Deep learning for medical imaging

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  - Paul Jaeger

Thank you!!

Previous Lecture
Validation

Validation

- Validation aims at evaluating the performance of an ML model
- Ideally, it should be representative of how the model would perform in real life
  - Difficult to achieve in practice, at least at the stage of research
- At the very least, it should provide an unbiased estimate to that used for training (but not the sma data of course!!!)

Metrics for classification/ regression

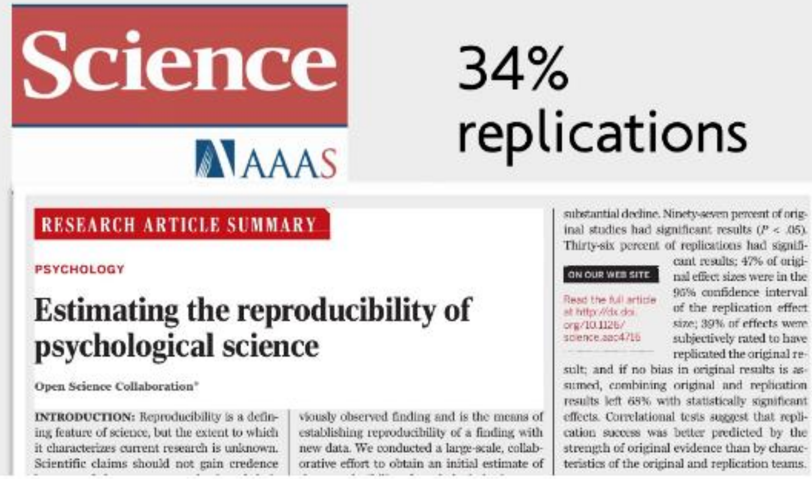
- Accuracy and BA are useful because they are easy to interpret. However, taken alone, they are not sufficient and can be misleading
- Same thing for F1
- Matthews Correlation Coefficient (MCC) is a good summary metric but probably less intuitive.

- RMSE, MAE good for regression models
- MAE is easier to interpret, RMSE will put more weight on rare large errors

Replication Crisis

AI in medicine is facing it too!

34% replications



Science

AAAS

RESEARCH ARTICLE SUMMARY

PSYCHOLOGY

Estimating the reproducibility of psychological science

Open Science Collaboration*

INTRODUCTION: Reproducibility is a defining feature of science, but the extent to which it characterizes current research is unknown. Scientific claims should not gain credence

viously observed finding and is the means of establishing reproducibility of a finding with new data. We conducted a large-scale, collaborative effort to obtain an initial estimate of

substantial decline. Ninety-seven percent of original studies had significant results ($P < .05$). Thirty-six percent of replications had significant results; 47% of original effect sizes were in the 95% confidence interval of the replication effect size; 39% of effects were subjectively rated to have replicated the original result; and if no bias in original results is assumed, combining original and replication results left 68% with statistically significant effects. Correlational tests suggest that replication success was better predicted by the strength of original evidence than by characteristics of the original and replication teams.

ON OUR WEB SITE

Read the full article at http://dx.doi.org/10.1126/science.aac4716

~11-25% replications

nature

International weekly journal of science

Raise standards for preclinical cancer research

C. Glenn Begley and **Lee M. Ellis** propose how methods, publications and incentives must change if patients are to benefit.

Efforts over the past decade to characterize the genetic alterations in human cancers have led to a better understanding of molecular drivers of this complex set of diseases. Although we in the cancer field hoped that this would lead to more effective drugs, historically, our ability to translate cancer research to clinical success has been remarkably low[1]. Sadly, clinical trials in oncology have the highest failure rate compared with other therapeutic areas. Given the high unmet need in oncology, it is understandable that barriers to clinical development may be lower than for other disease areas, and a larger number of drugs with suboptimal preclinical validation will enter oncology trials. However, this low success rate is not sustainable or acceptable, and investigators must reassess their approach to translating discovery research into greater clinical success and impact.

Many factors are responsible for the high failure rate, notwithstanding the inherently difficult nature of this disease. Certainly, the limitations of preclinical tools such as inadequate cancer-cell-line and mouse models[2] make it difficult for even

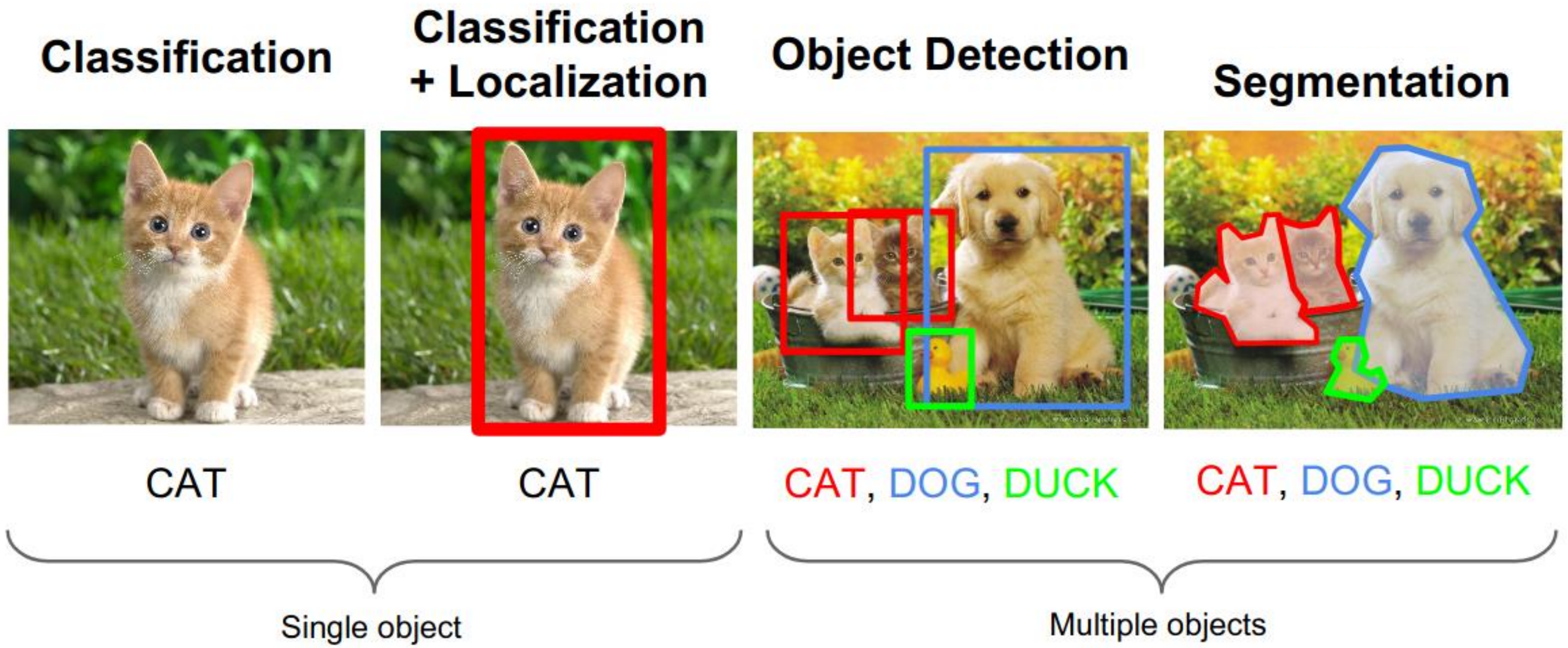
Part 4 – Segmentation

Outline

- Segmentation
  - Upsampling & Dilated Filters
  - Loss Functions
  - Evaluation Metrics
- Medical Imaging

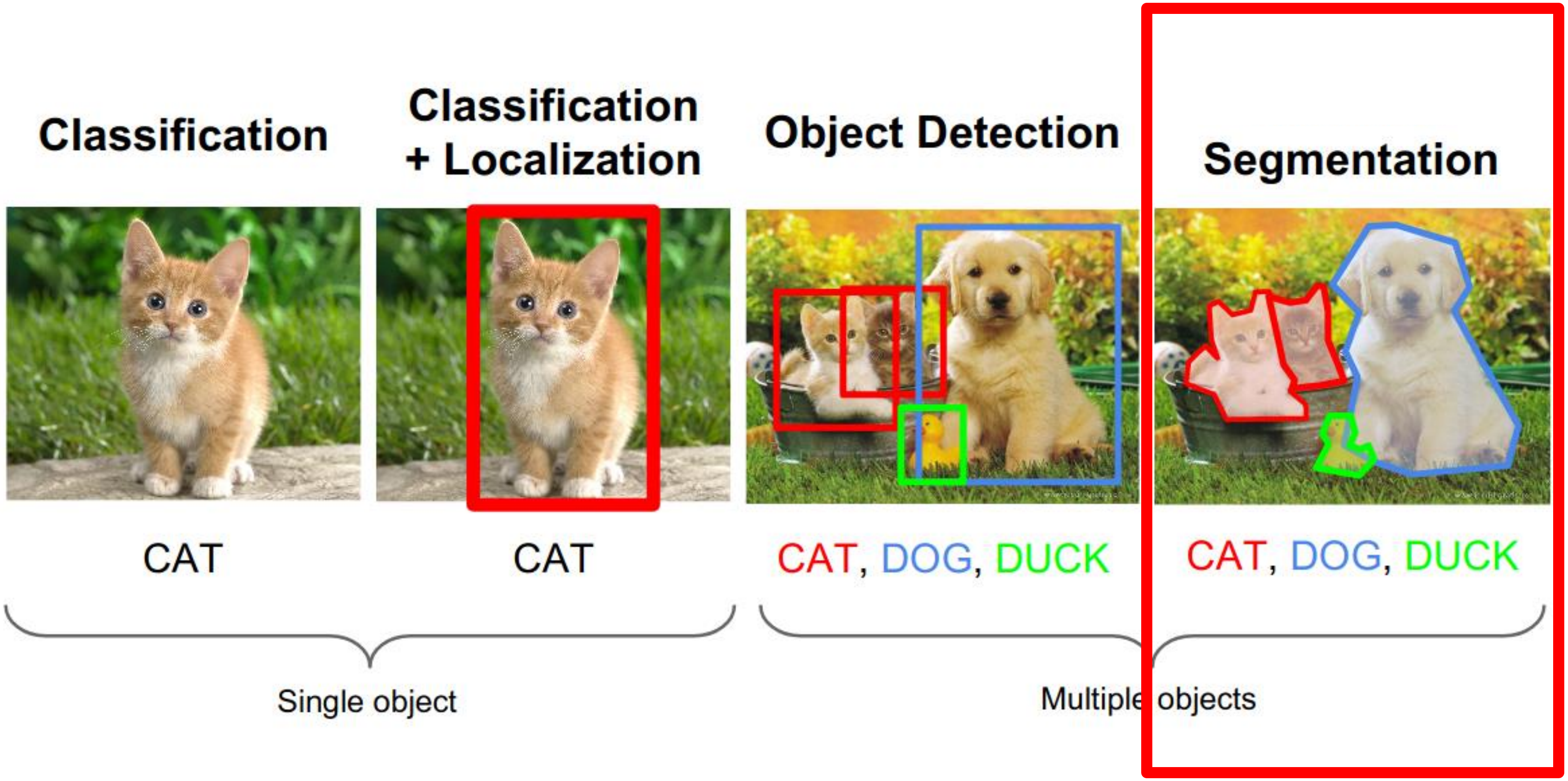
Introduction

- Different problems for vision



Introduction

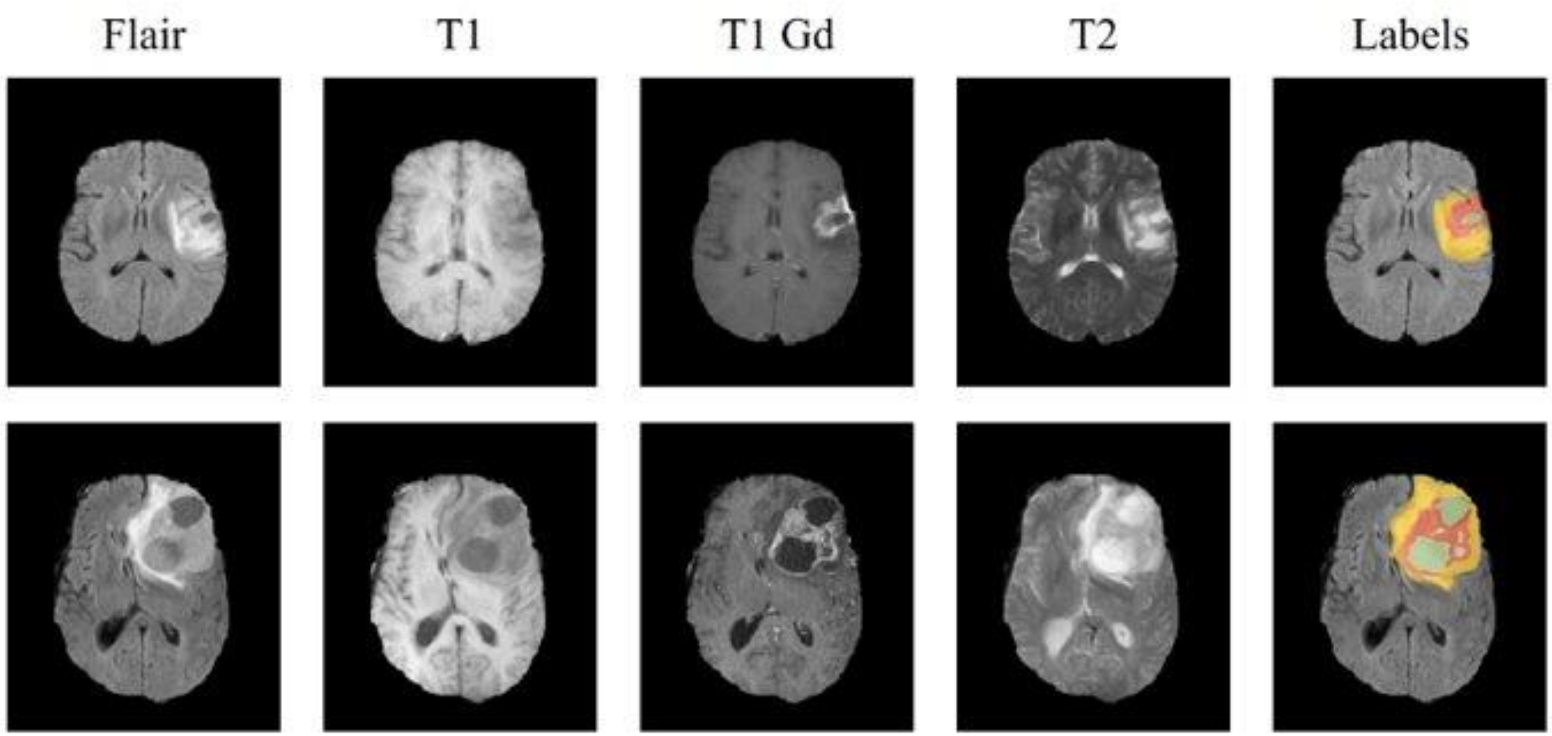
- Different problems for vision



Introduction

- Semantic Segmentation

  - Label each pixel in the image with a category label
  - Do not differentiate instances only care about pixels, we want to find the mesh of pixels with the same label

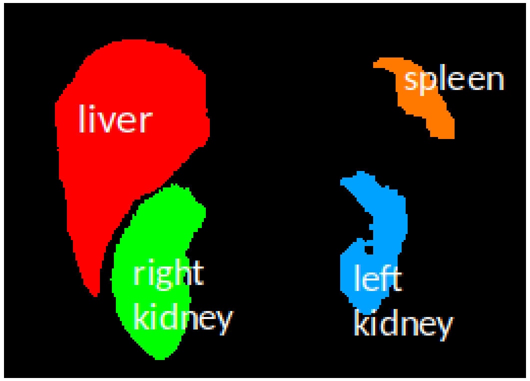


Introduction

- In Semantic Segmentation, a segmentated region is also assigned a **semantic meaning**
- This is in contrast to segmentation based on 'pure' clustering of image into coherent regions
- For this lecture, we are mostly interested in semantic segmentation

raw image

segmentation/clustering

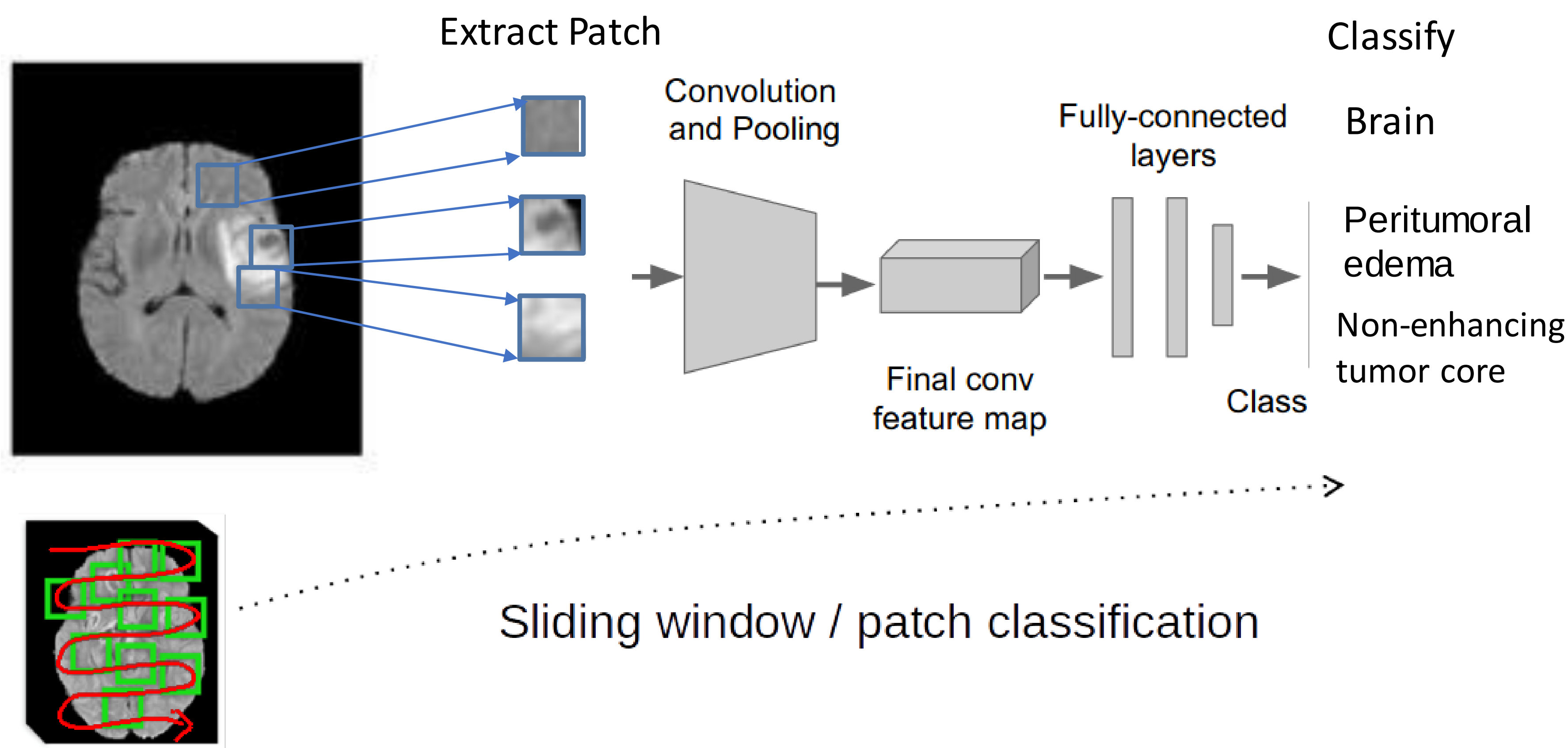


semantic segmentation

Introduction

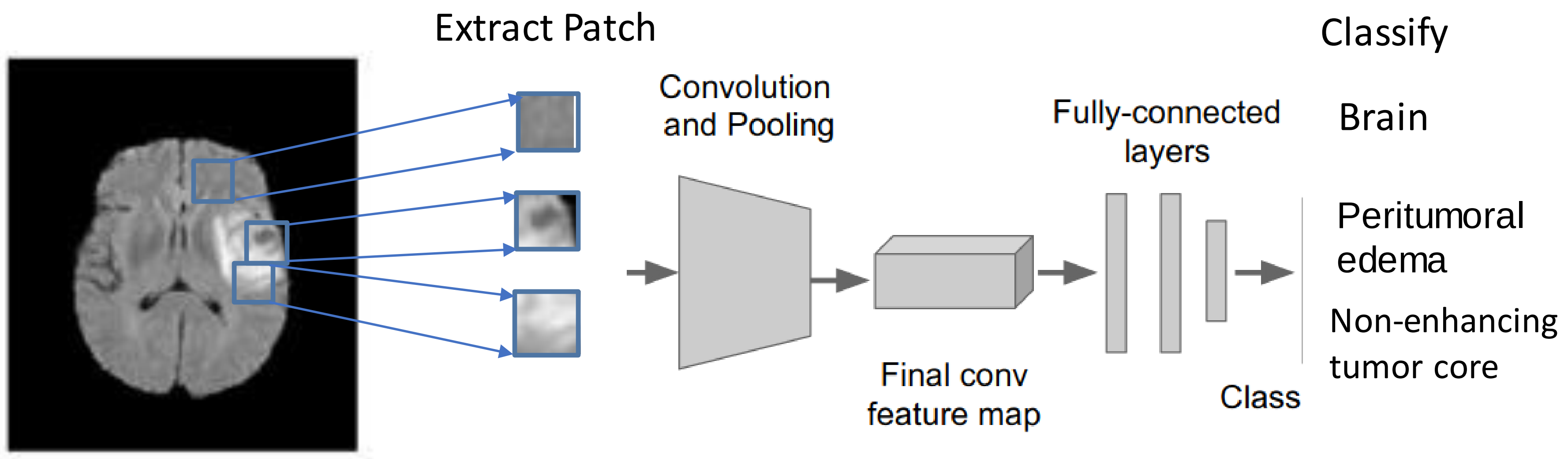
- Semantic Segmentation

- Idea #1: Image Segmentation as Classification using sliding window



Introduction

- Semantic Segmentation
- Idea #1: Image Segmentation as Classification using sliding window

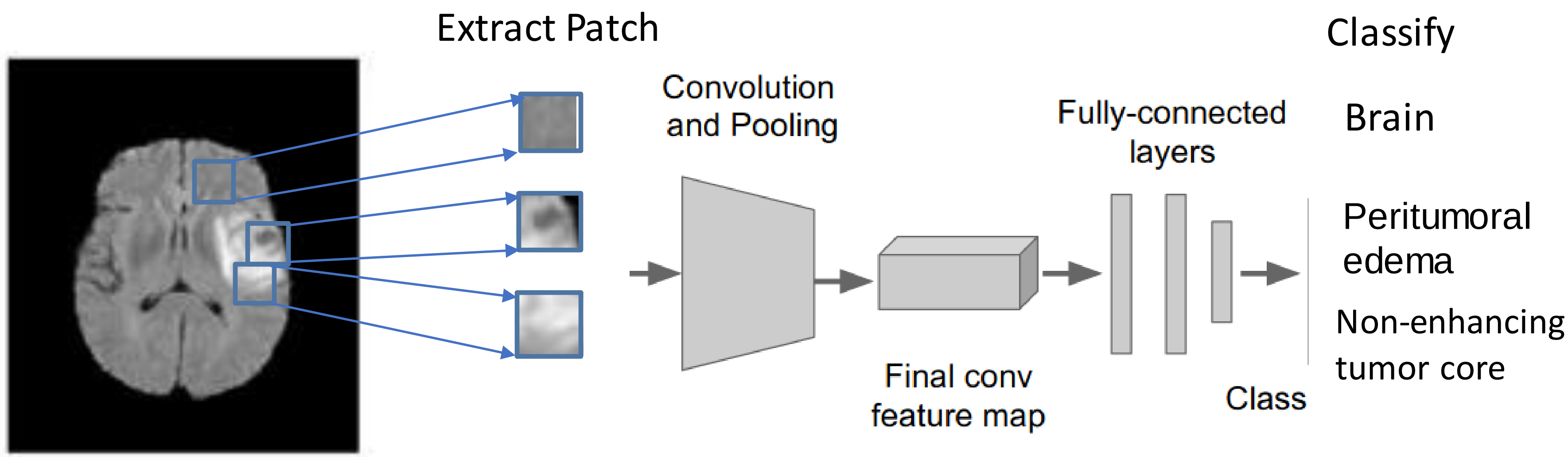


- Problems??

