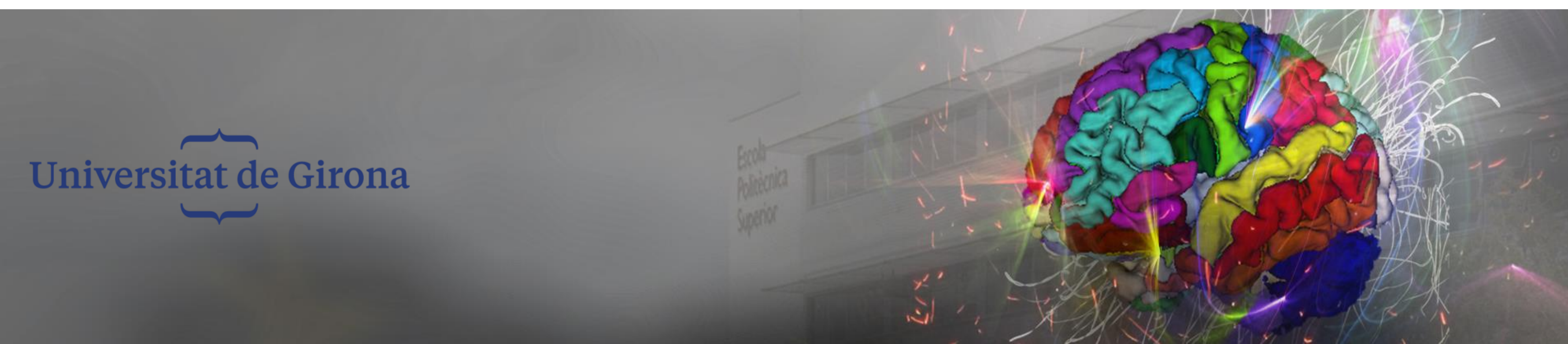
# Lecture Activity: Brain Cancer

Oleh Kozynets, Fakrul Islam Tushar

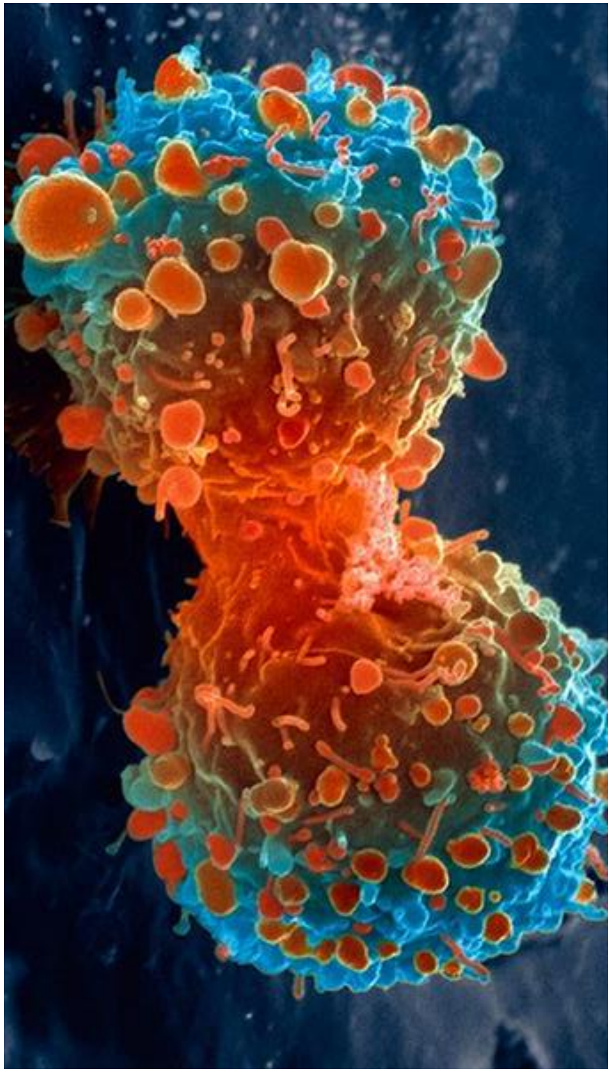


# Outline

1. Brain and Other Nervous System Cancer
2. CAD for Brain Cancer
3. Segmentation
4. Previous Studies, Deep Learning
5. DeepMedic
6. Dense Training
7. Deeper Network
8. Multi-Scale Pathway
9. Model Analysis
10. Results
11. Conclusion

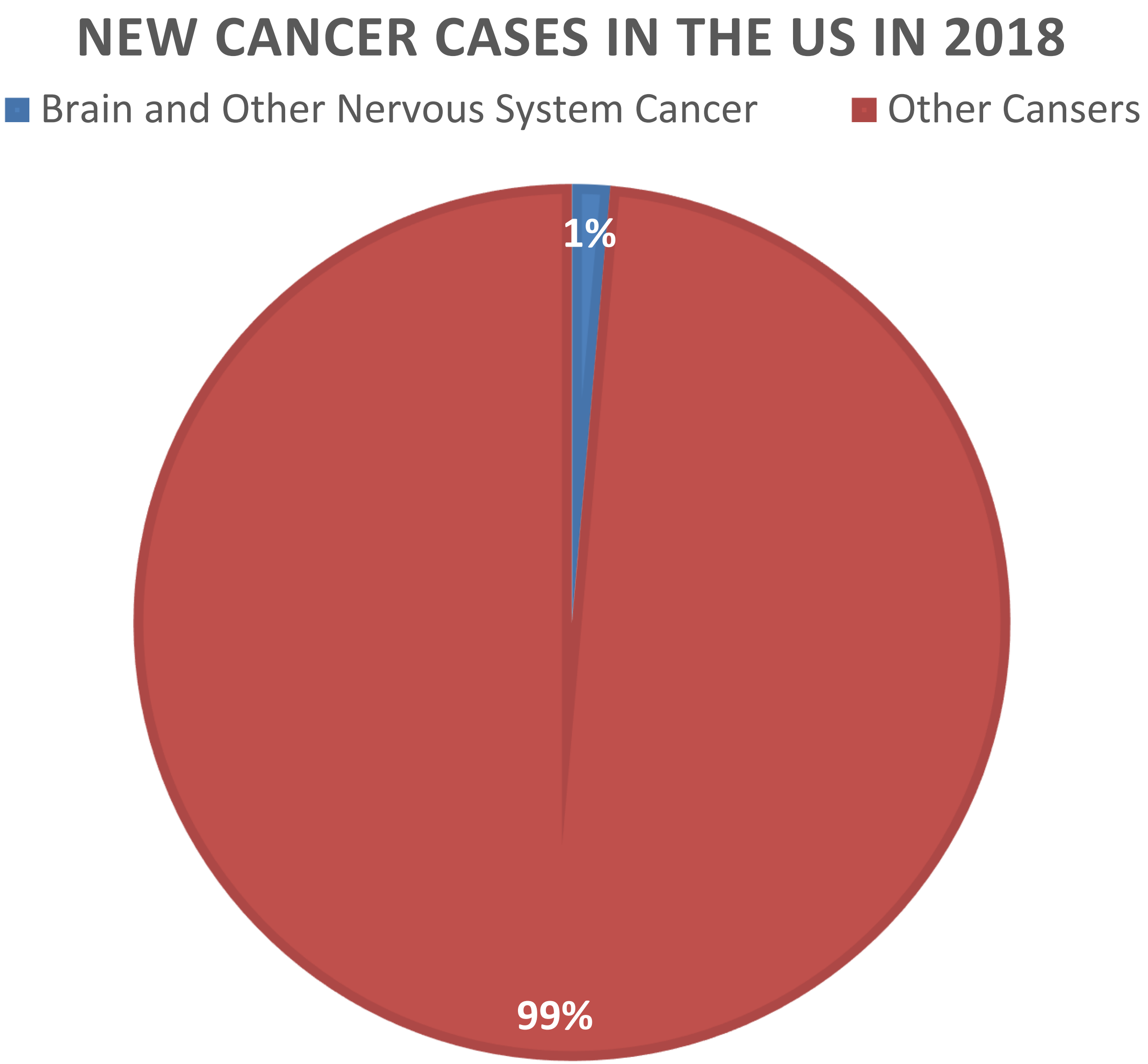
# 1.Brain and Other Nervous System Cancer

