TECHNIQUES FOR SAMPLING PERIPHERAL LESIONS

Michael J. Simoff, MD, FACP, FCCP
Director, Bronchoscopy and Interventional Pulmonology
Director, Lung Cancer Screening
Pulmonary and Critical Care Medicine
Henry Ford Medical Center
Professor of Medicine, FTA
Wayne State University of Medicine
Detroit, Michigan

DISCLOSURES

- Medical Consultant – Intuitive Surgical Robotics
- Medical Consultant – Gongwin Biopharm
- Medical Consultant – Spin@
- Grants:
  - NCI/NIH
    - "Center for Research to Optimize Precision Lung Cancer Screening in Diverse Populations."
  - Michigan Department of Health and Human Services
    - "Smoking cessation and lung cancer screening"

HENRY FORD MEDICAL CENTER
Detroit, Michigan USA

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THE HUMAN LUNG

- 22-24 generations
- >100,000 bronchi, bronchioles
- 1500 miles of airways
- 300-500 million alveoli
- 0.3mm in diameter
- Surface area $70m^2$
- Capillaries 616 miles end to end

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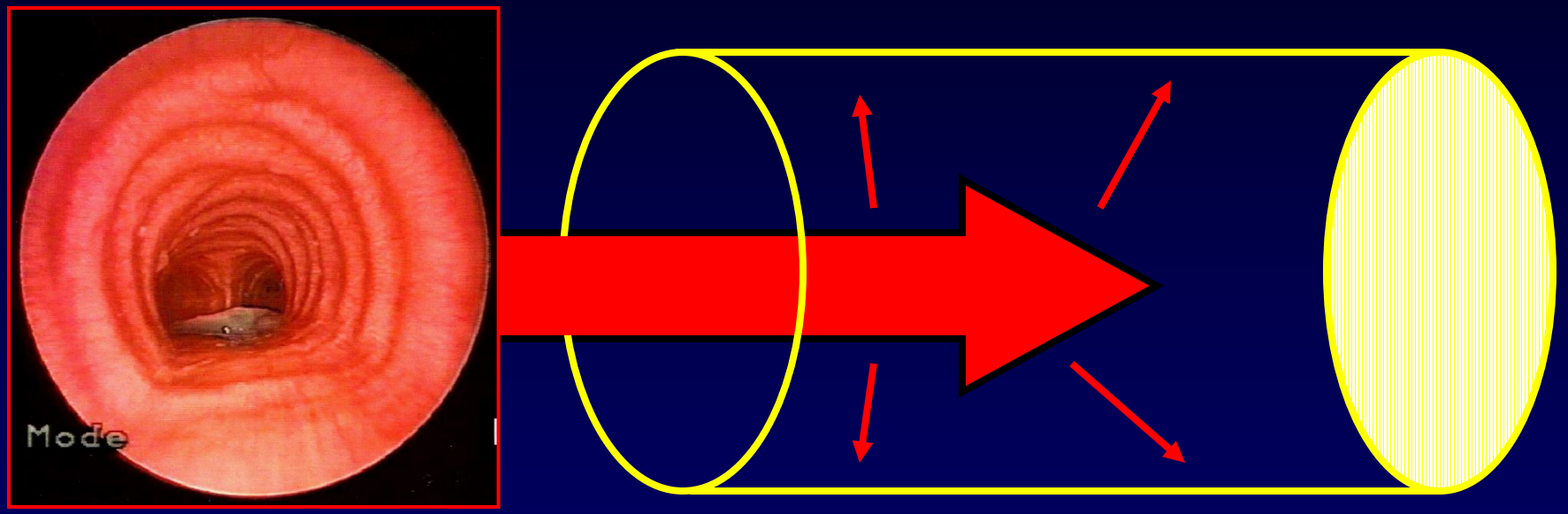
WHITE LIGHT BRONCHOSCOPY



Superficial airway evaluation

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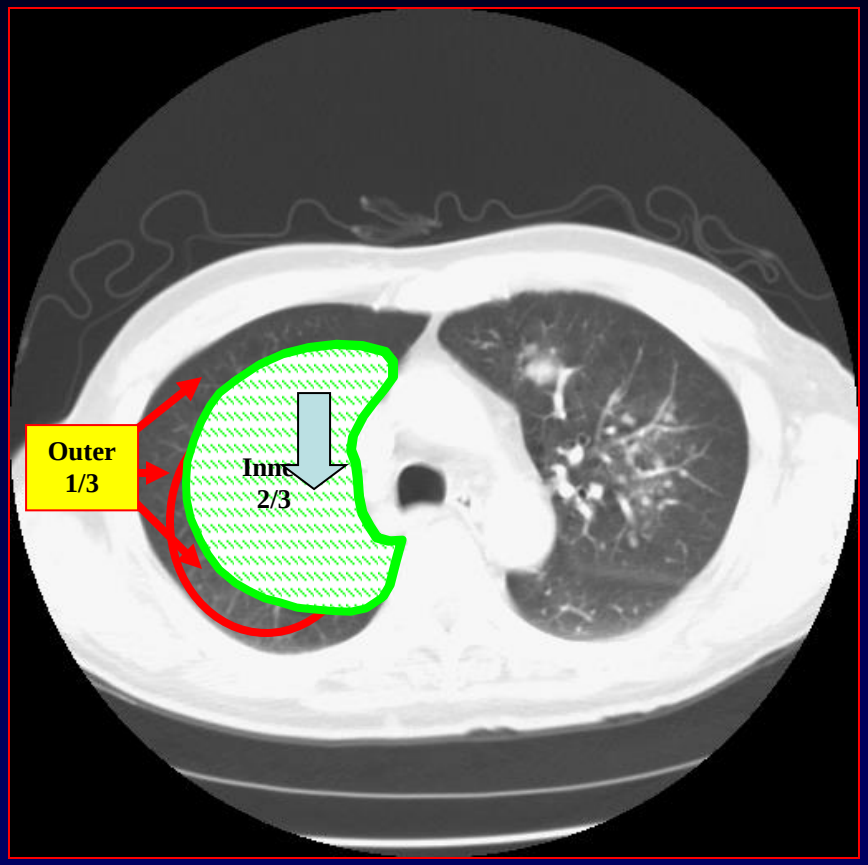
NODULE

- ≤3 cm in short axis
- Surrounded by aerated lung
- Identify location:
  - Inner 2/3 of lung
  - Outer 1/3 of lung
  - Lobe / Segment
- Air bronchogram through lesion
- Visible airway to lesion



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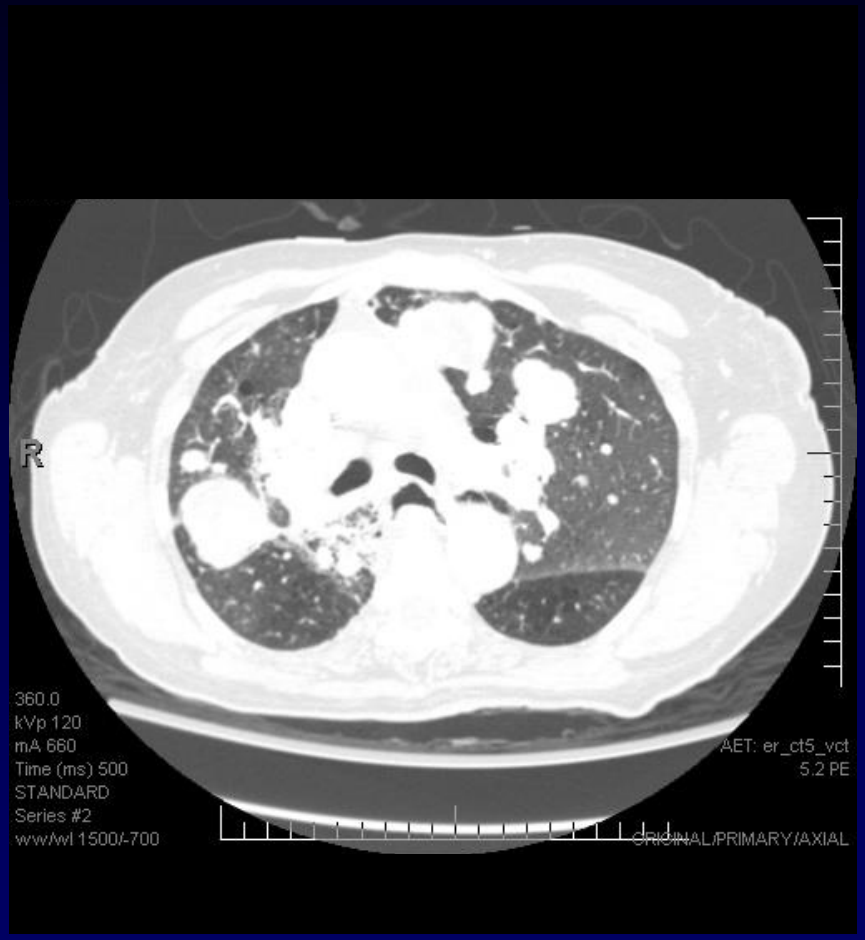
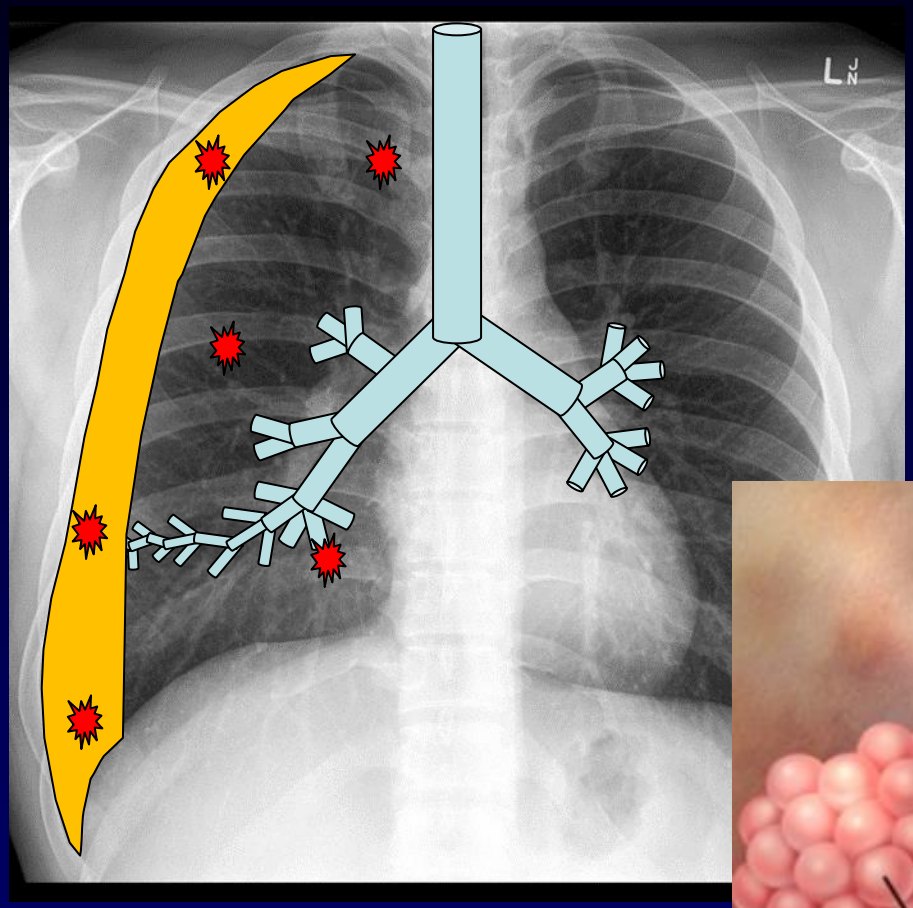
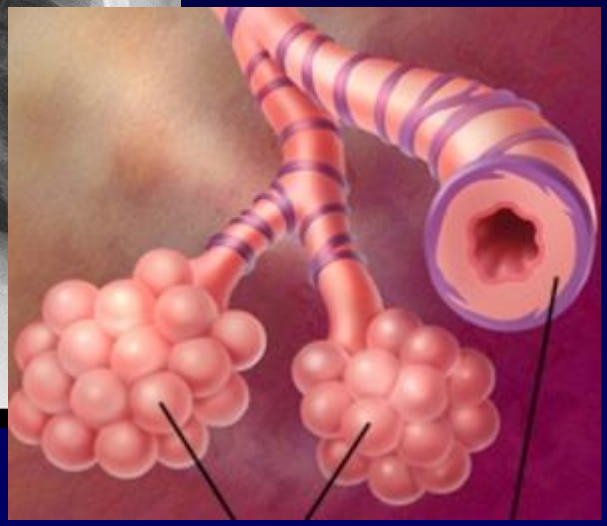
MASS

- Greater than 3 cm
- Identify location:
  - Inner 2/3 of the lung
  - Outer 1/3 of the lung
  - Lobe / Segment
- Air bronchogram through lesion
- Visible airway to lesion
- Atelectasis beyond lesion
- Involves mediastinal structures
- Involves vascular structures



WHERE ARE TUMORS AS THEY RELATE TO THE AIRWAYS?





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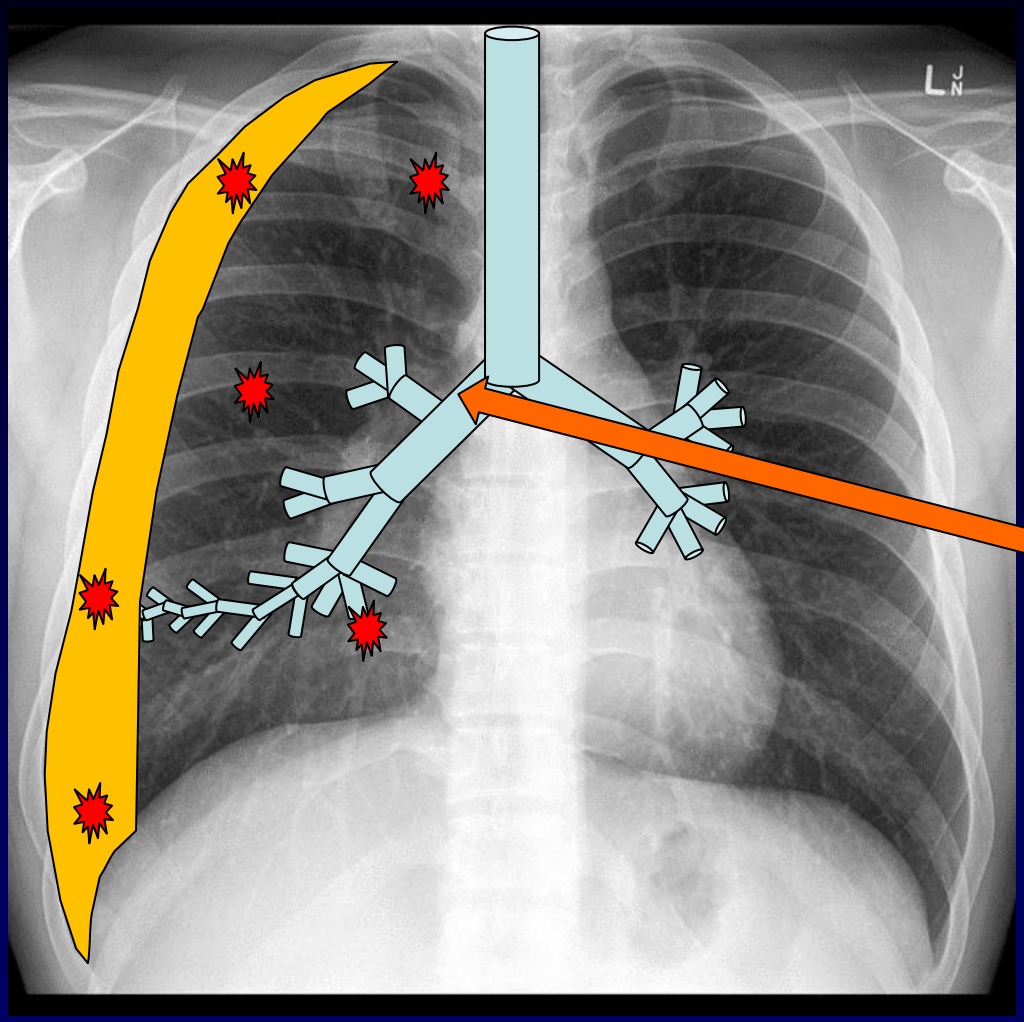
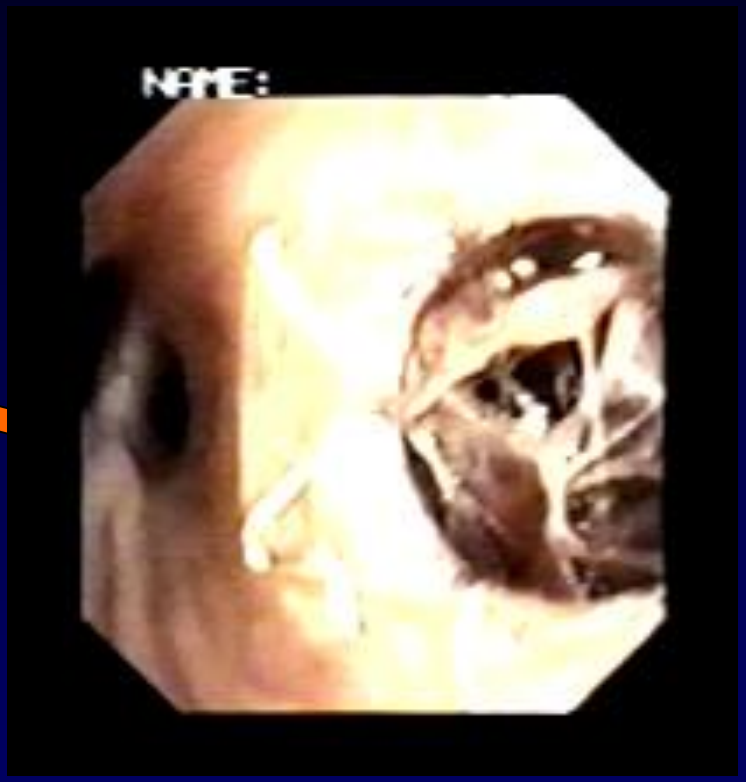
LUNG AND THE CENTRAL AIRWAYS





