PhD Qualifier
Fall 2020

Zafar Iqbal
Department of computer science
Georgia state university
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Committee

Dr. **Zhipeng Cai (Chair)**
Dr. **Ashwin Ashok**
Dr. Xiaolin Hu

Georgia State University

Papers

❑ Paper 1

- Zhe Guo, Xiang Li, Heng Huang, Ning Guo, Quanzheng Li “**Deep Learning-Based Image Segmentation on Multimodal Medical Imaging**” IEEE Transactions on Radiation and Plasma Medical Sciences, Volume: 3 , Issue: 2 , Page(s): 162 – 169, 2019

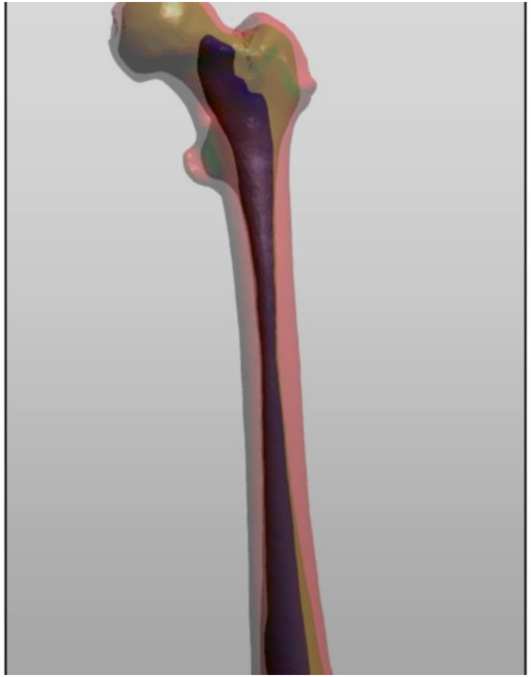
❑ Paper 2

- S. Pereira, A. Pinto, V. Alves, and C. A. Silva, “**Brain tumor segmentation using convolutional neural networks in MRI images**,” IEEE Transactions on Medical Imaging., vol. 35, no. 5, pp. 1240–1251, May 2016

Outline

- Introduction
- Motivation
- Paper 1 and Paper 2
  - Introduction
  - Proposed Approach
  - Experiments Results
  - Discussion and Future work
- Comparison of both the Journal Papers
- Conclusion

Introduction



- ✓ Image segmentation is a process to divide a digital image into different semantically meaningful segments based on the intensity, depth, color, or texture.
- ✓ It is typically used to find boundaries and locate objects in the image.

S: https://doi.org/10.1371/journal.pone.0079004.g005

Motivation

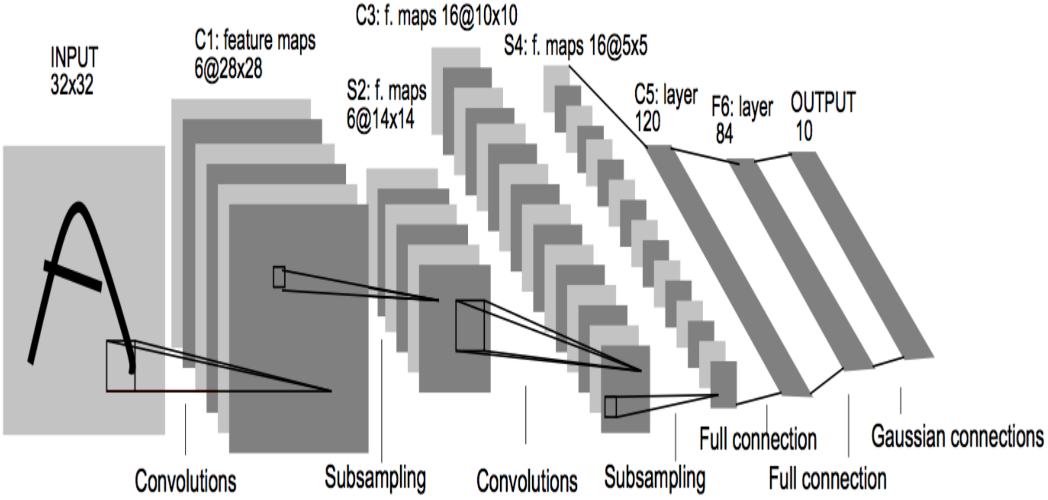
- ✓ Image segmentation in biomedical image analysis.

- ✓ Brain segmentation has countless clinical applications.
  - Measuring anatomical structures
  - Identify tumor regions
  - Monitor brain development
  - Assess risks of certain medical or surgical procedures etc.

Convolutional Neural Networks (CNN)

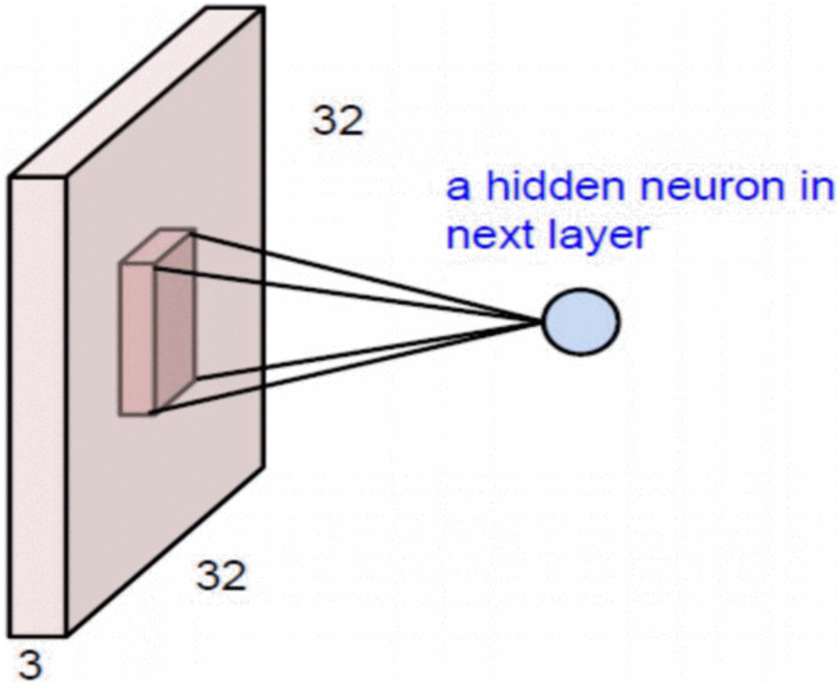
- ✓Successes in applying deep CNNs for medical image processing have been recently reported (Thrall et al., 2018).
- ✓CNNs have been applied to segmentation of tumors in brain, liver, breast , lung, and other regions.
- ✓Translation invariant (Guo, Li, Huang, Guo, & Li, 2019).