- Cancers are diseases characterized by unstoppable growth and spreading of the body's cells
- 5 years survival rate is 33.2%
- Most frequently diagnosed among people aged 55-64



https://seer.cancer.gov/statfacts/html/brain.html
Image by the US National Institutes of Health

# 1.Brain and Other Nervous System Cancer

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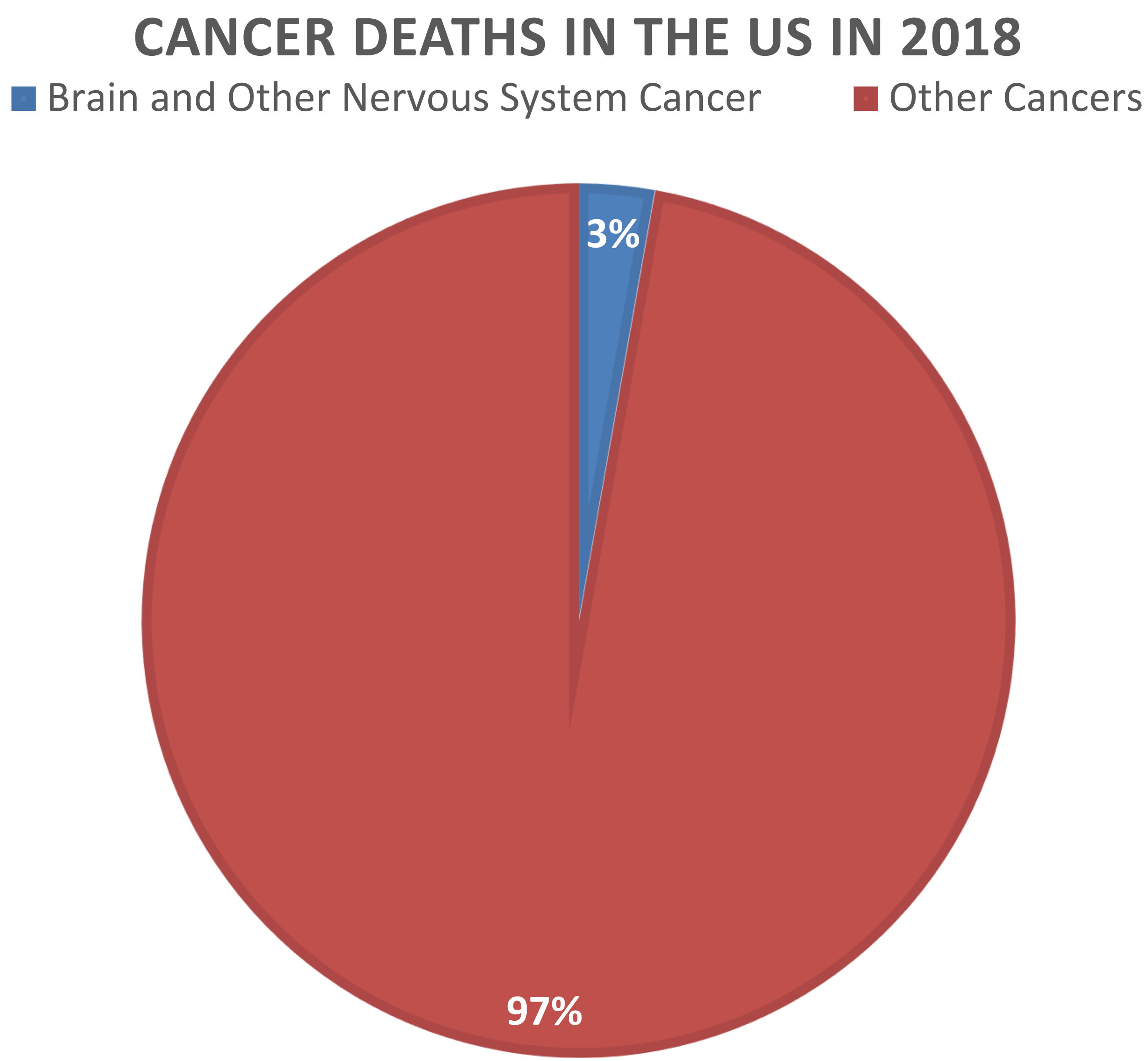
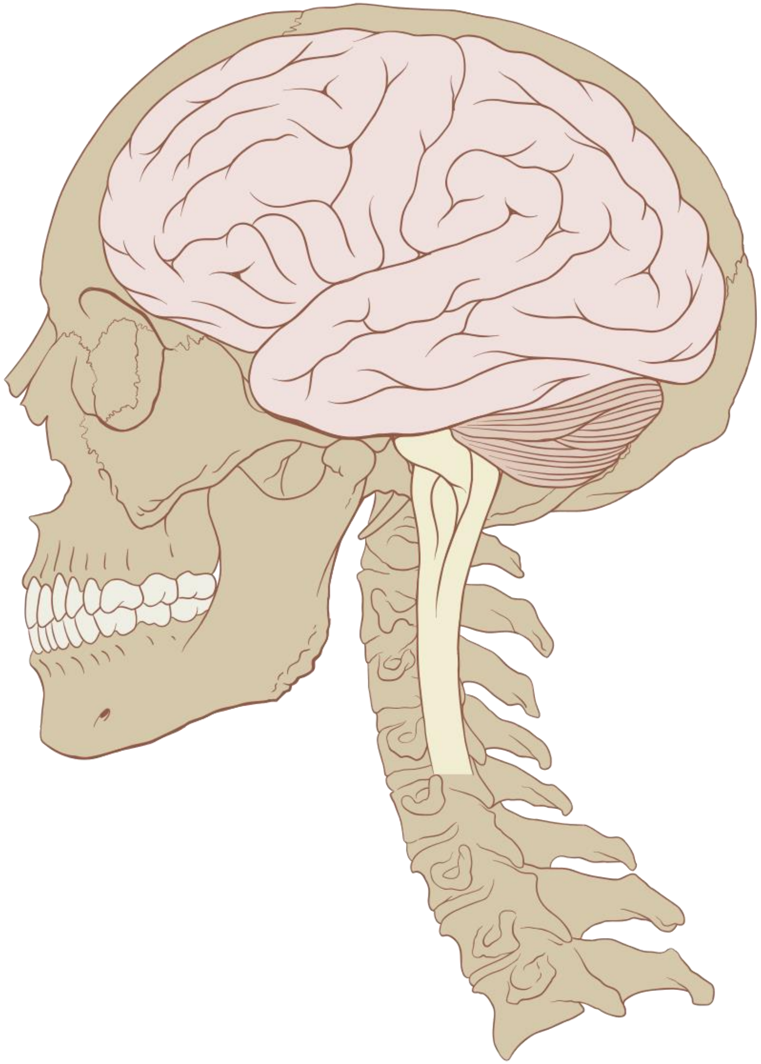
# 1.Brain and Other Nervous System Cancer




