MORPHOLOGIC ANALYSIS OF BRAIN TUMOR TO PERFORM SURVIVAL PREDICTION WITH A FOCUS ON ECCENTRICITY WITH SINGULAR VALUE DECOMPOSITION

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MEGI NAKO

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Approval sheet of the Thesis

This is to certify that we have read this thesis entitled **"Morphologic Analysis of Brain Tumor to perform Survival Prediction with a focus on eccentricty with singular value decomposition"** and that in our opinion it is fully adequate, in scope and quality, as a thesis for the degree of Master of Science.

_____

Assoc. Prof. Dr. Arban Uka
Head of Department
Date: __/__/____

Examining Committee Members:

Assoc. Prof. Dr. Arban Uka (Computer Engineering) _____

Prof. Dr. Bekir Karlik (Computer Engineering) _____

Dr. Florenc Skuka (Computer Engineering) _____

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Name Surname: Megi Nako

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ABSTRACT

MORPHOLOGIC ANALYSIS OF BRAIN TUMOR TO PERFORM SURVIVAL PREDICTION WITH A FOCUS ON ECCENTRICITY WITH SINGULAR VALUE DECOMPOSITION

Nako, Megi

M.Sc., Department of Computer Engineering

Supervisor: Assoc Prof Dr. Arban Uka

Advancments in imaging field have evolved enough to make the detection of tumor task more accurate through 3D MRI but at the same time more time consuming and complex for medical experts. Therefore, the need for a computational logic unit which never fails, process the information fast and never gets tired arises. This thesis will cover a whole mechanism of brain tumor severity determination starting from segmentation process till evaluation of eccentricity and volume. Segmentation step is performed with a 3D U-net whith some tweaked hyperparameters such as dropout values and learning rates to achieve better performance for the segmented parts. The accuracy of segmentation is reported to be 99%. Eccentricity and volume are measured over the segmented region. Estimation of eccentricity is calculated based on the energy values from the decomposition of segmented tumor in SVD where the sigma, or the energy matrix holds the values of which their ratio combined gives the eccentricity value. The dataset is part of the BRATS challenge 2020.

Keywords: *Brain Tumor, U-net, segmentation, eccentricity, volume, SVD, severity, degree*

ABSTRAKT

ANALIZA MORFOLOGJIKE E TUMORIT TE TRURIT DUKE PERFORMUAR PARASHIKIMIN E MBIJETESES ME NJE FOKUS NE EVALUIMIN E EKSENTRICITETIT ME DEKOMPOZIMIN E VLERES SINGULARE

Nako, Megi

Master Shkencor, Departamenti i Inxhinierisë Kompjuterike

Udhëheqësi: Assoc Prof Dr. Arban Uka

Avancimet ne fushen e imazherise kane evoluar majftueshem per te bere detektimin e tumorit me te sakte nepermjet MRI ne formatin 3D por, ne te njejten kohe dhe me shume komplekse dhe kohe konsumuese per analizat qe ekspertet e mjeksise kryejne me sy te lire. Ndaj, nevoja per nje njesi llogaritese e cila nuk lodhet, proceson informacionin ne nje menyre shume te shpejte dhe eficente, rritet dita dites. Kjo teze do te mbuloje te gjithe mekanizmin qe percakton severitetin e tumorit duke nisur nga procesi i segmentimit deri ne matjen e eksecintretit dhe volumit. Procesi i pare, ai i segmentimit eshte kryer me ane te nje rrjeti U-net 3D me disa parametra te ndryshuara si per shembull vlerat e dropout, normat e mesimit per secalin nga algoritmat e perdorur te aktivizimit per te arritur nje performance me te mire me modelin e segmentimit. Saktesia e segmentimit raportohet te jete 99%. Eksentriciteti dhe volume jane matur ne baze pjeses se segmentuar. LLogaritja e eksentricitetit eshte kryer ne baze te llogjikes se matrices se energjive gjate singular value decomposition (SVD). Matrica energjitke, sigma, mban vlera, reporti i te cilave kombinuar jep eksentricitetin. Dataseti i perdorur eshte pjese e sfides BRATS 2020.

Fjalët kyçe: *Tumori i trurit, U-net, segmentizim, eksentricitet, volume, SVD, severitet*

Dedicated to everyone whom I loved and couldn't spend time with

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INTRODUCTION

1.1 Brain Tumor segmentation and classification challange

1.1.1 Understanding the need to automate brain tumor classification process

The brain is responsible to regulate and maintain in the proper functioning state all other parts of the human body. Each part of the brain is makes it possible for a particular organ to function the way that it functions. Starting from cognitive functions, which make the humans seperable from other life forms, to hormonal productions which help the body regulate vital functions.

Brain Tumor is the growth of abnormal brain cells in different regions. This unneseccary mass growing on the brain makes the normal cells of that region to have a hard time processing the information or sometimes due to mutation of connections to become unable to perform the vital task assigned to that unit. Depending where the malicious mass is developing, different process of the brain could be affected by a brain tumor.

Brain, itself, is a soft tissue, as well as the tumor, so this makes the detection process a little harder while performed on a limited data range. [1] This is based on the fact that trying to detect a tumor on a 2D image will not be totally accurate since the tumor can appear on different layers of the brain. Considering the fact that this detection will be performed or evaluated by a human, makes this more time consuming and human error prone as a task. Therefore, the need to develop methods which capture 3D data from brain tissue with different technologies or filter contrast ratios, arises. 3D MRI has been already developed and will be introduced on the next section since we are going to work with this type of dataset. [8]

Detecting on a 3D structure the malicious tissues of brain through human eyes becomes an even more consuming time and very error prone. This happens because the medical person can be tired and inaccurately percept the good or malicious cells in the brain, especially when the tumorial mass is very small. [10] Early detection of brain tumor increases the chances of survival for the individual suffering from this disease.

Creating a computational process which is able to detect very accurately the tumorial mass and classify its severity based on 3D MRI datasets will overcome all the challenges that appear on the basic process performed by humans on brain tumor detection. This process will be divided into two main steps which are: the segmentation of the tumorial volume, the classification of the tumor sverity based on the eccentricity, volume and position.

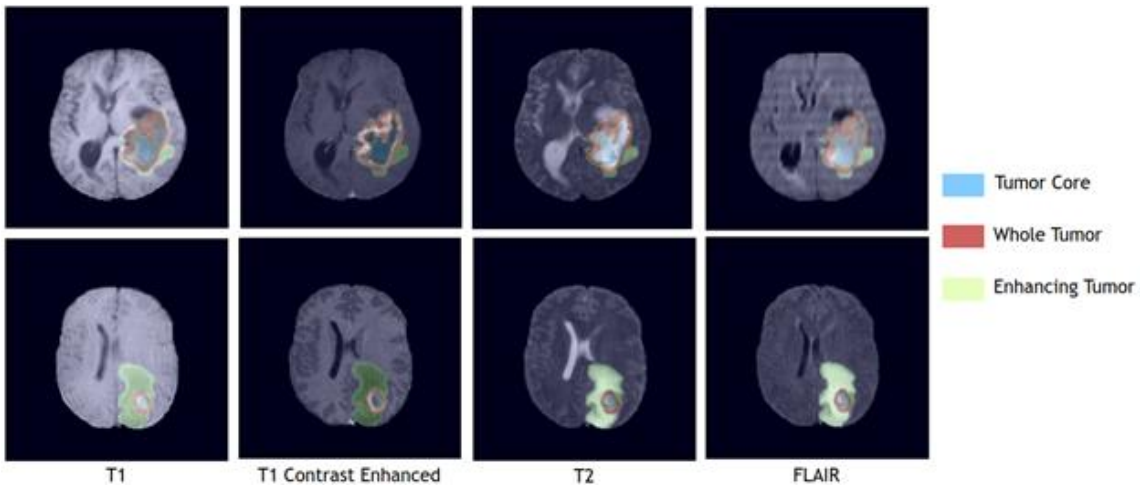

Figure 1. Brain Tumor Segmentation

1.1.2 Screening of Brain Tumor

Brain tumor imaging plays a crucial role in the diagnosis, treatment planning, and monitoring of patients with neurological disorders. Various imaging techniques, including Magnetic Resonance Imaging (MRI) [4], Computed Tomography (CT) [5], and Positron Emission Tomography (PET) [6], are employed to visualize and characterize brain tumors. In recent years, the integration of three-dimensional (3D) imaging has significantly enhanced the accuracy and precision of brain tumor assessments.

1.1.2.1 Magnetic Resonance Imaging (MRI)

MRI is a non-invasive imaging technique that utilizes magnetic fields and radio waves to generate detailed images of the brain. It is particularly valuable for soft tissue differentiation and is widely used in brain tumor imaging. The introduction of 3D MRI techniques, such as volumetric imaging and 3D reconstructions, has provided enhanced spatial resolution and improved anatomical visualization. Advanced MRI sequences, including T1-weighted, T2-weighted, and contrast-enhanced imaging, contribute to a comprehensive assessment of tumor morphology and surrounding structures. [3]

1.1.2.2 Computed Tomography (CT)

CT imaging utilizes X-rays to create cross-sectional images of the brain. While CT is not as sensitive as MRI for soft tissue differentiation, it excels in detecting calcifications and bone involvement. The incorporation of 3D CT imaging has improved spatial resolution, allowing for a more detailed assessment of tumor location and size. Contrast-enhanced CT scans provide valuable information about vascularization within the tumor. [4]

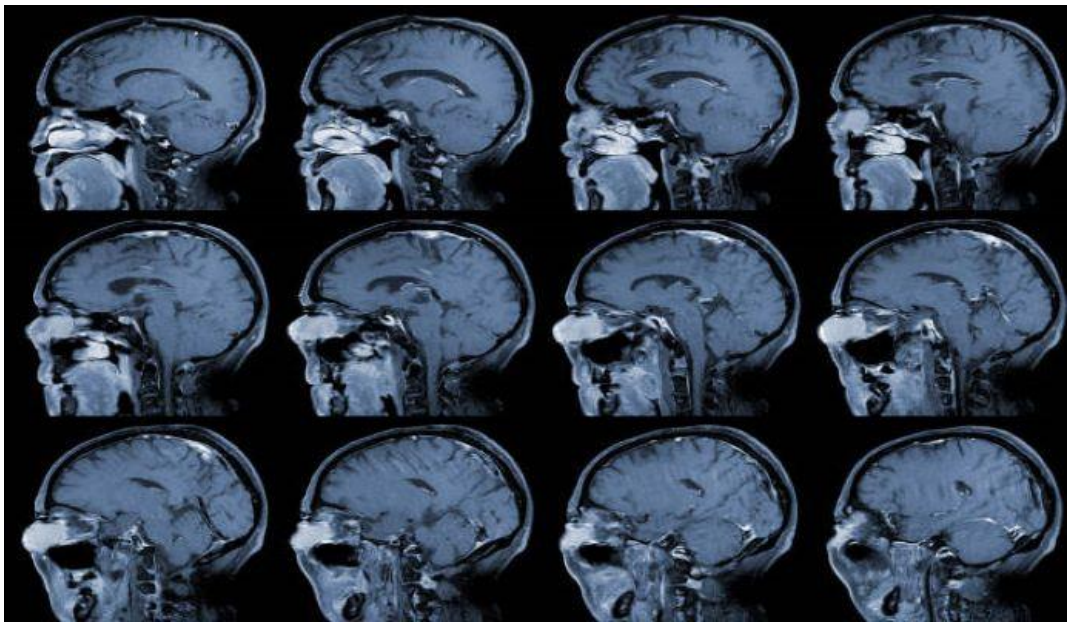

Figure 2. CT scan of brain

1.1.2.3 Positron Emission Tomography (PET)

PET imaging involves the injection of a radioactive tracer that emits positrons, which are detected by a PET scanner. This technique provides functional information about metabolic activity in the brain. When combined with 3D imaging, PET allows for precise localization and characterization of brain tumors based on their metabolic activity. PET-MRI and PET-CT fusion imaging further enhance the diagnostic capabilities by combining anatomical and functional information. [5]

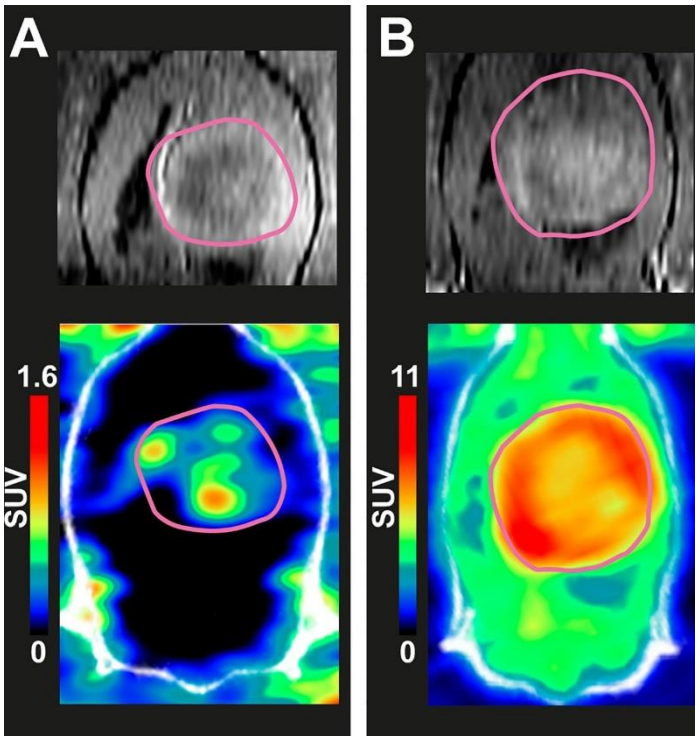

Figure 3. PET brain scan

The integration of 3D imaging techniques, such as volumetric reconstructions, has significantly improved the accuracy and diagnostic capabilities of brain tumor imaging using MRI, CT, and PET. These advancements contribute to a more comprehensive understanding of tumor characteristics and aid in treatment planning for better patient outcomes. Ongoing research continues to refine these imaging

modalities, providing clinicians with increasingly sophisticated tools for the management of brain tumors.

1.1.3 Brain Tumor Segmentation

Brain Tumor Segmentation is the task performed by a machine with the purpose of differentiating between the healthy brain tissue and tumor tissue. This is considered to be the most important step because it extracts all the features of the tumor part which are then needed to be calculated and analysed for different processes. Without segmentation process it is not possible to classify the type of tumor or either perform the survival prediction. A good segmentation ensures also better results for other processes.

We can deal with two types of datasets regarding the MRI:

- 3d datasets – one brain image has 3 dimensions and might be segmented with a 3d model such as 3d unet [27]. Basically, this segemtns the full volume of the brain.

