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Prediction of Glioblastoma Multiforme (GBM) Patient Survival Using MRI Image Features and Gene Expression

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Abstract:
PURPOSE
Glioblastoma multiforme has an extremely poor prognosis. The ability to predict patient survival after initial diagnosis could play an important role in choosing among treatment options. We used linear regression models incorporating MRI image features and tumor gene expression to predict patient survival.
MATERIALS & METHODS
The study is part of The Cancer Genome Atlas (TCGA) MRI characterization project of the National Cancer Institute. MRI images for 70 GBM patients made available through the National Biomedical Imaging Archive were reviewed independently by six neuroradiologists. The VASARI feature scoring system for human gliomas, developed at Thomas Jefferson University Hospital, was employed. 24 imaging features were scored. Patient tumor gene expression was from Verhaak et al. (*Cancer Cell* **17:** 98). A set of 620 genes associated with angiogenesis, a process critical for tumor growth, were used in this investigation. Survival times after diagnosis were obtained from the TCGA website. Median survival was 362 days. For statistical analyses, survival was recoded as a binary categorical variable: survival less than or greater than 1 year. Feature F1 (tumor location) was likewise subdivided into five features corresponding to specific brain regions.
Associations between imaging features and survival were assessed using linear regression models. Survival was the outcome; imaging features were the predictors.
RESULTS
Individually, 6 MRI features show association to survival with an unadjusted p-value < 0.05. Ependymal extension (F19), longest dimension of lesion size (F29), deep white matter invasion (F21) and the presence of satellites (F24) negatively correlate with survival.

Location of the tumor in the right (usually non-dominant) hemisphere (F2) is associated with better outcome. Patients with frontal lobe tumors (feature F1a) tend to survive longer than individuals with tumors elsewhere in the brain. Features best associated with survival are ependymal extension (P = 0.0012) and location in the frontal lobe (P = 0.0098).
An optimized multivariate linear regression model constructed by the stepwise addition and subtraction of features has F19, F29, F1a, F21 and F2 as predictors. This model has better accuracy (76.8% rate of correct predictions) and sensitivity (identification of 72.4% of patients with survival greater than 1 year) than any model based on a single feature.
We also examined linear regression models incorporating the most significant VASARI feature, F19, and expression of angiogenesis-related genes. A model based on ependymal extension, CCL5, ANG, TGFB2 and TNF correctly predicts survival for 82% of patients. Expression of ANG (angiogenin) and TGFB2 (TGF-beta 2) negatively correlate with survival, while CCL5 (chemokine (C-C motif) ligand 5) and TNF (tumor necrosis factor) positively correlate with survival.
CONCLUSIONS
A subset of VASARI imaging features correlate well with patient survival. Linear regression models incorporating multiple imaging features or a single VASARI feature (ependymal extension) and tumor gene expression can be used to predict patient survival. We are refining these models and are investigating whether including patient clinical characteristics into linear models can improve their predictive power.

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