https://seer.cancer.gov/statfacts/html/brain.html

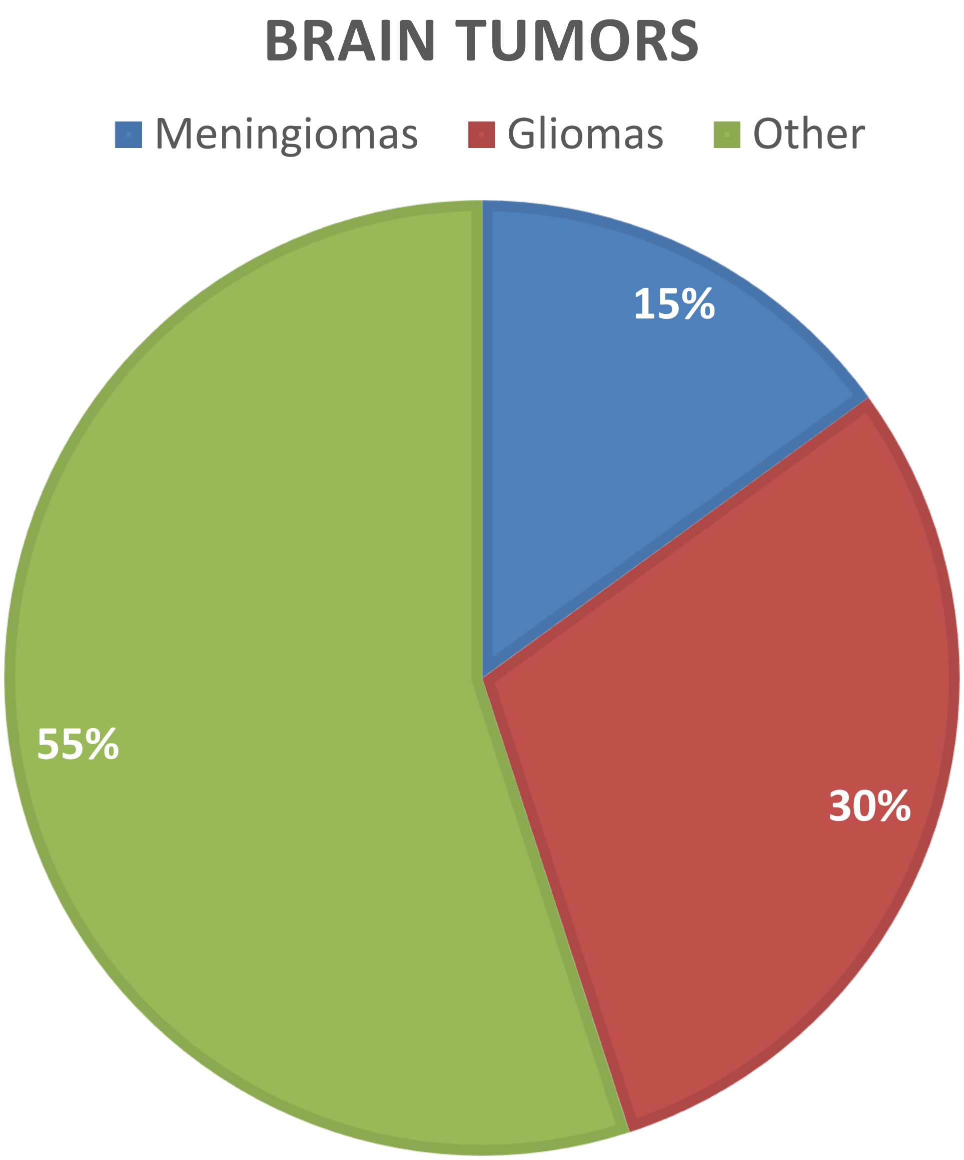
# 1.Brain and Other Nervous System Cancer

- 150 different brain tumors
- Primary and metastatic brain tumors
- Low (I, II) and high (III, IV) grade tumors according to WHO



https://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Brain-Tumors
Image by Patrick J. Lynch, medical illustrator

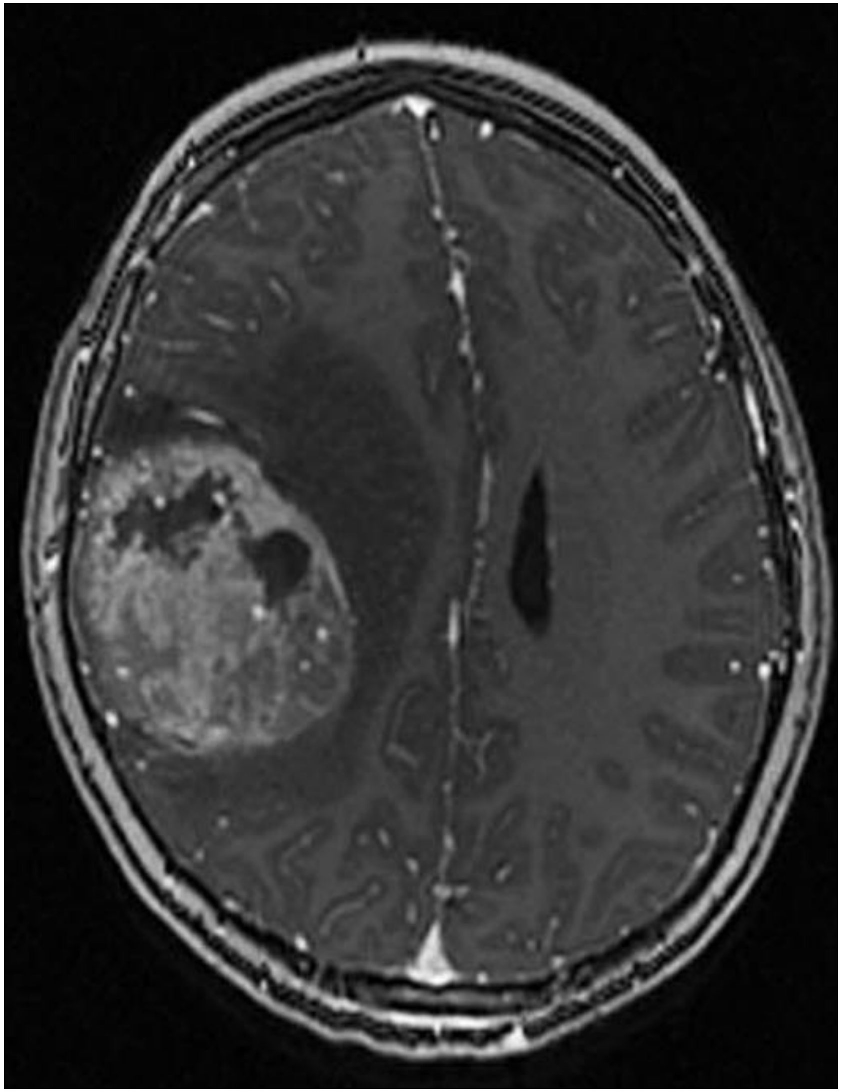
# 1.Brain and Other Nervous System Cancer




