Bias reduction in Y-90 PET with reconstruction that relaxes the non-negativity constraint

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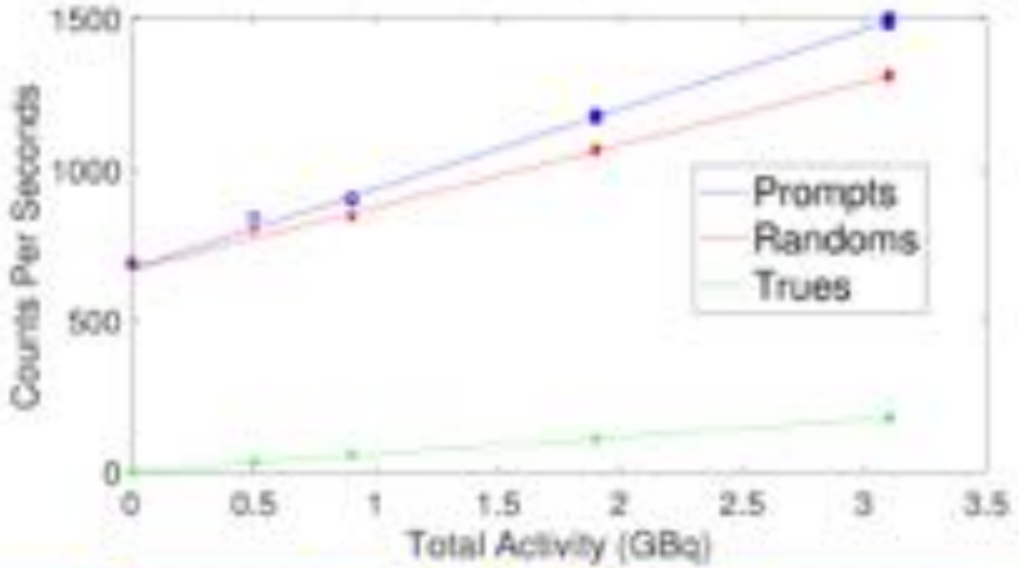
Particulars about Y-90 imaging

- Y-90: Radioisotope for radioembolization
  - Almost pure beta emitter
  - Very low probability of positron emission : 3.2×10^{-5}
  - ^{176}Lu and Bremsstrahlung photons contribute to random coincidences
    $\rightarrow$ Low true coincidence counts & very high random fraction

Figure: True/Random counts in measurement of our Y90 phantom study



Reported Problems

- Several Y-90 PET papers[1,2] reported bias in quantification
- Bias direction in calculation of the absorbed dose
  - Underestimation in hot (lesion) and warm (liver) region
    → Inaccurate absorbed dose-effect relationship
  - Overestimation in cold (no activity) region and total dose
    → False alarm due to high extra-hepatic (i.e., lung) deposition

[1] Carlier, Thomas, et al. "Y90 PET imaging: Exploring limitations and accuracy under conditions of low counts and high random fraction." Medical physics 42.7 (2015): 4295-4309.

[2] Pasciak, Alexander S., et al. "Radioembolization and the dynamic role of 90Y PET/CT." Frontiers in oncology 4 (2014)

Formulation of emission tomography

- Measurement follows Poisson statistical model:

$$Y_i \sim \mathrm{Poisson}(\bar{y}_i(\boldsymbol{x})), \quad i = 1, \dots, n_d$$
$$\text{where, } \bar{y}_i(\boldsymbol{x}) = [\boldsymbol{A}\boldsymbol{x}]_i + \bar{r}_i$$

- (Negative) Poisson log likelihood function $f(\boldsymbol{x})$:

$$f(\boldsymbol{x}) = \sum_{i=1}^{n_d} \bar{y}_i(\boldsymbol{x}) - y_i \log(\bar{y}_i(\boldsymbol{x}))$$

