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BRAIN DATA SCIENCE

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Deep Learning for NeuroImaging

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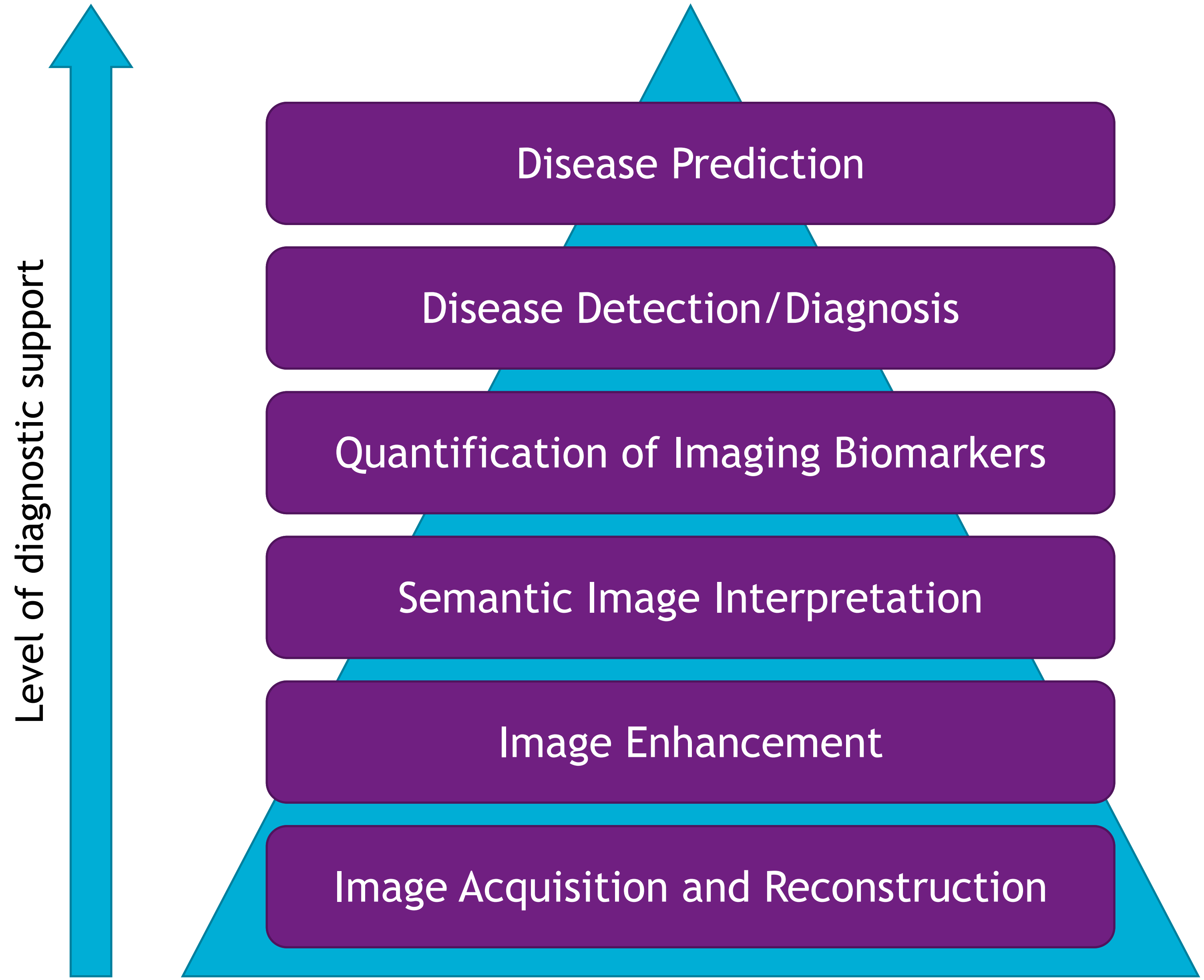
Inserm

SORBONNE UNIVERSITÉ

informatics mathematics

PR[AI]RIE
PaRis Artificial Intelligence Research InstitutE

Computer-aided neuro(radio)logy



Level	Application
Disease Prediction	Personalised prediction/prevention
Disease Detection/Diagnosis	Screening
Quantification of Imaging Biomarkers	Tumour quantification / Radiomics
Semantic Image Interpretation	Organ localisation / segmentation
Image Enhancement	Super-resolution
Image Acquisition and Reconstruction	Accelerated imaging

Source: Daniel Rueckert, Keynote talk @ PRIME 2019

Computer-aided neuro(radio)logy

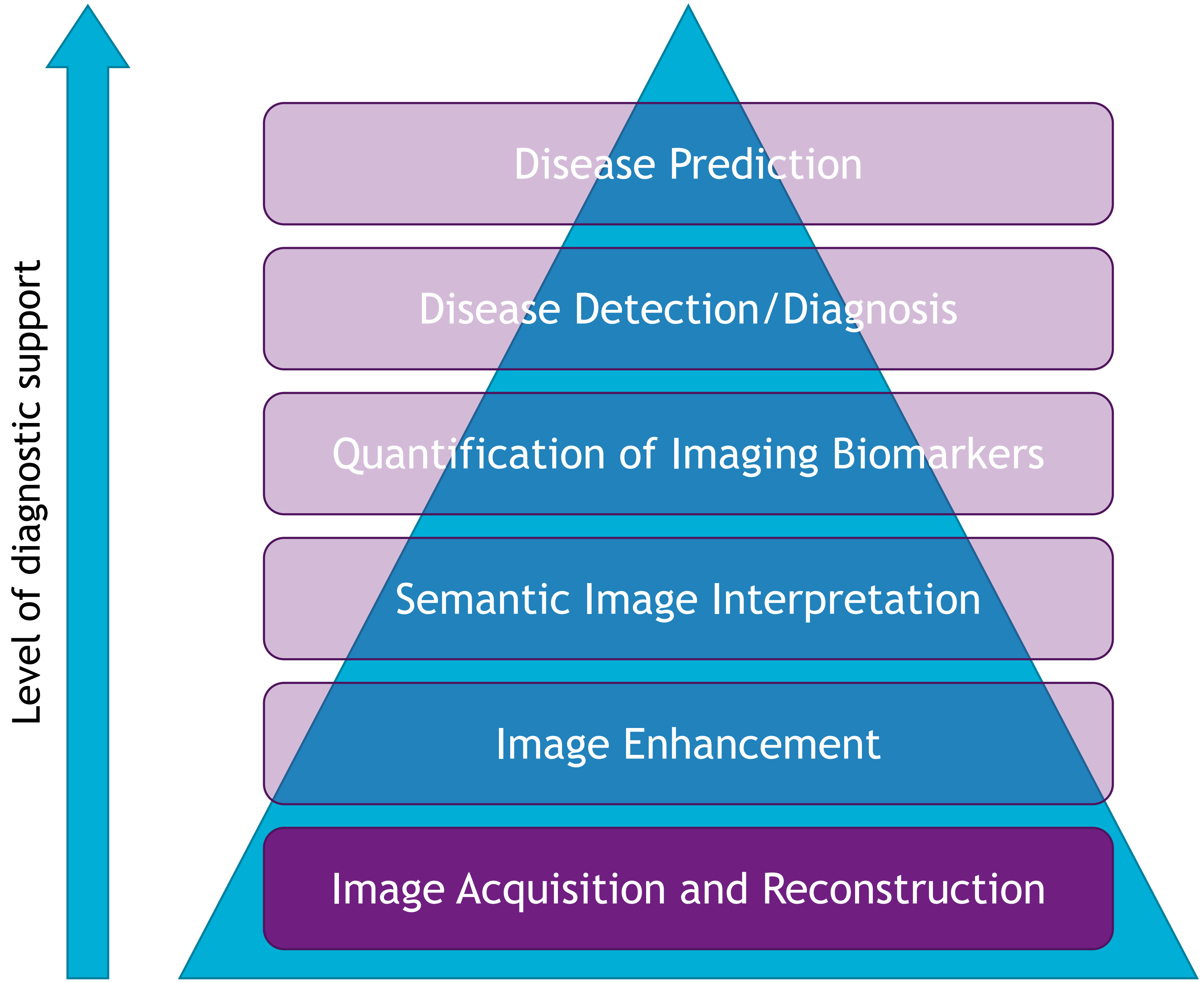
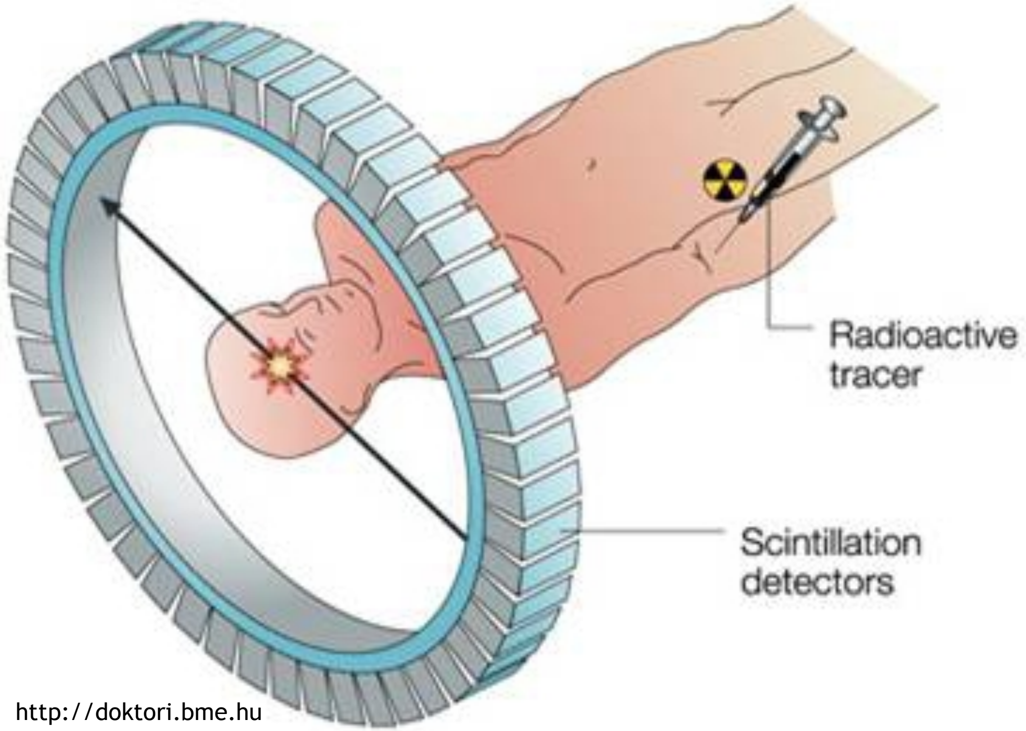
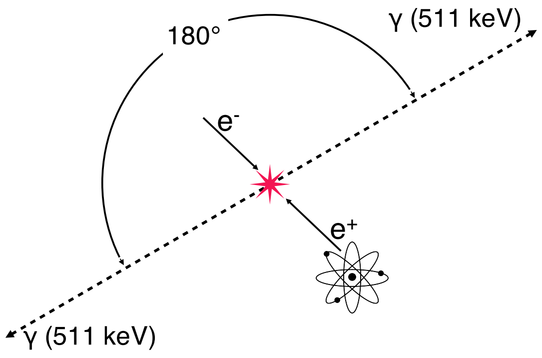


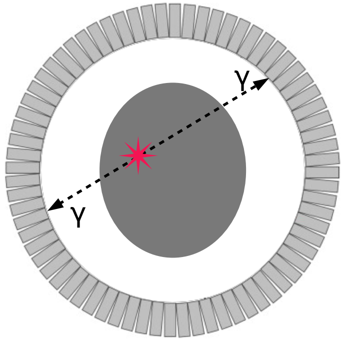
Image reconstruction

Positron emission tomography (PET)

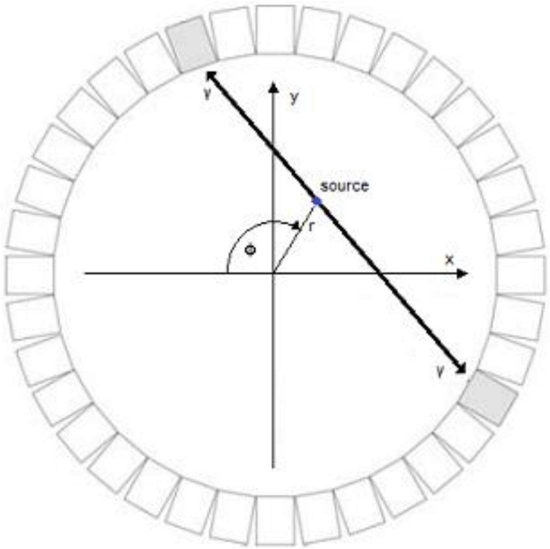


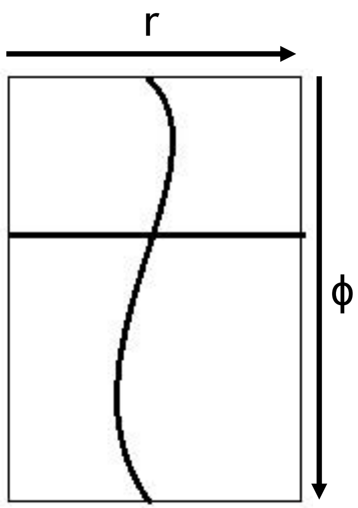
http://doktori.bme.hu





PET data detection





Sinogram

Słomski et al., BAMS, 2014

Image reconstruction

PET image reconstruction

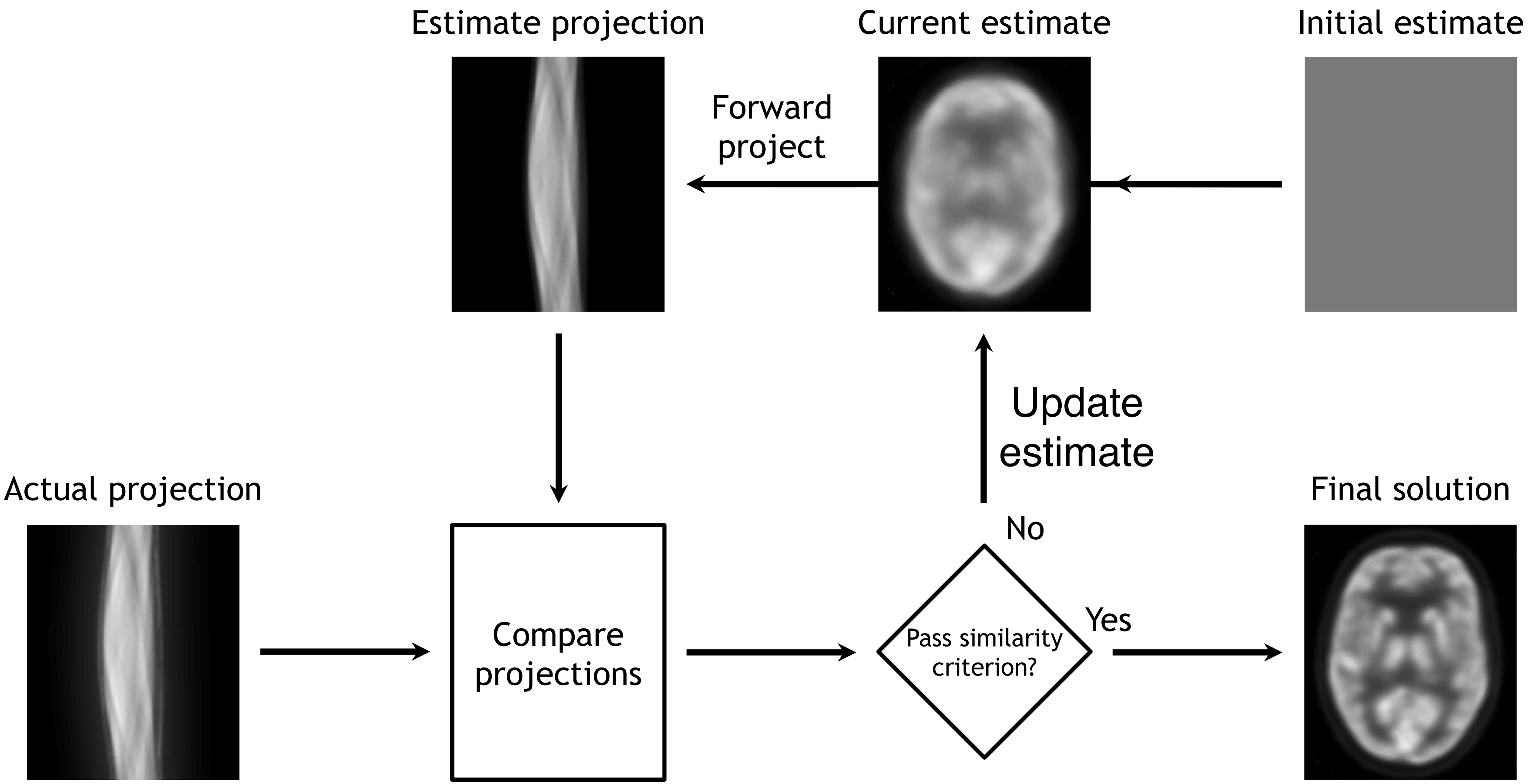
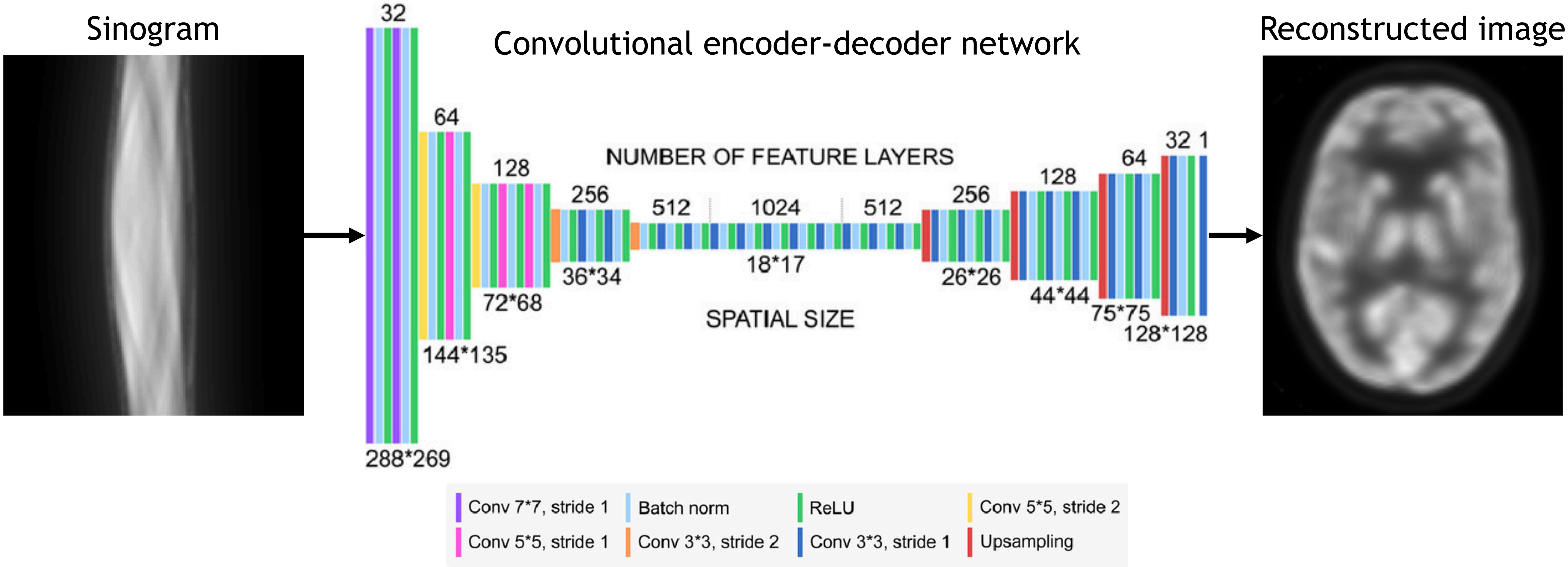


Image reconstruction

DeepPET: A deep encoder-decoder network for directly solving the PET image reconstruction inverse problem



Häggström et al., Medical Image Analysis, 2019

Batch normalisation

- **To improve the speed, performance, and stability of networks**
- **Batch normalisation layer:**

Input: Values of x over a mini-batch: $\mathcal{B} = \{x_{1\ldots m}\}$;
Parameters to be learned: γ, β

Output: $\{y_i = \mathrm{BN}_{\gamma,\beta}(x_i)\}$

$$\mu_{\mathcal{B}} \leftarrow \frac{1}{m}\sum_{i=1}^{m} x_i \qquad \text{// mini-batch mean}$$

$$\sigma_{\mathcal{B}}^2 \leftarrow \frac{1}{m}\sum_{i=1}^{m}(x_i - \mu_{\mathcal{B}})^2 \qquad \text{// mini-batch variance}$$

$$\widehat{x}_i \leftarrow \frac{x_i - \mu_{\mathcal{B}}}{\sqrt{\sigma_{\mathcal{B}}^2 + \epsilon}} \qquad \text{// normalize}$$

