2024 World Conference on Lung Cancer

SEPTEMBER 7-10, 2024 | SAN DIEGO, CA USA

Pulmonary From Diagnostics to Therapeutics

Nicholas Stollenwerk, MD
UCD Comprehensive Cancer Center

Overview: Pulmonary – From Diagnostics to Therapeutics

- Lung Cancer Screening. I have tried to avoid this topic, but there will be some overlap.
- **Evaluation of Pulmonary Nodules.**
  - How do we decide the following?
    - In which patients do we pursue biopsy?
    - Which nodules/abnormalities should be biopsied?
    - Which technique/technology should be used to perform the biopsy?
  - I am focusing most of this discussion on imaging and biomarkers that can help enrich the patient population in which invasive procedures will be pursued.
    - Currently, we can't (and shouldn't) perform a biopsy on every patient and every nodule.
  - I am, in general, avoiding discussion on the use of AI in lung cancer screening and evaluation of pulmonary nodules.
    - This is quite complex and is beyond the scope of this brief presentation.
- **Therapeutics.**
  - What interventions can Pulmonologists offer that can act as adjuncts to our colleagues in Medical Oncology, Thoracic Surgery, and Radiation Oncology.
    - In which patients and which treatments?

When (who and what) to Biopsy

The goal is to optimize (or “enrich”) the target patient population to improve diagnosis and minimize procedural complications.

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Control #: 1594

An Effective Multimodel Based on Cell-Free DNA Methylation for Risk Stratification of Pulmonary Nodules

Wenhua Liang, Jian-Bing Fan, Jianxing He

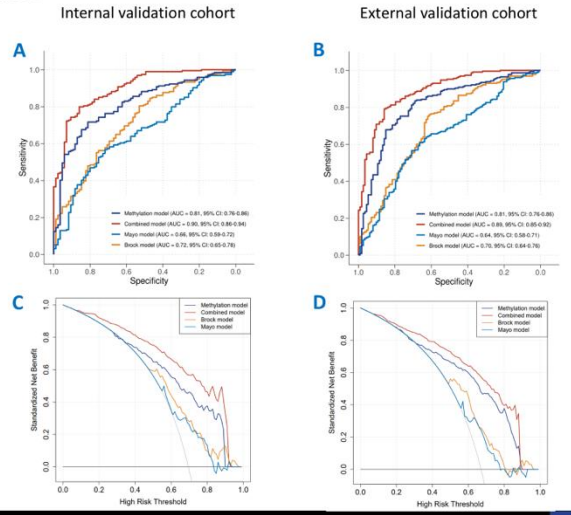
1. Department of Thoracic Surgery and Oncology, The First Affiliated Hospital of Guangzhou Medical University, China State Key Laboratory of Respiratory Disease & National Clinical Research Centre for Respiratory Disease, Guangzhou, China.
2. Department of Pathology, School of Basic Medical Science, Southern Medical University, China

- We know that low dose CT scan for lung cancer screening increases early-stage detection and decreases lung cancer mortality.
- However, most nodules are not malignant.
- Clinical prediction models (common models are Brock, Mayo, and VA) have a reported accuracy of 60-90%.
- For patients with low to intermediate risk nodules, difficult to biopsy nodules, or high-risk patients, additional assessment tools are needed to assist with evaluation.
- Liang, et al addressed this using a multimodel using Cell-Free DNA Methylation in combination with clinical prediction models.

Mini Oral Sessions: MA02.09

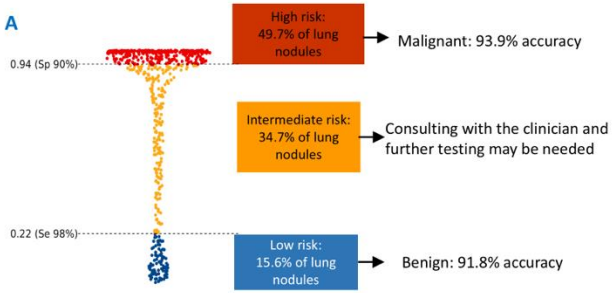
The multimodel for malignant identification

- **Methylation-only model:** (A,B)
  AUC=0.81 vs Myao Clinic (0.66) and Brock (0.72)
  Sensitivity=0.89 vs Myao Clinic (0.69) and Brock (0.81) when specificity fixed at 0.51.
  Accuracy=0.77 vs Myao Clinic (0.63) and Brock (0.72)
- **Combined model:** (A,B)
  AUC=0.89-0.90, with 0.08-0.09 increased.
  Sensitivity=0.95-0.97, with 0.06-0.07 increased.
  Accuracy=0.80-0.83, with 0.03-0.05 increased.
  PPV=0.80-0.82
  NPV=0.99 (10% prevelance)
- **Decision curve analysis (DCA): with a standardized net benefit of 79.1% from the combined model:** it means correctly identify approximately 79 individuals with malignant nodules from 100 people with lung cancer, if to consider an invasive procedure for a patient with a risk score more than the threshold of 0.40. (C, D)

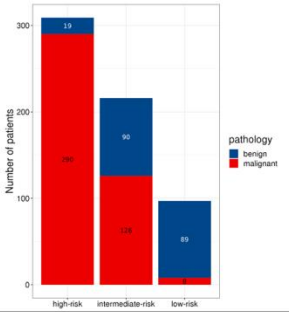


Two-threshold strategy for accurate risk stratification of pulmonary nodules

- **Two cutoffs simultaneously to classify pulmonary nodules into low-risk** (risk score <0.22)**, intermediate-risk** (risk score from ≥0.22 to <0.94)**, and high-risk** (risk score ≥0.94) **groups.** (A)
- **High risk nodules**: 49.7% of total; with 93.9% accuracy
  Low risk nodule: 15.6% of total; with 91.8% accuracy
  Intermediate risk: 34.7% of total; active follow up



Reduce unnecessary invasive surgeries	**90.4%** (89+90/198)
Malignant nodules misclassified and falls into surveillance	1.9% (8/424)
Benign nodules misclassified and undergone invasive surgeries	9.6% (19/198)



- Accuracy improved to 0.77
- NPV 0.99 (assuming 10% prevalence)
- Using the authors 2 threshold strategy: Misclassification of malignant nodules as low risk occurred 1.9% of the time.
  - Hence, low risk nodules will still need follow-up, but possibly follow up can be less intense.
- High risk nodules were malignant 93.9% of the time.
  - This is an enhanced patient pool, hence if the biopsy is negative, the repeat is likely warranted.

Background

Early detection of lung cancer utilizing low-dose computed tomography (LDCT) screening holds promise, however, its capacity to differentiate malignant potential often leads to unnecessary invasive interventions for benign lesions.

50-80 years old → **Smoking history** → **Low-dose CT**

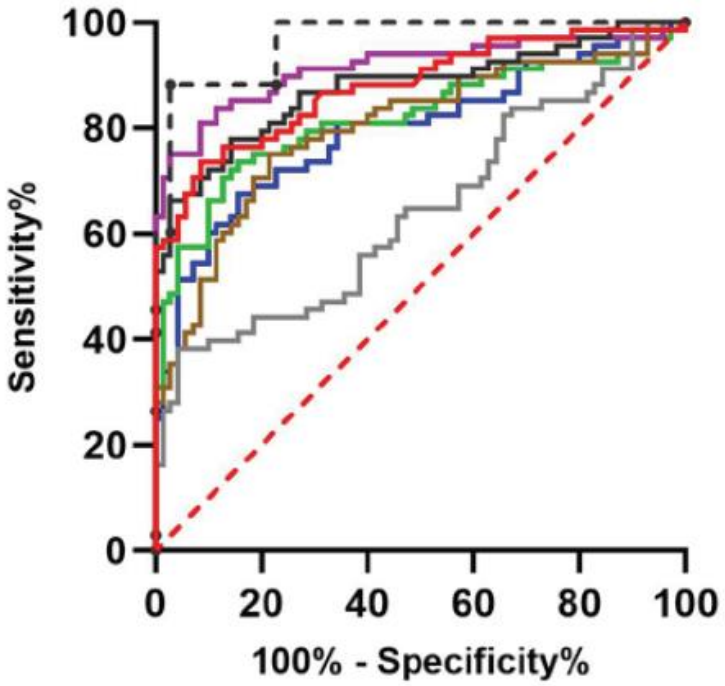
Benefits
- Reduction in lung cancer mortality (IRR 0.75 - 0.85)
- Sensitivity 59% - 100%
- Specificity 26.4% - 99.7%

Disadvantages
- False Positive: 49% - 96%
- Overdiagnosis: up to 67.2%
- Unnecessary invasive procedures or decision late
- Radiation exposure(~30mSv/year)

Aimed to address the diagnostic challenge by leveraging epigenetic insights from DNA methylation patterns in Bronchoalveolar Lavage Fluid (BALF) exosome specimens obtained from individuals suspected of having lung malignancies.

