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Real-Time Electromagnetic Navigation Bronchoscopy to Peripheral Lung Lesions Using Overlaid CT Images*

The First Human Study

Yehuda Schwarz, MD; Joel Greif, MD; Heinrich D. Becker, MD; Armin Ernst, MD; and Atul Mehta, MD

Study objectives: To characterize the feasibility, accuracy, and safety of the superDimension/Bronchus system (SDBS) [superDimension, Ltd; Hertzliya, Israel] in navigating to previously unreachable peripheral lung lesions and obtaining biopsy specimens.

Design: Open-label, prospective, controlled clinical study.

Setting: Pulmonary institute of a university-affiliated municipal hospital.

Patients: Thirteen adult candidates for nonemergency bronchoscopy who gave informed consent to participate.

Interventions: The patients underwent flexible bronchoscopy using the SDBS, which is based on real-time CT-guided electromagnetic navigation and is capable of reaching peripheral lung masses beyond the reach of the bronchoscope. A position sensor was used to navigate to and sample the various target lesions for biopsy.

Measurements and results: Three-dimensional chest CT was followed by SDBS methodology for marking anatomic landmarks and the target lesion on a virtual bronchoscopy screen and for sampling the lesion. The SDBS assisted in obtaining positive biopsy diagnoses in 9 of 13 cases (69%), with an average navigation accuracy of 5.7 mm. There were no SDBS-related adverse events.

Conclusions: The SDBS is safe and effective in navigating to peripheral lung lesions located beyond the optic limits of a standard flexible bronchoscope. (CHEST 2006; 129:988–994)

Key words: navigation bronchoscopy; peripheral lesion

Abbreviations: 3D = three dimensional; EWC = extended working channel; FFB = flexible fiberoptic bronchoscopy; FNA = fine-needle aspiration; LUL = left upper lobe; NSCLC = non-small cell lung carcinoma; RML = right middle lobe; RLL = right lower lobe; RUL = right upper lobe; SDBS = superDimension/Bronchus system; TBB = transbronchial biopsy

The flexible bronchoscope is used primarily to examine anatomic and pathologic structures inside the airways or to reach various lung lesions and acquire tissue samples for diagnosis. The instrument is also used to treat central airway obstructions by removing or cauterizing them with a laser. Standard flexible bronchoscopes, however, cannot reach most lung target lesions; more than two thirds of these masses are located at peripheral locations not accessible to the bronchoscope due to its diameter relative...
to the constantly narrowing branches of the bronchial tree. In a retrospective analysis, Hoffmann and Dienemann showed that almost 50% of the sampled lesions were benign. Radke et al reported that the number of benign lesions detected in screening programs exceeded 90%. Insofar as benign nodules do not require surgical resection, the ability to obtain specimens of isolated peripheral lung lesions via bronchoscopic technology could obviate the complications of more invasive biopsy procedures and inevitably reduce the number of unnecessary surgeries by ruling out malignancy.

The final and most critical stages of the advance of a bronchoscope through the bronchial tree to the lesion are performed in an essentially “blind” manner. The bronchoscope usually becomes wedged at a segment of the tree, and the endoscopic tools, such as diagnostic brushes or forceps, are pushed out toward the targeted lung area, guided by fluoroscopy. The fluoroscopic images, however, can neither provide depth perception nor can they depict the intricate anatomy of the bronchial tree. Determining lung opacity is also often problematic with standard bronchoscopic evaluations. These shortcomings establish the need for a tool that can provide navigational information with real-time positioning of the tip of the forceps as a guide to help the bronchoscopist grasp an endobronchially invisible peripheral lesion. Such a tool would facilitate diagnosis and obviate further interventional diagnostic procedures when that lesion is confirmed as being benign.

One of new technologies that allows an approach to the peripheral lung masses is electromagnetic navigation based on virtual bronchoscopy and real-time three-dimensional (3D) CT images. This technology was incorporated in the superDimension/Bronchus system (superDimension; Hertzliya, Israel) and has been shown to be capable of reaching peripheral lung masses beyond the reach of the standard bronchoscope in an animal model. The aim of the current study was to determine the feasibility, accuracy, and safety of the SDBS to navigate to peripheral lung lesions in humans and to examine its capability of increasing the diagnostic yield of the transbronchial biopsies (TBBs) in those patients.

