

# Brain Tumor Segmentation Using Deep Learning Models

by

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Submitted to the School of Engineering and Digital Sciences  
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## Abstract

Brain tumor is the abnormal growth of cells in a brain and they can be cancerous and non-cancerous. According to how fast these cells grow they are graded from 1 to 4. If 1 and 2 grades mean that they can be treated and cells grow slowly, 3 and 4 grade brain tumors are malicious and grow fast, and grow back even after treatment. Mostly, this disease occurs across older adults, but it can affect people of any age. Detection before grade 1 or 2 brain tumors can help to provide proper medical treatment and prevent from further spread of disease to other parts of body. In this work, the deep learning model called Unet will be used for 3D MR image brain tumor segmentation for finding the region of abnormalities in the brain tissue.

Thesis Supervisor: Martin Lukac

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# Chapter 1

## Introduction

A brain tumour is a growth of cells in the brain that multiplies in an abnormal, uncontrollable way. Brain tumours are graded according to how fast they grow and their severity. Grade 1 and 2 brain tumours, which are low grade and non-cancerous, and grade 3 and 4 tumours are cancerous, high grade tumors. Cancerous tumor grows slowly and is less likely to return after proper treatment, whereas non-cancerous brain tumors grow fast and can lead to fatal cases. The symptoms of brain tumor may differ according to the affected brain part, but mostly they include seizures, headaches, mental and behavioural changes, memory loss, weakness in the body, speech problems, and etc. The danger is that the brain tumor may develop very slowly and sometimes come without any symptoms. The problem in brain tumor treatment is that many people are suffering from this disease, not all countries have proper medical experts, and high grade tumors are serious disease which is not easily treated. Average lifespan of people who were diagnoses with brain tumor is 10 years. Magnetic Resonance (MR) imaging can be used to differentiate between normal and abnormal parts [17]. Brain tumors such as meningioma can be localised and segmented easily, whereas gliomas and glioblastomas can not because that they are more diffused and hard to detect when visualizing them using MR images.

Motivation for this work is early detection of brain tumor that would allow to start proper treatment as soon as possible, prevent from further development of high grade tumor, and to prevent further development of the existing tumor to higher

grade tumor and prevent fatal cases. Even though medical doctors are skilled and have high expertise, they may have thousand of patients and sometimes may overlook the progressing illness of individuals. In addition, MRI images may have a lot of noise and it is hard to detect brain tumor progression with naked eye.

The goal of this work is to find active tumor part from MRI images, therefore this work is mainly an image segmentation task. MICCAI Brats dataset will be used for having medically approved dataset with ground truth masks. Brats MRI brain scans are saved as voxels in nifti format. 3d-Unet will be used for doing segmentation due to finding malicious tumor part using the masks as labels.

## 1.1 Terminology

Medical image classification - Different features from images are extracted and fed to machine learning models to classify it to some specific class. In other words, one image has corresponding one label or class [25].

Medical image segmentation - Different features of images are extracted to fed them on machine learning or deep learning models to find the label for each pixel in an image. For example, in the image we can identify background and a tumor part, whereas in classification task we got the result predicting whether the image corresponds to brain tumor or not. In image segmentation process image is partitioned into multiple segments [22].

Multi-modality Imaging modalities - using two or more imaging modalities to get more information. For example, using combined X-ray computer tomography with magnetic resonance imaging modalities, because each imaging modality delivers various forms of information on the morphology, physiology, metabolism, chemical composition, or molecular pathways within biological tissue, on a specified spatial and temporal scale, and with a specific detection sensitivity. No single imaging modality can address all metrics of interest connected to a biological system. Therefore, acquiring images of the same subject using several modalities can be helpful [4].

Edema - Excessive fluid buildup in the intercellular gaps of subcutaneous tissue.

Increased permeability of the microvascular endothelium can cause vascular components to leak into tissue, resulting in this condition [8].

