Interventional Pulmonology

From Diagnostic to Therapeutic

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Consultant and Head of Respiratory Division
Department of Medicine
Queen Elizabeth Hospital
Respiratory Diseases: basic tools
Flexible Bronchoscopy

Mainly diagnostic
“Surgical” interventions

Rigid bronchoscopy:
- Airway stents
- Laser...etc.

Video-assist thoracoscopy:
- Lung resection
- Surgical pleurodesis..etc.

General Anaesthesia + Operation Theatre + Rigid instruments
Rapidly-growing interventional options

- Transbronchial needle aspiration (TBNA) and endobronchial ultrasound-guided (EBUS) TBNA
- Electrocautery/diathermy
- Argon plasma coagulation (APC)
- Laser
- Cryotherapy
- Cryoextraction
- Photodynamic therapy (PDT)
- Brachytherapy
- Tracheobronchial stents
- Electromagnetic navigation bronchoscopy (ENB)
- Endobronchial valves for emphysema
- Bronchial thermoplasty for asthma

BTS guidelines for Advanced Diagnostic and Therapeutic Flexible Bronchoscopy (2011)

Airway → Pleural space
Diagnostic → Therapeutic

Hsia D and Musani AI
Med Clin N Am (2011)
Just “New Toys”?

- Minimally invasive alternative(s)
- Flexible instruments
- Many can be performed as “day procedures”
- Local anaesthesia + conscious sedation
- Endoscopic suites
Pulmonary Interventions

EBUS-TBNA

Endobronchial Valves

Bronchial Thermoplasty

Autofluorescent Bronchoscopy

Cryoprobe / APC

Miniprobe

Pleuroscopy
Indwelling pleural catheter
Pulmonary Interventions

- Endobronchial Valves
- EBUS-TBNA
- Bronchial Thermoplasty
- Autofluorescent Bronchoscopy
- Cryoprobe / APC
- Miniprobe
- Pleuroscopy
  - Indwelling pleural catheter
Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration

Access beyond airway walls
The Equipment

- 6.9mm scope with 2mm instrument channel
- **Hybrid**: USG/Doppler + video-bronchoscope
- **Real-time USG-guided sampling** with 22G needle
Simultaneous Dual Display

Lymph node

Doppler

Conscious sedation + LA
Indications

1. **Staging of NSCLC**
   - Sampling of mediastinal and hilar lymph nodes (stations: 2-4, 7, 10-12)

2. **Diagnosis of mediastinal lesions**
   - Lymphoma
   - Sarcoidosis  (Wong M et al. ERJ 2013)
   - Tuberculosis

3. **Tumours adjacent to the airways**  (Chan JW et al. Hong Kong Med J 2014)
EBUS: a reliable diagnostic tool

Table 4—Characteristics of CT, PET, and EBUS-TBNA in the Correct Prediction of Mediastinal Lymph Node Staging

<table>
<thead>
<tr>
<th>Technique</th>
<th>Sensitivity (%)</th>
<th>Negative predictive value (%)</th>
<th>Prevalence (%) (range)</th>
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</thead>
<tbody>
<tr>
<td>CT</td>
<td>76.9</td>
<td>55.3</td>
<td>37.0</td>
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<tr>
<td>PET</td>
<td>80.0</td>
<td>70.1</td>
<td>46.5</td>
</tr>
<tr>
<td>EBUS-TBNA</td>
<td>92.3</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>84-88</td>
<td>77-81</td>
<td>61 (33-85)</td>
</tr>
</tbody>
</table>

*Cervical mediastinoscopy*

**Conventional TBNA**, 76-78 71-72 75 (30-100)

**EBUS-TBNA**, 90 76 68 (17-98)

**EUS-FNA**, 84-88 77-81 61 (33-85)

Data are presented as %. When the results of the three modalities were analyzed using $\chi^2$ tests describing the correct prediction of the lymph node status, the outcome was highly significant ($p < 0.00001$).

