Global Engage

5TH DIGITAL PATHOLOGY & AI CONGRESS: EUROPE

LONDON, UK

6-7 December 2018

Unlash the Power of Digital Pathology and Artificial Intelligence for Precision Medicine

Marilyn Bui, MD, PhD

About the Presenter

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Marilyn M. Bui | Moffitt Cancer Center
https://moffitt.org/providers/marilyn-bui/

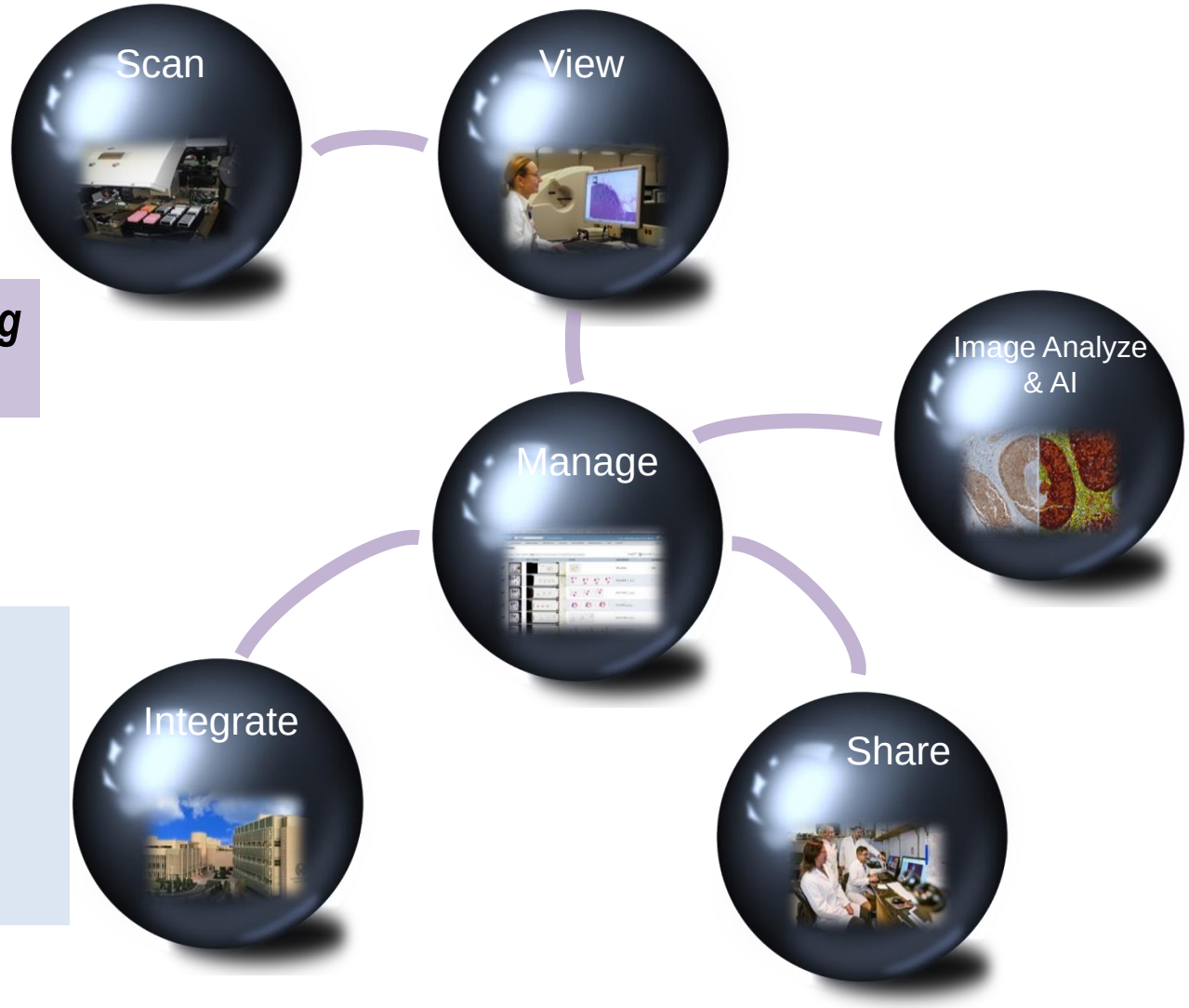
@DrBuiPathology

- Senior Member/professor of Pathology, Scientific Director of Analytic Microscopy Core, President of Medical Staff and Cytopathology Fellowship Program Director at the Moffitt Cancer Center https://moffitt.org in Tampa, Florida
- Chair of the College of American Pathologists (CAP) www.cap.org/ Guidelines Committee Expert Panel for Quantitative Image Analysis of HER2 Immunohistochemistry for Breast Cancer. Vice chair of the CAP Digital Pathology Committee
- President-elect of the Digital Pathology Association https://digitalpathologyassociation.org/

Objectives

- Review of the revolution of digital pathology (DP) and its impact on precision medicine
- Discuss lessons learned and challenges
- Looking forward to future opportunities and collaboration

Digital Pathology (DP)

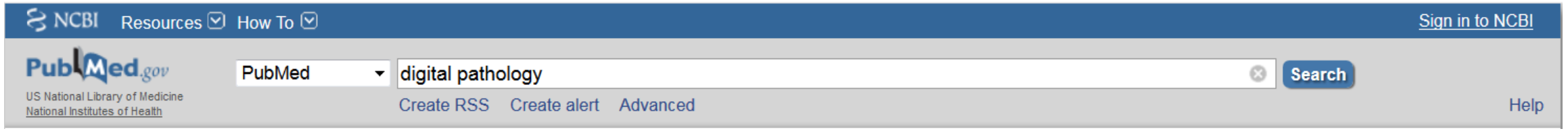


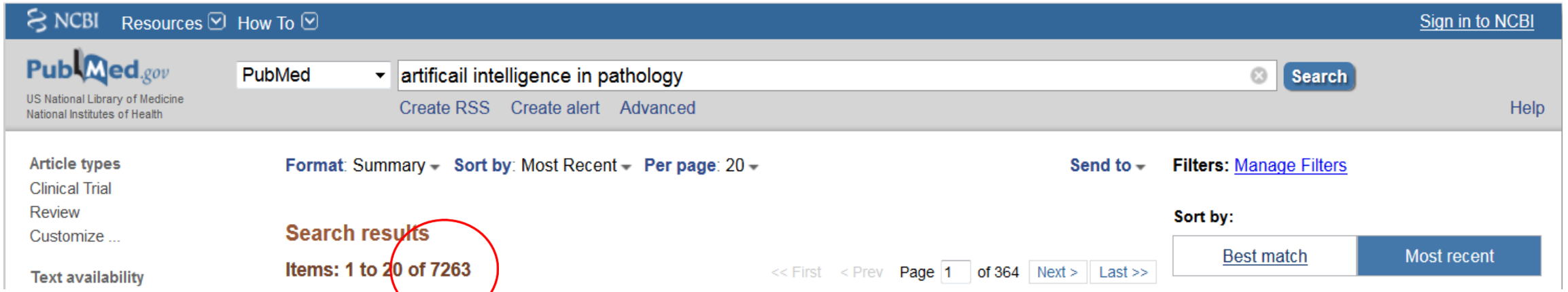
One of the most promising fields of digital medicine

- ***Integrated pathology informatics***
- ***Transform pathology data into clinically actionable knowledge***

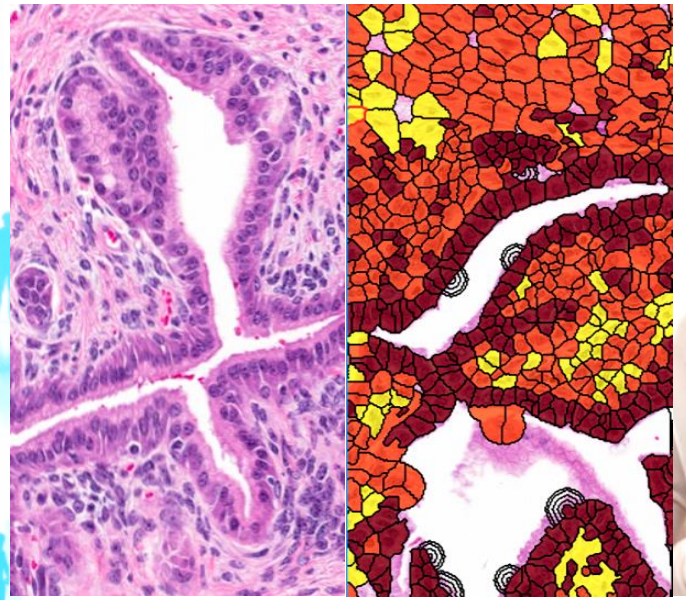
- ***Connectivity & accessibility***
- ***Image analysis, artificial intelligence and automation***
- ***Improved quality & efficiency***

Digital Pathology & Artificial Intelligence





A patient's medical journey begins with their diagnosis…



Pathologists are Leaders in Precision Medicine

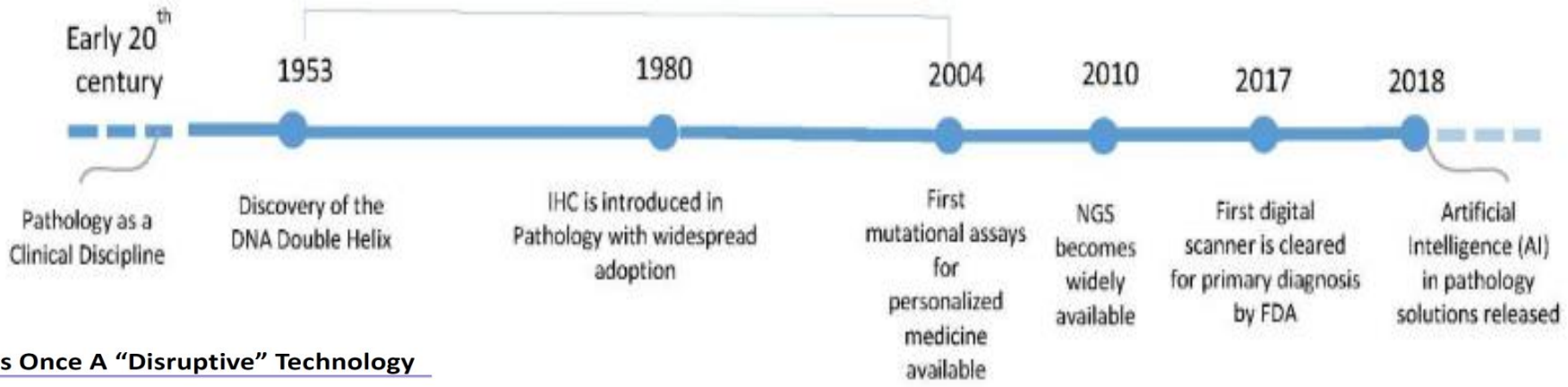
…Pathologists provide <u>forecast of</u>

Diagnosis

Prognosis

& Prediction of therapeutic response

Artificial Intelligence - The Third Revolution in Pathology



The Microscope Was Once A "Disruptive" Technology

"The use of the microscope in pathological investigations is an art so difficult that none but those who have especially cultivated it (and for a long time) can depend on it for correctness. On this account, it can never become employed in ordinary practice."

Alfred Stillé, 1848 – *Elements of General Pathology*

Courtesy Dr. Andy Evans

Artificial Intelligence - The Third Revolution in Pathology

Manuel Salto-Tellez, Perry Maxwell, Peter Hamilton

First published: 01 October 2018 | https://doi.org/10.1111/his.13760

Artificial Intelligence - The Third Revolution in Pathology

- Hereby we stress the importance of certified **pathologists** having learned from the experience of previous revolutions and be willing to accept such disruptive technologies, ready to innovate and **actively engage** in the **creation, application and validation of technologies** and **oversee** the safe introduction of AI into diagnostic practice.

Histopathology

Artificial Intelligence - The Third Revolution in Pathology

Manuel Salto-Tellez ✉, Perry Maxwell, Peter Hamilton

First published: 01 October 2018 | https://doi.org/10.1111/his.13760

DP & AI in Precision Medicine Delivery

Application

- Detection
- Quantification
- Classification
- Prognosis
- Prediction

Materials & Methods

- HE, special stain, IHC, fluorescence, live cells, etc.
- Image analysis through machine learning, deep learning/artificial intelligence

Desirable Results

- Improved quality & efficiency
- Pathology data → clinically actionable knowledge

Digital pathology is not just the transfer of histopathological slides into digital representations. The combination of different data sources (images, patient records, and *omics data) together with current advances in artificial intelligence/machine learning enable to make novel information accessible and quantifiable to a human expert, which is not yet available and not exploited in current medical settings.

Augmented Pathologist

Explainable Artificial Intelligence in Digital Pathology by Holzinger, Malle, Kieseberg, Roth, Muller, Reihs, Zatloukal

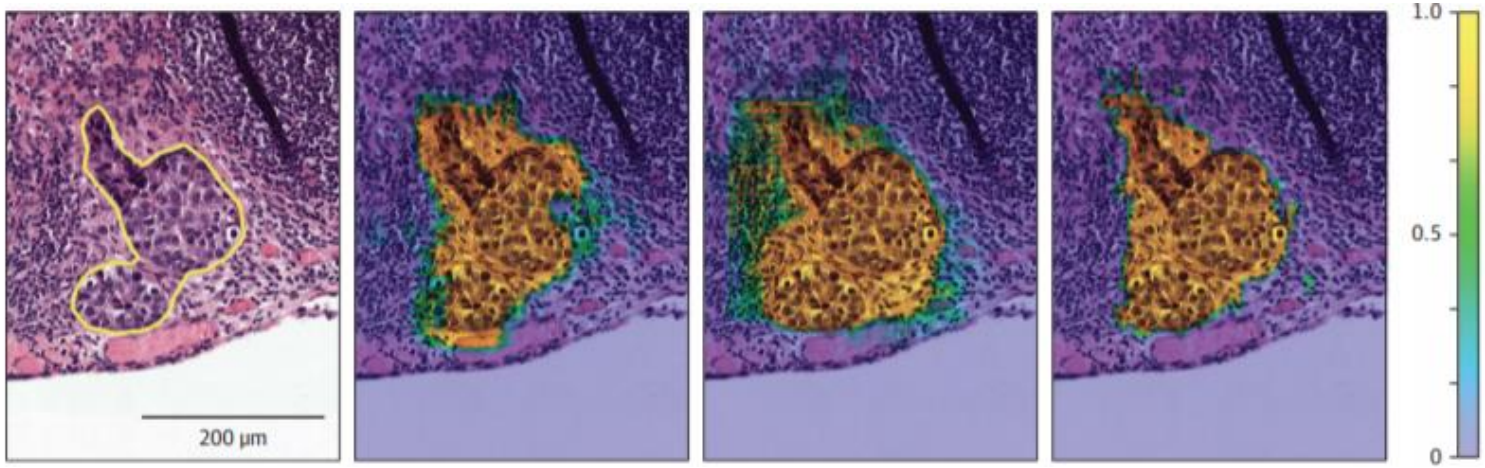
https://arxiv.org/pdf/1712.06657.pdf

Deep Learning in Breast Pathology

Automated classification of patients with metastatic breast cancer in lymph node

1. Babak Ehteshami Bejnordi, Mitko Veta, Paul Johannes van Diest, et al. and the CAMELYON16 Consortium. **Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer.** JAMA. 2017;318(22):2199–2210. DOI: 10.1001/jama.2017.14585

2. Peter Bandi, Oscar Geessink, Quirine Manson, et al. **From detection of individual metastases to classification of lymph node status at the patient level: the CAMELYON17 challenge.** IEEE-TMI (Early Access) DOI: 10.1109/TMI.2018.2867350



Downloading the data set

CAMELYON16 and CAMELYON17 data sets are open access and shared publicly on **GigaScience**, **Google Drive** and on **Baidu Pan.**

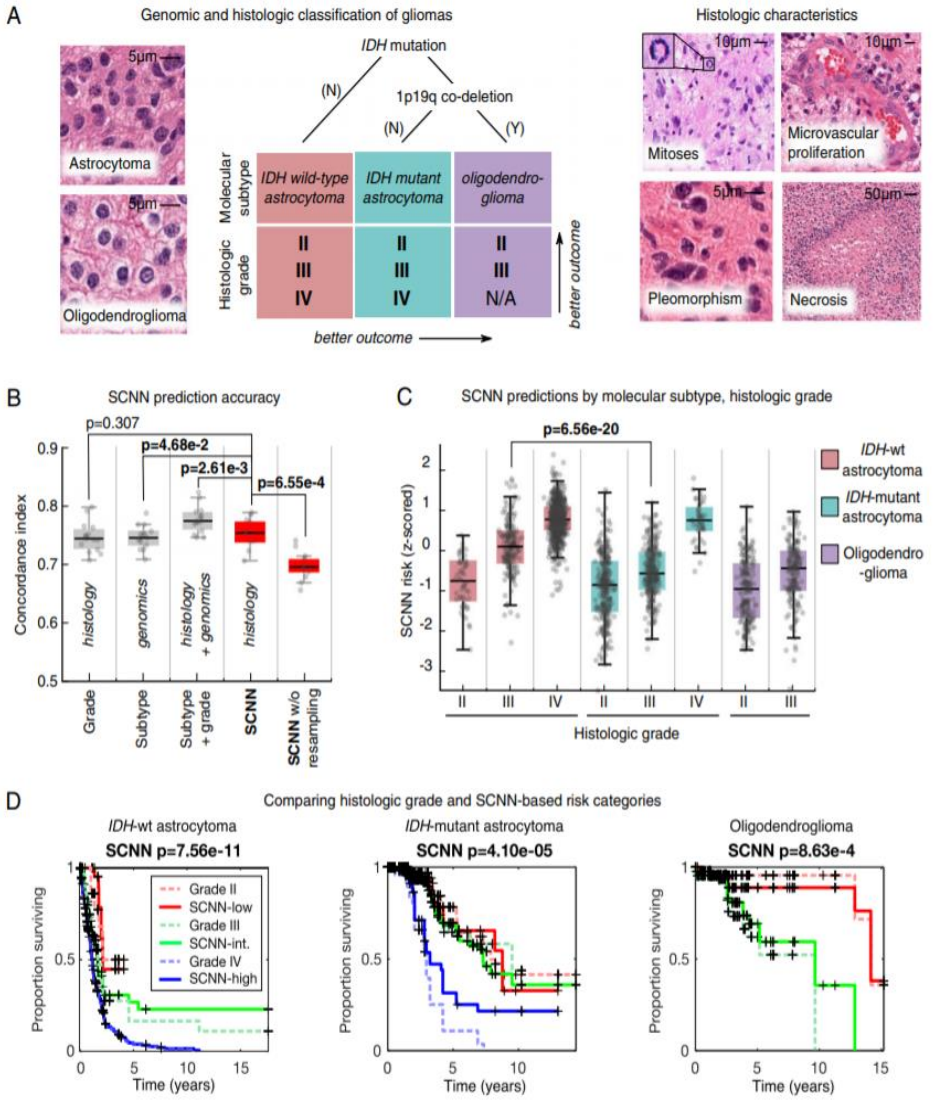
Prognostication Criteria for Diffuse Gliomas

Predicting cancer outcomes from histology and genomics using convolutional networks

Pooya Mobadersany[a], Safoora Yousefi[a], Mohamed Amgad[a], David A. Gutman[b], Jill S. Barnholtz-Sloan[c], José E. Velázquez Vega[d], Daniel J. Brat[e], and Lee A. D. Cooper[a,f,g,1]

www.pnas.org/cgi/doi/10.1073/pnas.1717139115 E2970–E2979 | PNAS | vol. 115 | no. 13

- A deep learning approach for learning survival directly from histological images and created a unified framework for integrating histology and genomic biomarkers for predicting time-to-event outcomes.
- Systematically evaluated the prognostic accuracy of this approaches in the context of the current clinical standard based on genomic classification and histologic grading of gliomas.
- **This approach rivals or exceeds the accuracy of highly trained human experts in predicting survival.**
- Improving the accuracy and objectivity of grading will directly impact patient care.



