Monaldi Archives for Chest Disease

eISSN 2532-5264 https://www.monaldi-archives.org/

Monaldi Arch Chest Dis 2024 [Online ahead of print]

To cite this Article:
Lanfranchi F, Michieletto L. **Peripheral pulmonary lesion: novel approaches in endoscopic guidance systems and a state-of-the-art review.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2024.3115

Peripheral pulmonary lesion:
novel approaches in endoscopic guidance systems and a state-of-the-art review

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Contributions: FL, data collection, writing and editing; LM, supervisioning and final draft editing. Both authors read and approved the final version of the manuscript.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: not applicable

Patient consent for publication: not applicable

Funding: none.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

Abstract

Diagnosis of peripheral pulmonary lesion (PPL) is the most challenging field in bronchoscopy and interventional pulmonology, which concerns early lung cancer diagnosis. Despite novel techniques and new approaches to the periphery of the lung, almost 25% of PPLs remain undiagnosed. Bronchoscopy with guide systems, virtual and/or electromagnetic navigation, robotic bronchoscopy, and transparenchymal nodule approaches tend to provide a higher percentage of reaching the lesion, but the diagnostic yield rarely exceeds 75%, regardless of the instruments used. Further studies are needed to evaluate what the main constraints of this discrepancy are and if a combined use of these techniques and instruments can provide an increased diagnostic yield.

Key words: peripheral pulmonary lesion, lung cancer, electromagnetic navigation bronchoscopy, virtual navigation bronchoscopy, bronchoscopic transparenchymal nodule access.

Introduction

Lung cancer is the most fatal and the second most common cancer worldwide. A lung nodule can represent the earliest detectable stage of lung cancer, defined as a peripheral pulmonary lesion (PPL). It has been well demonstrated that the stage of diagnosis is inversely related to prognosis, with early detection leading to significant improvements in survival [1]. Diagnosis of PPLs suspected of malignancy remains a challenge. However, there are no clear guidelines for these various endobronchial modalities.

Moreover, the ubiquitous use of diagnostic chest computed tomography (CT) scan and the implementation of lung cancer screening, the number of pulmonary nodules detected yearly continues to increase; as obvious, as the number of patients with lung nodules increases, there will be increased demand to perform tissue sampling.

Since the low diagnostic rate for which concerns PPLs, during time novel bronchoscopic approaches has been developed. We aimed to provide a comprehensive review of the novel bronchoscopic techniques and their diagnostic yield (DY). We performed a literature research in Pubmed by using the keywords “bronchoscopy” AND “lung cancer” AND “peripheral pulmonary lesion”.

This review focuses on bronchoscopic navigation techniques and innovative imaging/tumor detection techniques. We aimed to describe recent advancements including identification of knowledge gaps and future perspectives to improve the diagnosis and treatment of PPLs.

PPL is actually considered the most challenging field in bronchoscopy. Traditionally, there are three options for tissue sampling of the lung nodule: surgical resection, CT-guided transthoracic needle biopsy (CT-TTNB), or bronchoscopic biopsy.

During time, novel endoscopic approaches were developed to sample PPL.

The first of them was transbronchial lung biopsy (TBLB) with fluoroscopy, which consists in a radiologic confirmation of which direction the forceps are walking across.

Traditional TBLB, guided only by fluoroscopy, has historically had a low diagnostic yield, with diagnostic rates for nodules under 2 cm estimated to be 34% and still only 63% for lesions over 3 cm [2].

After that technique, advanced bronchoscopic technologies are developed, and include thin/ultrathin bronchoscopes, radial probe endobronchial ultrasound (R-EBUS) with or without guide sheath (GS), virtual bronchoscopic navigation (VBN), electro-magnetic navigational bronchoscopy (ENB), cone-beam CT (CBCT) assisted bronchoscopy, and robotic bronchoscopy.

Radial endobronchial ultrasound (R-EBUS) and guide sheath (GS)

R-EBUS is a thin, flexible catheter with a rotating ultrasound transducer that produces a 360-degree ("radial") image; the catheter easily passes through the working channel of the scope. This provides a 360-degree view in a 2D plane radiating laterally outward from the probe tip [2] (Figure 1).

A 2011 meta-analysis of R-EBUS guided bronchoscopy with 1420 patients reported a pooled diagnostic sensitivity of 73%. Complication rates were similar to non-guided bronchoscopy, with a pneumothorax rate of 1%, with less than half of those requiring chest tube placement [3].

The largest (and more recent) meta-analysis assessing R-EBUS for diagnosis of peripheral pulmonary lesions to date was in 2017 and found an overall weighted diagnostic yield of 70.6%. DY was higher in nodules >2 cm, malignant nodules, and those with a positive bronchus sign. Not surprisingly, the yield was higher when the probe had a concentric view rather than eccentric [4].

The benefit of R-EBUS lies in its ability to provide guided imaging to distal locations, allowing for real-time operator feedback regarding nodule location before the biopsy. Larger nodules and the ability to obtain a concentric view further increases the likelihood for higher diagnostic yield. A major limitation for R-EBUS is that an eccentric signature tells the operator that the nodule is next to the airway but we don't know where the nodule is (i.e., upper, lower, left, right). Thus, improved techniques such as bronchoscope manipulation and guide sheaths are needed for improved DY [5]. Although guide sheaths (GS) (Figure 2, [6]) may have improved the ability to find the same pathway towards the target lesion, in a meta-analysis a similar pooled diagnostic yield (72.7%) [7] was reported compared to R-EBUS without GS use (70.6%) [4] probably due to dislodgment of the guide sheath by the stiff biopsy tools [8].

