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Nanotechnology Enabled Image Guided Therapeutics in Lung Cancer

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Personalizing Cancer Medicine in 2015 *Feb 2nd, 2015*

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Disclosure

- Industry-sponsored grants
  - Educational and research grants from Olympus Medical Systems Corp.
- Consultant
  - Olympus America Inc.
  - Intuitive Surgical Inc.
  - Covidien
  - Johnson and Johnson
- Research Collaboration
  - Olympus Medical Systems Corp.
  - Novadaq Corp.
  - Veran Medical Technologies

Lung Cancer

- Lung cancer remains the leading cause of cancer death in the Western world
- Early detection is key to improved survival
- The detection rate of early-stage lung cancer is anticipated to increase with the introduction of CT screening

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Lung Cancer – New Problems

- How can we efficiently localize small lung cancer during MIS?

- What are other minimally invasive therapeutic options for high risk pts with lung cancer?

2009

2011

2012

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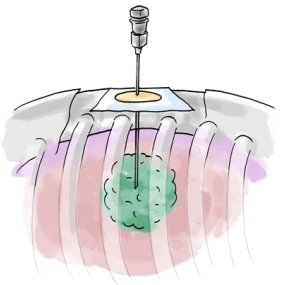
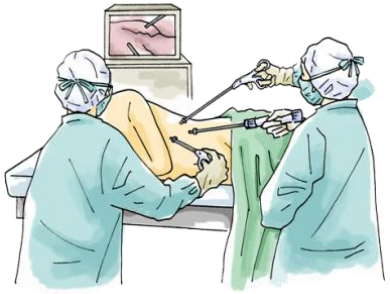
Diagnostic Approach to Pulmonary Nodules

- Minimally Invasive Biopsy
  - Bronchoscopic biopsy
  - CT guided FNA
- Surgical biopsy
  - VATS
  - Thoracotomy





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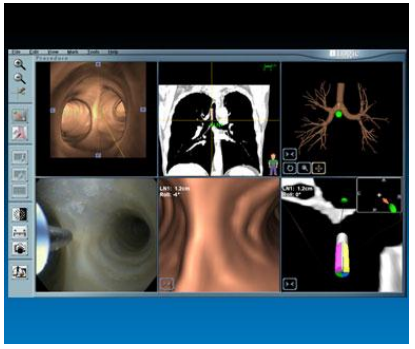
Bronchoscopic Biopsy

- Transbronchial biopsy

- EBUS-GS

- Electromagnetic Guidance



- Virtual Navigation

VATS (Video-assisted thoracoscopic surgery)

- Procedure of choice for surgical biopsy of peripheral pulmonary nodule

- Limitation
  - Identification of the nodule
  - Lack of digital palpation in small, non-solid deep nodules
  - May require conversion to thoracotomy

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Localizing Techniques - VATS

- Intraoperative imaging
  - CT
  - Thoracic ultrasound
- Preoperative CT guided marking
  - Liquid material (contrast media, colored adhesive agents, dyes)
  - Radionuclides
  - Wires (hookwires, microcoils)
- Preoperative bronchoscopic marking
  - Dye
  - Fiducials

Radiology 2002; 225: 511-518

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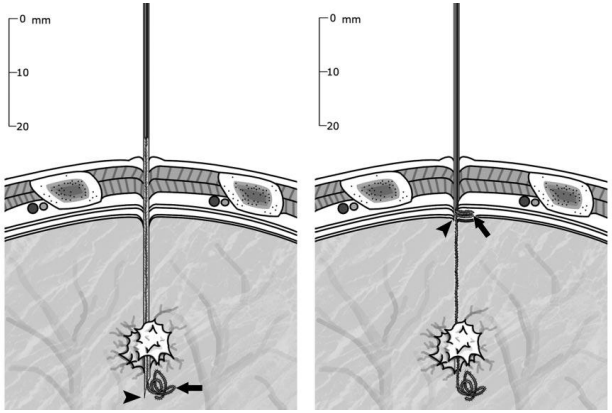
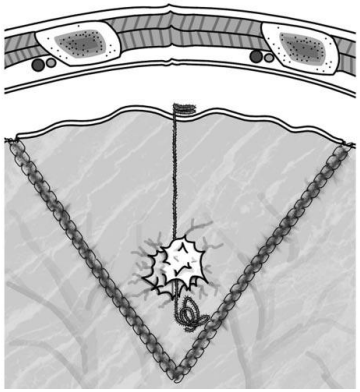
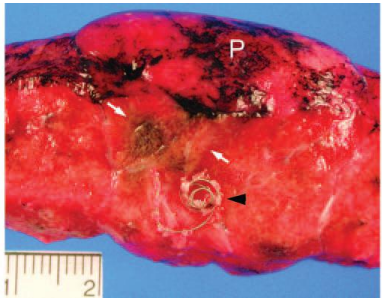
Wire Localization - Microcoil Localization







73/75 (97%) 4-24-mm nodules successfully removed
low rate of intervention (3%) for procedural complications

Radiology 2009; 250: 576-585

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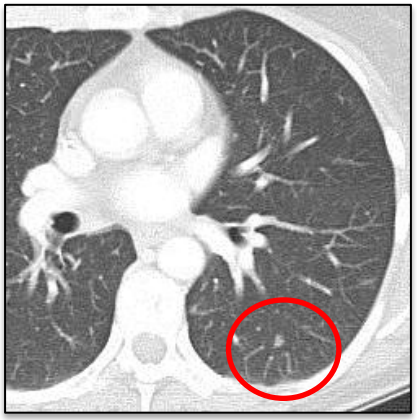
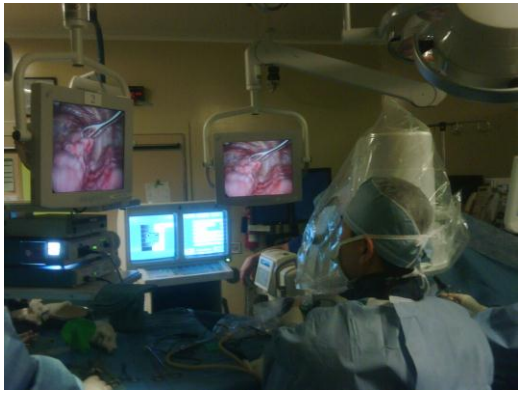
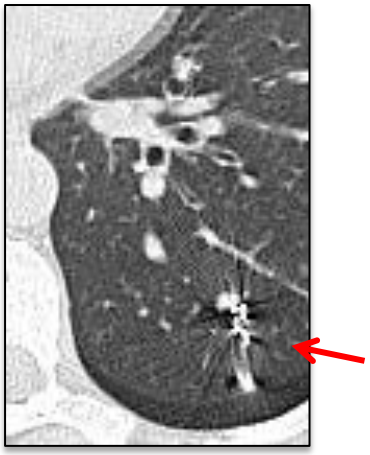
Microcoil Localization

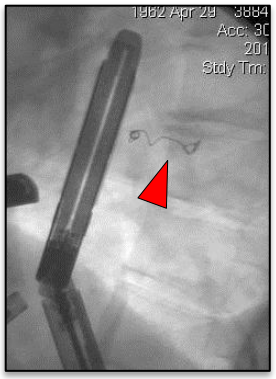




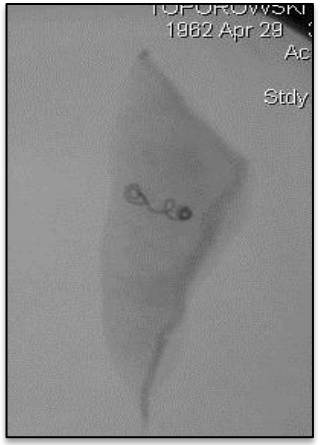


1. CT guided micro coil placement

2. VATS microcoil detection



3. Fluoroscopy guided VATS wedge resection



4. Confirmation of microcoil

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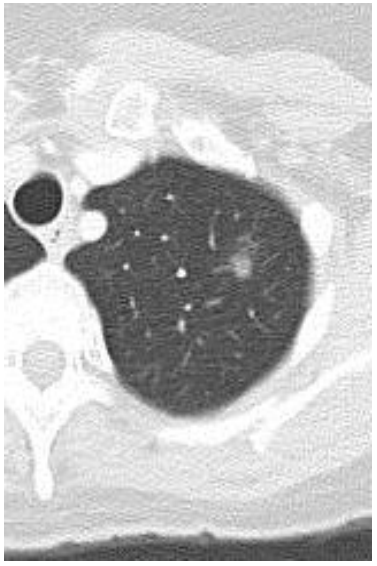
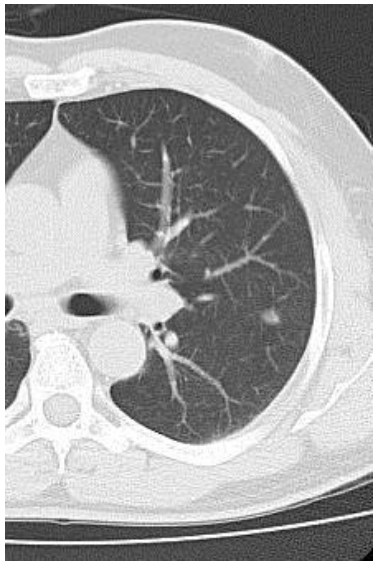
Microcoil Localization – Toronto Experience

