Future of Interventional Pulmonology

Atul C. Mehta, MBBS, FACP, FCCP
Professor of Medicine, Lerner College of Medicine
Staff, Respiratory Institute
Cleveland Clinic, Cleveland, Ohio, USA

Editor-in-Chief, Journal of Bronchology & Interventional Pulmonology
Conflict of Interest

- Participating in Coil Trial; PneumRx ® Corporation
- Editor in Chief: Journal of Bronchology and Interventional Pulmonology
“Future”

- “It is tough to make predictions, especially about the future!”
  Yogi Berra

- “The best prophet of the future is the past.”
  Lord Byron
Interventional Pulmonology
Past, Present and Future
Bronchoscopy

- **Early Years:** Rigid Scope: Foreign Body removal
- **Day before y’day:** Flexible Scope: Curiosity << RB
- **Yesterday:** Diagnostic tool FB>>RB
- **Today:** Diagnostic and Therapeutic Tool
- **Tomorrow:** Diagnostic, Therapeutic and Research tool Technology FB >>>>>RB
History

- 1807: Philipp Bozzini (German army surgeon): Light conductor, precursor of endoscopes
- 1828: Benjamin Guy Babington (British physician): “Glottiscope”
- 1800: Manuel Garcia (Spanish music teacher, singer): First laryngoscopy
- 1847: Horace Green inserted a gum-elastic catheter through the larynx and into the lower bronchi; expelled from the society
- 1867: G. Johnson: Extracted a penny impacted in a throat of a child using laryngoscope

Father of Bronchoscopy: Gustav Killian

- **1895**: Alfred Kirstein (Germany): first direct visualization of VC using esophagoscope (*autoscope*)
  - Examined trachea and main bronchi of a volunteer using Laryngoscope
  - Removed a bone from RMB using an esophagoscope
  - Removed 3 more FB in a similar fashion, same year and coined term “directe bronkoscopie”

- **1897**: Gustav Killian, (ENT, Freiburg, Germany):
  - Examined trachea and main bronchi of a volunteer using Laryngoscope
  - Removed a bone from RMB using an esophagoscope
  - Removed 3 more FB in a similar fashion, same year and coined term “directe bronkoscopie”

- **1898**: Algernon Coolidge (Harvard Medical School) used an open urethroscope, a head-mirror, and reflected sunlight to remove a hard-rubber cannula from RMB
Father of American Bronchoesophagology

Year: 1913

Cavalier Jackson
History

- **1904-20**: Chevalier Jackson (ENT surgeon, Professor x 5, Pittsburgh ➔ Philadelphia, USA) Modifications of RB, light at the distal end
  - Bronchoscopy: Hands-on-Courses!
- **Victor Negus** (British, Jackson’s student): Negus bronchoscope
- **C.L. Jackson, Jr.** (Laryngologist)-Founder:
  - Pan American Association of Otolaryngology
  - International Bronchoesophagological Society *
- **Edwin Boyles**: Optical Telescope with forward & angle viewing
- **Paul H. Holinger**: Bronchoscopic photography
History

- 1922: Yankauer → Brachytherapy
- 1976: Neel & Sanderson → Cryotherapy
- 1976: Laforet: Use of CO2 Laser on the trachea
- 1985: Hooper & Jackson → Endobronchial Electrosurgery

Beamis J, Mathur P, Interventional Pulmonology: Current Status and Future Direction
Major Milestones

- Fiberoptic Bronchoscope: 1968
- Transbronchoscopic Lung Biopsy: 1972
- TBNA: 1979
- Laser Therapy: 1981
- Lung Transplantation: 1982
- Endobronchial Stents: 1990
- EBUS:
  - Radial Probe: 1992
  - Convex probes: 2004
- EMN: 2003
- Bronchial Thermoplasty: 2006
Transbronchoscopic Lung Biopsy

Major Milestone: Fiberoptics

- 1872: Tyndall Effects
- 1957: Basil Hirschowitz (U of M): First gastro-fiberscope
- 1968: Shigeto Ikeda, T/S (Tokyo National Cancer Institute, Japan): Flexible Fiberoptic Bronchoscope
- 1970: First commercial Olympus FB model
- Late 1980’s: Video Bronchoscope

Flexible Transbronchial Needle Aspiration

- Based on Schipetti and Oho’s concept designed a needle for its application through the flexible scope
- Cytology and Histology needles
  - Mediastinal pathology
  - Peri-bronchial lesions (25% SmCCa)
  - Peripheral lesions (18%)
- Reduction in the number of mediastinoscopy