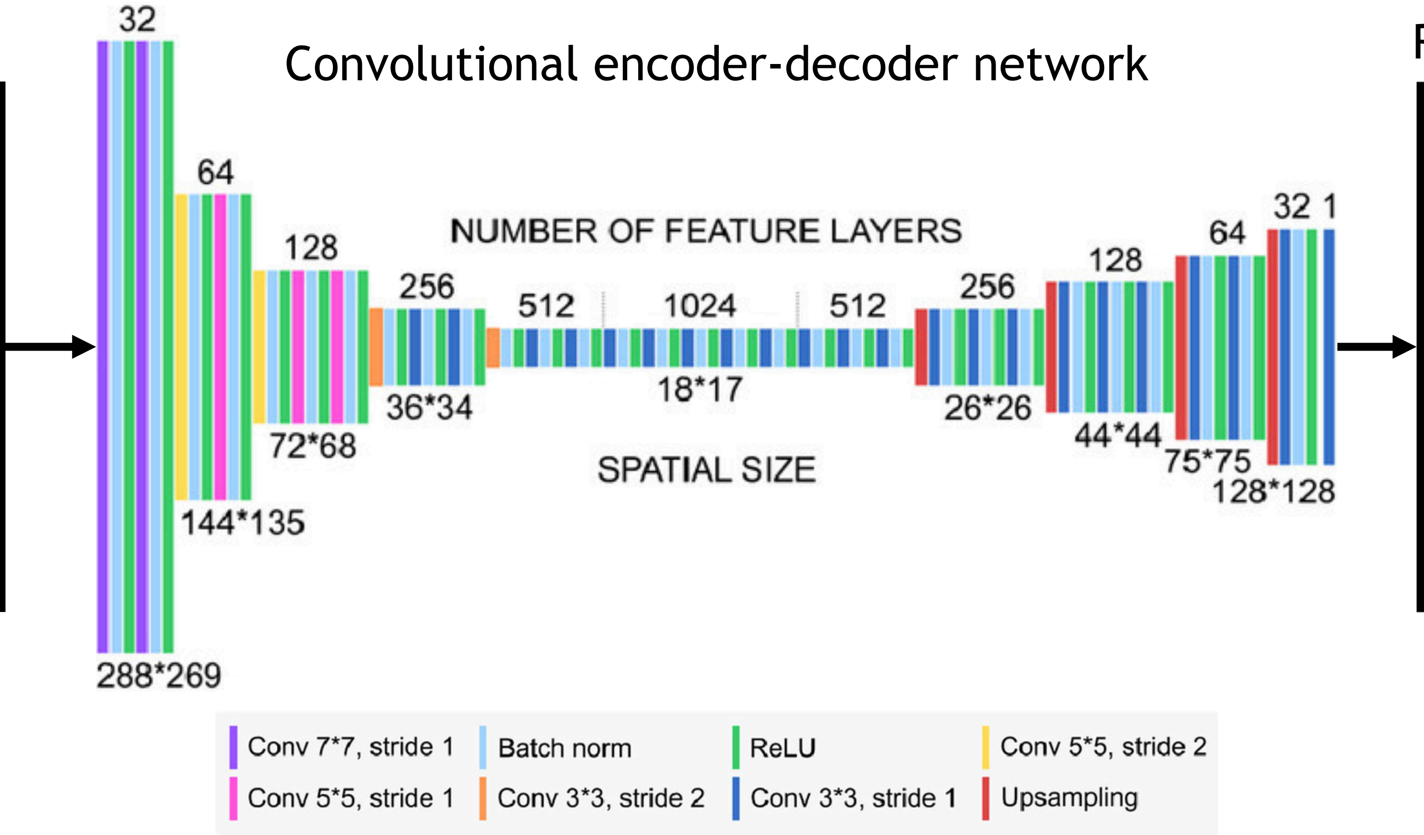
$$y_i \leftarrow \gamma\widehat{x}_i + \beta \equiv \mathrm{BN}_{\gamma,\beta}(x_i) \qquad \text{// scale and shift}$$

Ioffe and Szegedy, Batch Normalization: Accelerating Deep Network Training by Reducing Internal Covariate Shift, 2015

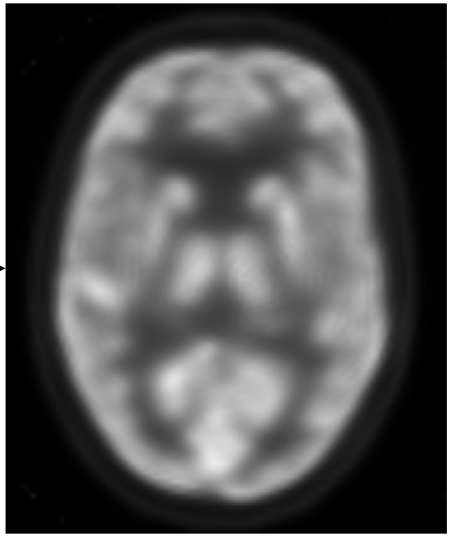
DeepPET: A deep encoder-decoder network for directly solving the PET image reconstruction inverse problem

Sinogram

Convolutional encoder-decoder network

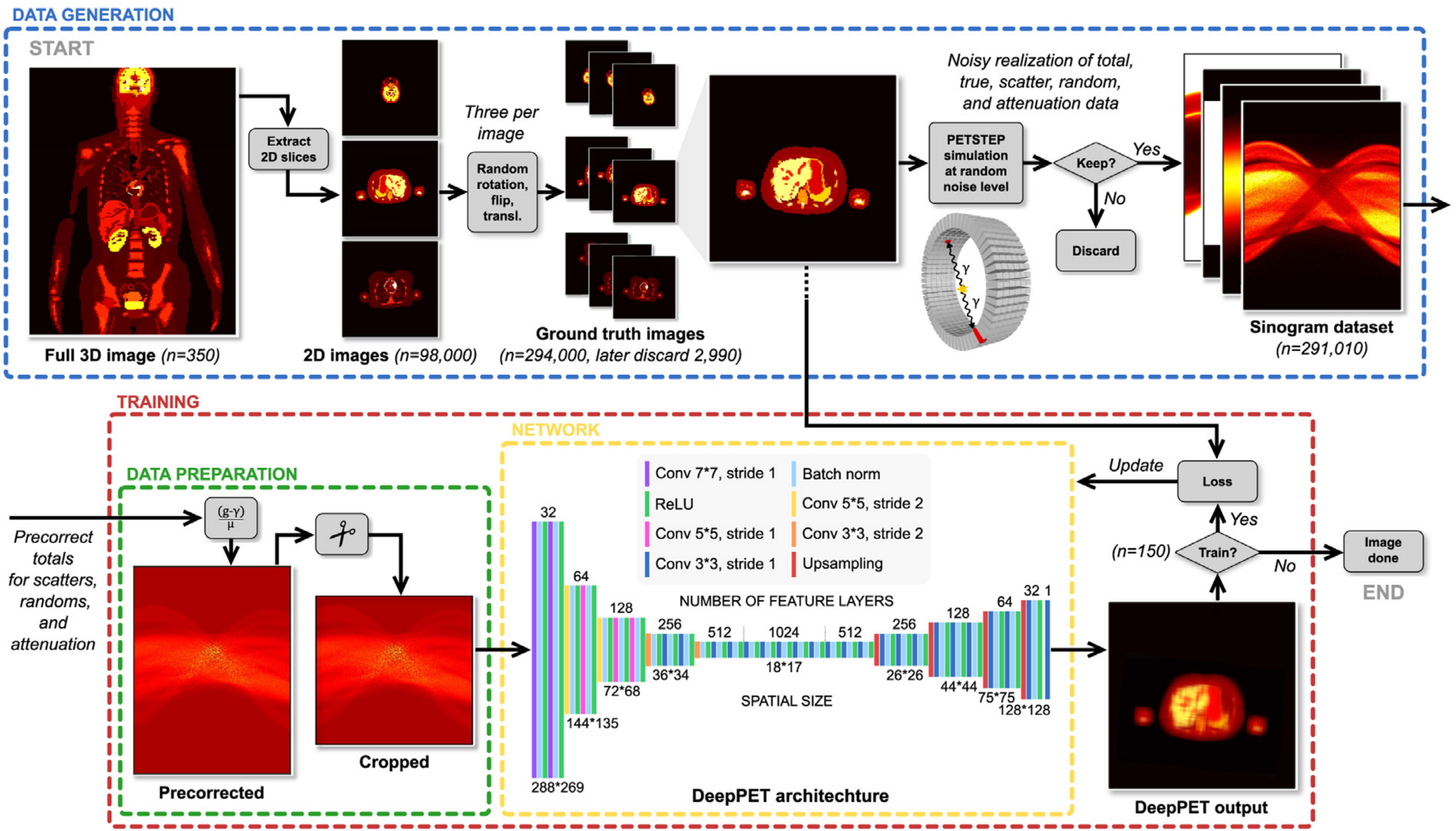


Reconstructed image



Häggström et al., Medical Image Analysis, 2019

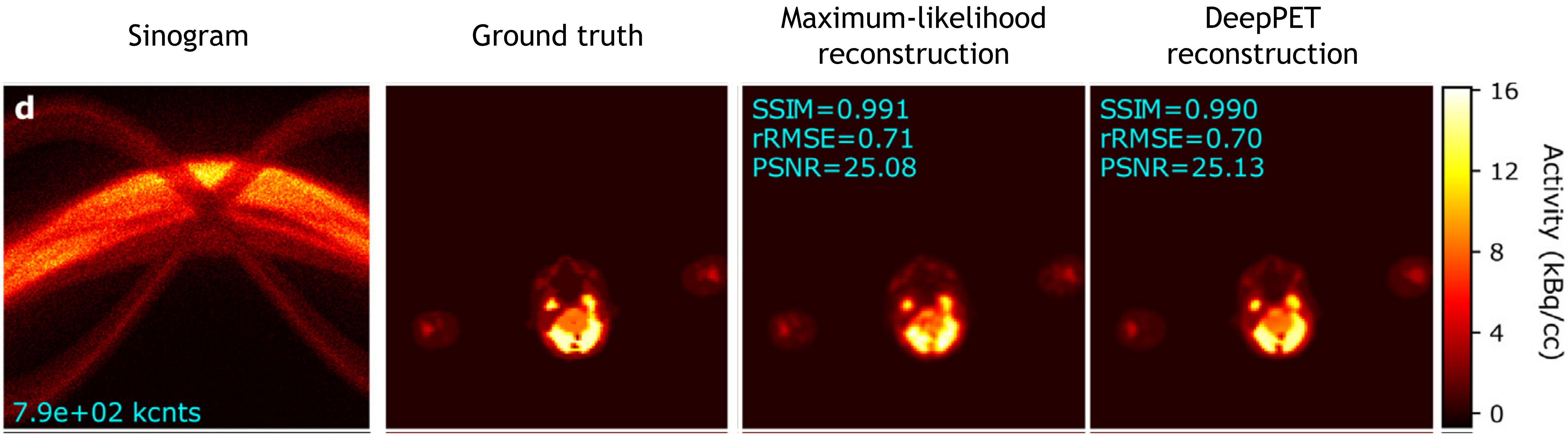
Image reconstruction



Häggström et al., Medical Image Analysis, 2019

DeepPET: A deep encoder-decoder network for directly solving the PET image reconstruction inverse problem

- Results on simulated data



Häggström et al., Medical Image Analysis, 2019

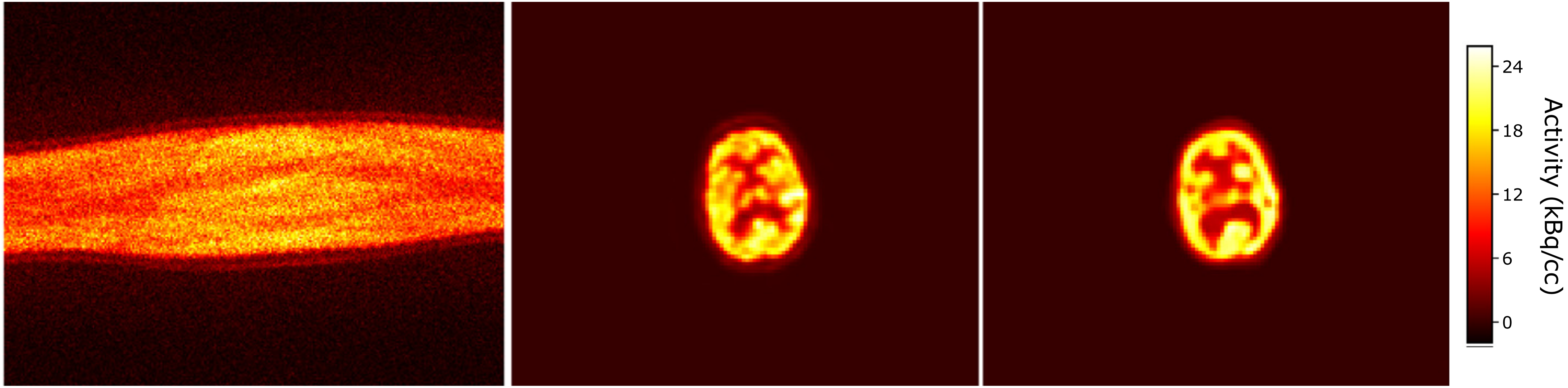
DeepPET: A deep encoder-decoder network for directly solving the PET image reconstruction inverse problem

- **Results on real data**

Sinogram

Maximum-likelihood reconstruction

DeepPET reconstruction



Häggström et al., Medical Image Analysis, 2019

Computer-aided neuro(radio)logy

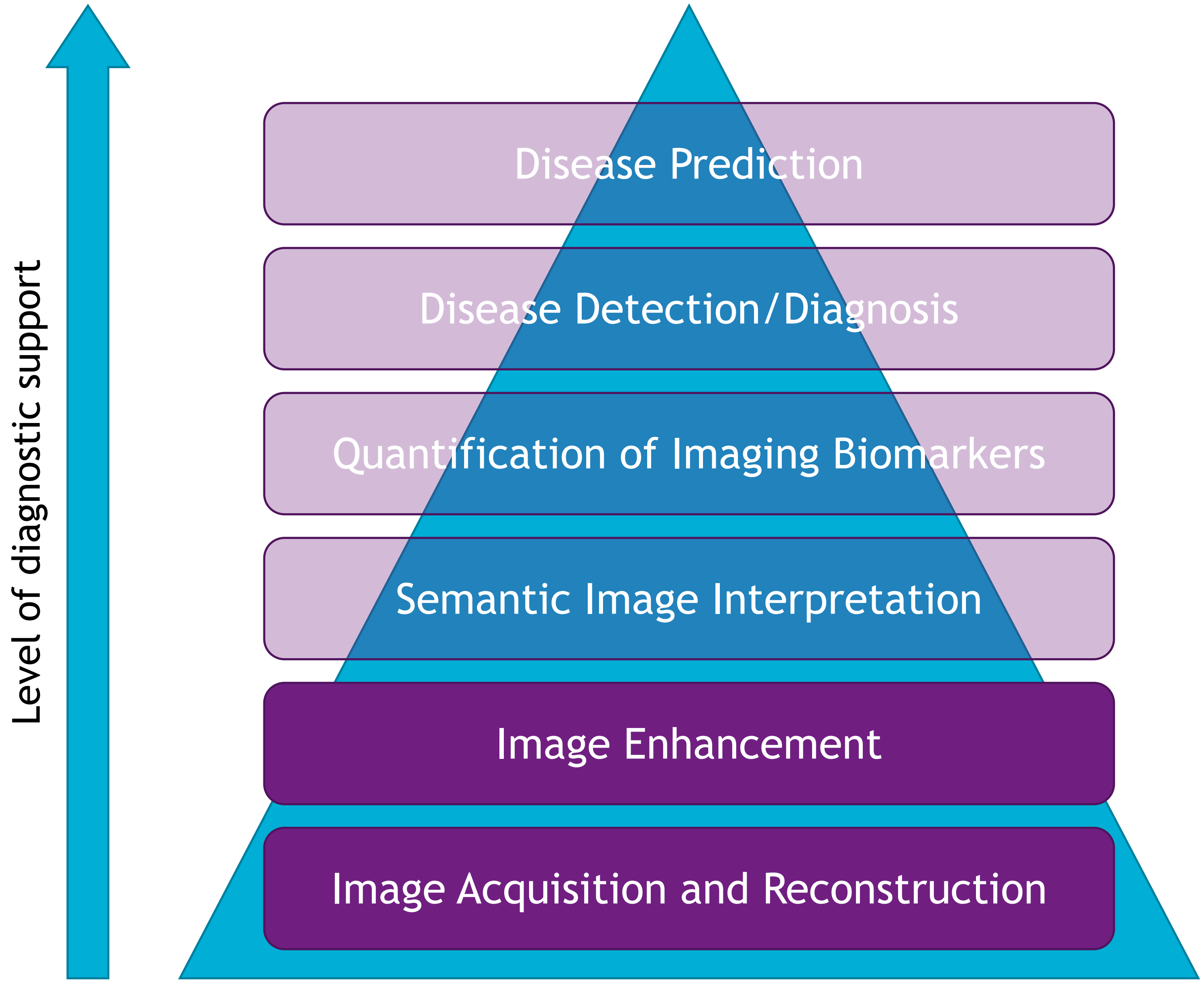
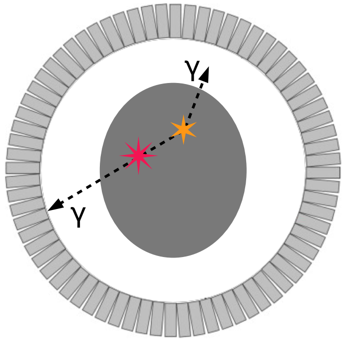
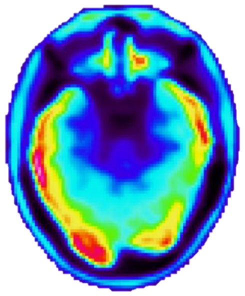


Image synthesis

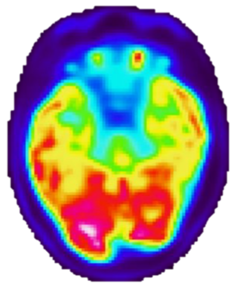
Attenuation correction for PET/MR scanners



