Artificial intelligence Applications in Gastrointestinal Pathology

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Disclosure:

Dr. Swanson owns stock and serves on the Scientific Advisory Board for Cogen Bioscience

Dr. Swanson lectures for the France Foundation/ASCP/ACCC (CME/AMA) on biomarker testing in colorectal carcinoma

Outline:

Opening Questions
Digital pathology
Artificial intelligence
General overview of applications in Surgical Pathology & GI
2 examples of research applications in GI Path→ future
Summary (opportunities, challenges)
Closing questions

What is a clinically validated example of AI an application in GI Path?

A) Pancreas cancer detection in core biopsies

B) Metastasis detection within lymph nodes of colorectal cancer resection specimens

C) Grading of dysplasia in Barrett's esophagus

D) Lymph node prediction in T1 polypectomy specimens

E) Eosinophil quantitation in esophageal biopsies

What are current examples of AI applications in GI Path?
Answer:

B) Metastasis detection within lymph nodes of colorectal cancer resection specimens

What are the minimum hardware and software needs to perform clinically validated AI in Surgical Pathology?

What are the minimum hardware and software needs to perform clinically validated AI in Surgical Pathology?

WSI scanners

Image management software

PACS (picture archiving and communication system)

Validated AI software

Current State of Digital Pathology Scanning at the University of Nebraska (UNMC)

2 Leica GT450s

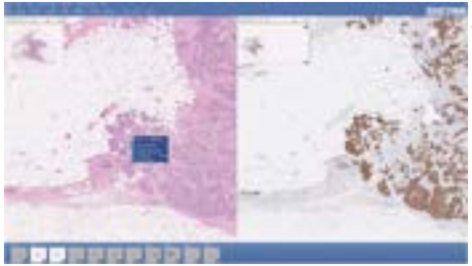
Maggie Sindelar
Lead Digital Pathology Histotech

Currently scanned cases:
-Placenta
-Autopsy
-Transplant biopsies
- Cardiovascular
-Retrospective cases (tumor boards, consults, education
~80 slides a day
~1,500-2,000 slides/month

UNMC's Digital Pathology Future: Fully Digital

GT450

Image Management Software
Must be scanner agnostic
Must be AI/ML agnostic



AI/ML integration

Storage (cloud, hot, cold, on-site, etc.)

<u>Integration with LIS/EMR</u>

Other Factors to Consider When Deploying Digital Pathology

Data architecture plan (on-premise, cloud, hot versus cold)

- Storage is expensive, most pathology departments that have gone fully digital have storage requirements in the petabytes

Who is going to load the scanners? Will need to have additional FTEs

How is your histology AP operations going to function/change to have minimal impact on turn around time?

How is your laboratory information system (LIS) support staff structured? Who will handle software and hardware issues?

$$$$$$$$

A Few Regional Institutions that Have Gone Fully Digital for Surgical Pathology

Memorial Sloan Kettering Cancer Center

utmb

CORE PLUS
SERVICIOS CLINICOS Y PATOLOGICOS

MAYO CLINIC

OHIO STATE

Apple and a PC

Circa 1985

Advantages of Primary Digital Signout

Remote consultation

Archiving slides for teaching

Tumor boards and associated conferences

Application to research

Only way to directly implement into AI algorithms

Business growth development: Technical only, international consults, etc.

Lui et al. "Applications of Artificial Intelligence in Breast Pathology" Arch. Pathol. Lab Med. 147, September 2023

Challenges in GI Pathology

High work volumes

Diagnosis complexity

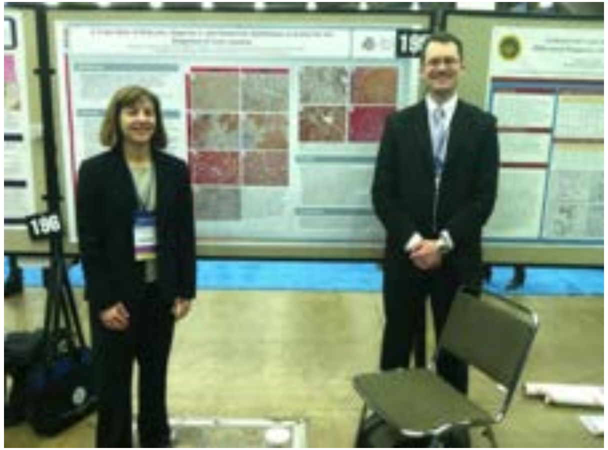
Tedious/repetitive tasks (like counting eosinophils)

Difficult to standardize biomarkers (Ki-67, Her2, PD-L1 etc.)

Grading dysplasia (Barrett's, IBD)

Inspired and partially adapted from: Lui et al. "Applications of Artificial Intelligence in Breast Pathology" Arch. Pathol. Lab Med. 147, September 2023

Limitations to Timely and Accurate GI Pathologic Diagnoses in 2024



- Nationwide shortage of Pathologists
- Differences in Pathologist's skills, diagnostic thresholds, fellowship training, experience
- Availability of ancillary molecular and immunohistochemical studies

Inspired and partially adapted from: Lui et al. "Applications of Artificial Intelligence in Breast Pathology" Arch. Pathol. Lab Med. 147, September 2023

Potential Clinical Applications of AI in GI Pathology Signout

Pre-screening difficult biopsies for cancer/dysplasia

- Example: Identification of H. pylori

Performing rudimentary/tedious tasks

- -Example: counting eosinophils
- Identifying micrometastasis in lymph nodes

Standardization of biomarkers

- Example: Ki-67

Predicting recurrence/chemoresistance/genetic profiles from WSI

Overview of Artificial Intelligence

Machine learning is a type of artificial intelligence

Deep learning is a type of machine learning

Generative AI is a type of deep learning

Transformers and large language models are part of generative AI

Chat GPT is a kind of large language

Machine Learning and Deep Learning

Is a subfield of artificial intelligence

- ML develops algorithms to learn repetitive data patterns from a large data set, then matches new cases to the learned data patterns

