
# Pathology: The Present State of Future

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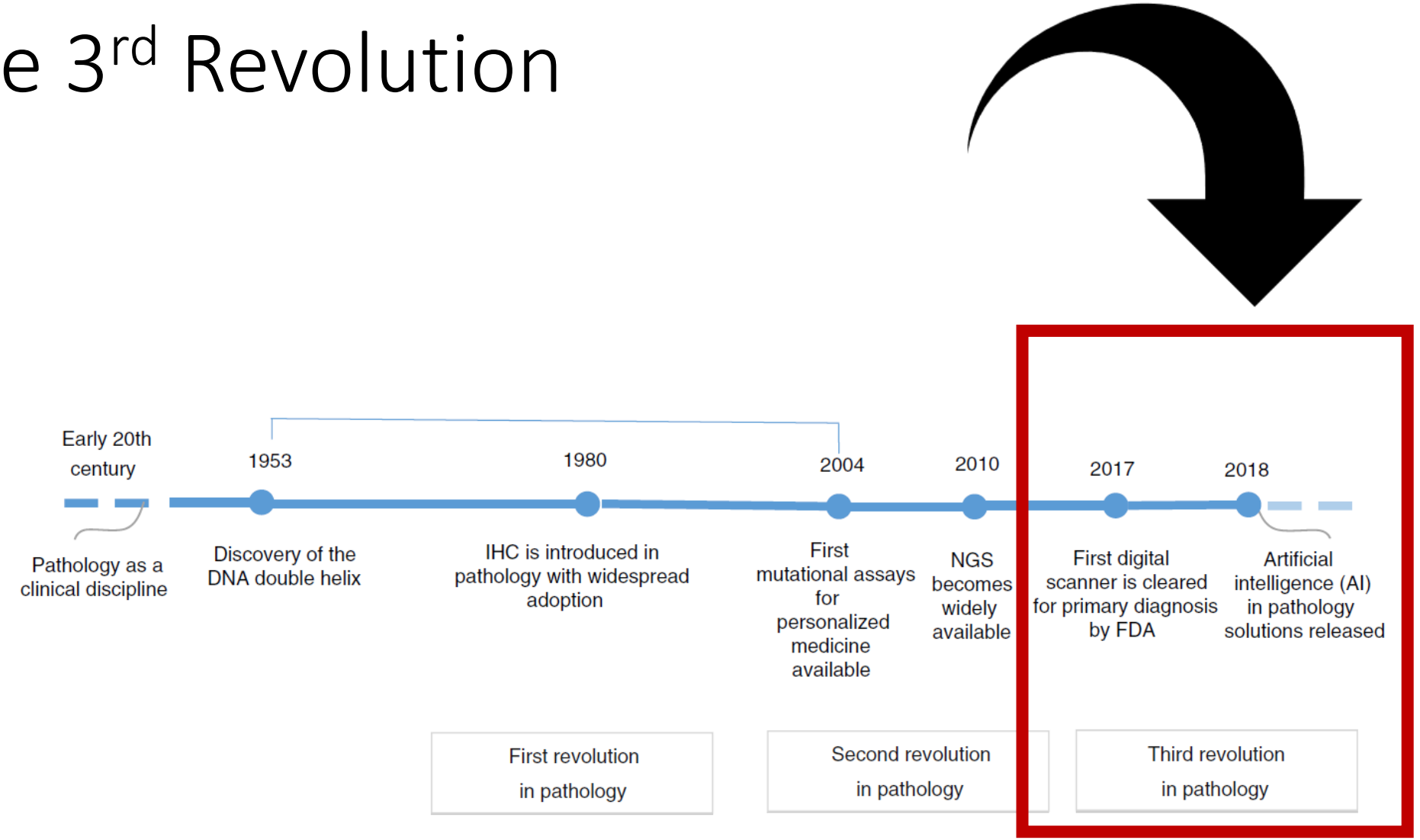
# The 3rd Revolution



