NATIONAL LUNG CANCER ROUNDTABLE

American Cancer Society®

Project ECHO®

Addressing Lung Cancer Biomarker Testing Through Project ECHO: 2022-2023 Expansion

Session Two: Central Time Combined Hub

Welcome to Session One: Central Time Combined Hub
ACS/NLCRT Lung Cancer Biomarker Testing Project ECHO

Each ECHO session will be recorded and will be posted on echo.cancer.org

You will be muted with your video turned off when you join the call.
Use the buttons in the *black* menu bar to unmute your line and to turn on your video.
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Today's materials will be made available on echo.cancer.org

Please type your name, email address and organization in the chat box

This ECHO session takes place on the Zoom platform.
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American Cancer Society®

Project ECHO®

Agenda Preview & Introductions

Pierre De Delva, MD

Chief of General Thoracic Surgery

University of Mississippi Medical Center

Today's Agenda

01	**Agenda Preview & Introductions** (15 min)
02	**Didactic Presentation: Barriers and Pathways to Biomarker Testing** (15 min)
03	**Didactic Q/A** (5 min)
04	**Case Presentation** (5 min)
04	**Case Presentation Recommendation/Discussion** (10 min)
05	**Post-Session Poll & Wrap Up** (5 minutes)

This ACS/NLCRT Lung Cancer Biomarker Testing ECHO series is made possible by funding provided by:

Additional thanks to Foundation Medicine

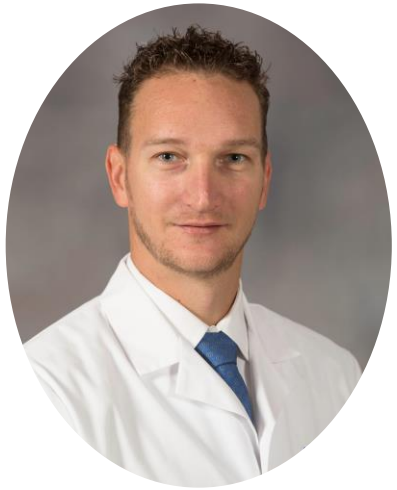
Introductions: Meet our Central Time Combined Hub Faculty

Pierre De Delva, MD
University Of Mississippi Medical Center
Cancer Center And Research Institute
Facilitator & NLCRT Faculty Member

Zhonglin Hao, MD, PhD
University of Kentucky
Markey Cancer Center
Facilitator & NLCRT Faculty Member

Eric Flenaugh, MD, FCCP
Grady Health System
NLCRT Faculty Member

Ray U. Osarogiagbon, MBBS FACP
Baptist Cancer Center
NLCRT Faculty Member



Michal Senitko, MD
University Of Mississippi Medical Center
Cancer Center And Research Institute
NLCRT Faculty Member

Ignacio Wistuba, MD
MD Anderson Cancer Center
NLCRT Faculty Member

Introductions: Meet our Central Time Combined Hub Faculty

Lynette Sholl, MD, FCAP
Brigham and Women's Hospital
Ad Hoc NLCRT Faculty Member

Farhood Farjah, MD, MPH
University of Washington
Ad Hoc NLCRT Faculty Member

Introductions: Meet our Central Time Combined Hub ACS Staff Team

Korey Hofmann, MPH
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ECHO Coordinator

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ECHO Tech Coordinator

Krista Kirksey Thomas
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Amy Williams
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ECHO Coordinator

Introductions: Meet our Arkansas Faculty

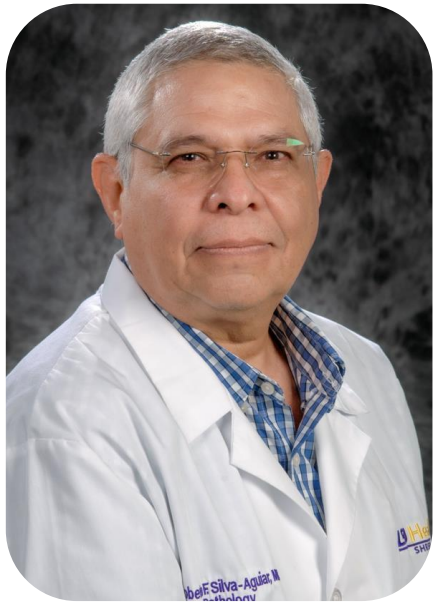
Sajjad A. Bhatti, MD
UAMS Winthrop P. Rockefeller Cancer Institute
Facilitator & Faculty Member

Sam Makhoul, MD
CARTI Cancer Center
Faculty Member

Humdum Durrani, MD
St. Bernards Cancer Center
Faculty Member

Introductions: Meet our Louisiana Faculty

Brian G. Fuller, MD
LSU Health
Faculty Member



Roberto Silva, MD
LSU Health
Faculty Member

Sarah Thayer, MD, PhD
LSU Health
Feist-Weiller Cancer Center
Faculty Member &
Facilitator

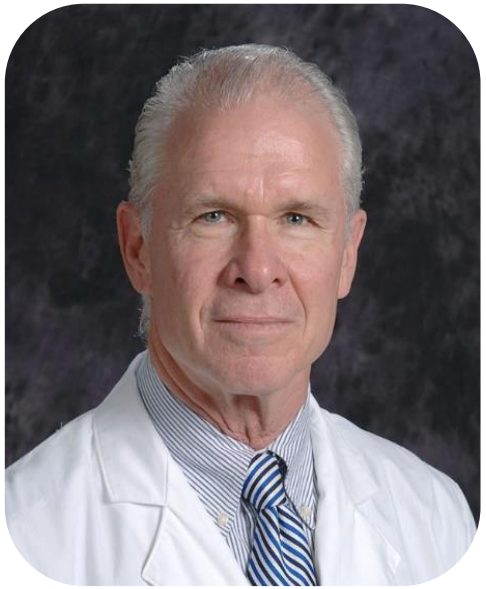
Troy Richards, MD
LSU Health
Faculty Member

Carlos Previgliano, MD
LSU Health
Faculty Member

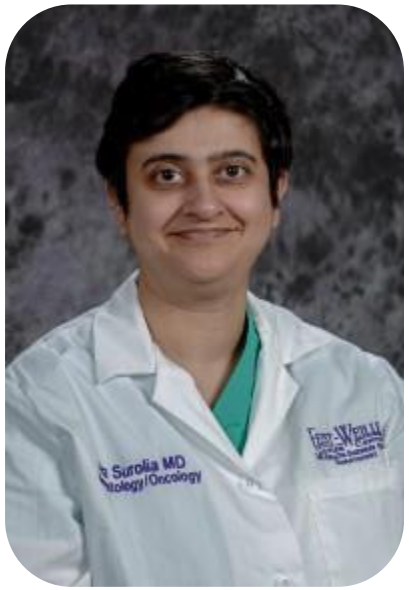
Introductions: Meet our Louisiana Faculty

