

Virtual bronchoscopy for evaluation of malignant tumors of the thorax

Steven E. Finkelstein, MD^a
Ronald M. Summers, MD, PhD^b
Dao M. Nguyen, MD^a
John H. Stewart IV, MD^a
Jean A. Tretler, RN^a
David S. Schrupp, MD^a

Objective: Virtual bronchoscopy is a novel technique making use of 3-dimensional reconstruction of 2-dimensional helical computed tomographic images for noninvasive evaluation of the tracheobronchial tree. This study was undertaken to evaluate the diagnostic potential of virtual bronchoscopy by comparing virtual bronchoscopic images with fiberoptic bronchoscopic findings in patients with thoracic malignant disease.

Methods: Thirty-two consecutive patients with thoracic malignant tumors underwent virtual bronchoscopy for evaluation of suspected tracheobronchial lesions. For each virtual bronchoscopic examination, 200 to 300 contiguous 1.25-mm images of the thorax were obtained in only one or two 17-second breath holds by using a multislice computed tomographic scanner. Virtual bronchoscopy images were reconstructed and interpreted blind to the actual endoscopic findings. Results of virtual bronchoscopy were compared with fiberoptic bronchoscopic findings in 20 patients.

Results: Anatomic computer simulation of the bronchial tree was successfully created in all patients. In 7 (35%) of 20 patients, results of fiberoptic bronchoscopy were found to be within normal limits. In all patients with normal anatomy, virtual bronchoscopy accurately correlated with the fiberoptic findings. Thirteen (65%) patients had a total of 22 abnormal findings on fiberoptic bronchoscopy. Virtual bronchoscopy detected 18 of 22 abnormal fiberoptic bronchoscopic findings: 13 of 13 obstructive lesions, 5 of 6 endoluminal lesions, and 0 of 3 mucosal lesions. The sensitivity of virtual bronchoscopy was 100% for obstructive lesions, 83% for endoluminal lesions, 0% for mucosal lesions, and 82% for all abnormalities; the specificity of virtual bronchoscopy was 100%.

Conclusions: Preliminary evaluation indicates that virtual bronchoscopy may be a promising and noninvasive modality for identifying bronchial obstructions and endoluminal lesions, as well as for assessing the tracheobronchial tree beyond stenoses. However, at present, virtual bronchoscopy does not enable the detection of subtle mucosal lesions, and as such, this modality may not be appropriate for identifying premalignant lesions in the respiratory tract. Although fiberoptic bronchoscopy remains the standard modality for evaluating airway patency and mucosal lesions, virtual bronchoscopy may provide additional information that may be useful in the management of pulmonary malignant tumors.

From the Thoracic Oncology Section, Surgery Branch, Center for Cancer Research,^a and the Diagnostic Radiology Department, Warren Grant Magnuson Clinical Center,^b National Institutes of Health, Bethesda, Md.

Presented in oral format at the Annual Meeting of the Society of Surgical Oncology, Washington DC, March 16, 2001

Received for publication June 13, 2001; revisions requested Aug 31, 2001; revisions received Oct 5, 2001; accepted for publication Oct 26, 2001.

Address for reprints: David S. Schrupp, MD, Head, Thoracic Oncology Section, Surgery Branch, National Cancer Institute, Building 10, Room 2B07, 10 Center Dr, Bethesda, MD 20892-1502 (E-mail: David_Schrump@nih.gov).

J Thorac Cardiovasc Surg 2002;123:967-72

Copyright © 2002 by The American Association for Thoracic Surgery

0022-5223/2002 \$35.00+0 12/1/121495

doi:10.1067/mtc.2002.121495

Virtual bronchoscopy (VB) is a novel technique making use of 3-dimensional (3-D) reconstruction of high-resolution helical computed tomographic (CT) images for noninvasive evaluation of the tracheobronchial tree. VB involves perspective surface or volume rendering of 2-dimensional (2-D) CT scan images to construct endoscopic-like visualization of the airway.¹ Because patients with malignant tumors of the thorax frequently have complete bronchial obstructions caused by endoluminal tumors and extrinsic compression, a noninvasive, reproducible, and objective method for sequentially evaluating these abnormalities might prove useful in guiding therapy and assessing treatment response in these individuals.²

Patients with mediastinal and central pulmonary lesions typically undergo conventional CT scanning of the chest, followed by fiberoptic bronchoscopy (FB).³ CT generates 2-D cross-sectional images of the thorax to provide information regarding peribronchial anatomy. In the evaluation of major endobronchial disease, CT scans have a sensitivity of 63% to 100% and a specificity of 61% to 99%.⁴⁻⁶ Sub-optimal scanning techniques, inappropriate slice thickness, and artifacts between sections may limit the accuracy of airway anatomy defined by conventional CT scans.⁷ FB remains the best modality for evaluation of endoluminal and mucosal lesions; however, endoscopy yields no information about the extent of extraluminal disease or airway patency distal to a high-grade stenosis.⁸ In addition, FB poses a potential risk to the patient (morbidity 0.8%) because some degree of sedation is required⁹; this risk may be increased in patients with advanced intrathoracic disease.

