Improved low count quantitative SPECT reconstruction with a trained deep-learning based regularizer

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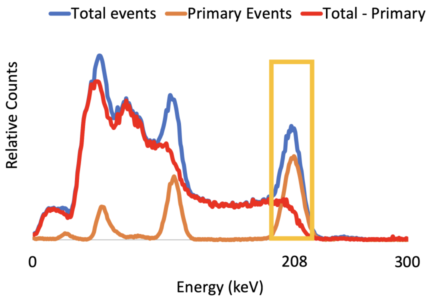
Benefits of improving low-count SPECT

1. Reduce scan duration: shorter scans
2. Enable pre-therapy theranostic imaging with radionuclides:
    - Y-90 (low bremsstrahlung yield)
    - Lu-177 (208 keV gamma: 10%)
3. Enable Whole Body SPECT. Currently not practical because of the long scan time.



LU-177 Energy Spectra

Approaches to low-count imaging

- Post-reconstruction filtering (used in clinic):
  Clinical choice is 3D 5-8mm FWHM Gaussian filter[1].
- Add regularization term to cost function:

$$\hat{\boldsymbol{x}} = \arg\min_{\boldsymbol{x} \geq \boldsymbol{0}} f(\boldsymbol{x}) + \mathrm{R}(\boldsymbol{x}),$$

where $\mathrm{R}(\boldsymbol{x})$ is a regularization term.

- Two families of $\mathrm{R}(\boldsymbol{x})$:
  1. Mathematically designed regularizer
  2. Learned (trained) regularizer

[1] Carlier, Thomas, et al. "90YPET imaging: Exploring limitations and accuracy under conditions of low counts and high random fraction." Medical physics 42.7 (2015): 4295-4309.

BCD-Net problem formulation

- BCD-Net[2] is inspired by following sparsity-based regularization with trained convolutional filters:

$$\hat{\boldsymbol{x}} = \arg\min_{\boldsymbol{x}} \min_{\boldsymbol{z}} f(\boldsymbol{x}) + \mathrm{R}(\boldsymbol{x}, \boldsymbol{z}) = \arg\min_{\boldsymbol{x}} \min_{\boldsymbol{z}} f(\boldsymbol{x}) + \beta\Big(\sum_{k=1}^{K} \|\boldsymbol{c}_k * \boldsymbol{x} - \boldsymbol{z}_k\|_2^2 + \alpha_k \|\boldsymbol{z}_k\|_1 \Big),$$

- Block Coordinate Descent (BCD) algorithm alternatively updates $\{\boldsymbol{z}_k : \boldsymbol{z}_1, ..., \boldsymbol{z}_K\}$ and $\boldsymbol{x}$. Then variable $\{\boldsymbol{z}_k\}$ and $\boldsymbol{x}$ updates become equivalent to following variable $\boldsymbol{u}$ and $\boldsymbol{x}$ updates with trained encoding, decoding filters $\{c_k\}, \{d_k\}$ and soft-thresholding values $\{\alpha_k\}$:

$$\boldsymbol{u}^{(n+1)} = \sum_{k=1}^{K} \boldsymbol{d}_k^{(n+1)} * \left(\mathcal{T}(\boldsymbol{c}_k^{(n+1)} * \boldsymbol{x}^{(n)}, \alpha_k^{(n+1)}) \right)$$

$$\boldsymbol{x}^{(n+1)} = \arg\min_{\boldsymbol{x}} f(\boldsymbol{x}) + \beta \left\| \boldsymbol{x} - \boldsymbol{u}^{(n+1)} \right\|_2^2 .$$

[2] Lim, H., Chun, I. Y., Dewaraja, Y. K., Fessler, J. A. (2019). Improved low-count quantitative PET reconstruction with a variational neural network. arXiv preprint arXiv:1906.02327.

