Physics of PET image generation

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Short Intro

- Academic background
  - Adjunct Professor (Title of Docent) in Medical Imaging Physics and Technology, University of Turku, 2021
  - PhD in Medical Physics and Engineering, University of Turku, 2018
  - MSc in Medical Physics, Technical University of Tampere, 2012

- Academic work experience
  - Currently an Academy of Finland Research Fellow in Turku PET Centre
  - Nara Institute of Science and Technology, Nara, Japan, 2022 - 2023
    - JSPS post-doctoral scholarship on deep learning for perfusion PET imaging
  - National Cerebral and Cardiovascular Research Centre, Osaka, Japan, 2014 – 2016
    - PhD level research visit to laboratory of Prof. Hidehiro Iida doing O-15 inhalation PET imaging
  - Turku PET Centre / GE Healthcare Finland, Turku, Finland, 2011 – 2012
    - Master's thesis from dual gating in PET/CT

- Research interests: medical physics and biomedical engineering, PET/MR & PET/CT technical research, image reconstruction, image quantification, phantom studies, image processing, motion correction, machine / deep learning and kinetic modelling

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Overview

- Superpower of PET – Quantitative PET
- Physical effects in data and why we need to correct them
- Reconstruction and data corrections
- Overview of multi-modality systems
- Questions!

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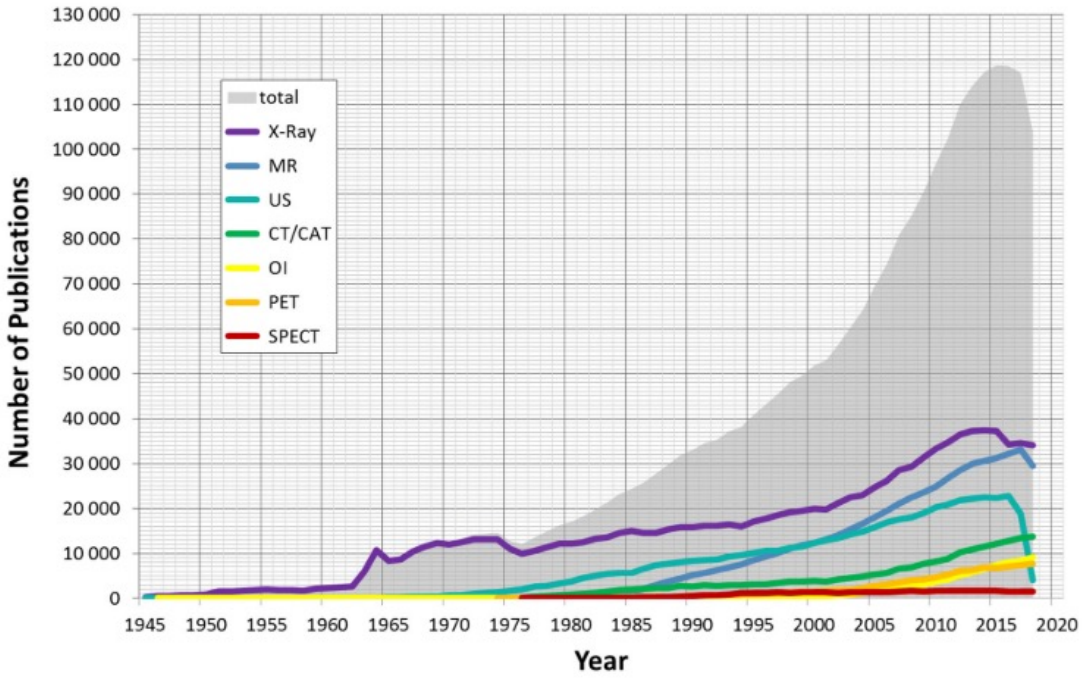
Why PET is Special?

- Large variety of tracers for different research and clinical applications
- PET is quantitative, meaning the actual values measured from the images have a relation to physical quantities
- Is a very sensitive method
- Is a functional method



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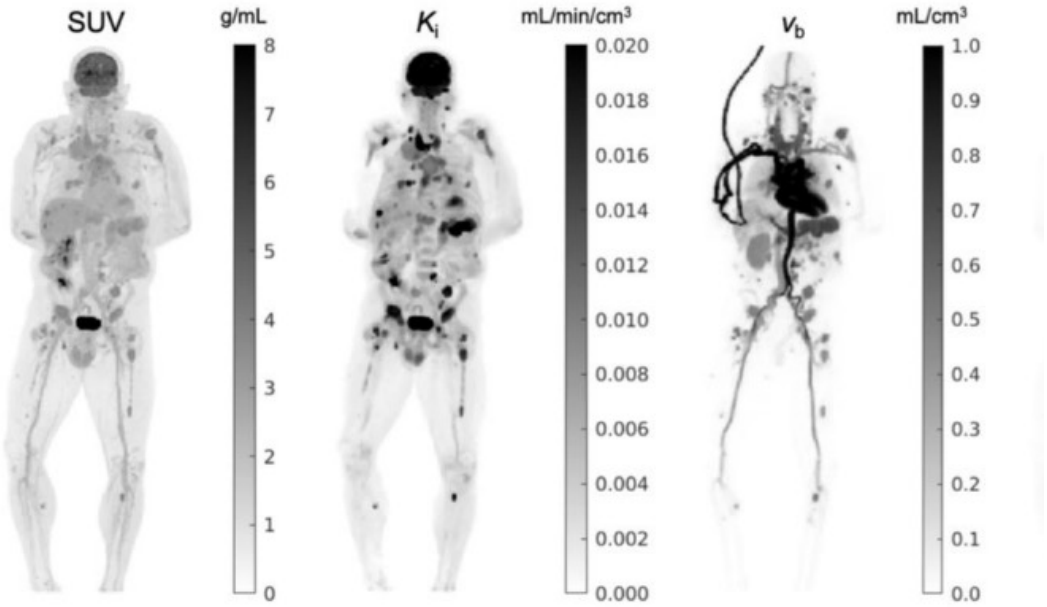
What can be studied?

- Tissue blood flow
- Tissue metabolism
- Enzyme activity
- Inflammation
- Receptor – ligand interactions
- Pharmacokinetics of different substances
- Gene expression



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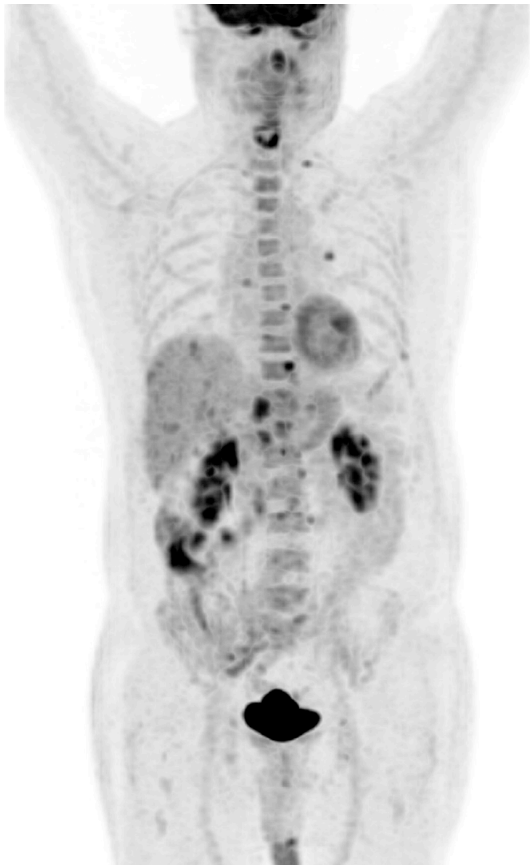
Clinical Application of PET

- Oncology, diagnosis and monitoring
- Neurology
- Inflammatory diseases
- Cardiovascular diseases
- Etc.



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But..?

- All of this works only if your images are quantitative

- According to Merriam-Webster:
  - Quantitative – adjective
  - Adjective - serving as a modifier of a noun (e.g PET) to denote a quality of the thing named, to indicate its quantity or extent, or to specify a thing as distinct from something else

- **Quantitative PET images are then:**
  - **1 :** of, relating to, or expressible in terms of quantity (uptake, standardized uptake value, K1, Ki)
  - **2 :** of, relating to, or involving the measurement of quantity or amount (radioactivity in a volume – kBq/mL)
  - **3 :** based on quantity (how much of this specific tracer has been bound to a receptor, or how much of this tracer flows in and out of a gram of tissue in mL in a minute)?

- As opposed to: “this spot looks brighter”

How do we get there?

- PET can be used to do many wonderful things - BUT it requires that anyone who is analyzing, interpreting or modelling the data *understands* how the data are generated and what the inherent inaccuracies in the data are. Thus, it is useful to understand the underlying physics of PET image generation.

- Before we get into a final PET image, we need to counter several physical effects which have occurred during the image acquisition process due to physical effects of the radiotracer in the object, as well as detection process, and the imperfections in the detector system *quam optime (as good as possible)*

- These effects need to be countered and corrected to achieve an accurate and quantitative representation of the underlying radioactivity distribution, often these days – in a functional (changing over time) sense

- Take home note:
  - You are dealing with a bit more than cat pictures downloaded from the internet
  - A lot of corrections were put in place to get the final image – corrections based on different models of physical interactions and assumptions, and sometimes these don't work perfectly
  - So keep your eyes open and look at the images!

Let’s start – concept time!