Deep Learning in Lung Cancer

nature medicine

ARTICLES

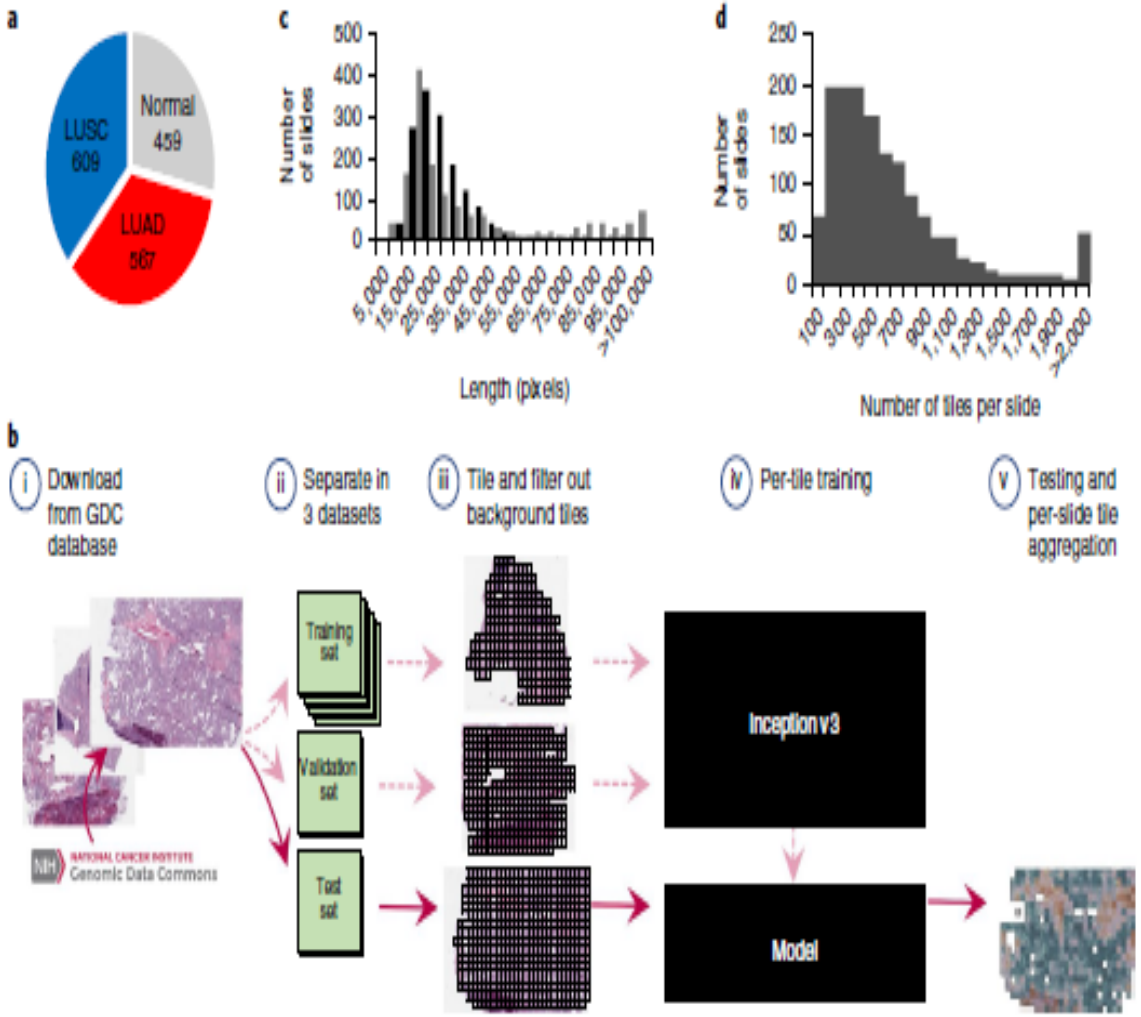
https://doi.org/10.1038/s41591-018-0177-5

NATURE MEDICINE | VOL 24 | OCTOBER 2018 | 1559–1567 | www.nature.com/naturemedicine

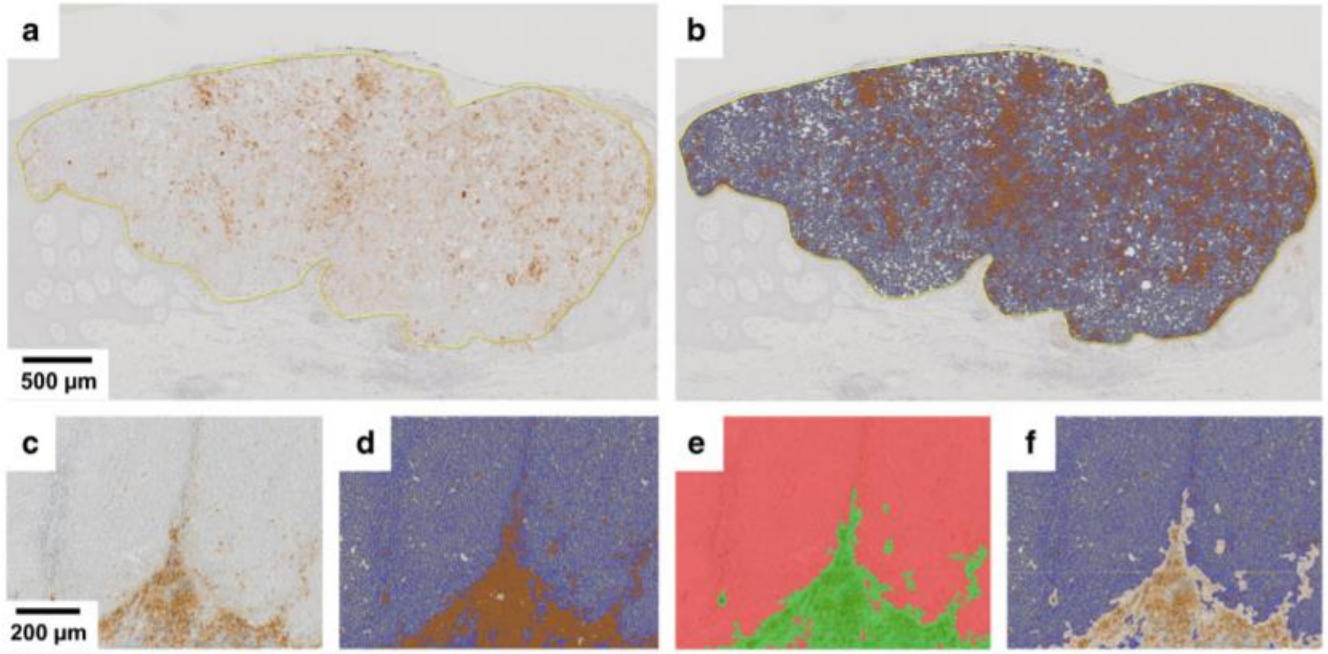
Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning

Nicolas Coudray[1,2,9], Paolo Santiago Ocampo[3,9], Theodore Sakellaropoulos[4], Navneet Narula[3], Matija Snuderl[3], David Fenyö[5,6], Andre L. Moreira[3,7], Narges Razavian[8*] and Aristotelis Tsirigos[1,3*]

Visual inspection of histopathology slides is one of the main methods used by pathologists to assess the stage, type and subtype of lung tumors. Adenocarcinoma (LUAD) and squamous cell carcinoma (LUSC) are the most prevalent subtypes of lung cancer, and their distinction requires visual inspection by an experienced pathologist. In this study, we trained a deep convolutional neural network (inception v3) on whole-slide images obtained from The Cancer Genome Atlas to accurately and automatically classify them into LUAD, LUSC or normal lung tissue. The performance of our method is comparable to that of pathologists, with an average area under the curve (AUC) of 0.97. Our model was validated on independent datasets of frozen tissues, formalin-fixed paraffin-embedded tissues and biopsies. Furthermore, we trained the network to predict the ten most commonly mutated genes in LUAD. We found that six of them—STK11, EGFR, FAT1, SETBP1, KRAS and TP53—can be predicted from pathology images, with AUCs from 0.733 to 0.856 as measured on a held-out population. These findings suggest that deep-learning models can assist pathologists in the detection of cancer subtype or gene mutations. Our approach can be applied to any cancer type, and the code is available at https://github.com/ncoudray/DeepPATH.



Assessment of PD-L1 Expression & Immune Cell Infiltrates



Virchows Archiv
https://doi.org/10.1007/s00428-018-2485-z

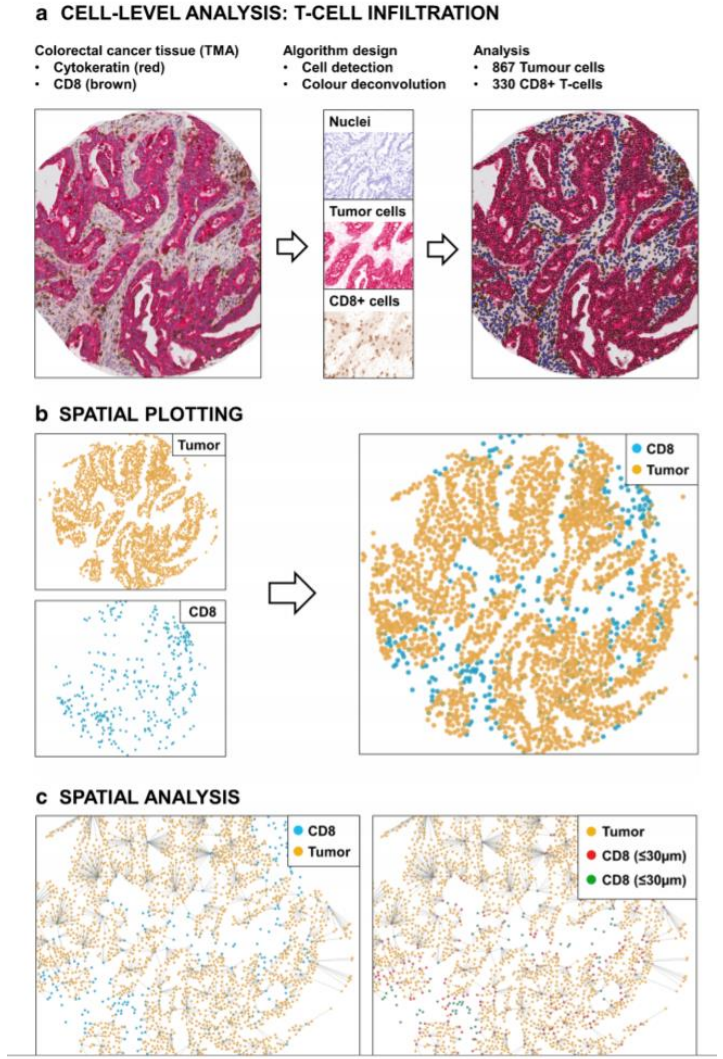
REVIEW ARTICLE

CrossMark

Precision immunoprofiling by image analysis and artificial intelligence

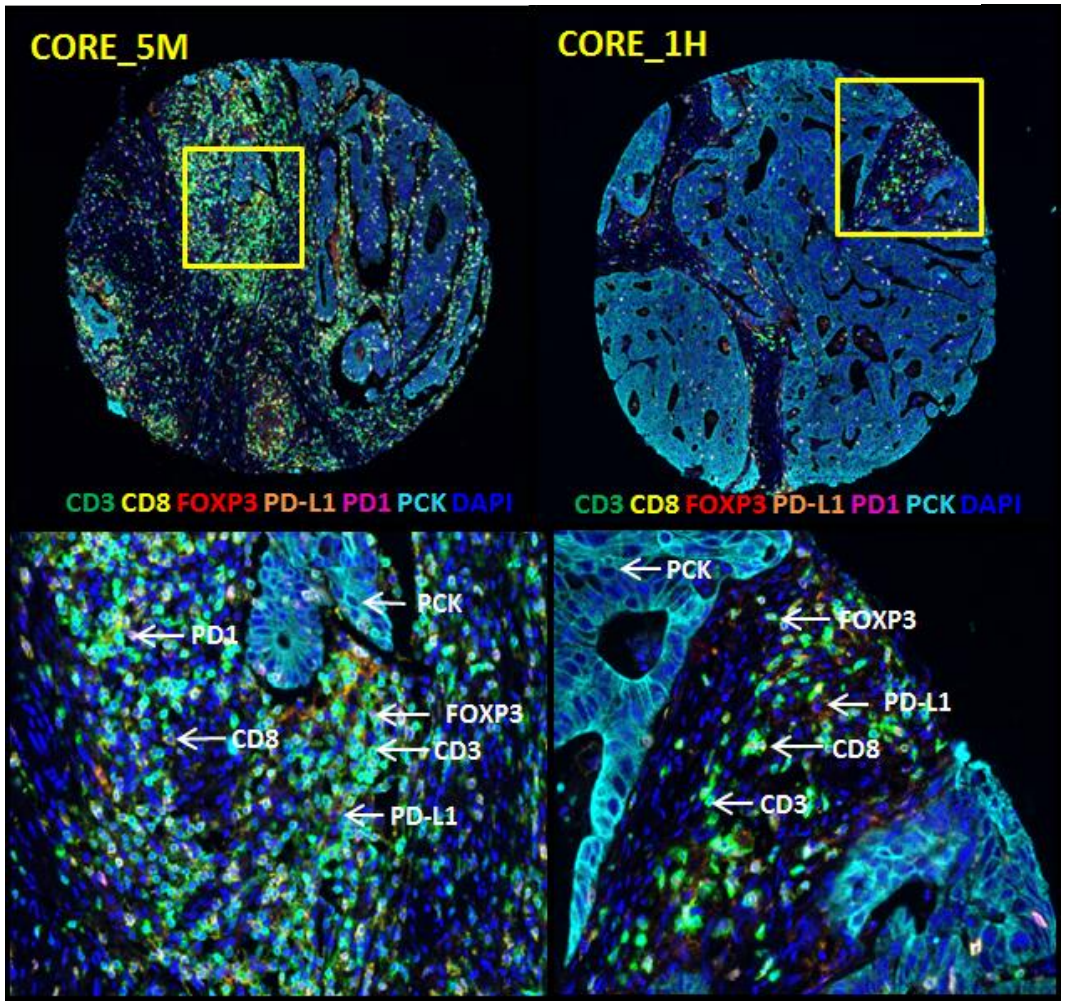
Viktor H. Koelzer[1,2] · Korsuk Sirinukunwattana[3] · Jens Rittscher[3,4,5] · Kirsten D. Mertz[6]

Received: 15 May 2018 / Revised: 6 November 2018 / Accepted: 9 November 2018

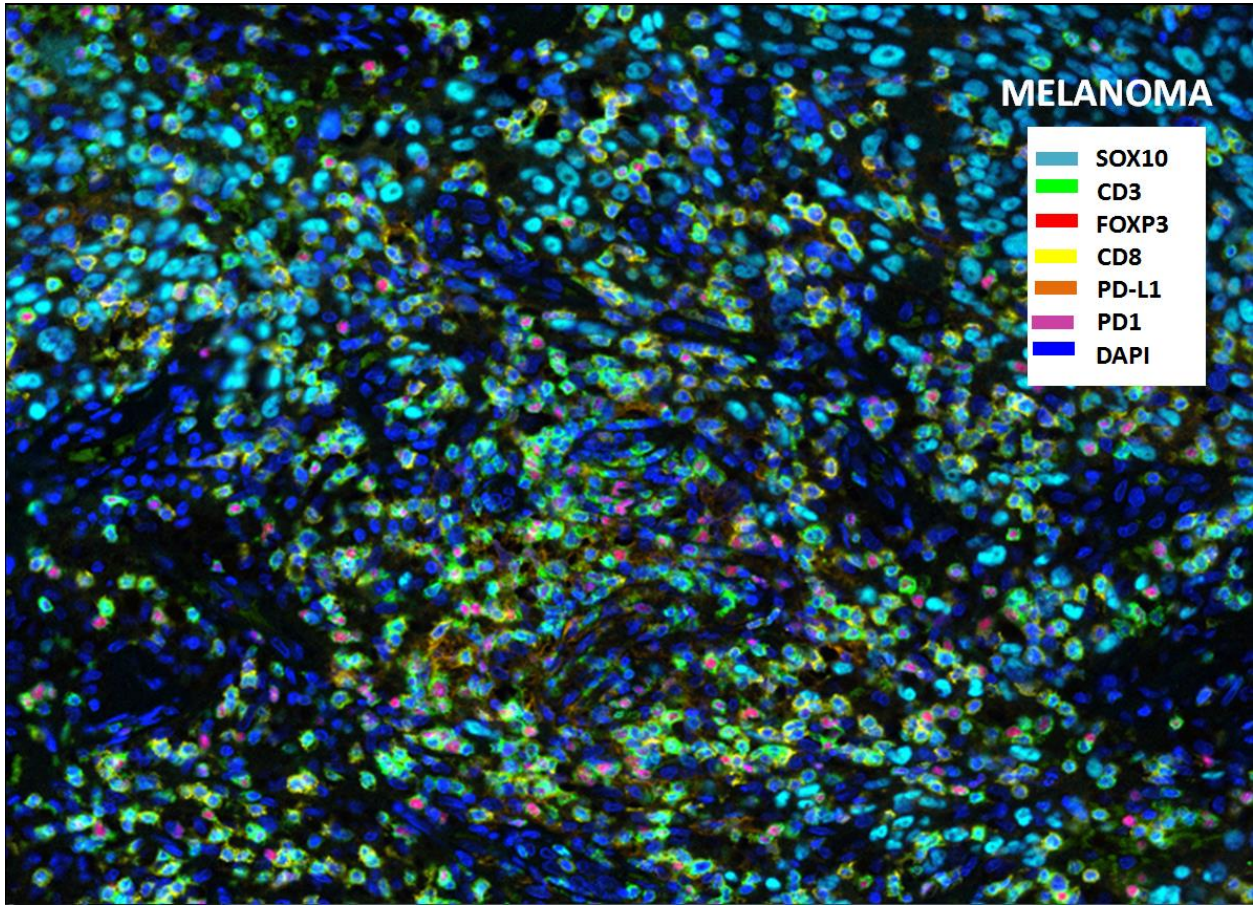


Multiplex IHC for Clinical Trials

Assessment of Immune Cells



Multiplex IHC Stained Section



Courtesy of Susan McCarthy of Moffitt Cancer Center using Vectra in a CLIA lab for clinical trials

Barriers to DP Adoption

- Regulatory
- Financial
- Technical
- Cultural

Breaking Regulatory Barriers

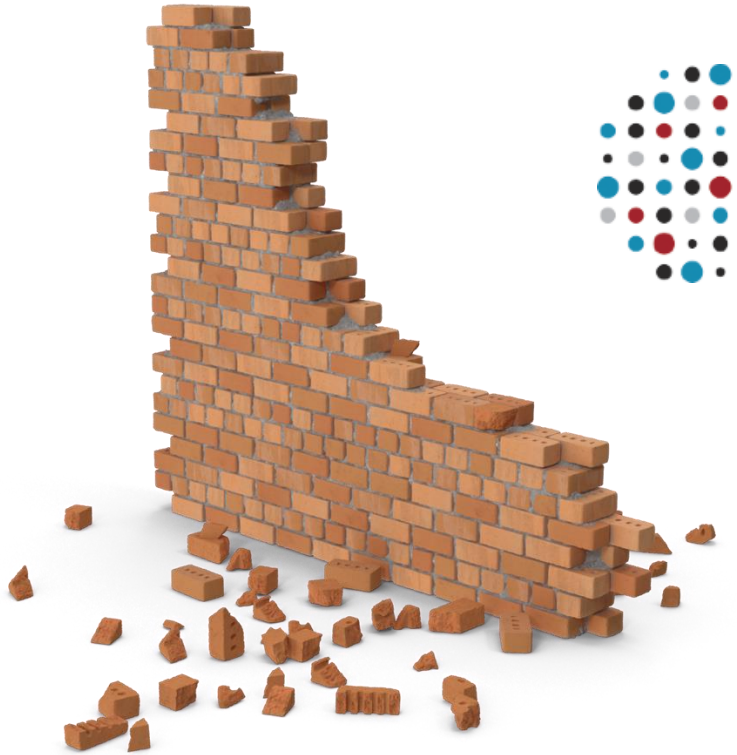
- Leading digital pathology companies have recently received **FDA approval** for whole slide imaging system for primary diagnosis in US or **CE certification** for routine pathology applications in the European Union under the In vitro diagnostic medical devices directive.

Quality and reliability of the imaging system

References:
1. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, Office of In Vitro Diagnostics and Radiological Health, Division of Molecular Genetics and Pathology MP and CB. [Internet]. Technical performance assessment of digital pathology whole slide imagingdevices; 2016. Available from: http://www.fda.gov/ downloads/MedicalDevices/DeviceRegulationandGuidance/ GuidanceDocuments/UCM435355.pdf
2. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. https:// ec.europa.eu/growth/single-market/european-standards/ harmonised-standards/iv-diagnostic-medical-devices_en.

