20th ANNUAL



ATLANTA

LUNG CANCER SYMPOSIUM

PRACTICAL APPLICATIONS OF ADVANCED DIAGNOSTIC APPROACHES IN LUNG CANCER

November 2026

Partners for Advancing Clinical Education

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PRACTICAL APPLICATIONS OF ADVANCED DIAGNOSTIC APPROACHES IN LUNG CANCER

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DISCLOSURE

1. No financial conflict

OBJECTIVE AND GOALS:

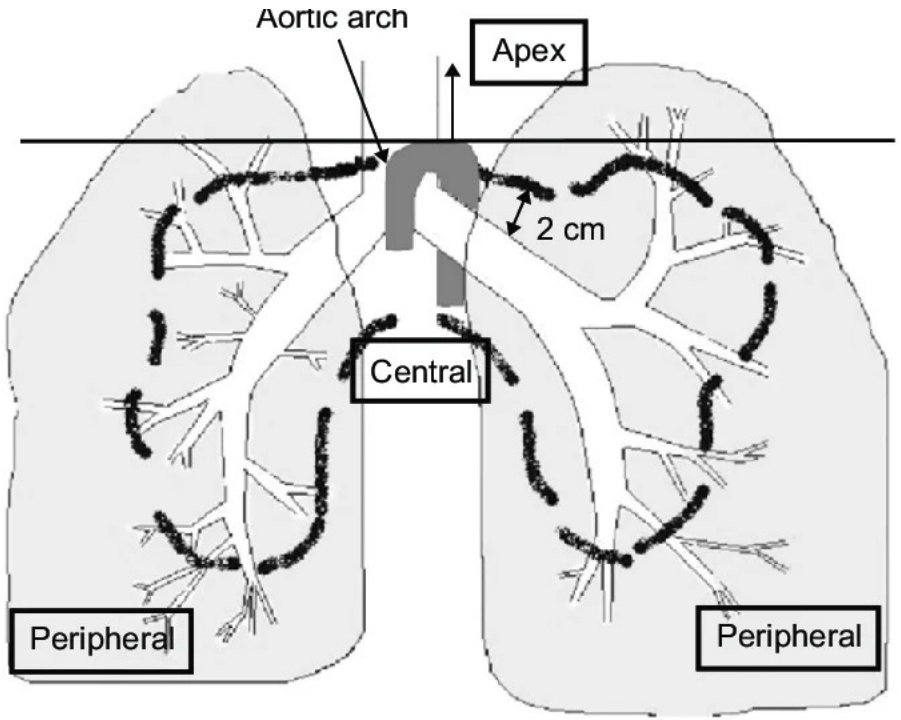
Overall Goal:

Review recent advances in advanced diagnostic bronchoscopy on tissue acquisition using endobronchial ultrasound (EBUS) and robotic-assisted bronchoscopy(RAB).

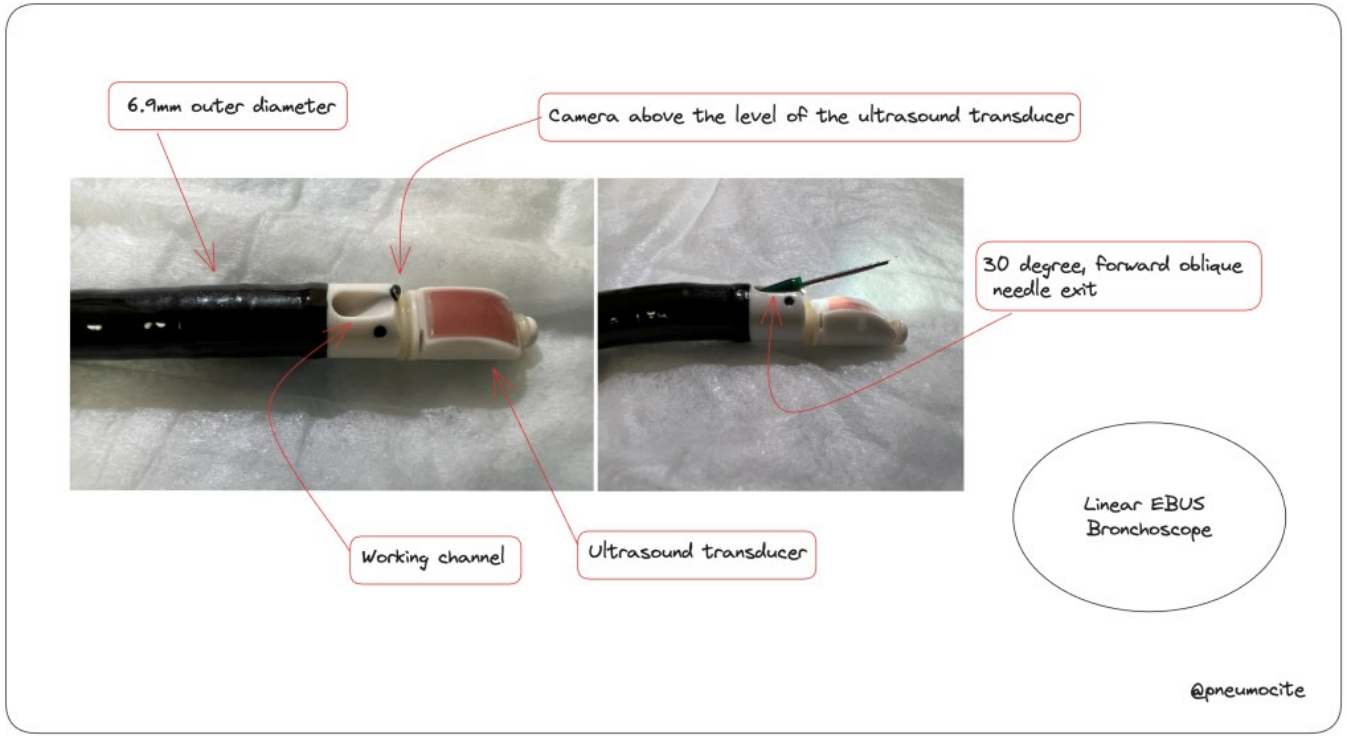
Objectives: By the end of this presentation, participants will be able to:

