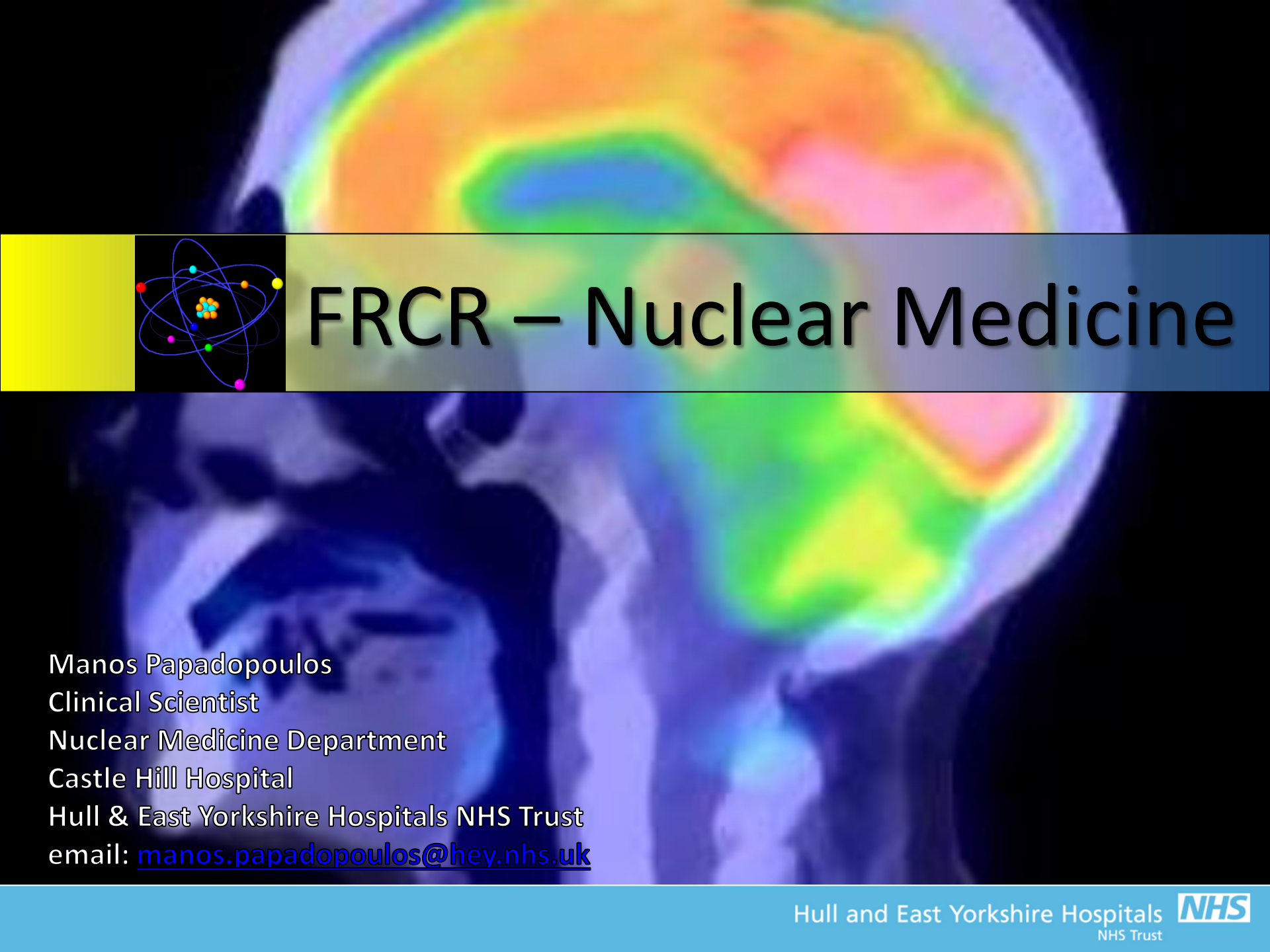

FRCR – Nuclear Medicine

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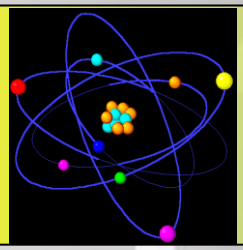
FRCR LECTURES

- Lecture I – 20/09/2016:
  - Nuclear Medicine and Image Formation
- Lecture II – 22/09/2016:
  - Positron Emission Tomography & QA
- Lecture III – 27/09/2016:
  - Radiation Detectors - Radiation Protection Molecular Imaging

BIBLIOGRAPHY

- Physics for Medical Imaging
  - P. Allisy-Roberts, J. Williams – *Farr's Physics for Medical Imaging*
- Radiological Physics
  - P. Dendy, B. Heaton – *Physics for Radiologists*
- Medical Imaging
  - J. Bushberg et al – *The Essential Physics of Medical Imaging*
  - S. Webb – *The Physics of Medical Imaging*
- Nuclear Medicine
  - S. Cherry – *Physics in Nuclear Medicine*
  - P. Sharp et al – *Practical Nuclear Medicine*



Nuclear Medicine

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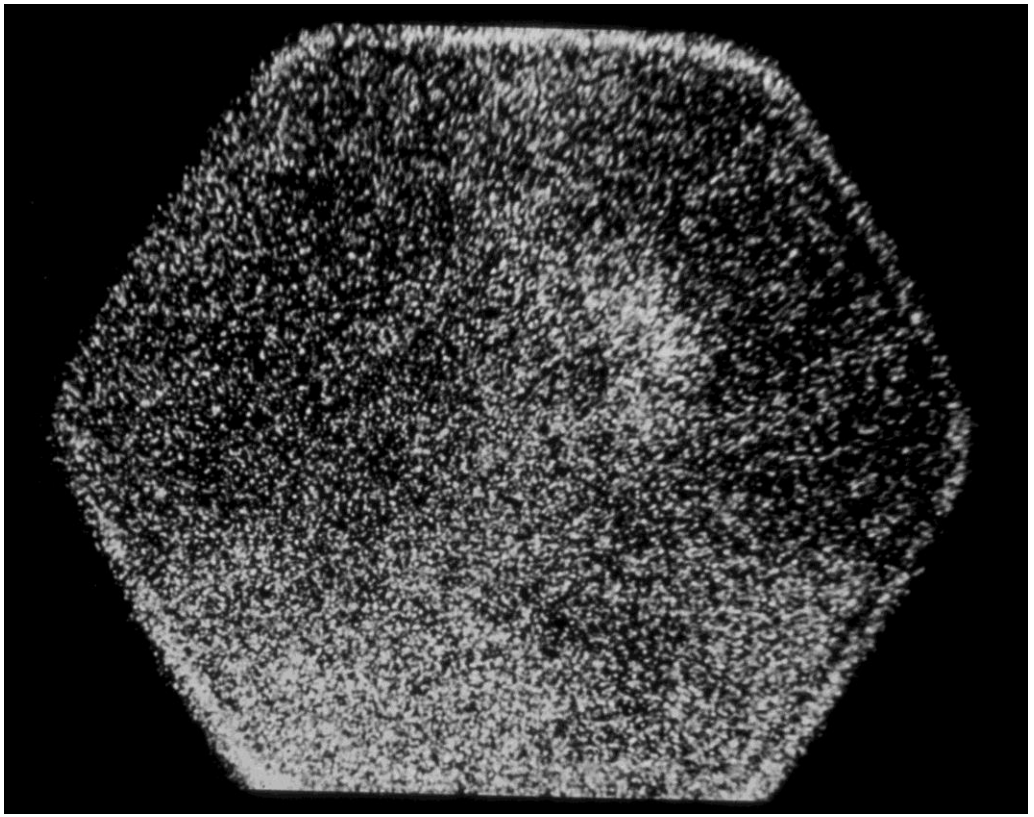
Nuclear Medicine or…

Unclear Medicine ?



Can you spot the difference?

Alive



Dead

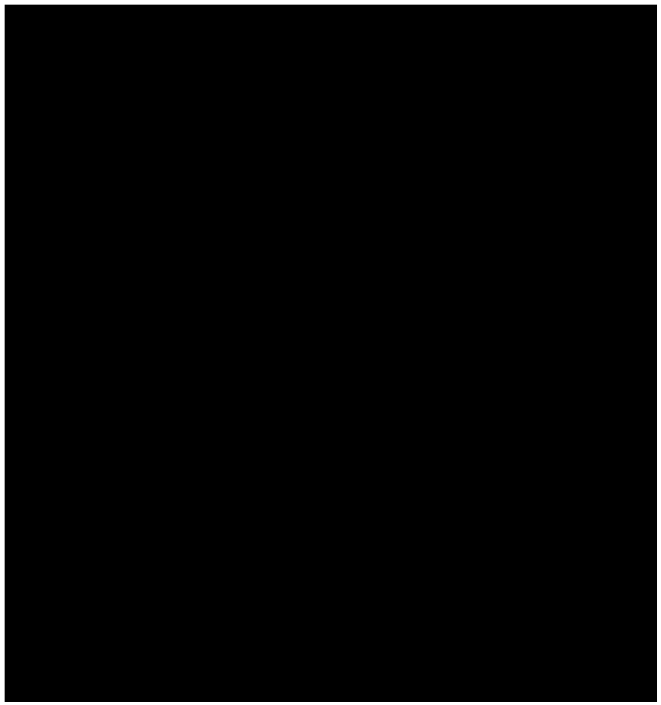


Nuclear Medicine Brain Imaging

Alive



Dead



An Intro to Functional Imaging

- To investigate regional tissue function
  - non-invasively
- Nuclear Medicine Imaging
  - SPECT, planar imaging
- Positron Emission Tomography
  - PET



Injection/ inhalation of radio-labelled molecules → **Detection of emitted γ-rays (photons) in tomographic scanner** → **Production of image (“map”) of radionuclide distribution** → **Production of functional image**

Radiopharmaceuticals

Pharmaceutical	Radionuclide
Physiological properties determine distribution in-vivo	Radiation emitter
Rapid and complete absorption by biological system of interest	Allows location of tracer to be determined
e.g. MIBI, HDP, MAG3	e.g. $^{99}Tc^{m}$, ^{123}I, ^{201}Tl

Radiopharmacy



The Ideal Radiopharmaceutical

- Radionuclide should
  - have a half-life similar to length of test
  - emit γ or X-rays
  - have no charged particle emissions
  - have energy between 100-200 keV
  - be chemically suitable
  - be readily available
- Pharmaceutical should
  - localise only in area of interest
  - elimination time similar to length of test
  - be simple to prepare





Commonly Used Radionuclides

Radionuclide	Production	Photon Energy (keV)	Half-life
^{67}Ga	Cyclotron	92, 182, 300, 390	78 hours
$^{99}Tc^{m}$	Generator	140	6 hours
^{111}In	Cyclotron	173, 247	2.8 days
^{123}I	Cyclotron	160	13 hours
^{131}I	Reactor	280, 364, 640	8 days
^{201}Tl	Cyclotron	68-80	73.5 hours

Radionuclide Generators

- Solution to the problem of supply
  - of short-lived radionuclides
- The principle is:

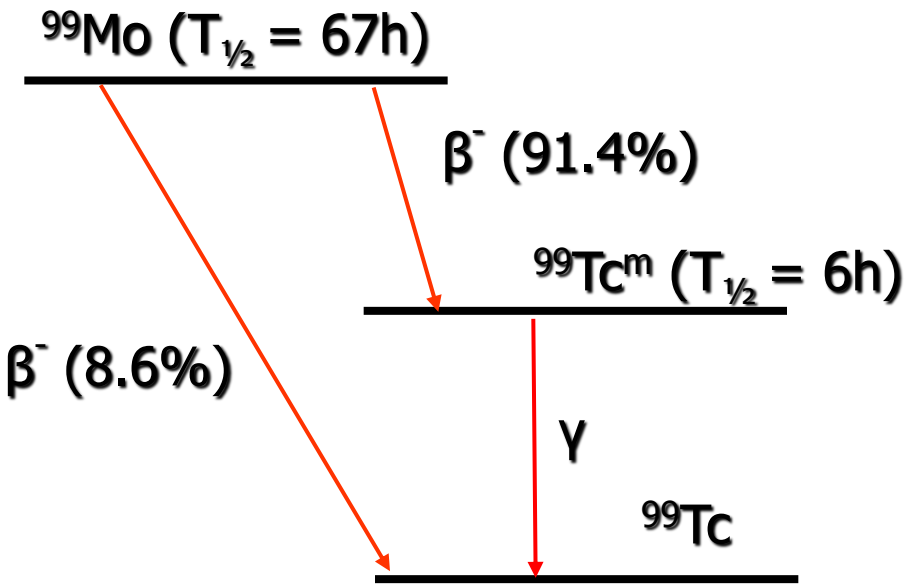
Relatively long-lived parent radionuclide

Decay

Daughter radionuclide with shorter half-life

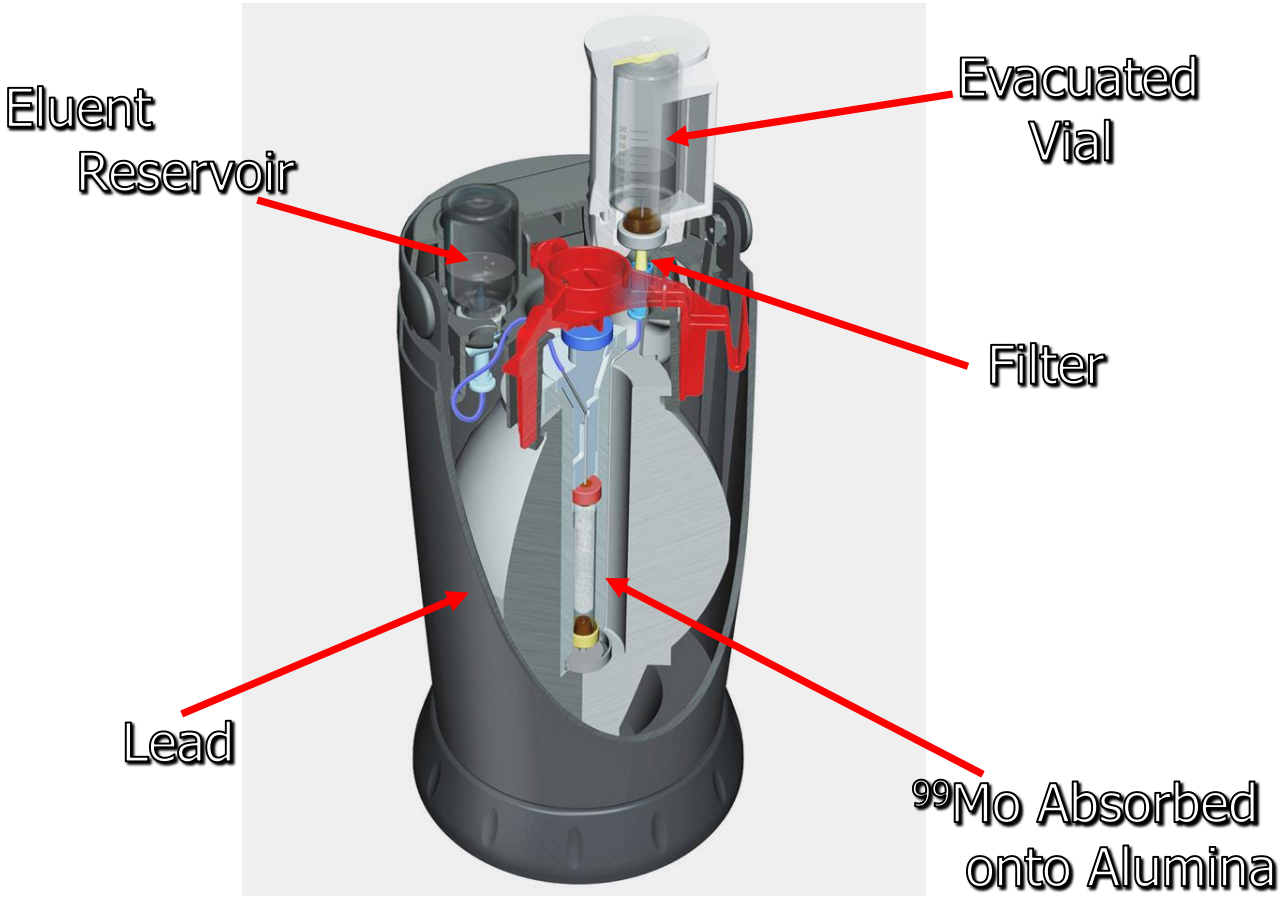


^{99}Mo Decay Scheme



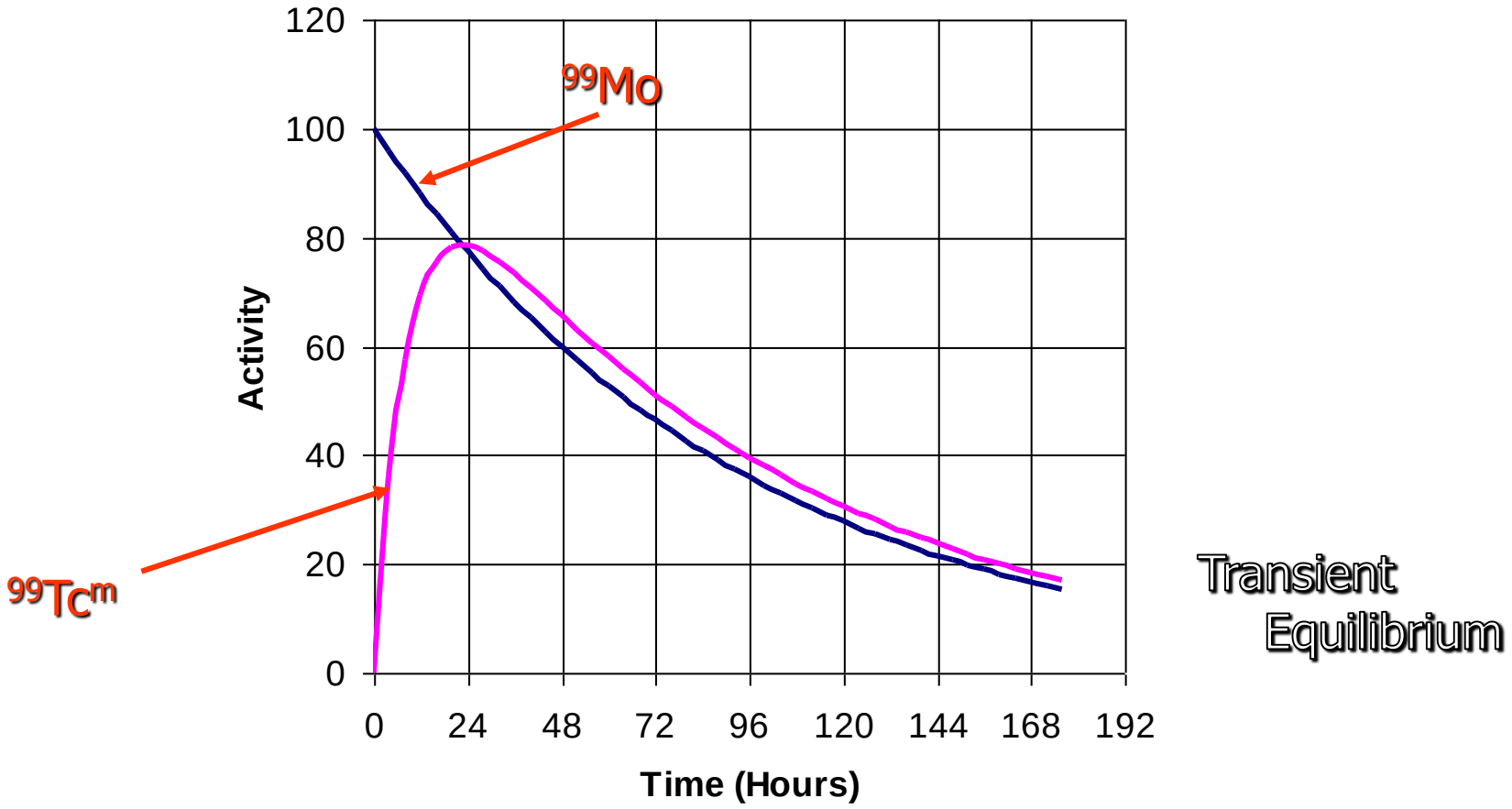
$^{99}Mo/^{99}Tc^{m}$ Generator



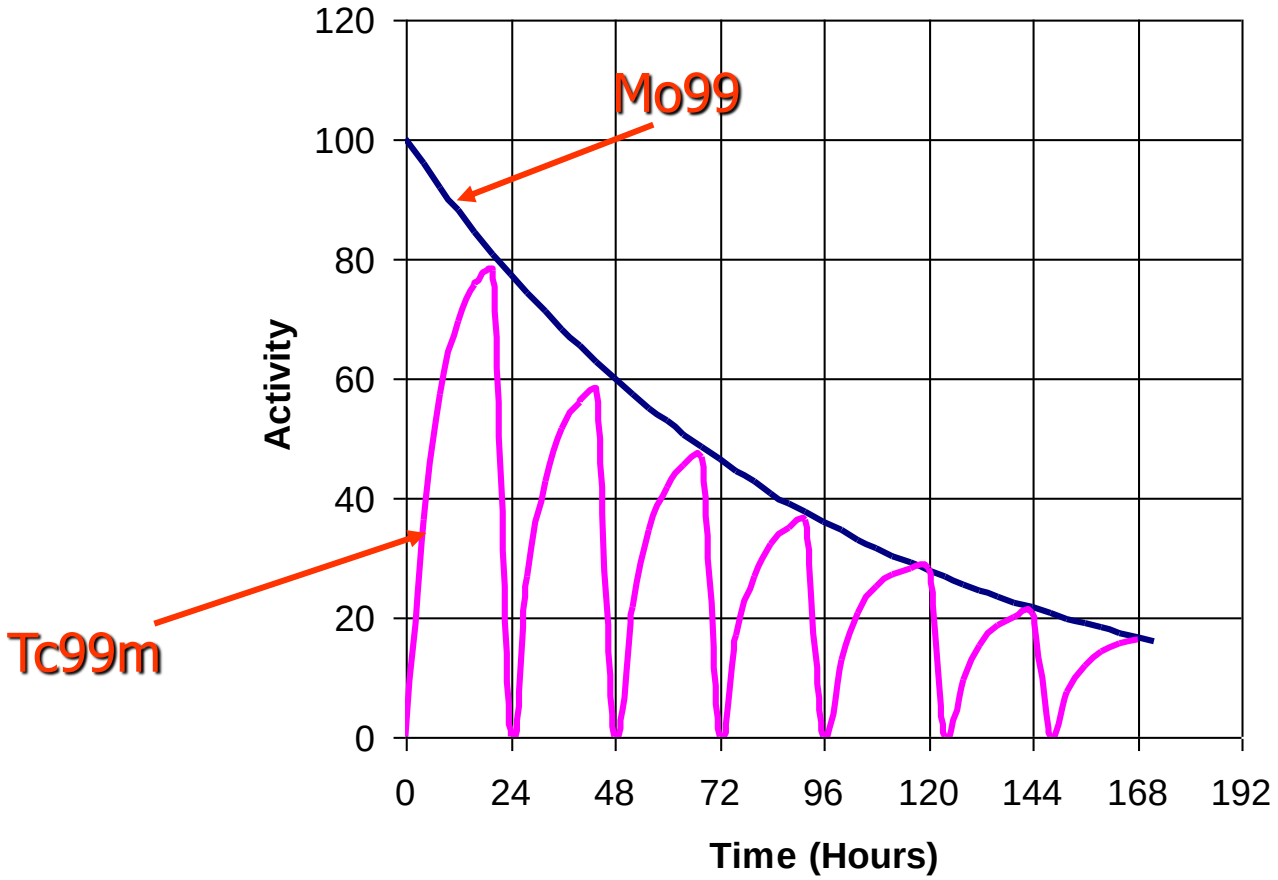


$Na^{+}Cl^{-}$ → **Generator** → $Na^{+}(TcO_4)^{-}$

$^{99}Mo/^{99}Tc^{m}$ Generator



$^{99}Mo/^{99}Tc^{m}$ Generator with Elution



Radiolabelling with $^{99}Tc^{m}$

- Cold (non-radioactive) kits
  - pre-packed set of sterile ingredients designed for the preparation of a specific radiopharmaceutical
  - Typical ingredients
    - compound to be complexed to $^{99}Tc^{m}$
      - e.g. methylene diphosphonate (MDP)

