TOGA:
“Tissue is the issue”

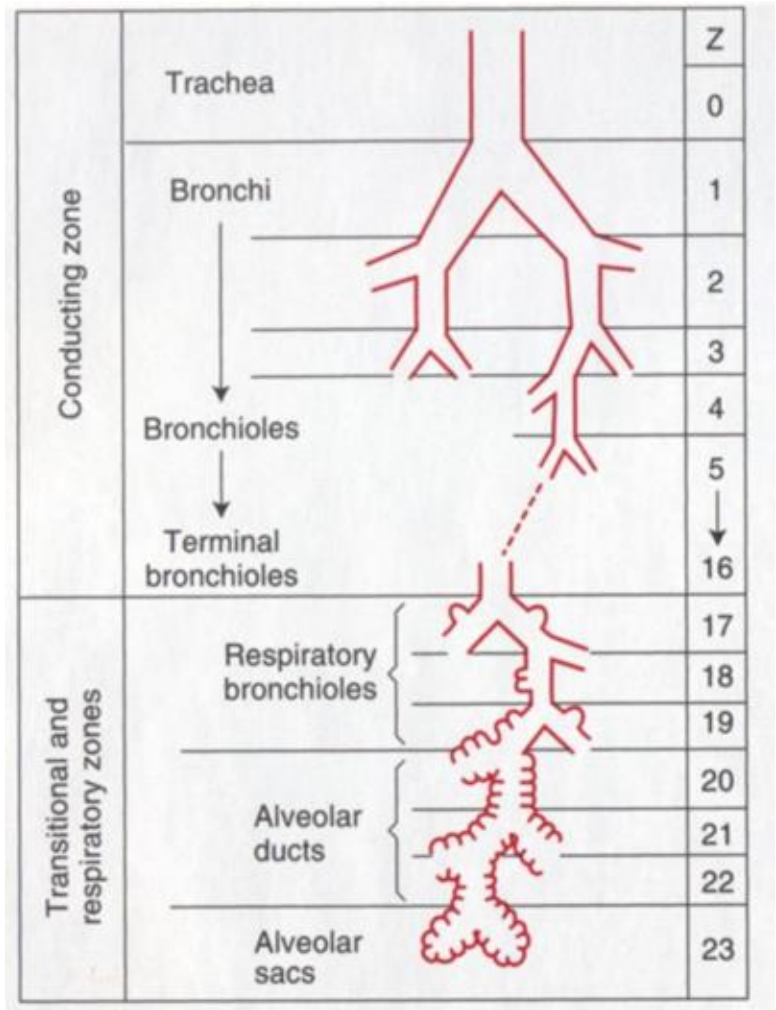
Reinier Wener

Department of pulmonary diseases

Reinier.wener@uza.be

Endobronchial techniques

- Conventional bronchoscopy
- (Ultra)thin bronchoscopy
- RP EBUS
- VBN and ENB
- Robotic bronchoscopy


Conducting zone
Transitional and respiratory zones
Trachea
Bronchi
Bronchioles
Terminal bronchioles
Respiratory bronchioles
Alveolar ducts
Alveolar sacs
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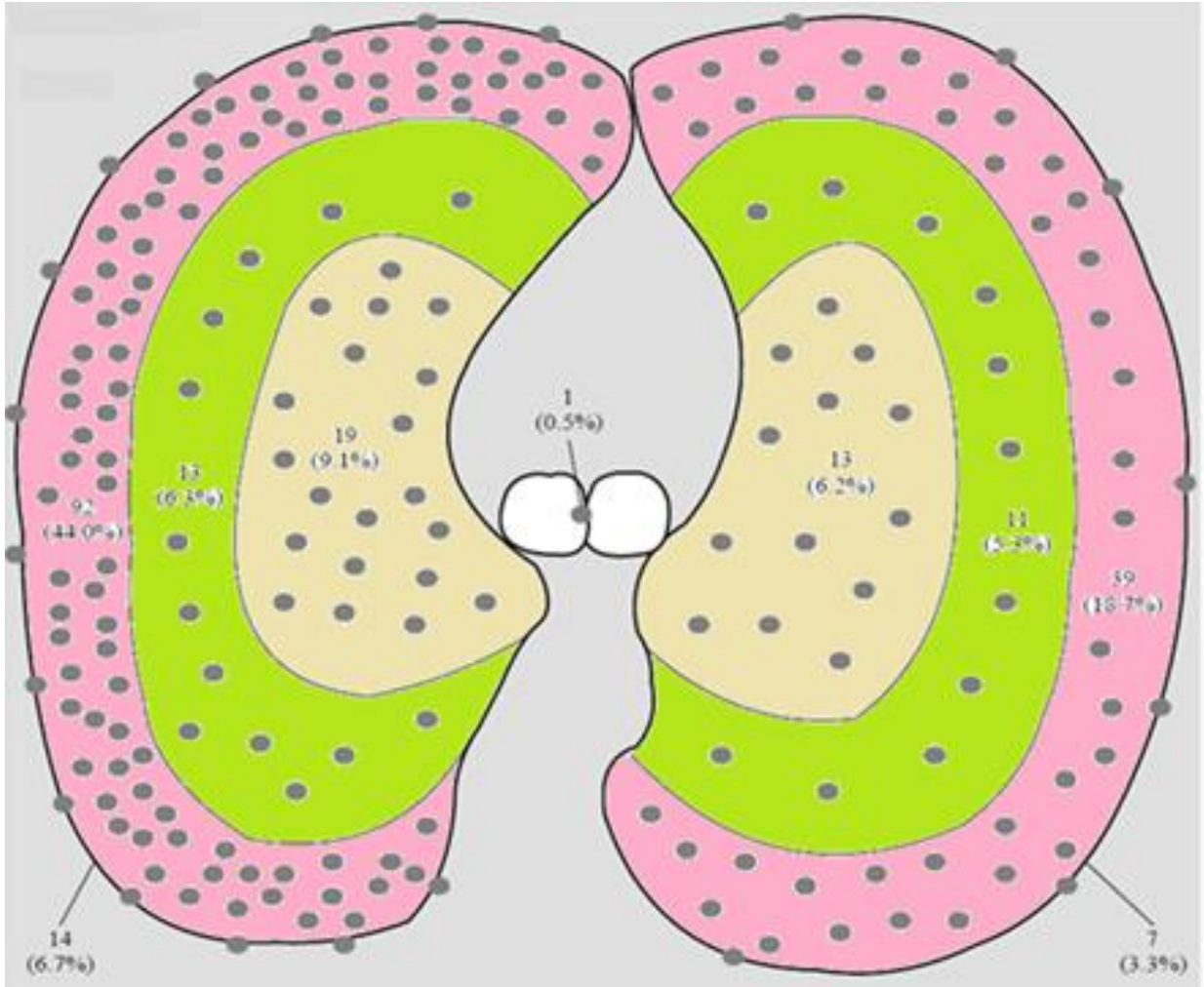
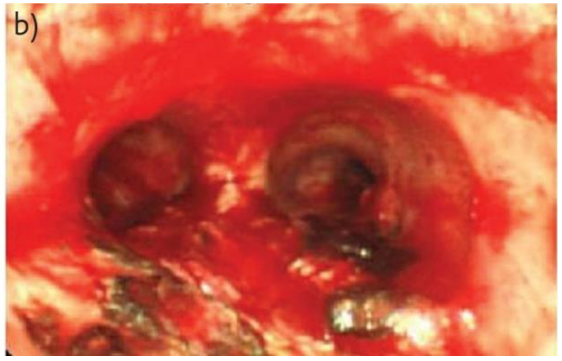

