

Digital Pathology Workflow/System at an Academic Medical Center

Douglas J. Hartman MD

October 15, 2018

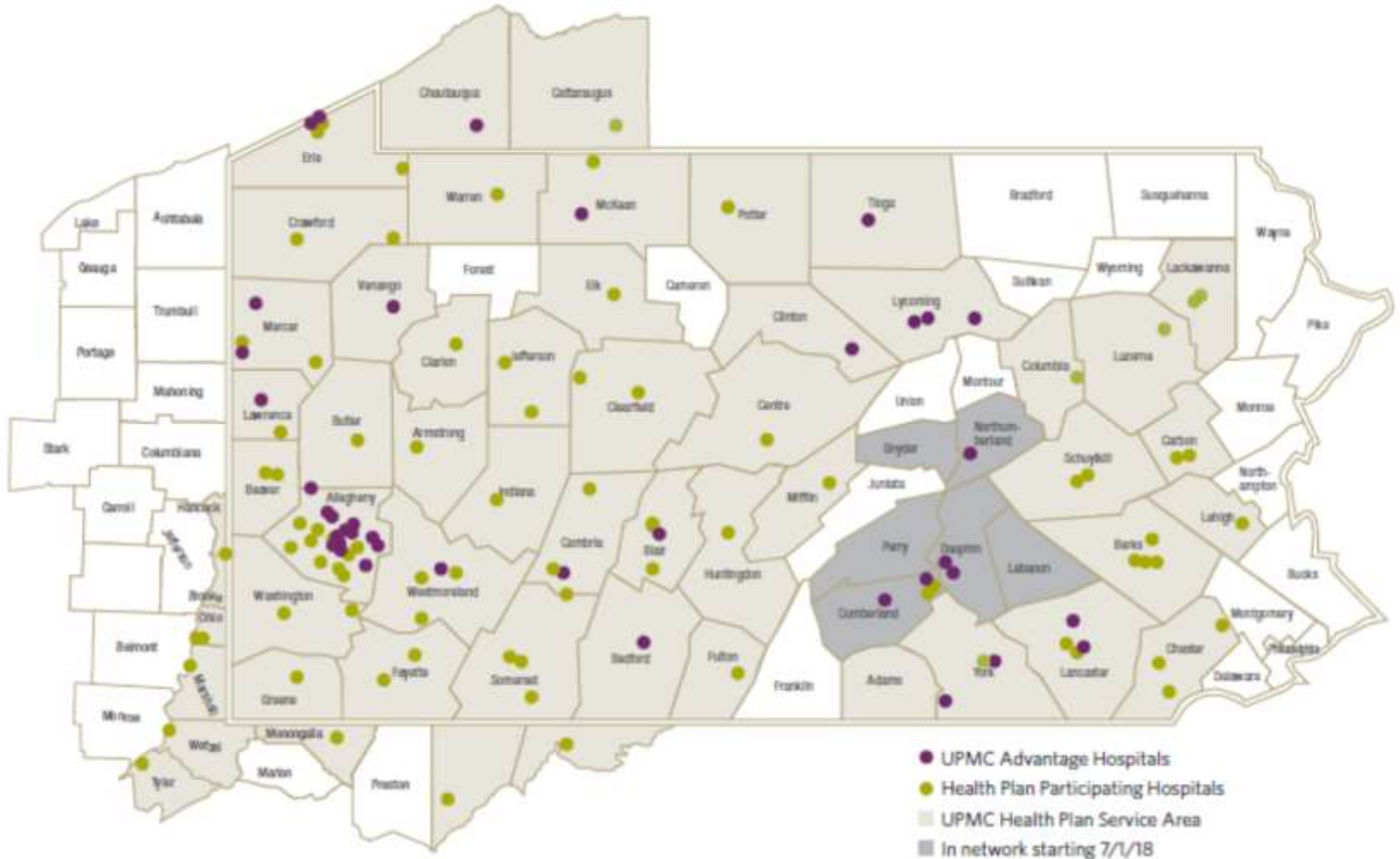
Objectives

- Describe the use of digital pathology within our hospital – prior implementations and current uses
- Describe the use cases that we have deployed
- Describe our future development items





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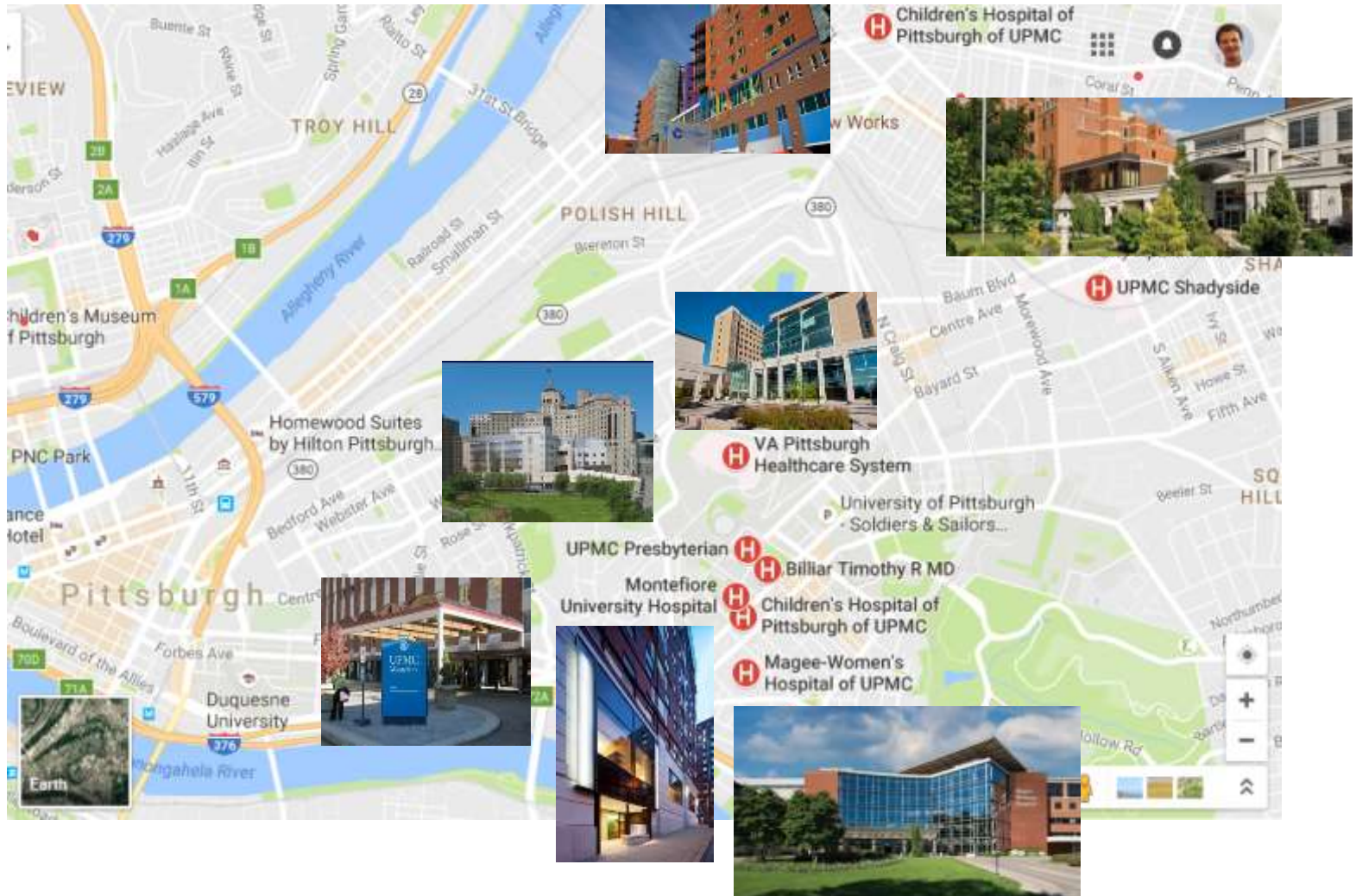
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Academic Hospitals - Subspecialty



Telepathology evolution

Static

Store & Forward
Still Images



Dynamic

Remote Microscopy

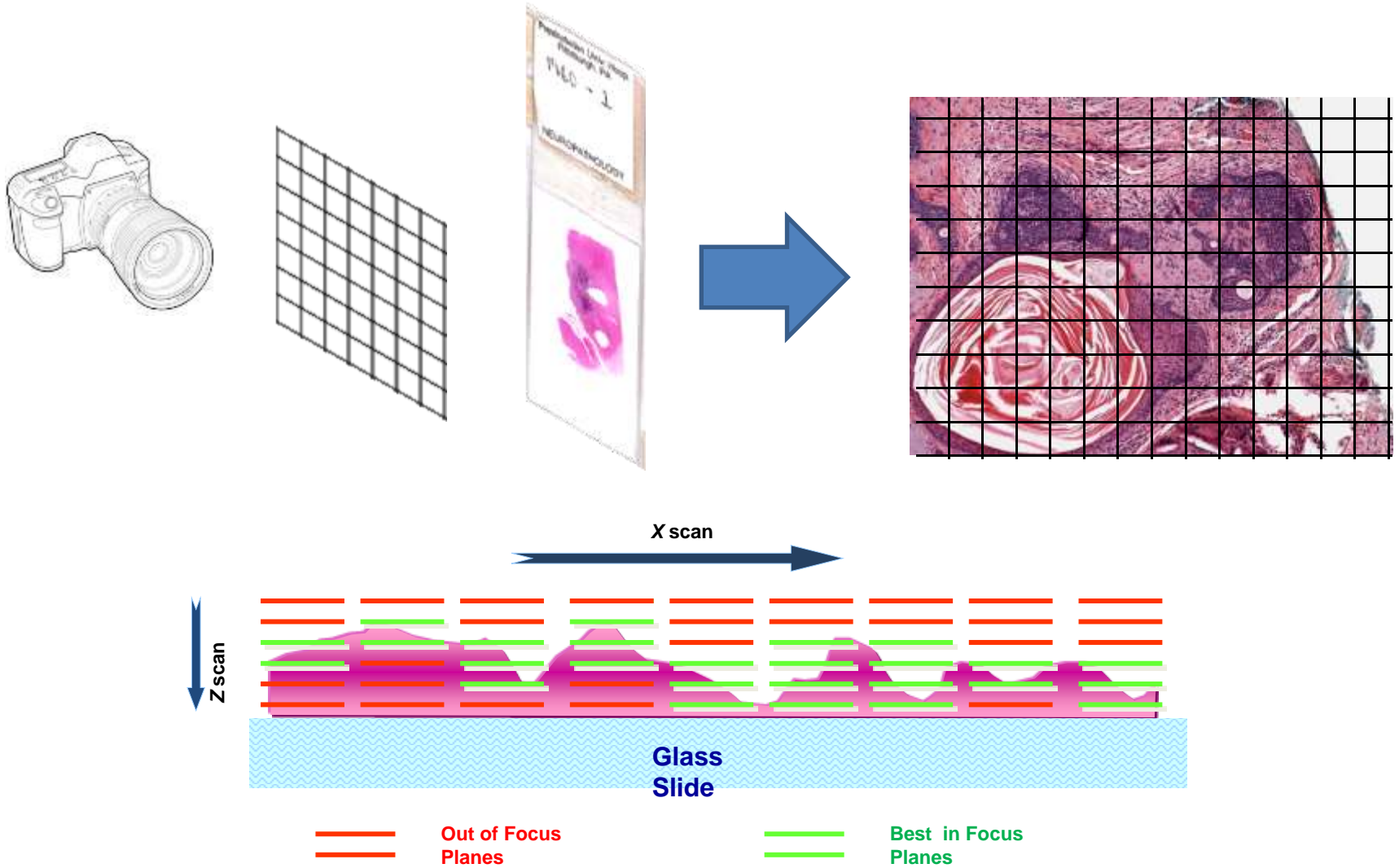


WSI

Whole Slide Imaging



What is a Whole Slide Image?



Whole Slide Imaging

ADVANTAGES

- Immediate Access
- Unbound by Location
- Workflow Automation
- Review by multiple users
- Area tracking
- CAD & added value SW

DISADVANTAGES

- Expensive
- Acquisition speed
- Image size and Storage
- Limited interoperability
- Workflow changes
- Additional staff

Background

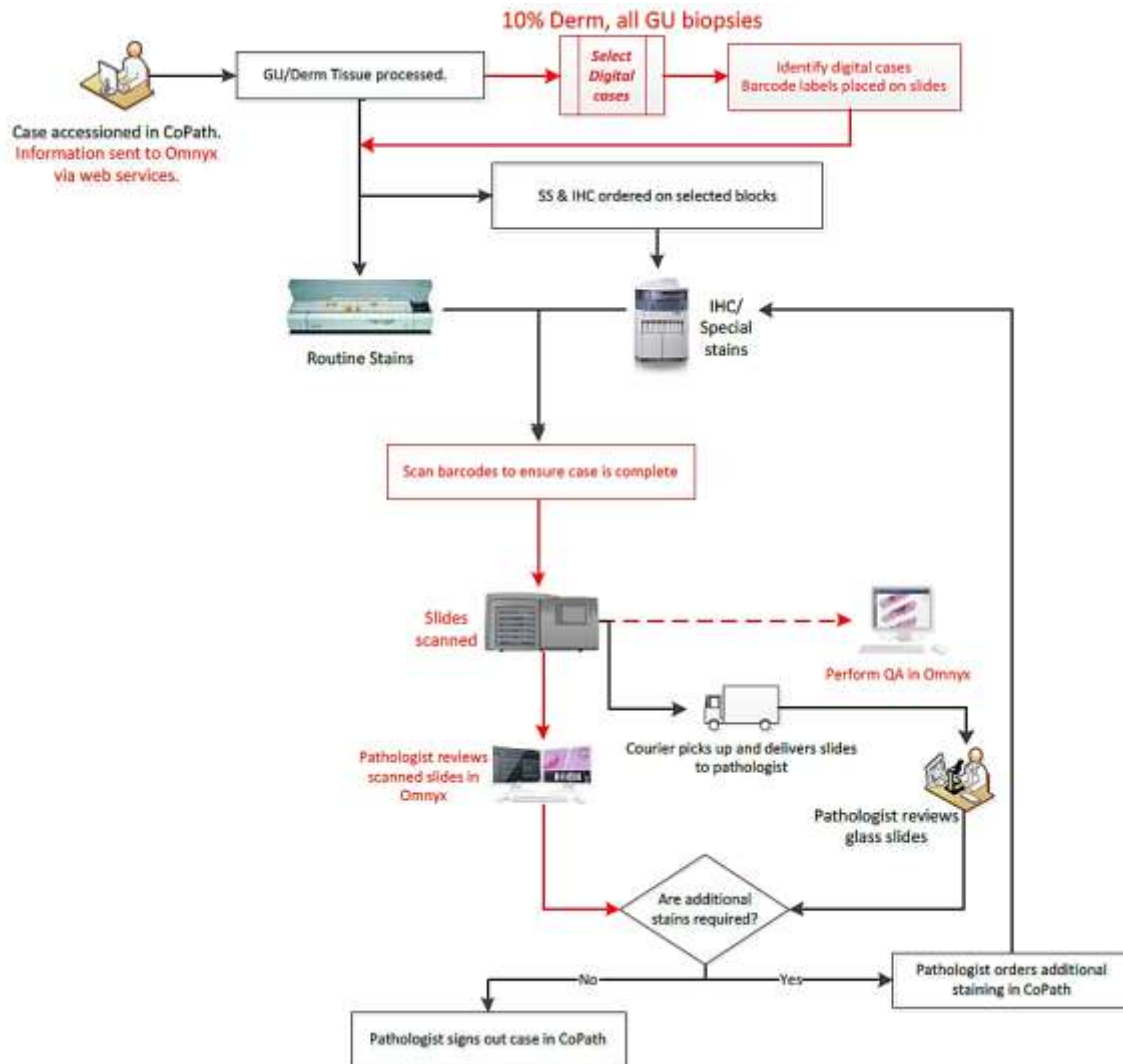
- ❑ **Primary diagnosis = use of WSI (and not glass slides) as the primary basis for establishing a pathologic diagnosis**
- ❑ **Very few AP labs in the USA have gone entirely digital for primary diagnosis**
- ❑ **UPMC has started conversion to a digital pathology platform for primary diagnosis sign out**
- ❑ **Several use cases were piloted and evaluated in different subspecialties (Dermatopathology, Gastrointestinal, Autopsy, Gynecologic/Breast, Pediatric Pathology, Genitourinary and Immunohistochemistry)**

