AI-based Computational Pathology Predicts Origins of Metastatic and Unknown Primary Cancers

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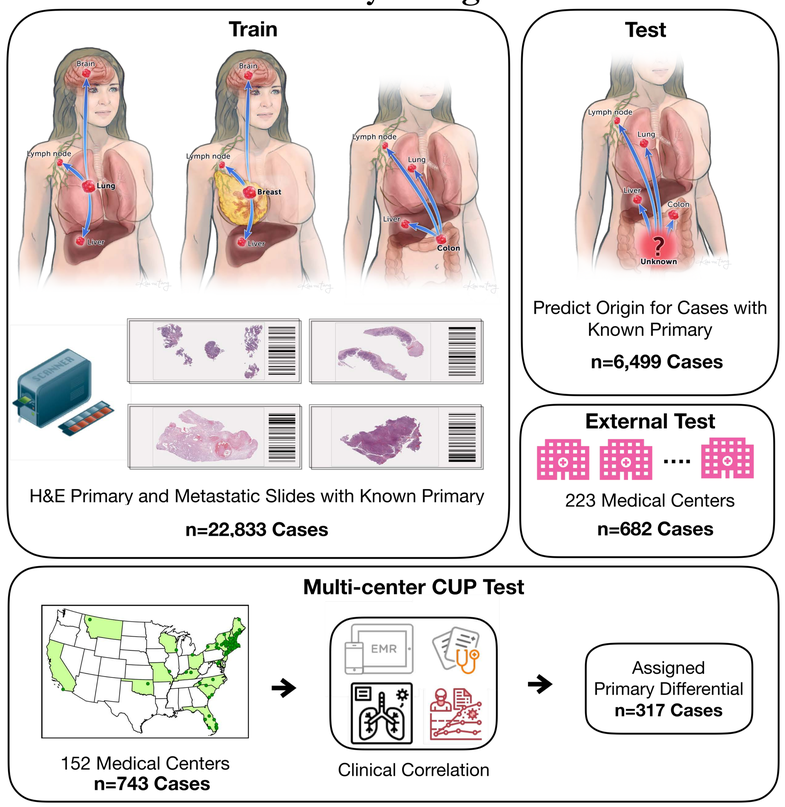
Motivation

- Cancers of Unknown Primary (CUP): an enigmatic group of diagnoses where the primary anatomical site of tumor origin is undetermined
- Median survival 2.7-16 months; patients undergo a complete workup of pathology, clinical, radiological, endoscopy, molecular testing etc. towards determining origin
- Typical workflow is resource intensive, might significantly delay administration of suitable treatment and is not always successful.