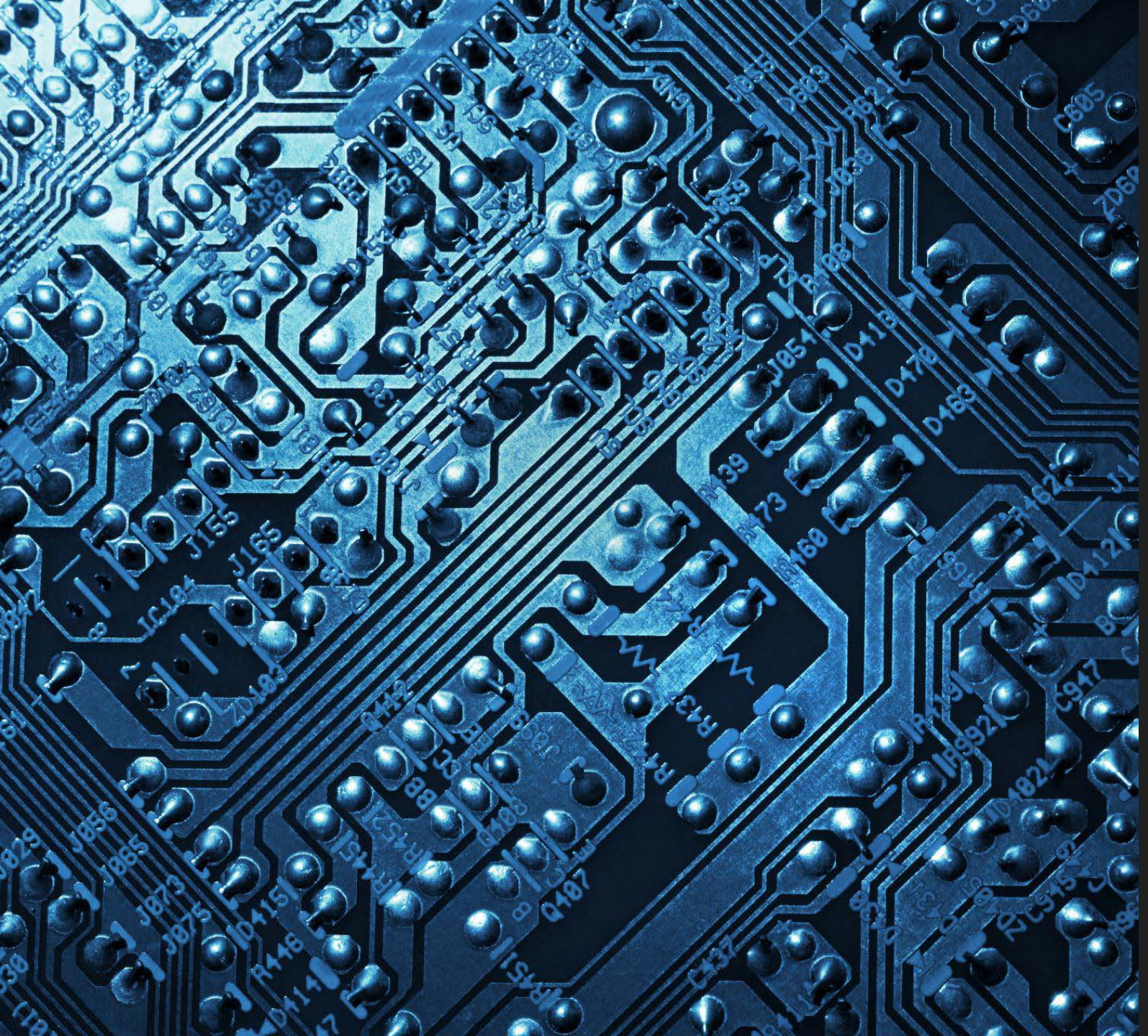

Histopathology 2019, 74, 372–376.

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

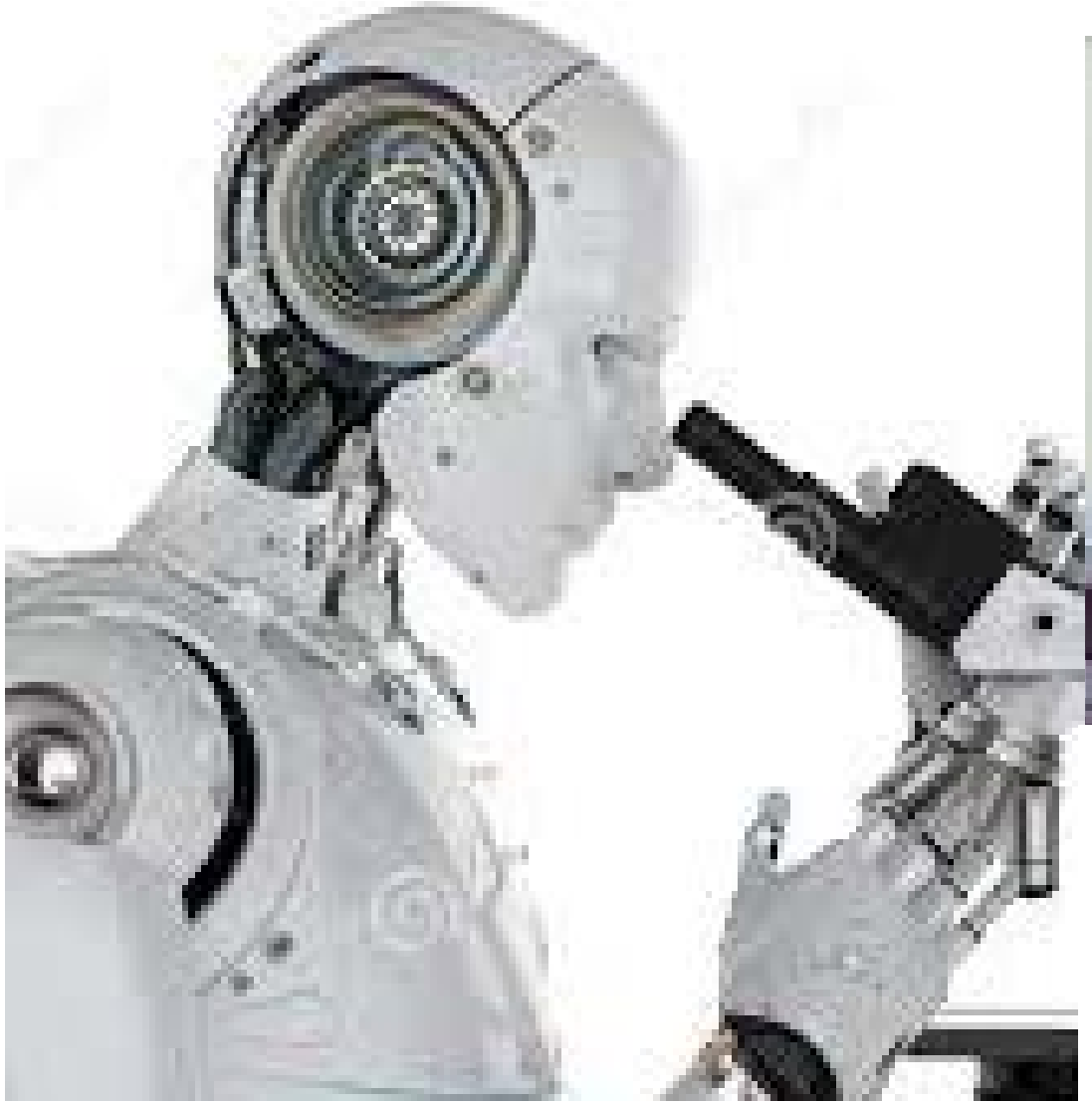
## A Key Milestone Is Reached and New Questions Are Raised

