

# Pulmonary – From Diagnostics to Therapeutics

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# NAVIGATE 24-Month Results

Electromagnetic navigation bronchoscopy for pulmonary lesions at 37 centers in Europe and the US

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**On behalf of the NAVIGATE Study Investigators**



2020 World Conference  
on Lung Cancer Singapore

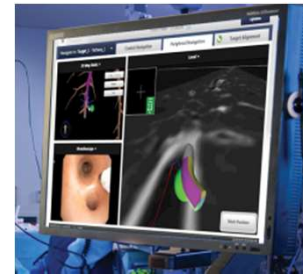
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# NAVIGATE

- Electromagnetic navigation bronchoscopy (ENB) using the superDimension™ navigation system versions 6.3 to 7.1
- Largest prospective ENB study conducted
- 1388 subjects at 37 academic and community sites
- 7 countries: Austria, Denmark, France, Italy, Spain, United Kingdom, United States.
- Pragmatic, real-world design (no directives on user methodology)
- 24-month final analysis

## Lung Lesion Biopsy

95.7% (1329/1388)



## Dye Marking

1.7% (23/1388)



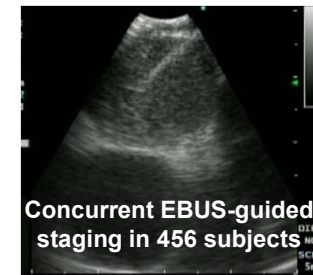
## Fiducial Placement

19.6% (272/1388)



## Lymph Node Biopsy

2.6% (36/1388)



# Regional Practice Pattern Variations

	Global 1388 subjects overall 1529 lesions in 1329 subjects undergoing ENB for biopsy	European Union* 175 subjects overall 187 lesions in 174 subjects undergoing ENB for biopsy	United States 1213 subjects overall 1342 lesions in 1155 subjects undergoing ENB for biopsy
Physician-estimated pretest probability of malignancy †			
Bronchus sign present on CT †	50.8 (777/1529)	<b>66.8</b> (125/187)	<b>48.6</b> (652/1342)
Lesions <20 mm †	49.7 (759/1528)	<b>53.5</b> (100/187)	<b>49.1</b> (659/1341)
General anesthesia	78.2 (1086/1388)	<b>56.6</b> (99/175)	<b>81.4</b> (987/1213)
Radial EBUS used	50.6 (703/1388)	<b>4.0</b> (7/175)	<b>57.4</b> (696/1213)
Fluoroscopy used †	85.0 (1299/1529)	<b>41.7</b> (78/187)	<b>91.0</b> (1221/1342)
Rapid on-site evaluation (ROSE) †	61.7 (777/1260)	<b>17.3</b> (29/168)	<b>68.5</b> (748/1092)
Prior ENB experience ≥5 cases per month before NAVIGATE	83.1 (1154/1388)	<b>21.7</b> (38/175)	<b>92.0</b> (1116/1213)
Total Procedure Time (min)	50.0 (34.0-69.0)	<b>40.0</b> (31.0-50.0)	<b>52.0</b> (35.0-71.0)

\* At the time of study enrollment (Austria, Denmark, France, Italy, Spain, United Kingdom)

† Lesion-specific data available in 1329 global subjects (1529 lesions) with attempted lung lesion biopsy.

**Not powered for statistical comparison testing**



# Procedure-Related Adverse Events

	Global (1388 Subjects)	European Union (175 Subjects)	United States (1213 Subjects)
Pneumothorax	4.7%	7.4%	4.3%
CTCAE Grade $\geq 2$ (Requiring Intervention or Hospitalization)*	3.2%	5.1%	2.9%
Bronchopulmonary Hemorrhage	2.7%	4.0%	2.5%
CTCAE Grade $\geq 2$ (Requiring Intervention or Hospitalization)	1.7%	2.3%	1.6%
Respiratory Failure	0.6%	0.0%	0.7%

- Despite regional differences in user experience, procedural methods, and patient selection, ENB continues to demonstrate a low complication risk.

