

Bronchoscopes of the Twenty-First Century

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KEYWORDS

- Bronchoscopy • Autofluorescence bronchoscopy
- Electromagnetic navigation • Narrow-band imaging
- Confocal fluorescence microendoscopy
- Endobronchial ultrasound-guided transbronchial needle aspiration • Endobronchial ultrasound

The bronchoscope has been an invaluable tool for the pulmonologist and surgeon for over a century. In the late 1800s, Dr Gustav Killian performed the first rigid bronchoscopy. The innovative procedure provided physicians with a new glimpse into human anatomy and sparked the growth of pulmonary medicine. Using a metal tube, electric light, and topical cocaine anesthesia, Killian removed a pork bone from a farmer's airway in 1897.

Before the invention of rigid bronchoscopy, over half of the patients who aspirated foreign bodies died, mostly of a postobstructive pneumonia. Rigid bronchoscopy with foreign body removal quickly evolved into the treatment of choice in these patients, with a clinical success rate above 98%.¹ During the early 1900s, Killian published extensively and lectured throughout the world. He further went on to adapt his bronchoscopes, laryngoscopes, and endoscopes, and first described techniques, such as using fluoroscopy and radiographs to define endobronchial anatomy. The design and functionality of the rigid bronchoscope was improved further in 1904 when Chevalier Jackson, the "father of American bronchoesophagology," first equipped his bronchoscope with a suction channel and a small light bulb at the distal tip to provide illumination.

Over the next 150 years, bronchoscopic technology continued to be refined. In 1966, at the 9th International Congress on Diseases of the Chest in Copenhagen, Shigeto Ikeda presented the first prototype flexible fiber-optic bronchoscope. In 1968, the first commercially available

flexible bronchoscope was made available by Machita and Olympus.² In 1980, Dumon presented his use of the neodymium-yttrium aluminum garnet (Nd:YAG) laser via the fiber-optic bronchoscope. Since then, the flexible bronchoscope has been widely used as both a diagnostic and a therapeutic tool for both diseases of the parenchyma and of the central airways. With the miniaturization of electronic devices, the first video bronchoscope was introduced in 1987. This development enabled endoscopic pictures to be taken and shared for educational purposes. Another major advance in the teaching of bronchoscopy came when physicians no longer needed to look through an eyepiece, but instead could transmit endoscopic images to monitors, enabling an entire bronchoscopy staff to witness procedures.

Although little has changed in the appearance of either the flexible or the rigid bronchoscope since 1968, new technological advances over the past decade have brought improvements to the field of bronchology. This article reviews the current advances in both rigid and flexible bronchoscopy and discusses the diagnostic and therapeutic implications of these tools.

NEW INNOVATIONS IN RIGID BRONCHOSCOPY

Though the design of the rigid bronchoscope has not significantly changed since Jackson first used it in 1897, current designs and accessories have helped make it possible to adapt the

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bronchoscope for new technologies. The rigid bronchoscope is made of a hollow cylindrical stainless steel tube with an equal diameter along its entire working length. The adult rigid bronchoscope is usually 40 cm long and has an external diameter ranging from 9 to 14 mm. The distal end has a beveled tip to enable lifting of the epiglottis and safer insertion through the vocal cords. This beveled end can also be used to dilate stenotic lesions and to “core” through tumors, thus achieving rapid airway patency. Fenestrations are present at the distal one third of the bronchoscope to enable contralateral lung ventilation when the bronchoscope is inserted into a mainstem bronchus. In comparison with the bronchoscope, a rigid tracheoscope is shorter—measuring 30 cm—enabling more maneuverability within the trachea to relieve central airway obstructions. Distal fenestrations are absent on the rigid tracheoscope because single lung ventilation is not required while operating within the trachea. The proximal end of the bronchoscope varies by manufacturer as discussed below. Most bronchoscope systems have several ports to enable passage of the telescope, suction catheters, and a variety of instruments for tumor destruction, tumor excision, dilation, and foreign body removal.

Over the past several years, new designs and modifications applied to the standard rigid bronchoscope have made it a more versatile tool for the interventional pulmonologist.