Robert Holladay, MD, FCCP
LSU Health
Faculty Member

David Chambers, MD
LSU Health
Faculty Member



Robert White, MD, FACS
LSU Health
Faculty Member



Ira Surolia, MD
LSU Health
Faculty Member

Kavitha Beedupalli, MD
LSU Health
Faculty Member

Introductions: Meet our Tennessee Faculty

Philip Edward Lammers, MD
Baptist Cancer Center
Facilitator & Faculty Member

J. Rob Headrick, MD
CHI Memorial Chest & Lung Cancer Center
Faculty Member

Melissa Johnson, MD
Sarah Cannon/Tennessee Oncology
Faculty Member

Raymond U. Osarogiagbon, MD
Baptist Cancer Center
Faculty Member

Introductions: Meet our Texas Faculty

Sheena Bhalla, MD
Facilitator & Faculty Member
UT Southwestern Medical Center

Farrah Kheradmand, MD
Facilitator & Faculty Member
Baylor College of Medicine

Linda Green, MD
Faculty Member
ME DeBakey VAMC

Bryan Burt, MD
Faculty Member
Baylor College of Medicine

Introductions: Meet our Arkansas Spoke Sites

CARTI
BRINGING THE FIGHT TO CANCER

UAMS
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES

ST. BERNARDS MEDICAL CENTER
Cancer Treatment Center

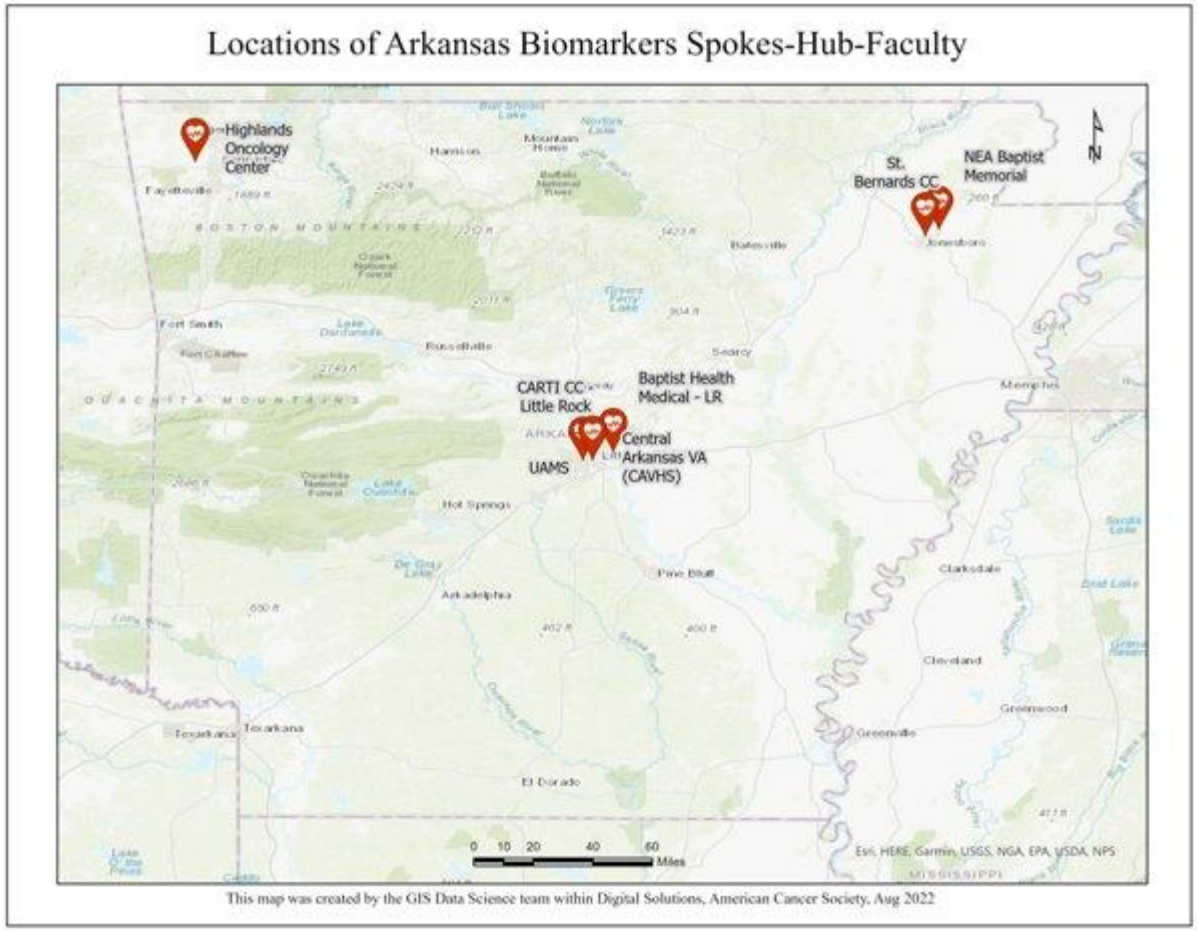
NEA BAPTIST

Baptist Health

HIGHLANDS ONCOLOGY

Jefferson Regional

Central Arkansas Veterans Healthcare System



Introductions: Meet our Louisiana Spoke Sites

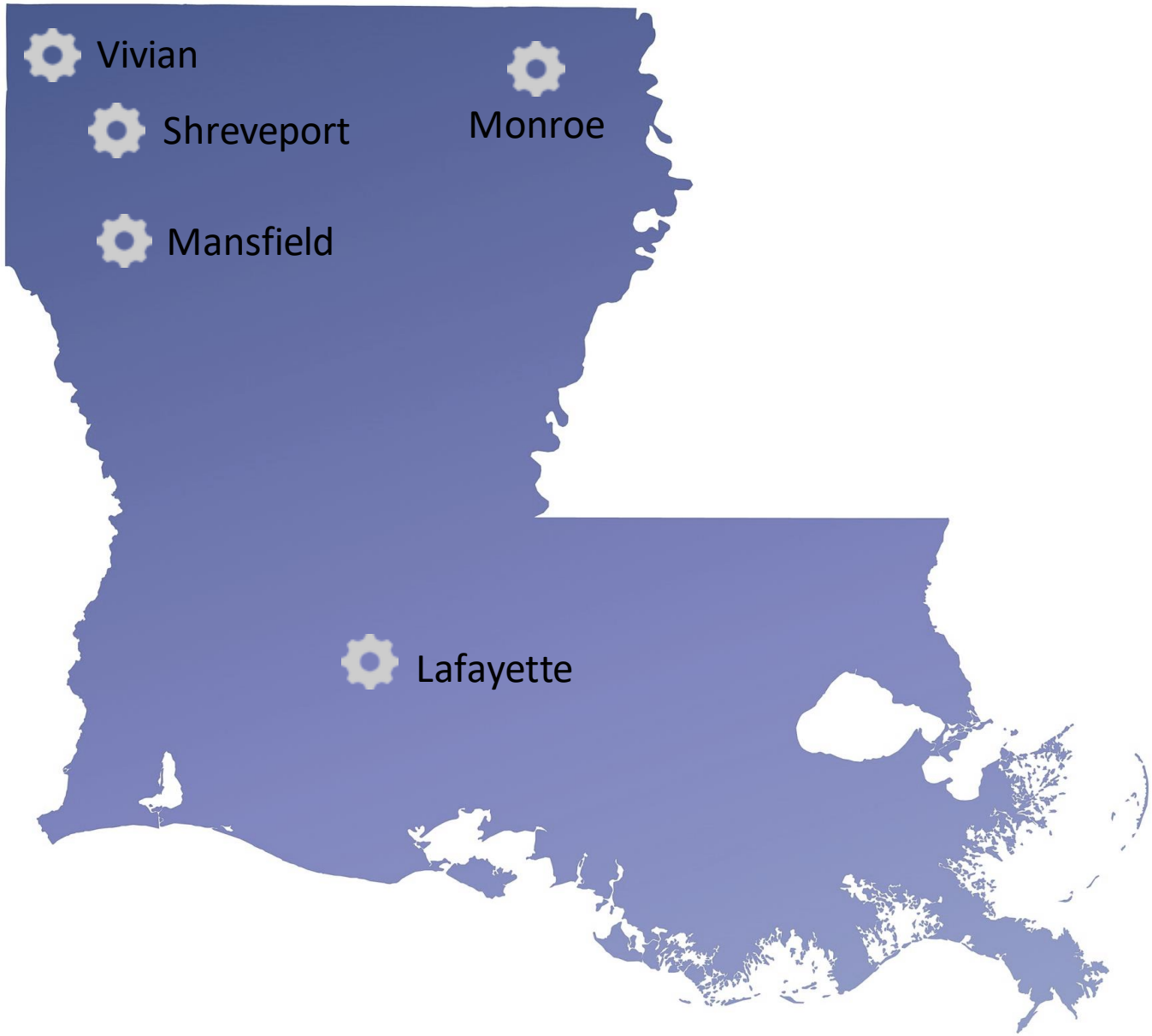
Ochsner Health

North Caddo Medical Center

Lourdes Physician Group

DeSoto Regional Health System
Improving Life Everyday

St. Francis Medical Center



Introductions: Meet our Tennessee Spoke Sites

Introductions: Meet our Texas Spoke Sites

- University Medical Center El Paso
- Hospitals of Providence
- CHRISTUS Trinity Mother Frances Health System

Reminder: Please type your *name, email address* and *organization* in the chat box

CENTRAL TIME COMBINED HUB SESSION 2

Didactic Presentation: *Specimen Adequacy for Biomarker Assays*

Eric Flenaugh, MD, FCCP

Director, Advanced Diagnostic & Interventional Pulmonary Medicine

Physician Director, Lung Nodule Program

Grady Cancer Center of Excellence

Disclosures

Specimen Adequacy for Biomarker Assays

Eric L. Flenaugh, MD, FCCP

Director, Advanced Diagnostic & Interventional Pulmonary

Physician Director, Lung Nodule Program

Grady Cancer Center of Excellence

Challenges

- Biomarker assay variability
- “Diagnostic adequacy” vs “BMT adequacy”
- Inability to reliably quantify cellularity on ROSE

Assay and Tumor Quantity Variability

- Biomarker Assays:
  - DNA-based mutational testing assay
  - RNA-based fusion assay
  - Protein-based immunostaining assays
  - FISH assays
- Tumor Variability

Method	Pros	Cons	Recommendation
IHC	Generally available Rapid turn-around-time Reimbursed	Significant false negatives and false positives	Not useful in detecting *RET* alterations due to low sensitivity and specificity
FISH	Generally available Rapid turn-around-time Reimbursed	High false positives and false negatives Requires significant validation efforts	Recommended if NGS or RT-PCR are not available
RT-PCR	Generally available Rapid turn-around-time Cheap	Limited to specified fusion partner detection Not commonly used in NSCLC workflow	Recommended, particularly if part of a multiplexed assay
5′/3′ differential expression	Multiplexable design Hybridization-based assay	Not commonly used in NSCLC workflow Requires significant validation efforts	Not recommended until more comparative data available
DNA-based NGS	Multiplexed and can detect SNVs as well as CNVs	Poor coverage of some intronic regions	Recommended, particularly as part of an RNA/DNA assay
RNA-based NGS	Unbiased fusion information without intron coverage issues	Highly dependent on RNA quality	Preferred method for fusion detection, including *RET*

NSCLC, non–small cell lung cancer; IHC, immunohistochemistry; FISH, fluorescence in situ hybridization; RT-PCR reverse transcriptase polymerase chain reaction; NGS, next-generation sequencing; SNVs, single nucleotide variants; CNV, copy number variations.