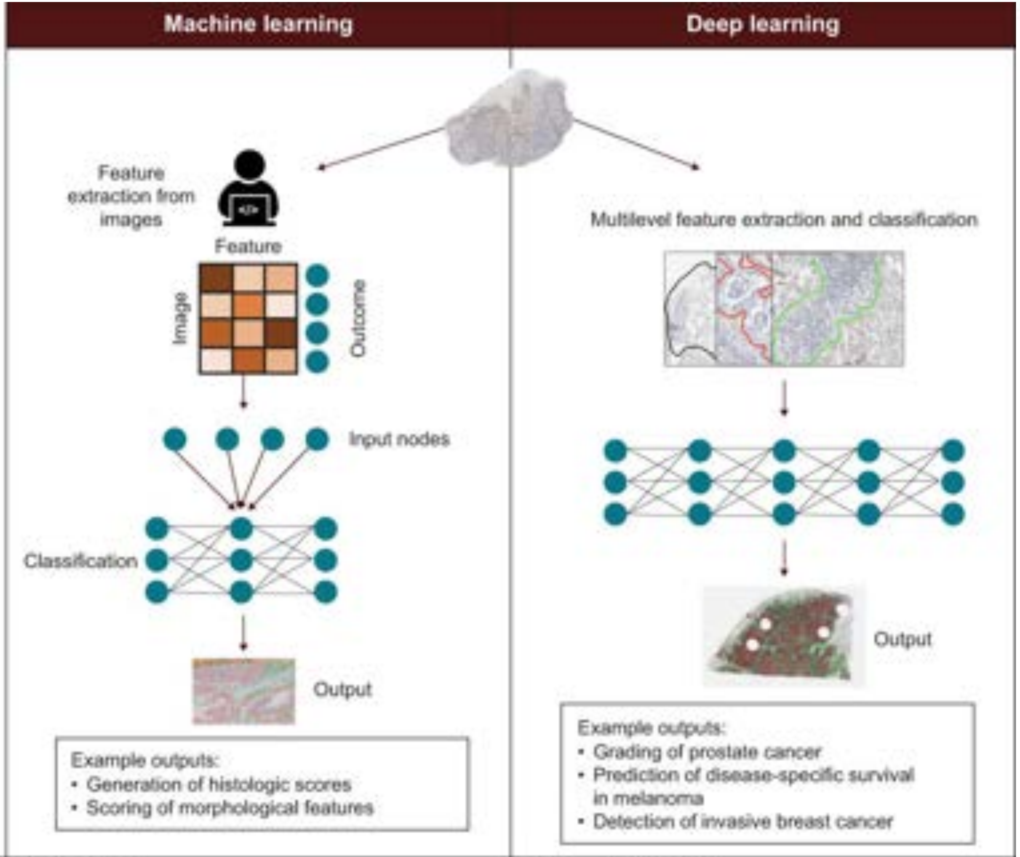
Deep learning is a subset of Machine learning

- Uses artificial neural networks composed of multiple layers (input layer, hidden layers, output layers) to extract progressively higher level features from data.
- The neural network learns data patterns by generating multiple hidden variables from data and also learns hierarchial representation of data that can't easily be recognized by humans.
- Deep learning includes supervised learning, unsupervised learning, semisupervised learning and transfer learning
- Compared to conventional ML, DL is simpler to conduct, performs with high-precision, and is cost-effective

Deep convolutional neural networks, a type of DL algortihm

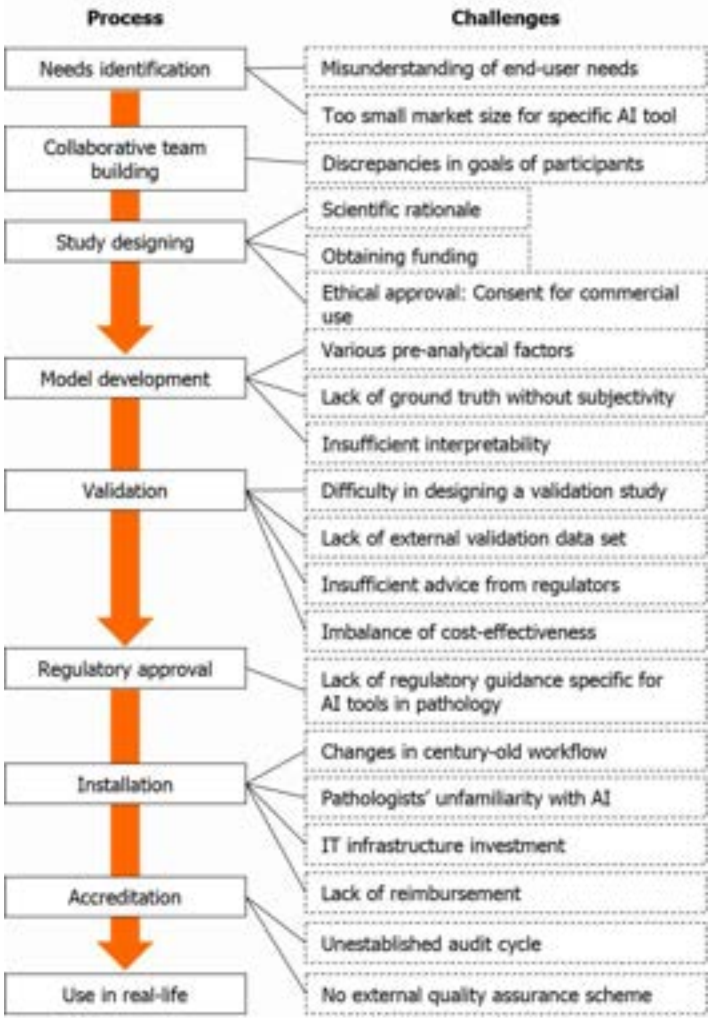
- Has shown superiority in image recognition and analysis

