Medical and Research Publications
International Open Access

Review Article **Journal of MAR Pulmonology (Volume 5 Issue 5)**

Diagnostic Accuracy of Radial Probe Endobronchial Ultrasound in Peripheral Pulmonary Lesions: Systematic Review and Meta Analysis

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Received Date: January 17, 2023

Published Date: February 01, 2023

DOI: 10.1027/marpy.2023.0225

Abstract

Background: *Increasing numbers of peripheral pulmonary lesions* ***(****PPLs****)*** *suggestive of early-stage lung cancer are being discovered thanks to lung cancer screening using computed tomography of the chest. PPLs may be sampled using radial endobronchial ultrasonography* ***(****R-EBUS****)*** *for early lung cancer diagnosis and treatment. Using R-EBUS has the potential to improve diagnostic accuracy, which justifies its use.*

Objective: *Examining how well R-EBUS performs in comparison to other diagnostic methods for PPLs was the focus of this research.*

Methods: *A meta-analysis and systematic review were performed. Original study providing a diagnostic accuracy of R-EBUS for PPLs found on computed tomography chest questionable for malignancy was sought for by a search of the Pubmed, Ovid, Cochrane, Medline, and Embase databases.* I^2 *was used to measure the degree of dissimilarity between the studies. Diagnostic accuracy was aggregated using random effects models. Meta-regression was used to investigate the factors that contributed to the diversity of study results. The impact of publication bias and the size of studies were evaluated.*

Results: *One hundred trials involving 3204 patients and 5566 PPLs. Overall diagnostic accuracy for R-EBUS was 72.4%* ***(****95% CI: 68-76.1****)*** *Less than 2% of complications were seen across all localization methods.*

Conclusion: *High diagnostic accuracy is combined with a high rate of successful PPL localization when using the R-EBUS probe. Diagnostic algorithms are the most practical choice for healthcare authorities.*

MeSH Keywords: *Pulmonary Lesion, Pulmonary Nodule or Peripheral pulmonary Lesion, Lung nodules or Lung tumor, Lung Cancer or Pulmonary Cancer, Probe radial Endobronchial Ultrasound or R- EBUS.*

Abbreviations

R- EBUS: Radial Probe Endobronchial Ultrasound

PPLs: Peripheral Pulmonary Lesions

CT: Computed Tomography Scan

CT- TTNB: Computedtomography guidedtransthoracicneedlebiopsy

ACCP: American College of Chest Physicians

ENB- Electromagnetic Navigational Bronchoscopy

PRISMA: Preferred Reporting Items for Systematic reviews and Meta-analysis

QUADAS: Quality Assessment of Diagnostic Accuracy Studies

CI: Confidence Intervals

Introduction

Background

CT **(**chest lung cancer**)** screening programs in Europe are detecting an increasing number of peripheral pulmonary lesions **(**PPLs**)** in current and past smokers that are suspicious for early-stage lung cancer **(**McWilliams et al., 2013; While et al., 2016**)**. For PPLs larger than 8 mm in these high-risk individuals, current clinical practise recommendations advise additional diagnostic examination **(**Postmus et al., 2017**)**. According to data from the National Lung Screening Trial **(**NLST**)**, screening computed tomography **(**CT**)** of the chest has a false-positive **(**FP**)** PPL rate that may approach 96.4%. This emphasises the need of a reliable histologic diagnosis of lung cancer for guiding lesion care and determining which patients would gain the most from curative-intent surgical lung resection **(**Ding et al., 2022**)**. Also, some people with early-stage lung cancer may be medically inoperable because of other health issues or because they have inadequate lung function. Noninvasive local treatments, such as external-beam radiation therapy, are an option in certain situations, but only if a proper diagnosis has been made **(**Rowell & Williams, 2001**)**.

Traditional biopsy techniques for PPL diagnosis include transbronchial biopsy guided by fluoroscopy and computed tomography of the chest-guided transthoracic needle biopsy (CT-TTNB). Care for patients with PPL is no longer recommended to be based only on flexible bronchoscopy as stated in the recommendations published by the American College of Chest Physicians (ACCP). This is related to its poor diagnostic yield, particularly for PPLs smaller than 20 mm in diameter and those with nonsolid density on CT of the chest (Planchard et al., 2019).Tobacco smokers with emphysema have additional hazards during CT-TTNB, including pneumothorax (collapse of the lung tissue), hemorrhage, and radiation overexposure (Lee et al., 2022).

Rationale

Image-assisted diagnostic tools for use with flexible bronchoscopy have been developed to improve diagnostic accuracy and patient safety as more peripheral lung nodules suspected for malignancy are found via lung cancer screening programmes. Bronchoscopy guided by radial endobronchial ultrasound (R-EBUS) is one example (Zheng et al., 2022).

Evaluation of peripheral lung lesions that cannot be accessed by conventional flexible bronchoscopy with R-EBUS is indicated in the ACCP recommendations for the diagnosis and treatment of lung cancer (Kurihara et al., 2022).Due to the high cost of ENB consumables per case in a single-payer public healthcare system, R-EBUS has a greater reach in Canada (McGuire et al., 2020).

The R-EBUS procedure for PPL biopsy entails inserting a micro (20-MHz) ultrasonic probe of 1.4 millimetres in diameter into the working channel of a flexible bronchoscope. This creates the opportunity for direct circular contact to be made with the small peripheral airways. This allows for the surrounding pulmonary structures and PPL to be seen by ultrasonography, which in turn makes it possible to do a biopsy with either forceps or an aspiration needle or cytology brush. R-EBUS offers the advantage of enhancing PPL diagnostic yield while eliminating radiation exposure from fluoroscopy or CT guided needle biopsy, in comparison to traditional flexible bronchoscopy and transbronchial biopsy (Jiang et al., 2020). When compared with CT-TTNB, the number of reports of concomitant bleeding and pneumothorax is likewise much reduced with R-EBUS (Jiang et al., 2020).

Combining computerized bronchoscopy airway architecture is required in order to perform R-EBUS for peripheral lung lesion biopsy, as explained in further detail by Tang et al. (2020).

It is allowed to get a visualization of the PPL and adjacent lung tissues while performing a biopsy. There are a number of studies that have been conducted at a single site and have reported the diagnostic yields and the rates of procedure complications for R-EBUS. In the past, a meta-analysis evaluating these outcomes was performed using one meta-analysis for each modality, respectively **(**Toennesen et al., 2022**)**.On the other hand, the test performance features of these various PPL localization systems have not been compared for the purpose of discussion in meta-analysis. At addition, after the release of the earlier findings, a number of additional studies that evaluated the effectiveness of R-EBUS in a single center and were reviewed by experts in the field have been made public.

Objectives

The major purpose of this study is to evaluate the relative effectiveness of R-EBUS biopsy in terms of successful localization and diagnostic accuracy. The secondary purpose is to identify the incidence of problems linked to biopsies for each method.

Hypothesis

Radial endobronchial ultrasound R-EBUS is not an accurate method for the biopsy/treatment of peripheral pulmonary lesions **(**PPLs**)**.

Outcomes

The primary exposures that will be evaluated are those that are governed by R-EBUS and PPL. The primary health outcomes that need to be reported are the diagnostic accuracy and sensitivity of each sample technique for malignancy. Complication rates for each technology are one of the secondary outcomes that need to be reported **(**bleeding, pneumothorax, aspiration pneumonitis, and respiratory failure**)**.

The results of this research might potentially be utilised to advise public health policy on the most effective image-guided way to discover peripheral pulmonary nodules that have been found on CT chest scans and get a biopsy of those nodules. The results of this study might potentially be included into clinical treatment algorithms for peripheral lung nodules that are discovered via CT lung cancer screening programmes.

Materials and Methods

Literature Search

The standard PRISMA procedure **(**Preferred Reporting Items for Systematic reviews and Meta-analysis**)**, which was developed by the Cochrane Collaboration, served as a guide for both the systematic review and the meta-analysis that was conducted. To find all of the studies that employed R-EBUS as a therapy for peripheral pulmonary lesions **(**PPLs**)** seen on CT chest, an electronic systematic search of the medical literature was carried out. From 1948 through 2023, the databases Pubmed, Ovid, Cochrane, Medline, and Embase were searched using a predetermined keyword search approach **(**Table 1**)**. In order to locate any and all articles that could be suitable for incorporation, a comprehensive manual search of all references included within the primary articles and review papers was carried out. The search was restricted to research involving human participants and to those that were available in full-text form in English. The use of the systematic search method resulted in the discovery of a total of 1065 articles.

Selection Criteria

The criteria for selection were decided upon in advance, and then the abstracts of all 1065 articles were assessed in line with those criteria. All of the following criteria were met by the papers that were put forth for consideration as candidates for a full-text review: A minimum of five patients were enrolled in the study by me; **(**ii**)** the histologic diagnostic yield of R-EBUS was reported for peripheral pulmonary lesions; **(**iii**)** the existence of the peripheral pulmonary lesions was confirmed by CT chest; and **(**iv**)** the study population included patients who were thought to have malignant peripheral pulmonary lesions. Only the abstracts that were able to meet all of these criteria were allowed to go on to the full-text article review step. The reference lists of the publications that were considered for exclusion from the study were manually searched for potentially additional relevant articles that matched the criteria for study inclusion. Although reviews, editorials, nonpeer reviewed papers, and meta-analyses were not considered for inclusion in the research, these types of articles were not considered for inclusion in the research.

After going over the entire texts of the studies, the ones that used linear EBUS to sample the mediastinal lymph nodes, did not use R-EBUS to sample the peripheral pulmonary lesions, and focused primarily on

benign diseases such as sarcoidosis were ruled out. In addition, studies were omitted from the final analysis if there was no reference standard used to compare the index test.

Study Quality Assessment

The Quality Assessment of Diagnostic Accuracy Studies **(**QUADAS**)** method was used to evaluate the quality of the studies that were included in the review **(**Whiting et al., 2003**)**. The QUADAS tool consists of 14 elements, each of which is documented per study as "absent" or "present." These elements are as follows: sufficient index test description and reference; representative study sample spectrum; reported reasons for study participant withdrawals and loss to follow-up; relevant clinical information; index and reference test interpretation blinding; definition of positive test result; complete verification of diagnosis with independent reference standard; avoided clinical review bias; appropriate clinical information; and appropriate clinical information. A total quality score between 11 and 14 was rated "excellent," 7 to 10 was considered "average," and 6 was considered "poor." The QUADAS elements that were present each received a score of 1 **(**Whiting et al., 2003**)**.

