Necrosis, Non-Enhancing, and Enhancing Tumor Features of Glioblastoma Tissue for Prediction of Overall Survival and Progression Free Survival

Abstract

Glioblastoma multiforme is an aggressive brain cancer. Only five percent of diagnosed patients live for longer than five years, with patients having an overall survival of only 14.2 months. The Stupp Protocol is the care standard used to treat glioblastoma, and it involves total resection of the tumor, chemotherapy, and radiation. The power of this protocol would be enhanced if we had a more accurate method of measuring the aggressiveness of the cancer. We can develop a more precise technique of measuring this aggressiveness by assessing a patient's predicted overall survival and progression-free survival. Linking these measurements to features of the cancer that can be measured by magnetic resonance imaging (MRI) would allow physicians to estimate prognosis according to glioblastoma's characteristics. This estimation would enable physicians to customize chemotherapy, providing for a better chance of survival as well as reduced side effects that could be caused by overtreatment. We wish to examine novel textural features of necrosis, non-enhancing, and enhancing tumor to evaluate their use as clinical outcome predictors. Using a dataset from the TCGA-GBM collection, We used T1-weighted contrast-enhanced MRI scans for a total of 212 patients. Algorithms were used to create segmentations for various heterogeneous histologic sub-regions, namely the necrosis, non-enhancing, and enhancing tumor. Clinical radiologists verified these segmentations. Textural readouts created using LifeX software for radiometric feature calculation in multimodality imaging were analyzed using a Receiver Operating Characteristic curve (ROC) and Kaplan-Meier analysis. Significant differences between diagnostic groups created by each

textural parameter were found for the histologic sub-regions necrosis, non-enhancing, and enhancing tumor.

Introduction

Glioblastoma(GBM) multiforme is the most malignant brain tumor, which develops from glial cells. Brain tumors may disrupt physical performance as well as one's mental state. These tumors grow and rupture nerves. Consequently, effects of GBM include seizuristic activity as well as pain. The tumor typically develops in the temporal lobe. Treatments include chemotherapy, radiotherapy, and tumor resection. Aside from the dangers of chemical exposure, complications in GBM treatment include maximizing resection while preserving quality of life. Some scans used for GBM include gadolinium enhanced T1 MRI as well as T2/Flair. Different features that have been used to predict survival include the amount of O^6-methylguanine DNA methyltransferase (MGMT) methylation status and ECOG performance status. ECOG status is a scale that assesses the patient's ability to perform everyday tasks to determine the severity of the tumor. Using necrosis, non-enhancing, and enhancing tumor texture as features to enhance GBM survival may help differentiate overall survival groups.. With knowledge of survival, physicians will administer more chemotherapy to the low survival groups while high survival groups will require more resections to avoid chemotherapy dangers, such as weakening heart conditions, nausea, and excessive dehydration from a rejection of the treatment. Thus a custom treatment will be beneficial to give patients the maximum likelihood of survival. Previous studies have tried Bounding Ellipsoid Volume Ratio(BEVR) and tumor volume as potential features but failed

to yield significant results. Current predictors of survival include older age and resection extent. However, these features aren't significant enough to be clinically used on their own predict survival. This study assessed texture for necrosis, T1 weighted non enhancing, and T1 weighted enhancing tumor as biomarkers to predict survival in GBM.

Methods

From The Cancer Imaging Archive (TCIA), a service which de-identifies and hosts a large archive of medical images of cancer accessible for public download, I requested access to data from the TCGA-GBM collection, which contains various MRI imaging data of post-operational and preoperational glioblastoma patients. The data consisted of FLAIR, T1-weighted, T1-weighted contrast enhanced, and T2-weighted MRI scans. We did not consider studying necrosis, non-enhancing, and enhancing tumor across multiple imaging modalities in this study, though this may be a place for future research. It also consisted of segmentation of various heterogeneous histologic sub-regions, namely the necrosis, non-enhancing, and enhancing tumor. We found that there were 212 patients that had the segmentations for these histologic sub-regions, PFS and OS data, and T1-weighted preoperational scans that we desired to be studied. We used LifeX imaging software, a software for radiomic feature calculation in multimodality imaging that accelerate advances in the characterization of tumor heterogeneity, to analyze the segmentation masks on the images. LifeX imaging software creates a textural readout from the 3D imaging analysis that provides data on GLCM texture, which measures patterns in combinations of gray levels that occur in an image. Various first order shape features

