PURPOSE: To create an imaging genomic map, linking MR imaging traits with gene and miRNA expression profiles, in GBM patients to determine genomic correlates of diffusion radiophenotype to find new genomic targets. Decreases in diffusion in GBM is associated with increased cellular density and higher nuclear to cytoplasm ratio. Here, we present the first study examining in a quantitative way MRI-diffusion genomics in GBM to determine targetable genomic biomarkers in GBM.

MATERIALS AND METHODS: We identified 80 treatment-naive GBM patients from The Cancer Genome Atlas (TCGA) who had both gene and miRNA expression profiles and pretreatment MR-neuroimaging specifically ADC maps. Image segmentation analysis was done in Slicer 3.6 using segmentation module, Fluid-Attenuated Inversion Recovery (FLAIR) was used for segmentation of the edema and post-contrast T1 weighted-imaging (T1WI) for segmentation of enhancement and necrosis. Diffusion was analyzed in Olea Sphere 2.3 and Conventional FLAIR/post contrast T1WI was registered to DWI/ADC maps. ADC, FLAIR, T1 Gadolinium enhancement values were measured using the ROI based method in the peri-tumoral edema/non-enhancing tumor and the enhancing tumor zones, dividing the peri-tumoral edema/non-enhancing tumor into 3 zones each of 1 cm width, 3 ROI measurements were taken from each zone. Multiple quantitative imaging features were identified and combined to create the imaging biomarker signature predictive for the invasion and poor prognosis of the tumor. All the genomic data was also analyzed to determine the most upregulated mRNAs/miRNAs using Ingenuity pathway analysis (IPA) in those with restricted diffusion.

RESULTS: Quantitative ADC values were in high correlation with biologically concordant functional genomic targets predicting the invasiveness and progression. CONCLUSIONS: The diffusion and conventional MR radiophenotype identified genes and miRNAs and corresponding molecular networks that were highly associated with tumor invasion. By these means we were able to identify possible key genes and miRNAs involved in the latter regulation.