Grading Airway Stenosis Down to the Segmental Level Using Virtual Bronchoscopy*

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Objective: To assess the sensitivity of noninvasive virtual bronchoscopy based on multirow detector CT scanning in detecting and grading central and segmental airway stenosis using flexible bronchoscopic findings as the reference standard.

Materials and methods: In a blinded controlled trial, multirow detector CT virtual bronchoscopy and flexible bronchoscopy were used to search for and grade airway stenosis in 20 patients. CT scan data were obtained with a multirow detector CT scanner using 4 × 1 mm collimation. Flexible bronchoscopy findings were graded by a pulmonologist and served as the reference standard for 176 central airway regions (ie, trachea, main bronchi, and lobar bronchi) and 302 segmental airway regions. The extent of airway narrowing was categorized as grade 0 (no narrowing), grade 1 (<50%), or grade 2 (≥50%).

Results: Flexible bronchoscopy revealed 30 stenoses in the central airways and 10 in the segmental airways. Virtual bronchoscopy detected 32 stenoses in the central airways (sensitivity, 90.0%; specificity, 96.6%; accuracy, 95.5%) and 22 in the segmental airways (sensitivity, 90.0%; specificity, 95.6%; accuracy, 95.5%). The number of false-positive findings was higher in the segmental airways (13 false-positive findings) than in the central airways (5 false-positive findings), which caused a lower positive predictive value for the segmental airways (40.9%) than for the central airways (84.4%). Flexible and virtual bronchoscopic gradings correlated better for central airway stenosis (r = 0.87) than for segmental airway stenosis (r = 0.61).

Conclusion: Although a high sensitivity was found for the detection of both central and segmental airway stenosis, the number of false-positive findings was higher for segmental airways. However, noninvasive multirow detector CT virtual bronchoscopy enables high-resolution endoluminal imaging of the airways down to the segmental bronchi.

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Abbreviation: HU = Hounsfield units
bronchoscopy with multirow detector CT scanning enables the reduction of scan collimation to produce high z-axis resolution despite a short scan time. Virtual bronchoscopy was found to be highly accurate in the detection of central airway stenosis and to correlate closely with flexible bronchoscopy in grading tracheobronchial stenosis.

Preliminary evidence indicates that multirow detector CT scanning enables virtual bronchoscopic evaluation of peripheral airways such as the segmental and subsegmental bronchi if adequate scanning parameters are used.3 In the present study, we evaluated the diagnostic accuracy of CT virtual bronchoscopy in detecting and grading stenoses of both the central and segmental bronchi using flexible bronchoscopy as the standard of reference.

Materials and Methods

Patient Population

This blinded retrospective trial comprised 20 consecutive patients (age range, 50 to 81 years; mean age, 61 years; 15 men and 5 women). Eight of these patients also had been included in a previous study.14 Three of these eight patients had new follow-up CT scans in which both the central and segmental bronchi were evaluated for the first time. In the other five patients, the CT scan data fulfilling the inclusion criteria for the present study were evaluated for the first time at the segmental level and were reevaluated blindly for the central airways. Patients were only included if they had undergone both CT scanning and flexible bronchoscopy. The mean interval between virtual bronchoscopy and flexible bronchoscopy was 5.4 days (range, 0 to 17 days). Eventually, 17 of the 20 patients had lung cancer as the final diagnosis. Histologic diagnoses included non-small cell lung cancer (14 diagnoses) and small cell lung cancer (3 diagnoses). Because both procedures were performed in the context of patient care and were evaluated in retrospect, no institutional review board approval or patient informed consent had to be obtained, according to the guidelines of our institution.

CT Scanning

CT scan examinations were performed using a multirow detector CT scanner (Asteion; Toshiba; Tokyo, Japan) with 4×1 mm collimation, pitch 1.375, 120 kV, 0.75-s rotation time, and 100 to 180 mA. Acquisition time was 25 to 35 s to enable complete acquisition during a single breathhold. The chest was scanned during inspiration in a caudocranial direction after a power injection of 80 mL (flow rate, 2 mL/s; scan delay, 30 s) of iopromide IV contrast medium containing 300 mg/mL iodine (Ultravist 300; Berlex Laboratories; Montville, NJ). The reconstruction interval and slice thickness were each 1 mm.

