Understanding PET images for segmentation tasks

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Conflict of Interest Disclosure

Nothing to disclose.

Outline: images and segmentation

Patient → **Data** → **Images** → **Interpretation**

PET scan **Reconstruction** **Observer**

- Patient: tracer distribution function
  - Randomly sampled from the tracer distribution
- Data: acquired by the PET scanner
  - Randomly sampled from the emissions
- Images: reconstructed from the data
  - Estimation choices
- Interpretation: answering the clinical question
  - Utility for the required task

Patient: tracer distribution

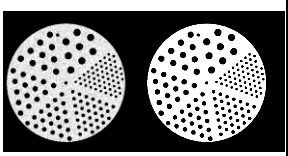
The signal is a random realization of the radioisotope distribution function.

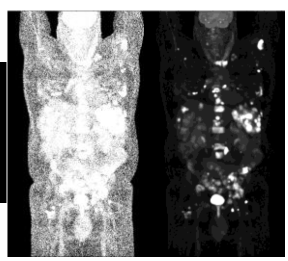
This distribution function is time varying and depends on:

- Tissue/tumor tracer kinetics
- Body habitus and motion

Note that tracer kinetics is often interpreted through the lens of a particular model.

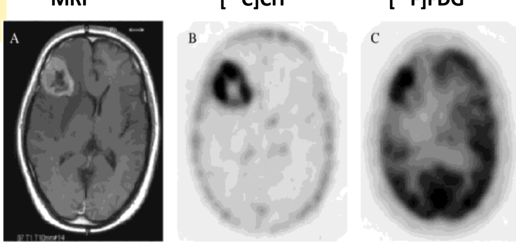
Tracer Distribution Function





One tumor, three images…

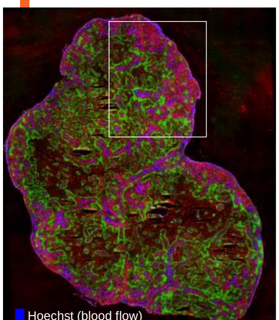
MRI | $[^{11}C]CH$ | $[^{18}F]FDG$

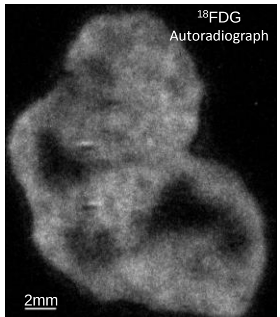


GBM in the right frontal lobe.

Tian M, et al. Mol Imag Biol. 2004;6:172-179

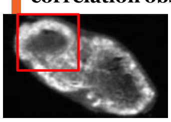
Tracer validation, heterogeneity, and microenvironment

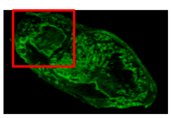


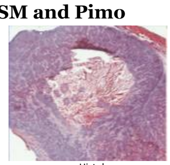


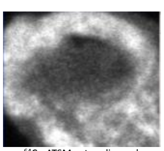
Courtesy Andrei Pugachev

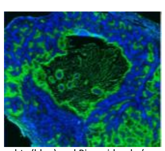
Poor agreement: No distinct correlation or anti-correlation observed in ^{64}Cu-ATSM and Pimo

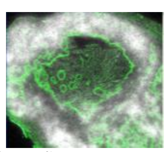

^{64}Cu-ATSM autoradiograph


Pimonidazole


Histology


^{64}Cu-ATSM autoradiograph


Hoechts (blue) and Pimonidazole (green)


^{64}Cu-ATSM vs Pimo

McCall, Keisha C., et al. "Copper-64-diacetyl-bis (N (4)-methylthiosemicarbazone) pharmacokinetics in FaDu xenograft tumors and correlation with microscopic markers of hypoxia." *International Journal of Radiation Oncology* Biology* Physics* 84.3 (2012): e393-e399.

