THE UNIVERSITY OF CHICAGO
CENTER FOR COMPUTATIONAL MEDICINE & CLINICAL ARTIFICIAL INTELLIGENCE

Artificial Intelligence to Determine Actionable Cancer States

Alexander T. Pearson MD PhD

DISCLOSURES

Advisory boards: Prelude Therapeutics, Ayala, Elevar Therapeutics, ThermoFisher

Research funds: Kura Oncology, Abbvie, Merck

Travel: Caris

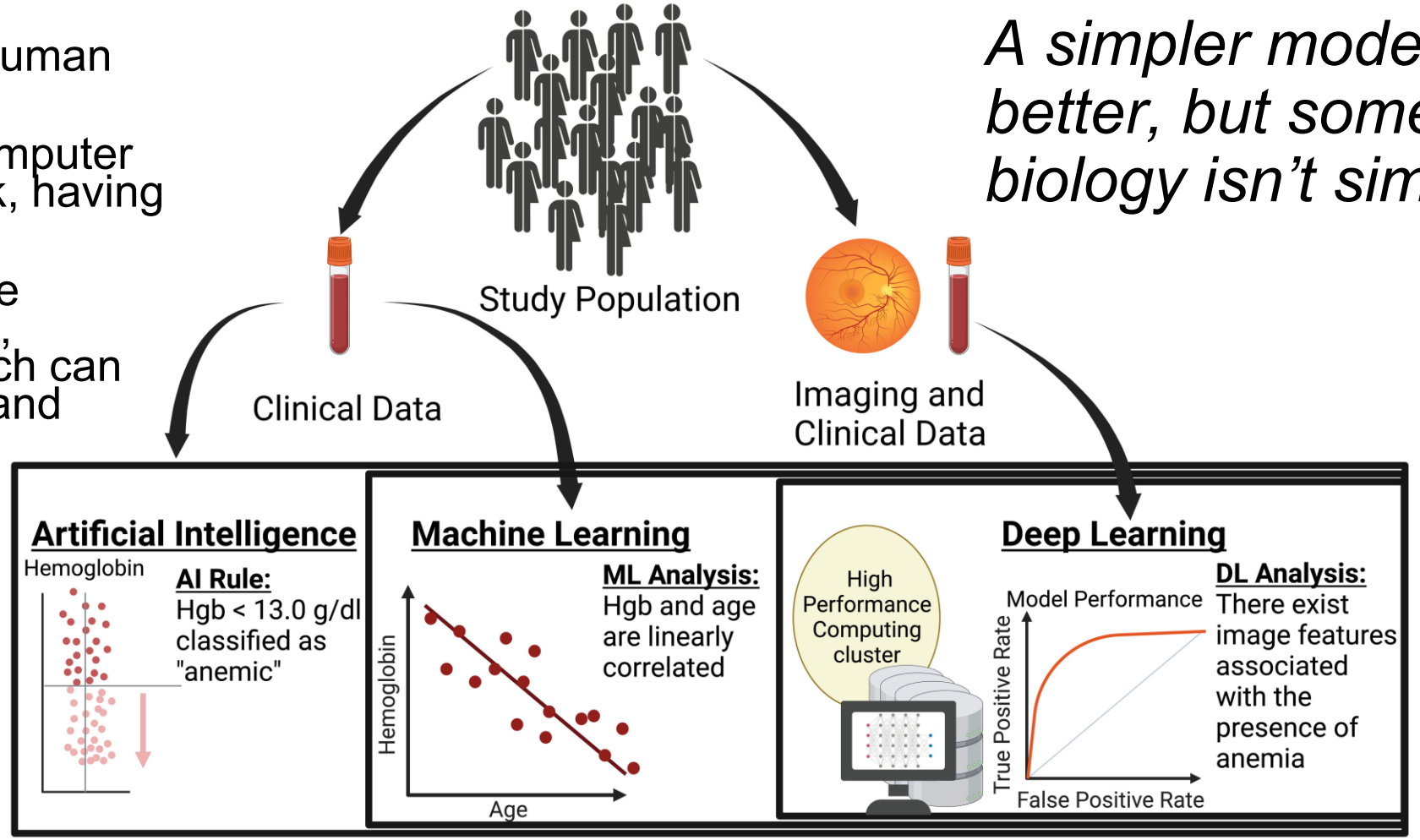
SAB: Fanconi Cancer Foundation, Breakthrough Cancer

Consulting: Abbvie

IP: University of Chicago pursuing patents related to digital pathology deep learning

AI IN CLINICAL MEDICINE

- *Artificial Intelligence*: A computer mimicking a human task
- *Machine Learning*: A computer mimicking a human task, having trained on data
- *Neural Networks*: Simple mathematical equations, connected in a way which can mimic animal neurons, and trained on data



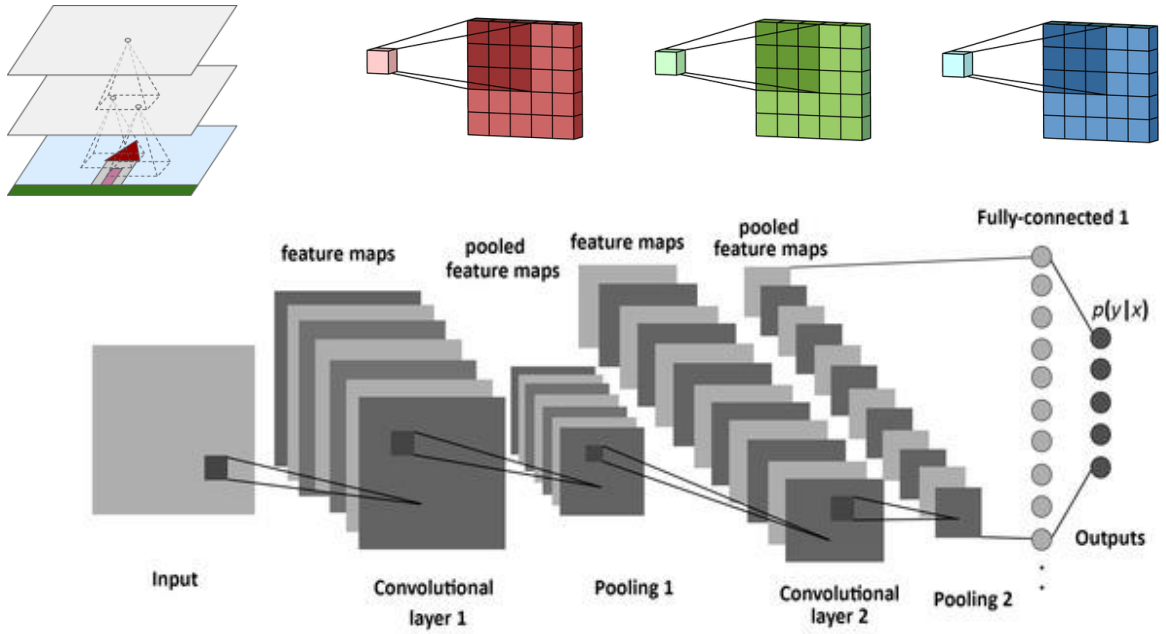
A simpler model is better, but sometimes biology isn't simple…

OUTLINE

- Extracting information from digital pathology images
- Clinical applications of AI in digital pathology
- Physician-assisting AI methods
- AI in Medicine at UChicago