- ✓ **Convolutional layers.**
  - ✓ Translation Invariant features
- ✓ **Fully connected layers**
  - ✓ Mapping between image features and labels



Original Image published in [LeCun et al., 1998]

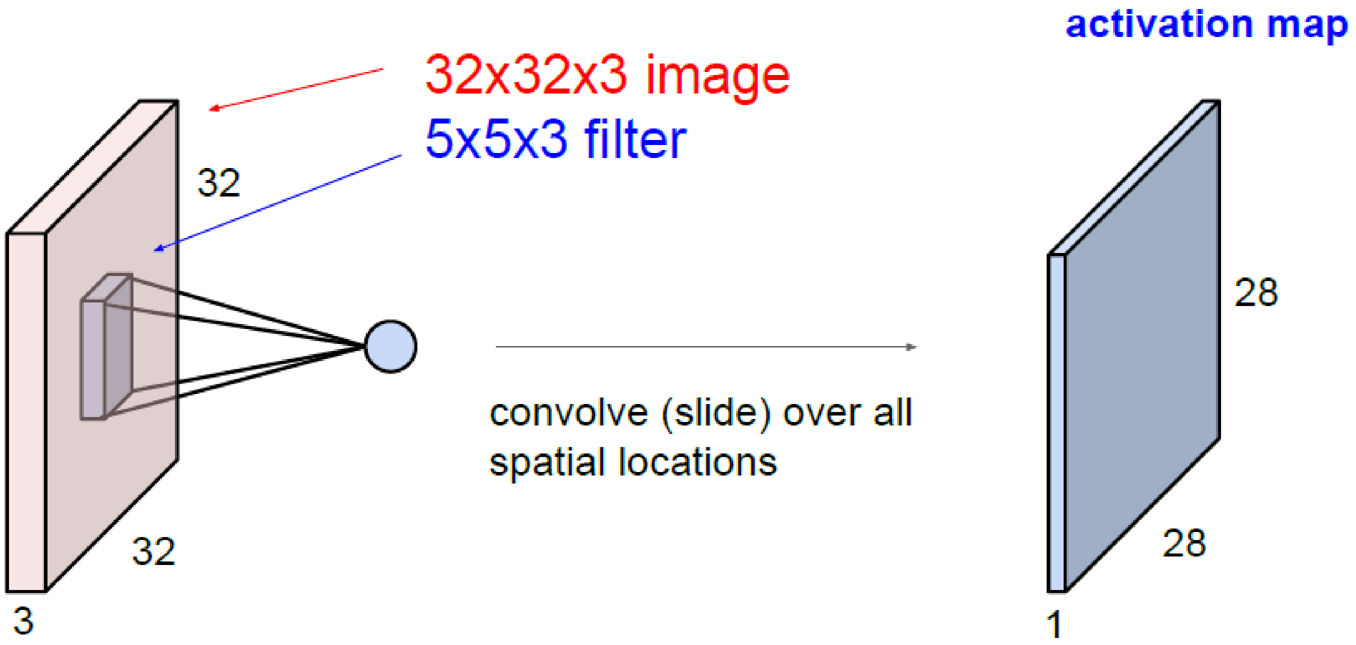
Convolutional layer



(Albawi, Mohammed, & Al-Zawi, 2017)

