td>Yes</td>
<td>Pathologist not required</td>
</tr>
<tr>
<td>Percentage of Margin Examined</td>
<td>~100%</td>
<td>&lt;1%</td>
<td>Entire margin</td>
</tr>
<tr>
<td>Time Required</td>
<td>~20 min</td>
<td>~20 min</td>
<td>&lt; 20 min</td>
</tr>
<tr>
<td>Interferes with pathology?</td>
<td>No</td>
<td>Yes</td>
<td>Non-destructive</td>
</tr>
<tr>
<td>Problematic with fatty tissues</td>
<td>No</td>
<td>Yes</td>
<td>Able to use on all tissues</td>
</tr>
<tr>
<td>Sensing Depth</td>
<td>Surface only</td>
<td>Up to 2 cm (focal)</td>
<td>1 - 2mm (standard of care)</td>
</tr>
</tbody>
</table>
Image Analysis and Predictive Model

A) Positive Margin

B) Positive Margin

C) Negative Margin

D) Negative Margin

ROC curve from cross-validated predictive model

Sensitivity = 80%
Specificity = 67%
AUC = 0.77
# Margin Classification Performance

(Results from 50 patients)

### Surgeon

<table>
<thead>
<tr>
<th></th>
<th>Path Positive</th>
<th>Path Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted Positive</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>Predicted Negative</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>34</strong></td>
<td><strong>21</strong></td>
</tr>
</tbody>
</table>

Sensitivity: 56%
Specificity: 24%

### Surgeon + Probe

<table>
<thead>
<tr>
<th></th>
<th>Path Positive</th>
<th>Path Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted Positive</td>
<td>32</td>
<td>7</td>
</tr>
<tr>
<td>Predicted Negative</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>34</strong></td>
<td><strong>21</strong></td>
</tr>
</tbody>
</table>

Sensitivity: 94%
Specificity: 67%

Use of the probe in conjunction with the surgeon’s judgment would result in:

- >7-fold reduction in false-negatives
- >2-fold reduction in false-positives
Summary and Conclusions

• Quantitative optical spectral imaging provides molecular composition maps of the specimen surface

• Imaging technology allows rapid, intra-operative coverage of the entire specimen surface

• Results from 50 patients show that in combination with the surgeon’s judgment, the probe reduces missed positive margins by 87% and unnecessary tissue removal by 56%
  – The probe alone reduces missed positives by 56% and unnecessary tissue removal by 53%

• Technology has a sensing depth (2 mm) that is consistent with standard-of-care pathology