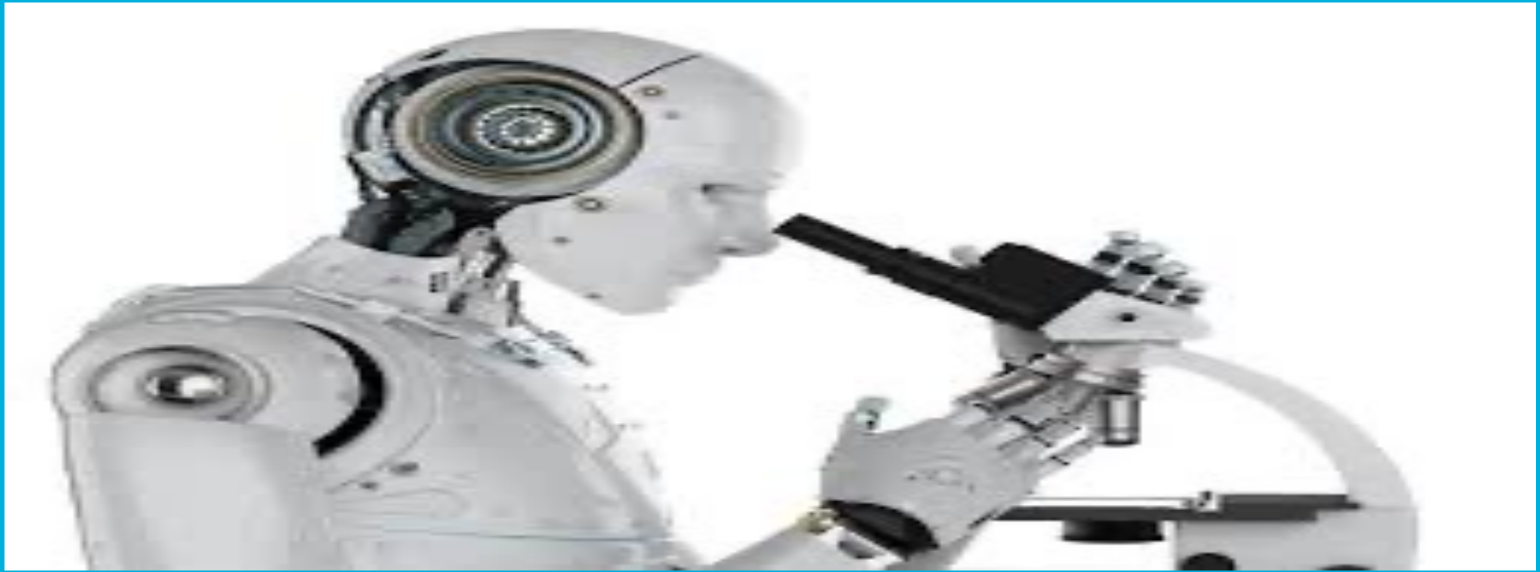


AI in modern pathology

Prof.dr. Iris Nagtegaal

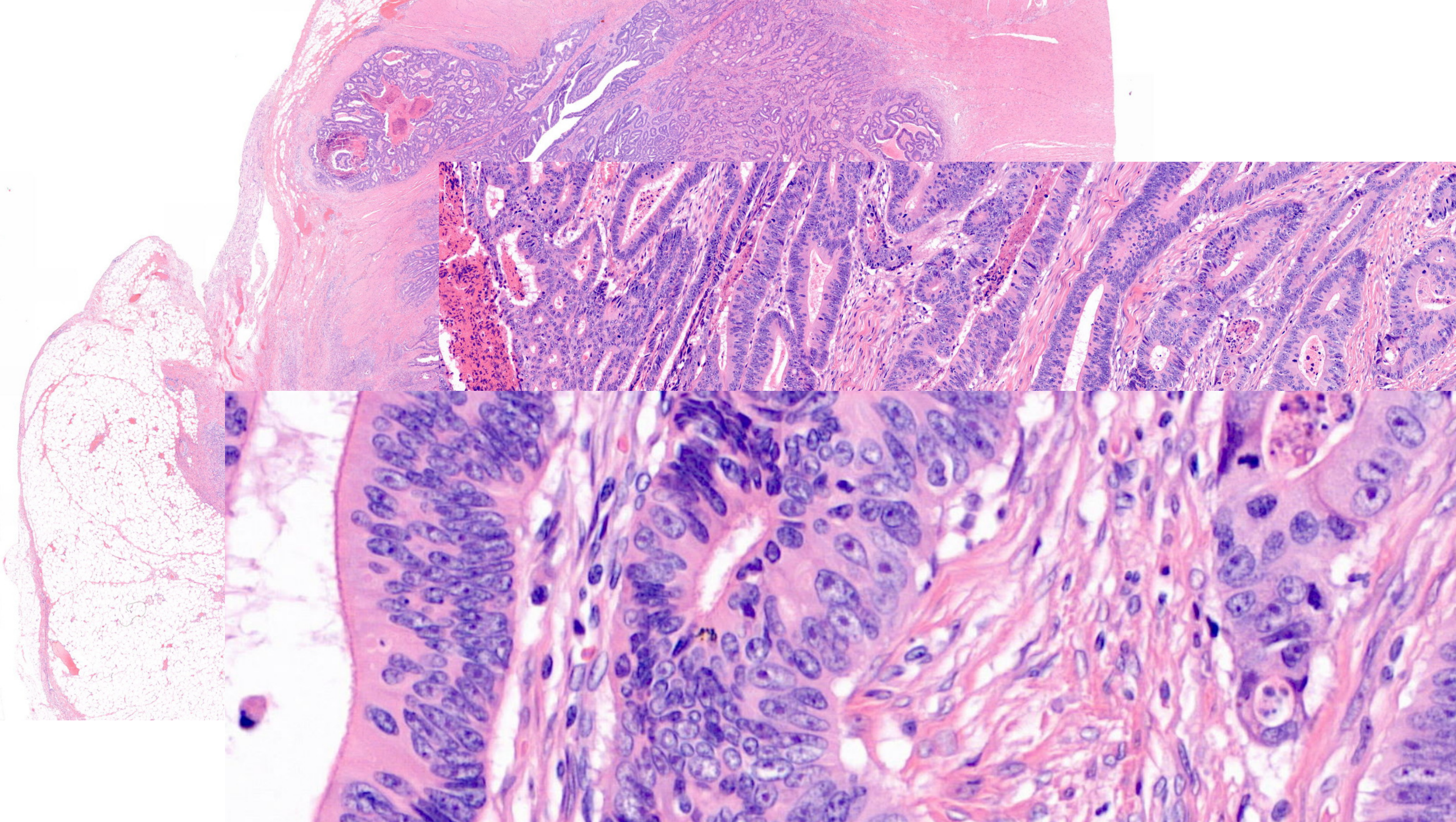
Radboudumc

MRO . ART

Modern Radiation Oncology: multidisciplinarity in the era of OMICS and AI guided oncology

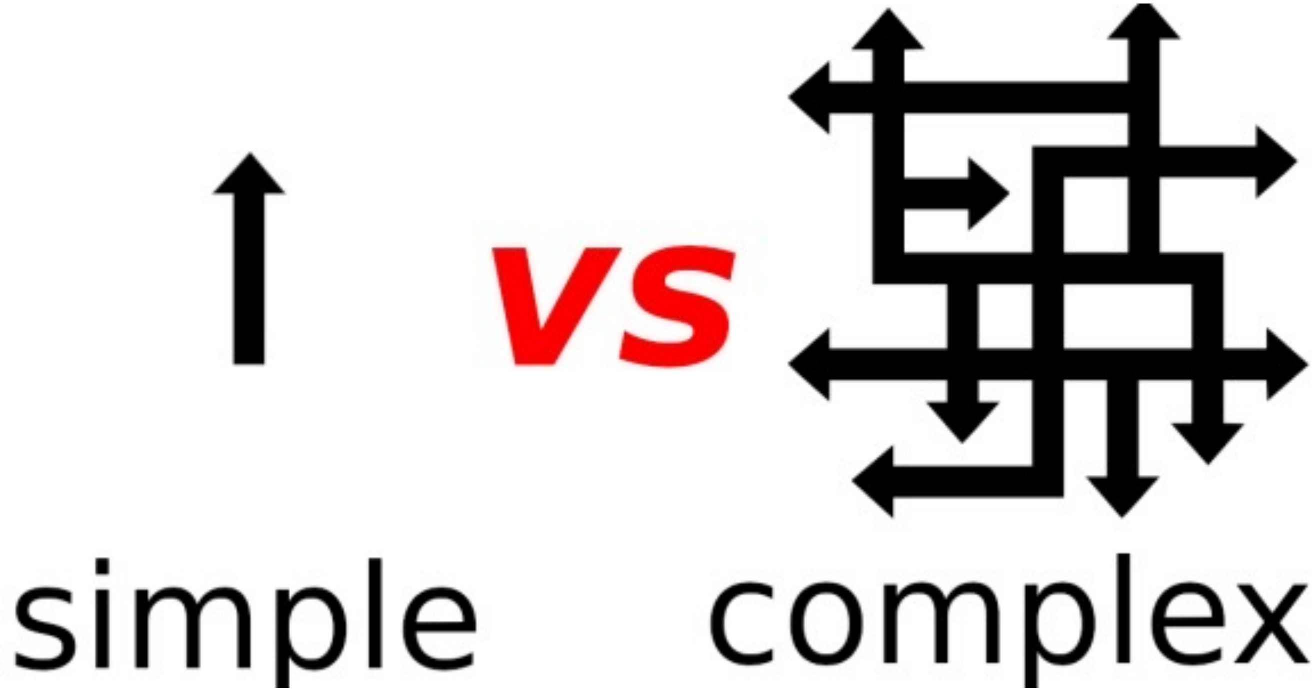
32° RESIDENTIAL COURSE

17 | 18 | 19 October 2022



Whole slide imaging

- A typical H&E slide is between 1 - 5 GB: for each resection 25-30 slides…
- X-ray: 10MB
- CT-series: 250-400MB
- MR series: 300-500MB


vs
simple
complex

Do Telephone Call Interruptions Have an Impact on Radiology Resident Diagnostic Accuracy?

Brad J. Balint, BS, Scott D. Steenburg, MD, Hongbu Lin, MS, Changyu Shen, PhD,
Jennifer L. Steele, MS, Richard B. Gunderman, MD, PhD

ORIGINAL ARTICLE Open Access

Check for updates

The performance costs of interruption during visual search are determined by the type of search task

