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Intraoperative fluorescent imaging detects cancer cells at tumor margins and lymph nodes

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Background:
Over half a million patients undergo cancer surgery each year. Positive margins and metastatic cancer deposits remain the single greatest challenge facing the Surgical Oncologist. In the operating room, surgeons have been limited by their eyes, hands and to ensure complete resection. We have developed a novel technology to fluorescently label tumor cells before surgery. We hypothesized that by fluorescently labeling tumor cells, surgeons can obtain better disease clearance of cancer deposits during surgery.

Methods:
A pilot study was performed on 10 consecutive patients with biopsy proven pulmonary adenocarcinoma. Preoperatively, these patients were injected with a folate molecule conjugated to fluorescein. A standard of care thoracotomy was performed and the chest cavity was inspected using a dual camera imaging system to identify tumor cells in the primary mass, lymph nodes and metastatic implants. After resection, the entire chest

cavity was again inspected for residual disease. Suspicious implants were biopsied. Histopathology and flow cytometry was used to validate all findings.

Results:
We found 9 out of 10 patients had folate (+) pulmonary adenocarcinomas. Imaging before surgery correctly identified all tumors (Figure 1). In addition, it identified metastatic disease in the lymph nodes of 3 out of 9 patients. Following standard of care pulmonary resection, intraoperative imaging detected one positive margin, which was thought to be disease-free by the surgeon. Histopathology confirmed all margins and lymph nodes. Flow cytometry demonstrated folate receptor alpha was present in >50% of the tumor cells in 9 out of 10 patients.

Conclusion:
Intraoperative fluorescence-guided surgery is safe and feasible. This approach can delineate tumor cells in primary lesions and lymph nodes and assist the surgeon in disease clearance. This represents a first in-human application for thoracic malignancies and will be broadly applicable in the future.
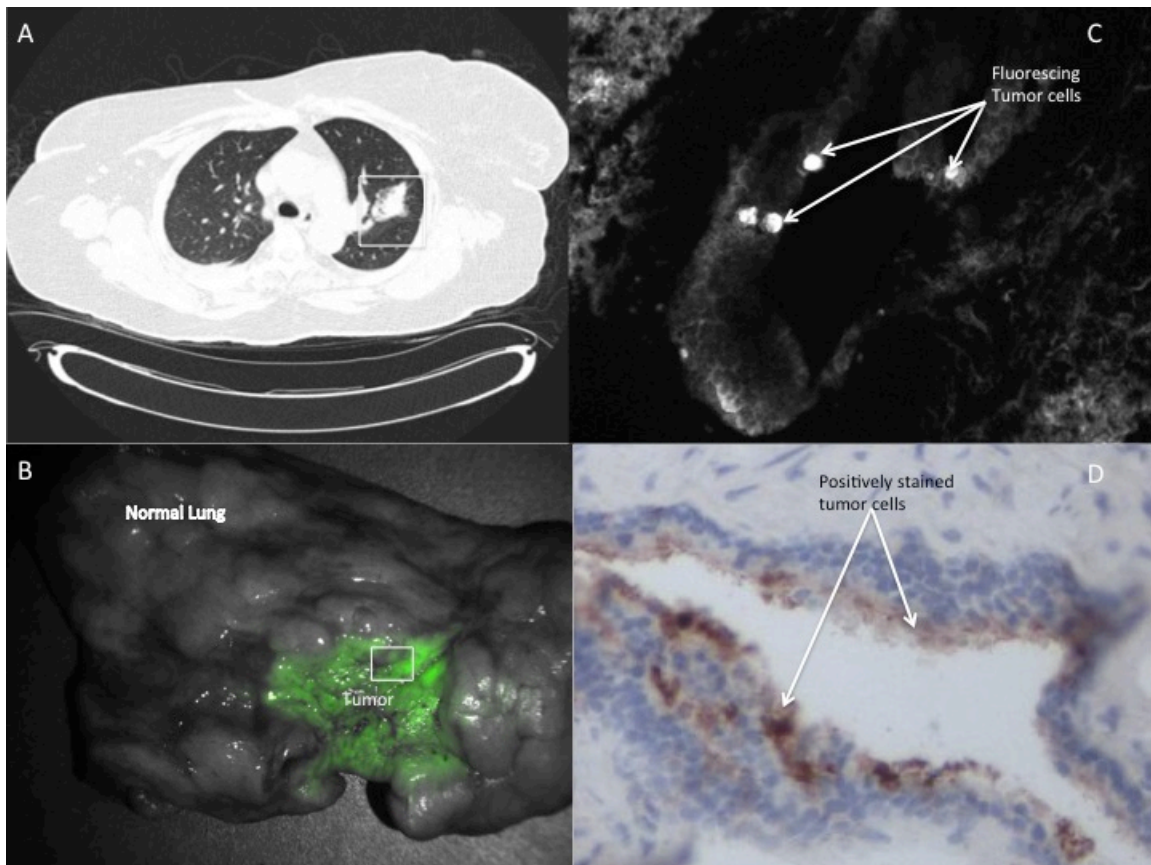

Figure 1: A: CT scan showing left upper lobe mass. B: Ex-vivo fluorescent imaging of left upper lobe clearly demonstrating signal from lung mass. C: Fluorescence microscopy of tumor sample gating for FITC showing positive glandular cells. D: immunohistochemistry of tumor sample for folate receptor alpha.