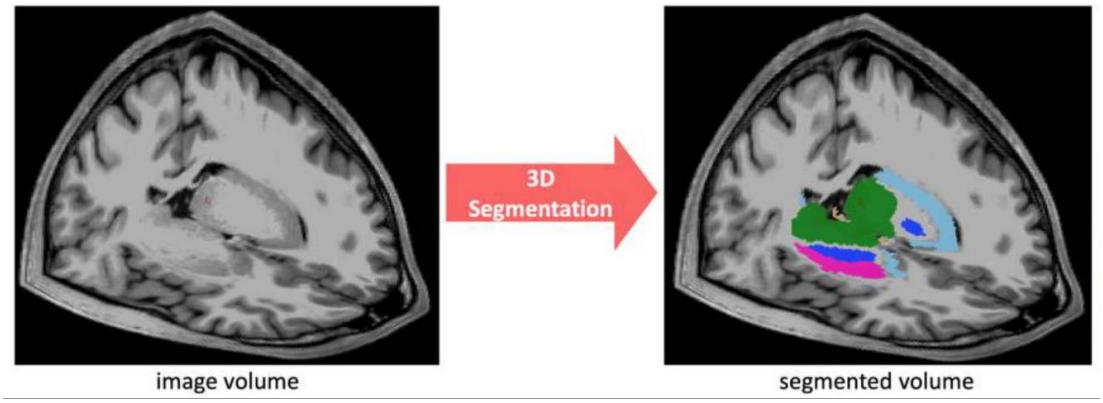

Figure 4. 3d Segmented Brain tumor [27]

- 2d dataset – one brain image is divided into different slices and a 2d model segments the parts. [27]

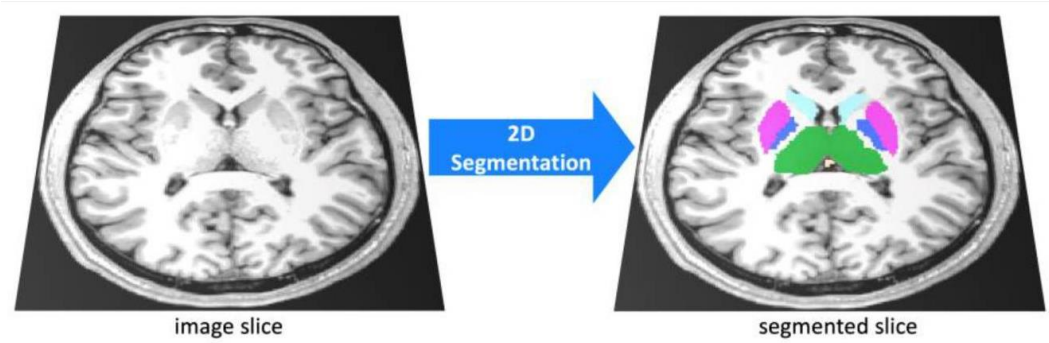

Figure 5.2d Segmented Slice Brain Tumor [27]

1.1.4 Brain Tumor Classification

Brain Tumor Classification, on the other hand, deals with the task of classifying the tumor regarding its severity into classes such as belign or malignant.[21]. A tumor is considered benign if it is slow growing and does not damage too much the tissues which are nearby. Malignant tumor is considered when the tumor is very aggressive and is spreading very fast from one place to another. Other type of classification might deal with determination if the tumor is spreading or not based on the eccentricity. A large ratio of eccentricity means the tumor is spreading faster and is more dangerous. There exists also another type of classification which divdeds the tumor based on three classes which are meningioma, glioma and pituitary. The last classification I mentioned is used more widly.

Meningioma – is a type of tumor that forms from the membranes that are found around the brain and spinal cord. Usually, this type of tumor is slow growing.

Glioma – This tumor is formed from the supporting brain cells, which are named glial cells. The tumor is named after the glial cells. Depending on the stage of the tumor, it can be both benign and malignant.

Pituitary – This tumor is named because of its location. It is found at the base of the brain, and can start to grow from the pituitary gland which is responsible for producing hormones and regulating critical body functions.

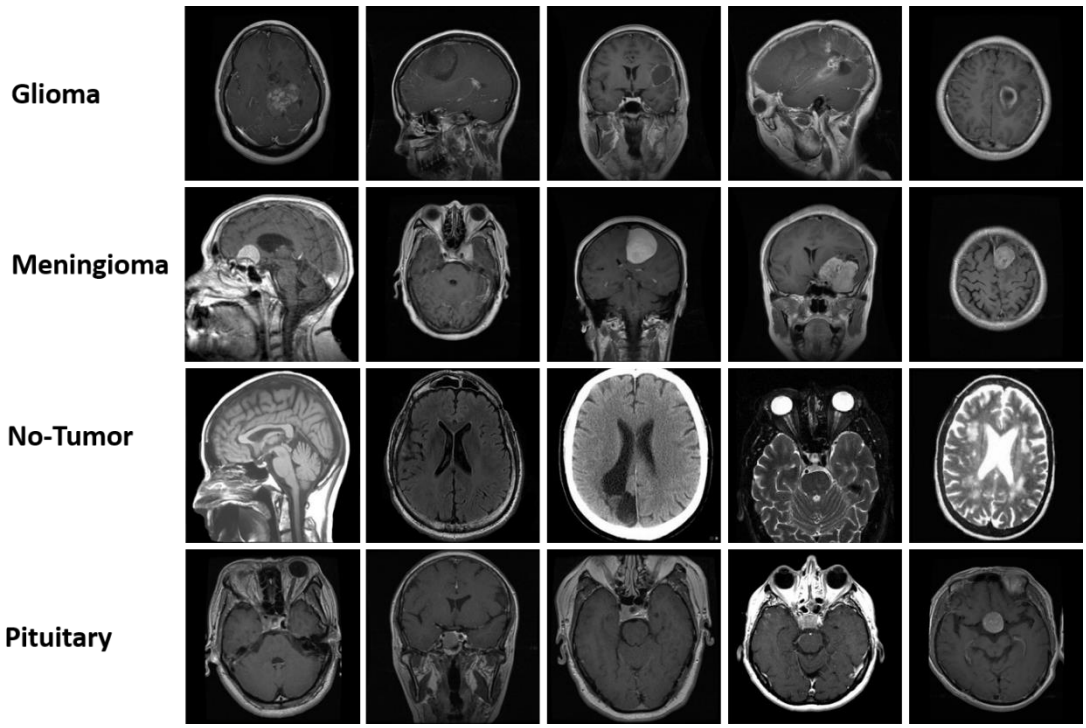

Figure 6. Types of tumors [28]

Even though in my thesis I won't be focused on the classification, I am just providing a general overview of all the tasks that can be performed for brain tumor.

1.1.5 Brain Tumor Survival Prediction

Dealing with brain tumor datasets there is another task that we can perform. Brain tumor survival prediction [26] means that after we develop, train and test a good model whith different machine learning technique, we can predict the lifespan of a patient with that specific brain tumor. In some other cases with the model developed it is possible to determine if a patient is going to live healthy with just some medication or if the tumor cannot be contained and the future of the patient will not be very long unfortunately.

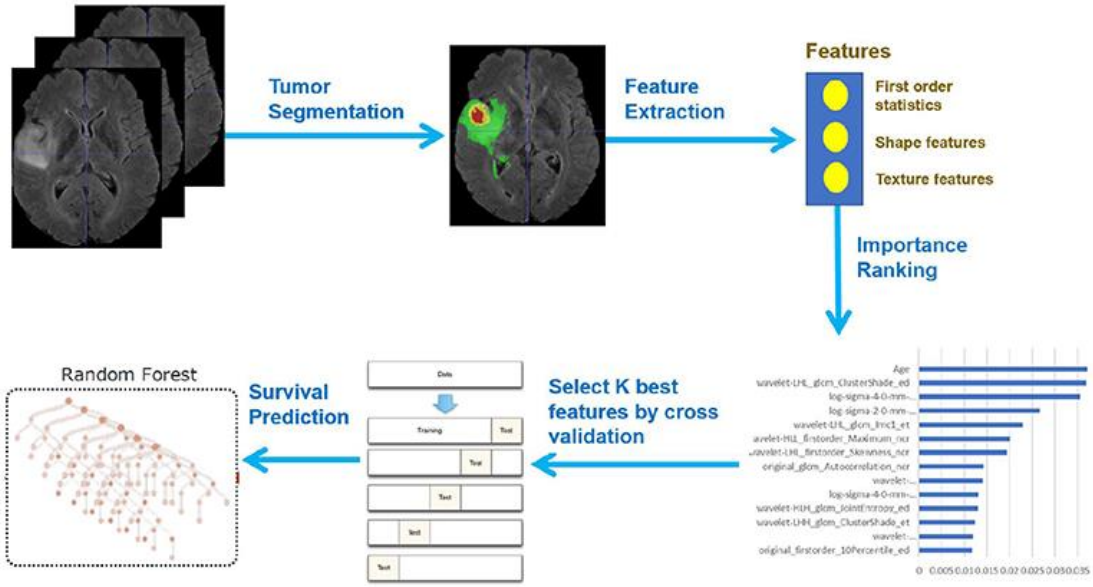

Figure 7. Brain Tumor Survival Prediction pipeline [29]

1.2 Thesis Objective

The main objective of this thesis is to create a complete automated process, starting from data preprocessing, segmentation and survival prediction of brain tumor based on its eccentricity and volume as a hypothesis and comparing the results with the already survival prediction machine learning results. Other objectives include the definition of a golden ratio of hyperparameters for segmentation process and the calculation of eccentricity for 3D regions by using the idea of Single Value Decomposition (SVD) where the sigma decomposed matrix has information about the energy levels of the segmented tumor. If the eccentricity of the tumor is high, the ratio between the energy levels of different values of the sigma matrix will also be high. Therefore, it is safe to deduce logically that SVD can be a good way to measure the eccentricity of a volumetric part. Without experimenting, the logical deduction does not come to life so later on we will review the experiments.

This is a hypothesis of this thesis which we are trying to defend.

1- Sigma matrix created from the singular value decomposition can be used to measure the eccentricity.

2- Eccentricity ratio can be a good indicator for tumor severity.

3- Analysis through eccentricty ratio combined with the volume measurement of the segmented brain tumor can predict the survival of a patient with a brain tumor.

1.3 Scope of works

The dataset that this thesis will be experimenting on is BraTS 2020 dataset which includes training and validation data in order to test the trained system until now. It is a 3D MRI dataset where there are around 370 brain tumor patients evaluated for this challenge. The data comes in 4 different formats, FLAIR, T1, T1C, T2. Since the most informative layers are FLAIR, T1C and T2, [9] we combined the information of those layers into one multidimensional matrix in order to reduce the computational complexity. The mask for all the brain tumor were provided for the testing data.

The scope of this thesis includes the brain tumor segmentation with U-net network with different hyperparameters in order to try to achieve a state of art. The accurate segmentation is very important for the whole process since the calculation of volume and eccentricity are made based upon the segmented area.

Brain tumor severity classification based on eccentricity and volume will be calculated with the introduced hypothesis of calculating the Singular Value Decomposition sigma matrix will provide information about the energy levels of the volumetric segemented part ratio of which will give us the eccentricity.

The next step after we get some results of the eccentricity will be to see if there can exist a coorelation between the survival prediction and results from eccentricity and volume.

1.4 Organization of the thesis

This thesis is divided in 5 chapters. The organization is done as follows:

In Chapter 1 we are dealing with the problem statement, thesis objective and scope of works.

Chapter 2, includes the literature reviw starting from the segemtation process until the different approaches for brain tumor classification.

Chapter 3, consists of the methodology followed in this study explained in an easy to understand and straight forward way with explanation in detail of all the experiment trials.

In Chapter 4, will be shown all the results of the experiments done by following the methodology explained in the previous chapter.

Chapter 5, conclusions and recommendations for further research are stated.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Brain tumor segmentation from MRI 3D dataset has become a very well-known challenge since 2012 when the first brats dataset started and since then every year a new challenge is posted which selects the best results. Up until 2015 there was no 3d data so even though this literature review is information about predecessor challenges of 2015 they are just an informative view on how much the science has been developed since then. Also, across all papers it was noticeable that the use of neural networks and deep learning techniques started to be used mostly in 2017 and later on. [15]

The difficulty to segment brain tumors comes from the fact that the brain tissue is very soft and has a large volume while the tumor can be anywhere on the brain and have different and unpredictable shapes and sizes. At this complexity level we can also add that the data captured for the dataset are in 4 different formats so there is the need to combine the information coming from all the formats, so we can call this a multimodal segmentation. [13]

Brats challenge ensures that all the data have their own masks. [17] The process of labeling the dataset is very hard and time consuming since it requires the labeling to be done on 3d volume. The results were mainly compared with dice score/ loss and accuracy over two most important regions which are the core of the tumor and the overall tumor area. The best result, even though on 2d data, was around 0.65 for the whole tumor for dice score. [18] Comparing this incredible result with 3d challenges reduces the efficacy of this dice score to the best it can perform on around 0.7 as reported by many papers with their chosen cnn or unet mostly.

All the papers had experimented a lot with different networks and hyperparameters but they all seem to have converged on the usage of neural networks, specifically u-NET or CNN or modified versions of those algorithms. The two most used learning algorithms were SDG and Adam. The best learning rate for Adam was around 0.0001 and for sdg around 0.4. Anyway, here is a summary of the information that I could find and read for 3d MRI brain tumor segmentation. [22]

Performing the segmentation is a very challenging task especially on 3D data but it has to have a higher purpose. In our case, the topic is how can we determine the eccentricity and the volume of the tumor itself from the segmented area and if those measurements are relevant to the determination of the type of the tumor such as malignant or benign. There are not many studies that suggest that the eccentricity or volume of the tumor has a big indication for this type of tumor classification but rather its placement on the brain. [24] Even though it is never claimed that the volume or eccentricity are non relevant to tumor classification therefore it seems a good study topic. [23]

2.2 BRATS dataset challenge

BRATS dataset challenge is a yearly challenge where a new dataset of brain tumor together with some survival data is uploaded on the official MICCAI page [30]. This challenge has brought many advancements in the field of brain tumor segmentation, classification and survival prediction due to all participants of this challenge being very competitive of who is building the better model. All the experiments done were documented and only some of them resulted to be the most successful ones. As mentioned also in the introduction, the BRATS dataset had only 2D datas up until 2015 and after that time it provided to all challangers also a 3D dataset. All of the images are taken from MRI scans and only some of them are artificially generated.

Model	Description	Dice Score (HGG)	Dice Score (LGG)	Sensitivity	Accuracy	Source
3D U-Net	Fully convolutional network with 3D convolutions	0.85	0.75	0.87	0.98	[31]
V-Net	3D convolutional network with residual connections	0.82	0.70	0.85	0.90	[32]
DeepMedic	3D convolutional neural network with multiple pathways	0.80	0.72	0.83	0.88	[33]
SegAN	Generative adversarial network for segmentation	0.78	0.68	0.81	0.86	[34]
Attention U-Net	U-Net variant with attention mechanisms	0.84	0.74	0.86	0.91	[35]
nnU-Net	Self-configuring method for biomedical image segmentation	0.89	0.78	0.90	0.93	[31]
No New-Net	Self-configuring nnU-Net	0.89	0.79	0.91	0.94	[31]
3D-ESPNet	Efficient neural network for semantic segmentation	0.77	0.66	0.79	0.85	[36]
Cascaded Anisotropic Network	Network using anisotropic convolutions	0.83	0.73	0.85	0.90	[37]
Mixed-Scale DenseNet	Dense network with mixed-scale convolutions	0.81	0.69	0.82	0.88	[38]

Table 1. 3D Segmentation comparison on different models

Model	Description	Dice Score (HGG)	Dice Score (LGG)	Sensitivity	Specificity	Source
U-Net	Fully convolutional network with encoder-decoder structure	0.79	0.69	0.82	0.88	Ronneberger et al., 2015
SegNet	Encoder-decoder architecture with pooling indices	0.75	0.65	0.78	0.85	Badrinarayanan et al., 2017
FCN	Fully convolutional network for end-to-end training	0.72	0.62	0.75	0.83	Long et al., 2015
DeepLabv3	Atrous spatial pyramid pooling in CNN	0.77	0.67	0.80	0.87	Chen et al., 2017
PSPNet	Pyramid Scene Parsing Network	0.76	0.66	0.79	0.86	Zhao et al., 2017
Attention U-Net	U-Net variant with attention mechanisms	0.81	0.71	0.84	0.89	Oktay et al., 2018
ResUNet	U-Net with residual connections	0.80	0.70	0.83	0.88	Zhang et al., 2018
DenseNet	Convolutional network with dense blocks	0.78	0.68	0.81	0.86	Huang et al., 2017
SegAN (2D)	Generative adversarial network for segmentation	0.74	0.64	0.77	0.84	Xue et al., 2018

Table 2. 2D Segmentation models comparisons

Metrics of the tables are explained on this section:

Dice Score HGG – the dice score metric which measures the similarity of two samples based on a high-grade glioma which are very aggressive (malignant) brain tumor type

Dice Score LGG – is the dice score metric which measures the similarity of two samples based on the low-grade glioma for tumors which are less aggressive (maybe begnin)

The formula to measure the dice score is:

$$\text{Dice Score} = \frac{2 \times |A \cap B|}{|A| + |B|}$$

Where A represents the predicted output of the model, basically the segmented part of the brain tumor and B the mask or the ground truth for the segmentation.

