Congresso Nazionale SIF, September 17th 2021

Denoising and dose reduction techniques for Positron Emission Tomography

L Presotto[1], E De Bernardi[2], V Bettinardi[1]

[1]Servizio di Medicina Nucleare, IRCCS Ospedale San Raffaele, Milano, Italia

[2]Dipartimento di Medicina e Chirurgia, Università di Milano Bicocca, Monza, Italia

Luca Presotto, PhD
Medicina Nucleare, IRCCS Ospedale San Raffaele, Milano

Luca Presotto
Medicina nucleare
IRCCS Ospedale San Raffaele, Milano

Outline

Noise in PET
Tomographic + Poisson

Hardware side
More counts, better information

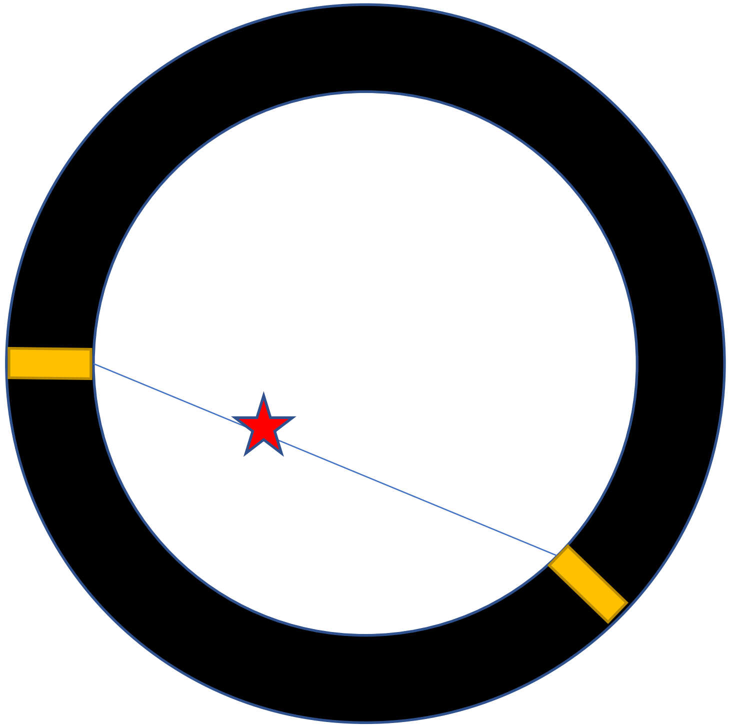
Image Reconstruction
Regularization technique

Artificial intelligence
Post processing / Deep Learning Recon

BACKGROUND

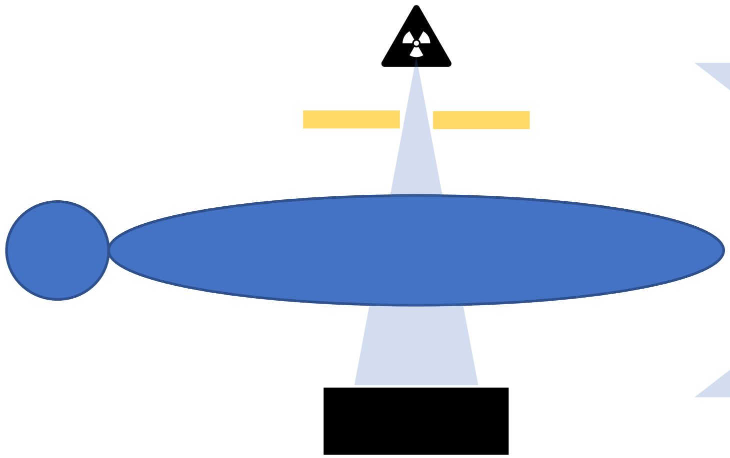
Detectors provide us with 3 kind of information

- Photons hit point
- Timing of the hits
- Energy of the photons



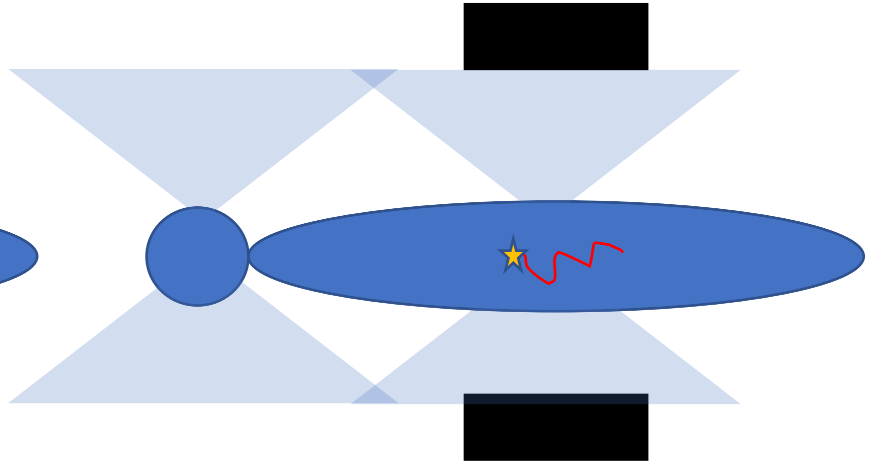
WHY NOT INCREASE COUNTS?

X - Ray



On only during data taking
Collimated to region under study

PET



Radiation for all biological/physical half life
Radiation to the whole body
Positron energy

Common tracers dosimetry:
18F-FDG: 1mSv/mCi

Tracer	Activity (MBq) (*)	Dose (mSv)
F-18 FDG	3.7 /kg	5-7.1
C-11 colina	400	1.8
C-11 metionina	740	3.7
Ga-68 PSMA	1.8–2.2 /kg	3.08
Ga-68 DOTA	200	4.2

POISSON NOISE

A common issue in emission tomography

In the measurement space

- The noise cannot be modelled as additive: $\mathrm{std}(\lambda) = \sqrt{\lambda}$
- It varies by many orders of magnitude
- It varies abruptly along structures contours
- The absolute variance is higher where the signal is higher

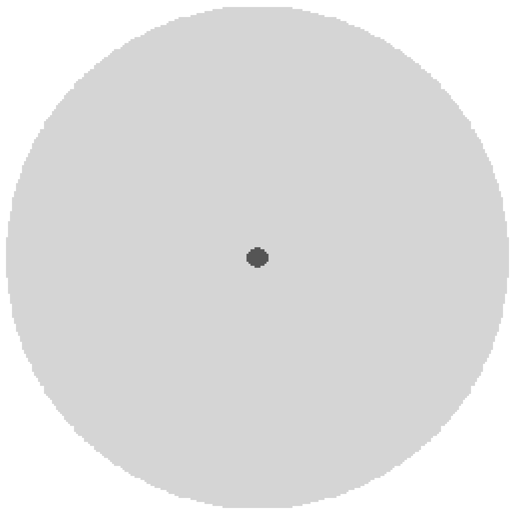
TOY EXAMPLE

A uniform circle (activity 1)

A target (12 mm diameter) with 4:1 contrast with background

Planar imaging (not tomography)

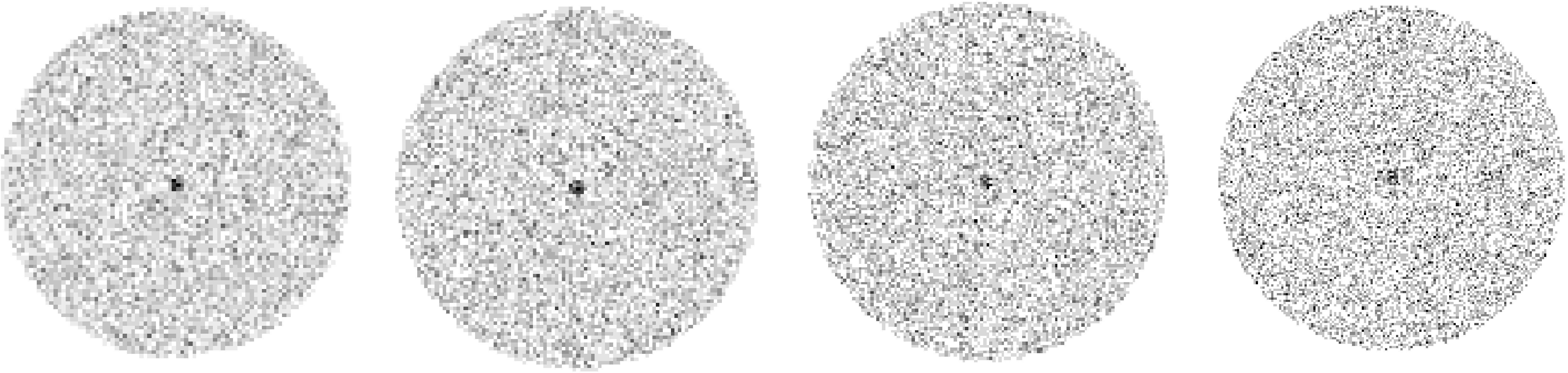
What happens if you keep the same number of counts and make the detector finer?



SPATIAL RESOLUTION AND NOISE

It's worse than it seems

3.5 mm | 3 mm | 2.5 mm | 2 mm

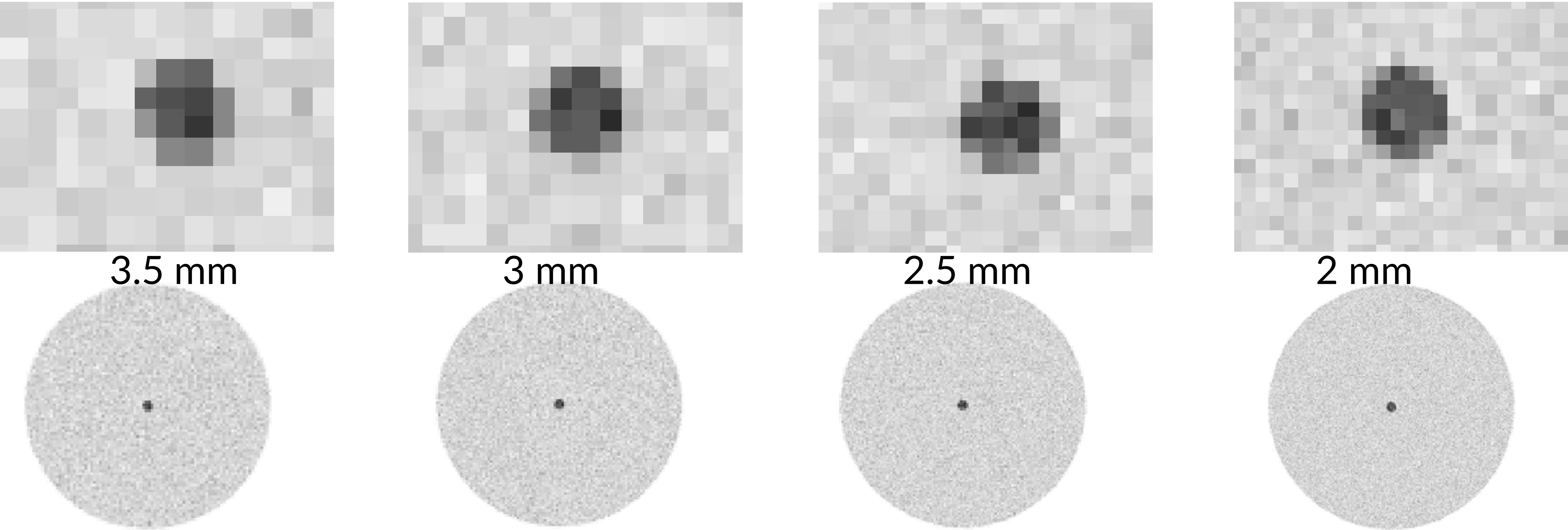


Noise $\propto {}^{1}/_{\Delta x}$

Poisson Noise

SPATIAL RESOLUTION AND NOISE

Increase counts quadratically

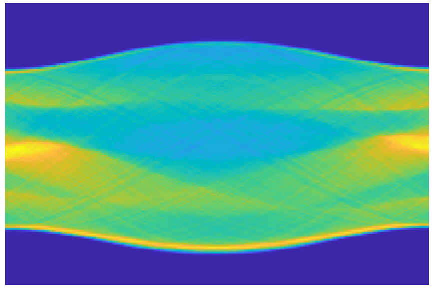


TOMOGRAPHIC PROBLEM

It gets even worse

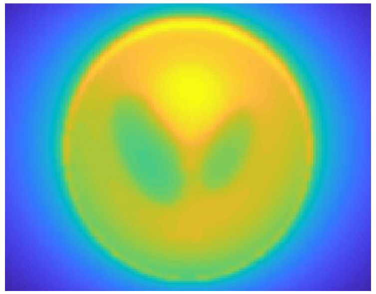
$y = H\lambda$

Forward projection



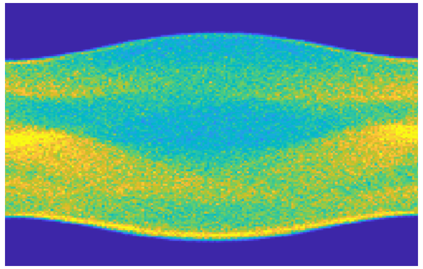
$H^T H\lambda$

Backprojection: $^1/_f$ lowpass filter



Analytical recon: high-pass ramp filer

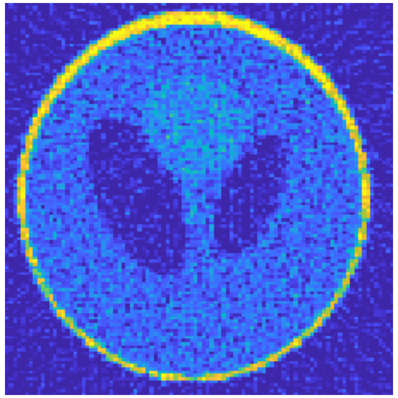
Noise in detector sinogram space?