- First case October 2008
- 64 cases
- Complete resection with VATS in 62/64 cases (97%)
- 100% diagnostic yield

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GTx (Guided Therapeutics) Program

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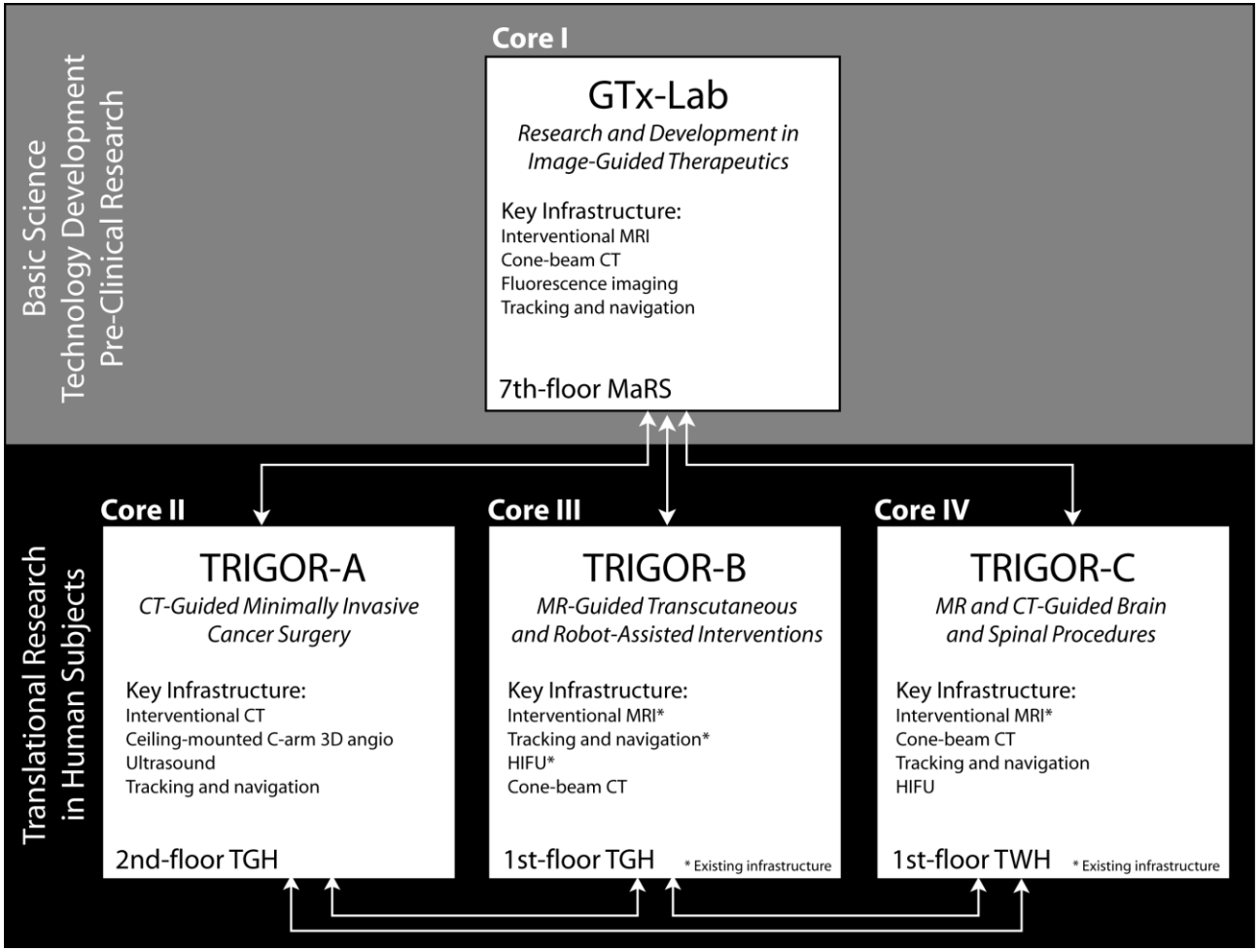
GTx Surgery Overview



TRIGOR = Translation Research Image Guided OR

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TRIGOR A Capabilities

Cone-Beam CT

Dual Source- Dual Energy CT

MIS, Endoscopic Technology

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TRIGOR A - GTx OR

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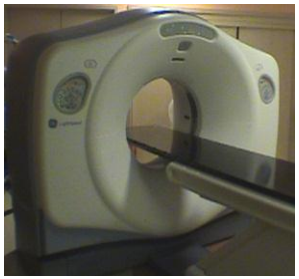
Multi-Modality Surgical Guidance

Pre-Operative Imaging



Intraoperative CBCT

Surgical Tool Tracking

Surgical Planning

Optical Imaging

Intraoperative localization

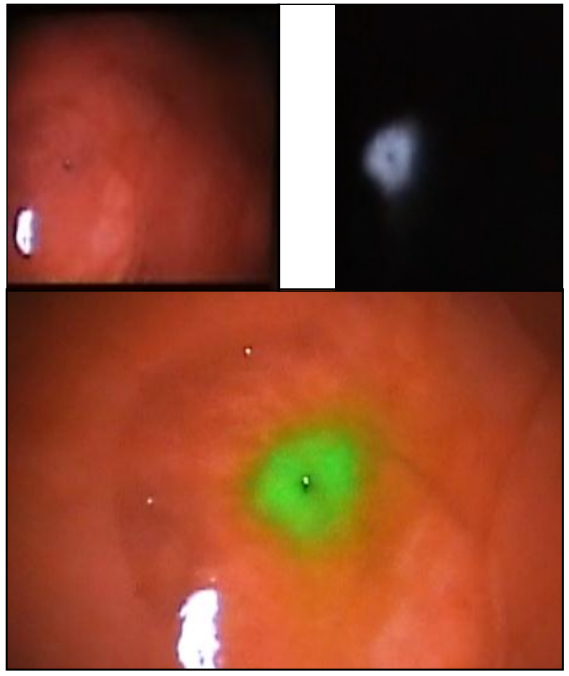
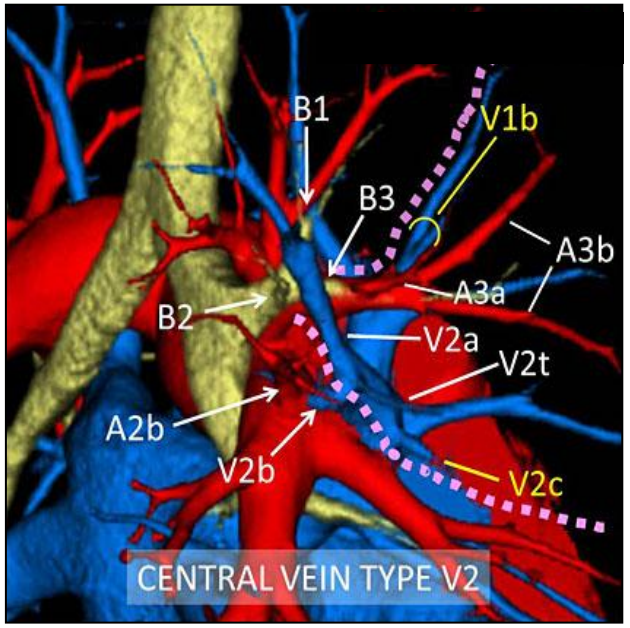
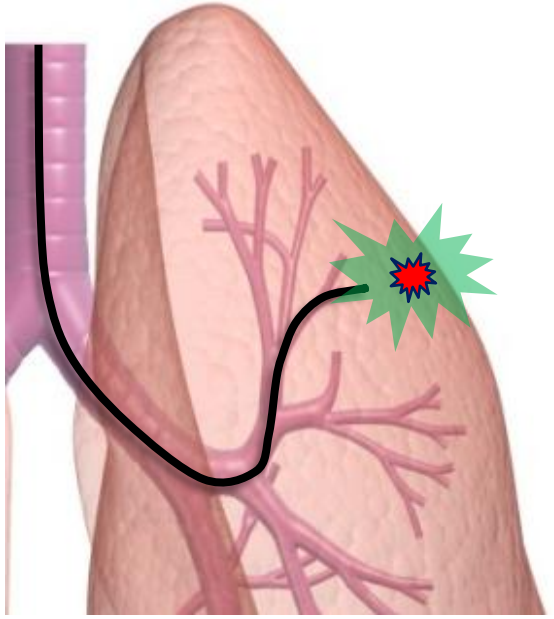


