COLLEGE of AMERICAN PATHOLOGISTS

Digital Frozen Sections in Surgical Pathology Practice: Issues and Challenges

Savitri Krishnamurthy, MD, FCAP
Andrew Evans MD, FCAP
Zoltan Laszik MD, PhD

July 2nd 2024

Conflict of Interest

- **The speakers on this webinar will discuss their conflict of interest within their presentations.**

The CAP Committee hosting this webinar

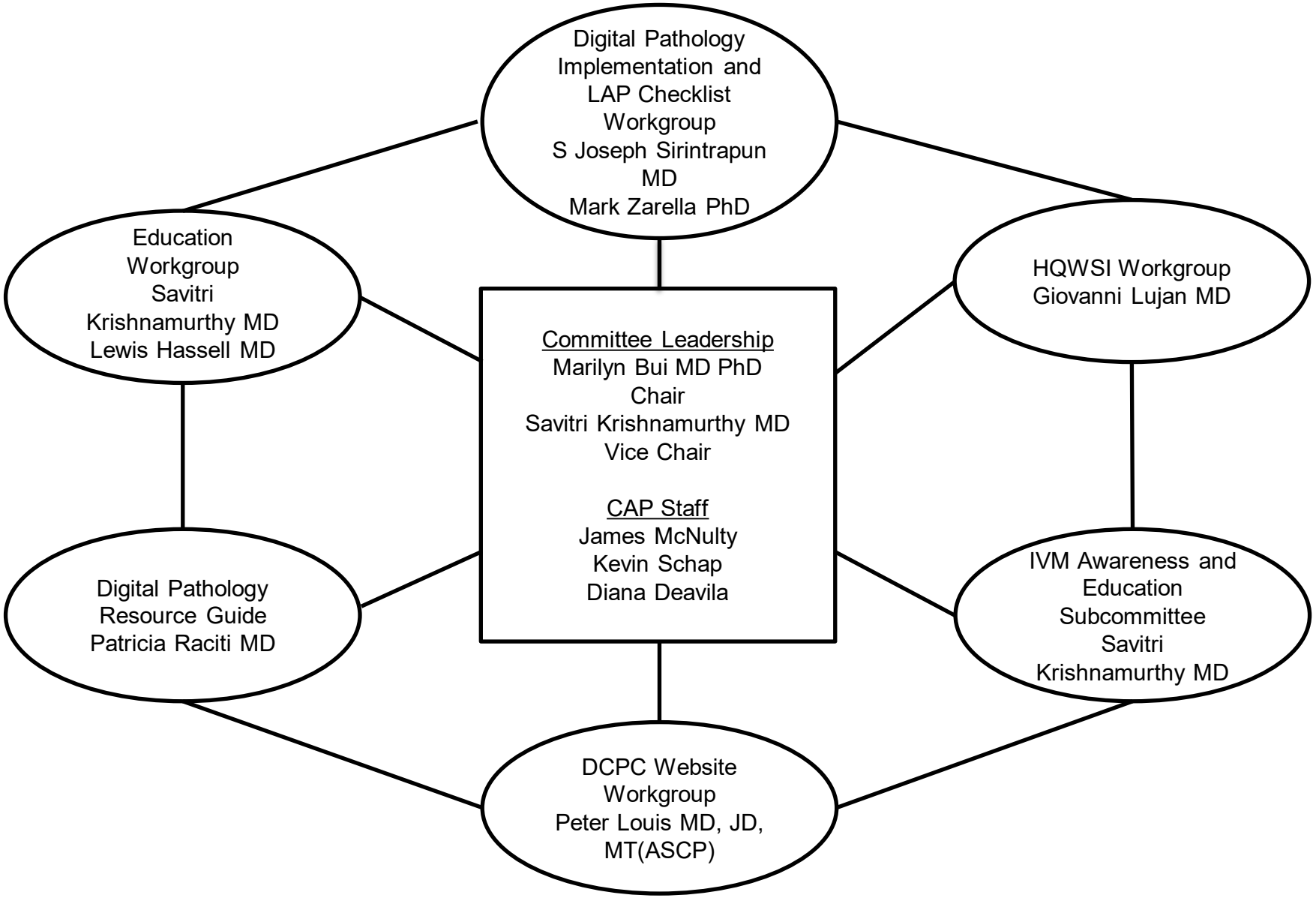
Digital and Computational Pathology Committee

- **The charge of the Digital and Computational Pathology Committee (DCPC) is to advance the adoption of digital pathology within the CAP and to serve as a respected resource for information and education for pathologists, patients and the public on the practice and science of digital pathology.**

<u>Committee Leadership</u>

- **Marilyn Bui, MD, PhD, FCAP Chair**
- **Savitri Krishnamurthy, MD, FCAP Vice Chair**

Digital and Computational Pathology Committee Structure



Composition of the DCPC

- Pathologists - 24 with variety of specialty interests/niches
- Junior members - 2
- Academic institutions - >18 represented.
- Private practice- at least 8 members, some with industry
- Expertise - Informatics, digital pathology use, development, standards, and validation, AI, IVM/EVM, etc.

Webinar agenda

TOPICS	PRESENTERS
Lessons learned from retrospective/prospective analysis leading to incorporation of WSI for FS evaluation in a large Breast Pathology practice	Savitri Krishnamurthy, MD, FCAP
The experience of using digital pathology for frozen section diagnosis in diverse practice settings	Andrew Evans, MD, PhD, FACP
Validating Whole Slide Imaging for Frozen Section Diagnoses: UCSF's Experience	Zoltan G. Laszik, MD, PhD
Moderated Questions	All Speakers

Learning Objectives

- To learn about different digital pathology options for intraoperative evaluation of frozen sections in surgical pathology practice.
- To understand the factors to consider when selecting a platform for digital frozen sections.
- To recognize the issues and challenges related to the use of digital frozen sections.

Savitri Krishnamurthy, MD, FCAP

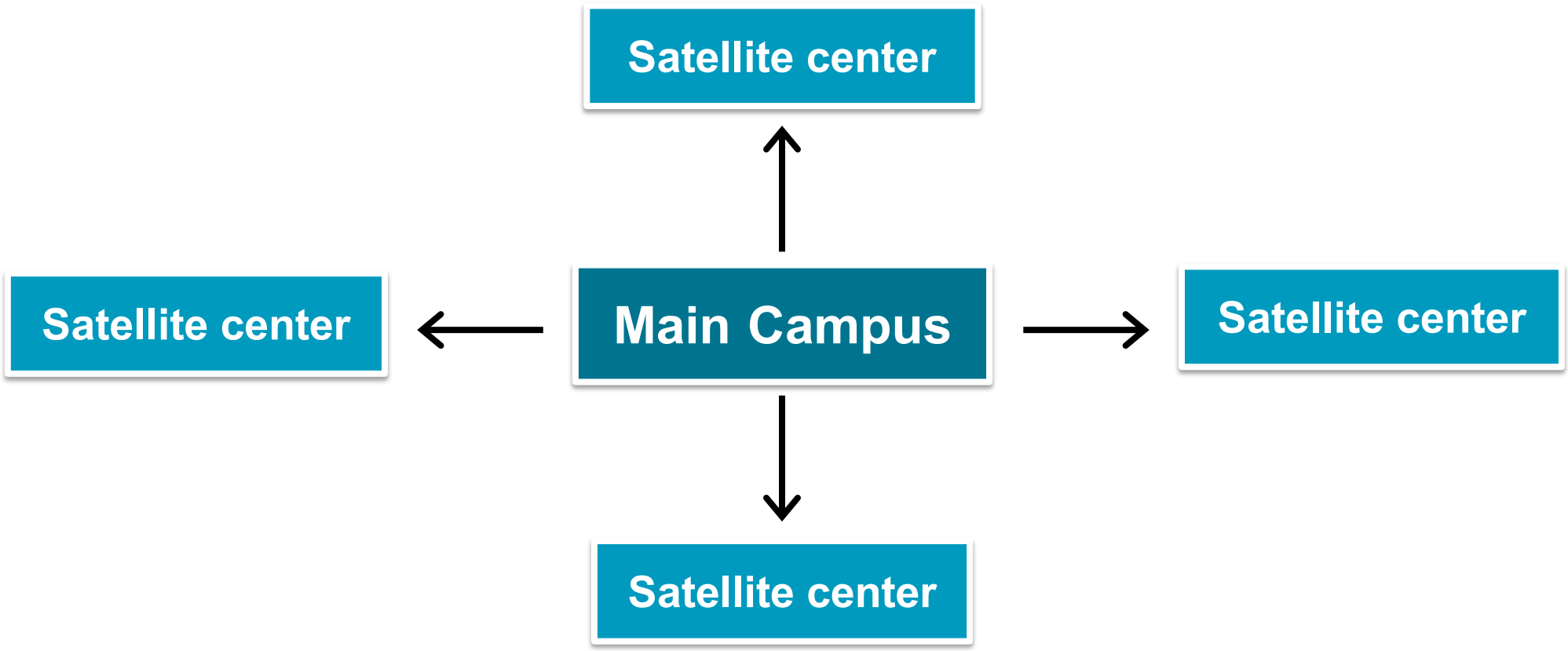
Dr. Krishnamurthy is the Vice Chair of the Digital and Computational Pathology Committee and is Professor of Pathology at The University of Texas MD Anderson Cancer Center in Houston, TX. She completed her Pathology residency training in New England Medical Center, Tuft's University in Boston followed by fellowship training in Oncologic Pathology at Memorial Sloan Kettering Cancer Center in New York and Cytopathology at the University of Texas MD Anderson Cancer Center.

Whole slide imaging for evaluation of frozen sections

Lessons learned from retrospective/prospective analysis leading to incorporation of WSI for FS evaluation in a large Breast Pathology practice

Digital Modalities for Frozen sections

Increasing need for remote interpretation of FSs in today's Anatomic Pathology practice



Choosing a Digital Modality

Camera based streaming of static images

Video camera based streaming of images

Whole slide Imaging

Robotic Microscopy

Live whole slide imaging

Robotic Microscopy/ whole slide imaging

Whole Slide Imaging for Frozen Section Evaluation in Breast Pathology practice

ADVANTAGES

- Ability of pathologists to navigate the slides themselves remotely
- Increasing familiarity using WSIs in standard of care practice
- Availability of scanners suitable for intraoperative use
- Acceptable image quality
- Integration into pathology information system
- Ease of obtaining second opinions in real time

Whole Slide Imaging for Frozen Section Evaluation

- Recognition of reported studies using different WSI platforms
- Feasibility, cost, time taken for acquisition of images, sensitivity and specificity, inter and intra observer agreement

Validation of a Portable Whole-Slide Imaging System for Frozen Section Diagnosis

Rajiv Kumar Kaushal[1], Sathyanarayanan Rajaganesan[1], Vidya Rao[1], Akash Sali[1,2], Balaji More[1], Sangeeta B. Desai[1]

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Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

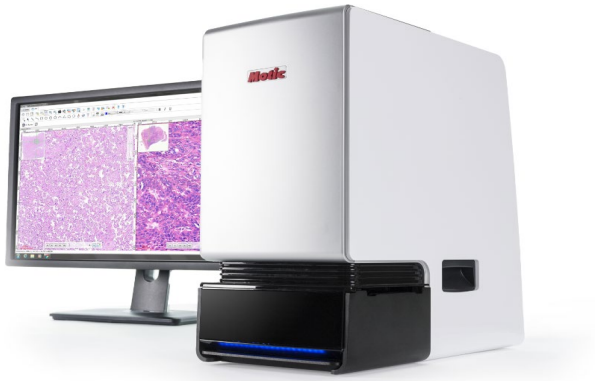
journal homepage: www.elsevier.com/locate/anndiagpath

Original Contribution

Validation of whole slide imaging for frozen section diagnosis of lymph node metastasis: A retrospective study from a tertiary care hospital in Thailand

Charinee Kantasiripitak[a], Thiyaphat Laohawetwanit[a,b,*], Sompon Apornvirat[a,b], Kongkot Niemnapa[c]

[a] Division of Pathology, Thammasat University Hospital, Pathum Thani, Thailand
[b] Division of Pathology, Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand
[c] Advanced Digital Simulation Center, Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand



Contents lists available at ScienceDirect

Journal of Pathology Informatics

journal homepage: www.elsevier.com/locate/jpi

Original Research Article

Establishment of a whole slide imaging-based frozen section service at a cancer center

Sue Chang, Evita Sadimin, Keluo Yao, Stanley Hamilton, Patricia Aoun, Raju Pillai, David Muirhead, Daniel Schmolze *

City of Hope National Medical Center, Department of Pathology, 1500 East Duarte Road, Duarte, CA 91010, USA

Whole Slide Imaging for Frozen Section Evaluation

Frozen Sections in Breast Pathology Practice

Sentinel and clipped axillary lymph nodes

Chemotherapy naïve

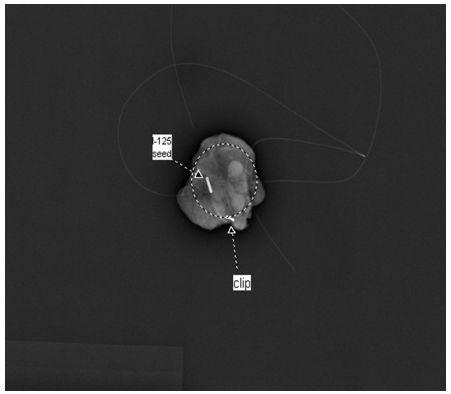
Invasive mammary carcinoma, ER/PR+,HER2-
Partial breast radiation

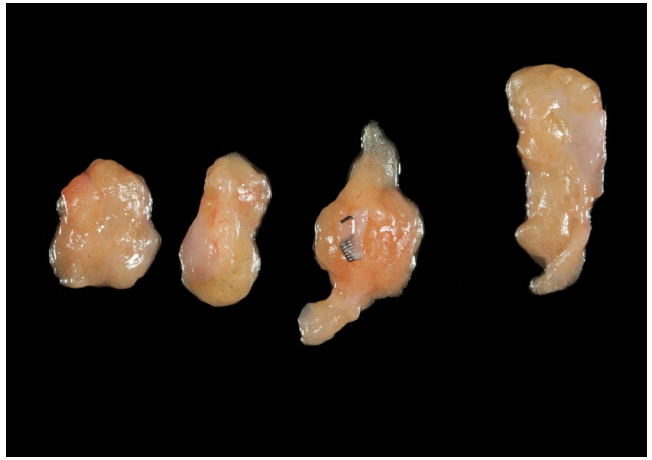
Invasive mammary carcinoma, ER/PR+, HER2+

Invasive mammary carcinoma ER/PR+, HER2-
Mastectomy

Post Neoadjuvant Chemotherapy

Targeted axillary dissection





Whole Slide Imaging for Frozen Section Evaluation

Retrospective analysis

39 patients, 109 Lymph nodes

Chemotherapy naïve : 17
Post neoadjuvant chemotherapy: 22

Real time prospective analysis

52 patients, 132 Lymph nodes

Chemotherapy naïve 13
Post neoadjuvant chemotherapy: 39

Incorporation into clinical practice

Whole Slide Imaging for Frozen Section Evaluation in Surgical Pathology Practice

Team of Experts

Information Technology

Informatics

Laboratory Information system

Surgical Pathology

Feasibility of Using WSI for Frozen Section Diagnosis

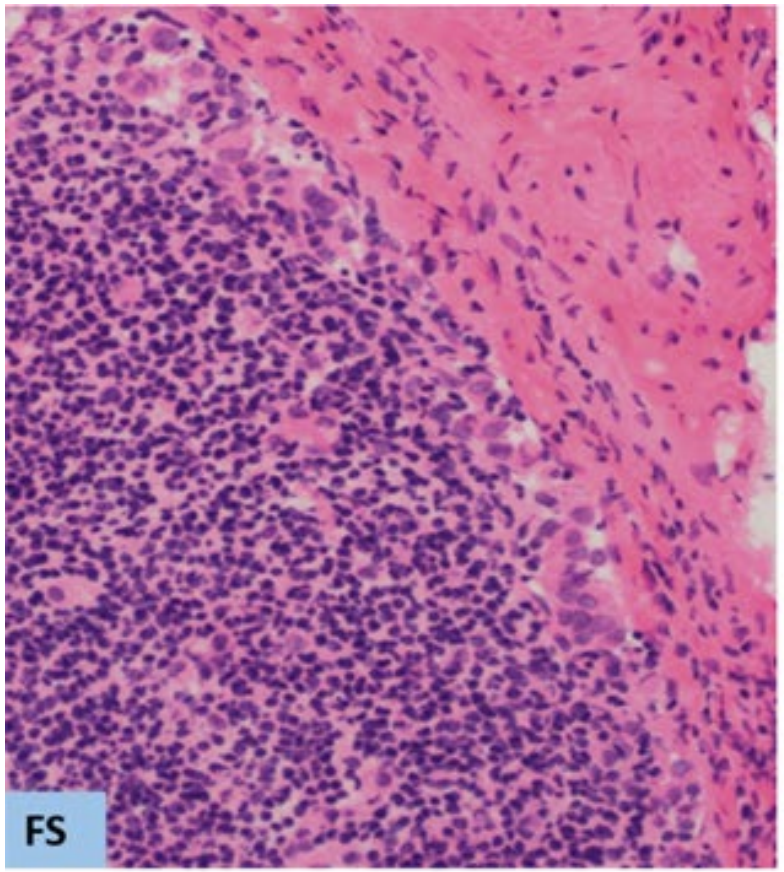
109 Axillary Sentinel Lymph nodes and Clipped lymph nodes
200 blocks, 200 levels

