Can virtual bronchoscopy be a complementary method for fiberoptic bronchoscopy?

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**Aims and objectives**

The usual diagnostic procedures for detection and diagnosis of tracheobronchial pathologies are computerized tomography (CT) and fiberoptic bronchoscopy (FOB) [1]. FOB is considered to be the 'gold standart' technique that allows direct visualization of the airway lumen and mucosa. Though its importance in the diagnosis of a variety of neoplastic, inflammatory, and infectious diseases, FOB has several limitations. It is invasive, time consuming, and it requires sedation [2]. Also, FOB may have some complications, especially in severely ill patients and some of the patients may not tolerate the procedure. Besides, the operator is unable to evaluate the airway calibre and morphology beyond the obstruction [3]. Physicians can now explore tracheobronchial tree on volumetric three-dimensional images with the increasing sophistication in CT technology [4]. Virtual bronchoscopy is a promising computer-assisted imaging technique that allows a three dimensional (3D) evaluation of tracheobronchial tree similar to those obtained during FOB. Although the technique was described in the mid 1990s, it is generating new interest as a result of improvements in multislice computed tomography and postprocessing technology [5]. Multidetector CT - unlike single-detector CT - has the advantage of providing high-resolution multiplanar reformatted images because of its high z-axis resolution [6]. It was found to be highly accurate in the detection of central airway stenosis and correlated closely with FOB in grading tracheobronchial stenosis [7]. This study explores the utility of VB to evaluate various tracheobronchial lesions and grading stenosis using FOB as the standart of reference.
Methods and materials

Patients

The population of this prospective study was 42 patients examined in our department between November 2013 and February 2014. The mean age of all patients was 62.7±11.9 years (median: 64 years; ranged between 30 to 80 years). 34 patients (80.9%) were male (mean age: 62.85±12.21, years; median age: 65 years; ranged between 30 to 80 years), 8 patients (20.1%) were female (mean age: 62.25±11.48 years; median age:63 years; ranged between 49 to 80 years). All patients underwent both CT and FOB. The inclusion criteria was the presence of a clinical indication for bronchoscopic evaluation. The clinical indications were cough, hemoptysis, persisting or recurrent pulmonary infections, suspicion of foreign-body aspiration, abnormal findings at physical examination and chest X-ray abnormality. Patients were only included if they had undergone both CT scanning and flexible bronchoscopy. Virtual bronchoscopy results were evaluated blindly and independently from those of FOB, which was performed at a different time not more than 30 days. The mean interval between virtual bronchoscopy and flexible bronchoscopy was 14.8+-9.1 days (median 14 days, ranged between 0 to 30 days). The local ethical committee had approved the study protocol and the patients had given informed consent before the examinations.

