Novel Bronchoscopic Therapies

Pallav L Shah

Royal Brompton Hospital
Chelsea & Westminster Hospital
Imperial College
**Clinical Features**

- 66 year old gentleman
- Longstanding breathlessness
- Exercise tolerance declined dramatically over last 12 months
- Breathless on daily task of living
- Repeated hospital admissions for respiratory exacerbations (4 over last 9 months)
- Ex-smoker 60 pack years stopped 12 months ago
## Vent Study Analysis

<table>
<thead>
<tr>
<th>Subset</th>
<th>Group</th>
<th>Vol Red</th>
<th>FEV1</th>
<th>6MWT</th>
<th>SGRQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population</td>
<td>Control</td>
<td>-1.7%</td>
<td>-1.9%</td>
<td>-1.5%</td>
<td>0.74%</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>-20.6%</td>
<td>5.3%</td>
<td>4.3%</td>
<td>-2.66%</td>
</tr>
<tr>
<td>&gt;10% heterogenous</td>
<td>control</td>
<td>-0.8%</td>
<td>-2.8%</td>
<td>-4.3%</td>
<td>0.95%</td>
</tr>
<tr>
<td></td>
<td>treatment</td>
<td>-23.3%</td>
<td>7.7%</td>
<td>4.5%</td>
<td>-2.33%</td>
</tr>
<tr>
<td>+lobar exclusion</td>
<td>treatment</td>
<td>-30.3%</td>
<td>12.4%</td>
<td>6.3%</td>
<td>-3.34%</td>
</tr>
<tr>
<td>+complete fissure</td>
<td>treatment</td>
<td>-56.9%</td>
<td>22.8%</td>
<td>5.3%</td>
<td>-5.01%</td>
</tr>
</tbody>
</table>
• Blinded Randomised Controlled study

• Sham procedure

• Selection based on Fissure Integrity

• All patients underwent Chartis procedure
Blinded RCT of EBV in Patients with Intact Fissures

50
Randomised

25
Sham Control

24 Completed Follow Up
- 1 SAE (Pneumothorax/ICU)

%ΔFEV1: 3.87 (0.66 to 7.08)
SGRQ -3.66 (-8.12 to 0.80)
6MWT -4 (-26 to 19)

25
Unilateral lobar Endobronchial valves

23 Completed Follow Up
- 2 RIP
1 Respiratory Failure (Removal)
1 COPD with Cor Pulmonale

%ΔFEV1: 24.77 (8.02 to 41.51)
SGRQ -8.71 (-17.22 to -0.21)
6MWT 29.0 (0-52)

Davey et al. Lancet 2015:386;1066
Change in FEV1

![Graph showing change in FEV1% from baseline for Treatment and Control groups. The graph indicates a statistically significant difference (p=0.033) between the two groups.]

Davey et al. Lancet 2015:386:1066c
Change in Secondary Endpoints

6MWD

Endurance cycle (t)

CAT

SGRQ

RV

TLco

Davey et al. Lancet 2015:386;1066c
Responder rate according to collateral ventilation status

<table>
<thead>
<tr>
<th></th>
<th>BLVR All (n=23)</th>
<th>BLVR CV-positive excluded (n=19)</th>
<th>Control (n=24)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEV₁</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;15% improvement</td>
<td>···</td>
<td>9 (47%)</td>
<td>1 (4%)</td>
<td>0.0044</td>
</tr>
<tr>
<td><strong>RV</strong></td>
<td>11 (48%)</td>
<td>···</td>
<td>7 (29%)</td>
<td>0.24</td>
</tr>
<tr>
<td>0.35 L reduction</td>
<td>···</td>
<td>11 (58%)</td>
<td>7 (29%)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>6MWD</strong></td>
<td>12 (52%)</td>
<td>···</td>
<td>4 (17%)</td>
<td>0.012</td>
</tr>
<tr>
<td>26 m improvement</td>
<td>···</td>
<td>12 (63%)</td>
<td>4 (17%)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Endurance cycle time</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>105 s improvement</td>
<td>···</td>
<td>9 (47%)</td>
<td>2 (8%)</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>SGRQc</strong></td>
<td>11 (48%)</td>
<td>···</td>
<td>11 (46%)</td>
<td>1.0</td>
</tr>
<tr>
<td>4 points reduction</td>
<td>···</td>
<td>11 (58%)</td>
<td>11 (46%)</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>CAT</strong></td>
<td>13 (57%)</td>
<td>···</td>
<td>7 (29%)</td>
<td>0.080</td>
</tr>
<tr>
<td>2 points reduction</td>
<td>···</td>
<td>13 (68%)</td>
<td>7 (29%)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