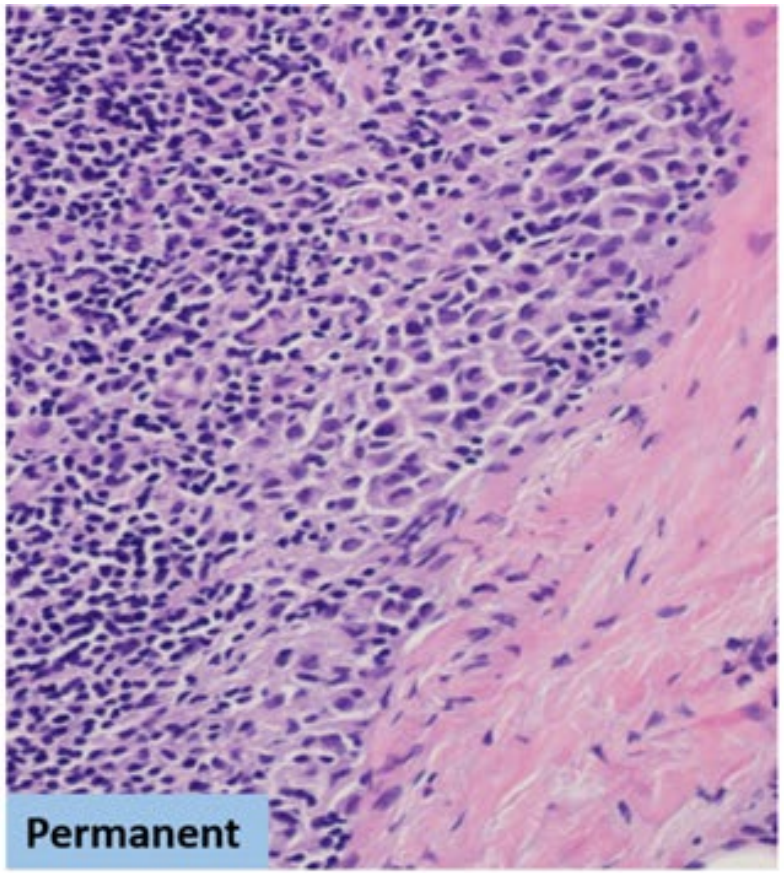
	Sensitivity		Specificity		PPV		NPV		Accuracy	
	WSI	LME	WSI	LME	WSI	LME	WSI	LME	WSI	LME
	(%)		(%)		(%)		(%)		(%)	
Pathologist 1	79	71	100	100	100	100	97	96	97	96
Pathologist 2	71	71	100	100	100	100	96	96	96	96
Pathologist 3	71	57	100	99	100	89	96	94	96	94
Pathologist 4	93	93	100	100	100	100	99	99	99	99
Pathologist 5	93	86	100	100	100	100	99	98	99	98

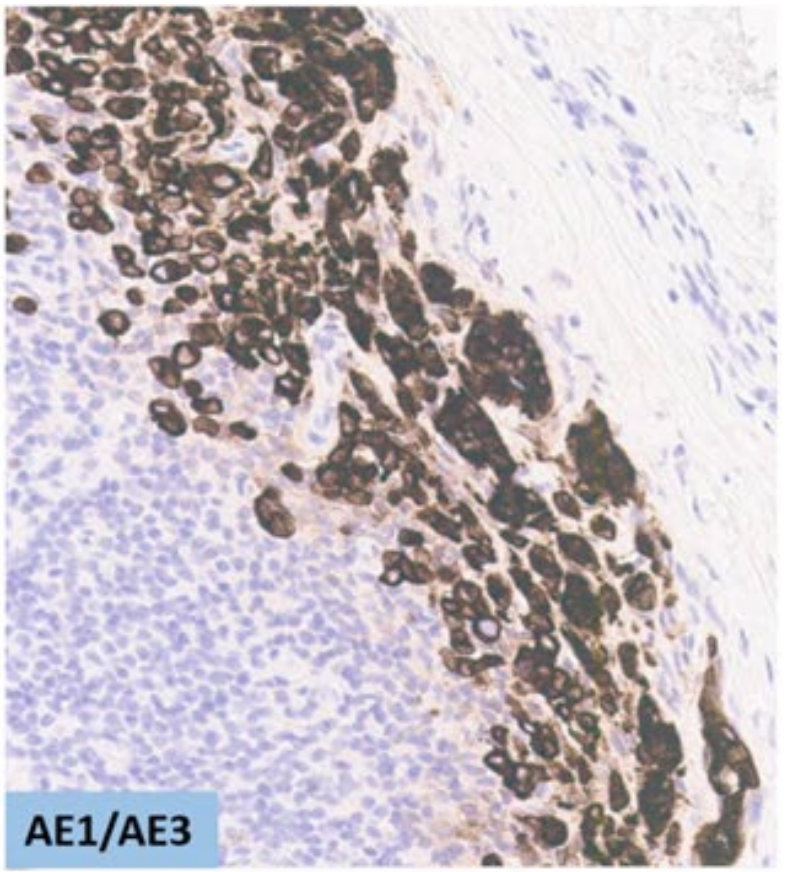
The performance of the pathologists was similar between WSI and LME. Time taken was significantly higher

Reader	Mean difference in time taken between WSI and LME (min)	P Value
Pathologist 1	5.4	<.0001
Pathologist 2	3.2	<.0001
Pathologist 3	1.4	<.0001
Pathologist 4	0.8	<.0001
Pathologist 5	0.7	<.0001

False negative WSI interpretation of sentinel lymph node FS







Prospective Feasibility Study of WSI of H&E Stained Frozen Sections of Sentinel Lymph Nodes (SLNs) and Clipped LNs in Breast Cancer

Primary Objectives

- Feasibility of using the WSI platform for intraoperative evaluation of SLNs and clipped LNs in breast cancer in real time
- Time required for scanning and acquisition of WSIs of H&E stained FSs of SLNs and clipped LNs
- Time taken to read digital WSIs in comparison to Light microscopic examination (LME) of H&E stained FSs of SLNs and clipped LNs
- Comparison of diagnosis between WSI and LME

Time Taken for Scanning and Diagnosis Using LME and WSI

	Scanning (Mean)	LME Diagnosis (Mean)	WSI Diagnosis (Mean)
LN (n=132)	6.04 min	3.51 min	3.95 min
1 Block (n=98)	4.16 min	2.59 min	3.04 min
2 Block (n=23)	8.43 min	4.84 min	5.98 min
>2 Block (n=11)	17.72 min	7.25 min	8.35 min

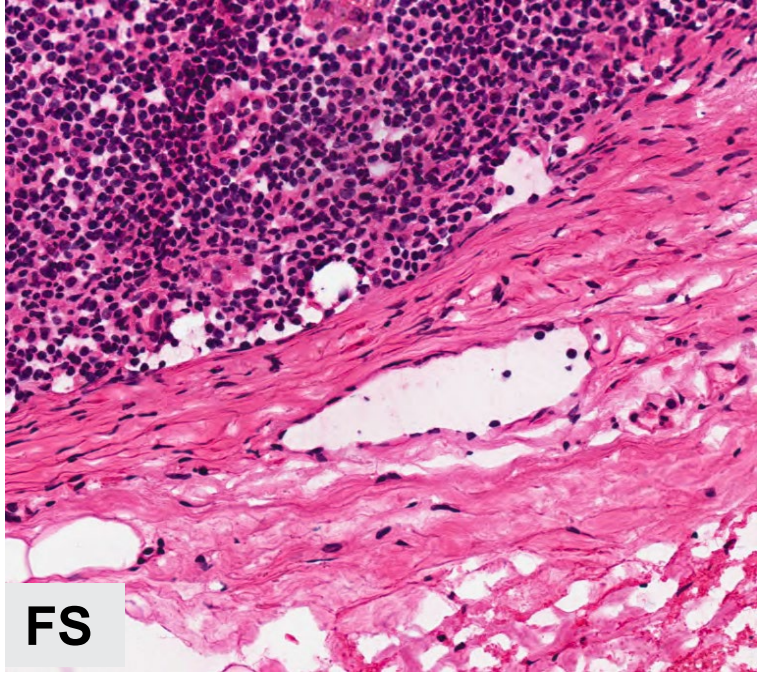
LME: Light microscopic examination
WSI: Whole slide images

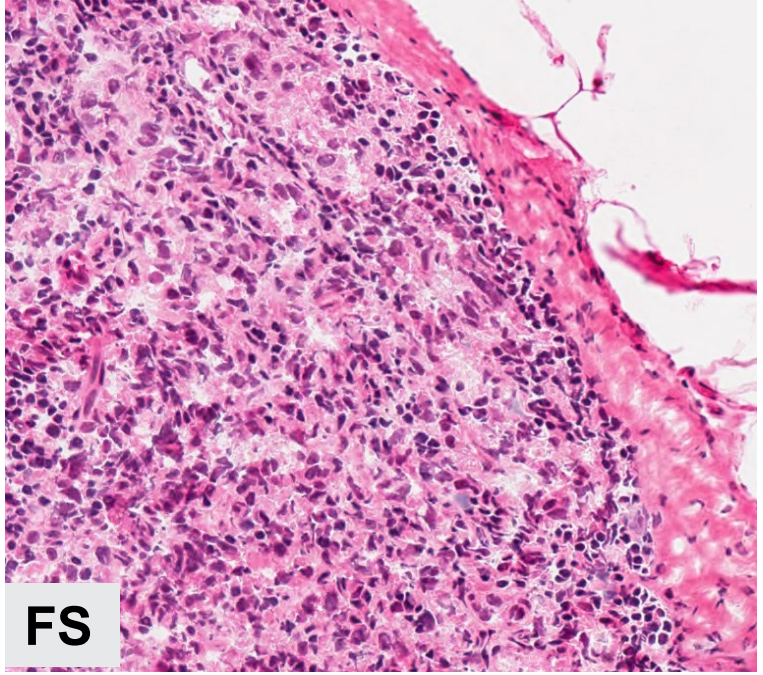
Comparison of Performance of Breast pathologists between WSI and Light microscopy

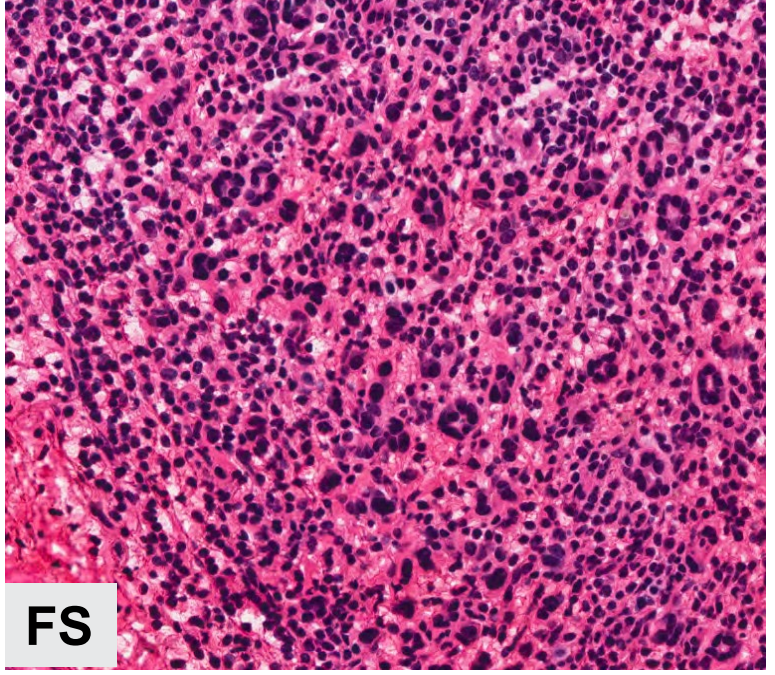
		Sensitivity, %		Specificity, %		PPV, %		NPV, %		Accuracy, %	
		WSI	LM	WSI	LM	WSI	LM	WSI	LM	WSI	LM
Prospective Analysis	Pathologist group	58	67	100	100	100	100	96	97	96	97

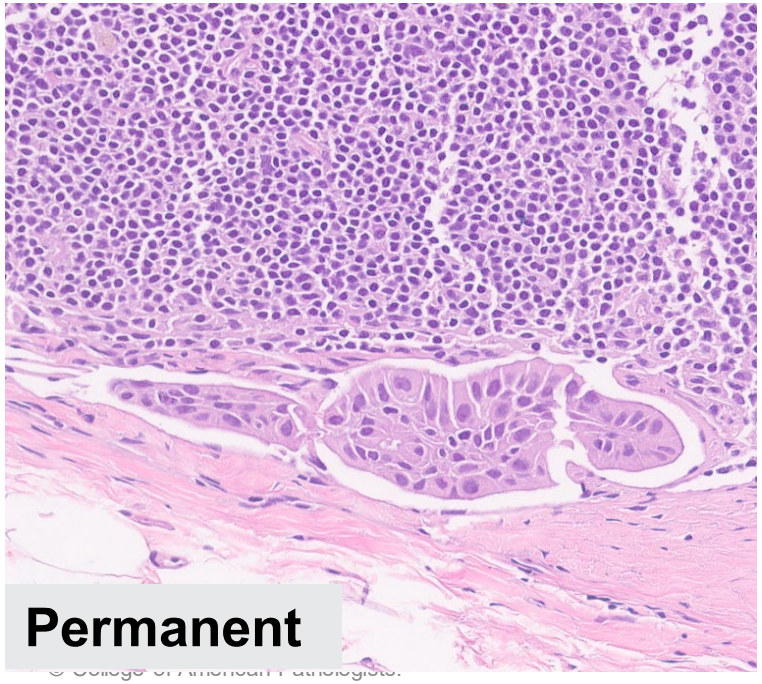
PPV, positive predictive value NPV, negative predictive value.

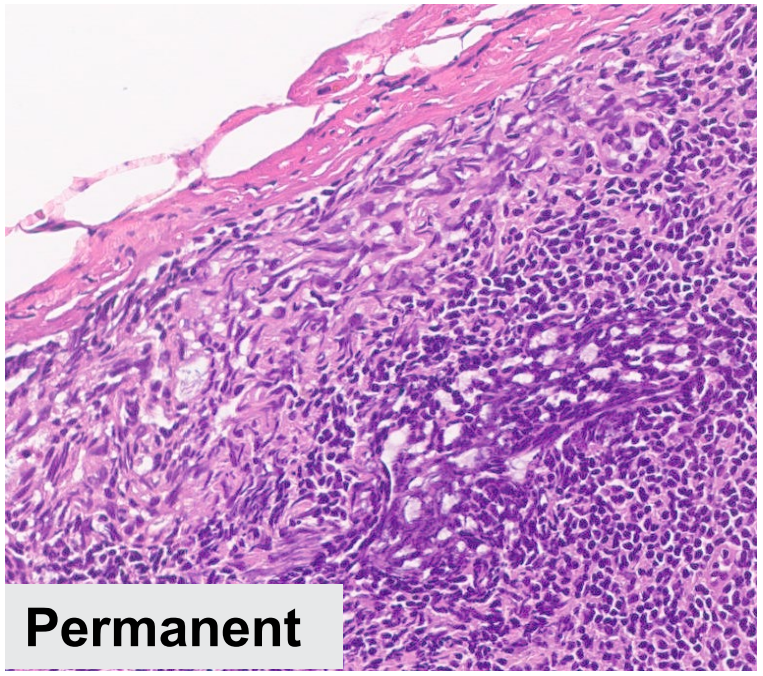
Comparable performance of pathologists between WSI and Light Microscopy

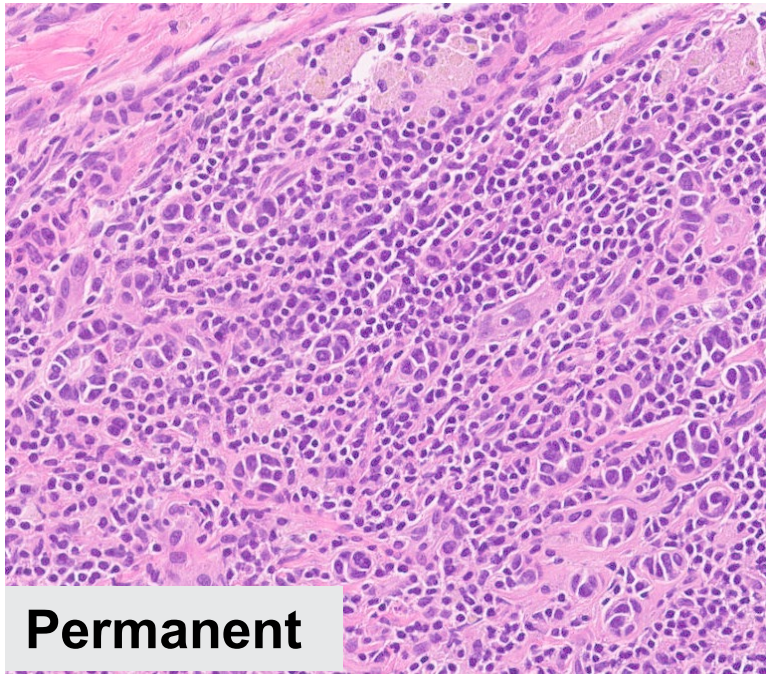












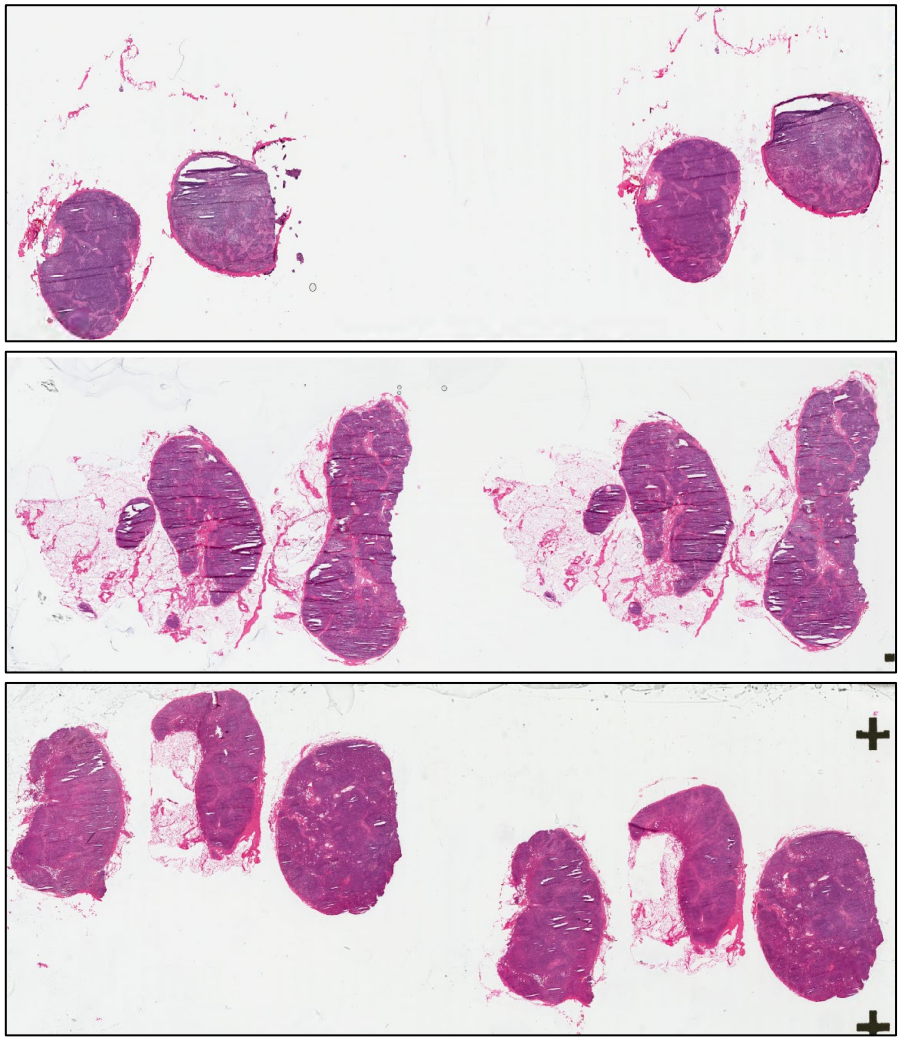
Details of performance of the breast pathologists between whole slide imaging and Light microscopy

		Final Diagnosis			
		Macrometastasis	Micrometastasis	ITCs	Negative
		(n =8)	(n = 4)	(n = 4)	(n = 116)
WSI	+	6	3	0	0
	–	2	1	4	116
LM	+	7	3	0	0
	–	1	1	4	116

ITCs, isolated tumor cells.

