

---

ABSTRACT 2

Associations Between MR Imaging and Genomic Features of Glioblastomas

Authors:

Scott N Hwang

Chad A Holder

Erich Huang

Bob Clifford

Dima Hammoud

Prashant Raghavan

Manal Jilwan

Max Wintermark

David A Gutman

Lee Cooper

Carlos Moreno

Justin Kirby

John Freymann

Seena Dehkharghani

Arun Krishnan

Carl Jaffe

Adam Flanders

Joel H Saltz

Daniel J Brat

## 1. Purpose

To identify imaging features of primary glioblastomas that may predict genomic features, including mutation status, gene expression, and DNA copy number variations.

## 2. Materials & Methods

MR images of 75 glioblastoma patients from The Cancer Genome Atlas (TCGA) of the National Cancer Institute (NCI) were each independently reviewed by at least 3 individuals from a panel of 6 neuroradiologists. Images were evaluated according to 26 imaging features (VASARI feature set, <https://wiki.nci.nih.gov/display/CIP/VASARI>). Multi-reader assessment of each tumor was reduced to a single score for each feature.

Genomic data for the tumors were obtained from TCGA's publicly available information (TCGA, Nature 455:1061, 2008), including mutation status (presence versus absence of a gene mutation) for the TP53, PTEN, EGFR, NF1, and IDH1 genes. On the basis of copy number data, subgroups were identified, including tumors with high-level EGFR gene amplification, with high-level PDGFRA amplification, with homozygous deletions of CDKN2A, and with deletions of NF1. Quantitative measurements of gene expression for TP53, PTEN, EGFR, NF1, IDH1, and TGFB2 were also obtained.

Applied statistical tests included Fisher's exact test, Student's t-test, and linear correlation.

## 3. Results

Compared to all the other tumors, TP53 mutant tumors had a decreased mean tumor size ( $p=0.002$ ), measured as the maximum tumor dimension in the T2-weighted or FLAIR images. A suggestion that EGFR mutation may be associated with larger tumor size was identified ( $p=0.08$ ). However, a comparison of tumors with the TP53 mutation versus tumors with the EGFR mutation demonstrated EGFR mutant tumors were significantly larger than TP53 mutant tumors ( $p=0.0005$ ). Enhancing pial involvement was also found to be more probable for EGFR mutant tumors ( $p=0.05$ ).

Fisher's exact test demonstrates an association between enhancing tumor (>5% proportion) and high-level EGFR amplification ( $p=0.01$ ). The presence of enhancing pial involvement was associated with high-level EGFR amplification ( $p=0.02$ ). There was a suggestion that having a >5% proportion of necrosis may be associated with high-level EGFR amplification ( $p=0.06$ ). Fisher's exact test demonstrated an association between the presence of CDKN2A homozygous deletion and the identification of an ill-defined nonenhancing tumor margin ( $p=0.007$ ). The presence of enhancing pial involvement was also associated with the

presence of a CDKN2A homozygous deletion ( $p=0.03$ ). No significant associations with PDGRFA amplification or NF1 deletions were identified. There were suggestions NF1 deletion was associated with the presence of edema ( $>5\%$  proportion) ( $p=0.06$ ) and with the presence of nonenhancing tumor ( $>5\%$  proportion) ( $p=0.06$ ).

A negative correlation between tumor size and IDH1 expression ( $r=0.33$ ,  $p=0.006$ ), and a positive correlation between tumor size (largest dimension on the basis of T2-weighted and/or FLAIR images) and EGFR expression ( $r=0.30$ ,  $p=0.02$ ) were statistically significant. Student's t-test demonstrated the mean IDH1 expression in tumors without a significant proportion of enhancement ( $\leq 5\%$  of the tumor volume) was less than the mean in tumors with  $>5\%$  enhancement ( $p=0.049$ ). No other statistically significant associations were found.

#### 4. Conclusion

Multiple statistically significant associations between imaging and genomic features in glioblastomas were identified. In particular, EGFR mutant tumors were significantly larger than TP53 mutant tumors, and were more likely to demonstrate pial involvement. CDKN2A homozygous deletion was associated with an ill-defined nonenhancing tumor margin and enhancing pial involvement.