Lui et al. "Applications of Artificial Intelligence in Breast Pathology" Arch. Pathol. Lab Med. 147, September 2023



	Machine learning	Deep learning
Hardware requirements	CPU for training	GPU required for training
Training time	Requires less time to train	Longer training time required
Training input	Annotated images	No operator input. Automated feature extraction is part of the learning process

Modern Pathology 2022 3523-32DOI: (10.1038/s41379-021-00919-2)



From: Yoshida, H. et al. "Requirements for implementation of artificial intelligence in the practice of gastrointestinal pathology"World J Gastroenterol 2021 June 7; 27(21): 2818-2833

OpenVMS Compaq VAX 7000

Circa 1995

Current Clinically Validated AI Applications in Surgical Pathology

Paige®

VISIOPHARM®

aiforia®
AI for image analysis

IBEX

Clinical Application in the US

Any software solution should be developed under the FDA's Quality System Regulation and Good Machine Learning Practices.

Current AI Applications in the United States

A single prostate algorithm currently FDA approved

Some of the "clinically validated" (as advertised on a company's website) algorithms have been approved in the European Union (CE IVD) but don't yet have FDA approval

-->Therefore, these would be considered for research only use only in the US

09/21/2021	DEN200080	Paige Prostate	Paige.AI	Pathology	QPN
05/17/2012	K120489	Tissue of Origin Test Kit FFPE	Pathwork Diagnostics, Inc.	Pathology	OIW

From: https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

11/19/2021	K211326	EndoScreener	Chengdu Wision Medical Device Co., LTD.	Gastroenterology & Urology	QNP
07/23/2021	K211951	GI Genius	Cosmo Artificial Intelligence - AI Ltd	Gastroenterology & Urology	QNP
04/09/2021	DEN200055	GI Genius	Cosmo Artificial Intelligence - AI, Ltd.	Gastroenterology-Urology	QNP
11/25/2019	K190529	SOZO	ImpediMed Limited	Gastroenterology-Urology	QJB
04/16/2018	K180126	SOZO	ImpediMed Limited	Gastroenterology-Urology	OBH
08/11/2017	K172122	SOZO	ImpediMed Limited	Gastroenterology-Urology	OBH
07/25/2023	K223473	ME-APDS™; MAGENTIQ-COLO™	Magentiq Eye LTD	Gastroenterology/Urology	QNP
05/19/2023	K231143	GI Genius System 100 and GI Genius System 200	Cosmo Artificial Intelligence - AI, Ltd.	Gastroenterology/Urology	QNP
04/07/2023	K230658	SKOUT® system	Iterative Scopes Inc.	Gastroenterology/Urology	QNP
03/17/2023	K223073	Alio	Alio, Inc.	Gastroenterology/Urology	DRG
08/12/2022	K213686	SKOUT Software	Iterative Scopes Inc	Gastroenterology/Urology	QNP

From: https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

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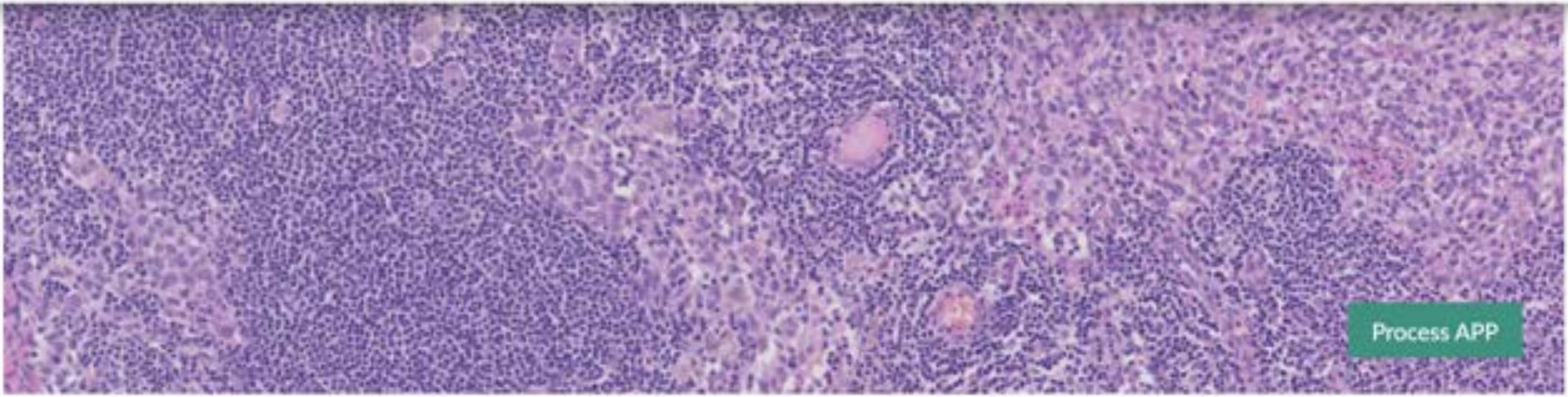


#90159

CE 2797

Metastasis Detection, AI

Certified under IVDR

AI/deep learning-assisted metastasis detection in Lymph nodes – simplifying lymph node assessment.

Approved in the EU, does not currently have FDA approval

Approved in the EU, does not currently have FDA approval

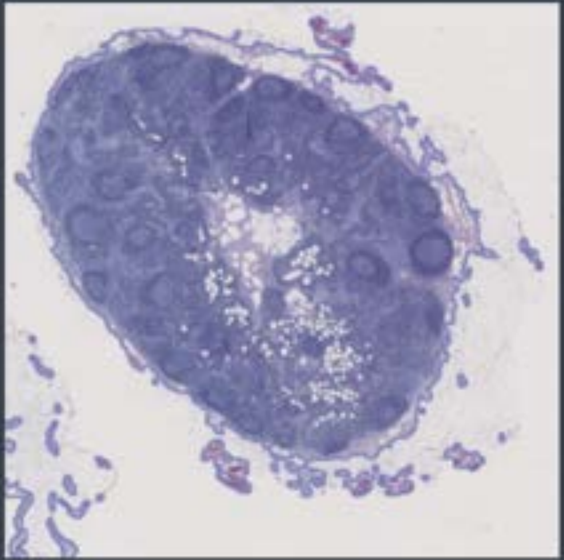


Figure 1

All relevant lymph node tissue is automatically outlined (in purple) for further analysis.