Conversely, a RCT conducted by Oki et al in which compared DY between TBLB plus GS and without GS revealed that the DY of histological specimens from the GS group was significantly higher than that from the non-GS group (55.3% versus 46.6%; p=0.033) [9].

The major limitations in R-EBUS procedures are misinterpretations of radial ultrasound signals in inexperienced operators and the fact that radial probe is more flexible than forceps; thus, after the lesion is identified, the forceps could not reach the target because of its stiffness.

Moreover, R-EBUS does not provide a real-time biopsy because when R-EBUS reaches the lesion, the probe has to be withdrawn to provide the biopsy tool insertion on the same working channel of the scope. An alternative option recently available is a real-time radial endobronchial ultrasonography with transbronchial needle aspiration (RT-R-EBUS-TBNA), in which TBNA and not TBLB can be performed, but a contemporary view (R-EBUS images and TBNA) is available; DY reported is 69% [10].

Thin/ultrathin bronchoscopy (TB/UTB)

The reasons to use TB/UTB lies in fact that the major limitation of conventional bronchoscopy is the anatomic constraints of the physical bronchoscope and its inability to reach distal subsegmental levels owing to the bronchoscope's large outer diameter (OD). Conversely, TB/UTB (OD < 3 mm) can go deeper to the lung periphery, often reaching the ninth bronchial generation, gaining improved access to peripheral lesions for tissue sampling [11]. TB/UTB is often combined with other guided techniques, such as CT guidance, virtual bronchoscopic navigation (VBN) and R-EBUS, to improve lesion localization.

One retrospective study comprising 44 of 338 patients who underwent bronchoscopy evaluated whether substituting a TB with the UTB during multimodal bronchoscopy improved lesion ultrasound visualization and diagnostic yield (DY). After substitution, in cases where the radial probe was within the target lesion (a concentric view), the DY was 80%. The yield decreased to 72% when the probe is adjacent to the lesion (eccentric). Overall DY was 65% [12]. This demonstrated that substitution of TB for UTB as needed improved position of R-EBUS probe. With an improvement in view, there was an increase in DY.

A 2015 trial from Japan randomized 310 patients who underwent TBLB with R-EBUS, fluoroscopy and VBN to either ultrathin bronchoscope (3 mm) or thin bronchoscope (4 mm) plus guide sheath (TB+GS). The UTB could reach more distal bronchi (median 5th vs. 4th generation) and had a higher DY of 74% compared to 59% of the TB+GS group. Complications occurred in 3% vs. 5%, respectively [13].

In a trial from 2019, patients were randomized to undergo R-EBUS, VBN and fluoroscopy-guided biopsy with a 3 mm UTB or a 4 mm TB. In the TB group, small forceps with GS or standard forceps without GS were allowed. Nevertheless, overall DY was higher in the UTB group (70.1% vs. 58.7%) and had a shorter procedure duration (24.8 vs. 26.8 min) with fewer complications (2.8% vs. 4.5%) [11]. Again, we observe that multimodal bronchoscopy with the aid of UTB allows for higher DY than using TB alone.

Complications of TB/UTB are bleeding and pneumothorax, because of their capability to reach sub pleural zones.

Virtual bronchoscopic navigation (VBN) and electromagnetic navigation (EMN)

Selecting the right branching bronchi from a two-dimensional CT- scan in order to accurately access the lung lesion in a real-life three-dimensional setting is challenging. Virtual bronchoscopic navigation (VBN) software creates a virtual map of the airway that describes the route with the highest probability to reach the lesion based on a pre-procedural CT-scan. During bronchoscopy, the navigational system recognizes the visual appearance of the airways and provides guidance towards the target lesion [14] (Figure 3). A limitation of VBN is that it

lacks a real-time adjustment mechanism for navigation errors and does not provide real-time biopsy tool localization feedback.

To overcome this limitation, electromagnetic navigation (EMN) combines a pre-procedural CT-scan to create a virtual tracheobronchial tree, similar to VBN, with an electromagnetic field for real-time guidance. An electromagnetic plate is placed around the patient's chest and biopsy instruments are guided towards the lesion based on the positional information of the electromagnetic sensor and pre-procedural CT-scan [14] (Figure 4, [15]).

The major limitations of these two techniques are the difference between the lesion localization on pre-procedural CT-scan and the real-time localization during the procedure due to respiration, body positioning, atelectasis and cardiac pulse (i.e., the CT-to-body-divergence) [16]; to overcome this divergence, there are many adjustments (i.e., anesthesia) or additional confirmatory tools that can be useful to reduce the difference between the CT scans and real images (R-EBUS, CBCT, AF) [17].

Multiple meta-analyses have been performed to demonstrate the usefulness of VBN and EMN but the outcomes are mostly based on small, single-center analyses with a frequent retrospective design.

One RCT performed VBN in conjunction with the UTB and fluoroscopy and did not demonstrate a significant higher DY in the VBN group (67.1% vs 59.9%), while another RCT used VBN in conjunction with fluoroscopy and R-EBUS showed a significant higher DY in the VBN group (80.4% vs 67.0%) [18, 19]. Lately, the first multi-center cohort study also prospectively evaluated the DY of EMN in 1157 lung lesions and reported a DY of 73% [20].

Cone beam CT and augmented fluoroscopy guided bronchoscopy

Fluoroscopy uses a C-arm X-ray for real-time, two-dimensional visualization of the target lesion and biopsy tools. Although the technique is widely used, few small randomized trials evaluated the use of fluoroscopy and suggest that complementary use of fluoroscopy does not result in an improved DY [21, 22]. This is probably the result of the two-dimensional imaging. The introduction of cone beam CT imaging (CBCT) seems to perform a better identification of the target and this should result in an augmented diagnostic yield.