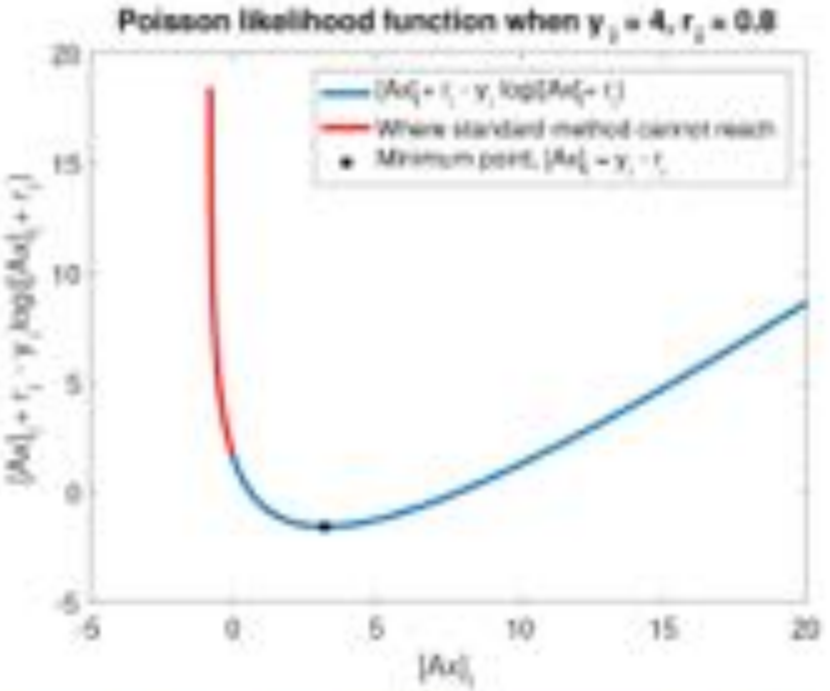
- Goal of conventional emission tomography:

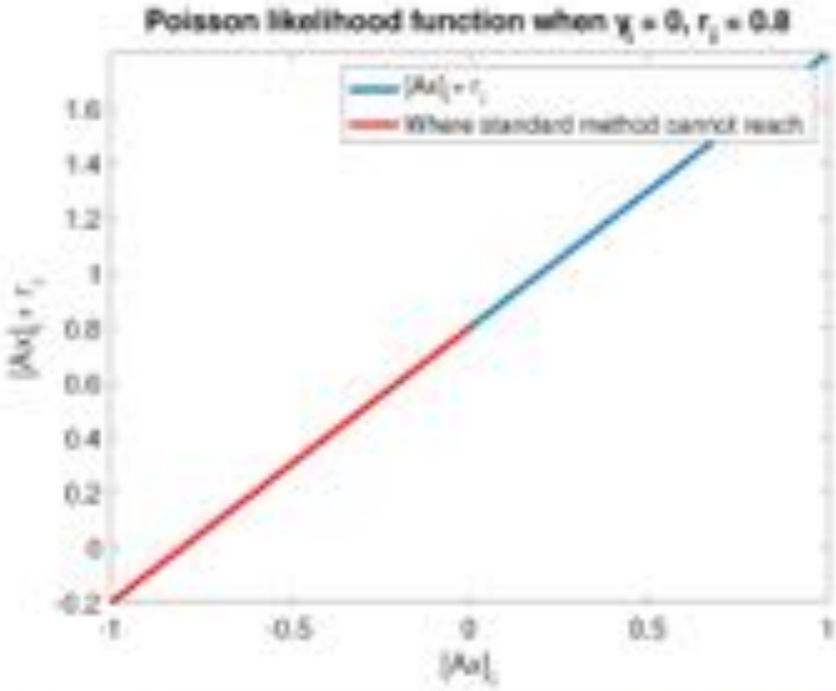
$$\hat{\boldsymbol{x}} = \underset{\boldsymbol{x}}{\operatorname{argmin}} f(\boldsymbol{x})$$
$$\text{subject to } \boldsymbol{x} \geq \boldsymbol{0}$$

