Semi-Automated Segmentation of Glioblastomas in Brain MRI Using Machine Learning Techniques

Naomi Joseph[1,2], Parita Sanghani[1], Hongliang Ren[1*]
[1]Biomedical Engineering,National University of Singapore Singapore
[2]University of Pittsburgh, Pittsburgh, United States of America
*Corresponding email: ren@nus.edu.sg

***Abstract*— Glioblastomas (GBMs) are cancerous brain tumors that require careful and intricate analysis for surgical planning. Physicians employ Magnetic Resonance Imaging (MRI) in order to diagnose glioblastomas. The segmentation of the tumor is a crucial step in surgical planning. Clinicians manually segment the tumor voxel-by-voxel; however, this is very time consuming. Hence, extensive research has been conducted to semi-automate and fully-automate this segmentation process. This project explores manual segmentation and utilizes k-means clustering technique for semi-automated segmentation. The accuracy of the k-means clustering segmentation was measured using the Dice Coefficient (DC). The results show that k-means clustering provides high accuracy for the segmentation of the enhanced region of tumor (which appears bright in the T1 post contrast MR image) and hence, it can be efficiently used to speed up manual segmentation.**

Keywords- segmentation; k-means clustering; glioblastomas; MRI

I. INTRODUCTION

Glioblastomas are aggressive brain cancers, which originate from glial cells and are supported by a large network of blood vessels. GBMs are grade IV gliomas and have very short median survival [1]. There are two types of GBMs: primary and secondary. Primary GBMs are more aggressive in nature and develop rapidly whereas secondary GBMs grow more slowly but can evolve into a high-grade tumor [2].

GBMs are diagnosed using MR images. For surgical planning, it is important to accurately segment and delineate the different pathological regions within the tumor on an MRI [3]. Different modalities like T1 (T1 pre-contrast), T1CE (T1 post-contrast), T2 and FLAIR (Fluid-Attenuated Inverse Recovery) are used for this segmentation as every modality provides different information regarding the tumor structure. Manual segmentation requires identification of the different tumor parts and labelling each part voxel-by-voxel, a process that is time taxing and subjective for clinicians. Thus, extensive research has been conducted to develop and test semi-automated and automated techniques to aid physicians in the qualitative diagnosis of the glioblastomas [3].

The tumor consists of four regions of interest (ROI): edema, necrosis, enhanced tumor and non-enhanced tumor. The four parts of a GBM can be identified from the combined efforts of four MRI scans: T1CE, T1, T2, and FLAIR. The relationship between the modalities is similar to a checks and balance system where an ROI may be initially identified by one modality but must be endorsed by another modality as well. The T1CE modality is used to distinguish the enhanced tumor which appears bright white on the scans due to contrast. T1 and T1CE are utilized together to determine the non-enhanced tumor and necrosis regions of the ROI. T2 and FLAIR are used to characterize the edema region, however in T2 while the edema is bright white, so are the ventricles of the brain. In some cases, when the edema overlaps with the ventricles this poses a problem when outlining the boundaries of the tumor for surgical planning. Therefore, FLAIR is employed to suppress the ventricles and still enhance the edema region of the ROI.

The purpose of this project was to learn manual segmentation of GBMs using four different MRI modalities. Alongside, a semi-automated technique of segmentation was performed using K-means clustering on the BRATS patient data set. The clustering performance accuracy was measured using the Dice Coefficient.

II. METHODS

A. Manual Segmentation

Manual segmentation was performed on The Cancer Genome Atlas (TCGA) data set of eighty-five patients. TCGA, the National Cancer Institute (NCI), and the National Human Genome Research Institute (NHGRI) collaborated to provide a public genomic data set for cancer research. The segmentation process began with identifying the tumor's location for each patient's set of MRI scans. Once the tumor was located, the contrast enhancing portion of the tumor was distinguished by its bright white color on the T1CE scan and dark grey color on the T1 scan. These voxels were labeled as CET (contrast enhancing tumor) and appear white in Fig. 3. If the T1CE contrast enhancing tumor was also bright white on the T1 scan, then these regions are considered contrast non-enhancing tumor and the voxels were labeled NET (non-enhancing tumor) and appear

purple in Fig. 3. Dark grey regions inside the contrast enhancing tumor ring on the T1CE scan that correlated with light grey regions of the T1 scan were labeled NET as well. Nearly black voxels on the T1CE scan, also inside the contrast enhancing ring, that were dark grey on the T1 scan and bright white on both the T2 and FLAIR scans were labeled as necrosis and appear yellow in Fig. 3. Finally, any region outside of the tumor that was bright white on both the T2 and FLAIR scans represented edema and swelling of the brain and appear blue in Fig. 3. Manually segmenting one patient took up to eighteen hours.