such as sphericity of tumor were also measured with the software. A total of 41 features were analyzed using LifeX imaging software. These features were tested in combination with each other. This was done by creating two combined feature groups, one associated with a low overall survival and one associated with high overall survival. The same was done using PFS values. Kaplan–Meier estimate survival curves, log-rank tests, and ROC analysis were used to compare the two groups. All statistical analysis was completed using textural readouts from LifeX imaging software and R code software.

Results

P values less than .05 was considered statistically significant. The log-rank test found that there is a significant difference (P = .0001) in between the necrosis low overall survival feature group and high overall survival feature group. There was a significant difference (P = .0017) between the non-enhancing tumor feature groups. There was also a significant difference (P = .001) between enhancing tumor feature groups. Necrosis was classified as a strong classifier according to ROC analysis (AUC = 0.89). Non-enhancing tumor was classified as a good classifier according to ROC analysis (AUC = 0.85). Enhancing tumor was also classified as a weak classifier according to ROC analysis (AUC = 0.66).

Conclusion

This study found an effect of necrosis, non-enhancing, enhancing tumor as it correlates to overall survival. Further studies are required to test significance in survival prediction of these

other features with the ones tested in this study. Furthermore, regularizine the features and giving more importance to some in the prediction may increase accuracy in the model. Using this feature in tandem with age, and volumetric features as survival indicators, treatment strategies can be planned accordingly to reduce risk. Patients with more contrast and angular heterogeneity had worse OS. In such cases, higher levels of chemotherapy would be administered to the patient as the severity of the condition grows. However, patients with lower overall survival will have more resections and less drug administration to reduce risk.

References

"Cancer Imaging Archive Wiki." TCGA-GBM - The Cancer Imaging Archive (TCIA) Public Access - Cancer Imaging Archive Wiki, wiki.cancerimagingarchive.net/display/Public/TCGA-GBM.

Chaddad, Ahmad, et al. "Prediction of Survival with Multi-Scale Radiomic Analysis in Glioblastoma Patients." SpringerLink, Springer Berlin Heidelberg, 19 June 2018, link.springer.com/article/10.1007/s11517-018-1858-4.

"Glioblastoma Multiforme Guide: Causes, Symptoms and Treatment Options." Drugs.com, www.drugs.com/health-guide/glioblastoma-multiforme.html.

Martin, Laura J. "Glioblastoma (Primary & Secondary): Symptoms, Treatments, Diagnosis."

WebMD, WebMD, 17 Dec. 2019, www.webmd.com/cancer/brain-cancer/what-is-glioblastoma#1.

Rajabpour, Mojtaba Vand, et al. "Prognostic Factors and Survival of Glioblastoma Multiform (GBM) in Iranian Patients." International Journal of Cancer Management, Kowsar, intjcancermanag.com/en/articles/6260.html.

Sanghani, Parita, et al. "Overall Survival Prediction in Glioblastoma Multiforme Patients from Volumetric, Shape and Texture Features Using Machine Learning." Surgical Oncology, Elsevier, 10 Sept. 2018, www.sciencedirect.com/science/article/abs/pii/S0960740418301002.

Sanghani, Parita, et al. "Overall Survival Prediction in Glioblastoma Multiforme Patients from Volumetric, Shape and Texture Features Using Machine Learning." Surgical Oncology, Elsevier, 10 Sept. 2018, www.sciencedirect.com/science/article/abs/pii/S0960740418301002.

Tixier, Florent, et al. "Preoperative MRI-Radiomics Features Improve Prediction of Survival in Glioblastoma Patients over MGMT Methylation Status Alone." Oncotarget, Impact Journals, 5 Jan. 2019,

www.oncotarget.com/index.php?journal=oncotarget&page=article&op=view&path[]=26578.

"What Is the Outlook and Survival Rate for Glioblastoma?" WebMD, WebMD, www.webmd.com/cancer/brain-cancer/qa/what-is-the-outlook-and-survival-rate-for-glioblastoma.