*Davey et al. Lancet 2015:386;1066*
Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation

Karin Klooster, Nick H.T. ten Hacken, M.D., Ph.D., Jorine E. Hartman, Ph.D., Huib A.M. Kerstjens, M.D., Ph.D., Eva M. van Rikxoort, Ph.D., and Dirk-Jan Slebos, M.D., Ph.D.
<table>
<thead>
<tr>
<th>Variable</th>
<th>EBV Group (N = 34)</th>
<th>Control Group (N = 34)</th>
<th>Between-Group Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in FEV$_1$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milliliters (95% CI)</td>
<td>161 (80 to 242)</td>
<td>21 (−9 to 52)</td>
<td>140 (55 to 225)</td>
<td>0.002</td>
</tr>
<tr>
<td>Percentage (95% CI)</td>
<td>20.9 (11.1 to 30.7)</td>
<td>3.1 (−0.4 to 6.6)</td>
<td>17.8 (7.6 to 28.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Response rate — %</td>
<td>59</td>
<td>24</td>
<td>—</td>
<td>0.003</td>
</tr>
<tr>
<td>Change in FVC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milliliters (95% CI)</td>
<td>416 (201 to 631)</td>
<td>69 (−50 to 187)</td>
<td>347 (107 to 588)</td>
<td>0.005</td>
</tr>
<tr>
<td>Percentage (95% CI)</td>
<td>18.3 (9.3 to 27.3)</td>
<td>4.0 (−0.7 to 8.6)</td>
<td>14.4 (4.4 to 24.3)</td>
<td>0.005</td>
</tr>
<tr>
<td>Change in distance on 6-min walk test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meters (95% CI)</td>
<td>60 (35 to 85)</td>
<td>−14 (−25 to −3)</td>
<td>74 (47 to 100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Percentage (95% CI)</td>
<td>19.6 (10.4 to 28.9)</td>
<td>−3.6 (−6.9 to −0.4)</td>
<td>23.3 (13.6 to 32.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Response rate — %</td>
<td>59</td>
<td>6</td>
<td>—</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Klooster et al. NEJM 2015:373;2325
Intention To Treat Analysis

Change from Baseline to 6 Mo (ml)

**FEV₁**
- EBV (N=34)
- Control (N=34)
- P=0.002

**FVC**
- EBV (N=34)
- Control (N=34)
- P=0.005

**6MWD**
- EBV (N=34)
- Control (N=34)
- P<0.001

MCID
Completed Treatment Only Analysis

- **FEV₁**
  - Change from Baseline to 6 Mo (ml)
  - EBV (N=25) vs Control (N=33)
  - P<0.001
- **FVC**
  - Change from Baseline to 6 Mo (ml)
  - EBV (N=25) vs Control (N=33)
  - P<0.001
- **6MWD**
  - Change from Baseline to 6 Mo (m)
  - EBV (N=23) vs Control (N=33)
  - P<0.001

- **RV**
  - Change from Baseline to 6 Mo (ml)
  - EBV (N=24) vs Control (N=33)
  - P<0.001
- **SGRQ Score**
  - Change from Baseline to 6 Mo (points)
  - EBV (N=24) vs Control (N=33)
  - P<0.001
- **CCQ Score**
  - Change from Baseline to 6 Mo (points)
  - EBV (N=24) vs Control (N=33)
  - P<0.001

Klooster et al. NEJM 2015:373;2325
<table>
<thead>
<tr>
<th>Event</th>
<th>EBV Group (N=34)</th>
<th>Control Group (N=34)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of serious events</td>
<td>23 (70)</td>
<td>5 (15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Pulmonary events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1 (3)‡</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>COPD exacerbation with hospitalization</td>
<td>4 (12)</td>
<td>2 (6)</td>
<td>0.67</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2 (6)</td>
<td>1 (3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>6 (18)</td>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>Resolved ≤14 days after onset, without drainage</td>
<td>1 (3)</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Resolved ≤14 days after onset, with drainage</td>
<td>2 (6)</td>
<td>0</td>
<td>0.49</td>
</tr>
<tr>
<td>Required temporary valve removal</td>
<td>1 (3)§</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Required permanent valve removal because of recurrent pneumothorax</td>
<td>1 (3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Required permanent valve removal, after temporary valve removal</td>
<td>1 (3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Other EBV-related events requiring permanent removal of all valves</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torsion of the bronchus</td>
<td>2 (6)¶</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Pneumonia distal to valve</td>
<td>1 (3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Increased sputum, dyspnea, or coughing without patient-perceived</td>
<td>2 (6)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Other EBV-related events requiring valve replacement</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve migration</td>
<td>2 (6)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Valve expectoration</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Valve dislocation due to formation of granulation tissue</td>
<td>1 (3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Increased sputum, dyspnea, or coughing</td>
<td>1 (3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (3)</td>
<td>2 (6)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Summary: Endobronchial Valves