Breaking Regulatory Barriers

- College of American Pathologists (CAP) set general guidelines on how to validate the imaging system to ensure the consistency of diagnose made by pathologists using the systems.



COLLEGE of AMERICAN PATHOLOGISTS

First step from computational pathology to clinical diagnosis

Breaking Financial Barriers

- ~ 12-13% (published) efficiency gain at pathologist level
- ~ Saving on retrieval of archived slides
- ~ Merger of departments/labs with flexible pathologist availability
- ~ Reduced turn around time changes patient pathways
  - reducing visits and in-patient time
  - better more efficient use of resources
- ~ Facilitates review improving diagnostic accuracy

J Pathol Inform

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Research Article

Can Digital Pathology Result In Cost Savings? A Financial Projection For Digital Pathology Implementation At A Large Integrated Health Care Organization

Jonhan Ho, Stefan M. Ahlers[1], Curtis Stratman[2], Orly Aridor[3], Liron Pantanowitz[4], Jeffrey L. Fine[4], John A. Kuzmishin[1], Michael C. Montalto[2], Anil V. Parwani[4]

Review

Future-proofing pathology part 2: building a business case for digital pathology

Bethany Jill Williams[1, 2], David Bottoms[3], David Clark[4], Darren Treanor[1, 2]

Breaking Technical Barriers

- Image quality
- Open software solutions
  - Open to many scanners
  - Open to many image analysis suites
- System (LIS/LIMS) integration
- Speed, file storage and IT infrastructure

Breaking Technical Barriers

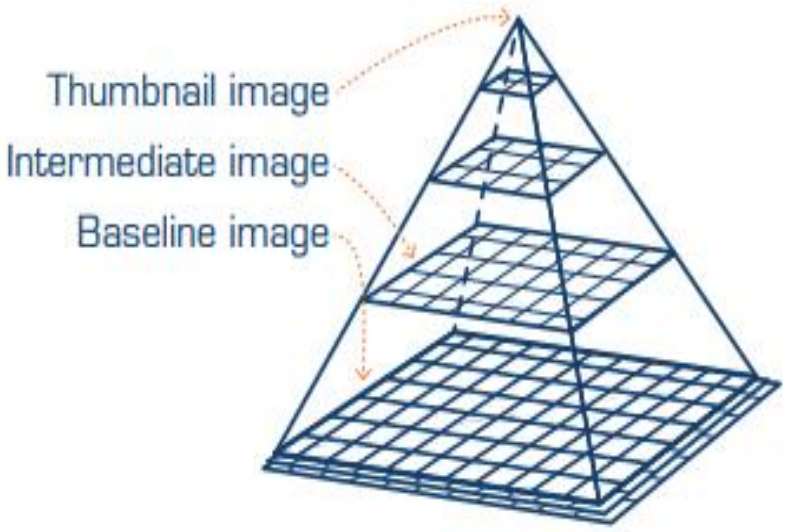
- ***Integrating the Heath Care Enterprise (IHE) Pathology and Laboratory Domain (PALM)***

  An initiative by healthcare professionals and industry to improve the way computer systems in healthcare share information; an international standards organization that bundles existing standards into profiles that solve particular medical communication problems

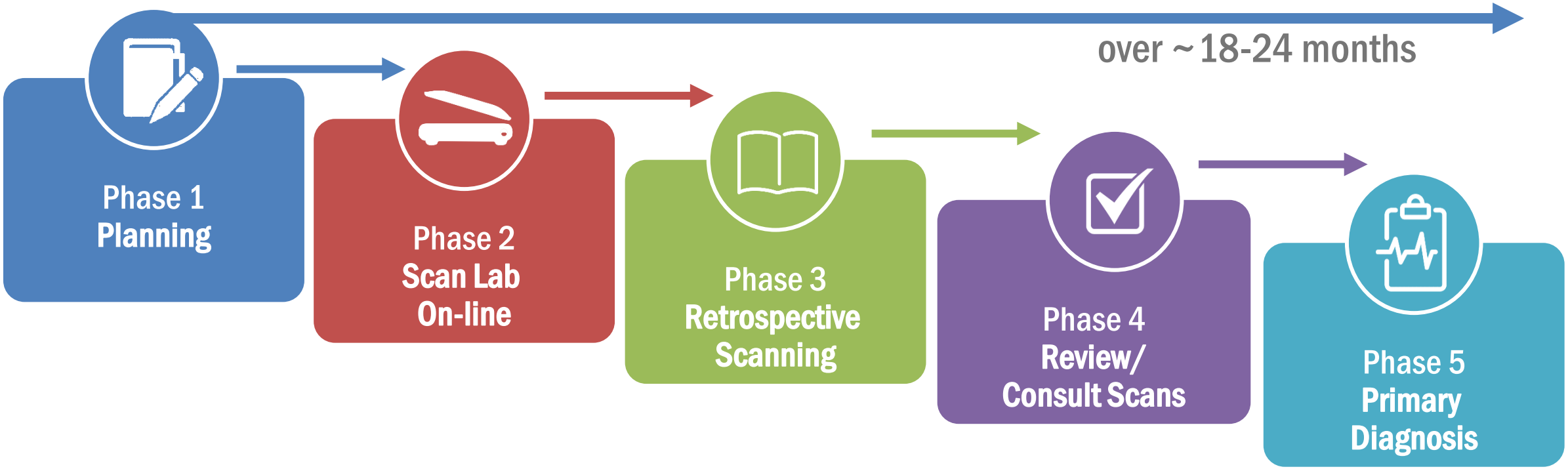
- ***Digital Imaging and Communication in Medicine (DICOM)***

  The standard file format definition and communication profile for radiological and many other medical images

- **IHE/PLAM & DICOM collaborative digital pat initiative starting in 2017 to create *interoperability for digital pathology***



Breaking Cultural Barriers



Proven Phased Adoption Strategy

Lessons Learned

Learning from early adopters who publish results

Optimizing throughput in the world's largest pathology imaging facility

Authors: Lloyd MC, Kellough D, Shanks T, Deshpande A, Singhal S, Parwani A

Sectioning Automation to Improve Quality and Decrease Costs for a High-Throughput Slide Scanning Facility

Authors: Cuddihy M, Shulgay T, Ferree L, Krueger G, Mack D, Pietryka K, Parwani A, Gill T, Lloyd MC

Computational Detection of Mitotic Figures using A Fusion of Deep Learning and Domain-Based Approaches

Authors: Harding D, Verma N, Mohammadi A, Monaco J, Lloyd MC, Tozbikian G, Li Z, Parwani A

Opportunities

Integrated Pathology Informatics Enables High-Quality Personalized and Precision Medicine

Digital Pathology and Beyond

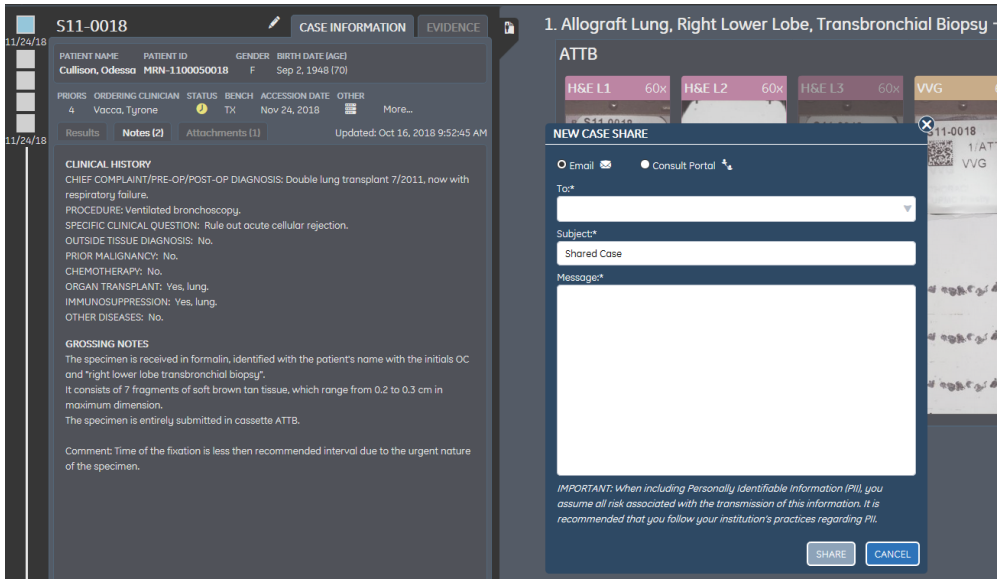
Zoya Volynskaya, PhD; Hung Chow, BSc, MLT; Andrew Evans, MD, PhD; Alan Wolff, MLT; Cecilia Lagmay-Traya; Sylvia L. Asa, MD, PhD

Arch Pathol Lab Med. 2018;142:369–382; doi: 10.5858/ arpa.2017-0139-OA

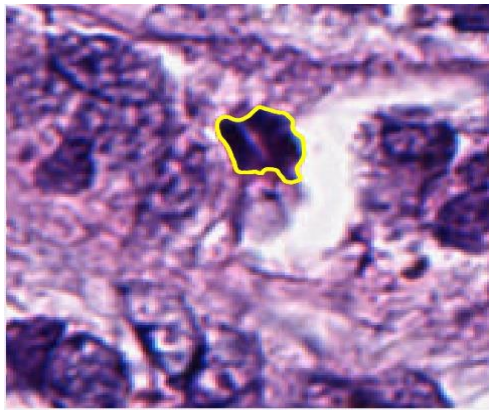
- The digitization of pathology in WSI will provide a huge source of data that will ultimately lead to computer-assisted diagnostics.
- The integration of all the various data obtained in laboratories is the future of pathology.
- The pathologist is a trained physician who has expertise in making the correct diagnosis, determining the likely prognosis, and, with the additional information derived from multiple tests, providing a consultative opinion about treatment approaches.
- As laboratory testing plays an increasing role in the era of personalized medicine, the role of the pathologist increases, and the need for consolidated interpretive reporting becomes critical.
- The depth of knowledge required to integrate these various ancillary technologies demands the insight of subspecialty pathology and promotes a critical role for pathologists in the implementation of precision medicine.

Opportunities

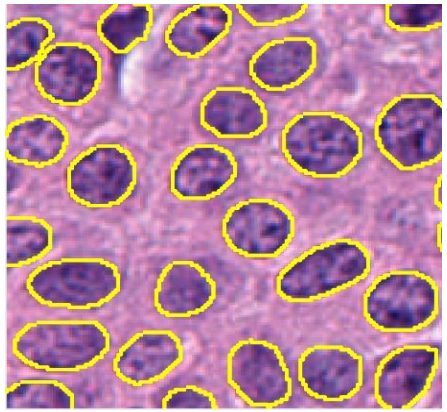
- Workflow efficiency; review current & priors cases instantly
- Telepathology and case sharing



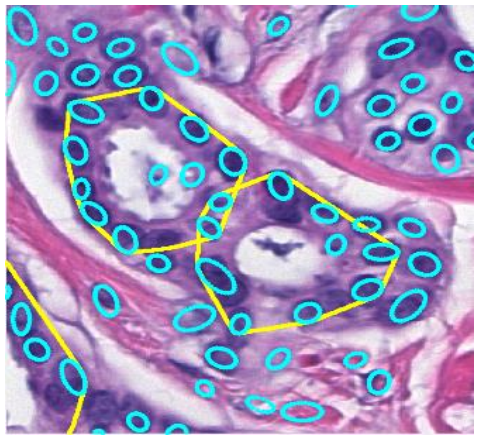
- Image analysis



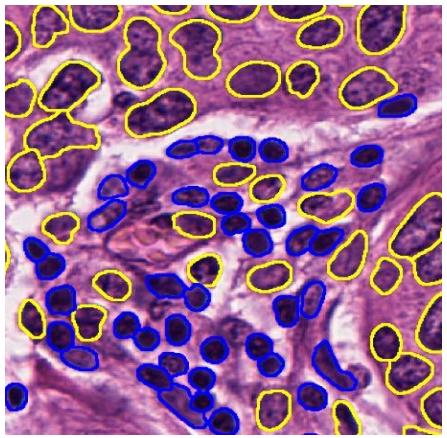
Mitosis analysis



Nuclear analysis



Tubule analysis



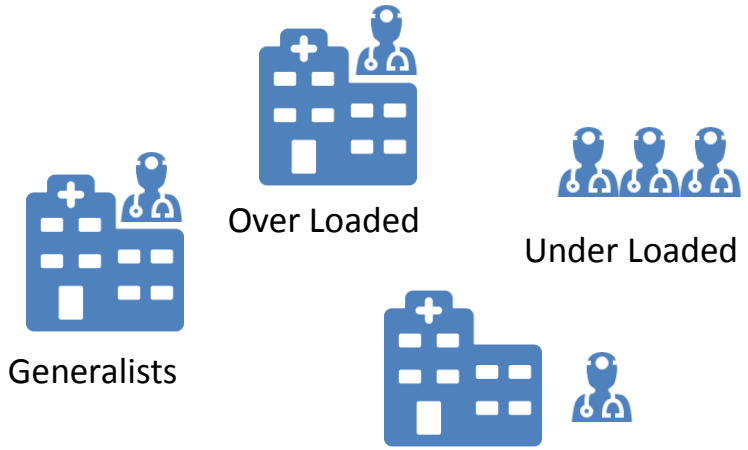
TIL analysis

Lloyd, Monaco ASCO 2018

Opportunities

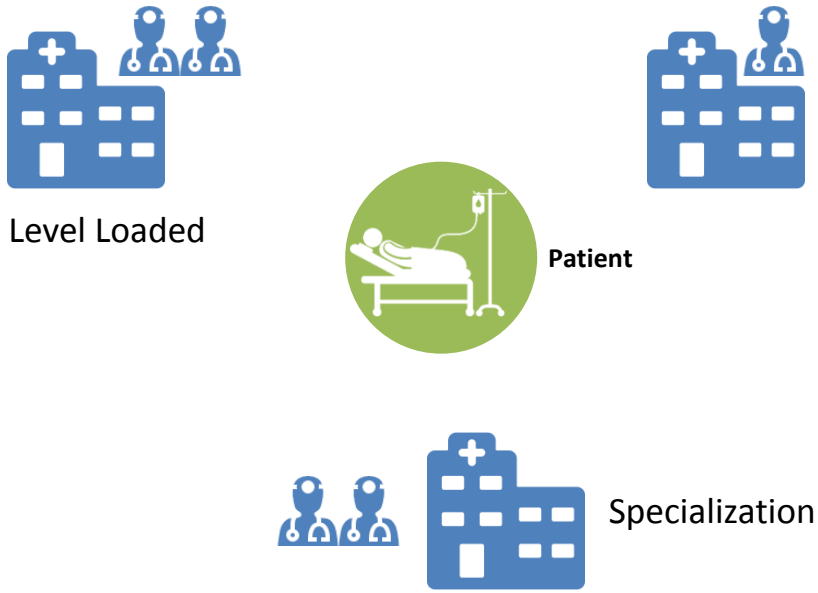
Integrated Digital Pathology Solutions

FROM PHYSICAL WORKFLOW



Dispersed, generalist

TO DIGITAL WORKFLOW



Optimised & patient centric

What's next?

Developing value-added tools

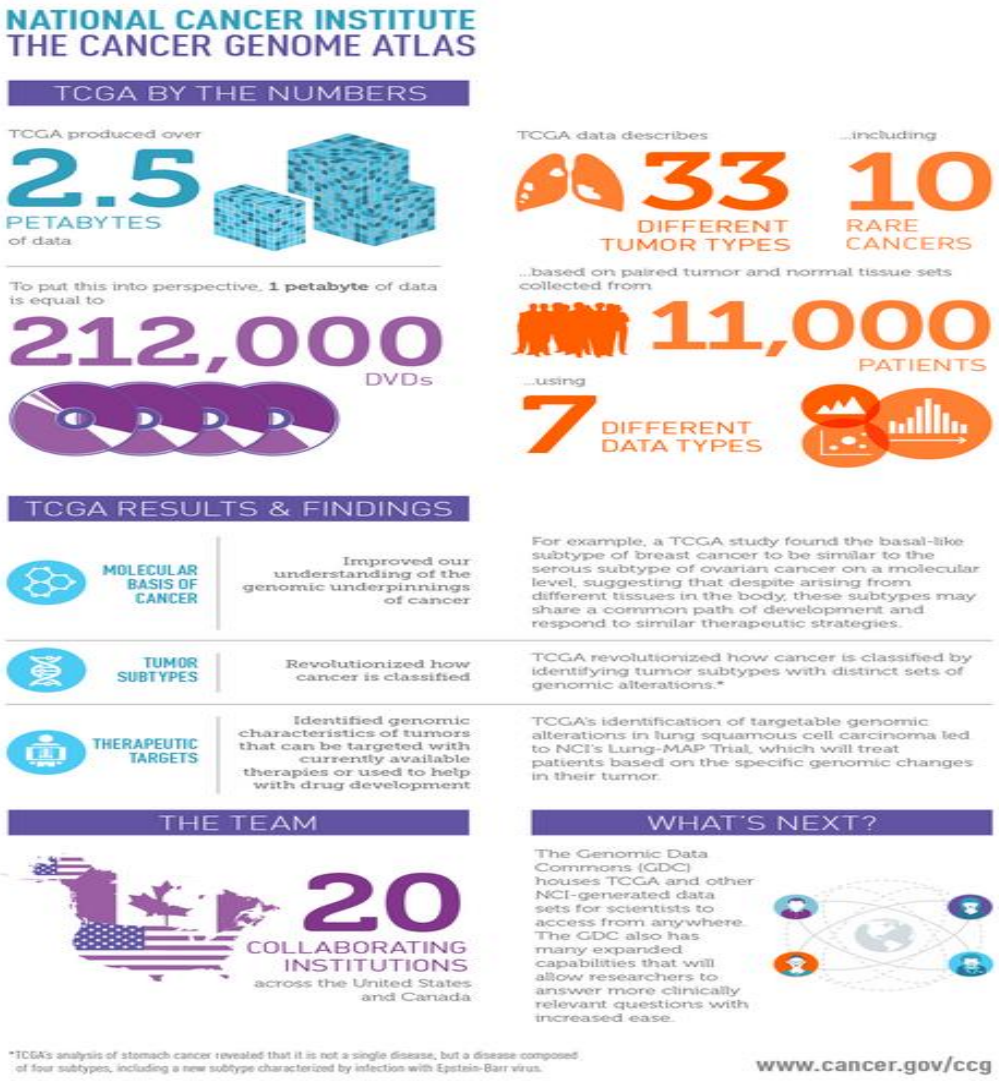
- Cancer finding tool
- Region of interest finder tool
- Mitotic count tool
- Pre-screening of IHC slides with quantitative scores
- Bug finder (e.g. mycobacteria)
- More accurate, faster measurements
- Tumor grading tools
- Application of image analysis to routine practice
- Image capture and export to the report

Opportunities: The Cancer Genome Atlas

The Cancer Genome Atlas (TCGA)

- A collaboration between the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI).
- **Free public dataset** with comprehensive, multi-dimensional maps of the key genomic changes in 33 types of cancer.
- Comprising more than two petabytes of genomic data.
- This **genomic information** helps the cancer research community to improve the prevention, diagnosis, and treatment of cancer.

https://wiki.nci.nih.gov/display/TCGA/Introduction+to+TCGA
http://cancer.digitalslidearchive.net/



