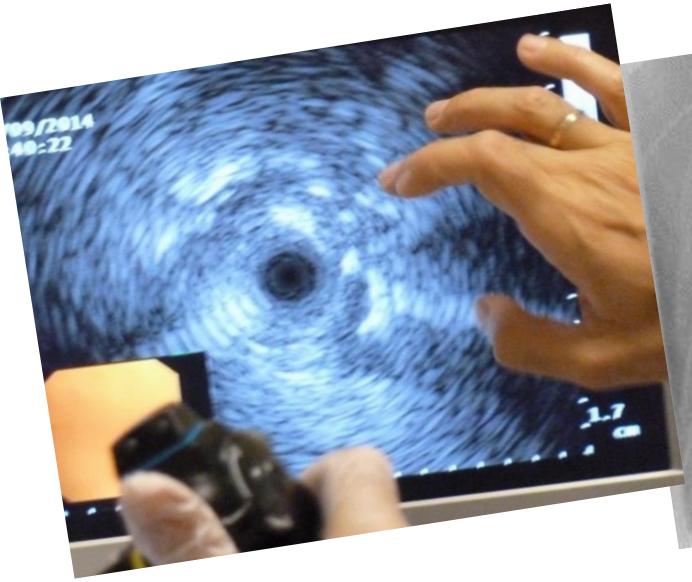
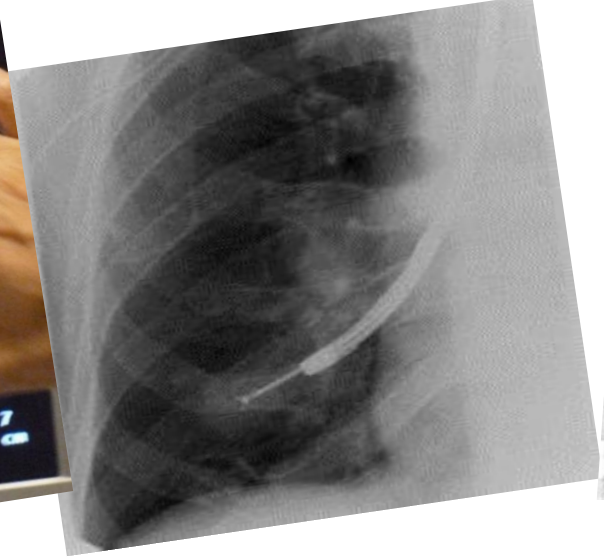
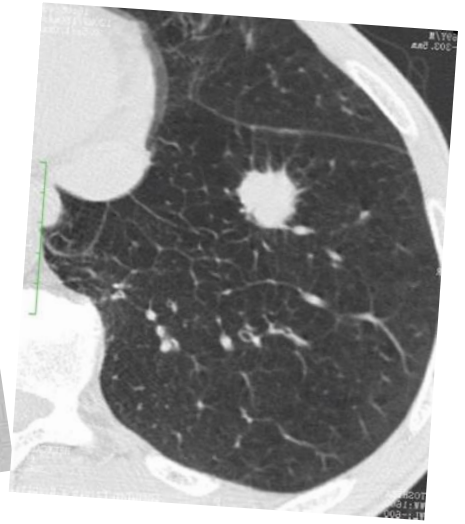





Assisted Access to the Lung Periphery (Nodules/lesions)

AI, CAD, CBCT, rEBUS, EMN, VB, UB, RB

and beyond.....

***Gr. Stratakos** MD, FCCP*

Professor of Respiratory Medicine

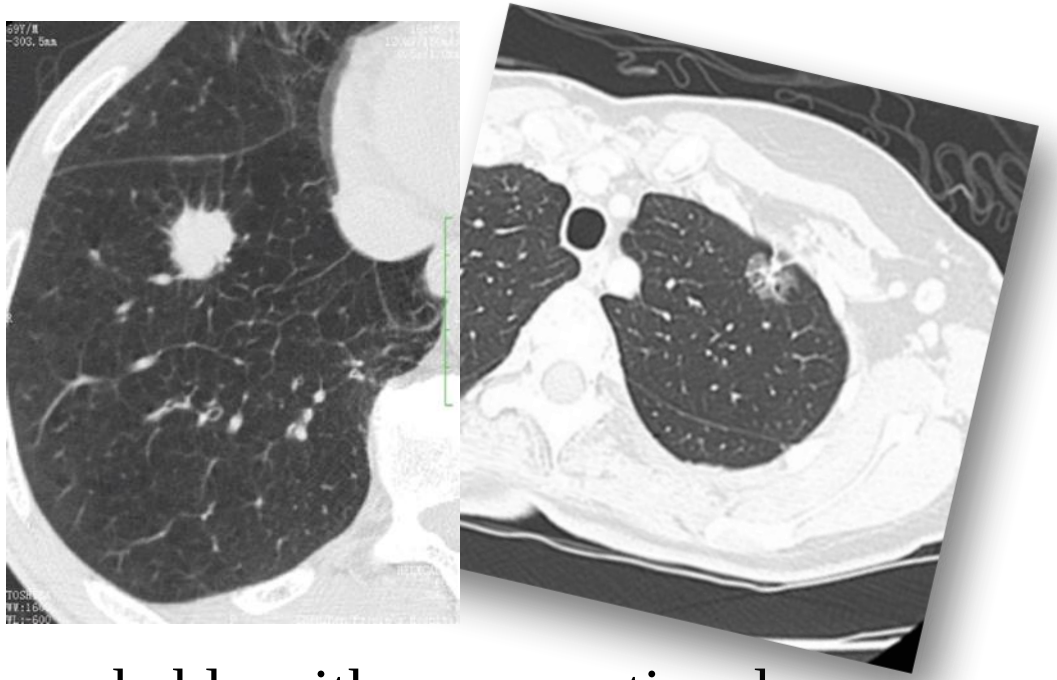
Head of the Interventional Pulmonology Unit

N. K. University of Athens, Greece

President EABIP

Εθνικό και Καποδιστριακό
ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

Definition of a “peripheral Nodule”



Node not reachable with a conventional Bronchoscope with OD >5mm.
Can be either solid, subsolid or ggo and guidelines for follow up distinguish between < 8 and > 8 mm

- **Solid node d ≤ 8mm**
- **Solid node d> 8mm**
- **Subsolid node-GGO**

PET-CT has not optimal PPV or NPV

Chest 2021 Aug 6;S0012-3692(21)03624-2

The Probability of Lung Cancer in Patients With Incidentally Detected Pulmonary Nodules

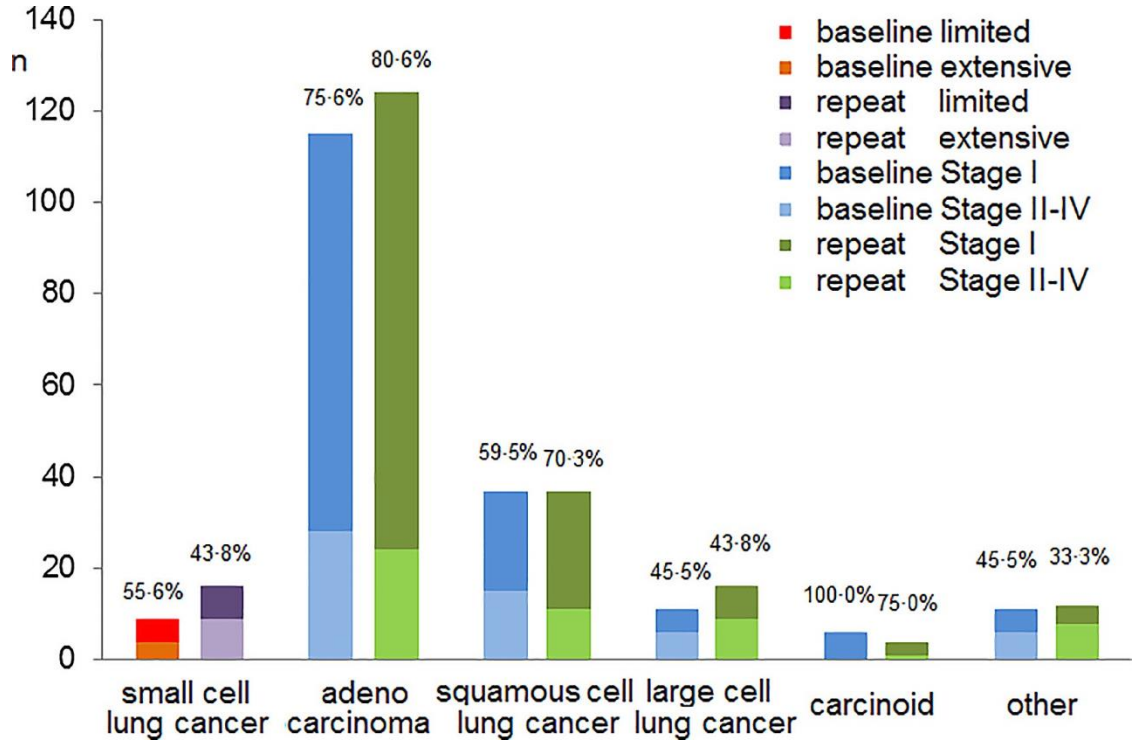
- 23,780 individuals with a nodule measuring > 8 mm, including
- Ca was diagnosed in 5.4% of never smokers, 12.2% of former smokers, and 17.7% of current smokers.
- Cancer was diagnosed in 5.7% of patients with nodules measuring 9 -15 mm, 12.1% of patients with nodules 15-20 mm, and 18.4% of patients with nodules 20-30 mm.
- The Mayo Clinic model) was more accurate than the Brock model ($p < .0001$). Both models overestimated the probability of cancer.
- **Almost 10% of patients with an incidental pulmonary nodule measuring > 8 mm in diameter will receive a lung cancer diagnosis.**

Early Lung Ca shift?

Pathology-specific differences in the proportion of early cancer between baseline and the repeat rounds. Data pooled from the Münster, Israel, Mayo, Toronto, NELSON & ITALUNGstudies.

Reasons for histological Dx before Surgical Management

- Benign etiology is always probable
- 25% of the pts are not fit for surgery
- Patients may qualify for neo-adjuvant strategy



PLOS ONE | DOI:10.1371/journal.pone.0164416 October 13, 2016

The NEW ENGLAND JOURNAL of MEDICINE

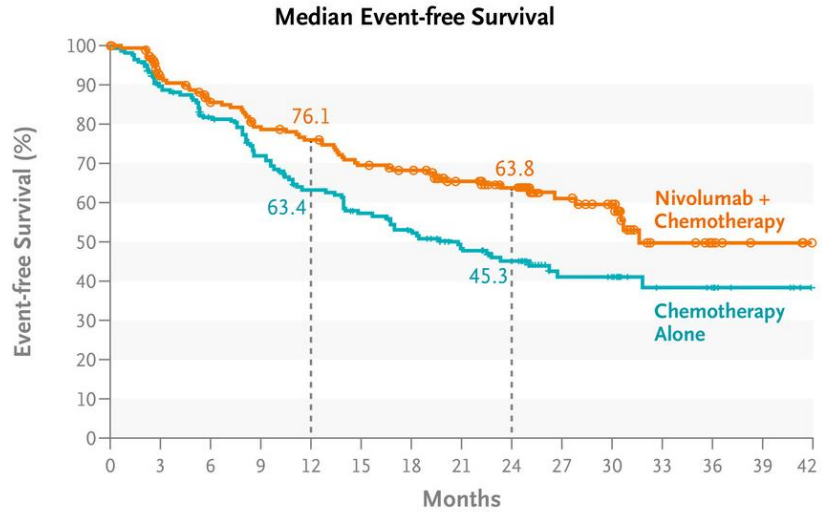
Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

Forde PM et al. DOI: 10.1056/NEJMoa2202170

Checkmate 816 (2022)

In patients with resectable NSCLC, Neoadjuvant Nivolumab plus Chemotherapy as well as Pembrolizumab plus chemotherapy followed by resection and adjuvant pembrolizumab , resulted in **significantly longer event-free survival** and a higher percentage of patients with a pathological complete response than chemotherapy alone.

The addition of nivolumab or Pembrolizumab to neoadjuvant chemotherapy did not increase the incidence of adverse events or impede the feasibility of surgery..



Keynote 671 (2023)

Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer

Heather Wakelee, M.D., Moishe Liberman, M.D., Ph.D., Terufumi Kato, M.D., Masahiro Tsuboi, M.D., Ph.D., Se-Hoon Lee, M.D., Ph.D., Shugeng Gao, M.D., Ke-Neng Chen, M.D., Ph.D., Christophe Dooms, M.D., Ph.D., Margarita Majem, M.D., Ph.D., Ekkehard Eigendorff, M.D., Gastón L. Martinengo, M.D., Olivier Bylicki, M.D., et al., for the KEYNOTE-671 Investigators*

Peripheral Pulmonary lesions

Non Interventional approach

Interventional approach

Input

Age 50 years

Sex ○ Female (0.6011)

● Male (0)

Family history of lung cancer ☑ (0.2961)

Emphysema ☑ (0.2953)

Nodule size 9 mm

Nodule type ○ Nonsolid or ground-glass (-0.1276)

● Partially solid (0.377)

○ Solid (0)

Nodule in upper lung ☑ (0.6581)

Nodule count 1 number

Spiculation ☑ (0.7729)

Results

Log odds -1.65

Cancer probability 16.13 %

Solitary Pulmonary Nodule (SPN) Malignancy Risk Score (Mayo Clinic Model)

☆

Predicts malignancy risk in solitary lung nodules on chest x-ray.

INSTRUCTIONS

Do not use in patients with prior lung cancer diagnosis or with history of extrathoracic cancer diagnosed within 5 years of nodule presentation.

When to Use

Age	50	years
Nodule diameter	9	mm
Current or former smoker	No 0	Yes +1
Extrathoracic cancer diagnosis ≥5 years prior	No 0	Yes +1
Upper lobe location of tumor	No 0	Yes +1
Nodule spiculation	No 0	Yes +1

FDG-PET
Optional, if performed

- PET not performed
- No uptake
- Faint uptake
- Moderate uptake
- Intense uptake

68.9 %

Probability of malignancy

One study suggests watchful waiting only at very low post-test probabilities (<2%), biopsy at "lower" post-test probabilities (2% to 20%), and surgery at higher post-test probabilities (>70%). See Next Steps.

Copy Results | Next Steps

BIMC Web Calculator
<Institute> 2009-2014

<LOGO>

Prior Probability of Malignancy (1-99%) 50

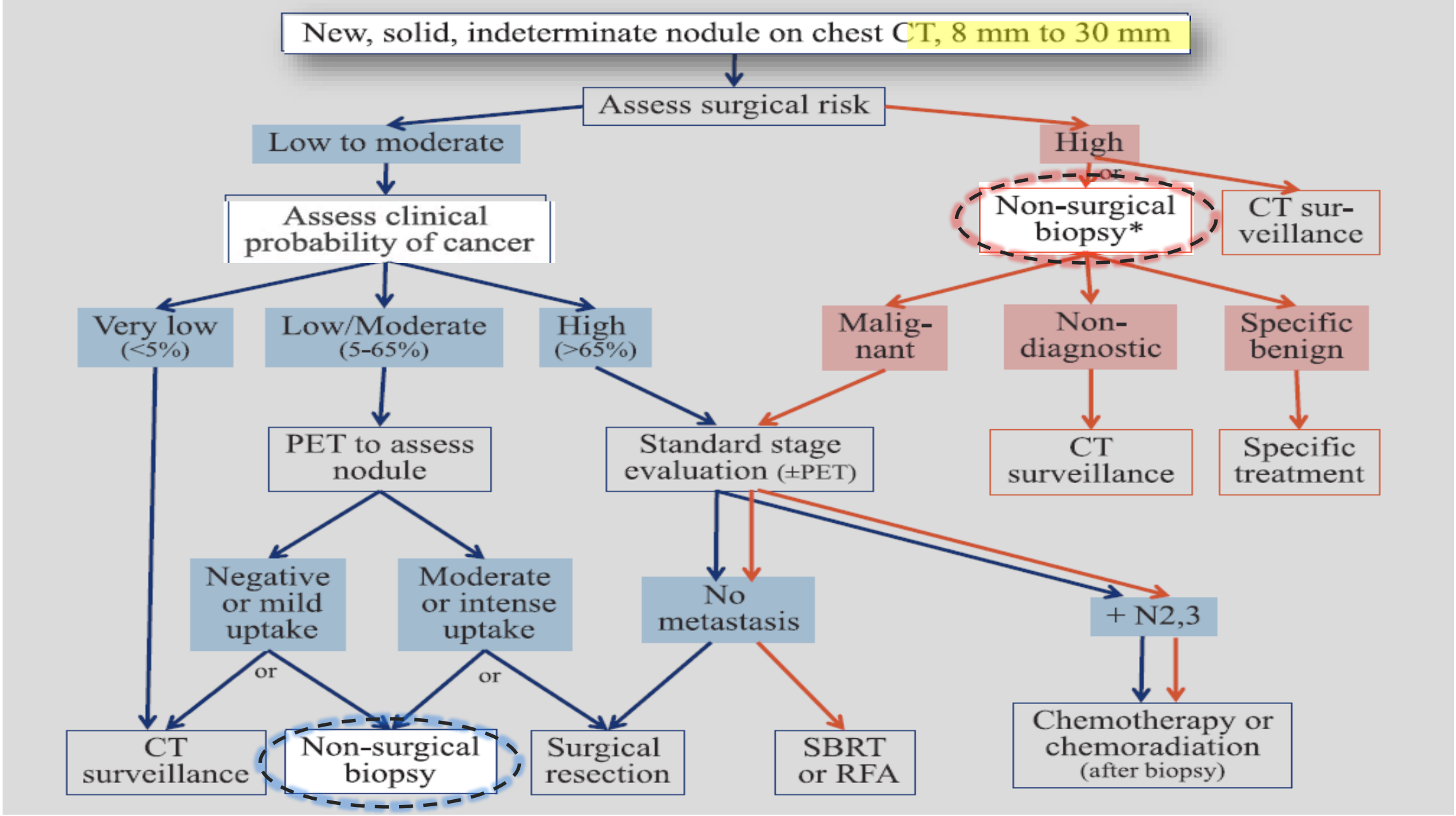
Estimated prevalence of disease in the referred population

Age:	40-49
Smoking (Pack-years)	>= 40
Hx Prev Malig:	No
Size (cm)	4-10 mm
Location	Superior
Edges	Lobulated
Volume Doubling Time (VDT)	401-900 d
Minimum Focal Density	between -60 and -30 HU
Enhancement	between 15 and 40 HU
FDG-PET	SUV between 1 and 2.5

Probability of Malignancy 68 %

Get BIMC result | Reset

Web Calculator version: v1



DIAGNOSIS AND MANAGEMENT OF LUNG CANCER, 3RD ED: ACCP GUIDELINES

15822 participants in NELSON trial (7915 LDCT screening vs 7907 no screening)