1 (0.5%)
19 (9.1%)
13 (6.3%)
13 (6.2%)
14 (6.7%)
7 (3.3%)

Conventional bronchoscopy era

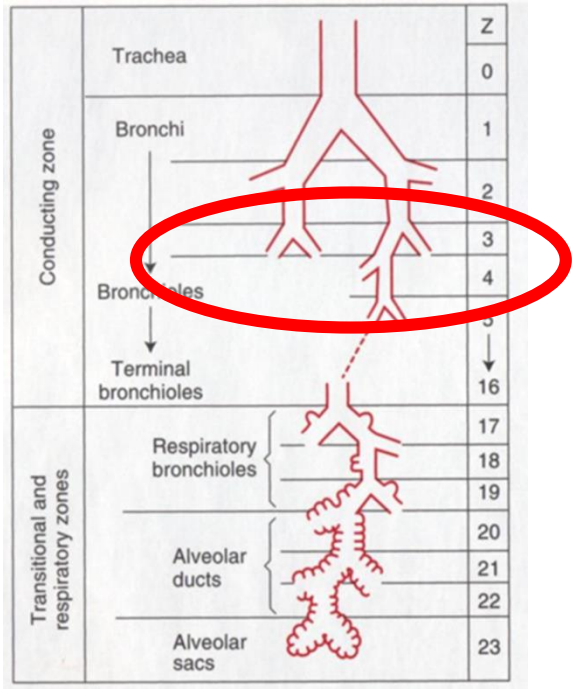
Conventional bronchoscopy

- Direct forceps biopsy sensitivity 74%
- Submucosal and peribronchial lesions are diffucult to diagnose by biopsy alone. Naald aspiratie verhoogd de diagnostiche opbrengst
- Sensitivity of central and visible endobronchial, submucosal en peribronchial lesions is 88%.



Chest. 2013;143:e142S-e165S

Conventional bronchoscopy



- 5,9 mm bronchoscope (standard) reaches 3th or4th generation bronchi

- Additional techniques: fluoroscopy, brush, transbronchial biopsy, transbronchial needle aspiration, alveolar lavage

- Laesion > 2 cm: 63%
- Laesion < 2 cm: 34% Chest. 2013;143:e142S-e165S

- Factors: size, location (yield 31% middle third, 14% peripheral third), bronchus sign (TBB met bronchus sign 59% zonder 18%), sampling techniques

Conventional bronchoscopy

- **Conclusion: conventional bronchoscopy has major limitations in diagnosing PPL's with exeption of visible lesions**

- Diagnostic yield 37,7 % for PPL's without bronchus sign
- Diagnostic yield 73% met bronchus sign

- Diagnostisic sensitivity of conventional bronchoscopy on average just 63,7 % in experienced hands.

Chest. 2018;154:1035-1043, Am J Respir Crit Care Med. 2016;193:68-77

CT guided biopsy

- CONVINCINGLY BETTER in diagnosing PPL's

- Pooled diagnostic accuracy 92%. Sens 92,1%; spec 100%; rare false positives
- Complication rate: Major complications were seen in 5.7% (95% CI 4.4–7.4%) of core biopsies and 4.4% (95% CI 2.7–7.0%) of fine needle aspirations (FNA)
- The risk of any pneumothorax was 25.3% (95% CI 22.2-28.6%) in core biopsy and 18.8% (95% CI 14.6-23.9%) in FNA

J Thorac Dis. 2015;7:S304-316; Eur radiol 2017;27:138-148

CT guided biopsy

- Hemorrhage: complicating 1.0% (95% CI 0.9-1.2%) of biopsies, 17.8% (95% CI 11.8-23.8%) of patients with hemorrhage required a blood transfusion