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ROBOTIC BRONCHOSCOPY TAKES US TO NEIGHBORHOODS NOT ADDRESSES

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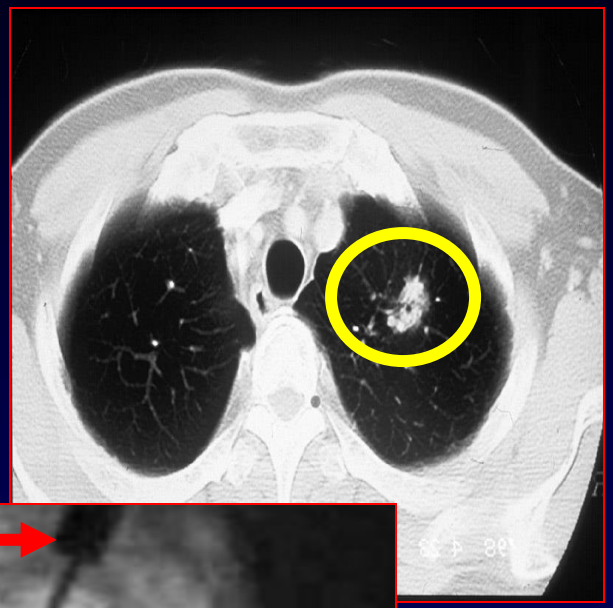
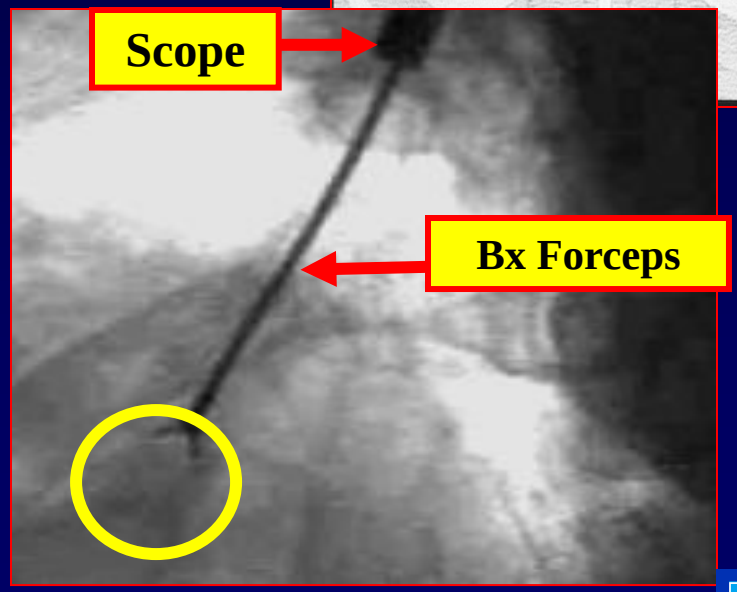
TRANSBRONCHIAL BIOPSY OF SPN

- Peripheral lesions are beyond bronchoscopic visualization
- Sampling techniques are guided using fluoroscopy
- Lesions that are $\leq$ 2 cm not visible with fluoroscopy





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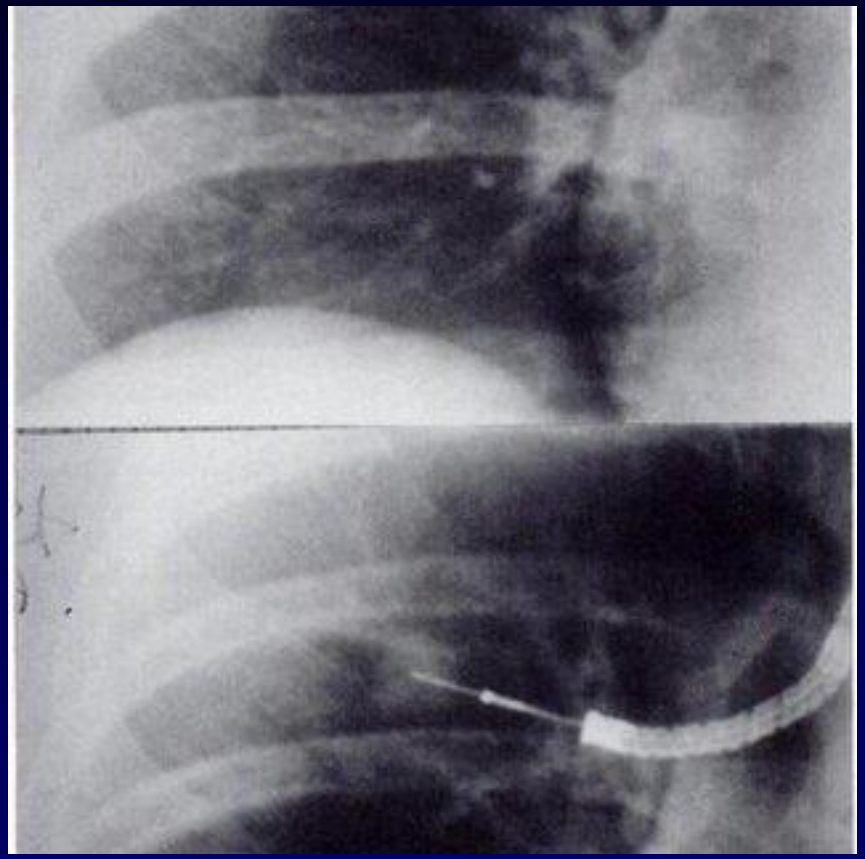
TRANSBRONCHIAL NEEDLE



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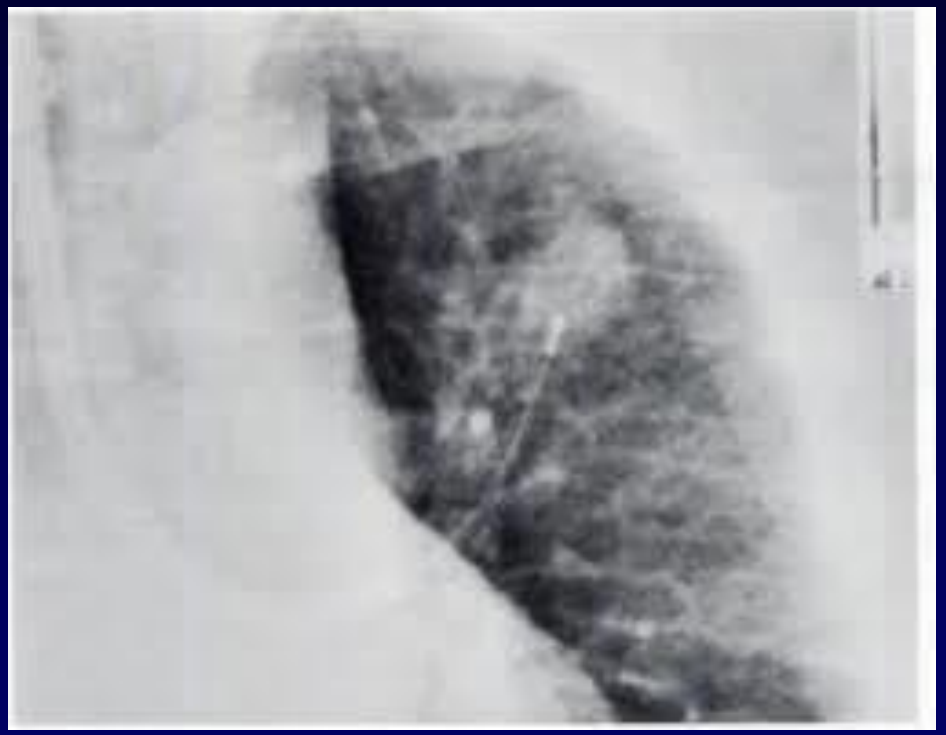
CYTOLOGY BRUSHING



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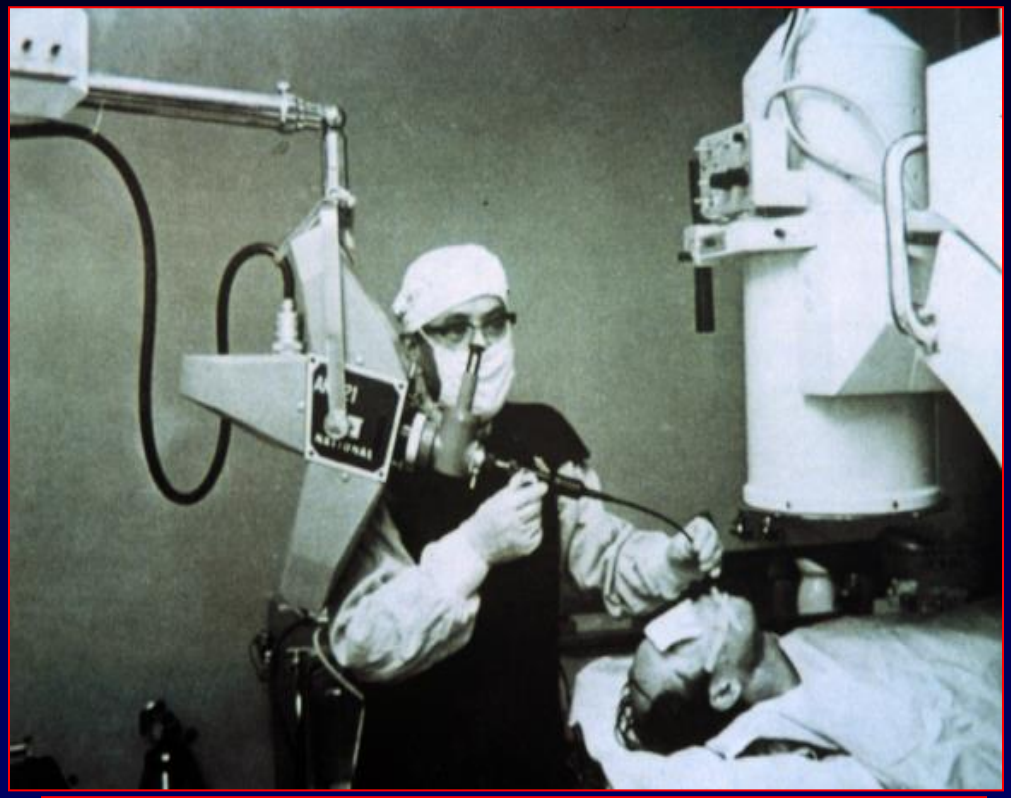
BRONCHOSCOPY FOR PERIPHERAL PULMONARY NODULES



Unchanged for previous 40 years

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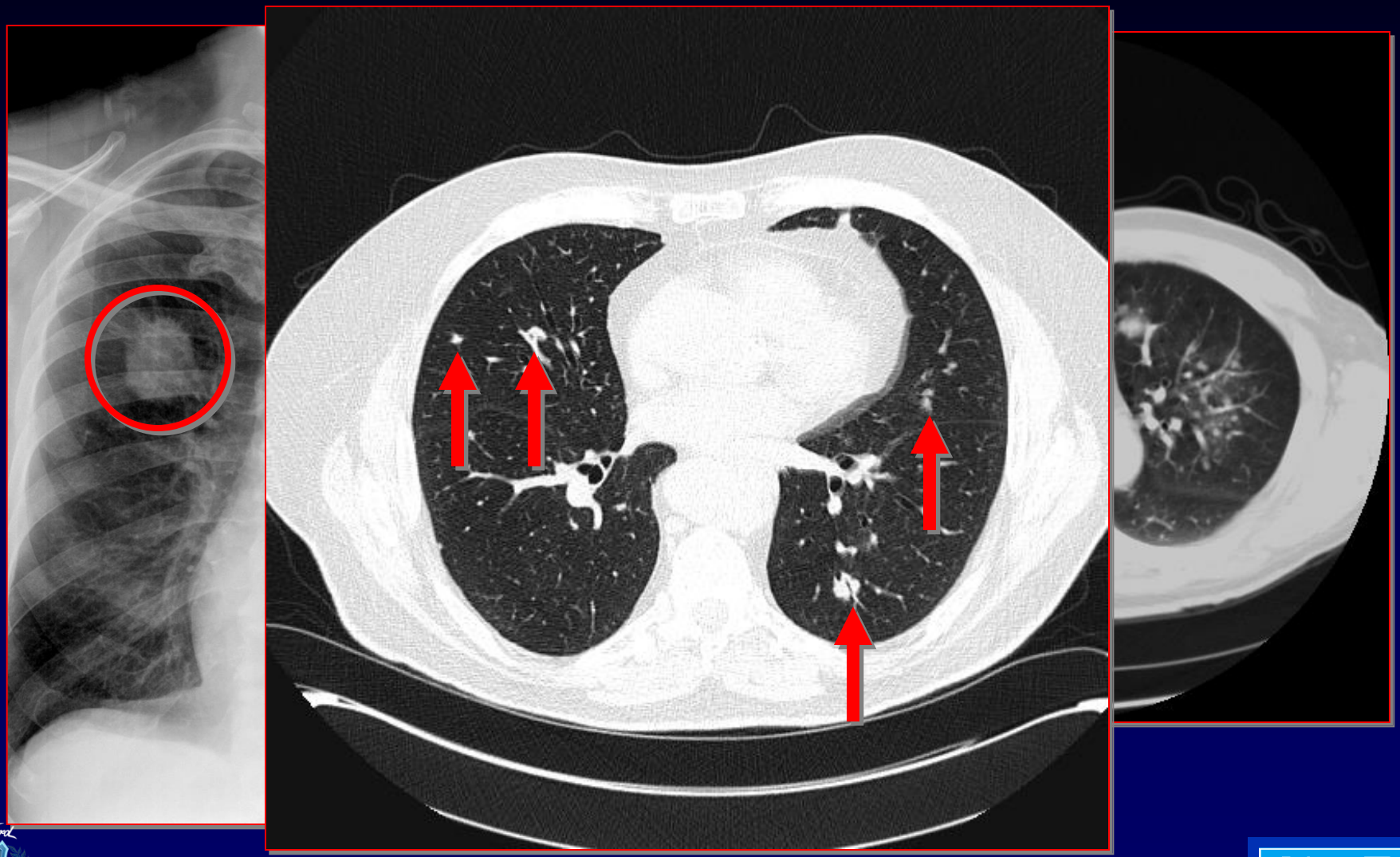
SOLITARY PULMONARY NODULES



