AI-Based Dx Could Enable Surgeons to Molecularly Classify Brain Tumors in Operating Room

DeepGlioma has shown it can classify brain tumors on the spot during surgery, and experts believe the AI-based imaging system can be useful for informing precision care.

By Catherine Shaffer

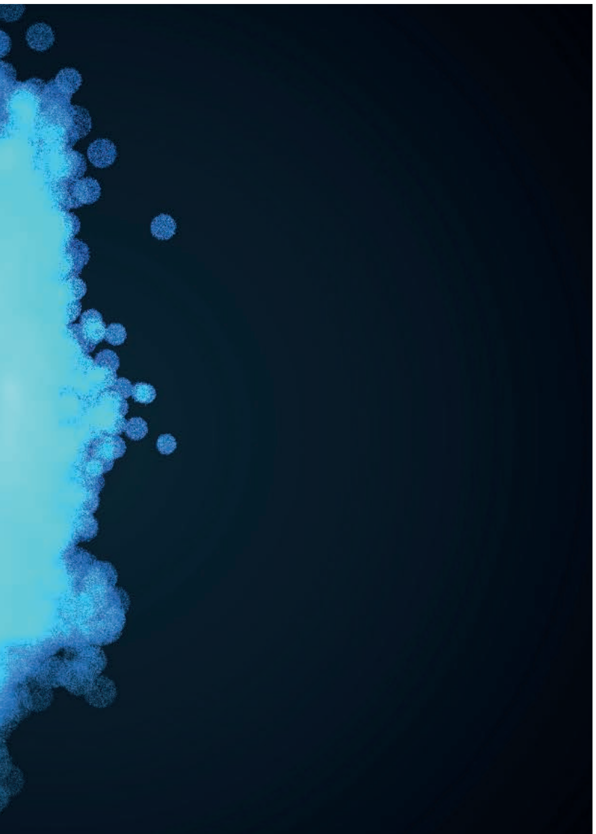
AN INVESTIGATIONAL AI-based diagnostic system has shown promise in molecularly classifying brain tumors from imaging data, providing results in as little as 90 seconds compared to the days or weeks for genetic testing.

According to the World Health Organization's 2021 guidelines, brain tumors should be classified primarily via molecular profiling, relegating histology-based classifications and immunohistochemistry methods to a supporting role. However, not all patients have access to molecular testing, especially outside the US, and even for those who have access, results often aren't available in time to help surgeons make critical decisions in the operating room.

> DeepGlioma may also have uses beyond informing surgical decisions.

"The WHO recognized in making a brain tumor classification scheme that requires molecular testing that this presents a public health problem, because now it mandates that all of these patients should have access to molecular testing," said Todd Hollon, a neurosurgeon at Michigan Medicine and assistant professor of neurosurgery at the University of Michigan Medical School.

Hollon believes AI-based diagnostic technology can fill the gap by predicting underlying molecular genetics based on imaging without access to genetic testing or a pathology laboratory. Moreover, the near-instant results from AI-based analysis can allow surgeons to use molecularly informed diagnostic information in the operating



room to tailor the surgical intervention to the patient's specific tumor type.

Hollon began his career in neurosurgery working with virus-based therapeutics as treatments for brain tumors, particularly in the context of intraoperative delivery during surgery, but his interests shifted as he realized that 21st century diagnostic tools for brain tumors were becoming more quantitative and computational. "I made the decision to convert from being a conventional molecular biologist to being a computational biologist and machine-learning researcher," Hollon said.

He connected with UM neurosurgeon Daniel Orringer, who was working on a technology for imaging brain tumor specimens in the operating room called stimulated Raman histology. Orringer's team was "generating this really good, high-resolution, clinical translational dataset for brain tumors," recalled Hollon.

Working with Orringer and other collaborators from UM, New York University, the University of California, San Francisco, and others, Hollon developed DeepGlioma, an AI-based diagnostic screening system that uses the NIO Laser Imaging System by Invenio to rapidly analyze tumor specimens taken during an operation and generate a molecular classification of the tumor.

Hollon and his colleagues published a study in *Nature Medicine* in March showing that DeepGlioma classified diffuse gliomas of 153 patients who underwent biopsy or surgical resection into molecular subgroups with an average accuracy of over 90 percent.