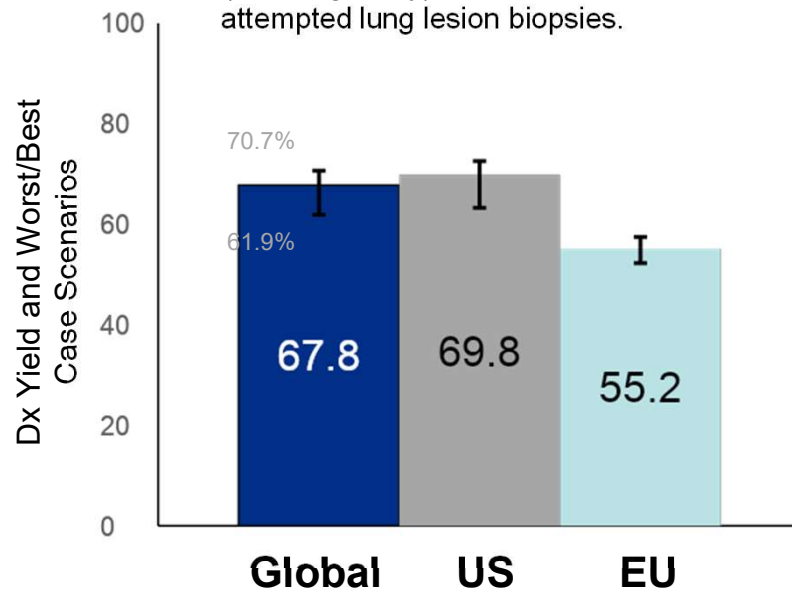
\* Grade  $\geq 2$  pneumothorax could also include subjects kept overnight in the hospital for observation only, without requiring a chest tube.



# Diagnostic Yield

**67.8% (822/1212)**

True positives (for malignancy) plus true negatives (for malignancy), based on follow-up, out of all attempted lung lesion biopsies.



## Multivariate Analysis of Predictors of Higher Diagnostic Yield

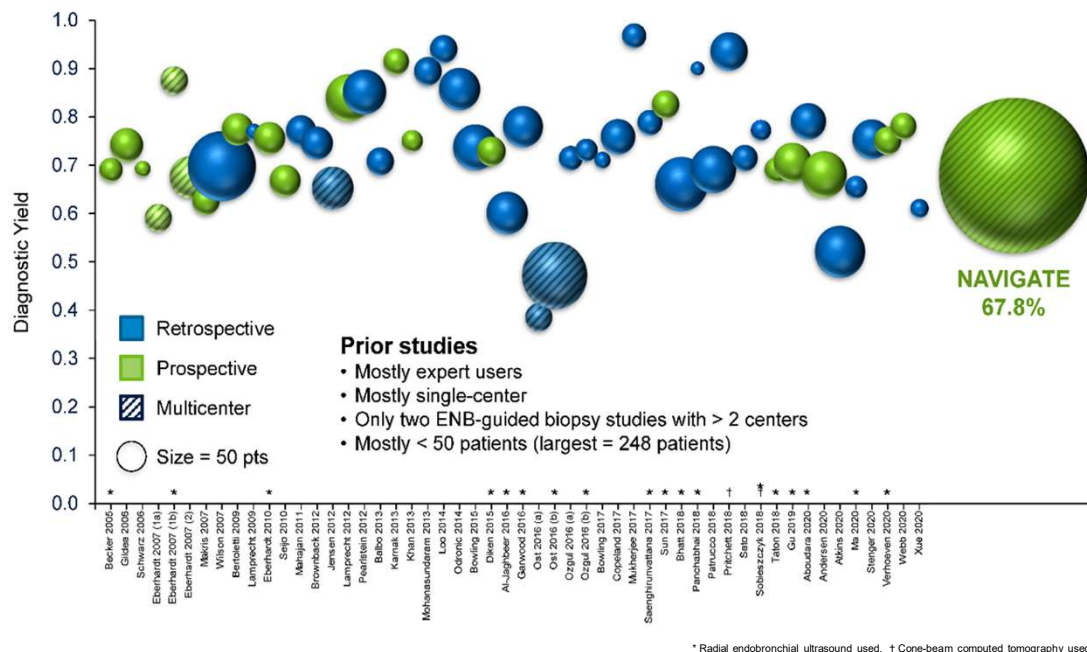
- ✓ Prior ENB Experience  $\geq 5$  cases/month
- ✓ Rapid On-Site Evaluation Use
- ✓ Concurrent Lymph Node Biopsy
- ✓ Biopsy of Multiple Lesions during ENB
- ✓ Average Lesion Size  $\geq 20$  mm
- ✓ Total Procedure Time  $\leq 60$  min
- ✓ Bronchus Sign Presence
- ✓ No Personal History of Cancer
- Upper Lobe Location (significant in univariate)
- Fluoroscopy Use (significant in univariate)
- Radial EBUS Use
- Cone-Beam CT Use
- Physician-Estimated Probability of Malignancy