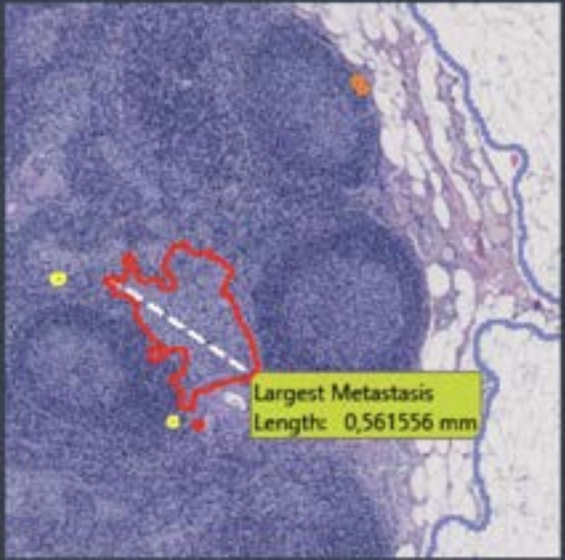


Figure 2

Metastases are identified as High Probability (red), Medium Probability (orange), Low Probability (yellow) and the largest is highlighted and measured.

VISIOPHARM®

> Mod Pathol. 2023 Oct;36(10):100285. doi: 10.1016/j.modpat.2023.100285. Epub 2023 Jul 18.

Performance of an Artificial Intelligence Model for Recognition and Quantitation of Histologic Features of Eosinophilic Esophagitis on Biopsy Samples

Luisa Ricaurte Archila [1], Lindsey Smith [2], Hanna-Kaisa Sihvo [3], Ville Koponen [3], Sarah M Jenkins [4], Donnchadh M O'Sullivan [5], Maria Camila Cardenas Fernandez [5], Yaohong Wang [6], Priyadharshini Sivasubramaniam [1], Ameya Patil [1], Puanani E Hopson [5], Imad Absah [5], Karthik Ravi [7], Taofic Mounajjed [8], Evan S Dellon [9], Albert J Bredenoord [10], Rish Pai [11], Christopher P Hartley [1], Rondell P Graham [1], Roger K Moreira [12]

Affiliations + expand

PMID: 37474003 DOI: 10.1016/j.modpat.2023.100285

EoE Paper Background

Often tedious to count eosinophils

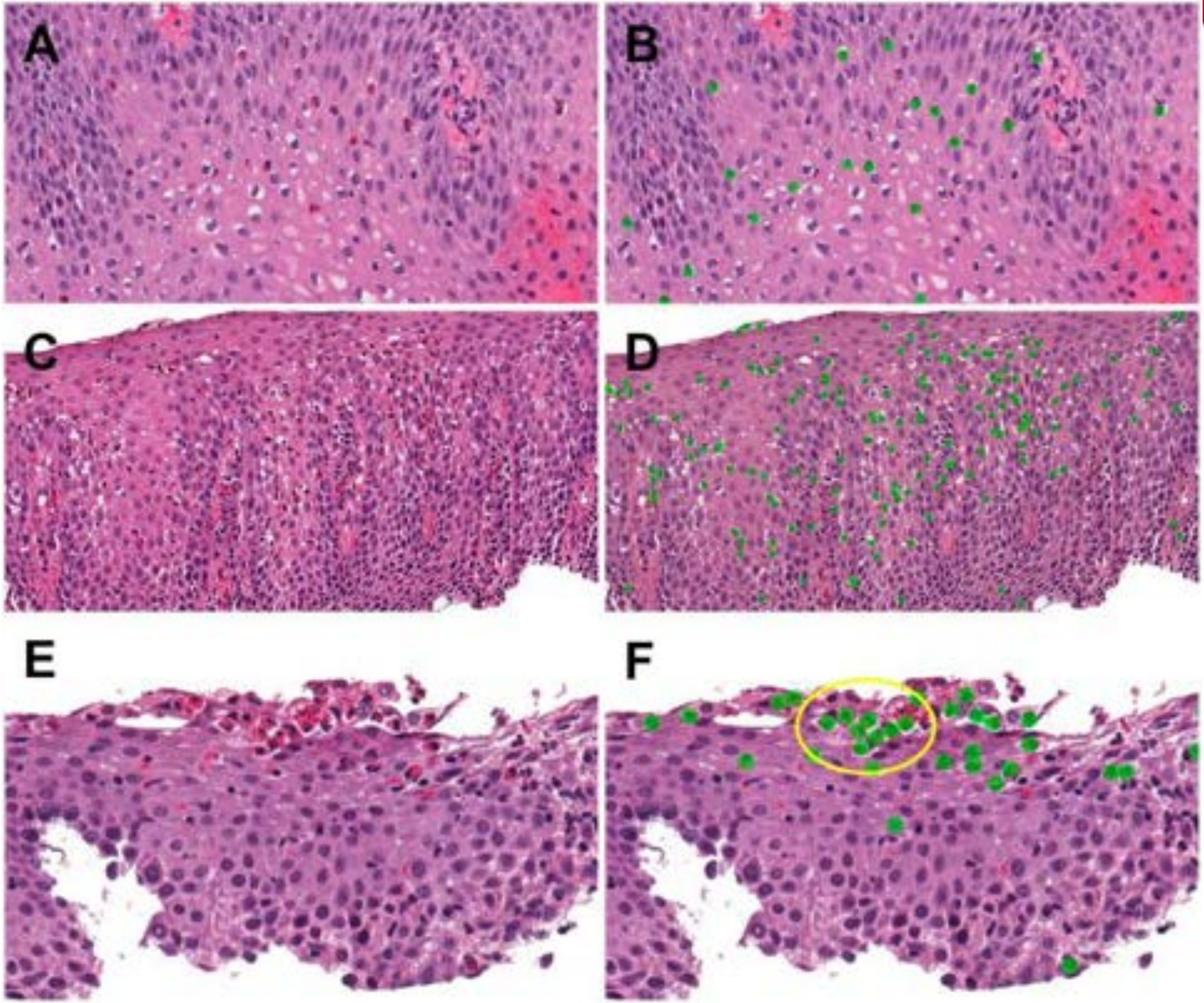
GI docs and clinicians want peak eosinophil count (PEC), also exists: EoEHSS