196 screen cancers were detected and another 34 in the 1st year after screening and 15 in the 2nd year after screening. Retrospective assessment of the last screening CT and clinical CT in 34 patients with interval cancer, showed that interval cancers **were not visible in 35%** of the cases or cancers **were visible when retrospectively assessed** but **were not diagnosed because of radiological detection and interpretation errors (50%) misclassification by the protocol (6%), participant non compliance (6%) and non adherence to protocol (3%).**

Artificial intelligence (AI) and pulmonary nodules

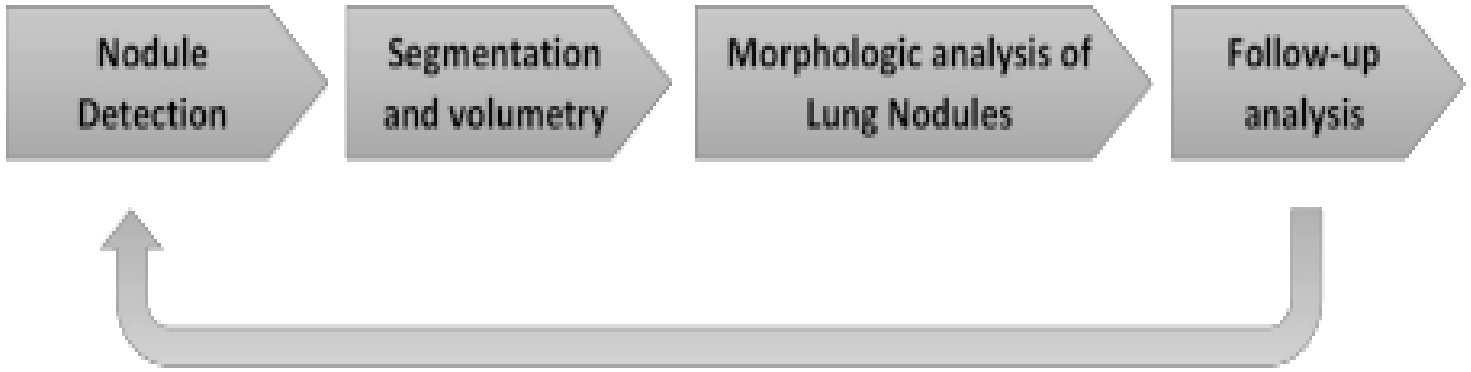
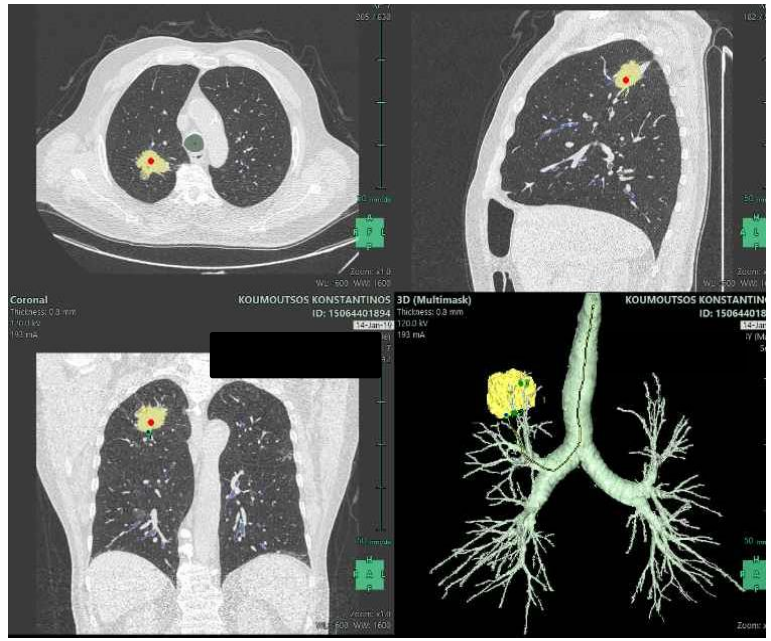


Figure 2 Steps in lung nodule management pathway where AI may play a role.



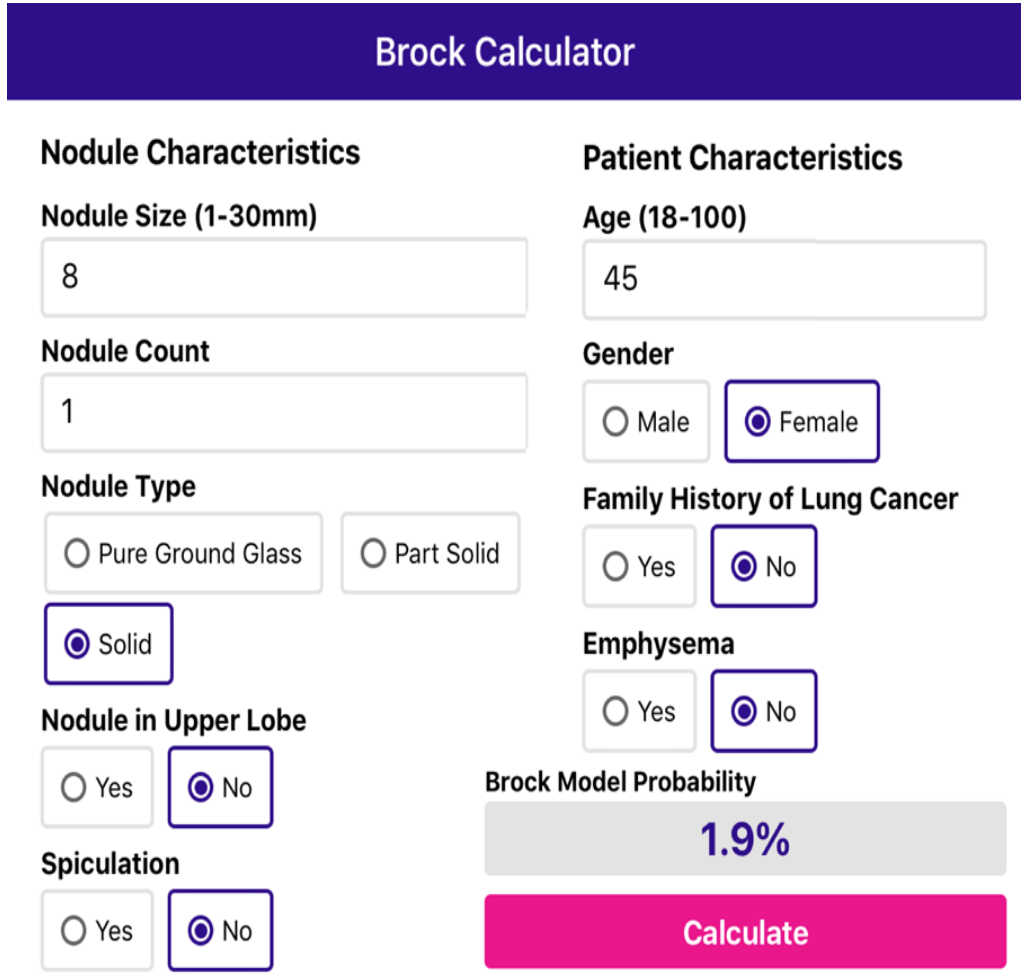
These protocols employ nodule volumetry, measurement of volume doubling time and morphology analysis.
Algorithms of artificial intelligence combine these parameters.

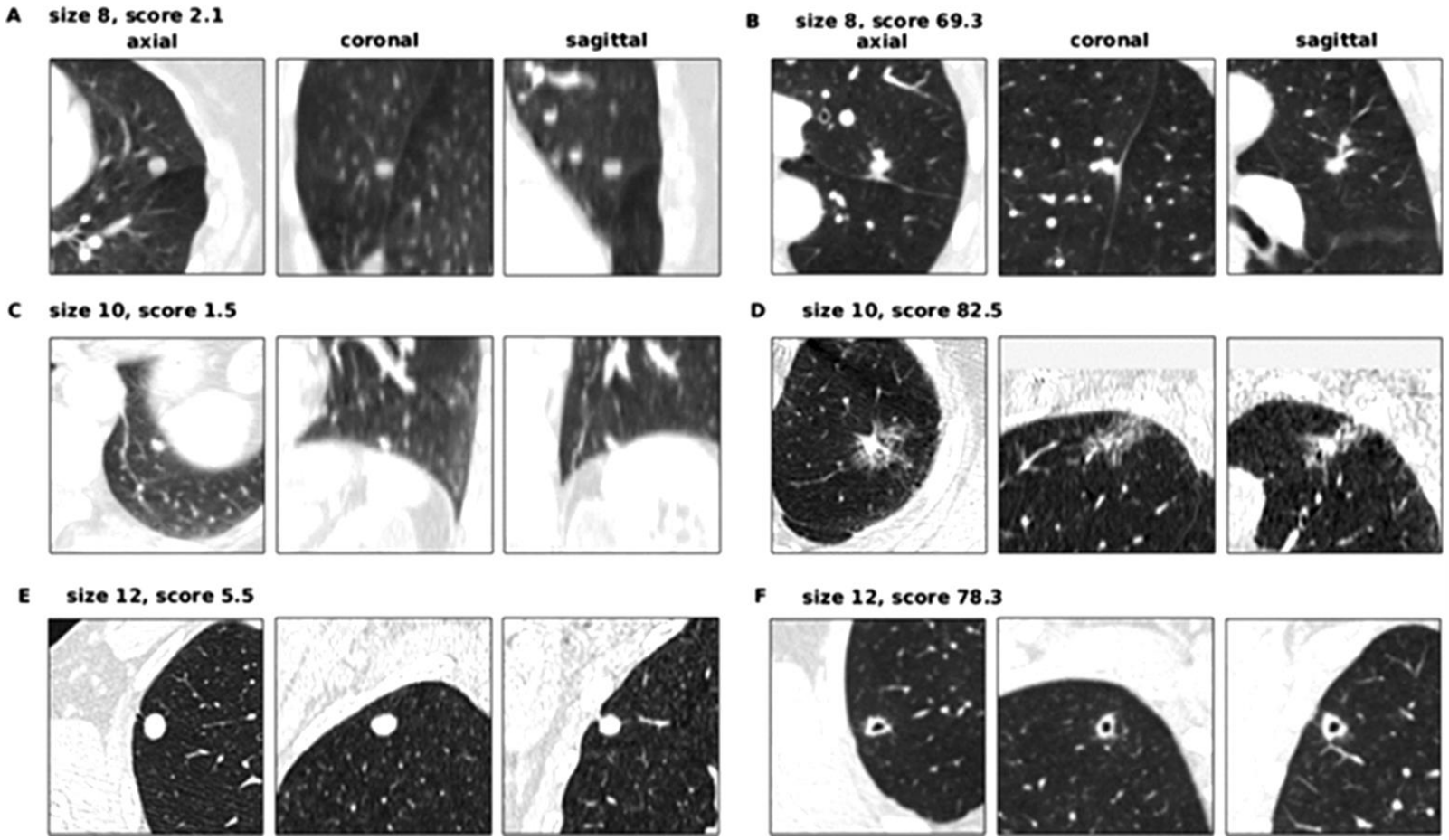
Clin Radiol . 2020 Jan;75(1):13-19.

External validation of a convolutional neural network artificial intelligence tool to predict malignancy in pulmonary nodules

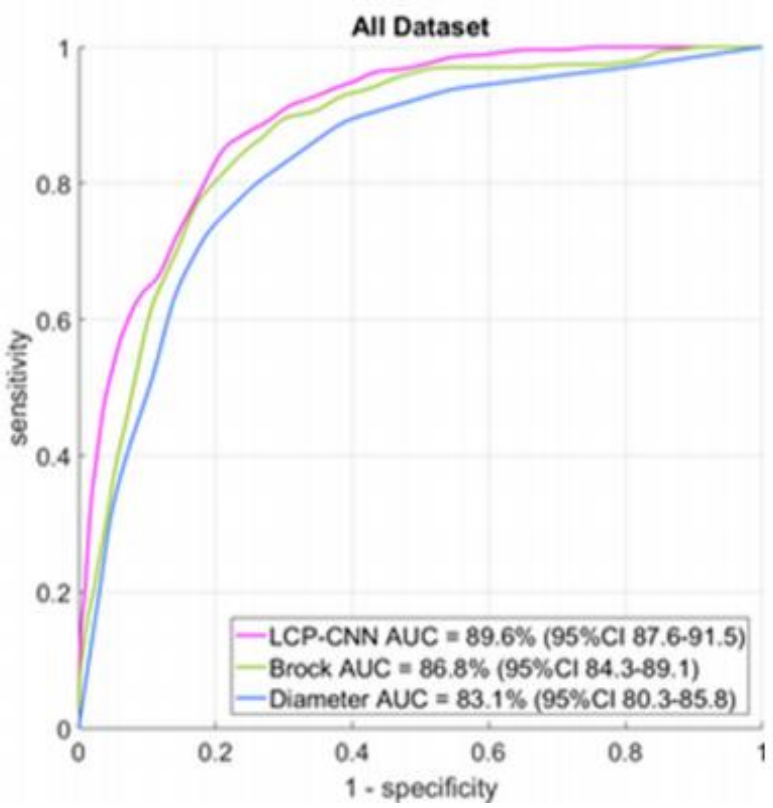
Baldwin DR, et al. Thorax 2020;75:306–312.

- ✓ Performance of an AI algorithm, the lung cancer prediction convolutional neural network (LCP-CNN) for nodules 5-15 mm, with that of the **Brock University model,** recommended in UK guidelines.
- ✓ The LCP-CNN is an AI tool that analyses parts of a CT scan around a nodule of interest and provides a score from 0 to 100 for that nodule



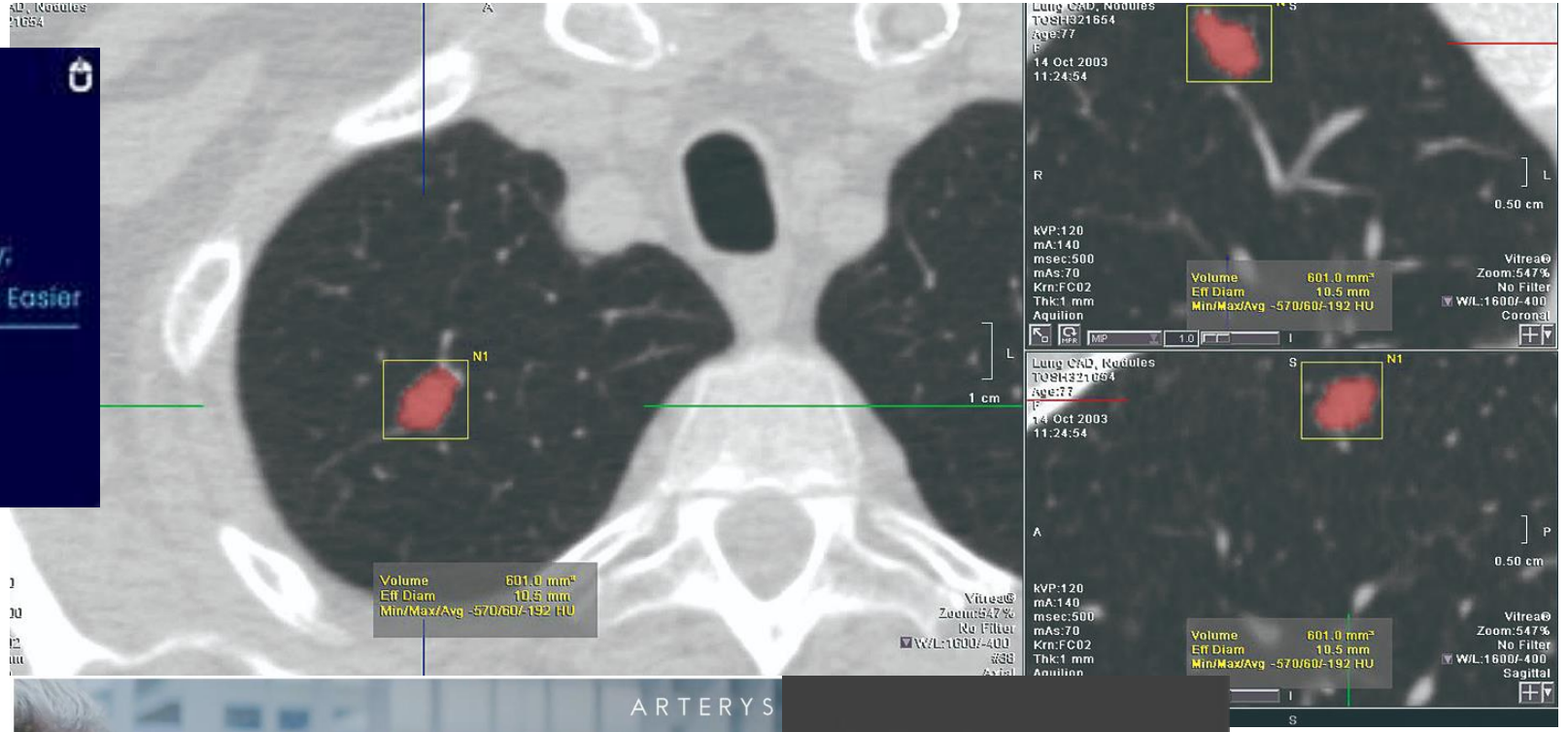


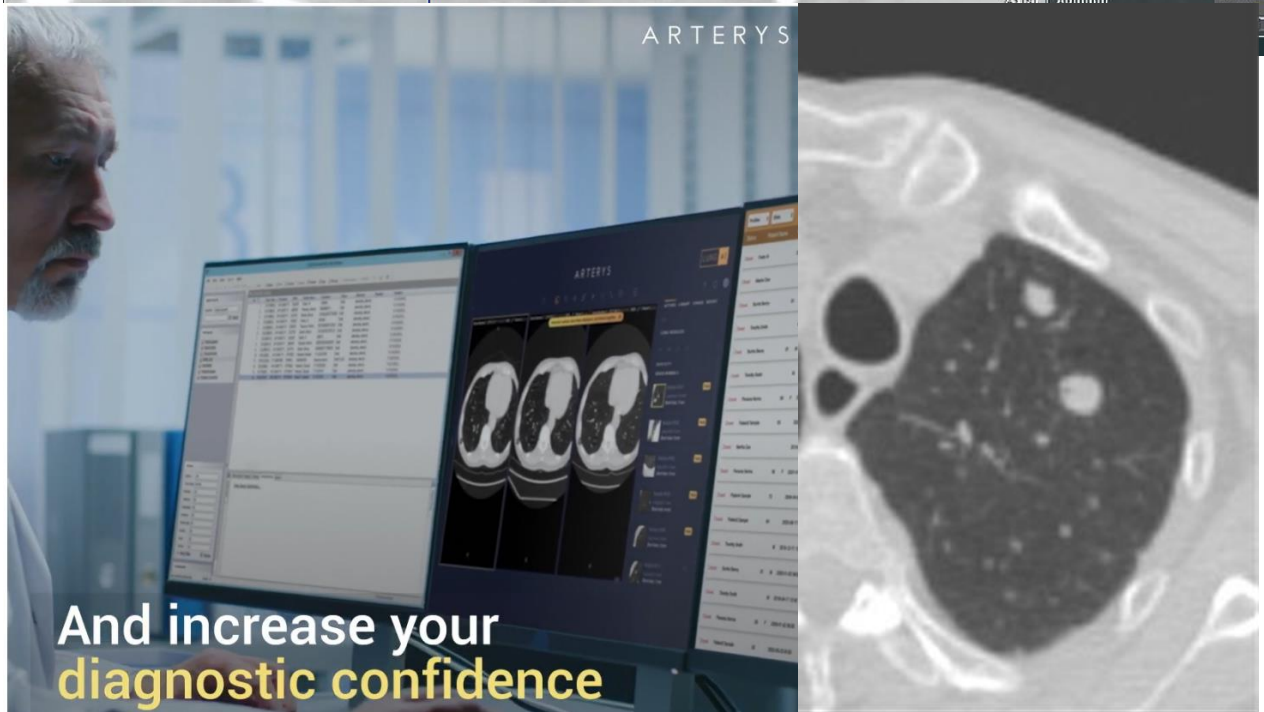
The LCP-CNN achieved an AUC of 89.6% , compared with 86.8% for Brock. ($p<0.005$).



