Bronchoscopic emphysema treatment: utility of thoracic CT

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Objectives

1. To review the different devices and techniques employed in the bronchoscopic emphysema treatment (BET) and discuss their indications and potential complications.
2. To describe the role of CT for patient selection and BET planning.
3. To illustrate the expected post-treatment imaging appearance and potential complications.
1. Introduction

Bronchoscopic treatments are new minimally-invasive approaches with great promise at reducing dyspnea in patients with severe emphysema, for which there is no therapeutic treatment option other than lung transplantation and, for a few, lung volume reduction surgery (LVRS). LVRS has shown a significant improvement in functional tests and life quality in patients with predominant upper lobes emphysema. Nevertheless, even in experienced centers it is associated with high morbidity (50%) and mortality (5-7.9 % in the first 90 days after procedure), and it is not indicated in patients with homogenous emphysema because of worse response and more rate of complications. In the attempt to achieve the benefits of LVRS with lesser risk and inclusion of a greater number of patients, several bronchoscopic procedures are developed. They look for a volume reduction in the pulmonary regions with severe emphysema, leading to expansion of less damaged lung and decreasing the dynamics of airway trapping. These techniques have different physiopathologic base, results and complications, and that explains their different indications depending on emphysema distribution (heterogeneous or homogeneous) and others clinical points that we are going to review.

2. Bronchoscopic emphysema treatment

a. Techniques:

• One-way valves

They block the air entry in the target emphysematous region, leading only a unidirectional flow out of air and secretions during the expiration. The isolation of the pulmonary treated segment induces atelectasis of parenchyma with the consequent lung volume loss, and redirection of flow to less emphysematous lung. There are two models in the market: a) umbrella shape prosthesis with a valve mechanism, and b) auto-expansible stent, with an incorporated valve in its proximal portion. Fig. 1 on page 10. Their insertion is bronchoscopy-guided, under local anesthesia and intravenous sedation, and only requires a short hospital stay. Fig. 2 on page 10. Candidates are patients with heterogeneous emphysema with predominance in upper lobes, looking for a similar physiologic effect to LVRS. There is controversy with respect to treat only one or both lungs, although there are data that support the recommendation of unilateral approach in the case of stent-valve and bilateral in umbrella-valve's case.
An improvement in respiratory function, dyspnea and life quality has been observed 1-3 months after implantation of bronchial valves, but they do not reach comparable results to LVRS. The main limiting factor for the lung volume reduction is the presence of anatomical communications between lobes that maintain a collateral ventilation of the treated lung despite bronchial obstruction. These communications are more frequent in emphysema, related to lung destruction. Complications are much less serious in comparison with LVRS. The most frequent adverse events are COPD exacerbation (5%-20%) and pneumothorax (7-11%).

- Biological and synthetic polymers

The instillation of polymers into the bronchi of emphysematous lung induces an inflammatory local reaction with posterior scarring, that collapses this parenchyma and remodels the lung. Biological polymers are made by a suspension of biopharmaceutical fibrinogen and thrombin solution that polymerizes in situ resulting in a hydrogel. This hydrogel contains polylysine and a hyaluronic acid complex that initiate an inflammatory reaction.

In our hospital the sealant foam is nowadays the endobronchial treatment of choice. It's formed by mixing air and a synthetic polymer (combination of amino alcohol and glutaraldehyde solutions) and it achieve the same results with significant less risk of morbidity. Fig. 3 on page 11

In all cases the procedure includes at least two sessions, separated by 3 months. Only 2 or 3 subsegmental not contiguous bronchi are treated at each session to avoid complications. The instillation is guided by bronchoscopy, under local anesthesia and sedation, requiring a short hospital stay. Fig. 4 on page 12

Scarring process develops in alveoli, and a reduction of functional volume lung is waited in approximately 6-8 weeks.

The sealant blocks the interalveolar and bronchioalveolar canals, trying to impede collateral ventilation effects seen with endobronchial valves; maybe this explains the improvement of respiratory function, not only in the heterogeneous but also in the homogeneous emphysema. Nonetheless, it's important to know that even in the homogenous emphysema the target of sealant is usually the upper regions of lung and the results are until now inferior to those obtained in heterogeneous emphysema.