B. K-Means Clustering

A semi-automated segmentation technique was performed on the GBM ROIs of the MRI scans. This technique was tested on the Brain Tumor Segmentation (BRATS) data set publicly provided by the Perelman School of Medicine at the University of Pennsylvania. These scans and their labels, which have been manually revised by neuroradiologists every year, were considered the ground truths throughout this project. The BRATS defines 3 clusters: enhancing tumor, edema, and a merged necrosis and non-enhancing tumor. Initially, the whole tumor region for each patient of the BRATS data set was delineated using the ground truth labels. This whole tumor mask consisted of all 4 ROIs as seen in Fig. 1. This mask was binarized to isolate the whole tumor from the surrounding brain as shown in Figure 1.

K-means clustering was performed within the whole tumor mask. Ten iterations of k-means clustering took two to three minutes per modality (Intel CORE i3 2.50GHz processor, with 6GB Ram). The concept of k-means clustering starts with understanding the grayscale spectrum of the MRI scan. The frequency of each voxel's intensity was plotted against the intensity range of the voxels in one type of MRI scan. Fig. 2 represents the histogram of the T1CE MRI masked by the whole tumor ROI.

K-means clustering initially assigns a specified number of random centroid points amongst the voxel intensity data set. The algorithm then calculates the distance between each centroid and every other point in the data set. It assigns the centroid with the smallest distance from each data point to that respective point. Next, it calculates the average point amongst the cluster of points assigned to one centroid; the old centroid is re-assigned to this new location. The algorithm is iterated until the change between the centroid location converges. This technique determines where the different clusters are located along the intensity range, given the number of clusters to be formed.

The code written to implement this concept first loaded two NIFTI files: the original MRI scan (T1, T1CE, T2, or FLAIR) and the binarized whole tumor mask. In the original MR image array, the voxels outside the whole tumor ROI were redundant and a part of the background, hence, they were assigned a value of zero. This was fed as input to the k-means clustering algorithm. The resulting background cluster was removed and assigned a value of 0. The new segmentation file was saved.

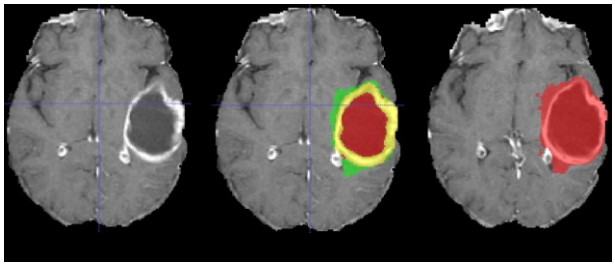

Figure 1. (a) Original T1CE modality (b) BRATS ground truth segmentation (c) Binarized whole tumor ROI mass

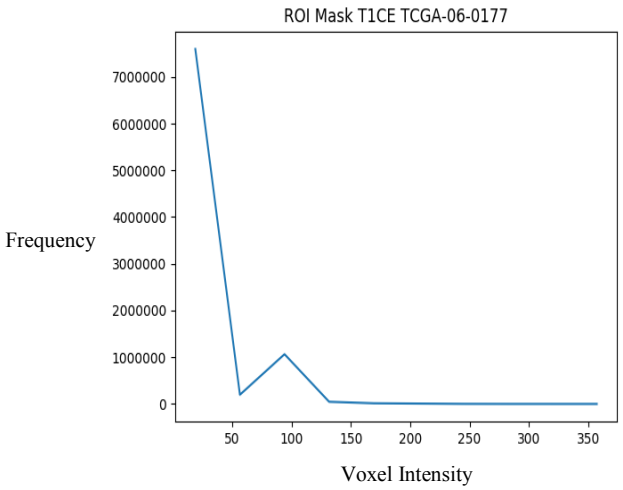

Figure 2. The Tumor ROI's Intensity Histogram

III. RESUTLS AND DISCUSSION

The first part of this project was focused on manual segmentation of the 4 different pathological parts of the GBM on MRIs. Fig. 3 illustrates the axial slice of an MRI of a patient where the segmentation was performed and verified by a neurosurgeon. Manual segmentation is a tedious process and also leads to inter-expert variability. Hence, a semi-automated segmentation approach was performed using the k-means clustering algorithm to determine the labels of each voxel within the whole tumor ROI. Fig. 4 represents the axial slice of the MRI from four modalities of a patient along with the results of K-means clustering implementation.

Due to time constraints, ten patients were randomly selected from the BRATS patient data set to undergo another round of k-means clustering. The T1CE and FLAIR modalities of the ten patients underwent a k-means clustering for 2 clusters. The T1CE modality's two clusters represented enhanced tumor and combined non-enhanced tumor and necrosis. FLAIR modality's two clusters represented edema and the remaining whole tumor ROI. These two segmentation masks were merged to produce a final segmentation mask. The merging order of the clusters was first combined non-enhance tumor and necrosis from T1CE, second edema from FLAIR, third enhanced tumor from T1CE.

Fig. 5 illustrates an example of the axial slice of one of these final masks alongside its ground truth from BRATS.