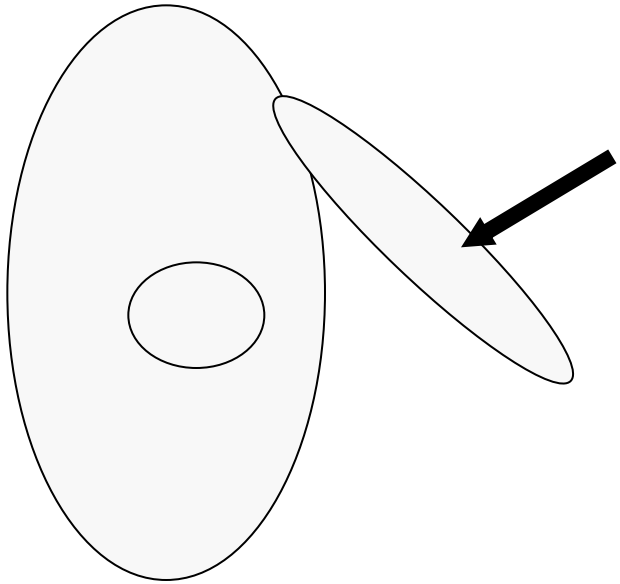
Radionuclide Calibrator

- Confirms correct activity prior to patient administration
- Well-type ionisation chamber
  - pressurised argon gas (increases efficiency)
- Electrometer
  - measures small ionisation currents
- Protective sleeve
  - removable if activity spilt
- “Dipper”
  - reduces finger dose
  - ensures fixed geometry
- Shielding
  - reducing background radiation
  - protects the user



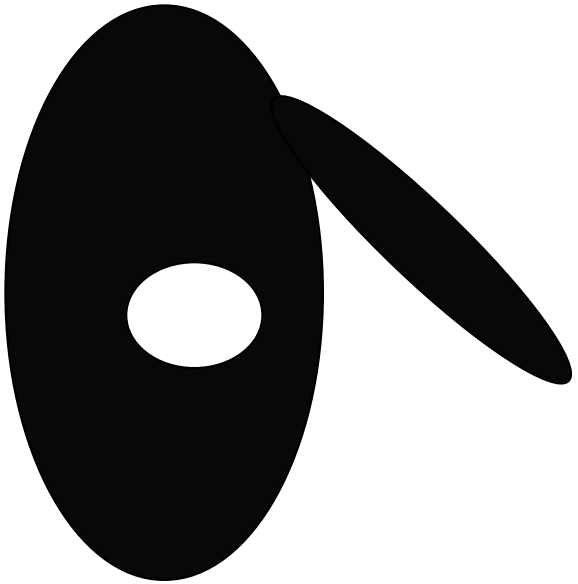
Nuclear Medicine Imaging

- Administration of radiopharmaceutical
  - usually intravenously



Nuclear Medicine Imaging

- Localisation and uptake
  - over time tracer concentrates to area of interest



Nuclear Medicine Imaging

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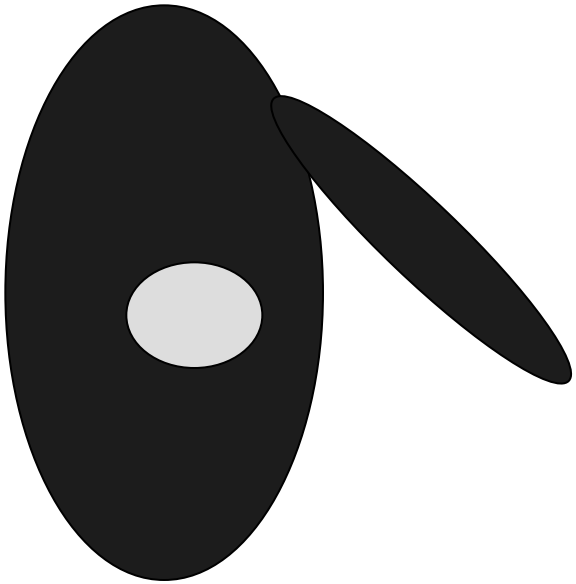

Nuclear Medicine Imaging

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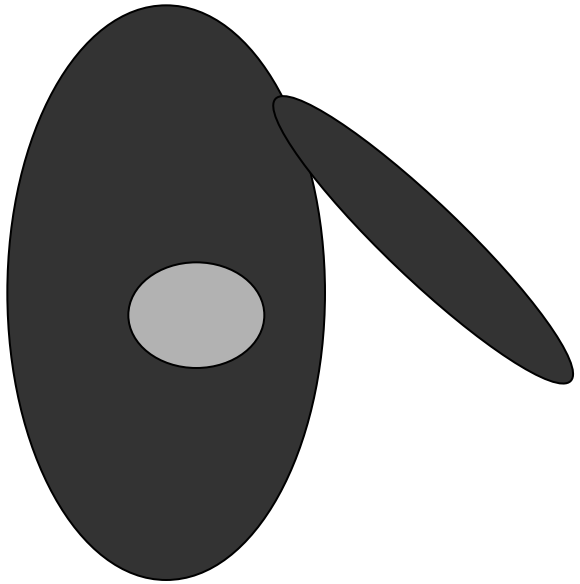

Nuclear Medicine Imaging

- Localisation and uptake
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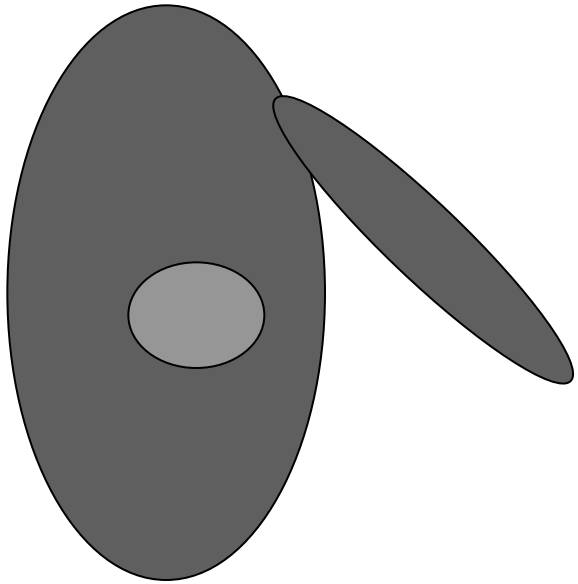

Nuclear Medicine Imaging

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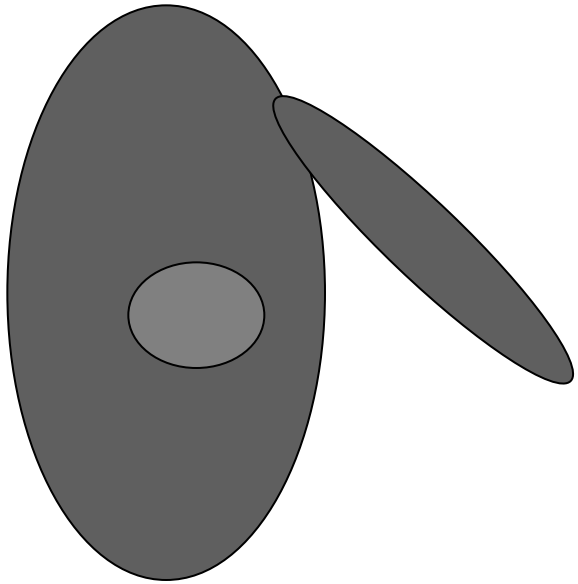

Nuclear Medicine Imaging

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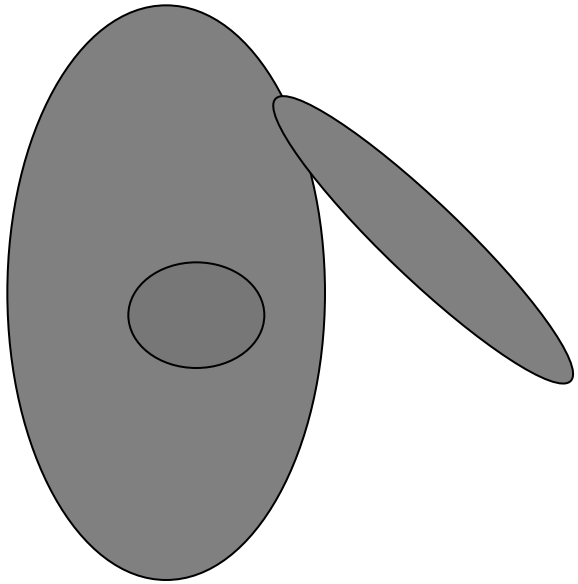
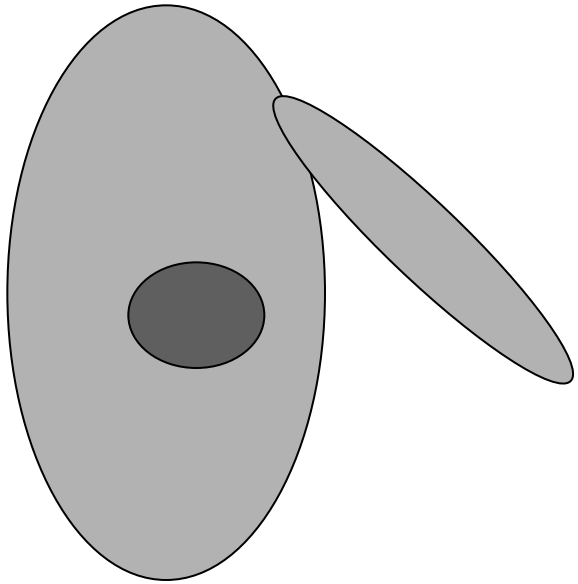


Nuclear Medicine Imaging

- Localisation and uptake
  - over time tracer concentrates to area of interest



Enhanced contrast between the area of interest and the rest of body

The Gamma (γ) Camera







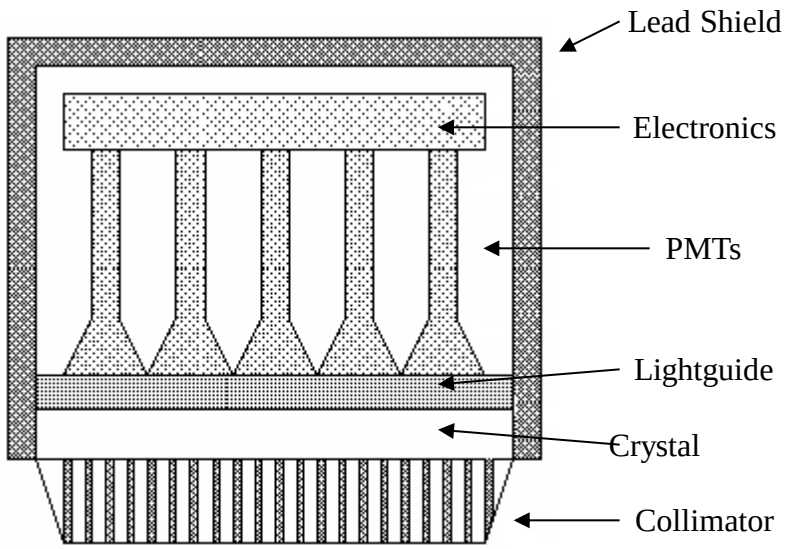
The Gamma (γ) Camera

- Principal instrument
  - in Nuclear Medicine
- Images distribution
  - of γ or X-ray emitters
- Consists of:
  - a gantry
  - at least one detector
  - a computer



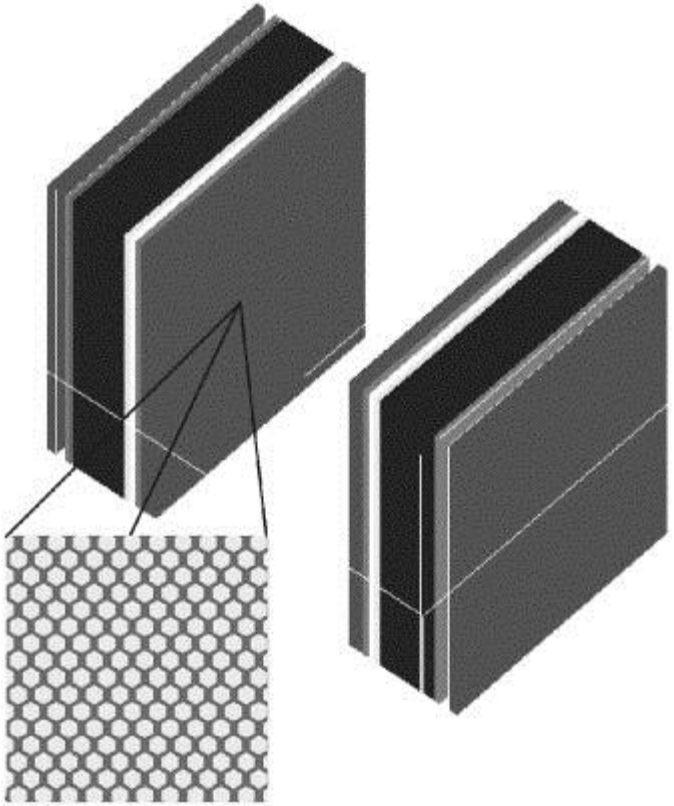
The Detector

- The components of a modern gamma camera are:
  - Collimator
  - Detector crystal
  - Optical light-guide
  - Photomultiplier tube array
  - Position logic circuits
  - Data analysis computer
  - Lead shield to minimise background radiation

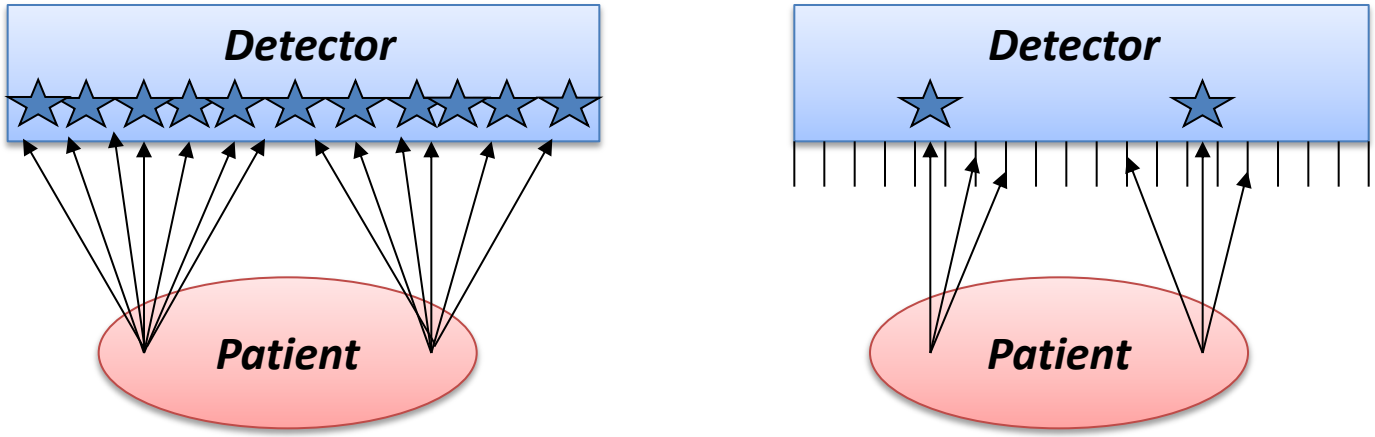


The Collimator

- The collimator consists of:
  - a lead plate
  - array of holes
- Selects direction of photons
  - incident on crystal
- Defines geometrical
  - field of view of the camera



The Collimator

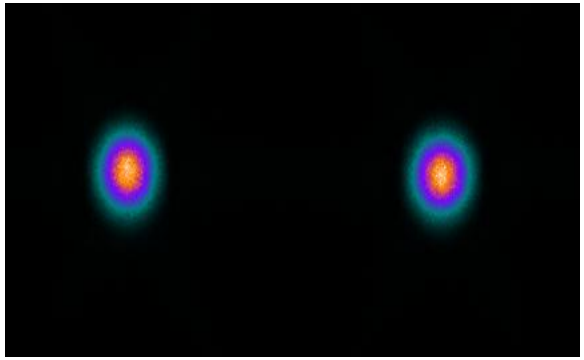


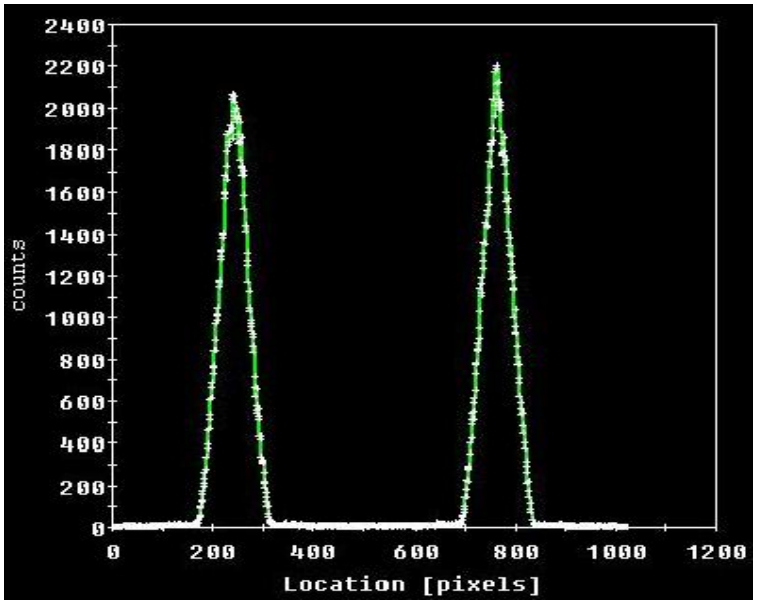
- In the **absence** of collimation:
  - no positional relationship between source – destination
- In the **presence** of collimation:
  - all γ-rays are excluded except for those travelling parallel to the holes axis – true image formation

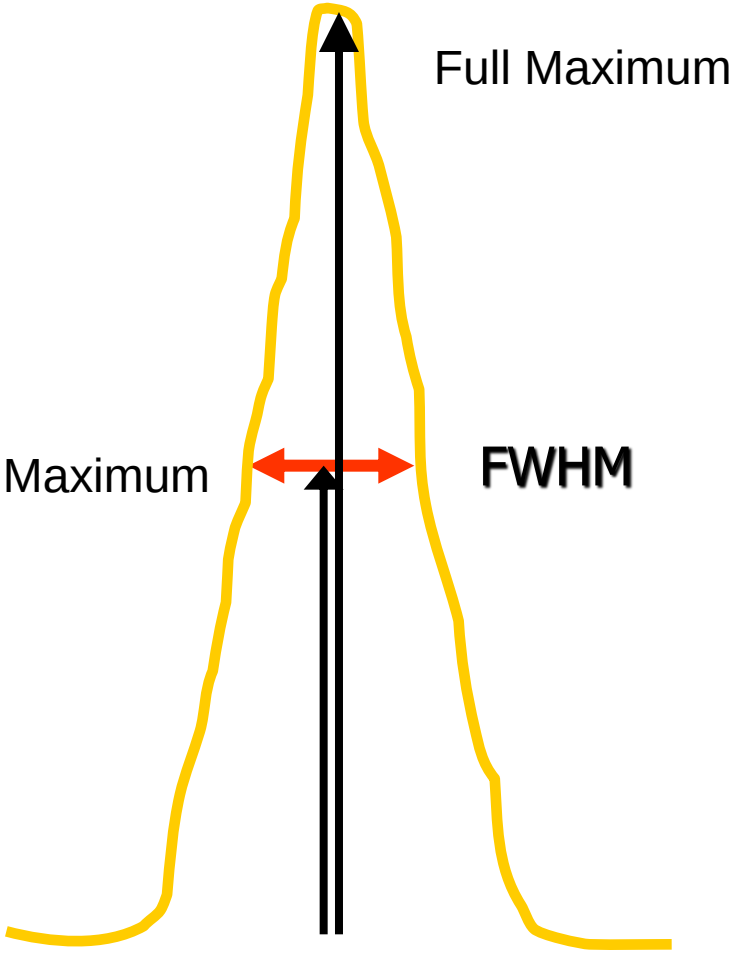
Collimator Parameters

- Spatial resolution (mm)
  - a measure of the sharpness of an image
- Sensitivity (cps/MBq)
  - the proportion of the emitted photons which pass through the collimator and get detected

