Friedrich-Alexander-Universität
Medizinische Fakultät

Closing the gap in the clinical adoption of computational pathology

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Friedrich-Alexander-Universität Erlangen-Nürnberg

MIRACUM DIFUTURE Kolloquium
07.10.2025

Learning objectives

- Understand the concepts of digital pathology and computational pathology

- Understand the challenges limiting the adoption of deep learning (DL) models in routine pathology diagnostics

- Understand the architecture and components of a standardized framework for deploying DL models in the diagnostic workflow of a fully digitized pathology department

The clinical context: histopathology

HISTOPATHOLOGY = Histos (tissue) + pathos (disease) + logos (study of)

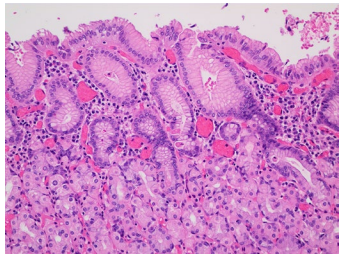
→ “The study of diseased cells and tissues using a microscope.” (NCI definition)

Histopathological glass slides

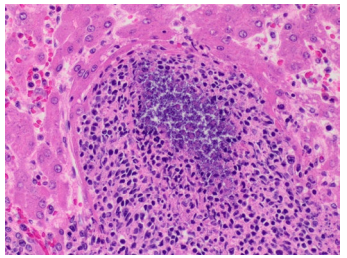
Picture from https://www.leica-microsystems.com/science-lab/industrial/he-staining-in-microscopy/

Microscopical examination

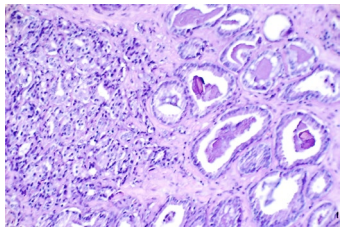
Picture from https://www.verywellhealth.com/histopathology-2252152.
Credit: Hero Images / Getty Images