Whole Slide Imaging for Frozen Section Evaluation in Surgical Pathology Practice

Good quality frozen sections



Whole slide imaging for frozen section evaluation in Surgical Pathology practice

- Support from team – IT, Informatics, vendor, pathologists
- Training laboratory support staff in scanning FS glass slides
- Encountering technical challenges :
  - Problems in scanning
  - Problems in integration of image into Epic Beaker
- Ready to face interruption in viewing images due to connectivity issues
- Good to have a back up plan with alternate imaging modality
- Administrative support to get approval for getting the imaging modality
- No special billing codes – charged as FS interpretation

Andrew Evans, MD, PhD, FACP

Dr. Evans is a former chair of the Digital and Computational Pathology Committee and current member of the Artificial Intelligence Committee and Council of Informatics and Pathology Innovation. He is an Associate Professor of Pathology at The University of Toronto and Chief of Pathology at Mackenzie Health in Toronto, ON. He completed his Pathology residency training at the University of Toronto and fellowship training in Genitourinary Pathology at University Health Network in Toronto.

Use of Digital Pathology for Frozen Section Diagnosis in Diverse Practice Settings

One Pathologist's Experience

Overview

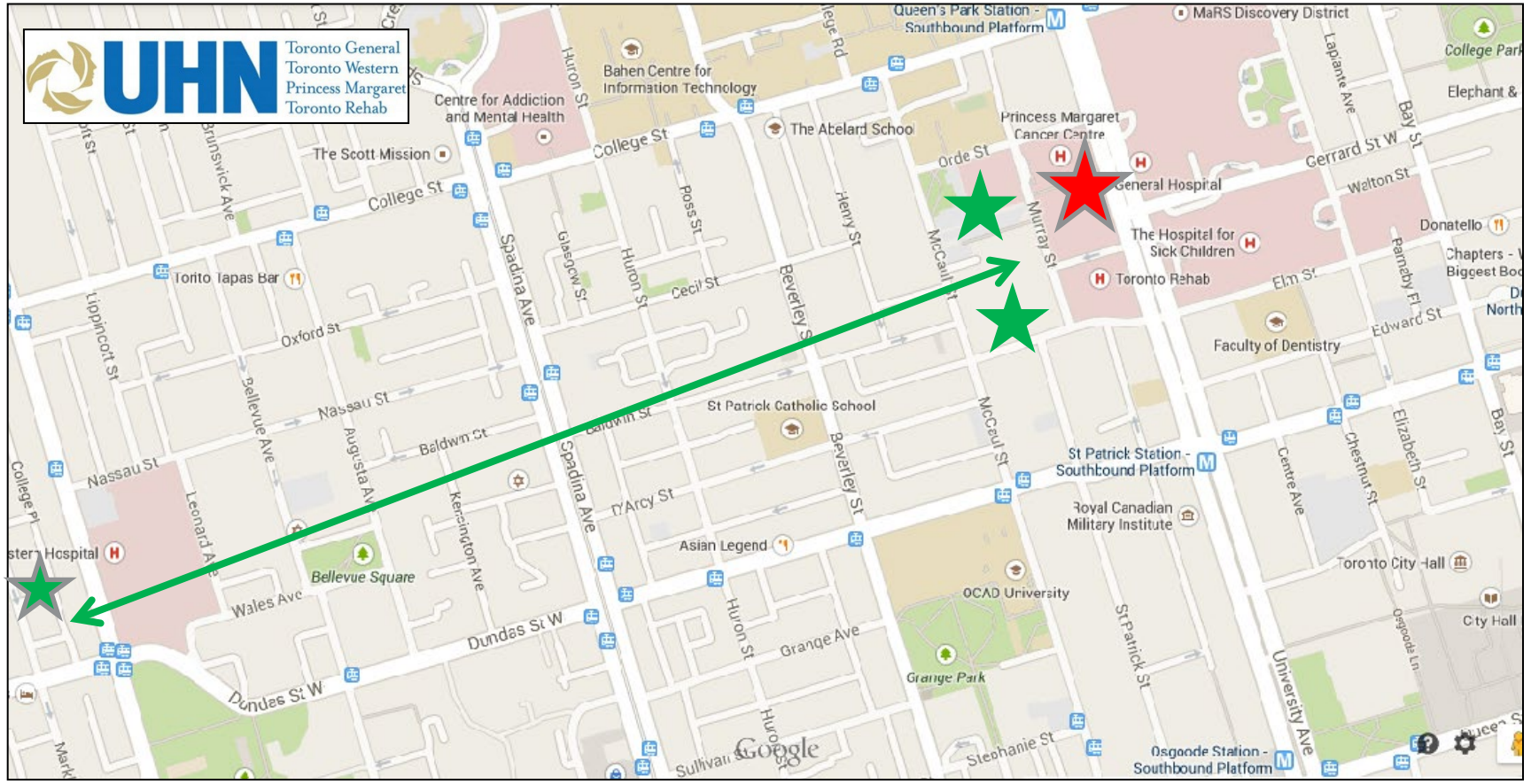
1) The presenter's experience with implementing digital pathology for frozen section review across different practice settings

2) Digital pathology modalities that can be used for frozen section diagnosis
   - robotic capture/forward, whole slide imaging, real-time video microscopy

Disclaimer

- **The content of this presentation reflects my experience over the last 19 years at University Health Network (2004-2020) and Mackenzie Health (2020-present).**

- **Depending on a variety of factors, the protocols and recommendations I will mention may/may not be practical or applicable in another institution.**



- Full departmental consolidation at TGH in early 2006
- No regular on-site pathologist at TWH as of 2004
- Move slides, move pathologists or go digital

Neuropathology Frozen Sections: Toronto Western Hospital

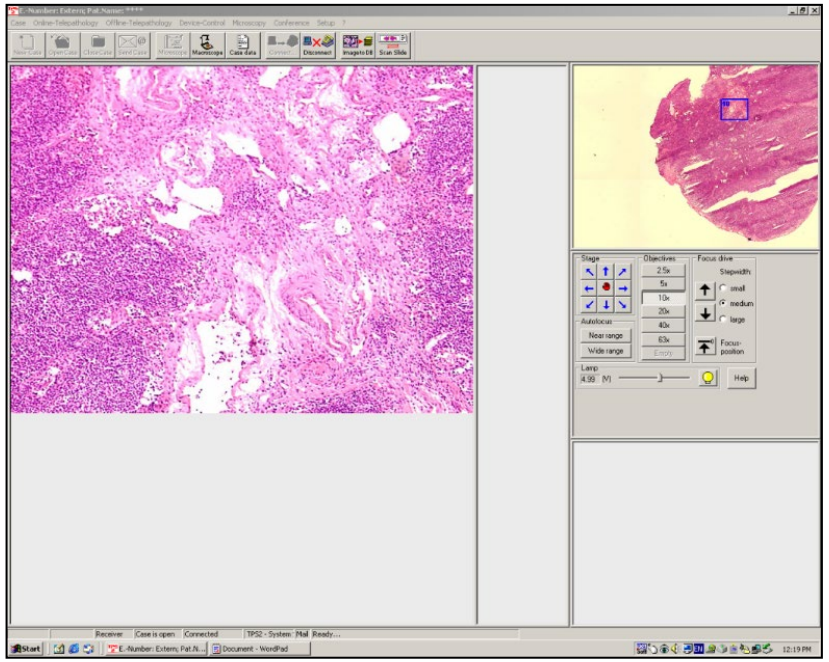
- **Upwards of 10 cases per week on average (range 2- 20)**

- **Probably the most challenging application we could have started with:**
  - **time-sensitive (i.e., TAT ≤ 20 minutes for single block in ≥ 90% of cases)**
  - **frozen section morphology (i.e., worse than paraffin sections)**
  - **greater chance of sub-optimal/crushed samples**
  - **one of the most stressful activities for pathologists**

Driving Factors For Going Digital

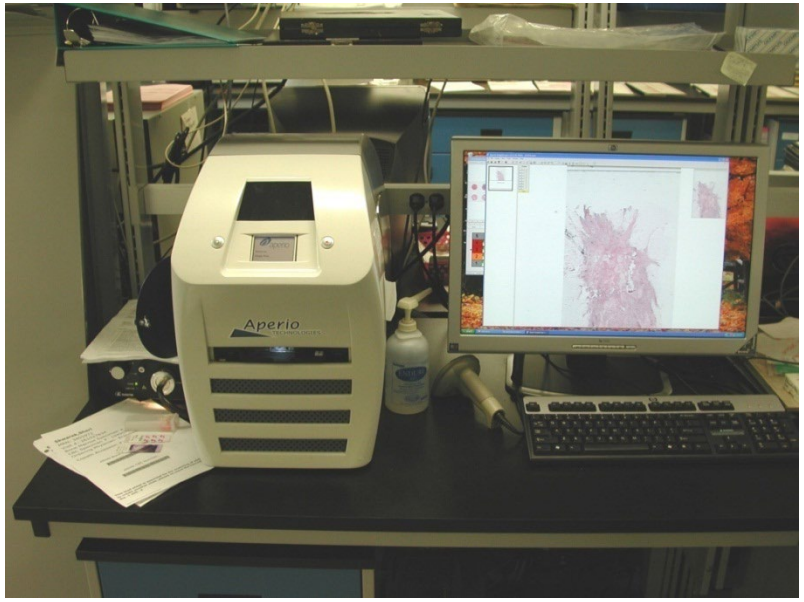
- **Single pathologist traveling from TGH to TWH**
  - **Inefficient - traveling and waiting**
  - **Disruptive to regular workflow at TGH**
    - **delays in regular sign-out <u>affecting other UHN patients</u>**
  - **No consultation on difficult cases**
    - **potential to <u>affect TWH surgical patients</u>**

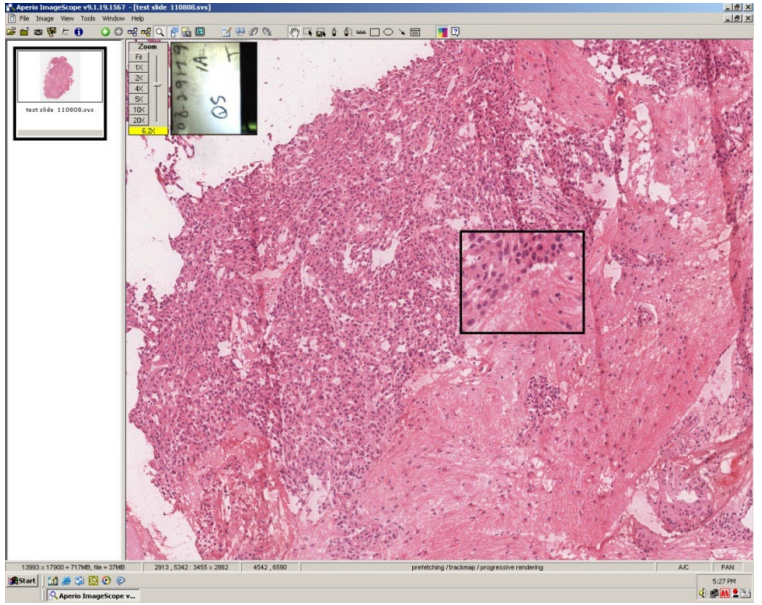
TWH Robotic Telepathology: 2004-2006



- 350 frozen sections
- slow (~ 10 minutes/slide)

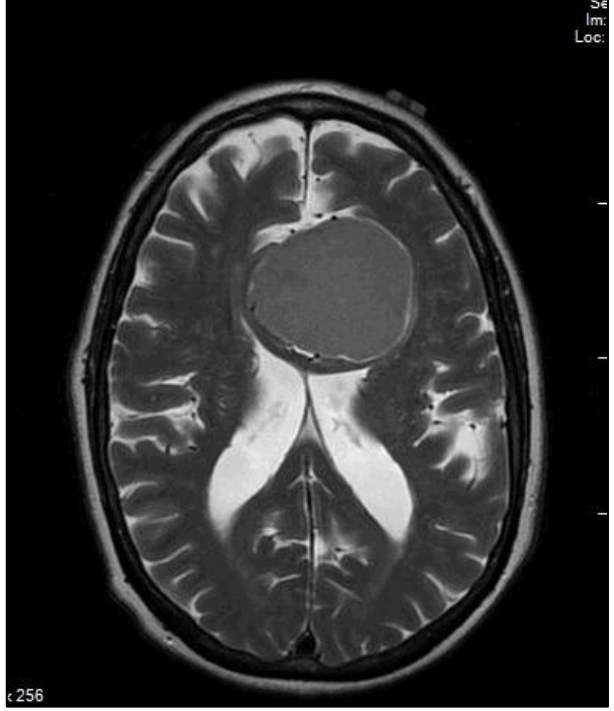
TWH Whole Slide Imaging: 2006-2021



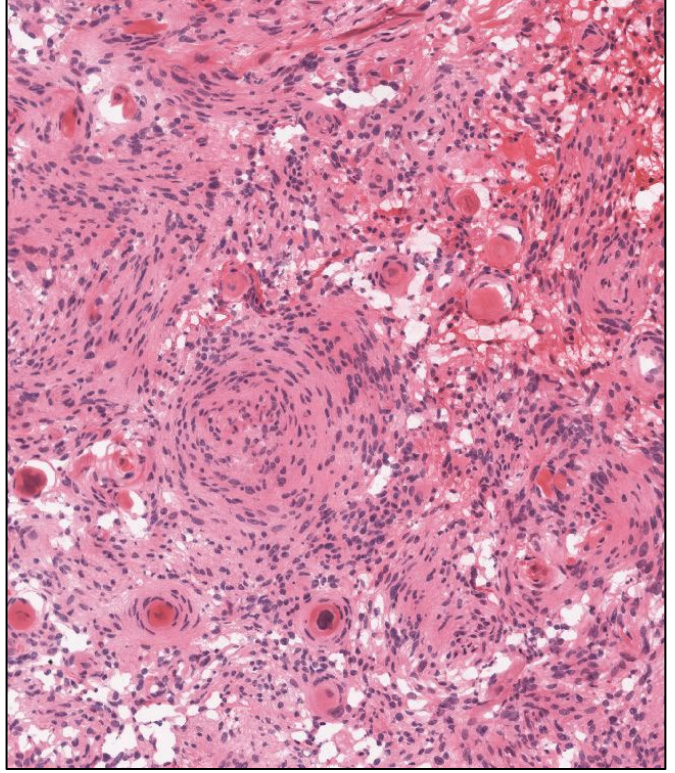


- > 6000 frozen sections
- > 90% from neurosurgery
- 0-2% discrepancy rate vs final diagnosis (year to year)

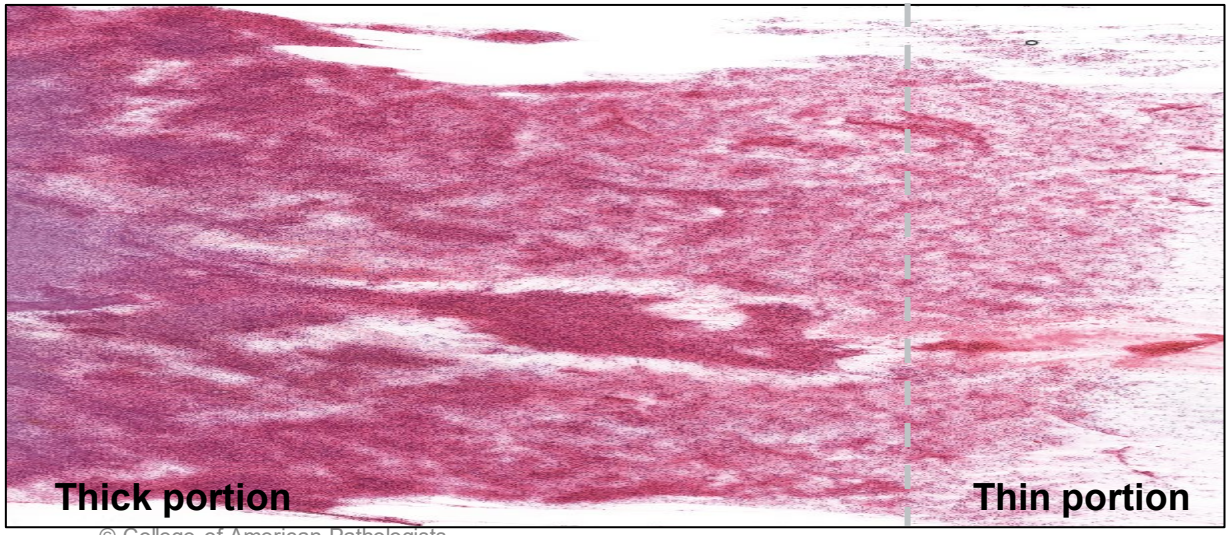
- 14-16 minute total turnaround time
- < 2% deferral rate
  - 2 pathologists can review all deferrals