Baldwin DR, et al. Thorax 2020;75:306–312.

- **Detection**
- **Segmentation**
- **Classification**
- **Qualification**
- **Quantification**
- **Anatomical Structure**
- **Risk Assessment**





SPN "Approach" – Non interventional techniques

Cancers (Basel). 2023 Feb; 15(4): 1000.
Published online 2023 Feb 4. doi: 10.3390/cancers15041000
PMCID: PMC9953844
PMID: 36831344

Qualitative and Semiquantitative Parameters of ^{18}F-FDG-PET/CT as
Malignancy in Patients with Solitary Pulmonary Nodule

J Clin Med. 2023 May; 12(10): 3536.
Published online 2023 May 18. doi: 10.3390/jcm12103536
PMCID: PMC10219568
PMID: 37240643

The Effects of Artificial Intelligence Assistance on the Radiologists' Assessment of Lung Nodules on CT Scans: A Systematic Review

Lotte J. S. Ewals,[1,2,*] Kasper van der Wulp,[1] Ben E. E. M. van den Borne,[3] Jon R. Pluyter,[4] Igor Jacobs,[5] Dimitrios Mavroeidis,[6] Fons van der Sommen,[2] and Joost Nederend[1]

J Digit Imaging. 2023 Apr;36(2):617-626. doi: 10.1007/s10278-022-00747-z. Epub 2022 Dec 7.

Multi-Modal Feature Fusion-Based Multi-Branch Classification Network for Pulmonary Nodule Malignancy Suspiciousness Diagnosis

Haiying Yuan [1], Yanrui Wu [2], Mengfan Dai [2]

Randomized Controlled Trial J Gene Med. 2023 Sep;25(9):e3529. doi: 10.1002/jgm.3529.
Epub 2023 May 16.

A combined diagnostic model based on circulating tumor cell in patients with solitary pulmonary nodules

J Natl Cancer Inst. 2023 Sep 7;115(9):1060-1070. doi: 10.1093/jnci/djad1

Circulating proteome for pulmonary nodule malignancy

Diagn Interv Imaging. 2023 Jan;104(1):11-17. doi: 10.1016/j.diii.2022.11.007.

Artificial intelligence: A critical review of applications for lung nodule and lung cancer

Constance de Margerie-Mellon [1], Guillaume Chassagnon [2]

Combined Clinical, Imaging and Biological markers

> J Natl Cancer Inst. 2023 Sep 7;115(9):1060-1070. doi: 10.1093/jnci/djad122.

Circulating proteome for pulmonary nodule malignancy

"Based on 4 international low-dose computed tomography screening studies, we assayed 1078 protein markers.. from 1253 participants based on a nested case-control design.. We identified 36 potentially informative circulating protein markers differentiating malignant from benign nodules, representing a tightly connected biological network"

Randomized Controlled Trial > J Gene Med. 2023 Sep;25(9):e3529. doi: 10.1002/jgm.3529. Epub 2023 May 16.

A combined diagnostic model based on circulating tumor cell in patients with solitary pulmonary nodules

"We confirmed the value of FR+CTC in diagnosing SPNs and developed a prediction model based on FR+CTC, demographic characteristics, and serum biomarkers for differential diagnosis of solitary pulmonary nodules"

> Lancet Digit Health. 2023 Aug 9:S2589-7500(23)00125-5. doi: 10.1016/S2589-7500(23)00125-5. Online ahead of print.

Accurate classification of pulmonary nodules by a combined model of clinical, imaging, and cell-free DNA methylation biomarkers: a model development and external validation study

*"We developed a combined clinical and imaging biomarkers (CIBM) model by machine learning... integrated with established circulating tumour DNA methylation model (PulmoSeek) to create a new combined model.. evaluated using decision curve analysis... **correctly identifying approximately 83 of 100 people with lung cancer**. Using the PulmoSeek Plus model to classify pulmonary nodules... **would have reduced 89% (105/118) of unnecessary surgeries and 73% (308/423) of delayed treatments**"*

> BMC Cancer. 2022 Apr 9;22(1):382. doi: 10.1186/s12885-022-09472-w.

Diagnostic value of circulating genetically abnormal cells to support computed tomography for benign and malignant pulmonary nodules

*"...The sensitivity (SE), **specificity (SP), and positive (PPV)** and negative (NPV) predictive values of the combined model were 61.0%, **94.1%, 94.7%** and 58.2%, respectively... higher diagnostic value than traditional tumour markers in early-stage lung cancer..."*

Interventional Techniques

- CT guided TTB (sens 65-94%)
- Radial EBUS (sens 70-75%)
- Ultrathin Bronchoscope (sens 70%)
- Virtual Navigation Bronchoscopy
- Electromagnetic navigation (sens 70%)
- Robotic Assisted Bronchoscopy (sens 75%)
- Combining rEBUS/EMN/VB/UB/Fluoroscopy (sens 88-90%)

+/- ROSE

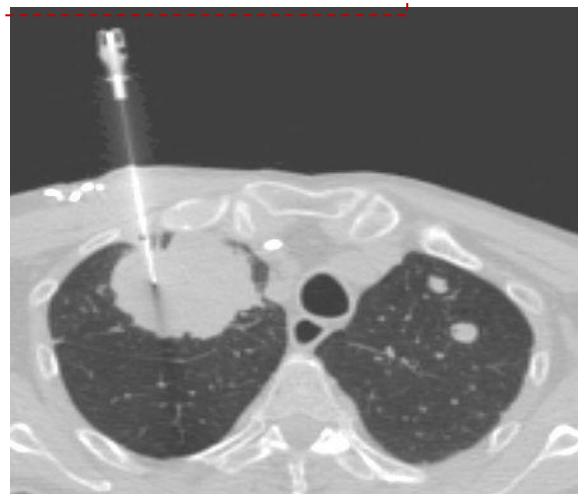
CT guided fine needle aspiration

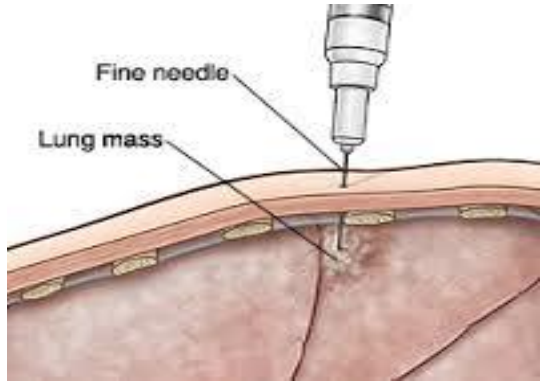
- **CT-FNA yields high sensitivity values around 90%, with a slightly lower sensitivity of 68–78% for smaller lesions (≤ 15 mm in diameter).**

- Sensitivity drops further with increasing distance between the nodule and pleura

Hofmann et al. Clin Lung Ca 2009.
Ost D et al. Chest 2008
Hautmann H et al.Respirology 2010

The overall complication rate for traversed lung depth ≥ 20.5 mm was 48% compared to 18% for traversed lung depth < 20.5 mm (p< 0.001).”





SPN Approach Update: CT Guided TTB

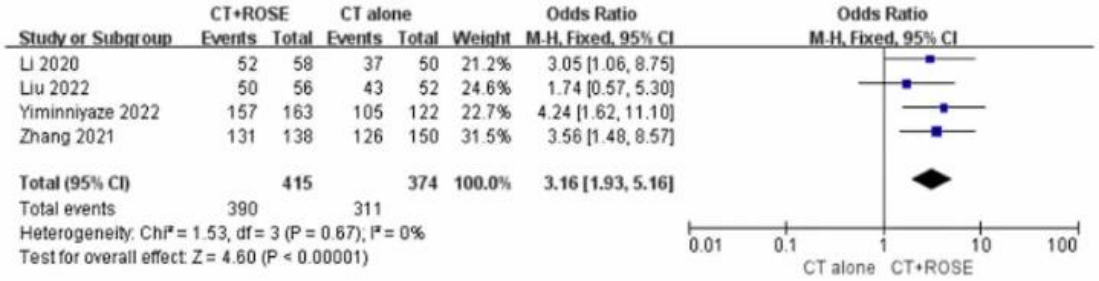
J Cardiothorac Surg. 2023 Apr 10;18(1):122. doi: 10.1186/s13019-023-02212-6.

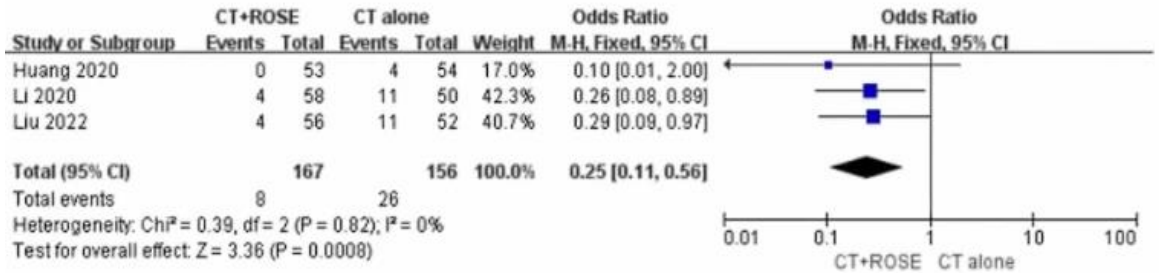
Computed tomography-guided lung biopsy with rapid on-site evaluation for diagnosis of lung lesions: a meta-analysis

Table 2 Baseline data of the patients in these studies

Author	Groups	Patients (n)	Mean age	Gender (M/F)	Mean diameter	Mean lesion-pleura distance	Final diagnoses (malignant/benign)
Huang [16]	CT + ROSE	53	64.5 y	30/23	Not given	Not given	49/4
	CT alone	54	64.4 y	33/21	Not given	Not given	Not given
Li [17]	CT + ROSE	58	59.8 y	30/28	1.4 cm	4.5 cm	32/26
	CT alone	50	59.3 y	28/22	1.3 cm	4.6 cm	28/22
Liu [18]	CT + ROSE	56	59.8 y	30/26	2.5 cm	4.4 cm	32/24
	CT alone	52	59.4 y	28/24	3.4 cm	4.7 cm	28/24
Peng [19]	CT + ROSE	132	57.3 y	86/46	Not given	Not given	61/71
	CT alone	102	56.4 y	66/36	Not given	Not given	54/48
Wang [20]	CT + ROSE	148	59.8 y	98/50	2.9 cm	4.2 cm	92/56
	CT alone	143	59.7 y	94/49	2.9 cm	4.0 cm	Not given
Yiminniyaze [21]	CT + ROSE	163	63 y	108/55	< / ≥ 3 cm: 36/127	Not given	157/6
	CT alone	122	64.5 y	85/37	< / ≥ 3 cm: 23/99	Not given	113/9
Zhang [22]	CT + ROSE	138	59.9 y	79/59	11.1 cm	Not given	95/43
	CT alone	150	60.1	96/54	10.9 cm	Not given	92/58

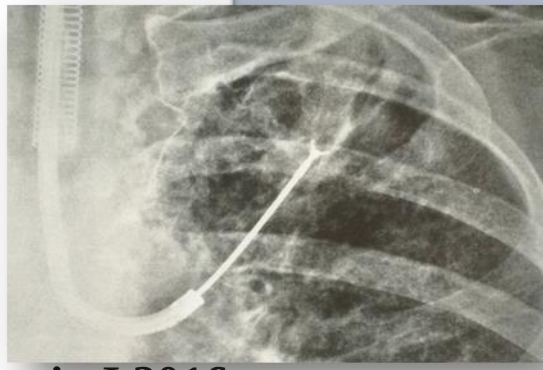
CT, computed tomography; M, male; F, female; ROSE, rapid on-site evaluation





- The meta-analysis included 6 studies
- A total of 748 and 673 patients who respectively underwent CT-guided LB procedures with and without ROSE
- Diagnostic yield was higher with ROSE vs no ROSE 94.0% vs. 83.2% with less biopsies needed in total

Transbronchial needle aspiration in peripheral pulmonary lesions: a systematic review and meta-analysis



Mondomi M et al. Eur Respir J 2016

Michele Mondoni[1], Giovanni Sotgiu[2], Martina Bonifazi[3,4], Simone Dore[4], Elena Maria Parazzini[1], Paolo Carlucci[1], Stefano Gasparini[3,4] and Stefano Centanni[1]

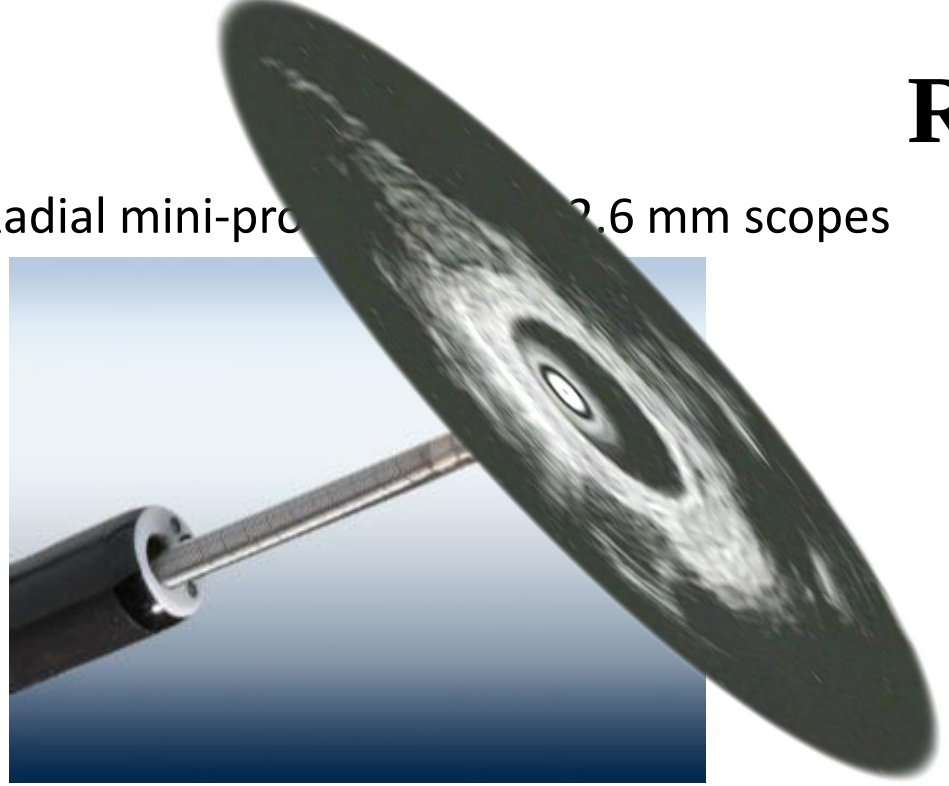
- **Higher diagnostic accuracy if :**

  - **There is bronchus sign 0.70 vs. 0.51**
  - **There is ROSE 0.62 vs. 0.51**
  - **Malignancy 0.55 vs. 0.17**
  - **Lesion > 30 mm 0.81 vs. 0.55**