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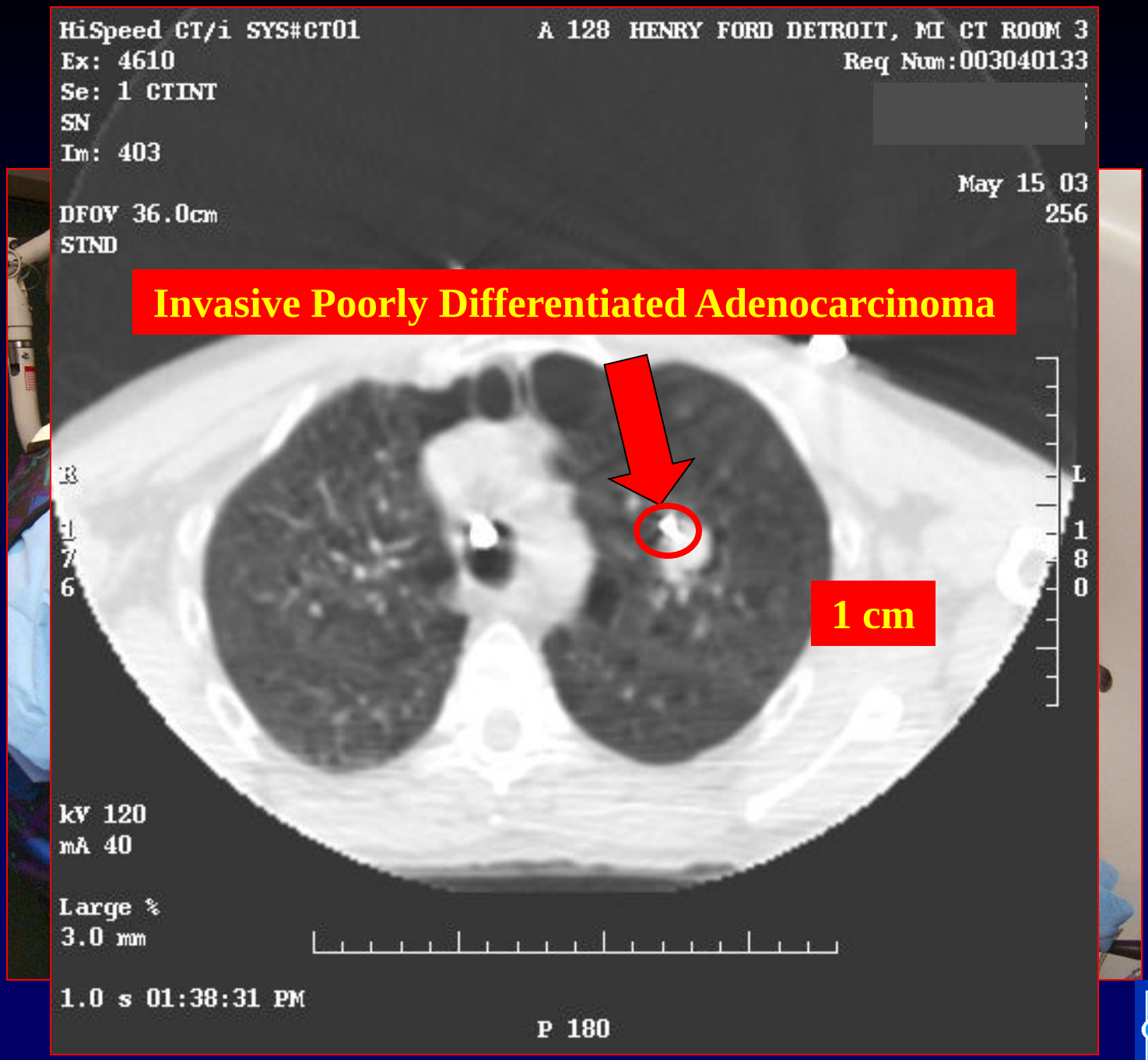
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Invasive Poorly Differentiated Adenocarcinoma
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mA 40
Large %
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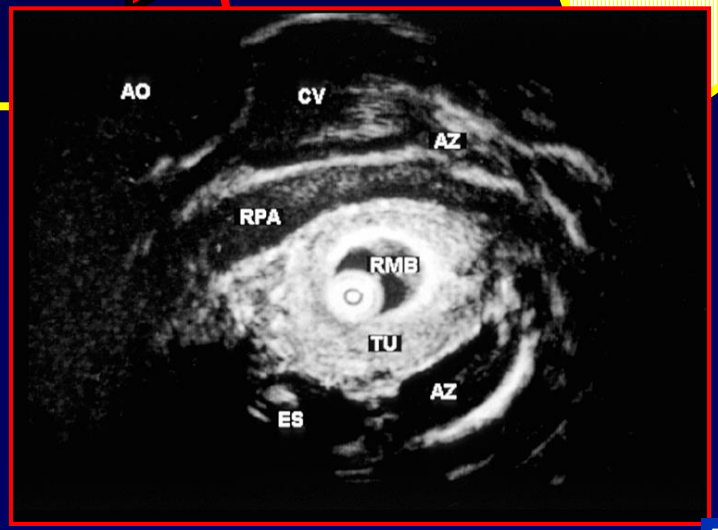
ENDOBRONCHIAL ULTRASOUND



Beyond the airway

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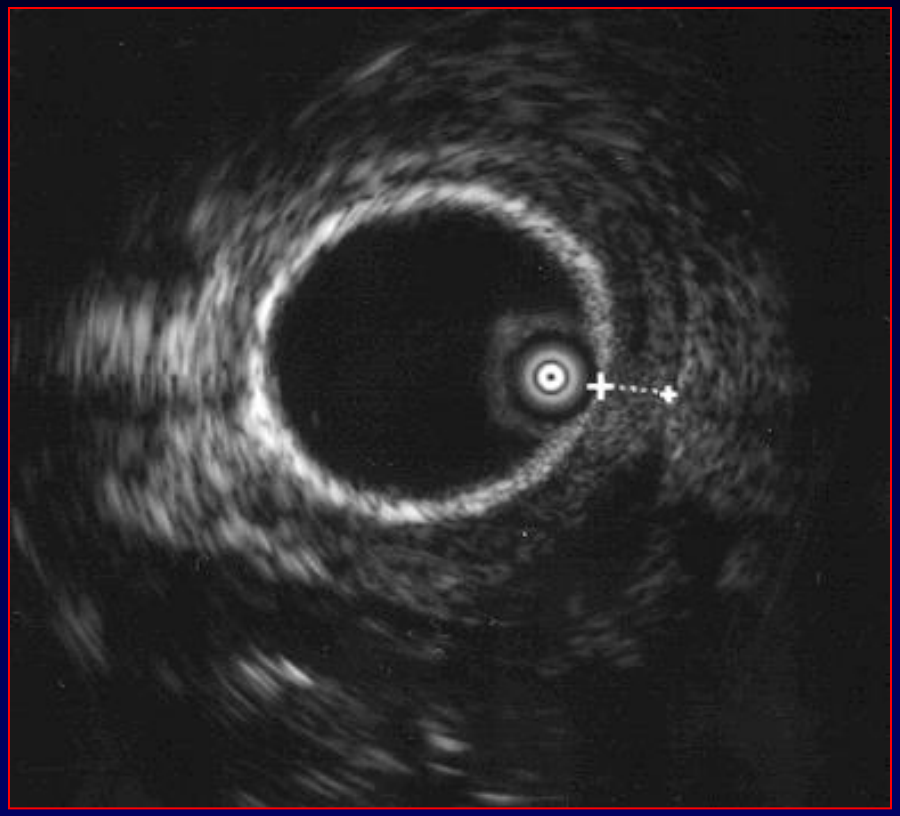
EBUS – CLINICAL USES

- Airway invasion
- Mediastinal structure invasion
- Transbronchial biopsy
- Ultrasound guided TBNA
- EBUS-TBNA



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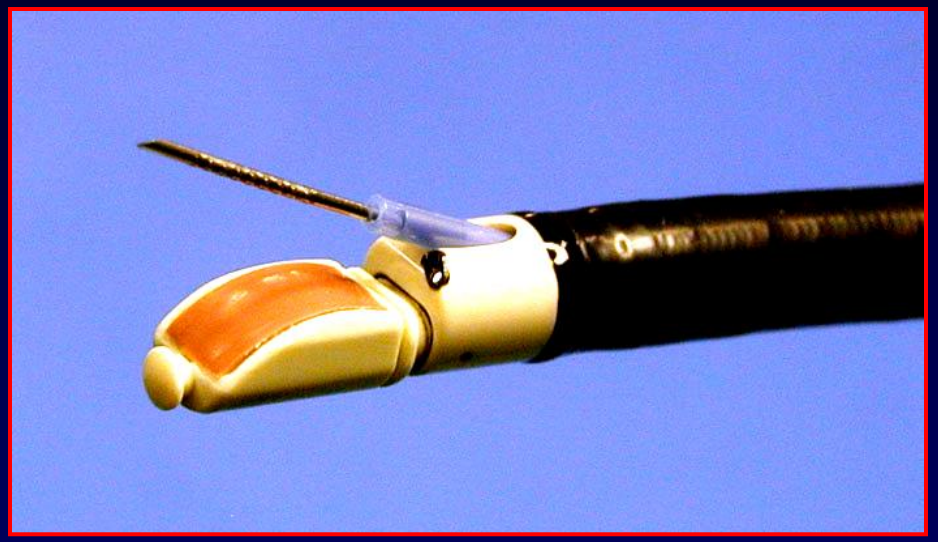
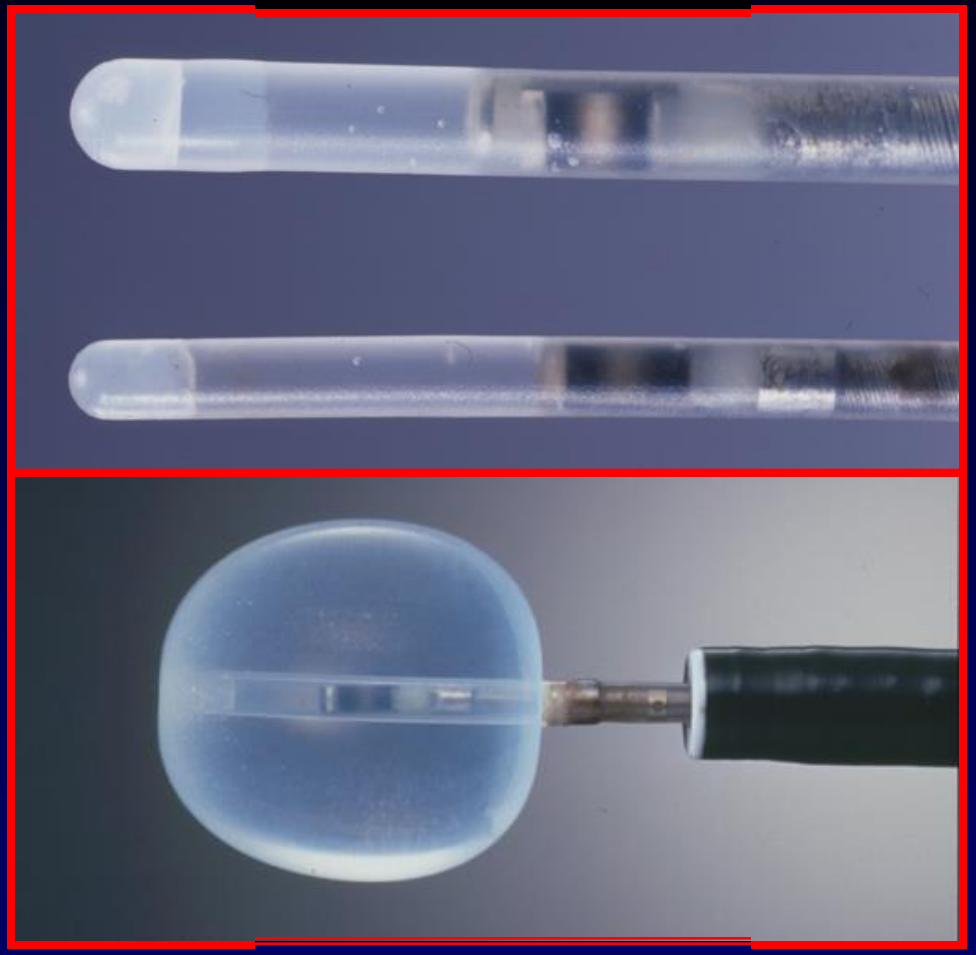
EBUS GUIDED TBNA

- Needle is extended with both visual and ultrasound imaging
- Incorporate a directional ultrasound probe into a bronchoscope
- Real time transbronchial specimens



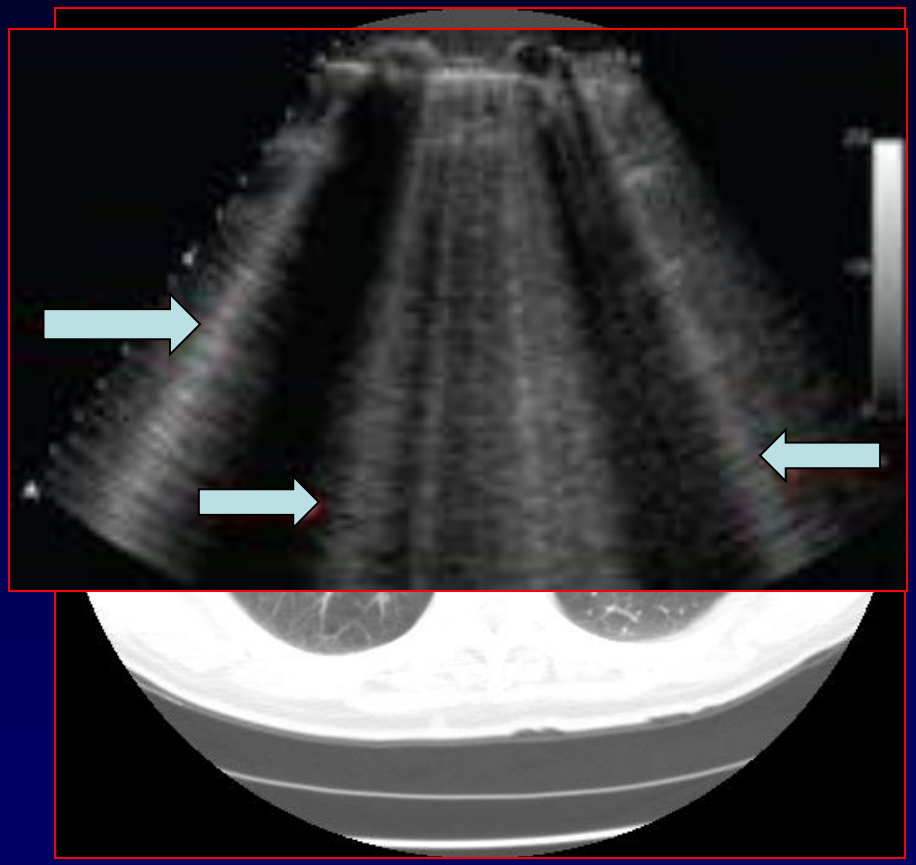
EBUS - EQUIPMENT

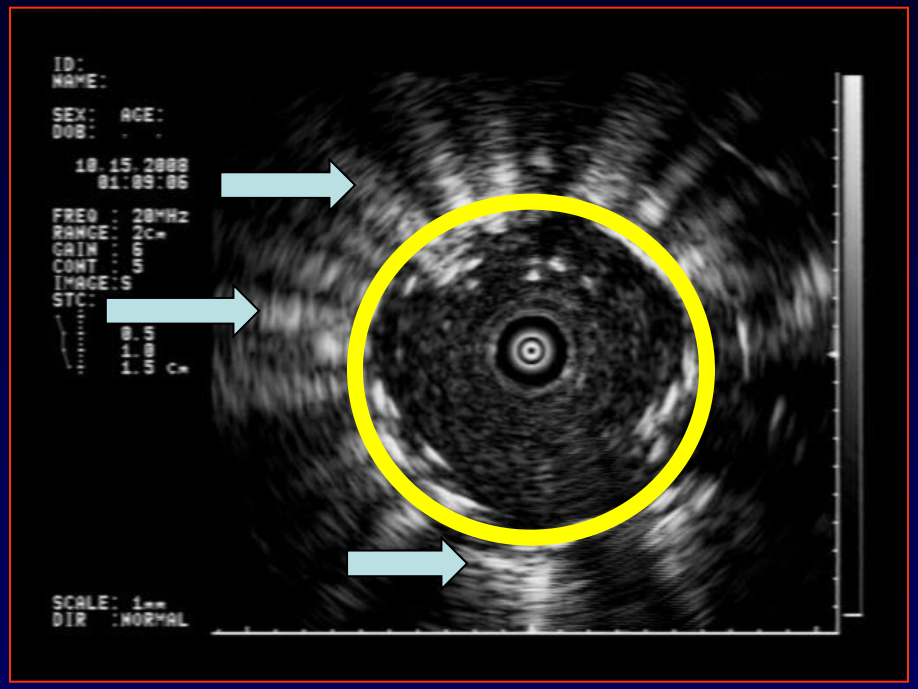
- **Processor:**
  - 20 mHz
  - 7.5 mHz
  - Combined (20&7.5 MHz)
  - Aloka (7.5 MHz)
- **Bronchoscope:**
  - 2.0 mm working channel
  - 2.8 mm working channel
- **Probes:**
  - Central
    - 20 MHz
    - 30 MHz
  - Peripheral – 20 MHz



Images courtesy Olympus Corp.