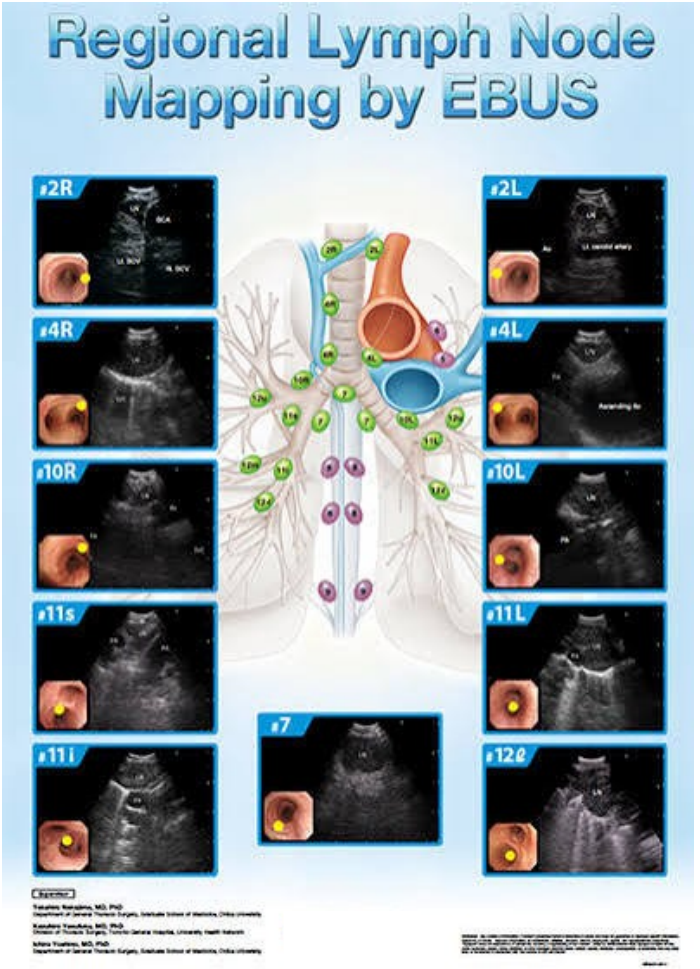
1. Compare at least 2 advanced bronchoscopic modalities for diagnosing thoracic lesions, including their clinical applications and limitations.
2. Critically appraise the results of at least 2 randomized controlled trials evaluating robotic or navigational bronchoscopy for peripheral pulmonary nodule biopsy, focusing on diagnostic yield and safety.

WHAT ARE WE BIOPSYING: LOCATION , LOCATION, LOCATION



CENTRAL AIRWAY LESIONS AND MEDIASTINAL LYMPH NODES: EBUS: ENDOBRONCHIAL ULTRASOUND





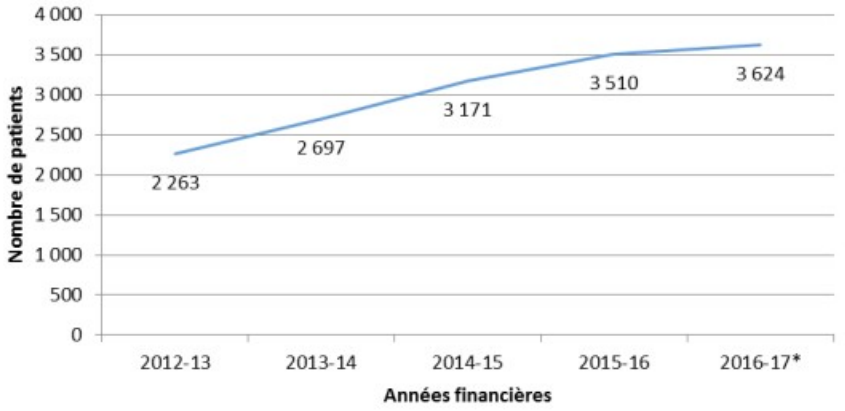
STAGING: EBUS

Modality	Sensitivity (%)	Specificity (%)	Invasiveness
CT scan	55	80	Non-invasive
PET-CT	80	90	Non-invasive
Cervical mediastinoscopy	78	100	Invasive
VATS	99	100	Invasive
EBUS-TBNA	89	100	Minimally invasive

Fiore C, Ayasa LA, Murn M, Swenson K. A comprehensive review of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA): staging, techniques, and future directions. J Thorac Dis. 2025 Dec 31

META ANALYSIS OF EBUS FOR DIAGNOSIS AND STAGING

- **Gu P et al. Eur J cancer 2009**
  - Pooled Sn 93 % and sp 100 % (11 studies)
- **Adams K et al thoracic 2009**
  - Pooled Sn 88 % and Specificity 100 % (10 studies)
- **Silvestri GS et al. Chest 2013; 143**
  - 26 studies/ 2756 patients
  - Median Sn 89 %, median sp 100 %, NPV 91 %
  - Median prevalence 58 %, Sn varies with prevalence



* Année financière estimée au 31 mars 2017.

INESSS Quebec report 2017

EBUS: SCORE STUDY

<u>Study comparing Systematic EBUS vs targeted EBUS</u>

Targeted approach: CT/PET guided

- Sensitivity 73 %

Systematic EBUS :

- Sensitivity 77 %
- Combines EUS-B after systematic EBUS Sn 82 %

Crombag et al. Eur Respir J 2019 53;1800800

ROLE OF MEDIASTINOSCOPY POST EBUS

Sanz- Santos et al annals ATS 2023:

After negative EBUS TBNA for lung cancer: confirmatory mediastinoscopy: Systematic review and met analysis

- 29 studies ; Sn 67 % for confirmatory VAM
- 96 % for combination of EBUS TBNA + conf VAM
- **HIGH Number Needed to treat (NNT) with VAM (24) after negative EBUS**
- **Conclusion:** Confirmatory VAM after negative EBUS-TBNA reduces the rate of unforeseen N2/3 disease, but with a high NNT, and it should be recommended only for certain cases yet to be defined.

