

Comparative Evaluation of Super High-Resolution CT Scan and Virtual Bronchoscopy for the Detection of Tracheobronchial Malignancies*

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Objectives: Novel imaging modalities are currently available for the noninvasive evaluation of the tracheobronchial tree. This study was undertaken to compare the diagnostic potentials of conventional CT scanning, super high-resolution CT (SHR-CT) scanning, and virtual bronchoscopy (VB) directly with fiberoptic bronchoscopy (FB) for the detection of tracheobronchial neoplasms.

Design: Prospective observer study, in which 44 consecutive patients with thoracic malignancies were evaluated using several diagnostic imaging modalities. Images of the thorax were interpreted by individuals blind to the results of FB for the detection of endoluminal, obstructive, or mucosal lesions.

Measurements and results: Image acquisition and simulation of the tracheobronchial anatomy were created successfully in all patients. Thirty-two patients who underwent both SHR-CT scanning and VB had correlative FBs within 1 month. In all nine patients who had a normal anatomy, SHR-CT scanning and VB accurately correlated with the FB findings. However, CT scanning demonstrated two false-positive obstructive lesions in one patient. Twenty-three patients had a total of 35 abnormal FB findings. The sensitivities of SHR-CT scanning and VB for the detection of endoluminal, obstructive, and mucosal lesions were 90%, 100%, and 16%, respectively. The overall sensitivities and specificities of SHR-CT scanning and VB were 83% and 100%, respectively. In contrast, CT scanning had sensitivities of 50%, 72%, and 0% for the detection of endoluminal, obstructive, and mucosal lesions with an overall sensitivity and specificity of 59%, and 85%, respectively. There was no case in which conventional CT scanning was better at detecting lesions than either SHR-CT scanning or VB.

Conclusions: SHR-CT scanning and VB are accurate, noninvasive methods for identifying obstructions and endoluminal lesions within the respiratory tract. Thus, these novel imaging techniques are valuable as complementary modalities to FB, providing information that is useful for the detection and management of airway malignancies. (CHEST 2003; 124:1834-1840)

Key words: bronchoscopy; cancer; CT; endoscopy; imaging; thoracic; virtual

Abbreviations: 3-D = three-dimensional; FB = fiberoptic bronchoscopy; FN = false negative; FP = false positive; SHR-CT = super high-resolution CT; TN = true negative; TP = true positive; VB = virtual bronchoscopy

Neoplasms involving the respiratory system cause significant morbidity and mortality. Primary lung cancers account for approximately 160,000 deaths annually in the United States.¹ In addition, nearly one third of all patients with neoplasms of nonpulmonary origin develop life-threatening pulmonary metastases.² Frequently, patients with primary or metastatic cancers involving the respiratory tract have partial or complete bronchial obstructions secondary to endoluminal tumors or extrinsic compression. Noninvasive, reproducible, and objective methods for sequentially evaluating these abnormalities may prove useful for directing therapy and assessing the treatment response in these individuals.

Patients with suspected tracheobronchial lesions

typically undergo diagnostic evaluation consisting of conventional CT scanning and fiberoptic bronchoscopy (FB).³ Conventional two-dimensional cross-sectional CT images of the chest have a reported sensitivity and specificity of 60 to 100% for the detection of obstructive lesions in the respiratory tract.⁴⁻⁶ The limitations of the accuracy of conventional CT scans include suboptimal scanning techniques, inappropriately thick slices, and artifacts between sections.⁷ Currently, FB remains the best modality for the evaluation of endoluminal and mucosal lesions in the respiratory tract. However, this imaging modality frequently provides little information concerning the extent of extraluminal disease or airway patency distal to high-grade bronchial stenoses.⁸

Novel imaging modalities, such as super high-resolution CT (SHR-CT) scanning and virtual bronchoscopy (VB), are currently available for the non-invasive evaluation of tracheobronchial neoplasms. SHR-CT scanning involves the acquisition of several hundred images of the chest using a multislice helical CT scanner. Indeed, conventional CT scans may acquire only 20 to 50 images of the entire chest. High-resolution CT scans may image 50 contiguous cuts through a specific area of concern within the thorax. SHR-CT scans acquire 200 to 300 contiguous 1.25-mm cross-sections of the entire thorax. The radiation dose associated with SHR-CT scans is the same or slightly less than that of a conventional CT scan.