## 1.2 Brain tumor

Tumors of the brain or spinal cord are known as brain tumors. They include abnormal neuron or glia cell growth in the cranial nerve system, the skull, the limbic system, the brain stem, or the spinal cord [9]. In the cortex, metastasis may occur. The severity of brain tumor varies widely according on its size, location, type, and stage of development at the time of identification. All of this is referred to as main brain tumor. The reason is that brain tumors are generally hidden from view because of the skull. That is why brain scan images are the only way to detect them. Another type of brain tumor is secondary brain tumor, which occurs when peripheral tumors, such as lung, breast, colon, and melanoma, spread to other parts in the body by metastasis to the brain. Primary brain tumor is one of the top ten most deadly malignancies, with more than 51,000 new cases diagnosed each year in the United States alone [9].

Although recent evidence suggests that these tumors arise either from neural stem cells or from other cells that take on many characteristics of neural stem cells as a result of malignant transformation caused by the activation of oncogenes and the inactivation of tumor suppressor genes within the cells. The cell of origin of commonly occurring brain tumors is unknown. Even if the main cause of brain tumor occurrence is not known, high-dose ionizing radiation, hereditary genetic disorders, and AIDS-related brain lymphomas are all proven risk factors for brain tumor [9].

The World Health Organization (WHO) terminology and grading criteria are used to classify these malignancies pathologically. Each of these tumor types can be histologically evaluated on a four-tiered scale of increasing malignancy from Grade I to IV. Grade I, for example, has a good prognosis after surgery, whereas Grade IV, glioblastoma multiforme, has several clinical aggressive characteristics and is usually incurable. Brain tumor types are wide and there are almost hundreds of varieties. For example, astrocytoma is the most frequent kind of brain tumor, with 75% of patients

dying within 5 years of diagnosis. Astrocytoma refers to tumors that have cytologic and histologic evidence of astrocytic differentiation and are the most common primary intracranial neoplasms. The neuropathological appearance of these patients varies greatly. On the other hand, glioblastoma, which is considered to be more dangerous brain tumor, has a median survival time of 14.6 months. Astrocytoma is Grade I, whereas glioblastoma multiforme is Grade IV tumor. Oligodendroglioma refers to tumors that show indications of oligodendroglial differentiation. Mixed oligoastrocytomas are tumors that have cells that are similar to both lineages.

A slow increasing focal neurological handicap or a nonfocal neurological illness such as headache, dementia, gait disorder, or seizure are the most typical symptoms that bring patients with a tumor developing in the brain to their doctor. Other systemic symptoms signal a tumor that has metastasized to the brain from somewhere else, as individuals with primary brain tumors rarely have systemic symptoms. Because primary brain tumors rarely exhibit any biochemical abnormalities, CT (computerized tomography) and MR (magnetic resonance) imaging are important diagnostic tools for detecting them. Mass effect, edema, and contrast media enhancement are all radiological characteristics of brain tumors. In the imaging of brain malignancies, positron emission tomography (PET) scanning and single photon emission computed tomography (SPECT) play supporting roles. Meningiomas and other slow-growing tumors can be discovered by chance on a CT or MRI scan, or they can cause a focal seizure, a slow-progressing focal impairment, or symptoms of increasing intracranial pressure [13].

Pathologists grade tumors by examining several characteristics of tumors using a light microscope. The most commonly assessed criteria are cytologic and architectural features. The nucleus size and shape, the ratio of the nucleus to the cytoplasm, and the mitotic index are all considered as cytologic properties. The tumor's histologic organization and its boundaries are considered as architectural properties. A well-differentiated tumor contains small nuclei as well as small nuclear volume compared to the entire cellular volume, a low number of proliferating cells, ordered organization in tumor architecture with well-formed glands, and well-defined tumor boundaries.



A poorly-differentiated tumor, on the other hand, contains large nuclei, large nuclear volume, a high proportion of dividing cells and disordered organization and it is hard to find tumor boundaries.