ADEQUACY OF EBUS- TBNA SPECIMENS FOR PD-L1 TESTING

- Sakata et al. CHEST 2018; 154 (4): 827-837
  - 61 pts who underwent EBUS TBNA followed by surgical resection
  - Sn EBUS TBNA 72 % for PDL1 > 1 % but 47 % for PDL1 > 50 %
- Smith et al JOBIP 2020; 27: 50-57
  - PD-L1 testing on 120 EBUS TBNA samples: 110 adequate
  - EBUS PD-L1 concordant with histology specimens in 14/18 (78 %) no FN
- Perrotta et al CHEST 2020: 158 1230-1239
  - Multicenter study: 95% EBUS TBNA samples adequate for PD-L1 testing

THORACIC ONCOLOGY ■

What Is the Sensitivity and Specificity of PD-L1 Testing in Cytologic vs Paired Histologic Specimens in Non-Small Cell Lung Cancer?

STUDY DESIGN

Meta-analyses of studies reporting the **pooled sensitivity and specificity of** programmed death ligand 1 **(PD-L1) testing on:**

Cytology Cell Block **vs** **Histology Specimen**

1,618 articles identified

↓

23 articles included

RESULTS

PD-L1 sample and cutoff		Sensitivity	Specificity
Histology specimens and cytology cell blocks **(n=1,064)**	≥1%	0.84 (95% CI, 0.77 to 0.89)	0.88 (95% CI, 0.82 to 0.93)
	≥50%	0.78 (95% CI, 0.69 to 0.86)	0.94 (95% CI, 0.91 to 0.96)
Paired specimens **without interval treatment** between histology and cytology **(n=946)**	≥1%	0.84 (95% CI, 0.76 to 0.90)	0.89 (95% CI, 0.82 to 0.94)
	≥50%	0.80 (95% CI, 0.71 to 0.89)	0.94 (95% CI, 0.91 to 0.96)

Cytologic specimens provide an accurate assessment of PD-L1 expression in most patients with non-small cell lung cancer, at both >1% and >50% cutoffs, when compared with histologic specimens.

Tajarernmuang P, et al. *CHEST* February 2024 | @journal_CHEST | https://doi.org/10.1016/j.chest.2023.09.013

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SWITCH GEAR TO PERIPHERAL LESIONS

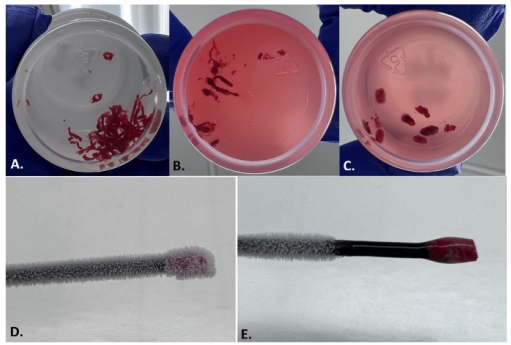


PERIPHERAL NODULE BIOPSY NAVIGATION:

Advances:

1. Navigation: Robotic: Reach, stability
2. Advanced Imaging: Intraoperative CT scan:
    1. Digital tomosynthesis
    2. Mobile and fixed Cone beam CT
    3. Augmented fluoroscopy
3. Tools: Cryoprobe





PERIPHERAL NODULE BIOPSY: ADVANCES #1: ROBOTIC NAVIGATION BRONCHOSCOPY







From left to Right: ION Rab, Noah Galaxy Rab, Monarch RAB

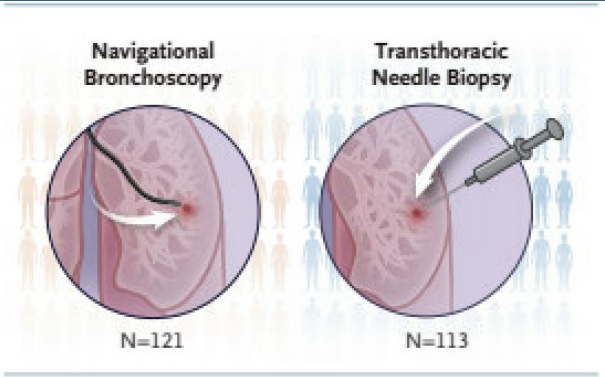
VERITAS TRIAL: RCT

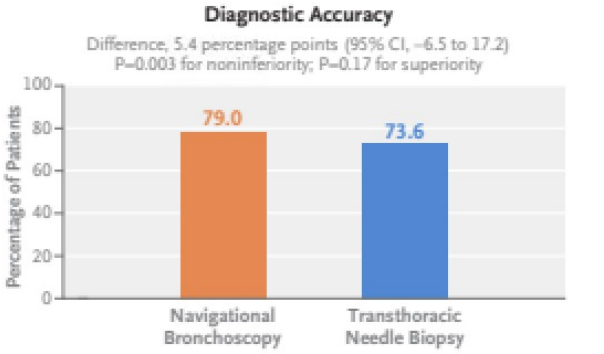
The NEW ENGLAND JOURNAL of MEDICINE

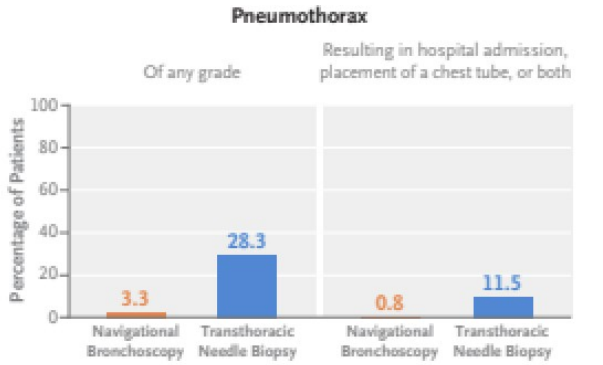
Navigational Bronchoscopy or Transthoracic Needle Biopsy for Lung Nodules

A Research Summary based on Lentz RJ et al. | 10.1056/NEJMoa2414059 | Published on May 18, 2025

- 7 US centers: Multicenter, randomized parallel group; non inferiority trial
- 234 patients: 10-30 mm diameter nodules intermediate- high risk nodules
- **Outcomes: Diagnostic accuracy 12 months and safety**
- **<u>Conclusion:</u> Nav Bronch was NON inferior to CT guided transthoracic needle biopsy for diagnosing peripheral lung nodules 10-30 mm, significant better safety profile**







Lentz RJ, et al NEJM 2025.