Table 1: Keyword search in electronic databases

Search ID	***Search Terms***
1	Pulmonary lesion
2	pulmonary nodule or peripheral pulmonary lesion
3	Lung's nodules or lung tumor
4	Lung cancer or pulmonary cancer
5	Probe radial endobronchial ultrasound or R-EBUS
6	All above and other related terms were searched

Data Extraction

Data were collected, to the extent that it was possible, on the following topics: study characteristics; a description of the study population; the results of the biopsy, which were categorized as positive **(**either malignant or benign**)**, nondiagnostic, normal lung tissue, or reported as inconclusive, or as requiring further tissue confirmation **(**chronic inflammation, organizing pneumonia, or atypical cells**)**; the complications, which were categorized as absent, bleeding that was self-limited **(**minor**)**, topical treatment **(**moderate**)**

The following intervention methods were extracted: sedation type, the number of times a biopsy was attempted on each lesion, sample methodology, examination length, supplementary guiding strategies, and a histology reference standard.

In order to compute the following for R-EBUS, respectively, selected study biopsy performance results were retrieved and used **(**Whiting et al., 2003**)**.

$$Diagnostic\ accuracy = \frac{malignant\ biopsy\ results\ confirmed\ correct\ by\ reference\ standard}{sampled\ nodules\ with\ known\ final\ diagnosis}$$

The findings of the index test **(**R-EBUS**)** and the reference test were used to classify the research participants, and two-by-two contingency tables were generated for each of the studies.

The data that were extracted were combined with weighted averages, where the weight of each research was determined by the size of its sample population.

Results

Study Selection

1065 results came up during the comprehensive search **(**Fig. 1**)**. After going over the abstracts of each article, we ultimately decided to look at 220 of them in their entirety. Out of these, 120 were disregarded because they did not pertain to the use of R-EBUS in the diagnosis accuracy for the treatment of peripheral pulmonary lesions; they did not pertain to the diagnostic yields of these technologies; or they were not unique research **(**review articles or editorial commentaries**)**. At long last, the meta-analysis was down to just 100 papers **(**Charvez et al., 2015**)**.

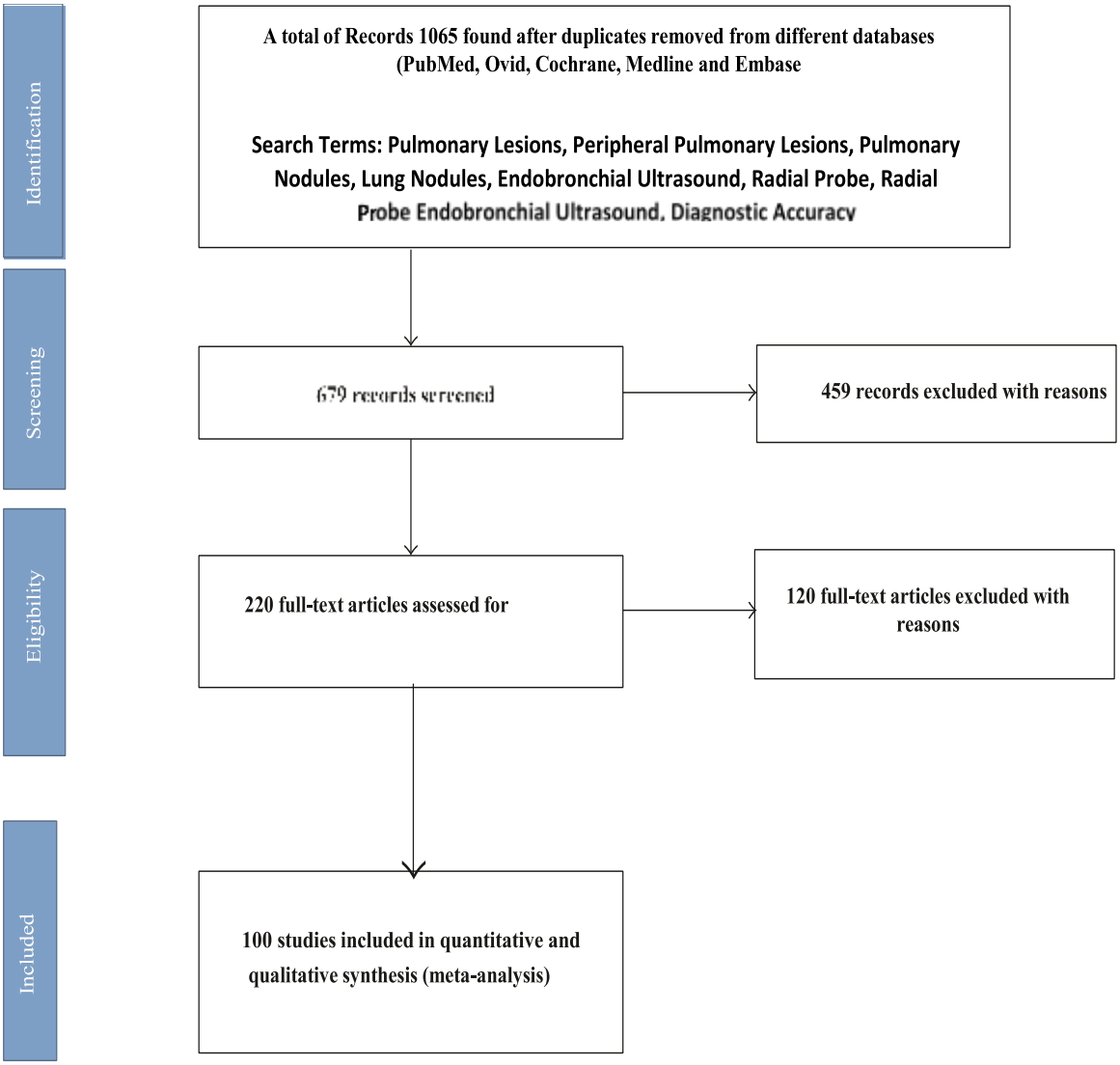

Fig1. Study flow chart following PRISMA guidelines.

Table 2. Study Participants and Peripheral Pulmonary Lesions Characteristics

References	Index Test	Participants	Study Design	Average Age %	Lung Cancer Prevalence %	Lung Lesions	Lesion Diameter (mm)
Agrawal et al. (2022)	R-EBUS	40	Prospective Case Series	65.1	88.7	55	23
Ankudavicius et al. (2022).	R-EBUS	48	Prospective Case Series	64.2	65	12	35
Avasarala et al. (2020).	R-EBUS	40	Prospective Case Series	67	38	50	36
Bailey et al. (2019).	R-EBUS	ND	Prospective Case Series	ND	56.3	49	23
Bellinger et al. (2021).	R-EBUS	91	Prospective Case Series	60	85	40	26
Bo et al. (2019).	R-EBUS	104	Prospective Case Series	66	58.1	31	22
Boonsarngsuk et al. (2020).	R-EBUS	248	Prospective Case Series	66	33.7	95	21
Chandrika & Yarmus (2020).	R-EBUS	13	Prospective Case Series	69	94.1	101	28
Chen et al. (2021).	R-EBUS	47	Prospective Case Series	63.1	78	25	26
Chen et al. (2020).	R-EBUS	58	Prospective Case Series	56	65	13	35
Chen et al. (2021).	R-EBUS	56	Prospective Case Series	32	28	56	36
Chen et al. (2022).	R-EBUS	93	Prospective Case Series	80	95	35	36
Chen et al. (2019).	R-EBUS	5	Prospective Case Series	65	68	13	321
Choi et al. (2022).	R-EBUS	52	Prospective Case Series	62	42	65	35
Choudhary et al. (2019).	R-EBUS	37	Prospective Case Series	35	27	38	36
Crombag (2019).	R-EBUS	32	Prospective Case Series	53	69	34	21
Dooms, C. (2019).	R-EBUS	12	Prospective Case Series	56	35	36	22
Fielding et al. (2019).	R-EBUS	24	Prospective Case Series	64	39	35	26
Folch et al. (2020).	R-EBUS	23	Prospective Case Series	56	654	65	25
Gasparini et al. (2022).	R-EBUS	58	Prospective Case Series	57	65	36	24
Giri et al. (2022).	R-EBUS	83	Prospective Case Series	86	38	362	21
Giri et al. (2021).	R-EBUS	61	Prospective Case Series	67	85	34	22
Gmehlin et al. (2022).	R-EBUS	27	Prospective Case Series	61	87	62	14
Han, J., & Lee, J. (2022).	R-EBUS	28	Prospective Case Series	65	52	34	16
Ho et al. (2022).	R-EBUS	48	Prospective Case Series	62	25	18	24
Hong et al. (2021).	R-EBUS	79	Prospective Case Series	69	65	34	26

Hong et al. (2021).	R-EBUS	15	Prospective Case Series	42	34	26	14
Hotta et al. (2022).	R-EBUS	72	Prospective Case Series	54	62	34	21
Huang et al. (2019).	R-EBUS	35	Prospective Case Series	25	35	95	25
Huang et al. (2019).	R-EBUS	32	Prospective Case Series	54	96	258	38
Haoran et al. (2022).	R-EBUS	38	Prospective Case Series	57	67	36	36
Ishiwata et al. (2021).	R-EBUS	56	Prospective Case Series	68	68	31	34
Ishiwata et al. (2021).	R-EBUS	94	Prospective Case Series	19	61	34	36
Ito et al. (2022).	R-EBUS	104	Prospective Case Series	62	25	321	32
Ito et al. (2021).	R-EBUS	40	Prospective Case Series	45	687	35	35
Ito et al. (2022).	R-EBUS	63	Prospective Case Series	24	65	62	14
Ito et al. (2021).	R-EBUS	35	Prospective Case Series	27	65	35	25
Jiang et al. (2022).	R-EBUS	36	Prospective Case Series	56	71	35	21
Juul et al. (2022).	R-EBUS	37	Prospective Case Series	54	65	32	25
Kalchiem-Dekel et al. (2022).	R-EBUS	47	Prospective Case Series	56	36	21	30
Katsis et al. (2020).	R-EBUS	15	Prospective Case Series	57	64	23	26
Kho et al. (2019).	R-EBUS	24	Prospective Case Series	86	85	65	20
Kim et al. (2023).	R-EBUS	51	Prospective Case Series	67	69	36	23.5
Kramer& Annema (2021).	R-EBUS	230	Prospective Case Series	61	94	95	18
Kuijvenhoven et al. (2020).	R-EBUS	24	Prospective Case Series	65	35	36	27
Kuijvenhoven et al. (2021).	R-EBUS	21	Prospective Case Series	62	92	94	28
Lee & Song (2022).	R-EBUS	54	Prospective Case Series	69	64	38	21
Lee et al. (2022).	R-EBUS	68	Prospective Case Series	42	37	36	33.5
Lee et al. (2019).	R-EBUS	104	Prospective Case Series	54	61	68	23
Leong et al. (2019).	R-EBUS	248	Prospective Case Series	25	35	68	35
Ruan (2019).	R-EBUS	13	Prospective Case Series	54	38	95	36
Li et al. (2019).	R-EBUS	47	Prospective Case Series	57	64	64	34
Li et al. (2022).	R-EBUS	58	Prospective Case Series	68	32	34	36