Limitation of conventional constraint

- Cases in negative Poisson log-likelihood function

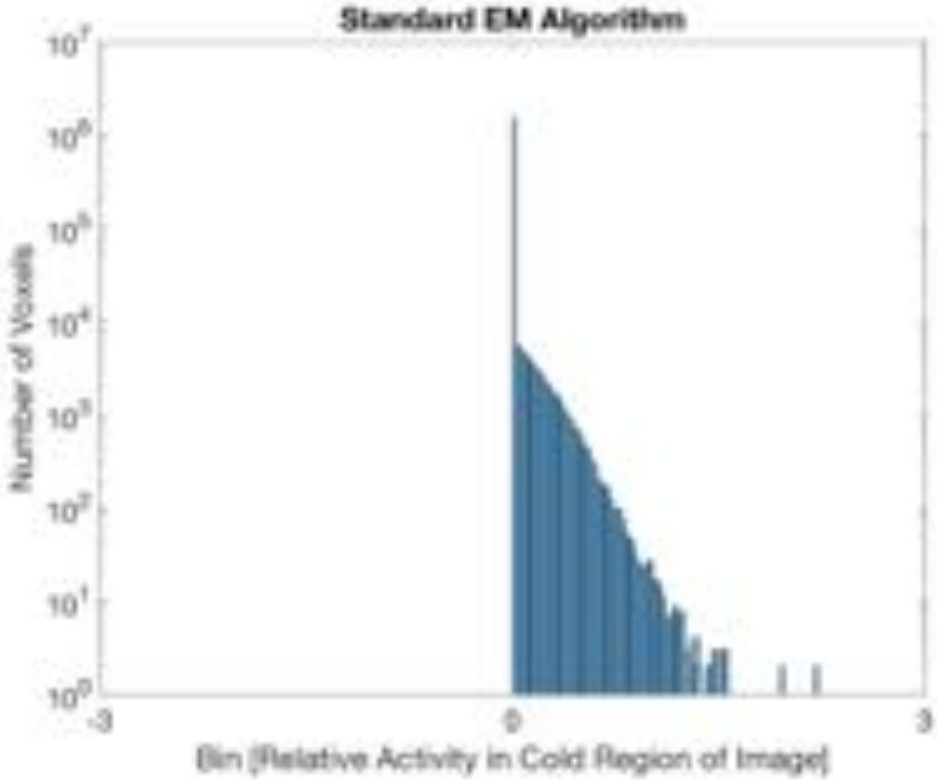
$$f(x) = \begin{cases} [\boldsymbol{A}\boldsymbol{x}]_i + \bar{r}_i - y_i \log([\boldsymbol{A}\boldsymbol{x}]_i + \bar{r}_i), & y_i > 0, \quad [\boldsymbol{A}\boldsymbol{x}]_i + \bar{r}_i > 0 \\ [\boldsymbol{A}\boldsymbol{x}]_i + \bar{r}_i, & y_i = 0 \\ \infty, & y_i > 0, \quad [\boldsymbol{A}\boldsymbol{x}]_i + \bar{r}_i \leq 0 \end{cases}$$





Bias introduced in cold region

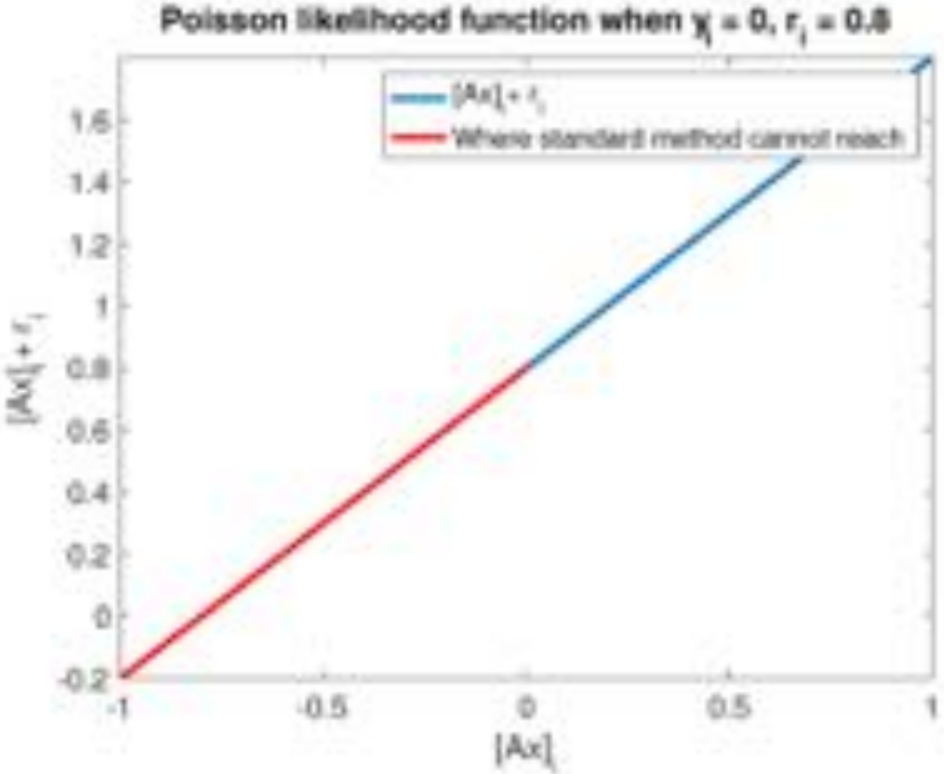
- Histogram in cold region (where there is no activity)