Gastritis



Liver inflammation



Prostate cancer

Histopathological analysis: main steps

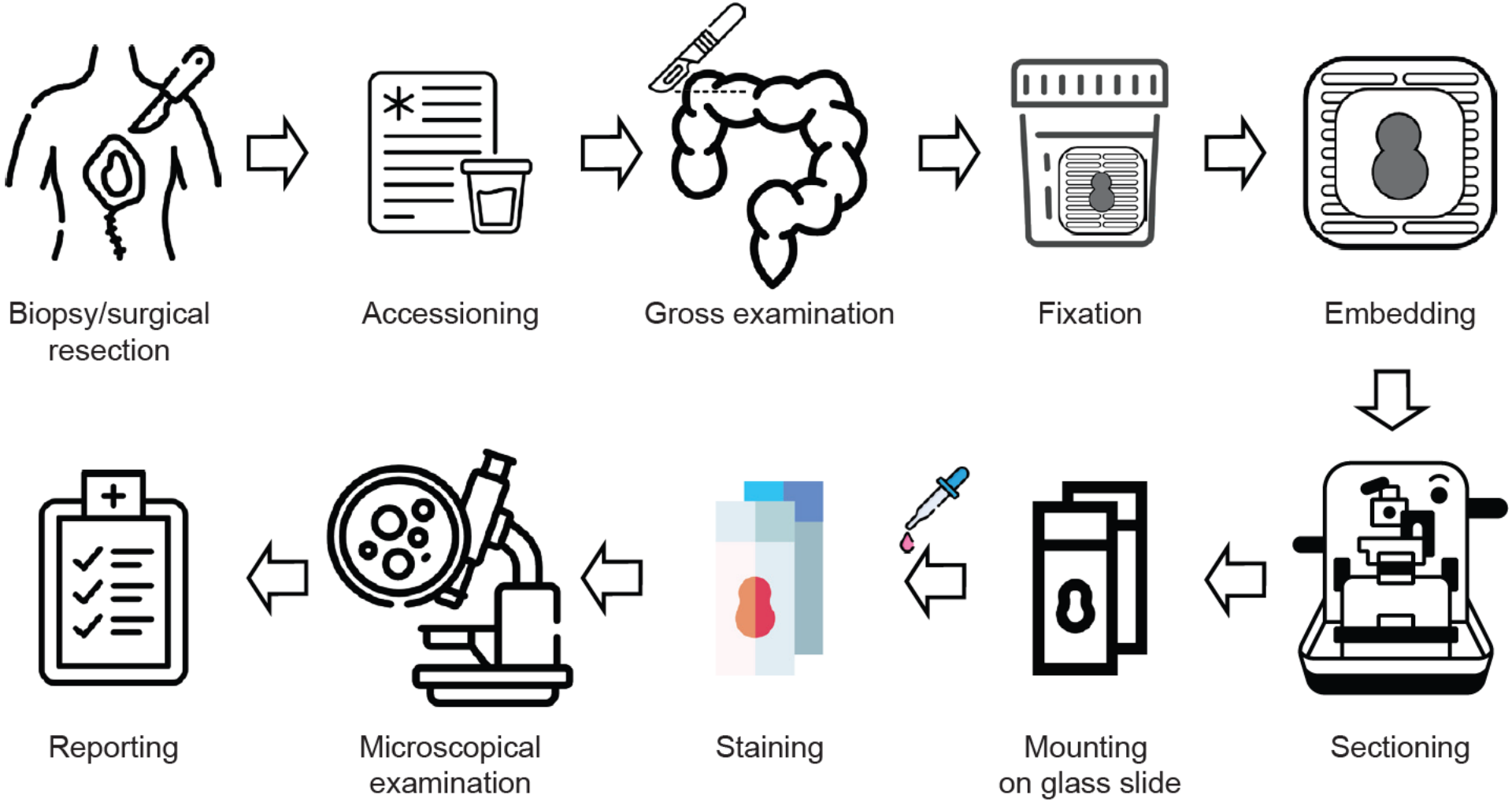


Image credits: M. Angeloni, PhD thesis, 2025

Digital pathology workflow

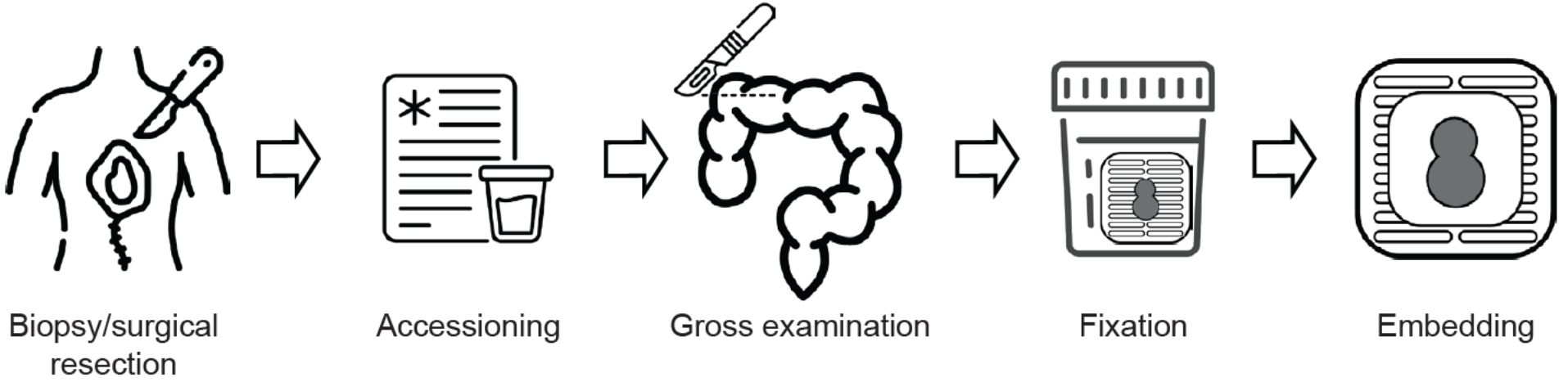


Image from SQD 12P Digital Pathology Slide Scanner – Cyan Biotech Pty Ltd

Image credits: M. Angeloni, PhD thesis, 2025

Digital pathology – a practical example

picture of FFPE material

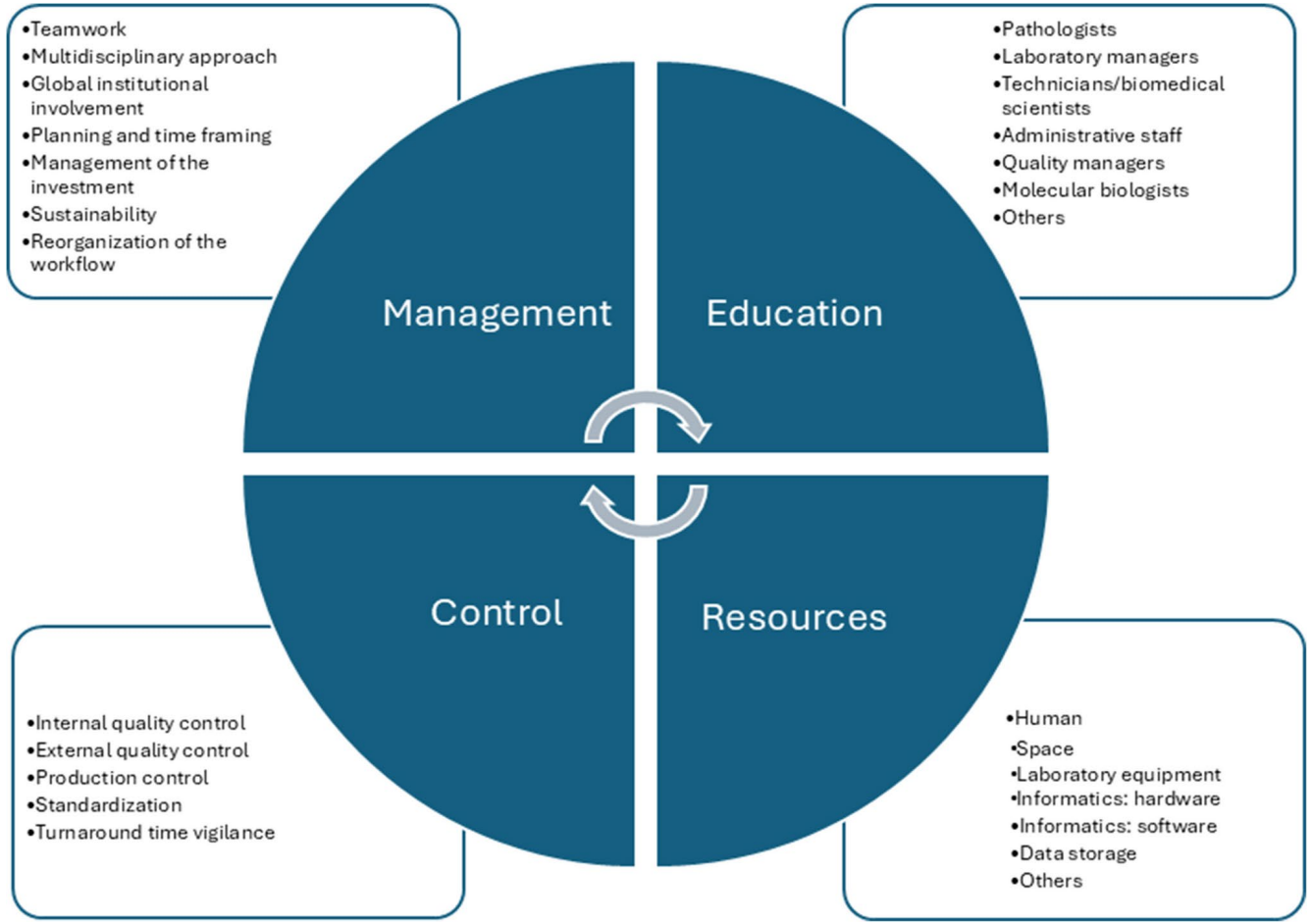
picture of scanned slide

pathologist's workspace

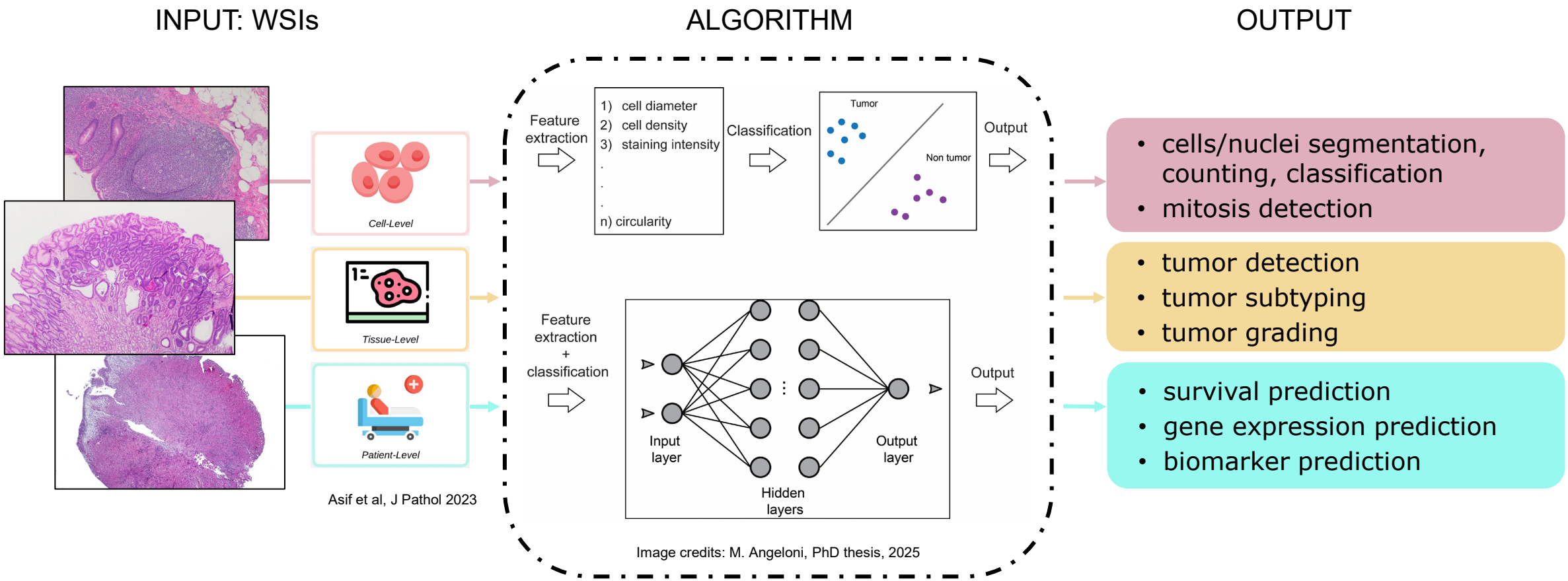
Caputo A et al. J Clin Pathol, 2023

Not just digitized slides, but a digitized pathology department

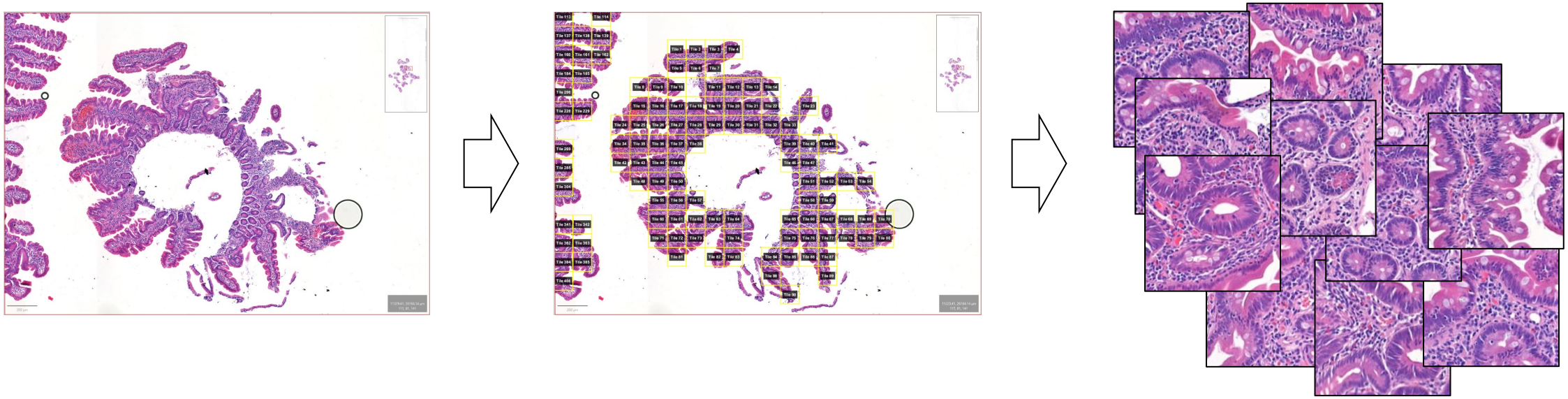
Eloy et al., Digital transformation of pathology - the European Society of Pathology expert opinion paper, Virchows Archiv, 2025