VB, also referred to as computerized tomographic bronchography, uses noninvasive high-resolution CT techniques exploiting the natural contrast between the air in the tracheobronchial tree and the soft tissue of the airway wall to establish a plane for generating the virtual airway⁶; the images are used to generate a 3-D model of airway anatomy. Once the virtual airway is created, the viewer can navigate through the airway in a 3-D manner analogous to standard FB. In addition, VB allows for unconventional images, such as retrograde views of endoluminal and extraluminal anatomy.⁸ The airway can be manipulated in space and evaluated from multiple angles.

In the present study we sought to examine the utility of VB relative to conventional diagnostic modalities in thoracic oncology patients. Herein we report that VB is an excellent, reproducible, and noninvasive modality that can be used to image tracheobronchial lesions, thus enabling sequential evaluation of treatment response in patients with malignant disease of the thorax. In addition, VB may be helpful in selecting patients for segmental lung resections or

ablation of high-grade bronchial stenoses with laser or photodynamic techniques.

Methods

Patients

Thirty-two consecutive patients with thoracic malignant disease were prospectively enrolled in institutional review board-approved National Institutes of Health (NIH) Protocol 96-CC-0021 and evaluated by means of VB between November 19, 1999, and January 2, 2001. Inclusion criteria were the presence of a malignant tumor of the thorax and willingness to undergo investigational imaging at the NIH. Informed consent was obtained from each participant. After VB images had been successfully acquired in 10 patients, an additional 22 individuals were accrued, with the intent of obtaining correlative FB images within 2 weeks of VB. Two of these 22 patients were subsequently excluded from analysis because correlative bronchoscopy was not obtained within 2 weeks after VB. The mean age of all patients was 54 years (median age, 54 years; SD, ± 12 years; age range, 29-88 years). Of these 32 patients, 23 (72%) were men (mean age, 54 years; median age, 57 years; SD, ± 11 years; range, 33-88 years), and 9 (28%) were women (mean age, 52 years; median, 51 years; SD, ± 15 years; range, 29-79 years). Histologic diagnoses included non-small cell lung cancer ($n = 12$), small cell lung cancer ($n = 3$), metastatic renal cell cancer ($n = 8$), metastatic melanoma ($n = 5$), metastatic thyroid cancer ($n = 2$), sarcoma ($n = 1$), and esophageal cancer ($n = 1$).

Examination Technique

For each FB, visualization of the tracheobronchial tree was achieved under the direction of the attending thoracic surgeons (D.S.S. and D.M.N.), who were blinded to results of VB. FB findings that were entered into the database included the presence or absence of obstructive lesions (defined as bronchial narrowing of $>50\%$), endoluminal masses (defined as a mass protruding into the lumen with $<50\%$ occlusion), or mucosal lesions (hemorrhage, erythema, or tissue friability).

For each VB, 200 to 300 contiguous 1.25-mm images of the thorax were obtained in only one or two 17-second breath holds by using a multislice helical CT scanner (G.E. LightSpeed QX/i, Milwaukee, Wis).¹⁰ The technique was 1.25 collimation, HS mode (helical pitch 6, 7.5-mm table motion per rotation, 120 kVp, 100 mAs, 0.8-second tube rotation, nonoverlapping reconstructions with a section interval of 1.25 mm and an effective z-axis resolution of approximately 1.6 mm). The manufacturer's standard reconstruction algorithm was used. The multiple scan average dose to the scanned volume was 1.58 rad at the surface and 0.78 rad in the center per examination. Radiation exposure from VB was calculated to be the same or slightly less than that with a conventional thoracic CT scan (James Vucich, Medical Physicist, NIH).

