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#DLUPC

Day 2 Lecture 5

Medical Imaging @UPC

At GPI with Verónica Vilaplana, Míriam Bellver, Xavier Giró

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Acknowledgments
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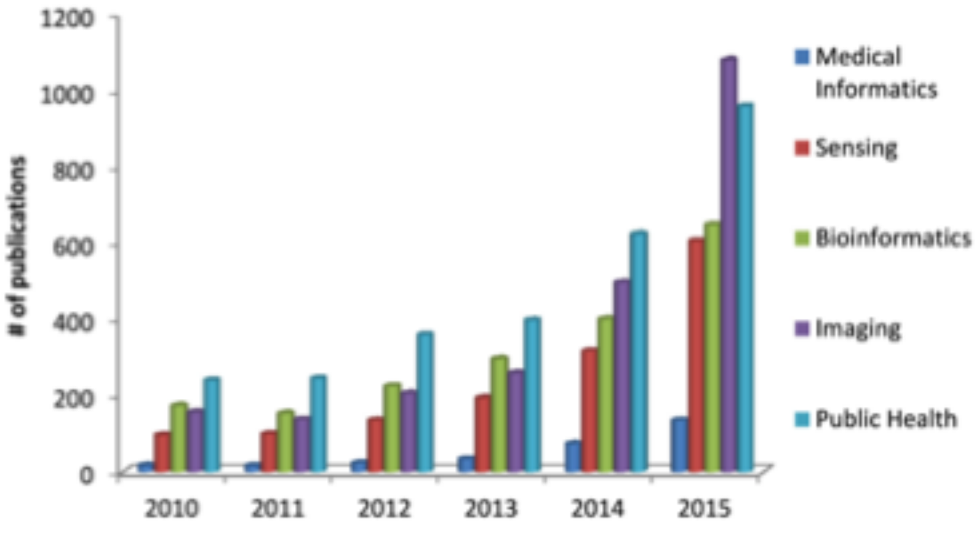
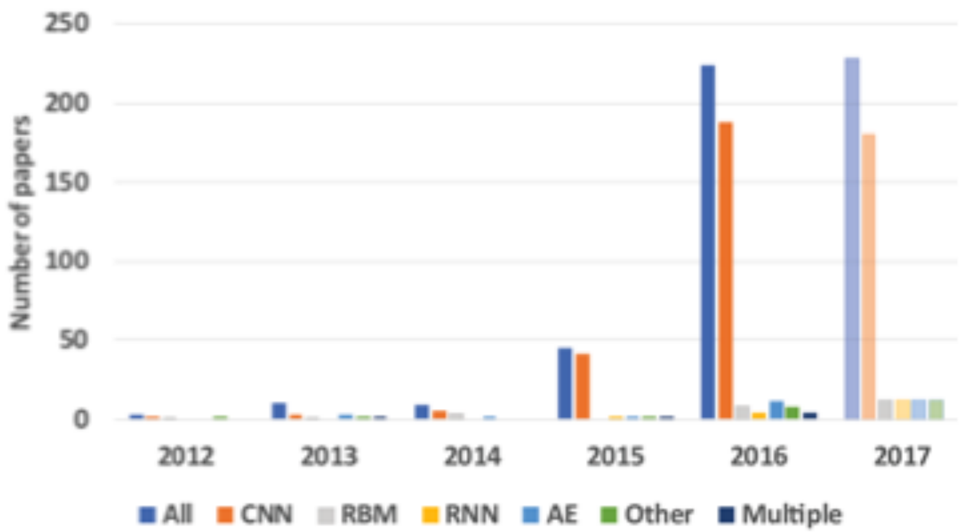
Outline

- Why DL for medical imaging?
- Challenges
- Some applications at UPC
    - Segmentation 1: brain tumor segmentation
    - Segmentation 2: brain tumor segmentation
    - Classification (Exam)1: Skin Classification
    - Super-Resolution 1: Brain MRI super-resolution
    - Segmentation 2: Liver Lesion Segmentation
    - Segmentation 3: Parasite Segmentation
    - Segmentation 4: Active Learning & Segmentation
    - Classification (Exam) 2: Impact of Segmentation in Exam (Skin)
- Datasets, challenges

Why deep learning for medical imaging?

Deep learning is providing exciting solutions for medical image analysis problems and is seen as a key method for future applications



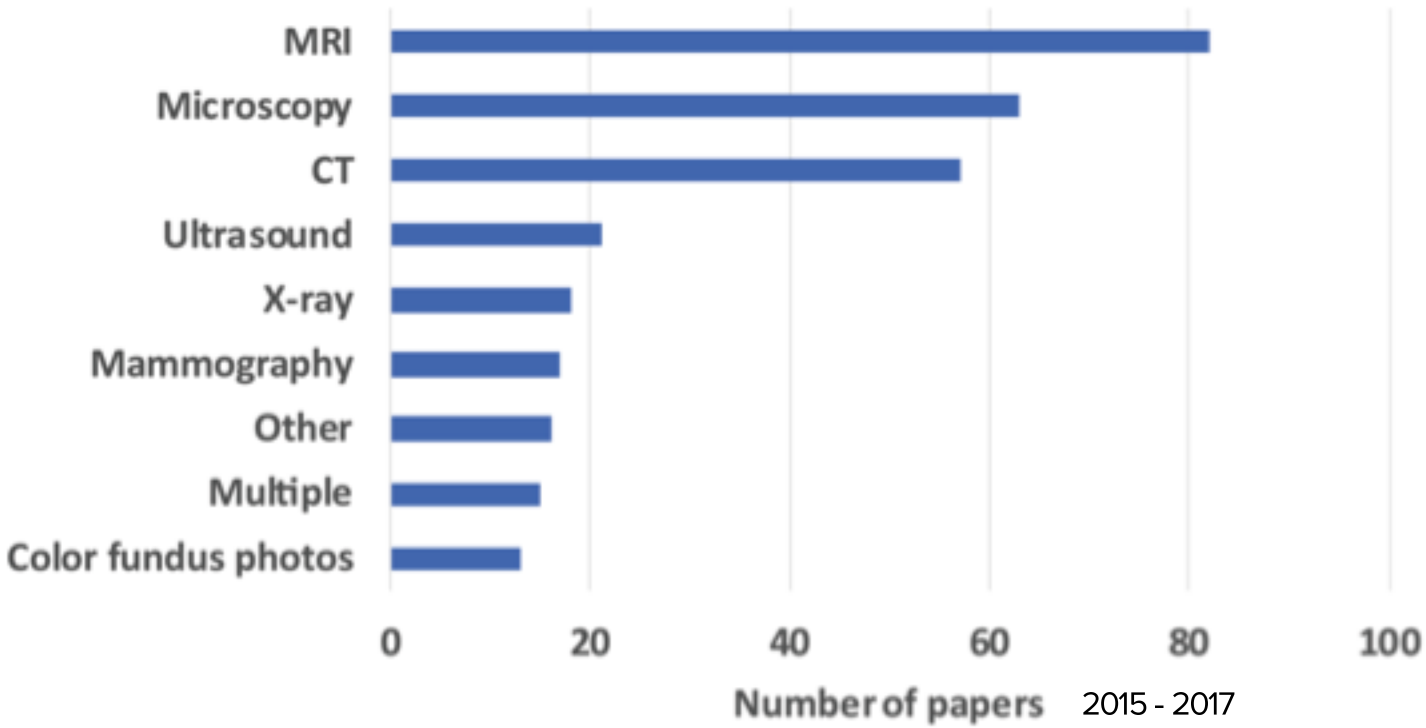


Papers that use deep learning in areas of health informatics / medical imaging

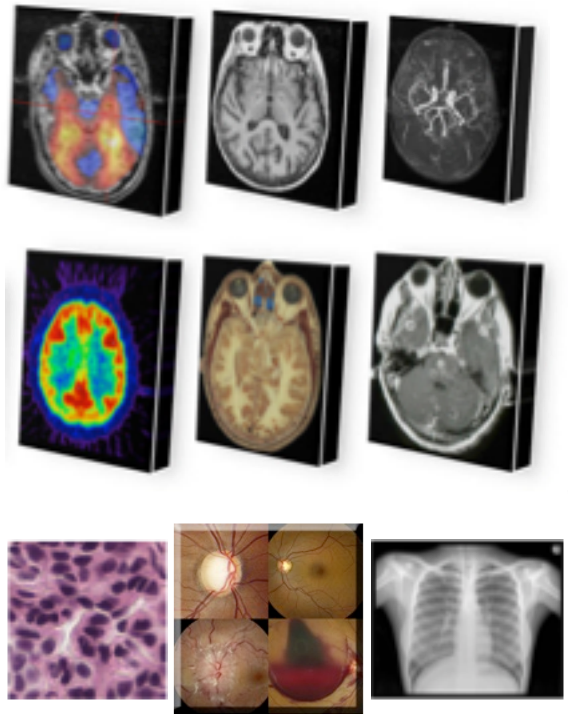
Ravi et al, [Deep Learning for Health Informatics](), JBHI, 2017
Litjens et al, [A Survey on Deep Learning in Medical Image Analysis](), June 4th , 2017

Why deep learning for medical imaging?