Image assistance during MIS/Robotic Surgery



Real time monitoring of minimally invasive thoracic intervention



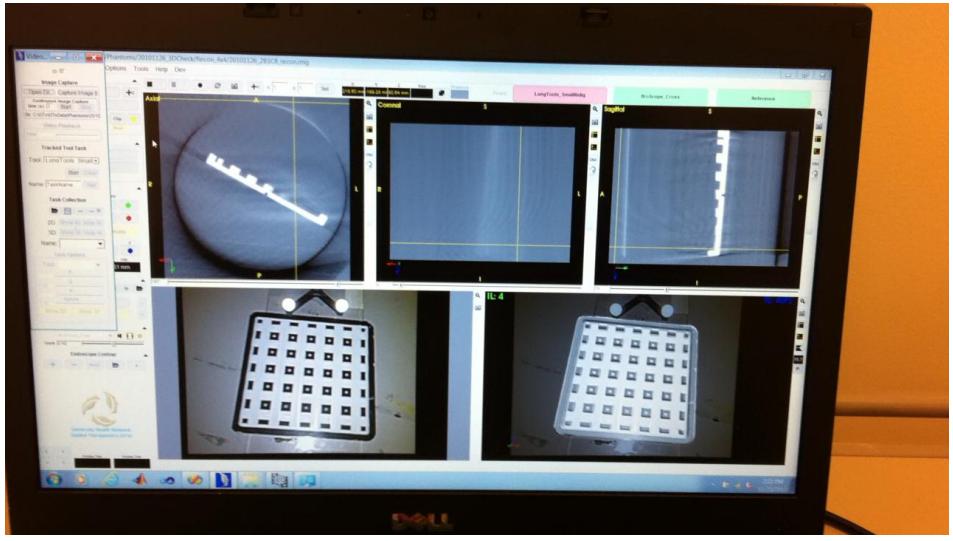
Optical Surgical Navigation

1. Preoperative CT imaging
2. Cone-beam CT nodule localization
3. Image registration with surgical navigation

Pre-Operative Imaging

Intraoperative CBCT

Surgical Tool Tracking



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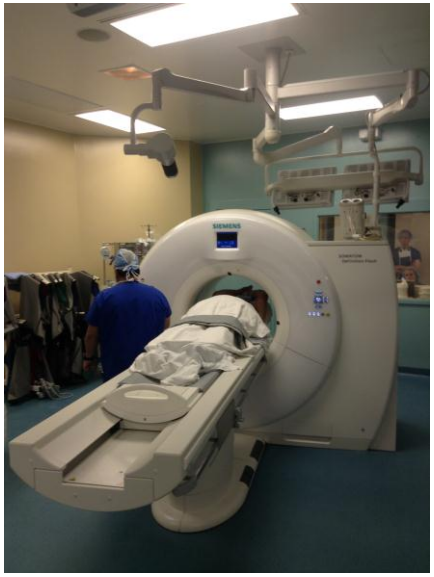
GTx OR – Image guided Transbronchial Interventions



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GTx OR – VATS localization

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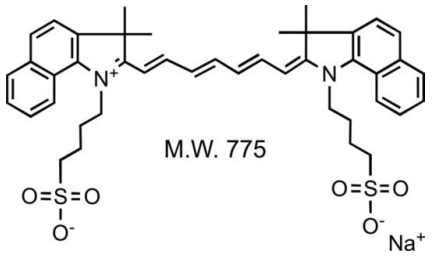
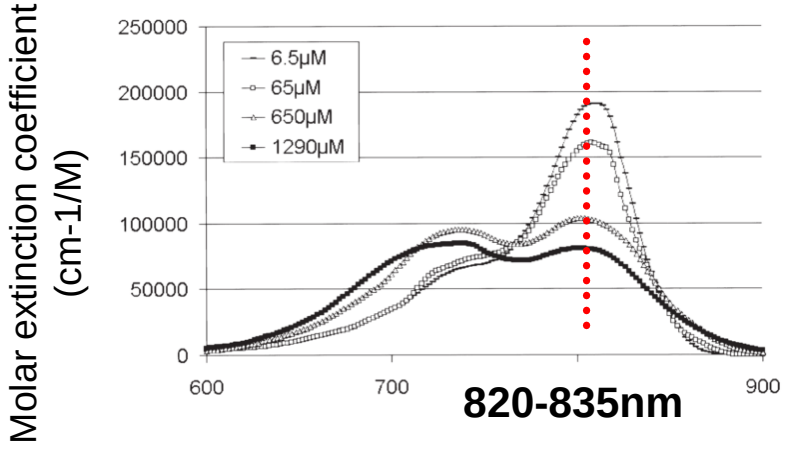
ICG and Near Infrared (NIR) Imaging