Multidetector CT Technique and CT Scan Image Analysis

CT examinations were performed on a 80-row detector CT (160 slice) scanner (Aquilion Prime, Toshiba Medical Systems, Nasu, Japan) with the following parameters; collimation, 4× 2 mm; pitch, 1.375; rotation time, 0.75 sec; 120 kVp; 100-180 mAs, and with a slice thickness of 0.5 mm. Acquisition time was roughly 20 sec to allow completion of the acquisition during a single breath-hold. The thorax was scanned during inspiration in a caudocranial direction after power injection of 80 mL (flow rate, 2 mL/sec; scan delay, 30 sec) of iopromide (Ultravist; Schering, Berlin, Germany) IV contrast medium containing 300 mg I/mL via automated injector (Missouri CT Injector, Ulrich Medical, Ulm, Germany). Adaptive Iterative Dose Reduction 3D (AIDR 3D) was used as an iterative dose reduction software and Sure Exposure 3D was used as a mA modulation software for all the examinations. Axial CT images were transferred to a workstation (Aquarius, TeraRecon Inc., San Mateo, CA, USA). Axial CT, coronal and sagittal MPR images with a slice thickness of 1 mm and with section intervals of 1 mm were reconstructed. Virtual bronchoscopic images obtained via the AquariusNET program (TeraRecon Inc., San Mateo, CA, USA) were evaluated simultaneously, dividing the computer screen into four equal quadrants in multiview mode. Two-dimensional views were evaluated by two radiologists (MBA, EU) with at least five year of experience, at the standard parenchymal window and mediastinal window for lesions' endobronchial extensions, relations with neighboring structures and accompanying pathologies independently from the FOB results. Assessed on ten randomly selected patients, the overall Pearson
correlation for interobserver reliability was 0.93 and intrarater reliability was 0.95, based on the evaluation of the same segments on different times by the same radiologist (MBA). 3D images were obtained by the volume-rendering technique. The lumen of the tracheobronchial tree was evaluated by moving from the proximal trachea using the 'SAT lung' programme. Tracheobronchial tree was divided into 27 regions (trachea, 8 central and 18 segmentary bronchus) and were evaluated both with FOB and VB in a blinded manner. The presence or absence of the endoluminal lesions (leading to <50% narrowing in the lumen), obstructive lesions (leading to >50% narrowing in the lumen), external compressions and mucosal lesions (ie, mucosal infiltration, anthracosis, chronic bronchitic changes) were recorded. Mucosal changes were noted if mucosal granularity and irregularity of the bronchial surfaces had been seen on VB. Also anatomical variations and diverticulas were noted on both VB and FOB.

**Fiberoptic Bronchoscopy**

For each FOB, visualization and interpretation of the tracheobronchial tree were achieved under the direction of the attending pulmonary physician who were blinded to the radiologist's interpretation of the imaging modalities. All FOB were performed with EPX-4400 Fujinon video endoscopy equipment in a bronchoscopy suite or in the intensive care units of our university hospital, with cardiopulmonary monitoring (pulse oximetry, non-invasive blood pressure measurement and three lead electrocardiography) by a pulmonary physician. All patients received sedation and local anesthesia during FOB. Midazolam (intravenous route) was used for conscious sedation and lidocaine (spray 10 mg/dose) was used for local anesthesia. The choice of sampling procedure during FOB was at the physician's discretion. Bronchial washing (BW) specimens were sent for acid-fast bacilli smear and culture for tuberculosis, bacterial culture, and cytological analyses. Bronchoalveolar lavage, transbronchial needle aspiration, mucosal and parenchymal biopsy samples were sent for pathological examination. Complications during FOB were also noted. Patients had chest roentgenograms after parenchymal biopsy to assess pneumothorax. Results of these procedures were recorded.

**Statistical Analysis**

Statistical analysis of virtual bronchoscopy revealing central and segmental airways stenosis in 42 patients using flexible bronchoscopy as the gold standart was performed. Qualitative results regarding the depiction of tracheobronchial narrowings and/or abnormalities with VB were defined as true-positive, true-negative, false-positive, and false-negative findings. A true-positive finding was classified as narrowing and/or abnormality noted at both image modalities (VB and FOB), whereas a true-negative finding was defined as absence of stenoses and/or airway abnormalities at FOB and multidetector VB. A false-positive finding was defined as an airway section noted as abnormal at VB but normal at FOB. A false-negative finding was defined as an airway section noted as normal at VB but abnormal at FOB. Sensitivity, specificity,
positive predictive value (PPV), negative predictive value (NPV) were calculated with 2x2 contingency tables. Pearson correlation coefficient (r) and significance (p values) were calculated between the variables. To analyze differences in the distribution of categorical data, $X^2$ test or Fisher Exact Test was used, as appropriate; p <0.05 was considered significant.
Results