- Line of response
- Events
- Data formats
  - Sinogram
  - List-mode

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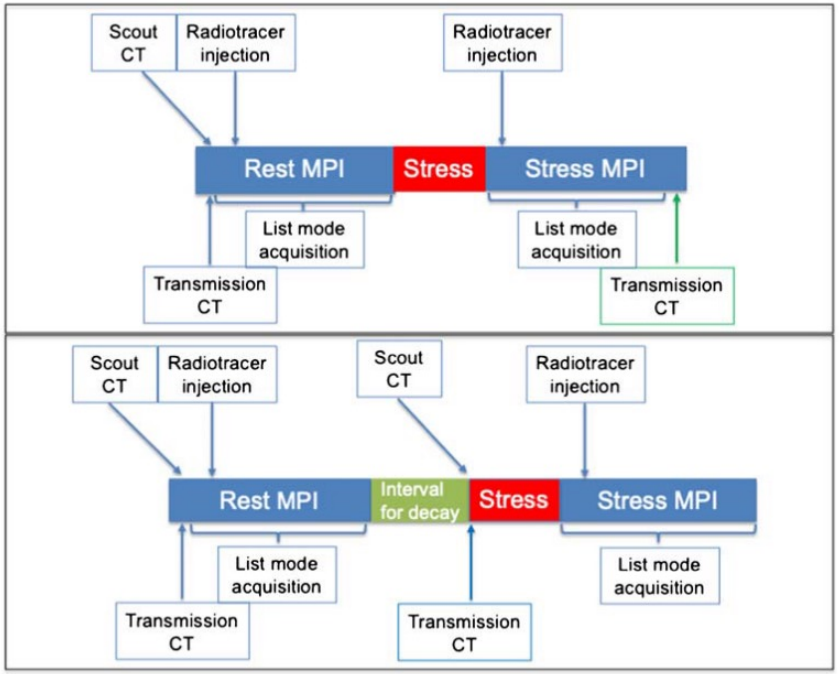
Imaging protocols

- Radiotracer is injected on the patient preparation bed, when imaging is conducted after a specific uptake period
  - Often this is done when conducting static imaging with 18F-FDG but can be also done when performing dynamic studies or modelling of late kinetics

- Radiotracer can be also injected on the scanner bed, and the imaging is started immediately from injection
  - Research studies for tracer kinetics
  - Dynamic imaging, e.g. for parametric studies using Patlak model
  - Cardiac perfusion and other perfusion studies



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LOR and Events

- A straight line which connects the centers of two detectors X and Y is called a line of response (LOR).
- The two 511 keV photons are detected in coincidence across a LOR, in the absence of an absorptive collimator.
- This technique is called electronic collimation.
- All coincident events recorded are collectively called as prompt (P) events, containing:
  - True events (T)
  - Random events (R)
  - Scattered (S)
  - Multicoincidence

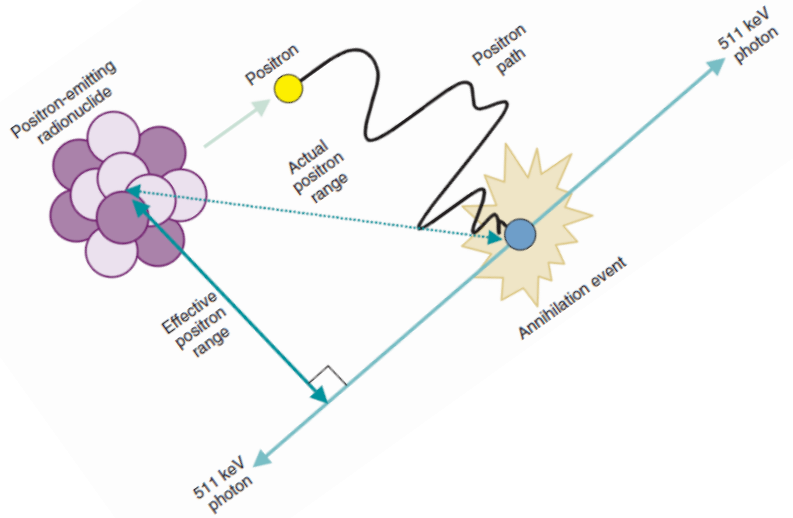

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Image Acquisition Process

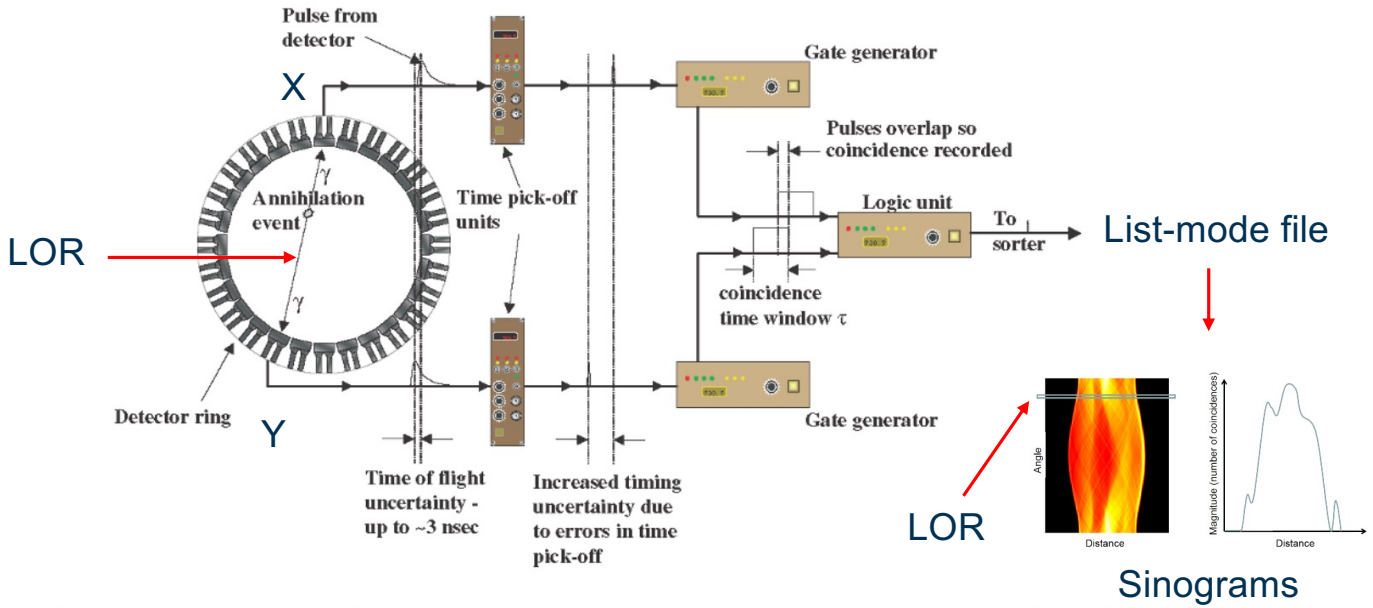

Figure 5.2. Figure 5.2 Example coincidence circuitry. Each detector generates a pulse when a photon deposits energy in it; this pulse passes to a time pick-off unit. Timing signals from the pick-off unit are passed to a gate generator which generates a gate of width τ. The logic unit generates a signal if there is a voltage on both inputs simultaneously. This signal then passes to the sorting circuitry.

Modified from : Quantitative Techniques in PET
Steven R Meikle and Ramsey D Badawi

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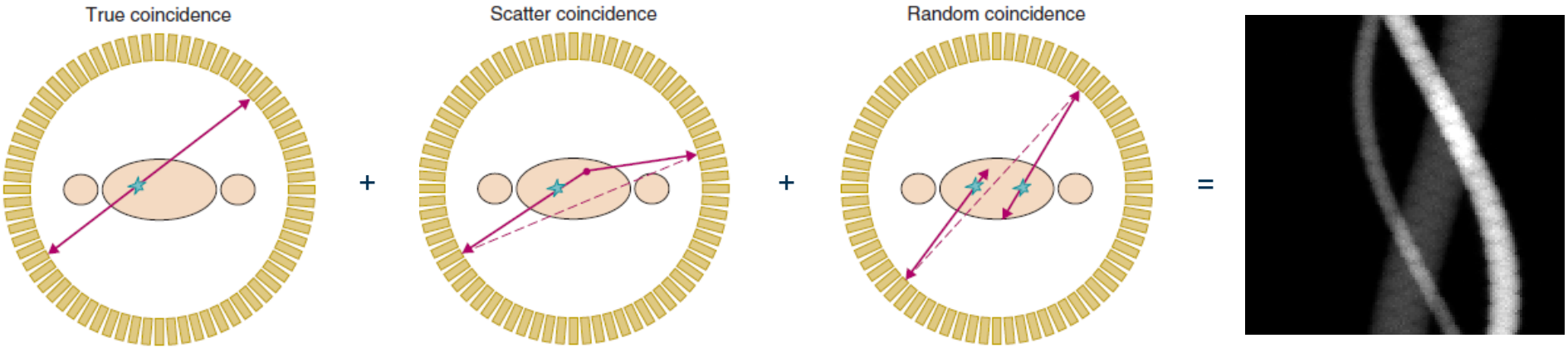
Events Collected in the Acquisition Process



Prompt events (data we eventually end up with) = Trues + Random + Scatter => motivation for data corrections

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Other Physical Events to be Corrected

- Attenuation
- Detector normalization
- Calibration
- Physical decay
- Geometrical effects
- Positron range
- Resolution recovery (PSF correction)
- Partial volume
- …

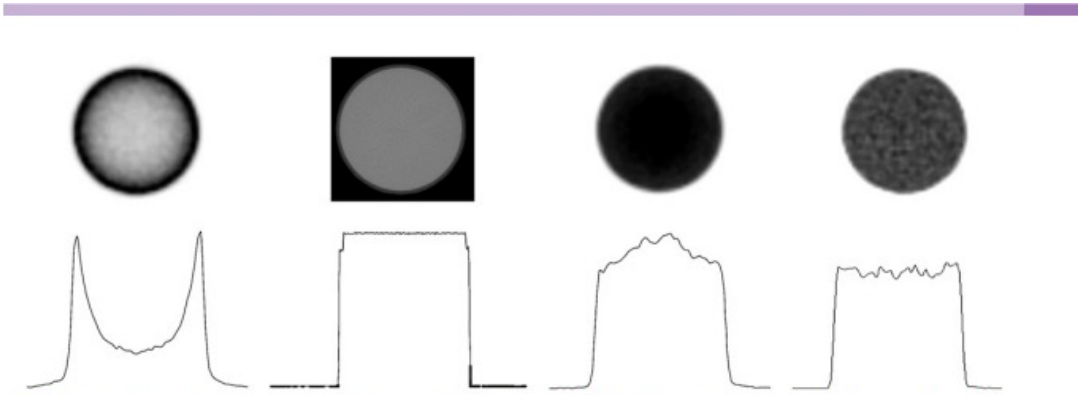

Fig. 1. Illustration of reconstruction artifacts resulting from the lack of attenuation correction for a uniform distribution of activity in a cylindric phantom (*top row*) and corresponding horizontal profiles drawn at the center of the cylinder (*bottom row*). From left to right: reconstructed image without attenuation correction, the CT-based attenuation map, the same slice after applying attenuation correction but without scatter correction, and finally the same slice after applying attenuation and scatter corrections. Note the loss of activity at the center of the cylinder on the noncorrected image, the overestimation of activity distribution at the center of the cylinder before scatter correction, and the recovery of a uniform activity distribution after attenuation and scatter corrections.