Attenuation



PET without
attenuation correction



PET with
attenuation correction

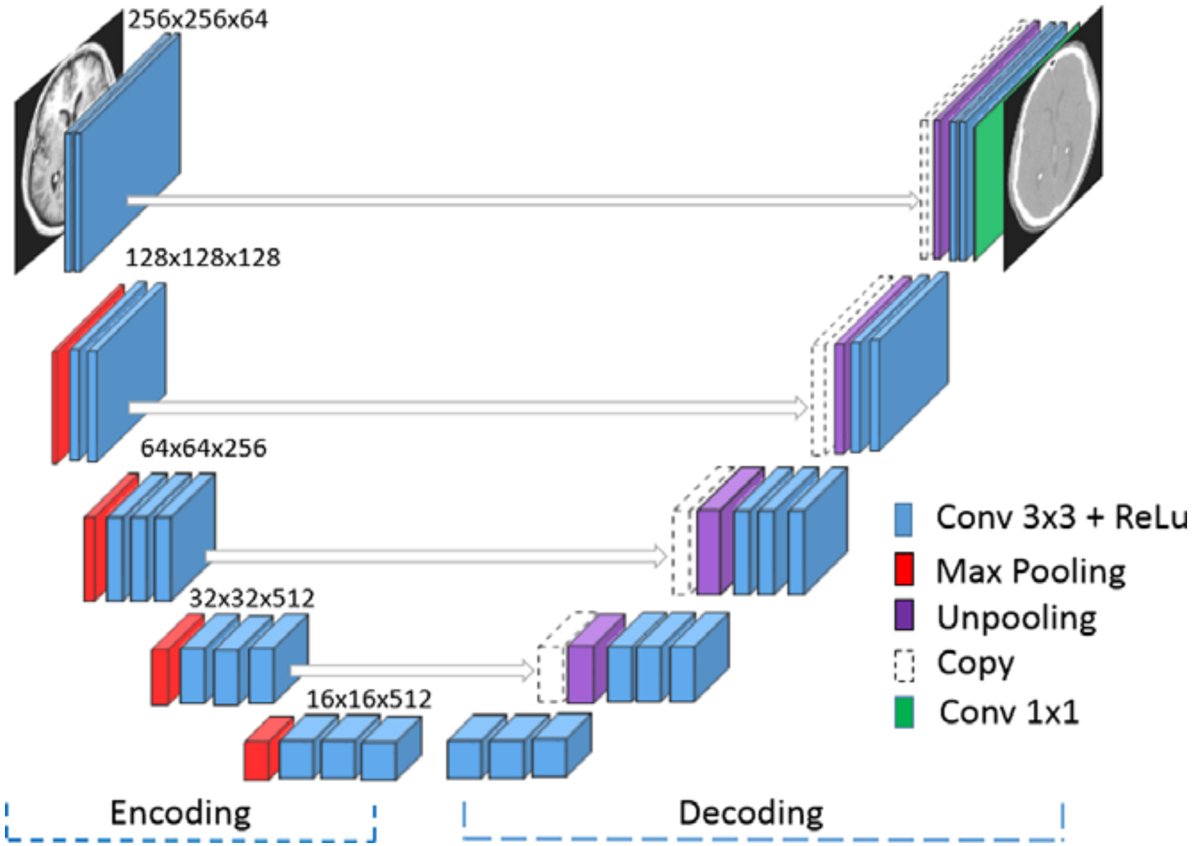
Solution

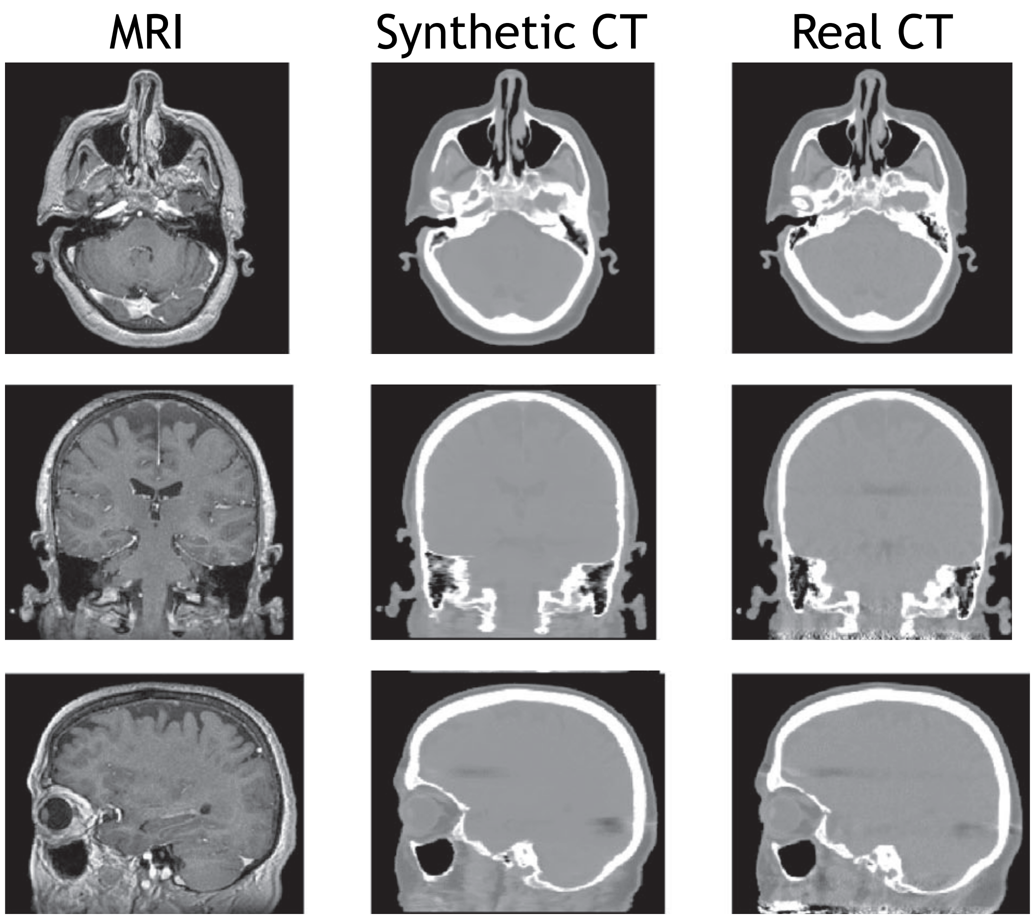
- ▷ Synthesise CT from MR images

MRI

CT

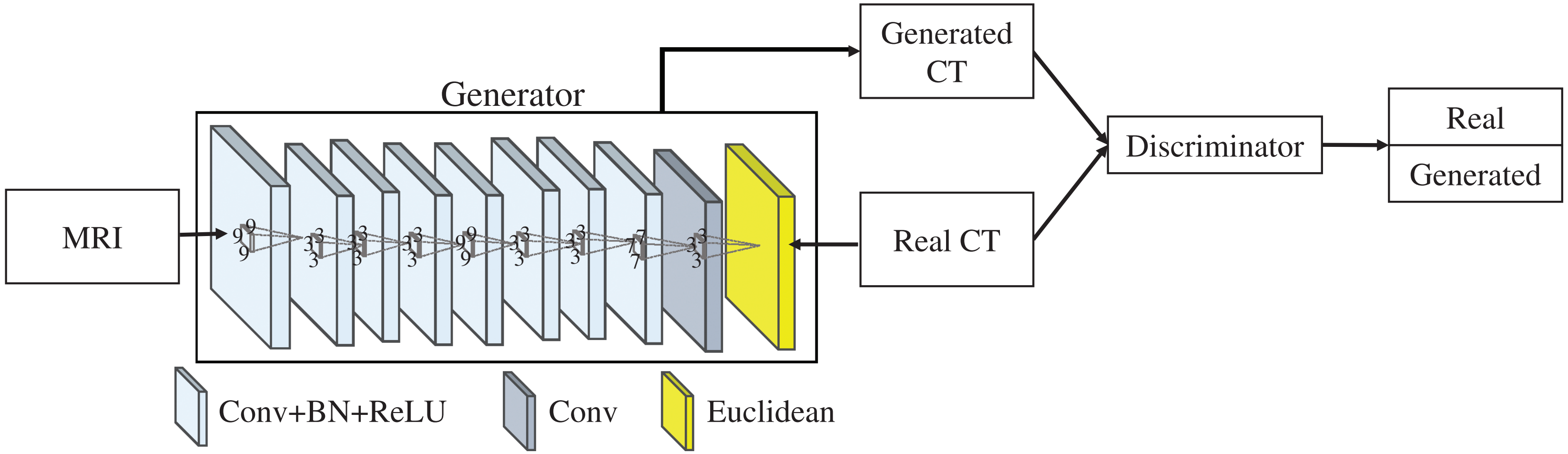
MR-based synthetic CT generation using a deep CNN method

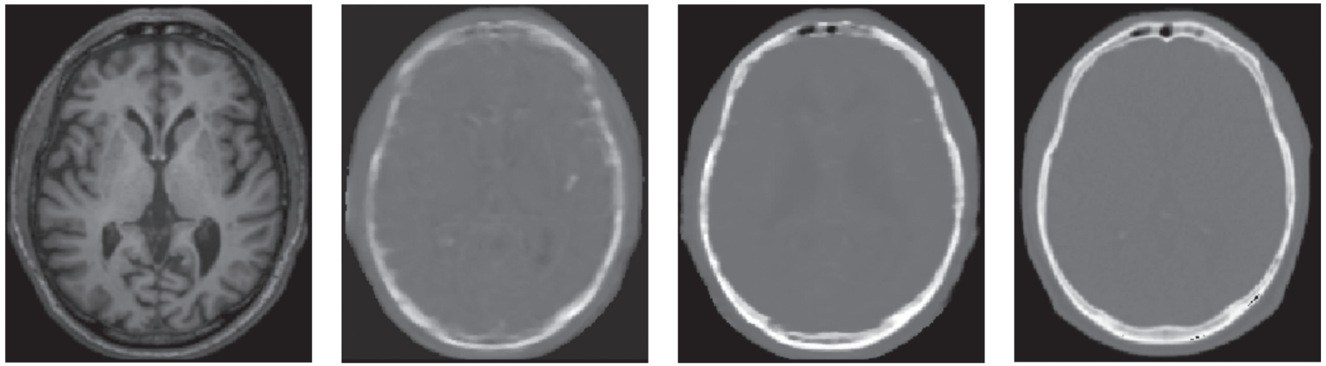




Han, Medical Physics, 2017

Medical Image Synthesis with Context-Aware GANs

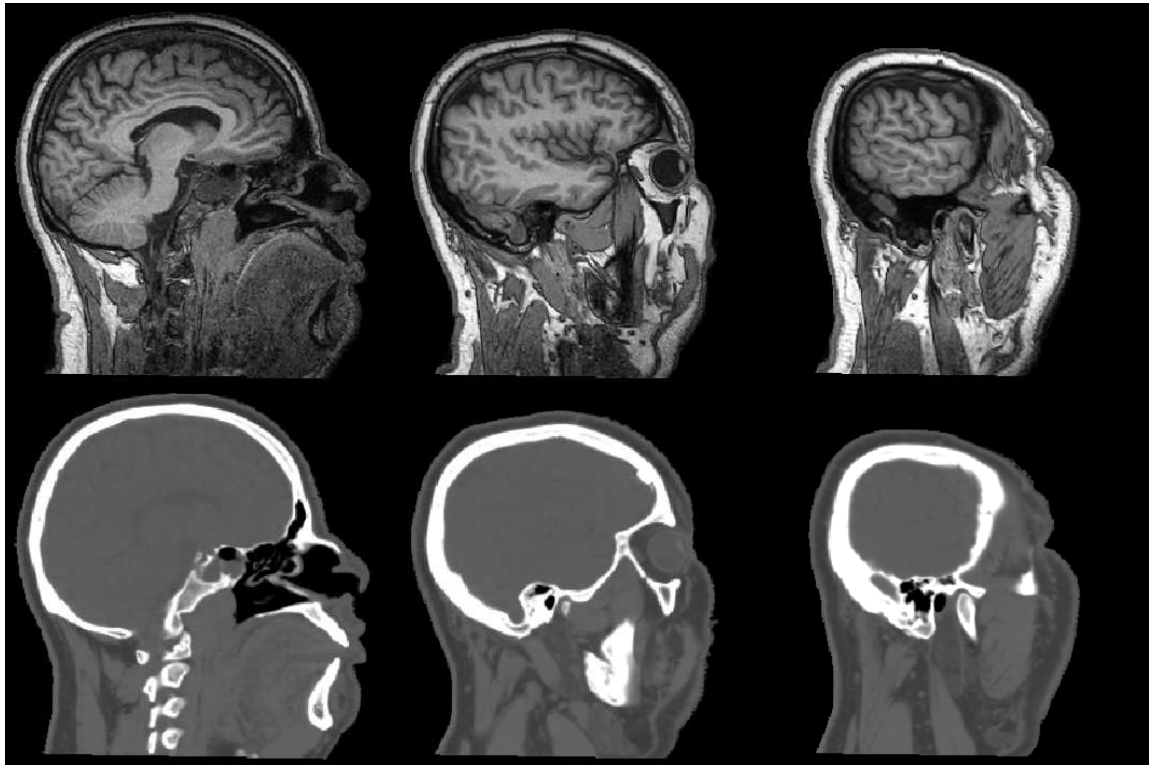




MRI FCN GAN Ground Truth

Nie et al., MICCAI, 2017

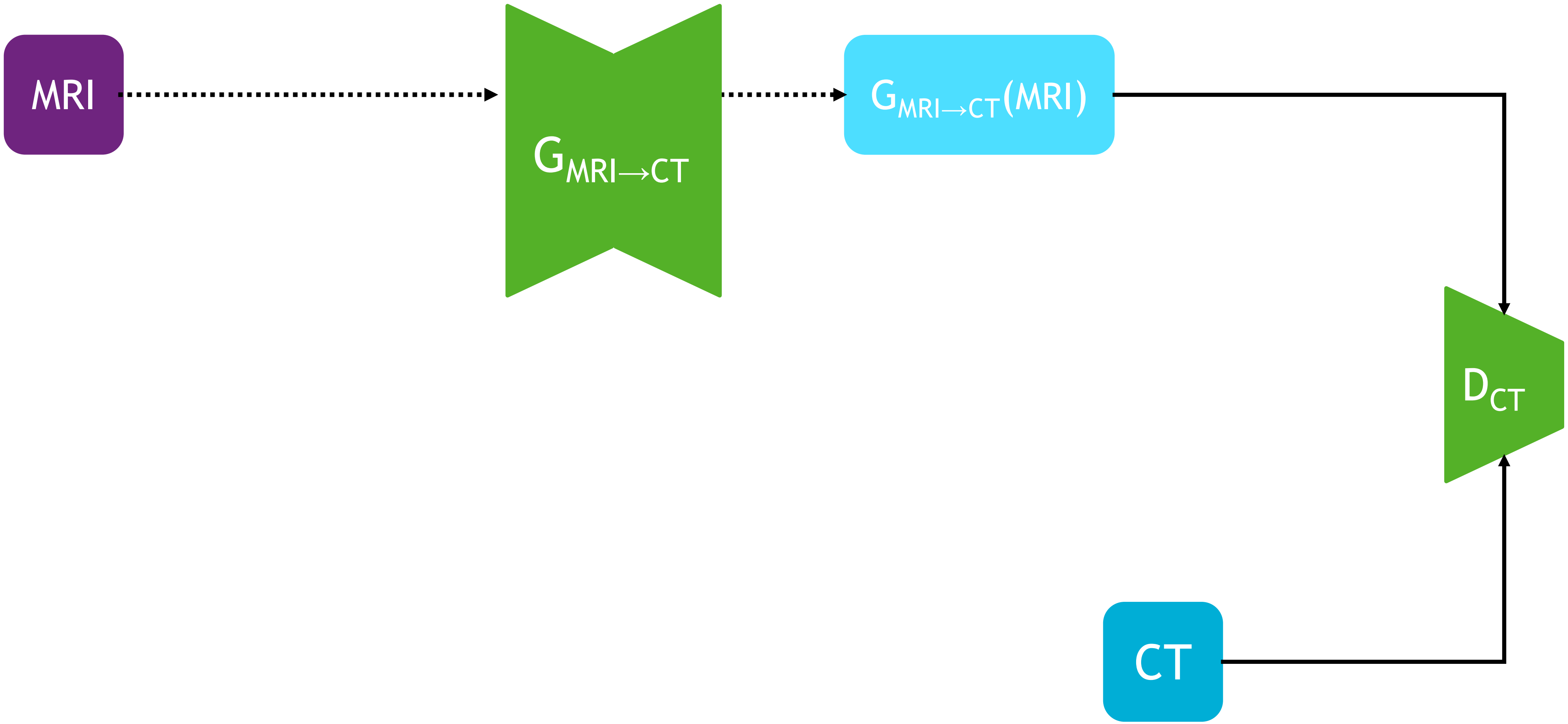
Deep MR to CT Synthesis using Unpaired Data



Wolterink et al., SASHIMI, 2017

Methodological parenthesis

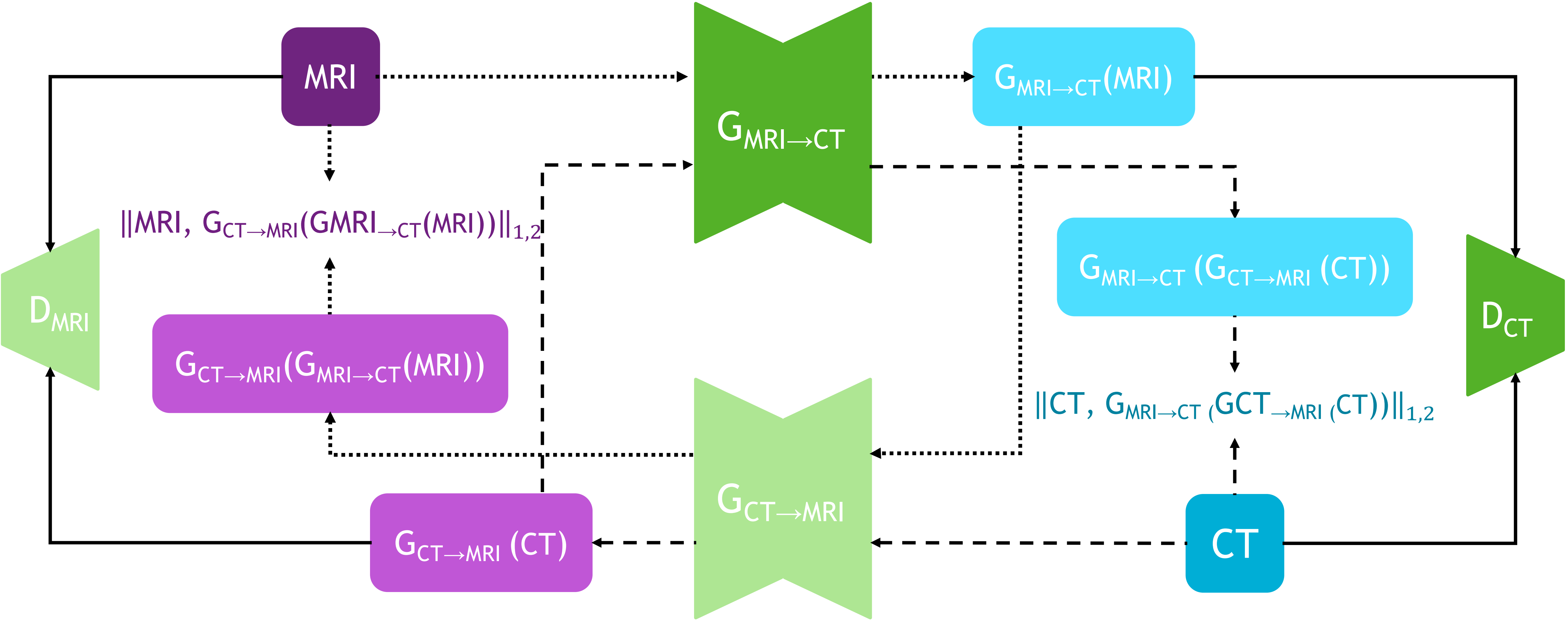
GANs



Isola et al., Image-to-Image Translation with Conditional Adversarial Networks, CVPR 2017

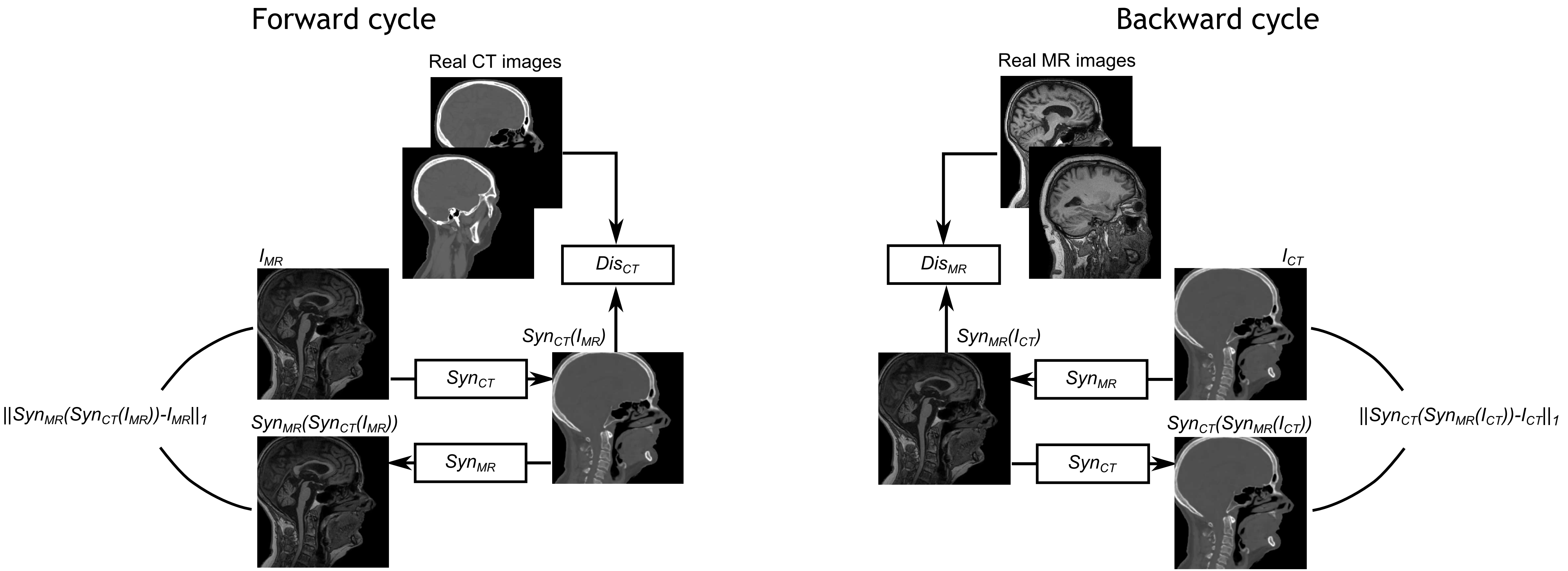
Methodological parenthesis

Cycle GANs



Zhu et al., Unpaired Image-to-Image Translation using Cycle-Consistent Adversarial Networks, ICCV 2017

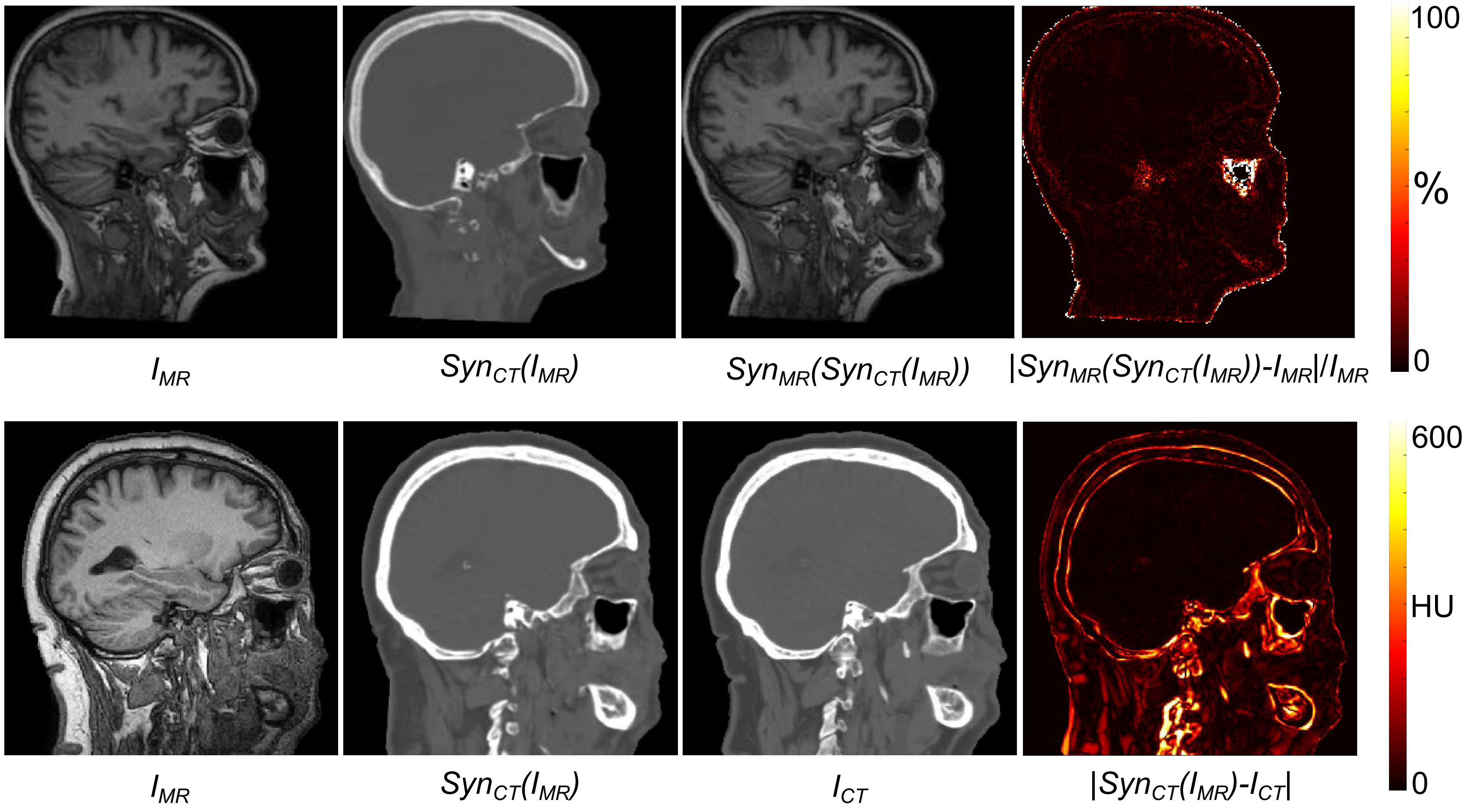
Deep MR to CT Synthesis using Unpaired Data



