

# Whole Slide Imaging/ Digital Pathology



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# Whole Slide Imaging/ Digital Pathology

Historical Perspective  
Advantages  
Obstacles  
Experience from our  
Demonstration Project



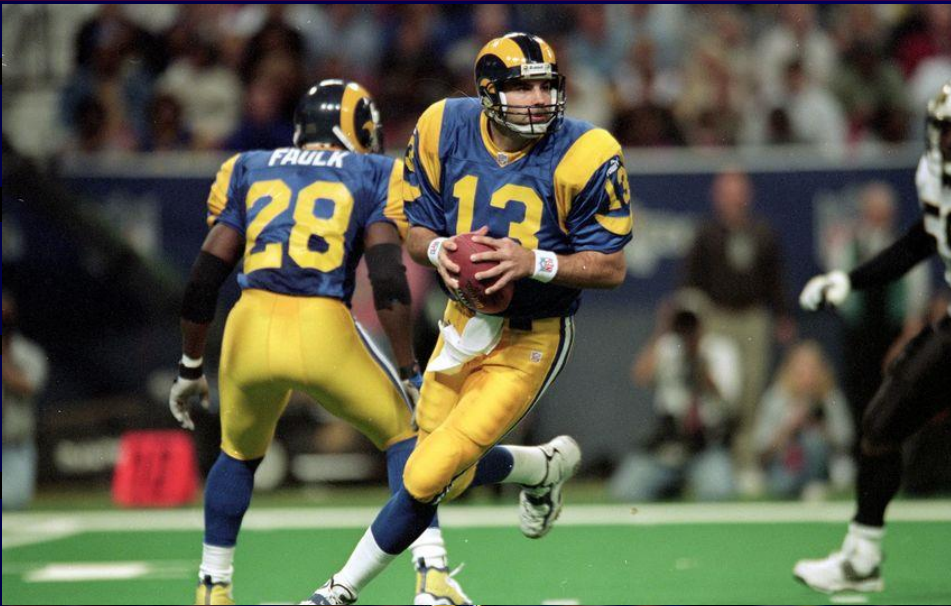
# Disclosures

**No financial relationship with any digital pathology company including Philips.**

**Member of the team evaluating the Philips Image Management System as part of a demonstration project with Sonora Quest Laboratories and Banner Health System.**



# The RAMS ARE BACK!





# And for you Dodger Fans!



I set my DVR to record 'The Biggest Loser' and it keeps recording Dodger games.

A black and white illustration of a man sitting on a chair, looking down at a dog lying on the floor next to him. The man is wearing a dark jacket and a hat.

som<sup>ee</sup>cards  
user card

YOU ONLY LIVE ONCE.  
DON'T WASTE IT BEING A...

A stylized illustration of a man's face and hand. He is pointing his index finger upwards. The illustration is in a high-contrast, orange and white style.

DODGERS FAN

# Objectives

- Review the historical time line/ evolution of digital pathology.
- Describe the advantages of whole slide imaging.
- What are the key elements/ obstacles for implementation.
- Knowledge gained from Philips-Banner-SQL Demonstration Project.

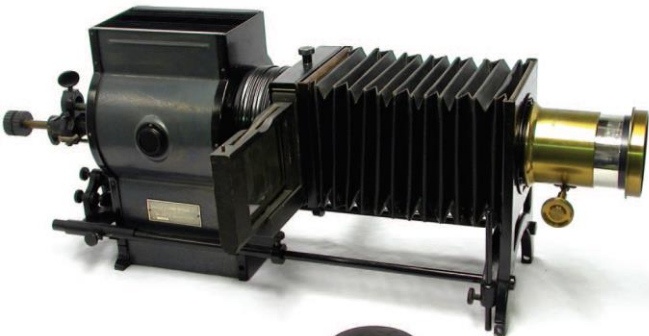


# 100 year span

Leitz Lantern Slide Camera, circa 1910



A



B

Bausch and Lomb Lantern Slide Projector, circa 1908

Morrison and Gardner:Arch Pathol Lab Med. 2015;139:1558

# Enter the 1930-1960s





# Enter the 1950-60s



photo by William Day,  
copyright 2007



© KenRockwell.com

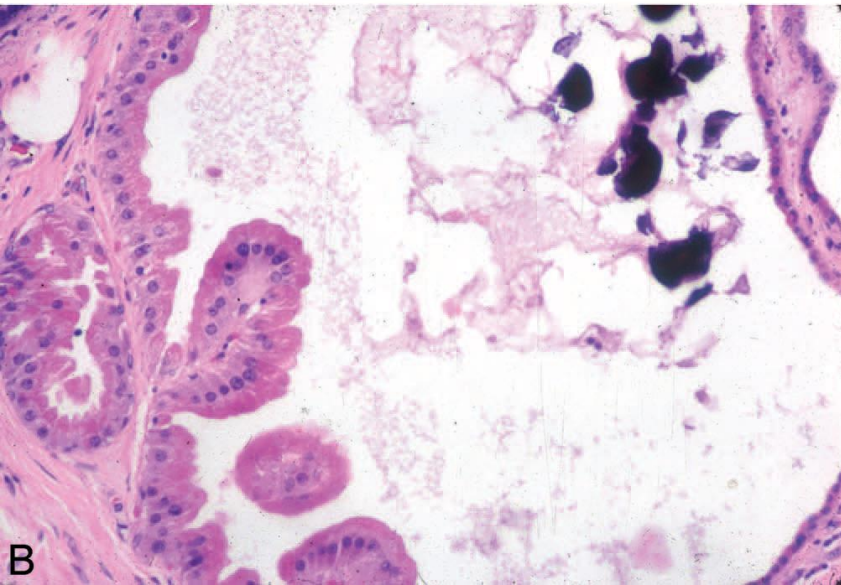




# Enter the 1980's



A



B



Morrison and Gardner: Arch Pathol Lab Med.  
2015;139:1558



# Enter the late 1990's



# Enter the 21 century

**MICROSCOPE WITH  
DIGITAL CAMERA**



**WHOLE SLIDE  
SCANNERS**



**ROBOTIC  
MICROSCOPES**

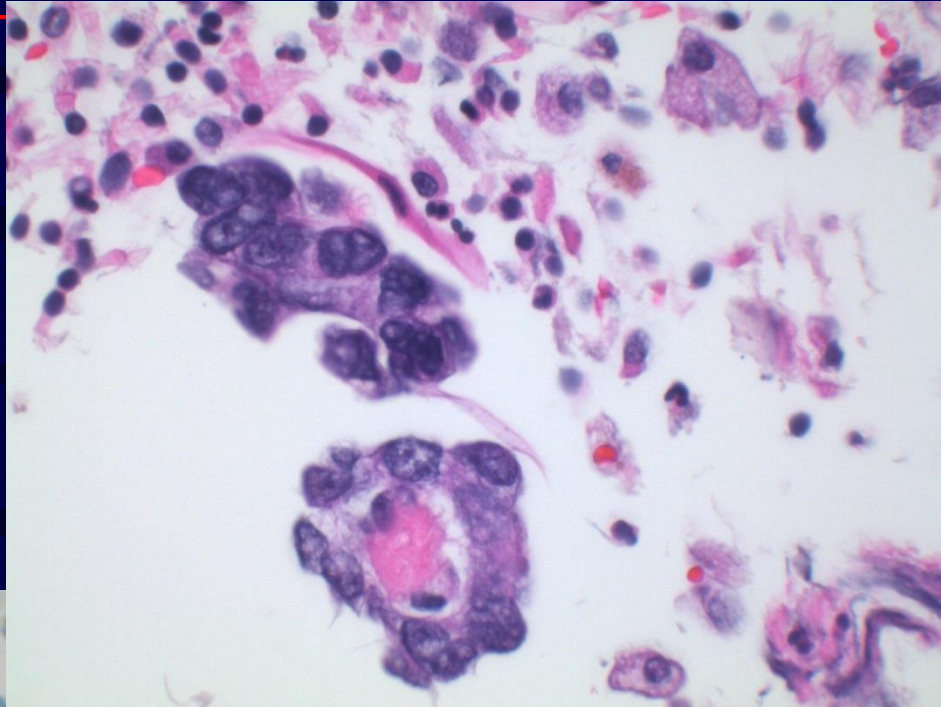


**IMAGE ANALYSIS  
SYSTEMS**





# Patient A BAL fluid



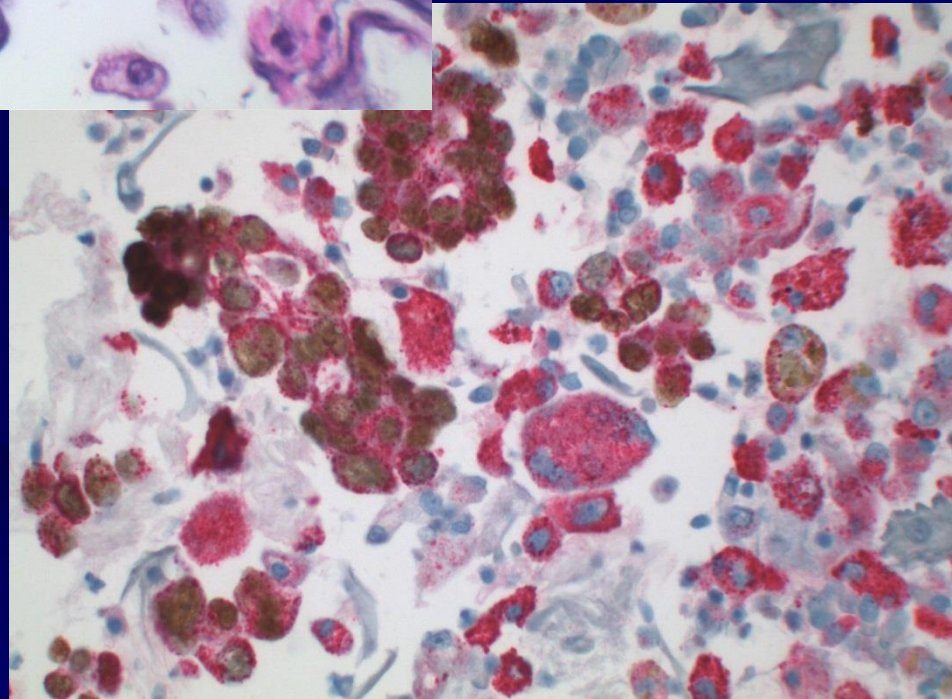
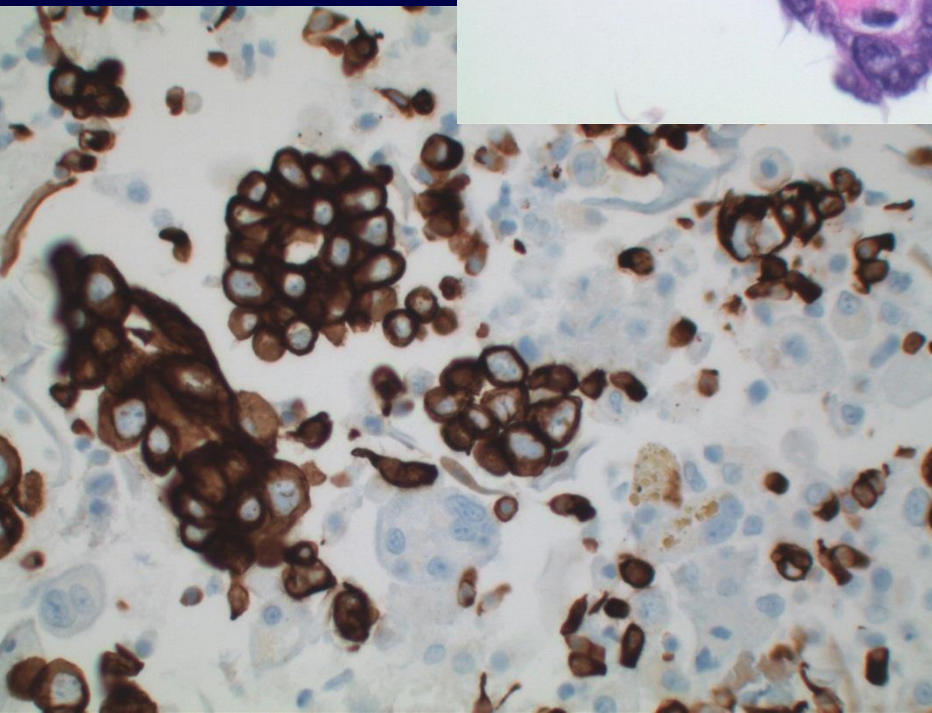
spot digital  
camera

Proof of  
Lung origin



TTF-1/ Napsin

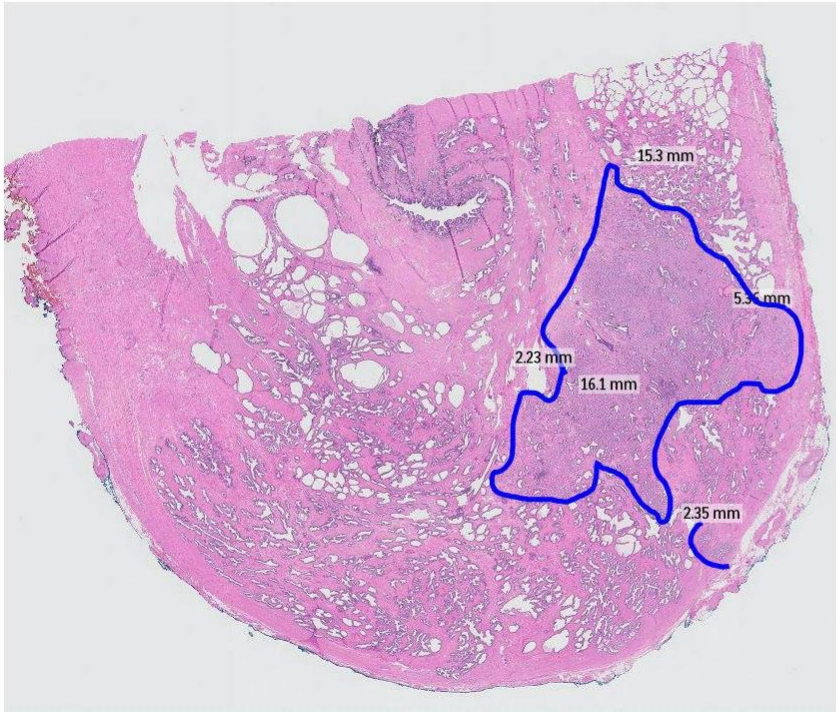
CK7











# Advantages to Whole Slide Imaging

Rapid availability of scanned images to the pathologist.

Eliminate courier time and  cost for labs with multiple remote sites.

Evaluation of multiple slides and regions simultaneously.

Rapid and easy measurement: depth of invasion, area, cell size.

Telepathology: Frozen sections, internal and external consults

Image analysis and application of deep learning tools.

Real time consultation and collaboration



# Considerations in Implementation

## Barriers to the Adoption of Whole Slide Imaging for Clinical Use

Cost: hardware, software, information technology support/infrastructure and maintenance

Pathologist perception of inferior performance compared to microscopy

Lack of standards and/or best practice guidelines

# Considerations in Implementation (2)

## Barriers to the Adoption of Whole Slide Imaging for Clinical Use

Regulatory issues: lack of US FDA approval  
(prior to late 2017)

Medicolegal liability, licensure, and credentialing issues

Absence of defined professional billing codes or business models



# Considerations: Implementing WSI for Diagnosis

Cost: hardware, software, information technology support/  
infrastructure and maintenance  
Pathologist perception of inferior performance compared to  
light microscopy  
Lack of standards and/or best practice guidelines  
Regulatory issues: lack of US Food and Drug Administration  
approval in the United States  
Medicolegal liability, licensure, and credentialing issues  
Absence of defined professional billing codes or business  
models

# Considerations: Implementing WSI for Diagnosis

Applications of WSI in patient care: where to start and how to assemble an implementation team: all slides; IHC, sp. stains etc.

Strategy for selecting a WSI scanner

Resources required to operate and maintain a clinical digital pathology program

Validation of the system to be used

Strategies to encourage adoption of WSI by pathologists

What to expect after going live, based on the experience of early adopters



# Considerations: Implementing WSI for Diagnosis

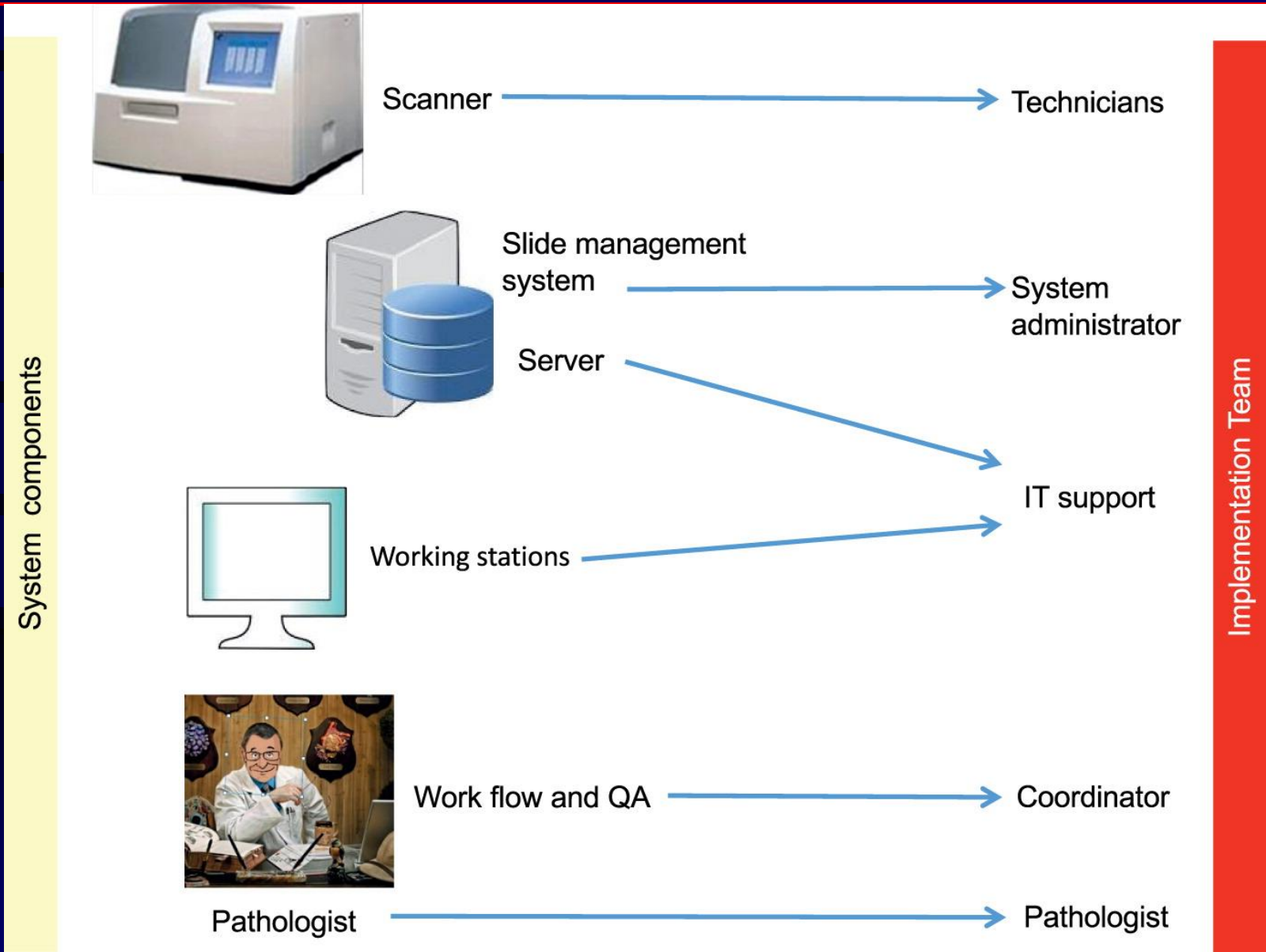
Applications of WSI in patient care: where to start and how to assemble an implementation team  
Strategy for selecting a WSI scanner  
Resources required to operate and maintain a clinical digital pathology program  
Validation of the system to be used  
Strategies to encourage adoption of WSI by pathologists  
What to expect after going live, based on the experience of early adopters