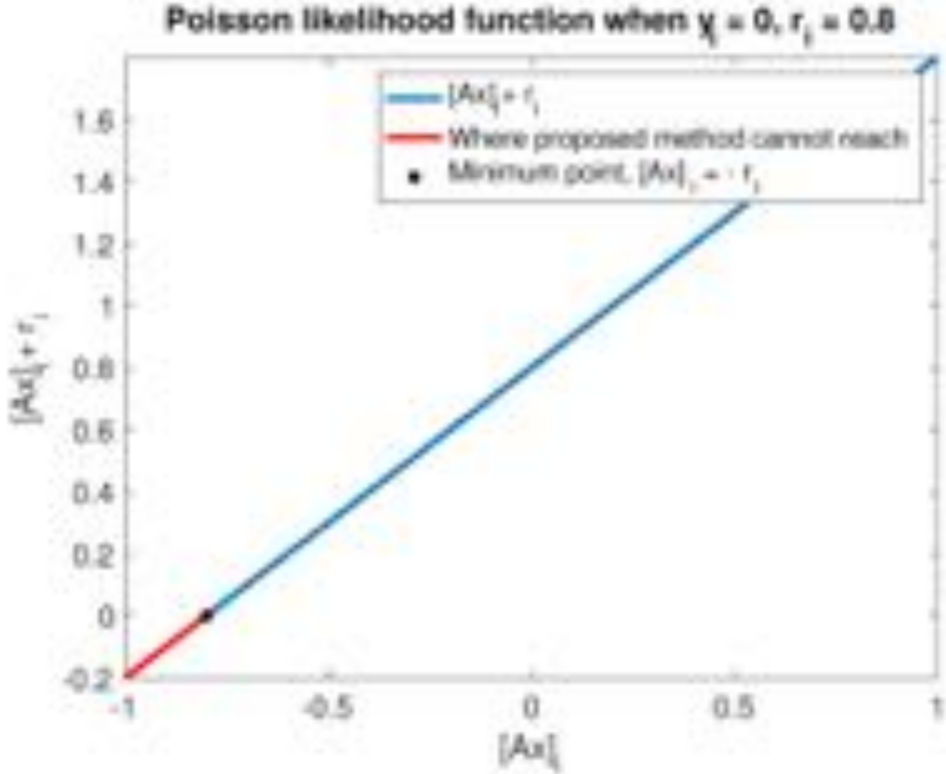
Proposed method

- Enforce non-negativity on projection space:

$$\hat{\boldsymbol{x}} = \underset{\boldsymbol{x}}{\operatorname{argmin}}\, f(\boldsymbol{x}), \quad \text{subject to } \boldsymbol{x} \geq 0 \quad \longrightarrow \quad \hat{\boldsymbol{x}} = \underset{\boldsymbol{x}}{\operatorname{argmin}}\, f(\boldsymbol{x}), \quad \text{subject to } \boldsymbol{A}\boldsymbol{x} + \bar{\boldsymbol{r}} \geq 0$$

