Tue Nov 29 2011 11:00AM - 11:10AM ROOM E451B

10) Radiogenomic Mapping in GBM: A Novel Quantitative Merge between Imaging and Genomics — The Creation of a Signature for Tumor Necrosis Using Image Genomic Analysis in 12, 764 genes and 555 microRNAs

R R Colen, MD, Boston, MA; P O Zinn, MD; J R Bruyere, BS,MA; B Mahajan, MBBS; F A Jolesz, MD (rrcolen@partners.org)

PURPOSE

To create a radiogenomic map, linking MR imaging traits with gene- and miRNA expression profiles, in patients with GBM to determine genomic correlates of necrosis to identify relevant MRI biomarkers and to find new genomic targets for GBM treatment. The introduction of gene microarrays, a method allowing for analysis of thousands of genes, has resulted in a greater insight into gliomagenesis, treatment response, and patient prognosis. However, specialized and invasive tissue sampling remains a limitation and bottleneck for its widespread use in the standard clinical realm. Here, we present the first study examining in a quantitative way radiogenomics in GBM to determine novel and targetable molecular necrosis correlates in GBM.

METHOD AND MATERIALS

We retrospectively identified 82 treatment naïve GBM patients from The Cancer Genome Atlas (TCGA) who had genetic- expression profiles and pre-treatment MR imaging. Image analysis was done on slicer 3.6 (slicer.org) and reviewed blindly-in consensus by 2 neuroradiologists. The post-contrast T1WI was used to quantitate necrosis volumes. Biostatistics analysis was performed for gene and miRNA sets where as the median necrosis volume was taken as the cutoff to define high and low groups. These groups were then analyzed by Comparative Marker Selection (Broad Inst.). A total of 12,764 genes and 555 microRNAs were analyzed. Among the whole gene set the most upregulated mRNAs/miRNAs (N=100), were analyzed with ingenuity pathway analysis (IPA).

RESULTS

IPA identified molecular networks, as well as canonical and functional pathways highly associated with cancer, cell death, cell cycle, and apoptosis in those patients with high necrosis.

CONCLUSION

The necrosis radiophenotype identified genes and miRNAs and corresponding molecular networks that were highly associated with cell death and apoptosis. By these means we were able to identify possible key genes and miRNAs involved in cell cycle regulation and cell death. The uncovered genes and miRNAs represent new insight into necrosis as seen on MRI and an underlying possible molecular mechanisms of GBM aggressiveness and novel therapeutic approaches.

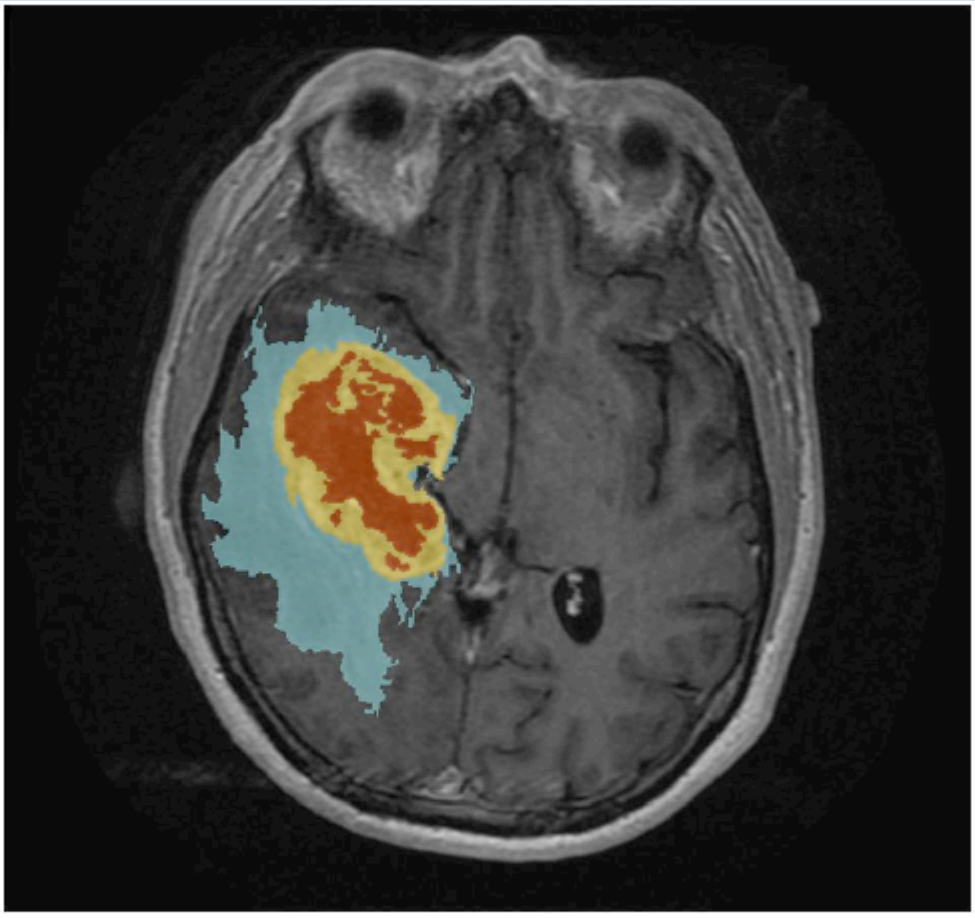
CLINICAL RELEVANCE/APPLICATION

Necrosis imaging biomarkers reflecting a specific molecular cancer composition will augment the predictive power for tumor aggressiveness and therapy response and identify novel targets GBM therapy.

FIGURE (OPTIONAL)

Uploaded Image

View Larger Image



Tumor Segmentation. 65 year old male patient with a right temporal GBM. Segmentation of tumor edema (blue), enhancement (yellow) and necrosis (red) was performed and the volume of necrosis was obtained.