Optical Intra-operative Assessment of Breast Tumor Margins

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Current Paradigm: Breast Conserving Surgery (BCS)

A positive margin is predictive of local recurrence

20 - 50% of women return for surgery

References:
Our Solution: Diffuse Reflectance Spectroscopy

EM SPECTRUM (METERS)

- NIR
- Visible
- Ultraviolet
- "Sort" X Rays
- "Hard" X Rays
- Infrared
- Gamma Rays

BREAST

- Cell scattering
- Blood absorption
- β-carotene absorption

Breast Cancer Changes³

- β-carotene absorption
- Blood absorption
- Scattering

Clinical Procedure
# Patient Demographics

<table>
<thead>
<tr>
<th>Characteristics of the Study Population</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (average)</td>
<td>57 (Range 30-78)</td>
</tr>
<tr>
<td>Primary Tumor Histology</td>
<td></td>
</tr>
<tr>
<td>Invasive Ductal</td>
<td>8 (17%)</td>
</tr>
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<td>Ductal Carcinoma in Situ</td>
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</table>
Representative Margin Image

DCIS

Adipose

[β-carotene] / scattering

Margin Size (mm)

Margin Size (mm)
Margin Level Histograms

[β-carotene] / scattering

Positive Margin

Negative Margin
Results of Prediction Algorithm

**Predictors**
- % of pixels < 6 \([\beta\text{-carotene}] / \text{scattering}\)
- % of pixels < 8 \([\text{THb}] / \text{scattering}\)

### Table: Predictors and Sensitivity/Specificity

<table>
<thead>
<tr>
<th></th>
<th>All Margins</th>
<th>Positive, IDC</th>
<th>Positive, DCIS</th>
<th>Positive, Other</th>
<th>All Positive</th>
<th>All Close</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Path Positive</td>
<td>Path Negative</td>
<td>Path Positive</td>
<td>Path Positive</td>
<td>Path Positive</td>
<td>Path Close</td>
</tr>
<tr>
<td>Probe Positive</td>
<td>27</td>
<td>7</td>
<td>11</td>
<td>8</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Probe Negative</td>
<td>7</td>
<td>14</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>79.4%</td>
<td></td>
<td>78.6%</td>
<td>88.9%</td>
<td>72.7%</td>
<td>82.4%</td>
</tr>
<tr>
<td>Specificity</td>
<td>66.7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</table>

\[\text{AUC} = 0.77\]

\[^4\] Wilke et al. *Rapid Non-invasive Optical Imaging of Tissue Composition in Breast Tumor Margins*. American Journal of Surgery. Accepted for publication.
Site Level Sources of Contrast

- Total Hb ($\mu$M)
  - Non-malignant: n=593
  - Malignant: n=27
  - p < 0.0002

- $\beta$ ($\mu$M)
  - Non-malignant: n=593
  - Malignant: n=27
  - p = 0.7

- $\mu_s$ (cm$^{-1}$)
  - Non-malignant: n=593
  - Malignant: n=27
  - p = 0.3

- Total Hb/$\mu_s$ ($\mu$M*cm)
  - Non-malignant: n=593
  - Malignant: n=27
  - p < 0.0008

- Beta/$\mu_s$ ($\mu$M*cm)
  - Non-malignant: n=593
  - Malignant: n=27
  - p = 0.4
# Summary and Conclusions

<table>
<thead>
<tr>
<th>Method / Technology</th>
<th>Optical Imaging Probe</th>
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<tr>
<td>Pathologist required in OR?</td>
<td>Pathologist not required</td>
</tr>
<tr>
<td>Percentage of Margin Examined</td>
<td>Entire margin</td>
</tr>
<tr>
<td>Time Required</td>
<td>&lt; 20 min</td>
</tr>
<tr>
<td>Interferes with pathology?</td>
<td>Non-destructive</td>
</tr>
<tr>
<td>Problematic with fatty tissues</td>
<td>Able to use on all tissues</td>
</tr>
<tr>
<td>Sensing Depth</td>
<td>Up to 2mm</td>
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<tr>
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Our optical imaging device has the potential to significantly impact breast cancer treatment during BCS.
Our Team and Sponsors

Lee Wilke  
Surgery

Nimmi Ramanujam  
Biomedical Engineering

Joseph Geradts  
Pathology

Bill Barry  
Bioinformatics and Statistics

Quincy Brown

Jennifer Gallagher

Lisa Richards

Marlee Junker

Duke Translational Medicine Institute

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CTSA Clinical & Translational Science Awards  
National Institutes of Health  
National Cancer Institute
Extra Slides
Solution: Light can Detect Positive Breast Tumor Margins in the O.R.

- 180,000 women
- Surgeons removes tumor
- Optical Device
- Post-op pathology of tumor margins
- New Practice
- 75,000 women return for re-operation
- < 37,000 women return for re-operation

Current Practice

- 75,000 women return for re-operation
- Post-op pathology of tumor margins
- Surgeons removes tumor
- 180,000 women
a. Margin dots
   - Green: Margin dots
   - Red: Research dots

   3mm

b. Transverse 3mm slice containing dots 1 & 3

c. Embed dot 1 in Paraffin Block

d. H&E stained slide for pathological review
Problem: Re-excision Rate of BCS

20 - 40% of women return for surgery

– Not all cancers are solitary “masses”
– Intra-operative specimen mammograms do not show the “extent” of microscopic disease
– “In-situ” or Stage 0 cancers cannot be felt or seen by the surgeon

Intra-operative Frozen Section/Touch Prep Cytology reduce re-excision rate to 20% but are not widely adopted

– A minority of hospitals have an on-site surgical pathologist with expertise in evaluating fatty breast tissue
– Greater than 20 minutes is required to evaluate all 6 sides of a breast specimen

All patients still undergo post-operative pathology


The Clinical Device

- Computer + software
- Xenon lamp + monochromator
- Probe interfaced with tissue
- Tissue interface
- Spectrograph
- CCD
### Characteristics of the Study Population

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<td><strong>Estrogen Positive</strong></td>
<td>38 (79%)</td>
</tr>
<tr>
<td><strong>HER-2/neu Positive</strong></td>
<td>6 (13%)</td>
</tr>
<tr>
<td><strong>Node Positive</strong></td>
<td>13 N1 (27%)</td>
</tr>
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<td><strong>Surgical Re-excision Rate</strong></td>
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<td><strong>Neoadjuvant Therapy</strong></td>
<td>Chemotherapy 6 (13%); Endocrine 2 (4%)</td>
</tr>
<tr>
<td><strong>Lumpectomy Volume (average)</strong></td>
<td>513 cm³ (Range 93-2237 cm³)</td>
</tr>
<tr>
<td><strong>Margins Assessed</strong></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>14 (25%)</td>
</tr>
<tr>
<td>Posterior</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>Superior</td>
<td>12 (22%)</td>
</tr>
<tr>
<td>Inferior</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Medial</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>Lateral</td>
<td>4 (7%)</td>
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