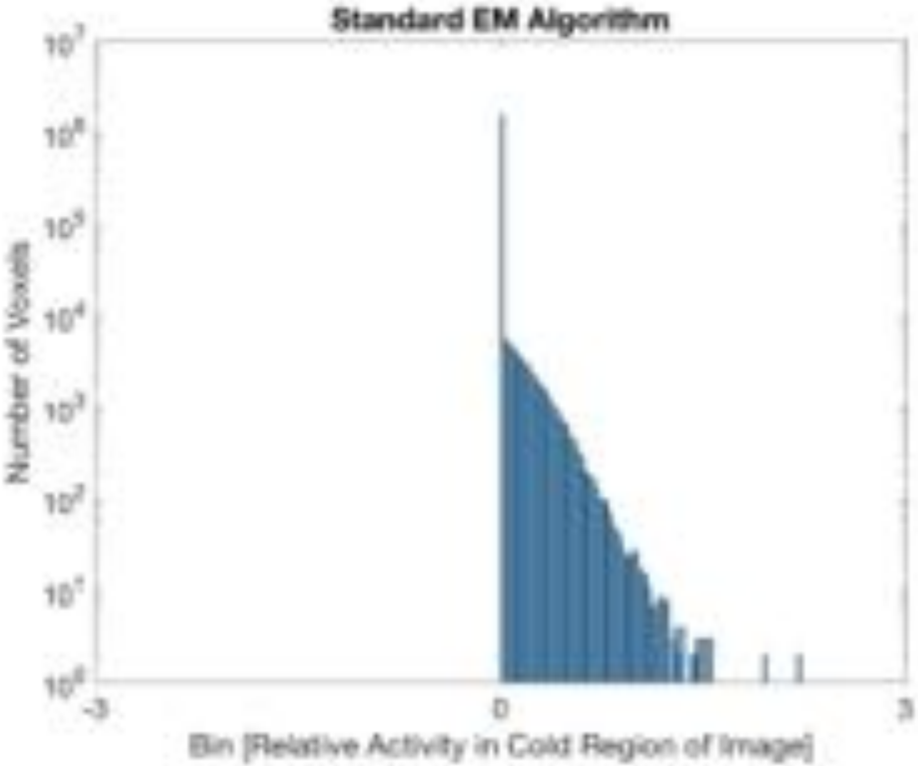


$\longrightarrow$

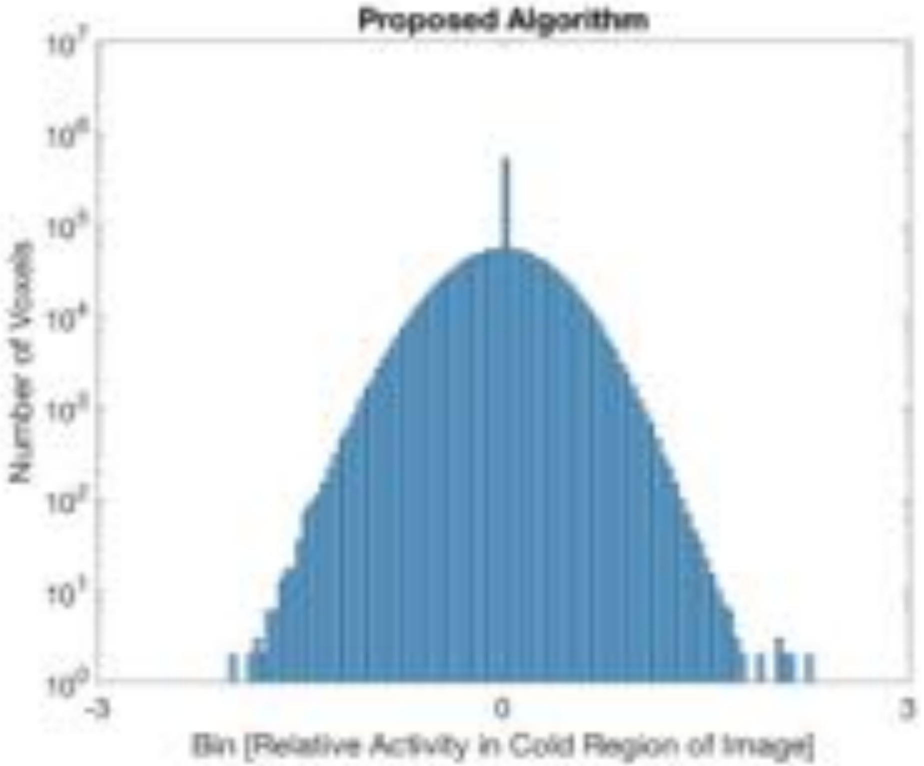


Overview of our proposed method

- Histogram in cold region (where there is no activity)



→



Changing the formulation to solvable form

- To solve the new formulation, we introduce a function $g(\cdot)$ and an auxiliary variable $\boldsymbol{v}$:

$$\hat{\boldsymbol{x}} = \underset{\boldsymbol{x}}{\operatorname{argmin}} f(\boldsymbol{x}), \quad \text{subject to } \boldsymbol{A}\boldsymbol{x} + \bar{\boldsymbol{r}} \geq 0$$

$$\Updownarrow$$

$$\hat{\boldsymbol{x}} = \underset{\boldsymbol{x}}{\operatorname{argmin}} f(\boldsymbol{x}) + g(\boldsymbol{A}\boldsymbol{x} + \bar{\boldsymbol{r}}), \text{ where } g(\boldsymbol{\eta}) = \begin{cases} \infty, & \text{any } \eta_i < 0 \\ 0, & \text{all } \eta_i \geq 0 \end{cases}$$

