Deep Learning based Iterative PET Image Recon:

Populational vs Personalize

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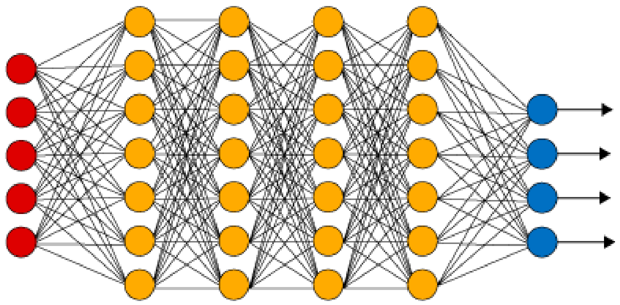
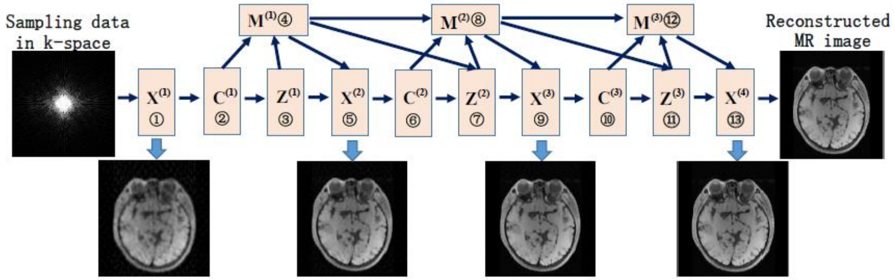
Introduction - Deep Neural Networks



Applications of deep learning in medical imaging

- Reconstruction



Sun, Jian, et al. "Deep ADMM-net for compressive sensing MRI." *Advances in Neural Information Processing Systems*. 2016.

- **Strong expression power**
  - **Good approximation of most complicated functions**

- Supervised Learning (pop)
  - Large Training Data with Labels
  - Annotation is bottle neck
- Unsupervised Learning
  - Large Training Data without Label (pop)
  - Single Training Data (same subject) w/o Label
- Semi-supervised Learning

- Structure
  - ResiNET
  - U-NET

- Not Covered
  - MRI/CT
  - System modeling
  - PET corrections (Attn, Scatters)

Introduction – Image Reconstruction

$$L(y\,|\,x)=\sum_{i=1}^{N} y_i \log([Px]_i + r_i + s_i) - ([Px]_i + r_i + s_i)$$

Data Model

$$P(x)=\frac{1}{Z}e^{-\beta U(x)}$$

Image Model

Cost Function MAP

$$\Phi(x,y)=L(y\,|\,x)-\beta U(x)$$

System Model

$$y=\mathbf{P}x$$

$$\mathbf{P}=\mathbf{P}_{norm}\mathbf{P}_{blur}\mathbf{P}_{attn}\mathbf{P}_{geom}\mathbf{P}_{range}$$

Optimization Algorithms

- OSEM
- Modified BSREM
- Relax OS-SPS
- PCG

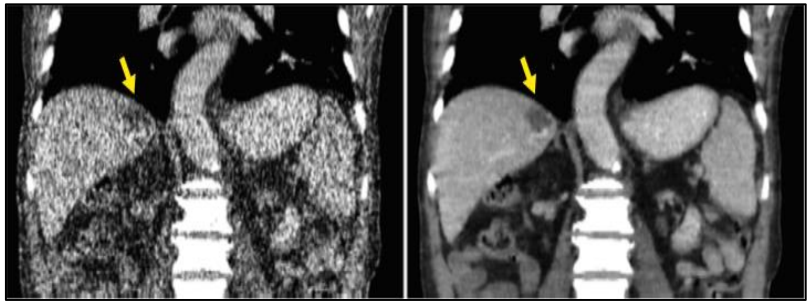
Statistical PET Reconstruction

Outline

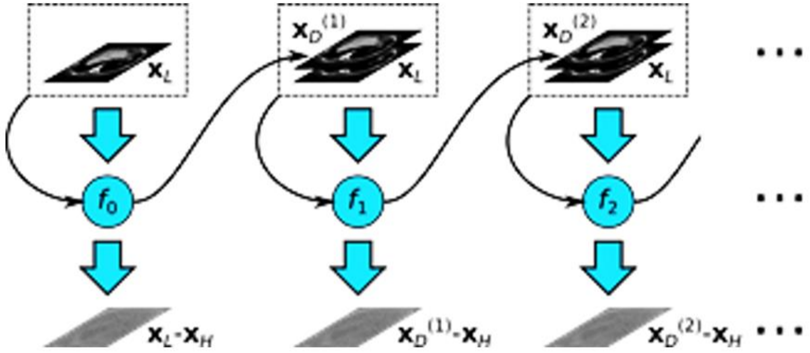
- Population based methods:
  - DL in penalty function
  - Kernel based method
- Personalized methods
  - Conditional deep image prior
    - Denoising
    - Static and parametric image recon
  - Noise2noise
    - Denoising
    - Static image recon
- Population based + Personalized

DL based PET Recon

- To improve PET image quality, various penalized methods have been proposed (Gindi *et al* 1993, Somayajula *et al* 2011)
- Convolutional neural networks (CNNs) are effective methods to improve medical image quality
  - Denoising (Chen *et al* 2017, Kang *et al* 2017)
    - *Cons: Smoothing out image details*
  - Plug-and-play or Unrolling (Venkatakrishnan *et al* 2013, Sun *et al* 2016, Diamond *et al 2017*)
    - *Cons: Time consuming in training*
  - Penalized reconstruction (Wu *et al* 2018, Kim *et al* 2018)
    - *Cons: Adjusting penalty parameter*



AAPM-net



➢ ***Noise levels in training & testing should be the same***

Preliminary reconstruction tests

- We first tried…

$$L(x) + \frac{\beta}{2}||x - x^D||^2 \le \boxed{\phi_L^{(n)}(x; x^n)} + \frac{\beta}{2}||x - \boxed{x^D}||^2$$

Majorizer by SQS

DnCNN image

1. Calculate x^D once from x^0 (OSEM image)
   - Guarantee convergence
   - No improvement compared to denoising
2. Calculate $x^D = DnCNN(x^n)$ in iteration
   - After certain # iterations, image suddenly get blurred significantly (out of noise boundary)

➡ ***Bias is significantly increased***

Local linear fitting

- Local linear fitting (LLF): patch based linear fitting

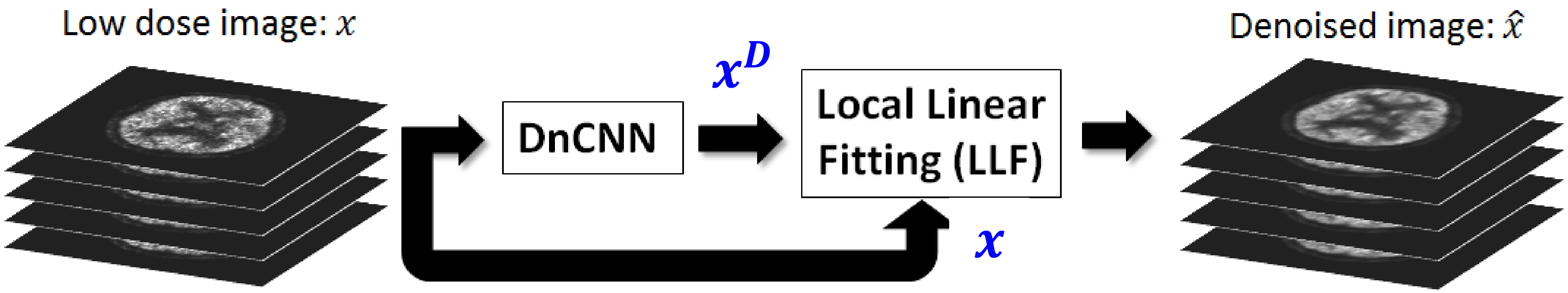
$$\hat{x}_k = q_i x_k^D + b_i, \forall k \in \boxed{p_i},$$

Patch with center pixel i

- ➢ ***Cost function***

$$E(q_i, b_i) = \sum_{k \in p_i} \left((q_i x_k^D + b_i - x_k)^2 + \epsilon q_i^2 \right)$$

Iterative reconstruction

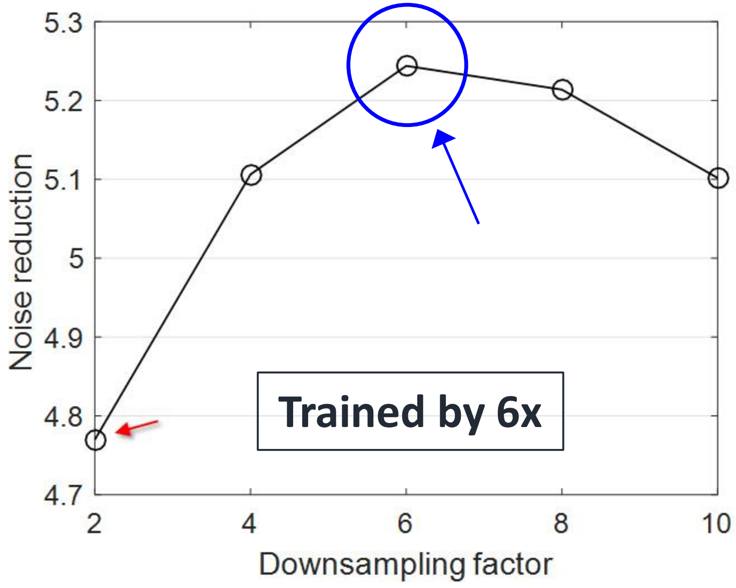


Cost function is the same as Guided filtering (K. He, 2013)

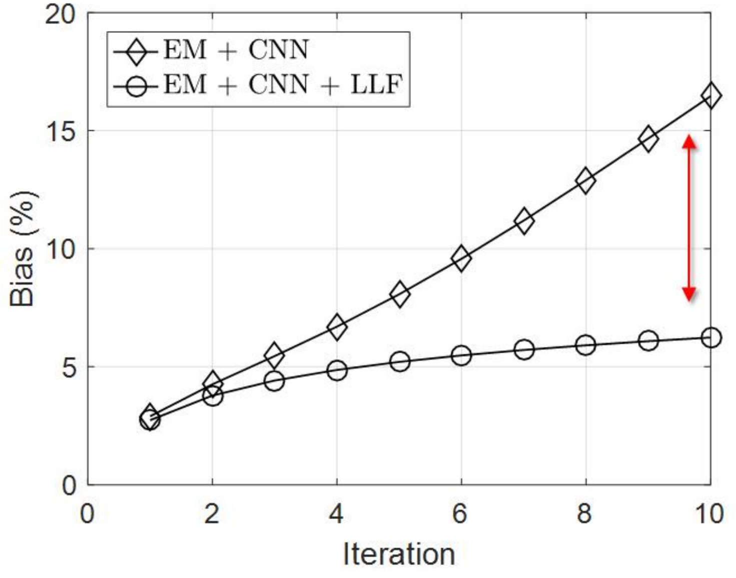
K. Kim, ... Q. Li, IEEE Transactions on Medical Imaging, vol. 37, pp 1478-1487, 2018

Simulation results

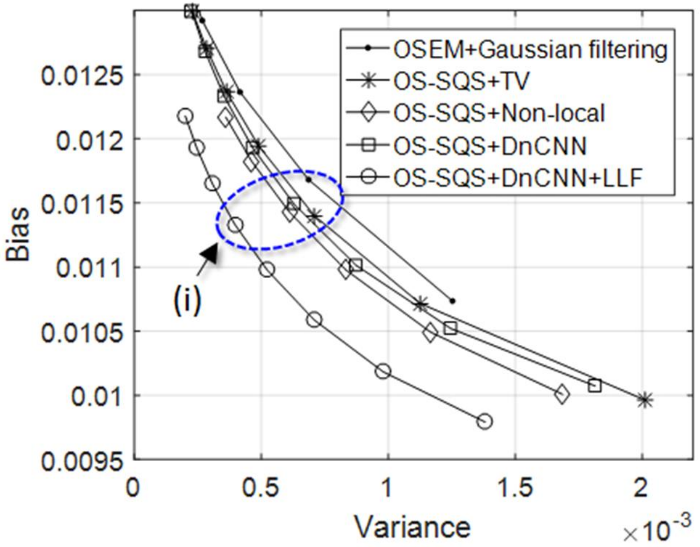
(a)



(b)



(c)



(a) Performance comparison of noise reduction for different downsampling datasets. (Network trained by 6x data)

(b) Bias increase by iteration

(c) Bias and variance graph

LLF significantly reduce bias!

