Ultrathin Bronchoscopy

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Contents

Abstract

Biopsy instruments can diagnose peripheral pulmonary lesions, but they must be precisely advanced through the bronchus to the target lesions by selecting the correct route among branching bronchi. Thinner bronchoscopes can navigate more peripheral bronchi while allowing direct visualization of bronchial branches, making the use of an ultrathin bronchoscope for diagnosing peripheral lesions a reasonable approach. Technological advances have led to the development of thinner bronchoscopes with larger working channels and improved visual quality compared to earlier models. Additionally, miniaturized biopsy instruments (e.g., cryoprobes and biopsy needles) and guidance devices (e.g., radial probe endobronchial ultrasound) that can be used through the working channel of ultrathin bronchoscopes have been introduced. Several randomized studies have demonstrated that ultrathin bronchoscopy offers superior diagnostic performance compared to larger bronchoscopes for small peripheral pulmonary lesions. The integration of multimodality and multiinstrumental ultrathin bronchoscopy significantly enhances the diagnostic yield for these lesions.

Keywords

Bronchoscopy · Cryobiopsy · EBUS-UT · Thin bronchoscope · Ultrathin bronchoscope · Ultrathin bronchoscopy

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1 Introduction

Since the introduction of flexible bronchoscopes by Shigeto Ikeda in 1966 [1], bronchoscopic technologies have evolved considerably. In the twentieth century, bronchoscopy for diagnosing peripheral pulmonary lesions was solely guided by fluoroscopy. The diagnostic yield of conventional bronchoscopy was limited [2], as fluoroscopy's two-dimensional display failed to precisely show the spatial relationship between the biopsy instrument and the target lesion. However, over the past two decades, advancements such as endobronchial ultrasound and navigation devices have significantly improved bronchoscopic diagnostic accuracy [3–5]. Navigation devices guide the bronchoscopic approach to the lesion, but advancing biopsy instruments through the indicated bronchus can be challenging due to the complexity of branching bronchi when using a large bronchoscope. Thinner bronchoscopes have the ability to navigate more peripheral bronchi along the navigation-indicated route under direct visualization. The use of an ultrathin bronchoscope in conjunction with navigation devices is highly advantageous, as it enhances the effectiveness of these devices. Conventional ultrathin bronchoscopes had limitations including restricted instrument availability, reduced suction power due to a small-caliber working channel, and poor visibility, but recent developments have addressed these issues. Recently developed ultrathin bronchoscopes feature larger working channels and improved endoscopic resolution compared to their predecessors [6]. Additionally, miniaturized biopsy instruments (e.g., cryoprobes and biopsy needles) and guidance devices (e.g., radial-probe endobronchial ultrasound [rEBUS]) are now available for use with ultrathin bronchoscopes. Consequently, integrating an ultrathin bronchoscope with advanced guidance devices and biopsy instruments is a promising strategy to enhance the diagnostic yield for small peripheral pulmonary lesions.

2 Definition of Ultrathin Bronchoscopes

As technology continues to evolve, the terminology for ultrathin bronchoscope is also likely to change over time. No formal definition has been determined for ultrathin bronchoscope, but recent publications have described bronchoscopes with an outer diameter ≤3.5 mm as ultrathin bronchoscopes [7, 8]. Bronchoscopes with an outer diameter of 3.6–4.5 mm are typically called thin bronchoscopes; those with an outer diameter ≥4.6 mm and a working channel with an inner diameter of approximately 2.0 mm are referred to as standard bronchoscopes; and those with a relatively large working channel with an inner diameter ≥2.6 mm are called therapeutic bronchoscopes (Fig. 1).