https://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Brain-Tumors

# 1.Brain and Other Nervous System Cancer

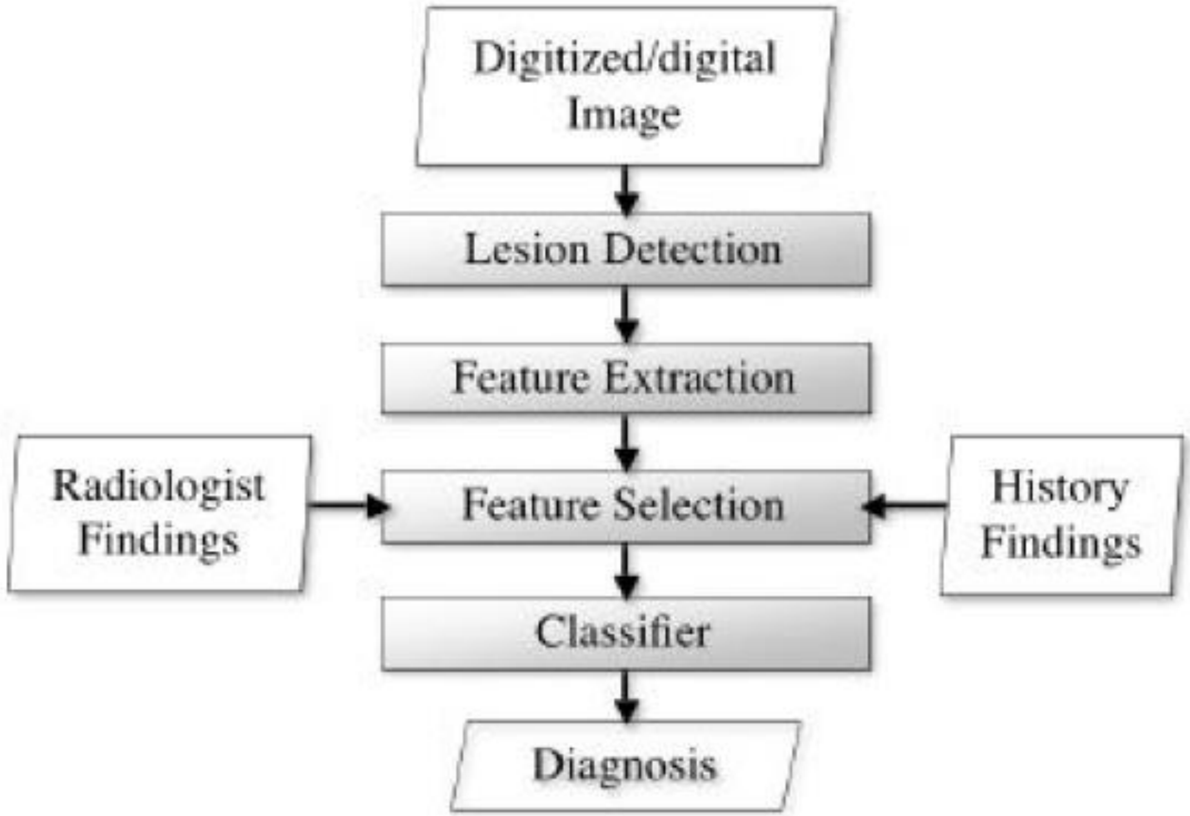
- T2 and FLAIR MRI
- T1-weighted post-Gadolinium MRI
- Perfusion MRI
- Diffusion MRI



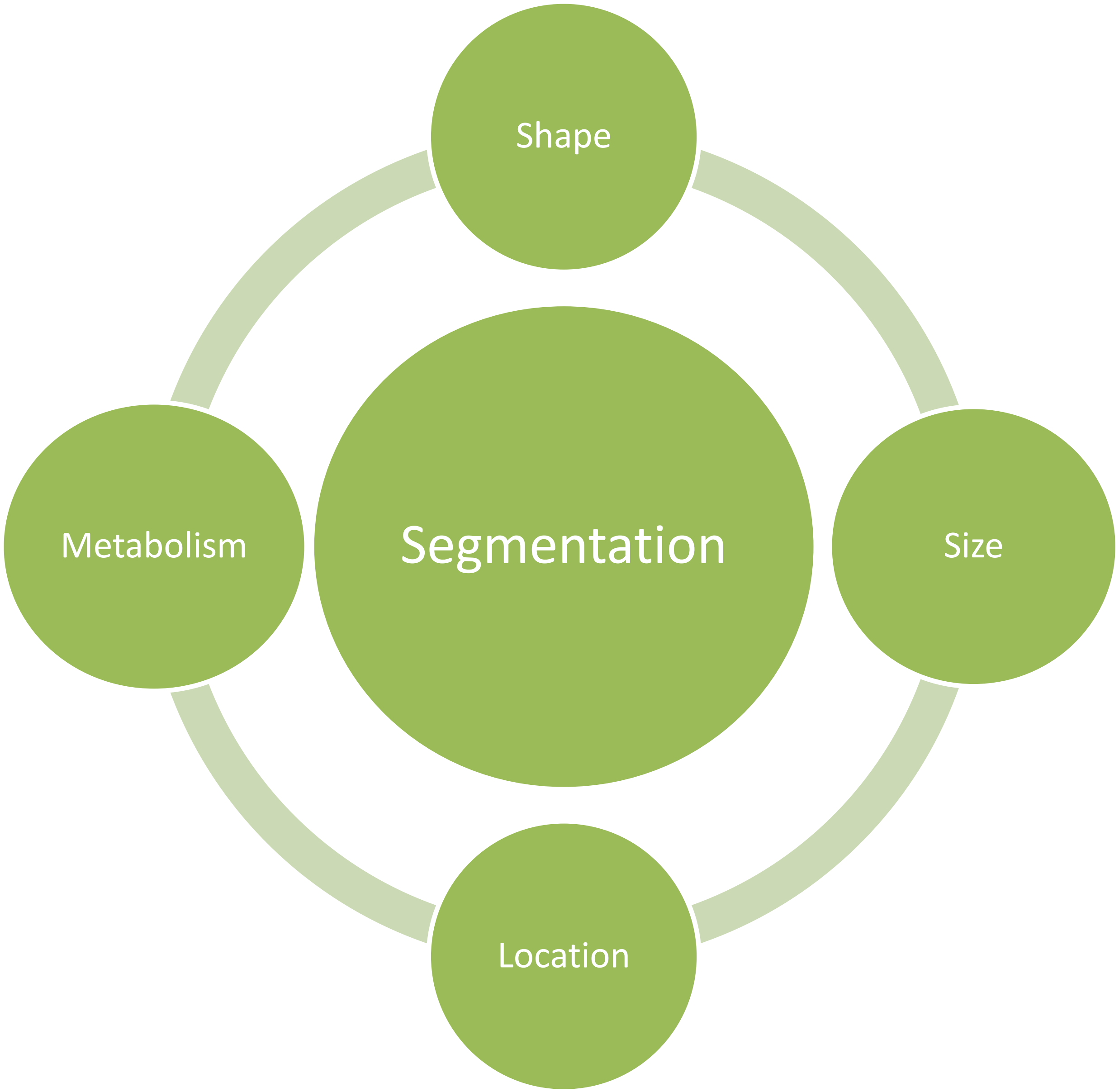
Epithelioid glioblastoma (Ep-GBM)
Grade IV, WHO

*[D. H. Louis et al.]* **WHO classification of tumours of the central nervous system WHO/IARC.,** ***Lyon, France, Tech. Rep., 2007.***

# 2.CAD for Brain Cancer



# 3.Brain Tumor Segmentation



# 4.Previous Studies

No training data required:

- Image registration
- Image synthesis
- Saliency based-method

Machine learning methods:

- Random Forests et al. (RF and atlas-based, RF and RMF)
- Deep Learning

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*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** ***Medical Image Analysis 36 (2017) 61–78***

# 4.PS: Deep Learning

2D CNNS

- Use neural network build for image processing
- 3D brain scan is achieved by processing each 2D slice independently