# Pathologist Discomfort with WSI

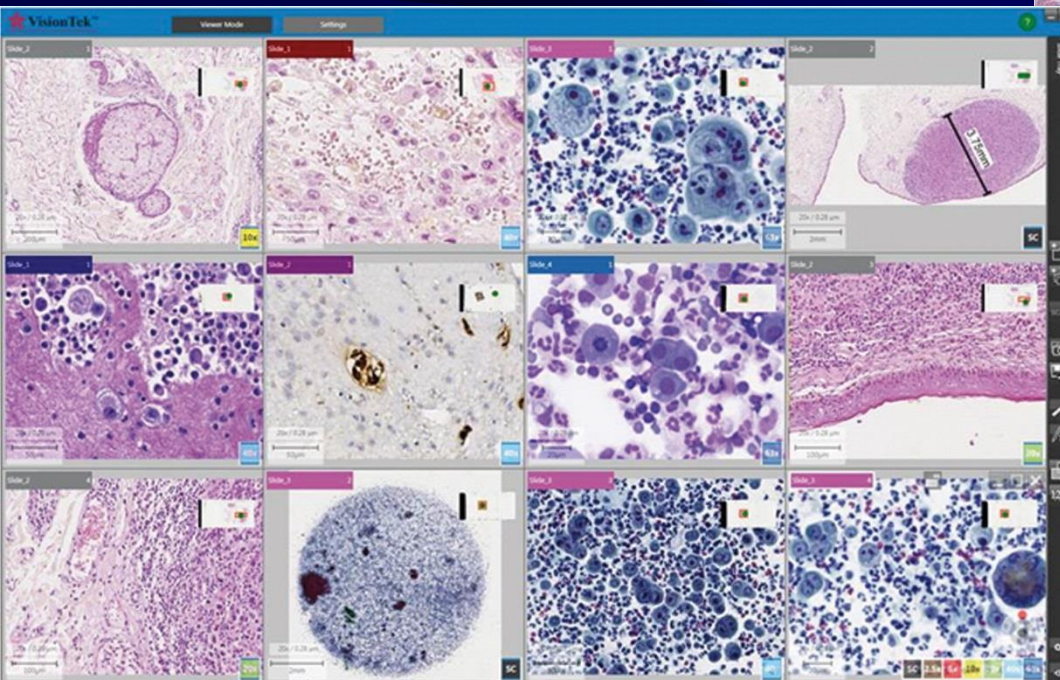
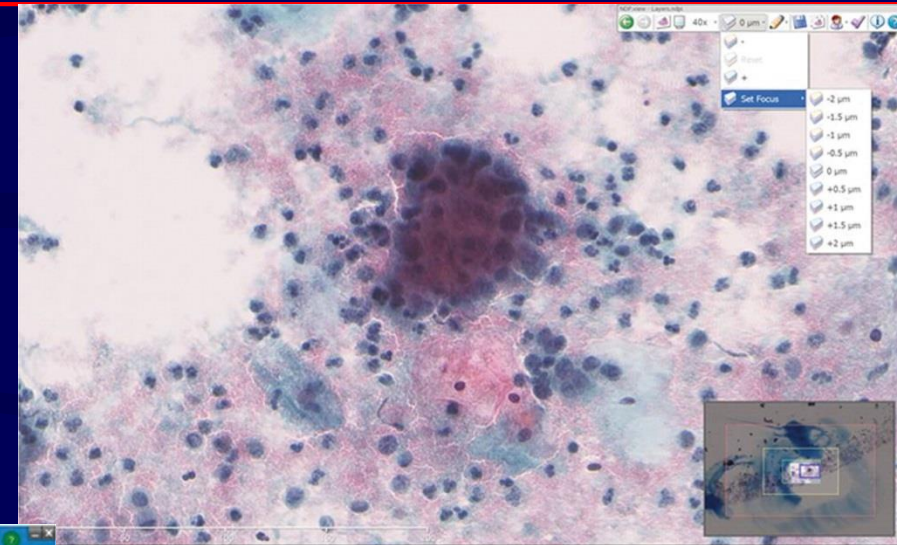
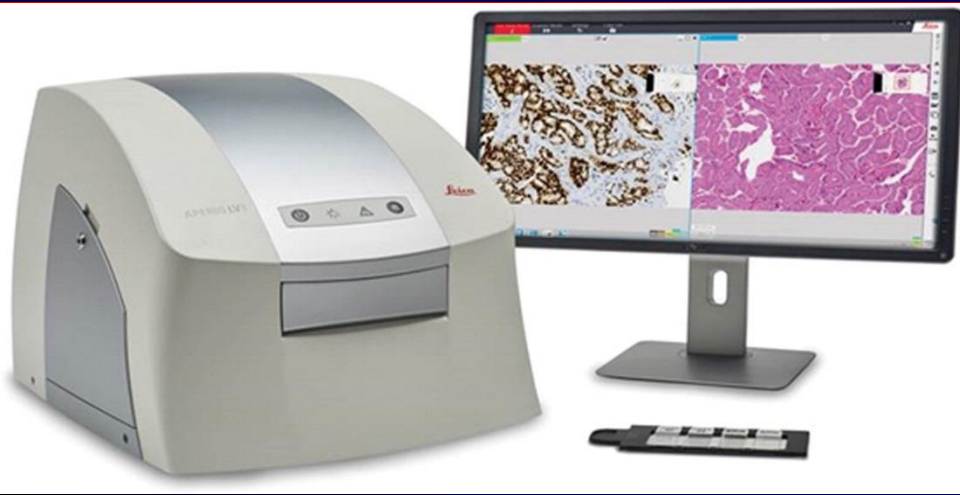
Lack of training or experience with the technology  
Time required to review cases by WSI such that confident diagnoses are rendered  
Fundamental mechanical and ergonomic differences between WSI and light microscopy  
Concern that WSI will introduce unfamiliar digital artifacts over and above those generated by routine histologic processing  
Lack of US Food and Drug Administration approval to use WSI for primary diagnosis in the United States ~~X~~



# Considerations: Implementing WSI for Diagnosis



# Applications: WSI



Aperio- upper left:  
View up to 4 slides

Hamatsu: upper right  
Cytology

Vision Tek-Sakura  
Multiple slides- modalities



# Whole Slide Imaging Philips Study

14 month randomized, blinded study using cases intended for routine surgical pathology diagnosis.

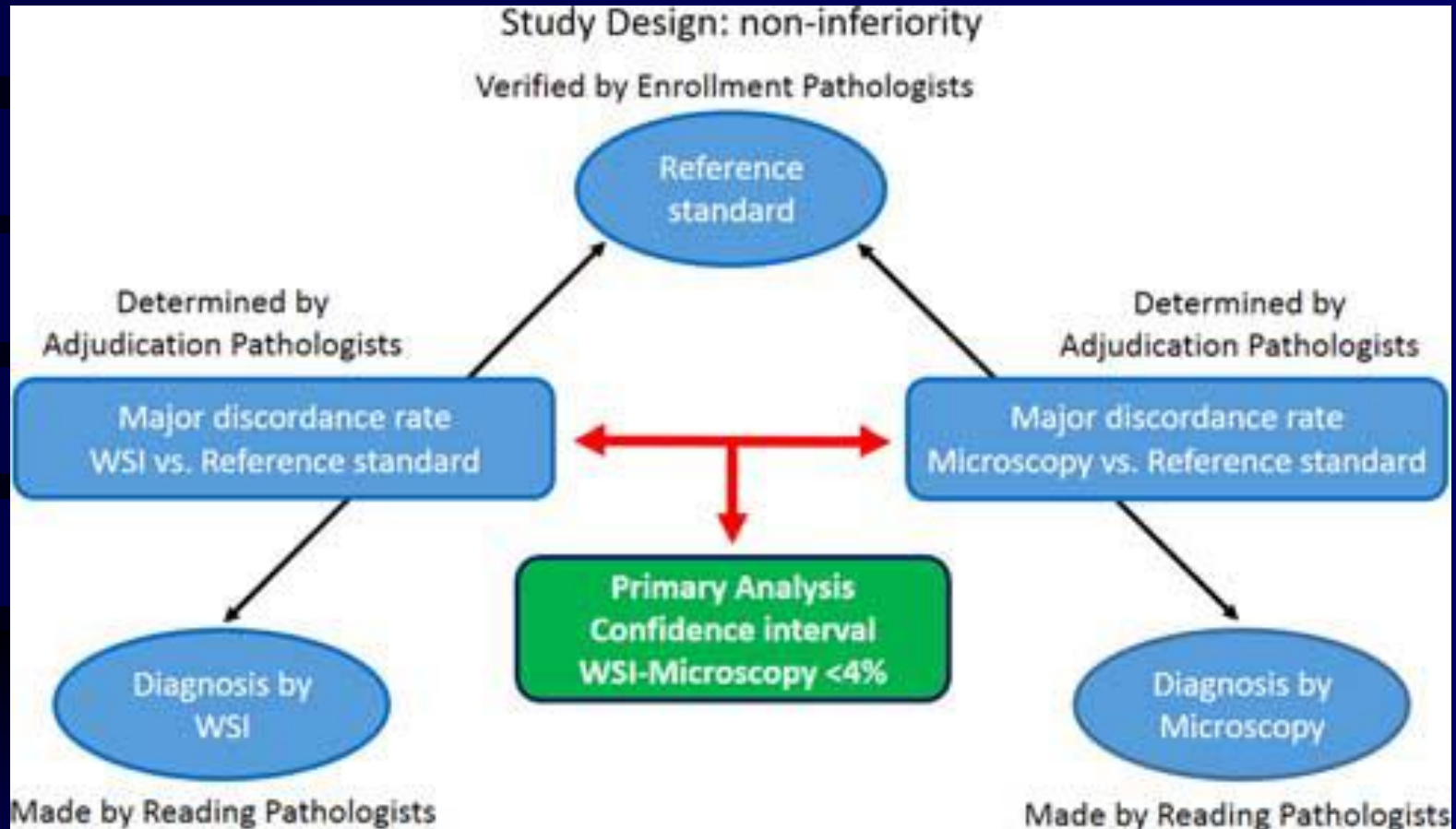
1992 cases read across 4 institutions and 16 pathologists

Philips Intellisite Pathology Solution: 15,292 reads

4 week washout period before re-read using alternative method (digital vs microscopy and vice versa)

73% of slides were HE, 27% IHC and histochemical test slides.

# Whole Slide Imaging Philips Study





# Whole Slide Imaging Philips Study

Digital slides were read in batches of 20.

Mean read time: microscopy: 74 seconds; digital: 84 sec

94% slides scanned adequately on first scan; 98.5% by 2 scans. Maximum # scans utilized was 5.

Reference standard: Original sign out Dx by microscopy.

Major discrepancy rate with ref. standard: 4.6% by microscopy and 4.9% by WSI.

# Whole Slide Imaging Philips Study (2)

## Differences by Organ System:

<1% **WSI discordance** > microscopy: Stomach, skin, brain, colorectal and prostate.

>1% **WSI discordance**: GYN (1.2), bladder (1.3), neopl. Kid (1.5); endocrine (1.8%)

<1% **microscopy discord** > WSI: Breast, respiratory, LN's

>1% **microscopy discord** > WSI: liver/biliary, salivary, perianal

**No difference**: peritoneal, appendix, gallbladder, soft tissue

# Philips- Demonstration Project

7 week evaluation of the Philips Intellesite Scanner and Image Management System (IMS): Sonorq Quest Labs; Banner Health

Scanned IHC, recut and special stain slides in first 4 weeks and then added selected up front HE slides

2 Pathologists at independent sites reading their own cases in parallel with glass slides, in no particular order, though usually digital slides first.

**Not** intended as a validation of the system or individual pathologists



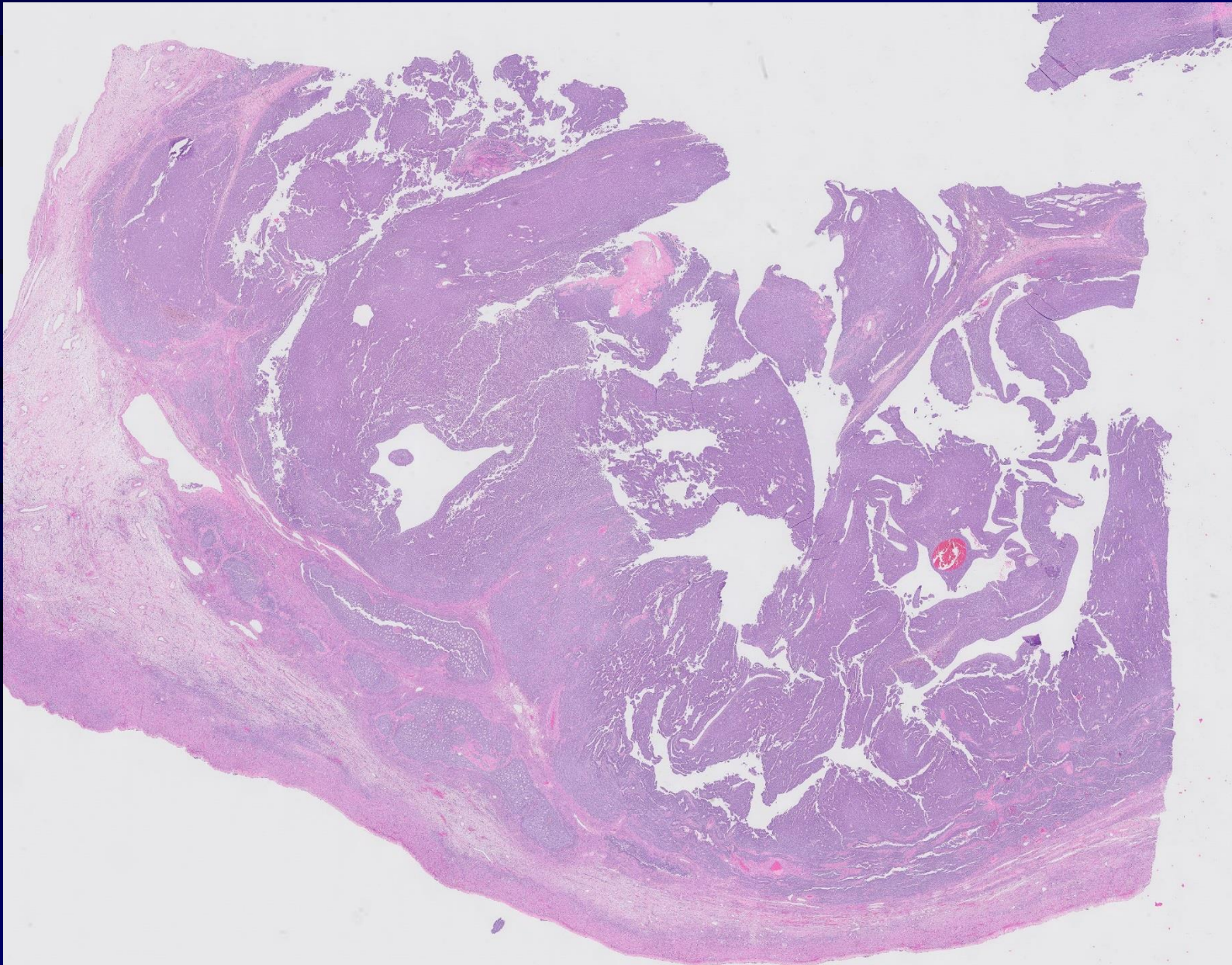
Slides scanned at the central SQL location into server on site.

IMS system application installed on each pathologist's current workstation and their current monitor was used.

The FDA approved workstation was intended for use but could not be installed in time for each pathologist. Available for demonstration, training and additional exploration at the central location, as time allowed.

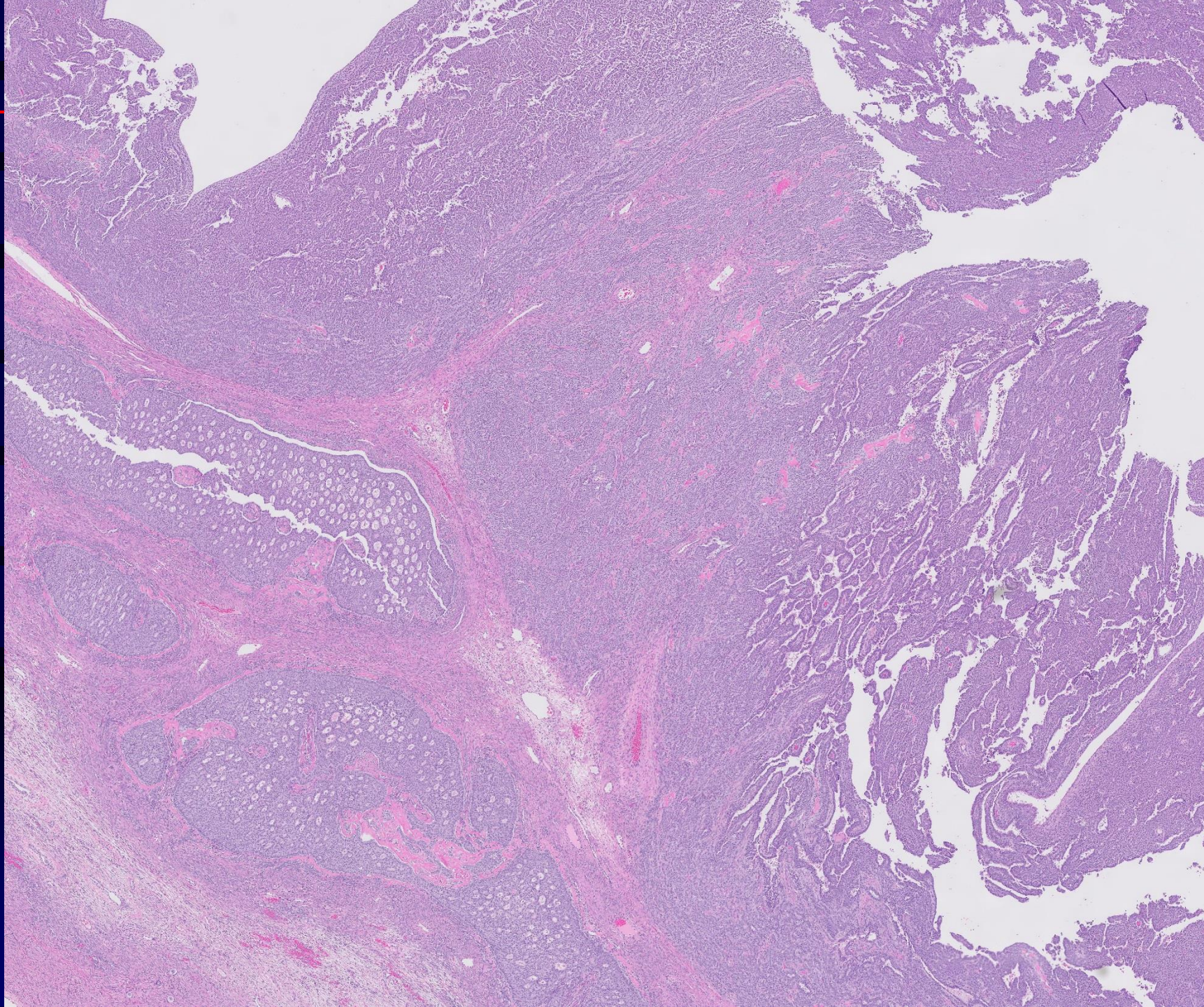
As of 4/2/18, number of cases and slides imaged and read per pathologist: 450 cases/ 1575 slides.