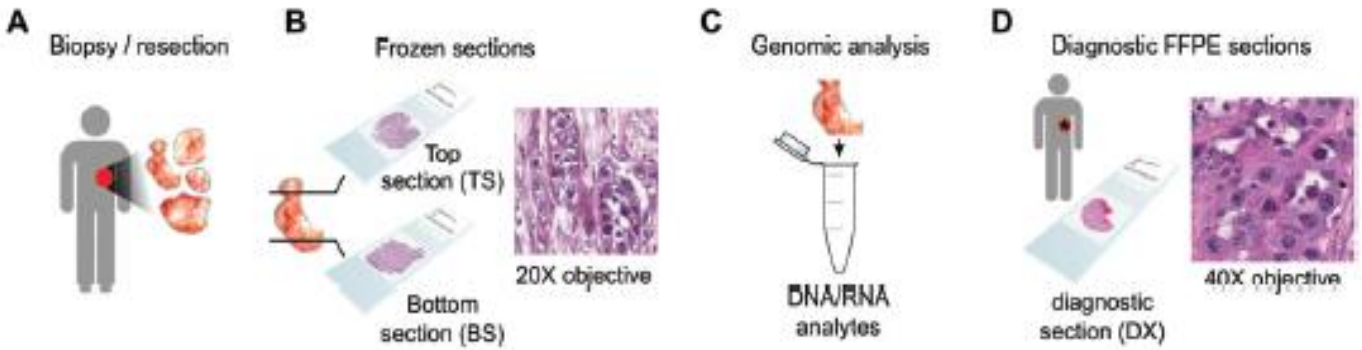
Opportunities: TCGA Data

Journal of Pathology
J Pathol 2018; **244:** 512–524
Published online 22 February 2018 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/path.5028

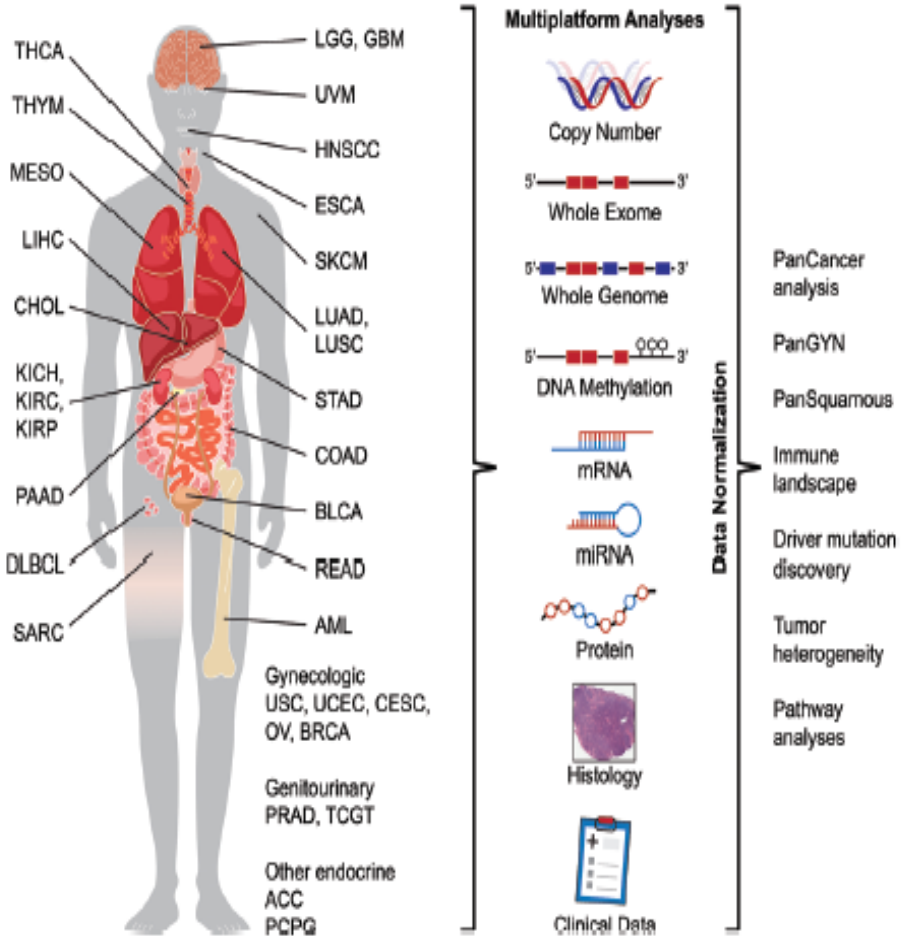
INVITED REVIEW

PanCancer insights from The Cancer Genome Atlas: the pathologist's perspective

Lee AD Cooper[1,2,3†], Elizabeth G Demicco[4†], Joel H Saltz[5], Reid T Powell[6], Arvind Rao[7,8] and Alexander J Lazar[9*]

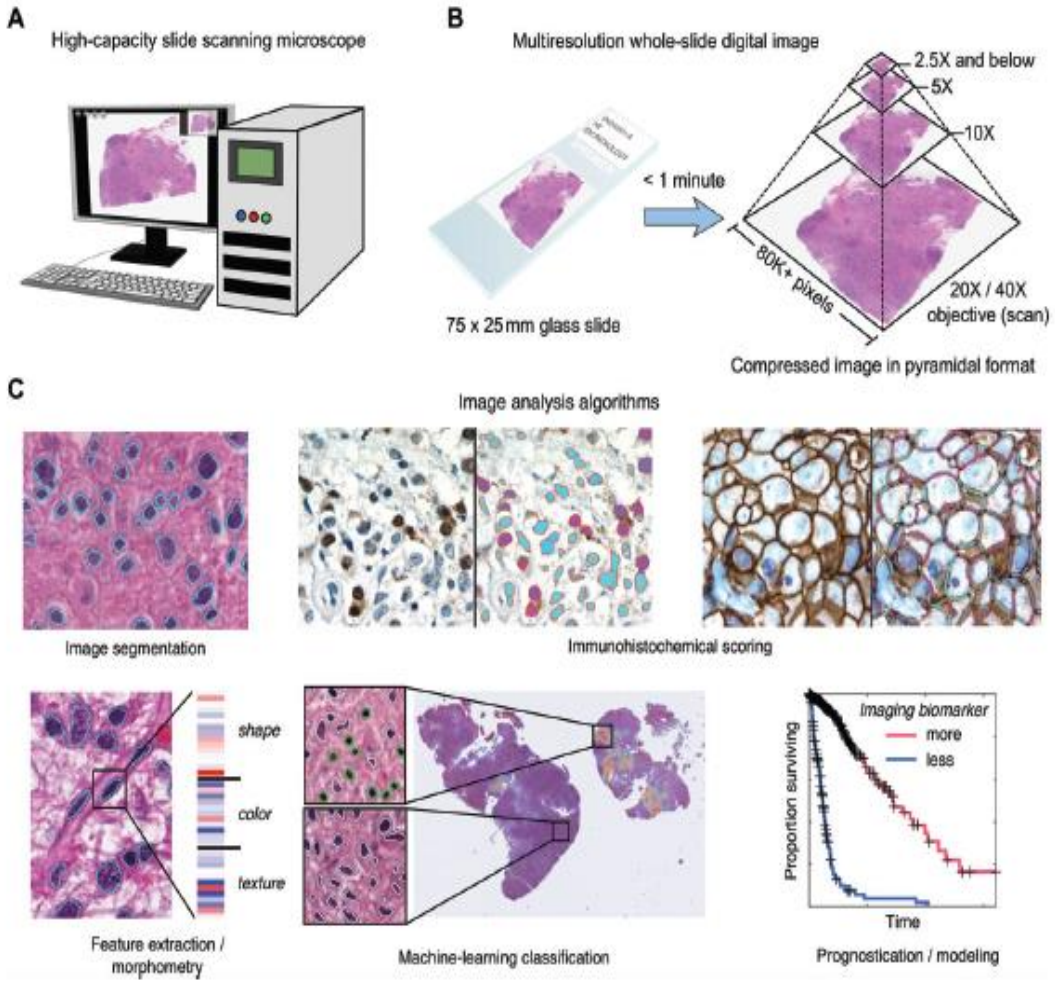


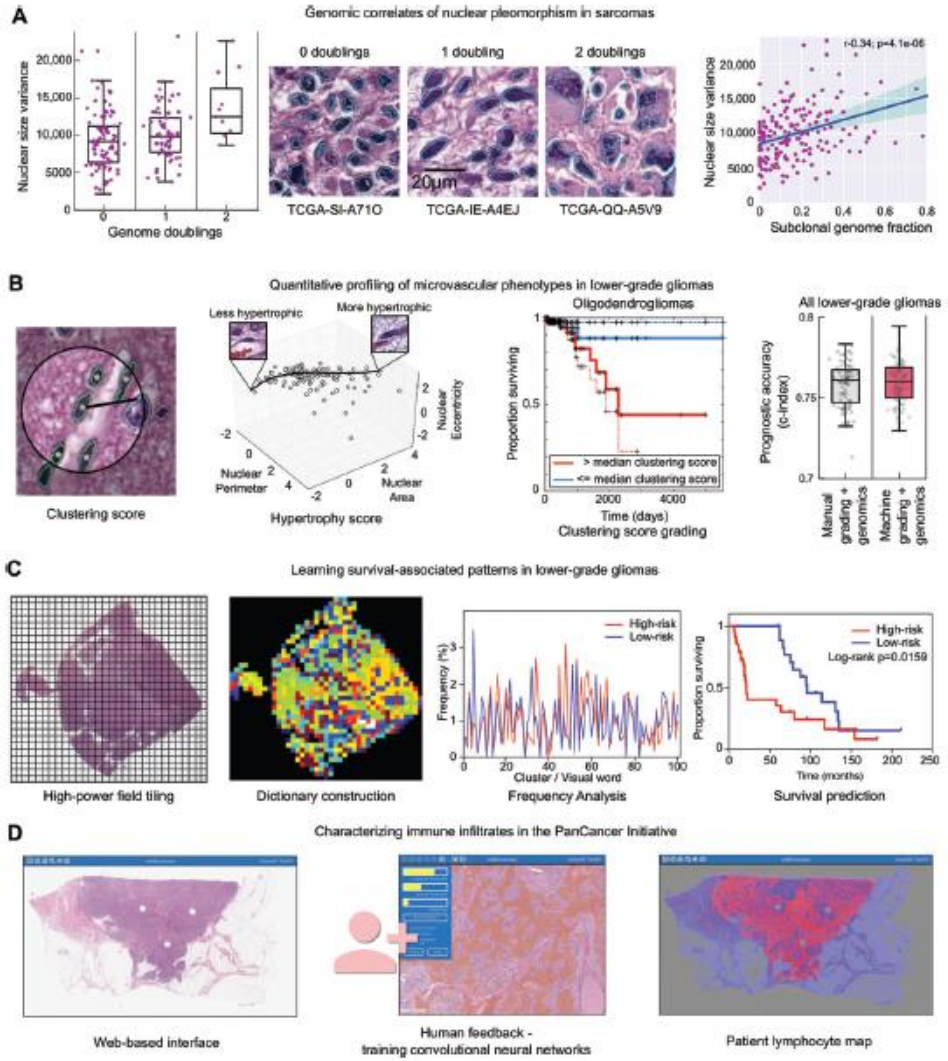
TCGA Tissue Procurement



TCGA Overview

Opportunities: TCGA Image Analysis

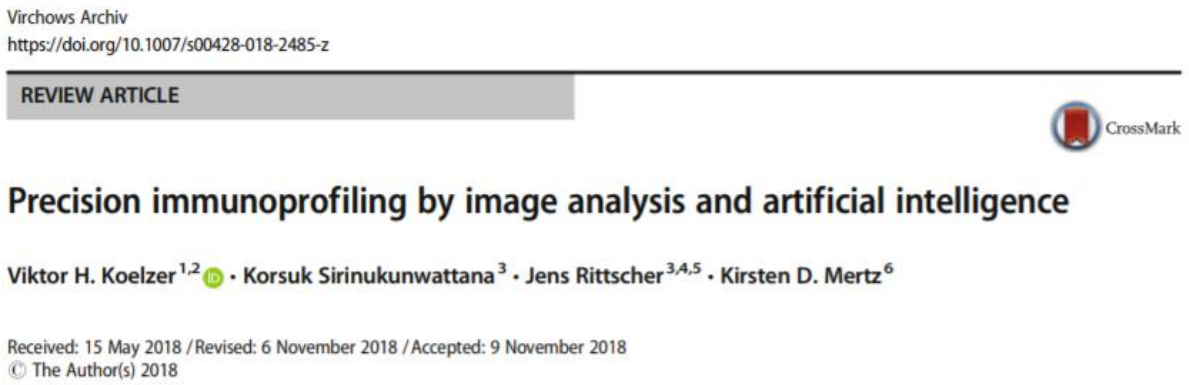




Future Collaborations

Future clinical demands will be best met by

- Dedicated research at the interface of pathology and bioinformatics, supported by professional societies
- Integration of data sciences and digital image analysis in the professional education of pathologists.



Virchows Archiv
https://doi.org/10.1007/s00428-018-2485-z

REVIEW ARTICLE

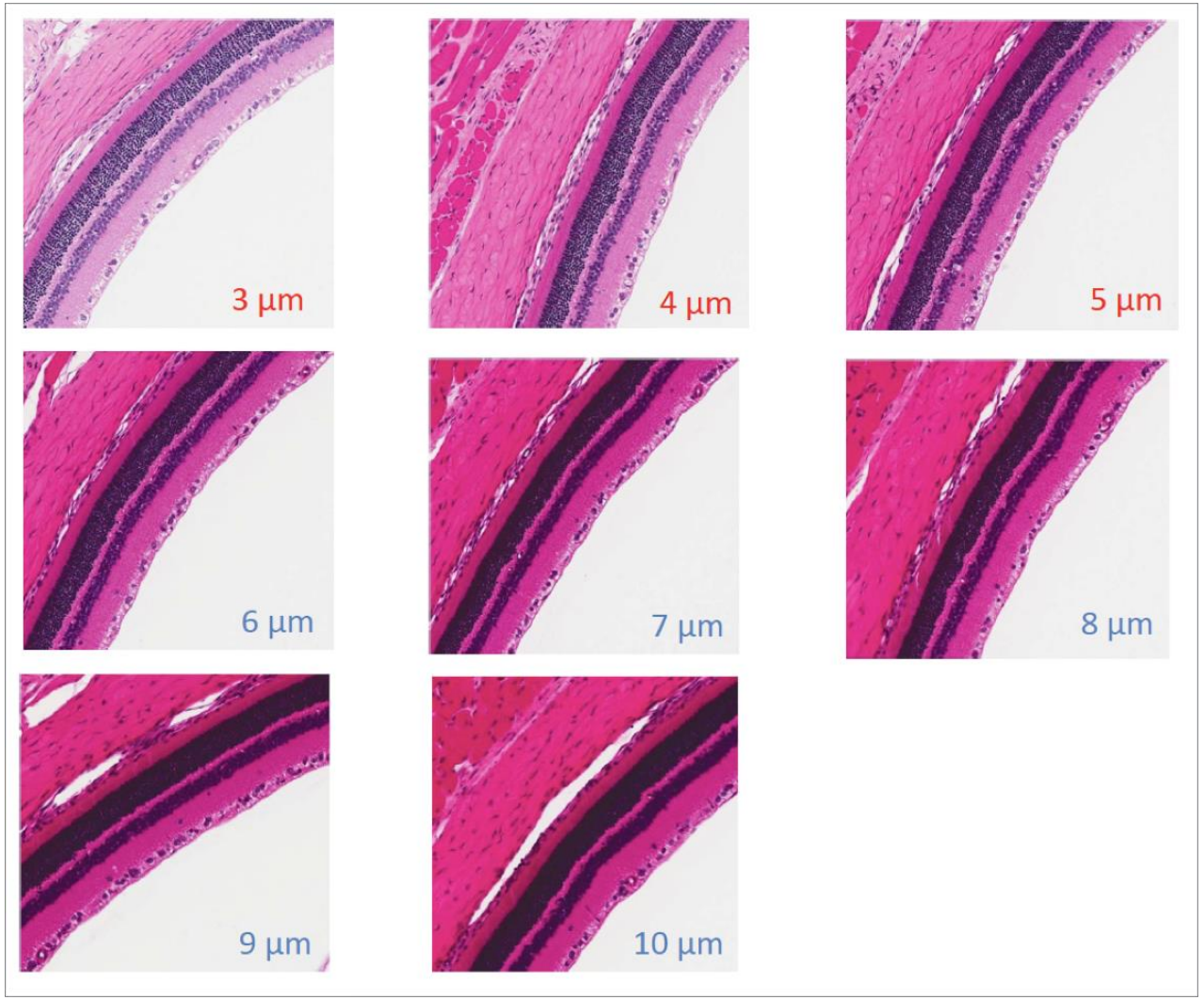
CrossMark

Precision immunoprofiling by image analysis and artificial intelligence

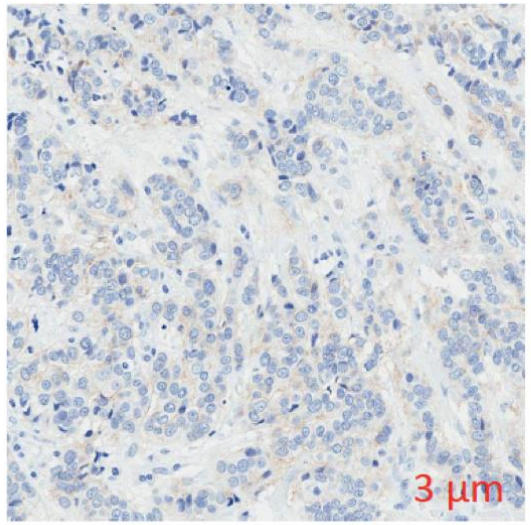
Viktor H. Koelzer[1,2] · Korsuk Sirinukunwattana[3] · Jens Rittscher[3,4,5] · Kirsten D. Mertz[6]

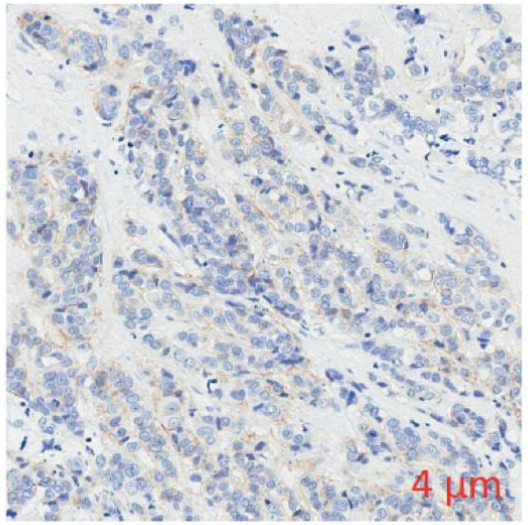
Received: 15 May 2018 / Revised: 6 November 2018 / Accepted: 9 November 2018

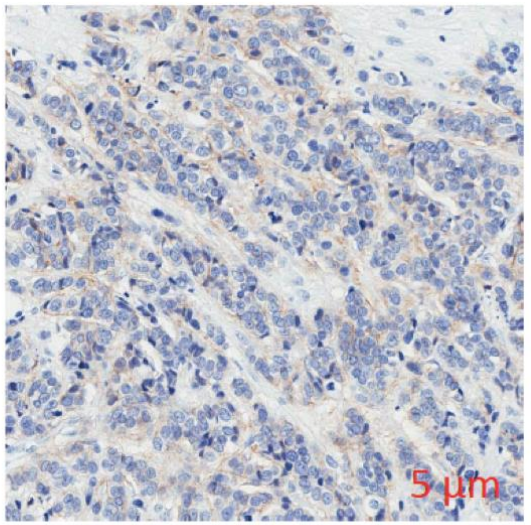
Preanalyticals Affect H&E

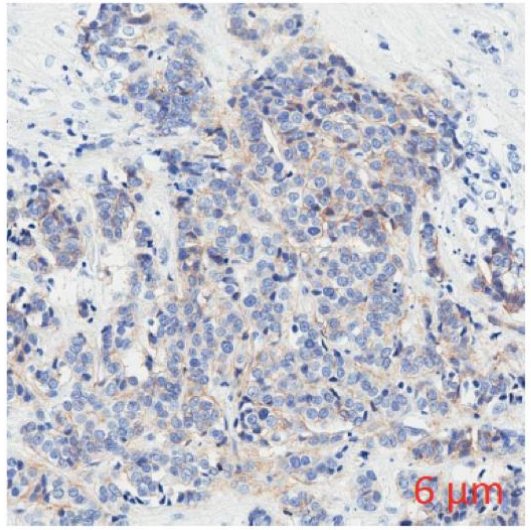


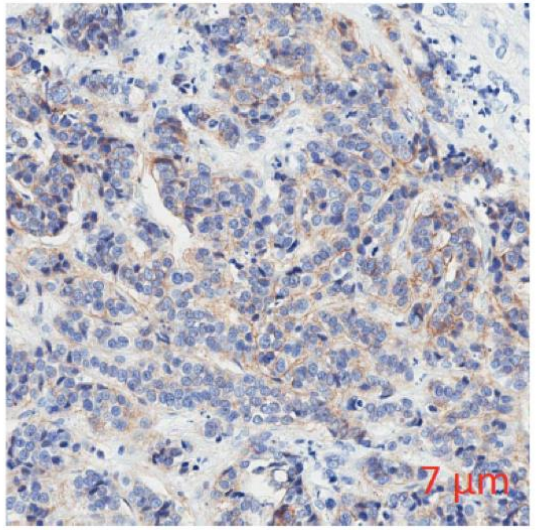
Preanalyticals Affect Immunostains

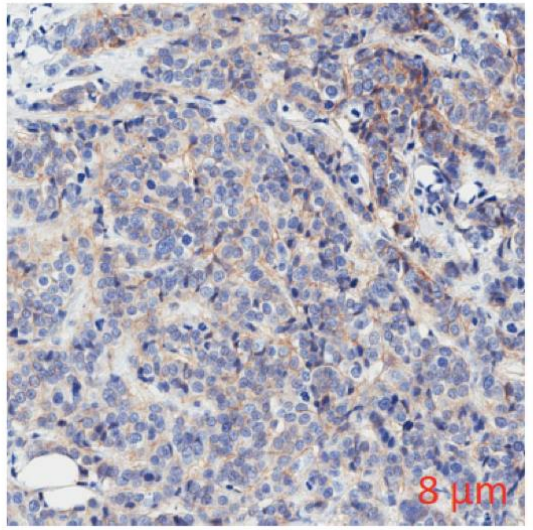












Preanalyticals Affect H&E and Immunostains

HISTOQIP

COLLEGE of AMERICAN PATHOLOGISTS
Laboratory Quality Solutions

2019 Surveys and Anatomic Pathology Education Programs

NEW

HQIP Whole Slide Image Quality Improvement Program HQWSI

Stain/Tissue	Program Code	Challenges per Shipment	
	HQWSI	A	B
H&E - Breast resection	▮	1	
H&E - Lung resection	▮	1	
H&E - Breast needle core biopsy	▮	1	
H&E - Prostate needle core biopsy	▮	1	
H&E - Colon resection	▮		1
H&E - Kidney resection	▮		1
H&E - Colon biopsy	▮		1
H&E - Skin punch biopsy	▮		1

Program Information

- Participant laboratories may submit up to four stained coverslipped glass slides and upload their scanned whole slide images per mailing
- Two shipments per year

CAP ER/PR and HER2 IHC TMA Survey

- The Centers for Medicine & Medical Services (CMS) regulates all lab testing preformed on humans in US through the Clinical Laboratory Improvement Amendments (CLIA)
- Proficiency Testing (PT) is one way that CMS monitors laboratories performance
- CAP Proficiency Testing (PT) specimens must be tested with the laboratory's regular workload, using routine methods, and testing the PT specimens the same number of times it routinely tests patient specimens.