Image Processing

Axial CT scan images were transferred to a workstation (Advantage for Windows 4.0; General Electric Medical Systems; Milwaukee, WI) running on appropriate hardware (Ultra Sparc 60; Sun Microsystems; Mountain View, CA) featuring two 450-MHz central processing units (Sun Ultra Sparc II) and 2 gigabytes of random access memory. Appropriate software (Navigator, version 2.03; General Electric Medical Systems) was used for the reconstruction of virtual bronchoscopic images. Image display used a surface-rendering algorithm and produced perspective grayscale images with a matrix of 512×512. Image segmentation was based on thresholding. All voxels with a density below the threshold level were considered to be within the bronchial lumen. An upper threshold between −400 and −550 Hounsfield units (HU) was used for endoluminal rendering of the central airways.15 For virtual bronchoscopic reconstruction of the peripheral airways, an upper threshold between −500 and −800 HU was used, depending on the caliber of the individual airways. To avoid the overestimation of airway stenosis, the upper threshold value was approached until the tracheobronchial wall was completely rendered without defects. Each bronchoscopic image simulated a coned-down view with an adjusted cone angle of between 50° and 80°, depending on the bronchial diameter and location within the tracheobronchial tree.

CT Scan Image Analysis

Table 1 shows the anatomic classification of the tracheobronchial tree, which was divided into 27 regions (9 central airway regions and 18 segmental airway regions). For image analysis, a virtual bronchoscopic fly-through of the tracheobronchial tree was performed in a central-to-peripheral direction by a fully board-certified radiologist specializing in chest radiology. For optimal orientation within the tracheobronchial tree and evaluation of the surrounding structures, virtual bronchoscopy was performed in the multiview mode in combination with dynamic axial and multiplanar reformatted imaging. The time for image analysis of a single patient ranged from 15 to 45 min. CT image analysis was performed in random order, and was blinded to flexible bronchoscopic findings and clinical history. Virtual bronchoscopy was evaluated using a flowchart that listed all airways to the segmental level. For each airway region, the estimated grade of stenosis was recorded using a 3-point scale as follows: grade 0, no stenosis; grade 1, luminal narrowing of <50%; or grade 2, luminal narrowing of ≥50%.16

Flexible Bronchoscopy

Flexible bronchoscopy was performed by a board-certified pulmonologist using a videobronchoscope (BF-1T200; Olympus Optical; Tokyo, Japan) under local anesthesia. The procedure time for bronchoscopy was about 30 min. The pulmonologist performing the procedure prospectively recorded the percentage of bronchial narrowing at all sites independent of CT scan data. Virtual bronchoscopic CT scan simulations of the airways were not available prior to flexible bronchoscopy, not directing the pulmonologist to particular areas of interest. Endobronchial photographs were obtained at stenotic sites. The presence and location of endoluminal mucus was routinely recorded on bronchoscopy reports. In retrospect, bronchoscopy reports were reviewed in random order without knowledge of the CT findings and clinical history, and for reasons of compatibility the grading of tracheobronchial narrowing was categorized as for virtual bronchoscopy using a 3-point scale as follows: grade 0, no stenosis; grade 1, luminal narrowing of <50%; or grade 2, luminal narrowing of 50% or more.

Statistical Analysis

The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of virtual bronchoscopy were calculated from 2×2 contingency tables, with confidence inter-
vals derived from binomial distribution. A Fisher exact test was used to test for significance in field entries smaller than five where the $\chi^2$ test was not applicable.

Assessments by virtual bronchoscopy were defined as overestimations or underestimations according to whether the particular stenosis was assigned a lower or higher grade on review of the findings of flexible bronchoscopy. The Spearman rank order correlation ($r$) was calculated to measure the strength of correlation between the results of virtual bronchoscopy and flexible bronchoscopy. A p value of $< 0.05$ was considered to be significant.