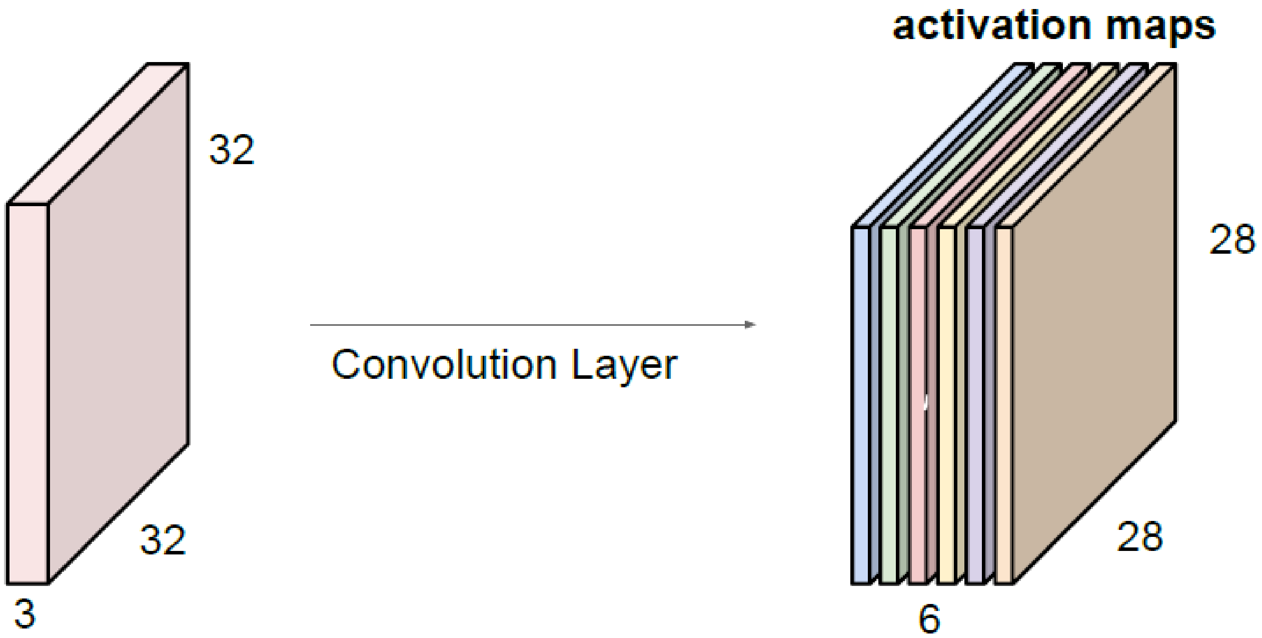
$$f(X, W) = WTX + b$$

Dot product between the filter and a small chunk of the image



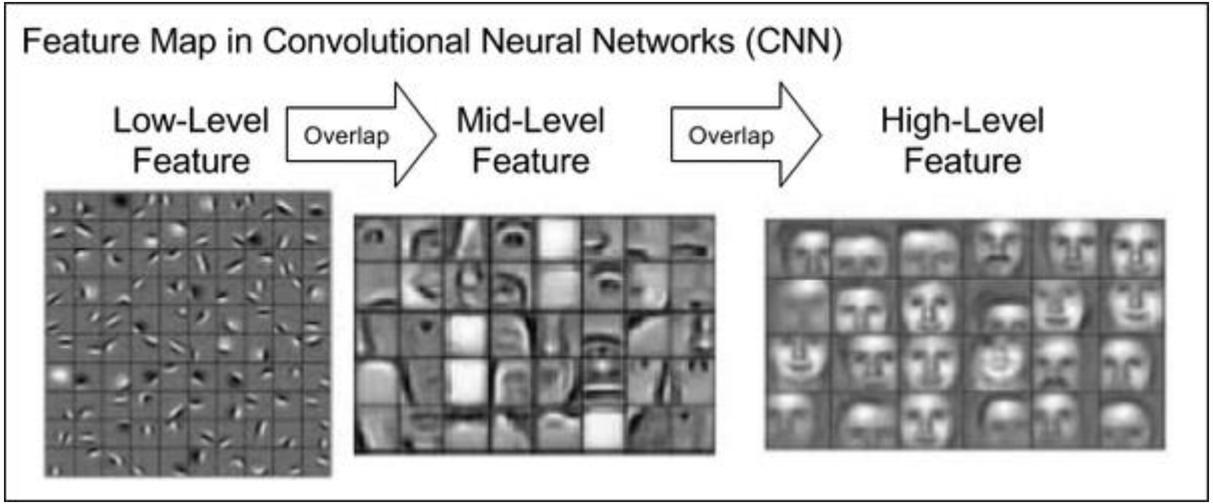
Source: http://cs231n.stanford.edu/slides/2017/cs231n_2017_lecture6.pdf

Stacking of Activation Maps



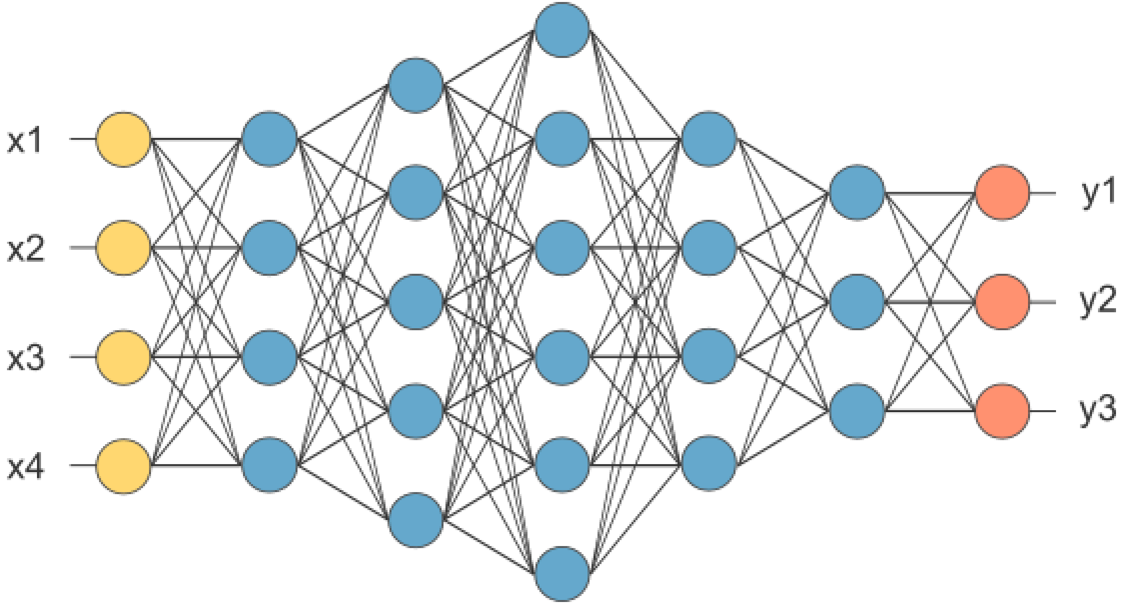
Source: http://cs231n.stanford.edu/slides/2017/cs231n_2017_lecture6.pdf

Low level and high-level features



Source: https://www.cnblogs.com/wangxiaocvpr/p/5847526.html

Fully connected layers



Source: https://medium.com/@RaghavPrabhu/understanding-of-convolutional-neural-network-cnn-deep-learning-99760835f148

Paper I

Deep Learning-Based Image Segmentation on Multimodal Medical Imaging

Introduction

- Combining different biomedical images.

- Use of more than one modality (i.e., multimodal) on the same target has become a growing field as more advanced techniques and devices have become available.

    - Each modality encompass different kind of information
    - Complementary to each other
    - PET + CT + MRI
    - MRI + EEG

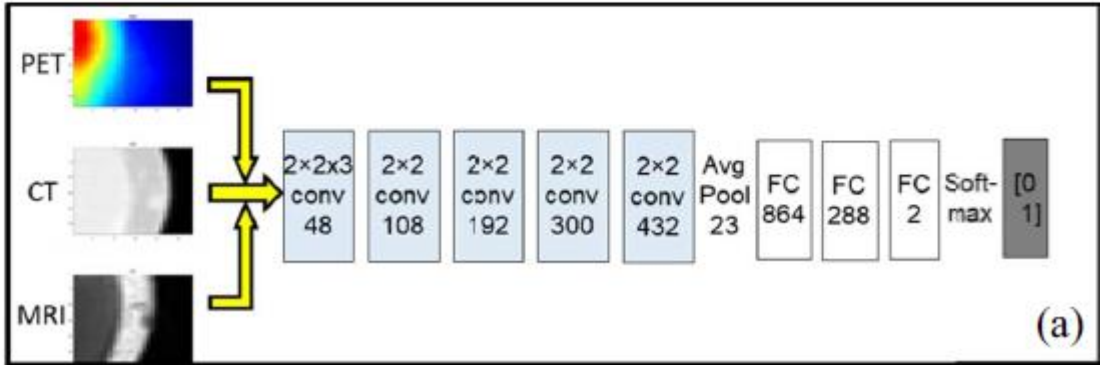
- This paper proposes an algorithmic architecture for **image fusion strategies** that can cover most supervised multimodal biomedical image analysis methods.

- Based on the main stages of machine learning models, this design includes fusion at three different levels:

    - ✓ Feature level
    - ✓ Classifier level
    - ✓ Decision-making level.

