# Multicenter European study for the treatment of advanced emphysema with bronchial valves

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**Online Depository**

**Inclusion/Exclusion criteria**

Inclusion:

- Aged 40 to 75 years;
- Predominantly upper lobe emphysema (confirmed by CT scan evaluation by investigator) and severe dyspnea;
- Satisfies the ATS/ERS Guidelines for Management of Stable COPD;
- Forced expiratory volume in one second ($FEV_1$) <45% of predicted,
- Total lung capacity (TLC) ≥100% of predicted and residual volume (RV) ≥150% of predicted;
- Able to perform a six-minute walking distance of ≥140 m;
- Abstained from smoking for the last four months and for the duration of the study

Exclusion

- $FEV_1$ and diffusion lung capacity for carbon monoxide (DLCO) <20% of predicted;
- Severe gas exchange abnormalities ($PCO_2$≥50 mm Hg, $PaO_2$ ≤ 45 mm Hg on room air (Denver criterion: $PaO_2$ ≤ 30 mm Hg);
- Two or more hospitalizations due to COPD exacerbations or respiratory infections in the past year;
- Bronchitis with sputum production >60 cc per day;
- active asthma (requiring >15 mg prednisone daily);
- giant bulla (>1/3 volume of lung);
- Severe pulmonary hypertension;
- Requirement for > 6 L $O_2$ to keep saturation ≥ 90% with exercise;
- Evidence of systemic disease or neoplasia expected to compromise survival during the 6-month study period;
- Prior lung volume reduction surgery or major lung procedures;
- Lung nodule anticipated to require evaluation or intervention during the study period;
- Diffuse emphysema with α1-antitrypsin deficiency;
- Any other major disease or condition which would have affected study participation or put the subject at risk during the bronchoscopic procedure or during exercise testing

**Randomsiation**

Before starting the study, the statistician created blocks of randomization sealed envelopes that were provided to each of the clinical sites. The envelopes were opened in numerical order only after the patient was anesthetized and the bronchoscopic evaluation of the airways was completed.

**Bronchial valve treatment algorithm**

The protocol directed that in each patient, all segments of the left upper lobe with the exception of the lingular segments should be occluded with valves. In the right upper lobe (RUL), all segments were occluded with the exception of one segment or sub-segment. The airway in the RUL not to be treated was determined by the investigator based upon evaluation of the distribution of emphysema, anatomy, or a subsegment of the anterior segment (Figure 1).

**Imaging Analysis**

Volumetric scanning was performed at 120 kVp, mAs 40, 1 or 1.25 mm slice thickness, spacing 1 or 1.25 mm (contiguous slices), no contrast media. Images were reconstructed using both a high and an intermediate spatial frequency and reconstruction algorithm.

Briefly, the lungs were segmented from the surrounding chest wall and mediastinal structures using standard threshold techniques. The individual lobes were automatically segmented within each lung (E1) and confirmed using visual editing. There were two experienced reviewers that individually confirmed or manually adjusted the segmentations. While these individuals could not be blinded to the presence or absence of valves, each case was verified by a second CT reviewer (i.e. one that did not perform the initial analysis) to confirm the lobar segmentation. Total lung and lobar volume was calculated by summation of the segmented pixel area (lung and lobe) in each slice and multiplying by the slice thickness. The CT endpoint for the study is therefore simply a volume measure and not a densitometry measure. Lung perfusion scans were obtained at baseline to confirm emphysema distribution as being upper lobe predominant. Chest X-rays were obtained prior to hospital discharge to evaluate the number and position of the valves, and to check for any pulmonary complications including lobar atelectasis and/or pneumothorax. Chest X-rays were repeated at the end of 3 months blinded treatment.

**Reference:**

E1. Zhang L, Hoffman EA, Reinhardt JM. Atlas-driven lung lobe segmentation in volumetric X-ray CT images. IEEE Trans Med Imaging. 2006 Jan;25(1):1-16.
**Figure 1: Valve placement treatment algorithm**