Challenges and Rewards of AI Software Applications in Pathology

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Park City, Feb. 9th 2022

1

Nothing to disclose related to this presentation

2

The case management cockpit

- Access to all data associated with diagnosis workup
- Clinical workup data sources:
  - Pathology slides and report
  - Laboratory test data
  - Radiology report and images
  - Electronic medical record system
- Pathology imaging data sources
  - Gross room images, light microscopy, fluorescent microscopy, electron microscopy
  - Laboratory medicine images: gel electrophoresis, bacterial/viral cultures, Ova & Parasites, etc.

3

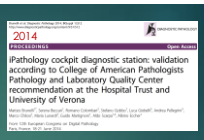
CAP

2013

Validating Whole Slide Imaging for Diagnostic Purposes in Pathology

Pantanowitz et al; Arch Pathol Lab Med : 137, p1710

- Validation should demonstrate that the WSI system 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.



2014

iPathology cockpit diagnostic station: validation according to College of American Pathologists Pathology and Laboratory Quality Center recommendation at the Hospital Trust and University of Verona

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2019

Models for implementing artificial intelligence in pathology practice
Douglas Hartman, U of Pittsburg

https://slidetodoc.com/models-for-implementing-artificial-intelligence-in-pathology-practice/

- Standardized measurements and techniques
- Standardized image formats and interchange
- Reference studies and datasets

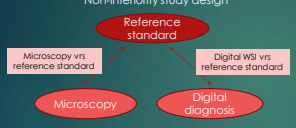
4

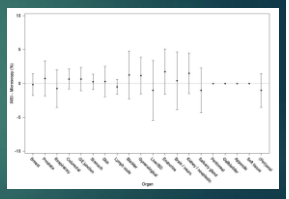
Whole Slide Imaging Versus Microscopy for Primary Diagnosis in Surgical Pathology
A Multicenter Blinded Randomized Noninferiority Study of 1992 Cases (Pivotal Study)

Am J Surg Pathol • Volume 42, Number 1, January 2018

(Mukhopadhyay et al. (Clive Taylor USC)

Non-inferiority study design

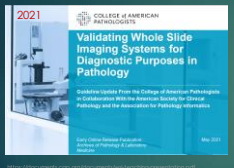




4 centers
8 enrolment pathologists verify primary diagnosis used as reference standard
16 reading pathologists (M (20 cases) → washout (4w) →digital WSI
3 pathologists to judge concordance

5

CAP ASCP api PATHOLOGY INFORMATICS



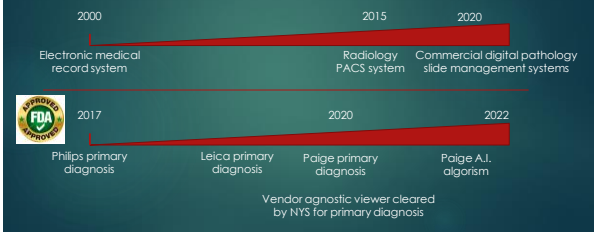
https://documents.cap.org/documents/wsi-teaching-presentation.pdf

What should be done to validate a whole slide digital imaging system for diagnostic purposes before it is placed in clinical service ?

- Pathologist must validate slide set of at least 60 H&E cases (FFPE, frozen, hemepath)
- & 20 IHC and special stain cases
- Concordance glass/digital ≥ 95% (2 week washout)
- Good practice standards from 2013 : each lab should do their own validation which must include a pathologist, emulate a real world situation and encompass the entire WSI workflow

6

Events forming digital pathology



7


Journal of the American Medical Informatics Association, 28(9), 2021, 1874–1884
doi: 10.1093/jamia/ocab085
Advance Access Publication Date: 14 July 2021
Research and Applications

AMIA

Research and Applications

Integrated digital pathology at scale: A solution for clinical diagnostics and cancer research at a large academic medical center

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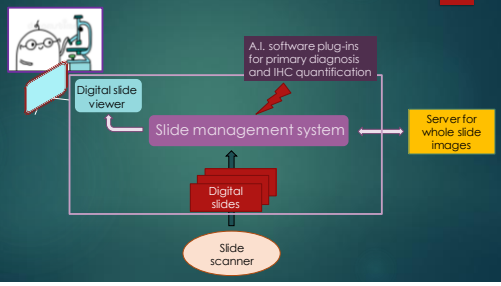
- Data on digital pathology implementation at a large tertiary care medical center
- Digital slide viewer installed at 4 hospital systems and used over 3yrs by 926 pathologists and researchers evaluating 288 903 digital slides.
- Integrated digital pathology solution for sign-out, research and education
- Different functionalities are required for the three end user groups
- Solution to assure data and patient privacy is most critical factor
- The framework includes A.I. software for diagnosis of prostate cancer, basal cell carcinoma & breast cancer metastasis