CBCT, with its rotating arm, scan the patient's chest and perform a 3D visualization of the bronchial anatomy, the lesion and the biopsy tools, in order to correctly reach the pulmonary lesion [23] (Figure 5). To have real-time guidance during biopsy passes, CBCT images of the target lesions can be overlaid on real-time fluoroscopy images, the so-called augmented fluoroscopy (AF) [23, 24]. This technique allows the fluoroscopic visualization of small lesions and GGO that are invisible for conventional fluoroscopy [24, 25]. Also, AF can be used for

confirmation of biopsy tools site, and a real-time evaluation of the biopsy site can be performed (Figure 6).

First studies performing CBCT with AF, either in conjunction with EMN and/or R-EBUS, report a DY ranging from 70.2% to 83.7% [25-27]; one study reported a significant improved navigational success using CBCT with AF and EMN of 89.9% but with a DY of 70.2%. This discrepancy between navigational success and diagnostic yield was attributed to the rigidity of the biopsy tools, breathing motions and manipulation of the endoscope, causing displacement of the instruments [26].

Recently, a navigation and augmented fluoroscopy system has been developed (Body Vision Medical LTD, Israel). This system integrates preprocedural high-resolution computed tomography to intraoperative real-time fluoroscopy using artificial intelligence algorithms. As a result, the system shows the exact projection of the target lesion on fluoroscopic image, facilitating nodule localization and thus increasing DY. However, as the other guidance systems, even if localization ratio of the nodule reaches 93-94%, its DY is still debated, ranging from 75% to 87% [27, 28].

Regarding the radiation exposure performing CBCT plus AF, for the total procedure it ranged from 11 to 29 mSv, which is comparable to average radiation from CT-scan guided lung biopsy [29, 30].

The major limitations of these techniques are their expensiveness, so an exhaustive analysis of number of procedures, single-procedure costs, and effective advantage have to be performed centre-by-centre.

Robotic bronchoscopy (RB)

Current available bronchoscopic guidance tools have demonstrated an improved approximation of the PPLs but the diagnostic yield remains limited. The innovative robotic bronchoscopic platforms (The Monarch™ platform, Auris Health and Ion™ Endoluminal System, Intuitive Surgical) have been developed to overcome the limitations of other guidance tools by redesigning the distal ends of the bronchoscope [31]. A cadaver study compared the peripheral reach of the robotic bronchoscope with a conventional thin bronchoscope with the same outer diameter and demonstrated a superior reach in all segmental bronchi compared to conventional thin bronchoscope [32]. One of the major differences between both platforms is the design of the scope and working channel. The Monarch™ platform has a 4.4-mm scope and a 2.1-mm working channel, while the Ion™ Endoluminal System has a 3.5-mm scope and a 2.0-mm working channel which is occupied by the camera during navigation. Another difference is about the navigation: while the Monarch™ platform uses EMN technology to

navigate, the Ion™ Endoluminal System records the catheter tip and overlay on the CT-scan to navigate.

The first prospective, multi-center study performed robotic bronchoscopy using the Monarch™ platform with R-EBUS in 54 patients with a median lesion size of 23 mm. In 51/53 patients (96.2%) the lesion was successfully localized using R-EBUS, but a diagnostic yield of 74.1% was reported [33]. Another study evaluated the Ion™ Endoluminal System in 130 patients with 159 lung lesions (median lesion size 18 mm) under R-EBUS and/or fluoroscopy guidance, and successful navigation was achieved in 157/159 (98.7%) lesions. An overall DY of 81.7% was reported with an 79.8% sensitivity for malignancy [34].

Although the results of both studies are encouraging, the difference between the identification of the lesion and diagnostic yield are still high, with 20% of PPLs undiagnosed. Moreover, also these techniques are disturbed by patient's breath, cardiac pulse, development of bleeding and/or atelectasis. Also, like CBCT, robotic bronchoscopy is very expensive and its widespread is limited by costs.

Bronchoscopic transparenchymal nodule access (BTPNA)

All the techniques mentioned above present a substantial limitation, that is bronchial anatomy: in fact, if the lesion is not reached by a bronchus, biopsy cannot be performed or cannot provide a diagnosis.

To overcome this limitation, bronchoscopic transparenchymal approaches have been developed to create a pathway towards the lesion.

Bronchoscopic transparenchymal nodule access (BTPNA) is part of the Archimedes VBN platform (Bronchus Medical, Inc, San Jose, California USA), allowing integration of bronchoscopic images, CT data and fluoroscopic images to generate a 3D transparenchymal route with avoidance of blood vessels. Based on the virtual guidance, a coring needle punctures the central airways to have direct access into the parenchyma. A balloon catheter dilates the point-of-entry, allowing a 2.0 mm working channel sheath with a stylet to be advanced to the target lesion under fluoroscopic/CT guidance. Via this tunneled tract, biopsy instruments are introduced and navigated safely towards the lesion [35] (Figure 7). The first study performed in humans was made by Herth and colleagues in 2015 [36]. In 10/12 patients (82%) the procedure was successfully performed with adequate tissue sampling. The most recent study of Sun performed in 114 patients, revealed a BTPNA diagnostic yield of 93.9% and sample adequacy for definite diagnosis in 75.4% of the cases [37].

The most recent study regarding Archimedes' VBN showed encouraging preliminary results, with a DY of 77% (7/9 patients) using Archimedes' VBN and BTPNA in patients that previously underwent to conventional bronchoscopy with R-EBUS and fluoroscopy, with no diagnosis

achieved. Interestingly, this study provided another way to sample PPL, by using miniforceps (CoreDx miniforceps, Boston Scientific, Watertown, MA) into the tunneled tract previously performed (FleXNeedle®, Broncus Medical©, San Jose, CA). This suggests a multimodal approach (needle, miniforceps), using different tools [38]. An alternative technique is the transbronchial access tool (TBAT, Medtronic, Minneapolis, Minnesota, USA) which can be integrated in the superDimension EMN system. To our knowledge, just few case series are reported with this technique [39-41].