3 History

In 1966, Shigeto Ikeda developed the first prototype flexible bronchoscope with an outer diameter of 5.0 mm [1]. In 1968, he developed the first prototype ultrathin fiberoptic bronchoscope, designed to be used with the Metras catheter originally intended for bronchography. This prototype had an outer diameter of 2.5 mm, lacked a working channel, and could be bent up to 30° [9]. In the 1980s and 1990s, Olympus released the BF-3C series bronchoscopes (3.3–3.6 mm in outer diameter) with a 1.2-mm working channel. These models were primarily used in

Fig. 1 Flexible bronchoscopes. Left to right: Ultrathin bronchoscope with a diameter of 2.8 mm and a working channel of 1.2 mm. Ultrathin bronchoscope with a diameter of 3.0 mm and a working channel of 1.7 mm. Thin bronchoscope with a diameter of 4.0 mm and a working channel of 2.0 mm. Standard bronchoscope with a diameter of 4.8 mm and a working channel of 2.0 mm. Therapeutic bronchoscope with a diameter of 5.9 mm and a working channel of 3.0 mm

pediatric patients and were referred to as pediatric bronchoscopes. The first clinical use of pediatric bronchoscope in adult patients was reported by Prakash in 1985 [10], who described three cases in which endobronchial lesions were not revealed by a standard-size bronchoscope but were successfully identified using the BF-3C4 (Olympus, Tokyo, Japan) pediatric bronchoscope. Since 1999, Olympus has introduced the BF-XP series (2.8–3.1 mm in outer diameter) with a 1.2-mm working channel, and the clinical utility of ultrathin bronchoscopes has been widely reported [11–14]. Conventional ultrathin bronchoscopes had a working channel up to 1.2 mm in inner diameter, which precluded the use of rEBUS. In 2009, Oki et al. [15] first reported the utility of rEBUS-guided ultrathin bronchoscopy (EBUS-UT) using a prototype 3.4-mm ultrathin bronchoscope with a 1.7-mm working channel. Finally, the newest generation of bronchoscope was released in 2017: this 3.0-mm ultrathin bronchoscope has a 1.7-mm working channel, which allows the use of rEBUS [6].

4 EBUS-UT Techniques

Before performing ultrathin bronchoscopy, the bronchus leading to the target lesion should be predicted using thin-slice CT images [16]. Ultrathin bronchoscopic procedures can be conducted under conscious sedation and local anesthesia. In the supine position, a 5.0-mm tracheal tube is inserted transnasally into the trachea under the guidance of ultrathin bronchoscopy. This established airway facilitates bronchoscope replacement, minimizes mucosal damage caused by bronchoscope movement, and supports the flexible portion of the ultrathin bronchoscope. After inspecting the trachea and central bronchus, the ultrathin bronchoscope is advanced through the predicted leading bronchus, as determined by preprocedural computed tomography (CT) and virtual bronchoscopic navigation (VBN), while confirming the location of the target lesion and the bronchoscope using fluoroscopy. Once the ultrathin bronchoscope is positioned close to the lesion, rEBUS is used to localize the target lesion. The rEBUS probe is inserted into the lesion, and once an image showing the probe within the lesion is obtained, the ultrathin bronchoscope is advanced further toward the lesion using the rEBUS probe as a guide wire [17]. Finally, bronchoscopic sampling is performed under fluoroscopic guidance until at least ten visible specimens are obtained.

5 Accessibility

Several studies have found that 2.8-mm or 3.0-mm ultrathin bronchoscopes can reach the median fifth-generation bronchi (sub-sub-subsegmental bronchi) [6, 14, 18], which are more distal than those accessible with a 4.0-mm thin bronchoscope (median fourth-generation bronchi, sub-subsegmental bronchi) [14, 18]. Ultrathin bronchoscopes can advance beyond the distal end of VBN images, whereas thin bronchoscopes cannot reach this distal region [18]. Therefore, to optimize the effectiveness of the VBN system, using an ultrathin bronchoscope is reasonable.

6 Diagnostic Yield

Numerous studies have demonstrated the utility of ultrathin bronchoscopy for diagnosing peripheral pulmonary lesions. Some of these studies were randomized trials, and their results are summarized in Table 1 [6, 14, 18–21].