Lab process

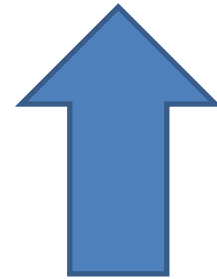
- Clinical Lab Building (CLB)
 - 24/6 processing
- Magee
 - 5AM - 5PM processing
- Children's Hospital
 - 5AM – 5 PM processing
- Dermatopathology
 - 5AM – 5 PM processing



Digital Workflow



Upstream



Changes Necessary



Downstream

Scanner Throughput - Calculations

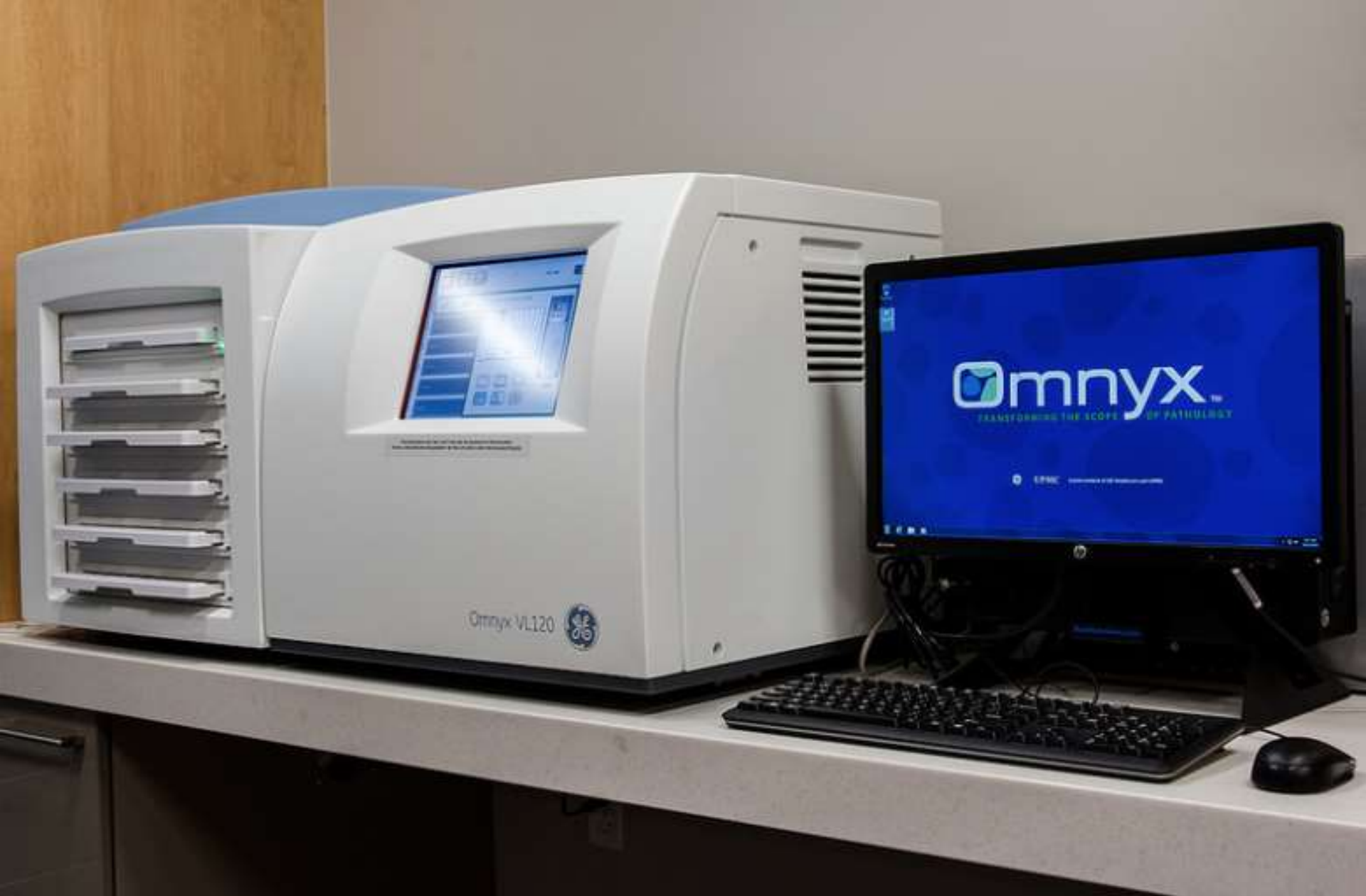
- Industry standard 15mm by 15mm
- Slide scanning only
- YMMV

Omnyx Production Use Cases

□ Begin utilizing Omnyx for Clinical Use Cases:

- **Start Date – (8/24/2015)**
 - Dermatopathology - 10 cases/day (~30 slides)
 - GI (quicks) - 10 cases/day (~30 slides)
- **Start Date - (9/21/2015)**
 - Autopsy – 1 case/day (~15 slides)
- **Start Date - (10/13/2015)**
 - Neuropathology – 1 autopsy case/day
- **Start Date – (10/19/2015)**
 - Pediatric Pathology (CHP) – 10 cases/day (max 3 parts) (~30 slides)
- **Start Date – (10/26/2015)**
 - GYN/Breast biopsies (Magee) – 10 cases/day (~10 slides)
- **Start Date – (11/16/2015)**
 - GU (prostate biopsies) – 2 cases/day
- **Start Date – (12/14/2015)**
 - UPMC St. Margaret's IHC Review
- **Start Date – (1/4/2016)**
 - UPMC Horizon IHC Review
- **Start Date – (2/2/2016)**
 - UPMC Passavant IHC Review
- **Start Date – (3/7/2016)**
 - UPMC Magee Placenta





Planning

- Engagement of key stakeholders**
 - Pathologists
 - Information Services Division
 - Lab supervisors & managers
 - Hospital administration
 - Enterprise decision-makers

- Budget considerations**
 - Hardware (scanners, workstations, servers, storage)
 - Software (licenses)
 - Hardware and Software Maintenance Support
 - Network Requirements
 - FTEs (pathologists, histology, IT)

- Need for flexibility**
 - Consolidation of hospital services
 - Changing technology
 - Regulatory environment (FDA)



Operations

Facility renovations

- Core lab (adequate bench space, located near slide production)
- Sign out areas (space, lighting, mounted monitors)

Hiring & training staff

- Pathologist (with information technology skills)
- Technologists (imaging experience & willing to work early shift)
- Information Technology (with imaging/PACS background)

Validation

- College of American Pathologists guideline satisfied
- Data capture for studies
- Evaluate actual throughput of scanners



Feedback Capture

The screenshot shows a web browser window displaying a feedback form for Omnyx. The browser's address bar shows the URL: <https://eps.slp.upmc.com/Omnyx/Lists/Pathologist%20Plot/NewForm.aspx?Source=https%3A%2F%2Feps.slp.upmc.com%2Fomnyx%2FLists%2FPathologist%2520Plot%2FAllItems%2Easpx&rootFolder=>. The page header features the UPMC logo and the text "LIFE CHANGING MEDICINE". The navigation menu includes "Home", "Notebook", "General Documents", "Recent", "Pathol. Features", "Priority Assignment", "Vigilance", "Pathol.", "Dr. Peiry's IHC", "Survey", "Pathologist Plot", "Survey", "Administrators", "Omnyx Training", "Checked Documents", and "SLP Contents".

The feedback form contains the following fields and questions:

- Pathologist/Resident/Fellow ***:
- Accession Number ***:
- Date ***:
- How satisfactory was the image quality? ***:
- How satisfactory was the Omnyx workflow? ***:
- Did you experience any technical problems? ***:
- If you answered yes above, please describe**:
- What is your diagnosis using Omnyx?**:
- Do you have any other comments?**:

At the bottom of the form are "Save" and "Cancel" buttons. The Windows taskbar at the bottom shows the time as 12:51 AM on 5/4/2016.

Faculty Engagement

- ❑ **Work culture:** Interested in digital pathology
- ❑ **Senior leadership:** Buy-in & support
- ❑ **Communication:** Grand rounds, memos
- ❑ **Incentives:** Validation studies



GI Pathology Early Adoption

❑ Rules

- Gastrointestinal Quicks (biopsies)
 - ❑ Selected in the histology lab from the routine output
- Cases with 3 or less parts
- No STAT cases
- Principally initial H&E stains only
- Without impact on slide delivery



Results

- 529 cases were reviewed prior to review of the glass slides
- Diagnosis was entered into sharepoint form



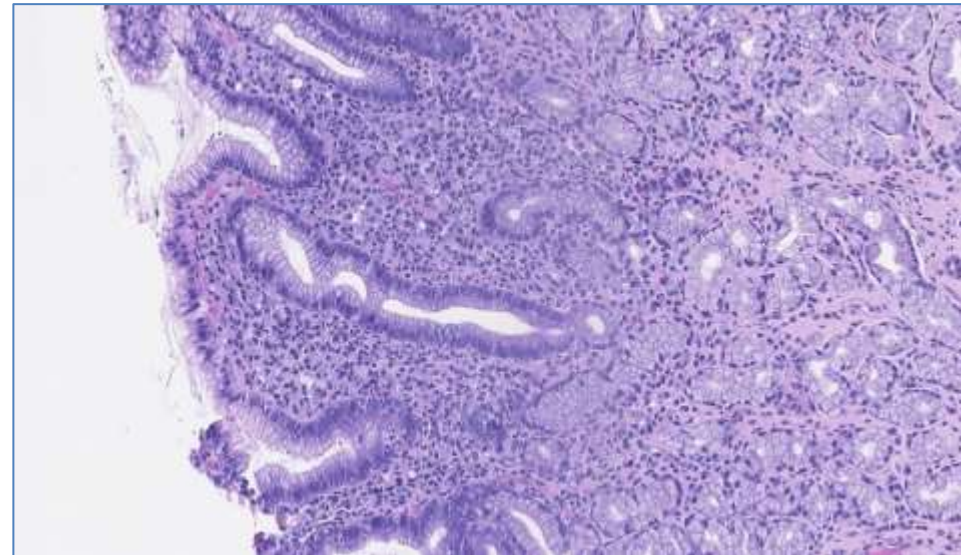
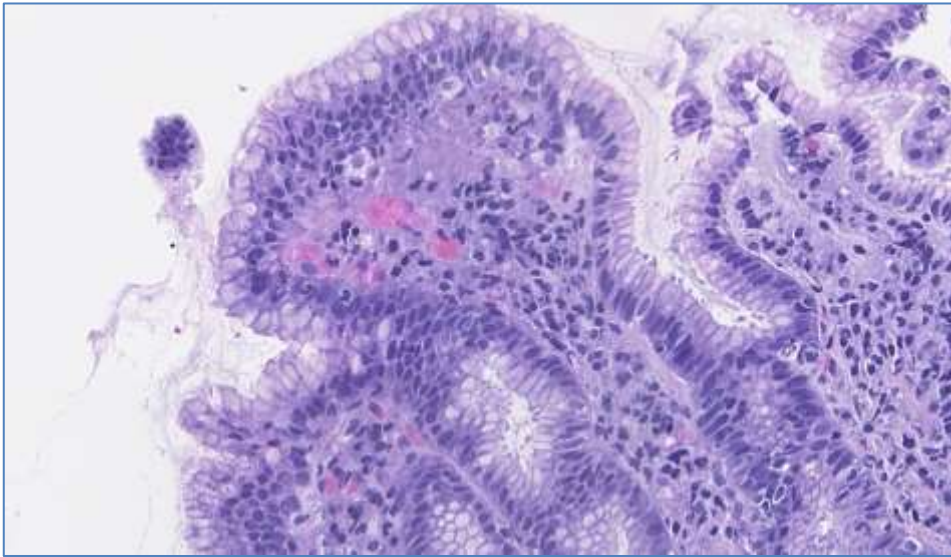
shutterstock · 130702703