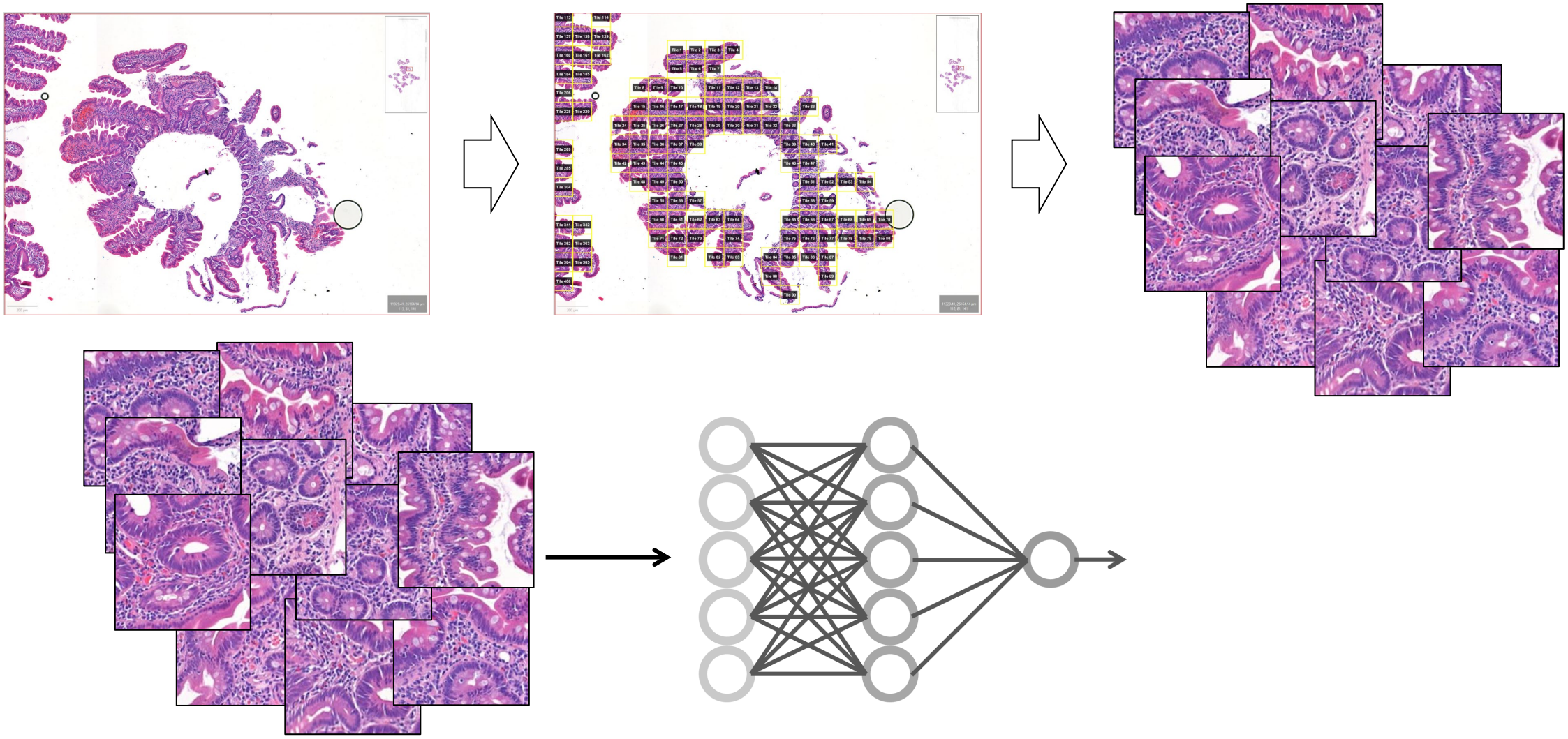
Computational pathology



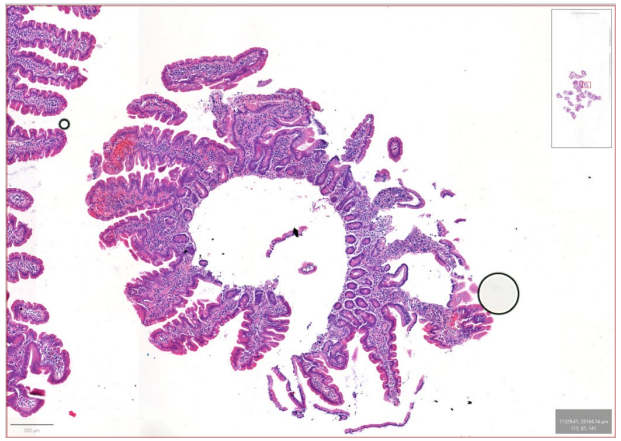
From WSIs to deep-learning models

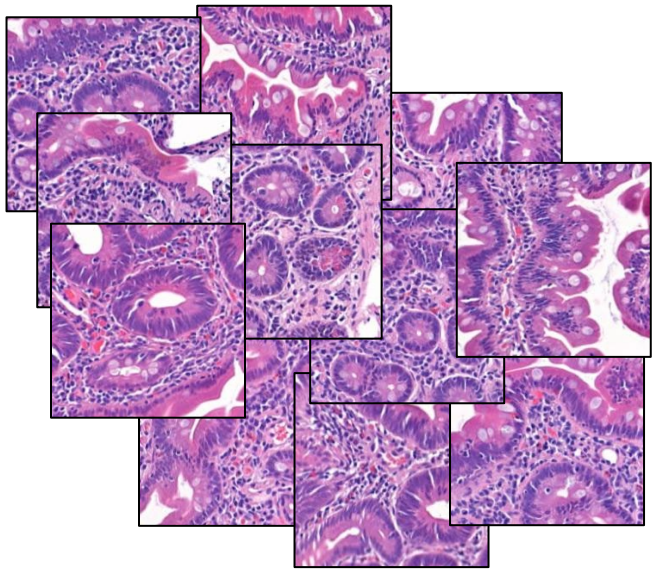


From WSIs to deep-learning models

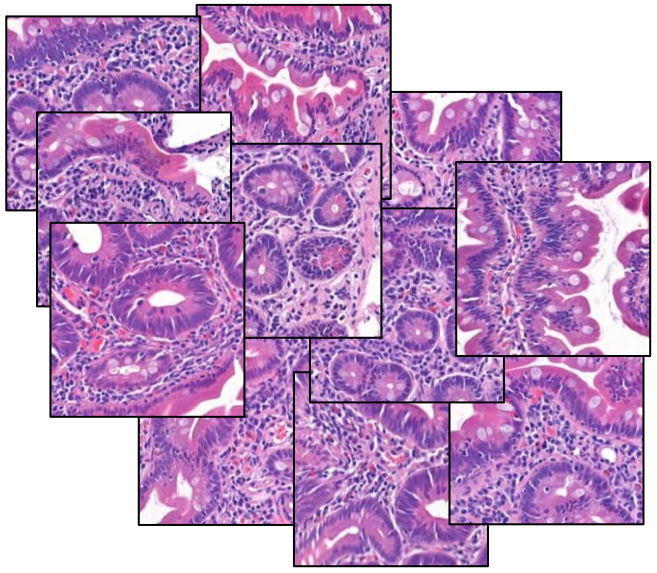


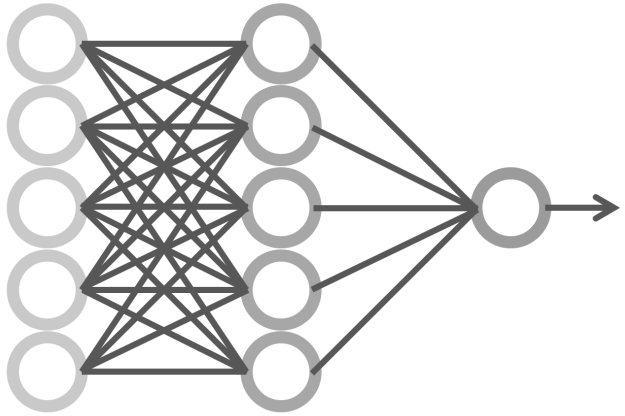
From WSIs to deep-learning models





Labels???

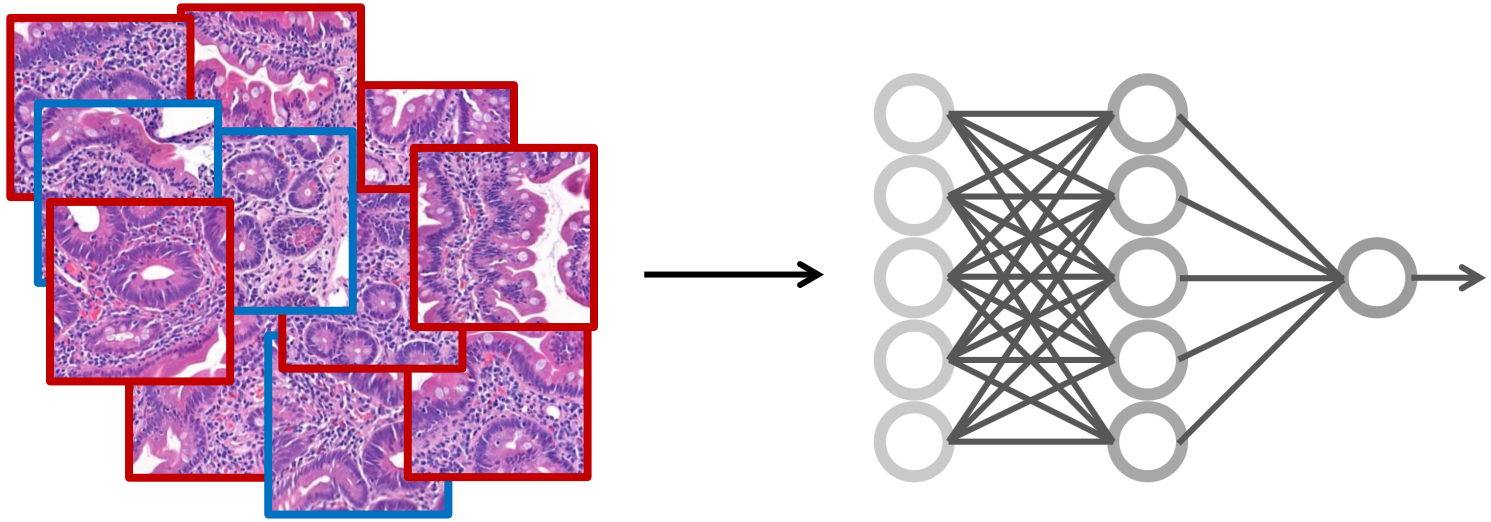




Patch-level vs slide-level predictions

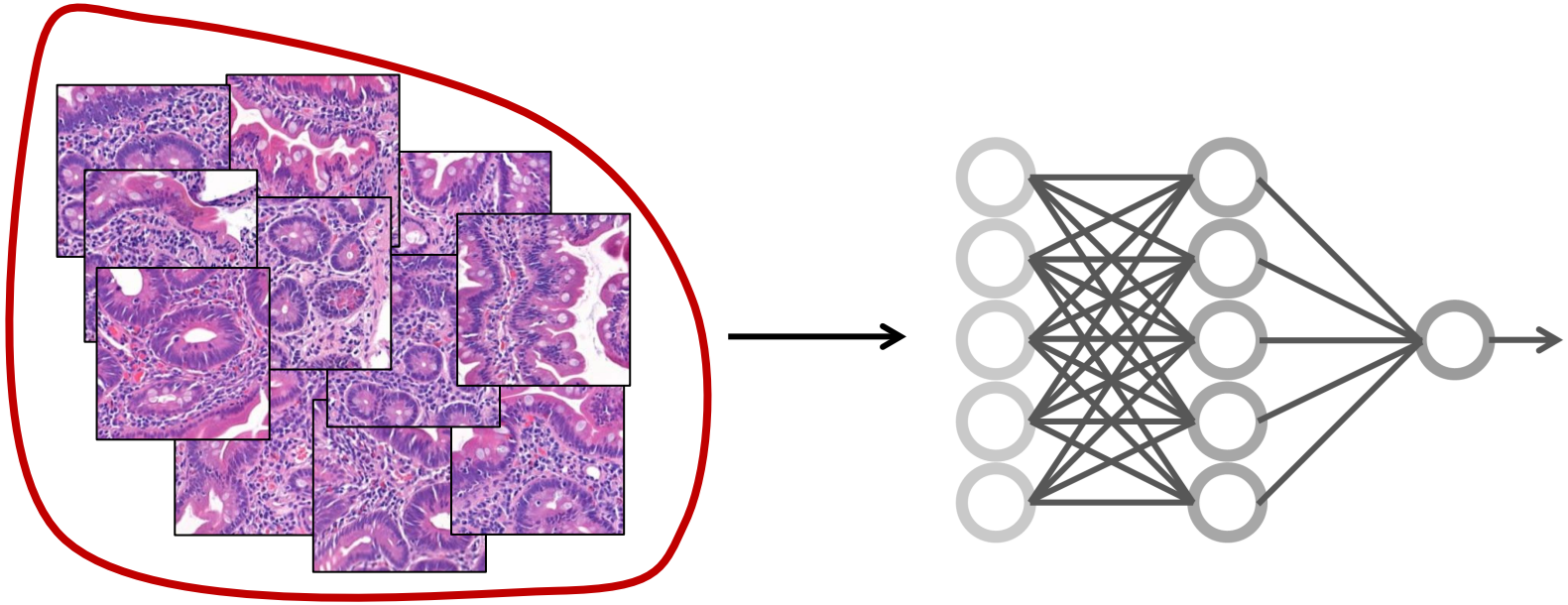
Patch-level

(strongly supervised)



Slide-level

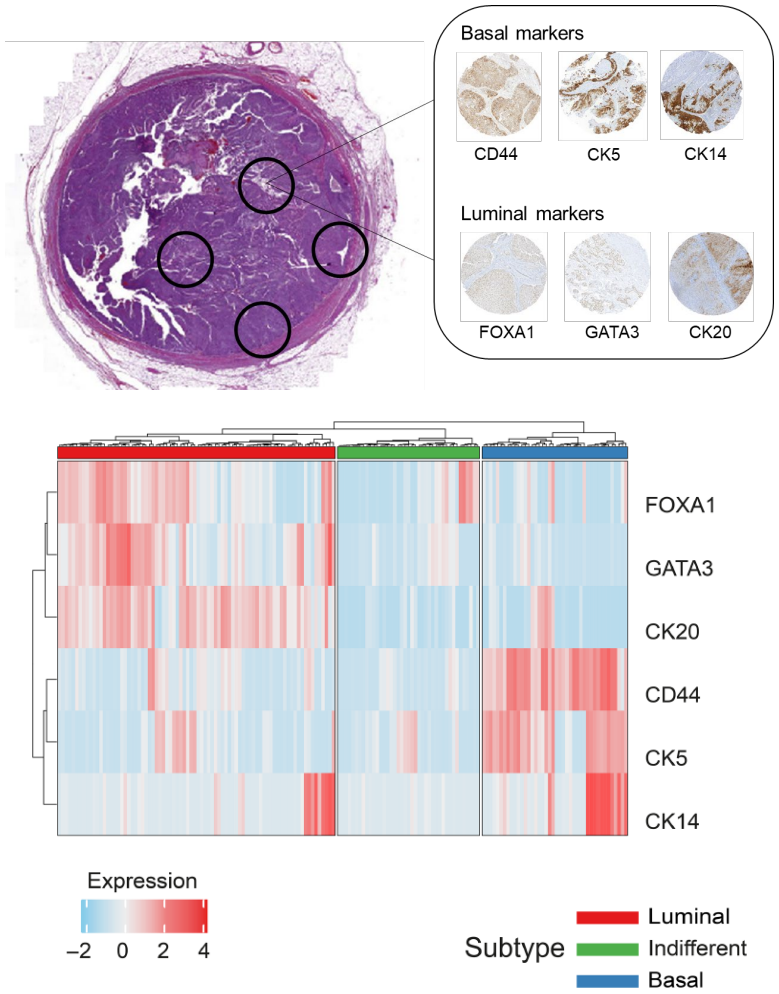
(weakly supervised)