Introduction

- Semantic Segmentation

- Idea #1: Image Segmentation as Classification using sliding window

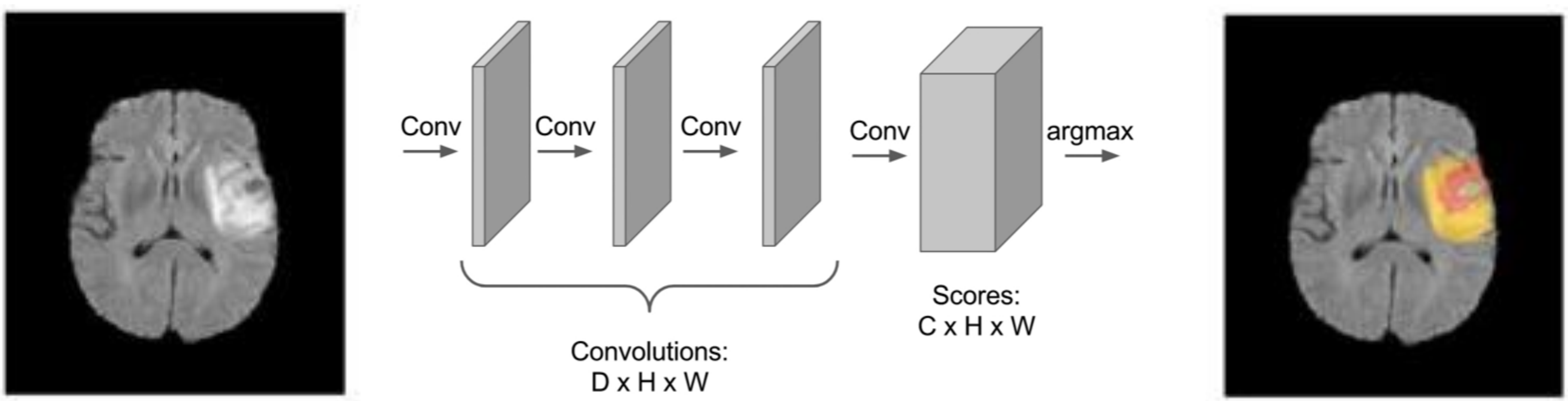


- Problems??
  - Very inefficient (both time and complexity)
  - Using information only in a small part of the image
  - Do not reuse shared features between overlapping patches

Introduction

- Semantic Segmentation

- Idea #2: Image Segmentation using Fully Convolutional Layers
    - Design a network as a bunch of convolutional layers to make predictions for pixels all at once!



Input HxW

Output HxW

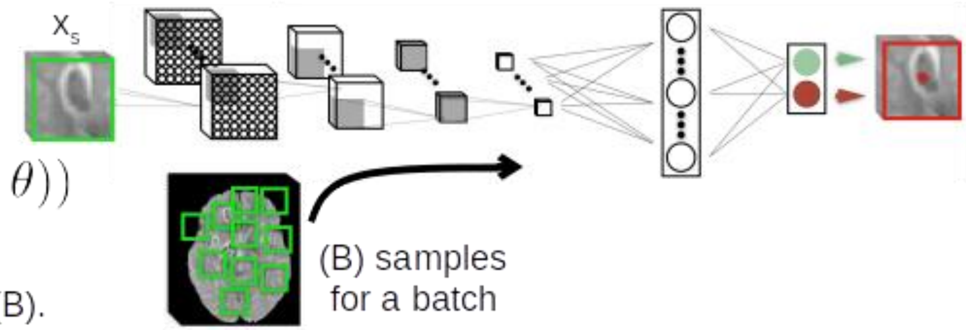
Problems?

Training

Training with single predictions on each sample:

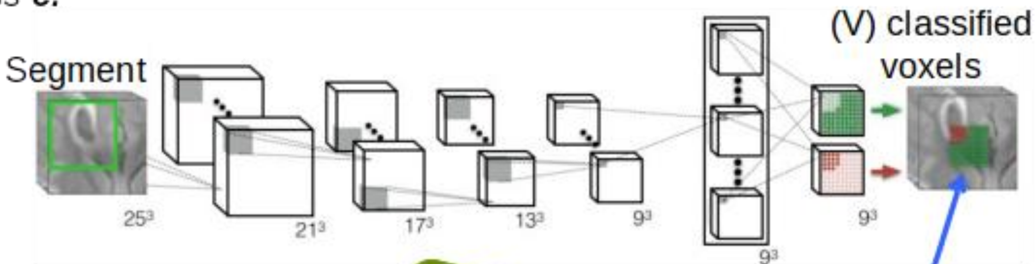
Learn parameters $\theta = \min_{\theta} \mathcal{L}$

$$\mathcal{L} = -\frac{1}{B}\sum_{s=1}^{B}\sum_{c}[c = y_s]log(f_c(x_s;\theta))$$



Cross Entropy over all the samples of a batch (B).
x*$_s$* a training sample (patch), ***y****$_s$* the true label of its central voxel.
f*$_c$**(x)* the CNN's confidence for predicting class ***c.***
[.] the indicator function.

Training on dense predictions:



Over the (B) segments (s) in a batch.

$$\mathcal{L} = -\frac{1}{B \cdot V}\sum_{s=1}^{B}\sum_{v=1}^{V}\sum_{c}[c = y_s^v]log(f_c(x_s^v;\theta))$$

Over the (V) classified voxels in a segment.

**Increase number of samples per batch.
Without linear increase in computation
(eg if loading V separate patches).**

Introduction

- Semantic Segmentation

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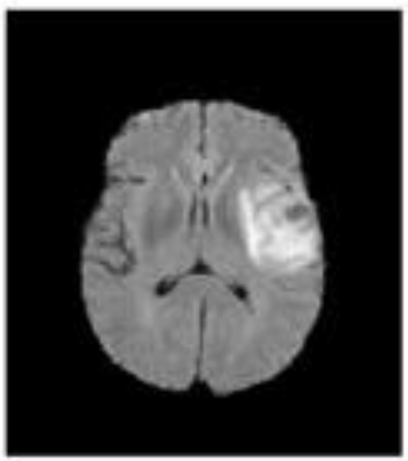
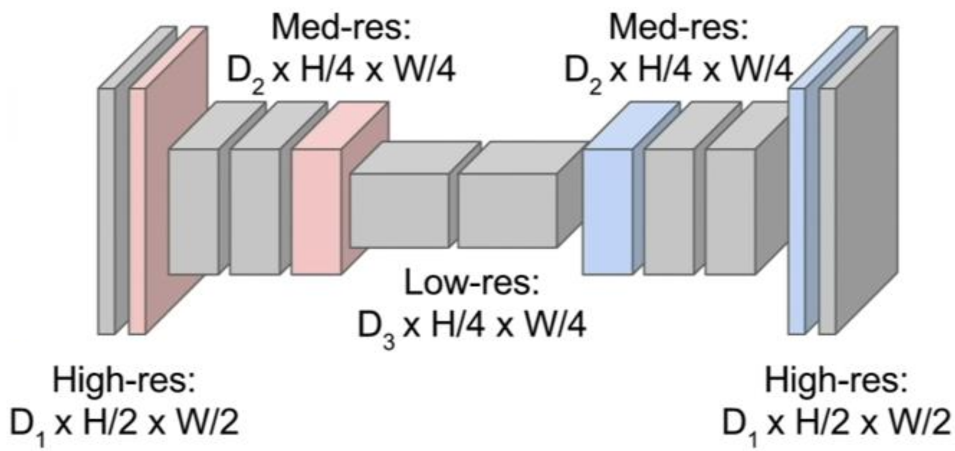
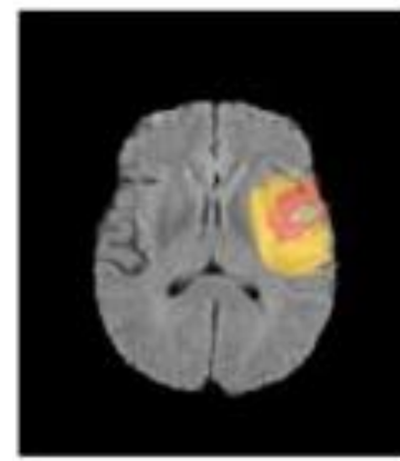
  - Design a network as a bunch of convolutional layers to make predictions for pixels all at once!



Input HxW





Output HxW

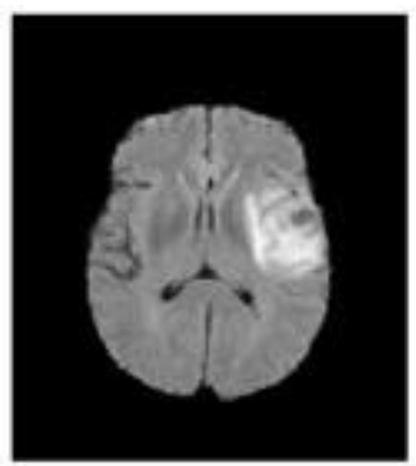
- Use Downsampling and upsampling inside the network!

Long, Shelhamer, and Darrell, "Fully Convolutional Networks for Semantic Segmentation", CVPR 2015
Noh et al, "Learning Deconvolution Network for Semantic Segmentation", ICCV 2015

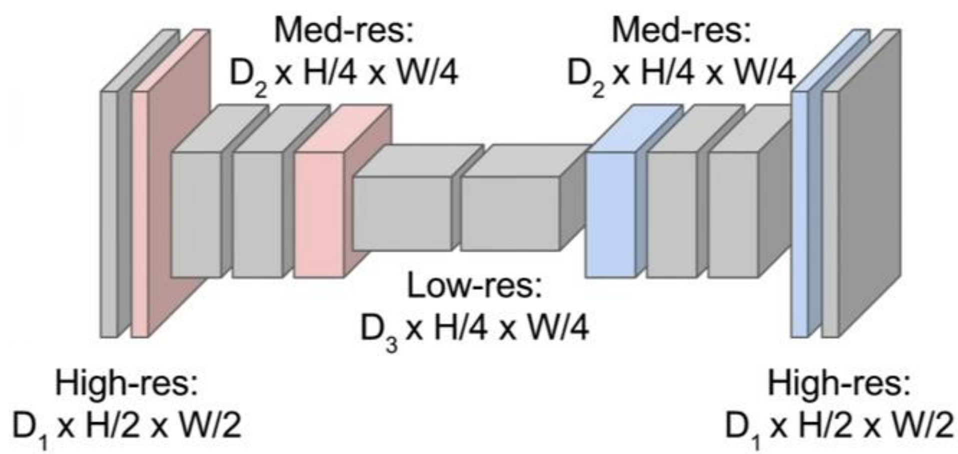
Introduction

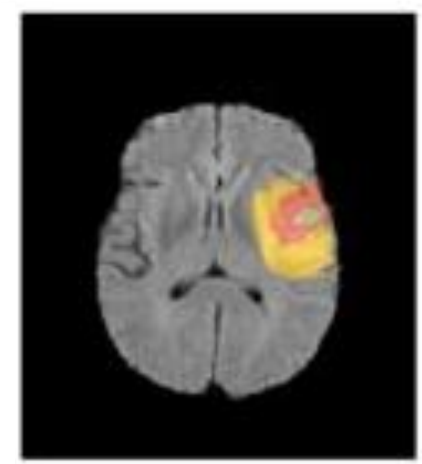
- Semantic Segmentation

- Downsampling: Pooling, strided convolution
- Upsampling ??



Input HxW





Output HxW

Upsampling

- In-Network upsampling: "Unpooling"

Nearest Neighbor

1	2
3	4

Input: 2 x 2

→

1	1	2	2
1	1	2	2
3	3	4	4
3	3	4	4

Output: 4 x 4

"Bed of Nails"

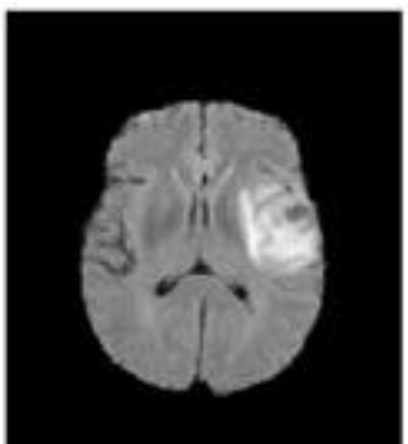
1	2
3	4

Input: 2 x 2

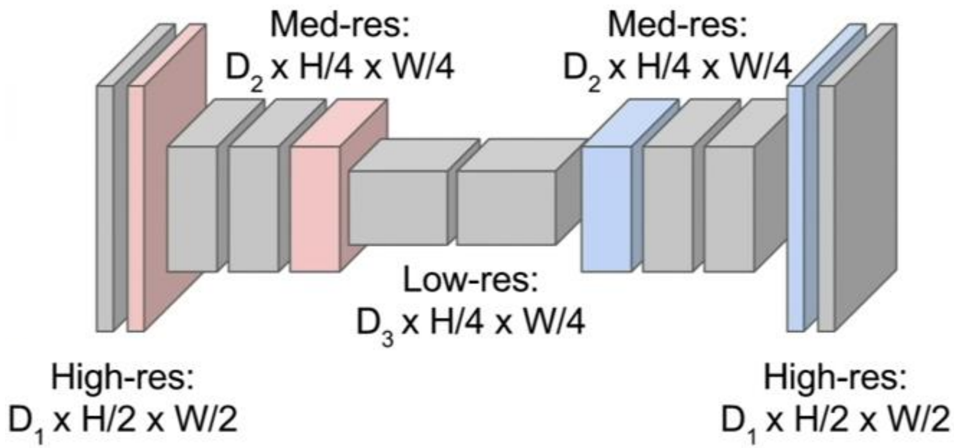
→

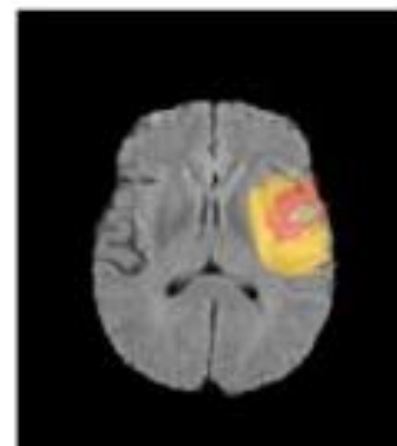
1	0	2	0
0	0	0	0
3	0	4	0
0	0	0	0

Output: 4 x 4



Input HxW





Output HxW

Upsampling

- Artefacts

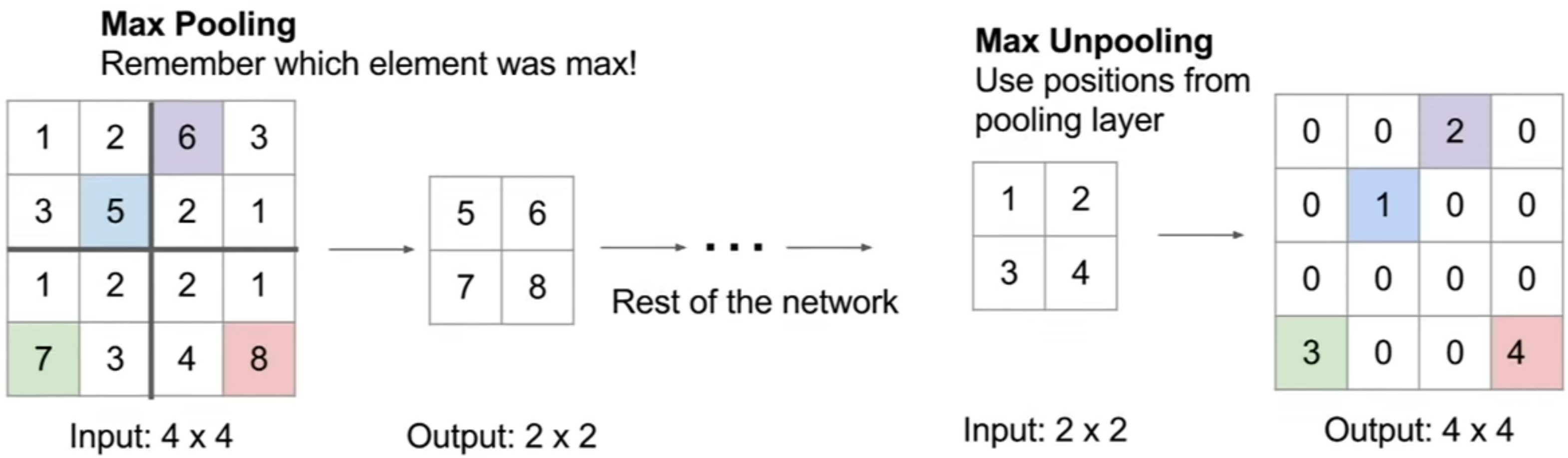
Transpose convolution with **zero-fill / “bed of nails”**

Transpose convolution with **nearest-neighbour-fill**

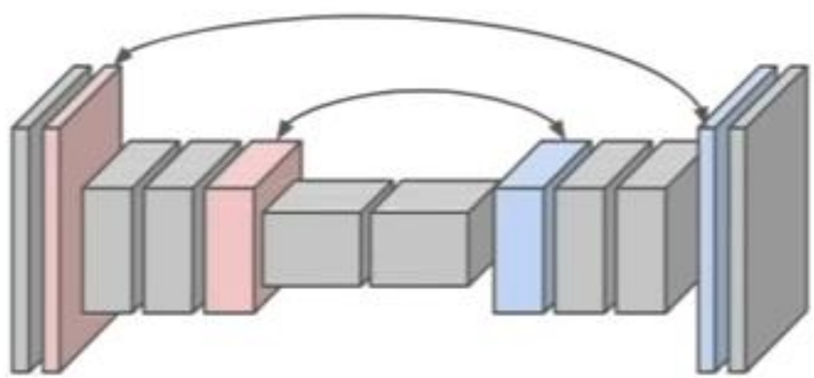
From: http://distill.pub/2016/deconv-checkerboard/

Upsampling

- In-Network upsampling: "Max Unpooling"



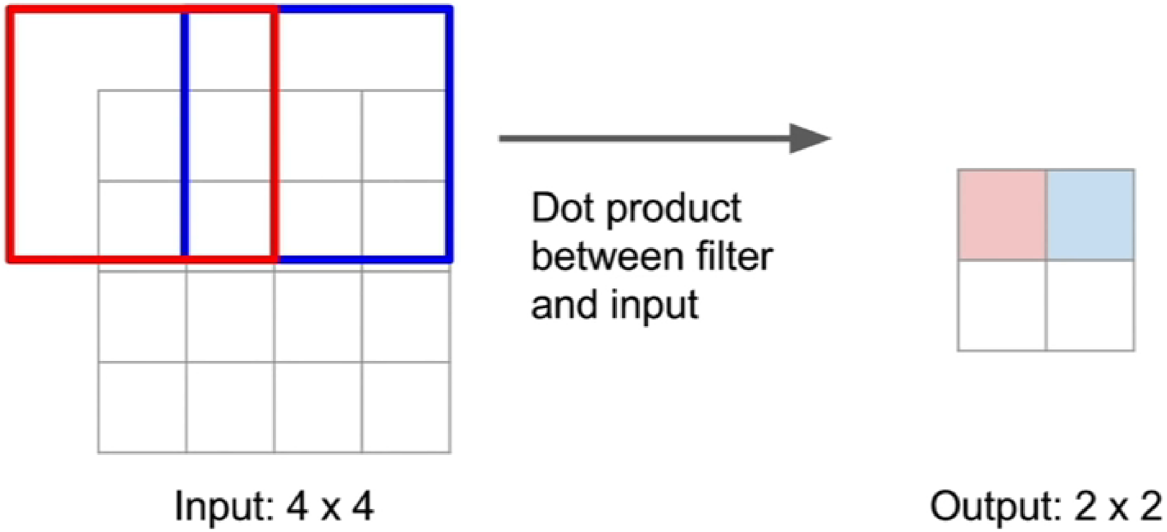
Corresponding pairs of downsampling and upsampling layers