3D CNNS

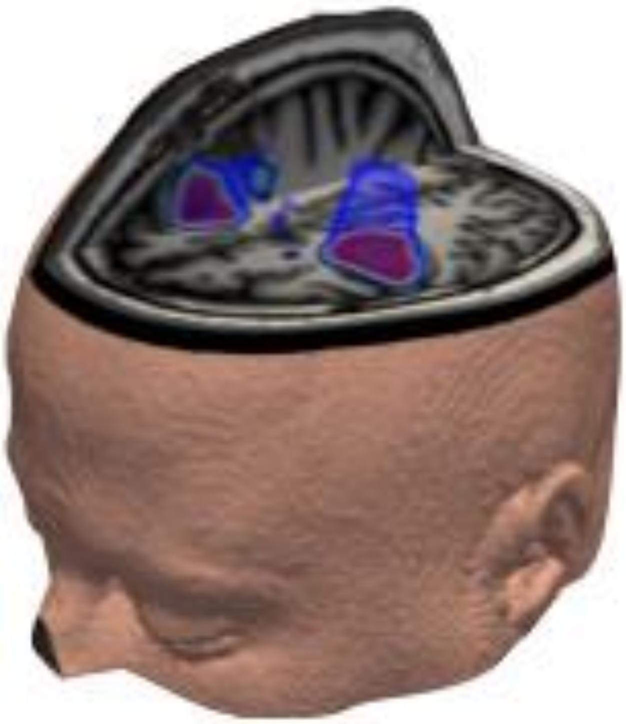
- Use 3D convolutions
- Increased number of parameters and significant memory and computational requirements

*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** ***Medical Image Analysis 36 (2017) 61–78***

**All images in the following slides are taken from this article.**

# 5.DeepMedic

- 11-layers deep 3D CNN for brain tumors segmentation
- Proposed by Konstantinos Kamnitsas et al. in 2017
- It was written in Python, using TensorFlow/Theano, NiBabel, NumPy et al.
- Among top-performers on the BRATS 2016 challenge
- BRATS 2017 challenge winners (DeepMedic, FCN, U-Net)



# 6.Dense Training

- Dense Training

$$\frac{1}{B.V}\sum_{s=1}^{B}\sum_{v=1}^{V}\log(P_{C_s^v}(x^v))$$

Where, B=Batch Size, V=Predicted voxels, $C_s^v$ = True level of the v-th voxel, $x^v$= Corresponding position in the FMs, $P_{C_s^v}$= Output of the softmax function

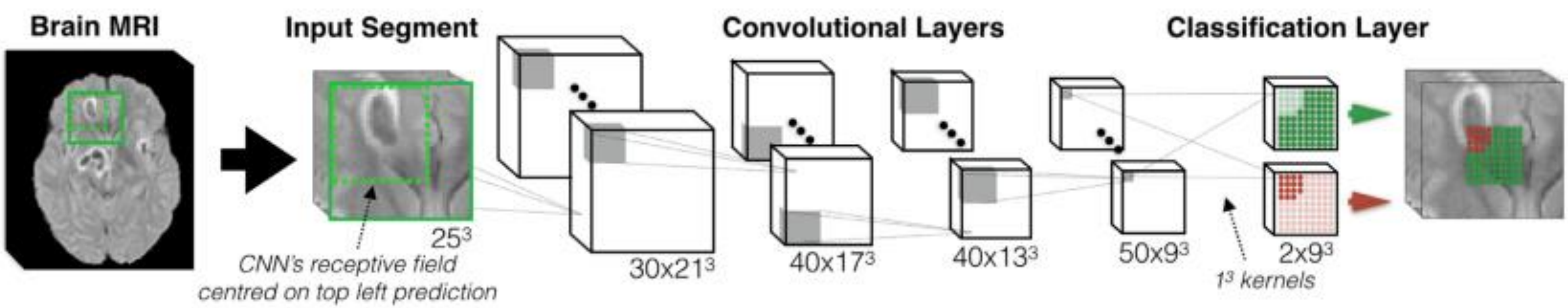



Fig. Baseline CNN

*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** *Medical Image Analysis 36 (2017) 61–78*

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# 6.Dense Training

- Segment based Sampling regulate class balance
- Relatively more background (green) is captured by larger segments and around smaller lesions (Red)

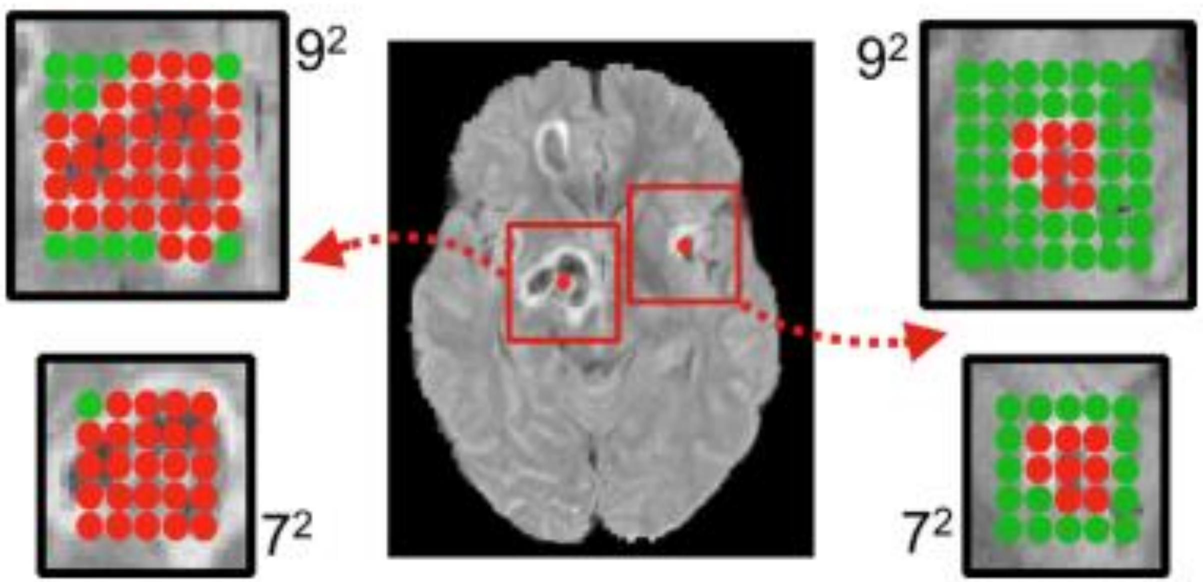



Fig: Consider a network with a 2D receptive field of $3^2$(for illustration) densely applied on the depicted lesion-centered image segments of size $7^2$or $9^2$

*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** *Medical Image Analysis 36 (2017) 61–78*