DL prediction of upper trait urothelial carcinoma (UTUC) protein-based subtypes

Hierarchical clustering to identify UTUC subtypes

N = 163 invasive UTUC samples (pT1+)



Angeloni,..., Ferrazzi*, Bahlinger*, J Pathol Clin Res, 2024

DL prediction of upper trait urothelial carcinoma (UTUC) protein-based subtypes

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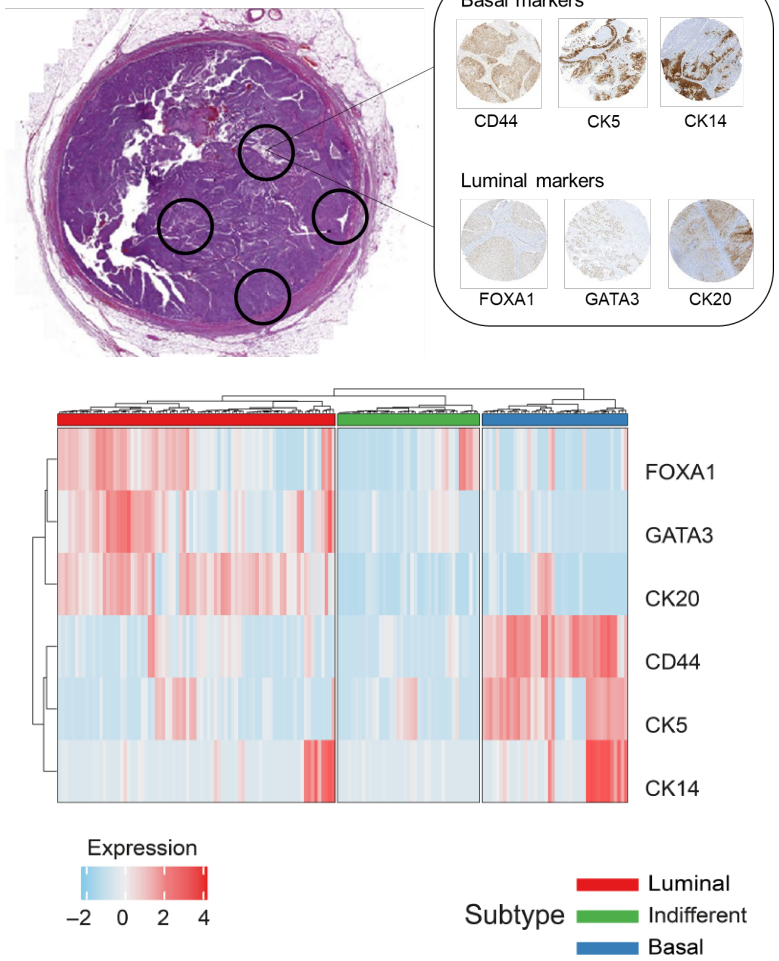
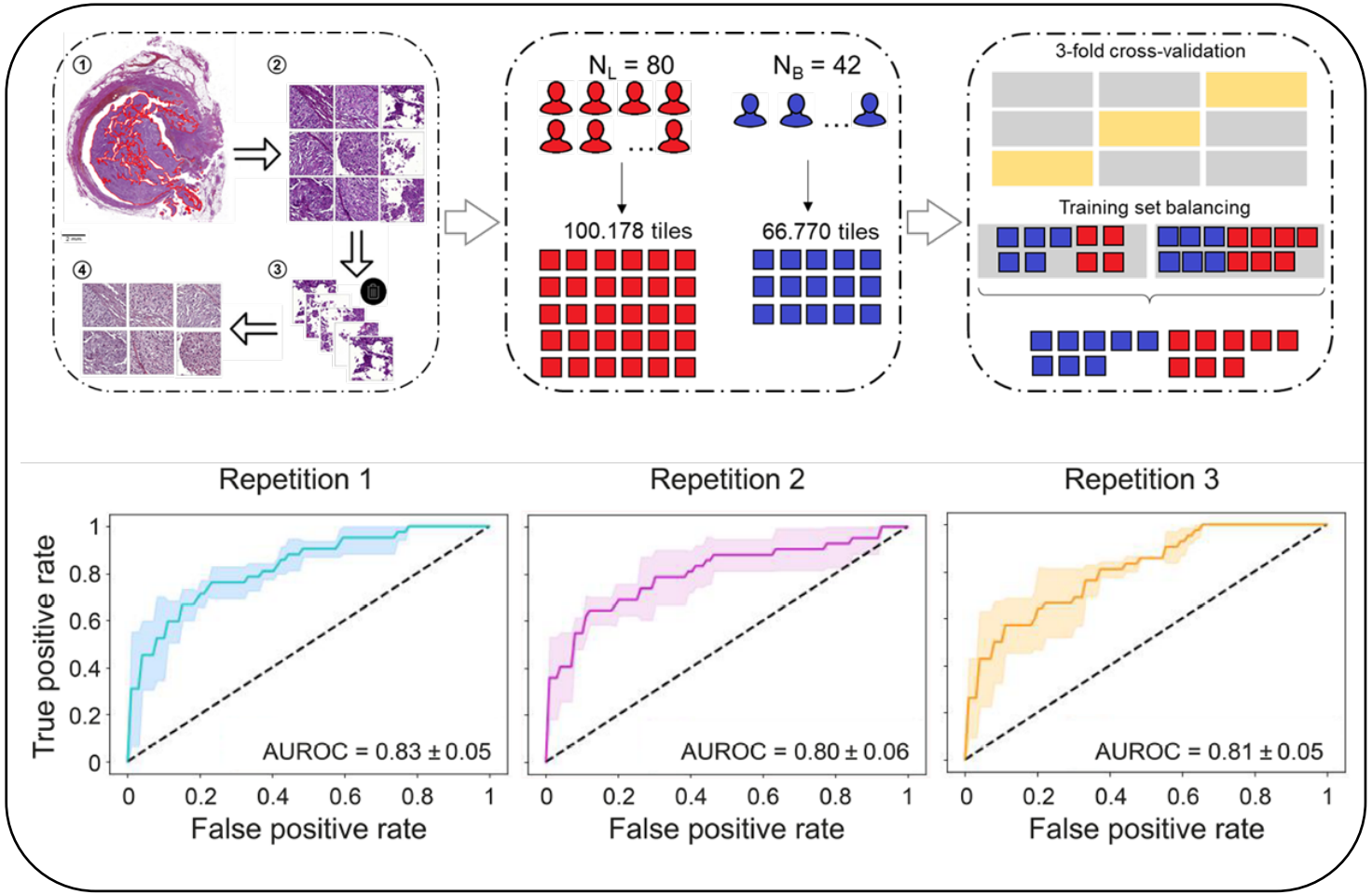


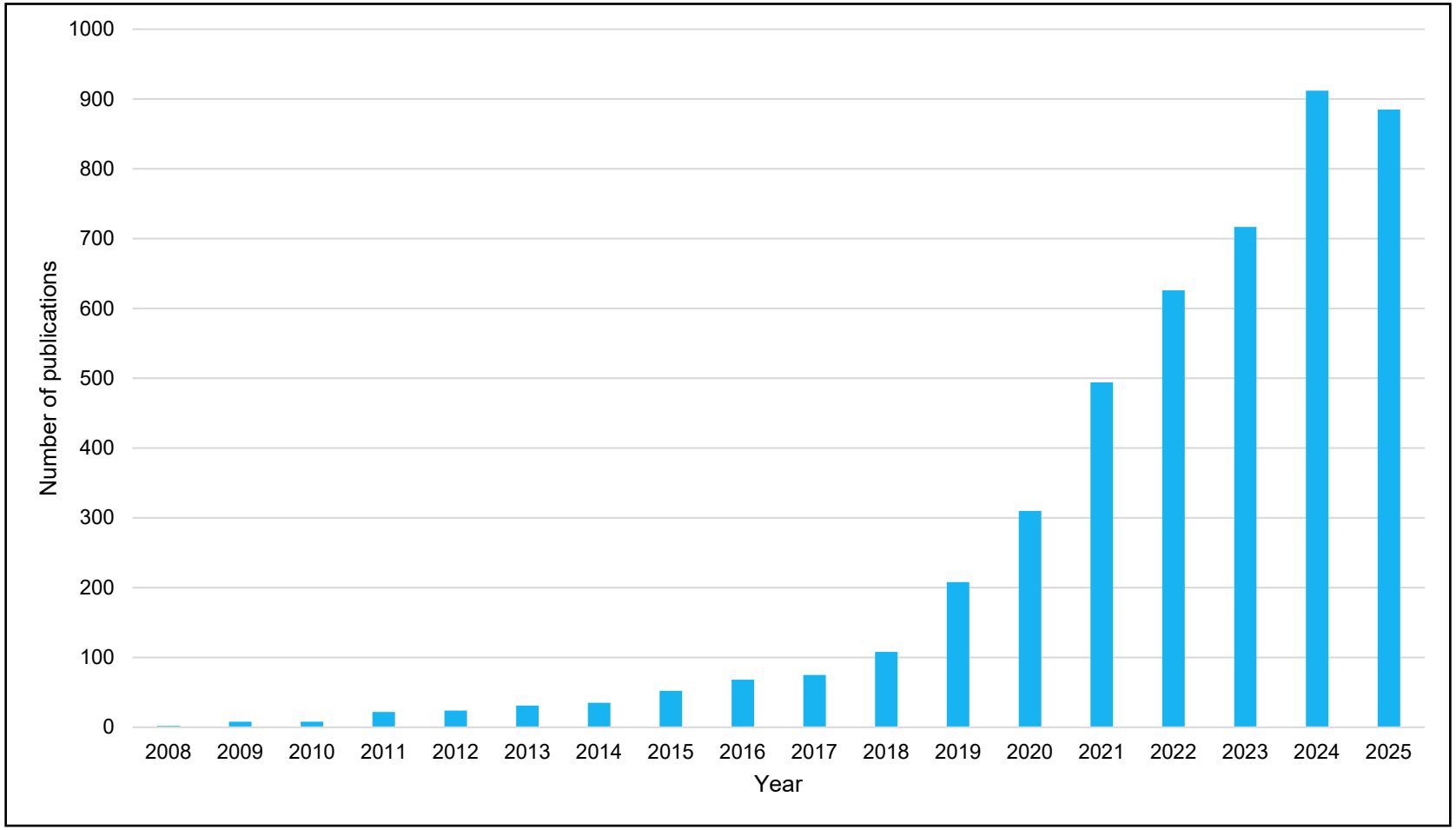
UTUC subtypes prediction from H&E slides