Biopsy tools

The more different are navigational systems, the same biopsy tools are available: biopsy forceps, miniforceps and TBNA needles are currently used and described in the studies mentioned above. Biopsy tools are a limiting factor that can explain the divergence between localization and DY ratios. The use of flexible and smaller (1.1 mm) cryoprobes (ErbeCryo®2, Erbe Elektromedizin GmbH 2023, Germany), moving its use from interstitial lung diseases (ILDs) to PPLs diagnosis, represent a promising tool to improve DY of navigational bronchoscopy systems. Description of biopsy tools are not the aim of the present review, but it is interesting to highlight the potential positive impact of cryobiopsy for PPLs. The 1.1 mm flexible cryoprobe (i.e., mini-cryo) allows to freeze and sample huge amount of tissue compared to conventional biopsy tools, increasing DY and obtaining adequate tissue for NGS [42]; its flexibility and dimensions make this probe suitable for all bronchoscopes (TB, UTB). Complications of cryobiopsy can be bleeding and pneumothorax, and consequently management of potentially life-threatening complications should be considered before performing cryobiopsy (Figure 8).

Conclusions

The field of interventional pulmonology for peripheral lung lesion analysis and treatment is evolving rapidly. A desirable future concept is the one-step bronchoscopic approach including navigation to the tumor, biopsy sample and diagnosis for future treatments. PPLs are the current challenge: several bronchoscopic guidance technologies have been developed that resulted in an improved DY of PPLs [33, 34] but data are still poor. Moreover, it is challenging to determine each individual technology's contribution to the diagnostic yield. Actually, whatever navigational technique used, DY now rarely exceeds 75% [33,34,43] with as key limiting factor the lack of needle in target lesion confirmation [44]. Thus, novel techniques regarding needle imaging might be helpful tools to identify malignant lesions and confirm the right place for biopsy, enabling optimal tissue acquisition [45]. However, the data on these techniques are preliminary and further research are needed.

In conclusion, in the last few years technological developments have implemented the options for bronchoscopic tumor navigation and treatment [46]. For which concerns the interventional pulmonology, the one-step bronchoscope approach to diagnose (and treat) will become the future clinical practice.

References

1. CDC. U.S. cancer statistics public use database. Available from: https://www.cdc.gov/united-states-cancer-statistics/public-use/index.html#:~:text=The%20U.S.%20Cancer%20Statistics%20public,developed%20by%20NCI's%20SEER%20Program.

2. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer. Chest 2013;143:e142S-65S.

3. Steinfort DP, Khor YH, Manser RL, Irving LB. Radial probe endobronchial ultrasound for the diagnosis of peripheral lung cancer: systematic review and meta-analysis. Eur Respir J 2010;37:902-10.

4. Ali MS, Trick W, Mba BI, et al. Radial endobronchial ultrasound for the diagnosis of peripheral pulmonary lesions: a systematic review and meta-analysis. Respirology 2017;22:443-53.

5. Kurimoto N, Miyazawa T, Okimasa S, et al. Endobronchial ultrasonography using a guide sheath increases the ability to diagnose peripheral pulmonary lesions endoscopically. Chest 2004;126:959-65.

6. Lachkar S, Guisier F, Roger M, Bota S, Lerouge D, Piton N, Thiberville L, Salaün M. A simple endoscopic method with radial endobronchial ultrasonography for low-migration rate coil-tailed fiducial marker placement. J Thorac Dis 2020;12:1467-74.

7. Zhang SJ, Zhang M, Zhou J, et al. Comparison of radial endobronchial ultrasound with a guide sheath and with distance by thin bronchoscopy for the diagnosis of peripheral pulmonary lesions: a prospective randomized crossover trial. J Thorac Dis 2016;8:3112-8.

8. Gildea TR. Lung lesion localization and the diagnostic drop. Ann Am Thorac Soc 2016;13:1450-2.

9. Oki M, Saka H, Imabayashi T, et al. Guide sheath versus non-guide sheath method for endobronchial ultrasound-guided biopsy of peripheral pulmonary lesions: a multicentre randomised trial. Eur Respir J 2022;59:2101678

10. Yarmus LB, Mallow C, Pastis N, et al. First-in-human use of a hybrid real-time ultrasound-guided fine-needle acquisition system for peripheral pulmonary lesions: a multicenter pilot study. Respiration 2019;98:527-33.

11. Oki M, Saka H, Asano F, et al. Use of an ultrathin vs thin bronchoscope for peripheral pulmonary lesions. Chest 2019;156:954-64.

12. Nishii Y, Nakamura Y, Fujiwara K, et al. Use of ultrathin bronchoscope on a need basis improves diagnostic yield of difficult-to-approach pulmonary lesions. Front Med 2020;7:588048.