$$\Updownarrow$$

$$\hat{\boldsymbol{x}} = \underset{\boldsymbol{x}}{\operatorname{argmin}} \min_{\boldsymbol{v}} \mathbf{1}^T(\boldsymbol{v} + \bar{\boldsymbol{r}}) - \boldsymbol{y}^T \log(\boldsymbol{v} + \bar{\boldsymbol{r}}) + g(\boldsymbol{v} + \bar{\boldsymbol{r}}) \quad \text{subject to } \boldsymbol{v} = \boldsymbol{A}\boldsymbol{x}$$

- We form augmented Lagrangian based on above minimization problem:

$$\Psi(\boldsymbol{x}, \boldsymbol{v}, \boldsymbol{\lambda}) = \mathbf{1}^T(\boldsymbol{v} + \bar{\boldsymbol{r}}) - \boldsymbol{y}^T \log(\boldsymbol{v} + \bar{\boldsymbol{r}}) + g(\boldsymbol{v} + \bar{\boldsymbol{r}}) + \boldsymbol{\lambda}^T(\boldsymbol{A}\boldsymbol{x} - \boldsymbol{v}) + \frac{\rho}{2}||\boldsymbol{A}\boldsymbol{x} - \boldsymbol{v}||_2^2$$

$$\hat{\boldsymbol{x}} = \underset{\boldsymbol{x}}{\operatorname{argmin}} \min_{\boldsymbol{v}} \max_{\boldsymbol{\lambda}} \Psi(\boldsymbol{x}, \boldsymbol{v}, \boldsymbol{\lambda})$$ [3]

[3] Lim, Hongki, Yuni K. Dewaraja, and Jeffrey A. Fessler. "A PET reconstruction formulation that enforces non-negativity in projection space for bias reduction in Y-90 imaging." Physics in medicine and biology (2018)

Comparison with related works

- Neg-ML[4] minimizes a modified data fit term $f_{\mathrm{N-ML}}(\boldsymbol{x})$:

$$f_{\mathrm{N-ML}}(\boldsymbol{x}) = \sum_{i=1}^{n_d} \tilde{\mathrm{q}}_i([\boldsymbol{A}\boldsymbol{x}]_i)$$

$$\tilde{\mathrm{q}}_i(t) = \begin{cases} t + \bar{r}_i - y_i \log(t + \bar{r}_i), & t + \bar{r}_i \geq \psi \\ \frac{(y_i - t - \bar{r}_i)^2}{2\psi} - y_i \log \psi + \psi - \frac{(y_i - \psi)^2}{2\psi}, & t + \bar{r}_i < \psi. \end{cases}$$

→ the Poisson distribution is replaced by Gaussian distribution when the estimated measurement is below than the parameter ψ.

[4] Nuyts, J., et al. "A dedicated ML-algorithm for non-attenuation corrected PET whole body images." Nuclear Science Symposium Conference Record, 2000 IEEE. Vol. 2. IEEE, 2000.

Regularization for extremely low-count imaging

- Add regularization term to cost function to penalize the roughness and control the noise:

$$\hat{\boldsymbol{x}} = \operatorname*{argmin}_{\boldsymbol{x}} f(\boldsymbol{x}) + \beta \mathrm{R}(\boldsymbol{x})$$
$$\text{subject to } \boldsymbol{A}\boldsymbol{x} + \bar{\boldsymbol{r}} \geq 0 \text{(proposed)}$$
$$\text{or } \boldsymbol{x} \geq 0 \text{ (conventional)}.$$

- Implemented a quadratic regularization for $\mathrm{R}(\boldsymbol{x})$:

$$\mathrm{R}(\boldsymbol{x}) = \sum_{k=1}^{K} \frac{([\boldsymbol{C}\boldsymbol{x}]_k)^2}{2}$$

where $\boldsymbol{C}$ is a $K \times n_p$ finite differencing matrix.

Evaluation metrics

- Contrast Recovery (CR):

$$\text{CR} = \frac{C_{hotsphere}/C_{\text{bkg}} - 1}{R - 1} \times 100(\%),$$

  - C_{hotspot}: Mean counts in hot spot.
  - C_{bkg}: Mean counts in background liver.
  - R: True activity concentration ratio between hot sphere and liver.