Image modalities



2015 - 2017



Litjens et al, [A Survey on Deep Learning in Medical Image Analysis](), June 4th , 2017

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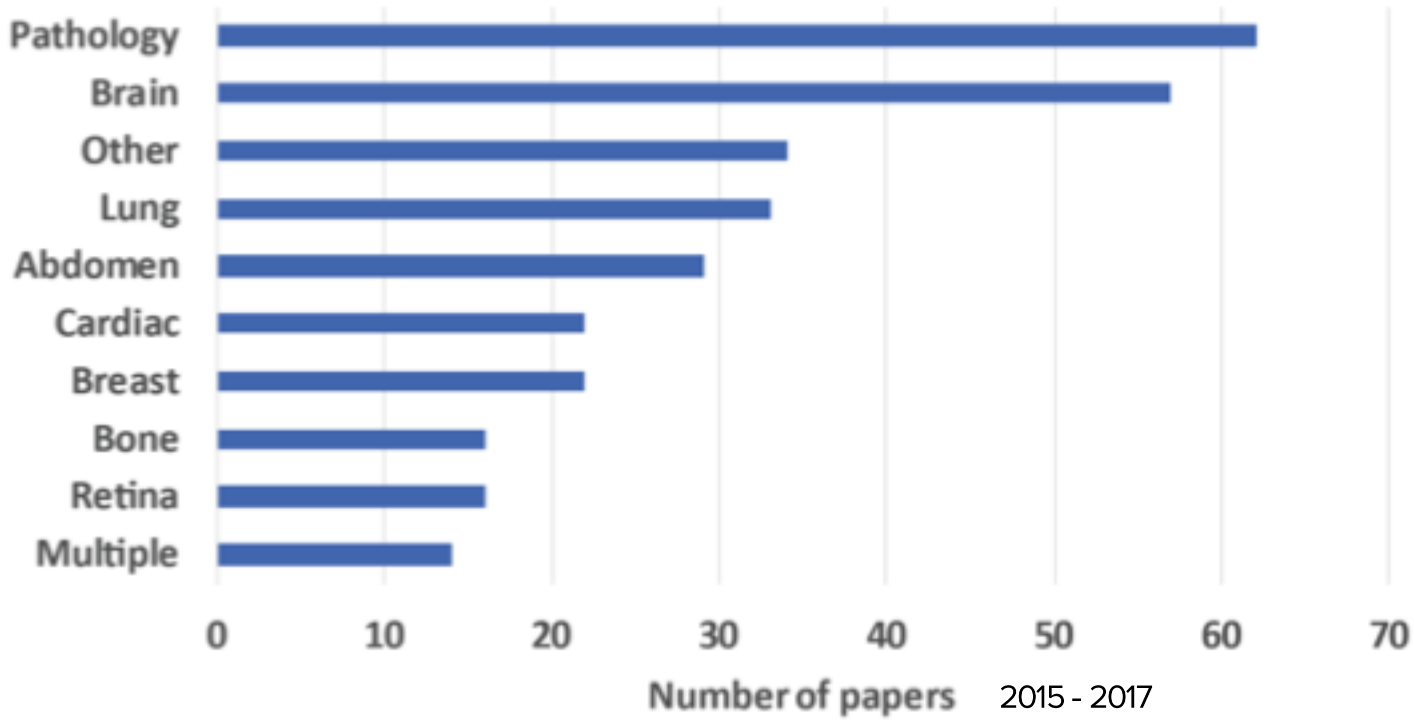
Why deep learning for medical imaging?

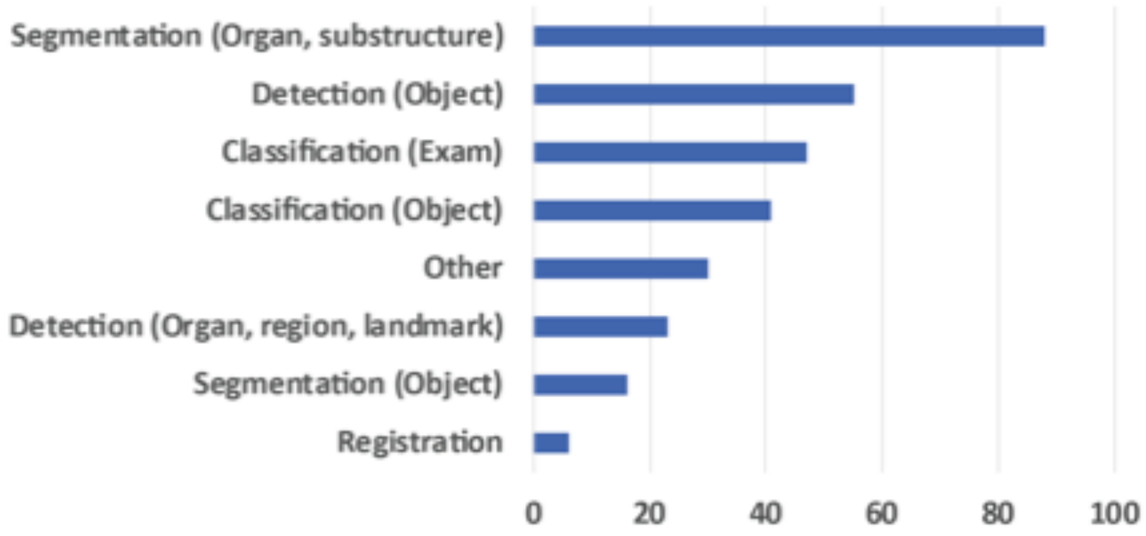
Anatomical application areas



2015 - 2017

Litjens et al, A Survey on Deep Learning in Medical Image Analysis, June 4th , 2017

Deep learning uses in medical imaging



Litjens et al, [A Survey on Deep Learning in Medical Image Analysis](), June 4th , 2017

Classification: Image / exam classification, object or lesion classification

Detection: organ, region and landmark localization, object or lesion detection

Segmentation: organ and substructure segmentation, lesion segmentation

Other tasks: registration, content based image retrieval, image generation and enhancement, combining image data with reports

Challenges

1. Problem definition and expertise

- **Relevance (clinician vs ML scientist)**
- Complexity of human physiology
- Difficulty in **modeling implicit knowledge and skills** of clinicians
- **Discrepancy** between experts and algorithms
- DL seen as a **black-box** which may lead to a lack of trust

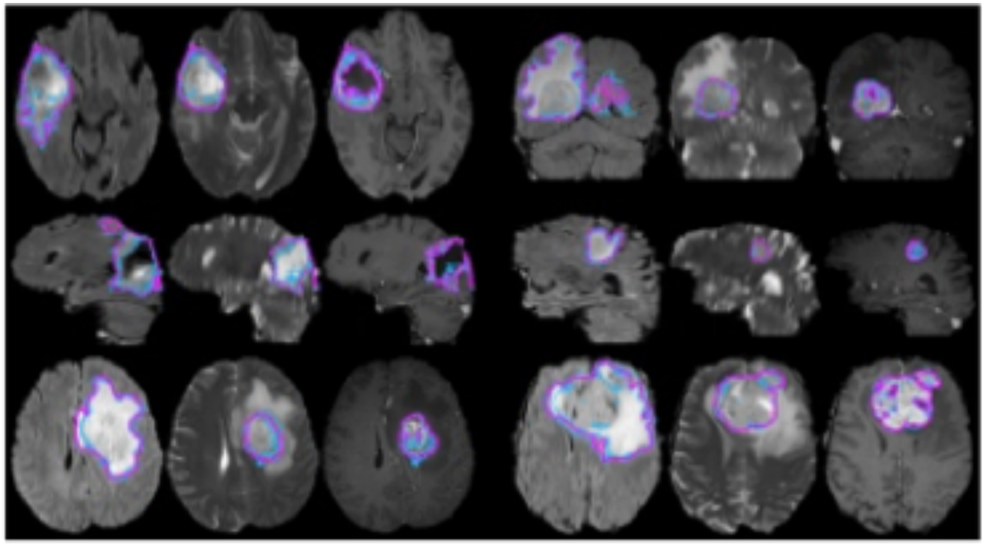
2. Data

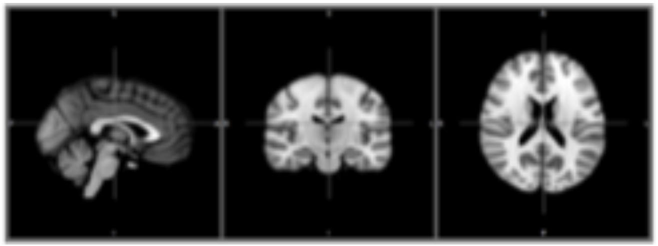
- Lack of large annotated datasets
  - Availability of datasets
  - Stringent **regulations**
  - **Annotations from experts** (expensive, time consuming)
- Large variability in images due to sensors and other factors
- Class imbalance: normal class is usually over represented

Segmentation 1: brain tumor segmentation

Gliomas are the most frequent primary brain tumors in adults

Challenges: lesions are defined through intensity changes relative to surrounding normal tissue, tumor structures vary in size, extension, localization (MRImages)



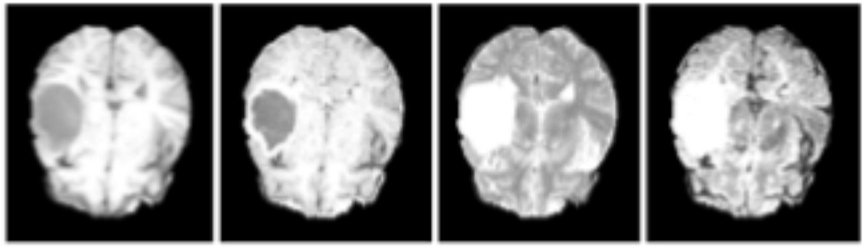


sagittal coronal axial

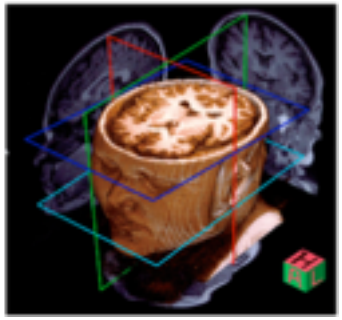
BRATS: Brain Tumor Segmentation Challenge (MICCAI Int. Conf. on Medical Image Computing and computer assisted intervention)

Segmentation 1: brain tumor segmentation

Multimodal MRI images (different biological information, 3D)

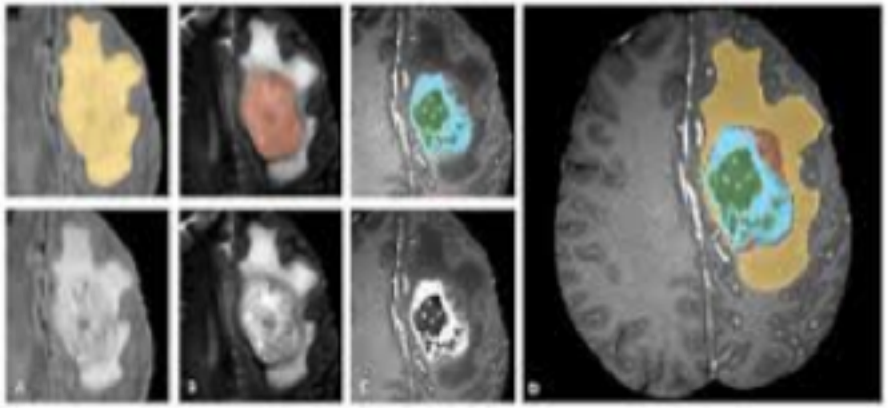


T1 T1* T2 FLAIR



BRATS challenge:

4 tumor regions + background



Whole tumor visible in FLAIR (A), the tumor **core** visible in T2 (B), enhancing tumor visible in T1c (blue), necrotic components of core (green). Segmentations combined to generate final labels (D): **edema** (yellow), **non-enhancing solid core** (red), **necrotic/cystic core** (green), **enhancing core** (blue)