Angeloni,..., Ferrazzi*, Bahlinger*, J Pathol Clin Res, 2024

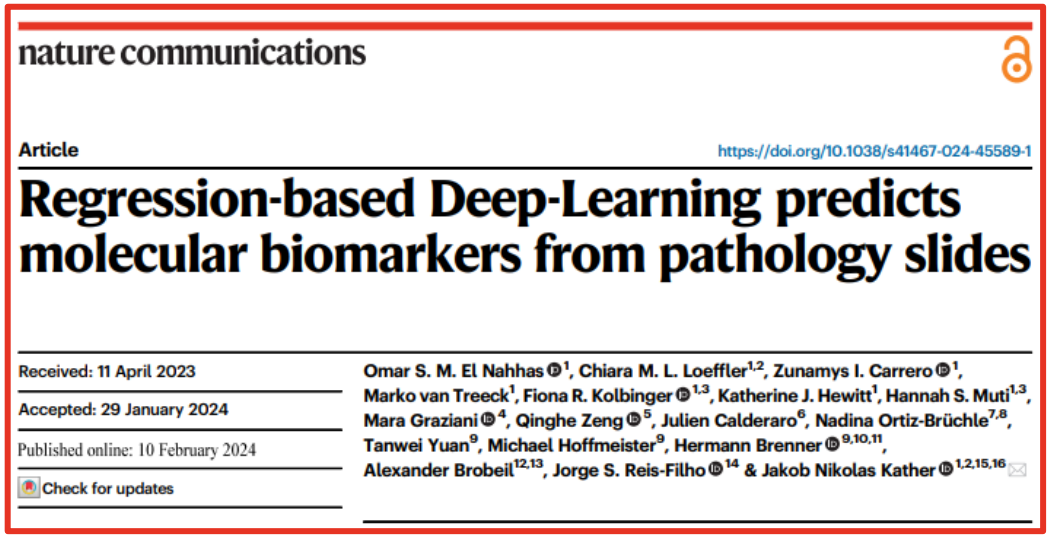
Increasing number of computational models in pathology

PubMed search: ("computational pathology" OR "digital pathology" OR "whole slide imag*") AND ("artificial intelligence" OR "machine learning" OR "deep learning" OR "image analysis") – last update: 29/09/2025



Computational pathology's impact

Prediction of molecular biomarkers



nature communications

Article

https://doi.org/10.1038/s41467-024-45589-1

Regression-based Deep-Learning predicts molecular biomarkers from pathology slides

Received: 11 April 2023

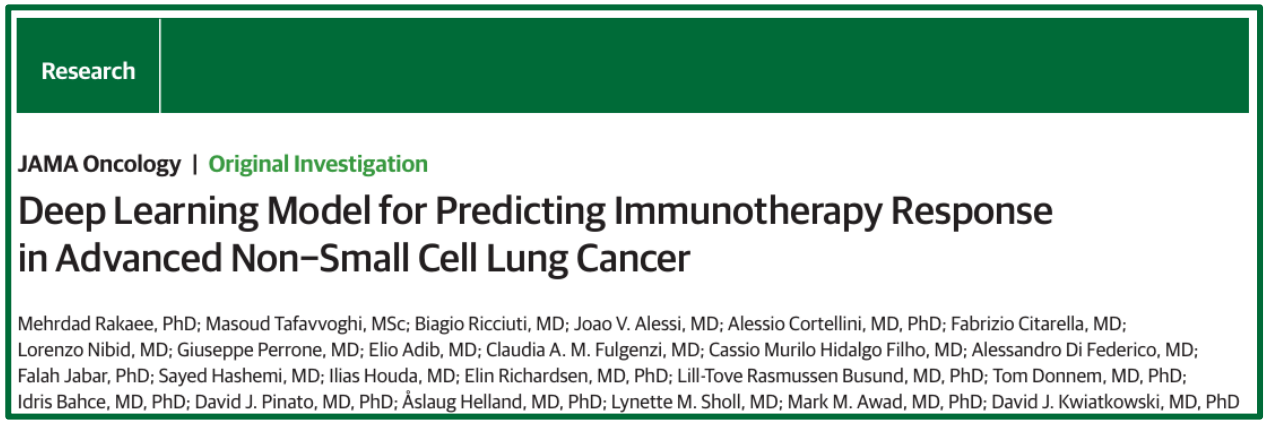
Accepted: 29 January 2024

Published online: 10 February 2024

Check for updates

Omar S. M. El Nahhas[1], Chiara M. L. Loeffler[1,2], Zunamys I. Carrero[1], Marko van Treeck[1], Fiona R. Kolbinger[1,3], Katherine J. Hewitt[1], Hannah S. Muti[1,3], Mara Graziani[4], Qinghe Zeng[5], Julien Calderaro[6], Nadina Ortiz-Brüchle[7,8], Tanwei Yuan[9], Michael Hoffmeister[9], Hermann Brenner[9,10,11], Alexander Brobeil[12,13], Jorge S. Reis-Filho[14] & Jakob Nikolas Kather[1,2,15,16]

Prediction of immunotherapy response



Research

JAMA Oncology | Original Investigation

Deep Learning Model for Predicting Immunotherapy Response in Advanced Non–Small Cell Lung Cancer

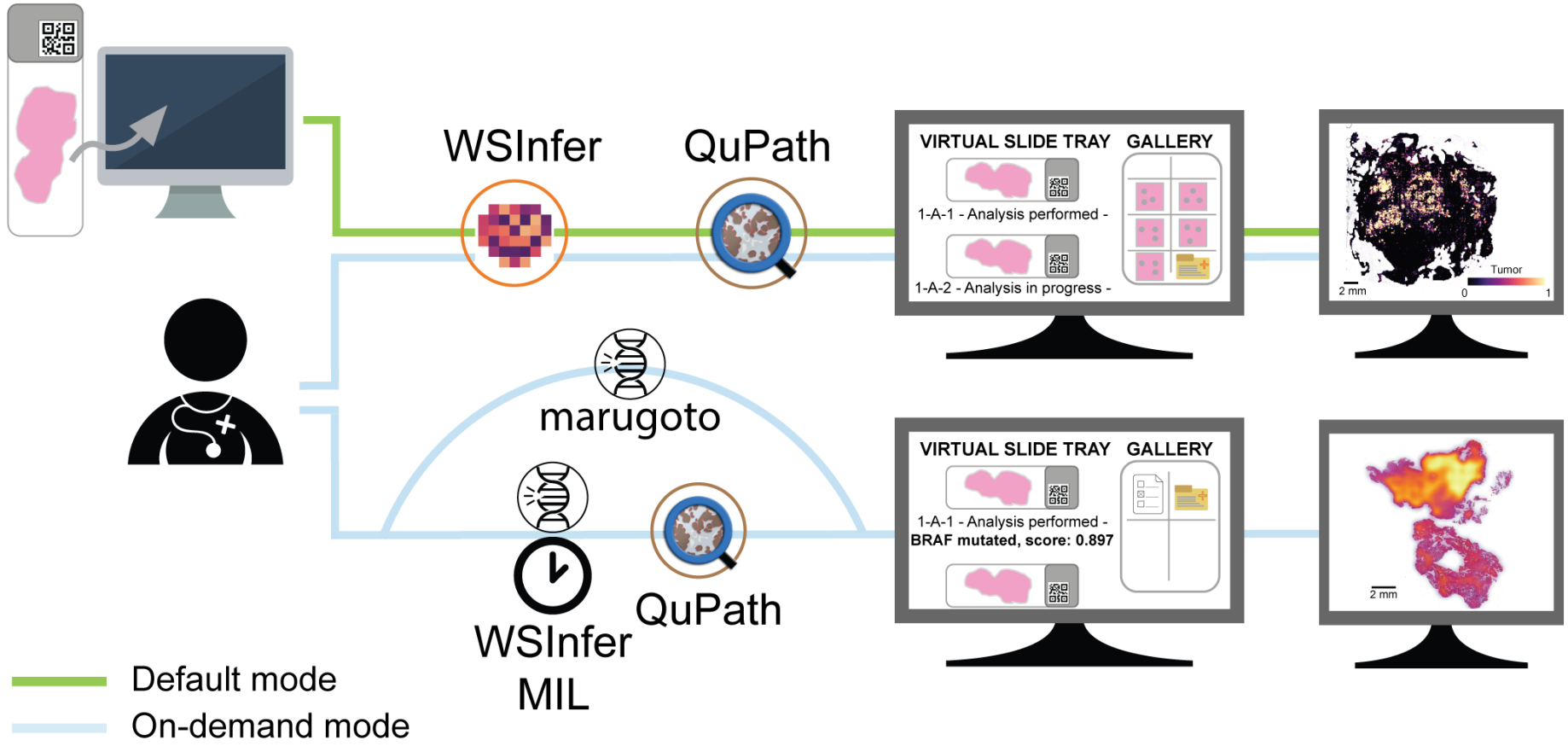
Mehrdad Rakaee, PhD; Masoud Tafavvoghi, MSc; Biagio Ricciuti, MD; Joao V. Alessi, MD; Alessio Cortellini, MD, PhD; Fabrizio Citarella, MD; Lorenzo Nibid, MD; Giuseppe Perrone, MD; Elio Adib, MD; Claudia A. M. Fulgenzi, MD; Cassio Murilo Hidalgo Filho, MD; Alessandro Di Federico, MD; Falah Jabar, PhD; Sayed Hashemi, MD; Ilias Houda, MD; Elin Richardsen, MD, PhD; Lill-Tove Rasmussen Busund, MD, PhD; Tom Donnem, MD, PhD; Idris Bahce, MD, PhD; David J. Pinato, MD, PhD; Åslaug Helland, MD, PhD; Lynette M. Sholl, MD; Mark M. Awad, MD, PhD; David J. Kwiatkowski, MD, PhD

JAMA Oncol. 2025;11(2):109-118. doi:10.1001/jamaoncol.2024.5356
Published online December 26, 2024.