Analyticals Affect Immunostain Interpretation

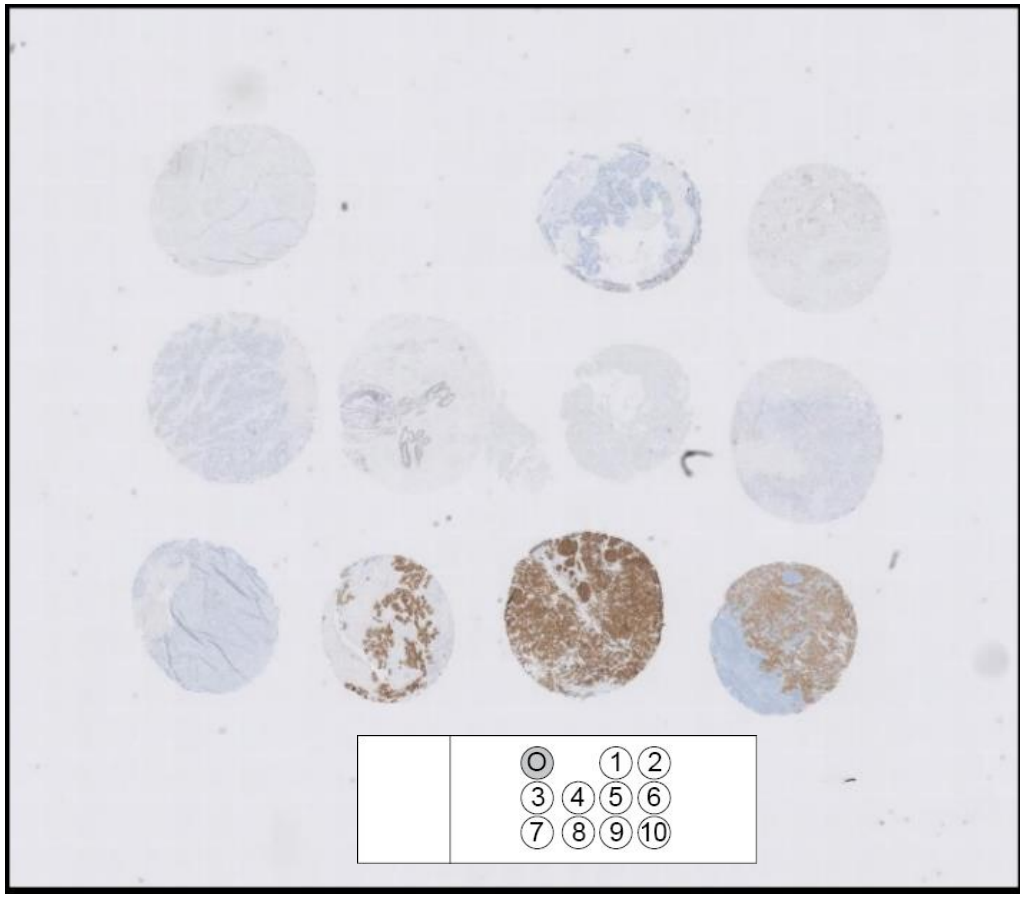
- **CAP ER/PR and HER2 Immunohistochemistry (IHC) Tissue Microarray (TMA) Survey**

One TMA for ER IHC containing 10 samples

PM2-02-2017-A

Stained at Moffitt Cancer Center (SP1 with antigen retrieval)

http://capatholo.gy/TMA1



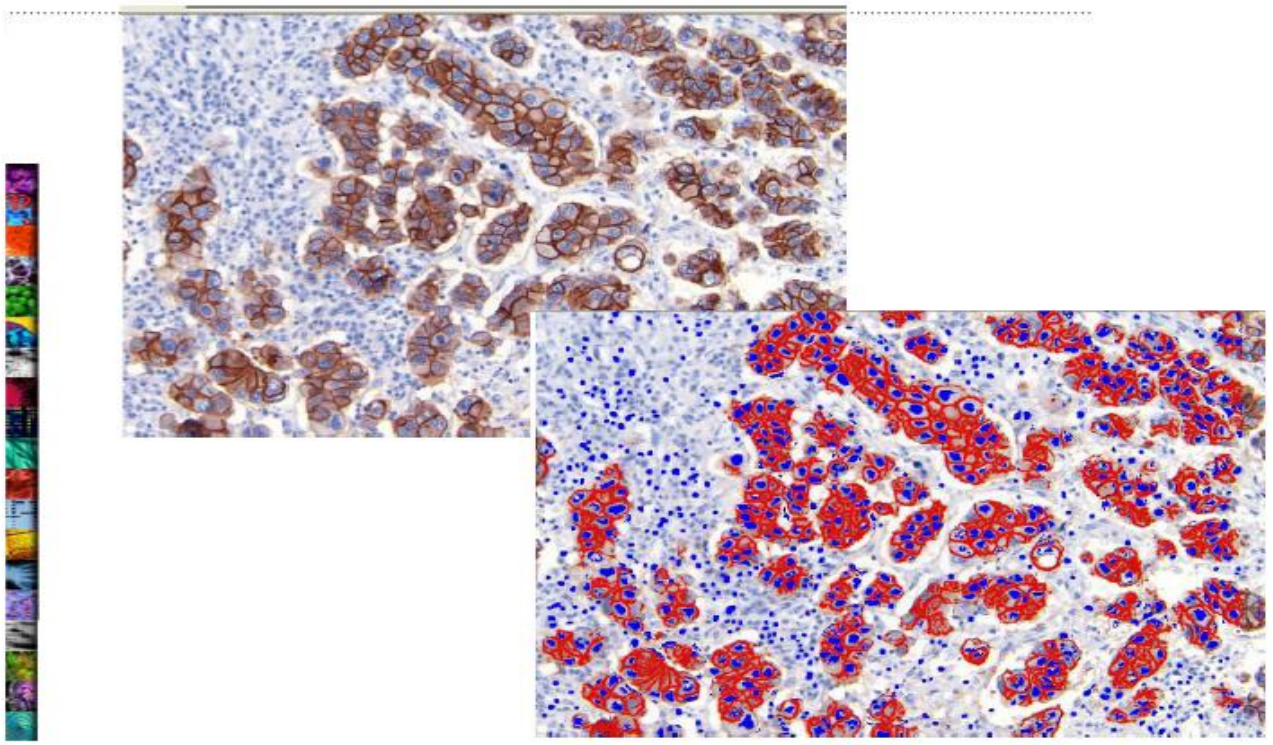
One TMA for HER2 IHC containing 10 samples

HER2-01-2017-A

Stained at Moffitt Cancer Center (4B5 PATHWAY)

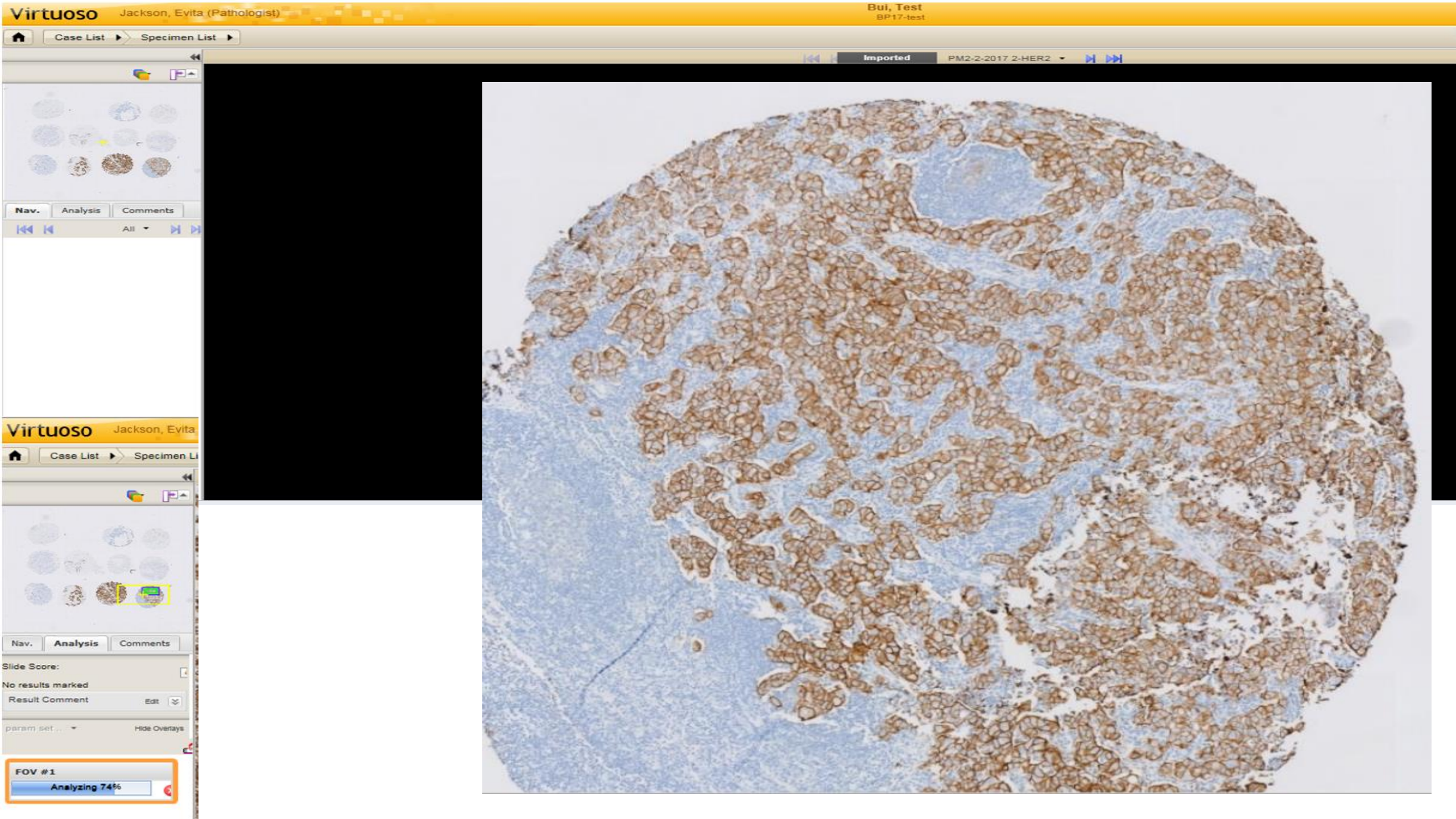
http://capatholo.gy/TMA2

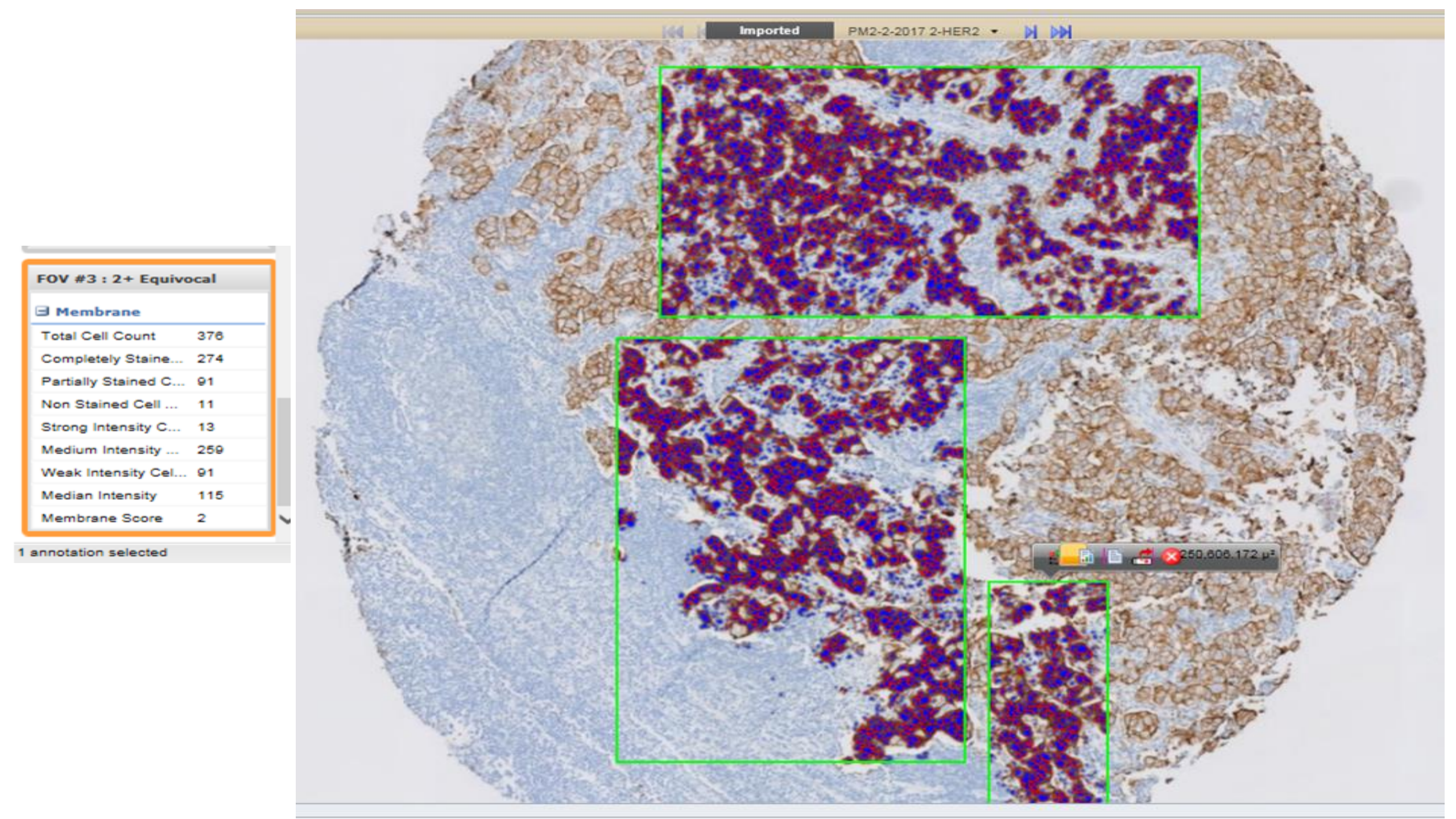
HER2 Quantiative Image Analysis Algorithms



A good quantitative image analysis (QIA) algorithm produces accurate, precise and reproducible result.

Date	K-Number	Tissue - Stain	Reagent	Application	
PATHIAM (BioImagene, Sunnyvale, CA)					
2010/10	K092333	Breast - P53/Ki-67	Dako		Image Analysis
2009/02	K080910	Breast - *HER2/neu*	Dako	Image Analysis	
2007/02	K062756	Breast - *HER2/neu*	Dako	Image Analysis (SW only)	
ScanScope XT System (Aperio Technologies, Vista, CA)					
2009/08	K080564	Breast - *HER2/neu*	Dako	*Tunable Image Analysis*	
2008/10	K080254	Breast - PR	Dako	*Reading on Monitor*	
2008/08	K073667	Breast - ER/PR	Dako Image Analysis		
2007/12	K071671	Breast - *HER2/neu*	Dako *Reading on Monitor*		
2007/10	K071128	Breast - *HER2/neu*	Dako	Image Analysis	
VIAS (Tripath Imaging, Burlington, NC)					
2006/09	K062428	Breast - *P53*	Ventana	Image Analysis	
2006/04	K053520	Breast - *Ki-67*	Ventana	Image Analysis	
2005/08	K051282	Breast - *HER2/neu*	*Ventana*	Image Analysis	
2005/05	K050012	Breast - ER/PR	Ventana	Image Analysis	
ARIOL (Applied Imaging, Santa Clara, CA)					
2004/03	K033200	Breast - ER/PR	Dako	Image Analysis	
2004/01	K031715	Breast - *HER2/neu*	Dako	Image Analysis	
ACIS (Clarient, Aliso Viejo, CA/Chroma Vision, San Juan Capistrano, CA)					
2004/02	K012138	Breast - ER/*PR*	Dako	Image Analysis	
2003/12	K032113	Breast - *HER2/neu*	Dako	*Image Analysis (system)*	
QCA (Cell Analysis, Highland Park, IL)					
2003/12	K031363	Breast - ER	Dako	Image Analysis (SW only)	


Virtuoso
Jackson, Evita (Pathologist)
Bui, Test
BP17-test
Case List
Specimen List
Imported
PM2-2-2017 2-HER2
Nav.
Analysis
Comments
All
Virtuoso
Jackson, Evita
Case List
Specimen Li
Nav.
Analysis
Comments
Slide Score:
No results marked
Result Comment
Edit
param set...
Hide Overlays
FOV #1
Analyzing 74%

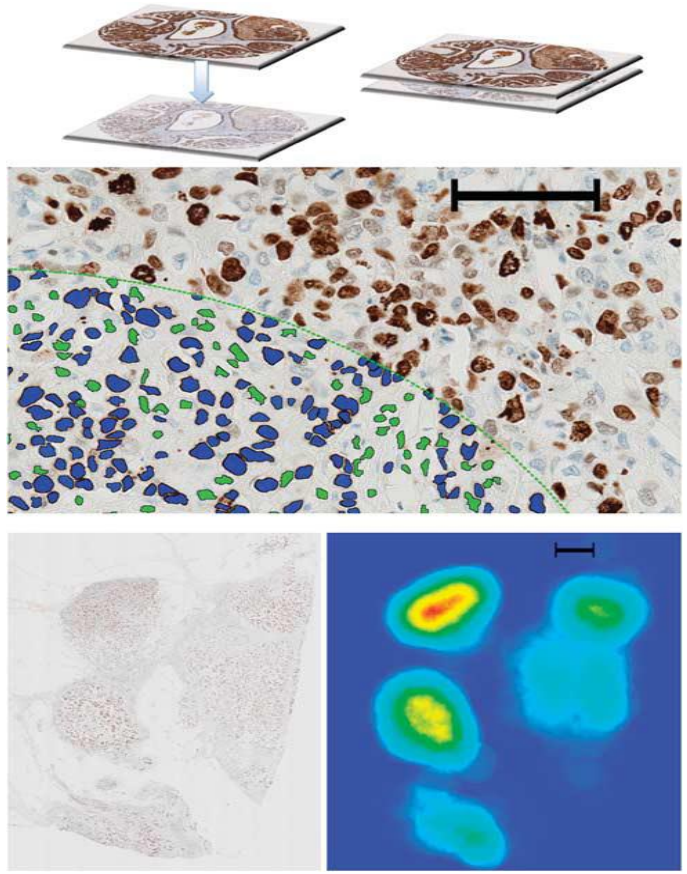

Imported
PM2-2-2017 2-HER2
FOV #3 : 2+ Equivocal
Membrane
Total Cell Count 376
Completely Staine... 274
Partially Stained C... 91
Non Stained Cell ... 11
Strong Intensity C... 13
Medium Intensity ... 259
Weak Intensity Cel... 91
Median Intensity 115
Membrane Score 2
1 annotation selected
250,606.172 µ²

Modern Pathology (2016) 29, 318–329

Digital image analysis outperforms manual biomarker assessment in breast cancer

Gustav Stålhammar[1,2], Nelson Fuentes Martinez[1,3], Michael Lippert[4], Nicholas P Tobin[5], Ida Mølholm[4,6], Lorand Kis[7], Gustaf Rosin[1], Mattias Rantalainen[8], Lars Pedersen[4], Jonas Bergh[1,5,9], Michael Grunkin[4] and Johan Hartman[1,5,7]

[1]Department of Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden; [2]St Erik Eye Hospital, Stockholm, Sweden; [3]Södersjukhuset, Stockholm, Sweden; [4]Visiopharm A/S, Hoersholm, Denmark; [5]Cancer Center Karolinska, Stockholm, Sweden; [6]Department of Applied Mathematics and Computer Science, Technical University of Denmark, Kongens Lyngby, Denmark; [7]Department of Clinical Pathology, Karolinska University Hospital, Stockholm, Sweden; [8]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden and [9]Department of Oncology, Karolinska University Hospital, Stockholm, Sweden



- In conclusion, the system for DIA evaluated here was in most aspects a superior alternative to manual biomarker scoring.
- It also has the potential to reduce time consumption for pathologists, as many of the steps in the workflow are either automatic or feasible to manage without pathological expertise.