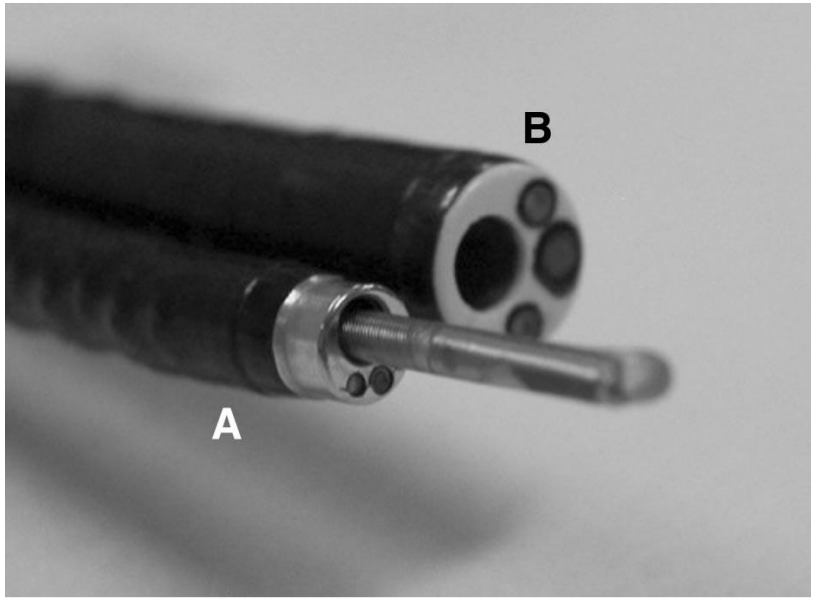
- The complication rate after forceps biopsy of PPLs was 1.79% including 0.63% of pneumothorax and 0.73% of hemorrhage.

- Overall, the complication rate of CT-TTNA is higher than conventional bronchoscopy in diagnosing PPLs

Ann intern Med. 2011;155:137-144, Respirology 2012;17:478-485

Current era…

Thin/Ultrathin bronchoscopy



- Ultrathin vs conventional diagnostic yield

  60% vs 54.3 % Yamamoto Lung Cancer. 2004;46:43-48.
- Bronchscope 3,5 mm outer and 1,7 inner

  diagnostic yield 73,5 %
- Ultrathin vs thin (randomized) diagnostic yield 74 vs 59% Am J Respir Crit Care Med. 2015;192:468-476

TABLE 2. Diagnostic Yield of EBUS-TBB with Thin Bronchoscope According to Lesion Size

	Lesions Diagnosed/Lesions Examined		
Lesion Size	Malignant	Benign	Total
<20 mm	4/6 (67)	1/8 (13)	5/14 (36)
>20 mm	31/38 (82)	13/19 (68)	44/57 (77)
Total	35/44 (80)	14/27 (52)	49/71 (69)

J Thorac Oncol. 2009;4:1274-1277.

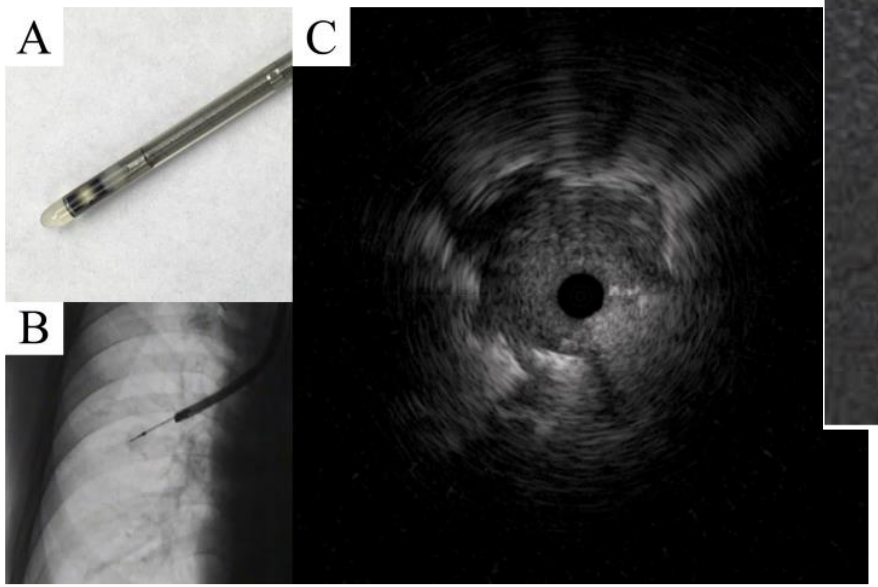
TABLE 3 Diagnostic yield of thin bronchoscopy according to lesion size

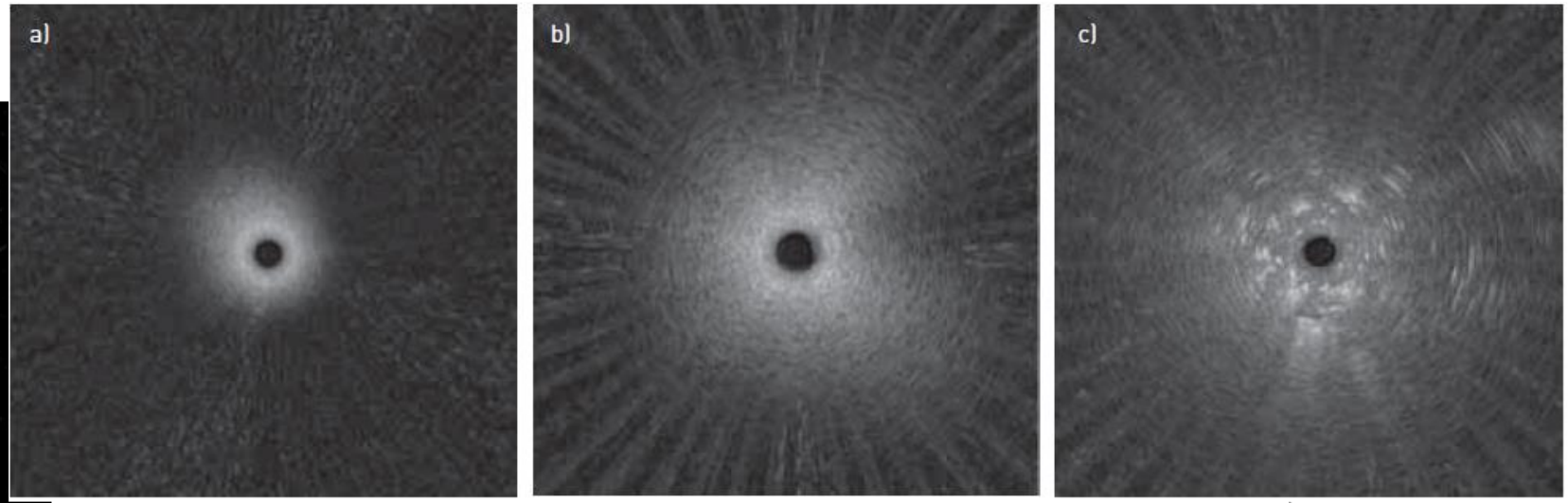
Lesion size	Lesions diagnosed/lesions examined		
	Malignant	Benign	Total
<20 mm	10/13 (77)	3/10 (30)	13/23 (57)
⩾20 mm	40/55 (73)	15/20 (75)	55/75 (73)
Total	50/68 (74)	18/30 (60)	68/98 (69)