K. Kim, ... Q. Li, IEEE Transactions on Medical Imaging, vol. 37, pp 1478-1487, 2018

Image comparison (HRRT FDG)

Full dose
(185 MBq)

Low dose
(10x)

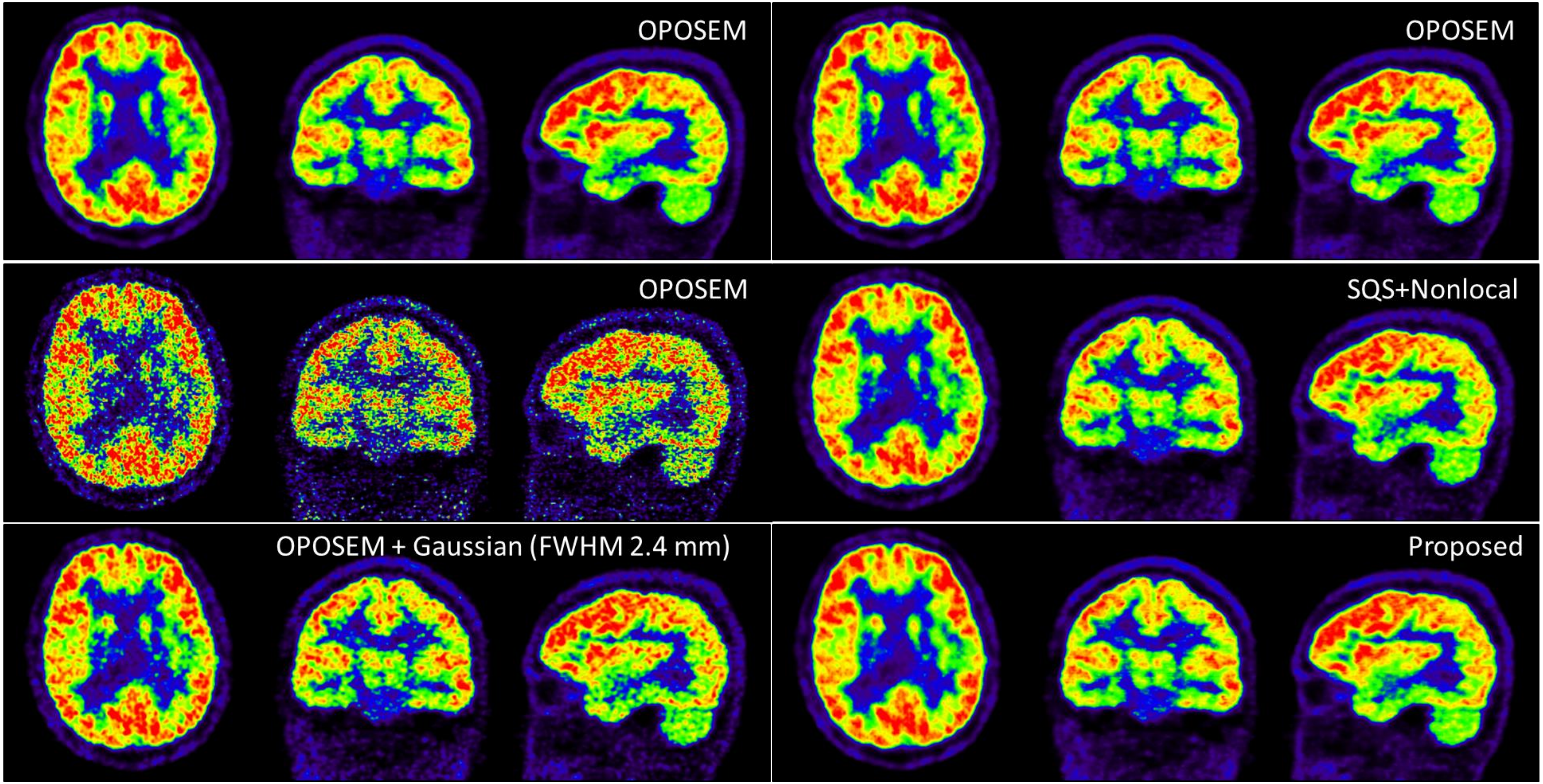


Image Model

- For image reconstruction inverse problems,

$$\boldsymbol{y} = \boldsymbol{P}\boldsymbol{x} + \boldsymbol{r}$$

- Change $\boldsymbol{x}$ to be the output of a network $f(\boldsymbol{z}|\boldsymbol{\theta})$,

$$\boldsymbol{y} = \boldsymbol{P} f(\boldsymbol{z}|\boldsymbol{\theta}) + \boldsymbol{r}$$

  - $\boldsymbol{z}$ is the input to the network, *unknown parameters*.
  - $\boldsymbol{\theta} = [\boldsymbol{w}, \boldsymbol{b}]$ are the parameters of the network, pre-trained using low-dose and high-does pairs.

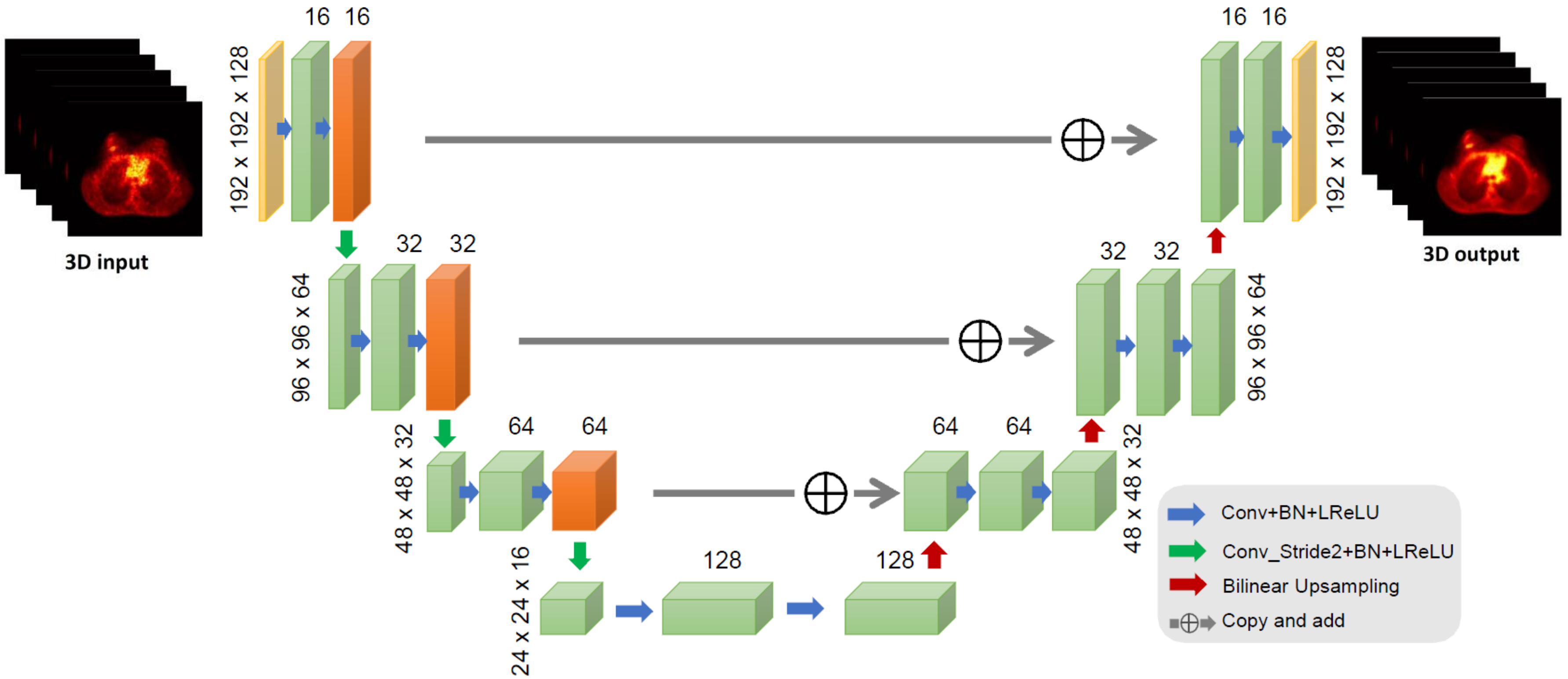
- Based on the distribution of the measurement data,

$$\hat{\boldsymbol{z}} = \arg\max_{\boldsymbol{z}} L(\boldsymbol{y}|f(\boldsymbol{z}|\boldsymbol{\theta})) \tag{1}$$

  - Directly optimizing (1) is difficult as the projector is coupled with network output

K. Gong, …, Q. Li, IEEE transactions on medical imaging 38 (3), 675-685

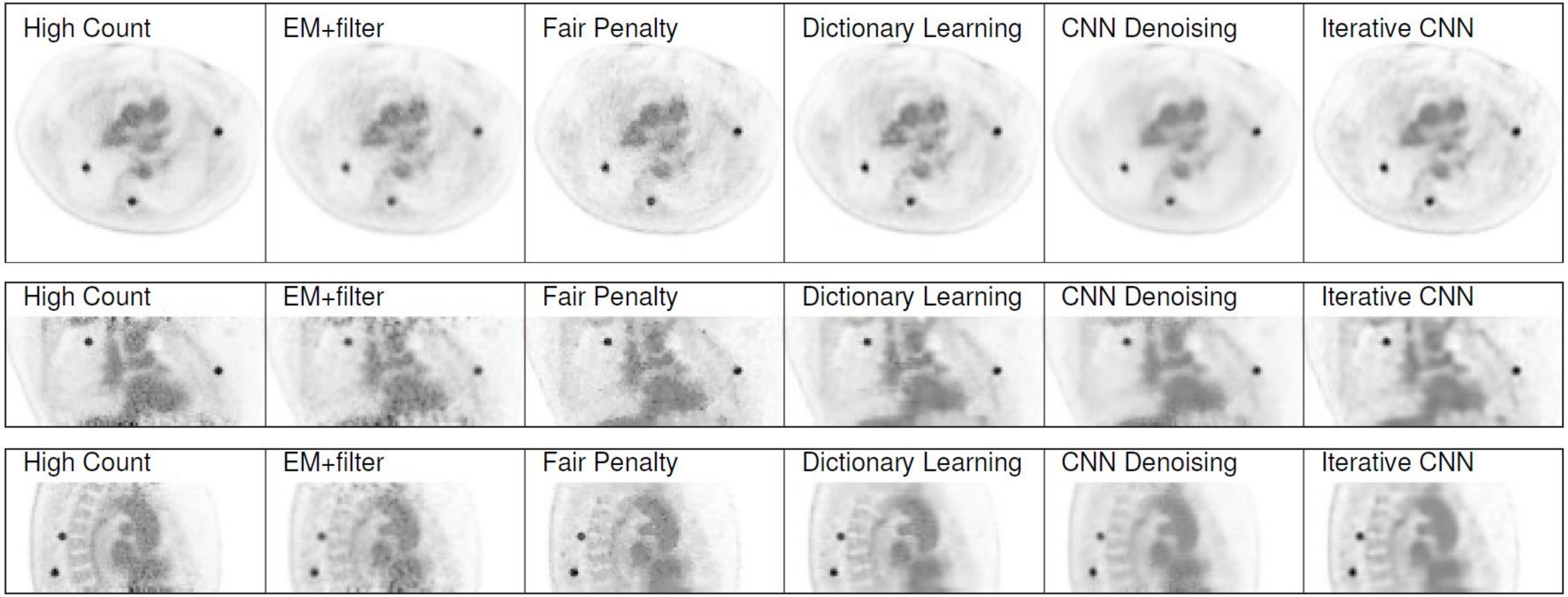
Network Structure



- 3D U-net was employed as the network structure, pretrained using high-quality training pairs.

K. Gong, …, Q. Li, IEEE transactions on medical imaging 38 (3), 675-685

Result: lung dataset

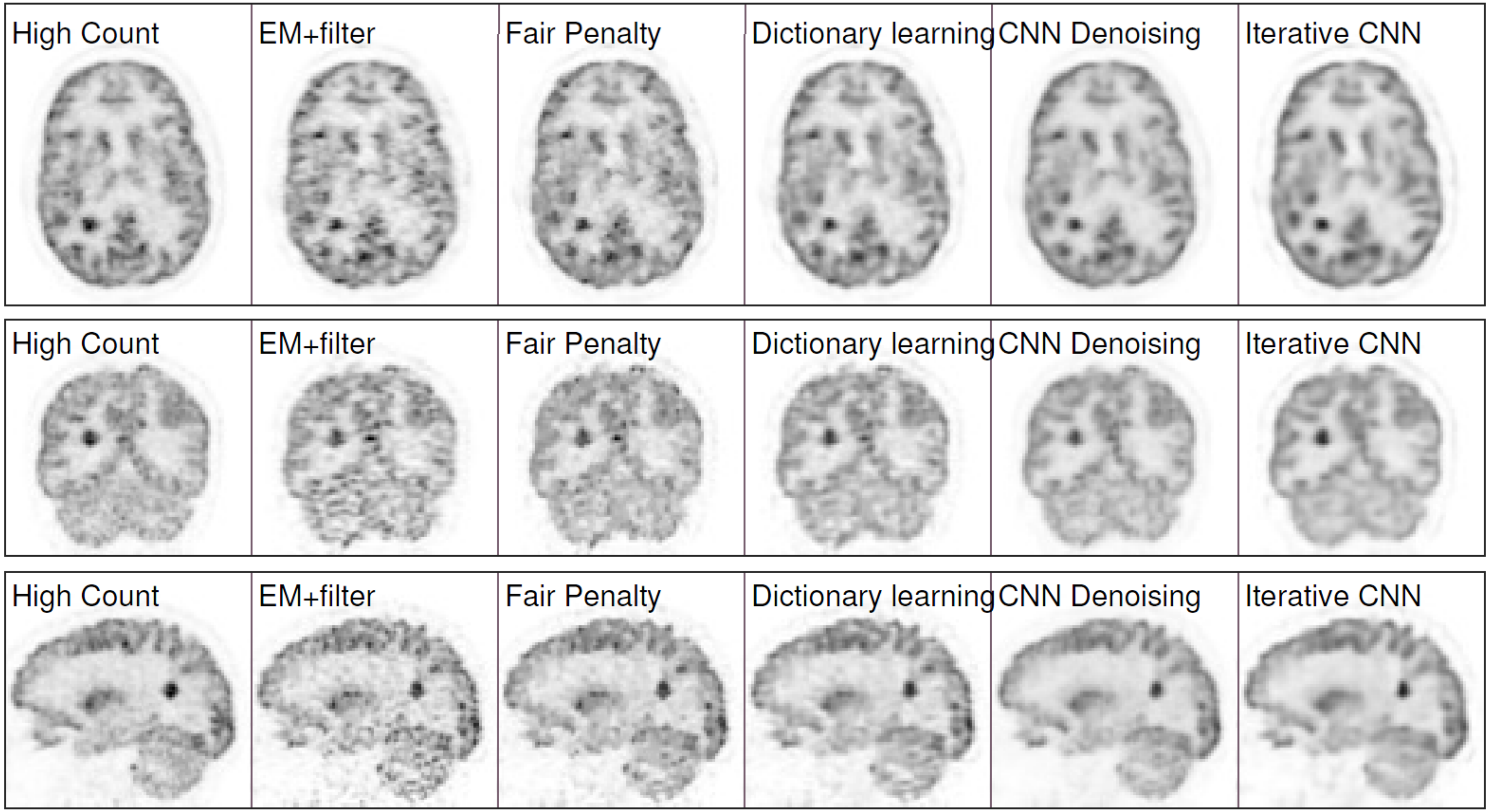


- Proposed Iterative CNN can have *higher uptake* in synthetic tumor and *lower noise*
  - Acquired from GE Discovery 690 PET-CT