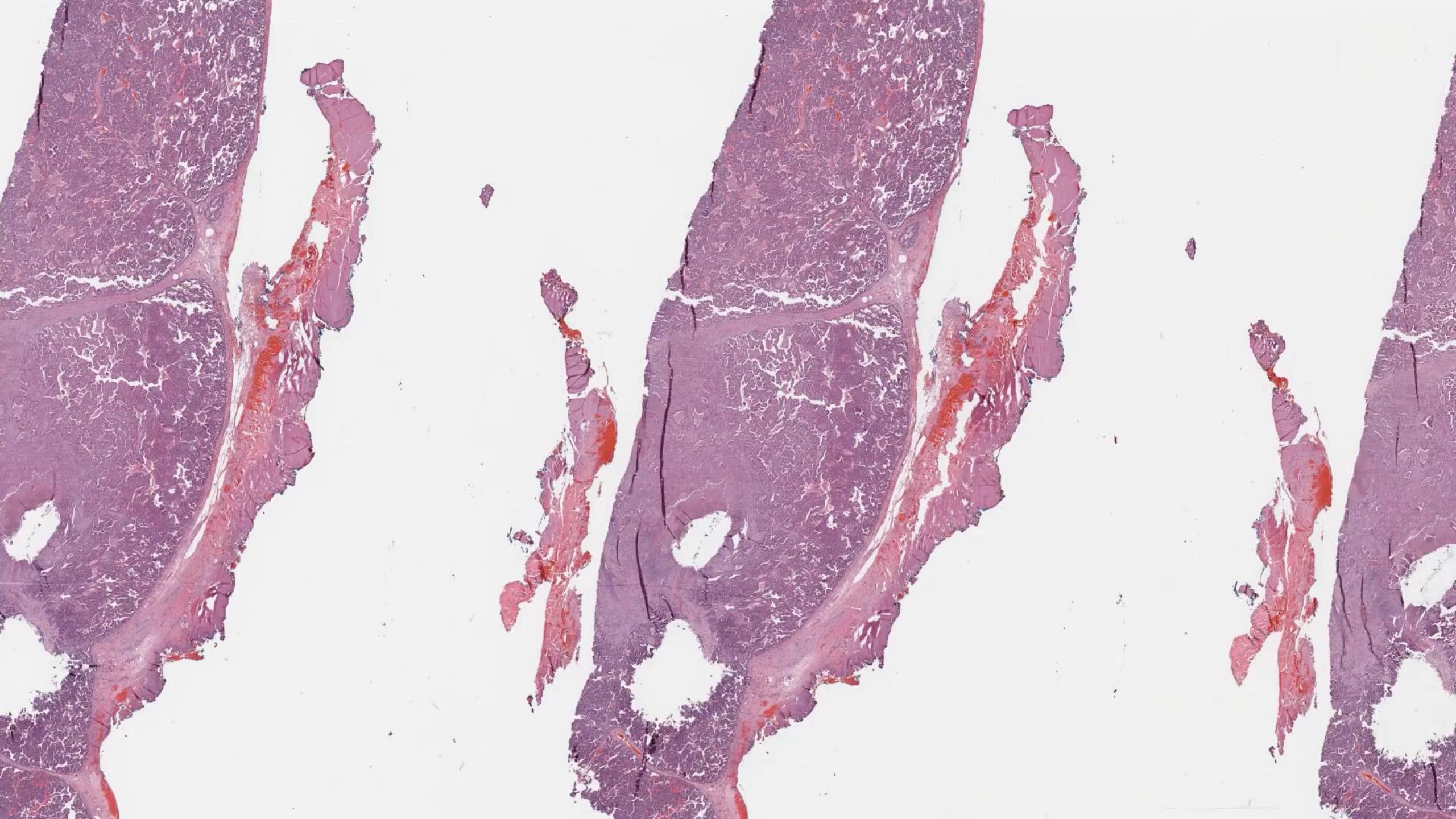
ARTIFICIAL INTELLIGENCE ARCHITECTURES LEARN TO INTERPRET IMAGES

Convolutional Neural Network



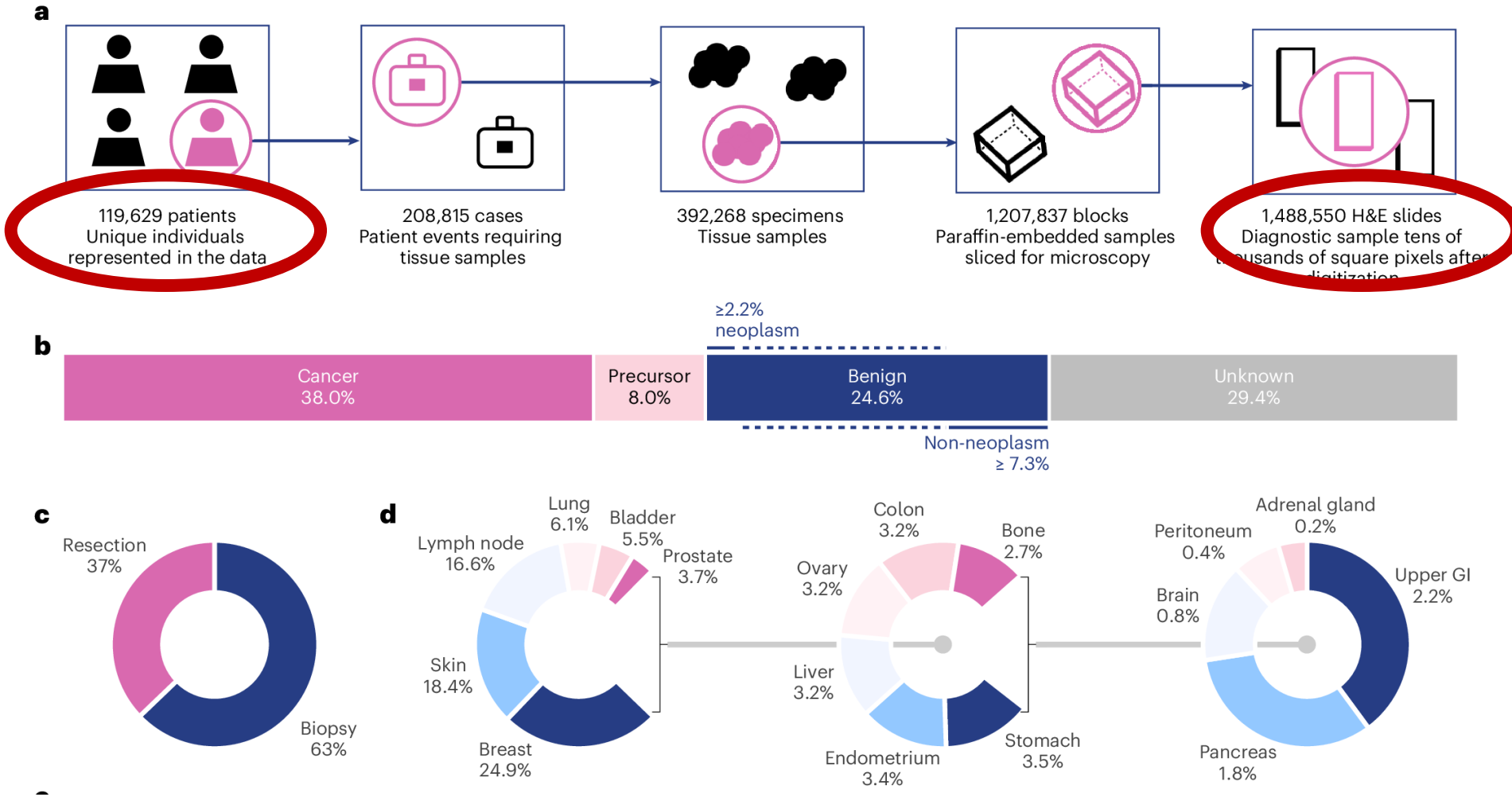
Vision Transformer

Géron, A. (2017). Hands-on machine learning with Scikit-Learn and TensorFlow : O'Reilly Media; Albelwi, S., & Mahmood, A. (2017). A framework for designing the architectures of deep convolutional neural networks. *Entropy*, *19*(6), 242; Looking inside neural nets. Retrieved September 2019, from https://ml4a.github.io/ml4a/looking_inside_neural_nets/; Satish Kumar, Analytics Vidhya



FOUNDATION MODELS REFLECT VAST DATA EXPOSURE

- FM produce a “feature vector” to represent the patterns in an image.
- This simple vector represents the “omics of visual data”.