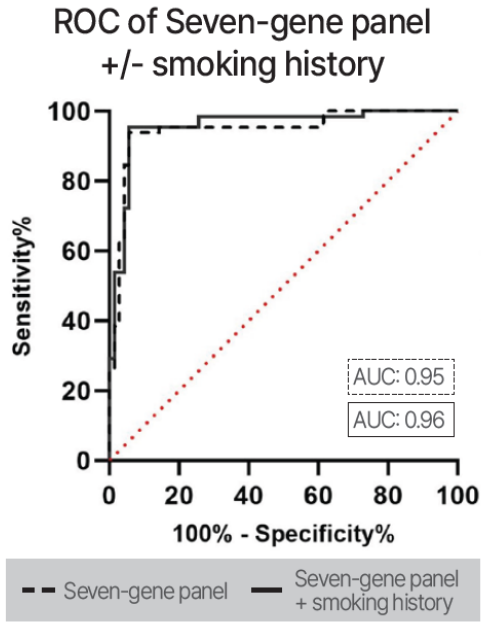
lveolar
.F) be used
cancer

Posters: P4.04C.02



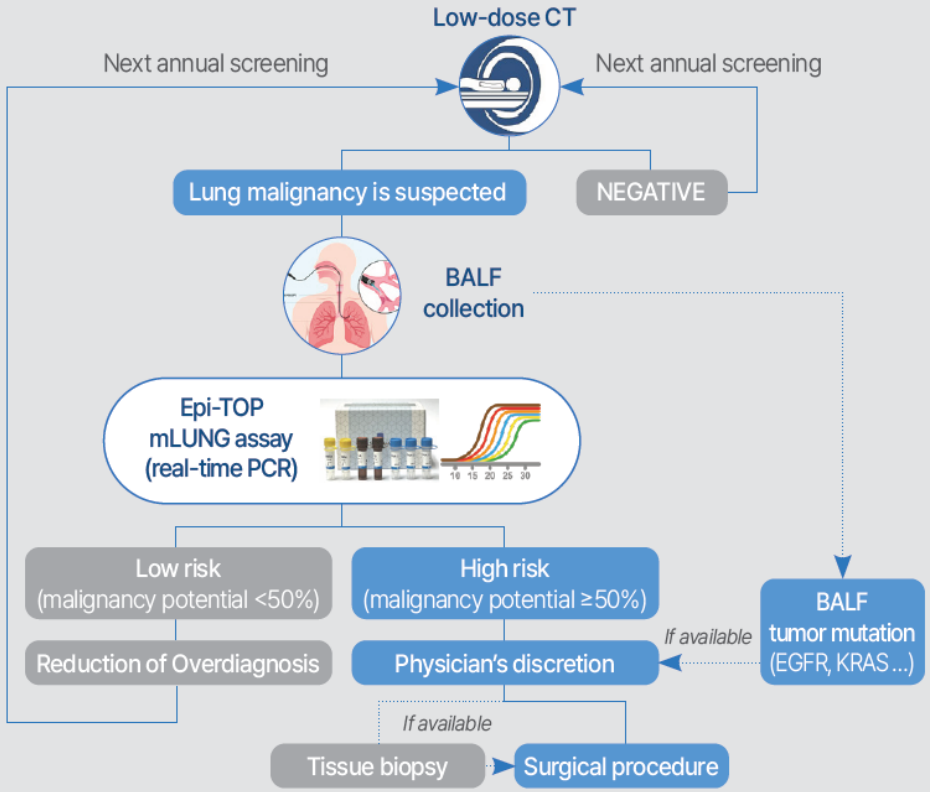
Gene	AUC	Sensitivity	Specificity
HOXA9	0.88	73.53%	91.43%
HOXD3	0.79	80.88%	65.71%
PCDH17	0.82	73.53%	84.29%
NID2	0.91	83.82%	88.57%
NPTX2	0.80	75.00%	77.14%
RASSF1A	0.64	38.24%	95.71%
SFRP2	0.87	77.94%	85.71%
Combined analysis	**0.97**	**88.24%**	**97.14%**

ROC for 7 gene panel. Improved to 92% sensitivity for early-stage LC when smoking history is included



Receiver Operating Characteristics and clinical performance of each gene

Assay workflow



Main barrier to mLUNG assay:

- This still requires bronchoscopy.
- Blood-based testing might be more appealing.

Advantages:

- Will require less resources, skill, risk, and likely cost, compared to more complex (Robotic Navigation) bronchoscopy.
- Could possible be used when bronchoscopy is being performed for other indications.

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Radiomics in Thoracic Oncology

Opportunities and Challenges

Jose Araujo-Filho, MD, PhD

Radiologist, Hospital Sirio-Libanes, Sao Paulo, Brazil
Global Outreach Committee – Society of Thoracic Radiology, USA

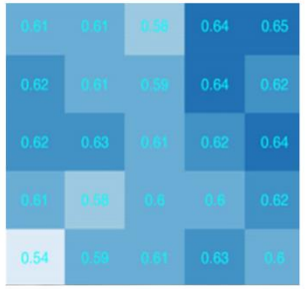
Since we are already obtaining radiographic and nuclear imaging, why not make better use of the information we already have?

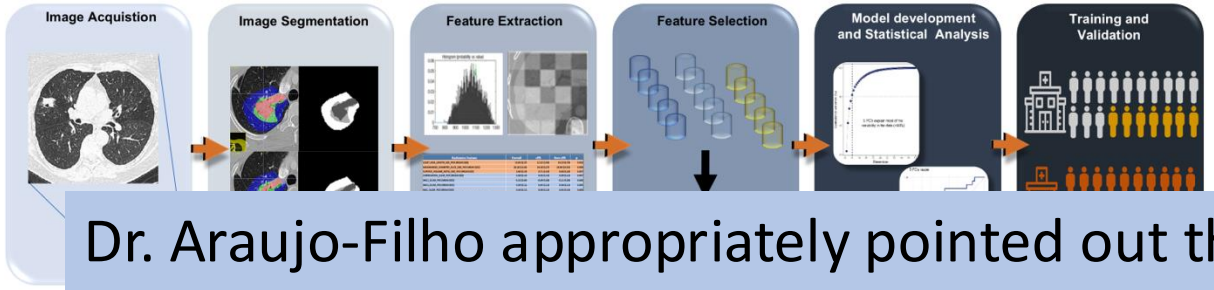
Educational Sessions: ES26.06

BASIC CONCEPTS

Radiomics is the process of extracting quantitative data (*radiomic features*) from medical images using data-driven algorithms

- Its workflow involves curation of clinical and imaging data and is a **stepwise process**
- **AI** methods are usually applied at various steps of this pipeline

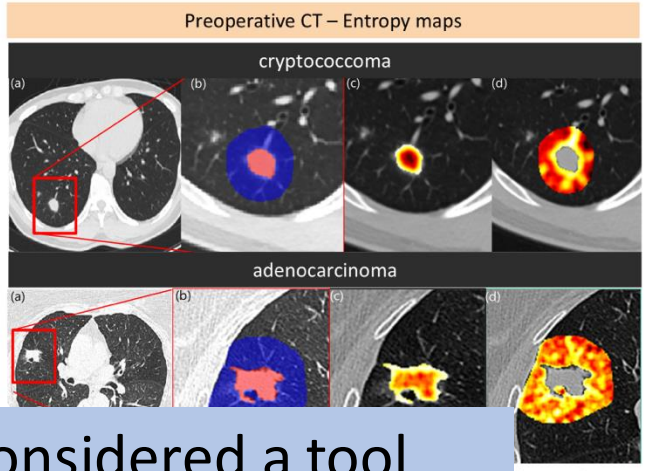




Tumor biology

Beyond the tumor size, there are other features potentially associated with worse clinical outcomes, such as **tumoral heterogeneity** and **tumor microenvironment** phenotypes

