Brain Tumor Diagnosis and Segmentation

Ellie Haber, Dennis Fenchenko, Erin Crowe

Problem Statement

The goal of this project is to develop, test, and evaluate a machine learning algorithm that will be able to perform brain tumor diagnosis and segmentation on a test set of MRI images of the brain.

It will classify cancerous and non-cancerous brain masses, mainly gliomas, and identify the different regions of the tumor, including: active tumor, edema, and necrosis. The most difficult aspect of tumor segmentation is the large imbalance of tumor labels in the training and test data. This leads to a large number of false-negative results, despite a relatively low percentage compared to the entirety of the data set.

We will utilize deep learning and convolutional neural networks to classify the MRI images, as well as a splice-layering technique to create a larger data set.

Brain Tumor Segmentation with Deep Neural Networks☆

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Abstract

In this paper, we present a fully automatic brain tumor segmentation method based on Deep Neural Networks (DNNs). The proposed networks are tailored to glioblastomas (both low and high grade) pictured in MR images. By their very nature, these tumors can appear anywhere in the brain and have almost any kind of shape, size, and contrast. These reasons motivate our exploration of a machine learning solution that exploits a flexible, high capacity DNN while being extremely efficient. Here, we give a description of different model choices that we've found to be necessary for obtaining competitive performance. We explore in particular different architectures based on Convolutional Neural Networks (CNN), i.e. DNNs specifically adapted to image data.

We present a novel CNN architecture which differs from those traditionally used in computer vision. Our CNN exploits both local features as well as more global contextual features simultaneously. Also, different from most traditional uses of CNNs, our networks use a final layer that is a convolutional implementation of a fully connected layer which allows a 40 fold speed up. We also describe a 2-phase training procedure that allows us to tackle difficulties related to the imbalance of tumor labels. Finally, we explore a cascade architecture in which the output of a basic CNN is treated as an additional source of information for a subsequent CNN. Results reported on the 2013 BRATS test dataset reveal that our architecture improves over the currently published state-of-the-art while being over 30 times faster.

Keywords:
Brain tumor segmentation, deep neural networks

1. Introduction

In the United States alone, it is estimated that 23,000 new cases of brain cancer will be diagnosed in 2015[2]. While gliomas are the most common brain tumors, they can be less aggressive (i.e. low grade) in a patient with a life expectancy of several years, or more aggressive (i.e. high grade) in a patient with a life expectancy of at most 2 years.

Although surgery is the most common treatment for brain tumors, radiation and chemotherapy may be used to slow the growth of tumors that cannot be physically removed. Magnetic resonance imaging (MRI) provides detailed images of the brain, and is one of the most common tests used to diagnose brain tumors. All the more, brain tumor segmentation from MR images can have great impact for improved diagnostics, growth rate prediction and treatment planning.

While some tumors such as meningiomas can be easily segmented, others like gliomas and glioblastomas are much more difficult to localize. These tumors (together with their surrounding edema) are often diffused, poorly contrasted, and extend tentacle-like structures that make them difficult to segment. Another fundamental difficulty with segmenting brain tumors is that they can appear anywhere in the brain, in almost any shape and size. Furthermore, unlike images derived from X-ray computed tomography (CT) scans, the scale of voxel values in MR images is not standardized. Depending on the type of MR machine used (1.5, 3 or 7 tesla) and the acquisition protocol (field of view value, voxel resolution, gradient strength, b0 value, etc.), the same tumorous cells may end up having drastically different grayscale values when pictured in different hospitals.

Healthy brains are typically made of 3 types of tissues: the white matter, the gray matter, and the cerebrospinal fluid. The goal of brain tumor segmentation is to detect the location and extension of the tumor regions, namely active tumorous tissue (vascularized or not), necrotic tissue, and edema (swelling near the tumor). This is done by identifying abnormal areas when compared to normal tissue. Since glioblastomas are infiltrative tumors, their borders are often fuzzy and hard to distinguish from healthy tissues. As a solution, more than one MRI modality is often employed, e.g. T1 (spin-lattice relaxation), T1-contrasted (T1C), T2 (spin-spin relaxation), proton density (PD) contrast imaging, diffusion MRI (dMRI), and fluid attenuation inversion recovery (FLAIR) pulse sequences. The con-