VB (also known as CT bronchography) employs three-dimensional (3-D) reconstruction of high-resolution helical CT images of the tracheobronchial tree.⁹ The contrast between the airway lumen and wall enables the generation of a 3-D anatomic model of tracheobronchial anatomy that provides views similar to those obtained during FB.⁶ Furthermore, VB enables the visualization of the tracheobronchial anatomy from multiple angles, thereby facilitating the analysis of bronchial lesions beyond the limits of FB and the assessment of airway patency distal to high-grade obstructions.⁸

Currently, limited information is available regarding the utility of SHR-CT scanning and VB relative to conventional diagnostic modalities of tracheobronchial lesions in oncology patients. Following an initial preliminary study to determine the feasibility of VB, the current study was undertaken to evaluate directly the diagnostic potential of conventional CT, SHR-CT scanning, and VB scans relative to FB for

the detection of tracheobronchial lesions. Thus, this study explores the utility of SHR-CT scanning and VB to evaluate the tracheobronchial anatomy with respect to the diagnosis and selection of patients for resection, dilation, and laser, or photodynamic ablation of high-grade stenoses, as well as enabling the sequential evaluation of treatment response in patients with tracheobronchial neoplasms. Indeed, a practical algorithm employing noninvasive techniques for patients who are at high risk for airway pathology may have important clinical benefits.

MATERIALS AND METHODS

Patient Population

Forty-four consecutive patients with thoracic malignancies were prospectively enrolled on an institutional review board-approved protocol evaluating novel imaging modalities between November 1999 and June 2001. The inclusion criteria included the presence of an intrathoracic malignancy and the willingness to undergo novel diagnostic imaging of the chest. After SHR-CT scans and VB images were successfully acquired in the first 10 patients, an additional 34 individuals were accrued with the intent of obtaining correlative FBs within 1 month of the noninvasive imaging. Two of these 34 patients were excluded from analysis due to a time delay between imaging and FB. Of the 32 patients who underwent correlative FBs, 25 (78%) had undergone standard conventional CT scans in addition to novel diagnostic imaging. Twenty of these subjects formed the basis of a preliminary evaluation of the VB technique.⁹

The mean (\pm SD) age of all patients was 52 ± 12.2 years (median, 53 years; range, 29 to 88 years). Thirty-two patients (73%) were men (mean age, 52 ± 11.3 years; median age, 54 years; age range, 29 to 73 years), 12 patients (27%) were women (mean age, 52 ± 14.8 years; median age, 51 years; age range, 38 to 88 years). Histologic diagnoses included non-small cell lung cancer (16 patients), small cell lung cancer (3 patients), metastatic renal cell cancer (12 patients), metastatic melanoma (7 patients), metastatic thyroid cancer (2 patients), sarcoma (1 patient), carcinoid (1 patient), teratoma (1 patient), and esophageal cancer (1 patient).

Procedures

For each FB, visualization and interpretation of the tracheobronchial tree were achieved under the direction of the attending thoracic surgeons (DSS and DMN) who were blinded to the radiologist's interpretation of the imaging modalities. FB findings, which were entered into the database, included the presence or absence of obstructive lesions (*ie*, a bronchial narrowing of $> 50\%$), endoluminal masses (*ie*, a mass protruding into the lumen with $< 50\%$ occlusion), or mucosal lesions (*ie*, hemorrhage, erythema, or tissue friability).

For each conventional CT scan, 20 to 50 images of the thorax were obtained, according to the standard of care. The technique was 5–10 collimation, HQ mode (*ie*, helical pitch, 1 to 3, 11.25 mm table motion per rotation, 120 kVp, 280 mA, 0.8 s tube rotation) and nonoverlapping reconstructions with a section interval of 5 to 10 mm in one held breath using a multislice helical CT scanner.