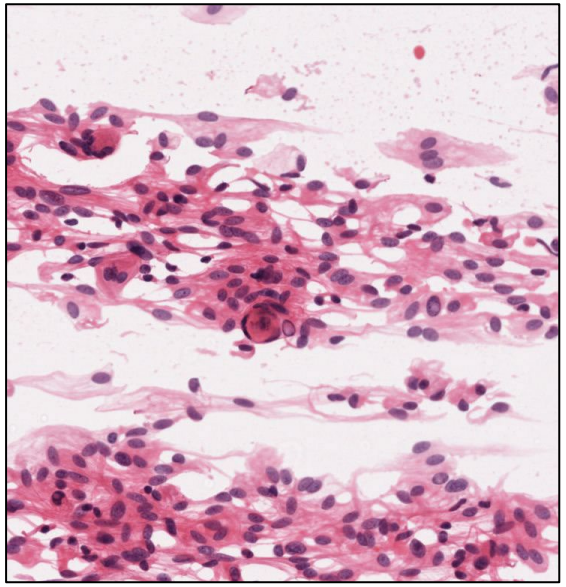


Meningioma



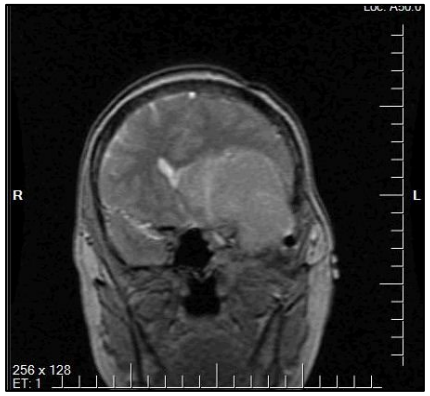
Frozen section

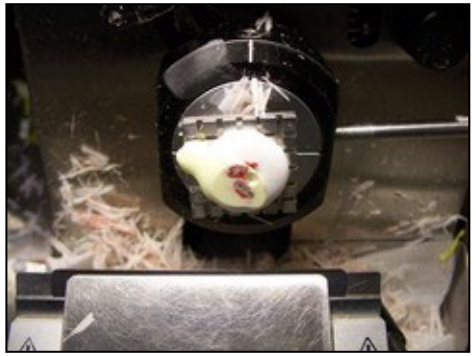


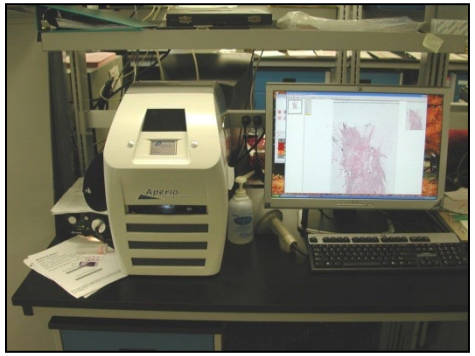


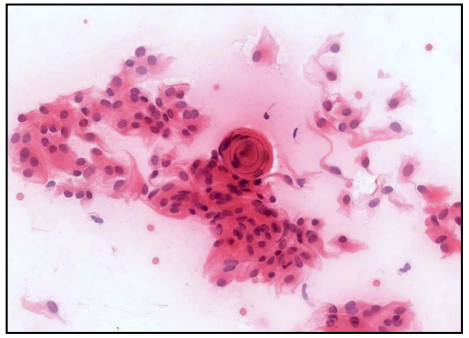
Smear

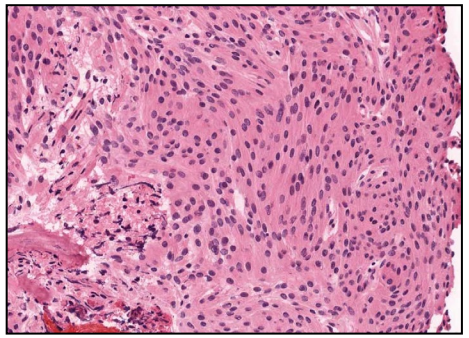
Intra-Operative Consultations: Workflow for Single Block Frozen Sections









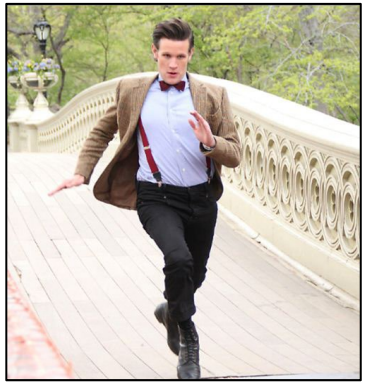


10-12 minutes

1-3 minutes

System Failure: Plan B

- Pathologist informs surgeon and goes to TWH if issue not resolved in 5 minutes
- A second pathologist works with the TWH histotechnologist in case the issue is resolved.

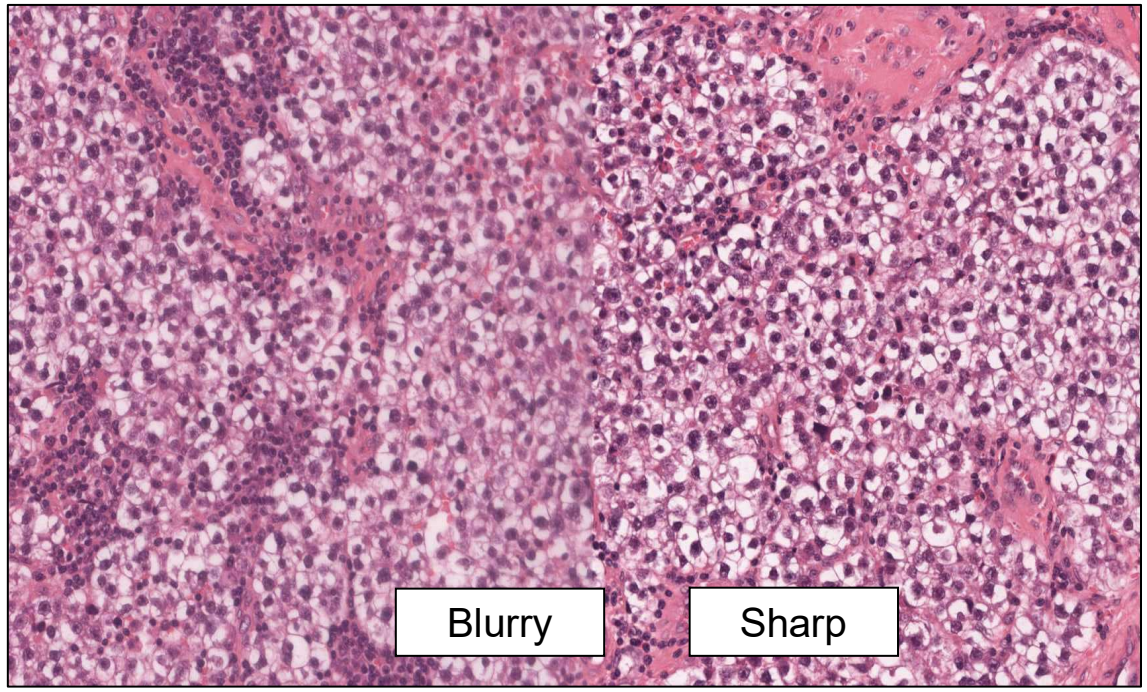



Mid Case System Failure

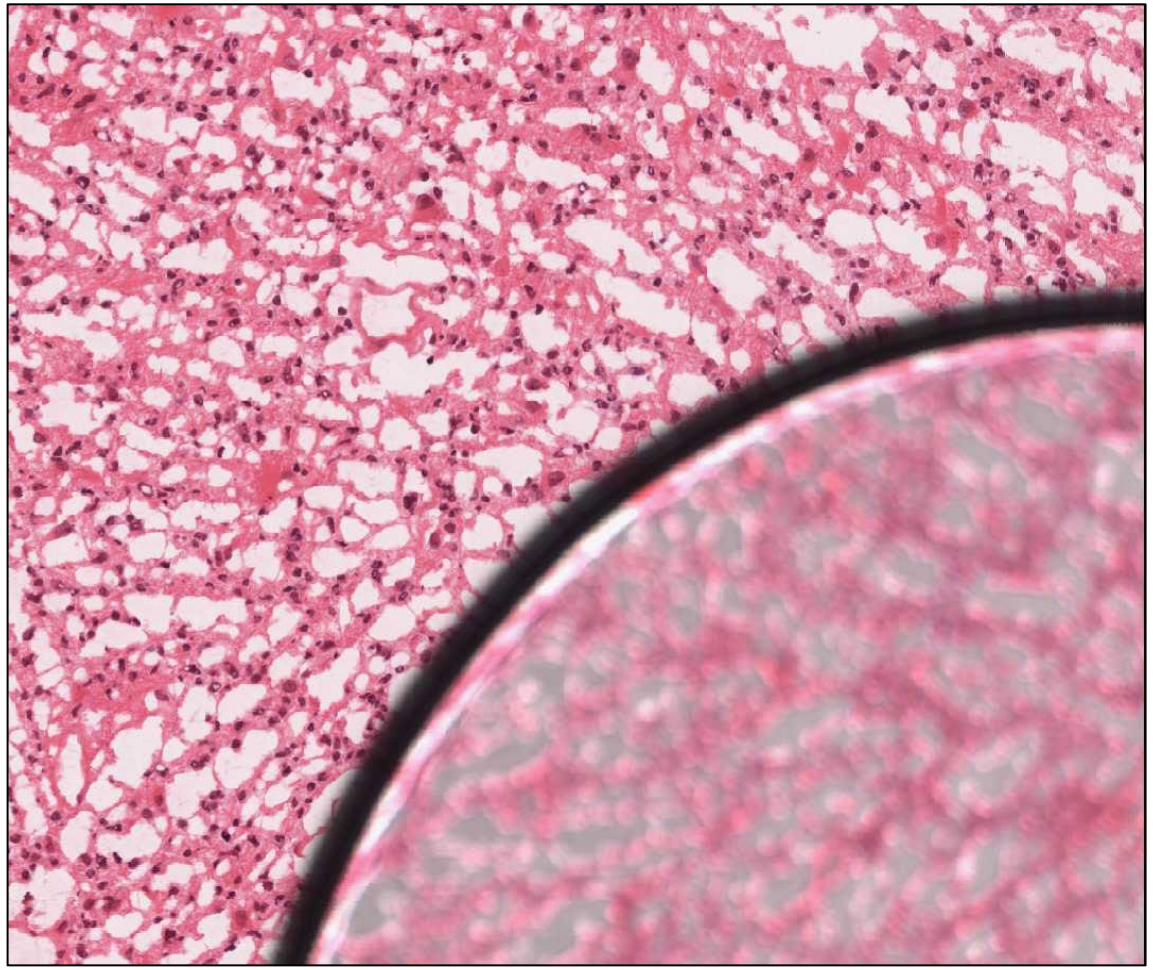
- < 20 episodes in over 6000 frozen sections (0.3% of cases) requiring a pathologist to go to TWH
  - small pale pieces of tissue
  - excess mounting media
  - burned out light bulb in the scanner
  - calibration errors
  - stage homing sensor failure

Lessons Learned: SOP and Histology

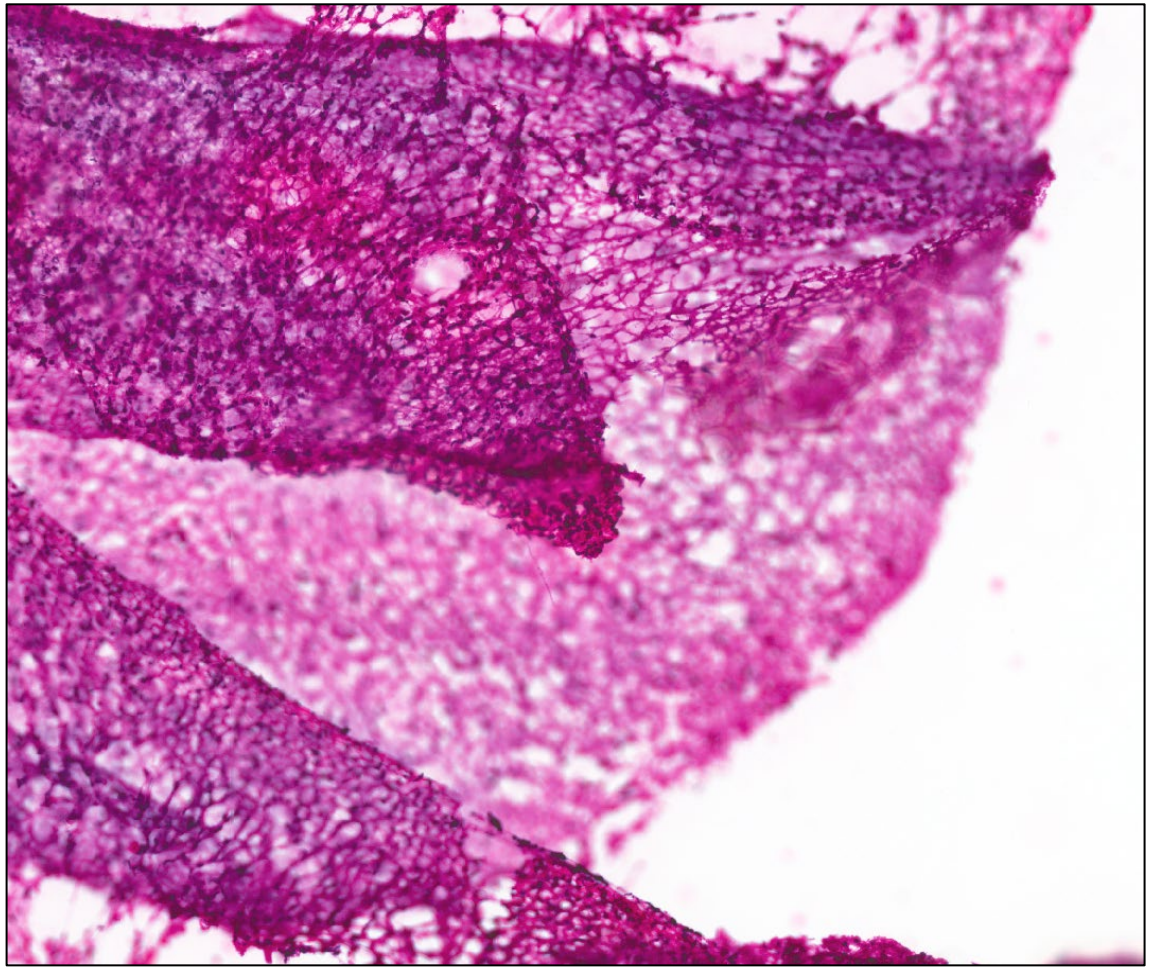
- Test slide scanned every morning
- Unexpected local network failure
- Scanner issues
  - dirty objective
  - background calibration



Air Bubbles



Tissue Folds



Contributing Factors for Success

- **Clearly-defined application**
- **Uncomplicated frozen section workflow**
- **18-month development period**
  - **thorough validation**
  - **time to build confidence/trust and develop a reliable workflow**
- **Team approach**
  - **committed group of pathologists, histotechnolologists/PA's to carry out delegated tasks**
  - **dedicated IT support**
  - **early engagement of TWH surgeons**

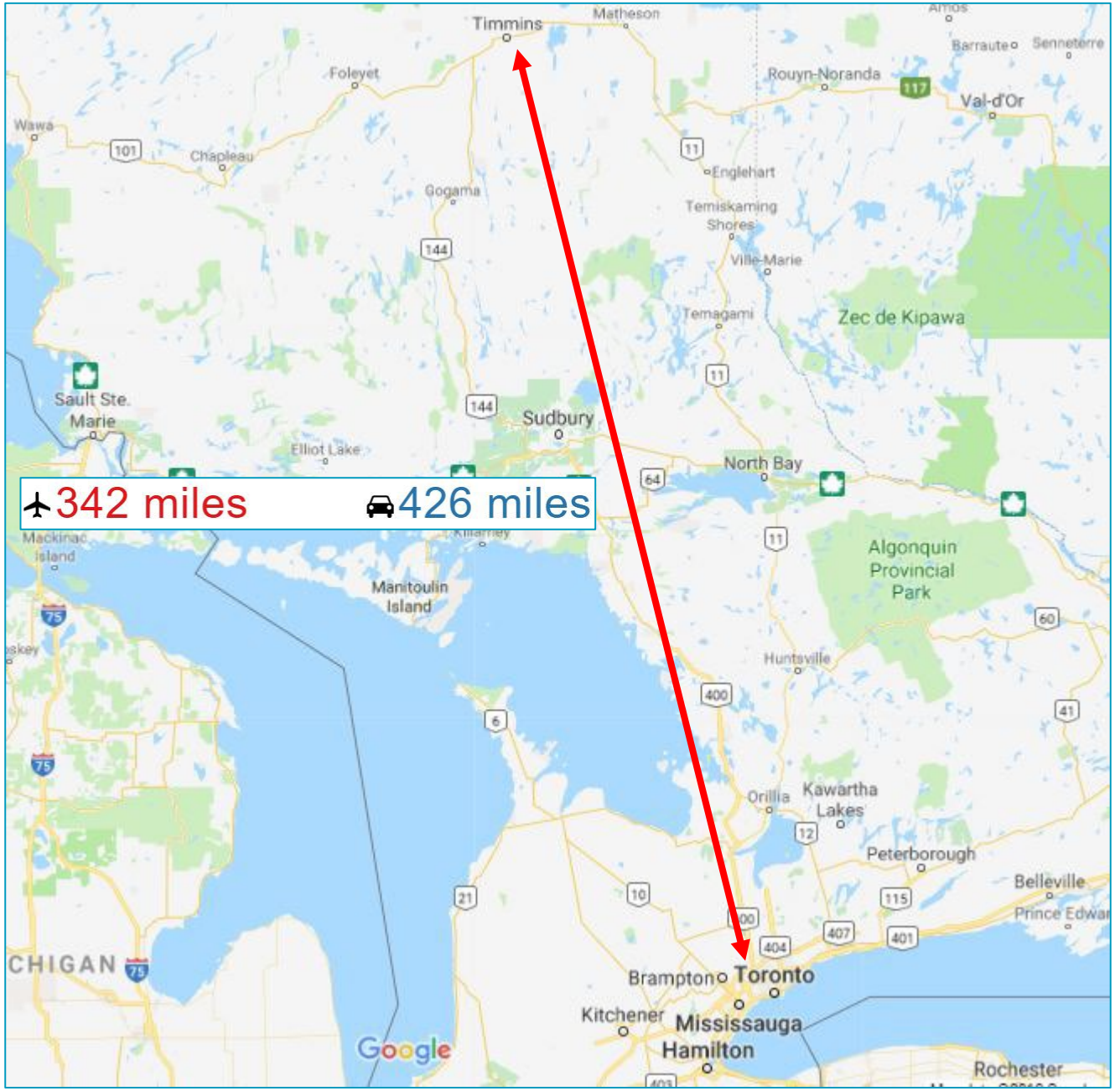
Frozen Sections Originating Outside Toronto