Wolterink et al., SASHIMI, 2017

Image synthesis

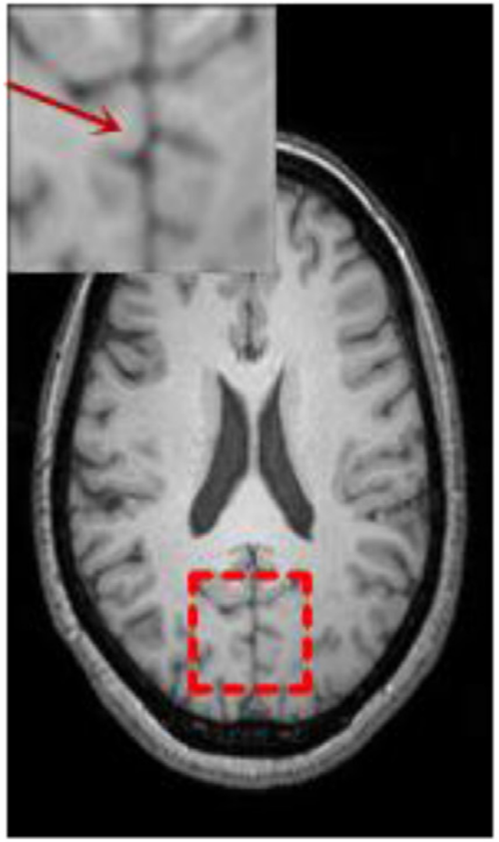
Deep MR to CT Synthesis using Unpaired Data



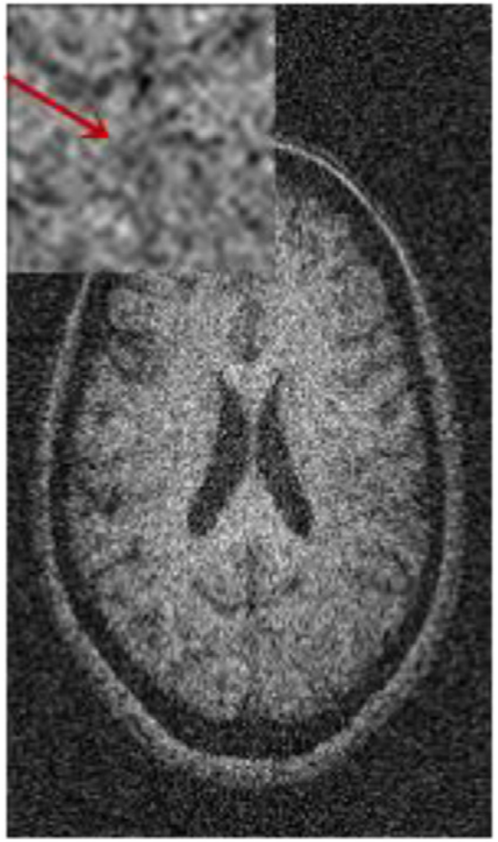
Wolterink et al., SASHIMI, 2017

Image denoising

Magnetic resonance imaging (MRI)



Noise-free MRI



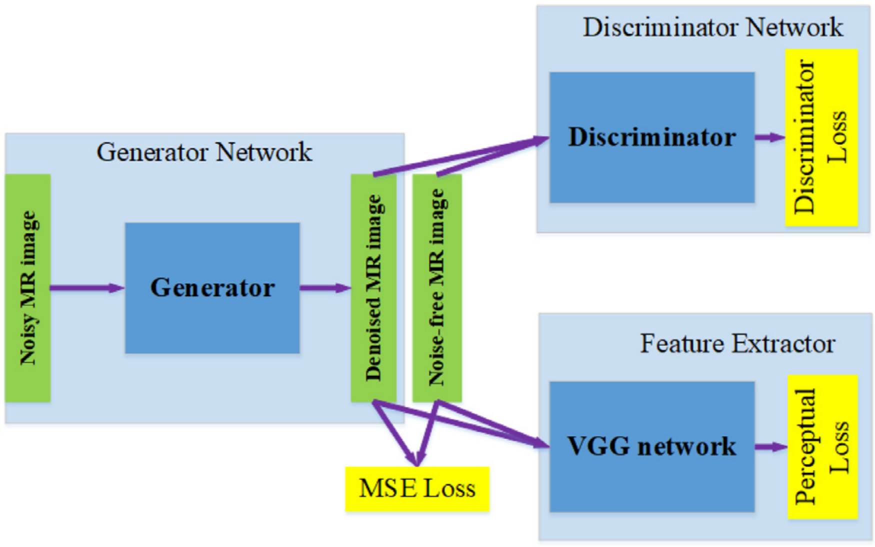
Noisy MRI

Ran et al., Medical Image Analysis, 2019

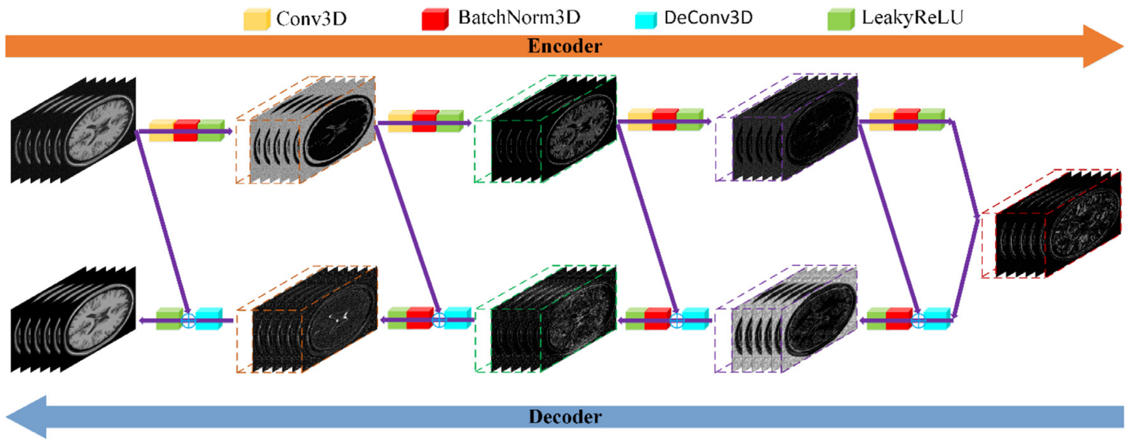
Image denoising

Denoising of 3D MRI using a residual encoder-decoder Wasserstein GAN

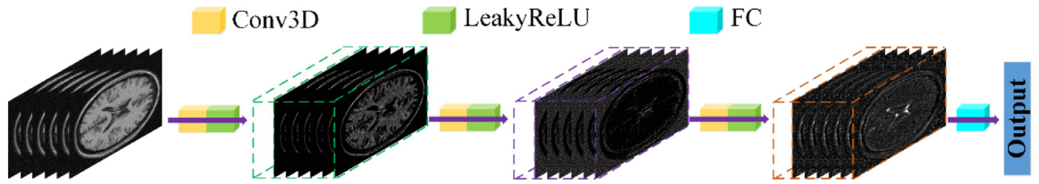
Overall architecture



Generator



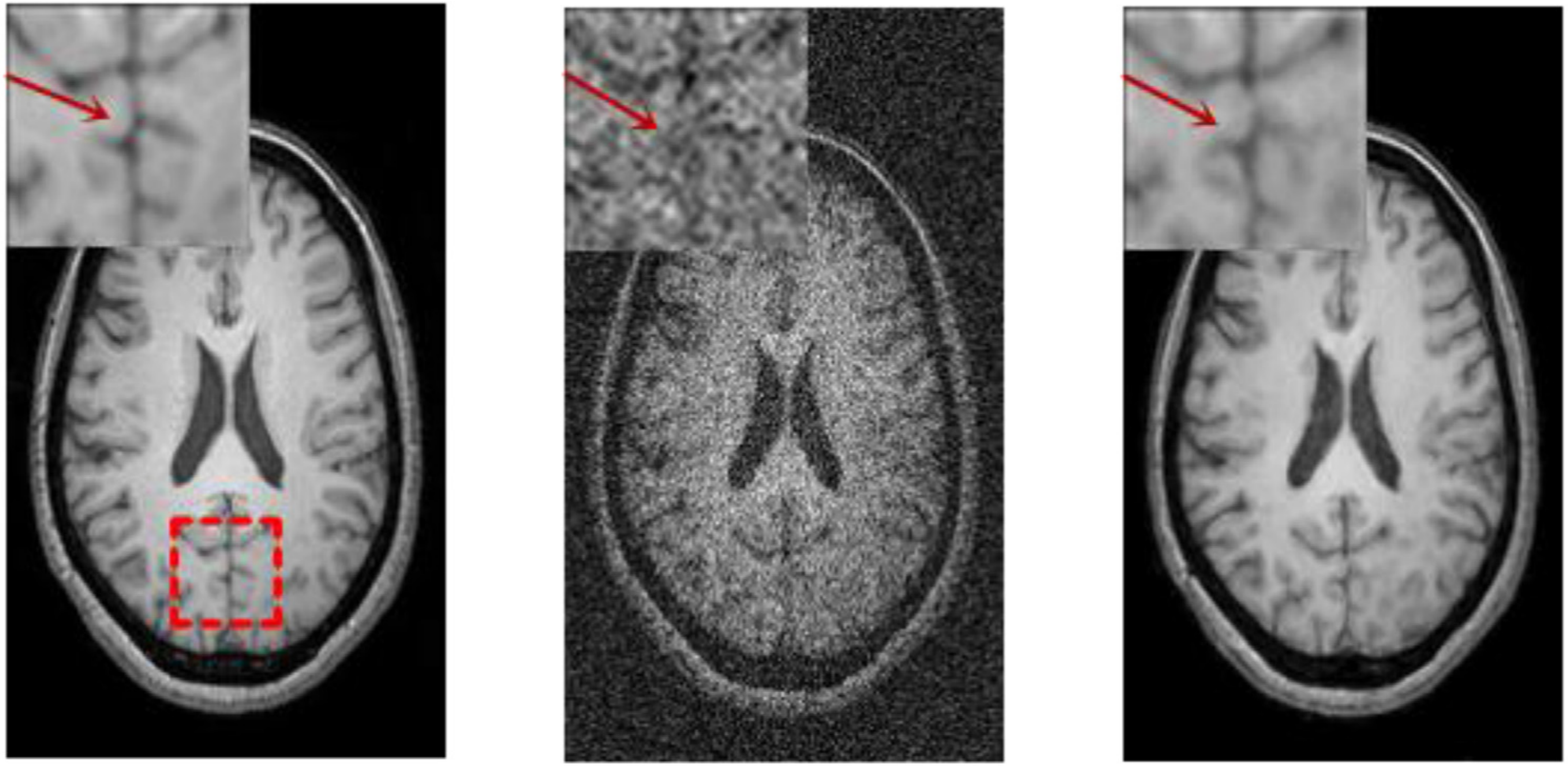
Discriminator



Ran et al., Medical Image Analysis, 2019

Image denoising

Denoising of 3D MRI using a residual encoder-decoder Wasserstein GAN

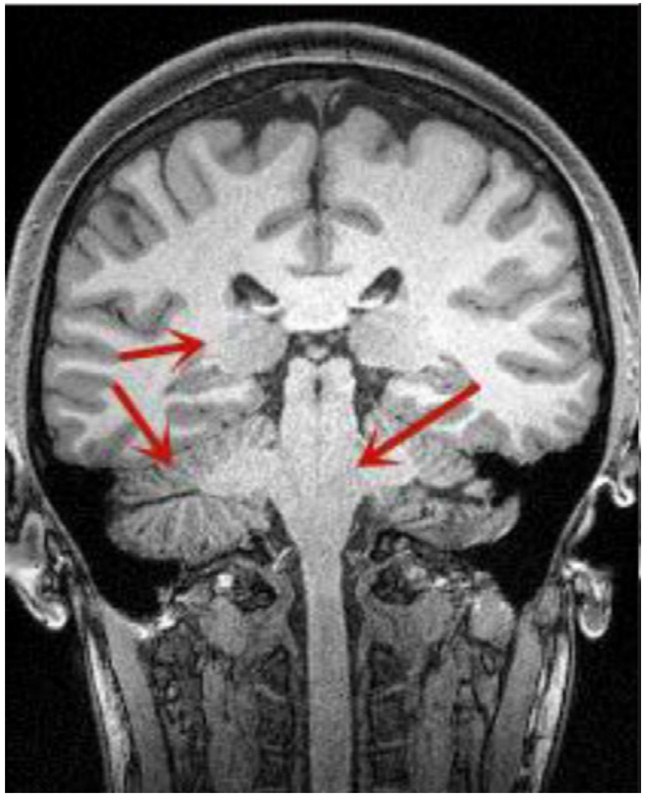


Noise-free MRI | Noisy MRI | Denoised MRI

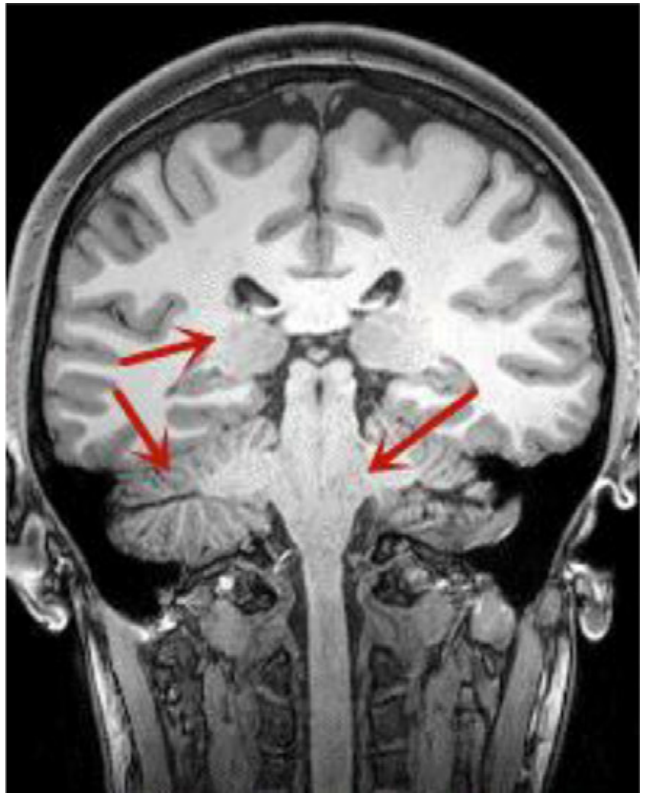
Ran et al., Medical Image Analysis, 2019