Table 2 Molecular 'intrinsic' breast cancer subtypes and surrogate definitions by immunohistochemical profile

Intrinsic subtype	*Surrogate IHC classification*
Luminal A	ER ≥ 1% and/or PR ≥ 20% and HER2 'negative' and Ki67 'low'
Luminal B	1. ER ≥ 1% and/or PR ≥ 20% and HER2 'negative' and Ki67 'high' or 2. ER ≥ 1% and PR < 20% and HER2 'negative.' Any Ki67 or 3. ER ≥ 1% and/or PR ≥ 1% and HER2 'positive.' Any Ki67
HER2-enriched	ER < 1% and PR < 1%. HER2 'positive.' Any Ki67
Basal-like	ER < 1% and PR < 1%. HER2 'negative.' Any Ki67

% = Proportion of tumor cells stained with the respective biomarker. 'Positive' and 'negative' = as defined by the American Society of Clinical Oncology and College of American Pathologists recommendations for human epidermal growth factor receptor 2-testing in breast cancer.[30] 'High' and 'low' = as defined by each laboratory's own reference data,[3,6,17] with threshold generally in the range of 14–29%.[4,5,19–21]

HER2 Quantitative Image Analysis (QIA)

- QIA has been shown to improve consistency and accuracy of interpretation than manual scoring by pathologists, but has not gained widespread acceptance

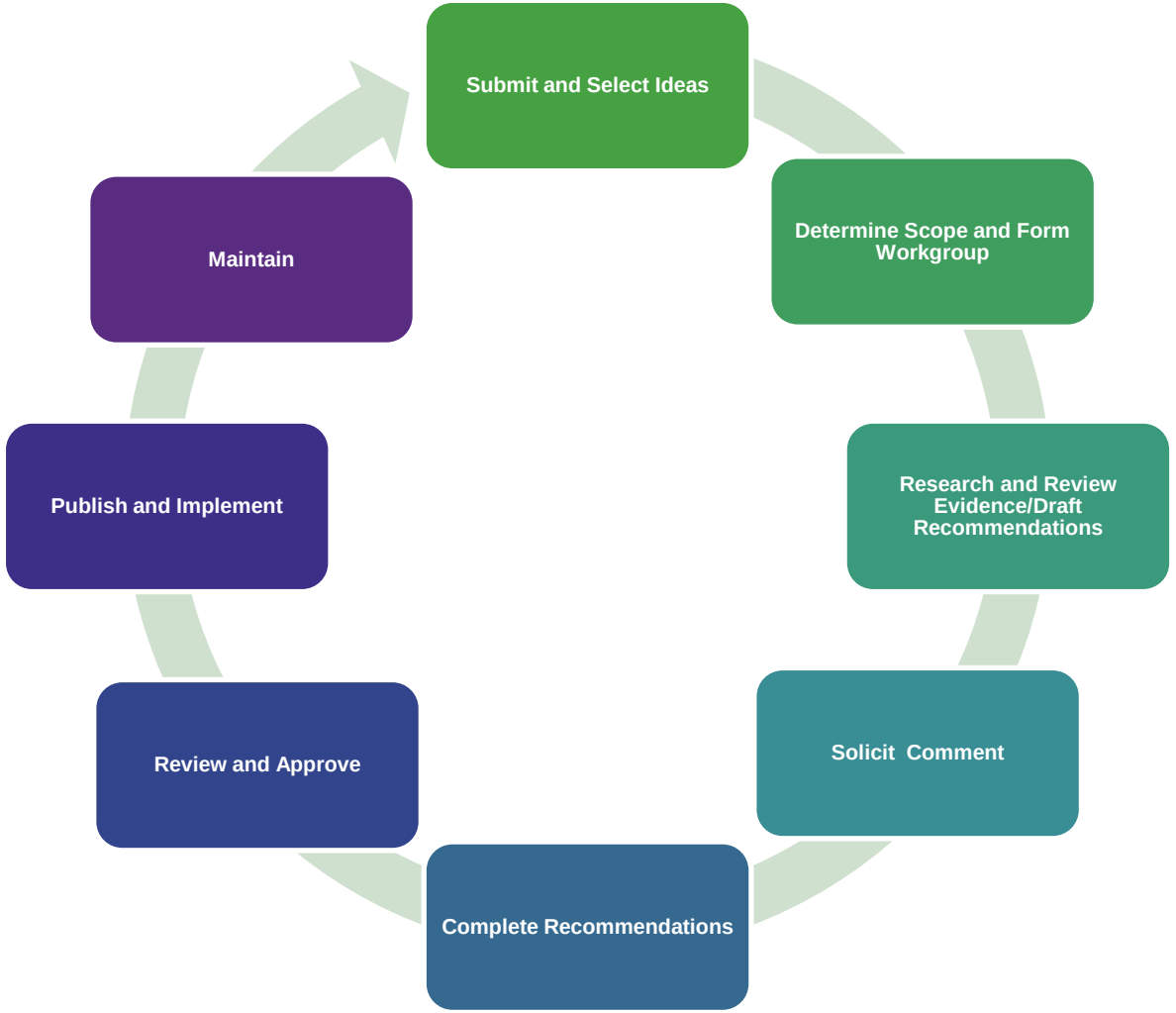
  In 2016, 183 (22.1%) of the 826 laboratories enrolled in the CAP HQIP-A mailing, reported using QIA

- While the ASCO/CAP HER2 testing guidelines addressing the key pre-analytical and IHC related issues, there is a need of guideline for HER2 IHC QIA

CAP QIA Guideline Scope:

- to provide recommendations for improving accuracy, precision and reproducibility in the interpretation of HER2 IHC where QIA is employed

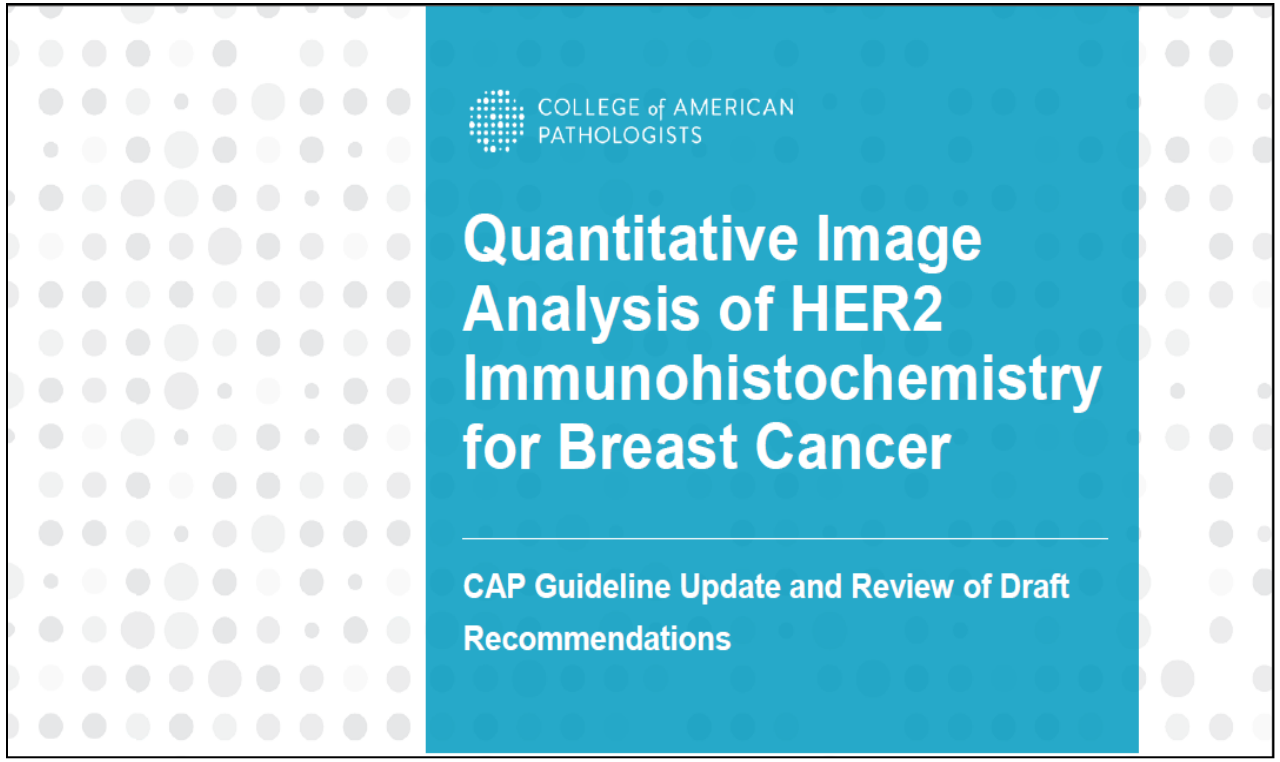
CAP Center Guideline Methods



CAP HER2 QIA Guideline Key Questions

1. What equipment validation and daily performance monitoring is needed?
2. What training of staff and pathologists is required? What are the competency assessments needs over time?
3. How does one select or develop an appropriate algorithm for interpretation?
4. How does one determine the performance of the image analysis?
5. How should image analysis be reported?

CAP HER2 QIA Guideline



https://digitalpathologyassociation.org/_data/files/API/QIA_-_API_2017_CAP_DPA_Bui.pdf

CAP ARCHIVES of Pathology & Laboratory Medicine

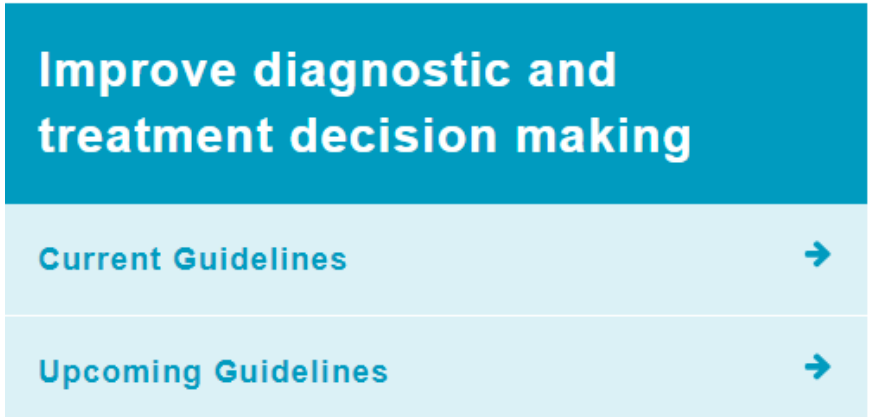
Bui M, Riben MW, Allison KH, et al. Quantitative image analysis of HER2 immunohistochemistry for breast cancer: guideline from the College of American Pathologists. *Arch Pathol Lab Med.* In press.

11 recommendations
- 7 recommendations (based on laboratory accreditation requirements)
- 4 expert consensus opinions

CAP Helps Pathologists and Laboratories Adopting DP

- **Digital Pathology Committee**
- **Pathology and Laboratory Quality Center Committees**

  CAP Evidence-Based Guidelines –
  - Revisions to whole slide imaging validation guidelines
  - Quantitative imaging analysis of HER2 immunohistochemistry for breast cancer guidelines



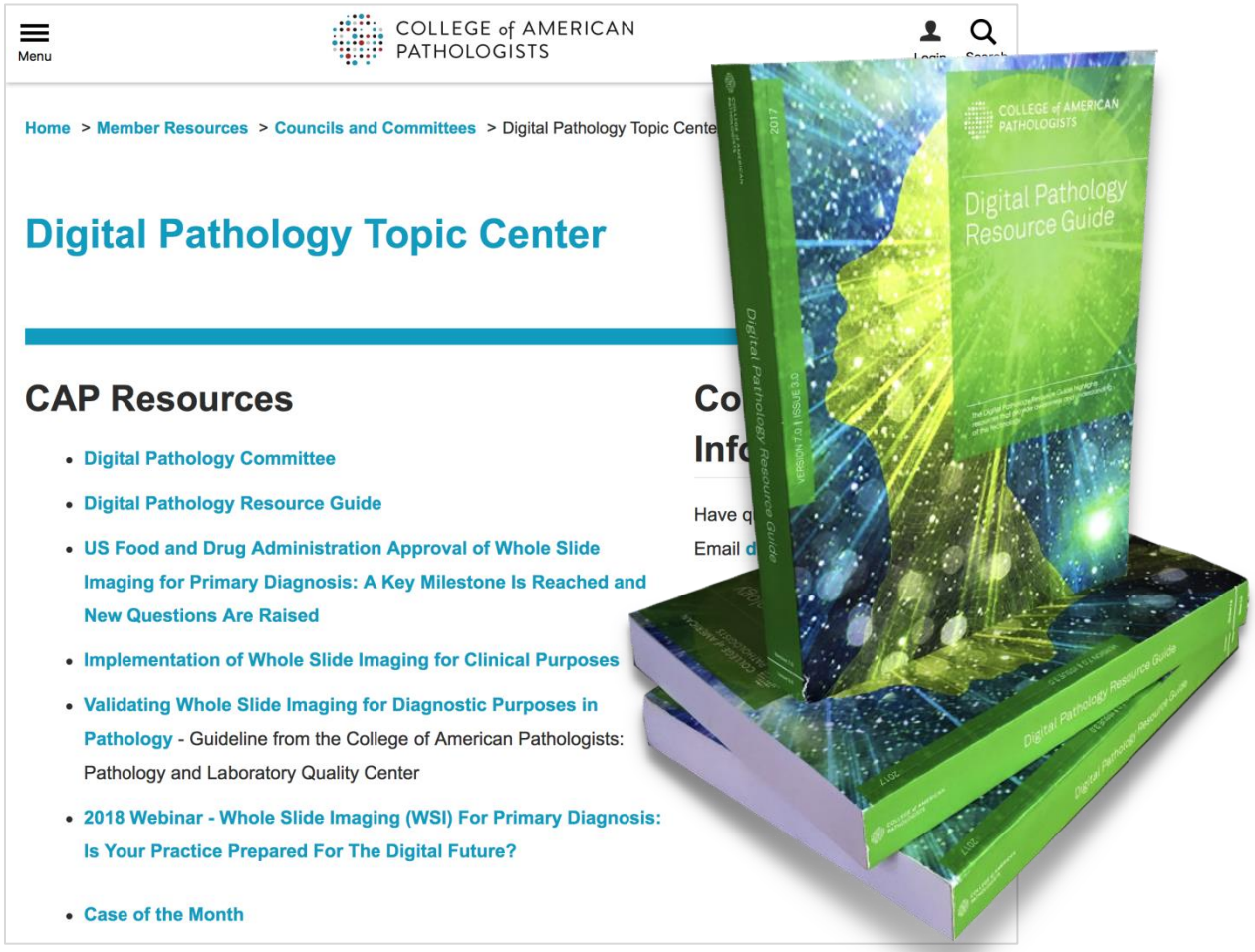
CAP Helps Pathologists and Laboratories Adopting DP

Digital Pathology Committee

Digital Pathology Topic Center

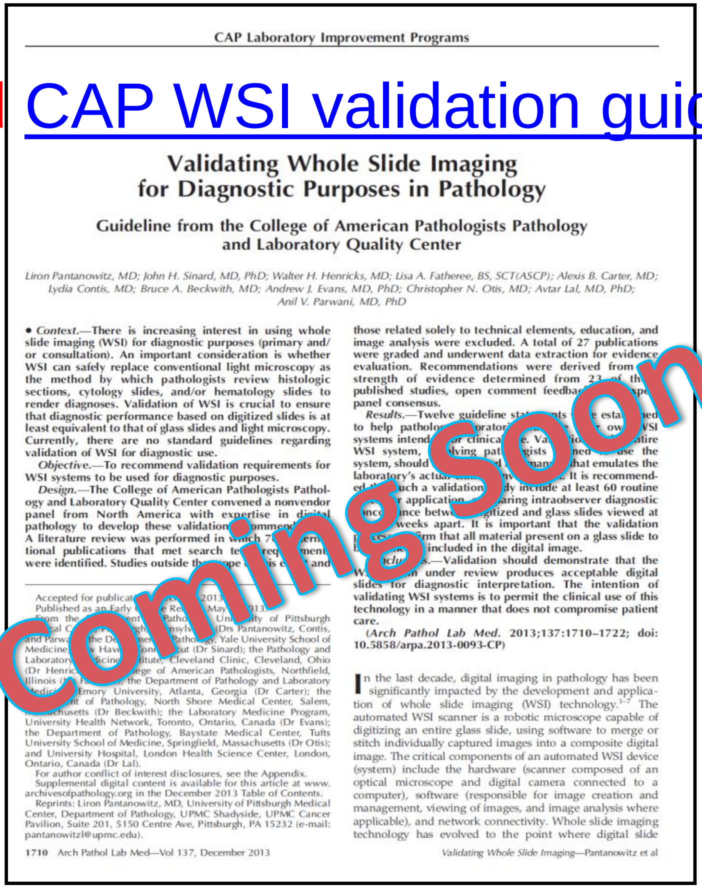
Charge:

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.



CAP and Other Pathology Societies *Guidelines*

Updated [CAP WSI validation guidelines](http://www.archivesofpathology.org/doi/full/10.5858/arpa.2013-0093-CP).



Validating Whole Slide Imaging for Diagnostic Purposes in Pathology

Guideline from the College of American Pathologists Pathology and Laboratory Quality Center

Liron Pantanowitz, MD; John H. Sinard, MD, PhD; Walter H. Henricks, MD; Lisa A. Fatheree, BS, SCT(ASCP); Alexis B. Carter, MD; Lydia Contis, MD; Bruce A. Beckwith, MD; Andrew J. Evans, MD, PhD; Christopher N. Otis, MD; Avtar Lal, MD, PhD; Anil V. Parwani, MD, PhD

• *Context.*—There is increasing interest in using whole slide imaging (WSI) for diagnostic purposes (primary and/or consultation). An important consideration is whether WSI can safely replace conventional light microscopy as the method by which pathologists review histologic sections, cytology slides, and/or hematology slides to render diagnoses. Validation of WSI is crucial to ensure that diagnostic performance based on digitized slides is at least equivalent to that of glass slides and light microscopy. Currently, there are no standard guidelines regarding validation of WSI for diagnostic use.