For each SHR-CT scan, 200 to 300 contiguous 1.25-mm images of the thorax were obtained in one or two 17-s breathhold maneuvers (LightSpeed QXI multislice helical CT scanner;

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Dr. Summers has patents pending or has been awarded patents in the subject area of this article.

This research was supported by a Cancer Research Foundation of America, Young Investigator Travel Grant Award, and by the intramural research programs of the Diagnostic Radiology Department, National Institutes of Health, Bethesda, MD, and was a recipient of the Cecile Lehman Research Finalist Award at Chest 2002.

Presented in part at Chest 2002, San Diego, CA, November 5, 2002.

Supplemental movie materials are available online at <http://www.chestjournal.org/cgi/content/full/124/5/1834/DC1>.

Manuscript received February 10, 2003; revision accepted May 19, 2003.

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General Electric; Milwaukee, WI).¹⁰ The technique was 1.25 collimation, HS mode (helical pitch, 6, 7.5 mm table motion per rotation, 120 kVp, 100 mA, and 0.8 s 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. The calculated radiation dose with this technique was the same or slightly less than that of a conventional thoracic CT scan.⁹

VB images were converted to 3-D endoscopic views using commercial software (Navigator; General Electric) on a workstation (Advantage Windows; General Electric). The VB was derived from the SHR-CT axial images of the thorax with no further radiation exposure necessary. The radiologist (RMS), who was blinded to the findings of the other modalities, first placed the viewpoint in the proximal trachea. Retrograde inspection of the subglottic area of the trachea was performed. Subsequent analysis consisted of sequential antegrade inspection of the trachea, mainstem bronchi, lobar bronchi, and segmental bronchi. Little additional time was needed to perform and interpret the images. For the purpose of this study, the interpretation of the VB reconstruction was kept to < 10 min for all cases.

All detected abnormalities in the tracheobronchial tree were

recorded in the database. All SHR-CT and VB scans and FBs were interpreted in a blinded manner. The presence or absence of obstructive lesions (*ie*, bronchial narrowing of > 50%), endoluminal masses (*ie*, a mass protruding into the lumen with < 50% occlusion), or mucosal lesions (*ie*, hemorrhage, erythema, or tissue friability) were recorded. In addition, the anatomic locations of the detected lesions were noted.

Statistical Analysis

The results of the imaging modalities were compared directly with actual FB findings at the same anatomic sites. A true-positive (TP) result occurred when the finding of the imaging modality equaled that of FB, when FB visualized a lesion. A true-negative (TN) result occurred when the finding of the imaging modality equaled that of FB, when the FB finding was within normal limits. A false-negative (FN) result occurred when an imaging modality failed to detect a lesion that had been documented during FB. A false-positive (FP) result occurred when an imaging modality demonstrated an abnormality but FB had revealed the area to be normal. The overall sensitivity (*ie*, TP/[TP + FN]) and specificity (*ie*, TN/[TN + FP]) of each imaging modality was determined. A subanalysis was performed for obstructive lesions, endoluminal masses, and mucosal lesions.