TABLE 1 | Molecular testing methods to detect RET and other gene fusions in NSCLC.

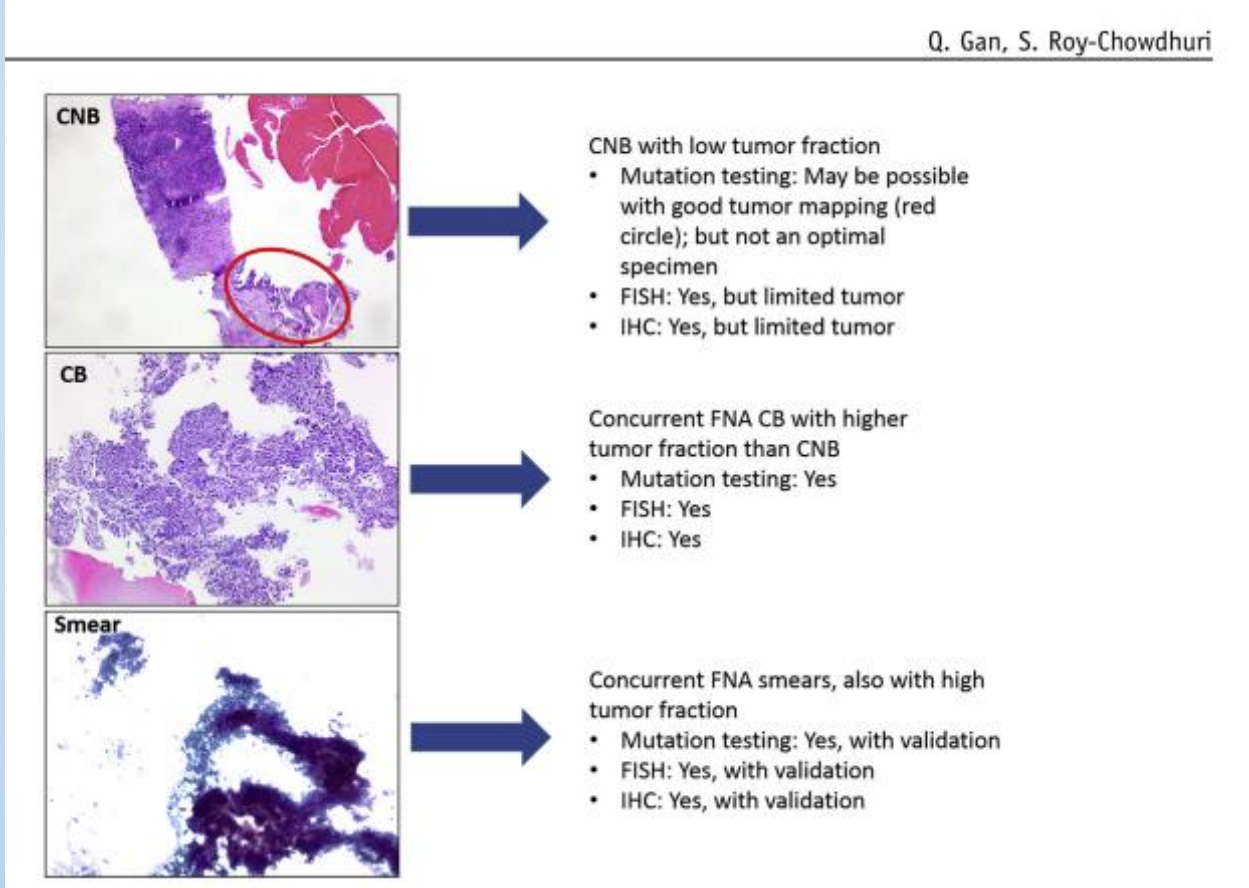
Published in Frontiers in Medicine 2020

Specimen Preparation Limits ROSE

Table 1 Small specimens used for biomarker testing.

Variable	Specimen type				
	Small biopsy (CNB; punch biopsy; forceps biopsy)	Cytology: CB	Cytology: touch imprint; direct smears	Cytology: cytospins; LBC	Cytology liquid biopsy (FNA supernatant; exfoliative supernatant; eg, CSF, urine, effusion)
ROSE for adequacy assessment	No[a]	No	Yes	No	No
Fixation	Formalin[b]	Formalin[c]	Varies[d]	Varies[d]	None
Processing	Paraffin embedding	Paraffin embedding	Varies[e]	Varies[e]	None
Biomarker testing (yes/no)					
DNA-/RNA-based assays	Yes	Yes	Yes[f]	Yes[f]	Yes[f]
FISH	Yes	Yes	Yes[f]	Yes[f]	No
Gene expression	Yes	Yes	Yes[f]	Yes[f]	Yes[f]
IHC	Yes	Yes	Yes[g]	Yes[f]	No

Does ROSE Help or Give False Security?



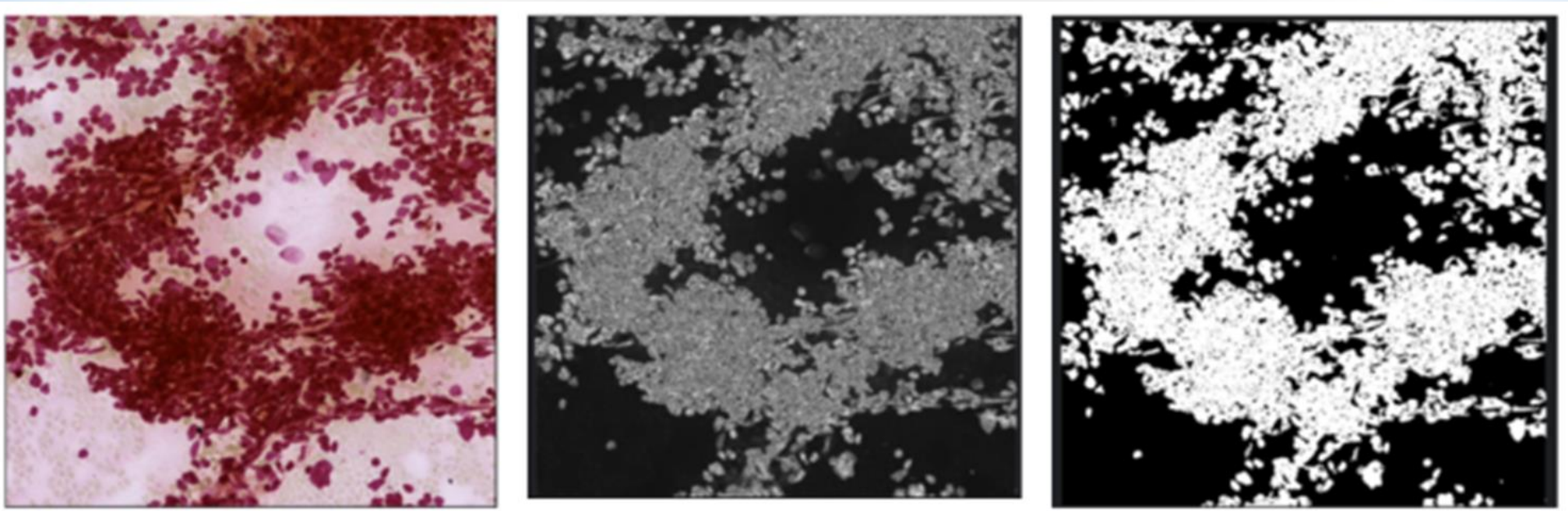
- How many passes needed?
  - Smears
  - Cell Block
  - Core
- Does each pass have adequate tissue for:
  - Diagnosis?
  - Quantity for BM Assays?
- Practice adjustments
  - Only review one slide
  - Recover from slides
  - Serum assay ‘backup’