DEEP LEARNING USE CASE: PATHOLOGY DATA FLOW FROM PHYSICAL TO DIGITAL

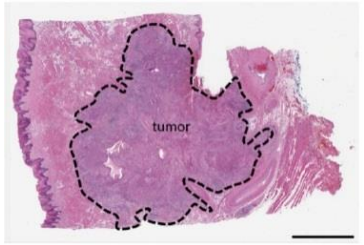
Digital slide scanner image capture of tumor regions

Automated digital slide image processing

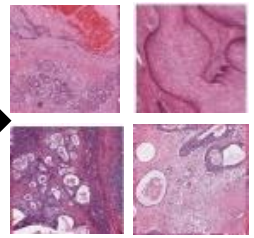
Foundation models built on millions of unlabeled images to extract features

Deep learning model fine-tuning for specific tasks

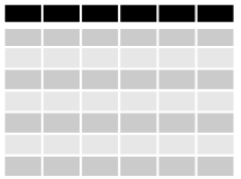
1) H&E Stained Slides



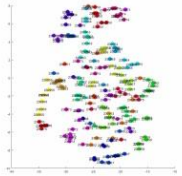
2) Optional pathologist annotation



3) Optional tiling based on algorithm



4) High-dimensional spreadsheet of derived features



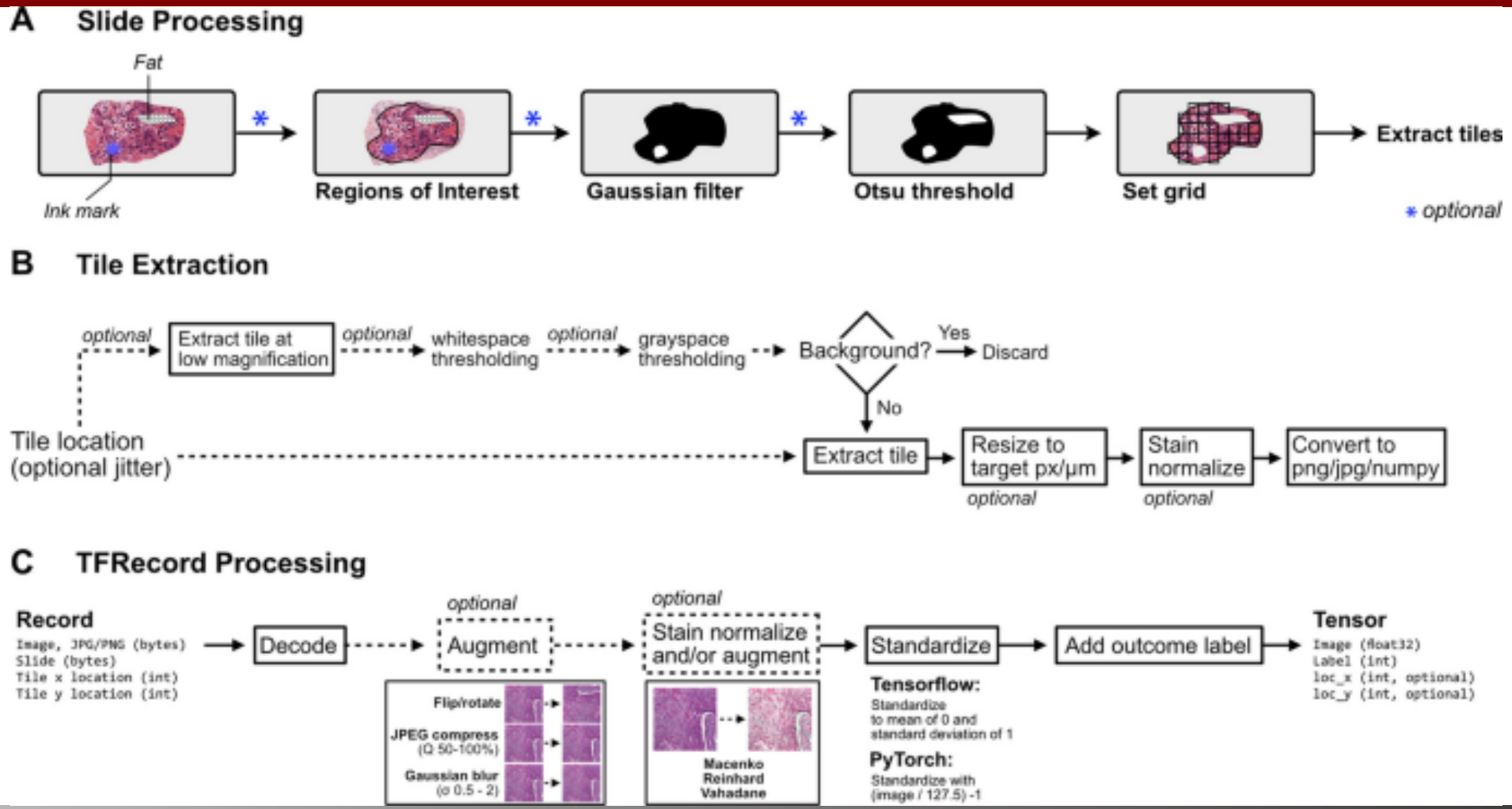
5) Statistical analysis output

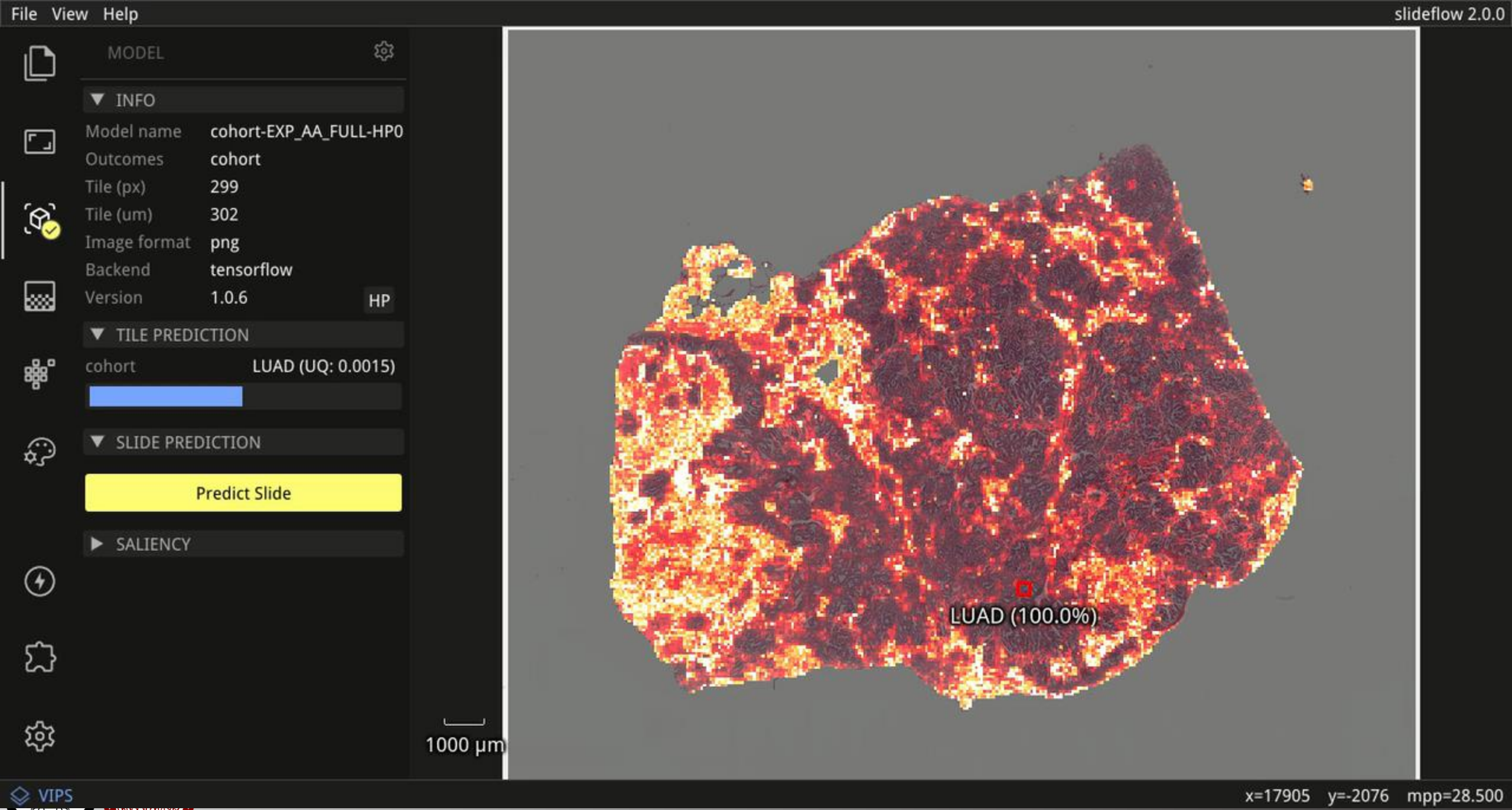
OPEN SOURCE PIPELINE FOR TRAINING PATHOLOGY DEEP LEARNING MODELS

Slideflow

www.slideflow.dev

www.slideflow.ai




File View Help
slideflow 2.0.0
MODEL
INFO
Model name cohort-EXP_AA_FULL-HP0