K. Gong, …, Q. Li, IEEE transactions on medical imaging 38 (3), 675-685

Result: brain datasets

- Acquired from GE Signa PET-MR



- Proposed Iterative CNN can have *higher uptake* in synthetic tumor and *lower noise*

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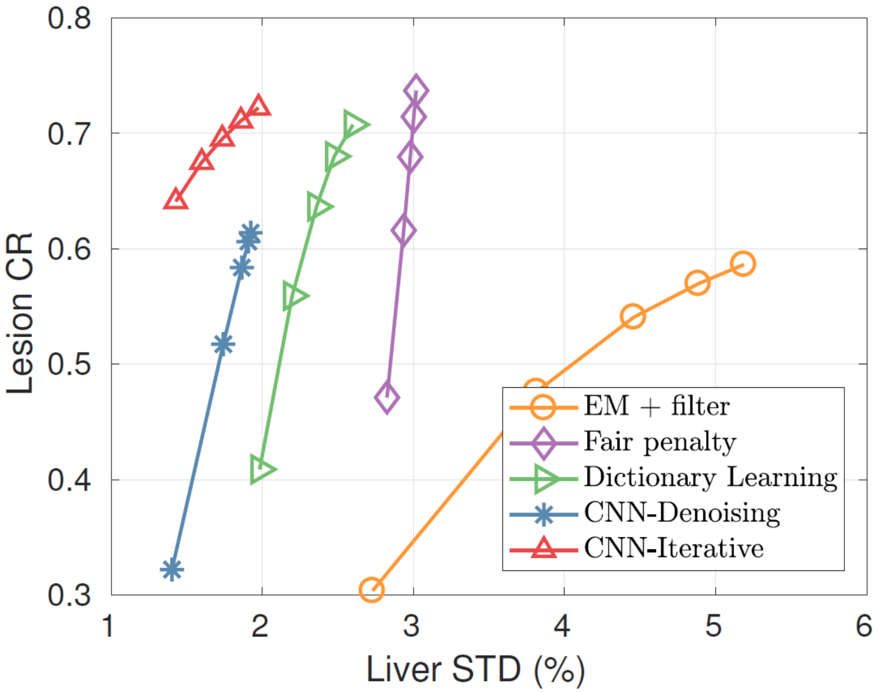
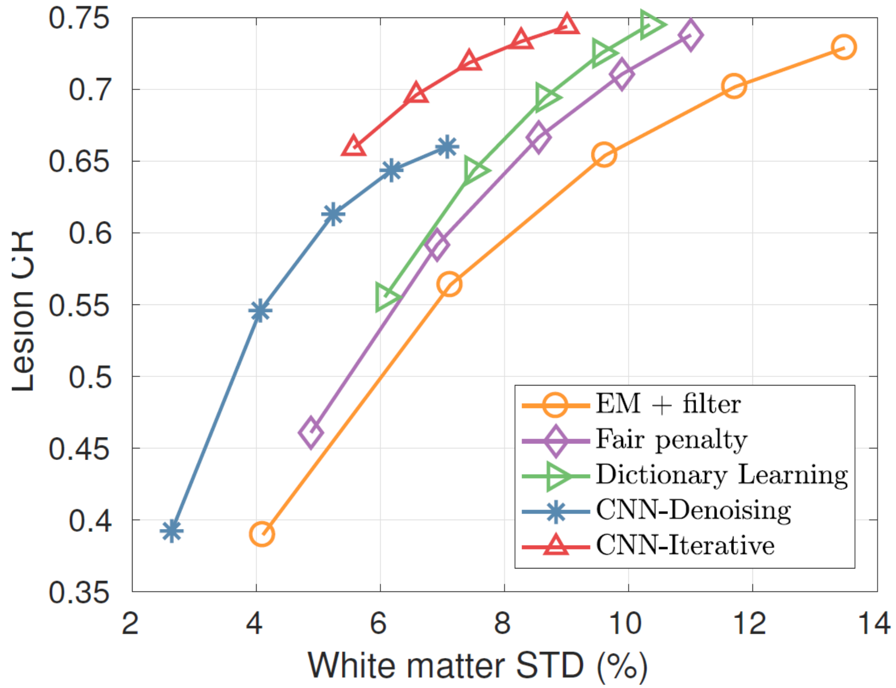
Result: quantification

Lung data set



Brain data set



- Proposed Iterative CNN can have *better quantification* regarding bias-variance trade-off.

K. Gong, …, Q. Li, IEEE transactions on medical imaging 38 (3), 675-685

Outline

- Population based methods:
  - DL in penalty function
  - Kernel based method
- Personalized methods
  - Conditional deep image prior
    - Denoising
    - Static and parametric image recon
  - Noise2noise
    - Denoising
    - Static image recon
- Population based + Personalized

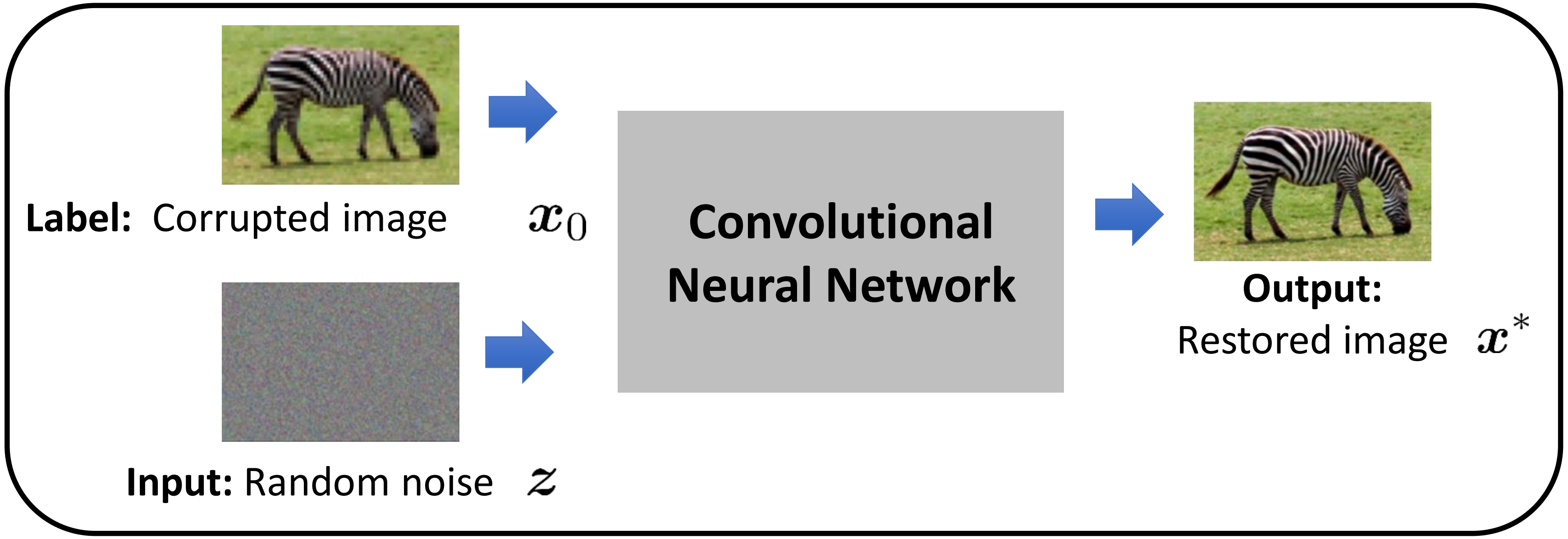
Method: Deep Image Prior

- Deep image prior framework (*Ulyanov et al 2017*) shows that CNN can *learn intrinsic structures* from corrupted images.

- It tries to restore clean image from its corrupted version by only *employing random noise as network input.*

$$\underbrace{\boldsymbol{\theta}^*}_{} = \arg\min_{\boldsymbol{\theta}} \|\boldsymbol{x}_0 - f(\boldsymbol{\theta}|\boldsymbol{z})\|^2 \qquad \boldsymbol{x}^* = f(\boldsymbol{\theta}^*|\boldsymbol{z})$$

Corrupted image *Network parameters* *Network input* *Restored image*



K. Gong, ... Q. Li, IEEE Transactions on Medical Imaging, Dec, 2018

Proposed Method

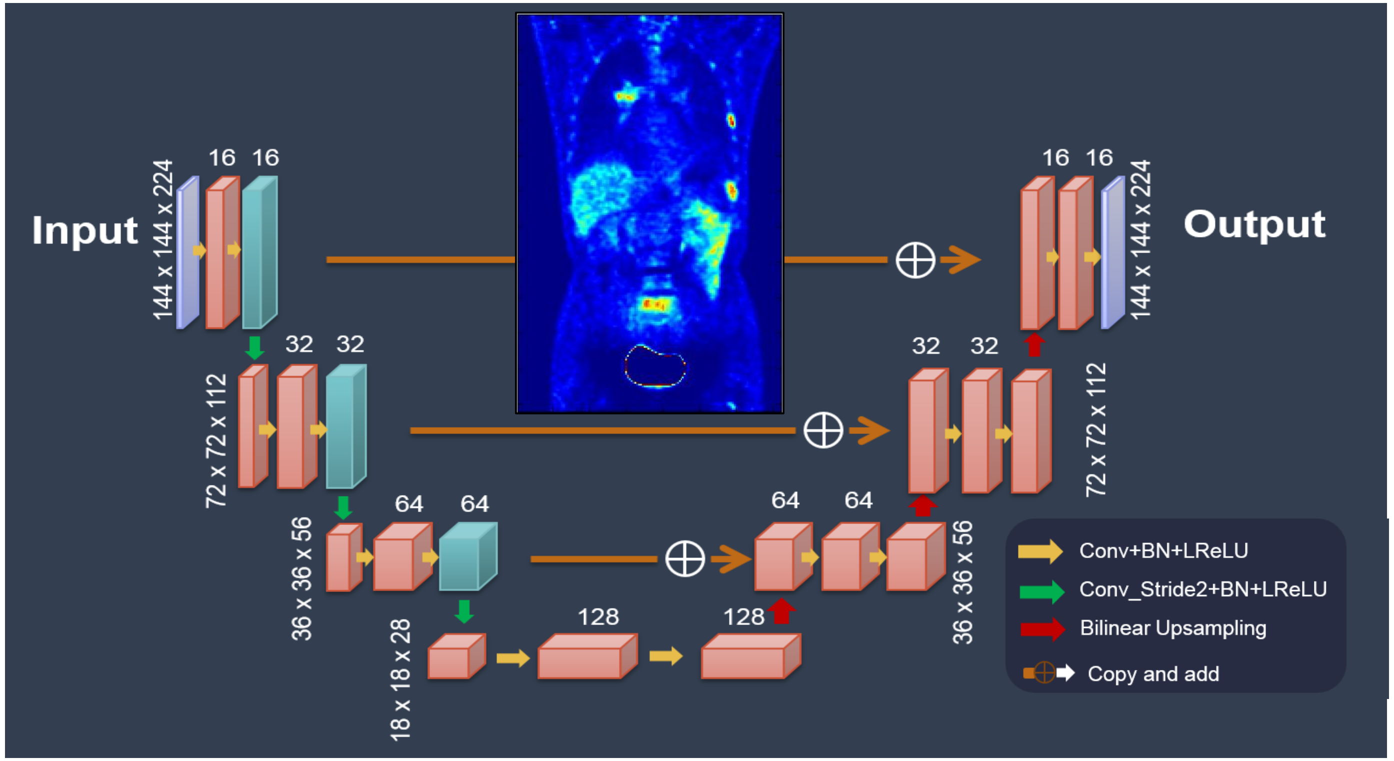
- Denoising process :

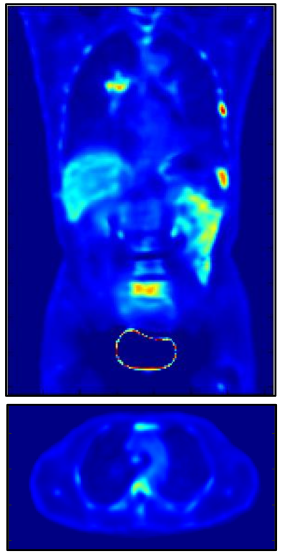
$$\hat{\theta} = arg\min_{\theta} \|x_0 - f(\theta|z)\|$$

$$\hat{x} = f(\hat{\theta}|z)$$

- $f(\theta|z)$: untrained modified 3D Unet[2]
- $\hat{\theta}$: network parameters
- z: input (**co-registered CT/MR image**)
- x_0: noisy PET image (training label)
- $\hat{x}$: denoised PET image