Study:

Authors had previously developed an AI algorithm using WSI to count eosinophils (supervised deep learning using AI platform (Aiforia)

Prospective study: 203 eosophagus bx. With eosinophilia (91 adult and 112 kids) as well as 10 normal controls

Compared results against expert GI pathologist and central reviewing pathologist


A
B
C
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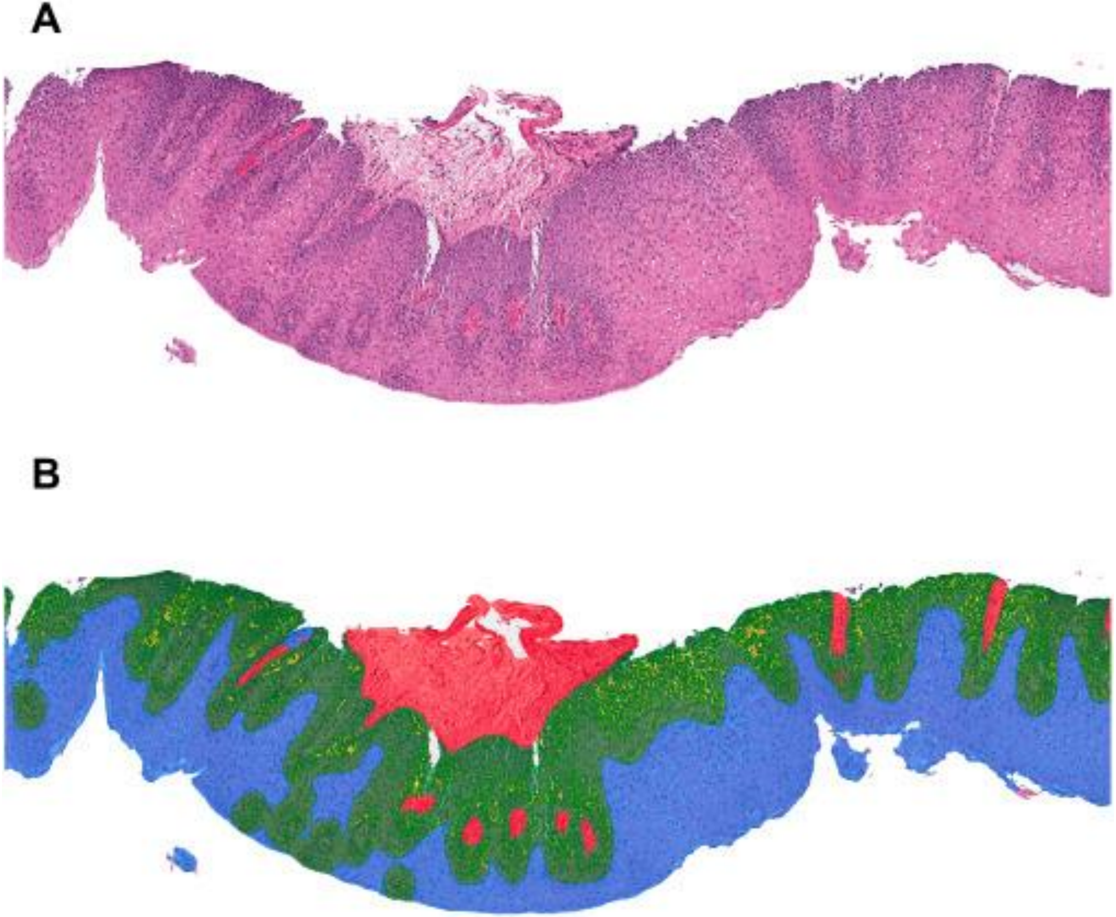

Figure 2. Artificial intelligence model segmentation layers. A, original hematoxylin and eosin stain; B, model segmentation of lamina propria (red), basal zone (green), dilated intercellular spaces (yellow), and surface layer (blue).