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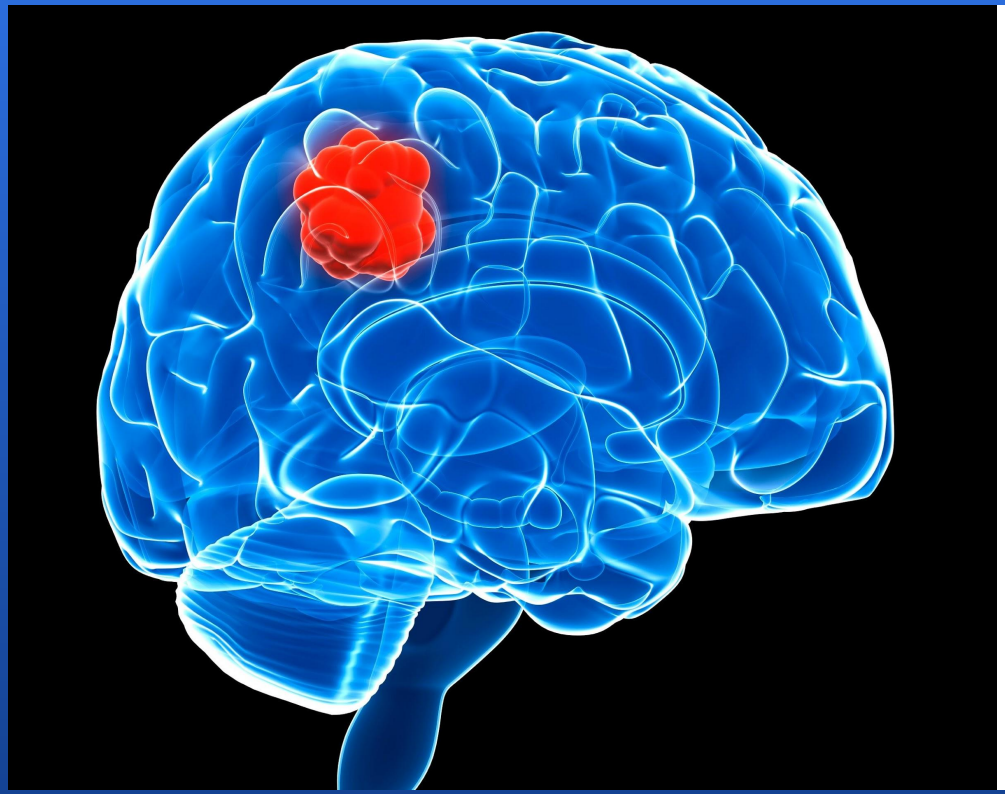
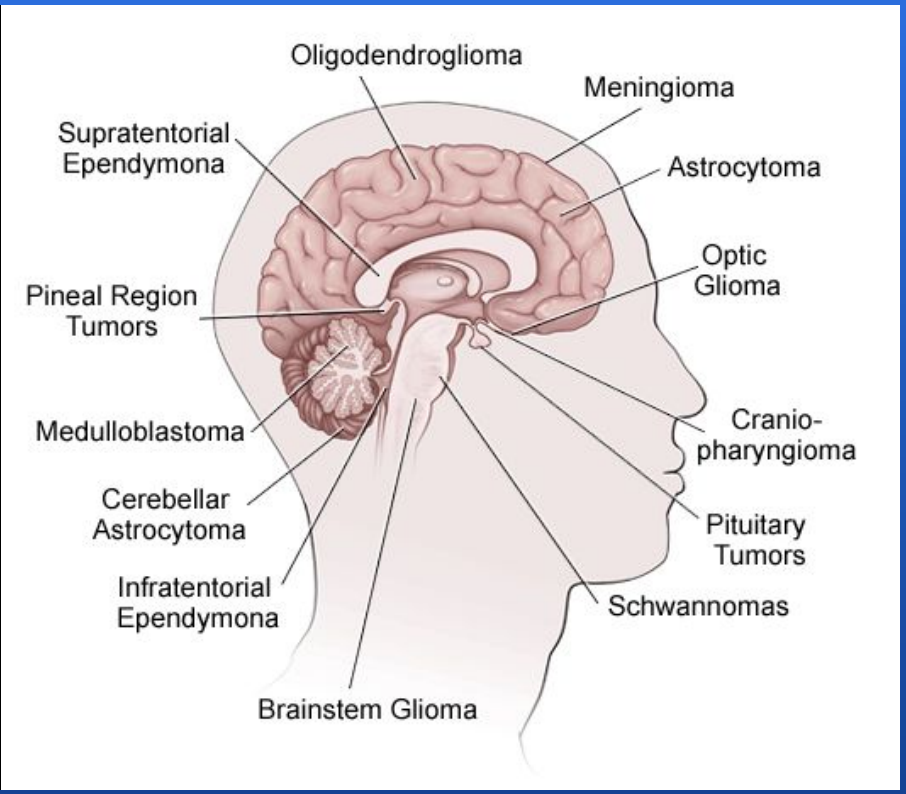
Brain Tumor Types





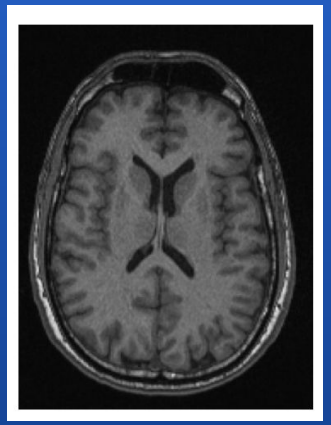
University of Texas MD Anderson Cancer Center

Approach

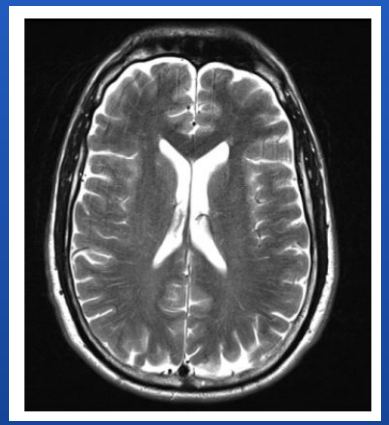
- Data
  - Initially had a relatively small data set (~30-40 images), compared to other traditional machine learning problems, but this was handled by slicing each MRI image into 2D axial images. Each image was subdivided into ~200 slices, yielding a more appropriately-sized data set.
  - Dataset has both HG and LG images, with HG dimensions being (176, 261, 160) and LG dimensions being (176, 196, 216).
- Normalization / Preprocessing
  - Filter out patches with that are 0's (non-tumor patches).
  - Subtract the mean and divide by the standard deviation within each slice.
- Patches
  - Perform mini-batch gradient descent on the patches of each slice.
- Convolutional Neural Network (CNN)
  - Create two CNNS with cascading-architecture, where the output of the first CNN will act as the input of the second.

Problem Formulation: Training Data

- Our project uses training data adopted from BRATS challenge 2013 dataset, consisting of 30 patient datasets, 50 synthetic datasets as well as ground truth data.
- Augment dataset using slicing. Perform segmentation in axial slices.
- Utilizing four different image modalities namely: T1, T2, T1C, and FLAIR.