Adaptive BCD-Net: 1. Normalization and scaling

- It is important for trained methods to be able to generalize to a wide range of count levels.
- We propose normalization and scaling scheme:

$$\boldsymbol{u}^{(n+1)} = \sum_{k=1}^{K} \boldsymbol{d}_k^{(n+1)} * \left(\mathcal{T}_{\alpha_k^{(n+1)}} \left(\boldsymbol{c}_k^{(n+1)} * g_1(\boldsymbol{x}^{(n)}) \right) \right)$$

$$\boldsymbol{x}^{(n+1)} = \operatorname*{arg\,min}_{\boldsymbol{x} \geq \boldsymbol{0}} f(\boldsymbol{x}) + \beta \left\| \boldsymbol{x} - g_2(\boldsymbol{u}^{(n+1)}) \right\|_2^2,$$

where the normalization function $g_1(\cdot)$ is defined by $g_1(\boldsymbol{v}) := \frac{1}{\sum_j \bar{v}_j} \bar{\boldsymbol{v}}$ $(\boldsymbol{1}^T g_1(\boldsymbol{v}) = 1)$, and the scaling function $g_2(\cdot)$ is defined by $g_2(\boldsymbol{v}) := \hat{s}\boldsymbol{v}$ with $\hat{s} = \arg\min_s f(s \cdot \boldsymbol{v})$.

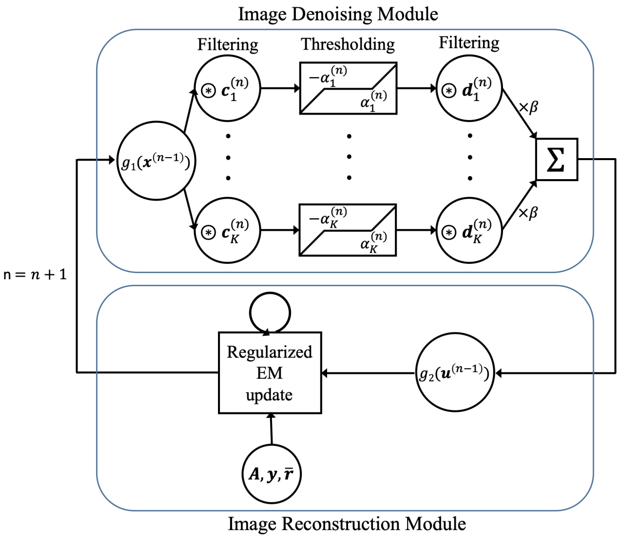
Adaptive BCD-Net: 2. Adaptive regularization parameter selection

- We set the β value based on evaluation on current gradients of data-fidelity term and regularization term:

$$\beta^{(n')} = \frac{\left\| \nabla_{\boldsymbol{x}} f(\boldsymbol{x}^{(n')}) \right\|_2}{\left\| \nabla_{\boldsymbol{x}} \mathrm{R}(\boldsymbol{x}^{(n')}) \right\|_2} \cdot c$$

where c is a constant specifying how we balance between the data-fidelity term and regularization term and n' denotes n'th iteration in $\boldsymbol{x}$-update.
$\rightarrow$ Regularization parameter value is adaptively chosen for each patient data.

Architecture of BCD-Net



Related works

- Mathematically designed regularizer TV (Total Variation) improved low-count SPECT[3].
- Many related works use single image denoising (deep) neural network (e.g., U-Net) as a post-reconstruction processing (input: noisy image, output: clean image).

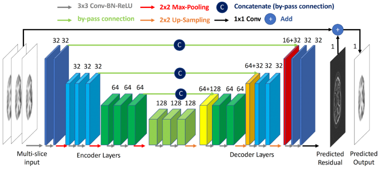


Fig. 2. Overall architecture of our proposed network.

U-Net architecture[4]

- We implemented non-recurrent (single forward pass) 3-D version of U-Net.

[3] Wolf, Paul A., et al. "Few-view single photon emission computed tomography (SPECT) reconstruction based on a blurred piecewise constant object model." Physics in Medicine Biology 58.16 (2013): 5629.