Objective.—To recommend validation requirements for WSI systems to be used for diagnostic purposes.

Design.—The College of American Pathologists Pathology and Laboratory Quality Center convened a nonvendor panel from North America with expertise in digital pathology to develop these validation [illegible]. A literature review was performed in which [illegible] tional publications that met search te[illegible] were identified. Studies outside th[illegible] and those related solely to technical elements, education, and image analysis were excluded. A total of 27 publications were graded and underwent data extraction for evidence evaluation. Recommendations were derived from strength of evidence determined from 23 of th[illegible] published studies, open comment feedba[illegible] panel consensus.

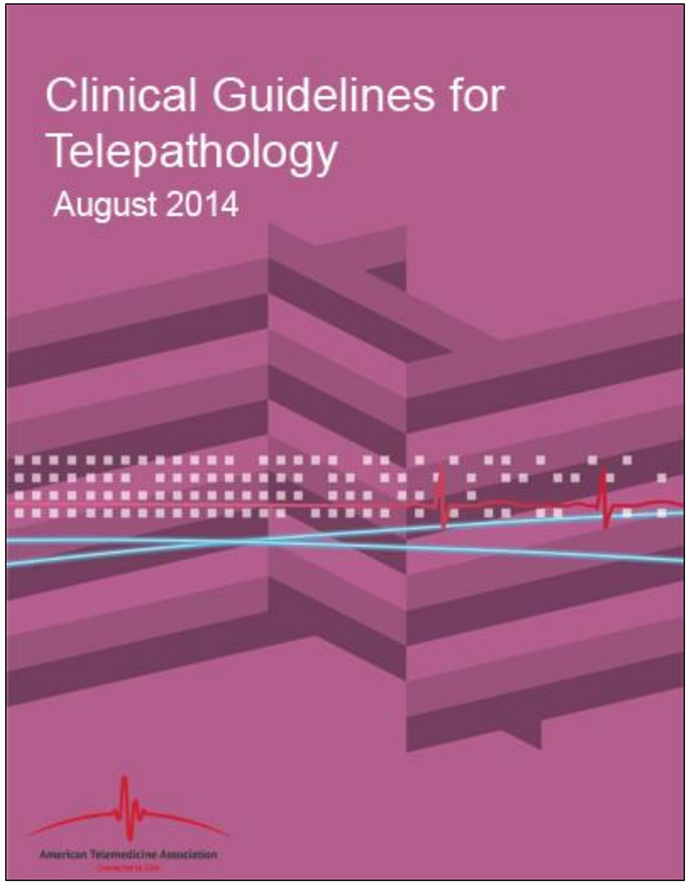
Results.—Twelve guideline sta[illegible] to help patholo[illegible] systems intend[illegible] WSI system, [illegible] system, should [illegible] that emulates the laboratory's actua[illegible]. It is recommended [illegible] such a validation [illegible] include at least 60 routine [illegible] application [illegible] intraobserver diagnostic [illegible] between [illegible] gitized and glass slides viewed at [illegible] weeks apart. It is important that the validation [illegible] firm that all material present on a glass slide to [illegible] included in the digital image.

Conclusions.—Validation should demonstrate that the W[illegible] under review produces acceptable digital slides for diagnostic interpretation. The intention of validating WSI systems is to permit the clinical use of this technology in a manner that does not compromise patient care.

(*Arch Pathol Lab Med.* 2013;137:1710–1722; doi: 10.5858/arpa.2013-0093-CP)

In the last decade, digital imaging in pathology has been significantly impacted by the development and application of whole slide imaging (WSI) technology.[1–7] The automated WSI scanner is a robotic microscope capable of digitizing an entire glass slide, using software to merge or stitch individually captured images into a composite digital image. The critical components of an automated WSI device (system) include the hardware (scanner composed of an optical microscope and digital camera connected to a computer), software (responsible for image creation and management, viewing of images, and image analysis where applicable), and network connectivity. Whole slide imaging technology has evolved to the point where digital slide

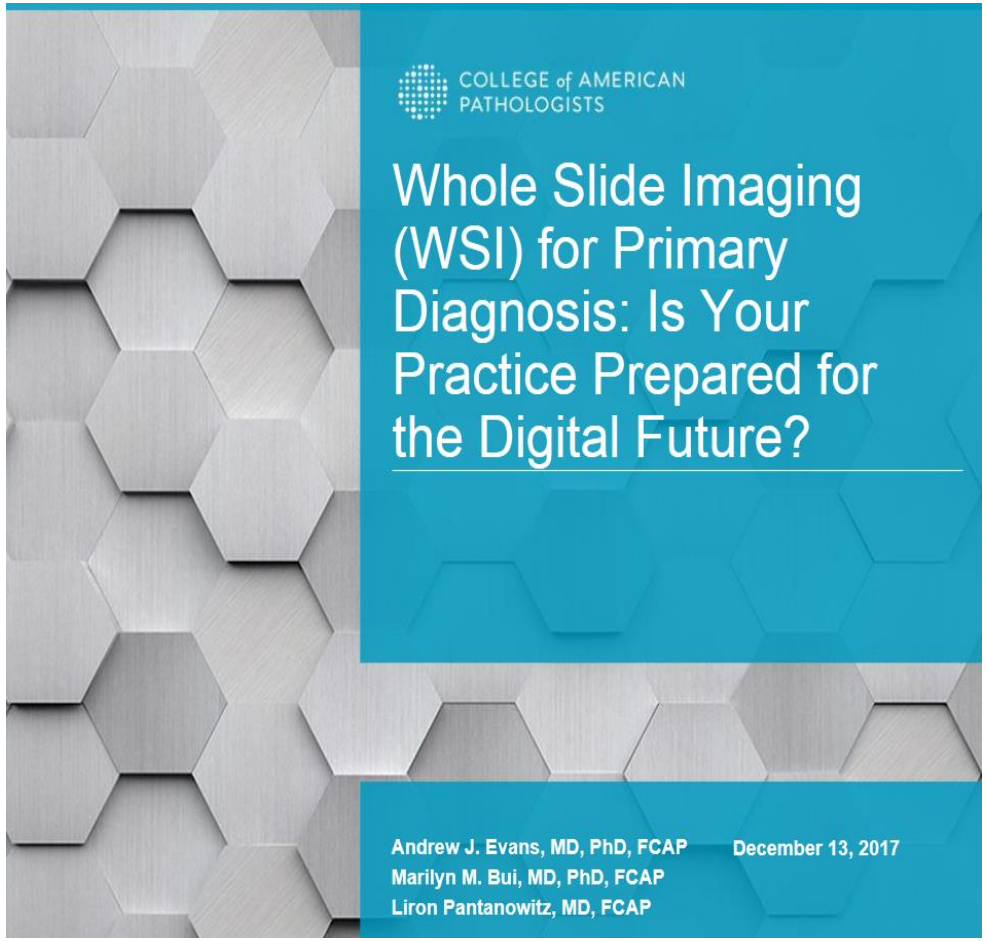
Accepted for publicat[illegible] 2013.
Published as an Early [illegible] May [illegible] 2013.
From the [illegible] University of Pittsburgh [illegible] (Drs Pantanowitz, Contis, and Parwa[illegible]); the De[illegible] Patho[illegible], Yale University School of Medicine, [illegible] Have[illegible] Conn[illegible]ut (Dr Sinard); the Pathology and Laboratory [illegible] Institute, Cleveland Clinic, Cleveland, Ohio (Dr Henric[illegible] [illegible] ege of American Pathologists, Northfield, Illinois ([illegible]); the Department of Pathology and Laboratory Medic[illegible] Emory University, Atlanta, Georgia (Dr Carter); the [illegible] of Pathology, North Shore Medical Center, Salem, [illegible]chusetts (Dr Beckwith); the Laboratory Medicine Program, University Health Network, Toronto, Ontario, Canada (Dr Evans); the Department of Pathology, Baystate Medical Center, Tufts University School of Medicine, Springfield, Massachusetts (Dr Otis); and University Hospital, London Health Science Center, London, Ontario, Canada (Dr Lal).
For author conflict of interest disclosures, see the Appendix.
Supplemental digital content is available for this article at www.archivesofpathology.org in the December 2013 Table of Contents.
Reprints: Liron Pantanowitz, MD, University of Pittsburgh Medical Center, Department of Pathology, UPMC Shadyside, UPMC Cancer Pavilion, Suite 201, 5150 Centre Ave, Pittsburgh, PA 15232 (e-mail: pantanowitzl@upmc.edu).



http://www.archivesofpathology.org/doi/full/10.5858/arpa.2013-0093-CP

http://www.jpathinformatics.org/article.asp?issn=2153-3539;year=2014;volume=5;issue=1;spage=39;epage=39;aulast=Pantanowitz

CAP DP Committee



http://capatholo.gy/2Agehmu

US Food and Drug Administration Approval of Whole Slide Imaging for Primary Diagnosis

A Key Milestone Is Reached and New Questions Are Raised

Andrew J. Evans, MD, PhD; Thomas W. Bauer, MD, PhD; Marilyn M. Bui, MD, PhD; Toby C. Cornish, MD, PhD; Helena Duncan, BBA, MJ; Eric F. Glassy, MD; Jason Hipp, MD, PhD; Robert S. McGee, MD, PhD; Doug Murphy, MT (ASCP); Charles Myers, MD; Dennis G. O'Neill, MD; Anil V. Parwani, MD, PhD; B. Alan Rampy, DO, PhD; Mohamed E. Salama, MD; Liron Pantanowitz, MD

• April 12, 2017 marked a significant day in the evolution of digital pathology in the United States, when the US Food and Drug Administration announced its approval of the Philips IntelliSite Pathology Solution for primary diagnosis in surgical pathology. Although this event is expected to facilitate more widespread adoption of whole slide imaging for clinical applications in the United States, it also raises a number of questions as to the means by which pathologists might choose to incorporate this technology into their clinical practice. This article from the College of American Pathologists Digital Pathology Committee reviews frequently asked questions on this topic and provides answers based on currently available information.

(*Arch Pathol Lab Med.* 2018;142:1383–1387; doi: 10.5858/arpa.2017-0496-CP)

CAP DP Committee

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Implementation of Whole Slide Imaging for Clinical Purposes

Issues to Consider From the Perspective of Early Adopters

Andrew J. Evans, MD, PhD; Mohamed E. Salama, MD; Walter H. Henricks, MD; Liron Pantanowitz, MD

• *Context.*—There is growing interest in the use of digital pathology, especially whole slide imaging, for diagnostic purposes. Many issues need to be considered when incorporating this technology into a clinical laboratory. The College of American Pathologists (CAP) established a Digital Pathology Committee to support the development of CAP programs related to digital pathology. One of its many initiatives was a panel discussion entitled "*Implementing Whole-Slide Imaging for Clinical Use: What to Do and What to Avoid,*" given for 3 years at the CAP annual meetings starting in 2014.

Objectives.—To review major issues to consider when implementing whole slide imaging for clinical purposes as covered during the panel discussion.

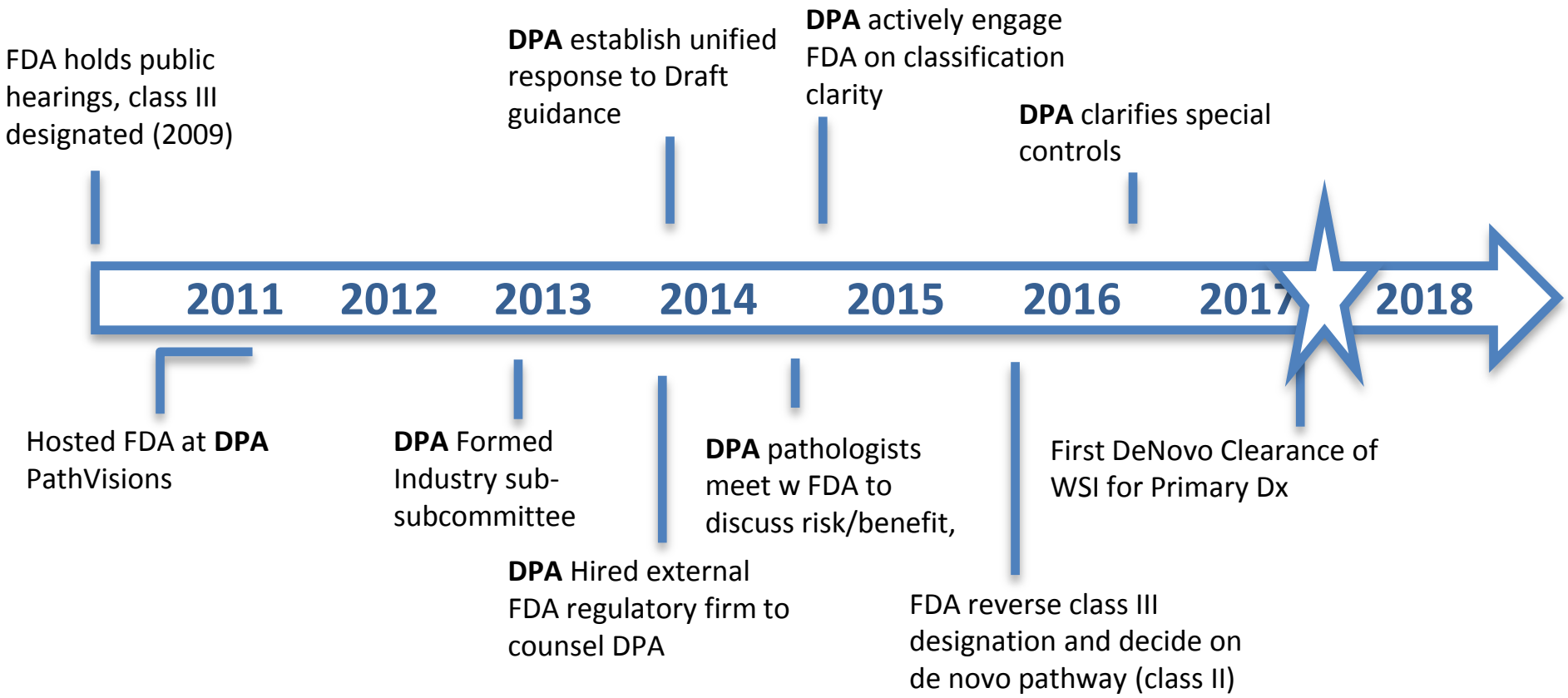
Design.—The views expressed and recommendations given are based primarily on the personal experience of the authors as early adopters of this technology. It is not intended to be an exhaustive review of digital pathology.

Results.—Implementation is best approached in phases. Early efforts are directed toward identifying initial clinical applications and assembling an implementation team. Scanner selection should be based on intended use and budget. Recognizing pathologist concerns over the use of digital pathology for diagnostic purposes, ensuring adequate training, and performing appropriate validation studies will enhance adoption. Once implemented, the transition period from glass slide to image-based diagnostics will be associated with challenges, especially those related to a hybrid glass slide–digital slide workflow.

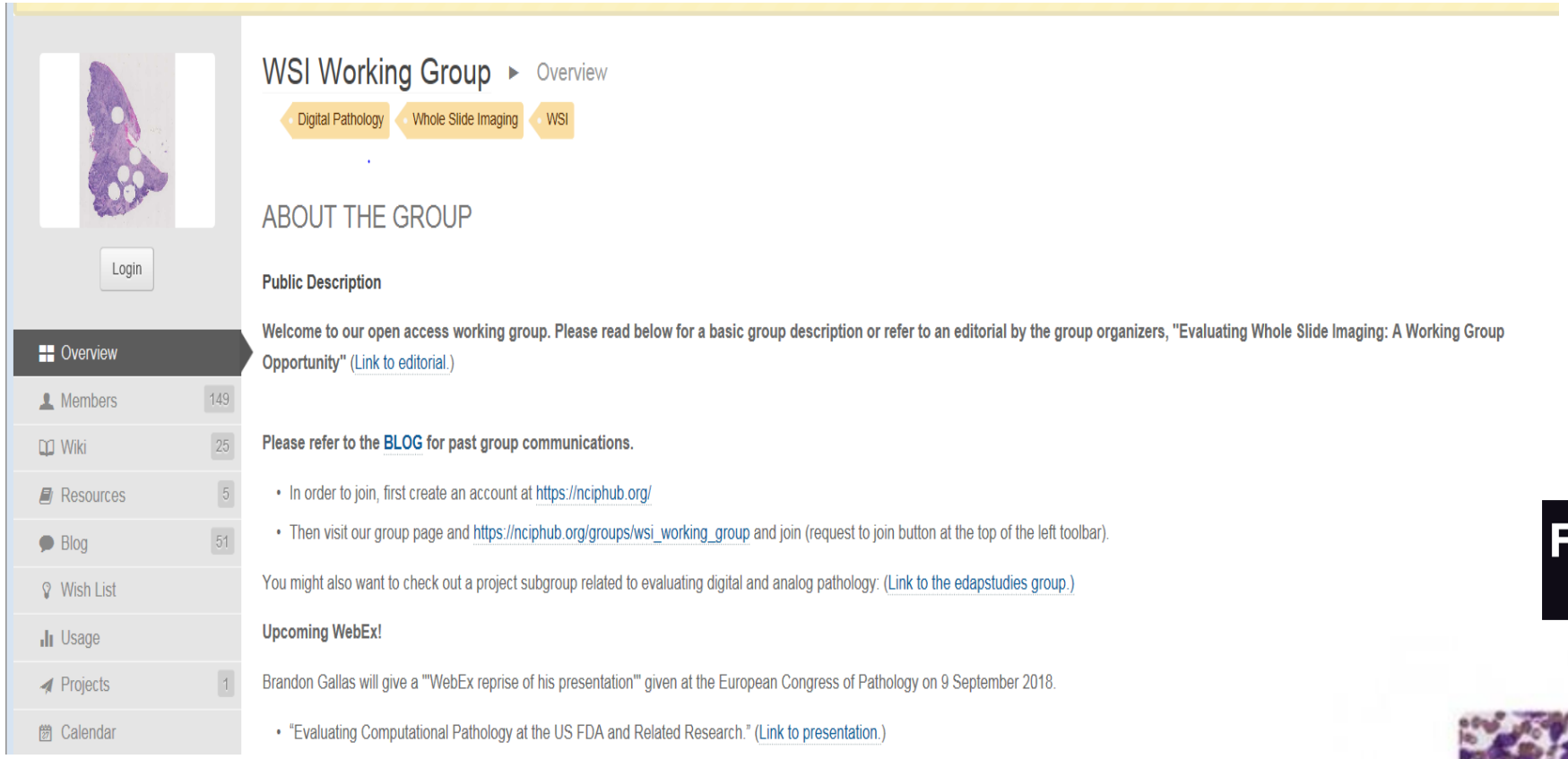
Conclusions.—With appropriate preparation, planning, and stepwise implementation, whole slide imaging can be used safely and reliably for frozen sections, consultation, quality assurance, and primary diagnosis.

(*Arch Pathol Lab Med.* 2017;141:944–959; doi: 10.5858/arpa.2016-0074-OA)

DPA in Advocacy for Regulatory Path Clarity



Next Task: Regulatory Path for AI



WSI Working Group ▸ Overview

Digital Pathology | Whole Slide Imaging | WSI

Login

Overview
Members 149
Wiki 25
Resources 5
Blog 51
Wish List
Usage
Projects 1
Calendar

ABOUT THE GROUP

Public Description

Welcome to our open access working group. Please read below for a basic group description or refer to an editorial by the group organizers, "Evaluating Whole Slide Imaging: A Working Group Opportunity" (Link to editorial.)

Please refer to the BLOG for past group communications.

- In order to join, first create an account at https://nciphub.org/
- Then visit our group page and https://nciphub.org/groups/wsi_working_group and join (request to join button at the top of the left toolbar).

You might also want to check out a project subgroup related to evaluating digital and analog pathology: (Link to the edapstudies group.)

Upcoming WebEx!

Brandon Gallas will give a ""WebEx reprise of his presentation"" given at the European Congress of Pathology on 9 September 2018.

- "Evaluating Computational Pathology at the US FDA and Related Research." (Link to presentation.)

Facilitate bringing safe and state-of-the art pathology algorithms to the market in an efficient way.