13. Oki M, Saka H, Ando M, et al. Ultrathin bronchoscopy with multimodal devices for peripheral pulmonary lesions: a randomized trial. Am J Respir Crit Care Med 2015;192:468-76
14. Reynisson PJ, Leira HO, Hernes TN, et al. Navigated bronchoscopy: a technical review. J Bronchology Interv Pulmonol 2014;21:242-64.
15. Katsis JM, Rickman OB, Maldonado F, Lentz RJ. Bronchoscopic biopsy of peripheral pulmonary lesions in 2020: a review of existing technologies. J Thorac Dis 2020;1:3253-62.
16. Asano F, Eberhardt R, Herth FJF. Virtual bronchoscopic navigation for peripheral pulmonary lesions. Respiration 2014;88:430-40.
17. Pritchett MA, Bhadra K, Calcutt M, Folch E. Virtual or reality: divergence between preprocedural computed tomography scans and lung anatomy during guided bronchoscopy. J Thorac Dis 2020;12:1595-611
18. Ishida T, Asano F, Yamazaki K, et al. Virtual bronchoscopic navigation combined with endobronchial ultrasound to diagnose small peripheral pulmonary lesions: a randomised trial. Thorax 2011;66:1072-7.
19. Asano F, Shinagawa N, Ishida T, et al. Virtual bronchoscopic navigation combined with ultrathin bronchoscopy. A randomized clinical trial. Am J Respir Crit Care Med 2013;188:327-33.
20. Folch EE, Pritchett MA, Nead MA, et al. Electromagnetic navigation bronchoscopy for peripheral pulmonary lesions: one-year results of the prospective, multicenter NAVIGATE study. J Thorac Oncol 2019;14:445-58.
21. Zheng X, Xie F, Li Y, et al. Ultrathin bronchoscope combined with virtual bronchoscopic navigation and endobronchial ultrasound for the diagnosis of peripheral pulmonary lesions with or without fluoroscopy: a randomized trial. Thorac Cancer 2021;12:1864-72.
22. Tachihara M, Tamura D, Kiriu T, et al. Bronchoscopy using virtual navigation and endobronchial ultrasonography with a guide sheath (EBUS-GS) with or without fluoroscopy for peripheral pulmonary lesions. Kobe J Med Sci 2018;63:E99-104.
23. Setser R, Chintalapani G, Bhadra K, Casal RF. Cone beam CT imaging for bronchoscopy: a technical review. J Thorac Dis 2020;12:7416-28.
24. Cheng GZ, Liu L, Nobari M, et al. Cone beam navigation bronchoscopy: the next frontier, J Thorac Dis 2020;12:3272-8.
25. Yu KL, Yang SM, Ko HJ, et al. Efficacy and safety of cone-beam computed tomography-derived augmented fluoroscopy combined with endobronchial ultrasound in peripheral pulmonary lesions. Respiration 2021;100:538-46.

26. Verhoeven RLJ, Fütterer JJ, Hoefsloot W, van der Heijden E. Cone-beam CT image guidance with and without electromagnetic navigation bronchoscopy for biopsy of peripheral pulmonary lesions. J Bronchol Interv Pulmonol 2021;28:60-9.
27. Cicenia J, Bhadra K, Sethi S, et al. Augmented fluoroscopy: a new and novel navigation platform for peripheral bronchoscopy. J Bronchology Interv Pulmonol 2021;28:116-23.
28. Pritchett MA. Prospective analysis of a novel endobronchial augmented fluoroscopic navigation system for diagnosis of peripheral pulmonary lesions. J Bronchology Interv Pulmonol 2021;28:107-15.
29. Kheir F, Thakore SR, Uribe Becerra JP, et al. cone-beam computed tomography-guided electromagnetic navigation for peripheral lung nodules. Respiration 2021;100:44-51.
30. Casal RF, Sarkiss M, Jones AK, et al. Cone beam computed tomography-guided thin/ultrathin bronchoscopy for diagnosis of peripheral lung nodules: a prospective pilot study. J Thorac Dis 2018;10:6950-9.
31. Kent AJ, Byrnes KA, Chang SH. State of the art: robotic bronchoscopy. Semin Thorac Cardiovasc Surg 2020;32:1030-5.
32. Chen AC, Gillespie CT. Robotic endoscopic airway challenge: REACH assessment. Ann Thorac Surg 2018;106:293-7.
33. Chen AC, Pastis NJ, Mahajan AK, et al. Robotic bronchoscopy for peripheral pulmonary lesions: a multicenter pilot and feasibility study (BENEFIT). Chest 2021;159:845-52.
34. Kalchiem-Dekel O, Connolly JG, Lin IH, et al. Shape-sensing robotic-assisted bronchoscopy in the diagnosis of pulmonary parenchymal lesions. Chest 2022;161:572-82.
35. Silvestri GA, Herth FJ, Keast T, et al. Feasibility and safety of bronchoscopic transparenchymal nodule access in canines: a new real-time image-guided approach to lung lesions. Chest 2014;145:833-8.
36. Herth FJF, Eberhardt R, Sterman D, et al. Bronchoscopic transparenchymal nodule access (BTPNA): first in human trial of a novel procedure for sampling solitary pulmonary nodules. Thorax 2015;70:326-32.
37. Sun J, Criner GJ, Dibardino D, et al. Efficacy and safety of virtual bronchoscopic navigation with fused fluoroscopy and vessel mapping for access of pulmonary lesions. Respirology 2022;27:357-65.
38. Lanfranchi F, Mancino L, Foltran G, et al. Use of the Archimedes navigation system to diagnose peripheral pulmonary lesions: preliminary Italian results. Front Oncol 2024;14:1394022.
39. Anciano C, Brown C, Bowling M. Going off road: the first case reports of the use of the transbronchial access tool with electromagnetic navigational bronchoscopy. J Bronchol Interv Pulmonol 2017;24:253-6.