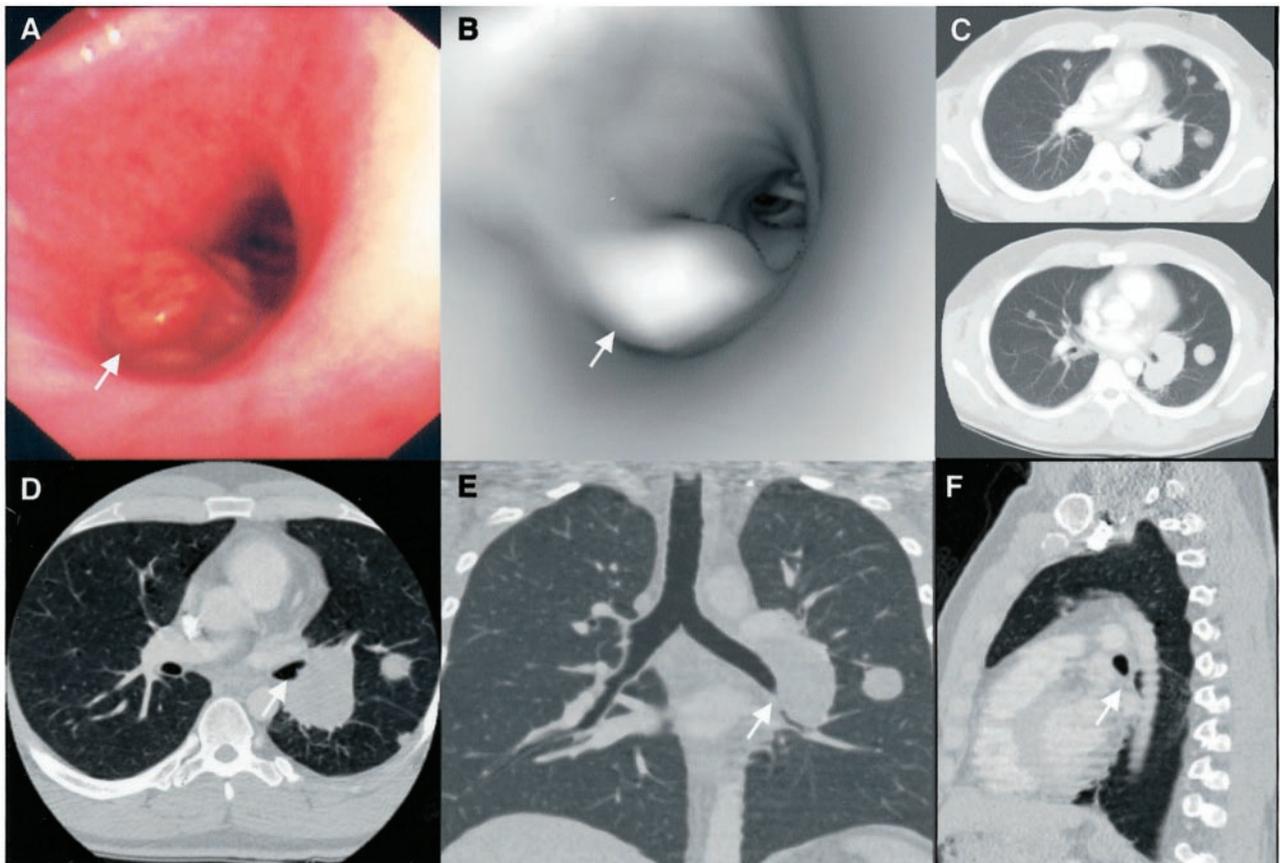


FIGURE 1. Endoluminal lesion obstructing the superior segment of the left lower lobe in a 30-year-old gentleman in whom metastatic melanoma has been diagnosed. The visualization of this lesion (white arrow) took place by FB (*top left*, A), VB (*top middle*, B), and SHR-CT scan (*bottom left*, D: axial section; *bottom middle*, E: coronal section; and *bottom right*, F: sagittal section). However, this lesion was not seen by consecutive conventional CT sections (*top right*, C).

RESULTS

Image Acquisition

Image acquisition and anatomic simulation of the tracheobronchial tree were successful in all patients. No adverse events were noted in the study group. There were no respiratory or cardiac motion artifacts that precluded image reconstruction.

SHR-CT and VB

Of the 32 patients who underwent correlative FBs, 9 (28%) had normal examination findings. In all patients with normal anatomy, the results of SHR-CT scans and VB accurately correlated with those of FBs (Web movie 1; available online at <http://www.chestjournal.org/cgi/content/full/124/5/1834/DC1>).

In the remaining 23 patients, a total of 35 abnormal FB findings were detected (Figs 1 and 2). With respect to the location of FB findings, there were 20 lesions (57%) in the right lung, 12 lesions (34%) in the left lung, and 3 lesions (9%) in the trachea/carina. There appeared to be some clustering of lesions (13 of 35 lesions [37%]) at the right mainstem and right upper lobe. Of these 13 lesions, 9 were obstructive, 2 were endoluminal, and 2 were mucosal. Lesions beyond the proximal segmental bronchi were difficult to visualize by FB due to the size of the endoscope (Fig 3).