Ko Pen Wang, 1978
Major Milestone: Use of LASER

- 1981: First reported use of Nd-YAG Laser in the airways
- Designed newer type of rigid bronchoscope
- Silicon Stents and Stent insertion instrument


Rigid Bronchoscope & Endobronchial Stent

Dumon JF. A dedicated tracheobronchial stent. Chest. 1990;97:328
Radial Probe-EBUS
Becker HD, New Perspective on EBUSm J Ultraschall Med, 1996; 17: 106

Heinrick Becker, MD, Heidelberg, Germany
Hunter T, Hanrath P, Endobronchial Sonography, Feasibility & Preliminary Results
Thotax, 1992, (47): 565
CP-EBUS

Yasufuku K, Chhajed P, Real-time EBUS-TBNA of mediastinal & hilar lymph nodes
Chest. 2004;126:122
Electromagnetic Navigation

Yehuda Swrtz, MD, Tel Aviv, IS

EMN Diagnostic Bronchoscopy: A Prospective Study. Am J Respir Crit Care Med. 2006; 174(9)982
Bronchial Thermoplasty
Cox G, AJRCCM, 2006
Today

- Most commonly performed diagnostic procedure by the pulmonologist
- There is no single pulmonary ailment a flexible bronchoscope can not either diagnose, cure or palliate! (Asthma, COPD,.....)
Today

Success of Lung Transplantation cannot be imagined without the Flexible bronchoscope

E P Trulock; The role of TBBx in Rx of LTx recipients
An analysis of 200 consecutive procedures, Chest. 1992;102(4):1049
Bronchoscopic Management of Dehiscence

Short-Term Deployment of Self-Expanding Metallic Stent Facilitates Healing of Bronchial Dehiscence. Amer J of Respir & Critic Care Med 2005; 172:768
Interventional Pulmonology

- Well established sub-sub specialty
- Fellowship programs
- First ever IP Board Exam (# 75)
- National & international organizations: [WABIP, AABIP, EABIP, IABIP, ...]
- National & International Seminars [WCBIP]
- JOBIP is now Indexed
- Guidelines and Consensus statements
Cleveland Clinic had the honor of hosting the 17th World Congress for Bronchology and Interventional Pulmonology (WCBIP) — and the 17th World Congress for Bronchoesophagology — on June 15-18, 2012. The World Congress takes place every other year, and this is only the fourth time that it has come to the United States.
Bronchoscopy Today

- **Level IV**: Basic Diagnostic: Wash, Brush, EBB, TBB, C-TBNA, NBI
- **Level III**: Advanced Diagnostics: Level IV plus EMN, RP-EBUS, CP-EBUS
- **Level II**: Therapeutic bronchoscopy: Level III plus, SEMS, APC, EBES, Laser-PR, Bronchoplasty, Cryo, EBVR, Thermoplasty, FB removal
- **Level I**: Advanced Therapeutics: Level II plus Rigid Bronch, Silicon stent placement, SEM Remova; Staging EBUS, Adrenal Gland Bx, EUS, PEG
Interventional Pulmonology

- **Fostering Team Approach:**
  - Anesthesiology
  - Radiation Oncology
  - Cytopathology
  - Thoracic surgery
  - Radiology/Interventional Radiology

- **Competing Disciplines:**
  - GI: EUS, Adrenal Gland Bx, PEG Tubes
  - Thoracic Surgery: Pleuroscopy
  - Otolaryngology: T Tube placement
  - Pathology

Gasparini S, The Role of the Pulmonologist in ROSE Evaluation of TBNA, A Prospective Study CHEST, 2014, 145(1) 60
Today

What is the largest foreign body a pulmonologist has ever removed from the endobronchial tree?
Today

- Removal of the endobronchial foreign body and the mediastinal staging of NSCCA, no longer remain in the domain of the thoracic surgeons.

- Answer: Thoracic Surgeon

Annema, J, Mediastinoscopy vs Endosonography for Mediastinal Nodal Staging of Lung Cancer: A Randomized Trial, JAMA.2010, 304 (20): 2245
Future

Future belongs to ideas and innovations.

Yet!

People who don’t remember the past are condemned to repeat it!
“All Innovations are History Forgotten!”

Lord Ganesha:

- First case of:
  - Solid organ transplantation
  - Facial transplantation
  - Xenotransplantation
  - (?) Cushing’s Syndrome
“All Innovations are History Forgotten!”