Image denoising

Denoising of 3D MRI using a residual encoder-decoder Wasserstein GAN



Original noisy MRI

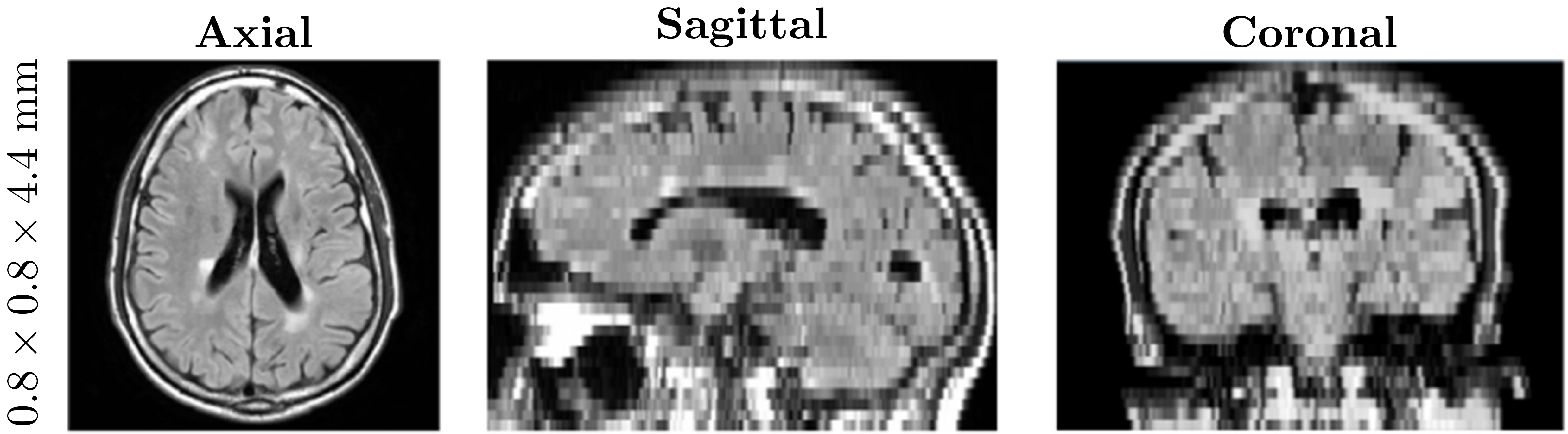


Denoised MRI

Ran et al., Medical Image Analysis, 2019

Image super-resolution

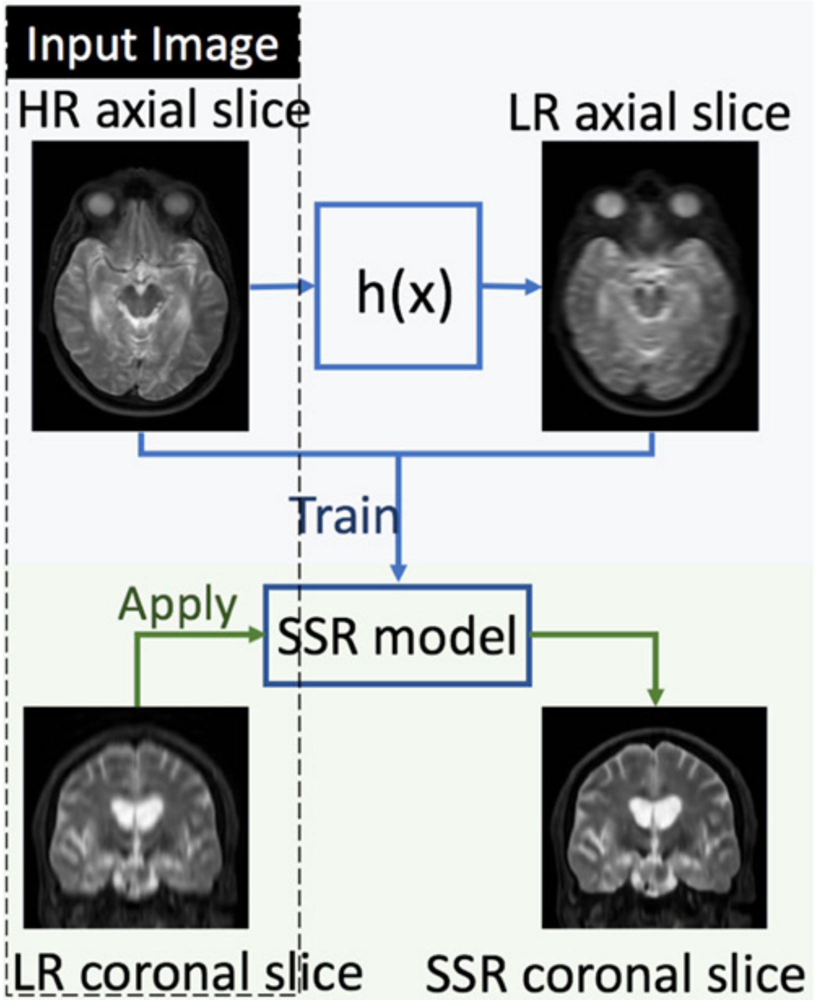
2D MRI

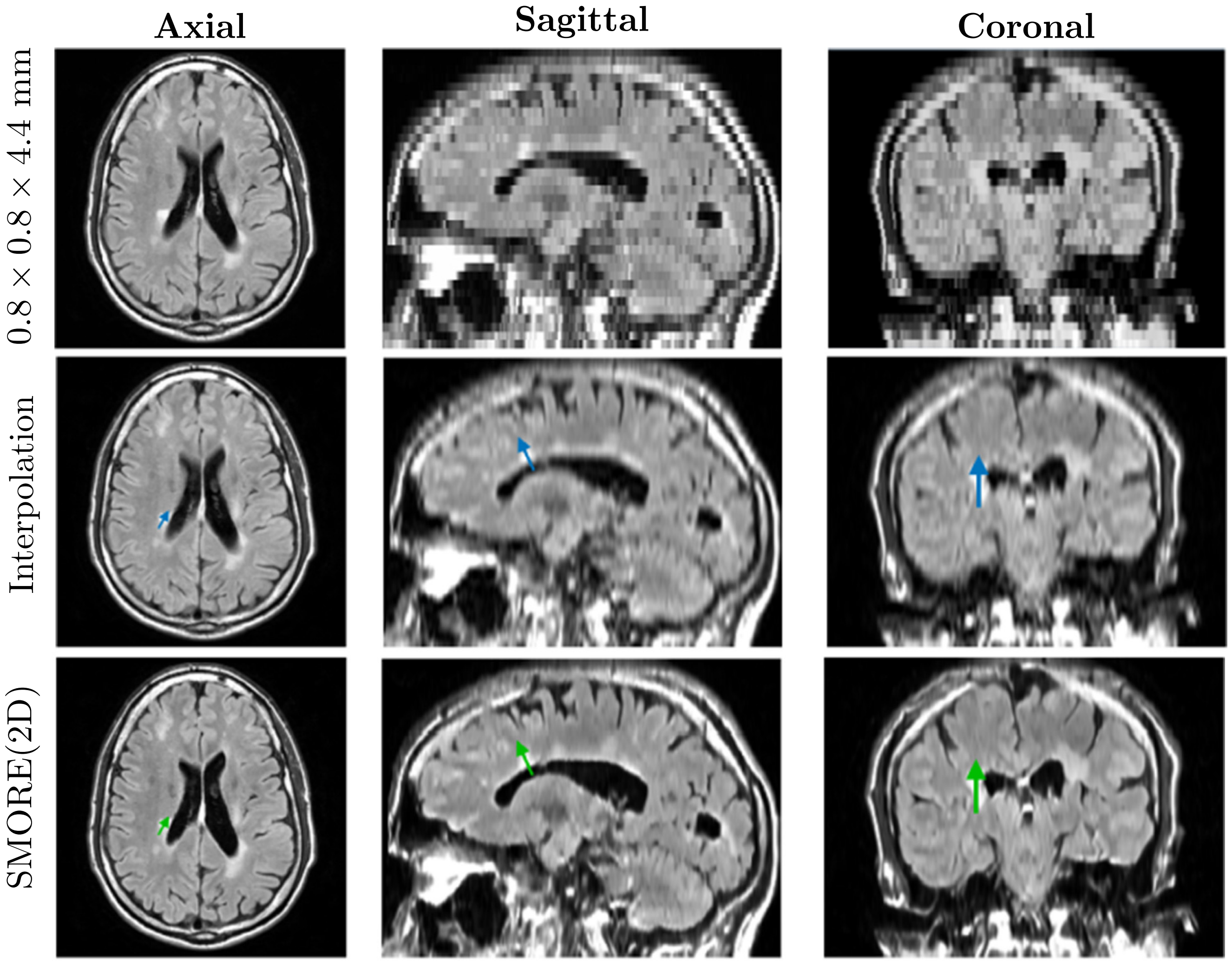


Zhao et al., Magnetic Resonance Imaging, 2019

Image super-resolution

Self super-resolution for MRI

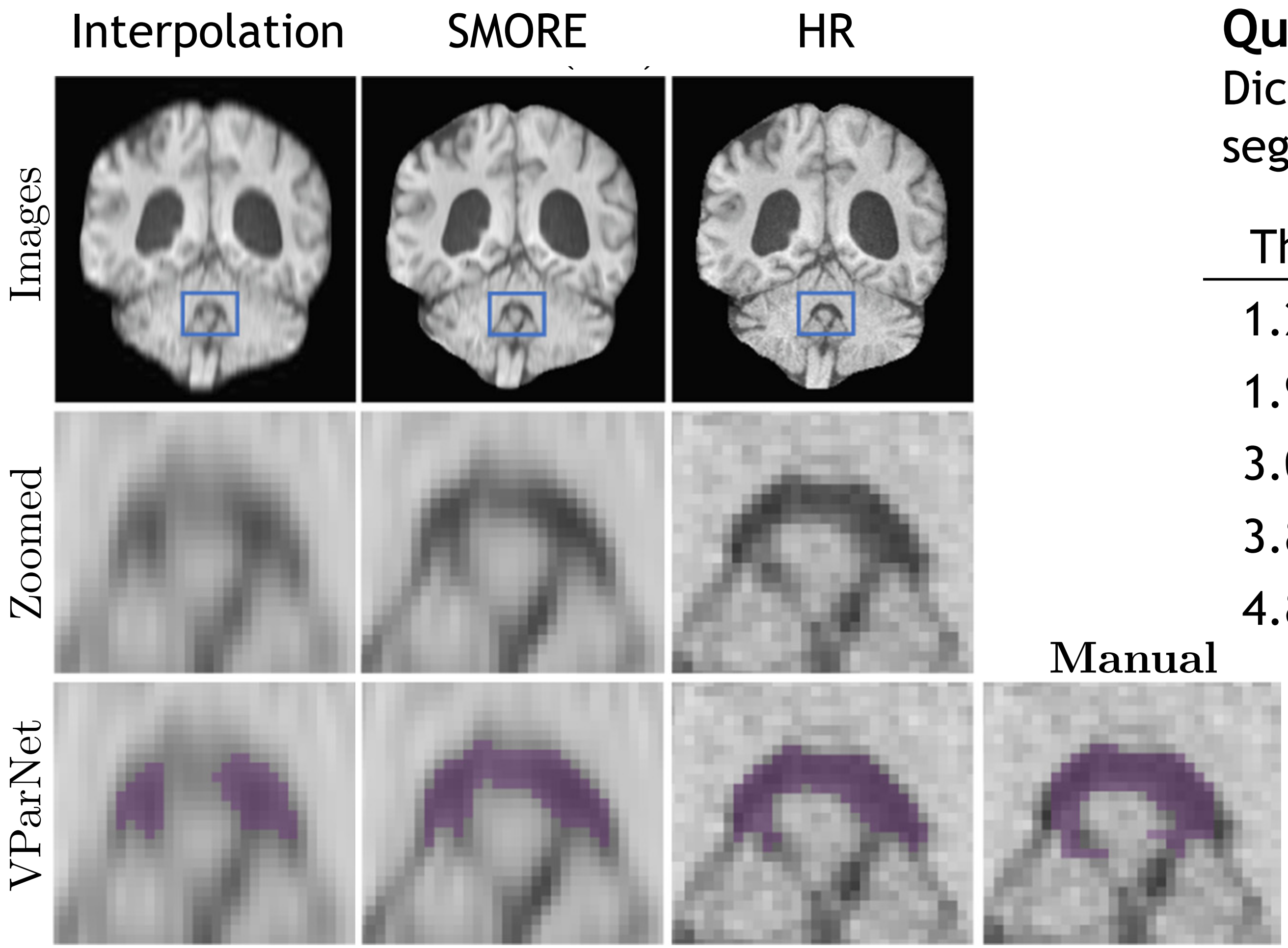




Zhao et al., Magnetic Resonance Imaging, 2019

Image super-resolution

Self super-resolution for MRI



Quantitative results

Dice score (overlap between manual and automatic segmentations)

Thickness	Interpolation	SMORE	HR (0.9 mm)
1.205 mm	0.969	0.9696	0.9699
1.928 mm	0.9665	0.9690	
3.0125 mm	0.9602	0.9675	
3.856 mm	0.9524	0.9632	
4.82 mm	0.9408	0.9607	

Zhao et al., Magnetic Resonance Imaging, 2019

Computer-aided neuro(radio)logy

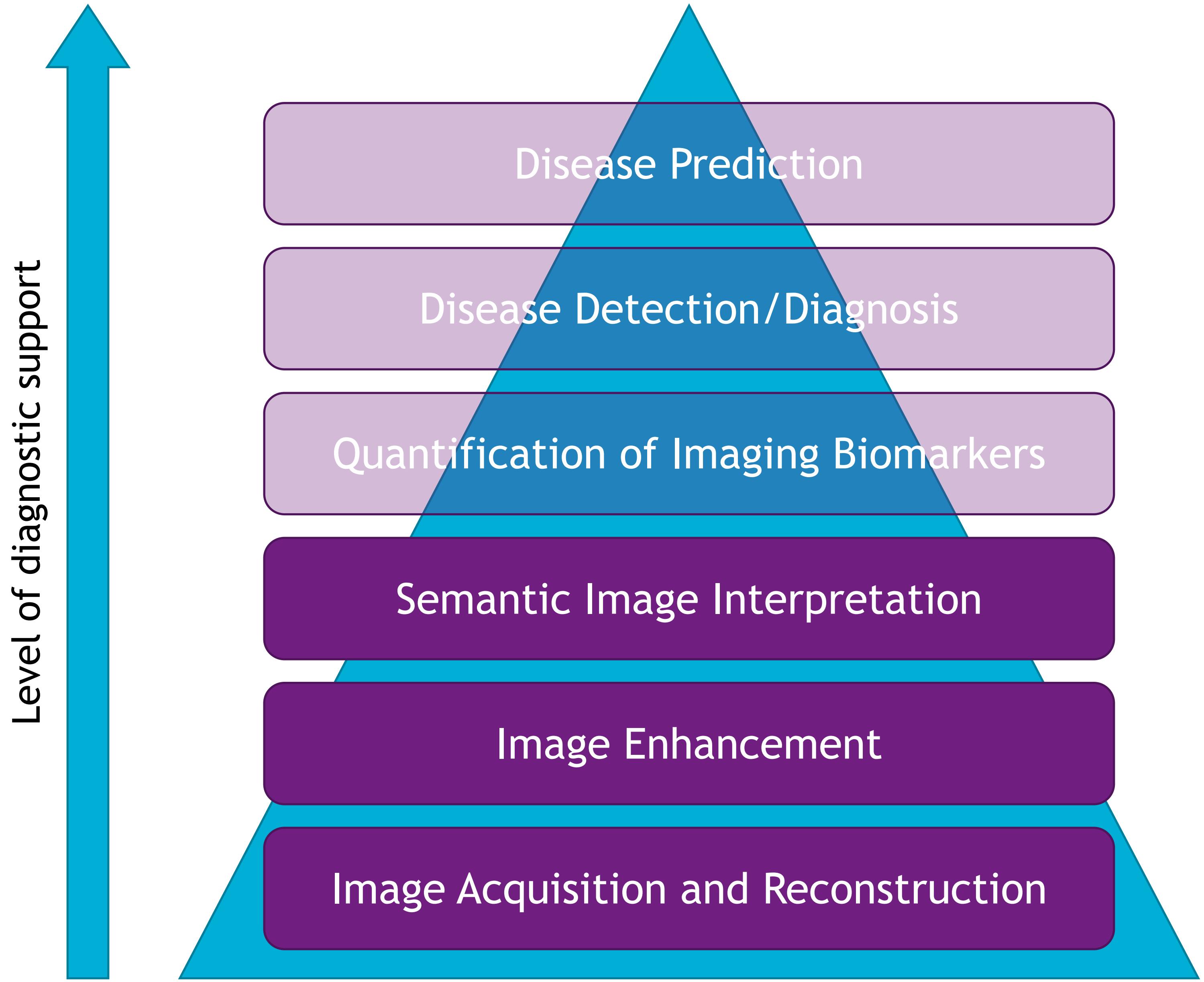
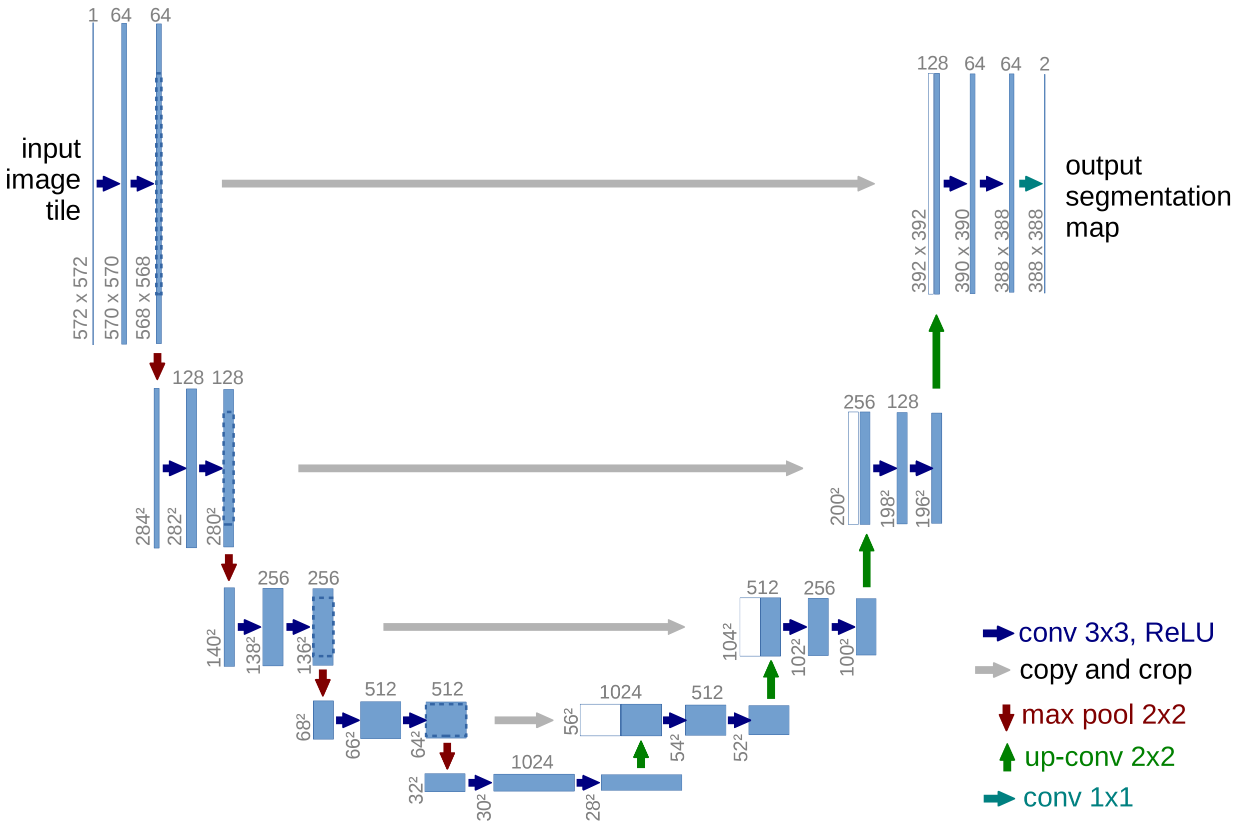


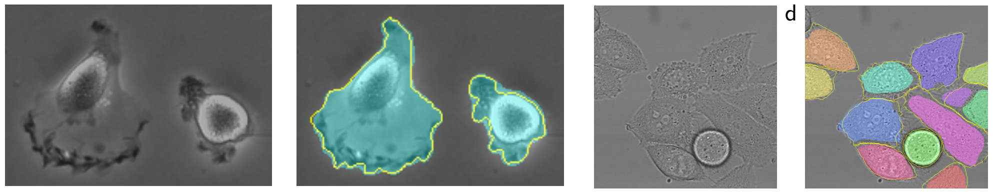
Image segmentation

U-Net: Convolutional Networks for Biomedical Image Segmentation



Results on the ISBI cell tracking challenge

“PhC-U373” data set | “DIC-HeLa” data set



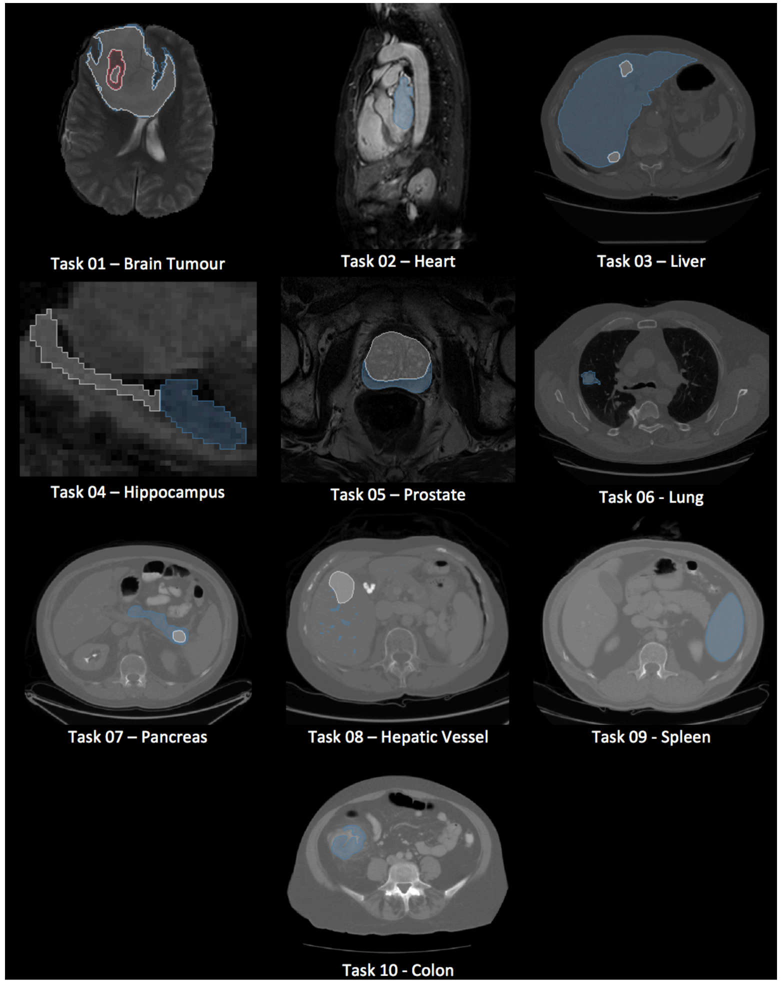
Segmentation results (IOU “intersection over union”)

Name	PhC-U373	DIC-HeLa
IMCB-SG (2014)	0.2669	0.2935
KTH-SE (2014)	0.7953	0.4607
HOUS-US (2014)	0.5323	-
second-best 2015	0.83	0.46
u-net (2015)	**0.9203**	**0.7756**

Ronneberger et al., MICCAI, 2015 (**12076** citations on 05/03/2020)

Image segmentation

Medical Segmentation Decathlon

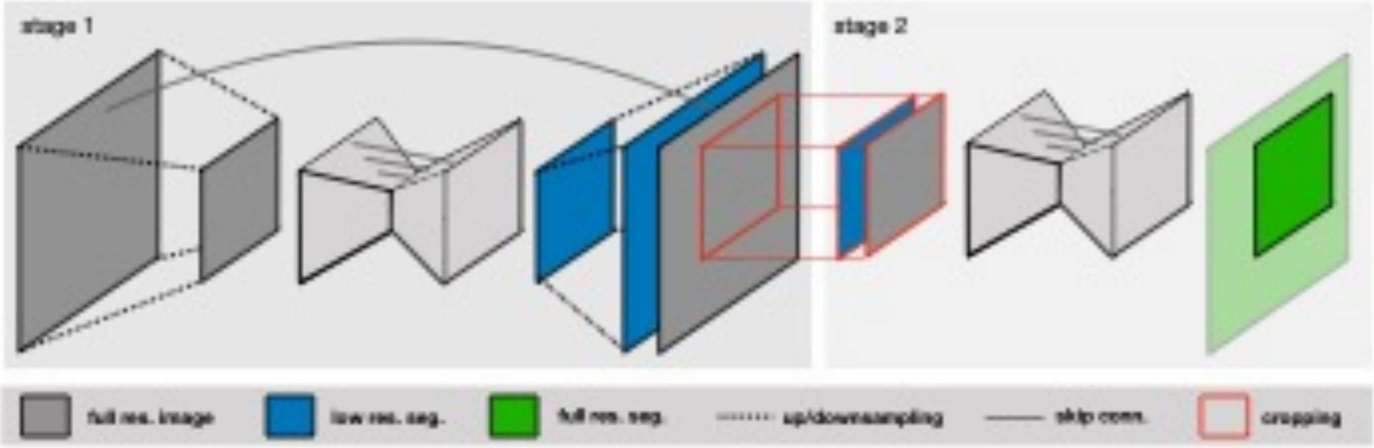


Simpson et al., arXiv:1902.09063, 2019

And the winner is:

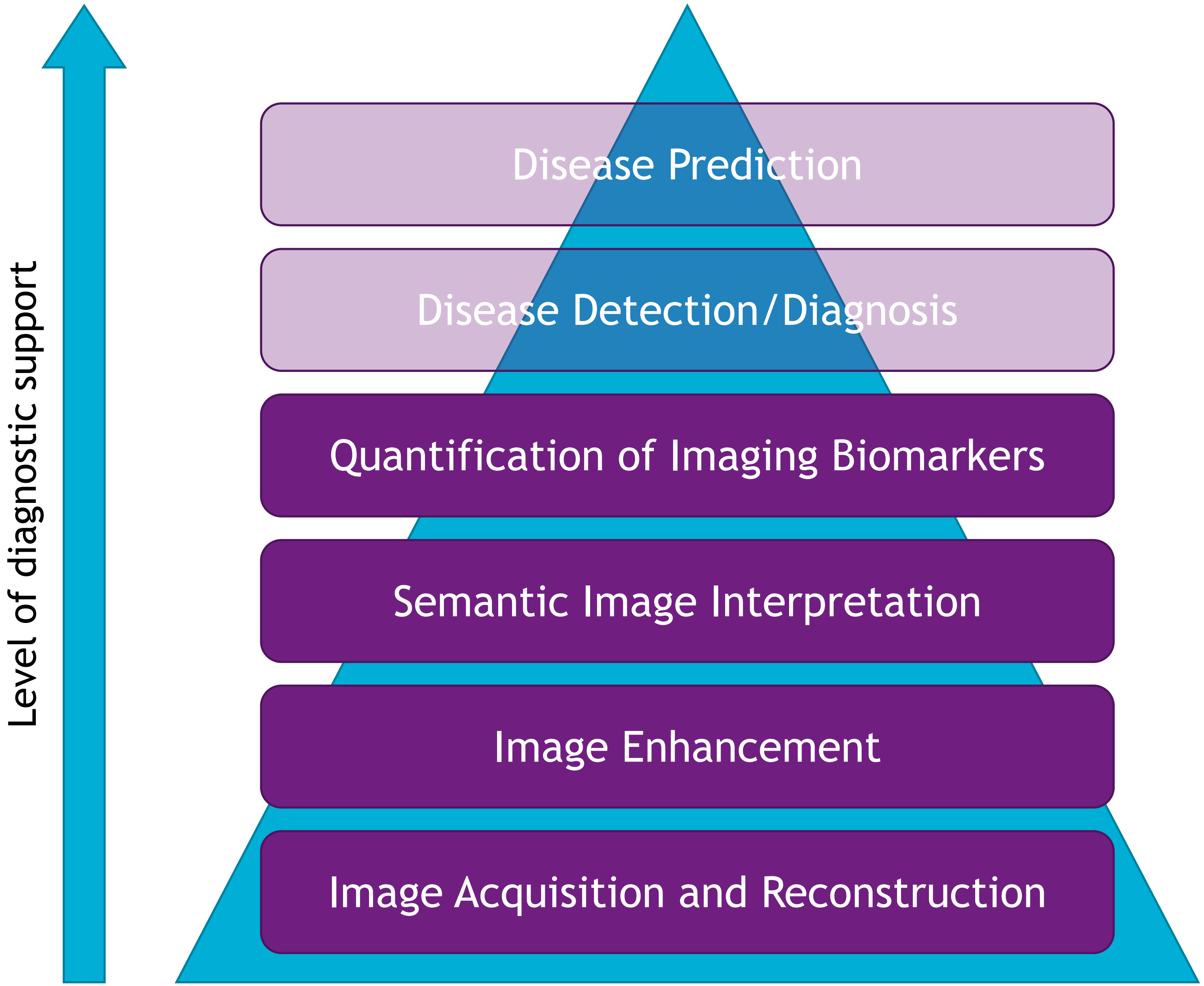
nnU-Net: Self-adapting Framework for U-Net-Based Medical Image Segmentation

"We consider a pool of basic U-Net architectures consisting of a 2D U-Net, a 3D U-Net and a U-Net Cascade."



