DM Seminar
Bronchoscopic Techniques For Evaluation Of Pulmonary Nodules

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Topics To Be Discussed

- Lung nodule management
- Role of non surgical biopsy- When to opt for?
- Diagnostic bronchoscopy techniques
- Current evidence
- Pros and Cons of available techniques

Setting In which pulmonary nodules are found

- Incidental
- Lung cancer screening
- During Evaluation of respiratory symptoms

Wiener D. C et al ., CHEST 2020

Pulmonary Nodule On Imaging
The next question?

Should we/when to intervene?

Incidental Pulmonary Nodule

- Fleischer society guidelines
- BTS guidelines
- ACCP guidelines

Nodules detected during lung cancer screening

LUNG RADS scoring

During W/U of respiratory symptoms

Clinical feature/ Management change

Wiener D. C et al ., CHEST 2020

Modalities For Tissue Diagnosis

Surgical resection/Biopsy

Non Surgical Biopsy

- CT-guided Trans Thoracic Needle Biopsy(through the chest wall)
- Bronchoscopic techniques(through the airway)

Katsis et al ., Journal of Thoracic Disease 2020

Non Surgical Biopsy

- Intermediate/High risk of malignancy (patient not fit for surgical biopsy)
- Benign aetiology suspected which would require treatment e.g., PTB, Fungal pneumonia
- Irrespective of risk of malignancy/aetiology if diagnosis desired by patient

Which Procedure To opt For – Trans-thoracic/Bronchoscopic

Location of lesion

Central

Peripheral

Relation of nodule to airway

Size of lesion

Availability and Expertise for the procedure

Patient factors

Which Procedure To opt For – Trans-thoracic/Bronchoscopic

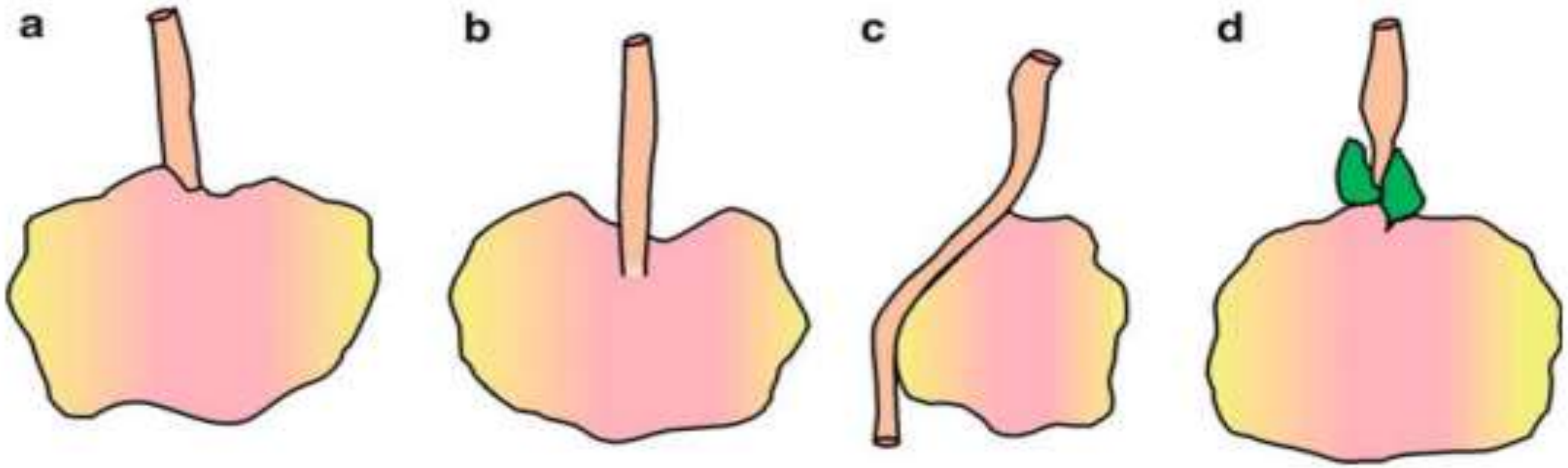

Fig. 2.2 Tumor–bronchus relationship: (**a**) Type I: bronchus is patent up to the tumor, (**b**) Type II: the bronchus is contained within the tumor mass, (**c**) Type III: the bronchus is compressed, narrowed and displaced by the tumor mass, but the bronchial mucosa is intact (**d**) Type IV in which the proximal bronchus is narrowed by the submucosal and peribronchial spread of the tumor, fibrosis, or enlarged lymph nodes

Bronchoscopic Techniques For Pulmonary Nodule Evaluation

Central lesions	Peripheral lesions
FOB Endobronchial biopsy	Radial EBUS
	Virtual Navigation Bronchoscopy
	Electro Magnetic Navigation
	Bronchoscopic Trans Parenchymal Nodule access
	Cone Beam Computed Tomography
	Robotic Bronchoscopy
	Fluoroscopy Based Navigation
	Ultra Thin Bronchoscope

Kurman et al., Semin Respir Crit Care Med 2018;

Central Pulmonary Nodule/Lesions

3.2.2.1. In patients suspected of having lung cancer, who have a central lesion, bronchoscopy is recommended to confirm the diagnosis. However, it is recommended that further testing be performed if bronchoscopy results are non-diagnostic and suspicion of lung cancer remains (Grade 1B).

Rivera et al ., CHEST 2013

Central Pulmonary Nodule (Endobronchial lesions)

- 35 Studies with central/endobronchial lesion included
- Central lesion identified as one presenting as exophytic growth / submucosal spread or causing extrinsic compression
- 4,507 patients were included in the analysis
- Direct forceps biopsy, brushings, washings and EBNA were the sampling techniques performed

Rivera et al ., CHEST 2013

Central(Endobronchial lesions)

- Analysis of data showed overall sensitivity of 88%
- Among the sampling techniques endobronchial biopsy had highest sensitivity(at least 3 samples)
- EBNA used in cases with submucosal tumour spread or peri bronchial tumour increased overall sensitivity

			Sensitivity (%)				
First Author	Year	No. of Patients[a]	All Methods	Endobr Biopsy	Brush	Wash	EBNA/ TBNA
Buccheri [96]	1991	708	-	80	35	31	-
Jones[127]	2001	514	89	72	72	48	-
Oswald[77]	1971	434	-	61	-	-	-
Lam[102]	1983	329	94	82	74	76	-
Pilotti[73]	1982	286	-	-	78	-	-
Gellert[104]	1982	218	-	78	-	-	-
Zavala[109]	1975	193	94	97	93	-	-
Govert [94]	1996	177	85	81	48	43	-
Mak[98]	1990	125	87	76	52	50	-
Saita[100]	1989	105	-	48	30	-	-
Popp[97]	1991	99	-	93	79	-	-
Karahalli[126]	2001	98	90	83	68	32	69
Chaudhary[74]	1978	95	-	76	53	78	-
Schenk[72]	1987	91	71	56	40	29	45
Utz[5]	1993	88	-	-	-	-	36
Win[124]	2003	78	85	61	27	45	42
Stringfield[107]	1977	78	-	85	-	-	-
Wagner[71]	1989	72	67	58	39	35	36
McLean[92]	1998	71	-	82	-	-	-
Kvale[108]	1976	71	-	71	77	63	-
Bilaceroglu[93]	1997	68	96	-	66	-	90
Govert[91]	1999	57	95	74	-	63	82
Sing[70]	1997	53	-	-	64	-	-
Gay[99]	1989	53	-	-	-	-	23
Chopra[75]	1977	51	-	66	72	51	-
Zisholtz[103]	1983	51	73	67	65	44	-
Gaber[125]	2002	39	90	79	74	54	-
Castella[95]	1995	39	-	-	-	-	87
Cox[101]	1984	33	94	84	83	76	-
Dasgupta[90]	1999	32	97	-	-	-	78
Hsu[123]	2004	24	-	-	-	-	71
Bungay[89]	2000	24	92	-	-	-	-
Baaklini[88]	2000	22	82	-	-	-	-
McDougall[105]	1981	16	-	50	23	-	-
Radke[106]	1979	15	87	-	-	-	-
Summary		**4,507**	**88**	**74**	**61**	**47**	**56**

Rivera et al ., CHEST 2013

Peripheral Pulmonary Nodule evaluation

CT guided Trans Thoracic needle biopsy

Bronchoscopic techniques

Trans Thoracic Needle Aspiration/Biopsy –Role in peripheral pulmonary nodule

Study	**Population**	**Outcome**	**Results**
Systematic Review	48 articles 10,383 lesions	Diagnostic accuracy Complications	92.1% Pneumothorax 20.5% (ICTD requiring 7.3%) Haemorrhage 2.8%

Size/Nature of lesion	**<2cm**	**<1cm**	**GGO**
Diagnostic accuracy	92.8%	92.6%	92.5%

DiBardino DM et al., J Thorac Dis 2015

Disadvantage Of TTNB

- Complications
- Inability to perform simultaneous mediastinal staging
- Risk factors associated with increased incidence of pneumothorax include – Old age > 60 yr, presence of emphysema, deeper location, need to traverse fissure, smaller lesion size, number of times pleura was punctured

DiBardino DM et al., J Thorac Dis 2015

Peripheral Pulmonary Nodule – Bronchoscopic techniques

Central lesions	Peripheral lesions
FOB Endobronchial biopsy	Radial EBUS
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	Fluoroscopy Based Navigation
	Ultra Thin Bronchoscope