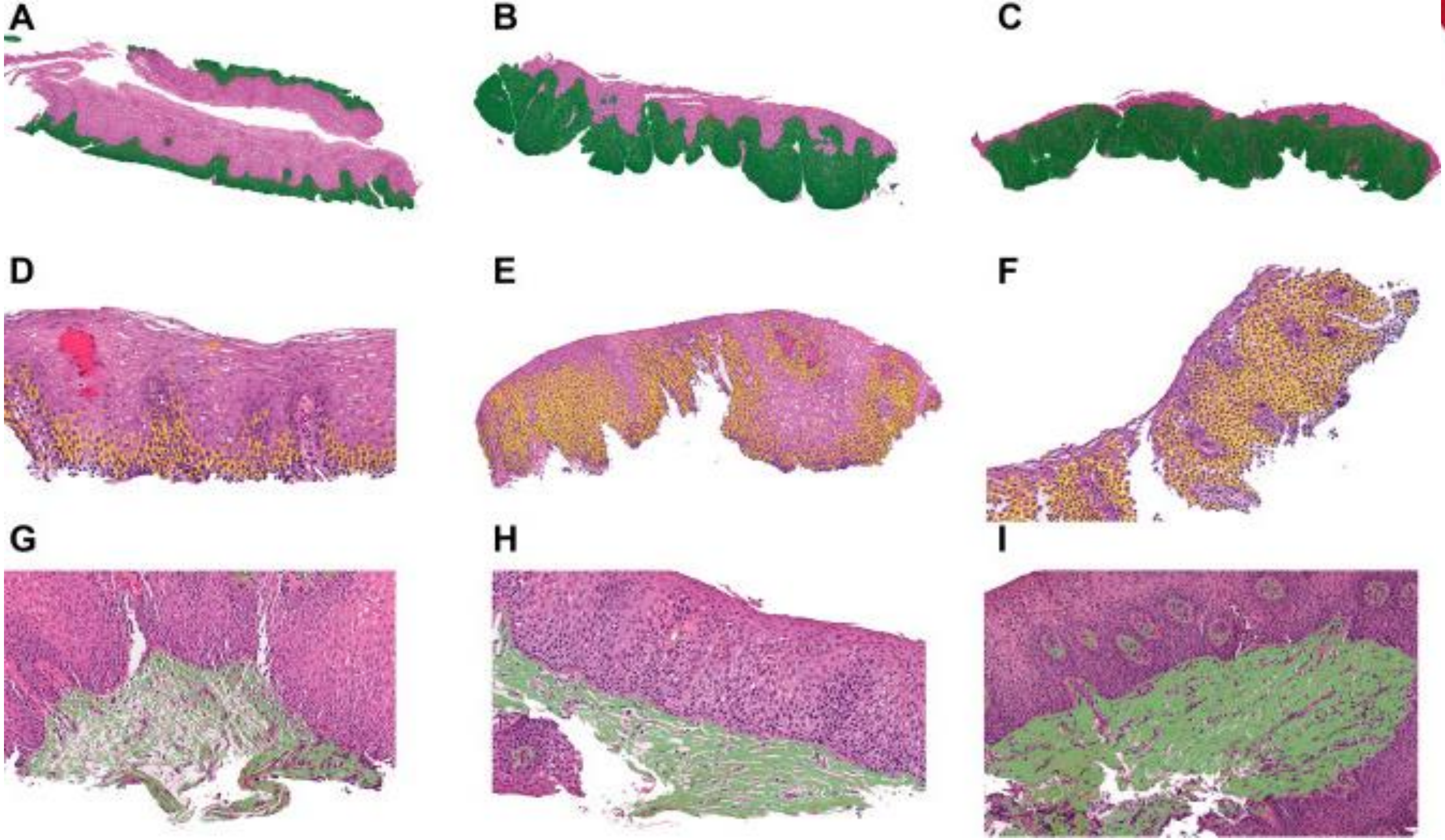

Figure 1. Artificial intelligence model recognition of eosinophilic esophagitis-related segmentation features. A-C, basal zone (green) (A, normal; B, mild to moderate; and C, severe). D-E, dilated intercellular spaces (yellow) (D, mild; E, moderate; F, severe). Lamina propria fibrosis (light green) (G, none; H, mild to moderate; I, severe). Whole slide images, hematoxylin, and eosin stain.

Results

- **AI looked at median of 187 HPF areas per biopsy slide**
- Inter-rater correlation coefficient between the AI and CP was 0.55
- After AI HPF grid method, increased to 0.96.
- AI model identified 6 of 19 (31.5%) grade 1 cases as grade 2 (≥ 15 eosinophils per HPF).
- Re-review by CP with AI guided identification of the area of highest eosinophil concentration confirmed the presence of 15 eosinophils or greater in **three of the six cases.**

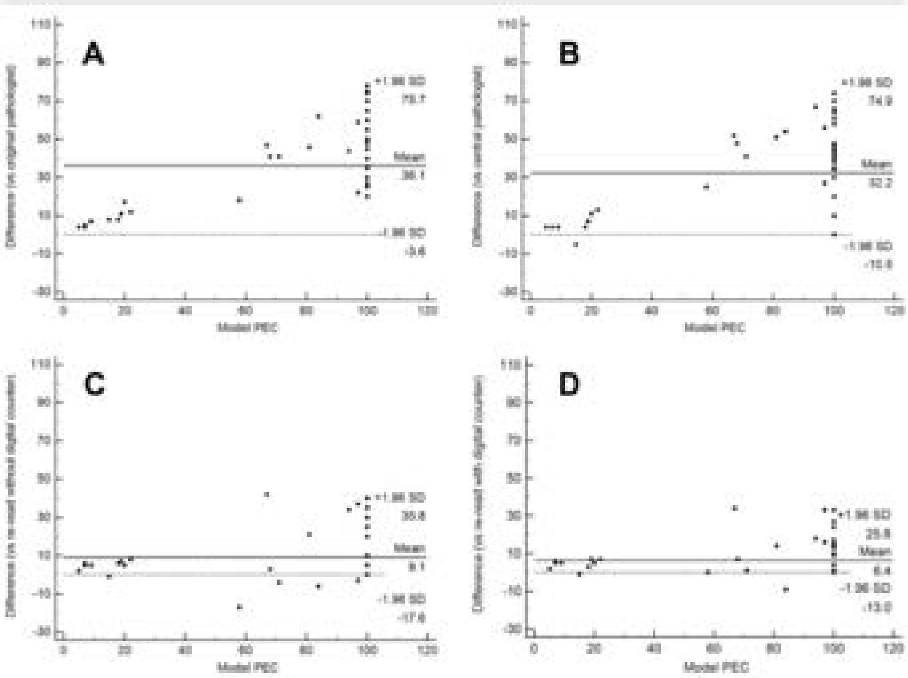

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Figure 4. Bland-Altman plot showing mean differences between pathologists' PEC (A, original pathologist's read, and B, central pathologist's read) and AI model PEC. After recount of PEC (by the central pathologist) based on the location of HPF with highest concentration of eosinophils indicated by the AI model, the mean PEC difference between model and pathologists decreased from 32 eosinophils/HPF to 9.1 and 6.4 eosinophils/HPF (without [C] and with [D] digital dotting tool, respectively). Abbreviations: PEC, peak eosinophil count; SD, standard deviation.