Indocyanine green



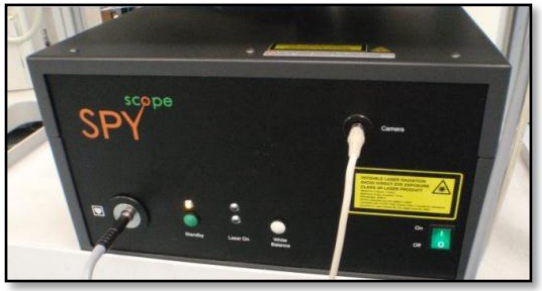
M.W: 775

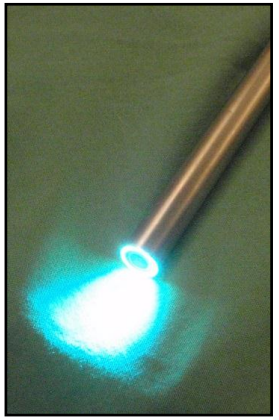


Surv Opthalmol, 2000

NIR thoracoscope

SPY scope, Novadaq Technologies™





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ICG - SPY Localization

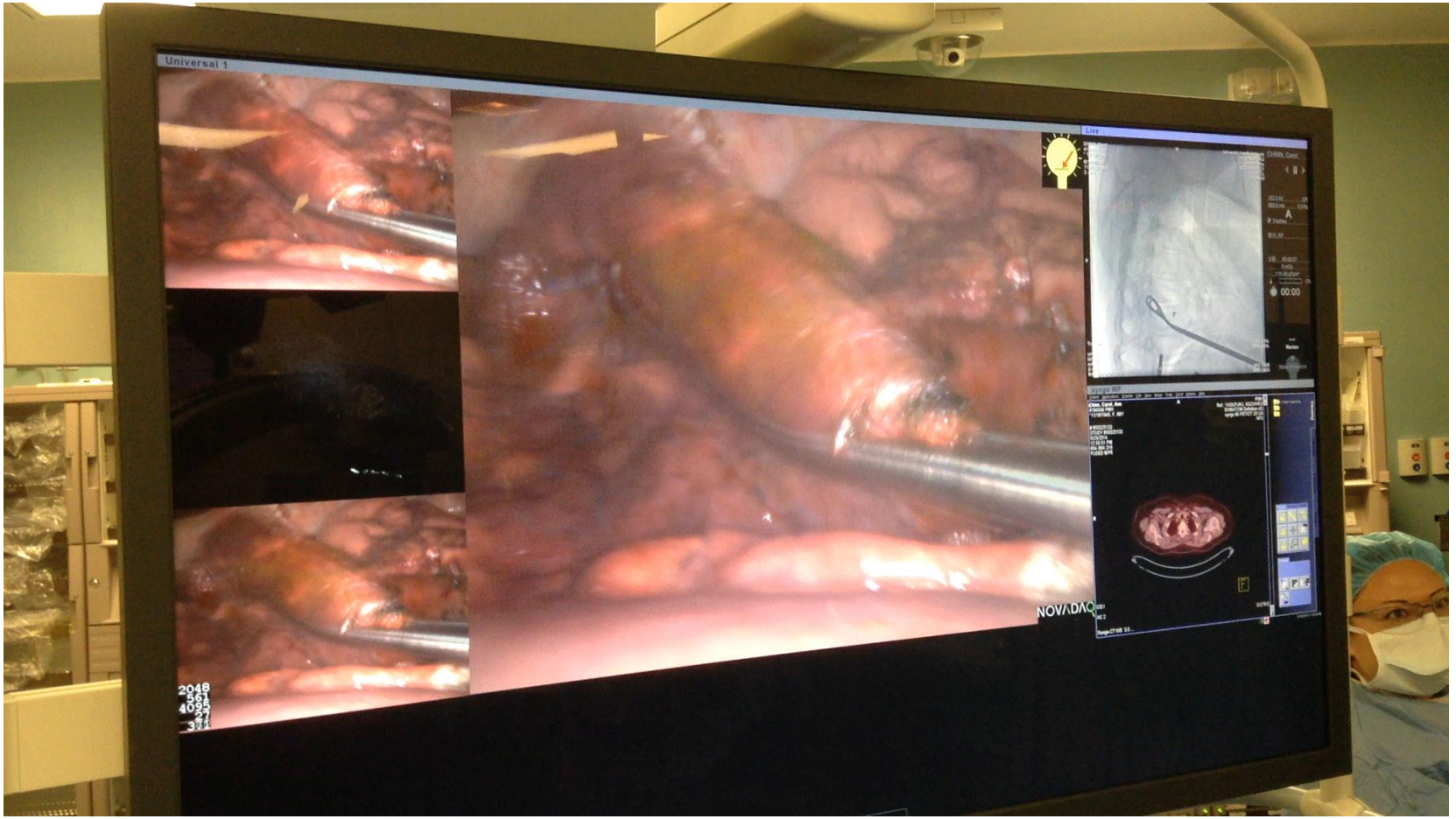

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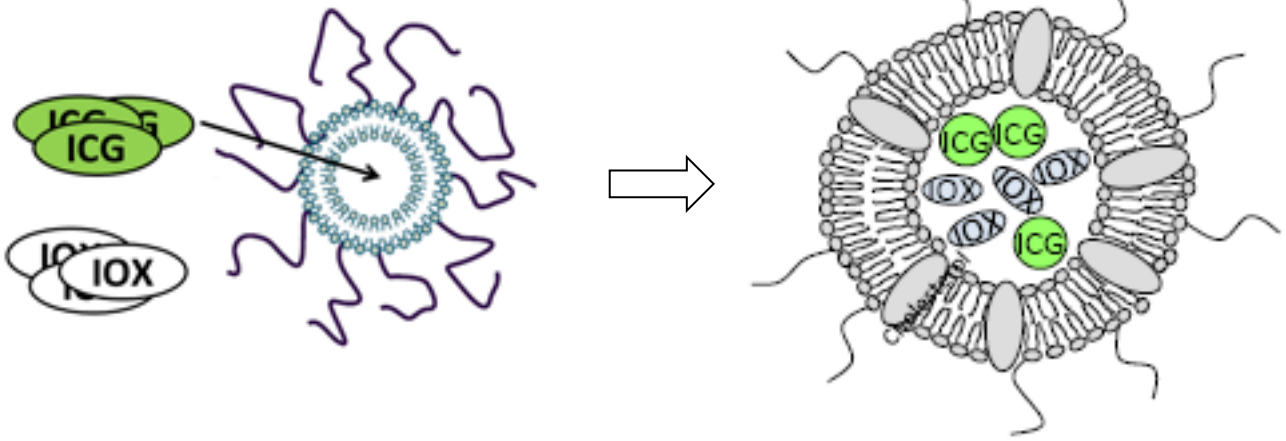
Image-guided Localization Platform for Minimally Invasive Lung Cancer Surgery

Multi-modal liposomal nanoparticle(C800) - ICG Liposome



Size (nm)	Iodine concentration (mg/mL)	ICG concentration (μg/mL)
99.2 ± 1.8	53.2 ± 1.4	94.6 ± 7.8

The phospholipid nanoparticle, coated with polyethylene glycol, encapsulates ICG and CT contrast (iohexol, labelled IOX
The prolonged intravascular half-life allows for longitudinal CT and NIR imaging

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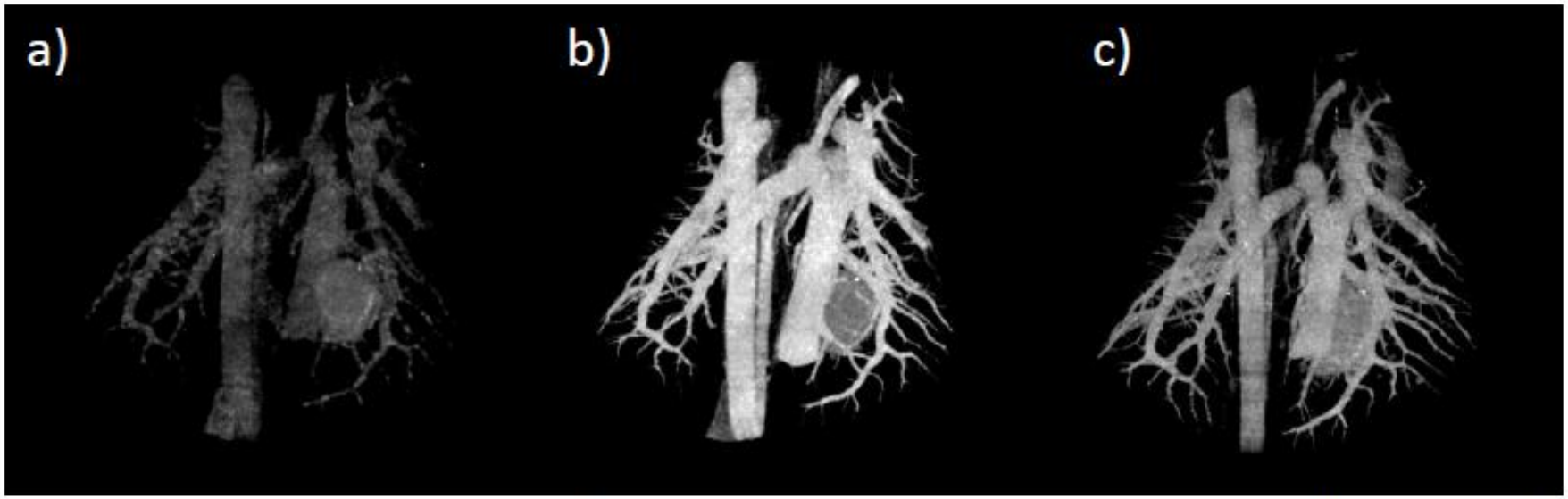
Image Assistance – 3D Reconstruction

Pre-injection | 5 min post-injection | 3 days post-injection



Administered CF800 continuously remains in both vasculature and the tumor in a rabbit, allowing for successful 3D reconstruction even at 3 days post injection

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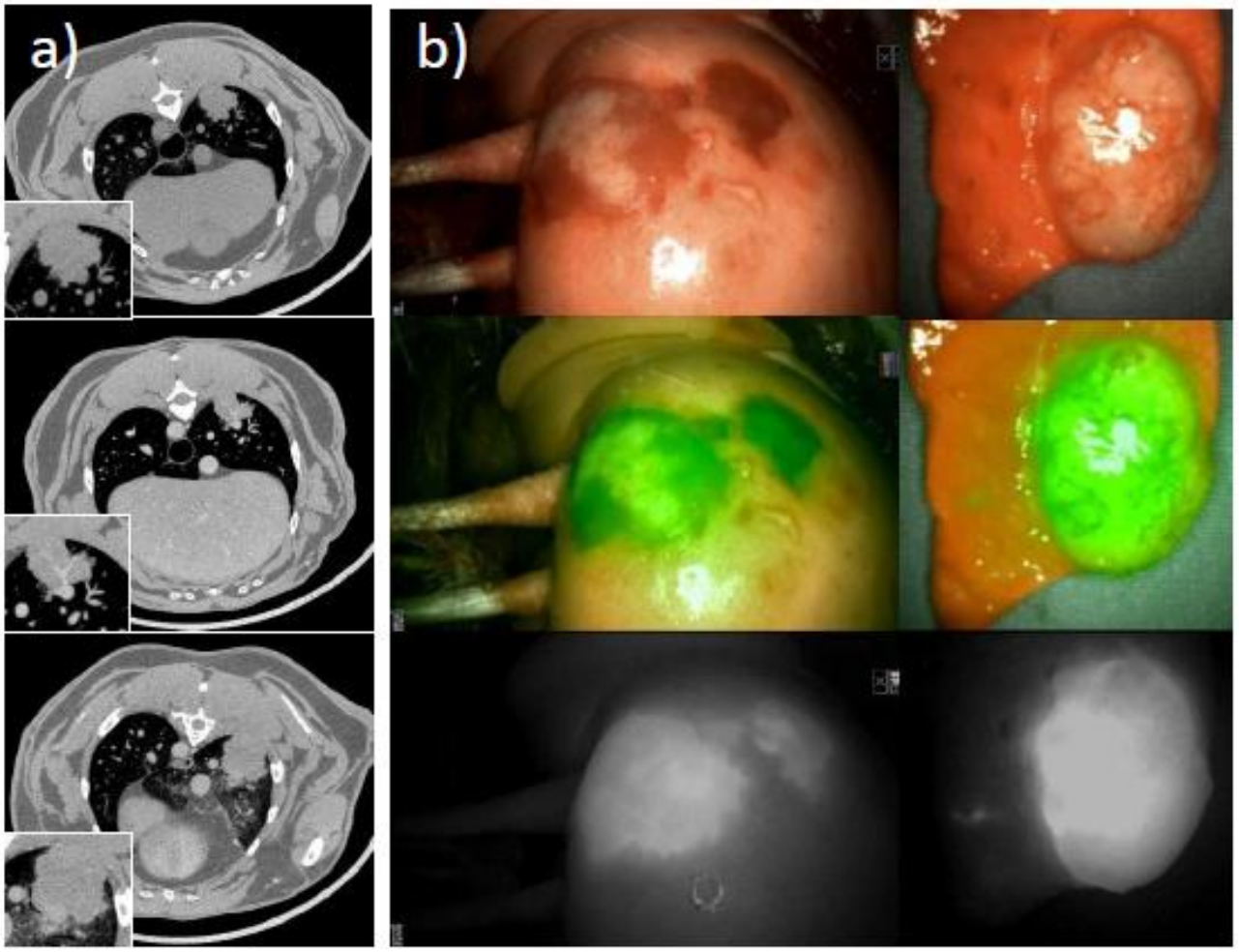
NIR imaging of Lung Cancer



4 days post-injection of CF800

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Ultra-minimally Invasive multi-modal image guided phothermal ablation of lung cancer