EBUS AND PERIPHERAL LESIONS





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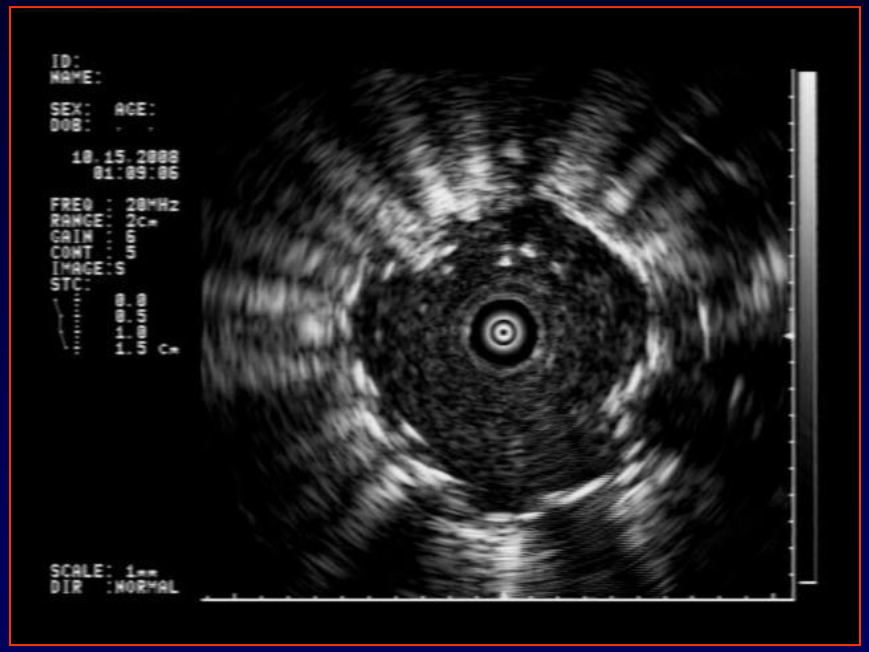
PERIPHERAL ULTRASOUND

- Comparison of fluoroscopic transbronchial biopsies vs. peripheral EBUS
- Herth et al.
  - 50 consecutive patients with SPN
  - Patients randomly distributed between Fluoroscopic vs. EBUS guided transbronchial biopsies



FLUOROSCOPIC BIOPSY VS. PERIPHERAL ULTRASOUND

	Lesion < 3 cm	Lesion >3 cm
Patients n	21	29
EBUS n (%)	17 (80)	23 (79)
Fluoroscopic n (%)	12 (57)	26 (89)

Herth et al. Eur Respir J 2002

EBUS GUIDED TRANSBRONCHIAL BIOPSY OF PERIPHERAL LUNG LESIONS

Series	Technique	n	Size (*mm*)	Diagnostic Yield (%)
Herth and colleagues (3)	EBUS—transbronchial forceps biopsy	50	All	80
		21	< 30	80
		29	> 30	79
Kurimoto and colleagues (4)	EBUS with guide sheath and fluoroscopy ± curette—forceps biopsy/brush	150	All	77.3
		81	< 20	72.8
		43	20–30	77
		26	> 30	92
Kikuchi and colleagues (5)	EBUS with guide sheath and fluoroscopy ± curette—forceps biopsy/brush	24	< 30	58.3
		15	< 20	53.3
		9	20–30	66.7
Yang and colleagues (6)	EBUS—transbronchial forceps biopsy	122	All	65.6
		11	< 20	54.5
		103	> 20	66.0
Asahina and colleagues (7)	EBUS with guide sheath, virtual bronchoscopy navigation and fluoroscopy ± curette—forceps	30	< 30	63.3
		18	< 20	44.4
		12	20–30	91.7
Paone and colleagues (				78.7
				71
				75
		40	> 30	82.8
Herth and colleagues (9)	EBUS—transbronchial forceps biopsy	54	Fluoroscopically invisible, mean 22 ± 0.7	70.3

Yields: 53.3% - 92%

GUIDE SHEATH

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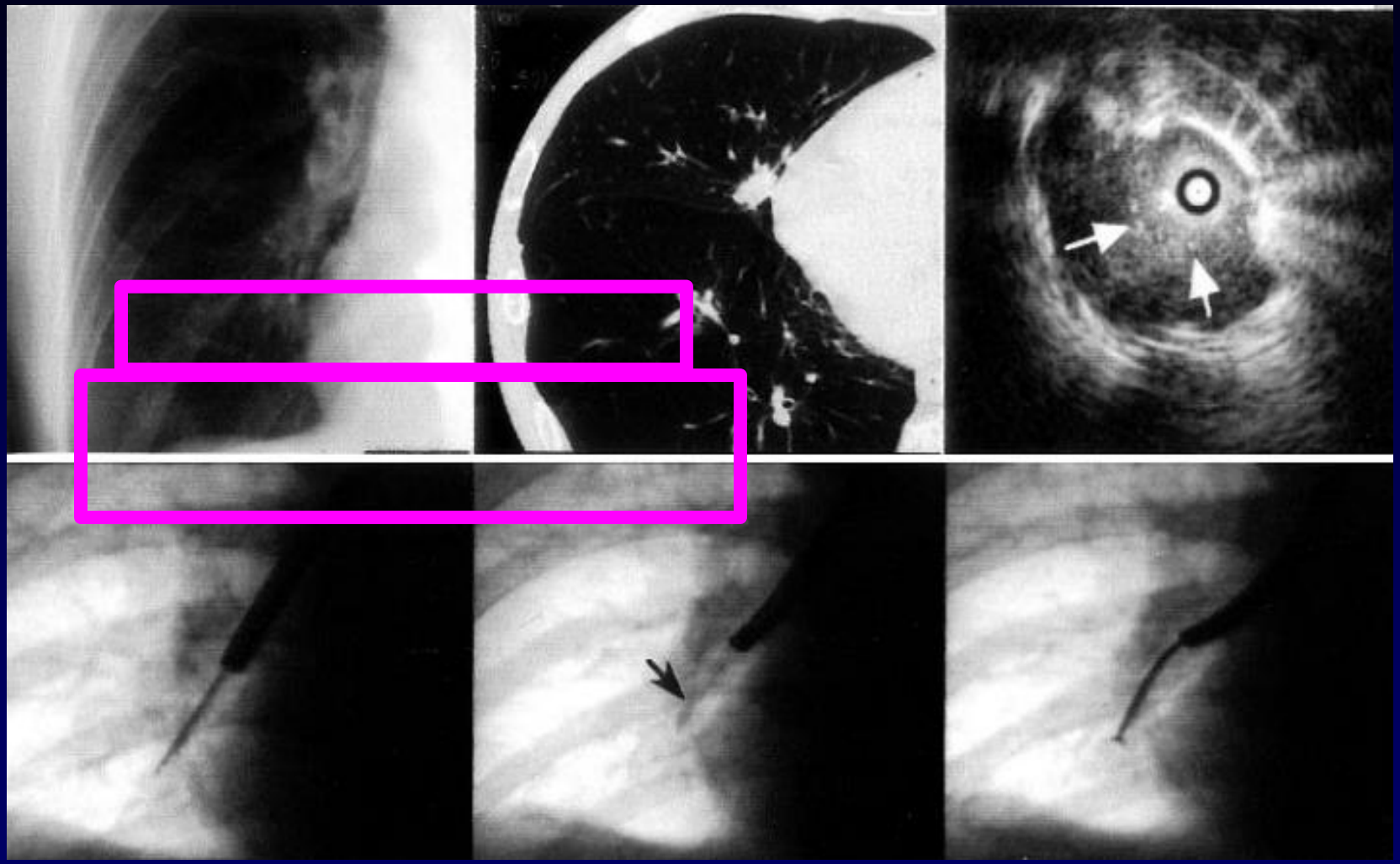
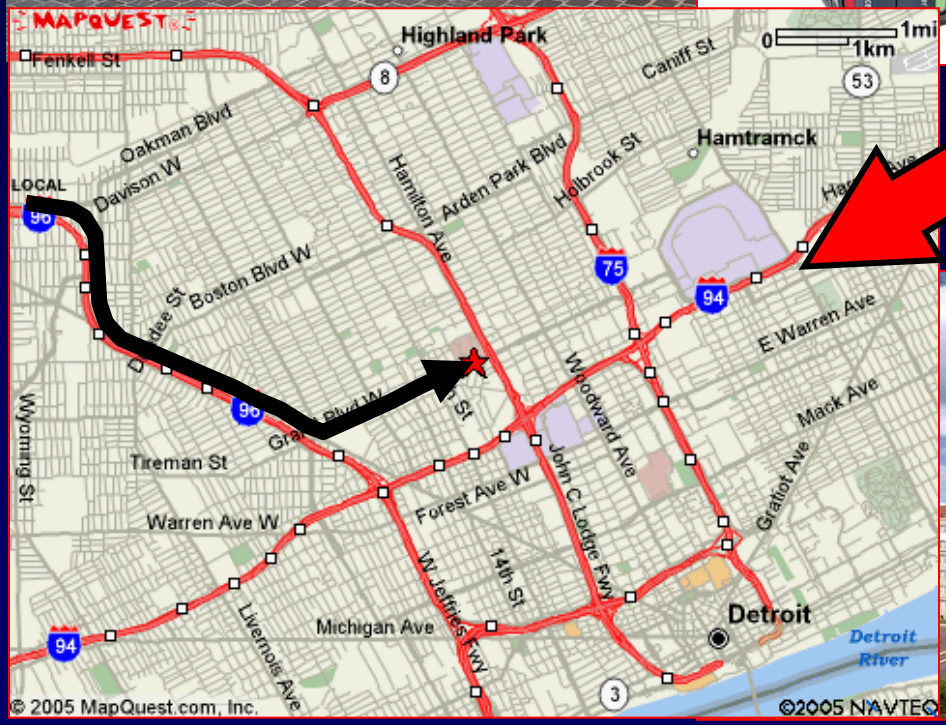
PERIPHERAL LESIONS – EBUS-GUIDE SHEATH

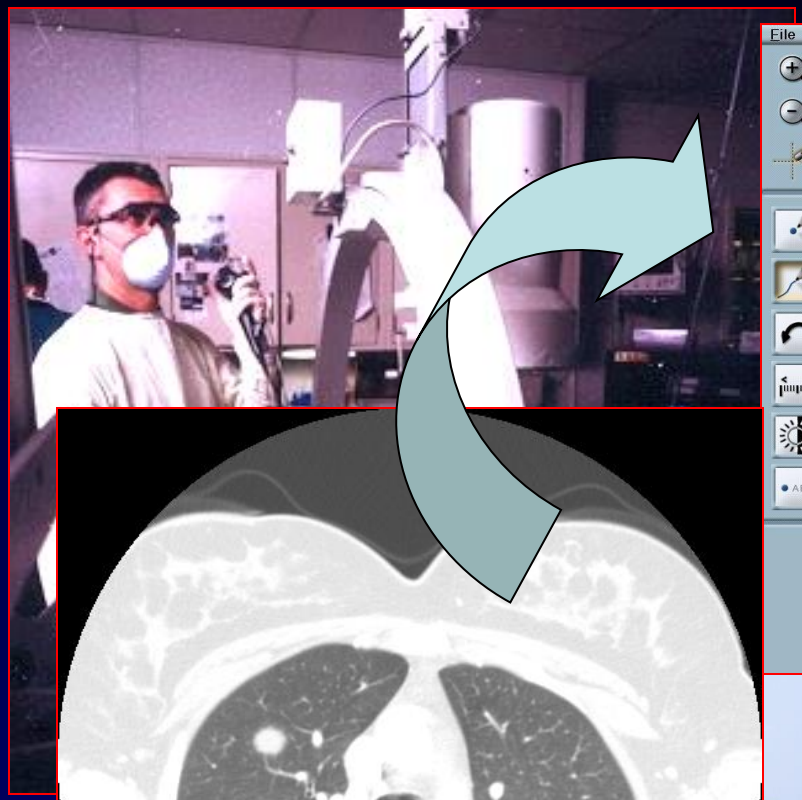


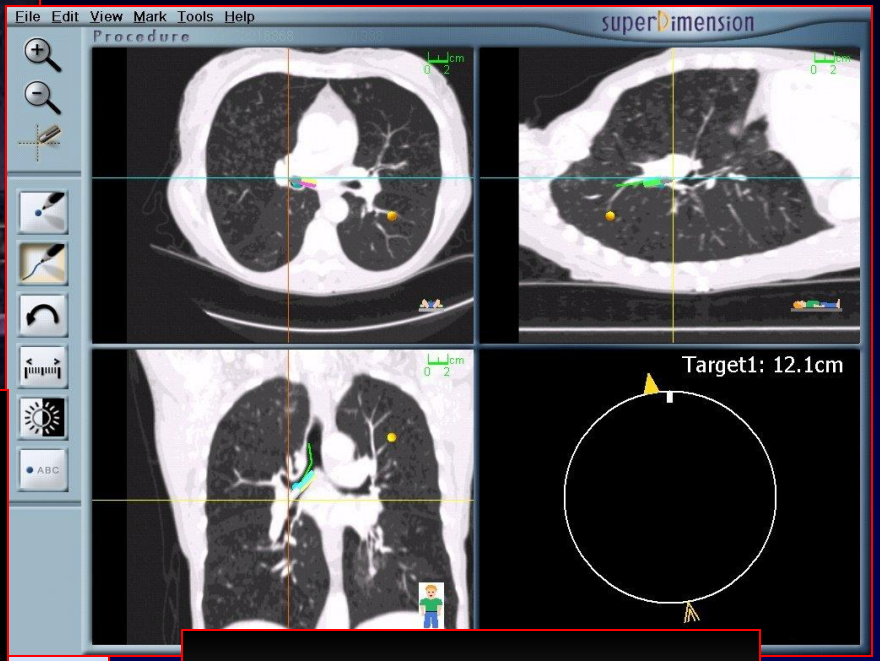
Kurimoto N. *Chest* 2004.

