A noninvasive approach may identify glioblastoma patients suitable for antiangiogenic therapy

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Radiomics, an approach that combines imaging and computation, can stratify patients with recurrent glioblastoma into those who are likely to benefit from the antiangiogenic therapy bevacizumab (Avastin) and those who do not, according to a study published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

"Radiomics is a noninvasive approach that applies advanced computational methods to convert medical images of cancerous tissues into a large number of quantitative descriptors encompassing a wealth of hidden information, much more than what is visible when looking at the images with the naked eye," said Philipp Kickingereder, MD, a radiology resident in the Department of Neuroradiology at the University of Heidelberg Medical Center in Germany, who was lead author of this study. "These image features are then subjected to machine-learning and supervised-learning algorithms to create predictive models that may allow patient stratification and aid personalized medicine.

"Our study revealed that radiomic features subjected to machine-learning algorithms identified imaging signatures that defined a subset of patients with recurrent glioblastoma who may gain the most benefit from antiangiogenic therapy," Kickingereder said. "This stresses the role of radiomics as a novel tool for improving decision-support in cancer treatment at low cost and provides a direction for further research on radiomics of glioblastoma."

Angiogenesis, a process of blood vessel development that promotes tumor growth and malignant transformation, is a pathological hallmark of glioblastoma, and has therefore been considered a priority therapeutic target, Kickingereder said. Initial phase II studies in patients with recurrent glioblastoma treated with the antiangiogenic drug bevacizumab showed promising results; however, later studies failed to demonstrate an overall survival benefit, and recent studies showed that only patients who have tumors with distinct molecular subtypes may benefit from bevacizumab treatment, he added.

Glioblastoma is the most common and most aggressive primary brain tumor. Prognosis of this disease remains dismal despite aggressive therapy, with median overall survival rates of less than 1.5 years, said Martin Bendszus, MD, a professor of neuroradiology at University of Heidelberg Medical Center, and one of the study's senior authors. Bevacizumab is an FDA-approved therapeutic for this disease. The researchers investigated whether radiomics can help identify an imaging signature to stratify and predict the outcome of patients with recurrent glioblastoma receiving bevacizumab.

The team analyzed radiographic images from 172 patients using a high throughput approach to automatically extract and calculate nearly 5,000 quantitative magnetic resonance imaging (MRI) features for each patient that included information on the shape, intensity, and texture of the tumor.

Patients were divided into a discovery set and a validation set (2:1) with matching clinical and survival characteristics. They then performed a supervised principal component (superpc) analysis to stratify patients in the discovery set based on treatment outcomes [progression-free survival (PFS) and overall survival (OS)] and validated those findings in the validation set. PFS and OS were measured from the time of treatment with bevacizumab until disease progression and death or last follow-up.

The superpc analysis identified 72 radiomic features that were most important in predicting outcomes, and divided the patients in the discovery set who received bevacizumab into two groups: those in the low-risk group had a median PFS and median OS of 5.9 and 11.8 months, respectively; those in the high-risk group had a PFS and OS of 3.8 and 6.5 months, respectively.

The utility of the superpc analysis was confirmed in the validation set, where patients allocated to the low-risk group had a median PFS and median OS of 5.6 and 11.6 months, respectively; those in the high-risk group had a PFS and OS of 2.7 and 6.5 months, respectively. Patients with unfavorable radiomic signature (high-risk group) were 1.85 times more likely to have tumor progression and 2.6 times more likely to have died during bevacizumab treatment.

"Radiologic examinations are noninvasive and arbitrarily repeatable, which is of advantage compared to invasive biopsy required for molecular or histological analysis," Kickingereder noted. "Sophisticated imaging analysis may in the future provide valuable complementary information to histological and molecular data." The team is conducting further studies with the inclusion of a control arm to clarify the value of the radiomic signature as a truly predictive imaging biomarker.

A limitation of this study is that the results need to be validated in large multicenter studies to confirm the independence of the identified signature from different clinical protocols, Kickingereder noted.

More information: Large-scale Radiomic Profiling of Recurrent Glioblastoma Identifies an Imaging Predictor for Stratifying Anti-Angiogenic Treatment Response. DOI: 10.1158/1078-0432.CCR-16-0702