On the Horizon

- The Role of ROSE is Crucial for Procedure Efficiency
- Confirmation Takes More Than Just Navigation
- Localization Yield Doesn’t = Pathologic Yield

AI ROSE in Bronchoscopy

AI ROSE in Bronchoscopy: Training the System



Input Image | Binary Image | morph_binary (output for OTSU method)

Experimental results with Blue ratio and adaptive thresholding with OTSU

SCC_DC -- Patch # 771

Malignant Cells Segmentation with Dilated Recurrent Residual U-Net for Lung Cancer Detection from Fine-needle Aspiration

Md Zahangir Alom[1], Theus Aspiras[1], Gabriela Oprea-Ilies[2], TJ Bowen[3], Vijayan K. Asari[1,3], Eric L. Flenaugh[4]
[1]Department of Electrical and Computer Engineering, University of Dayton, OH, USA
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Abstract

Histopathological image analysis considered as a standard for cancer diagnosis. In this paper, we use Dilated Recurrent Residual U-Net (DR2U-Net) for malignant cells segmentation for lung cancer obtained using 4-D tip-tracked navigation guided needle biopsy of suspicious lung nodules. The segmentation masks of the input images are generated with blue ratio and adaptive thresholding methods and then labeled samples are verified by the expert pathologist. After training the DR2U-Net, the model is tested on completely new samples and the experimental results shows 0.9869 F1-score and 0.9301 Intersection over Union (IOU) for malignant segmentation tasks.

Background: The lung cancer is one of the leading cancers of death for men and women in USA [1]. New technology uses 4-D CT scan image mapping of small lung tumors and combines real-time navigation guided needle lung biopsy that were previously too small to sample. Despite this technology, the histopathological image analysis is the most important and widely used approach for confirmation of a lung cancer diagnosis. In this study, we have used samples collected from 4-D navigation tracked needle biopsy to detect the malignant cells from whole slide image.

Method: The DR2U-Net is an extension of the R2U-Net model with the multi-scale dilation techniques are incorporated in the bottleneck layer of the R2U-Net model [2]. The number of filters in each layer of DR2U-Net multi-layer model is as follows: 3→32→64→128→256→512→256→128→64→32→1. In each layer, we have used 3×3 size of kernels. The total number of parameters is 17M.

Results: We have collected around 188,160 images and corresponding masks and verified by the expert pathologist where 80 percent are used for training and remaining 20 are used validation and testing the model. The size of the samples is 128×128 pixels. The model is trained for 75 epochs with batch size of 128, Adam optimizer, and using binary cross entropy loss. The qualitative results are shown in Figure 1, the results show that even if the model is trained on weakly annotated samples which is shown in second row in Figure 1, the proposed method shows very accurate segmentation results in third row of Figure 1.

Conclusions: The proposed DR2U-Net shows around 99.45 F1-score and qualitative results demonstrate very accurate segmentation results.

References:

1. Cancer Facts & Figures, Amer. Chem. Soc., Washington, DC, USA, 2018.
2. Alom, M. Z., Yakopcic, C., Hasan, M., Taha, T. M., & Asari, V. K. (2019). Recurrent residual U-Net for medical image segmentation. *Journal of Medical Imaging*, *6*(1), 014006.

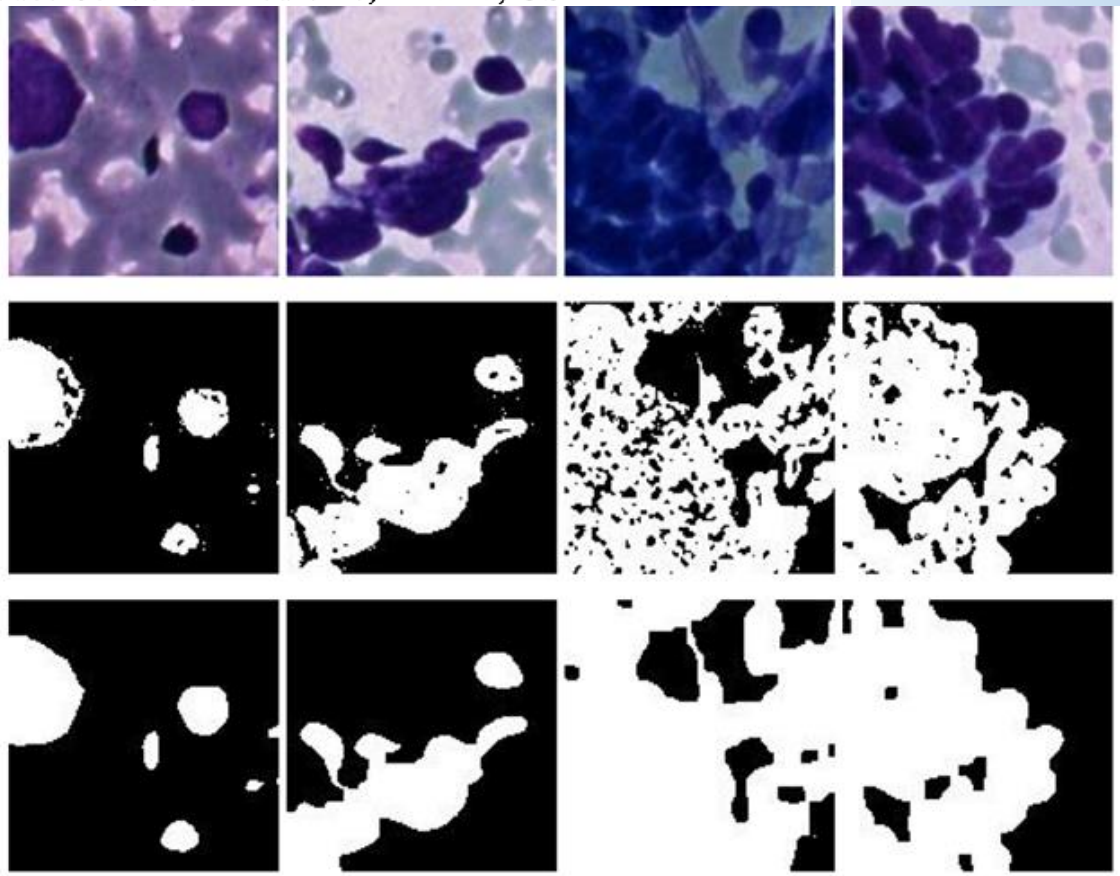
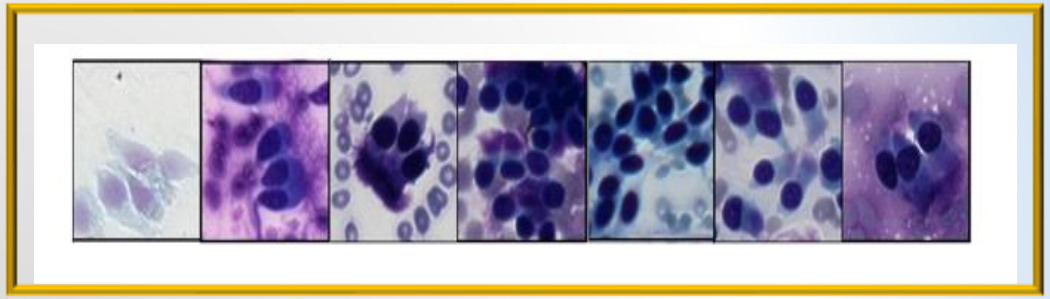


Figure 1. Experimental results: first row represents the input images, second row shows the annotated masks generated with blue ratio and adaptive thresholding, and third row shows the DR2U-Net outputs.

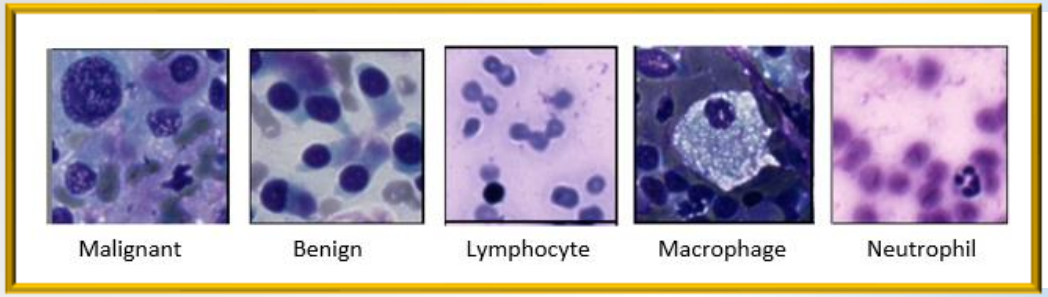
AI ROSE in Bronchoscopy

- Digital microscope Grundium OCUS20 scanned uncovered diff-quik slides during procedure
- Whole Slide Imaging (WSI) in 3-4 minutes. Images divided into 128 x 128 pixel tiles.
- 47 slides scanned (135,000 tiles / slide) for a total of 6.3 MM tiles
- The cytopathologist reviewed and labeled tiles
- The 47 slides yielded 51,241 classified and reviewed tiles, of which 70% were used.