Advances in Attenuation Correction Techniques in PET, by Habib Zaidi et al. 2007

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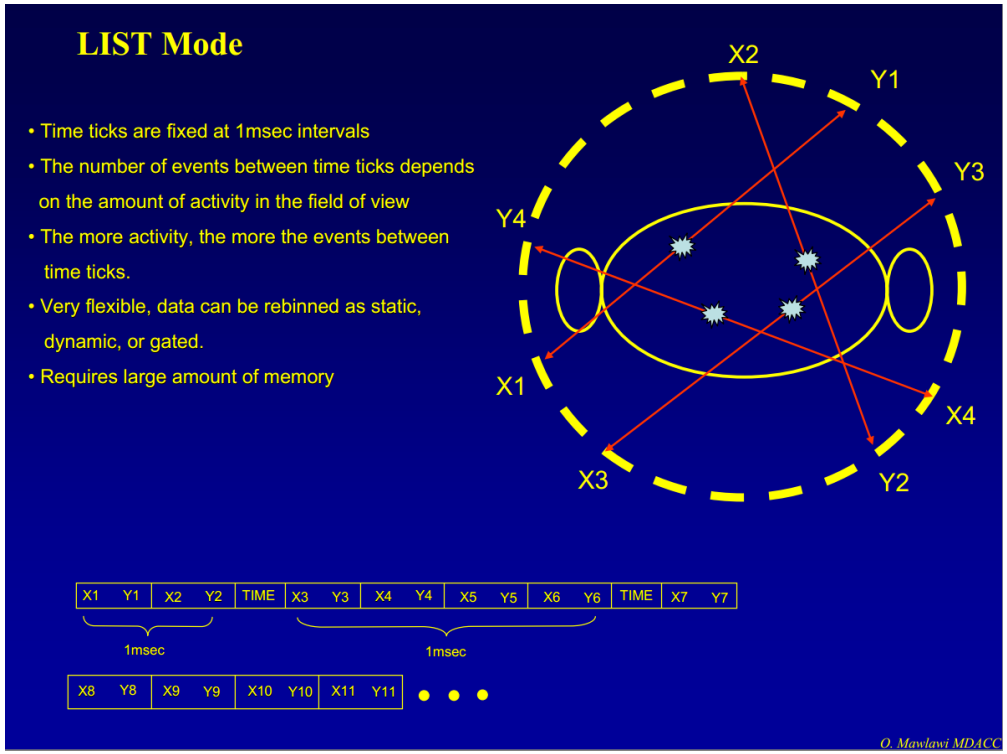
PET Data Formats – List mode and Sinogram

- In list-mode acquisition, digitized X- and Y- signals are coded with “time marks” as they are received in sequence.
- Signals are stored as individual events as they occur, containing timing and crystal location (axial, transaxial position) information.
- After the acquisition is completed, data can be histogrammed (re-binned) to individual sinograms, using the information coded in the list-mode data.
- In sinogram, the imaged object f(x,y) is now represented as a set of projections p(s,ϕ) of the radioactivity distribution.
- In image reconstruction we want to recover the original imaged object f(x,y) from this set of projections p(s,ϕ).

Visual Representation of List-mode data



https://www.aapm.org/meetings/amos2/pdf/42-11881-66890-783.pdf

PET Scan Types

- The acquired data, if collected in list-mode can be histogrammed again to sinograms using different types of acquisition modes
- *Static* => one single image from the entire acquisition duration
- *Dynamic* => a 4D time-series of images with certain duration (from seconds to minutes) from the acquisition duration
- *Gated* => a series of images divided by recorded respiratory or cardiac signal
- Dynamic + Gated => possible to be combined (typically research setting only) but statistics will become an issue!

Framing Schema, Examples

Table 3 Examples of framing schemes for re-binning of dynamic list mode acquisitions

Reference	Tracer	Frame sequence	Total time
Kajander S et al. [59]	[^{15}O]water	14 × 5 s; 3 × 10 s; 3 × 20 s; 4 × 30 s	4 min 40 s
Danad I et al. [60]	[^{15}O]water	1 × 10 s; 8 × 5 s; 4 × 10 s; 2 × 15 s; 3 × 20s; 2 × 30 s; 2 × 60 s	6 min
Clinical protocol in Aarhus, Amsterdam, Uppsala	[^{15}O]water	1 × 10 s; 8 × 5 s; 4 × 10 s; 2 × 15 s; 3 × 20s; 2 × 30 s	4 min
Muzik O et al. [38]	[^{13}N]NH_3	12 × 10 s; 4 × 15 s; 4 × 30 s; 3 × 300 s	20 min
Hutchins GD et al. [40]	[^{13}N]NH_3	12 × 10 s; 4 × 30 s; 1 × 360 s	10 min
DeGrado TR et al. [39]	[^{13}N]NH_3	12 × 10 s; 4 × 30 s; 3 × 120 s; 2 × 300 s	20 min
Sciagrà R et al. [61]	[^{13}N]NH_3	24 × 5 s; 2 × 30 s; 1 × 60; 1 × 300 s	9 min
El Fahkri et al. [62]	^{82}Rb	24 × 5 s; 86 × 30 s	6 min
Lortie et al. [63]	^{82}Rb	12 × 10 s; 2 × 30 s; 1 × 60 s; 1 × 120 s, 1 × 240 s	10 min
Dekemp RA et al. [64]	^{82}Rb	9 × 10 s; 3 × 30 s; 1 × 60 s; 1 × 120 s	6 min
Dekemp RA et al. [64]	^{82}Rb	12 × 10 s; 2 × 30 s; 1 × 60 s; 1 × 120 s	6 min
Dekemp RA et al. [64]	^{82}Rb	12 × 5 s; 6 × 10 s; 4 × 20 s; 4 × 40 s	6 min
Armstrong IS et al. [52]	^{82}Rb	1 × 10 s; 8 × 5 s; 3 × 10 s; 2 × 20 s; 4 × 60 s	6 min
Gaudieri V et al. [65]	^{82}Rb	12 × 5 s; 6 × 10 s; 4 × 20 s; 4 × 40 s	6 min

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Practical Example
One 2D Sinogram – Static Image

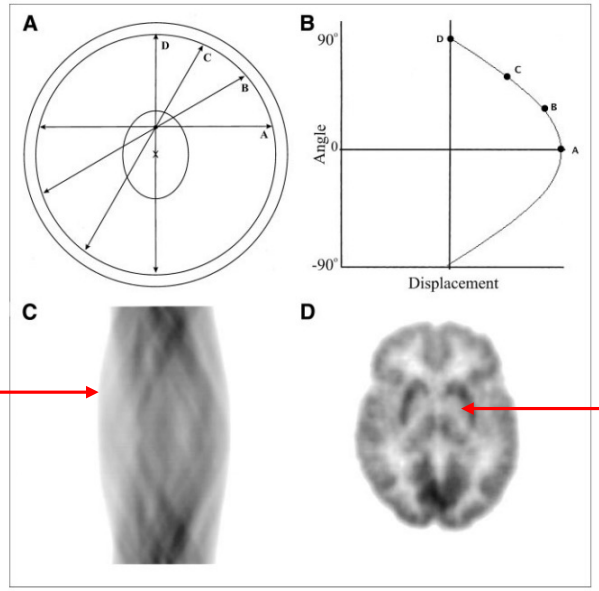

FIGURE 1. Sinogram formation. Coincidence events in PET scanner are categorized by plotting each LOR as function of its angular orientation versus its displacement from center of gantry. (A) Center of gantry is noted by cross (X), and locus of interest (e.g., tumor) is noted by ellipse. Four LORs passing through locus of interest are labeled A, B, C, and D. (B) These 4 LORs are plotted on this sinogram where angular orientation is on *y*-axis and displacement from center of gantry is on *x*-axis. If all possible LORs that pass through this point are plotted, it maps out half of sine wave turned on its side as shown here. (C) Sinograms of more complicated objects, such as sinogram of brain scan shown, are composed of many overlapping sine waves. (D) Reconstructed brain image corresponding to sinogram in (C) is shown.

The sinogram is a two-dimensional histogram of the LORs in distance and angle coordinates

Each sinogram represents the data acquired for a slice across all angles

After data corrections and image reconstruction, the image is a pixel-by-pixel representation of the radiotracer concentration at scan time.