David Alonso*, Mark Lavelle and Trafton Drew

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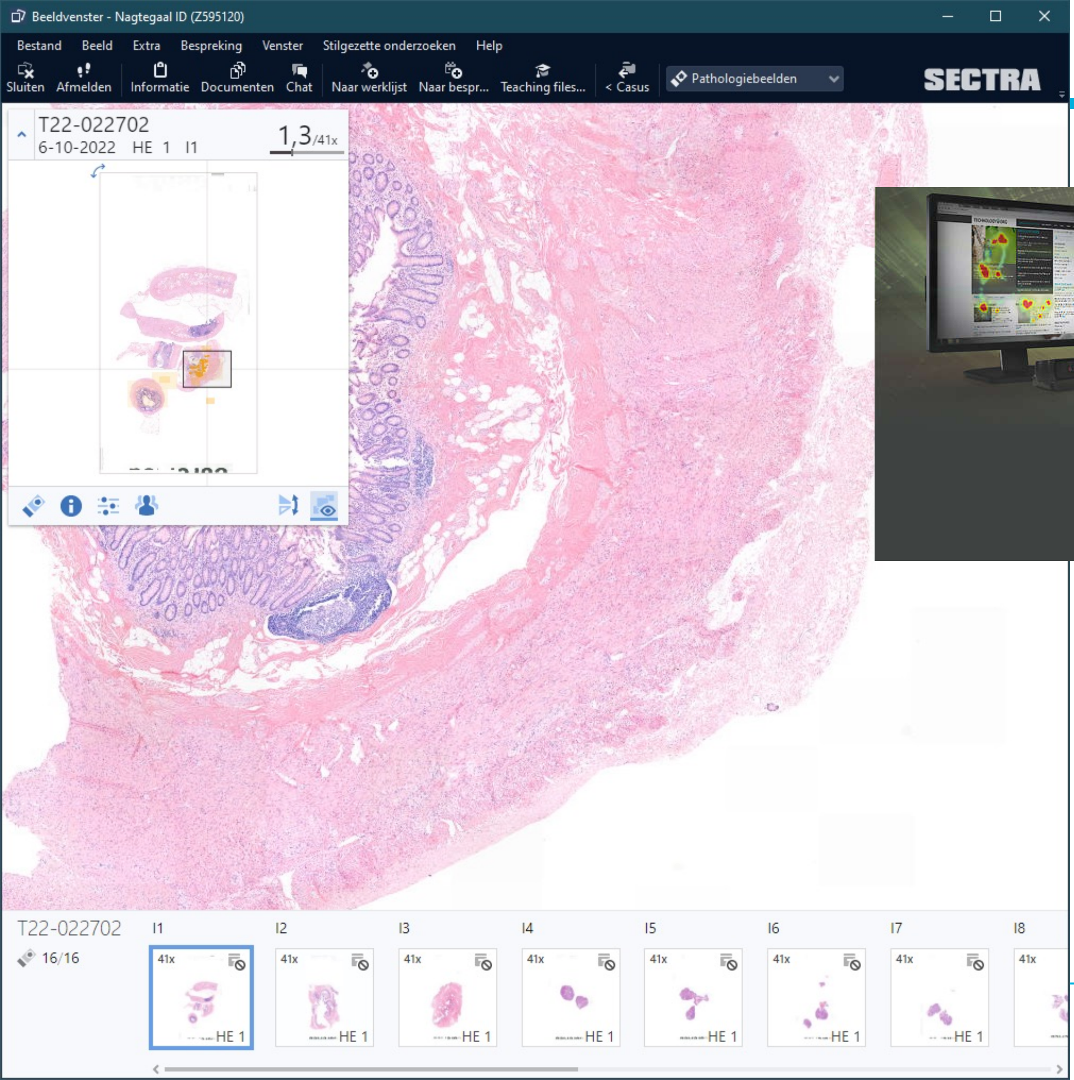
Beeldvenster - Nagtegaal ID (Z595120)
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Informatie
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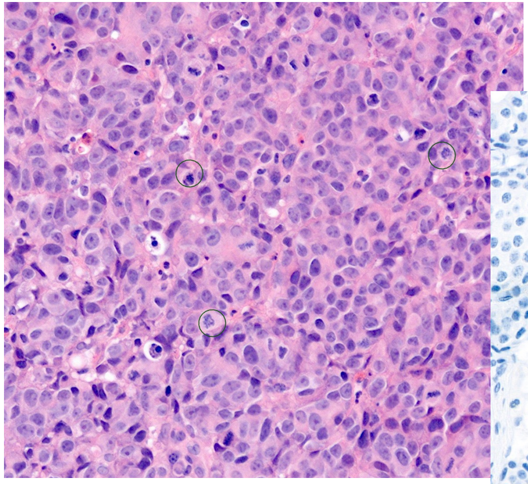
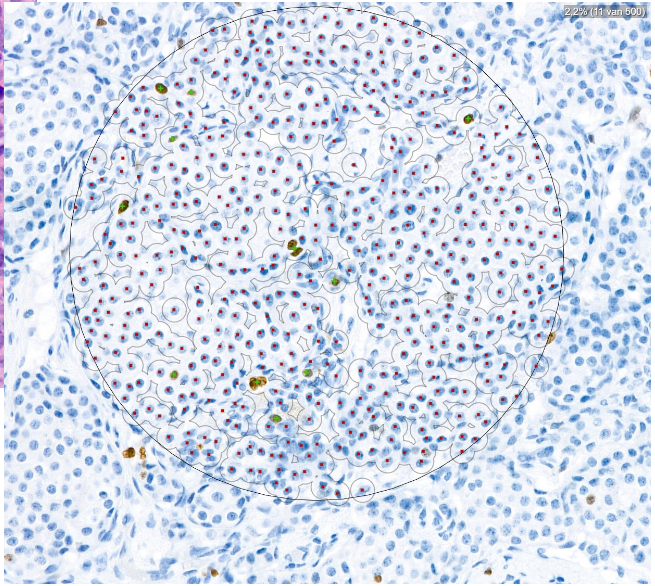
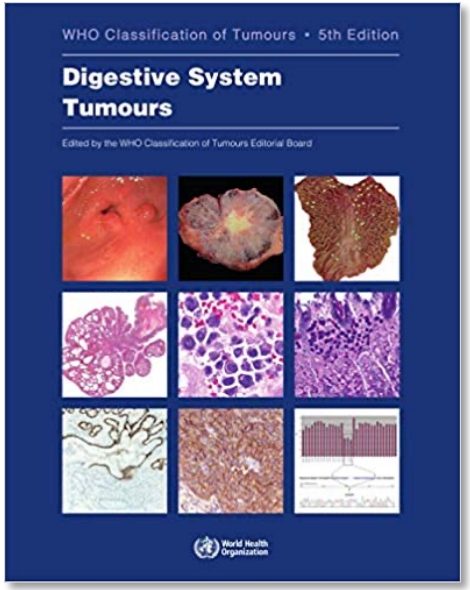
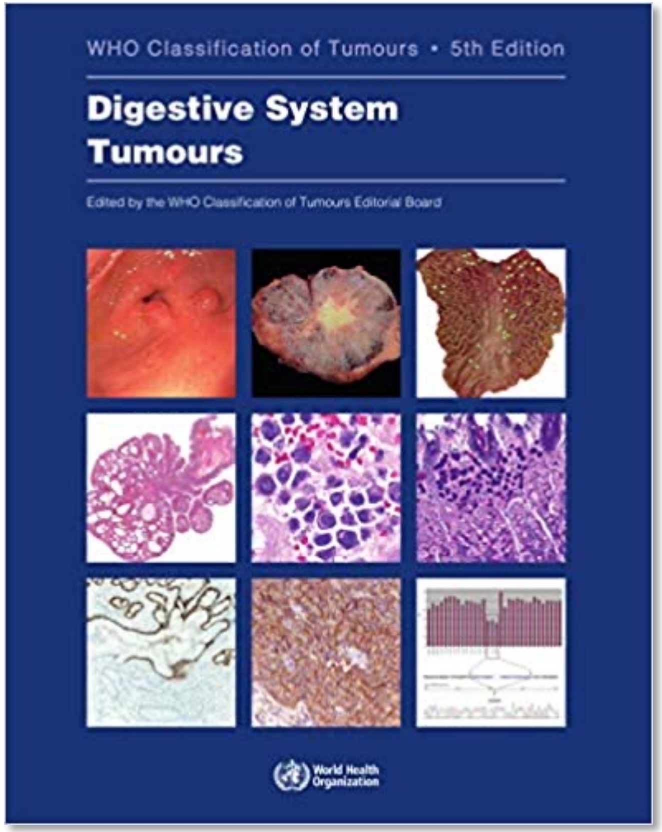
Tracking....