Data: PET data acquisition

In PET, data quality can be assessed from the data's deviation from the idealized PET model.

$$\bar{g}(u,\varphi)=\int f(\mathbf{x})h(u,\varphi,\mathbf{x})d\mathbf{x}$$

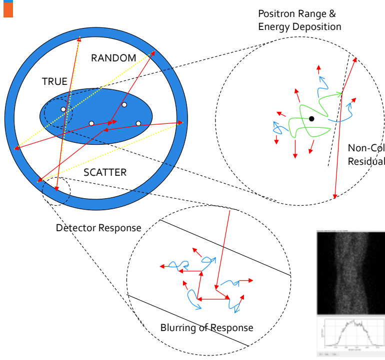
data mean value

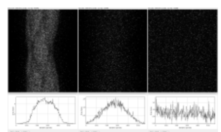
tracer distribution

transport kernel

- Particle/photon transport
  - Positron range, non-colinearity, patient attenuation, and detector localization
  - Additive counts: scatter and random events (and cascade)
- System geometry and detector performance
  - Non-uniform sensitivity
  - Energy resolution
  - Timing resolution

PET data acquisition



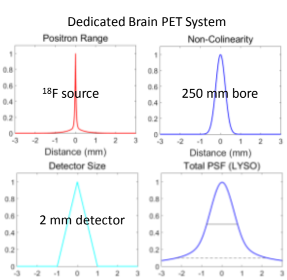


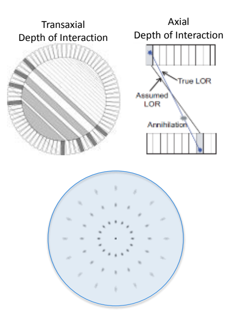
Each detected event is a random realization of the tracer distribution, and detection likelihood (patient attenuation and detector response).

Important data quality metrics

- Spatial resolution
  - Spatially variant
- Sensitivity: number of counts per unit activity
  - Solid angle
  - Detector efficiency/photon stopping
- Noise equivalent counts: data signal-to-noise ratio
  - Count statistics
  - Signal independence

Sources of Spatial Resolution Loss





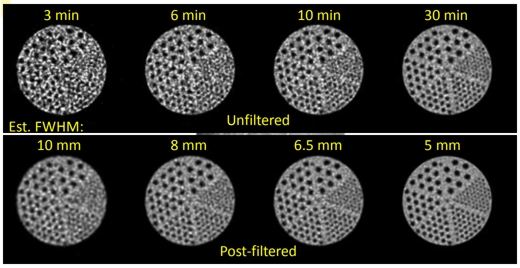
$$\sigma_{total} \approx \sqrt{\sigma_{\det}^2 + \sigma_{pos,{}_A^ZX}^2 + \sigma_\theta^2 + \sigma_\parallel^2}$$

Schmidtlein et al. "Initial performance studies of a wearable brain positron emission tomography camera based on autonomous thin-film digital Geiger avalanche photodiode arrays." *J Med Imag* 4.1 (2017).

Upper Image 1: Gillam and Rafecas. "Monte-Carlo simulations and image reconstruction for novel imaging scenarios in emission tomography." *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* 809 (2016): 76-88.
Upper Image 2: https://www.intechopen.com/books/mammography-techniques-and-review/positron-emission-mammography

Noise/resolution tradeoff: sensitivity

ACR Phantom rod sizes: 4.8, 6.4, 7.9, 9.5, 11.1, 12.7

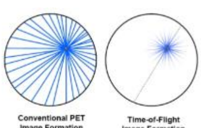


Data quality metric: NEC

Noise Equivalent Counts (NEC): Represents the signal (true counts) degraded by the noise (additive counts, e.g. scatter and random counts).

$$NEC = \frac{T^2}{T+S+R}$$

Effective NEC: An improved estimate of NEC provided the signal's timing resolution (TOF), and support (region within the patient) are known.



Count localization

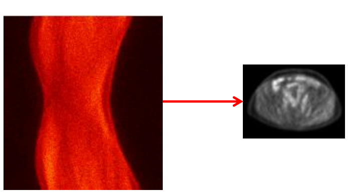
$$NEC_{eff} = \left(\frac{D}{\min(c\Delta t/2, D)}\right)\left(\frac{T+S+(D/D_{FOV})R}{T+S+(D/D_{FOV})^2 R}\right) NEC$$

Random rejection

Image: http://clinical.netforum.healthcare.philips.com/global/Explore/Clinical-News/PetCT/Generation-3-Time-of-Flight-now-shipping.