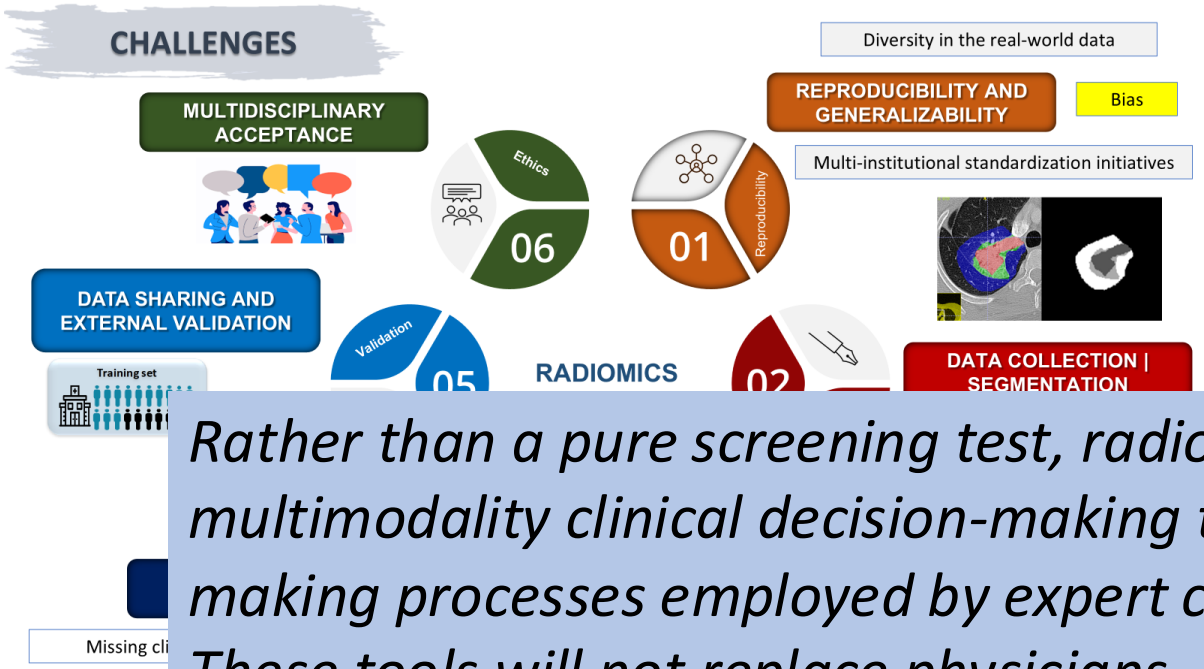
- **Intratumoral** radiomics features can predict pathologic (histology, invasiveness, etc) and clinical outcomes
- **Peritumoral** radiomics features can



lho et al. 2021

Dr. Araujo-Filho appropriately pointed out that radiomics must be considered a tool that provides complimentary information, but does not replace conventional biopsies.

It is early in the application of this technology, hence there are going to be a lot of challenges/barriers.



Currently radiomics is an adjunct that provides additional data for consideration. Per Dr. Araujo-Filho, “nice to have”, but is it a “must have”?

- The clinical benefit of radiomics and cost are not yet defined.
- This is new, so it is not clear when clinicians will accept this data
- ration when using
- oration across
- y, regulatory

Rather than a pure screening test, radiomics should be part of a multimodality clinical decision-making tool, similar to the decision making processes employed by expert clinicians and radiologists. These tools will not replace physicians, but should help to make us better.

Educational Sessions: ES26.06

How to Biopsy

Association of FDG-PET/CT findings with sufficient amount of tissue samples for gene panel testing in TBB/TBNA

Akiko Tamura[1,2], Ryo Ko[1], Hirotsugu Kenmotsu[1], Takuya Kawata[1], Suguru Matsuda[1]
Meiko Morita[1], Motoki Sekikawa[1], Kosei Doshita[1] Michitoshi Yabe[1], Hiroaki Kodama[1]
Keita Miura[1], Yuko Iida[1], Nobuaki Mamesaya[1], Haruki Kobayashi[1], Kazushige Wakuda[1]
Akira Ono[1], Tateaki Naito[1], Haruyasu Murakami[1], Hiroshi Nokihara[2], Masayuki Hojo[2]
Toshiaki Takahashi[1]

1) Shizuoka Cancer Center, Shizuoka, Japan
2) National Center for Global Health and Medicine, Tokyo, Japan

Mini Oral Sessions: MA08.08

Many of us are already using PET-CT to help us guide biopsy in a qualitative manner.

This supports this practice and specifically looked at gene panel testing, rather than just the presence of malignant cells.

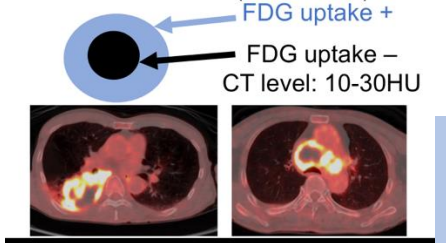
Study design

Patients

- Stage IV NSCLC, Jan 2022 - Jan 2024
- TBB/EBUS-TBNA for gene panel testing
- TBB: EBB/TBLC/EBUS-GS-TBB/Others

PET/CT parameters

- SUVmax
- Presence of necrosis (PET-necrosis)



Primary outcome

- Panel-biopsy failure
- inadequate or negative tissue samples
- requiring re-biopsy, single-plex testing, or gene panel testing by cell blocks

Other factors reported to contribute to panel-biopsy failure

- TBB: tumor locations
  (central vs peripheral, right vs left, upper/middle lobe vs lower lobe)
- EBUS-TBNA: biopsy site
  (N1/primary lesion vs N2/N3)

Summary

PET-necrosis was associated wit
EBUS-GS-TBB) and TBNA.

Why in EBUS-GS-TBB?
- small sample size - limited area of tumor is biopsied
- guide sheath are often pushed to the tumor core to prevent falling out

In choosing biopsy sites for gene panel testing, FDG-PET/CT findings had better be considered, and lesions of PET-necrosis might be not optimal target of biopsy.

Results

Stage 4 NSCLC biopsied for panel gene testing (N=239)

- Failure N=48 (TBB N=33, TBNA N=15)
- Success N=157 (TBB N=121, TBNA N=36)
- ※ N=34

Patient characteristics

	Failure (N=48)	Success (N=157)	P value
Median age, year (IQR)	72 (68-75)	73 (67-77)	0.67
Female, n (%)	18 (37.5)	47 (29.9)	0.38
Smoking status, n (%)			0.21
Current / Former	32 (67)	121 (77)	
Never	16 (33)	36 (23)	
Histologic subtype, n(%)	Ad 37 (77.1) Sq 5 (10.4) Others 6 (12.5)	Ad 115 (73.2) Sq 26 (16.6) Others 16 (10.2)	0.61
Type of procedures, n (%)			0.0087
TBB - endobronchial biopsy (EBB)	2 (4.2)	30 (19.1)	
TBB – EBUS guide sheath (GS)	21 (43.8)	38 (24.2)	
		17 (10.8)	
		36 (22.9)	
		36 (22.9)	
		6 (3-6)	0.70
		3 (1.9)	0.054

These findings should encourage us to integrate PET anatomy into our diagnostic procedure planning. This is done qualitatively, but possibly this data should be quantitatively integrated into our procedural plans. It should also remind us to be cognizant of the biopsy techniques we use – FNA vs core or transbronchial biopsy vs cryobiopsy.

				value
				0.5
				0.026
Tumor location				
central/peripheral	0.78 (0.36-1.70)	0.54	0.87 (0.33-2.27)	0.77
right/left	1.31 (0.60-2.85)	0.49	0.97 (0.36-2.65)	0.95
upper and middle/lower	3.10 (1.40-6.88)	0.0053	3.54 (1.35-9.23)	0.0099

Subgroup	Adjusted OR of PET-necrosis (95%CI)	p value
EBB	0.0 (0.0-Inf)	1
EBUS-GS-TBB	6.52 (0.95-44.60)	0.056
TBLC	679000000 (0.0-Inf)	1
Others	1.45 (0.08-25.50)	0.8

EBUS TBNA

Variables	Unadjusted OR (95%CI)	p value	Adjusted OR (95%CI)	p value
SUVs	0.98 (0.87-1.11)	0.75	1.04 (0.91-1.19)	0.59
PET-necrosis	5.52 (1.00-30.50)	0.05	7.89 (1.17-53.2)	0.034
Biopsy site (N1/primary lesion or N2/N3)	1.26 (0.12-13.2)	0.85	0.32 (0.02-4.92)	0.42

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Bronchoscopy for Diagnosis and Approach to Mediastinal Staging