Arch Pathol Lab Med. 2018;142:1383–1387

• 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.



# So what does Digital Pathology look like ?

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# Digital Pathology Components

## Ultra Fast Scanner

- High quality images
- Ready for volume and speed
- Easy to use
- Fully automated scanning

## Image Management System Viewer

- Enhanced viewing experience
- Streamlined digital workflow
- Smart caseload management
- Real-time collaboration


## Image Management System Server and Storage software

- Cost effective deployment
- Tailored scalability
- Versatile integration
- Multi-site harmonization

# Whole Slide Imaging Versus Microscopy for Primary Diagnosis in Surgical Pathology

*A Multicenter Blinded Randomized Noninferiority Study of 1992 Cases (Pivotal Study)*

Am J Surg Pathol 2018;42:39–52

# Validating Whole Slide Imaging for Diagnostic Purposes in Pathology

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

Arch Pathol Lab Med. 2013;137:1710–1722

# Fully Automated Labs

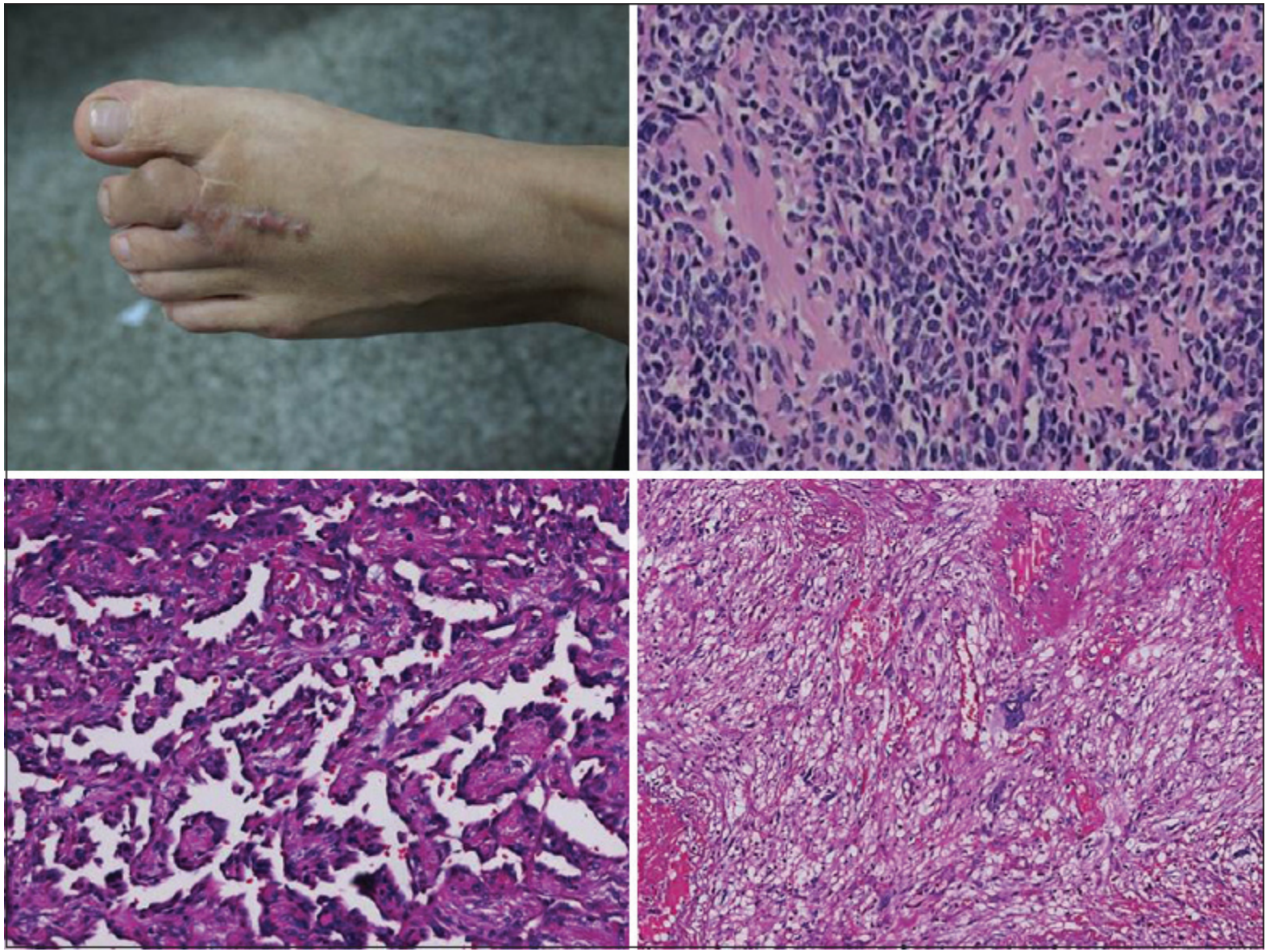
- Sweden – 2 labs completely digital for primary diagnosis
- Department of Pathology at the Utrecht University Medical Center – 2016
  - All the Netherlands Pathology Centers to become digital
- Memorial Sloan Kettering Cancer Center (MSKCC), NY – retrospective
- University Hospital Centre of Montreal (CHUM) – moving towards digitization
- …….