8

Digital pathology infrastructure

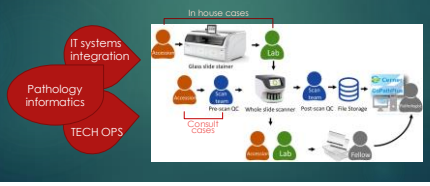


9

Clinical implementation of digital pathology requires a team

CHALLENGES for DIGITAL pathology

- Integration of the digital pathology computer and software systems with other laboratory information systems in pathology



10

Clinical implementation of digital pathology requires a team

CHALLENGES for COMPUTATIONAL pathology

- To bring research grade algorithms into clinical practice

A.I. Algorithm development and validation → Algorithm testing in independent cases → Algorithm refinement in thousands of cases → API plugin for deployment → Post-market evaluation

Computer vision research | Commercial development

11

Why should pathologists adopt digital pathology ?

- Efficiency
- Accuracy
- Structured, accessible information and slide organization
- Job satisfaction of pathologists and lab personnel
- Client satisfaction
- Improved communication
- Research opportunities
- Education

12

Resistance to digital sign out in pathology

- Distrust of algorithm and computer assistance
- Less control over sign out process
- Less interactions with colleagues
- Speed
- Ergonomics
- Joy of microscopy
- Change in workflow

13

How to overcome resistance and move to a digital sign out

- Partnership between pathologists
- Discovering value in DP
- Educational materials
- Partnership with slide management systems vendor
- Customized interfaces
- High-quality DP products (requires evaluation)
- Internet speed and ergonomics

DIGITAL PATHOLOGY DPA ASSOCIATION

PIc alliance

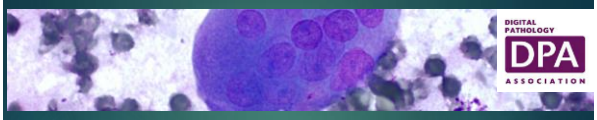
14

What do I need to sign out cases at home

1. March 2020, CMS temporarily waived the requirement for remote locations to have separate CLIA licenses. Advocacy by CAP committees to convert temporary to permanent regulation.
2. The validation study using 60 H&E cases and 20 IHC cases with glass and digital reads. > 95% concordance for diagnostic components affecting patient management
3. Remote readiness:
   - Computer/workstation with large monitor and fast network bandwidth
   - Remote desktop connection through institutional virtual private network with 2-factor authentication

15

Digital Pathology and education



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Digital Anatomic Pathology Academy

Cloud-based platform which provides annotated digital slides with diagnosis and relevant information of morphology and ancillary testing

16

Digital pathology and regulatory science

CAP

A regulatory science initiative to harmonize and standardize digital **pathology** processes to speed up innovation to patients.

Pathology Innovation Collaborative Community

The Alliance for Digital Pathology and AI/ML

You value Collaborations	You have a Regulatory Science Project	You propose your project to Picc	You present to steering committee	Picc helps organize the project	Picc is a network to find interested collaborators
	Focus is NOT on competitive product development			Picc does NOT actively participate in your project All interested members are	

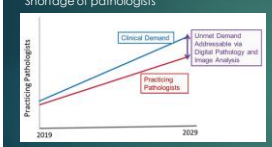
Picc is a collaborative community that provides the infrastructure to connect stakeholders

FDA

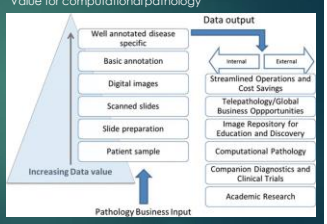
17

Value proposition of digital pathology

Shortage of pathologists

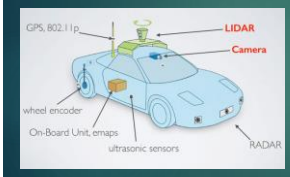


Value for computational pathology



18

What is computational pathology ?



Mechanics
Electronics

DIGITAL PATHOLOGY
engine — Slide management system (SMS)
wheels — Slide scanners

COMPUTATIONAL PATHOLOGY
Data input — Digital slides
Data output — Algorithms

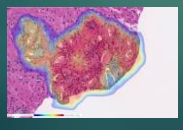
19

FDA approves algorithm for prostate cancer diagnosis

Paige

September 21st, 2021

- Algorithm can be used as second opinion for cancer detection
- approval based on a study where 6 pathologists examined 527 digitally scanned prostate biopsy slides. The pathologist made two assessments, one with and one without the program's help.
- The software improved detection of cancer on individual slide images by 7.3% on average compared to unassisted reads.