Lucia Viola
FNC – CTIC
Colombia

Fundación Neumológica COLOMBIANA

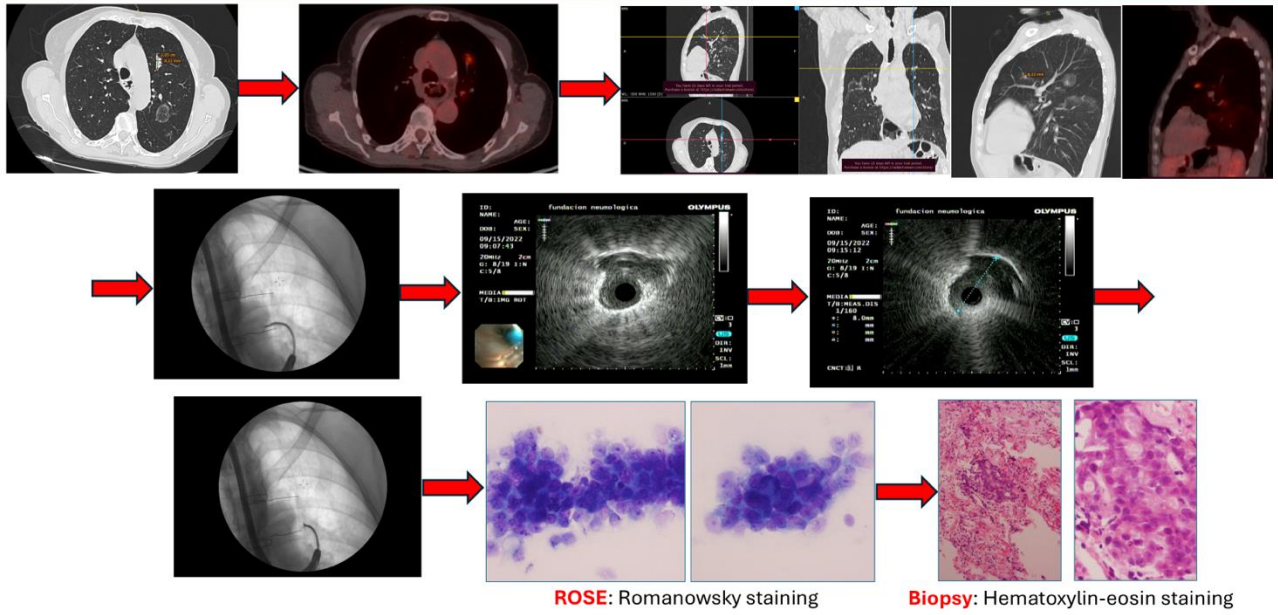
CENTRO DE TRATAMIENTO E INVESTIGACIÓN SOBRE CÁNCER LUIS CARLOS SARMIENTO ANGULO

Summary and Recommendations:

- Bronchoscopic approach allows for diagnosis and staging in a single procedure
- ROSE is essential (we will review)
- Radial and CP-EBUS should be used. They are operator dependent.
- Mediastinoscopy and EBUS have similar diagnostic yield, but there is absolutely still a role for mediastinoscopy
- Tissue is still the issue.

BEST OF WCLC 2024

Education Sessions: ES08.06



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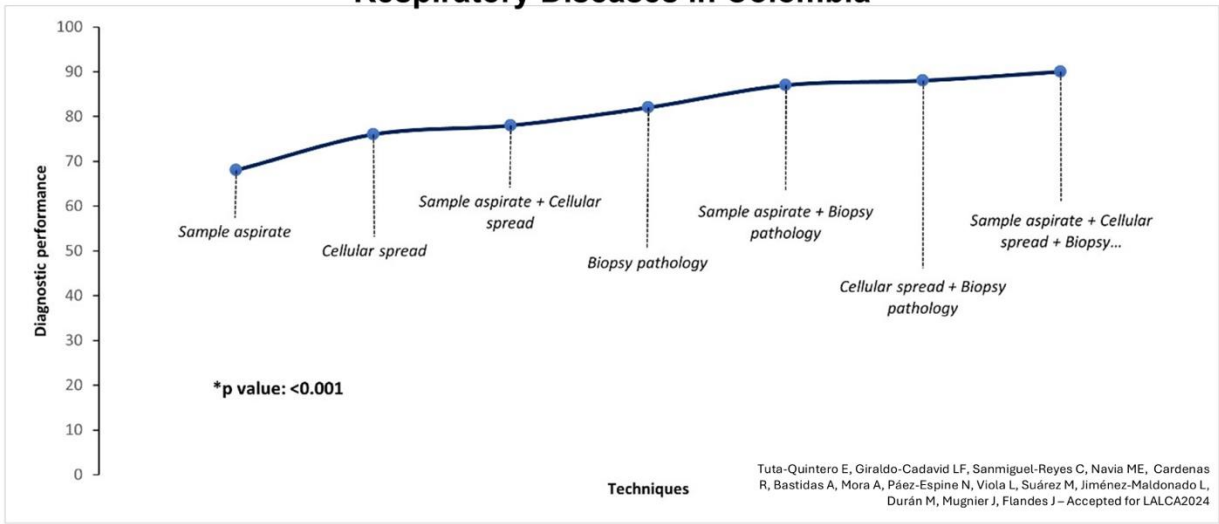
Effect of the addition of multiple sampling tools on the diagnostic accuracy of combined linear/radial endobronchial ultrasonography in a reference center for Respiratory Diseases in Colombia



Tuta-Quintero E, Giraldo-Cadavid LF, Sanmiguel-Reyes C, Navia ME, Cardenas R, Bastidas A, Mora A, Páez-Espine N, Viola L, Suárez M, Jiménez-Maldonado L, Durán M, Mugnier J, Flandes J – Accepted for LALCA2024

- Confirmation that you are in the correct location is key!
- This can be done with ultrasound, fluoroscopy, cone beam CT, and pathologist giving you feedback (Rapid On-site Evaluation; ROSE).
- More biopsies and more tools improves yield.
  - There is a balance. More biopsies and more tools = more risk and more monetary cost.

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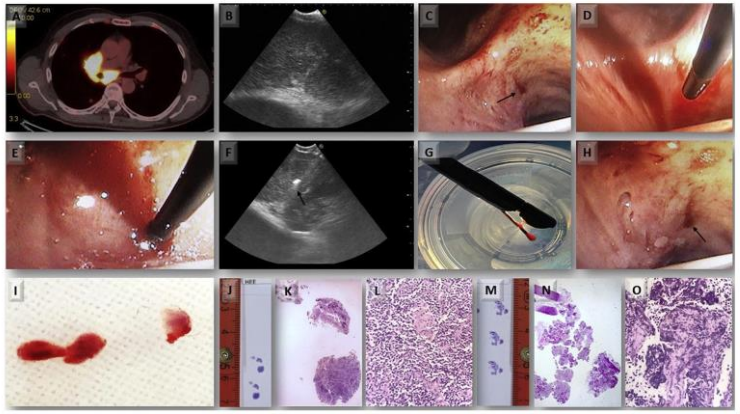
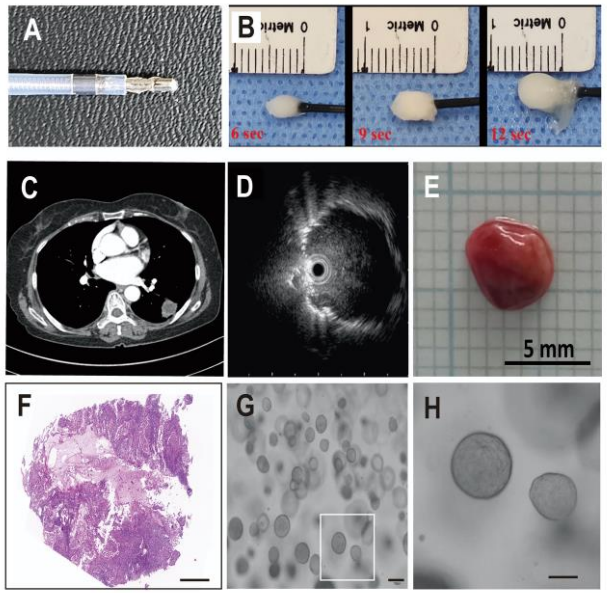
Transbronchial Mediastinal Cryobiopsy





Archivos de Bronconeumología 2022
Cellis **2023**

Experience with cryobiopsy is increasing. This has now been expanded to mediastinal biopsies under CP-EBUS.

Reported yield and safety are good.

This can break equipment and creates a much larger puncture site. Unclear what will occur when more universally employed.

This needs to be studies in a more structured manner.

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Transthoracic versus transbronchial approaches for diagnosis of pulmonary nodules located in the middle lung zone

Tsukasa Ishiwata[1], Alexander Gregor[1], Thomas Waddell[1], Kazuhiro Yasufuku[1], Kasia Czarnecka-Kujawa[1,2]

[1]Division of Thoracic Surgery, [2]Division of Respirology, Toronto General Hospital, University Health Network, Toronto, ON, Canada

Traditionally, it has been the experience that pulmonary nodules in the outer 1/3rd of the lung are best approached using CT guided needle biopsy.

How to approach the middle lung zone is less defined.

It should also be noted that bronchoscopic diagnosis of pulmonary nodules, especially peripheral nodules, is very operator dependent.