The American Joint Commission on Cancer (AJCC) has advised that most malignant tumors be graded on a scale ranging from well differentiated to undifferentiated, depending on the amount of malignant features present. The GX to G4 scale is the most used among radiologists and can be interpreted as follows: Grade X (GX) – Grade cannot be assessed

Grade 1 (G1) – Well differentiated (Low-grade and less aggressive)

Grade 2 (G2) – Moderately differentiated (Intermediate-grade and moderately aggressive)

Grade 3 (G3) – Poorly differentiated (High-grade and moderately aggressive)

Grade 4 (G4) – Undifferentiated (High-grade and aggressive)

For most tumors, the World Health Organization (WHO) experts have advocated analogous systems and instead of GX-G4 they use Roman numbers from I to IV. Sometimes grades 3 and 4 are merged in some cases, therefore a three-tiered approach may be also applied [6].

## 1.3 Brain tumor imaging

Nowadays, brain tumor is identified using different methods. One of such methods is MRI imaging. However, there are other medical imaging techniques which are available for identification of the tumor. Those methods are magnetic resonance spectroscopy, magnetic resonance angiography, magnetic resonance venography, diffusion tensor imaging (DTI), functional MRI, CT scan or CT angiography, Positron emission tomography (PET) scan, angiogram. [cite] Also, lumbar puncture (spinal tap), electroencephalogram, vision and hearing tests and brain tumor biopsy may be used [17].

The most used and conventional imaging approach for diagnosis is MRI, which is still considered to be the cornerstone of brain tumor imaging. An MRI scanner

uses magnets and strong radio waves to produce the detailed pictures of the brain from different angles. A special dye, known as contrast, might be put into the vein during the MRI, or might be given as a fluid or pill to swallow. The dye is used for getting clear pictures of the brain. It also facilitates the process of differentiating between normal and abnormal brain tissues. MRI with and without contrast is the most appropriate imaging in cases when a brain tumor is possibly developing but not diagnosed yet, where there are symptoms such as chronic headache, or new onset headache with optic disc edema, nontraumatic sudden attack of illness, probably a stroke or an epileptic fit in individuals older than 40, or focal neurologic deficit. CT scans can be utilized in an emergency room or to check for calcification in some patients [18].

If there is a need for histopathologic diagnosis, the MRI can not diagnose them. Therefore, biopsies or surgery for histopathologic diagnosis is used in case of specific diagnosis, however low and high grade lesion differentiation is more important than histopathologic diagnosing which is taken only in case of a molecular studies and surgery for treatment [18]. There is a preference of MRI to diagnose the brain tumors, because the imaging using different sequences or planar views such as 3D isotropic T1w, T2, T2w, FLAIR is recommended by the imaging protocol consensus. Other imaging methods such as PET or CT can be also useful for precise diagnosis. Surgical planning can not go without MRI, whereas DTI or fMRI imaging modalities are also can be helpful. During the cutting out of a tissue or a part of tumor, or in other words, in tumor resection, intraoperative MRI can better this process and prognosis. Postoperative imaging is needed to check up the cut off area and provide the patients with follow-up after tumor resection. The main reason for follow-up is to observe the size of enhancing or non-enhancing lesion/tumor part which can be seen on MRI TW2 or FLAIR sequences. After the surgery it is useful to take into the consideration the radiation necrosis which can have effect on brain, because the treatment, pseudoresponse, pseudoprogession and timeframe can be different for each individual. DWI and perfusion images are used to observe the recurrence of tumor after the surgery and can be helpful to detect treatment-related changes in a tissue.

Imaging can be used to evaluate the treatment response, because different tumor types may have different progression and can vary according to the histopathological type, grade, use of immunotherapy, so they all need different assessment.

Magnetic resonance spectroscopy (MRS) helps to identify whether the tissue is part of growing tumor or mass of scar tissue. It shows the metabolites, which are the chemical changes, inside the tumor. [cite]

Magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) are the type of MRI which show the brain's blood vessels. Patients should lie flat inside the large tunnel-like magnetic resonance imaging scanner. For clear view of blood vessels contrast will be added to the bloodstream. Sometimes the contrast is given using intravenous (IV) needle. MRA or MRV may be useful for planning surgery [23].