Ramp filter!

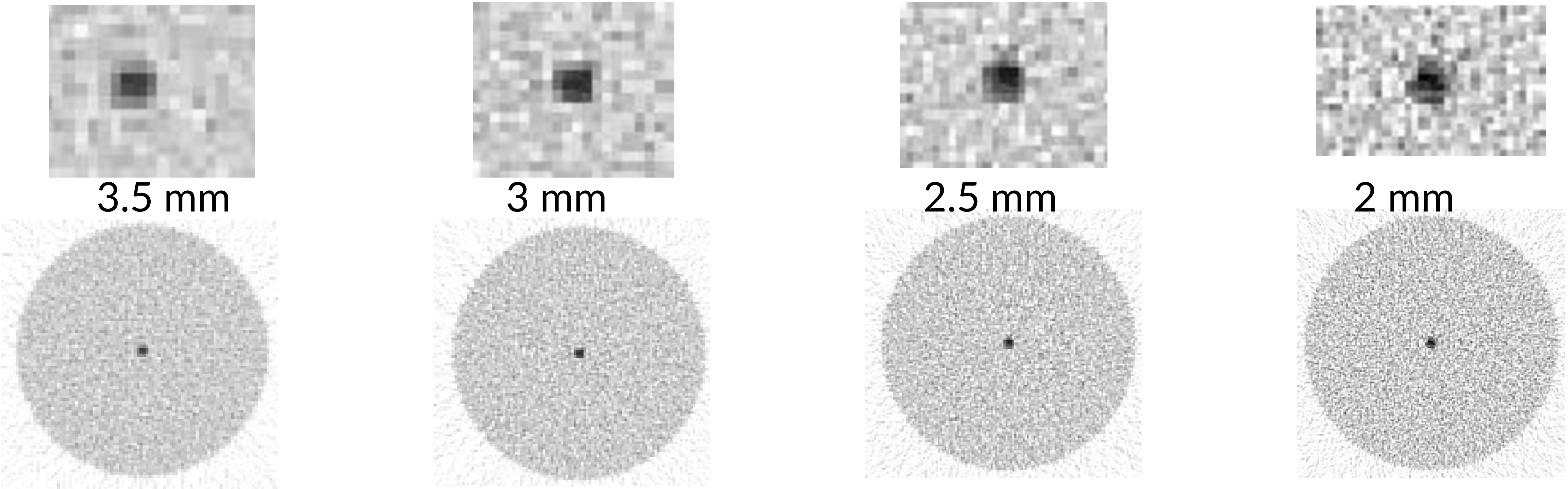
$$\lambda_{rec} = \lambda_{true} + (H^T H)^{-1} H^T noise$$

Noise is strongly amplified at high frequencies



Tomographic Noise

CONSTANT COUNTS



NOISE: TAKE AWAY MESSAGE

Summary

- The joint effect of the Poisson statistics and of tomographic noise makes achieving high resolution extremely hard.
- Need to scale the counts more than quadratically with resolution (in 2D….)
- Sensitivity is the n° 1 design desire for PET

NEW HARDWARE DEVELOPMENTS

Timing Resolution

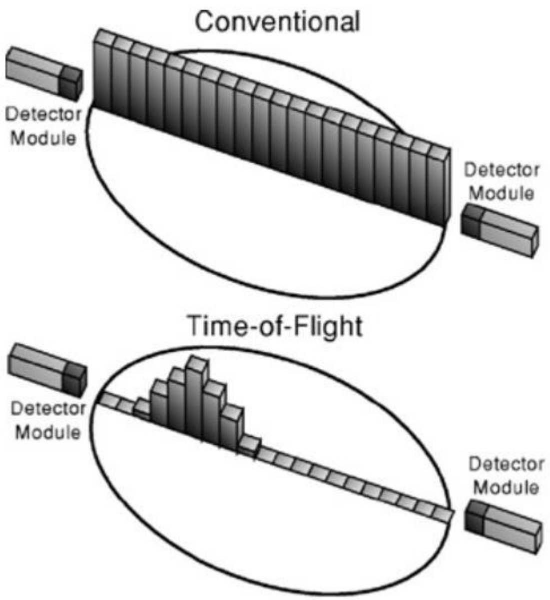
Energy Resolution

Extended Axial FOV

TITOLO SEZIONE

Timing Resolution

TOF principle



uniform probability on line-of-response

$$\Delta x = c\,\frac{\Delta t}{2}$$

500 ps $\rightarrow$ 7.5 cm

Current commercial systems

- Mostly limited by crystal thickness
  - Vendor A: 25 mm → 400 ps
  - Vendor B: 20 mm → 250 ps
  - (20 mm : 66ps at the speed of light)
- SiPM and LYSO are pushing the limit of timing resolution

BENEFITS OF TOF

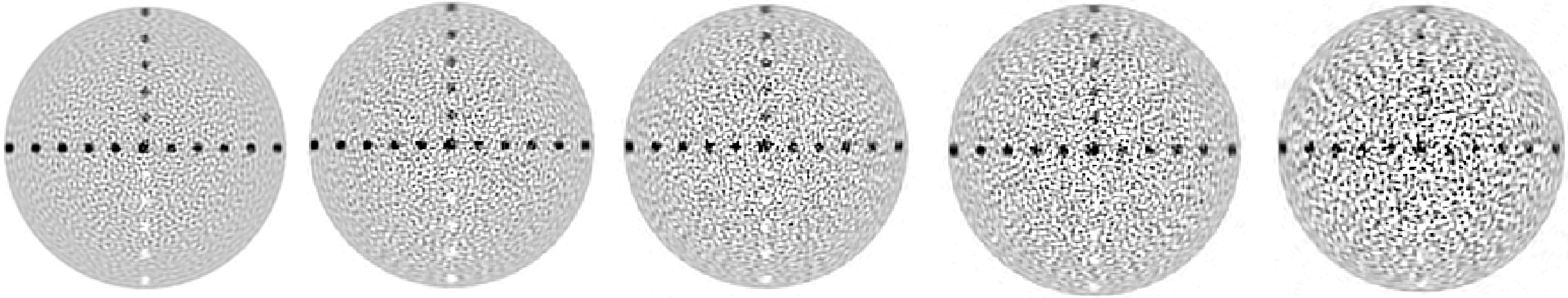
- Reduces noise
- Provides redundant information
- Makes reconstruction *much* more robust towards errors in the calibration of detector pairs, including attenuation

- Noise Reduction:
- $\sqrt{\frac{D}{D_{eff}}}$ $$D_{eff} = \frac{\sqrt{2\pi}}{\sqrt{8 \ln 2}} \frac{c}{2} \Delta t$$

TOF AT CONVERGENCE

Constant counts
Different timing resolution
Reconstruction at convergence

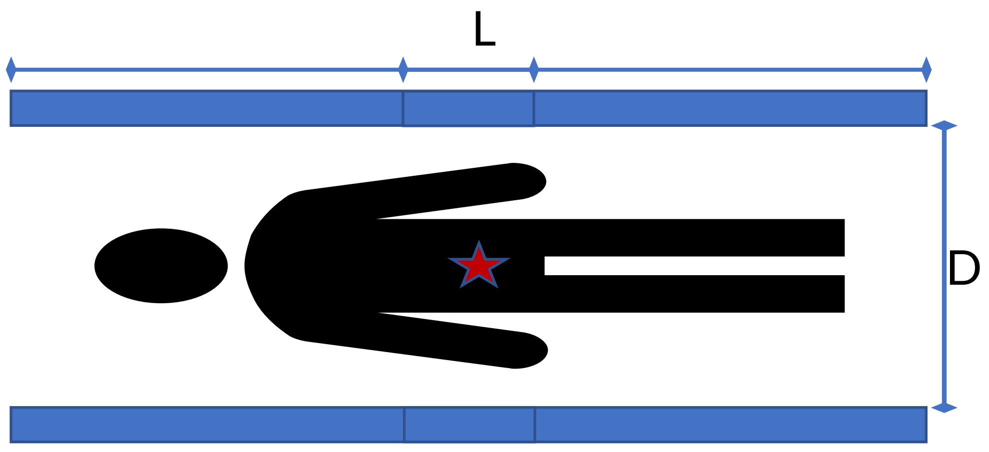
100 ps | 200 ps | 400 ps | 650 ps | non-TOF



EXTENDED AXIAL FOV

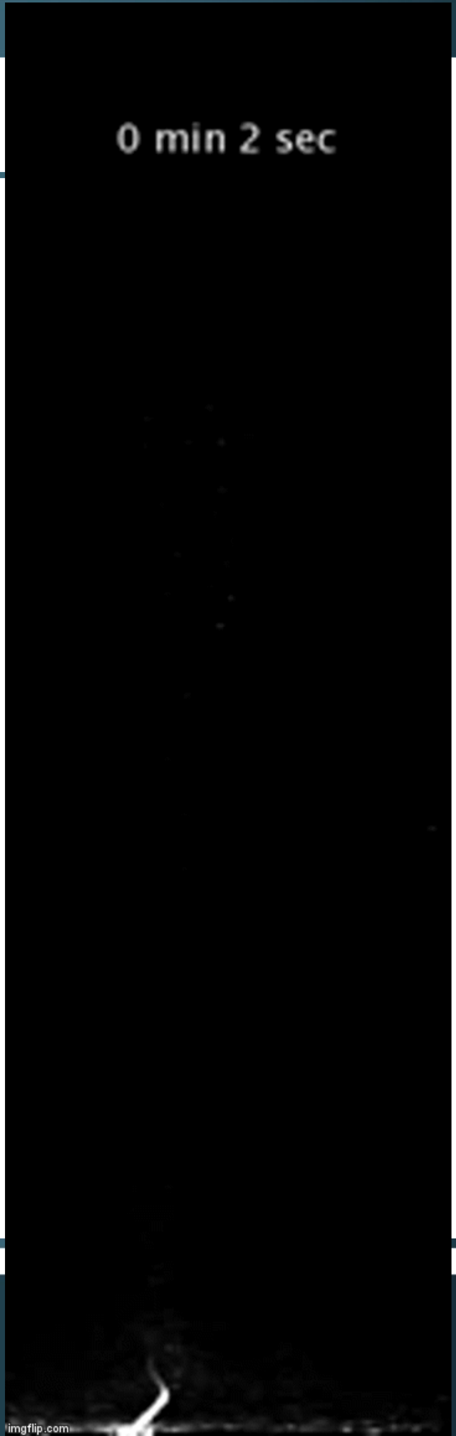
Getting More Counts

- Organ specific geometric efficiency:
  - $\frac{2}{\pi} atan\left(\frac{L}{D}\right)$ (fraction of solid angle)
- Whole body efficiency:
  - $\approx\propto L^2$
- 2m system gain:
  - Adult WB: 42x
  - Pediatrics WB: 20x
  - Cardiac: 5x
  - Brain: 5x



Poon et al, Phys Med Biol, 57:4077-4094, 2012

WHAT TO DO WITH 40X MORE COUN



- Fixed dose: SNR improved by 6.5x
  - Better images
  - More spatial resolution
  - Dynamic imaging (down to 0.1 s frames!)
- Long dynamic range
  - Acquire for 5 half lives!
- Fast acquisitions
  - No motion artefacts
- Ultra-low dose acquisitions
  - Inject 1/40 x -> 0.2 mSv scan / less than a flight!