Data Acquisition in PET Imaging, Frederic H. Fahey

Let’s go a bit deeper

- Reconstruction
- Main concepts:
  - Forward projection
  - Backprojection
- MLEM reconstruction example
- Examples of data corrections

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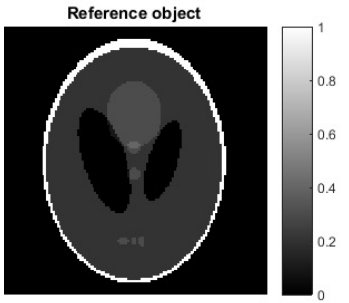
PET Reconstruction

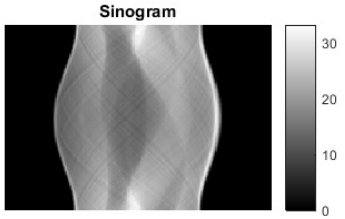
- Analytical algorithms
  - Rarely used anymore, expect for performance testing and reference method evaluation
  - Linear behavior, but low image quality
  - Most frequently used analytic reconstruction algorithm is the filtered backprojection (FBP) algorithm

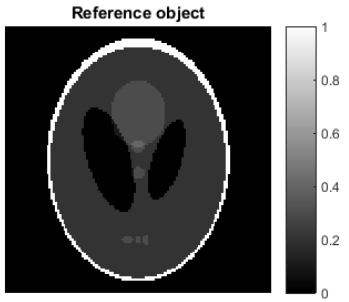
- Iterative algorithms
  - MLEM and later OSEM
  - Good image quality
  - Common standard are OSEM derivates
  - Non-linear behavior => FBP is considered “gold standard” in certain measurements

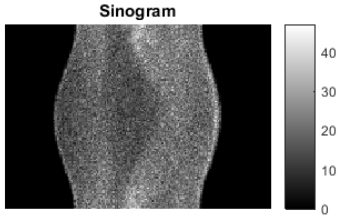
- Deep-learning based reconstruction

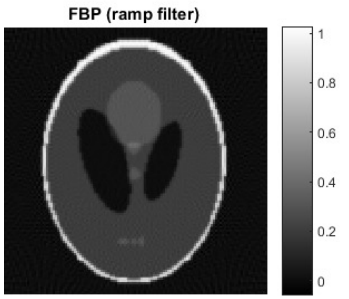
FBP Example – Noiseless vs Noisy Case

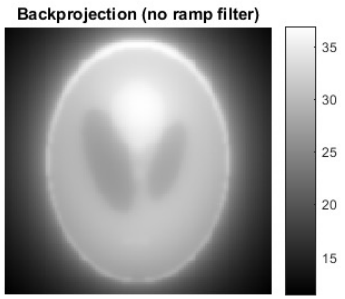


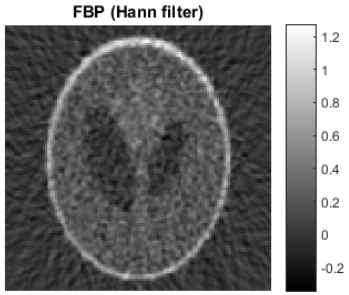


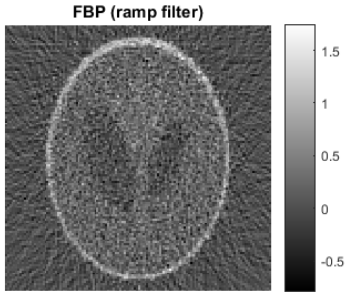












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Sinogram Formation, Forward Projection

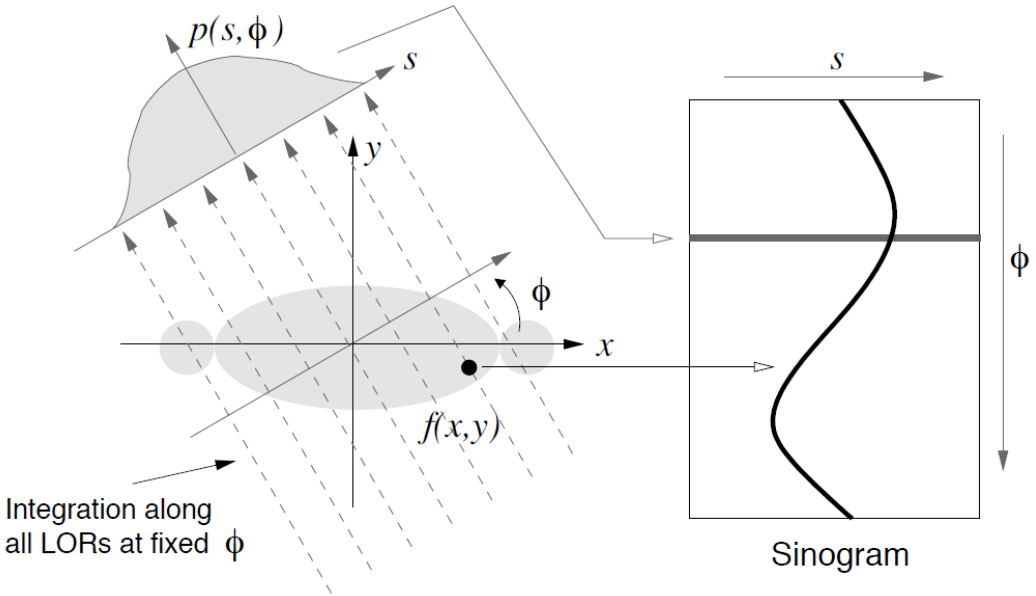
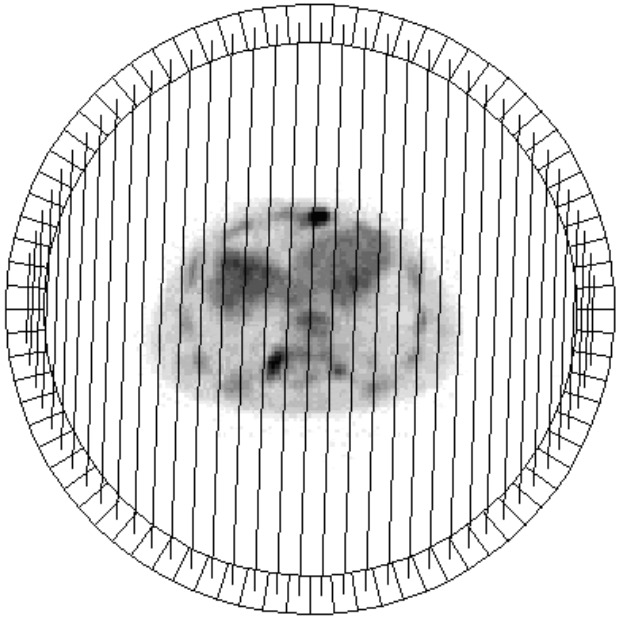


Figure 2. A projection, $p(s,\phi)$, is formed from integration along all parallel LORs at an angle ϕ. The projections are organized into a sinogram such that each complete projection fills a single row of ϕ in the sinogram. In this format, a single point in $f(x,y)$ traces a sinusoid in the sinogram.

PET Image Reconstruction
Adam Alessio and Paul Kinahan

Lines of response between PET detectors



Corresponding location in sinogram

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Backprojection

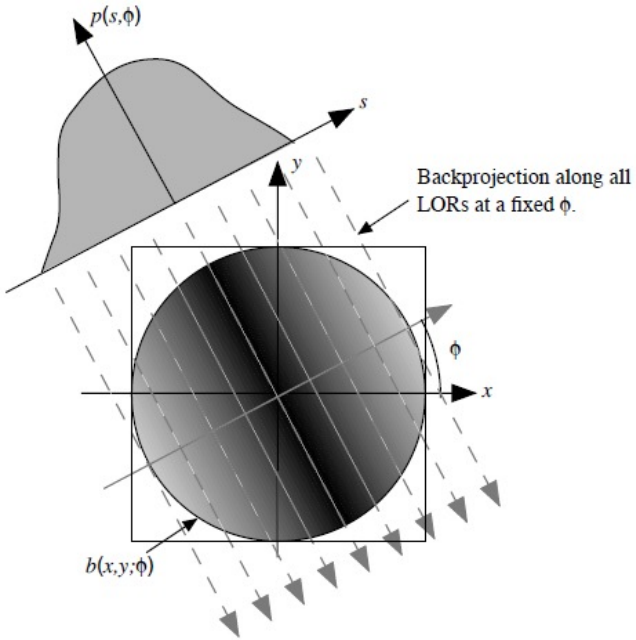
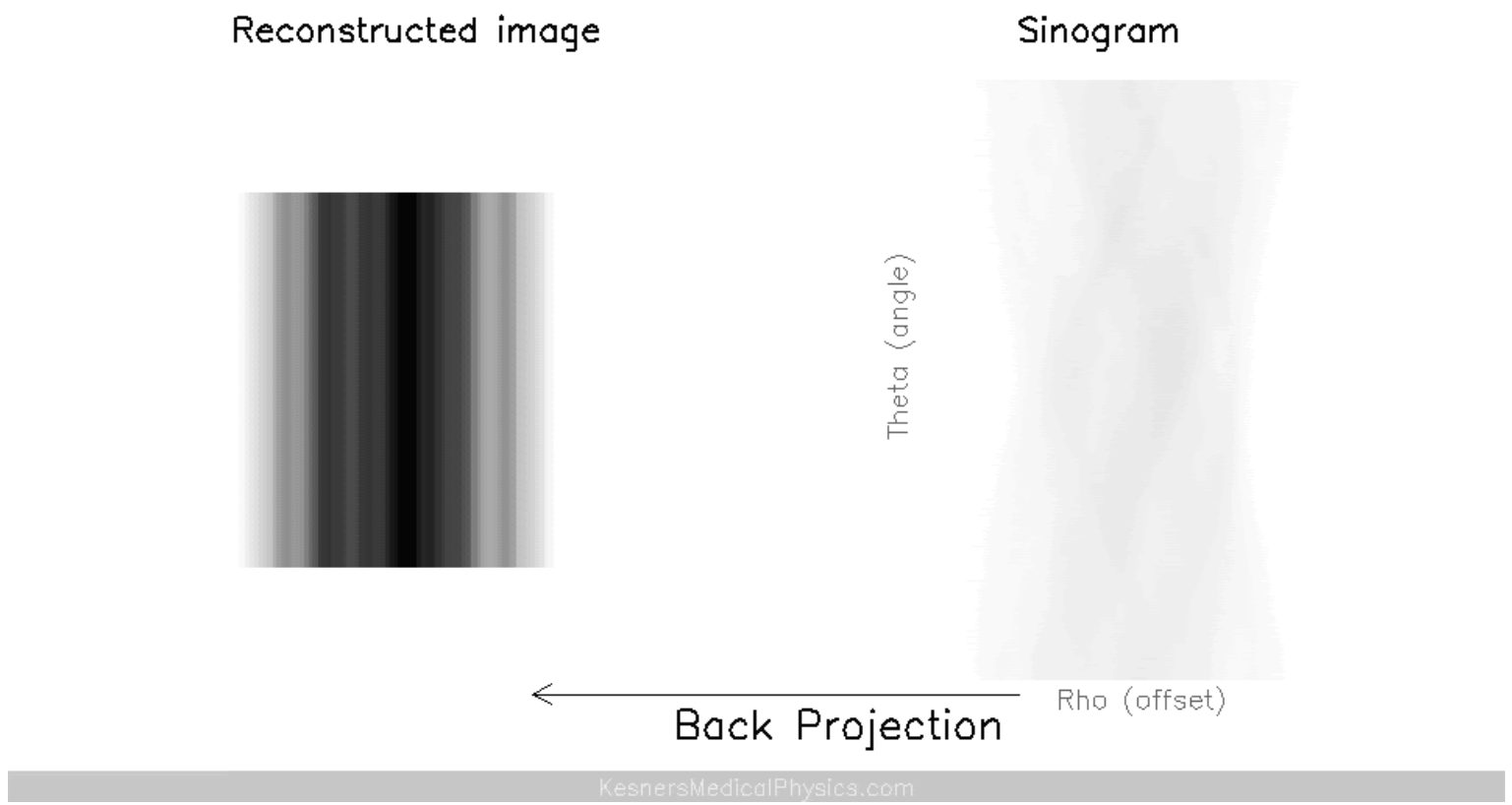