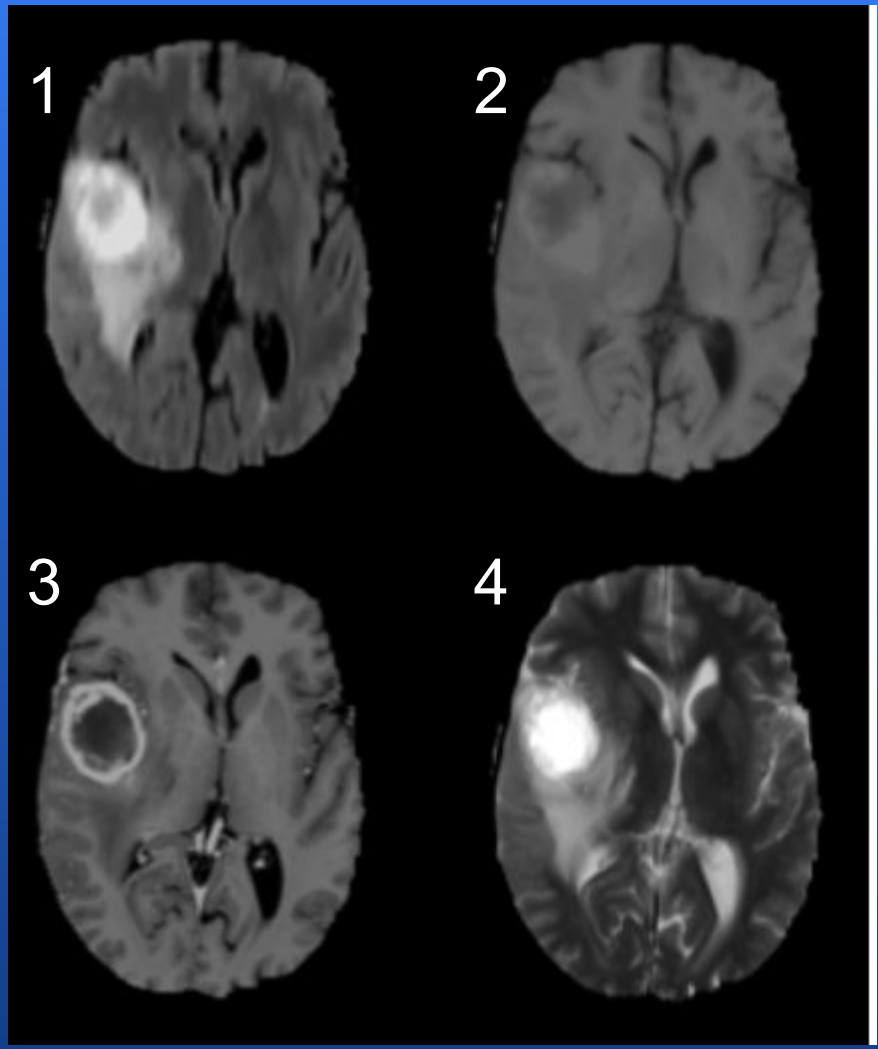


T1: Axial



T2: Axial

("Brain Magnetic Resonance Imaging Technique"2019)



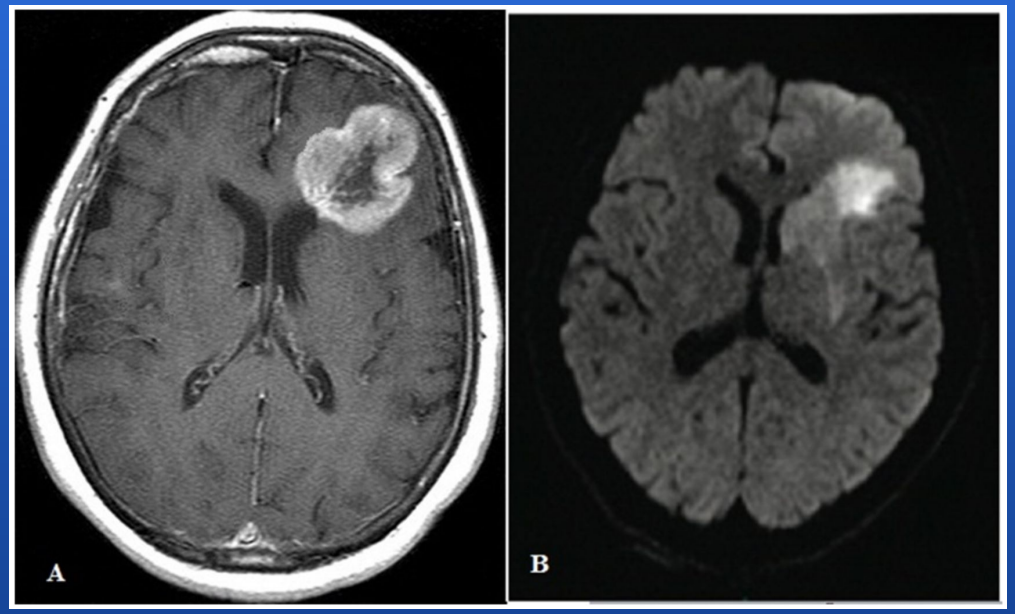
Here is an example of each of the four imaging modalities.

1) FLAIR (Fluid Attenuated Inversion Recovery)
2) T1
3) T1-C
4) T2

Nicole Aldeborgh, 2017

To Visualize...

This is a T1 MRI displaying a high grade glioma in a brain.