CHALLENGES

Why now?

Explorer HW:

- Crystals N°: ~6 10^5
- SiPMs: 54k
- Lines of Response N°: 92 x 10^9

Explorer Recon:

- 9 Recon servers, each:
  - 96GB RAM
  - 2 V100 Tesla GPU
  - 2 Xeon 6126 CPU
- 10 min scan :
  - 100 GB Data, 15 Minutes Recon
- 60 min dynamic:
  - 2 TB data, several hrs

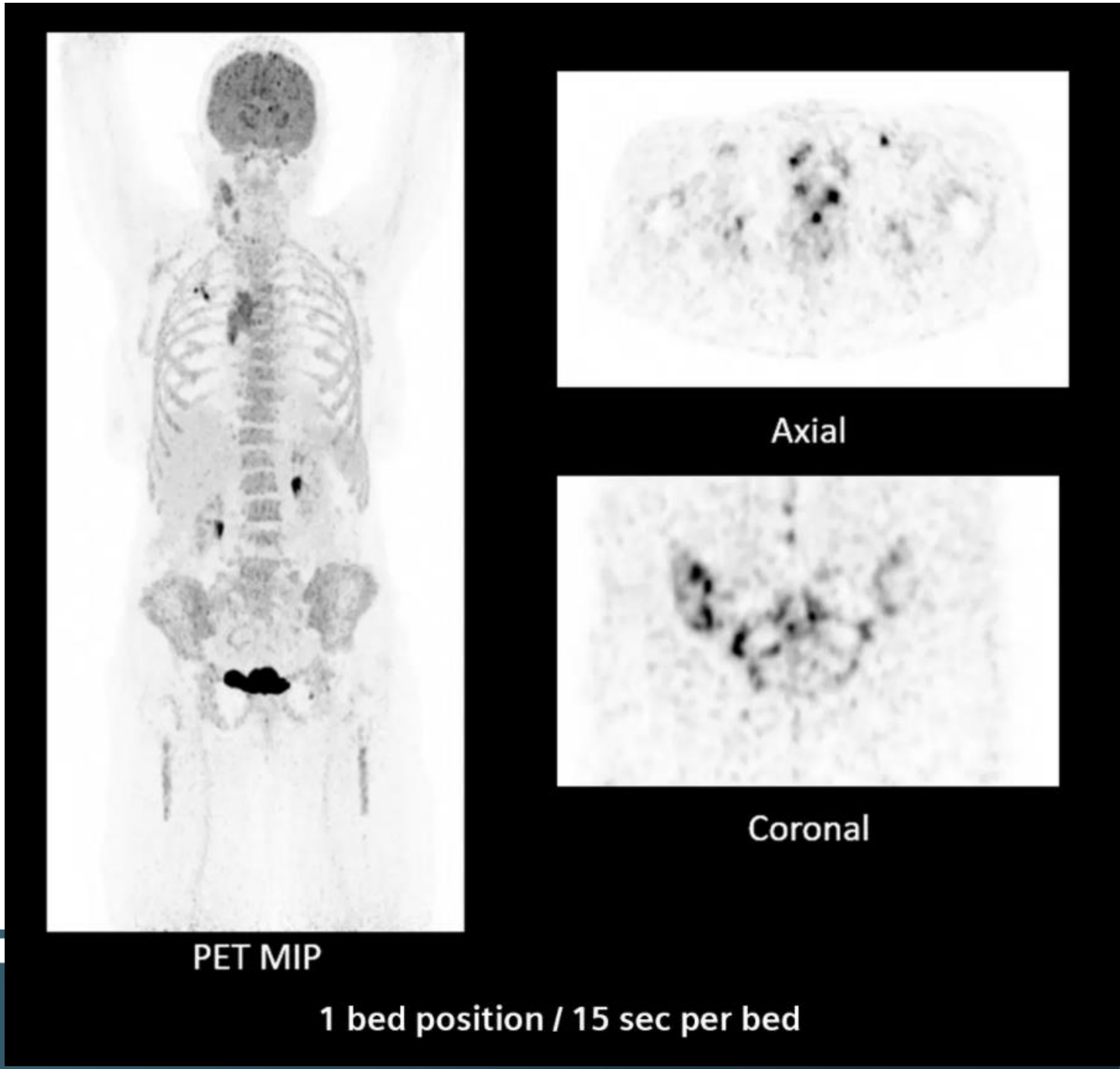
EXISTING SYSTEMS

United Imaging explorer: 2 m scanner (research only?)

PennPET Explorer: 1.4 m scanner (not commercial)

Commercial systems: 106 cm

- Sensitivity: ~5x a 25 cm scanner / 10x a 15 cm one
- Can acquire eyes to thigh in 1 steps!
- Dynamic scans always include the aorta



REGULARIZED RECONSTRUCTION

Early Stopped OSEM is not enough

WHY DO WE STOP EARLY?

OSEM-recon proprieties

- Recon time
- Visually less «noisy»
- Mathematically:

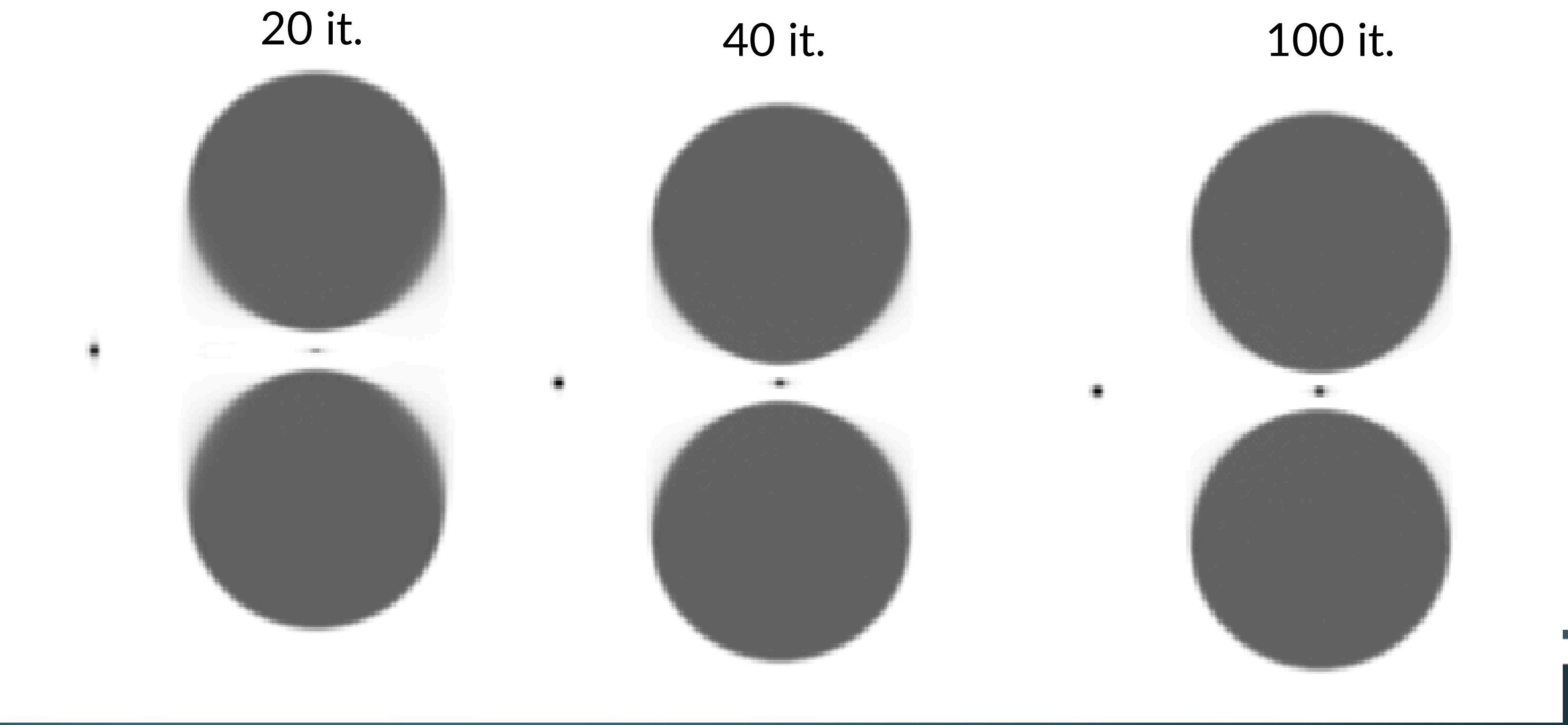
$$\lambda^{k+1} = [H^T W y]\mathrm{diag}\left(\lambda^k\right) \text{ with } W = \mathrm{diag}\left(1/H\lambda^k\right)$$

1. Hot contrast converges faster than cold
2. Larger background → Slower convergence
3. Smaller signal → Slower convergence

Presotto, Luca, Valentino Bettinardi, and Elisabetta De Bernardi. "A Simple Contrast Matching Rule for OSEM Reconstructed PET Images with Different Time of Flight Resolution." Applied Sciences 11.16 (2021): 7548.

IMPACT OF EARLY STOPPING ON QUANTIFICATION

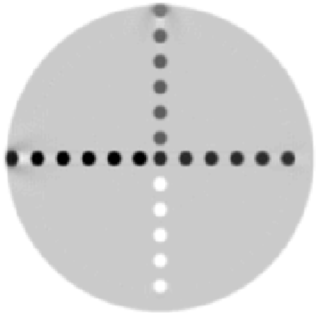
Same field of view, 2 identical signals in air and within a hot background.



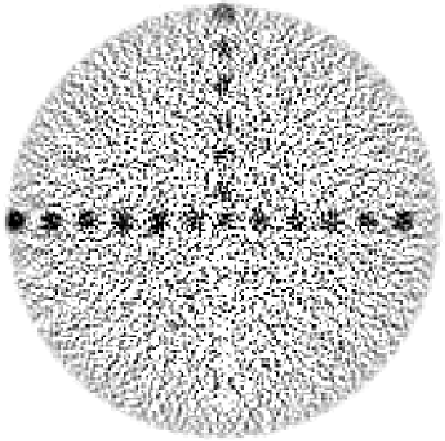
EARLY STOPPING: VISUAL NOISE

ML solution

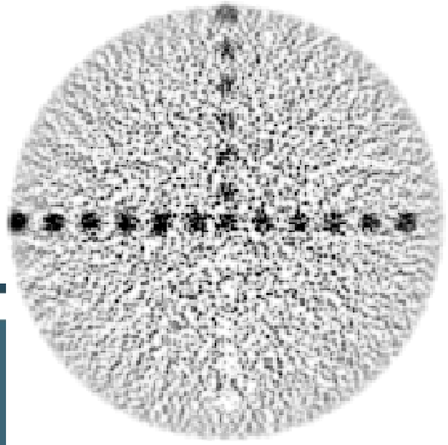
Reference:



Direct output



Gaussian smoothing 4 mm FWHM



REGULARIZATION

Can we get to convergence while limiting noise?

- *Unconstrained* image reconstruction with resolution modelling does not have a unique solution
- Why don't we add a constraint?
- Basic implementations are known not to work well
- Suppose we maximize $L(y,\lambda) + \beta\lambda' R\lambda$?
- $E[\lambda] = [H'D(^1/_{y_i})H + \beta R]^{-1} H'D(^1/_{y_i})H\lambda^{true}$

Spatial Resolution Properties of Penalized-Likelihood
Image Reconstruction: Space-Invariant Tomog
Fessler & Rogers, IEEE TMI, **1996**

REGULARIZATION

How we can get to convergence

- In a Poisson experiment more counts → Higher variance (even if lower relative error).
- In PET «signal» is «hot» → Penalize high variance → Suppress signal!!