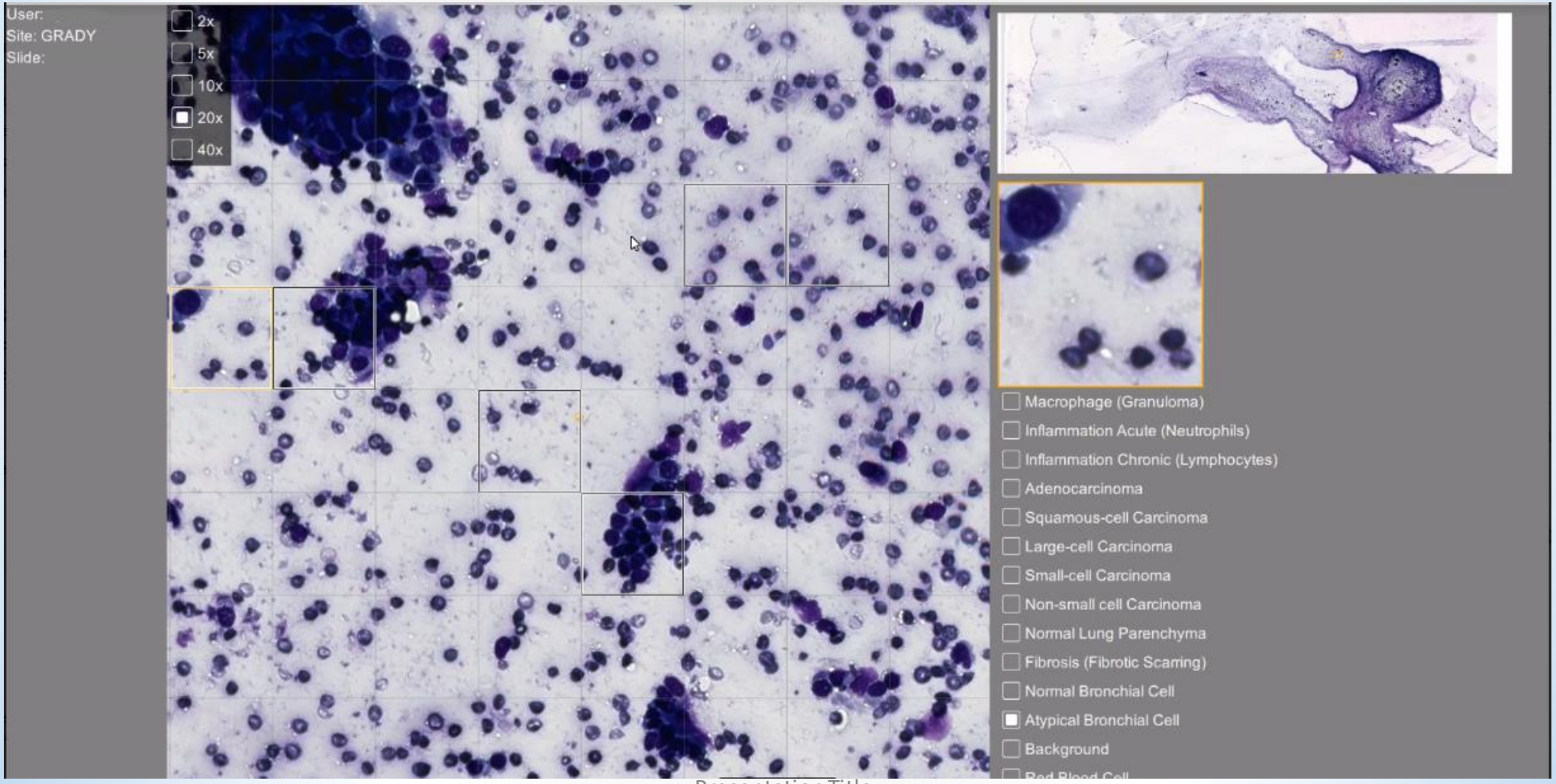
Variation in staining



Classification of cells

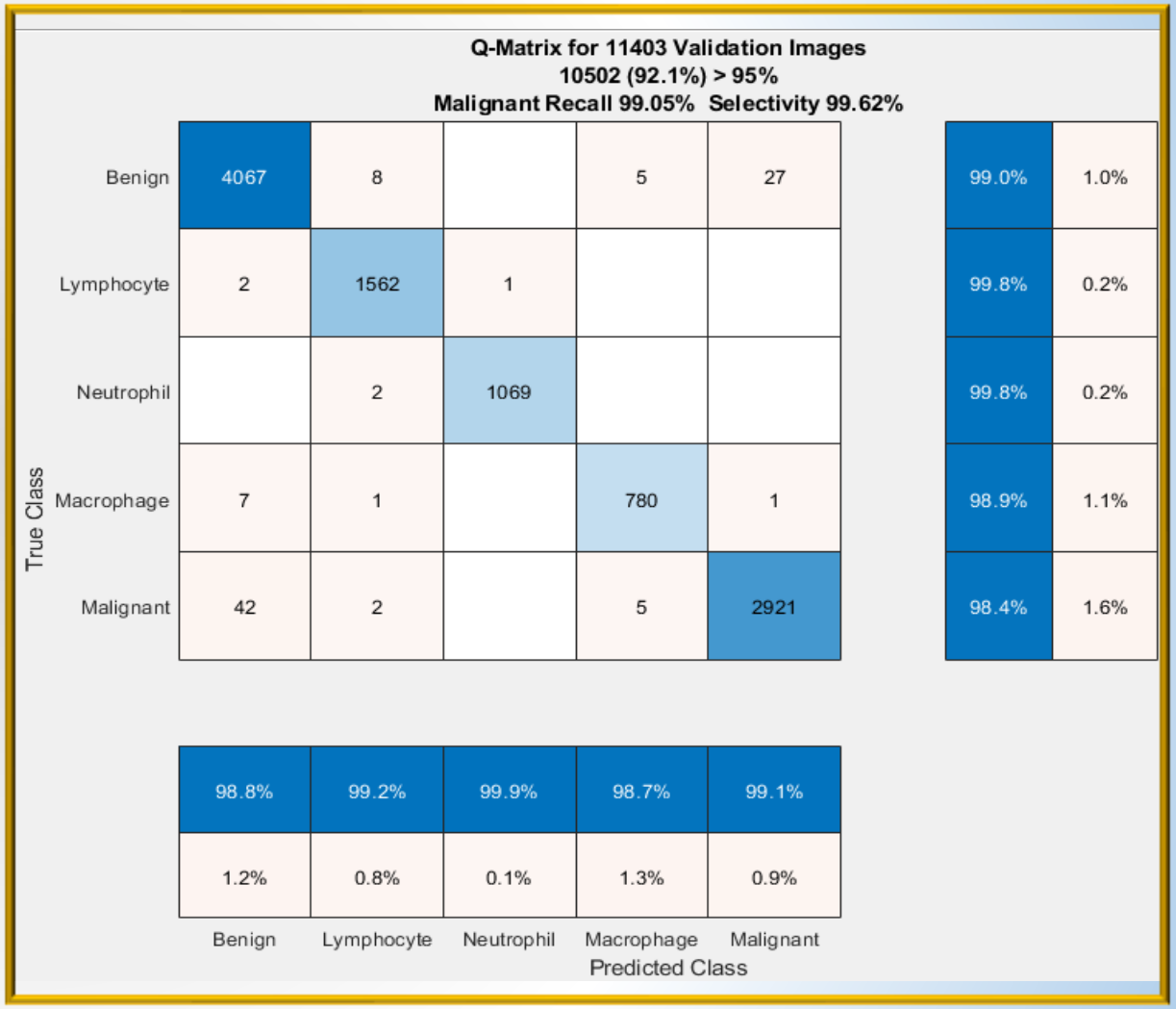


AI ROSE and “Atypical”/ Non-Diagnostic

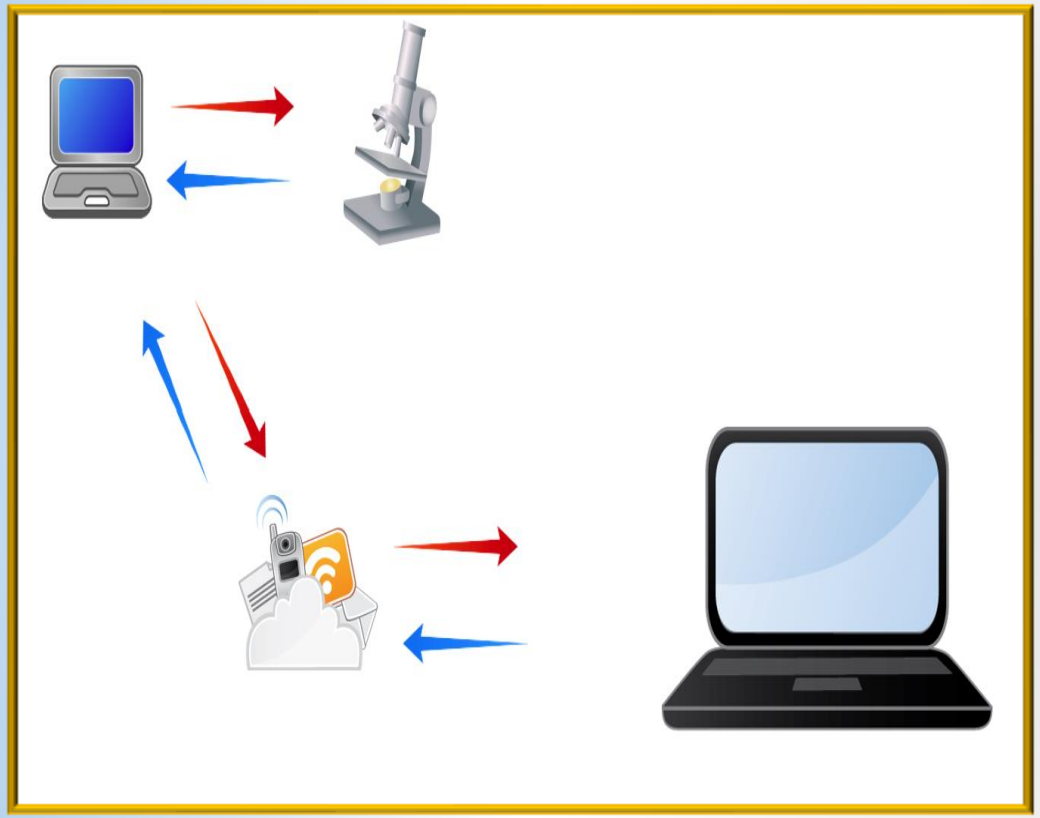


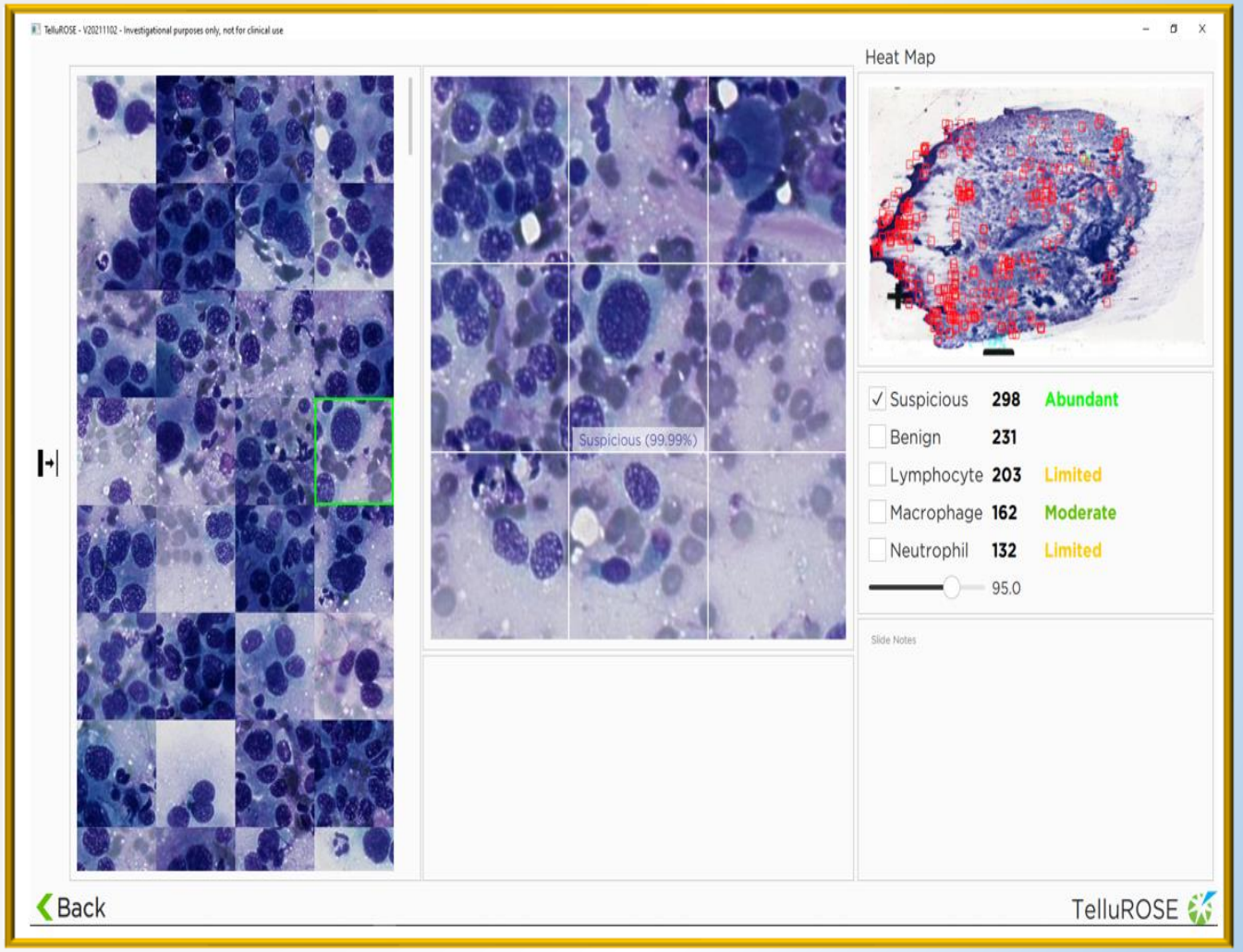
AI ROSE in Bronchoscopy

- Training AI classification algorithm:
  - cytopathologist reviewed 35,868 tiles
- Validation:
  - 15,373 reviewed tiles
- 99.0% recall (true-positive rate)
- 99.0% specificity (true-negative rate)
- AI was able to give amounts of material on slide



