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

Patient Demographics: LUM015 injection

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<tr>
<th>Median age</th>
<th>61 years (range 48-78)</th>
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<tbody>
<tr>
<td>IDC with DCIS</td>
<td>70% (7/10)</td>
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<tr>
<td>IDC + ILC with DCIS</td>
<td>10% (1/10)</td>
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<tr>
<td>DCIS only</td>
<td>20% (2/20)</td>
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<tr>
<td>Mean tumor size</td>
<td>1.6 cm (range 0.4-2.5)</td>
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• Image acquisition for each margin required approximately 1 second with a 2.5 cm field of view
• Total scanning time for entire lumpectomy cavity was ~1 minute
• No significant baseline breast tissue auto-fluorescence
• No adverse effects in patients injected with LUM015

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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<td>Residual fluorescence in the lumpectomy cavity (in vivo) correlated with residual IDC in the corresponding cavity shaved margin</td>
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<td>High fluorescence in a 1.9 cm region from an ex vivo lumpectomy transaction correlated with tumor configuration on pathology</td>
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<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 images in vivo (A1 – A2) and ex vivo (B1 – B2, C1 – C2)

Figure 2: Mean fluorescent signal based on LUM015 dosage and tissue type

Figure 3: LUM system in use

LUM System performance

• 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

ACKNOWLEDGEMENT

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• Lumicell provided training for the use of the LUM system and performed the imaging data analysis for this study.