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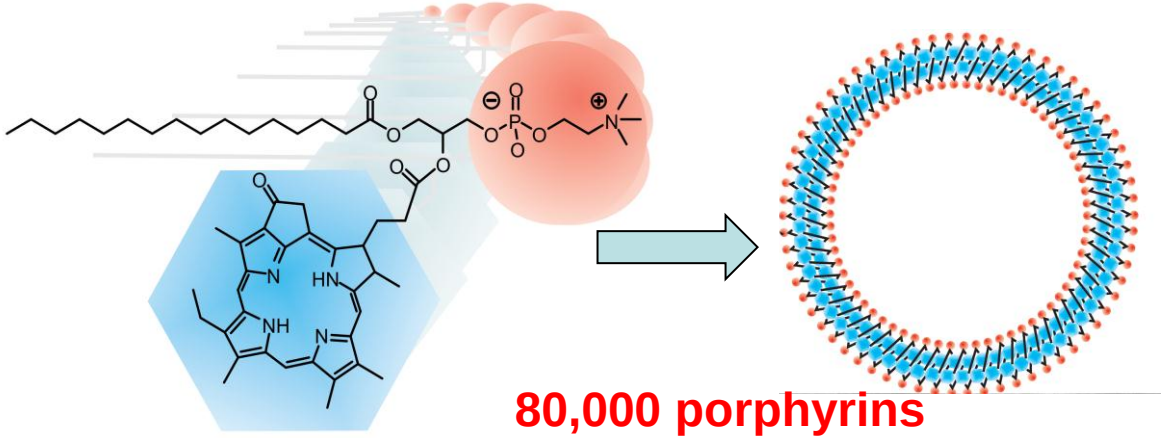
Porphysomes : Liposomes like bilayer porphyrin-phospholipid

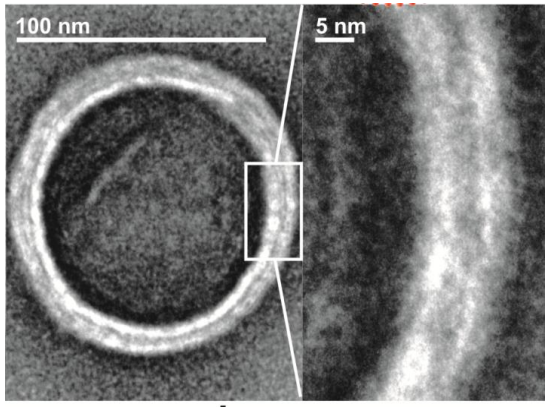
ARTICLES
PUBLISHED ONLINE: 20 MARCH 2011 | DOI: 10.1038/NMAT2986
nature materials

Porphysome nanovesicles generated by porphyrin bilayers for use as multimodal biophotonic contrast agents

Jonathan F. Lovell[1,2], Cheng S. Jin[1,2], Elizabeth Huynh[2,3], Honglin Jin[2,3], Chulhong Kim[4], John L. Rubinstein[3,5], Warren C. W. Chan[1], Weiguo Cao[6], Lihong V. Wang[4] and Gang Zheng[1,2,3]*



80,000 porphyrins



Works as both fluorophore and photo-enhancer

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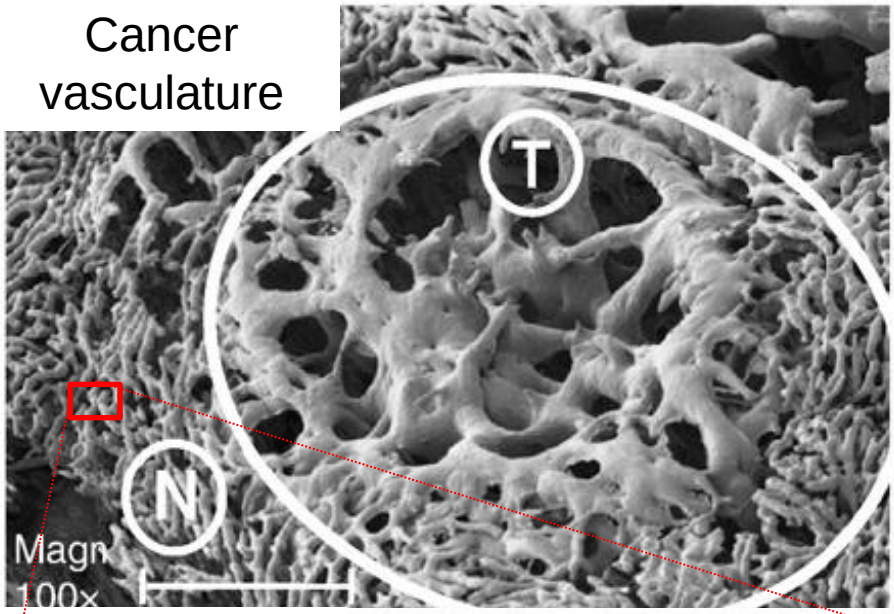
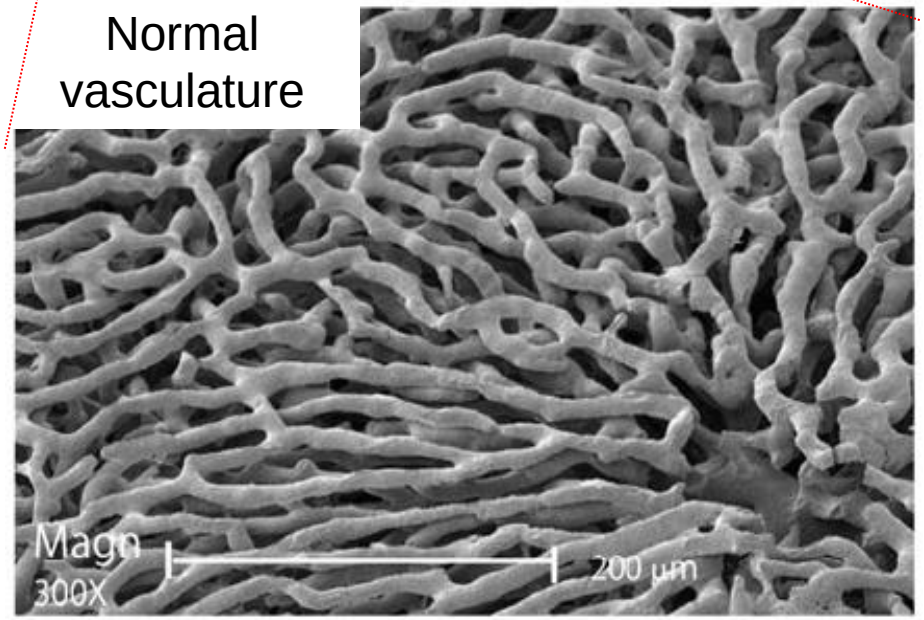
EPR effect;
Enhanced Permeability and Retention Effect