Segmentation 1: brain tumor segmentation

UPC Paper:
Casamitjana et al, 3D Convolutional Networks for Brain Tumor Segmentation: a comparison of multiresolution architectures, 201

Fully 3D Convolutional NN: to account for 3D correlation
Hybrid training: take image patches and densely train them (due to memory constraints)
Dense inference: segment the whole volume in a single forward pass.
Pre-processing: normalize each input channel (mean, std).
Post-processing: remove small connected components (100 voxels)

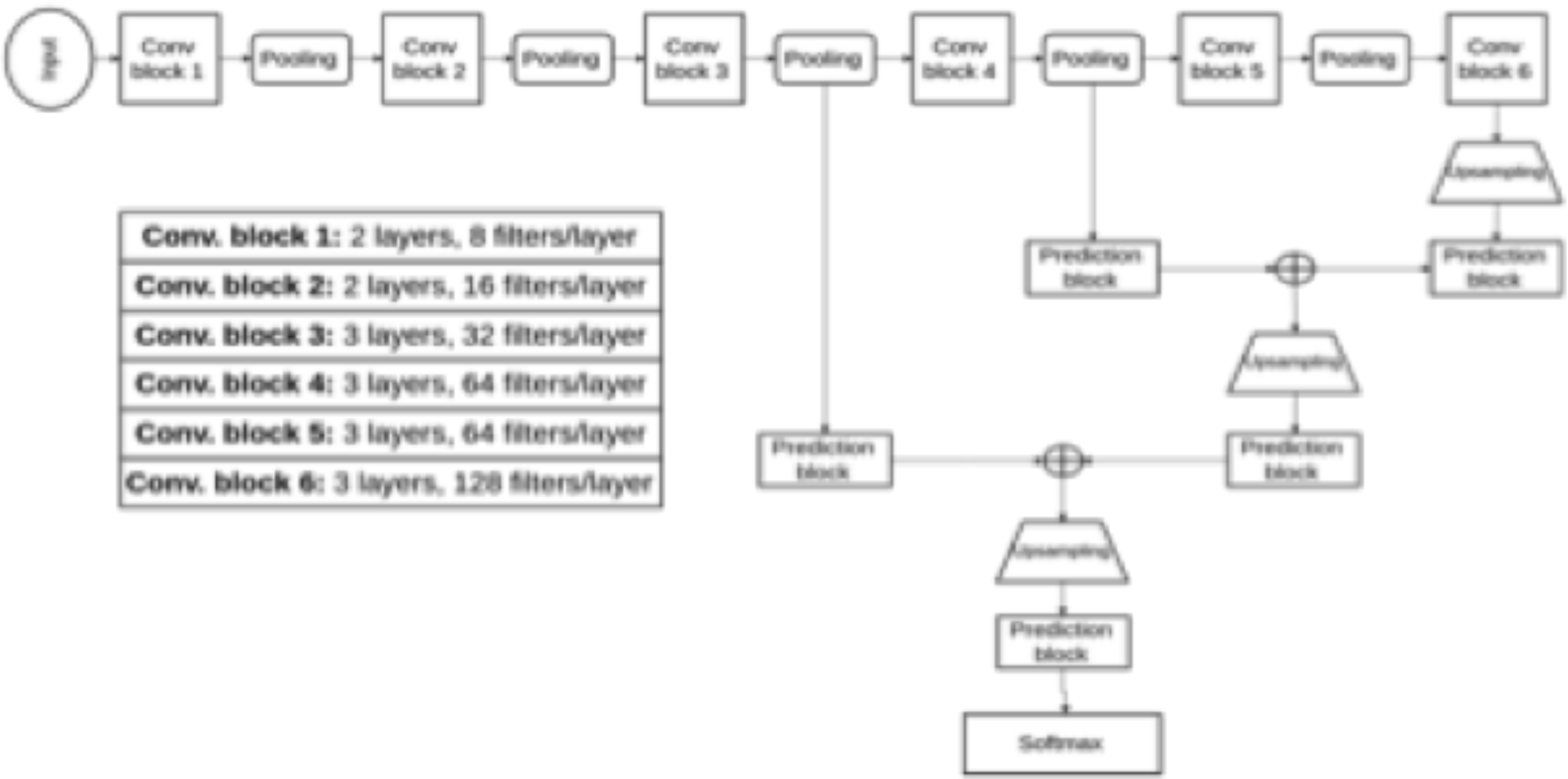
Architectures:

- 3D-Net1: 3D extension of FCN8 Long
- 3D-Net2: 3D extension of U-Net
- 3D-Net3: based on two-paths 2D (1), DeepMedic 3D (2)

(1) Havaei et al, Brain tumor segmentation with Deep Neural Networks, 2016
(2) Kamnitsas, Efficient Multi Scale 3D CNN with fully connected CRF for Accurate Brain Lesion Segmentation, 2016

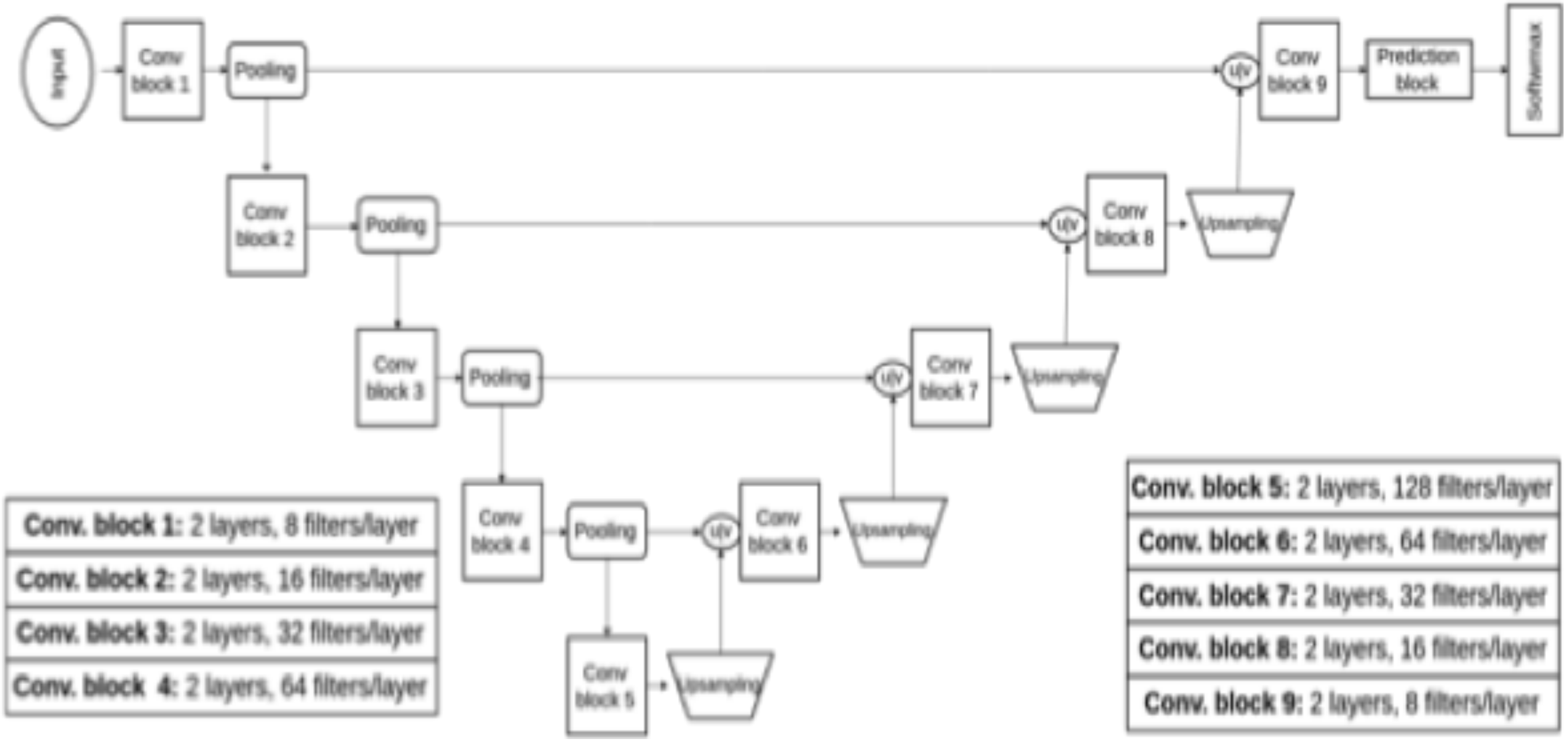
Segmentation 1: brain tumor segmentation

3D-Net1



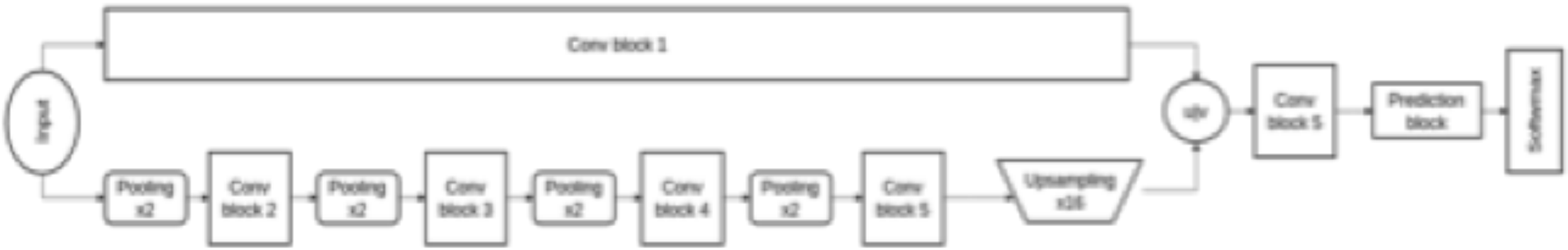
Segmentation 1: brain tumor segmentation