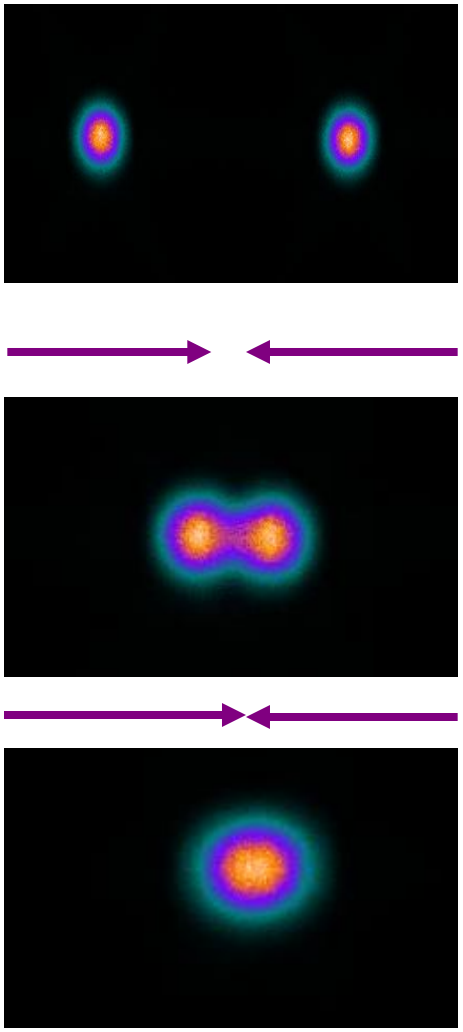
Spatial Resolution

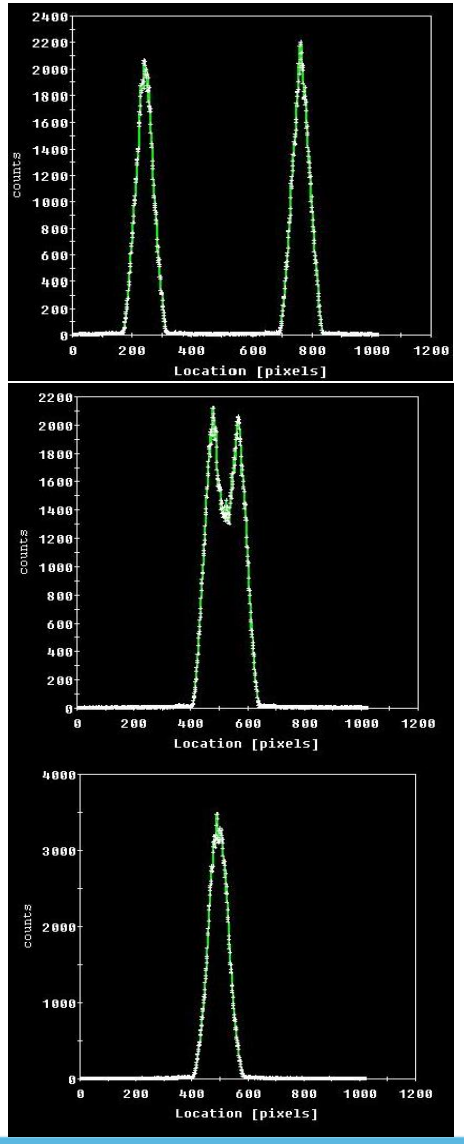




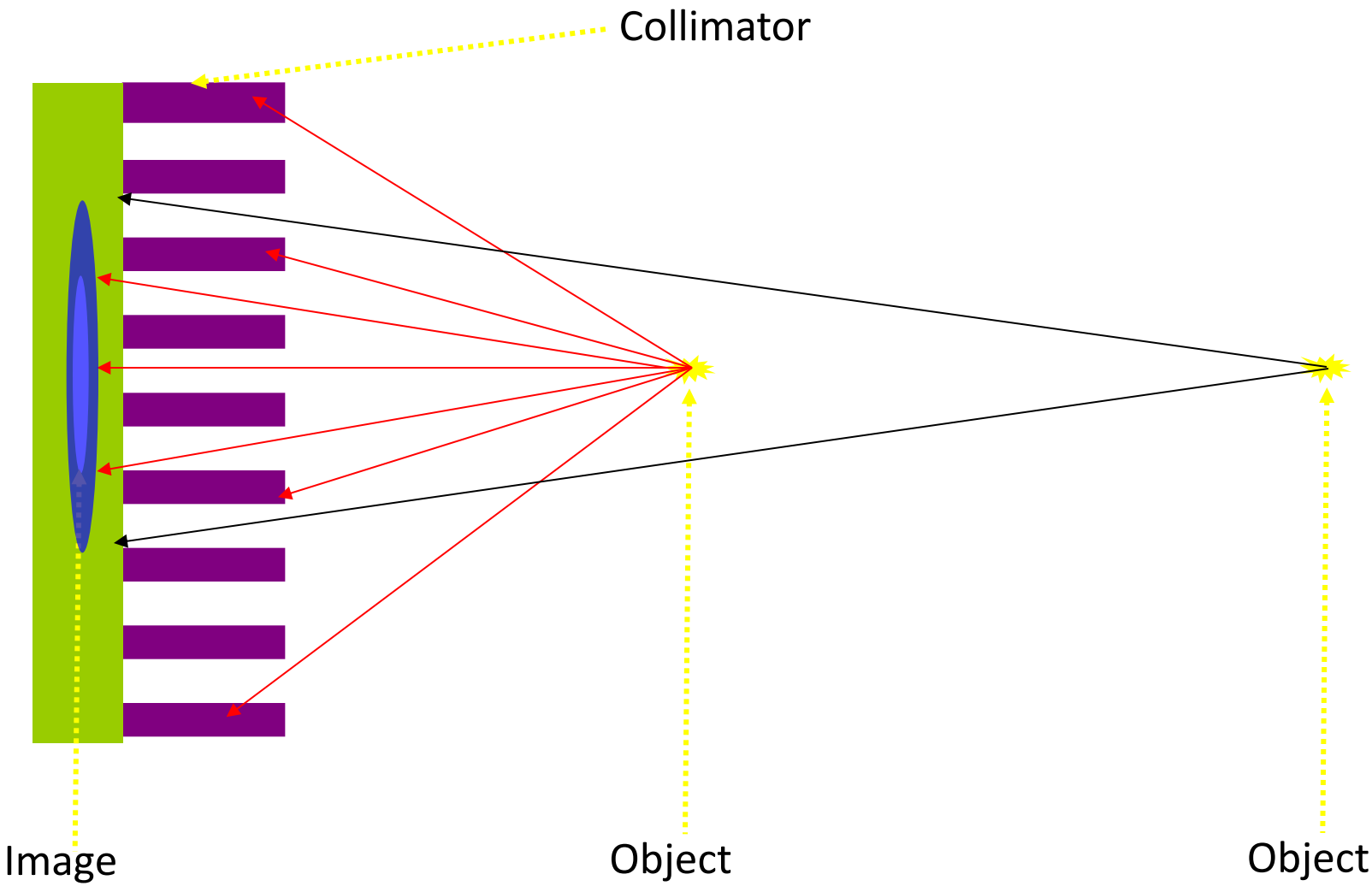


Significance of FWHM

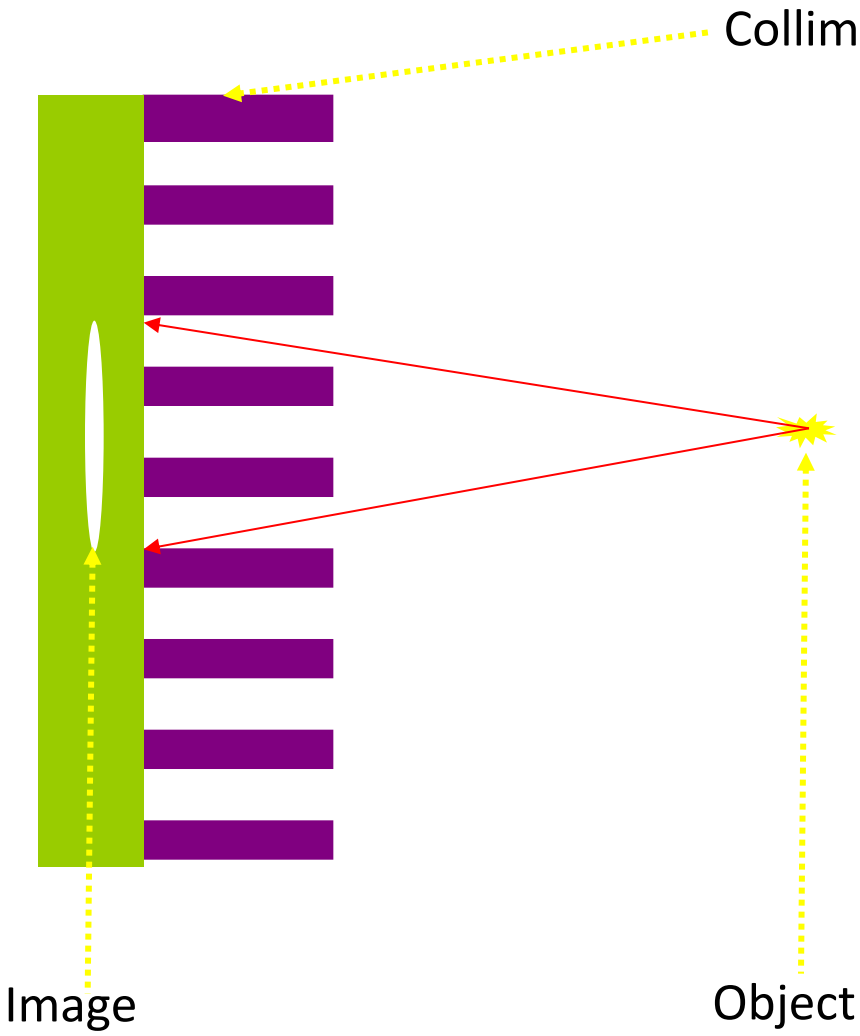




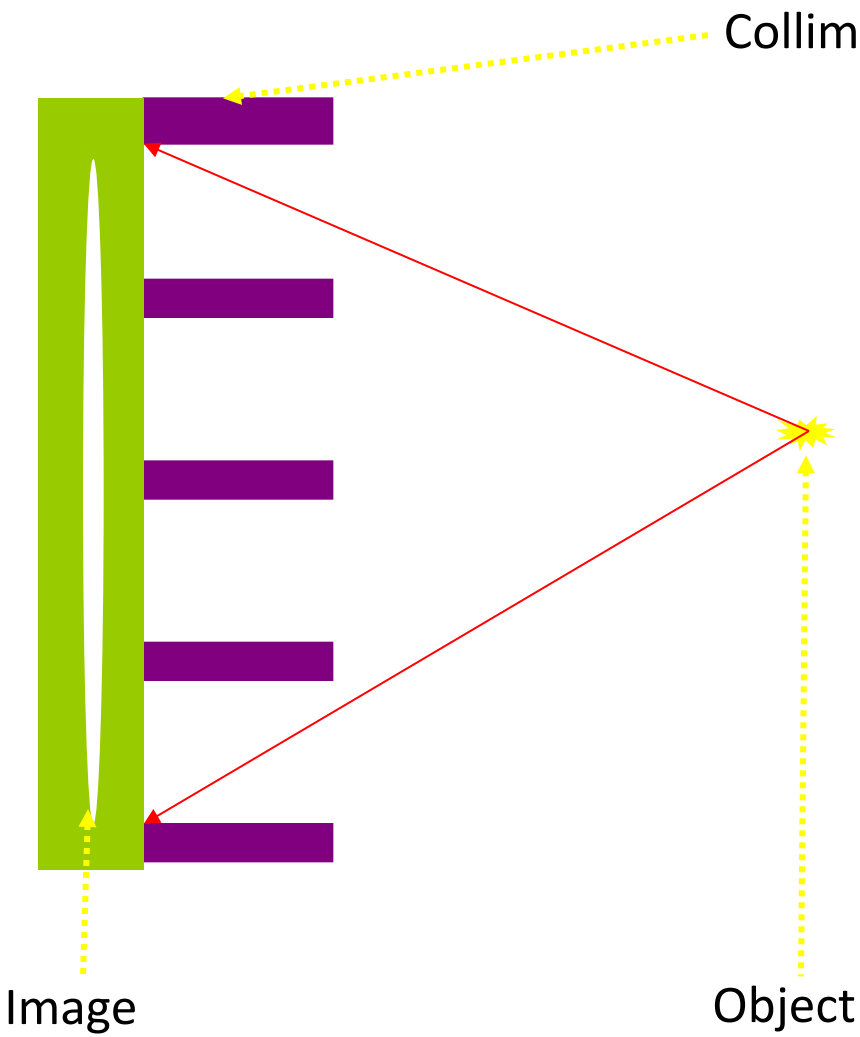
Distance from Collimator



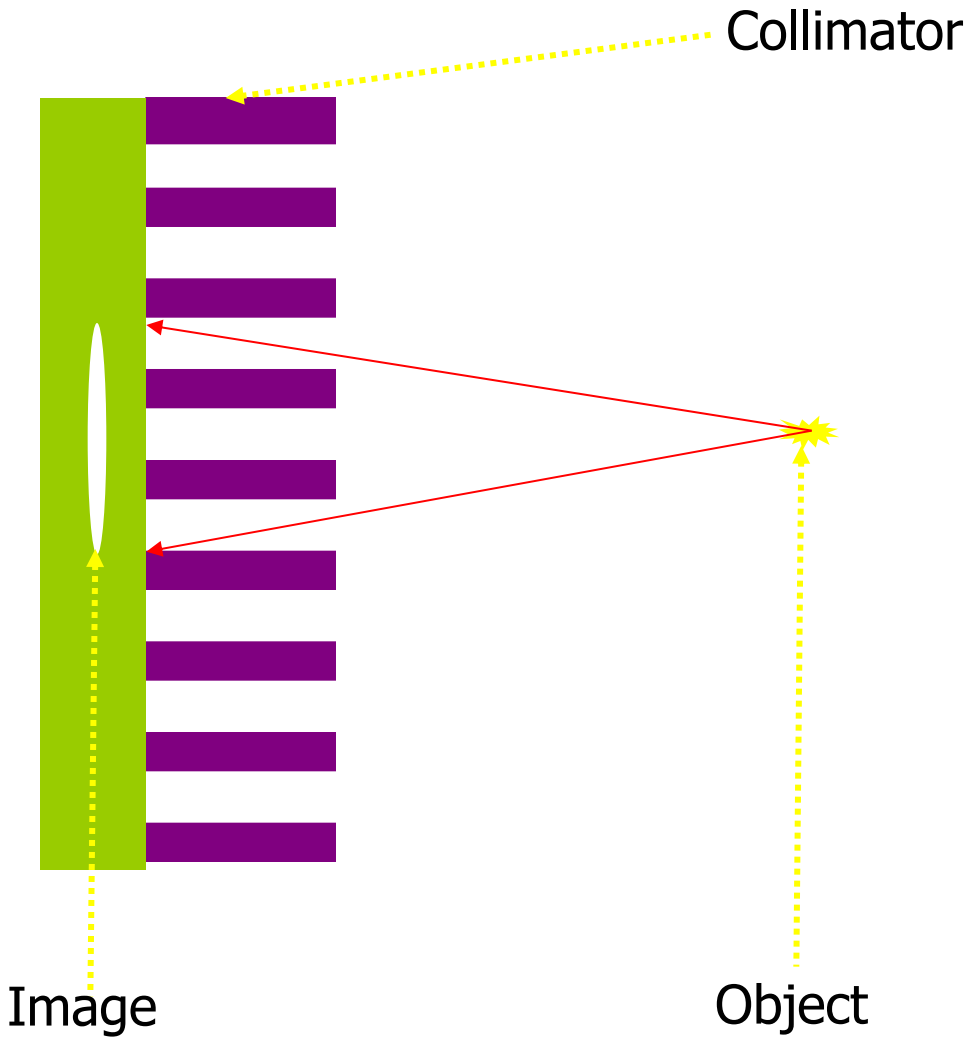
Hole Size



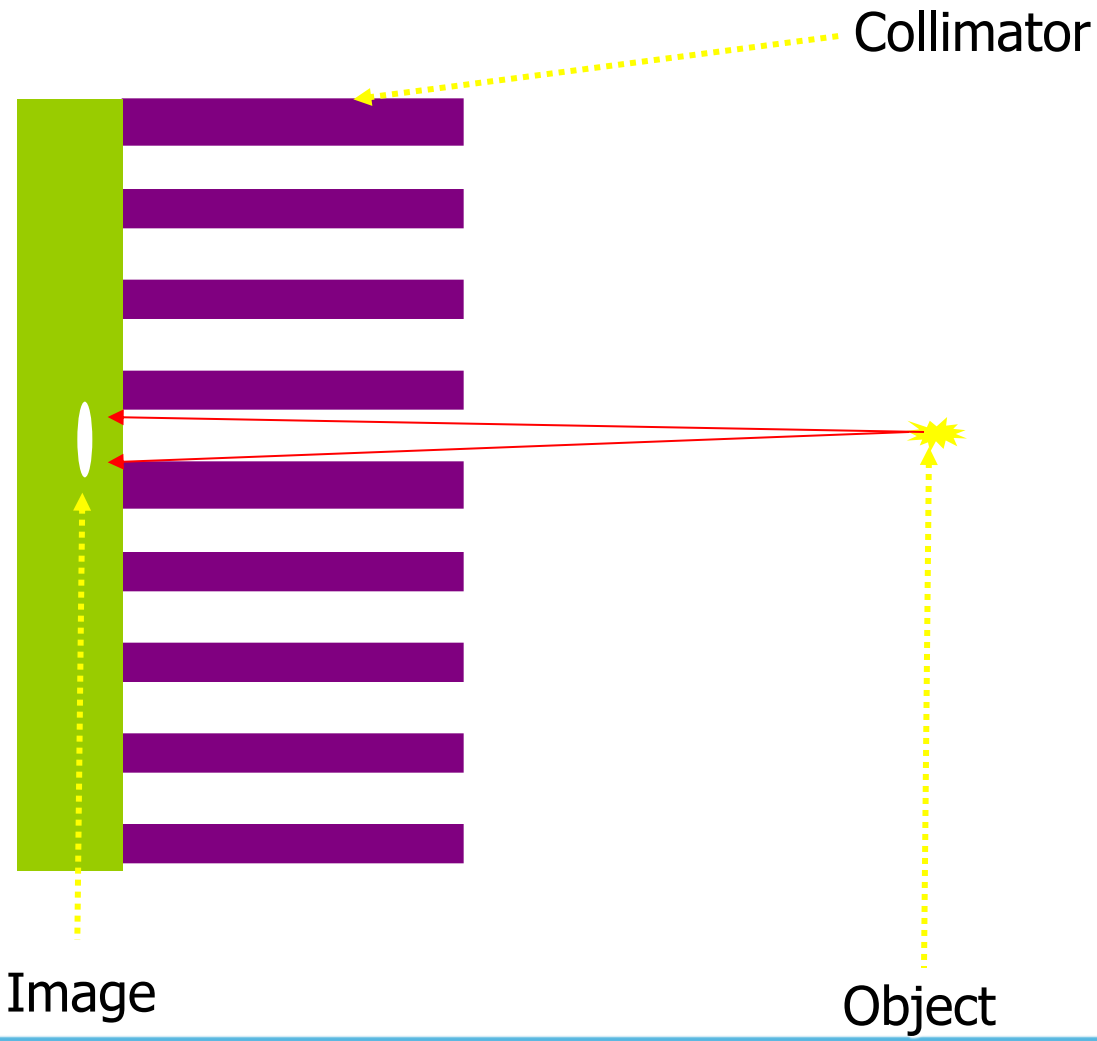
Hole Size



Hole Length

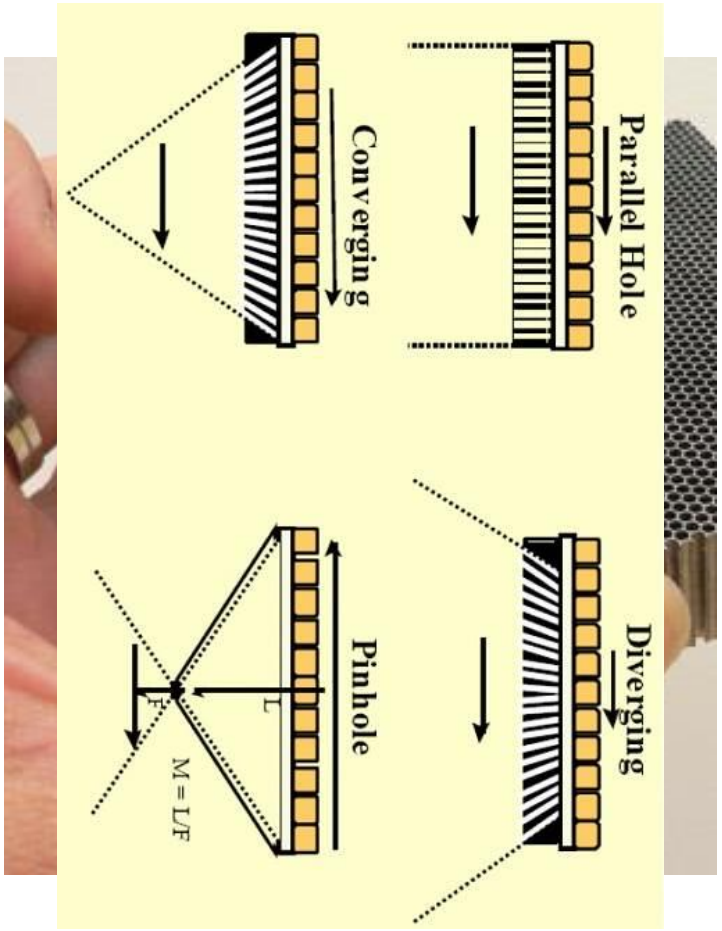


Hole Length



Types of Collimators

- There are several types of collimators:
  - Parallel-Hole collimator
  - Converging collimator
  - Diverging collimator
  - Pin-Hole collimator
- Depending on the energy:
  - LE: 0 keV < energy < 200 keV
  - ME: 200 keV < energy < 300 keV
  - HE: 300 keV < energy < 400 keV



Collimators: Performance Factors

Type	Hole Size (mm)	Number of Holes	Hole Length (mm)	Septal Thickness (mm)
LEHR	1.5	86,300	35	0.20
LEGP	1.9	56,560	35	0.20
MEGP	3.0	15,210	58	1.05
HEGP	4.0	7,410	66	1.80

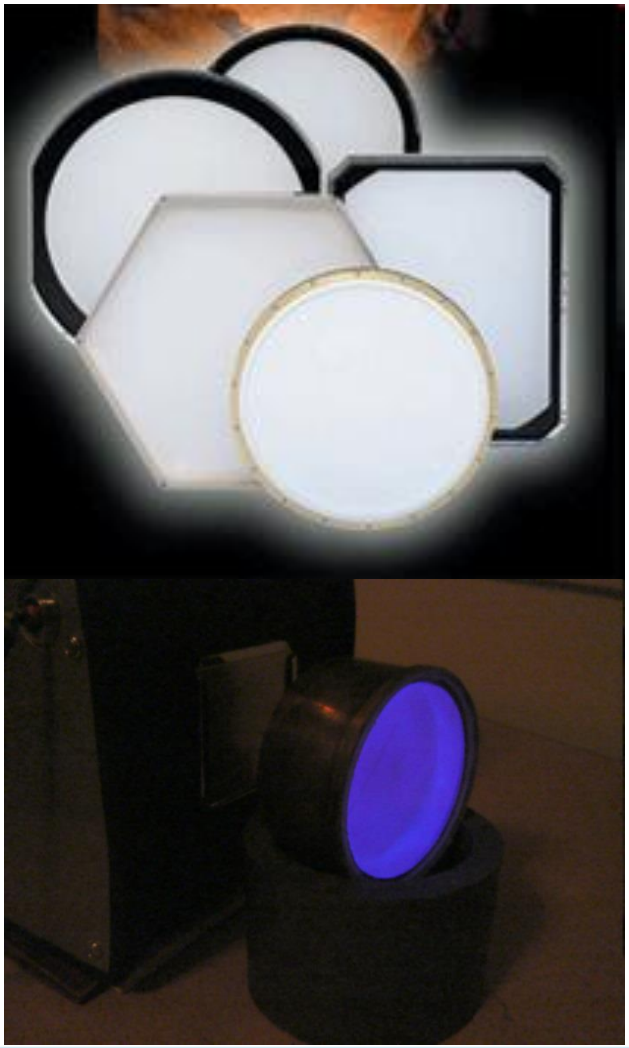
Collimators: Performance Factors

Type	Resolution* (mm)	Sensitivity (cps/MBq)
LEHR	7.4	72.0
LEGP	9.0	121.5
MEGP	9.4	64.8
HEGP	10.7	65.25

*spatial resolution at 10 cm from collimator face

The Scintillation Crystal

- γ-ray photon
  - detected by interacting with crystal
  - converted into scintillations
- Crystal shape:
  - circular
  - rectangular
- The crystal size
  - ~ 60 x 45 cm^2
  - FOV ~ 54 x 40 cm^2
- Crystal thickness
  - ~ 9.5 mm (3/8 inch)



Scintillation Crystal Properties

- **Desirable Properties of the scintillation crystal**:
  - High stopping efficiency for γ-rays
  - Stopping should be without scatter
  - High conversion of γ-ray energy into visible light
  - Wavelength of light should match response of PMTs
  - Crystal should be transparent to emitted light
  - Crystal should be mechanically robust
  - Thickness of scintillator should be short

Properties of NaI(Tl) Scintillator

- **The crystal – NaI(Tl)**
  - emits blue light at 415 nm
  - high attenuation coefficient
    - intrinsic efficiency:

      90% at 140 keV
  - conversion efficiency:

    10-15%



Disadvantages of NaI(Tl) crystal

- **NaI(Tl) crystal suffers from the following drawbacks**:
  - Expensive (approximately £50,000)
  - Fragile
    - sensitive against mechanical stresses
    - sensitive against temperature changes
  - Hygroscopic
    - encapsulated in aluminium case

Lightguide and Optical Coupling

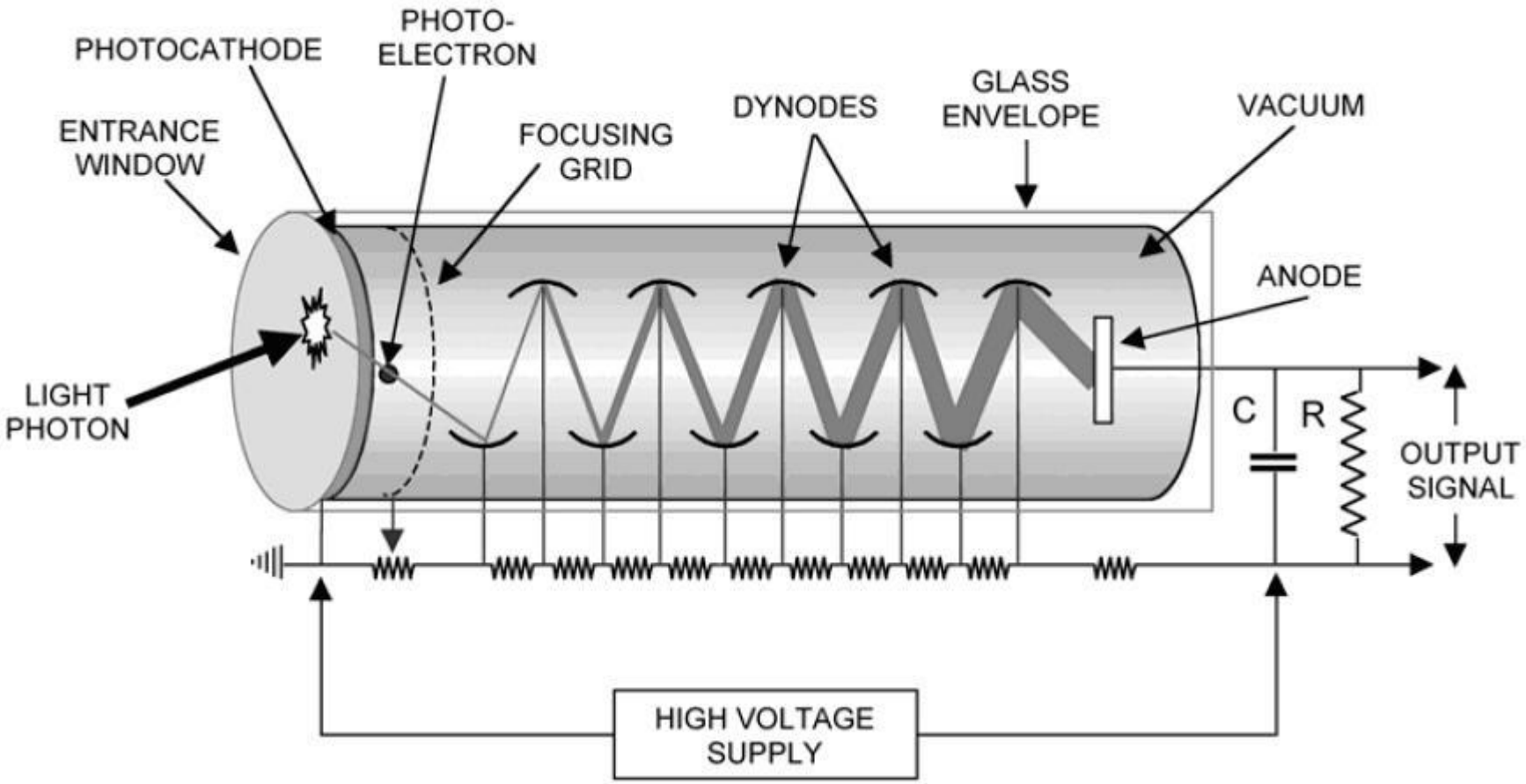
- Lightguide
  - acts as optical coupler
  - usually quartz doped plexiglass (transparent plastic)
  - should be as thin as possible
  - should match the refractive index of scintillation crystal
- Silicone grease between
  - exit window of scintillation crystal and lightguide
  - lightguide and the PMTs
- No air bubbles trapped in the grease
  - photon reflections
  - reduced light transmission

The Photomultiplier Tube

- A PMT is an evacuated glass envelope
- It consists of:
  - a photocathode
  - an anode
  - ~ 10 dynodes