Liam et al. (2021).	R-EBUS	56	Prospective Case Series	19	35	36	35
Lin et al. (2022).	R-EBUS	93	Prospective Case Series	62	68	38	33
Liu et al. (2022).	R-EBUS	5	Prospective Case Series	45	64	39	32
Lou et al. (2022).	R-EBUS	52	Prospective Case Series	24	35	34	32
Ma et al. (2020).	R-EBUS	37	Prospective Case Series	27.00	69	37	23
Matsumoto et al. (2021).	R-EBUS	32	Prospective Case Series	56	94	36	32
McGuire et al. (2020).	R-EBUS	12	Prospective Case Series	54	92	64	30
Miotto et al. (2020).	R-EBUS	24	Prospective Case Series	64.2	67	37	26
Mondoni et al. 2022).	R-EBUS	23	Prospective Case Series	67	74	61	20
Moon et al. (2019).	R-EBUS	65	Prospective Case Series	ND	72	35	23.5
Muñoz-Largacha et al. 2021).	R-EBUS	24	Prospective Case Series	60	76	38	18
Oki et al. (2019).	R-EBUS	32	Prospective Case Series	66	6	64	27
Park et al. (2020).	R-EBUS	248	Prospective Case Series	66	67	32	28
Paul & Munavvar (2020).	R-EBUS	31	Prospective Case Series	69	38	35	21
Poudel et al. (2021).	R-EBUS	93	Prospective Case Series	63.1	81	68	33.5
Pritchett (2021).	R-EBUS	4	Prospective Case Series	78	83	64	22
Qian et al. (2020).	R-EBUS	35	Prospective Case Series	66	64	35	36
Qian et al. 2020)	R-EBUS	16	Prospective Case Series	40	90	56	35
Rahman, N. (2019).	R-EBUS	64	Prospective Case Series	56	34	54	33
Reisenauer et al. (2022).	R-EBUS	54	Prospective Case Series	54	61	56	33
Ren et al. (2020).	R-EBUS	58	Prospective Case Series	85	94	57	34
Samaranayake et al. (2020)	R-EBUS	150	Prospective Case Series	64	35	86	26
Shanthikumar et al. (2019).	R-EBUS	146	Prospective Case Series	62	60	67	22
Shinagawa (2019).	R-EBUS	240	Prospective Case Series	56	64	61	35
Shyang et al. (2019).	R-EBUS	145	Prospective Case Series	59	35	65	14
Simon et al. (2021).	R-EBUS	238	Prospective Case Series	57	65	62	15

Song et al. (2022).	R-EBUS	125	Prospective Case Series	53	35	69	19
Song et al. (2021).	R-EBUS	104	Prospective Case Series	64	18	42	17
Sryma et al. (2021).	R-EBUS	248	Prospective Case Series	58	65	32	26
Styrvoky et al. (2022).	R-EBUS	13	Prospective Case Series	29	38	36	20
Sumi et al. (2020).	R-EBUS	47	Prospective Case Series	61	19	34	23.5
Tanaka et al. (2022).	R-EBUS	58	Prospective Case Series	36	64	40	18
Tsujimoto et al. (2022).	R-EBUS	56	Prospective Case Series	38	35	36	27
Heijden & Verhoeven (2022).	R-EBUS	93	Prospective Case Series	62	64	90	28
Verhoeven et al. (2021)..	R-EBUS	5	Prospective Case Series	55	51	68	21
Wagh et al. (2020).	R-EBUS	52	Prospective Case Series	52	52	69	33
Weng et al. (2020).	R-EBUS	37	Prospective Case Series	50	35	62	20
Xu et al.. (2021).	R-EBUS	32	Prospective Case Series	54	61	35	18
Xu et al. (2019).	R-EBUS	12	Prospective Case Series	45	56	66	32
Yarmus et al. (2020).	R-EBUS	24	Prospective Case Series	65	75	35	16
Yu et al. (2021).	R-EBUS	23	Prospective Case Series	69	65	36	15
Yuan et al. (2019).	R-EBUS	56	Prospective Case Series	78	61	34	14
Zarogoulidis et al. (2022).	R-EBUS	68	Prospective Case Series	56	85	42	12
Zheng et al. (2020).	R-EBUS	225	Prospective Case Series	25	35	25	16
Zhou et al. (2022	R-EBUS	21	Prospective Case Series	58	61	22	25
Zuñiga et al. (2020).	R-EBUS	10	Prospective Case Series	34	68	56	26
Nishii et al. (2020).	R-EBUS	25	Prospective Case Series	36	91	85	24

Study Description

The most significant findings of the study are broken down into categories and shown in tables 2 and 3. The total number of people who participated in the study of peripheral pulmonary lesions was 6379, and they had a total of 5566 lung lesions amongst them. The average age was 55 years old (and the standard deviation). Many different countries were represented among the people who took part in the survey.

The maximal diameter of pulmonary lesions was measured to be 28.35 millimetres on average (standard deviation). The overall frequency of lung cancer was shown to be 70.33 %, according to the research.

Aurora system All of the R-EBUS studies utilised either the 20-MHz mechanical radial probe (XUM-S20– 17R; Olympus; Tokyo, Japan) with an external diameter of 1.4 mm (that is, a probe with an external diameter of 1.4 mm) or the 20-MHz mechanical radial-type probe (UMS20–20R; Olympus) with an external diameter of 1.7 mm (that is, a probe with an external diameter of 1.7 (Hautmann et al., 2005). The diagnostic reference standard in a number of studies consisted of either surgical resection, other biopsy methods, or prolonged follow-up with CT chest.

Table 3. Details of Procedure

References	Index Test	Examination Durarion (min)	Biopsy method	Sedation	No. of Biopsiese	Adverse Events	Reference standards	Additional tools for Guidance
Agrawal et al. (2022)	R-EBUS	21.2	Forceps	CS	5	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Ankudavicius et al. (2022).	R-EBUS	ND	Forceps	CS	2.3	Bleeding	Surgical resection or follow-up to radiologic resolution	Fluoroscopy
Avasarala et al. (2020).	R-EBUS	28.3	Forceps	CS	3	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Bailey et al. (2019).	R-EBUS	ND	Forceps	CS	3.4	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Bellinger et al. (2021).	R-EBUS	ND	Forceps	CS	6	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Bo et al. (2019).	R-EBUS	25.72	Forceps	CS	6.5	Bleeding	ND	Fluoroscopy
Boonsarngsuk et al. (2020).	R-EBUS	22.3	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy

Chandrika & Yarmus (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Chen et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Chen et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Chen et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Chen et al. (2022).	R-EBUS	22.5	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Chen et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Choi et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Choudhary et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Crombag (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Dooms, C. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Fielding et al. (2019).	R-EBUS	ND	Forceps	CS	3	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Folch et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or	Fluoroscopy

							radiologic surveillance	
Gasparini et al. (2022).	R-EBUS	ND	Forceps	CS	2	Bleeding	Surgical resection or follow-up to radiologic resolution	Fluoroscopy
Giri et al. (2022).	R-EBUS	28.32	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Giri et al. (2021).	R-EBUS	26.55	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Gmehlin et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Han, J., & Lee, J. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	ND	Fluoroscopy
Ho et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Hong et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Hong et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Hotta et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Huang et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Huang et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Haoran et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy

Ishiwata et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Ishiwata et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Ito et al. (2022).	R-EBUS	32.5	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Ito et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Ito et al. (2022).	R-EBUS	ND	Forceps	CS	2.8	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Ito et al. (2021).	R-EBUS	ND	Forceps	CS	5	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Jiang et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection or follow-up to radiologic resolution	Fluoroscopy
Juul et al. (2022).	R-EBUS	ND	Forceps	CS	3	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Kalchiem-Dekel et al. (2022).	R-EBUS	ND	Forceps	CS	4	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Katsis et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy

Kho et al. (2019).	R-EBUS	ND	Forceps	CS	4.1	Bleeding	ND	Fluoroscopy
Kim et al. (2023).	R-EBUS	ND	Forceps	CS	4.2	Bleeding	Surgical resection	Fluoroscopy
Kramer& Annema (2021).	R-EBUS	ND	Forceps	CS	5	Bleeding	Surgical resection	Fluoroscopy
Kuijvenhoven et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Kuijvenhoven et al. (2021).	R-EBUS	32.35	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Lee & Song (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Lee et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Lee et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Leong et al. (2019).	R-EBUS	ND	Forceps	CS	6.4	Bleeding	Surgical resection or follow-up to radiologic resolution	Fluoroscopy
Ruan (2019).	R-EBUS	32	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Li et al. (2019).	R-EBUS	21	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Li et al. (2022).	R-EBUS	18.25	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy

Liam et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	ND	Fluoroscopy
Lin et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Liu et al. (2022).	R-EBUS	ND	Forceps	CS	ND	None	Surgical resection	Fluoroscopy
Lou et al. (2022).	R-EBUS	ND	Forceps	CS	2.8	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Ma et al. (2020).	R-EBUS	ND	Forceps	CS	6	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Matsumoto et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
McGuire et al. (2020).	R-EBUS	ND	Forceps	CS	2	Bleeding	Surgical resection	Fluoroscopy
Miotto et al. (2020).	R-EBUS	ND	Forceps	CS	4	Bleeding	Surgical resection	Fluoroscopy
Mondoni et al. 2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Moon et al. (2019).	R-EBUS	ND	Forceps	CS	4.1	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Muñoz-Largacha et al. 2021).	R-EBUS	ND	Forceps	CS	4.2	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Oki et al. (2019).	R-EBUS	ND	Forceps	CS	5	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Park et al. (2020).	R-EBUS	ND	Forceps	CS	2	Bleeding	Histology by alternate means or	Fluoroscopy

							radiologic surveillance	
Paul & Munavvar (2020).	R-EBUS	ND	Forceps	CS	3	Bleeding	Surgical resection or follow-up to radiologic resolution	Fluoroscopy
Poudel et al. (2021).	R-EBUS	ND	Forceps	CS	3.6	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Pritchett (2021).	R-EBUS	ND	Forceps	CS	6	None	Histology by alternate means or radiologic surveillance	Fluoroscopy
Qian et al. (2020).	R-EBUS	ND	Forceps	CS	5	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Qian et al. 2020)	R-EBUS	ND	Forceps	CS	9	Bleeding	ND	Fluoroscopy
Rahman, N. (2019).	R-EBUS	ND	Forceps	CS	6.3	Bleeding	Surgical resection	Fluoroscopy
Reisenauer et al. (2022).	R-EBUS	ND	Forceps	CS	6.4	Bleeding	Surgical resection	Fluoroscopy
Ren et al. (2020).	R-EBUS	ND	Forceps	CS	2.5	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Samaranayake et al. (2020)	R-EBUS	ND	Forceps	CS	5.3	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Shanthikumar et al. (2019).	R-EBUS	ND	Forceps	CS	5.7	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Shinagawa (2019).	R-EBUS	ND	Forceps	CS	6	Bleeding	Surgical resection	Fluoroscopy
Shyang et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy

Simon et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Song et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Song et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Sryma et al. (2021).	R-EBUS	ND	Forceps	CS	ND	None	Histology by alternate means or radiologic surveillance	Fluoroscopy
Styrvoky et al. (2022).	R-EBUS	ND	Forceps	CS	2	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Sumi et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Tanaka et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection or follow-up to radiologic resolution	Fluoroscopy
Tsujimoto et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Heijden & Verhoeven (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Verhoeven et al. (2021)	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy

Wagh et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	ND	Fluoroscopy
Weng et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Xu et al.. (2021).	R-EBUS	ND	Forceps	CS	4.3	Bleeding	Surgical resection	Fluoroscopy
Xu et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Yarmus et al. (2020).	R-EBUS	ND	Forceps	CS	ND	None	Histology by alternate means or radiologic surveillance	Fluoroscopy
Yu et al. (2021).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Yuan et al. (2019).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Zarogoulidis et al. (2022).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Surgical resection	Fluoroscopy
Zheng et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Zhou et al. (2022	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Zuñiga et al. (2020).	R-EBUS	ND	Forceps	CS	ND	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy
Nishii et al. (2020).	R-EBUS		Forceps	CS	5.2	Bleeding	Histology by alternate means or radiologic surveillance	Fluoroscopy

Heterogeneity Assessment

The trials were determined to have a high degree of heterogeneity **(**I^2 varied from 66-94% while P value was less than 0.001**)**. Overall and stratified by peripheral pulmonary lesions localization approach, values of sensitivity and other diagnostic characteristics for lung cancer were pooled using random-effects models. This action was taken because there was substantial evidence of study-to-study variation.

Study Quality and Bias

Total QUADAS scores were low, suggesting that the majority of included studies were of poor or intermediate quality in terms of their methodology **(**Fig. 2**)**. The average QUADAS score was 4.4, with a standard deviation of 0.4. **(**1.3**)**. The lowest possible score was 2, and the best was 7.

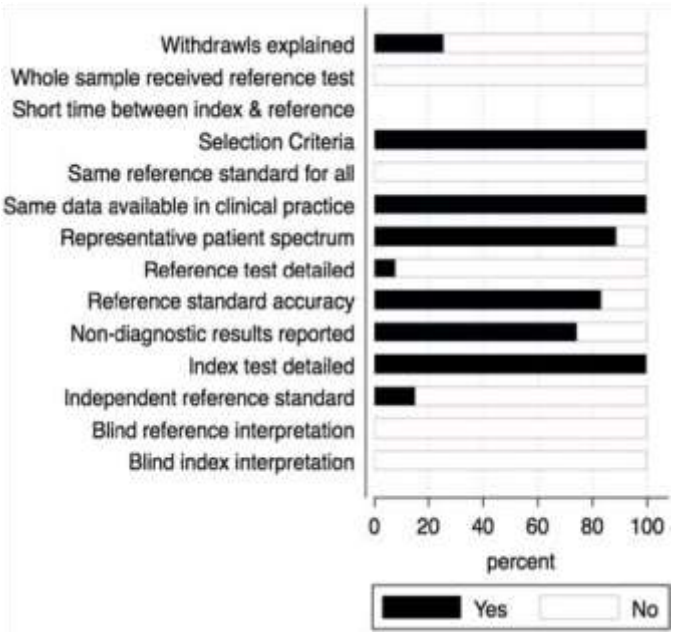

Fig 2. Fourteen studies were assessed for quality using the QUADAS criteria. An Analysis of the Studies' Methodological Quality Regarding Diagnostic Accuracy Found That Most Were Moderate to Poor There was an overall 4.4 %age point drop in QUADAS scores **(**1.4**)**. **(**1.3**)**. The minimum was a two and the maximum a seven.

Confirmation of the lung lesion found by histology using a different means, such as surgery, was not part of the criteria that determined whether or not a research study reached the "gold standard." The testing carried out in comparison to the reference standard was not documented in sufficient detail to make a repeatable process possible. Even though the vast majority of studies claimed to have access to clinical patient data, it was difficult to do an analysis for selection bias since it was unclear whether or not research participants were typical of patients who had R-EBUS biopsies in clinical practise. It was also perplexing that there was a lack of clarity on the standardisation of processes for the interpretation of index and reference tests, such as observer blinding. An Egger funnel plot was used in order to evaluate the results of individual, underpowered study **(**Fig. 3**)**. Both the bottom symmetrical funnel plot and the Begg statistic P-value of 0.001 are powerful indications of very little study impacts that are associated with less accurate baseline evaluations.

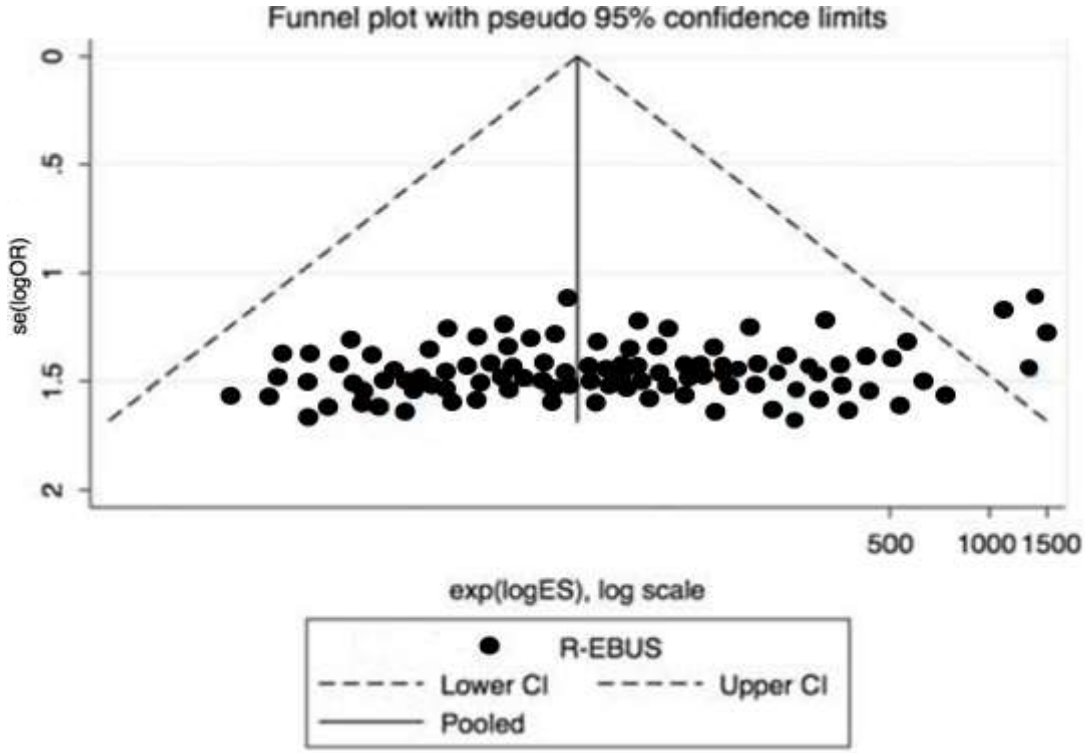

Fig 3.A funnel plot may be used to evaluate the publishing bias. In the examination of publication bias using the funnel plot, it was found that the meta-analysis lacked big studies with a high degree of accuracy. When applied to studies of small sizes, the funnel plot had a foundation that was symmetrical. The Begg statistic for the small study effect indicated a P-value of 0.001, giving strong evidence, which is consistent with the evaluation of the funnel plot, that the meta-analysis was consisted of small studies with lower baseline precision estimations. CI denoted as confidence interval; R-EBUS, radial-endobronchial-ultrasound.

Performance Outcomes

The diagnostic accuracy for the treatment of peripheral pulmonary lesions based on the given reference standard likewise varied greatly from research to study, ranging anywhere from 58.3% to 96.8%. The overall diagnostic accuracy of the pooled data for R-EBUS was 72.4% **(**95%, CI= 68.7-76.1**)**. Fig 4. depicts the forest plot that was used to determine the diagnosis accuracy.

Exploration of Heterogeneity

A meta-regression was carried out in order to investigate the factors that led to the heterogeneity. This showed that there was only a small amount of evidence to suggest that the covariates of **(**1**)** maximal nodule size **(**P=0.0695**)** and **(**2**)** biopsy method employed to sample the target lesion once it was localised **(**forceps, brush, or aspiration needle use, P=0.0572**)** contributed to the heterogeneity found between studies. There was evidence that was moderately strong **(**P=0.0450**)** that using multiple different biopsy methods for one lung lesion sampling procedure **(**for example, using forceps alone versus using forceps plus brushings**)** contributed to between-study heterogeneity. This was found in the context of a comparison between using forceps alone and using forceps plus brushings.

Safety

In none of the studies that were chosen, participants had significant bleeding that required surgical intervention to manage. There was one occurrence of pulmonary hematoma that was recorded and it was managed with careful surveillance **(**Wilson & Bartlett, 2007**)**. At the time of flexible bronchoscopy, there were no instances in which the patient had any little bleeding that was either self-limiting or needed the use of a simple topical hemostatic agent soon after the procedure. In order to treat the bleeding, chest tubes were not necessary. A topical treatment for bleeding that was applied promptly on the airway using the flexible bronchoscope, such as dilute epinephrine, was administered in 100 of the total occurrences of mild hemorrhage.

Discussion

Summary

With regard to the successful PPL localization, a random-effects meta-analysis indicated an overall successful localization rate of R-EBUS 90.2%. The successful PPL localization rate was high for both technologies. The combination of the two methods showed a diagnostic accuracy of around 71% when used to the identification of malignant PPL on CT chest scans. When contrasted with the lower sample sizes of selected research, the R-EBUS estimate's 95% confidence intervals may indicate enhanced accuracy as a result of bigger lung nodule sample sizes. This is in contrast to the smaller sample sizes of certain of the studies.

If the physician who is doing the surgery does not have enough expertise in the application of all aspects of the technology used for localization and sampling, the performance of the diagnostic test will not be at its highest possible level.