# WSI Telepathology

- UPMC Experience:
  - Transplant biopsies from Italy (Mediterranean transplant Institute) are read at UPMC
  - Excellent concordance
- International WSI Telepathology Consultations – iPath (Univ of Basel)
- UPMC – KingMed, China TeleConsultation Center
- A digital pathology consultation portal (https://pathconsult.upmc.com/)

Pantanowitz L, Wiley CA, Demetris A et al. Experience with multimodality telepathology at the University of Pittsburgh Medical Center. J. Pathol. Inform. 2012; 3; 45

Zhao C, Wu T, Ding X, Parwani AV, et al. International telepathology consultation: Three years of experience between the University of Pittsburgh Medical Center and KingMed Diagnostics in China. J Pathol Inform 2015;6:63



**(Top left) recurrent acral myxoinflammatory fibroblastic sarcoma. The clinical image shown in this case was supplied by KingMed upon request.**

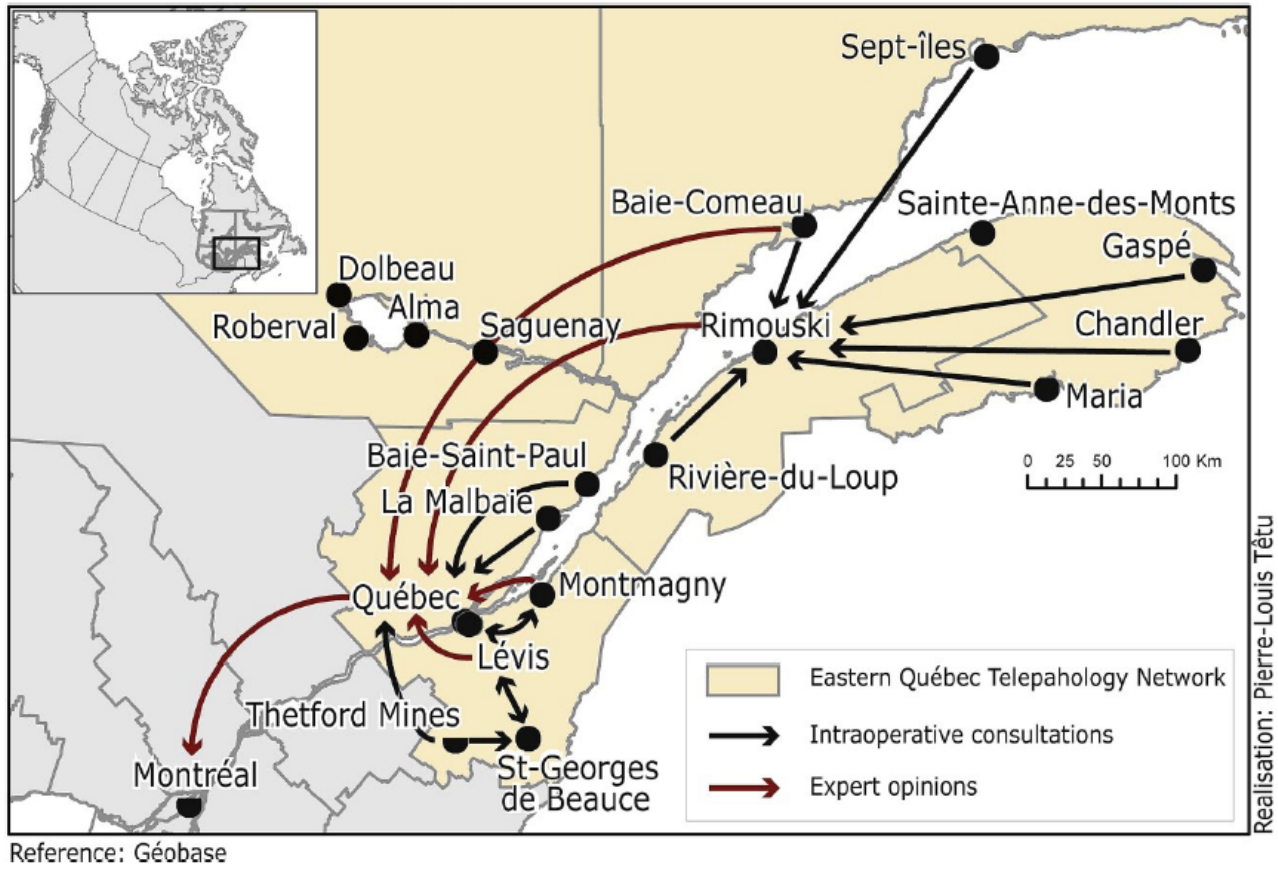
**(Top right) Extraskeletal mesenchymal chondrosarcoma.**