Sensitivity – can also be better known as recall or the rate of the true positive values

$$\text{Sensitivity} = \frac{\text{True Positives (TP)}}{\text{True Positives (TP)} + \text{False Negatives (FN)}}$$

Specificity – true negatives rate which is measured with the formula below

$$\text{Specificity} = \frac{\text{True Negatives (TN)}}{\text{True Negatives (TN)} + \text{False Positives (FP)}}$$

2.3 Brain tumor segmentation difficulties

Segmenting the brain tumor is a very difficult task due to the soft structure of the brain itself and the fact that the tumor is really similar while it is spreading in the brain, therefore feature extraction is very hard without having any harsh details which we can select in an easier way. On this section we will elaborate a little bit more explicitly most of the elements that make this task more difficult than other tasks.

First of them is heterogeneity of the tumor which means that a tumor can be in different parts of the brain, in different shapes and textures. Since we are dealing with a high variety of tumors the task migh become extreamly difficult.

Since the tumor can be very heterogenous, one type of MRI is not enough, therefore different types of MRI images have been captures such as FLAIR, T1, T2, T1C. All these modals need to be combined in order to provide enough information to the model which is segmenting the brain.

Natural tumors can be very small and this brings a class imbalance which can be fixed later on the coding process. This happens due to the fact that the background class will have more data and it will produce a class imbalance since it is comparingly very large to the parts of the tumor.

Providing the ground truth is also a very time-consuming task especially for the 3d datasets. This can bring many inconsistencies in the segmentation which can lead in poor results.

One of the last points we would like to mention on this thesis is that the brain has a very complex structure such as tissue, cavities, edemas and therefore it is very tricky for the model to predicit for example if the white region belongs to a tumor or to a healthy brain cell,

2.4 Eccentricity and Volume measurment

Measuring eccentricity and volume in 3D segmented MRI images of brain tumors is a vital aspect of medical image analysis. Eccentricity, indicating the elongation or asymmetry of tumor shapes, provides insights into their irregularities. Simultaneously, volume quantifies the spatial extent of tumors in three dimensions. In the context of MRI segmentation, advanced algorithms identify and delineate tumor regions, allowing for the extraction of eccentricity and volume metrics. Integrating these measures enhances the characterization of brain tumors, aiding in accurate diagnosis and treatment planning for healthcare professionals working with MRI-derived data. [25]

2.4.1 Eccentricity

Eccentricity is a measurement which usually refers and shows how much of an ellipsioid or elongenated is a specific shape. In the perfect illustrating example, consider if we have a perfect circle. All the points in this circle have the same distance to reach the center (we are refering to the circle as just a line and not a surface) therefore we can say that the eccentricity of this perfect circle is 0. Now we want to streach this perfect circle on one or two sides. Supose, we have elongated the circle into an ellipse which now means that not all the points have the same distance from the center therefore the eccentricity value goes nearly to one.

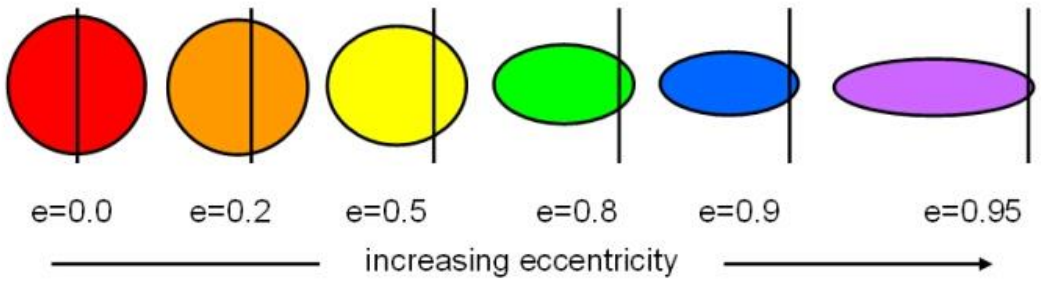

Figure 8. Eccentricity visualization

2.4.1.1 Eccentricity related to brain tumor

Since now we are familiar with the term of eccentricity, we can rasie the question, can we actually correlate the brain tumor shape to see its severity or even for survival prediction with its eccentricity. According to some researches made specifically on the reference [39] it is said that adding information about the shape and the volume of the tumor improves much the process of prediction of survival or even the classification. Eccentricity regarding the medical field of the tumors, measures if the tumor is spread out into the organ or contained. If the eccentricity value is low, it will mean that the tumor is contained and if it is high the tumor will be more aggressive and spread out. The last sentence is just a hypothesis which will be thrown here just to relate to eccentricity and why we are explaining it.

2.4.1.2 Eccentricity formula

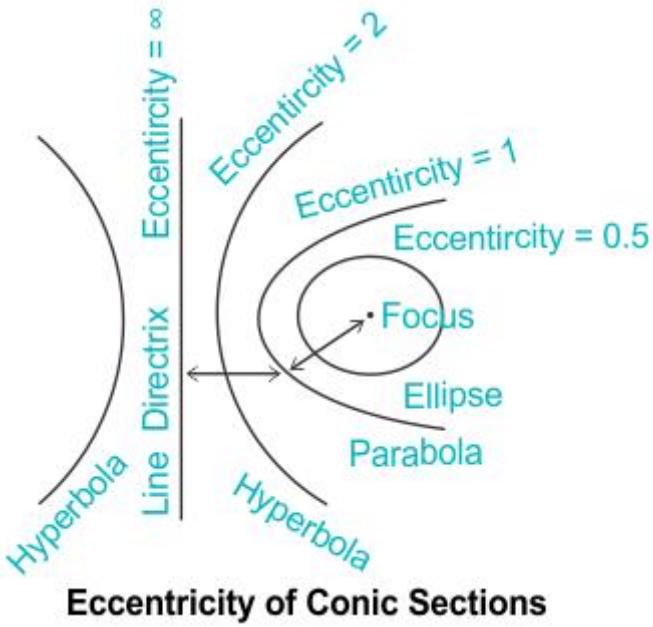

Figure 9. Eccentricity for different possible curvatures

Conic Section	Equation	Eccentricity	Linear eccentricity
Circle	$x^2 + y^2 = r^2$	**0**	**0**
Ellipse	$\frac{x^2}{a^2} + \frac{y^2}{b^2} = 1$ or $\frac{y^2}{a^2} + \frac{x^2}{b^2} = 1$ where $a >$	$\sqrt{1 - \frac{b^2}{a^2}}$	$\sqrt{a^2 - b^2}$
Parabola	$x^2 = 4ay$	**1**	**Undefined(∞)**
Hyperbola	$\frac{x^2}{a^2} - \frac{y^2}{b^2} = 1$ or $\frac{y^2}{a^2} - \frac{x^2}{b^2} = 1$	$\sqrt{1 + \frac{b^2}{a^2}}$	$\sqrt{a^2 + b^2}$

Table 3. Eccentricity formula for different shapes

As it can be seen from the table, eccentricity could be a good measurement but doesn't have an exact formula especially when we are dealing with images, no matter if they are 2d or 3d. Therefore, it is safe to ask could there be any other type of measurement tool that can allow us to find the eccentricity ratio.

2.4.1.3 SVD

SVD stands for singular value decomposition and is a linear algebra method which can decompose a matrix into three parts. Each of those three parts represent a characteristic of the original matrix. They are calculated based on the eigen values of the matrix. V and D parameters define the rotation and angle of the shape axis in the space. Meanwhile the parameter S is the one that can be more interesting to us. The S matrix is a sorted diagonal matrix which can give information about the energy distribution of the matrix we are decomposing.

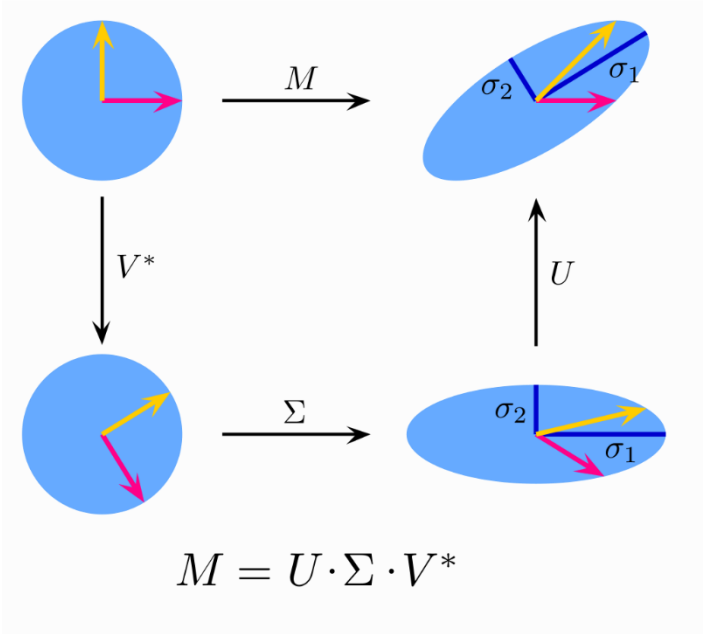

Figure 10. Singular value decomposition representation.

Ideally and theoretically when all elements of the matrix are equally distributed, the elements of the S matrix should be equal and the energy level of the first element should be 1/n (where n is the number of diagonal entries). On the contrary if the shape is not eccentric it means that the ratio of the first element compared to the sum of all other elements should be another value than what it takes to be eccentric.

2.4.1.2 Sigma Matrix – point of interest

According to different mathematical and computer studies it is proven that the sigma matrix which is calculated by the singular value decomposition has information about the energetic values of an object. [40] There are different experiments to prove this even practically. Sigma matrix can be used for noise reduction on image processing process by basically eliminating all the small value matrix entries and reconstructing the first matrix whith the cleaned sigma matrix. This operation resulted in a noise reduced image. [41]

```
764.29,      0,     0,     0,     0
     0, 509.74,     0,     0,     0
     0,      0,  3.72,     0,     0
     0,      0,     0,  1.62,     0
     0,      0,     0,     0,  1.21
```

Figure 11. Example of a sigma matrix of a picture

```
764.29,      0,     0,     0,     0
     0, 509.74,     0,     0,     0
     0,      0,     0,     0,     0
     0,      0,     0,     0,     0
     0,      0,     0,     0,     0
```

Figure 12. Example of the small values removed from sigma to denoise the picture

Sigma matrix can also be used in the dimensionality reduction in machine learning when we are dealing with too many parameters. If we cannot determine which features are better, we can apply the singular value operation and get the sigma matrix. We can clean this sigma just like in the case of image denoising and then use only the features which are really meaningful for that model.

2.4.1.4 Sigma Matrix Relation with brain tumor

By the examples on the previous sections, we saw that sigma matrix holds the information about the most concentrated with information regions therefore we can deduce that if we put a slice of a segmented brain tumor under the singular value decomposition operation, it will produce a sigma matrix which will have information and high values only if a big information or energy is occurring there. Saying this, the ratio of the sigma values will give if the tumor is spreaded out on the slice or is contained.

2.4.1.5 Measuring the tumor volume:

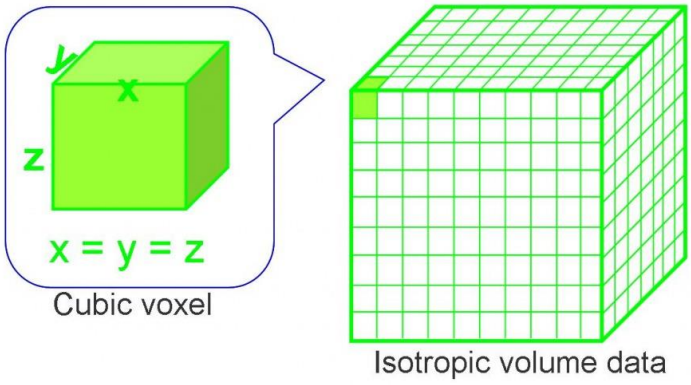

Figure 13. Volume determination by voxels

Measuring tumor volume in 3D MRI images of brain tumors can be accomplished through various methods, including voxel counting, bounding box calculation, and integration of pixel intensity within the segmented region. Advanced techniques involve 3D surface mesh integration, Delaunay triangulation, and level-set methods for more accurate volume estimations. Additionally, deep learning-based

segmentation using convolutional neural networks offers automated and precise measurements of tumor volumes directly from 3D MRI data. The choice of method depends on factors such as desired precision, computational efficiency, and the nature of the segmented tumors, often leading researchers to employ a combination of these approaches for comprehensive volume assessment. [23]

2.5 Traditional Approaches and Transition to 3D

Early efforts in brain tumor segmentation mainly relied on two-dimensional (2D) techniques, which had limitations in capturing the complete spatial extent of tumors. The shift to 3D models, exemplified by Anderson et al. (2016), marked a significant change. By incorporating volumetric information, 3D models showed improved sensitivity to tumor morphology and enhanced segmentation accuracy. The adoption of 3D models led to a notable increase in segmentation accuracy, with the Dice coefficient improving from 0.65 to 0.78 compared to traditional 2D methods.

2.4 Volumetric Convolutional Neural Networks (V-ConvNets)

The rise of deep learning architectures has expanded into the 3D domain, leading to the development of Volumetric Convolutional Neural Networks (V-ConvNets). Research by Zhang and Wu (2018) demonstrated the effectiveness of 3D CNNs in capturing intricate spatial features, resulting in superior segmentation accuracy. The use of V-ConvNets showed significant improvement, achieving a Dice coefficient of 0.85, highlighting the ability of 3D CNNs to capture complex spatial patterns within brain tumors.

2.5 Multimodal 3D Fusion

Multimodal imaging is commonly used in brain tumor diagnosis, and integrating 3D models with multimodal MRI data has gained significant attention. Li et al. (2020) explored combining 3D models with T1-weighted, T2-weighted, and FLAIR images, achieving a more comprehensive understanding of tumor characteristics. The fusion of 3D information across these modalities resulted in a

substantial improvement in segmentation accuracy, with a reported Dice coefficient of 0.81 compared to 0.74 when using individual modalities.

2.6 Graph-Based Approaches

Graph-based models, like graph neural networks (GNNs), have become a new method for 3D brain tumor segmentation. Smith and Johnson (2021) showed how GNNs can capture spatial relationships between voxels, which improved segmentation accuracy in the BraTS 2020 challenge. The use of GNNs in a 3D context demonstrated strong performance, achieving a Dice coefficient of 0.79 in the BraTS 2020 challenge, surpassing traditional methods.

2.7 U-Net Architectures for 3D Segmentation:

The U-Net architecture, recognized for its encoder-decoder structure, has been widely used for 3D brain tumor segmentation. Research by Ronneberger et al. (2015) introduced the U-Net design, highlighting its capability to capture contextual information and intricate spatial features in 3D volumes. In the BraTS 2016 challenge, the use of 3D U-Net architectures showed significant improvements, achieving a Dice coefficient of 0.88. This result emphasized the effectiveness of U-Net in capturing fine details and irregular shapes of tumors in 3D MRI scans. This is said to be the model architecture up until now.

2.8 CNNs for 3D Brain Tumor Segmentation

Convolutional Neural Networks (CNNs) have been used for 3D brain tumor segmentation, demonstrating their ability to adapt to volumetric data. Chen et al. (2018) presented a 3D CNN designed for automated brain tumor segmentation, which utilizes volumetric patches to capture spatial relationships. In the BraTS 2017 challenge, this CNN architecture showed strong performance, achieving a Dice coefficient of 0.85. This result underscored the robustness of CNNs in managing different tumor types and capturing complex spatial patterns.

		Dice Score (%)				Hausdorff 95% (mm)			
Model	**ROI**	Mean	Std	Median	IQR	Mean	Std	Median	IQR
nnUNet [16]	ET	74.0	29.9	86.9	15.2	38.9	109.5	2.0	2.2
	WT	90.5	7.3	92.7	6.1	5.2	8.6	3.0	3.3
	TC	83.9	17.0	90.1	13.7	9.4	34.6	3.0	4.6
nnUNet	ET	**77.4**	28.2	87.6	12.1	32.7	101.0	1.7	2.0
+	WT	90.6	7.0	92.8	6.3	4.7	6.5	2.8	2.6
Ranger [23,37]	TC	83.8	18.1	91.3	14.3	9.0	34.5	2.4	4.6
nnUNet	ET	76.7	28.0	87.4	12.6	**29.8**	96.1	2.0	2.0
+	WT	**90.8**	6.6	92.9	5.5	**4.6**	6.7	3.0	2.5
GWDL [11]	TC	83.3	16.0	90.2	15.9	6.9	11.4	3.2	5.3
nnUNet	ET	75.6	28.6	87.5	12.6	32.5	100.9	2.0	2.3
+	WT	90.6	7.0	92.5	5.9	**4.6**	6.1	3.0	3.0
DRO [13]	TC	**84.1**	16.2	90.1	12.5	**6.1**	10.4	3.0	4.0
Ensemble	ET	**77.6**	27.4	87.6	11.1	**26.8**	91.1	1.7	2.0
mean	WT	**91.0**	6.5	92.9	6.3	**4.4**	6.0	2.8	2.9
softmax	TC	**84.4**	15.6	90.8	12.4	**5.8**	10.2	2.8	4.3

Table 4. Results comparison between different model for segmentation performance

2.9 Survival Prediction

Survival prediction in brain tumor is a task which referres to the process of segmenting and after that of being able to predict the time that a patient with a specific tumor has to live or even just being able to tell if this patient is going to live or not.