[4] Xu, Junshen, et al. "200x low-dose pet reconstruction using deep learning." arXiv preprint arXiv:1712.04119 (2017).

Experimental setting: Training data

- We used three Lu-177 patient studies with multiple acquisitions on a Symbia SPECT/CT.
- We resampled[5] the high-count (25-minutes scan) measurement data with Poisson resampling factor of 1/9 and 1/25 to generate 3-minutes and 1-minute equivalent scans.
- Total number of high-count (25 minutes) scans: 10
- Total number of low-count realizations: 20 (10 scans $\times$ 2 count-level).

Table: Primary counts range in training dataset: 3 patients (patient A, B, C) studies with multiple acquisition time points

Data	Count-level	Day0	Day5
Patient A,B,C	High (25 minutes scan)	12.3M - 26.5M	2.7M - 6.1M
	Low (3 minutes scan)	2.2M - 2.9M	410K - 680K
	Low (1 minute scan)	800K - 1.1M	150K - 250K

[5] White, Duncan, and Richard S. Lawson. "A Poisson resampling method for simulating reduced counts in nuclear medicine images." Physics in Medicine Biology 60.9 (2015): N167.

Experimental setting: Testing data

- We used the following Lu-177 phantom and patient studies:
  - Measurement with hot spheres (lesions) in the warm liver of a torso-phantom
  - Measurement with six hot spheres (2,4,8,16,30 and 113 mL) in a warm background
  - Two patient studies not used for training
- We resampled the high-count measurement data with Poisson resampling factor of $1/9$ and $1/25$ to generate low-count measurements:
  - Generates 5 realizations with each measurement to assess the noise across realizations.

Table: Primary counts range in testing dataset: 2 phantom studies and 1 patient (patient D, E) study

Data	Primary counts
Patient D	110 - 303K
Patient E	81K - 224K
Liver phantom	370K - 1.0M
Sphere phantom	1.3M - 3.7M

BCD-Net training details

- $\boldsymbol{x}^{(0)}$: An image estimated with EM algorithm using 50 iterations
- 5 outer loop
- 10 inner-iterations in $\boldsymbol{x}$-update
- 3D Filters and soft-thresholding values are trained with
  - Pytorch deep-learning library
  - ADAM optimization
  - epoch number: 500, mini-batch size: one 3-D image ($128 \times 128 \times 81$)
  - Learning rate: Encoding(1e3), Decoding(1e0), Thresholding(1e5)
  - Learning rate decay method is used (lr = lr $\times$ 0.9 every 20 epoch)
  - Filter size: $3 \times 3 \times 3$, Filter number (K): 3^5

Evaluation metrics

- Activity Recovery:

$$\text{AR} = \frac{\text{Estimated } C_{VOI}}{\text{True } C_{VOI}} \times 100(\%),$$

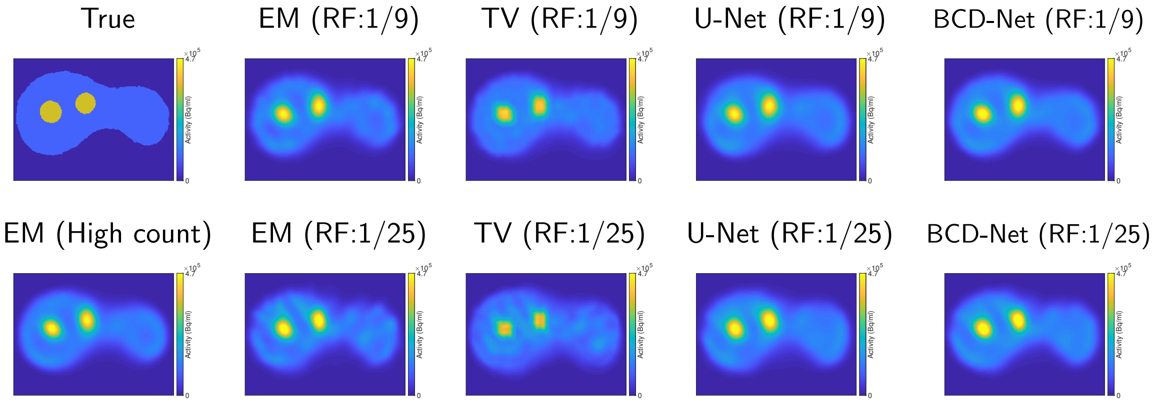
  where C_{VOI} is mean counts in the volume of interest (VOI)