Figure 6. Backprojection, $b(x,y;\phi)$, into an image reconstruction array of all values of $p(s,\phi)$ for a fixed value of ϕ.



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MLEM Algorithm

Image at nth iteration

Measured data (emission sinogram)

$$f_j^{(n+1)} = \frac{\hat{f}_j^{(n)}}{\sum_{i'} H_{i'j}} \sum_i H_{ij} \frac{p_i}{\sum_k H_{ik} \hat{f}_k^{(n)}}$$

Updated image

System matrix

Forward projected image at nth iteration

OSEM Algorithm

$$f_j^{(n+1)} = \frac{\hat{f}_j^{(n)}}{\sum_{i' \in S_b} H_{i'j}} \sum_{i \in S_b} H_{ij} \frac{p_i}{\sum_k H_{ik} \hat{f}_k^{(n)}}$$

MLEM
Example of One Iteration

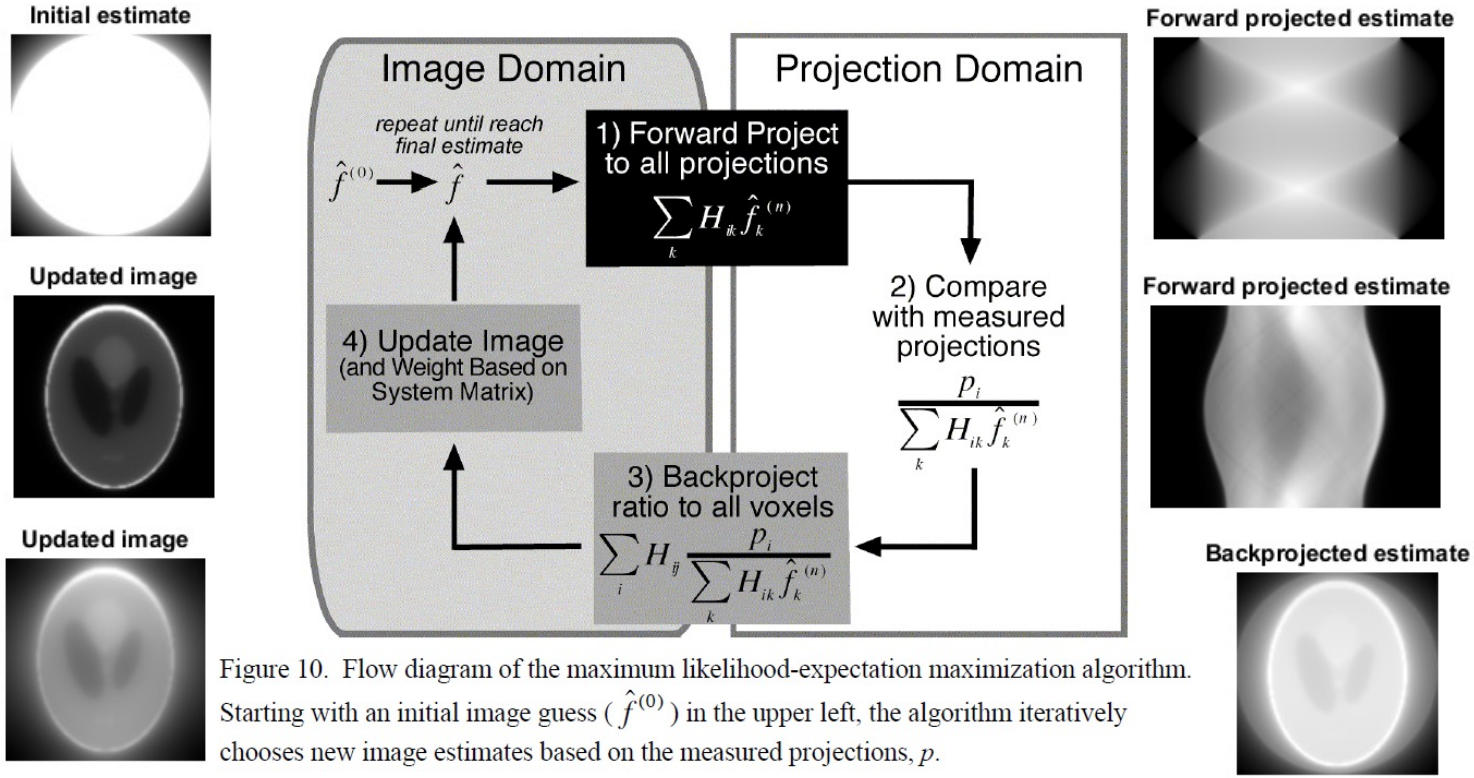

Figure 10. Flow diagram of the maximum likelihood-expectation maximization algorithm. Starting with an initial image guess ($\hat{f}^{(0)}$) in the upper left, the algorithm iteratively chooses new image estimates based on the measured projections, p.

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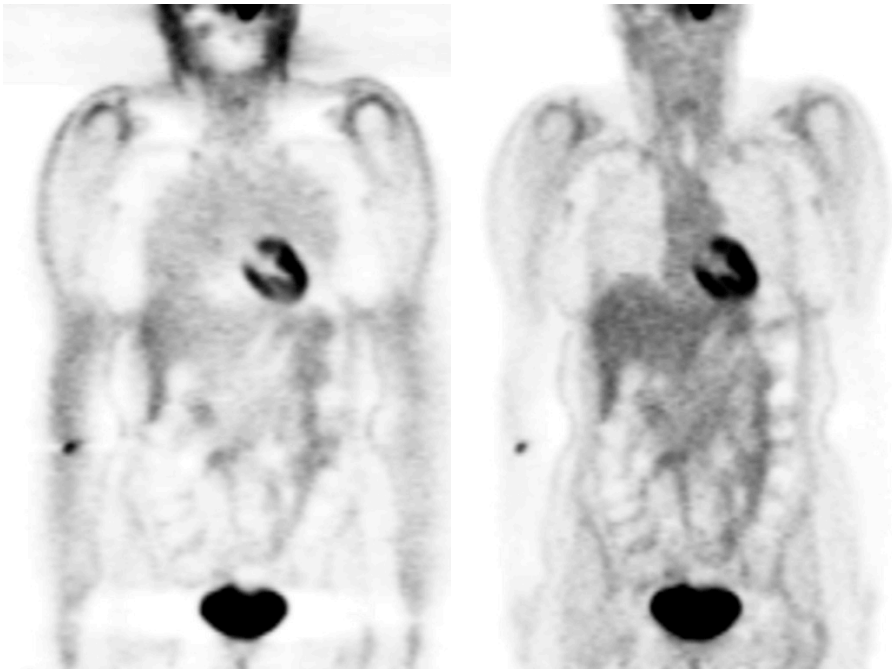
Data Corrections

- The collected data contains several physical effects which need to be collected during image reconstruction
  - Attenuation of the photons inside the object
  - Scattering
  - Randoms
  - Losses in the detector due to e.g. dead-time
  - Detector geometry, normalisation of detector efficiencies, calibration to uptake units, radioactive decay
- Taking into account of TOF and resolution recovery (PSF) corrections
- Corrections are incorporated in the reconstruction loop in iterative algorithms