Feature level fusion

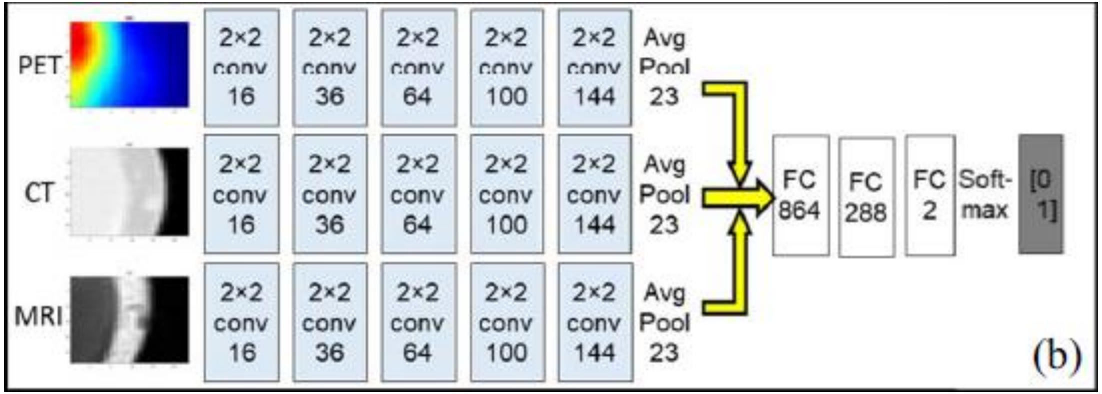
- Multimodality images are used together to learn a **unified image feature set**.



Source: (Guo, Li, Huang, Guo, & Li, 2019)

Classifier level fusion

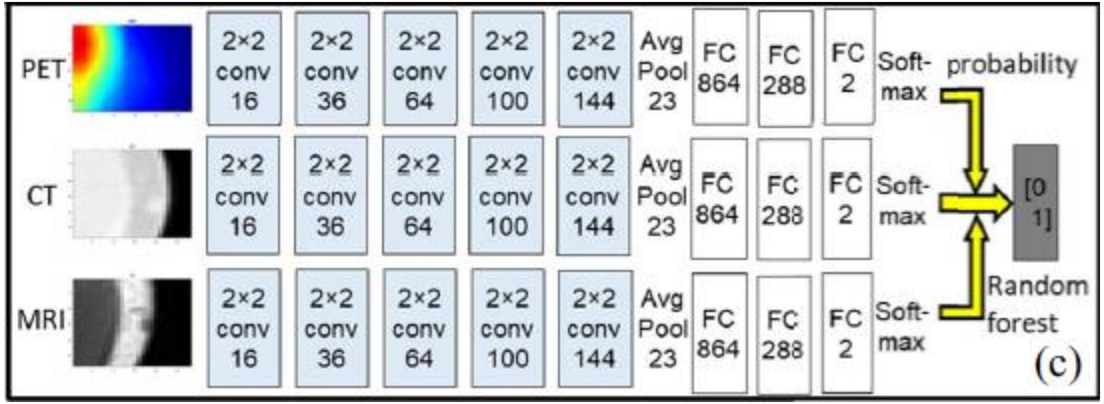
- Images of each modality are used as separate inputs to learn **individual feature sets**..



Source: (Guo, Li, Huang, Guo, & Li, 2019)

Decision-making level fusion

- Images of each modality are used independently to learn a single modality classifier (and the corresponding feature set).
- The final decision based on "voting".



Source: (Guo, Li, Huang, Guo, & Li, 2019)

Dataset Description

Soft-tissue Sarcoma (STS)

- ✓ 50 subjects
- ✓ The STS dataset contains a total of four imaging modalities:
  - ✓ PET
  - ✓ CT
  - ✓ MRI (T1-weighted).
  - ✓ MRI (T2-weighted).
- ✓ Gross tumor volume (GTV) is **manually annotated for T2 weighted images** and then corresponding contours for other modalities are obtained using MIM software.

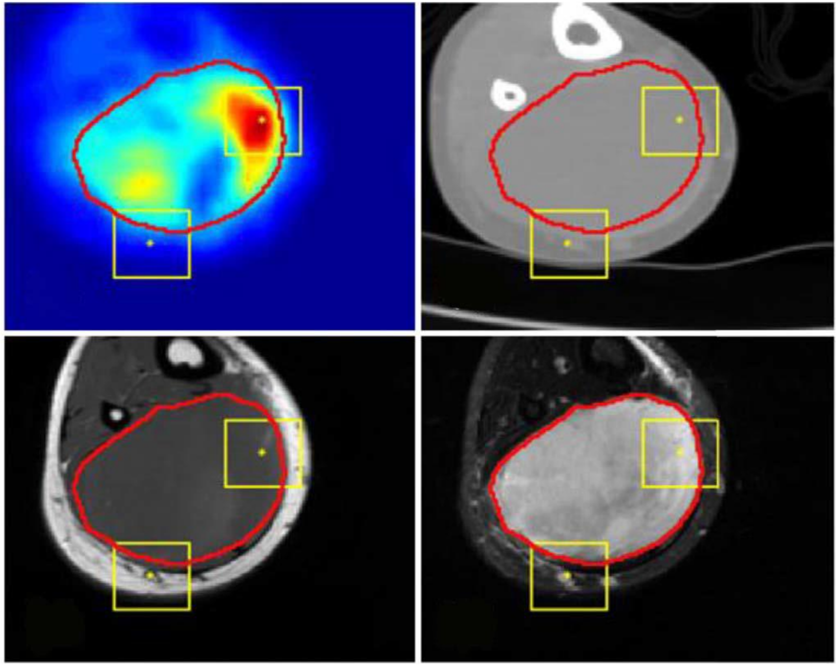
Dice Similarity coefficient

Measures the similarity between predicted region and annotation region.

$$DSC = \frac{2TP}{FP + 2TP + FN}$$

Multimodal images on the same position

- Top-left: PET
- Top-right: CT
- Bottom-left: T1
- Bottom-right: t2
- Yellow boxes: Patches (28 *28)



Source: (Guo, Li, Huang, Guo, & Li, 2019)

- ✓ On average, around **1 million patches** were extracted from each subject, with around **0.1 million** positive patches.

- ✓ During the training phase, to balance the number of positive and negative patches, they **randomly selected negative patches to the same number of positive patches**.

- ✓ During the testing phase, They used all the patches for segmentation.