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# Take-Home Message



- Largest prospective ENB study to date
- Only multinational analysis, 2-year follow-up
- NAVIGATE elucidates ENB usage patterns, safety, and diagnostic yield across Europe and the United States
- Diagnostic yield is moderate (67.8%) with the ENB system versions used in this study
- Yield is impacted by user experience, lesion characteristics, and procedural factors
- ENB has low complication rates even in a heterogeneous population and remains a valuable tool for peripheral nodule evaluation
- Newer technologies with advanced visualization and real-time location correction may improve both the safety and effectiveness of ENB

**ENB Sensitivity for Malignancy**  
 Meta-Analysis of 3342 Patients in 40 Studies = 77%  
 (Folch et al. Chest. 2020;158:1753-69)







# Factors Affect the Diagnostic Yield of Robot-Assisted Bronchoscopy for Pulmonary Lesions

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**Zucker School of Medicine at Hofstra/Northwell**  
**NY, USA**



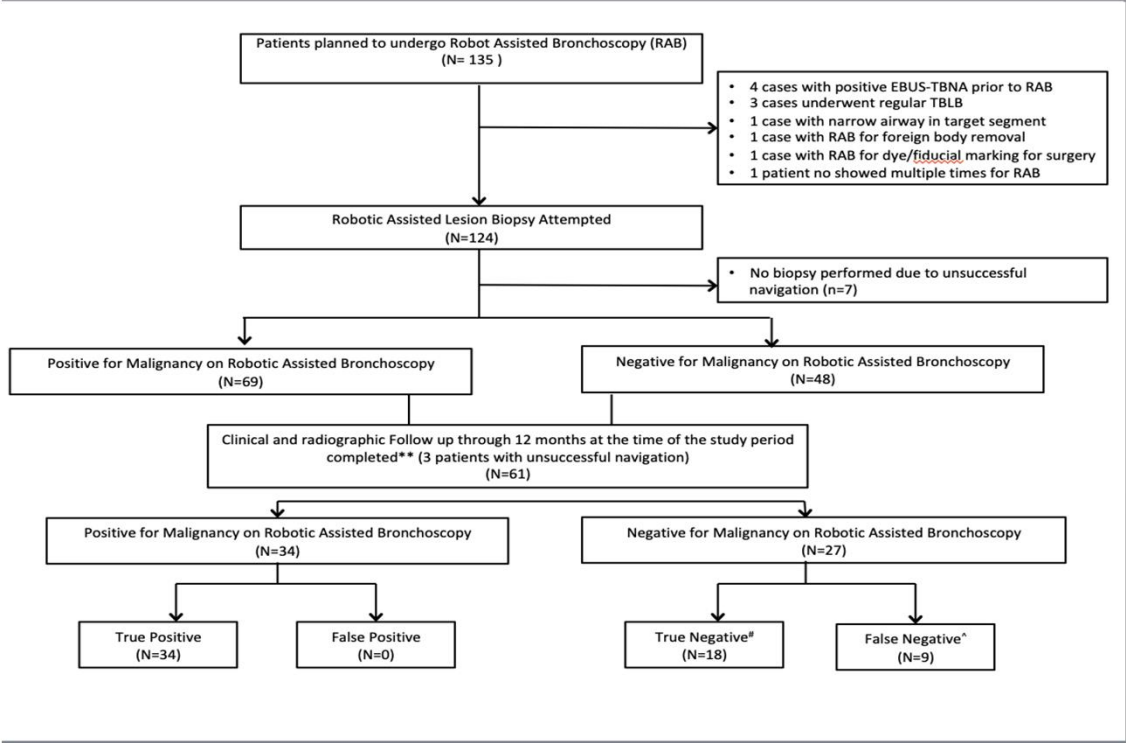


# Background & Methods

- Robotic Assisted Bronchoscopy (RAB) has the potential to overcome several limitations of contemporary guided-bronchoscopic technologies for the diagnosis of lung lesions.
- We retrospectively reviewed data on consecutive cases at the University of Chicago (UC) in whom RAB (Auris Monarch Endoscopy Platform) was used to sample lung lesions between June 15th, 2018 until December 15th, 2019.
- Diagnostic yield for all procedures as well as twelve month yield, sensitivity, specificity, negative and positive predictive values was calculated.
- Multivariate logistic regression was performed to assess for various factors.
- Procedure related complications were analyzed.