Using the NIO Laser Imaging System, DeepGlioma captures and analyzes images from a custom microscope slide onto which a patient's freshly excised tumor tissue specimen has been loaded. In about 90 seconds, while a surgeon is removing a tumor from a patient's brain in the operating room, the system produces results about the tumor's molecular classification – a huge advance from standard practice, according to Hollon. "Normally we have our best guess as to what the tumor is likely to be based on the MRI scan and the patient's age and demographics," he said. "But it's not a definitive guess."

> Michigan's Todd Hollon believes his team's recently published study represents the first "serious attempt" to show that AI-based tools can change how doctors diagnose brain tumors.

The uncertainties at the time of surgery include whether the tumor is a primary tumor or a metastasis and whether the tumor type is a glioblastoma, astrocytoma, or oligodendroglioma. Those three types of gliomas require different surgical management. For example, a patient with an astrocytoma, which is defined by certain IDH mutations and a lack of a 1p/19q deletion, will benefit from the maximum possible resection of the tumor that can be done safely.

In contrast, patients with glioblastoma and oligodendroglioma may not benefit from an aggressive resection. For example, if a patient is elderly and has an aggressive glioblastoma that lacks an IDH mutation, the patient is unlikely to gain additional survival benefit from an aggressive resection, which can cause neurologic deficits.

Patients with oligodendrogliomas – tumors that have an IDH mutation with a 1p/q19 deletion – have the best prognosis. They tend to respond well to radiation and chemotherapy and are also less likely to benefit from an aggressive resection.

DeepGlioma may also have uses beyond informing surgical decisions. Certain investigational precision therapies such as oncolytic viruses and gene therapies can be administered during surgery or immediately after, and patients' molecular tumor classifications will be important to deciding which patients should get these drugs, according to Hollon.

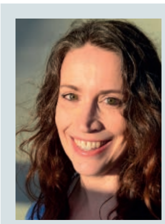
"We're going to need an ability to identify candidates for investigational treatments that require delivery in the artery as soon as possible," he said. "We need to know right away if they meet the inclusion criteria for the study … [DeepGlioma's] effect on trial enrollment will be important."

In developing DeepGlioma, Hollon and his colleagues innovated on the typical computer-based vision methods by using a technique called contrastive learning, which is based on contrasting samples with other samples to find shared and differing attributes between data classes. The technique is optimized using knowledge of the genomic landscapes of gliomas, for example, including which mutations co-occur and which tend to be mutually exclusive.

"The problem is that if you're training neural networks like you normally do, you're not providing any of that information and all the model is doing is looking at an image and trying to produce an accurate prediction," Hollon said. However, DeepGlioma is "adapted in such a way that it's optimally tuned for training with these specific stimulated histology images," he said.

Approximately 15 NIO imagers are in use in the US and Europe, according to Hollon. While the device has been cleared by the US Food and Drug Administration for interoperative microscopy, DeepGlioma is still investigational. Hollon's team is partnered with Invenio, working toward possible FDA approval and commercialization of the test.

He believes his team's recently published study represents the first "serious attempt" to show that AI-based tools can change how doctors diagnose brain tumors. Hollon is optimistic that many more AI-based diagnostic tools will follow DeepGlioma. "Until now, we've been almost exclusively reliant on laboratory tests," he said. "With the tools that are coming out of AI, we're really going to be able to open up clinical medicine and biomedical research to some of these AI-based technologies to improve patient care and improve research, as well." PMQ



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Catherine has been a reporter with *Precision Oncology News* since 2022 where she focuses on the latest advances in genomics and drug discovery as they relate to the development of personalized medicines for cancer. Prior to that, she covered science and biotechnology for a number of other publications, including *Genetic Engineering and Biotechnology News*, *Nature Biotechnology*, and *BioWorld Today*, as well as on-air regional news for NPR affiliate WUOM in her hometown of Ann Arbor, Michigan. Catherine is also an award-winning science fiction author. Her stories have appeared in numerous magazines and anthologies *Analog* and *Nature's Futures*. Catherine has a bachelor's degree in biochemistry from Michigan State University and a master's in biological chemistry from the University of Michigan.