Toloza EM, et al. CHEST 2003
Detterbeck FC, et al. CHEST 2007
Medford AR, et al. Respirology 2010
EBUS-TBNA: Evaluations

**Pros**
- Daycase
- No GA required
- In endoscopy suite
- ↓ Procedural time
- Even ↑ Diagnostic value if combined with EUS

Rintoul RC et al. ERJ 2005  
Lee YT et al. HKMJ 2010

**Safe:**
- Overall complication rate ~1%  
  Shah A et al. CHEST 2011

**Cons**
- ↓ Negative predictive value than mediastinoscopy

Smaller sample size

↑ Initial setup costs
Endobronchial USG for peripheral lesions

Yield for conventional flexible bronchoscopy only ~ 30%
EBUS radial probe (miniprobe)

- A small radial USG probe inserted via bronchoscope (+/-) guide sheath

- "Extended working channel" to lesions along or adjacent to small airways

- Enable biopsy, brush, bronchial aspirate, needle aspiration and curette
Peripheral lesions: “Additional guides”

- Fluoroscopic guidance
- Virtual Bronchoscopy
- Navigational tools
Mechanisms of AFI

<table>
<thead>
<tr>
<th>Light intensity</th>
<th>Display color (Detection Light)</th>
<th>R (G' Reflected light)</th>
<th>G (Auto Fluorescence)</th>
<th>B (G' Reflected light)</th>
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<tbody>
<tr>
<td>Normal</td>
<td>green</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer, Dysplasia</td>
<td>red</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchitis</td>
<td>red</td>
<td>green</td>
<td></td>
<td>blue</td>
</tr>
</tbody>
</table>

Yasufuku K. Clin Chest Med 2010
Potential indications of AFI

1. Detection of **early lung cancer** with abnormal sputum cytology
2. Surveillance after curative resection of lung cancer
3. Guidance to endoscopic ablative procedures like Cryotherapy

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**Table: Sputum atypia group**

<table>
<thead>
<tr>
<th></th>
<th>WLB</th>
<th>AFB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sputum atypia group</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>57.1 (20–88)</td>
<td>85.7 (42–99)</td>
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<tr>
<td>Specificity</td>
<td>44.9 (31–60)</td>
<td>26.5 (15–41)</td>
</tr>
<tr>
<td>PPV</td>
<td>12.9 (4–31)</td>
<td>14.3 (6–29)</td>
</tr>
<tr>
<td>NPV</td>
<td>88.0 (68–99)</td>
<td>93.0 (64–100)</td>
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</table>

**Suspicious sputum cells group**

<table>
<thead>
<tr>
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<th>WLB</th>
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<tbody>
<tr>
<td><strong>Suspicious sputum cells group</strong></td>
<td></td>
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<tr>
<td>Sensitivity</td>
<td>60.0 (17–93)</td>
<td>100 (46–100)</td>
</tr>
<tr>
<td>Specificity</td>
<td>58.8 (32–81)</td>
<td>35.3 (15–61)</td>
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<tr>
<td>PPV</td>
<td>30.0 (8–65)</td>
<td>31.3 (12–59)</td>
</tr>
<tr>
<td>NPV</td>
<td>83.3 (57–97)</td>
<td>100 (52–100)</td>
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</tbody>
</table>

**Whole group**

<table>
<thead>
<tr>
<th></th>
<th>WLB</th>
<th>AFB</th>
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</thead>
<tbody>
<tr>
<td><strong>Whole group</strong></td>
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<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>58.3 (29–84)</td>
<td>91.7 (60–100)</td>
</tr>
<tr>
<td>Specificity</td>
<td>50.0 (38–62)</td>
<td>26.4 (17–38)</td>
</tr>
<tr>
<td>PPV</td>
<td>16.3 (7–31)</td>
<td>17.2 (9–29)</td>
</tr>
<tr>
<td>NPV</td>
<td>87.8 (73–95)</td>
<td>95.0 (73–100)</td>
</tr>
</tbody>
</table>

Lam B et al.  ERJ 2006
AFI: limitations

- ↓ specificity
- ↓ central tumours
- Varying accuracies with different pre-cancerous lesions
- Addition of Narrow Band Imaging (NBI) might improve the performance

<table>
<thead>
<tr>
<th>Technique</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WLB</td>
<td>26.5</td>
<td>63.9</td>
<td>34.4</td>
<td>54.9</td>
</tr>
<tr>
<td>AFI</td>
<td>52</td>
<td>79.6</td>
<td>64.4</td>
<td>69.9</td>
</tr>
<tr>
<td>NBI</td>
<td>66</td>
<td>84.6</td>
<td>75.4</td>
<td>77.7</td>
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<tr>
<td>AFI+NBI</td>
<td>86.1</td>
<td>86.8</td>
<td>84.4</td>
<td>88</td>
</tr>
</tbody>
</table>