Eur Respir J. 2008;32:465-471.

Radial probe EBUS

- Tissue contact
- Characterisation tissue density surrounding the
- Alveolar airspace: snowstorm
- GGO blizzard sign





Eur Respir J 2015;45:1661-1668

Radial probe EBUS

- Mismatch positioning and biopsy location.

- Development: GS

Radial probe EBUS

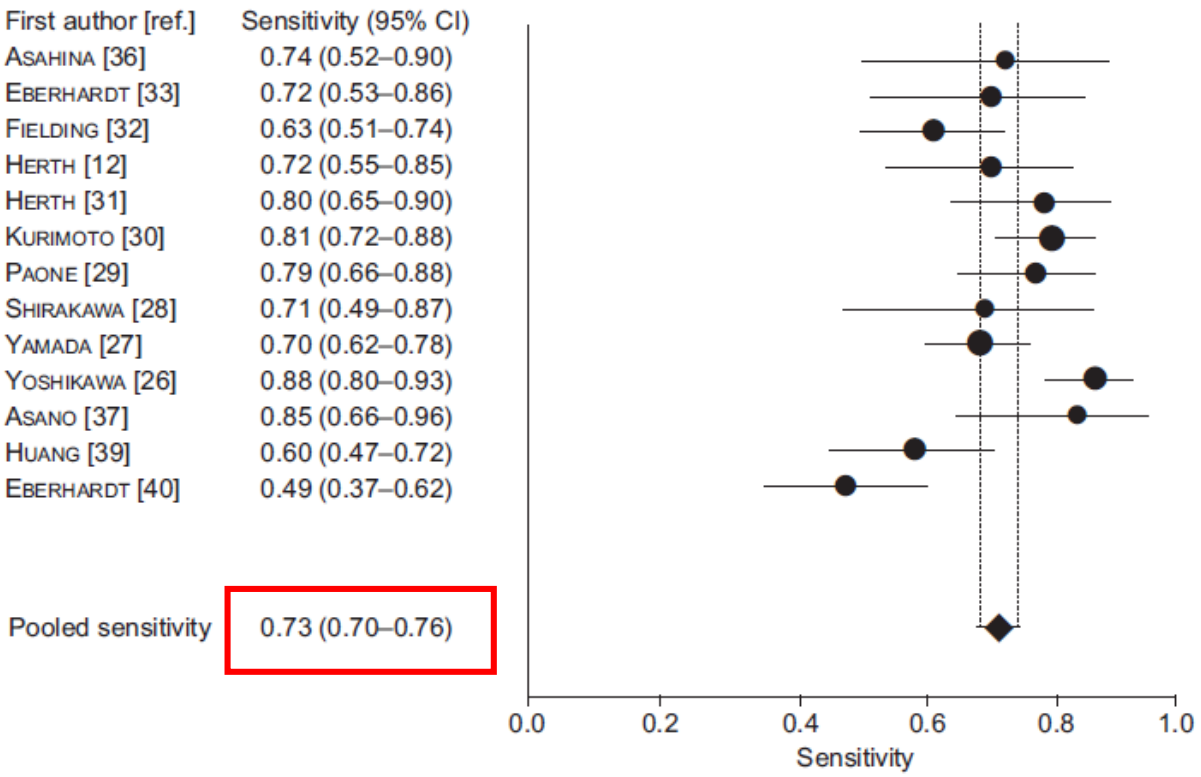


Table 2—*Inverse Weighted Diagnostic Yield Overall and by Modality*

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

See Table 1 legend for expansion of abbreviations.

Eur Respir J. 2011;37:902-910.

Chest. 2012;142:385-393

Radial probe EBUS

- Diagnostic yield: location, lesion size, location probe vs target

- Factors influencing localization:

- Size PPL <20 mm
- Distance to hilum >50 mm

- Highest predictor yield: location van de RP EBUS probe vs target

Radial probe EBUS, conclusions

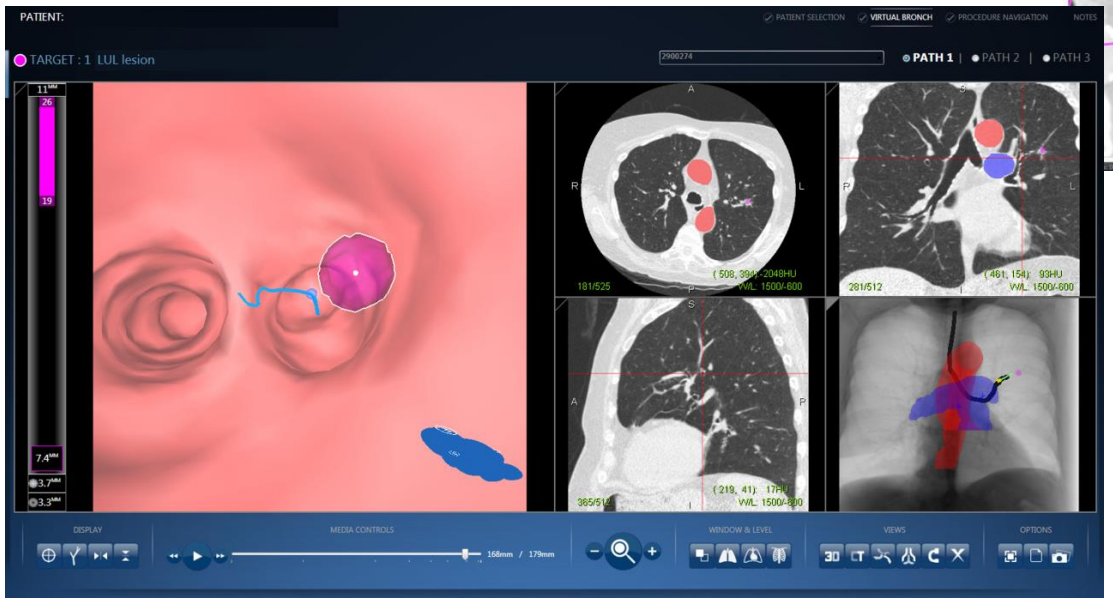
- RP EBUS is NOT a navigation tool
- Often used in combination met navigation tools (VBN en ENB)
- NO real time biopsy visualisation
- Dexterity of endoscopist has a big role
- Learing curve
- Most RP EBUS data from “expert centers”
- Generalizability?

Am J Respir Crit Care Med. 2007;176:36-41.

Future?!

Navigation bronchoscopy

- Virtual bronchoscopic navigation
- ENB



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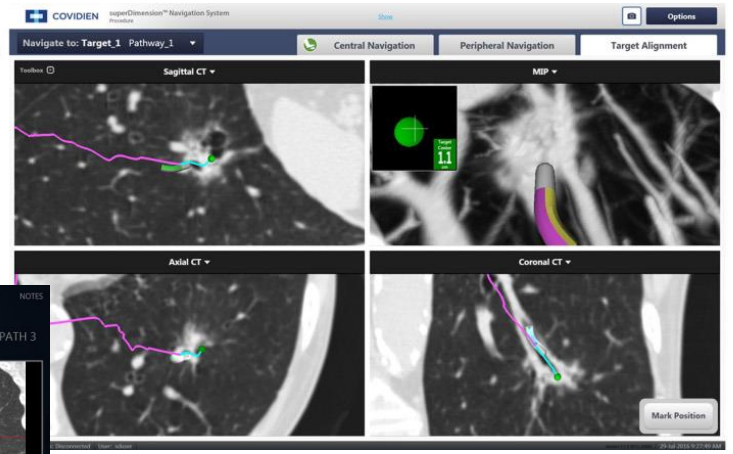

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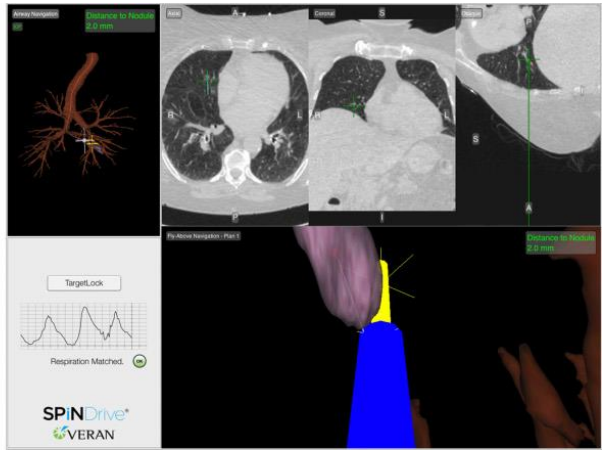


Navigation bronchoscopy, VBN

TABLE 3. DIAGNOSTIC YIELD ACCORDING TO EACH SAMPLING PROCEDURE

	VBNA	NVBNA	*P* Value
Total	112/167 (67.1)	100/167 (59.9)	0.173
Forceps biopsy	98/167 (58.7)	89/167 (53.3)	0.321
Forceps cytology	47/119 (39.5)	47/116 (40.5)	0.873
Brushing	65/143 (45.5)	65/136 (47.8)	0.695
Washing	41/141 (29.1)	37/133 (27.8)	0.818
Lobe			
Right upper	39/48 (81.3)	25/47 (53.2)	0.004
Posterior–anterior radiograph			
Invisible	24/38 (63.2)	17/42 (40.5)	0.043
Location			
Peripheral	77/119 (64.7)	63/121 (52.1)	0.047

Am J respir crit Care Med. 2013;188:327-333.

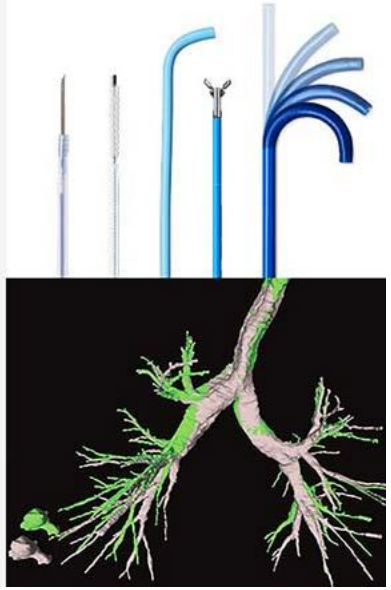
Table 3 Diagnostic yield according to lesion size in the per-protocol population

	Bronchoscopic diagnosis		
Lesion size	**VBNA**	**NVBNA**	**p Value**
<20 mm	44/58 (75.9)	35/59 (59.3)	0.056
20–30 mm	36/41 (87.8)	29/36 (80.6)	0.382
Total	80/99 (80.8)	64/95 (67.4)	0.032

Thorax 2011;**66**:1072–1077. doi:10.1136/thx.2010.145490

Navigation bronchoscopy, ENB

- Virtual 3D reconstructions + electromagnetic sensor tracked during bronchoscopy.
- Position sensor superimosed onto virtual image