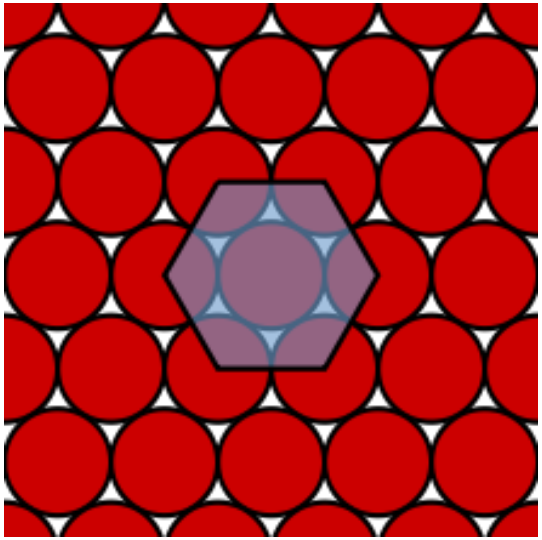


The Photomultiplier Tube



The Photomultiplier Tube

- Hexagonal array of detectors
- PMTs mounted on the crystal
- Cross Section of PMT
  - Circular or **hexagonal**
- Arrays of 7, 19, 37, 61 and 91
- The number of PMTs affects the spatial resolution of the camera
  - smaller diameter – improved resolution
  - increased number – uniformity problems



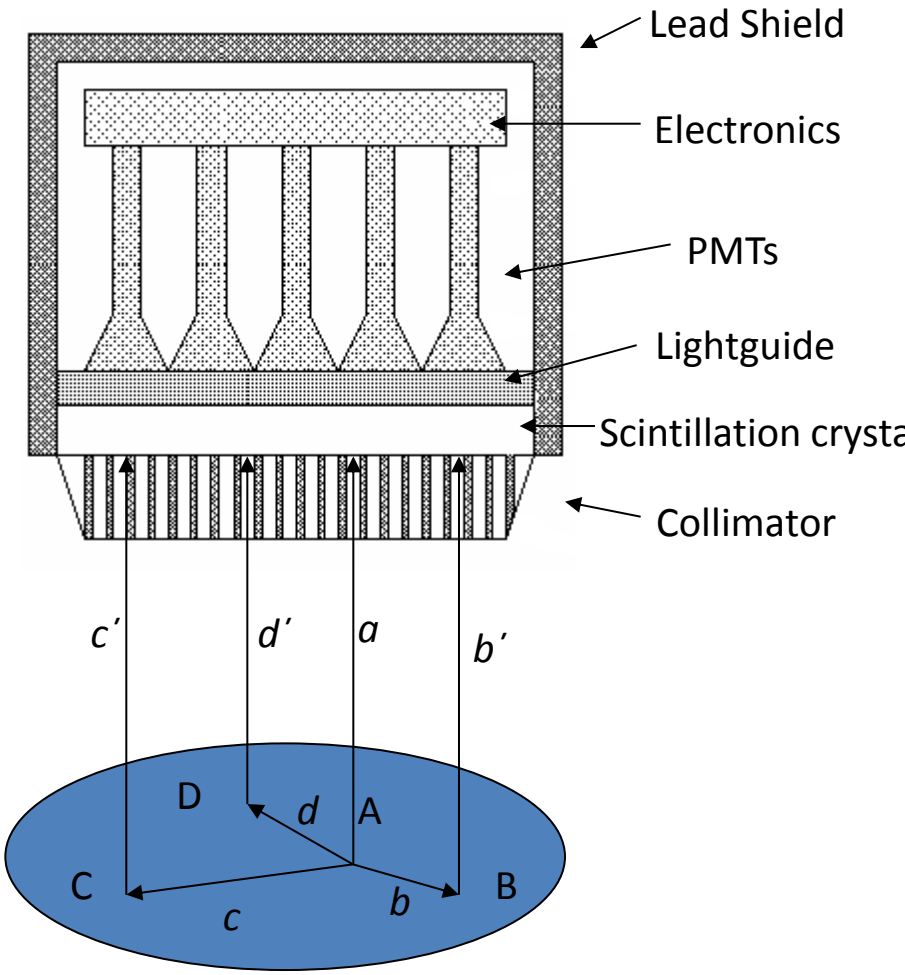
Positional and Energy Co-ordinates

- PMT signals processed
  - spatial information – X and Y signals
  - energy information – Z signal
- Z signal – the sum of the outputs of all PMTs
  - proportional to the total light output of the crystal

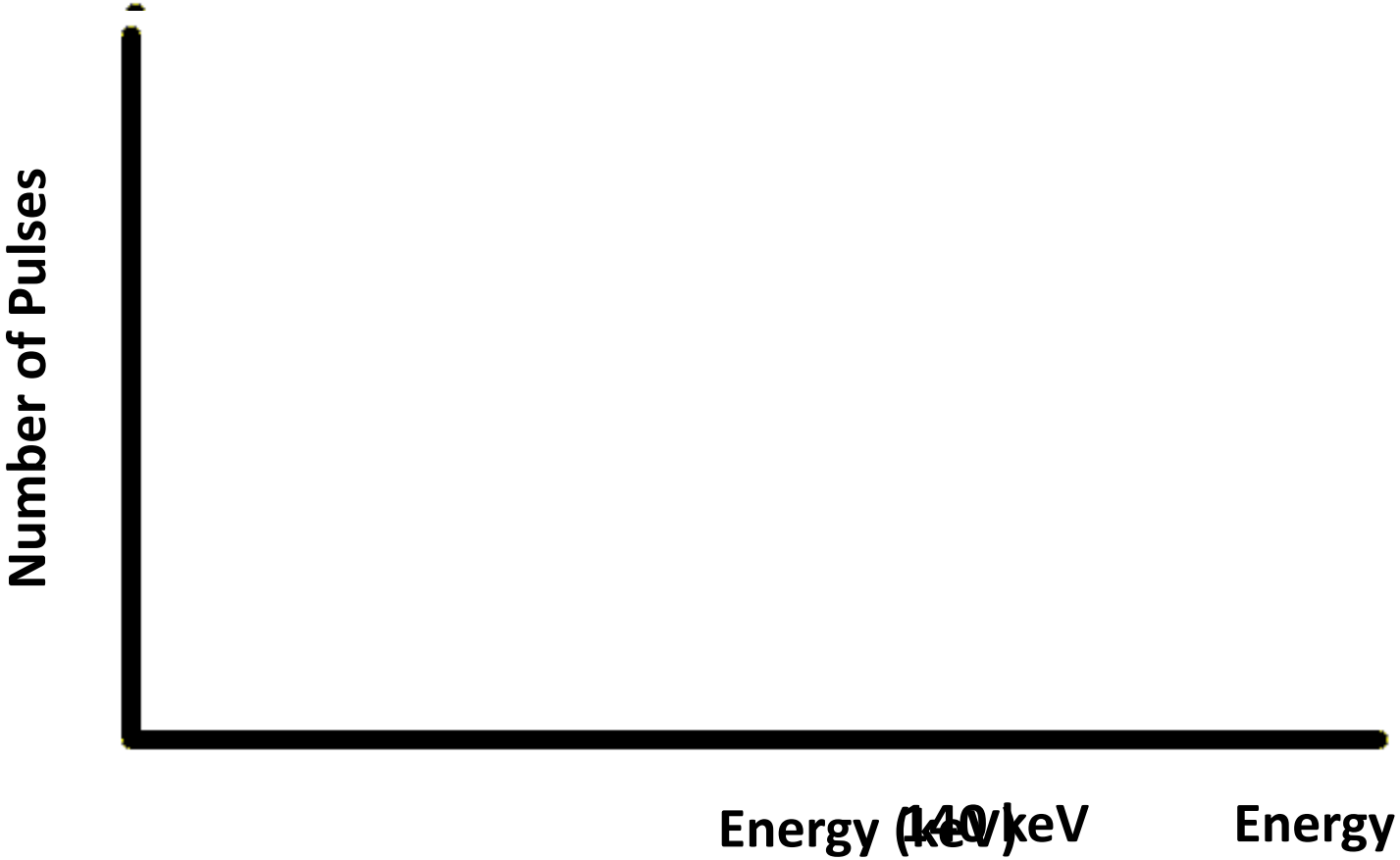


Pulse Height Analysis

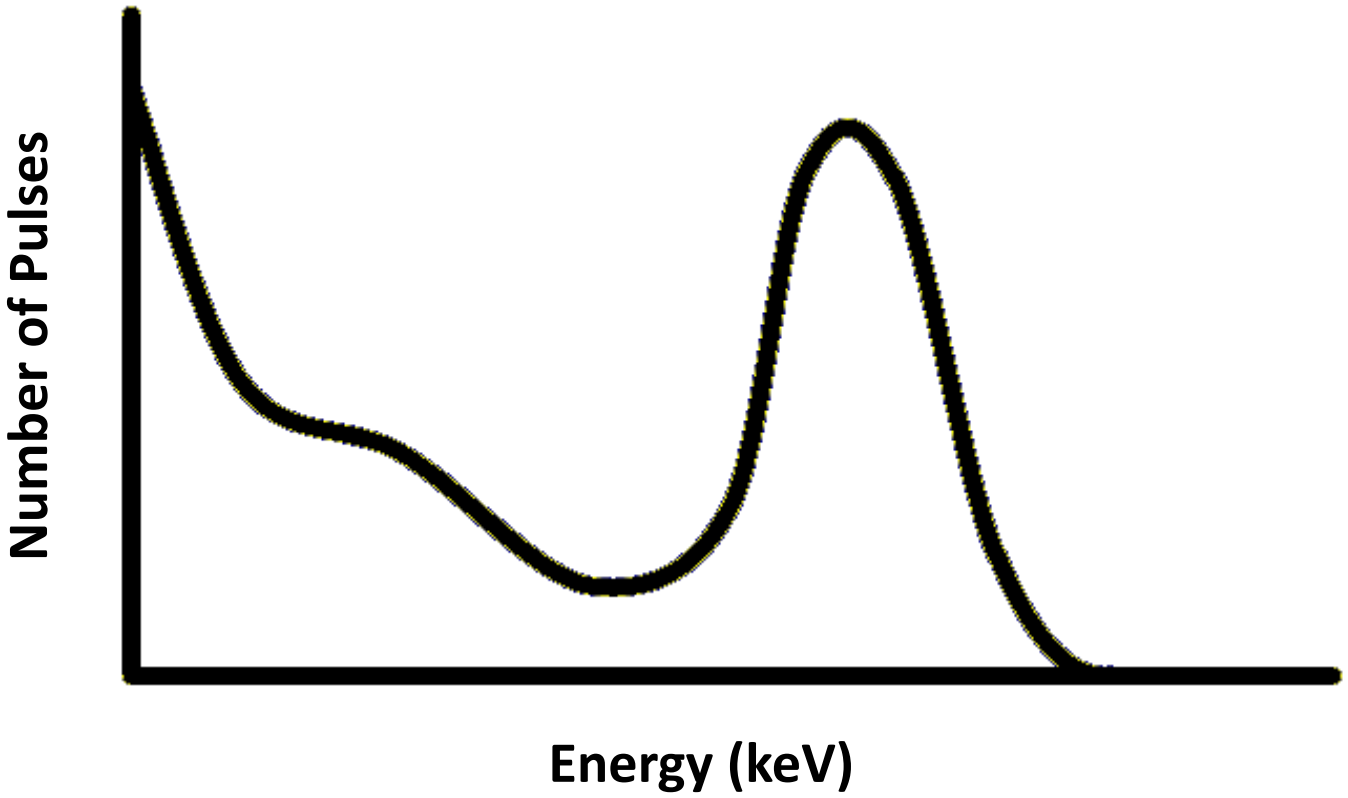
- Z-signal goes to PHA
- PHA sets
  - energy window
- PHA checks
  - the energy of the γ-ray
- If Z-signal acceptable
  - γ-ray is detected
  - position determined by X and Y signals
- 20% energy window
  - 30% scattered photons



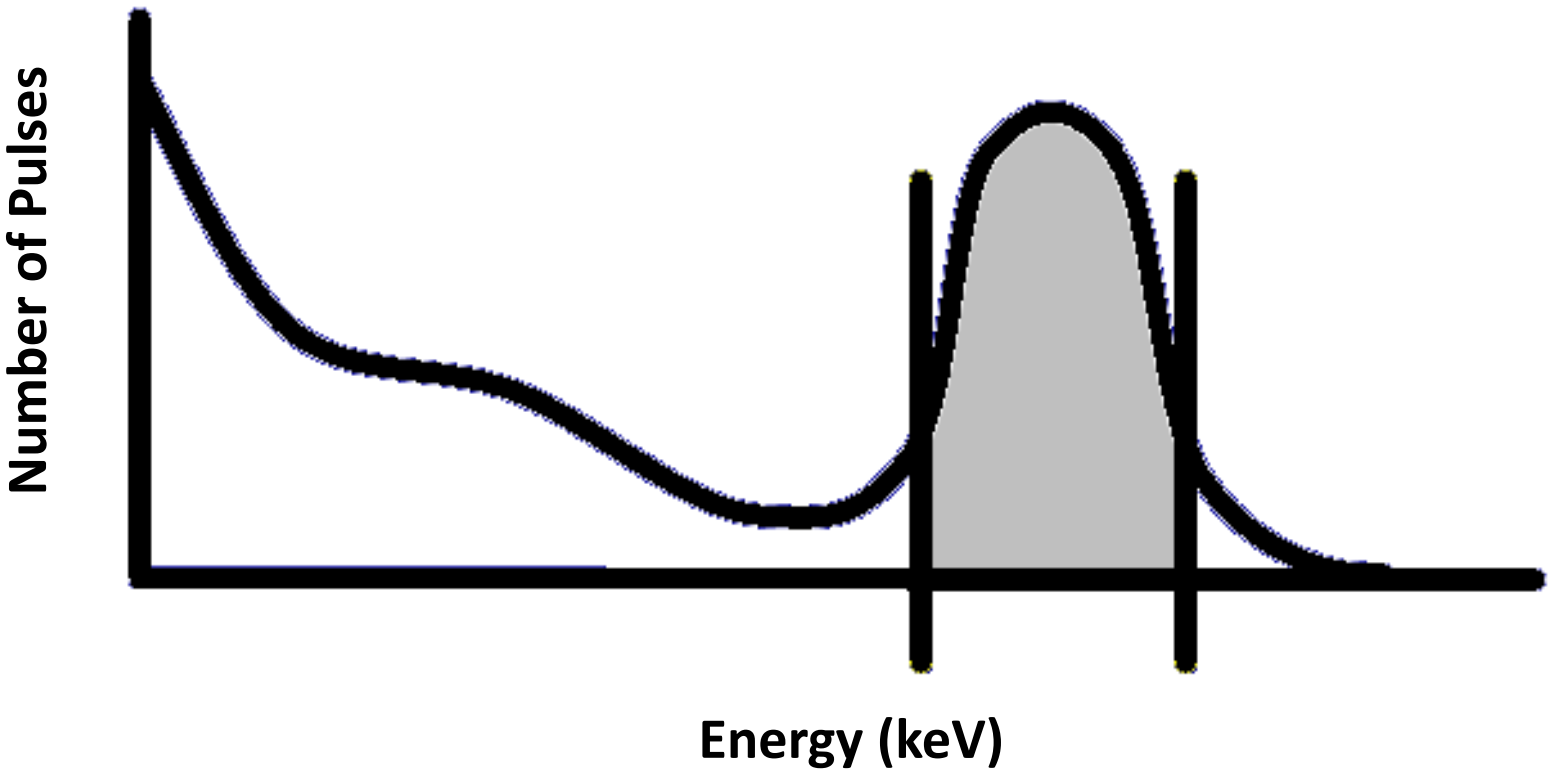
THEORETICAL $^{99}Tc^{m}$ SPECTRUM



Actual $^{99}Tc^{m}$ SPECTRUM



ENERGY WINDOWS



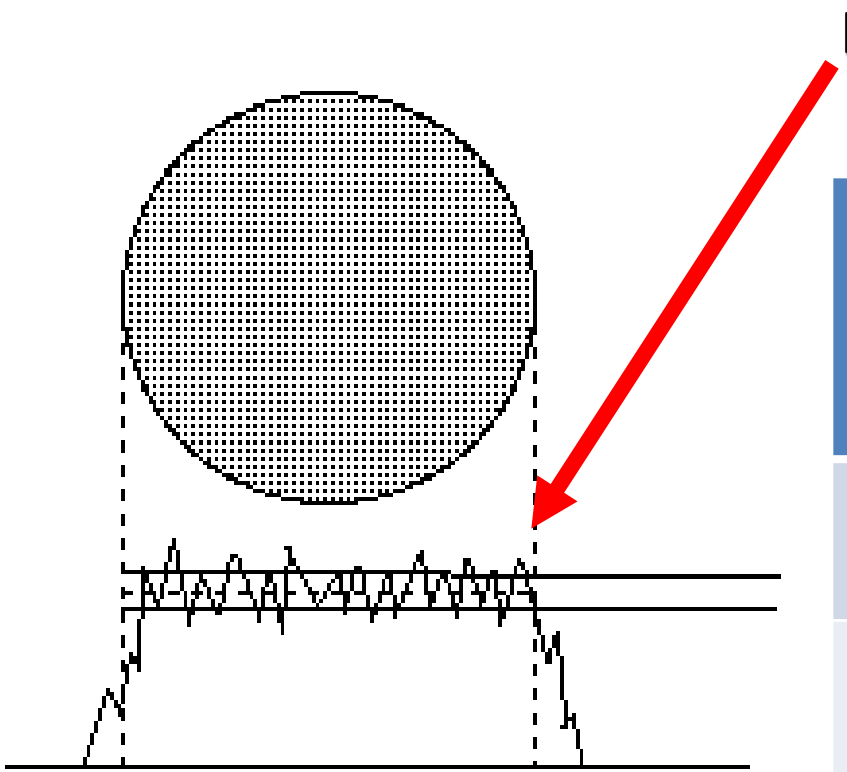
Physical Measures of Image Quality

- Noise
  - Statistical uncertainty in the number of counts recorded
- Contrast
  - Difference in intensity in parts of the image corresponding to different concentrations of activity within the patient

Image Quality: Noise

- An imaging system is subject to statistical variations at all of its stages
  - Radioactive decay
  - Number of scintillation photons in crystal
  - Number of photoelectrons emitted from PMT photocathode / dynodes

Image Quality: Noise

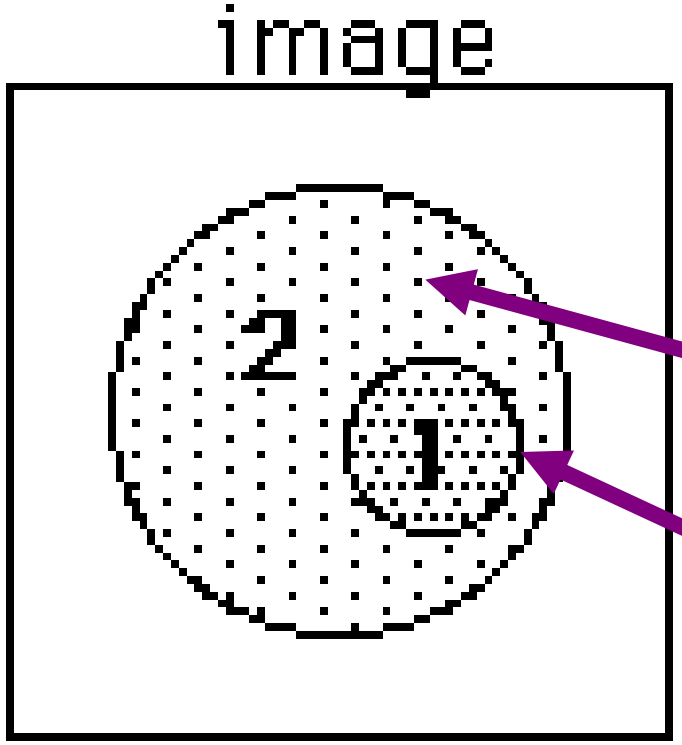


Noise = √(Average Pixel Count)

Mean Pixel Count	Absolute Noise	Noise (%)
100	10	10
10,000	100	1

Increased Counts → Reduced Noise

Image Quality: Contrast



$$Contrast = \frac{(R_1 - R_2)}{R_2}$$

R_2: Background

R_1: Lesion

Image Quality: Recorded Counts

- Administered activity
  - diagnostic reference levels – ARSAC
- Uptake of tracer
  - radiopharmaceutical properties
- Attenuation / Scatter
  - patient size
- Acquisition time
  - typical imaging times: 3-60 minutes

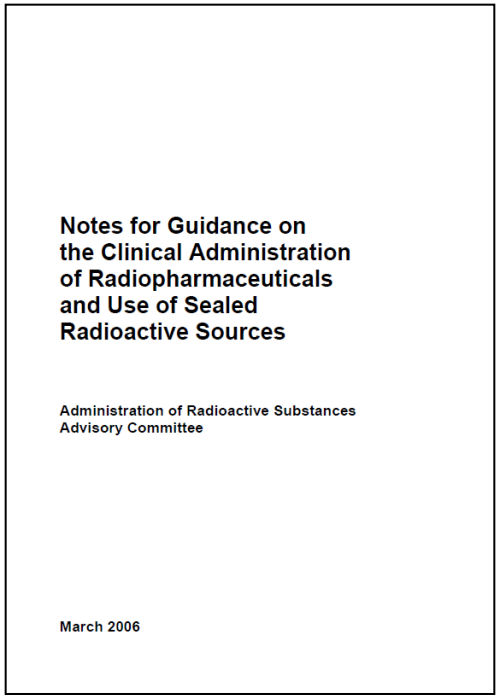


Image Quality: Patient Motion

- Long imaging times
  - limit to time patient can remain still
- Physiological motion
  - cardiac gating
  - respiratory gating

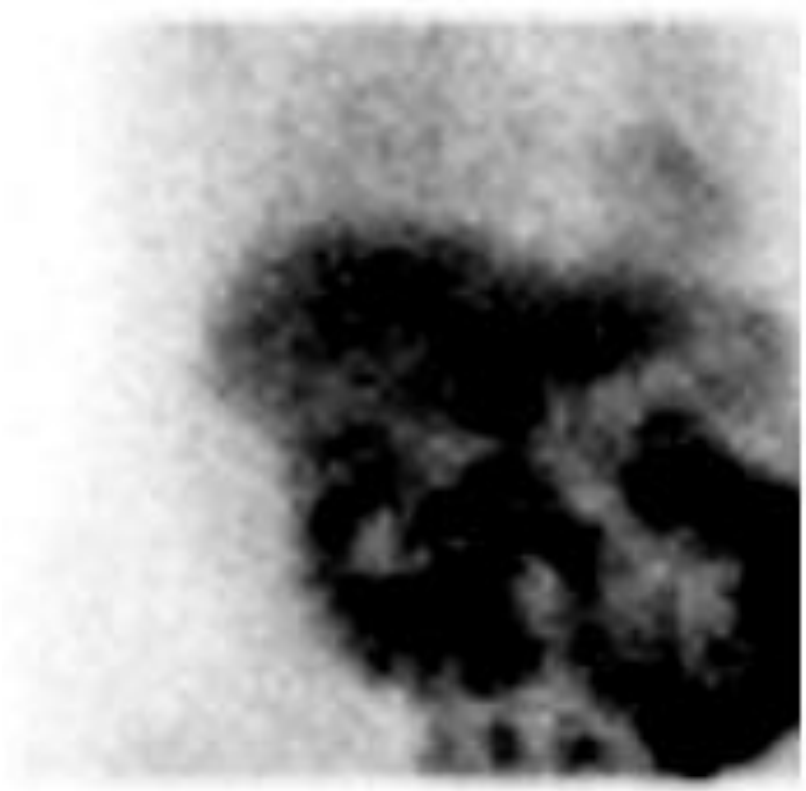


Image Acquisition Techniques

- Planar Imaging
  - Static
  - Dynamic
  - Multiple Gated (MUGA)
  - Whole Body
- Tomographic Imaging
  - Single Photon Emission Tomography (SPECT)
  - Positron Emission Tomography (PET)