The Bryan-Dumon Series II rigid bronchoscope represents the first major modification to the rigid bronchoscope since the rigid bronchoscope first appeared. The Bryan-Dumon Series II

bronchoscope features an operator head with a universal instrumentation barrel. The operator head (**Fig. 1**) is an interchangeable piece that can be placed on the proximal end of any of the color-coded bronchial and tracheal tubes within the Dumon series. The universal instrumentation barrel is also equipped with three side ports for instruments, ventilation, and anesthesia. In addition, the barrel has a channel for the telescope. The multiple ports of access permit physicians to use various endoscopic tools while maintaining the visualization capabilities of the rigid telescope. The system also has a stent introducer system for the placement of silicone tracheobronchial stents.

Another rigid bronchoscope recently introduced is the Texas R.I.B. (Rigid Integrated Bronchoscope) from Wolff. This bronchoscope features separate channels for optics and instruments to enable access to a larger working area with uninterrupted visualization. The design combines the operator head with the camera, which limits the loss of working space within the bronchoscope channel taken up by the larger optics. This design may also increase efficiency during procedures because the telescope does not need to be removed before the insertion of accessories. However, the telescope cannot extend distally past the lumen of the bronchoscope and thus vision is limited to only areas at the distal end of the rigid bronchoscope. There is also an irrigation port at the proximal operator end to enable washing of the distal lens for optimal visualization. At the distal tip of the bronchoscope are additional fenestrations to provide 360° viewing.

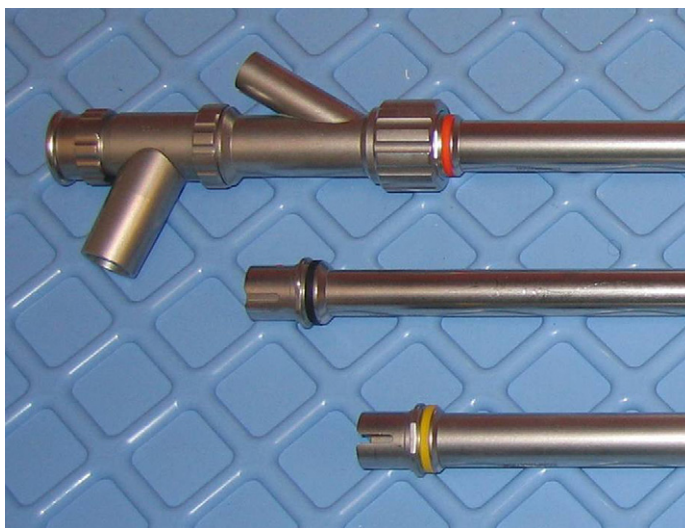


Fig. 1. The Bryan-Dumon Series II bronchoscope's universal operator head with multiple ports, which enable jet or volume ventilation as well as passage of a variety of instruments.

VENTILATION AND MONITORING DURING RIGID BRONCHOSCOPY

Ventilation during rigid bronchoscopy can be achieved in several ways. In 1967, Sanders³ developed a method of low-frequency jet ventilation to enable effective ventilation and oxygenation while keeping the proximal end of the bronchoscope free for passage of the instruments. In the 1990s, a shift away from this mode followed reports of hypoxemia during spontaneous assisted ventilation with intravenous anesthesia during rigid bronchoscopy in patients with central airway obstruction. Jet Venturi ventilation reemerged as a favored method.⁴ Because the system is open to atmosphere, room air is also entrained into the bronchoscope, resulting in a variable fraction of inspired oxygen (FiO₂).⁵ Although a safe oxyhemoglobin saturation is usually easily obtained, potential downsides to this system are a limited ability to monitor FiO₂, minute ventilation, and airway pressures. As such, there is a potential increased risk of iatrogenic pneumothorax due to dynamic hyperinflation distal to a stenotic airway.⁶

The Hemer bronchoscope introduced by Wolff is adapted with a measuring port that enables sampling of carbon dioxide and oxygen and monitoring of pressure fluctuations during the procedure. The peak inspiratory pressure of entrained air and jet-pressurized air reaches a plateau within the rigid bronchoscope at a distance of approximately 10 cm from the proximal end of the bronchoscope. By measuring pressure distal to that point, an estimate of mean inspiratory pressure is obtained. The adapted Hemmer bronchoscope has an internal port at 14 cm from the proximal end of the bronchoscope and can be connected to pressure transducers and gas sensors to monitor end-tidal carbon dioxide, enabling real-time monitoring.