Upsampling

- Learnable Upsampling: Transpose Convolution *(Deconvolution)*

Recall: Normal 3 x 3 convolution, stride 2 pad 1

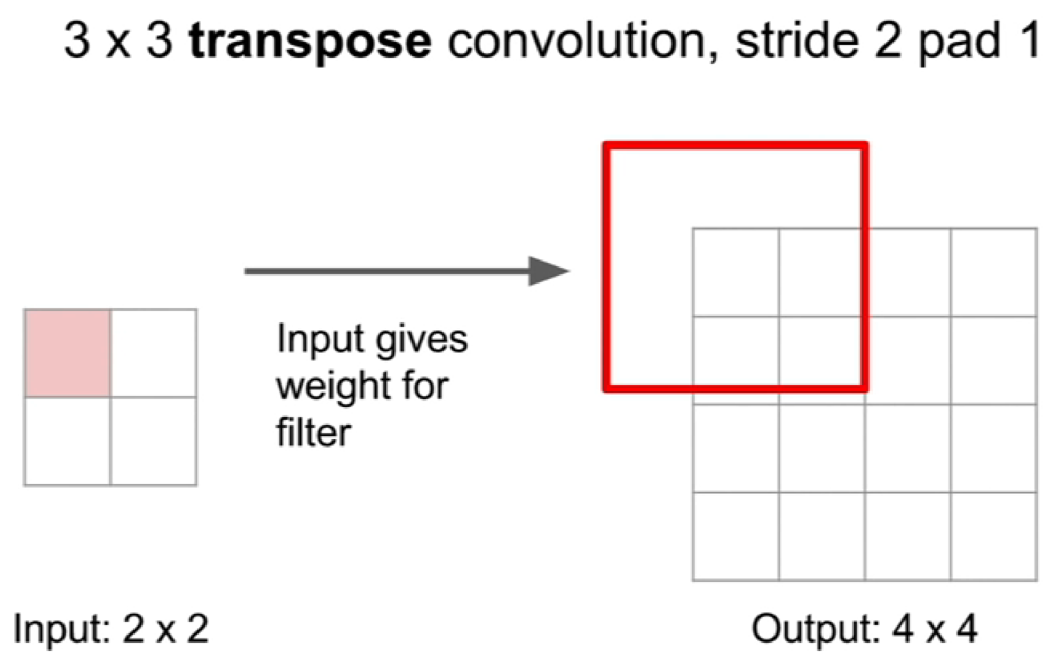


Filter moves 2 pixels in the input for every one pixel in the output

Stride gives ratio between movement in input and output

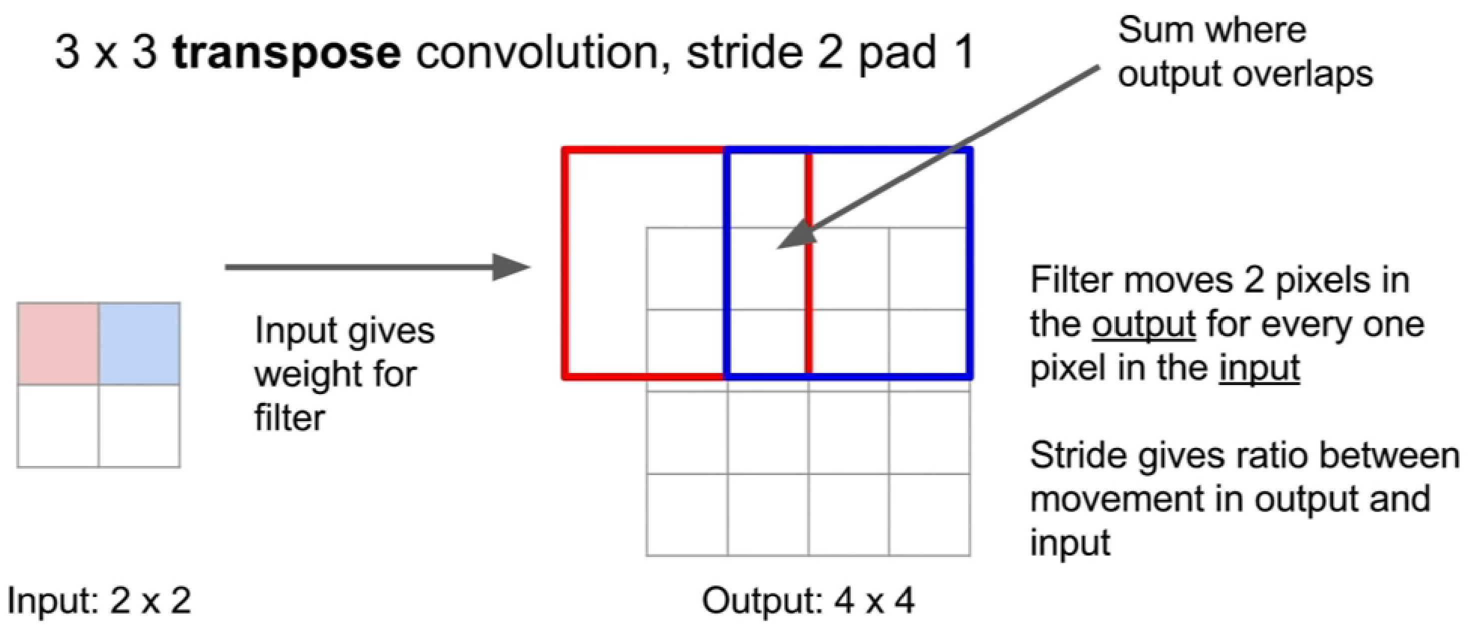
Upsampling

- Learnable Upsampling: Transpose Convolution *(Deconvolution)*



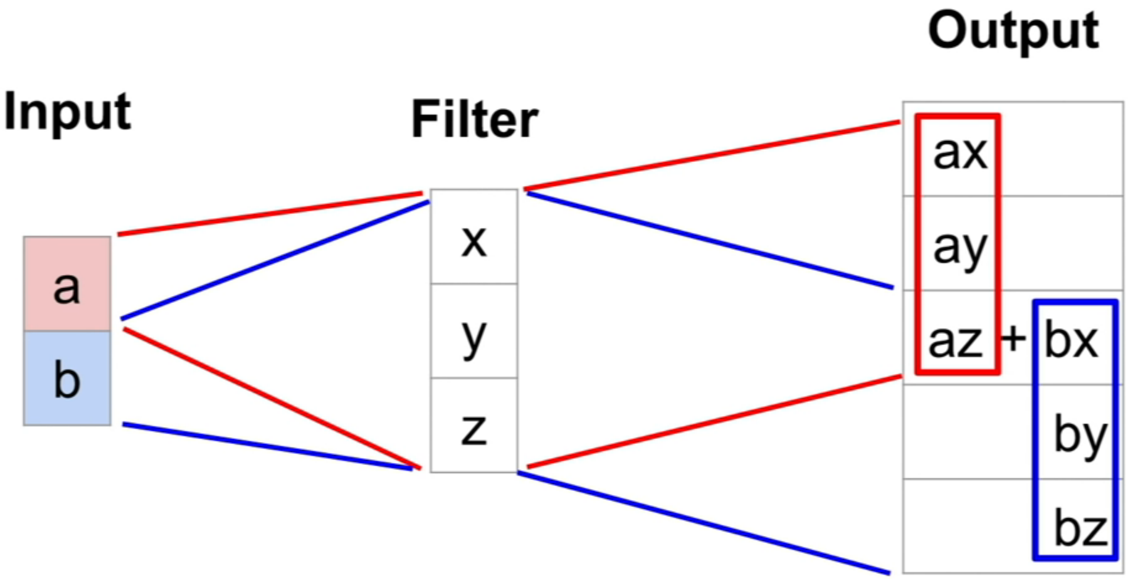
Upsampling

- Learnable Upsampling: Transpose Convolution *(Deconvolution)*



Upsampling

- Transpose Convolution: 1D Example

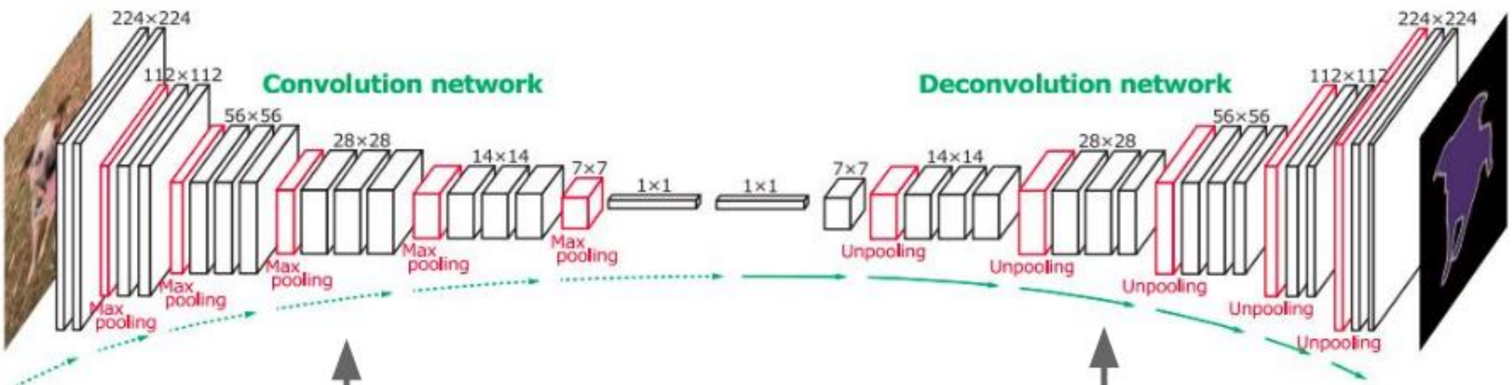


Output contains copies of the filter weighted by the input, summing at where at overlaps in the output

Need to crop one pixel from output to make output exactly 2x input

Upsampling

- Example:



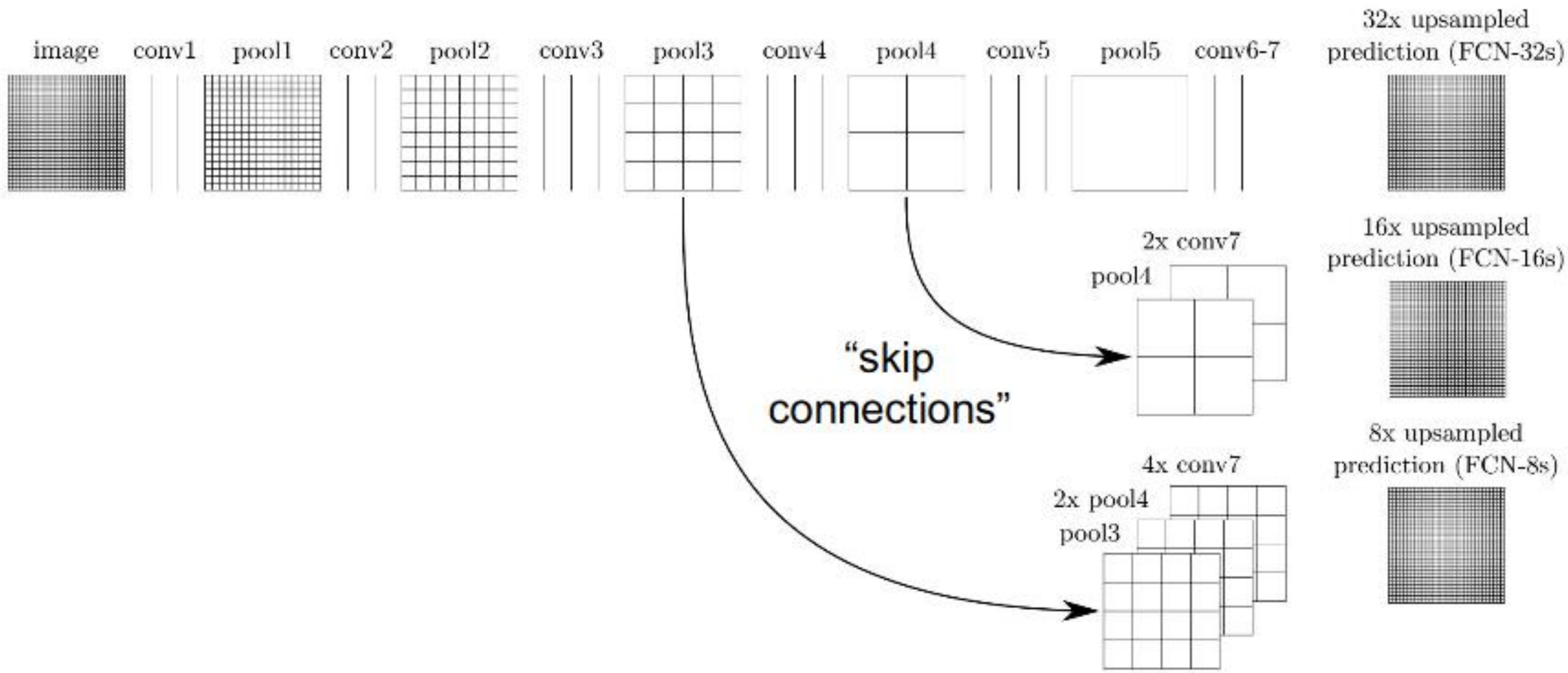
Normal VGG

"Upside down" VGG

Noh et al, "Learning Deconvolution Network for Semantic Segmentation", ICCV 2015

Upsampling

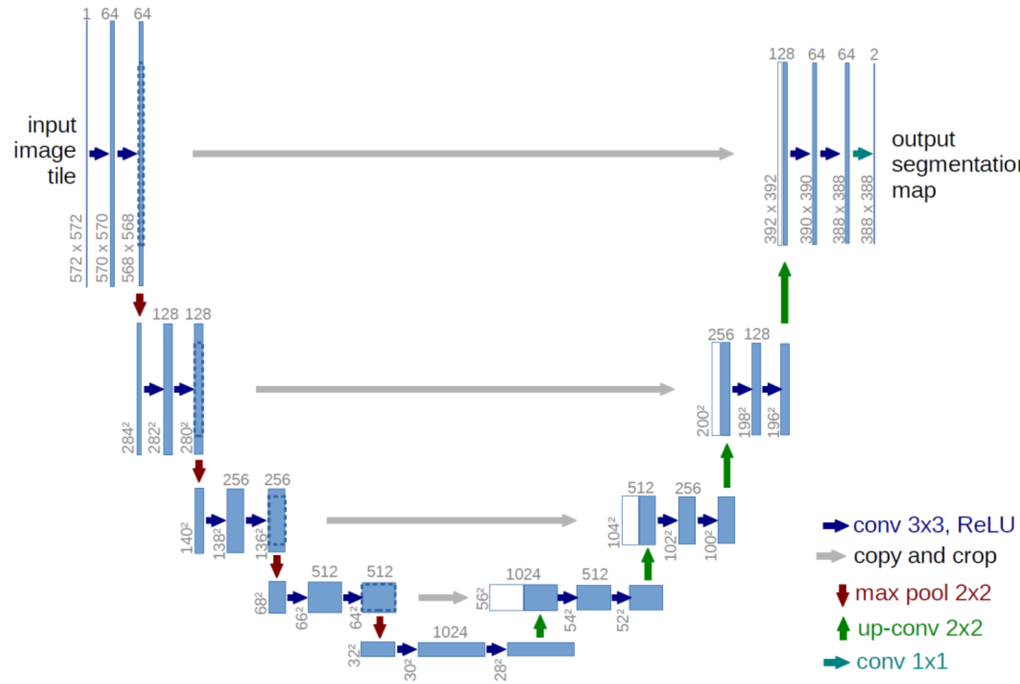
- For better performance preserving more details on the boundaries usually it is combined with skip connections



Long, Shelhamer, and Darrell, "Fully Convolutional Networks for Semantic Segmentation", CVPR 2015

UNET

- Ronneberger et al. "U-Net: Convolutional Networks for Biomedical Image Segmentation"

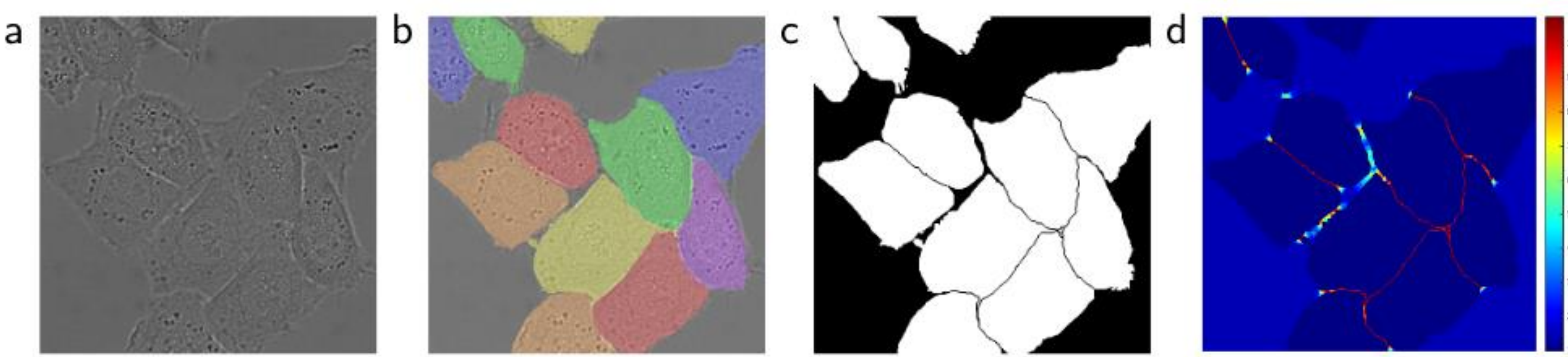


Loss function

$$E = \sum_{\mathbf{x}\in\Omega} w(\mathbf{x}) \log(p_{\ell(\mathbf{x})}(\mathbf{x}))$$

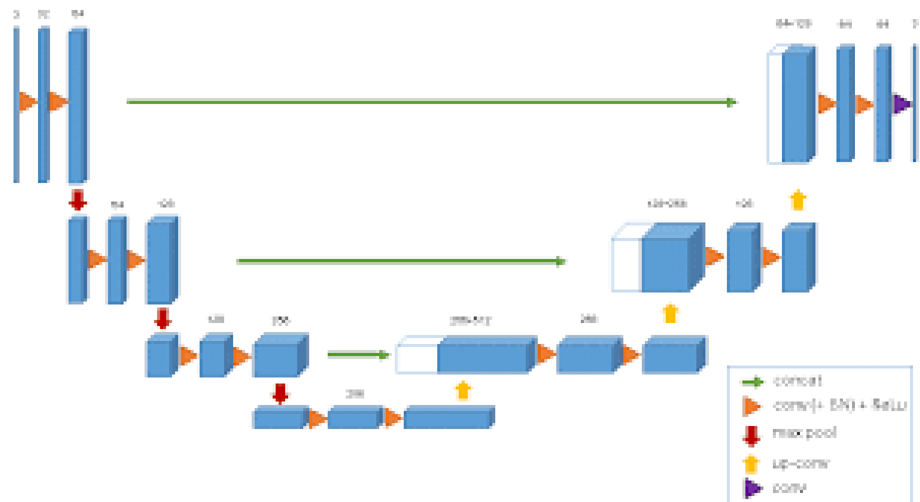
Weighted strategy

$$w(\mathbf{x}) = w_c(\mathbf{x}) + w_0 \cdot \exp\left(-\frac{(d_1(\mathbf{x}) + d_2(\mathbf{x}))^2}{2\sigma^2}\right)$$



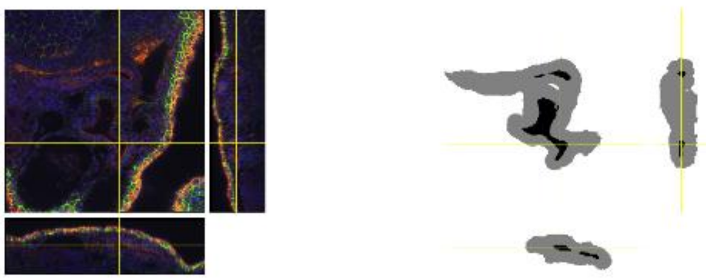
3D-UNET

- Cicek et al. "3D U-Net: Learning Dense Volumetric Segmentation from Sparse Annotation"



Loss Function

$$E = \sum_{\mathbf{x}\in\Omega} w(\mathbf{x}) \log(p_{\ell(\mathbf{x})}(\mathbf{x}))$$



(a) (b)

Fig. 3: **(a)** The confocal recording of our 3rd *Xenopus* kidney. **(b)** Resulting dense segmentation from the proposed 3D u-net with batch normalization.

