

Artificial intelligence system may improve diagnosis of complicated metastatic cancers

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To improve diagnosis for patients with complex metastatic cancers, especially those in low-resource settings, researchers from the Mahmood Lab at the Brigham and Women's Hospital developed an artificial intelligence (AI) system that uses routinely acquired histology slides to

accurately find the origins of metastatic tumors while generating a "differential diagnosis," for cancer of unknown primary patients.

In 1 to 2 percent of cancer cases, the primary site of tumor origin cannot be determined. Because many modern cancer therapeutics target primary tumors, the prognosis for a cancer of unknown primary (CUP) is poor, with a median overall survival of 2.7-to-16 months. In order to receive a more specific diagnosis, patients often must undergo extensive diagnostic workups that can include additional laboratory tests, biopsies and endoscopy procedures, which delay treatment. To improve diagnosis for patients with complex metastatic cancers, especially those in [low-resource settings](#), researchers from the Mahmood Lab at the Brigham and Women's Hospital developed an artificial intelligence (AI) system that uses routinely acquired histology slides to accurately find the origins of metastatic tumors while generating a "differential diagnosis," for CUP patients. Research findings are described in *Nature*.

"Almost every patient that has a cancer diagnosis has a histology slide, which has been the diagnostic standard for over a hundred years. Our work provides a way to leverage universally acquired data and the power of [artificial intelligence](#) to improve diagnosis for these complicated cases that typically require extensive diagnostic work-ups," said corresponding author Faisal Mahmood, Ph.D., of the Division of Computational Pathology at the Brigham and an assistant professor at Harvard Medical School.

The deep-learning-based algorithm developed by the researchers, called Tumor Origin Assessment via Deep Learning (TOAD), simultaneously identifies the tumor as primary or metastatic and predicts its site of origin. The researchers trained their model with gigapixel pathology whole-slide images of tumors from over 22,000 cancer cases, and then tested TOAD in about 6,500 cases with known primaries and analyzed increasingly complicated [metastatic cancers](#) to establish utility of the AI

model on CUPs. For tumors with known primary origins, the model correctly identified the cancer 83 percent of the time and listed the diagnosis among its top three predictions 96 percent of the time. The researchers then tested the model on 317 CUP cases for which a differential diagnosis was assigned, finding that TOAD's diagnosis agreed with pathologists' reports 61 percent of the time and top-three agreement in 82 percent of cases.

TOAD's performance was largely comparable to the performance reported by several recent studies that used genomic data to predict [tumor](#) origins. While genomic-based AI offers an alternative option for aiding diagnoses, genomic testing is not always performed for patients, especially in low-resource settings. The researchers hope to continue training their histology-based model with more cases and engage in clinical trials to determine whether it improves diagnostic capabilities and patients' prognoses.

"The top predictions from the model can accelerate [diagnosis](#) and subsequent treatment by reducing the number of ancillary tests that need to be ordered, reducing additional tissue sampling, and the overall time required to diagnose patients, which can be long and stressful," Mahmood said. "Top-three predictions can be used to guide pathologists next steps, and in low-resource settings where pathology expertise may not be available the top prediction could potentially be used to assign a [differential diagnosis](#). This is only the first step in using whole-slide images for AI-assisted [cancer](#) origin prediction, and it's a very exciting area with the potential to standardize and improve the diagnostic process."

More information: AI-based pathology predicts origins for cancers of unknown primary, *Nature*, [DOI: 10.1038/s41586-021-03512-4](https://doi.org/10.1038/s41586-021-03512-4)

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