6.1 Ultrathin Bronchoscopy Without rEBUS Guidance

Conventional ultrathin bronchoscopes have a small-caliber working channel, up to 1.2 mm in diameter, which precludes the use of rEBUS. Several studies have investigated the diagnostic efficacy of conventional ultrathin bronchoscopy guided solely by fluoroscopy [12, 20]. Yamamoto et al. [12] performed ultrathin bronchoscopy, followed by bronchoscopy using 5.3–6.3-mm bronchoscopes under fluoroscopic guidance in 35 patients: the diagnostic yields for ultrathin bronchoscopy, standard bronchoscopy, and their combination were 60.0%, 54.3%, and 62.8%, respectively. In a small randomized study by Franzen et al. [20] (Table 1), involving 20 patients in each arm, the diagnostic yields for ultrathin bronchoscopy and bronchoscopy using 5.0–6.0-mm bronchoscopes were 55% and 80%, respectively. These results suggest that the diagnostic performance of ultrathin bronchoscopy, when guided only by fluoroscopy, may be limited. The two-dimensional fluoroscopic images, even when using a C-arm fluoroscopy, cannot accurately confirm the spatial relationship between lung lesions and biopsy instruments. Therefore, to enhance the effectiveness of ultrathin bronchoscopy, additional guidance methods such as VBN, CT, and cone-beam CT (CBCT) are necessary. In a randomized study involving 350 patients, Asano et al. [14] evaluated the utility of VBN during conventional ultrathin bronchoscopy (Table 1): the difference in diagnostic yields between VBN-assisted ultrathin bronchoscopy and ultrathin bronchoscopy without VBN was not statistically significant (67.1% vs. 59.9%, $p = 0.173$), but VBN-assisted ultrathin bronchoscopy provided higher diagnostic yields for right upper lobe lesions, lesions not visible on chest radiographs, and lesions located in the peripheral third of the lung field. Additionally, a retrospective study using propensity score-matched analysis by Kawakita et al. [22] found that the diagnostic yield of CBCT-guided ultrathin bronchoscopy

Table 1 Randomized trials on ultrathin bronchoscopy

Author/ year	Scope/ channel diameter (mm)	Study arms	Common guidance method in each arm	Sampling instruments	Median lesion diameter (mm)	No. diagnosed/ examined	Yield (%)	P-value	No. diagnosed/ examined for lesions <2 cm	Yield (%)	P-value	Malignancy (%)	Complications
Oki/ 2012 [19]	3.4/1.7	UTB	Flu, rEBUS	For, Bru	26.0	66/101	65	ND	10/25	40	ND	76	PTX (3), PNA (1), bleeding (1)
	4.0/2.0	TB + GS		For, Bru	27.5	63/102	62		16/27	59		80	PNA (2)
Asano/ 2013 [14]	2.8/1.2	UTB	Flu	For, Bru	17	100/167	59.9	0.173	62/110	56.4	0.190	90.4	PTX (1), lidocaine intoxication (1), PNA (1)
	2.8/1.2	UTB + VBN		For, Bru	18	112/167	67.1		74/114	64.9		85.6	PTX (1), bleeding (2), bradycardia (1)
Oki/ 2015 [6]	3.0/1.7	UTB	Flu, rEBUS, VBN	For	19.0	111/150	74	0.044	52/80	65	0.037	82	PTX (3), PNA (1), chest pain (1)
	4.0/2.0	TB + GS		For	19.4	92/155	59		40/82	49		70	PTX (5), bleeding (2)
Franzen/ 2016 [20]	2.8/1.2	UTB	Flu	For, Bru	27	11/20	55.0	0.18	6	ND		40	Severe coughing (2), blocked working channel (3), hypertension (1)
	5.0–6.0/ 2.2–2.8	SB		For, Bru	24	16/20	80.0		6	ND		40	Bleeding (1)
Oki/ 2019 [18]	3.0/1.7	UTB	Flu, rEBUS, VBN	For	18.9	124/177	70.1	0.027	64/102	62.7	0.12	80.2	PTX (2), PNA (2), bleeding (1)
	4.0/2.0	TB ± GS		For, Ne	19.1	105/179	58.7		52/101	51.5		78.2	PTX (2), PNA (1), bleeding (2), vomiting (1), nausea (1), myocardial infarction (1)
Zheng/ 2021 [21]	3.0/1.7	UTB	rEBUS, VBN	For, Bru	Mean 26.3	44/60	73.3	0.38	10/17	58.8	0.47	76.7	0
	3.0/1.7	UTB + Flu		For, Bru	Mean 29.0	49/60	81.7		11/15	73.3		90.0	0

Bru brush, *Flu* fluoroscopy, *For* forceps, *GS* guide sheath, *ND* no data, *Ne* needle, *PNA* pneumonia, *PTX* pneumothorax, *rEBUS* radial-probe endobronchial ultrasound, *SB* standard-size bronchoscope, *TB* thin bronchoscope, *UTB* ultrathin bronchoscope, *VBN* virtual bronchoscopic navigation

was significantly higher than that of CT-guided ultrathin bronchoscopy (72.9% vs. 47.9%, $p = 0.012$).