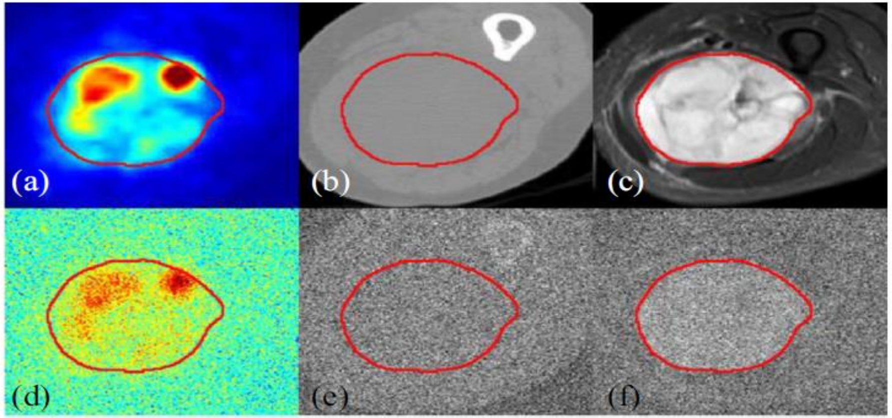
Additional benefits of Multimodality

- It is expected that multimodal imaging should offer **additional information** resulting in better performance compared with single-modality methods.

- Extending multimodality on low quality images.

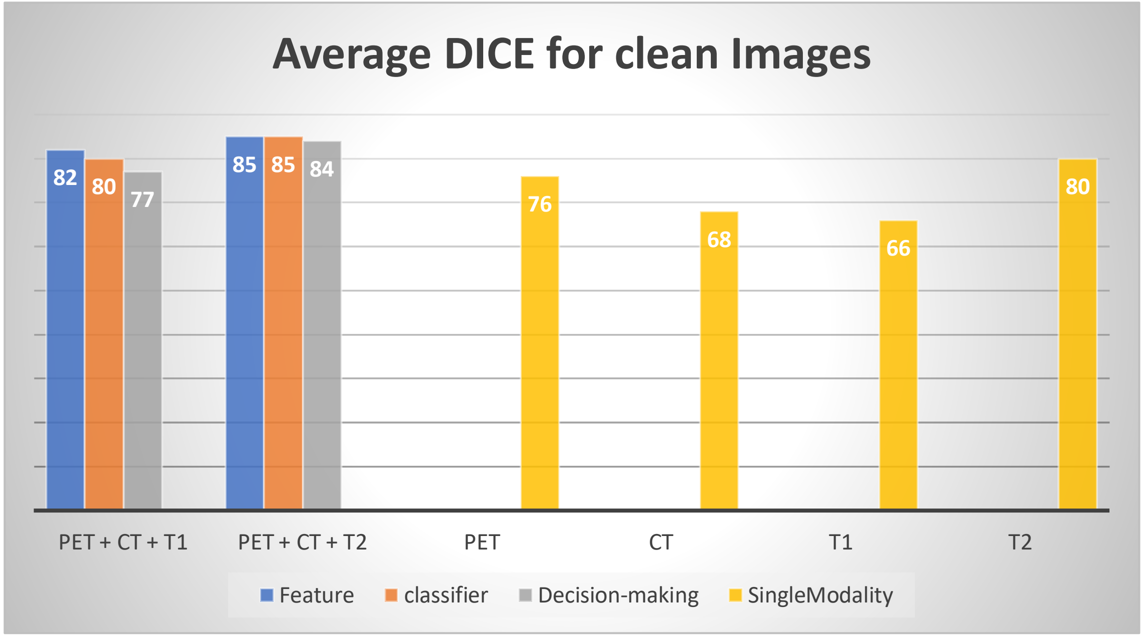
Noised Images

- ✓ Added random Gaussian noise.
- ✓ (a-c): Original PET, CT, T2
- ✓ (d-f): Noised PET, CT, T2



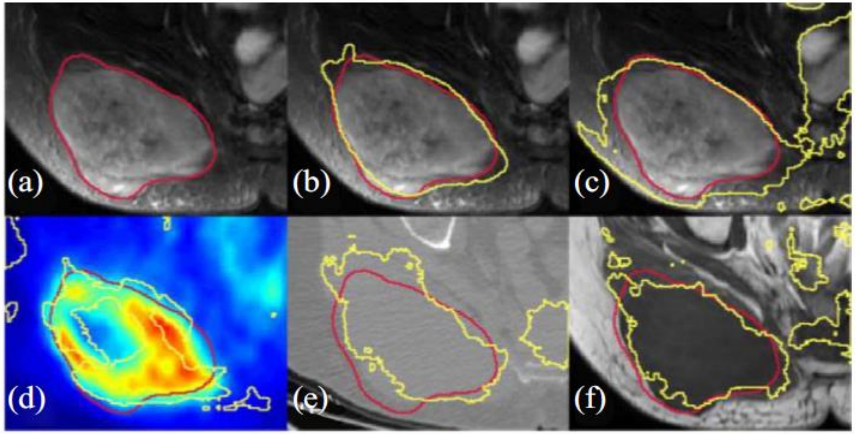
Source: (Guo, Li, Huang, Guo, & Li, 2019)

Experimental Results



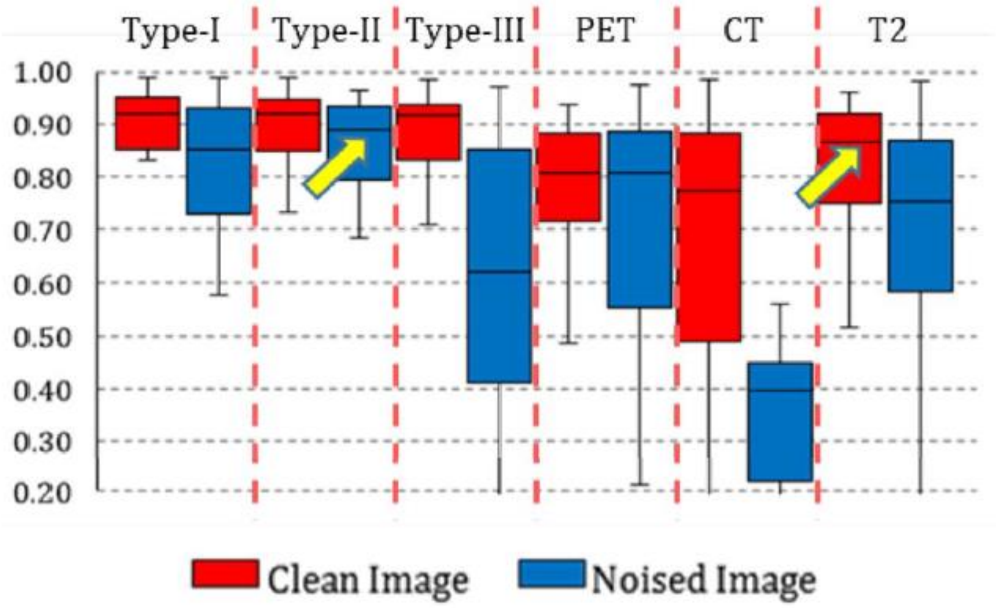
Segmentation results on an example

a) Ground truth on T2
b) Classifier-level fusion (PET+CT+T1) result
c) T2
d) PET
e) CT
f) T1



