Feasibility of the LUM Imaging System for real-time, intraoperative detection of residual breast cancer in lumpectomy cavity margins

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INTRODUCTION

- 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
- There is a significant unmet need for tools to identify residual tumor at lumpectomy margins during the initial surgery
- We assessed LUM015 (optical contrast agent) and the LUM2.6 Imaging Device, for real-time, intraoperative detection of residual tumor in breast cancer patients

METHODS

- 40 Patients were enrolled following IRB and FDA approval
- Auto-fluorescence group: 25 patients without LUM015 injection had ex-vivo imaging of excised breast specimens
- Study group: in vivo imaging of lumpectomy cavity margins
  - 5 control patients, no LUM015 injection
  - 10 patients injected with LUM015, a cathepsin-activatable fluorescent agent, 2-6 hrs prior to surgery at 0.5 mg/kg or 1.0 mg/kg
- Lumpectomy cavity walls were scanned in vivo and shaved cavity margins (SCM) were imaged using the LUM system
- Sites of fluorescence were correlated with histopathology

RESULTS

- 40 Patients were enrolled following IRB and FDA approval
- Auto-fluorescence group: 25 patients without LUM015 injection had ex-vivo imaging of excised breast specimens
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LUM system achieved 100% detection of residual cancer

<table>
<thead>
<tr>
<th>In vivo positive margin</th>
<th>Ex vivo detection Invasive Ductal</th>
<th>Ex vivo detection DCIS</th>
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<tbody>
<tr>
<td>A1</td>
<td>B1</td>
<td>C1</td>
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<tr>
<td>Residual fluorescence in the lumpectomy cavity (in vivo) correlated with residual IDC in the corresponding cavity shaved margin</td>
<td>High fluorescence in a 1.9 cm region from an ex vivo lumpectomy transaction correlated with tumor configuration on pathology</td>
<td>Two sub-millimeter spots separated by 0.1 cm identified by the LUM Imaging System corresponded to 2 foci of DCIS</td>
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Figure 1: Representative histopathology and correlated intraoperative LUM image in vivo (A1 – A2) and ex vivo (B1 – B2, C1 – C2)

- 100% sensitivity for tumor detection at or near the margin (<2mm)
- No false negative readings
- Invasive ductal, invasive lobular, and DCIS lesions were visualized
- Tumors were visualized in pre-and post-menopausal women
- 2 study lumpectomies (20%) had positive margins with 'ink on tumor' on standard histopathology and underwent re-excision
- In both cases the LUM system correctly identified residual tumor in lumpectomy cavity walls during the initial surgery
- Re-excision pathology confirmed residual tumor
- Signal was observed in some benign tissue
- Tumor associated macrophages
- Some fibrocystic lesions
- Refinement of detection algorithms are under way

CONCLUSIONS

- LUM015 is tumor selective, safe in humans, and demonstrated 100% sensitivity for tumor detection in a pilot study
- The LUM system is a promising tool for real-time detection of residual breast cancer during lumpectomy surgery for breast cancer
- These results support our ongoing feasibility trial using the LUM Imaging System to guide the extent of lumpectomy margin resection in breast cancer patients (NCT02438356)

ACKNOWLEDGEMENT

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- Luminicell provided training for the use of the LUM system and performed the imaging data analysis for this study