Solution

- Penalize relative differences
- Weight regularization based on attenuation

Nuyts, J., Beque, D., Dupont, P., & Mortelmans, L. (2002). A concave prior penalizing relative differences for maximum-a-posteriori reconstruction in emission tomography. *IEEE Transactions on nuclear science*, *49*(1), 56-60.

REGULARIZATION

What if we don't want to stop early?

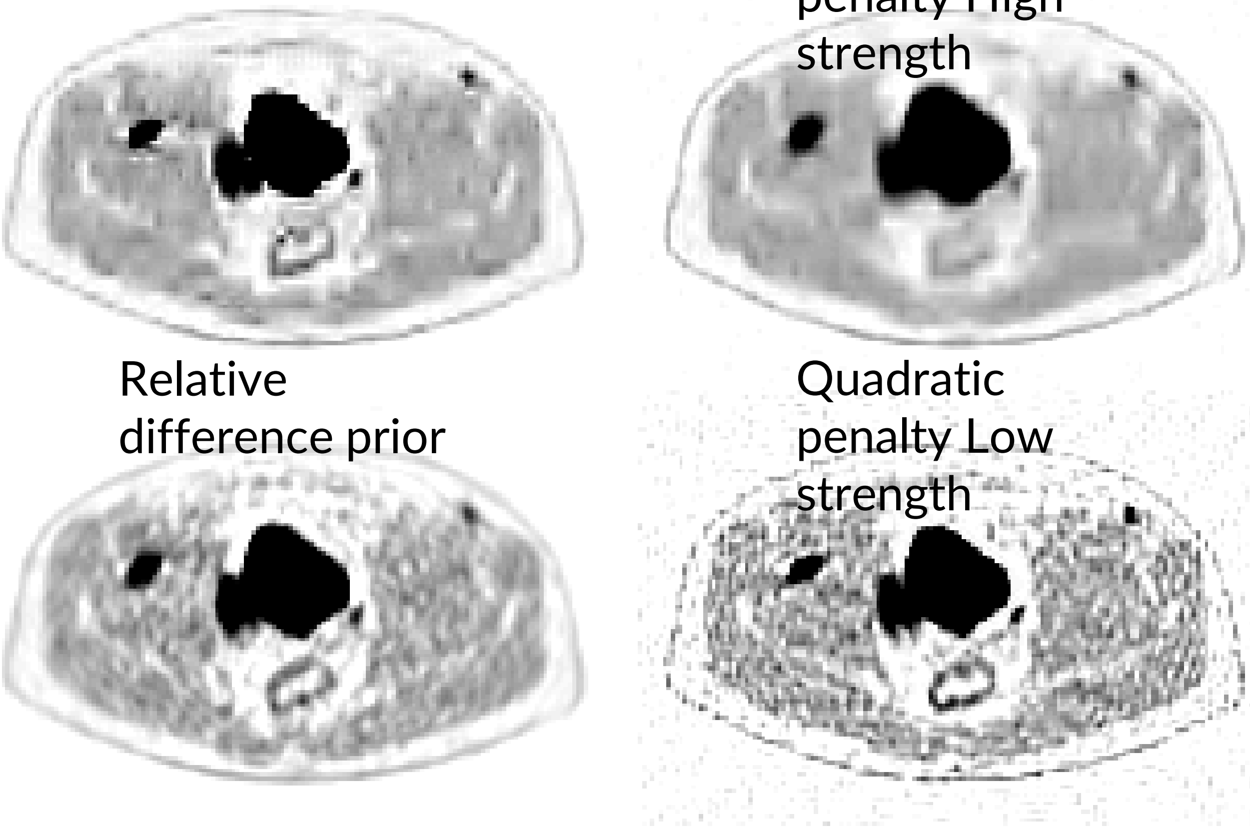
Variance is proportional to activity

Suppress variance

- Suppress hot signals!

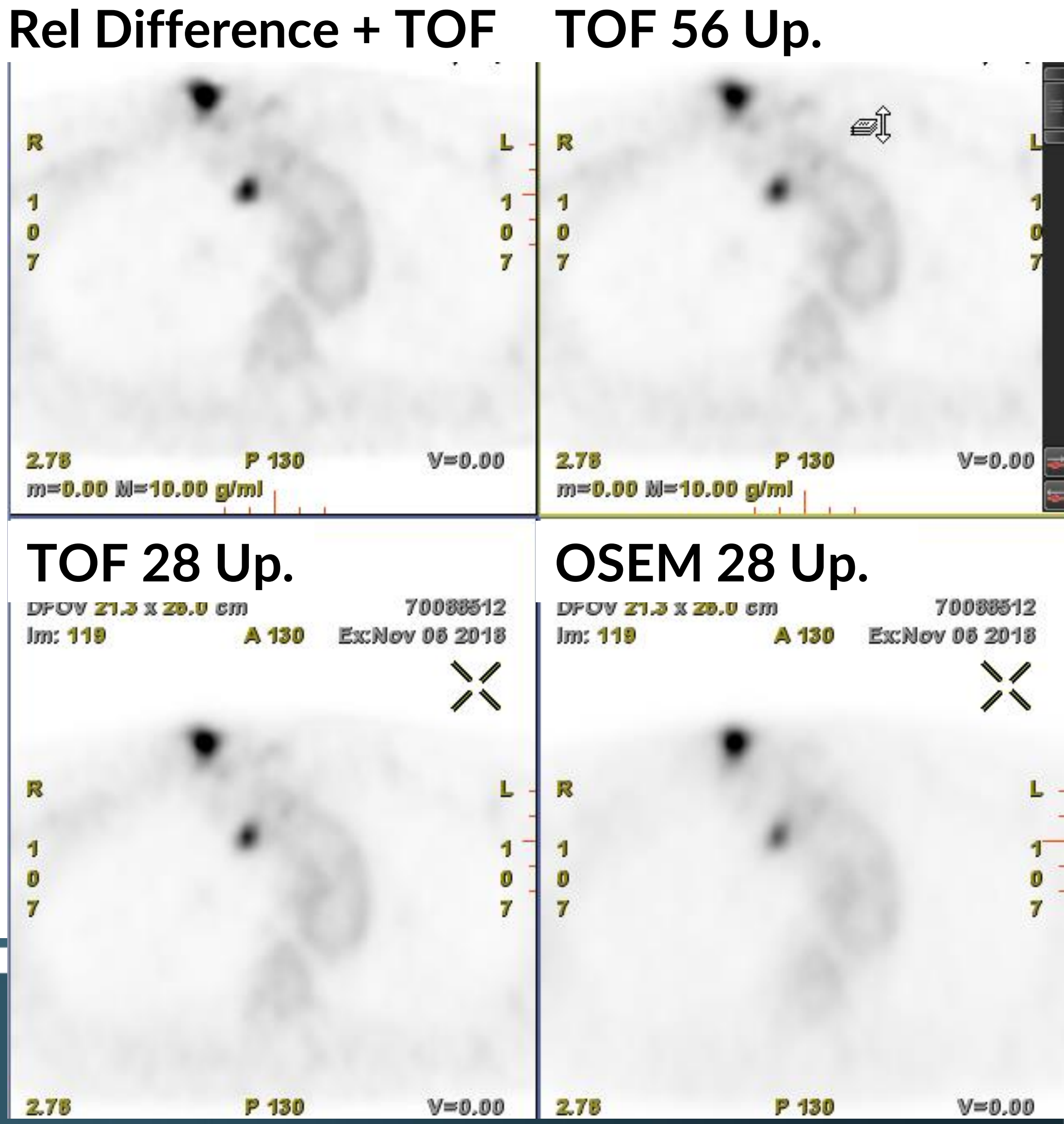
Solution

- Penalize relative differences



CLINICAL EXAMPLES

- Normal body patient
- Head/neck lesion
  - (High contrast/very low background)



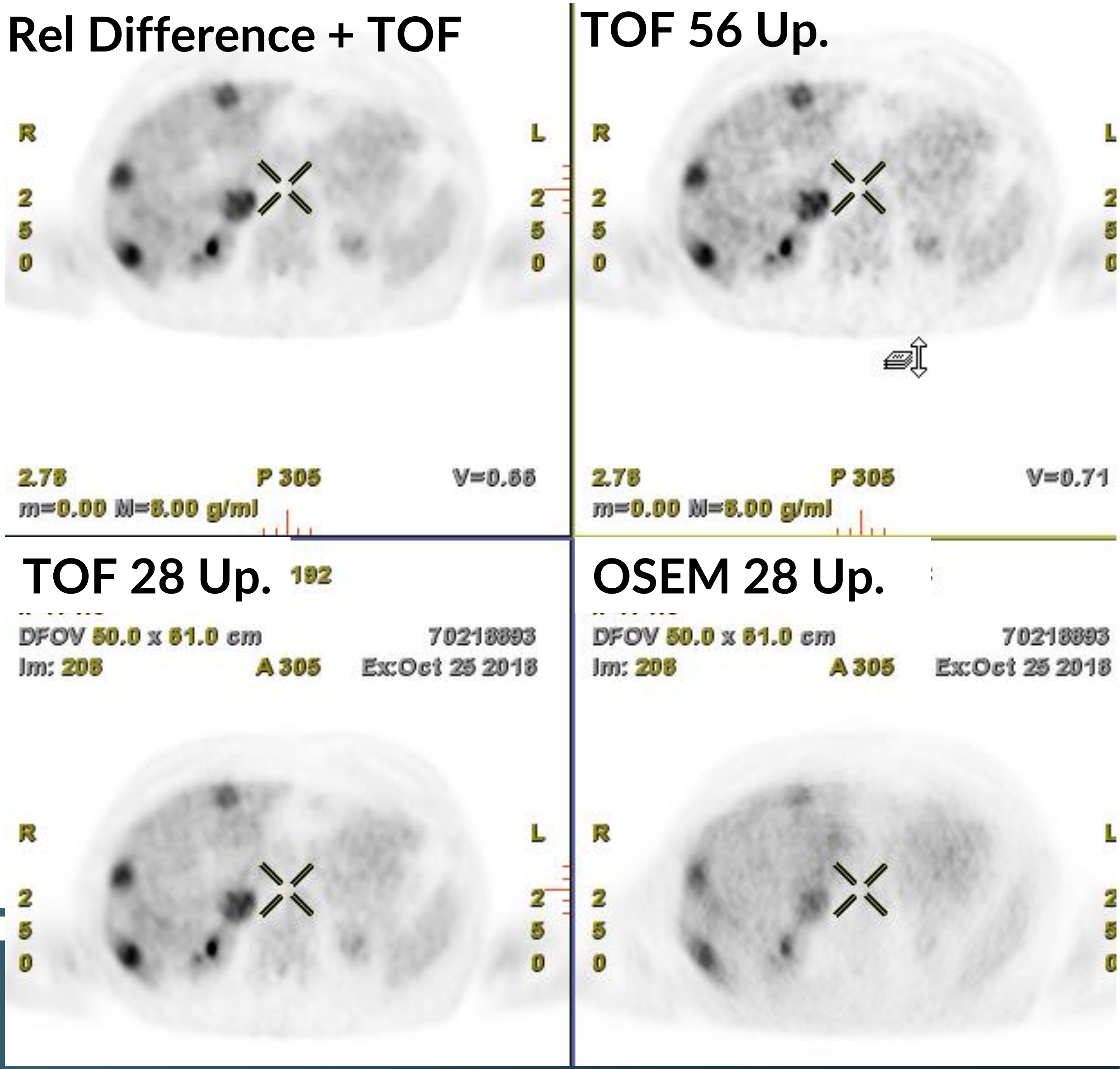
CLINICAL EXAMPLES

Normal Weight Patients

Arms downs

Hepatic lesions (low contrast)