A sum of 1115 airway segment of 42 patients were evaluated. 1 patient had right pneumonectomy and 1 patient had right upper lobectomy. One of them had 3 segmentary bronchus of the left upper lobe bronchus, one had two segments of right upper lobe, and 3 segments of the right lower lobe bronchus. While 5 out of 42 cases (11,9%) were evaluated as normal on both VB and FOB, a total of 44 pathologies were detected in 37 patients(88%) by FOB (Table 1). Based on the findings, 4 of the patients had endoluminal, 17 had obstructive lesions, 3 had external compressions, 17 had mucosal changes, 3 had anatomical variations and 5 of the patients had normal bronchoscopic findings. 14 patient had malign pathologies; 3 adenocarcinoma, 5 squamous cell carcinoma, 3 small cell carcinoma, 1 had squamous metaplasia, 1 had nonsmall cell cancer but couldn't subtyped, 1 had carcinomatous infiltration but couldn't typed, and 4 had chronic inflammation. 2 of the patients had diverticula according to VB and couldn't be seen by FOB. One had tracheal diverticula (figure 1) and the other had diverticula in the left second carina. All of the anatomical variations were depicted on both VB and FOB as they were mentioned above. The sensitivity and specificity values for detection of endoluminal lesions 66,6%, 92,3 %, for diagnosis of obstructive lesions was 88,8% and 96,7%, and for mucosal changes they were 41,1% and 96%. While VB detected 2 of the endoluminal lesions, FOB found 3; but, VB couldn't find 1 milimetric endoluminal lesion. VB found 5 other endoluminal lesions, but these lesions were containing air spaces and they were spike-shaped or had lobulated contours. So, they were thought to be mucus plaques. VB found 16 of the 18 obstructive lesions. In our study, obstructive malign tumoral extension in the segmentary bronchus of left lower lobe in 2 patients were depicted by VB which couldn't be displayed with FOB (figure 2). VB couldn't see one of the external compressions, we believe that it may be due to the deep inspiration during the CT imaging. In evaluating external compressions VB found 6, while FOB found 3. While FOB detected 17 mucosal lesions, VB detected 7 of them (figure 3). Due to the effectiveness in detecting extraluminal structures and poststenotic segment evaluation, VB found 6 external compressions, but FOB found 3. VB couldn't see one of these external compressions, it may be due to the deep inspiration during the CT imaging. Based on these findings, accuracy of VB for diagnosis of obstructive lesions was highest (figure 4), however VB was less effective in detecting mucosal changes (Table 1, 2).
Table 1: Sensitivity, specificity, positive and negative predictive values of VB in detecting endoluminal, obstructive and mucosal lesion.

<table>
<thead>
<tr>
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<th>Endoluminal lesion</th>
<th>Obstructive lesion</th>
<th>Mucosal lesion</th>
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<tbody>
<tr>
<td>VB</td>
<td>2</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>FOB</td>
<td>3</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>True positive</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>True negative</td>
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<td>30</td>
<td>24</td>
</tr>
<tr>
<td>False positive</td>
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<td>1</td>
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</tr>
<tr>
<td>False negative</td>
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<td>10</td>
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<td>Sensitivity (%)</td>
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<tr>
<td>Specificity (%)</td>
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<tr>
<td>Positive predictive value (%)</td>
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<tr>
<td>Negative predictive value (%)</td>
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### Table 2

<table>
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<tr>
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<th>Anatomical variation and diverticula</th>
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<tr>
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<td>FOB</td>
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<tr>
<td>Positive</td>
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<td>3</td>
</tr>
<tr>
<td>Negative</td>
<td>37</td>
<td>39</td>
</tr>
</tbody>
</table>

*FOB: Fiberoptic bronchoscopy, VB: Virtual bronchoscopy*

Table 2. Detection of external compression, anatomical variations and diverticula with VB and FOB
Figure 1: A 2 cm diverticula located in the right posterolateral wall of the trachea was demonstrated on the sagittal reformatted CT image (A), its outer sight on virtual bronchoscopy (B), its inner aspect on axial CT (C) and on virtual bronchoscopy (D). This lesion couldn’t be demonstrated by FOB, maybe due to its small neck as displayed here on image D.

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Figure 2: Squamous cell carcinoma case; left lower lobe superior segment and all the basal segmentary bronchus was obstructed with the lesion. FOB demonstrated the lower lobe and lower lobe superior segmentary bronchial obstruction but VB showed all the basal and superior segmentary bronchial obstructions.