Limited application of DL models in routine pathology practice

- A fully digital workflow is required
- Lack of prospective clinical validation and required regulatory approval for clinical use of AI-based assays
- Lack of/limited reimbursement for AI use
- Missing protocol for the integration of computational pathology solutions
- Difficulty in re-using publicly available DL models
- Black-box nature of AI tools

Closing the gap in the clinical adoption of computational pathology



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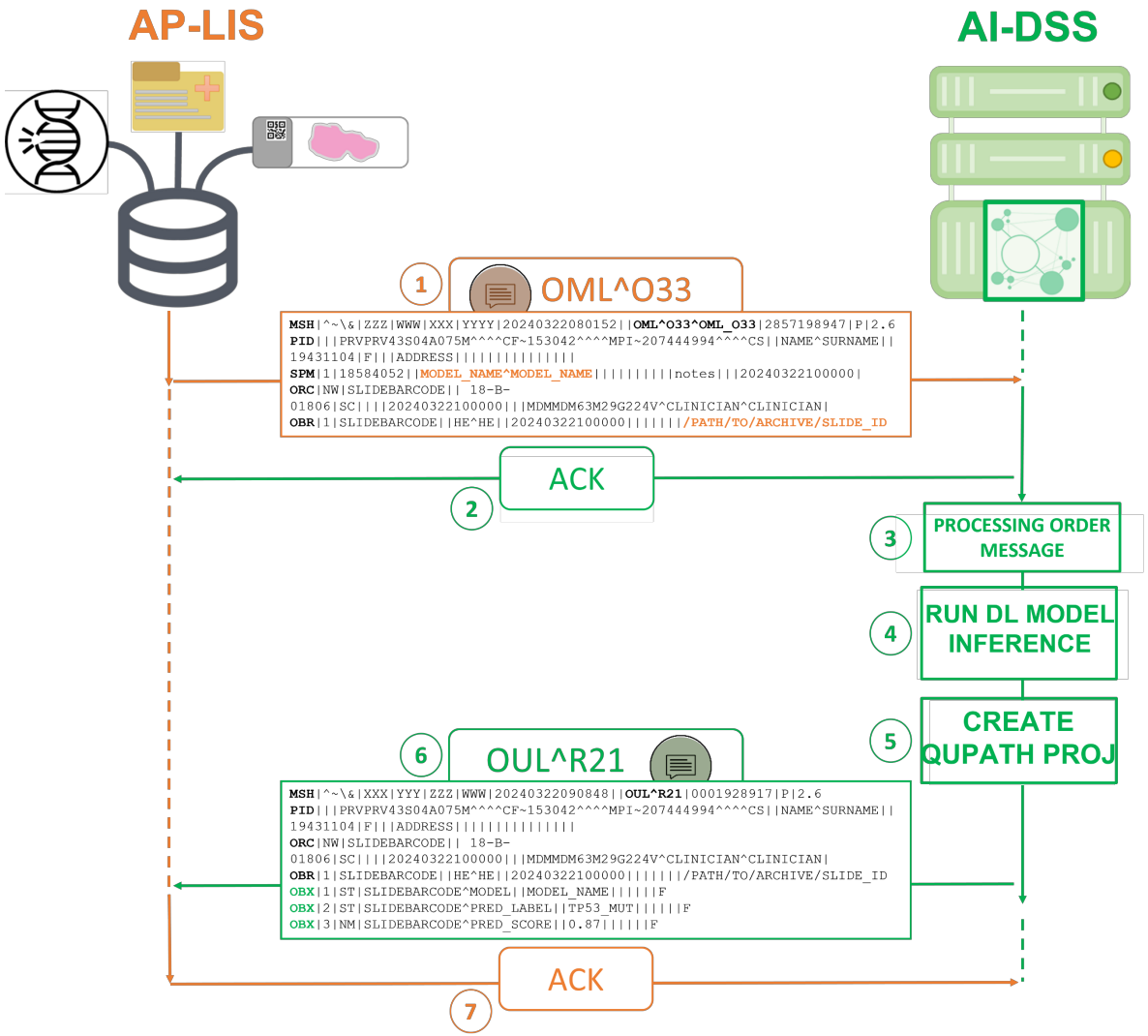
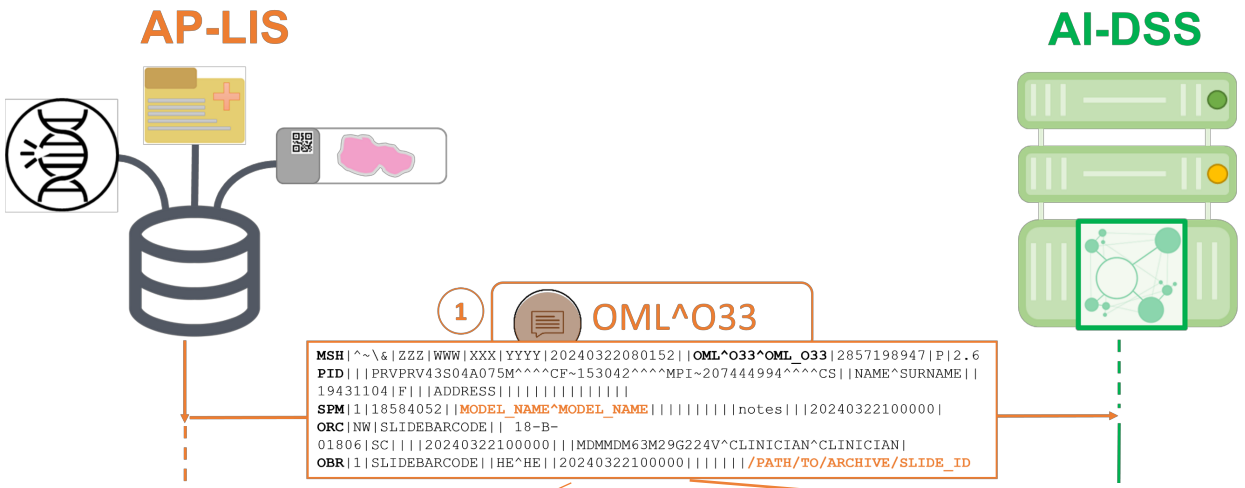
HL7-based integration framework scheme

- **portable and standardized integration framework**
- inclusion of publicly available and custom developed DL models
- implementation of intuitive visualization strategies



Angeloni,..., Ferrazzi*, Fraggetta*, Genome Med, 2025

Request: laboratory order message (OML^O33) from AP-LIS to AI-DSS



specimen

observation request

MSH|^~\&|ZZZ|WWW|XXX|YYYY|20240322080152||OML^O33^OML_O33|2857198947|P|2.6

PID|||PRVPRV43S04A075M^^^^CF~153042^^^^MPI~207444994^^^^CS||NAME^SURNAME||194

31104|F|||ADDRESS|||||||||||||||

name of DL model to deploy

SPM|1|18584052||**MODEL_NAME^MODEL_NAME**|||||||||notes|||20240322100000|

ORC|NW|SLIDEBARCODE|| 18-B-01806|SC||||20240322100000|||MDMMDM63M29G224V

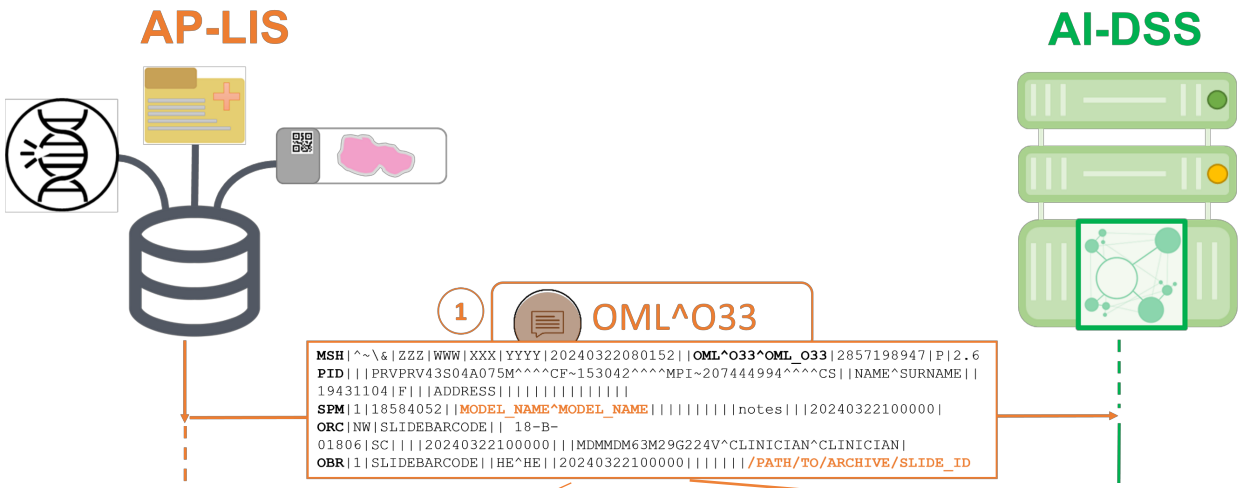
^CLINICIAN^CLINICIAN|

path to WSI to analyze

OBR|1|SLIDEBARCODE||HE^HE||20240322100000|||||||**/PATH/TO/ARCHIVE/SLIDE_ID**

Angeloni,..., Ferrazzi*, Fraggetta*, Genome Med, 2025

Request: laboratory order message (OML^O33) from AP-LIS to AI-DSS



- **default-mode**: correspondence table between tissue type, staining and DL models
- **on-demand**: drop-down menu in AP-LIS

specimen

observation request

MSH|^~\&|ZZZ|WWW|XXX|YYYY|20240322080152||OML^O33^OML_O33|2857198947|P|2.6

PID|||PRVPRV43S04A075M^^^^CF~153042^^^^MPI~207444994^^^^CS||NAME^SURNAME||194 31104|F|||ADDRESS|||||||||||||||

SPM|1|18584052||**MODEL_NAME^MODEL_NAME**|||||||||notes|||20240322100000|

ORC|NW|SLIDEBARCODE|| 18-B-01806|SC||||20240322100000|||MDMMDM63M29G224V ^CLINICIAN^CLINICIAN|

OBR|1|SLIDEBARCODE||HE^HE||20240322100000|||||||**/PATH/TO/ARCHIVE/SLIDE_ID**

name of DL model to deploy

path to WSI to analyze

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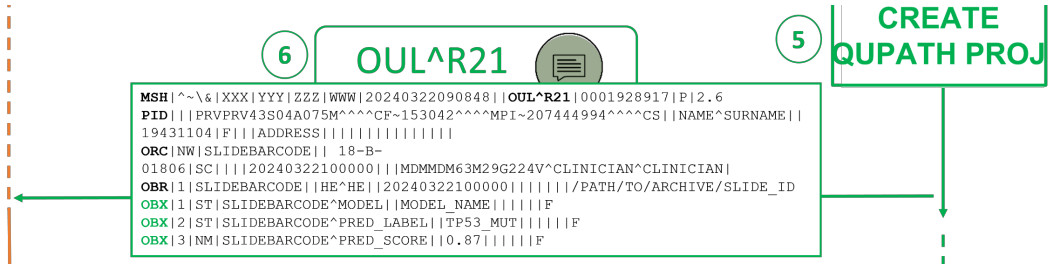
Results – patch-level models: unsolicited laboratory observation message (OUL^R21) from AI-DSS to AP-LIS