- Noise:

$$\text{Noise} = \frac{STD_{bkg}}{C_{bkg}} \times 100(\%)$$

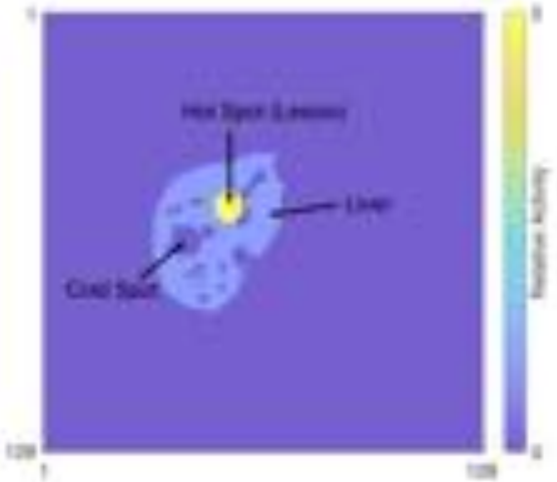
  - STD_{bkg}: Standard deviation of counts in background liver.

- Contrast to Noise Ratio (CNR):

$$\text{CNR} = \frac{C_{hotsphere} - C_{\text{bkg}}}{STD_{bkg}}$$

Simulation results summary

- Lim, Hongki, Yuni K. Dewaraja, and Jeffrey A. Fessler. "A PET reconstruction formulation that enforces non-negativity in projection space for bias reduction in Y-90 imaging." Physics in medicine and biology (2018).
- Simulated Y-90 PET with XCAT phantom



	Patient A		Patient B	
	CR	Noise	CR	Noise
NEG-ML-Reg ($\psi = 4$)	80.0	**12.1**	54.3	**6.2**
NEG-ML-Reg ($\psi = 10^{-3}$)	91.6	40.9	87.2	39.9
Proposed (ADMM-Reg)	**91.7**	41.6	**87.3**	40.0

Experimental setting

- A liver/lung torso phantom setting

- Lung: 5% lung shunt
- Liver: 1.2 MBq/mL at Day 0
- 3 hepatic lesions: 6.5 MBq/mL at Day 0
- Scanned for 30 minutes

- Acquisition at two time points

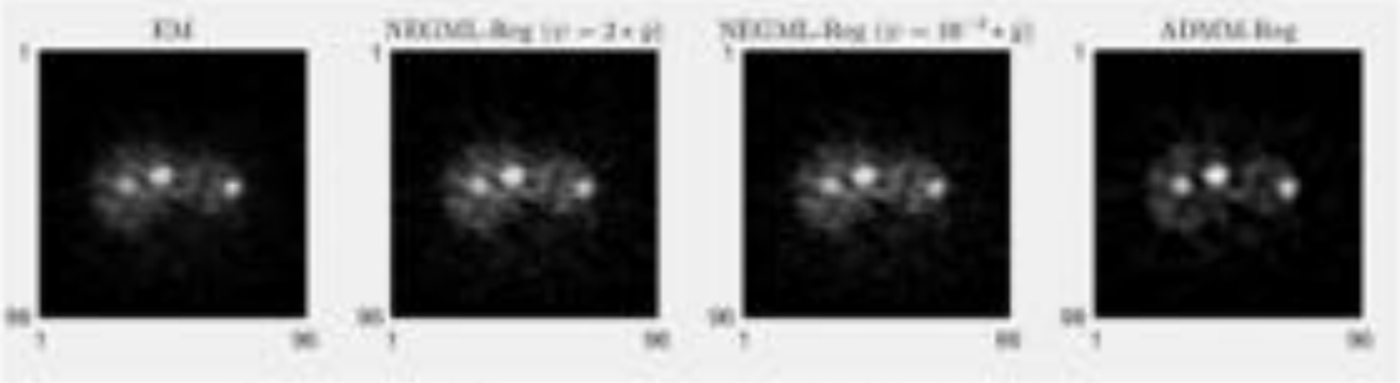
	Day 0	Day 3
Total Y-90 activity (GBq)	1.96	0.96
Total Net Trues	220K	120K
Total Randoms	2.1M	1.7M
Total Prompts	2.3M	1.8M
Random Fraction (%)	91	94