Outcomes cohort
Tile (px) 299
Tile (um) 302
Image format png
Backend tensorflow
Version 1.0.6
HP
TILE PREDICTION
cohort LUAD (UQ: 0.0015)
SLIDE PREDICTION
Predict Slide
SALIENCY
LUAD (100.0%)
1000 µm
VIPS
x=17905 y=-2076 mpp=28.500

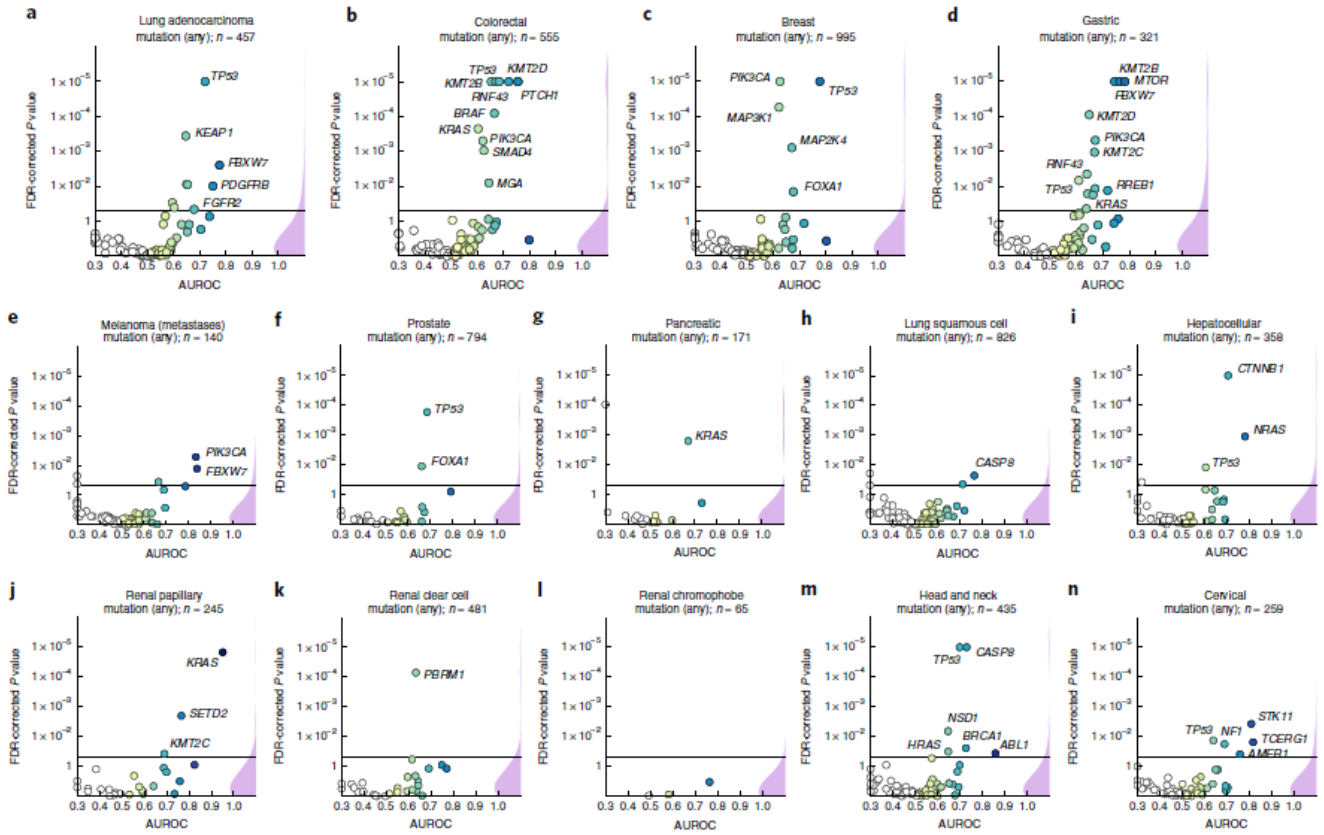
SUMMARY #1

- Deep learning AI tools can be applied to digital pathology data
- Foundation Models (FMs) leverage huge data sets to learn a language of image patterns
- Open source FMs can be applied through open source tools for analytical tasks

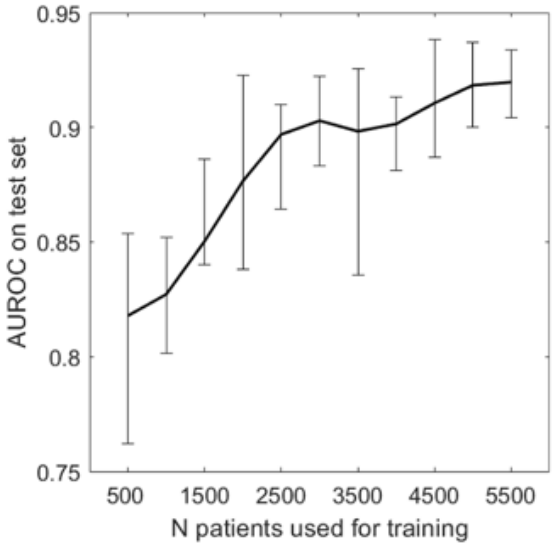
2. INTEGRATING AI MODELS INTO CANCER TREATMENT PLANNING

CLINICAL APPLICATION #1:
Pan-Cancer "Digital NGS" from digital histopathology

- Next generation sequencing (NGS) is costly and time consuming?
- Can we predict actionable mutations directly from pathology?
- Trained models of every OncoKB actionable cancer alteration in >4000 pts.