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ORC|NW|SLIDEBARCODE|| 18-B-01806|SC||||20240322100000|||MDMMDM63M29G224V^CLINICIAN^CLINICIAN|

OBR|1|SLIDEBARCODE||HE^HE||20240322100000|||||||/PATH/TO/ARCHIVE/SLIDE_ID

OBX|1|ST|SLIDEBARCODE^MODEL||breast-tumor-resnet34.tcga-brca|||||F name of model

OBX|2|ED|SLIDEBARCODE^RUN||b‘run_metadata.json’|||||F metadata

OBX|3|ED|SLIDEBARCODE^MASK||b‘mask.jpg’|||||F tissue mask

OBX|4|ED|SLIDEBARCODE^TABLE||b‘models_output.csv’|||||F tile-level predictions

OBX|5|ED|SLIDEBARCODE^TILE||b‘tile1.jpg’|||||F

OBX|6|ED|SLIDEBARCODE^TILE||b‘tile2.jpg’|||||F

OBX|7|ED|SLIDEBARCODE^TILE||b‘tile3.jpg’|||||F

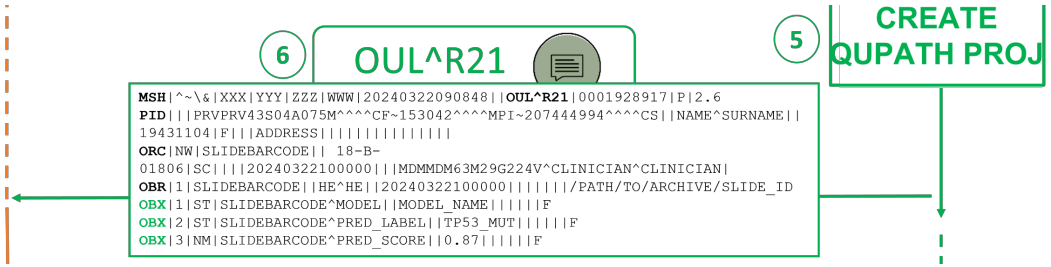
OBX|8|ED|SLIDEBARCODE^TILE||b‘tile4.jpg’|||||F

OBX|9|ED|SLIDEBARCODE^TILE||b‘tile5.jpg’|||||F

OBX: observation result segments

Angeloni,..., Ferrazzi*, Fraggetta*, Genome Med, 2025

Results – patch-level models: unsolicited laboratory observation message (OUL^R21) from AI-DSS to AP-LIS



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OBX|1|ST|SLIDEBARCODE^MODEL||breast-tumor-resnet34.tcga-brca|||||F name of model

OBX|2|ED|SLIDEBARCODE^RUN||b‘run_metadata.json’|||||F metadata

OBX|3|ED|SLIDEBARCODE^MASK||b‘mask.jpg’|||||F tissue mask

OBX|4|ED|SLIDEBARCODE^TABLE||b‘models_output.csv’|||||F tile-level predictions

OBX|5|ED|SLIDEBARCODE^TILE||b‘tile1.jpg’|||||F

OBX|6|ED|SLIDEBARCODE^TILE||b‘tile2.jpg’|||||F

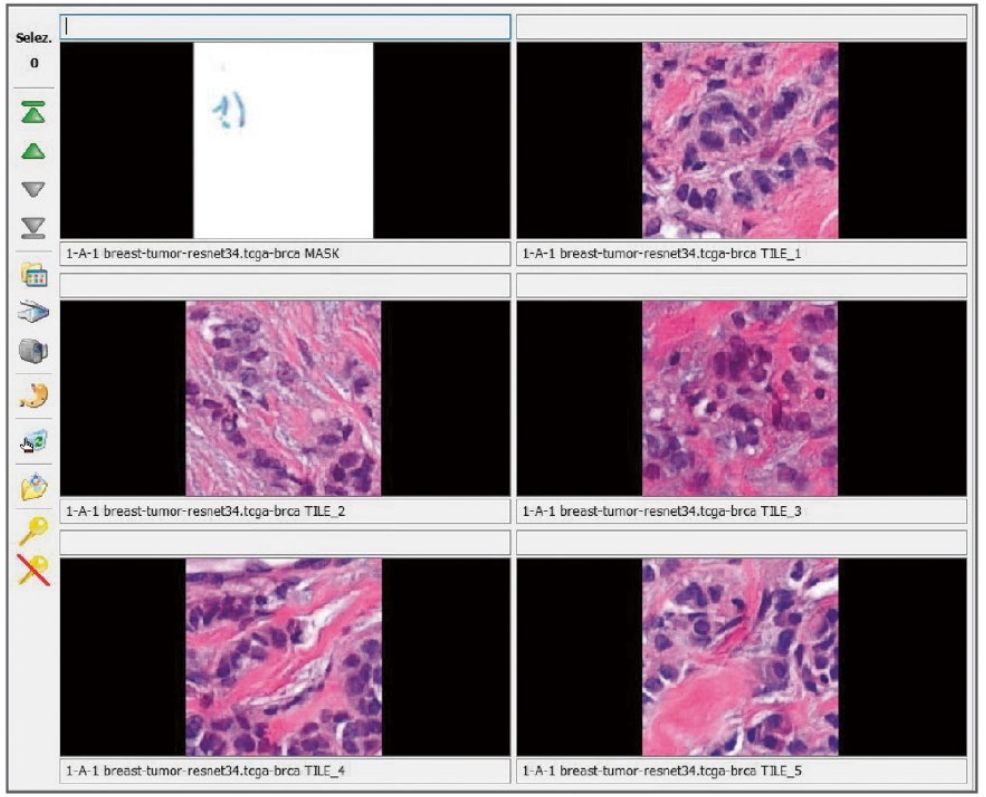
OBX|7|ED|SLIDEBARCODE^TILE||b‘tile3.jpg’|||||F

OBX|8|ED|SLIDEBARCODE^TILE||b‘tile4.jpg’|||||F

OBX|9|ED|SLIDEBARCODE^TILE||b‘tile5.jpg’|||||F

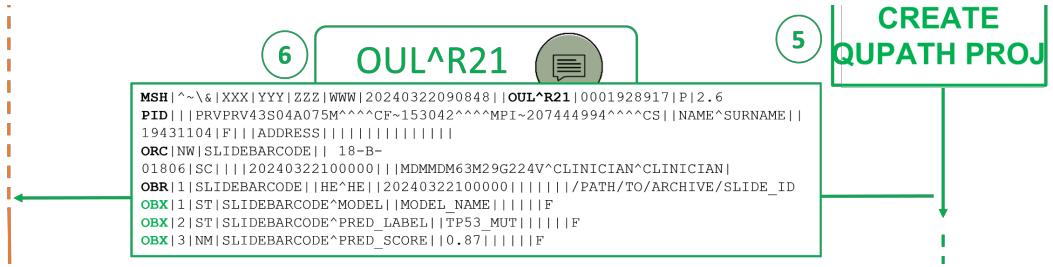
OBX: observation result segments

for binary models: top 5 predicted tiles in the LIS patient gallery



Angeloni,..., Ferrazzi*, Fraggetta*, Genome Med, 2025

Results – slide-level models: unsolicited laboratory observation message (OUL^R21) from AI-DSS to AP-LIS



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OBR|1|SLIDEBARCODE||HE^HE||20240322100000|||||||/PATH/TO/ARCHIVE/SLIDE_ID

OBX|1|ST|SLIDEBARCODE^MODEL||msi-attMIL-marugoto|||||F

OBX|2|ST|SLIDEBARCODE^PRED_LABEL||isMSIH_MSIH|||||F

OBX|3|NM|SLIDEBARCODE^PRED_SCORE||0.9310635|||||F

LIS virtual tray

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N = 16 DL models currently integrated

- portable and standardized integration framework
- **inclusion of publicly available and custom developed DL models**
- implementation of intuitive visualization strategies

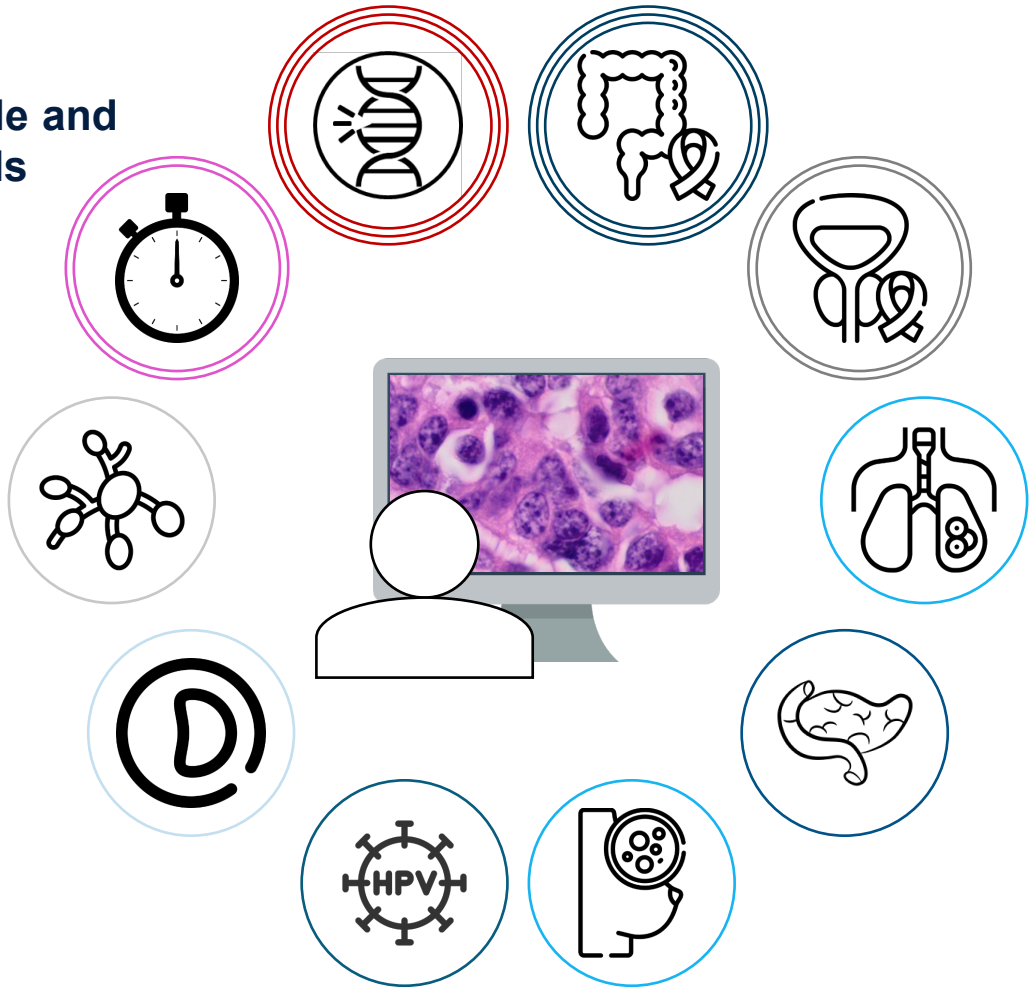


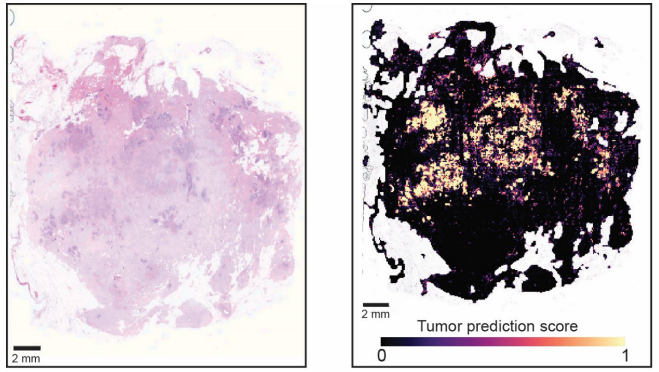
Image created using resources from Flaticon.com

DL models currently integrated:

- discriminate between different tissue types or conditions;
- predict the status of clinical biomarkers;
- predict the risk of cancer death.