Electromagnetic Navigation



NAVIGATION

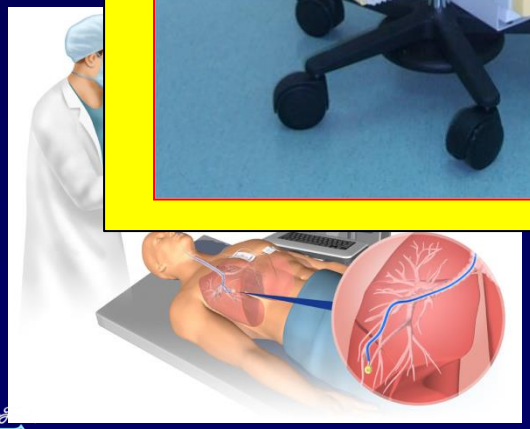



File Edit View Mark Tools Help
superDimension
Procedure
Target1: 12.1cm

ELECTROMAGNETIC NAVIGATION

- O
- L
- V
- su

- superDimension LTD
- Five Systems released first year
- HFH
- 2005



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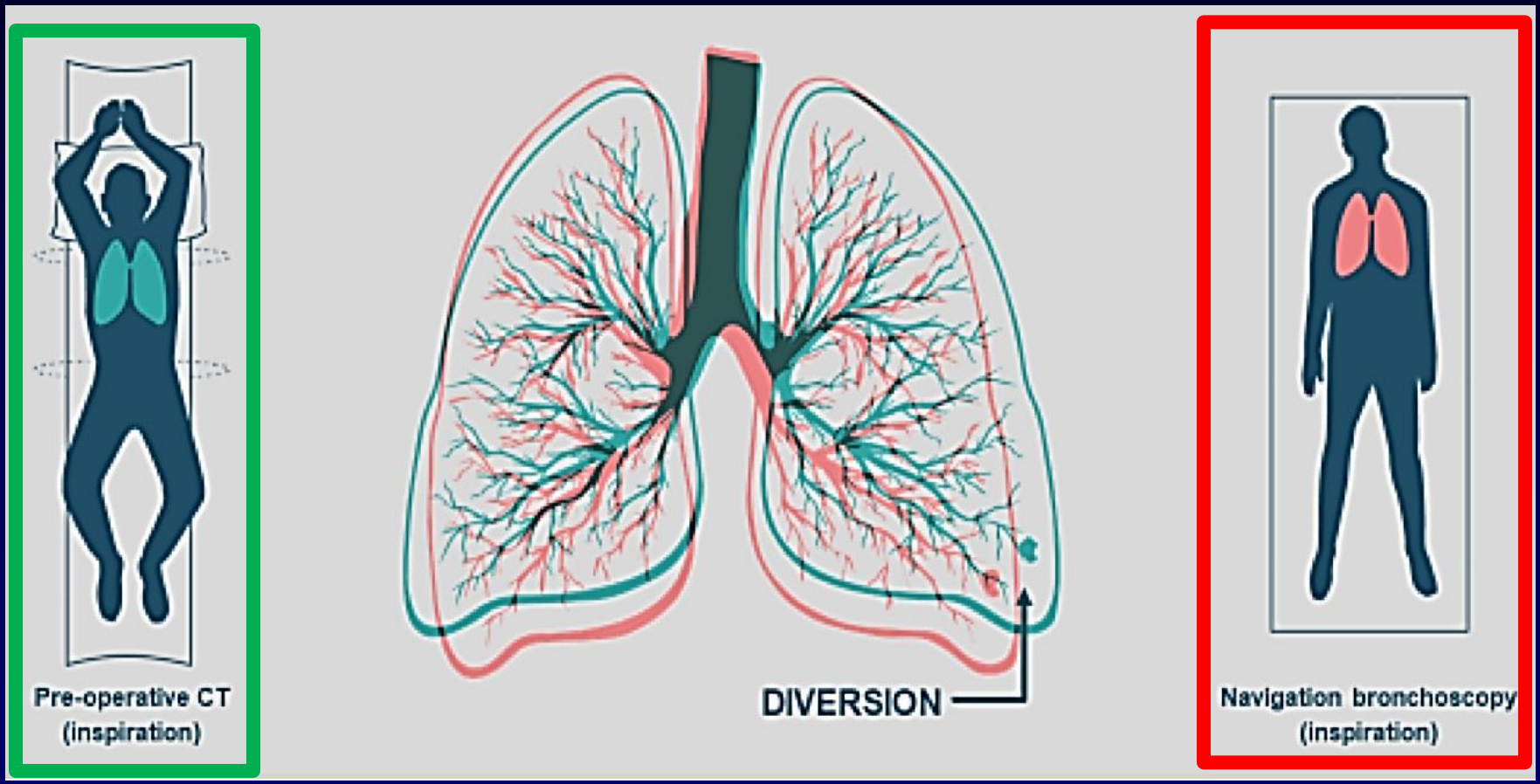
CURRENT DIAGNOSTIC YIELDS FOR ELECTROMAGNETIC NAVIGATION

- Clinical experience trials: Becker 2005, Schwarz 2006, Gildea 2007, Makris 2007, Eberhart 2007, Wilson 2007, Weiser 2008, Bertoletti 2009, Lambrecht 2009, Eberhardt 2009, Zhang 2015
- All authors with yields in the 70-75% range
- 4 meta-analyses report 70% average yield
- These studies were at academic centers
- Studies of all users have demonstrated yields of <50%

LIMITATIONS OF ELECTROMAGNETIC NAVIGATION

- Deviation of electromagnetic field as passes through body, creating intrinsic error
- Dynamic changes in the target lesion from the time of imaging to procedure
- Suboptimal scans
- Ferrometalic interference
- Poor registration technique
- Difficult-to-see ground glass lesions
- Respiratory motion
- Atelectasis
- Positional changes with instrumentation

CT TO BODY DIVERGENCE



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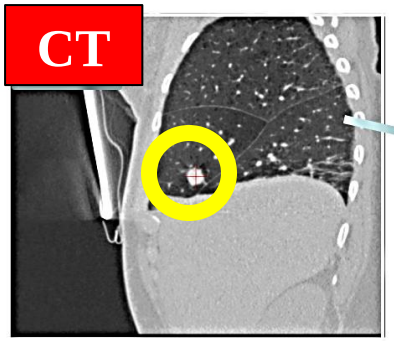
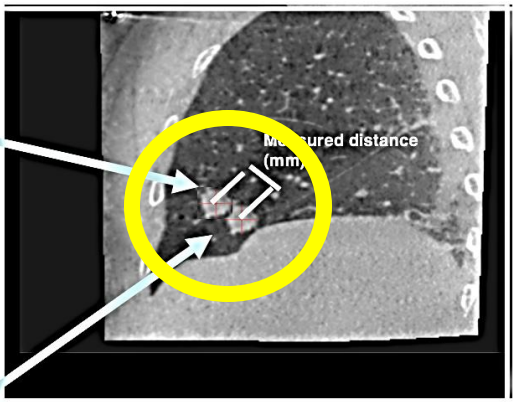
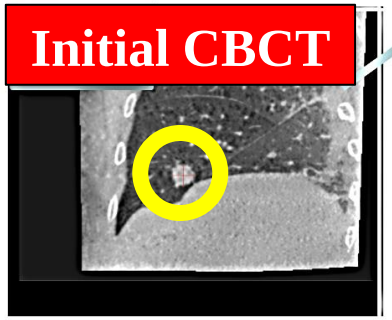
NODULE MOVEMENT

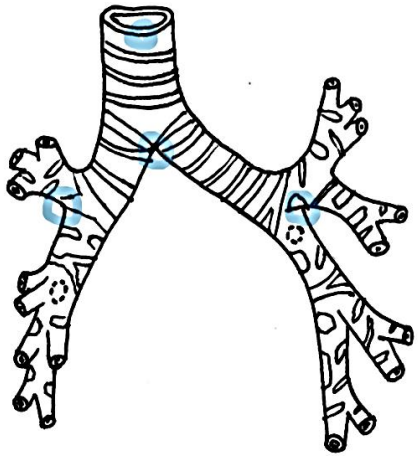
Nodule Movement Measurements







- CT to CT comparison in 3-dimensions
- Registration based central airway



Lobe	Divergence (mm) Avg (range)
Upper Lobes	12.6 (2.64-35.9)
Lower Lobes	18.4 (9.56-28.89)

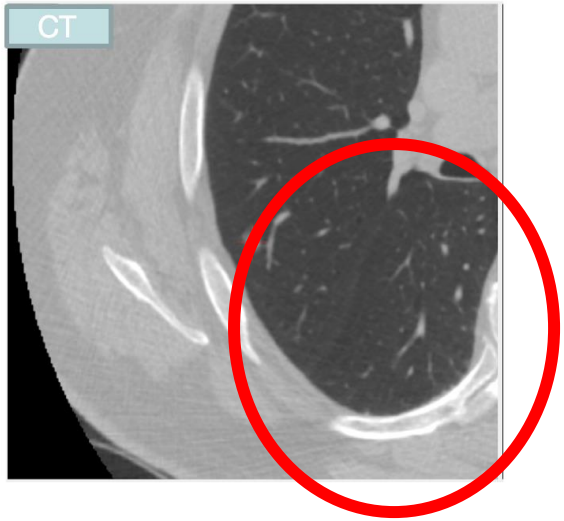
WCLC 2018

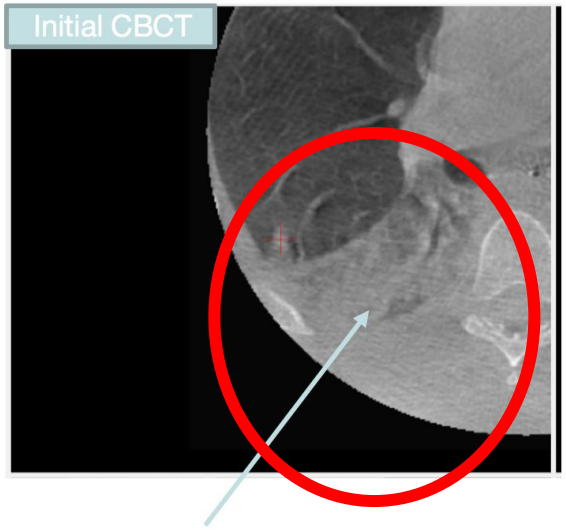
ATELECTASIS

Case: 180214
Gender: Male
Age: 60
Nodule location: RUL
Nodule size: 9 mm

Atelectasis During Bronchoscopy

Pre-procedure CT to Intra-procedure CBCT Divergence: 24 mm





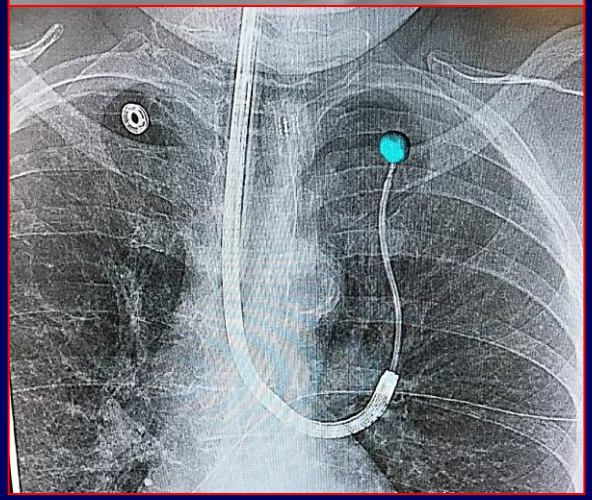
WCLC 2018

FLUORSCOPIC NAVIGATION

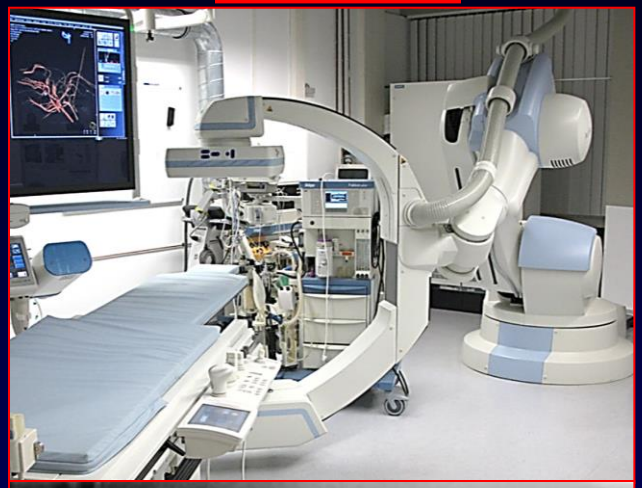
- Tomosynthesis with software algorithms to enhance the visibility of the targeted region
- Tight focus on area of interest provides more precise registration to compensate for local CT to body divergence
- Once nodule location is “confirmed”, a new navigation path is generated and the user may navigate to the target
- “Local registration”

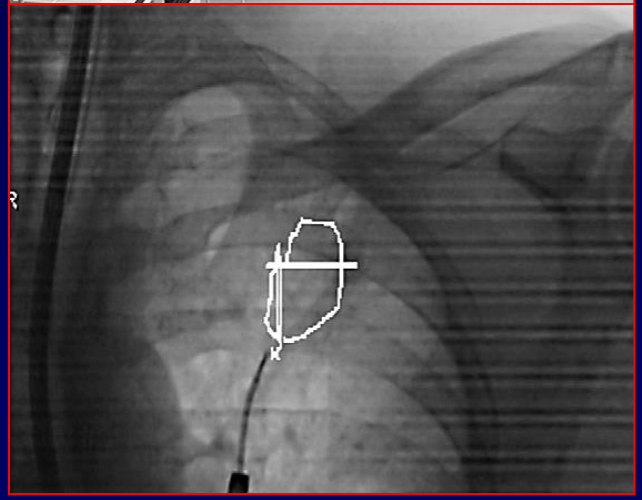
CONE BEAM CT

Philips



Siemens





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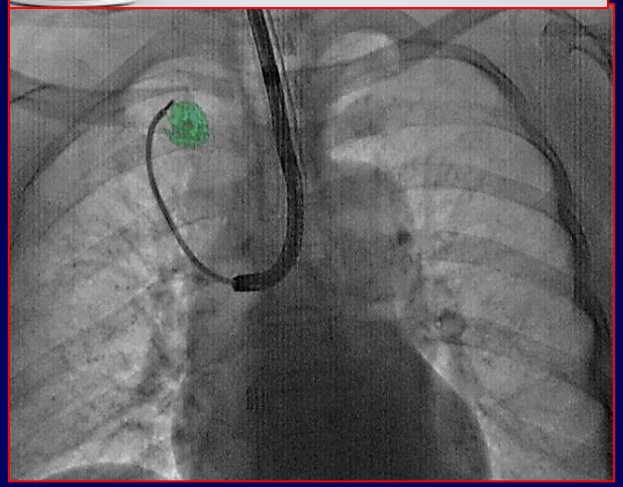

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CHEST® JOURNAL
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Pulmonary Procedures | October 2014

Cone-Beam CT Scanning with Electromagnetic Navigation Bronchoscopy

Michael Pritchett, DO, MPH
Pinehurst Medical Clinic & FirstHealth Moore Regional Hospital – Chest Center of the Carolinas, Pinehurst, NC

PURPOSE/BACKGROUND

Electromagnetic Navigation Bronchoscopy (ENB) has been shown to have superior yield in diagnosing peripheral nodules compared to conventional bronchoscopy. Standard fluoroscopy is most commonly used during these procedures to assist in visualization. Cone-beam CT (CBCT) is increasingly utilized by interventional radiology for percutaneous biopsy, placement of fiducials and application of ablative therapy for lung malignancies. There has been no case study with the use of ENB and CBCT used in conjunction.

CASE PRESENTATION

A 60-year-old male with a 30-pack-year history of smoking presents with a 1cm pleural based nodule in the right upper lobe (figure 1). A PET scan showed significant metabolic activity in this small peripheral nodule with an SUV of 3.3 (figure 2).

FIGURES


FIGURE 1

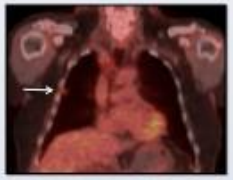


FIGURE 2


FIGURE 3


FIGURE 4

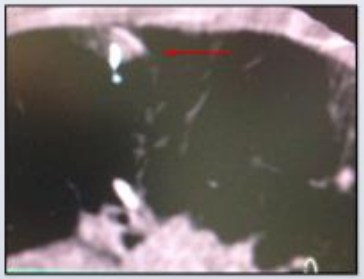


FIGURE 5

METHODS

We performed ENB using the superDimension iLogic system in conjunction with a 90-degree Edge catheter. Cone-beam images acquired with the Philips Allura Xper FD20 system (figure 3). After successful navigation to the lesion a brush was deployed for sampling. With the brush extending in the sampling position, a rotational scan was performed to acquire the cone-beam CT images. The images were manipulated for immediate viewing, which showed the brush in the center of the 1cm lesion (Figures 4 & 5).

CONCLUSIONS

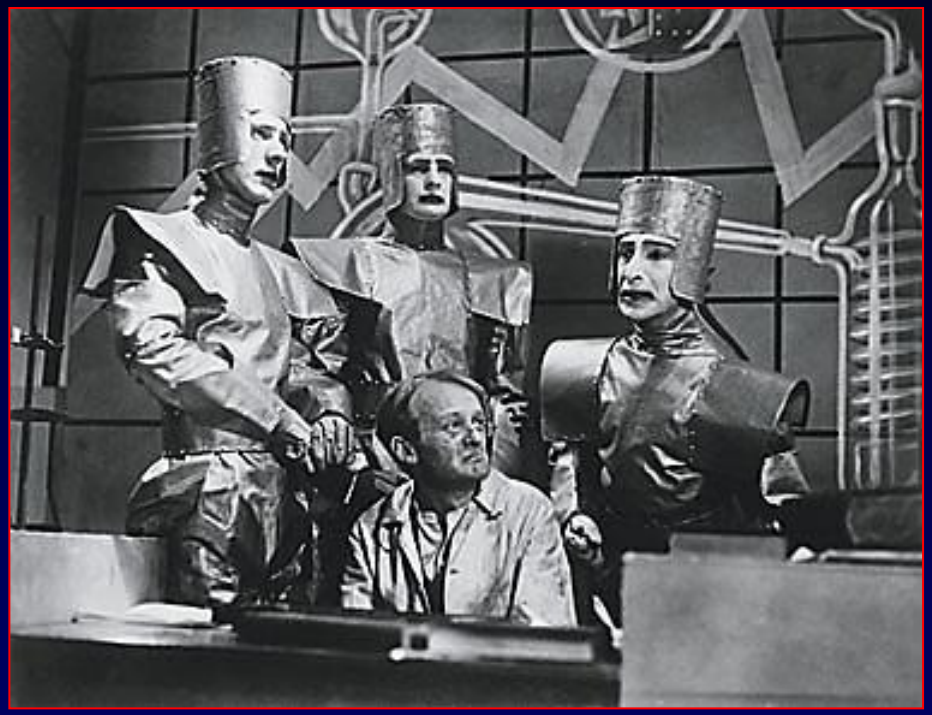
To the best of our knowledge this is the first use of CBCT in conjunction with ENB in humans. Recent case studies have shown increasing use of CBCT with conventional bronchoscopy using this itself as a mode of navigation. We feel that these two modalities used in combination have significant potential to both increase diagnostic yield and eventually to confirm location for use of endobronchial-guided ablative therapies for early-stage lung cancer, such as radiofrequency or microwave ablation.