**Results**

Of the 20 examined patients, 17 had bronchial carcinoma (non-small cell lung cancer, 14 patients; small cell lung cancer, 3 patients) and had at least one tracheobronchial stenosis. Three patients did not have bronchial carcinoma and did not have airway stenosis. A total of 176 central airway regions and 302 segmental airway regions were evaluated. Four central airway regions and 51 segmental airway regions were excluded because complete luminal obstruction of the proximal airways made flexible bronchoscopic assessment impossible. In six patients, the right lower lobar medial basal segmental bronchus (B VII) was absent due to anatomic variation. In one patient, the right upper lobar apical segmental bronchus (B I) and right upper lobar posterior segmental bronchus (B II) had a common bronchial stem due to anatomic variation. The quality of CT data sets was good in all patients. None of the patients exhibited major breathing artifacts. Moderate cardiac motion artifacts were observed in all patients. They appeared as regular ring structures in the region of the tracheal bifurcation and lingula bronchi.

**Central Airways**

Flexible bronchoscopy revealed a total of 30 central airway stenoses. Thirteen stenoses were judged to be grade 1, and 17 were judged to be grade 2. Virtual bronchoscopy detected a total of 32 stenoses. Fourteen stenoses were judged to be grade 1, and 18 were judged to be grade 2. Figure 1 shows a grade 2 stenosis of the right main bronchus. Twenty-seven findings were true-positive, five were false-positive (ie, trachea, right upper lobe bronchus, intermediate bronchus, middle lobe bronchus, and left main bronchus), and three were false-negative (ie, right main bronchus, intermediate bronchus, and right lower lobe bronchus) [Table 2]. In four of the five false-positive stenoses, mucus was noted on flexible bronchoscopy, which was removed through irrigation and suction. Virtual bronchoscopy had 95.5% accuracy, 90.0% sensitivity, and 96.6% specificity for the detection of central airway stenosis. The positive predictive value was 84.4%, and the negative predictive value 97.9%.

As shown in Table 3, 168 of 176 central airway regions were correctly graded with virtual bronchoscopy (Fig 2). Virtual bronchoscopy correctly graded 25 of 27 verified stenoses. Two stenoses in the intermediate bronchus were graded too high. The correlation between virtual bronchoscopic and flexible bronchoscopic grading of central airway stenosis was good ($r = 0.87$; p $< 0.0001$).

**Segmental Airways**

Flexible bronchoscopy revealed a total of 10 segmental airway stenoses. Three stenoses were judged to be grade 1 and seven were judged to be grade 2.
Virtual bronchoscopy found a total of 22 peripheral airway stenoses. Fourteen stenoses were judged to be grade 1 and 8 were judged to be grade 2. Figure 3 demonstrates a grade 2 stenosis of the left upper lobar posterior segmental bronchus (B II). Nine findings were true-positive, and 13 were false-positive. The 13 false-positive findings were for the left upper lobar apicoposterior segmental bronchus (B I/III) [two patients], the left upper lobar anterior segmental bronchus (B III) [two patients], the right lower lobar superior segmental bronchus (B VI), the right upper lobar apical segmental bronchus (B I) [two patients], the right upper lobar posterior segmental bronchus (B II), the right upper lobar anterior segmental bronchus (B III), the left lower lobar anteromedial segmental bronchus (B VII/VIII), the right lower lobar medial basal segmental bronchus (B VII), the middle lobar medial segmental bronchus (B IV), and middle lobar lateral segmental bronchus (B V). In seven of the 13 false-positive stenoses, mucus was noted on flexible bronchoscopy, which was removed through irrigation and suction. One false-negative finding was made in the left lower lobe superior segmental bronchus (B VI). The sensitivity (90.0%), accuracy (95.5%), and negative predictive value (99.6%) of virtual bronchoscopy for the diagnosis of segmental airway stenosis were similar to those for the central airways. The positive predictive value, however, was lower for the segmental airways (40.9%) than for the central airways (54.4%).

Virtual bronchoscopy correctly graded 286 of 302 airway regions. It correctly graded all nine true-positive stenoses. The correlation between virtual bronchoscopic and flexible bronchoscopic grading of peripheral airway stenosis was lower ($r = 0.61$; $p < 0.0001$) than for grading of central airway stenosis ($r = 0.87$; $p < 0.0001$).