Conclusion

Strong correlation between PEC by the AI model and pathologists.

AI absolute counts were significantly and consistently higher than the pathologists’ PEC in both adult and pediatric populations.

Overestimated EAs (could improve accuracy in future versions.)

AI performed similar to GI pathologist

AI assisted identification of PEC “significantly more accurate”

> Dig Endosc. 2023 Nov;35(7):902-908. doi: 10.1111/den.14547. Epub 2023 Apr 10.

Whole slide image-based prediction of lymph node metastasis in T1 colorectal cancer using unsupervised artificial intelligence

Yuki Takashina [1], Shin-Ei Kudo [1], Yuta Kouyama [1], Katsuro Ichimasa [1] [2], Hideyuki Miyachi [1], Yuichi Mori [1] [3], Toyoki Kudo [1], Yasuharu Maeda [1], Yushi Ogawa [1], Takemasa Hayashi [1], Kunihiko Wakamura [1], Yuta Enami [1], Naruhiko Sawada [1], Toshiyuki Baba [1], Tetsuo Nemoto [4], Fumio Ishida [1], Masashi Misawa [1]

Paper: T1 WSI prediction of LN metastasis

When submucosal invasion identified during a polypectomy, it is important to determine if a patient needs a colectomy due to lymph node metastasis risk

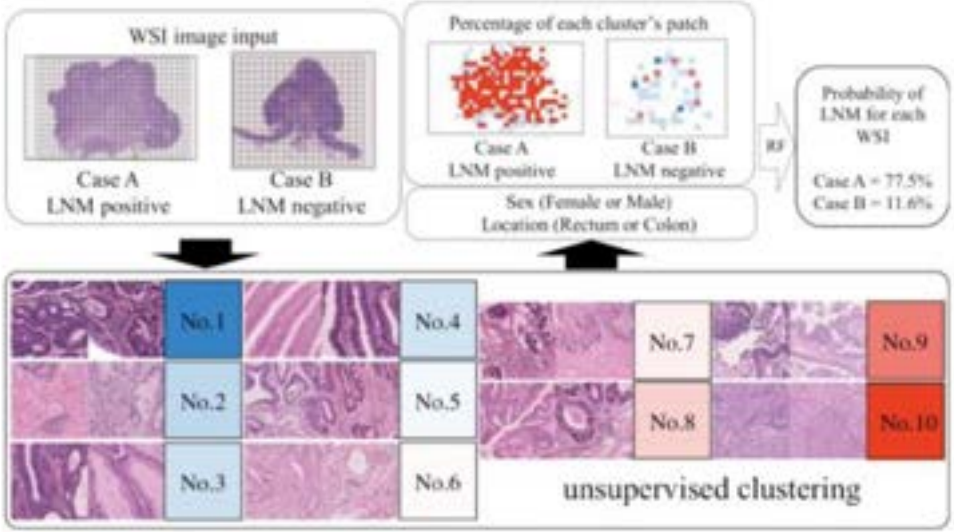
Approximately 10% of T1 CRC will have LN mets

Current pathologic features to predict LNM: poor differentiation, tumor budding, lymphovascular invasion

Paper: T1 WSI prediction of LN metastasis

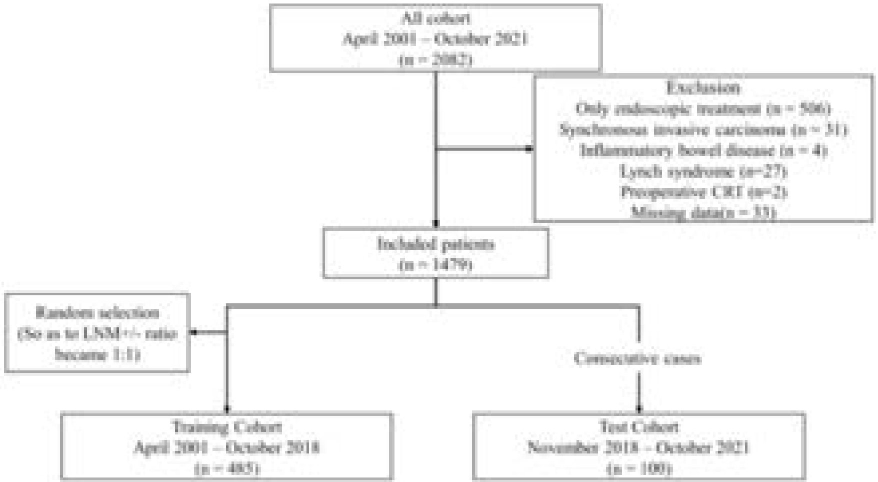
Retrospective single center study
Used 100 each T1 and T2 colon resections
Used 1:1 cohort of LN+ (50) and LN- (50) cases
Used single slide with deepest invasion
1st step) Invasive carcinoma was annoted
2nd step) Pathology images were used to pretrain a convolutional neural network to create a feature extractor
3rd step) Conducted unsupervised training using K-means, a nonhierarchical clustering method--> risk of LNM stratified into 10 categories
Made 10 clusters and calculated the percentage of LNMC positive patches in each cluster
Sex and tumor location also used for LNM prediction

Whole slide image-based prediction of lymph node metastasis in T1 colorectal cancer using unsupervised artificial intelligence



Digestive Endoscopy, Volume: 35, Issue: 7, Pages: 902-908, First published: 11 March 2023, DOI: (10.1111/den.14547)

Whole slide image-based prediction of lymph node metastasis in T1 colorectal cancer using unsupervised artificial intelligence