3D-Net2



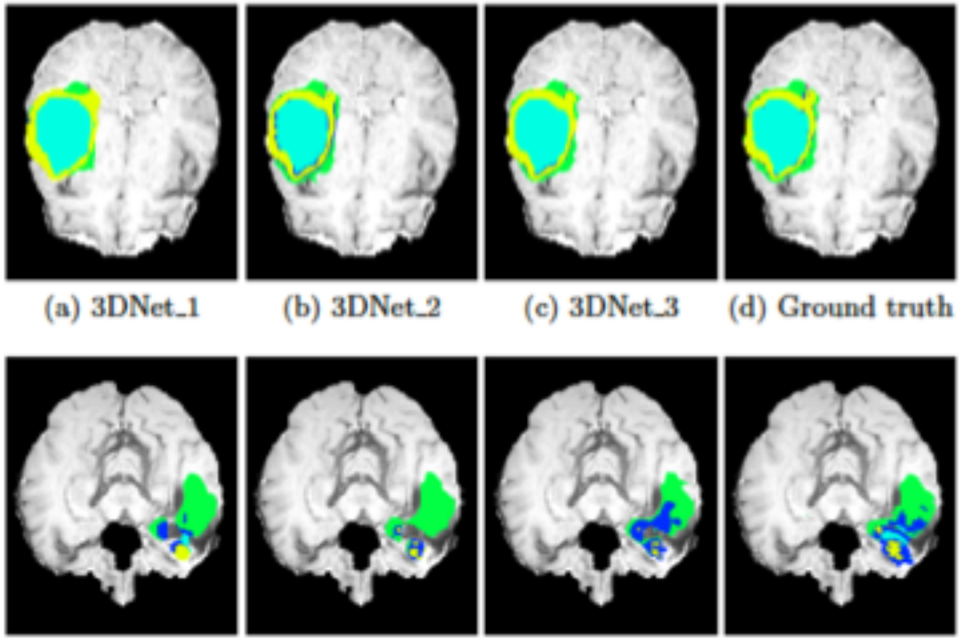
Segmentation 1: brain tumor segmentation

3D-Net3



Conv. block 1: 8 layers, 8 filters/layer
Conv. block 2: 2 layers, 16 filters/layer
Conv. block 3: 2 layers, 32 filters/layer
Conv. block 4: 2 layers, 32 filters/layer
Conv. block 5: 2 layers, 64 filters/layer
Conv. block 6: 2 layers, 16 filters/layer

Segmentation 1: brain tumor segmentation


(a) 3DNet_1 (b) 3DNet_2 (c) 3DNet_3 (d) Ground truth
(e) 3DNet_1 (f) 3DNet_2 (g) 3DNet_3 (h) Ground truth

	Accuracy	Dice score		
		Whole	Core	Active
3DNet_1	99.69	89.64	76.87	63.12
3DNet_2	**99.71**	91.59	69.90	73.89
3DNet_3	**99.71**	**91.74**	**83.61**	**76.82**

$$Dice\ score = \frac{2 * |X \cap Y|}{|X| + |Y|}$$

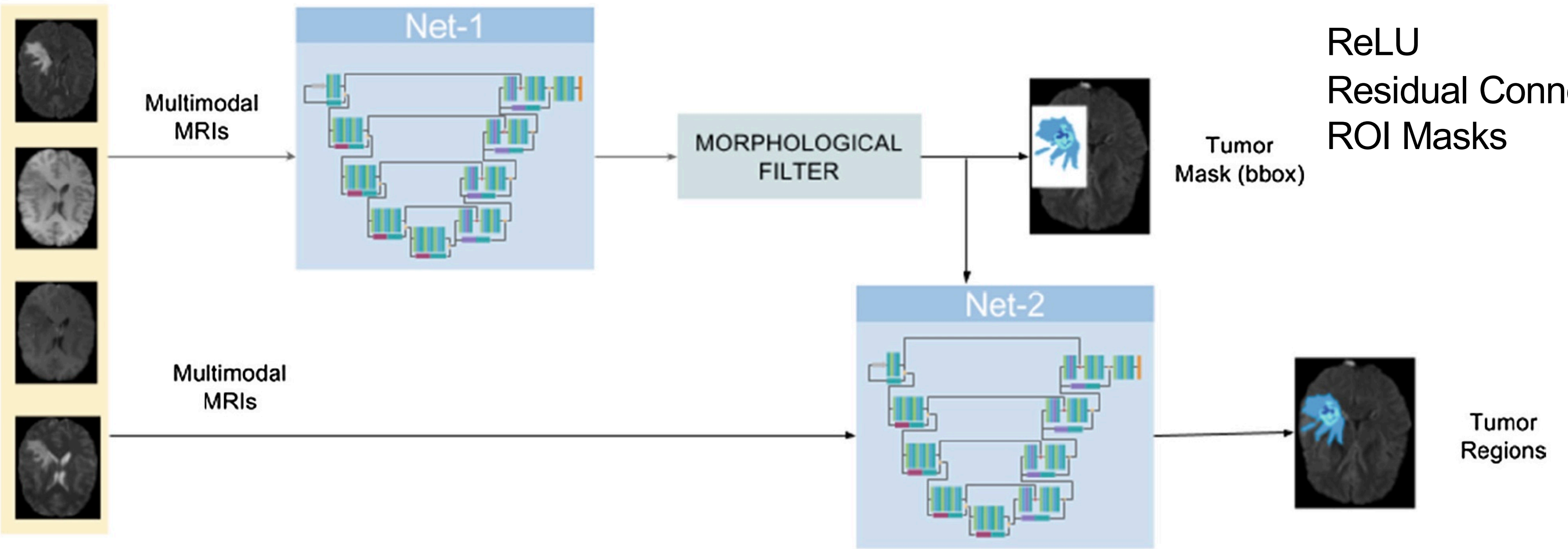
Y: Ground Truth. X: Predicted Segmentation

Segmentation 2: brain tumor segmentation

UPC Paper:

Casamitjana et al, Cascaded V-Net Using ROI Masks for BrainTumor Segmentation, 2018

Whole Image (dense training)
Smaller filter size 3x3x3
ReLU
Residual Connections
ROI Masks



Segmentation 2: brain tumor segmentation

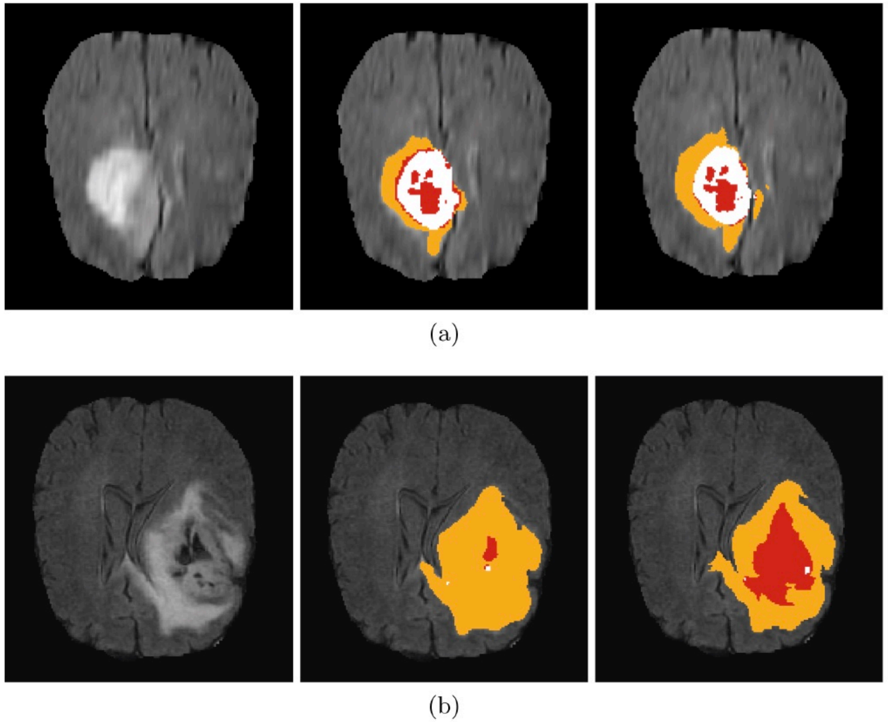


Fig. 5. Segmentation results of two subjects: (a) TCIA 479 (b) TCIA 109. From left to right we show the FLAIR sequence, followed by Prediction and GT tumor segmentation. We distinguish intra-tumoral regions by color-code: enhancing tumor (white), peritumoral edema (orange) and necrotic and non-enhancing tumor (red). (Color figure online)

Table 1. Results for BraTS 2017 data. Dice and Hausdorff metrics are reported.

	Dice			Hausdorff		
	ET	WT	TC	ET	WT	TC
Development set	0.671	0.869	0.685	7.145	6.410	9.584
Validation set	0.714	0.877	0.637	5.434	8.343	11.173

Table 2. Results for BraTS 2017 data. Sensitivity and specificity are reported.

	Sensitivity			Specificity		
	ET	WT	TC	ET	WT	TC
Development set	0.735	0.851	0.664	0.998	0.994	0.997
Validation set	0.723	0.879	0.619	0.998	0.994	0.998

Classification (Exam)1: Skin Classification

UPC Paper: Combalia M. Vilaplana V.,
Monte-Carlo Sampling applied to Multiple Instance Learning for whole Slide Image Classification, 2018

Task: Classify between Sun Exposed and Not Sun Exposed Pieces of Skin

Whole Slide Tissue Image: High Resolution Image, high computational cost to evaluate, to reduce it MIL is used.

Multiple Instance Learning (MIL)**:** An input set of N bags, where each bag contains M instances

Bag: Images / Instances: Patches

Sampling of Patches: Grid- Sampling

Uniform Sampling

Monte-Carlo Sampling

Architecture:

- Shallow ResNet (8 Layers)
- Patch Size (50x50)

Classification (Exam)1: Skin Classification

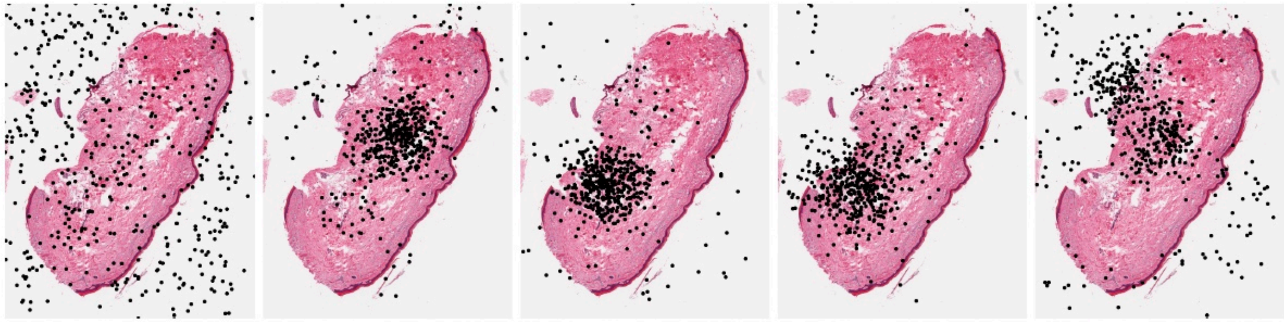


Figure 1: Black points corresponds to the centroids' positions at epochs 2, 6, 8, 37 and 72 in the training process of the neural network.