As mentioned above, the prediction is made based on the segmented image therefore we need to have a perfect and non errornes segmented tissue to predict the survival. Since the segmentation was explored previously, I will not go in details here and just skip to explaining some prediction models.

The pipeline is very simple just as shown on the picture below:

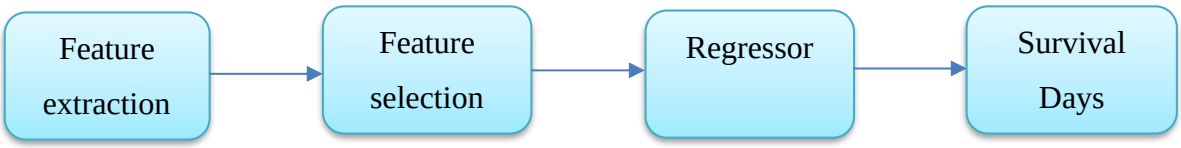

Figure 14. Piple for survival prediction

Feature extraction

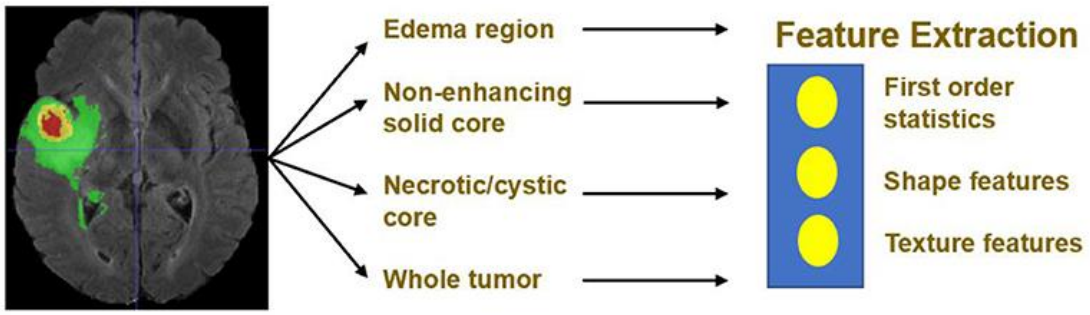

Figure 15. Features which are extracted [44]

One network example that will also be used on the experiments part of this thesis will also be the network shown below:

Figure 16. Survival Prediction network

As we can see, this network has all the pipeline stages that we need to perform the task of the brain tumor survival prediction. Firstly, it gathers the information from all picture modals such as flair, t1, t2, and t1c. Then as we can see it goes into some convolution steps and at the end it concatenates the age input from the ground truth data and at the end it predicts the days.

The reported accuracy using this model on an experimented paper and github was reported to be around 55%. [45]

CHAPTER 3

METHODOLOGY

3.1 Brain Tumor Segmentation

3.1.1 Data Preprocessing

The BraTS 2020 dataset contains 4 format of data which are FLAIR, T1, T1C, T2 and the mask which serves as a ground truth for training the model. The most useful information, the images where the features are most prominent and dominant resulted to be only FLAIR, T1C, T2 so we dicarded the information we get from T1 due to its low information provided. This helps also with the reduction of computation complexity.

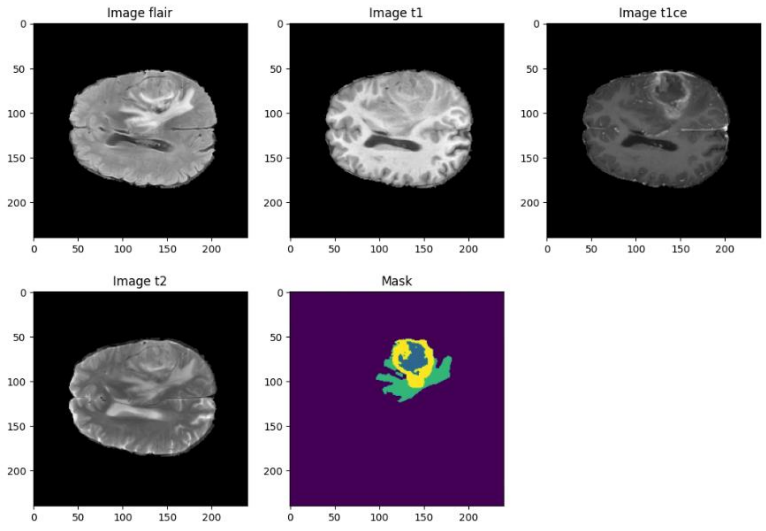

Figure 17. BRATS 2020 Dataset visualization

A combination of FLAIR, T1C, T2 into a multimatrix was used in order to combine the whole information from all the layers in the same time. By combining the data formats (can be usually found with the term modals) we create a multimodal structure which has feature from 3 different sources.

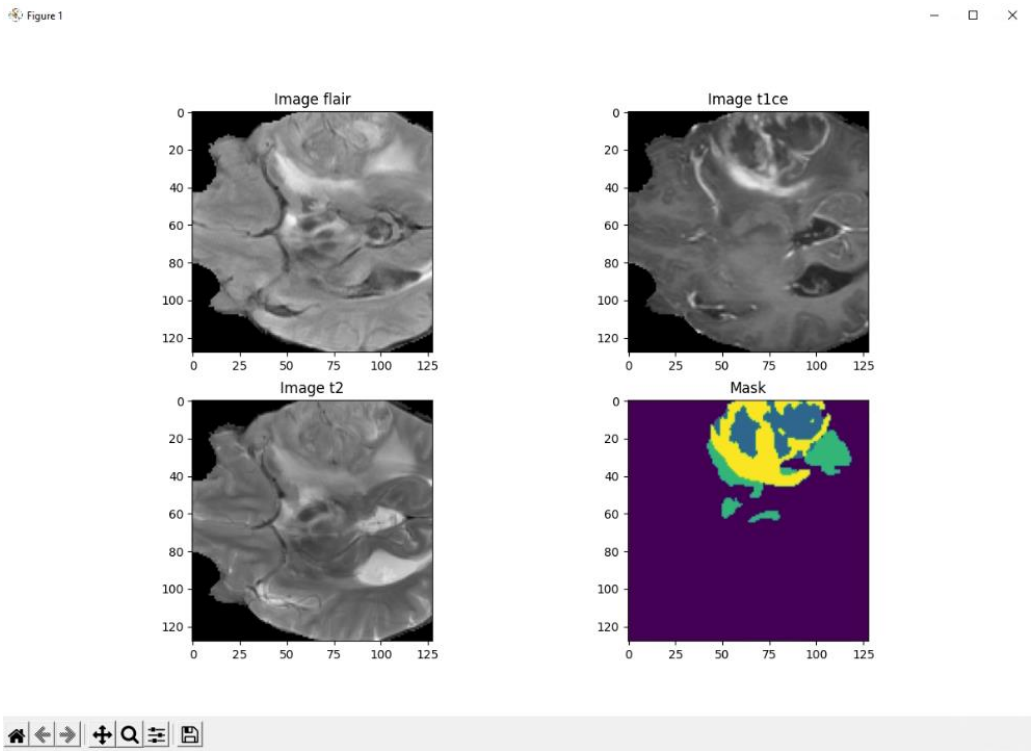

Figure 18. The datas to be used

This multimatrix then is cropped in the format 128 x 128 x128 and comverted from a nii file to a numpy array which will make the computational easier. A min-max scaler was used to scale those images while cropping them to the desired format. We also used a Standard scaler (usually found by the name of Z-score scaler) just for the sake of performance.

3.1.2 Network

The network we used was a 3D U-net network. On this network we tried to tweek the parameters such as the pooling technique from Max Pooling to Average

Pooling and the activation function even though the one who worked better was Max Pooling technique and relu function. The dropout values were also changed in order to experiment and see which produces the best result.

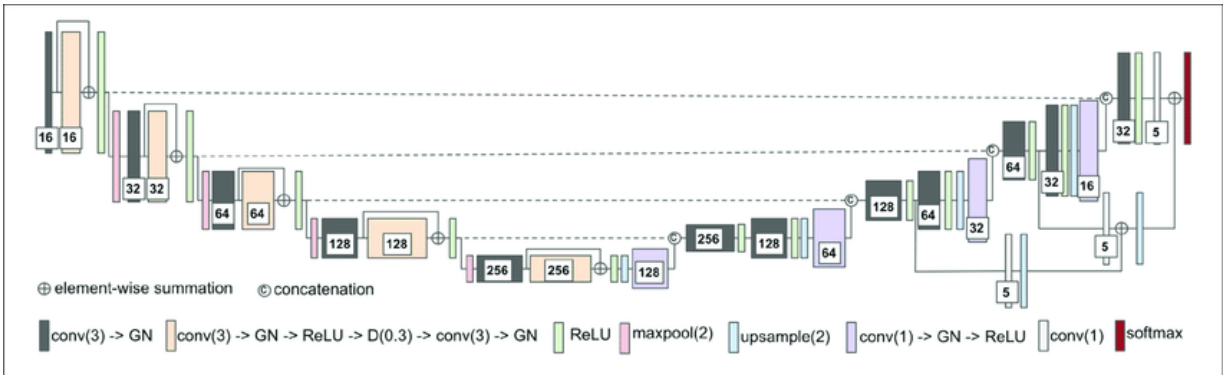

Figure 19. The network model we are using

3.1.3 Hyperparameters

To conduct the best training, we tried different batch sizes ranging from 2 – 16. It is advised that for large datasets, especially the 3D datasets, to have a smaller batch size since the computational complexity is very high and the accuracy of accuracy, loss and iou score is better measured when the batch size is smaller.

The learning rate and learning function are a big indicator on the segmentation process. This thesis will exploit two learning rates for our model. Adam learning rate with different parameters in range from 0.01 to 0.00001 and SDG learning algorithm with parameters ranging from 0.1 to 0.6.

Activation layer for inner nodes of the network we tried and most commonly we kept the Relu and for activation function of the outer layer we used a sigmoid function.

3.1.4 Visualization

In order to visualize our resuls for the segmentation process we ploted the original image divided on random slices together with the corresponding mask and segmentation. For each brain tumor segmentation there are 128 layers which are

impossible to compare one by one, therefore we created gif imgaes and small vidoes in order to compare all the slices and the segmented data in the same time one by one.

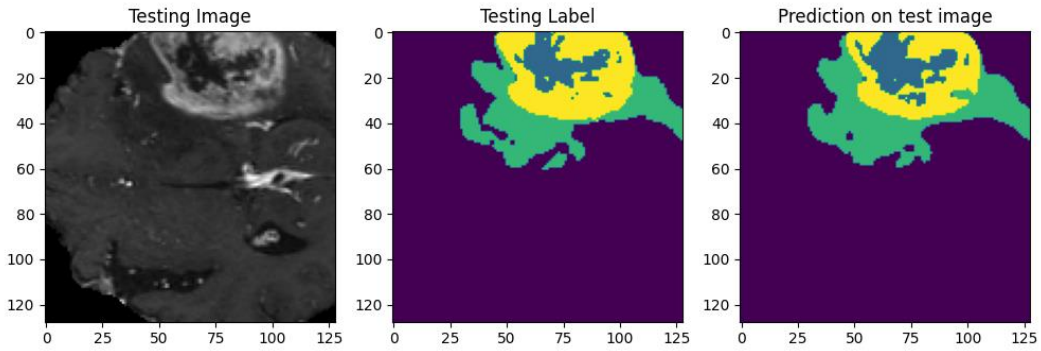

Figure 20. Example of segmented result

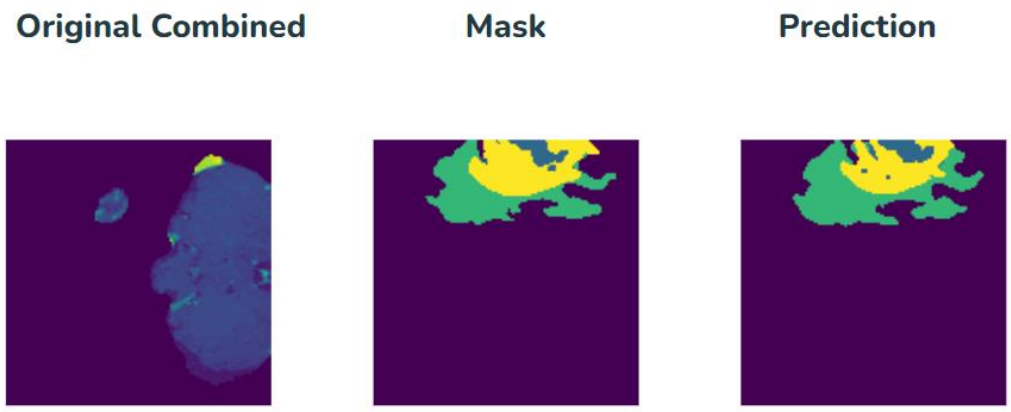

Figure 21. Generated gifs to compare all layers of mask and prediction

3.2 Shape Parameters Measurment

3.2.1 Volume measurement

The process of measuring the volume of the segmented 3D segmented brain tumor can be divided into simple steps such as:

1 – Voxel counting: Calculate the volume by counting the number of voxels within the segmented tumor region. Each voxel represents a three-dimensional pixel in the dataset.

2 – Finding the ratio between a voxel and a real-life tumor: Convert voxel count to physical units (e.g., cubic millimeters or cubic centimeters) by multiplying the voxel count by the volume of each voxel. The voxel dimensions are usually available in the DICOM header or can be determined from the acquisition parameters.

Example calculation:

If the voxel dimensions are 1 mm x 1 mm x 1 mm, and the segmented region contains 5000 voxels, the tumor volume would be 5000 mm^3

3.2.2 Surface Area

Marching Cubes Algorithm

Surface area parameter is calculated based on the 3D segmented brain tumor. The method of calculation is marching cube algorithm. This algorithm iterating every voxel of the image and creats a cube for every voxel and its 7 adjacent neighbours. This means that the cubes will intersect each other. here are 256 possible ways (or configurations) the isosurface can intersect a cube, but these can be reduced using symmetries to 15 unique configurations. Now the aim is to create a mesh that fully covers the 3D shape of the segmented brain tumor. To achieve this goal, the algorithm defines a set of triangles that approximate the surface within a cube. The next step is to connect all the traingles within voxel boxes. The connection of all triangles gives us a mesh over the whole segmented brain tumor.