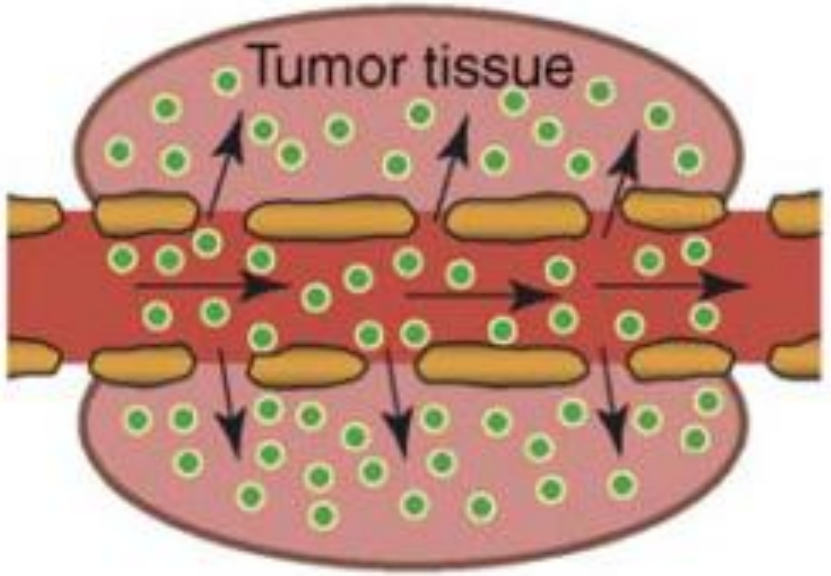
Cancer vasculature



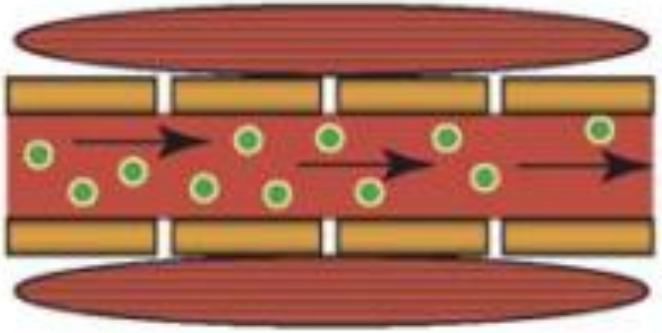
Normal vasculature



Cancer vasculature



Normal vasculature



1, Adv Drug Deliv Rev, 2011
2. Drug Dis Today, 2006

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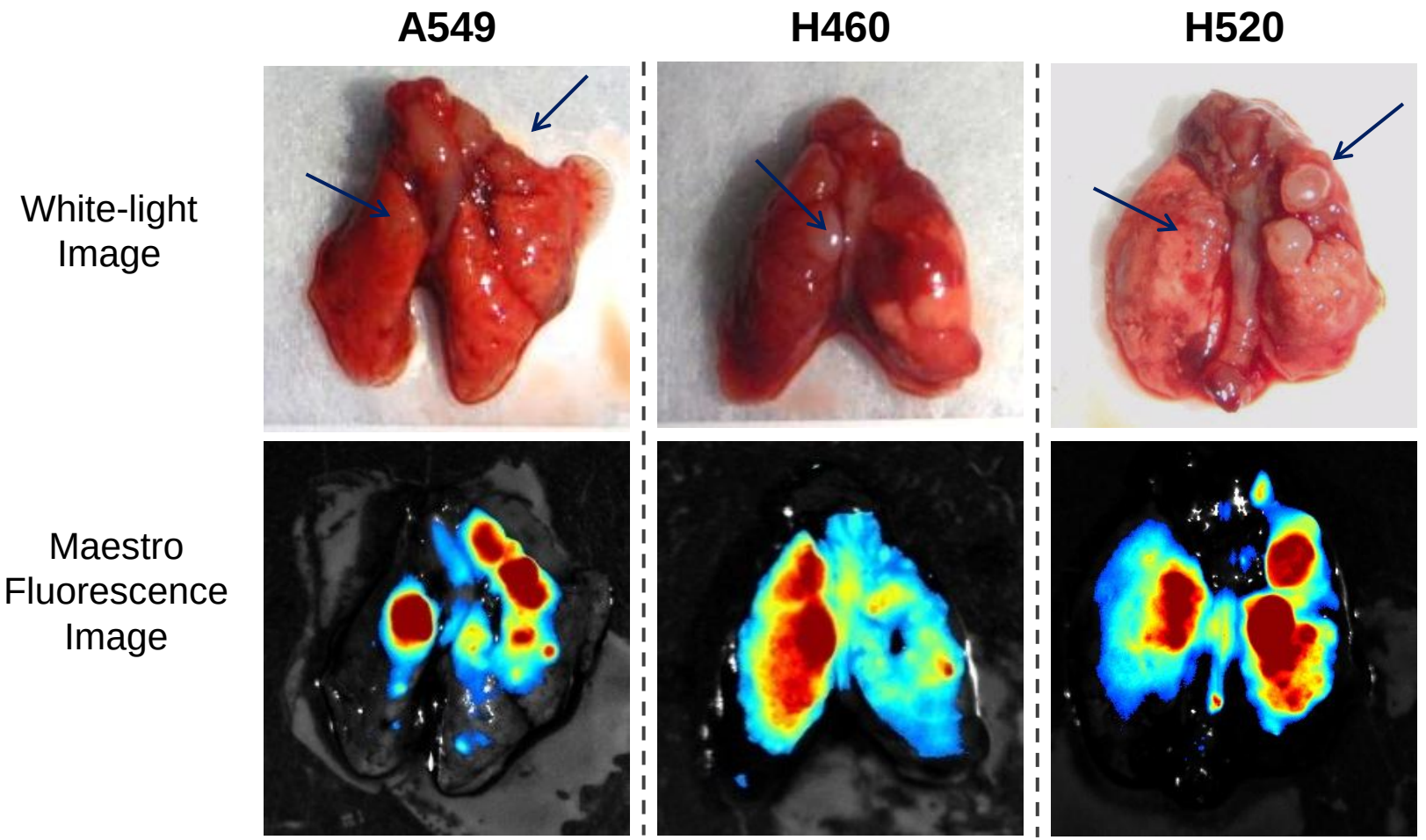
Porphysome distribution in Orthotopic lung cancer Xenograft models



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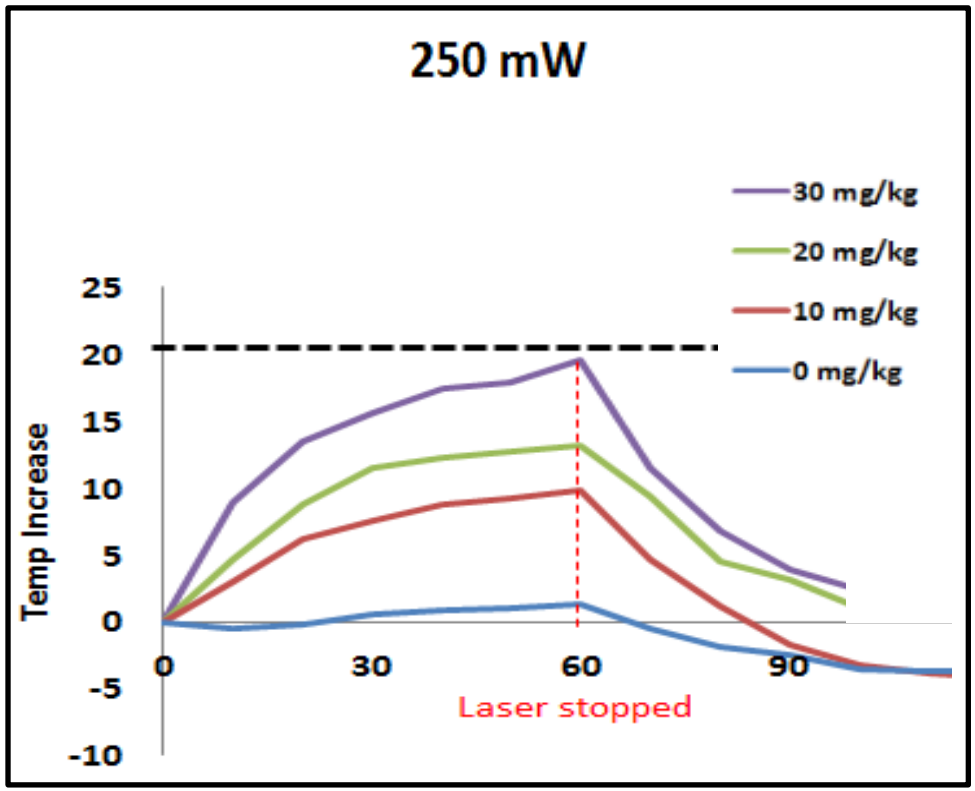
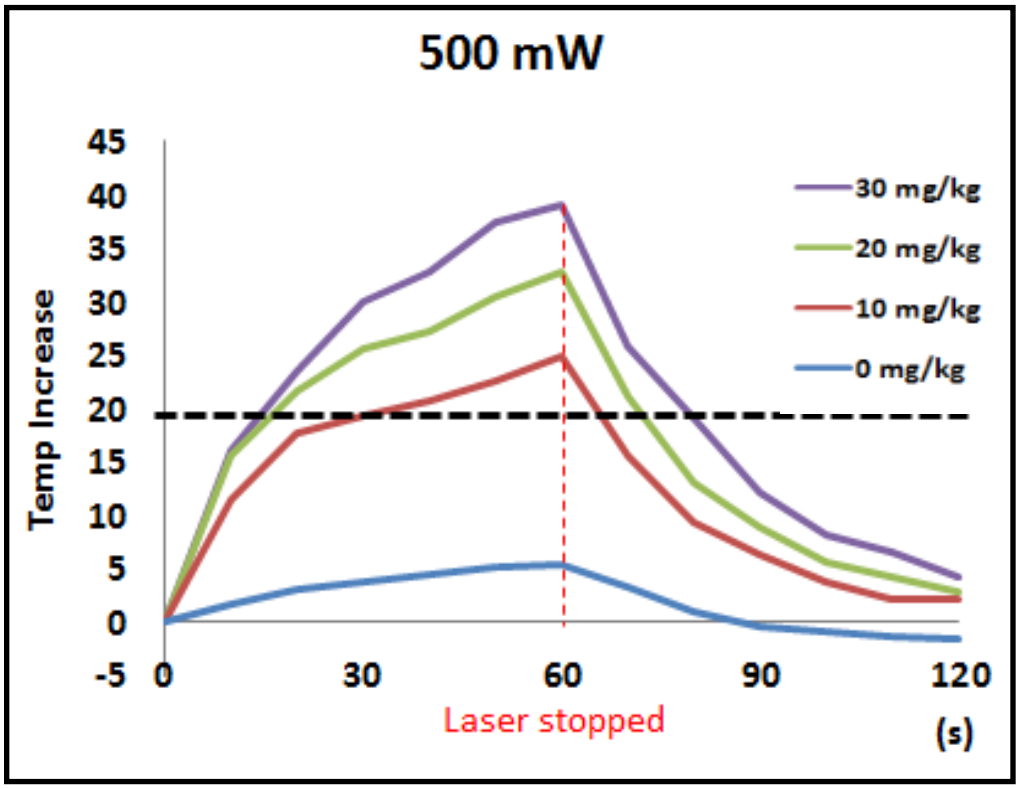
Porphysome thermal effect on resected VX2 tumor tissue (ex-vivo)