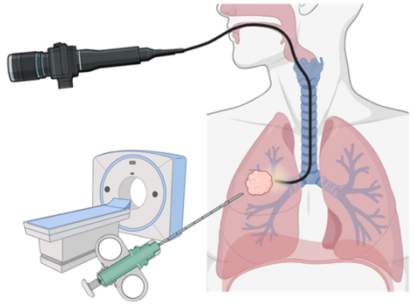
Mini Oral Sessions: MA08.07

Background

- **Transbronchial** and **transthoracic** approaches are selected for diagnosis of pulmonary nodules

	Transbronchial	Transthoracic
Pro	Less complications	High diagnostic yield
Con	Lower diagnostic yield in the peripheral region	High complication rate in the central region
	Favored for **central**	Favored for **peripheral**

Which approach is better for the middle lung zone?



Note the Pros and Cons of transbronchial vs transthoracic approaches.

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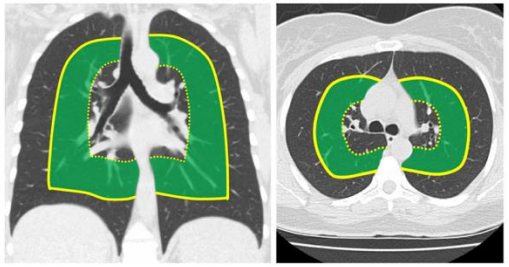
Methods



Concentric lines from the hilum divide hemithorax into central/middle/peripheral third.
Shin, *et al.* Eur Respir J. 2019;53(3):1801508.
Casal, *et al.* Eur Respir J. 2019;53(5):1802220.

Nodule location was determined by three independent clinicians.

- Single-center, retrospective, observational [2015-2016]
- Multidisciplinary triage program determined appropriate approaches
- Pulmonary nodules in the middle-third

Comparison

Transbronchial-approach-first
vs.
Transthoracic-approach-first

Outcomes

- Diagnostic yield
- Complications
- Diagnostic workup duration
- Costs

The middle lung zone.
Study design.

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Complications (throughout entire diagnostic process)	Transbronchial-first N = 108	Transthoracic-first N = 99	P
Pneumothorax, all	3 (2.8%)	28 (28.3%)	**<0.0001**
Pneumothorax requiring chest tube placement	0 (0.0%)	8 (8.1%)	**0.0023**
Bleeding (Moderate or severe)	11 (10.2%)	18 (18.2%)	0.1115
Endobronchial bleeding			
Moderate	6 (5.6%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	
Pulmonary hemorrhage			
Moderate	6 (5.6%)	18 (18.2%)	
Severe	0 (0.0%)	0 (0.0%)	
Hospitalization	0 (0.0%)	8 (8.1%)	**0.0023**
Diagnostic workup duration (days)			
Referral to the first procedure	19.8 ± 9.9	30.0 ± 15.4	**<0.0001**
Referral to diagnosis completion			
Total	30.6 ± 19.1	44.0 ± 29.1	**0.0001**
Nodal staging for malignancy			
With pathological nodal staging	30.9 ± 20.9	45.0 ± 16.7	**0.0024**
With imaging only	28.9 ± 10.5	35.8 ± 14.9	0.0727
Costs (US dollars, adjusted with inflation)			
Total	N = 108 $1,791 [1,274-2,612]	N = 99 $1,658 [954-2,875]	0.6773
Patients with pathological nodal staging	N = 63 $2,122 [1,724-2,875]	N = 28 $3,022 [2,384-3,459]	**0.0002**

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Results

804 Requiring pathological diagnosis for lung nodules (18 months)

Location of nodules

Middle	Central	Peripheral
247	122	435

Excluded cases diagnosed from sites other than lungs

First diagnostic approach

Transbronchial	Transthoracic
108	99

	Transbronchial-first N = 108	Transthoracic-first N = 99	P
Pulmonary nodule size, mm	43.4 ± 19.2	35.3 ± 23.6	**0.0087**
≤20 mm	12 (11.1%)	28 (28.3%)	**0.0025**
Bronchus sign, positive	102 (94.4%)	67 (67.7%)	**<0.0001**
Final diagnosis			
Malignant	98 (90.7%)	84 (84.8%)	0.2078
Benign	9 (8.3%)	13 (13.1%)	0.3872
Undiagnosed	1 (0.9%)	2 (2.0%)	
Nodal staging for malignancy			
Required	83 (84.7%)	68 (81.0%)	0.5033
Not required	15 (15.3%)	16 (19.0%)	
Diagnostic yield of the first approach	84/108 **(77.8%)**	89/99 **(89.9%)**	**0.0238**
Subsequent approach after first approach failure			
CT-guided biopsy	18 (85.7%)	7 (70.0%)	
Bronchoscopy	0 (0.0%)	2 (20.0%)	
Mediastinoscopy	1 (4.8%)	0 (0.0%)	
Direct to surgical resection	0 (0.0%)	1 (10.0%)	
Direct to radiotherapy	1 (4.8%)	0 (0.0%)	
Follow up chest imaging	1 (4.8%)	0 (0.0%)	

- Bronchoscopy vs transthoracic approaches had similar yield.
- EBUS can be done at the same time as the transbronchial approach, hence is more efficient – both cost and time – comparted to the TTNA.
- There were fewer complications in the bronchoscopic approach.
- It should not be understated that this was an experience group of bronchoscopists. This will not likely be reproduced in many community settings.

RESULTS

Figure 2: Participant Flow Diagram

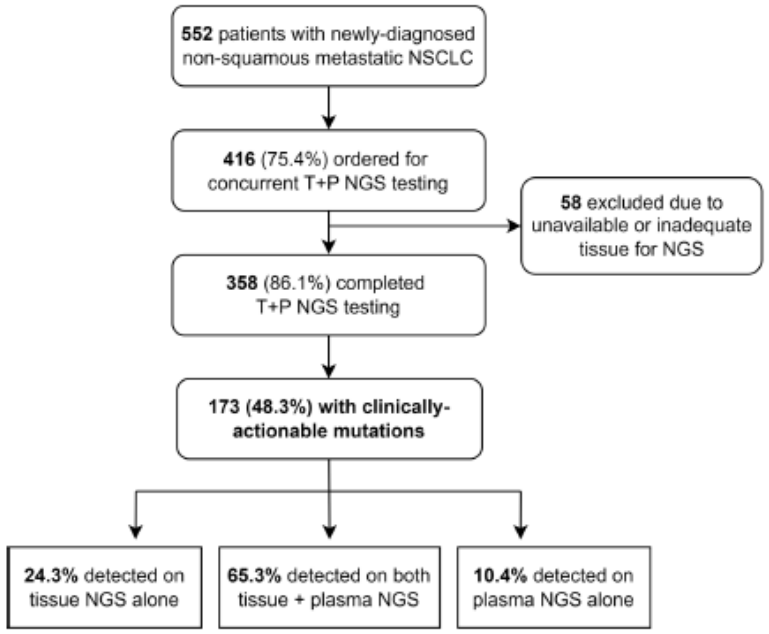
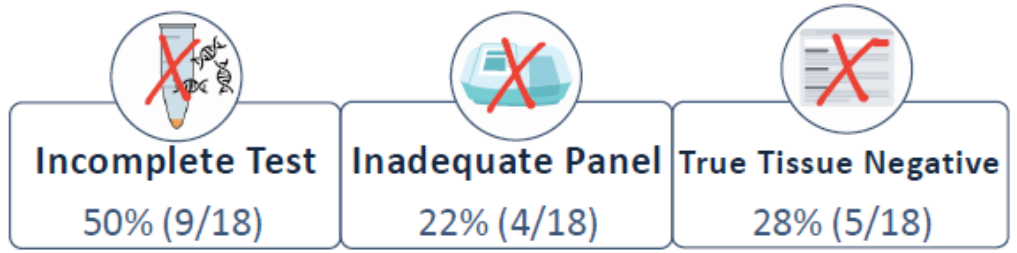


Figure 3: Etiology of Discrepant Results



- 44% (8/18) received 1st line targeted therapy due to an alteration detected only in plasma-based NGS
- Site of biopsy in patients with plasma-based NGS exclusive alterations: 10 pulmonary lesions, 5 thoracic lymph nodes, 2 bone metastases, and 1 liver metastasis

62	F	White	Former	Lung	Insertion	ErbB2	Incomplete Testing	Chemo+IO
63	F	White	Former	Liver	Point	KRAS	Inadequate Panel	Deceased
79	F	White	Former	Bone	Insertion	ErbB2	Inadequate Panel	IO
78	F	White	Never	Lung	Point	BRAF	Inadequate Panel	Targeted
44	M	Asian	Former	Lung	Deletion	EGFR	Inadequate Panel	Targeted