Laser Photoresection
Future

Future belongs to the Innovations

- Endobronchial Volume Reduction: Patient selection
- Virtual Bronchoscopic Navigation
- Bio-absorbable Stents
- 3-D Printing
- Tracheal Transplantation
- Stem Cell Therapy
- Confocal Bronchoscopy
- OCT (?)
Endobronchial Volume Reduction: Valves

- Use of EBV for Emphysema remains investigational in USA
- EBV are routinely used in select European and Middle Eastern “Center(s) of Excellence”
- EBV have been approved in the compassionate management of prolonged air leak in the USA
- Trials on “Biochemical” agents Thermal Vapor have been abandoned in USA
- Newer modalities for EBVR are emerging: Coils
A Randomized Study of Endobronchial Valves for Advanced Emphysema (Zephyr Valve®)

- **VENT Trial**
- N=321, 2:1 randomization (220:101)
- Centers: 31
- Dec 2004-April 2006
- Age: 40-75
- Upper lobe Heterogeneous disease
- FEV1: 15-45%, TLC: >100%, RV: 150%
- Unilateral Upper lobe Rx
Euro VENT Trial
Euro Respi J 2012, 39 1334

- 23 sites
- N=171
  - 111 EBV
  - 60 Control

Overall results
- Modest benefit in overall cohort
- Consistent with findings in US VENT

Complete fissures
- Greater clinical benefit compared to whole cohort

Complete fissures + lobar occlusion
- Highest benefit
Complete Fissure (N=56)

<table>
<thead>
<tr>
<th></th>
<th>Lobar Occlusion (20)</th>
<th>No Lobar Occlusion (17)</th>
<th>P</th>
<th>Control (19)</th>
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<tr>
<td>6 months</td>
<td></td>
<td></td>
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<tr>
<td>Target Lobe VR</td>
<td>-80%</td>
<td>-29%</td>
<td>&lt;0.0001</td>
<td>0</td>
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<tr>
<td>&gt;55% Reduction</td>
<td>79 %</td>
<td>18%</td>
<td>0.0002</td>
<td>0</td>
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<tr>
<td>FEV1 Change</td>
<td>26</td>
<td>6</td>
<td>0.004</td>
<td>3</td>
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<tr>
<td>&gt;15% Change</td>
<td>67%</td>
<td>8%</td>
<td>0.002</td>
<td>6%</td>
</tr>
<tr>
<td>6 MWD</td>
<td>22</td>
<td>-2</td>
<td>0.03</td>
<td>19</td>
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<tr>
<td>&gt;35 meter</td>
<td>56%</td>
<td>25%</td>
<td>0.1</td>
<td>38</td>
</tr>
<tr>
<td>SGRQ</td>
<td>-10</td>
<td>-2</td>
<td>0.02</td>
<td>3</td>
</tr>
<tr>
<td>&gt;4 points</td>
<td>67%</td>
<td>40</td>
<td>0.4</td>
<td>17%</td>
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</table>

Euro Respi J 2012, 39 1334
Survival Advantage

**FIGURE 1.** Atelectasis following bronchoscopic lung volume reduction was associated with improved survival (p=0.026).

**FIGURE 2.** Survival comparison between patients with and without visible fissures. O: censored patients; |: alive patients.
Lung Volume Reduction Coil System

- CE Mark: 2010
- > 600 pts Rxed (total)
- French MOH: 2013 Cost effectiveness & reimbursement study
- Approved for a US IDE Pivotal Clinical Trial: Pts are being recruited

Shape memory Nitinol implant
CHEST 2012; 142(3):574–582
Lung Volume Reduction Coil System

Compresses diseased tissue in emphysematous lung

- Restore elastic recoil
  - Improve lung compliance
  - Shift preferential filling of air from diseased to healthier tissue

- Reduce hyperinflation
  - Radially suspends & tethers airways open to reduce air trapping