# 38 yo: abnl vaginal bleeding and ovarian mass

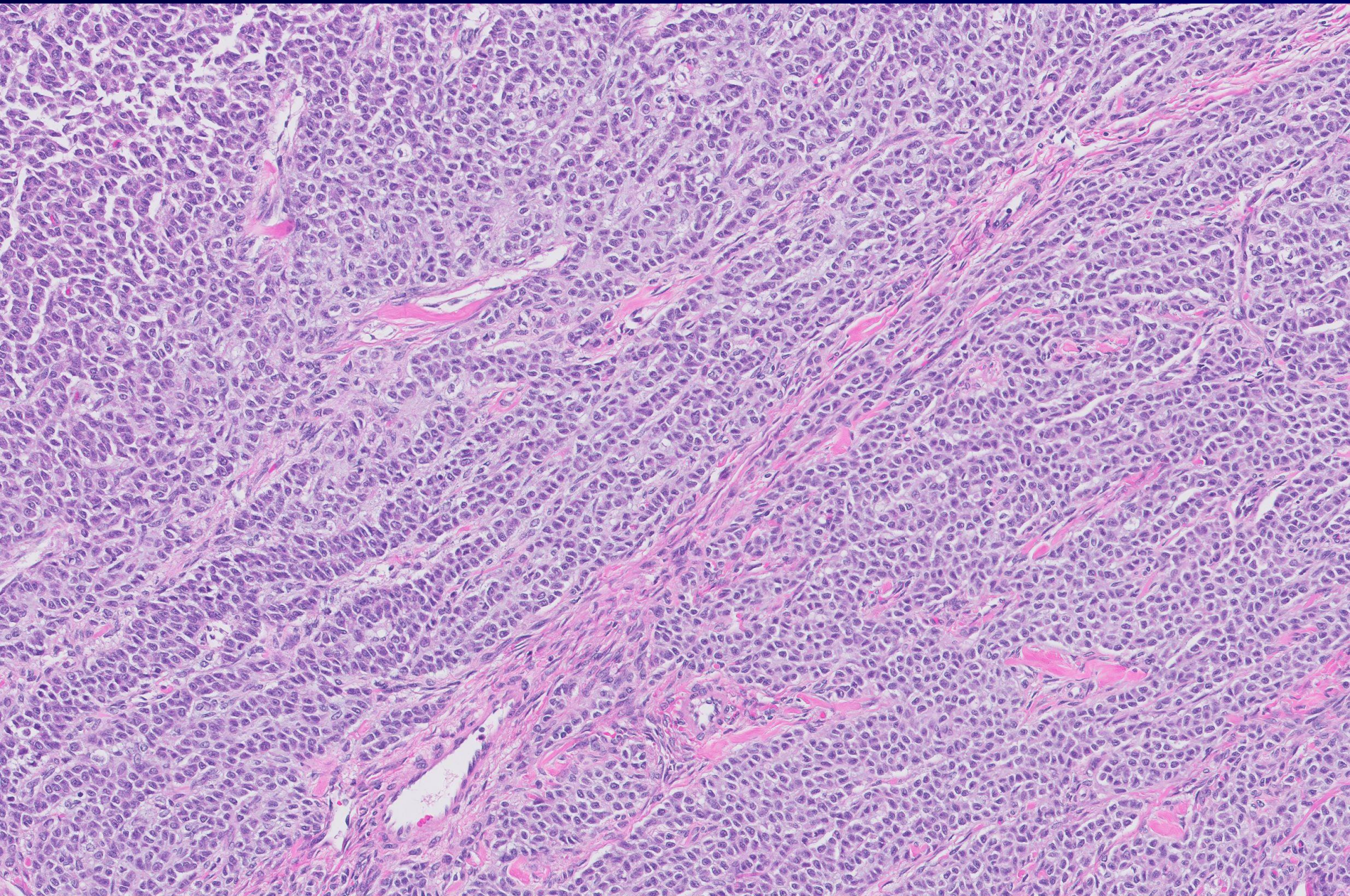


Exported  
snapshots  
from the  
whole  
scanned  
slide

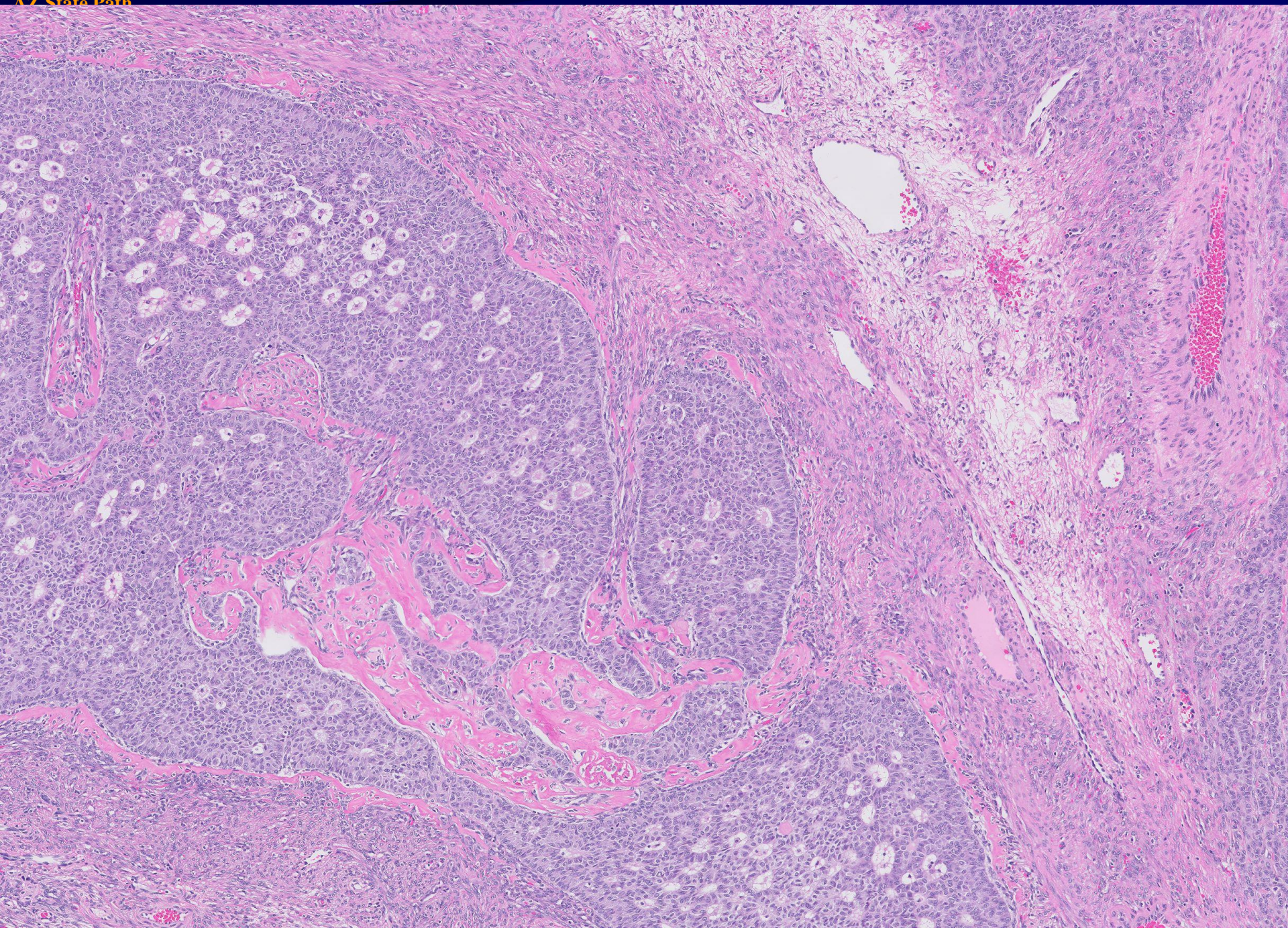




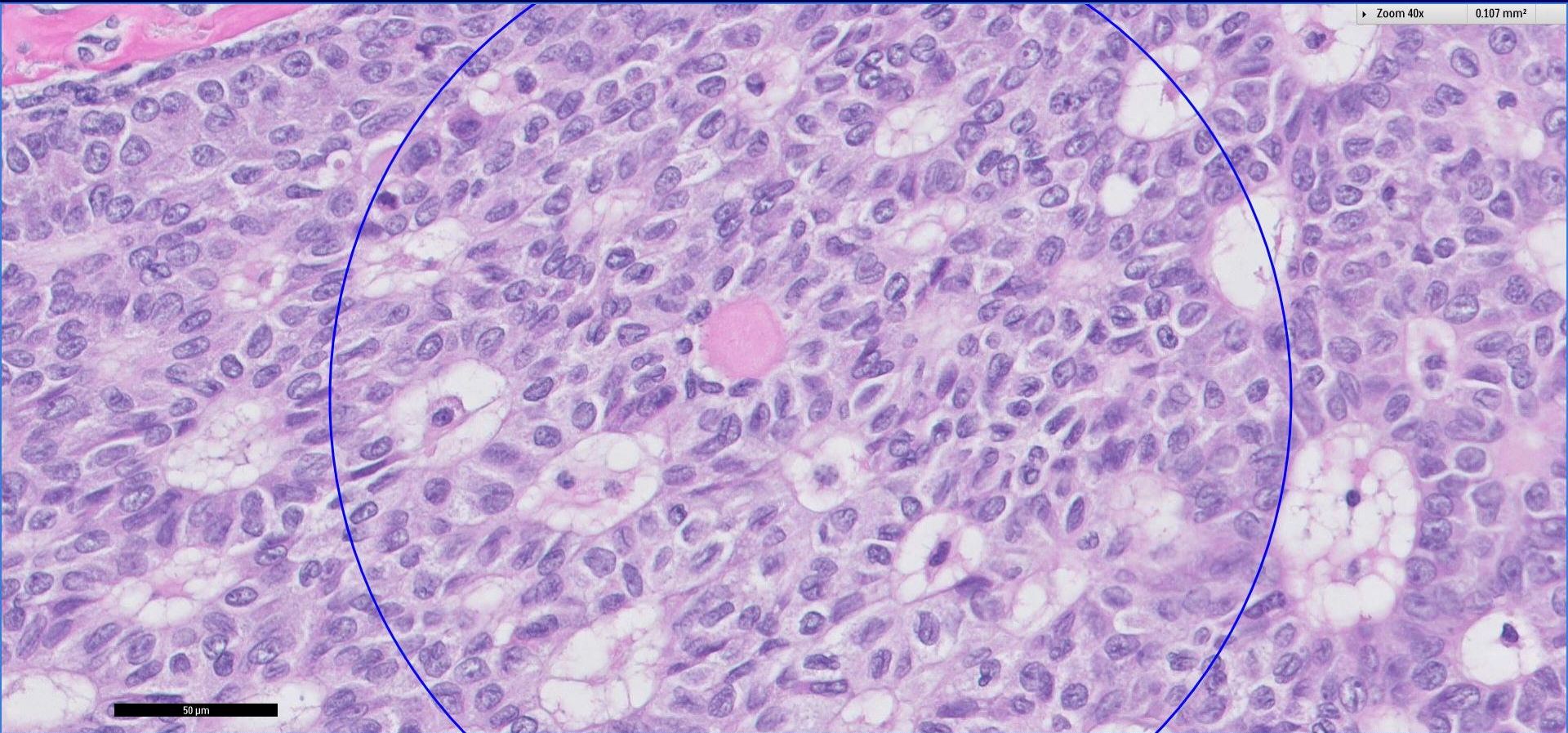




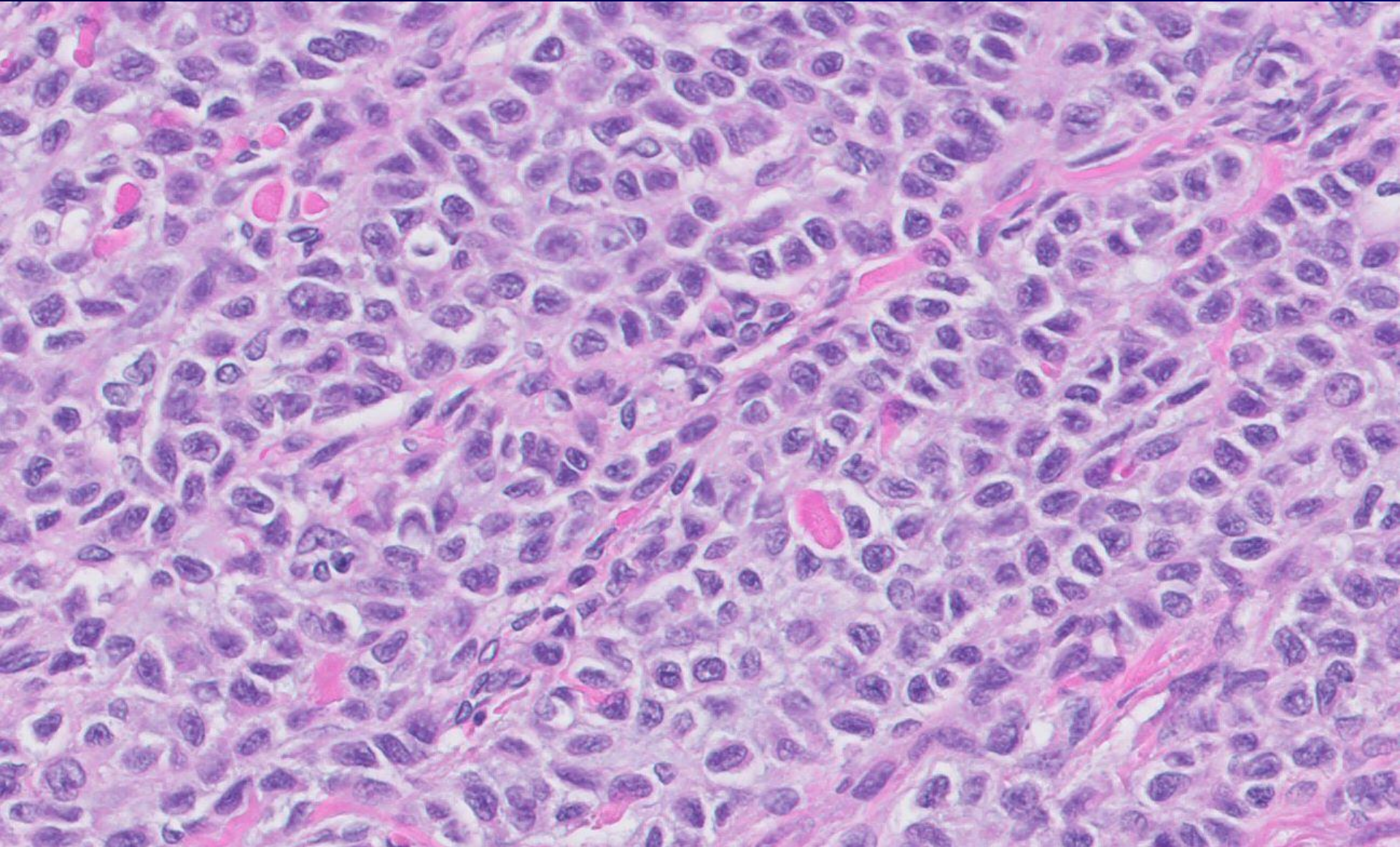








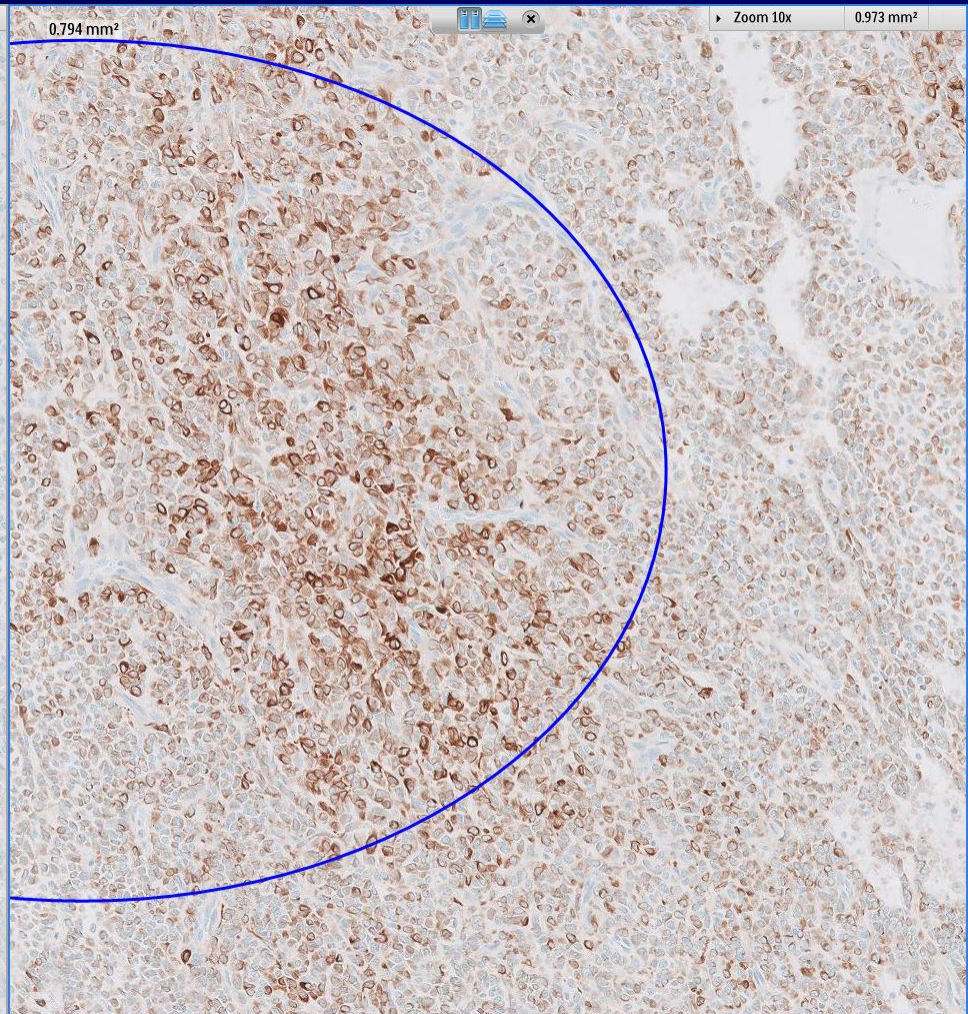
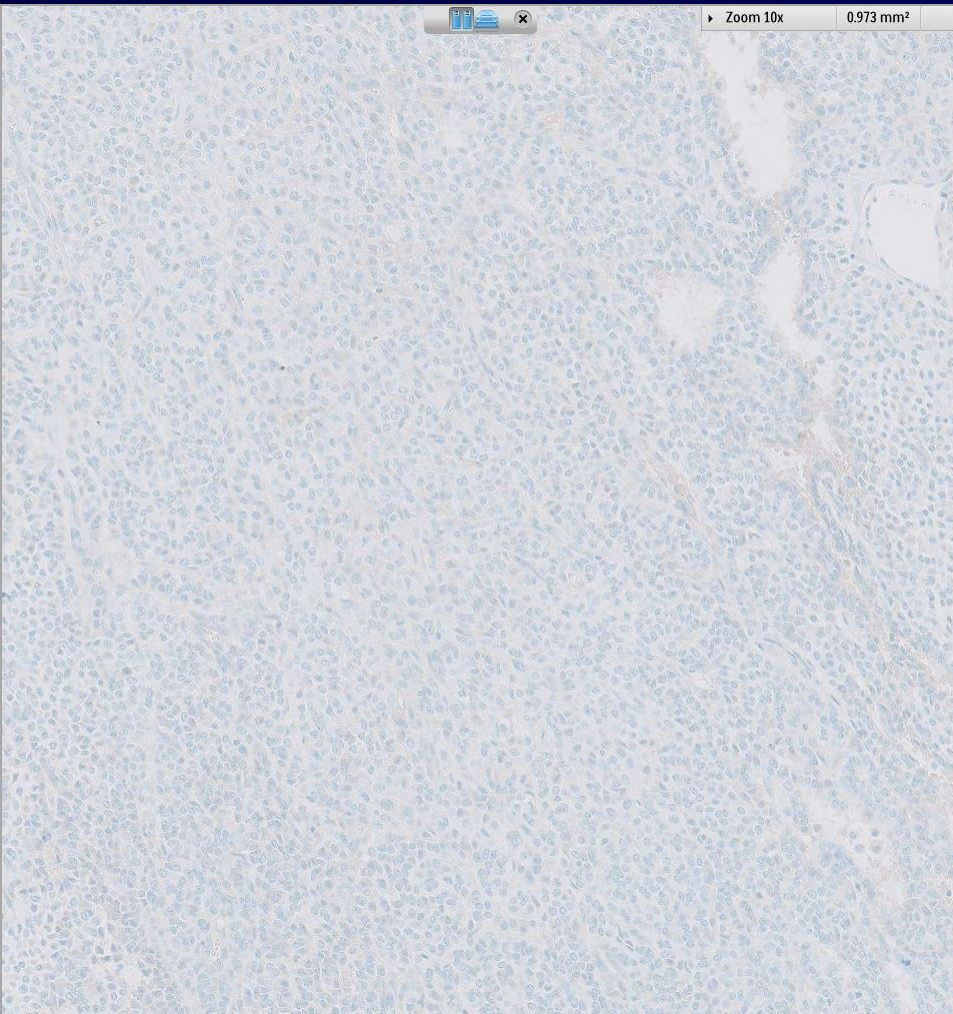