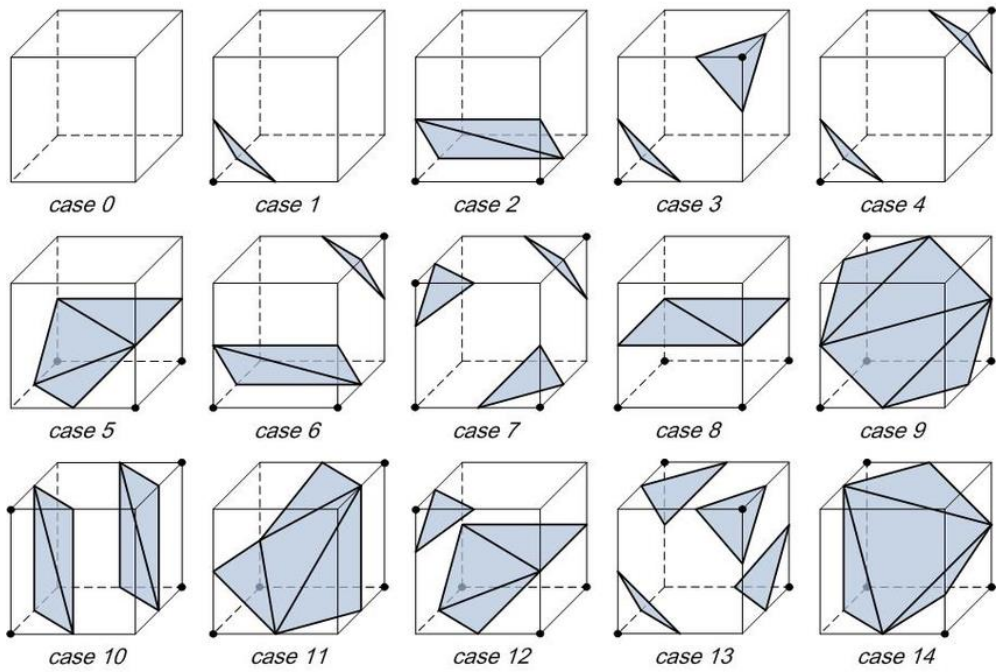

Figure 22. Marching cubes algorithm (online source [46])

Once the mesh is generated, it is very simple to calculate the surface area for the shape we are interested. The calculation is done just by summig the surfaces of all triangles on the mesh. The surface of the triangle is calculated with Heron Formulas or or vector cross product for the triangle's sides.

3.2.3 Sphericity

On this thesis, we are focused on eccentricity and how we can calculate it with different methods, but it is logically related mostly with a 2D shape rather than a 3D one. Therefore, the equivalent measurement of eccentricity for a 3D shape is sphericity. Sphericity itself if a measurement that determines how close to a perfect sphere is a shape. For a perfect sphere the sphericity is 1.

$$\Psi = \frac{\boldsymbol{\pi^{\frac{1}{3}}(6V)^{\frac{2}{3}}}}{A}$$

where

V → is the volume measurment on the first section

A → is the surface area which is measured using marching cube es explained in the previous section.

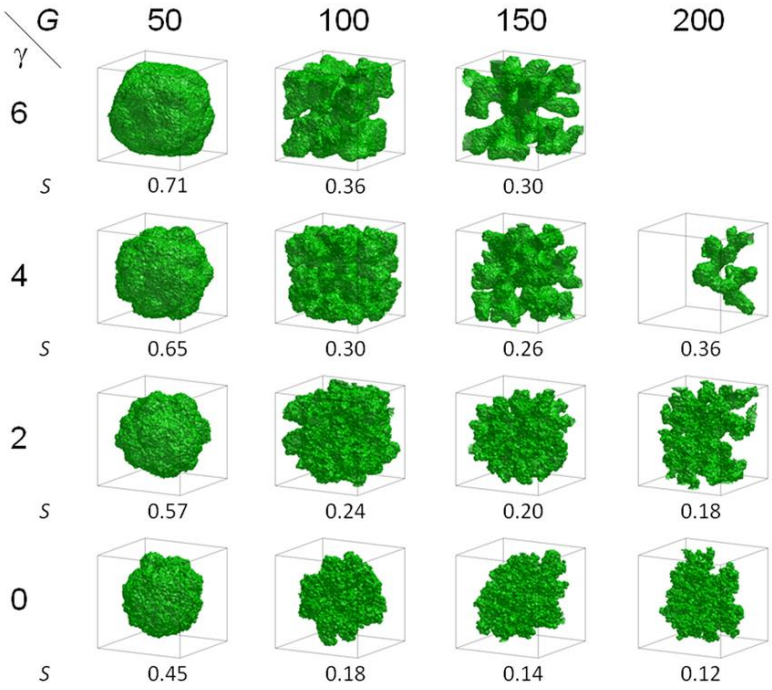

Figure 23. Sphericity values for tumors. [47]

3.2.4 Bounding Box Volume and Extent

Bounding box volume is a measurement that finds the volume of the most well fitted box that contains the whole segmented brain tumor inside. This parameter might not look that it has a straight forward impact in morphologic analysis of a brain tumor, but in fact, it impacts it in an indirect way. Since we have the brain tumor volume itself and the volume of the bounding box, we can measure the extent. The extent will be the ratio between both volumes. For instance, if we have a shape which has many elonganated slim parts extened out of the core tumor, it means that the bounding box volume will be much higher than the volume of the shape itself. This leads to an optional calculation for the sphericity and eccentricity of a 3D shape.

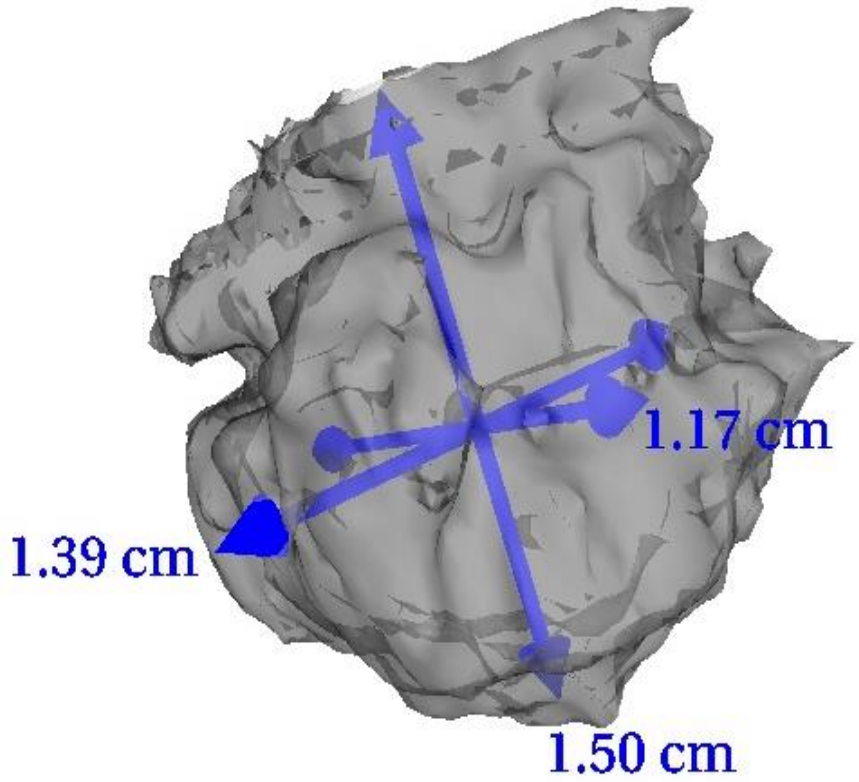

Figure 24. Extent visualization [48]

3.2.5 Eccentricity with Area and Perimeter on each slice

All the methods above calculate the shape parameters on a 3D shape, what if we switch our focus to 2D images to calculate each slice of the brain tumor?

The shape parameter that I want to focus on my thesis is eccentricity and ways how we can measure it. Inspired by the bounding box volume and extent calculation, eccentricity of a 2D slice can be calculated based on the surface and perimeter of segemented tumors. Basically, if the ratio of area over the perimeter is large it means that the brain tumor image has a much larger area than perimeter, it means that the tumor is more contained and does not have many extensions. On the other hand, if the ratio is smaller, it means that the perimeter is bigger. Logically this means that the tumor has many extended parts.

$$EccentricityAP = \frac{A}{P}$$

Where A is the area of the segmented slice and P is the perimeter of the segmented brain tumor.

3.2.6 Eccentricity with SVD of random points on the contours

Performing the singular value decomposition over some random points over the contours of the segmented brain tumor, means that we have to execute two processes. The first one is to identify the contours of the shape and then select some random points on those contours. The tricky part here is that a brain tumor can have disconnected segmented shapes and the random points would converge to one contour which could be the smallest one. If it is the smallest contour, it will not capture the most problematic brain tumor part. In my experiments I have always taken the largest contour to avoid the above-mentioned problem, even though it is partially correct, since a part of the small contour which can be far away can have some impact on the eccentricity. Anyway, since here we are dealing with slices, that small contour will

somehow be conneted to the full body of tumor. Later on, when we calculate the whole mean, the contribut the small contour has will be taken in consideration.

Contours are found by using the measure library of python which provides a method to find all the contours.

The higher the number of random points selected, the higher will be the the chance to capture the extension of the tumor, therefore I have tested with 16, 32 and 64 random points for each contour.

A matrix constructed with the values of the random points selected is decomposed with SVD. The result of the SVD contains the ∑ matrix which contains the energetic values for that matrix.

The formula used for eccentricity is as below:

$$Eccentricity1 = \sqrt{1 - (\frac{\sigma[1]}{\sigma[0]})^2}$$

3.2.7 Eccentricity with SVD for each whole slice

Eccentricity is a measure of how much an object deviates from being perfectly circular. In the context of image analysis and using Single Value Decomposition (SVD), eccentricity can be calculated from the singular values obtained through SVD. The eccentricity can be computed as the ratio of the largest singular value to the smallest singular value.

$$A=U\cdot\Sigma\cdot V^{T}$$

Σ is a diagonal matrix where the singular values are arranged in descending order. Eccentricity (e) is calculated as the ratio of the largest singular value σ_{max} to the smallest singular value $\sigma_{min.}$

$$\text{Eccentricity (e)} = \sigma_{max} / \sigma_{min}$$

Regarding the technical part of implementing this theory I have used the linalg.svd method of the numpy library. The difficulty here stands that the model that I segment is a 3d shape specifically 128 x 128 x 128 and the calculation of the SVD can be performed only in two ways:

- Calculate SVD of each slice regarding one axis for each class of the tumor

After calculating the svd, I need the S matrix. Since it is a diagonal matrix, the numpy library has simplified the view of it by just producing an 1d array representing the entries of the original diagonal matrix. To calculate the eccentricity, we need to perform a simple ratio. Since we always know that the first element of the S matrix will be the biggest one we can perform a ratio like this formula: s[0] / sum(s), there are two cases:

- The matrix is eccentric: since there are 128 possible slots for matrix S values and for a matrix to be eccentric it needs to full fill the following formula: x / x*n (where x is a value which is same for all entries and n is 128, number of possible slots) By simple math reduction we can deduce that if the value of the ratio is around 1/128 the matrix is eccentric and basically the tumor is very contained an not distributed in extensions.

- The matrix is not eccentric: we have a ratio which is bigger than 1/128.

In my thesis I have measured the eccentricity with two methods.

- The ratio of the major axis over the sum of all axis:
- (% of energy in the first element)

$$Eccentricity2 = \frac{\sigma[0]}{\sum_{i}^{128} \sigma[i]}$$

- The ratio of major and minor axis as on the equation on the above section.

3.3 Experiments

The experiments that were tried for this thesis were concentrated on the segmentation and volume measumerments of the segmented tumor part.

Below, there is a table with all the hyperpameter for our trials.

First Batch of trails

Version	Batch Size	Epochs	Optimizer	Threshold	Pooling Layer	Activation Function	Learning Rate
V1	2	100	adam	0.5	max pooling 3D	Relu	0.0001
V6	2	100	adam	0.5	avg pooling 3D	Relu	0.0001
V7	8	100	adam	0.5	max pooling 3D	Softrelu	0.0001
V8	2	100	sgd	0.5	max pooling 3D	Relu	0.0001
V9	2	100	rms	0.5	max pooling 3D	Relu	0.0001

Table 5. First batch of Trials

This training time for this batch of trials took from 1 hour and 30 minutes to 2 hours per each trial.

Second Batch of trials

Version	Batch Size	Epochs	Optimizer	Threshold	Normaliza	Activation Function	Learning Rate
V10	4	100	adam	0.5	Z - Score	Relu	0.0001
V11	4	100	adam	0.5	Z - Score	Relu	0.001
V12	4	100	adam	0.5	MinMax	Relu	0.001
V13	4	100	adam	0.5	MinMax	Relu	0.001
V14	4	100	rms	0.55	MinMax	Relu	0.0001

Table 6. Second batch of trials

This training time for this batchof trials took 2 hours per each training.

SVD Experiments

The first experiment I conducted was firstly made on a mask rather than just the segmented model itself. This decision was made because the mask has a more accurate segmentation. If the experiments work with this then we can safely apply the method into the segmented part.

Python only allows to use the singular value decomposition on 2D data and therefore we needed to work only on slices. The segemented data array is a 4D matrix which has information about all the pixels and the last dimension is about the class to whom that data belong to. Since we have 4 classes I experimented with all of them except the background class which does not fall in the scope of our interest.

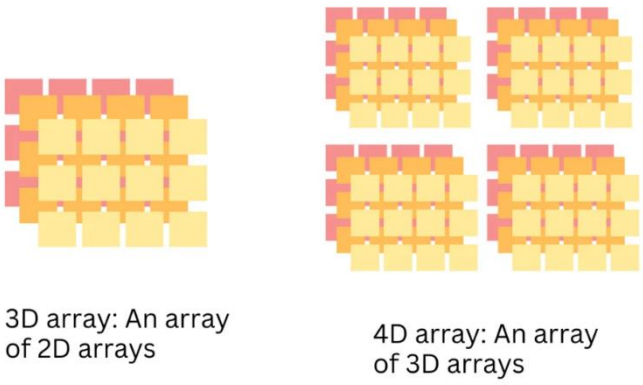

Figure 25. Representation of 3D and 4D arrays in programming

If we keep one of the classes fixed on the 4D matrix, we still have a 3D matrix where we cannot apply singular value decomposition so we need to determine which axis we have to keep fixed. Through many trials and erros on this table I have tried to summarize the best combination for each class:

Class	X - axis fixed	Y – axis fixed	Z - axis fixed
1	Not much information provided	Many 0 values, not stable	When the ratio is high, tumor parts are spread all around. Low ratio, small dots.
2	Not meaningful combination	When eccentricity is just an empty circle, eccentricity is small (0.1) but if it is a shape we have a higher value of eccentricity (0.4)	Not meaningful combination
3	Same deduction as 2Y	Same deduction as 2Y	Same deduction as 2Y

Table 7. Combinations of all axis and classes to perform 2d arrays

Ratio formula I used for the svd:

$Sigma_{Max}$/ Sigma[0 - n]

Basically, just the ratio of the biggest Sigma value over the whole sum of sigma.

Python creates the sigma matrix in a very creative way by giving us only one array with sorted data. The detail that I noticed is that when the tumor is bigger, more array positions are filled with a value which is meaningful (not zero).

While applying the SVD to the entire slice of the segmented brain tumor, I have applied also another formula except the ratio one. This formula is described on the section 3.2.7, formula number 2.

SVD of random points over the contours.

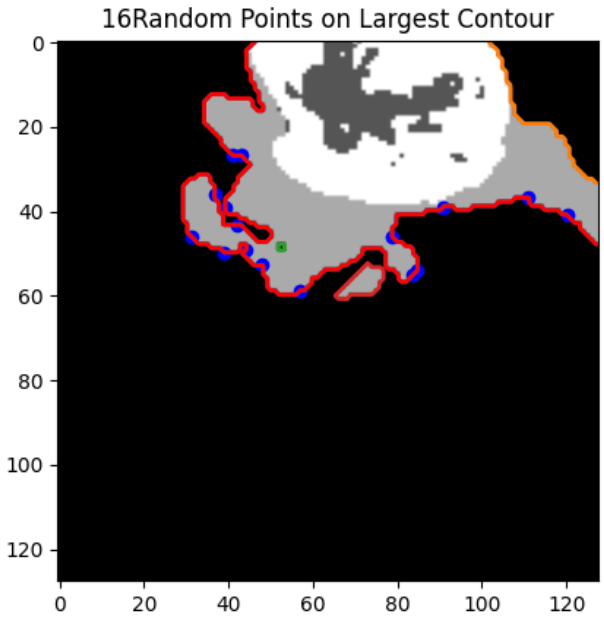

Figure 26. Blue points are the random points generated over the contour.