40. Bowling MR, Brown C, Anciano CJ. Feasibility and safety of the transbronchial access tool for peripheral pulmonary nodule and mass. Ann Thorac Surg 2017;104:443-9.
41. Sobieszczyk MJ, Yuan Z, Li W, Krimsky W. Biopsy of peripheral lung nodules utilizing cone beam computer tomography with and without trans bronchial access tool: a retrospective analysis. J Thorac Dis 2018;10:5953-9.
42. Oki M, Saka H, Kogure Y, et al. Ultrathin bronchoscopic cryobiopsy of peripheral pulmonary lesions. Respirology 2023;28:143-51.
43. Sainz Zuniga PV, Vakil E, Molina S, et al. Sensitivity of radial endobronchial ultrasound-guided bronchoscopy for lung cancer in patients with peripheral pulmonary lesions: an updated meta-analysis. Chest 2020;157:994-1011.
44. Yarmus L, Akulian J, Wahidi M, et al. A prospective randomized comparative study of three guided bronchoscopic approaches for investigating pulmonary nodules: the PRECISION-1 study. Chest 2020;157:694-701.
45. Fernandes S, Williams G, Williams E, et al. Solitary pulmonary nodule imaging approaches and the role of optical fibre-based technologies. Eur Respir J 2021;57:2002537.
46. Villalba AJA, Ost DE. Bronchoscopic treatment of early-stage peripheral lung cancer. Curr Opin Pulm Med 2024;30:337-45.

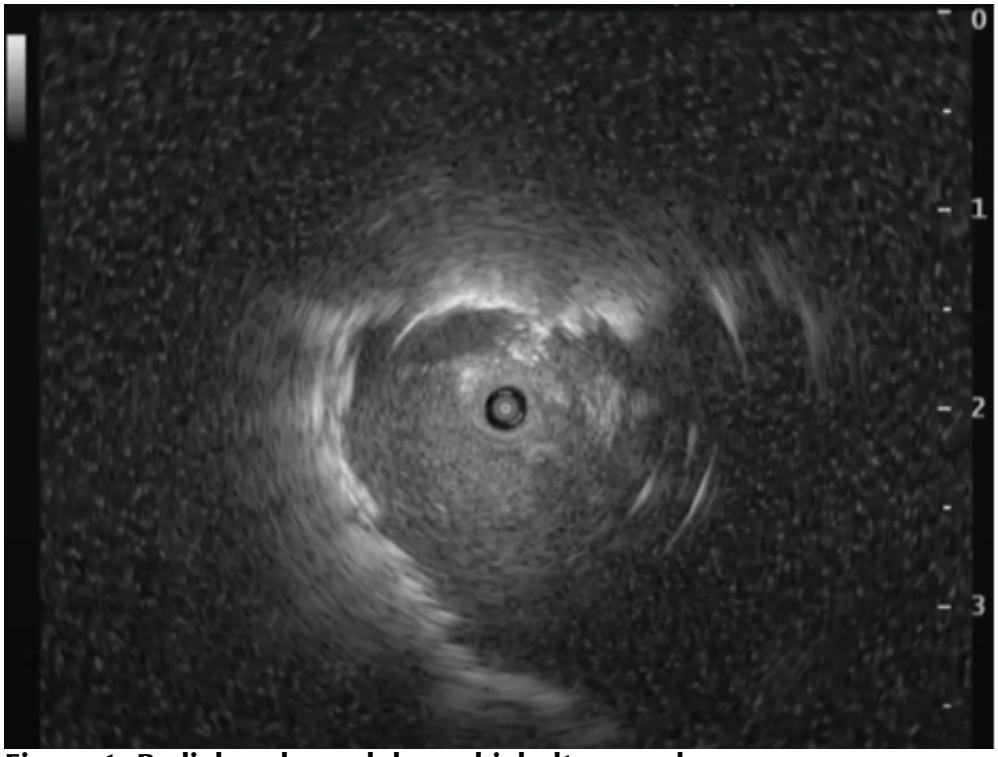

Figure 1. Radial probe endobronchial ultrasound

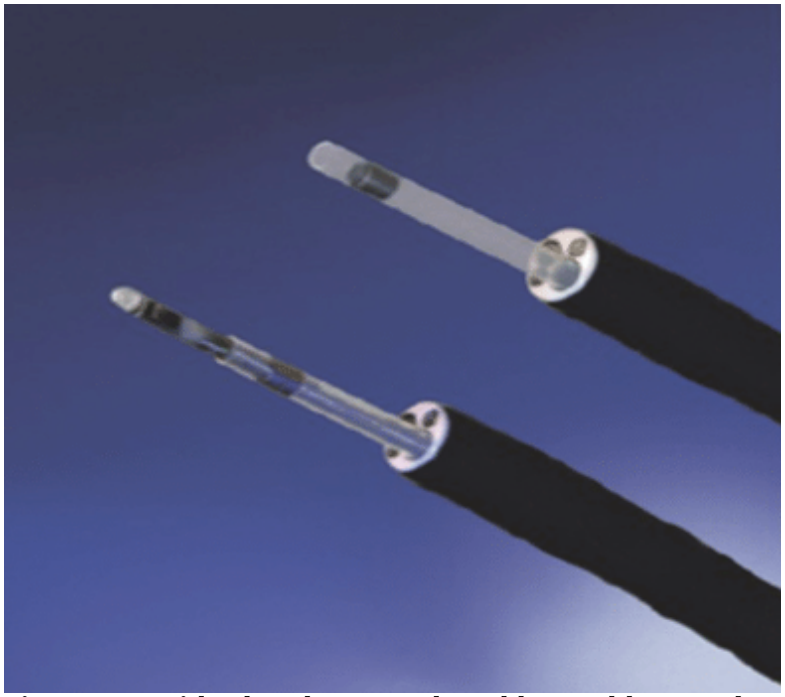
Figure 2. Guide sheath. Reproduced by Lachkar *et al.* (2020).