**(Bottom left) retiform hemangioendothelioma.**

**(Bottom right) Pleomorphic hyalinizing angiectatic tumor**

# Canadian Experience

- The Eastern Quebec Telepathology Network is the largest network in the World - 2011
- 22 sites
- Primary diagnosis
- Intraoperative consultation
- 2nd opinions
- Eductaion




Pare G, Meyer J, Trudel MC, Tetu B. Impacts of a large decentralized telepathology network in Canada. Telemed. J. E. Health. 2016; 22; 246–250.

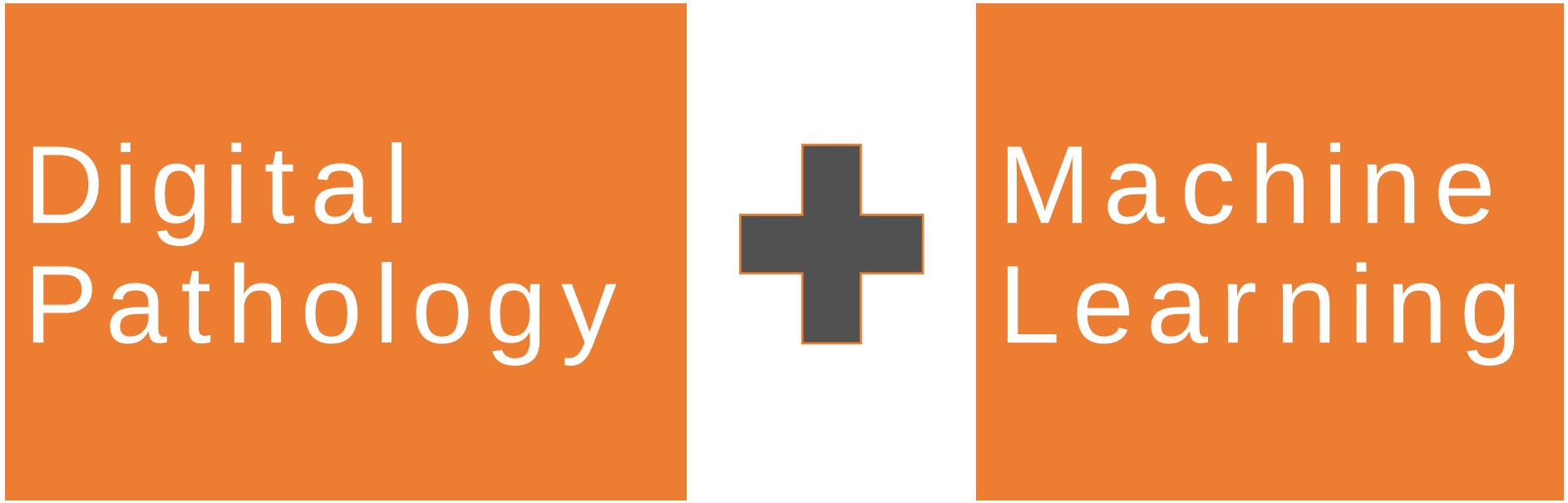
# KHSC Experience

- Intraoperative frozen section consultation with UHN for Neurosurgery cases

# Challenges in digital pathology

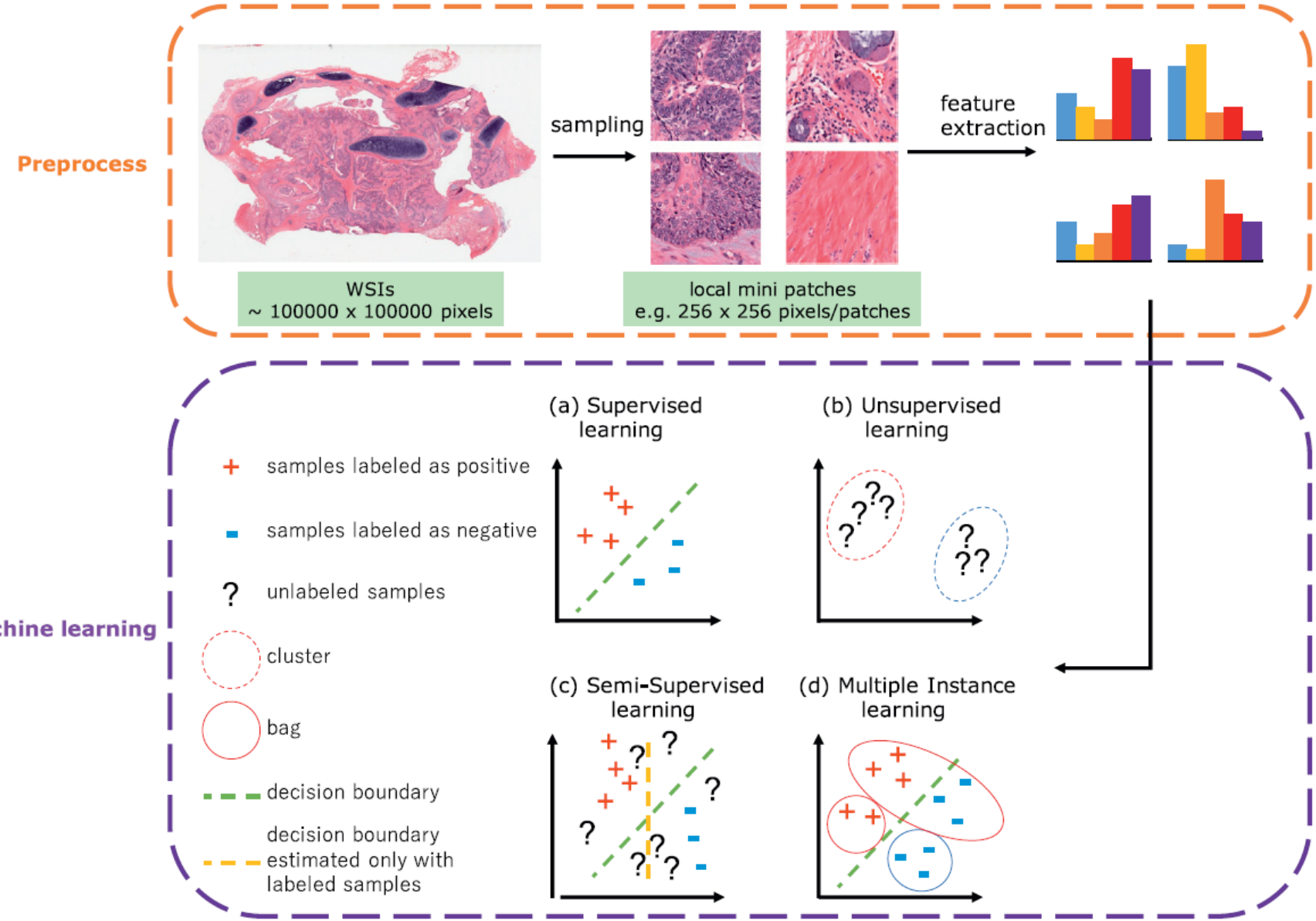
- Cost – additive to glass slides
- Large image size – technical issues, storage issues
- Challenges related to tissue processing
- Specific diagnostic categories
  - Dysplasia – focal, high power changes altered
  - Focal findings/ diagnostic changes
- Pathologist confidence in the technology

Bethany J. Williams, Philip DaCosta, Edward Goacher, and Darren Treanor (*2017*) A Systematic Analysis of Discordant Diagnoses in Digital Pathology Compared With Light Microscopy. Archives of Pathology & Laboratory Medicine: December 2017, Vol. 141, No. 12, pp. 1712-1718




*“Creativity is intelligence having fun.”*
Albert Einstein