Source: (Guo, Li, Huang, Guo, & Li, 2019)

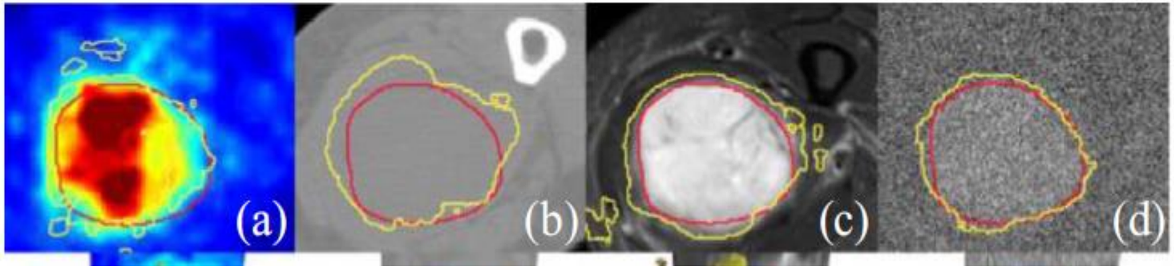
Clean vs Noised Images



Source: (Guo, Li, Huang, Guo, & Li, 2019)

Performance on Noised Images

a) PET
b) CT
c) T2
d) PET+ CT + T2



Source: (Guo, Li, Huang, Guo, & Li, 2019)

Summary

- Multimodal approach
- Three level fusion
- Evaluated models on clean and noised images.

Strengths and Weaknesses

Strength

- ❑ Type I and Type II fusion performed well
  - ▪ Complement each other
- ❑ Fusion based networks produced comparable results to single modal networks using clean images
- ❑ Computationally economical.

Weakness

- ❑ Tested on only one Dataset
  - ▪ Couldn’t generalize results
- ❑ Why decision-making level fusion performed worst?
  - ▪ No suitable Justification
- ❑ Experiments were performed on a well registered dataset
  - ▪ Real data is messy

Future Work

- The proposed method could be tested on other imaging datasets.
- Type III fusion performed worst consistently. Other ensembled methods like bagging, Boosting, stacking could be explored to enhance the performance.
- The proposed fusion strategies could be used for unsupervised learning.
- 3D convolution could be helpful in extracting spatial features in 3 dimensions.

Paper II

Brain Tumor Segmentation Using Convolutional Neural Networks in MRI Images

INTRODUCTION

- **Glioma is a specific type of tumor** which occurs in the brain and nervous system including the spinal cord. It can severely impact the functionality of brain.

- There are **four different grades of Gliomas**. Grade I and II are categorized as **Low-Grade Gliomas** while grade III and IV are termed as **High-grade gliomas**.

- In comparison to LGG, **HGG are more aggressive** and they grow rapidly throughout the brain.

Problem statement

- Magnetic resonance imaging (MRI) could be used to identify these kind of tumors.

- Manual segmentation challenging.

- Automated segmentation methods are required.

- In this paper, two deep learning-based architectures are proposed.

- ✓ Pre-Processing,
  - ✓ intensity normalization
  - ✓ data augmentation

- ✓ Convolutional neural networks.
  - ✓ Xavier Initialization
  - ✓ Max-pooling
  - ✓ Regularization (drop out)
  - ✓ Loss function (categorical cross entropy)
  - ✓ Optimizer (Stochastic gradient descend)
  - ✓ Activation function (Leaky ReLU)

Preprocessing

- MRI images are altered by the **bias field distortion**.
  - Intensity values vary for the same tissues.

- **N4ITK** method.
  - To correct bias field distortion

- **Intensity normalization**
  - To make the contrast and intensity ranges more similar across patients and acquisitions

Preprocessing..

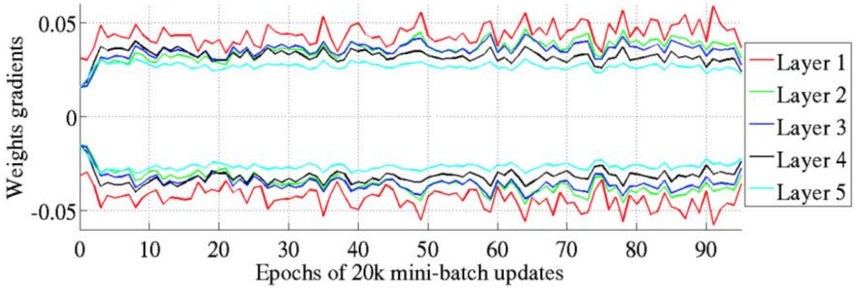
Data Augmentation

- It can be used to increase the size of training data and avoid overfitting.
  - Flip, crop, rotate, translate, resize, etc.
- In this paper, they have done only rotation operations.

Weights initialization

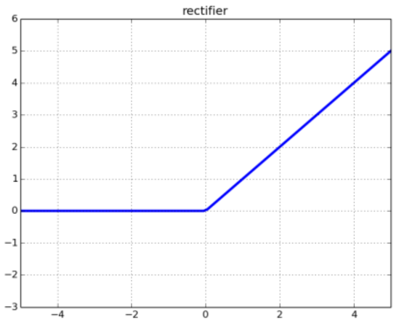
Xavier Initialization

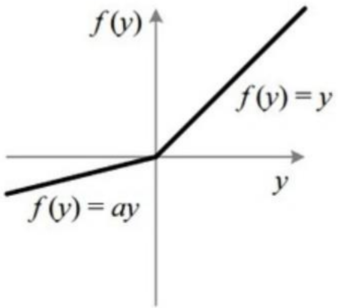
- Fast convergence
- With this, the activations and the gradients are maintained in controlled levels
    - Back-propagated gradients doesn't vanish or explode.



Source: (X Glorot et al. , 2010)

Activation function:





S : https://www.quora.com/What-is-leaky-ReLU

- To add non- linearity into the network.
- To restrict the output of a layer in a certain range.