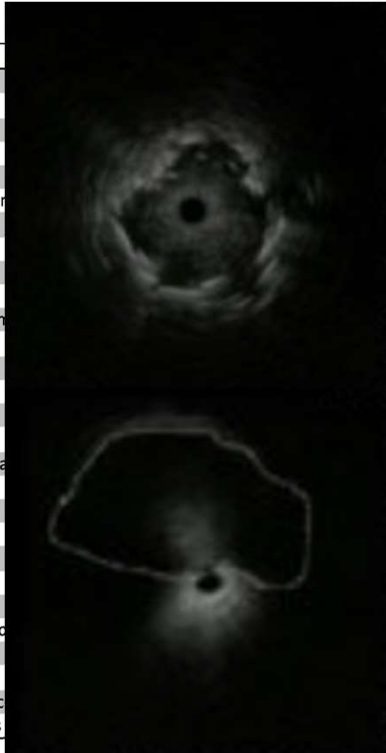


# Results

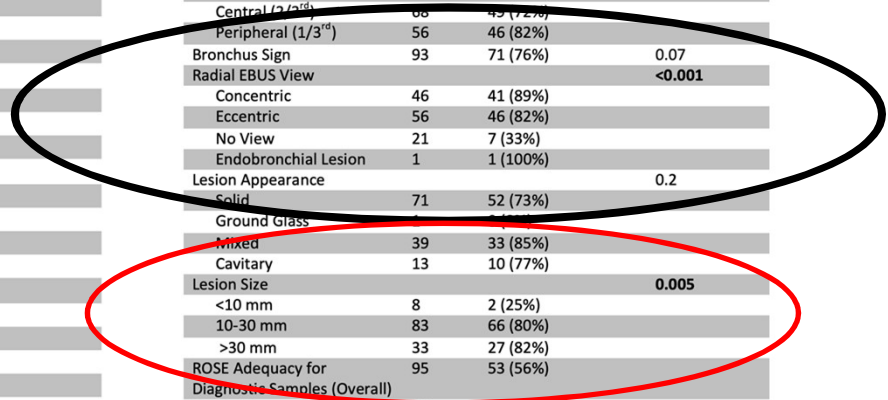


# Results

<b>Diagnostic Findings</b>
<b>N</b>
<b>Malignant Findings</b>
Lung cancer
Adenocarcinoma
Squamous Cell Cancer
Lung NOS/Poorly Differentiated
Small Cell Cancer
Neuroendocrine Tumor
Melanoma
Lymphoma
Appendiceal Adenocarcinoma
Thyroid Cancer
Plasma Cell Neoplasm
Atypical Cells *
Hamartoma
<b>Benign Findings</b>
Non-necrotizing Granuloma
Fungal Infection
Organizing Pneumonia
Inflammation <sup>#</sup>
<b>Non-diagnostic Findings</b>
<b>N</b>
Unable to Navigate/Unable to Advance
Non-diagnostic Inflammation <sup>#</sup>
Alveolated Lung with Anthracosis
Benign Others, Reactive Cells



Variables	Total	RAB/Diagnostic (Diagnostic Yield)	P value
Patients undergoing RAB	124	95 (77%)	
Lesion Location (Lobe)			0.9
Right Upper Lobe	44	35 (80%)	
Right Middle Lobe	10	7 (70%)	
Right Lower Lobe	22	17 (77%)	
Left Upper Division	24	19 (79%)	
Lingula	8	5 (62%)	
Left Lower Lobe	16	12 (75%)	
Lesion Location			0.2
Central (2/3 <sup>rd</sup> )	68	45 (72%)	
Peripheral (1/3 <sup>rd</sup> )	56	46 (82%)	
Bronchus Sign	93	71 (76%)	0.07
Radial EBUS View			<0.001
Concentric	46	41 (89%)	
Eccentric	56	46 (82%)	
No View	21	7 (33%)	
Endobronchial Lesion	1	1 (100%)	
Lesion Appearance			0.2
Solid	71	52 (73%)	
Ground Glass	24	21 (88%)	
Mixed	39	33 (85%)	
Cavitary	13	10 (77%)	
Lesion Size			0.005
<10 mm	8	2 (25%)	
10-30 mm	83	66 (80%)	
>30 mm	33	27 (82%)	
ROSE Adequacy for Diagnostic Samples (Overall)	95	53 (56%)	
ROSE Adequacy for Diagnostic Samples (Malignancy)	69	48 (70%)	