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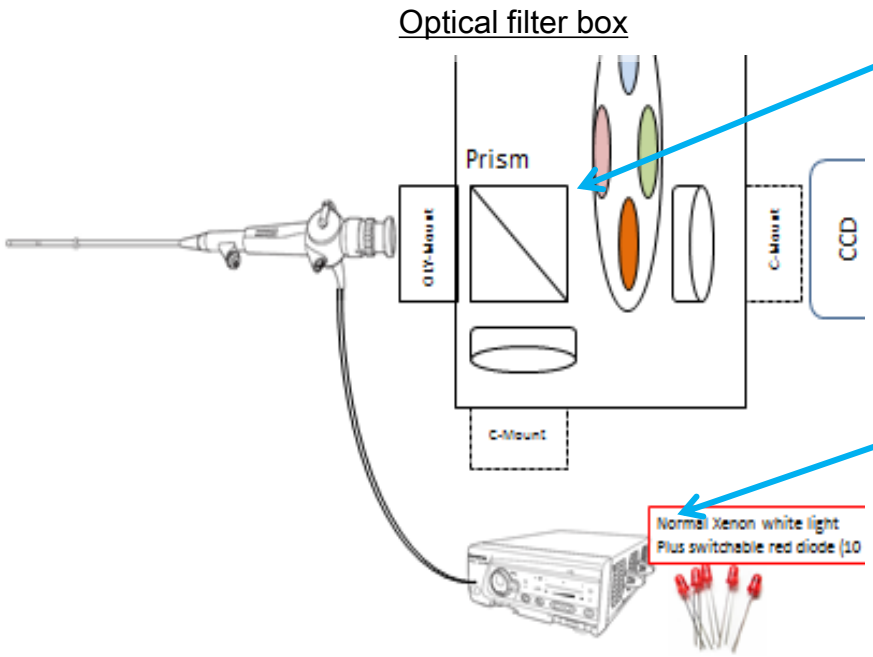
Development of prototype bronchoscope for visualization of porphysome fluorescence

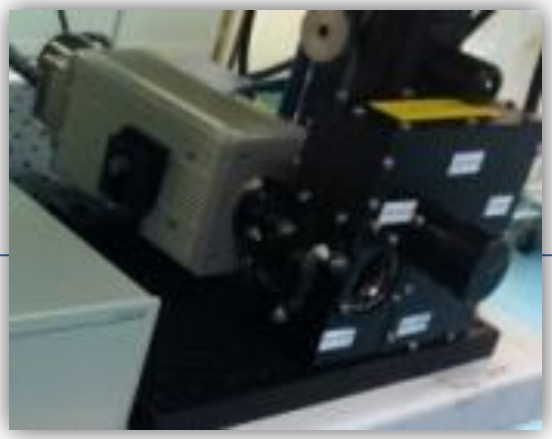


Emission (bronchoscope side) :

A long pass filter : 678-1000nm

Exitation (light source side):

Red diode of 10 mW output
A band-pass filter : 650-670nm



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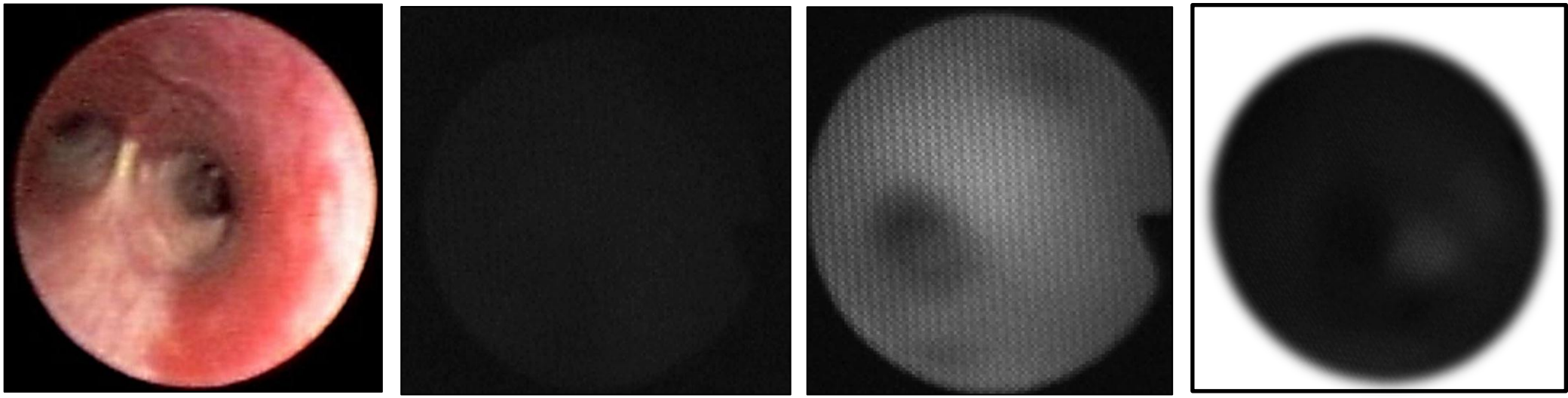
In-vivo model

Prototype fluorescence bronchoscope

WL | 0 time | 24hr | 48hr



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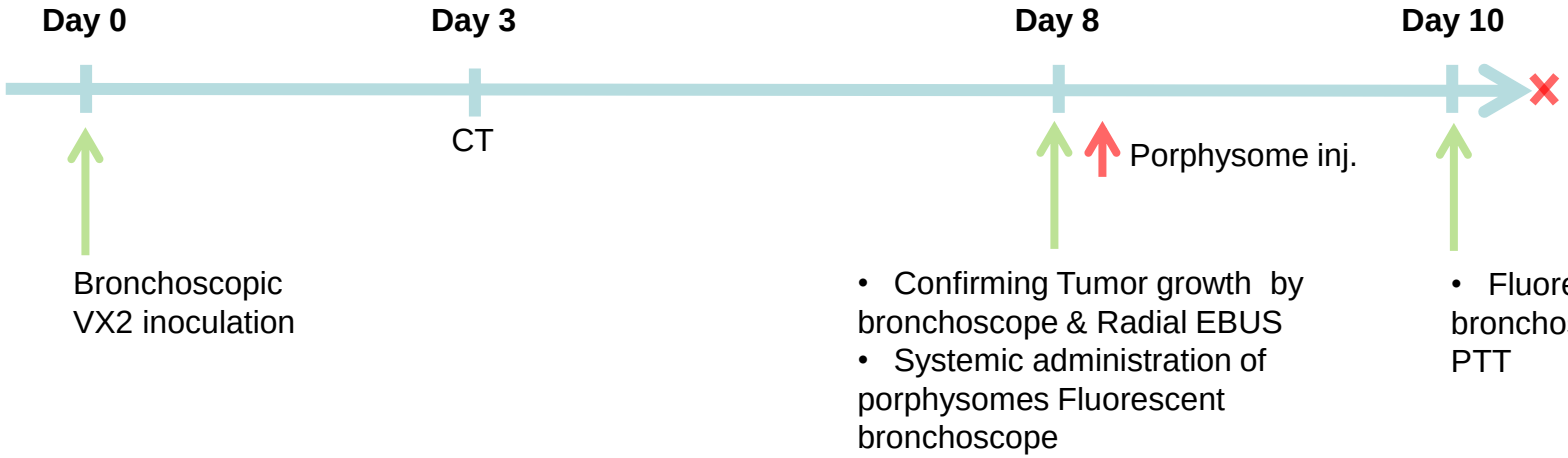
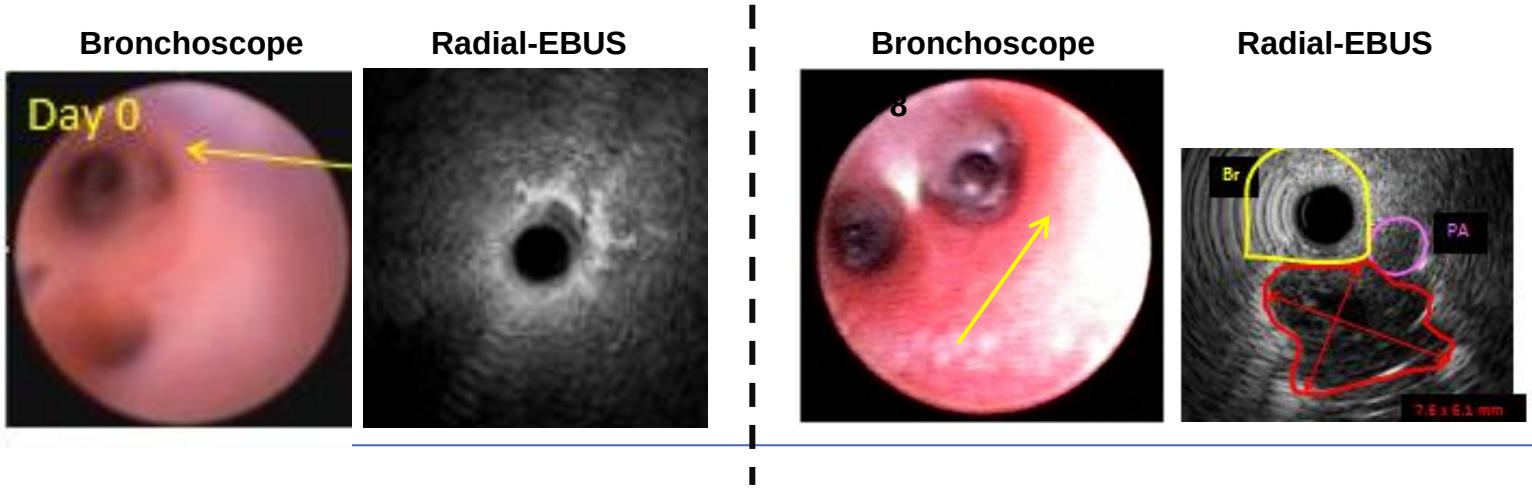
Experimental Design