ACKNOWLEDGEMENTS

The authors would like to thank Covidien (superDimension), our cytology techs, OR staff and respiratory therapists for their support and dedication.

HISTORY OF ROBOTS

- Robot originates from the Slavonic term robota which means forced labor
- “Robot” was made famous by Karel Capek in 1921 – Rossum’s Universal Robots



ROBOTIC BRONCHOSCOPY

Requirements for Robotic Bronchoscopy

- Reach
- Access
- Control Stablity
- Location feedback
- Ability to perform procedures

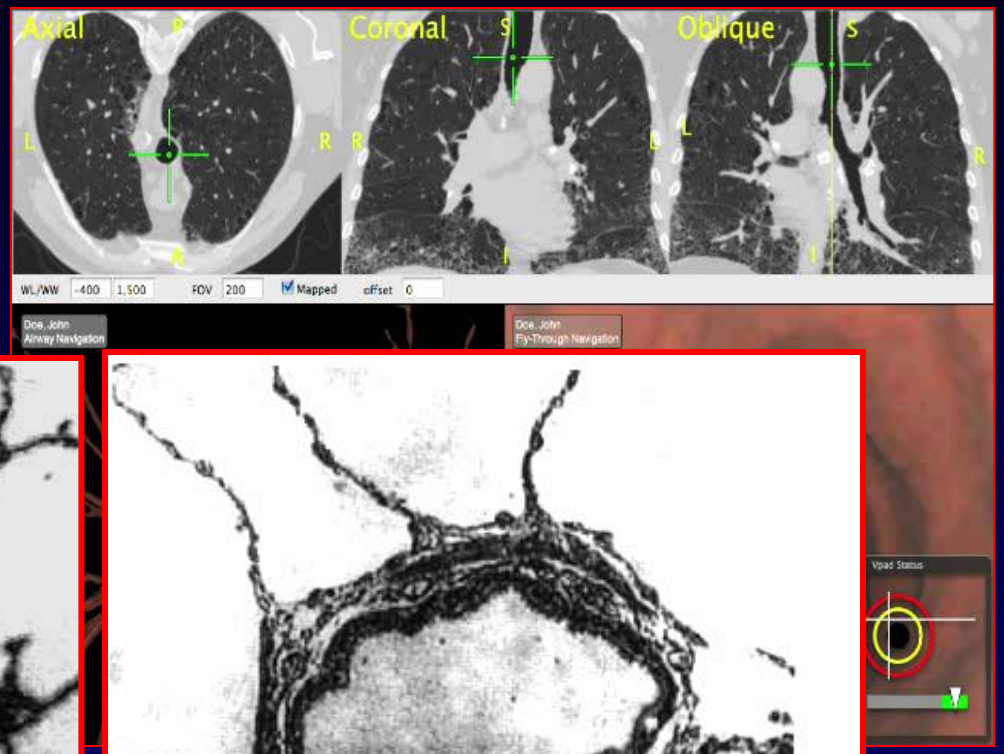
HISTORY OF MEDICAL ROBOTS

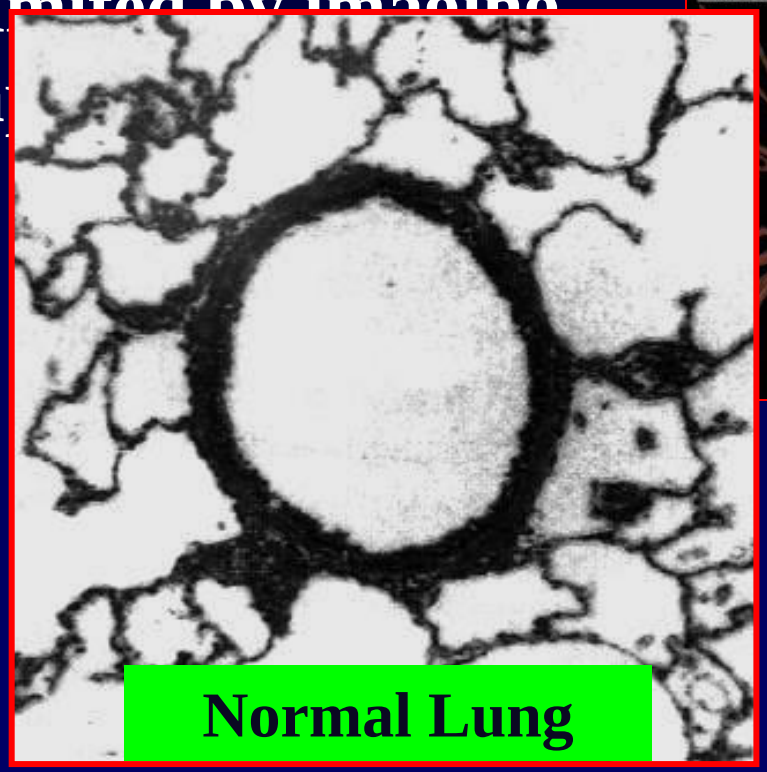
AMES Research Center - NASA and Stanford Research Institute

- **After review of casualties of Vietnam War identified that if field surgery was available then more soldiers might have been saved**
- **Idea of combining virtual reality with surgical robotics or tele-presence surgery**
- **Department of Defense funded the biomedical program to develop a tele-surgery unit for the field**

ROBOTIC BRONCHOSCOPY: REACH

- Integrate CT scans of the lung to create road maps
- Limited by imaging ca



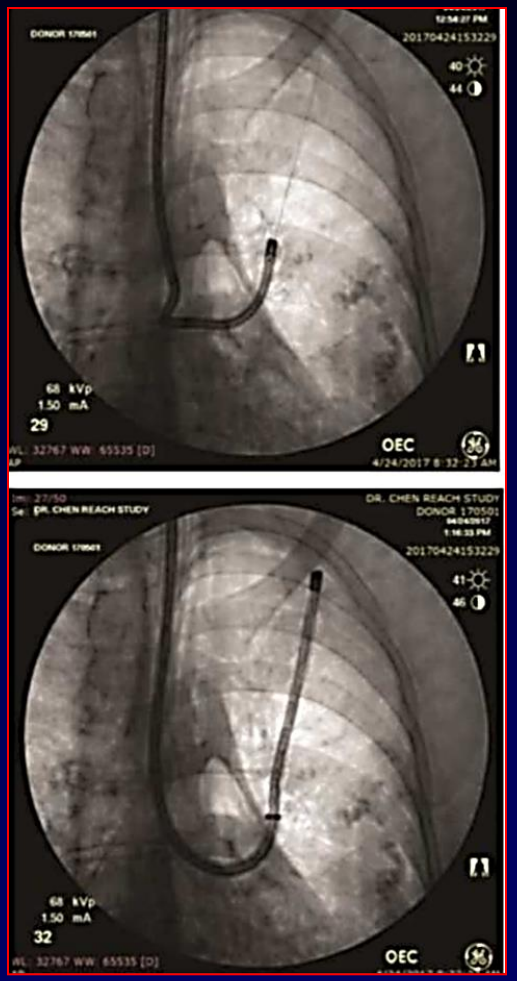


Normal Lung

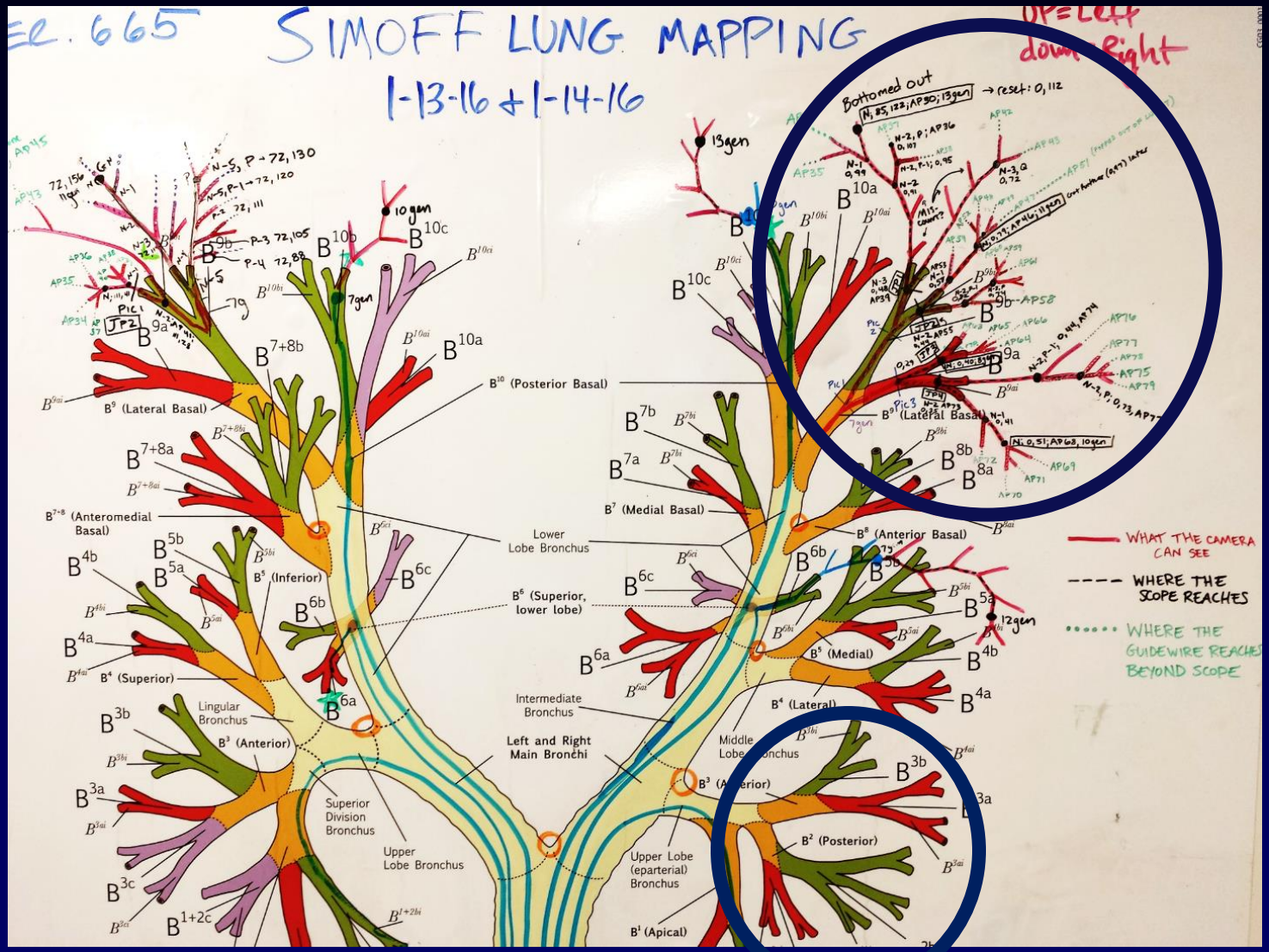
Emphysema

Robotic Endoscopic Airway Challenge: REACH

- 10 operators performed bronchoscopy on 5 different cadavers using both the BF-P190 bronchoscope and Monarch system
- Peripheral access measured:
  - Generation count
  - Distance from main carina
  - Measure with external fluoroscopy



ACCESS STUDY



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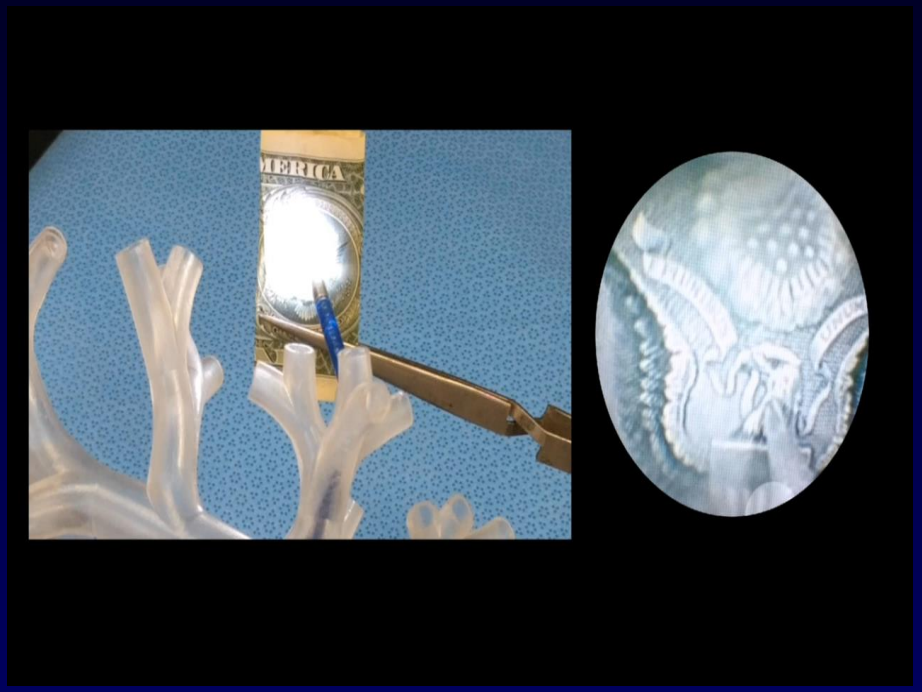
ROBOTIC BRONCHOSCOPY: CONTROL/STABILITY

**Probe 1.4mm /
Gold fiducial is 0.8mm**

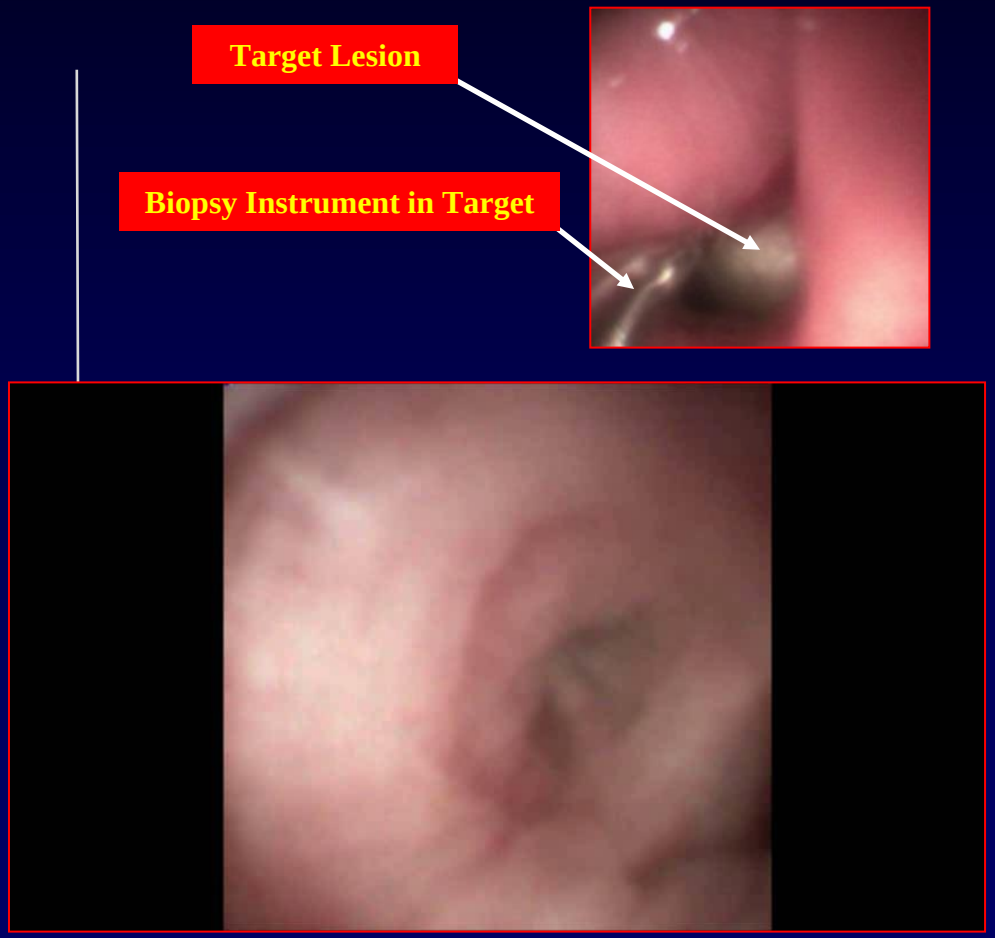


**Precision Instrument
Manipulation**

FIRST-IN-MAN FEASIBILILITY STUDY: AURIS

- 2014
- Proof of concept
- Robotic endoscopy performed in 15 patients with pulmonary lesions
- Specimens successfully obtained in 14/15 patients using the robotic platform
- No serious adverse events noted