Strategy
- Unilateral occlusion

Selection
- intact fissure or absent collateral ventilation
- heterogeneity (greater than 15% difference in degree of destruction between upper & lower lobes)

Survival
- atelectasis of target lobe indicative of response & long term survival
Endobronchial Coil Procedure

Tools
Emphysema: Case Study

Case PH
Emphysema: Case Study

- 54 year old florist, increasing dyspnoea over last 18 months
- ex smoker stopped 10 years ago with a previous of 15 pack years
- maximal medical treatment
- Has to stop after walking every 50 metres
- Losing contracts due to ill health
- Has not been away on a holiday for last 5 years
Emphysema: Case Study

Case PH
Emphysema: Case Study

Results: 30 days post coil insertion

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>0.61</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td>FVC</td>
<td>3.08</td>
<td>3.59</td>
<td></td>
</tr>
<tr>
<td>RV</td>
<td>5.28</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>TLC</td>
<td>8.21</td>
<td>7.53</td>
<td></td>
</tr>
<tr>
<td>RV/TLC</td>
<td>0.65</td>
<td>0.47</td>
<td></td>
</tr>
<tr>
<td>6MWT</td>
<td>200m</td>
<td>282m</td>
<td></td>
</tr>
<tr>
<td>SGRQ</td>
<td>64</td>
<td>56</td>
<td></td>
</tr>
</tbody>
</table>

- Walking has improved
- Even able to load flowers into the van
- Improved self esteem
- Planning holiday first holiday

Case PH
Endobronchial coils for the treatment of severe emphysema with hyperinflation (RESET): a randomised controlled trial

Pallav L Shah, Zaid Zoumot, Suveer Singh, Stephen R Bicknell, Ewen T Ross, John Quiring, Nicholas S Hopkinson, Samuel V Kemp, for the RESET trial Study Group

Multicenter, randomized, controlled study
Safety and effectiveness
1:1 randomisation, Treatment or Control
45 subjects
Controls cross over to treatment at 3 months
## RESET Trial: Efficacy Outcomes
(Change from Baseline at 90 Days)

<table>
<thead>
<tr>
<th></th>
<th>RePneu Coil Treatment n=23</th>
<th>Control Group n=23</th>
<th>Between-Group Difference in Change from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number (95% confidence interval)</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>Corrected for Difference between Groups at Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change in SGRQ</td>
<td>-7.43 (-12.48 to -2.37)</td>
<td>-0.35 (-5.52 to 4.82)</td>
<td>-7.08 (-14.06 to -0.09)</td>
</tr>
<tr>
<td></td>
<td>-0.35 (-5.52 to 4.82)</td>
<td>-7.08 (-14.06 to -0.09)</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary outcome</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change in TLC (L)</td>
<td>-0.28 (-0.57 to 0.00)</td>
<td>-0.21 (-0.50 to 0.08)</td>
<td>-0.08 (-0.43 to 0.28)</td>
</tr>
<tr>
<td>Mean change in RV (L)</td>
<td>-0.61 (-0.93 to 0.29)</td>
<td>-0.04 (-0.37 to 0.28)</td>
<td>-0.57 (-0.97 to -0.17)</td>
</tr>
<tr>
<td>Mean change in 6MWT (m)</td>
<td>47.14 (23.40 to 70.87)</td>
<td>-5.00 (-28.67 to 18.67)</td>
<td>52.14 (21.78 to 82.50)</td>
</tr>
<tr>
<td>Mean percent change in FEV₁</td>
<td>14.20 (7.52 to 20.89)</td>
<td>1.99 (-4.98 to 8.96)</td>
<td>12.22 (3.51 to 20.92)</td>
</tr>
</tbody>
</table>
### Table 3: Responder analysis of primary and secondary efficacy outcomes in the intent-to-treat population (change from baseline at 90 days after final treatment)