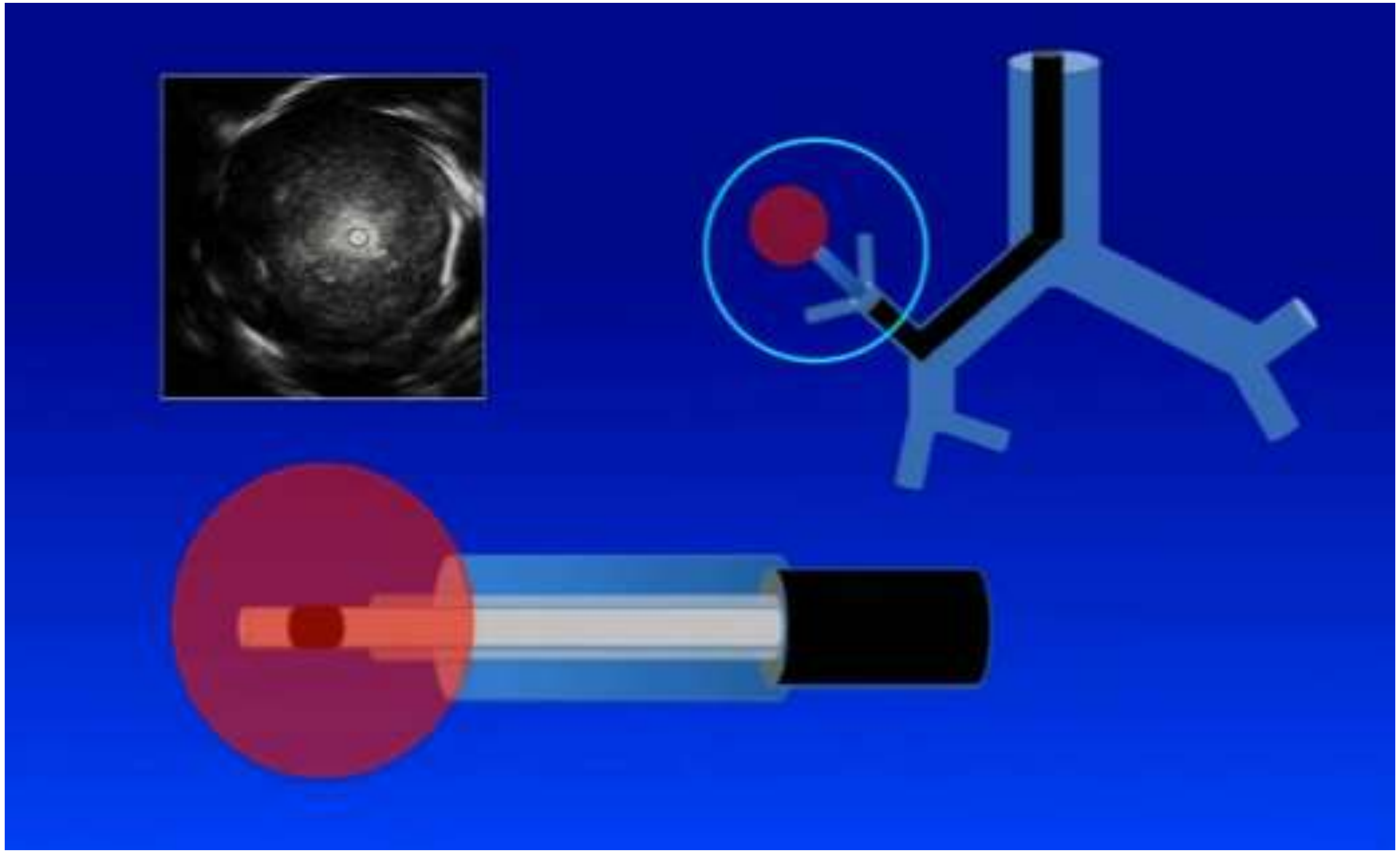
Kurman et al., Semin Respir Crit Care Med 2018;

Radial Endo Bronchial Ultra Sound(r-EBUS)

- r-EBUS employs flexible catheter that houses rotating 20 MHz US transducer
- 360° image of airway wall and surrounding structure is produced by US
- r-EBUS probe can be advanced directly or through guide sheath
- Once lesion is identified radial probe is removed and biopsy instrument are introduced

Chen A et al., Ann Am Thorac Soc 2014

Radial Endo Bronchial Ultra Sound(r-EBUS)

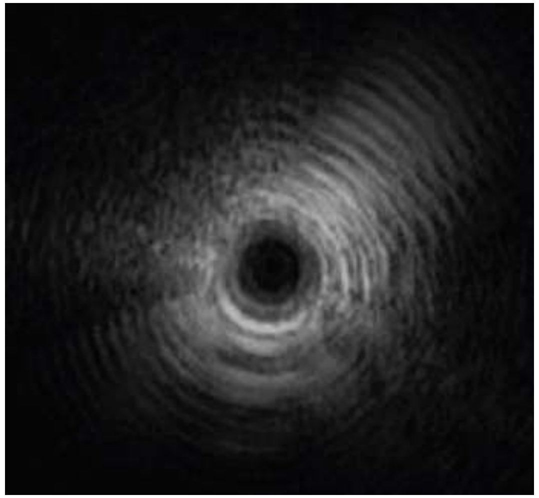


Once within the lesion hyperechoic line represents junction b/w normal lung and lesion

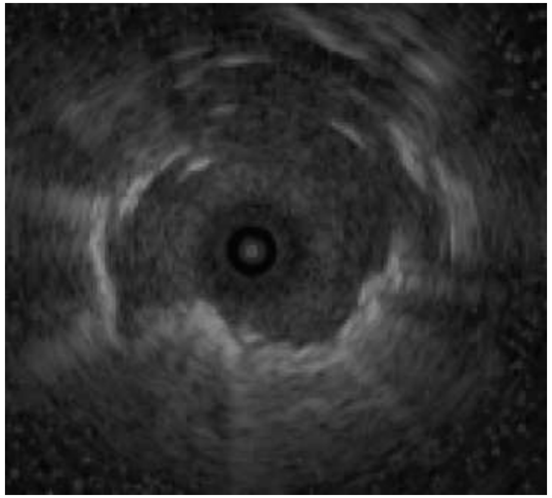
Type of US image generated depends upon
Location of lesion
Nature of lesion

Chen A et al., Ann Am Thorac Soc 2014

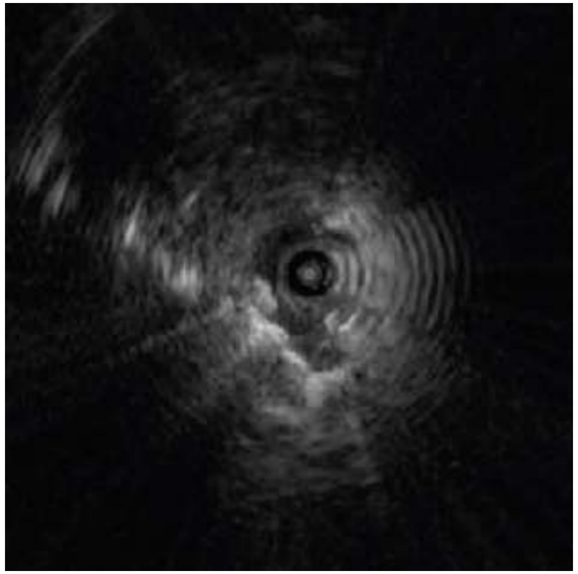
Radial Endo Bronchial Ultra Sound(r-EBUS) images



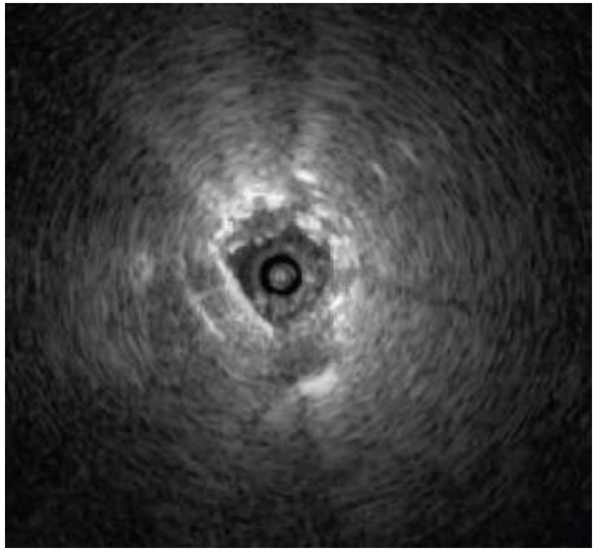
Normal



Concentric solid lesion



Eccentric solid lesion



GGO

Chen A et al., Ann Am Thorac Soc 2014

Diagnostic Yield Of r-EBUS

Study	Population	Intervention	Outcome
Retrospective review	467 cases with Peripheral pulmonary lesions	Only r-EBUS for diagnosis	96% nodules identified Diagnostic yield – 69% Complication rate Pneumothorax – 2.8% ICTD required - 1.7%

	1-2cm	2.1-3cm	3.1-4cm	4.1-5cm	>5cm
Diagnostic(%)	83(58)	99(72)	54(77)	41(87)	35(88)

→ Diagnostic yield increased with increasing size of lesion

Chen A et al., Ann Am Thorac Soc 2014

Factors affecting yield from r-EBUS

Diagnostic yield with concentric view – 84%

Diagnostic yield with eccentric view - 48%

Diagnostic yield with guided sheath – 72%

Diagnostic yield with 4mm bronchoscope – 70%

Sampling instruments used – TBNA + CDP v/s CDP – 78.4% v/s 60.6%

Chen A et al., Ann Am Thorac Soc 2014

Factors affecting yield from r-EBUS

Factors	Chavez et al., 2015[26]		Tamiya et al., 2013[10]		Yamada et al., 2007[19]		Umeda et al., 2014[27]		Okachi et al., 2016[28]		Minezawa et al., 2015[7]		Yoshikawa et al., 2007[16]		Kurimoto et al., 2004[4]		Fielding et al., 2008[29]	
	Diagnostic rate (%)	P	Diagnostic rate (%)	P	Diagnostic rate (%)	P	Diagnostic rate (%)	P	Diagnostic rate (%)	P	Diagnostic rate (%)	P	Diagnostic rate (%)	P	Diagnostic rate (%)	P	Diagnostic rate (%)	P
Probe position																		
Within	68	0.001	92.1	0.004	83	<0.001	80.9[c]	<0.0001	77.1	<0.001	-	-	-	-	87	<0.0001	-	-
Adjacent/invisible	54		60.0		61/4		7.7[d]		68.9/19.4		-		-		42		-	
Bronchus sign																		
Positive	-	-	-	-	71	0.211	74.2	0.0002	68.8	0.005	-	-	67.3	<0.01	-	-	-	-
Negative	-		-		45		44.0		41.9		-		0		-		-	
Lesion size by diameter (mm)																		
≥20, ≤30	71	0.179	74.1	0.534	91[a]	<0.001	-	-	71.3[e]	0.031	82.6	0.01	75.6[e]	<0.01	77	0.99/0.41 /0.96	-	-
<20	62		80.5		68[b]		-		55.6[f]		63.8		29.7[f]		76/76/69[g]		-	
Consistency																		
Solid	68	1.000	91.7	0.007	-	-	71.6	0.017	68.6	0.061	73.2	0.24	67	<0.05	-	-	-	-
GGO (pure/ part-solid)	67		62.5		-		52.8		48.4/42.9		66.7		35		-		-	
Lobe location																		
Upper (right/left)	66	0.803	82.4	0.382	60/76	0.66	65.3	0.23	65.6	0.662	71.4[i]	0.82	48.6/68.2	<0.05	40[k]	0.003	-	-
Middle/lingula	73		80.0		67		84.2		70.6		73.1[j]		90/80		54-100[l]		-	
Lower	67		70.8		67/65		64.4		60.0				54.8/72.2					
Relationship with pleura																		
Not touching	77	0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	74	<0.01
Touching/ within 10 mm[h]	55		-		-		-		-		-		-		-		35	
Visibility under fluoroscopy																		
Clearly visible	-	-	-	-	-	-	-	-	-	-	81.9	0.01	-	-	67	0.96	-	-
Vague/invisible	-		-		-		-		-		63.6		-		74		-	
Relationship between lesion and bronchus																		
A	-	-	-	-	-	-	-	-	-	-	83.7	0.001	-	-	-	-	-	-
B	-		-		-		-		-		65.3		-		-		-	
C	-		-		-		-		-		28.6		-		-		-	
SUV_{max}																		
<2.8	-	-	-	-	-	-	46.8	<0.0001	-	-	-	-	-	-	-	-	-	-
≥2.8	-		-		-		75.5		-		-		-		-		-	