Timmins and District Hospital

Kingston General Hospital

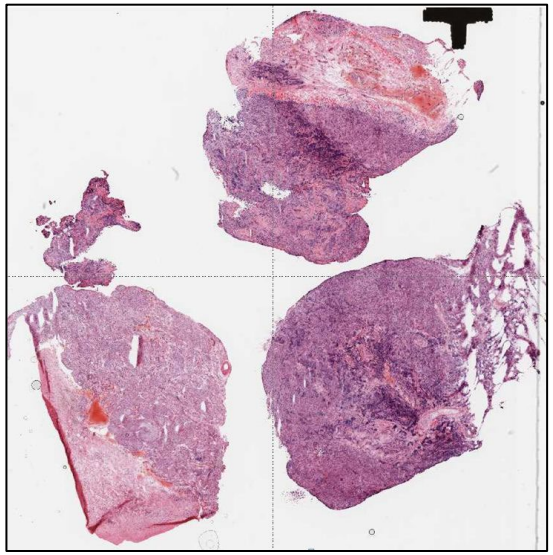
Lakeridge Health

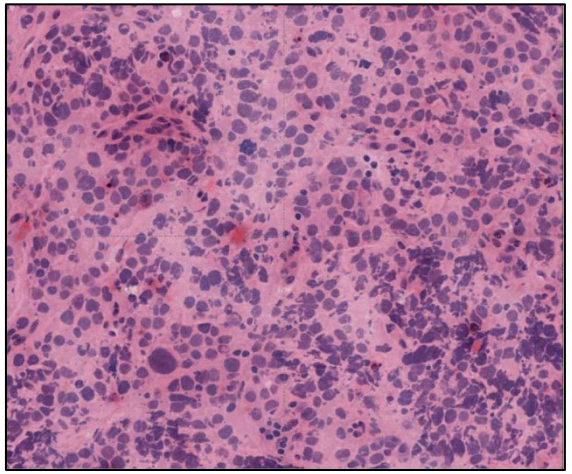
TIMMINS AND DISTRICT HOSPITAL
L'HÔPITAL DE TIMMINS ET DU DISTRICT

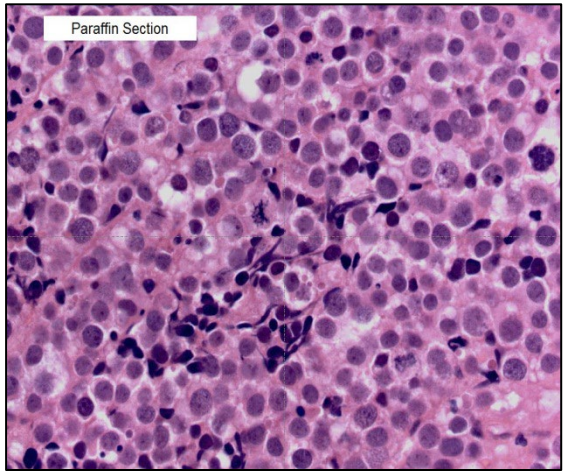


Frozen Section Workflow

- Initiated by a pager (~ 15 minutes before tissue is sent)
- No on-site pathologist
  - report directly to surgeon in the O.R. by telephone
- Pathologist-to-pathologist consultation when pathologist is on site:
  - confirm the on-site pathologist's opinion
  - help with a difficult case

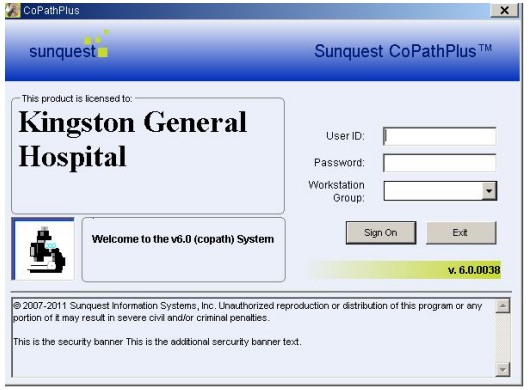


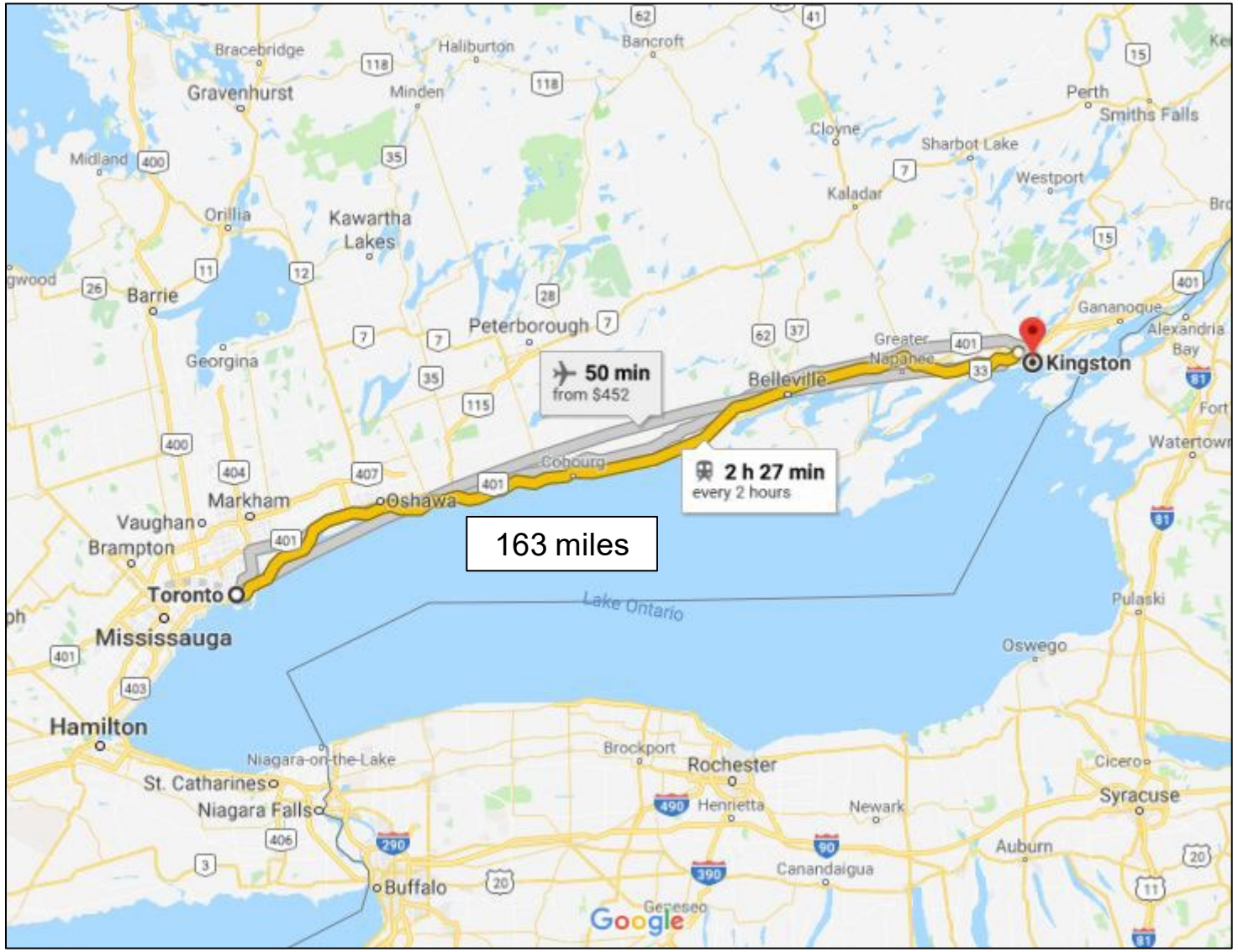




Kingston General Hospital (Queen's University)

- Academic pathology department
- Neuropathology frozen sections (1-5 per week)
- 1 staff neuropathologist to cover all frozen sections
- Need for back-up during vacation, CME leave, etc
- UHN pathologists given limited consulting privileges
  - remote access to EPR/diagnostic imaging
  - remote access to KGH LIS

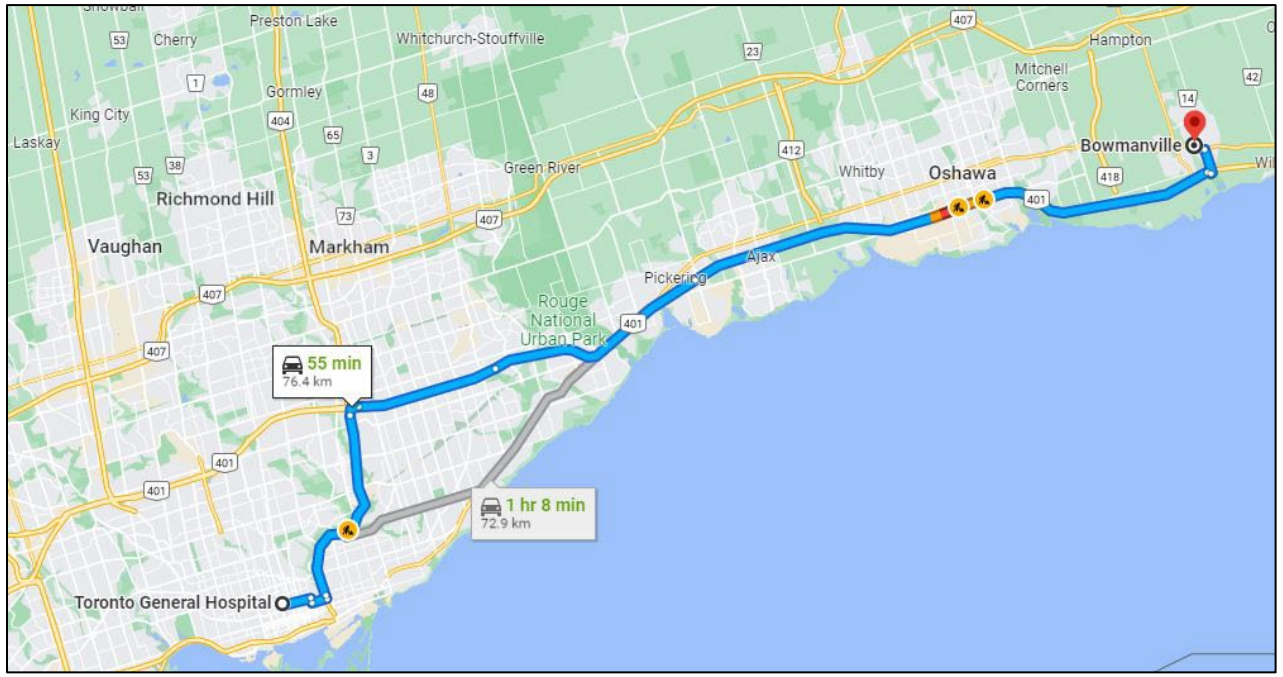


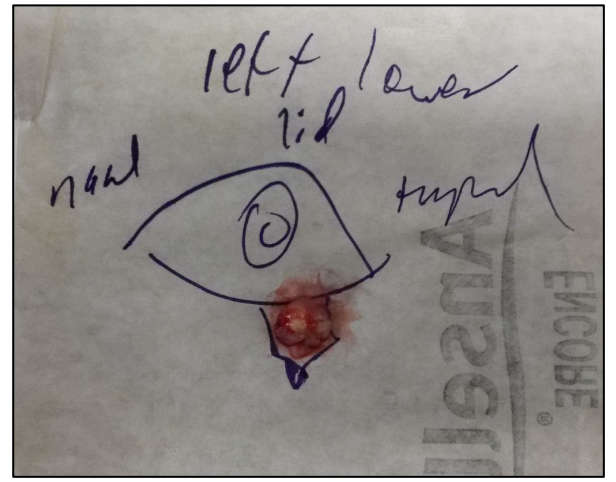


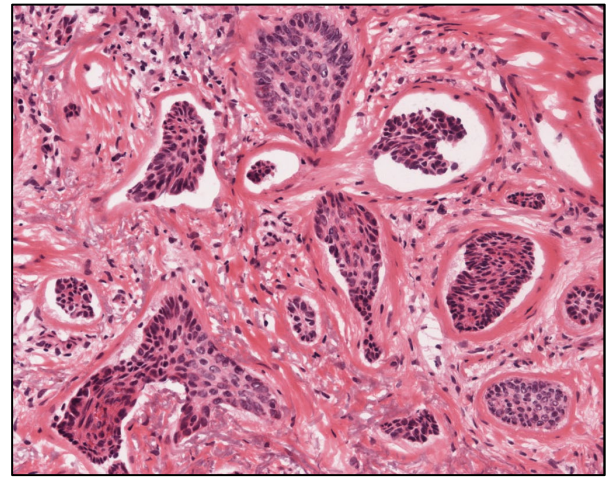
Plan B for System Failure

- Always on-site pathologists at KGH
- No mid-case failures in 8 years

Lakeridge Health







Basal Cell Carcinomas

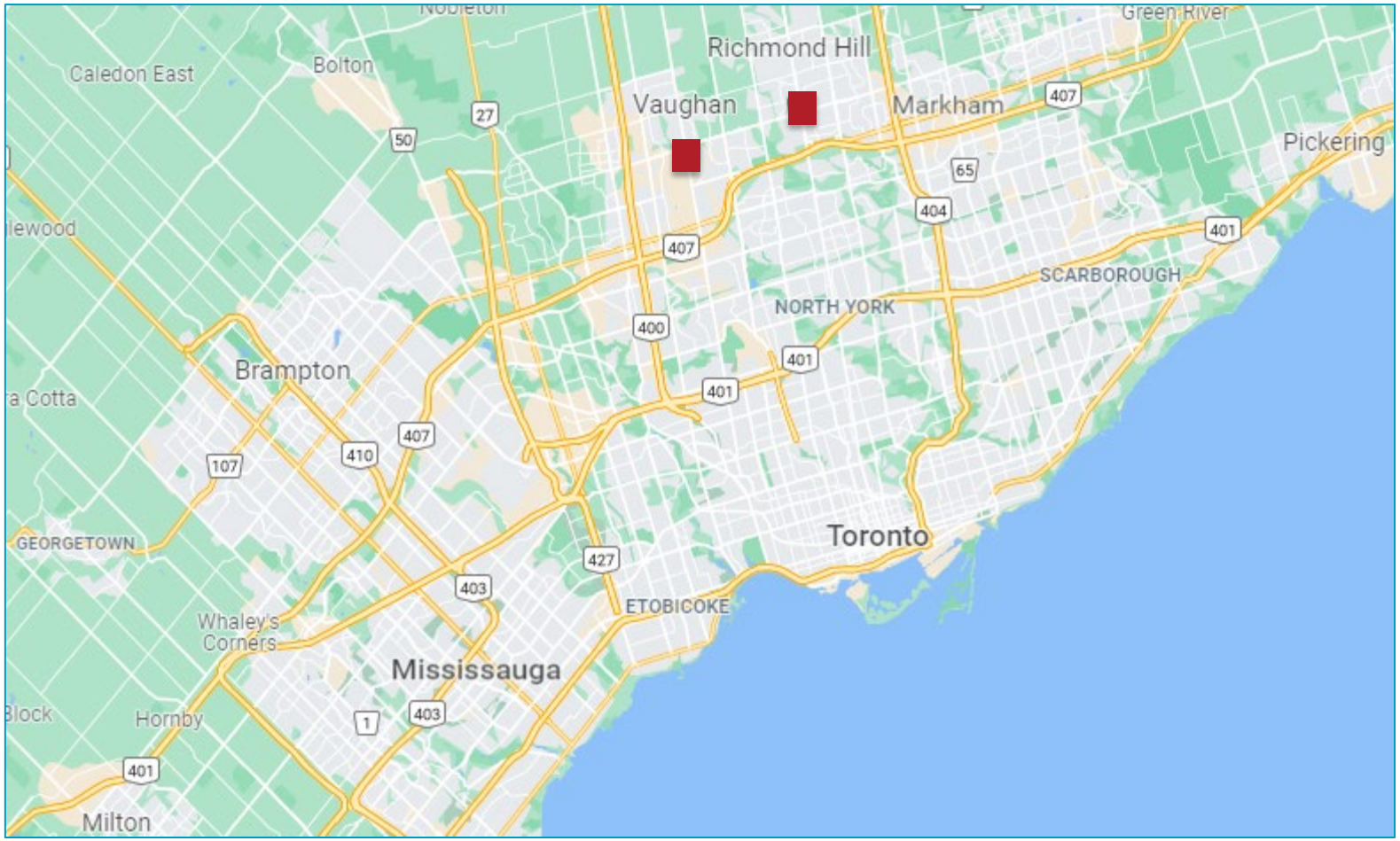
- surgeon-oriented skin ellipses
- Leica/Aperio Scanscope CS
- 20x scans