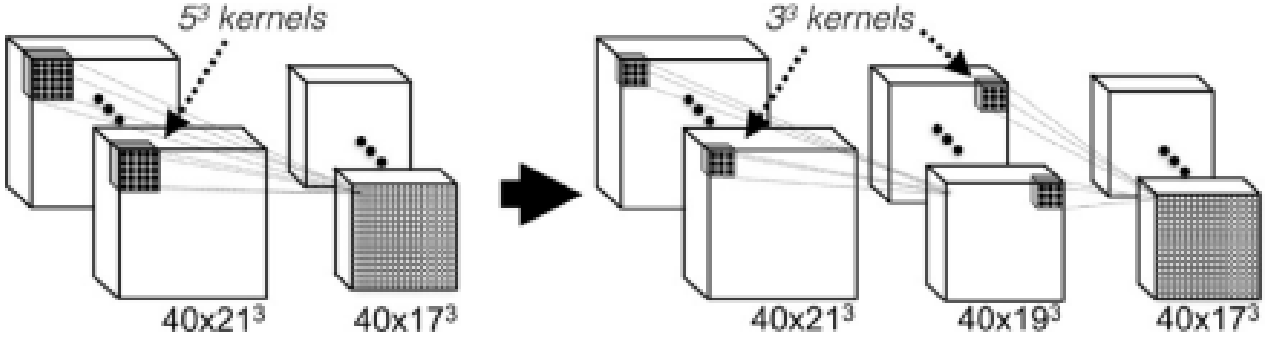
# 7.Deeper Network

- More layers, more power! More computation, more difficult to train

1. Use Smaller kernels
2. Use Batch Normalization
3. Use ReLu-Specific initialization
4. Solution

# 7.Deeper Network: Use Smaller Kernel

- In order to build a deeper 3D architecture, They adopt the $3^3$ kernels that are faster to convolve with and contain less weights




*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** *Medical Image Analysis 36 (2017) 61–78*

# 7.ReLu Specific initialization Scheme

- In Case of Deeper CNN The Forward and Backwards propagated signal may explode or vanish if care is not given to retain its variance (Glorot and Bengio, 2010)

- **ReLu Specific initialization Scheme**

Initialize the kernel weights by sampling from normal distribution (Glorot and Bengio, 2010)

$$\mathrm{N}(0, A = \sqrt{2/n_l^{in}})$$

Where, $n_l^{in}$= number of weights through which a neuron of layer *l* is connected to its input

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# 7.Building Deeper Model

| Shallow | Deep | Shallow+ | Deep+ | BigDeep | DeepMedic |
|---|---|---|---|---|---|
| 4 layer Baseline CNN $5^3$ Kernels Initialization | 9 Layer CNN $3^3$ Kernels | **Shallow** + **ReLu Specific initialization Scheme** + **Batch Normalizatio n** | **Deep** + **ReLu Specific initialization Scheme** + **Batch Normalizatio n** | **Deep+** + Two Hidden layers | **Deep+** + $2^{nd}$ CNN pathway + Two hidden for combining the multi-scale features before the classification layer, Total 11 layers. |

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# 8.Multi-Scale Via Parallel Pathways

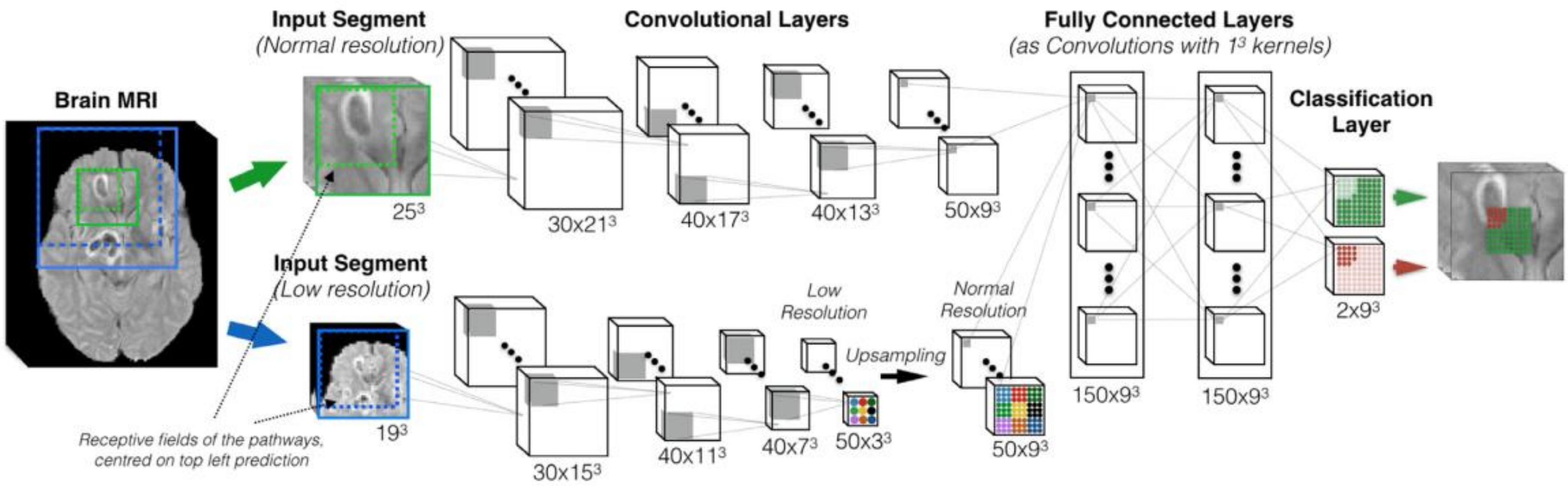
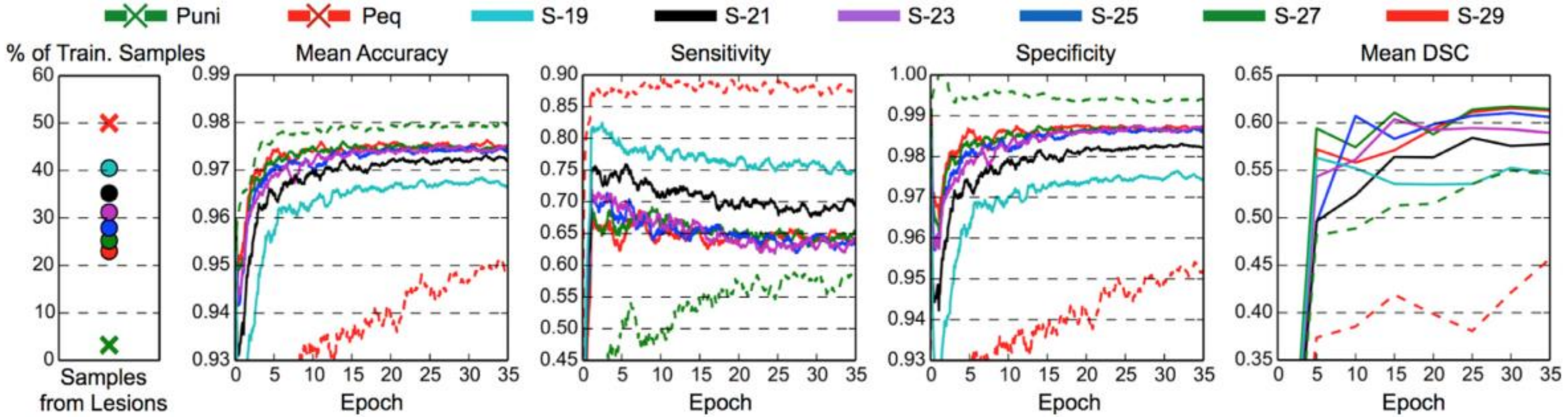



Fig: Multi-scale 3D CNN with two convolutional pathways

*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** ***Medical Image Analysis 36 (2017) 61–78***