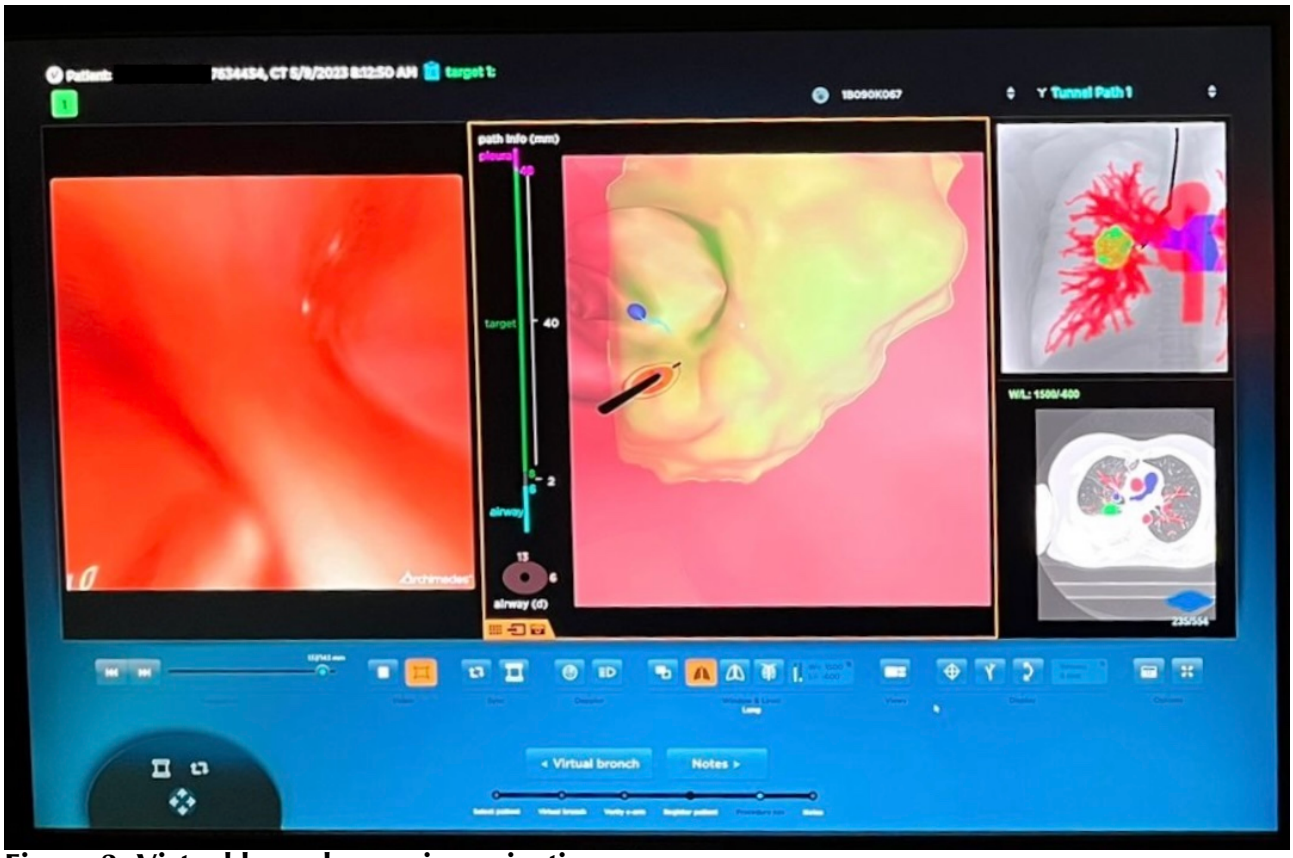

Figure 3. Virtual bronchoscopic navigation.