Mackenzie Health

Mackenzie Richmond Hill Hospital

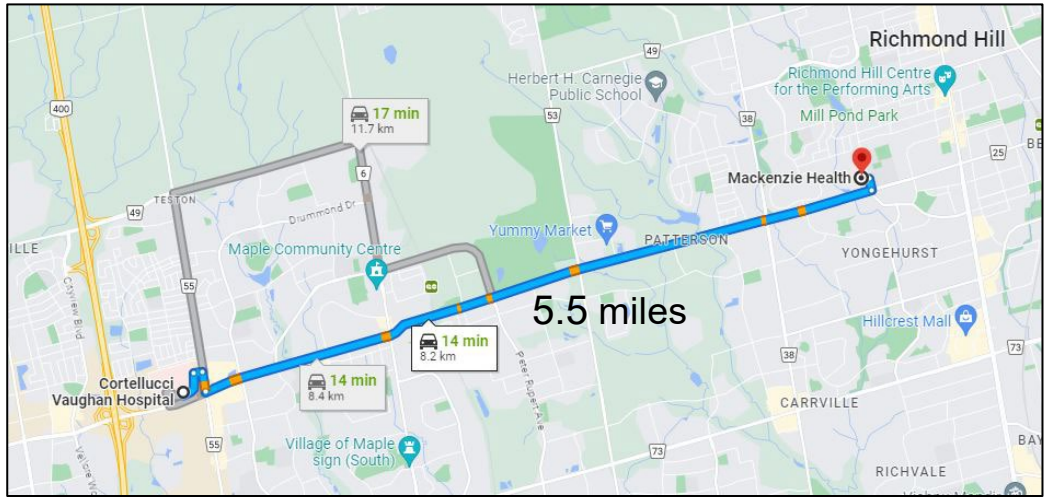
Cortellucci Vaughan Hospital

Mackenzie Health

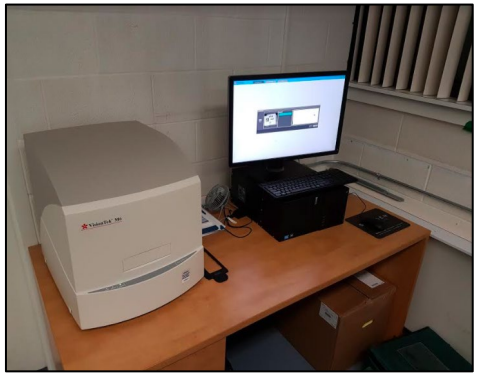


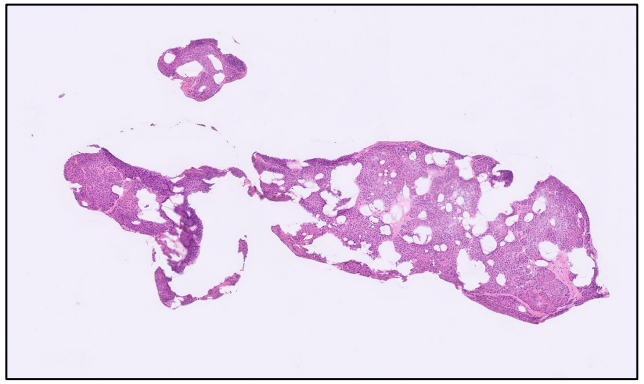
- 2-site community hospital - 682 beds (eventually 900 beds)
- Serving > 0.5 M people
- Mackenzie Richmond Hill Hospital (MRHH) - 1963
- Cortellucci Vaughan Hospital (CVH) - February, 2021 (with the consolidated pathology department).

MRHH Frozen Sections - January 2021-Present

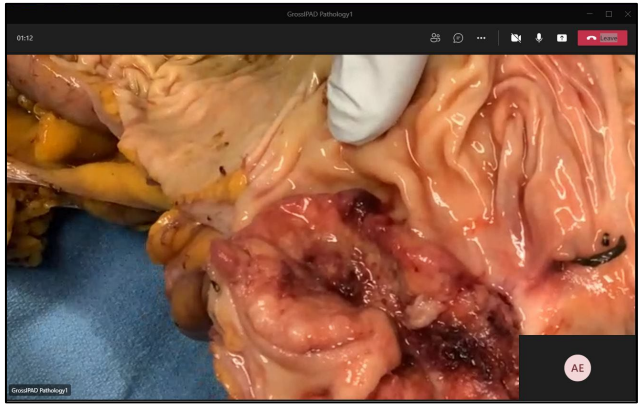


Sakura MRH





- No on-site pathologist
- Pathologist assistants and medical laboratory technologists on-site



Gross Review

- iPad
- MS Teams

Preparation Before Going Live

- ✓ **Training for all users of the system**
- ✓ **Validation - frozen section slides representing mix of cases to be expected**
- ✓ **Finalization of SOP**
  - **workflow and assignment of tasks for processing specimens**
  - **use of high-resolution webcam for gross specimen review**
  - **dry runs to establish TAT benchmarks - 20 minutes (receipt of tissue to diagnosis)**
  - **downtime procedure - pathologist travels to MRH from CVH**
- ✓ ***Engagement of surgical colleagues***

✓ **Completed in 6 weeks prior to go live in January of 2021**

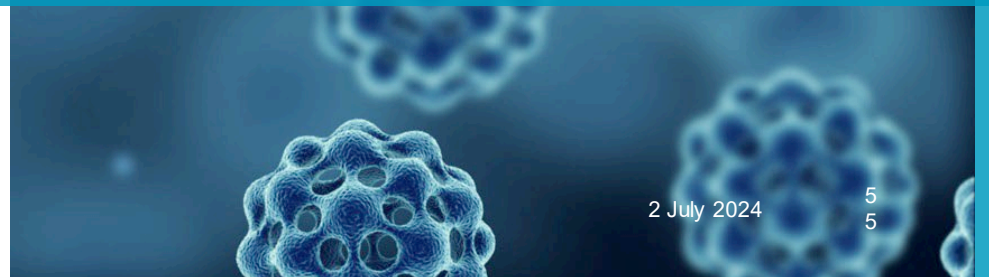
Value of Daily Connectivity Check

IT department made changes to TeamViewer user profiles for all users

- no advance notice was issued
- blocked Sakura access - central password resets required
- IT “unaware” of the frozen section system
- problem discovered through daily system check

Take Home Points

1. Several different digital pathology modalities can be safely used to review frozen sections at remote sites located 1 to over 400 miles away from the reviewing pathologist
2. In addition to validation, the implementation process should include early engagement of surgical colleagues
3. Running daily test slides before frozen sections arrive is essential
4. System failures are rare, however there is an absolute need to have a plan B
5. CAP benchmark TAT's are easily attainable with proper planning



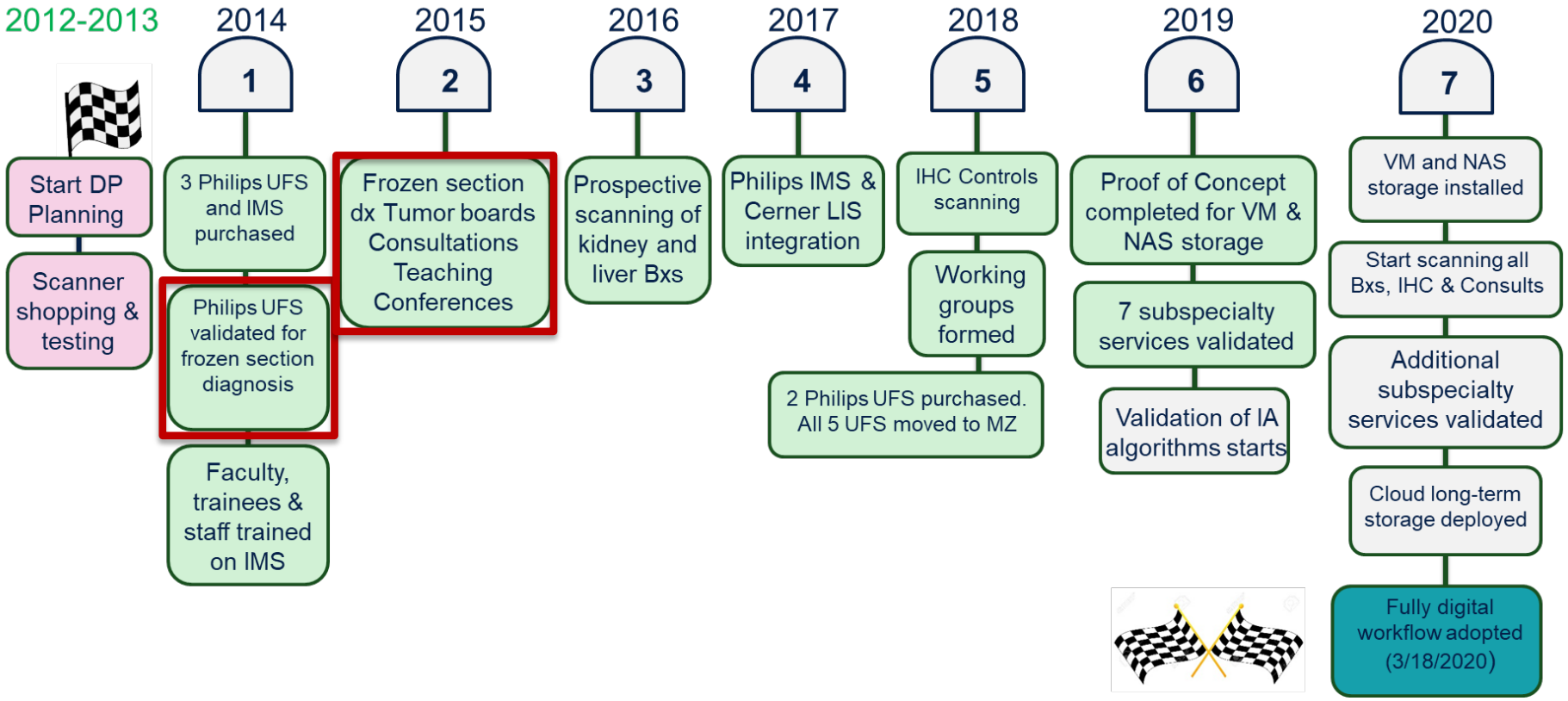
Zoltan G. Laszik, MD, PhD

Dr. Laszik is a Professor of Pathology at the University of California San Francisco. Under his leadership as the Director of Digital Pathology, UCSF deployed a fully digital workflow for primary diagnosis in March 2020. He is also the Director of the Renal Pathology and Electron microscopy services. His research lab is adopting and developing novel tissue interrogation technologies, including multiplexing immunofluorescence, to study various renal and other diseases. He completed his residency training at the University of Oklahoma and 4 years of renal pathology fellowship with Dr. Fred Silva.

Validating WS Digital Imaging for Frozen Section Diagnoses

UCSF Experience, 2014-2024

The digital journey at UCSF
From start to finish



Why go digital?

Background

- Whole-slide scanners introduced in late 1990s
- Interest in whole-slide digital imaging (WSDI) for:
  - Routine surgical pathology/Cytopathology
  - Consultation by telepathology
  - Computational pathology
  - Frozen section diagnosis
- WSDI has high *diagnostic accuracy* and concordance with LM

Study aims

- To validate the Philips Ultra-Fast Scanner (UFS) and Image Management System (IMS) for routine frozen section diagnosis

CAP guidelines for validation of WSDI for diagnostic Use

- Include at least 60 routine cases
- Confirm that all material present on a glass slide to be scanned is included in the digital image
- Demonstrate that the WSDI system produces acceptable digital slides for diagnostic interpretation
- Examine *intra*-observer diagnostic concordance between digitized and glass slides, viewed at least 2 weeks apart

Pantanowitz *et. al. Arch Pathol Lab Med*. 2013;137:1710–1722

Historical data on digital interpretation of frozen sections

Reference	Country	Type of Study	Scanner	Size	Concordance	Accuracy
Tsuchihashi et. al., Diagn Pathol, 2008	Japan	Prospective pilot	VASSALO by CLARO, Inc.	15 cases	100%	Not reported
Slodkowska et. al, Folia Histochem, 2009	Poland	Prospective *inter*-observer	Aperio Scan Scope	33 FSs	100%	100%
Evans et. al., Hum Pathol,2009	Canada	Retrospective *Inter*-observer	Aperio Scan Scope CS	633 FSs	Not reported	100%
Fallon et. al, Arch Pathol Lab Med, 2010	USA	Retrospective *inter*-observer	MIRAX Desk, Carl Zeiss	71 FSs	Not reported	100%
Ribback et. al., Pathol Res Pract, 2014.	Germany	Retrospective *Inter-observer*	MIRAX Desk, Carl Zeiss	1204 FSs	Not reported	98.5%

Philips Ultra Fast Scanner and Image Management System

- Average scanning time: 2 min for 10 x 13 mm tissue size
- 0.25 µm/pixel resolution
- Easy 2-step‘load and scan’ operation
- 1 Gb/s shared bandwidth between sites

Specific study aims

- Phase 1 (QC): To assess whole-slide FS digital image quality, rate of image flaws, and root causes of flaws
- Phase 2: To examine intra-observer diagnostic concordance between digitized and glass slides

Phase 1: Digital image quality control

- 2158 frozen sections from 541 consecutive cases (890 parts (“cases”]) (years 2012-2013), including a variety of tissue types
- WSDIs (Philips, UFS) evaluated by a single pathologist for diagnostic image quality
- Characteristics and root causes of image flaws classified
- Suboptimal images with a potential to impede the diagnosis rescanned and re-evaluated

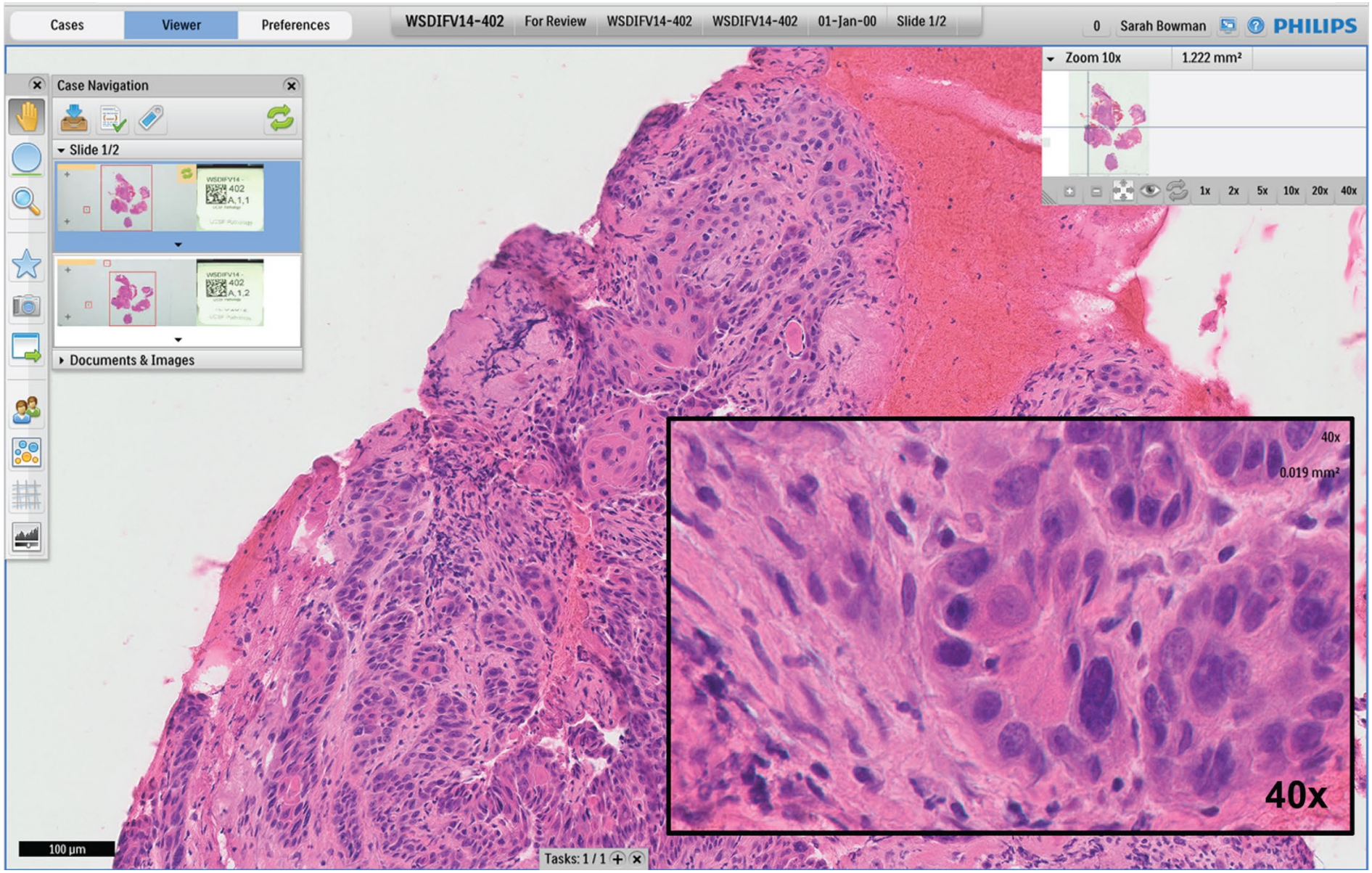
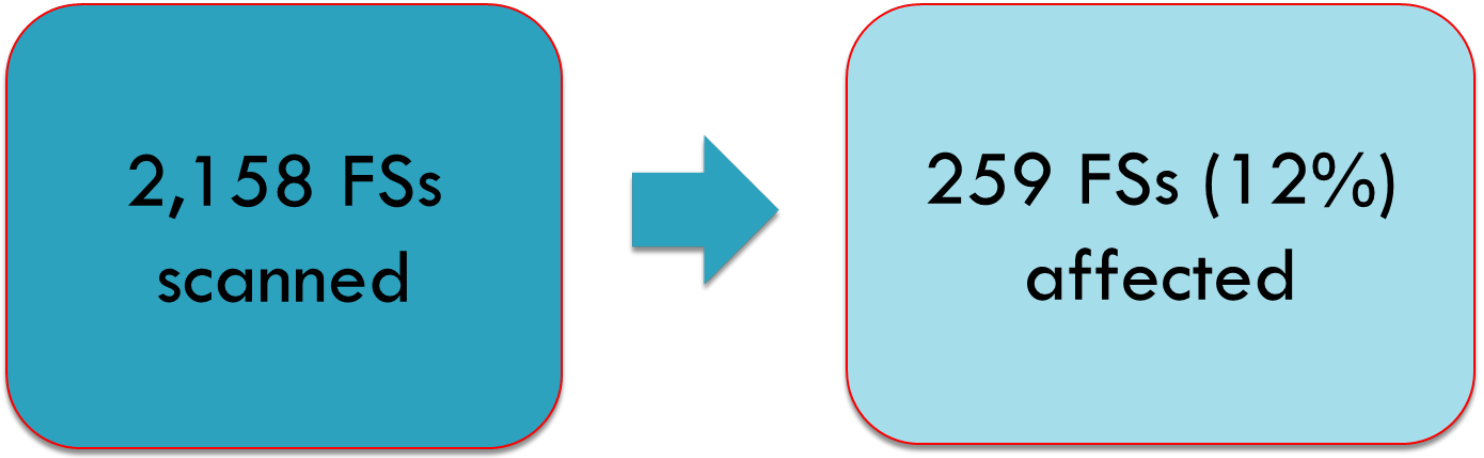
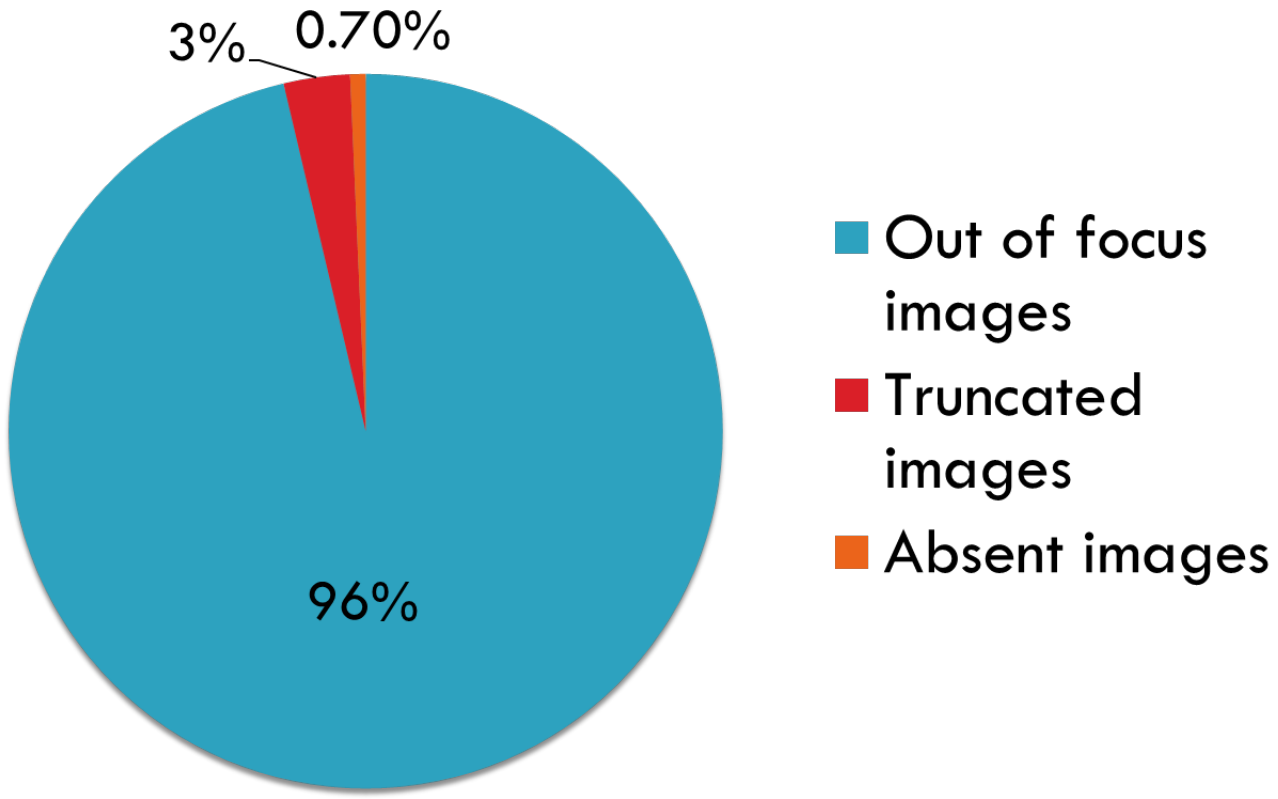