- Image-ensemble-noise across realizations:

$$\text{Noise} = \frac{\sqrt{\frac{1}{J_{\text{BKG}}} \sum_{j \in \text{BKG}} \left(\frac{1}{M-1} \sum_{m=1}^{M} (\hat{\boldsymbol{x}}_m[j] - \frac{1}{M} \sum_{m'=1}^{M} \hat{\boldsymbol{x}}_{m'}[j])^2 \right)}}{\frac{1}{J_{\text{BKG}}} \sum_{j \in \text{BKG}} \frac{1}{M} \sum_{m=1}^{M} \hat{\boldsymbol{x}}_m[j]} \times 100\ \%.$$

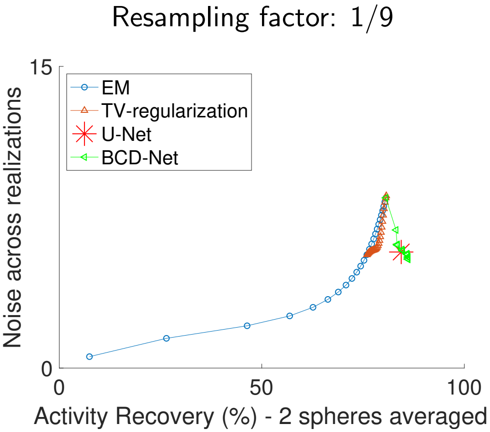
  where M is total number of realizations and J_{BKG} is the total number of voxels in uniform background region.