Philips and Paige team up to bring Artificial Intelligence (AI) to clinical pathology diagnostics: Dec 2019


Preprocess
sampling
feature extraction
WSIs
~ 100000 x 100000 pixels
local mini patches
e.g. 256 x 256 pixels/patches
Machine learning
samples labeled as positive
samples labeled as negative
unlabeled samples
cluster
bag
decision boundary
decision boundary estimated only with labeled samples
(a) Supervised learning
(b) Unsupervised learning
(c) Semi-Supervised learning
(d) Multiple Instance learning

# Artificial Intelligence–Based Breast Cancer Nodal Metastasis Detection

## Insights Into the Black Box for Pathologists

*Yun Liu, PhD; Timo Kohlberger, PhD; Mohammad Norouzi, PhD; George E. Dahl, PhD; Jenny L. Smith, MD; ash Mohtashamian, MD; Niels Olson, MD; Lily H. Peng, MD, PhD; Jason D. Hipp, MD, PhD; Martin C. Stumpe, PhD*

(Arch Pathol Lab Med. doi: 10.5858/arpa.2018-0147-OA)

# Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer

*(JAMA.* 2017;318(22):2199-2210)

- Camelyon16 and 17 challenges
- LYNA algorithm

nature medicine

ARTICLES

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

# 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*]

- TCGA tissue sets
- AdenoCa vs Sq Ca vs normal lung tissue – AUC 0.97
- Potential to predict 6/10 most common mutations in adenoca
- **STK11, EGFR, FAT1, SETBP1, KRAS and TP53**