PET image reconstruction

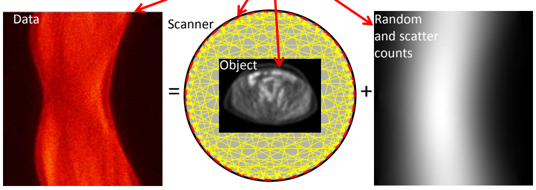
- Why reconstruct?
  - PET data is not interpretable by humans



The PET data equation

The PET data model is deceptively simple. It is a linear system where all the physics is hidden in the system matrix. Calculating the data given the object is known as the forward problem. Its quick and accurate calculation is easy.

$$g = \mathbf{A}f + \gamma$$



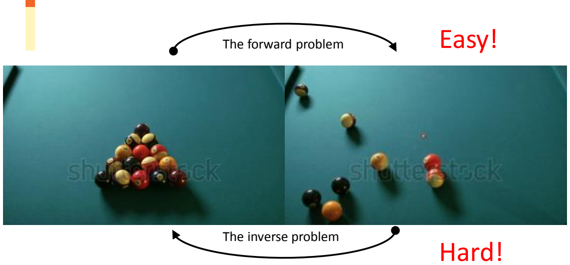
Unfortunately, we want to estimate the object given the data. This is known as an inverse problem and is hard.

Inverse problems

An **inverse problem** in mathematics is the process of calculating from a set of observations the causal factors that produced them.

Images and video taken from Shutterstock.
http://www.shutterstock.com/video/clip-883594-stock-footage-this-is-an-overhead-shot-of-billiards-balls-breaking-this-was-shot-with-a-fish-eye-lens.html

Inverse problems



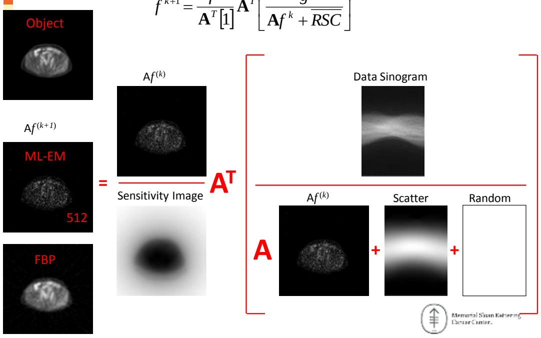
Easy!

Hard!

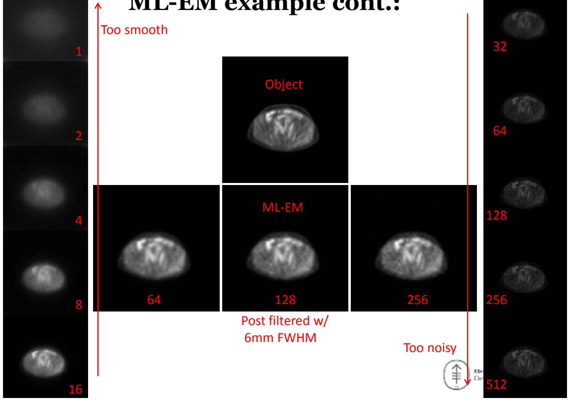
Images and video taken from Shutterstock.
http://www.shutterstock.com/video/clip-883594-stock-footage-this-is-an-overhead-shot-of-billiards-balls-breaking-this-was-shot-with-a-fish-eye-lens.html

ML-EM example cont.:

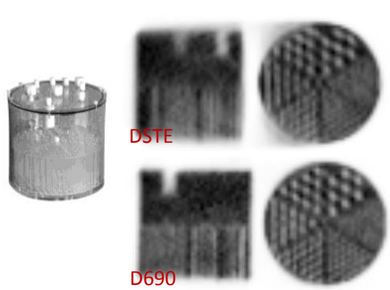
$$f^{k+1} = \frac{f^k}{\mathbf{A}^T[1]}\mathbf{A}^T\left[\frac{g}{\mathbf{A}f^k + RSC}\right]$$



ML-EM example cont.:

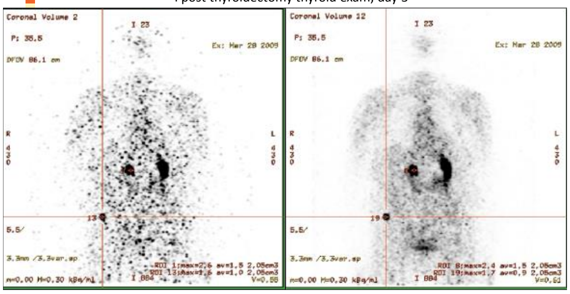


Example: under converged



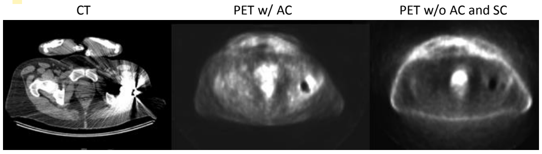
Fitting noise

^{124}I post thyroidectomy thyroid exam, day 3

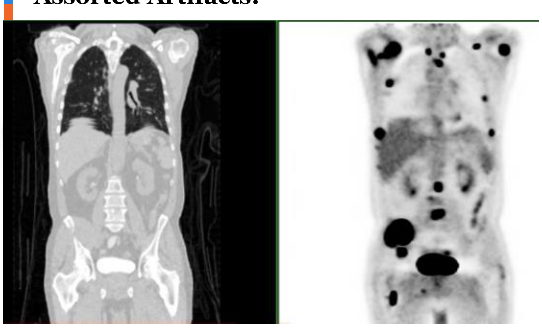


Attenuation correction artifacts

CT | PET w/ AC | PET w/o AC and SC



Assorted Artifacts:



The problem of over-fitting

Maximum likelihood methods always fits the noise.

- The less data the more over-fitting becomes a problem.
- Convergence is a spatially variant noise/resolution tradeoff problem.
  - Optimal stopping depends on local statistics (spatially dependent)
  - Under-converged images have uptake dependent resolution and noise properties
  - There are no optimal stopping rules

Post-filtering the images is mandatory.

- Post-filtering damages spatial resolution.

Nonetheless, most clinical statistical reconstruction systems stop the iterations short before convergence to avoid over-fitting.

Regularization, penalties, and priors

Regularization: numerical instability and over-fitting avoidance

Penalty Function: objective function term that increases in response to an undesirable image feature(s)

Prior: a priori information weighting the likelihood function

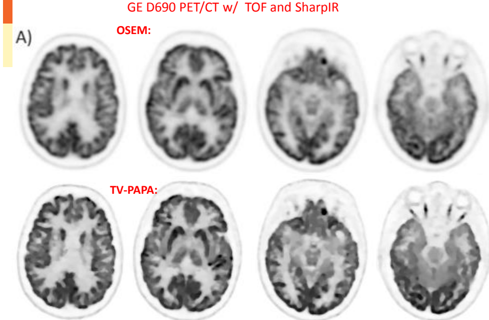
In a practical sense they all basically do the same thing:

Add additional constraints to the model to limit the deviation of the output from the underlying source, to avoid over-fitting, and to penalize model complexity.

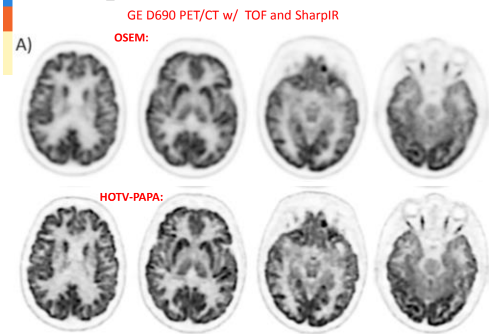
Edge preserving penalties
- Differentiable/convex: Relative difference
- Non differentiable/convex: total variation
- Non differentiable/non convex: hat function

Example: edge preserving brain

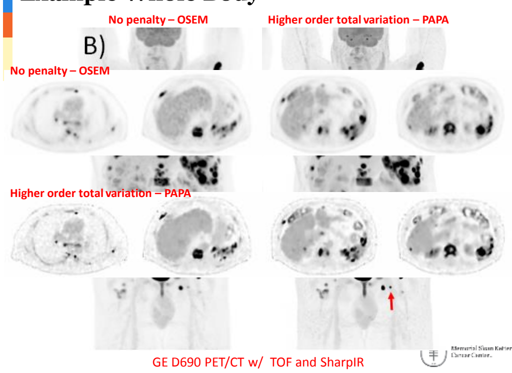
GE D690 PET/CT w/ TOF and SharpIR



Example: brain



Example Whole Body



Interpretation of the data

- What is the purpose of the segmentation?
  - Response assessment
  - Target definition
  - Sub-region identification
- This is a question of whether one wishes to:
  - Classify (avoid missing tumor)
  - Quantify (avoid normal tissue)

Differing observer emphasis

- Response assessment: nuclear medicine physicians generally prefer smaller margin to avoid biasing measurements.
- Target definition: radiation oncologists generally prefer large margins to avoid missing tumor.

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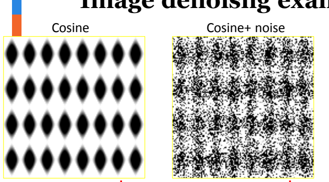
Thank you!

Sparse representation

Sparse representation is the idea that the salient features in images are important because they have structure.