RELIANT TRIAL

STUDY DESIGN

411	10%	1
patients randomized	noninferiority margin	centre (Vanderbilt)

Design
Investigator-initiated, unblinded, pragmatic cluster-randomized noninferiority trial (NCT05705544). Two operating rooms were each randomized every morning; one OR-day = one cluster. Enrolled Mar 2023 – Apr 2024.

Population
Patients undergoing diagnostic bronchoscopy for a peripheral pulmonary lesion.

Intervention
Shape-sensing robotic-assisted bronchoscopy (RAB).

Comparator
Electromagnetic navigation bronchoscopy (ENB) with integrated digital tomosynthesis.

Outcomes
Primary: diagnostic yield (procedures yielding lesional tissue). Secondary: procedure duration. Safety: complications within 7 days.

RESULTS

Outcome	RAB (n=203)	ENB (n=208)	Difference
Diagnostic yield	**77.8%** (158/203)	**75.5%** (157/208)	+2.3 points noninferiority p = 0.007
Median procedure time	**37 min**	**32 min**	+5 min (95% CI 2.0 – 7.7)

COMPLICATIONS / SAFETY

Event (within 7 days)	RAB	ENB	Comment
Pneumothorax	**4** (≈2.0%*)	**6** (≈2.9%*)	Comparable between groups
Haemorrhage, respiratory failure, anaesthesia complications	assessed	assessed	Counts not retrieved; see full text

KEY CAVEATS

- **Noninferiority, not superiority.** RAB did not improve yield (+2.3 points) and procedures ran about 5 min longer.
- **Single academic centre, expert operators, unblinded.** Generalisability to other settings is uncertain.
- **Wide 10% margin.** A published letter (Bertolaccini et al.) questioned the margin and some subgroup findings; the authors reply that the 2.3-point difference would meet stricter margins and that small subgroups limit inference.
- **Safety is descriptive.** Event counts (4 vs 6 pneumothoraces) are too few for a reliable safety comparison.
- **No integrated cone-beam CT in the RAB arm.** Newer integrated-imaging platforms are being tested in the ongoing RELIANT 2 trial.

In trained hands, robotic bronchoscopy was noninferior to electromagnetic navigation for diagnostic yield (77.8% vs 75.5%) with similar pneumothorax counts (4 vs 6); both are reasonable options for peripheral pulmonary lesions.

Paez R, Lentz RJ, Duke JD, Siemann JK, Salmon C, Dahlberg GJ, et al.; Maldonado F. Robotic versus electromagnetic bronchoscopy for peripheral pulmonary lesions: a randomized trial (RELIANT). Am J Respir Crit Care Med 2025;211(9):1644-1651. PMID 40460390. doi:10.1164/rccm.202409-1846OC

*Percentages calculated from reported counts. Prepared from the abstract, a trial summary and related correspondence (full text was not accessible). Verify against the paper.

CONFIRM STUDY

INTERVENTIONAL PULMONOLOGY ■ Thorax 2026;81(3):267 | Visual summary 1 of 2

Does shape-sensing robotic bronchoscopy with integrated mobile cone-beam CT reliably sample small peripheral lung nodules? (CONFIRM)

STUDY DESIGN

155	14 mm	99.4%
patients, 6 centres	median nodule size	tool-in-lesion

Design
Prospective, observational, multicentre; consecutive enrolment (NCT05562895).

Population
Patients with a peripheral pulmonary nodule (PPN) ≤20 mm suspicious for malignancy. 54.8% upper lobe; CT bronchus sign in 25.8%; median 8.2 mm to nearest pleura.

Intervention
Shape-sensing robotic-assisted bronchoscopy (ssRAB) integrated with mobile cone-beam CT (mCBCT) to correct CT-to-body divergence. Median 2 mCBCT spins.

Comparator
None (single-arm).

Outcomes
Tool-in-lesion (TIL), diagnostic yield (ATS/ACCP), sensitivity for malignancy, pneumothorax and airway bleeding. Non-malignant biopsies followed 12 months.

RESULTS

Outcome	Result	95% CI	n / N
Tool-in-lesion (TIL) confirmation	**99.4%**	96.5 – 100.0	154 / 155
Diagnostic yield (ATS/ACCP definition)	**89.0%**	83.0 – 93.5	138 / 155
Sensitivity for malignancy	**91.5%**	86.4 – 96.5	—

COMPLICATIONS / SAFETY

Event	Rate	95% CI	n
Pneumothorax	**0%**	0.0 – 2.4	0
Airway bleeding, Nashville grade 3	**1.3%**	[illegible]	2
Radiation (mCBCT), median dose-area product	**25.7 Gy·cm²**	IQR 11.0 – 46.7	—