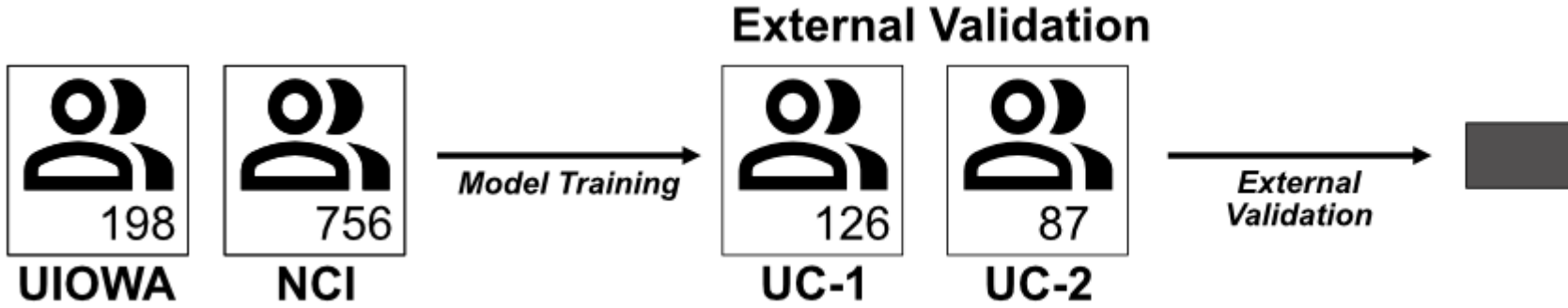


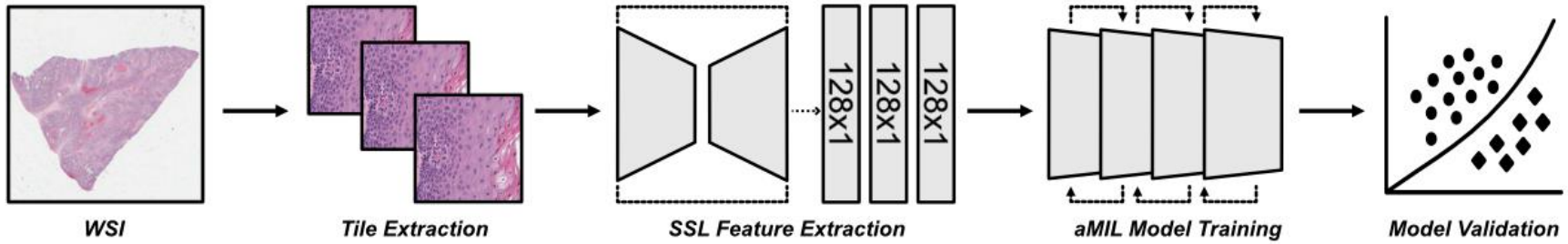
- Model performance improves with access to more data:

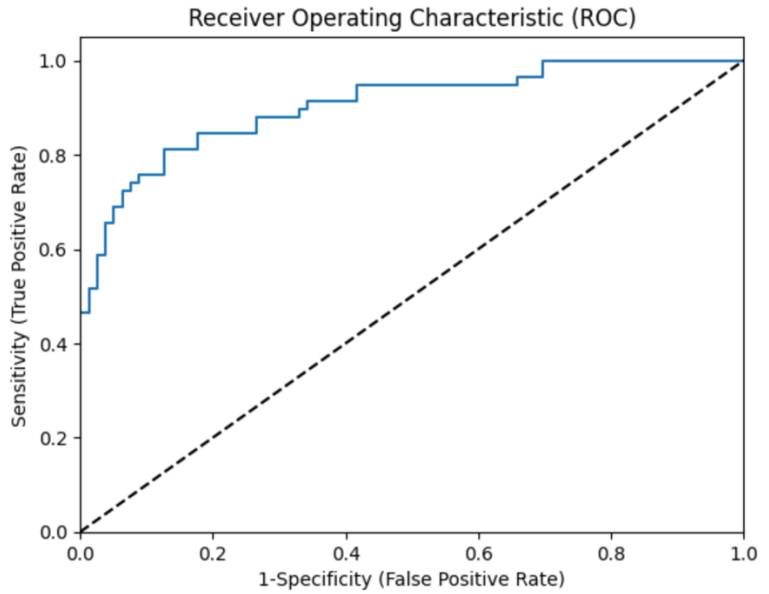


3/21/2019: Conceptualized *pan-cancer* deep learning for actionable alterations
11/8/2019: Posted BioRXiv Pre-print
4/17/2020: Manuscript Accepted in *Nature Cancer* DOI: 10.1101/833756

CLINICAL APPLICATION #2: Cancer progression prediction in OPL





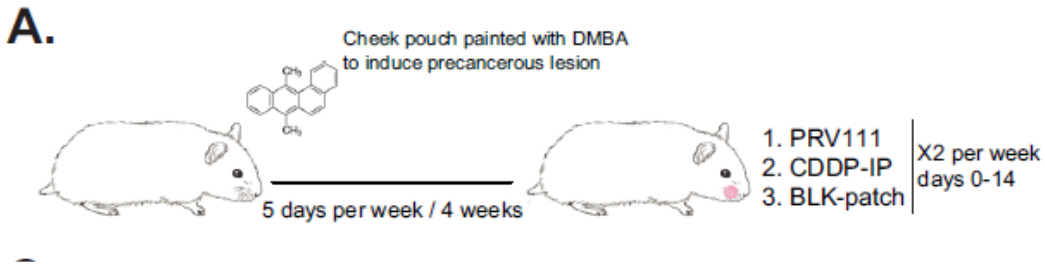


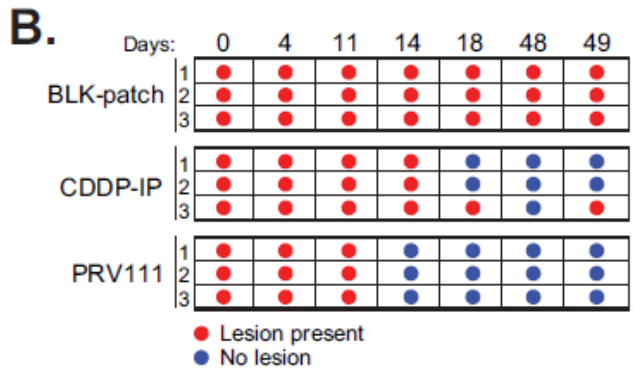
EXTERNAL VALIDATION
AUROC = 0.905, a Highly specific rule-in test?
Performance exceeds human grading

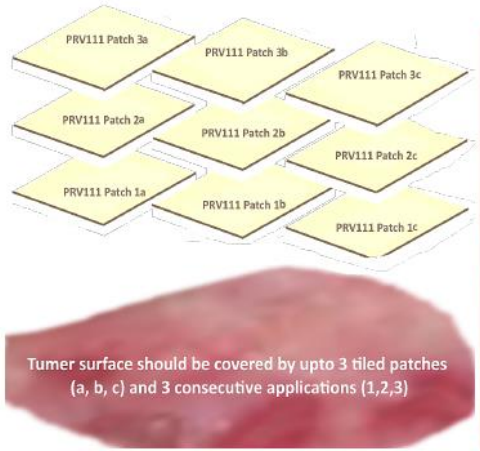
Ramesh S et. al. *JCO Global Oncology* 2023 DOI: 10.1200/GO.2023.9.Supplement_1.90

CLINCIAL APPLICTAION #2: Selecting Topical Chemo Candidates

- PRV111 is a cisplatin-embedded nanoparticle emitting patch
- Reverses dysplasia in 4NQO murine models
- Now in active Phase 1/2 trial at UChicago for CIS







NCT05893888; Goldberg M *Nature Communications* 2022

3. CLINICIAN-FACING COMPUTATIONAL TOOLS

TRUSTWORTHY DIAGNOSTICS: Explainable AI

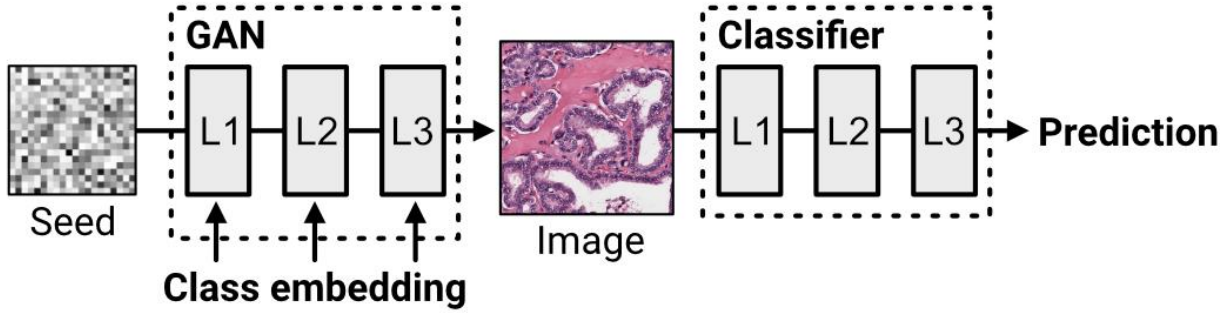
- Many neural networks are not inherently explainable
- Can we trust the results of an algorithm enough to make an important clinical decision for patient care?