# Results

## Outcomes at 12 Months (N=64)

<b>12-month diagnostic yield for malignancy* ([TP + TN] / All patients undergoing RAB*)</b>	81.3% (52/64)
<b>Sensitivity for Malignancy (TP/[TP + FN])</b>	79.1% (34/43)
<b>Specificity for Malignancy (TN/[FP + TN])</b>	100% (18/18)
<b>Positive Predictive Value (TP / [TP + FP])</b>	100% (34/34)
<b>Negative Predictive Value (TN / [FN + TN])</b>	66.7% (18/27)



# Take Home Messages

- Our study suggests that RAB has a diagnostic yield of at least 77% for diagnosing pulmonary nodules, which is higher than previous diagnostic yield from ENB guided bronchoscopy platforms.
- Similar to prior analyses, a bronchus sign and lesion size predict a higher diagnostic yield using flexible bronchoscopy.
- However, contrary to prior studies, in this study the diagnostic yield was >80% even in patients with an eccentric r-EBUS view, which may explain the higher diagnostic yield using the RAB platform.
- The 12 month diagnostic yield for malignancy was 81.3%, with high sensitivity.
- Complication rates are similar to prior reports on guided bronchoscopy.



# Initial Experience of Hybrid Operating Room Cone-Beam CT guided Bronchoscopic Microwave Ablation of Peripheral Small Lung Lesions



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Siu, E Yuan, S Liu, J Choi, CM Chu, Calvin SH Ng