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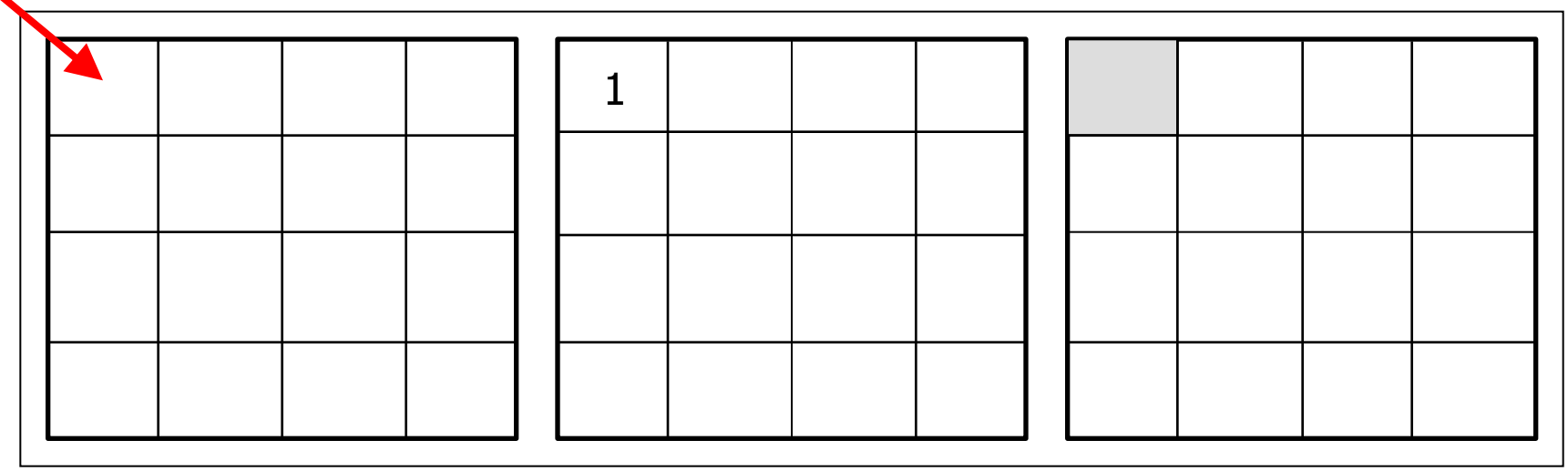
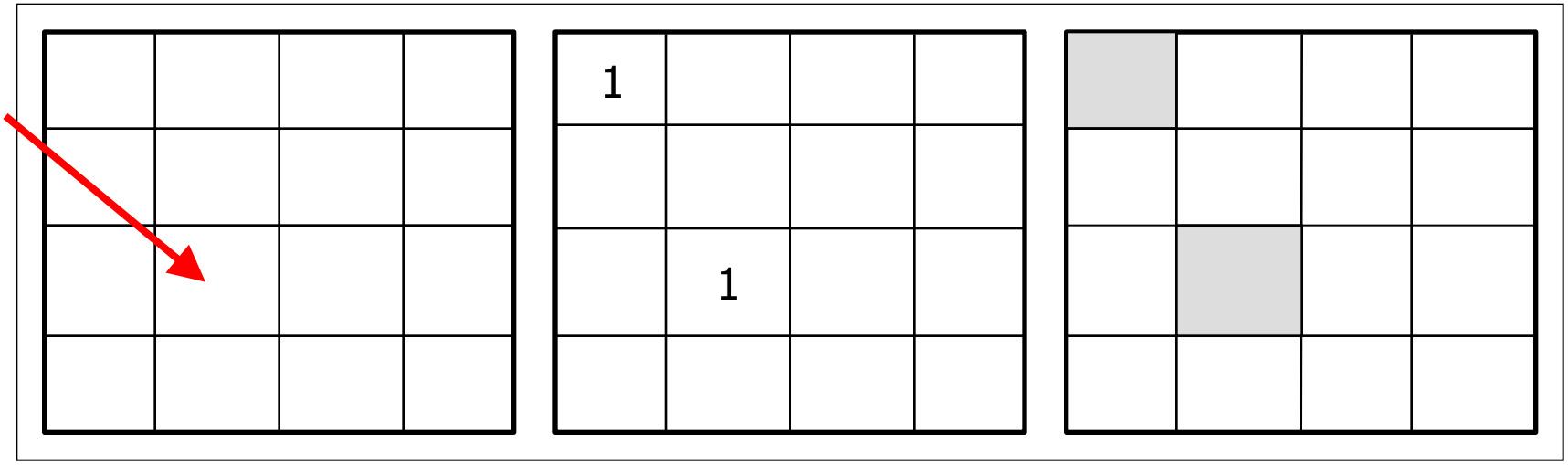
Static Imaging (Planar)



- Camera FOV divided into regular matrix of pixels
- Each pixel stores number of gamma rays detected at corresponding location on detector
- Typical matrix sizes: 256^2, 128^2, 64^2

Static Imaging (Planar)



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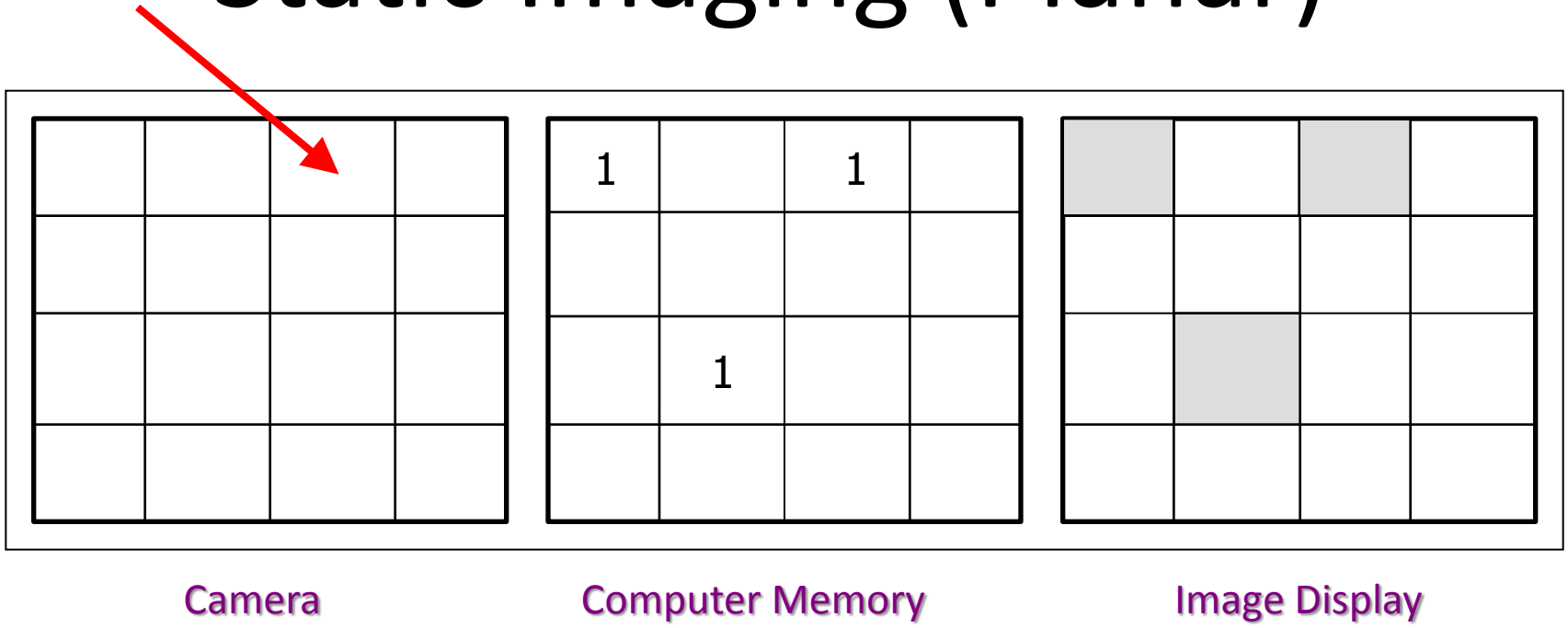

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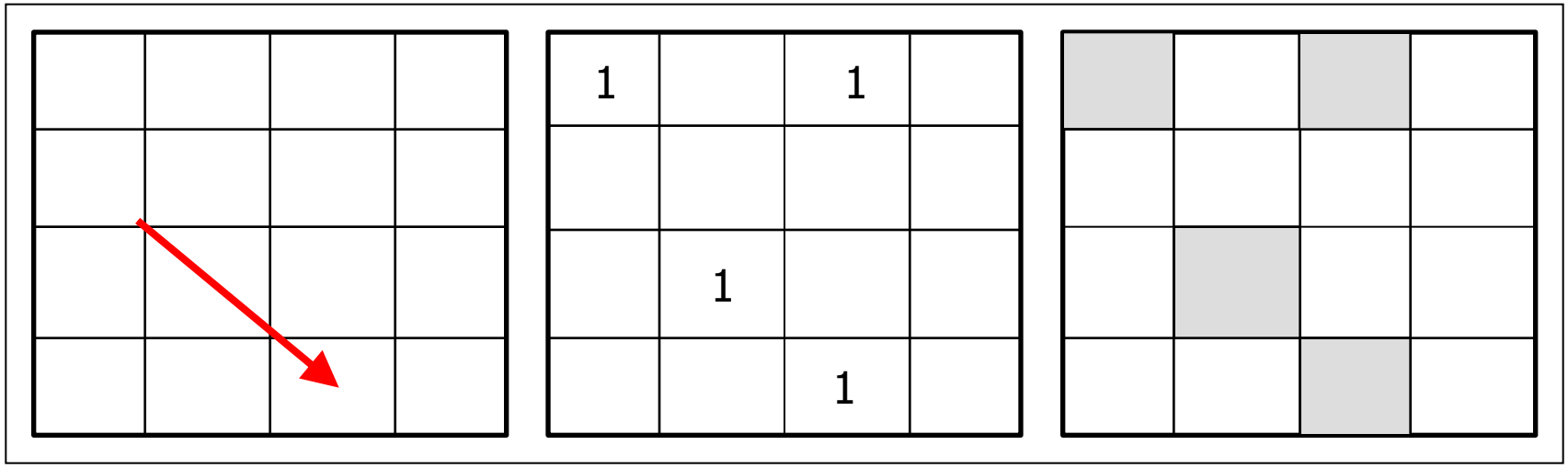

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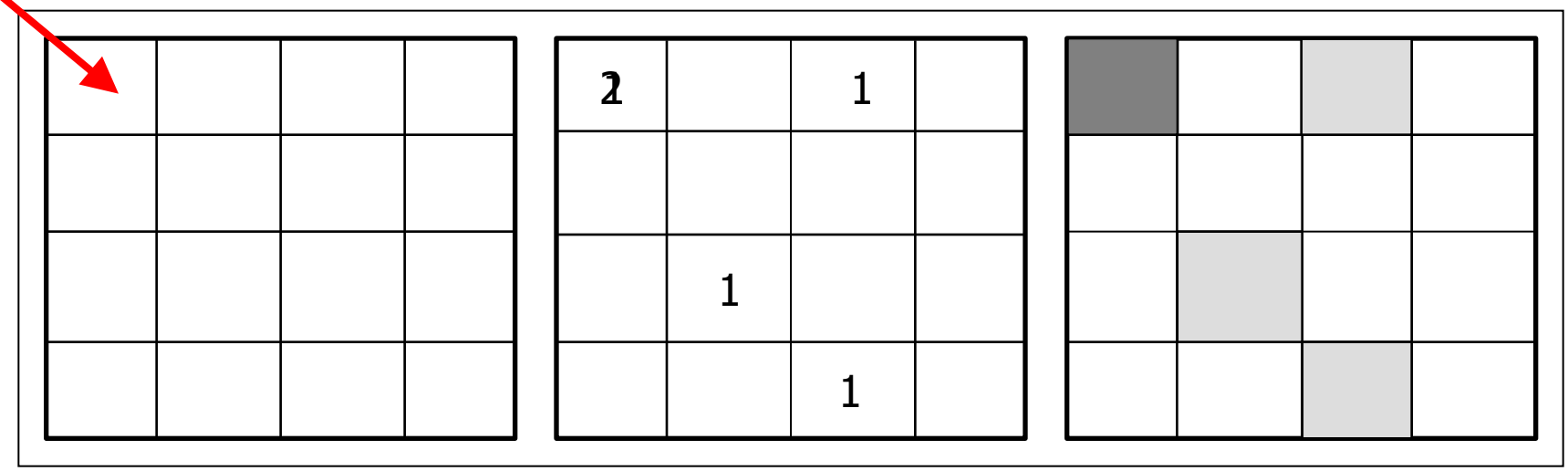

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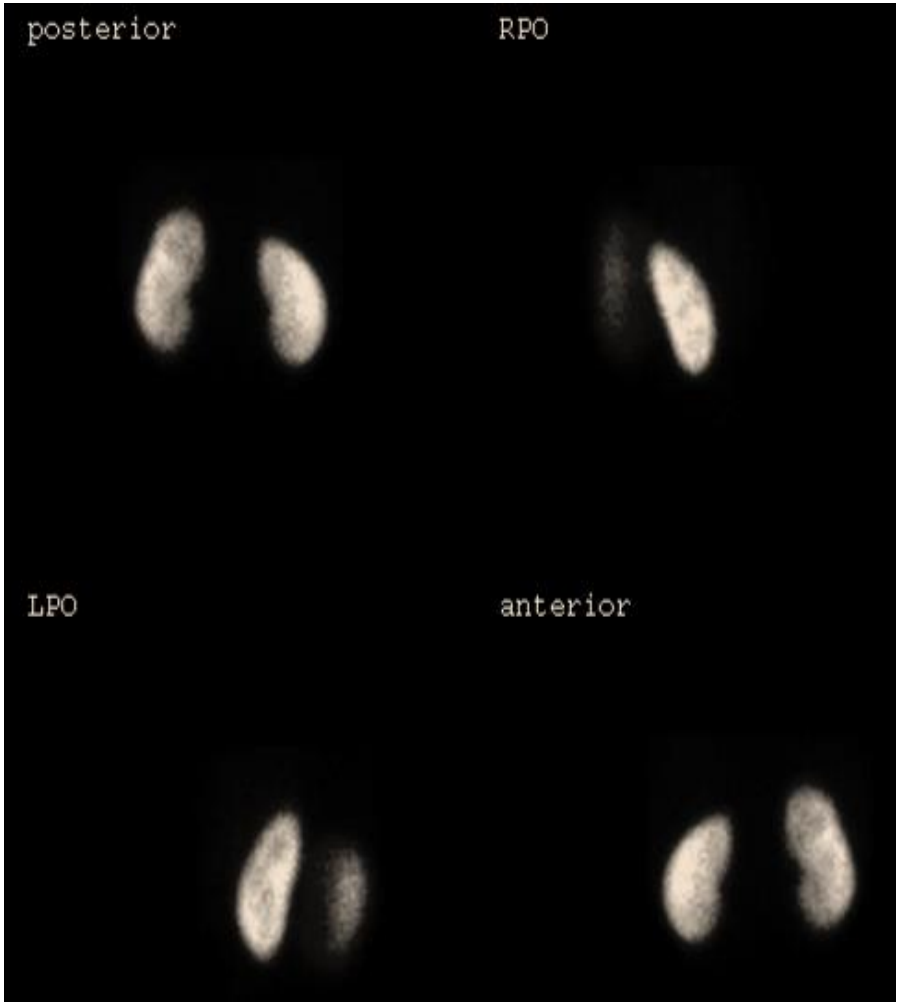
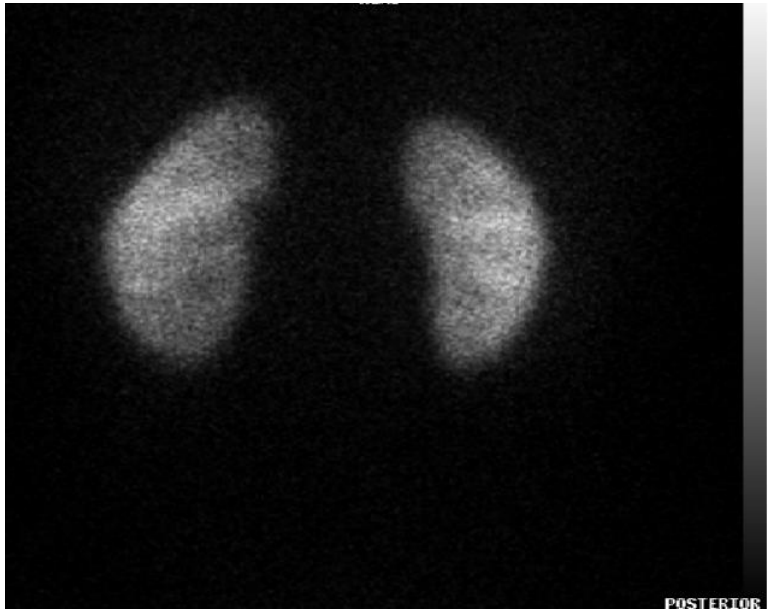
DMSA Renal Imaging

- Radiopharmaceutical
  - $^{99}Tc^{m}$-DMSA
- Imaged at 3-4 hours
- Effective dose
  - 0.7 mSv
- Investigates
  - renal scarring
  - non-functioning tissue
  - divided renal function
- Useful post UTIs



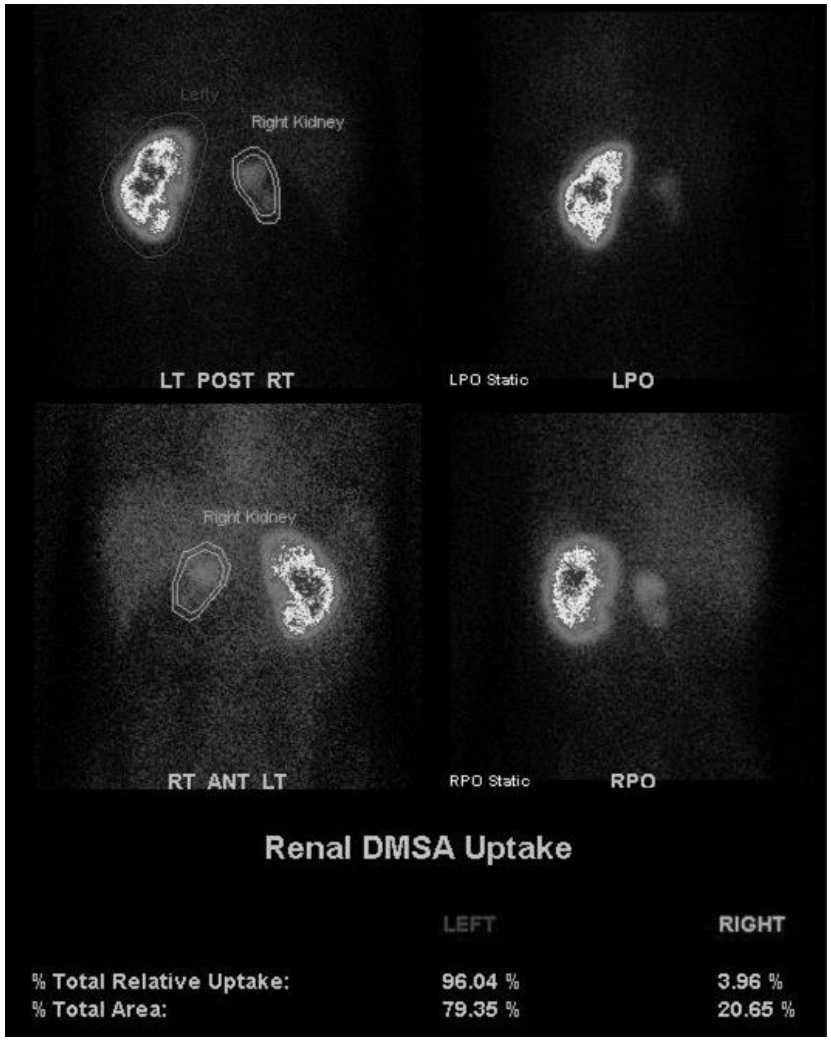
Case 1 – Normal Scan

- Divided function
  - Normal range: 45 - 55%
- Normal scan
  - bilateral smooth renal outlines
  - equal sized kidneys



Case 2 – Renal Scarring

- More sensitive than
  - ultrasound
- Focal scarring in
  - left kidney
- Atrophic
  - right kidney



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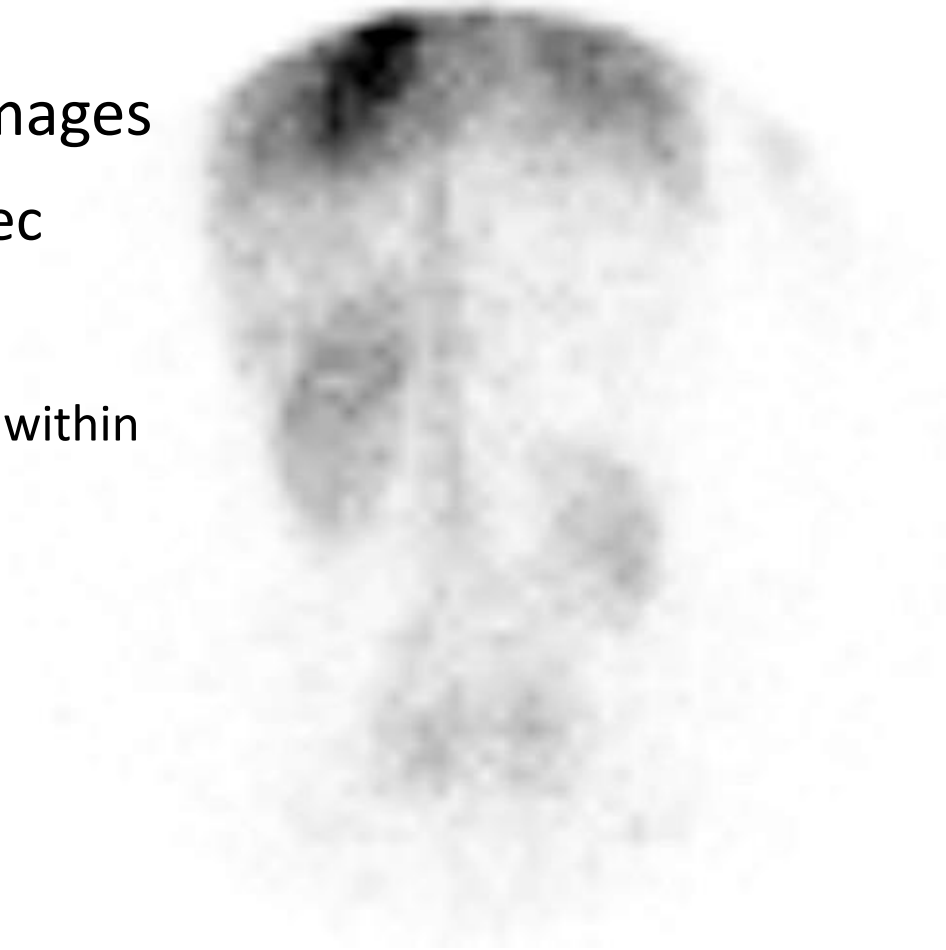
Dynamic Imaging

- Series of sequential static images
  - e.g. 90 frames each of 20sec
- Images
  - changing distribution of activity within the patient
- Examples include:
  - gastric emptying studies
  - lymphoscintigraphy
  - diuretic renography

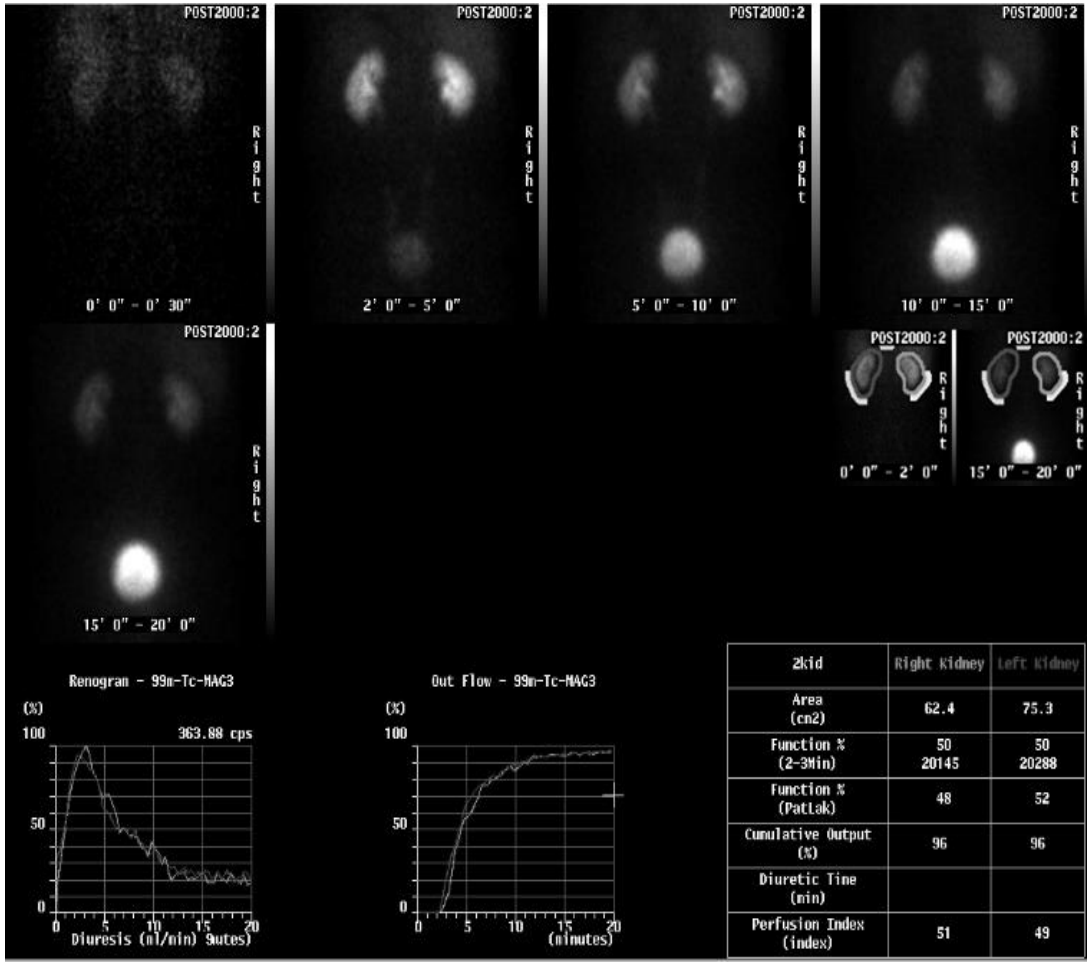


Diuretic Renography

- Radiopharmaceutical
  - $^{99}Tc^{m}$-MAG3
- Imaged immediately
- Effective dose
  - 0.7 mSv
- Investigates
  - suspected obstruction
  - dilated system
  - pre-transplant donor assessment