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>Treatment (n=23)</th>
<th>Usual care (n=23)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGRQ ≥4-point improvement</td>
<td>15 (65%)</td>
<td>5 (22%)</td>
<td>0.01</td>
</tr>
<tr>
<td>SGRQ ≥8-point improvement</td>
<td>13 (57%)</td>
<td>3 (13%)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Secondary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory volume: ≤0.35-L reduction</td>
<td>13 (57%)</td>
<td>4 (17%)</td>
<td>0.01</td>
</tr>
<tr>
<td>6-min walk test: ≥26-m improvement</td>
<td>17 (74%)</td>
<td>4 (17%)</td>
<td>&lt;0.0003</td>
</tr>
<tr>
<td>FEV₁: ≥10% improvement</td>
<td>13 (57%)</td>
<td>6 (26%)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Data are n (%). *Fisher’s Exact Test. SGRQ=St George’s Respiratory Questionnaire. FEV₁= forced expiratory volume in 1 s.
Summary: Endobronchial Coils

Strategy

- insertion of 8-12 coils per lung
- staged procedure unilateral then treat contra-lateral side when required

Selection

- broad patient selection
- homogenous to heterogenous disease
- avoid very bullous disease

Survival

- long term effect on coil tension is unclear (longest follow up about 72 months but effect lost in Revolens Study within 12 months)
Mechanism of Action

Tissue sealant

Foam Sealant flows into the alveolar compartment as a liquid, polymerizes and seals the target area

Small airways and collateral channels are obstructed

Gas in the sealed area is absorbed leading to volume reduction

Volume reduction decreases hyperinflation, improving lung function and quality of life
Summary: Ariseal

Strategy

• Upper lobe treatment
• Total 2 non adjacent upper lobe sub-segments in each lobe (total of 4 sub-segments)

Selection

• Upper lobe predominant heterogenous disease
• Homogenous disease where <17% perfusion to upper lobe and FEV1>20% predicted

Survival

• Long term effects are unclear
• Need for RCT (suspended due to lack of finance)
Steam for Emphysema
Bronchoscopic Thermal Vapour Ablation

- Delivering calculated quantities of energy to target lobe to produce volume reduction using steam
- Disposable catheter
- Resusuable vapour generator and handle

Therapy delivered through natural anatomic channels
STEP-UP RCT: Efficacy

**STEP-UP**

<table>
<thead>
<tr>
<th>FEV1 % Pred Improvement</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3 Month</strong></td>
<td><strong>6 Month</strong></td>
</tr>
<tr>
<td>Treated from Baseline (BL)</td>
<td>7.8%</td>
</tr>
<tr>
<td>Control from Baseline (BL)</td>
<td>-0.3%</td>
</tr>
<tr>
<td>Treated vs. Control</td>
<td>8.1%</td>
</tr>
</tbody>
</table>

**SGRQ Improvement**

<table>
<thead>
<tr>
<th>SGRQ Improvement</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3 Month</strong></td>
<td><strong>6 Month</strong></td>
</tr>
<tr>
<td>Treated from Baseline (BL)</td>
<td>-7.2</td>
</tr>
<tr>
<td>Control from Baseline (BL)</td>
<td>-0.6</td>
</tr>
<tr>
<td>Treated vs. Control</td>
<td>-6.6</td>
</tr>
</tbody>
</table>

A lifetime of specialist care
Summary: Vapour Therapy

Strategy
- Upper lobe treatment
- Single procedure

Selection
- Upper lobe predominant heterogenous disease
- Segmental treatment

Survival
- Efficacy observed for up to 12 months
- Longer term effects unclear
Stents for Emphysema
Explanted Emphysematous Lung

<table>
<thead>
<tr>
<th>Inspiratory</th>
<th>Expiratory</th>
<th>Expiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Post-Airway Bypass</strong></td>
</tr>
</tbody>
</table>

Airway Bypass Tools
## PFT, 24 hours post airway bypass

<table>
<thead>
<tr>
<th></th>
<th>before</th>
<th>after</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, L</td>
<td>0.74 (21%)</td>
<td>1.46 (42%)</td>
</tr>
<tr>
<td>FVC, L</td>
<td>3.17 (71%)</td>
<td>4.78 (107%)</td>
</tr>
<tr>
<td>TLC, L</td>
<td>10.1 (152%)</td>
<td>9.24 (140%)</td>
</tr>
<tr>
<td>RV, L</td>
<td>7.11 (302%)</td>
<td>4.39 (187%)</td>
</tr>
<tr>
<td>RV/TLC</td>
<td>70.6 (189%)</td>
<td>47.5 (127%)</td>
</tr>
<tr>
<td>mmRC</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>6MWT</td>
<td>338</td>
<td>538</td>
</tr>
</tbody>
</table>
Primary Endpoint Components