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Acknowledgements:
- Thoracic Center for Excellence at Penn Medicine
- Study participants and their families
- Perelman Center for Advanced Medicine staff

Posters: P3.06D.06

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SingHealth DukeNUS ACADEMIC MEDICAL CENTRE
Lung Centre

Augmented Imaging Techniques for Peripheral Nodules

CARRIE LEONG

INTERVENTIONAL PULMONOLOGY AND PLEURAL SERVICE
SINGAPORE GENERAL HOSPITAL

SINGHEALTH LUNG CENTER

Education Sessions: ES26.03

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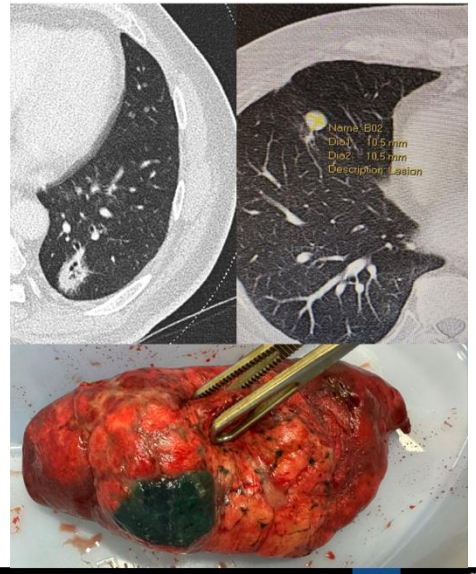
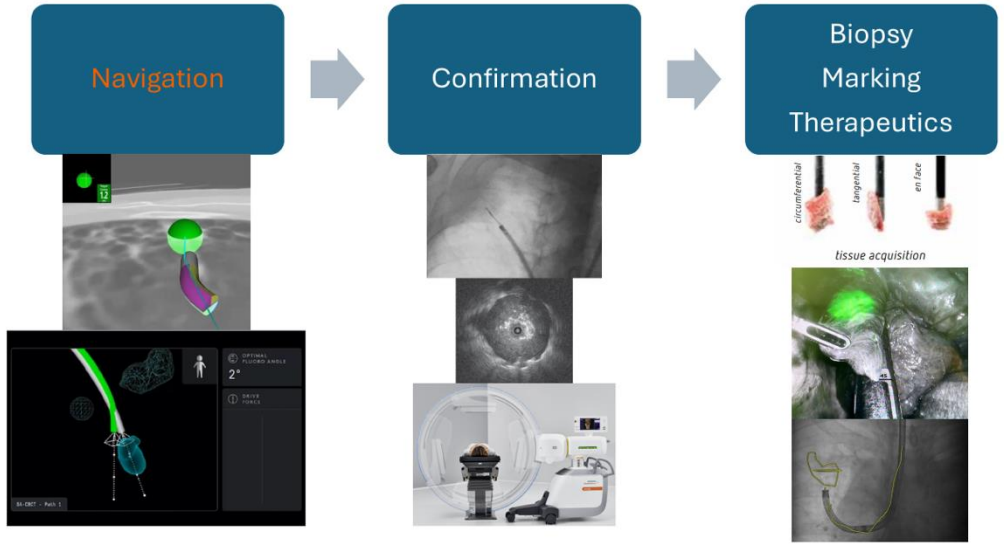
Navigational Bronchoscopy for peripheral nodules

Navigational Bronchoscopy for peripheral nodules: Indications

- Biopsy of lung nodules
- Nodule marking for intraoperative localization during thoracic surgery
- Therapeutics
  - Ablation
  - Chemotherapy injection



igational Bronchoscopy for peripheral nodules



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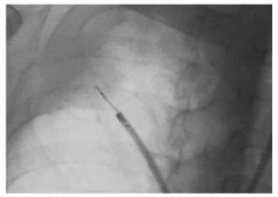
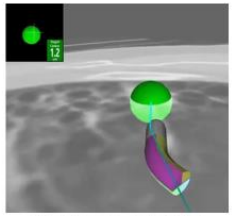
Evolution of navigational bronchoscopy



Transbronchial lung biopsy

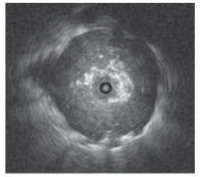


Electromagnetic navigation

Transparenchymal nodule access

Cone beam CT and Augmented imaging

Radial endobronchial ultrasound



Ultrathin bronchoscopes

Robotic navigation

All of these approaches are still used.

As mentioned, bronchoscopy is operator dependent.

Determining which technology to use will depend on operator skill, the health system, procedure availability, and patient ability to tolerate the procedure.

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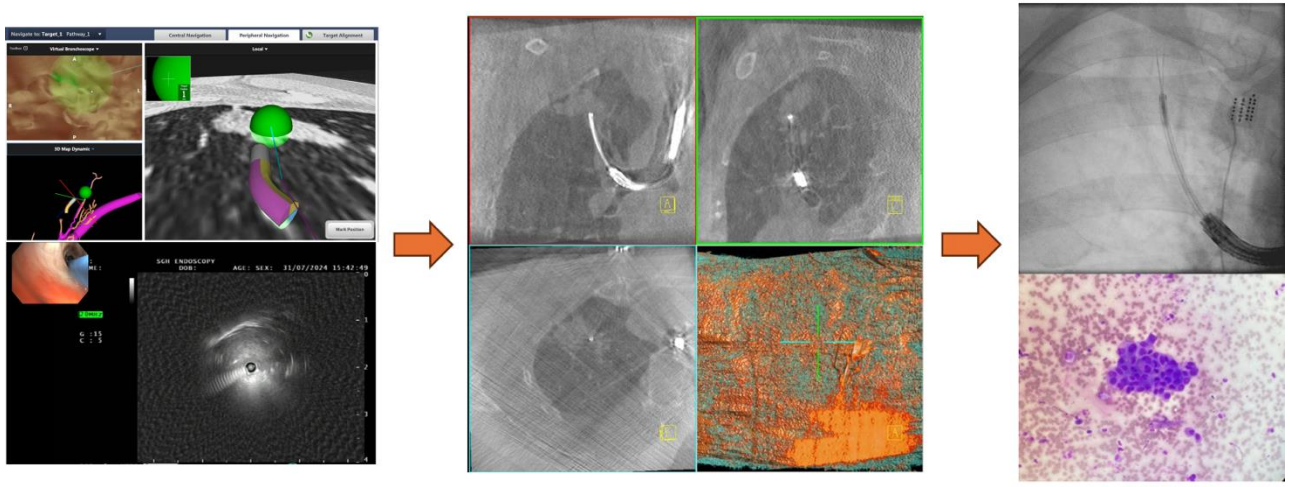
Navigational Bronchoscopy with Mobile Cone Beam CT



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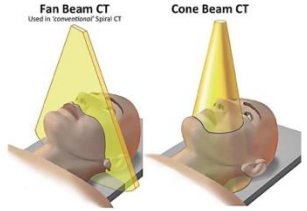
Cone Beam CT (CBCT)

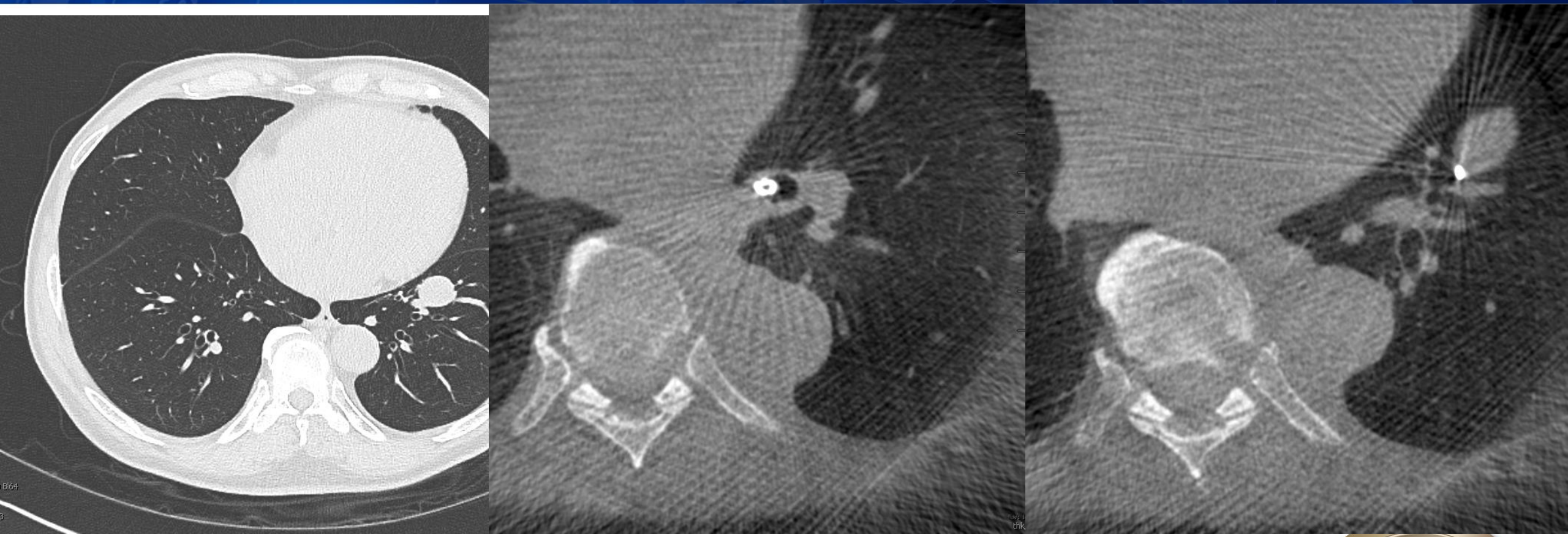
- Cone-shaped X-ray beam that projects onto a flat detector sensing two dimensions
- Single rotation, shorter duration but reduced contrast ratio vs conventional multi-slice CT