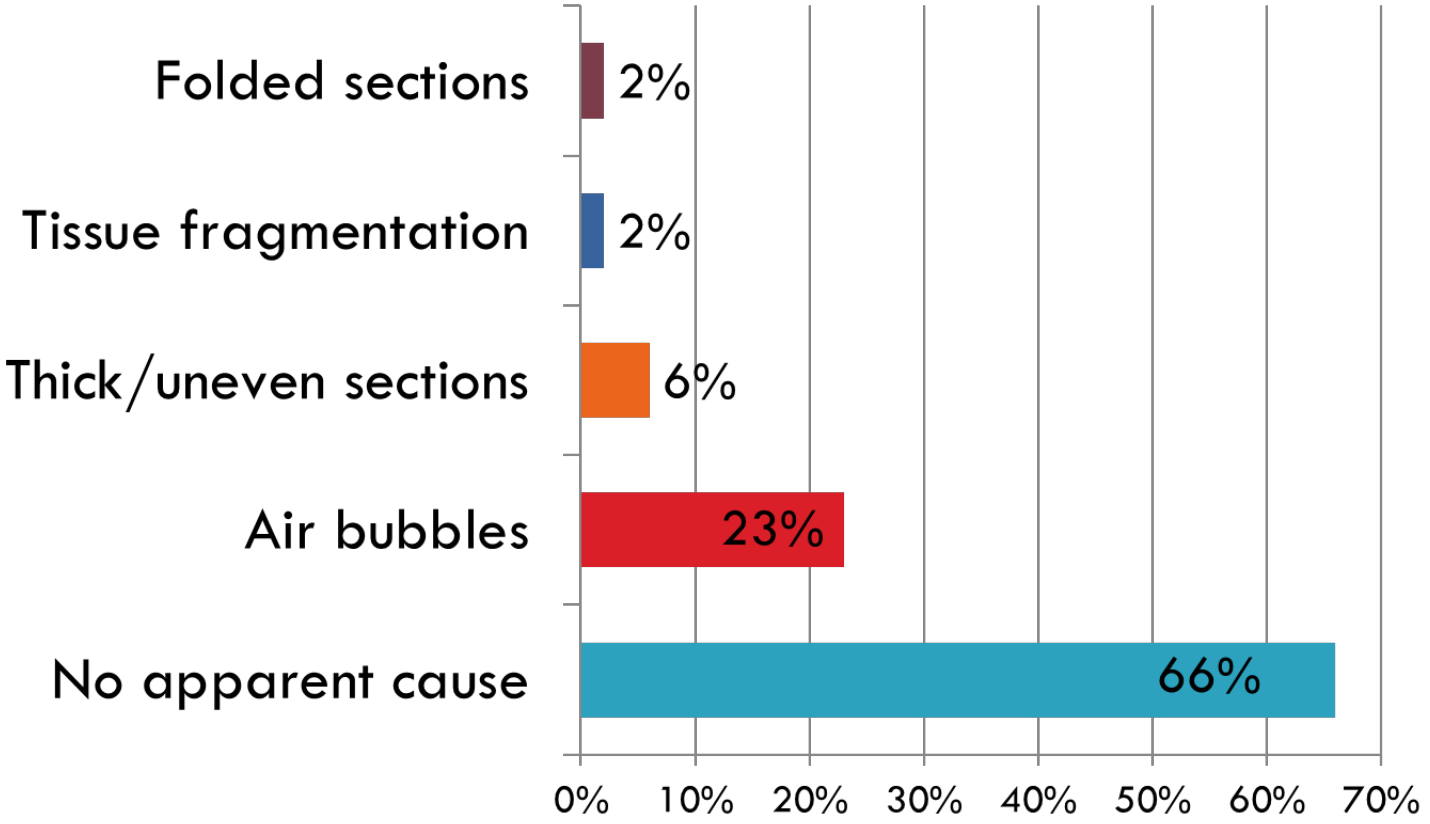
Image flaw rate



Results: What were the types of scanned image flaws?

