**Emphysema**

**Endoscopic lung volume reduction**

**JM VERGNON M.D, PhD.**
Chief, department of chest diseases and thoracic oncology.

Genève 2010

**INSERM IFR 143**

1. Abnormal size increase of distal alveolar spaces starting in terminal bronchioles.
2. Lung parenchyma destruction
3. No fibrosis

**Physiological concepts**

- Bronchial obstruction
  - Airflow limitation
  - Thoracic distension
  - Dyspnea
  - Muscular activity reduction
  - Muscular deconditionning
The surgical approach

Lung volume reduction surgery (LVRS): tested in the NETT study (National Emphysema Treatment Trial)

**Functional benefit:**
- Quality of life
- Exercise capacity

- Survival
  - Heterogeneous emphysema
  - Upper lobes
  - Limited exercise capacity

⇒ Place for minimal invasive techniques?
⇒ Techniques where we can go back...?

The medical approach

- Insert bronchus blockers
  - One-way valves:
    - Zephyr valves
    - Spiration valves
    - Spigots
  - Stick the lobe: Aeris system
- Create new bronch/bronchial fenestration
  - Bronchus system
- Other systems:
  - PneumoRx
**Theoretical action**

Start this way...

Reduction of volume targeted lobe

Improves ventilation

Improves exercise and QOL

Mechanical benefit → Clinical benefit

---

**Zephyr® valves**

---

**Valve insertion**
**International Endobronchial Valve for Emphysema Palliation (VENT) Trial**

- **Type of study**
  - Clinical randomized and prospective multi-centric study.

- **Population**
  - ≥ 270 patients

- **Inclusion centers**: 25

- **Randomization ratio**: 2/1 (Treatment/Control)

- **Selection**
  - Heterogeneous emphysema assessed on strict CT scan criteria.

- **Main end-points**:
  - 6 months after inclusion
  - FEV1 improvement
  - 6 min walking test improvement.

---

**Results at 6 months**

<table>
<thead>
<tr>
<th>Main end-points:</th>
<th>Treatment n = 220</th>
<th>Control n = 101</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Change in FEV1</td>
<td>5.8 ± 27.7%</td>
<td>-0.6 ± 27.3%</td>
<td>0.0047</td>
</tr>
<tr>
<td>% Change in 6MWT</td>
<td>1.7 ± 30.3%</td>
<td>-4.0 ± 28.1%</td>
<td>0.0073</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary end-points:</th>
<th>Treatment n = 220</th>
<th>Control n = 101</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGFRQ</td>
<td>-2.6 ± 13.0</td>
<td>0.4 ± 10.5</td>
<td>0.0186</td>
</tr>
<tr>
<td>Max Workload (w)</td>
<td>0.75 ± 15.0</td>
<td>-4.4 ± 11.5</td>
<td>0.0003</td>
</tr>
<tr>
<td>mMRC</td>
<td>-0.1 ± 1.0</td>
<td>0.3 ± 0.8</td>
<td>0.0024</td>
</tr>
<tr>
<td>Supplemental O2 (l/day)</td>
<td>9.7 ± 953.4</td>
<td>116.2 ± 736.1</td>
<td>0.0392</td>
</tr>
</tbody>
</table>
Main end points at 12 months

- VEMS % Change:
  - Δ = 11.7%
  - Univariate p = 0.0001
  - Longitudinal, multivariate p = 0.0001*

- 6MWT % Change:
  - Δ = 3.3%
  - Univariate p = 0.0001
  - Longitudinal, multivariate p = 0.0001*

Safety results: Main complications at 6 and 12 months compared to controls.