Table 1: Training and validation accuracies for the various sampling strategies

Sampling technique	Train acc	Validation acc
Grid sampling	**0.967**	0.826
Uniform sampling	0.929	0.920
Monte-Carlo sampling	0.946	**0.942**

Super-Resolution 1: Brain MRI super-resolution

UPC Paper: Sánchez I. Vilaplana V., [Brain MRI super-resolution using 3D generative adversarial networks](), 2018

Task: Generate Brain MRI High Resolution Images from low Resolution Images

Generative Adversarial Network: SRGAN Model (1) extended to 3D

Discriminator: least squares adversarial loss

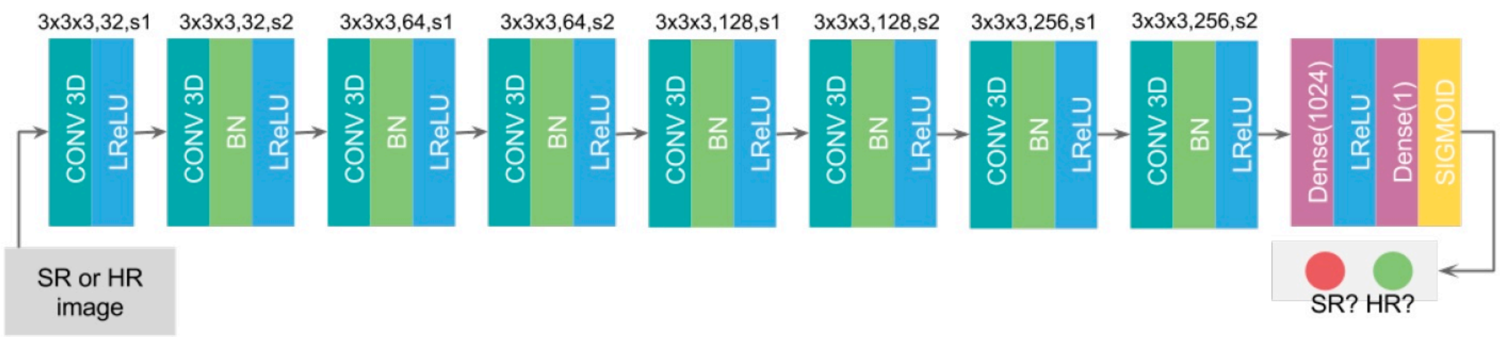


Figure 1: Architecture of the Discriminator network. For each convolutional layer: kernel size (3x3x3), number of filters, stride (s).

Super-Resolution 1: Brain MRI super-resolution

Generator: least squares adversarial loss and a content term

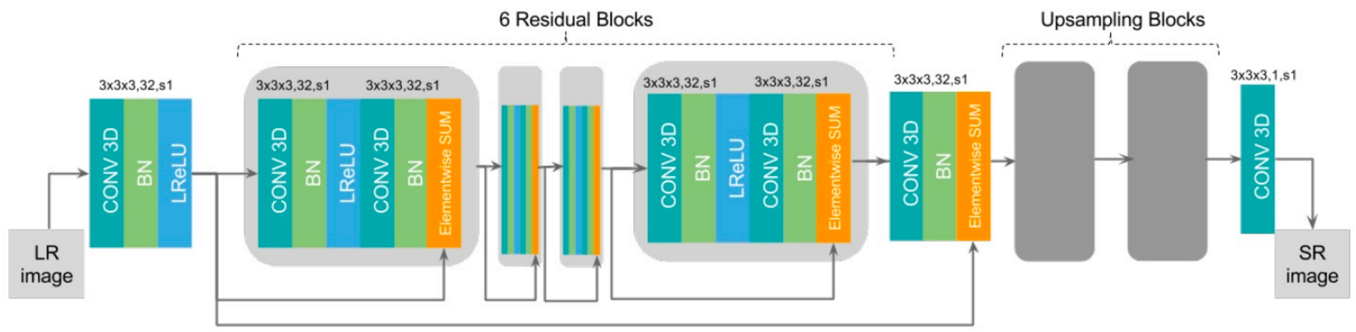


Figure 2: Architecture of the Generator network. For each convolutional layer: kernel size (3x3x3), number of filters, stride (s).

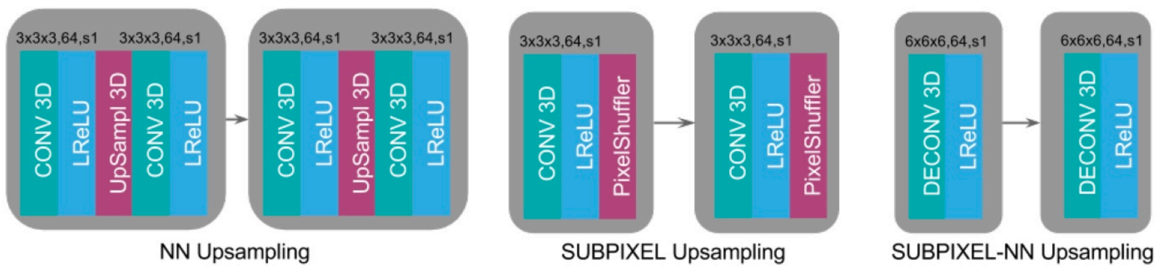


Figure 3: Architecture of the different upsampling methods.

Super-Resolution 1: Brain MRI super-resolution

Results

	Upsample x2							
	Cubic Int.		Resize Conv.		Subpixel		Subpixel-NN	
	PSNR	SSIM	PSNR	SSIM	PSNR	SSIM	PSNR	SSIM
Mean	38.06	0.9848	39.11	**0.9913**	39.09	0.9898	**39.28**	0.9849
Std	1.2085	0.0020	1.0608	0.0014	1.0203	0.0016	1.0724	0.0028
Min	34.65	0.9792	35.93	0.9868	36.61	0.9855	36.65	0.9781
Max	41.45	0.9897	41.88	0.9940	42.39	0.9933	42.54	0.9907
	Upsample x4							
	Cubic Int.		Resize Conv.		Subpixel		Subpixel-NN	
	PSNR	SSIM	PSNR	SSIM	PSNR	SSIM	PSNR	SSIM
Mean	31.76	0.9412	33.33	**0.9688**	32.86	0.9638	**33.58**	0.9582
Std	0.9948	0.0078	1.1813	0.0070	1.2241	0.0085	1.1456	0.0097
Min	29.78	0.9312	30.54	0.9531	29.96	0.9462	31.01	0.9388
Max	33.74	0.9534	36.86	0.9816	36.51	0.9787	37.23	0.9770