Since the perimeter of the contour can be large, I have experimented with different number of random points such as 32 and 64 to have a higher coverage. Here are the random points generated:

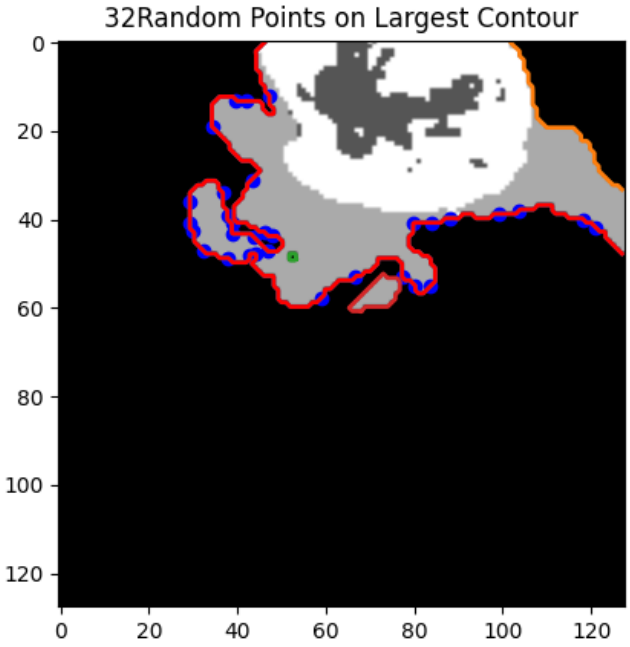

Figure 27. 32 Points generated over the contours.

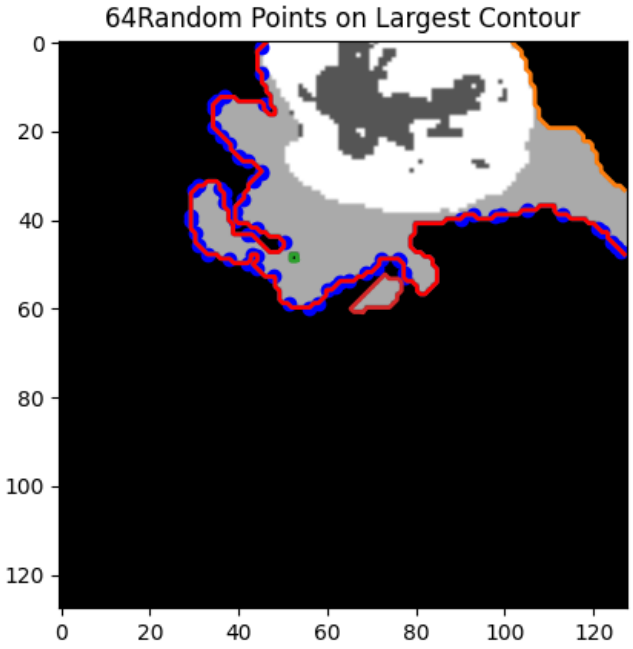

Figure 28. 64 points generated over the contours.

3D Shape parameters experiments

Experiments are made for all the segmented brain tumor parts and csv files are generated for each of the metric measured. The explanation of each method is made on the previous section and the results are found on the results section.

3.4.1 Survival Prediction

There are different ways to predict the survival of brain tumor diagnosed patient, through machine learning.

Classification

The classification of the survival prediction is made by firstly training the model shown in the picture:

Figure 29. The network for survival prediction

For this model we will use the segmented dataset slice by slice since the model for the survival prediction is only 2D and does not accept 3D segemented data. In this case this is good for us since we can measure the eccentricity only through 2D arrays.

CHAPTER 4

RESULTS AND DISCUSSIONS

4.1 Results

Segmentation

The results that are achieved until now for this thesis can be reported to be on the values of an achieved accurarcy of 99%, the metric of dice loss + (1 * focal loss) resulted to be 0.77, the iou score for the best last epochs run was 0.8 and the meanIou for one of the best trails is reported to be 0.8102. (cross binary)

Below we can see two diagrams which plot the training and validation accuracy through scaning the dataset and training the U-net on one of our best runs. While the other graphic shows the training and validation loss through the training process while scanning the dataset and training the U-net with the specified hyperparameters.

Figure 30. Training and validation graph for accuracy

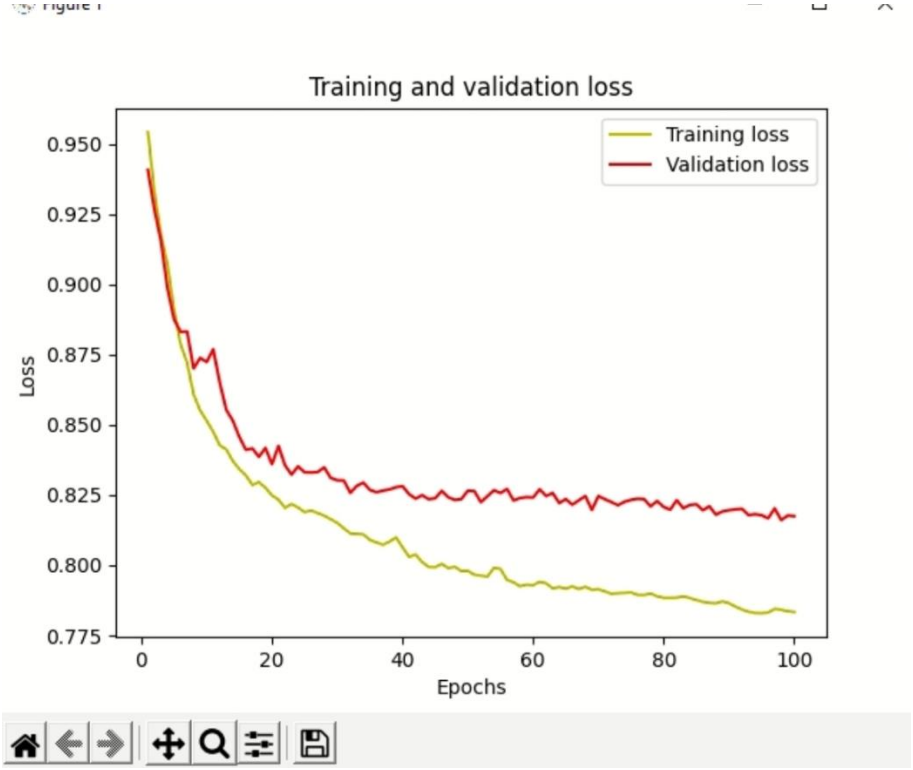

Figure 31. Training and validation graph for loss

Best achieved results with 3D unet for brats2020 dataset segmentation challenge:

	Accuracy	Dice loss + 1*focal	İou score
Best achieved	0.99	0.77	0.8

Mean Iou: 0.8102

Visual Results

The following results will be shown as two results for the same brain tumor dataset. The first picture will be from slice number 65 and the other one from slice 55.

Testing Image 1

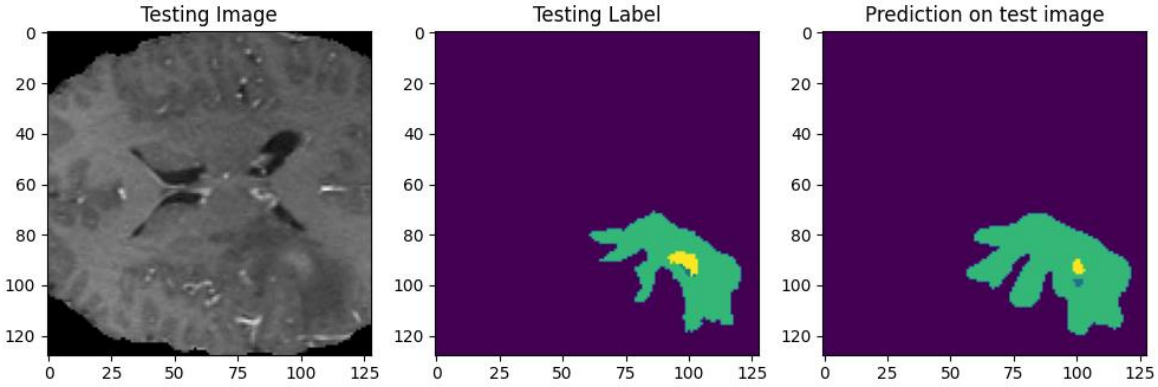

Figure 32. Slice 65 for brain tumor segmentation 1

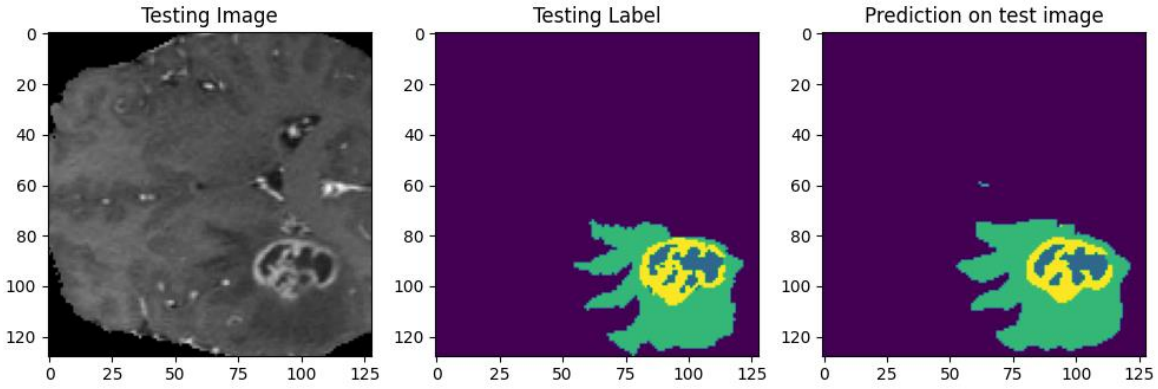

Figure 33. Slice 65 for brain tumor segmentation 1

Testing Image 2

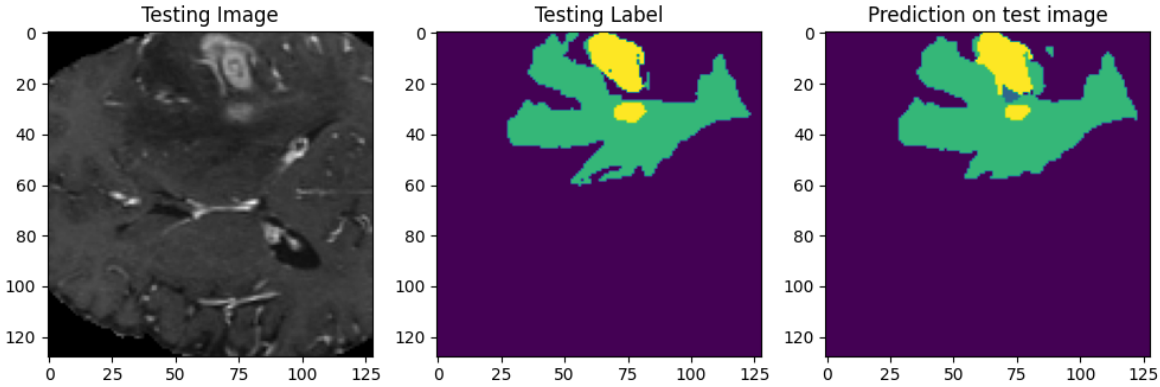

Figure 34. Slice 65 for brain tumor segmentation 2

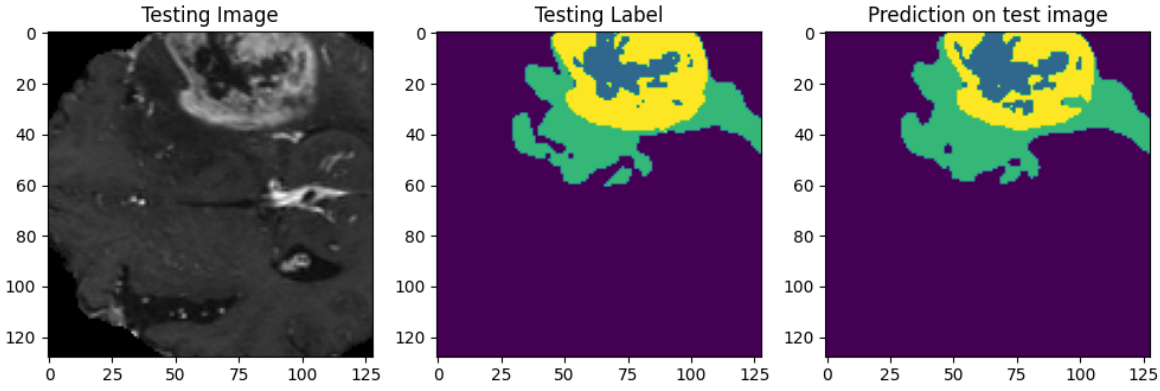

Figure 35. Slice 25 for brain tumor segmentation 2

Volume

The normal volume of the brain is around 1300 cm^3. Every value of tumor volume we got was inside a logical range depending on the tumor size and shape from the segmentation masks. For smaller tumors we got values like 33 cm^3 and for larger tumors we got bigger volumetric values such as 600 cm^3. If we imagine the tumor mass as a perfect sphere with radius of 2 cm, by spehere volume formula we can calculate the volume which will be around 33 cm^3. Comparing this with the segmented tumor makes common sens. To be more accurate, for the dataset we are using there are no labeled data to check the correct volume of the tumor.

3D Segmented brain tumor shape measurement

Volume	Surface Area	Sphericity	Bbox volume	Extent	Figure number
202	226.4797723	0.735115564	525	0.384761905	#100
71531	17237.77869	0.483428617	252168	0.283664065	#100
1	1.732050505	2.792052454	1	1	#100
16	37.97396263	0.808620712	25	0.64	#100
1	1.732050505	2.792052454	1	1	#100
38009	8840.118752	0.618420182	157920	0.240685157	#110
1	1.732050505	2.792052454	1	1	#110
9	20.41348344	1.025011355	18	0.5	#110
157878	29254.8748	0.482873781	520768	0.303163789	#111
1	1.732050505	2.792052454	1	1	#111

Table 8. Results of the 3D Shape Measurments.

As it can be seen from the table, the figure number is replicated sometimes in the table. This happens because sometimes python segements the volume in components if they are not connected with each other.

Eccentricity Surface and Perimeter of 2D Slice

Since we are dealing with 2D slices, I have saved the information for all the slices of each image and then calculated their mean eccentricity.

For image with number 111 in the dataset, here is the table for each slice with surface, perimeter and eccentricity calculated based on them:

Surface	Perimeter	Eccentricity A/P
3.57E+02	3.05E+03	8.55E+00
3.67E+02	3.11E+03	8.48E+00
3.55E+02	3.13E+03	8.81E+00
3.75E+02	3.19E+03	8.51E+00
3.81E+02	3.23E+03	8.47E+00
4.03E+02	3.24E+03	8.04E+00
4.32E+02	3.29E+03	7.61E+00
4.75E+02	3.36E+03	7.08E+00
4.92E+02	3.42E+03	6.95E+00
5.18E+02	3.48E+03	6.71E+00
5.18E+02	3.55E+03	6.86E+00
4.89E+02	3.64E+03	7.44E+00
4.77E+02	3.71E+03	7.79E+00
4.99E+02	3.73E+03	7.48E+00
4.89E+02	3.74E+03	7.64E+00
4.99E+02	3.70E+03	7.41E+00

Table 9. Values of surface, perimeter and eccentricity for slices from slice 45 – 60.

Average eccentricity for image 111 is 3.22.

Eccentricity with Random points per slice

16 Random	32 Random	64 Random
9.49E-01	8.94E-01	9.27E-01
9.67E-01	9.64E-01	9.74E-01
9.53E-01	9.62E-01	9.58E-01
9.64E-01	9.49E-01	9.51E-01
9.56E-01	9.60E-01	9.49E-01
9.66E-01	9.56E-01	9.48E-01
9.67E-01	9.35E-01	9.51E-01
9.39E-01	9.25E-01	8.61E-01
7.93E-01	8.10E-01	8.72E-01
8.62E-01	7.77E-01	7.89E-01
9.10E-01	8.25E-01	8.85E-01
8.93E-01	9.03E-01	8.72E-01
8.52E-01	8.38E-01	8.34E-01
7.86E-01	8.25E-01	7.99E-01
8.64E-01	7.82E-01	7.88E-01
7.88E-01	7.81E-01	8.09E-01

Table 10. Eccentricity with random points for image 111 for slices 45 – 60.