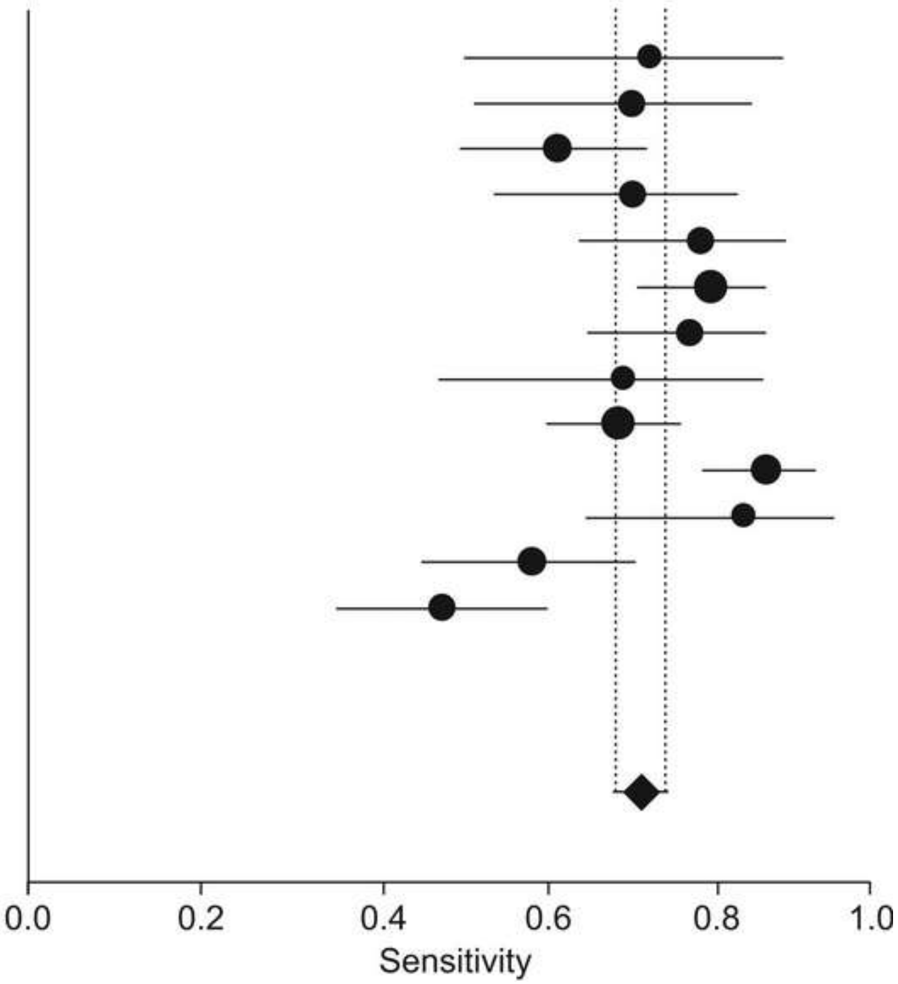
[a]15-30 mm, [b]≤15 mm, [c]Within and adjacent, [d]Invisible, [e]>20; ≤30 mm, [f]≤20 mm, [g]≤10 mm/>10; ≤15/>15 mm; ≤20 mm, [h]From the costal visceral pleura, [i]Upper lobe or superior segment of lower lobe, [j]Middle or lower lobe except for superior segment, [k]Left upper apical posterior segment, [l]Other location. GGO: Ground-glass opacity, SUV_{max}: Maximum standardized uptake value of ^{18}F-FDG uptake, ^{18}F-FDG: Fluorine-18 fluorodeoxyglucose

→ Concentric view most important factor affecting the yield

Zhang et al ., Endosc US 2017

Diagnostic Yield Of r-EBUS

First author [ref.]	Sensitivity (95% CI)
Asahina [36]	0.74 (0.52–0.90)
Eberhardt [33]	0.72 (0.53–0.86)
Fielding [32]	0.63 (0.51–0.74)
Herth [12]	0.72 (0.55–0.85)
Herth [31]	0.80 (0.65–0.90)
Kurimoto [30]	0.81 (0.72–0.88)
Paone [29]	0.79 (0.66–0.88)
Shirakawa [28]	0.71 (0.49–0.87)
Yamada [27]	0.70 (0.62–0.78)
Yoshikawa [26]	0.88 (0.80–0.93)
Asano [37]	0.85 (0.66–0.96)
Huang [39]	0.60 (0.47–0.72)
Eberhardt [40]	0.49 (0.37–0.62)
Pooled sensitivity	0.73 (0.70–0.76)



Pooled pneumothorax rate of 1%

Steinfort D P et al., ERJ 2011

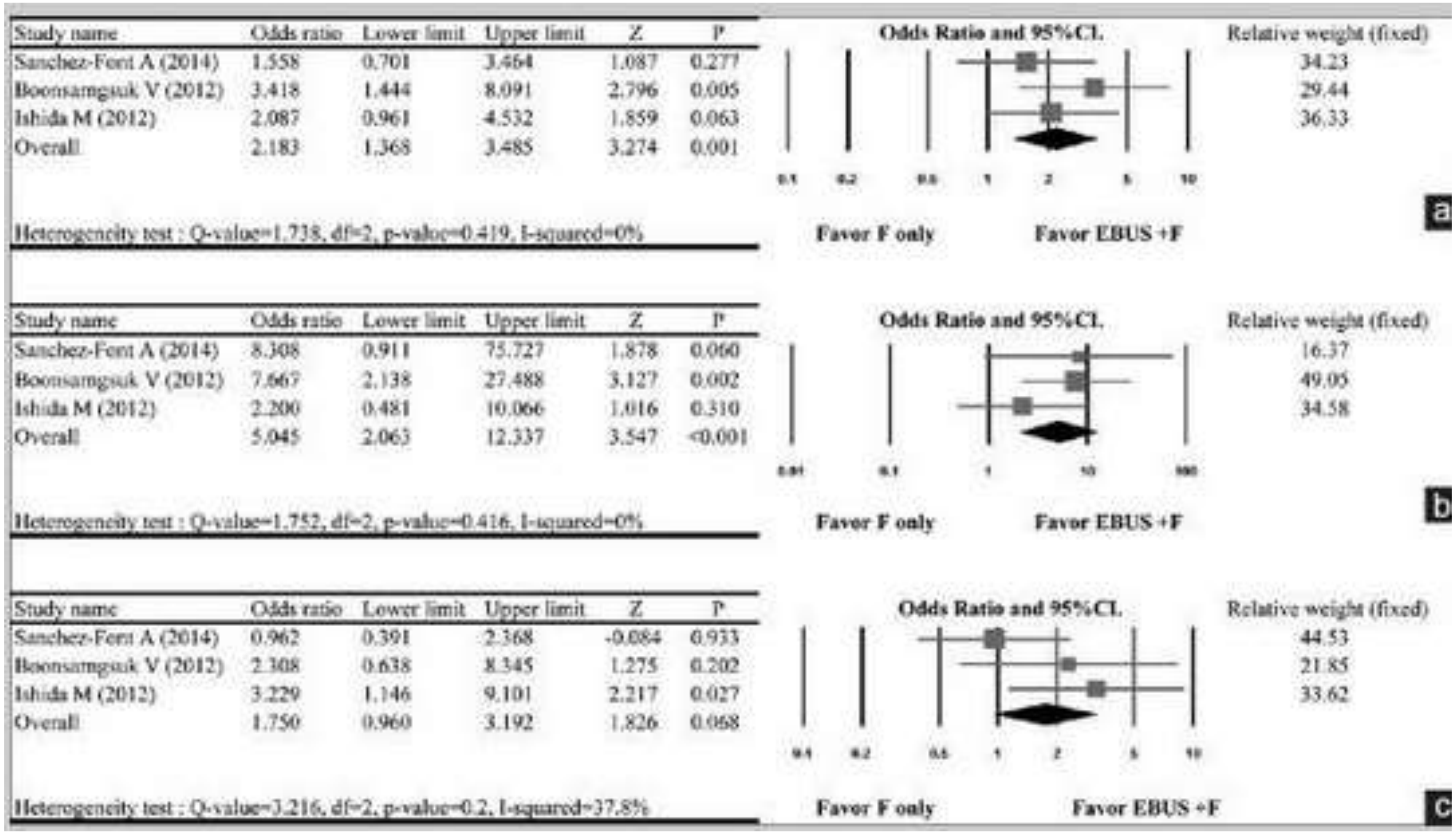
Diagnostic Yield Of r-EBUS

—Inverse Weighted Diagnostic Yield Overall and by Modality

Technology	Studies, No.	Weighted Proportion, %	95% CI	Q Statistic	Q *P* Value
VB	10	72.0	(65.7-78.4)	21.0	.01
ENB	11	67.0	(62.6-71.4)	13.3	.21
GS	10	73.2	(64.4-81.9)	63.8	< .0001
U	11	70.0	(65.0-75.1)	15.2	.12
R-EBUS	20	71.1	(66.5-75.7)	84.2	< .0001
All	39	70.0	(67.1-72.9)	119.4	< .0001

Wang Memoli et al., CHEST 2013

Metaanalysis r-EBUS+ Fluoro guided TBB V/s Fluoro TBB



Study name	Odds ratio	Lower limit	Upper limit	Z	P	Relative weight (fixed)
Sanchez-Font A (2014)	1.558	0.701	3.464	1.087	0.277	34.23
Boonsarngsuk V (2012)	3.418	1.444	8.091	2.796	0.005	29.44
Ishida M (2012)	2.087	0.961	4.532	1.859	0.063	36.33
Overall	2.183	1.368	3.485	3.274	0.001	

Heterogeneity test : Q-value=1.738, df=2, p-value=0.419, I-squared=0%

Study name	Odds ratio	Lower limit	Upper limit	Z	P	Relative weight (fixed)
Sanchez-Font A (2014)	8.308	0.911	75.727	1.878	0.060	16.37
Boonsarngsuk V (2012)	7.667	2.138	27.488	3.127	0.002	49.05
Ishida M (2012)	2.200	0.481	10.066	1.016	0.310	34.58
Overall	5.045	2.063	12.337	3.547	<0.001	

Heterogeneity test : Q-value=1.752, df=2, p-value=0.416, I-squared=0%

Study name	Odds ratio	Lower limit	Upper limit	Z	P	Relative weight (fixed)
Sanchez-Font A (2014)	0.962	0.391	2.368	-0.084	0.933	44.53
Boonsarngsuk V (2012)	2.308	0.638	8.345	1.275	0.202	21.85
Ishida M (2012)	3.229	1.146	9.101	2.217	0.027	33.62
Overall	1.750	0.960	3.192	1.826	0.068	

Heterogeneity test : Q-value=3.216, df=2, p-value=0.2, I-squared=37.8%

Combination of r-EBUS with fluoroscopy guided TBB improved diagnostic yield

OR~5 especially for nodules<20mm

Jian Y et al ., Ann Thorac Med 2017

Diagnostic Yield Of r-EBUS

Study	Population	Intervention	Outcome
Prospective, Randomized trial	N=197 Lung nodule 1.5- 5cm	85 Std Bronch-Fluoro 112 Thin Bronch-rEBUS	Diagnostic yield 37.7% v/s 49.1% (p=0.11) 46 patients who had non diagnostic report in Std arm crossed over 7 of them were diagnosed