  - **Combined with TBNA in the mediastinum**

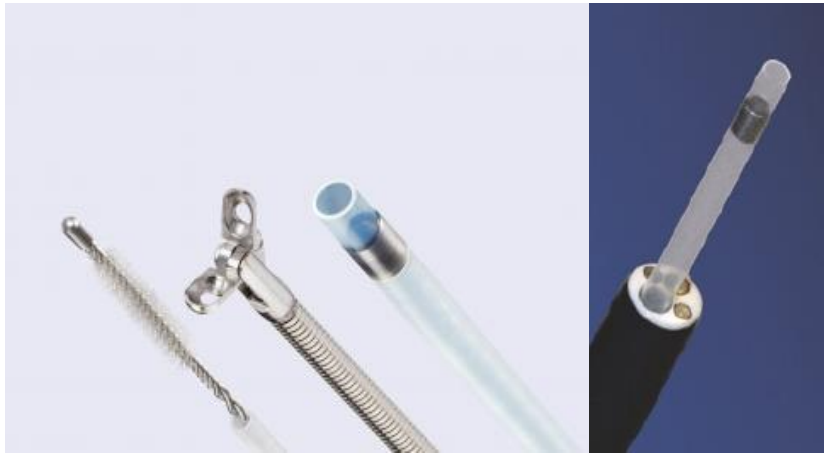
Radial EBUS

Radial mini-pro .6 mm scopes



Driving unit

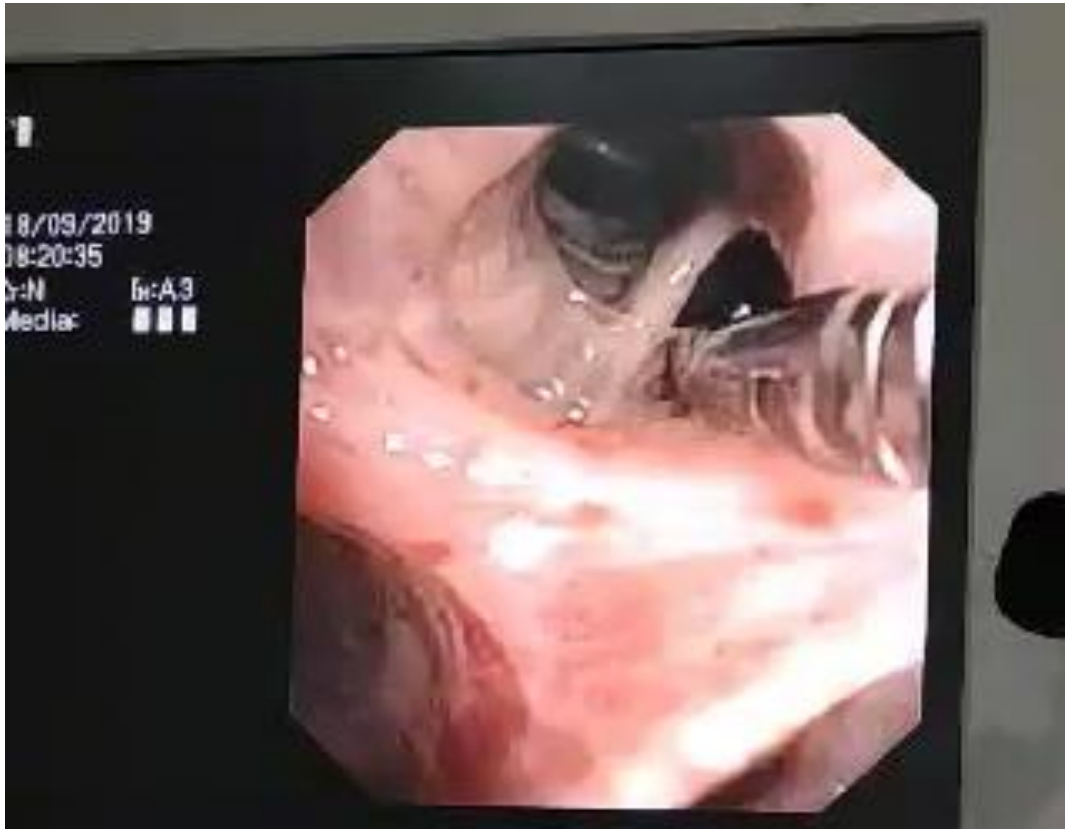
Guide sheath- brush- needle- forceps

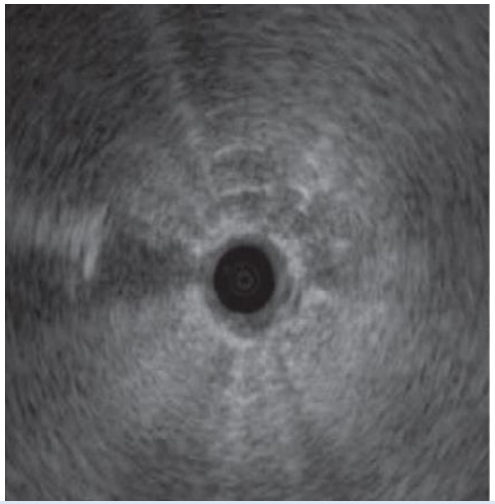


Positioning device for the guide sheath

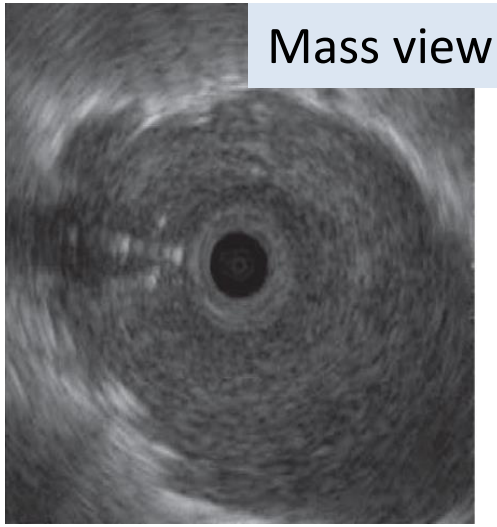
Radial EBUS

360° Degrees rotating view





Lung (snowstorm) view



Mass view

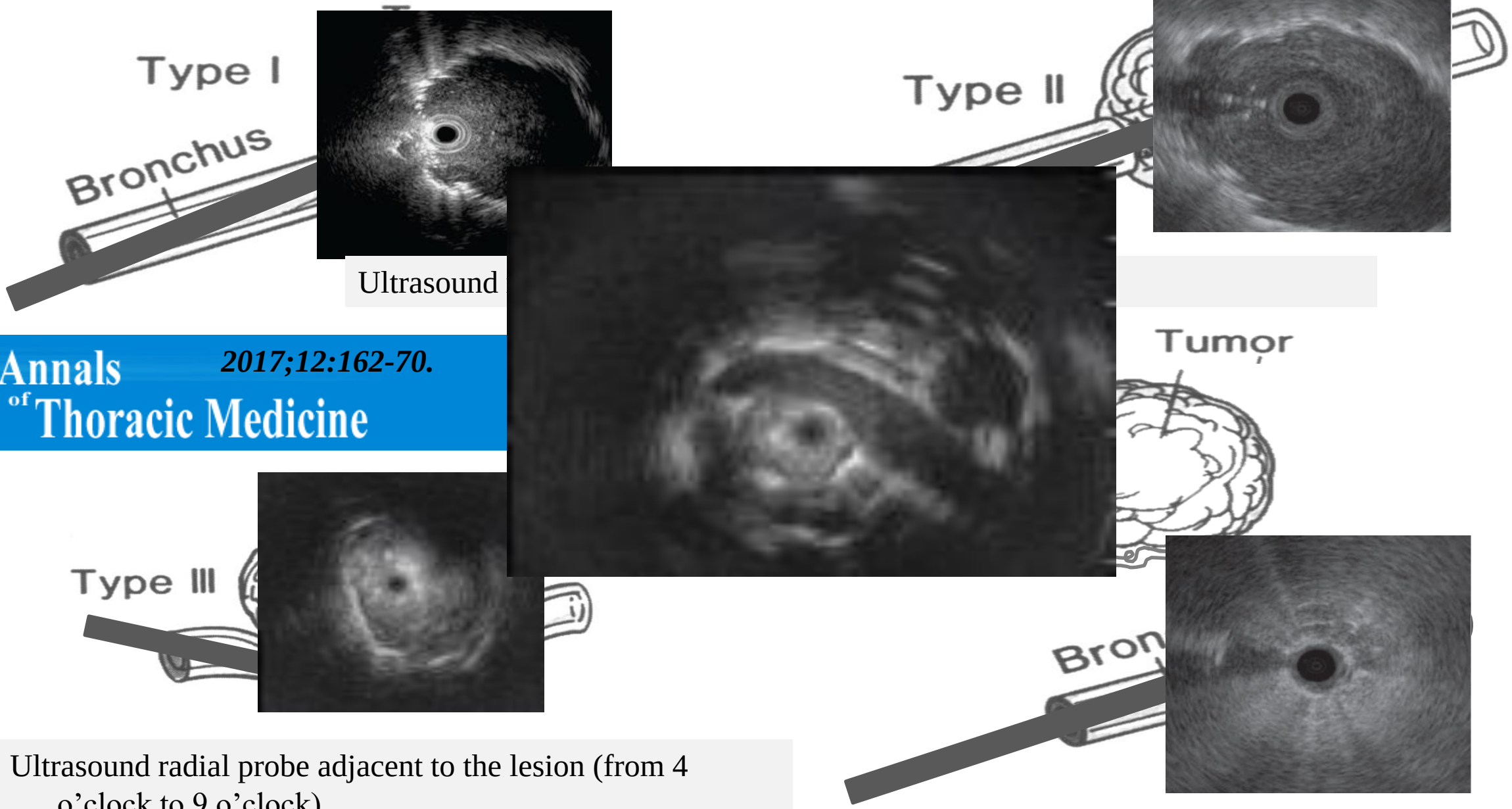
Table 1. Studies evaluating the diagnostic yield of radial probe endobronchial ultrasound since 2014

Study	Year	Pro/Retro*	Number of lesions	Diameter mean	Diameter median	Diagnostic yield %	Guide sheath	Fluoro*	Other tools*
Boonsarngsuk *et al.* [26]	2014	Retro	174	25.1 mm (SD 10.7 mm)	NR	79.9% overall	+	+	Forceps, brush, BAL
Ikezawa *et al.* [27]	2014	Retro	67	21 mm (SD 8 mm)	NR	57% overall	+	+	Double-hinged curette, forceps, brush
Chen *et al.* [28]	2014	Retro	467	NR	NR	69% overall	+/−	−	Forceps, brush, TBNA
Hayama *et al.* [29]	2015	Retro	965	NR	25 mm (range 6–107)	64.4% overall, 77.1% for malignancy	+	+	Forceps, brush, TBNA, VNB, ROSE
Durakovic *et al.* [30]	2015	Retro	147	28 mm (SD 18 mm)	NR	26.5% for malignancy	−	−	Forceps, brush, BW
Casutt *et al.* [31]	2015	Retro	51	25.8 mm (range 8–67 mm)	NR	72.5% overall	−	+	Forceps, brush, BAL/BW, TBNA
Chavez *et al.* [32]	2015	Retro	212	20.45 mm (SD 5.45 mm)	NR	67.5% for malignancy	+	+	Forceps, brush, TBNA, ROSE

*Pro, prospective; Retro, retrospective.
BAL, bronchoalveolar lavage; BW, bronchial washing; Fluoro, fluoroscopy; GS, guide sheath; NR, not reported; r-EBUS, radial probe endobronchial ultrasound; ROSE, rapid on-site evaluation; TBNA, transbronchial needle aspiration; VNB, virtual navigational bronchoscopy.

Variability 26,5-79,9% (depends on the size butmostly location regarding the bronchus)

Curr Opin Pulm Med 2016, 22:000–000



Ultrasound

Annals of Thoracic Medicine 2017;12:162-70.

Ultrasound radial probe adjacent to the lesion (from 4 o'clock to 9 o'clock),

SPN Approach Update: rEBUS vs CT Guided TTB

Review > Clin Respir J. 2021 Jan;15(1):3-10. doi: 10.1111/crj.13275. Epub 2020 Oct 5.

Endobronchial ultrasound-guided versus computed tomography-guided biopsy for peripheral pulmonary lesions: A meta-analysis

Yu-Fei Fu [1], Jing-Hao Zhang [2], Tao Wang [1], Yi-Bing Shi [1]

Study	Year	Design	Country	Patients number	Quality assessments: Jade score	Quality assessments: Newcastle–Ottawa score
Steinfort[13]	2011	RCT	Australia	48	3	–
Fielding[14]	2012	RCT	Australia	70	3	–
Wang[15]	2015	Retrospective	China	213	–	6
Wang[16]	2016	Retrospective	China	108	–	8
Zhang[17]	2017	Retrospective	China	513	–	8
Wang[18]	2018	RCT	China	160	3	–
Gupta[19]	2018	RCT	India	50	5	–
Zhu[20]	2018	Prospective non-RCT	China	335	–	7
Zhu[10]	2019	Retrospective	China	529	–	7

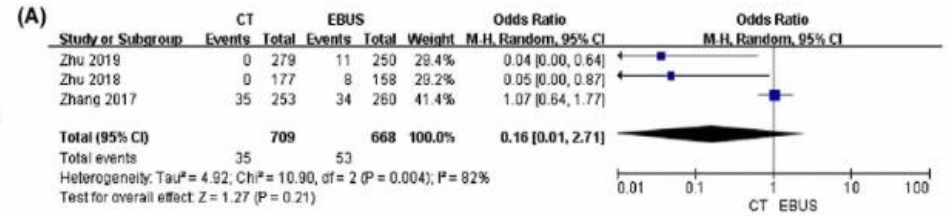
Abbreviations: RCT, randomized controlled trial.

2025 pts

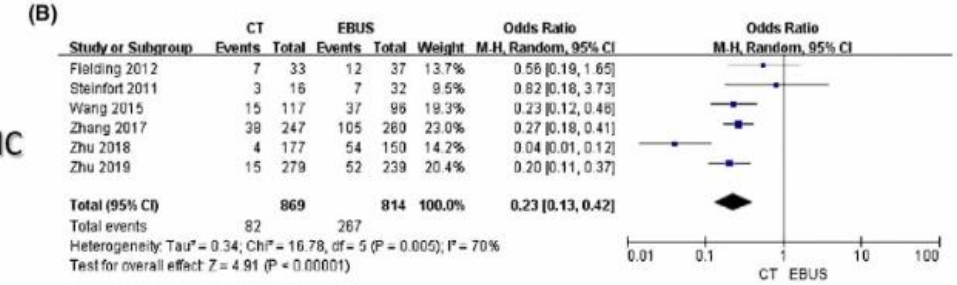
9 TRIALS (RCTs & Retrospective)

CT-TTNB was associated with:
- higher diagnostic yield (OR: 0.23; P < 0.00001)
- greater accuracy (OR: 0.43; P = 0.002), and
- higher rates of complications (OR: 7.27; P < 0.00001)