Diffusion tensor/weighted imaging (DTI) is also one type of MRI. It is used for seeing the cellular structure of the brain. It is helpful for surgeons during planning of tumor removal.[cite]

In positron emission tomography (PET) scan the radioactive substance is put to the blood through vein. The logic behind that test is that if radioactive substance is absorbed quickly, then it means that the tissue has tumor. A PET scan tells whether the tissue is active growing tumor or scar tissue.[cite]

After getting results from one of the tests described above, the obtained images are examined by radiologists: considering the shape, area of deep white area on MRI, they suggest the existence of lump or tumor.



# Chapter 2

## Previous work

Nowadays many researchers propose method of CNN, machine learning models, image classification and segmentation techniques to analyse brain tumor. Medical doctors may have thousand of patients and sometimes may overlook the progressing illness of individuals even though they may have high expertise. In addition, MRI images may have a lot of noise and it is hard to detect brain tumor progression with the naked eye. In order to solve some of these problems, several researcher groups have been actively proposing automated methods that would obtain classification and segmentation results of brain tumor MRI images. Firstly we should differentiate between image classification and image segmentation problems. They may analyse the brain tumor, whereas they are somehow different.

### 2.1 Brain tumor classification

First, in this work we will do segmentation task of MRI images. However, I want to introduce the image classification works, because many authors were doing brain tumor classification with prior or post segmentation. The topics are closely related that's why I will give brief overview on classification problems and continue with brain tumor segmentation.

Classification task concentrates on finding whether image has brain tumor or not, unlike segmentation task where the main purpose is to find the region of brain tumor.

Below several works are introduced which concentrated on classification task. Firstly, Somaya A. El-Feshawy, Waleed Saad, normalized MR images, augmented by rotating the images to 90 degrees and resized to  $224 \times 224$ , then fed to proposed 3D CNN and classified as malignant and benign. The malignant cases were 155, whereas benign image amount was 98. Their classification accuracy is 96% [7].

Using the same dataset from the first work, other researchers proposed a custom CNN and compared it with VGG16. The obtained accuracies were 93% and 97%, respectively. They did data augmentation and had 1085 tumorous and 980 non-tumorous images. They converted the MRI images to grayscale, removed noise using dilations and erosions, smooth the data of images with Gaussian blur, extracted the largest contour, found the extreme points of the contoured images, resized, cropped the image using extreme points, splitted the dataset, and trained on CNN, VGG16 for tumor/non tumor classification [10].

It should be noted that some authors tried to increase their classification results by prior segmentation of MR images. One of them, is the research was done by G.Hemanth, M.Janardhan [12], who did pixel based segmentation, bilateral segmentation on MR images, after trained on CNN.

As well as that, S. P Archa, C. Sathish Kumar, did CNN classification of images, whereas they did segmentation after finding brain tumor and then found the contours of malicious region using canny edge detector and Wavelet transform. There is no accuracy information, just info how they filtered the brain images, and found the lesion segment [1].

Fluid-Attenuated Inversion Recovery (FLAIR) is one of the brain MRI modalities and used for capturing periventricular region near to cerebrospinal fluid and periphery of the hemisphere. In the works of [15], the main idea was to achieve better segmentation by using Anisotropic filter, denoising.

In the works of Ashfaq Hussain, Ajay Khunteta, they did brain image segmentation and then classification. Their method differs with using watershed segmentation. But they did not have masks or ground truth. They did preprocessing of jpeg images using Median filtering, then applied skull stripping. After that watershed segmen-

tation was done to get region of brain tumor. However they did not evaluate the accuracy of actual brain tumor part with predicted brain tumor region. That's why their segmentation accuracy is not known. However, their binary classification after segmentation shows good results with SVM and reached 97,2% accuracy [14].

## 2.2 Brain tumor segmentation

Now, I want to introduce the works who did pure segmentation:

Yida Yin did partial view segmentation on brain tumor 3D MR slices saved in Nifti format. He extracted 2d segments of brain tumor region out of 3D slices. There were 4 sequences: FLAIR, T2, T1, T1gd and 3 categories: the GD-enhancing tumor, the peritumoral edema, and the necrotic non-enhancing tumor core. However, we also should note the background in the MR slices, that is why his model predicted the MR scans to 4 labels. Also, to solve imbalance in data, he considered that tumor region is on average 20% of all brain size, that is why his model was better at segmenting the tumor region with 88.15%, 58.51%, 54.11% and 57.11% accuracy for four different labels after 500 epochs [26].