Bivariate Analyses

Factors	Bronchoscopic Diagnosis	
	No. (%)	*P* Value
Lobulated		
No (n = 142)	142 (50.0)	.008
Yes (n = 55)	55 (29.1)	
Size of lesion		
15-25 mm (n = 65)	20 (30.8)	.002
26-35 mm (n = 62)	27 (43.6)	
36-50 mm (n = 70)	40 (57.1)	
R-EBUS imaging		
Ecentric (n = 61)	19 (31.2)	.014
Concentric (n = 113)	57 (50.4)	

Multivariable Logistic Regression Model

Factors	OR	95% CI
Study arm (TB-EBUS vs SB-F)	1.74	0.87-3.46
Lobulated (no vs yes)	3.35	1.51-7.43
Size of lesion	1.06	1.02-1.09

Tanner N T et al., CHEST 2018

r-EBUS

Advantages	Disadvantages
Comparatively safe and feasible technology	Precise localization of eccentrically located nodule is difficult
Real time visualisation feasible prior to biopsy	Lacks navigation platform
Yield better than conv. bronchoscopy	Ground glass nodules are difficult to visualise

Virtual Bronchoscopic Navigation

- 3 dimensional images of tracheobronchial tree are generated from helical CT scan data obtained from patient

- Starting point and target point are selected on CT

- VBN software creates a virtual bronchoscopic route to the lesion

- During bronchoscopy the navigation system guides the user to make correct turns on the way to target lesion

Katsis et al ., Journal of Thoracic Disease 2020

Virtual Bronchoscopic Navigation

- Currently available VBN systems include

Bf-NAVI

LungPoint

DirectPath

- VBN consists of three phases

Planning phase

Guidance phase

Biopsy phase

Katsis et al ., Journal of Thoracic Disease 2020

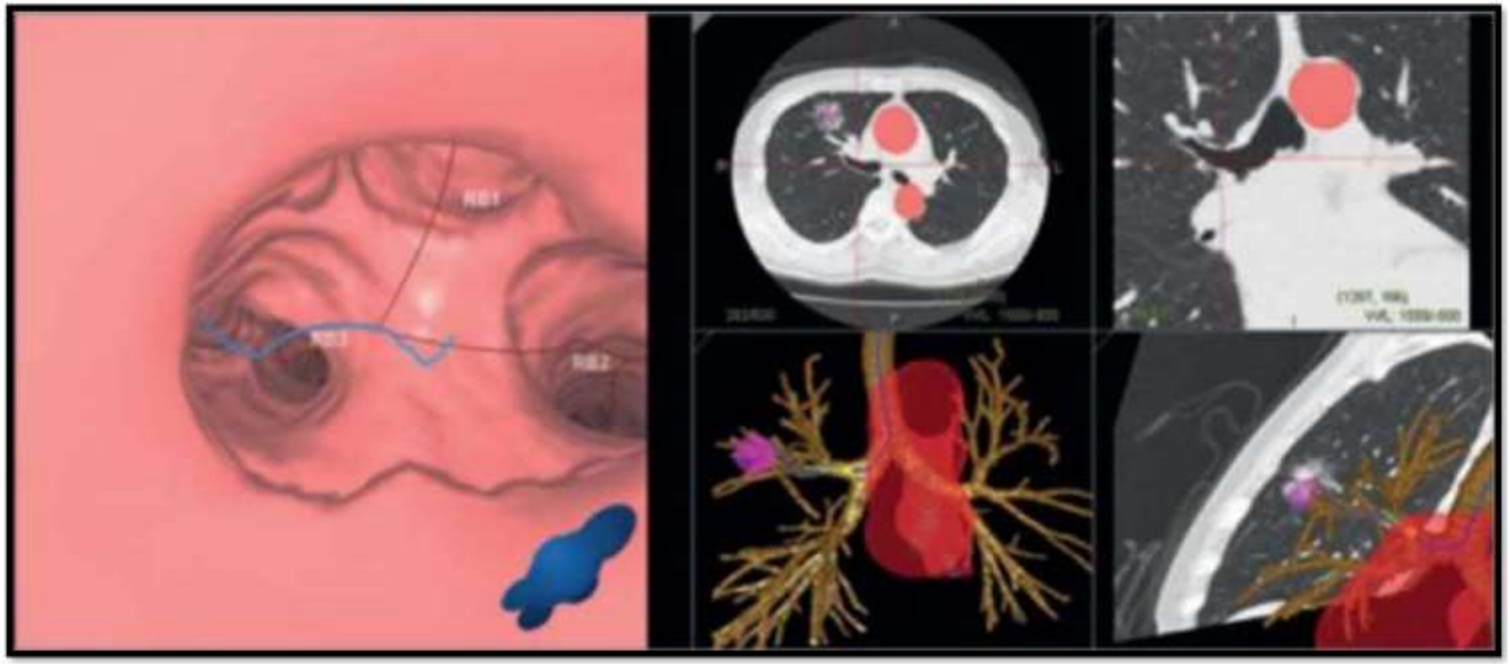
Virtual Bronchoscopic Navigation

Planning Phase	Guidance Phase	Biopsy Phase
CT images are acquired according to a specific protocol Images are utilised by specialized software to create virtual bronchoscopic pathway to target lesion	Virtual images of airway are synchronised with real time images during bronchoscopy	Lesion sampled either as it is or after confirmation with r-EBUS and fluoroscopy

Asano F et al ., Respiration 2014

Virtual Bronchoscopic Navigation

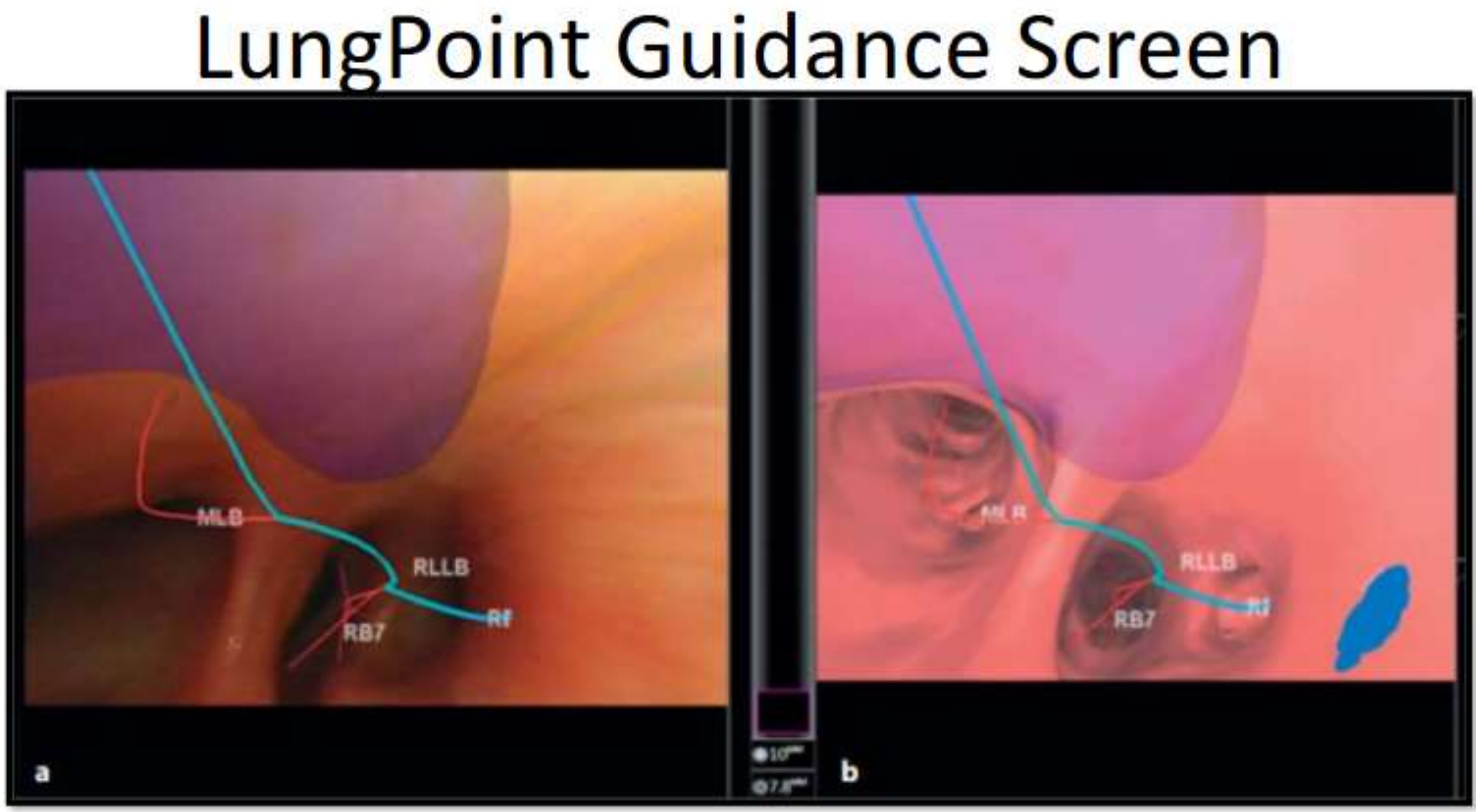
Lungpoint Planning Screen



- Target site is marked
- Virtual pathway to lesion is generated

Asano F et al ., Respiration 2014

Virtual Bronchoscopic Navigation



- Real time and virtual images are displayed side by side to guide the user to target

Asano F et al ., Respiration 2014

VBN Evidence Pooled analysis of data

Studies of VBN for the diagnosis of PPLs

First author	Year	Study design	VBN system	Bronchoscope external diameter	Confirmation of arrival	Lesion size selection	Lesions, n	Diagnostic yield	Lesions <2 cm, n	Diagnostic yield for lesions <2 cm	Complications, n	Complication rate	Complications
Shinagawa [16]	2004	Pro	Not used	2.8 mm	CT	<2 cm	26	65.4%	26	65.4%	0	0.0%	None
Asahina [26]	2005	Pro	Not used	4.0 or 5.3 mm	EBUS	≤3 cm	30	63.3%	18	44.4%	0	0.0%	None
Asano [11]	2006	Pro	Bf-NAVI	2.8 mm	CT	≤3 cm	38	81.6%	26	80.8%	n/a	n/a	n/a
Shinagawa [17]	2007	Pro	Bf-NAVI	2.8 mm	CT	<2 cm	71	70.4%	71	70.4%	1	1.4%	1 PTX
Tachihara [29]	2007	Pro	Bf-NAVI	2.8 or 5.2 mm	Flu	≤3 cm	96	62.5%	77	54.5%	0	0.0%	None
Asano [10]	2008	Pro	Bf-NAVI	4.0 mm	EBUS	n/a	32	84.4%	15	73.3%	0	0.0%	None
Eberhardt [33]	2010	Pro	LungPoint	2.8 mm	Non-Flu	n/a	25	80.0%	n/a	n/a	1	4.0%	1 PTX (0 CTI)
Omiya [30]	2010	Retro	Bf-NAVI	2.8 and 4.0 mm	Flu	≤3 cm	37	75.7%	13	76.9%	n/a	n/a	n/a
Iwano [31]	2011	Retro	Not used	2.8 mm	Flu	n/a	122	78.7%	30	73.3%	n/a	n/a	n/a
Oshige [27]	2011	Pro	Bf-NAVI	4.0 or 5.9 mm	EBUS	n/a	57	84.2%	22	72.7%	0	0.0%	None
Ishida [24]	2011	RCT	Bf-NAVI	4.0 mm	EBUS	≤3 cm	99	80.8%	58	75.9%	0	0.0%	None
Asano [32]	2013	RCT	Bf-NAVI	2.8 mm	Flu	≤3 cm	167	67.1%	114	64.9%	4	2.4%	1 PTX (0 CTI), 2 Hemo, 1 Brad
Tamiya [28]	2013	Pro	LungPoint	4.0 mm	EBUS	≤3 cm	68	77.9%	27	74.1%	n/a	n/a	n/a
Summary							868	73.8%	497	67.4%		1.0%	

Brad = Bradycardia; CTI = chest tube insertion; Flu = fluoroscopy; Hemo = hemorrhage; n/a = not available; Pro = prospective study; PTX = pneumothorax; Retro = retrospective study.