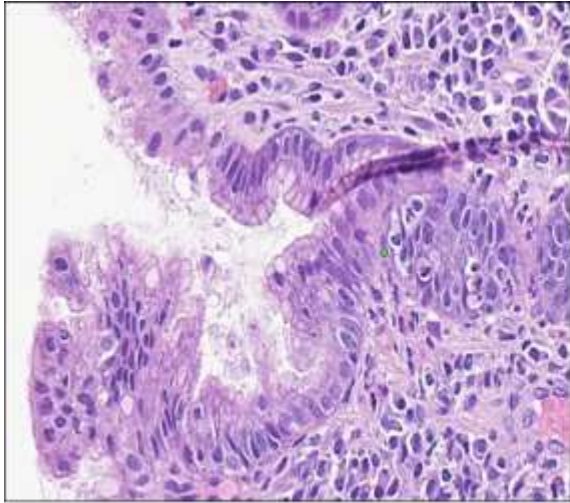
Results: Digital vs. Glass

- ❑ 470 cases (91%) were interpreted the same for the digital slides as the glass slides
- ❑ No major discrepancies occurred
- ❑ Of 54 cases with minor discrepancy, the majority involved evaluation of inflammation or lack of confidence in identifying helicobacter organisms

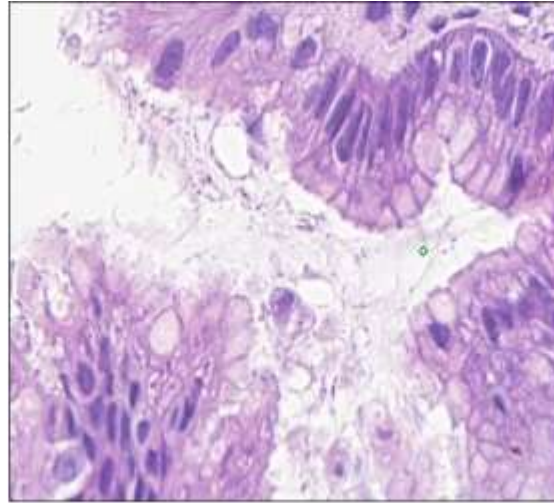


Helicobacter Organisms

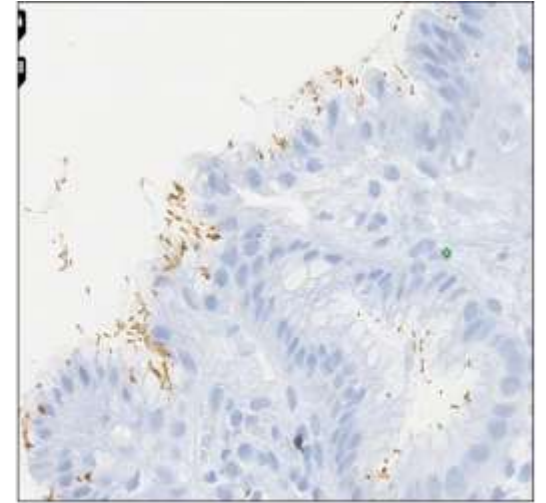




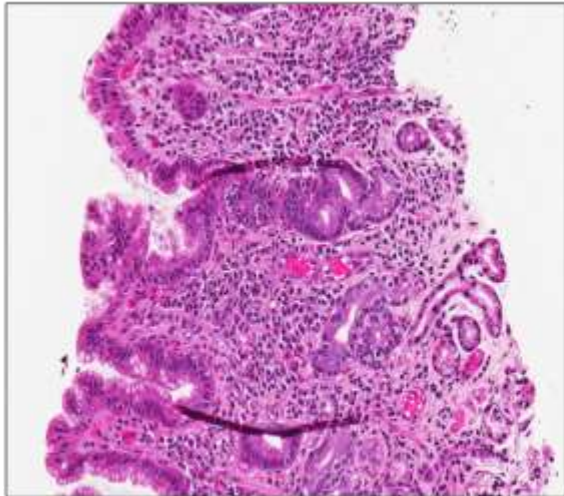
Omnyx - 40x



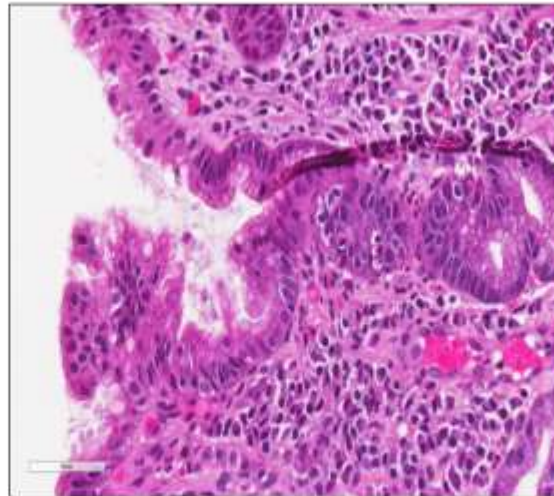
Omnyx - 60x



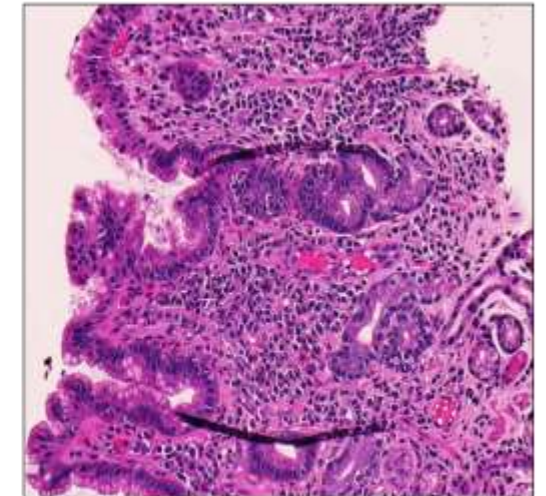
Omnyx - 40x (IHC)



Aperio - 20x



Aperio - 40x

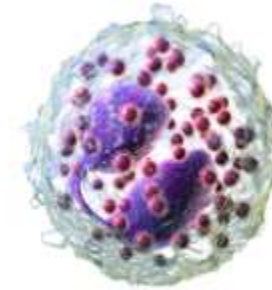
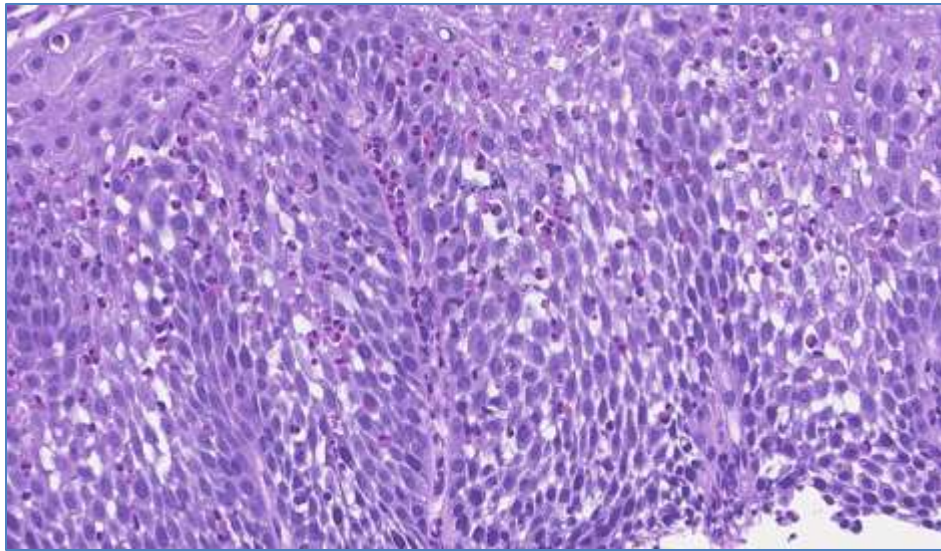


NanoZoomer - 20x

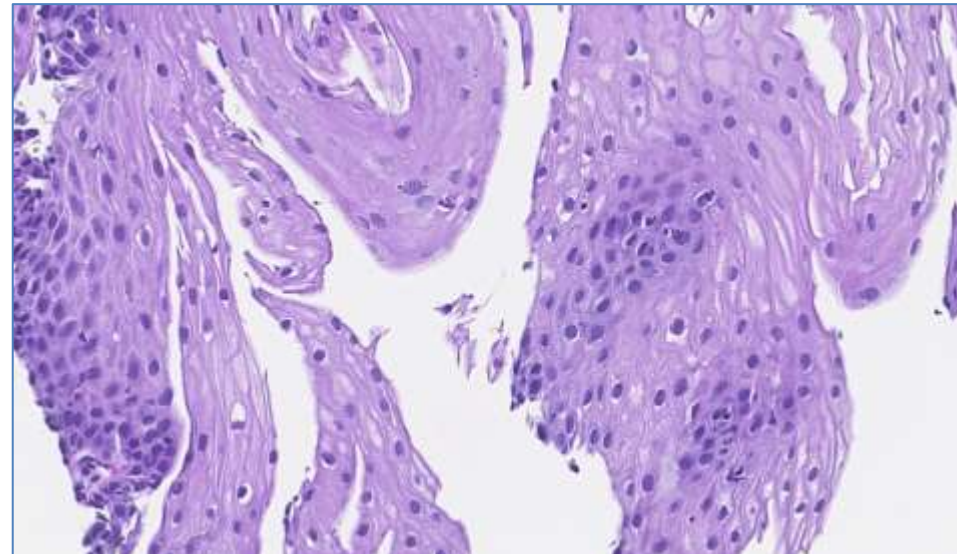
Helicobacter by Magnification and WSI Scanner

Modality	Omnyx (n=20)		Aperio (n=20)		NanoZoomer(n=20)
	40x	60x	20x	40x	20x
% Agreement H&E slide	92.5%	92.5%	75%	82.5%	92.5%
% Agreement IHC slide	92.5%	82.5%	92.5%	87.5%	90%
% of cases with image quality (score $\geq 5/10$) – H&E slide	80%	100%	25%	95%	100%
% of cases with image quality (score $\geq 5/10$) - IHC slide	82.5%	100%	67.5%	100%	100%