3-D Reconstruction and Analysis

VB images were reconstructed to 3-D endoscopic views by using commercial software (G.E. Navigator on a G.E. Advantage Windows workstation). The radiologist (R.M.S.) first placed the viewpoint in the proximal trachea. Retrograde inspection of the subglottis was done. The following were reviewed sequentially: antegrade inspection of the trachea, right main stem bronchus,

right upper lobe apical B1, right upper lobe posterior B2, right upper lobe anterior B3, bronchus intermedius, right middle lobe, right middle lobe lateral B4, right middle lobe medial B5, right lower lobe superior B6, right lower lobe medial basal B7, right lower lobe anterior basal B8, right lower lobe lateral basal B9, right lower lobe posterior basal B10, left main stem bronchus, left upper lobe, left upper lobe superior division, left upper lobe apical posterior B1+2, left upper lobe anterior B3, lingular, left upper lobe superior lingular B4, left upper lobe inferior lingular B5, left lower lobe superior B6, left lower lobe anteromedial basal B7-8, left lower lobe lateral basal B9, and left lower lobe posterior basal B10.

Abnormalities in the tracheobronchial tree were recorded. The radiologist interpreted all VB images blind to the actual FB results. The presence or absence of obstructive lesions (defined as bronchial narrowing of >50%), endoluminal masses (defined as a mass protruding into the lumen with <50% occlusion), or mucosal lesions (hemorrhage, erythema, or tissue friability) were entered into the database.

The results of VB were compared with actual FB findings at the same anatomic sites. True-positive (TP) results occurred when VB equaled FB when FB visualized a lesion. True-negative (TN) results occurred when VB equaled FB when FB was within normal limits. False-negative (FN) results occurred when VB failed to detect a lesion documented during FB. False-positive (FP) results occurred when VB demonstrated an abnormality, but FB revealed the area to be normal. Sensitivity (TP/[TP+FN]) and specificity (TN/[TN+FP]) of VB were computed.

Results

Anatomic computer simulation of the bronchial tree was successfully created in all patients. There were no significant respiratory or cardiac motion artifacts precluding 3-D image reconstruction. Of the 20 patients who had correlative FBs, 7 (35%) had normal examination results (Figure 1). In all patients with normal anatomy, results of VB accurately correlated with results of FB.

Thirteen (65%) patients had a total of 22 abnormal FB findings. VB detected 18 of these 22 abnormalities, including 13 of 13 obstructive lesions, 5 of 6 endoluminal masses, and 0 of 3 mucosal lesions (Figures 2 and 3). VB did not reveal 4 abnormalities identified during FB: a small peripheral endoluminal mass in 1 patient, benign mucosal inflammation after induction chemotherapy (which resolved within 2 weeks) in 1 patient, and the presence of blood in 2 patients (with no evidence of distal endobronchial lesions). However, VB revealed 7 obstructive lesions that were not visualized by means of FB because of size limitation of the bronchoscope (5 patients) and lesions beyond stenoses (2 patients, Table 1). Overall, the sensitivity of VB was 100% for obstructive lesions, 83% for endoluminal masses, 0% for mucosal lesions, and 82% for all abnormalities; the specificity of VB was 100%.

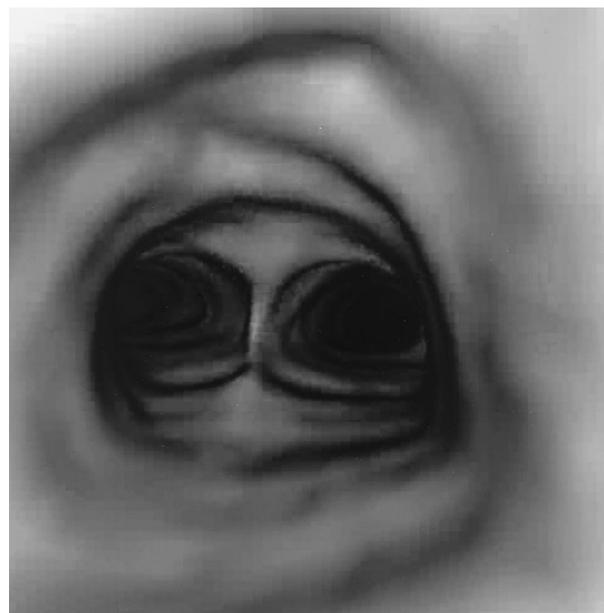


Figure 1. VB of normal anatomy. Viewpoint is in trachea above carina looking into right and left main stem bronchi.

Discussion

Standard preoperative diagnostic procedures in patients with malignant disease of the thorax include CT scanning of the chest and FB. Although these methods are highly reliable, both have technical limitations that may lead to inaccurate characterization of airway pathology. With advances in medical imaging, multislice helical CT scanners allow for 3-D reconstruction of tracheobronchial anatomy without an increase in radiation exposure.

