Magnetic resonance imaging-genomic mapping reveals gender-specific molecular determinants of necrosis in GBM

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Introduction

Despite recent discoveries of new molecular targets and pathways, the search for an effective therapy for Glioblastoma Multiforme (GBM) continues. A newly emerged field, radiogenomics, links gene expression profiles with MRI phenotypes. MR T1 post-contrast imaging can evaluate the active versus the necrotic parts of the entire tumor. Cell death in GBM can either be associated with tumor suppressor or oncogenes, since increased cell death can be caused by an aggressive cellular growth (lack of oxygen/nutrients) or by the presence of tumor suppressor genes inducing apoptosis. Thus, an imaging genomic necrosis screen has the potential to uncover novel molecular determinants of cell death in GBMs. Here, we present the first comprehensive radiogenomic analysis using quantitative necrosis MRI volumetrics and large-scale gene- and microRNA expression profiling in GBM.

Methods

Based on The Cancer Genome Atlas (TCGA) and The Cancer Imaging Archive (TCIA) gene, microRNA, and quantitative MR-imaging data sets were created based on a total of 78 patients. Top concordant genes and microRNAs correlated with high Necrosis volumes were further analyzed using Ingenuity Pathway Analysis and cognate microRNA-gene networks were created.

Learning Objectives

1) Necrosis in GBM: Friend or Foe?

2) Necrosis in GBM: Gender bias!

3) Necrosis in GBM: Survival and molecular determinants - men versus women!

Results

Female patients demonstrated significantly lower volumes of necrosis than male patients. Thus, a gender specific analysis was chosen and revealed that female patients with high necrosis had a significantly shorter survival compared to both females with lower necrosis or males with high necrosis, while survival in males was similar in patients with high versus low tumor necrosis. The genomic analysis revealed that predominantly oncogenic pathways (MYC) were associated with necrosis in female patients, while male patients showed a strong association with tumor suppressor pathways (TP53), while gender independent necrosis pathways showed equal distribution of both tumor suppressors and oncogenes.

Conclusions

Here, we propose a novel diagnostic method to screen for molecular correlates of necrosis in GBM. Interestingly, our findings also have potential therapeutic significance since the understanding of cell death molecular gene and microRNA signatures can improve therapy and patient survival in GBM.

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