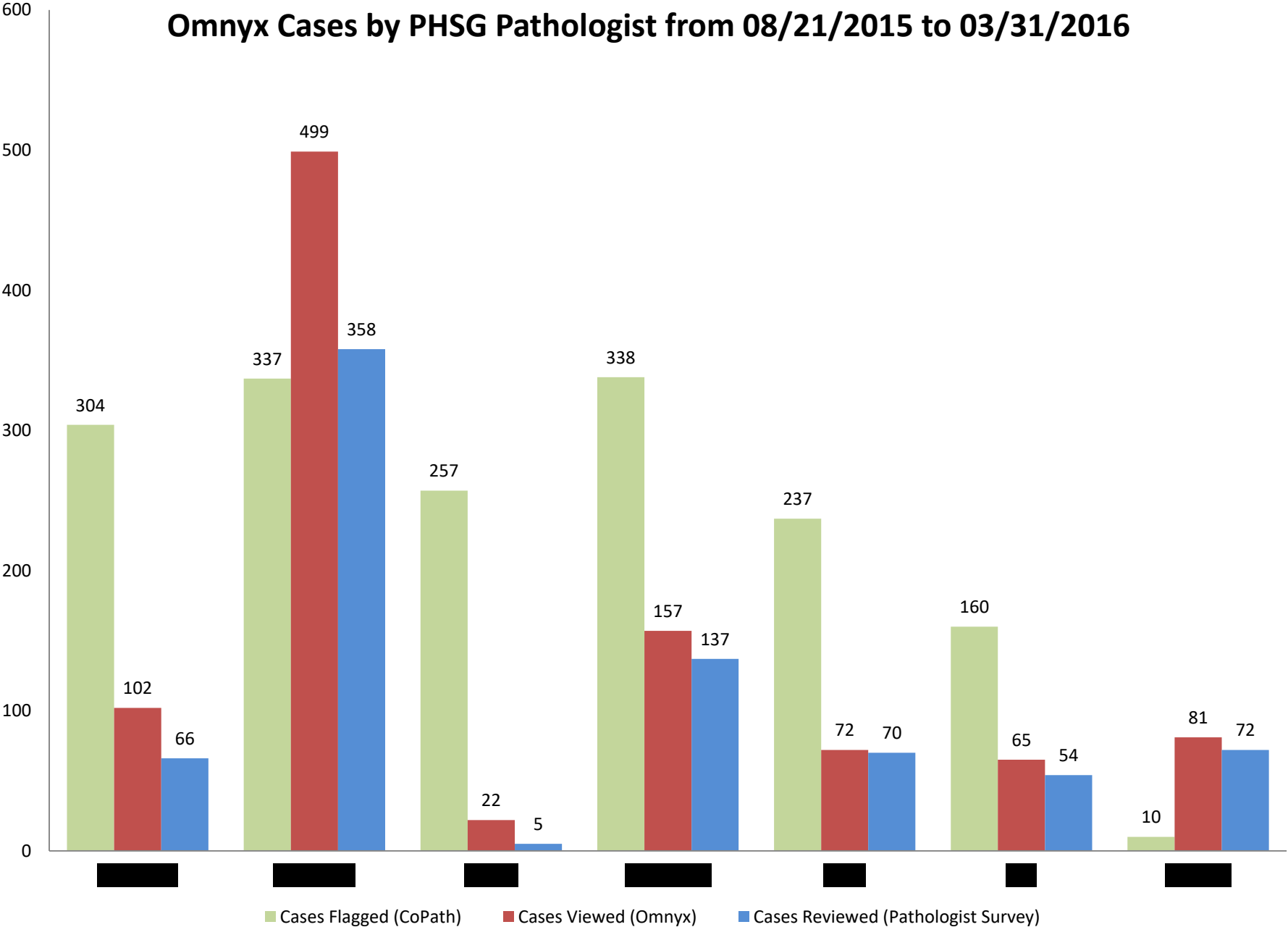
Inflammatory Cells



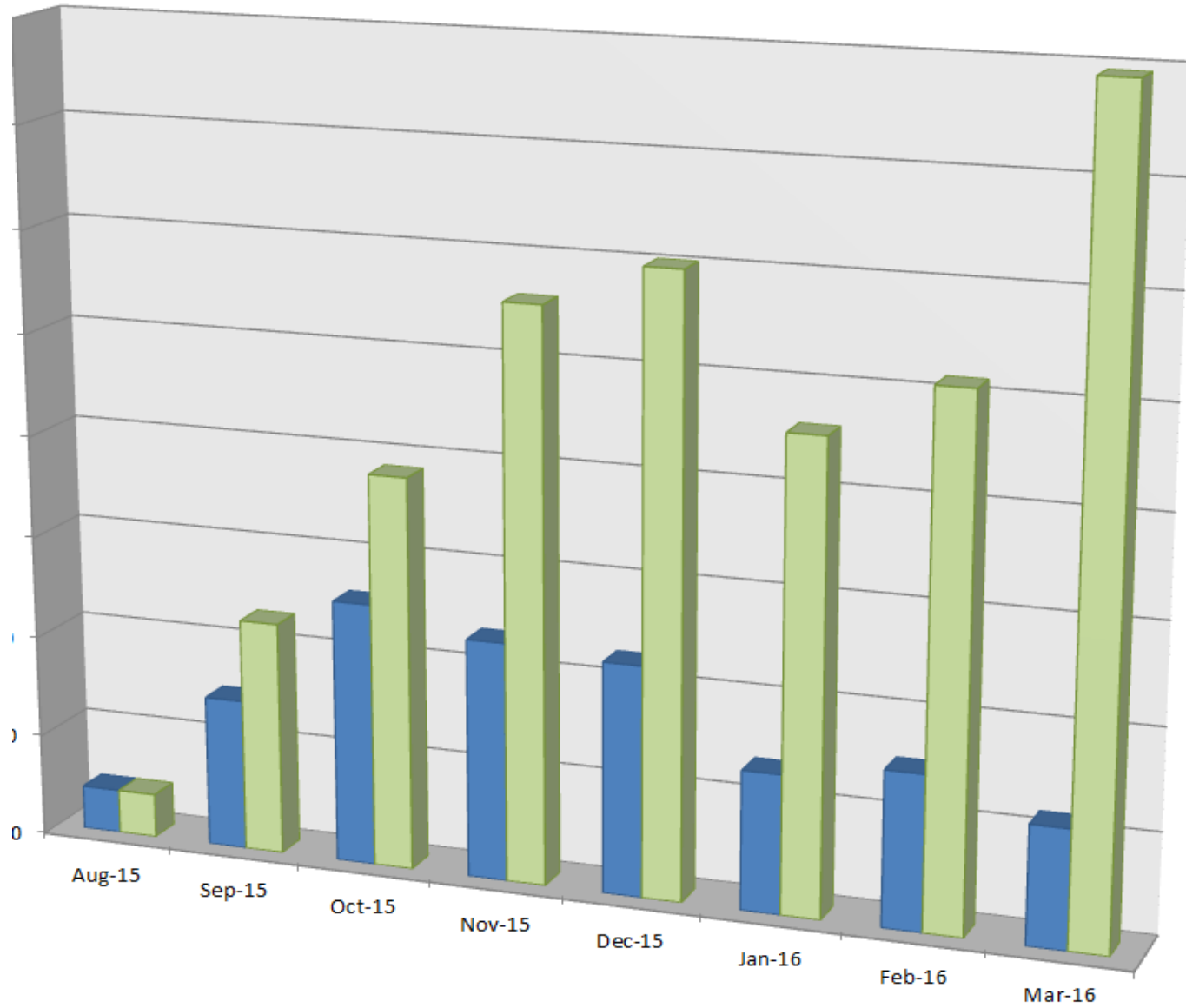
Eosinophil



Omnyx Cases by PHSG Pathologist from 08/21/2015 to 03/31/2016



Omnyx Cases Aug '15 - Mar '16



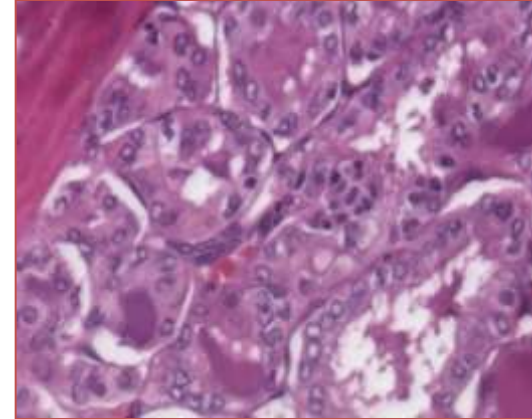
WSI - Rate of Adoption

Accelerated Rollout		Incremental Adoption	
Advantages	Disadvantages	Advantages	Disadvantages
Full Span	Higher Upfront Cost	Lower Upfront Cost	Limited Span
Focused Rollout Support	Immature Adoption	Mature Adoption	Extended Rollout Support
Fast Adoption	Limited Use Cases	Lower Refresh Cost	Slow Adoption
Focused Change Management	Impact on Operations	More Time For Clinical Validation	Long Change Management

WSI - Size Challenges



Avg. Size of Radiology Study: 0.1 Gb



Avg. Size of Pathology Case: 1.0 Gb

- ❖ Acquiring
- ❖ Storing
- ❖ Retrieving
- ❖ Streaming
- ❖ Analyzing

Handling Large Volumes of Large Images is Key to Enabling Digital Pathology

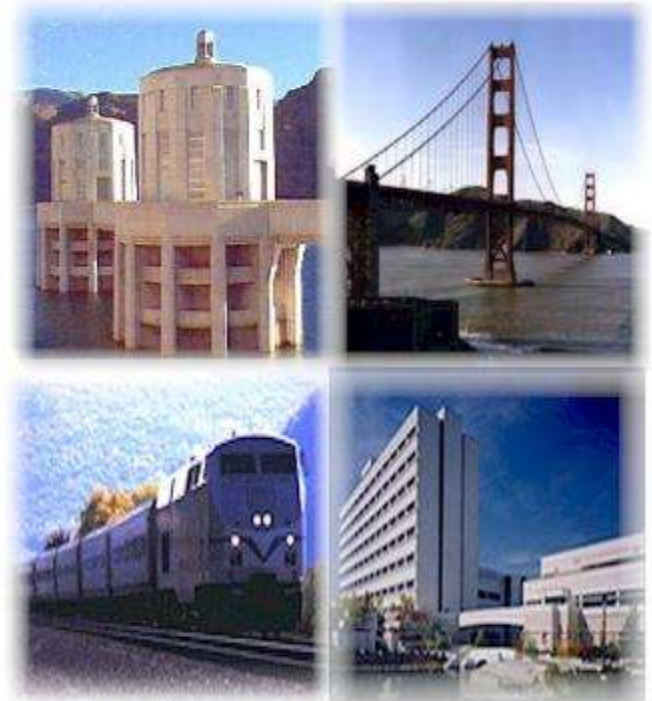
WSI - Scanner Challenges

- ❑ **Cost:** WSI scanners require high upfront investment
- ❑ **Throughput:** This is the average speed to process a slide.
- ❑ **Logistics:** Large scanners require adequate space planning to maximize efficiency in usage and serviceability
- ❑ **Resources:** Large WSI scanners in a full digital workflow require dedicated personnel



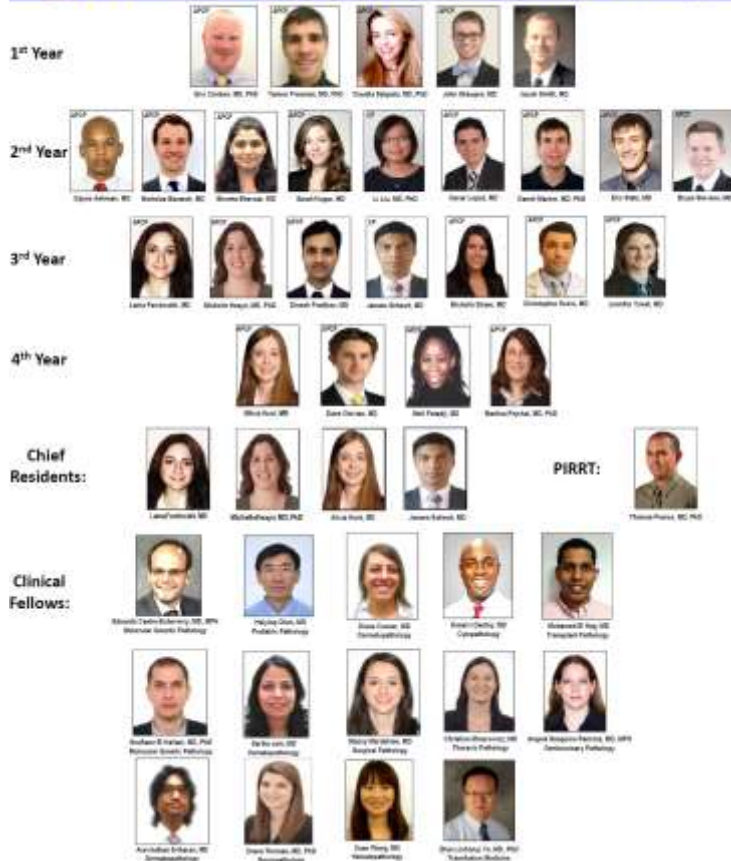
WSI - Infrastructure

- ❑ **Network:** Boosting network connectivity for scanners
- ❑ **Storage:** Large storage requirements, may require short and long term strategies
- ❑ **Servers:** physical location of servers and connectivity may be critical if on multiple sites.
- ❑ **Workstations:** different requirements in hardware and layout for histology, pathologist's offices, sign out areas and education
- ❑ **Scanners:** space and layout considerations are important especially for large scanners to ensure adequate installation, access and service.
- ❑ **Spare Parts:** Plan on site for spare parts of different mechanical components that may fail.
- ❑ **Workflow Continuity:** Scanner downtime can be significant in the event of mechanical or hardware failure.



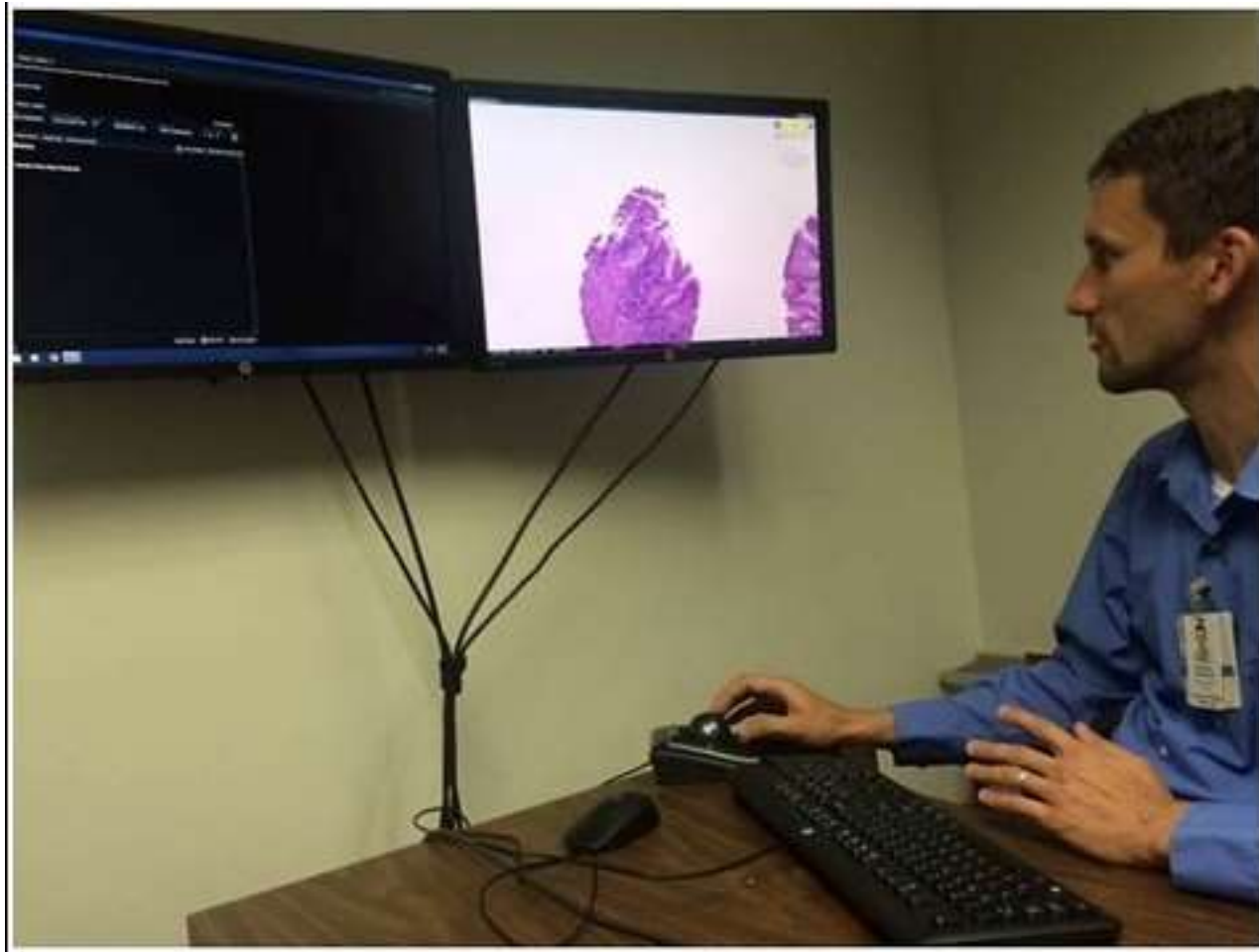
Housestaff?