Table 1: Numerical Results

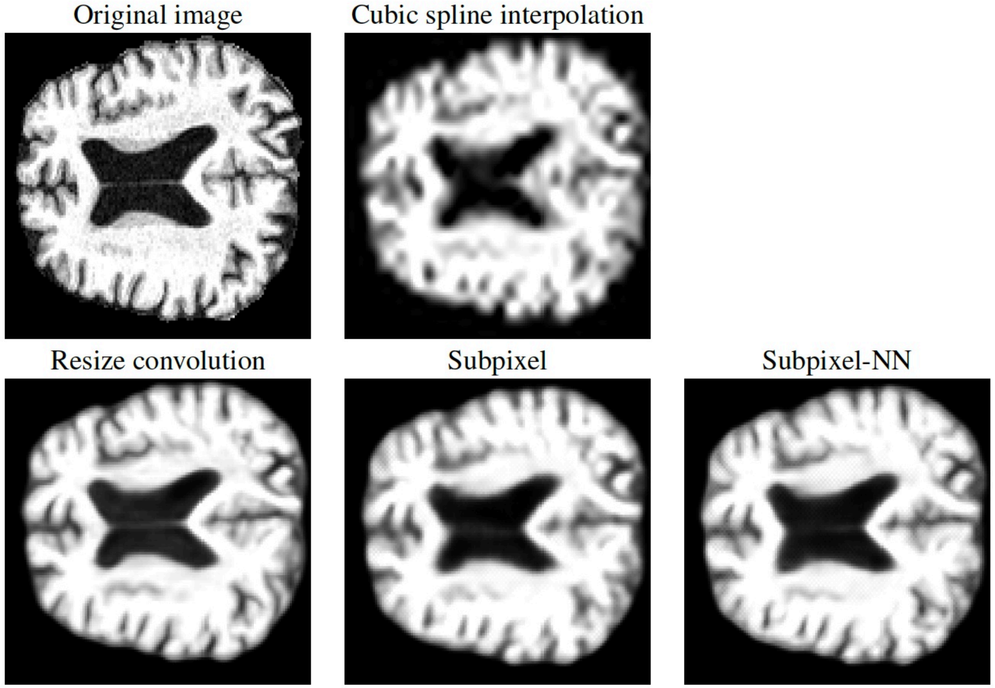


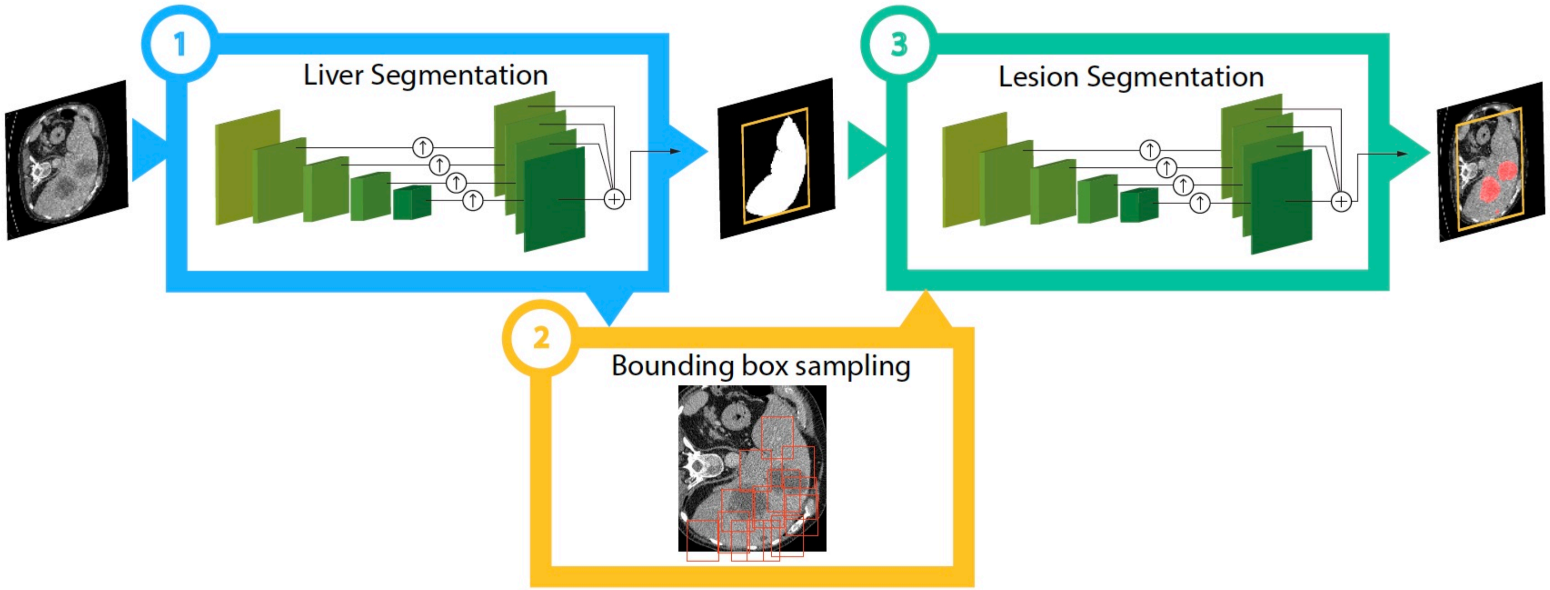
Figure 4: Illustration of SR results using a downsampling factor of 4. The first row shows the original high resolution image and the result of cubic spline interpolation. The next row presents the results of applying our GAN with the three proposed upsampling methods: resize convolution, sub-pixel and subpixel-NN.

Segmentation 2: Liver Lesion Segmentation

UPC Paper: Bellver M. et al. Detection-aided liver lesion segmentation using deep learning, 2017

Task: Segmentation of Lesions of Liver in CT Images

Architecture: Cascade networks (based on DRIU, 1) for Liver and Lesion Segmentation



(1) Maninis, K. K., et al. (2016, October). Deep retinal image understanding. In International Conference on Medical Image Computing and Computer-Assisted Intervention (pp. 140-148). Springer International Publishing

Segmentation 2: Liver Lesion Segmentation

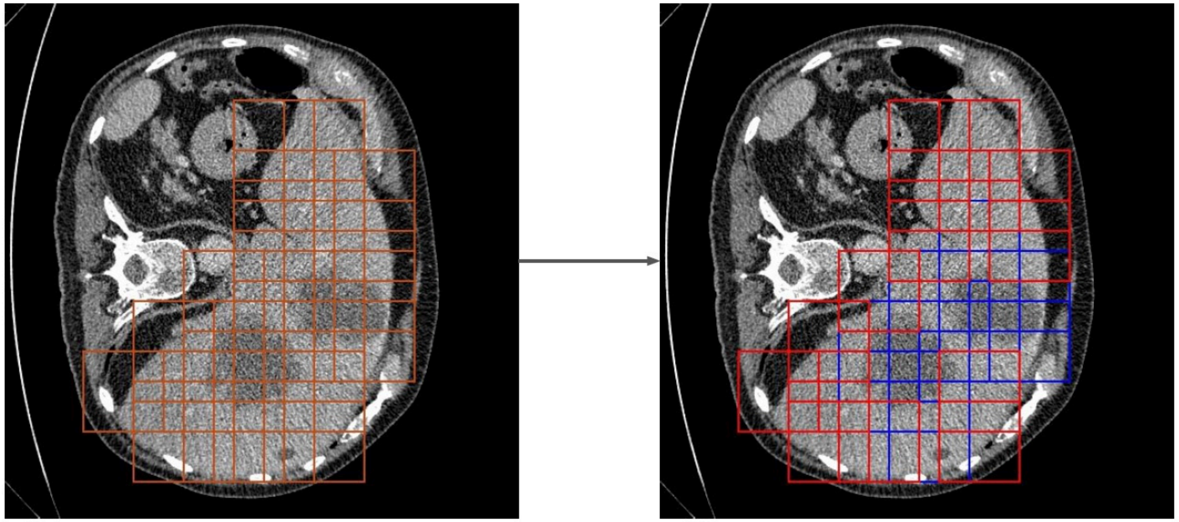
Detection Network

Used to keep context around lesion tissues

Pre Trained Resnet 50 for Image Net without classification layer

Single Neuron determining if it's a healthy tissue or not

Reduces false positives



Segmentation 2: Liver Lesion Segmentation

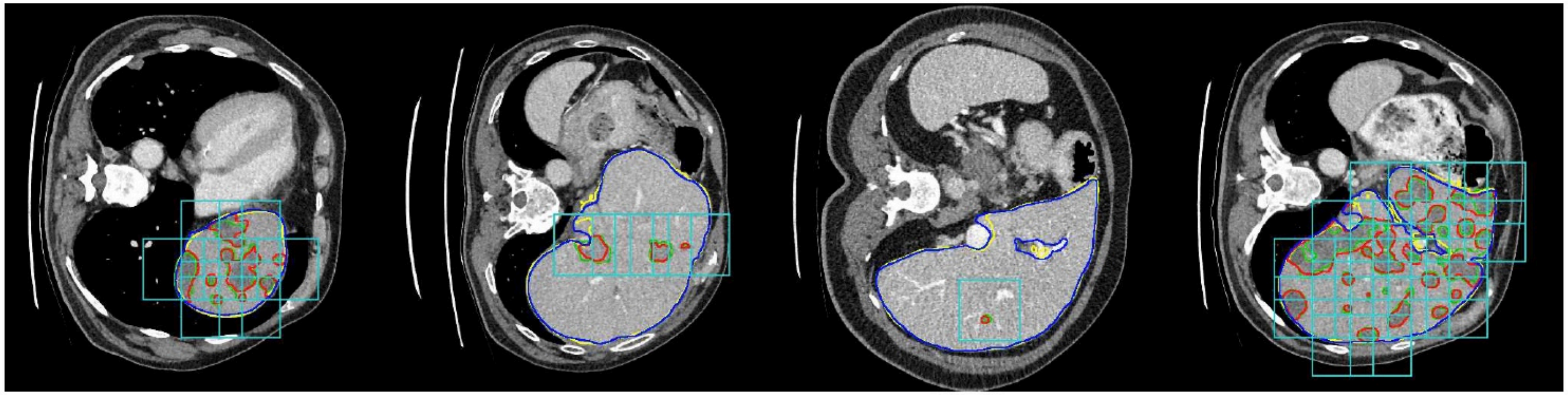
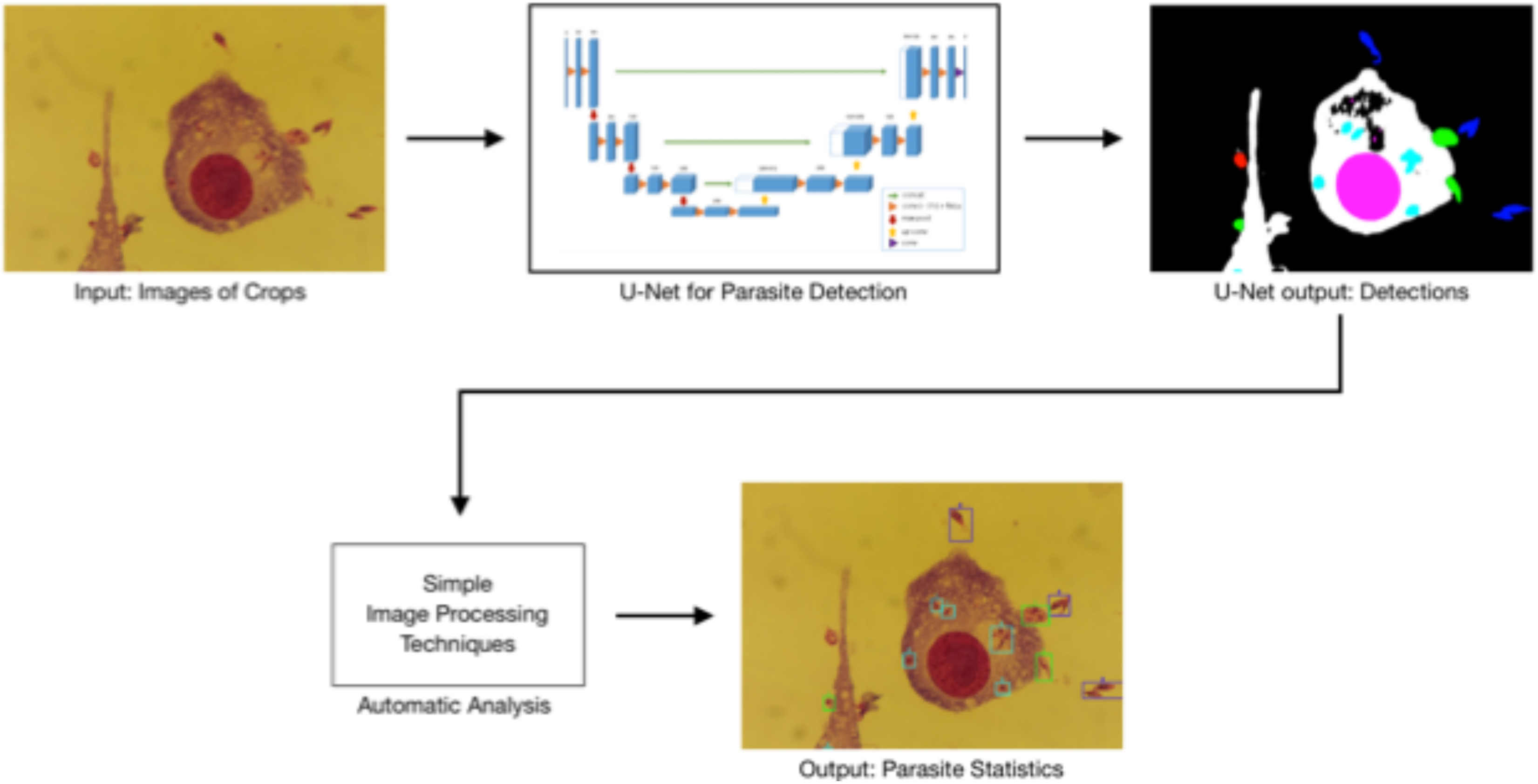


Figure 2: Results of the lesion detection network. Blue and red lines indicate the liver and lesion ground truth, respectively. Yellow and green lines are the segmentation results for liver and lesion. The light blue bounding boxes are the windows detected as having a lesion. All positive pixels at the output of the segmentation network will be removed if they disagree with the results of lesion detection.