The main disadvantage of sealant is the irreversibility of the procedure. On the other hand, due to the novelty of the technique, the evolution of changes in the long term is not known, and a diminution of consolidation and recuperation of lung volume secondary to material degradation, is not dismissed.

In a great number of patients, leukocytosis, fever and/or sickness are present in the first 12-24 hours. Patients may have pleuritic chest pain, especially in case of peripheral treatment with inflammatory reaction in proximity or contact to pleura. The following effect in frequency is the COPD exacerbation (22%), followed by bronchoaspiration and pneumonia.
• **Thermoablation**

Vapor emission in airways generates an inflammatory reaction with the consequent loss of volume of the treated segment. The target bronchus is isolated by a balloon lodged in the lumen, and the response is occurring in the alveoli, like in the case of polymers, avoiding partially the problem of collateral ventilation described with the valves. There are few patients treated with this method; even if they improved their symptoms, the waited changes in functional respiratory tests and imaging were poor. The most frequent adverse effects are COPD exacerbation and pneumonia.

• **Endobronchial Coils** [Fig. 5 on page 12]

They block the airway, in regard to treat both heterogeneous and homogeneous emphysema, obtaining the maximal lung volume reduction in 2-4 weeks. Until now, the results, in few patients, show an improvement in respiratory function and life quality without pneumothorax neither more severe complications. However, the bronchial distortion secondary to coils is suspected to promote the development of bronquiectasis and vessel tortuosity with the potential risk of thrombosis and infarct.

• **Others not in use nowadays:** **bronchial fenestrations and blockers**

**Bronchial fenestrations**: by-pass [Fig. 6 on page 13]

The aim of airway wall fenestration in low resistance bronchi is allow the exit of air trapped resulting of the high resistance to flow by its natural airway. The bronchoscopy-guided procedure consists in the fenestration of the walls followed by the implantation of mural stents to guarantee the flow, and it needs general anesthesia. The described fails in stent implantation, added to variable results and other complications have led this technique to fall into disuse.

**Bronchial blockers** (silicone balloons, stents with a central occlusive sponge)

They obstruct bronchial lumen so the entry and exit of air and secretions is not allowed in the treated lung. They are currently unused because of description of a high rate of material migrations and cases of postobstructive pneumonia.

See [Table 1 on page 26](#) : summary of the bronchoscopic treatment modalities, indications and more frequent complications.

b. **Inclusion and exclusion criteria** See [Table 2 on page 26](#) [Table 3 on page 27](#)
In patients with advanced emphysema and symptoms not responding to treatment, the combination of functional parameters and imaging findings permit to select those who will benefit from a lung volume reduction.

• Clinical status
• Functional respiratory tests
• Thoracic CT
• Perfusion scintigraphy

3. Thoracic CT imaging

Our protocol for candidates to BET includes a thoracic CT before the procedure and a follow-up thoracic CT at 3, 6 and 12 months after the treatment; patients also a clinical exam and respiratory functional tests pre-treatment and 3, 6, 9 and 12 months after the procedure.

a. Technical parameters

**Acquisition**: 0.8 mm collimation and 1 pitch; 120 kV and 70 reference mAs (low dose); only more mAs if obese.
Low dose is not a problem for us to visual identification of emphysema, in agree with some authors.
The same technique is used in the follow-up to procure reproducibility, and it is especially recommended in case of emphysema quantification.
In practice, if a patient has a recent thoracic CT we do not repeat the study pre-treatment. Contrast injection is not necessary and it could produce beam hardening artifacts that bias the quantification results; we use only when it is indicated because of the clinical suspicion.

**Reconstructions** send to PACS:
- 1 mm contiguous slices with an appropriate filter and window for lung.
- 2 mm slices with 1 mm-overlapping and an appropriate filter and window for mediastinum.

**Additional reconstructions**:
- Minimum Intensity Projections (MinIP) in transverse and coronal plane with a slice thickness of 5-10 mm are obtained from images with overlapping. These reconstructions facilitate the identification of emphysema.

b. **Pre-treatment assessment**: See **Table 4** on page 27
Thoracic CT provides crucial information for the selection of patients and optimal guide for treatment.