Table 1: Cross validation results for semi-automated segmentation (IoU)

test slices	3D w/o BN	3D with BN	2D with BN
subset 1	0.822	0.855	0.785
subset 2	0.857	0.871	0.820
subset 3	0.846	0.863	0.782
average	0.842	0.863	0.796

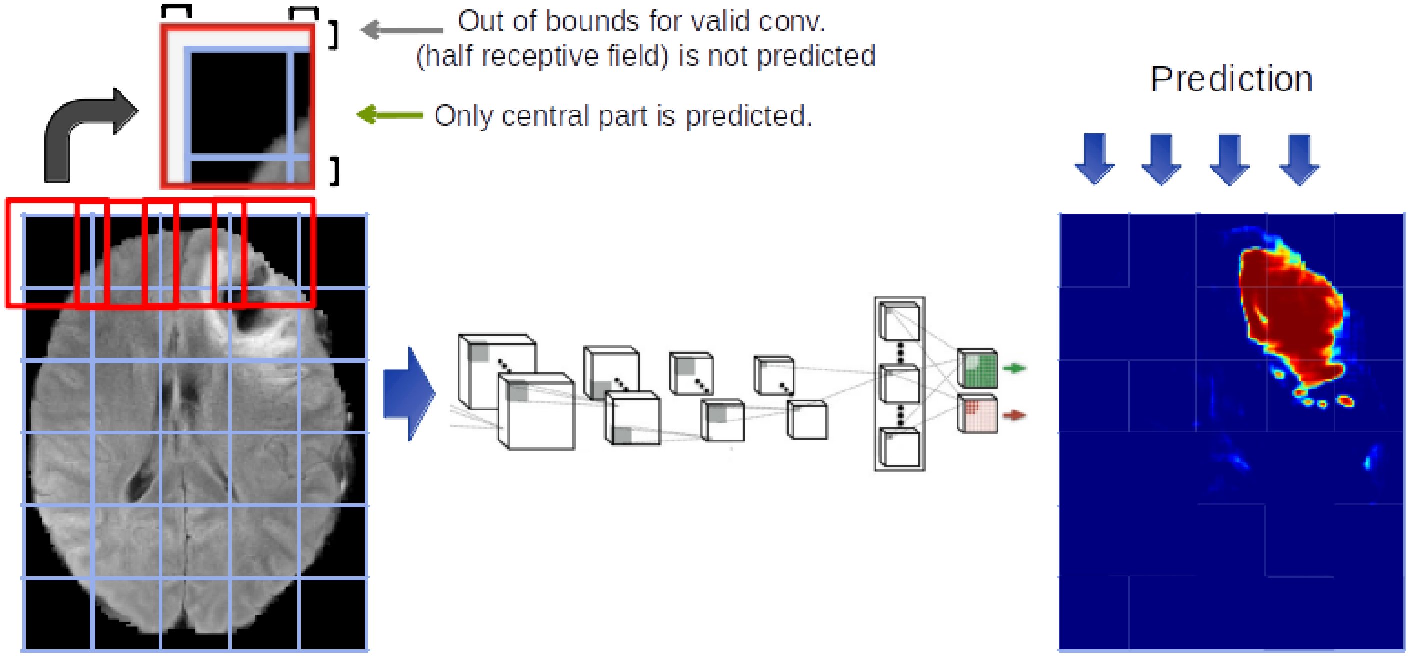
Table 2: Effect of # of slices for semi-automated segmentation (IoU)

GT slices	GT voxels	IoU S1	IoU S2	IoU S3
1,1,1	2.5%	0.331	0.483	0.475
2,2,1	3.3%	0.676	0.579	0.738
3,3,2	5.7%	0.761	0.808	0.835
5,5,3	8.9%	0.856	0.849	0.872

Table 3: Cross validation results for fully-automated segmentation (IoU)

test volume	3D w/o BN	3D with BN	2D with BN
1	0.655	0.761	0.619
2	0.734	0.798	0.698
3	0.779	0.554	0.325
average	0.723	0.704	0.547

Tiling for 3D networks



Bigger input tiles (or segments):

- Require more memory (FMs expand)
- But fewer redundant computations (less overlap)

Tile size during testing can be different from training

Dilated Convolutions

- Recall discrete convolution

$$S(i,j) = (I * K)(i,j) = \sum_m \sum_n I(m,n) K(i-m, j-n)$$

- Dilated Convolution

$$S(i,j) = (I *_l K)(i,j) = \sum_m \sum_n I(m,n) K(i-lm, j-ln)$$

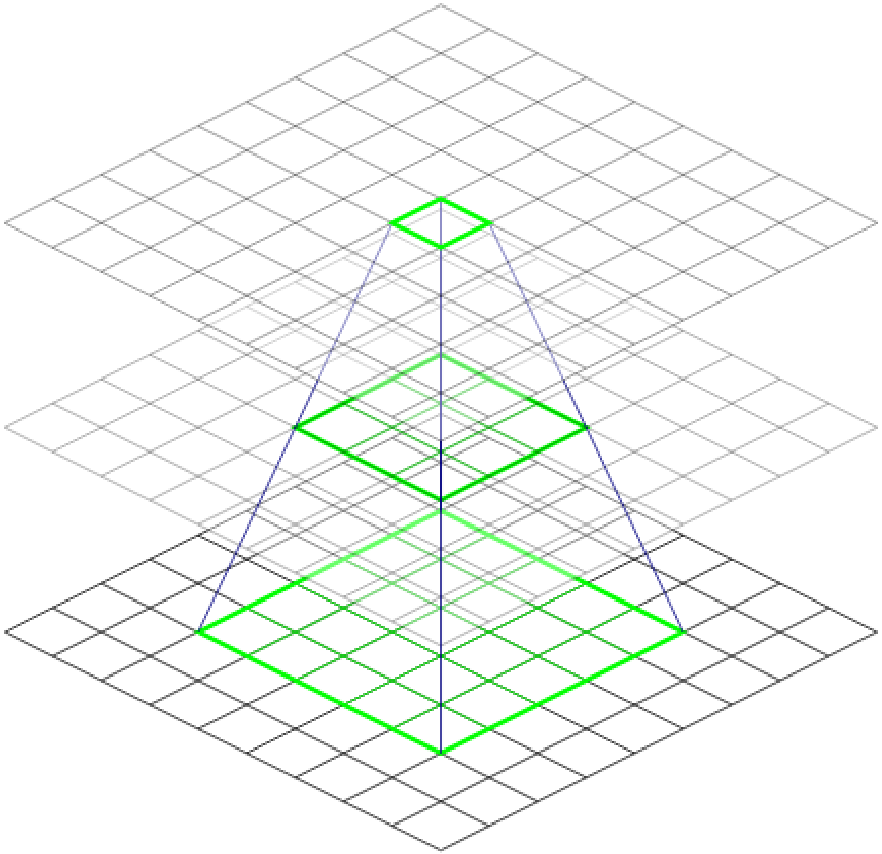
L is a dilation factor

- Very old idea going to the 80s wavelet theory literature

Regular Convolutions

- Regular Convolution
  - s: stride
  - k: kernel
  - r: receptive field

$$r_{(i-1)} = s_i \times r_i + (k_i - s_i)$$

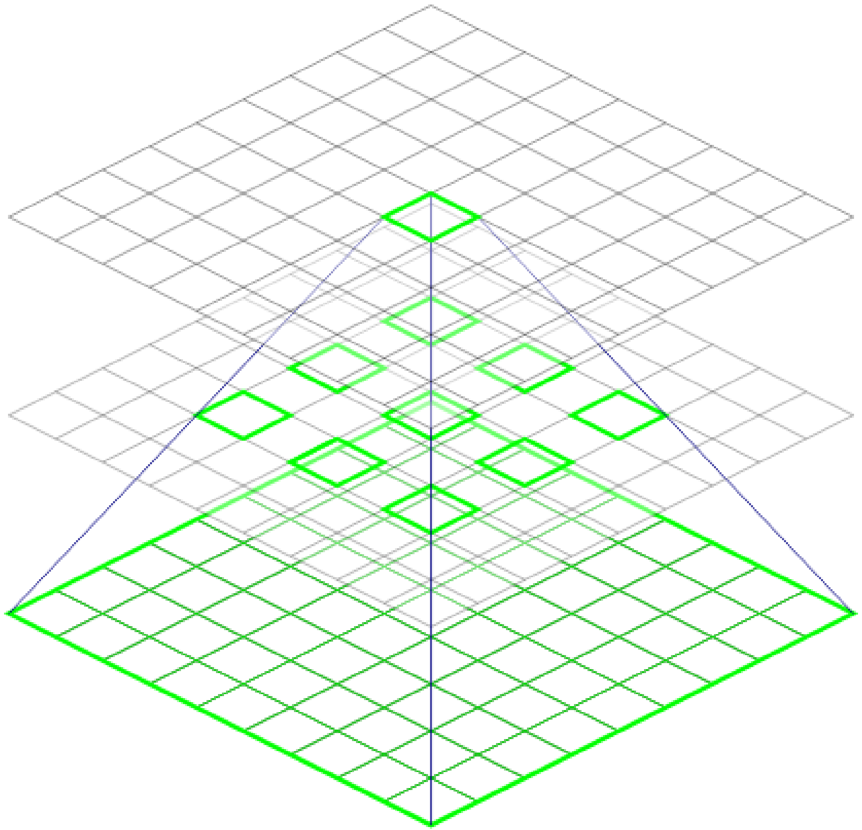


The unit on the third layer has an effective receptive field of size 5x5

Dilated Convolutions

- Dilated Convolution
  - k: kernel
  - r: dilation

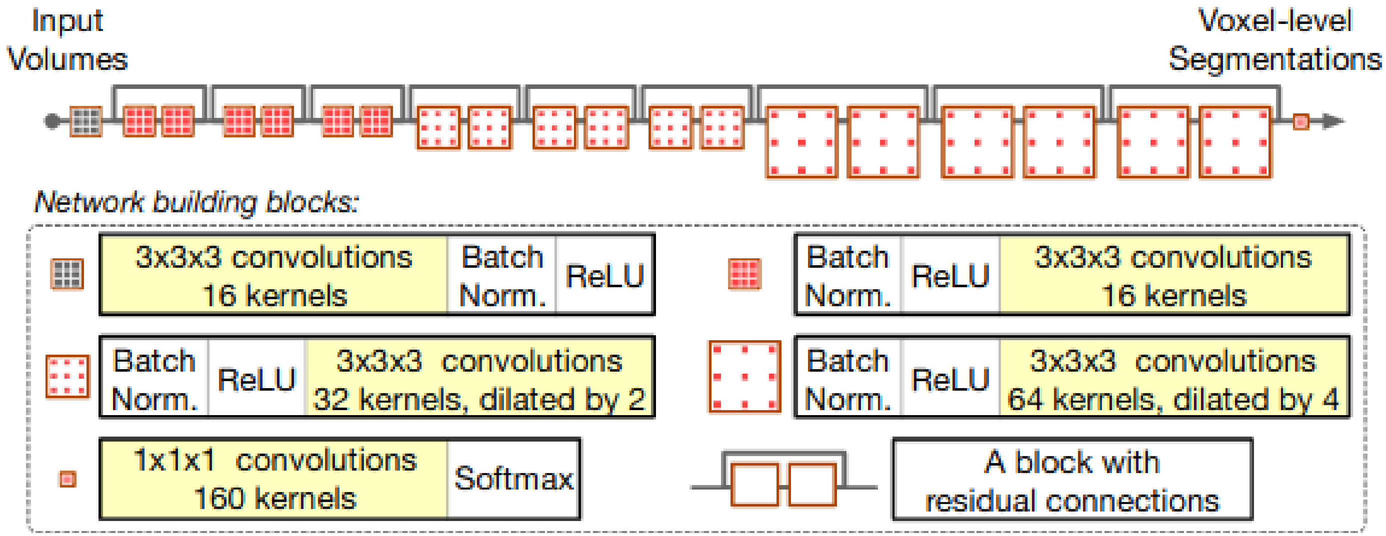
$$k' = r(k-1) + 1$$

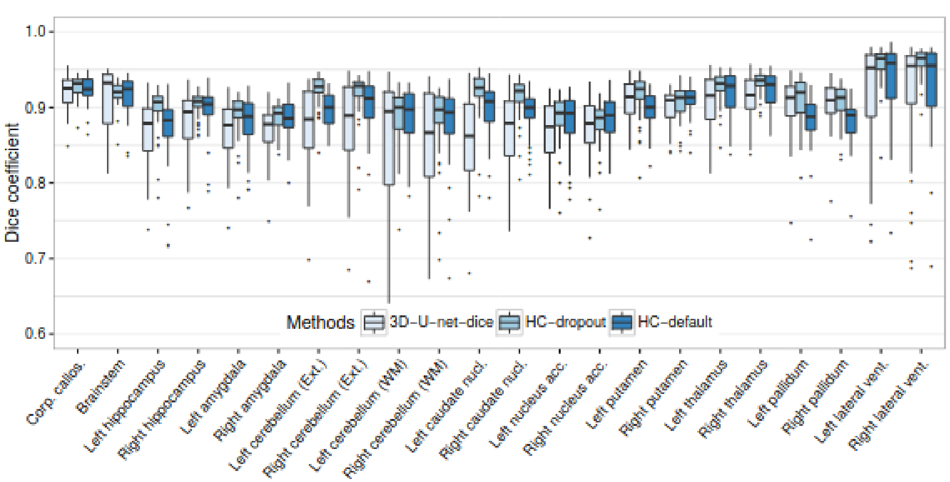


The unit on the third layer has an effective receptive field of size 9x9

HighRes3DNet

- Li et. al, "On the Compactness, Efficiency, and Representation of 3D Convolutional Networks: Brain Parcellation as a Pretext Task", IPMI 2017





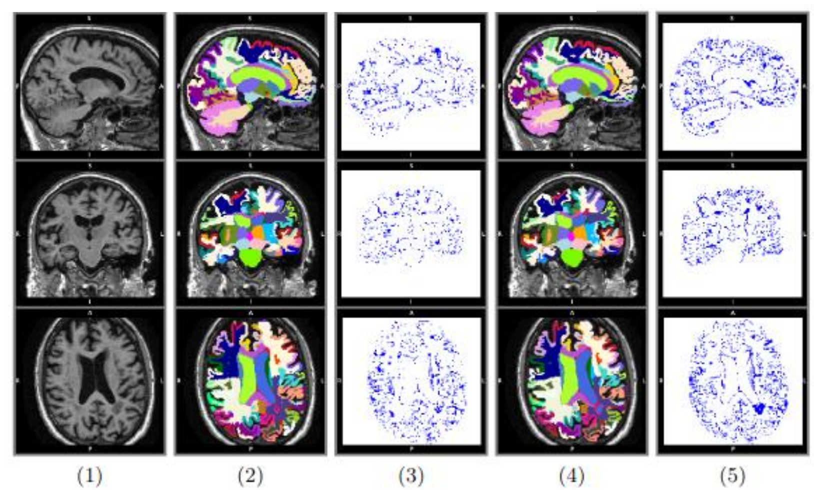
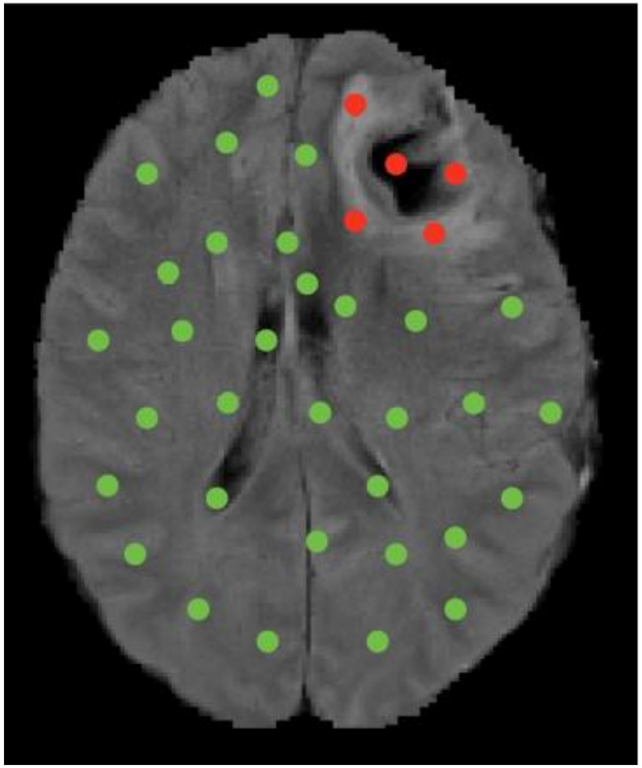


Fig. 4. Visualisations of segmentation results. (1) slices from a test image volume, segmentation maps and false prediction maps generated by HC-dropout (2, 3), and 3D U-net-dice (4, 5).

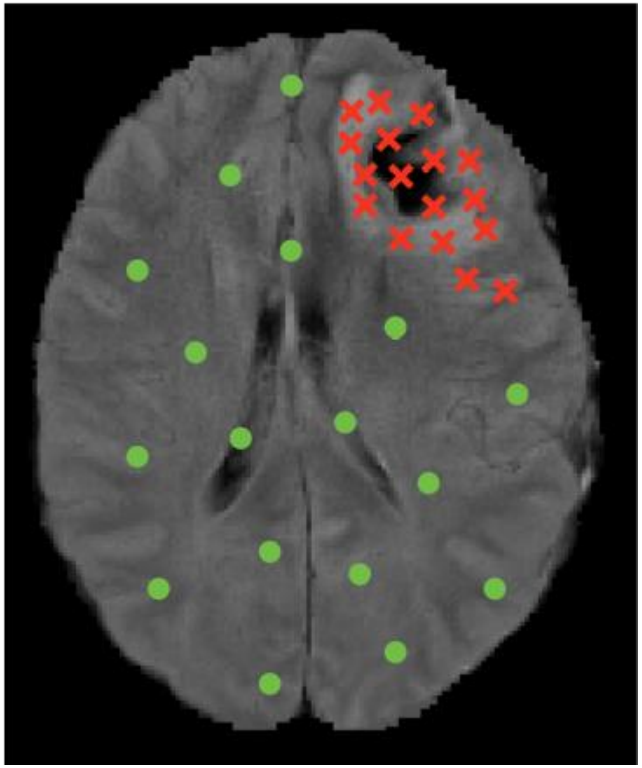
Loss Functions

Class Imbalance and Sampling

Uniform sampling



Weighted sampling: 50/50



Additional Losses

- **Dice Loss** [Milletari et al., 2016]

$$D = \frac{2\sum_i^N p_i g_i}{\sum_i^N p_i^2 + \sum_i^N g_i^2} \qquad \frac{\partial D}{\partial p_j} = 2\left[\frac{g_j\left(\sum_i^N p_i^2 + \sum_i^N g_i^2\right) - 2p_j\left(\sum_i^N p_i g_i\right)}{\left(\sum_i^N p_i^2 + \sum_i^N g_i^2\right)^2}\right]$$

g_n the value of segmentation at n and p_n the predicted probabilistic map

Additional Losses

- **Dice Loss** [Milletari et al., 2016]

$$D = \frac{2\sum_i^N p_i g_i}{\sum_i^N p_i^2 + \sum_i^N g_i^2} \qquad \frac{\partial D}{\partial p_j} = 2\left[\frac{g_j\left(\sum_i^N p_i^2 + \sum_i^N g_i^2\right) - 2p_j\left(\sum_i^N p_i g_i\right)}{\left(\sum_i^N p_i^2 + \sum_i^N g_i^2\right)^2}\right]$$

g_n the value of segmentation at n and p_n the predicted probabilistic map

- **Generalized Dice Loss** [Sudre et al., 2017]

$$\mathrm{GDL} = 1 - 2\frac{\sum_{l=1}^2 w_l \sum_n r_{ln} p_{ln}}{\sum_{l=1}^2 w_l \sum_n r_{ln} + p_{ln}}, \qquad \frac{\partial \mathrm{GDL}}{\partial p_i} = -2\frac{(w_1^2 - w_2^2)\left[\sum_{n=1}^N p_n r_n - r_i \sum_{n=1}^N (p_n + r_n)\right] + N w_2 (w_1 + w_2)(1 - 2r_i)}{\left[(w_1 - w_2)\sum_{n=1}^N (p_n + r_n) + 2N w_2\right]^2}$$

r_n the value of segmentation at n, p_n the predicted probabilistic map, $w_l = 1/\Sigma(r_{ln})^2$

Used to deal with the correlation that exists between the size of the segment and the result of the dice!

Additional Losses

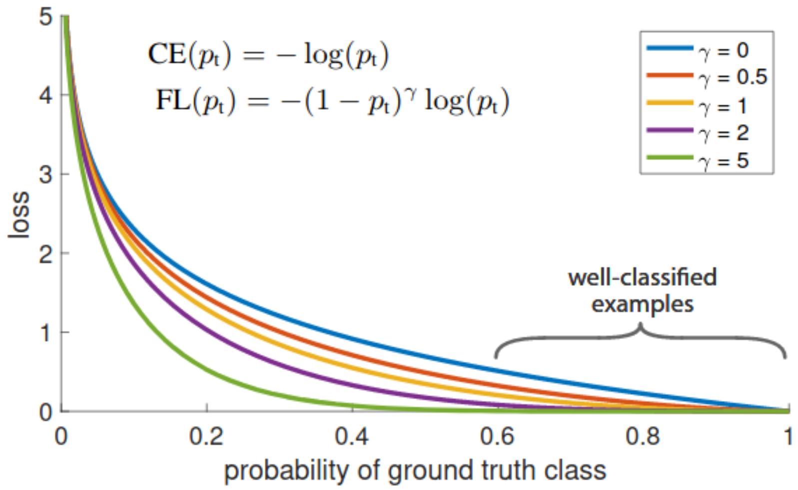
- Most of the losses balance the importance of positive/negative examples without integrating the importance between easy/ hard examples.
- **Focal Loss** [Lin et al. 2018]
  - Propose to reshape the loss function to down-weight easy examples and thus focus training on hard negatives.