Case 1: Normal Study



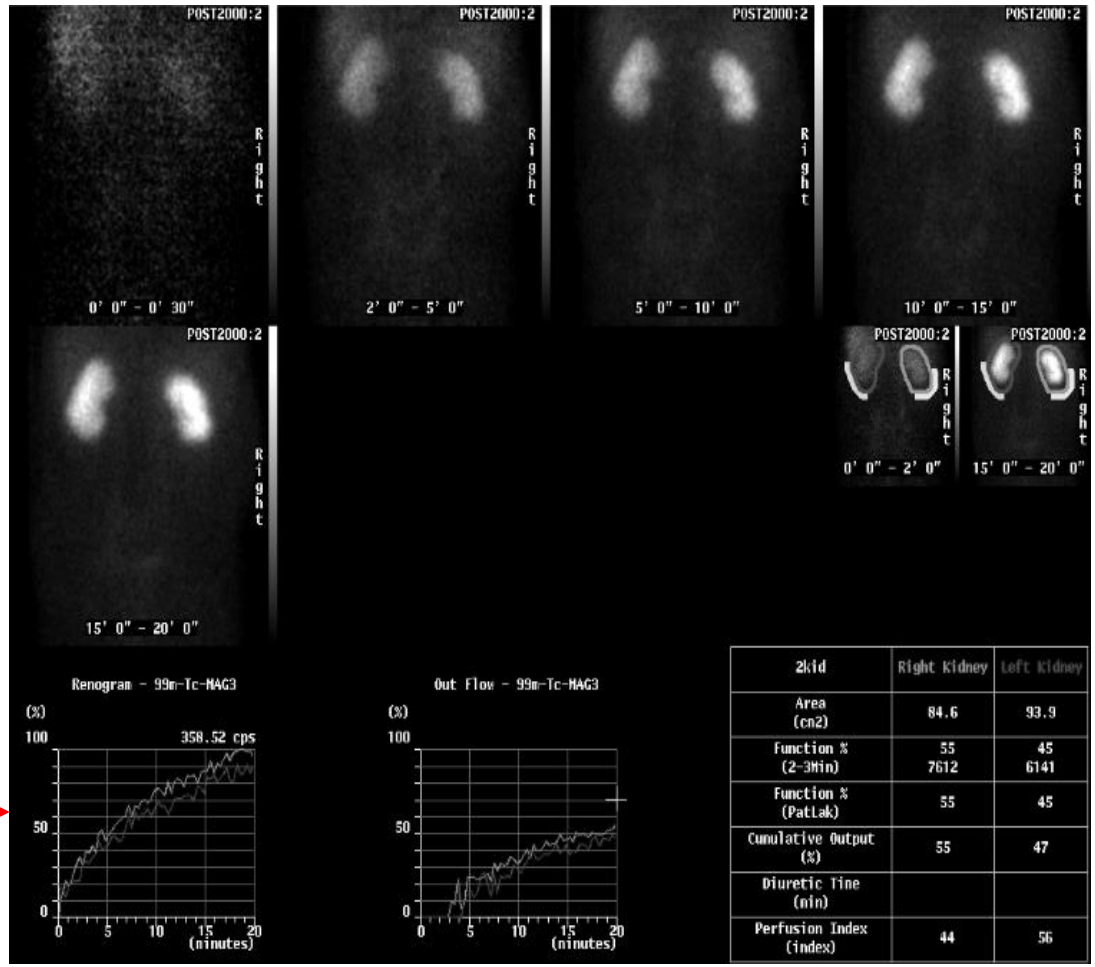
Regions of Interest (ROI)

Curves showing changing renal activity over time

Split Renal Function

Case 2: Obstructed System

Rising time-activity curves on both kidneys



2kid	Right Kidney	Left Kidney
Area (cn2)	84.6	93.9
Function % (2-3Min)	55 7612	45 6141
Function % (PatLak)	55	45
Cumulative Output (%)	55	47
Diuretic Time (min)		
Perfusion Index (index)	44	56

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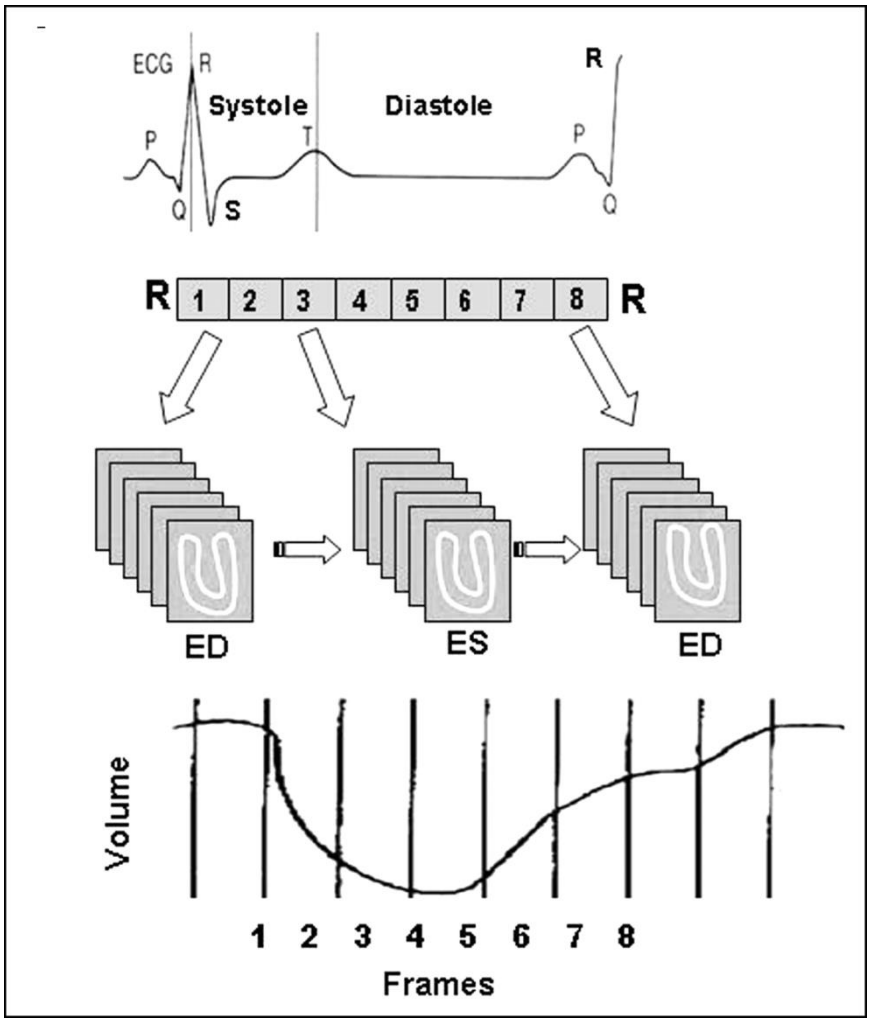
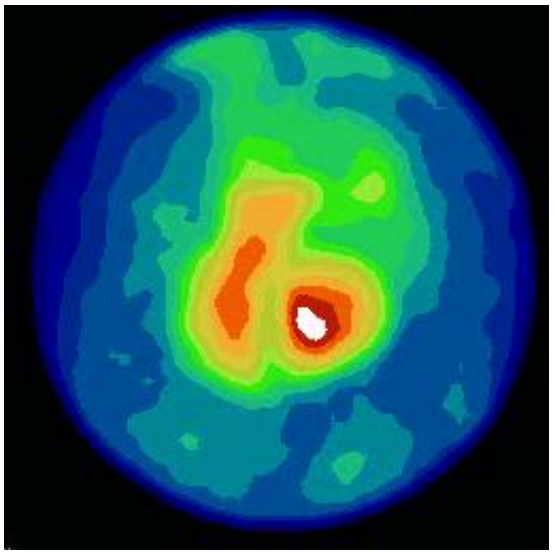
Multiple Gated Imaging (MUGA)





- Multiple images/frames acquired over set time period
- Acquired over many cycles

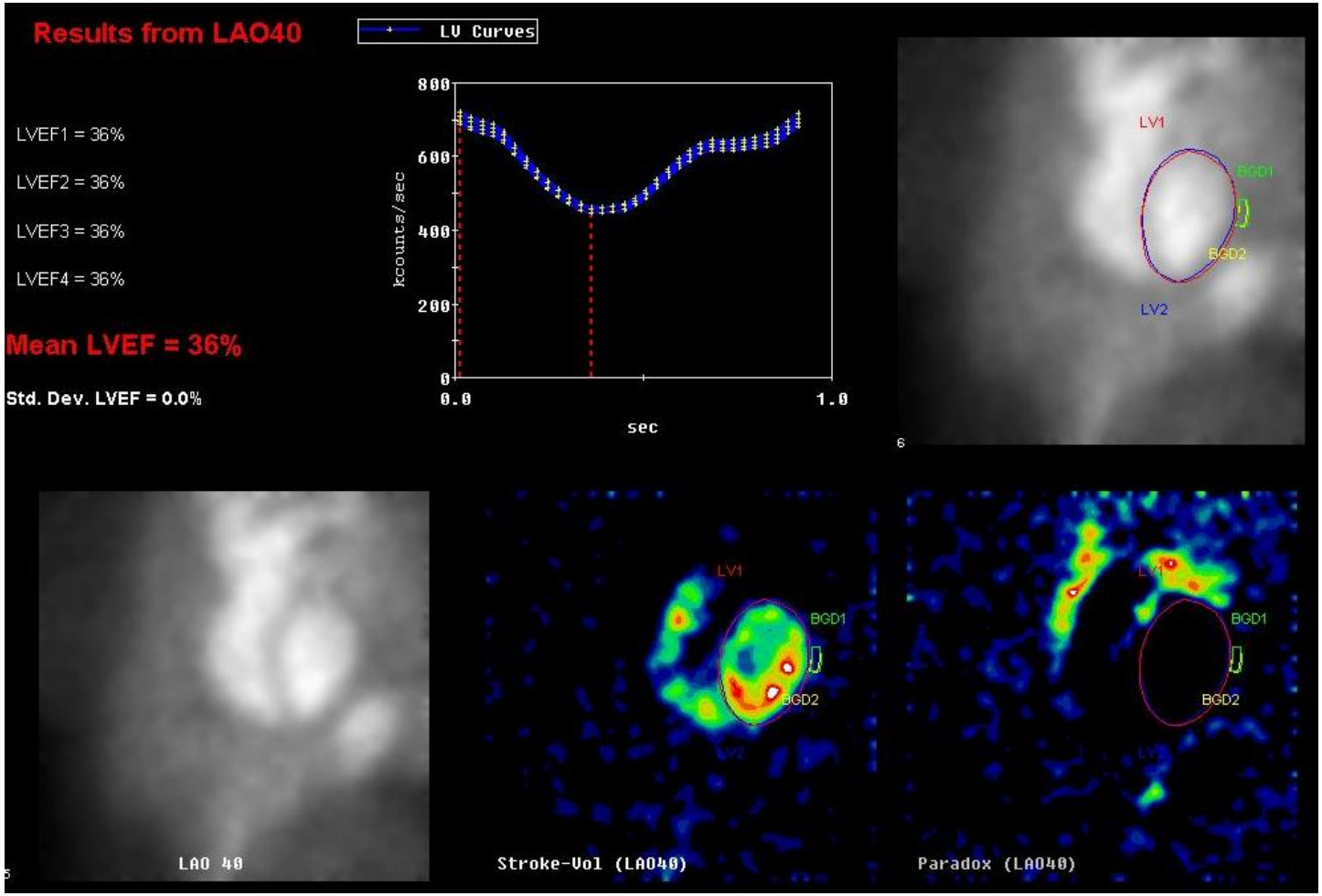
Radionuclide Ventriculography

- Radiopharmaceutical
  - Tc-99m labelled red cells
- Imaged immediately
- Effective dose
  - 6 mSv
- Investigates
  - left ventricular function
  - regional wall motion



- Allows precise/repeatable measurement of LVEF
  - left venrtricular ejection fraction

Radionuclide Ventriculography



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Whole Body / Continuous Imaging

- A window (or ramp)
  - opens along the camera face
  - and then slowly scans down the body
- Ramps down as camera
  - reaches the preset end of the body
- Sensors on the camera
  - ensure detectors remain close to the patient



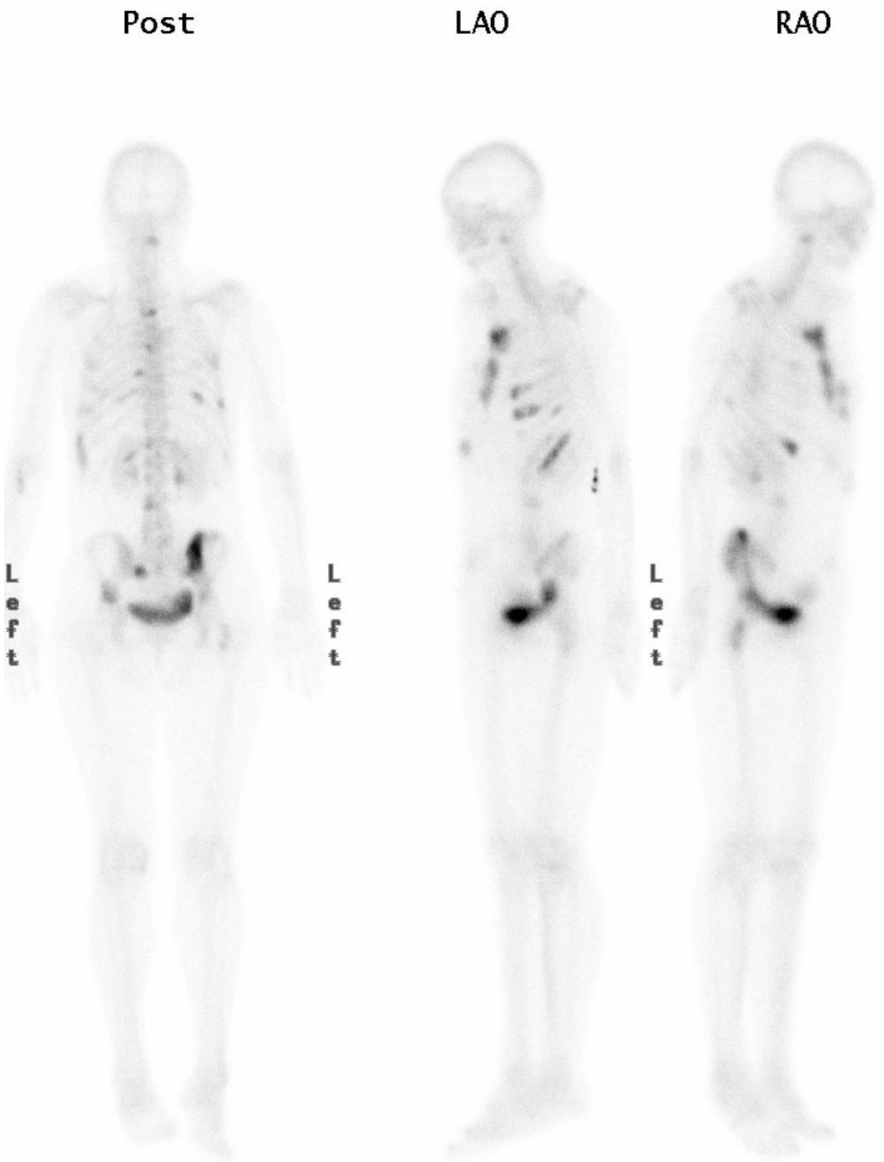
Case 1

- Radiopharmaceutical
  - $^{99}Tc^{m}$-HDP
- Imaged at 3-4hrs
  - High Bone/Soft tissue ratio
- Effective dose 3 mSv
- Symmetry
- Kidneys and bladder



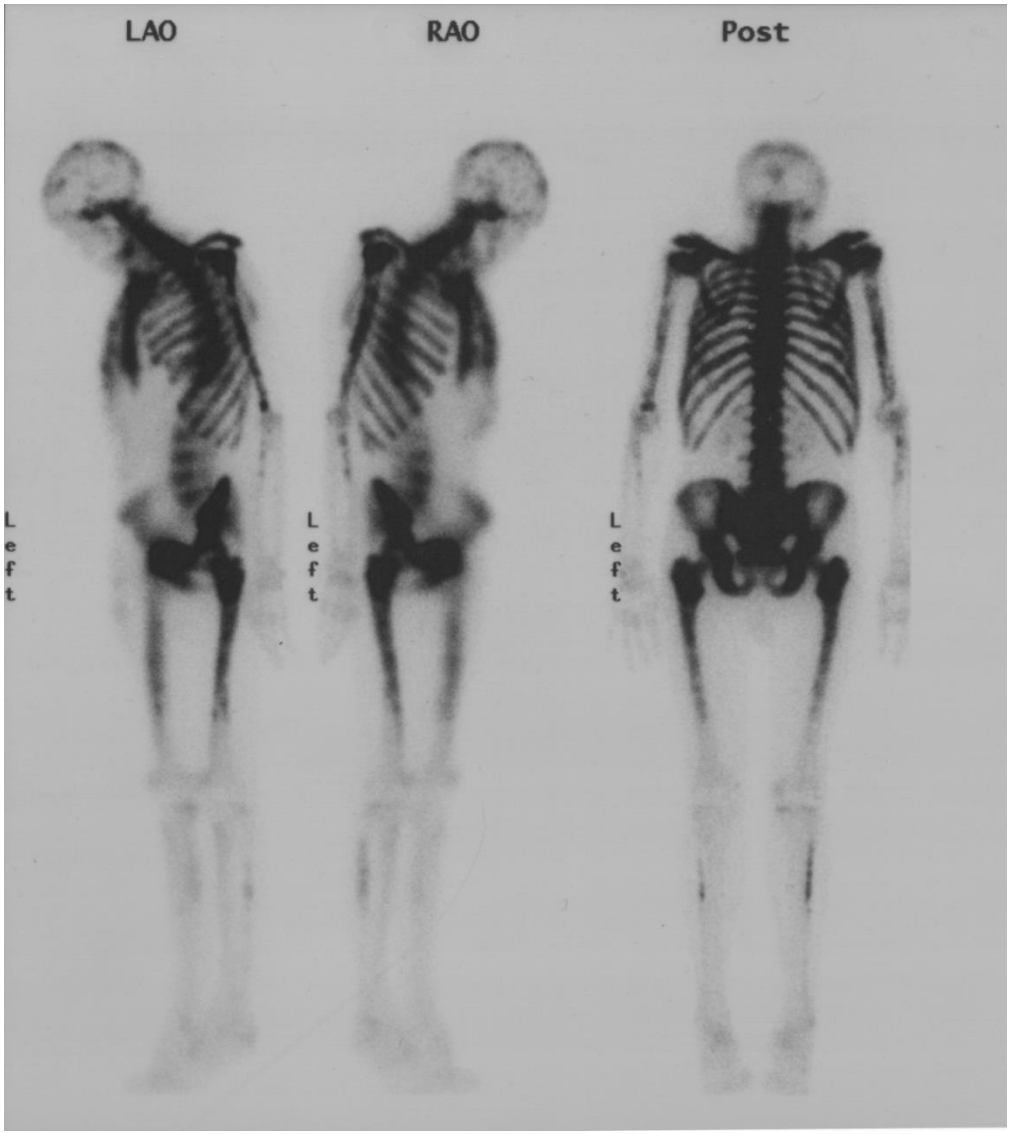
Case 2

- Focal uptake
  - throughout axial skeleton
- Osteo*blastic* metastases
  - breast and prostate
  - high sensitivity
- Osteo*lytic* metastases
  - Renal, breast, lung, myeloma
  - Reduced sensitivity

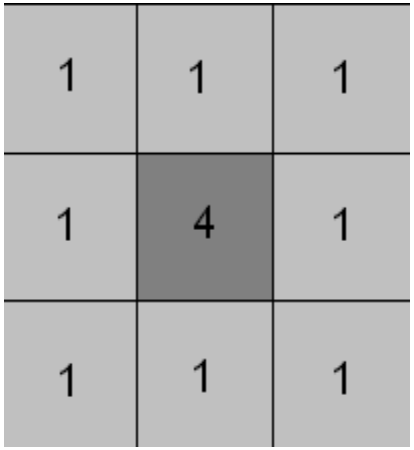


Case 3

- Superscan
- Non-visualisation of
  - kidneys
  - soft tissue
- Poor visualisation of
  - limb bones
- Diffusely increased
  - Skeletal uptake
- Causes
  - widespread metastases

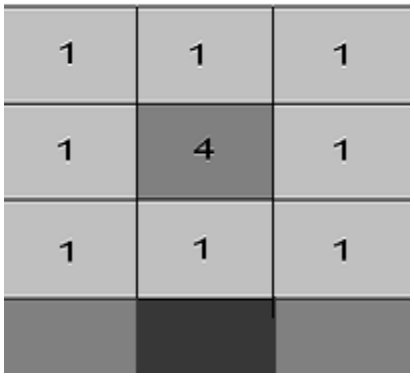


Pitfalls of Planar Imaging



- Planar imaging
  - 2D representation of 3D distribution of activity
  - No depth information
  - Structures at different depths are superimposed
    - Loss of contrast

Pitfalls of Planar Imaging



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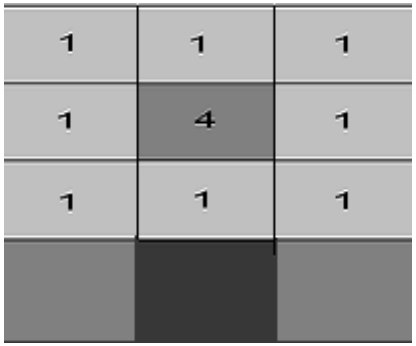

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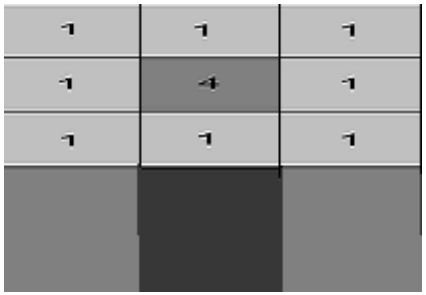

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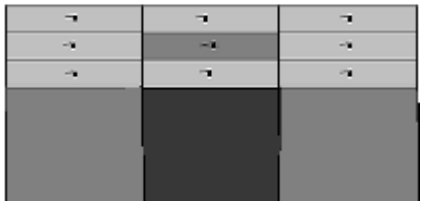

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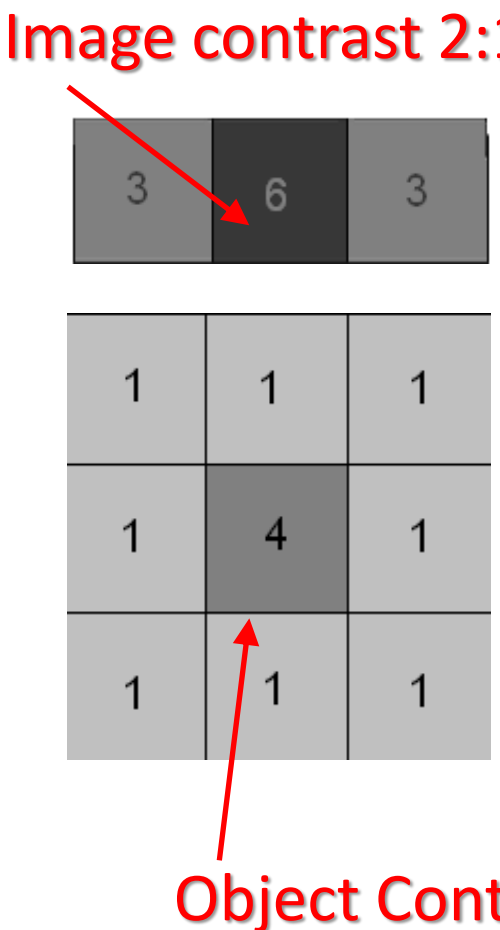