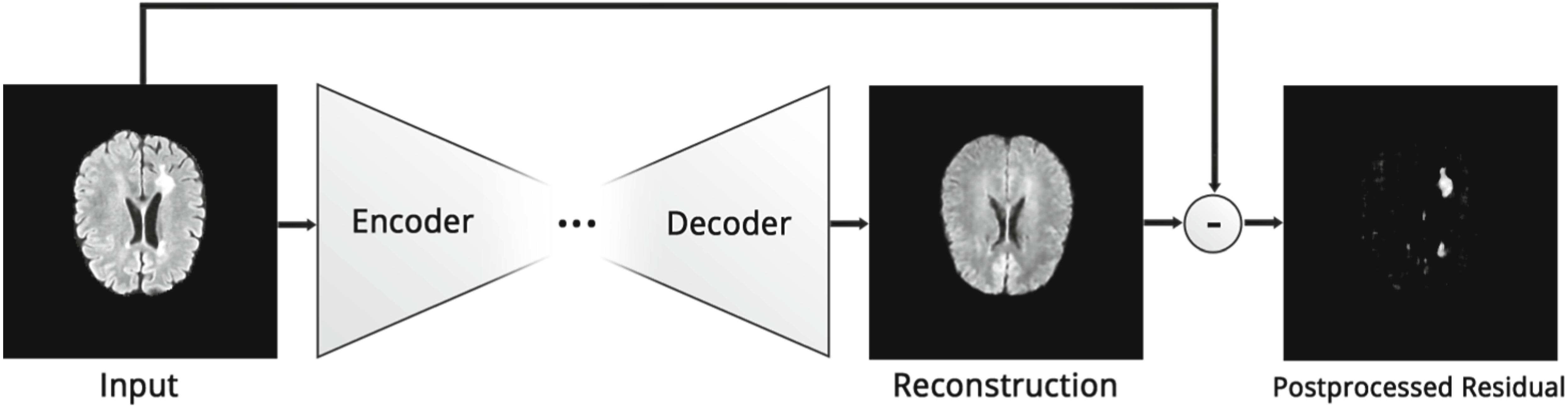
Isensee et al., arXiv:1809.10486, 2018

Computer-aided neuro(radio)logy



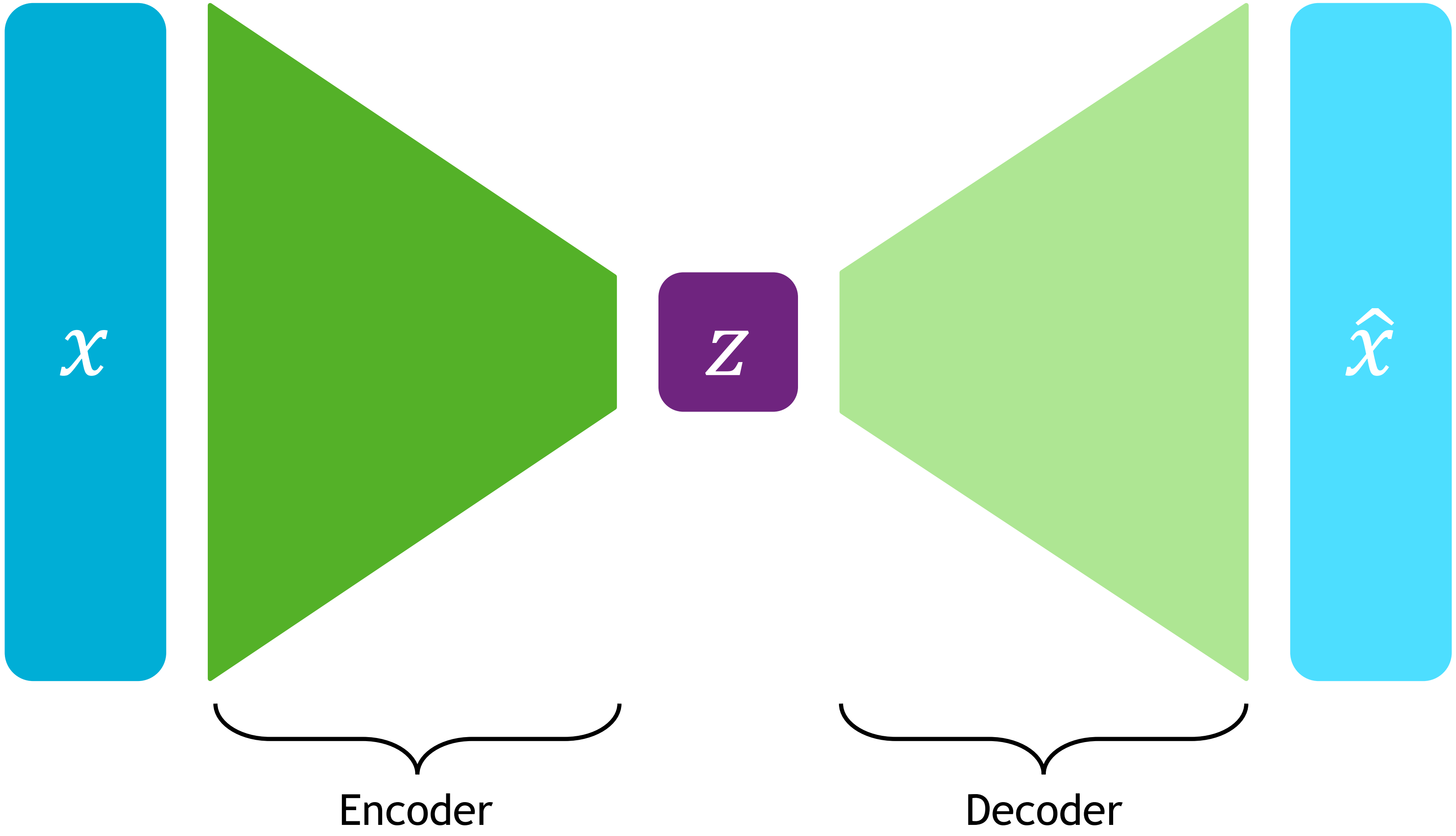
Anomaly detection

Deep autoencoding models for unsupervised anomaly segmentation in brain MR images



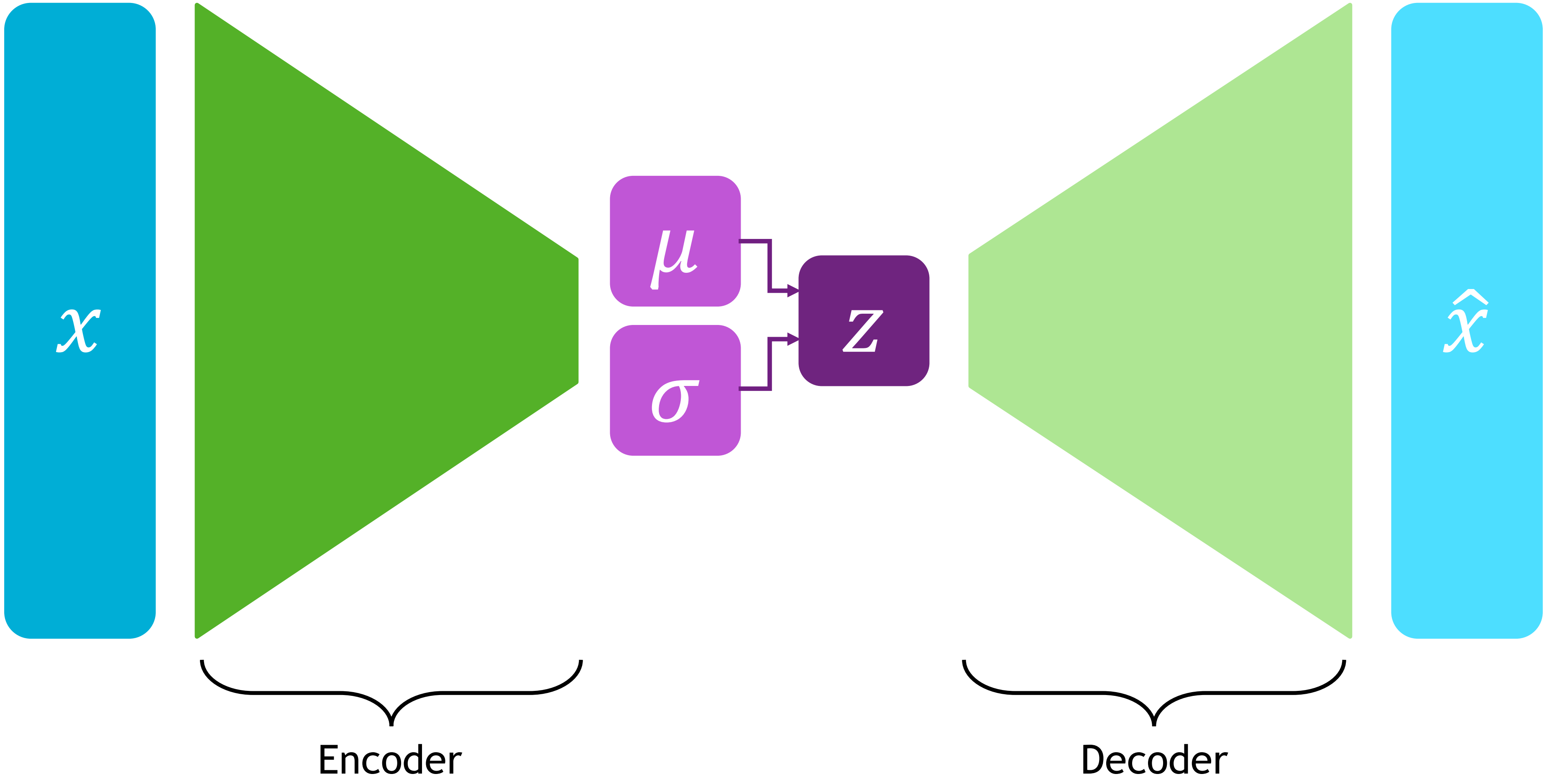
Baur et al., MICCAI Brainlesion Workshop, 2019

Autoencoder



Methodological parenthesis

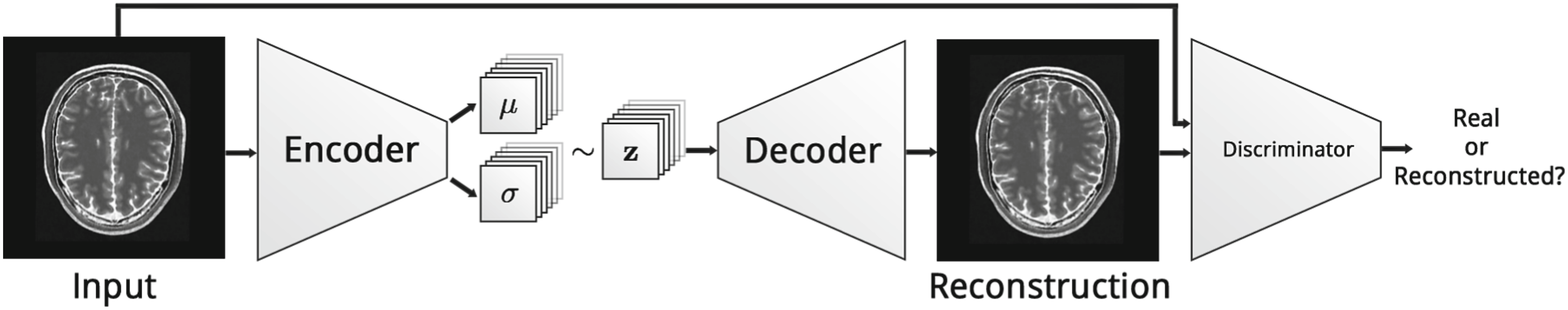
Variational autoencoder (VAE)



Anomaly detection

Deep autoencoding models for unsupervised anomaly segmentation in brain MR images

VAE-GAN for anomaly segmentation



Baur et al., MICCAI Brainlesion Workshop, 2019

Anomaly detection

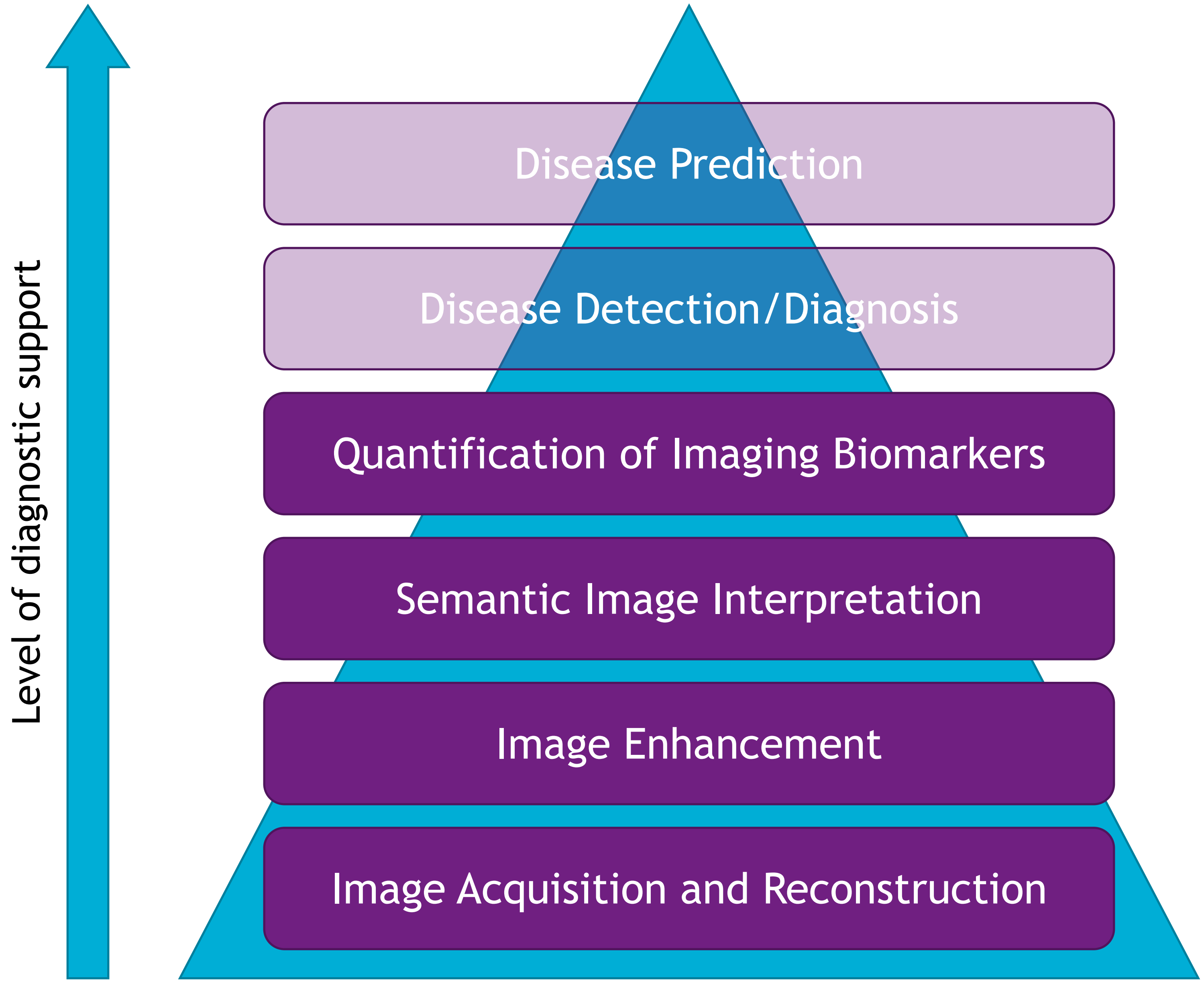
Deep autoencoding models for unsupervised anomaly segmentation in brain MR images

Input image | Ground-truth segmentation | Input - Reconstruction | Resulting segmentation overlaid on input image

True Positives False Positives False Negatives

Baur et al., MICCAI Brainlesion Workshop, 2019

Computer-aided neuro(radio)logy



Parenthesis on Alzheimer's disease

What is dementia?

- Disorders caused by abnormal brain changes
- Trigger decline in cognitive abilities, severe enough to impair daily life
- Affect behaviour, feelings and relationships
- Progressive

Common types of dementia

- Alzheimer's disease: 60 to 80% of dementia cases
- Vascular dementia
- Lewy body dementia
- Frontotemporal dementia
- Posterior cortical atrophy
- Primary progressive aphasia

Parenthesis on Alzheimer's disease

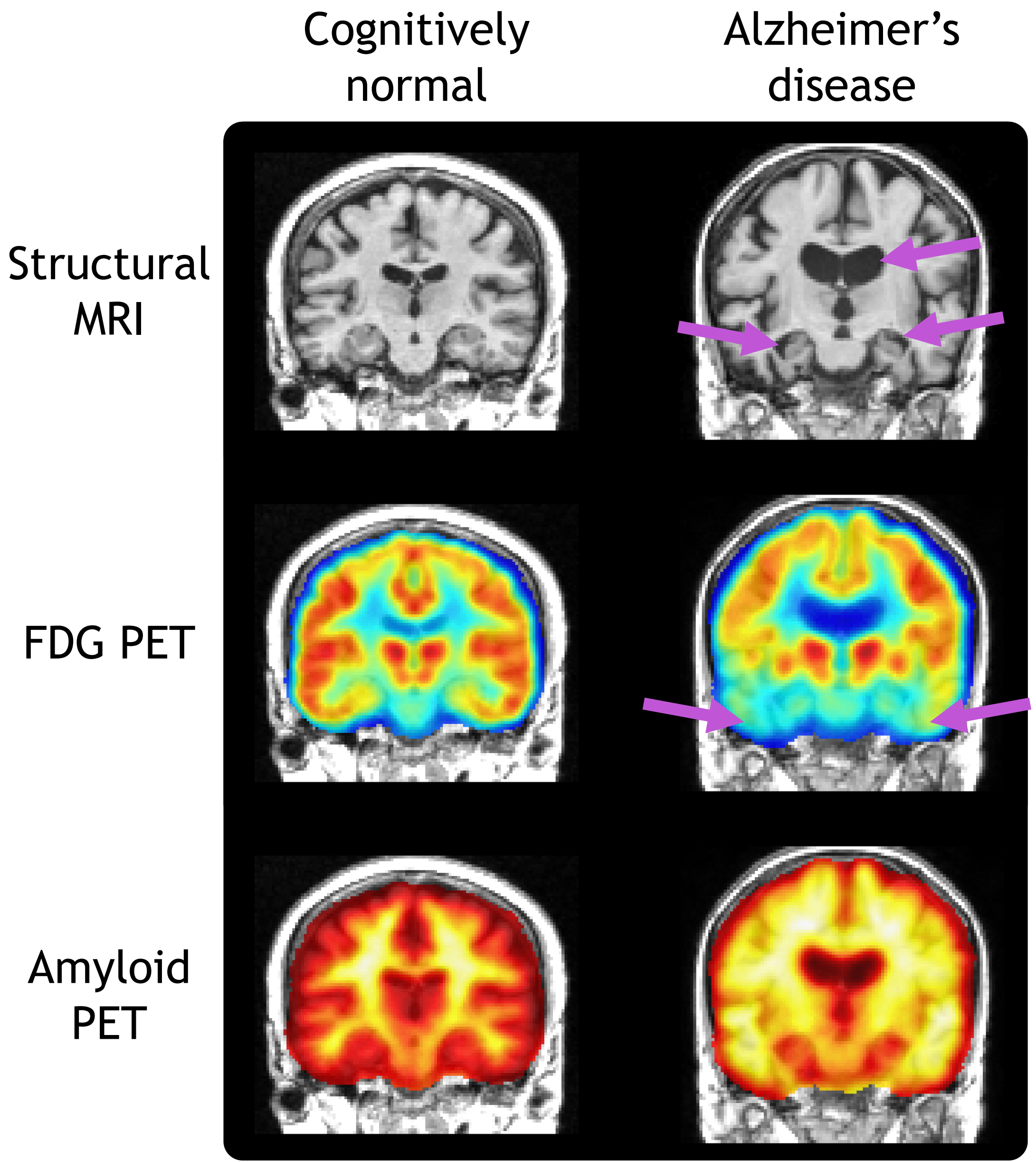
Current diagnosis of dementia

- Clinical consultation
  - Questions about the person's concerns, symptoms, general health and medical history
  - Discussion with a relative about the person' symptoms
  - Physical check-up
  - Completion of some pen-and-paper tests to check memory, language and problem-solving skills
- Other possible tests
  - Brain scans
  - Blood tests
  - Lumbar puncture

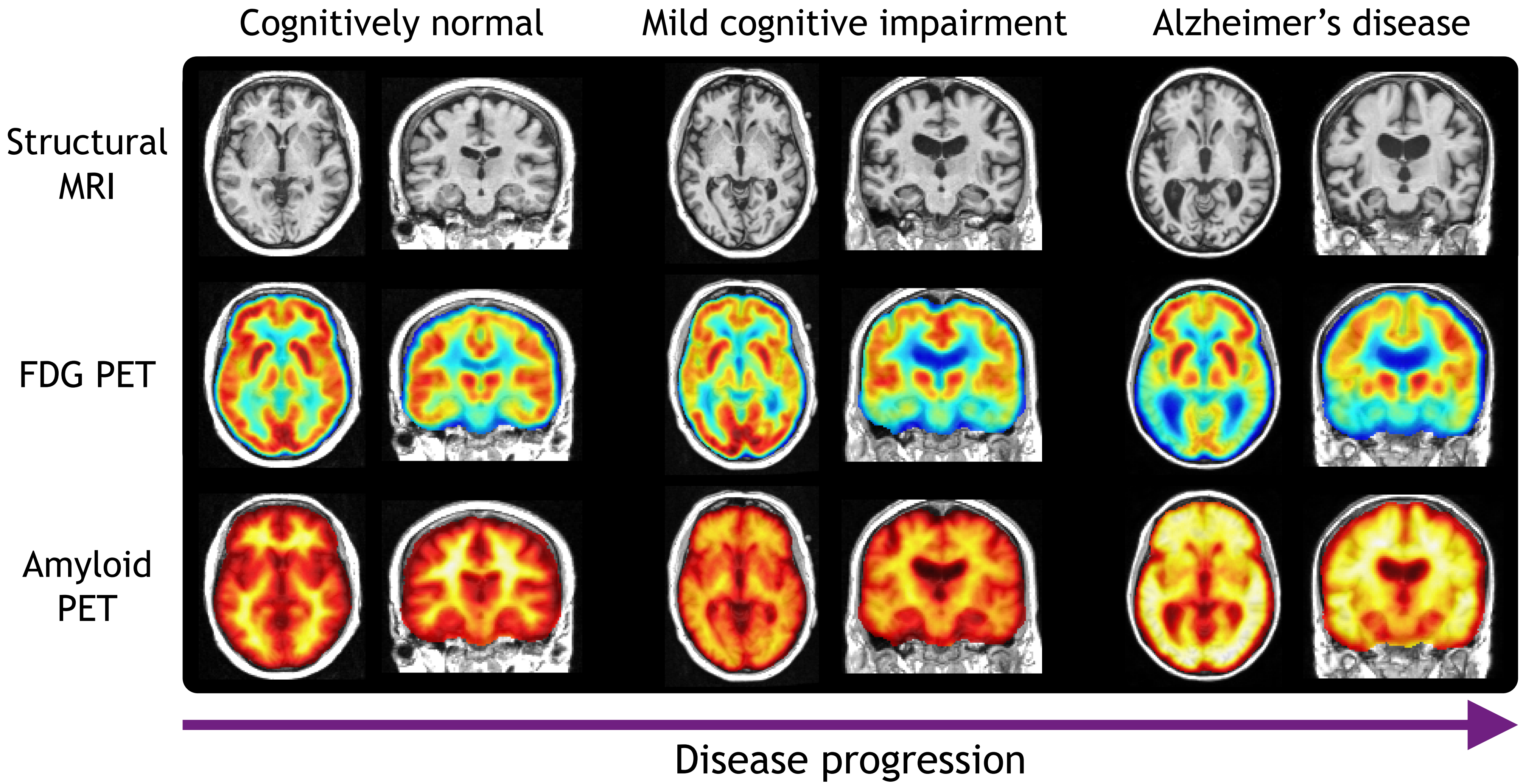
Imaging in Alzheimer's disease

- Magnetic resonance imaging
  - **Structural MRI**
    - Atrophy
  - **Diffusion MRI**
    - White matter integrity