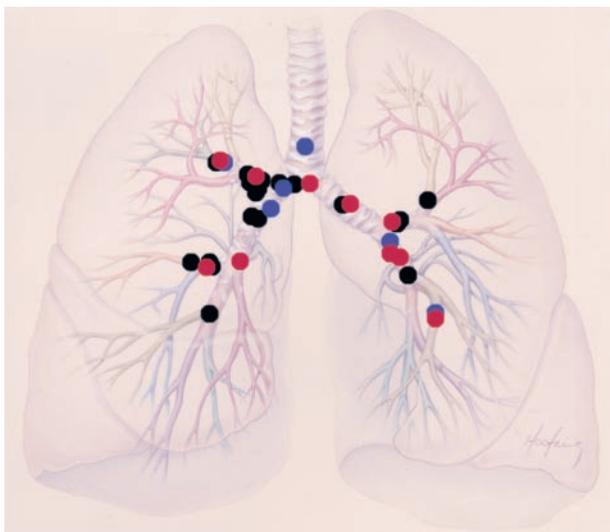


FIGURE 2. Location of lesions by FB. Each circle represents the anatomic location of a lesion, as follows: the black circle (19 lesions) represents an obstructive lesion (*ie*, a bronchial narrowing of > 50%); the red circle (10 lesions) represents an endoluminal mass (*ie*, a mass protruding into the lumen with < 50% obstruction); and the blue circle ($n = 6$) represents a mucosal lesion (*ie*, hemorrhage, erythema, abnormal color, or tissue friability).

VBs and SHR-CT scans exhibited an identical pattern of detection for these lesions (Fig 1) [Web movies 2 and 3; available online at <http://www.chestjournal.org/cgi/content/full/124/5/1834/DC1>]. These modalities detected 29 of these abnormalities (83%) [19 of 19 obstructive lesions; 9 of 10 endoluminal masses; and 1 of 6 mucosal lesions]. The sensitivities of SHR-CT scans and VBs were 100% for obstructive lesions, 90% for endoluminal masses, 17% for mucosal lesions, and 83% for all abnormalities. The specificities of SHR-CT scanning and VB were 100% (Table 1).

Six FN lesions were identified by FBs and were not detected by SHR-CT scans or VBs (Fig 3, *top left, A*, and *top middle, B*). These included a small peripheral endoluminal mass in one patient that was located in the left lower lobe, mucosal inflammation in two patients, and the presence of blood with no evidence of distal endobronchial lesions in three patients. With respect to these three cases of hemoptysis, it is possible that bleeding was intermittent and thus not present on the day of imaging, but was present on the day of FB.

On the other hand, SHR-CT scans revealed 10 additional lesions, and VB demonstrated 11 additional lesions that were not evaluable by FB (Fig 3, *bottom left, D*, and *bottom middle, E*) due to the size limitation of the bronchoscope (9 cases) or to the location distal to high-grade stenoses (2 cases). Because many patients went on to undergo resection of a lesion for palliation or cure, pathologic correlation was attainable in nine cases. Of these nine cases, six obstructive lesions (67%) that had not been detected by FB but were visualized by SHR-CT scans and VBs were confirmed to be positive by pathology. With respect to the location of these pathology-proven distal lesions, two were located in the right lower lobe, two were located in the left lower lobe, one was located in the right middle lobe, and one was located in the left upper lobe (Fig 3, *bottom left, D*, and *bottom middle, E*).

Conventional CT Scanning

Of the 32 patients who underwent correlative FBs, 25 (78%) obtained conventional CT scans in addition to SHR-CT scan and VBs. Seven patients (28%) had normal examination findings by FB. The results of conventional CT scans correlated with those of FBs in six of these patients (specificity, 85%). Conventional CT scans demonstrated two FP obstructive lesions in one patient (Table 1).