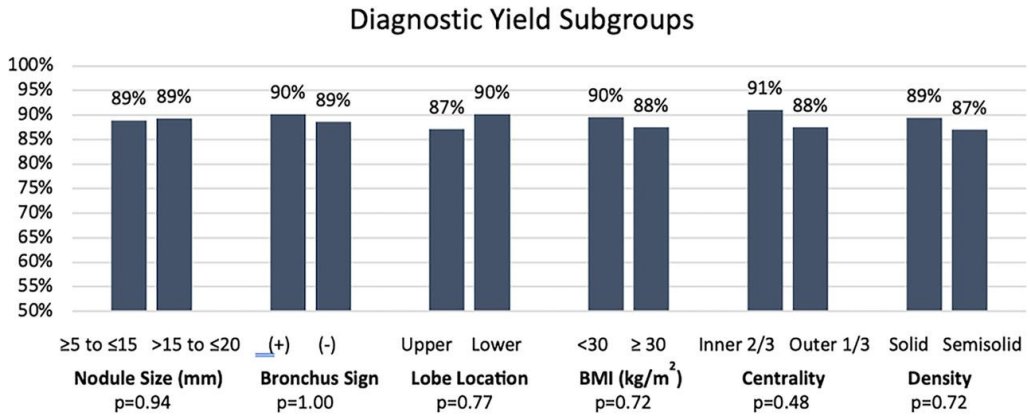
KEY CAVEATS

- **Single-arm, observational.** No comparator group; the comparison with transthoracic biopsy is indirect (cross-study).
- **Industry funding and ties.** Intuitive Surgical funded the sites and the independent statistical analysis; several authors report grants or consulting fees from the company, and one is a part-time employee.
- **Generalisability.** 155 patients at 6 centres; performance in lower-volume settings or without mCBCT access is not addressed by this study.
- **Trade-offs not summarised in the abstract:** added radiation, cost and procedure time; results are descriptive statistics only.

Integrated ssRAB + mCBCT reached the target in 99.4% of small nodules with 89.0% diagnostic yield and no pneumothorax, which the authors interpret as outcomes similar to transthoracic biopsy with a more favourable safety profile.

Husta BC, Cheng GZ, Batra H, Reisenauer JS, Bartek WM, Kalchiem-Dekel O, et al. Shape-sensing robotic-assisted bronchoscopy with integrated mobile cone-beam CT for small nodules: results from the prospective multicentre CONFIRM study. Thorax 2026;81(3):267.

Prepared from the published abstract and author disclosures (full text was not accessible). Verify against the full paper before citing.



TOOLS: CRYOBIOPSY: FROSTBITE 2 TRIAL

JAMA

QUESTION Is the diagnostic yield of transbronchial lung biopsy higher with use of a 1.1-mm cryoprobe compared with 2.0-mm forceps?

CONCLUSION This clinical trial found that the diagnostic yield of transbronchial lung biopsy was significantly higher with use of a 1.1-mm cryoprobe vs 2.0-mm forceps in patients with pulmonary nodules or masses, lung transplant, and diffuse parenchymal lung disease.

POPULATION

252 Males
248 Females

Adults ≥18 years undergoing transbronchial biopsy for lung nodules or masses, lung transplant, or diffuse parenchymal lung disease

Mean age: 62.6 years

LOCATION

9
Medical centers
in the United States

INTERVENTION

500 Patients randomized
490 Patients analyzed

250
Cryoprobe
Transbronchial biopsy using a 1.1-mm cryoprobe

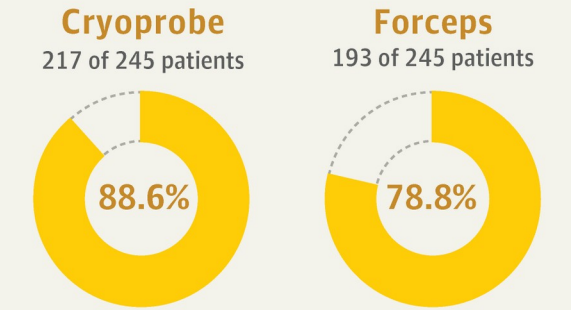
250
Forceps
Transbronchial biopsy using 2.0-mm forceps

PRIMARY OUTCOME

Diagnostic yield, defined as the percentage of patients for whom the transbronchial biopsy sample led to a specific diagnosis based on histologic examination

FINDINGS

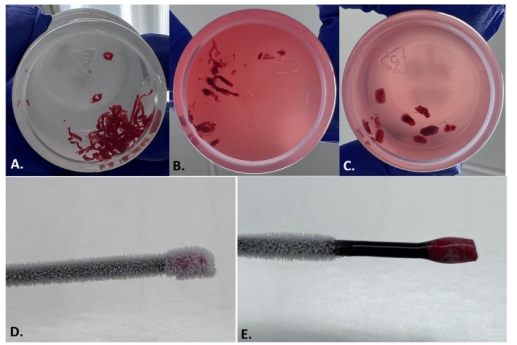
Rate of overall diagnostic yield



Diagnostic yield was significantly higher with a 1.1-mm cryoprobe vs 2.0-mm forceps:
Absolute difference, 9.8%
(95% CI, 3.3% to 16.3%); *P* = .003

© AMA

Thiboutot J, Kapp CM, Illei P, et al; Interventional Pulmonary Outcomes Group. Cryobiopsy vs forceps for bronchoscopic lung biopsy: the FROSTBITE-2 randomized clinical trial. *JAMA*. Published online May 18, 2026. doi:10.1001/jama.2026.7908



WHY CARE ABOUT NAVIGATION BRONCHOSCOPY ?

LETTERS TO THE EDITOR · Volume 23, Issue 7, P1225-1226, July 2026 Download Full Issue

Toward Safer Tissue Acquisition in Peripheral Lung Nodule Evaluation

Jacob Schwartz, MD, MPH · Irene Riestra, MD · Uzair K. Ghori, MD · Otis B. Rickman, DO · Abesh Niroula, MBBS

Affiliations & Notes Article Info

Diagnostic Yield

Study	Design	n	Bronchoscopy	Imaging	DY
Ost, 2026 (PRECIsE)	Prospective Multicenter Cohort	305	ssRAB	2D Fluoroscopy	Strict: 74%
Husta, 2025 (CONFIRM)	Prospective Multicenter Cohort	155	ssRAB	Integrated mCBCT C-arm	Strict: 89%
Chambers, 2022	Retrospective Single Center Cohort	79	ssRAB	mCBCT O-arm	Lenient: 77%
Patel, 2026	Retrospective Single Center Comparative	375	ssRAB	Fixed CBCT	Strict: 90%
Lentz, 2023 (VERITAS)	Prospective Multicenter Comparative	121	EMN-B	AF-DT	Strict: 79%