Large lesions



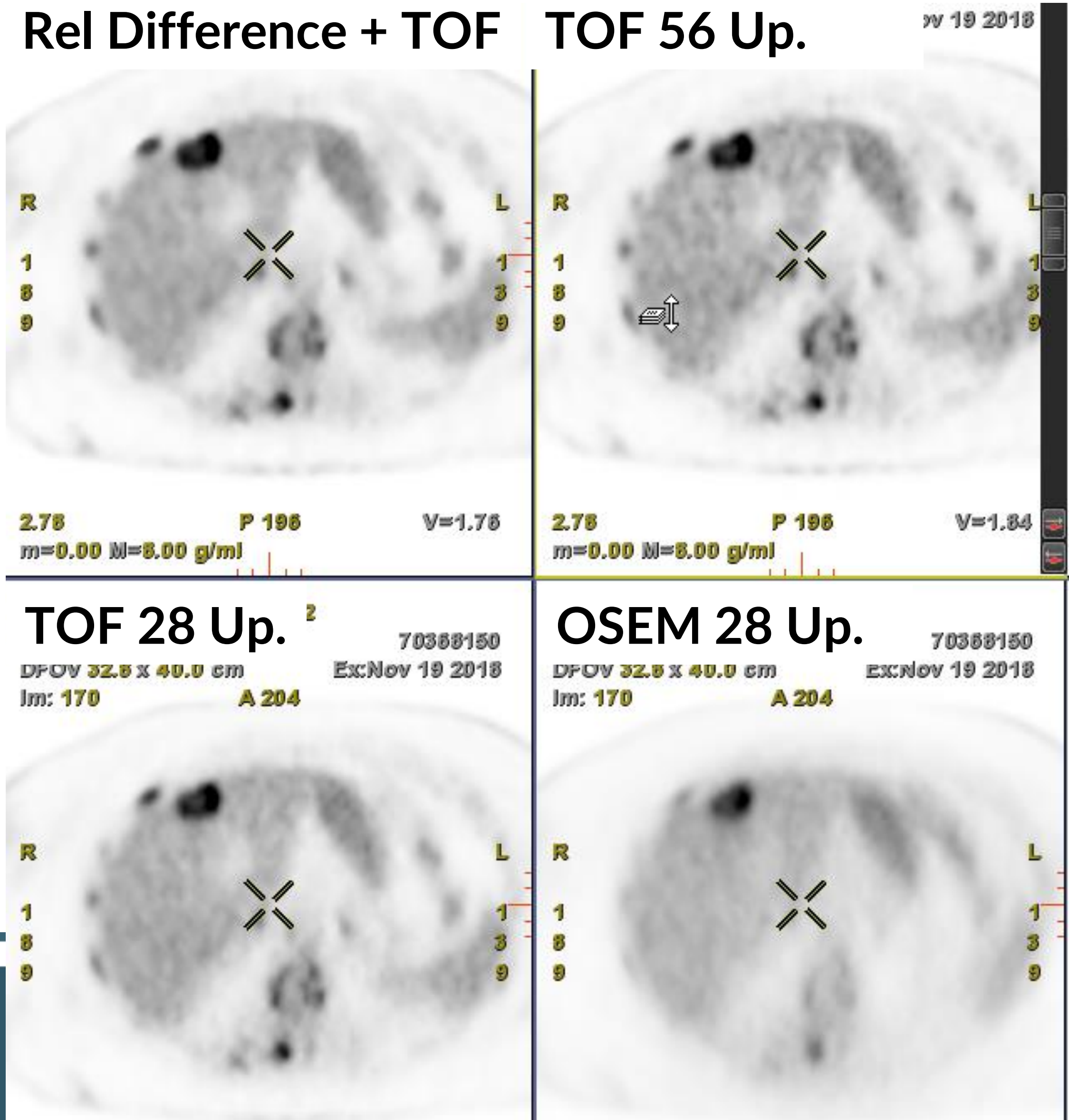
CLINICAL EXAMPLES

Obese patient

Arms downs

Hepatic lesions (low contrast)

Large lesions



ARTIFICIAL INTELLIGENCE DENOISING

Artificial intelligence denoising

CONVOLUTIONAL NEURAL NETWORKS

AMYLOID PET DENOISING

- Standard U-NET with residual approach
- 40 pts (32/8 train/val, 5 fold xVal)
- Output: Standard acq (20 min, 300 MBq)
- Input: 1/100 of the events + mpMRI
  - (3 MBq or 12 s acquisition)

Chen, Kevin T., et al. "Ultra–low-dose 18F-florbetaben amyloid PET imaging using deep learning with multi-contrast MRI inputs." Radiology 290.3 (2019): 649-656.

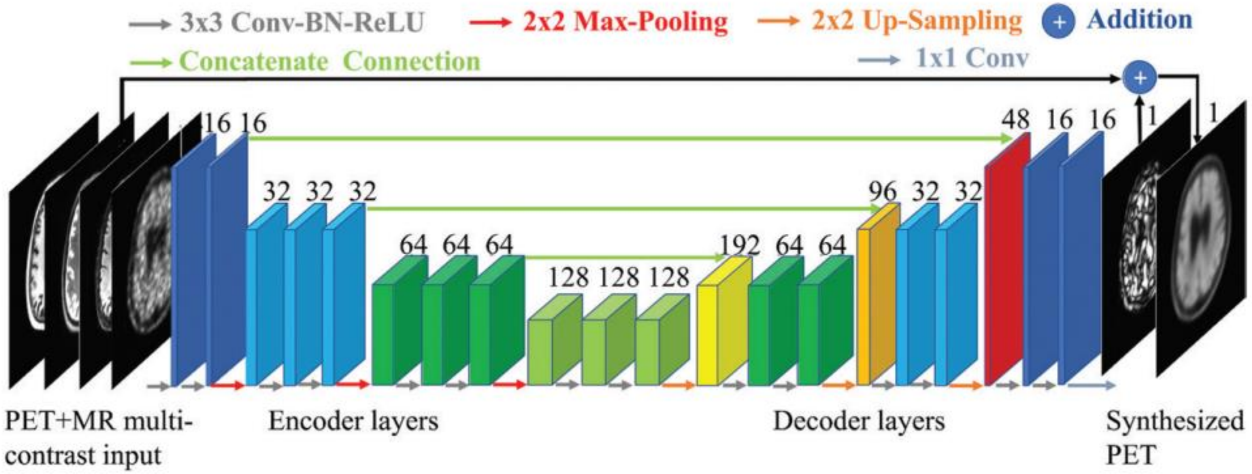


Figure 1: A schematic of the encoder-decoder convolutional neural network used in this work. The arrows denote computational operations and the tensors are denoted by boxes with the number of channels indicated above each box. Conv = convolution, BN = batch normalization, ReLU = rectified linear unit activation.

Artificial intelligence denoising

RESULTS

Amyloid PET Denoising

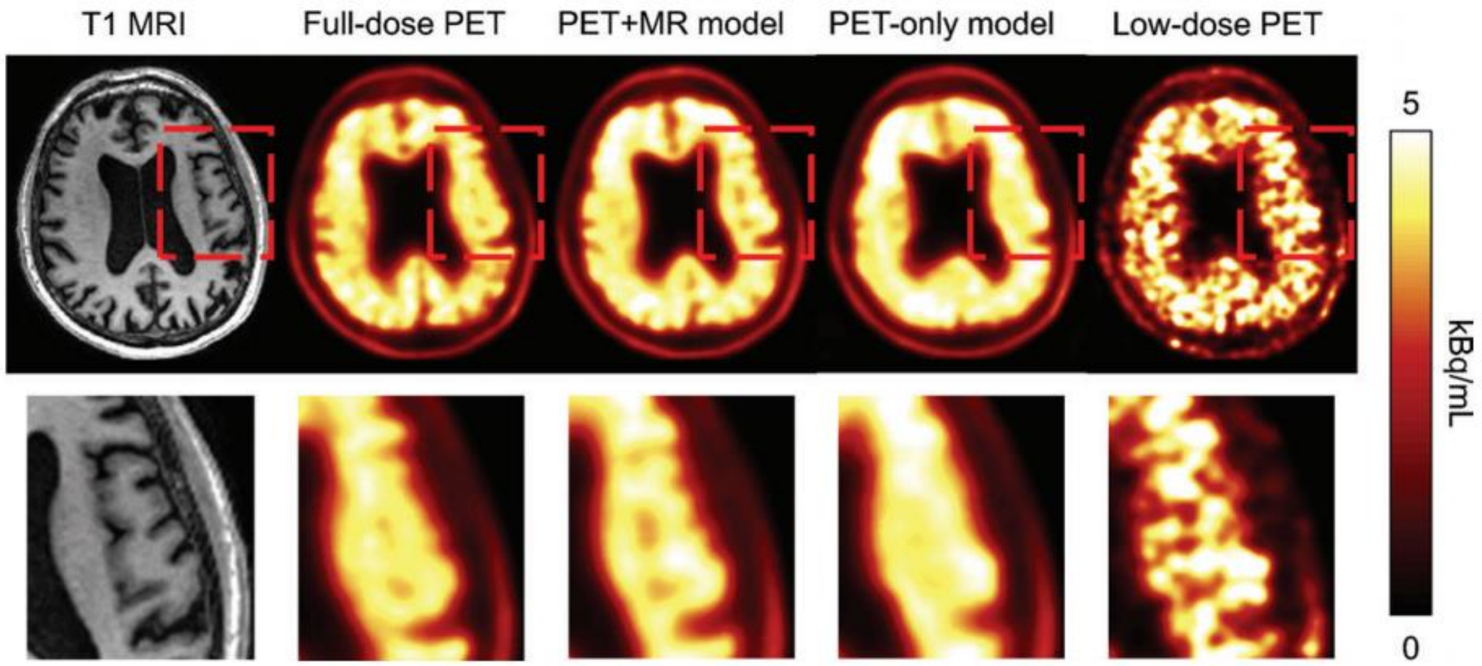


Figure 4: Amyloid-positive PET image in a 58-year-old male patient with Alzheimer disease, with the T1-weighted MR image (left) shown as reference. The region within the red box in the images in the top row is enlarged and shown in the bottom row. The synthesized PET images show significantly reduced noise compared with the low-dose PET images, while the images generated from the PET+MR model were superior in reflecting the underlying anatomic patterns of the amyloid tracer uptake compared with the images generated from the PET-only model.

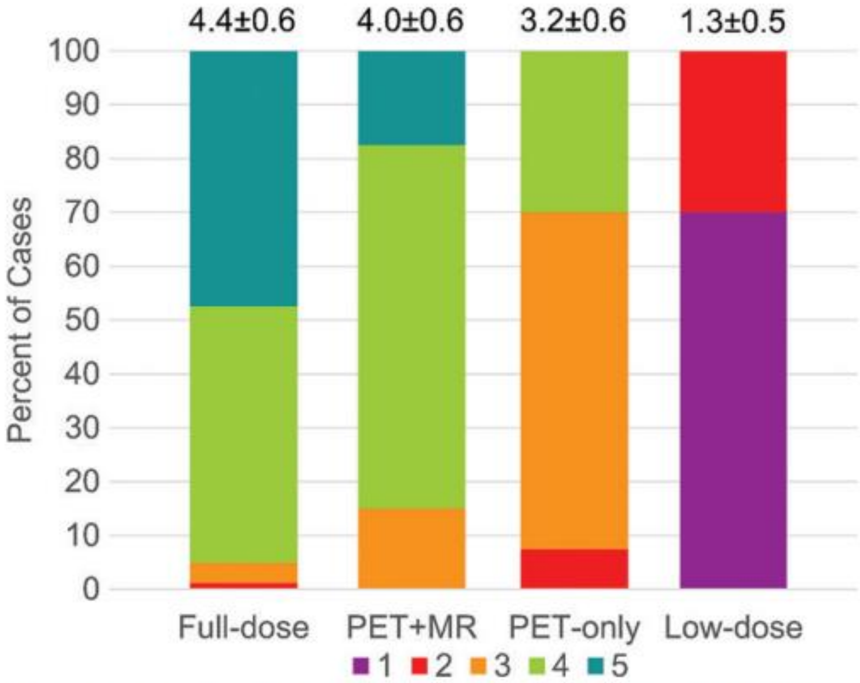


Figure 6: Clinical image quality scores (1 = uninterpretable/low, 5 = excellent/high; mean scores and standard deviation of all readings presented at top of each bar) as independently assigned by the two readers.

Chen, Kevin T., et al. "Ultra–low-dose 18F-florbetaben amyloid PET imaging using deep learning with multi-contrast MRI inputs." Radiology 290.3 (2019): 649-656.

