Endobronchial Ultrasound Reliably Differentiates Between Airway Infiltration and Compression by Tumor*

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Objective: A frequent problem in patients with intrathoracic malignancies neighboring central airways is the question of whether the airway wall is infiltrated by the tumor or if it is merely compressed. This distinction can often not be made with certainty with the help of chest CT alone, but frequently necessitates surgical biopsy or exploration. We prospectively studied the utility of endobronchial ultrasound (EBUS) in this clinical circumstance.

Methods and patients: Between May 1999 and July 2000, 131 consecutive patients with central thoracic malignancies potentially involving the airways were enrolled into the study. Patients underwent chest CT followed by standard bronchoscopy together with EBUS and subsequent surgical evaluation. The bronchoscopists did not know the radiologist’s interpretation of the chest CT before performing EBUS. The ability of chest CT and EBUS to distinguish between compression and infiltration was measured against the histologic results.

Results: One hundred five patients completed the trial by undergoing surgery. In 81 patients (77%), the CT scan was read as consistent with tumor invasion. EBUS only showed invasion in 49 cases (47%). Histology after surgery revealed a specificity of 100%, a sensitivity of 89%, and an accuracy of 94% for EBUS. Chest CT was far inferior, with a specificity of 28%, a sensitivity of 75%, and an accuracy of 51%.

Conclusion: We conclude that EBUS is a highly accurate diagnostic tool and superior to chest CT in evaluating the question of airway involvement by central intrathoracic tumors. In the hands of experienced endoscopists, EBUS may become the procedure of choice for this question.

Key words: chest CT; diagnosis; endobronchial ultrasound; lung cancer

Abbreviation: EBUS = endobronchial ultrasound

Lung cancer is a common disease, and exact staging is of extreme importance in order to plan therapy and assess patients for potentially curative surgical resection. A frequent problem in assessing the extent of tumor spread is the question of infiltration vs compression of central airways by central tumors. Chest CT as the general imaging procedure of choice is often not helpful with this question, as it cannot delineate the layers of the airway wall. Regular bronchoscopy also cannot reliably identify intramural disease and differentiate it from external compression. Patients in this situation often require surgical exploration to establish final staging and may find themselves nonsurgical candidates who had to undergo surgical procedures in order to establish this fact.

Endobronchial ultrasound (EBUS) has been available for several years, and we were interested if the addition of EBUS to regular bronchoscopy can help differentiate between airway infiltration and external compression and as such contribute to less-invasive patient staging. EBUS seems intuitively well suited for this question with its submillimeter resolution and exquisite visualization of all layers of the bronchial wall, as well as the surrounding parabronchial structures. As EBUS is a relatively new technique, very little controlled data currently exist addressing this very important issue.
Patients

All patients who presented for evaluation and treatment of a central tumor within the chest as evidenced on a plain chest radiograph were enrolled in this prospective study. Central tumor was defined as a mass next to the trachea or within the tracheobronchial angles. After written informed consent was obtained, all patients underwent CT of the chest, followed by bronchoscopy with EBUS. All findings were correlated with final histology on surgical specimens.

Methods

The CT imaging was performed on a Siemens Somatom Plus (Siemens; Munich, Germany) by spiral technique and 5-mm cuts after contrast injection. The chest CTs were reviewed by a chest radiologist. The mass neighboring the airways was classified as infiltrating the airway wall vs just compressing it. Infiltration was assumed if no plane between mass and airway could be identified. The results were documented separately and unknown to the bronchoscopist. The hard copies of the CT scans were available for review to the bronchoscopists.

Bronchoscopy was then performed in the usual manner with only one type of bronchoscope (P20, T40; Olympus; Tokyo, Japan). After a thorough airway examination with white light bronchoscopy an EBUS examination was performed. Details of the technique and sonographic anatomy are available elsewhere. A flexible 20-MHz probe (Olympus) was passed through the working channel of the bronchoscope. With a 360° view, the bronchial wall and its layers were visualized (Fig 1). Tumor infiltration was determined to be present if at least the outermost layer of the airway wall had become indistinguishable (Fig 2, 3). The information obtained by chest CT and EBUS regarding infiltration of the airways was not used in assessing the need for surgical exploration or resection. Bronchoscopic and EBUS examinations were performed by the authors only with a combined experience of >5,000 EBUS examinations.

After a standard workup, most patients underwent surgical resection or staging procedures, at which time specimens of the airway in question were also sampled. Patients who were excluded from surgery are listed in Table 1. The patient population undergoing surgery was used for statistical assessment. Final pathologic findings were compared to findings by chest CT and EBUS. Patients excluded from surgery were not included, as surgical correlation with EBUS and CT findings would not be established. The pathologist was blinded to the results of CT scan and EBUS examination. Tumor involvement of at least the outermost layer of the airway was considered infiltration by the pathologist.

Statistical Analysis

Means, SEs, and percentages are presented as appropriate. Spearman rank correlations for nonparametric samples were used to correlate the different classifications with the postoperative result.

Results

Between May 1999 and July 2000, 131 patients were examined with central tumors on chest radiography and potential airway involvement. There were 89 male and 32 female patients, with an average age of 60.1 years (range, 32 to 82 years). Of these, 105 patients (78 male and 27 female; average age, 59.2 years; range, 32 to 82 years) underwent surgery following the chest CT and bronchoscopic examination and could thus be analyzed. Table 1 lists the findings excluding 26 patients from further surgical intervention.