CT/MR image
144×144×224
Z





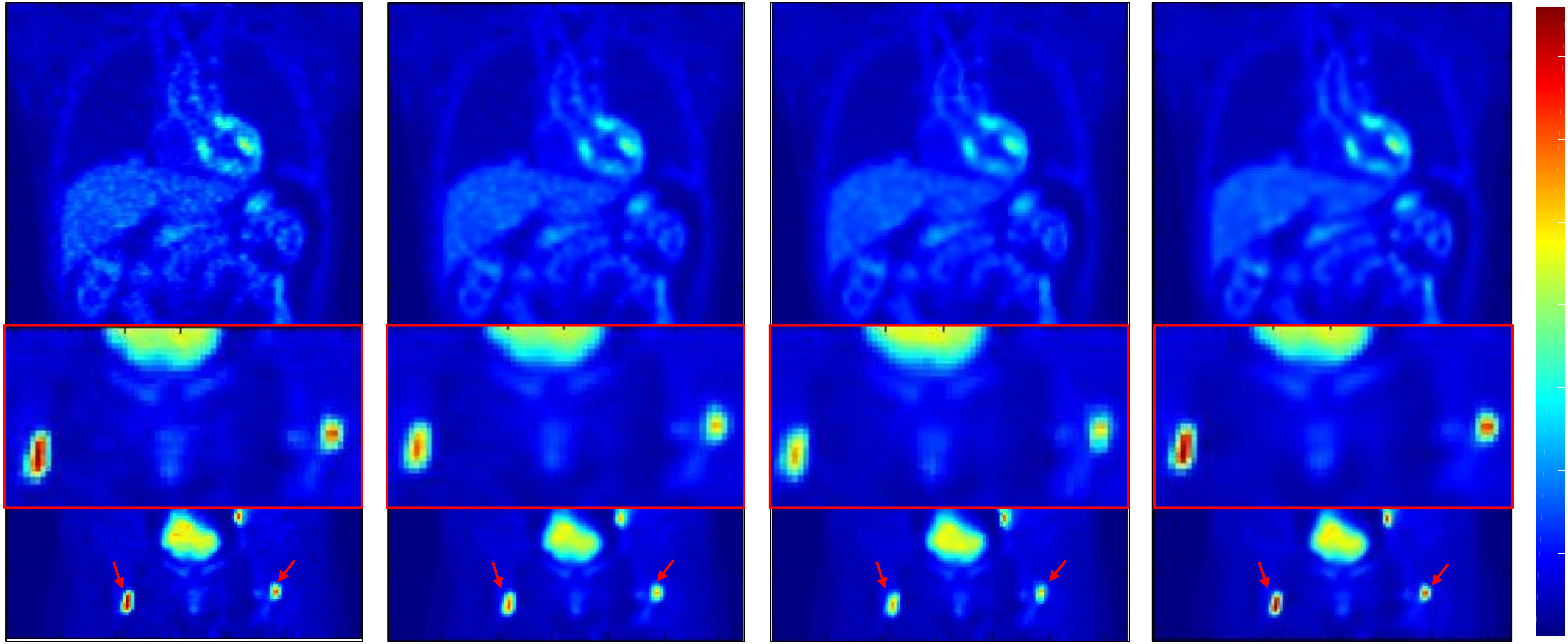
Denoised PET image
144×144×224

Optimization algorithm: L-BFGS

[2] Çiçek, Özgün, et al. "3D U-Net: learning dense volumetric segmentation from sparse annotation." International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, Cham, 2016.

J. Cui, ..., Q. Li, IEEE MIC 2018

Results-PET/MR



Noisy PET

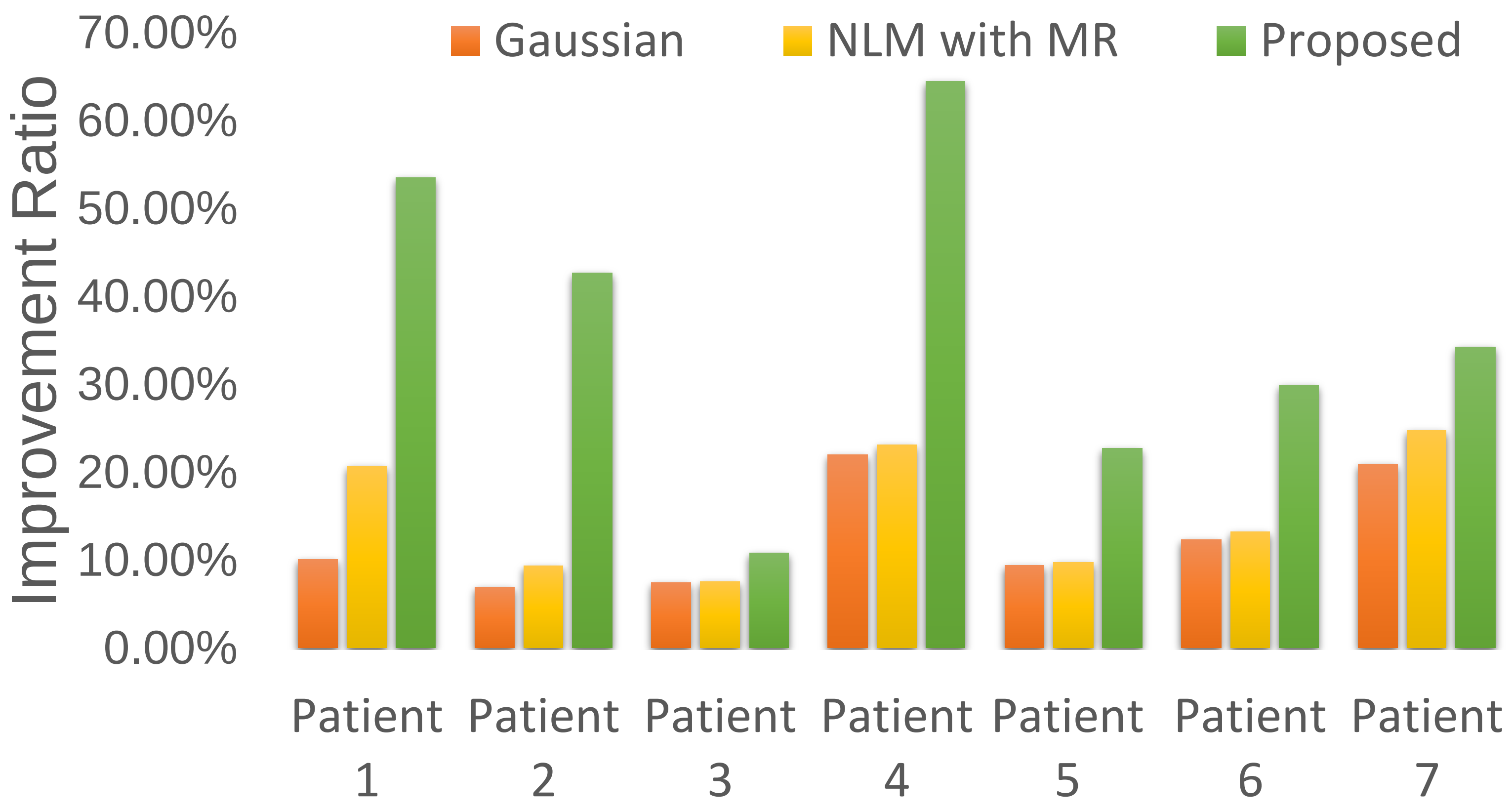
Gaussian
FWHM = 0.7

NLM with CT
window size:
3×3×3

Proposed
700 epochs

J. Cui, ..., Q. Li, IEEE MIC 2018

Results - CNR improvement ratio



CNR improvement ratios for 7 patients data sets

J. Cui, ..., Q. Li, IEEE MIC 2018

Image Model

- For image reconstruction inverse problems,

$$\boldsymbol{y} = \boldsymbol{P}\boldsymbol{x} + \boldsymbol{r}$$

- Change $\boldsymbol{x}$ to be the output of a network $f(\boldsymbol{z}|\boldsymbol{\theta})$,

$$\boldsymbol{y} = \boldsymbol{P} f(\boldsymbol{z}|\boldsymbol{\theta}) + \boldsymbol{r}$$

  - $\boldsymbol{z}$ is the input to the network. Here we use prior information as input.
  - $\boldsymbol{\theta} = [\boldsymbol{w}, \boldsymbol{b}]$ are the parameters of the network.

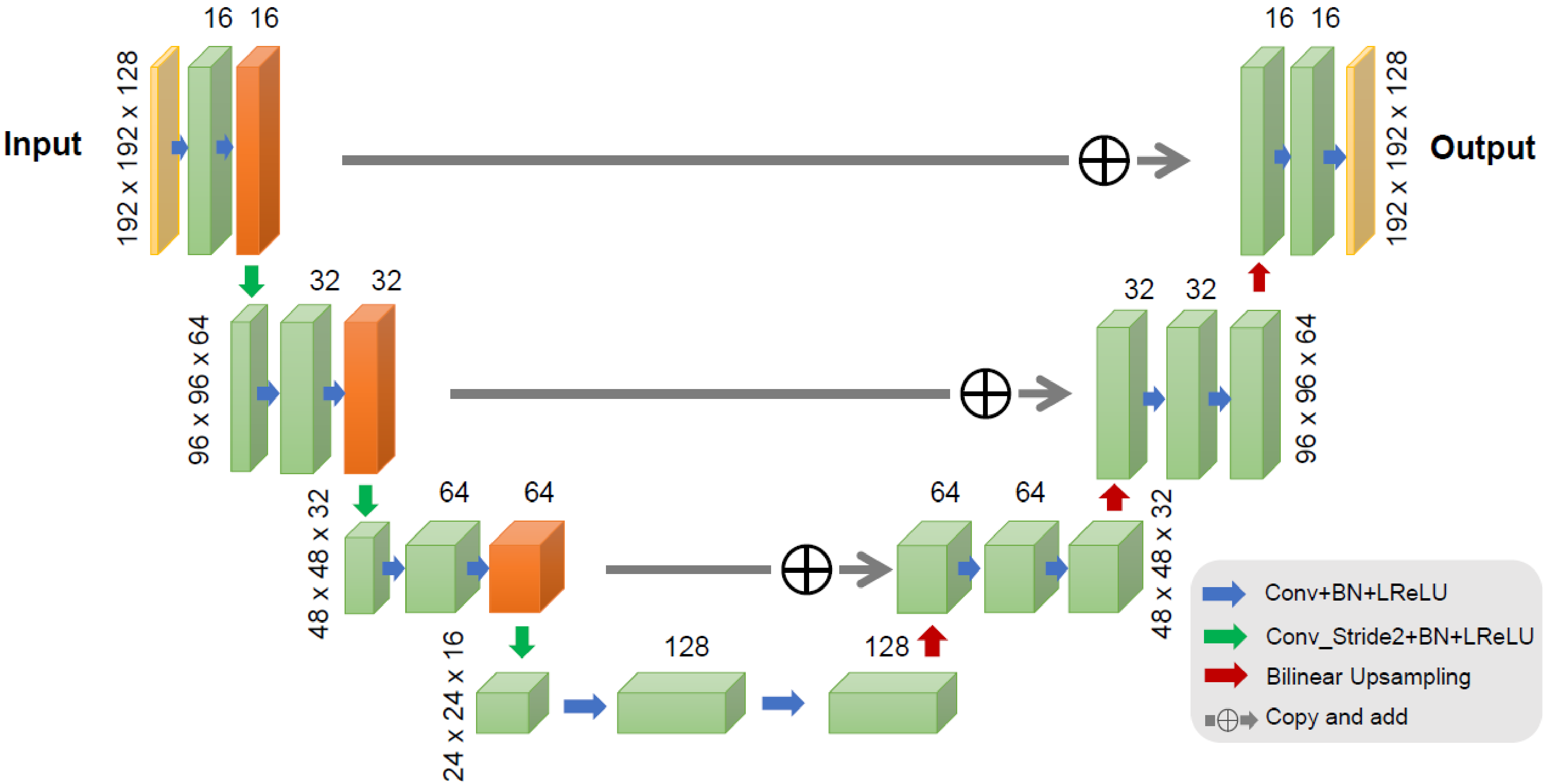
- Based on the distribution of the measurement data,

$$\hat{\boldsymbol{\theta}} = \arg\max_{\boldsymbol{\theta}} L(\boldsymbol{y}|f(\boldsymbol{z}|\boldsymbol{\theta})) + R(\boldsymbol{\theta}) \tag{1}$$

- Directly optimizing (1) is difficult as the projector is coupled with network output

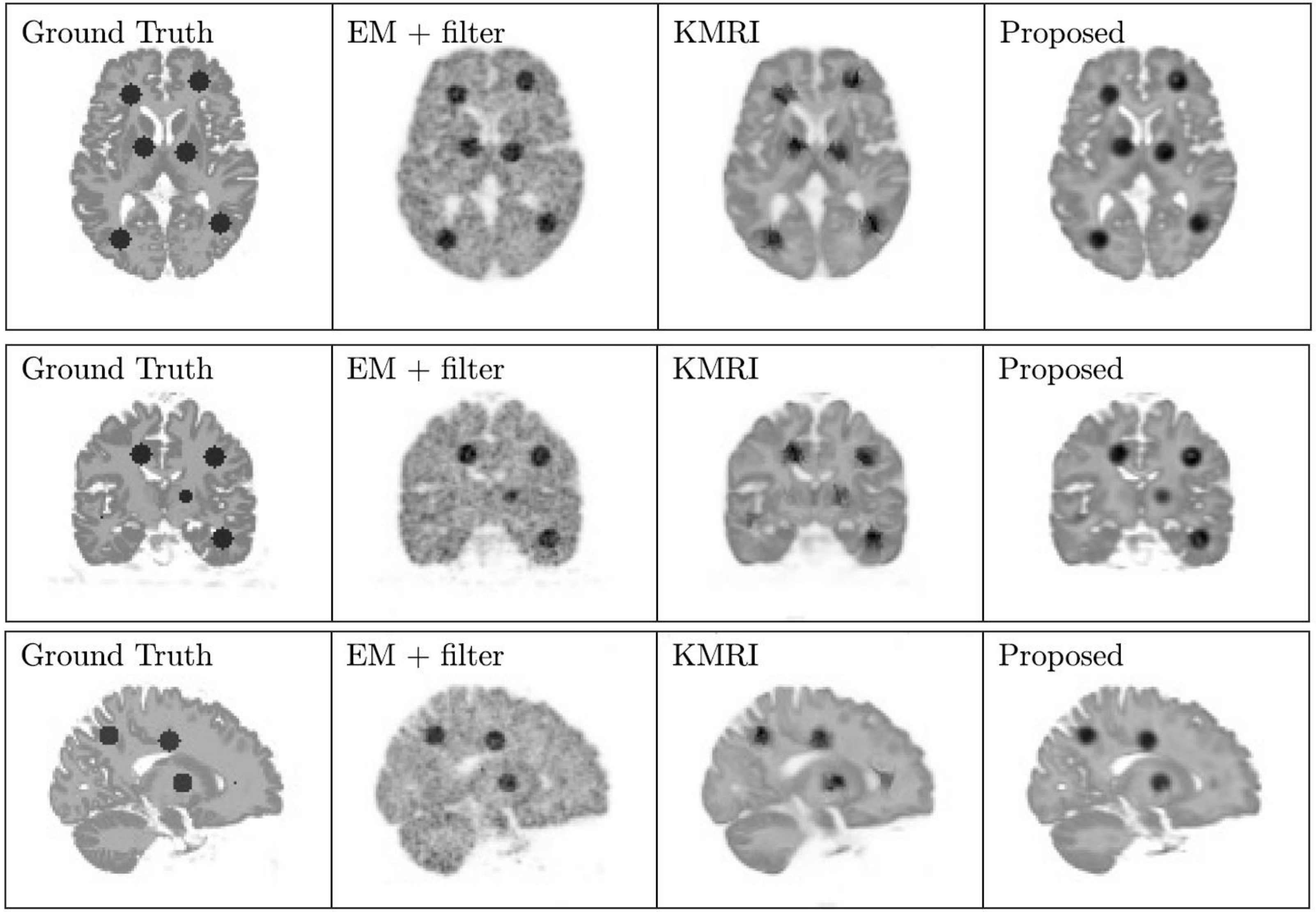
K. Gong, ... Q. Li, IEEE Transactions on Medical Imaging, Dec, 2018