AI ROSE in Bronchoscopy





The End

Didactic Questions

Melissa Johnson, MD

Program Director, Lung Cancer Research

Sarah Cannon Cancer Institute

Susan Garwood, MD

Pulmonologist

TriStar Centennial Medical Center

Sarah Cannon Cancer Institute

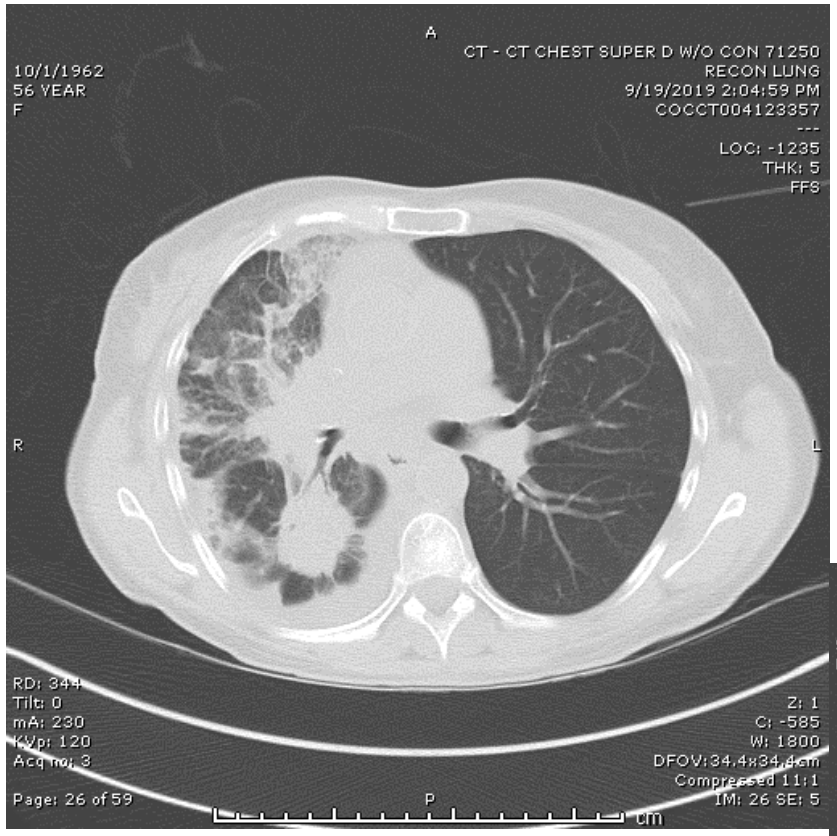
Lauren Ventola, MD

Interventional Pulmonologist

TriStar Centennial Medical Center

Sarah Cannon Cancer Institute

- 59 yo female who smokes daily presents with abdominal pain, swelling to osh
- 30 years ½ ppd =15 pack years
- Exam palpable large abdominal mass
- CT abd/pelvis 13.5x14.1x11.7 complex ovarian mass
- CT chest 4.6 cm RLLL mass, hilar and med adenopathy, R supraclavicular node
- CEA 294 CA 125 236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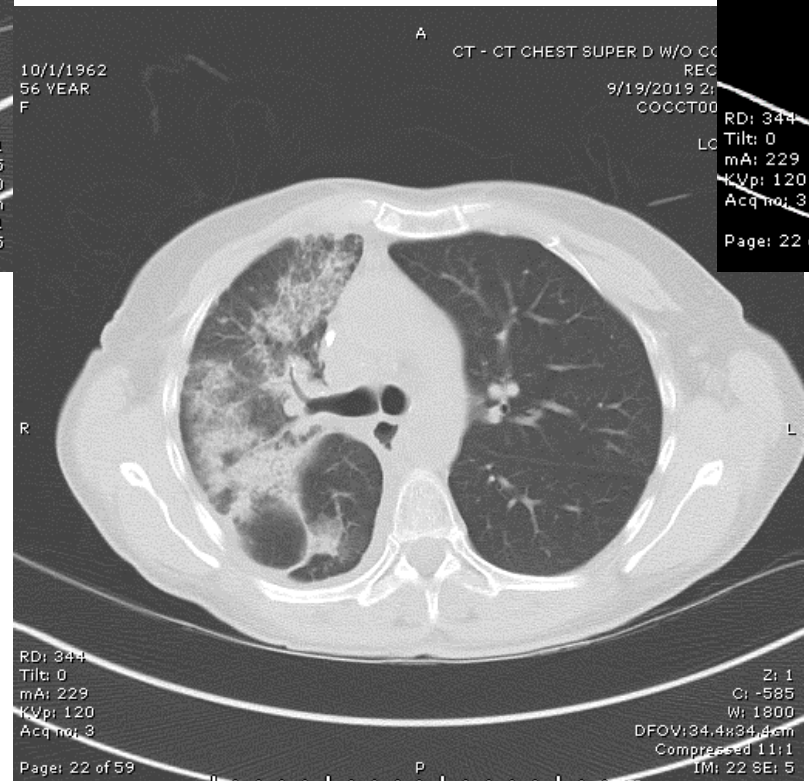
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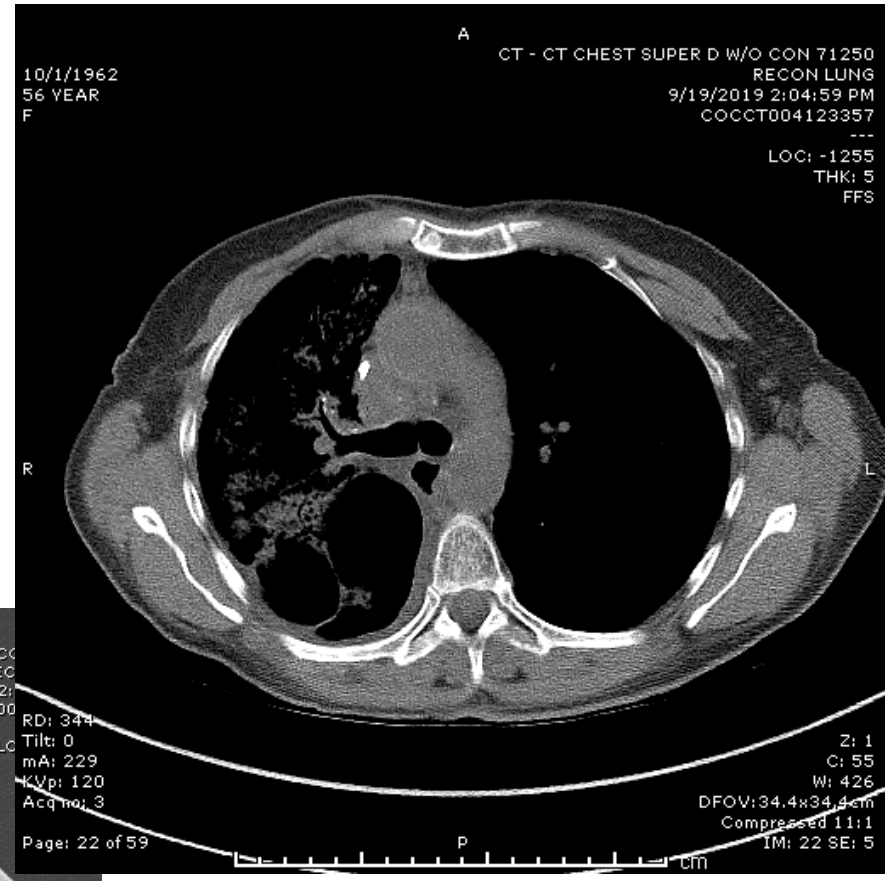
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- FNA of supraclavicular adenocarcinoma NOS
- Induction chemo 3 cycles carbo/taxol followed by BSO, TAH and omentectomy
- Path: right ovary high grade carciomma with clear cell features with focal tubal involvement, omentum negative, uterine serosal involvement
- Palliative chemo recommended
- Referal for robotic nav bronch and ebus-RUL, RLL, 10R, 4R, 7 positive for lung adenocarcinoma

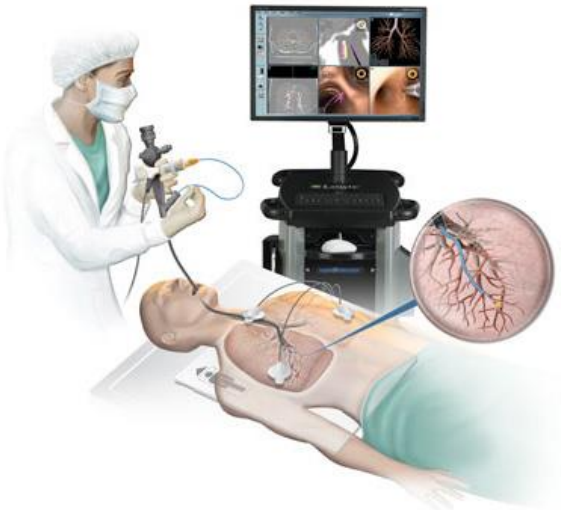
- Molecular profile-NGS-EGFR Exon 19 mutated, PDL 1-25%, all others negative
- Bone scan –metastatic disease
- Carbo, alimta, keytruda-changed to osimertinib when egfr returned
- Continues on monotherapy osimertinib
- Serum NGS 9/20222 no EGFR mutation noted

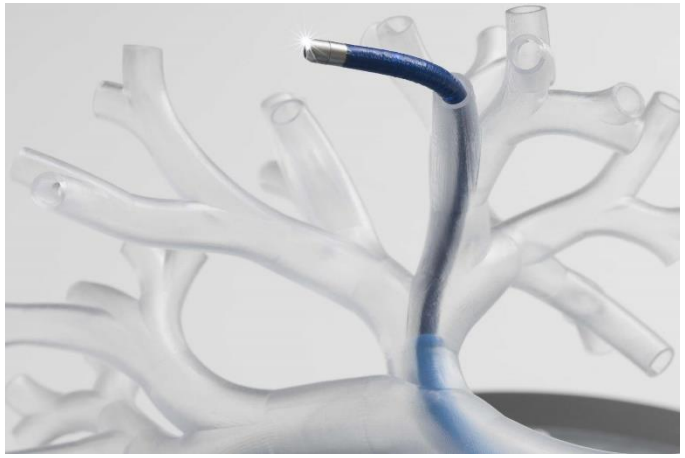
TISSUE IS THE ISSUE

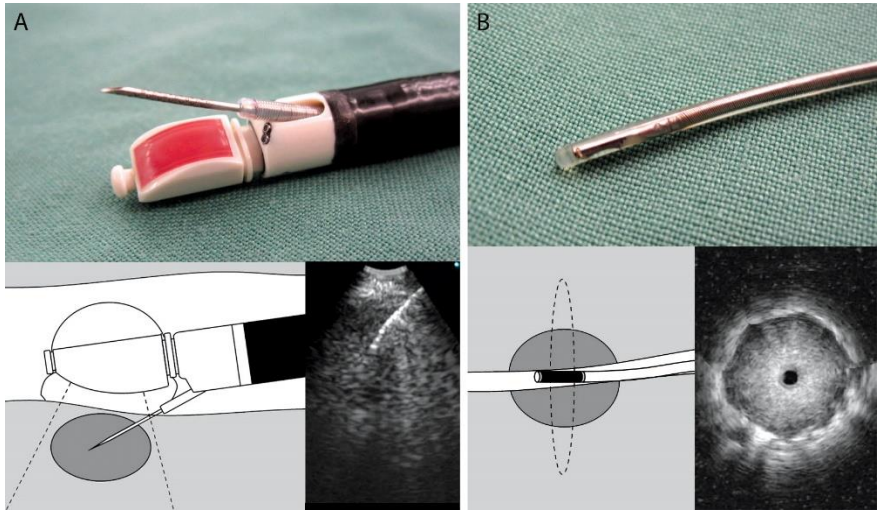
- Biopsy type
  - Endobronchial ultrasound (EBUS)
  - Navigational bronchoscopy
    - Robotic navigation
    - Non-robotic navigational platform
    - Advanced imaging options
      - Cone beam CT
      - Cios Spin
      - Computer tomography
      - Radial probe ultrasound (rEBUS)
  - Thin scope with rEBUS
  - Dye marking for surgical wedge
  - Interventional radiology for ct or us guided bx