Materials and Methods

Fifteen subjects (7 men and 8 women; age range, 26 to 81 years) were originally enrolled into an open-label, prospective, single-group, controlled clinical study from June 2003 to May 2004. The study was approved by the Tel Aviv Sourasky Medical Center Helsinki Committee, and informed consent was obtained from all the subjects prior to bronchoscopy. Bronchoscopy was performed on an outpatient basis under conscious sedation with midazolam or propofol. Patient selection was based on nonendoscopically visible lesions, regardless of the lesion size or lobe location, since the main objective of this study was to evaluate the feasibility of the SDBS to visualize these masses.

Electromagnetic Navigation System

The electromagnetic navigation system is an image-guided localization device that assists the endobronchial accessories (forceps, brush, needle) in reaching the desired areas of the lung. A detailed description of this system has appears in an earlier publication.

Electromagnetic Location Board: The system uses low-frequency electromagnetic waves that are emitted from a 1-cm-thick, 47 × 56-cm electromagnetic board that is placed under the cephalad end of the mattress of the bronchoscopy table (Fig 1).

Sensor Probe (Locatable Guide): A sensor probe (diameter, 1 mm; length, 8 mm) mounted on the tip of a flexible metal cable constitutes the main assembly of the device. Once placed within the electromagnetic field, its position in the X, Y, and Z planes as well as orientation (roll, pitch, and yaw movements) is captured by the SDBS. This information is then displayed on a monitor in real time at a rate of 166 frames per second, superimposed on previously acquired CT images. The locatable guide also has an added feature that allows its distal section to be steered in a complete circle (360°). Four separate wires control the movement of the probe from the proximal end of the device using a rotating knob and a control lever. The locatable guide also provides a socket for connecting a wire, which relays the information from the sensor to the computer. The probe, which is fully retractable, is incorporated into the tip of a flexible
catheter 130 cm in length and 1.9 mm in diameter, and serves as an extended working channel (EWC) for easy access for bronchoscopic accessories once placed at the targeted area guided by the navigation system (Fig 2).

**Computer Software and Monitor:** The bronchoscopist is able to view the reconstructed 3D CT images in coronal, sagittal, and axial views together with superimposed graphic information depicting the position of the sensor probe as well as the preidentified anatomic landmarks and the position of the target lesion. The monitor also displays the latter in a “tip-view” orientation from the sensor probe (Fig 3).

**System Application**

Maneuvering the probe to reach the lesion as displayed on the CT scan images requires that it be in alignment with the subject’s anatomy prior to the bronchoscopic procedure. This was carried out by the following steps:

**Radiologic Mapping (Planning):** The digitized information from the CT scan was downloaded into the SDBS software in digital imaging and communications in medicine format. This information was then used to reconstruct axial, coronal, and sagittal views of the chest and virtual images of the bronchial tree. Between five and seven anatomic landmarks were marked as coordinates on the corresponding CT as well as on the virtual bronchoscopy image. In addition, the target lesion was identified and marked at its center in a similar fashion (Fig 4).

**Endobronchial Mapping (Registration):** Bronchoscopy was performed under conscious sedation. Once the subject was placed on the examination table, three reference sensors were fixed on the subject’s thorax for compensation for respiratory movements and possible movement on the table. A flexible bronchoscope (Olympus BF 1T40; Olympus; Tokyo, Japan) was inserted into the trachea through the nasal approach. The locatable guide was inserted via the working channel of the flexible bronchoscope. The same “radiologic landmarks” selected on the virtual bronchoscopy image were identified in vivo and touched with the probe to register their location in the software for establishing alignment. Registration of all the above information into the computer software automatically synthesized a navigation scheme to approach the lesion with precision (Fig 5).

**Real-time Navigation:** Following successful mapping, the bronchoscope with the sensor probe was advanced toward the segmental bronchus, where the lesion could be seen projecting from the distal end of the sensor. The three CT views were displayed for the corresponding CT slice according to the actual position of the sensor. Once having reached the wedge position, the sensor probe was advanced together with the EWC and steered toward the target under guidance of the display on the three perpendicular CT views and especially following the tip-view orientation (Fig 3; track marked in green). Once the sensor probe reached the location closest to the target, fluoroscopy was performed in an anteroposterior view to confirm that the sensor probe had reached the designated target. In addition, the EWC was fixed at the entrance of the biopsy channel of the bronchoscope by a lock, and a flexible forceps or brush was inserted in order to obtain histologic and cytologic specimens. The position of the endoscopic tools was verified by fluoroscopy. Accuracy of navigation was further calculated by assessment of the fiducial target registration error.