Eighteen patients (72%) had a total of 29 abnormal FB findings. Conventional CT scans detected only 17 of these 29 abnormalities, including 13 of 18 obstructive lesions, 4 of 8 endoluminal masses, and 0

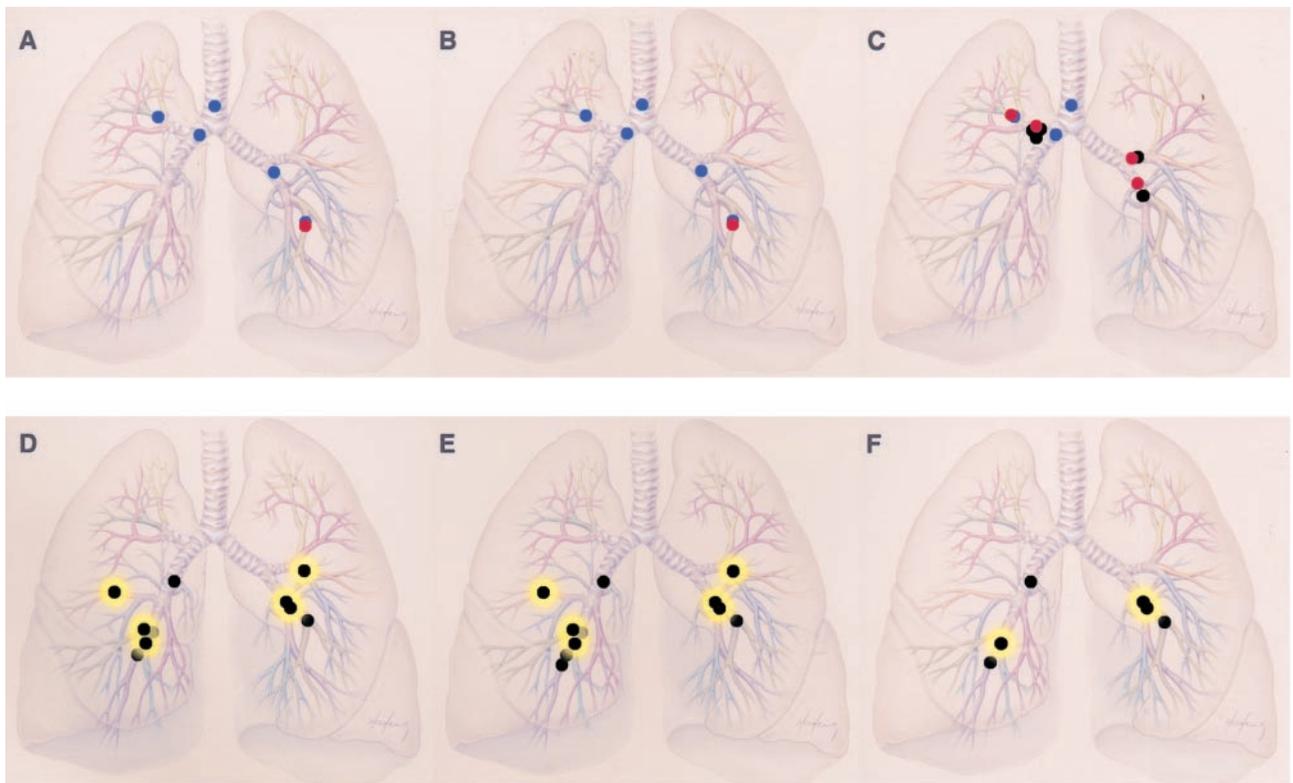


FIGURE 3. Location of FN lesions determined by SHR-CT scan (top left, A), VB (top middle, B), and CT scan (top right, C). Location of additional distal lesions not reachable by FB but nevertheless visualized by SHR-CT scan (bottom left, D), VB (bottom middle, E), and CT scan (bottom right, F). A black circle represents an obstructive lesion, a red circle represents an endoluminal lesion, and a blue circle represents a mucosal lesion. Lesions highlighted in yellow were confirmed to be positive by pathology.

of 3 mucosal lesions. In contrast to SHR-CT scans and VBs, the sensitivity of conventional CT scanning was 72% for obstructive lesions, 50% for endoluminal masses, 0% for mucosal lesions, and 59% overall (Table 1). Of the 12 FN lesions identified by FB and not detected by conventional CT scanning, only 3 abnormalities were not visualized by SHR-CT scanning and VB. This was due to the fact that conventional CT scanning was not obtained in those patients, and not because conventional CT scans could visualize the lesions missed by SHR-CT scans and/or VBs. Indeed, there was no case in which conventional CT scanning improved on the findings of either SHR-CT scans or VBs (Fig 3).