FDG CARDIAC PET DENOISING

- Standard U-NET
- Input: PET + CT
- Note: fully 3D (400M parameters)
- Training: 168 patients (112/28/28)
- Counts reduction: 10%, 1%
- Full statistics Images/ Gated Images
- 300 MBq 10 min acquisition

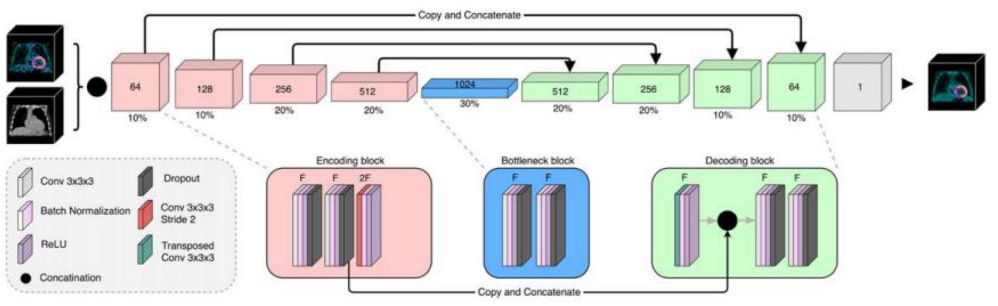


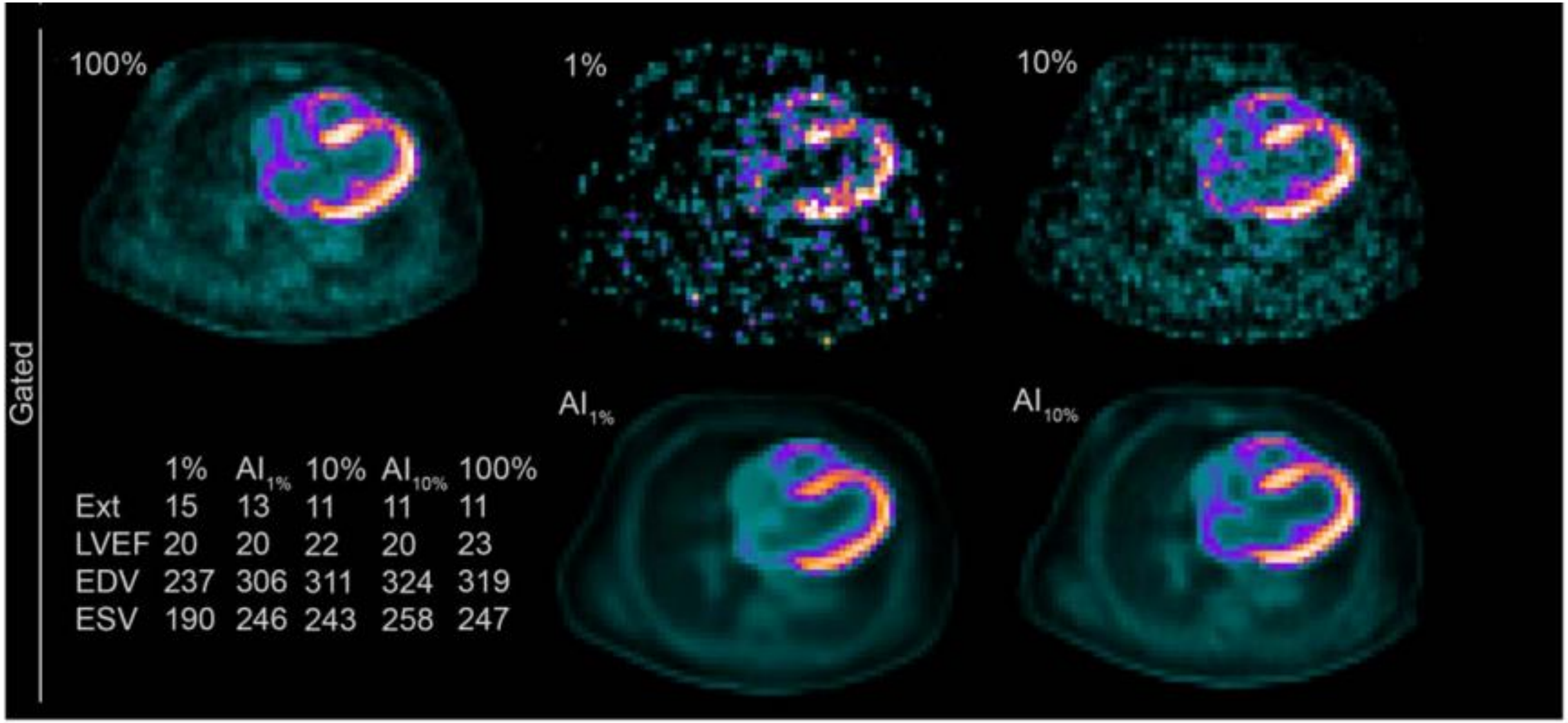
Figure 1. Schematic illustration of the model architecture. The model accepts two-channel input consisting of full volume low-dose PET and CT images (128 × 128 × 112 × 2) and outputs the de-noised PET image. The number inside each block represents the number of filters/kernels (F) applied in the convolution (Conv) layers and the percentage shown below each block represents the dropout fraction used.

Ladefoged, Claes Nøhr, et al. "Low-dose PET image noise reduction using deep learning: application to cardiac viability FDG imaging in patients with ischemic heart disease." Physics in Medicine & Biology 66.5 (2021): 054003.

Artificial intelligence denoising

RESULTS

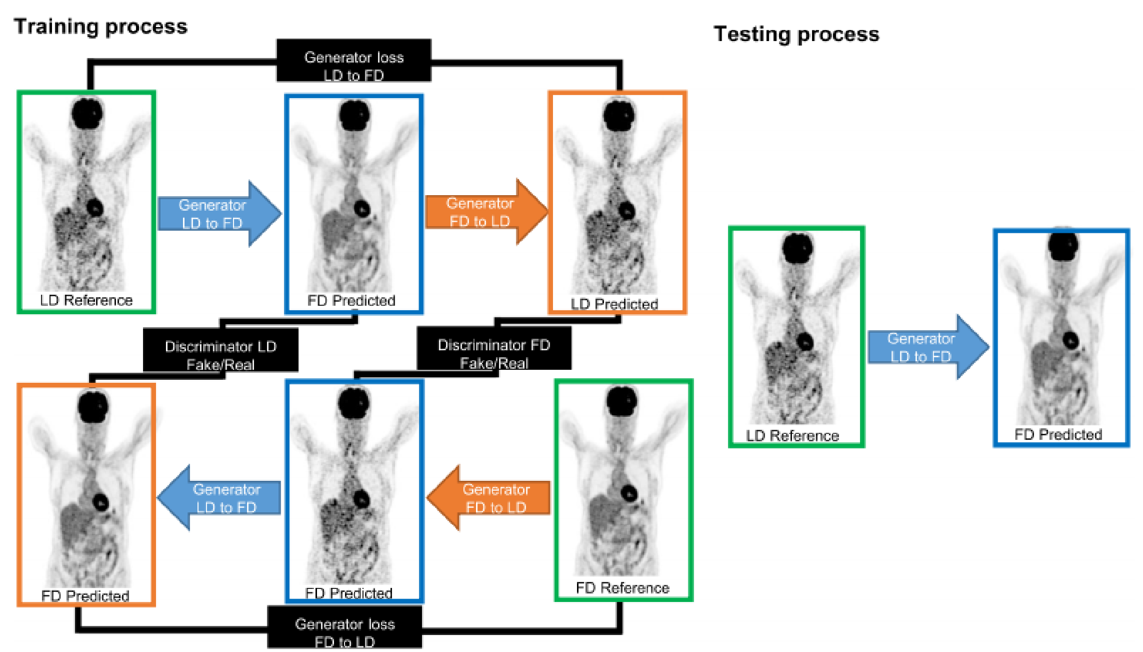
FDG Cardiac PET Denoising



Ladefoged, Claes Nøhr, et al. "Low-dose PET image noise reduction using deep learning: application to cardiac viability FDG imaging in patients with ischemic heart disease." Physics in Medicine & Biology 66.5 (2021): 054003.

ADVANCED METHODS: CYCLE GAN

- GAN learn the noise pattern best
- Cycle GAN do not need paired training examples
- Potentially poorer quantitative performance?
- Training: 85 oncological pts (60/15/10)
- Compared with standard Res-UNET

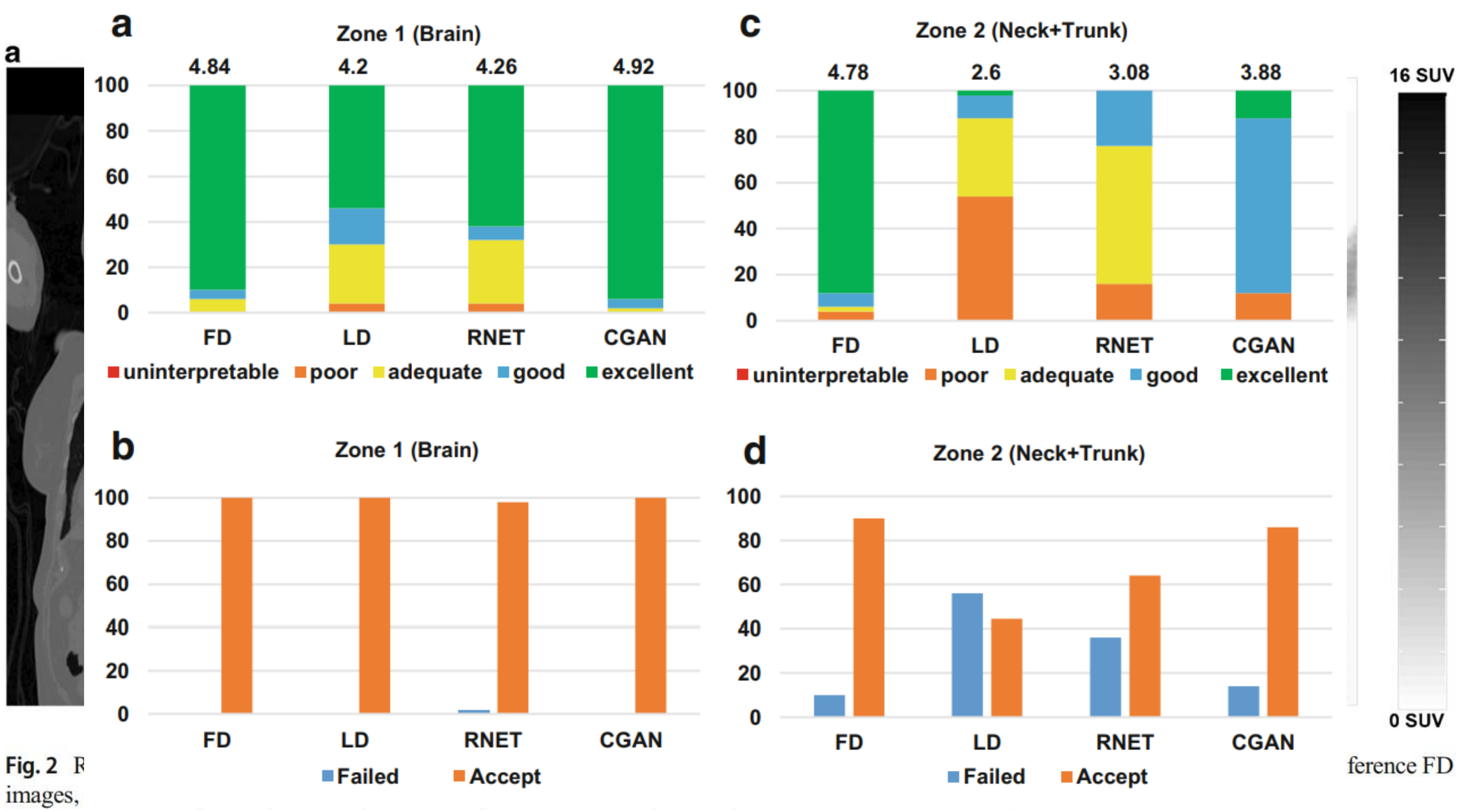


Sanaat, Amirhossein, et al. "Deep learning-assisted ultra-fast/low-dose whole-body PET/CT imaging." European Journal of Nuclear Medicine and Molecular Imaging (2021): 1-11.CC

Artificial intelligence denoising

RESULTS

Advanced Methods: Cycle GAN



Sanaat, Amirhossein, et al. "Deep learning-assisted ultra-fast/low-dose whole-body PET/CT imaging." European Journal of Nuclear Medicine and Molecular Imaging (2021): 1-11.CC

CONCLUSIONS

Exciting new times!