Mean eccentricity for 16 random points: 5.03

Mean eccentricity for 32 random points: 4.9

Mean eccentricity for 64 random points: 5.59

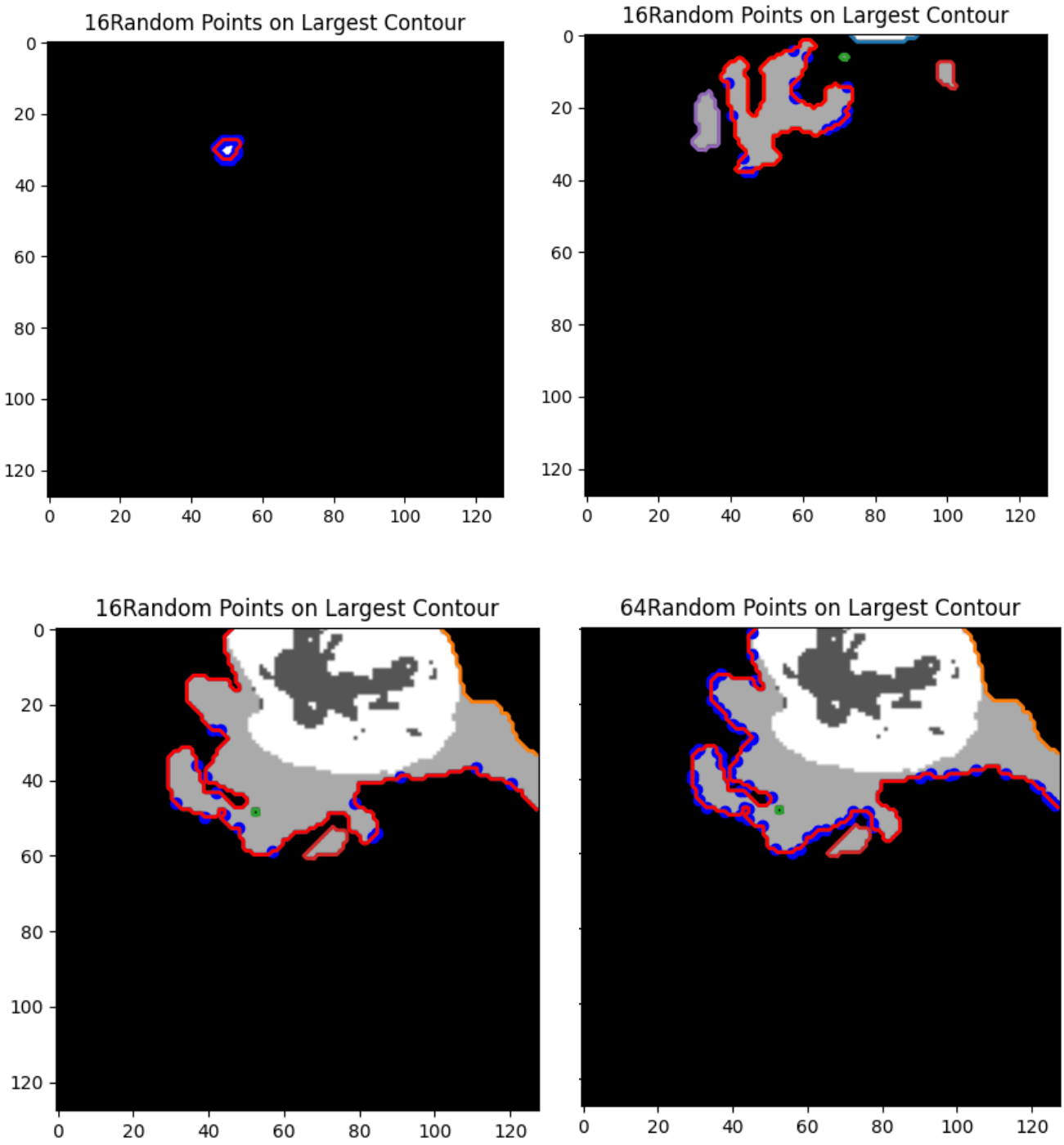

Figure 36. Different images for 16 points on different contour lengths

Eccentricity measurement with SVD on full slice

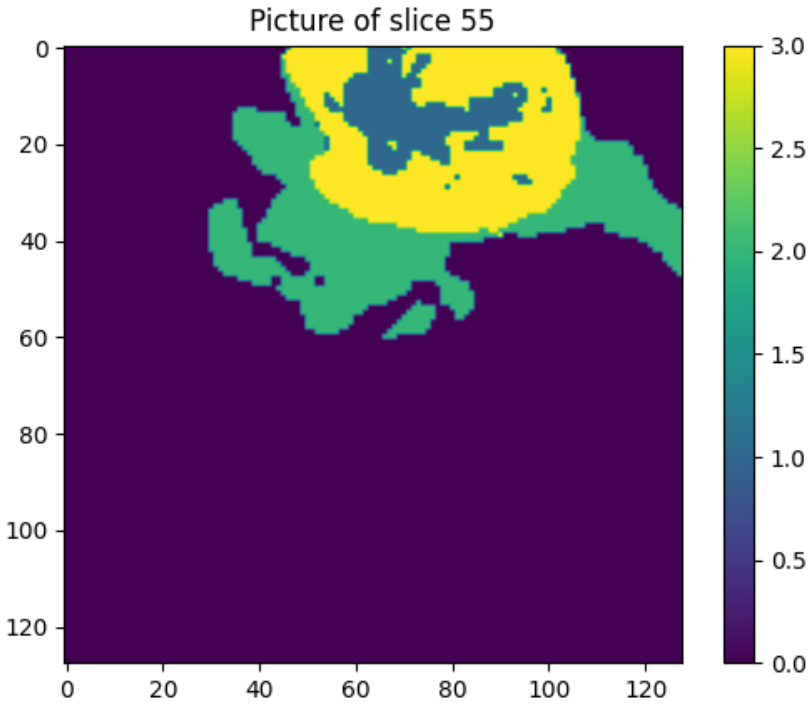

Figure 37. Representation of the 55th slice from the mask of a picture from the dataset

The S matrix for this slice has those values:

Check Apendix 1 for the full sigma array

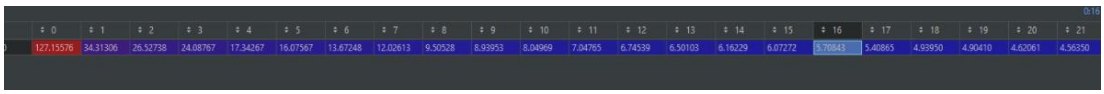

Figure 38. Screen Capture of the sigma array produced by the operation

The ratio value for the formula described earlier is: 0.287553
60 Slots have a value rather than 0.

Now lets see another slice:

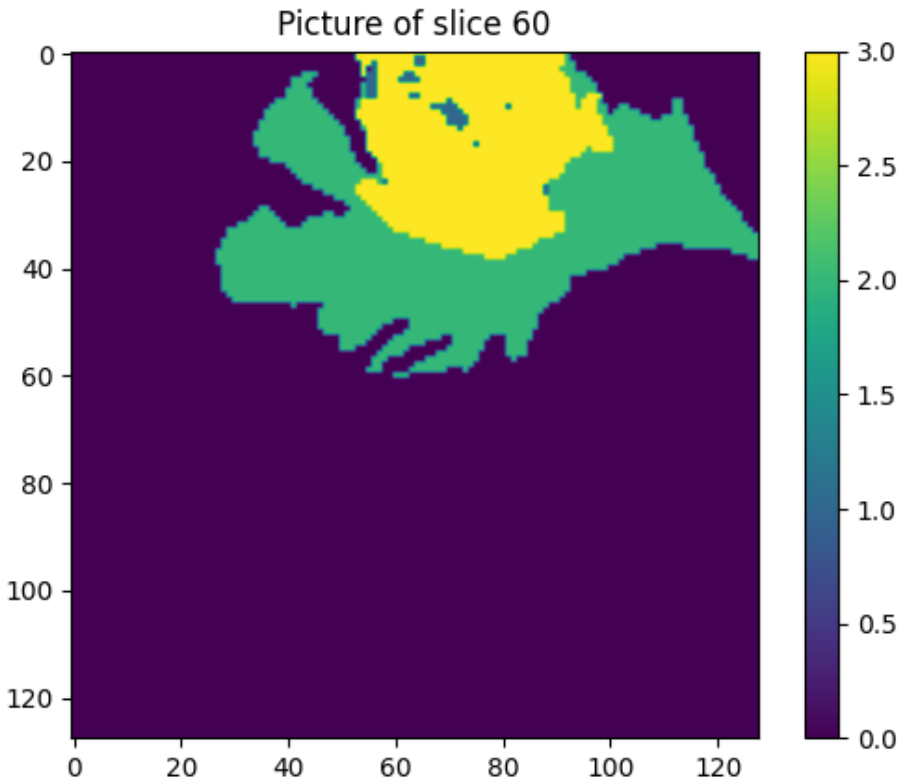

Figure 39. Representation of the 60th slice from the mask of a picture from the dataset

As an eye checking result, we can see that differently from the slice 55, this slice has a bigger green zone.

Ratio value: 0.3210913

Check Apendix 2 for the full sigma array

Now we are going to see another experiment where we have a very small part of a segmented tumor:

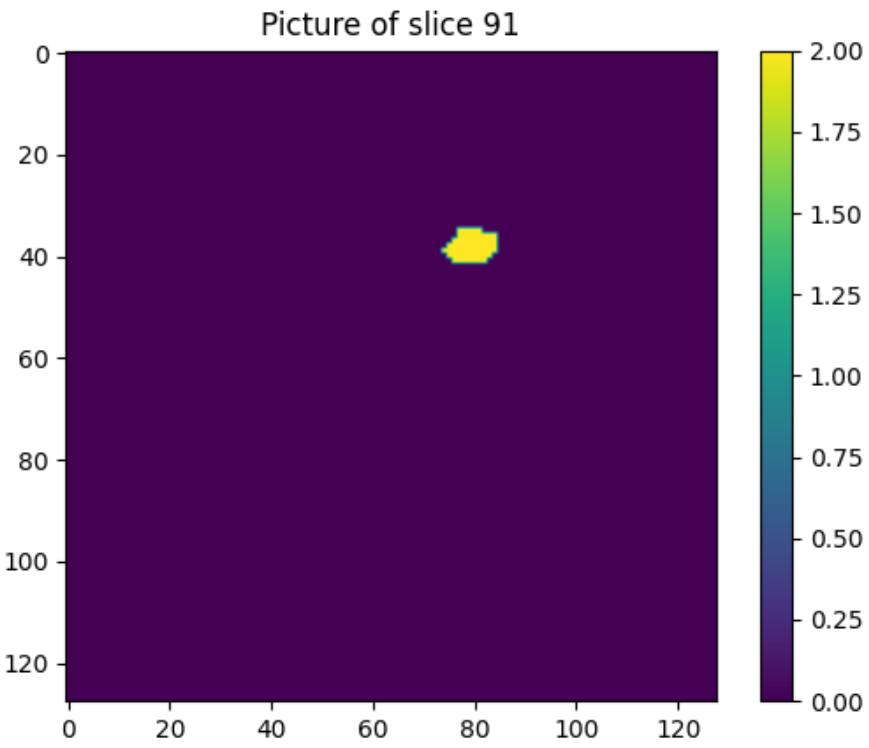

Figure 40. Representation of the 91th slice from the mask of a picture from the dataset

Ratio value: 0.5593745

Slots other than value 0: 7

Check Apendix 3 for the full sigma array

Based on those experiments, we can see a correlation between the tumor size and the number of array positions which have a meaningful value. Together with the ratio value we can deduce that some thresholds must be applied in order to classify if the tumor is growing or not.

Slice number	Ratio Value	Positions filled	Description
55	0.28	60	The tumor is round but big
60	0.32	57	Tumor is a little bit more spread out but has a smaller surface
91	0.55	7	Tumor is just a small dot

Table 11. Eccentricity ratio and slots number correlation

From the data of this table, we can deduce that when the number of positions filled is above 50 and the ratio eccentricity is more than 0.25, the tumor is more aggressive.

Ratio with Sum Eccentricity	Ratio of minor and major eccentricity	Mahotas Eccentricity
2.91E-01	9.68E-01	8.73E-01
2.82E-01	9.67E-01	8.69E-01
2.92E-01	9.65E-01	8.64E-01
2.81E-01	9.64E-01	8.48E-01
2.74E-01	9.65E-01	8.30E-01
2.68E-01	9.66E-01	8.18E-01
2.63E-01	9.66E-01	7.97E-01
2.59E-01	9.64E-01	7.75E-01
2.65E-01	9.63E-01	7.60E-01
2.69E-01	9.64E-01	7.57E-01
2.81E-01	9.65E-01	7.64E-01
2.88E-01	9.63E-01	7.74E-01
2.93E-01	9.63E-01	7.79E-01
3.00E-01	9.68E-01	7.78E-01
3.04E-01	9.73E-01	7.83E-01

Table 12. Eccentricity methods for the full slice svd for slices 45-60.

The mean eccentricity for all images is represented on the table below

Ratio with Sum Eccentricity	Ratio of minor and major eccentricity	Mahotas Eccentricity	Image number
0.145747889	0.416032775	0.334500211	#100
0.127890761	0.339171493	0.297804826	#110
0.189691345	0.572087309	0.509905143	#111
0.218996432	0.600043155	0.476401119	#113
0.188667938	0.497198241	0.468178587	#114
0.122620123	0.405365221	0.382847975	#12
0.171056032	0.530257949	0.430343945	#120
0.163126553	0.381028782	0.289976841	#126
0.170822489	0.436223726	0.288199538	#130
0.183370699	0.537039667	0.315709561	#132
0.175902065	0.525177662	0.477734682	#133
0.167025161	0.536912326	0.427966646	#137
0.176725824	0.528833632	0.281620153	#142
0.152114077	0.43664355	0.373223468	#145
0.237396535	0.691711694	0.685885625	#147

Table 13. Mean eccentricies for some images

Survival Prediction Model Training

First run:

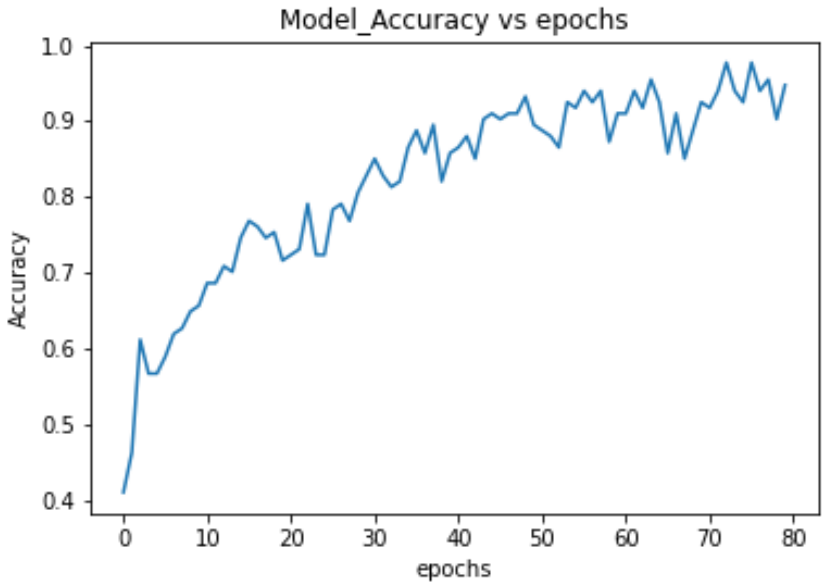

Figure 41. Model training for survival prediction parameter accuracy

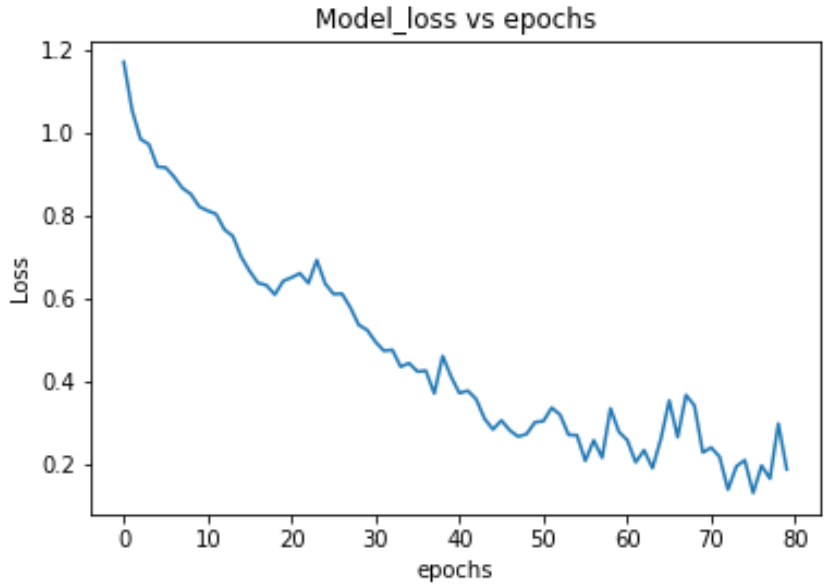

Figure 42. Model training for survival prediction parameter loss

Results for survival prediction training model:

Run #	Accuracy	Loss
1st run	0.97	0.3
2nd run	0.98	0.4

Table 14. Results of survival prediction model

	Survival Pred.	Eccentricity Ratio Sum	Slots of σ	Volume
Img 1	Yes	0.11	2	0.2 cm^3
Img 2	Yes	0.98	0	0 cm^3
Img 3	No	0.40	63	10 cm^3
Img 4	Yes	0.16	3	0.4 cm^3
Img 5	No	0.30	57	6 cm^3
Img 6	No	0.38	65	8 cm^3

Table 15. Correlation between survival prediction and Eccentricity of ratio sum, slots and volume.