Colorectal neuroendocrine neoplasms









Box 6.02 Essential and desirable diagnostic criteria for colorectal cancer

- Histological subtype
- Differentiation grade: Low/high
- Invasion depth: According to TNM, specify if invasion in other organs (pT4) or tumour perforation
- Presence of (lympho)vascular invasion: Intramural vascular invasion, extramural vascular invasion, lymphatic invasion
- Perineural growth: Present/absent
- Resection margin status (proximal, distal, circumferential): Positive, negative, distance in cm
- Diameter of the tumour
- Site/localization of the tumour
- Quality of the resection specimen
- Number of investigated lymph nodes
- Number of positive lymph nodes
- Presence of treatment response: Yes/no; if yes, partial or complete response
- Microsatellite status / presence of DNA mismatch repair proteins (MLH1, MSH2, MSH6, PMS2): Microsatellite-stable or -instable, staining for mismatch repair proteins present or absent
- Tumour budding status
- Immune response
- Presence or absence of relevant mutations

Deep learning can predict microsatellite instability directly from histology in gastrointestinal cancer

Jakob Nikolas Kather[1,2,3,4,5*], Alexander T. Pearson[4], Niels Halama[2,5,6], Dirk Jäger[2,3,5], Jeremias Krause[1], Sven H. Loosen[1], Alexander Marx[7], Peter Boor[8], Frank Tacke[9], Ulf Peter Neumann[10], Heike I. Grabsch[11,12], Takaki Yoshikawa[13,14], Hermann Brenner[2,15,16], Jenny Chang-Claude[17,18], Michael Hoffmeister[15], Christian Trautwein[1] and Tom Luedde[1*]

Deep learning model for the prediction of microsatellite instability in colorectal cancer: a diagnostic study

Rikiya Yamashita, Jin Long, Teri Longacre, Lan Peng, Gerald Berry, Brock Martin, John Higgins, Daniel L Rubin, Jeanne Shen**

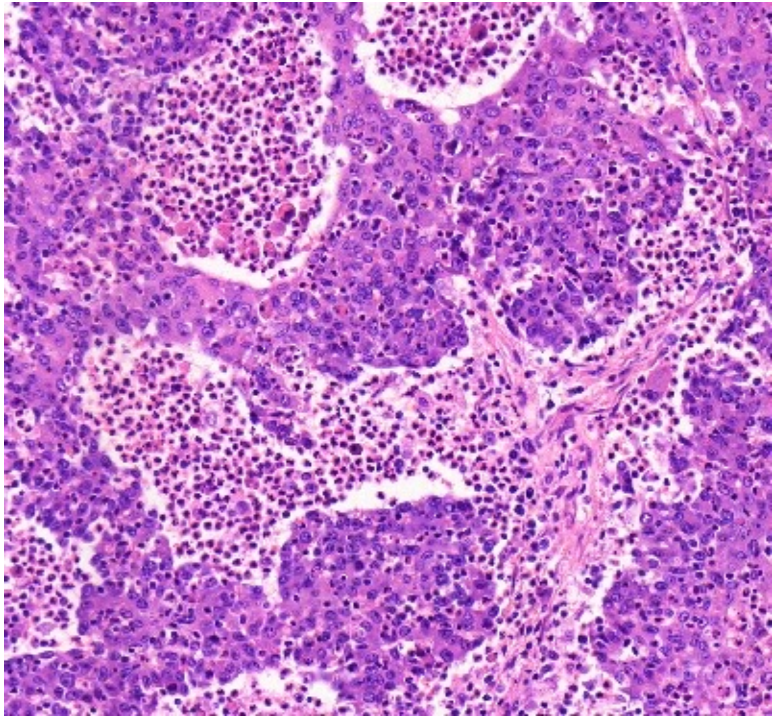
Artificial Intelligence for Histology-Based Detection of Microsatellite Instability and Prediction of Response to Immunotherapy in Colorectal Cancer

Lindsey A. Hildebrand [1], Colin J. Pierce [1], Michael Dennis [1,2], Munizay Paracha [1] and Asaf Maoz [1,3,*]

Review

Artificial Intelligence for Predicting Microsatellite Instability Based on Tumor Histomorphology: A Systematic Review