The overall diagnosis accuracy with R-EBUS was 72.4%, taking into account both the malignant and benign diagnoses. Despite the fact that the %age is larger when compared to Probe R-EBUS, the 95% confidence intervals are much broader for this estimate, which indicates a lack of accuracy. This is again most likely owing to the limited sample size, which makes it more difficult to discern from the target lesion when using radial ultrasonography. In addition, this underlines how important it is to confirm a benign diagnosis using a secondary way of tissue diagnosis if there is a strong suspicion that the PPL on CT chest is malignant tissue **(**McGuire et al., 2020**)**.

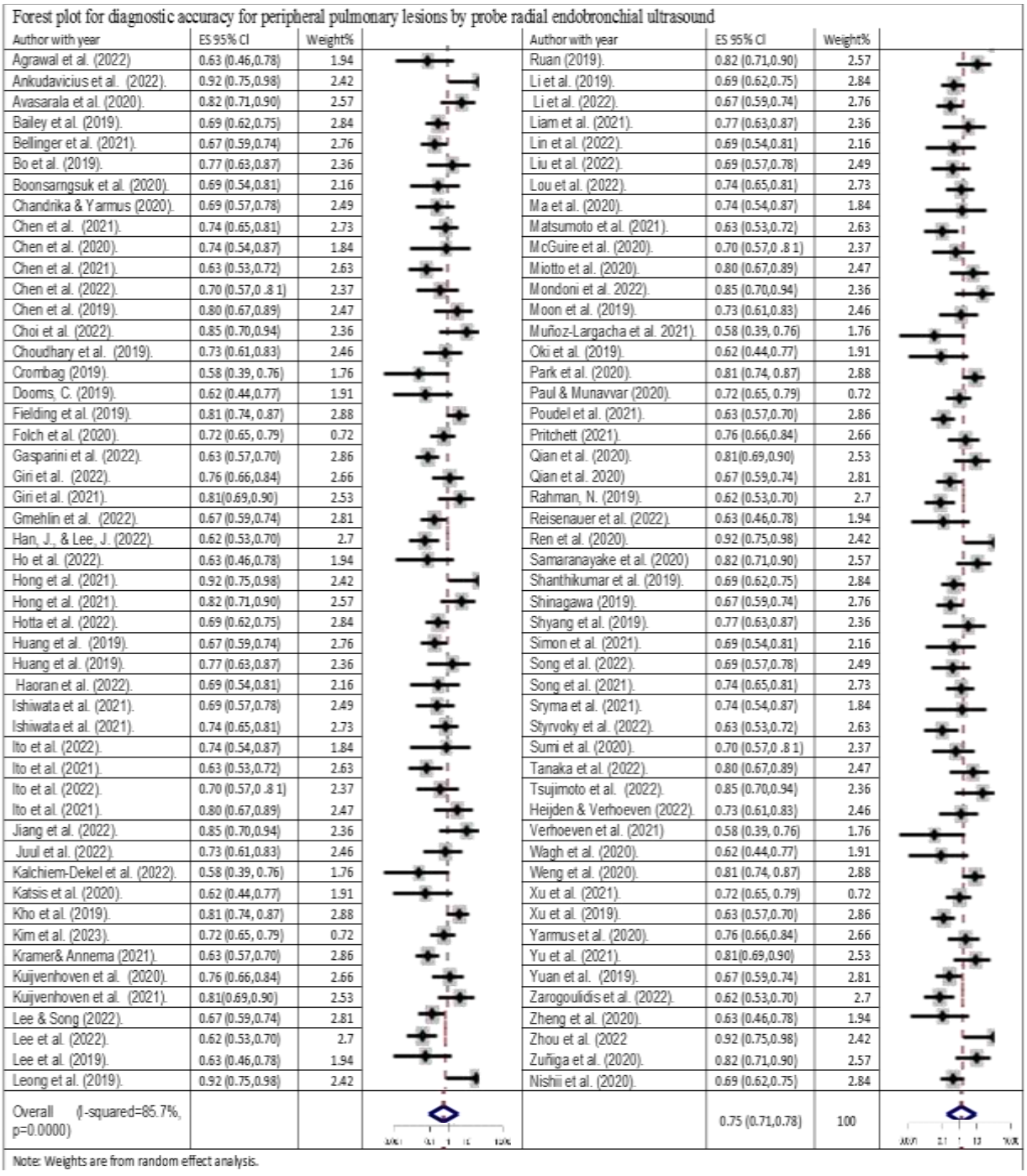

Fig 4. A forest plot to improve the accuracy of cancer diagnostics using technology **(**probe R-EBUS**)**. Diagnostic accuracy for peripheral pulmonary lesions, depending on the reference standard that was presented, likewise varied greatly from research to study, ranging anywhere from 58.3 % to 96.8 %. Accuracy of the pooled overall diagnostic test for R-EBUS was 72.4 % **(**95%, CI: 68.7-76.1**)**. CI: confidence interval.

Limitations

One of the limitations of this meta-analysis is that the majority of the studies that were made available for selection were of a low quality; the QUADAS scores of the investigations were used to establish the level of quality of the research. For example, several studies didn't have a trustworthy reference standard, which made it difficult to validate the R-EBUS test's performance characteristics. In addition, the reporting for either the index or the reference test was not carried out in a blind method.

The high degree of heterogeneity that occurred across the many investigations, as shown by the I^2 statistic, is one of the things that holds this study back, making it one of its weaknesses. The importance of this study is still drawn from the methodical endeavours made to analyse, using meta-regression, the variables that lead to the heterogeneity that is demonstrated across studies. With the use of this technique, we are able to create precise explanations that explain the observed heterogeneity; nevertheless, we are unable to quantify the exact amount to which each discovered variable contributes to the overall effect. We were able to determine, via the use of meta-regression, that the observed between-study heterogeneity was the result of a mixture of variables; these factors included, but were not limited to, the size of the PPLs as well as the sampling strategy **(**forceps, needle, brush**)**.

There were also hints of publishing bias favouring more limited research, as the funnel diagram in Figure 3 indicates. The bulk of the studies that were selected had a limited number of participants in their samples, therefore the accuracy of their estimations was severely compromised. Because of this, the pooled and stratified study estimates that were observed had a lower degree of accuracy than they otherwise would have had. Due to the fact that we wanted for this to be the most in-depth evaluation and analysis possible, we felt that it was essential to include analyses of some of the less popular series. It is possible that integrating these studies will be of tremendous use due to the fact that more limited research on diagnostic test performance characteristics tends to focus on groups who have a higher cancer incidence.

Conclusions

The results of the research allow for some tentative inferences to be drawn; however, it is important to keep in mind the constraints of the study. A large %age **(**more than 90 %**)** of R-PPL EBUS's translations have been successful. The accuracy of the diagnosis was more than 72%. The rate of problems was lower than the standard deviation of minus 2%. The R-EBUS treatment for peripheral pulmomary lesions is an approach that is economical. A future prospective study in the form of a randomised trial comparing the

test performance of each technology for a sampling of PPLs compared with a well-defined reference standard is warranted, and it should be compared with other methods such as electromagnetic navigation bronchoscopy. Given the balance with respect to the overall diagnostic superiority of R-EBUS, a future prospective study should compare R-EBUS with other methods such as EMNB (ENB).

References

1. McWilliams, A., Tammemagi, M. C., Mayo, J. R., Roberts, H., Liu, G., Soghrati, K., ... & Lam, S. (2013). Probability of cancer in pulmonary nodules detected on first screening CT. New England Journal of Medicine, 369(10), 910-919.

2. Wille, M. M., Dirksen, A., Ashraf, H., Saghir, Z., Bach, K. S., Brodersen, J., ... & Pedersen, J. H. (2016). Results of the randomized Danish lung cancer screening trial with focus on high-risk profiling. American journal of respiratory and critical care medicine, 193(5), 542-551.

3. Postmus, P. E., Kerr, K. M., Oudkerk, M., Senan, S., Waller, D. A., Vansteenkiste, J., ... & Peters, S. (2017). Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology, 28, iv1-iv21.

4. Ding, E., Zhang, D., &Bluyssen, P. M. (2022). Ventilation regimes of school classrooms against airborne transmission of infectious respiratory droplets: A review. Building and Environment, 207, 108484.

5. Rowell, N. P., & Williams, C. (2001). Radical radiotherapy for stage I/II non-small cell lung cancer in patients not sufficiently fit for or declining surgery (medically inoperable). Cochrane Database of Systematic Reviews, (1).

6. Planchard, D., Popat, S., Kerr, K., Novello, S., Smit, E. F., Faivre-Finn, C., ... & Peters, S. (2019). Correction to:"Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up". Annals of Oncology, 30(5), 863-870.

7. Lee, J., Kim, C., Seol, H. Y., Chung, H. S., Mok, J., Lee, G., ... &Eom, J. S. (2022). Safety and Diagnostic Yield of Radial Probe Endobronchial Ultrasound-Guided Biopsy for Peripheral Lung Lesions in Patients with Idiopathic Pulmonary Fibrosis: A Multicenter Cross-Sectional Study. Respiration, 101(4), 401-407.

8. Zheng, X., Cao, L., Zhang, Y., Xie, F., Yang, H., Liu, J., ... & Sun, J. (2022). A Novel Electromagnetic Navigation Bronchoscopy System for the Diagnosis of Peripheral Pulmonary Nodules: A Randomized Trial. Annals of the American Thoracic Society, (ja).

9. Kurihara, Y., Tashiro, H., Takahashi, K., Tajiri, R., Kuwahara, Y., Kajiwara, K., ... &Sueoka-Aragane, N. (2022). Factors related to the diagnosis of lung cancer by transbronchial biopsy with endobronchial ultrasonography and a guide sheath. Thoracic Cancer.

10. McGuire, A. L., Myers, R., Grant, K., Lam, S., & Yee, J. (2020). The diagnostic accuracy and sensitivity for malignancy of radial-endobronchial ultrasound and electromagnetic navigation bronchoscopy for sampling of peripheral pulmonary lesions: systematic review and meta-analysis. Journal of bronchology& interventional pulmonology, 27(2), 106-121.

11. Jiang, S., Liu, X., Chen, J., Ma, H., Xie, F., & Sun, J. (2020). A pilot study of the ultrathin cryoprobe in the diagnosis of peripheral pulmonary ground-glass opacity lesions. Translational Lung Cancer Research, 9(5), 1963.

12. Tang, L., Zhang, Y., & Wang, Y. (2022). Intraoperative identification of pulmonary nodules during minimally invasive thoracic surgery: a narrative review. Quantitative Imaging in Medicine and Surgery, 12(11), 5271.

13. Toennesen, L. L., Vindum, H. H., Risom, E., Pulga, A., Nessar, R. M., Arshad, A., ... &Clementsen, P. F. (2022). Learning curves for electromagnetic navigation bronchoscopy using CUSUM analysis. Journal of Bronchology& Interventional Pulmonology, 29(3), 164-170.