WLB = White light videobronchoscopy, AFI = Autofluorescence imaging videobronchoscopy, NBI = Narrow band imaging videobronchoscopy, PPV = Positive predictive value, NPV = Negative predictive value

Pulmonary Interventions

- EBUS-TBNA
- Endobronchial Valves
- Bronchial Thermoplasty
- Autofluorescence Bronchoscopy
- Cryoprobe / APC
- Miniprobe
- Pleuroscopy Indwelling pleural catheter
Mechanism of Cryotherapy

- $\text{N}_2\text{O}$ vaporizes at the metal tip of the cryoprobe with ↓↓ pressure
- → cooling (Joule- Thomsen) effect (-89°C)
- “Cryo-destruction”: freeze/thaw action + vascular damage
- Cartilage is cryo-resistant: ↓↓ bronchial perforation
- “Cryo-adhesive” effect

Vergnon JM et al. ERJ 2006
Indications

- Relief of **malignant major airway obstruction**: de-bulking +/- “cryo-recanalization”
  

- **Treatment of early superficial carcinoma or carcinoma-in-situ**
  
  Deygas N et al. Chest 2001; Vergnon

- **Cryo-biopsy**: bronchial / transbronchial
  
  Babiak A et al. Respiration 2009; Franke KJ et al. Lung 2009

- **Removal of foreign bodies**
Cryotherapy: evaluations

- Safe
- Few adverse effects:
  - cough
  - fever
  - airway oedema
  - Bleeding
- Delayed effects
- Multiple sessions
Argon Plasma Coagulation (APC)

- High-frequency electrical current via ionized argon delivered to target tissue
- **Self-limiting depth** (≤5mm)
- **Flexibility**: Direction determined by the shortest distance between the jet and tissue (not direction of applicator)

A: Desication
B: Coagulation
C: Devitalization
Indications

- **Haemoptysis**  Morice RC et al. Chest 2001
- **Symptomatic airway obstruction**  Morice RC et al. Chest 2001

**Others:**
- Benign tumours (e.g. carcinoid)  Miller SM et al. J Bronchol Interv Pulmonol 2013
- Stent overgrowth or ingrowth (malignancy or granulation tissue)  Colt HG. J Bronchol 1998
- Cicatricial stenosis  Yasuo M et al. Respirology 2006

- **Not much evidence for treatment of early superficial cancer**
APC: Potential risks

- Uncommon
- Airway wall perforation
  - Leading to mediastinal and subcutaneous emphysema
- Burnt bronchoscopic tips
- Endobronchial burn (airway fires)
- MI, Stroke
- Gas embolism (rare)  
  
<table>
<thead>
<tr>
<th>Techniques</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical Removal</td>
<td>• Standard biopsy forceps</td>
<td>• Bleeding may cause less accurate management</td>
</tr>
<tr>
<td>Nd-YAG Laser</td>
<td>• Deep necrosis</td>
<td>• Relatively expensive</td>
</tr>
<tr>
<td></td>
<td>• Immediate result</td>
<td>• Skill &amp; expertise needed</td>
</tr>
<tr>
<td>Electrocautery and Argon Plasma Coagulation</td>
<td>• Simple &amp; inexpensive facility</td>
<td>• “Overkill,” fibrosis, and scarring</td>
</tr>
<tr>
<td></td>
<td>• Immediate visible result</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Flexibility (angulation)</td>
<td></td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>• Simple &amp; inexpensive facility</td>
<td>• Superficial necrosis</td>
</tr>
<tr>
<td></td>
<td>• Lethal effect (mm)</td>
<td>• Thermal fibrosis and scarring</td>
</tr>
<tr>
<td></td>
<td>• Safe for cartilage</td>
<td></td>
</tr>
<tr>
<td>High-Dose-Rate Brachytherapy</td>
<td>• Simple treatment</td>
<td>• Expensive facility</td>
</tr>
<tr>
<td></td>
<td>• Short sessions</td>
<td>• Normal tissue damage</td>
</tr>
<tr>
<td></td>
<td>• “Accurate” dosimetry calculation</td>
<td>• Multiple treatment sessions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lack feedback dosimetry for catheter movement during irradiation</td>
</tr>
<tr>
<td>Photodynamic Therapy</td>
<td>• Simple treatment</td>
<td>• Relatively expensive, elaborate facility</td>
</tr>
<tr>
<td></td>
<td>• Deep necrosis</td>
<td>• Complex dosimetry</td>
</tr>
<tr>
<td></td>
<td>• Vascular thrombosis</td>
<td>• Late necrosis, cleanup bronchoscopy</td>
</tr>
<tr>
<td></td>
<td>• Safe for cartilage</td>
<td>• Skin photosensitivity (hematoporphyrin)</td>
</tr>
</tbody>
</table>

