Prediction of Glioblastoma Multiforme (GBM) Patient Time to Recurrence 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 time to recurrence 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 time to recurrence.

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.

Associations between imaging features and time to recurrence were assessed using linear regression models. Time to recurrence was the outcome; imaging features were the predictors. Linear regression models were constructed with imaging features and the expression of angiogenesis-related genes.

RESULTS
Times to recurrence values after diagnosis were obtained for 15 patients. Median time to recurrence was 263 days. Individually, two MRI features show association to time to tumor recurrence with an unadjusted p-value < 0.05. Localization of the tumor to the left hemisphere correlated positively with time to recurrence ($P = 0.0084$); the presence of ependymal extension correlated negatively with time to recurrence ($P = 0.0445$).

The optimal model constructed by the stepwise addition and subtraction of variables has the MRI feature for localization to the left or right hemisphere and the expression of the STAT1, ARHGAP24 and SSTR2 genes. Predicted time to tumor recurrence based on the model show a Pearson correlation of 0.972 ($P = 1.42e{-}09$) with observed times to recurrence. In contrast, tumor localization to the left hemisphere alone shows a correlation of 0.652 ($P = 8.43e{-}03$) with time to recurrence.

CONCLUSIONS:
A subset of VASARI imaging features correlate well with patient time to recurrence. Linear regression models incorporating multiple imaging features or a single VASARI feature and tumor gene expression can be used to predict patient time to recurrence. We are refining these models and are investigating whether including patient clinical characteristics into linear models can

improve their predictive power.