Binary Cross entropy

$$\mathrm{CE}(p, y) = \begin{cases} -\log(p) & \text{if } y = 1 \\ -\log(1-p) & \text{otherwise.} \end{cases}$$

Focal Loss

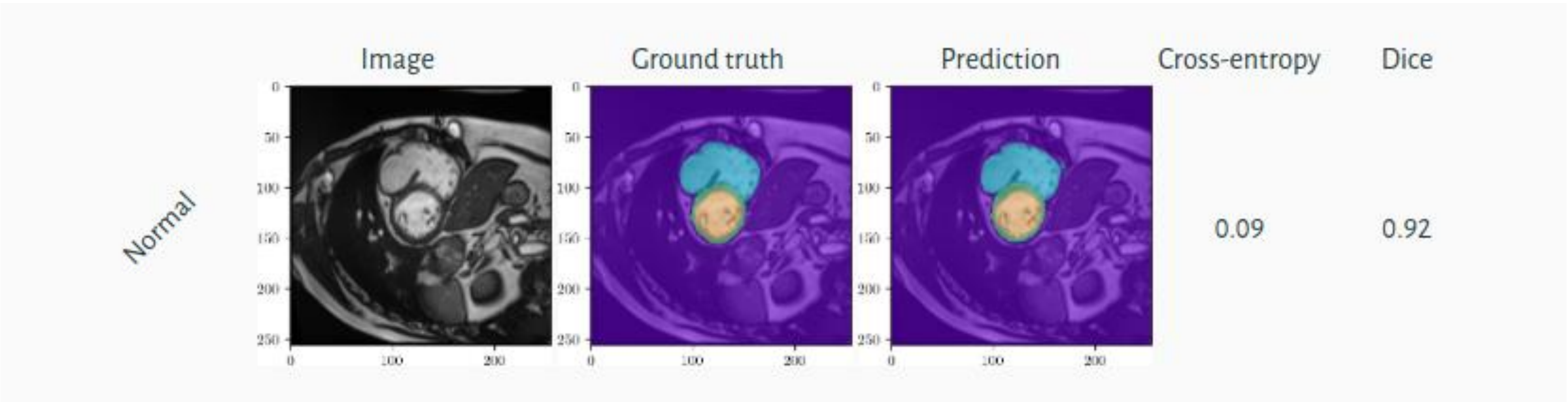
$$\mathrm{FL}(p_t) = -(1-p_t)^\gamma \log(p_t).$$



Where $\gamma \geq 0$.
when an example is misclassified and p is small
the modulating factor is near 1 and the loss is unaffected. As p -> 1, the factor goes to 0 and the loss of the well-classified examples is down-weighted

Be carefull however

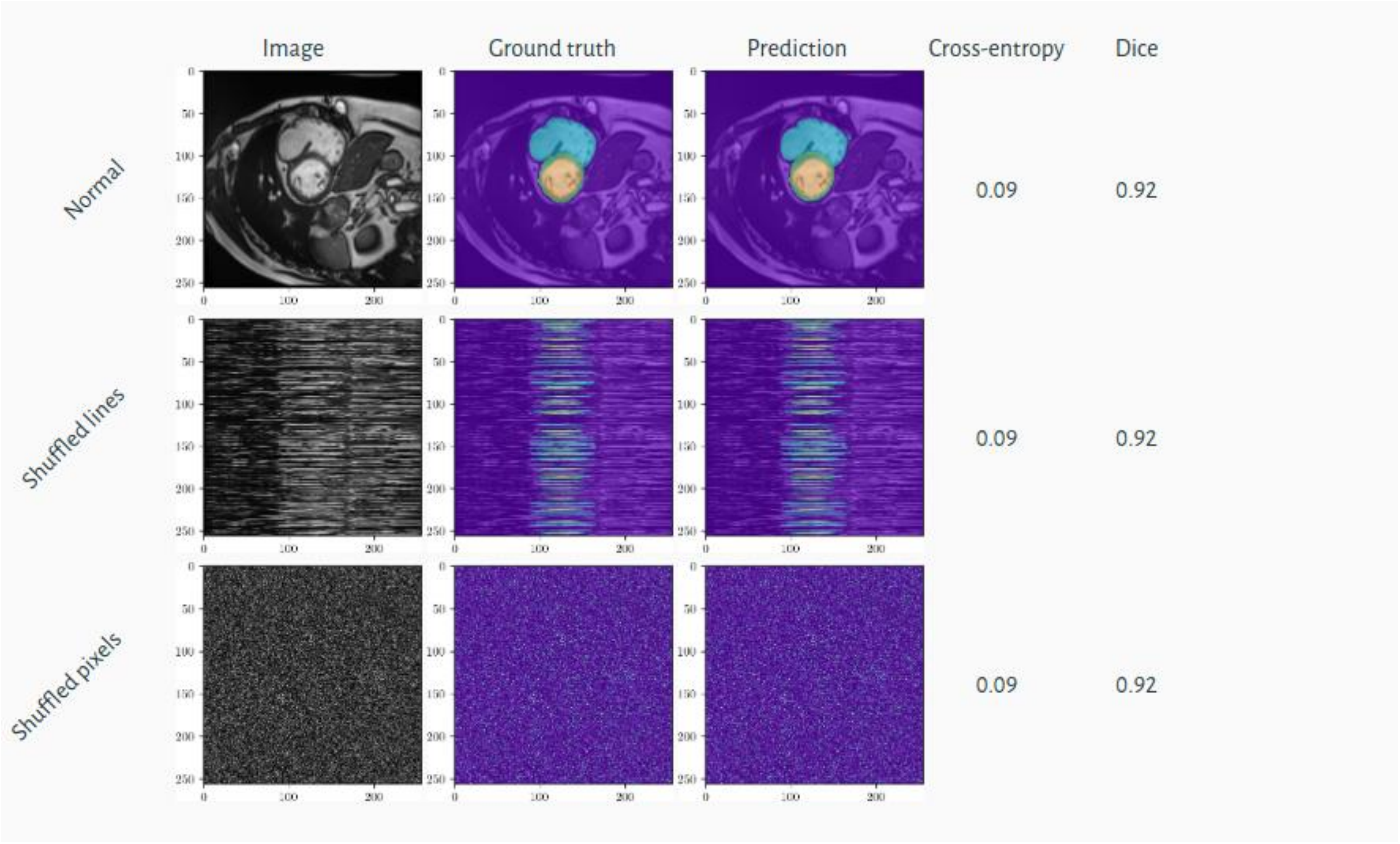
- Standard losses treat segmentation as independent classification



Slide inspired by: Hoel Kervadec

Be carefull however

- Standard losses treat segmentation as independent classification



Slide inspired by: Hoel Kervadec

Introduce shape descriptors

General *shape* moment:

$$\mu_{p,q}^{(k)}(s_\theta) := \sum_{i \in \Omega} s_\theta{}^{(i,k)} x_{(i)}^{p} y_{(i)}^{q},$$

p, q	moments order;
s_θ	softmax predictions;
k	class;
$i \in \Omega$	pixels in the image;
x, y	pixels-coordinates (2D).

Volume:

$$\mathfrak{V}^{(k)}(s_\theta) := \mu_{0,0}^{(k)}(s_\theta) = \sum_{i \in \Omega} s_\theta^{(i,k)}.$$

Centroid: "average" of pixels coordinates

$$\mathfrak{C}^{(k)}(s_\theta) := \left(\frac{\mu_{1,0}^{(k)}(s_\theta)}{\mu_{0,0}^{(k)}(s_\theta)}, \frac{\mu_{0,1}^{(k)}(s_\theta)}{\mu_{0,0}^{(k)}(s_\theta)} \right)$$

Slide by: Hoel Kervadec

Introduce shape descriptors

General *central* moment:

$$\bar{\mu}_{p,q}^{(k)} := \sum_{i \in \Omega} s_\theta^{(i,k)} \left(x_{(i)} - \frac{\mu_{1,0}^{(k)}}{\mu_{0,0}^{(k)}} \right)^p \left(y_{(i)} - \frac{\mu_{0,1}^{(k)}}{\mu_{0,0}^{(k)}} \right)^q,$$

p, q	moments order;
s_θ	softmax predictions;
k	class;
$i \in \Omega$	pixels in the image;
x, y	pixel coordinates (2D).

Average distance to the centroid: "standard deviation" of pixels coordinates

$$\mathfrak{D}^{(k)}(s_\theta) := \left(\sqrt[2]{\frac{\bar{\mu}_{2,0}^{(k)}(s_\theta)}{\mu_{0,0}^{(k)}(s_\theta)}}, \sqrt[2]{\frac{\bar{\mu}_{0,2}^{(k)}(s_\theta)}{\mu_{0,0}^{(k)}(s_\theta)}} \right).$$

https://github.com/HKervadec/shape_descriptors

Slide by: Hoel Kervadec

Evaluation Metrics

Dice Similarity Coefficient

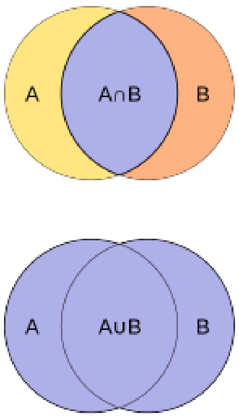
- Most widely used measure for evaluating segmentation
- Assume is the reference, and the prediction

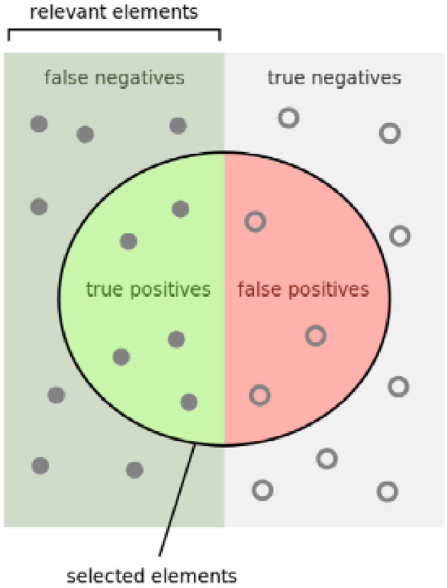
$$DSC = \frac{2|A \cap B|}{|A| + |B|}$$

- $|A| = TP + FN$
- $|B| = TP + FP$
- $|A \cap B| = TP$

$$DSC = \frac{2TP}{2TP + FP + FN} = F_1$$

DSC is equivalent to F1 score!





Other Measures

Tana & Hanbury: "Metrics for evaluating 3D medical image segmentation: analysis, selection, and tool"

volume similarity

$$VS = 1 - \frac{\big||A| - |B|\big|}{|A| + |B|} = 1 - \frac{|FN - FP|}{2TP + FP + FN}$$

surface distance measures

- **Hausdorff distance**

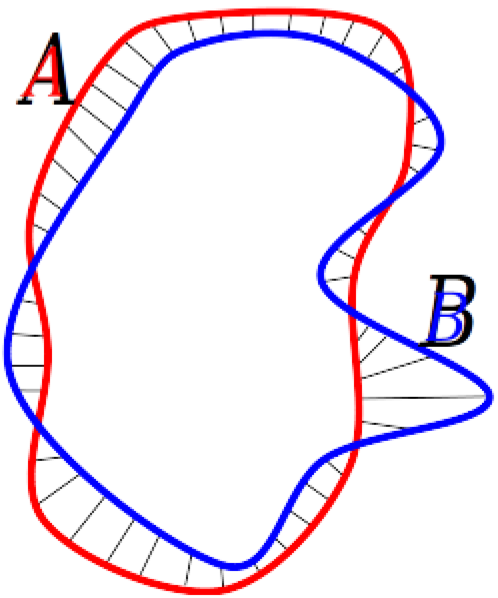
$$HD = \max\big(h(A,B), h(B,A)\big)$$

$$h(A,B) = \max_{a \in A} \min_{b \in B} \|a - b\|$$

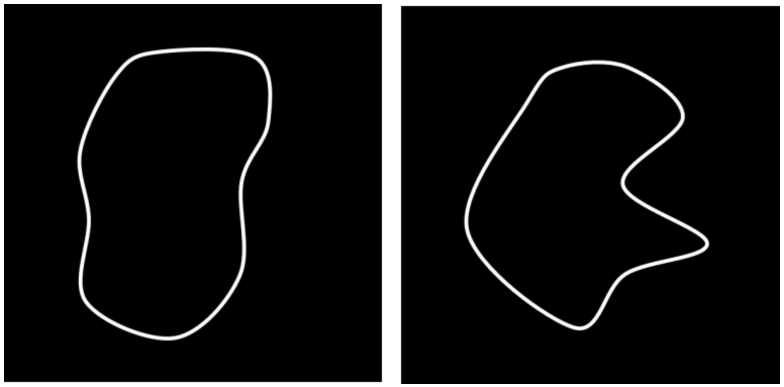
- **(symmetric) average surface distance**

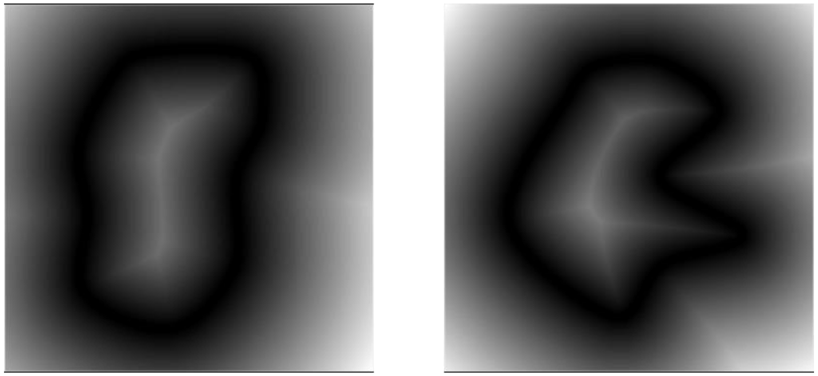
$$ASD = \frac{d(A,B) + d(B,A)}{2}$$

$$d(A,B) = \frac{1}{N} \sum_{a \in A} \min_{b \in B} \|a - b\|$$



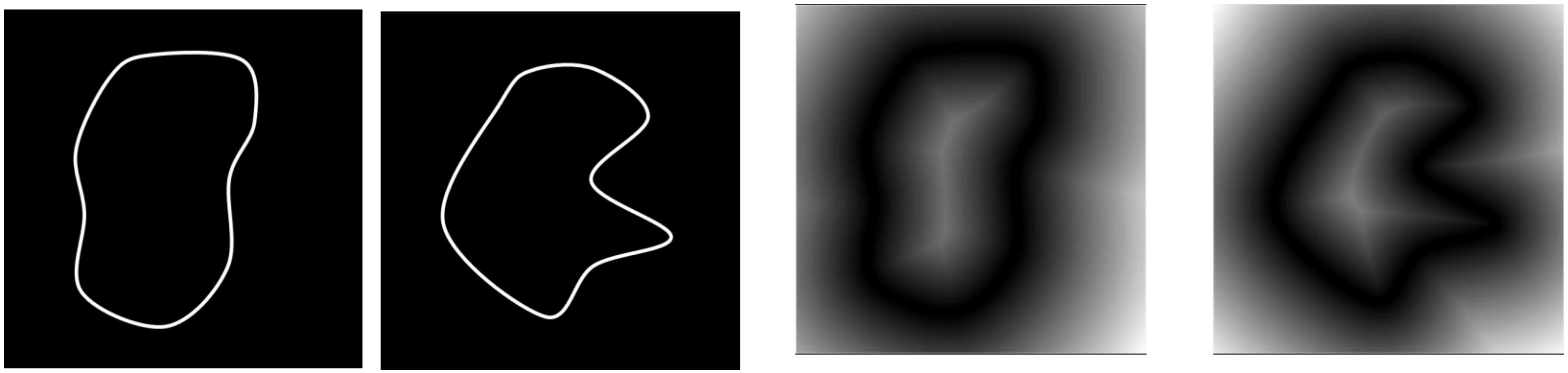
Surface Distance



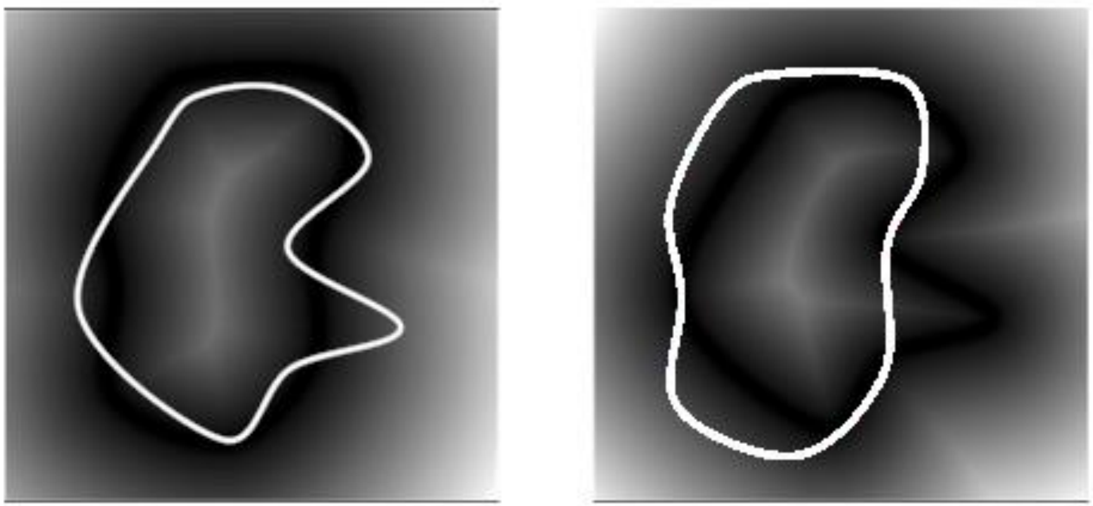


Euclidean Distance Maps

Surface Distance



Euclidean Distance Maps



Sum up distances along pixels on the boundaries of one contour overlaid on the distance map of the other.

Metrics for segmentation

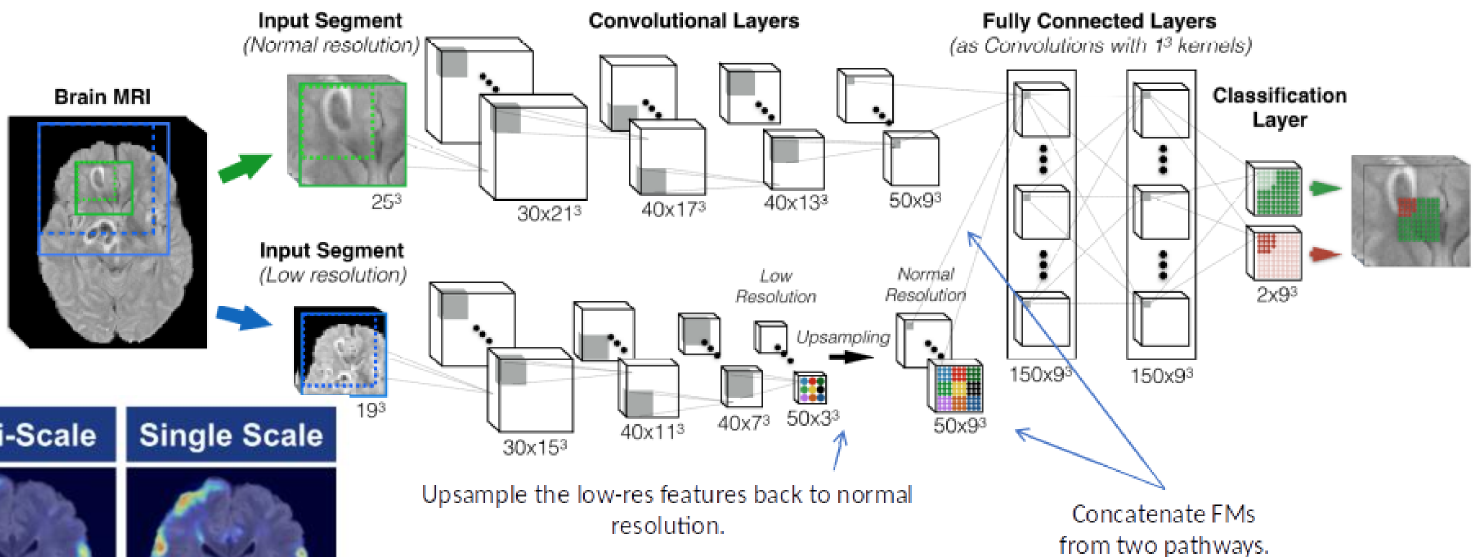
More information about choice of metrics

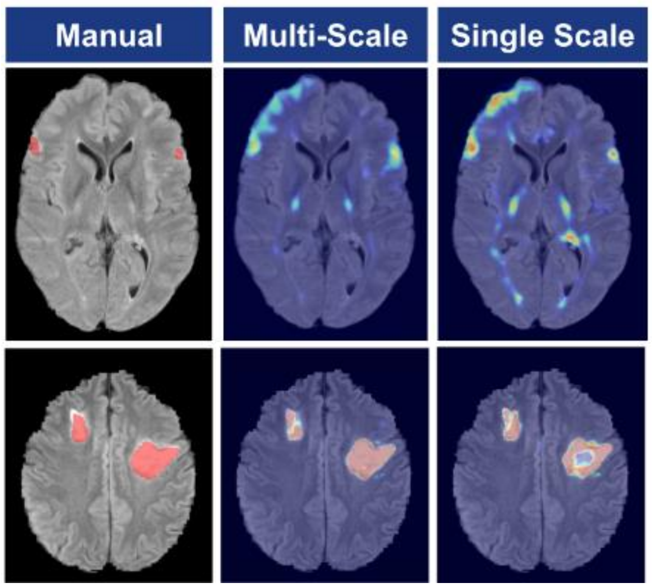
- Maier-Hein et al, "Metrics reloaded: Pitfalls and recommendations for image analysis validation.", Preprint, 2022

More Papers

Multi-Scale Processing

- How can we make the network to "see" more context?
- **Idea:** Add more pathways which process downsampled images