Ji Hyun Park [1], Eun Young Kim [2], Claudio Luchini [3,4], Albino Eccher [5], Kalthoum Tizaoui [6], Jae Il Shin [7,*] and Beom Jin Lim [8,*]



Other things we can do ourselves…

- Lymph node evaluation
- Immunoscore
- Tumor budding

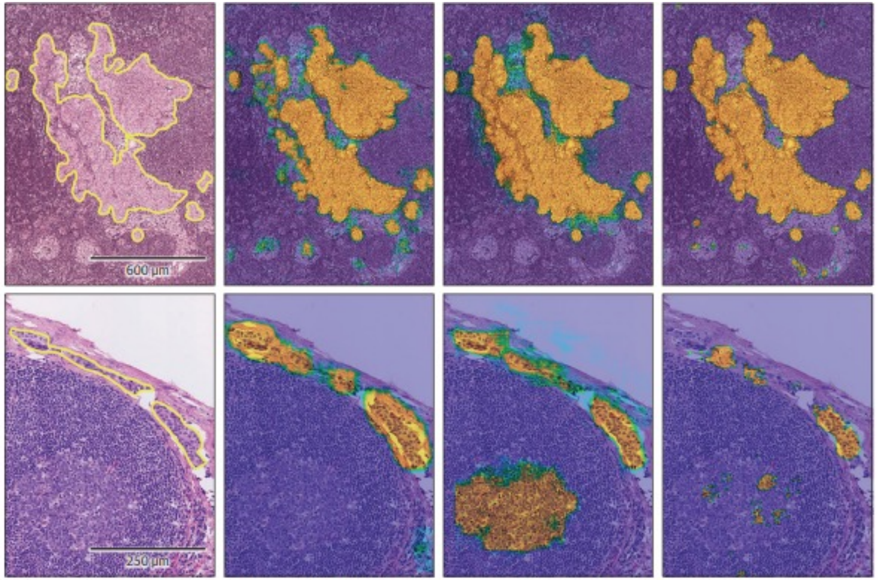
Incentives and resources

"It is like when you learn to drive and you have like a parking assistant that is really good. What if it is not there anymore? Then you cannot park anymore. Teaching to colleagues, like if you grew up with this, if you grew up using an algorithm, are you really learning pathology?"

"You have to learn how to use the technology, just like you have to learn how to use cruise control and navigation with driving lessons. Yes, in the past you did not have them and you had to learn how to drive just by using the pedal and reading a map, but nowadays you do not have to do that anymore, so it is better to understand how to use cruise control and set navigation safely, than to have to do that when you are done and actually have been instructed in that."

Pathologists'first opinions on barriers and facilitators of computational pathology implementation in histopathology (Swillens et al, submitted)

Lymph node assessment is possible



For abbreviations, see the legend of Figure 3. The color scale bar (top right) indicates the probability for each pixel to be part of a metastatic region. For additional examples, see eFigure 5 in the Supplement. A, Four annotated micrometastatic regions in whole-slide images of hematoxylin and eosin–stained lymph node tissue sections taken from the test set of Cancer Metastases in Lymph Nodes Challenge 2016 (CAMELYON16) dataset. B-D, Probability maps from each team overlaid on the original images.

JAMA | Original Investigation

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

Babak Ehteshami Bejnordi, MS; Mitko Veta, PhD; Paul Johannes van Diest, MD, PhD; Bram van Ginneken, PhD; Nico Karssemeijer, PhD; Geert Litjens, PhD; Jeroen A. W. M. van der Laak, PhD; and the CAMELYON16 Consortium

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But is it really necessary?

A Preliminary Diagnosis Service Provides Prospective Blinded Dual-Review of All General Surgical Pathology Cases in an Academic Practice

Jamie A. Weydert, MD, Barry R. De Young, MD, and Michael B. Cohen, MD

TABLE 4. Summary of Errant Diagnoses Prevented by Hot Seat Review

No.	Hot Seat Diagnosis	Attending Pathologist Diagnosis	Final Diagnosis	Comment
Case no. 1: Duodenal biopsy	Cytomegalovirus cytopathic effect	Nonspecific duodenitis	Cytomegalovirus cytopathic effect	Immunocompromised patient
Case no. 2: Lip resection	Moderate squamous dysplasia	Superficially invasive squamous cell carcinoma	Moderate squamous dysplasia	Resection margin of a cutaneous lesion
Case no. 3: Axillary lymph node dissection	Metastatic carcinoma in 3 of 9 axillary lymph nodes	No metastatic carcinoma identified	Rare tumor cell clusters present in 3 of 9 lymph nodes	The patient received adjuvant chemotherapy based on the presence of micrometastatic disease
Case no. 4: Axillary lymph node dissection	Metastatic carcinoma in 6 axillary lymph nodes	Metastatic carcinoma in 3 lymph nodes	Metastatic carcinoma in 6 axillary lymph nodes	Change in diagnosis changed stage of disease
Case no. 5: Gastric biopsy	Gastritis with *Helicobacter pylori*	Gastritis without *Helicobacter pylori*	Gastritis with *Helicobacter pylori*	Patient received anti-*Helicobacter pylori* therapy