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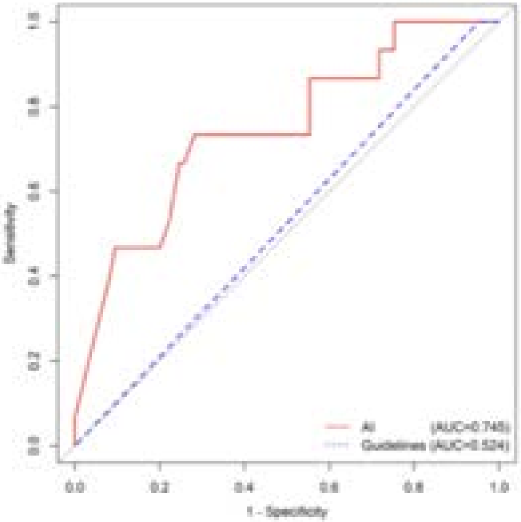

Digestive Endoscopy, Volume: 35, Issue: 7, Pages: 902-908, First published: 11 March 2023, DOI: (10.1111/den.14547)

Paper: T1 WSI prediction of LN metastasis

AUC prediction of LNM by the AI was 0.745

Using traditional pathologic scoring: AUC is 0.524

This model could theoretically reduce the rate of surgery by 3.4%

Limitations:

- Single center retrospective design
- Also used T2 cases, which isn't really applicable to polypectomy specimens
- Didn't account for the size of the tumor
- Need to validate this study with an external data set

BMC Gastroenterology

BMC

BMC Gastroenterol. 2020; 20: 417.
PMCID: PMC7731757
Published online 2020 Dec 11. doi: 10.1186/s12876-020-01494-7
PMID: 33308189

Journal Article

Deep learning for sensitive detection of *Helicobacter Pylori* in gastric biopsies

Sebastian Klein,[#1,2] Jacob Gildenblat,[#3] Michaele Angelika Ihle,[2] Sabine Merkelbach-Bruse,[2] Ka-Won Noh,[2] Martin Peifer,[4] Alexander Quaas,[2] and Reinhard Büttner[2]

> APMIS. 2022 Jan;130(1):11-20. doi: 10.1111/apm.13190. Epub 2021 Nov 22.

Automated assessment of Ki-67 proliferation index in neuroendocrine tumors by deep learning

Tiina Vesterinen [1] [2], Jenni Säilä [2], Sami Blom [3], Mirkka Pennanen [1], Helena Leijon [1], Johanna Arola [1]

Affiliations + expand

PMID: 34741788 PMCID: PMC9299468 DOI: 10.1111/apm.13190

Summary

Prospective digitization of slides needed to perform clinically validated AI algorithms

- Most pathologists in the US still use glass slides, but this is evolving
- Investment in scanners, IMS, storage, etc.

Currently one FDA approved algorithm (prostate biopsy screening), many more coming in the near future (next 1-2 years)

Generizability of research studies to population at large

Reimbursement?

Pathologist's Efficiency?

QC/QA

Business opportunities with AI and Digital Pathology

What is a clinically validated example of AI an application in GI Path?

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B) Metastasis detection within lymph nodes of colorectal cancer resection specimens

C) Grading of dysplasia in Barrett's esophagus

D) Lymph node prediction in T1 polypectomy specimens

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What are current examples of AI applications in GI Path?
Answer:

B) Metastasis detection within lymph nodes of colorectal cancer resection specimens

What are the minimum hardware and software needs to perform clinically validated AI in Surgical Pathology?

What are the minimum hardware and software needs to perform clinically validated AI in Surgical Pathology?

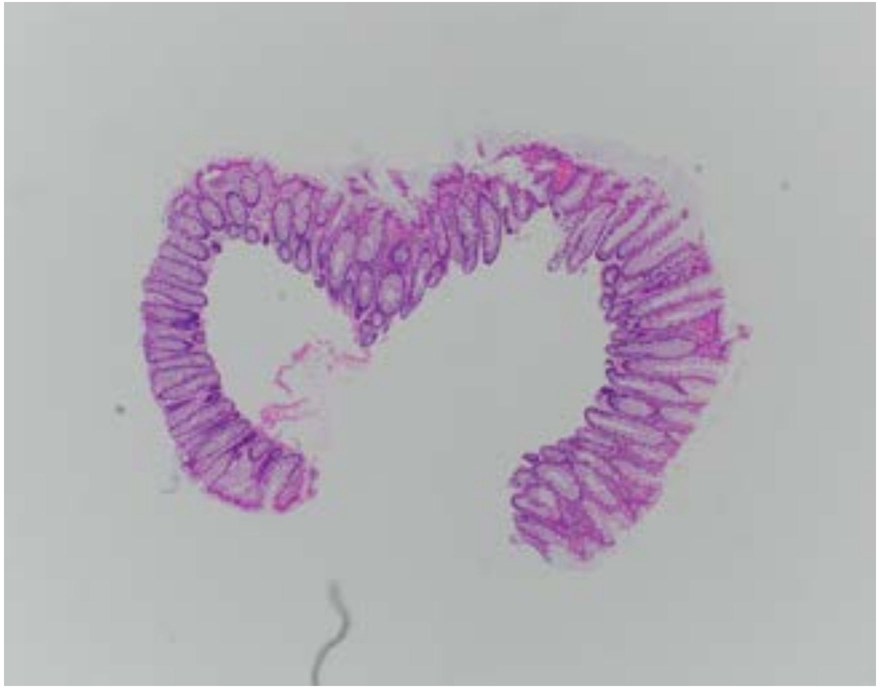
WSI scanners

Image management software

PACS (picture archiving and communication system)

Validated AI software

Questions?



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Lui et al. "Applications of Artificial Intelligence in Breast Pathology" Arch. Pathol. Lab Med. 147, September 2023

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Vesterinen et al. “Automated assessment of Ki-67 proliferation index in neuroendocrine tumors by deep learning.” APMIS 2021 130:11-20

Takashina et al. ”Whole slide image-based prediction of lymph node metastasis in T1 colorectal cancer using unsupervised artificial intelligence.” Digestive Endoscopy 2023; 35: 902-908

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