Network Structure



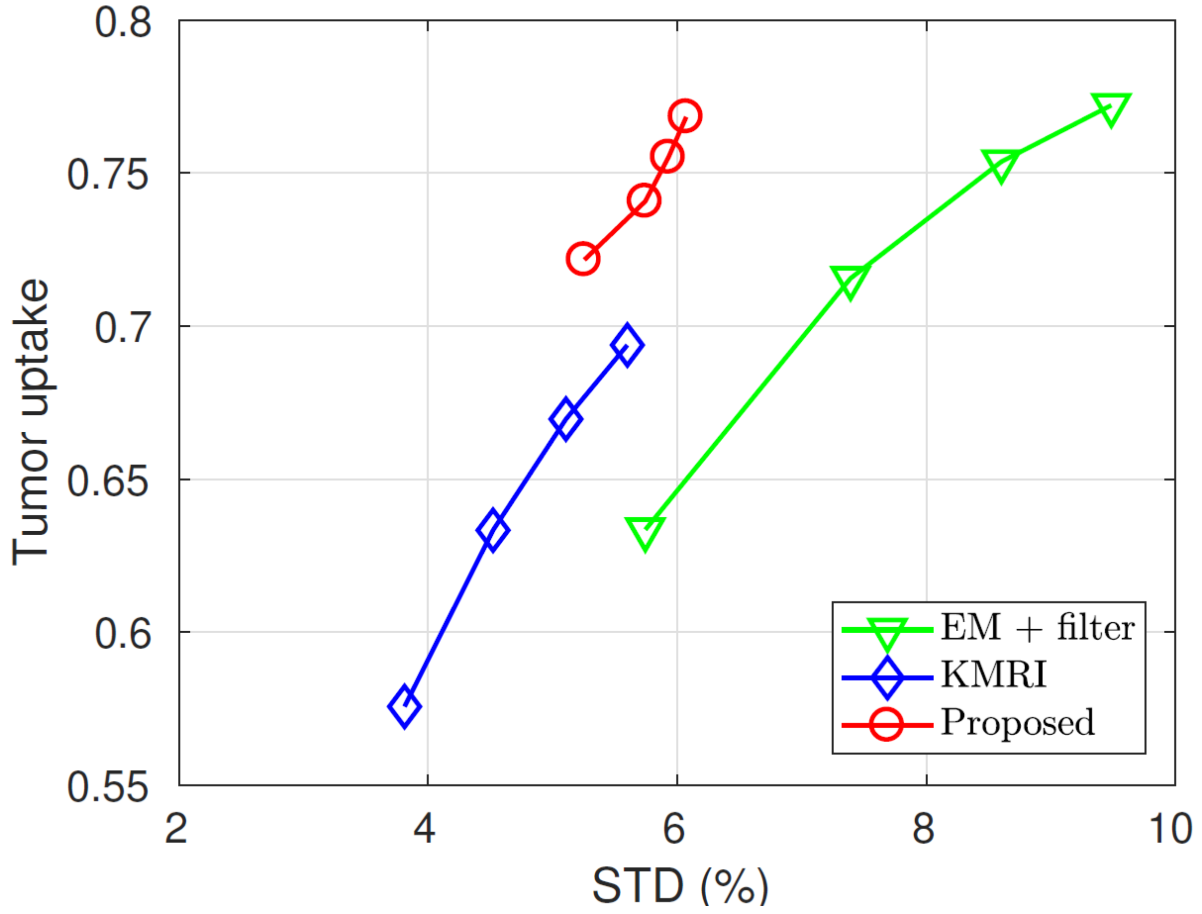
K. Gong, ... Q. Li, IEEE Transactions on Medical Imaging, Dec, 2018