Diagnostic Yield - Subsolid

	Study	Design	# Lesions	Navigation	Diagnostic Yield
Mobile CBCT	Husta, 2025 (CONFIRM)	Prospective Cohort	17	ssRAB	87%*
	Fernandez-Bussy, 2025 (DYSTRICT)	Retrospective Comparative	115	ssRAB	74%*
	Fernandez-Bussy, 2026 (2000)	Retrospective Cohort	324	ssRAB	76%*
	Zhang, 2026	Retrospective Cohort	55	ssRAB	87%*
Fixed CBCT	Kawakita, 2025	Retrospective Cohort	157	VB	69%
	Patel, 2026	Retrospective Comparative	90	UTB or EMN-RAB	88%*
DT	Lentz, 2025 (VERITAS)	Prospective Randomized	22	EMN-B	68%*

MOLECULAR MARKERS ADEQUACY NODULE: BRONCHOSCOPY

- Supplementary Table 5. Overall and Per-Sampling Tool Adequacy and Performance Success Rates for Predictive Marker and Driver Mutation Assays[a]

Assay	Platform	Assay Success Threshold	Overall Assay Success Rate[b]	Individual Sampling Tool Assay Success Rate[c]		
				TBNA	TBFB	TBCB
ALK IHC	Cell Signaling Technology Clone D5F3®		199/202 99.0%	22/22 100%	152/152 100%	31/31 100.0%
PD-L1 IHC	Ventana® SP263 Clone		203/210 96.6%	23/25 92.0%	158/163 96.9%	32/32 100.0%
Adequacy for molecular studies	Visual estimation	Tumor cell proportion ≥20%	216/242 89.2%	109/202 53.6%	176/198 88.9%	47/49 95.9%
KRAS PCR	Idylla™ KRAS Mutation Assay	Mutation variant frequency ≥5%	146/159 91.8%	16/18 88.9%	110/115 95.6%	24/30 80.0%
EGFR PCR	Idylla™ EGFR Mutation Assay	Mutation variant frequency ≥5%	144/157 91.7%	17/20 85.0%	101/105 96.1%	28/33 84.8%
EGFR exons 19 and 20, ERBB2/HER2 exon 20 insertion/deletion PCR	EGFR/ERBB2 Sizing Assay (Fragment Analysis)	Tumor cell proportion ≥10%	40/46 86.9%	4/5 80.0%	25/27 92.6%	12/16 75.0%
Next-generation sequencing	MSK-IMPACT™	Tumor cell proportion ≥10% Exon sequence coverage ≥100×	154/165 93.3%	11/14 78.5%	115/122 94.2%	32/35 91.4%
Gene fusion RNA-seq panel	Archer FusionPlex™	Tumor cell proportion ≥10%	27/28 96.4%	3/4 75%	15/16 93.7%	9/9 100%

EMORY REAL-WORLD TBCB PERFORMANCE one year data 2024-2025

STRICT Diagnostic yield, lesion characteristics and procedural safety

STRICT DIAGNOSTIC YIELD

Population	TBCB yield	95% CI
All lesions	82.5% 321/389	78.7–86.3%
Nodules <30 mm	81.8% 248/303	77.5–86.2%

TBCB YIELD BY LESION CHARACTERISTIC

Lesion type	Diagnostic	Non-diagnostic
Solid	84.1% (227/270)	15.9%
Part-solid	75.0% (39/52)	25.0%
Ground-glass	88.3% (15/17)	11.7%
Cavitary/cystic	81.6% (40/49)	18.4%

COMPLICATIONS (n=361)

Pneumothorax	1.0% 4/361
Clinically significant bleeding	1.0% 4/361
Post-procedural hypoxemia	1.0% 4/361
Post-procedural admission	2.2% 8/361