- Total n = 6300
- Including lots of biopsies

Actually: no data on reliability of lymph node assessment

Am J Surg Pathol • Volume 29, Number 6, June 2005

Immunoscore

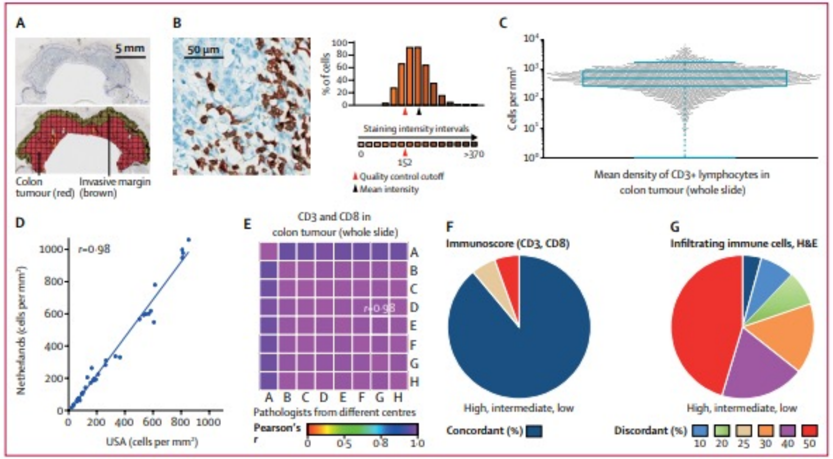
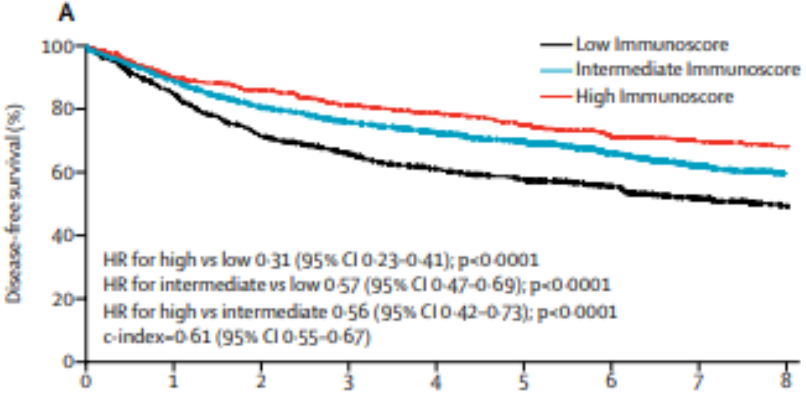


***Figure 2:* Determination of the immune cell densities by image analysis software with a dedicated Immunoscore module**
(A) The colon tissue is divided into tiles, with tumour tissue highlighted in red and the invasive margin highlighted in brown. (B) Representative immunohistochemistry of CD3+ cells infiltrating a colonic tumour (left, in brown), and a histogram of the staining intensities of positive cells detected by the software in a case with an adequate immunostaining intensity, leading to a valid counting (right; mean intensity >152 arbitrary units; black triangle). (C) Histogram of the mean density of CD3+ T cells in the colon tumour for all patients of the cohort (training set plus internal validation set plus external validation set, 3539 patients). (D) Example of a 2×2 correlation of the mean densities for CD3+ cells in the tumour between pathologists from the USA and the Netherlands (r=0·98). (E) Correlation matrix illustrating the reproducibility of the CD3+ and CD8+ cell counting in a set of control slides with colon tumour sections by eight pathologists (tagged A–H) from five centres. The mean of all 2×2 correlations between the eight pathologists doing digital pathology is r=0·97. (F–G) H&E stain evaluation for immune-cell infiltration was done by 11 independent evaluators on 268 representative cases that were randomly selected (n=135 in cohort 1; n=133 in cohort 2). Each evaluator investigated all cases using the same set of nine referent slides (three for each Immunoscore category). Pie charts show the degree of agreement between (F) Immunoscore and (G) H&E stain evaluation for tumour-infiltrating T cells by independent evaluations. Cases with more than 50% discordance between evaluators were considered ambiguous. H&E=haematoxylin and eosin.

International validation of the consensus Immunoscore for the classification of colon cancer: a prognostic and accuracy study



Tumor budding

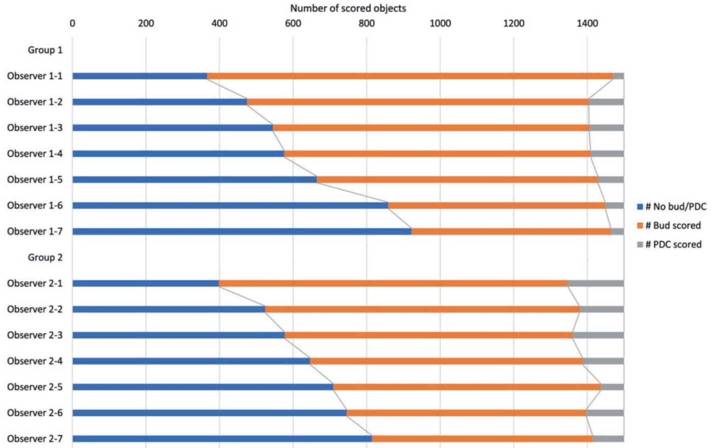


Fig. 3 TB, PDC and neither scores in the 2 × 1500 immunohistochemistry dataset per observer.

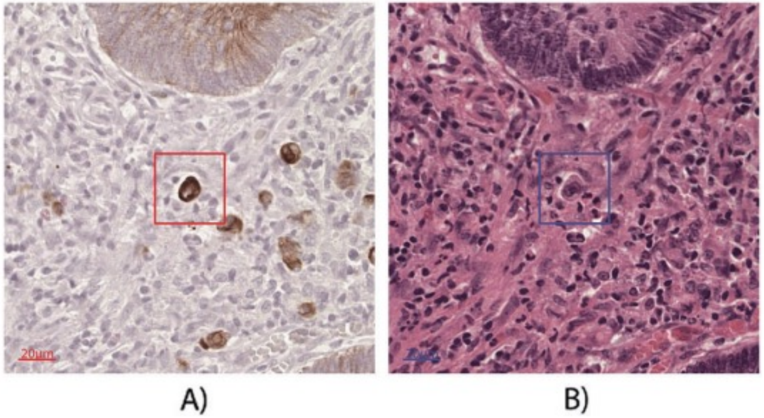


Fig. 1 Example of TB-candidate in IHC and re-stained H&E. Example of TB-candidate in **a** immunohistochemistry, and **b** restained H&E.