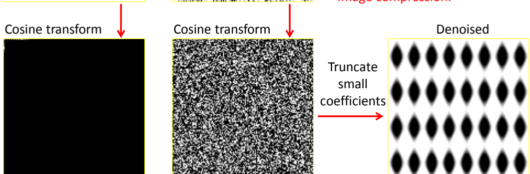
- Structure implies pattern and redundancy.
- This indicates a transform space where the object can be sparsely/compactly represented exists.
- Noise has no pattern or redundancy and thus cannot be compactly represented by any transform.

Image denoisng example



In this case, the transform was matched to the image. In general we don't have this information ,but certain transforms have been shown to be very effect for a large class of images.

This is what JPEG uses for image compression.



Distribution recovery: a thought experiment

Fessler's perfect detector:

We inject a patient with a radiotracer and at some time point after this we sample the patient and record the results.

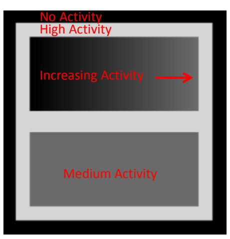
Now let's imagine that we have perfect detection of the events: we can perfectly localize their origin (*i.e.* no point spread function or timing uncertainty).

Is the list of detected events enough?

We note that repeating the scan would produce a different list of events.

Fessler's Perfect Detector Example

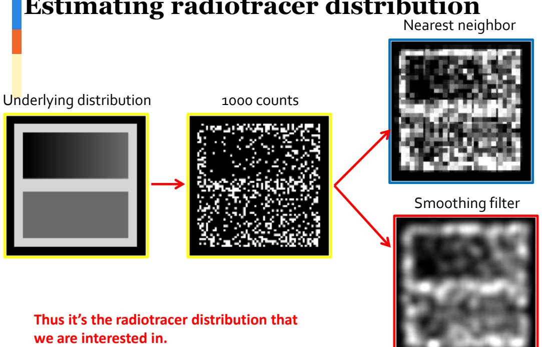
- Activity distribution



- Perfect detector with 1000 counts

Example taken from Jeff Fessler's image reconstruction lectures.
https://web.eecs.umich.edu/~fessler/papers/talk.html

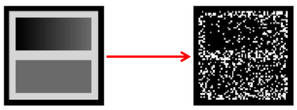
Estimating radiotracer distribution



Thus it's the radiotracer distribution that we are interested in.

Perfect detector revisited

Nearest neighbor | Smoothing post-filter | Sparse representation

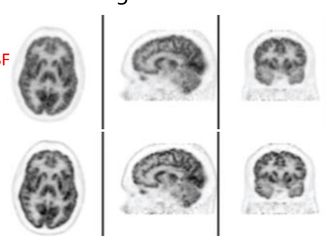


Point spread function information

Modeling the scanner's intrinsic resolution improves the system model used in the reconstruction algorithm.

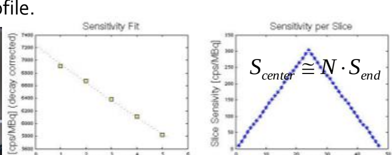
Without PSF

With PSF



Improving system sensitivity: FOV

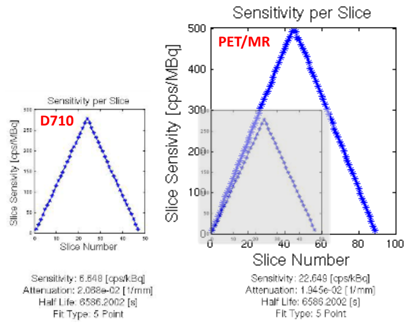
The sensitivity profile in a 3D PET/CT is roughly a pyramid profile.



Larger axial FOV adds additional sensitivity.

- Most current scanners have ~15 cm axial FOV
- Adding 5 cm to the axial FOV gives ~1.3x sensitivity
- Adding 10 cm to the axial FOV gives ~1.6x sensitivity
- A future 1.0 m design should have ~3.8x sensitivity

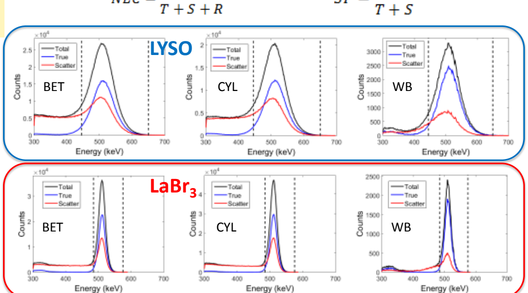
Example: sensitivity comparison



1.7x more sensitive due to geometry. Oblique patient attenuation will take some of that back.