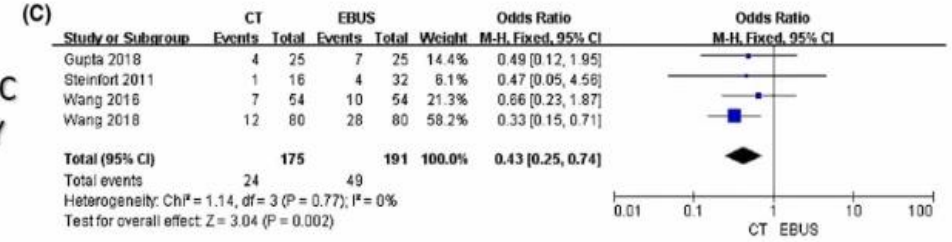
TECHNICAL SUCCESS



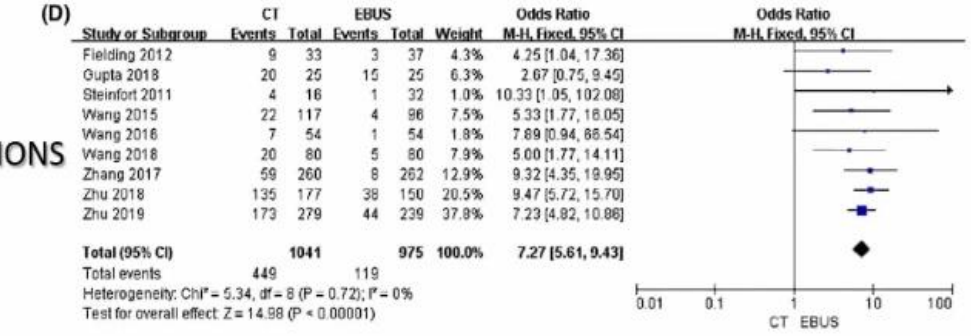
DIAGNOSTIC YIELD



DIAGNOSTIC ACCURACY

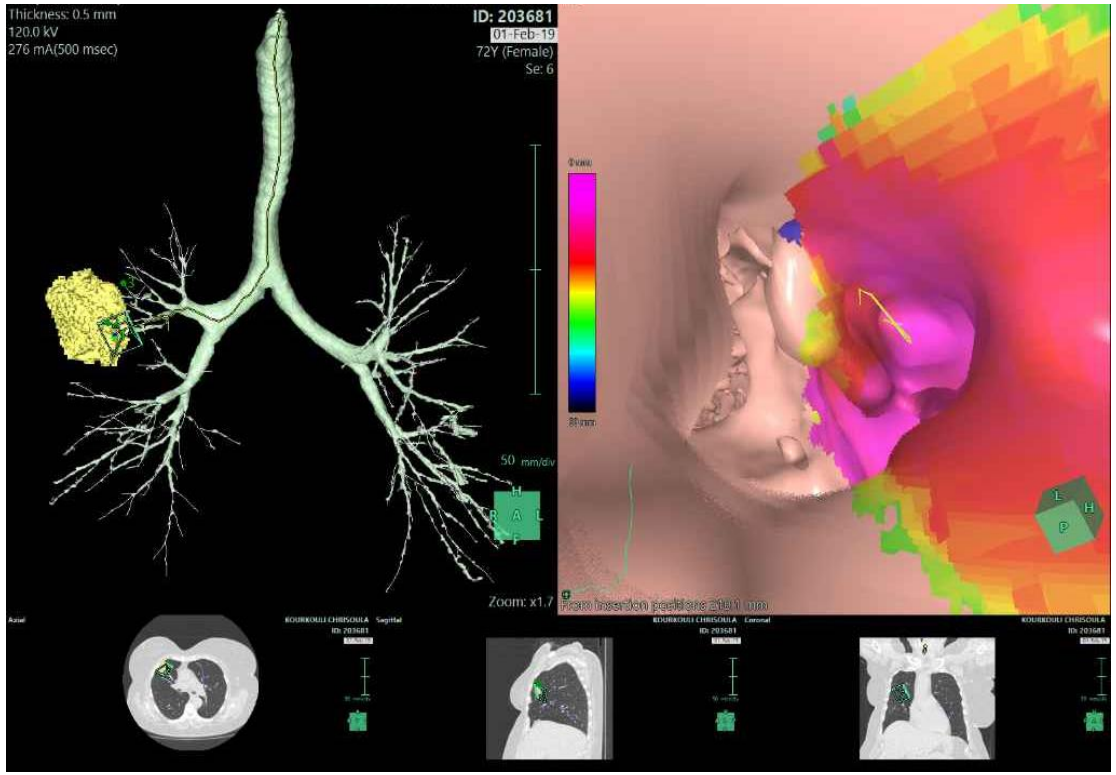


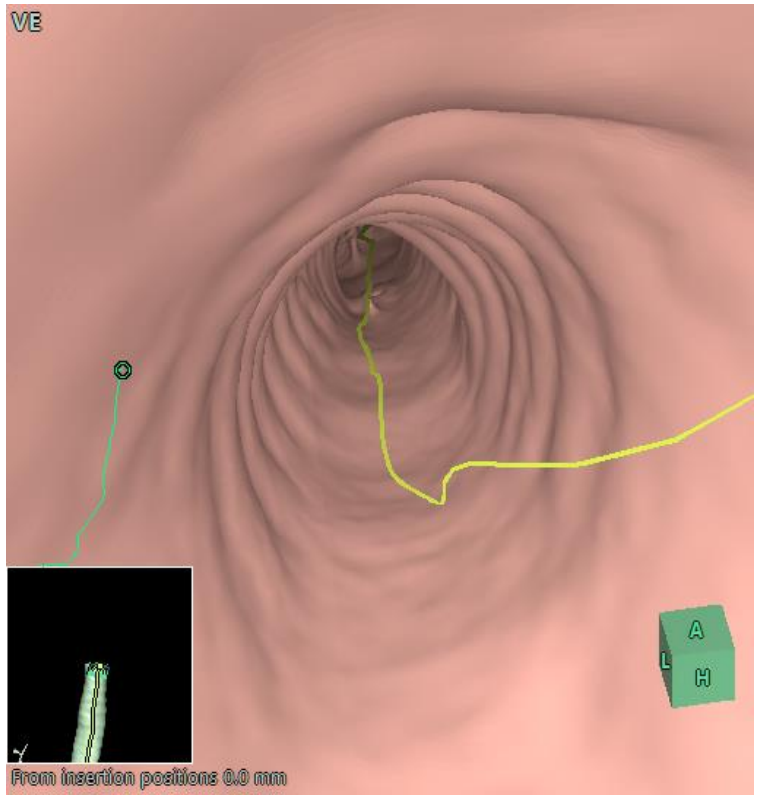
COMPLICATIONS



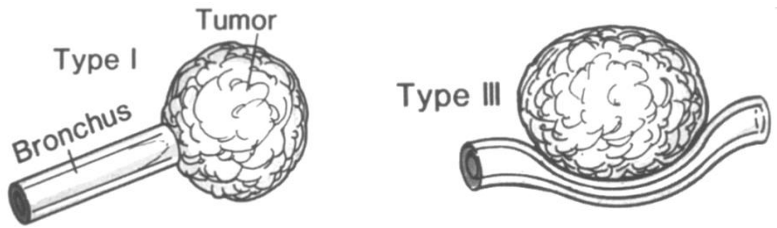
Pathway Selection

Virtual Bronchoscopic navigation based on CT scan





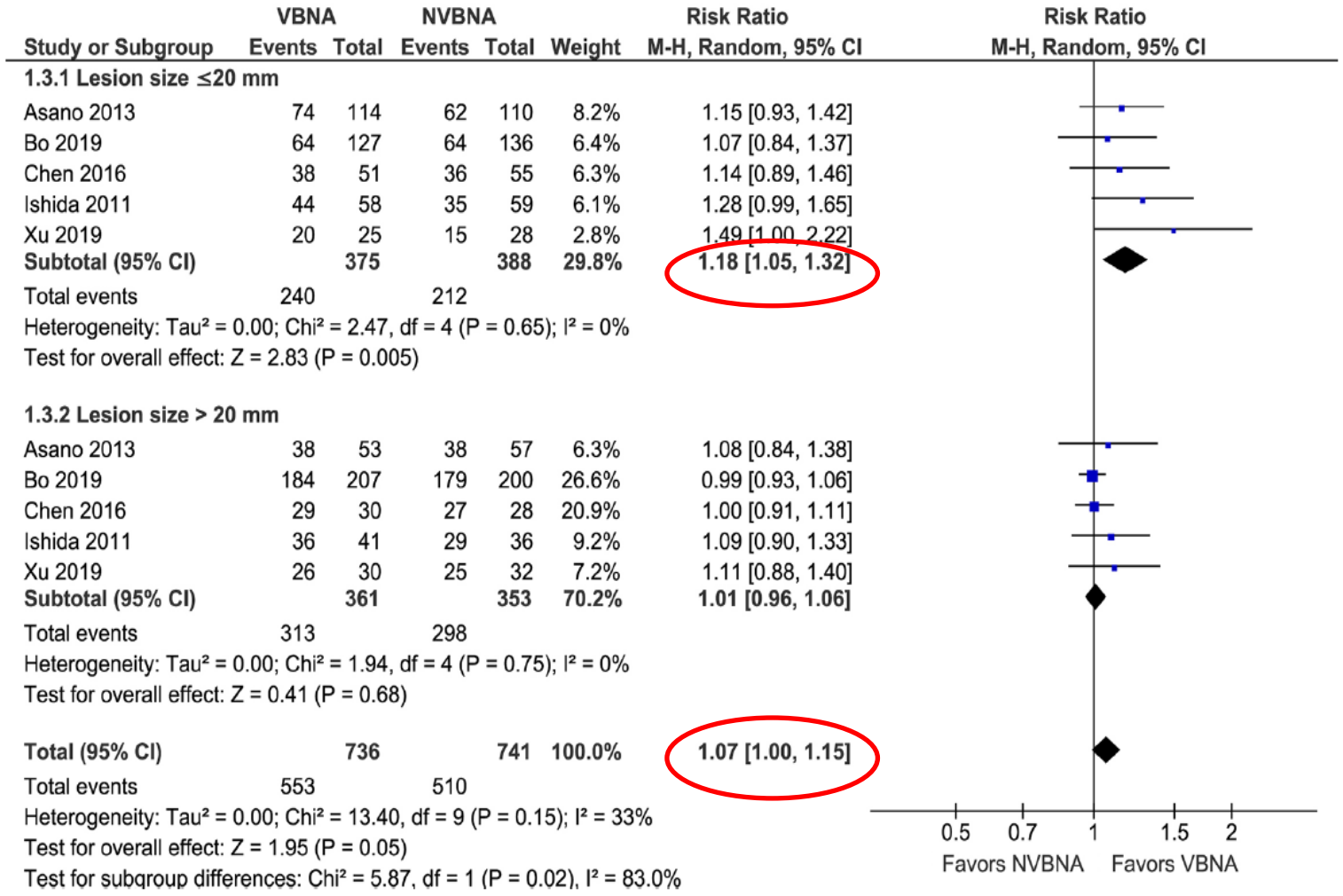
A color code indicates the relationship and the distance of the lesion from the respective bronchus.



VB navigation versus non-VB navigation bronchoscopy for the diagnosis of peripheral pulmonary lesions: a systematic review and meta-analysis

- Six RCTs with 1626 patients (Japanese and Chinese centers).
- Overall diagnostic rate although higher, did not reach statistical significance in the VBNA (74.2%) vs NVBNA (69.5%) groups.
- In the VBNA group, the total examination time was significantly shorter.

- **Superiority of VBNA over NVBNA was evident among patients with pulmonary nodules ⩽ 20 mm.**



Ther Adv Respir Dis 2021, Vol. 15: 1–11

Real time check of the pathway to the lesion

bronchoscopy under CT fluoroscopy

Advantages

- Direct visualization

  - **Diagnostic yield 70-73%**[1]

  - Depending on:
  - Size, location disparity while according

  Ost D et al. Chest 2008 does not add significantly to standard bronchoscopy

Disadvantages

- Radiation for both doctor and patient
- Time consuming in the CT department
- Logistics…

- Duhig N et al. J Bronchol 2002
- Shinagawa N et al. Chest 2004
- Ost D et al. Chest 2008
- Hautmann H et al. Respirology 2010

The Utility of Virtual Bronchoscopy Using a Computed Tomography Workstation for Conducting Conventional Bronchoscopy: A Retrospective Analysis of Clinical Practice

- *C*onsecutive patients who underwent bronchoscopy for small PPLs (major diameter ≤30 mm) were retrospectively reviewed.
- 69 patients underwent bronchoscopy without VB and 56 patients underwent bronchoscopy with VB.
- **The VB group had a significantly higher diagnostic yield than the non-VB group (57.1 vs. 33.3%; *p* = 0.008)**. In the multivariate analysis, VB was identified as a significant factor affecting the diagnostic yield (odds ratio: 3.30, *p* = 0.011).
- In the conventional bronchoscopy settings, VB using the CT workstation is efficient for the diagnosis of PPLs when other guided-bronchoscopy techniques are unavailable.

Table 2. Results of the bronchoscopic examination of VB and non-VB groups

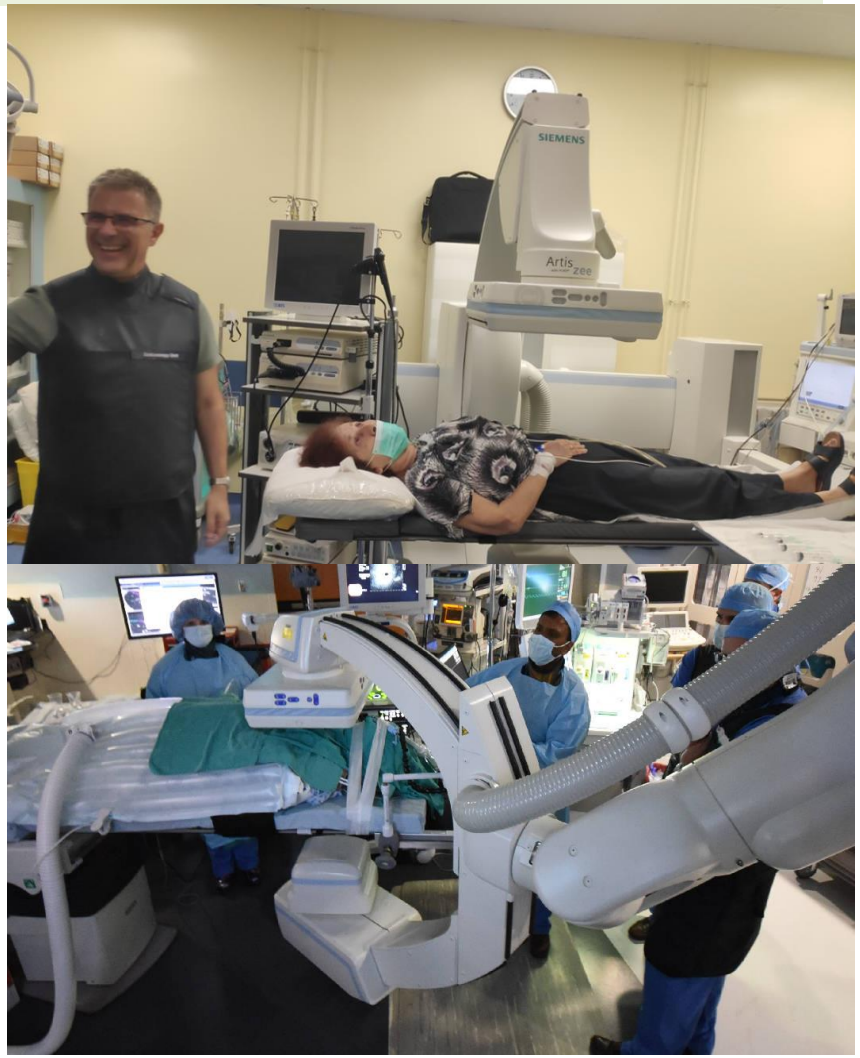
	VB group (*n* = 56)	Non-VB group (*n* = 69)	*p* value
Diagnostic yields, *n* (%)	32 (57.1)	23 (33.3)	0.008
Achievement rate of biopsy, *n* (%)	42 (75.0)	36 (52.2)	0.009
Procedure time (median, range), min	27 (11–60)	25 (7–69)	0.488

Respiration 2019;97:52–59

Real time check of the pathway leading to the lesion
Cone beam CT and augmented fluoroscopy bronchoscopy

- The CT image is acquired after one convolution around the patient.
- Analysis very close to conventional CT
- Less radiation
- Less time needed for time acquisition.

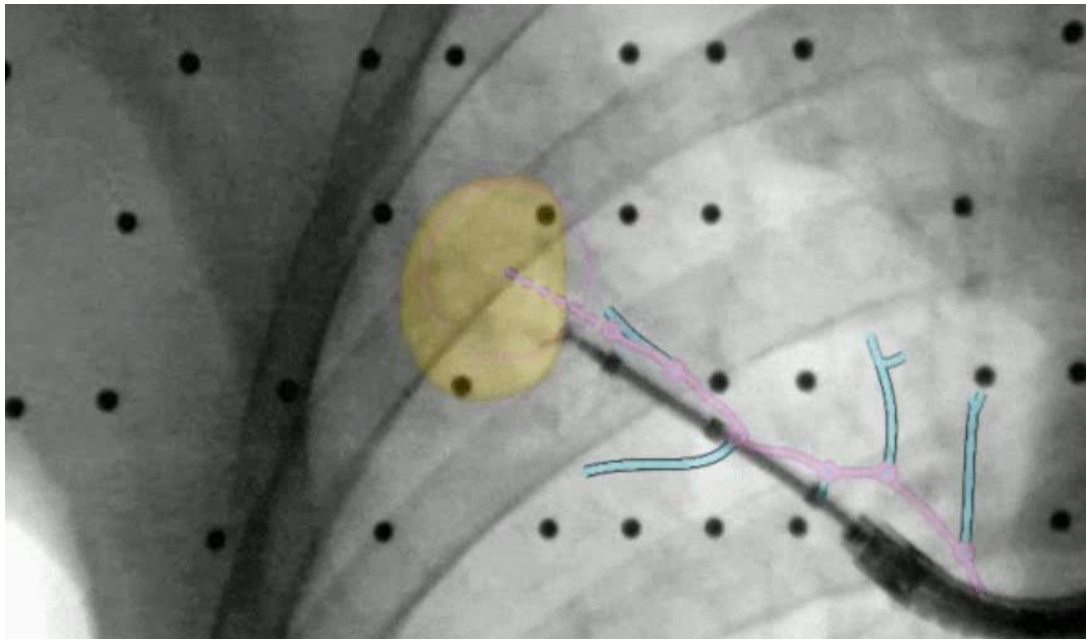
- Reconstruction of image and use of it in a 3D hybrid fluoroscopy, in order to confirm exact positioning of biopsy tools (needle, forceps).

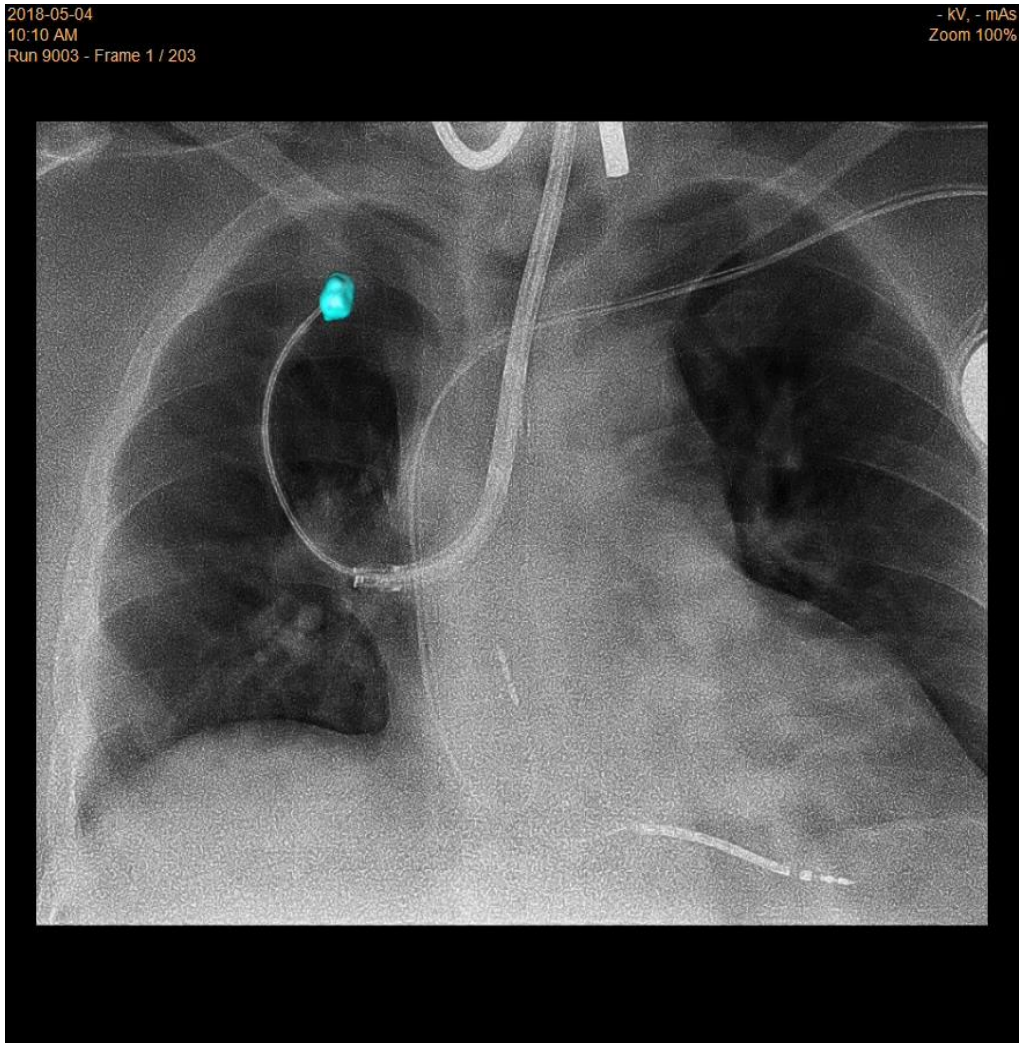


The first rotation produces image acquisition and segmentation (identification) of targeted nodule. Tracking and positioning of tools with 3D fluoroscopy and segmentation of the nodule projected follows.