Navigatie bronchoscopie ENB

CT Scan

- DICOM data

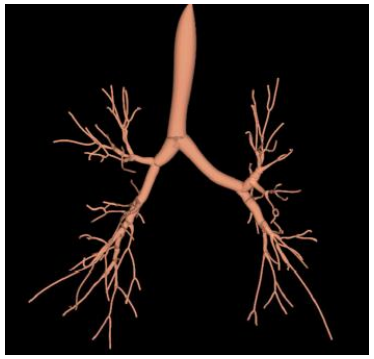
Plan

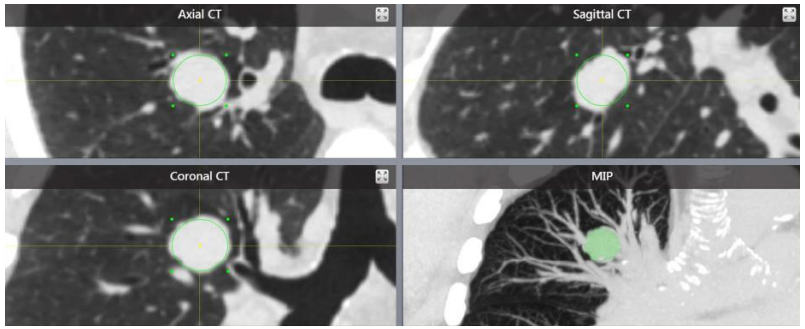
- Create a plan for the ENB procedure

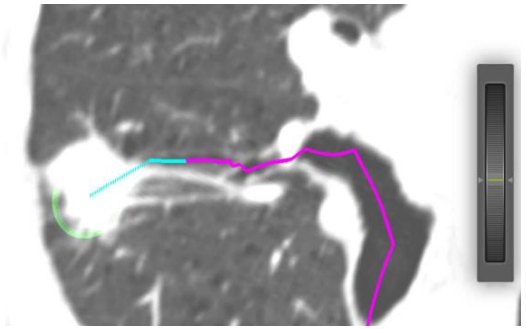
Navigate

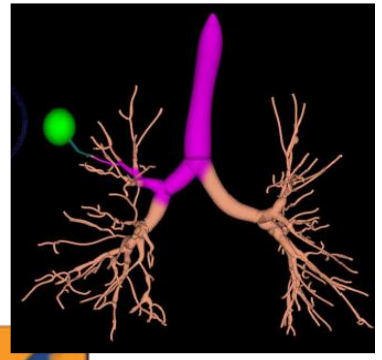
- Sample
- Localize

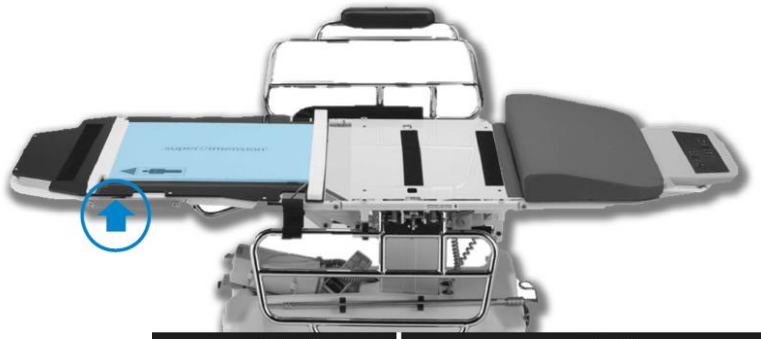
Navigation bronchoscopy, ENB

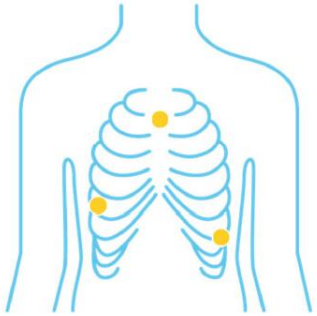


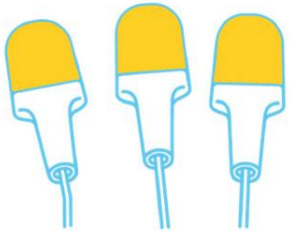


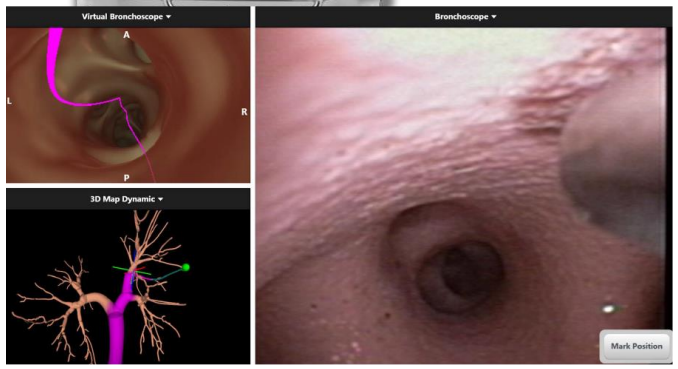


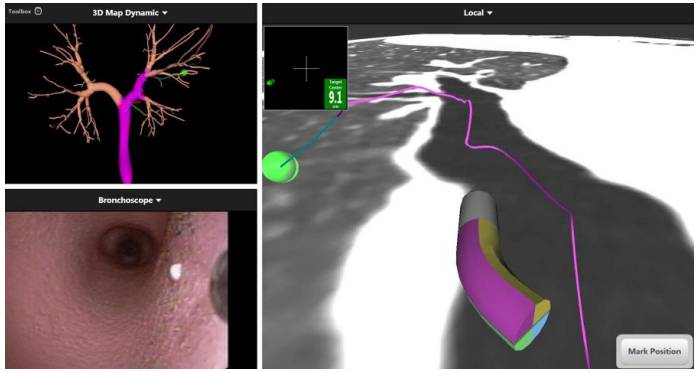


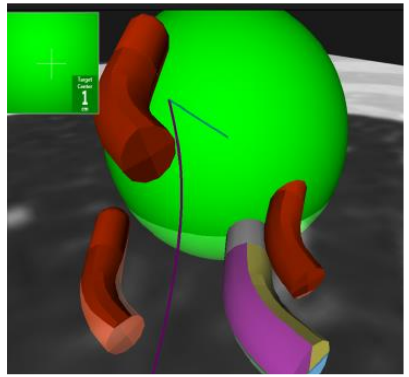












Navigation bronchoscopy, ENB, indications

- SAMPLING TARGET LESIONS
- Transthoracic needle aspirations (high pneumothorax rate >20%)
- Placement of fiducial markers for limited stage lung cancer with SBRT
- Dyemarking prior to surgery
- Foreign body removal in the distal airway