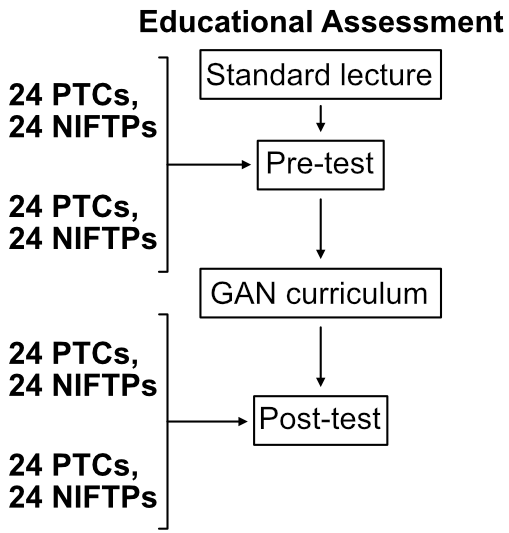
(a) Husky classified as wolf

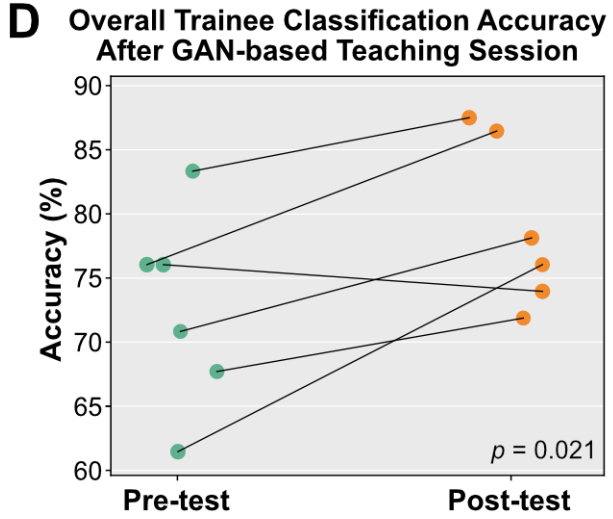
(b) Explanation

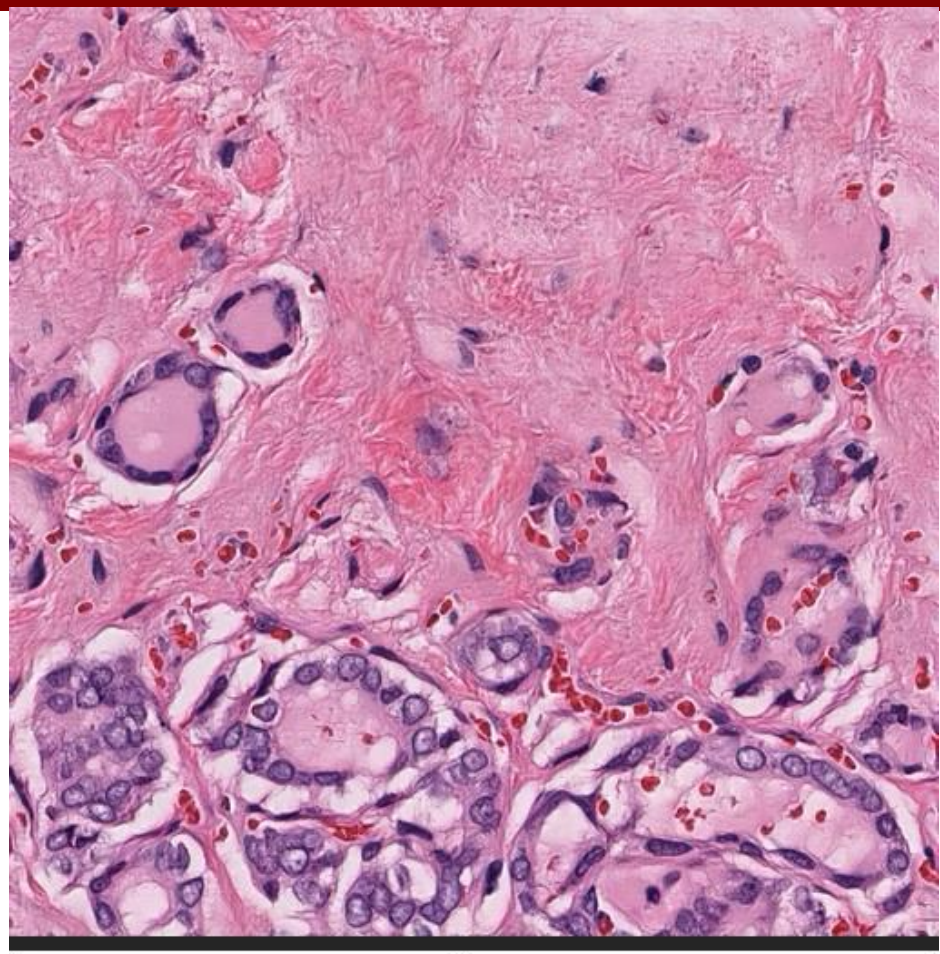
TRUSTWORTHY DIAGNOSTICS: Generative AI Explanations

AI based generative imaging can create images with enough information to train human pathologists