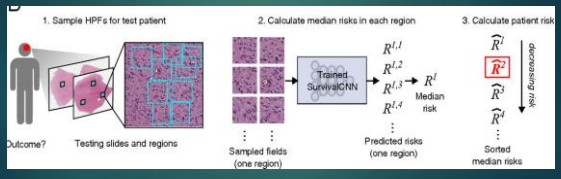


IBEX

20

How do machine learning algorithms work ?

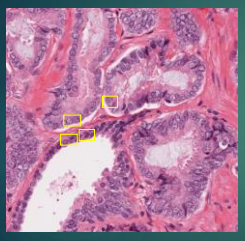
Level 1 : counting positive cells in IHC stained slides
Level 2 : cancer diagnosis and outline of cancer regions
Level 3 : prognosis and treatment recommendation



Predicting cancer outcomes from histology and genomics using convolutional networks. Mobadersany & Lee Cooper PNAS, 2018

21

Pathologist-inspired algorithm development



1. Criteria established by pathologist do diagnose prostate cancer:
   - Loss of basal cell layer
   - Nuclear enlargement
   - Nucleolus
   - Luminal border

2. Force algorithm to learn features of these criteria

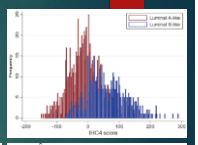
3. Visualize features that the algorithm learned

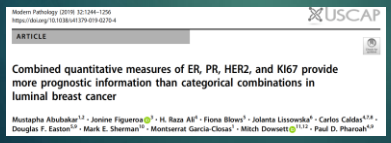
4. This specific approach does not work for grading, which is based on gland architecture

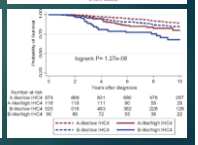
22

IHC quantification

- FDA approved algorisms since 2007
- Algorithm linked to slide scanner
- Home – grown systems
- Semi-automated, pathologists marks region to quantify
- Ki-67, breast panel, PD-L1







23

Automated PD-L1 scoring workflow

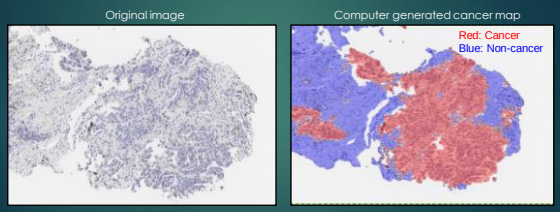
24

Step 1- The computer learns to overlap images from different slides

Step 2: outline areas of necrosis

25

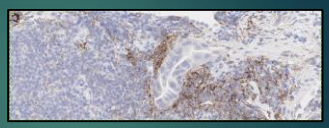
Step 3 - Computer learns to outline cancer regions

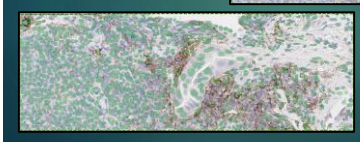


26

Examples of computer-generated annotations in IHC slides – step 4

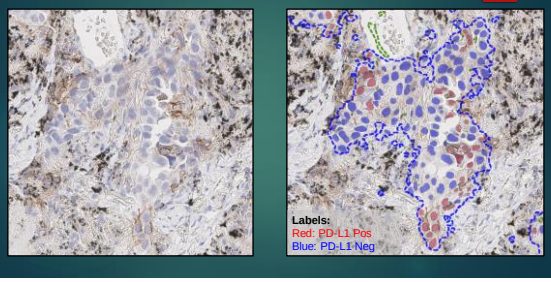
Nuclear outlines and immune cell infiltration





27

Quantification of PD-L1 positive cells – step 5



28

Performance evaluation of the algorithm is critical at your practice location

- Don't trust vendors (yet)
- Algorithms are challenging to optimize
- Off the shelf commercial algorithm need to be tested at your practice location for its performance
- Performance has to be evaluated for each step in the algorithm if there is a problem with the algorithm
- Be involved in testing to understand what the algorithm does
- Data migration into pathology reports

29

Future opportunities in digital and computational pathology

- Automation of anatomic pathology
- Increased efficiency
- Increased accuracy (reimbursement for using algorithm)
- Fast second opinion
- Quantitative data from slides
- Prognostic and treatment related information
- May be able to replace certain expensive genomic testing

30

Future challenges in digital and computational pathology

- Expensive infrastructure
- Integration into existing IT structure
- New operational workflows
- Acceptance by pathologists
- Regulatory framework
- Pricing and cost efficiency

31

Thank you for your attention

QUESTIONS ?

32