WHERE DO WE GO?

- Image r
- Better
- Improv
- Long S
- Artifici …tion

New era for Positron Emission Tomography?

Questions?

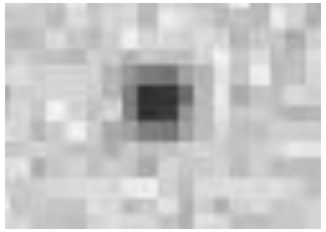
Email: presotto.luca@outlook.it

Luca Presotto, PhD
Medicina Nucleare, IRCCS Ospedale San Raffaele, Milano

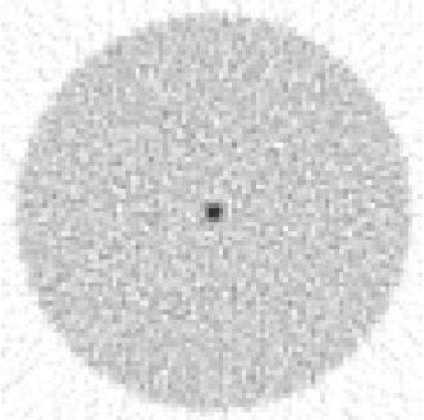
BACKUP

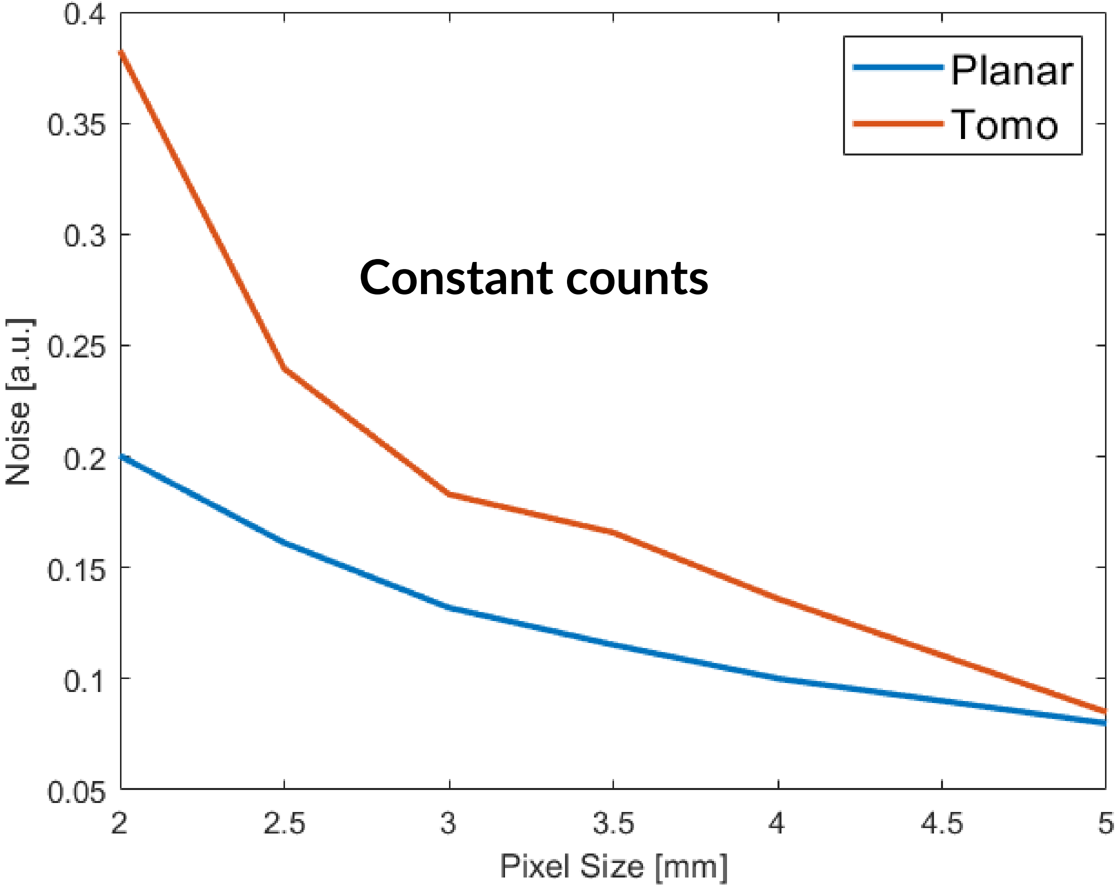
Tomographic Noise

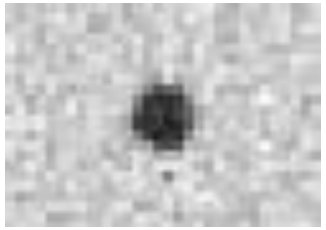
CUBIC COUNT INCREASE



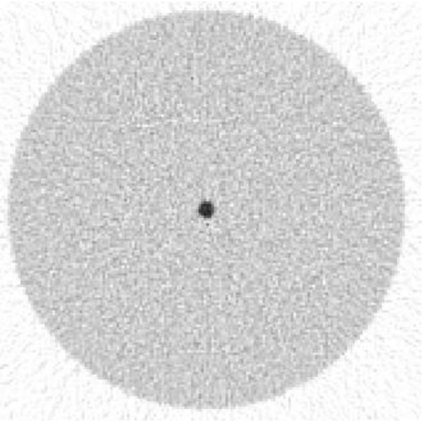
3.5 mm







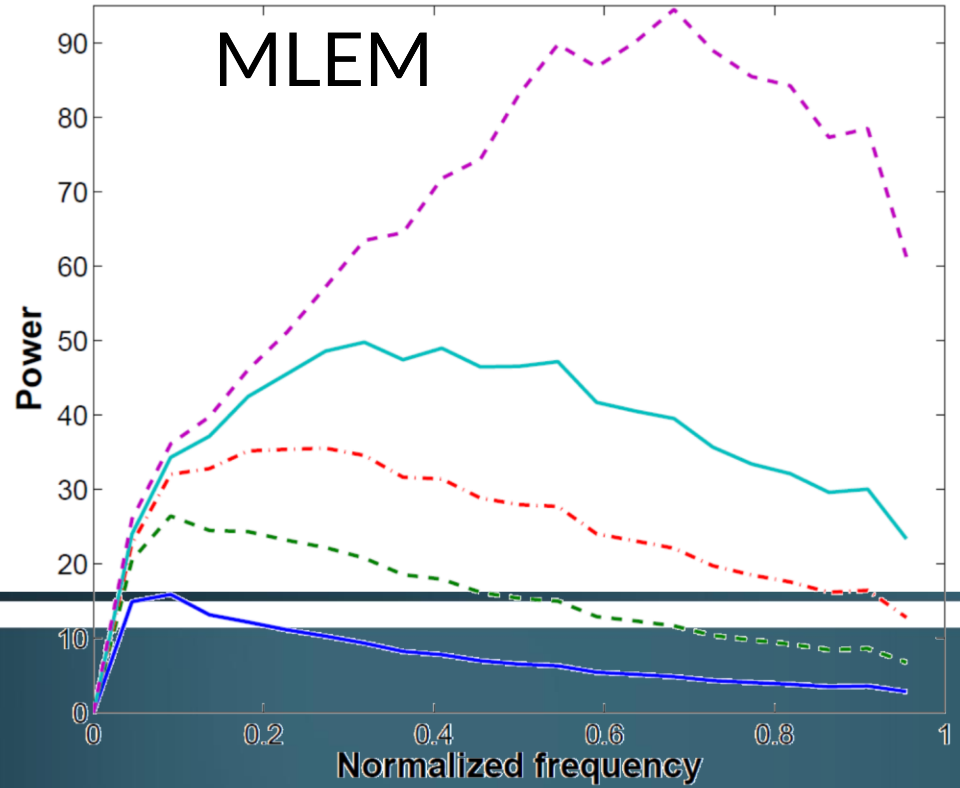
2 mm

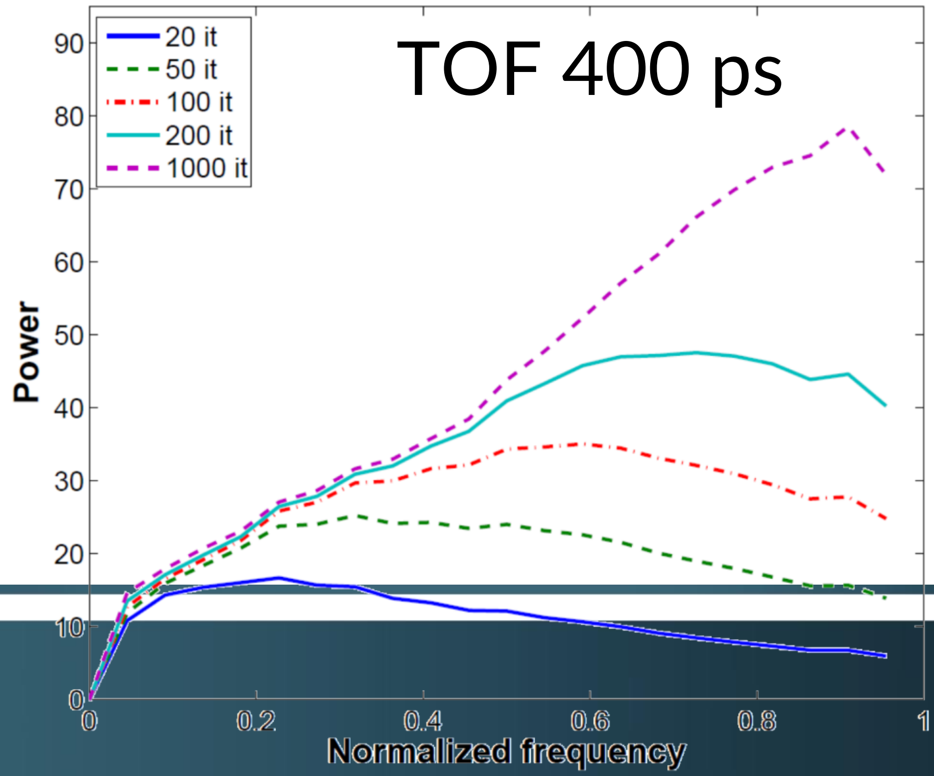


ENERGY RESOLUTION

- Scatter is the highest confounding factor
  - Up to 40% of non-random coincidences for systems with 10% energy resolution
- Research on narrowing the energy window

- L'NPS è mal definito ma… Misuriamolo in un rettangolo centrale del fantoccio uniforme

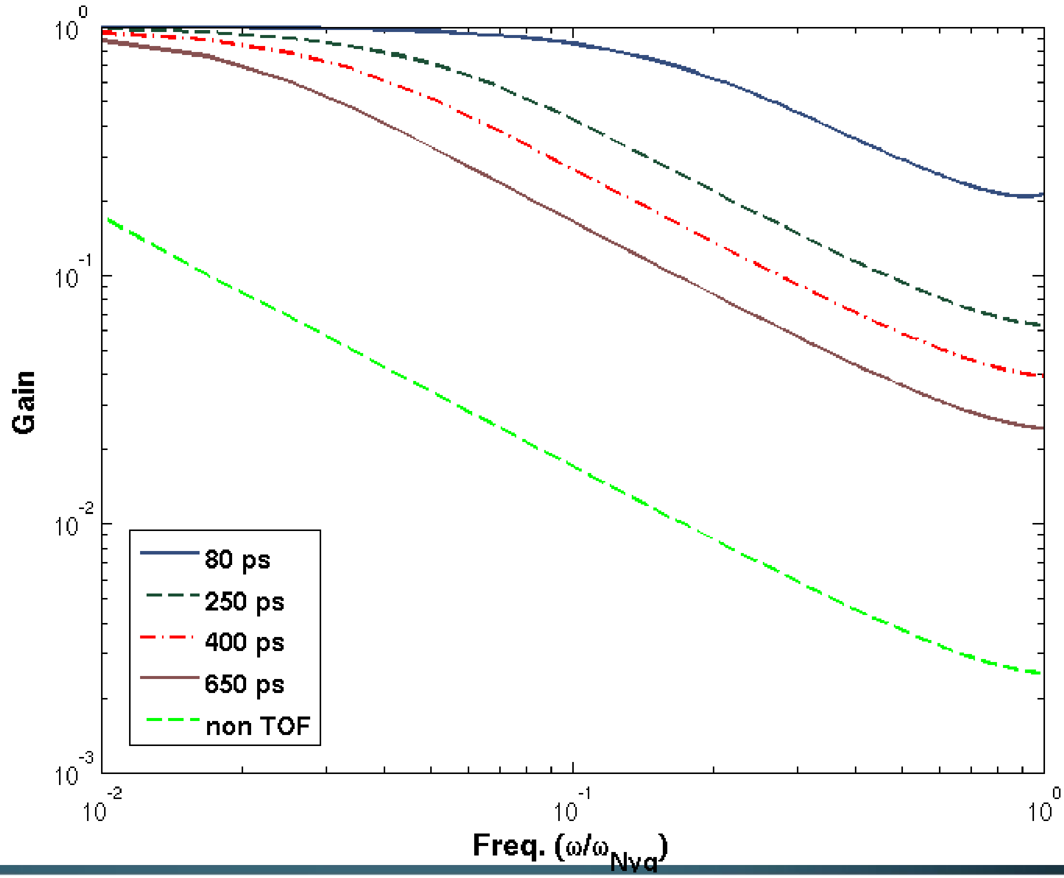




- Without regularization the image is way too noisy
- What do we expect from maximizing $L(y,\lambda)+\beta\lambda' R\lambda$?
- $E[\lambda]=[H'D(1/y_i)H+\beta R]^{-1}H'D(1/y_i)H\lambda^{true}$
- First Huge problem!! $< y_i > \propto \lambda_j$ ➔The more counts a pixel has the higher the influence of the penalty (whatever *R* we use…)
- Second problem: *H* includes attenuation correction factors. Which vary by a factor ~100 for different sinogram bins
- Third problem: the more counts we have the more our penalty acts!
- Any Bayesian-like regularization we can come up with does not satisfy our requests for a clinical reconstruction!!!