14. Whiting, P., Rutjes, A. W., Reitsma, J. B., Bossuyt, P. M., &Kleijnen, J. (2003). The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC medical research methodology, 3(1), 1-13.

15. Wilson, D. S., & Bartlett, R. J. (2007). Improved diagnostic yield of bronchoscopy in a community practice: combination of electromagnetic navigation system and rapid on-site evaluation. Journal of Bronchology& Interventional Pulmonology, 14(4), 227-232.

16. Chavez, C., Sasada, S., Izumo, T., Watanabe, J., Katsurada, M., Matsumoto, Y., &Tsuchida, T. (2015). Endobronchial ultrasound with a guide sheath for small malignant pulmonary nodules: a retrospective comparison between central and peripheral locations. Journal of thoracic disease, 7(4), 596.

17. Hautmann, H., Schneider, A., Pinkau, T., Peltz, F., &Feussner, H. (2005). Electromagnetic catheter navigation during bronchoscopy: validation of a novel method by conventional fluoroscopy. Chest, 128(1), 382-387.

18. Agrawal, A., Ho, E., Chaddha, U., Demirkol, B., Bhavani, S. V., Hogarth, D. K., &Murgu, S. (2022). Factors Associated With Diagnostic Accuracy of Robotic Bronchoscopy With 12-Month Follow-up. The Annals of Thoracic Surgery.

19. Ankudavicius, V., Miliauskas, S., Poskiene, L., Vajauskas, D., &Zemaitis, M. (2022). Diagnostic Yield of Transbronchial Cryobiopsy Guided by Radial Endobronchial Ultrasound and Fluoroscopy in the Radiologically Suspected Lung Cancer: A Single Institution Prospective Study. Cancers, 14(6), 1563.

20. Avasarala, S. K., Aravena, C., & Almeida, F. A. (2020). Convex probe endobronchial ultrasound: historical, contemporary, and cutting-edge applications. Journal of Thoracic Disease, 12(3), 1085.

21. Bailey, N., Krisnadi, Z., Kaur, R., Mulrennan, S., Phillips, M., &Slavova-Azmanova, N. (2019). A pragmatic application of endobronchial ultrasound-guided transbronchial needle aspiration: a single institution experience. BMC Pulmonary Medicine, 19(1), 1-9.

22. Bellinger, C., Poon, R., Dotson, T., & Sharma, D. (2021). Lesion characteristics affecting yield of electromagnetic navigational bronchoscopy. Respiratory Medicine, 180, 106357.

23. Bo, L., Li, C., Pan, L., Wang, H., Li, S., Li, Q., ... &Jin, F. (2019). Diagnosing a solitary pulmonary nodule using multiple bronchoscopic guided technologies: a prospective randomized study. Lung Cancer, 129, 48-54.

24. Boonsarngsuk, V., Petnak, T., So-Ngern, A., Saksitthichok, B., &Kanoksil, W. (2020). Comparison of different transbronchial biopsy sampling techniques for the diagnosis of peripheral pulmonary lesions with radial endobronchial ultrasound-guided bronchoscopy: a prospective study. Respiratory Investigation, 58(5), 381-386.

25. Chandrika, S., & Yarmus, L. (2020). Recent developments in advanced diagnostic bronchoscopy. European Respiratory Review, 29(157).

26. Chen, A. C., Pastis Jr, N. J., Mahajan, A. K., Khandhar, S. J., Simoff, M. J., Machuzak, M. S., ... & Silvestri, G. A. (2021). Robotic bronchoscopy for peripheral pulmonary lesions: a multicenter pilot and feasibility study (BENEFIT). Chest, 159(2), 845-852.

27. Chen, A. C., Pastis, N. J., Machuzak, M. S., Gildea, T. R., Simoff, M. J., Gillespie, C. T., ... & Silvestri, G. A. (2020). Accuracy of a robotic endoscopic system in cadaver models with simulated tumor targets: ACCESS study. Respiration, 99(1), 56-61.

28. Chen, C. C., Bai, C. H., Lee, K. Y., Chou, Y. T., Pan, S. T., & Wang, Y. H. (2021). Evaluation of the diagnostic accuracy of bronchial brushing cytology in lung cancer: A meta-analysis. Cancer cytopathology, 129(9), 739-749.

29. Chen, H., Yu, Y., Yu, X., Li, S., Zheng, L., Zhang, S., ... & Chen, Z. (2022). An Innovative Method: Predicting the Visibility of Radial Endobronchial Ultrasound for Peripheral Pulmonary Nodules by Virtual Bronchoscopic Navigation. Technology in Cancer Research & Treatment, 21, 15330338221141790.

30. Chen, X., Wan, B., Xu, Y., Song, Y., Zhan, P., Huang, L., ... &Lv, T. (2019). Efficacy of rapid on-site evaluation for diagnosing pulmonary lesions and mediastinal lymph nodes: a systematic review and meta-analysis. Translational Lung Cancer Research, 8(6), 1029.

31. Choi, J., Zo, S., Kim, J. H., Oh, Y. J., Ahn, J. H., Kim, M., ... & Lee, H. Y. (2022). Nondiagnostic, radial-probe endobronchial ultrasound-guided biopsy for peripheral lung lesions: The added value of radiomics from ultrasound imaging for predicting malignancy. Thoracic Cancer.

32. Choudhary, R., Marwah, V., Behal, P., Sengupta, P., Malik, V., Verma, S., ... &Wasan, A. (2022). Endobronchial ultrasound-guided transbronchial needle aspiration in diagnosing mediastinal lymphadenopathy: Experience from a tertiary care centre. Medical Journal Armed Forces India.

33. Costa Jr, A. D. S., Palomino, A. L. M., Suzuki, I., Scordamaglio, P. R., Gregorio, M. G., &Jacomelli, M. (2019). Endobronchial ultrasound: a minimally invasive technology to assist diagnosis of thoracic diseases. Einstein (São Paulo), 17.

34. Crombag, L. (2019). ES07. 03 Radial Endosonography. Journal of Thoracic Oncology, 14(10), S29.

35. Dooms, C. (2019). ES07. 04 Predictive Molecular Testing on Small Biopsy Samples. Journal of Thoracic Oncology, 14(10), S29-S30.

36. Fielding, D. I., Bashirzadeh, F., Son, J. H., Todman, M., Chin, A., Tan, L., ... & Sung, A. W. (2019). First human use of a new robotic-assisted fiber optic sensing navigation system for small peripheral pulmonary nodules. Respiration, 98(2), 142-150.

37. Folch, E. E., Labarca, G., Ospina-Delgado, D., Kheir, F., Majid, A., Khandhar, S. J., ... & Fernandez-Bussy, S. **(**2020**)**. Sensitivity and safety of electromagnetic navigation bronchoscopy for lung cancer diagnosis: systematic review and meta-analysis. Chest, 158**(**4**)**, 1753-1769.

38. Gasparini, S., Mei, F., Bonifazi, M., &Zuccatosta, L. **(**2022**)**. Bronchoscopic diagnosis of peripheral lung lesions. Current Opinion in Pulmonary Medicine, 28**(**1**)**, 31-36.

39. Giri, M., Huang, G., Puri, A., Zhuang, R., Li, Y., & Guo, S. **(**2022**)**. Efficacy and Safety of Cryobiopsy vs. Forceps Biopsy for Interstitial Lung Diseases, Lung Tumors, and Peripheral Pulmonary Lesions: An Updated Systematic Review and Meta-Analysis. Frontiers in medicine, 9.

40. Giri, M., Puri, A., Wang, T., Huang, G., & Guo, S. **(**2021**)**. Virtual bronchoscopic navigation versus non-virtual bronchoscopic navigation assisted bronchoscopy for the diagnosis of peripheral pulmonary lesions: A systematic review and meta-analysis. Therapeutic advances in respiratory disease, 15, 17534666211017048.

41. Gmehlin, C. G., Kurman, J. S., & Benn, B. S. **(**2022**)**. Size and vision: Impact of fluoroscopic navigation, digital tomosynthesis, and continuous catheter tip tracking on diagnostic yield of small, bronchus sign negative lung nodules. Respiratory Medicine, 202, 106941.

42. Han, J., & Lee, J. **(**2022**)**. EP13. 01-003 Diagnostic Yield of Radial Probe Endobronchial Ultrasonography without Fluoroscopic guidance in Peripheral Pulmonary Lesions. Journal of Thoracic Oncology, 17**(**9**)**, S520.

43. Ho, A. T. N., Gorthi, R., Lee, R., Chawla, M., &Patolia, S. **(**2022**)**. Solitary Lung Nodule: Ct Guided Transthoracic Biopsy Vs Transbronchial Biopsy With Endobronchial Ultrasound and Flexible Bronchoscope, a Meta-analysis of Randomized Controlled Trials.

44. Hong, K. S., Ahn, H., Lee, K. H., Chung, J. H., Shin, K. C., Jin, H. J., ... &Ahn, J. H. **(**2021**)**. Radial Probe Endobronchial Ultrasound Using Guide Sheath-Guided Transbronchial Lung Biopsy in Peripheral Pulmonary Lesions without Fluoroscopy. Tuberculosis and Respiratory Diseases, 84**(**4**)**, 282.

45. Hong, K. S., Lee, K. H., Chung, J. H., Shin, K. C., Jin, H. J., Jang, J. G., &Ahn, J. H. **(**2021**)**. Utility of radial probe endobronchial ultrasound guided transbronchial lung biopsy in bronchus sign negative peripheral pulmonary lesions. Journal of Korean Medical Science, 36**(**24**)**.

46. Hotta, T., Kurimoto, N., Shiratsuki, Y., Amano, Y., Hamaguchi, M., Tanino, A., ... &Isobe, T. (2022). Deep learning-based diagnosis from endobronchial ultrasonography images of pulmonary lesions. Scientific Reports, 12(1), 1-7.

47. Huang, C. T., Tsai, Y. J., Ho, C. C., & Yu, C. J. (2019). Atypical cells in pathology of endobronchial ultrasound-guided transbronchial biopsy of peripheral pulmonary lesions: incidence and clinical significance. Surgical Endoscopy, 33(6), 1783-1788.

48. Huang, Z., Huang, H., Ning, Y., Han, J., Shen, Y., Shi, H., ... &Sapalidis, K. (2019). Radial probe endobronchial ultrasound assisted conventional transbronchial needle aspiration in the diagnosis of solitary peribronchial pulmonary lesion located in the segmental bronchi. Journal of Cancer, 10(3), 634.

49. Ishiwata, T., Gregor, A., Inage, T., &Yasufuku, K. (2019). Advances in interventional diagnostic bronchoscopy for peripheral pulmonary lesions. Expert review of respiratory medicine, 13(9), 885-897.