Zhenyi Wang did segmentation on data set with 2 labels: tumor or background, that's why he did binary segmentation with graph cut on the 64 MRI brain scans and cropped them to 128\*128 pixel size images and overall got 27294 image crops for training and 7050 for validation sets. This was done to reduce imbalance between tumor area and background area in the images. All this crops were trained on U-net: one slice and three slice crops. Three slice crops were concatenated and middle slice of a ground truth were used as a ground truth. The accuracy results of IoU are 0.72 and 0.75 on single slice and three slice images [24].

There are also works with medical image segmentation. This work was done using new approach called TransFuse. CNN has a lot of layers and loses information of low level features during down-sampling, so the authors of TransFuse architecture used the fusion of features from both CNN and Transformers to do the medical image segmentation [27].

In the work of Bo Zhou et al., they did synthetic segmentation with the AccSeg-Net framework. The novelty of this framework is that they did not use the ground truth for the images. Instead they used anatomy-constraint and patch contrastive learning, then their images can be trained with correct anatomical content. However, their framework is for 2-D medical volumetric CT/PET/MRI/CBCT images [28].

In the works of Nimrod Sagie et al. transfer learning was used for getting better segmentation results on 3-D chest CT scans. Initially there were a 3-D chest CT scans, then the pre-trained network produced the 3-D segmentation mask for the lungs and infections. After getting the 3-D segmentation masks for the test set, they compared it to the ground truth reference mask. The ImageNet and MedicalNet as a pretrained network was giving the highest of 0.799 dice score [20].

In the works of Wenjun Shen et al. implemented a two-stage registration network, where the first sub-network registers the global information, the second sub-network registers the tumor structures of DCE-MRI series. Then, recurrent alignment framework was applied. Experimental results demonstrate that the proposed method achieves significant performance in segmentation and Dice Similarity Coefficient reveals the 80.12% [21].

In the study of Federica Proietto Salanitri et al., they proposed 3D fully-convolutional network for pancreas segmentation from MRI and CT scans. They have used the encoding-decoding strategy to generate segmentation masks for the target class. Their data was volumetric 3D MRI images and they aggregated those volumes to the size of 1024-8-32-32 and generated multiple intermediate segmentation maps in the hierarchical encoding stage. Then all intermediate masks are concatenated along the channel dimension and in the end merged through a convolutional layer to predict the final segmentation mask for all input slices. Their model called PankNet outperformed existing 3D-U-net model and on average was showing dice score of 77.46% and maximum of 89%. Their volumetric image segmentation architecture can be applied to other 3D object segmentation problems in medical domain [19].

The deep learning methods may be helpful for identifying brain tumor very accurately, and image segmentation techniques will be of great use for comparing the



each pixel of MRI images and finding malicious region. In this work U-Net will be used to do semantic segmentation detect area of brain tumor.