NEW INNOVATIONS IN FLEXIBLE BRONCHOSCOPY

Since its first introduction by Ikeda in 1967, the flexible bronchoscope has rapidly emerged as the most adaptable tool for the practicing pulmonologist. Since that time, the field has seen a steady stream of advances. Recently, technological advances have begun to open more doors toward not only improved diagnostic interventions for malignant disease but also for the detection of premalignant lesions. As additional studies are performed and as new data become available, such modalities as endobronchial ultrasound (EBUS), electromagnetic navigation, autofluorescence bronchoscopy, narrow-band imaging, and

confocal fluorescence microscopy are emerging as important new technologies for the bronchoscopist.

MODERN VIDEO BRONCHOSCOPES

Despite great advances in the technology within the bronchoscope, the overall appearance of the instrument resembles that of the original fiber-optic design. The external diameter of most working flexible bronchoscopes varies from approximately 4 mm to 6.3 mm. Ultrathin bronchoscopes are also available, with an external diameter of 2.7 mm, and are especially helpful in bypassing obstructing airway lesions to assess distal patency. The diameter of the working channel ranges from 1.2 mm to 3.2 mm. A working channel 2.8 mm or more is recommended for more therapeutic flexible bronchoscopy, as well as EBUS, as it enables better suction and the passage of larger instruments. Most flexible bronchoscopes can flex 180° up and 130° down. Olympus is developing an “endocotoscopy” bronchoscope that provides high-magnification of 450× and a horizontal resolution of 4.2 μm, providing cellular imaging and the possibility of an “optical biopsy.”

ENDOBONCHIAL ULTRASOUND BRONCHOSCOPY AND THE DIAGNOSIS OF LUNG CANCER

Lung cancer remains the leading cause of cancer deaths in the United States and accounted for approximately 161,840 deaths in 2008.⁷ It is estimated that 2009 figures will show 219,440 new cases of lung cancer for the year. Meanwhile, the number of lung cancer deaths continues to increase amongst women in the United States.⁸ Bronchoscopy has been an invaluable tool in the diagnosis and staging of lung cancer. Transbronchial needle aspiration (TBNA) of mediastinal and hilar lymph nodes has been shown to be an effective means of both diagnosing and staging lung cancer.^{9–11} The procedure has consistently been shown to be minimally invasive, safe, and less costly than mediastinoscopy. Also, the procedure can preclude surgery in up to 29% of patients.¹² Despite these facts, the procedure remains underused. A survey performed in 1991 showed that only 12% of pulmonologists routinely use TBNA in evaluating malignant disease. This reluctance to use TBNA is likely due to concerns over lack of training, fear of injuring the bronchial tubes or puncturing a blood vessel, and lack of adequate procedural support.¹³ Although traditional TBNA is a safe and effective procedure, the inability to directly visualize mediastinal and hilar lymph

nodes as well as surrounding vasculature and lung tissue has been a limitation.

The invention of the integrated EBUS in 2002 used for real-time guidance TBNA solved this issue. The role of EBUS-guided TBNA (EBUS-TBNA) in mediastinal staging and restaging of lung cancer is discussed in detail in the article by Herth and colleagues elsewhere in this issue. The design of the EBUS convex probe flexible bronchoscope differs from that of the standard flexible bronchoscope in widespread use today. The Olympus EBUS bronchoscope is a hybrid bronchoscope incorporating both fiber-optic and video imaging technologies. The bronchoscope incorporates a 7.5-MHz convex transducer, which produces a linear curved array. By making direct contact with the airway wall or by using a water-filled balloon that lies over the tip of the ultrasound transducer, transbronchial ultrasound images of mediastinal and hilar structures can be obtained.