Augmented Fluoroscopy & Lung Vision™

3D-real time
image guidance

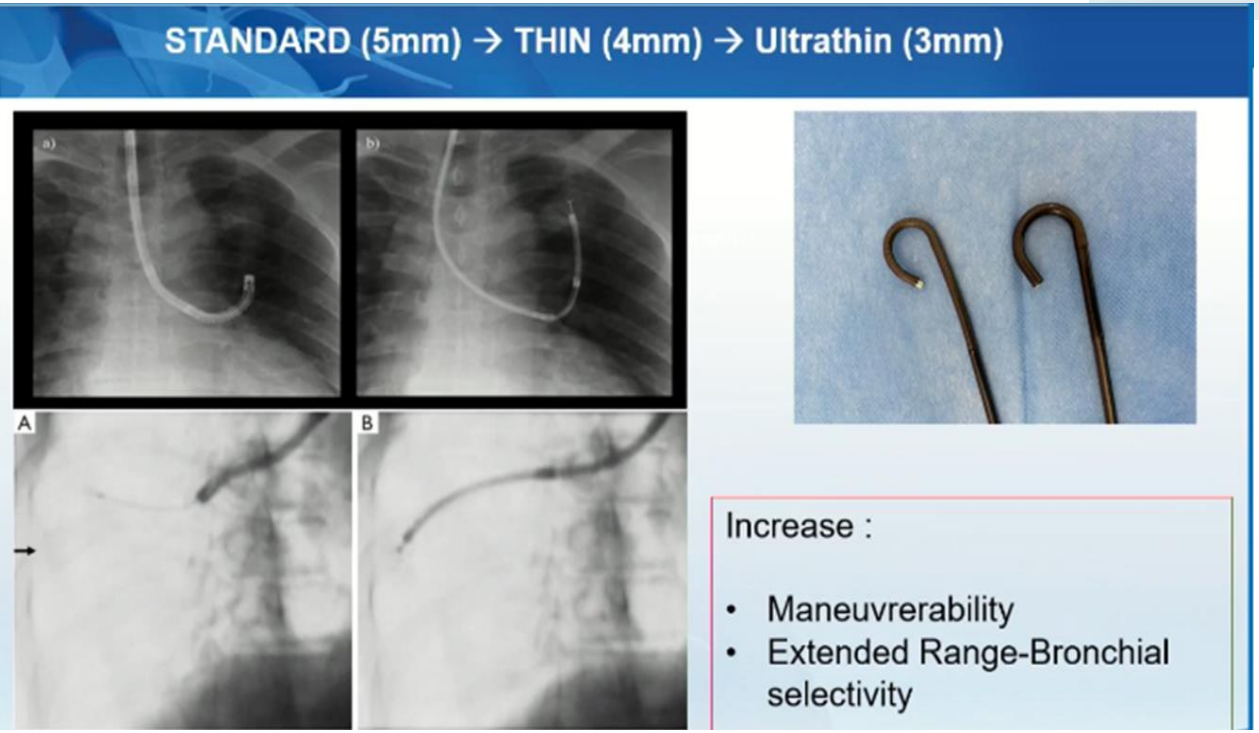




Vehicle selection

Distal end outer diameter (mm)	6,1	6,2	5,5	4,8	4,2	3,1	3,0
Working channel diameter (mm)	3,2	2,8	2,0	2,0	2	1,2	1,7

therapeuthic | standard | Thin | Ultra-Thin



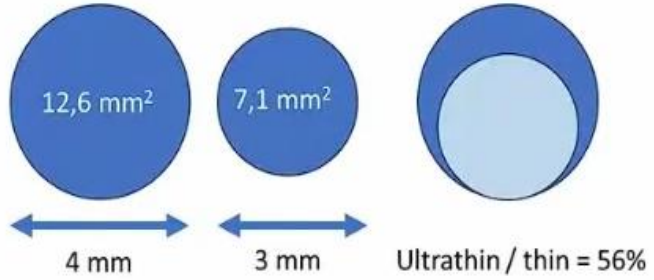
Video by Dr Sh. Lachcar

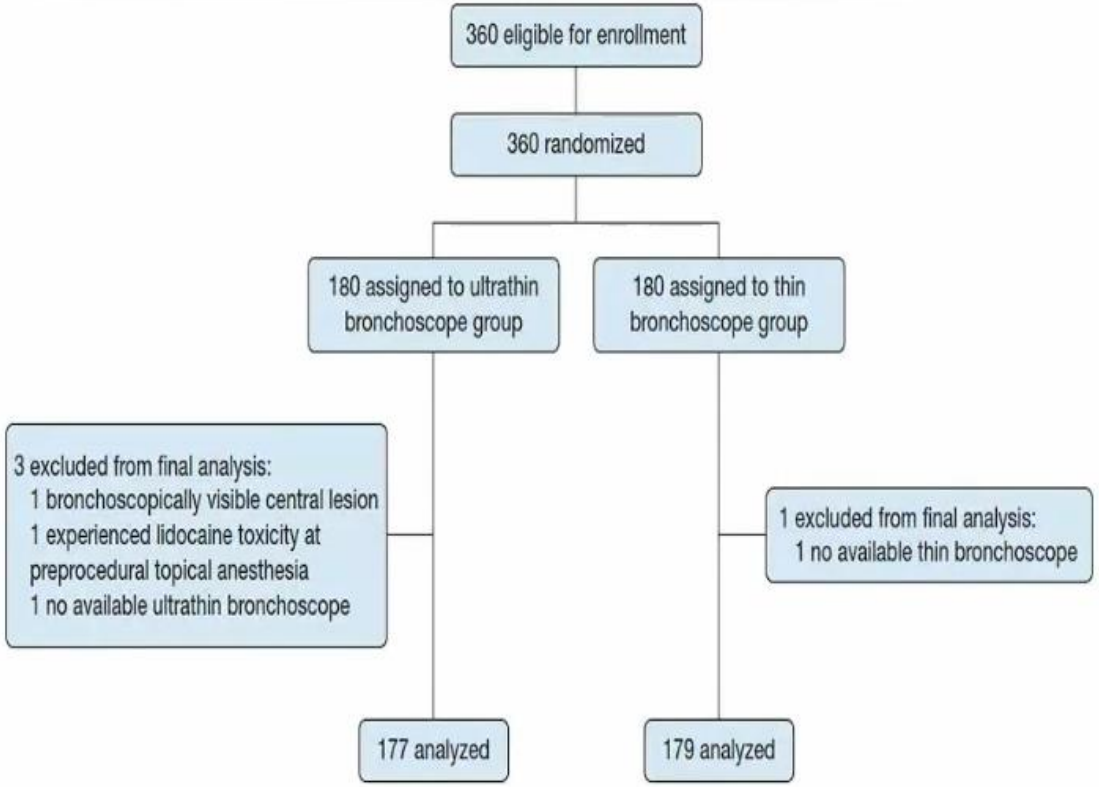
SPN Approach Update: Ultrathin bronchoscopy (UTB)

Randomized Controlled Trial > Chest. 2019 Nov;156(5):954-964. doi: 10.1016/j.chest.2019.06.038. Epub 2019 Jul 26.

Use of an Ultrathin vs Thin Bronchoscope for Peripheral Pulmonary Lesions: A Randomized Trial

Masahide Oki [1], Hideo Saka [1], Fumihiro Asano [2], Chiyoe Kitagawa [1], Yoshihito Kogure [1], Akifumi Tsuzuku [2], Masahiko Ando [3]



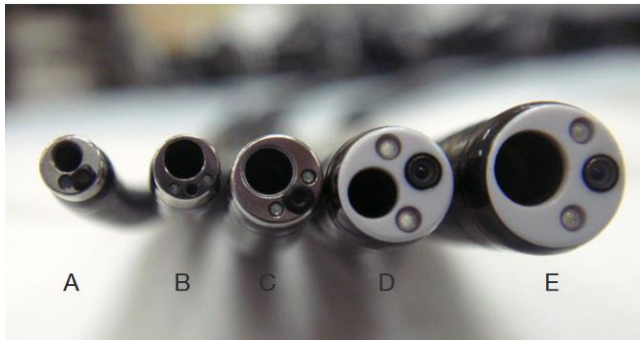


- Patients (n=360) with peripheral pulmonary lesions <30 mm
- Randomized 1:1 to undergo rEBUS, virtual bronchoscopy and fluoroscopy-guided bronchoscopy
- Diagnostic yield was significantly higher in the UTB group than in the thin bronchoscope group (70.1% vs 58.7%)
- UTB → 5 generations of bronchi deeper
- Complication rates were 2.8% and 4.5%, respectively

Study	Year	Study design	Bronchoscope diameter (mm)	Guidance method	Mean lesion diameter (mm)	No. lesions	No. diagnosed	Yield (%)	No. lesions <2 cm	No. lesions <2 cm diagnosed	Yield for lesions <2 cm (%)	Prevalence of malignancy (%)
Shinagawa (6)	2004	Pro	2.8	CT, VBN	13	26	17	65	26	17	65	69
Yamamoto (4)	2004	Pro	2.8	Flu	ND	67	40	60	ND	ND	ND	76
Asano (7)	2006	Pro	2.8	Flu, CT, VBN	19	38	31	82	26	21	81	55
Shinagawa (8)	2007	Pro	2.8	CT, VBN	14	71	50	70	71	50	70	72
Tachihara (9)	2007	Pro	2.8	Flu, VBN	16	58	33	57	46	21	46	ND
Oki (28)	2008	Pro	3.5	Flu	34	98	68	69	23	13	57	69
Oki (29)	2009	Pro	3.4	Flu, rEBUS	31	71	49	69	14	5	36	62
Eberhardt (10)	2010	Pro	2.8	VBN	28	25	20	80	ND	ND	ND	
Matsuno (16)	2011	Retro	2.8	Flu, CT	ND	166	113	68	ND	ND	ND	
Oki (30)	2012	RCT	3.4	Flu, rEBUS	26	101	66	65	25	10	40	
Asano (12)	2013	RCT	2.8	Flu	17	167	100	60	110	62	56	
		RCT	2.8	Flu, VBN	18	167	112	67	114	74	65	
Oki (19)	2015	RCT	3.0	Flu, rEBUS, VBN	19	150	111	74	80	52	65	82
Franzen (32)	2016	RCT	2.8	Flu	20	20	11	55	6	ND	ND	40
Diez-Ferrer (14)	2019	Pro	2.8/3.1	Flu, VBN	23	55	26	47	26	11	42	60
		Retro	2.8/3.1	Flu	25	110	44	40	46	11	24	78
Ali (18)	2019	Pro	2.8	Flu, VBN, CBCT	20	40	36	90	ND	ND	ND	63
Sehgal (20)	2019	Retro	3.0	rEBUS	16	34	19	56	ND	ND	ND	ND
Oki (21)	2019	RCT	3.0	Flu, rEBUS, VBN	19	177	124	70	102			
Sumi (22)	2020	Retro	3.0	Flu, rEBUS	20	102	77	75	65			
Summary						1,717	1,130	66%	780			

PPL, peripheral pulmonary lesion; CBCT, cone-beam computed tomography; Flu, fluoroscopy; ND, no data; PNA, RCT, randomized controlled trial; rEBUS, radial-probe endobronchial ultrasound; Retro, retrospective study, VBN, v

59%



Review Article on Advance in Bronchoscopy for Peripheral Pulmonary Diseases

Diagnostic value of ultrathin bronchoscopy in peripheral pulmonary lesions: a narrative review

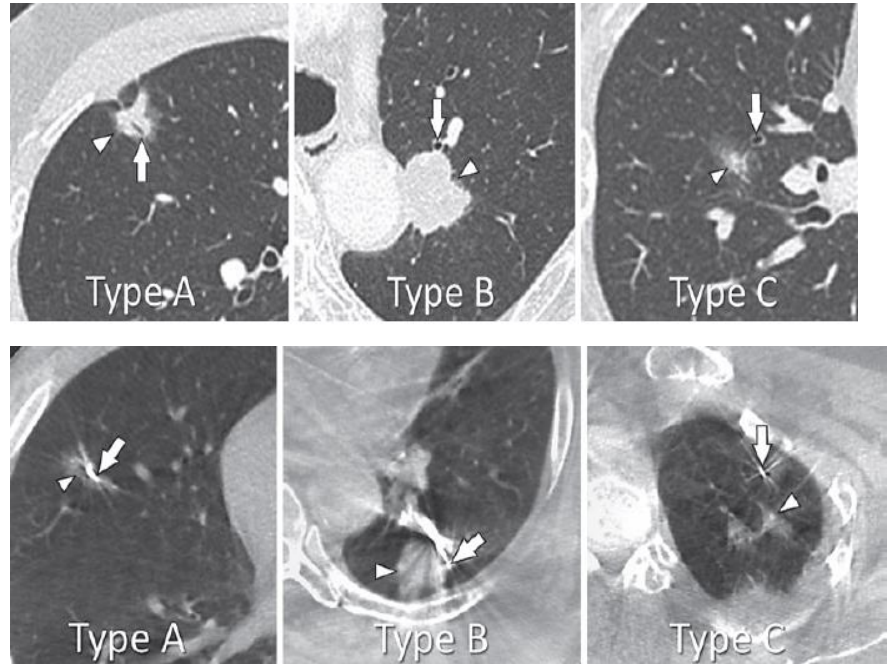
Masahide Oki[1], Hideo Saka[1,2]

J Thorac Dis 2020;12(12):7675-7682 |

Respiration 2019;98(4):321-328

Transbronchial Biopsy Using an Ultrathin Bronchoscope Guided by Cone-Beam Computed Tomography and Virtual Bronchoscopic Navigation in the Diagnosis of Pulmonary Nodules

Eman A.A. Ali[a, c] Hiromitsu Takizawa[a] Naoya Kawakita[a] Toru Sawada[a]



Although the target lesions were invisible by conventional C-arm fluoroscopy in 29 patients, CBCT visualized all 40 lesions.

The overall diagnostic yield was 90.0%, and diagnostic yields for malignant and benign lesions were 92.0 and 86.7%, respectively. Diagnostic yields for CBCT target-forceps sign types A, B, and C were 100, 75.0, and 0%, respectively. Four undiagnosed patients proceeded to other diagnostic procedures based on the CBCT target forceps sign (type B: n = 2, type C: n = 2) and were correctly diagnosed without delay.

Transbronchial biopsy using an ultrathin bronchoscope guided by CBCT and VBN showed a very high yield in the diagnosis of pulmonary nodules.

SPN Approach Update: Cryobiopsy with rEBUS vs CT Guided TTB

Randomized Controlled Trial > Intern Med J. 2023 Aug;53(8):1390-1399. doi: 10.1111/imj.15833. Epub 2022 Jul 21.

Cryobiopsy with radial-endobronchial ultrasound (Cryo-Radial) has comparable diagnostic yield with higher safety in comparison to computed tomography-guided transthoracic biopsy for peripheral pulmonary lesions: An exploratory randomised study

Table 1 Demographic data between the two arms

Characteristic	Radial-Cryo arm ($n = 26$)	CT-TTB arm ($n = 22$)	*P*-value
Sex			
Female	11 (42.3%)	10 (45.5%)	0.827
Male	15 (57.7%)	12 (54.4%)	
Age	63.5 (SD 10.5)	Mean 65.6 (SD 14.4)	0.572
COPD	14 (53.8%)	10 (45.5%)	0.562
FEV1	2.27 (SD 0.79)	1.9 (SD 0.93)	0.266
Non-smoker	7 (27%)	8 (36%)	0.76
Current smoker	8 (30.8%)	4 (4.5%)	
Ex-smoker	11 (42.3%)	9 (40.9%)	

Table 2 CT characteristics of the pulmonary lesion between the two arms

	Radial-Cryo arm ($n = 26$)	CT-TTB arm ($n = 22$)	*P*-values
Size (largest diameter in axial images) (mm)	33.6 mm (SD 21.6)	38.6 mm (SD 24.2)	0.456
Location of lesion on axial CT			
Inner 1/3	7 (26.9%)	2 (9.1%)	0.193
Middle 1/3	5 (19.2%)	8 (36.4%)	
Outer 1/3	14 (53.8%)	12 (54.5%)	
Lobar location: UL	16 (61.5%)	14 (63.6%)	0.994
Lobar location: LL/RML	10 (38.5%)	8 (36.4%)	
Presence of air bronchograms	13 (50.0%)	6 (27.3%)	0.083
No air bronchogram	12 (46.2%)	11 (50%)	
Not recorded	1 (3.8%)	5 (22.7%)	

LL, lower lobe; RML, right middle lobe

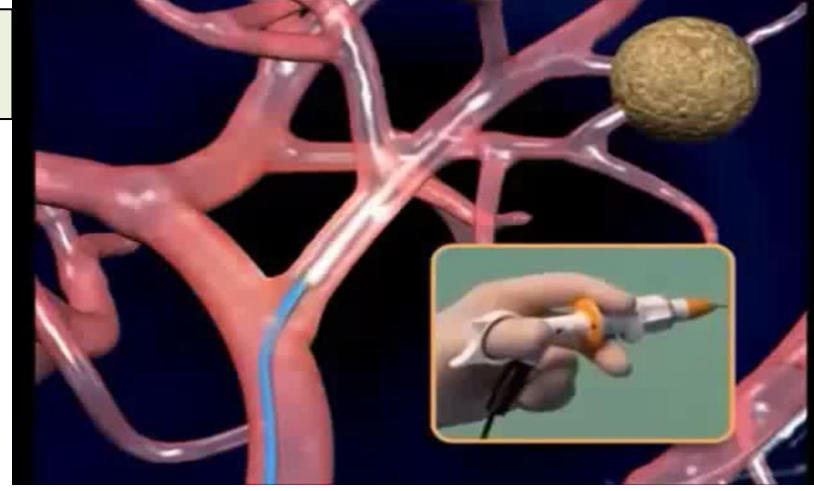
Table 3 Comparing the logistics and resources required in both arms

	Cryo-Radial	CT Bx
Place of procedure	Operating rooms, 19/25 (76%) Endoscopy suite, 6/25 (24%)	Radiology department, 16/16 (100%)
Airway usage	13/25 (52%) had a rigid bronchoscopy in place, 7/25 (28%) Laryngeal Mask Airway (LMA), 1/25 (4%) Endotracheal tube (ETT) and 4/25 (16%) had their own airway	Own airway, 16/16 (100%)
Imaging used to detect the lesion	4/26 (15%) of patients undergoing Cryo-Radial procedure had fluoroscopy	16/16 (100%) had a repeat CT of the chest
No passes done of the lesion	No. biopsies done using cryo-probe: 1 pass (6/16), 2 passes (9/16) and 3 passes (1/16) for cryo-biopsy Out of the six patients who had one pass, four did not yield diagnostic material. Only 2/6 (33%) had a successful diagnosis All patients having two or more passes had a successful diagnosis 10/10 (100%)	No. passes done: CT-guided biopsy, 2 passes (1/15), 3 passes (10/15), 4 passes (2/15) and 5 passes (1/15).
Time taken for the procedure	49.8 (SD 17.9) min, $P < 0.01$ Paired *t* test	16.1 (SD 17.6) min

- Randomized prospective study in 46 patients
- The diagnostic yield was CT-TTB 93.8% (15/16) vs Cryo-Radial 85% (17/20) p=0.6
- For 5/13 (38%), a diagnosis was solely made on cryobiopsy
- Eleven (78%) of 14 in CT-TTB versus 7/10 (70%) Cryo-Radial were suitable for EGFR testing p=0.6
- Time taken substantially longer for Cryo-R vs CT-TTB ~50min vs 16min
- Complications less with Cryo-R vs CT-TTB

Electromagnetic navigation

- Lead tools to peripheral target
- Using CT "roadmap" for real time navigation
- Enable tool: real-time location and steerability
- Navigate: towards target, overlaid on CT images



CT-Scan ➡ DICOM CD

Software ➡ Planned Pathway File

Navigation ➡ Biopsy ➡ Treatment

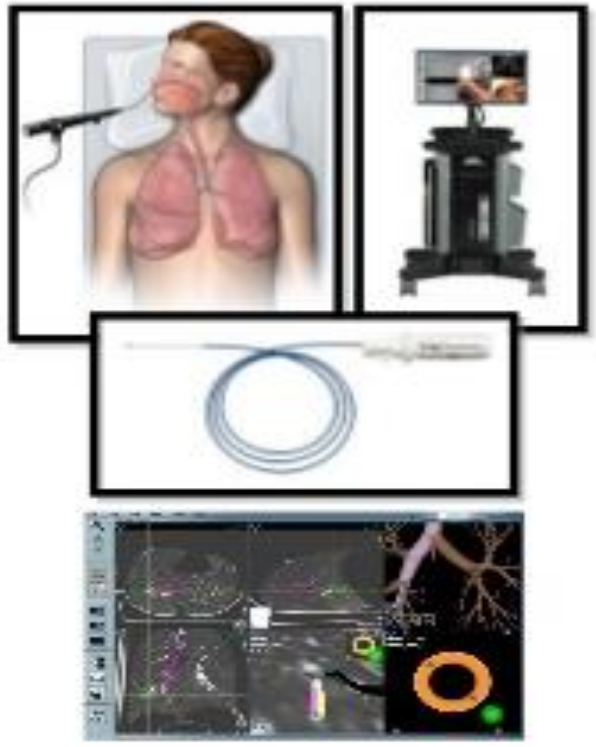


Table 2. Large studies evaluating the diagnostic yield of EMN since 2012

Study	Year	Pro/ Retro*	Number of lesions	Diameter mean	Diameter median	Diagnostic yield %	Other tools*
Brownback *et al.* [40]	2012	Retro	55	NR	30 mm (range 1.1–7.8 cm)	74.5% overall, 69.4% for malignancy	Forceps, brush, BW, TBNA, F, ROSE
Jensen, *et al.* [41]	2012	Retro	92	26.1 mm (SD 14.2 mm)	NR	65.2% overall	Forceps, brush, BAL, TBNA
Lamprecht *et al.* [42]	2012	Pro	112	27.1 mm (SD 1.3 mm)	NR	83.9% overall	Forceps, brush, TBNA
Pearlstein *et al.* [43]	2012	Retro	101	NR	28 mm (range 8–10 mm)	85.1% overall	Forceps, brush, TBNA, ROSE
Loo *et al.* [39]	2014	Retro	50	26 mm (range 3–80 mm)	NR	94% overall	Forceps, brush, TBNA, ROSE
Bowling *et al.* [44]	2015	Retro	91	NR	NR	74% overall	Forceps, brush, BAL, TBNA, F
Steinfort, *et al.* [45▪▪]	2015	Pro	57	19.1 mm (SD 6.8 mm)	NR	15.8% overall	r-EBUS with GS, forceps, brush, BW, F

*Pro, prospective; Retro, retrospective.
BAL, bronchoalveolar lavage; BW, bronchial washing; F, fluoroscopy; GS, guide sheath; NR, not reported; r-EBUS, radial probe endobronchial ultrasound; ROSE, rapid on-site evaluation; TBNA, transbronchial needle aspiration.