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**Percutaneous Ablation**

More readily available, widely researched

Interventional radiologists

**Bronchoscopic Ablation**

Less pleural-based complications

Surgeons / Interventional pulmonologists

Radiofrequency Ablation

**Microwave Ablation**

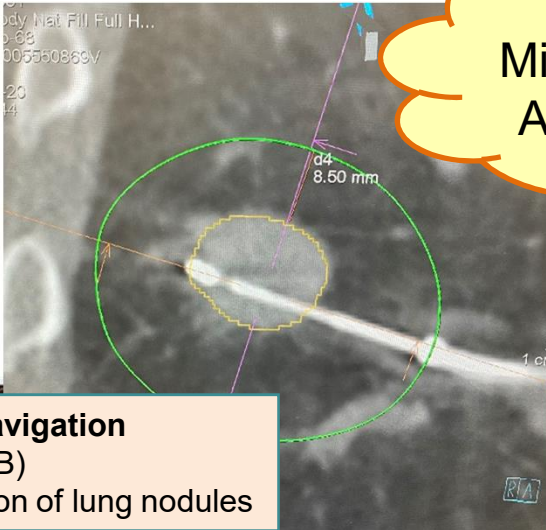
Larger and faster ablation zones

Less affected by impedance

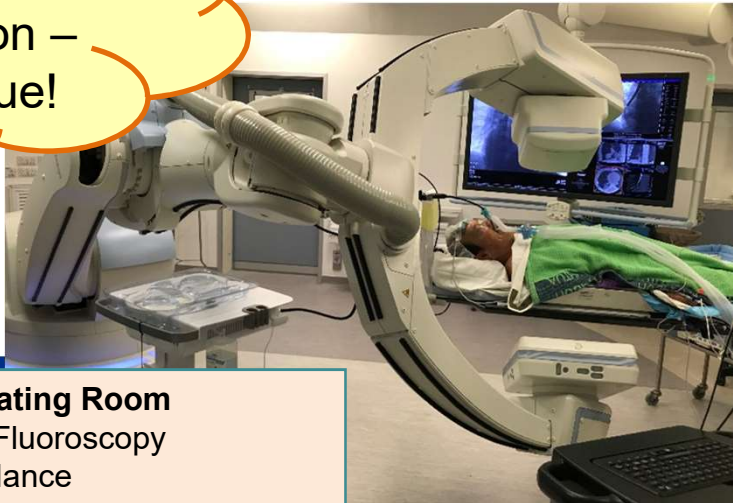
Less heat-sink

More researched

**Bronchoscopic Microwave Ablation – A Novel Technique!**



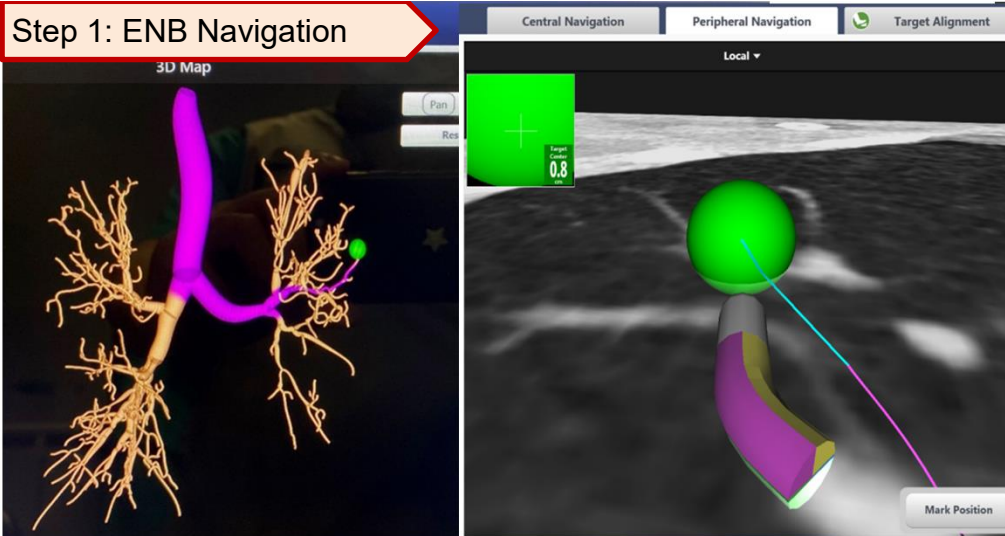
**Electromagnetic Navigation Bronchoscopy (ENB)**  
→ accurate localization of lung nodules



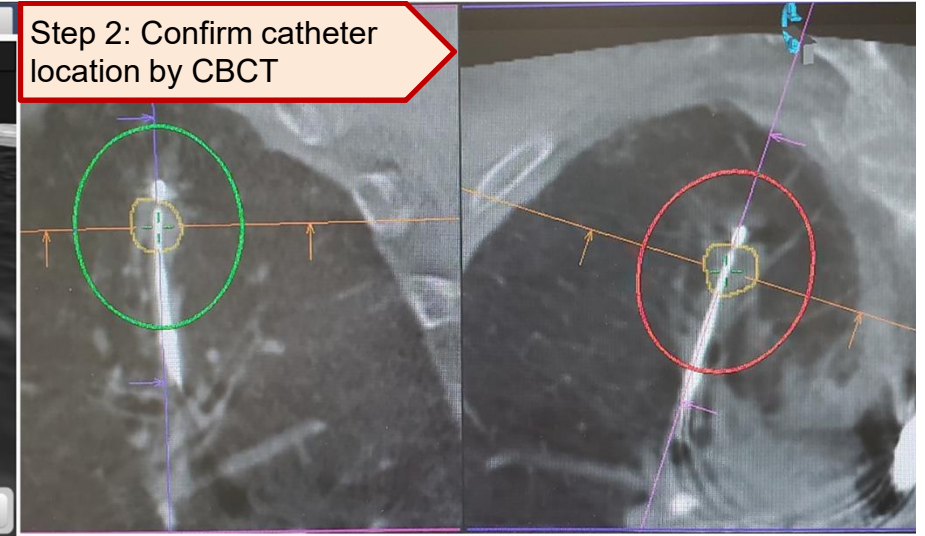
**Hybrid Operating Room**  
 Real-time Fluoroscopy  
 CBCT guidance



Step 1: ENB Navigation



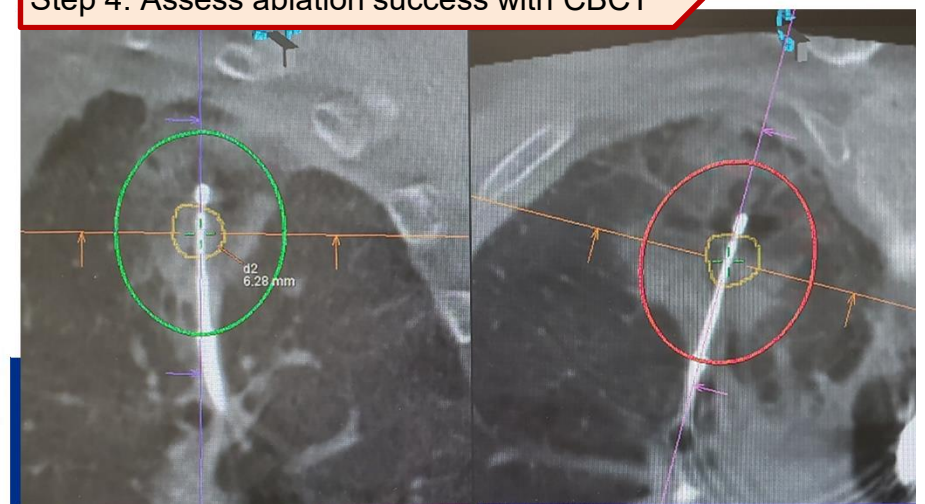
Step 2: Confirm catheter location by CBCT