Department of Pathology Residents & Clinical Fellows 2016-2017

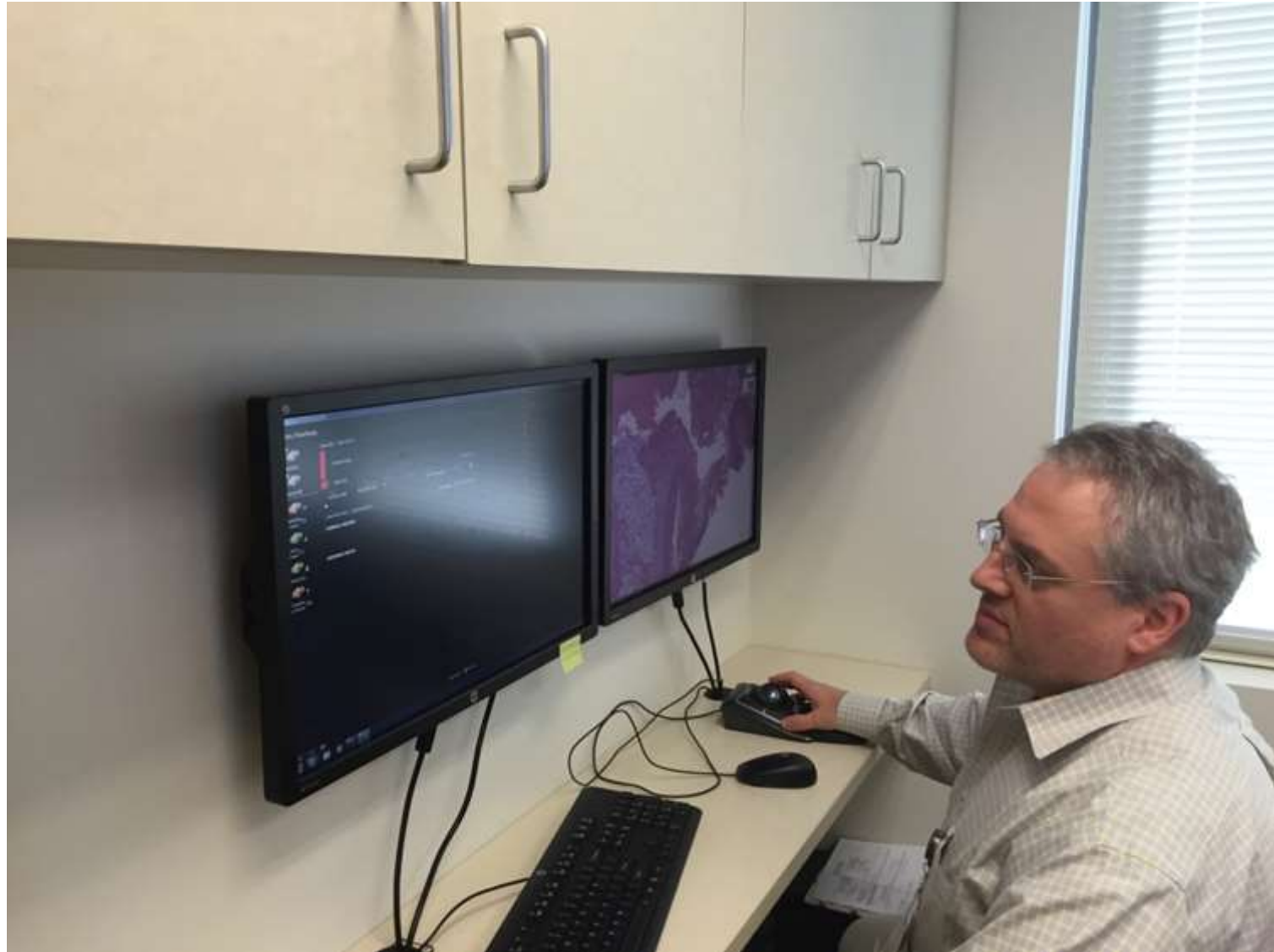


- Nearly all medical schools teach pathology with WSI
- Anatomic pathology residency revolves around learning glass slides
- What should the workflow be?

Workstation #1



Workstation #2



Workstation #3 - Option A



Workstation #3 - Option B



Imaging Lab

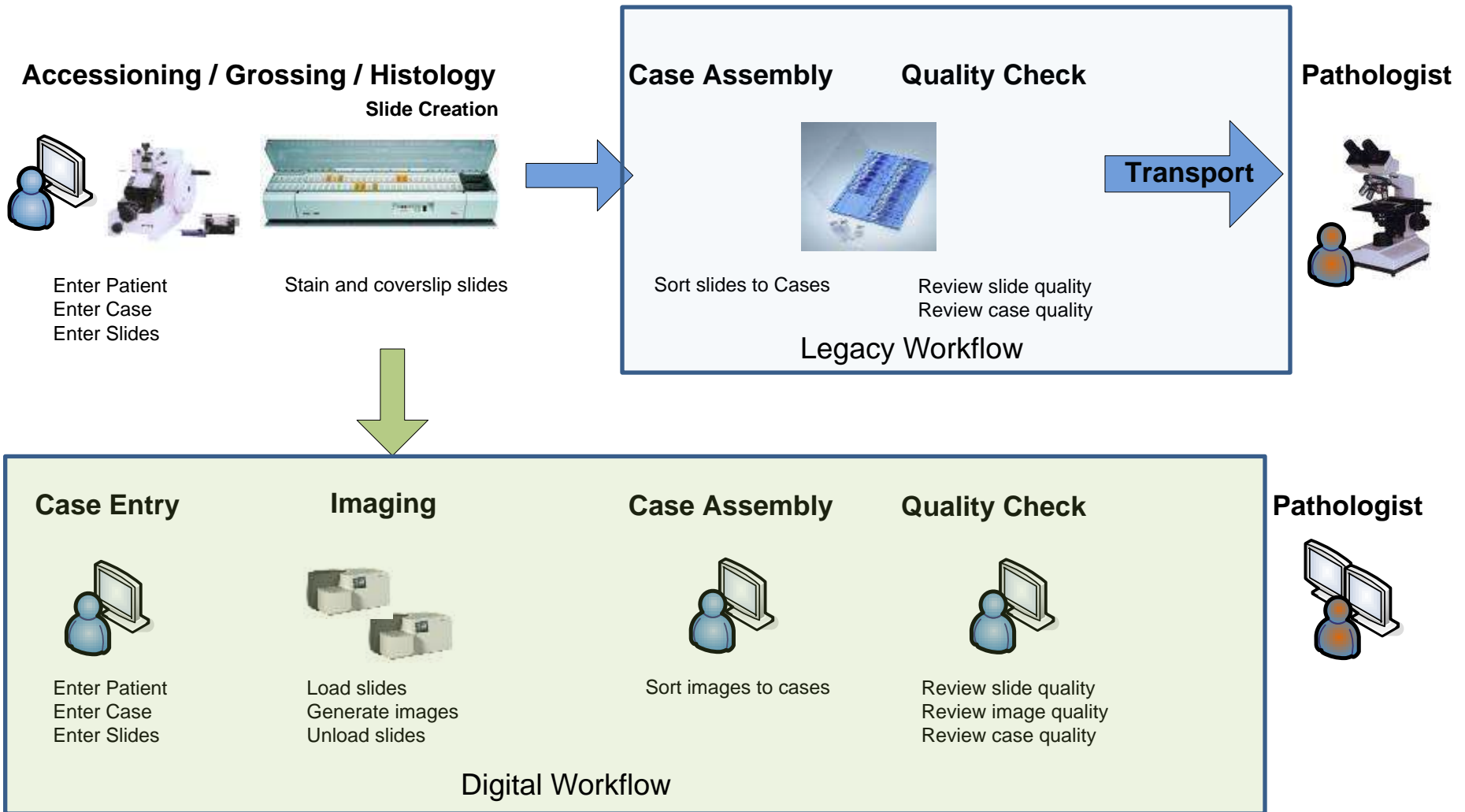


Pre-Imaging Workflow

- ❑ **Histology Legacy Tasks** - Digital workflow does not eliminate the legacy tasks, histology techs still need to stain and prepare slides
- ❑ **Scan preparation** - Slides need to be loaded in cassettes to be digitized
- ❑ **Issue Management** - Scanner needs to be monitored against errors and mechanical failures. Scanner errors and interruptions need to be resolved.
- ❑ **QA and Calibration** - Raw Images need to be assessed for quality and optics require periodic calibration



Pre-Imaging Workflow



Digital Implementation Strategies

- Although primary diagnosis has been approved, different strategies may be applied by institutions depending on use case
 - Upfront “In-line” scanning (i.e. scanning as soon as the slides leave the stainer)
 - Post-signout scanning (i.e. Scanning slides after the cases have been signed out but before the filing)
 - Archival scanning (i.e. Pulling cases from slide files and scanning them)



Challenges

Hardware /Gripper Issues

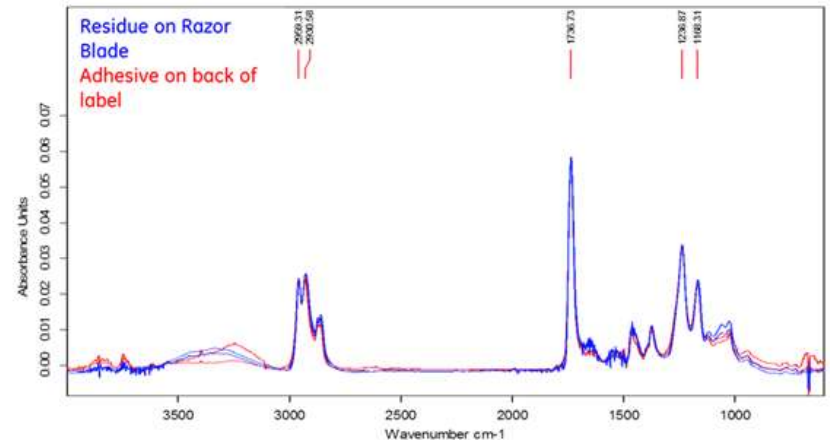
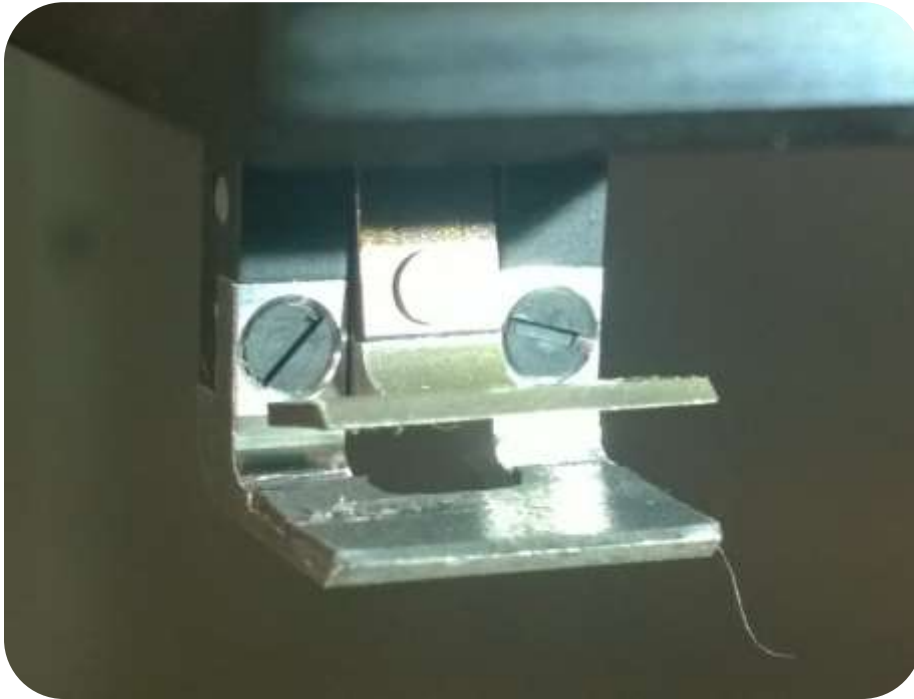
- ❑ **Label overhang** – a slight overhang of a label may cause slides to not be scanned correctly
- ❑ **Glue** - Glue on the back can gum up the gripper which resulted in slides not being able to be picked up properly by the robotic arm

Software

- ❑ **Query Latency** – Integration issues can result in inconsistent behavior and delays in data populating from the LIS
- ❑ **Scrolling** –delays in the ability to scroll through an image may affect productivity
- ❑ **Noticeable image tiling** – Image focus issues can cause noticeable tiling



Scanner Problems



Advancements in Technology

❑ Prior:

- Robotic telepathology

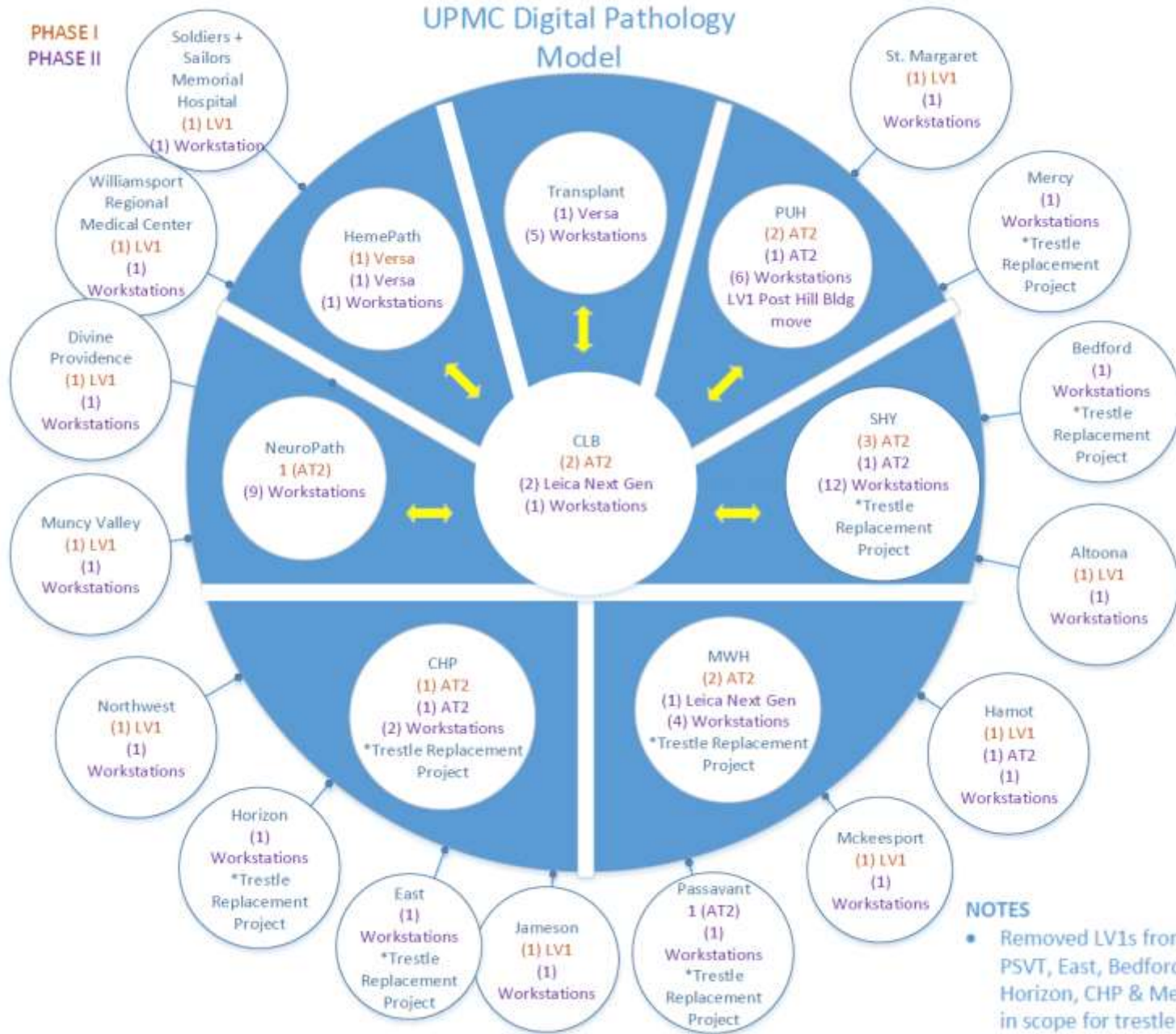


❑ New:

- Hybrid (robotic telepathology and WSI)



UPMC Digital Pathology Model



NOTES

- Removed LV1s from SHY, PSVT, East, Bedford, Magee, Horizon, CHP & Mercy LV1s; in scope for trestle project

UPMC Use Cases

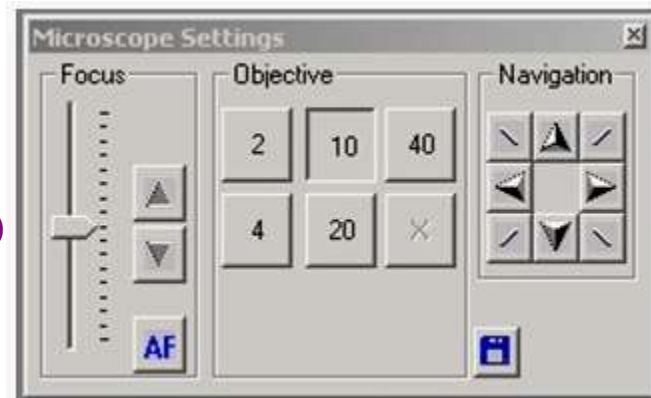
- 1. Remote Frozen Sections**
2. Telecytology for ROSE
3. International Consultation

Robotic Telepathology System



Digital/video camera

Networked PC
↔
(server software)

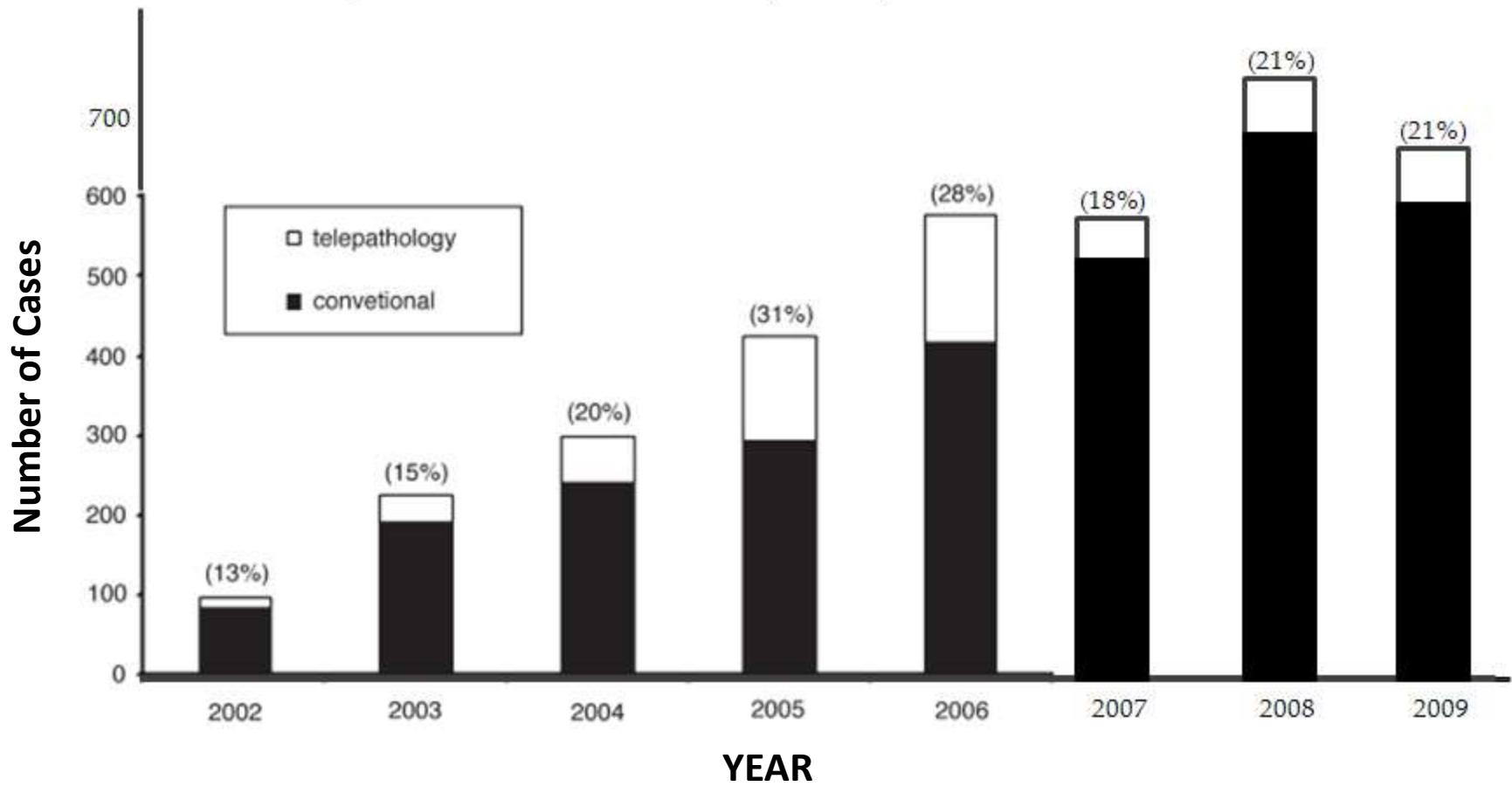


Remote Microscope Controls
(Viewing software required)

Robotic (motorized) microscope
(1-4 slides)

UPMC Neuropathology Frozen Section Rate

Pantanowitz et al. J Pathol Inform 2012; 3:45

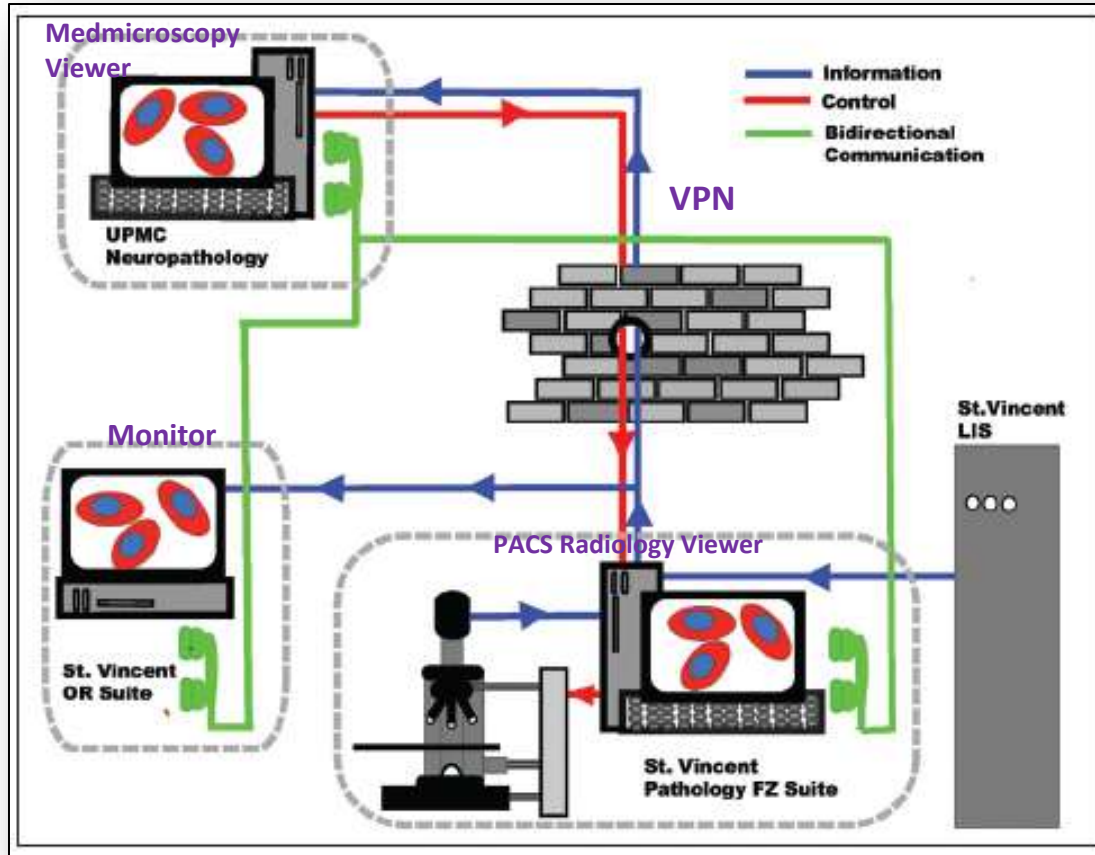


Interinstitutional Teleneuropathology

Wiley et al. J Pathol Inform 2011; 2:21



9 neuropathologists



4-slide Zeiss
Axiomager

370
miles

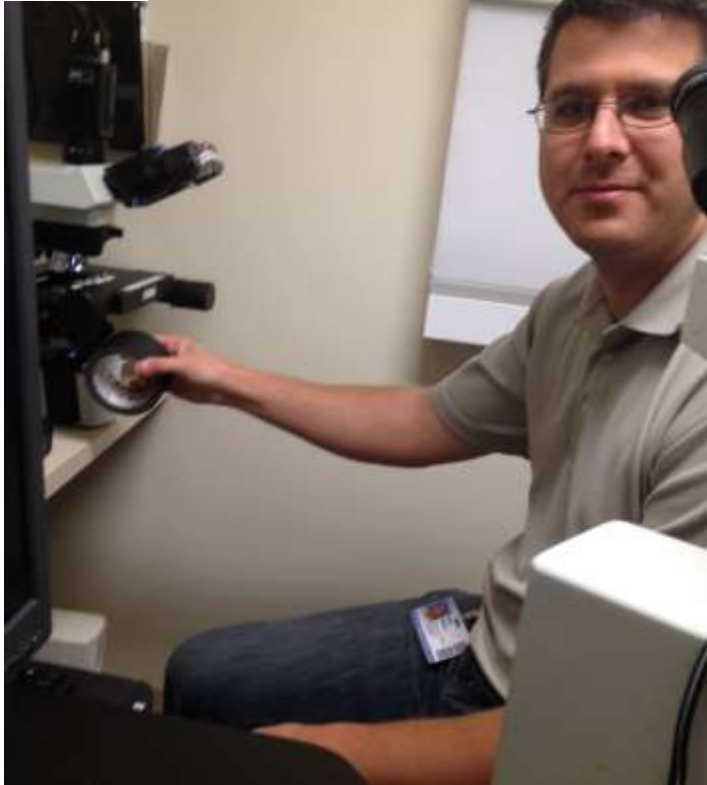


1 neuropathologist



Adopting Hybrid Technology

Trestle
(Robotic only)



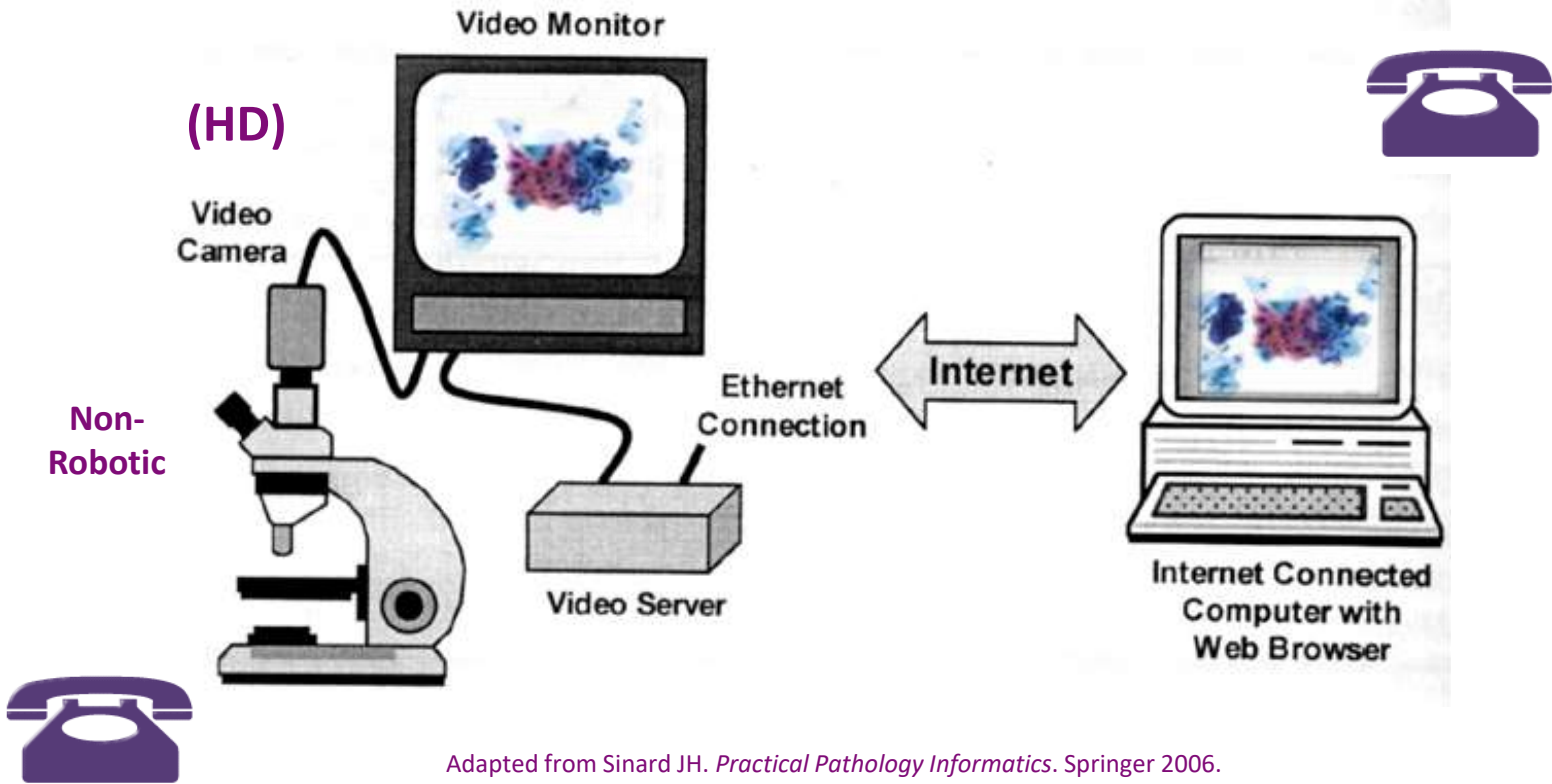
Hybrid LV1 scanner
(Robotic + WSI)