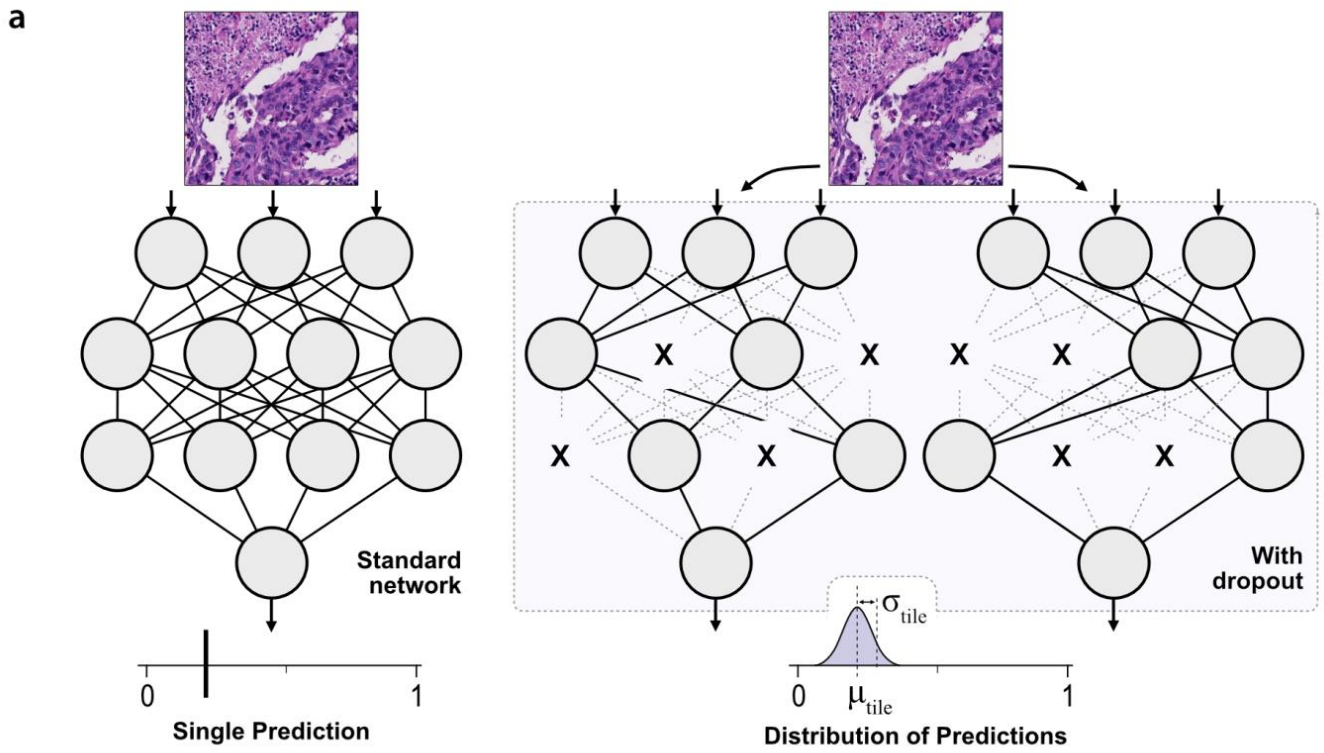


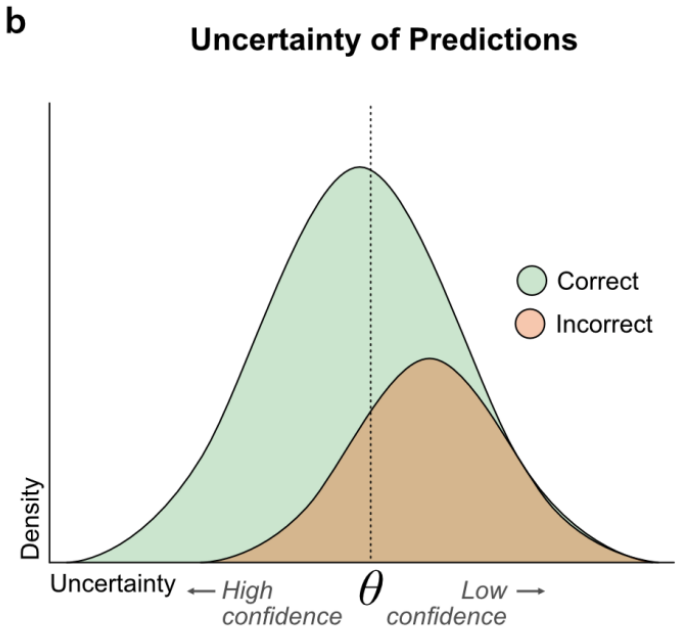




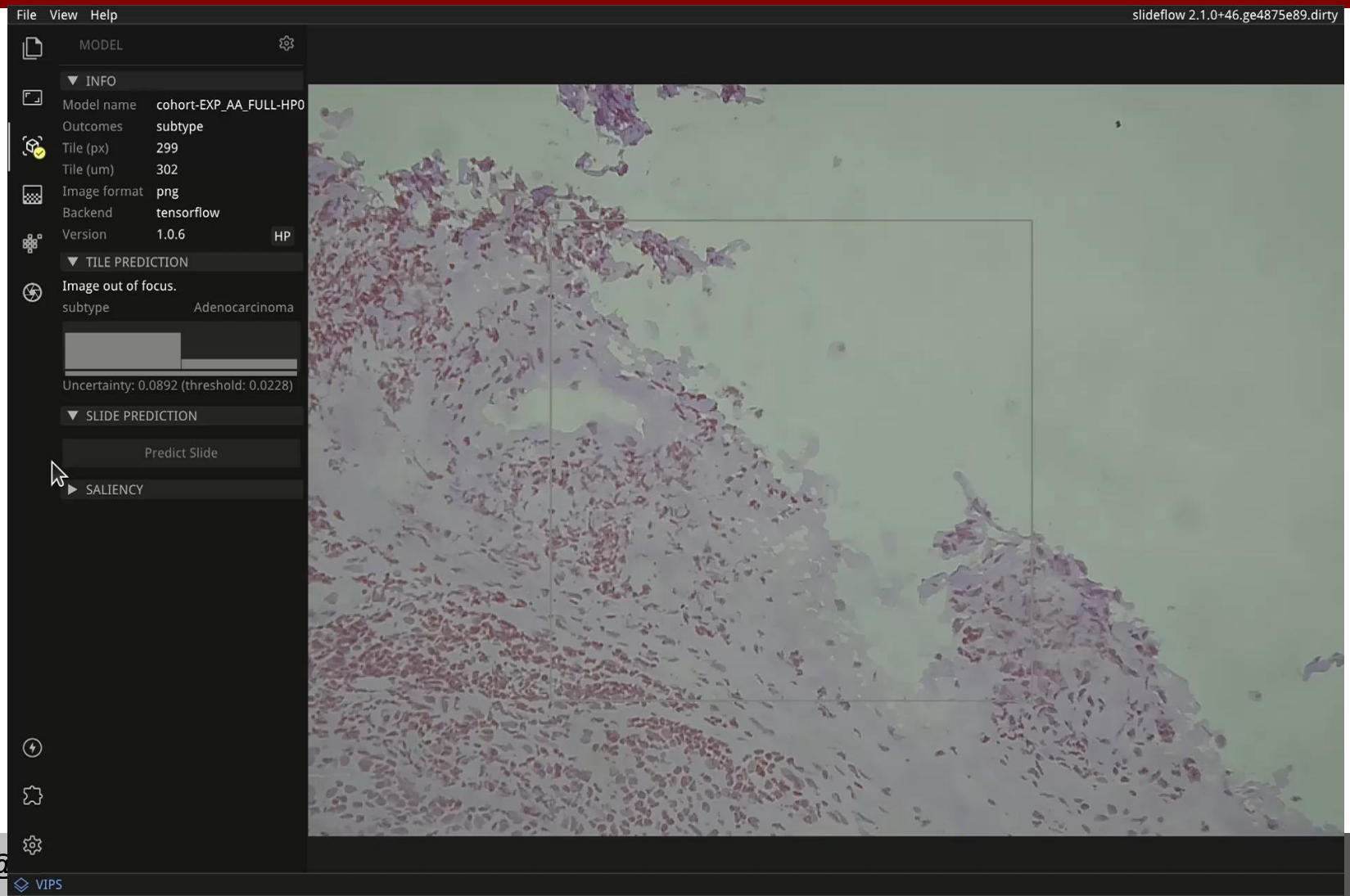
Dolezal et. Al., *npj Precision Oncology* 2023

TRUSTWORTHY DIAGNOSTICS: Excluding Non-Trustworthy Predictions





TRUSTWORTHY DIAGNOSTICS: Uncertainty Quantification in Real Time



LOCALLY-PRODUCED OPEN-SOURCE LOW-COST DEPLOYMENT

HNSCC

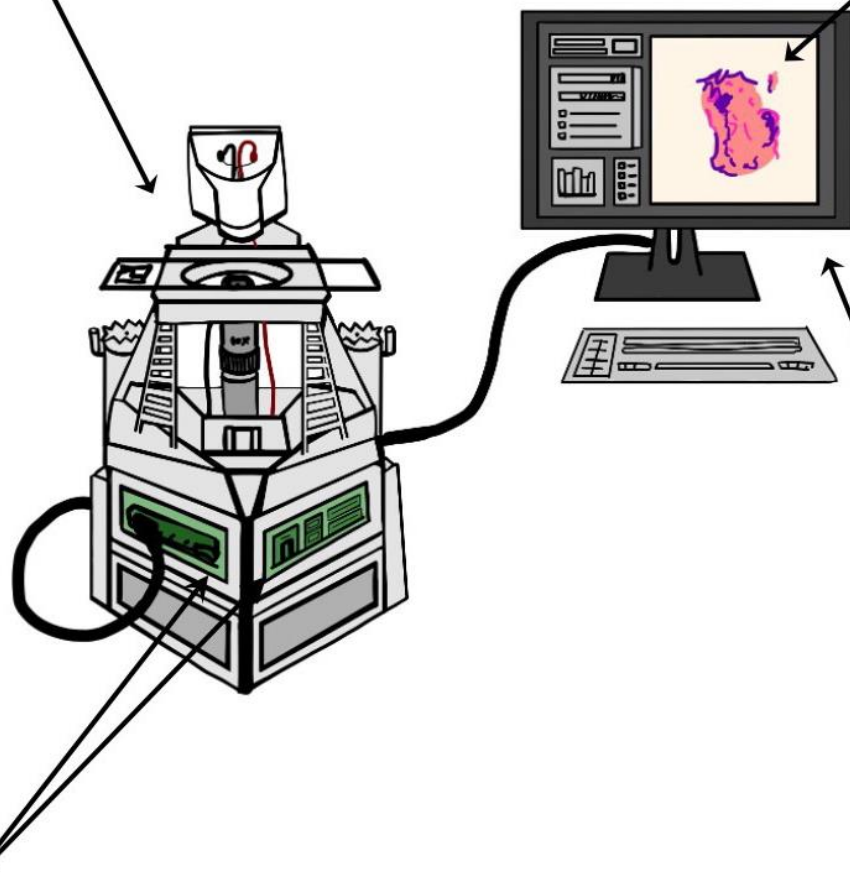
OpenFlexure Microscope
Cost: $100
License: Creative Commons Attribution 4.0 International License (CC BY 4.0)