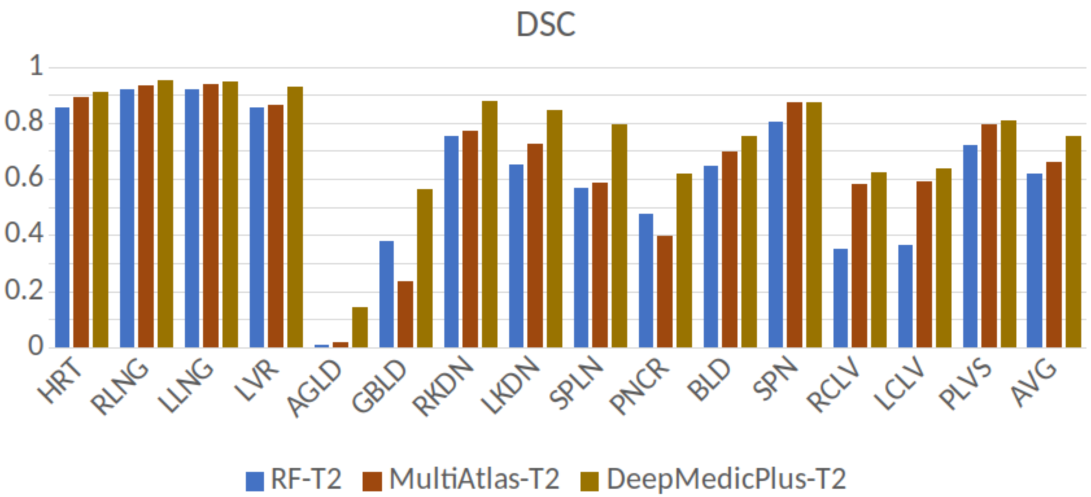


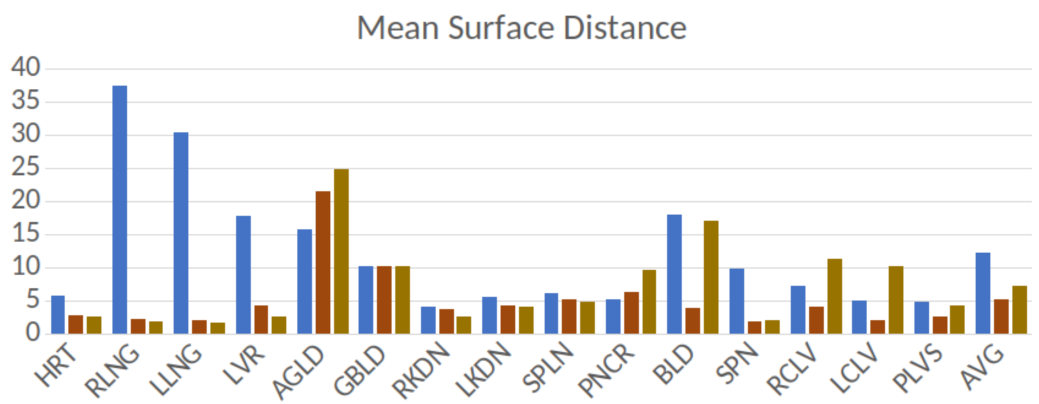


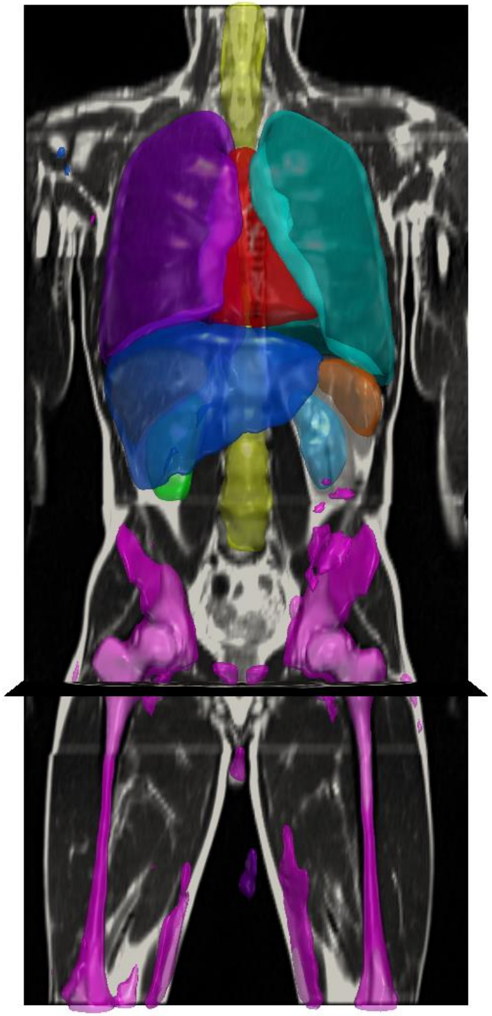
Kamnitsas et al, "Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation", MedIA, 2017
Source code: https://github.com/Kamnitsask/deepmedic

Multi-Organ Segmentation

Lavdas et al. "Fully automatic, multiorgan segmentation in normal whole body magnetic resonance imaging (MRI), using classification forests (CFs), convolutional neural networks (CNNs), and a multi-atlas (MA) approach"

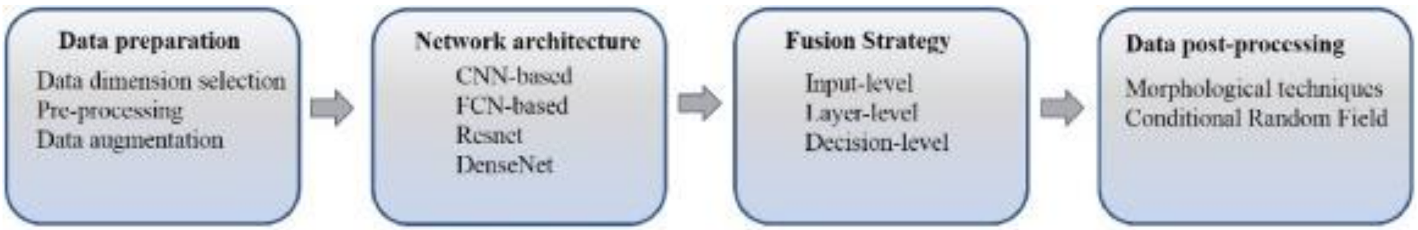


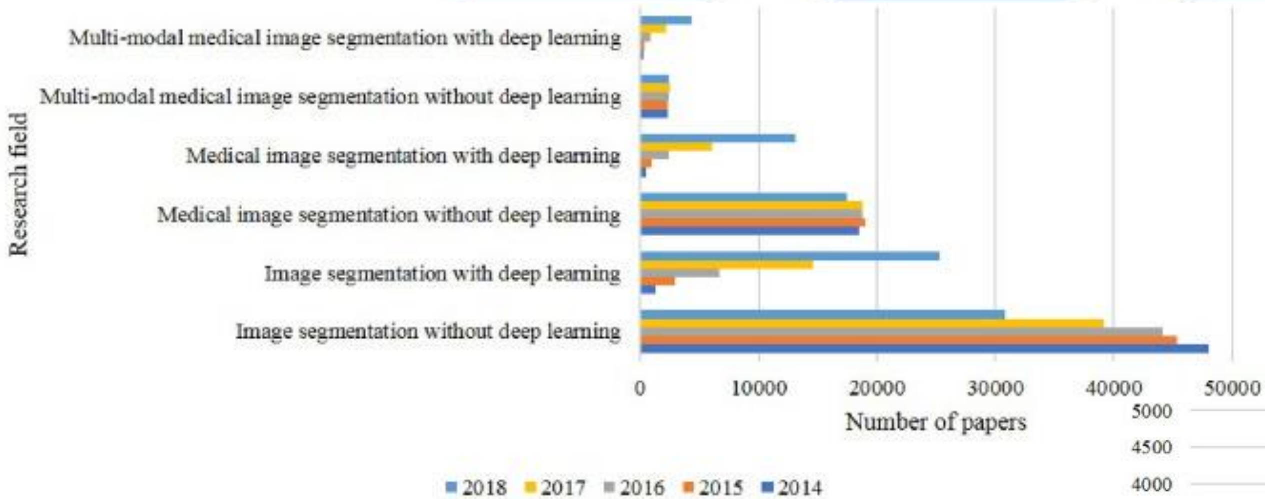


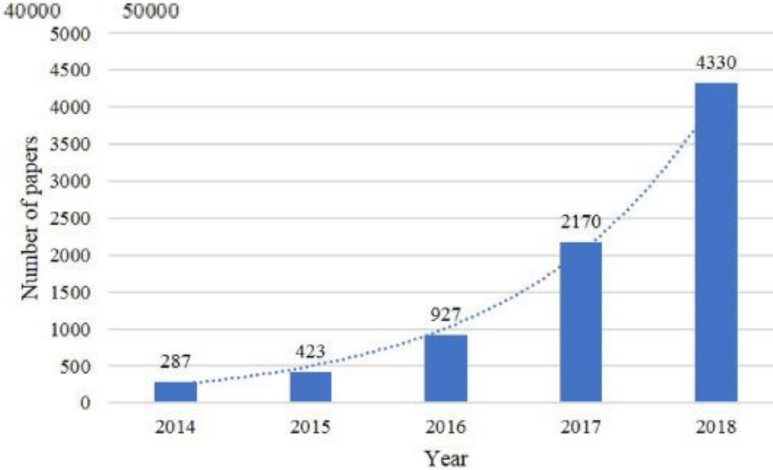


Interesting Points

Zhou et al. "A review: Deep Learning for medical image segmentation using multi-modality fusion"

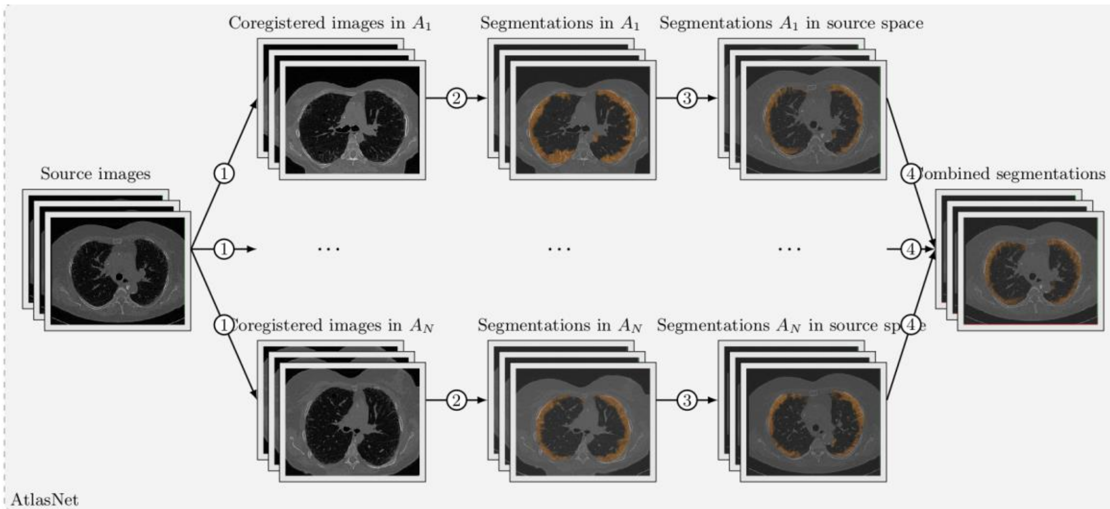


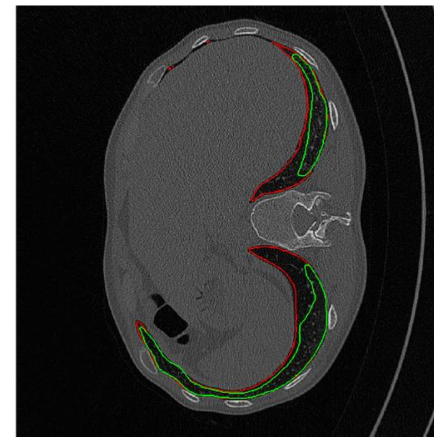


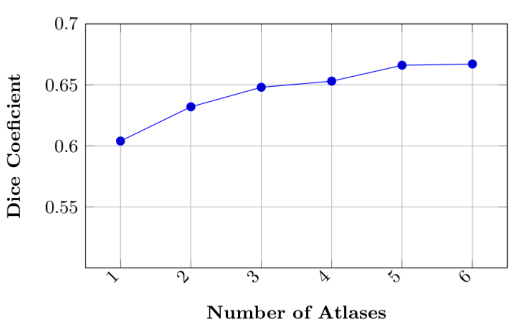


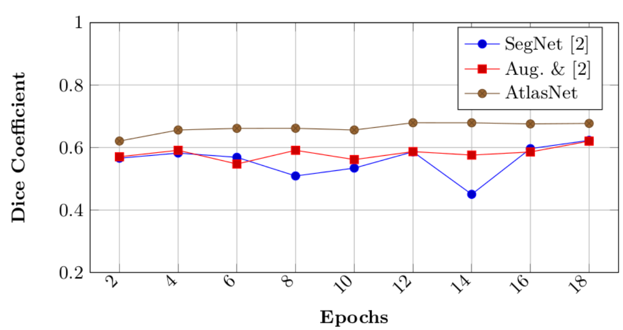
AtlasNet

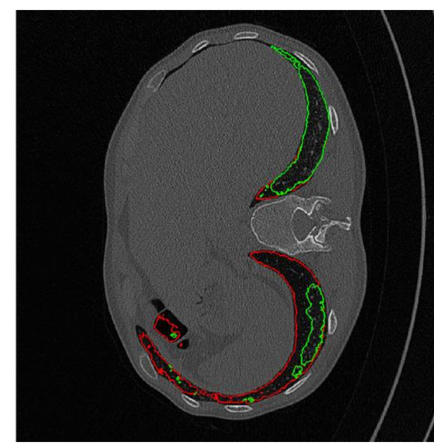
Vakalopoulou et al. "AtlasNet: Multi-atlas Non-linear Deep Networks for Medical Image Segmentation"









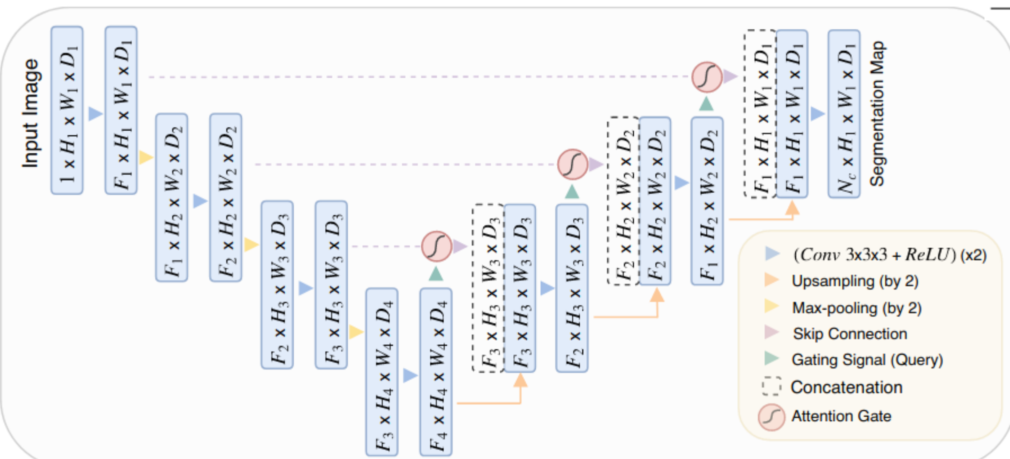


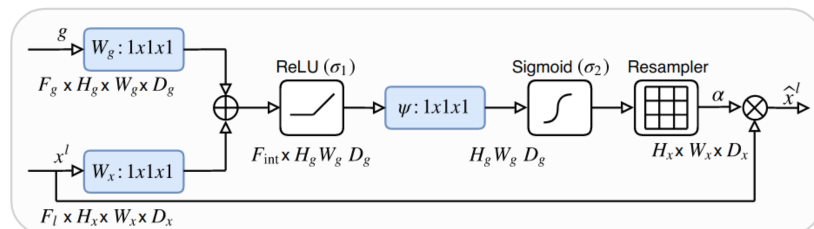
Attention U-Net

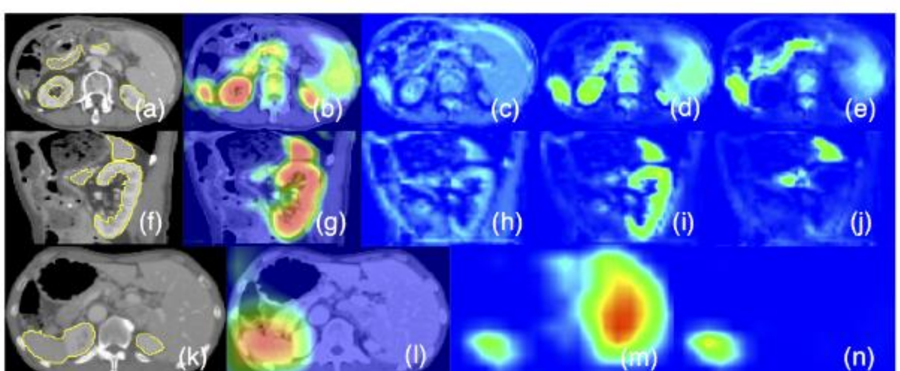
Oktay et al. "Attention U-Net: Learning Where to Look for the Pancreas"

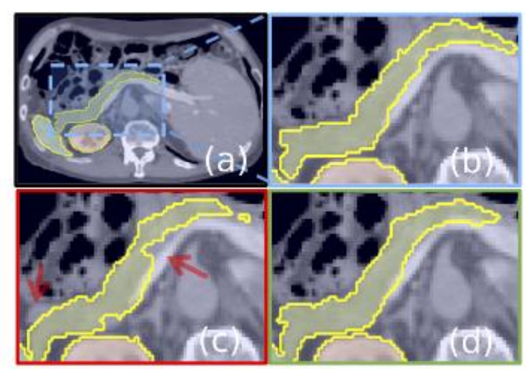
$$q_{att}^{l} = \psi^{T}\left(\sigma_1\left(W_x^T x_i^l + W_g^T g_i + b_g\right)\right) + b_\psi$$
$$\alpha_i^l = \sigma_2(q_{att}^l(x_i^l, g_i; \Theta_{att})),$$

	Method	Dice Score	Precision	Recall	S2S Dist (mm)
BFT	U-Net [24]	0.690±0.132	0.680±0.109	0.733±0.190	6.389±3.900
BFT	Attention U-Net	**0.712±0.110**	0.693±0.115	**0.751±0.149**	**5.251±2.551**
AFT	U-Net [24]	0.820±0.043	0.824±0.070	0.828±0.064	2.464±0.529
AFT	Attention U-Net	**0.831±0.038**	0.825±0.073	**0.840±0.053**	**2.305±0.568**
SCR	U-Net [24]	0.815±0.068	0.815±0.105	0.826±0.062	2.576±1.180
SCR	Attention U-Net	0.821±0.057	0.815±0.093	**0.835±0.057**	**2.333±0.856**



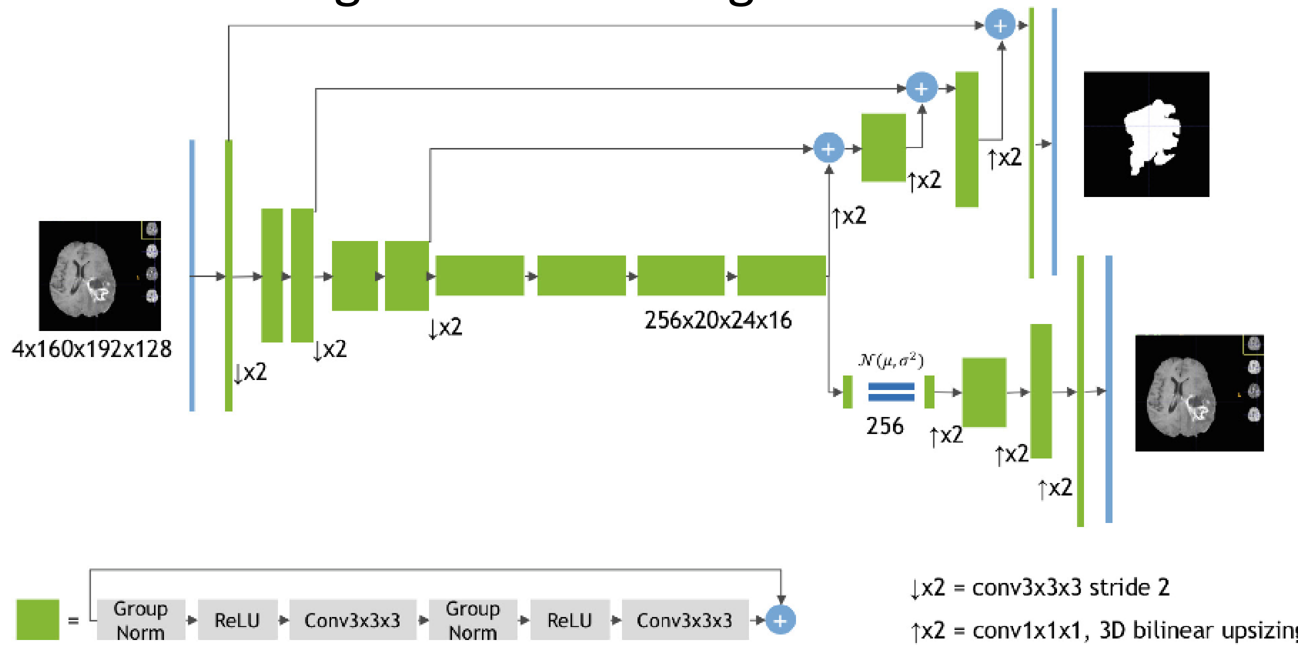




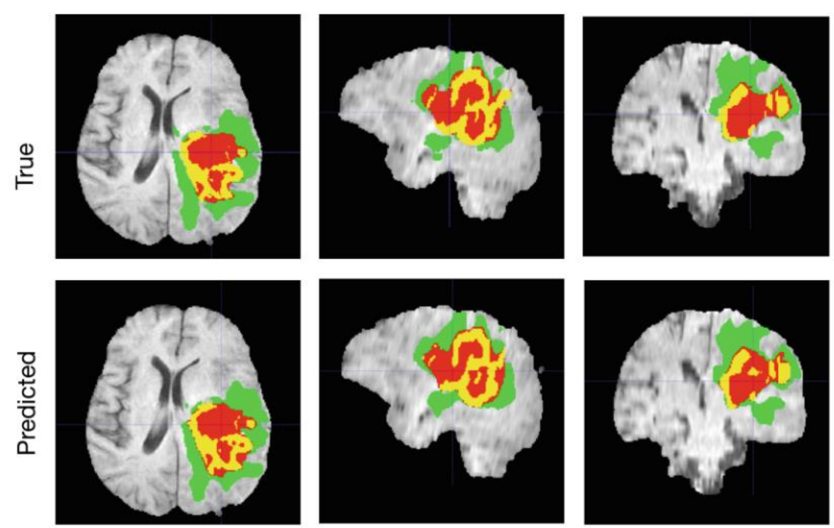


Multi-Task

Myronenko "3D MRI Brain Tumor Segmentation Using Autoencoder Regularization"

