TITLE:
AI-based Prognostic Stratification of Glioblastoma using Hematoxylin & Eosin-Stained Whole Slide Images

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BACKGROUND:
Glioblastoma is the most common and aggressive malignant adult brain tumor, with median overall survival (OS) of 14 months. Despite optimizations in the treatment regime and technological advancements, patient OS has remained unchanged for the last 20 years. Here we seek the prognostic stratification of glioblastoma patients, by virtue of distinct morphological patterns apparent in histopathology Hematoxylin & Eosin (H&E)-stained whole slide images (WSI) alone.

METHODS:
We selected 271 (n_{training}/n_{hold-out-test}= 216/55) frozen digitized tissue sections, at 10x magnification, of untreated primary glioblastoma (IDH-wildtype) adult cases from the TCGA-GBM collection, without history of previous glioma and with post-operative OS > 30 days. The median OS across cases was used to divide them into short- (< 324 days) and long- (> 390 days) survivors, after excluding 5 percentiles of cases around this median. Each WSI was partitioned in non-overlapping 256x256 patches. A pre-trained VGG16 AI model automatically extracted a 512-dimensional feature vector from each patch. Dimensionality was reduced, from 512 to 8, using principal component analysis, and distinct groups of morphological patterns were identified with unsupervised clustering. The number of distinct groups was decided based on the silhouette coefficient, assessing goodness of clustering. The proportions of these patterns within each WSI, describing the tumor’s spatial heterogeneity, were used to distinguish between short- and long-survivors using gradient boosting.

RESULTS:
We identified morphological patterns of 5 distinct groups, descriptive of cellularity differences as well as artifactual content. Quantification of these patterns’ proportions resulted in a classification accuracy of 72.72% (short- vs long-survivors).

CONCLUSIONS:
We identified morphologic patterns within a WSI, associated with shorter and longer OS. These may allow the clinical neuropathologist to i) provide additional prognostic information gleaned during microscopic assessment to the treating team, and ii) suggest avenues for further biological investigations towards contributing to our mechanistic understanding and potentially treating of glioblastoma.