FDA U.S. FOOD & DRUG ADMINISTRATION

DIGITAL PATHOLOGY DPA ASSOCIATION

https://nciphub.org/groups/wsi_working_group

DPA in Education Partnership with NHS

DPA, in collaboration with NSH, developed the first ever certificate program for digital pathology

174 Course Registrations
In 8 months!

NOW AVAILABLE!

DIGITAL PATHOLOGY DPA ASSOCIATION

DPA in Interoperability with DICOM

- **DPA hosted the first Connectathon at Pathology Visions 2017**
- **Formation of DICOM & Standards Task Force**

CAP TODAY
The one publication most important to your job!

"We learned more in this one event than we did in the past 7 year"

Dr. David Clunie, DICOM WG 26 Co-chair

'Connectathon' opens door to interoperability in digital pathology

Valerie Neff Newitt

December 2017—With the FDA having approved whole slide imaging for primary diagnosis this year, one obstacle to full acceptance of digital pathology remains: lack of interoperability. To topple that barrier, the Digital Pathology Association, the CAP through its Digital Pathology Committee, and DICOM Working Group 26 convened in October, during the Pathology Visions conference, the first Connectathon for digital pathology.

"The uptake of digital pathology hasn't been as rapid as everyone had anticipated," says Liron Pantanowitz, MD, professor of pathology and biomedical informatics, University of Pittsburgh Medical Center. "Many pathology departments know that if they purchase a digital pathology system it will not be easy to bring it back to the lab, plug it in, and get it to interact with everything else. There has been no plug-and-play option in digital pathology, and that has been a huge stumbling block."

Dr. Pantanowitz, a member of the CAP Digital Pathology Committee, says Connectathon was a milestone almost as big as the FDA's recent approval itself. "Connectathon not only provided a venue for connecting machines able to talk to each other, but also it connected an entire industry with a commitment to move digital pathology forward."


Dr. Parwani

Anil Parwani, MD, PhD, MBA, a member of the CAP committee and a professor of pathology, vice chair of anatomic pathology, and director of pathology informatics and digital pathology shared resources, Ohio State University Wexner Medical Center, says of Connect-athon: "We thought it would be great if we could bring vendors together and have them show us that, yes, they can all connect and, yes, we can use standards"—in the way radiology does, for example—"and, yes, we can share these images."

PATHOLOGY DPA ASSOCIATION

DPA in Education and Awareness

Publication & White Papers

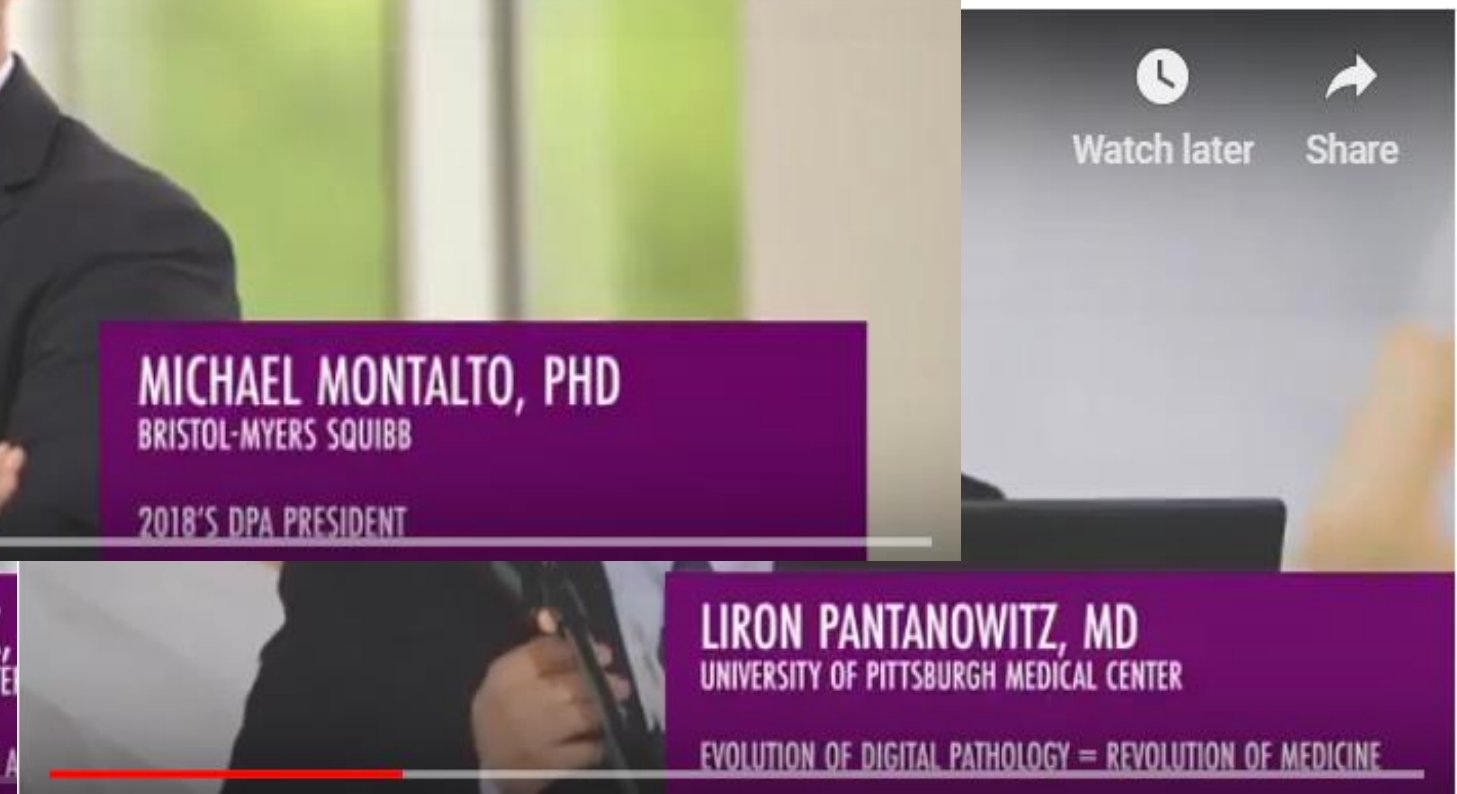
- Abstracts of all Pathology Visions presentation are published in the *Journal of Pathology Informatics* since 2017.
- Member publication posting on DPA website is available per request.
- Previous white paper presentations are on DPA website.
- Various new white papers are in progress.

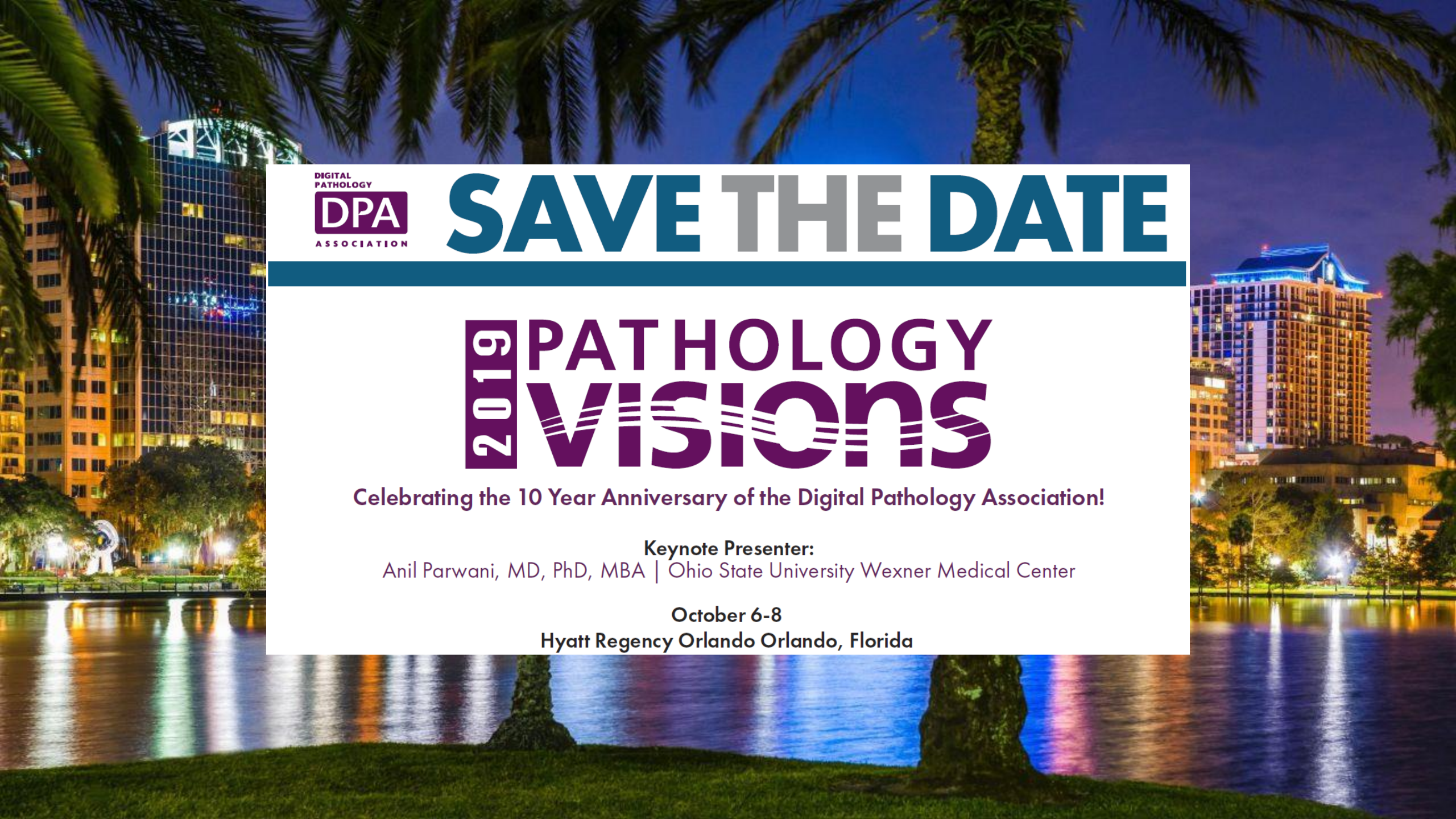
Webinars & Blogs

- DPA members have access to all archived webinars.
- DPA members are welcome to post blogs.

DIGITAL PATHOLOGY DPA ASSOCIATION

Pathology Visions





DIGITAL PATHOLOGY DPA ASSOCIATION

SAVE THE DATE

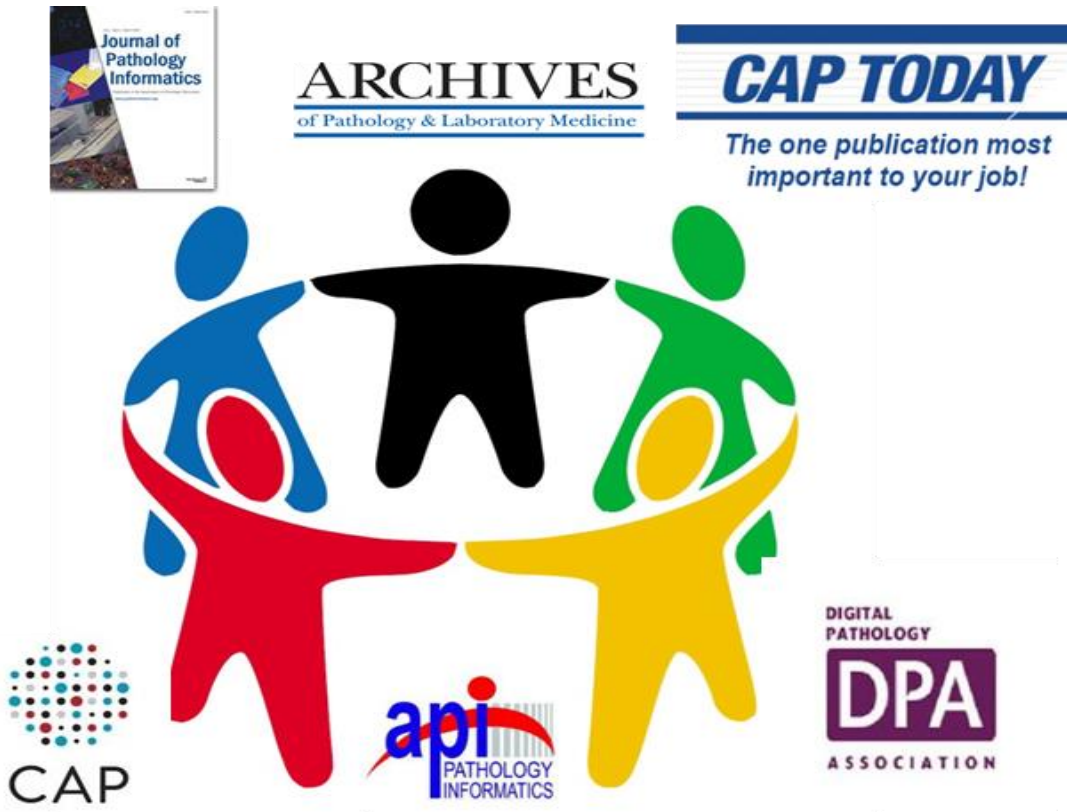
2019 PATHOLOGY VISIONS

Celebrating the 10 Year Anniversary of the Digital Pathology Association!

Keynote Presenter:
Anil Parwani, MD, PhD, MBA | Ohio State University Wexner Medical Center

October 6-8
Hyatt Regency Orlando Orlando, Florida

Conclusions



- Digital pathology and artificial intelligence are here to stay and will continuously transform the delivery of precision medicine.
- Collaboration of pathologists, scientists and industry are important to move the field forward in an impactful way.
- Each individual can make a difference.

Catalyst for change

Facilitator for collaboration

DIGITAL PATHOLOGY DPA ASSOCIATION

Any Questions ?

Marilyn M. Bui, MD,PhD, FCAP
Email: Marilyn.Bui@Moffitt.org

Marilyn M. Bui | Moffitt Cancer Center
https://moffitt.org/providers/marilyn-bui/

@DrBuiPathology

- Senior Member/professor of Pathology, Scientific Director of Analytic Microscopy Core, President of Medical Staff and Cytopathology Fellowship Program Director at the Moffitt Cancer Center https://moffitt.org in Tampa, Florida
- Chair of the College of American Pathologists (CAP) www.cap.org/ Guidelines Committee Expert Panel for Quantitative Image Analysis of HER2 Immunohistochemistry for Breast Cancer. Vice chair of the CAP Digital Pathology Committee
- President-elect of the Digital Pathology Association https://digitalpathologyassociation.org/

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DIGITAL PATHOLOGY ASSOCIATION

DPA

CAP

Analytic Microscopy Core

Scientific Director:
Marilyn M. Bui, MD, PhD

Joseph Johnson, MS: Core Manager
Tingan (Anna) Chen, PhD: Microscopy Specialist III
Aga Kasprzak, MS: Microscopy Specialist III
Jonathan Nguyen, MS: Microscopy Specialist III

MRC 4058

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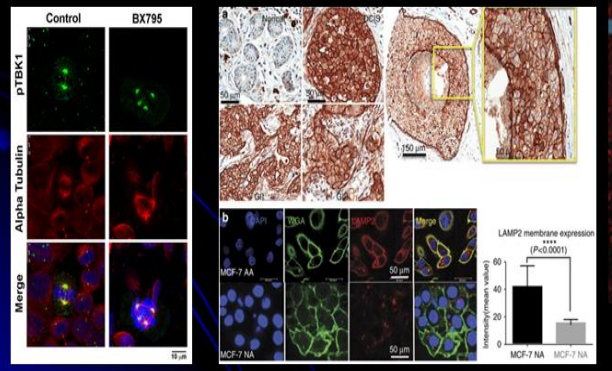
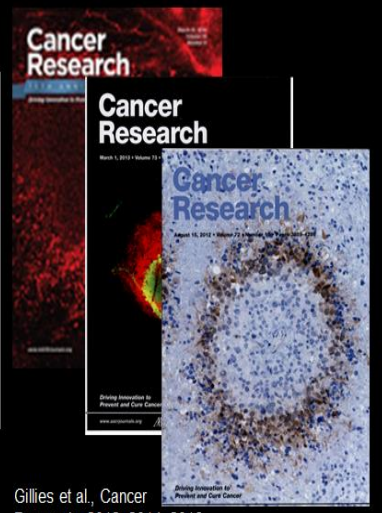
- Multiple image analysis software platforms
- 4 dedicated staff members that provide assistance, training, consultation, and experiment design services
- During previous CCSG period:
  - Supported by over 100 unique PIs including members of all 5 research programs
  - 47% increase in usage hours
  - Contributed on more than 150 publications including:

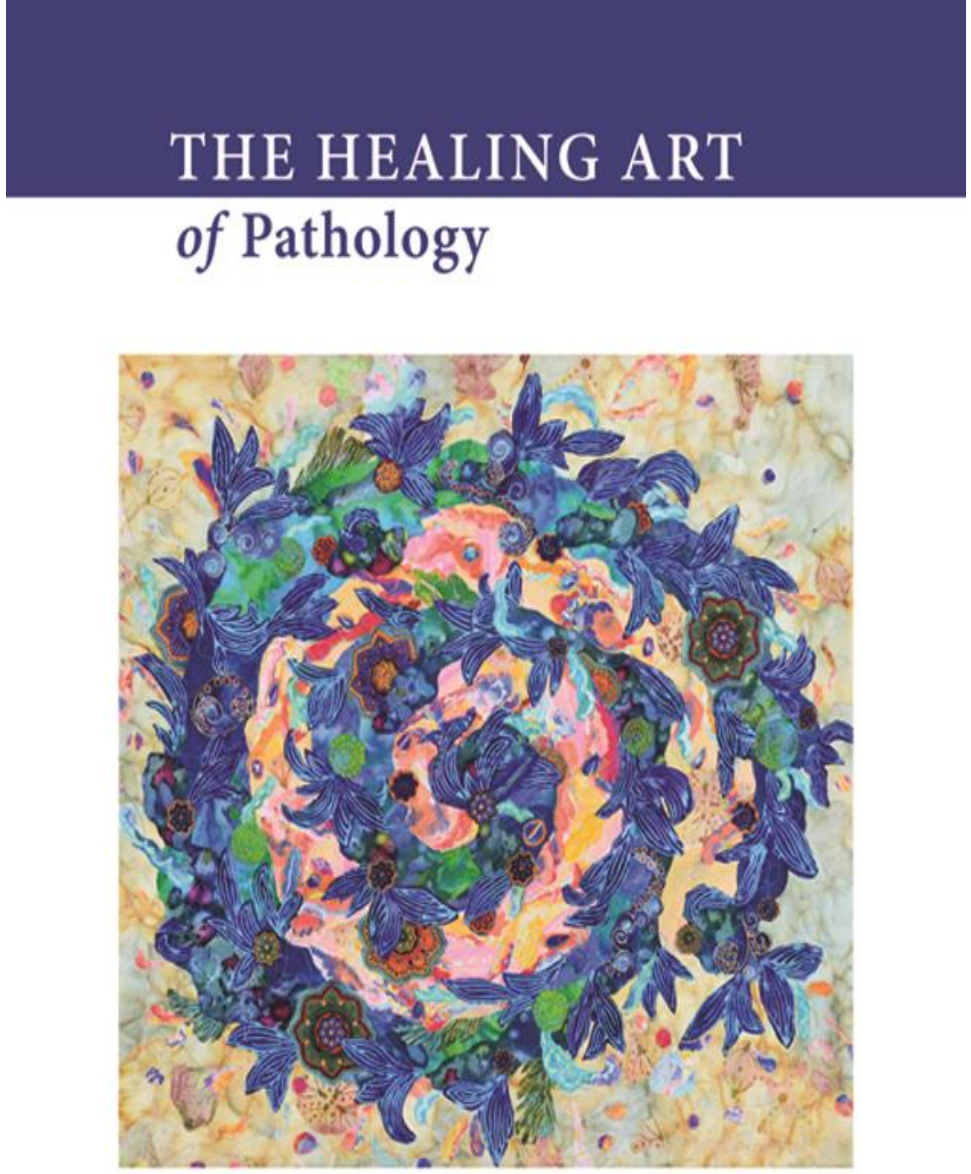


Chellappan et al., Nature Communications, 2015

Gillies et al., Nature Communications, 2016



Gillies et al., Cancer Research, 2012, 2014, 2016



https://www.amazon.com/HEALING-ART-PATHOLOGY-FCAP-Marilyn/dp/0983706883

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