Pulmonary Interventions

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- Autofluorescence Bronchoscopy
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- Miniprobe
- Pleuroscopy
  - Indwelling pleural catheter
Pleuroscopy (Medical Thoracoscopy): Semi-rigid instrument

- Handing ~ flexible bronchoscope
- 1 port of entry
- Flexible trocar

Distal 5 cm: 160° up/130° down
Outer diameter: 7mm
Working channel: 2.8mm
Common Indications

Diagnostic
- Exudative pleural effusions of unknown origin
- Suspected pleural secondaries (staging)

Therapeutic
- Talc pleurodesis for malignant pleural effusion
The procedure
Pleuroscopy: evaluation

**Pros:**
- **Yield 79-96%**
  - rigid ~ semi-rigid
    - [Lee et al. 2007; Munavvar et al. 2007; Law WL, Chan JW et al. 2008]
  - Superior to pleural biopsy and pleural tapping
- **Safe**
  - Mortality (0.09-0.24%)
  - Complications: mild and self-limiting
  - Commonest: Fever and SC emphysema
    - [Law WL, Chan JW et al. HKMJ 2008]

**Cons:** (semi-rigid pleuroscope)
- Possibly ↓ yield with mesothelioma or lymphoma
- Difficulty with dense adhesions or loculations
- ↓ Bleeding control
Pulmonary Interventions

EBUS-TBNA

Endobronchial Valves

Bronchial Thermoplasty

Autofluorescence Bronchoscopy

Cryoprobe / APC

Miniprobe

Pleuroscopy

Indwelling pleural catheter
Malignant Effusions: pleurodesis

- Symptom relief with drainage + prevention of recurrence
- Might not be the best solution:
  - “trapped lung”
  - Inability to tolerate surgical procedure
  - Significant failure rate
  - Adverse reactions
  - Hospitalizations

Davies HE and Lee GYC. Curr Opin Pul Med 2013
Indwelling (Tunneled) Pleural Catheter (IPC)

- Day procedure and ambulatory drainage
- Tunneled catheter connected to vacuum containers
IPC Outcomes

- 90% symptoms-free at 30-D without additional interventions
- ~50% “auto-pleurodesis” at 2-6 weeks
  
  Temblay A et al. Chest 2006

- Non-inferior to talc pleurodesis for dyspnoea control and QOL
  
  Davies HE et al. JAMA 2012

- More cost-effective
  

- Lower direct costs: ↓ hospitalizations
  
  Boshuizen RC et al. Respiration 2013

- Few complications: infections (<5%)
  
  Fysh ET et al. Chest 2013
Pulmonary Interventions

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A ONE-WAY VALVE:
Isolate the lobe →
Lobe shrinkage →
Complete collapse →
Volume reduction
Lung volume reduction (LVR) in emphysema

- **Hyperinflation in emphysema:**
  - ↓ chest wall compliance
  - ↓ function respiratory muscles
  - Leading to SOB, ↓ exercise tolerance and QOL

- **LVR surgery** [Fishman A et al. NEJM 2003]
  - Improves functional capacity and survival in a subgroup
  - Upper lobe predominant disease and poor baseline lung function
  - Substantial operative risks
EBV for emphysema (Bronchoscopic Lung Volume Reduction)

- Modest \(\uparrow\) lung function, exercise tolerance and symptoms
  - \(\uparrow\) success rate with heterogeneous emphysema, lobar exclusion (with complete lobar fissure) and -ve collateral ventilation

- \(\uparrow\) adverse events
  - EBV-related events: pneumothorax > 7 days (2.2%), “distal” pneumonia (1.9%); haemoptysis (0.6%)
Other Options?

Figure 5  Algorithm for bronchoscopic lung volume reduction in patients with severe emphysema. BLVR, biological lung volume reduction; FEV$_1$, forced expiratory volume in 1 s; HRCT, high-resolution CT; LVRC, lung volume reduction coil; RV, residual volume.