Navigation bronchoscopy, ENB

- Early reports ENB (2014); diagnostic yield van 64.9% (95% CI 59.2–70.3)
- NAVIGATE trial, pragmatic prospective multicenter single arm cohort
- 12 month diagnostic yield 73%
- Complications:

  Pneumothorax requiring intervention 2,9% (35/1215). Any pneumothorax 4.3%

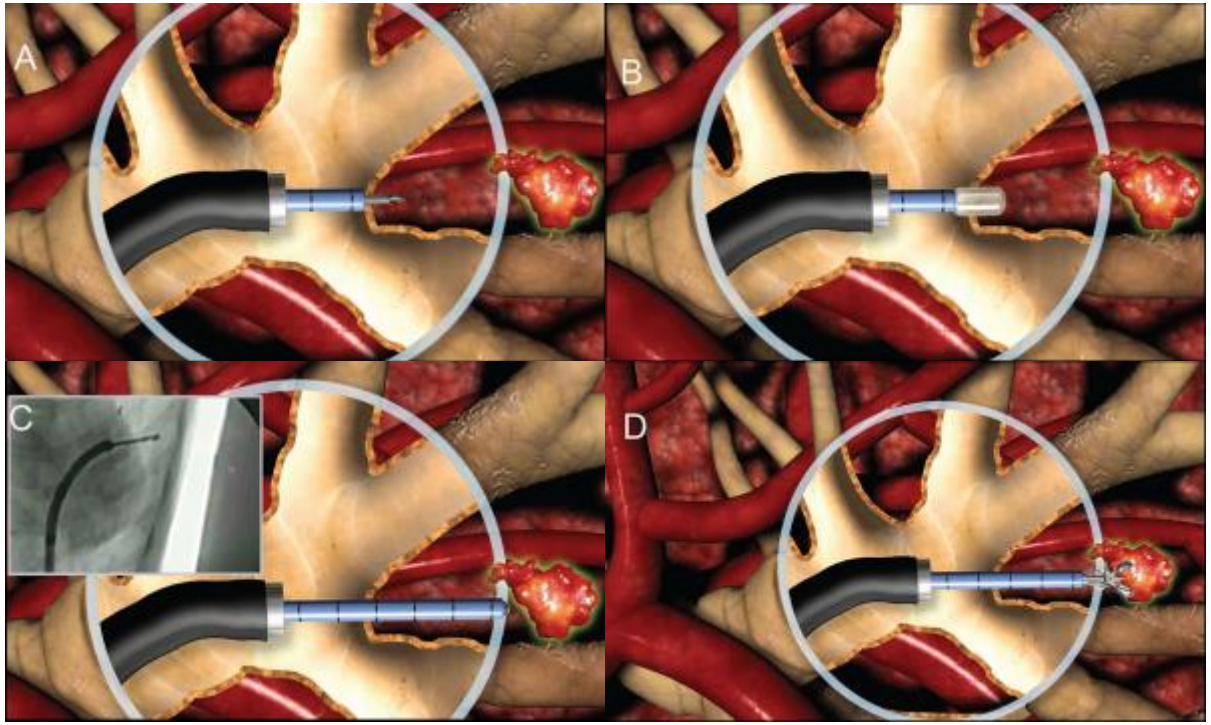
  Bronchopulmonary hemorrhage 1,5% grade 2 or higher

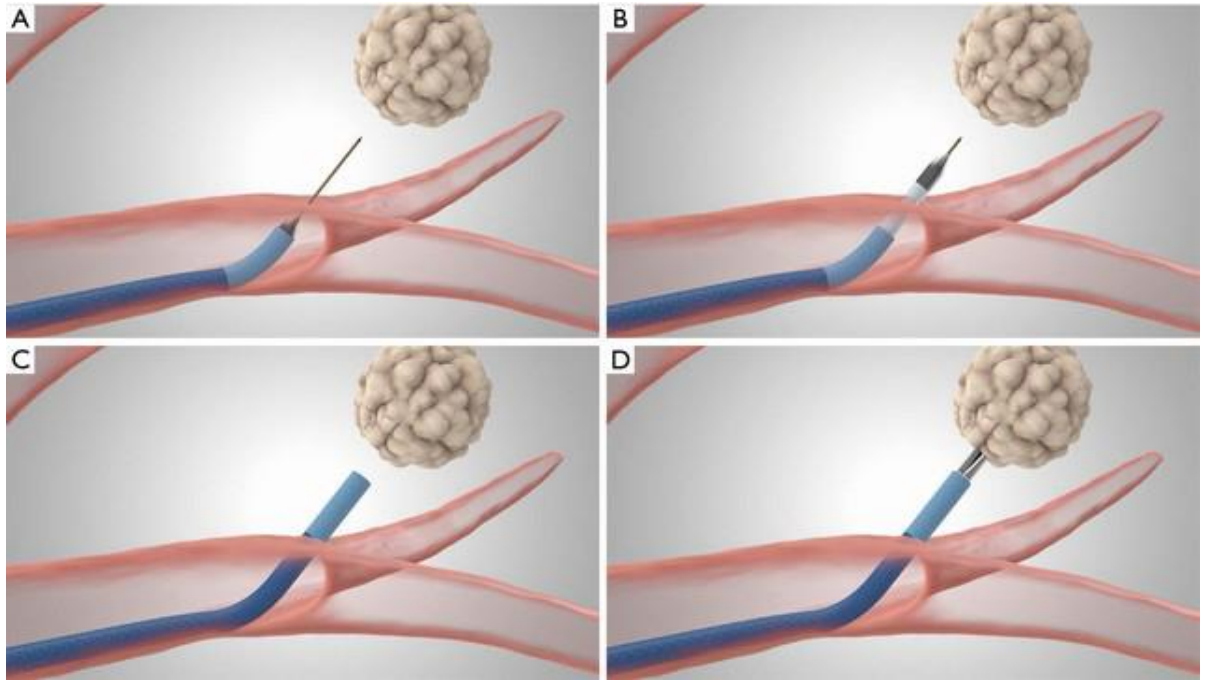
  Respiratory failure grade 4 or higher 0,7%