- Positron emission tomography
  - **FDG PET ('glucose' PET)**
    - Hypometabolism
  - **Amyloid & tau PET**
    - Accumulation of amyloid-ß and tau proteins



Imaging in Alzheimer’s disease

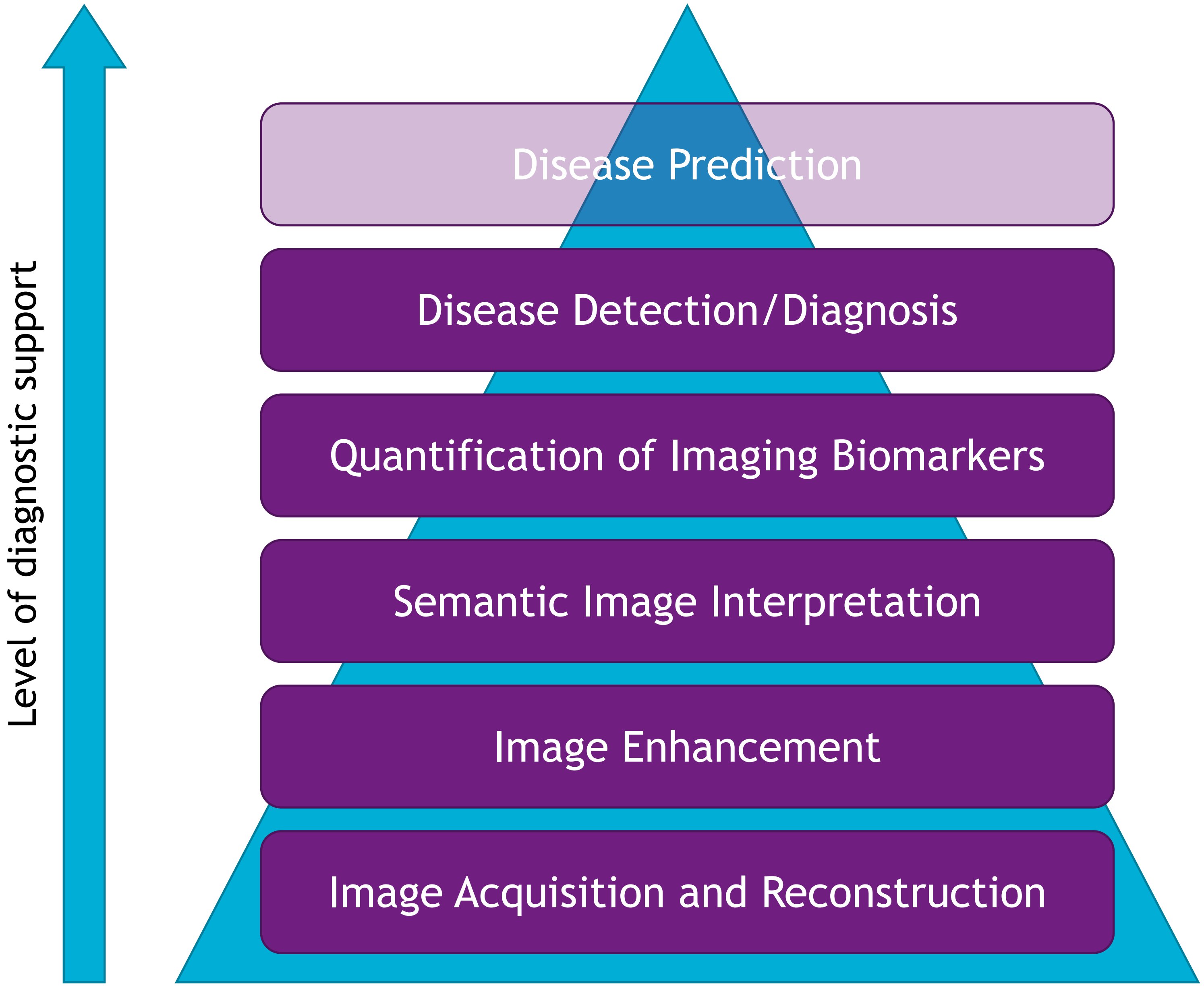


Parenthesis on Alzheimer’s disease

Machine learning for the diagnosis and prognosis of AD

- ‘Diagnostic’ classification task
  - Differentiate cognitively normal (CN) subjects from patients with AD: CN vs AD
  - Not clinically relevant but useful when developing algorithms
- ‘Predictive’ classification task
  - Different patients with mild cognitive impairment (MCI) that will stay stable (sMCI) from the ones that will progress to AD dementia (pMCI): sMCI vs pMCI
  - Clinically relevant but more difficult

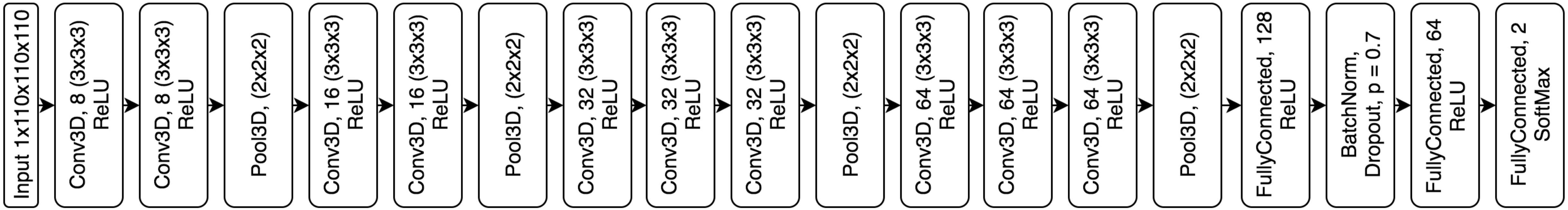
Computer-aided neuro(radio)logy



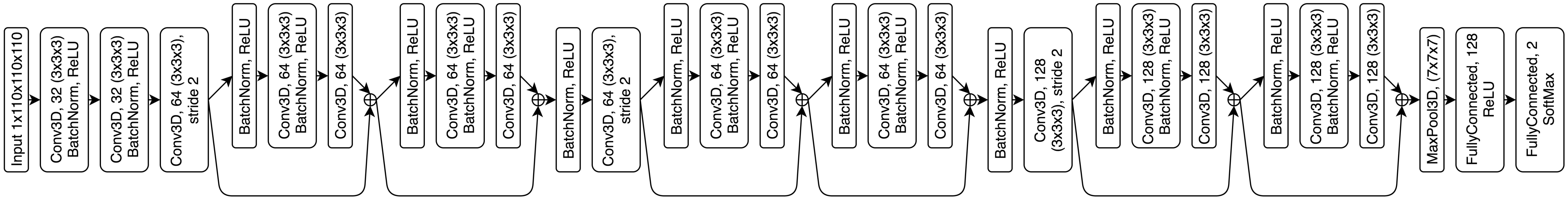
Computer-aided diagnosis

Residual and plain convolutional neural networks for 3D brain MRI classification

VoxCNN:



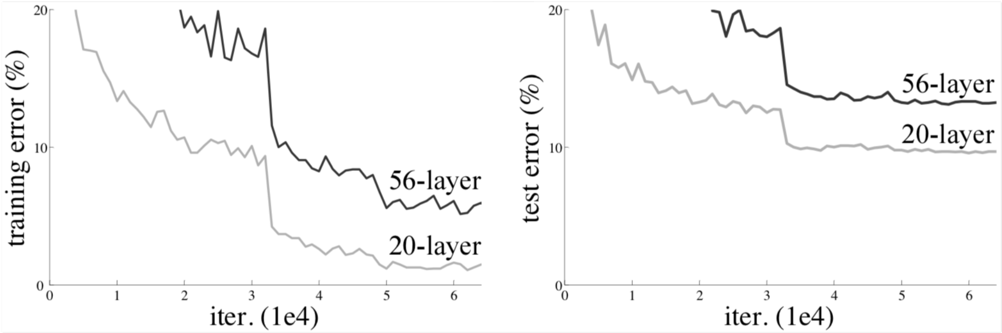
ResNet:

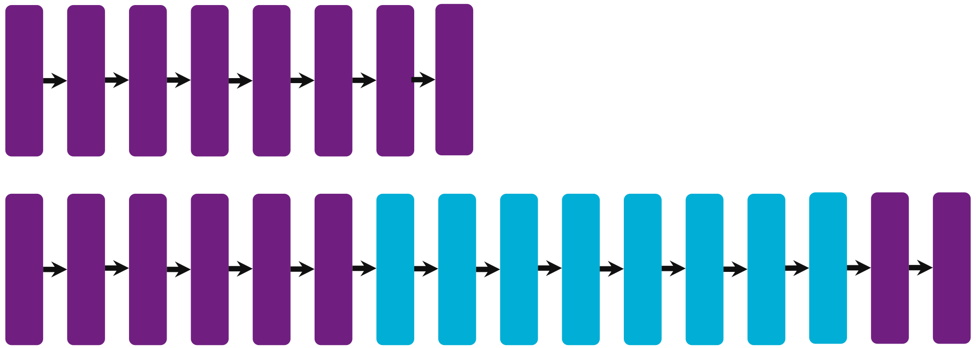


Korolev et al., ISBI, 2017

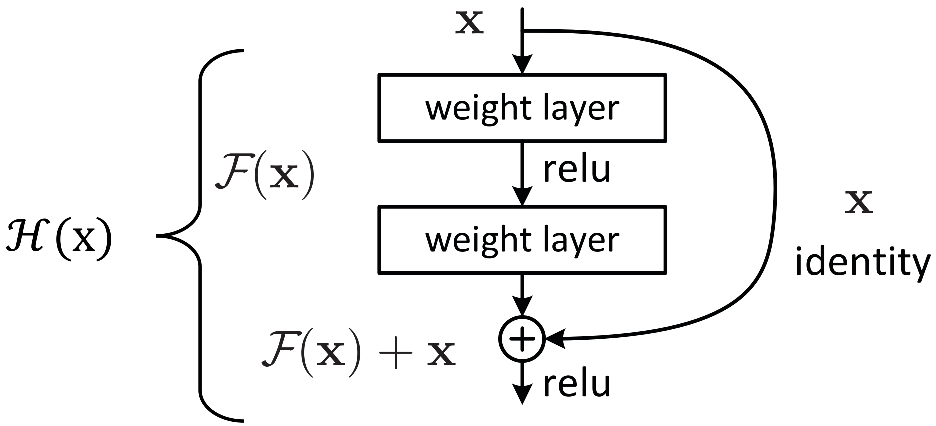
Residual learning

Degradation problem: with the network depth increasing, accuracy gets saturated and then degrades rapidly





Solution: Residual block



Residual = Output − Input

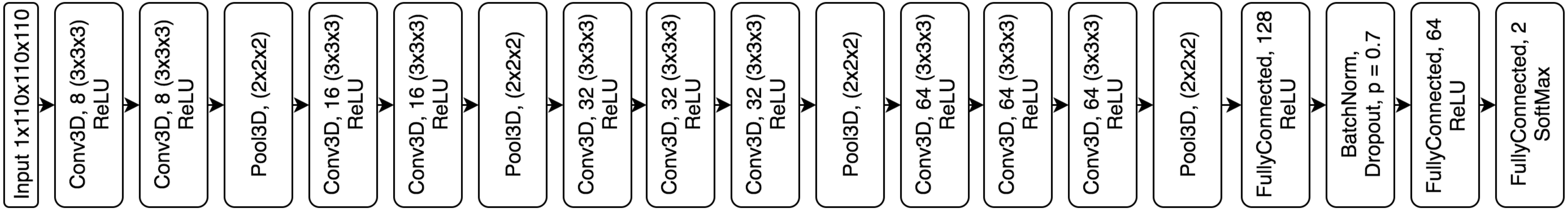
$$\mathcal{F}(\mathrm{x}) = \mathcal{H}(\mathrm{x}) - \mathrm{x}$$

$$\mathcal{H}(\mathrm{x}) = \mathcal{F}(\mathrm{x}) + \mathrm{x}$$

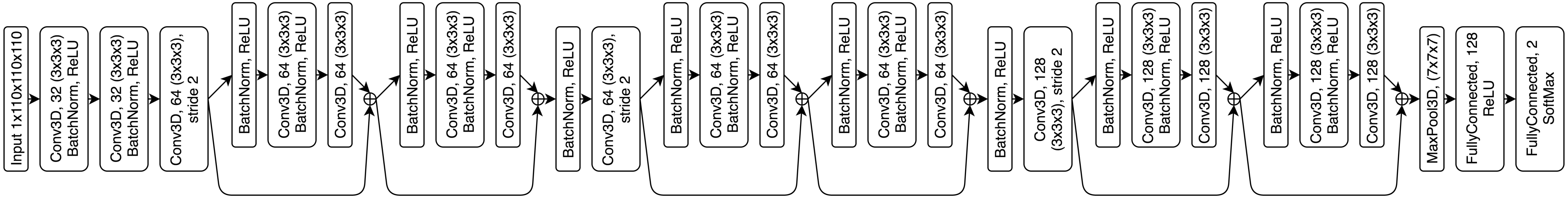
He et al., Deep Residual Learning for Image Recognition, 2015

Residual and plain convolutional neural networks for 3D brain MRI classification

VoxCNN:



ResNet:



Korolev et al., ISBI, 2017

Residual and plain convolutional neural networks for 3D brain MRI classification

	VoxCNN		ResNet	
	AUC	Acc.	AUC	Acc.
AD vs NC	$.88 \pm .08$	$.79 \pm .08$	$.87 \pm .07$	$.80 \pm .07$
AD vs EMCI	$.66 \pm .11$	$.64 \pm .07$	$.67 \pm .13$	$.63 \pm .09$
AD vs LMCI	$.61 \pm .12$	$.62 \pm .08$	$.62 \pm .15$	$.59 \pm .11$
LMCI vs NC	$.67 \pm .13$	$.63 \pm .10$	$.65 \pm .11$	$.61 \pm .10$
LMCI vs EMCI	$.47 \pm .09$	$.56 \pm .11$	$.52 \pm .11$	$.52 \pm .09$
EMCI vs NC	$.57 \pm .12$	$.54 \pm .09$	$.58 \pm .09$	$.56 \pm .07$

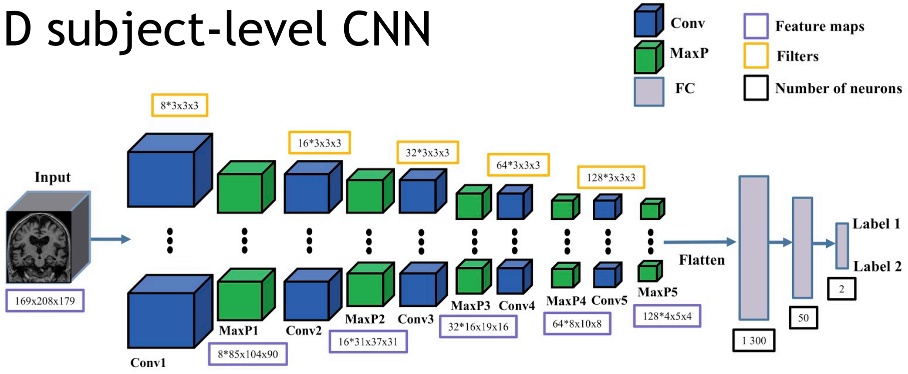
"Both networks show similar results within a standard deviation."

Korolev et al., ISBI, 2017

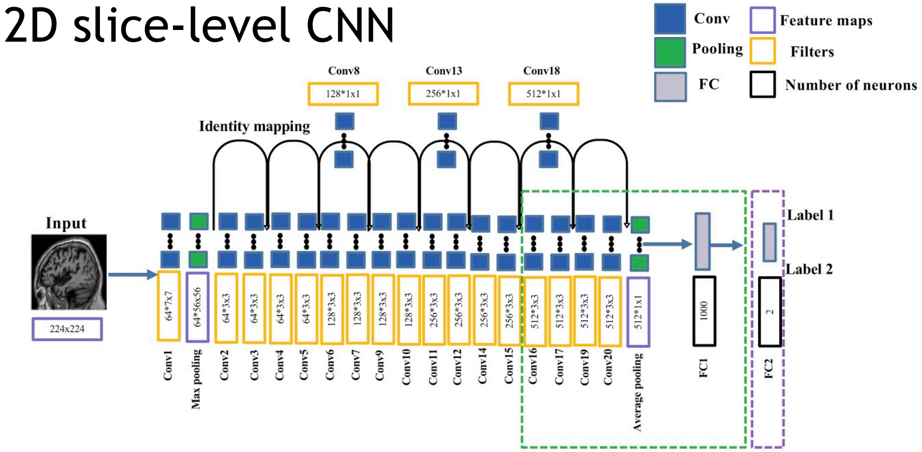
Computer-aided diagnosis

CNNs for Classification of Alzheimer's Disease: Overview and Reproducible Evaluation

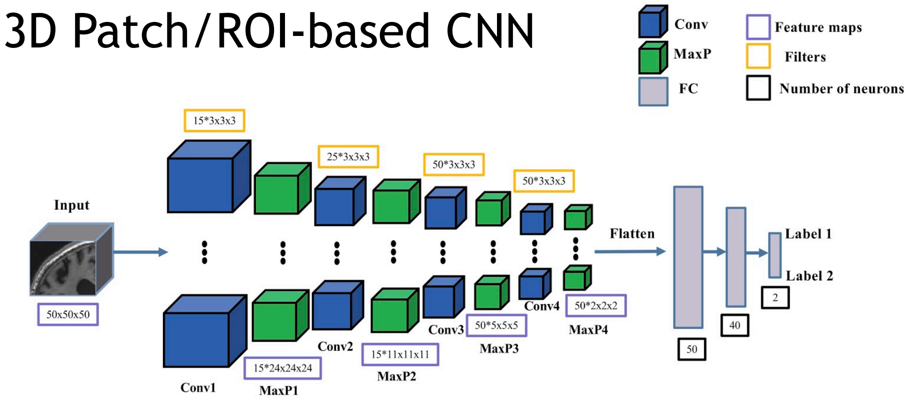
3D subject-level CNN



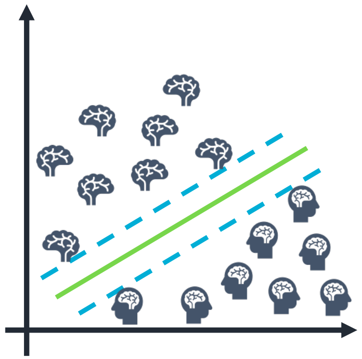
2D slice-level CNN



3D Patch/ROI-based CNN



SVM

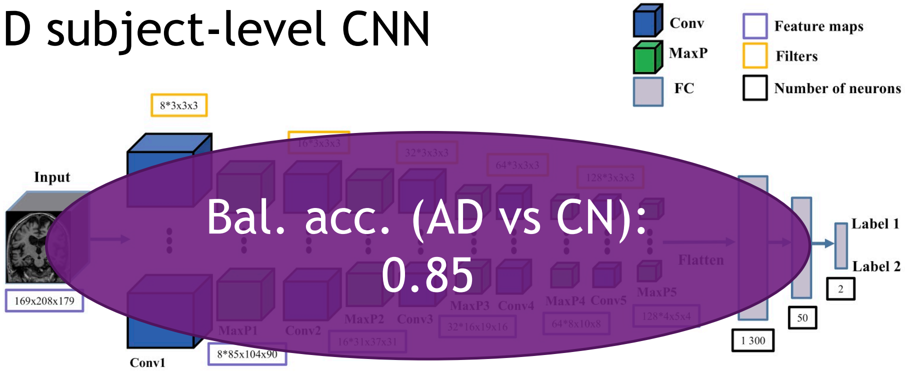


Wen, Thibeau-Sutre et al., arXiv:1904.07773 (under minor revision at Medical Image Analysis), 2019

Computer-aided diagnosis

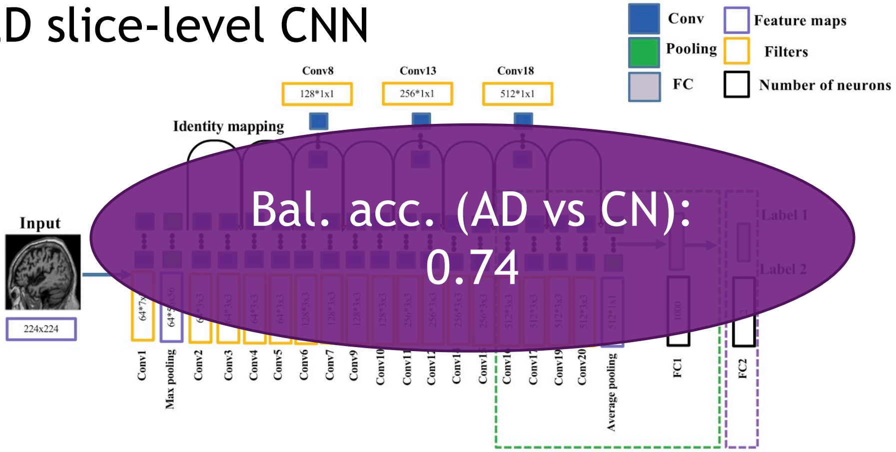
CNNs for Classification of Alzheimer's Disease: Overview and Reproducible Evaluation