Assessment of individual tumor buds using keratin immunohistochemistry: moderate interobserver agreement suggests a role for machine learning

J. M. Bokhorst[1] · A. Blank[2] · A. Lugli[2] · I. Zlobec[2] · H. Dawson[2] · M. Vieth[3] · L. L. Rijstenberg[1] · S. Brockmoeller[4] · M. Urbanowicz[5] · J. F. Flejou[6] · R. Kirsch[7] · F. Ciompi[1] · J. A. W. M. van der Laak[1,8] · I. D. Nagtegaal[1]

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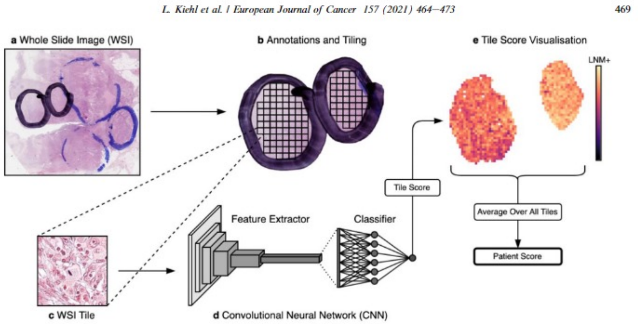
Lymph node prediction

- In particular for pT1 tumors
- Currently: grade, invasion depth, budding, LVI
- Relevant in population screening



Deep learning can predict lymph node status directly from histology in colorectal cancer

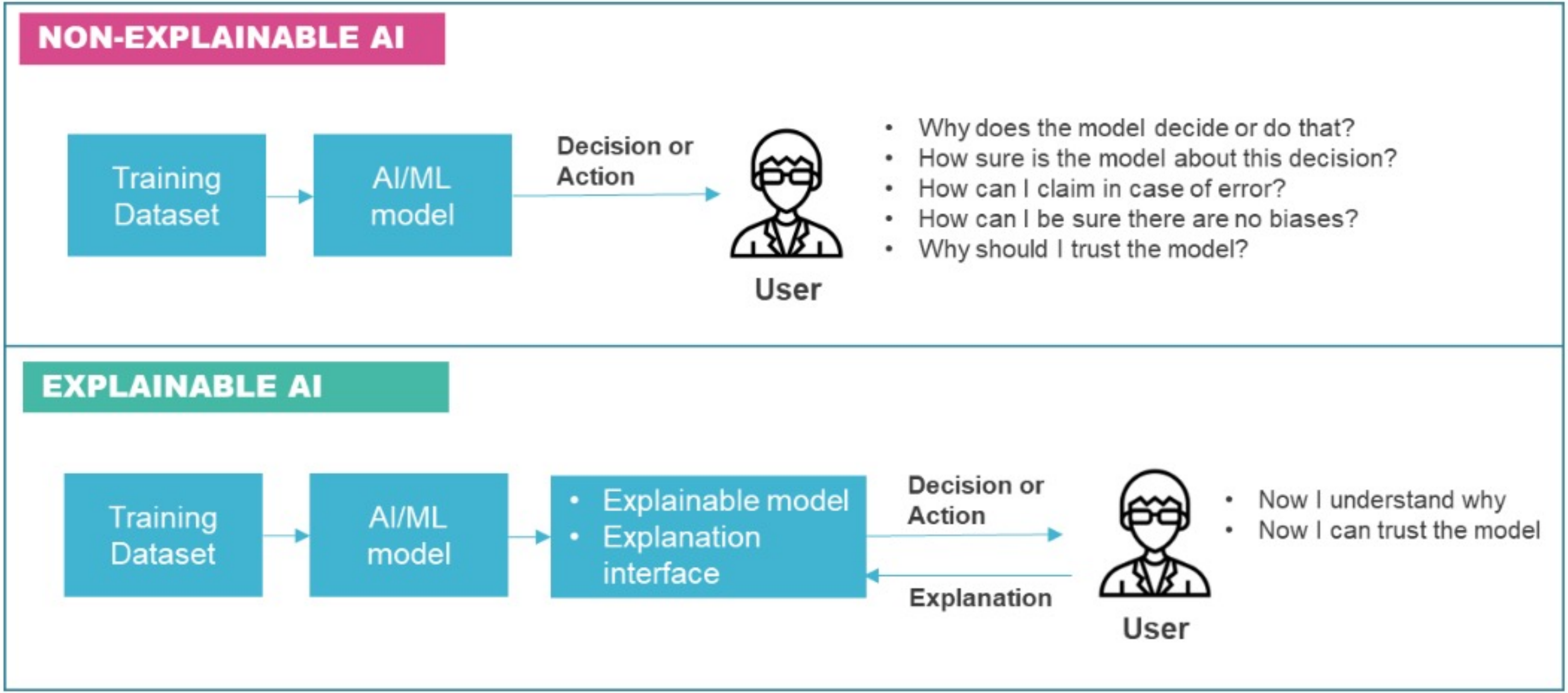
Lennard Kiehl [a,1], Sara Kuntz [a,1], Julia Höhn [a], Tanja Jutzi [a], Eva Krieghoff-Henning [a], Jakob N. Kather [b], Tim Holland-Letz [c], Annette Kopp-Schneider [c], Jenny Chang-Claude [d,e], Alexander Brobeil [f,g], Christof von Kalle [h], Stefan Fröhling [i], Elizabeth Alwers [j], Hermann Brenner [j,k,l], Michael Hoffmeister [j,1], Titus J. Brinker [a,l,*,1]

Deep Convolutional Neural Network-Based Lymph Node Metastasis Prediction for Colon Cancer Using Histopathological Images