Tumor-growth



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Porphysome enhanced transbronchial PTT

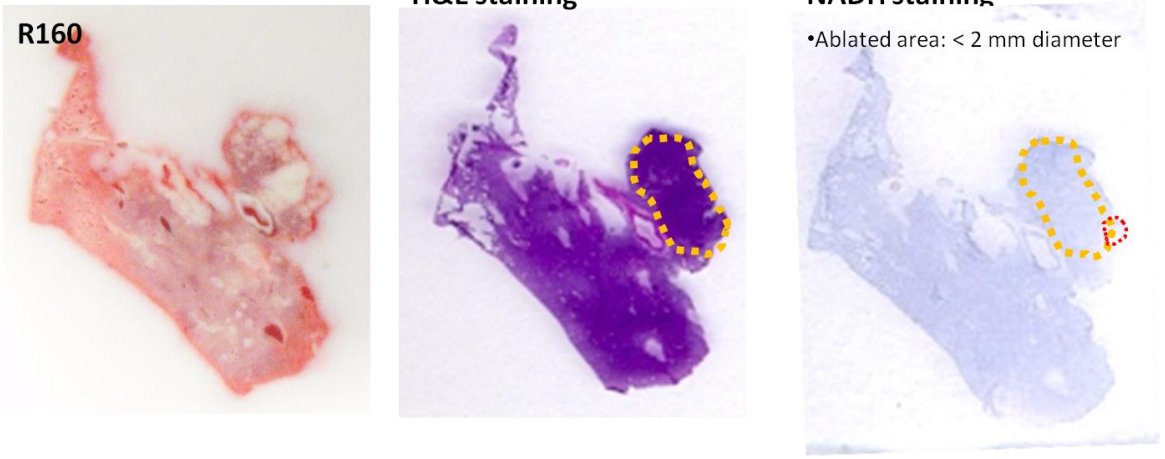
Laser Control

R160

H&E staining

NADH staining

•Ablated area: < 2 mm diameter



Porphysome-PTT

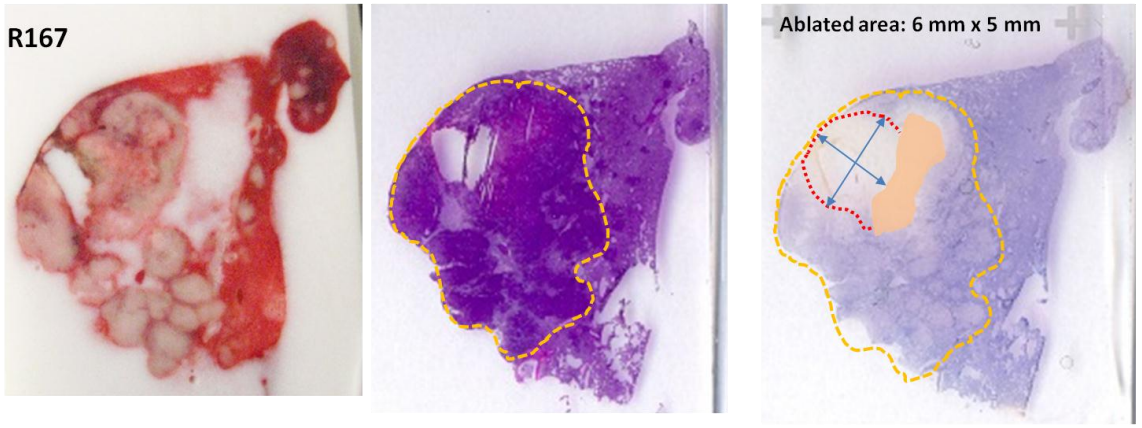
Lung Slide

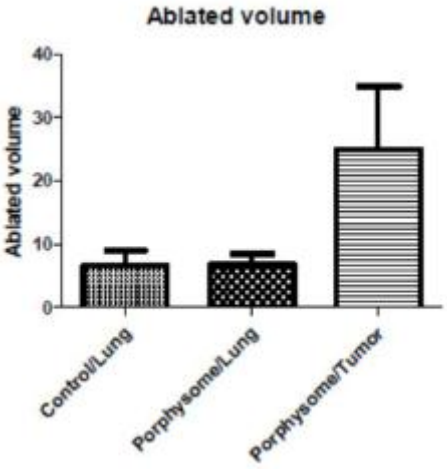
H&E Staining

NADH Staining

R167

Ablated area: 6 mm x 5 mm





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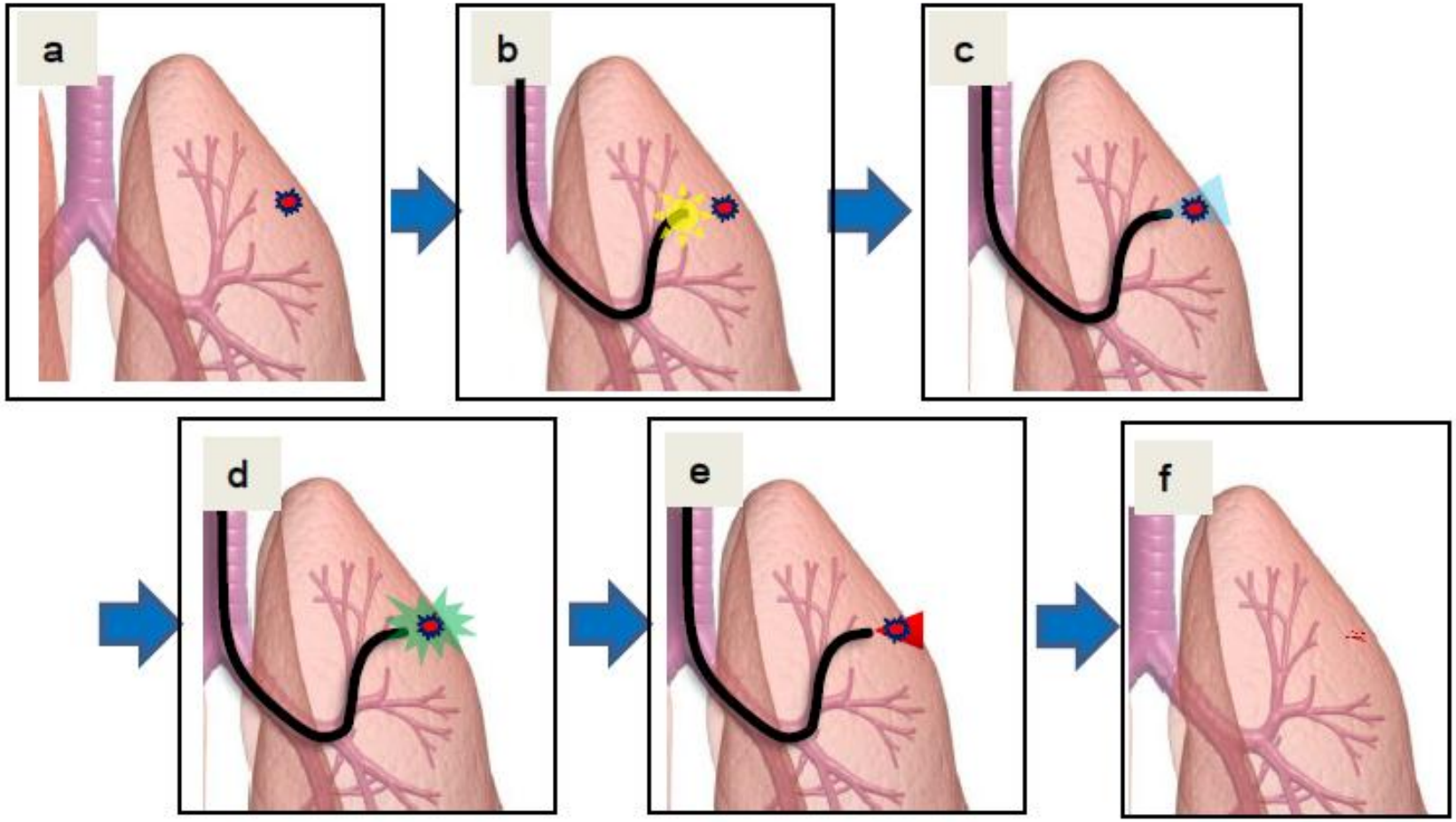
Ultra-minimally invasive multi-modal image guided phothermal ablation of lung cancer



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Summary

- Advances in nanotechnology and image guidance will enable intraoperative localization of small peripheral nodule and also assist surgeons during MIS

- New transbronchial ablation technologies are in development and can potentially be used for minimally invasive treatment of early stage lung cancer

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Acknowledgement

Toronto General Hospital

Doctors of Thoracic Surgery (DOTS)

- Shaf Keshavjee
- Tom Waddell
- Gail Darling
- Andrew Pierre
- Marc de Perrot
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