3D Simulation



K. Gong, ... Q. Li, IEEE Transactions on Medical Imaging, Dec, 2018

CRC-STD Quantification

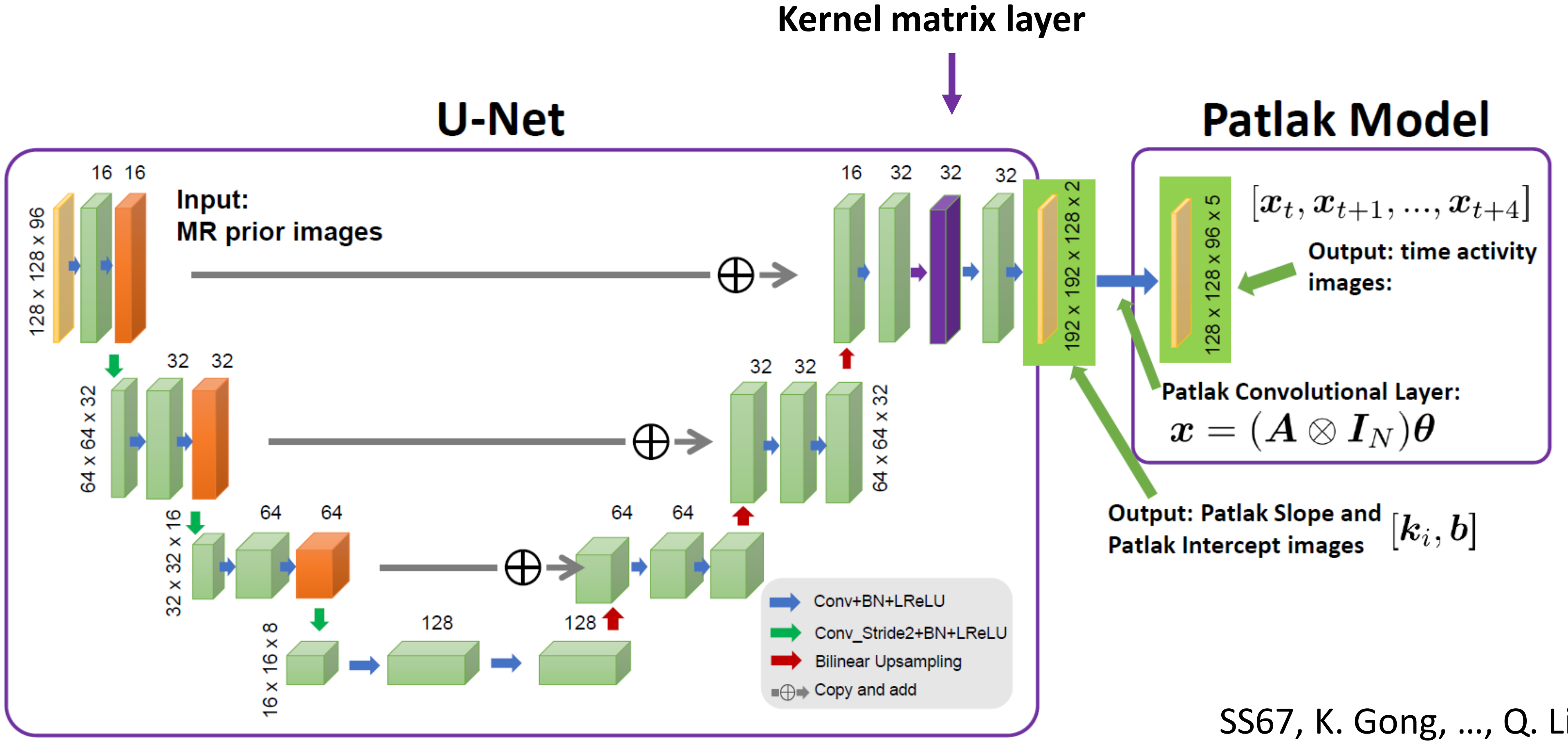


Tumor Region

K. Gong, ... Q. Li, IEEE Transactions on Medical Imaging, Dec, 2018

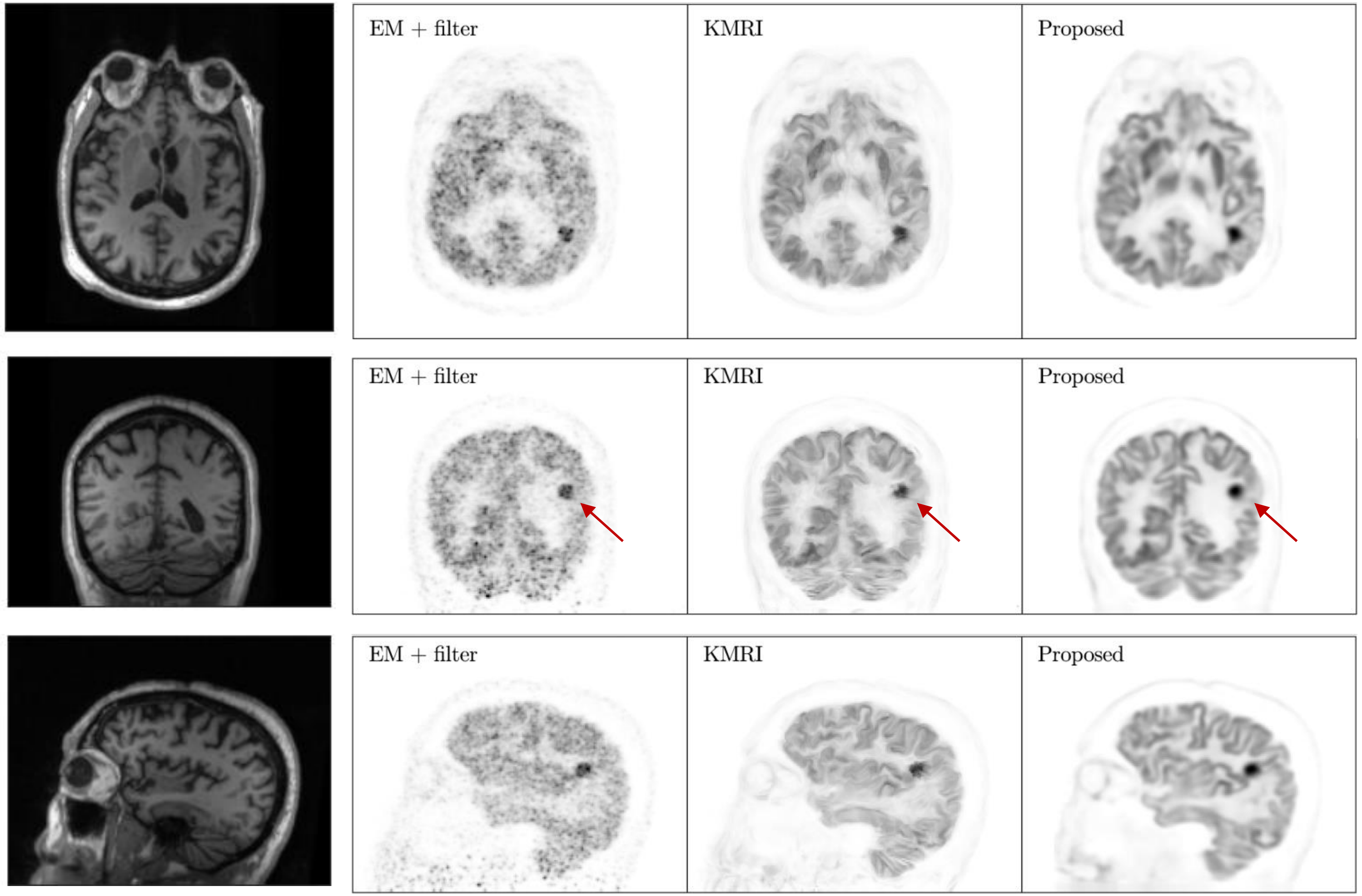
Network Structure

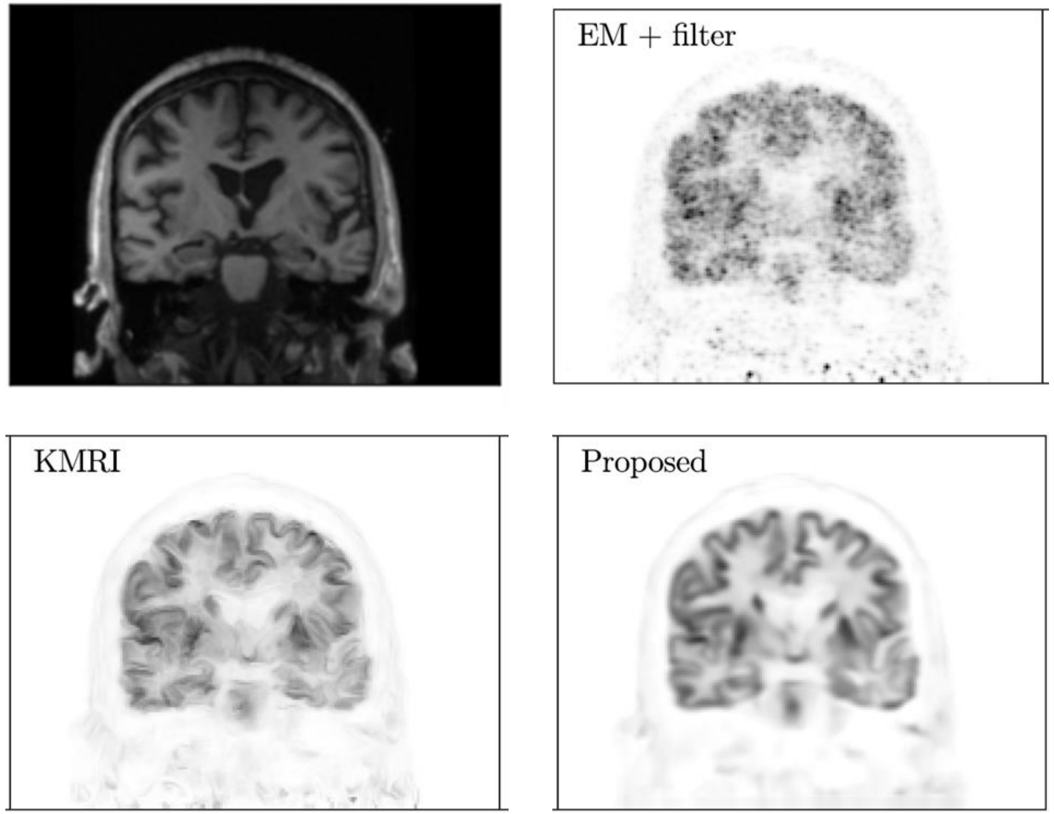
- 3D modified U-net structure (Ronneberger *et al* 2015) is employed as part of the network $f(\boldsymbol{\theta}|\boldsymbol{z}, \boldsymbol{A}, \boldsymbol{K})$:
- Backpropagation of the Kernel matrix layer is $\boldsymbol{K}'\boldsymbol{x}$.
- Patlak layer is 1x 1 x 2 convolution.



SS67, K. Gong, ..., Q. Li, SNMMI 2019

Clinical Data Results

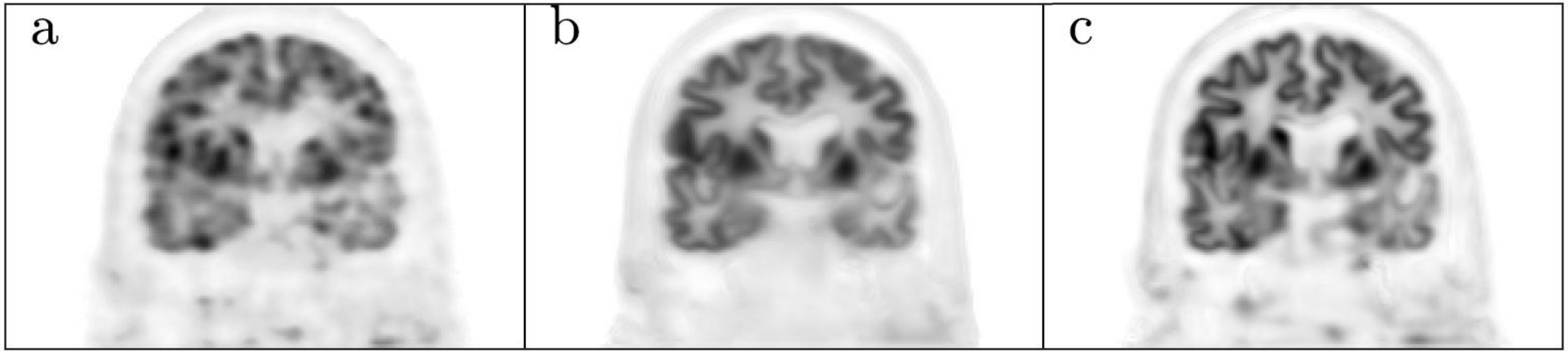




SS67, K. Gong, …, Q. Li, SNMMI 2019

Method: Deep Image Prior

- Unlike natural images, *prior images of the same subject*, instead of random noise, can be employed as network input, which should further improve the results.
- Instead of using the corrupted image as training labels, *sinogram data can be utilized* as training labels and training function can be formulated based on maximum likelihood *(Gong et al 2018).*



(a) Denoising with random noise as network input

(b) Denoising with MR prior as network input

(c) Reconstruction with MR prior as network input

K. Gong, ... Q. Li, IEEE Transactions on Medical Imaging, Dec, 2018

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Noise2noise training

- Motivation
  - Under some circumstances we do not have access to high-quality images
    - Dynamic imaging: PET kinetics, CT perfusion, Material images of spectral CT, etc.
- Noise2noise (Lehtinen et al. 2018)
  - Using labels with another noise realization is equivalent to using clean labels.

- Conventional training

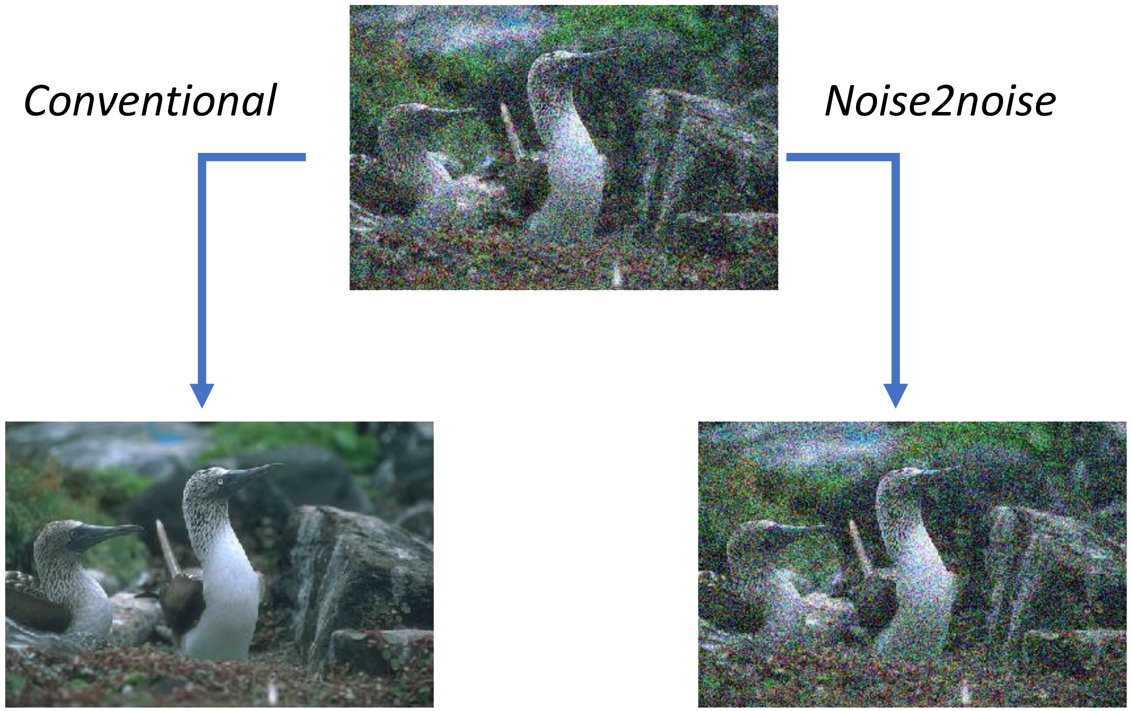
$$\boldsymbol{\Theta}_c = \underset{\boldsymbol{\Theta}}{\operatorname{argmin}} \frac{1}{N} \sum_{i=1}^{N} \| f(\mathbf{x}_i + \mathbf{n}_i; \boldsymbol{\Theta}) - \mathbf{x}_i \|_2^2 ,$$

  - $\mathbf{x}_i$ - noiseless image; $\mathbf{n}_i$ - noise.

- Noise2noise training

$$\boldsymbol{\Theta}_n = \underset{\boldsymbol{\Theta}}{\operatorname{argmin}} \frac{1}{N} \sum_{i=1}^{N} \| f(\mathbf{x}_i + \mathbf{n}_{i1}; \boldsymbol{\Theta}) - (\mathbf{x}_i + \mathbf{n}_{i2}) \|_2^2 ,$$

  - $\mathbf{n}_{i1}$ - noise realization 1; $\mathbf{n}_{i2}$ - noise realization 2.
  - The only difference is that training label has noise.



PET Denoising

- Motivation
  - Under some circumstances we do not have access to high-quality images
    - Dynamic imaging: PET kinetics, CT perfusion, Material images of spectral CT, etc.

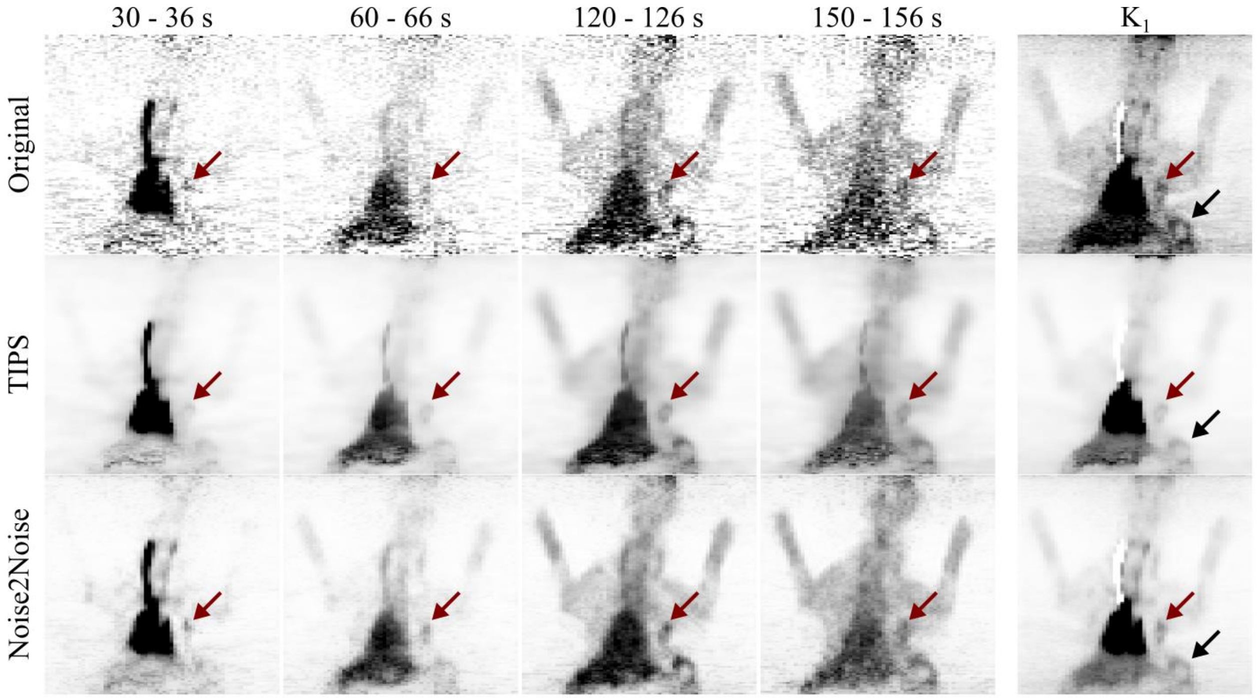


Fig. 1. Denoising results of the ^{15}O water PET time frames and averaged K1 images from three injections.The primary tumor is pointed by the black arrows. A metastasis is pointed by the red arrows, which is almost smoothed out in the TIPS results. The hyperparameters for TIPS and Noise2Noise were chosen based on visual appearance. The display windows for time frames and K_1 are [0, 7.5×10^3] Bq/ml and [0, 0.04] s^{-1}, respectively.

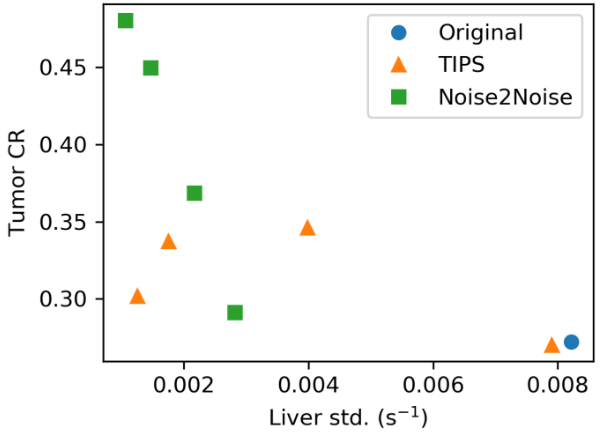


Fig. 2. Contrast recovery (CR) of the tumor versus standard deviations inside liver of the K_1 images, with different hyperparameters of TIPS and Noise2Noise.