There are currently two Olympus EBUS bronchoscopes available. The Olympus BF-UC160F was the first model widely produced by Olympus. This bronchoscope is larger than standard bronchoscopes. The distal tip has an outer diameter of 6.9 mm and the insertion tube has an outer diameter of 6.2 mm. The working channel is 2.0 mm. The optical vision has a 35° forward oblique view due to the ultrasound transducer at the tip of the bronchoscope and an 80° field of view. This angulation is different from that of standard bronchoscopes and can make the insertion of the bronchoscope into the vocal cords technically more challenging, as discussed below. Recently, Olympus introduced the second-generation EBUS bronchoscope. The BF-UC180F has the same outer dimension as the original model. The working channel is larger at 2.2 mm, enabling better suctioning and accommodating larger-bore needles. The newer bronchoscope is also compatible with the more powerful Olympus Aloka ultrasound system.

Pentax has recently introduced the EB-1970UK EBUS bronchoscope. The Pentax EBUS bronchoscope has a 6.3-mm insertion tube diameter and a 2.0-mm working channel. The angle of view is 100°. The imaging technology on the Pentax bronchoscope uses an all video imaging processor as compared with the hybrid imaging on the Olympus bronchoscopes. This technology allows for a finer visual image at the expense of a slightly larger outer diameter.

Both systems use a dedicated EBUS-TBNA needle. Olympus has produced a 22-gauge needle and recently introduced a 21-gauge TBNA needle. Pentax offers a 22-gauge needle through Medi-Globe.

From a technical standpoint, the EBUS bronchoscope is operated in a slightly different manner than the traditional bronchoscope. This means clinicians must take time to understand the ultrasound anatomy and become familiar with the dedicated needle system.¹⁴ The distal end of the bronchoscope is larger in diameter and the forward view is 30° oblique instead of 0° (straight ahead). As a result, the most distal portion of the bronchoscope cannot be directly visualized, adding an additional challenge when inserting the bronchoscope through the vocal cords.

ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION IN OTHER DISEASES

Initial data examining the yield of EBUS-TBNA primarily concentrated on the diagnosis and staging of lung cancer. As EBUS has become more established, multiple studies have examined its use beyond the scope of lung cancer diagnosis. These applications include those related to sarcoidosis, lymphoma, and pulmonary emboli.^{15–17} Several recent studies have shown that EBUS-TBNA may be the preferred diagnostic modality for the investigation of pulmonary sarcoidosis.^{15,18,19} One study showed a sensitivity of 85% for the diagnosis of sarcoidosis using EBUS-TBNA as a first-line diagnostic test.¹⁵ A randomized trial by Tremblay and colleagues¹⁸ examined the diagnostic efficacy of EBUS-TBNA versus standard TBNA in sarcoidosis and found an increase in diagnostic yield to 83% from 54% with an increase in sensitivity to 83% from 61% by using EBUS. A recent study by Aumiller and colleagues¹⁷ performed EBUS on patients with computed tomography (CT)-confirmed central pulmonary emboli and reconfirmed the diagnosis in 96% of the cases. Although an interesting finding, the clinical utility of this finding is not yet established.

ENHANCED BRONCHOSCOPIC NAVIGATION

Traditionally, small distal parenchymal lesions less than 2 cm have been difficult to sample bronchoscopically.²⁰ Often, these lesions must be either followed radiographically or surgically resected.²¹ As the large majority of peripheral lung nodules are not malignant, the ability to obtain a minimally invasive diagnosis would significantly reduce the number of unnecessary surgeries.²² One of the main limitations of bronchoscopy for peripheral lesions is that the size of the bronchoscope precludes direct inspection of distal airways and, as a result, the operator is unable to visualize these lesions. Traditionally, fluoroscopy and, more

recently, CT-guided fluoroscopy and radial probe EBUS have been used to attempt localization of peripheral lesion, but these methods were still limited by the bronchoscope's ability to guide a biopsy device successfully to the distal lesion. An electromagnetic guidance system has been adapted to be used with the flexible bronchoscope to assist with peripheral nodule sampling and is discussed in detail in the article by Schwarz and colleagues elsewhere in this issue.