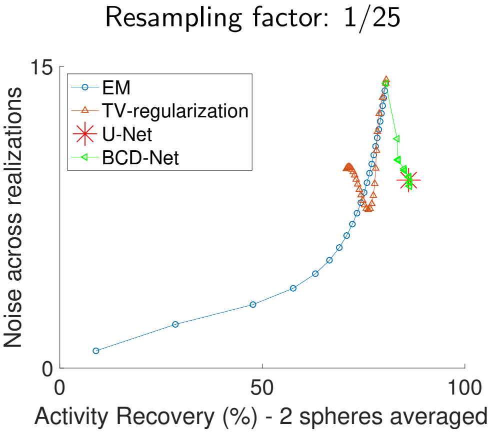
Visual comparison: Liver phantom study



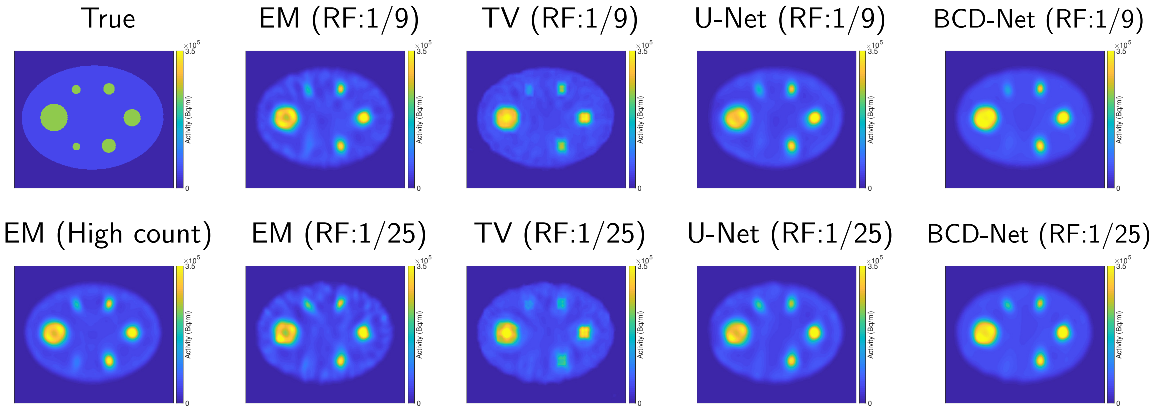
* RF: Resampling factor

Quantitative evaluation result: Liver phantom study



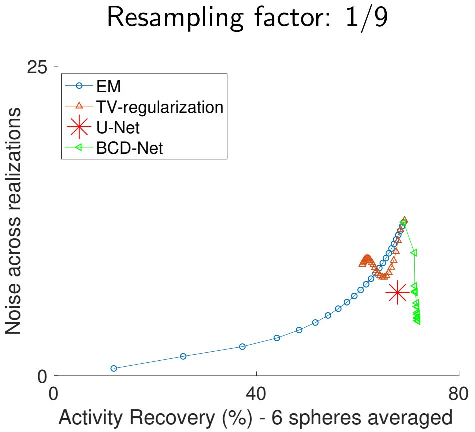


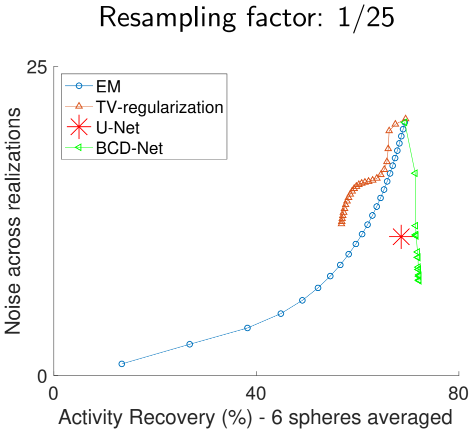
Visual comparison: Sphere phantom study



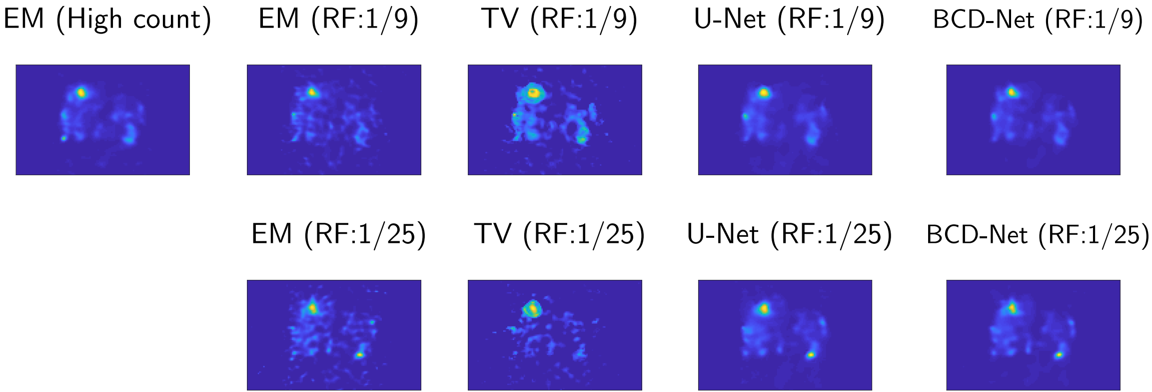
* RF: Resampling factor

Quantitative evaluation result: Sphere phantom study



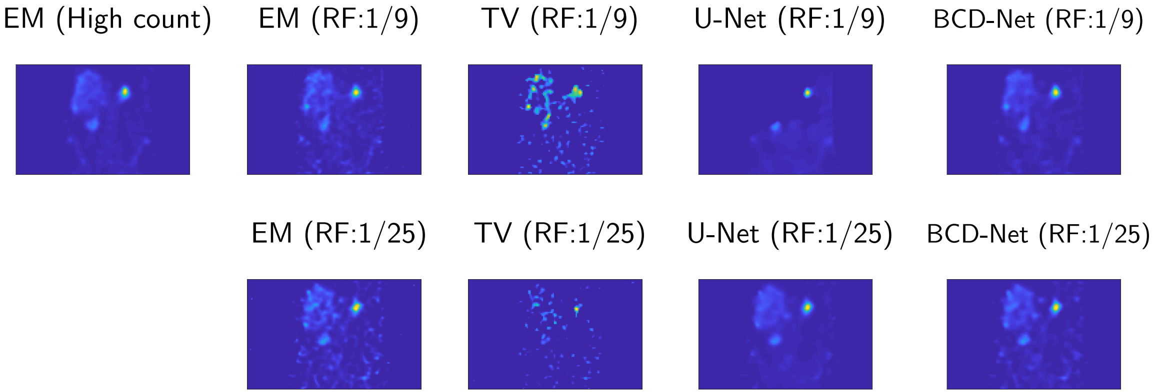


Visual comparison (coronal view): Patient D day5 study



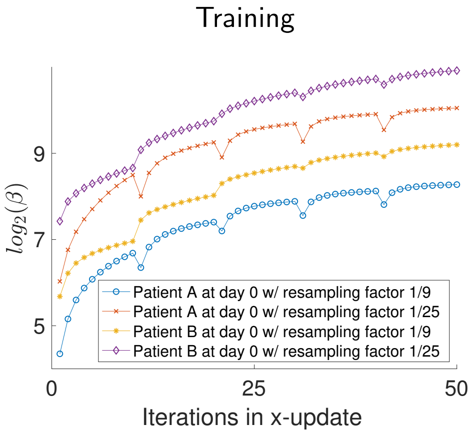
* RF: Resampling factor

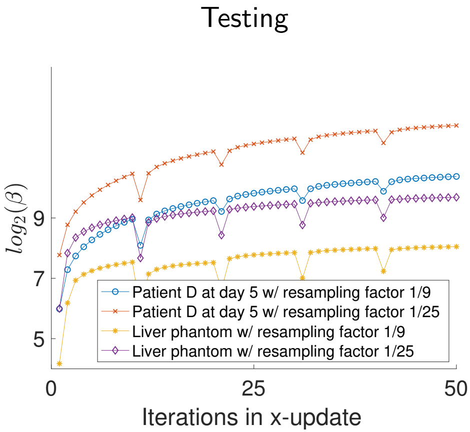
Visual comparison (coronal view): Patient E day8 study



* RF: Resampling factor

Efficacy of adaptive regularization parameter selection scheme





- We set $c = 0.07$ and regularization parameter value is adaptively chosen based on the count-level (more regularization when count-level is lower).

Summary & Acknowledgement

- BCD-Net improved activity recovery for a hot sphere and reduced noise at the same time.
- BCD-Net showed robustness to noise-level (count-level).
- BCD-Net has 67K $\left((3 \times 3 \times 3 \times 243 \times 2 + 243) \times 5\right)$ trainable parameters whereas U-Net has 40M trainable parameters ($\sim$ 600 $\times$ BCD-Net).
- The performance of U-Net was slightly worse than that of BCD-Net in quantitative evaluation on phantom stuies. Moreover, U-Net had a test case (patient E study with RF 1/9) showing non-robust generalization performance.
- Imaging with 1/9 reduction in counts will enable a 3-4 min SPECT acquisition compared to current standard 25-30 min scan, considerably reducing imaging burden to patient and clinic. Also possibility for whole body SPECT with 3 acquisitions.
- Imaging with 1/25 reduction in counts will enable pre-therapy diagnostic Lu-177 SPECT with tracer quantities (5-10 mCi).
- We acknowledge Jeremy Niedbala, Gerrid Rosebush for all help in measurements
- This work is supported by NIH(NIBIB) grant R01EB022075

Thank You

- Slides are here:
  `https://limhongki.github.io`
- Derivation details:
  Hongki Lim, et al. (2019). Improved low-count quantitative PET reconstruction with a variational neural network. arXiv preprint arXiv:1906.02327.