Yasaman Arjmand, Pooya Torkian, Ali Keipourfard

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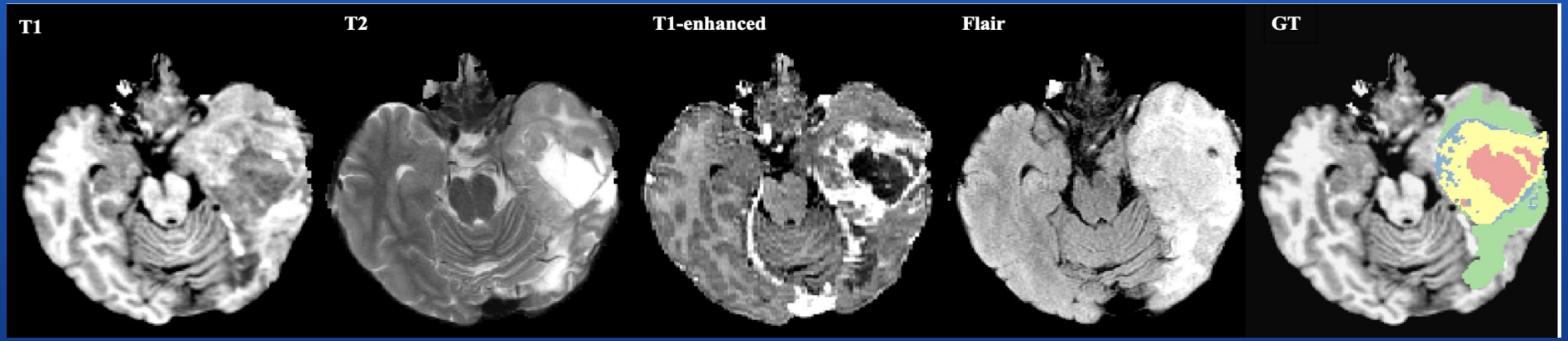
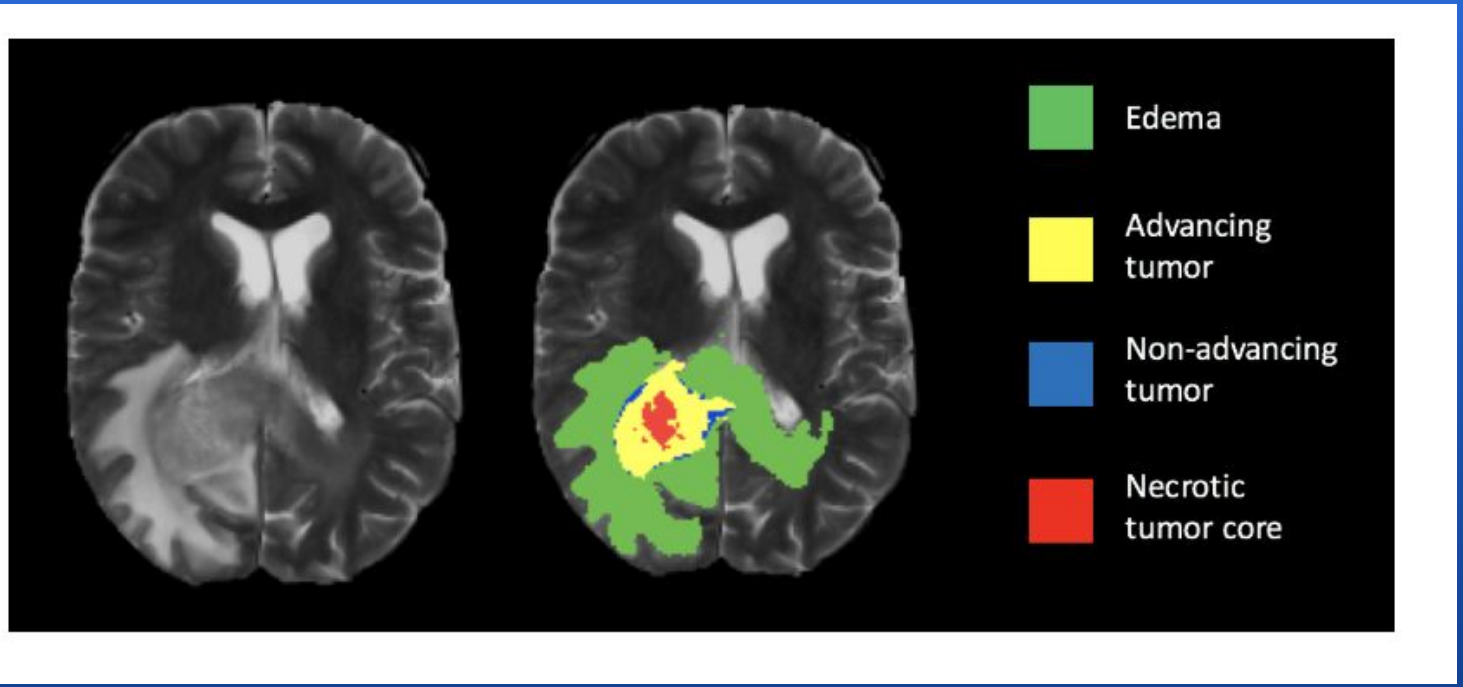
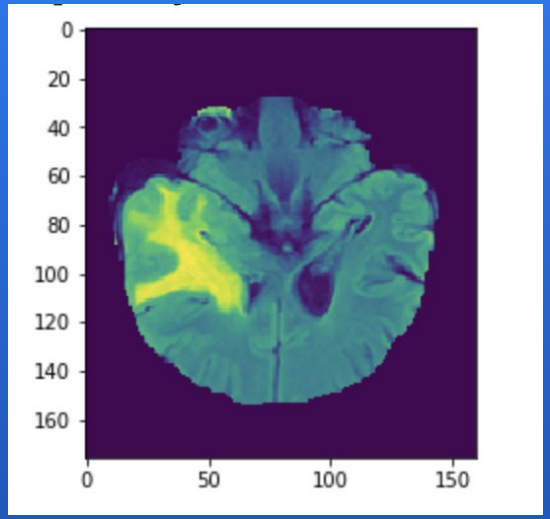