UPMC Use Cases

1. Remote Frozen Sections
- 2. Telecytology for ROSE**
3. International Consultation

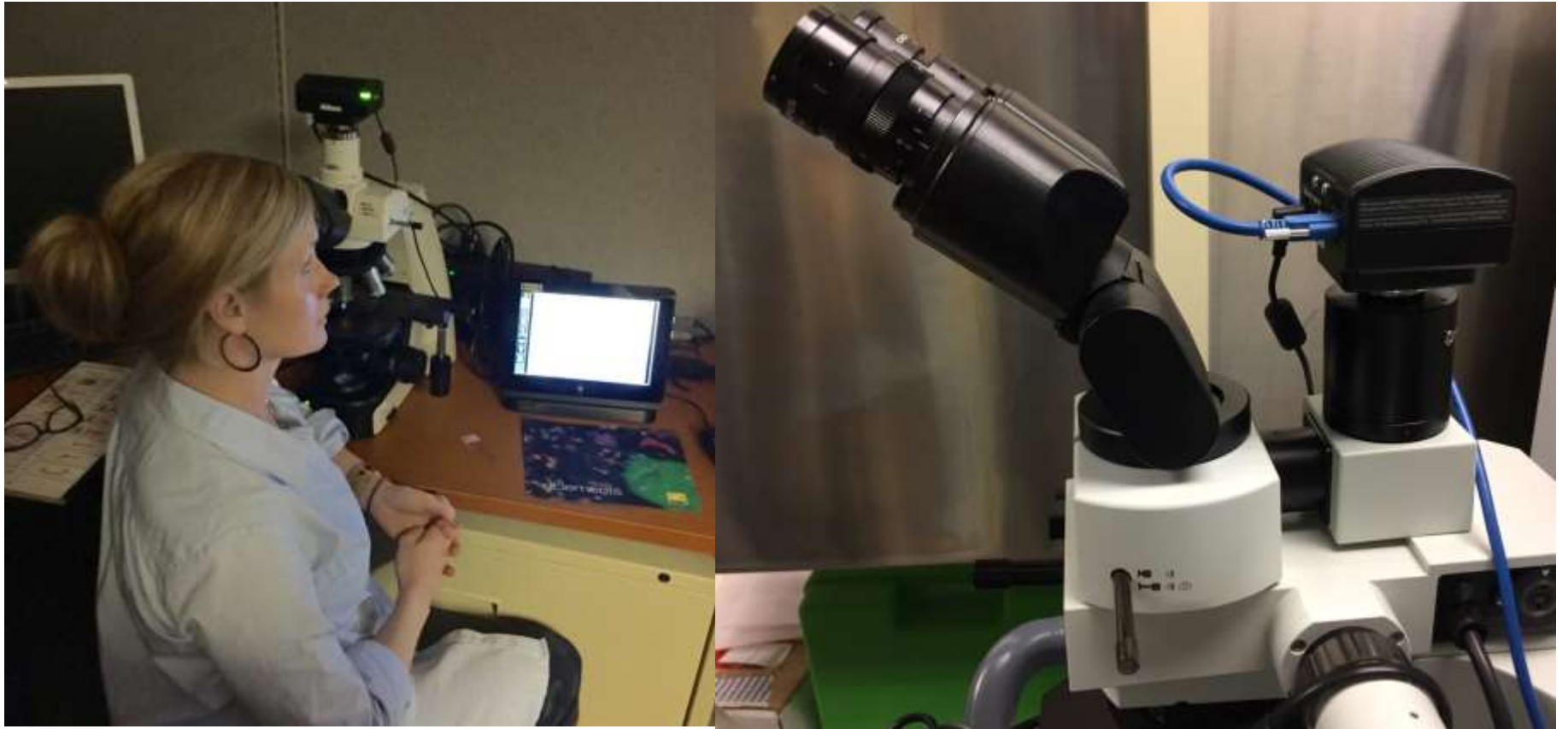
Dynamic Video Microscopy System



Adapted from Sinard JH. *Practical Pathology Informatics*. Springer 2006.

UPMC Telecytology

Web-based streaming via WiFi

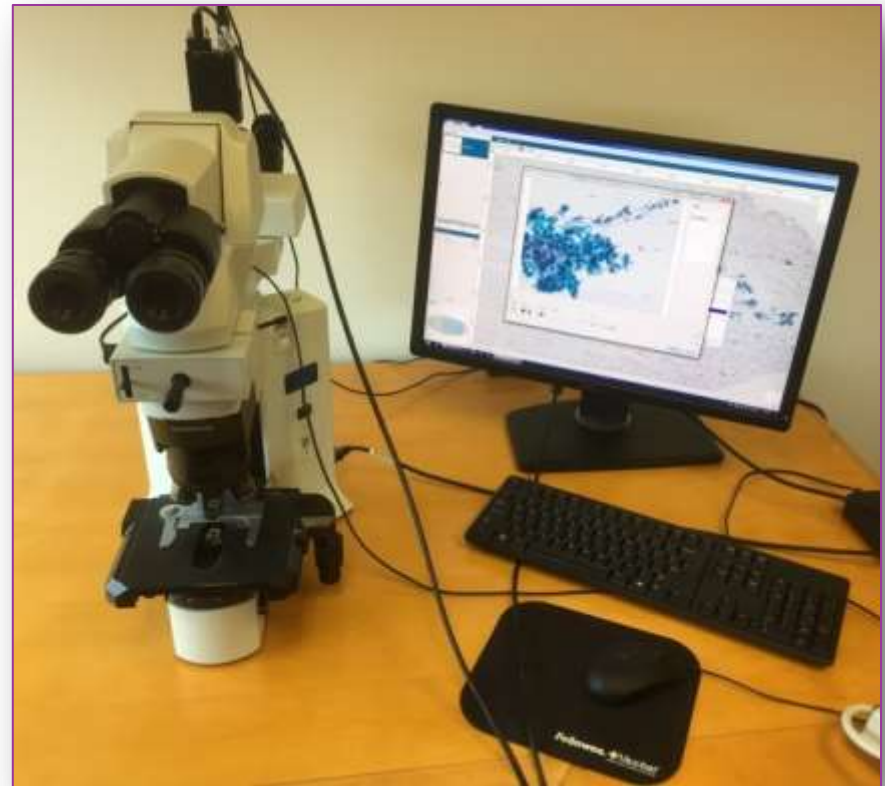


"Cyto to Go"

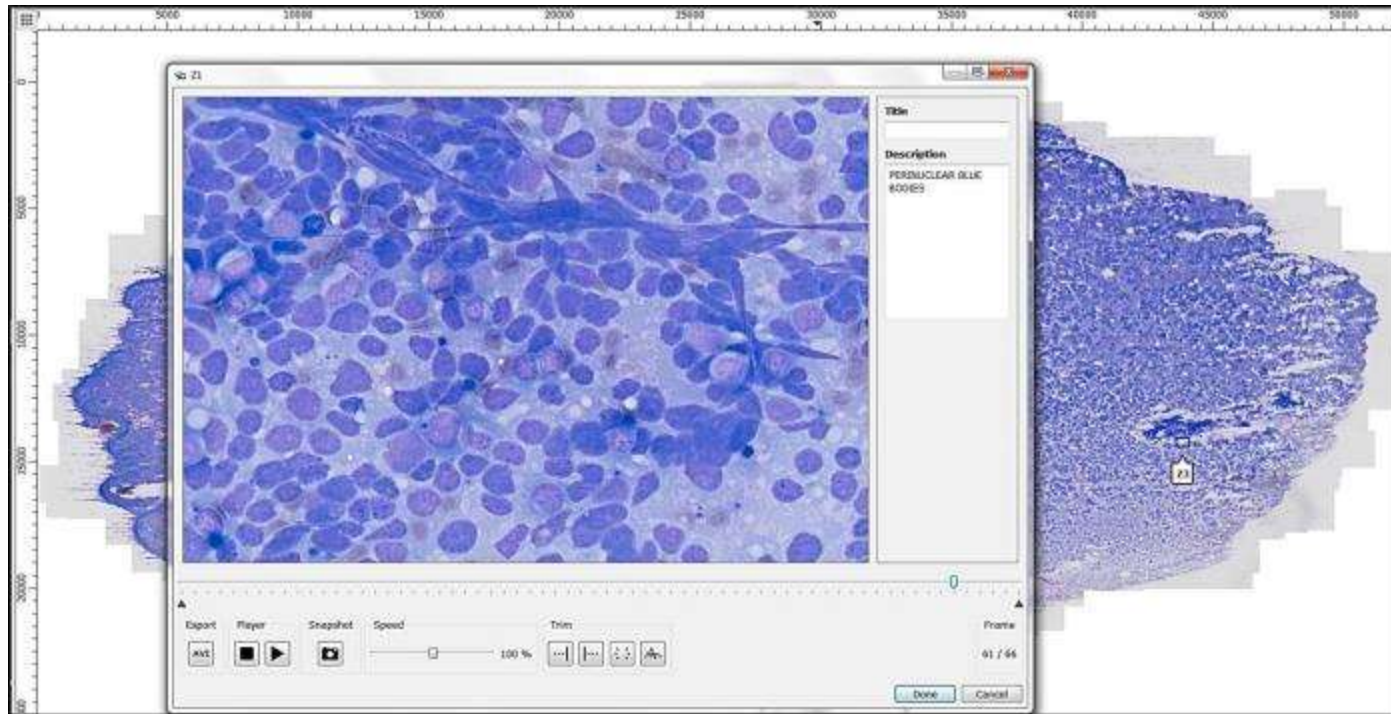


Panoptiq System

- Panoptiq allows users to create digital files combining low power panoramic images with ROI imaged using high power z-stacks.
- Allows fine focusing of thick smears and cell clusters.
- Acquisition of images requires a trained cytologist to create panoramic image.



Panoptiq combined low and high magnification image



Liver FNA showing metastatic small cell carcinoma (DQ stain)

UPMC Use Cases

1. Remote Frozen Sections
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Digital Pathology Consultation Portal

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DIIGITAL

UPMC Digital Pathology Consultation Portal

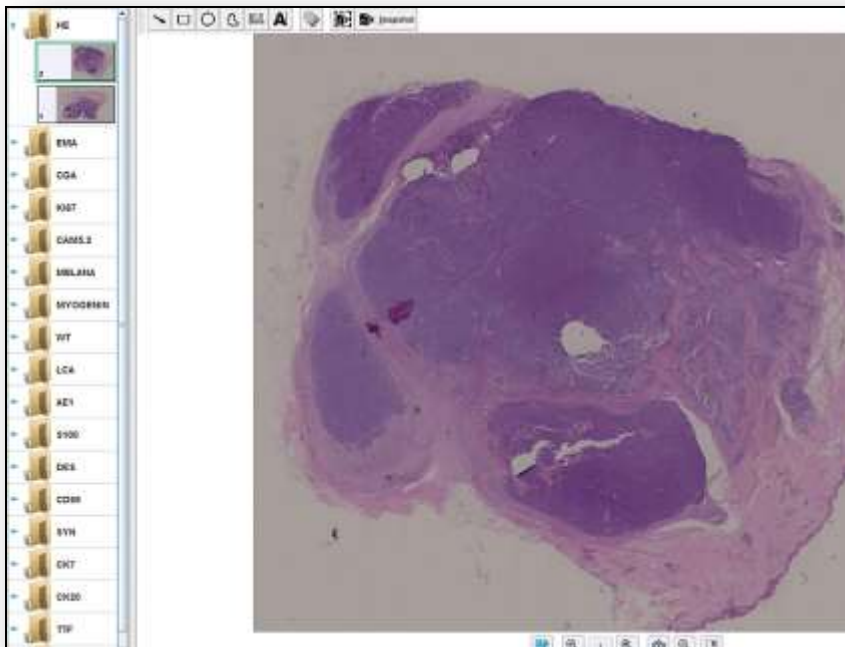
Now it's easier than ever to send your slides electronically and let UPMC Pathology experts be your second set of eyes for diagnosis and treatment.

The UPMC Digital Pathology Consultation Portal gives you a valuable second opinion necessary to be accurate and efficient in both diagnosis and treatment.