Fleiter and colleagues¹¹ reported a series of patients with thoracic malignant disease who underwent VB with a double-detector CT unit and correlative FB. VB images were successfully created in 19 of 20 patients. In one patient a strong heart pulsation produced a motion artifact that prevented accurate reconstruction. Sites of high-grade stenosis were accurately detected with both techniques. VB allowed for accurate anatomic visualization beyond stenoses. Discrete malignant infiltration and extraluminal compression were not visualized by means of VB in 5 patients. Liewald and coworkers¹² evaluated 30 patients with lung cancer using VB and FB. Three-dimensional images were created in all patients. Thirteen obstructive lesions were seen equally well with VB and FB. VB delineated tracheobronchial anatomy beyond high-grade stenosis in 2 patients. However, mucosal lesions were not visualized by means of VB.¹² Rapp-Bernhardt and associates¹³ compared VB with FB in 21 patients with esophageal carcinoma infiltrating the tracheobronchial tree. These authors found no statistically significant difference in the location or grading of stenoses when comparing VB with FB. These same authors also

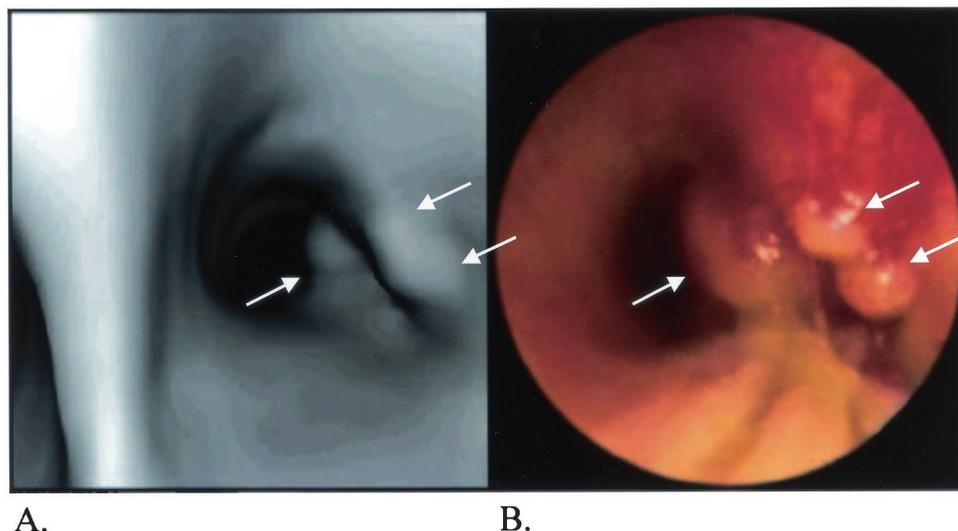


Figure 2. A, VB; B, FB. Endoluminal lesion in a 51-year-old man with metastatic renal cell carcinoma to the right hilum. The lesion consists of both large and small components in the right main stem bronchus (arrows) with complete obstruction of the right upper lobe bronchus. Note corresponding morphology at VB compared with at FB.

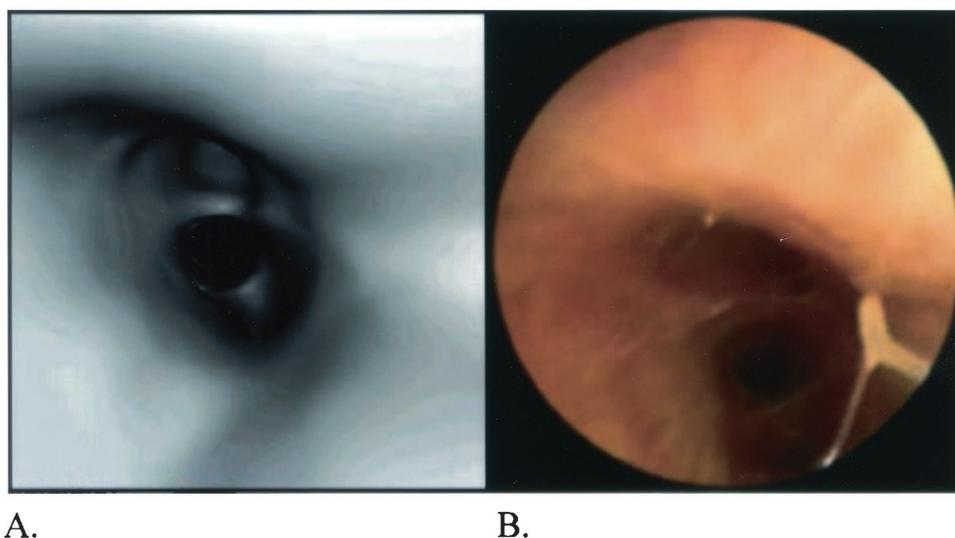


Figure 3. A, VB; B, FB. Normal anatomy beyond poststenotic area. Viewpoint is in right lower lobe bronchus looking toward right lower lobe segmental bronchi.