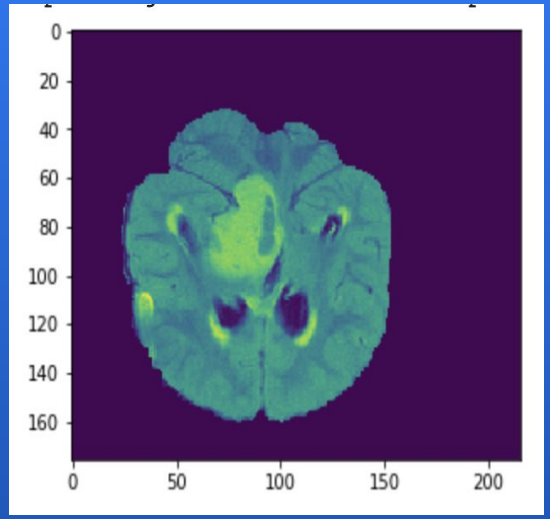
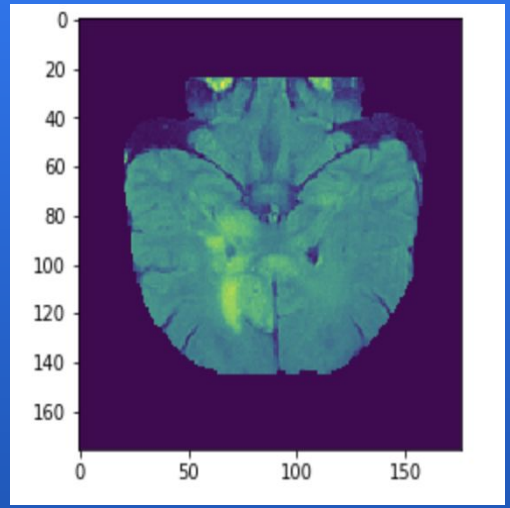
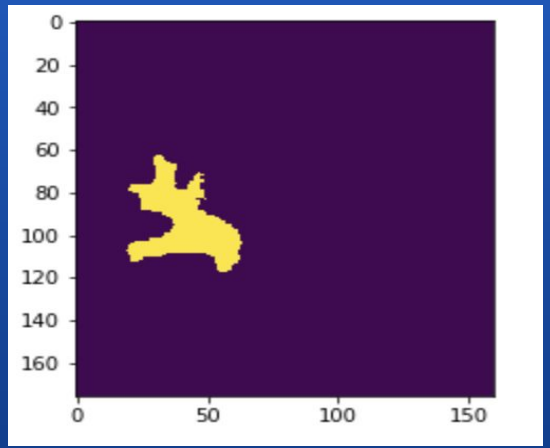
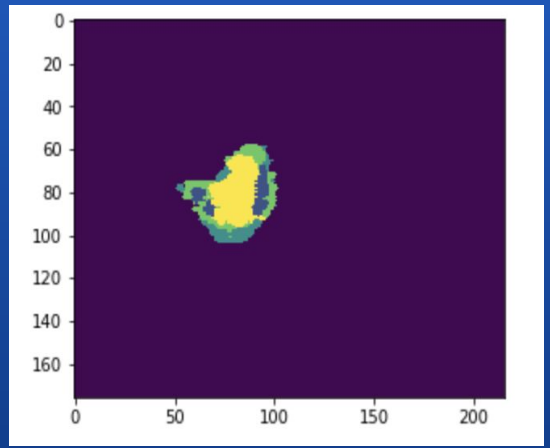
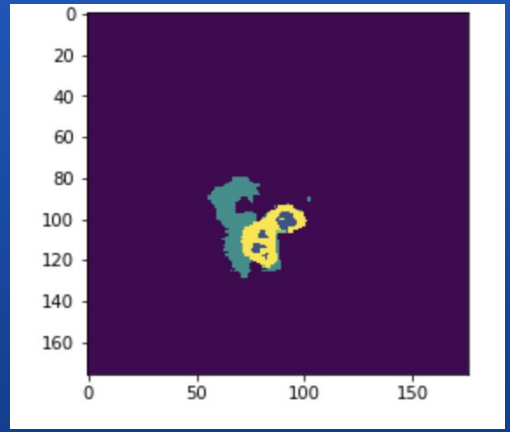
Training Data, continued…