Overall diagnostic yield 73.8%

Complication rate 1%

Asano F et al ., Respiration 2014

VBN Evidence

Study	Population	Intervention	Outcome
RCT Ishida et al, 2011	N= 200 PPL<3cm	VBN assisted group v/s Non VBN assisted group 4mm bronchoscope EBUS-GS plus fluoro used	Diagnostic yield 80.4% v/s 67.4%(p=0.03) Higher yield in lesion <20mm
RCT Asano et al, 2013	N=350 PPL<3cm	VBN assisted group v/s Non VBN assisted group 2.8mmbronchoscope Fluoro used	Diagnostic yield 67.1% v/s 59.9%(p=0.173) Complication rate 1%

Factors affecting diagnostic yield in VBN

- Yield was low in left lower lobe sup seg lesions
- Yield was low in non solid lesions
- Yield was low in eccentric lesions

Advantages Of VBN

- Technically Simple procedure
- Safe
- Diagnostic yield better than conventional bronchoscopy

Limitations

- Pre planned images are used to reach the lesion(No real time navigation)

Electro-magnetic Navigational Bronchoscopy

- Involves creating electromagnetic field around the chest which is utilized to localize or guide a endoscopic tool

- Two systems of EMN available are

  Super dimension system

  SpinDrive system

Becker H D et al., Respiration 2003

Components Of Electro-magnetic Navigational Bronchoscopy

- Virtual bronchoscopy planning software
- Location board which generates electromagnetic field
- Extended working channel
- Eight way steerable catheter
- Locatable guide containing sensors

Fong K M et al., Journal Of Thoracic Dis 2012

Electro-magnetic Navigational Bronchoscopy
Planning phase

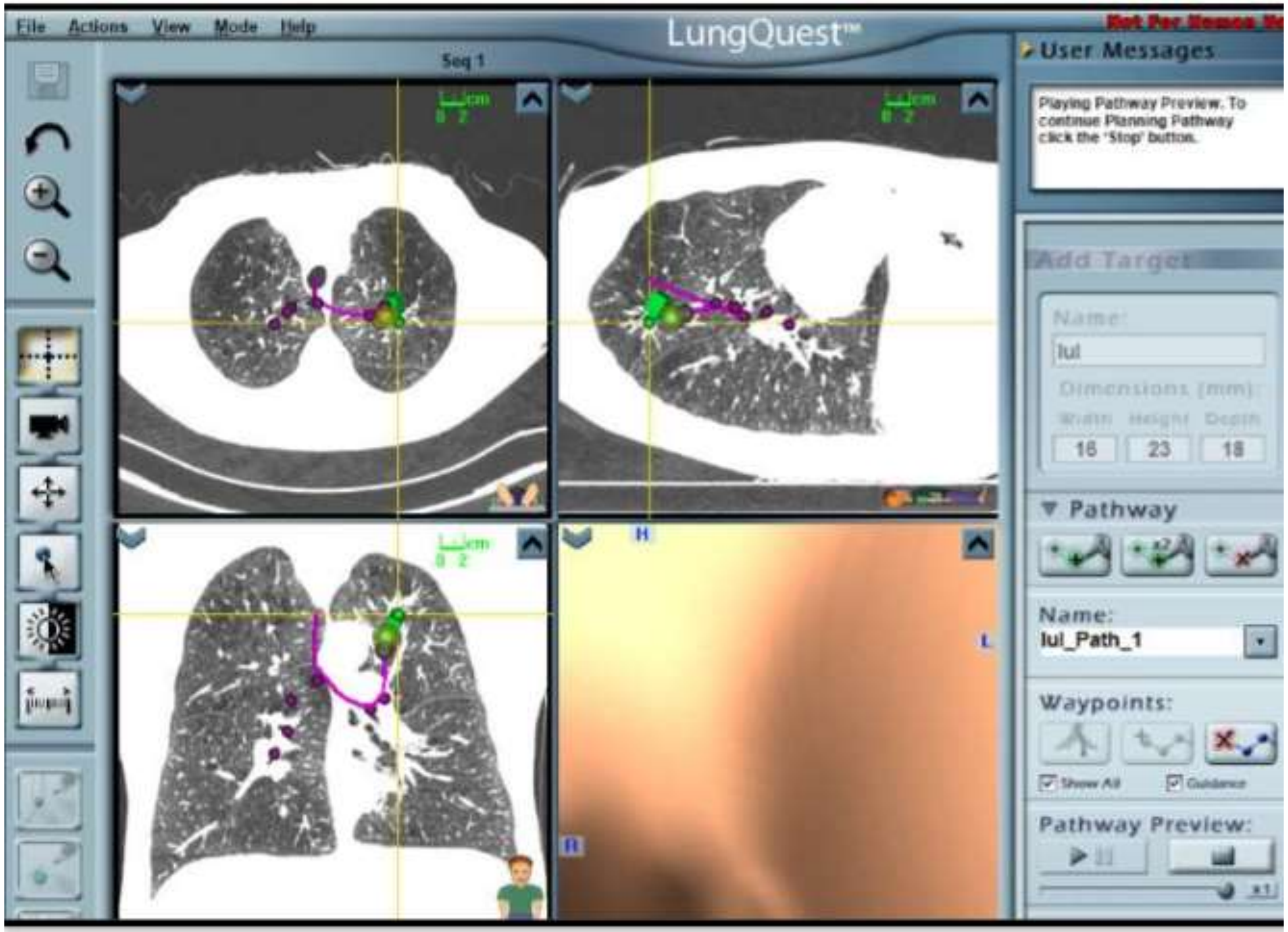
- CT scan obtained with specific slice thickness is loaded into navigation software

- Axial, sagittal, coronal and virtual endobronchial views are generated

- 6-7 easily locatable registration points are marked

Fong K M et al., Journal Of Thoracic Dis 2012

Electro-magnetic Navigational Bronchoscopy



Fong K M et al., Journal Of Thoracic Dis 2012

Electro-magnetic Navigational Bronchoscopy
Navigation phase

- Extended working channel and locatable guide are inserted through working channel of bronchoscope

- CT images and real time bronchoscopic images are matched by a process called registration

- Registration is measured as AFTRE(Average fiducial target registration error) and should be <5mm

- Bronchoscope is wedged into the subsegment leading to the lesion

Fong K M et al., Journal Of Thoracic Dis 2012

Electro-magnetic Navigational Bronchoscopy
Navigation phase

- Extended working channel and locatable guide are slowly advanced by keeping the selected way point in the centre of circle shown on tip view

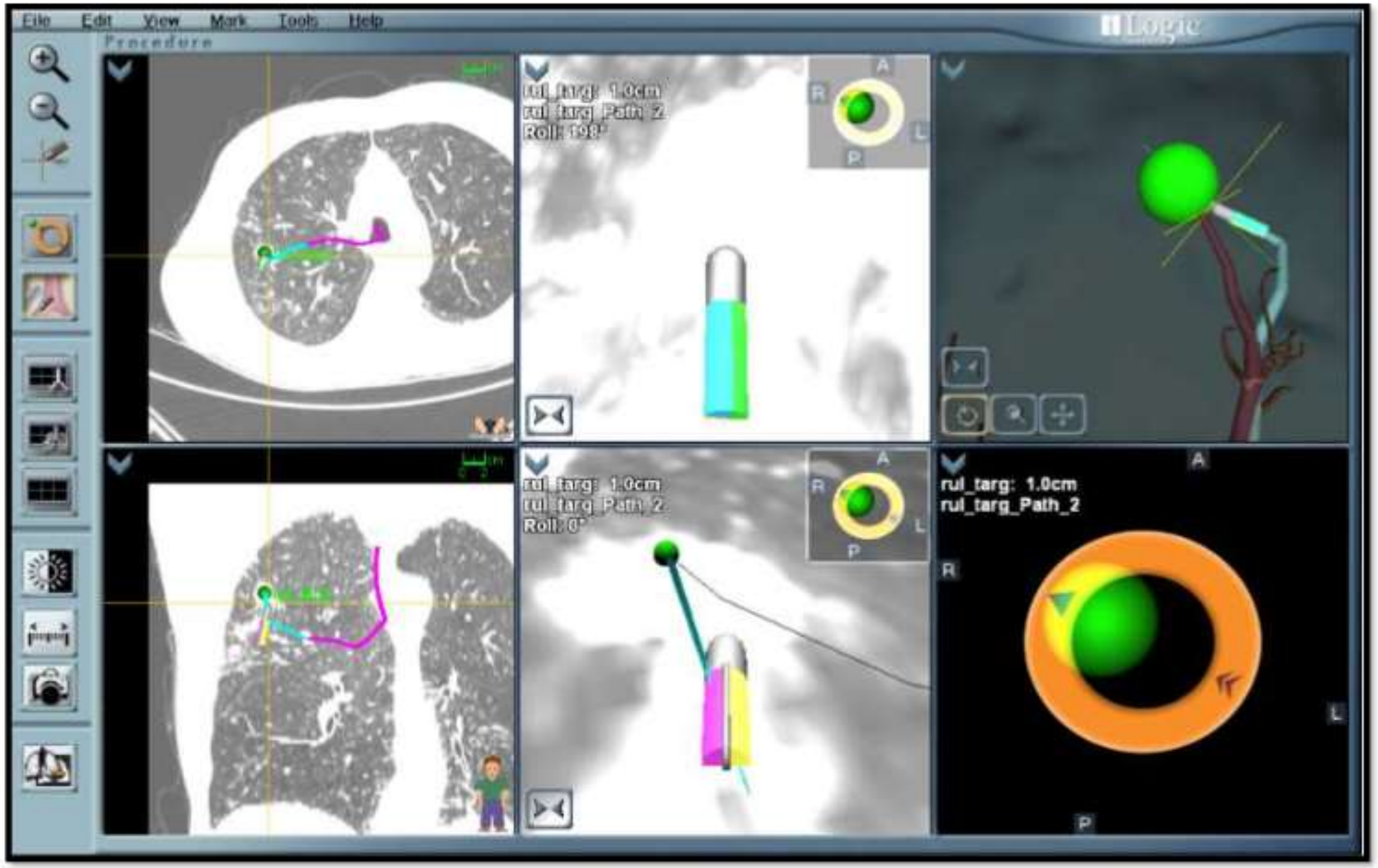
- Locatable guide can be steered to obtain correct orientation