# Chapter 3

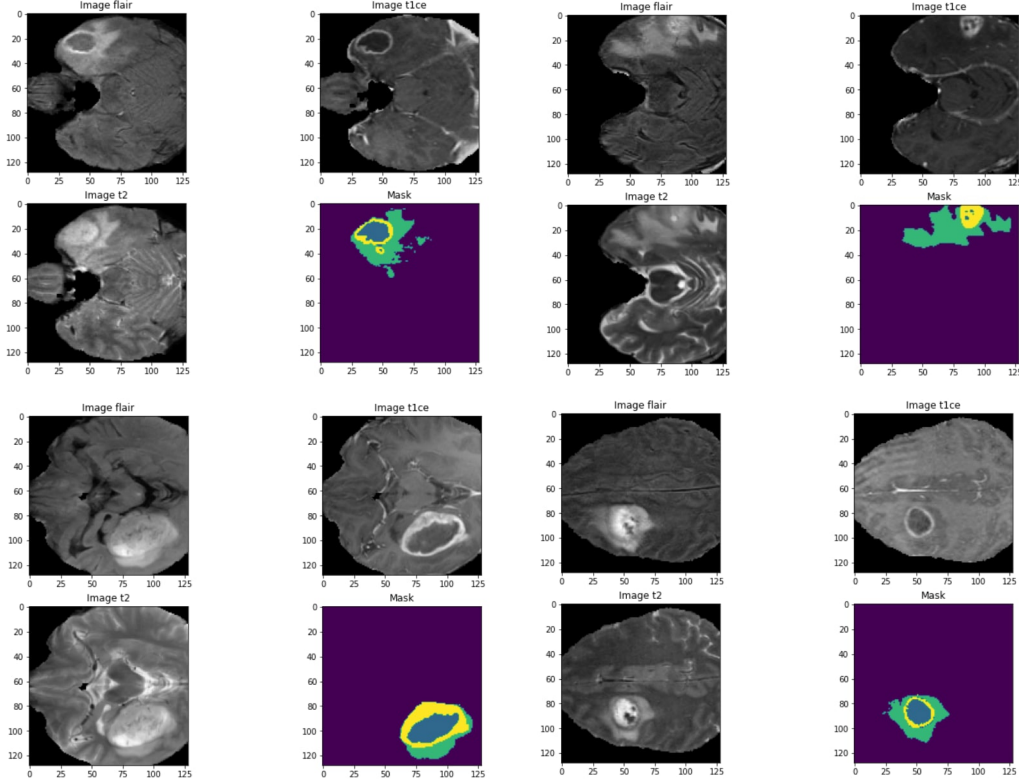
## Methodology

3D segmentation can be classified into three types: instance, part and semantic segmentation [11]. In this work we did semantic segmentation on MRI data. We find regions of brain image containing tumor. In comparison with classification task, where there is single input with single output, in segmentation, we have separate output for each pixel. In semantic segmentation task we classify each pixel.

### 3.1 Dataset

In this work, we use BraTS brain tumor dataset [16] from medically approved source, which is publicly available in a website of Perelman School of Medicine University of Pennsylvania and Center for Biomedical Image Computing & Analytics (CBICA).

BraTS dataset for segmentation task contains the brain tumor MR images in four contrasts: T1, T1ce, T2, FLAIR. In this work we will use 3 contrasts: T1ce, FLAIR, T2. This is the representation of brain in different planes: sagittal, coronal, transverse. Brain tumor images are in 3d volumes and they are called voxels.



Those images contain the segmentation masks, and annotations for them, which were done manually by one to four raters, and were medically approved by neuro-radiologists. Annotations consists of 4 labels: background, enhancing tumor, edema, non-enhancing tumor core. In the annotations they are introduced as the GD-enhancing tumor (ET — label 4), the peritumoral edema (ED — label 2), and the necrotic and non-enhancing tumor core (NCR/NET — label 1), and background as label 0. Everything is described in more detail in the BraTS 2012-2013 TMI paper [16] and in the latest BraTS summarizing paper [2][3].

## 3.2 Processing

BraTS has training and validation datasets contains 371 and 127 samples, respectively. In this work, we use only training set, because validation data has no segmentation masks. Training set was split to 75% and 25%. Each sequence including masks had the (240, 240, 155) size. To get all the supportive information from 3 sequences, leaving out only t1 sequence, they were stacked together to (240,240,150,3) sized

array and were cut to (128,128,128,3) and masks were cut from (240,240,155) to (128,128,128). Mask labels were 0- background, 1- non enhancing tumor core, 2- edema, 4 - enhancing tumor. There were no 3 label, that's why we replaced 4 with 3, and then the corresponding labels were (0,1,2,3).

All the images are cropped in order to contain the brain area, and remove non-brain sections. The reason is that the four modalities captured brain from different angles, and unnecessary background is also presented in the MR images. Also, only three modalities were chosen to do segmentation, because t1 sequence contains incorrect brain tumor areas, so that they were removed and recommended to do so by the Brats dataset authors [2].