LESION SIZE DISTRIBUTION (n=424) — YIELD BY SIZE NOT REPORTED

<10 mm	10–20 mm	20–30 mm	>30 mm
16.7%	37.7%	23.3%	22.2%

Emory MOLECULAR ADEQUACY: REAL-WORLD CARIS EXPERIENCE

Institutional NSCLC testing — quantity not sufficient (QNS) rates

2025

93.5%

MOLECULAR TESTING ADEQUATE



QNS: 6.5% | 22 QNS cases*

341 total NSCLC cases

2026 YTD

92.1%

MOLECULAR TESTING ADEQUATE



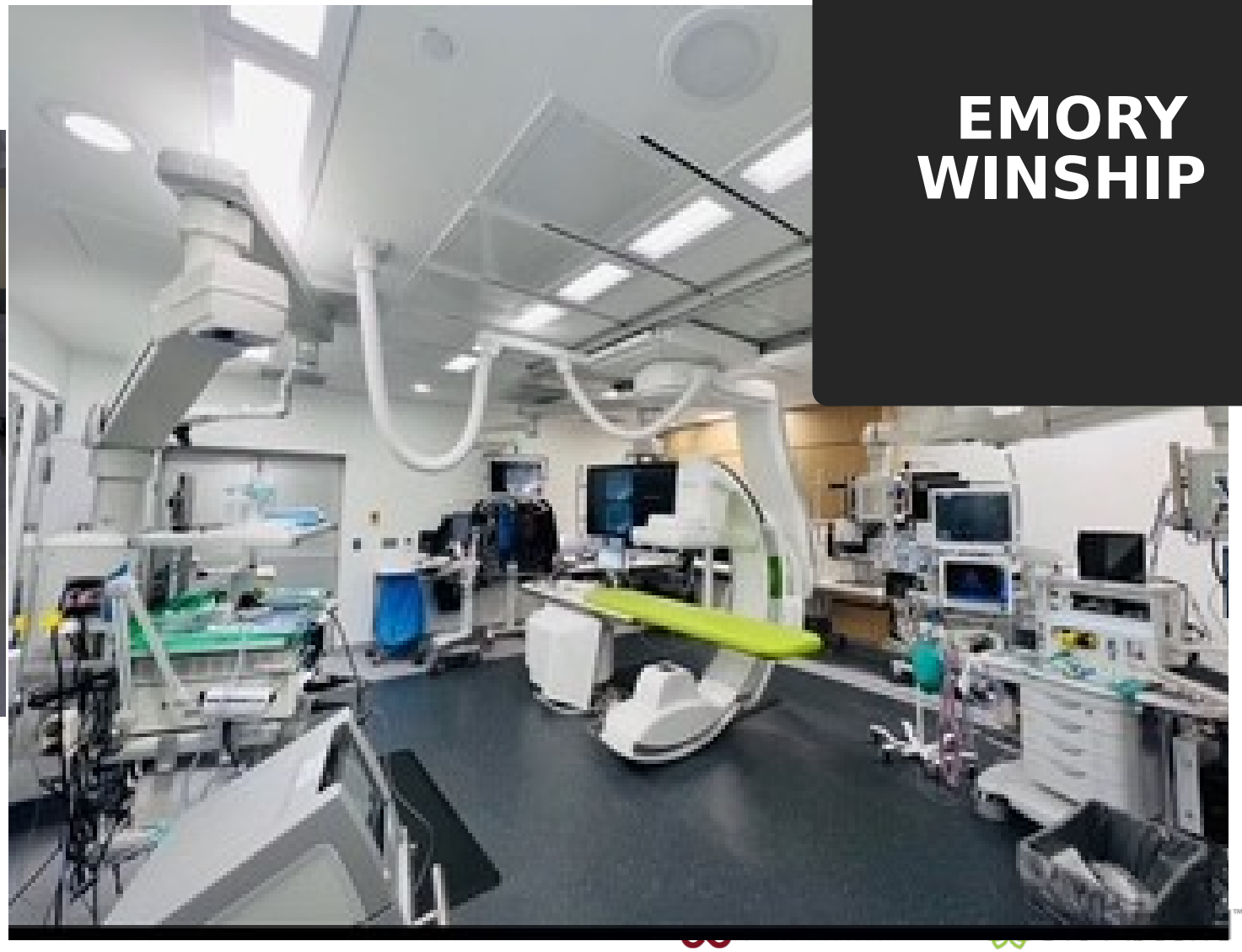
QNS: 7.9% | 29 QNS cases

366 total NSCLC cases

More than 9 in 10 NSCLC cases had adequate material for molecular testing

HOW LUNG CANCER DIAGNOISS/ STAGING LOOKS LIKE IN 2026



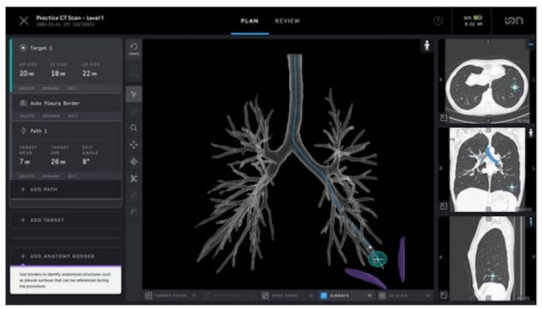


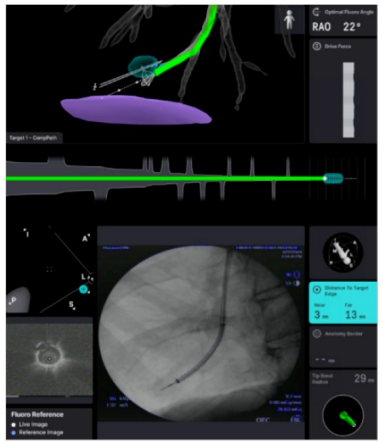
EMORY WINSHIP

20th ANNUAL ATLANTA LUNG CANCER SYMPOSIUM