• **Emphysema: type and distribution. Presence of giant bulla**

CT permits diagnose of emphysema, characterized by focal low attenuation due to pulmonary destruction and vascular disruption, and shows its extension and distribution. Emphysema quantification is useful if we have robust software; in this case that provides more consistency and reproducibility than visual graduation. Usually a threshold of -950 HU is used, and voxels with a density below this value are considered emphysema. Patients most likely to benefit from a lung volume reduction are those with heterogenous emphysema with upper lobe predominance. Fig. 7 on page 14 Treatment is usually address to the most heterogeneous lobe or lung, avoiding areas of extensive bullous emphysema or giant bulla larger than 10 cm, where good results are not expected. Fig. 8 on page 14.

Response in homogeneous emphysema is worse, with less lung volume reduction. It's thought that is related to greater collateral ventilation. In these patients, reduction by bronchial biological or synthetic sealants is the existing available technique with the best functional and clinical results.

• **Fissures state** Fig. 9 on page 15

Lack of fissures also indicates the presence of interlobar communications that allows collateral ventilation, associated to lesser possibility of lung volume reduction with endobronchial valves. But it is important to remind that probably, reduction of volume is not the only mechanism responsible for improvement with these therapies.

• **Signs of pulmonary artery hypertension and right cardiac overload**

CT also provides information about the existence of pulmonary artery hypertension, frequent in patients with severe emphysema (diagnosed by pulmonary artery diameter > 29 mm or pulmonary artery/Aorta diameter >1), and about right ventricle overload and failure (wall thickness > 4 mm and dilatation RV/LV>1).

• **Other possible findings** (for example lung nodules and coronary calcifications) have to be reported, not like an exclusion criterion, but important for patient management.

• **Lung volume quantification**

**c. Post-treatment assessment:** See Table 5 on page 28
CT is useful in evaluation of response, showing inflammatory consolidations, atelectasis and lung volume reduction, and makes evident possible complications.

- **Location and permeability (valves)**

Endobronchial valves are generally placed in segmental or subsegmental bronchi, depending on the anatomy. Radiologist can confirm the correct disposition of the valves Fig. 10 on page 16 and look for the consequent segmental or subsegmental atelectasis. In most cases lobar atelectasis are not seen due to the collateral ventilation and incomplete lobar fissures.

- **Consolidation and atelectasis (polymers)**

In case of sealant and thermoablation, consolidations in the treated segments are expected, formed by inflammatory reactive tissue and atelectasis of adjacent parenchyma. These consolidations usually have a round or elongated morphology and well-defined margins without air bronchogram; they can simulate neoplastic masses if we ignore the antecedent of bronchoscopic treatment Fig. 11 on page 16 Occasionally the inflammatory tissue is poor and only little nodular opacities are seen, without atelectasis neither volume reduction. Fig. 12 on page 17 In some cases we have not appreciate any change in the treated segment probably due to lack of inflammatory response. In our patients, treated with synthetic sealant, we have seen air-filled spaces within consolidated lung. Pseudocavities probably correspond to trapped residual emphysema, or air from adjacent communicated bronchi secondary to remodeling and retraction by the inflammatory tissue. Fig. 13 on page 18 and Fig. 14 on page 19 They can appear both in 3 and in 6 months-CT, and we have observed that they usually disappear or diminish spontaneously, but we do not have long-term follow-up. We have not seen an association between this finding and clinical or functional changes. It is important to know that this finding is frequent and it is not an infection. If the bronchoscopic sealant treatment is unknown this image can be misinterpreted, and other diagnosis like aspergilosis, invasive infections or even adenocarcinoma could be suggested. On the other hand, necrosis secondary to exaggerated inflammatory response, can participate in the formation of pseudocavities. We have registered a patient with an extensive cavitation associated to sterile necrosis. Follow-up chest X-Ray was interpreted like a pneumonia with abscess formation, because clinical data were unknown. Nevertheless, the clinical-radiological discordance and the quick radiologic improvement were the key to discard this diagnosis. Fig. 15 on page 20 Fig. 15 on page 20 and Fig. 16 on page 21

- **Lung volume reduction**: qualitative and quantitative evaluation

Loss of volume can be visually recognized by displacement of fissures, vessels, mediastinum and anterior pleural line (examples Fig. 17 on page 22 Fig. 18 on page 22 Fig. 19 on page 23 Fig. 20 on page 24). Using a specific software, lung volume can be calculated and compared to basal CT. However, due to complexity of the
gas exchange in severe emphysematous patients, the correlation between symptoms, functional respiratory tests and lung volume reduction is not good. In our experience, some of the patients treated with polymers, get clinically and functionally better without a significative reduction of lung volume in CT. This can be explicated because exclusion of ventilation of the most affected areas, even without atelectasis, reduces physiologically the death space, redirecting air to lesser emphysematous segments.