evaluated 18 patients with bronchogenic carcinoma. CT and VB were used to evaluate tracheobronchial stenoses that had been detected by means of FB. CT of the chest was found to have a sensitivity of 92.9% and a specificity of 100%. VB was found to have a sensitivity of 93.8% and a specificity of 99.7%.¹⁴

Our experience confirms that of previous investigators who have evaluated the feasibility and utility of VB in patients with primary or metastatic cancers involving the lungs and mediastinum. We noted that the sensitivity of VB

was 100% for obstructive stenotic lesions and that VB was effective for visualizing obstructive lesions in poststenotic sites. VB was also effective at detecting peripheral obstructive lesions beyond the size limits of the endoscope in 5 patients. Our study demonstrated that VB had an overall sensitivity of 82% for detecting any abnormality in the tracheobronchial tree. VB was not effective for detection of subtle mucosal abnormalities, including erythema and tissue friability. It is important to note that VB was able to detect 5 of 6 endoluminal lesions. This represents the first report

TABLE 1. Comparison of VB findings with FB findings in 20 patients with thoracic malignancy

Patient No.	Age (y)	Sex	Diagnosis	VB results	FB results
1	49	M	Sarcoma	O	NV
2	38	F	Melanoma	E	E
3	58	M	NSCLC	E, O , O , O	E, O , O , O
4	44	M	NSCLC	N	N
5	53	F	NSCLC	O	NV, <u>M</u>
6	40	F	Melanoma	O , O	O , O
7	44	F	RCC	E, O	E
8	66	M	Melanoma	N, N	<u>M</u> , <u>E</u>
9	69	M	NSCLC	N	N
10	40	F	NSCLC	O	NV
11	88	F	NSCLC	O , O	O , NV
12	44	M	RCC	N	<u>M</u>
13	58	M	RCC	O , O	NV, NV
14	73	M	NSCLC	N	N
15	56	M	RCC	E, O	E, O
16	50	M	RCC	O	O
17	64	M	RCC	N	N
18	59	M	SCLC	O	O
19	52	M	RCC	E, O	E, O
20	54	F	NSCLC	O , O , O	O , O , O

Letters in bold indicate lesions visualized by VB but not by FB. Underlined and italicized letters indicate lesions visualized by FB but not by VB. *O*, Obstructive lesion (defined as bronchial narrowing of >50%); *NV*, not visible because of technical issues; *E*, endoluminal mass (defined as a mass protruding into the lumen with <50% obstruction); *N*, within normal limits; *M*, mucosal lesion (defined as hemorrhage, erythema, abnormal color, or tissue friability).

that VB may be useful for reliably detecting endoluminal disease not advanced enough to cause atelectasis or distal pneumonitis detectable by conventional imaging techniques. Hence this modality may be helpful in guiding bronchoscopic evaluation of patients with intermittent hemoptysis.

There are several advantages of VB. The technique is noninvasive, and no additional radiation exposure occurs relative to standard CT scans of the chest. Commercial software allows for the seamless interactivity of 2-D and 3-D images, thereby enhancing the detection of extraluminal and intraluminal disease. Indeed, for every endoluminal position of the virtual endoscope, it is possible to refer to the corresponding cross-sectional images or to other multiplanar reconstructions to evaluate structures outside the bronchial lumen that may have clinical significance. Although this issue was not specifically addressed in the present study, interpretation of VB by radiologists, thoracic surgeons, and pulmonologists should be highly reproducible and reliable, given the objectivity of the imaging techniques and the software used for data analysis. As such, VB may prove to be a highly effective, objective, and reproducible means of assessing treatment response in patients enrolled in clinical protocols. Furthermore, because VB provides accurate information regarding the length of obstructing lesions and the anatomy distal to an obstruction, this modality may prove to be useful for assessing the feasibility of anatomic segmentectomy, as well as that of endobronchial

laser or photodynamic therapy, in thoracic oncology patients.