  1 anesthesia related death due to grade5 hypoxic respiratory failure in pt with multiple comorbidities

J Thorac Oncol. 2019 Mar;14(3):445-458

Trans Bronchial Access Tool





Case series: feasibility study 10/12 (83%) successful tunneling (no complications), second report 5/6 patients successful biopsie (2 pneumothorax), 8/12 diagnosis, TBAT + CBCT +REBUS 7/7 diagnosis

Thorax. 2015;70:326-332; Respiration. 2016;91:302-306; J Thorac Dis. 2018;10:5953-5959

Cone-beam computed tomography (CBCT)

- New modality; 2D projecties + volumetric projections, C-arm
- Advances: lower costs and radiation dose

- CBCT + conventional bronchoscopy – RP EBUS

  diagnosic yield 70%

- Guidance CBCT vs fluoroscopy

  absolute 20% increase in diagnostic yield

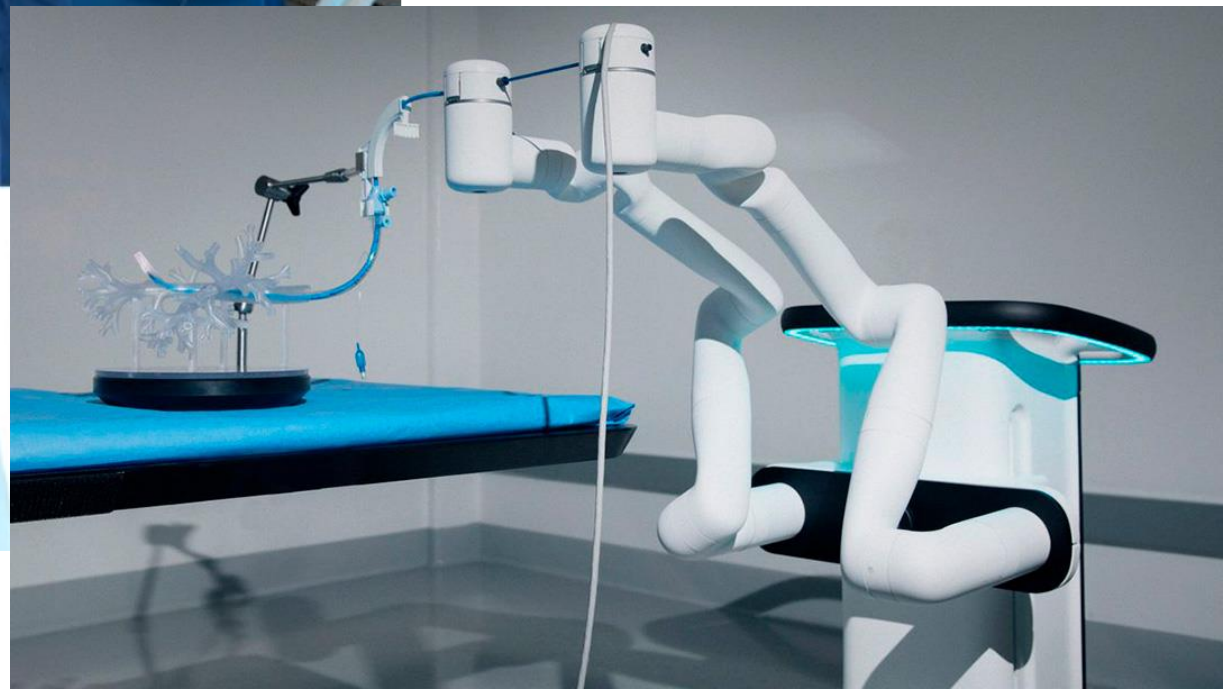
(Far) future??

Robotic bronchoscopy

A

B

C



Robotic bronchoscopy

- Monarch system 97% (65/67) succeded in acquiring tissue
- Human cadavers using ENB and RP EBUS for target localization

Chest annual meeting 2018

- Intuitive: 30 pts with PPLs of 12.5 mm.
- Diagnostic yield was 83% No device related adverse events

Chest annual meeting 2017

- Pro: Deeper in the airways, ability to maintain static position close to target lesion, future opportunities for treatment
- Con: Unexpected events during intervention, cost effectiveness

Diagnostische yield

- MAXIMUM with all available and combined techniques

73%

Diagnostische yield

- MAXIMUM with all available and combined techniques

73%

Acceptable??

Diagnostische yield

- MAXIMUM with all available and combined techniques

73%

Acceptable??

NO!!

Basic principles for accurate diagnosis of PPL's

1. Selecting the correct airway
2. Approaching the target as close as possible
3. Confirming the location of the target before sampling
4. Sampling the same place as confirmed earlier

Basic principles for accurate diagnosis of PPL

1. Selecting the correct airway → VNB en ENB
2. Approaching the target as close as possible → ultrathin bronchoscopy, robotic bronchoscopy
3. Confirming the location of the target before sampling → RP-EBUS and CBCT
4. Sampling the same place as confirmed earlier → real time sampling

Thank you for your attention.

Reinier.wener@uza.be