EMA

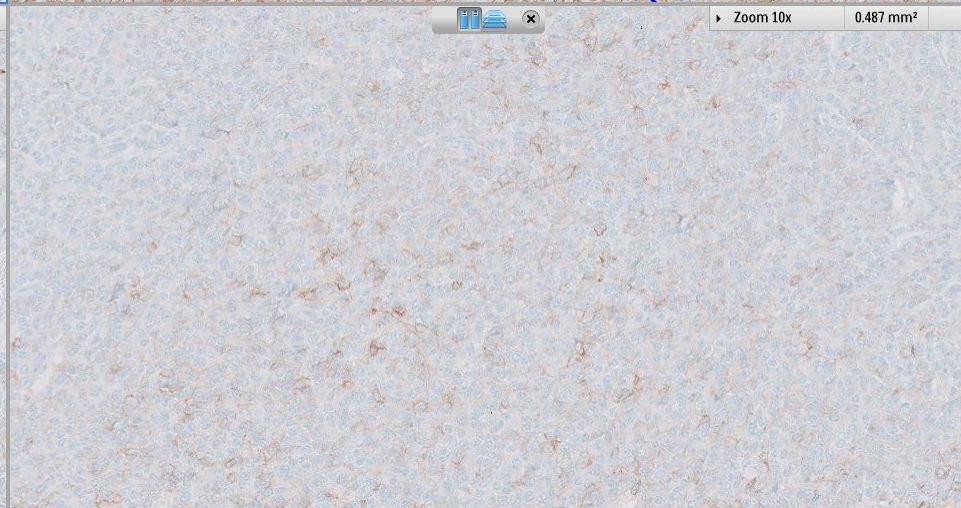
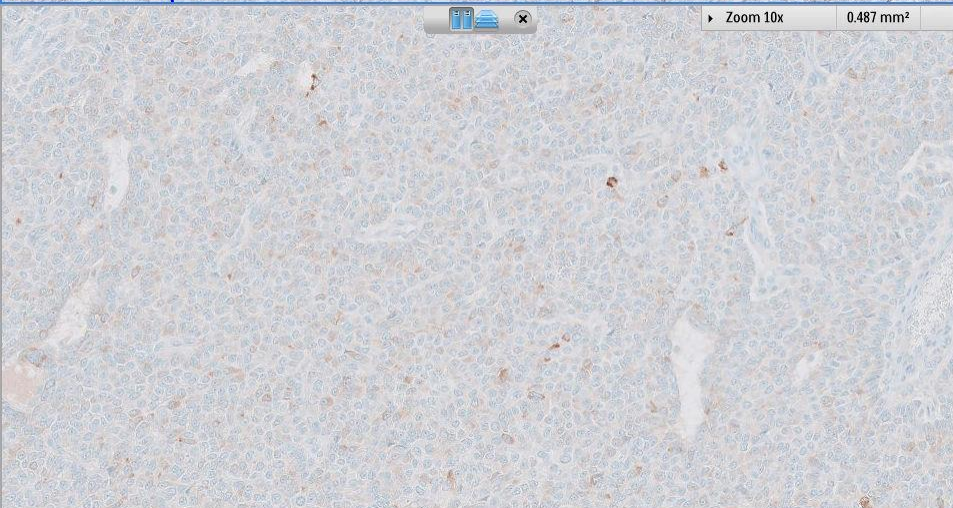
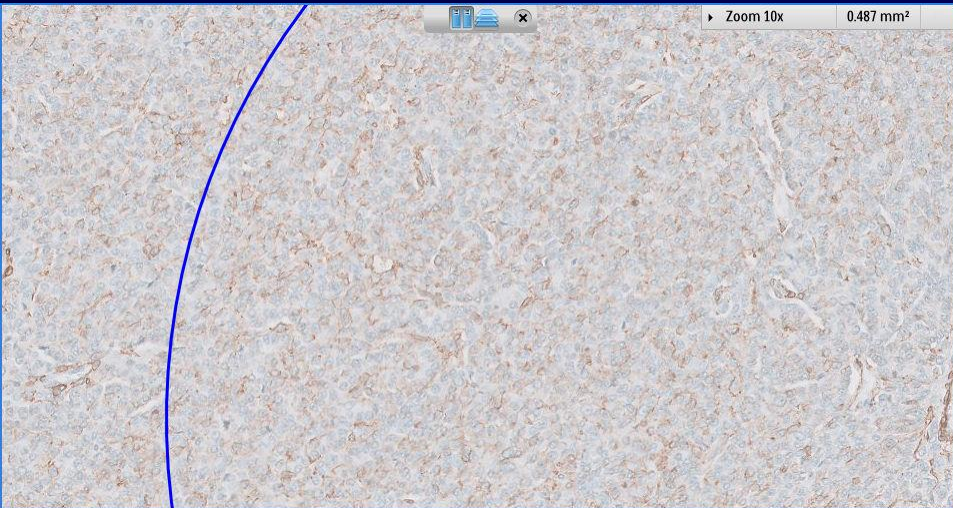
Cam5.2





SMA

CD99



inhibin

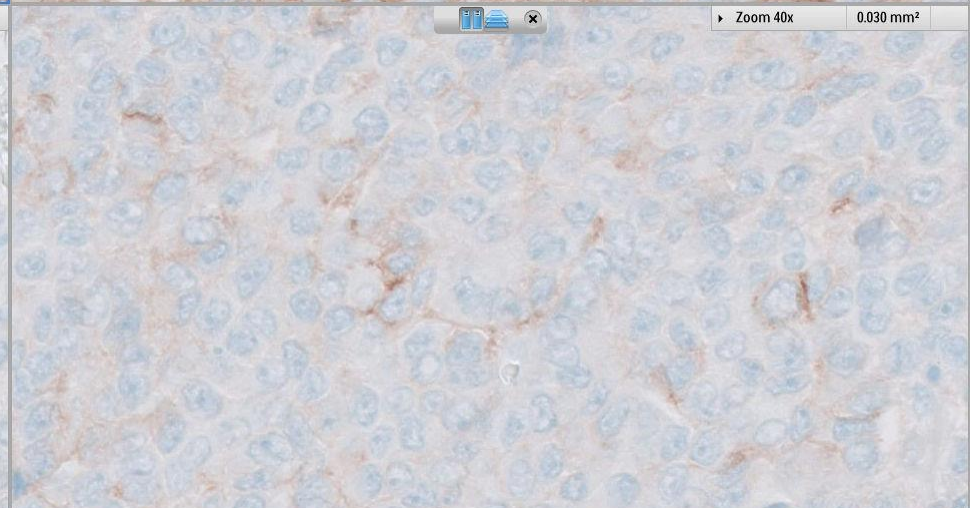
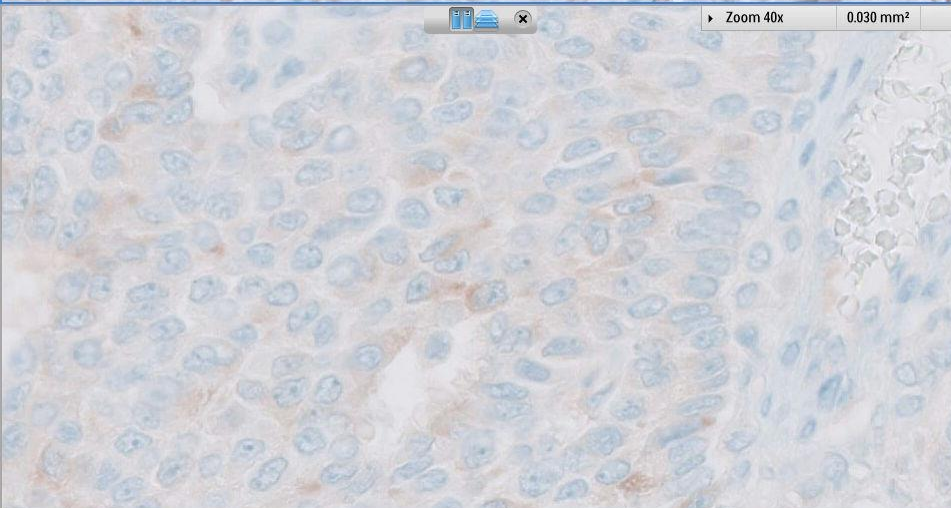
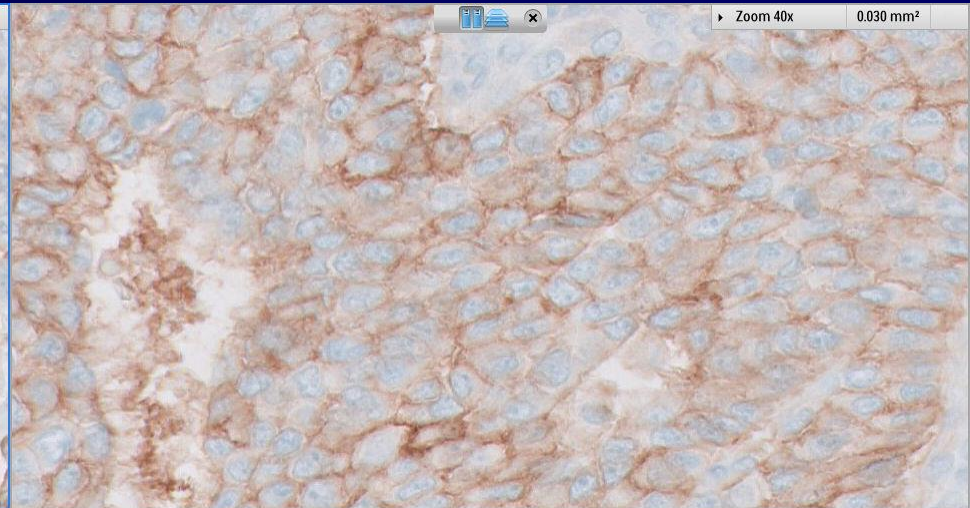
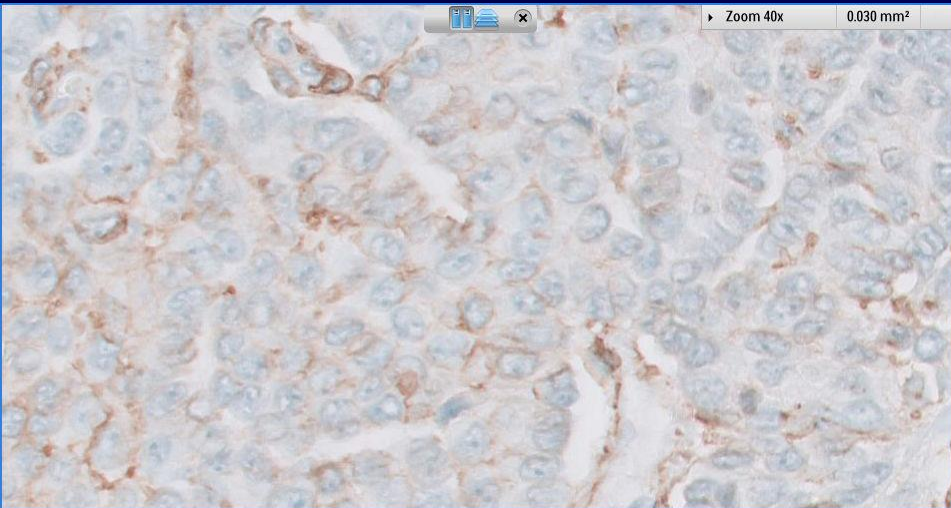
CD56



# Granulosa cell tumor

SMA

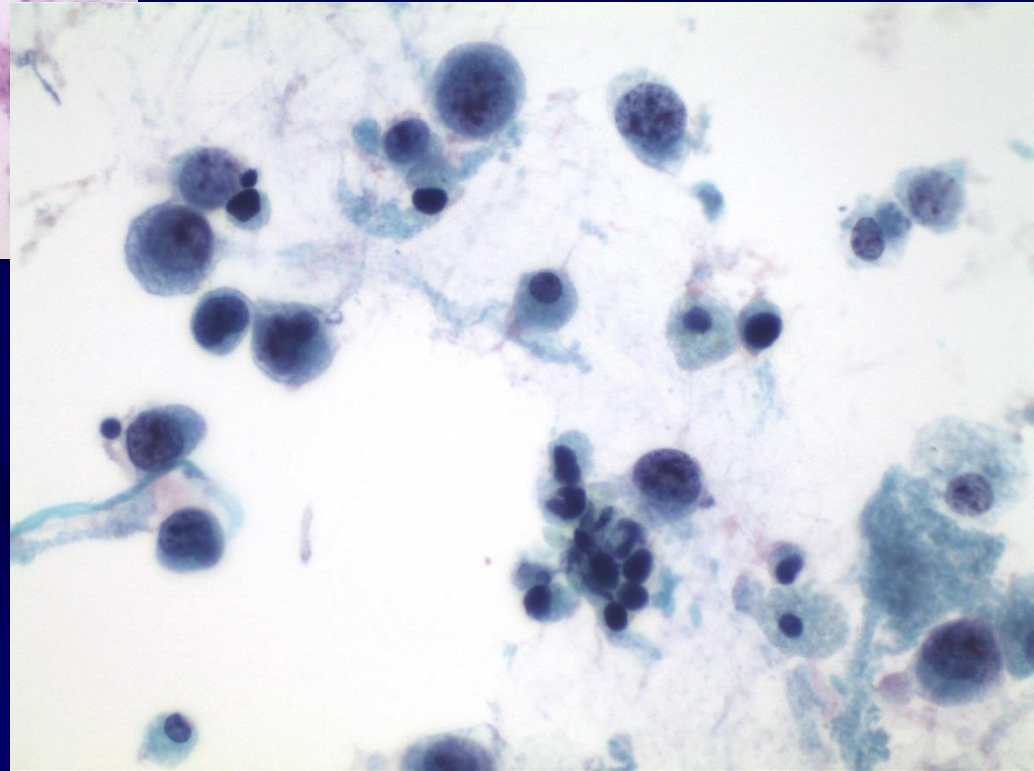
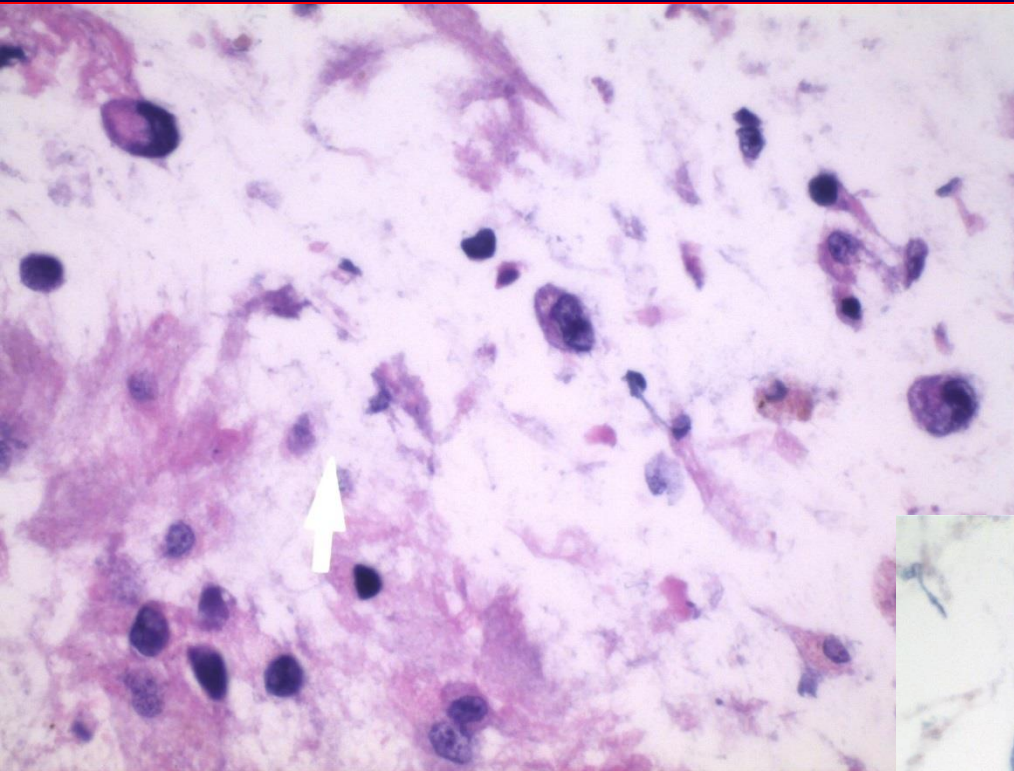
CD99