Step 3: Microwave Ablation



Step 4: Assess ablation success with CBCT

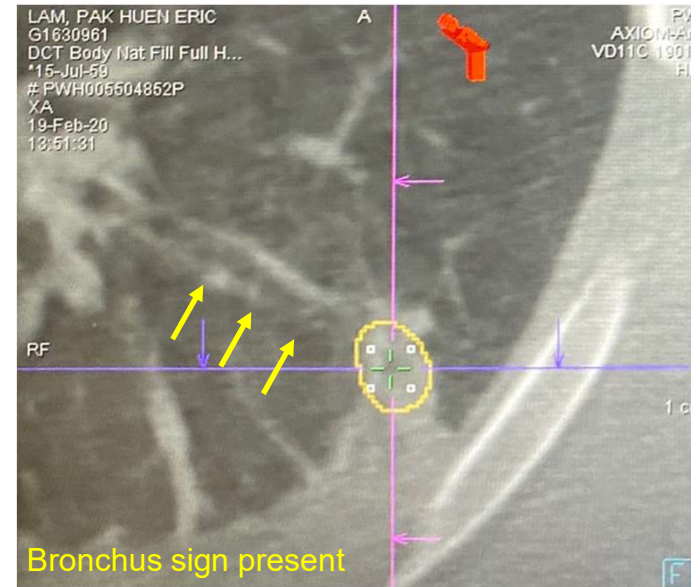


# Methods & Results

- **Study Design:** Retrospective single-center analysis
- **Selection Criteria**
  - Patient factors: unfit for / refuse surgical resection
  - Lesion type: T1N0M0 primary lung cancer / isolated lung oligometastases / radiologically suspicious
  - Nodule factors: bronchus sign present (preferably), <3cm tumour size

## Baseline characteristics

- 41 nodules
- Age: mean 68 years (range 40-86)
- 28 (68%) in the peripheral 1/3 of lung
- Lesion maximal diameter: mean 15.3mm (range 7-29)