For Airway Bypass, FVC increases day 1
Returns to baseline by Month 3
Control unchanged

mMRC decreases in both groups after baseline
No differences between groups

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>SC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate</td>
<td>16.4</td>
<td>5.2</td>
</tr>
<tr>
<td>1</td>
<td>13.4</td>
<td>11.3</td>
</tr>
<tr>
<td>2</td>
<td>11.8</td>
<td>11.6</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>11</td>
</tr>
</tbody>
</table>
Summary: Airway Bypass

**Strategy**
- Bilateral treatment with at least 6 stents

**Selection**
- Homogenous disease
- With moderate to high level destruction
- High degree of collateral ventilation

**Survival**
- Good acute benefit but shortlived
- Need technological improvements to maintain stent patency
Role of Parasympathetic Nerves in COPD
Targeted Lung Denervation (TLD) defined

**Denervation**
- Disrupt parasympathetic nerves to decrease release of acetylcholine

**Lung**
- Decrease smooth muscle tone
- Decrease mucus production

**Targeted**
- Anatomically to only the lung
- To a depth where the nerves are located
TLD designed to decrease airway smooth muscle tone

COPD After TLD

Acetylcholine release

X
Gen1: Holaira TLD Catheter

Thermocouple and Power Line

Coolant Inflow Conduit

Catheter Shaft

Balloon

Electrode

Coolant Outflow Conduit
TLD – RF Electrode positioning

Electrode fluoroscopic view

Electrode bronchoscopic view
Safety – Airway Effects

TLD - Left main bronchus

Pre Tx  |  TLD  |  PostTx  |  90days
TLD Efficacy – FEV1

Data presented as mean (SEM), * indicates p<0.05 vs. baseline
Conclusions

• First-in-human clinical trial of targeted lung denervation (TLD)
• TLD was safe with 16 SAEs reported through 1-year of follow-up for all patients
  • 8 COPD exacerbations
  • 3 respiratory infections
• TLD showed improvements in the 20W group at 1-year
  • FEV1 of +11.6 ± 32.3 %
  • Sub-maximal cycle endurance of +6.8 ± 12.8 minutes
  • SGRQ of −11.1 ± 9.1 points
• Benefit tended to be greater in the 20W vs. 15W group
A cardinal feature of asthma is narrowing of the airways caused by contraction of airway smooth muscle. 

- Reduction of excessive airway smooth muscle (ASM) 
  - Reduced ability for bronchoconstriction 
  - Reduced asthma symptoms and exacerbations 
  - Improved asthma control and quality of life
Trial Design: Pivotal Trial

AIR2 Study

• Study Design: Sham Controlled, Double Blind
  — 2 : 1 randomization; BT: Sham
  — BT Group (ICS + LABA + BT)
  — Sham Group (ICS + LABA + Sham)

• Study Size: 297 Subjects / 30 centers (International)

• All analysis done with Bayesian statistics

• Length of Follow-up:
  — One year
  — 5-year safety follow-up for BT subjects
AIR 2 Trial

Healthcare Utilization for Respiratory Symptoms Post-Treatment Period (Events/Subject/Year)

- Posterior Probability of Superiority = 95.6%

Bronchial Thermoplasty Trials

**Feasibility**

- Well Tolerated
- Lung Function
- Symptom Free Days
- Persistent Effect

*(n = 16)*

**AIR**

- AQLQ
- Exacerbations
- Rescue Medications
- Symptom Free Days

*(RCT; n = 108)*

**RISA**

- AQLQ
- ACQ
- Rescue Medications
- Oral Steroids *(p=0.12)*

*(RCT; n = 32)*

**AIR 2**

- AQLQ
- Severe Exacerbations
- ER visits
- Days lost work/school

*(RCT; n = 297)*

*AJRCCM, v173, May 2006*

*NEJM, v356, Mar 2007*

*AJRCCM, v176, Sep 2007*

*AJRCCM v181 Jan 2010*

All of the above were shown to be significant *(p < 0.05)*, except where noted.
Conclusions

• **Short term risks:**
  — Treatment adverse events related to transient worsening of asthma
  — Typically occur within one day and resolve within one week with standard care

• **Long term benefits; improvements in:**
  — AQLQ
  — Severe exacerbations
  — ER visits
  — Days lost from work/school/activities
  — Patients reporting asthma (multiple symptoms) adverse events
  — Respiratory adverse events *lower* for BT compared to Sham during long-term follow-up

• **Longer term benefits outweigh short term risks**
Thank You

Pallav L Shah

Royal Brompton Hospital
Chelsea & Westminster Hospital
Imperial College