inhibin

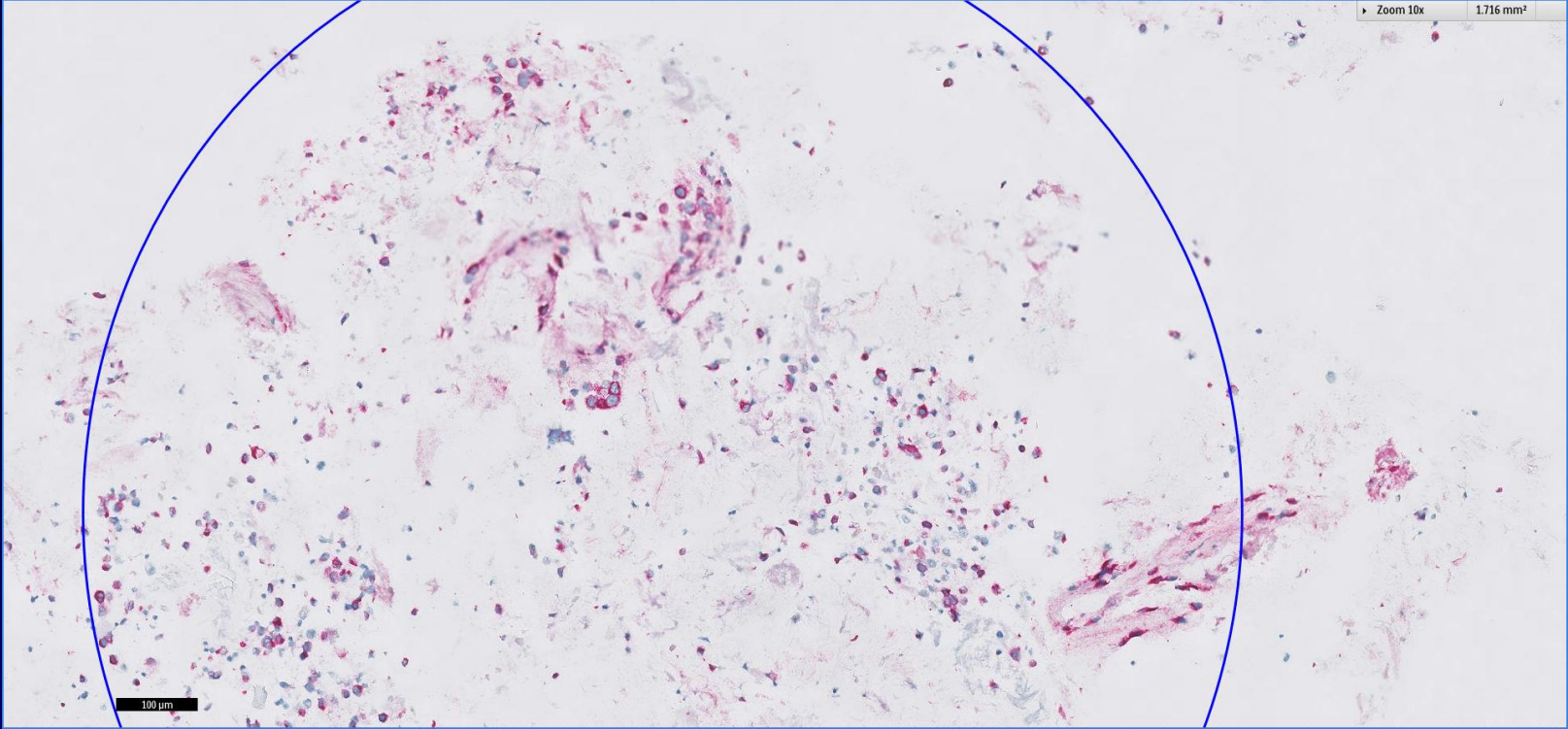
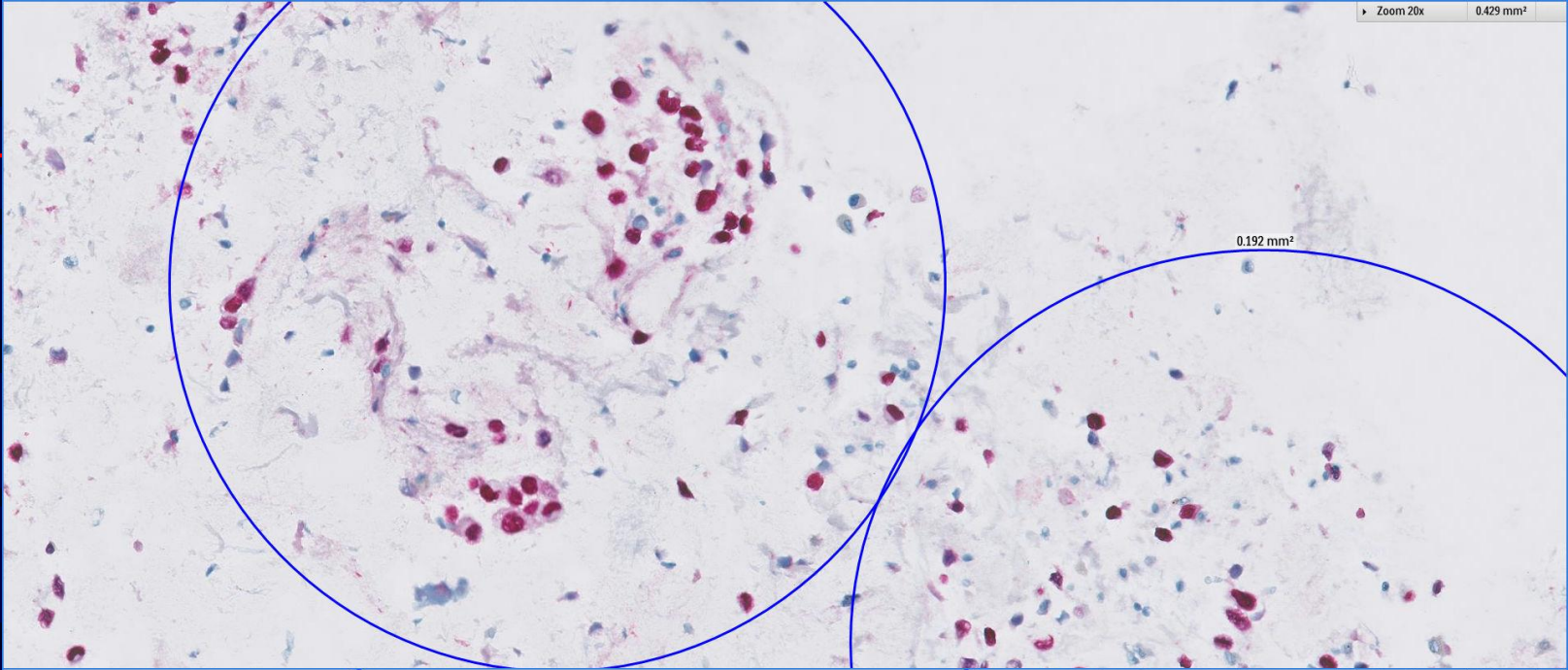
CD56

# 60 year old with pulmonary consolidation- BAL





60 yo  
BAL  
SOX-  
10



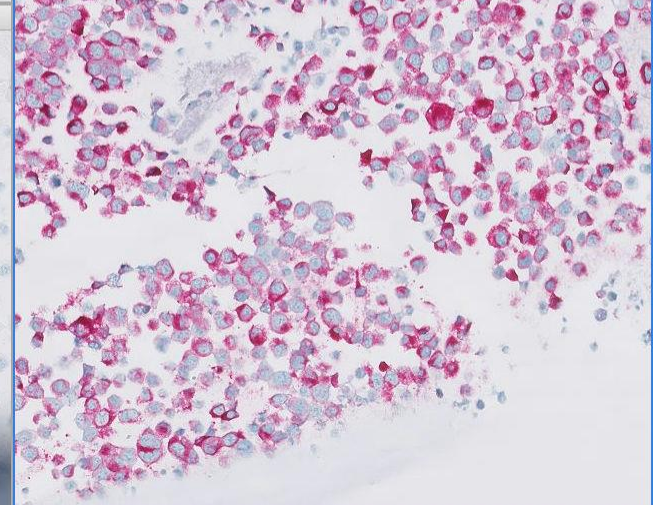
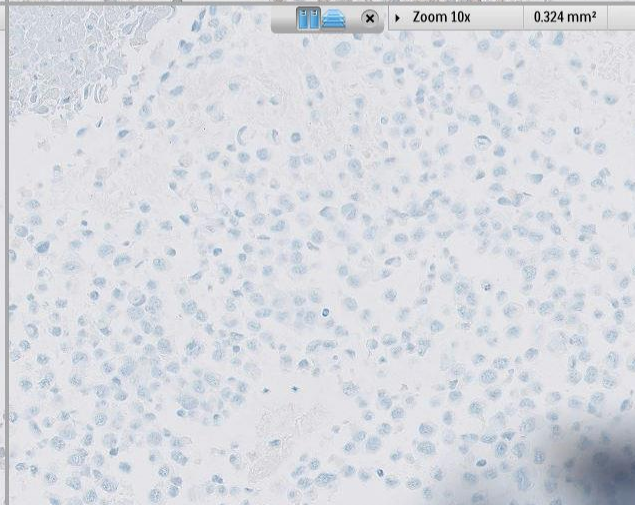
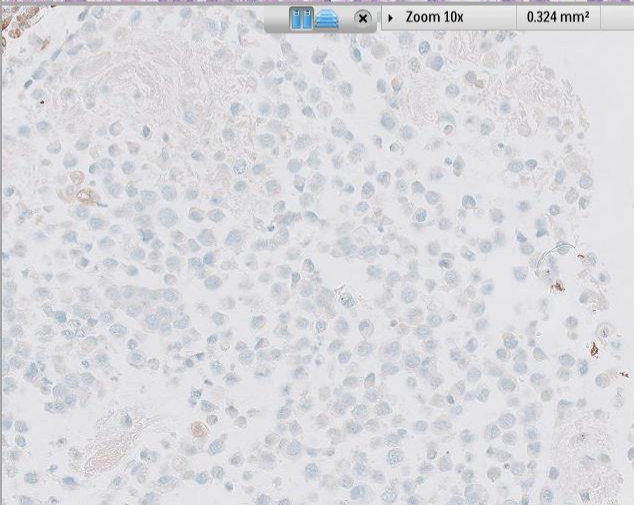
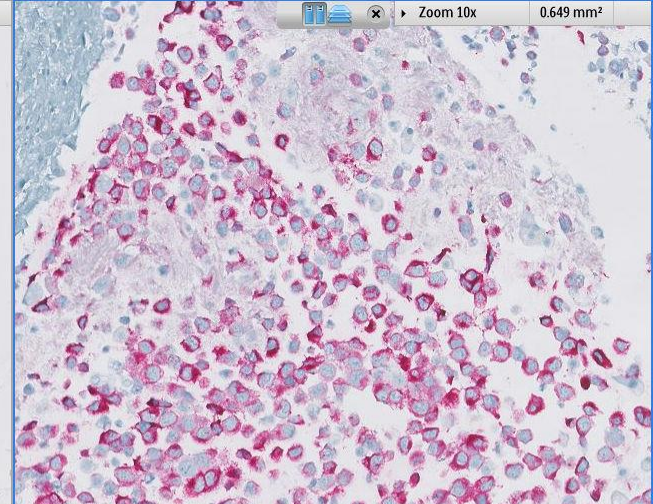
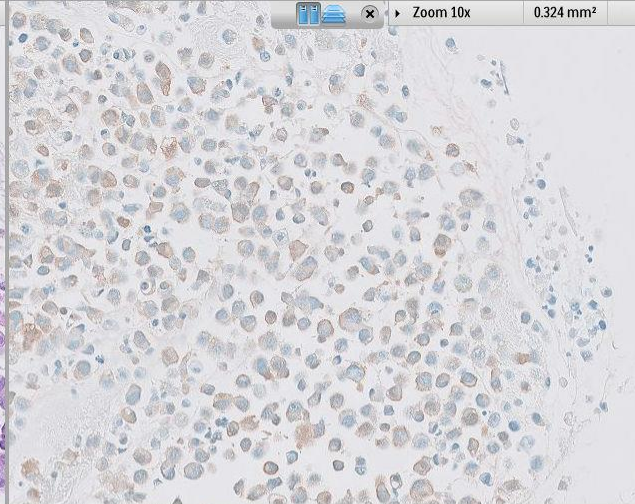
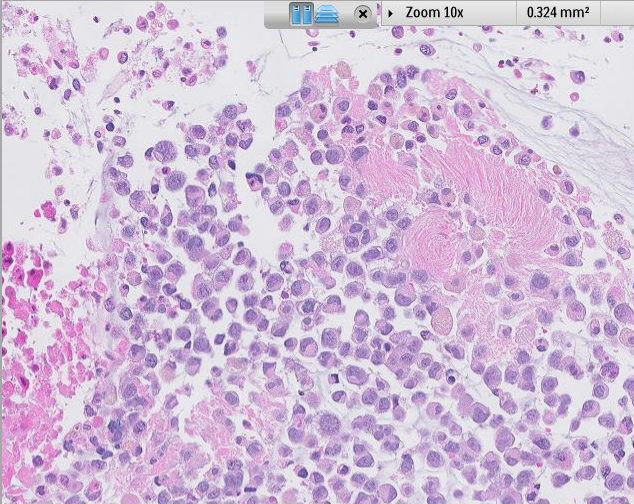
60 yo  
BAL  
Melan  
A



# 60 year old with pulmonary consolidaton- BAL

S-100

Melan A



CK 5/6

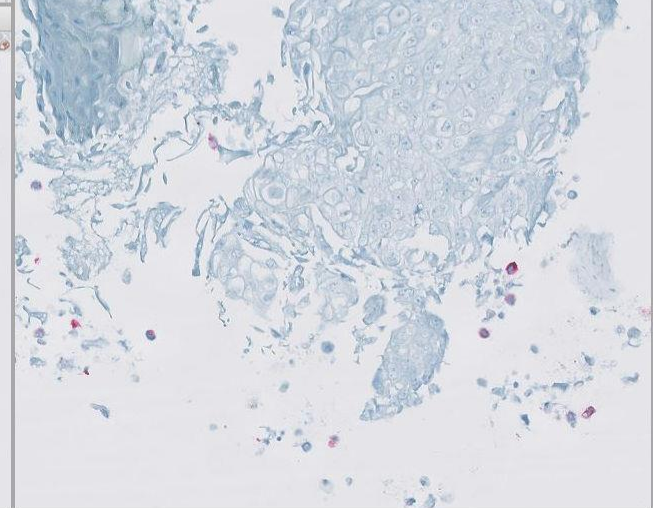
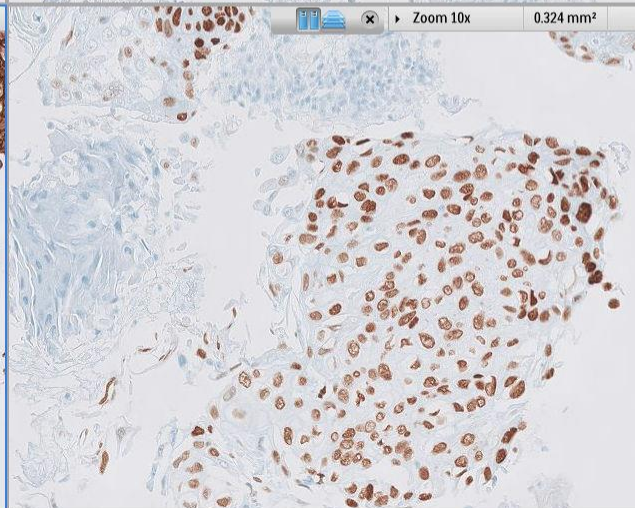
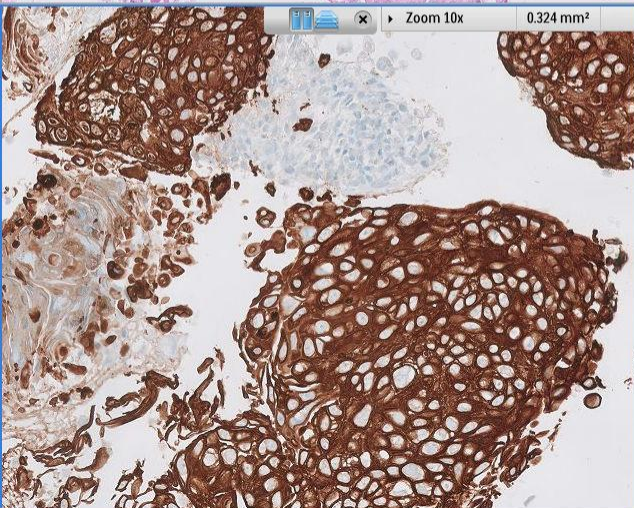
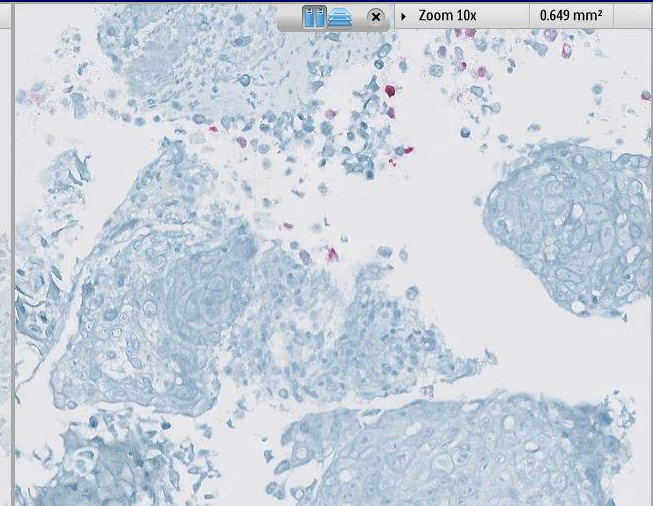
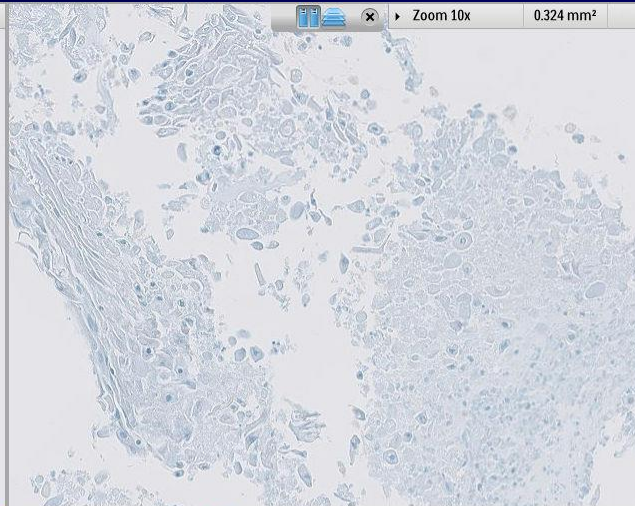
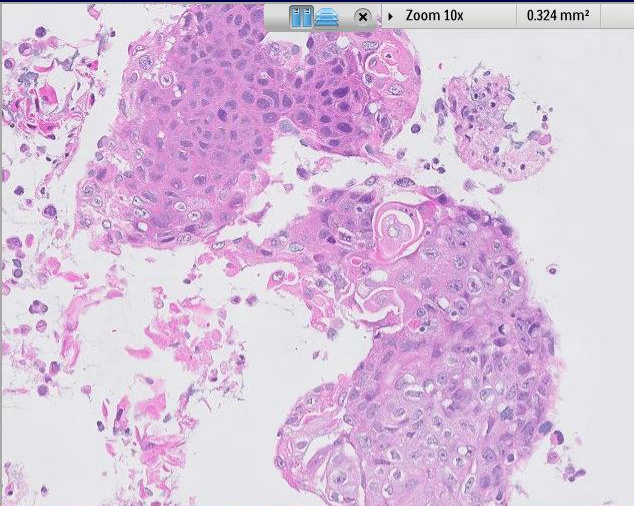
p40