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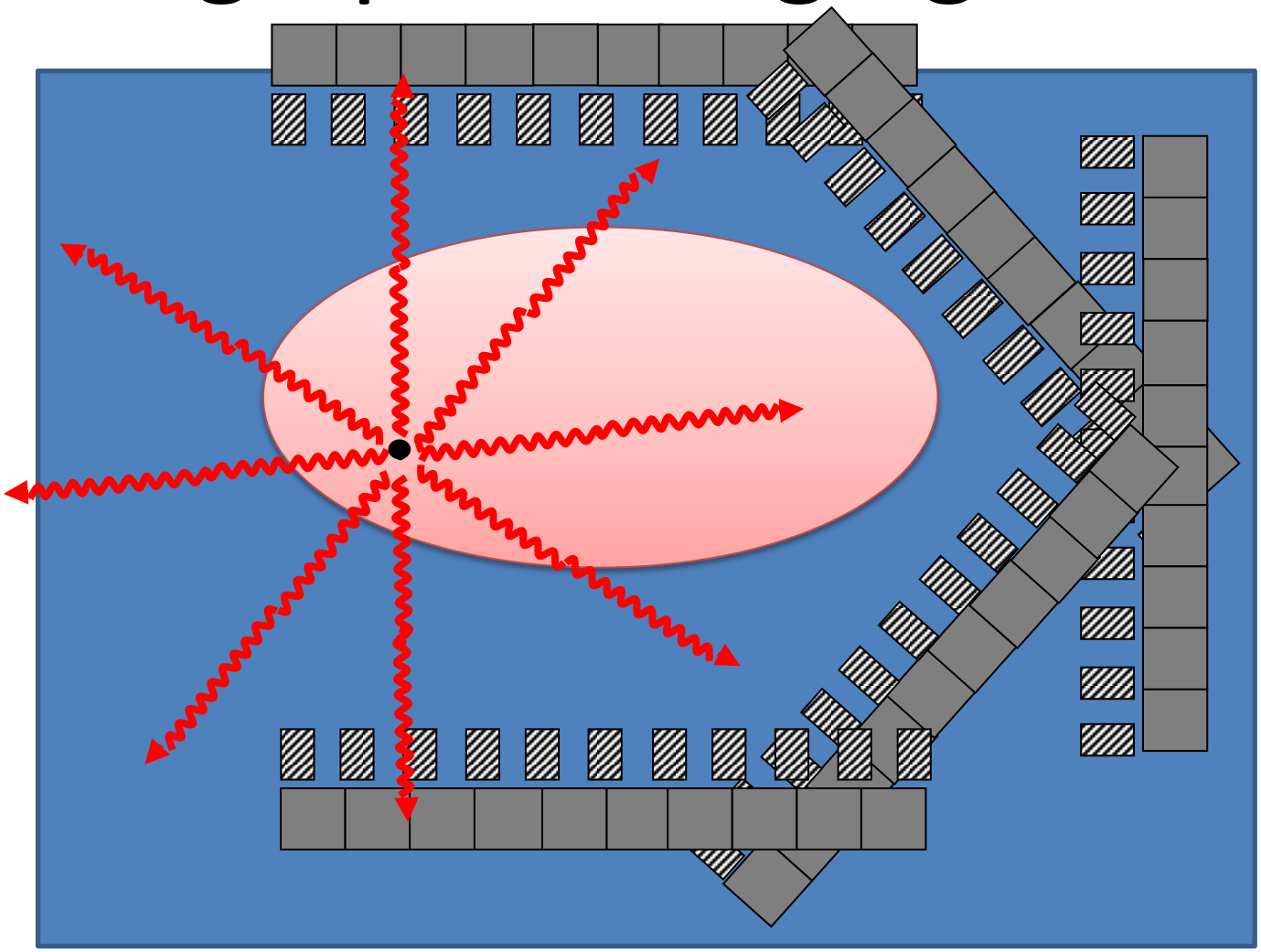
Tomographic Imaging - SPECT

γ/X-rays → SPECT

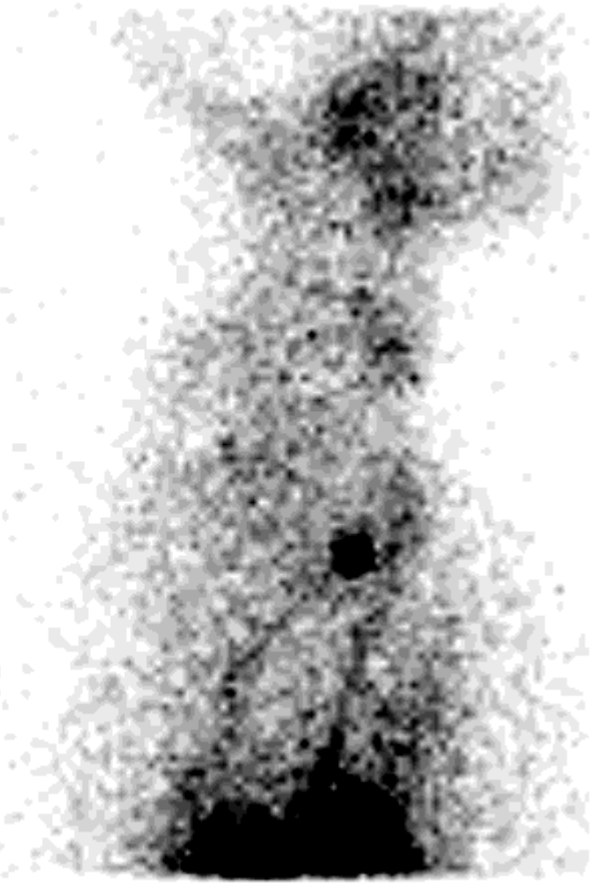
Isotope	Half-life (hr)	Energy (keV)
$^{99}Tc^{m}$	6.0	140
^{111}In	67.3	171 & 245
^{123}I	13.2	159
^{201}Tl	73.0	69-83

Tomographic Imaging - SPECT



Tomographic Imaging - SPECT

- Multiple planar images (projections)
  - acquired at several angles around the patient
- Projections processed
  - Filtered Backprojection
  - Iterative Reconstruction



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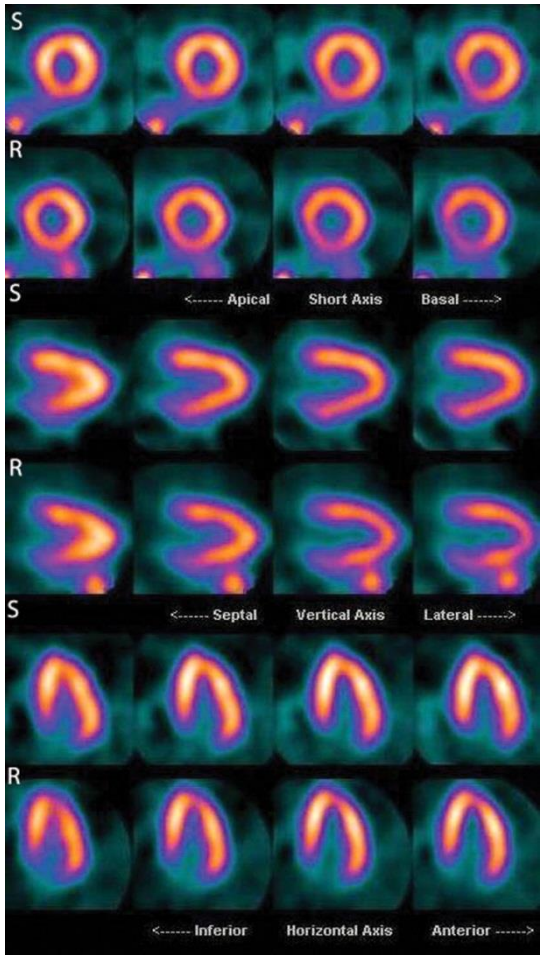
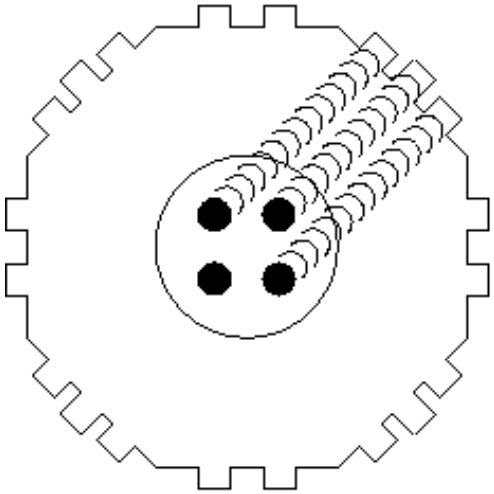
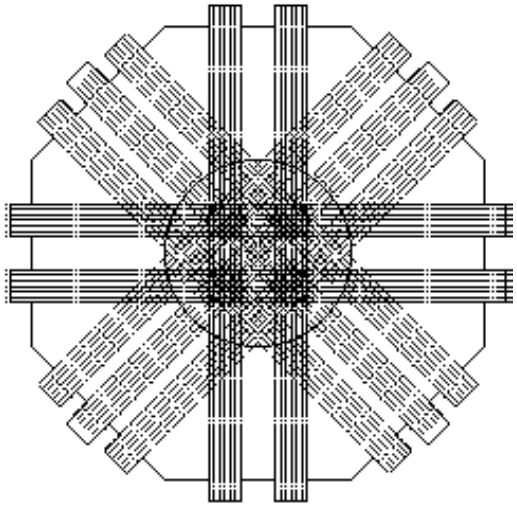


Filtered Backprojection

- Simple Backprojection
  - mathematical method to reconstruct a tomographic image

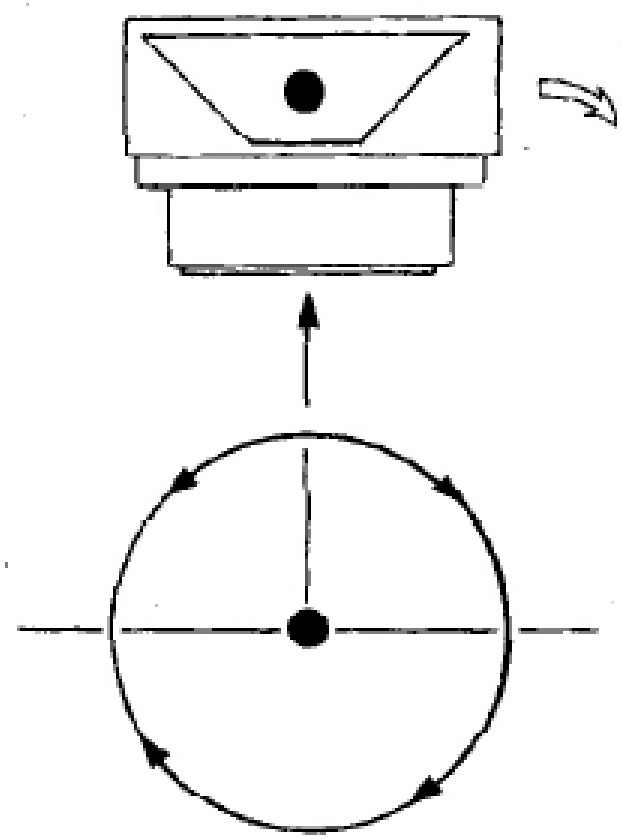


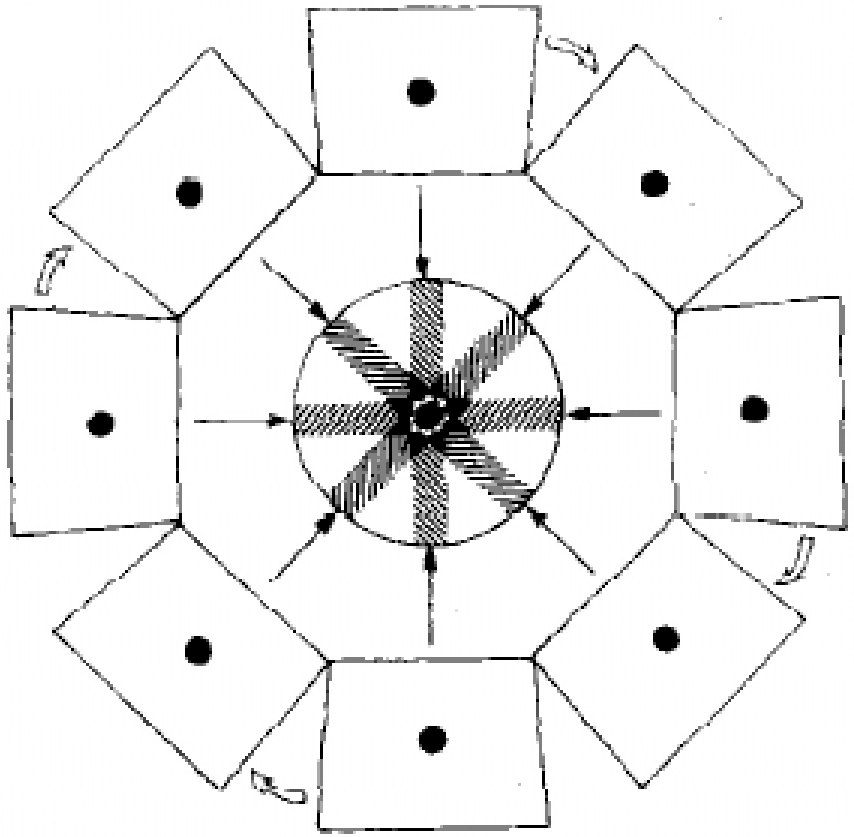
Projection



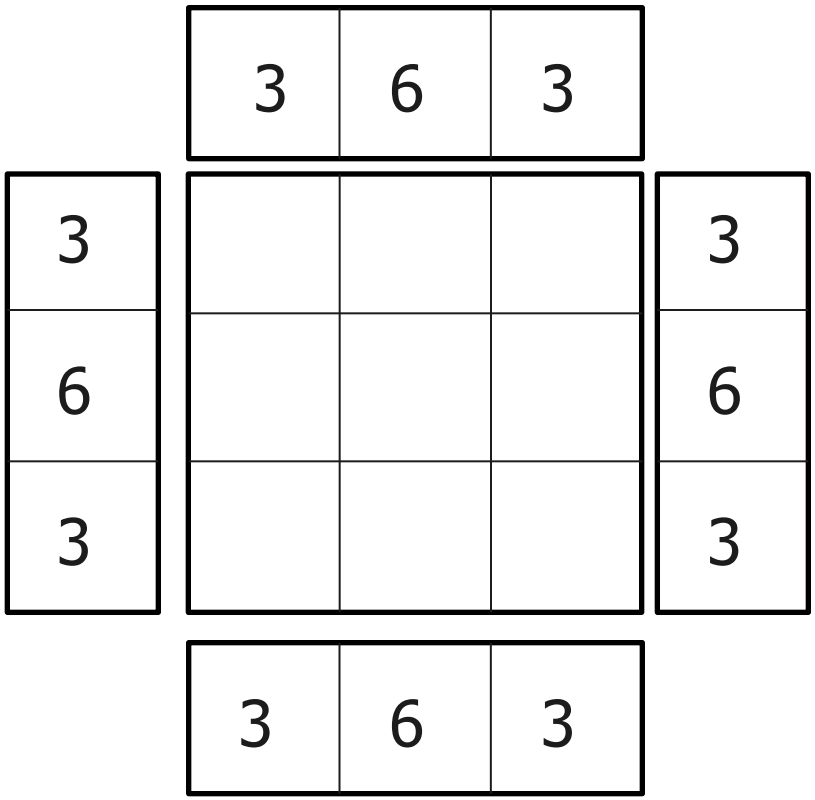
Backprojection

Backprojection





Backprojection



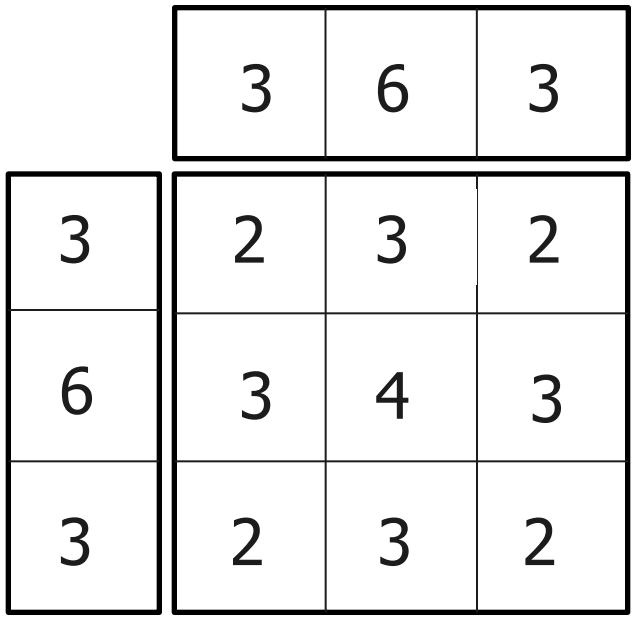
- Backproject each planar image onto three dimensional image matrix

Backprojection

3	6	3
1	2	1
1	2	1
1	2	1

- Backproject each planar image onto three dimensional image matrix

Backprojection



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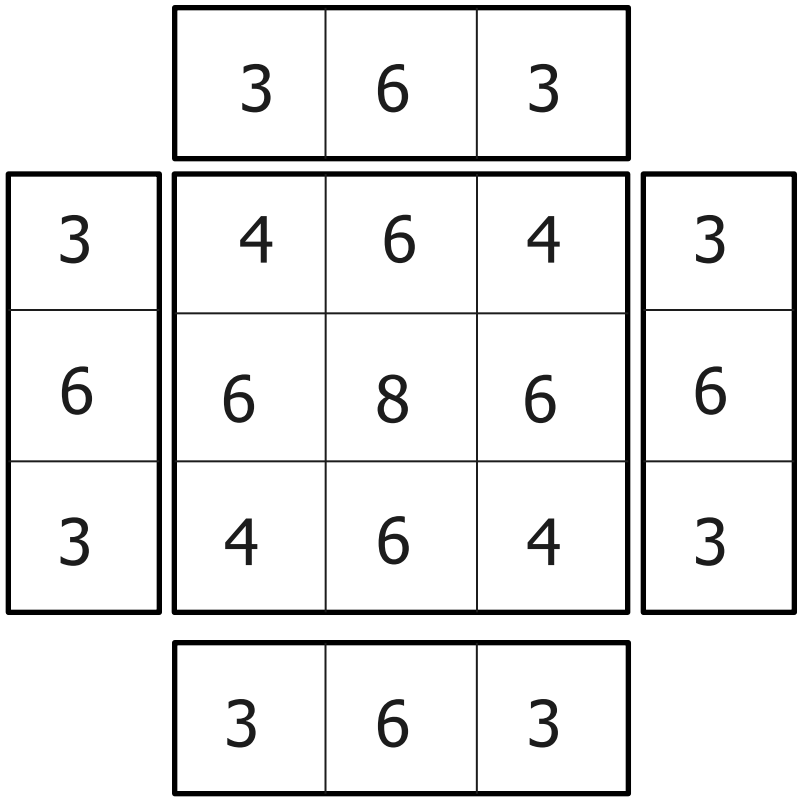

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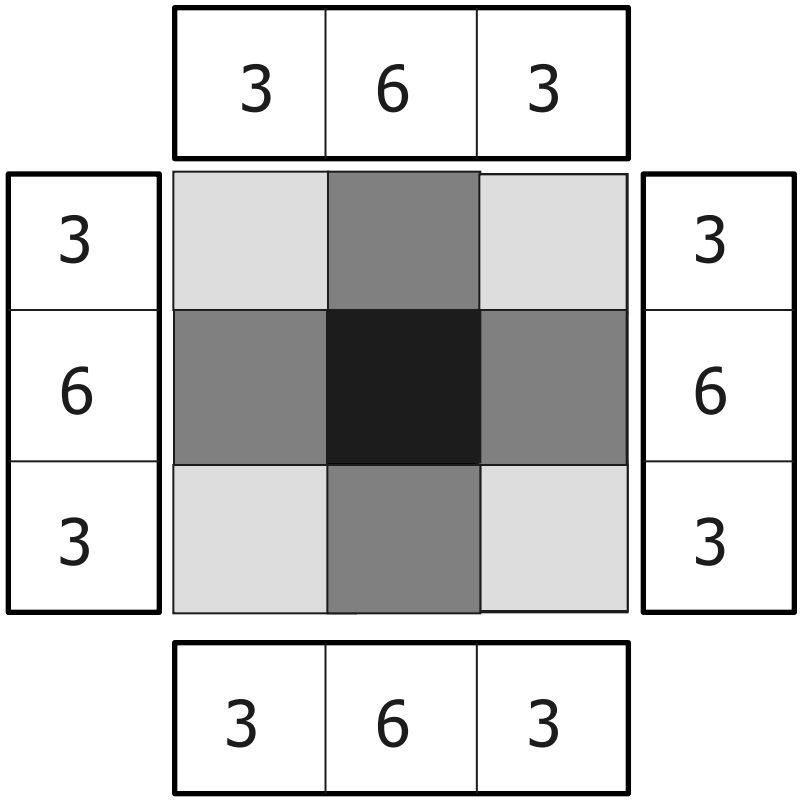

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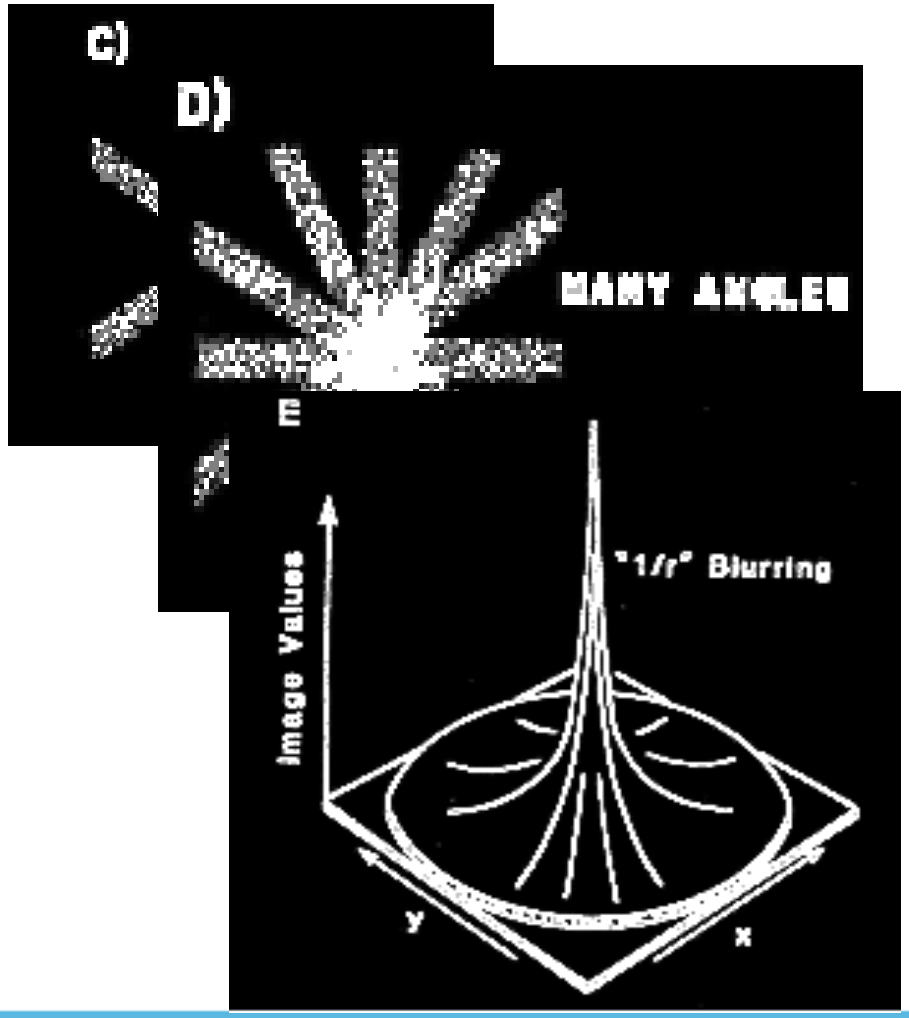
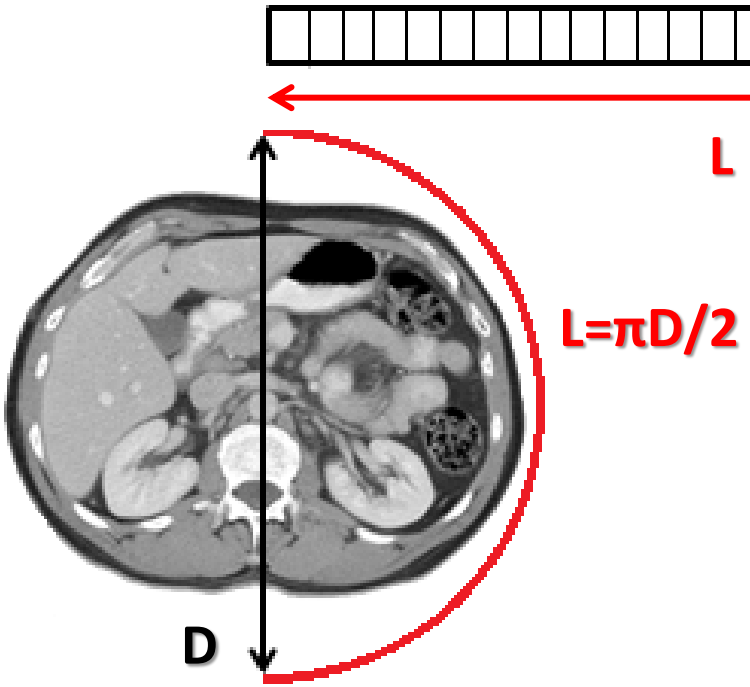
Backprojection