* Random Fraction = (Total randoms / Total prompts) × 100

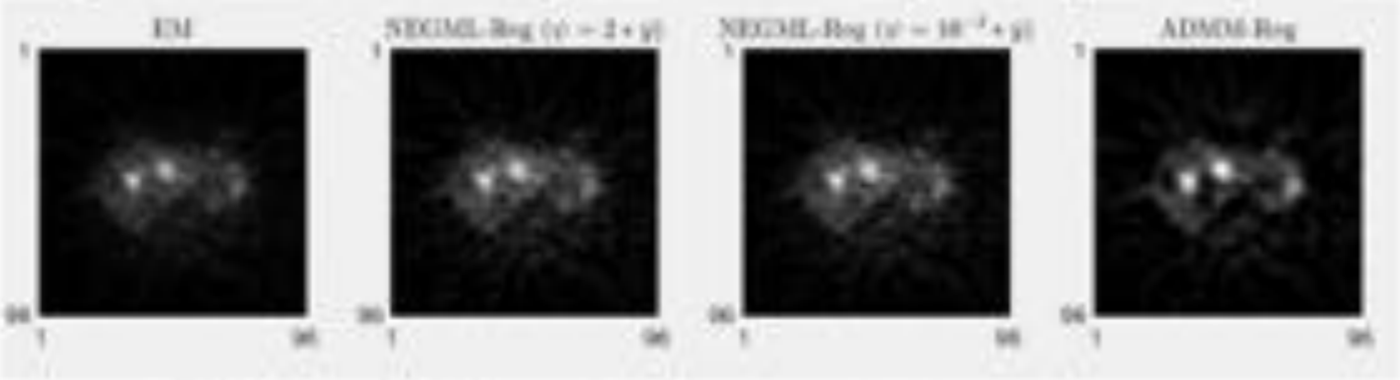
- Reconstructed with TOF data and TOF system model (13 time bins)

Reconstructed images at Day 0 & Day 3

- For visualization, iteration number selected to achieve highest CNR
- Day 0 images: Proposed method improved CNR by 12.9% compared to EM



- Day 3 images: Proposed method improved CNR by 16.2% compared to EM



- NEGML gave lower CNR than EM at both acquisition points

Evaluation results

- CR-H1/H2/H3: Contrast recovery at 29/16/8 ml hot spheres
- Selected iteration number to achieve equivalent noise
- Proposed method achieved highest contrast recovery in both data acquisition points.

Table: Evaluation results on methods

	Day 0				Day 3			
	CR-H1	CR-H2	CR-H3	Noise	CR-H1	CR-H2	CR-H3	Noise
EM	49.9	41.8	41.6	55.0	50.9	40.0	37.1	85.6
NEG-ML-Reg[1]	48.1	40.5	39.2	54.3	51.1	40.7	37.8	85.9
NEG-ML-Reg[2]	48.0	40.5	39.2	54.0	51.2	40.8	37.9	85.6
Proposed method	**65.5**	**50.5**	**49.1**	55.1	**74.9**	**53.8**	**46.8**	85.4

- NEG-ML-Reg[1]: $\psi := 2\times$mean counts of sinogram
- NEG-ML-Reg[2]: $\psi := 10^{-3}\times$mean counts of sinogram

Evaluation results

- CR-H1/H2/H3: Contrast recovery at 29/16/8 ml hot spheres
- Evaluate the converged images (100 iterations)
- Proposed method achieved highest contrast recovery in both data acquisition points.

Table: Evaluation results on methods

	Day 0				Day 3			
	CR-H1	CR-H2	CR-H3	Noise	CR-H1	CR-H2	CR-H3	Noise
NEG-ML-Reg[1]	51.9	43.8	43.6	97.6	54.8	42.5	43.2	146.5
NEG-ML-Reg[2]	51.9	43.8	43.6	95.0	54.5	42.4	42.5	136.8
Proposed method	**66.4**	**51.6**	**51.0**	**62.2**	**80.0**	**57.6**	**52.3**	**106.2**

- NEG-ML-Reg[1]: $\psi := 2\times$mean counts of sinogram
- NEG-ML-Reg[2]: $\psi := 10^{-3}\times$mean counts of sinogram

Discussion & Conclusion

- Our proposed algorithm is distinct in avoiding modifying or approximating the Poisson log-likelihood used in the data term compared to related works (NEG-ML, AB-EMML).
- Applicable to other low true count rates and high random fractions imaging situations
  - Ion-beam therapy
- Future works
  - Implement and test ordered subsets version
  - Use matched TOF projector for regularized methods

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Thank You