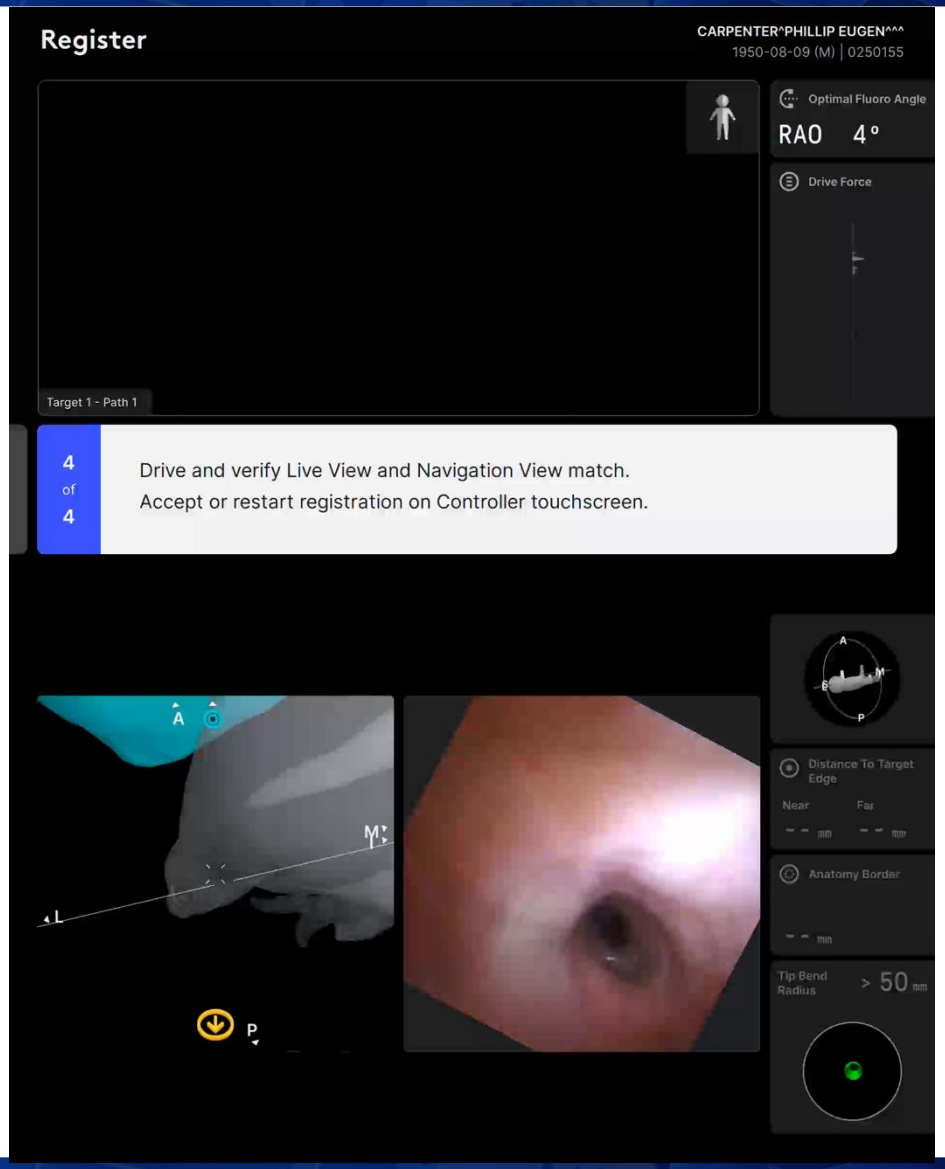


1. Journal of Physics: Conference Series. 884. 012041.
2. Diagnostics (Basel). 2023 Aug 3;13(15):2580.
3. Ann Transl Med. 2023 Aug 30;11(10):361.

CT to body divergence has been a major barrier with navigation bronchoscopy over the past 15 years.

Navigational bronchoscopy + Cone Beam CT are key to making future bronchoscopic therapeutics possible.





Therapeutics

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Radiotherapy improves survival in NSCLC following oligoprogression on immunotherapy: A cohort study

Lauren J Brown, Julie Ahn, Bo Gao, Harriet Gee, Adnan Nagrial, Ines Pires da Silva, Eric Hau

Dr Lauren Julia Brown MBBS MClinTRes FRACP
Westmead and Blacktown Hospitals
Sydney, Australia

THE UNIVERSITY OF SYDNEY | The Westmead Institute FOR MEDICAL RESEARCH | NSW GOVERNMENT Health Western Sydney Local Health District

As reminder, I am a pulmonologist, not a Radiation Oncologist or Medical Oncologist.

I am showing this because it is exciting. It also shows that non-systemic treatments have the potential to positively augment systemic therapy in advanced stage disease.

Oral Sessions: OA05.04

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Radiotherapy improves PFS2 and OS for OligoPD

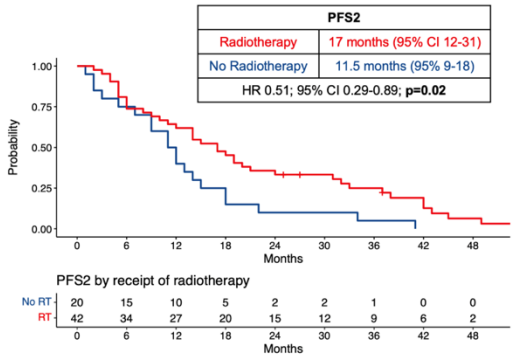

Figure 1: PFS2 in patients with OligoPD by receipt of radiotherapy

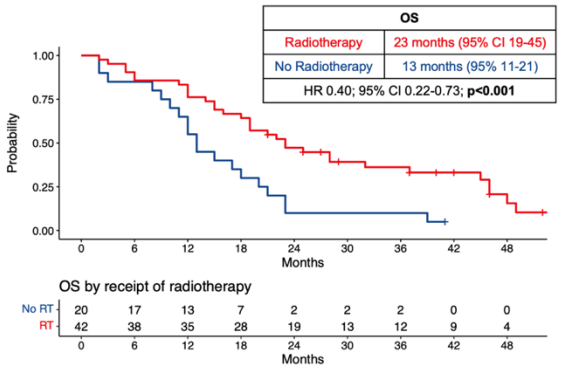

Figure 2: OS in patients with OligoPD by receipt of radiotherapy

Radiotherapy does not improve PFS2 and OS for Systemic PD

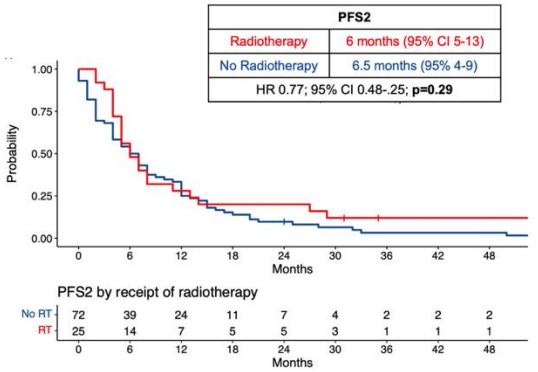

Figure 1: PFS2 in patients with Systemic PD by receipt of radiotherapy

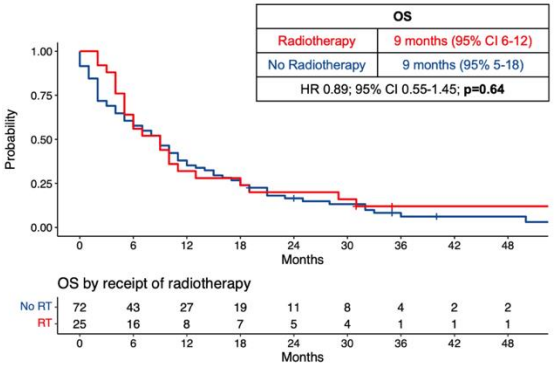

Figure 2: OS in patients with Systemic PD by receipt of radiotherapy

Methods

Retrospective cohort study at two high-volume cancer centres in Australia

Inclusion Criteria:

- Metastatic NSCLC without EGFR/ALK or ROS1 mutation
- Progressed following **first-line** PD-(L)1 inhibitors +/- chemotherapy
- Patients were treated between January 2017 - January 2022

Aims

1. To characterise the frequency and location of oligoprogression (OligoPD) in NSCLC treated with 1L ICIs
2. Determine overall survival (OS) following radiotherapy vs. no radiotherapy in oligoprogressive NSCLC following 1L ICIs

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Ablation to oligo-residual sites plus ICIs improved survival of patients with advanced NSCLC : preliminary results of the phase II BOOSTER trial

Shuo Yang, Bin Chen, Jia Yu, Xiaozhen Liu, Tao Jiang, Fengying Wu, Aiwu Li, Guanghui Gao, Xiaoxia Chen and Shengxiang Ren.

Shanghai Pulmonary Hospital, Shanghai/China

Background:

- Oligo-residual disease is prevalent in immunotherapy.
- Abscopal effect has been observed in thermal ablations.
- Local ablations augment efficacy of IO via multiple mechanisms.
  - Directly reduction tumor burden.
  - Simulating anti-tumor response.
  - Switching immunosuppressive tumor micro-environment.

Oral Sessions: OA05.03

Study Design

Key Eligibility Criteria

Inclusion Criteria:
- Advanced/metastatic NSCLC
- Administrated with first line immunotherapy (with or without chemotherapy)
- Residual lesions suitable for complete ablation

***N=137**

Endpoints

Primary:
- PFS

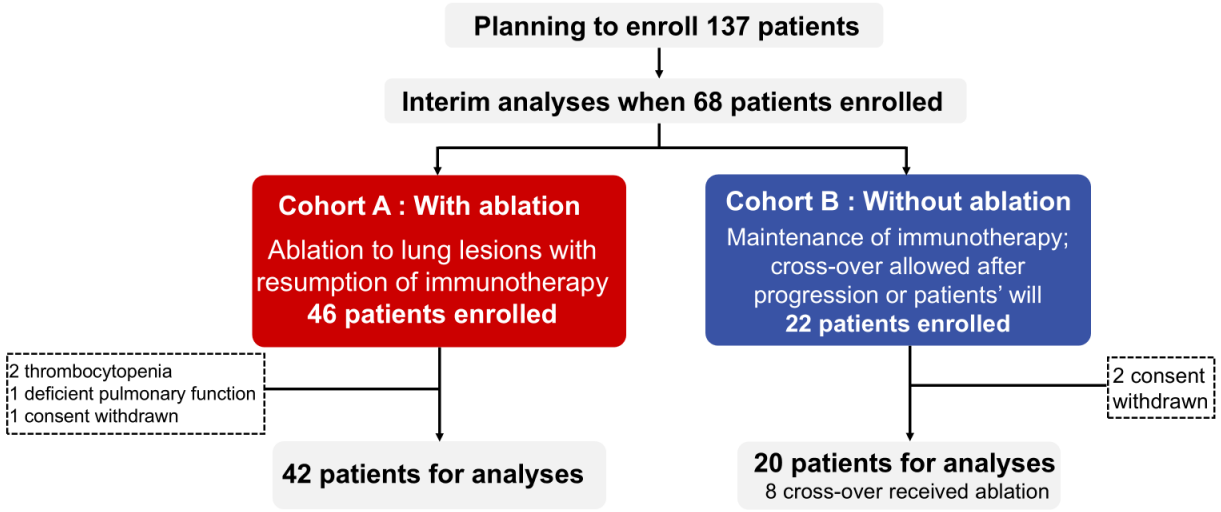
Secondary:
- OS
- LRFS
- Safety of ablation

Interim analyses was planned when half of the patients were enrolled.

***Statistical consideration: A lengthened PFS of 6 months expected in cohort of Arm A with estimated PFS of Arm B as 6 months since randomization. With randomization ratio as 2:1 and expulsion rate as 10%, total sample size of 137 patients (91 for Arm A and 46 for Arm B) might achieve desired statistical power.**

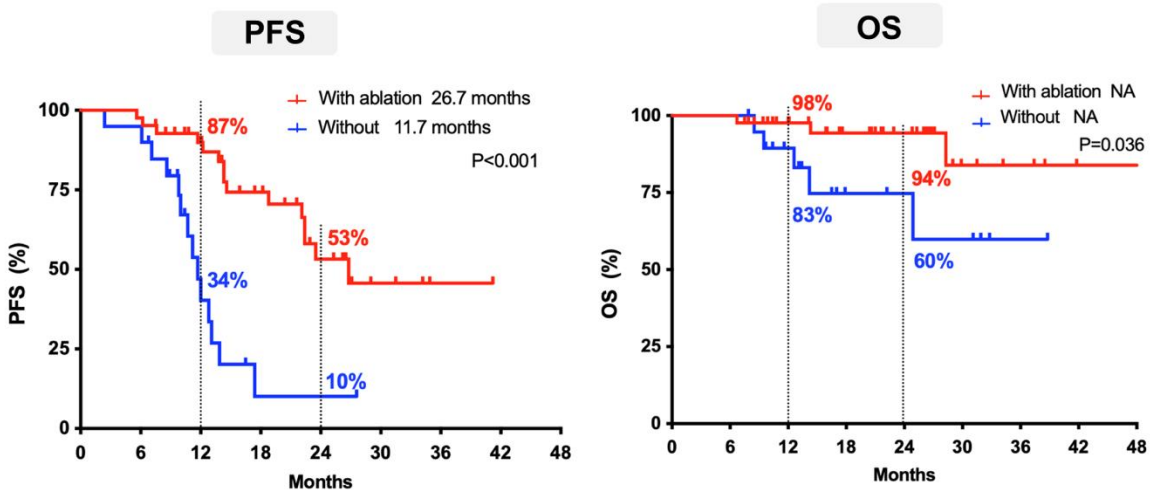
R: randomization; LAT: local ablation treatments ; PFS: progression-free survival ; OS: overall survival; LRFS: local recurrence free survival

Patient Disposition



Oral Sessions: OA05.03

PFS & OS — Since Immunotherapy Initiation



Adverse Events

LRAEs	Event
Pneumothorax (G3)	1
Pneumothorax (G2)	3
Pleural effusion (G2)	3
Pleurodynia (G2)	2
Bronchopulmonary hemorrhage (G2)	1

	Cryoablation (n=13)	Thermal ablation (n=29)
Pneumothorax		
0	7 (53.8)	20 (69.0)
1	6 (46.2)	9 (31.0)
Transthoracic drainage		
No drainage	12 (92.3)	23 (79.3)
Catheter	1 (7.7)	5 (17.2)
Chest tube	0	1 (3.4)
Time to immunotherapy	30.9±20.4	34.8±20.4

Take home message from authors:

- Oligo-residual disease is prevalent in patients administered with IO as first line.
- Ablation to ORD sites was associated with significantly improved PFS and OS over IO alone in highly selected patients.
- Cryoablation plus IO may have better survival benefit than thermal ablation plus IO.
- Further large-scale trials are warranted to confirm findings.

Additional thought and discussion:

Bronchoscopic ablation is no longer only occurring in the clinical research setting.
Needles that can be used via CT guided needle and bronchoscopic navigation have FDA 510(k) approval for the application of Pulsed Electrical Field ablation.

Bronchoscopic ablative therapies have to be done with high accuracy.

- A false negative biopsy will delay care and result in the need for a repeat procedure.
- This is an unfortunate, but acceptable part of diagnostic testing, and usually leads to minimal harm.
- A misguided therapeutic intervention is not acceptable. There is potential therapeutic toxicity, without the benefit of treatment.
    - For this, and multiple other reasons, bronchoscopic ablations are currently adjunctive and may become salvage.
- Bronchoscopic trials are done at at high volume, high skill, and high functioning centers.
- The experience in the community is generally not as successful.

I would seek my intervention at an experienced center.

- This is an exciting and promising adjunct, but it needs to be implemented properly.