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

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Rai U[1], Tang R[1], Plichta JK[1], Merrill AL[1], Rice-Stitt T[1], Gadd MA[2], Specht MC[1], Brachtel EF[2], Smith BL[1]

From the [1]Departments of Surgical Oncology and [2]Pathology at Massachusetts General Hospital, Boston, MA

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

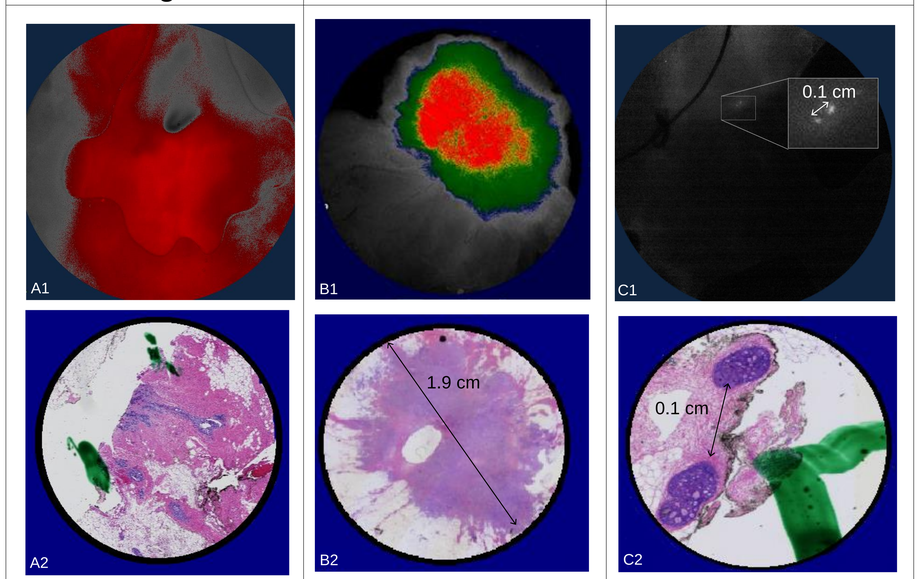
- 40 Patients were enrolled following IRB and FDA approval
- Auto-fluorescence group: 25 patients without LUM015 injection had ex-vivo imaging of excised breast specimens
- Study group: in vivo imaging of lumpectomy cavity margins
  - 5 control patients, no LUM015 injection
  - 10 patients injected with 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	
Median age	61 years (range 48-78)
IDC with DCIS	70% (7/10)
IDC + ILC with DCIS	10% (1/10)
DCIS only	20% (2/20)
Mean tumor size	1.6 cm (range 0.4-2.5)

- **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



Residual fluorescence in the lumpectomy cavity (in vivo) correlated with residual IDC in the corresponding cavity shaved margin

High fluorescence in a 1.9 cm region from an ex vivo lumpectomy transection correlated with tumor configuration on pathology

Two sub-millimeter spots separated by 0.1 cm identified by the LUM Imaging System corresponded to 2 foci of DCIS

Figure 1: Representative histopathology and correlated intraoperative LUM image in vivo (A1 – A2) and ex vivo (B1 – B2, C1 – C2)

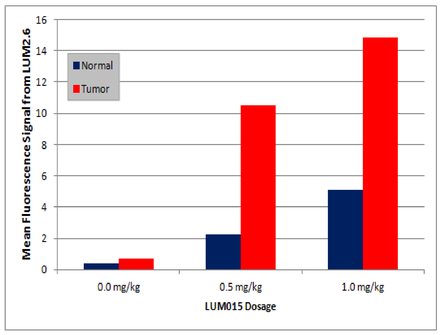


Figure 2: Mean fluorescent signal based on LUM015 dosage and tissue type

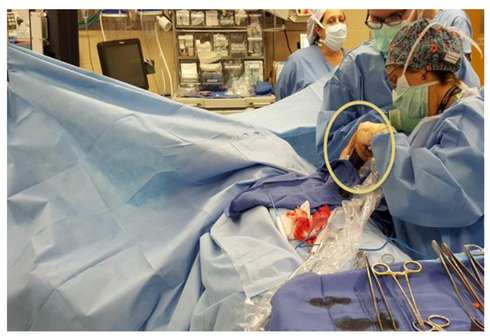


Figure 3: LUM system in use

RESULTS

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 (NCT02438358)

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