**Fig. 2**

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Figure 3: A 80 years old female patient, FOB was reported severe anthracosis and mucosal irregularity. When compared to the normal mucosal surface of a 51 years old female patient (E) VB was able to show these changes on figure B.

**Fig. 3**
Figure 4: A 59 years old male patient with endoluminal obstructive lesion in the left upper lobe bronchus. Axial, coronal, sagittal MPR images on the mediastinal window and virtual image was shown on A, FOB reported left upper lobe bronchus was obstructed with a necrotic endobronchial lesion (B).

Fig. 4
Conclusion

In this study, various tracheobronchial pathologies were evaluated comparatively with VB and FOB. VB can be used to display normal anatomic features of the tracheobronchial tree and to identify anatomical variants [[8], [9], [10]]. In the study by Heyer et al, the sensitivity and specificity of VB in the evaluation of stenosis by tracheobronchomalacia in children were 86% and 85% [11]. In the present study, 3 anatomical variations were demonstrated using both FOB and VB, but when VB displayed 2 diverticulas -one was on trachea and one was on the left second carina- but none of them could be identified on FOB (picture 1). It may be due to the difficult visualization of the small neck of these diverticulas endoscopically, but because of VB can show its' extraluminal extension. An advantage of VB over fiberoptic bronchoscopy is the ability to image beyond the site of obstruction and to visualize the smaller airways, which are not accessible with FOB. According to the study by Finkelstein et al. VB depicted 5 peripheral obstructive lesions beyond the size limitation of the endoscope [12]. Although VB is considered superior to FOB for distal airway visualization, if the evaluation is carried out in conjunction with MPR and axial images, the performance can be further enhance [13]. In addition, it can evaluate the extraluminal extension of the lesion, neighbouring structures with the help of multiplanar reformatted images (MIP) on coronal and sagittal planes [11]. For these reasons, VB provides a road map for bronchoscopy as a guide for transbronchial biopsy, stent placement, laser therapy or radiotherapy. There are some limitations for VB. First, the natural color is absent, changes such as surface infiltration cannot be recognized, and the spatial resolution is limited, still less than FOB. The radiation exposure is involved because VB image is based on CT examination. Retained secretions could occasionally be mistaken for obstructive lesions leading to false-positive results [2]. In addition, VB quality is dependent on CT source data and recommended Digital Imaging and Communications in Medicine (DICOM) parameters may be unavailable [14]. CT virtual imaging can be used to achieve excellent mucosal and lesion detail when volume rendering is used, with the transition zone (mucosa) reconstructed separately from the wall and the lumen as we used in the present study to visualize the mucosa as a separate structure with lifelike colors, which adds image depth and lesion relief to the virtual images [15]. Although pervious studies declared that VB was not able to depict mucosal changes [[5], [16]], this study provides elaborate assessment of the mucosal changes like anthracosis, chronic bronchitic changes and mucosal infiltration. We defined abnormal mucosa if the mucosa had excessive granularity or irregularity (picture 3). Unfortunately, VB is not effective for the detection of subtle mucosal abnormalities such as erythema or early mucosal infiltrations. As mentioned in the study, VB failed to display malign mucosal infiltration in 2 patients. Further investigations with large scale studies and age-matched control groups are needed to evaluate the effectiveness of VB on mucosal changes. It may be a good idea to subject all pertinent cases to MDCT first, make a reasonably accurate diagnosis and filter out those cases that actually need conventional bronchoscopy. The MDCT images along with VB help facilitate pre-bronchoscopy planning and navigation during bronchoscopy.
In conclusion; multidetector CT virtual bronchoscopy is a safe, noninvasive and sensitive diagnostic modality for endoluminal assessment of tracheobronchial tree. In selected patients whom cannot tolerate or have contraindications for FOB, it can be used as an initial method. By developing large scale studies, VB will have wider acceptance, including its use as a complementary method with FOB.
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