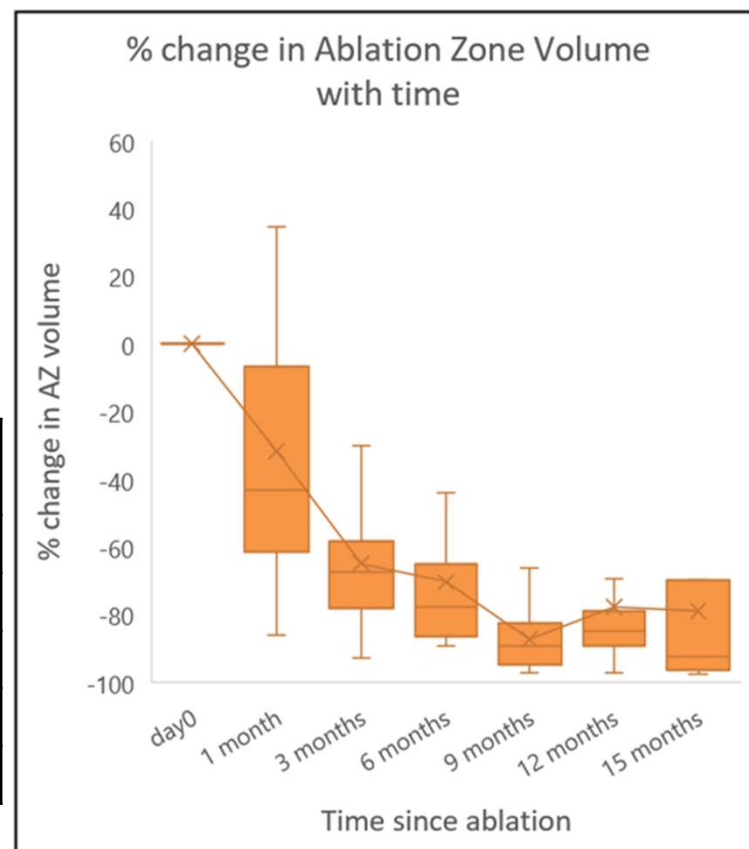


# Results

- **Technical success 100%** (8 required double ablations)
- Minimal predicted margin: mean 6.1mm
- Minimal actual margin: mean 5.4mm
- **Speedy discharge:** 76% discharged on day 1, 95% discharged within 3 days

Complications	
Mild pain	7 (17%)
Pneumothorax	4 (9.8%)
Fever/Post-ablation reaction	2 (4.9%)
Self-limiting hemoptysis	1 (2.4%)
Bronchopleural fistula	1 (2.4%)
N.B. CTCAE grade 3 events: 4 cases	

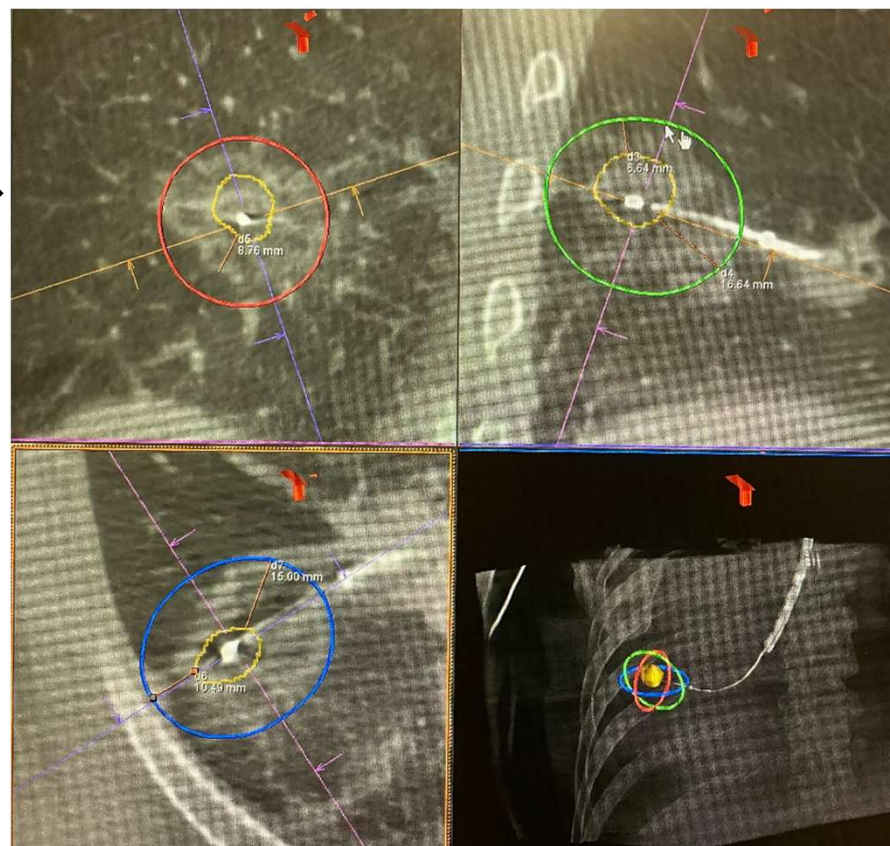
1-Year Response Rate (n=16)	
mRECIST criteria	
Complete Response	2
Partial Response	13
Stable Disease	6
Progressive Disease	0





# Take Home Message

- ✓ Bronchoscopic Approach + Microwave Ablation → combines the best of two worlds
- ✓ ENB allows accurate navigation and localization within target lung nodules, especially in hybrid operating room
- ✓ 100% technical success rate
- ✓ Low complication rate
- ✓ A promising novel technique for local treatment of early primary lung cancers / lung metastases



# Take Home Messages

- The largest study evaluating the most widely used Bronchoscopic Navigation System had a diagnostic yield of only 67.8%. (similar to previous studies)
- Robotic Navigation Bronchoscopy may increase yield to > 80%
- Combining the best Bronchoscopy platforms with radial EBUS and Cone Beam CT should improve diagnostic yield and may allow for reliable bronchoscopic tumor ablation, not now, but perhaps in the future