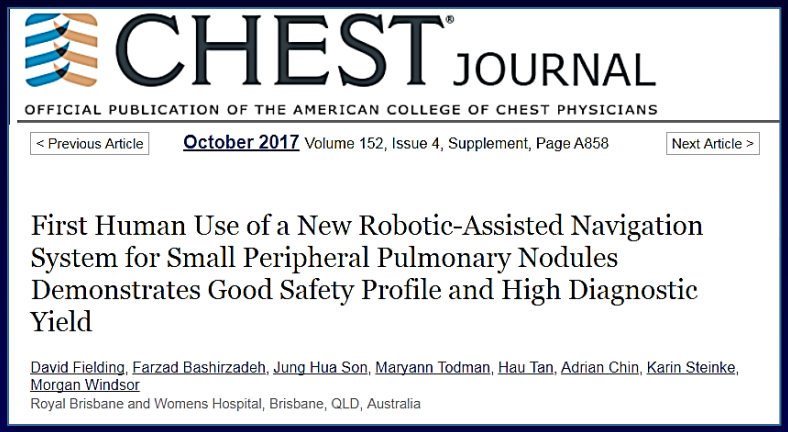
Direct Visualization of Biopsy in Periphery of Lung



Rojas-Solano J, et al. J Bronchology Interv Pulmonol. 2018

FIRST-IN-MAN FEASIBILILITY STUDY: INTUITIVE

Primary Endpoints	**Feasibility** Facilitate sampling of SPNs ≥10 mm to <30 mm in largest diameter **Safety** Pneumothorax and excessive bleeding
Sample Size	30 patients
Follow-up	Up to 6 months
Exclusion	Central pulmonary nodules within the 1st three airway generations



CHEST JOURNAL

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First Human Use of a New Robotic-Assisted Navigation System for Small Peripheral Pulmonary Nodules Demonstrates Good Safety Profile and High Diagnostic Yield

David Fielding, Farzad Bashirzadeh, Jung Hua Son, Maryann Todman, Hau Tan, Adrian Chin, Karin Steinke, Morgan Windsor

Royal Brisbane and Womens Hospital, Brisbane, QLD, Australia

FIRST-IN-MAN INTUITIVE: RESUTS

Nodule Demographics

Nodule Location

- 7th ± 1.5 Generation
- 66.7% UL's
- 10% RML
- 23.3% LL's

Bronchus sign present

- 60%

Nodule Size

- Largest Oblique ⌀:
- 14.8 mm [10 - 26.4mm]
- Largest Cardinal ⌀:
- 12.3 mm [4.5 – 26.4mm]

Primary End Points: Feasibility and Safety

97% Feasibility

0% Pneumothorax or Excessive Bleeding

Subject and Sample Results: Clinical Diagnosis through 6 month F/U

80% Diagnostic Yield – System Sample

89% Diagnostic Yield - Malignancy

Average size: 14 mm

D. Fielding. First Human Use of a New Robotic-Assisted Navigation System for Small Peripheral Pulmonary Nodules Demonstrates Good Safety Profile and High Diagnostic Yield. CHEST 2017 Conference

CURRENTLY AVALIABLE BRONCHOSCOPIC ROBOTS

Auris Monarch

Intuitive Ion

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ROOM SCAN

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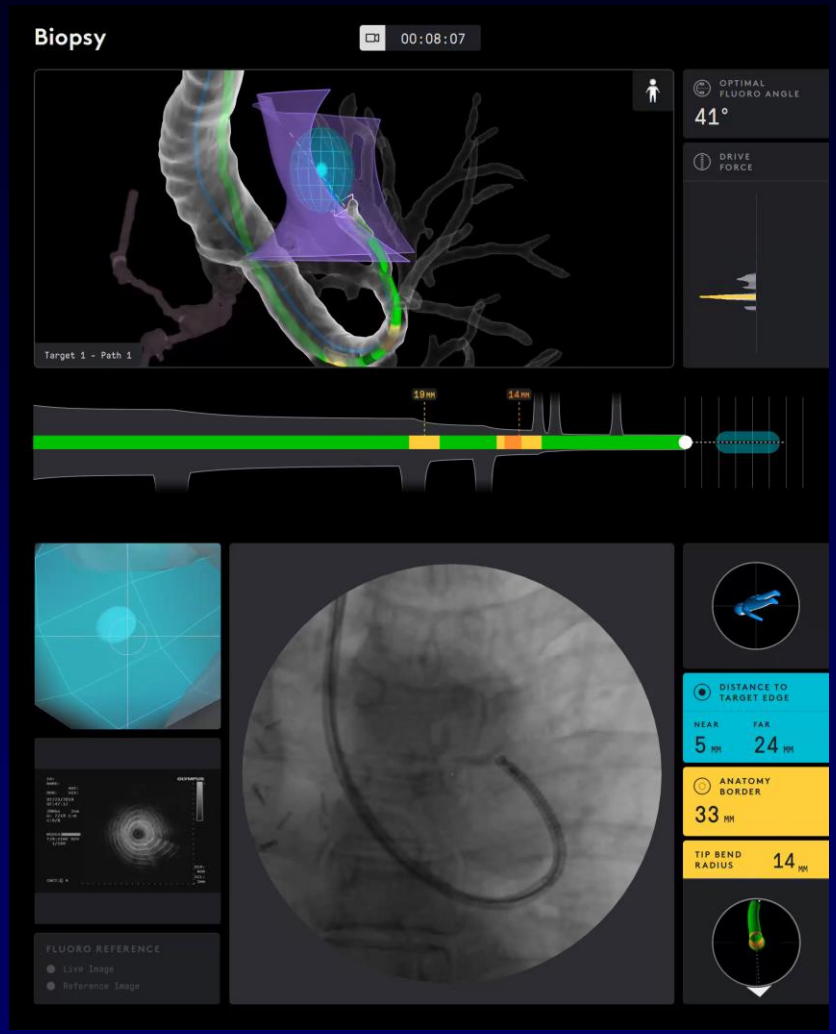
NEEDLE PASS



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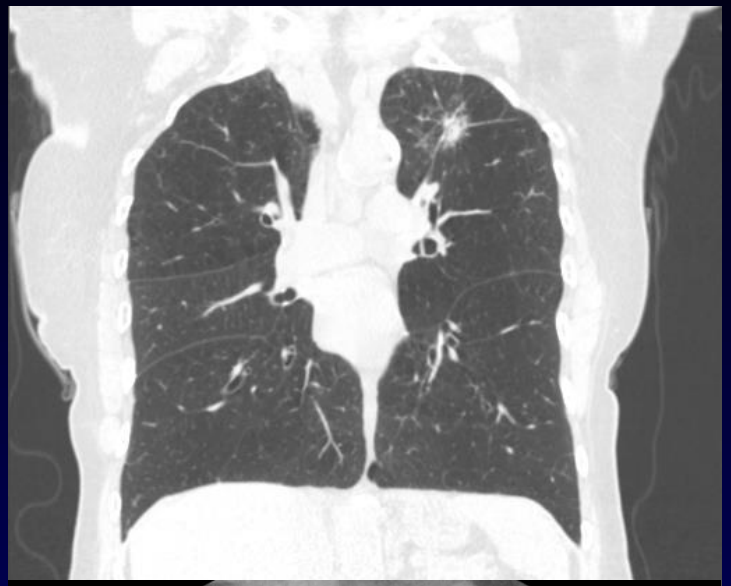
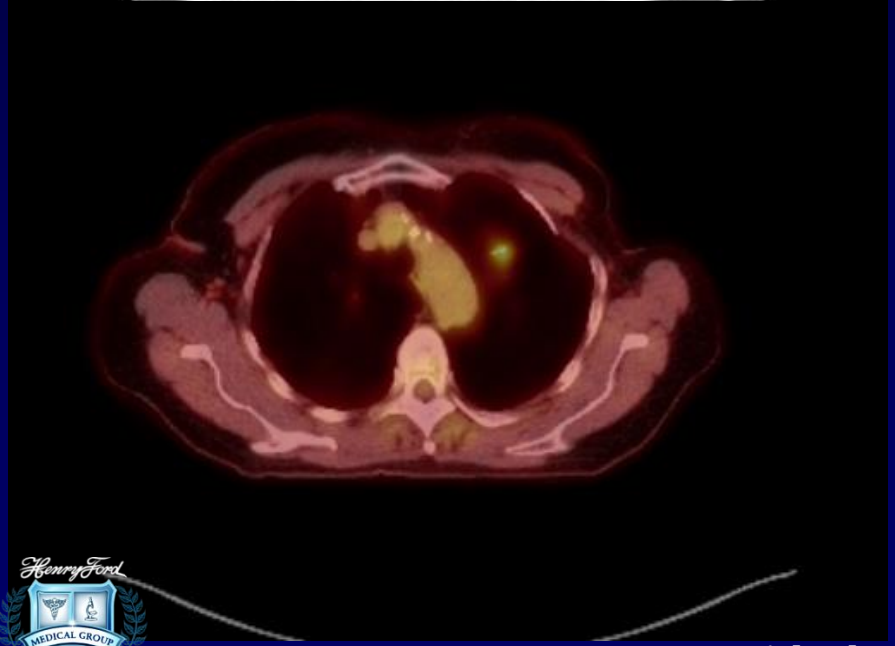
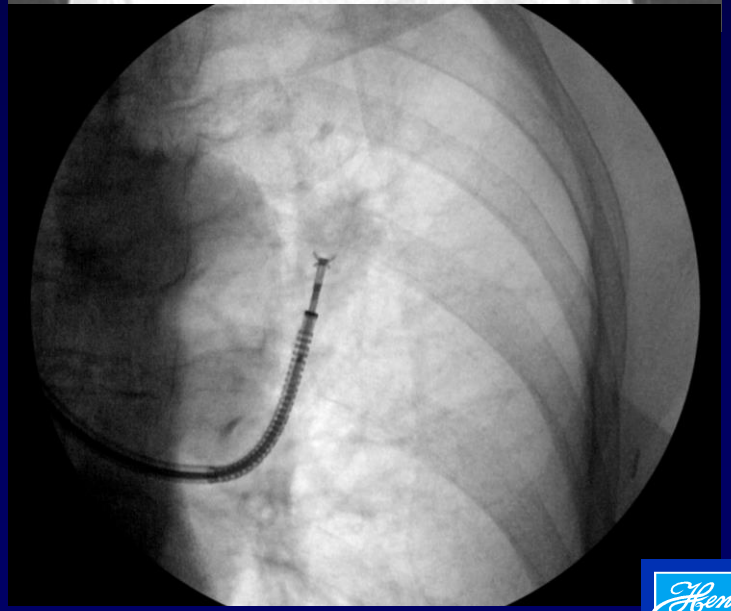
CASE 1: LUL NODULE







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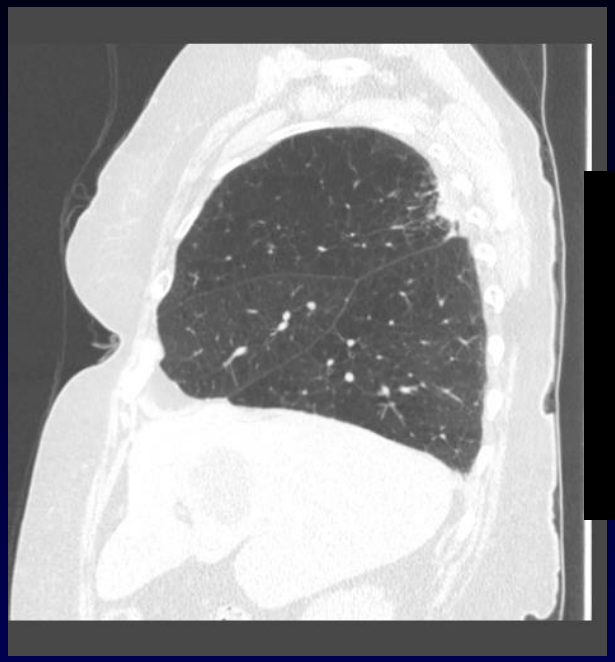
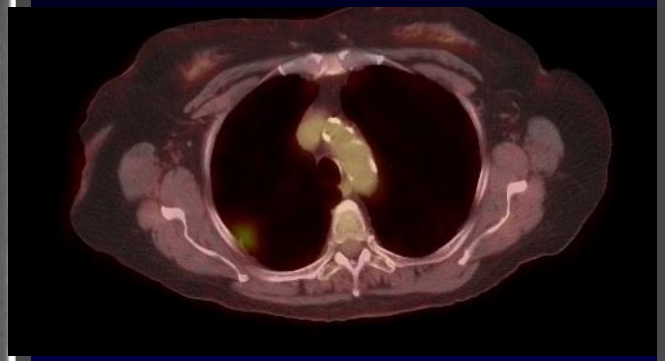
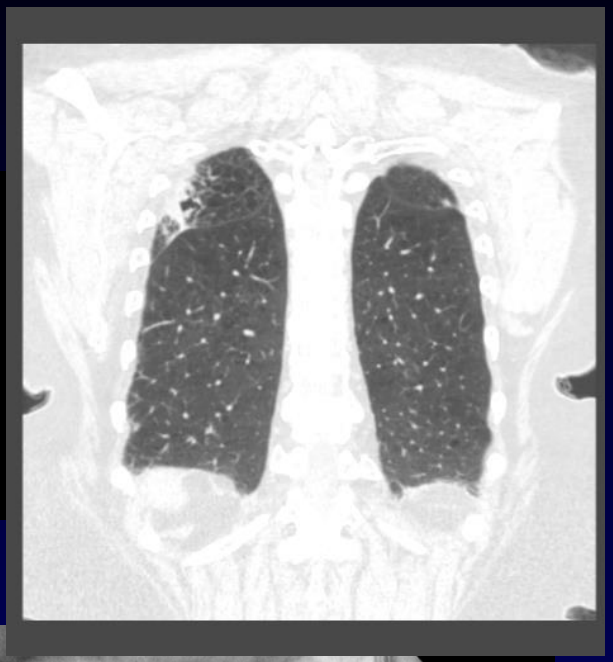
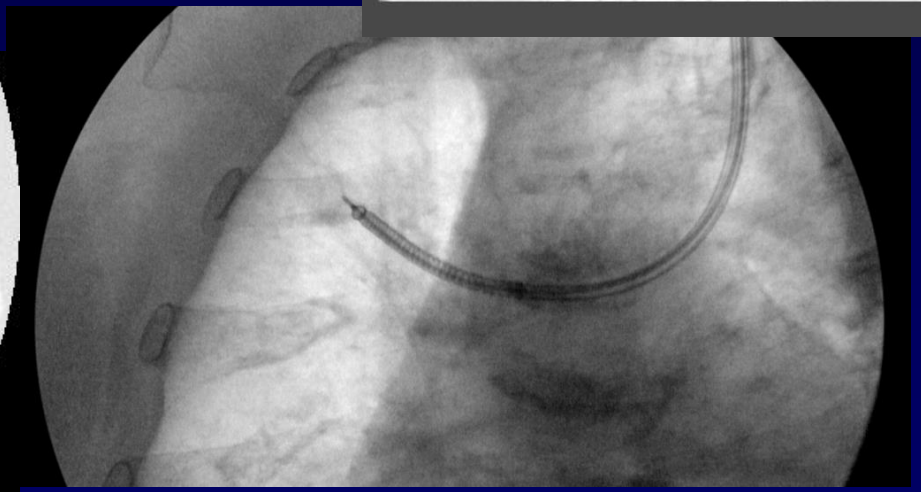
CASE 2: PLEURAL BASED NODULE