# 9.Model Analysis

- Effect of Dense Training

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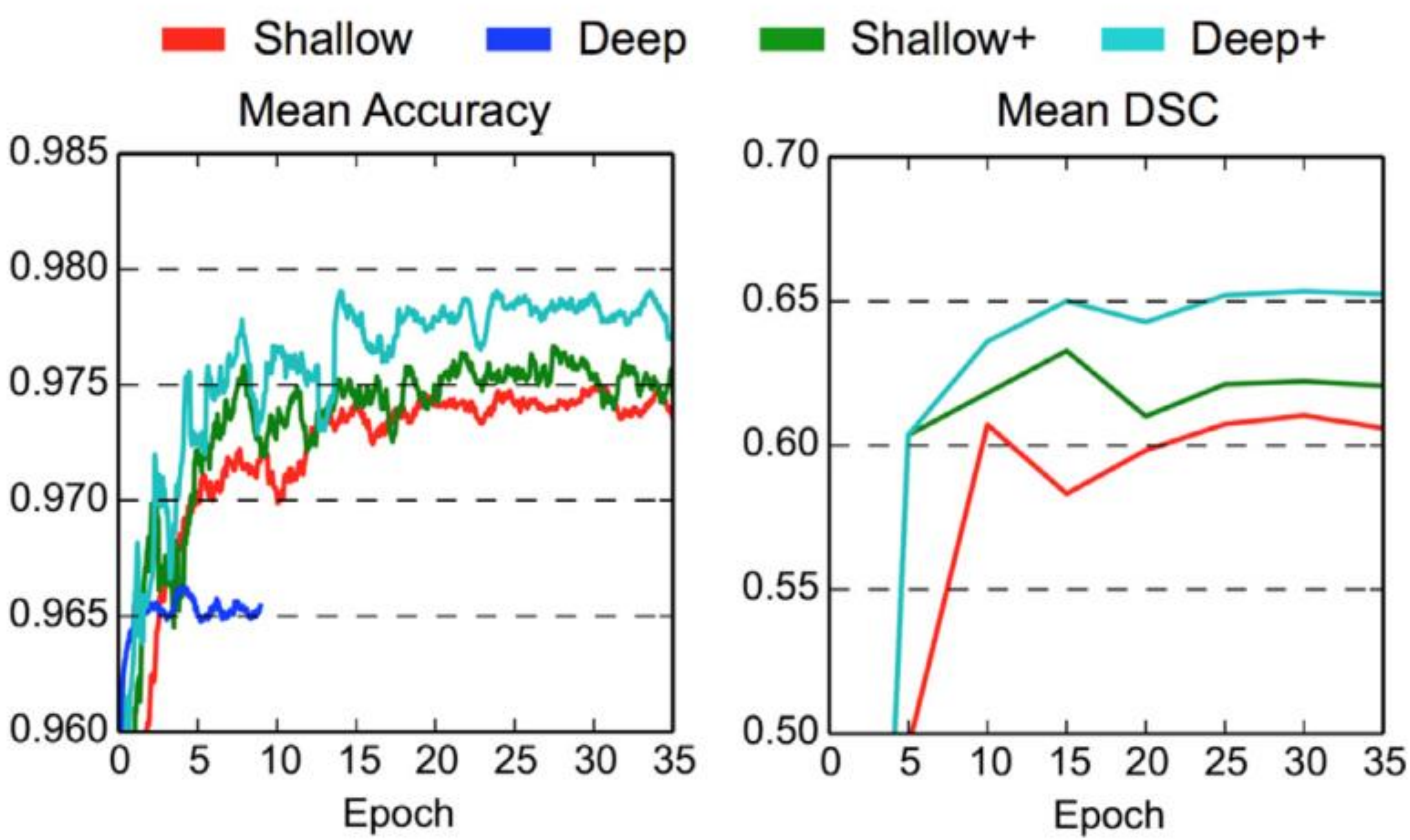
# 9.Model Analysis

- Effect of Deeper Network

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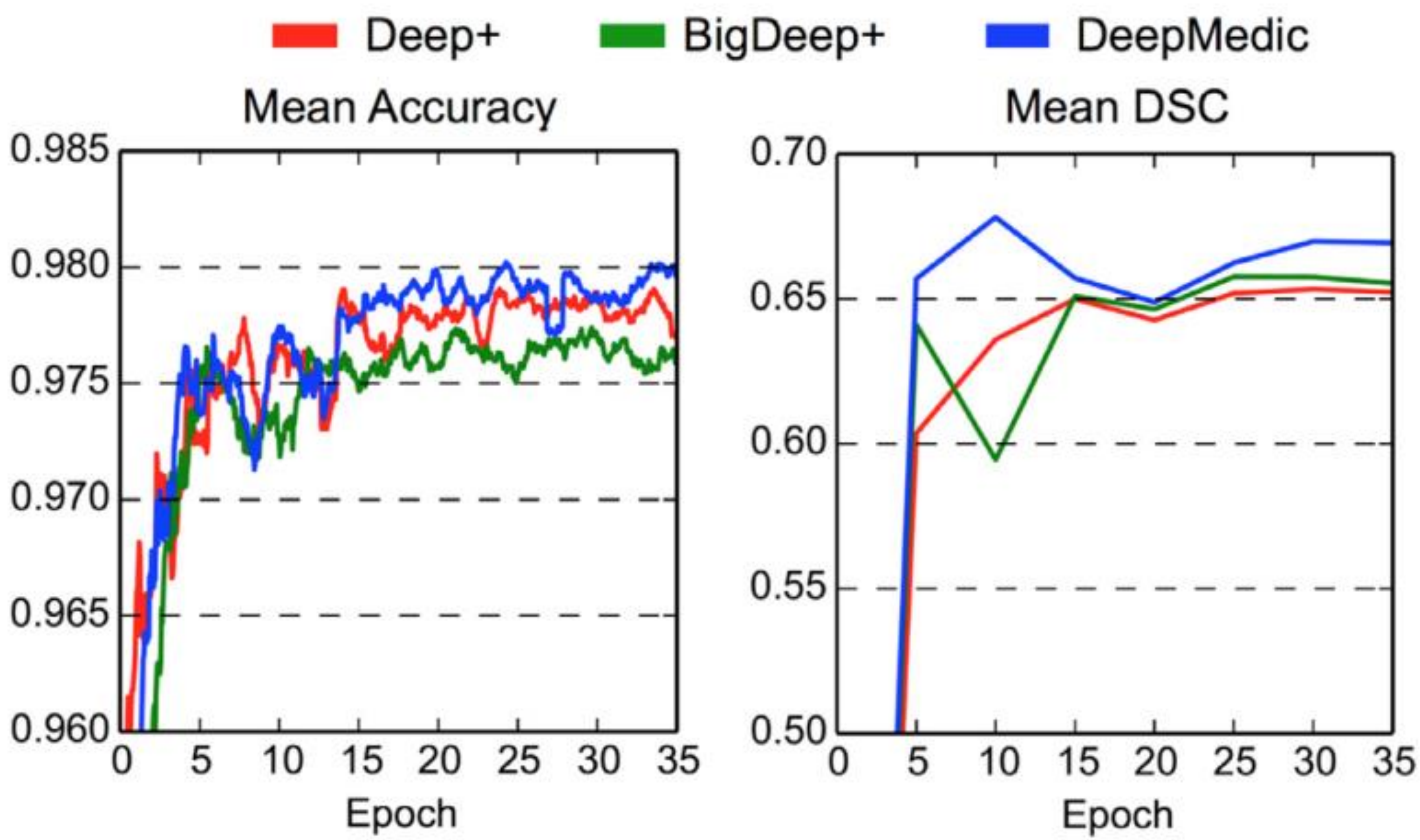
# 9.Model Analysis

- Effect of Multi-Scale Pathways

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# 10.BRATS 2015

- **Multimodal Brain Tumor Image Segmentation (BRATS) challenge** . Link: https://sites.google.com/site/braintumorsegmentation/home/brats2015
- Training Data 220 cases
- Testing Data 110 cases
- **Multi-class problem**
  - necrotic core
  - Edema
  - non-enhancing core
  - Enhancing core