Great variability: 15,8-94% (depending on the size, location and patient selection)

Sensitivity and Safety of Electromagnetic Navigation Bronchoscopy for Lung Cancer Diagnosis

Systematic Review and Meta-analysis

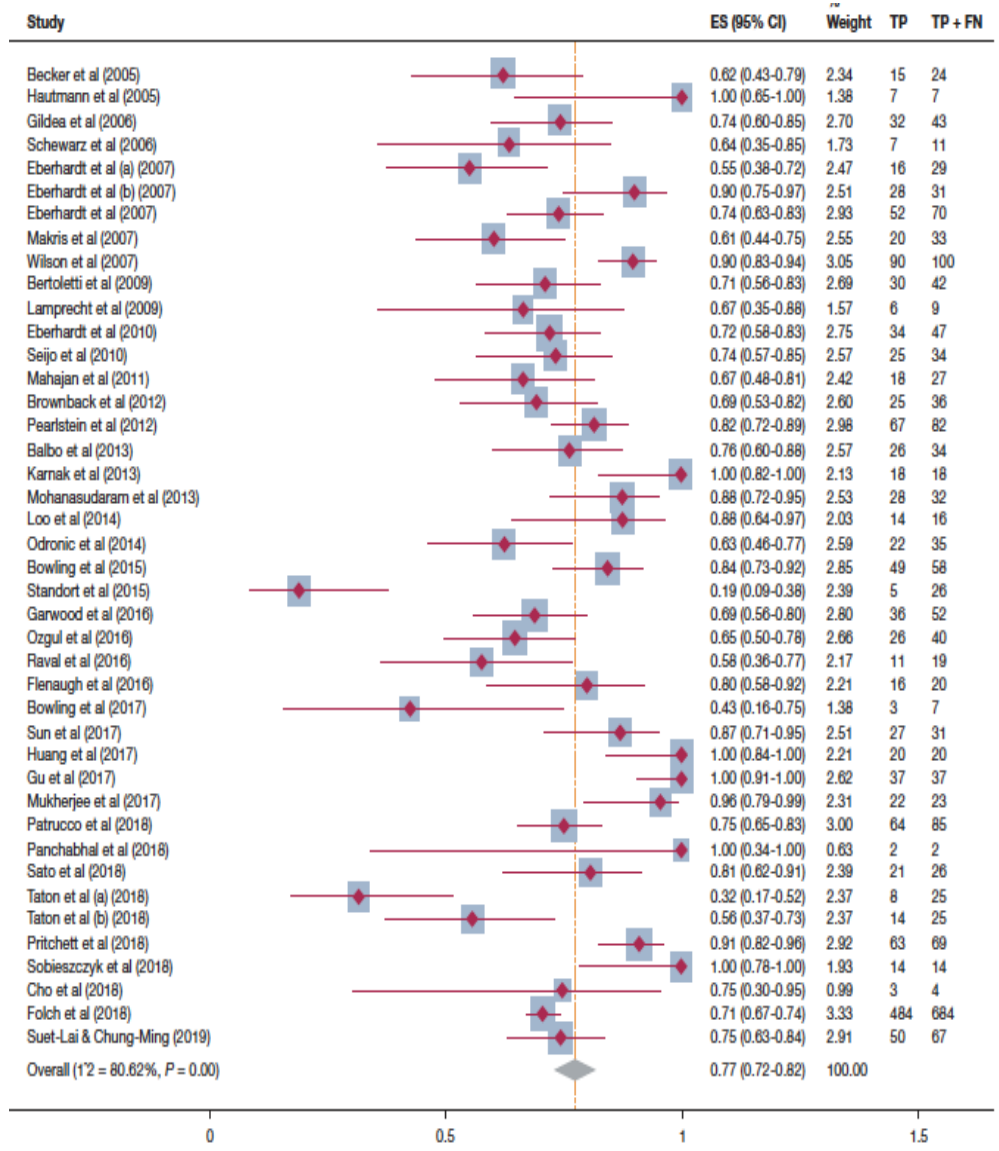
Chest 2020;158(4):1753-69

Erik E. Folch, MD; Gonzalo Labarca, MD; Daniel Ospina-Delgado, MD; Fayez Kheir, MD; Adnan Majid, MD; Sandeep J. Khandhar, MD; Hiren J. Mehta, MD; Michael A. Jantz, MD; and Sebastian Fernandez-Bussy, MD

Included 40 studies and 3342 patients

- ENB reported a **pooled sensitivity of 77%** (95% CI, 72%-82%), PTX risk 2%

Subgroup	Sensitivity (%)	95% CI (%)	I^2 Value (%)	Intergroup heterogeneity
ROSE				
Yes	72	66-76	34.07	Nonsignificant
No	74	65-80	84.92	
EBUS use				
Yes	80	74-83	73.1	Nonsignificant
No	72	66-76	85.5	
Fluoroscopy guidance				
With fluoroscopy	71	60-79	85.25	Nonsignificant
Without fluoroscopy	74	69-77	24.66	
Navigation system				
Super dimension	78	73-83	81.30	Nonsignificant
Another platform	70	54-84	N.A.	
No. of techniques				
1	67	53-79	75.14	Significant
2	72	60-83	82.24	
3	83	76-89	75.14	
4	91	82-96	N.A.	
5	72	69-76	N.A.	



Bronchoscopic transparenchymal nodule access (BTPNA): first in human trial of a novel procedure for sampling solitary pulmonary nodules

Felix JF Herth,[1,2] Ralf Eberhardt,[1,2] Daniel Sterman,[3] Gerard A Silvestri,[4] Hans Hoffmann,[5] Pallav L Shah[6,7,8]

BTPNA procedure was successfully completed in 10 patients (83%), and a positive biopsy was successfully obtained in all 10 cases in which a tunnel was successfully created from the POE

Herth FJF, *et al*. *Thorax* 2015;**70**:326–332.

Table 1 CBCT combined with navigation for diagnosis peripheral pulmonary lesions

Studies	Design	Procedural modalities	CBCT used	Overall diagnostic yield	Lesions	Nodule size	Radiation information
Pritchett *et al.*	Retrospect study	CBCT + ENB + AF	Allura Xper FD20; Philips	83%	93	Median nodule size 20 (range, 7–55) mm	2.0 mSv per CBCT run, average 1.5 runs, 3.5 mSv
Sobieszczyk *et al.*	Retrospective study	CBCT + ENB + R-EBUS + TBAT	Not reported	77.2%	22	Median nodule size 21 (range, 7–52) mm	Not reported
Casal *et al.*	Prospective observational cohort study	CBCT + R-EBUS + Ultrathin Bronchoscope	Not reported	70%	20	Median nodule size 21 (range, 11–30) mm	Estimated to range between 8.6 to 23 mSv, average fluoroscopy time 8.6 minutes (range, 5–15.4 minutes)
Bowling *et al.*	Retrospect study	CBCT + ENB + TBAT	Artis Zeego; Siemens	71%	14	Median nodule size of 18 (range, 9–30) mm	4.3 mSv (range, 3 to 5 mSv), and the average fluoroscopic time was 17 minutes (range, 2 to 44 minutes)
Ali *et al.*	Prospective study	CBCT + VBN + Ultrathin Bronchoscope	Artis Zeego; Siemens	90%	40	Median nodule size 20 (range, 9–30) mm	Not reported

CBCT, cone beam computed tomography; ENB, electromagnetic navigation bronchoscopy; R-EBUS, radial endobronchial ultrasound; AF, augmented fluoroscopy; TBAT, Trans Bronchial Access Tool.

Has the diagnostic yield of guided bronchoscopy for PPL improved over the past decade???

CHEST JOURNAL

CHEST 2023 Jun;163(6):1589-1598

Guided Bronchoscopy for the Evaluation of Pulmonary Lesions: An Updated Meta-analysis

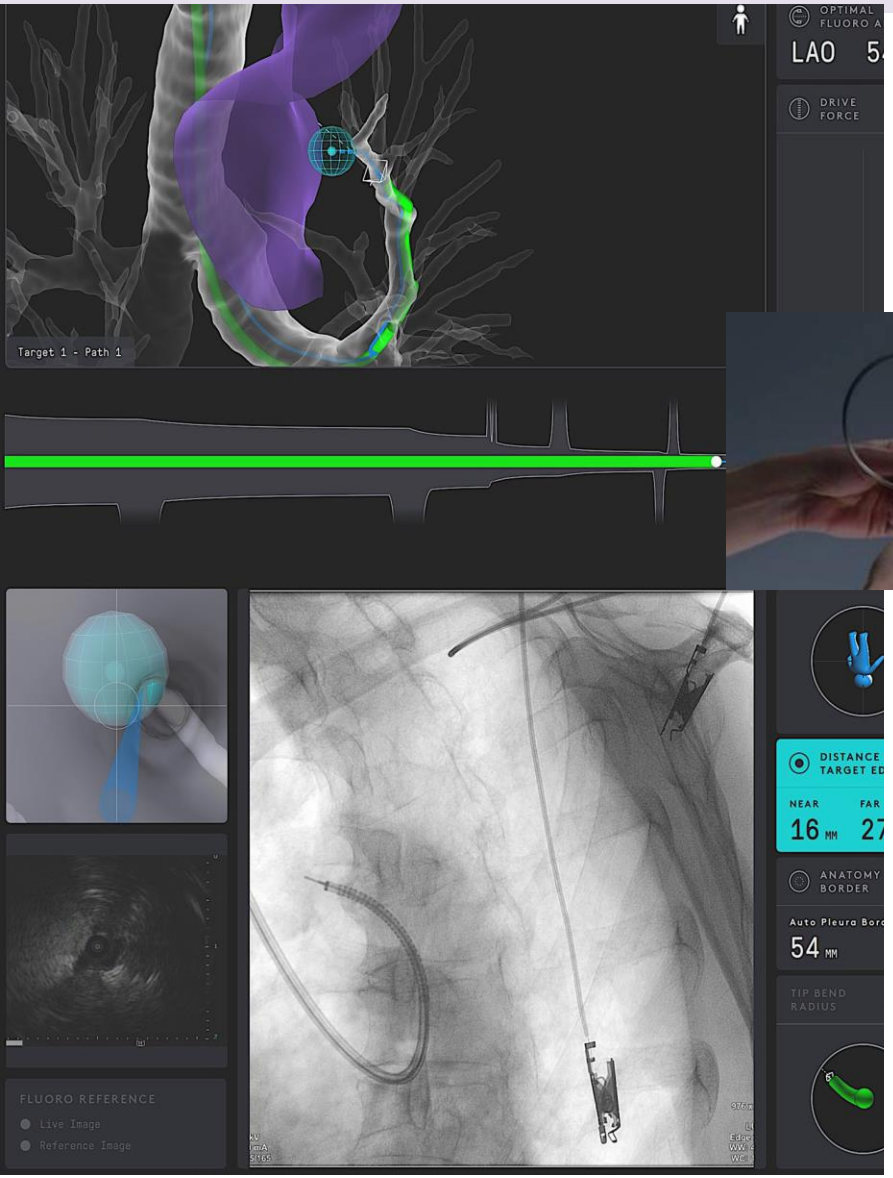
Tejaswi R Nadig [1], Nina Thomas [2], Paul J Nietert [3], Jessica Lozier [1], Nichole T Tanner [4], Jessica S Wang Memoli [5], Nicholas J Pastis [6], Gerard A Silvestri [7]

- 16,389 lesions from 126 studies were included.
- There was no significant difference in diagnostic yield prior to 2012 (39 studies; 3,052 lesions; yield 70.5%) vs after 2012 (87 studies; 13,535 lesions; yield 69.2%) (P > .05).
- There was no significant difference in yield when comparing different technologies.
- Lesion size > 2 cm, presence of bronchus sign, and high prevalence of malignancy in the study population were associated with significantly higher diagnostic yield.

Robotic Bronchoscopy

Robots in the way

Simoff *et al. BMC Pulm Med (2021) 21:322*



Shape-sensing robotic-assisted bronchoscopy for pulmonary nodules: initial multicenter experience using the Ion™ Endoluminal System

…hoff[1*], Michael A. Pritchett[2,3], Janani S. Reisenauer[4], David E. Ost[5], Adnan Majid[6], Colleen Keyes[7], …sal[5], Mihir S. Parikh[6], Javier Diaz-Mendoza[1], Sebastian Fernandez-Bussy[8] and Erik E. Folch[7]

60 subjects with 67 nodules < 20 mm were targeted for biopsy. **Most nodules were extraluminal and distance from the outer edge of the nodule to the pleura or nearest fissure was 4.0 mm** Median bronchial generation count to the target location was 7.0 (IQR: 6.0, 8.0). Procedure duration was 66.5 min. Distance from the catheter tip to the closest edge of the virtual nodule was 7.0 mm.

Biopsy completion was 97.0%.

No pneumothorax or airway bleeding was reported.

Pragmatic and Observational Research

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Real-World Impact of Robotic-Assisted Bronchoscopy on the Staging and Diagnosis of Lung Cancer: The Shape of Current and Potential Opportunities

Gabriel Ortiz-Jaimes[1,*], Janani Reisenauer[1,2,*]

2023:14 75–94

	Ion Robotic Bronchoscopy System	Monarch Robotic Bronchoscopy System	Galaxy System
Technology Type	Shape-sensing	Electromagnetic Navigation	Electromagnetic Navigation
Catheter Diameter	3.5 mm	Mother- Daughter configuration, 4.2mm Inner extension, 6mm outer catheter	4.0 mm (disposable catheter)
Working Channel	2 mm	2.1 mm	2.1 mm
Maneuverability/flexion	180 °	Outer catheter: 130° Inner catheter 180°	N/A
Endobronchial vision during Navigation	Yes, 1.8 mm vision probe (90–120 degrees field of view)	Yes	Yes
Endobronchial vision during Biopsy	No	Yes	Yes
Controller interface	Console pedestal with secondary screen. Trackball and scroll wheel controller	Video game-like handheld controller	Video game-like handheld controller
Imaging features	Cone Beam CT integration Augmented fluoroscopy under investigation	Cone Beam CT Digital tomosynthesis under investigation	Digital tomosynthesis – augmented fluoroscopy proprietary system. TiLT™ (tool-in lesion technology)

Table 2 Studies Reporting the Diagnostic Yield and Performance of Robotic Bronchoscopy in Pulmonary Lesions

Study	Lesions (N)	Diagnostic Yield (DY)	Size mm (Diameter/ Range)	Bronchus Sign	Pneumothorax/ Intervention	Prevalence of Malignancy	Comment
Ion Endoluminal System							
Fielding 2019[45]	29	88%	14.8 (10–26.4)	58.6%	0%/0%	88%	Feasibility Study. Successful navigation 96.6%
Benn 2021[46]	52	86%	21.9 (7–60%)	46%	3.8%/1.4%	65%	Prospective. Successful navigation 85%, 15% repositioning with CBCT
PRECISE Study 2021[47]	69	88%	17 (10–30)	25			
Reisenauer 2021[35]	270	–	18.2 (10–30)	–			
Reisenauer 2021[48]	30	93.3%	17.5 (10–30)	40			
Bajwa 2021[49]	76	92%	17 (0.6–70)	-	-	59%	R-EBUS 100%, 91% of inflammatory lesions resolved
Kalchiem-Dekel 2021[50]	131	81.7%	18 (13–27)	62.9%	1.5%/1.5%	56.6%	Fluoroscopy: 2D 80%, 3D 20%, R-EBUS 85%
Oberg 2022[51]	120	90%	22 (8–34.3)	48.3%	5.4%/2.7%	46.7%	Retrospective. R-EBUS + 2D fluoroscopy. Cryobiopsy with 1.1 mm probe.
Styrvoky 2022[52]	209	91.4%	22.6 (7–73)	-	1%/0.5%	64.1%	Retrospective. R-EBUS and CBCT in 100%.
Low 2022[26]	143	77%	17 (12–27)	40%	1.5%/1.5%	54.5%	Retrospective comparative cohort vs Digital tomosynthesis ENB. 100% R-EBUS and 2D fluoroscopy

Table 2 Studies Reporting the Diagnostic Yield and Performance of Robotic Bronchoscopy in Pulmon

Study	Lesions (N)	Diagnostic Yield (DY)	Size mm (Diameter/ Range)	Bronchus Sign	Pneumothorax/ Intervention	Prevalence of Malignancy	
Monarch System							
Rojas Solano 2018[53]	15	-	26 (10–63)	100%	0%/0%	60%	Feasibility study, successful biopsy in 93%
Chaddha	165	69.1%	25 (10–40)	63.5%	3.6%/2.4%	63.5%	Retrospective. R-EBUS signal and bronchus sign predicted success, no CBCT.
					3.7%/1.9%	82.5%	Prospective multicentric feasibility. R-EBUS + 2D fluoroscopy. 96.2% localization rate.
					-	76%	Retrospective.
Agrawal 2022[55]	124	77%	20.5 (13–30)	75%	1.6%	61%	Retrospective, 2D fluoroscopy, R-EBUS in 82%. Accuracy after 12-month follow-up overall sensitivity for malignancy 69%, specificity 100%
Cumbo-Nacheli 2022[56]	20	86% Sensitivity	22 (15–29)	50%	-	75%	Retrospective. CBCT + R-EBUS. Pre-navigation CBCT, 100% navigation success.
Khan 2023[41]	264	Index: 85.2% 12 months: 79.4%	19.3 (3.2–72.5)	30%	5.7%/3.8%	58%	Retrospective. R-EBUS in 93.9%, CBCT in 3.4%