6.2 EBUS-UT

The clinical use of ultrathin bronchoscopy has increased since the introduction of the ultrathin bronchoscope with a 1.7-mm working channel, which allows the passage of a rEBUS probe. No date, no direct comparative studies have been conducted on the new 1.7-mm channel model and the conventional 1.2-mm channel model, but the 1.7-mm channel ultrathin bronchoscope appears to provide higher diagnostic yields [8, 23]. Several studies have compared ultrathin bronchoscopy with larger-diameter bronchoscopes. In two large randomized studies (Table 1), Oki et al. [6] demonstrated the diagnostic superiority of ultrathin bronchoscopy over thin bronchoscopy under rEBUS, VBN, and fluoroscopy guidance for diagnosing peripheral pulmonary lesions <30 mm in diameter: factors such as lesion size >20 mm, presence of a bronchus sign, and malignancy were associated with a higher diagnostic yield in ultrathin bronchoscopy. Sumi et al. [18] conducted a retrospective comparison of ultrathin bronchoscopy and standard 4.8-mm bronchoscopy under rEBUS and fluoroscopy guidance in 168 patients with peripheral pulmonary lesions <30 mm in diameter [24]. They found that ultrathin bronchoscopy had a significantly higher diagnostic yield compared to the standard bronchoscope (74.5% vs. 59.1%, $p = 0.04$). While rEBUS, when combined with fluoroscopy, is generally effective in confirming lesion location, it does not always localize the lesion, such as with small pure ground-glass nodules. In cases where the lesion is not visible on rEBUS, the spatial relationship between the rEBUS probe and the target lesion remains uncertain. CBCT enables more precise three-dimensional positioning of target lesions and biopsy instruments, potentially enhancing the diagnostic yield of EBUS-UT. Kawakita et al. [25] conducted a prospective pilot study on CBCT-guided rEBUS-ultrathin bronchoscopy with 20 patients and reported a diagnostic yield of 85%.

6.3 Role of EBUS-UT as a Second Procedure

Although ultrathin bronchoscopes provide excellent accessibility to peripheral lung regions, they have some limitations, including limited availability of biopsy instruments, weak suction power due to the relatively small working channel, inferior visibility, and reduced maneuverability because of their flexible design. Consequently, in clinical practice, ultrathin bronchoscopy is often used as a second-line procedure when first-line procedures with larger bronchoscopes are unsuccessful [26]. Nishii et al. [27] conduced a retrospective study involving 53 patients in whom rEBUS could not be inserted into the pulmonary lesion (the lesion was not visible or the probe was adjacent to but not within the lesion) using a thin bronchoscope; these patients underwent ultrathin bronchoscopy in the same setting. The ultrathin bronchoscope successfully provided a "within" lesion rEBUS image in 59.1% of cases and a definitive diagnosis in 65.9%. Similarly, in a prospective study by Oki et al. [28], ultrathin bronchoscopy was performed on 87 peripheral pulmonary lesions where the rEBUS probe could not be inserted during thin bronchoscopy (the lesion was not visible, or the probe was adjacent to the lesion). The rEBUS probe could be successfully inserted into the lesions ("within" lesion rEBUS image) in 55% of cases, and the diagnostic yield increased from 13% to 41% when ultrathin bronchoscopy was added to thin bronchoscopy. Thus, EBUS-UT is valuable for diagnosing small peripheral pulmonary lesions, both as a first-line and a second-line procedure.