50. Ishiwata, T., Ujiie, H., Gregor, A., Inage, T., Motooka, Y., Kinoshita, T., ... &Yasufuku, K. (2021). Pilot study using virtual 4-D tracking electromagnetic navigation bronchoscopy in the diagnosis of pulmonary nodules: a single center prospective study. Journal of Thoracic Disease, 13(5), 2885.

51. Haoran, E., Chen, J., Sun, W., Zhang, Y., Ren, S., Shi, J., ... & Chen, C. (2022). Three-dimensionally printed navigational template: a promising guiding approach for lung biopsy. Translational Lung Cancer Research, 11(3), 393.Ito, T., Matsumoto, Y., Okachi, S., Nishida, K., Tanaka, M., Imabayashi, T., ... & Hashimoto, N. (2022). A Diagnostic Predictive Model of Bronchoscopy with Radial Endobronchial Ultrasound for Peripheral Pulmonary Lesions. Respiration, 101(12), 1148-1156.

52. Ito, T., Okachi, S., Ikenouchi, T., Ushijima, F., Ohashi, T., Ogawa, M., ... & Hashimoto, N. (2021). The Value of Additional Conventional Transbronchial Biopsy in the Negative Results of Rapid On-site Evaluation During Endobronchial Ultrasound With Guide Sheath to Diagnose Small Peripheral Lung Cancer. Technology in Cancer Research & Treatment, 20, 15330338211043040.

53. Ito, T., Okachi, S., Iwano, S., Kinoshita, F., Wakahara, K., Hashimoto, N., & Chen-Yoshikawa, T. F. (2022). Diagnostic value and safety of endobronchial ultrasonography with a guide sheath transbronchial biopsy for diagnosing peripheral pulmonary lesions in patients with interstitial lung disease. Journal of Thoracic Disease, 14(11), 4361.

54. Ito, T., Okachi, S., Kimura, T., Kataoka, K., Suzuki, Y., Kinoshita, F., ... &Kondoh, Y. **(**2021**)**. Endobronchial ultrasonography with a guide sheath transbronchial biopsy for diagnosing peripheral pulmonary lesions within or near fibrotic lesions in patients with interstitial lung disease. Cancers, 13**(**22**)**, 5751.

55. Jiang, L., Xu, J., Liu, C., Gao, N., Zhao, J., Han, X., ... & Zhao, J. **(**2021**)**. Diagnosis of peripheral pulmonary lesions with transbronchial lung cryobiopsy by guide sheath and radial endobronchial ultrasonography: a prospective control study. Canadian respiratory journal, 2021.

56. Juul, A. D., Falster, C., Rasmussen, T. R., Hilberg, O., Jacobsen, N., Arshad, A., &Laursen, C. B. **(**2022**)**. Does the Addition of Radial Endobronchial Ultrasound Improve the Diagnostic Yield of Electromagnetic Navigation Bronchoscopy? A Systematic Review. Respiration, 1-9.

57. Kalchiem-Dekel, O., Connolly, J. G., Lin, I. H., Husta, B. C., Adusumilli, P. S., Beattie, J. A., ... &Bott, M. J. **(**2022**)**. Shape-sensing robotic-assisted bronchoscopy in the diagnosis of pulmonary parenchymal lesions. Chest, 161**(**2**)**, 572-582.

58. Katsis, J. M., Rickman, O. B., Maldonado, F., & Lentz, R. J. **(**2020**)**. Bronchoscopic biopsy of peripheral pulmonary lesions in 2020: a review of existing technologies. Journal of Thoracic Disease, 12**(**6**)**, 3253. Livi, V., Barisione, E., Zuccatosta, L., Romagnoli, M., Praticò, A., Michieletto, L., ... &Corbetta, L. **(**2019**)**. Competence in navigation and guided transbronchial biopsy for peripheral pulmonary lesions. Panminerva Med, 61**(**3**)**, 280-289.

59. Kho, S. S., Chan, S. K., Yong, M. C., & Tie, S. T. **(**2019**)**. Performance of transbronchial cryobiopsy in eccentrically and adjacently orientated radial endobronchial ultrasound lesions. ERJ open research, 5**(**4**)**.

60. Kim, S. H., Kim, J., Pak, K., &Eom, J. S. **(**2023**)**. Ultrathin Bronchoscopy for the Diagnosis of Peripheral Pulmonary Lesions: A Meta-Analysis. Respiration, 102**(**1**)**, 34-45.

61. Kramer, T., & Annema, J. T. **(**2021**)**. Advanced bronchoscopic techniques for the diagnosis and treatment of peripheral lung cancer. Lung Cancer, 161, 152-162.

62. Kuijvenhoven, J. C., Leoncini, F., Crombag, L. C., Spijker, R., Bonta, P. I., Korevaar, D. A., & Annema, J. T. **(**2020**)**. Endobronchial ultrasound for the diagnosis of centrally located lung tumors: a systematic review and meta-analysis. Respiration, 99**(**5**)**, 441-450.

63. Kuijvenhoven, J. C., Livi, V., Szlubowski, A., Ninaber, M., Stöger, J. L., Widya, R. L., ... & Annema, J. T. **(**2021**)**. Endobronchial ultrasound for T4 staging in patients with resectable NSCLC. Lung Cancer, 158, 18-24.

64. Lee, J., & Song, J. U. **(**2022**)**. Diagnostic yield of radial probe endobronchial ultrasonography-guided transbronchial biopsy without fluoroscopy in peripheral pulmonary lesions: A systematic review and meta-analysis. Thoracic Cancer.

65. Lee, J., Kim, C., Seol, H. Y., Chung, H. S., Mok, J., Lee, G., ... &Eom, J. S. **(**2022**)**. Safety and Diagnostic Yield of Radial Probe Endobronchial Ultrasound-Guided Biopsy for Peripheral Lung Lesions in Patients with Idiopathic Pulmonary Fibrosis: A Multicenter Cross-Sectional Study. Respiration, 101**(**4**)**, 401-407.

66. Lee, K. M., Lee, G., Kim, A., Mok, J., Lee, J. W., Jeong, Y. J., ... &Eom, J. S. **(**2019**)**. Clinical outcomes of radial probe endobronchial ultrasound using a guide sheath for diagnosis of peripheral lung lesions in patients with pulmonary emphysema. Respiratory research, 20**(**1**)**, 1-9.

67. Leong, T. L., Loveland, P. M., Gorelik, A., Irving, L., &Steinfort, D. P. **(**2019**)**. Preoperative Staging by EBUS in cN0/N1 Lung Cancer. Journal of Bronchology& Interventional Pulmonology, 26**(**3**)**, 155-165.

68. Li, N., Peng, Y., Chen, Y., Lv, Y., Xu, G., & Ruan, T. **(**2019**)**. Diagnostic Value of Non-Real-Time Radial Probe Endobronchial Ultrasound **(**RP-EBUS**)** Guided Positioning Method for Peripheral Pulmonary Lesions. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research, 25, 9721.

69. Li, X., Pan, J., Ma, Y., Ren, Y., & Gao, B. L. **(**2022**)**. Diagnosis of diffuse parenchymal lung diseases using transbronchial cryobiopsy guided by endobronchial ultrasound compared to clinicoradiological diagnosis. Quantitative Imaging in Medicine and Surgery, 12**(**2**)**, 1139.

70. Liam, C. K., Lee, P., Yu, C. J., Bai, C., &Yasufuku, K. **(**2021**)**. The diagnosis of lung cancer in the era of interventional pulmonology. The International Journal of Tuberculosis and Lung Disease, 25**(**1**)**, 6-15.

71. Lin, C. K., Fan, H. J., Yao, Z. H., Lin, Y. T., Wen, Y. F., Wu, S. G., & Ho, C. C. **(**2022**)**. Cone-Beam Computed Tomography-Derived Augmented Fluoroscopy Improves the Diagnostic Yield of

Endobronchial Ultrasound-Guided Transbronchial Biopsy for Peripheral Pulmonary Lesions. Diagnostics, 12(1), 41.

72. Liu, Y., Wang, F., Zhang, Q., & Tong, Z. (2022). Diagnostic yield of virtual bronchoscope navigation combined with radial endobronchial ultrasound guided transbronchial cryo-biopsy for peripheral pulmonary nodules: a prospective, randomized, controlled trial. Annals of Translational Medicine, 10(8).

73. Lou, L., Huang, X., Tu, J., & Xu, Z. (2022). Endobronchial ultrasound-guided transbronchial needle aspiration in peripheral pulmonary lesions: a systematic review and meta-analysis. Clinical & Experimental Metastasis, 1-8.

74. Ma, L., Fang, Y., Zhang, T., Xue, P., Bo, L., Liu, W., & Fu, E. (2020). Comparison in efficacy and safety of forceps biopsy for peripheral lung lesions guided by endobronchial ultrasound-guided sheath (EBUS-GS) and electromagnetic navigation bronchoscopy combined with EBUS (ENB-EBUS). American journal of translational research, 12(8), 4604.

75. Matsumoto, Yuji, Toshiyuki Nakai, Midori Tanaka, Tatsuya Imabayashi, TakaakiTsuchida, and YuichiroOhe. "Diagnostic outcomes and safety of cryobiopsy added to conventional sampling methods: an observational study." Chest 160, no. 5 (2021): 1890-1901.

76. McGuire, A. L., Myers, R., Grant, K., Lam, S., & Yee, J. (2020). The diagnostic accuracy and sensitivity for malignancy of radial-endobronchial ultrasound and electromagnetic navigation bronchoscopy for sampling of peripheral pulmonary lesions: systematic review and meta-analysis. Journal of bronchology& interventional pulmonology, 27(2), 106-121.

77. Miotto, A., Perfeito, J. A. J., Leite, R. P., Latorraca, C. D. O. C., &Riera, R. (2020). Minimally invasive interventions for pulmonary nodule biopsy: A systematic review protocol.

78. Mondoni, M., Rinaldo, R. F., Carlucci, P., Terraneo, S., Saderi, L., Centanni, S., &Sotgiu, G. (2022). Bronchoscopic sampling techniques in the era of technological bronchoscopy. Pulmonology, 28(6), 461-471.

79. Moon, S. M., Choe, J., Jeong, B. H., Um, S. W., Kim, H., Kwon, O. J., & Lee, K. (2019). Diagnostic performance of radial probe endobronchial ultrasound without a guide-sheath and the feasibility of molecular analysis. Tuberculosis and Respiratory Diseases, 82(4), 319-327.

80. Muñoz-Largacha, J. A., Batra, H., & Wei, B. (2021). Navigational bronchoscopy with interventional pulmonologists and thoracic surgeons. Innovations, 16(2), 117-122.

81. Oki, M., Saka, H., Asano, F., Kitagawa, C., Kogure, Y., Tsuzuku, A., & Ando, M. (2019). Use of an ultrathin vs thin bronchoscope for peripheral pulmonary lesions: a randomized trial. Chest, 156(5), 954-964.