As with SHR-CT scans and VBs, additional obstructive lesions were appreciated by CT scans that were not visualized by FB. Three of six of these obstructive lesions (50%) were confirmed to be positive by histologic evaluation. The locations of these lesions were in the left lower lobe (two lesions) and the right lower lobe (one lesion) [Fig 3, bottom right, F].

DISCUSSION

Rapid technological advances in image processing have permitted the simulation of endoscopic proce-

Table 1—Comparison of Imaging Modalities for Detection of Tracheobronchial Malignancies

	Sensitivity				Specificity (Patient TN)
	Endoluminal	Obstructive	Mucosal	Overall	
CT scan	50% (4/8)	72% (13/18)	0% (0/3)	59% (17/29)	85% (6/7)
SHR-CT scan	90% (9/10)	100% (19/19)	16% (1/6)	83% (29/35)	100% (9/9)
VB	90% (9/10)	100% (19/19)	16% (1/6)	83% (29/35)	100% (9/9)

Table 2—Summary of Literature for VB Detection of Tracheobronchial Malignancies

Study/year	No.	Diagnosis	Results	Sensitivity	Specificity
Fleiter et al ¹² /1997	20	Thoracic malignancies	Images successfully created in 19/20 patients; high-grade stenoses accurately detected; discrete malignant infiltration and extraluminal compression not visualized in five patients	Not reported	Not reported
Liewald et al ¹³ /1998	30	Lung cancer	Thirteen obstructive lesions seen equally well by VB and FB; VB visualized anatomy beyond high-grade stenosis in two patients; mucosal lesions not visualized	Not reported	Not reported
Rapp-Bernhardt et al ¹⁴ /1998	21	Esophageal carcinoma	No statistically significant difference in the location or grading of stenoses comparing VB with FB	Not reported	Not reported
Rapp-Bernhardt et al ¹⁵ /2000	18	Bronchogenic carcinoma	CT scan and VB used to evaluate tracheobronchial stenoses that had been detected by FB	CT scan, 93%; VB, 94%	CT scan, 100%; VB, 99.7%
Finkelstein et al ⁹ /2002	20	Thoracic malignancies	Images successfully created in all patients; high-grade stenosis and endoluminal lesions accurately detected; difficulty detecting subtle mucosal lesions	VB, 82%	VB, 100%

dures using sophisticated, but relatively inexpensive, computer workstations. In thoracic imaging, the trachea, mainstem bronchi, and many of the segmental bronchi can be readily visualized by new diagnostic modalities.¹¹ Although standard methodologies are readily available, their limitations may lead to an inaccurate characterization of airway pathology.

Preliminary studies reported by Finkelstein et al,⁹ Fleiter et al,¹² Liewald et al,¹³ Rapp-Bernhardt and colleagues,^{14,15} and Seemann et al¹⁶ have demonstrated the feasibility and utility of VB in patients with primary or metastatic cancers involving the lungs and mediastinum (Table 2). However, limited information is available comparing SHR-CT scanning to other imaging modalities in this clinical context. Our current study was performed to directly compare in a prospective manner the diagnostic potentials of standard CT scanning, SHR-CT scanning, and VB relative to FB for the detection of tracheobronchial neoplasms. We observed that SHR-CT scanning and VB are excellent imaging modalities with sensitivities of 100% for the detection of obstructive stenotic lesions. Furthermore, these modalities are highly effective for assessing airway patency distal to high-grade stenoses and for identifying lesions in subsegmental bronchi. Therefore, SHR-CT scanning and VB had overall sensitivities of 83% for the detection of any abnormality in the tracheobronchial tree. However, these techniques are presently not effective for the detection of subtle mucosal abnormalities such as erythema or early sessile lesions. SHR-CT scans and VB may not

be appropriate for identifying premalignant lesions in the respiratory tract. Nevertheless, technologies such as fiberoptic confocal microscopy, optical CT scanning, high-resolution ultrasonography, and positron emission tomography may complement the detection of these lesions in the near future.¹¹