NAC AC

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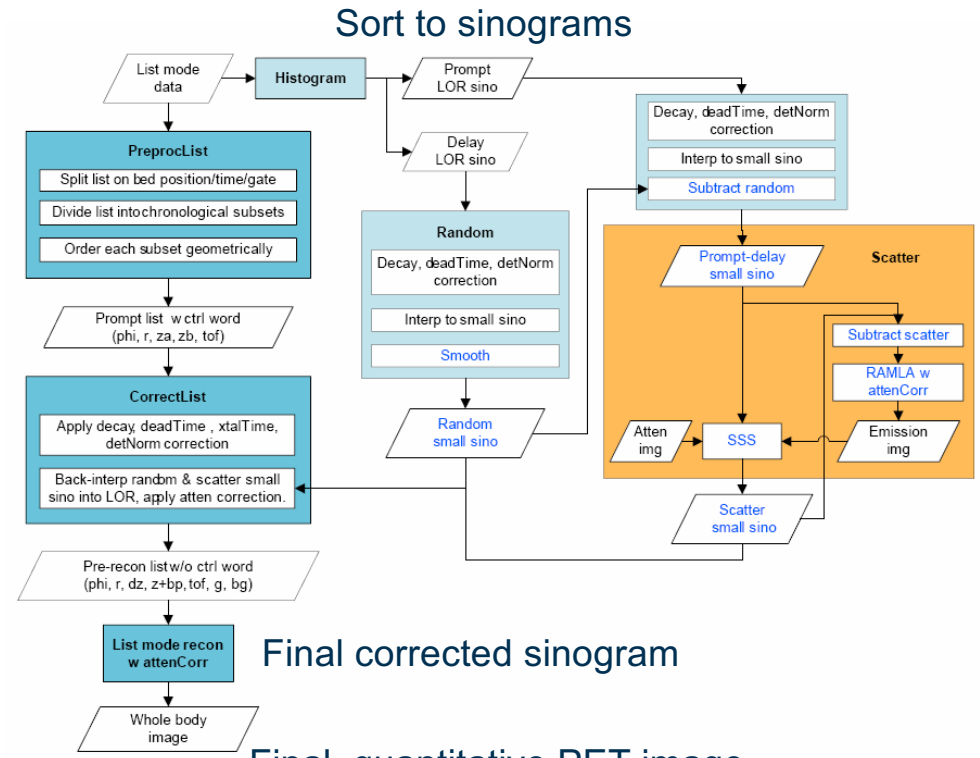
Data Corrections

Data corrections



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Examples – Attenuation correction

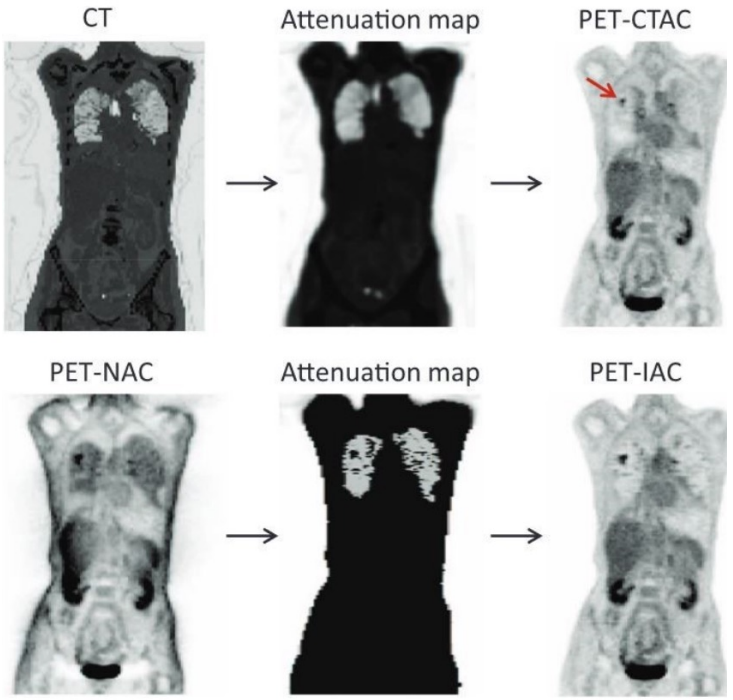
- Magnitude of photon attenuation:

$$I(x) = I_0 e^{-\int_0^x \mu(x)dx} \quad (1)$$

$$\alpha = e^{-\int_0^{A+B} \mu(x)dx} \quad (2)$$

$$C_x = \alpha \int C_o(x)dx \quad (3)$$

- Where, C_x is the uncorrected emission counts for a given LOR, expressed as an integral of attenuated point sources C_o multiplied by α expressing the attenuation of intensity of radiation
- Thus, to recover the un-attenuated distribution, $C_x * 1/\alpha$, where $1/\alpha = ACF$, the attenuation correction factor (ACF)
- What α includes are the μ-values, the linear attenuation coefficients covering the whole imaging volume
- The μ-values need to be either measured (CT scan! / Transmission scan!) or calculated or otherwise approximated (MR scan)



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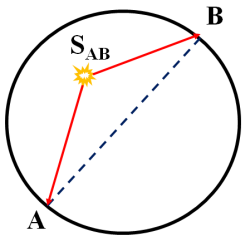
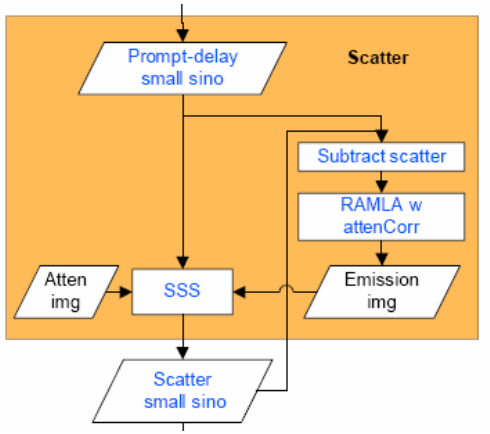
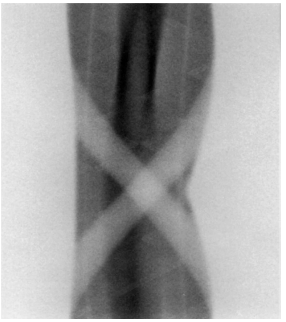
Examples – Scatter correction

- Define activity and attenuation distribution from the scatter-uncorrected emission and transmission image.
  - Randomly distribute scatter points within the scatter volume.
  - Select an LOR e.g. between A and B
- For a given scatter point (Sab), calculate the number of events it contributes to this LOR from the following and using :
  - activity distribution estimate, (emission image)
  - Klein–Nishina cross section,
  - Compton scattering relationships,
  - solid angles,
  - scatter medium distribution.(attenuation image)
- Repeat for all scatter points and add all contributions to the LOR.
- Repeat steps for all LORs.
- Interpolate in LOR space to obtain the scatter sinogram.
- Scale and subtract the scatter sinogram from the measured sinogram.
- Reconstruct the image







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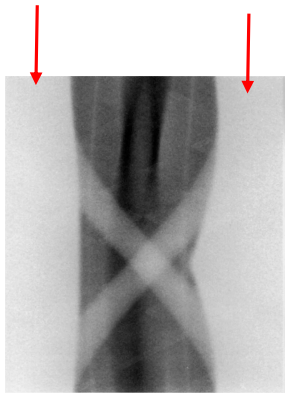
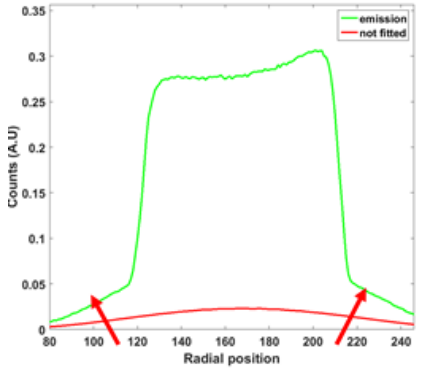
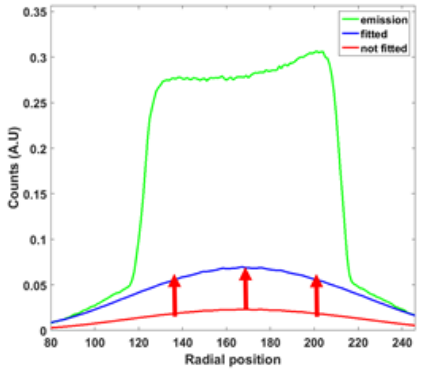
Examples – Scatter correction

- SSS allows to derive the spatial distribution of scatter in relative scale for each detector pairs
- Therefore, the scatter count rates are calculated within a scaling coefficient, which can be of form (ax) or (ax + b)
- Commonly used method is to extract the background region (assumed to consist purely of scattered events) from the emission sinogram
- The background region is called the “sinogram tail” region, which can be used to calculate appropriate scaling coefficient e.g. by taking the ratio of integral of emission tails vs integral of scatter tails
- The tail scaling takes into account multiple scatter as well, although this relation cannot be proven theoretically
- Alternative methods based on Monte Carlo simulation (MC-SSS) have been proposed





Sinogram tail regions



Estimate scaling coefficient and fit

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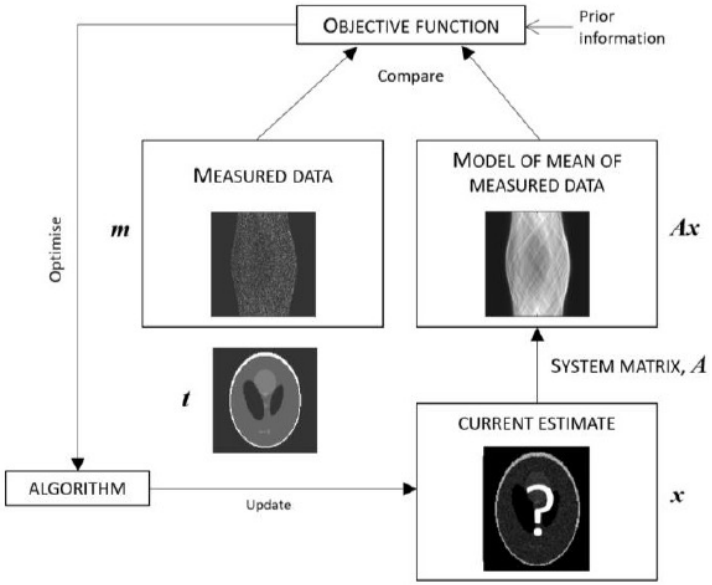
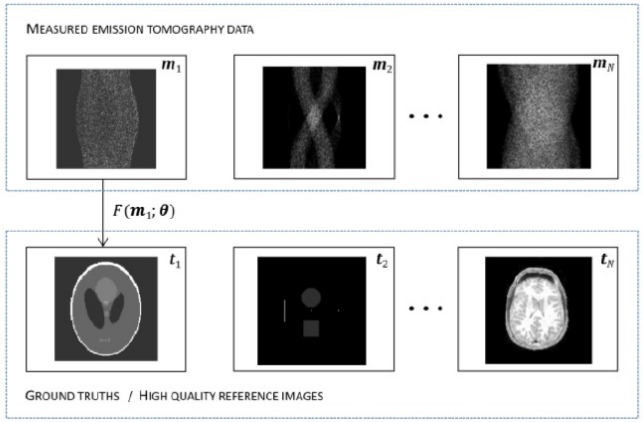
Deep Learning for PET Recon