More recently, newer methods of sampling peripheral lesions have emerged. These take advantage of improved CT imaging and complex computer programs, enabling accurate reconstruction of the airways. The distinct advantage of these systems as compared with the electromagnetic guidance systems is that they require no additional guidance equipment during the procedure. A virtual bronchoscopy is created with CT imaging and mapped pathways are determined (Fig. 2). Using a flexible ultrathin bronchoscope and the image guidance, the clinician can gain access to small peripheral nodules. In 2006, Asano and colleagues²³ published the first study in the literature using the technology. By using CT virtual bronchoscopy in conjunction with a computer program that generated a pathway to the lesion and an ultrathin bronchoscope, they were able to advance the bronchoscope into the planned route in 36 of 38 cases (94.7%), with a diagnostic rate of 81.6%. A latter study by the same group combined this technology with radial probe EBUS and guide-sheath technology. In this study of 31 patients, 32 peripheral pulmonary lesions were evaluated. The newer program was able to produce virtual images out to a seventh-order bronchi. In all patients, the ultrathin bronchoscope was successfully guided to the lesion. A pathologic diagnosis was obtained in 27 (84.4%) of the samples. With a median total examination time of 22.3 minutes, the procedure time did not appear to be significantly lengthened with the use of the virtual technology.²⁴

AUTOFLUORESCENCE BRONCHOSCOPY

For most types of lung neoplasm, surgical resection remains the primary curative modality. Recent efforts have been directed at earlier diagnoses with the hope that such malignancies, caught in earlier stages, could be cured without resection or be surgically removed with a higher likelihood of cure.²⁵ Early detection of preinvasive lesions within the central airways can be achieved with the autofluorescence.²⁶ By using blue light (520 nm) instead of white light, dysplasia and carcinoma in situ will appear darker than the surrounding normal tissue because of a loss of normal autofluorescence (Fig. 3). There are several autofluorescence devices currently available, including the Laser Induced Fluorescence Endoscope (LIFE) system, the D-Light system, the SAFE-1000 system, and the Autofluorescence Imaging (AFI) system.^{27,28} Unfortunately, autofluorescence technology is unable to differentiate between early preinvasive lesions and inflammatory or infectious changes in the epithelium that are benign, thus significantly reducing its specificity.²⁹ There are several classes of tissue findings in autofluorescence: normal (class I); inflammation and mild dysplasia (class II); and moderate to severe dysplasia, carcinoma in situ, or invasive cancer (class III).²⁷ To date, this classification does not correlate with degree of invasion or propensity toward a neoplastic process.³⁰ Because of its poor specificity, and high degree of inter- and intraobserver variability, autofluorescence is not considered an acceptable screening modality, even in high-risk patients, and the utility of this procedure in the lower airway remains in question.^{31,32}

NARROW-BAND IMAGING

Narrow-band imaging is a light technology that uses specialized filters to separate wavelengths of white light and select out red, green, and blue

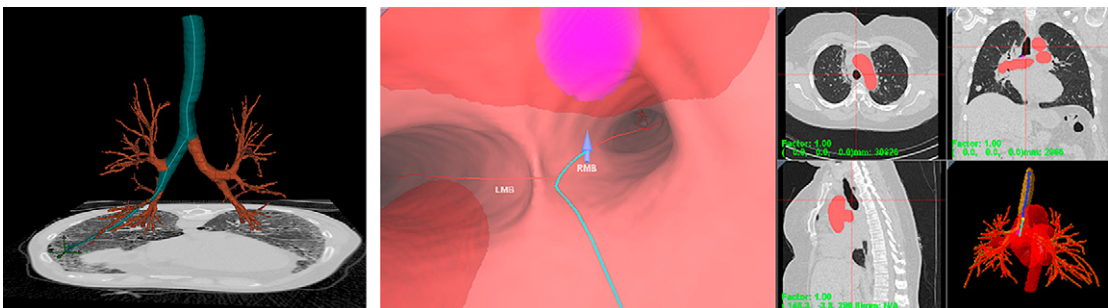


Fig. 2. Virtual bronchoscopic navigation. ([Left] Courtesy of Vida Diagnostics; with permission. [Right] Courtesy of Bronchus Technologies; with permission.)