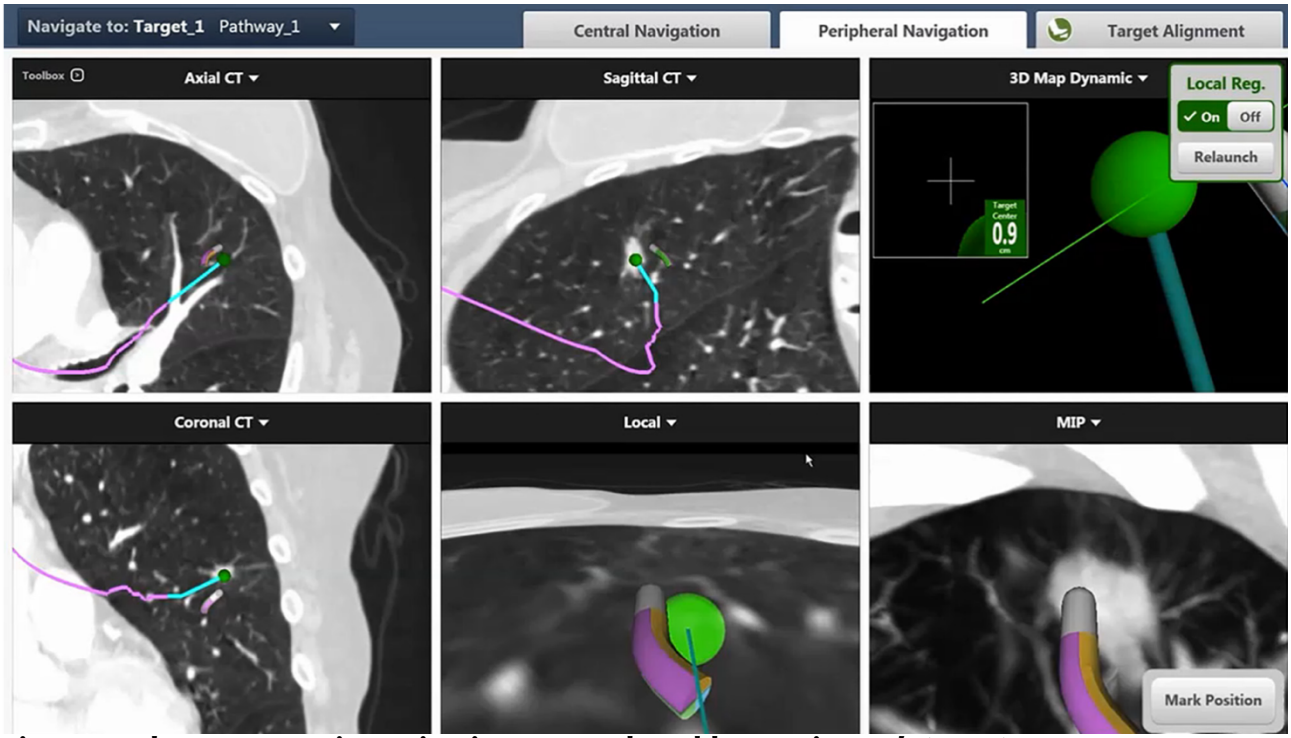

Figure 4. Electromagnetic navigation. Reproduced by Katsis *et al.* (2020).

Figure 5. Cone-beam computed tomography. Reproduced with permission from Siemens Healthcare GmbH.

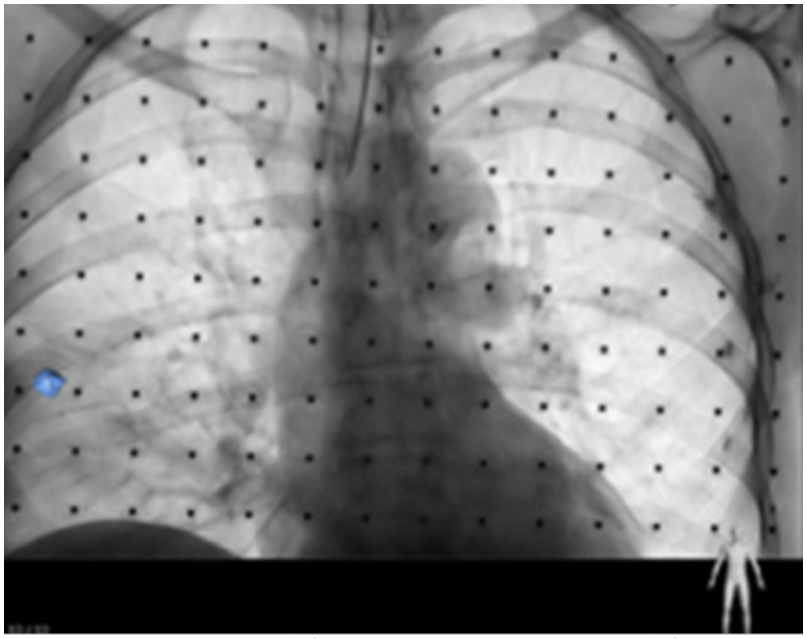

Figure 6. Augmented fluoroscopy. Reproduced from Cheng *et al.* (2020).

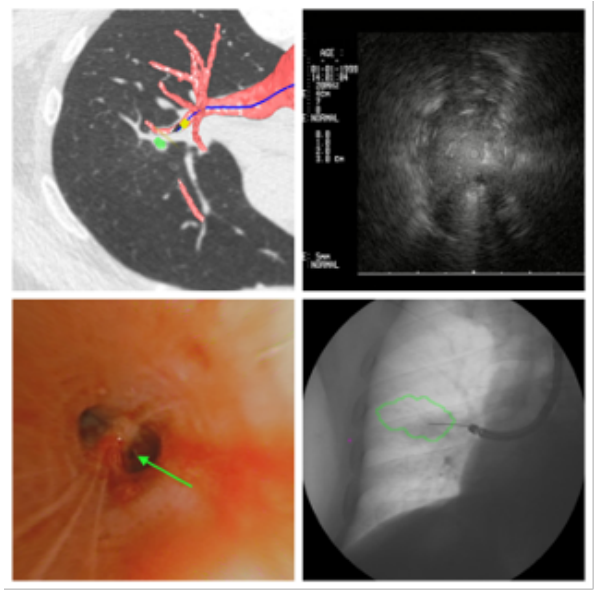

Figure 7. Bronchoscopic transparenchymal nodule access.

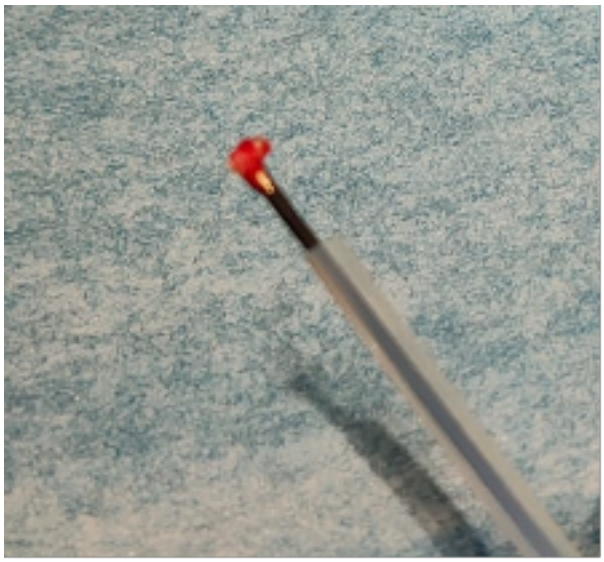

Figure 8. Cryobiopsy.