Deep Learning for PET Image Reconstruction

Andrew J. Reader, Guillaume Corda, Abolfazl Mehranian, Casper da Costa-Luis, Sam Ellis and Julia A. Schnabel, *IEEE Senior Member*





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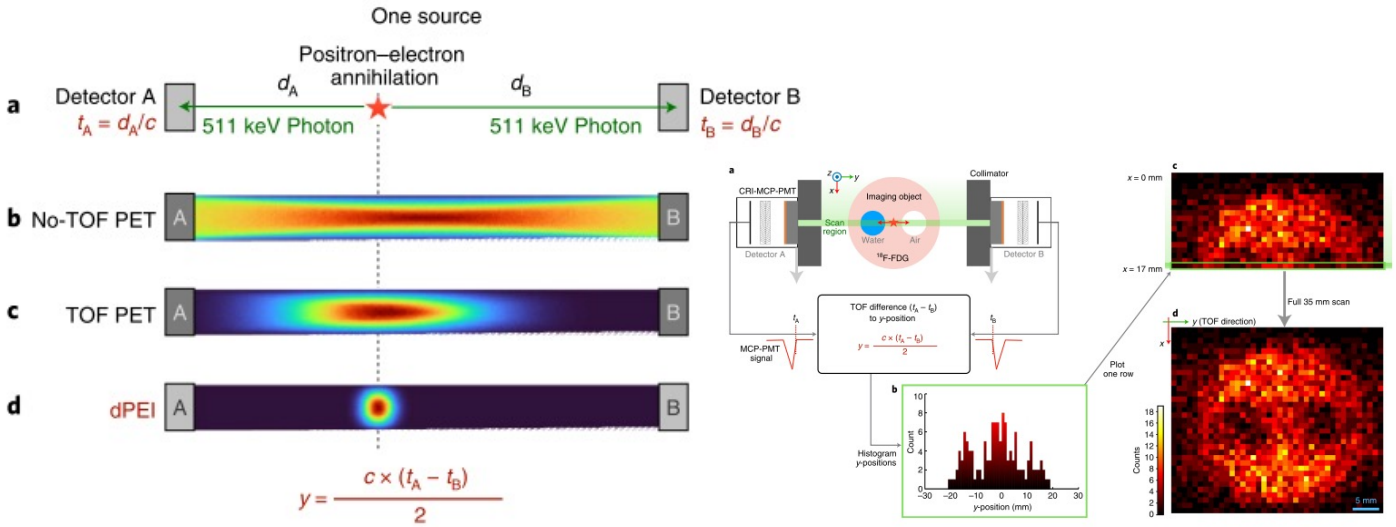
Reconless Reconstruction?

Ultrafast timing enables reconstruction-free positron emission imaging

Sun Il Kwon[1,5], Ryosuke Ota[2,5], Eric Berg[1,5], Fumio Hashimoto[2], Kyohei Nakajima[3], Izumi Ogawa[3], Yoichi Tamagawa[3], Tomohide Omura[2], Tomoyuki Hasegawa[4] and Simon R. Cherry[1]



Time to relax

- Multi-modality systems
- PET/CT
- PET/MR
- High-resolution / experimental / pre-clinical
- Total-body or large axial field of view systems (LAFOV-PET)

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Multi-modality Systems

- PET-only whole-body systems are nearly extinct, but experimental PET-only brain systems and inserts exist
- Multi-modality systems contain either CT or MRI in addition to PET system in a single gantry
- Modalities are complementary in nature, allowing advantages over PET-only systems
- PET/CT install base far surpasses the install base of PET/MR
- Large field of view systems extending over 24 – 30 cm FOV are becoming more popular

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PET/CT

- CT and PET in a single gantry
- Several advantages:
  - CT offers anatomical localization
  - PET has functional and metabolic information
  - CT can be used for attenuation correction
- Sequential and fast acquisition, allowing efficient workflow

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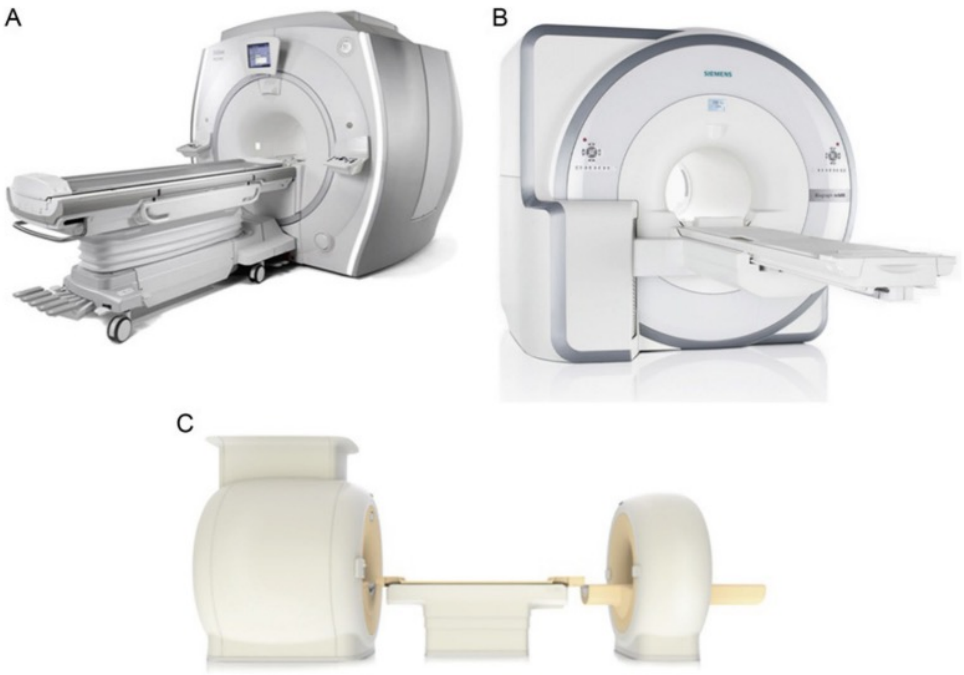
PET/MRI

- Current PET/MR systems: PET contained inside MRI gantry
- Fully simultaneous imaging, meaning PET and MRI can be acquired at the same time
- Advantages:
  - MRI has excellent soft tissue contrast
  - Modalities complement each other
  - Possibilities for research applications
- Disadvantages:
  - Costly modality compared to PET/CT
  - MRI acquisitions require more time
  - Clinical applications not so clear cut compared to PET/CT
  - Previously: attenuation correction issues



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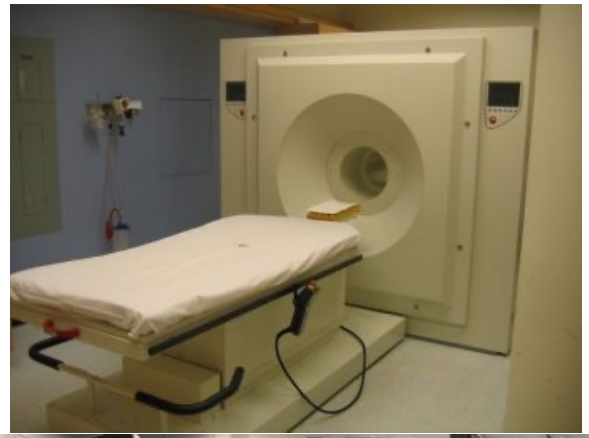
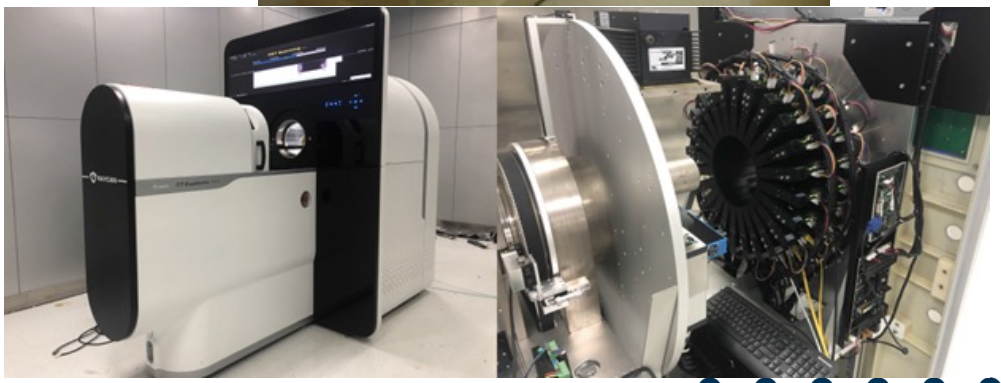
Experimental and Pre-clinical Systems

- Brain PET systems dedicated to brain only imaging
  - HRRT > 20 years
  - New systems under development
- Preclinical systems for small animal imaging
- More specific systems dedicated to single application
- I’ve also included PET inserts to this category
  - Use existing MRI with an insert for PET/MR imaging





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Total Body PET/CT Systems

- Paradigm shift in PET imaging
- Improved sensitivity: the Biograph Quadra provides a NEMA sensitivity that is about 5 times that of the Biograph Vision in MRD 85 and about 10 times in MRD 322 mode
- Simultaneous functional imaging of all organs in the FOV
- Static imaging in very short acquisition time
- Good platform for methodological developments
- Requires new ways things need to be thought out in case of acquisition, analysis and diagnosis (and methodological research)!