**RESULTS**

The SDBS navigation procedure was performed in 13 of the 15 originally enrolled subjects. One subject was dropped after severe bronchoconstriction developed as a result of propofol sedation, and the other subject was dropped for poor virtual bronchoscopy findings due to excessive mucopurulent secretions in the bronchial airways. Data from both subjects were excluded from the analyses.

The size of lesions was from 1.5 to 5 cm (average, 3.35 ± 1.1 cm) [Table 1]. The location of the lesions was as follows: four lesions were located at the left upper lobe (LUL), three at the right upper lobe (RUL), five at the right lower lobe (RLL), and one at the right middle lobe (RML). All lesions were displayed on the chest CT and were beyond the reach of a standard bronchoscope as required in the current study protocol. Average duration of the intervention was 46 min (range, 25 to 68 min).

In nine cases (9 of 13 subjects, 69%), the diagnoses established by the help of the SDBS were true-

**Figure 2.** The sensor probe (locatable guide [LG]) incorporated in a flexible catheter: the EWC. At the proximal end of the device, a handle with a rotating knob and a control lever to bend the distal tip.
Figure 3. SDBS real-time navigation screen.

Figure 4. SDBS planning screen.
positive (Table 1): six non-small cell lung carcinomas (NSCLCs), one tuberculous lesion, one carcinoid mass, and one case of atypical epithelial cells. Note-worthy, the SDBS procedure led to a definitive diagnosis in 2 of the 13 cases in which other diagnostic procedures (one routine bronchoscopy and one CT-guided fine-needle aspiration [FNA]) failed to provide a diagnosis. The diagnoses established by the help of the SDBS were false-negative in 4 of the 13 cases. These cases were subsequently diagnosed by CT-guided FNA (n = 4) or surgery (n = 1) as two NSCLCs, one large cell neuroendocrine carcinoma, and one squamous cell carcinoma.

Two of the lesions were located behind the blood vessels, and one lesion was surrounded by granulomatous tissue, making the navigation process very difficult in these patients. No biopsy tool reached the lesion in one patient, probably due to the technical problems, and this patient subsequently underwent CT-guided FNA.

No device-related adverse events were reported during or up to 48 h after the study. The accuracy of the navigation process, as expressed by the average of fiducial as target registration error value, was 5.7 mm.

### Table 1—Size, Location, and Biopsy Results of the Peripheral Lung Lesions With Navigation Guidance of the SDBS

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Lesion Location</th>
<th>Lesion Size, cm</th>
<th>Lesion Biopsy Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LUL</td>
<td>3.8</td>
<td>Normal tissue</td>
</tr>
<tr>
<td>2</td>
<td>RUL</td>
<td>5.0</td>
<td>NSCLC</td>
</tr>
<tr>
<td>3</td>
<td>RLL</td>
<td>1.5</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>4</td>
<td>LUL</td>
<td>4.2</td>
<td>Inflammation</td>
</tr>
<tr>
<td>5</td>
<td>RUL</td>
<td>2.7</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>6</td>
<td>RLL</td>
<td>3.5</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>7</td>
<td>LUL</td>
<td>3.2</td>
<td>Atypical epithelial cells</td>
</tr>
<tr>
<td>8</td>
<td>RLL</td>
<td>3.7</td>
<td>Carcinoid</td>
</tr>
<tr>
<td>9</td>
<td>RML</td>
<td>4.3</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>10</td>
<td>RLL</td>
<td>2.4</td>
<td>Normal tissue</td>
</tr>
<tr>
<td>11</td>
<td>RUL</td>
<td>1.8</td>
<td>Normal tissue</td>
</tr>
<tr>
<td>12</td>
<td>LUL</td>
<td>3.0</td>
<td>NSCLC</td>
</tr>
<tr>
<td>13</td>
<td>RLL</td>
<td>4.2</td>
<td>NSCLC</td>
</tr>
</tbody>
</table>
the steerable system of the locatable guide enabled us to advance through the intricate bronchial tree by executing more turns and bends until the targeted lesion had been reached. The use of the EWC facilitates several attempts at introducing the forceps directly up to the lesion area. Should the EWC be dislodged, it is easy to repeat the navigation process and continue in the effort to grasp tissue for diagnosis.