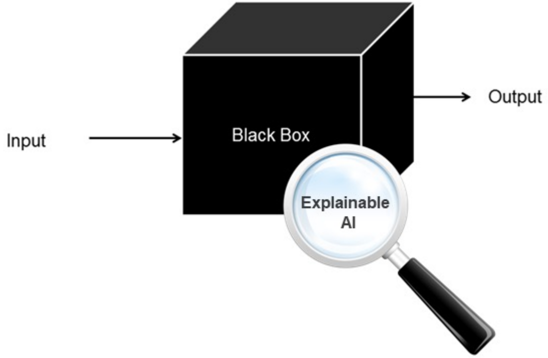
Min Seob Kwak [1], Hun Hee Lee [1], Jae Min Yang [2], Jae Myung Cha [1], Jung Won Jeon [1], Jin Young Yoon [1] and Ha Il Kim [1]*

Prediction of lymph node metastasis in early colorectal cancer based on histologic images by artificial intelligence

Manabu Takamatsu[1,2], Noriko Yamamoto[1,2], Hiroshi Kawachi[1,2], Kaoru Nakano[1,2], Shoichi Saito[3], Yosuke Fukunaga[4] & Kengo Takeuchi[1,2,5]

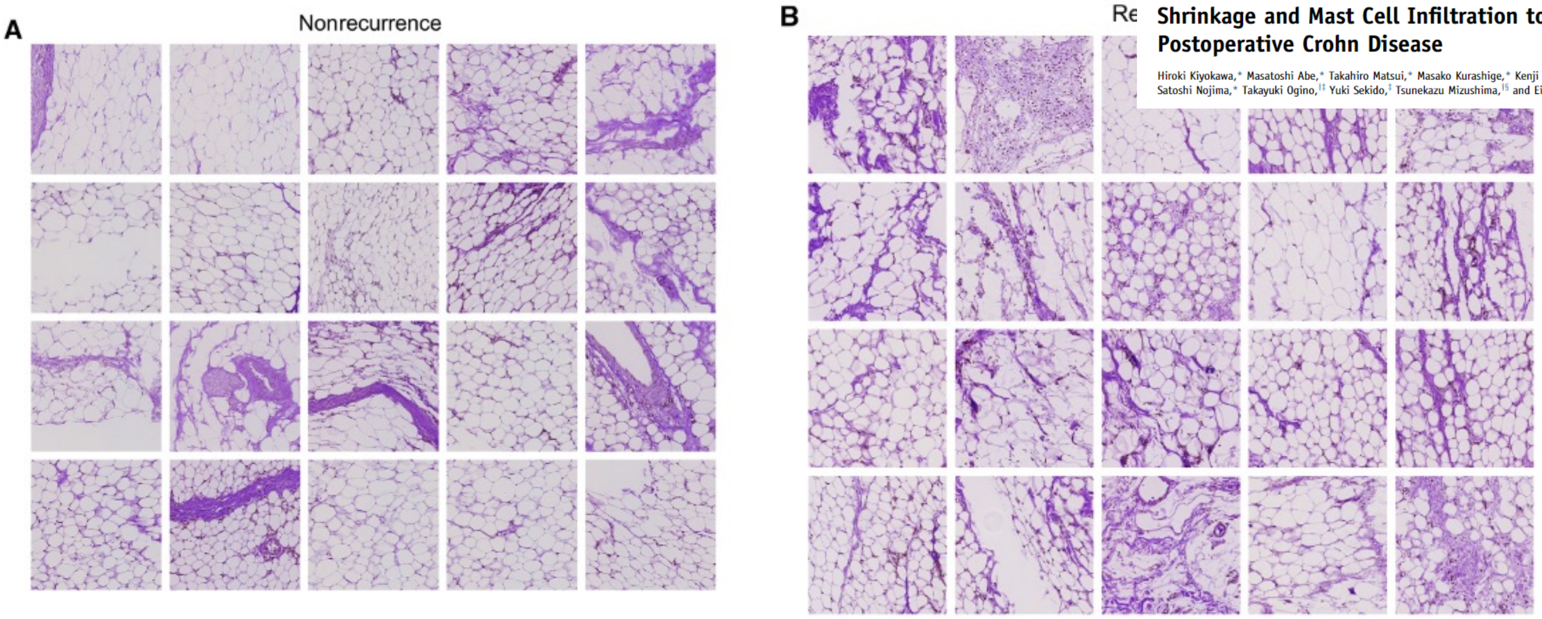

NON-EXPLAINABLE AI
Training Dataset
AI/ML model
Decision or Action
User
Why does the model decide or do that?
How sure is the model about this decision?
How can I claim in case of error?
How can I be sure there are no biases?
Why should I trust the model?
EXPLAINABLE AI
Training Dataset
AI/ML model
Explainable model
Explanation interface
Decision or Action
Explanation
User
Now I understand why
Now I can trust the model

Explainable AI



Company / Organisation	End Users / Consumers	Regulators
Improve understanding	Increase trust	Compliance and regulations
Improve performance	Increase transparency	Provide trust and transparency
Evaluate the quality of the data used	Understand the importance of their actions	Ensure the proper use of sensible data
Avoid bias	Be aware of the data they share	Avoid bias and discrimination

Research: new frontiers



The American Journal of Pathology, Vol. 192, No. 6, June 2022

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The American Journal of PATHOLOGY

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MACHINE LEARNING, COMPUTATIONAL PATHOLOGY, AND BIOPHYSICAL IMAGING

Check for updates

Deep Learning Analysis of Histologic Images from Intestinal Specimen Reveals Adipocyte Shrinkage and Mast Cell Infiltration to Predict Postoperative Crohn Disease

Hiroki Kiyokawa,* Masatoshi Abe,* Takahiro Matsui,* Masako Kurashige,* Kenji Ohshima,* Shinichiro Tahara,* Satoshi Nojima,* Takayuki Ogino,†‡ Yuki Sekido,† Tsunekazu Mizushima,†§ and Eiichi Morii*

Conclusions

- AI can help with standardisation
- AI can improve quality of care
- AI is already implemented in small part of lower GI pathology
- AI has potential for more extensive implementation
- AI can add knowledge (explainable AI)