3D subject-level CNN



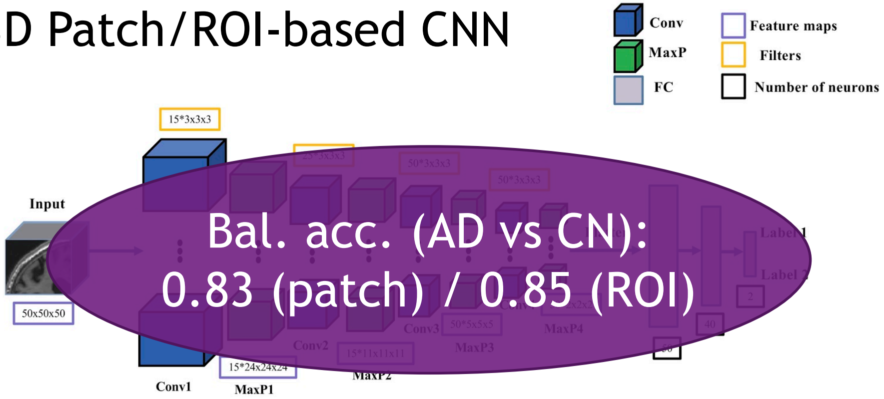
Bal. acc. (AD vs CN): 0.85

2D slice-level CNN



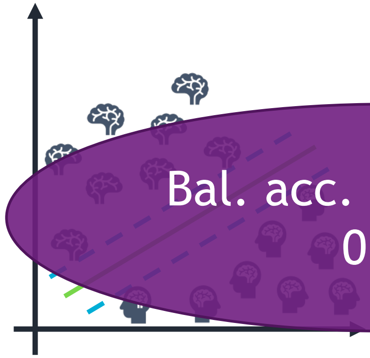
Bal. acc. (AD vs CN): 0.74

3D Patch/ROI-based CNN



Bal. acc. (AD vs CN): 0.83 (patch) / 0.85 (ROI)

SVM



Bal. acc. (AD vs CN): 0.87

Wen, Thibeau-Sutre et al., arXiv:1904.07773 (under minor revision at Medical Image Analysis), 2019

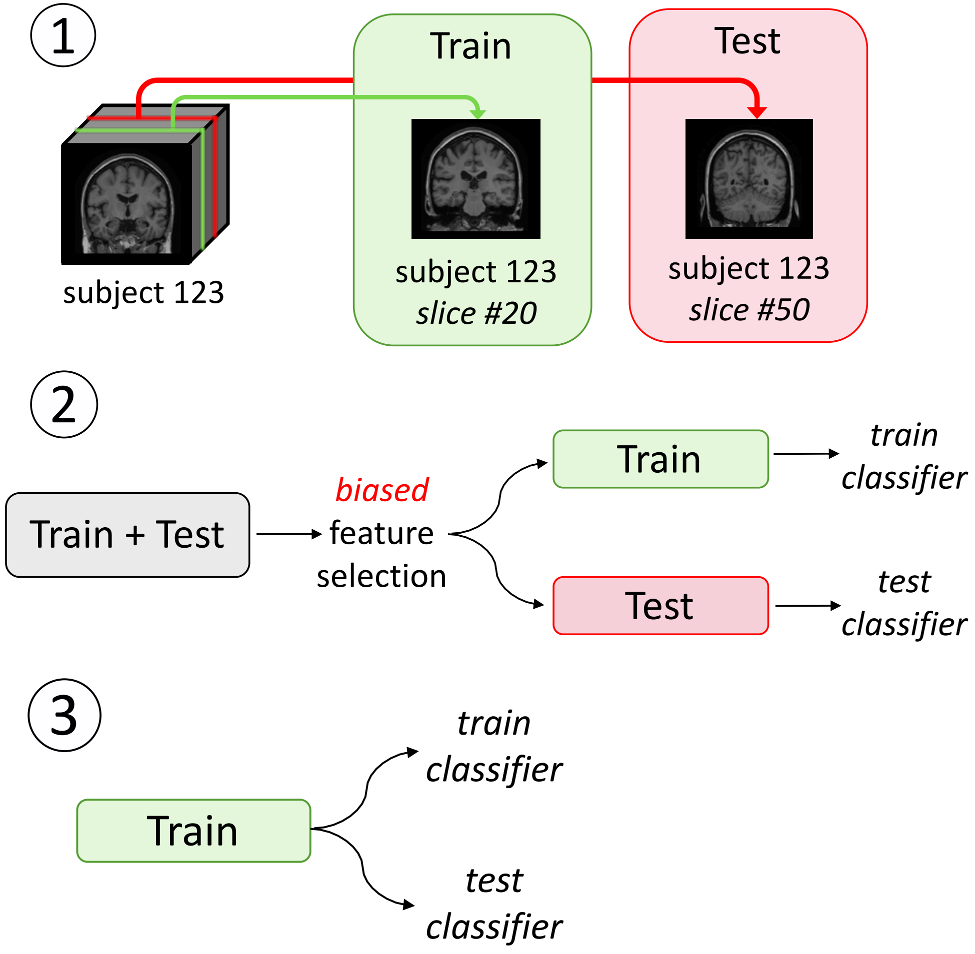
CNNs for Classification of Alzheimer's Disease: Overview and Reproducible Evaluation

3 categories identified:

1. **Biased split**
Data extracted from the same original is distributed in both the train and test sets

2. **Late split**
Test / train split is performed after another procedure (feature selection, pretraining, etc.)

3. **No independent test set**
Performance is evaluated on the train and / or validation sets



Wen, Thibeau-Sutre et al., arXiv:1904.07773 (under minor revision at Medical Image Analysis), 2019

Parenthesis on data leakage

CNNs for Classification of Alzheimer's Disease: Overview and Reproducible Evaluation

Study	Performance					Approach	Data leakage	Number of citations
	AD vs CN	sMCI vs pMCI	MCI vs CN	AD vs MCI	Multi-class			
(Aderghal et al., 2017b)	ACC=0.84	--	ACC=0.65	ACC=0.67†	--	ROI-based	None detected	16
(Aderghal et al., 2018)	BA=0.90	--	BA=0.73	BA=0.83	--	ROI-based	None detected	9
(Bäckström et al., 2018) *	ACC=0.90	--	--	--	--	3D subject-level	None detected	20
(Cheng et al., 2017)	ACC=0.87	--	--	--	--	3D patch-level	None detected	12
(Cheng and Liu, 2017)	ACC=0.85	--	--	--	--	3D subject-level	None detected	8
(Islam and Zhang, 2018)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	None detected	23
(Korolev et al. [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	72
(Li et al., [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	12
(Li et al., 2018)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	7
(Lian et al., 2018)	ACC=0.90	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	None detected	30
(Mingxia Liu et al., 2018a)	ACC=0.91	ACC=0.78†	--	--	--	3D patch-level	None detected	59
(Mingxia Liu et al., 2018c)	ACC=0.91	--	--	--	--	3D patch-level	None detected	26
(Qiu et al., 2018)	--	ACC=0.83†	--	--	--	2D slice-level	None detected	8
(Senanayake et al., 2018)	ACC=0.76	--	ACC=0.75	ACC=0.76	--	3D subject-level	None detected	3
(Shmulev et al., 2018)	--	ACC=0.62	--	--	--	3D subject-level	None detected	5
(Valliani and Soni, 2017)	ACC=0.81	--	--	--	ACC=0.57[2]	2D slice-level	None detected	8

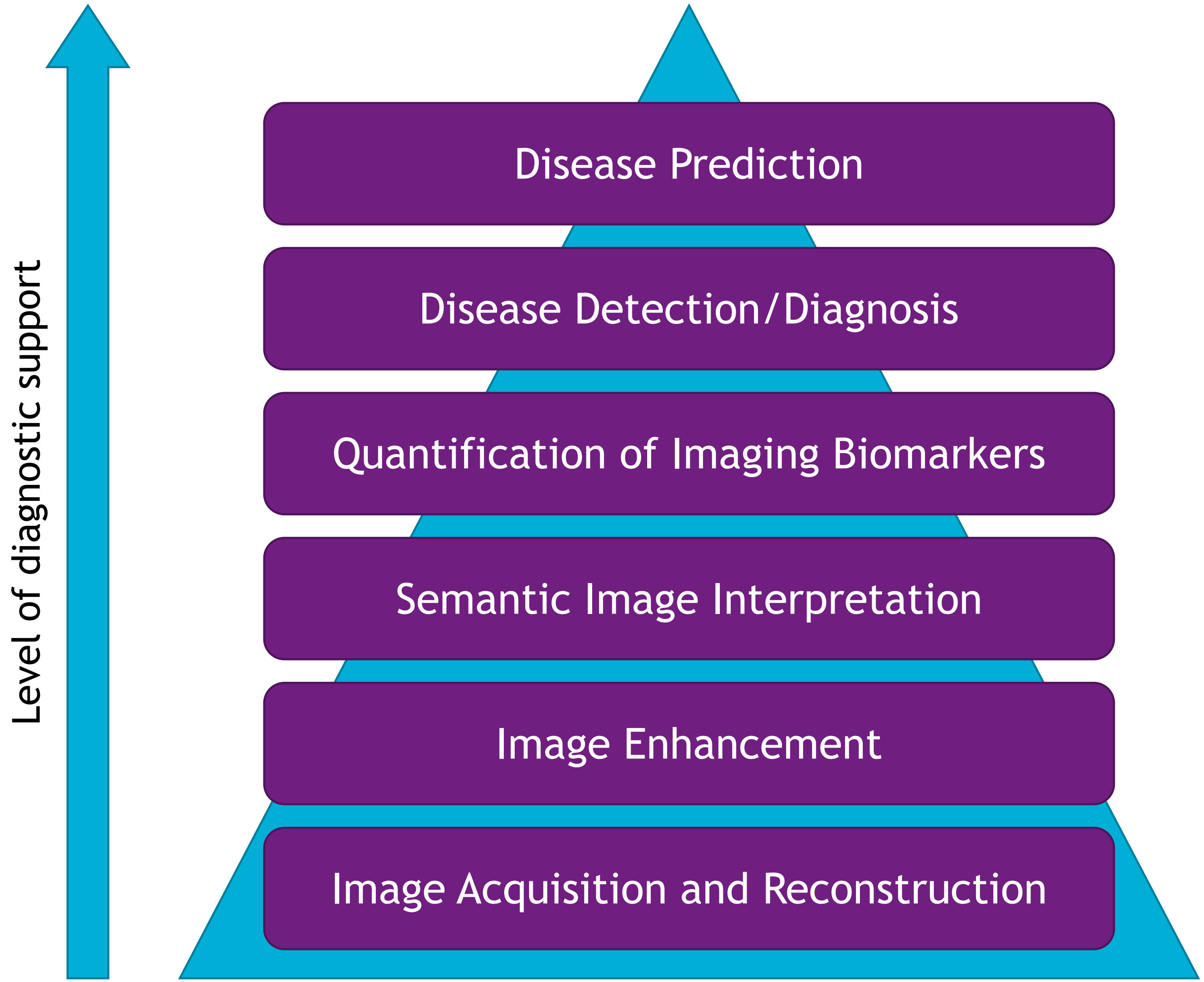
Average ACC (AD vs CN) :
86.4%

Study	Performance					Approach	Data leakage (type)	Number of citations
	AD vs CN	sMCI vs pMCI	MCI vs CN	AD vs MCI	Multi-class			
(Aderghal et al., 2017a)	ACC=0.91	--	ACC=0.66	ACC=0.70	--	ROI-based	Unclear (b,c)	13
(Basaia et al., 2019)	BA=0.99	BA=0.75	--	--	--	3D subject-level	Unclear (b)	25
(Hon and Khan, 2017)	ACC=0.96	--	--	--	--	2D slice-level	Unclear (a,c)	32
(Hosseini Asl et al., 2018)	ACC=0.99	--	ACC=0.94	ACC=1.00	ACC=0.95[2]	3D subject-level	Unclear (a)	107
(Islam and Zhang, 2017)	--	--	--	--	ACC=0.74[1]†	2D slice-level	Unclear (b,c)	23
(Lin et al., 2018)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Unclear (b)	22
(Manhua Liu et [illegible] 2018 [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	39
(Taqi et a [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	16
(Vu et al., 2017)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	20
(S.-H. Wang et al., 2018)	ACC=0.98	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Unclear (b)	49
(Bäckström et al., 2018)*	ACC=0.99	--	--	--	--	3D subject-level	Clear (a)	20
(Farooq et al., 2017)	--	--	--	--	ACC=0.99[3]†	2D slice-level	Clear (a,c)	31
(Gunawardena et al., 2017)	--	--	--	--	ACC=0.96[2]	3D subject-level	Clear (a,b)	8
(Vu et al., 2018)	ACC=0.86	--	ACC=0.86	ACC=0.77	ACC=0.80[2]	3D subject-level	Clear (a,c)	8
(Wang et al., 2017)	--	--	ACC=0.91	--	--	2D slice-level	Clear (a,c)	11
(Wang et al., 2019)	ACC=0.99	--	ACC=0.98	ACC=0.94	ACC=0.97[2]	3D subject-level	Clear (b)	17
(Wu et al., 2018)	--	--	--	--	0.95[4]†	2D slice-level	Clear (a,b)	7

Average ACC (AD vs CN) :
93.8%

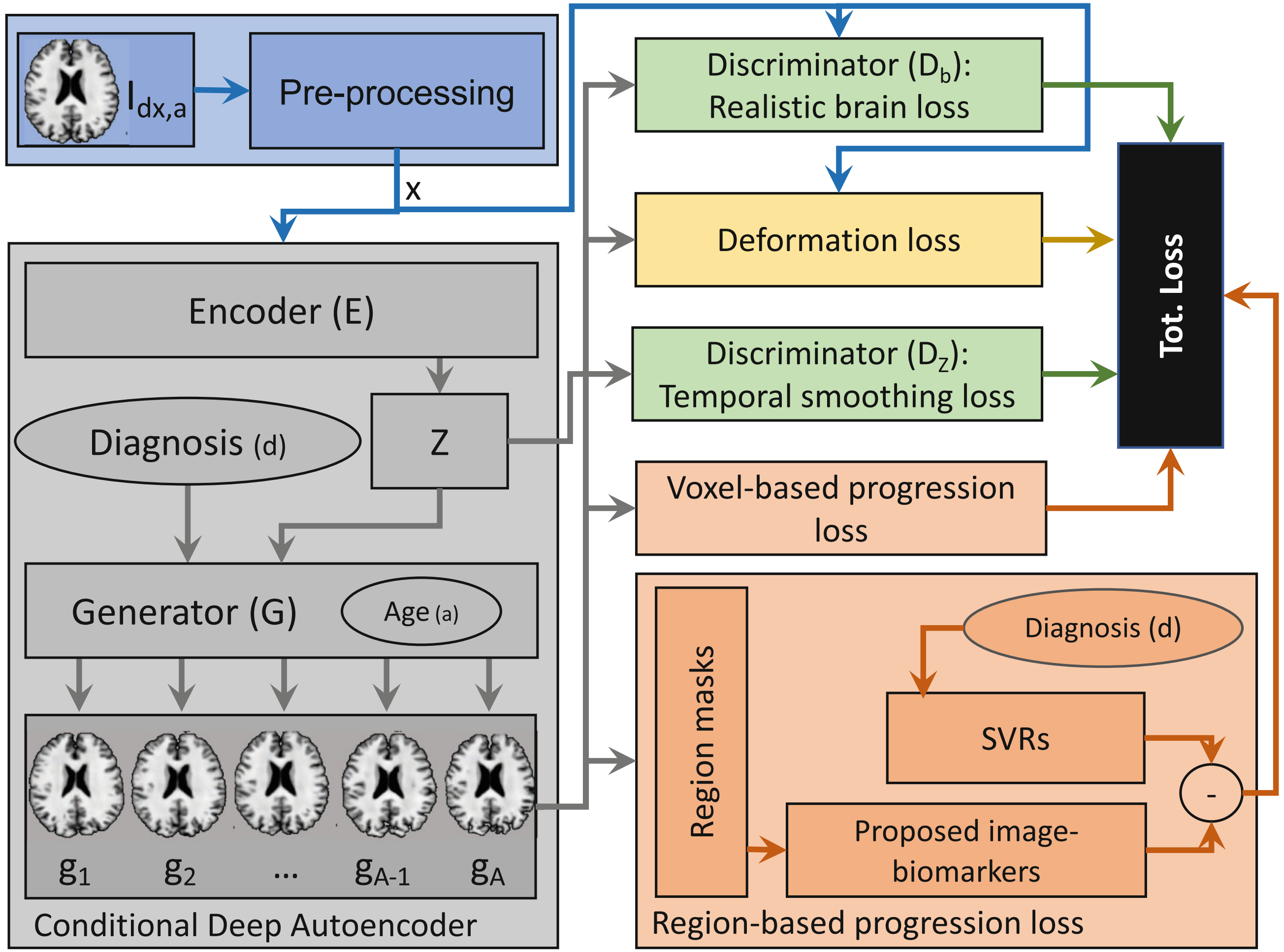
Wen, Thibeau-Sutre et al., arXiv:1904.07773 (under minor revision at Medical Image Analysis), 2019

Computer-aided neuro(radio)logy



Simulation of disease progression

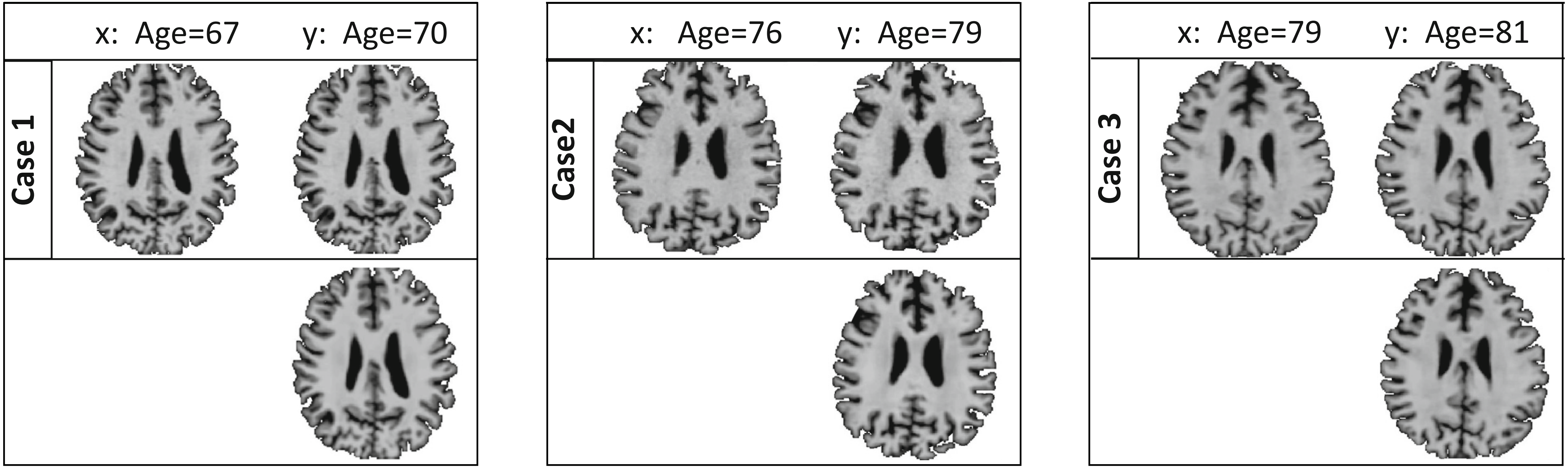
Degenerative Adversarial NeuroImage Nets: Generating Images that Mimic Disease Progression



Ravi et al., MICCAI, 2019

Simulation of disease progression

Degenerative Adversarial NeuroImage Nets: Generating Images that Mimic Disease Progression



Ravi et al., MICCAI, 2019

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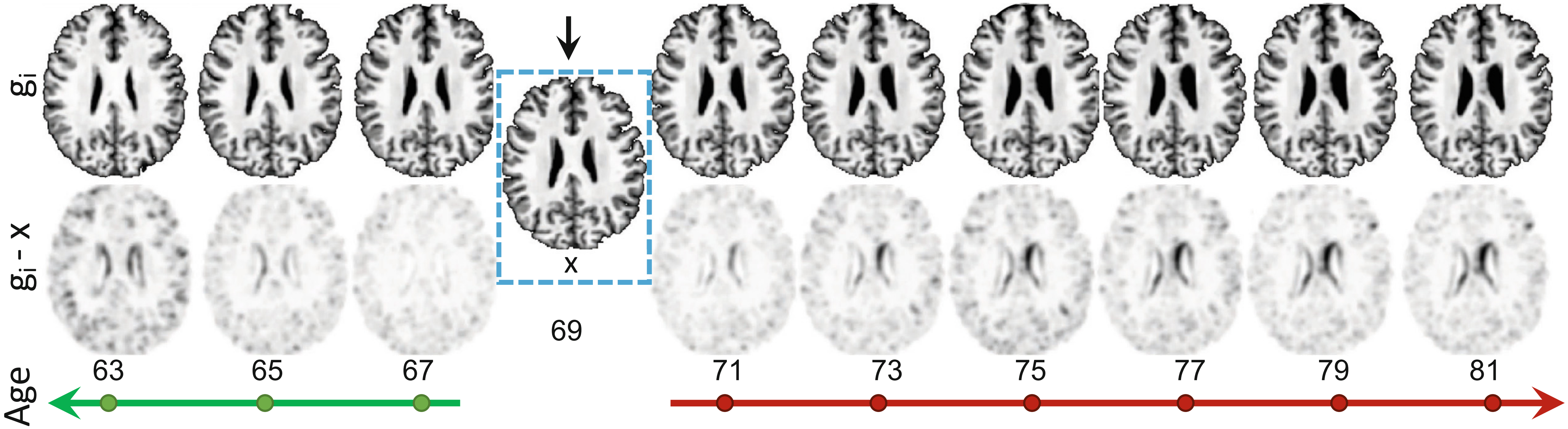

Neurodegeneration simulation of a 69-year old ADNI participant

Ravi et al., MICCAI, 2019

Computer-aided neuro(radio)logy