<table>
<thead>
<tr>
<th>Major Complication Composite (MCC)</th>
<th>Control 6 months</th>
<th>EBV 6 months</th>
<th>p value</th>
<th>Additional Safety Analysis 12 months (cumulative)</th>
<th>Control 12 months</th>
<th>EBV 12 months</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.0%</td>
<td>2.4%</td>
<td>0.0748</td>
<td>4.6%</td>
<td>10.4%</td>
<td>0.1724</td>
<td></td>
</tr>
<tr>
<td>Empyema</td>
<td>0.0%</td>
<td>0.0%</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Massive Hemoptysis</td>
<td>0.0%</td>
<td>0.0%</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Distal Pneumonia</td>
<td>NA</td>
<td>1.4%</td>
<td>—</td>
<td>—</td>
<td>NA</td>
<td>4.2%</td>
<td>—</td>
</tr>
<tr>
<td>Pneumothorax/air leak &gt;7 days</td>
<td>1.2%</td>
<td>1.4%</td>
<td>1.0000</td>
<td>1.2%</td>
<td>1.9%</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>Resp. Failure ≥ 24 hours went</td>
<td>1.2%</td>
<td>1.9%</td>
<td>1.0000</td>
<td>2.3%</td>
<td>2.8%</td>
<td>1.0000</td>
<td></td>
</tr>
</tbody>
</table>

*By interaction with heterogeneity

**Modified Intention to Treat:** Randomized patients receiving study-directed treatment and had any follow-up.

Frequent events in valve group
**Fissure integrity**

- HR CT scan can control fissure integrity
- Fissure integrity is highly correlated with the percentage of lung volume reduction and with the FEV1 improvement.

**Target lobe volume change**

*Subjects with HRCT available*

**Target lung volume reduction (TLAS) and fissure integrity**
Valve group: FEV1 6-month change

Control (n=52)                     Treatment (n=115)
% Change @ 6 mo  Δ = 12.2%  p = 0.0001

FEV1 change according to heterogeneous emphysema score

% Change @ 6 mo  Δ = 12.2%  p = 0.0001
Control (n=52)  Treatment (n=115)  4.8%  10.3%

% Change @ 12 mo  Δ = 19.0%  p = 0.0001
Control (n=52)  Treatment (n=115)  4.1%  15.0%

6 mn walking test change according to heterogeneous emphysema score

% Change @ 6 mo  Δ = 12.1%  p = 0.0043
Control (n=52)  Treatment (n=115)  4.3%  7.0%

% Change @ 12 mo  Δ = 19.7%  p = 0.0131
Control (n=52)  Treatment (n=115)  12.5%  3.9%
Technical point of view: bronchial closure failure

SPIRATION valve
- Umbrella
- Polyurethane membrane
- Nitinol armature
- Efficacy study on 98 patients (659 valves)
- QOL improvement (SGRQ) without FEV1 change
- Seal: better distribution of airflows in healthier lung parts


Valve insertion

Valve is deployed in bronchial segments via catheter delivery
Valve seat expands to seal and eliminate air leaks
Valve is deployed in bronchial segments via catheter delivery
Valve seat expands to seal and eliminate air leaks
Valve is deployed in bronchial segments via catheter delivery
Valve seat expands to seal and eliminate air leaks
Valve is deployed in bronchial segments via catheter delivery
Valve seat expands to seal and eliminate air leaks
Valve is deployed in bronchial segments via catheter delivery
Valve seat expands to seal and eliminate air leaks
Endobronchial blockers

- Silicone "Spigots" of Watanabee
  - Tested in broncho-pleural fistulas
  - Limited experience in emphysema...

Toma et al. Am J Respir Crit Care Med 2002;165(suppl).
Watanabe Y, LVRS with WBA. Presented at: World Congress of Bronchology, June 2002, Boston

Silicone "Spigots" NOVATECH

To stick the lobes

- Obstruction of emphysematous lobes with glue:
  - Endobronchial injection through a flexible bronchoscope of polymers (fibrin hydro-gel and thrombin, bi-component system)
  - Sheep trial:atelectasis foci and fibrosis
  - Human trial (Aeris study) 50 patients: positive results on FEV1, FVC, RV/TLC, 12 weeks after treatment with an acceptable tolerance.

Bronchial fenestration (Bronchus system)
- To improve expiration
- Dynamic hyper-inflation


EASE trial « in progress »

Lung retraction (PneumoRx system)

Back home messages
- Surgery : selected indications on heterogeneous upper lobe emphysema.
- One-way valves useful on more and more selected patients : heterogeneous emphysema, fissure analysis, collateral ventilation analysis...
- Emphasys group fails but the Zephyr
  valves distribution starts again with a new group PulmonX. Collateral ventilation analysis is now proposed to a better assessment.
- Biological blockers could have a fruitful future.
- In homogeneous emphysema: fenestration or lung retraction ? Studies should be completed.
Thanks for your attention