Analysis Per Patient

Eventually, 17 of the 20 patients had lung cancer as final diagnosis, and 12 patients had at least one stenosis. The per patient sensitivity of virtual bronchoscopy was 91.7% (11 of 12 patients) for the detection of airway stenoses due to bronchial carcinoma ($p < 0.001$). In one patient, a stenosis of the left lower lobe superior segmental bronchus (B VI) was not detected. In another patient, a false-positive stenosis was found in the right upper lobe bronchus. Accordingly, per patient specificity was 87.5%, and per patient accuracy was 90.0%.

Discussion

We evaluated the success rate of noninvasive, multirow detector CT virtual bronchoscopy in de-
tecting and grading central and segmental airway stenosis. In our present study, virtual bronchoscopy enabled high-resolution endoluminal imaging of the airways including segmental bronchi. Virtual bronchoscopy of segmental airway stenosis provides important additional information on the tracheobronchial tree and was not evaluated in earlier reports, where it has been applied exclusively for the detection of central airway stenosis. A preliminary study concluded that virtual bronchoscopy can render stenosis in anatomic detail, but that further studies were needed to evaluate its diagnostic potential. Other studies have found virtual bronchoscopy to have a high sensitivity (90%) and specificity (98%) in detecting central airway stenosis in patients with bronchial carcinoma. The results of these studies were confirmed by our investigations, showing a sensitivity of 90% for detection of central airway stenosis. Additionally, we found a sensitivity of 90% for the detection of segmental airway stenosis, although the number of false-positive findings here was higher. Segmental airway stenosis had not been evaluated in any of the previously conducted studies.

There are several reasons for the misinterpretation of virtual bronchoscopic findings on stenosis. The present study had three false-positive findings of stenosis located in the middle lobar bronchus. It has been reported that stenoses occurring in the middle lobar bronchi and lingula may lead to the inaccurate estimation of the bronchial caliber. This occurs because these airways lie parallel to the axial scan plane and their walls are less well-depicted than those of bronchi running perpendicular to the scanning plane, such as the intermediate bronchi. Similarly, one false-positive and one false-negative finding of stenosis in the right inferior lobar superior segmental bronchus (B VI) may have been misread because of the difficulty in assessing this segmental airway using virtual bronchoscopy. False-positive readings in

<table>
<thead>
<tr>
<th>Variables</th>
<th>Central Airways</th>
<th>Segmental Airways</th>
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<tbody>
<tr>
<td>Total graded airway regions, No.</td>
<td>176</td>
<td>302</td>
</tr>
<tr>
<td>Correctly graded airway regions, No.</td>
<td>167</td>
<td>296</td>
</tr>
<tr>
<td>Airway regions graded too low, No.</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Airway regions graded too high, No.</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Correlation (r) between virtual bronchoscopy and flexible bronchoscopy when grading airway stenosis</td>
<td>0.87</td>
<td>0.61</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.53–0.91</td>
<td>0.53–0.68</td>
</tr>
<tr>
<td>p value</td>
<td>&lt; 0.0001</td>
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these bronchi may lead to further diagnostic studies with potential morbidity.

Compared to the central airways, we found a higher rate of false-positive stenoses in the segmental bronchi. In our study, intraluminal mucus deposition caused more false-positive segmental airway readings (seven) than false-positive central airway readings (four). It has been reported that the segmental airways seem to be more susceptible to the deposition of mucus and coagulated blood, which can only be removed by irrigation and suction on flexible bronchoscopy. This may explain why we found a lower positive predictive value for segmental airway stenosis (40.9%) than for central airway stenosis (84.4%).

Interindividual variation of the bronchial caliber, which may cause misinterpretation of the bronchial lumen, may be more frequent on the level of the segmental bronchi. This also may contribute to our finding of a better correlation between flexible and virtual bronchoscopy in the grading of stenoses within the central \( r = 0.87 \) than in the segmental airways \( r = 0.61 \).

Although virtual bronchoscopy with single-detector helical CT scanning is reported to have excellent sensitivity and specificity in detecting central airway stenosis, it is limited by the relatively long scanning times needed for a narrow collimation. This is more likely to cause breathing and motion artifacts, especially in patients with airway disease that may restrict their ability to hold their breath for a sufficient length of time. This may lead to the misinterpretation of the tracheobronchial lumen and false-positive findings. Scanning time can be kept short using multirow detector CT scanning despite a thin collimation, which enhances z-axis resolution of the CT data set and consequently improves the quality of virtual bronchoscopic images. This enables the expanded use of virtual bronchoscopy not only for the central airways, but also for the segmental and subsegmental airways. When a thin collimation (eg, 4 × 1 mm) is used, virtual bronchoscopy can be reconstructed from any routine chest multidetector CT scan in retrospect, and radiograph exposure does not exceed that of a normal chest CT scan.