# Metastatic Melanoma and SCCA- BAL

S-100

Melan A

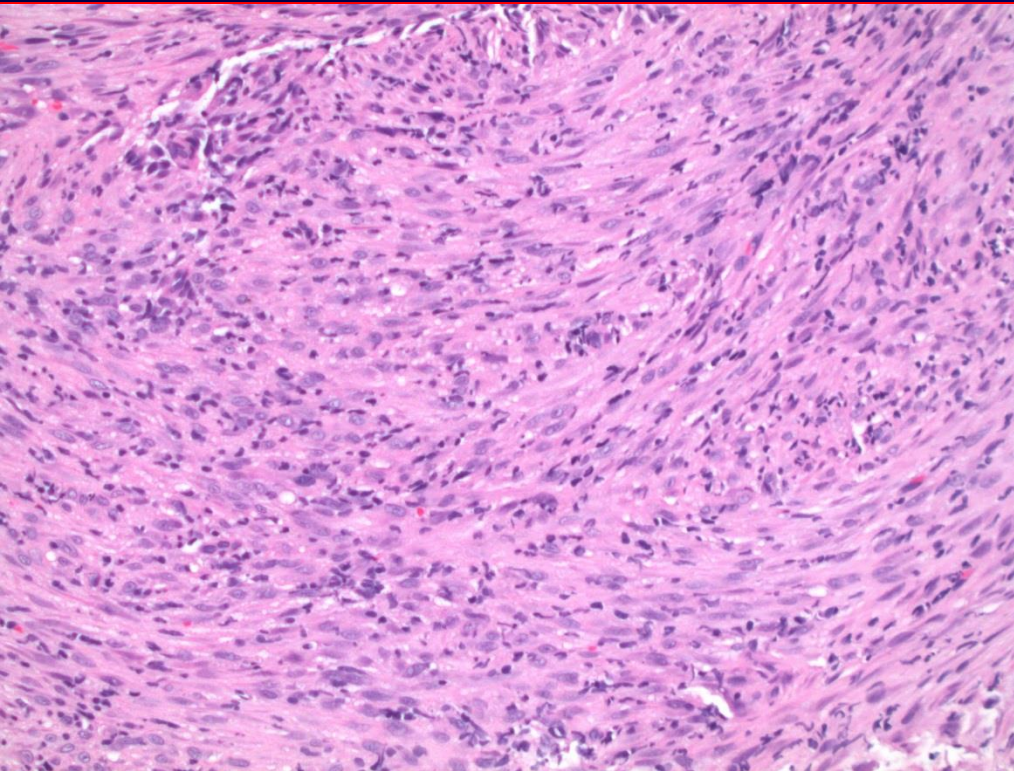


CK 5/6

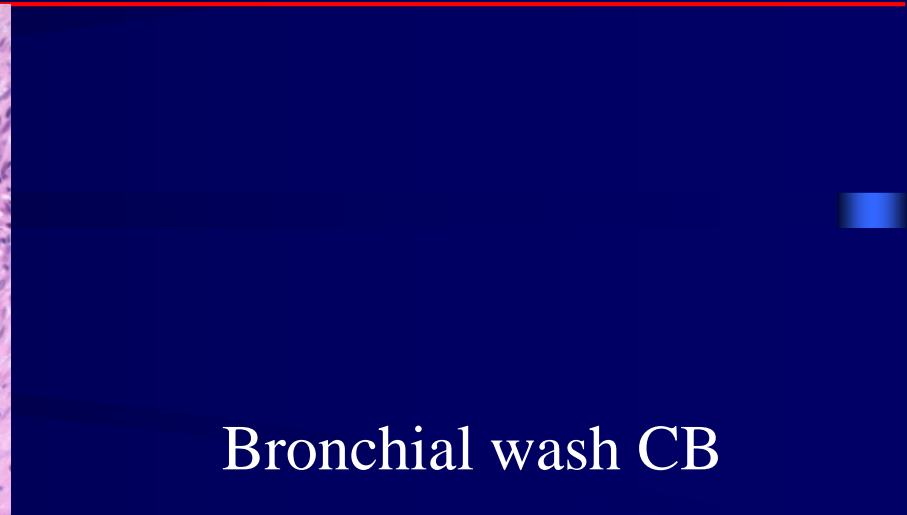
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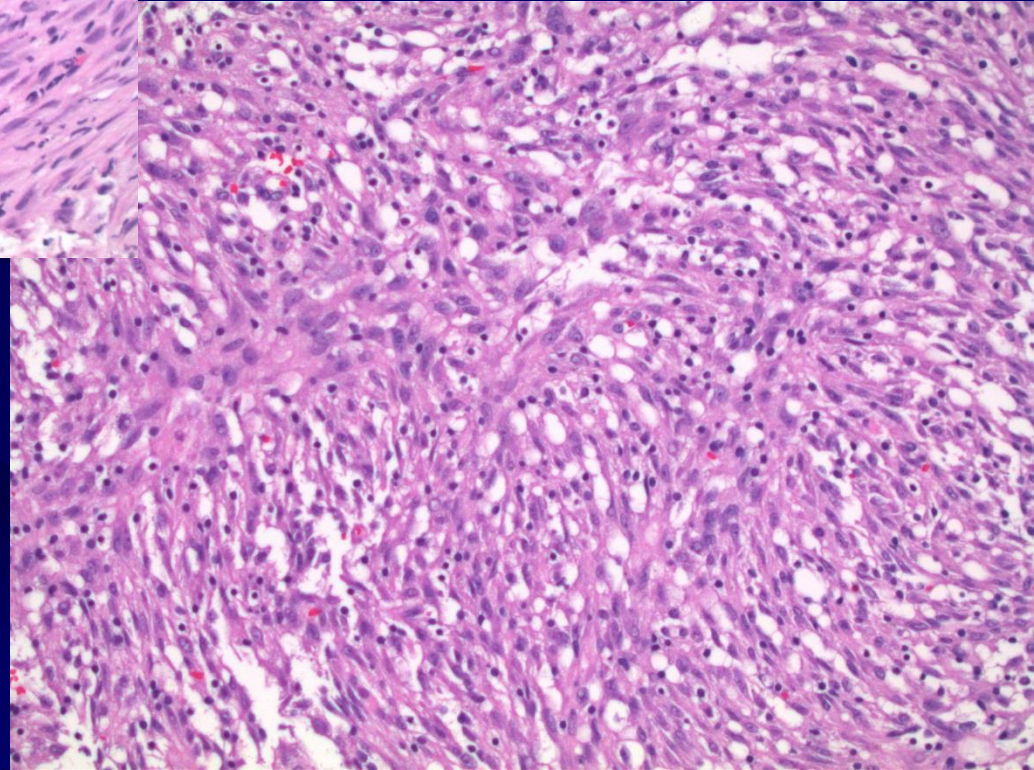
# Inflammatory myofibroblastic tumor