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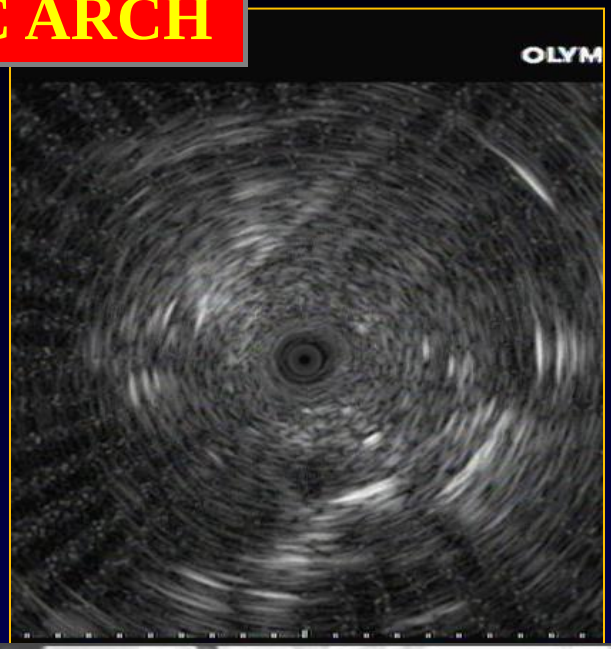
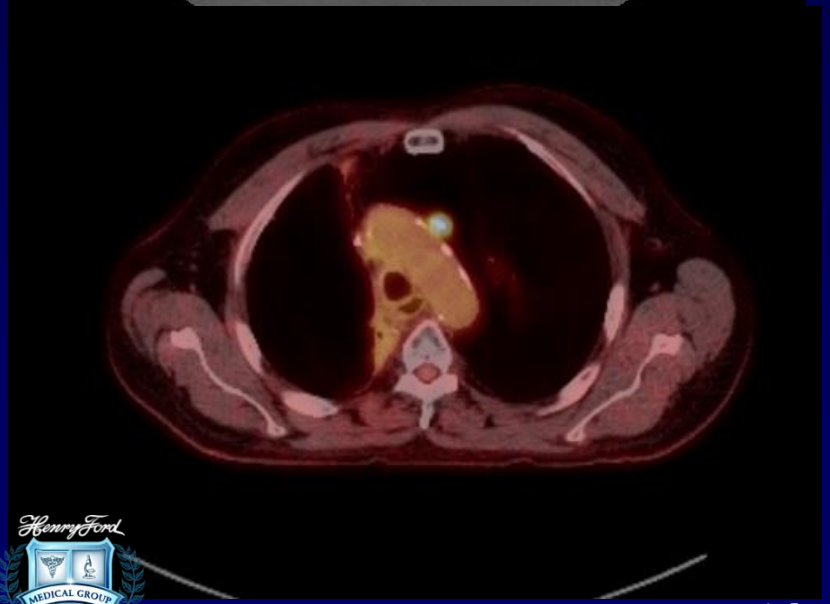
CASE 3: AORTIC ARCH





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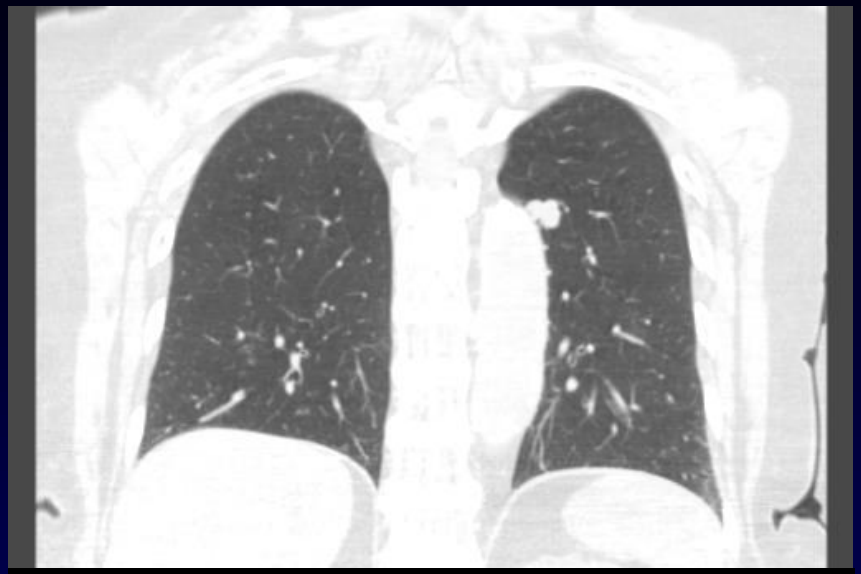
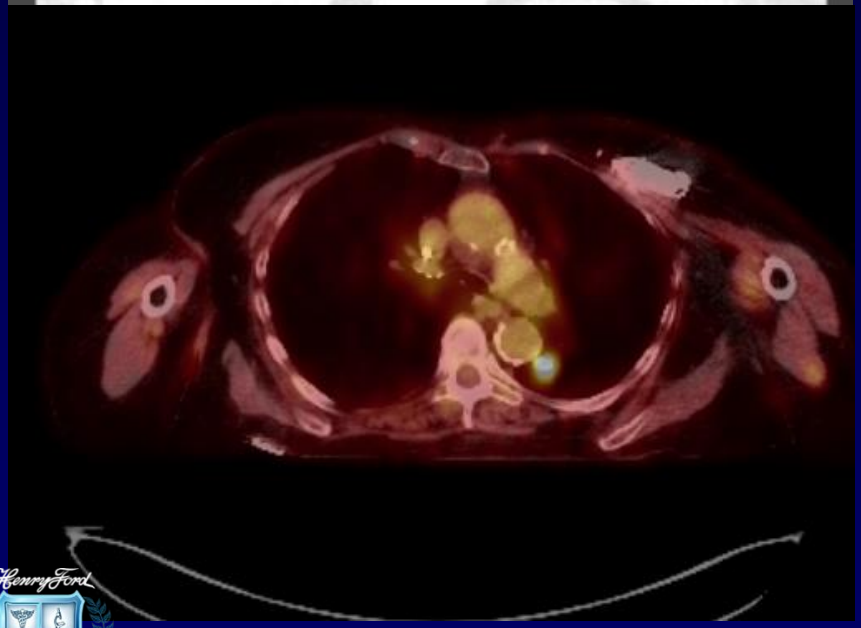
CASE 4: DECENDING AORTA





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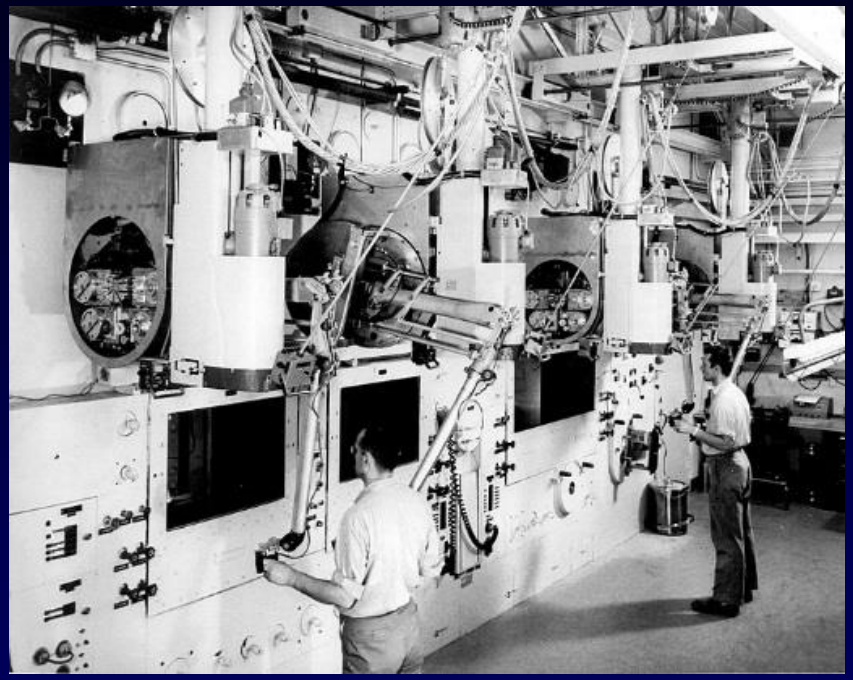
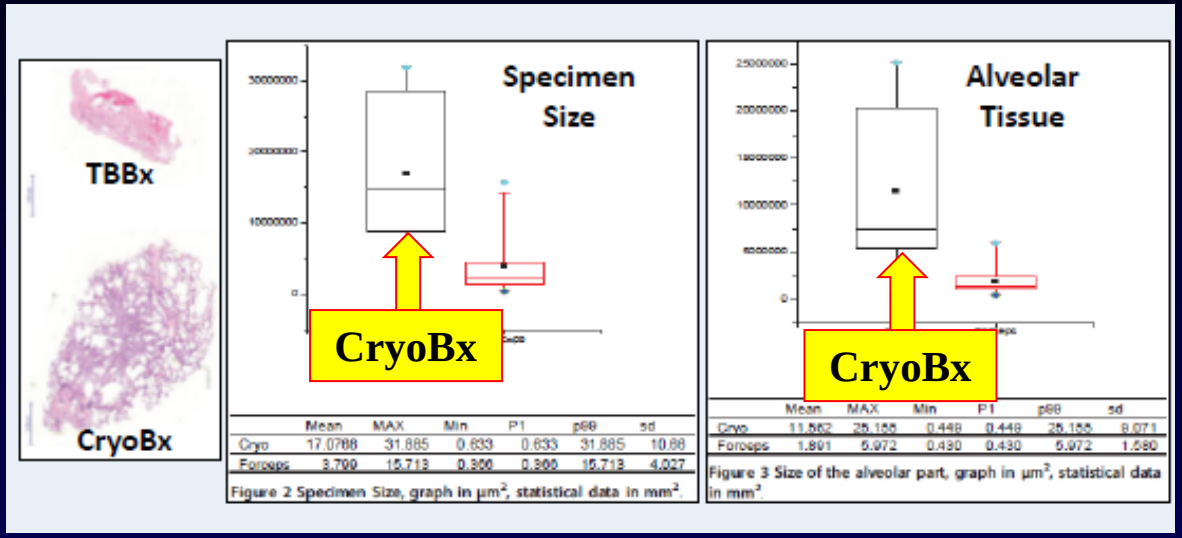
HISTORY OF MEDICAL ROBOTS

- "True" robots have independent motions or preprogramed actions
- Surgical robots are better described as computer-enhanced tele-manipulator systems
- First master-slave manipulator use in Argonne National Laboratory to work with radioactive material in 1945



CRYOBIOPSY vs. TRANSBRONCHIAL BIOPSY

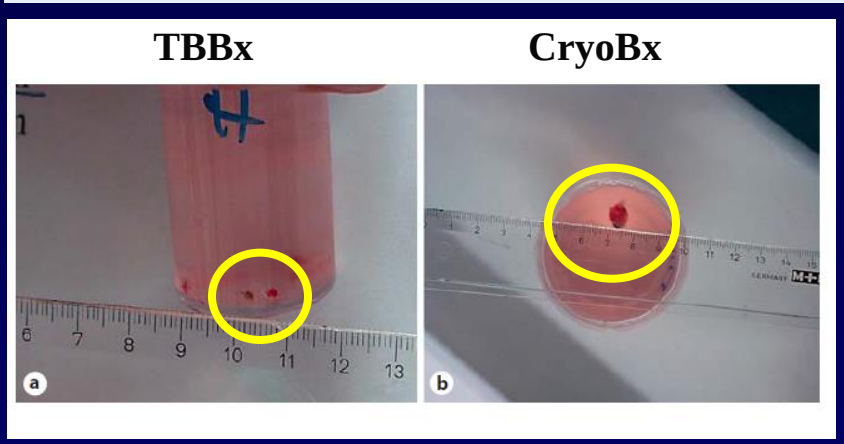


	Mean	MAX	Min	P1	p99	sd
Cryo	17.0788	31.885	0.633	0.633	31.885	10.66
Forceps	3.799	15.713	0.366	0.366	15.713	4.027

Figure 2 Specimen Size, graph in μm^2, statistical data in mm^2.

	Mean	MAX	Min	P1	p99	sd
Cryo	11.562	25.155	0.448	0.448	25.155	8.071
Forceps	1.891	5.972	0.430	0.430	5.972	1.680

Figure 3 Size of the alveolar part, graph in μm^2, statistical data in mm^2.



Cryobiopsy on average is 3x the size of TBBx

Babiak A, et al. *Respiration* 2009; 78: 203–8

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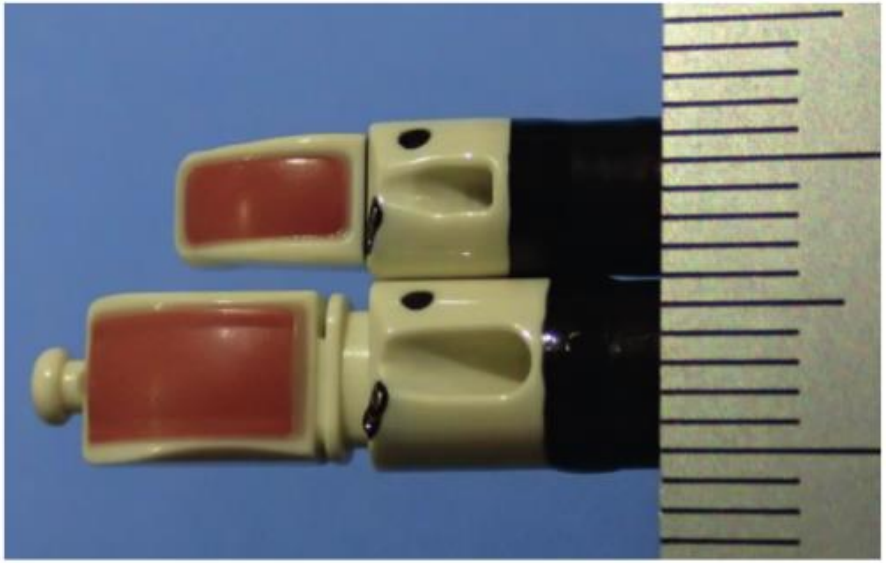
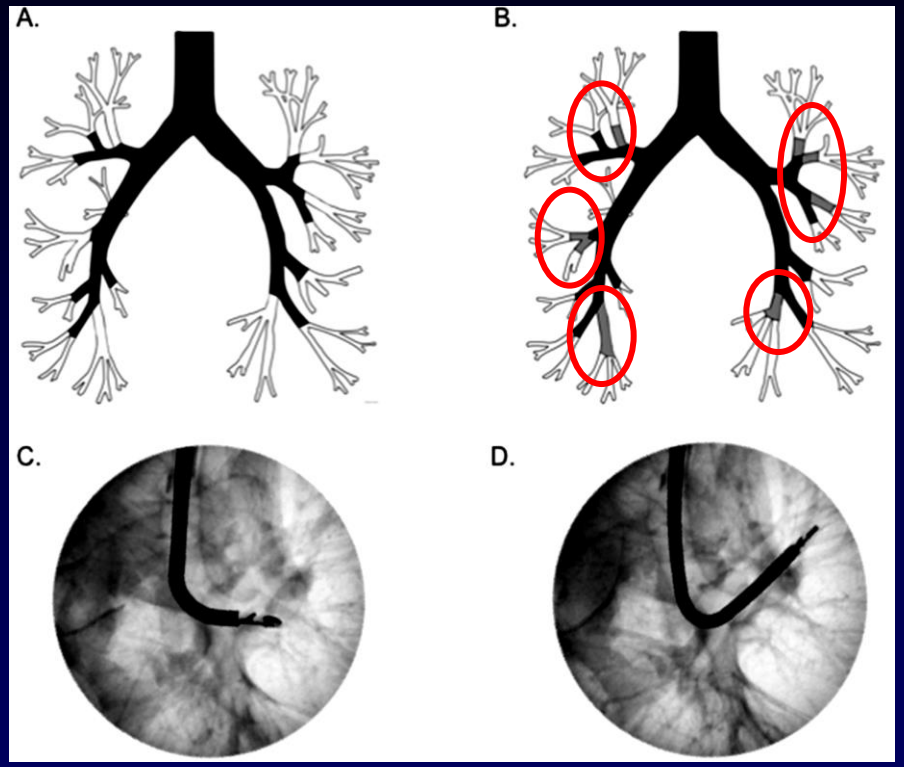
CRYOBIOPSY SUMMERY

- Average size: 5-7mm
- Less artifact
- Easier immunohistochemical evaluation
- Complex pathology: UIP, NSIP, DIP
- Consider as alternative to open lung biopsy

THIN CONVEX ULTRASOUND PROBE

Figure 1: The appearance of both the thin convex probe endobronchial ultrasound to the current convex probe endobronchial ultrasound





Thank You

Michael J. Simoff, MD, FACP, FCCP
Professor of Medicine
Director, Interventional Pulmonology
Director, Lung Cancer Screening
Pulmonary and Critical Care Medicine
Henry Ford Medical Center
Wayne State University, School of Medicine
313-916-4406
MSimoff1@hfhs.org

Michael J. Simoff, M.D.