### 3.3 Semantic Segmentation

Image consists of height, width, channel information. However, MRI images has 4 sequences, because MRI images show information in different planes: sagittal, coronal (frontal), transverse (horizontal). There x, y,z stands for 3d volume information and 4rd channel represents the sequence information. Therefore 4d format MRI scans are named as voxels. The fourth channel gives information about corresponding sequence: Flair, T1, T2, T1gd. Integer values for ground truth labels: 0- background, 1-edema, 2- non-enhancing tumor, 3- enhancing tumor.

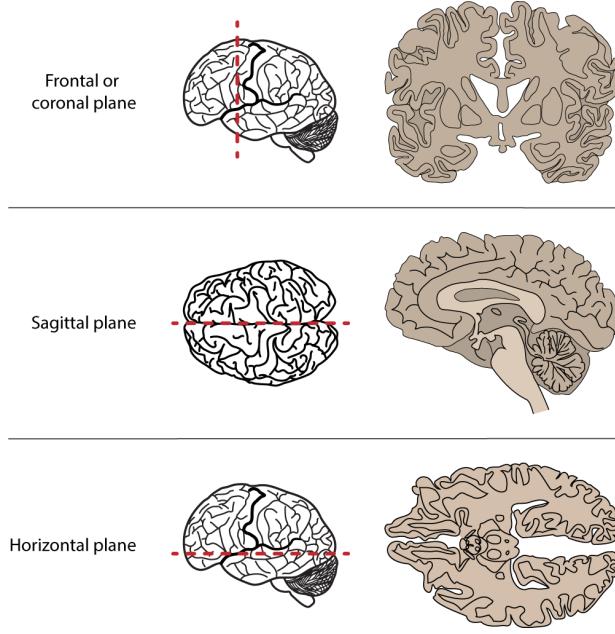


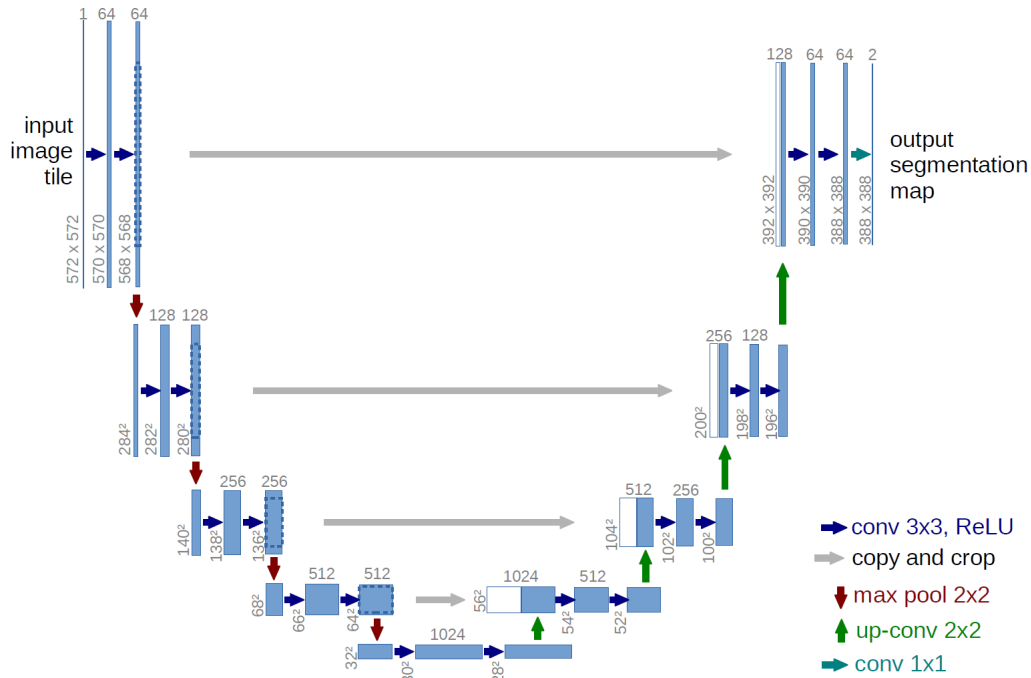
Image classification architectures perform downsampling as they go deeper, Fully convolutional neural networks (FCN) architecture will have lower resolution, however we should preserve each pixel label to obtain a class for each pixel. In order to save the pixel labels, we do upsampling [11].