Study Design



Evaluation on Tumors of Known Primary

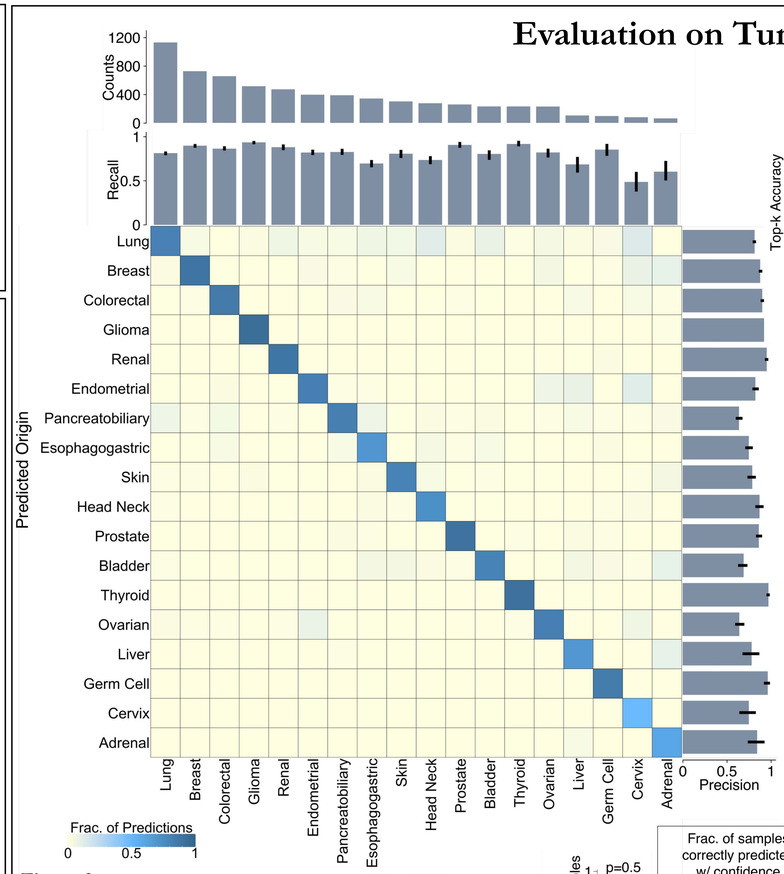
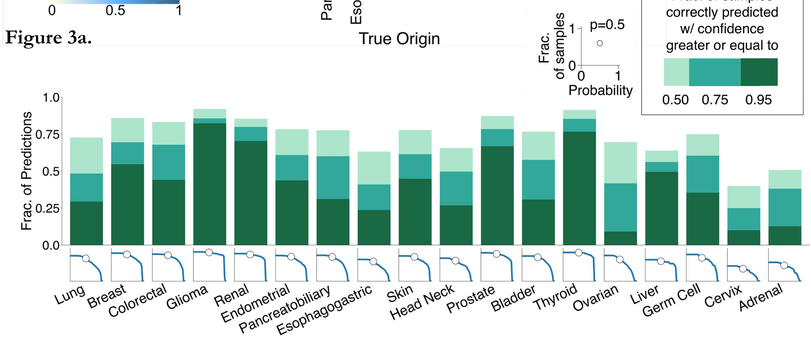
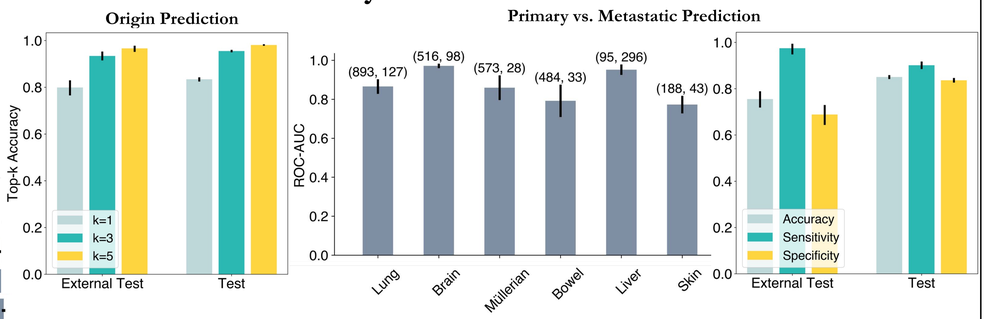
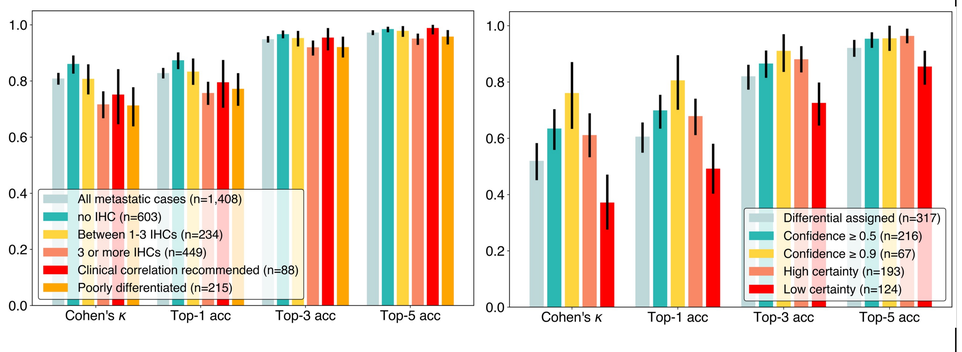


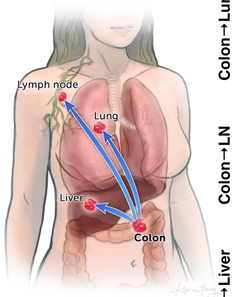
Figure 3a.