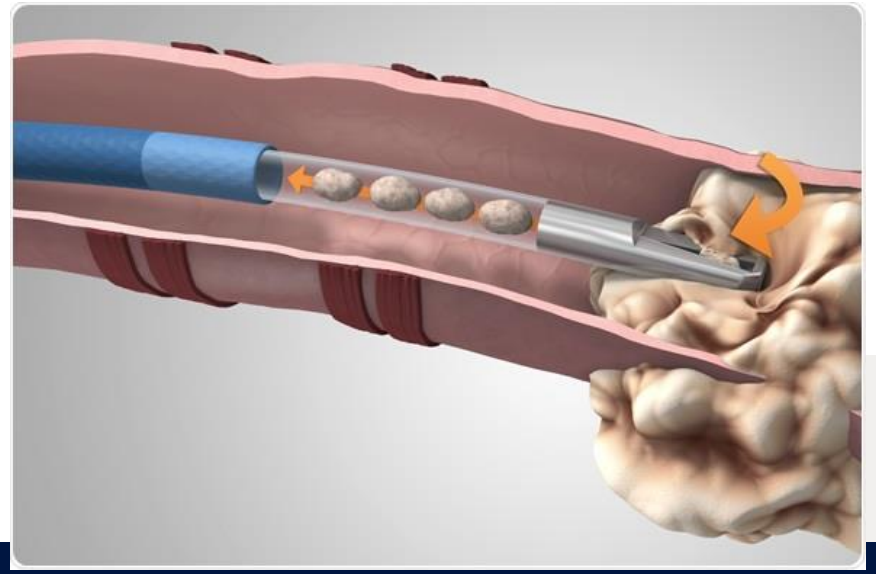
- Location selection
  - PET/CT to guide best location
    - Diagnosis
    - Staging
    - Molecular
  - Safety
  - Feasibility of success
    - Accessible
    - Vascularity
    - Degree of necrosis
    - Patient characteristics
      - Co-morbidities, medications

New Innovations in Diagnostics



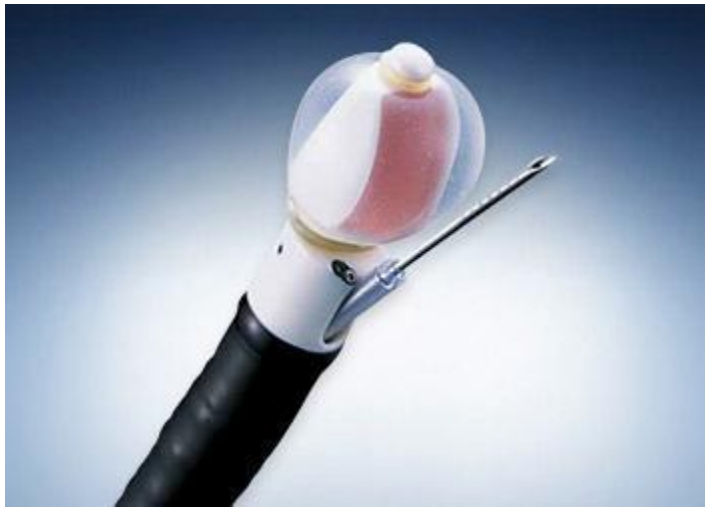


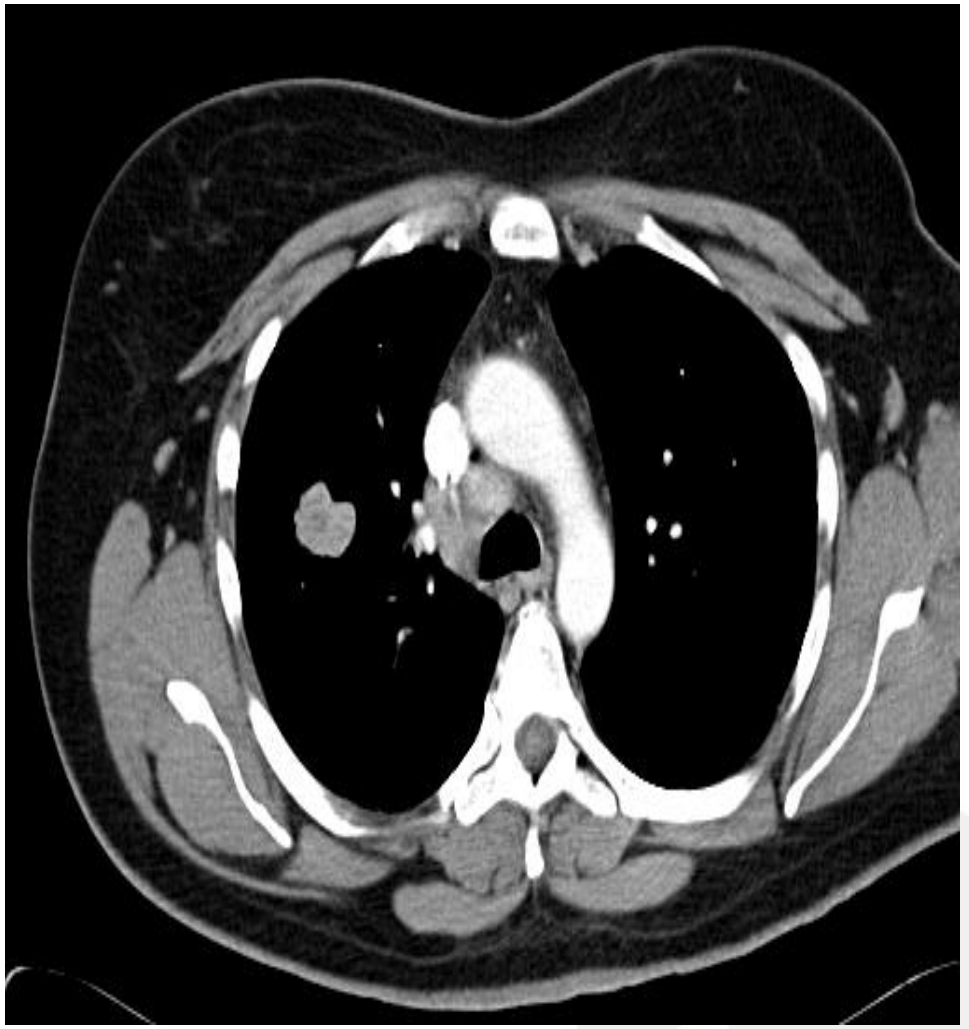




HCA®

EBUS NEEDLE ASPIRATION SYSTEM





ROSE ASSESSMENT

QUALITATIVE

- Degree of necrosis
- Degree of blood
- Degree of contaminant
- Percentage viable tumor

QUANTITATIVE

- Visual cues from container
- Number of biopsies required
- Tool selection for largest volume sampling

Case Presentation Discussion

Specific Question(s) to the Faculty	
Q1	What are the main reasons your center struggles with tissue adequacy?
Q2	
Q3	
Q4	

Wrap-Up & Post-Session Poll Questions

A Few Reminders

Next ECHO Session: 01/27/2022, 10:00am CST

Next Didactic Presenter: *Ignacio Wistuba, MD, Choice of Panel, Interpretation of Results and Next Steps*

Materials and Resources will be made available soon.
All resources will be available on the [ACS ECHO Website]

Spokes: Interested in scheduling your Case Presentation? Let us know.
Faculty: All future case presentations will be shared with you at least 24-hours in advance

Additional Feedback on Today's Session? Tell us in the Post Session Feedback Forum
(URL in chat box)

Questions: Contact korey.hofmann@cancer.org

THANK YOU & HAPPY HOLIDAYS!
SEE YOU JANUARY 27 @ 10AM CT