Predicting Ki67 and Cellular Density via MR images as a prognostic indicator

Emily Blitz[1], Adrian Celaya[2], Dawid Schellingerhout[3] MBChB BSc, David T. Fuentes[2] Ph.D.

University of Arkansas[1], Fort Smith, AR
Department of Imaging Physics, The University of Texas MD Anderson Cancer Center[2], Houston, TX
Department of Neuroradiology, The University of Texas MD Anderson Cancer Center[3], Houston, TX

Background

Ki67 is present at all proliferative phases of the cell cycle[1], thus making it a useful indicator of cellular division. The ability to measure Ki67 expression to determine the rate of cellular division allows it to be used as a prognostic tool in some tumors[2,10] and previous studies have linked higher Ki67 expression to higher tumor grade[3]. Traditionally, the Ki67 index is measured through staining and manual counting of positively stained tumor cells, a method that requires biopsy/resection of tumor tissue[4]. This study looks at the potential for using medical imaging to predict Ki67 index and cellular density as well as correlating the results with other common prognostic tools such as IDH mutation status, chromosomal 1p/19q codeletion status, and WHO grade.

Hypothesis

Higher predictions of Ki67 index should positively correlate with IDH WT status, normal 1p/19q chromosome, and higher WHO grade.

This correlation can be made through MRIs using image processing, allowing us to provide doctors with more information about a patient's tumor prior to performing surgery.

Methods

MR Images

Obtained MR Images of 46 patients from Erasmus Glioma Database (EGD)[5]. Each patient had 4 structural MRIs plus a tumor mask provided in the dataset. IDH mutation status, 1p/19q codeletion status, and WHO grade was provided when known.

Image processing

Skull stripped > registered > normalized > Ki67 and CD predicted via random forest regression

Analysis

Predicted Ki67 intensity and Cellular Density for each patient were analyzed for descriptive statistics via Matlab. Data presented is for values that lied within the tumor mask provided by EGD. Some tumor masks were manually segmented via SimpleITK v3.6.0 [12] or BrainLab. Others were automatically segmented using all four registered, structural MRIs available and a CNN.

Results

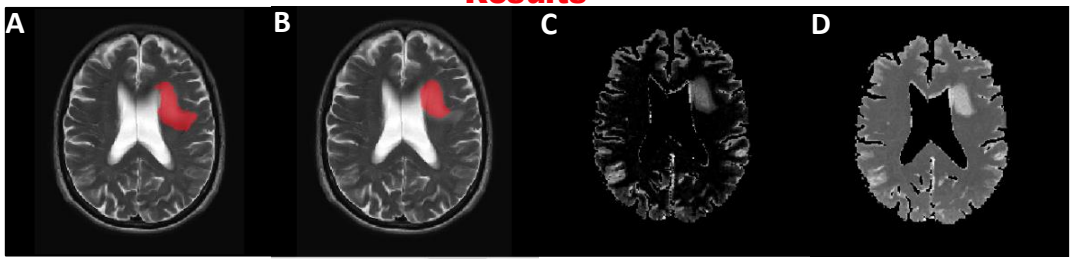

Image 1: ITKSnap Images of **A)** FLAIR Image with overlaid tumor mask as provided by EGD, **B)** FLAIR image with overlaid tumor mask as generated by docker, **C)** Intensity map of predicted Ki67 intensities, and **D)** Map of predicted cellular density

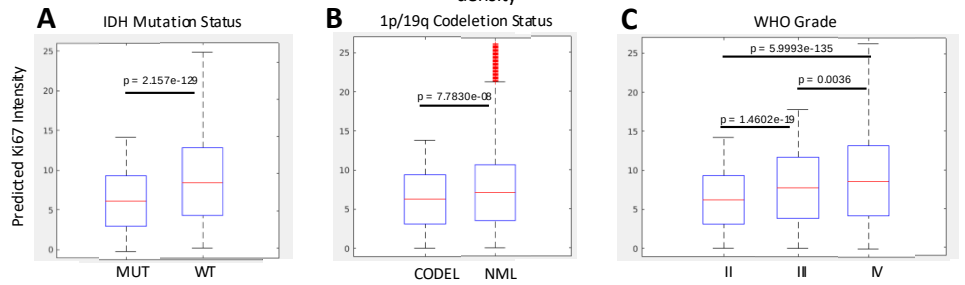

Fig 1: Ki67 intensity vs **A)** IDH mutation status(med_{MUT} = 5.95, $mode_{MUT}$ = 0.3, avg_{MUT} = 6.072)(med_{WT} = 8.275, $mode_{WT}$ = 0.6, avg_{WT} = 8.927), **B)** 1p/19q chromosome codeletion status(med_{CODEL} = 6.39, $mode_{CODEL}$ = 0.15, avg_{CODEL} = 6.437)(med_{NML} = 6.76, $mode_{NML}$ = 0.20, avg_{NML} = 7.478), and **C)** WHO grade (med_{II} = 5.91, $mode_{II}$ = 0.3, avg_{II} = 6.025) (med_{III} = 7.80, $mode_{III}$ = 0.05, avg_{III} = 7.970) (med_{IV} = 8.20, $mode_{IV}$ = 0.6, avg_{IV} = 8.792)

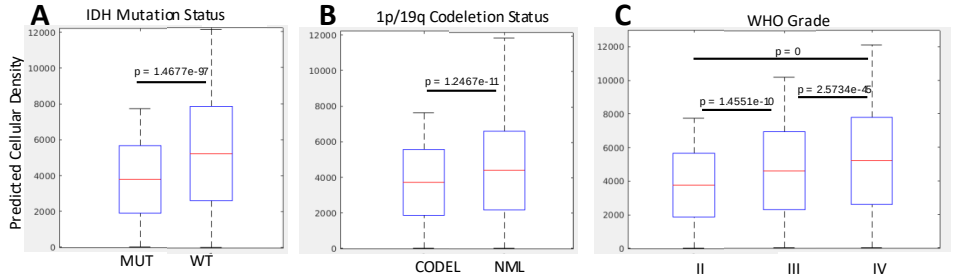

Fig 2: Cellular Density vs **A)** IDH mutation status(med_{MUT} = 3800, $mode_{MUT}$ = 300, avg_{MUT} = 3798)(med_{WT} = 5240, $mode_{WT}$ = 300, avg_{WT} = 5302), **B)** 1p/19q chromosome codeletion status(med_{CODEL} = 3755, $mode_{CODEL}$ = 300, avg_{CODEL} = 3762)(med_{NML} = 4445, $mode_{NML}$ = 300, avg_{NML} = 4584), and **C)** WHO grade (med_{II} = 3800, $mode_{II}$ = 300, avg_{II} = 3795) (med_{III} = 4620, $mode_{III}$ = 150, avg_{III} = 4727) (med_{IV} = 6650, $mode_{IV}$ = 2550, avg_{IV} = 6692)

Conclusions

It has been shown previously that IDH WT status, normal chromosomal 1p/19q status, and higher WHO grading all are linked to poorer prognoses for patients. It is unsurprising that we see a positive correlation between these prognostic indicators and higher Ki67/higher cellular density values within the tumor. These links support further research in this field of radiomics in hopes to provide surgeons with more detail on a patient's tumor in order to perform safer, more effective biopsies/surgeries.

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Acknowledgements: This presentation is supported by the National Cancer Institute through the U54 CA096297/CA096300: UPR/MDACC Partnership for Excellence in Cancer Research Training Program. For further information, please contact Emily Blitz at emilyblitz197@gmail.com.