The histologic findings for the primary tumor in the 105 patients who underwent surgery are shown in Table 2.
The most frequent histology was squamous cell carcinoma. In 60 patients (57%), a pneumonectomy was performed, 29 patients (27%) underwent a right upper-lobe sleeve resection, 6 patients (6%) underwent bilobectomy, 5 patients (5%) had a left upper lobe sleeve resection, and 5 patients (5%) had a left-sided lower lobe Y-sleeve resection.

The distribution of areas of suspected airway involvement is shown in Table 3. The CT scan was read in 81 patients (77%) as being consistent with tumor invasion of the airway and with tumor impression in 24 patients (23%) [Table 4].

Tumor invasion as evidenced by EBUS examination was shown to be present in 49 patients (47%) and tumor impression in 56 patients (53%). The pathologic examination after surgery showed tumor invasion in 55 patients (52%) and tumor impression in 50 patients (48%). All patients classified as having tumor invasion by EBUS were confirmed (Table 5). EBUS showed six false-negative examinations for tumor invasion, all located within the trachea.

Examination of the tracheobronchial tree with EBUS for possible infiltration by a central tumor yielded an accuracy of 94%, a sensitivity of 89%, and a specificity of 100% (Table 4). Chest CT scanning for the same indication yielded an accuracy of 51%, a sensitivity of 75%, and a specificity of 28%.

**Figure 2.** Top left: example of a chest CT with central mass abutting the airway. This mass was classified as infiltrating the airway, as no plane could be identified between tumor and airway; R = right. Top right: the corresponding EBUS examination demonstrates an intact outermost airway layer and as such no evidence of infiltration. The EBUS finding was confirmed at time of surgery. Bottom: magnified EBUS image demonstrating the intact bronchial wall.
The correlation between the EBUS classification and the postoperative classification of airway involvement was statistically highly significant (correlation 0.89, \( p < 0.01 \)). There was a statistically nonsignificant correlation between chest CT and postoperative classification (correlation 0.06, \( p = 0.4 \)). The EBUS examinations added an average of 3.5 min (range, 2.4 to 5.9 min) to the time needed for a standard bronchoscopy, and no complications associated with the use of EBUS occurred.

**Discussion**

Lung cancer is a common disease, and surgical resection currently is the only reasonable hope for cure except for patients with small cell carcinoma. Accurate staging is crucial for appropriate patient selection and therapy planning. Also, surgical staging should be minimized for patients who can be ruled out for surgical resection by noninterventional means.

A special problem presents itself in the evaluation of central lesions with possible involvement of the airway wall. Anatomically, the airway wall consists of several layers that cannot be visualized with conventional imaging methods. This shortcoming may explain the inability to assess the issue of infiltration vs compression accurately.

This report confirms the limited ability of even modern chest CT to accurately image the airway wall. Currently, most of these patients need to...
undergo surgical evaluation for staging after unsuccessful bronchoscopic biopsy attempts.

EBUS with its excellent resolution and imaging of the layers of the bronchial wall has previously been evaluated for this purpose on few patients only. Our study is the largest to date comparing state-of-the-art chest CT and EBUS followed by histologic confirmation in determining airway wall infiltration. EBUS is highly specific and sensitive. Only six false-negative results were obtained (impression on imaging, but infiltration on surgery). They all occurred in the trachea, and in all cases this was believed to be due to insufficient circular contact of the probe with the airway wall because of a very large tracheal diameter. This technical shortcoming could easily be overcome in the future by using larger-diameter balloons to achieve full contact. No patients determined to have infiltrated airway walls by EBUS proved to be falsely assessed.

Our study suggests that EBUS, if performed by experienced endoscopists for the question of airway wall infiltration or compression, is highly accurate and superior to chest CT in assessing potential airway infiltration by malignant tumor. This study was designed to evaluate the ability of EBUS to contribute in the evaluation of patients with an airway wall possibly infiltrated by cancer. Even though we found EBUS to be highly accurate and superior to CT in this circumstance, it will need to be evaluated further concerning changes in therapy stemming from the information. Patients may be excluded from surgical resection for a variety of other reasons, such as carinal involvement, contralateral disease, and others. The addition of EBUS hypothetically could be of significant help in cases of questionable tracheal involvement to prove nonresectability or in questionable mainstem involvement to guide the extent or feasibility of resection. After the accuracy of this imaging modality has been established in this trial, further studies addressing this important topic are warranted.

### References


### Tables

**Table 3—Areas Suspicious for Airway Involvement**

<table>
<thead>
<tr>
<th>Location</th>
<th>Patients, No. (%)</th>
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<tbody>
<tr>
<td>Trachea</td>
<td>26 (25)</td>
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<tr>
<td>Right main bronchus</td>
<td>41 (39)</td>
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<tr>
<td>Left main bronchus</td>
<td>38 (36)</td>
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**Table 4—Correlation of CT Findings With Postoperative Findings in All Patients Undergoing Surgery (n = 105)**

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<th>Impression</th>
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<td>40</td>
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<tr>
<td>Impression</td>
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<tr>
<td>Total</td>
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**Table 5—Correlation of EBUS Findings With Postoperative Findings in All Patients Undergoing Surgery**

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<th>Invasion</th>
<th>Impression</th>
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</tr>
<tr>
<td>Impression (n = 56)</td>
<td>6</td>
<td>50</td>
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<tr>
<td>Total (n = 105)</td>
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