Rectified Linear Unit (ReLU)

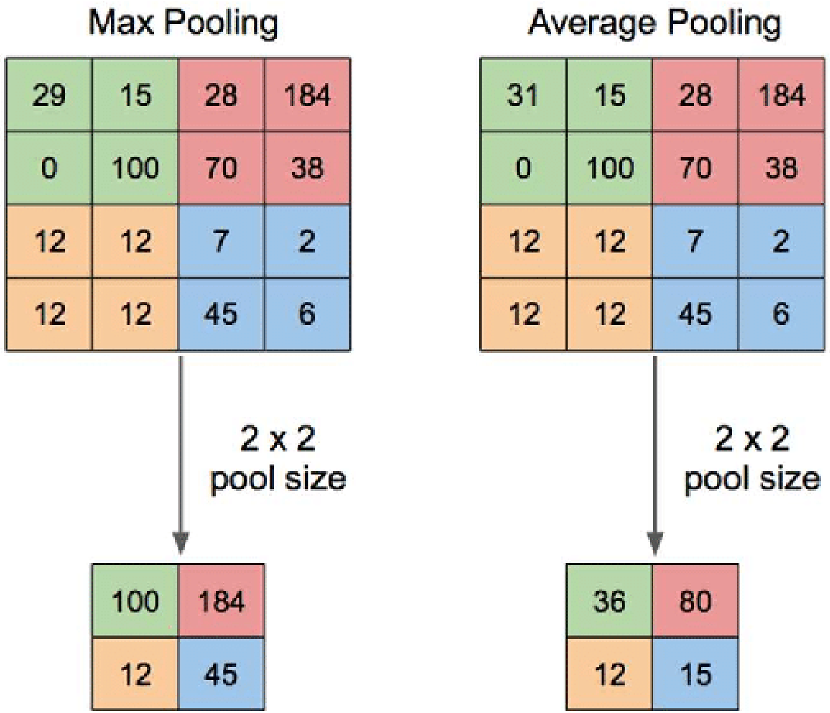
- $f(x) = \max(0x, x)$

Leaky Rectified Linear Unit (ReLU)

- $f(x) = \max(0.01x, x)$

Pooling

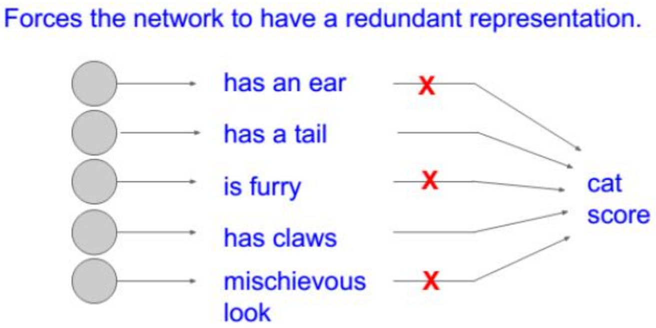
- Makes the representation smaller and more manageable.
- Operates over each activation map independently

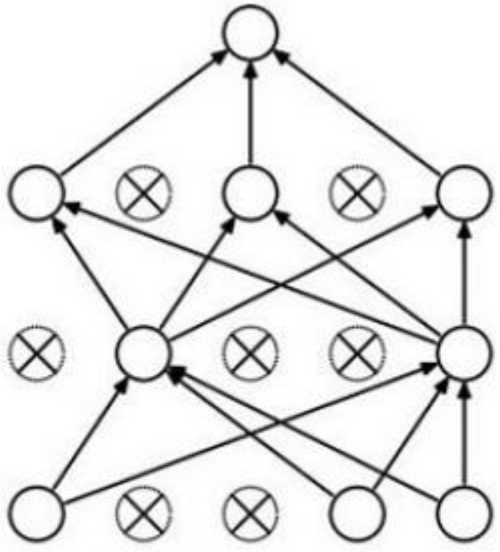


Source: (Yani, 2019)

Regularization (Drop Out)

- It is used to reduce overfitting.
- Randomly set some neurons to zero in the forward pass.





Srivastava, Nitish, et al. ”Dropout: a simple way to prevent neural networks from overfitting”, JMLR 2014

Loss function (categorical cross Entropy)

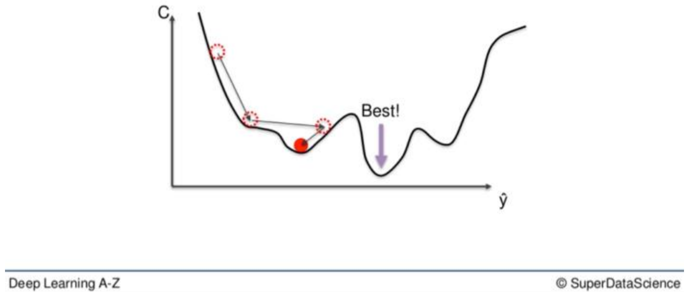
- Commonly used loss function for classification tasks
- Appropriate for Multi-class classification

$$L(\phi) = \sum_{i=1}^{K} y_i log(\hat{y}_i)$$

Optimizer

Stochastic Gradient Descent

- Used to minimize the cost function
  - take steps to the negative of the gradient at the current point
- SGD uses one or subset of samples to update the parameters.
- To overcome saddle point and local minima problem
  - Nestrov's accelerated Momentum



BRATS 2013 and BRATS 2015 DATABASES

- Four MRIs available
  - ✓ T1
  - ✓ T1C (T1 with gadolinium enhancing contrast)
  - ✓ T2
  - ✓ FLAIR

- BRATS 2013

  Training (20 HGG, 10 LGG), Leaderboard(21 HGG, 4 LGG), challenge (10 HGG)

- BRATS 2015

  Training(220 HGG, 54 LGG), Challenge(53 cases including both grades)

- Class Labels:
  - necrosis, edema, non-enhancing, and enhancing tumor, normal tissue.

- The classes are imbalanced. So, they used all samples from the underrepresented classes and randomly sampled from the other.

- Patches extracted:
  - 450,000 HGG
  - 335,000 LGG

- Data augmentation increased the training data roughly four times.