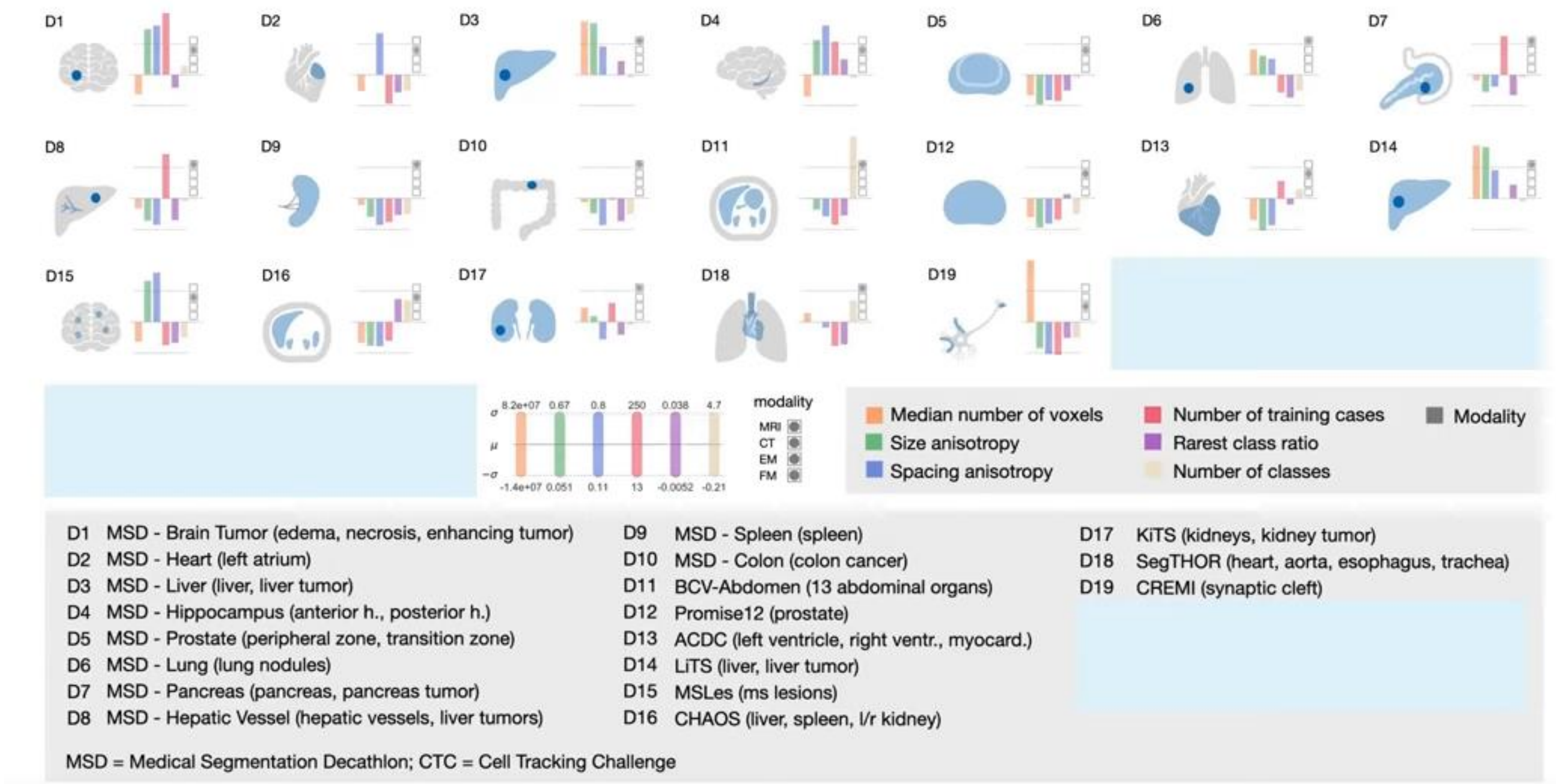


$$\mathbf{L} = \mathbf{L}_{dice} + 0.1 * \mathbf{L}_{\mathrm{L2}} + 0.1 * \mathbf{L}_{\mathrm{KL}}$$



nnU-Net

Isensee et al. "nnU-Net: Self-adapting Framework for U-Net-Based Medical Segmentation"
Isensee et al. "Automated Design of Deep Learning Methods for Biomedical Image Segmentation"



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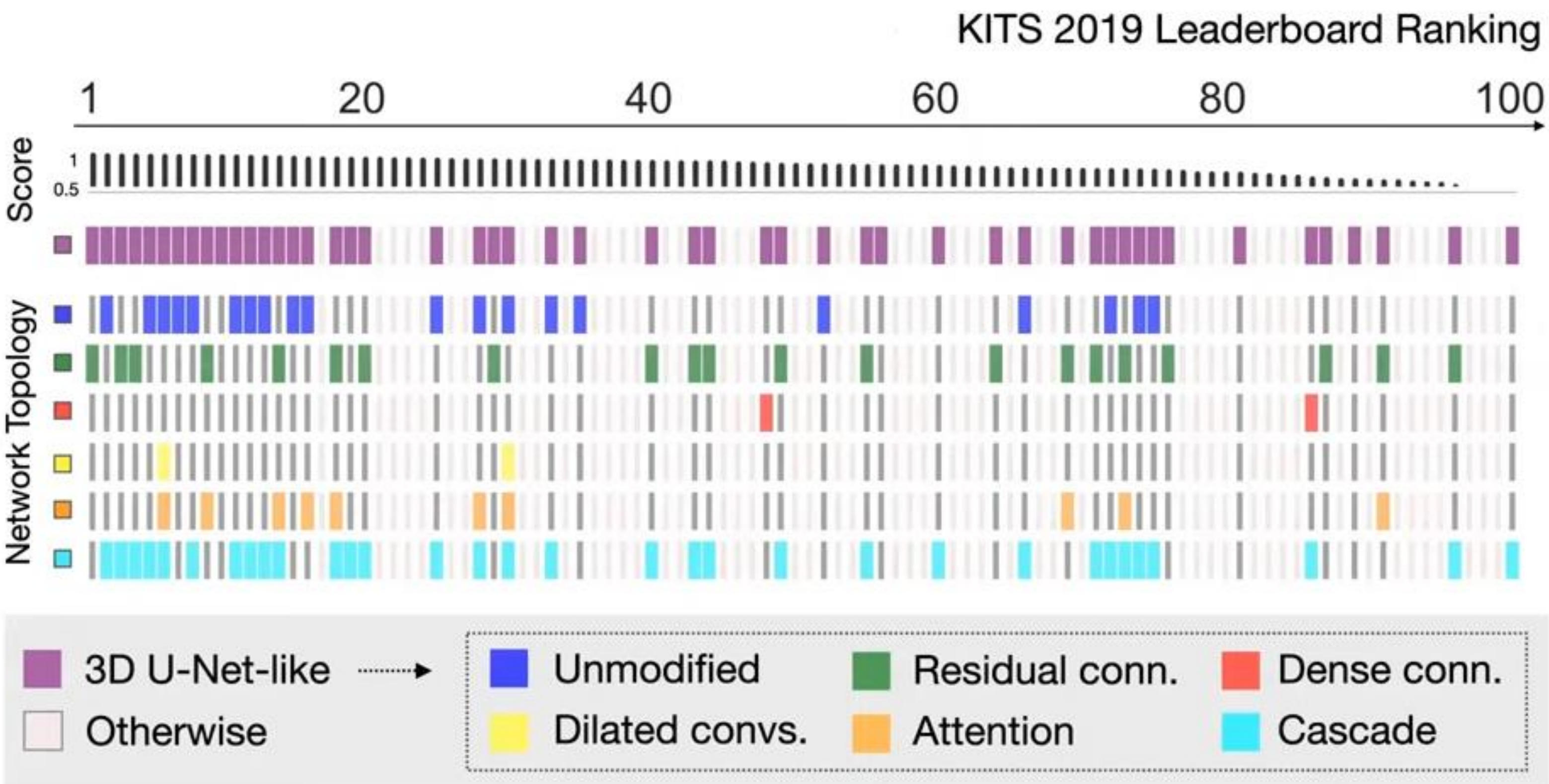


nnU-Net

Overall observations

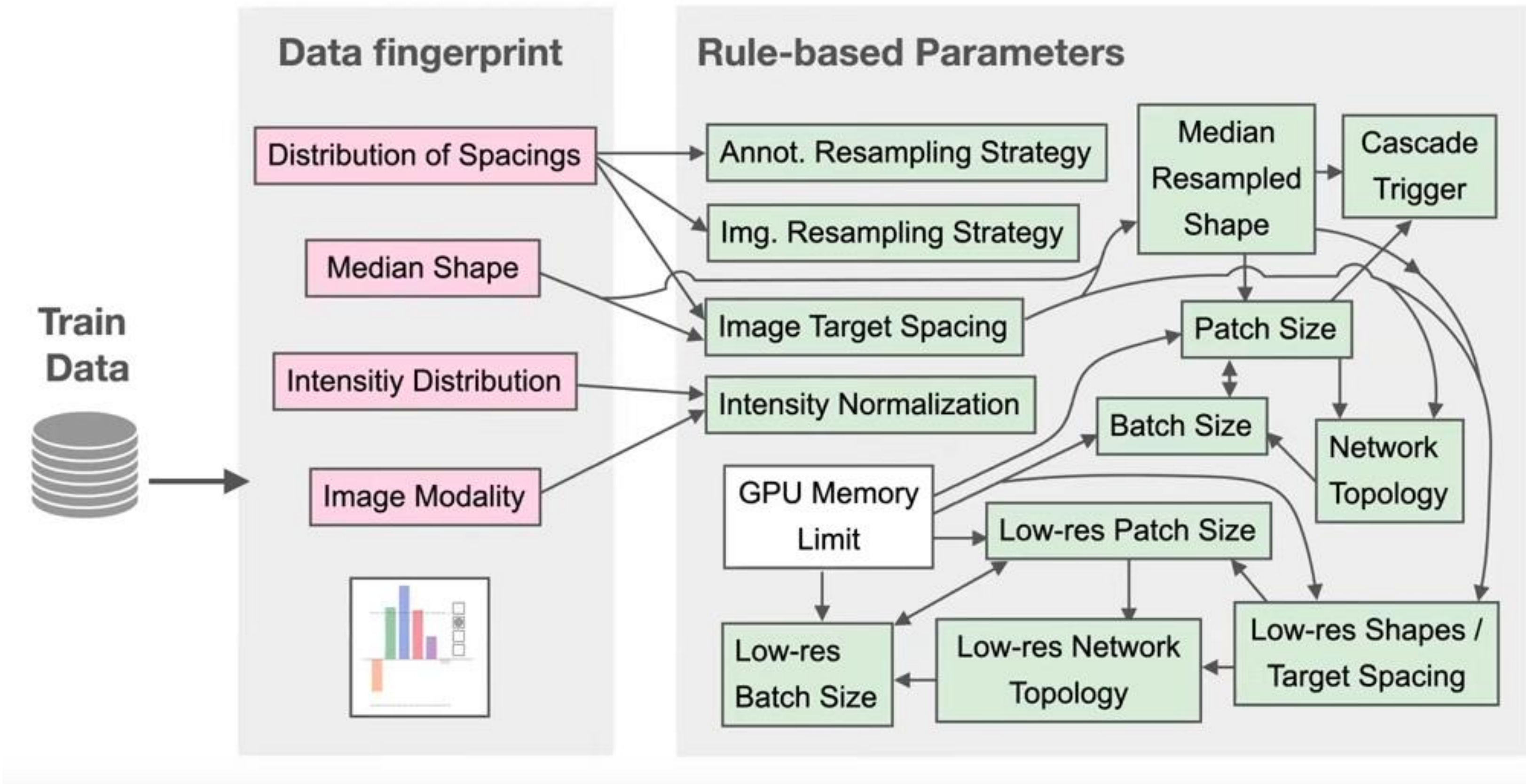
- Time consuming trial-and-error-process
- Success depends on experience of the researcher
- Needs to be repeated on every dataset

nnU-Net: Proposed recipe

- **Fixed Parameters:** Collect design decisions that do not require adaptation betweeen datasets and identify a robust common configuration
- **Rule-based Parameters:** For as many of the remaining decisions as possible formulate explicit dependencies between specific dataset properties ("dataset fingerprint") and design choices ("pipeline fingerpring") in the form of heuristic rules to allow for almost instant adaptation on application.
- **Empirical Parameters:** Learn only the remaining decisions empirically from the data

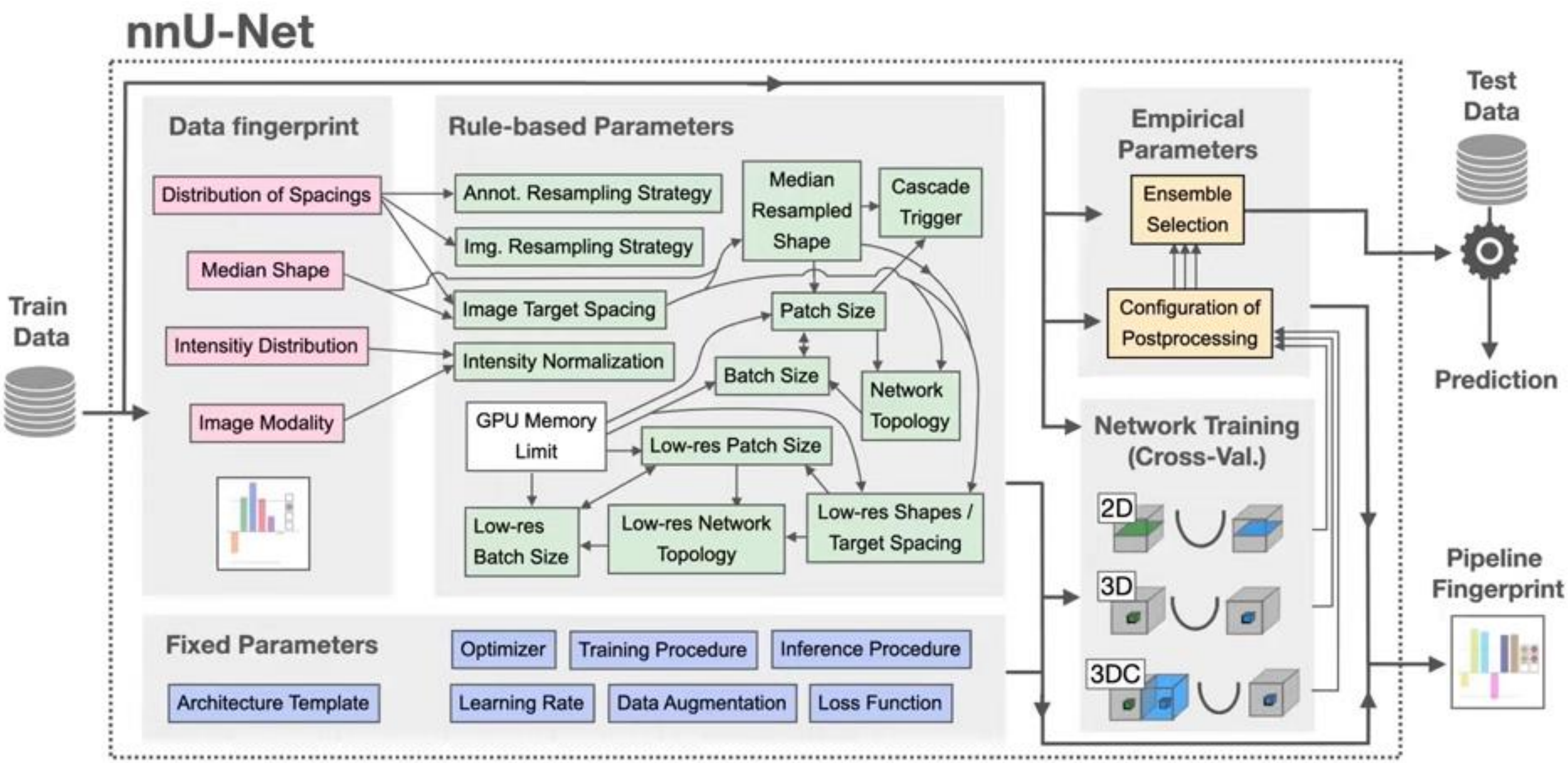
nnU-Net

Rule-based Parameters



nnU-Net

Overall Method



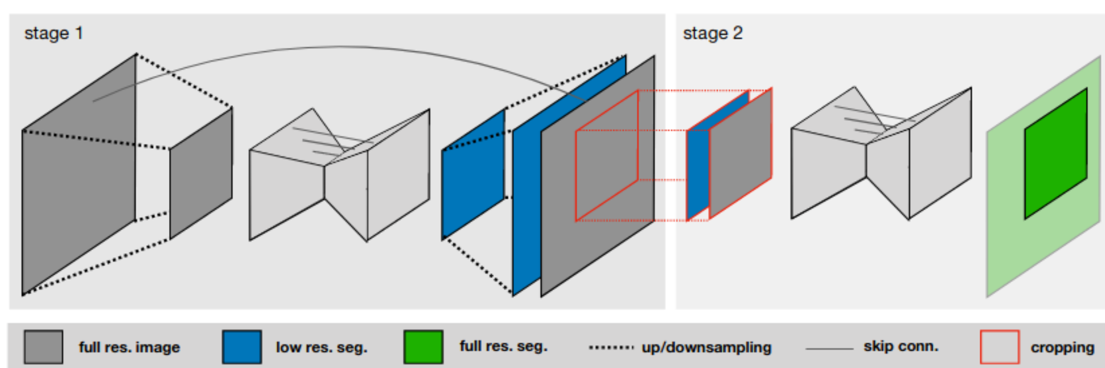
nnU-Net

Isensee et al. "nnU-Net: Self-adapting Framework for U-Net-Based Medical Segmentation"

$$\mathcal{L}_{total} = \mathcal{L}_{dice} + \mathcal{L}_{CE}$$

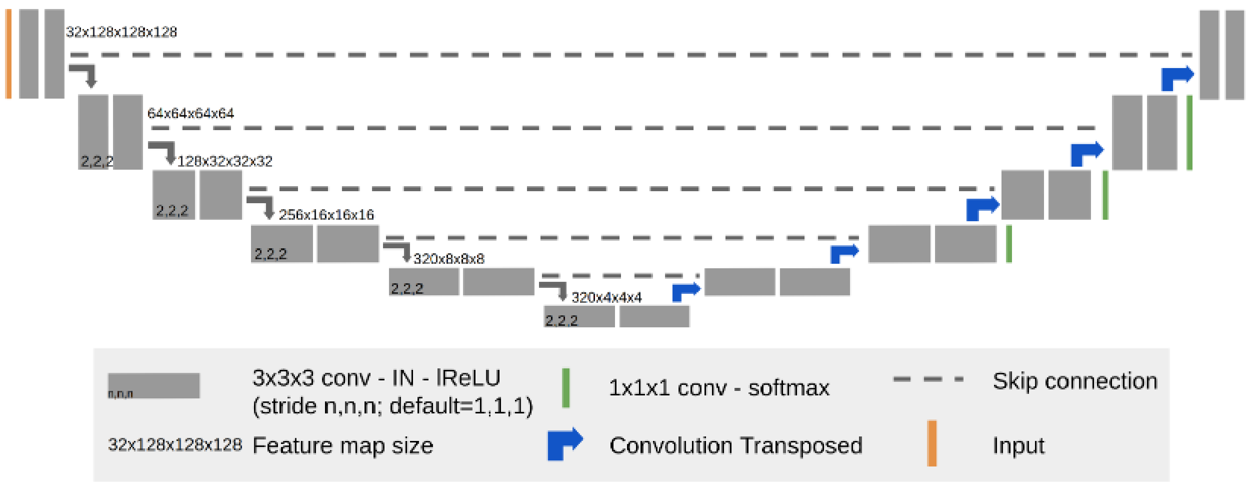
		2D U-Net	3D U-Net	3D U-Net lowres
BrainTumour	median patient shape	169x138	138x169x138	-
	input patch size	192x160	128x128x128	-
	batch size	89	2	-
	num pool per axis	5, 5	5, 5, 5	-
Heart	median patient shape	320x232	115x320x232	58x160x116
	input patch size	320x256	80x192x128	64x160x128
	batch size	33	2	2
	num pool per axis	6, 6	4, 5, 5	4, 5, 5
Liver	median patient shape	512x512	482x512x512	121x128x128
	input patch size	512x512	128x128x128	128x128x128
	batch size	10	2	2
	num pool per axis	6, 6	5, 5, 5	5, 5, 5
Hippocampus	median patient shape	50x35	36x50x35	-
	input patch size	56x40	40x56x40	-
	batch size	366	9	-
	num pool per axis	3, 3	3, 3, 3	-
Prostate	median patient shape	320x319	20x320x319	-
	input patch size	320x320	20x192x192	-
	batch size	26	4	-
	num pool per axis	6, 6	2, 5, 5	-
Lung	median patient shape	512x512	252x512x512	126x256x256
	input patch size	512x512	112x128x128	112x128x128
	batch size	10	2	2
	num pool per axis	6, 6	4, 5, 5	4, 5, 5
Pancreas	median patient shape	512x512	96x512x512	96x256x256
	input patch size	512x512	96x160x128	96x160x128
	batch size	10	2	2
	num pool per axis	6, 6	4, 5, 5	4, 5, 5

	BrainTumour			Heart	Liver		Hippoc.		Prostate		Lung	Pancreas	
label	1	2	3	1	1	2	1	2	1	2	1	1	2
2D U-Net	78.60	58.65	77.42	91.36	94.37	53.94	88.52	86.70	61.98	84.31	52.68	74.70	35.41
3D U-Net	**80.71**	**62.22**	**79.07**	92.45	94.11	61.74	**89.87**	**88.20**	60.77	83.73	55.87	77.69	42.69
3D U-Net stage1 only (U-Net Cascade)	-	-	-	90.63	94.69	47.01	-	-	-	-	65.33	79.45	49.65
3D U-Net (U-Net Cascade)	-	-	-	92.40	95.38	58.49	-	-	-	-	**66.85**	**79.30**	**52.12**
ensemble 2D U-Net+ 3D U-Net	80.79	61.72	79.16	**92.70**	94.30	60.24	89.78	88.09	**63.78**	**85.31**	55.96	78.26	40.46
ensemble 2D U-Net+ 3D U-Net (U-Net Cascade)	-	-	-	92.64	95.31	60.09	-	-	-	-	61.18	78.79	45.46
ensemble 3D U-Net+ 3D U-Net (U-Net Cascade)	-	-	-	92.63	**95.43**	**61.82**	-	-	-	-	65.16	79.70	49.14
test set	67.71	**47.73**	**68.16**	**92.77**	**95.24**	**73.71**	**90.37**	**88.95**	**75.81**	**89.59**	**69.20**	**79.53**	**52.27**



nnU-Net for Brain Tumor Segmentation

Isensee et al. "nnU-Net for Brain Tumor Segmentation"



Additional Modifications:

- Region-based training [R] : training on the validated classes
- Postprocessing especially on the enhancing tumor (remove predictions smaller than a threshold)
- Biger batch size
- More data augmentation [DA]
    - Increase probability for rotation, scalling
    - Brightness augmentation
    - Elastic deformations

nnU-Net for Brain Tumor Segmentation

Isensee et al. "nnU-Net for Brain Tumor Segmentation"

Additional Modifications

- Batch normalization [BN] (instead of instance normalization)
- Batch dice [BD] Calculate the dice for the entire mini-batch and not per sample. It helps with the cases with very small number of segmentations.