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- Population based + Personalized

Proposed Method

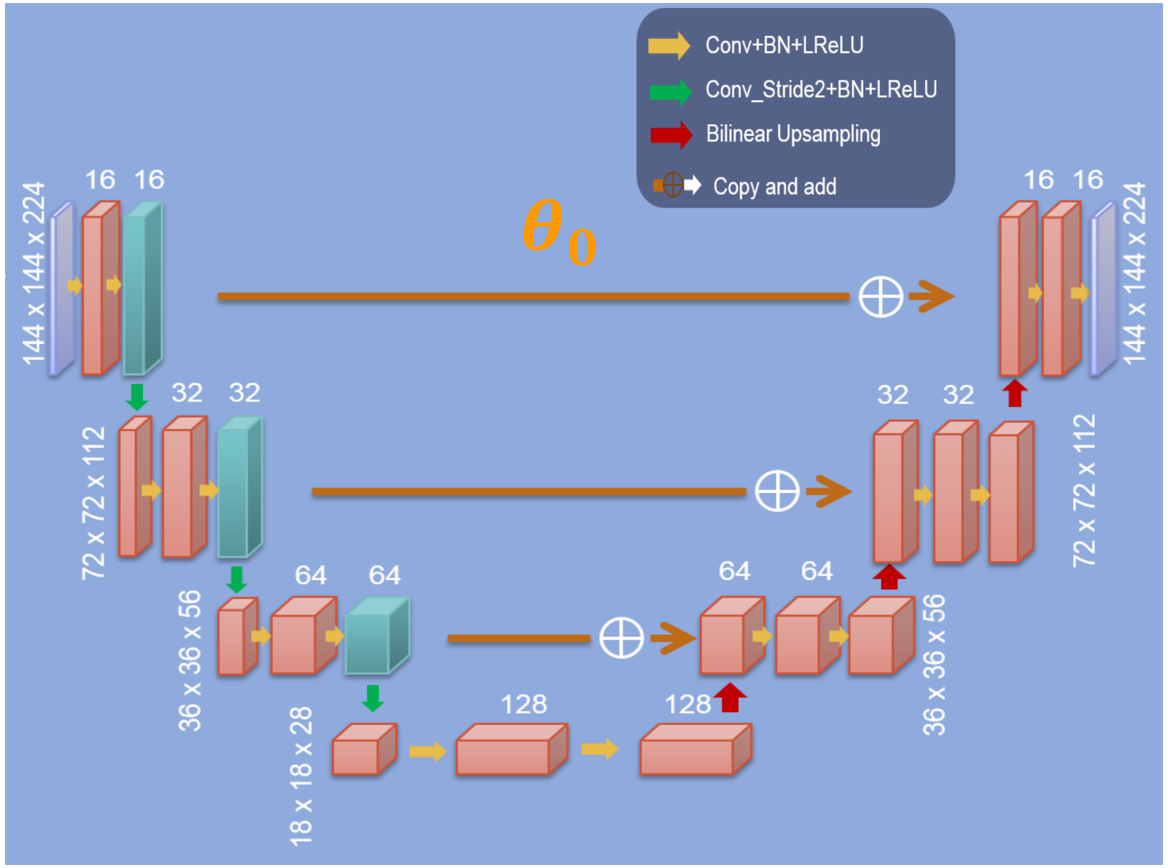
➢ Pre-training

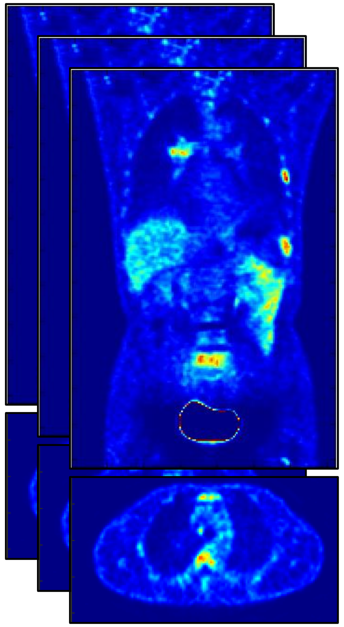
$$\theta_0 = arg\min_{\theta} \left\| x_0^{train} - f\left(\theta | \alpha^{train}\right) \right\|^2$$

- f: untrained modified 3D Unet
- θ: network parameters
- α^{train}: training input (**co-registered CT/MR images**)
- x_0^{train}: noisy PET images (training labels)

CT/MR images

α^{train}





Noisy PET images

x_0^{train}

Optimization algorithm: Adam

Çiçek, Özgün, et al. "3D U-Net: learning dense volumetric segmentation from sparse annotation." International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, Cham, 2016.

Proposed Method

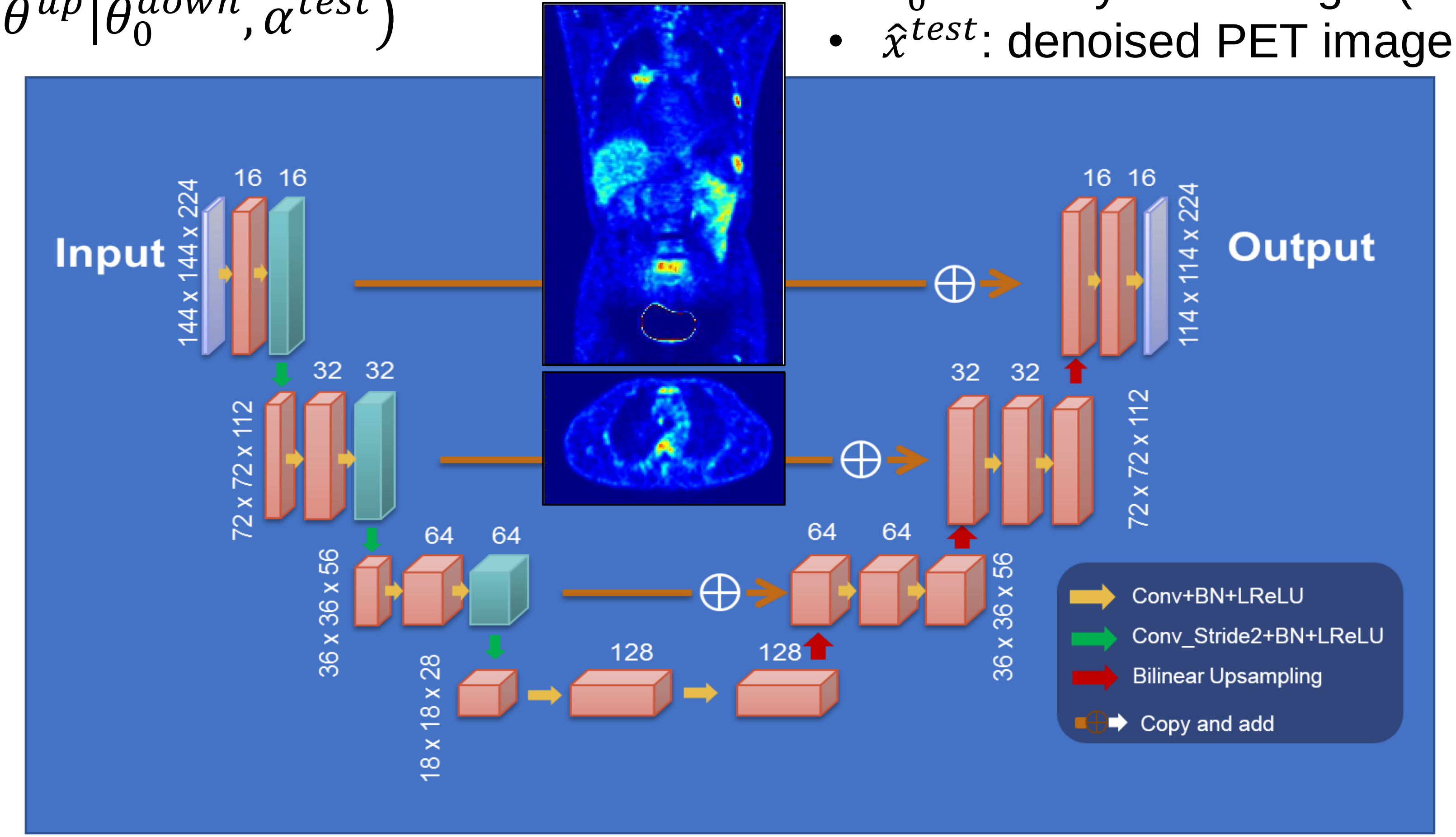
➢ Fine-tune process :

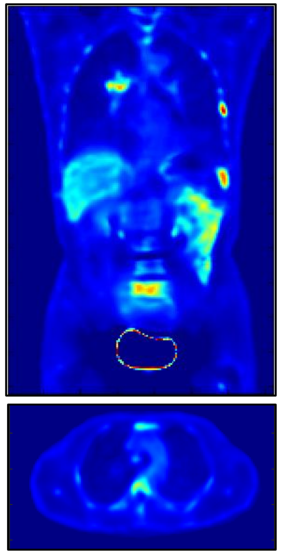
$$\hat{\theta}^{up} = \arg\min_{\theta} \left\| x_0^{test} - f\left(\theta^{up} \middle| \theta_0^{down}, \alpha^{test}\right) \right\|$$

$$\hat{x}^{test} = f\left(\hat{\theta}^{up} \middle| \theta_0^{down}, \alpha^{test}\right)$$

- f: modified 3D Unet[2]
- θ_0: pre-trained network parameters(**fixed θ_0^{down}**)
- α^{test}: test input (**co-registered CT/MR image**)
- x_0^{test}: noisy PET image (test label)
- $\hat{x}^{test}$: denoised PET image

CT/MR image



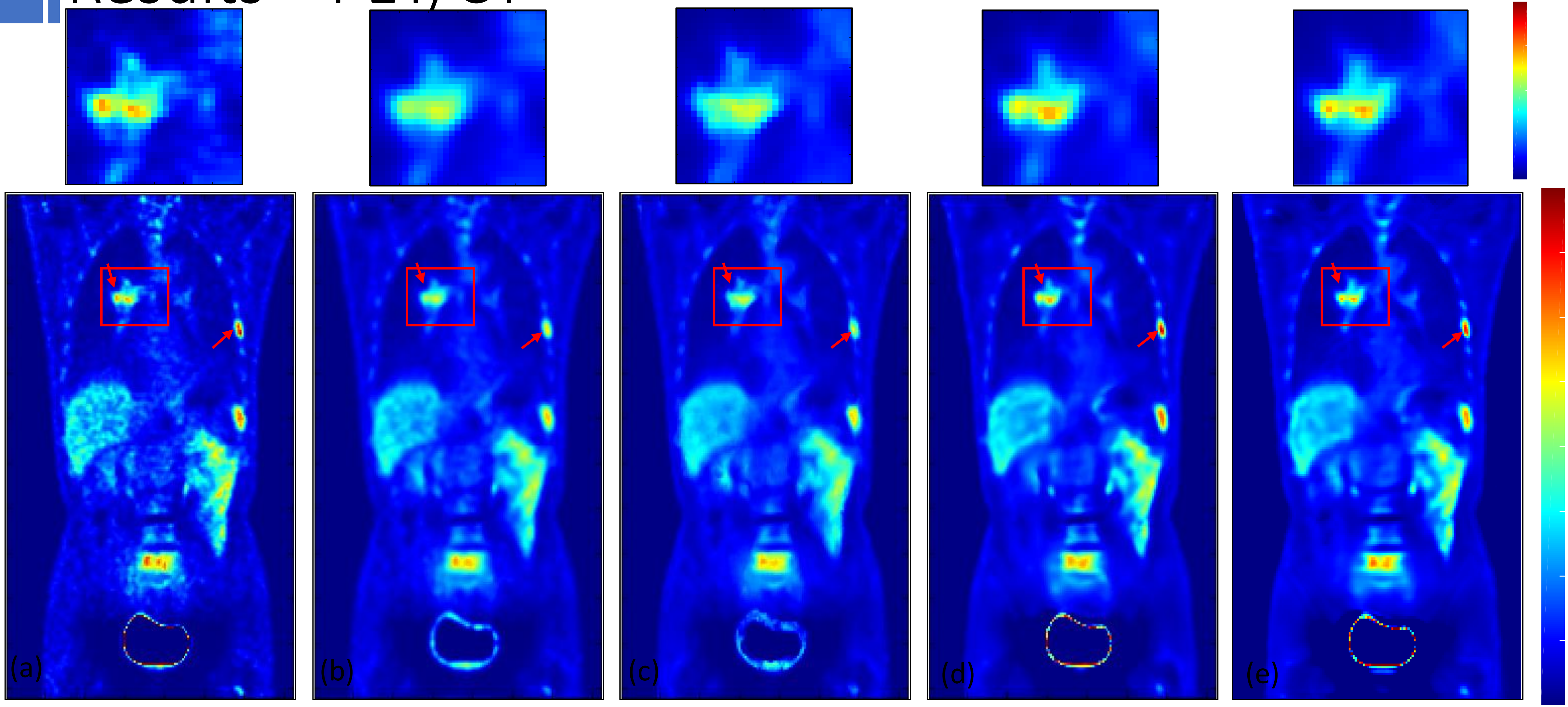


Denoised PET image

Optimization algorithm: L-BFGS

[2] Çiçek, Özgün, et al. "3D U-Net: learning dense volumetric segmentation from sparse annotation." International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, Cham, 2016.