- Once LG tip is in close proximity to lesion, it is removed

- EWC position can be confirmed with fluoroscopy/R-EBUS and sampling done

Fong K M et al., Journal Of Thoracic Dis 2012

Electro-magnetic Navigational Bronchoscopy
Navigation phase



Fong K M et al., Journal Of Thoracic Dis 2012

Electro-magnetic Navigational Bronchoscopy Evidence

Respiration

Review

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DOI: 10.1159/000355710

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Diagnostic Yield and Safety of Electromagnetic Navigation Bronchoscopy for Lung Nodules: A Systematic Review and Meta-Analysis

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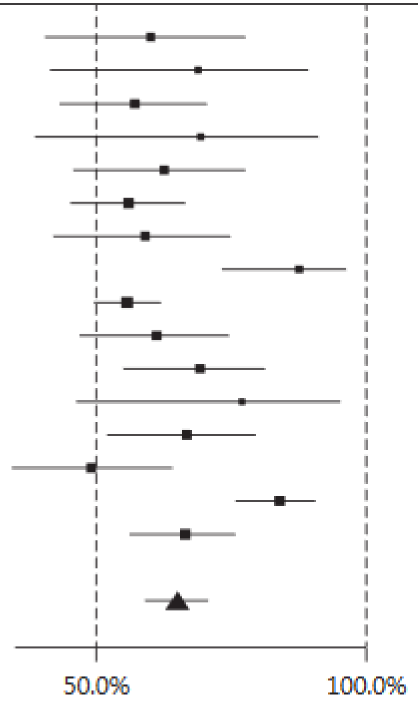
15 Trials with 1033 lung nodules included

GEX G et al ., Respiration 2014

Electro-magnetic Navigational Bronchoscopy

Study, first author	Number/ total	Diagnostic yield (95% CI)
Becker, 2005 [3]	18/30	60.0 (40.6; 77.3)
Hautmann, 2005 [13]	11/16	68.8 (41.3; 89.0)
Gildea, 2006 [14]	32/56	57.1 (43.2; 70.3)
Schwarz, 2006 [15]	9/13	69.2 (38.6; 90.9)
Makris, 2007 [16]	25/40	62.5 (45.8; 77.3)
Eberhardt, 2007 [17]	52/93	55.9 (45.2; 66.2)
Eberhardt, 2007 [18]	23/39	59.0 (42.1; 74.1)
Eberhardt, 2007 [18]	35/40	87.5 (73.2; 95.8)
Wilson, 2007 [19]	151/271	55.7 (49.6; 61.7)
Bertoletti, 2009 [20]	33/54	61.1 (46.9; 74.1)
Eberhardt, 2009 [21]	38/55	69.1 (55.2; 80.9)
Lamprecht, 2009 [22]	10/13	76.9 (46.2; 95.0)
Seijo, 2010 [23]	34/51	66.7 (52.1; 79.2)
Mahajan, 2011 [24]	24/49	49.0 (34.4; 63.7)
Lamprecht, 2012 [26]	94/112	83.9 (75.8; 90.2)
Pearlstein, 2012 [25]	67/101	66.3 (56.2; 75.4)
Pooled (random effects) $I^2 = 66\%$		64.9 (59.2; 70.3)

Forest plot



GEX G et al ., Respiration 2014

Electro-magnetic Navigational Bronchoscopy

Reported significant predicting factors in univariate analysis
Location in lower lobe [18] Size of the nodule [23] Bronchus sign [23] AFTRE [16] Nodule visualization with radial-probe EBUS [18, 21] Catheter suction technique versus forceps biopsies [21]
Reported significant predicting factors in multivariate analysis
Bronchus sign [23]

[1] Distance between the tip of the sensor and the center of the nodule.

Table 5. Study level characteristics associated with significant modification of ENB's performance

		Studies, n	Pooled outcome (95% CI)	p values
General anesthesia			diagnostic yield	
	yes	9	69.2% (60.6–76.7)	0.02
	no	7	57.5% (53.2–61.8)	
ROSE			sensitivity for malignancy	
	yes	4	80.2% (72.1–86.4)	0.006
	no	10	66.3% (60.3–71.8)	
Fluoroscopy			diagnostic yield	
	yes	6	56.3% (51.5–60.9)	0.006
	no	10	68.8% (61.3–75.4)	

Pneumothorax occurred in 3.1% patients 1.6% requiring ICTD

GEX G et al ., Respiration 2014

EMN – NAVIGATE Trial

Study	Population	Characteristics	Outcome
Prospective , Multicentre cohort study	29 sites / n = 1157 patients	Median lesion size 20mm ENB using Superdimension system Fluoroscopy – 90% R-EBUS – 57%	12 month diagnostic yield 73% Pneumothorax rate 2.9 %

Folch E E et al ., JTO 2018

Electro-magnetic Navigational Bronchoscopy

Benefits	Drawbacks
Effective	Expensive
Safe	?Safety in patients with pacemaker/defibrillator
	CT to body divergence (movement of nodule with respiration)

Ultra Thin Bronchoscope

- Smaller variants of flexible bronchoscope ranging in size from 2.8-3.5mm
- By virtue of their smaller diameter can be inserted beyond subsegmental bronchi
- Have better manoeuvrability and wider reach

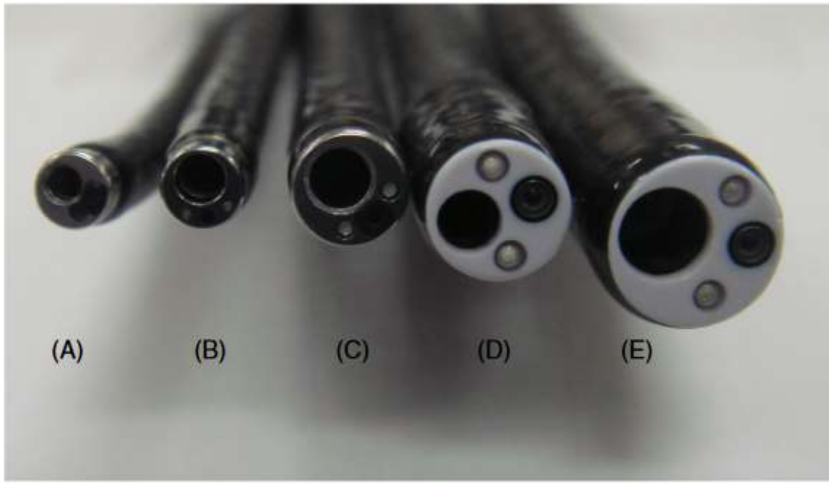


Figure 1 Flexible bronchoscopes. (A) A 2.8-mm bronchoscope with a 1.2-mm channel; (B) a 3.0-mm bronchoscope with a 1.7-mm channel; (C) a 4.0-mm bronchoscope with a 2.0-mm channel; (D) a 4.8-mm bronchoscope with a 2.0-mm channel; and (E) a 5.9-mm bronchoscope with a 3.0-mm channel.

Katsis et al ., Journal of Thoracic Disease 2020

Ultra Thin Bronchoscope

[Original Research **Thoracic Oncology**]

CHEST

Use of an Ultrathin vs Thin Bronchoscope for Peripheral Pulmonary Lesions

A Randomized Trial

Check for updates

Masahide Oki, MD; Hideo Saka, MD; Fumihiro Asano, MD; Chiyoe Kitagawa, MD; Yoshihito Kogure, MD; Akifumi Tsuzuku, MD; and Masahiko Ando, MD

Study	Population	Intervention	Outcome
RCT	N=356 Nodule <30 mm	Thin bronchoscope(4mm) v/s Ultra thin bronchoscope(3mm) EBUS/Fluoro/VBN guidance used	Diagnostic yield Procedure duration Complication

OKI M et al ., CHEST 2019

Ultra Thin Bronchoscope

Variables	UTB Group (n = 177)		Thin Bronchoscope Group (n = 179)		P Value	P Value for Interaction
Total	124/177 (70.1)		105/179 (58.7)		.027	
Lesion size in the largest diameter on CT scan						
≤ 20 mm	64/102 (62.7)	P = .004	52/101 (51.5)	P = .027	.120	P = .664
> 20 to ≤ 30 mm	62/75 (82.7)		53/78 (67.9)		.041	
Lesion nature						
Malignant	111/142 (78.2)	P < .001	99/140 (70.7)	P < .001	.173	P = .172
Benign	13/32 (40.6)		6/37 (16.2)		.032	
Unknown	0/3 (0)		0/2 (0)		...	
Lobar location						
Upper lobe	56/85 (65.9)	P = .244	61/97 (62.9)	P = .212	.757	P = .089
Other	68/92 (73.9)		44/82 (53.7)		.007	
Lesion location from the hilum						
Intermediate	29/40 (72.5)	P = .701	26/37 (70.3)	P = .107	> .999	P = .163
Peripheral	95/137 (69.3)		79/142 (55.6)		.019	
Locational relationship with pleura						
Apart from the pleura	73/102 (71.6)	P = .608	67/105 (63.8)	P = .096	.368	P = .448
Abutting on the pleura	51/75 (68.0)		38/74 (51.4)		.046	
Bronchus sign						
Present	97/130 (74.6)	P = .028	87/133 (65.4)	P = .002	.109	P = .549
Absent	27/47 (57.4)		18/46 (39.1)		.098	
Appearance on CT scan						
Solid	107/148 (72.3)	P = .141	94/153 (61.4)	P = .067	.051	P = .784
Part-solid nodule	17/29 (58.6)		11/26 (42.3)		.285	

Overall yield 70.1% v/s 58.7%

Procedure duration

Complication

Favoured Ultra thin bronchoscope arm

OKI M et al ., CHEST 2019

Bronchoscopic Trans parenchymal Nodule Access(BTPNA)

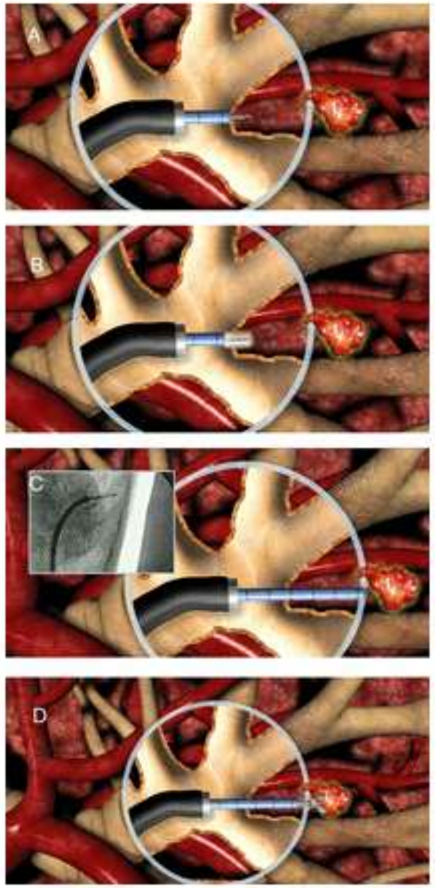
- Newer modality for nodules without air bronchus sign or nearby patent airway
- BTPNA generates a route from airway to nodule across parenchyma avoiding vessels after analysing the CT
- Point of Entry(POE) in airway is identified using BTPNA software
- During bronchoscopy POE is reached under VB guidance
- Coring needle is used to penetrate the wall and avascular track to nodule is created