Raspbian-OpenFlexure OS (OpenFlexure Connect)
Cost: Free
License: GNU General Public License (v3)

Raspberry Pi 4 Model B
Cost: $35
License: Creative Commons Attribution-NoDerivatives 4.0 International (CC BY-ND)

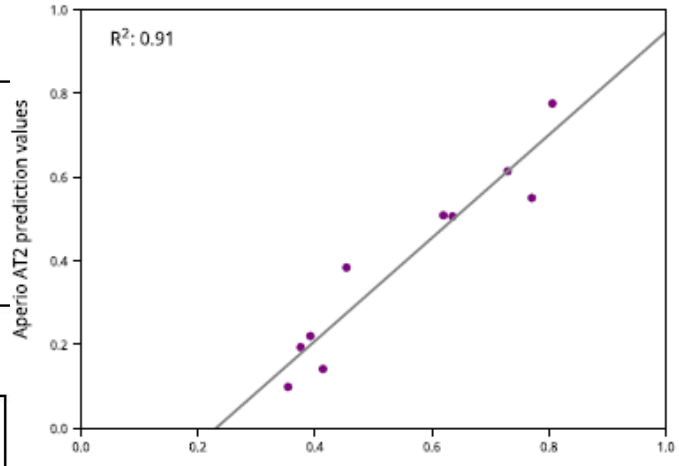
Raspberry Pi Camera Module
Cost: $65
License: Creative Commons Attribution-NoDerivatives 4.0 International (CC BY-ND)

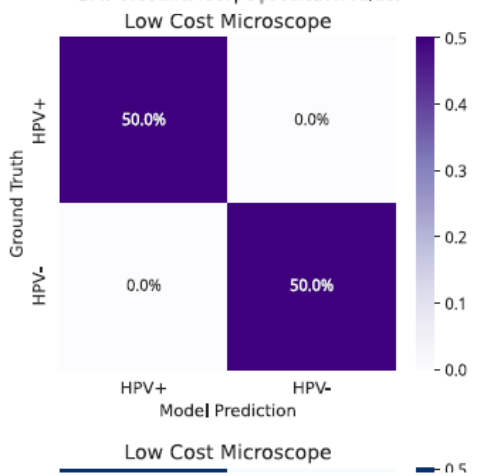
Raspberry Pi OS
Cost: Free
License: The 3-Clause BSD License



Slideflow and Slideflow Studio GUI
Cost: Free
License: GNU General Public License v3.0

Monitor
Monitor connects to OpenFlexure microscope
Cost: <$100
License: Variable





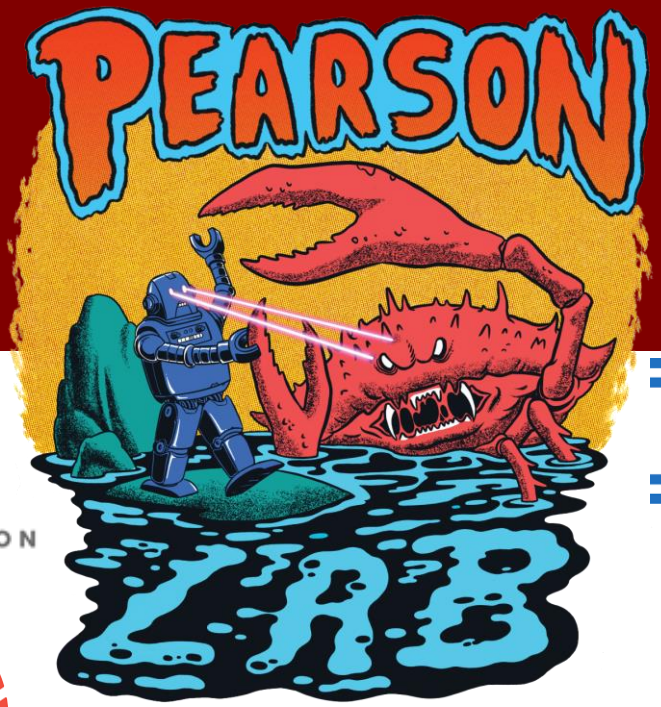
Low Cost Microscope

Choudhury D, *eBioMedicine* 2024

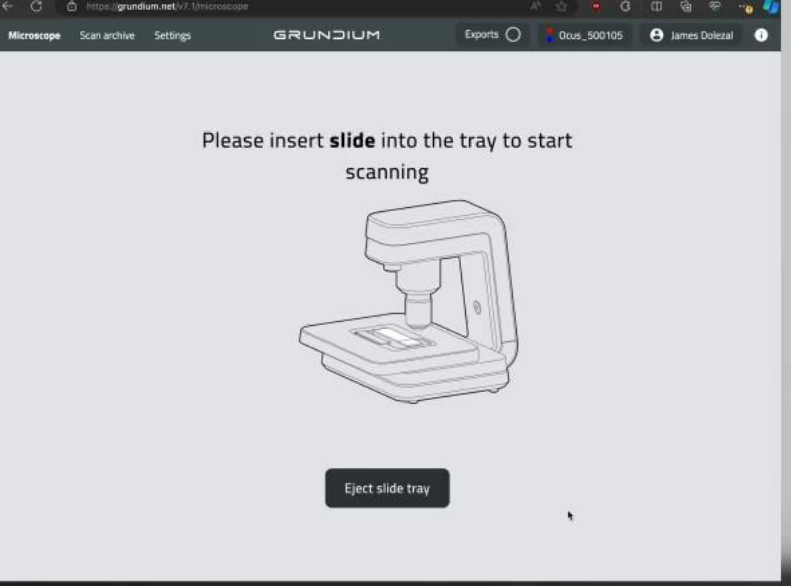
Summary #2

- Physician adoption of AI models may be augmented by improved trustworthiness.
- Algorithmic Explainability and Uncertainty Quantification can improve model transparency and reliability.
- Innovation on the full data acquisition and analysis continua will be required for medical AI to reach its full global potential.

THANKS!



- Sara Kochanny
- Matteo Sacco
- Lilly Li
- Erik Wolf
- Anran Li
- Hanna Hieromnimon
- Sid Ramesh, MD
- Grace Li
- Frank Wen, MD PhD
- Meghan Hutch, PhD
- Emma Dyer
- Dmitry Karpyev, PhD
- Divya Choudhury
- Caroline Montag
- Lawrence He
- Juliana Byanyima



(Near) Real-Time AI Deployment

- Hardware: Grundium
- Software: Grundium API, SlideFlow Studio (OS)
  - Dolezal J, *BMC Bioinformatics* 2024
- Model: Vision Transformer MSI prediction (OS)
  - Wagner SJ, *Cancer Cell* 2023