One limitation of VB pertains to the inability to evaluate the mucosal surface of the tracheobronchial tree. Although form can be detected, mucosal color, irregularity, or friability cannot be assessed. Hence at present VB may not be a reliable modality for the detection of premalignant tracheobronchial lesions. However, with continued refinements in acquisition capabilities and image display techniques, such as high-resolution ultrasonography, magnetic resonance imaging, or positron emission tomography scanning, it may soon be possible to evaluate the mucosal surface by means of VB. If this occurs, VB may prove to be an efficient modality for early detection of airway malignant tumors and for assessing response in patients enrolled in chemoprevention protocols. However, because VB does not enable acquisition of tissue samples for histologic or microbiologic analysis, this modality will never completely replace FB for evaluation of lesions in the respiratory tract.

As technology advances, we must justify clinical indications for new and potentially expensive methods. Our current study indicates that VB is an accurate and noninvasive method for evaluating obstructions, endoluminal masses, and poststenotic areas within the airway. Although FB remains the best modality for examining airway patency and mucosal lesions, VB yields additional information regarding bronchial anatomy that may prove useful in the management of patients with malignant disease of the thorax.

We thank the Radiology technicians for patient care and scanning, Betty Wise for data management, and Sharyn A. Childs, Surgery Branch, NCI, for manuscript preparation.

References

1. Rubin GD, Beaulieu CF, Argio V, Ringl H, Norbash AM, Feller JF, et al. Perspective volume rendering of CT and MR images: applications for endoscopic imaging. *Radiology*. 1996;194:871-7.
2. Shepard JA. The bronchi: an imaging perspective. *J Thorac Imaging*. 1995;10:236-54.
3. Shure D. Fiberoptic bronchoscopy: diagnostic applications. *Clin Chest Med*. 1987;8:1-13.
4. Colice GL, Chappel GJ, Frenchman SM, Solomon DA. Comparison of computerized tomography with fiberoptic bronchoscopy in identifying endobronchial abnormalities in patients with known or suspected lung cancer. *Am Rev Respir Dis*. 1985;131:397-400.
5. Naidich DP, Lee JJ, Garay SM, McCauley DI, Aranda CP, Boyd AD. Comparison of CT and fiberoptic bronchoscopy in the evaluation of bronchial disease. *AJR Am J Roentgenol*. 1987;148:1-7.
6. Harponik EF, Aquino SL, Vining DJ. Virtual bronchoscopy. *Clin Chest Med*. 1999;20:201-17.
7. Colletti PM, Beck S, Howell WD Jr, Radin DR, Yamauchi DM, Ralls PW, et al. Computed tomography in endobronchial neoplasms. *Comput Med Imaging Graph*. 1990;14:257-62.
8. Aquino SL, Vining DJ. Virtual bronchoscopy. *Clin Chest Med*. 1999; 20:725-30.
9. Pue CA, Pacht ER. Complications of fiberoptic bronchoscopy at a university hospital. *Chest*. 1995;107:430-2.
10. Summers RM, Sneller MC, Langford CA, Shelhamer JH, Wood BJ. Improved virtual bronchoscopy using a multi-slice helical CT scanner. In: Chen C-T, Clough AV, editors. *Medical imaging 2000: physiology and function from multidimensional images*. Proceedings of SPIE Press. Vol. 3978. San Diego: 2000. p. 117-21.
11. Fleiter T, Merkle EM, Aschoff AJ, Lang G, Stein M, Gorich J, et al. Comparison of real-time virtual and fiberoptic bronchoscopy in patients with bronchial carcinoma: opportunities and limitations. *AJR Am J Roentgenol*. 1997;169:1591-5.
12. Liewald F, Lang G, Fleiter TH, Sokiranski R, Halter G, Orend KH. Comparison of virtual and fiberoptic bronchoscopy. *Thorac Cardiovasc Surg*. 1998;46:361-4.
13. Rapp-Bernhardt U, Welte T, Budinger M, Bernhardt TM. Comparison of three-dimensional virtual endoscopy with bronchoscopy in patients with oesophageal carcinoma infiltrating the tracheobronchial tree. *Br J Radiol*. 1998;71:1271-8.
14. Rapp-Bernhardt U, Welte T, Doehring W, Kropf S, Bernhardt TM. Diagnostic potential of virtual bronchoscopy: advantages in comparison with axial CT slices, MPR, and MIP? *Eur Radiol*. 2000; 10:981-8.