6.4 Sampling Methods

Forceps biopsy has traditionally been the standard sampling technique during ultrathin bronchoscopy, but several studies have demonstrated that incorporating additional sampling techniques can enhance diagnostic yield. Notably, cryobiopsy and transbronchial needle aspiration (TBNA) show promising potential. In a prospective study, Oki et al. [29] evaluated forceps biopsy and cryobiopsy on 50 lesions (median length: 17.9 mm) with diameters ≤30 mm during EBUS-UT. The diagnostic yields for forceps biopsy, cryobiopsy, and their combination were 54%, 62%, and 74%, respectively. In another study, Sumi et al. [30] conducted forceps biopsy and cryobiopsy on 66 lesions ≤30 mm in diameter during EBUS-UT, achieving a diagnostic yield of 81.8% with the combined technique. Sumi et al. [31] also explored the addition of TBNA to forceps biopsy during EBUS-UT. In this retrospective study, the diagnostic yields for forceps biopsy, TBNA, and their combination were 72.5%, 68.6%, and 86.3%, respectively. TBNA proved particularly useful for cases with lesions adjacent to the EBUS image, as combining TBNA with forceps biopsy increased the diagnostic yield by up to 21.5% (forceps biopsy, 57.1%, combined forceps biopsy and TBNA, 78.6%).

6.5 Molecular Testing

The latest ultrathin bronchoscopes feature a 1.7-mm working channel, which is larger than that of conventional ultrathin bronchoscopes but still smaller than the 2.0-mm working channel of a standard bronchoscope. This advancement allows for the use of 1.5-mm biopsy forceps, although standard 1.8- or 1.9-mm biopsy forceps are not compatible. Specimens obtained with the smaller 1.5-mm forceps are

generally suitable for single gene expression analysis [32]. However, the success rate of multiplex gene expression analyses, such as next-generation sequencing, is lower for specimens obtained from 1.5-mm forceps compared to those obtained with standard-size biopsy forceps [33, 34]. For molecular testing, technical modifications may be necessary to obtain larger tissue samples. These modifications could include increasing the number of biopsies, incorporating biopsies with a larger bronchoscope, or utilizing cryobiopsy techniques [35].

7 Complications

The complication rates associated with ultrathin bronchoscopy are comparable to those of larger bronchoscopes. The incidence of pneumothorax during ultrathin bronchoscopy has been reported at 2%, with an overall complication rate of 3% [7, 8]. The mechanism of pneumothorax in ultrathin bronchoscopy can differ from that seen with standard bronchoscopes. Due to their smaller diameter, ultrathin bronchoscopes can sometimes reach the visceral pleura and may directly injure it. Oki et al. [36] reported pneumothorax in 6 of 410 patients who underwent ultrathin bronchoscopy using a 2.8-mm bronchoscope, with direct injury to the visceral pleura occurring in two cases. To minimize the risk of such complications, it is crucial to handle the ultrathin bronchoscope gently and carefully, especially in areas close to the pleura.

8 Indications Other Than the Diagnosis of Peripheral Lung Lesions in Adult Patients

The primary advantage of ultrathin bronchoscopes over standard bronchoscopes is their thin body, which allows them to navigate through small airways. This feature has made them valuable for both diagnostic and therapeutic procedures in pediatric patients [37]. In adults, ultrathin bronchoscopes have proven useful for various applications, including retrieving foreign bodies from peripheral lung regions [38], directly observing and administering drugs into cavitary lesions [39, 40], and planning therapeutic interventions by visualizing peripheral airways beyond stenotic areas during therapeutic bronchoscopy [41, 42] and preoperative localization of small peripheral lung lesions [43].

9 Conclusions

Previously, conventional ultrathin bronchoscopes with a 1.2-mm working channel did not accommodate rEBUS, which limited their clinical utility. However, advancements in bronchoscope design have led to the development of new-generation ultrathin bronchoscopes with a larger working channel, enabling the use of EBUS-UT. Additionally, newer guidance modalities such as VBN and CBCT, as well as smaller sampling instruments such as thinner needles and cryoprobes, are now available for these ultrathin bronchoscopes. The integration of these multimodal and multi-instrumental capabilities significantly enhances the diagnostic yield of bronchoscopy, making it a valuable tool both as a first-line and second-line procedure for diagnosing small peripheral pulmonary lesions.

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