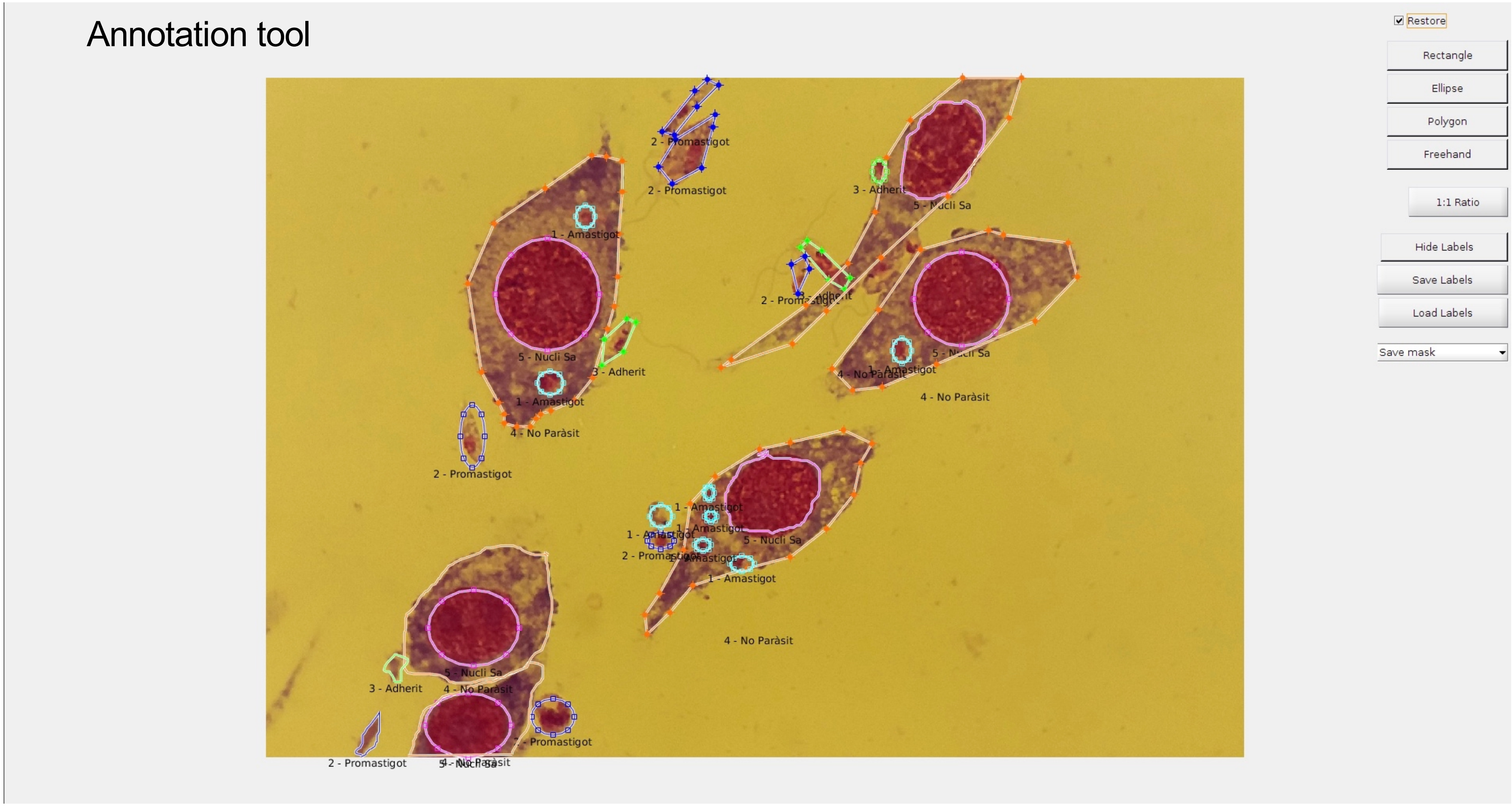
	Dice
Segmentation-only baseline	0.41
Segmentation-only 3-i/o + BP in liver	0.54
Segmentation-only 3-i/o + BP in liver + Detector	0.57
Segmentation-only 3-i/o + BP in liver + Detector + 3D-CRF	0.59

Segmentation 3: Leishmaniasis Parasite Segmentation

UPC Paper: Górriz M. et al., Leishmaniasis Parasite Segmentation and Classification using Deep Learning, AMDO 2018



Segmentation 3: Parasite Segmentation



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Segmentation 3: Parasite Segmentation

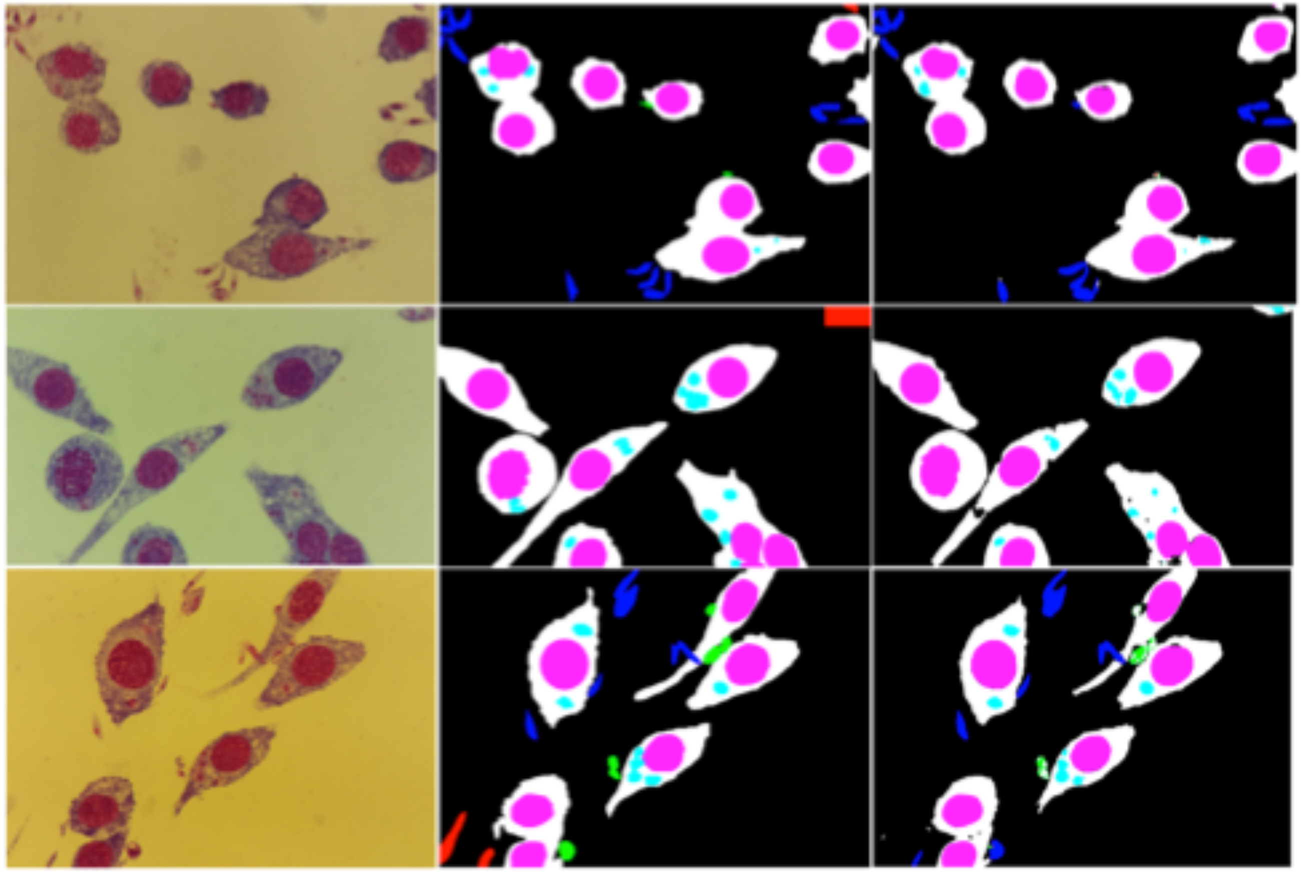


Table 2. Evaluation of pixel-wise classification in terms of Dice score, precision, recall and F1-score and the percentage of pixels per class.

Class	Dice score	Precision	Recall	F1-score	Pixels
Background	0.981	98.31 %	97.79 %	98.05 %	97.07 %
Cytoplasm	0.896	88.17 %	91.25 %	89.62 %	1.96 %
Nucleus	0.950	93.82 %	96.38 %	95.01 %	0.79 %
Promastigote	0.495	51.21 %	47.63 %	49.13 %	0.07 %
Adhered	0.707	67.74 %	37.92 %	45.68 %	0.05 %
Amastigote	0.777	75.67 %	82.29 %	77.71 %	0.06 %

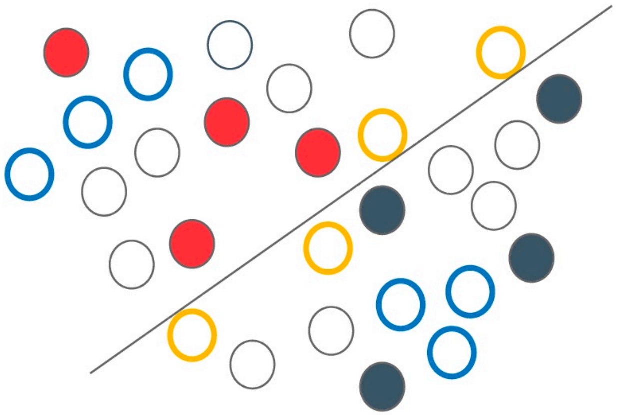
Segmentation 3: Active Learning & Segmentation

UPC Paper: Górriz M. et al. Active Deep Learning for Medical Imaging Segmentation, NIPS 2017

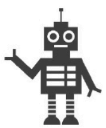
Task: Use Active Learning when not enough labeled data is available or is explensive

Active Learning: auto-selection of useful instances to be labeled in order to achieve similar performance with few data

Cost Effective Methodology: Automatically Select and Pseu-Annotate good Unlabeled samples using the output of the network



Uncertain. Samples near border between classes. More **dubitative** for the classifier. **Labeled by human**.