The current success rate in diagnostic bronchoscopies for peripheral lesions is very low.\textsuperscript{4,6–8} The accuracy of diagnosing peripheral pulmonary lesions from retrieved tissue samples using transbronchial biopsy (TBB) is reportedly 20 to 84\% in cases of malignant lesions, and 35 to 56\% in cases of benign lesions. The yield of TBB is even lower in small lesions.\textsuperscript{9–15} Thus, Baaklini et al\textsuperscript{9} reported that lesions \(\leq 2.0\) cm in diameter had a diagnostic yield of 14\% when located in the peripheral third, compared with 31\% when located in the inner two thirds of the lung. The patients in whom the diagnostic bronchoscopy has failed are usually referred to more invasive procedures, such as CT-guided percutaneous biopsies or a surgical biopsy, both associated with much higher costs and greater risk for the patient.\textsuperscript{16–19} Moreover, the great majority of patients who are candidates for investigation of peripheral lesions have some degree of emphysematous changes and poor pulmonary function, putting them at increased risk of pneumothorax by percutaneous techniques.

The need to accurately reach peripheral lung locations via bronchoscopy has been documented in numerous scientific articles and is a prevailing topic at most pulmonology conferences.\textsuperscript{20–23} Reports on sporadic attempts to resolve this need continue to appear in the literature.\textsuperscript{24–25} CT-guided TBB or cytology was developed to overcome the problem of incorrect positioning of the forceps or curette.\textsuperscript{26} An ultrathin bronchoscope was developed that can be inserted into more peripheral bronchi than conventional bronchoscopes under direct vision.\textsuperscript{27–31} Recently, the working channel of an ultrathin bronchoscope has become wider, extending the possibility for the collection of peripheral tissue specimens. In addition, rapid progress in computer technology has resulted in advances in diagnostic imaging. Virtual bronchoscopy is the application of 3D display techniques to the airways, enabling the simulation of actual bronchoscopic procedures.\textsuperscript{5,27}

The current study results show that the SDBS can be effectively used as an aid in guiding other tools to peripheral lung lesions. The system was now also shown to be safe during the procedures in humans as it had been in animal trials.\textsuperscript{5}

The lesions targeted in this study were all beyond the optical range of routine bronchoscopic procedures. Such lesions are usually sampled by more invasive techniques, such as CT-guided FNA or surgery, approaches that involve higher risks and costs; for example, there is a 20\% (13 to 25\%) risk of pneumothorax in patients undergoing FNA.\textsuperscript{32–33} The results of our current and earlier studies\textsuperscript{5} indicate that the new technology could help to establish diagnosis in peripheral lung lesions as an extension of standard FFB without resorting to these techniques and with high success rates. An accurate diagnosis by TBB may obviate unnecessary surgery under general anesthesia for the diagnosis of benign nodules. Importantly, even video-assisted thoracoscopic biopsy bears considerable risk for elderly patients or patients with poor respiratory or cardiac function.

Other problems in diagnosing small peripheral pulmonary lesions that are invisible under fluoroscopic radiograph guidance are related to the difficulty in maneuvering within the angles of the bronchial tree and in identifying accessible bronchial branches for reaching the lesion. If there were navigational information with real-time position of the tip of the forceps as a guide to help the bronchoscopist to grasp peripheral lesion (invisible endobronchially), a diagnosis could be reached easily and further interventional diagnostic procedures could be prevented.

It should be emphasized that in addition to all the above-mentioned limitations, small peripheral lung opacities are being increasingly observed due to the growing popularity of CT scans (6.7 million CT scans in the United States in 2001) and also to the popular shift to filtered cigarettes, which is believed to increase the relative proportion of peripheral (vs central) lung lesions, with the smaller, filtered particles being considered to penetrate deeper within the bronchial tree.\textsuperscript{34} Considering the fact that both cancer and emphysema are directly related to smoking, the importance of diagnosing small peripheral pulmonary lesions goes without saying. Despite spectacular medical advances in the last 50 years, lung cancer causes more deaths than any other cancer in both men and women. It is now the most common form of cancer diagnosed in the United States and a major cause of death, accounting for 14\% of all cancers and 31\% all cancer deaths in males.\textsuperscript{35}

The ability of the SDBS to reach peripheral lesions with a high success rate is probably due to two factors. The first is the use of a “road map” that reduces trial-and-error effects in the navigation of tools in the airways. The second is the innovative locatable guide, which is steerable. This allows active manipulation of the tool inside the airways, facilitating navigation through difficult curves, such as the upper lobes of the lungs. We believe that this
technology has much potential in increasing the diagnostic yield of FFB for peripheral lung lesions.

In conclusion, SBDS appears to be an effective and safe tool in the diagnosis of peripheral lung lesion beyond standard endoscopic vision, avoiding the need to refer patients for more risky procedures when the biopsy identifies a benign lesion. The SBDS can greatly improve the diagnostic accuracy of a standard FFB and obviate the need for more invasive measures.

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