# Mitoses

Predicting breast tumor proliferation from whole-slide images: the TUPAC16 challenge

http://tupac.tue-image.nl

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npj | Digital Medicine

www.nature.com/npjdigitalmed

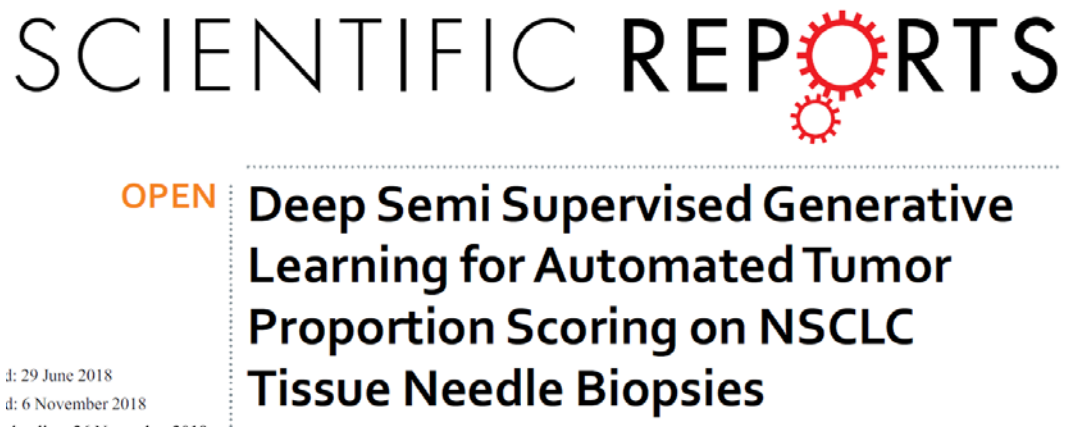
ARTICLE OPEN

Similar image search for histopathology: SMILY

Google - Similar Medical Images Like Yours (SMILY)

# PD-L1 Staining Assessment

www.nature.com/scientificreports




Scientific REPORTS | (2018) 8:17343

Automated image analysis of NSCLC biopsies to predict response to anti-PD-L1 therapy

Althammer et al. Journal for ImmunoTherapy of Cancer. (2019) 7:121

Automated
Double staining – CD8/PD-L1

# Clinical Trials

The Journal of Pathology: Clinical Research
*J Pathol Clin Res;* April 2019; **5:** 81–90
Published online 25 March 2019 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/cjp2.127

**PERSPECTIVE**

## The use of digital pathology and image analysis in clinical trials

Robert Pell[1], Karin Oien[2], Max Robinson[3], Helen Pitman[4], Nasir Rajpoot[5], Jens Rittscher[1], David Snead[6†], and Clare Verrill,[1†*]
on behalf of the UK National Cancer Research Institute (NCRI) Cellular-Molecular Pathology (CM-Path) quality assurance working group[‡]

# A deep learning image-based intrinsic molecular subtype classifier of breast tumors reveals tumor heterogeneity that may affect survival

Mustafa I. Jaber[1], Bing Song[2], Clive Taylor[3], Charles J. Vaske[4], Stephen C. Benz[4], Shahrooz Rabizadeh[1,2], Patrick Soon-Shiong[2] and Christopher W. Szeto[4*]

1. The image analysis predicts PAM50 subtypes
2. Also identified significant heterogeneity within the slides/ cases to predict survival (luminal A vs basal-like)