- Maintain airway patency
  - Preserve distal access & flow
<table>
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<tr>
<th></th>
<th>N</th>
<th>180 Days (N=113)</th>
<th>p-value</th>
<th>N</th>
<th>360 Days (N=75)</th>
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<tbody>
<tr>
<td><strong>Change vs. Baseline, Actual Value</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>FEV1, L</td>
<td>106</td>
<td>0.11L ±0.16</td>
<td>&lt; 0.0001</td>
<td>73</td>
<td>0.10L ±0.22</td>
<td>0.0003</td>
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<tr>
<td>RV, L</td>
<td>112</td>
<td>-0.59L ±0.76</td>
<td>&lt; 0.0001</td>
<td>74</td>
<td>-0.52L ±0.77</td>
<td>&lt;0.0001</td>
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<tr>
<td>6MWT, m</td>
<td>110</td>
<td>43.9m ±66.7</td>
<td>&lt; 0.0001</td>
<td>71</td>
<td>50.6m ±62.4</td>
<td>&lt;0.0001</td>
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<tr>
<td>SGRQ, points</td>
<td>111</td>
<td>-11.2pts ±11.6</td>
<td>&lt; 0.0001</td>
<td>74</td>
<td>-10.1pts ±12.2</td>
<td>&lt;0.0001</td>
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<tr>
<td><strong>% Change vs. Baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1, L</td>
<td>106</td>
<td>14.92% ±22.01</td>
<td>&lt; 0.0001</td>
<td>73</td>
<td>13.16% ±27.07</td>
<td>&lt;0.0001</td>
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<tr>
<td>RV, L</td>
<td>112</td>
<td>-10.49% ±13.02</td>
<td>&lt; 0.0001</td>
<td>74</td>
<td>-9.2% ±13.55</td>
<td>&lt;0.0001</td>
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<tr>
<td>6MWT, m</td>
<td>110</td>
<td>17.9% ±27.9</td>
<td>&lt; 0.0001</td>
<td>71</td>
<td>19.0% ±25.9</td>
<td>&lt;0.0001</td>
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<tr>
<td>SGRQ, points</td>
<td>111</td>
<td>-18.9% ±21.2</td>
<td>&lt; 0.0001</td>
<td>74</td>
<td>-17.9% ±24.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
ELVR – Lessons learned - SGRQ

![Graph showing various treatments over time](chart.png)
Virtual Bronchoscopy Navigation

McLennan G, Ferguson JS, Use of MDCT-based computer aided pathway finding mediastinal & perihilar LN Biopsy: A randomized controlled prospective trial, Respiration 2007;74:423
Carinal Replacement with Fresh Aortic Grafts

Carinal Replacement

- Continuous mucociliary epithelium:
- Ciliated cells
- Goblet cells

Tracheal Transplantation (Tissue Engineering)
At 5 months
Tissue Engineering
Distant Future or Tomorrow’s Treatment?

1. Synthetic scaffold cultured with autologous human bone marrow mononuclear cells
2. Bronchoscopy at 1 week
3. Histology at 2 months:
   - Respiratory epithelium
   - Mucus-secreting cells

AJRCCM 2013, (187) : 468-475
Endobronchial Stent: 3D Printing: Silicon Stent

Cleveland Clinic
Bioabsorbable Airway Splint Created with 3-D Printer

Zopf et al, NEJM 2013

- 2 month old child with severe TBM
- 3-D printing using polycaprolactone
- Normal airways at 1 year follow up
Tracheal Replacement in Humans Using Autologous Tissues: An 8-Year Experience

Tracheal Replacement in Humans Using Autologous Tissues: An 8-Year Experience

- Trachéal substitution with tube made up of forearm fascio-cutaneous flap vascularized by radial vessels, re-anastomosed to internal mammary vessels, reinforced by rib cartilage implanted into the subcutaneous tissue
- No immunosuppression
- No synthetic materials
- N=12 (8 years)
- Tracheal neoplasms: 8
- 7 –12 cm resection
- All extubated on POD 1
- 8 are alive at a mean of 36 months, 2 with trach
In Vivo Imaging of the Bronchial Wall Microstructure Using Fibered Confocal Fluorescence Microscopy

Luc Thiberville, et al.

Mosaicing reconstruction of a normal area of the bronchial wall (right upper lobe carina) in a patient at high risk for lung cancer, as visualized by fibered confocal fluorescence microscopy during a bronchoscopy.

Alterations in the fluorescence structure of the bronchial basement membrane zone are frequently found in individuals at high risk for lung cancer.

Am J Respir Crit Care Med 2007; 175:22–31
Endoscopic Microscope

“Future of Bronchoscopy lies in the Colon of the patient!”
Challenges of the Future

“The future ain’t what it used to be!” Yogi Berra

- Radiology: HRCT
- Cost vs Reimbursement
- Education: Training, Credentialing
- Overenthusiasm
- Maldistribution between needs and resources
- Innovations: Electronic nose, Molecular Radiology, Serology
Editorial Comments

- Interventional Pulmonology is more than just interventions [EBTB, EB Sarcoid, GPA, IBD, Infections]
- You have to be a good bronchoscopist to be an interventionalist; interventions don’t make you a better bronchoscopist
- Because it could be done that doesn’t mean it should be done
- One has to be larger than his or her abilities
- Pt’s welfare >> self gratification, “Adrenalizing”
- A good bronchoscopist is the one who knows when not to perform the procedure
- Reducing health care cost is a civic responsibility
Still I am learning