- The training brains come with ground truth for which 5 segmentation labels are provided, namely non-tumor, necrosis, edema, non-enhancing and enhancing tumor.
- In total our model iterates over about 2.2 million examples of tumorous patches and 3.2 million healthy patches, the distribution of examples from all 5 classes is uniform.
- Our model was trained using 2D slices since MRI volumes in the dataset do not possess an isotropic resolution and spacing in the third dimension is not consistent across the data.



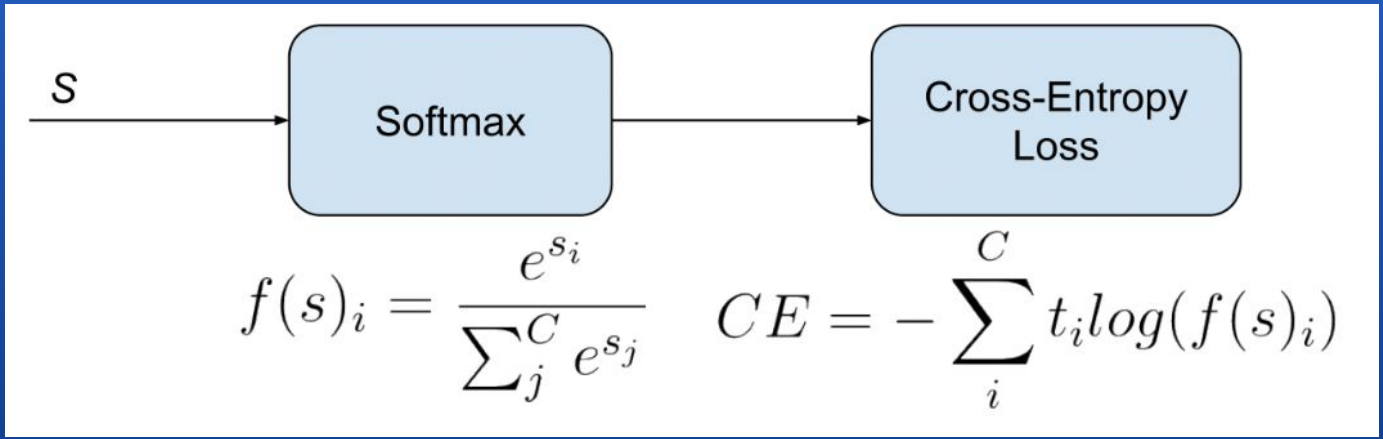
To Visualize… Sample Segmentation



Loss Function

- We chose a categorical cross-entropy loss function to use slice by slice on the MRI image pixels.
- Then a weighted loss function was used on the entire set to counteract the skewed nature of the dataset toward healthy voxels instead of tumor tissue.



Training Procedure…

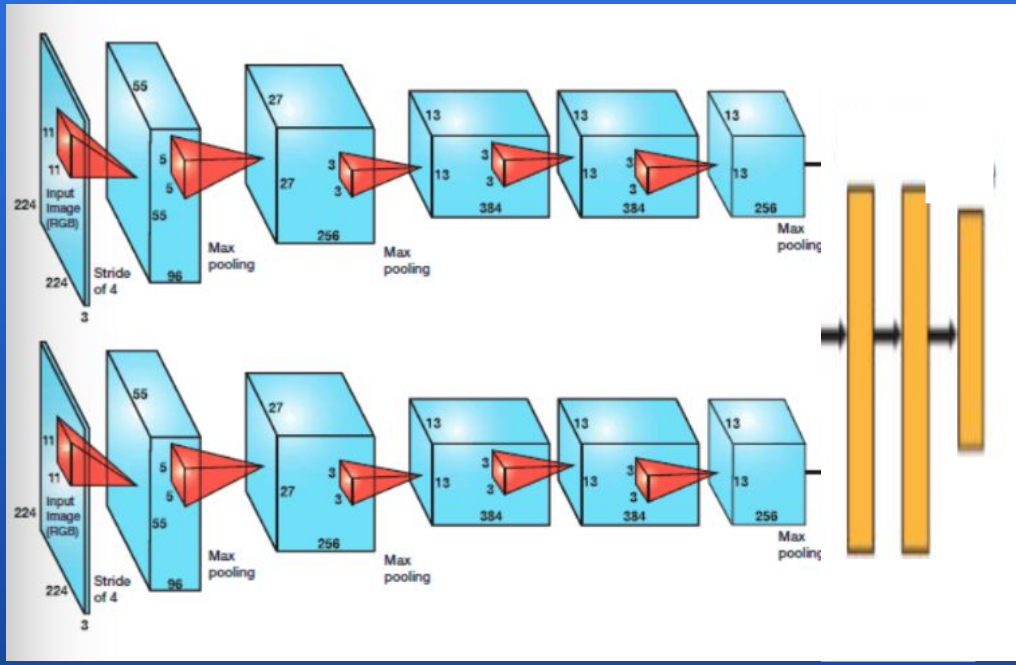
- The benefit of using cascading architecture with CNNs is that we are able to achieve a higher degree of discrimination on the images, while still operating at a relatively high performance level.
- Our training criteria is to maximize the probability of all of all labels in our training set which is equivalent to minimizing negative log-probability for each label in the brain, we accomplish this with stochastic gradient descent.
- Due to highly imbalanced nature of our data in the first phase we construct our patches dataset such that all labels are equiprobable. In the second phase we re-train only the output layer, keeping kernels of other layers fixed.

Training Procedure…

- We used L1/L2 regularization and Dropout to prevent overfitting.
- Softmax function as activation for output layer of model
- Relu non-linear activation function is used for hidden layer convolutions
- Valid mode convolutions implemented
  - Filter response for pixels less than N/2 pixels from the image border aren't computed
- Kernels are hyperparameters that we set based on the paper's specifications
- Gradient clipping to prevent exploding gradients (caused by large parameter gradient)
- Global Path vs Local Path
  - Global: (13x13) prediction of pixel label based upon larger context of its location in the scan
  - Local (7x7) visual details of the direct region surrounding the pixel