Synchronous Telepathology

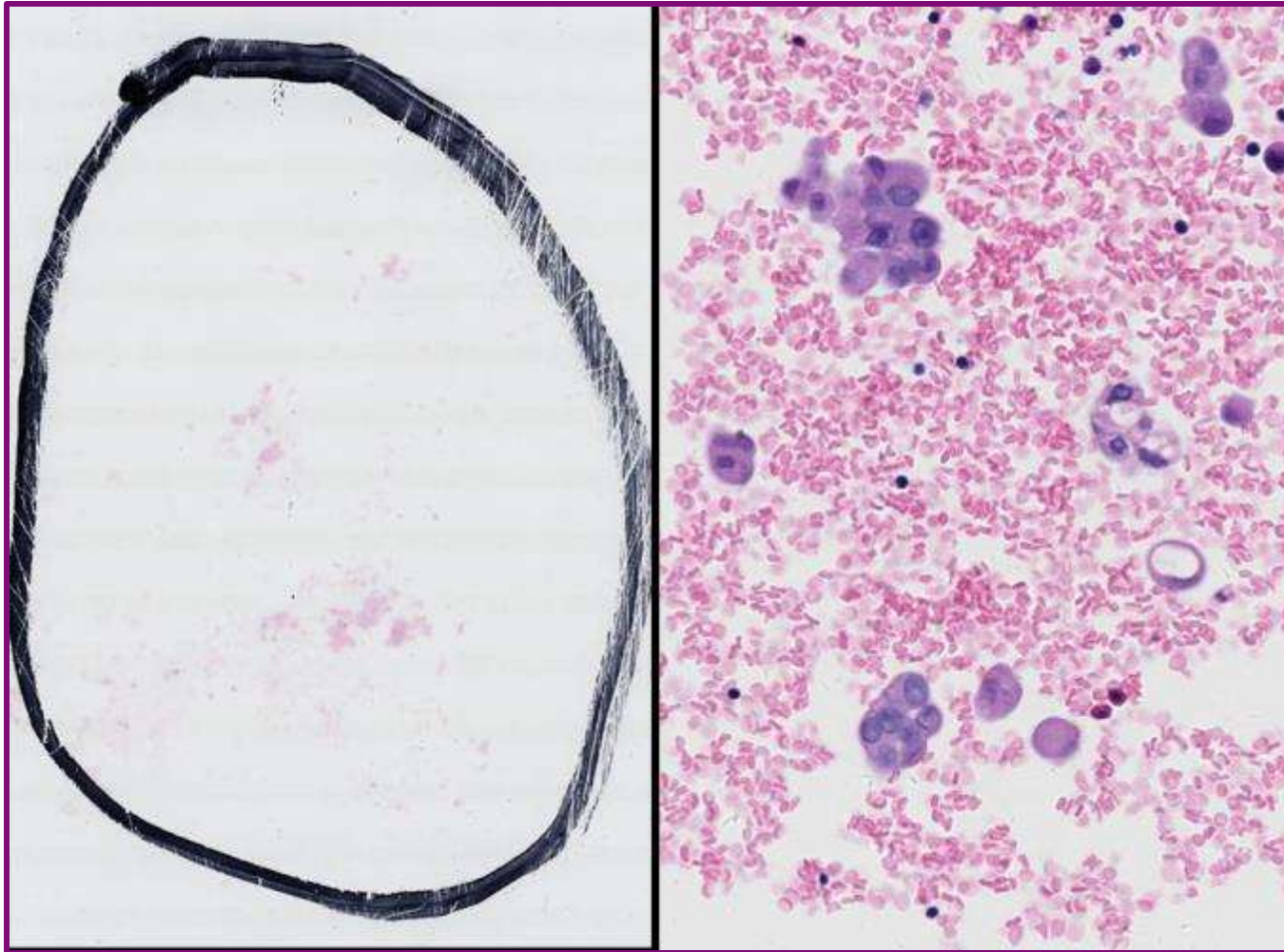
Referring Pathologist



Consulting Pathologist



Feasibility Using Digitally Scanned Cell Block Slides



International Telepathology at UPMC

□ Current “portals”

- ISMETT (Italy)
- Direct (ad-hoc)
- KingMed (China)
- Qingdao (China)



What have we done

Consults Completed:

- 4140 KingMed cases
- 241 ISMETT cases
- 24 general portal

Expanded Viewer

Adoption of OpenSlide functionality



Referral Nature of Cases Submitted

Zhao C et al. J Pathol Inform 2015; 6:63

Individuals requesting consultation	Case number	Percentage
Primary pathologists in China	958	61.4
Clinicians in China	576	36.9
Patients in China	27	1.7
Total	1561	100

Original Article

International telepathology consultation: Three years of experience between the University of Pittsburgh Medical Center and KingMed Diagnostics in China

Chengquan Zhao¹, Tao Wu², Xiangdong Ding², Anil V. Parwani¹, Hualin Chen², Jeffrey McHugh¹, Anthony Piccoli¹, Qinling Xie², Gonzalo Romero Lauro¹, Xiaodong Feng², Douglas J. Hartman¹, Raja R. Seethala¹, Shangwei Wu², Samuel Yousem¹, Yaoming Liang², Liron Pantanowitz¹

¹Departments of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA, ²KingMed Diagnostics, Guangzhou, Guangdong, China

E-mail: *Liron Pantanowitz - pantanowitzl@upmc.edu, *Chengquan Zhao - zhaoc@upmc.edu

*Corresponding author

- Hematopathology, Bone/Soft Tissue and Breast/Gyn are the most frequent specimen types
- Turnaround time initially was 7 days and then was lowered to 5 days

Sample Diagnoses from GI Cases

- Several cases of Neuroendocrine Carcinoma in stomach, esophagus, colon
- Poorly differentiated carcinoma with neuroendocrine features in colon
- Gastrointestinal stromal tumor, myxoid type
- Autoimmune chronic pancreatitis
- Numerous GI adenocarcinomas
- Poorly differentiated mesenchymal neoplasm
- High grade dysplasia and adenocarcinoma in gallbladder
- Solid pseudopapillary tumor in pancreas
- Low grade mesenchymal proliferation
- Paraganglioma and ganglioneuroma
- Mixed adenocarcinoma and neuroendocrine carcinoma (MANEC)
- Benign inflammatory fibrotic process
- Schwannoma
- Rhabdomyosarcoma, poorly differentiated embryonal type
- Low grade appendiceal mucinous neoplasm
- Pancreas with papillary and micropapillary features

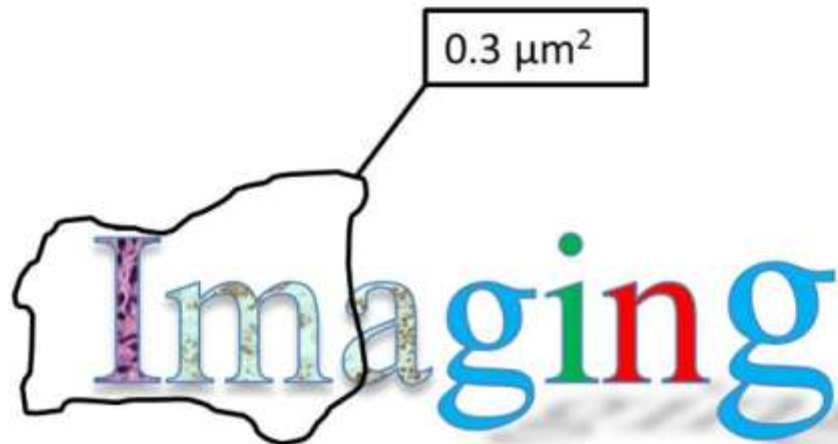
Image Analysis

- Rapidly expanding area
- Buzzwords:
 - Machine Learning
 - Artificial Intelligence
 - “Centaur pathologists”
- ?Driver for digital pathology adoption



Hot Topics

0.3 μm^2



Algorithms

- **Identify rare events (e.g. screening for microorganisms)**
- **Quantitative measurements**
 - **Score biomarkers (e.g. ER, PR, Her2/neu, Ki67, CD34, PD-L1)**
 - **Tissue measurements (e.g. mitotic counts, quantify fibrosis/steatosis)**
- **Analyze spatial patterns and feature distribution (e.g. neuroscience)**
- **Automated grading (of tumors)**
- **CAD (e.g. prostate cancer diagnosis, detect Barrett's esophagus with dysplasia)**
- **Workflow (smart) algorithm (e.g. triage cases, automate downstream steps like LCM)**
- **Miscellaneous (research & novel) algorithms (e.g. TMAs, 3D image reconstruction)**

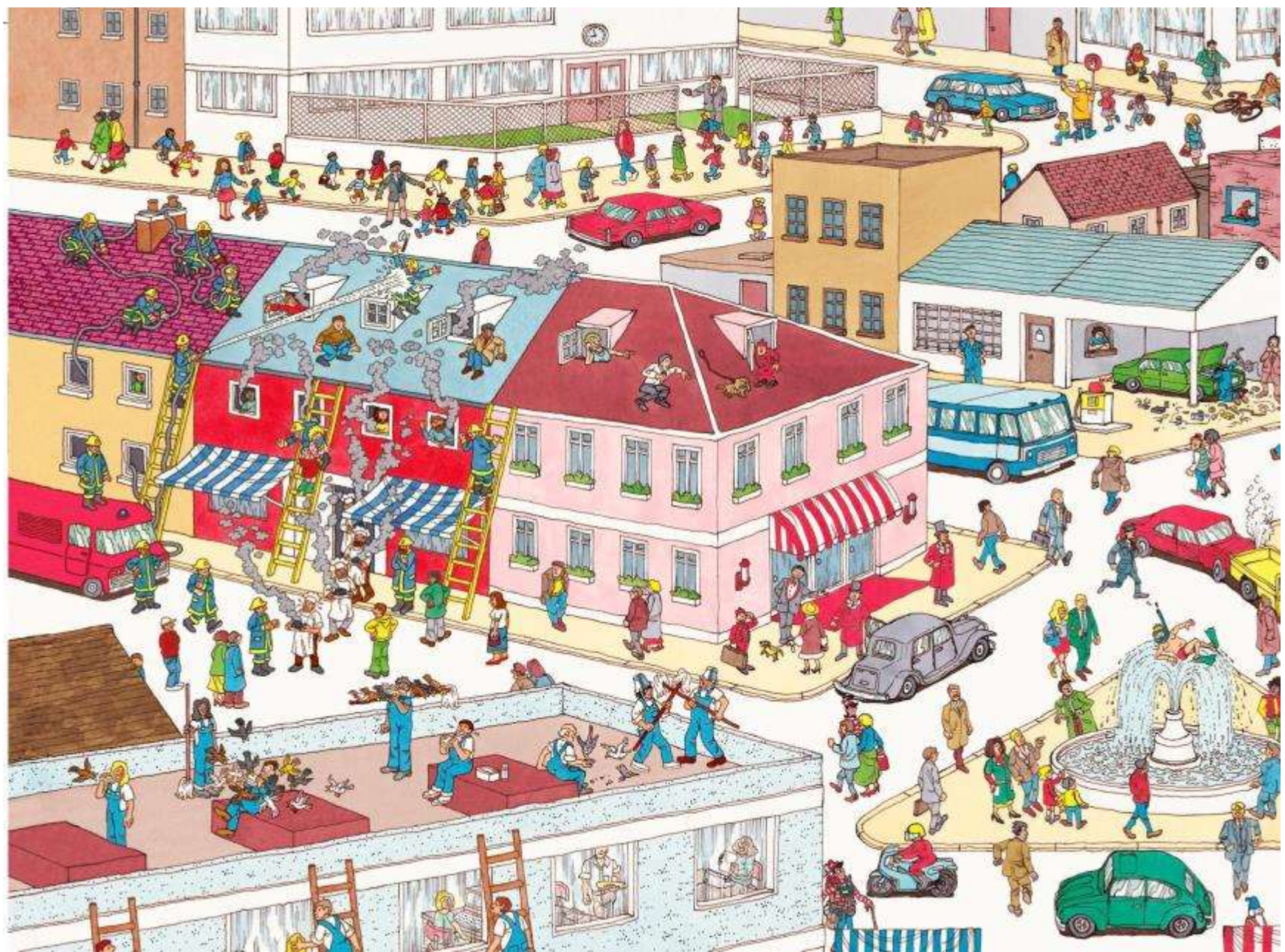




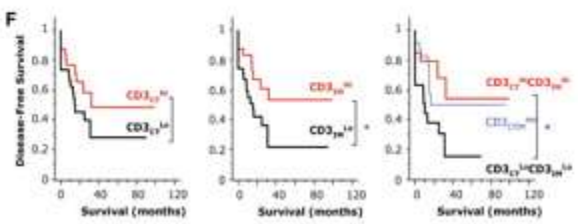
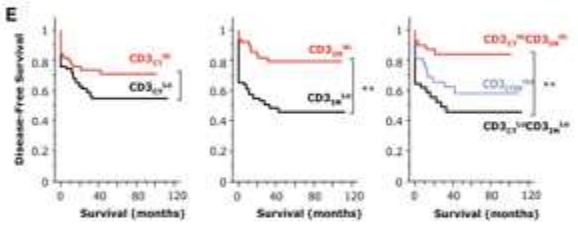
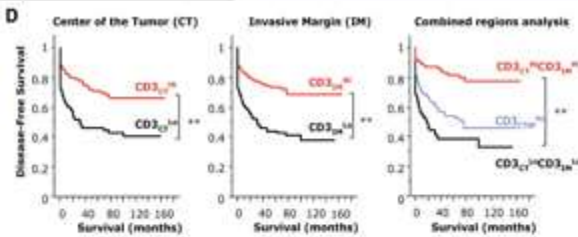
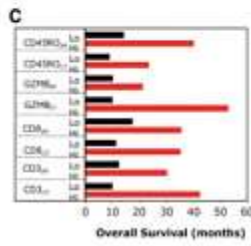
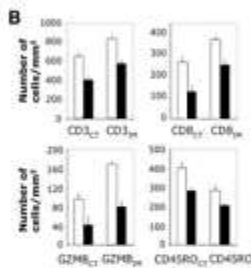
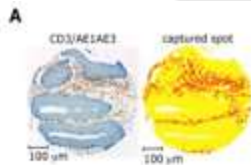
Image J

The screenshot displays the ImageJ software interface with several open windows:

- ImageJ**: The main application window with a menu bar (File, Edit, Image, Process, Analyze, Plugins, Window, Help) and a toolbar. The status bar shows "Location = (144,85), value=0,66,200".
- mri.gif (2:1)**: A grayscale MRI brain scan with a yellow outline tracing a specific region.
- FluorescentCells.jpg**: A multi-color fluorescence microscopy image showing green and red filaments and blue nuclei.
- 1D Gel**: A grayscale image of a 1D gel electrophoresis pattern with a yellow vertical line indicating a lane.
- blobs.gif**: A grayscale image with red blobs representing segmented objects.
- Drawing...**: A drawing window showing the segmented blobs from the previous window, each labeled with a red number from 1 to 6.
- Results**: A window displaying a table of measurements for the six segmented objects.

File	Area	Mean	Major	Minor	Angle
1	425	195.95	28.02	19.31	71.22
2	426	201.84	31.33	17.31	17.59
3	676	198.99	35.72	24.10	166.25
4	361	197.21	23.70	19.39	172.83
5	610	189.72	46.20	16.81	64.39
6	641	192.62	39.75	20.53	122.64

Immunoscore



roach for cancer



tegrative Cancer Immunology
rance



News

July, 2014 Natural and therapy-induced anticancer immunosurveillance: the Immunoscore, Paris, France

January, 2014 Tumor immunology symposium: The Immunoscore in cancer, Doha, Qatar

Image Analysis Benefits

- **Better accuracy (more precise measurements)**
- **Standardization (more reproducible results)**
- **Automation (reduce time consumption for pathologists)**
- **Enhance efficiency (triage cases - weed out negative cases)**
- **CAD (help pathologists find, diagnose & grade cancer)**
- **Enable Big Data approach (images for biomarker discovery)**



Conclusions

- ❑ **Changes in workflow can be significant and histology labs require additional staff to manage a digital workflow**
- ❑ **Scanner reliability may impact workflow continuity and redundancy may be costly**
- ❑ **LIS Integration and computer assisted diagnosis will be the game changers in digital pathology enhancing diagnosis and speed**
- ❑ **Telepathology is not as easy as it looks...**
- ❑ **Imaging Analysis adds another use case for digital pathology**



Questions and Answers



Douglas J. Hartman MD

hartmandj@upmc.edu