• **Complications**

The main complication of the valves is the pneumothorax. Its mechanism has not been yet clarified, and maybe it is secondary to pleural adherences and rupture of blebs and bulla after relaxation of non treated segments, or perhaps it is due to a delay in the remodeling process after a significative atelectasis of treated segments. The pneumothorax can be very small, hidden on chest X-Ray and only visualized in CT. Frequently secretions are seen in the distal lumen of stent. Fig. 21 on page 25 Occasionally a hyperplastic granulation tissue can be observed in the proximal portion of the stent, where the valve is lodged.

After sealant treatment, the principal adverse events are bronchoaspiration, pneumonia, and less frequently pneumothorax. Until now we have not seen these complications in our patients.
**Fig. 1:** Commercialized unidirectional endobronchial valves models. A. Umbrella-shaped valve. Its expansion during inspiration prevents air inflow (arrows) and its contraction during expiration allows air outflow and secretions clearance. B and C: Duckbill-shaped valve, placed in the proximal portion of an autoexpandible container, designed to be opened during low pressures, expiration, and facilitate air outflow (blue in B) and to be closed quickly during inspiration due to flow inversion.

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Fig. 2: Bronchoscopic placement of endobronchial valves. A: Endobronchial valves are placed using a delivery catheter (asterisk) which is inserted through a flexible standard bronchoscope. B. Duckbill-shaped valve (arrow) placed in the proximal portion of the stent.

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Fig. 3: Synthetic adhesive (Aeriseal®) A: Mixture of solutions (step 1). Combination of air and polymers to obtain a foam (steps 2 and 3). B: Instillation through a catheter, under direct bronchoscopic visualization.

© Aeriseal

Fig. 4: Bronchoscopic foam sealant instillation. Foam sealant (arrow) is injected through the delivery catheter (asterisk). After this procedure, air has to be immediately introduced to produce a peripheral distribution of the product. Complete polymerization is expected in 1 minute before removing the bronchoscope and look for another treatment objective.

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Fig. 5: Endobronchial coils. A. Nitinol coils of 10 to 20 cm in length, are placed by endoscopy in less than 2 minutes. B: Chest x-ray with bilateral multiple coils (red arrows) released in subsegmental bronchi of upper lung zones.

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Fig. 6: Bronchial fenestrations. Endoscopic perforation of bronchial wall and stent placement to allow trapped air to flow out without resistance.

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Fig. 7: Heterogeneous and homogeneous emphysema. Lung coronal minIP reconstructions of two patients with different types of emphysema. A: Heterogeneous emphysema with upper lobes predominance. B: Homogeneous emphysema. Severity is similar in all lung lobes with uniform distribution.

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Fig. 8: Bullous emphysema in left lung. Cross-sectional slices, upper (A) and lower (B). These segments were not candidates to sealant treatment due to bullae (asterisk). Recently, sealant treatment is accepted in areas with bullae up to 10 cm.

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**Fig. 9:** Absent fissure. Cross-sectional images, upper (A) and lower (B). Hyperinsuflation of lower right lobe (LID) and displacement of middle lobe (LM) and upper right lobe (LSD). Minor fissure is not defined. See complete contralateral fissure (green arrows).

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![Image](image1.png)

**Fig. 10:** Duckbill-shaped valve, correctly positioned in segmental bronchi of right lower lobe. A y B: cross-sectional images of lung; see the characteristic morphology in its longitudinal axis (red arrow) and transversal axis (yellow arrow, proximal portion in A and distal portion in B). C y D: MIP coronal reconstructions may help to visualize placement of the valves. Stent structure is appreciated (red arrows).

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**Fig. 11:** Sealant instillation, 3-month follow-up CT. Heterogeneous emphysema with upper lobe predominance in left lung. Cross-sectional images (up) and coronal MIP images (down). Inflammatory consolidation-atelectasis in two not adjacents subsegments in apical lower left lobe (upper - red arrow- and lower-blue arrow-).