Navigation

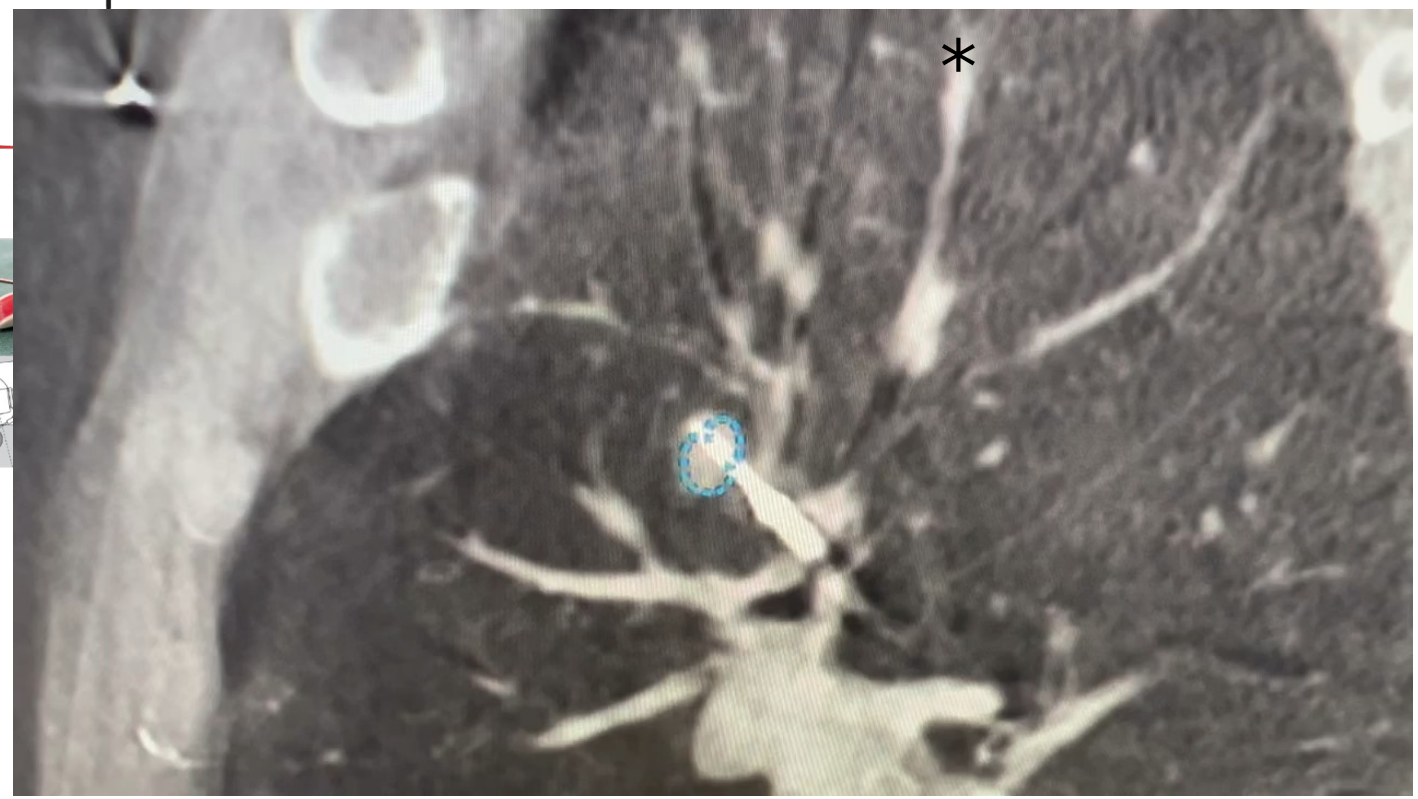
Planning





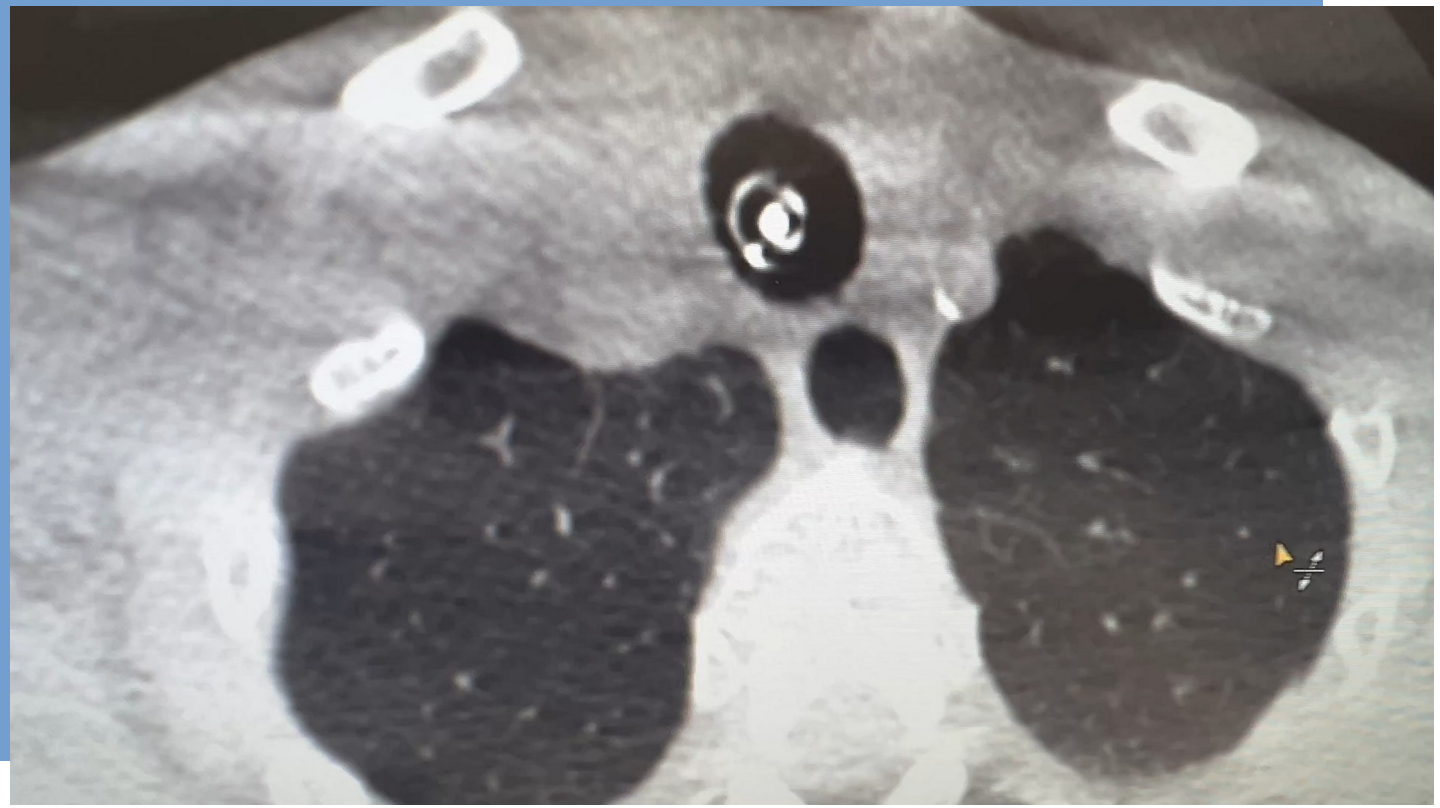
Biopsy





PHILLIPS AZURION FIXED CBCT: 74 YRS OLD WITH GROWING RIGHT FISSURAL NODULE: TOOL IN LESION





CONCLUSIONS

- **The future of lung cancer diagnosis:**
  - **It's not just WHERE we biopsy. It's HOW we biopsy.**
- Central lesions: EBUS for diagnosis and staging.
- Peripheral lesions: Robotic bronchoscopy + advanced imaging + appropriate sampling tools.
- Tissue matters: Obtain adequate material for molecular profiling and treatment selection.
- Teamwork matters: Multidisciplinary planning to choose the safest and most effective biopsy approach.
- **One procedure. Diagnosis, staging, and molecular information.**