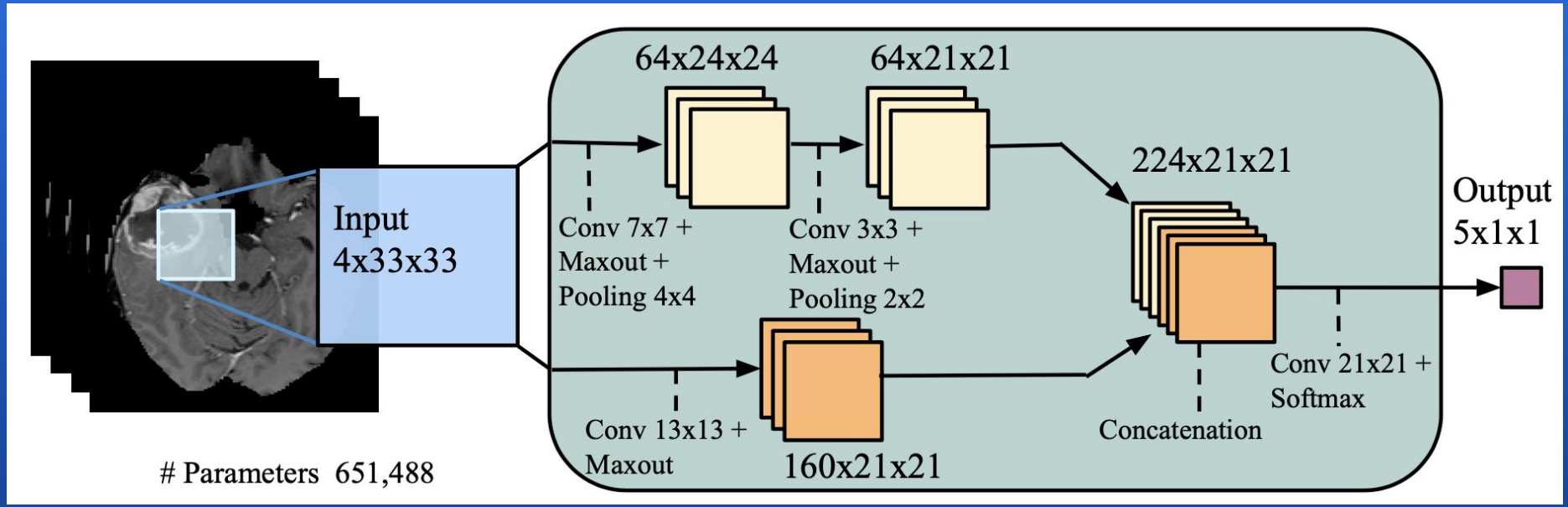
Training Procedure, continued…

The two-path CNN is derivative of multipath convolutional neural network architecture. It creates two paths, one to take source images as input, and the other to take filtered images, then the two paths were concatenated after all the layers were completed. This allows the algorithm to achieve a more comprehensive understanding and classification of image features than if a single-path approach was used. A simple diagram of a classic CNN is shown.