Categories of supported DL models and visualizations

- portable and standardized integration framework
- inclusion of publicly available and custom developed DL models
- **implementation of intuitive visualization strategies**



measurement maps
binary classifiers

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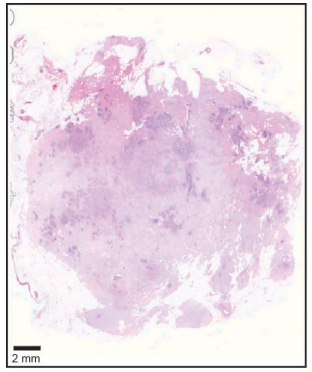
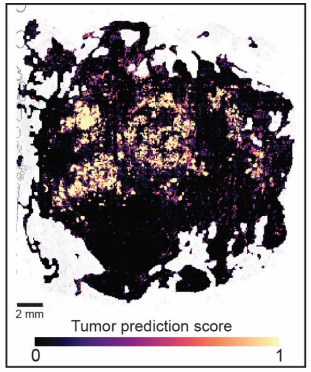
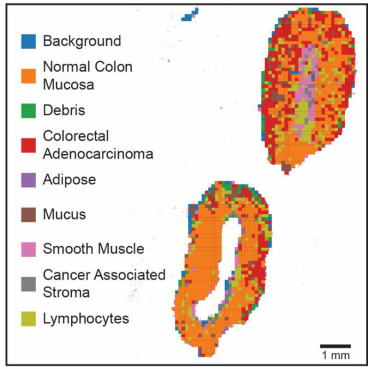
Categories of supported DL models and visualizations

- the establishment of an integration framework
- the inclusion of publicly available DL models
- **the implementation of intuitive visualization strategies**





measurement maps
binary classifiers



color maps
multi-class classifiers

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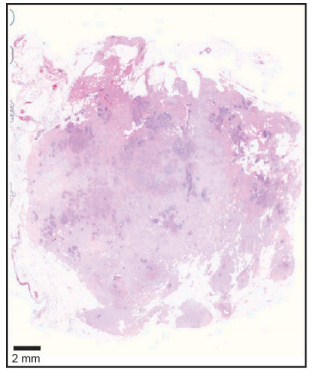
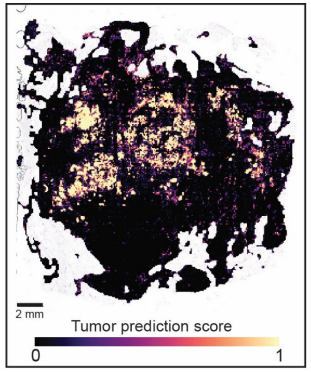
Categories of supported DL models and visualizations

- the establishment of an integration framework
- the inclusion of publicly available DL models
- **the implementation of intuitive visualization strategies**





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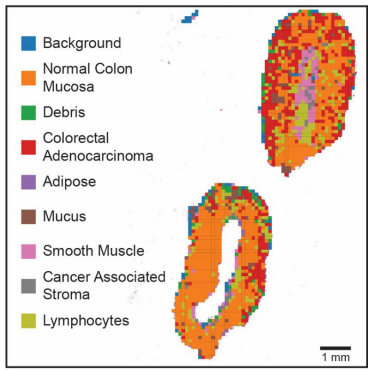

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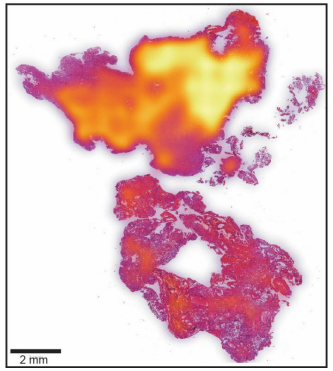

density maps
attention-based MIL classifiers

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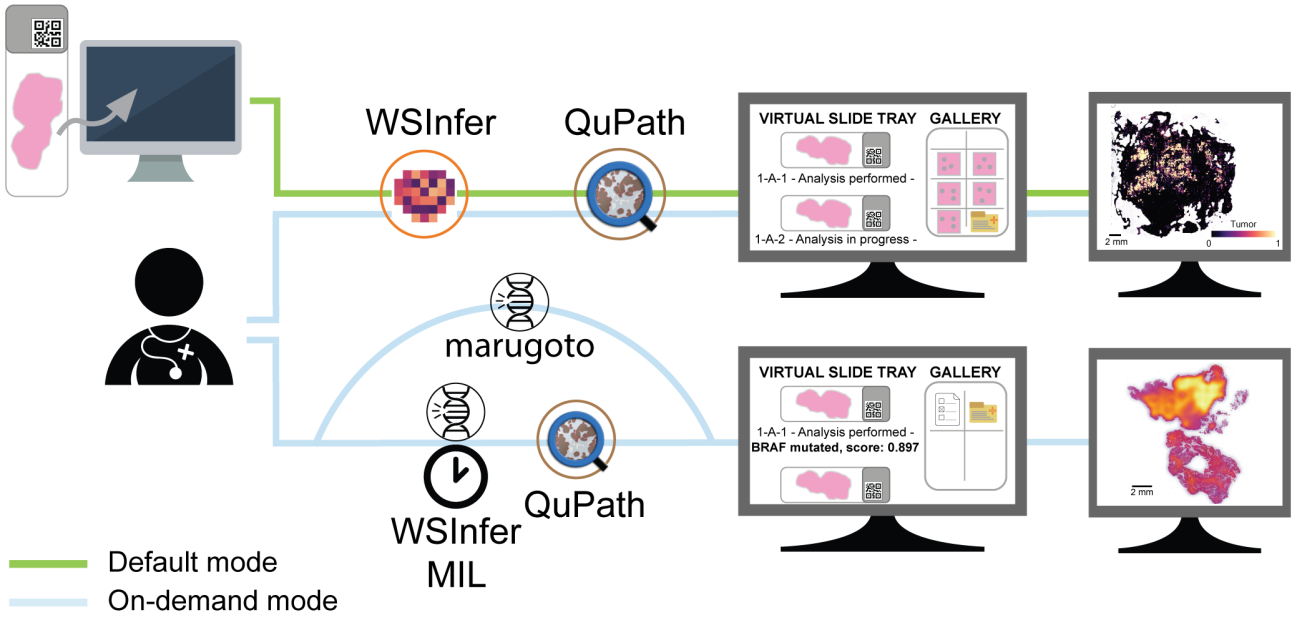
Conclusions

Our proof-of-concept framework addressed three key challenges:

- the establishment of an integration framework
- the inclusion of publicly available and custom DL models
- the implementation of intuitive visualization strategies



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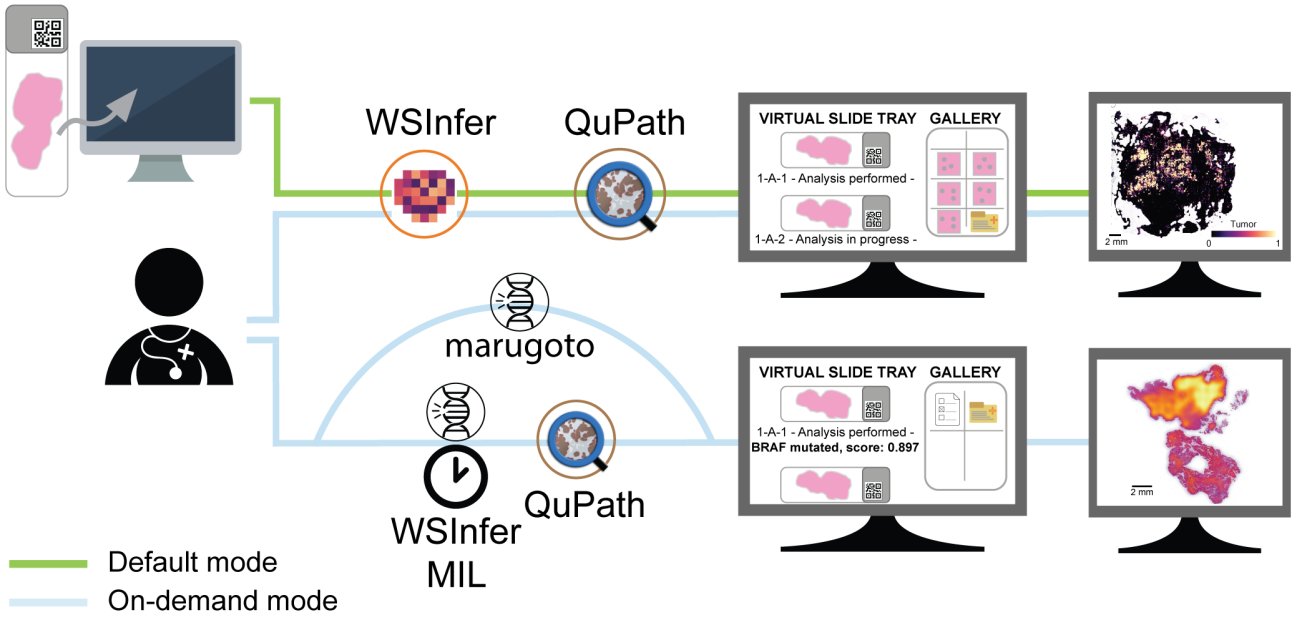

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LIMITATIONS:

- Research-only framework
- How to include DL-based assessment in diagnostic reports?
- Digitization of the pathology department required
- Pathologists' acceptance and AI proficiency

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