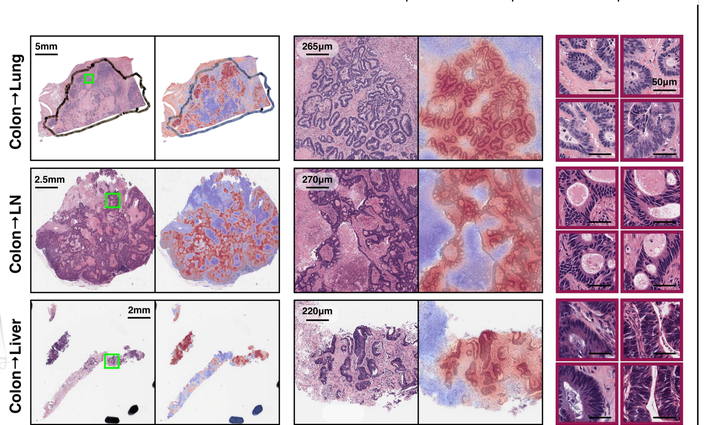




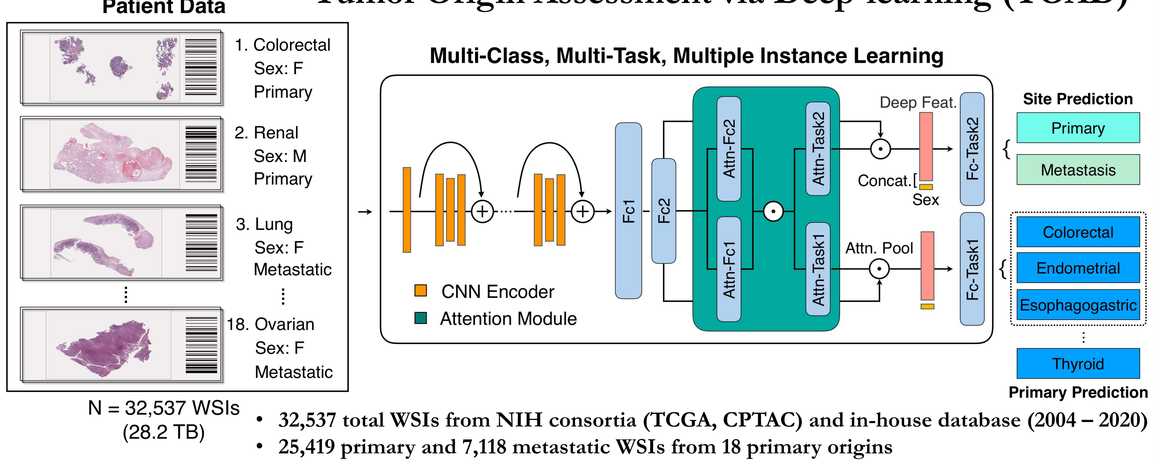
Performance on Metastatic Tumors and CUPs







Tumor Origin Assessment via Deep-learning (TOAD)



- 32,537 total WSIs from NIH consortia (TCGA, CPTAC) and in-house database (2004 – 2020)
- 25,419 primary and 7,118 metastatic WSIs from 18 primary origins

Clinical Utility: Assisting Physicians in Differential Diagnosis

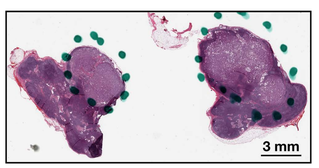
Typical Work-up

Tissue Site: Lymph Node

Gender: ♀ F

IHC demonstrates the following:

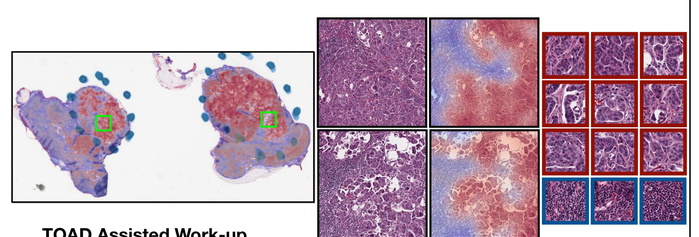
- CK20, ER, TTF1, CDX2, p53 (heterogeneous), WT1, RCC, TTF1, GCDFP, mammoglobin, GATA3 (focal, weak), CD10, p63, HPV DNA ISH
- \+ PAX8 (strong), SMAD4 (intact), CK7, p16, CEA, CK903



Clinical Correlation:

Prior cervical lesion, but current tumor negative for HPV DNA.

Differential includes tumors of müllerian, renal and thyroid origin. Müllerian preferred.



TOAD Assisted Work-up

Top-3 TOAD Differentials

Ovarian	0.718
Breast	0.267
Lung	0.012

IHC demonstrates the following:

- \+ PAX8 — Confirms Müllerian
- \- GATA3, TTF1 — Rules Out Breast, Lung