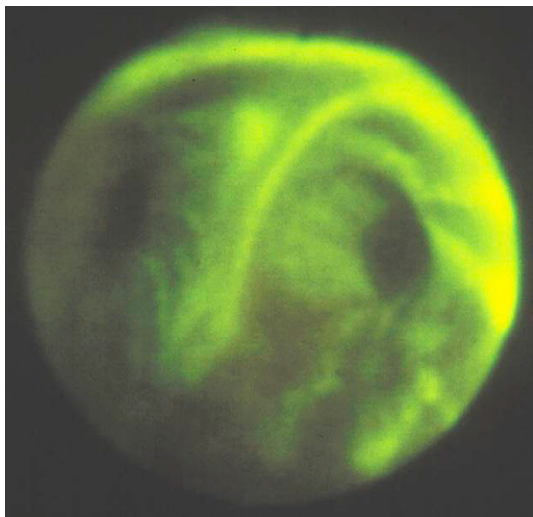


Fig. 3. Carcinoma in situ as seen with autofluorescence bronchoscopy.

bands. Additional filtering technology then intensifies the blue band. By selectively engaging these bands of light, the microvasculature is more clearly visible (**Fig. 4**).³³ This technology has been used to help identify premalignant lesions within the airways.³⁴ Dysplastic or premalignant lesions have been shown to have abnormal levels of angiogenesis compared with the surrounding normal tissue.^{35,36} In a recent pilot study by Vincent and colleagues,³⁴ narrow-band imaging was compared with white-light bronchoscopy in 22 patients with known or suspected bronchial dysplasia or malignancy. Endobronchial biopsies of lesions suspicious for dysplastic, malignant, and normal (control) areas were then performed. There were four dysplastic and one malignant

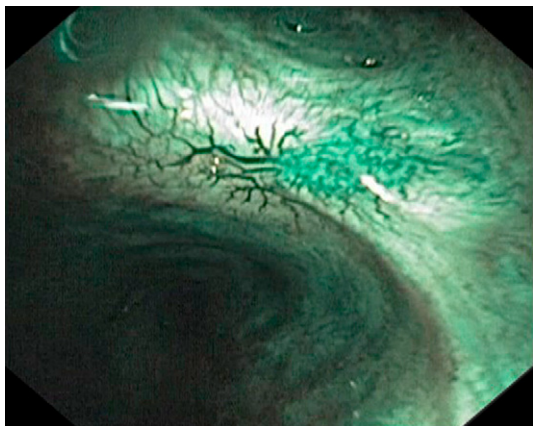


Fig. 4. Neovascularization seen with narrow-band imaging.

lesions in 22 patients detected by narrow-band imaging when findings by white-light imaging were considered normal, which increased the rate of detection of dysplasia and malignancy by 23%. As in the case of autofluorescence, a better understanding of the progression of these lesions and improved specificity is needed before this technology can be recommended for widespread use.

CONFOCAL FLUORESCENCE MICROENDOSCOPY

Alveoloscopy or confocal laser fluorescence microendoscopy (CFM) is a newer technology that enables *in vivo* microscopic observation of the airways and alveoli. The technology was introduced in 1957 but only in the last decade has the device been adapted for use with bronchoscopy. Similar to autofluorescence, the device uses a blue laser, which has been adapted within a small probe that can be advanced through the working channel of the bronchoscope into the distal airways and alveoli to induce tissue fluorescence. Optical slices of the observed tissue are obtained and *in vivo* magnified images of the alveoli can be observed.³⁷