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**Fig. 12**: Small consolidations after sealant instillation (red arrows), without a significative loss of volume. Findings related to a poor inflammatory response. A and B images belong to the same patient; even in absence of significant changes in CT, the Total Lung Capacity (TLC), Residual Volume (RV) and TLC/RV ratio improved.

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Fig. 13: Pseudocavitation. Cross-sectional CT images, at 3 months (A and C, on the right) and 6 months (B and D, on the left) after the sealant instillation in two subsegments of upper left lobe. Example of images smaller than 1 cm within the inflammatory consolidations, that practically resolved at 6 months.

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**Fig. 14:** Pseudocavitation. CT cross-sectional images (A-B) and coronal minIP (D) at 3 months (A), 6 months (B and D) and 9 months (C) after the first sealant bronchial instillation. Second instillation at 3 months. Inflammatory consolidations (red asterisks) in apical segment of lower left lobe and anterior segment of upper left lobe. Pseudocavitation in the apical lower left lobe consolidation is seen at 6 months (red arrows) and resolved at 9 months.

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**Fig. 15:** Cavitation. Chest X-ray on the 14th day (A) 17th day (B) and 21st day (C) after treatment, and coinciding with a COPD exacerbation. In an area of homogeneous emphysema the inflammatory response promoted a communication with the airway larger than usual, probably related to sterile necrosis. Image was misinterpreted as an abscess. In the contralateral lung there are other consolidations from a previous session.

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**Fig. 16:** …Cavitation. Same patient of Fig.15 Follow-up CT at 3 months. A: Cross-sectional image and B: coronal MIP reconstruction. Residual pneumatocele (blue arrow) within a small atelectasis, and loss of volume despite this evolution, compared to previous CT (C).

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**Fig. 17:** Loss of volume: displacement of fissure and anterior pleural junction line. Imágenes transversales del pulmón en el mismo plano, Cross-sectional CT images at the same plane, A: pretreatment and B: 3 months after instillation of sealant. Consolidation with parenchymal retraction (red arrow) and secondary volume loss; see fissure and anterior pleural junction line displacement (green arrows)

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**Fig. 18:** Loss of volume: fissure displacement. Cross-sectional CT images at the same plane, A: pretreatment and B: 3 months after instillation of sealant. Consolidation with parenchymal retraction (red arrow) and secondary volume loss; see fissure and anterior pleural junction line displacement (green arrows)

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Fig. 19: Loss of volume: displacement of fissure, anterior pleural junction line, and chest wall. Upper lobes panacinar emphysema. Cross-sectional CT images pre-treatment (A and C, on the left) and 3 months after sealant instillation (B and D, on the right). Consolidation with parenchymal retraction (red arrow) and secondary volume loss; see fissure, anterior pleural junction line and chest wall displacement (green arrows)

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Fig. 20: ... Loss of volume: displacement of fissure, anterior pleural junction line, and chest wall. Upper lobes panacinar emphysema. Min IP coronal reconstructions of the same patient in previous figure. Basal study (A and C, on the left) and 3 months after sealant instillation (B and D, on the right). Consolidation with pseudocavities and parenchymal retraction (red asterisk). Secondary volume loss; see fissure, mediastinum and chest wall displacement (green arrows). Lung volume reexpansion of lower right lobe (blank asterisk)

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**Fig. 21:** Secretions inside the lumen of the endobronchial valves. Cross-sectional images, upper level (A) and lower level (B) showing mucus-filled valves (yellow arrows). C: Another patient with occupation of the luminal valve (yellow arrow).

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<table>
<thead>
<tr>
<th>Modality</th>
<th>Indications</th>
<th>Common complications</th>
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<tr>
<td><strong>Endobronchial valves</strong></td>
<td>Heterogeneous emphysema</td>
<td>COPD exacerbation. Pneumonia/Bronchitis. Air leaks/Pneumothorax, pneumomediatinum. Hemorrhage</td>
</tr>
<tr>
<td><strong>Biological and synthetical sealants</strong></td>
<td>Homogeneous and heterogeneous emphysema</td>
<td>COPD exacerbation. Pneumonia/Bronchoaspiration.</td>
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<tr>
<td><strong>Thermoablation</strong></td>
<td>Heterogeneous emphysema</td>
<td>COPD exacerbation. Pneumonia.</td>
</tr>
<tr>
<td><strong>Endobronchial stents</strong></td>
<td>Heterogeneous emphysema</td>
<td>Blocker migration. Post-obstructive pneumonia.</td>
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</tbody>
</table>

**Table 1:** BET: modalities, indications and complications.

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Table 2: Required tests and results prior to bronchoscopic treatment.