Because virtual bronchoscopy has an interactive design, we used the multiview mode at the workstation in combination with axial CT scan slices and multiplanar reformats for analysis of the airways. This is particularly useful for orientation within the tracheobronchial tree, and permits differentiation between intraluminal tumor growth and extraluminal airway compression. Furthermore, axial and reformatted CT scan slices are an indispensable tool for thoracic CT diagnosis, providing important anatomic and pathologic information beyond the lumi-

Figure 2. A 73-year-old woman with non-small cell lung cancer of the left upper lobe causing a grade 2 (≥50%) stenosis accompanied by atelectasis of the left upper lobe including the lingula. CT virtual bronchoscopy (top) and flexible bronchoscopy (middle) both reveal an obstruction of the left upper lobe bronchus (arrows), which was correctly classified as a grade 2 stenosis with virtual bronchoscopy. Bottom: coronal reformatted CT scan image demonstrates left upper lobe atelectasis (arrow).
nal view of a bronchoscope, and permitting the detection of adenopathy and neighborhood infiltration.

Virtual bronchoscopy uses surface rendering, which takes advantage of the natural contrast between the airway and surrounding tissues. Therefore, the level of thresholding is important for displaying accurate simulations. For displaying the central airways, we used an upper threshold between $-400$ and $-550$ HU. For virtual bronchoscopic reconstruction of segmental bronchi, we adapted the threshold to lower values of between $-500$ and $-800$ HU, depending on the individual caliber of the airways. We cannot fully exclude that this somewhat subjective choice may have caused overestimation or underestimation of the airway diameter.

An intrinsic limitation of virtual bronchoscopy is its inability to permit therapeutic and diagnostic maneuvers. As observed in our study, especially the segmental bronchi may be susceptible to the deposition of mucus and coagulated blood, which may be misinterpreted as stenosis on virtual bronchoscopy. These depositions can be removed through irrigation and suction on flexible bronchoscopy. Flexible bronchoscopy procedures, however, can be uncomfortable for the patient and may require sedation. In addition, complications relating to the procedure itself and anesthesia have been described. The complications of flexible bronchoscopy must therefore be weighed against the considerable amount of diagnostic and therapeutic information gained from the procedure.

As demonstrated in our study, virtual bronchoscopy may be used for the evaluation of both central and segmental airway stenosis. This enables the evaluation of the segmental airways distal to a stenosis, which is impassable for flexible bronchoscopy. Other potential clinical uses of virtual bronchoscopy include the planning of flexible bronchoscopy, the identification of abnormal airways and pathologic lymph nodes, and the follow-up of airway stenosis over time, in response to treatment, or in patients too ill to tolerate flexible bronchoscopy. Flexible bronchoscopy and virtual bronchoscopy should not be pitted against each other but, rather, should be used as complementary techniques.

In conclusion, virtual bronchoscopy with multirow detector CT scanning enables high-resolution endoluminal imaging of both central and segmental bronchi. It is slightly more accurate at assessing central airway stenosis than segmental airway stenosis. Virtual bronchoscopy may be used clinically in individual cases, such as in cases of an impassable stenosis in patients undergoing flexible bronchoscopy. In the near future, improved multirow detector CT scanners with a higher longitudinal resolution
and reduced scanning times should further enhance the resolution of virtual bronchoscopy, especially for segmental bronchi of small caliber that lie parallel to the axial scan plane. Furthermore, it remains to be studied whether inhalation and expectoration maneuvers of the patient prior to virtual bronchoscopy may help to evacuate secretions from the lumen of smaller bronchi, which could reduce false-positive findings. This may well improve the virtual bronchoscopic assessment of segmental and subsegmental airways for stenosis, allowing for the visualization of more distal airways and thus enabling the detection of endobronchial lesions distal to the reach of a flexible bronchoscope.23

REFERENCES