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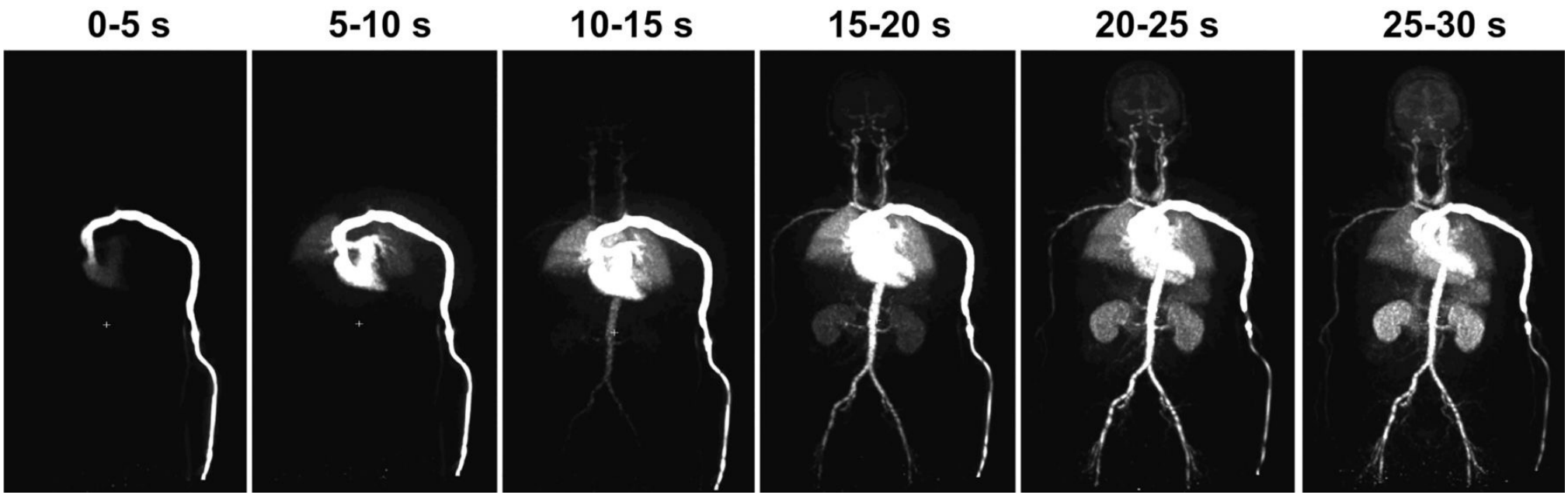

https://doi.org/10.2967/jnumed.122.264870

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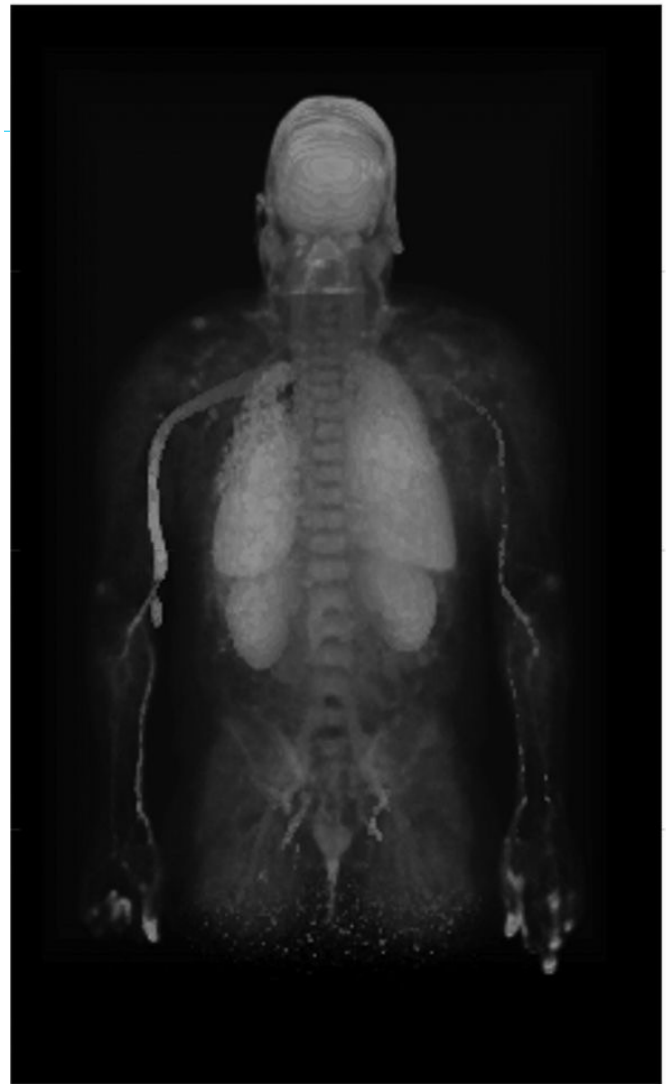
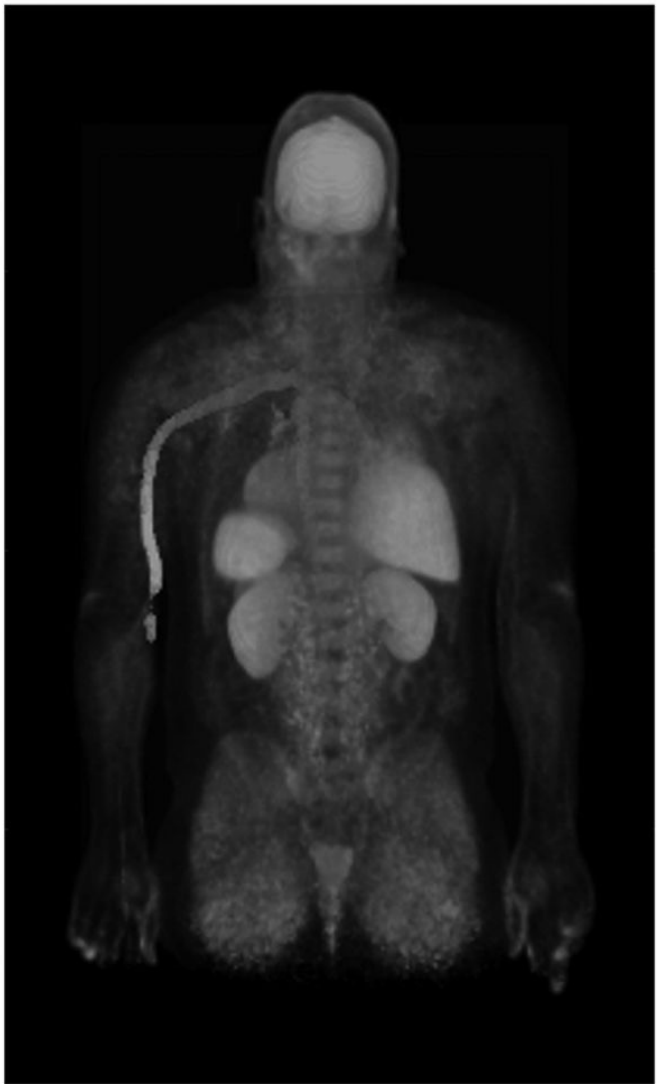
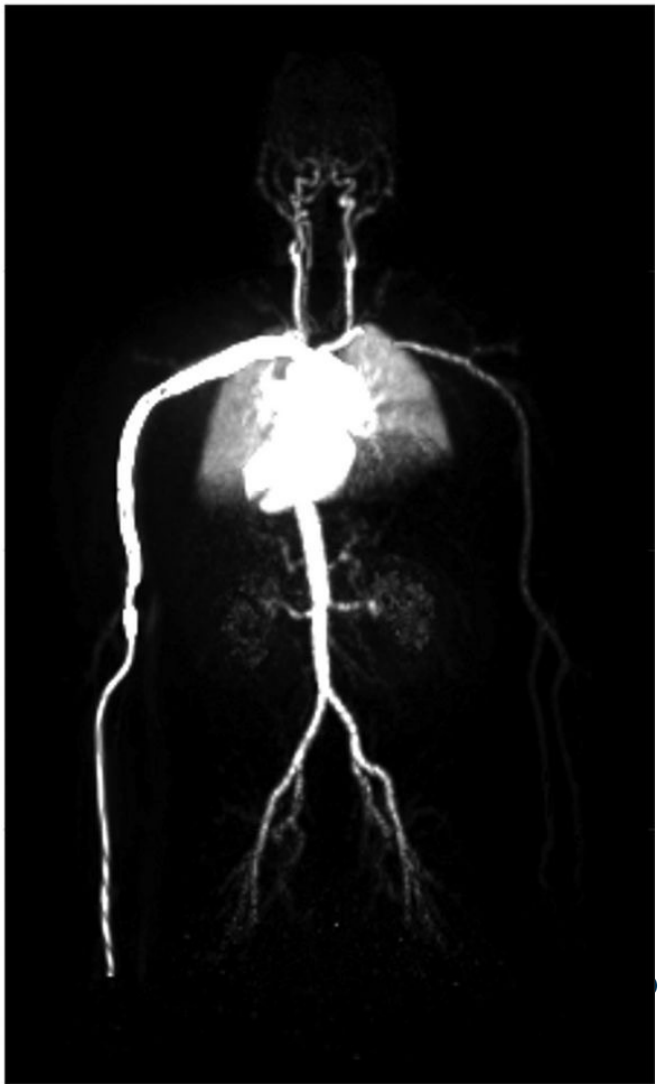
Perfusion (K_1-flow)



Perfusable Tissue Fraction (PTF)



Arterial blood volume (V_a)



Time for Questions

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