Gompelmann et al., JTO 2019

Bronchoscopic Trans parenchymal Nodule Access(BTPNA)

- Sheath is introduced under fluoroscopic guidance to the lesion

- Biopsy forceps are introduced to sample the lesion



Gompelmann et al., JTO 2019

Bronchoscopic Trans parenchymal Nodule Access(BTPNA) Feasibility Studies

Study	Population	Device	Outcome
Herth F J et al., Thorax 2015	N=12 Nodules of size 10mm to 40mm 1cm from pleural surface	Archimedes VBN system	Adequate biopsy in 10 patients(83%) No adverse events
Harzheim D et al., Respiration 2016	N=6	Archimedes VBN system	Adequate biopsy in 5/6 2 pneumothorax 1 requiring ICTD

Trans Bronchial Access Tools(TBAT)

- Tool similar to BTPNA
- Uses ENB to generate virtual pathway to lesion across parenchyma
- Multicentre trial utilizing above modality is ongoing – EAST 2 trial

Katsis et al ., Journal of Thoracic Disease 2020

Cone Beam C T and Augmented Fluoroscopy

- Fluoroscopy can be utilized for real time sampling of radiopaque lesions
- However localization of small and ground glass nodules is difficult
- Cone beam CT is a variant of CT which utilizes cone shaped x ray beam and two dimensional detectors
- CBCT enables acquiring of more volumetric data with fewer rotations
- Use of ENB to navigate to lesion plus use of fluoro and CBCT to confirm position within target lesion be combined greater diagnostic yield can be achieved

Cone Beam C T and Augmented Fluoroscopy

ORIGINAL INVESTIGATION

OPEN

Cone-Beam CT With Augmented Fluoroscopy Combined With Electromagnetic Navigation Bronchoscopy for Biopsy of Pulmonary Nodules

Michael A. Pritchett, DO, MPH,† Stéphanie Schampaert, PhD,‡*
Joris A.H. de Groot, PhD,‡ Charles C. Schirmer, MD,§
and Imramsjah van der Bom, PhD‡

Single centre study

CBCT with fluoroscopy combined with ENB

Feasibility and efficacy study

Prittchett et al ., J Bronchol Intervent Pulmonol 2018

Cone Beam C T and Augmented Fluoroscopy

- Procedure was done under GA
- From baseline CT target lesion was characterized
- CT data was loaded onto EMN system
- CBCT was acquired post intubation, in which lung nodule was highlighted in a process called segmentation
- Bronchoscope was introduced into airway and navigated towards nodule using EMN
- Nodule segmentation was visualized in an overlay with live fluoroscopy
- Final position was confirmed with fluoroscopy

Prittchett et al ., J Bronchol Intervent Pulmonol 2018

Cone Beam C T and Augmented Fluoroscopy

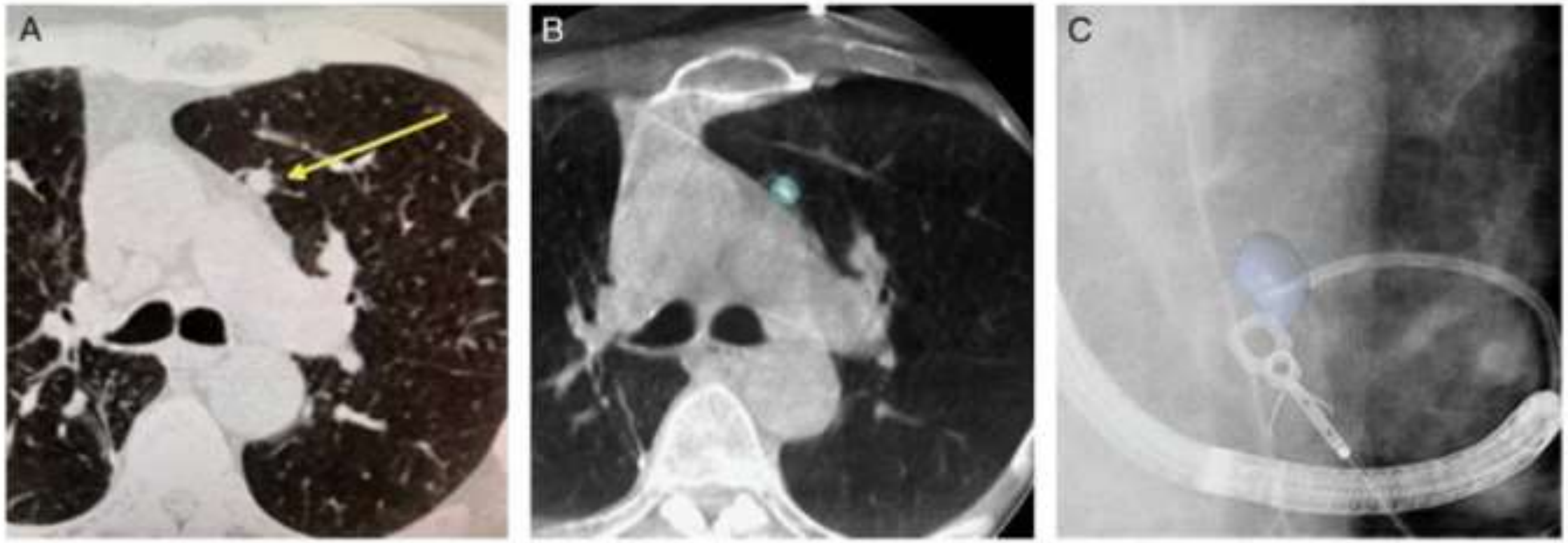


FIGURE 1. Illustration of the different imaging sources involved using CBCT with AF during ENB-guided biopsy procedures. CT data were acquired before the procedure (Yellow arrow shows the target nodule) (A). Intraoperative CBCT data were acquired and 3-dimensional nodule segmentation was performed (B). Three-dimensional nodule segmentation was visualized in overlay with live fluoroscopy: AF (C). AF indicates augmented fluoroscopy; CBCT, cone-beam computed tomography; ENB, electromagnetic navigation bronchoscopy.

Prittchett et al ., J Bronchol Intervent Pulmonol 2018

Cone Beam C T and Augmented Fluoroscopy

TABLE 3. Diagnostic Performance of ENB and CBCT With Augmented Fluoroscopy

Diagnostic Performance	Diagnostic Yield (95% CI)	Diagnostic Accuracy (95% CI)*
All lesions (n = 92) (mm)	83.7% (74.8%-89.9%)	93.5% (86.5%-97.0%)
Lesions ≤ 10 (n = 19)	84.2% (62.4%-94.5%)	89.5% (68.6%-97.1%)
Lesions ≤ 20 (n = 65)	83.1% (72.2%-90.3%)	90.8% (81.3%-95.7%)
Lesions > 20 (n = 27)	96.3% (81.7%-99.8%)	100% (87.5%-100%)
Minimum sensitivity for malignancy†	91.3% (82.3%-96.0%)	
Maximum sensitivity for malignancy‡	95.5% (87.5%-98.4%)	
Minimum prevalence of malignancy‡	71.7% (61.8%-79.9%)	
Maximum prevalence of malignancy†	75.0% (65.3%-82.7%)	
Minimum negative predictive value	79.3% (61.6%-90.2%)	
Maximum negative predictive value	89.7% (73.6%-96.4%)	

*Diagnostic accuracy represents the malignant and benign lesions as well as the indeterminate lesions confirmed as benign with clinical and radiographic follow-up divided by the total number of lesions biopsied.

†Minimum sensitivity and maximum prevalence were based on the assumption that patients with uncompleted follow-up (n = 3) actually had lung cancer (ie, were false negative).

‡Minimum sensitivity and prevalence were based on the assumption that patients with uncompleted follow-up (n = 3) actually had lung cancer (ie, were false negative).

CBCT indicates cone-beam computed tomography; CI, confidence interval; ENB, electromagnetic navigation bronchoscopy.

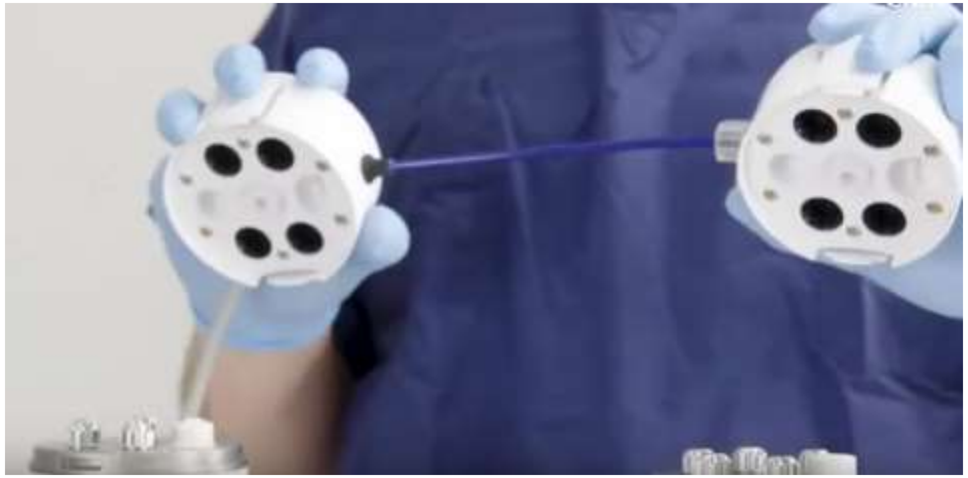
Prittchett et al ., J Bronchol Intervent Pulmonol 2018

Robotic Bronchoscopy

- Robotic bronchoscope consists of robotic arms that contain rotatory pulleys that drive the bronchoscope

- Available robotic system – Auris monarch and Intuitive

Robotic arm



Endoscope attached

Prittchett et al ., J T O 2018

Robotic Bronchoscopy

- Robotic scope is propelled using a hand held controller
- Scope has an outer and inner sheath, has optical capabilities and a separate suction channel
- EMN is used for guidance

Prittchett et al ., J T O 2018

Data On Robotic Bronchoscopy

	Population	Outcome	Adverse events
Single centre Feasibility study Rojas solano et al ., J Bronchol Intervent Pulmonol 2018	N=15 Peripheral lung nodules with bronchus sign (size -2.6cm)	Biopsy sample obtained in 93% patients	Nil
Feasibility study Fielding D et al ., CHEST 2018	N=30 Nodule size 12.5mm +/- 4.3mm with bronchus sign	Diagnostic yield – 83%	Nil

Robotic Bronchoscopy

Advantage	Drawbacks
Direct visualisation of peripheral airways and biopsy tools	Limited data
Precise control of biopsy instruments	Cost
	Availability and learning curve

Role Of Cryo Biopsy

- Larger sample and due to deeper effect lesion adjacent to airway can be sampled