<table>
<thead>
<tr>
<th>Test</th>
<th>Parameters</th>
</tr>
</thead>
</table>
| SPIROMETRY            | FEV1/FVC < 70% predicted  
                        | FEV1 : 20-50% predicted                                                   |
| PLETHYSMOGRAPHY       | TLC > 100% predicted  
                        | RV > 135 % predicted                                                     |
| DLCO                  | 20-60 % predicted                                                         |
| THORACIC CT           | Lung destruction with severe emphysema                                     |
|                       | - Valves: heterogenous emphysema required                                   |
|                       | - Sealant: heterogeneous or homogeneous emphysema, but at least 2 segments |
|                       | available for treatment                                                    |
| PERFUSION SCINTIGRAPHY| Perfusion ≤ 17% at least in one upper lobe, in case of homogenous emphysema |

Table 3: Exclusion criteria

1. Active respiratory infection
2. COPD exacerbation or broncospasm
3. Bronchoscopy intolerance
4. Allergy to any component of the device
5. Main diagnosis of asthma, chronic bronchitis or bronchiectasis
6. Frequent exacerbations (>2 last year)
7. Need for assisted ventilation
8. Active smoker
9. FEV1 < 20% ref and DLCO > 20% pre-treatment
10. If valves: homogeneous emphysema
11. If sealant: homogeneous emphysema with perfusion ≥ 17% in both upper lobes (scintigraphy quantification)
<table>
<thead>
<tr>
<th>FINDINGS</th>
<th>DESCRIPTION</th>
</tr>
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<tbody>
<tr>
<td>Type of emphysema</td>
<td>Centrilobular/paraseptal/panlobular/bullous</td>
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<tr>
<td>Distribution of emphysema</td>
<td>Heterogeneous (upper/lower lobes predominance) / Homogeneous</td>
</tr>
<tr>
<td>Most heterogeneous lobe or lung</td>
<td>-</td>
</tr>
<tr>
<td>Bullae &gt; 5 y 10 cm</td>
<td>Yes (location)/No</td>
</tr>
<tr>
<td>Fissures</td>
<td>Absent/Incomplete/Complete</td>
</tr>
<tr>
<td>Pulmonary artery hypertension signs</td>
<td>Yes/No (describe)</td>
</tr>
<tr>
<td>Right cardiac overload signs</td>
<td>Yes/No (describe)</td>
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<tr>
<td>Other findings</td>
<td>Lung/pleura/mediastinum lesions. Coronary calcifications</td>
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<tr>
<td>Volume quantification (each lobe)</td>
<td>_ cc</td>
</tr>
<tr>
<td>(if software available)</td>
<td></td>
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</table>

**Table 4:** Pre-treatment radiology CT report.

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<table>
<thead>
<tr>
<th>FINDINGS</th>
<th>DESCRIPTION</th>
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<tr>
<td>Valves</td>
<td>Describe location and permeability of valves</td>
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<tr>
<td>Atelectasis</td>
<td>Absent/laminar/segmental o subsegmental/lobar</td>
</tr>
<tr>
<td>Sealant</td>
<td>Describe location and size</td>
</tr>
<tr>
<td>Consolidation-atelectasis</td>
<td>Describe pseudocavitation or cavitation</td>
</tr>
<tr>
<td>Loss of volume (qualitative evaluation)</td>
<td>Determine if displacement of fissure/anterior pleural line/mediastinum/chest wall</td>
</tr>
<tr>
<td>Complications</td>
<td>Absente/infection/pneumothorax/others</td>
</tr>
<tr>
<td>Volume quantification (each lung lobe)</td>
<td>_ cc _ % of volume reduction</td>
</tr>
<tr>
<td>(if available software)</td>
<td></td>
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</tbody>
</table>

**Table 5:** Post-treatment radiology CT report.

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Conclusions

BETs are new developing techniques that improve quality-of-life in severely emphysematous patients with a low rate of complications. The radiologist needs to know the imaging findings of appropriate candidates, post-treatment pulmonary changes and possible complications.