Advanced Transbronchial Interventions
- What to Expect in the Near Future

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Transbronchial Diagnostic Modalities
Endoscopic Staging - EBUS-TBNA

- Access to all LN stations accessible by Med as well as N1 nodes
- A minimally invasive modality
- Sensitivity 85-96%
- Real time procedure
- Doppler mode enables differentiation of LN from vessels
- Adopted in over 2500 centers

Ultrasound Imaging Modes

**B-mode**
- Images structures in black and white

**M-mode**
- Displays motion over time

**Color-doppler**
- Shows blood flow color-coded

**Harmonic Imaging**
- Based on non-linear echoes

**Elastographic Imaging**
- Evaluation of stiffness (Elasticity)

**Contrast-agent Imaging**
- Microbubbles are used for evaluation of tumor lesion
EU-ME2

H-FLOW  Pulse wave Doppler  Elastography

Soft  Hard
Assessment of Mediastinal Lymph Nodes

Benign LN

Malignant LN
Assessment of Mediastinal Lymph Nodes

Benign LN

Malignant LN
Principle of Spectrum Analysis

1) Midband-fit (dB, value of the regression line at the center frequency),
2) Slope (dB/MHz),
3) Intercept (dB, extrapolation to zero frequency)
Quantitative Ultrasound – Tumor vs Normal lung tissue

Midband-fit

Intercept

Slope

Wada et al, WCBIP 2014, abstract
Staging Beyond the Mediastinum
LN not assessable by EBUS

N1 LNs
part of 12, 13, 14
Thin EBUS-TBNA scope

outer diameter 6.9mm

outer diameter 5.9mm

Wada et al, JOBIP 2014
Prototype TCP-EBUS in human lung

Percent of Assessable Lobar Bronchi

PATIENT EBUS

Right Lung
Left Lung

Percent of Assessable Segmental Bronchi

PATIENT EBUS

Right Lung
Left Lung

Newer Technologies
Archimedes (Broncus) - Transparenchymal Access
Cone Beam CT Guided Bronchoscopy

Navigation Yield
91%

Diagnostic Yield
<2cm (15 +3mm) 75%
>2cm (30 +11mm) 67%

Hohenforst-Schmidt et al, J Cancer 2014; 5: 231-41
Cone Beam CT Guided Bronchoscopy

SPiN Perc – EMN TTNA
ETTNA

• Multicentre, randomized control study
  • Small peripheral nodules (< 3cm)
  
  • Dx yield higher in VBN group
    80.4% vs 67.0% (p=0.032)
  
  • Shorter time in VBN group
    24.0min vs 26.2min (p=0.016)

Yarmus et al, J Thorac Dis 2016; 8: 186-194
Robotic Bronchoscopy?

- Robotic Platform for endoluminal surgery
Transbronchial Therapeutics
Transbronchial Ablative Technology

• Radiofrequency Ablation (RFA)
• Microwave Ablation
• Cryo Ablation
• Vapor Ablation
• Photodynamic Therapy (PDT)
• Photothermal Therapy (PTT)
Nanomedicine

Multi-Modal Liposomes

- Optical Imaging
- Active Targeting
- CT Imaging
- MR Imaging
- Radionuclide Imaging

Multi-Modal Porphysomes

- Surface Functionalization and Targeting
- Mn for MRI
- Cu for PET imaging
- Photothermal therapy
- Photocoustic imaging

Encapsulated Drug/Contrast

Liposome

Courtesy: Dr. Shawn Stapleton

Courtesy: Dr. Jinzi Zheng (TECHNA)

Courtesy: Dr. Gang Zheng (TECHNA)
Enhanced permeability and retention effect (EPR Effect)

Cancer cell

Tumor

Normal capillary: polymer molecules can not be permeable

highly permeable neo-vascularture:

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## Characteristics of Nanoparticles

<table>
<thead>
<tr>
<th></th>
<th>ICG liposome Nanovista-CF800 (Dr. David Jaffray/ Dr. Christine Allen)</th>
<th>Porphysome (Dr. Gang Zheng)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>100 nm</td>
<td>100 nm</td>
</tr>
<tr>
<td>Emission wavelength</td>
<td>820-835 nm</td>
<td>680 nm</td>
</tr>
<tr>
<td>Intravascular half-life</td>
<td>25-35h (mouse) 60-70h (rabbit)</td>
<td>12h (mouse) 12h (rabbit)</td>
</tr>
<tr>
<td>Structure</td>
<td><img src="image1.png" alt="Structure Diagram" /> Co-encapsulate ICG and iohexol</td>
<td><img src="image2.png" alt="Structure Diagram" /> Porphyrin packed bilayer structure</td>
</tr>
<tr>
<td>Main role</td>
<td>Fluorescence Imaging agent for tumor imaging</td>
<td>Photosensitive agent for laser therapy</td>
</tr>
</tbody>
</table>

NIR Fluorescence-guided Tumor Localization (ICG liposome)

Mouse Orthotopic lung cancer model

Rabbit VX2 lung cancer model

Patel P, Yasufuku K et al. Plos one 2016
Nanotechnology-enabled fluorescence-guided transbronchial photothermal therapy of peripheral lung cancer
Photothermal Therapy of Lung Cancer

**Transbronchial** (straight-cut type fiber)

**Transpleural** (cylindrical diffuser type fiber)

Porphysome/Tumor

Cylindrical diffuser

Cryo-section

HE staining

NADH staining

Phase I Clinical Trials under Development

- Transbronchial PDT for Peripheral Lung Cancer

- **Vapor** Ablation for Localized Cancer Lesions of the Lung (VAPORIZE)

- Transbronchial RFA
Summary

• Advances in bronchoscopy will allow surgeons to navigate out into peripheral lung lesions with ease

• 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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Thank you