4.2 Discussion

During the work with this thesis, it was found out that the way of how the brain tumor is segmented is very important for the whole after process such as volumetric and eccentricity measurement. This happens because the measurments are done based on the segmented part.

The best way to measure the volume of the brain tumor is by counting the voxels in the segmented tumor part and then multiplying the voxel with a real-life representation. Basically, each voxel that has a different color from the background is counted as a tumor voxel. The voxel size is then translated to real life units and the the volume is found. Volumetric data for the tumor are a big indicator of severity of the tumor.

By eccentricities with svd experiments, we need to add some constraints when we measure the eccentricity of the tumor. For instance, slice 90 has a bigger ratio value by which we can deduce two things:

1) the energy intensity of the segmented part is concentrated in a very few pixels and the ratio is very big when we have few pixels labeled as brain tumor.

2) The number of slots which have a value other than 0 determines the size of the segmented tumor. A bigger number of slots with a meaningful value, the bigger the size of the tumor.

3) Since the S matrices which have more slots with value other than 0 produce a lower ratio rather than the ones which have less slots it means that we need to create a threshold in order to qualify if a tumor is risky or not.

Threshold

Each Slice has dimensions 128 x 128 and the sigma array that we produce is 128, and by the experiments it was observed that when half of the slots have a meaningful value (other than 0 value) the segmented brain tumor part is considerably large. Basically, every number of slots from 50 and above is considered to be a huge tumor. Considering the ratio, when we deal with 50 or more occupied slots, and the ratio is between 0.2 – 0.4 the tumor can be considered as huge, meanwhile if we have a lower number of occupied slots, we can raise the threshold of ratio. From this we can deduce that ratio and number of slots are in a indirect relation which means that when we have a larger number of slots, the ratio is lowered but when we have small number of slots the ratio is higher. Further experiments need to be done in order to understand the practical thresholds and specific values.

Even though the above explained method is promising, the more metrics we have the better it is since the measurement is more accurate. Therefore, even the 3D shape parameters are very meaningful.

CHAPTER 5

CONCLUSIONS

5.1 Conclusions

In this thesis it was aimed to create the full process of a brain tumor detection and severity measurement based on volumetric and eccentricity. The unexplored topic that this thesis is showing is the eccentricity evaluation through the singular value decomposition. Basically, if we can decompose the matrix of voxels created by the segmented brain tumor data with the SVD principles, we can find the sigma matrix which basically has information about the energetic values of the tumor. Their ration can give the eccentricity on different parts.

The segmentation was performed with the standard U-net even though we tweaked most of the hyperparameters in order to achieve the best result for the segmented brain tumor. The best way of measuring the volume of the brain tumor is by finding the real measurement representation of the voxel and the counting all the voxels in the part of the brain tumor segemted part. Then, we can calculate the volume.

5.2 Recommendations for future research

Future research is always possible on every topic that we can ever think of. In my thesis case I would suggest that if the segmented process could reach a better state than it currently is. More metrics should be added to the whole process.

There need to be more research on finding a strong relation between the brain tumor severity and if it eccentricity is a feature that provides enough information to help the survival prediction process. If those researches support the efficacity of the eccentricity ratio there need to be more experiments and studies if the eccentricity ratio, number of sigma array slots filled with meaningful information and volume correlates with an exact result of the survival prediction.

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6 Appendix

[1] Sigma array of 55th slice for figure 33

[127.15576,34.31306,26.52738,24.08767,17.34267,16.07567,13.67248,12.02613,9.50528,8.93953,8.04969,7.04765,6.74539,6.50103,6.16229,6.07272,5.70843,5.40865,4.93950,4.90410,4.62061,4.56350,4.14283,3.94744,3.85133,3.74233,3.53416,3.32100,3.21807,3.19680,3.04381,2.96552,2.76771,2.70739,2.60833,2.55643,2.31788,2.26514,2.15290,2.11348,2.07189,1.90487,1.82076,1.81399,1.73470,1.71141,1.58078,1.53456,1.43973,1.38900,1.31891,1.22434,1.19902,1.16978,0.99848,0.97363,0.83117,0.82197,0.75317,0.67078,0.41389,0.00000]

[2] Sigma array of 60th slice for figure 35

[133.47381,29.09722,27.13240,22.75600,14.98516,13.26793,11.02881,10.02789,9.41773,7.95419,7.38380,6.70393,6.08325,6.02768,5.92004,5.72740,4.96033,4.80042,4.37397,4.07011,3.94432,3.86796,3.66160,3.53546,3.31357,3.25243,3.21861,3.08692,3.04363,2.95781,2.85738,2.71521,2.59745,2.52070,2.45819,2.41575,2.22277,2.16919,2.04486,1.99347,1.90499,1.81493,1.75040,1.70077,1.64789,1.49123,1.37855,1.27302,1.24723,1.21046,1.17079,1.12888,1.02501,0.97126,0.83331,0.76777,0.72067,0.58146,0.00000,0.0

0000,0.00000,0.00000]

[3] Sigma array of 91th slice for figure 36

[14.45613,3.43415,2.70752,1.94433,1.64272,0.97418,0.68435,0.00000]

Testing Image 3

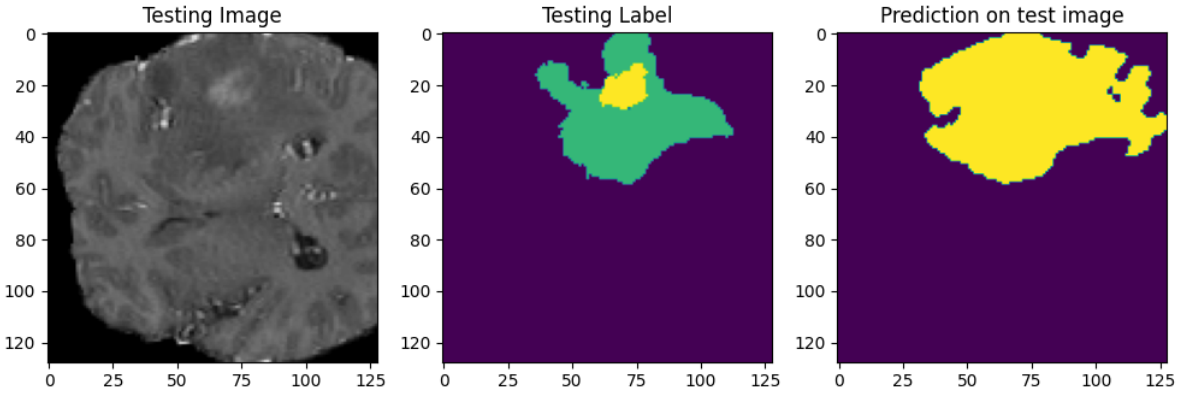

Figure 43. Slice 65 for brain tumor segmentation 3

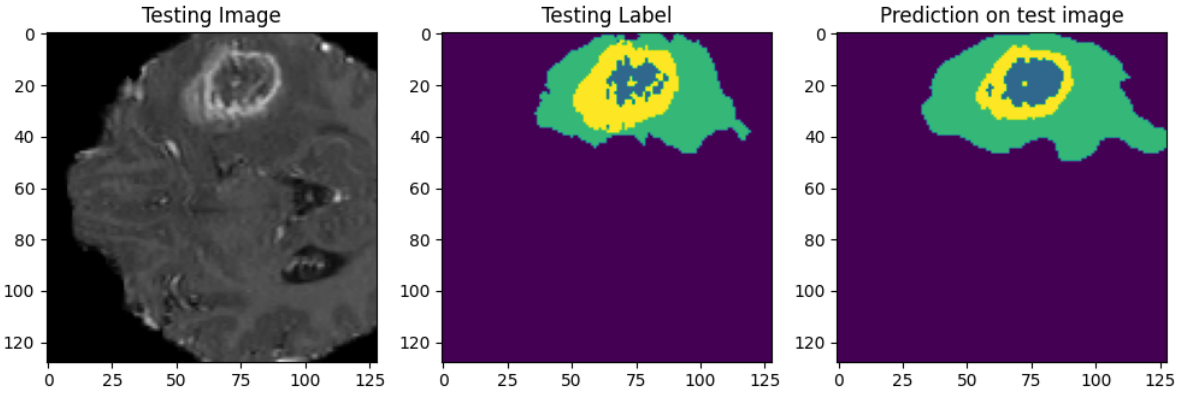

Figure 44. Slice 55 for brain tumor segmentation 3

Testing Image 4

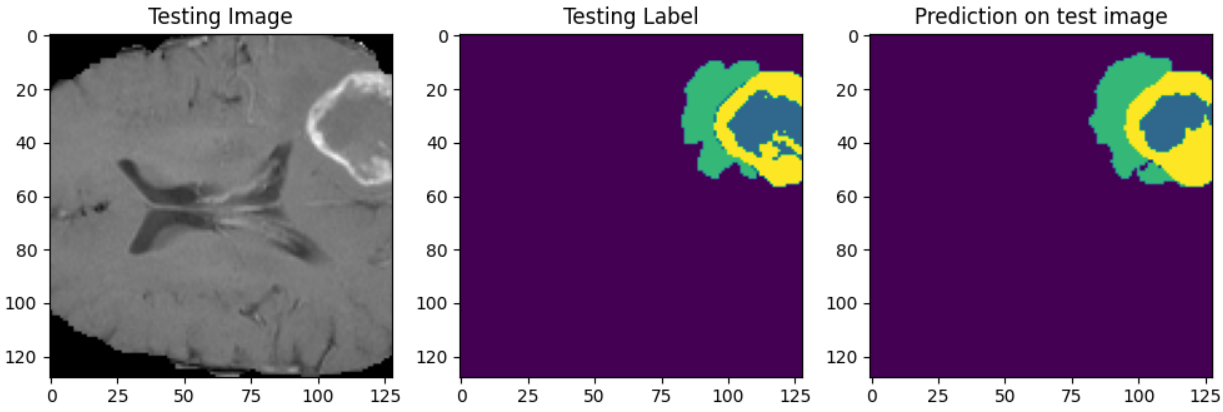

Figure 45. Slice 65 for brain tumor segmentation 4

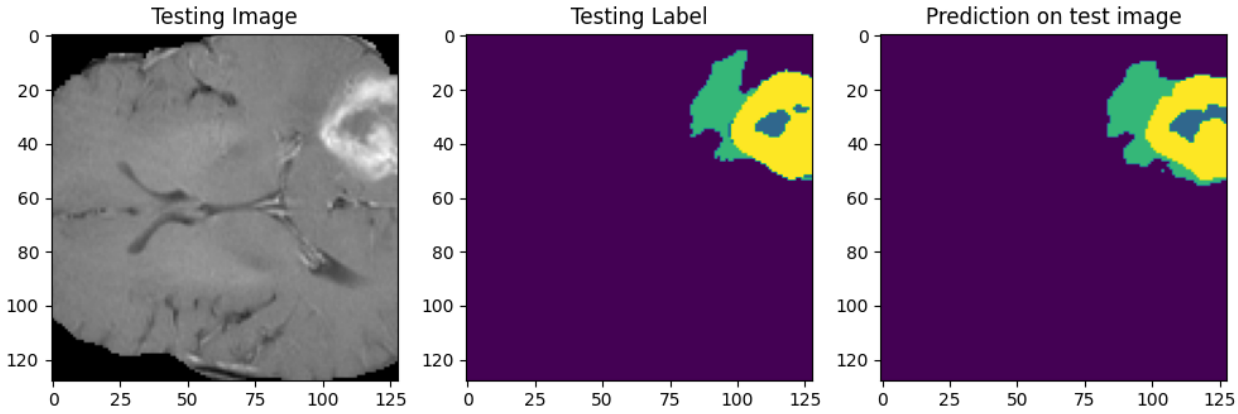

Figure 46. Slice 55 for brain tumor segmentation 4

Bad Predictions

During our experiments we had also bad results such as the below results.

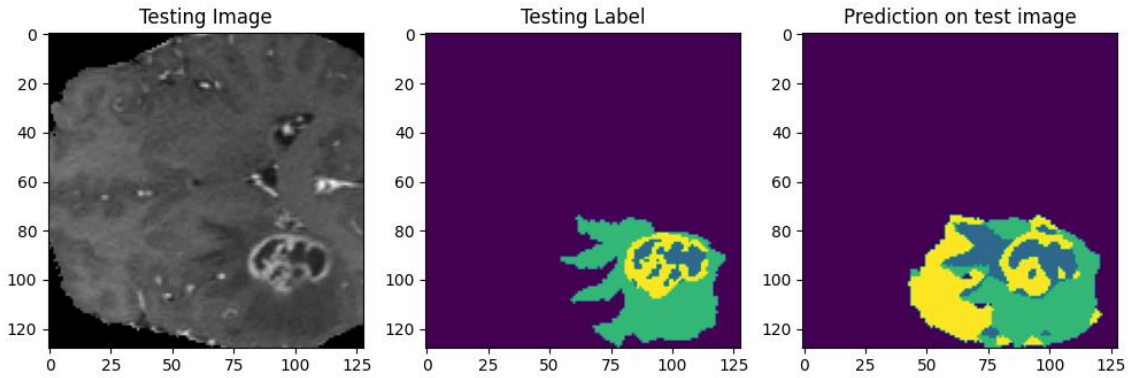

Figure 47. Bad prediction 1

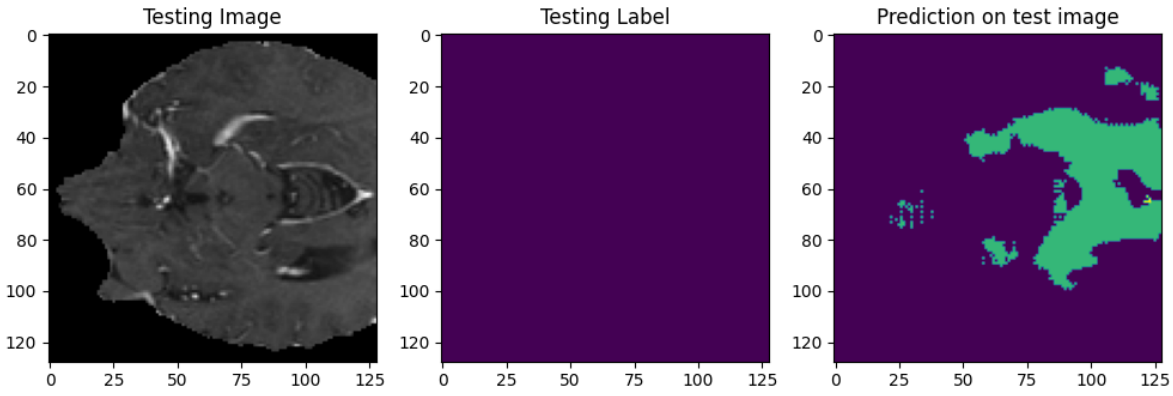

Figure 48. Bad prediction 2