82. Oki, M., Saka, H., Imabayashi, T., Himeji, D., Nishii, Y., Nakashima, H., ... & Ando, M. (2022). Guide sheath versus non-guide sheath method for endobronchial ultrasound-guided biopsy of peripheral pulmonary lesions: a multicentrerandomised trial. European Respiratory Journal, 59(5).

83. Park, S., Yoon, H. Y., Han, Y., Wang, K. S., Park, S. Y., Ryu, Y. J., ... & Chang, J. H. (2020). Diagnostic yield of additional conventional transbronchial lung biopsy following radial endobronchial ultrasound lung biopsy for peripheral pulmonary lesions. Thoracic cancer, 11(6), 1639-1646.

84. Paul, S., & Munavvar, M. (2020). Flexible bronchoscopy. Medicine, 48(4), 257-262.

85. Poudel, B., Desman, J., Aihara, G., Weidman, D. I., Tsang, A., Kovrizhkin, K., ... & Liddell, R. P. (2021). Adequacy of samples obtained via percutaneous core-needle rebiopsy for EGFR T790M molecular analysis in patients with non-small cell lung cancer following acquired resistance to first-line therapy: A systematic review and meta-analysis. Cancer Treatment and Research Communications, 29, 100470.

86. Pritchett, M. A. (2021). Prospective analysis of a novel endobronchial augmented fluoroscopic navigation system for diagnosis of peripheral pulmonary lesions. Journal of Bronchology& Interventional Pulmonology, 28(2), 107.

87. Qian, K., Krimsky, W. S., Sarkar, S. A., & Deng, Y. (2020). Efficiency of electromagnetic navigation bronchoscopy and virtual bronchoscopic navigation. The Annals of Thoracic Surgery, 109(6), 1731-1740.

88. Qian, K., Krimsky, W. S., Sarkar, S. A., & Deng, Y. (2020). Efficiency of electromagnetic navigation bronchoscopy and virtual bronchoscopic navigation. The Annals of Thoracic Surgery, 109(6), 1731-1740.

89. Rahman, N. (2019). ES07. 01 Transthoracic Ultrasonography. Journal of Thoracic Oncology, 14(10), S29.

90. Reisenauer, J., Simoff, M. J., Pritchett, M. A., Ost, D. E., Majid, A., Keyes, C., ... & Folch, E. E. (2022). Ion: technology and techniques for shape-sensing robotic-assisted bronchoscopy. The Annals of thoracic surgery, 113(1), 308-315.

91. Ren, H. Y., Zhang, X. J., Zhang, K., Li, T. X., Gao, B. L., & Chen, Z. X. (2020). Endobronchial Ultrasound Combined with Clinical Data for Predicting Malignant Peripheral Pulmonary Lesions. Cancer Management and Research, 12, 9837.

92. Samaranayake, C. B., Wright, C., Erigadoo, S., Azzopardi, M., Putt, M., &Bint, M. (2020). A randomized controlled trial on optimal sampling sequence in radial guide sheath endobronchial ultrasound lung biopsy. Journal of Bronchology& Interventional Pulmonology, 27(3), 205-211.

93. Shanthikumar, S., Massie, J., Ranganathan, S., Schuhmann, M., Eberhardt, R., Irving, L. B., ... &Steinfort, D. P. (2019). Utility of endobronchial ultrasound in assessment of intrathoracic lesions in paediatric patients. Respiration, 98(4), 340-346.

94. Shinagawa, N. (2019). A review of existing and new methods of bronchoscopic diagnosis of lung cancer. Respiratory investigation, 57(1), 3-8.

95. Shyang, K. S., & Teck, T. S. (2019). Radial probe endobronchial ultrasound (r-ebus) guided transbronchial cryobiopsy in the diagnosis of peripheral solitary pulmonary nodule. Med J Malaysia, 74(4), 349.

96. Simon, M., Simon, I., Tent, P. A., Todea, D. A., &Haranguș, A. (2021). Cryobiopsy in Lung Cancer Diagnosis—A Literature Review. Medicina, 57(4), 393.

97. Song, J. Y., Shin, S. H., Yoo, H., Jeong, B. H., Um, S. W., Kim, H., ... & Lee, K. (2022). Efficacy of Combining Multiple Electromagnetic Navigation Bronchoscopy Modalities for Diagnosing Lung Nodules. Journal of Clinical Medicine, 11(24), 7341.

98. Song, N., Yang, L., Wang, H., Jiang, L., Zhao, L., Colella, S., ... & He, Y. (2021). Radial endobronchial ultrasound-assisted transbronchial needle aspiration for pulmonary peripheral lesions in the segmental bronchi adjacent to the central airway. Translational Lung Cancer Research, 10(6), 2625.

99. Sryma, P. B., Mittal, S., Madan, N. K., Tiwari, P., Hadda, V., Mohan, A., ... & Madan, K. (2021). Efficacy of Radial Endobronchial Ultrasound (R-EBUS) guided transbronchial cryobiopsy for peripheral pulmonary lesions (PPL's): A systematic review and meta-analysis. Pulmonology.

100. Styrvoky, K., Schwalk, A., Pham, D., Chiu, H. T., Rudkovskaia, A., Madsen, K., ... & Abu-Hijleh, M. **(**2022**)**. Shape-Sensing Robotic-Assisted Bronchoscopy with Concurrent use of Radial Endobronchial Ultrasound and Cone Beam Computed Tomography in the Evaluation of Pulmonary Lesions. Lung, 200**(**6**)**, 755-761.

101. Sumi, T., Ikeda, T., Sawai, T., Shijubou, N., Kure, K., Yamada, Y., ... & Takahashi, H. **(**2020**)**. Comparison of ultrathin bronchoscopy with conventional bronchoscopy for the diagnosis of peripheral lung lesions without virtual bronchial navigation. Respiratory Investigation, 58**(**5**)**, 376-380.

102. Tanaka, M., Matsumoto, Y., Imabayashi, T., Kawahara, T., &Tsuchida, T. **(**2022**)**. Diagnostic value of a new cryoprobe for peripheral pulmonary lesions: a prospective study. BMC Pulmonary Medicine, 22**(**1**)**, 1-9.

103. Tsujimoto, Y., Matsumoto, Y., Tanaka, M., Imabayashi, T., Uchimura, K., &Tsuchida, T. **(**2022**)**. Diagnostic value of bronchoscopy for peripheral metastatic lung tumors. Cancers, 14**(**2**)**, 375.

104. van der Heijden, E. H., & Verhoeven, R. L. **(**2022**)**. Robotic Assisted Bronchoscopy: The Ultimate Solution for Peripheral Pulmonary Nodules?. Respiration, 101**(**5**)**, 437-440.

105. Verhoeven, R. L., Fütterer, J. J., Hoefsloot, W., & van der Heijden, E. H. **(**2021**)**. Cone-beam CT image guidance with and without electromagnetic navigation bronchoscopy for biopsy of peripheral pulmonary lesions. Journal of bronchology& interventional pulmonology, 28**(**1**)**, 60.

106. Wagh, A., Ho, E., Murgu, S., & Hogarth, D. K. **(**2020**)**. Improving diagnostic yield of navigational bronchoscopy for peripheral pulmonary lesions: a review of advancing technology. Journal of thoracic disease, 12**(**12**)**, 7683.

107. Weng, X., Zhi, L., An, X., Xu, M., Zhang, H., Long, K., & Gao, P. **(**2020**)**. Diagnostic value of rapid on-site evaluation in interventional pulmonology: A protocol for systematic review and meta analysis. Medicine, 99**(**29**)**.

108. Xu, C., Wang, Y., Wang, W., Yuan, Q., Hu, H. D., & Li, L. **(**2021**)**. Improved diagnostic yield of transbronchial lung biopsy in peripheral pulmonary lesions using a combination of endobronchial ultrasound and rapid on-site evaluation. Journal of International Medical Research, 49**(**3**)**, 0300060521999535.

109. Xu, C., Yuan, Q., Wang, Y., Wang, W., Chi, C., Zhang, Q., ... & Zhang, X. (2019). Usefulness of virtual bronchoscopic navigation combined with endobronchial ultrasound guided transbronchial lung biopsy for solitary pulmonary nodules. Medicine, 98(7).

110. Yarmus, L., Akulian, J., Wahidi, M., Chen, A., Steltz, J. P., Solomon, S. L., ... & Group, I. P. O. (2020). A prospective randomized comparative study of three guided bronchoscopic approaches for investigating pulmonary nodules: the PRECISION-1 study. Chest, 157(3), 694-701.

111. Yu, K. L., Yang, S. M., Ko, H. J., Tsai, H. Y., Ko, J. C., Lin, C. K., ... & Shih, J. Y. (2021). Efficacy and safety of cone-beam computed tomography-derived augmented fluoroscopy combined with endobronchial ultrasound in peripheral pulmonary lesions. Respiration, 100(6), 538-546.

112. Yuan, M. L., Yang, X., Yin, W., Hu, H. L., Li, X. Y., & Hu, Y. (2019). The effectiveness of rapid on-site cytological evaluation (ROSE) on the diagnostic yield of bronchoscopy in peripheral pulmonary lesions: a systematic review and meta-analysis. Int J Clin Exp Med, 12(4), 3283-3293.

113. Zarogoulidis, P., Huang, H., Chen, W., Petridis, D., Matthaios, D., Hohenforst-Schmidt, W., ... & Bai, C. (2022). Radial Endobronchial Ultrasound for Lung Cancer Diagnosis: Tips and Tricks. Journal of Cancer, 13(4), 1307.

114. Zheng, X., Wang, L., Chen, J., Xie, F., Jiang, Y., & Sun, J. (2020). Diagnostic value of radial endobronchial ultrasonographic features in predominant solid peripheral pulmonary lesions. Journal of thoracic disease, 12(12), 7656.

115. Zhou, L., Wang, F., Wang, Z., Xu, L., & Tong, Z. (2022). Utility of Radial Endobronchial Ultrasound with a Guide Sheath for Peripheral Pulmonary Lesions in Patients with Pulmonary Emphysema: A Retrospective Study.

116. Zuñiga, P. V. S., Vakil, E., Molina, S., Bassett Jr, R. L., & Ost, D. E. (2020). Sensitivity of radial endobronchial ultrasound-guided bronchoscopy for lung cancer in patients with peripheral pulmonary lesions: an updated meta-analysis. Chest, 157(4), 994-1011.

117. Nishii, Y., Nakamura, Y., Fujiwara, K., Ito, K., Sakaguchi, T., Suzuki, Y., ... &Hataji, O. (2020). Use of ultrathin bronchoscope on a need basis improves diagnostic yield of difficult-to-approach pulmonary lesions. Frontiers in Medicine, 7, 588048.