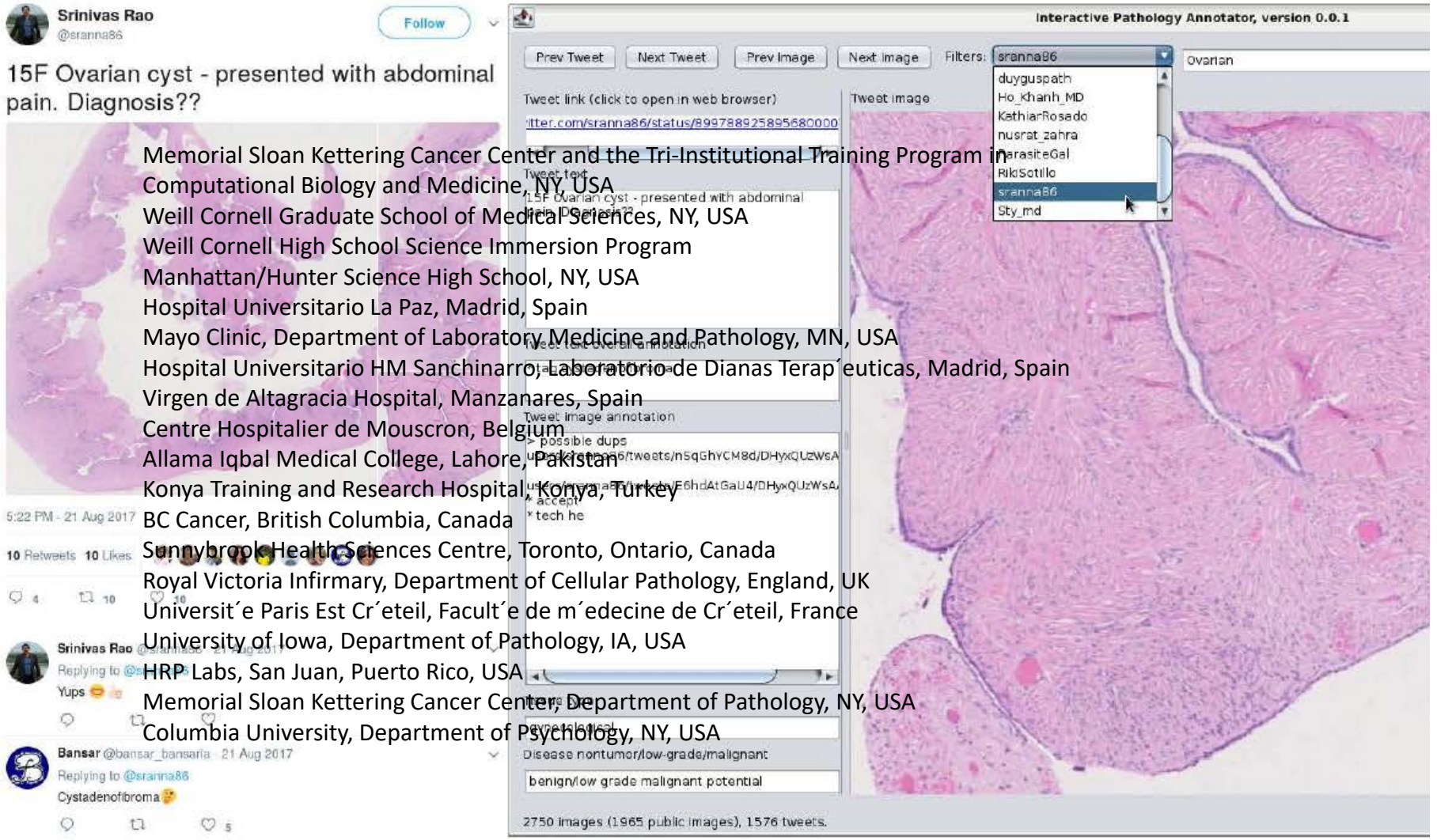
Breast Cancer Research (2020) 22:12

# Challenges and Limitations of AI

# Annotation of digital images – biggest time intensive step


- Garbage in garbage out

# Large-Scale Annotation of Histopathology Images from




Memorial Sloan Kettering Cancer Center and the Tri-Institutional Training Program in Computational Biology and Medicine, NY, USA
Weill Cornell Graduate School of Medical Sciences, NY, USA
Weill Cornell High School Science Immersion Program
Manhattan/Hunter Science High School, NY, USA
Hospital Universitario La Paz, Madrid, Spain
Mayo Clinic, Department of Laboratory Medicine and Pathology, MN, USA
Hospital Universitario HM Sanchinarro, Laboratorio de Dianas Terap´euticas, Madrid, Spain
Virgen de Altagracia Hospital, Manzanares, Spain
Centre Hospitalier de Mouscron, Belgium
Allama Iqbal Medical College, Lahore, Pakistan
Konya Training and Research Hospital, Konya, Turkey
BC Cancer, British Columbia, Canada
Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
Royal Victoria Infirmary, Department of Cellular Pathology, England, UK
Universit´e Paris Est Cr´eteil, Facult´e de m´edecine de Cr´eteil, France
University of Iowa, Department of Pathology, IA, USA
HRP Labs, San Juan, Puerto Rico, USA
Memorial Sloan Kettering Cancer Center, Department of Pathology, NY, USA
Columbia University, Department of Psychology, NY, USA

# Limitations

- Some algorithms are black boxes
- Overfitting and other inherent errors
- Over-reliance without clinical context
  - ESR, CRP, high platelets or any  number of examples
- Ethics issues
  - Data confidentiality, data ownership, data sharing
  - Digitization and storage of data are new facets for REBs
  - Evolving standardized guidelines


# Will I be replaced ?

# NO

- ML is a screening and support tool for Pathologists
- Validation, appropriate clinical query and integration
- New roles integrating computation and pathology

Journal List › J Pathol Inform › v.7; 2016 › PMC5027737

Journal of Pathology Informatics
Publication of Association for Pathology Informatics, USA
Home | Browse articles | Instructions | Submit articles

J Pathol Inform. 2016; 7: 39.
Published online 2016 Sep 1. doi: 10.4103/2153-3539.189704

PMCID: PMC5027737
PMID: 27688930

## A novel leadership fellowship in digital pathology

Bethany Jill Williams[1,*] and Darren Treanor[1]

Leeds Teaching Hospitals NHS Trust, Leeds, UK

# Uses

- Screening
- Measurements – tumor size, distance from margins etc
- Prognostication – mitotic count
- Predictive  - assess the immune infiltrate and help with the scoring (PD-L1 inhibitor)
- Decision support tool – e.g. fibroadenoma vs benign phyllodes tumor

# Thank You