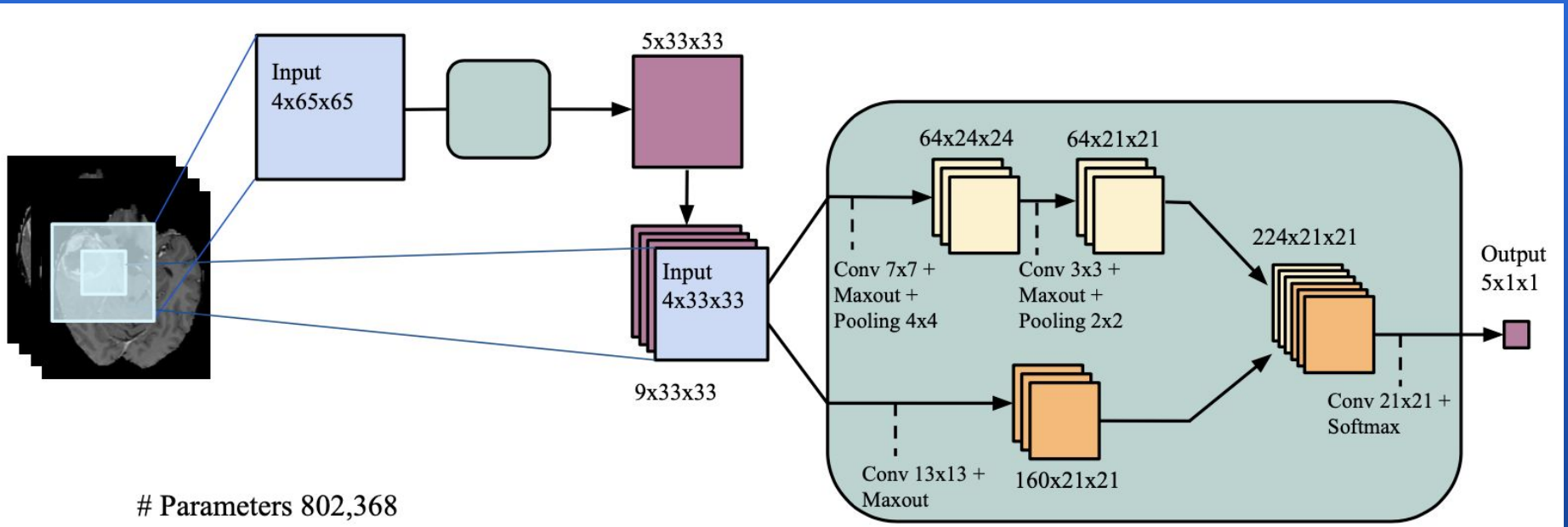


General form of the two-path CNN

Another Visualization of Two-Pathway CNN

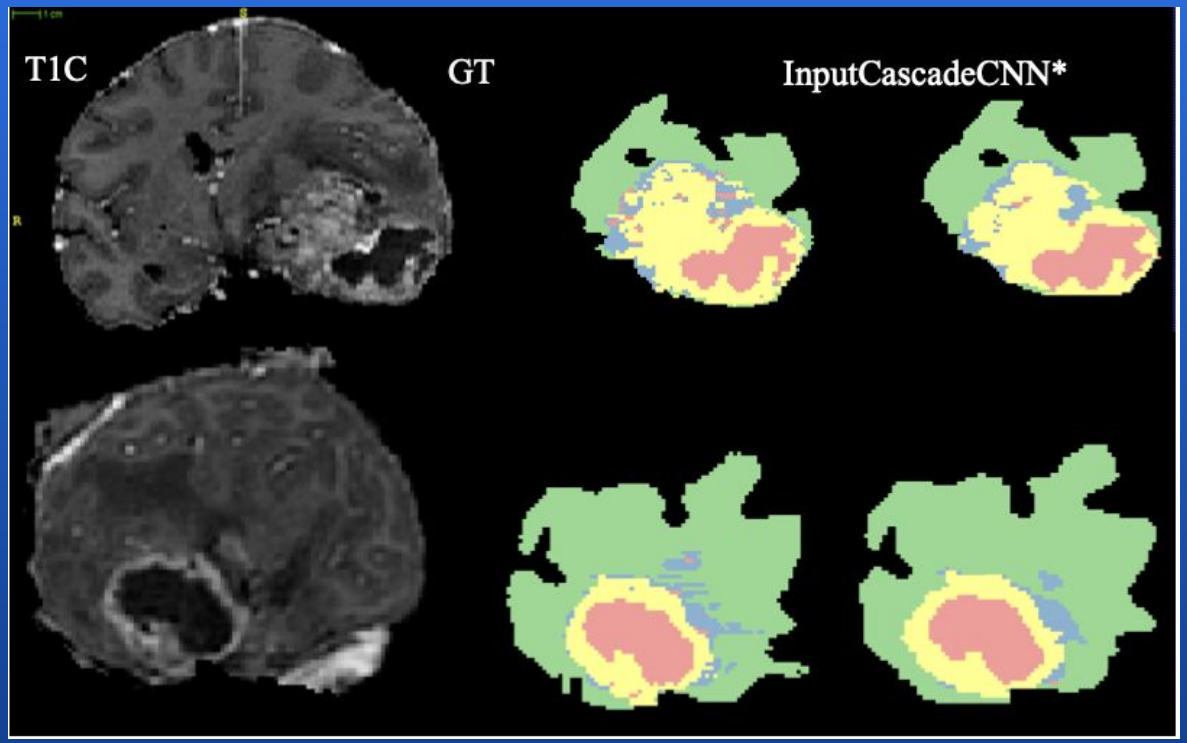


Input Cascade CNN



(a) Cascaded architecture, using input concatenation (InputCascadeCNN).

Evaluation Results Visualization



	BRAIN SLICE	F1 SCORE
0	HG 0004 Slice 113	0.8995
1	HG 0004 Slice 96	0.8375
2	HG 0011 Slice 113	0.9288
3	LG 0004 Slice 113	0.9591
4	LG 0004 Slice 111	0.9626
5	HG 0007 Slice 113	0.9676
6	HG 0007 Slice 96	0.9794
7	LG 0013 Slice 78	0.9878
8	LG 0013 Slice 113	0.9519

Evaluation Results Explained

- The functionality of our model was evaluated by the f1 score. Which takes into the consideration the precision (p) and recall (r) to compute a ratio between 0, and 1. The ideal f1 score is exactly 1, or as close as possible.
- Because our data was an unbalanced class, f1 was more valuable than other evaluation metrics.
- As an intermediary step, the accuracy was used to ensure that the model was working correctly at the epoch level.
    - Can't use accuracy as testing value due to the skewed nature of the dataset (98%:2% ratio of healthy voxels to unhealthy ones).
    - In theory, we could still achieve a high accuracy despite misclassifying images as false negatives, because the number of positive results is so small compared to the rest of the dataset.
- Of the f1 scores on the previous slide, the average value = 0.9375.

Evaluation Results Explained

- Ways to improve accuracy:
  - Perform n4ITK bias correction on T1 and T1C images
    - Removes artifacts in MRI data/intensity gradient
  - Remove images with highest and lowest 1% of intensities
    - Perform K-fold cross validation for training to account for the distribution of intensities in dataset
- Run training model with more of the dataset
  - Training takes very long (200 slices per image with 5 epochs per slice)
  - Will help to improve computational segmentation edges
- Find F1 score for segmentation of each component of the tumor rather than tumor as a whole (will help for seeing accuracy of individual regions/edges)

References

"Are All Gliomas Malignant, Low & High-Grade: Moffitt." *Moffitt Cancer Center*, moffitt.org/cancers/brain-cancer/faqs/are-all-gliomas-malignant/.

https://github.com/jadevaibhav/Brain-Tumor-Segmentation-using-Deep-Neural-networks

https://github.com/naldeborgh7575/brain_segmentation

"Astrocytoma Tumors." *AANS*, www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Astrocytoma-Tumors

Chen, Shengcong, et al. "Dual-Force Convolutional Neural Networks for Accurate Brain Tumor Segmentation." *Pattern Recognition*, Pergamon, 14 Nov. 2018, www.sciencedirect.com/science/article/pii/S0031320318303947.

Havaei, Mohammed, et al. *Brain Tumor Segmentation with Deep Neural Networks*. BRATS-MICCAI, 20 May 2016, arxiv.org/pdf/1505.03540.pdf.

Nikki, Aldeborgh 2017, Automatic TUmor Segmentation, https://github.com/naldeborgh7575/brain_segmentation

Wadhwa, Anjali, et al. "A Review on Brain Tumor Segmentation of MRI Images." *Magnetic Resonance Imaging*, Elsevier, 11 June 2019, www.sciencedirect.com/science/article/pii/S0730725X19300347.

"Figure 2f from: Irimia R, Gottschling M (2016) Taxonomic Revision of Rochefortia Sw. (Ehretiaceae, Boraginales). Biodiversity Data Journal 4: e7720. Https://Doi.org/10.3897/BDJ.4.e7720." doi:10.3897/bdj.4.e7720.figure2f.

Figure 1. A: T1-Weighted MRI Shows Enhanced Lesion with Peripheral Edema on Left Frontal Area, Compatible with High Grade Glioma. B: Left Frontal Area of Same Patient Has Hyper Intense Signal in Diffusion Weighted Imaging (DWI), Compatible with Ischemic Area : Radiologic Evaluation of Patients with Glioblastoma Multiforme Who Initially Presented with Ischemic Stroke: A Case Series : Science and Education Publishing, http://pubs.sciepub.com/ajmcr/5/1/3/figure/1.

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