Herth FJ et al. Respiration 2011 (Sealant)
Snell G et al. ERJ 2012 (thermal vapour ablation)
Shah PL et al. Lancet Resp 2013 (endobronchial coils)
EBV for persistent air leaks in pneumothorax
EBV in persistent air leaks: the evidence

- Mostly case series or reports
- Shorten LOS
- Relatively safe and non-invasive
- Air leaks reduced or resolved in >90% (Travaline JM et al. Chest 2009)
  - Mean time from EBV placement to drain removal: 21 days (median 7.5; IQR 3-29)
Pulmonary Interventions

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Airway Smooth Muscle (ASM) on Asthma

Normal Airway

Asthma Attack
Bronchial Thermoplasty: Actions and effects

Reduces Airway Smooth Muscle

Reduces Bronchoconstriction

Reduces Asthma Exacerbations

Improves Asthma Quality of Life
Bronchial Thermoplasty: Catheter and RF Controller

- **Catheter** – a flexible tube with an expandable wire array at the tip (introduced through a standard bronchoscope)

- **Radiofrequency (RF) Controller** – supplies energy via the Catheter to heat the airway wall
Clinical Studies

- **Over 800** Procedures Performed
- **3** Randomized Controlled Studies
- **Over 10** Publications

**Pivotal Study**
AIR2: $n=190$
treated patients
at 30 sites

1. (Castro, AJRCCM, 2010)
2. (Castro, AAAI, 2011)
3. (Cox, NEJM, 2007)
4. (Cox, AJRCCM, 2006)

AIR = Asthma Intervention Research Study
RISA = Research in Severe Asthma Study
Clinical Outcomes

- Improved asthma-related quality of life
- Improved clinical outcomes:
  - 32% ↓ severe exacerbations
  - 84% ↓ ER visits
  - 73% ↓ hospitalization
  - 66% ↓ days off work / school / other daily activities
- Slightly short-term asthma related morbidities
- No device-related serious adverse events or deaths
- No complications + stable lung fx at 5 years

Cox et al. NEJM 2007
Pavord et al. AJRCCM 2007
Castro et al. AJRCCM 2010
Thomson NC et al. BMC Pul Med 2011
Pavord ID et al. AJRCCM 2011
Potential therapeutic option in severe asthmatics

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
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<tbody>
<tr>
<td><strong>As needed rapid-acting β₂-agonist</strong></td>
<td><strong>As needed rapid-acting β₂-agonist</strong></td>
<td><strong>As needed rapid-acting β₂-agonist</strong></td>
<td><strong>As needed rapid-acting β₂-agonist</strong></td>
<td><strong>As needed rapid-acting β₂-agonist</strong></td>
</tr>
<tr>
<td><strong>Controller options</strong>*</td>
<td><strong>Controller options</strong>*</td>
<td><strong>Controller options</strong>*</td>
<td><strong>Controller options</strong>*</td>
<td><strong>Controller options</strong>*</td>
</tr>
<tr>
<td>Select One</td>
<td>Select One</td>
<td>Add one or more</td>
<td>Add one or both</td>
<td>Add one or both</td>
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<tr>
<td>Low-dose inhaled ICS*</td>
<td>Low-dose ICS plus long-acting β₂-agonist</td>
<td>Medium or high-dose ICS plus long-acting β₂-agonist</td>
<td>Oral glucocorticosteroid (lowest dose)</td>
<td>Oral glucocorticosteroid (lowest dose)</td>
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<td>Leukotriene modifier**</td>
<td>Medium or high-dose ICS</td>
<td>Leukotriene modifier</td>
<td>Anti-IgE treatment</td>
<td>Anti-IgE treatment</td>
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<tr>
<td>- Low-dose ICS plus leukotriene modifier</td>
<td>Sustained release theophylline</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

*ICS = inhaled glucocorticosteroids
** = Receptor antagonist or synthesis inhibitors
*** = Preferred controller options are shown in shaded boxes

GINA 2012
Interventional Pulmonology: Conclusions

- A growing field
  - From airway to pleura
  - From diagnostic to therapeutic
- Attractive alternatives for patients with borderline performance status
  - ↓ invasiveness
  - ↓ risks
  - ↓ hospitalization
  - ↑ Cost-effectiveness
Acknowledgments

- Dr. David CL Lam (QMH)
- Dr. WL Law (QEH)
- Members of the Special Interest Group of Bronchology and Interventional Pulmonology of HKTS/ACCP (HK & Macau Chapter)

THANK YOU!