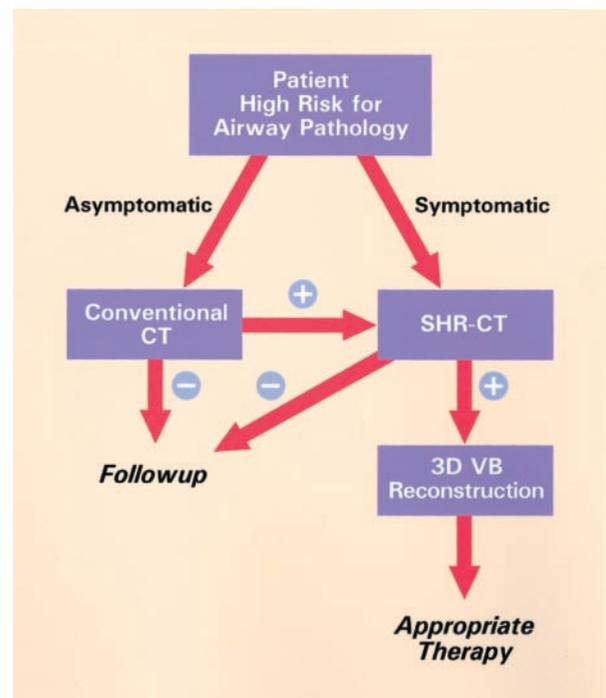


FIGURE 4. Algorithm utilizing CT scanning, SHR-CT scanning, and VB for patients who are at high risk for airway pathology.

Although SHR-CT scanning and VB presently cannot be utilized for the identification of preneoplastic lesions, these imaging modalities have a tremendous potential for clinical application. SHR-CT scanning and VB are noninvasive. The radiation exposure associated with these scans is comparable if not less than that of conventional CT scans of the chest. SHR-CT scanning and VB provide unique opportunities to assess extraluminal and intraluminal airway pathology by allowing visualization from multiple angles. Thus, highly effective, objective, and reproducible investigation of poststenotic regions beyond the reach of endoscopy with either SHR-CT scanning or VB is possible. As these modalities provide accurate information regarding tracheobronchial anatomy, SHR-CT scanning and VB may become invaluable for assessing the feasibility of resections as well as laser or photodynamic ablations of airway stenoses.

Our data indicate that SHR-CT scanning and VB are powerful, objective, and reproducible imaging modalities that can complement FB for the evaluation of tracheobronchial malignancies. As such, we propose the following algorithm for patients who are at high risk for airway pathology (Fig 4). Asymptomatic patients should undergo screening using conventional chest CT scans. Symptomatic individuals should undergo SHR-CT scans. If abnormalities are detected, VB can be used to further define and simulate airway anatomy before FB or surgery. This algorithm may limit the number of unnecessary SHR-CT scans and 3-D VB reconstructions while optimizing the decisions regarding appropriate therapeutic interventions with curative or palliative intent. Follow-up SHR-CT scans and VB would enable the serial evaluation of the treatment response in these individuals.

Emerging technologies often precede advances in patient care. As clinicians, we must justify the indications for novel, potentially expensive medical procedures. This study demonstrates that SHR-CT scanning and VB are accurate, noninvasive methods for evaluating obstructions, endoluminal masses, and poststenotic areas within the airway. These novel imaging modalities provide information regarding bronchial and peribronchial anatomy that may prove beneficial in the management of patients with thoracic malignancies.

ACKNOWLEDGMENT: The authors acknowledge the Radiology Department technicians for patient care and scanning, Betty

Wise for data management, and Donald Bliss and Alan Hoofring for original medical illustration.

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