Improving NECR

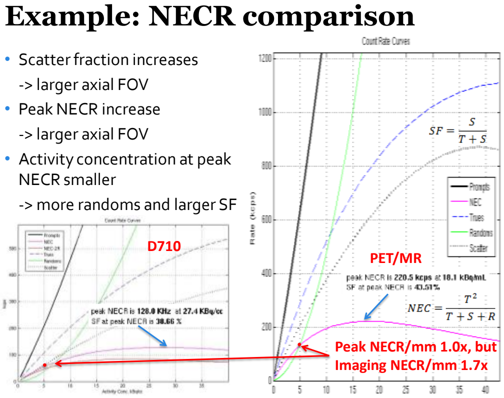
$$NEC = \frac{T^2}{T+S+R} \qquad SF = \frac{S}{T+S}$$



Schmidtlein, C Ross., et al. "Initial performance studies of a wearable brain positron emission tomography camera based on autonomous thin-film digital Geiger avalanche photodiode arrays." *Journal of Medical Imaging* 4.1 (2017).

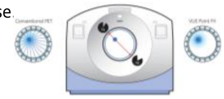
Example: NECR comparison

- Scatter fraction increases
  -> larger axial FOV
- Peak NECR increase
  -> larger axial FOV
- Activity concentration at peak NECR smaller
  -> more randoms and larger SF



What about time-of-flight?

With sufficiently timing resolution (fast scintillator light decay) the origin of annihilation photon can be determined along a line-of-response



$$\Delta x = c\,\Delta t/2$$

- Clinical systems (~600 ps): localization ~9 cm
- Prototype detectors (< 300 ps): localization ~ 4.5 cm

What is the advantage?

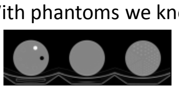
- Resolution?
  - No, not till timing < 50 ps
- NEC!

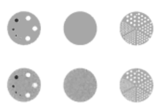
$$NEC_{TOF} = \frac{D}{\Delta x} NEC = \frac{2D}{\Delta t} NEC$$

Image: http://www3.gehealthcare.com.sg/en-gb/products/categories/pet-ct/pet-ct_applications/vue_point_fx

ACR Phantom for Objective IQ

With phantoms we know the true object via the CT.





CT derived object

GE D690 PET/CT w/ TOF and SharpIR

- Hot/Uniform/Jaszczak:
- Thus we can measure the RMSE for phantoms:

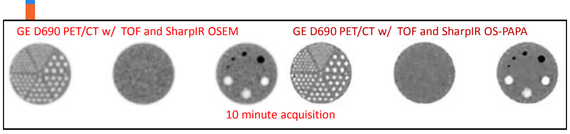
$$RMSE = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(IMAGE_i - OBJ_i)^2}$$

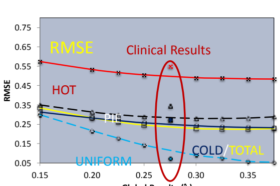
- How about resolution in a phantom?

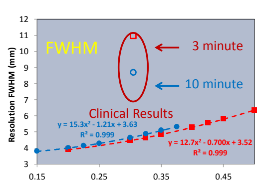
Using edge information from the Jaszczak region.

$$FWHM^* = \underset{FWHM>0}{\arg\min}\left\{\left\| IMAGE_i - N\left(0, \frac{FWHM}{2\sqrt{2\ln 2}}\right) * OBJ_i \right\|_1\right\}$$

ACR Phantom RMSE/FWHM

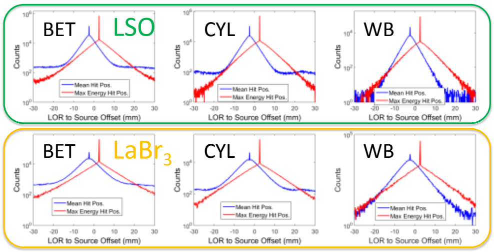






Improved Spatial Resolution

Monte Carlo estimates

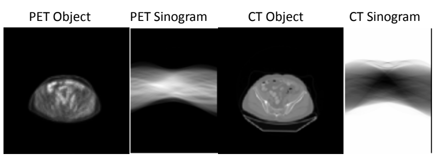


Blue: centroid of hit locations

Red: maximum energy hit locations

The red and blue curves are shifted by ± 2.5mm for clarity.

ML-EM simulation example:



$$A[\bar{f}]+\bar{S}+\bar{R}=g$$