Architecture for HGG

	Type	Filter size	HGG Stride	# filters	FC units	Input
Layer 1	Conv.	3× 3	1× 1	64	-	4× 33× 33
Layer 2	Conv.	3× 3	1× 1	64	-	64× 33× 33
Layer 3	Conv.	3× 3	1× 1	64	-	64× 33× 33
Layer 4	Max-pool.	3× 3	2× 2	-	-	64× 33× 33
Layer 5	Conv.	3× 3	1× 1	128	-	64× 16× 16
Layer 6	Conv.	3× 3	1× 1	128	-	128× 16× 16
Layer 7	Conv.	3× 3	1× 1	128	-	128× 16× 16
Layer 8	Max-pool.	3× 3	2× 2	-	-	128× 16× 16
Layer 9	FC	-	-	-	256	6272
Layer 10	FC	-	-	-	256	256
Layer 11	FC	-	-	-	5	256

(Pereira, Pinto, Alves, & Silva, 2016)

Architecture for LGG

	LGG Type	Filter size	Stride	# filters	FC units	Input
Layer 1	Conv.	3× 3	1× 1	64	-	4× 33× 33
Layer 2	Conv.	3× 3	1× 1	64	-	64× 33× 33
Layer 3	Max-pool.	3× 3	2× 2	-	-	64× 33× 33
Layer 4	Conv.	3× 3	1× 1	128	-	64× 16× 16
Layer 5	Conv.	3× 3	1× 1	128	-	128× 16× 16
Layer 6	Max-pool.	3× 3	2× 2	-	-	128× 16× 16
Layer 7	FC	-	-	-	256	6272
Layer 8	FC	-	-	-	256	256
Layer 9	FC	-	-	-	5	256

(Pereira, Pinto, Alves, & Silva, 2016)

Evaluation

The evaluation is performed for:

- The enhancing tumor,
- The core (necrosis + non-enhancing tumor + enhancing tumor),
- The complete tumor (all classes combined).

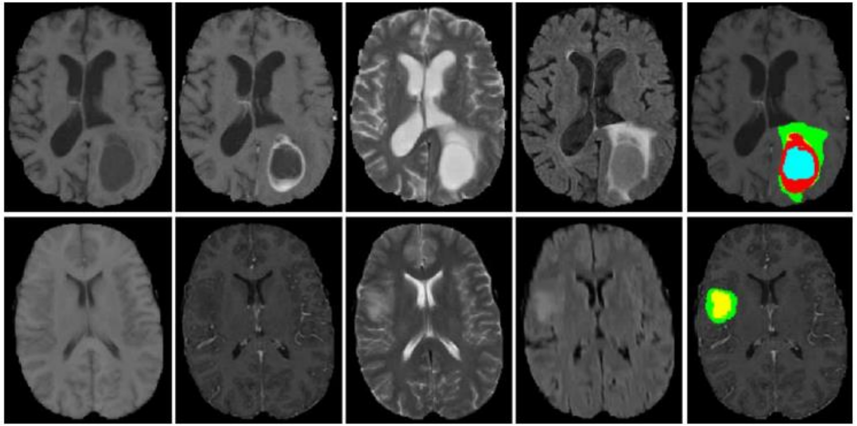
The evaluation metrices were DSC, PPV and Sensitivity.

Results (BRATS 2013 Challenge)

Dataset	Method	DSC (complete)	DSC (core)	DSC (Enhanced)	Position
Leaderboard	Proposed	0.84	0.72	0.62	1
	Kwon et al.[18]	0.86	0.79	0.59	2
	Zhao et al. [4]	0.83	0.73	0.55	3
	Aganm1	0.83	0.71	0.54	4
	Havam2	0.82	0.69	0.56	5
	Urban et.al.	0.70	0.57	0.54	17
	Havaei et.al.[19]	0.84	0.71	0.57	--
	Davy et. al	0.72	0.63	0.56	--
Challenge	Proposed	0.88	0.83	0.77	1
	Kwon et. al. [18]	0.88	0.83	0.72	2
	Zhao et. al. [4]	0.87	0.78	0.74	3
	Aganm1	0.88	0.78	0.73	4
	Havam2	0.87	0.78	0.70	5
	Urban et.al.	0.86	0.75	0.73	12
	Havaei et.al. [19]	0.88	0.79	0.73	--
	Davy et. al.	0.85	0.74	0.68	--

(Pereira, Pinto, Alves, & Silva, 2016)

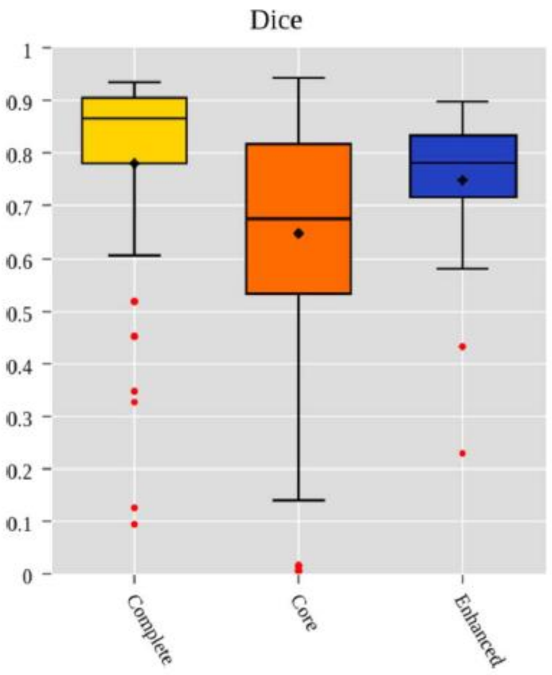
- First Row: HGG
- Second Row: LGG
- T1, T1C, T2, FLAIR, and segmentation (from left to right)
- **Class labels:** Green- edema, blue-necrosis, yellow-non-enhancing tumor, Red-enhancing tumor



(Pereira, Pinto, Alves, & Silva, 2016)

Results (BRATS 2015 challenge)

- DSC score of 0.78, 0.65, and 0.75 in the complete, core, and enhanced regions, respectively
- Secured second position



(Pereira, Pinto, Alves, & Silva, 2016)

Strengths and Weaknesses

Strength

- ❑ Reduced no. of parameter
  - ▪ Smaller filters
- ❑ Overlapping Pooling
  - ▪ Help retaining important information
- ❑ LReLU
  - ▪ Fixed dying Relu problem
- ❑ Won BRATS 2013 challenge

Weakness

- ❑ Extracted 2D patches.
- ❑ Modest results in sensitivity
  - ▪ class imbalance problem not fully addressed by data augmentation
- ❑ Not a winner if all the metrices are considered

Future Work

- Dilated convolution could be used.

- 3D convolution could be helpful in extracting spatial features in 3 dimensions.

Papers Comparison

Paper 1	Paper 2
CNN based Segmentation	CNN based Segmentation
Multimodality	Single modality
2D convolution	2D convolution
2D patches	2D patches

Conclusion

- Paper 1 proposed image fusion strategies for the task of segmentation on biomedical images.
  - Significant improvement over single modality-based networks.
  - Less sensitive to low quality images.

- Paper 2 proposed two different CNN based architecture for the task of segmentation of LGG and HGG tumors.
  - Secured 1st position in BRATS 2013 challenge.










Thank you!!