Study	Population	Outcome
Schumann et al ., ERJ 2014	N=31 1.2mm Cryoprobe used	Larger sample size (yield 74.2%) 11.17mm2 v/s 4.69mm2 1 moderate bleed
Herath S et al ., Respirol 2018	N=6 1.9mm Cryoprobe used	Larger sample size No complication
Kho et al ., ERJ 2019	N=114 1.9mm Cryoprobe used	Diagnostic yield in eccentric lesion better with cryobiopsy 75% v/s 48.8% Moderate bleed in 8%

Meta analysis/Pooled analysis of bronchoscopy procedures for diagnosis of pulmonary nodules

Study	Sites/Patients	Yield/Sensitivity
2012 Meta analysis [1]	39 studies / 3004 patients	Overall -70% >2cm – 81% <2cm – 61% Pneumothorax rate – 1.5%
2013 ACCP guidelines [2]	35 studies / 4507 patients	Central lesion – 88%
	34 studies / 5742 patients	Peripheral lesion – 78%
	10 studies / 1367 patients	< 2cm – 34% >2cm – 63%

1 Weng memoli et al . , CHEST 2012

2 Rivera et al ., CHEST 2013

Diagnostic Yield Of bronchoscopy procedures

—Inverse Weighted Diagnostic Yield Overall and by Modality

Technology	Studies, No.	Weighted Proportion, %	95% CI	Q Statistic	Q *P* Value
VB	10	72.0	(65.7-78.4)	21.0	.01
ENB	11	67.0	(62.6-71.4)	13.3	.21
GS	10	73.2	(64.4-81.9)	63.8	< .0001
U	11	70.0	(65.0-75.1)	15.2	.12
R-EBUS	20	71.1	(66.5-75.7)	84.2	< .0001
All	39	70.0	(67.1-72.9)	119.4	< .0001

Wang Memoli et al., CHEST 2013

Analysis of bronchoscopy procedures for diagnosis of pulmonary nodules

Study	Sites / Patients	Yield / Sensitivity
AEGIS Trial [1]	28 sites / 639 patients	Overall – 69% < 2cm – 59% 2-3cm – 62% >3cm – 78%
AQuIRE Registry [2]	15 sites / 531 patients	Overall -64%

1 Silvestri et al . , NEJM 2015

2 Ost et al ., AJRCCM 2015

Bronchoscopic techniques for evaluation of GGO

Study	Characteristics	Outcome
Ikezawa et al ., Resp 2014	67 GGN Mean size 21mm	75% identified with EBUS 73% of these diagnosed
Ikezawa et al ., Ann Thorac Med 2017	169 GGN Mean size 23mm VBN Fluoro used for navigation	92% identified with EBUS 69% of these diagnosed

Bronchoscopic Sampling Techniques

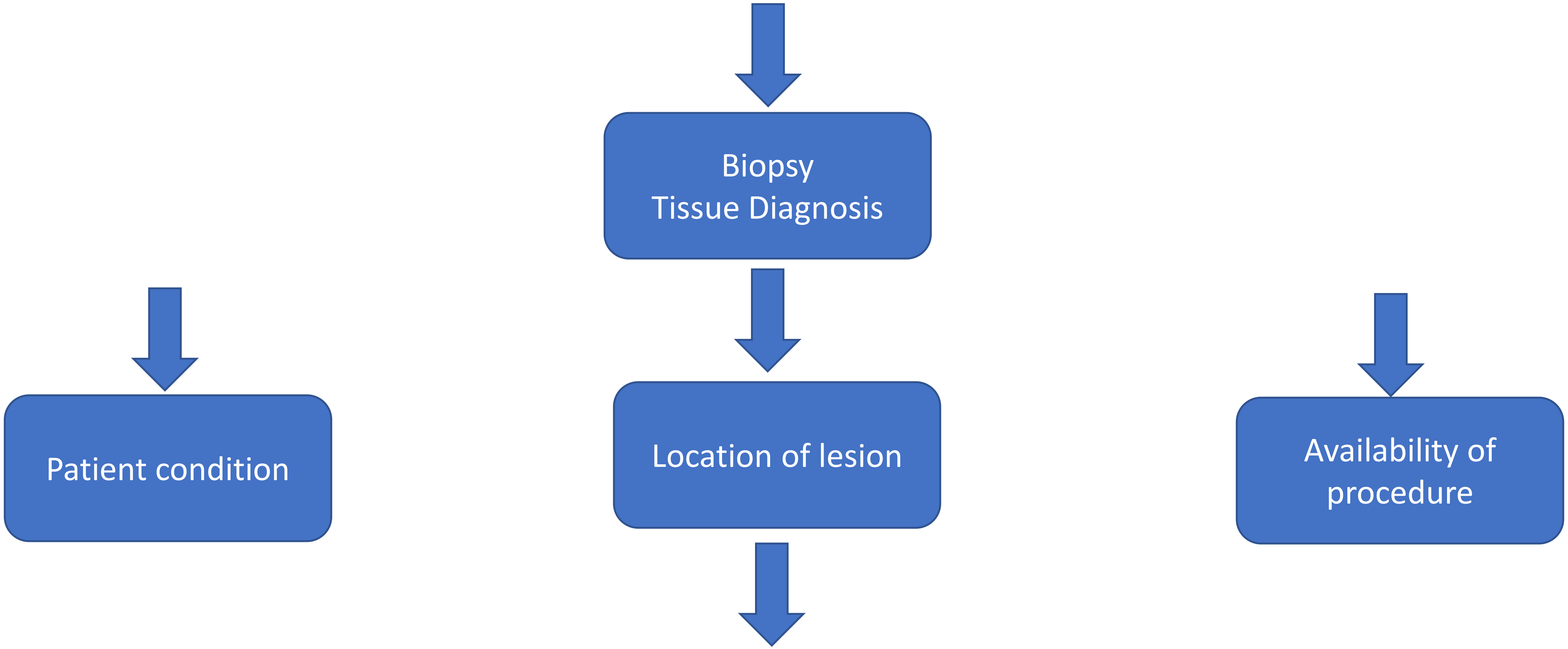
	Study	Comparison
Conventional Bronchoscopy	Rivera et al ., CHEST 2013 Mondoni M et al ., ERJ 2016	TBNA v/s Forceps biopsy v/s brushing 65% v/s 57% v/s 54% TBNA – 53%
Guided Bronchoscopy	Chao et al ., CHEST 2009 Chen et al ., Ann Am Thorac Soc 2014 Ost D E et al ., AJRCC 2016	TBNA use provided 17% higher yield Yield with TBNA was higher TBNA added 9.5% to diagnostic yield

Bronchoscopic techniques for pulmonary nodules

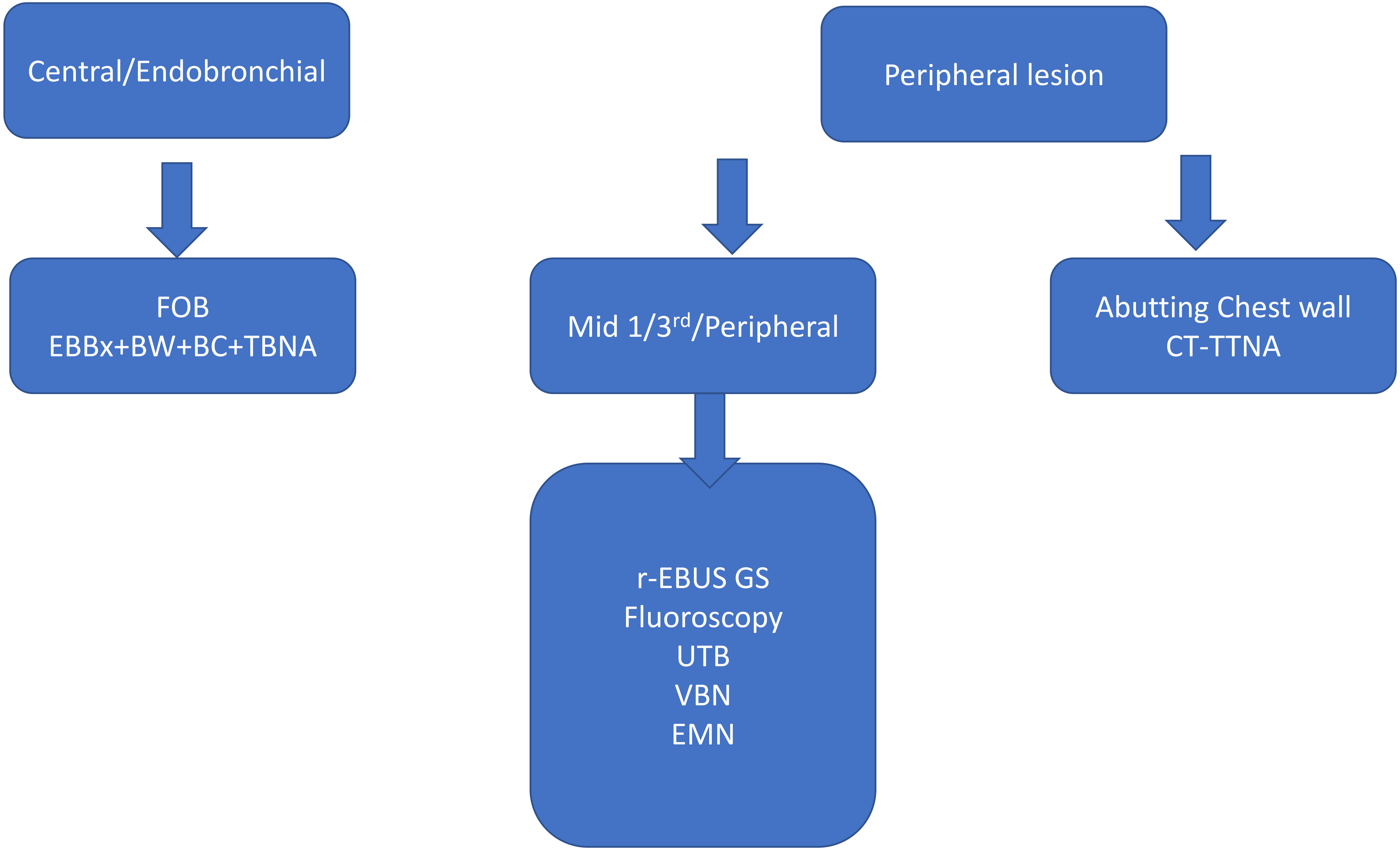
	Navigation(Get to the lesion)	Confirm position in the lesion	Real time sampling
FB	-	+	+
R-EBUS	-	+	-
VBN	+	-	-
ENB	+	-/+	-
BTPNA	+	-/+	-
CBCT + Aug Fluoro	+	+	+
Robotic bronchoscopy	+	+	+

Pulmonary Nodule On Imaging
The next question?

- Is it malignant?



Pulmonary Nodule On Imaging



Conclusion

- Bronchoscopy is procedure of choice for central/endobronchial lesions
- Yield of bronchoscopy overall is between 50-70% for peripheral nodules
- Yield from various procedure depends on patient selection, characteristic of lesion
- Most of the evidence is from high volume centres with expertise ? generalisability