In segmentation we should preserve the location of each class in comparison with the classification problem. For example, if we had the classification problem, for us it would be unnecessary to know where the tumor is located, our work would be concentrated on finding whether the image has tumor or not. In comparison, segmentation task is about finding where the tumor is located, therefore we should preserve the spatial information to find the label for each pixel. In this work we do semantic segmentation. It requires to do downsampling and upsampling of an image. Downsampling is realized through maxpooling operations or using strided convolutions. Thus, we will reduce the image size, because otherwise it would be hard and computationally tiresome to classify each pixel. Also, it takes a lot of memory. After we get the labels, we can upsample the image to return to its original size.

Various architectures in recent years for doing semantic segmentation are FCN, SegNet, U-Net, PSP-Net, DeepLab and Mask R-CNN.

### 3.3.1 U-Net

Medical images are mostly trained on 2d or 3d U-Net models and in average they show good results even with the little amount of training data. [11] Medical images are not similar to ordinary images. They saved in different formats such as dicom, nifti or etc. BraTS 2021 segmentation challenge task data was saved in nifti format and we stacked the (128,128,128)-FLAIR,(128,128,128)- T1ce,(128,128,128)- T2 sequences together and got additional channel, and overall got 4d array tensors represented as (128,128,128,3). Then using U-Net from segmentation models library from official keras, tensorflow with 2d Convolutions we trained data and compared them with ground truth masks.



The

u-net architecture comprises of an encoder-decoder parts. Encoder part is used for contraction, which reduces the dimensionality of an image. This helps to analyze the medical image. In our case, encoder part contracts the (128,128,128,3) shaped data. After that U-Net uses decoder part, which comprised of up-convolutions to expand the contracted data to produce a full-resolution segmentation for each pixel in an image [5].

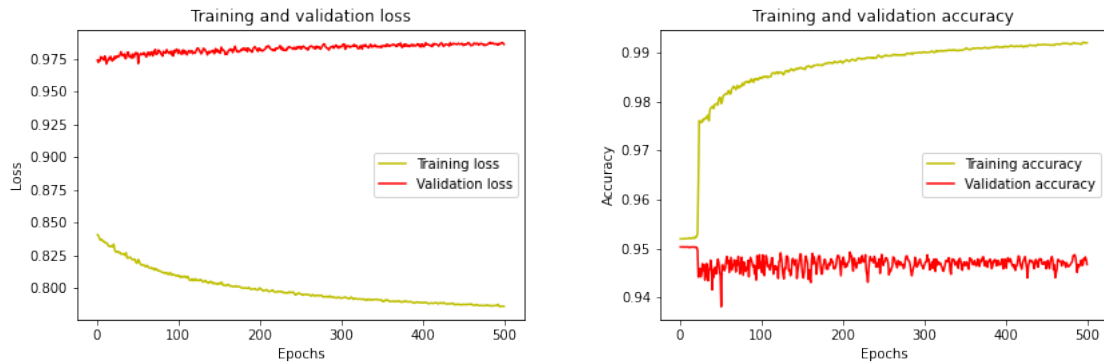
### 3.4 Evaluation

In contrast with the classification task, in segmentation we should find accuracy for each pixel label. Therefore, Mean Intersection-over-Union (meanIoU), Dice similarity coefficients are used to compute the accuracy of a segmentation model. In this work we used Mean Intersection-Over-Union as an evaluation metric, which initially finds the Intersection-over-Union score and then takes an average for all number of classes. IOU is defined as follows:

$$IOU = truePositive / (truePositive + falsePositive + falseNegative)$$

U-net model after training on 258 samples and evaluated on 86 samples got the loss: 0.7864 - accuracy: 0.9920 - iou score: 0.7909 - val loss: 0.9865 - val accuracy: 0.9483 - val iou score: 0.2521

Mean IoU was 25%



### 3.5 Conclusion

During the preprocessing masks and actual images were incorrectly stacked, so labels do not match actual images. I should stack them properly. It will be done in this week. But U-Net model works and trains correctly. Only labels failed to match.



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