Diagnostic yield
ION 77-93%
Monarch 69-96%

CHEST 2021; 159(2):845-852

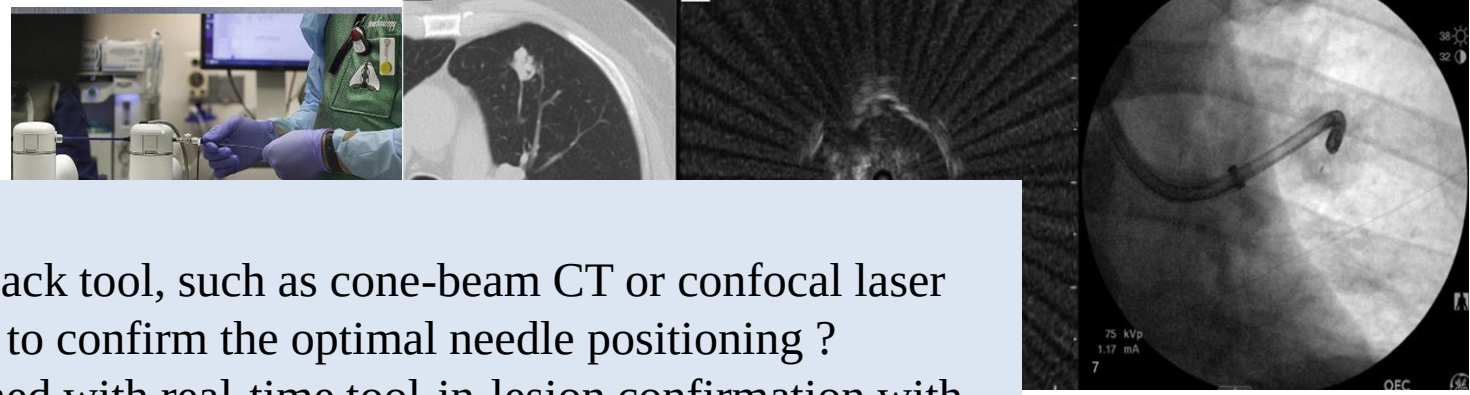
CHEST

Robots on the way

Robotic Bronchoscopy for Peripheral Pulmonary Lesions

A Multicenter Pilot and Feasibility Study (BENEFIT)

Alexander C. Chen, MD; Nicholas J. Pastis Jr, MD; Amit K. Mahajan, MD; Sandeep J. Khandhar, MD; Michael J. Simoff, MD; Michael S. Machuzak, MD; Joseph Cicenia, MD; Thomas R. Gildea, MD; and Gerard A. Silvestri, MD



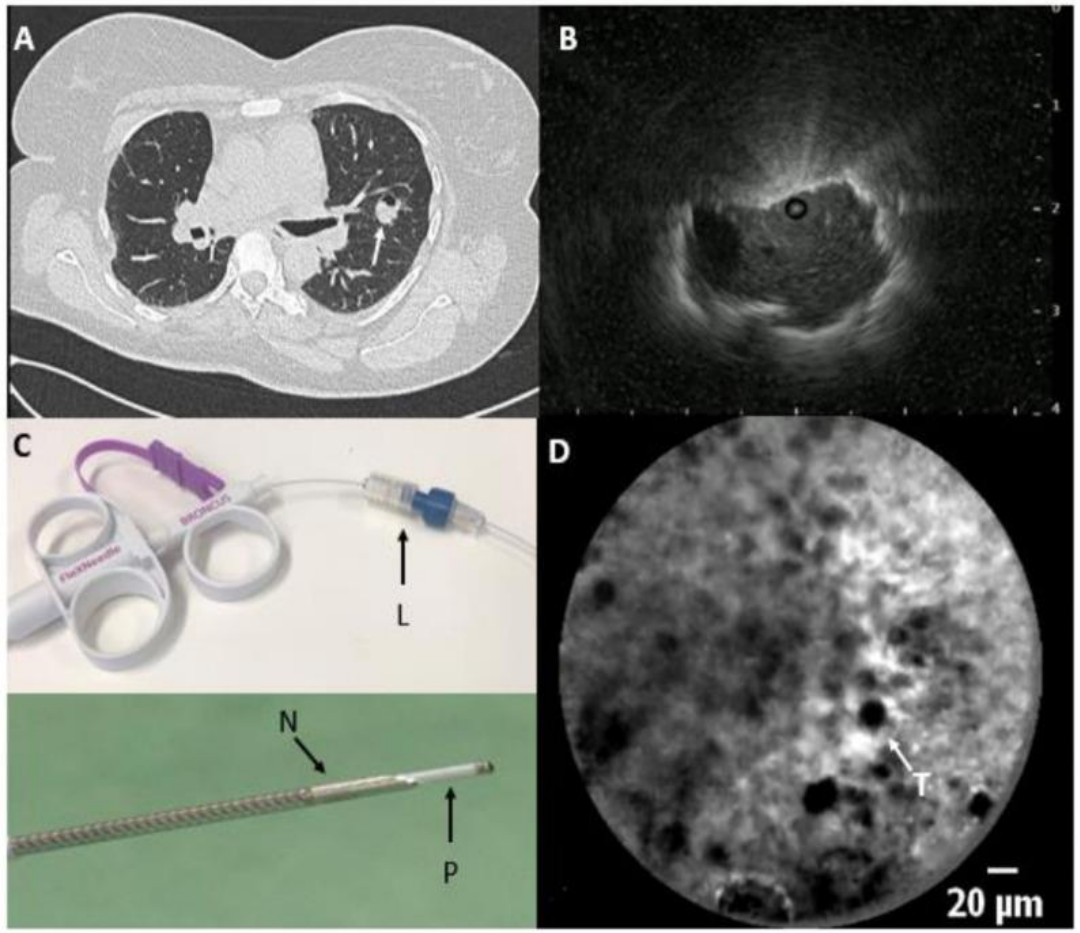
Do we need a real-time feedback tool, such as cone-beam CT or confocal laser endomicroscopy (CLE) to confirm the optimal needle positioning ?
Robotic bronchoscopy combined with real-time tool-in-lesion confirmation with the use of needle based CLE imaging is now prospectively evaluated in an ongoing trial
(ClinicalTrials.gov NCT04441749)

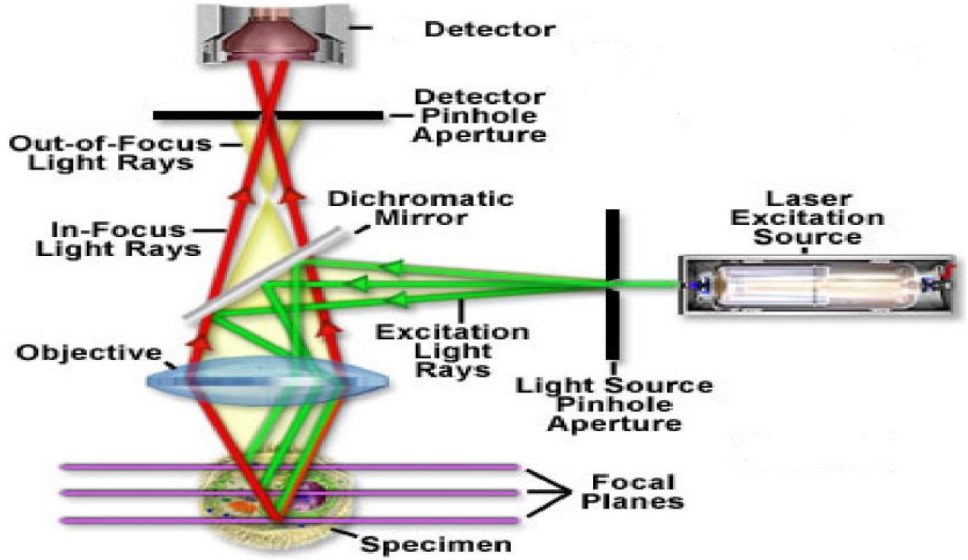
54 patients y. TBNA and ROSE per TBNA alo was performed with the us . R-EBUS images were available in 53/54 cases . Lesion localization successful in 51/53 patients **(96.2%).** Pneumothorax was reported in 2/54 of the cases (3.7%); No additional adverse events occurred. Diagnosis was obtained in 40/54 patients **(74.1%).**

Original research

Bronchoscopic needle-based confocal laser endomicroscopy (nCLE) as a real-time detection tool for peripheral lung cancer

Tess Kramer,[1] Lizzy Wijmans,[1] Martijn de Bruin,[2] Ton van Leeuwen,[2] Teodora Radonic,[3] Peter Bonta,[1] Jouke T Annema[1]

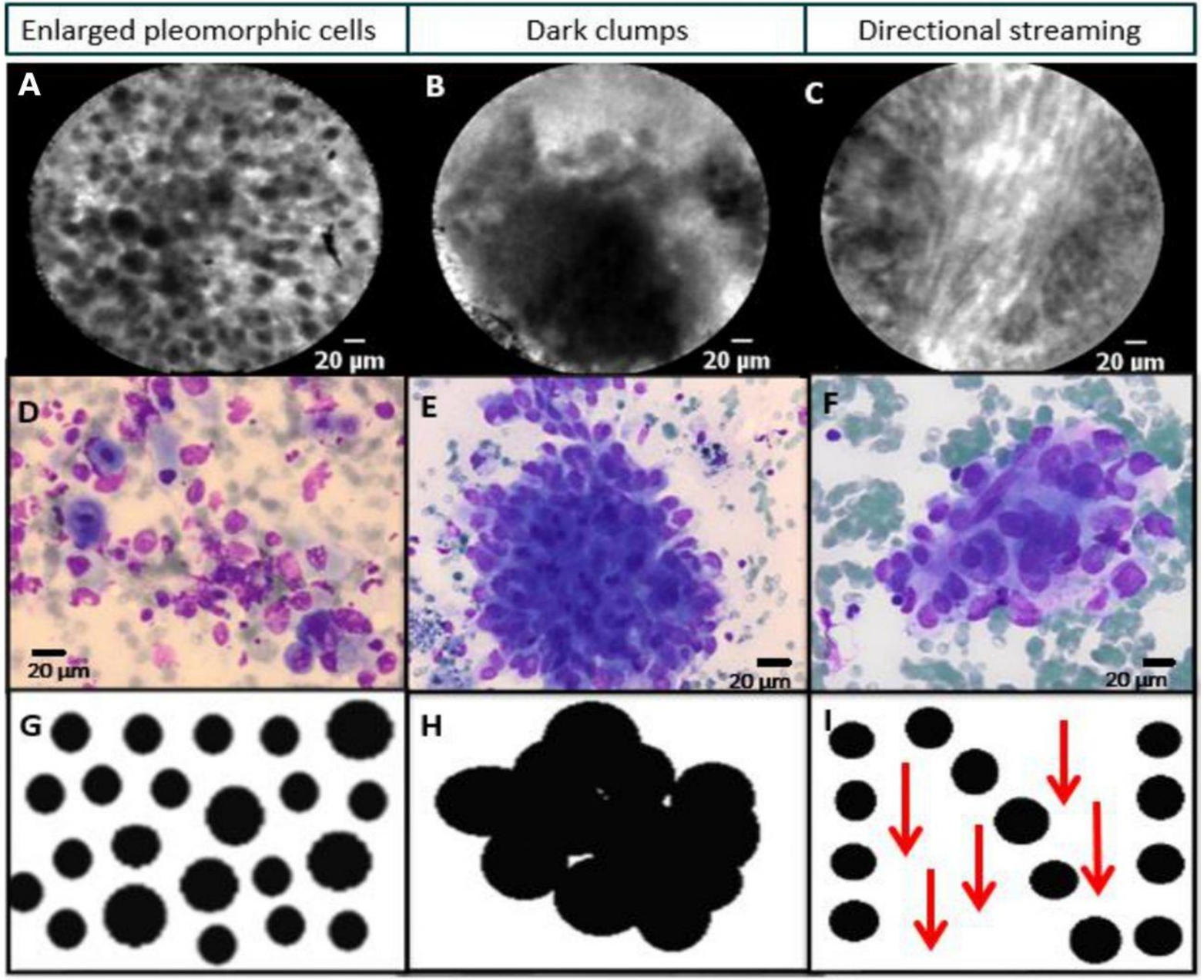


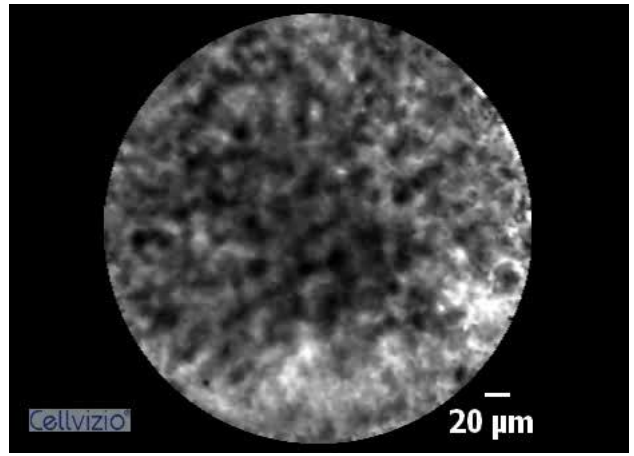


Patients with suspected peripheral lung Ca underwent rEBUS and FOB under fluoroscopy. After rEBUS lesion detection, an 18G needle loaded with the CLE probe was inserted in the selected airway under fluoroscopic guidance. The nCLE videos were obtained at the needle tip, followed by aspirates and biopsies.

The nCLE imaging was performed in 26 patients. No adverse events. The nCLE imaging detected malignancy in 22 out of 23 patients with lung cancer. Blinded raters differentiated nCLE videos of malignancy from airway/ lung parenchyma (280 ratings) with a 95% accuracy.

Kramer T, et al. Thorax 2022;77:370–377

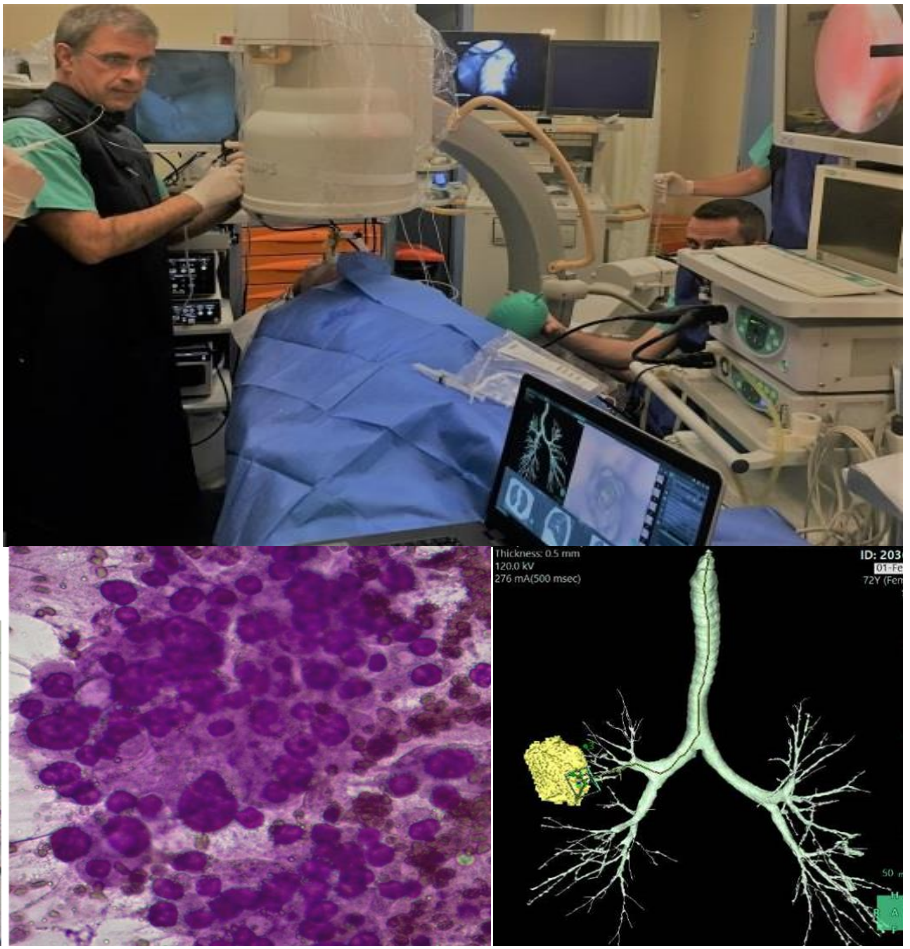


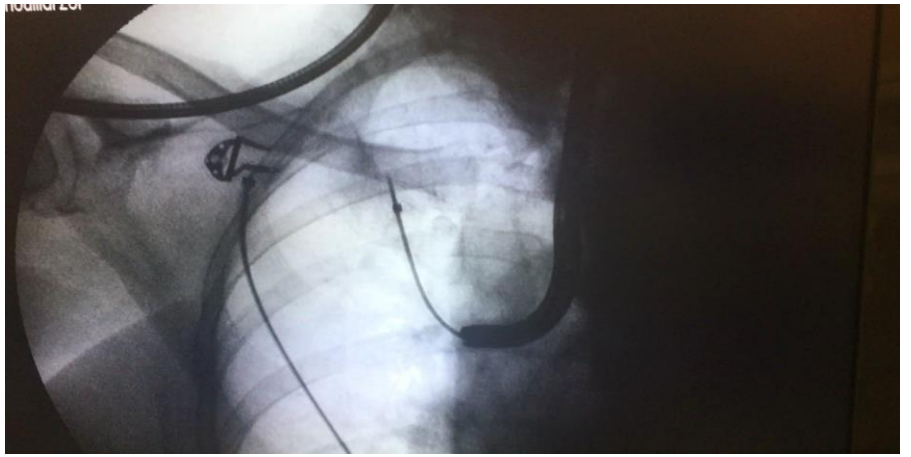


Real-time needle-based CLE imaging of different lung tumours demonstrating the two ‘static’ nCLE malignancy criteria (enlarged pleomorphic cells and dark clumps) and the ’dynamic’ phenomenon of directional streaming .

Kramer T, et al. Thorax 2022;77:370–377

Conclusions- “the secret recipe” Multimodality approach





- Exclude any mediastinal involvement (EBUS/bEUS) +ROSE
- Assessment of PPL with VB and rEBUS under fluoroscopy or CBCT + ROSE. Consider UB
- Use biopsy forceps, needle or thin cryoprobe through the radial EBUS sheath.

Segmentation and pathway analysis, Radial EBUS, fluoroscopic Confirmation and ROSE

Thank you for your attention