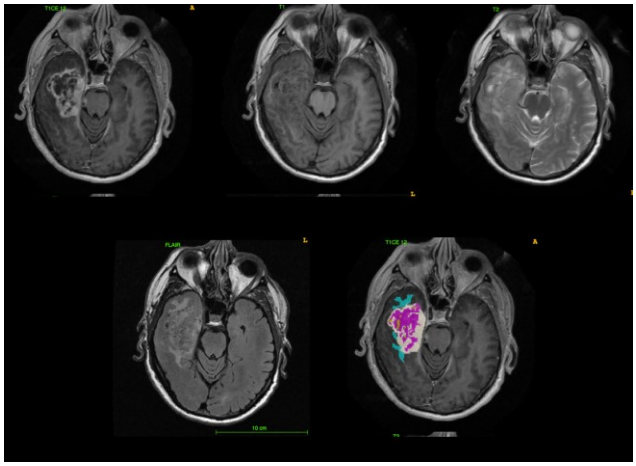

Figure 3. (a) T1CE (b) T1 (c) T2 (d) FLAIR (e) Manual Segmentation on the T1CE modality where CET, NET, necrosis, and edema appear white, purple, yellow, and blue respectively)

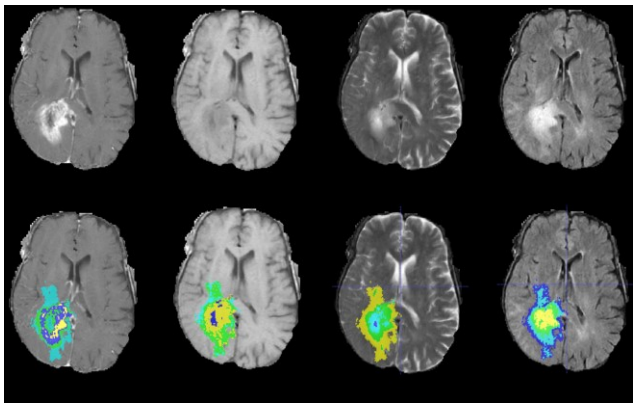

Figure 4. (a) T1CE (b) T1 (c) T2 (d) FLAIR of a BRATS patient (e-h) Corresponding K-means Clustering Segmentation result with four clusters for the four modalities respectively. The different colors in each segmentation mask represent the different clusters formed by k-means clustering

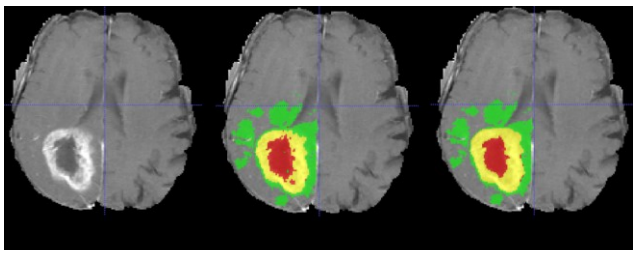

Figure 5. (a) T1CE (b) K-means Clustering Final Combined Mask (c) BRATS Ground Truth

The dice coefficient analyzes the accuracy of the k-means clustering technique with respect to the ground truth labels provided in the BRATS data set. Equation 1 illustrates the dice coefficient for all the ten selected patients.

$$\text{Dice Coefficient} = 2*|A \cap B| / [|A| + |B|] \quad (1)$$

In (1), $|A|$ and $|B|$ represents the number of elements in the ground truth's enhanced tumor region and the k-means clustering final segmentation mask's enhanced tumor region. Table 1 displays the dice coefficient results for each of the ten patients.

TABLE I. DICE COEFFICIENT ACCURACY CALCULATED FOR TEN PATIENTS

Patient ID	DC Accuracy
TCGA-02-0037	0.7705
TCGA-02-0064	0.9095
TCGA-02-0086	0.865
TCGA-02-0106	0.7717
TCGA-06-0145	0.7196
TCGA-06-0149	0.7839
TCGA-06-0238	0.9141
TCGA-12-0616	0.7781
TCGA-19-2631	0.8977
TCGA-76-4932	0.822
Average	0.82321

As mentioned previously, manual segmentation is time consuming. Hence, K-means clustering techniques are considered a possible automated segmentation alternative. Due to time constraints, only ten patients were fully analyzed by the proposed methodology set forth initially. One of the drawbacks of K-means clustering is that it randomly assigns its centroid points within the tumor ROI. This allows for MRI segmentation mask labels to differ between patients making it almost impossible to later merge the four modality masks to create a final simulated segmentation mask. Since necrosis/non-enhancing tumor and enhancing tumor are easily distinguishable on the T1CE modality and the edema region was identifiable from the FLAIR modality, only the T1CE and FLAIR modalities of the ten patients underwent k-means clustering for 2 clusters per modality. These labels of these segmentation masks were manually entered into another simulation to merge the T1CE and FLAIR masks. These final masks were qualitatively compared with the ground truths and it was evident that the non-enhancing tumor/necrosis and edema regions were overlapping and inaccurate. Thus, dice coefficient was measured for the enhancing tumor regions of the final combined segmentation masks and the ground truths. According to Table I, the accuracy of k-means clustering for the enhancing tumor of the ROI is 82% on average. Therefore, it is beneficial to perform k-means clustering for this region of the tumor and then manually segment the remaining three regions of the tumor.

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