Model	Training set				Validation set			
	rank based on mean Dice		BraTS ranking		rank based on mean Dice		BraTS ranking	
	value	rank	value	rank	value	rank	value	rank
BL	86.55	8	0.3763	8	84.18	6	0.4079	8
BL*	86.09	9	0.3767	9	83.76	9	0.4236	9
BL*+R	86.73	5	0.3393	5	84.13	7	0.4005	7
BL*+R+DA	87.07	**1**	0.3243	3	84.73	5	0.3647	5
BL*+R+DA+BN	86.82	3	0.3377	4	85.20	3	0.3577	4
BL*+R+DA+BD	86.79	4	0.3231	2	84.12	8	0.3726	6
BL*+R+DA+BN+BD	86.87	2	0.3226	**1**	85.11	4	0.3487	3*
BL*+R+DA*+BN	86.68	6	0.3521	6	85.58	**1**	0.3125	**1***
BL*+R+DA*+BN+BD	86.64	7	0.3595	7	85.29	2	0.3437	2*

Transformers for segmentation

- Hatamizadeh et. al, "UNETR: Transformers for 3D Medical Image Segmentation", CVPR 2022

- The medical input is separated in multiple 3D patches $\mathbf{x} \in \mathbb{R}^{H \times W \times D \times C}$ used as input to the transformer

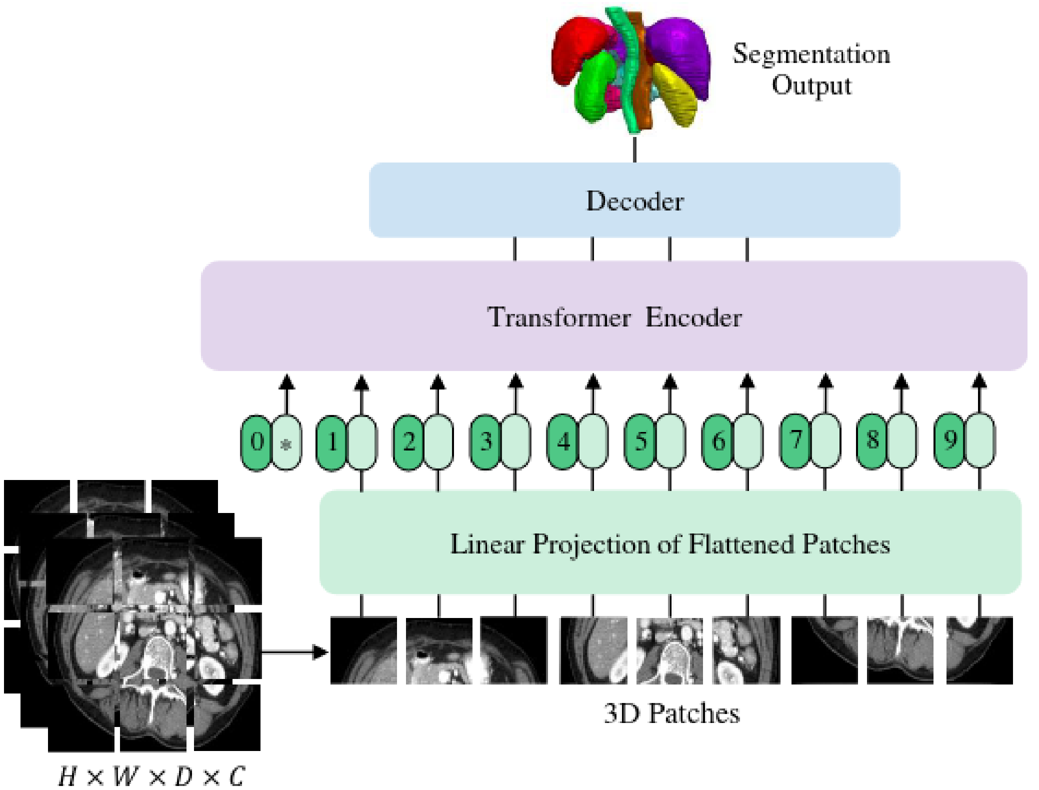
$$\mathbf{E}_{pos} \in \mathbb{R}^{N \times K}$$

$$\mathbf{E} \in \mathbb{R}^{(P^3.C) \times K}$$

$$\mathbf{z}_0 = [\mathbf{x}_v^1\mathbf{E}; \mathbf{x}_v^2\mathbf{E}; \ldots; \mathbf{x}_v^N\mathbf{E}] + \mathbf{E}_{pos},$$

$$\mathbf{z}'_i = \mathrm{MSA}(\mathrm{Norm}(\mathbf{z}_{i-1})) + \mathbf{z}_{i-1}, \quad i = 1 \ldots L,$$

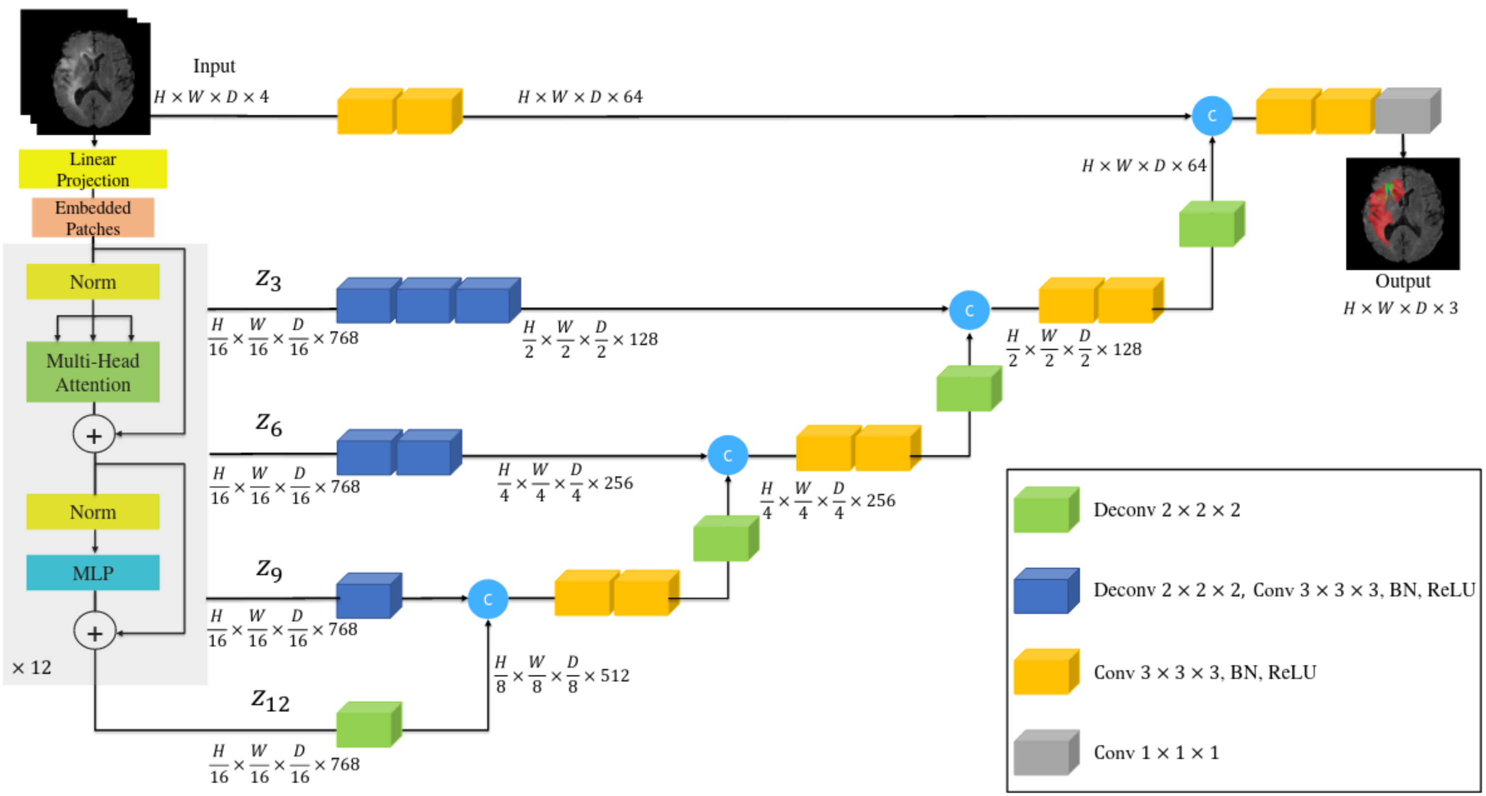
$$\mathbf{z}_i = \mathrm{MLP}(\mathrm{Norm}(\mathbf{z}'_i)) + \mathbf{z}'_i, \quad i = 1 \ldots L,$$



- MSA: multi-head self-attention, MLP: two linear layers with GELU activation

Transformers for segmentation

- Hatamizadeh et. al, "UNETR: Transformers for 3D Medical Image Segmentation", CVPR 2022



- Transformer-based encoder and convolutional decoder with skip connections to restore the spatial resolution of the images.

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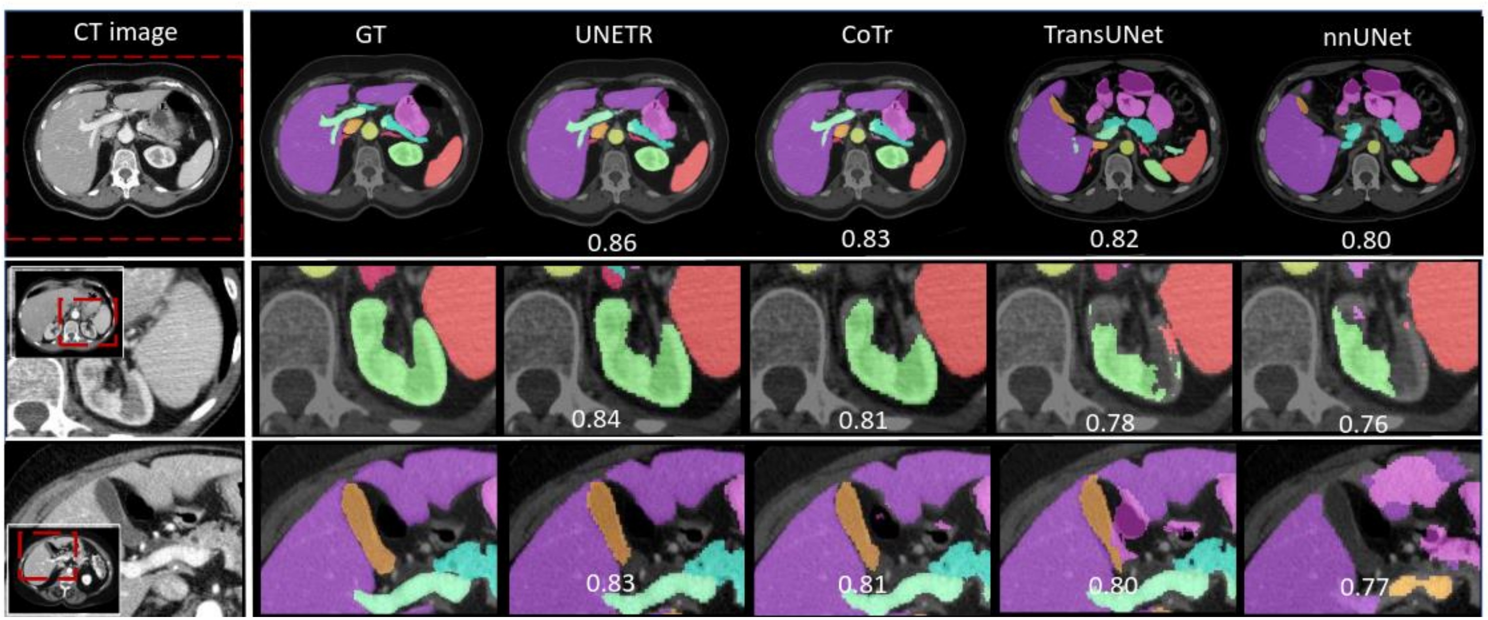
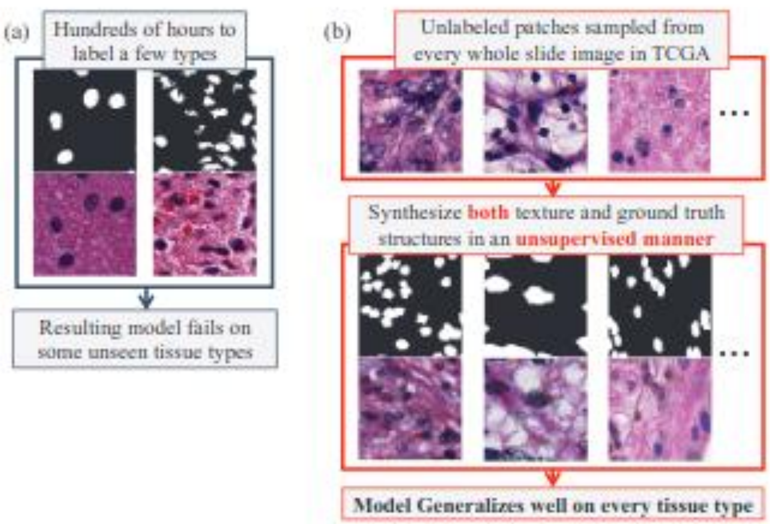
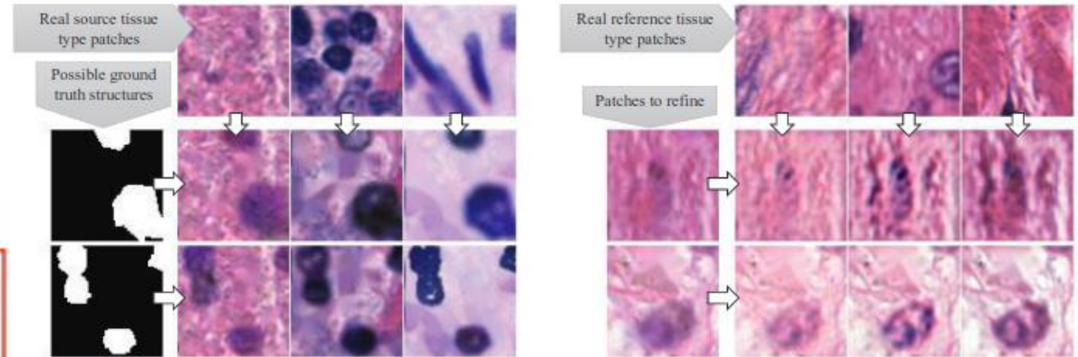
Task/Modality	Spleen Segmentation (CT)		Brain tumor Segmentation (MRI)							
Anatomy	Spleen		WT		ET		TC		All	
Metrics	Dice	HD95	Dice	HD95	Dice	HD95	Dice	HD95	Dice	HD95
UNet [36]	0.953	4.087	0.766	9.205	0.561	11.122	0.665	10.243	0.664	10.190
AttUNet [34]	0.951	4.091	0.767	9.004	0.543	10.447	0.683	10.463	0.665	9.971
SETR NUP [52]	0.947	4.124	0.697	14.419	0.544	11.723	0.669	15.192	0.637	13.778
SETR PUP [52]	0.949	4.107	0.696	15.245	0.549	11.759	0.670	15.023	0.638	14.009
SETR MLA [52]	0.950	4.091	0.698	15.503	0.554	10.237	0.665	14.716	0.639	13.485
TransUNet [7]	0.950	4.031	0.706	14.027	0.542	10.421	0.684	14.501	0.644	12.983
TransBTS [43]	-	-	0.779	10.030	0.574	9.969	0.735	8.950	0.696	9.650
CoTr w/o CNN encoder [47]	0.946	4.748	0.712	11.492	0.523	9.592	0.698	12.581	0.6444	11.221
CoTr [47]	0.954	3.860	0.746	9.198	0.557	9.447	0.748	10.445	0.683	9.697
UNETR	**0.964**	**1.333**	**0.789**	**8.266**	**0.585**	**9.354**	**0.761**	**8.845**	**0.711**	**8.822**



Synthesize

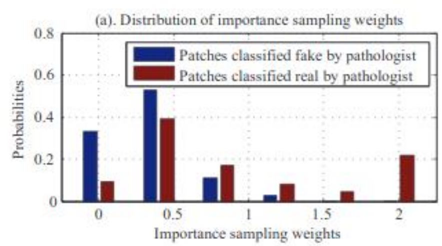
Hou et al. "Robust Histopathology Image Analysis: to Label or to Synthesize?"

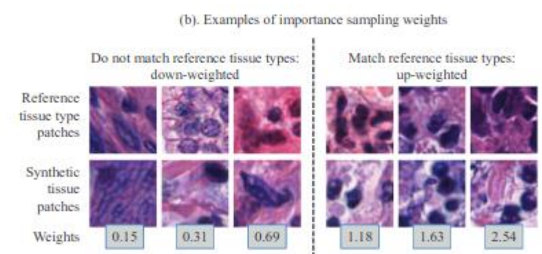




(a). Utilizing textures in various tissue types during the initial synthesis step.

(b). Refining the initial synthetic patches to be more like the reference type.





Nucleus segmentation methods	DICE Avg.
No hard examples	0.7476
No reference patch during refinement	0.7410
No importance weights	0.7533
Universal CNN (proposed)	**0.7612**

Lymphocyte detection methods	AUROC
Level Set features + supervised net [67]	0.7132
Fine-tuning VGG16 (supervised) [52]	0.6925
Universal CNN (proposed)	**0.7149**

Agony of Choice

- Architecture: depth, width, scales, residuals, ….
- Loss function: (weighted) cross entropy, IoU, Dice, …
- Sampling strategy: equally per class, fore/background, uniform, …
- Optimization: optimizer, learning rate, momentum, regularization, ...
- Data normalization: z-score, bias field correction, histogram matching, …
- Post-processing: CRFs, ensemble of networks, ….

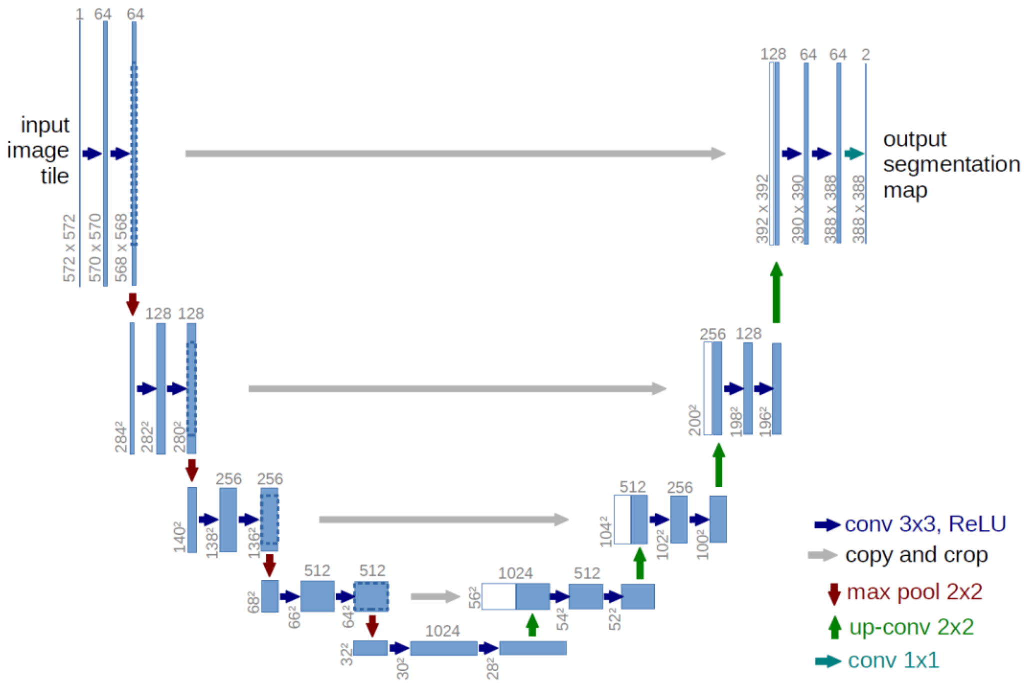
Conclusions

- Semantic Segmentation is one of the most studied problems in medical imaging.
  - Conducting **quantitative analyses**, e.g. measuring the volume of the ventricular cavity.
  - Determining the precise **location and extent** of an organ or a certain type of tissue, e.g. a tumour for treatment such as radiation therapy.
  - Creating **3D models** used for **simulation**, e.g. generating a model of an abdominal aortic aneurysm for simulating stress

- A lotttt of open challenges on these topics.

Lab Session!

- Brain tumor segmentation
  - U-Net



TorchVision

Deep learning for medical imaging

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