Bronchial biopsy

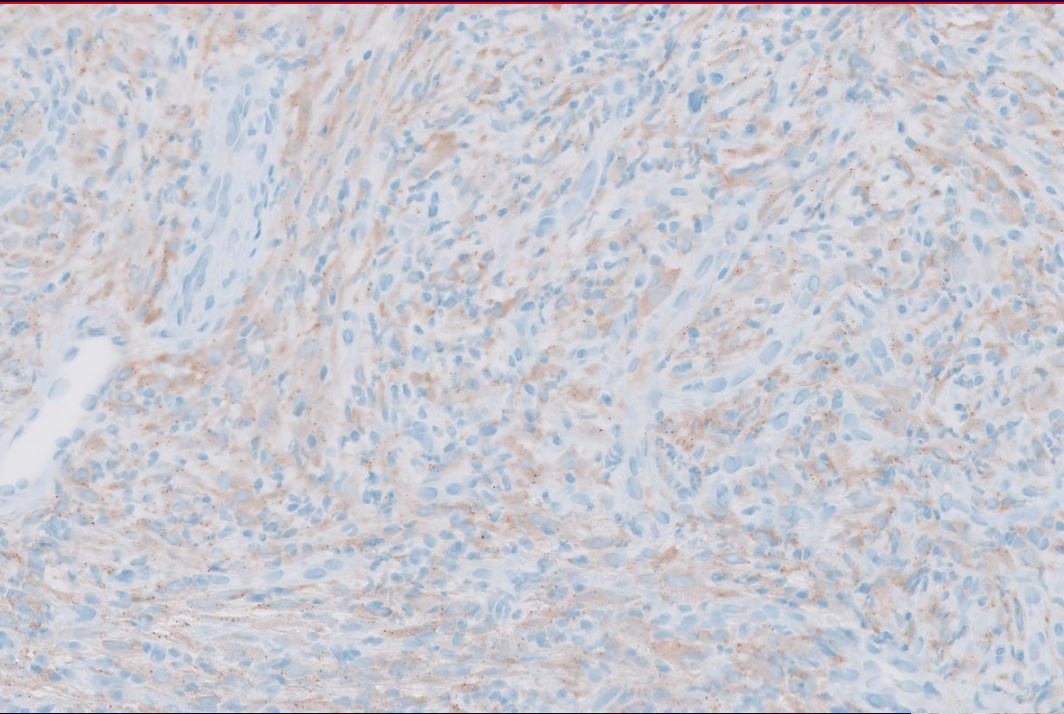


Bronchial wash CB



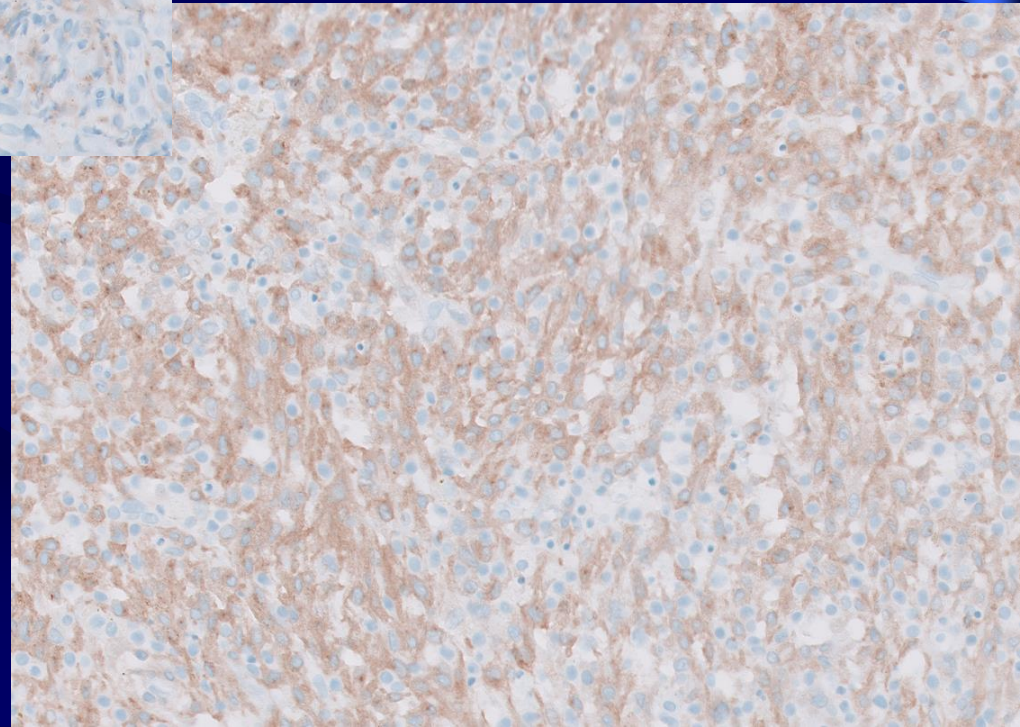


# IMT: ALK IHC images exported



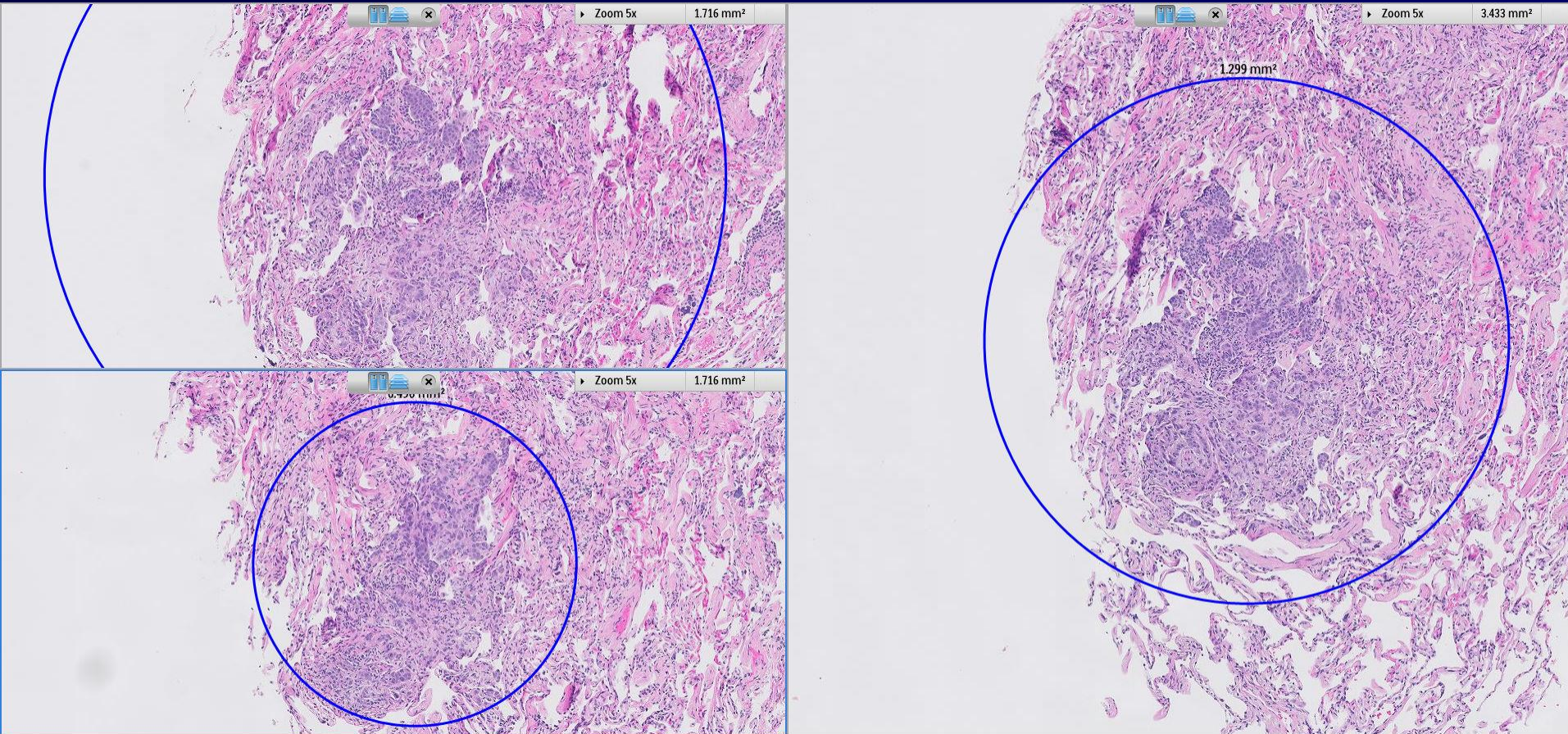
Bronchial wash CB

Bronchial biopsy





# Comparing levels: images exported

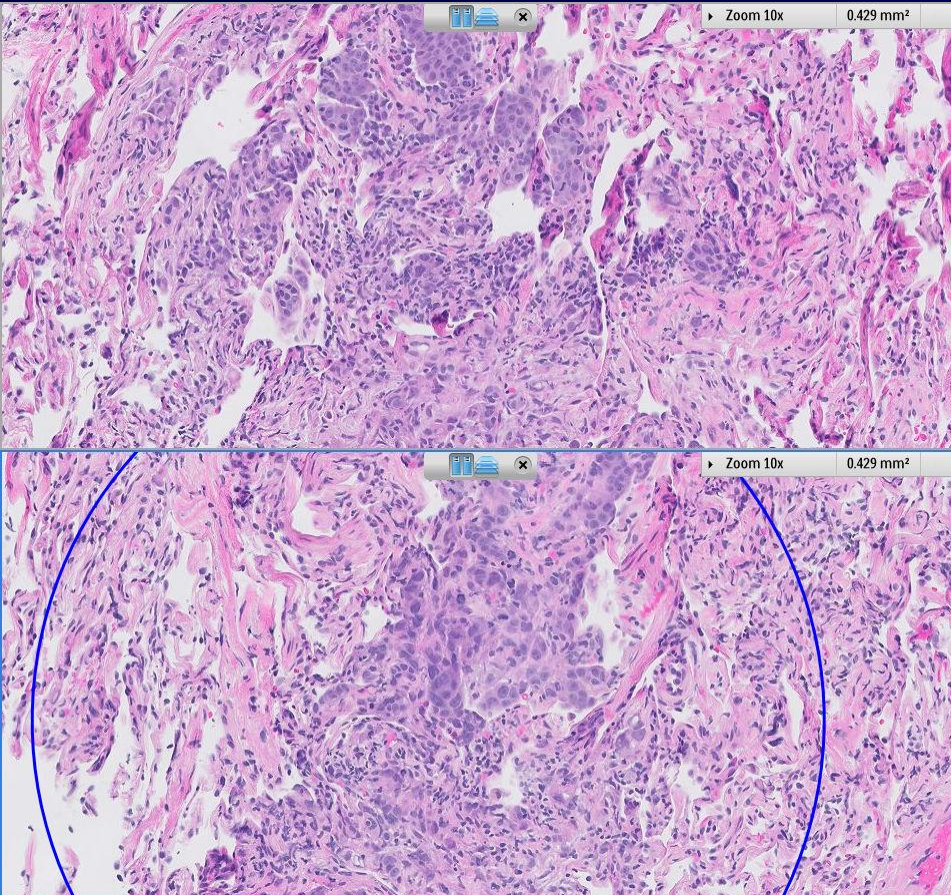


Bronchial biopsy- metastatic breast carcinoma 5X

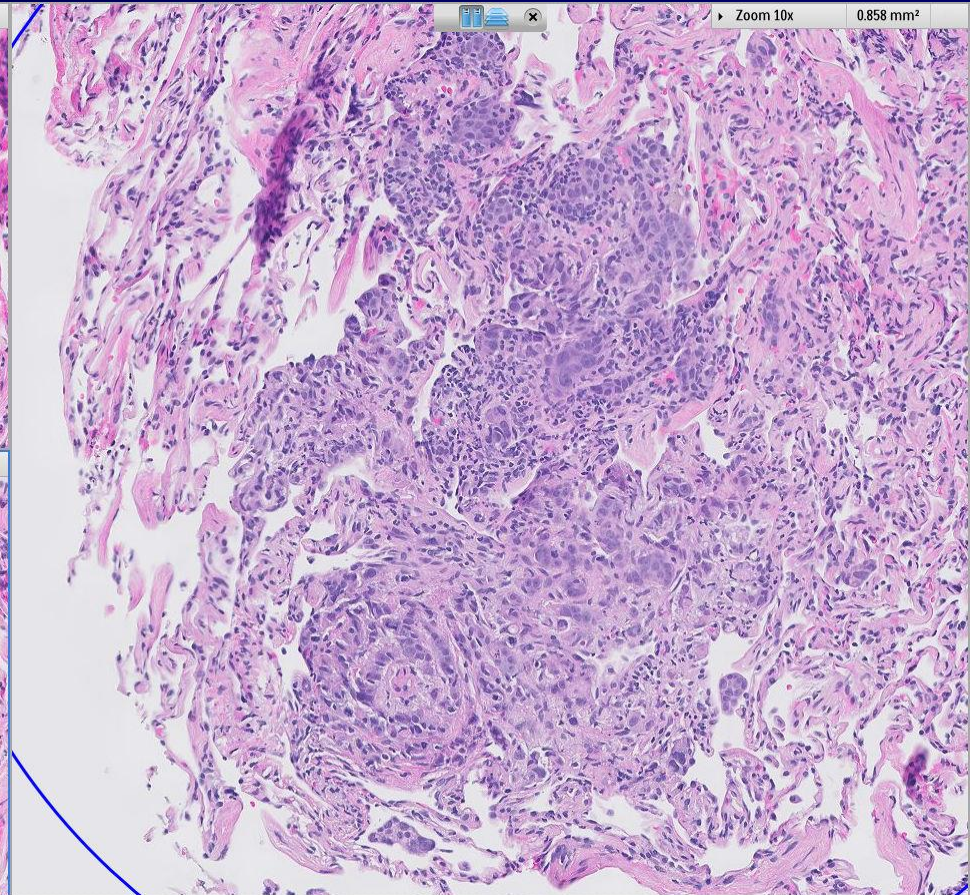


# Comparing levels: images exported

Level 1



Level 3

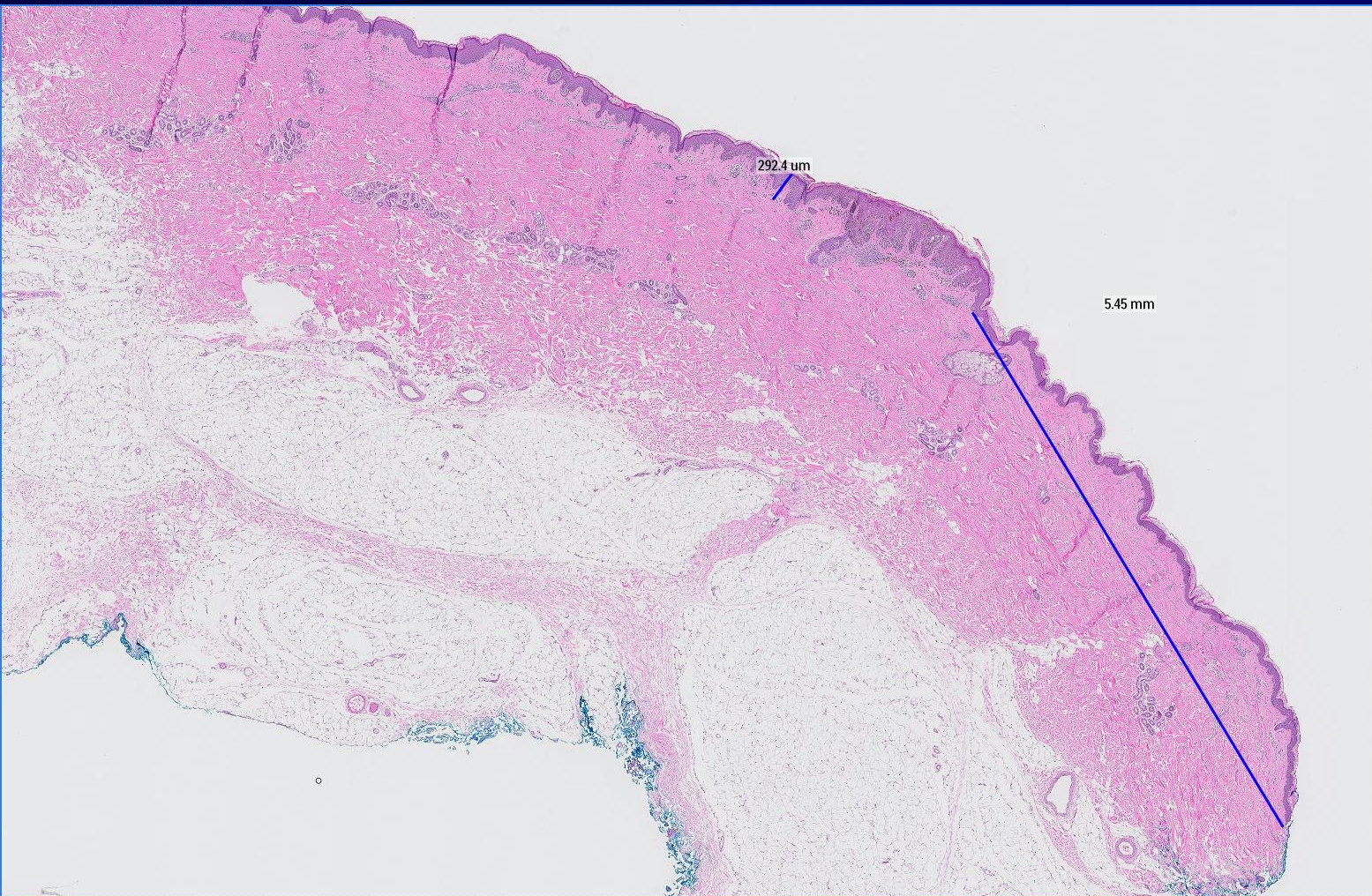


Level 2

Bronchial biopsy- metastatic breast carcinoma- 10X



# Measurements

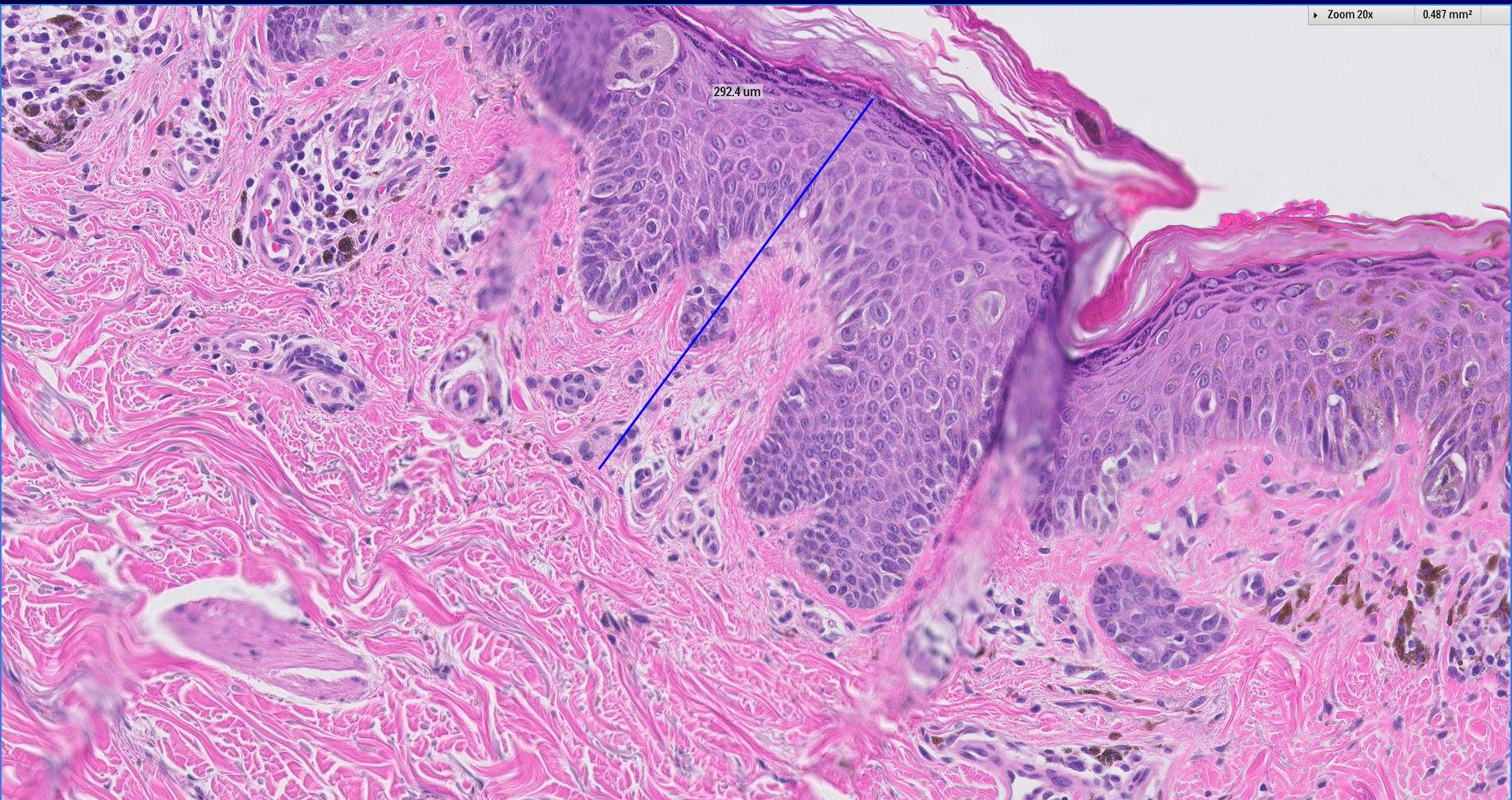


Zoom 1x 124,600 mm<sup>2</sup>

5.45 mm lateral margin



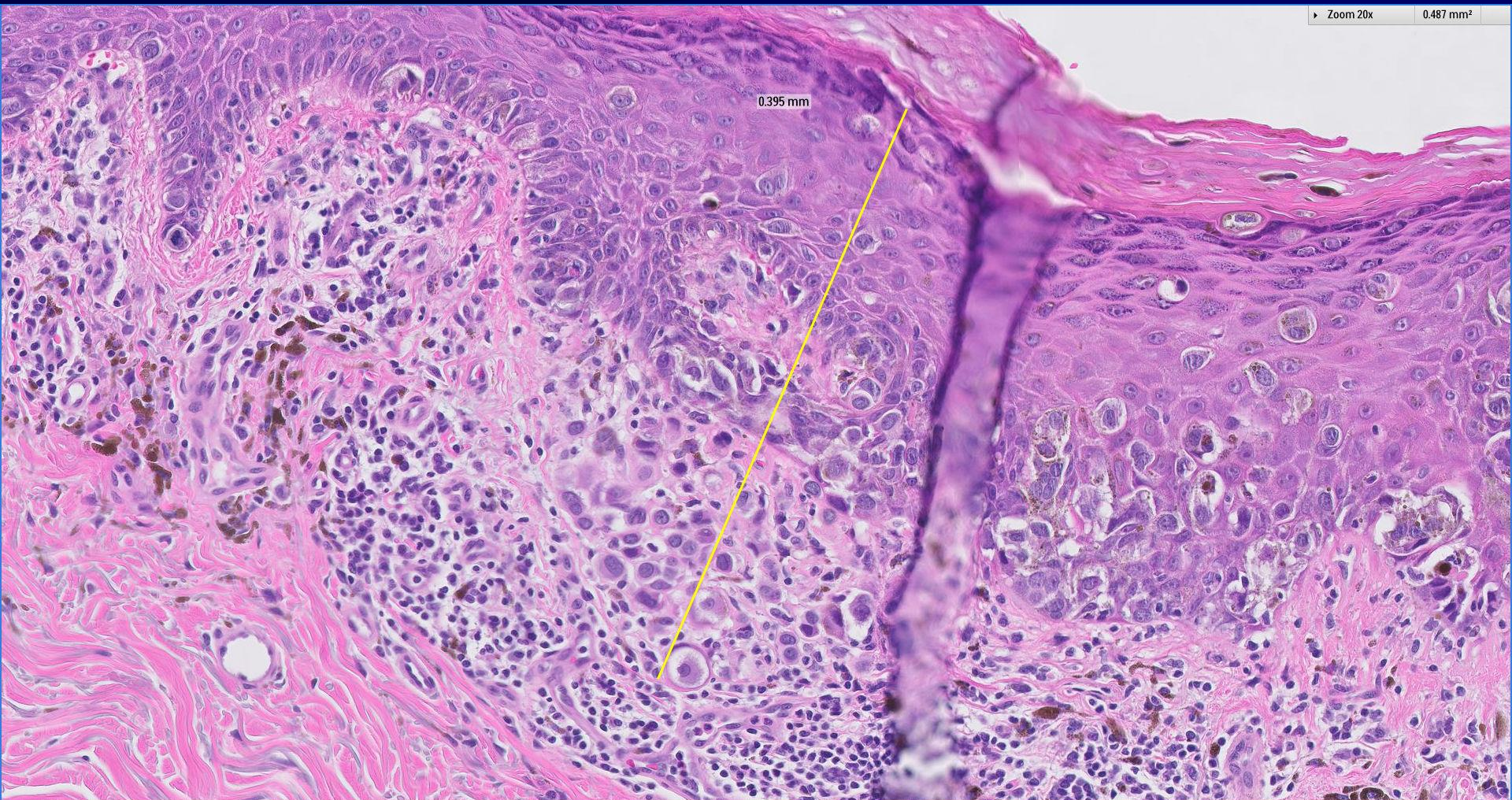
# Measurements



0.2924 mm (292.4 um) depth



# Measurements



0.395 mm depth

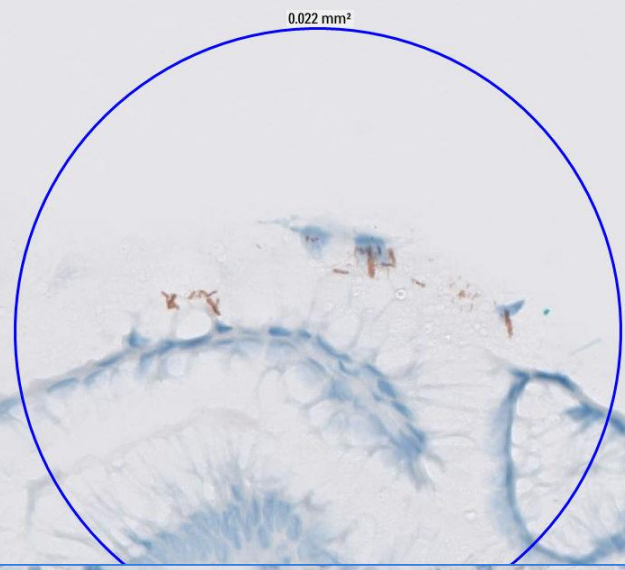




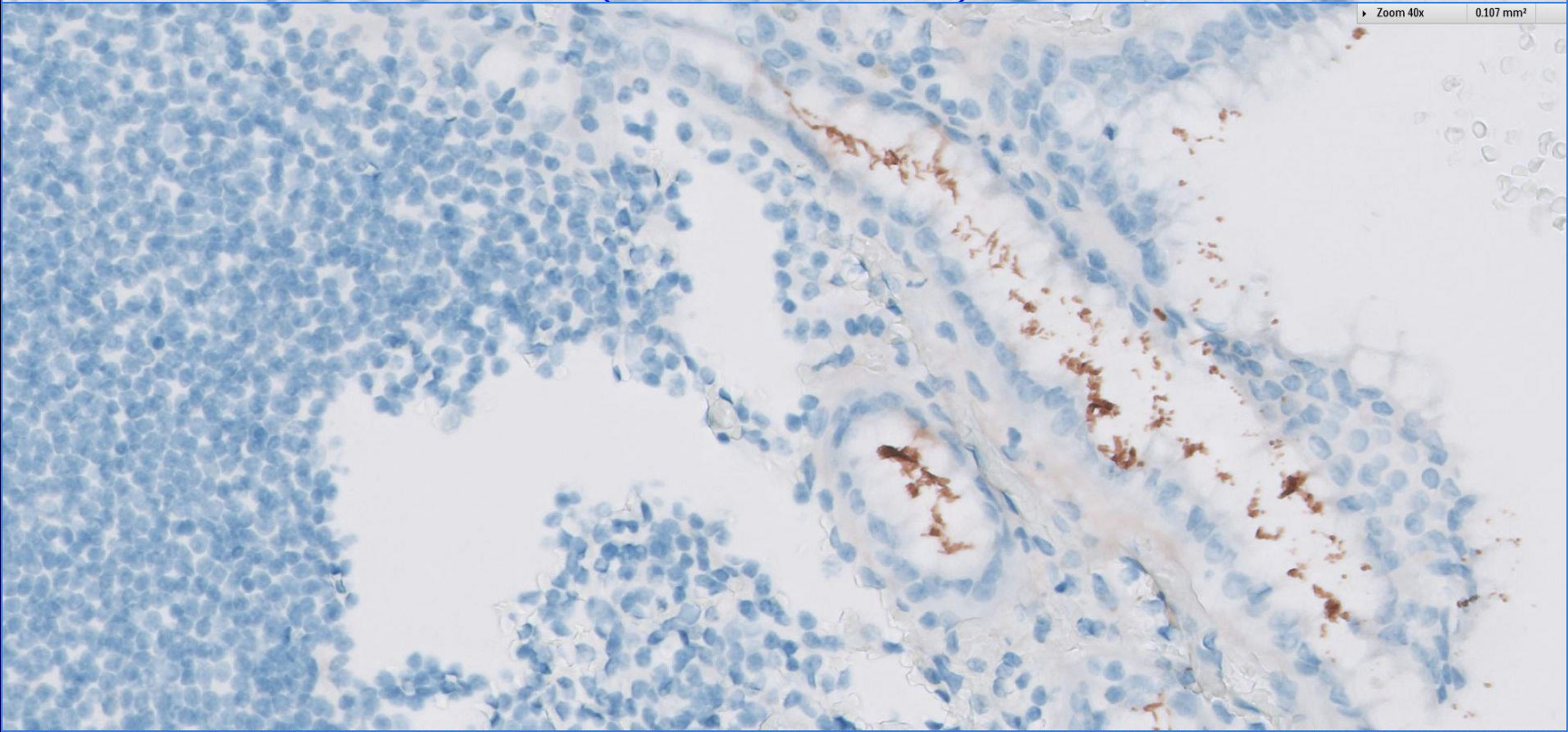
H. Pylori



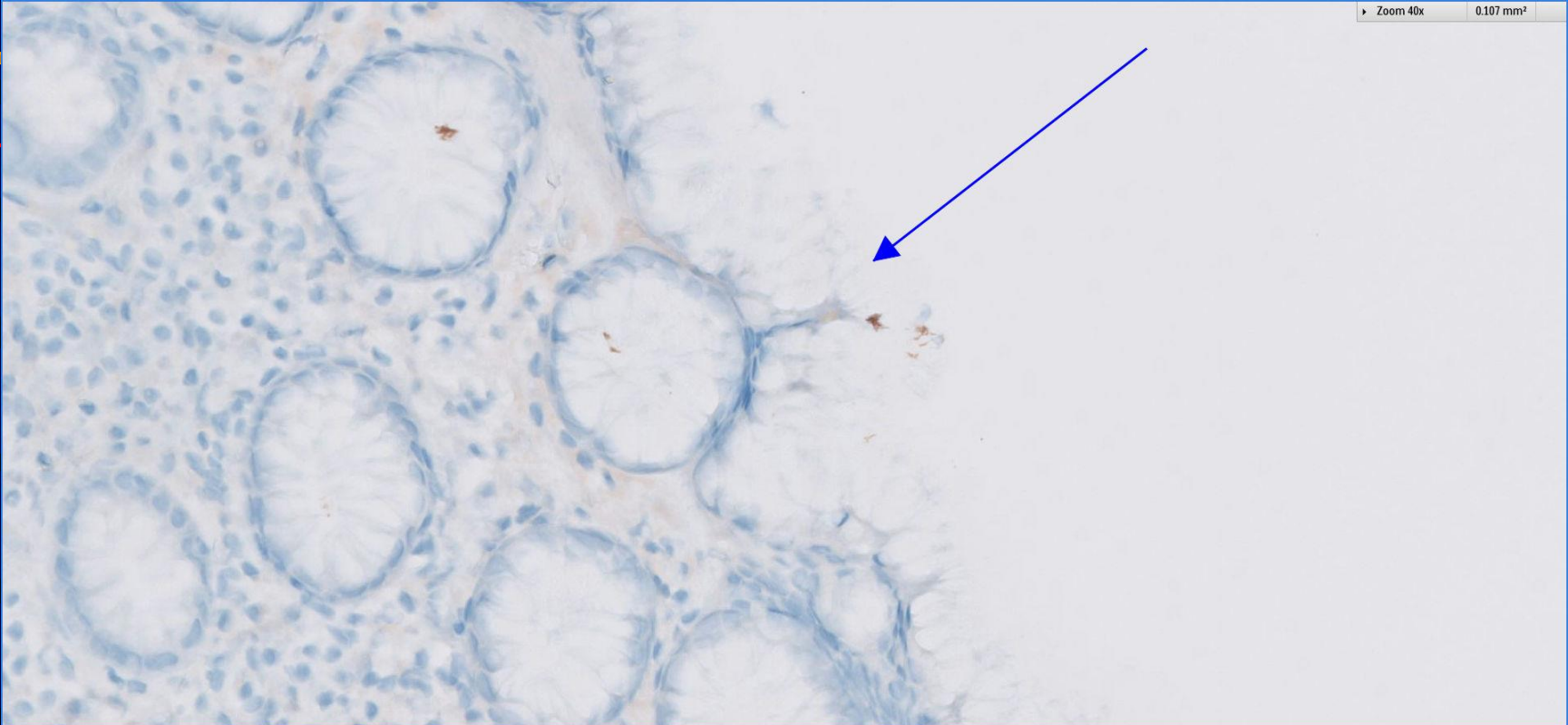
Hpy  
Pt.



Hpy  
cont



Hpy  
Pt.



Hpy  
Pt.