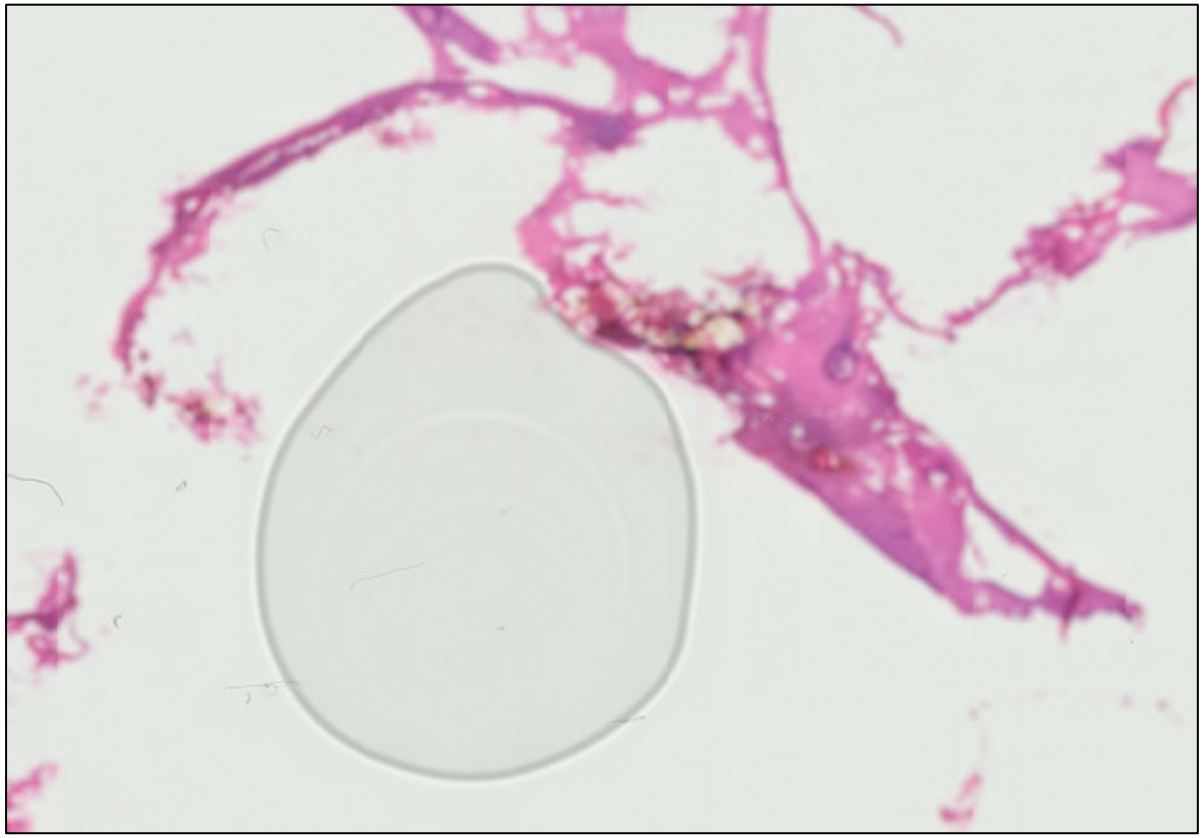


Out-of-focus images: Root causes



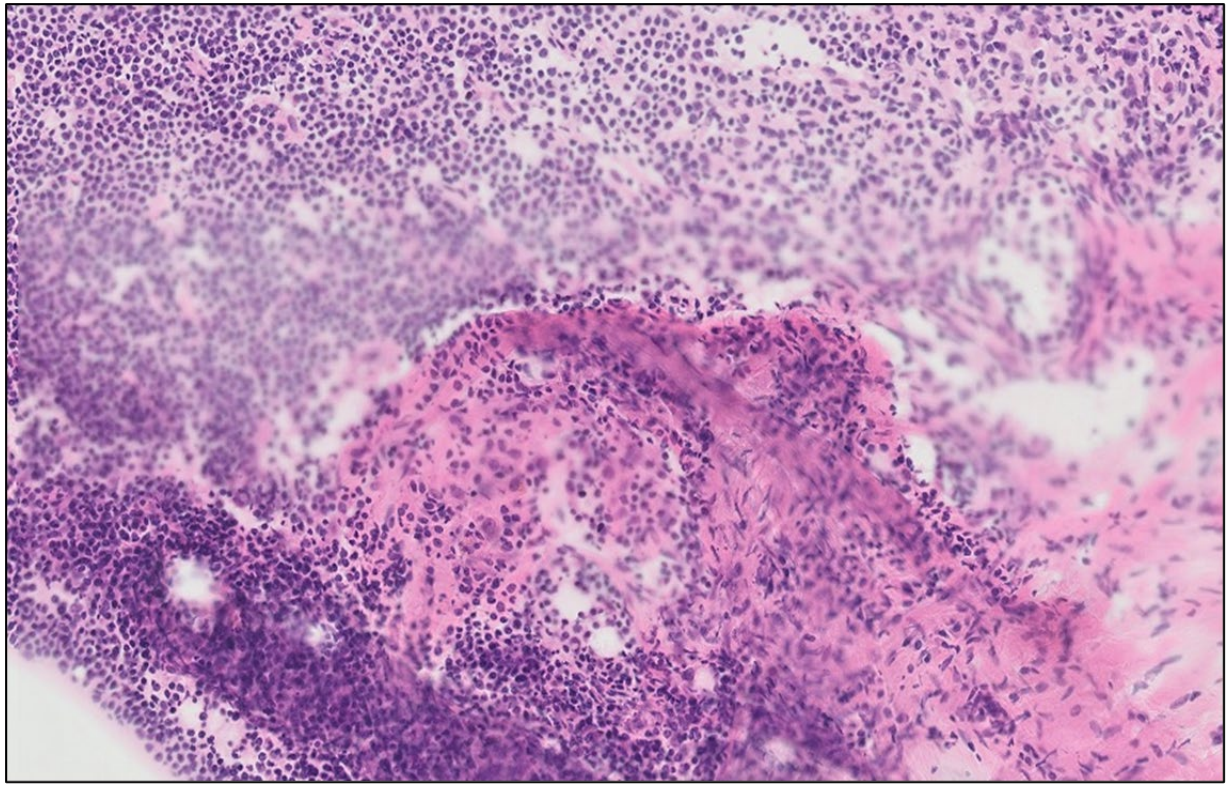
Out-of-focus images: Root causes

- Air bubbles

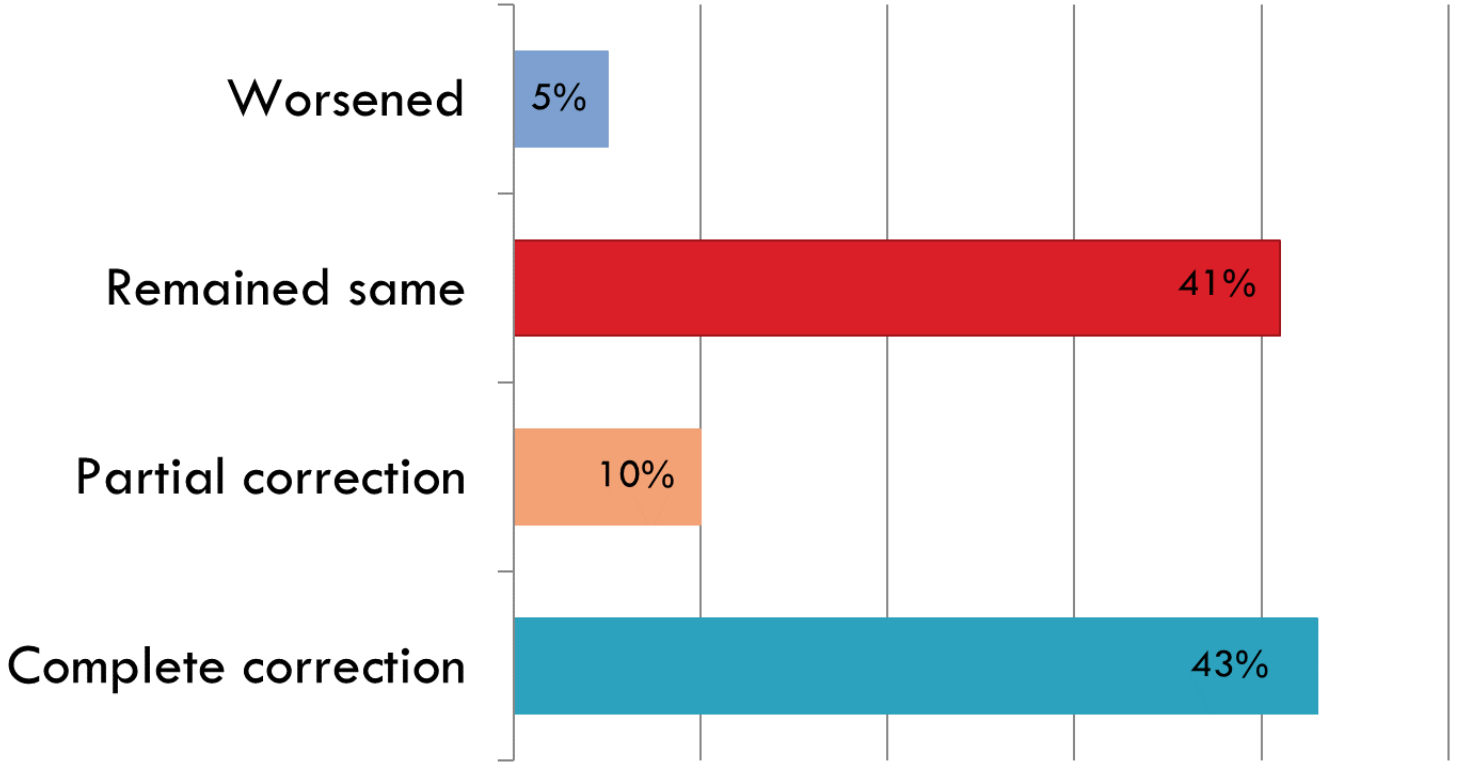


Out-of-focus images: Root causes

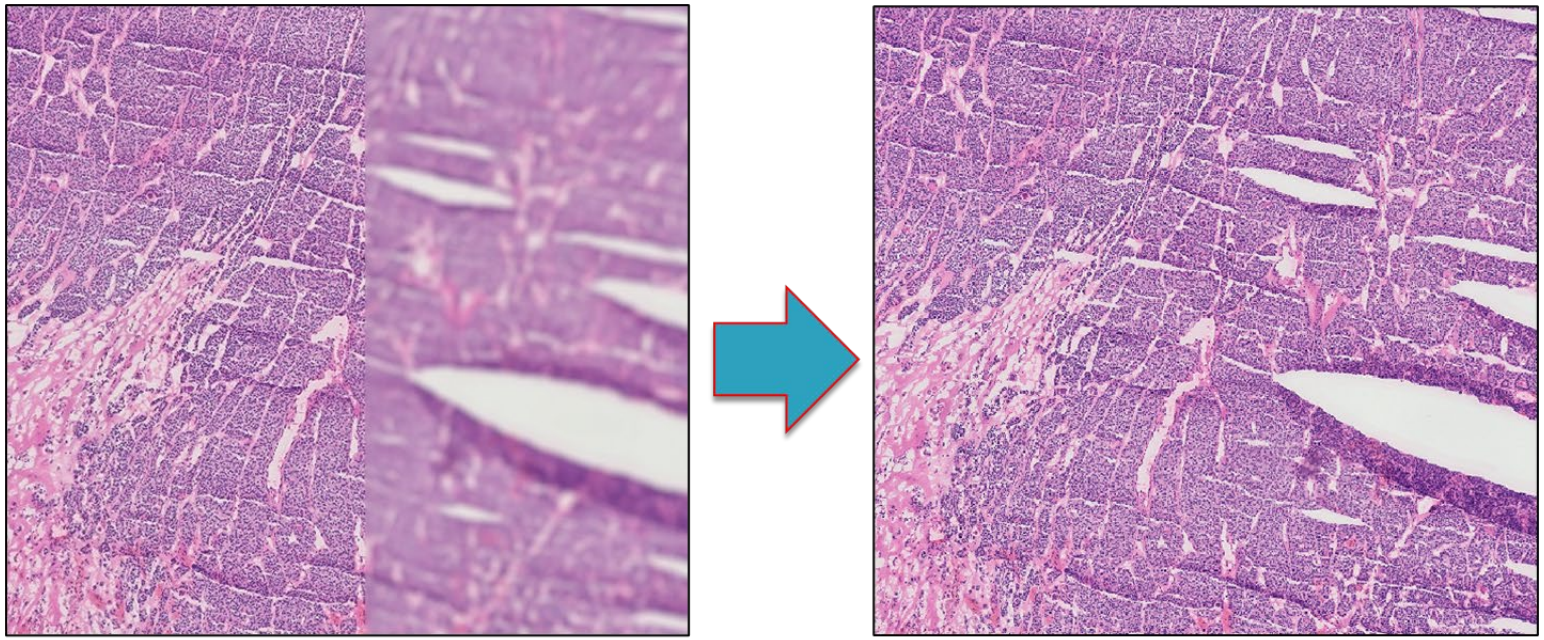
- Thick/ uneven sections



For how many slides did rescanning correct the flaw?



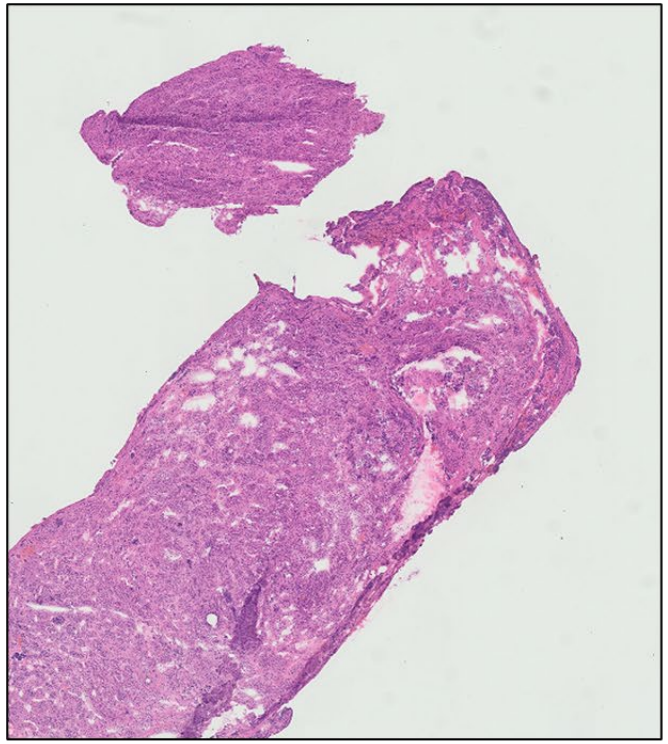
Scanned image flaws: Examples



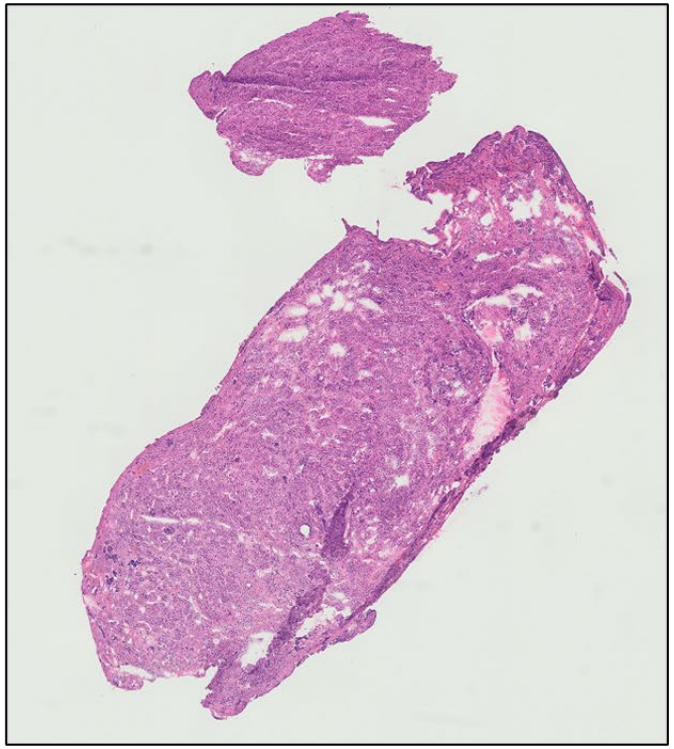
Out-of-focus image

Rescanned image

Scanned image flaws: Examples



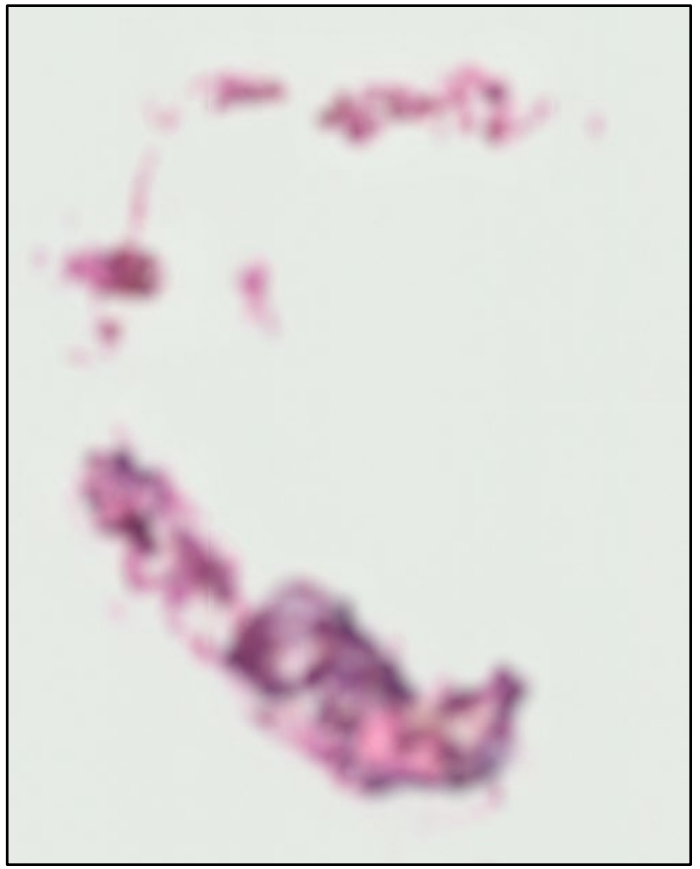
Truncated image



Rescanned image

How many cases were non-diagnostic due to image flaws?

- 22 slides (out of 2158 sides) were non-diagnostic due to image flaws (~1.0% of all FSs)
- *However,* only 1 case of 890 cases was nondiagnostic (0.1% of all cases)



Summary, phase 1

- 88% of slides had no image flaws upon initial scanning
- Image flaws did NOT render the slide non-diagnostic in overwhelming majority (99%) of cases
- Diagnostic WSDIs require high-quality frozen section slide preparation

Study aims

- Phase 1 (QC): To assess whole-slide FS digital image quality, rate of image flaws, and root causes of flaws
- Phase 2: To examine *intra*-observer diagnostic concordance between digitized and glass slides

Hypothesis (concordance design)

- Interpretation of FSs using whole slide digital images (WSDI) by Philips' UFS scanner is comparable to conventional LM interpretation using glass slides

Specific aims, Phase 2

- To show that WSDI interpretation of FSs is comparable to that of conventional glass slide interpretation by demonstrating a high degree of concordance between diagnoses made on digital versus glass slides
- To assess potential minor and major discrepancies between FS diagnoses based on conventional glass slide versus WSDI interpretation

De-identification of slides, coding and scanning

- Each case was de-identified and assigned a unique study identification number carried on a bar code
- The slides with the unique barcodes were scanned in and stored on the Philips server
- After initial QC, the assigned cases with the digital slides were made available on the network for the pathologists to evaluate

Study design, Phase 2

- 31 participating pathologists from UCSF
  - Surgical pathologists (n=26)
  - Neuropathologists (n=5)
- 889 cases enrolled (~30 cases assigned to each pathologist)

Cases enrolled for the FS validation study

Organ	# of cases (511 cases; 890 parts)	% of cases
Breast	31	5.7
Bone and soft tissue	63	11.6
Gynecologic	8	1.5
Head and neck	58	10.7
Hematology	20	3.7
Kidney and male genitalia	8	1.5
Liver and gallbladder	24	4.4
Upper GI	18	3.3
Lower GI	8	1.5
Lung	40	7.4
Prostate	10	1.8
Pancreas	18	3.3
Skin	9	1.7
Thymus and salivary gland	64	11.8
Neuropathology	132	24.4

Study design

Phase 2, digital arm

- WSDIs reviewed by pathologists at one of the 2 designated Philips workstations using HR monitors
- Relevant clinical and “gross” information provided to emulate real-world clinical environment
- The pathologists were asked to record the diagnoses and the time spent with each slide/case
- Philips workstation/software training for each pathologist participating in the study was conducted prior to their first session evaluating the WSDIs

Study design

Phase 2, glass slide arm

- Two to six weeks after completing the digital review
- Relevant clinical and “gross” information provided to emulate real-world clinical environment
- The pathologists were asked to record the diagnoses and also the time spent with each slide/case

Data collection, analysis

- Diagnoses (WSDI and LM) were entered into a database
- The concordance rate between the two diagnostic modalities calculated
- Discrepancies between WSDI and LM diagnoses assessed and classified according to the criteria from the Association of Directors of Anatomic and Surgical Pathology that have been adopted by CAP for laboratory accreditation purposes

Diagnostic Discrepancies

- WSDI showed discrepancies with correct Gold Standard diagnosis in 31 cases out of 886 (3.4%)
  - 11 major (1.2%) and 20 minor (2.2%)
- Upon review by an expert panel, all 31 cases were diagnostic on WSDIs
- 4 cases with discrepant diagnoses were excluded from the analysis (the Gold Standard diagnosis or both Gold Standard and WSDI diagnoses were incorrect)

Examples of major diagnostic discrepancies

Organ	WSDI diagnosis	GS diagnosis	Nature of discordance
Head and neck	Neoplastic	Benign resp. mucosa	Overcall
Lung	Squamous cell ca.	Reactive mesothelial hyperplasia	Overcall
Thyroid/parathyroid	Probable thyroid ca.	Parathyroid	Overcall
Pancreas	Adenocarcinoma	Chronic pancreatitis	Overcall
Pancreas	Adenocarcinoma	Chronic pancreatitis	Overcall
Bladder	Focal ca *in situ*	No tumor	Overcall
Lung	Atypical glands	Adenocarcinoma	Undercall
Bladder	Non-diagnostic	*In-situ* carcinoma	Undercall
Breast/lymph node	Benign lymph node	Microscopic tumor focus, < 0.5 mm	Undercall
Lung	Spindle cell lesion; defer to IHC	Malignant spindle cell tumor	Undercall
Brain	Fibrous tissue	Recurrent glioma	Undercall

Hypothesis (non-inferiority study design)

- The difference between (1) historical discrepancy rates for conventional LM FS interpretation (historical control data) and (2) actual discrepancy rates for WSDI technology (i.e., actual discrepancy rates for FS diagnosis by WSDI and "gold standard" diagnosis by LM in study population) (control accuracy rate minus WSDI accuracy rate), the amount by which the control is superior to WSDI, is less than the pre-specified non-inferiority margin (WSDI is not inferior to conventional LM interpretation of FSs)

28 cases flagged for the 890 study cases for the original GS FS reading

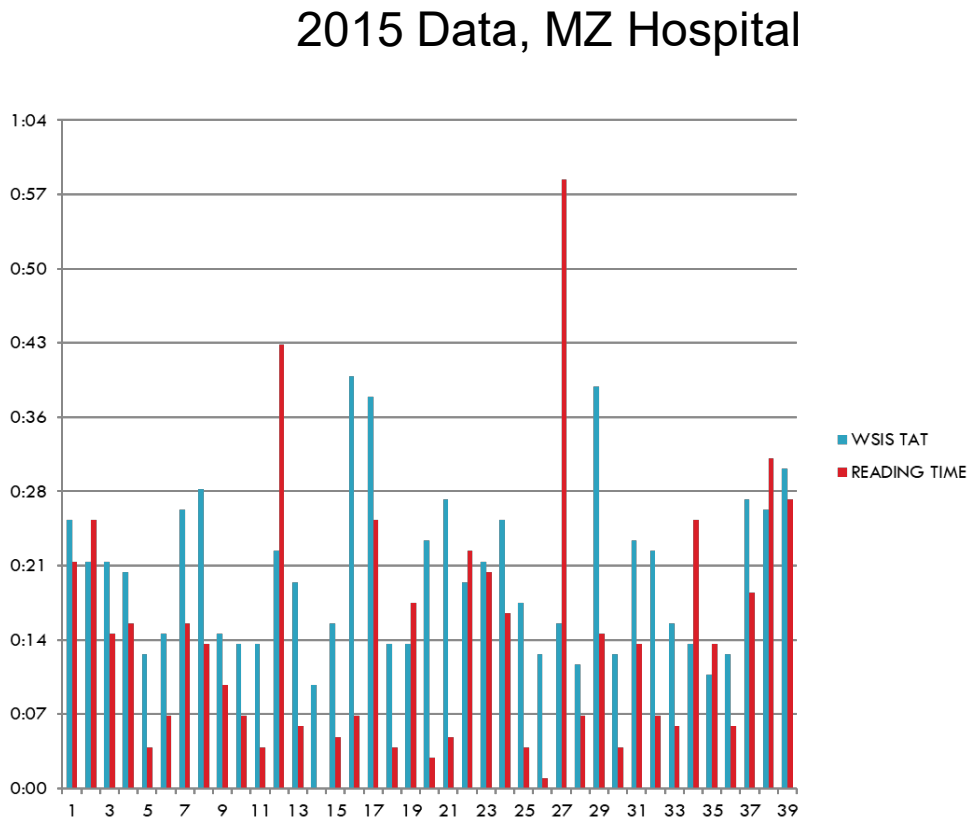
- The number of flagged cases (28/890) for the original GS FS diagnosis in the study set is similar to that of combined major and minor diagnostic discrepancies for the digital reading (31/886)
- Number of major diagnostic discrepancies due to diagnostic misinterpretation:
  - 6/890 (0.67%) for the GS FS reading
  - 11/886 (1.2%) for the WSDI readings

Summary, Phase 2

- WSDI is applicable for frozen section diagnosis (diagnostic in 99.8% cases)
- WSDI had discrepancies with correct glass-slide diagnosis in 31 (11 major, 20 minor) cases, albeit the scanned images were of diagnostic quality
- WSDI frozen section service deployed in 2014 in 1 hospital (MZ)

Post-implementation WSDI FS TATs comparable to that of LM FS TATs

- WSDI TATs comparable to that of LM with a few outliers



Operational challenges with WSDI for routine FS service

- Multiple part FS cases with a large number of slides
- Multiple “conventional” (GS) and WSDI FS cases processed parallel

Post-implementation, evolution

2014-2018	2018-2022	2022-2024
	 + 	 +  
Philips UFS	Philips UFS Microscan	Philips UFS Motic Microscan as backup

Questions?

Thank You

The DCPC will be producing more digital pathology educational content in 2024.

- **In addition to webinars, the committee will produce podcasts on digital pathology implementation and create a section for frequently asked questions (FAQ) on digital pathology for our updated and enriched website.**
  - **DCPC Website**

We are excited to announce that we are updating the Digital Pathology Resource Guide and we invite you to be part of this collaborative effort. Your insights and contributions are valuable to us. Please reach out if you are interested in assisting with this effort.

To become a DCPC member, please apply during the upcoming committee appointment cycle.

COLLEGE of AMERICAN PATHOLOGISTS