Results – PET/CT



Noisy PET

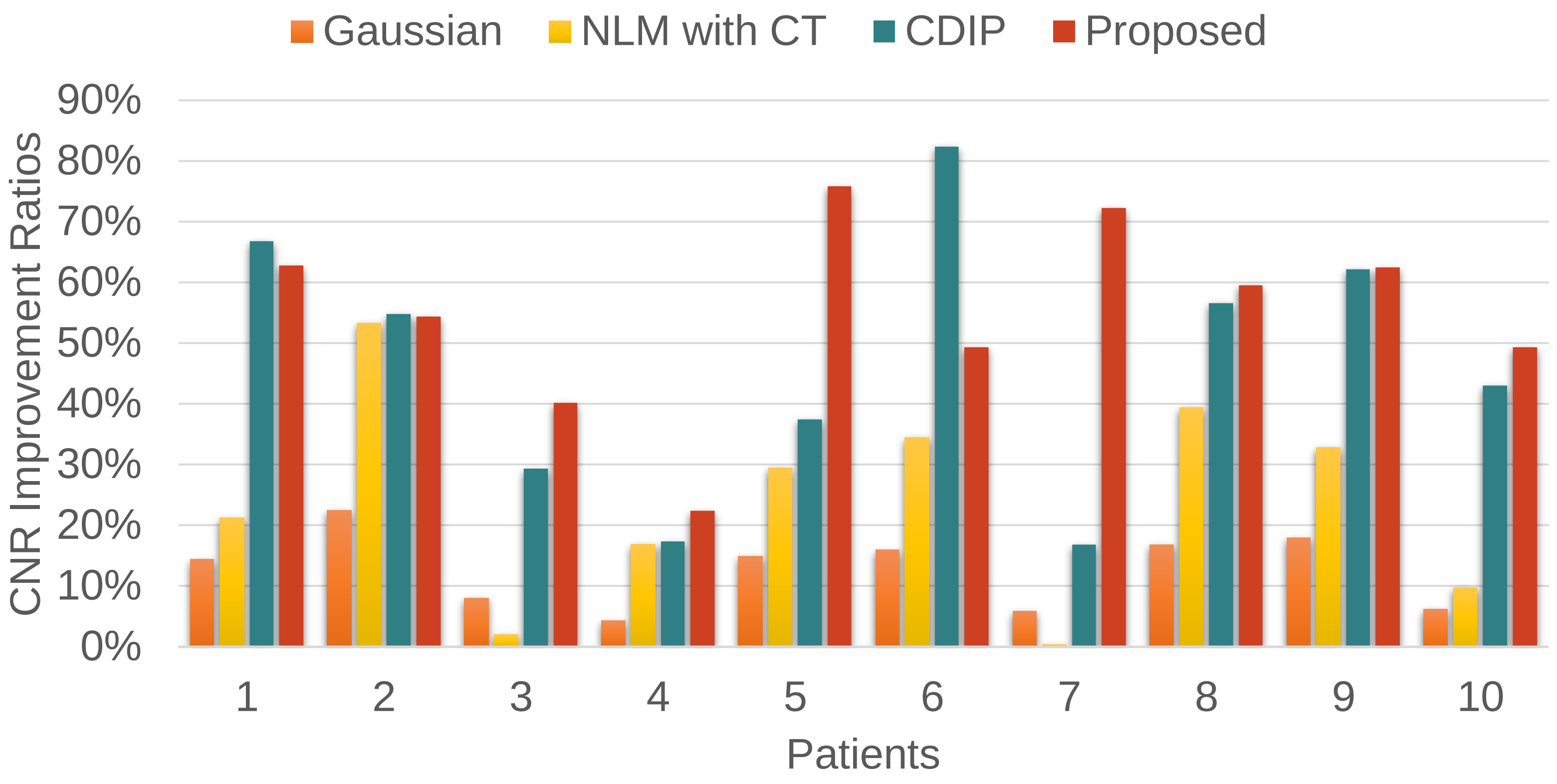
Gaussian
FWHM = 1

NLM with CT
window size:
5×5×5

CDIP
700 epochs

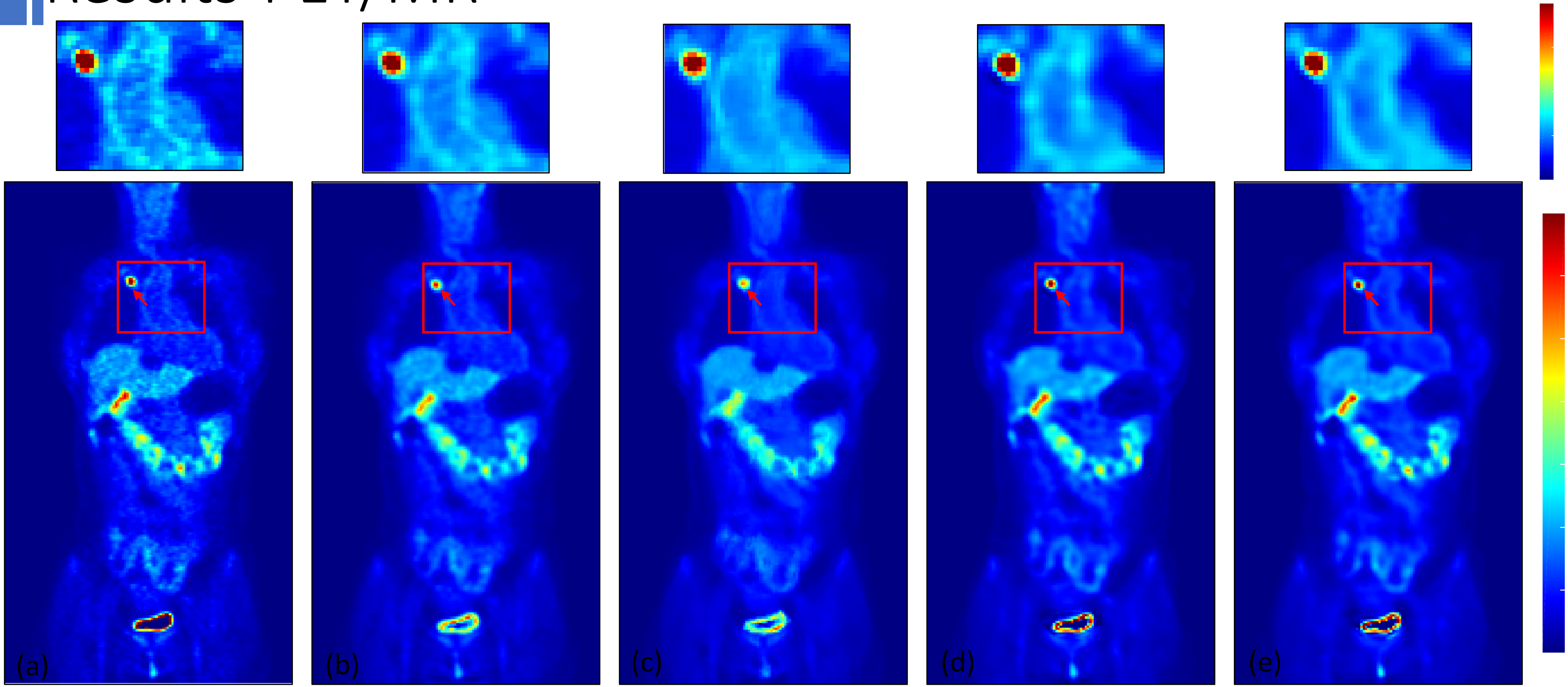
Proposed
pre-train: 50 epochs
finetune: 700 epochs

Results – PET/CT



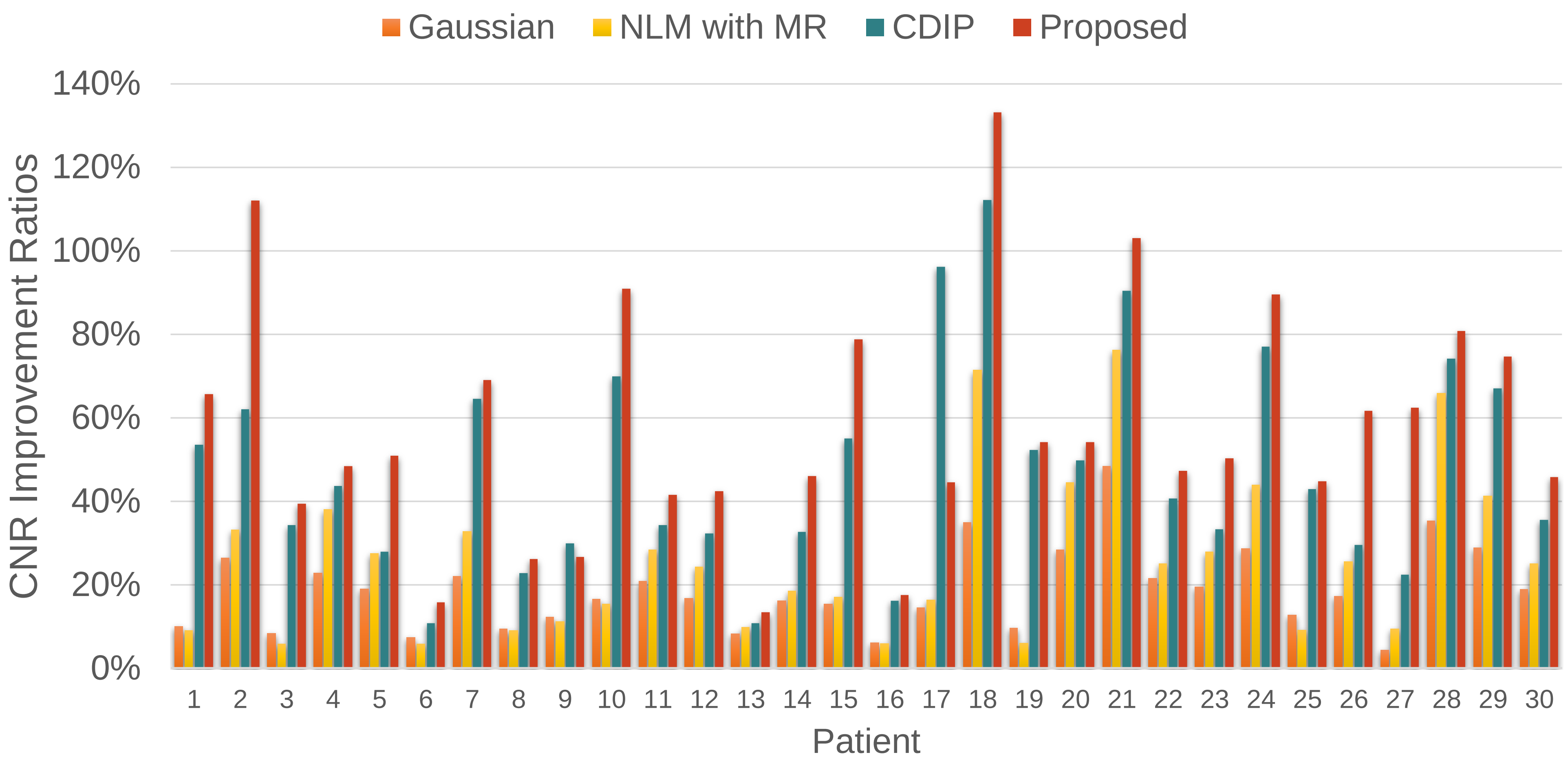
The proposed method has the highest CNR among most patients.

Results-PET/MR



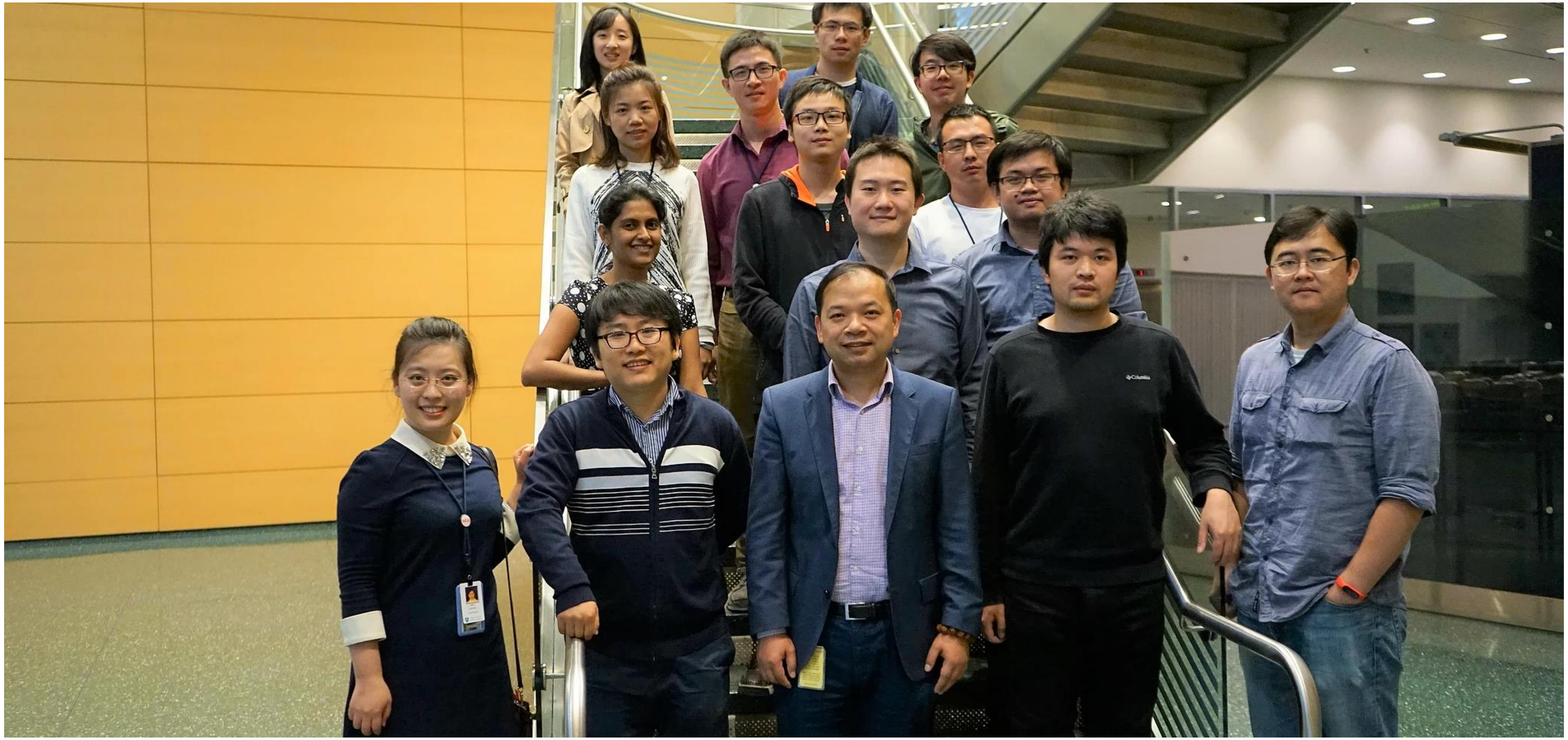
Noisy PET	Gaussian FWHM = 1	NLM with CT window size: 5×5×5	CDIP 700 epochs	Proposed pre-train: 50 epochs finetune: 700 epochs

Results – PET/MR



The proposed method has the highest CNR among most patients.

Thanks for your attention!



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