Although the technology will theoretically enable histologic interpretation of *in vivo* tissue, several technical issues remain. These need to be resolved before the technology can be put in widespread use. Currently, to adequately fluoresce this live tissue, a contrast dye must be administered within the pulmonary parenchyma and, given the limits of standard bronchoscopy and live imaging, the placement of the confocal probe within the correct area of study cannot yet be accurately controlled. The current data within the pulmonary literature remain limited to studies by Thiberville and colleagues.³⁷ In 2007, their group performed *in vivo* CFM bronchoscopically on 29 patients at high risk for lung cancer. The investigators recognized several microscopic patterns that may help in the recognition of dysplastic tissue. In 2009, the same group performed confocal fluorescence microscopy in 41 healthy subjects, including 17 active smokers. *In vivo* acinar microimaging was obtained from multiple lung segments (**Fig. 5**). The investigators reported that alveolar macrophages were not detectable in nonsmokers, whereas a specific tobacco tar-induced fluorescence was observed in smoking subjects.³⁸ Although this technology does appear to have promise, given the currently limited data, its accuracy in detecting lung pathology has yet to be defined.

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) is an imaging technology similar to ultrasound. Instead of measuring the intensity of back-reflected sound, OCT uses an infrared light to obtain cross-sectional images of tissue. Compared to ultrasound, the resolution of OCT within the airways is significantly higher, which enables a more detailed evaluation of depth of invasion in endobronchial disease (Fig. 6).³⁹ OCT resolution, between 4 and 20 nm in the airway, is approximately 25 times higher than that of other available modalities.⁴⁰ It is also an optically based technology. This means it does not require direct contact with tissue for transmission of a signal and can therefore easily be used within the airways.⁴¹

OCT's ability to assess the microstructure of the eye has an established role in ophthalmology and has only recently been adapted to the airways.⁴² Its potential to produce in vivo images or "optical biopsies" of the microstructure of the lung without the risk of tissue biopsy could be a very useful modality in such fields as interstitial lung disease and lung transplantation.^{43,44} As in the other modalities discussed above, further studies are needed to before its true clinical efficacy can be determined.

SUMMARY

Bronchoscopy continues to evolve at a rapid pace and remains an invaluable tool for the practicing pulmonologist. Recent advances have enabled the diagnosis and staging of our patients in a minimally invasive fashion with higher specificity than

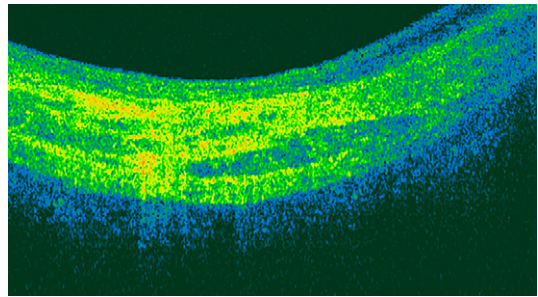


Fig. 6. OCT showing human main bronchus. Scan direction: perpendicular to airway. Image size: 1.5 mm × 4 mm. (Courtesy of Tomophase Corp; with permission.)

ever. Further advances and studies in electromagnetic guidance systems, OCT, and CFM may one day allow the bronchoscopist to obtain in vivo diagnoses without tissue destruction. As Chevalier Jackson said:

In the future, as at present, the internist will tap and look and listen on the outside of the chest; the roentgenologist will continue to look through the patient; but in continually increasing proportions of cases, the surgeon, the internist and the roentgenologist will ask the bronchoscopist to look inside the patient.¹

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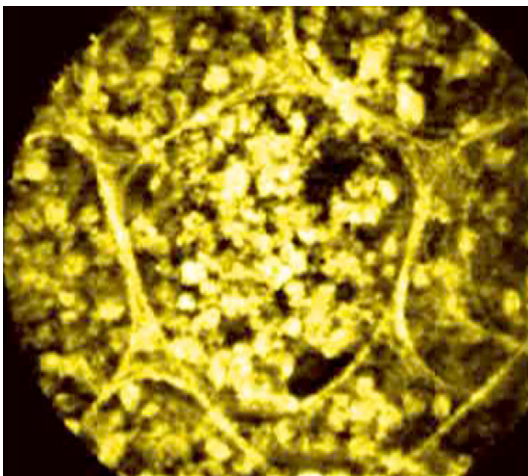


Fig. 5. Confocal microendoscopy showing alveolar septae and alveolar macrophages.

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