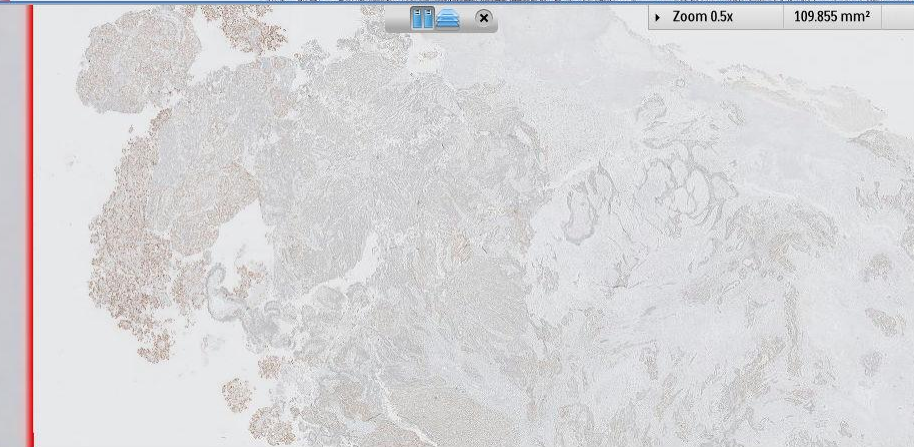
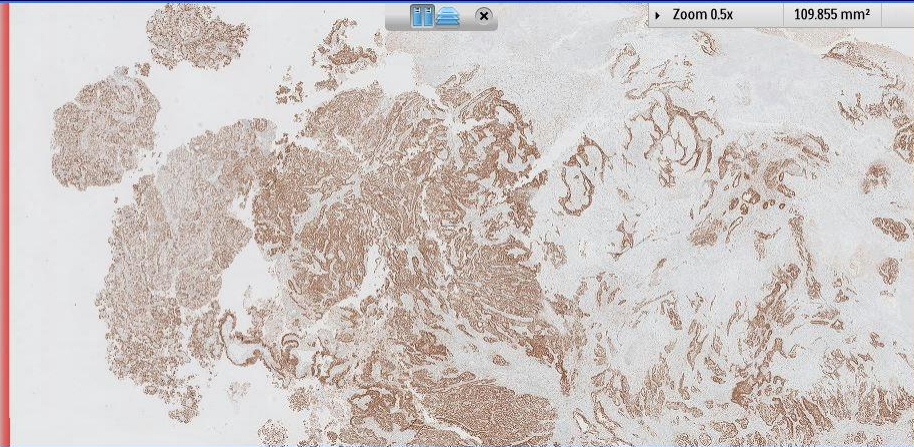
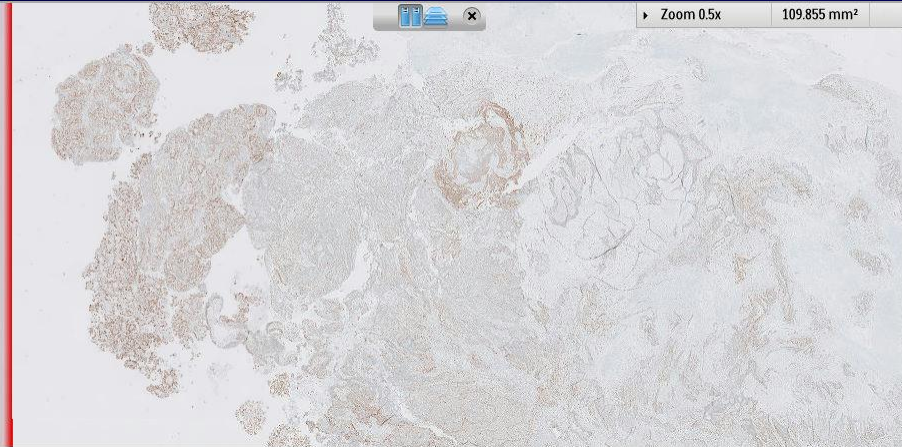


# Endometrial CA MMR, 0.5X

MLH1

Aligned slides

MSH6



MSH6

PMS2

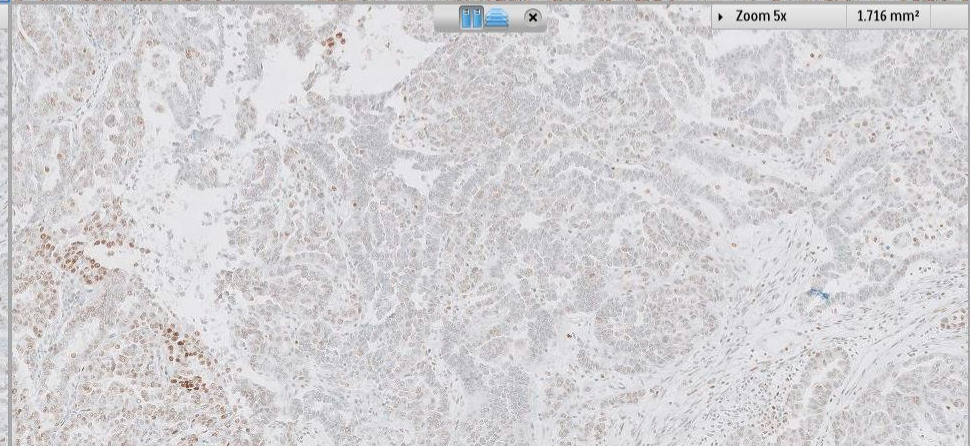
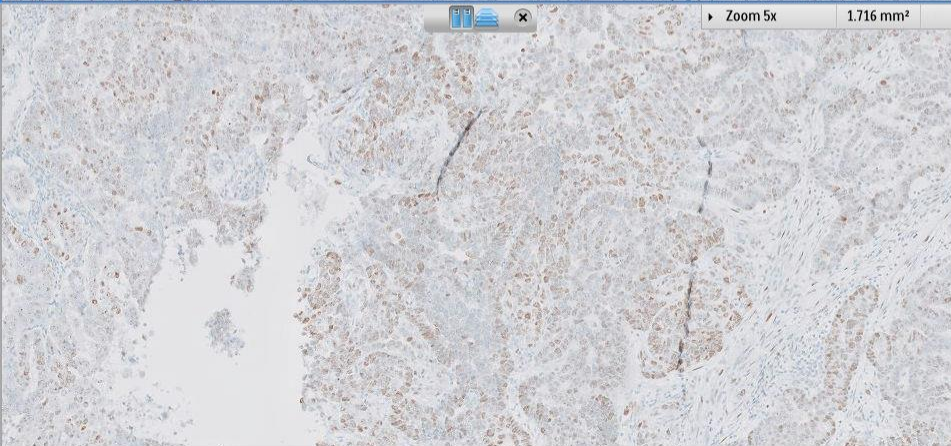
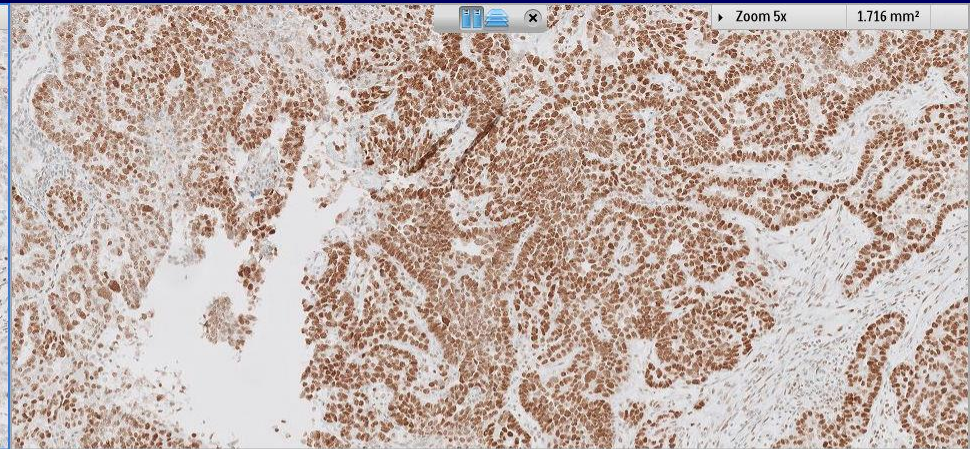
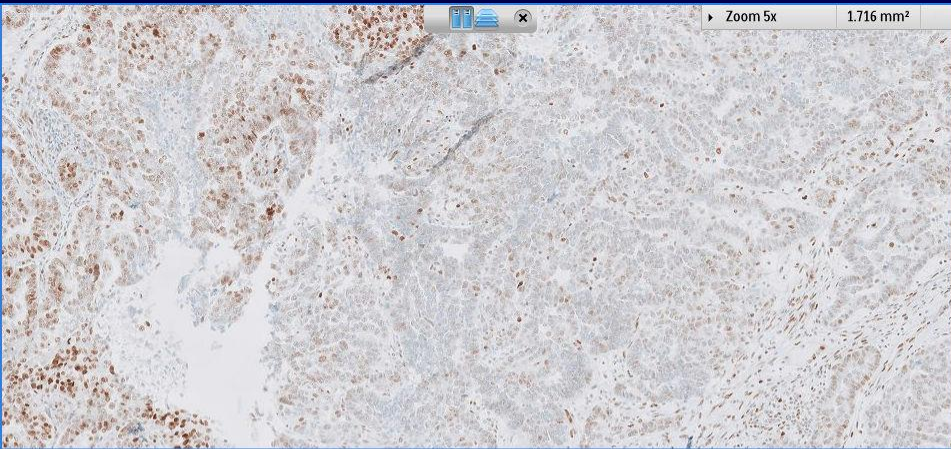


# Endometrial CA MMR, 5X

MLH1

Aligned slides

MSH6



MSH6

PMS2

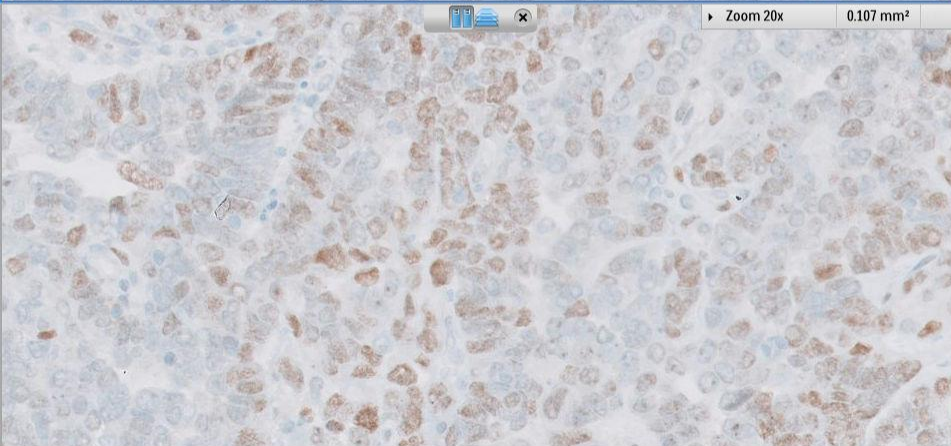
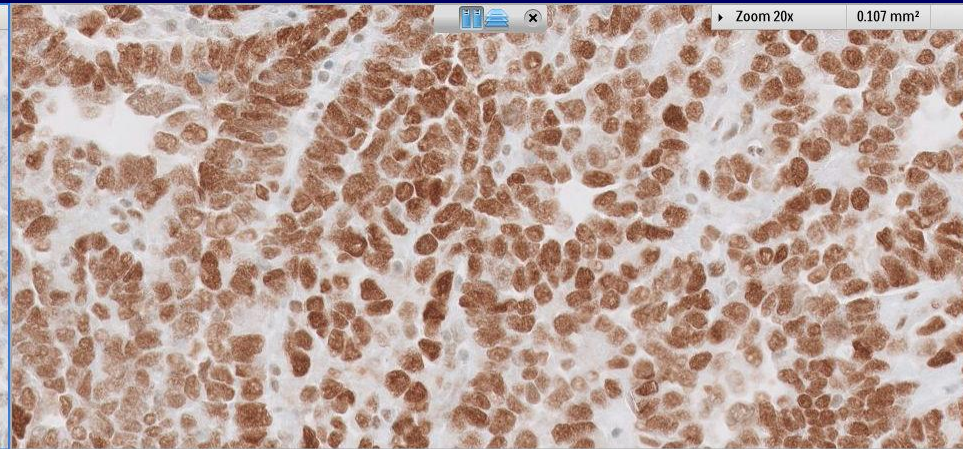
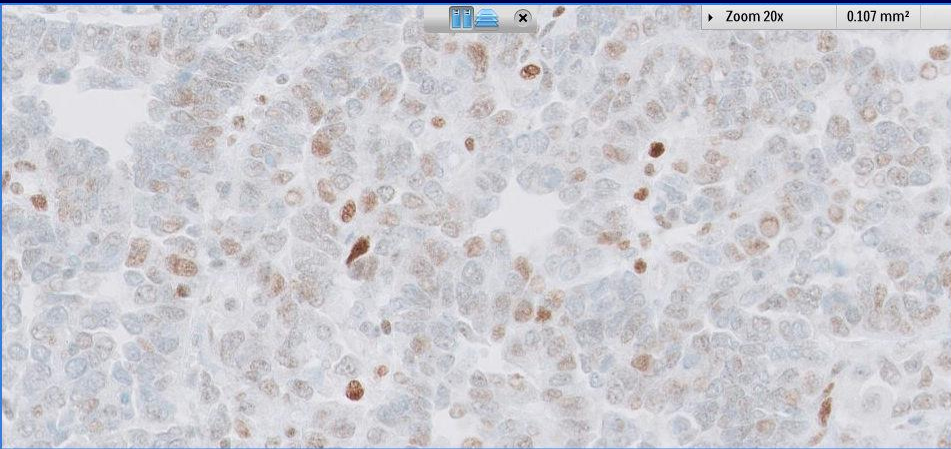


# Endometrial CA MMR, 20X

MLH1

Aligned slides

MSH6

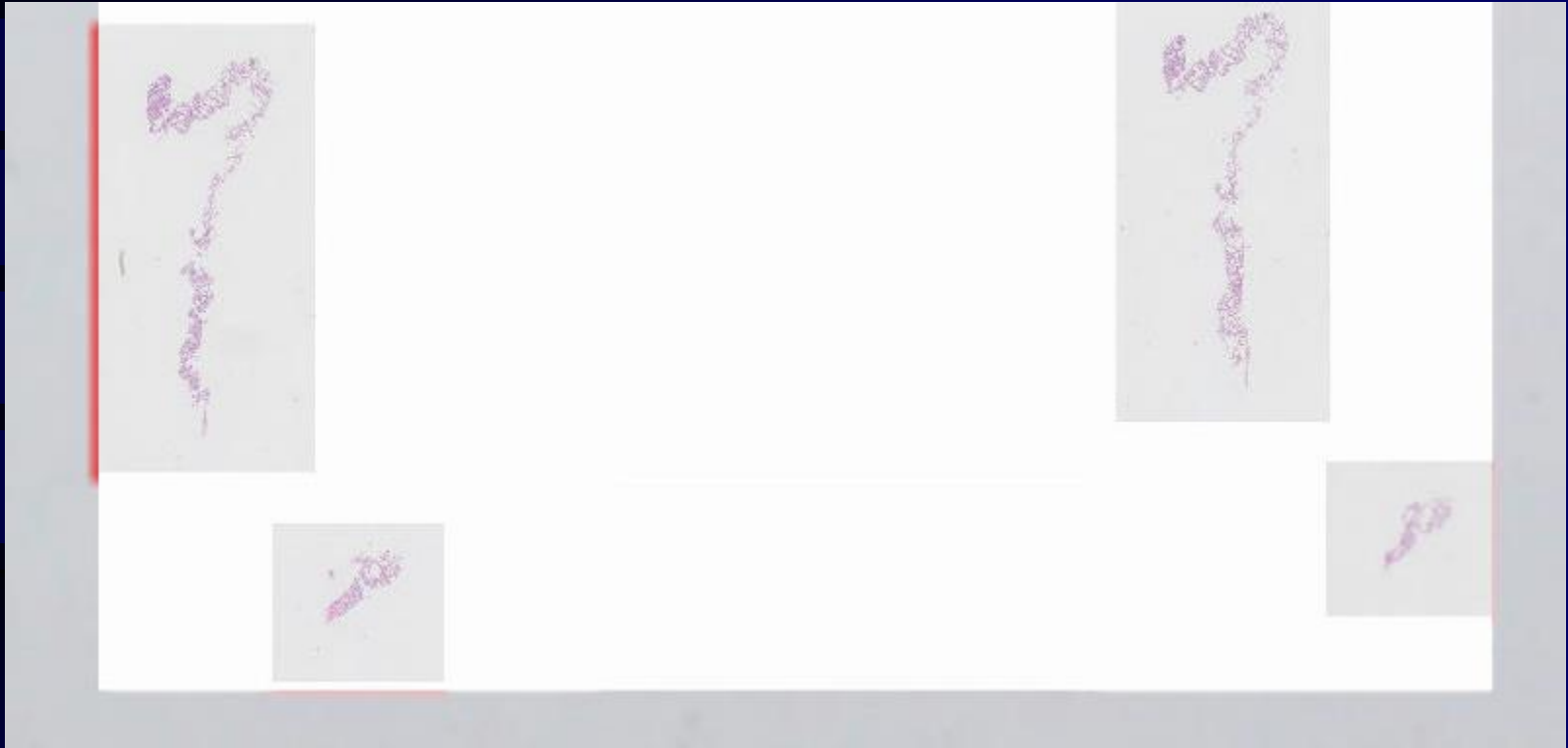


MSH6

PMS2

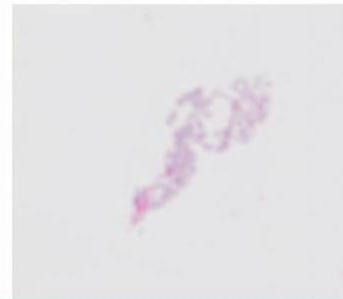
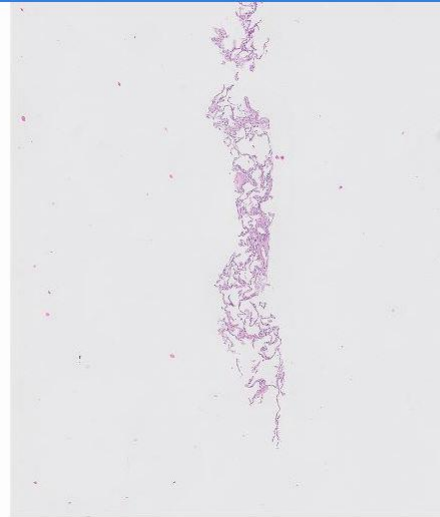


# small fragments in focus





# Next level small fragments out of focus



Zoom 1x 109.855 mm<sup>2</sup>

# Philips Demonstration Project: Take Aways

Selecting the appropriate implementation team is critical.

IT support is paramount: ensuring proper bandwidth and workstations and troubleshooting.

WSI is a powerful tool with equivalence to glass slide reading for diagnosis in routine surgical pathology. Cytology, frozen sections, hematopathology smears not yet FDA approved.

Some lag time and minimal image quality issues exist versus the optimized FDA approved workstation (not prohibitive for proof of concept in the project).

Rare out of focus issue with very small fragments of tissue.



# Philips- Demonstration Project Team!

Project Manger: William Desalvo, SQL

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SQL Histology: Tamara Stahn, Dawn Stapley, Nelly Melendez Rosario and Steven Stubblefield.

SQL and Banner IT: Calley McCoy, Bart Mika, Khai Dao, Diane Blasko

Philips Corporation: Cynthia Marr, Steve Sorenson, Nora Mansoorian and Lisa Cuomo.

Banner Lab Managers: Gabrielle Siciliano (BTMC) and Denise Waltrip (BDMC)

Pathologists: Holly McDaniel (BDMC) and Richard Eisen (BTMC).

# Whole Slide Imaging: References

Evans AJ, Salama ME, et al. Implementation of Whole Slide Imaging for Clinical Purposes: Issues to Consider From the Perspective of Early Adopters. *Arch Pathol Lab Med*. 2017;141:944–959.

Hedvat CV. Digital Microscopy. Past, Present, and Future. *Arch Pathol Lab Med*. 2010;134:1666–1670.

Mukhopadhyay S, Feldman MD, et al. Whole Slide Imaging Versus Microscopy for Primary Diagnosis in Surgical Pathology. A Multicenter Blinded Randomized Noninferiority Study of 1992 Cases (Pivotal Study). *Am J Surg Pathol* 2018;42:39–52.



# Whole Slide Imaging: References (2)

Morrison AO and Gardner JM. Microscopic Image Photography Techniques of the Past, Present, and Future. Arch Pathol Lab Med. 2015;139:1558–1564.

Thrall M, Pantanowitz L and Khalbuss W. Telecytology: Clinical applications, current challenges, and future benefits. J Pathol Inform 2011, 2:51.

Bauer TW, Schonefeld L, et al. Validation of Whole Slide Imaging for Primary Diagnosis in Surgical Pathology. Arch Pathol Lab Med. 2013;137:518–524.



THE END