Real-time, intraoperative detection of residual breast cancer in lumpectomy cavity margins using the LUM Imaging System: Results of a feasibility study

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BACKGROUND
- Tumor-free margins are critical for local control in breast conserving surgery
- 20-40% of lumpectomy patients have positive margins that require surgical re-excision
- Tools are needed to identify residual cancer in the tumor cavity intraoperatively
- We assessed LUM015 (protease-activated dye) and the LUM2.6 Imaging System for intraoperative detection of residual tumor in the tumor cavity of breast cancer patients

METHODS
- Breast cancer lumpectomy patients were injected with 1.0 mg/kg LUM015 4±2 hours prior to surgery
- Standard lumpectomy was performed
- All lumpectomy cavity surfaces were imaged with the handheld probe
- Areas of high-fluorescence were detected, analyzed, and excised. Lumicell images and standard histopathology were compared (Figure 3)
- 2.6 cm diameter image acquisition, analysis and display required only ~1 second

RESULTS

Table 1
<table>
<thead>
<tr>
<th>Patient Demographics (n=45)</th>
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<tbody>
<tr>
<td>Median age (years)</td>
</tr>
<tr>
<td>Invasive carcinoma</td>
</tr>
<tr>
<td>Ductal Carcinoma in situ (DCIS) only</td>
</tr>
<tr>
<td>Mean tumor size (cm)</td>
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Figure 2: LUM optical head with sterile barrier

Figure 3: LUM Imaging compared to Standard Histopathology

- Invasive ductal, invasive lobular, and ductal carcinoma in situ lesions were visualized
- Tumors were visualized in pre- and post-menopausal women
- 569 cavity margin surface images were evaluated
  - 100% sensitivity
  - 73% specificity
- Signal was observed in some benign tissue (~15%) including:
  - Macrophages associated with healing biopsy sites
  - Fibrocytic changes with usual ductal hyperplasia and cysts
- 8 of 45 patients had positive margins by standard histopathology, corresponding LUM intraoperative readings are shown in Table 2
- 1 adverse event: extravasation of LUM015 during IV injection
- Blue staining of the forearm that resolved in ~3 months

Table 2
<table>
<thead>
<tr>
<th>Positive margin histopathology reading</th>
<th>LUM Imaging result of cavity beyond margin</th>
<th>Action taken</th>
<th>Tumor found in resected tissue</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCIS &lt;2mm from Ink</td>
<td>LUM guided shave</td>
<td>+</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>DCIS &lt;2mm from Ink</td>
<td>LUM guided shave</td>
<td>-</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>DCIS &lt;2mm from Ink</td>
<td>Re-excision</td>
<td>+</td>
<td>B</td>
<td>B</td>
</tr>
<tr>
<td>IDC on Ink</td>
<td>Re-excision</td>
<td>+</td>
<td>(mastectomy)</td>
<td>B</td>
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</table>

RESULT - A: Residual tissue presented. B: Surgeon declined to take additional lumicell-guided margin. C: No tumor found in second surgery, LUM Imaging System predicted negative margin.

Figure 1: LUM Imaging System in use

Figure 2: LUM optical head with sterile barrier

CONCLUSIONS
- No positive margins containing invasive cancer or DCIS were missed by the LUM Imaging System
- Taking Lumicell guided margins prevented re-excision surgeries
- A multi-center Phase III/Pivotal clinical trial of this approach is funded and will start shortly

ACKNOWLEDGEMENTS
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- Lumicell provided training for the LUM System and conducted the imaging data analysis
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