- $[H^T H]$ lowpass filter with varying TOF

- Frequencies suppressed here have noise enhanced during reconstruction



TOF EFFECT ON POISSON STATISTICS

Poisson Likelihood Hessian diagonal: $\sum_i c_{i,j}^2 \frac{y_i}{\bar{y}_i^2}$ $(\bar{y}_i = \sum c_{i,j}\lambda_j + r_i + s_i)$

- The fewer counts the steeper the curvature
- The better the TOF the fewer the counts "related to pixel j "
- The timing coordinate, at good CTR, constrains results much more than the "tomographic" part
- $\frac{\sigma_{STD}}{\sigma_{TOF}} = \sqrt{\frac{D}{D_{eff}}}$

Pro:

- Extremely robust to inconsistencies
  - Normalization/dead time
  - Attenuation
- Randoms become negligible

Con:

- Very sensitive to time-critical corrections
  - Timing coordinate
  - Timing resolution
  - Scatter

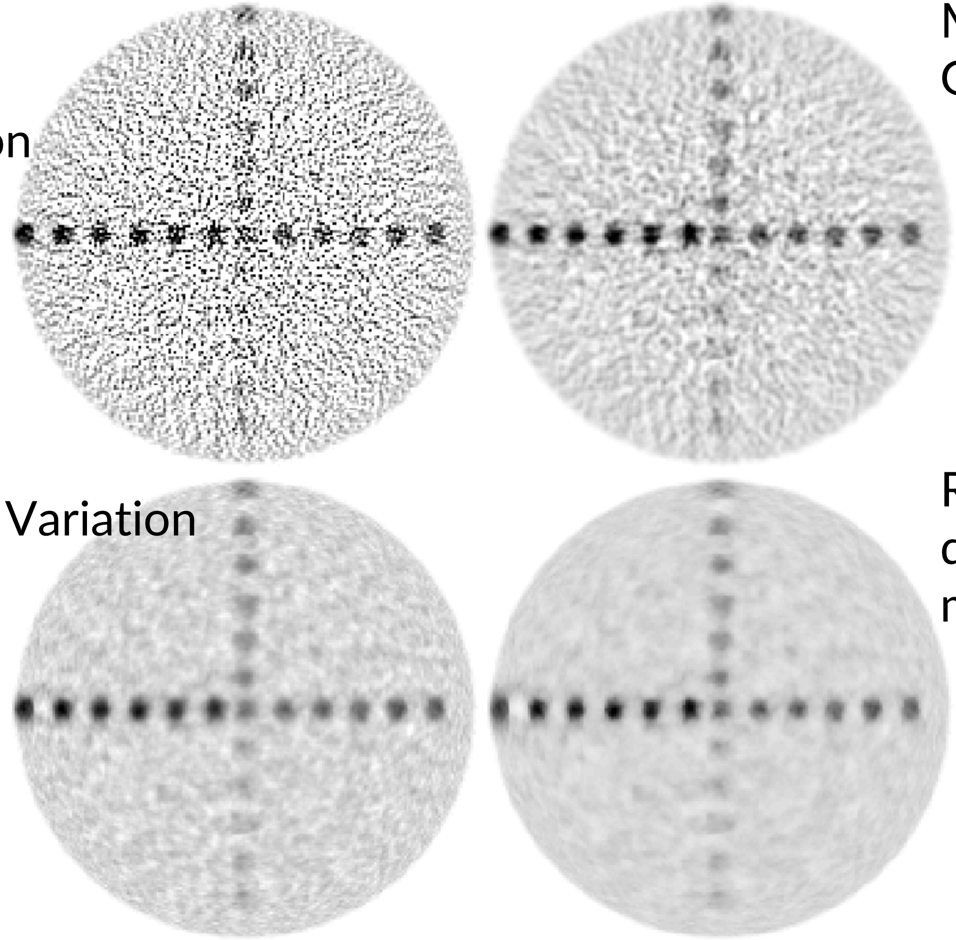
EXAMPLE OF REGULARIZATION STRATEGIES

Contrast: 2, 3, 4, 6

Diameter: 45 cm

Attenuation: Water

Single noise realization



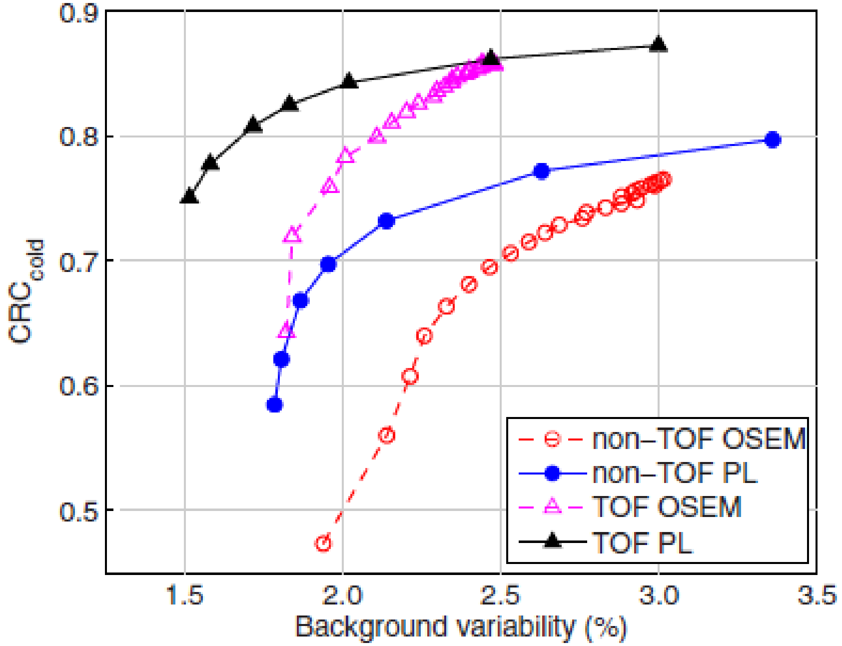
CLINICAL IMPLEMENTATION

OSEM Diff

Rel. Diff

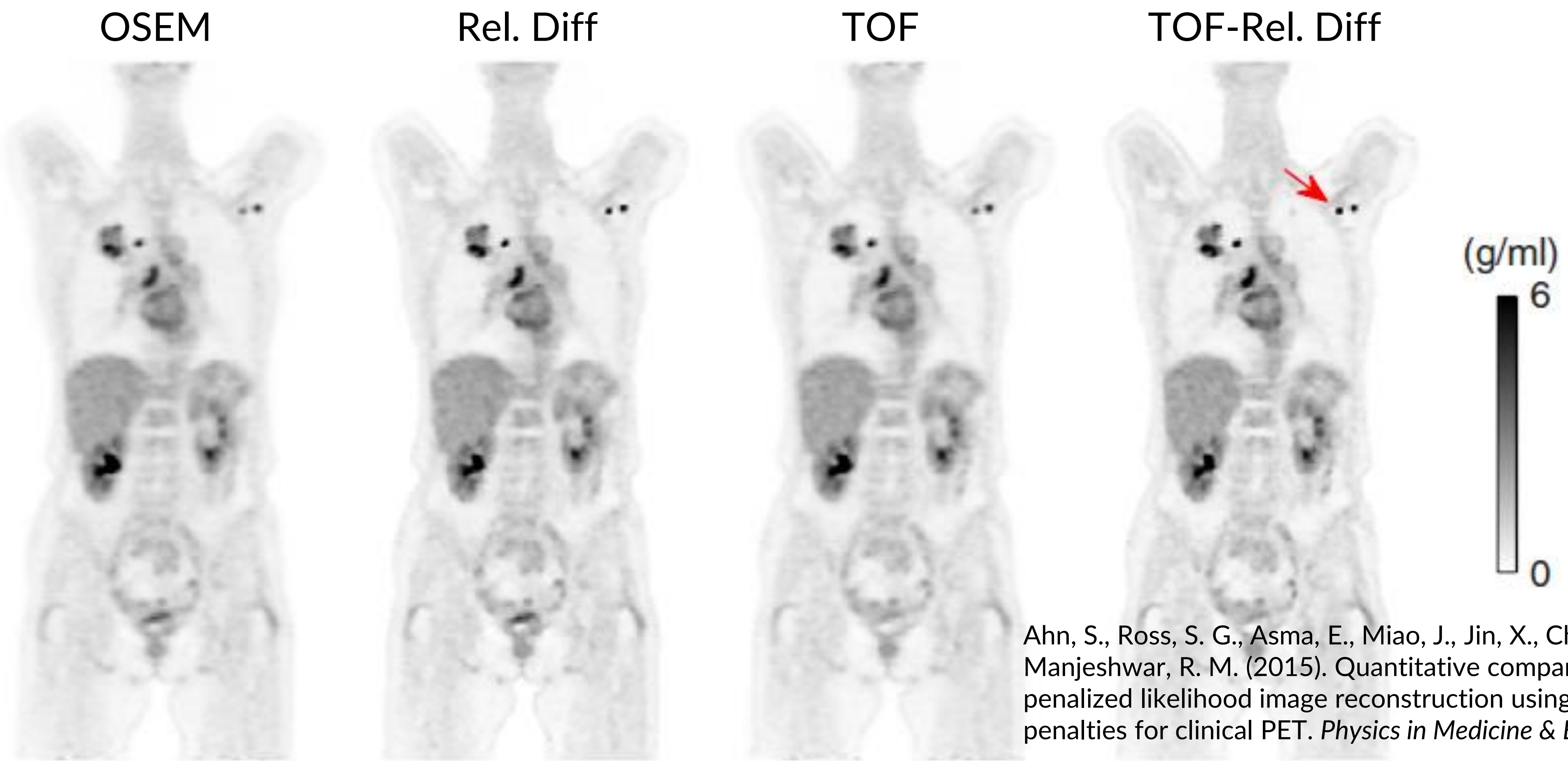
TOF

TOF-Rel.



Ahn, S., Ross, S. G., Asma, E., Miao, J., Jin, X., Cheng, L., ... & Manjeshwar, R. M. (2015). Quantitative comparison of OSEM and penalized likelihood image reconstruction using relative difference penalties for clinical PET. *Physics in Medicine & Biology*, *60*(15), 5733.

CLINICAL IMPLEMENTATION



Ahn, S., Ross, S. G., Asma, E., Miao, J., Jin, X., Cheng, L., ... & Manjeshwar, R. M. (2015). Quantitative comparison of OSEM and penalized likelihood image reconstruction using relative difference penalties for clinical PET. *Physics in Medicine & Biology*, *60*(15), 5733.

EXAMPLE: WRONG ATTENUATION