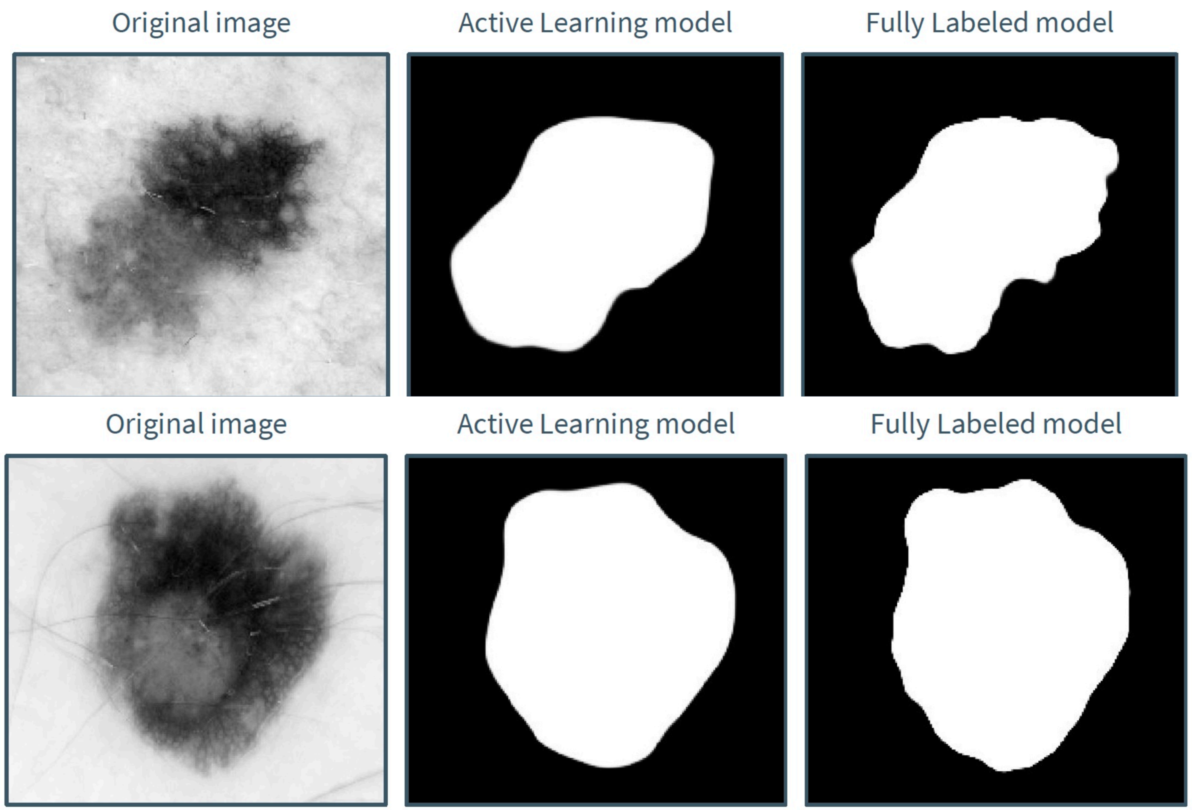
Certain. Samples far from the border between classes. **Easier** for the classifier. **Labeled by itself (Pseudo Labeling)**.

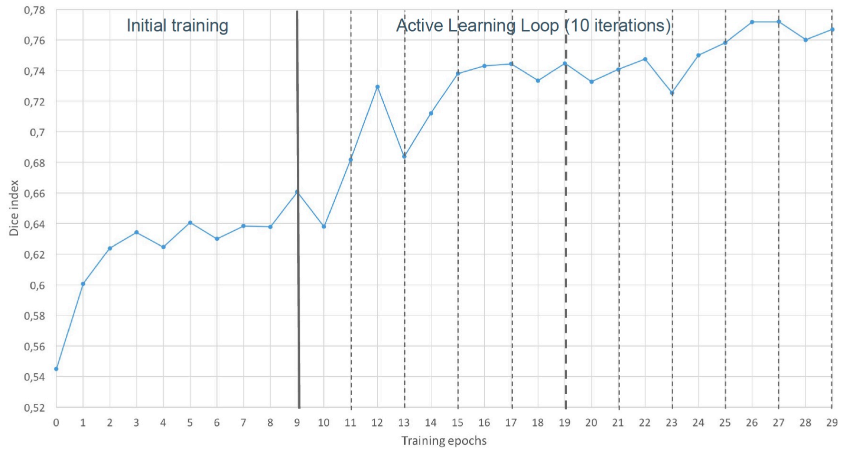
Keze Wang, Dongyu Zhang, Ya Li, Ruimao Zhang, and Liang Lin. Cost-effective active learning for deep image classification. CoRR, abs/1701.03551, 2017.

Segmentation 3: Active Learning & Segmentation

Architecture: U-NET

Qualitative evaluation

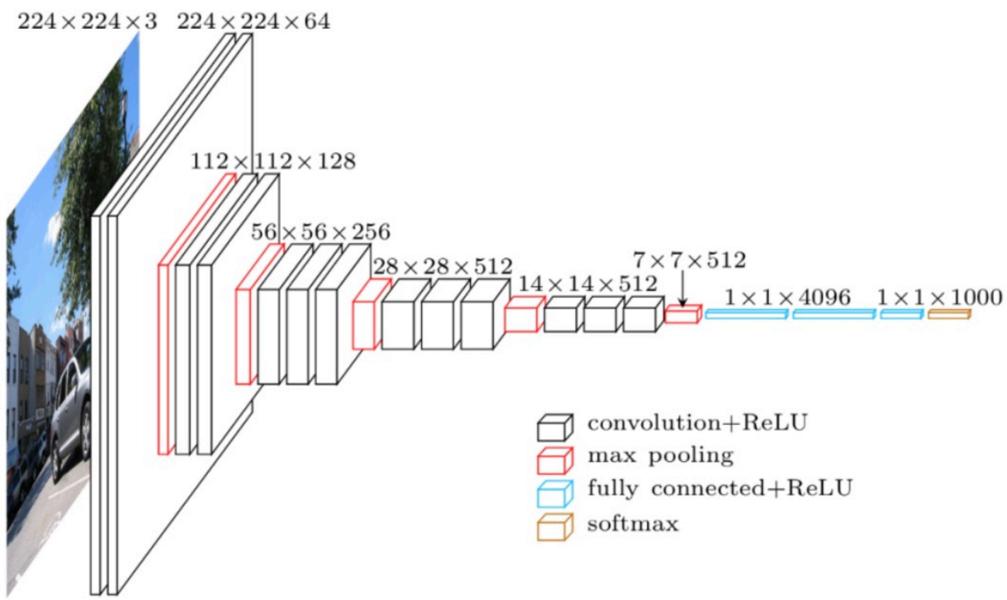




Classification (Exam) 2: Impact of Segmentation in Exam

UPC Paper: Burdick J. et al. [The Impact of Segmentation on the Accuracy and Sensitivity of a Melanoma Classifier Based on Skin Lesion Images](), SIIM 2017

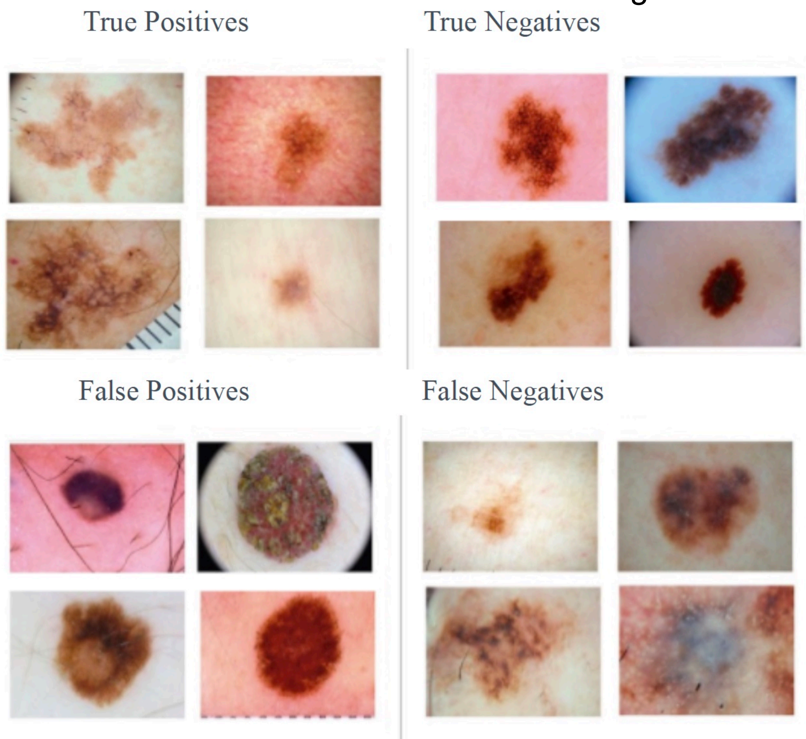
- Pretrained VGG16
  (Simonyan & Zisserman, 2014)
- Transfer Learning



Original VGG. This method uses a single sigmoid for classification

Classification (2) : Impact of Segmentation in Classification

Perfect Segmentation PS+25 Unsegmented



	Sensitivity	Accuracy	AUC
Perfect Segmentation	45.3%	58.7%	62.2%
+25	53.3%	61.3%	64.2%
+50	56.0%	60.7%	62.6%
+75	57.3%	59.3%	60.8%
+100	34.7%	55.3%	57.9%
Unsegmented	24.0%	51.3%	53.2%

Resources

- **Datasets**
  - The cancer imaging archive
  - Alzheimer's Disease Neuroimaging Initiative (ADNI)
  - Open-access Medical Image repositories
- **Challenges**
  - Grand challenges in Biomedical Image Analysis
  - Medical Image Computing and Computer Assisted Interventions (MICCAI)
  - Int. Symposyum on Medical Imaging (ISBI)
- **Survey papers: DL in Medical imaging**
  - Ravi et al, Deep Learning for Health Informatics, JBHI, 2017
  - Litjens et al, A Survey on Deep Learning in Medical Image Analysis, 2017
  - Zhou et al Ed., Deep learning for Medical Image Analysis, Elsevier, 2017

Thank You!!

Questions?