# 10.Results

- BRATS 2015 training Result

Average performance of our system on the training data of BRATS 2015 as computed on the online evaluation platform and comparison to other submissions visible at the time of manuscript submission. Presenting only teams that submitted more than half of the 274 cases. Numbers in bold indicate significant improvement by the CRF, according to a two-sided, paired $t$-test on the DSC metric ($^{*}p < 5 \cdot 10^{-2}$, $^{**}p < 10^{-3}$).

| | DSC | | | Precision | | | Sensitivity | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Whole | Core | Enh. | Whole | Core | Enh. | Whole | Core | Enh. | Cases |
| Ensemble+CRF | **90.1*** | 75.4 | **72.8*** | 91.9 | 85.7 | 75.5 | 89.1 | 71.7 | 74.4 | 274 |
| Ensemble | 90.0 | 75.5 | 72.8 | 90.3 | 85.5 | 75.4 | 90.4 | 71.9 | 74.3 | 274 |
| DeepMedic+CRF | **89.8**** | 75.0 | **72.1*** | 91.5 | 84.4 | 75.9 | 89.1 | 72.1 | 72 .5 | 274 |
| DeepMedic | 89.7 | 75.0 | 72.0 | 89.7 | 84.2 | 75.6 | 90.5 | 72.3 | 72.5 | 274 |
| bakas1 | 88 | 77 | 68 | 90 | 84 | 68 | 89 | 76 | 75 | 186 |
| peres1 | 87 | 73 | 68 | 89 | 74 | 72 | 86 | 77 | 70 | 274 |
| anon1 | 84 | 67 | 55 | 90 | 76 | 59 | 82 | 68 | 61 | 274 |
| thirs1 | 80 | 66 | 58 | 84 | 71 | 53 | 79 | 66 | 74 | 267 |
| peyrj | 80 | 60 | 57 | 87 | 79 | 59 | 77 | 53 | 60 | 274 |

*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** ***Medical Image Analysis 36 (2017) 61–78***

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# 10.Results

- BRATS 2015 test Result

Average performance of our system on the 110 test cases of BRATS 2015, as computed on the online evaluation platform. Numbers in bold indicate significant improvement by the CRF, according to a two-sided, paired $t$-test on the DSC metric ($^{*}p < 5 \cdot 10^{-2}$, $^{**}p < 10^{-3}$). The decrease of the mean DSC by the CRF and the ensemble for the "Core" class was not found significant.

| | DSC | | | Precision | | | Sensitivity | | |
|---|---|---|---|---|---|---|---|---|---|
| | Whole | Core | Enh. | Whole | Core | Enh. | Whole | Core | Enh. |
| DeepMedic | 83.6 | 67.4 | 62.9 | 82.3 | 84.6 | 64.0 | 88.5 | 61.6 | 65.6 |
| DeepMedic+CRF | **84.7**** | 67.0 | 62.9 | 85.0 | 84.8 | 63.4 | 87.6 | 60.7 | 66.2 |
| Ensemble | 84.5 | 66.7 | 63.3 | 83.3 | 86.1 | 63.2 | 88.9 | 59.9 | 67.3 |
| Ensemble+CRF | **84.9**** | 66.7 | **63.4*** | 85.3 | 86.1 | 63.4 | 87.7 | 60.0 | 67.4 |

*[K. Kamnitsas et al. 2017]* **Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation.** *Medical Image Analysis 36 (2017) 61–78*

# 10.Results

- Examples of DeepMedic's segmentation from its evaluation on the training datasets of BRATS 2015.

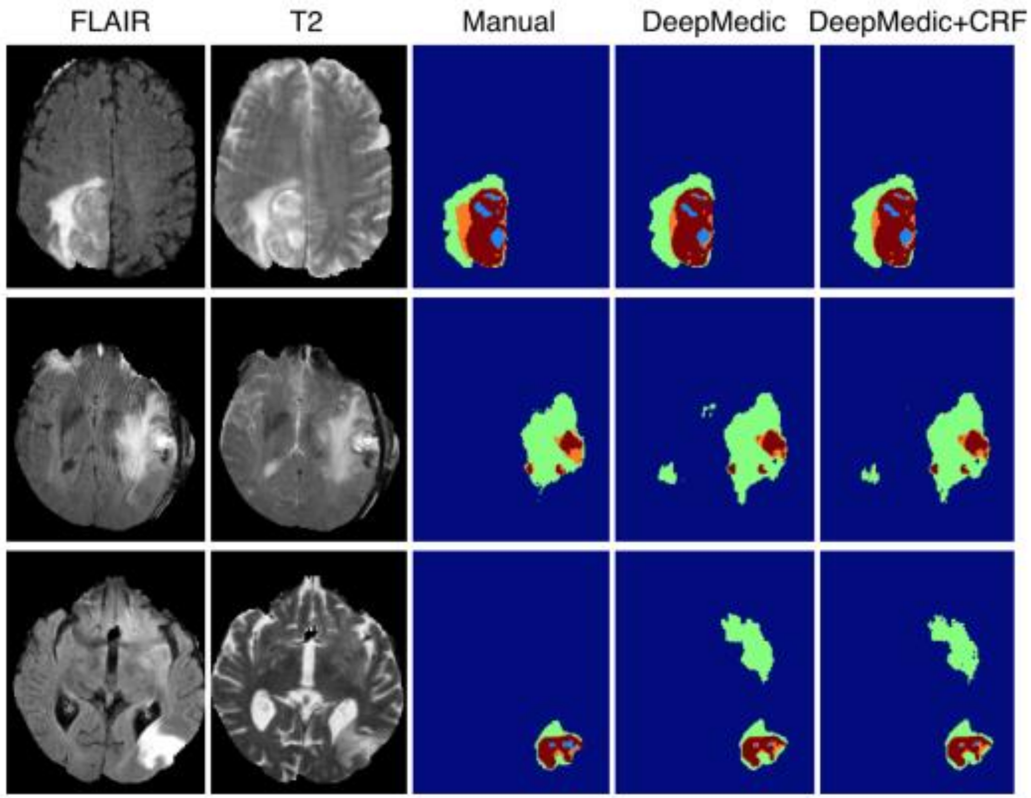


Fig: cyan: necrotic core, green: oedema, orange: non-enhancing core, red: enhancing core. (top and middle) Satisfying segmentation of the tumour, regardless motion artefacts in certain sequences. (bottom) One of the worst cases of over-segmentation observed. False segmentation of FLAIR hyper-intensities as oedema constitutes the most common error of DeepMedic

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# 11.Conclusion

- Deep learning  approaches Proven to be better than conventional approaches in comparison of results
- Deeper network has more advantages where as it comes with more computation expenses and complexity
- Dense training approaches using segments is proven to be better and using  equal distribution of  lesion and non lesion pixels over uniform distribution fails
- Designing deeper network importance need to given to the initialization steps and parameters to be trained

# To know more…

- **Konstantinos Kamnitsas**, Christian Ledig, Virginia F.J. Newcombe, Joanna P. Simpson, Andrew D. Kane, David K. Menon, Daniel Rueckert, and Ben Glocker, "Efficient Multi-Scale 3D CNN with Fully Connected CRF for Accurate Brain Lesion Segmentation", *Medical Image Analysis, 2016*.
- GitHub: https://github.com/Kamnitsask/deepmedic
- YouTube: [MISS 2016] Ben Glocker - Deep Learning for Brain Lesion Segmentation

MAIA

# Thank You