- More views – better reconstruction
- Blurring, even with infinite number of views

Sampling Theorem

- Angular sampling interval should be
  - approximately same as linear sampling distance



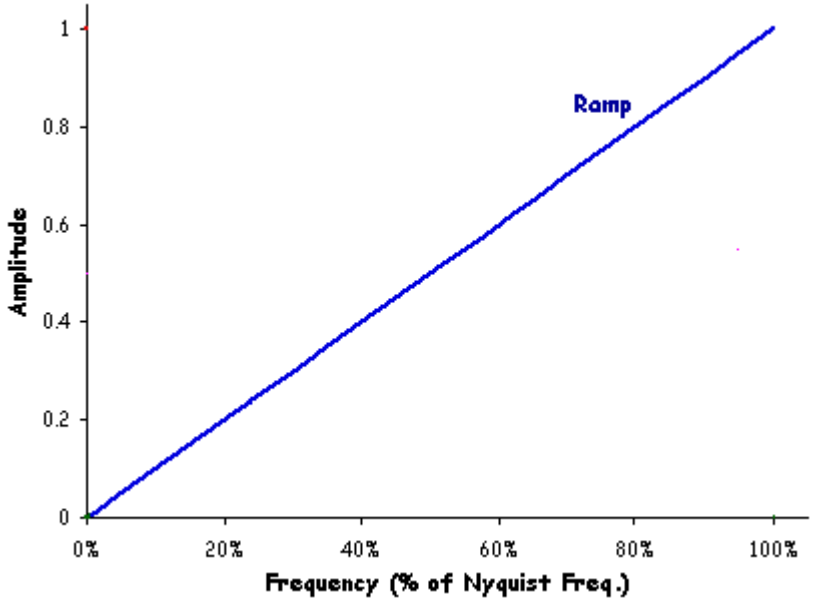
Linear sampling distance is pixel size, Δr

$N_{views} > L/\Delta r$

$N_{views} > \pi D/2\Delta r$

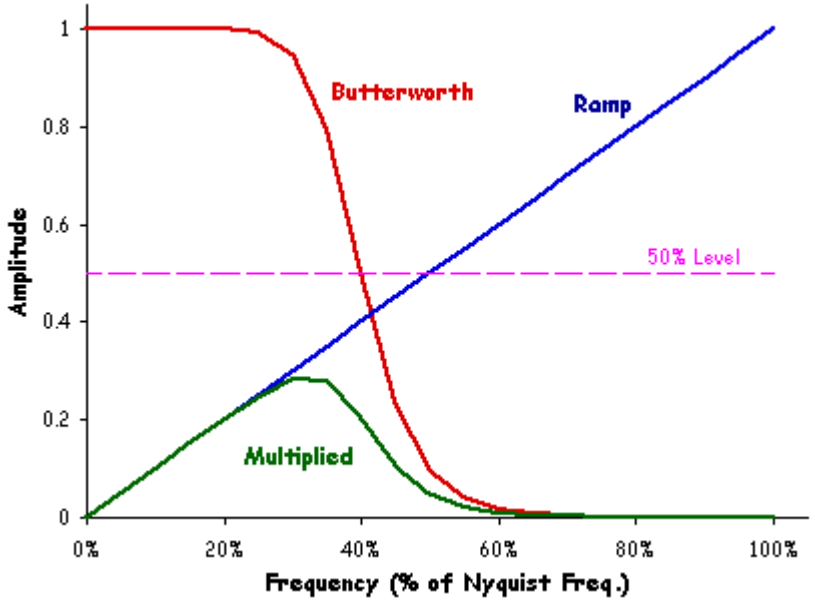
Filtered Backprojection

- Utilises a RAMP filter
  - Used to supress blurring
  - Used for all routine tomographic reconstructions



Filtered Backprojection

- RAMP filter + User selected filter is used
  - goal is to create an image easier to “read”



Pitfalls of Filtered Back Projection

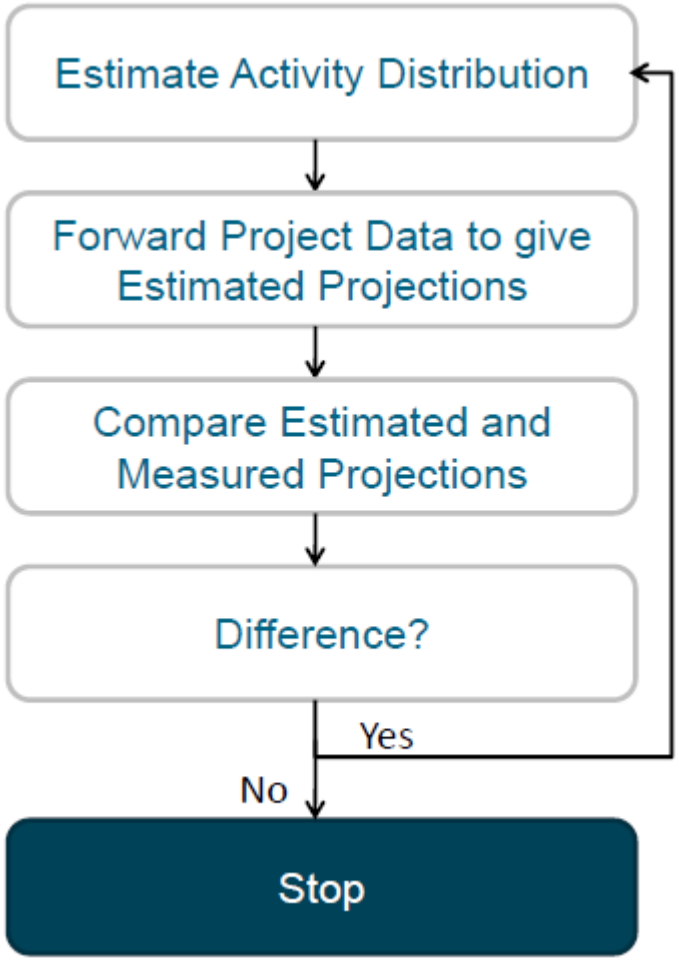
- Back projection is mathematically correct *but*
  - introduces noise and streaking artefacts
  - cannot apply attenuation correction techniques
- Filtered Back Projection can reduce noise and artefacts
  - but may degrade resolution

Iterative Reconstruction

- It is NOT a new technique
  - pre-dates filtered backprojection
- Computationally intensive
  - long reconstruction times
  - requires fast computers for reconstruction

What is Iterative Reconstruction?

- It is a method based on
  - successive “guesses” of the image
- Processing computer forms image
  - by refining expected projections in comparison to those recorded
- This form of iterative reconstruction is known as
  - “Maximum Likelihood Expectation Maximisation” (MLEM)



Iterative Reconstruction

- Filtering
  - post reconstruction – data may need smoothing
- Since iterative reconstruction makes estimates
  - it can be used to correct for image degradation due to
    - Attenuation
    - Scatter
    - Loss of image resolution

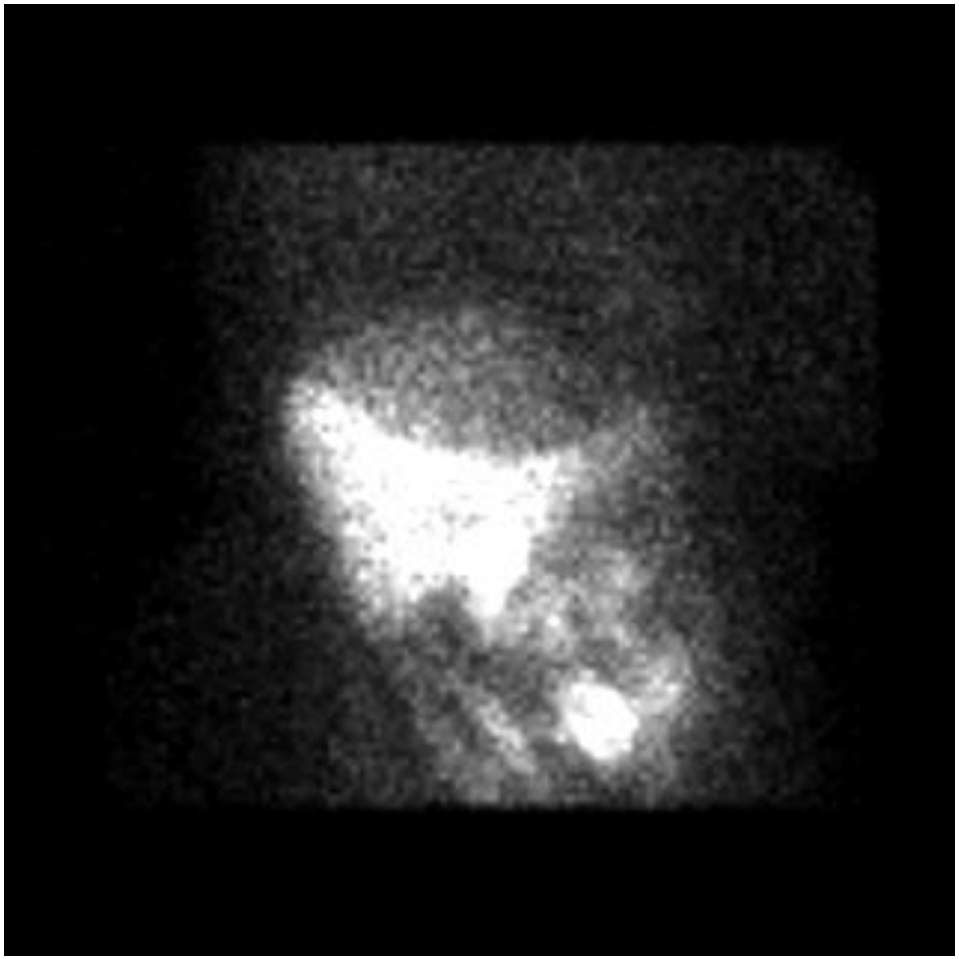
PHOTON ATTENUATION

- The removal of photons from a beam of photons
  - as it passes through matter
- Attenuation is caused by
  - absorption
  - scattering

} of photon beam



PHOTON ATTENUATION



ATTENUATION CORRECTION

- Aim
  - to correct for attenuation from tissue surrounding the organ of interest
- Attenuation correction
  - reduces the artifactual decrease in activity
  - image appearance represents actual activity in area of interest
  - leads to
    - improved quantitation
    - improved image quality

ATTENUATION CORRECTION

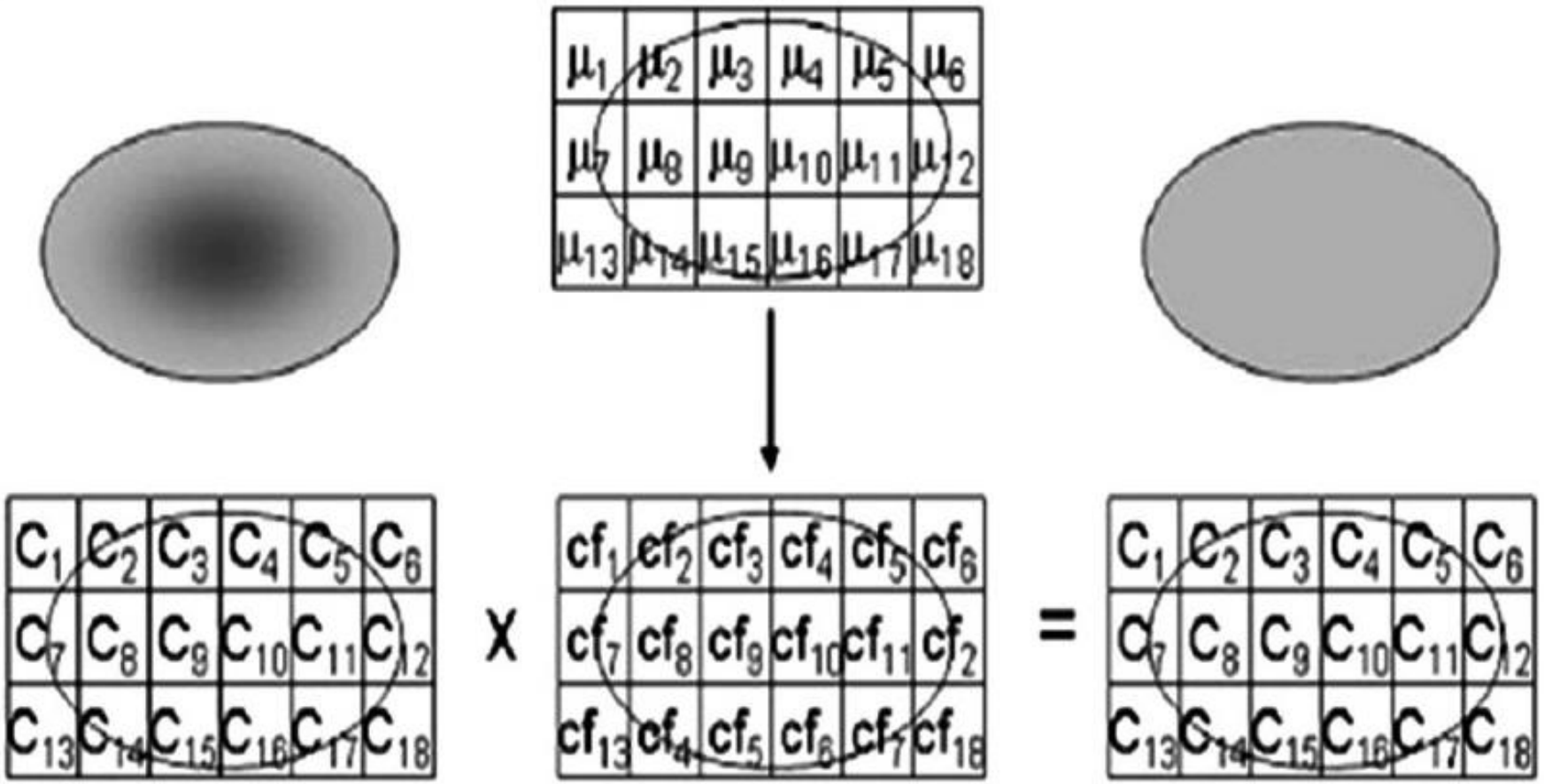
- Attenuation effects
  - can be interpreted correctly through references to normal images and training
- Correction
  - may improve the diagnostic accuracy of a study

CT-BASED METHOD

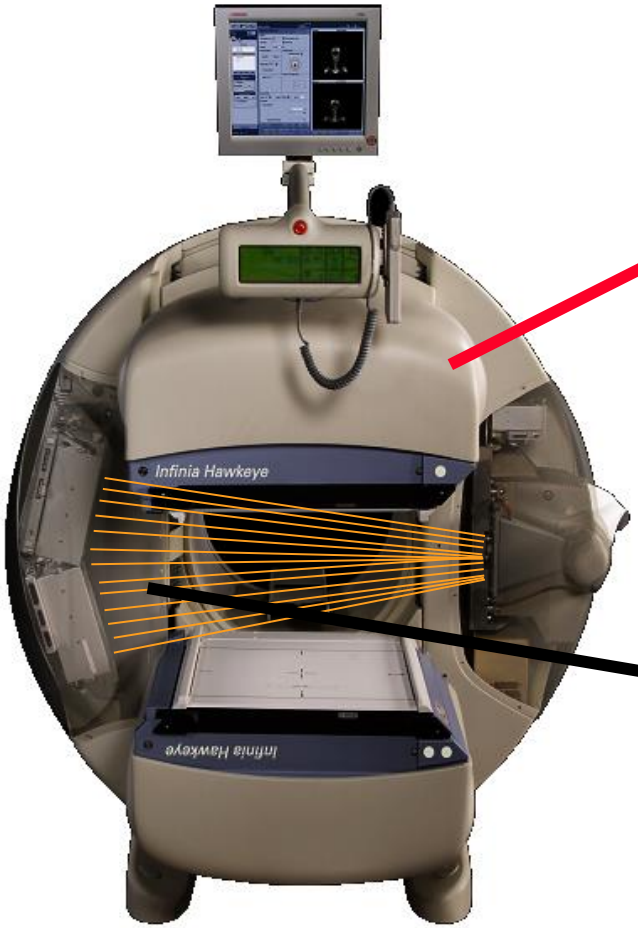
- A Computed Tomography image is
  - a measure of attenuation profiles at different angular projections
- The reconstructed image is
  - a 2D map of linear attenuation coefficients

$$\text{CT - number} = \frac{\mu - \mu_{\text{water}}}{\mu_{\text{water}}} \cdot 1000$$

CT-BASED METHOD

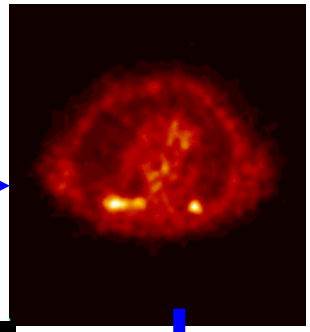


CT-BASED METHOD

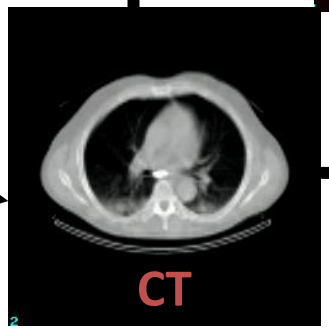




Attenuation Correction

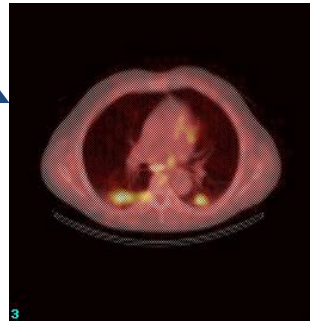


1) AC image



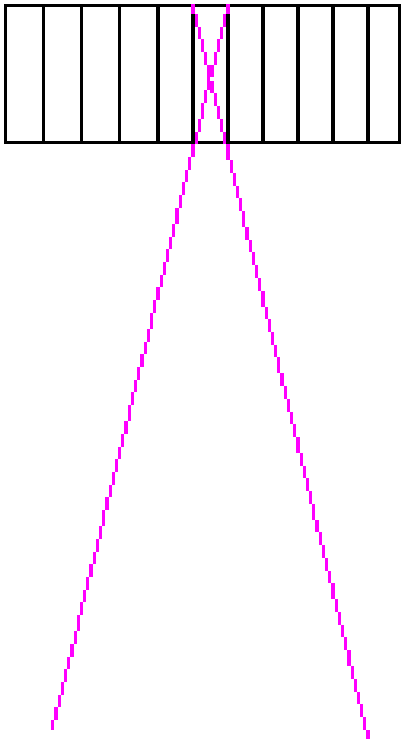
Inherent Image Registration (Fusion)

2) Fused image



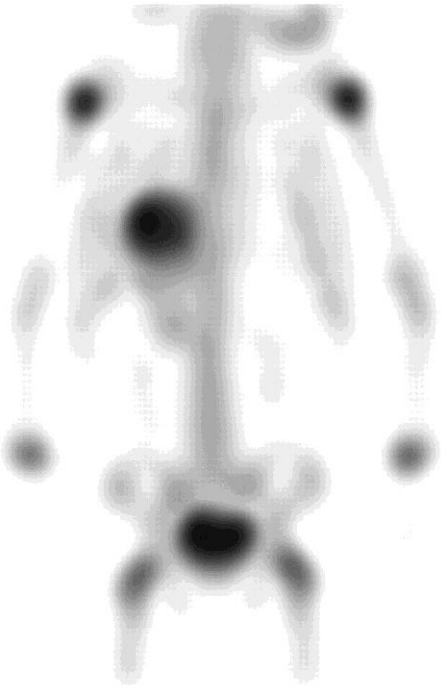
Resolution Recovery

- Spatial resolution
  - worsens with increasing distance from the collimator
- Resolution losses modelled
  - put into iterative reconstruction

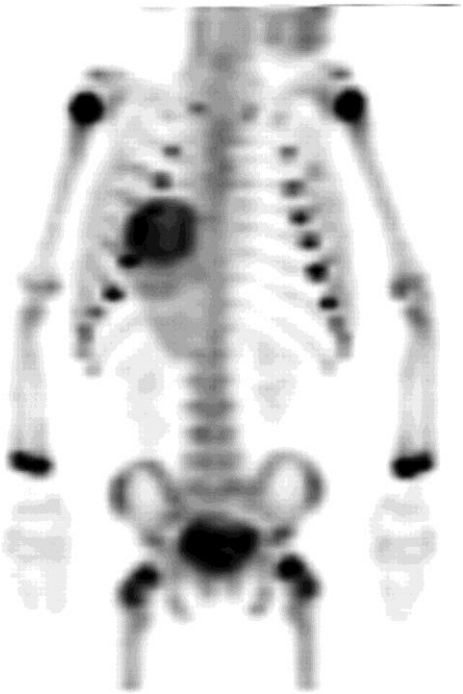


Resolution Recovery

- Better modelling means better images
- Fewer counts needed to get acceptable images
  - shorter acquisitions
  - lower doses



Full counts
FBP



Half counts
OSEM 3D

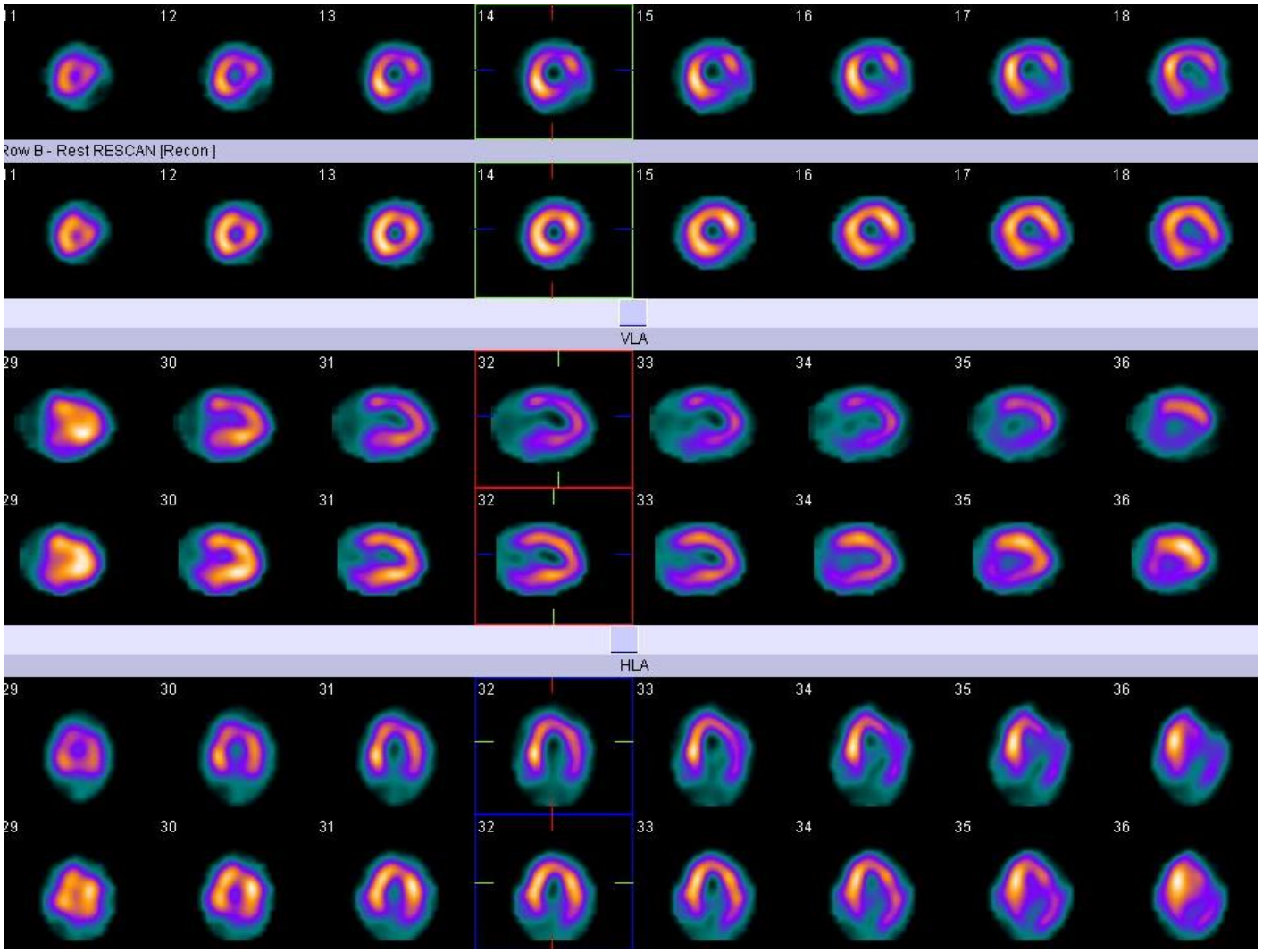
SPECT Applications

SPECT Applications Cardiology

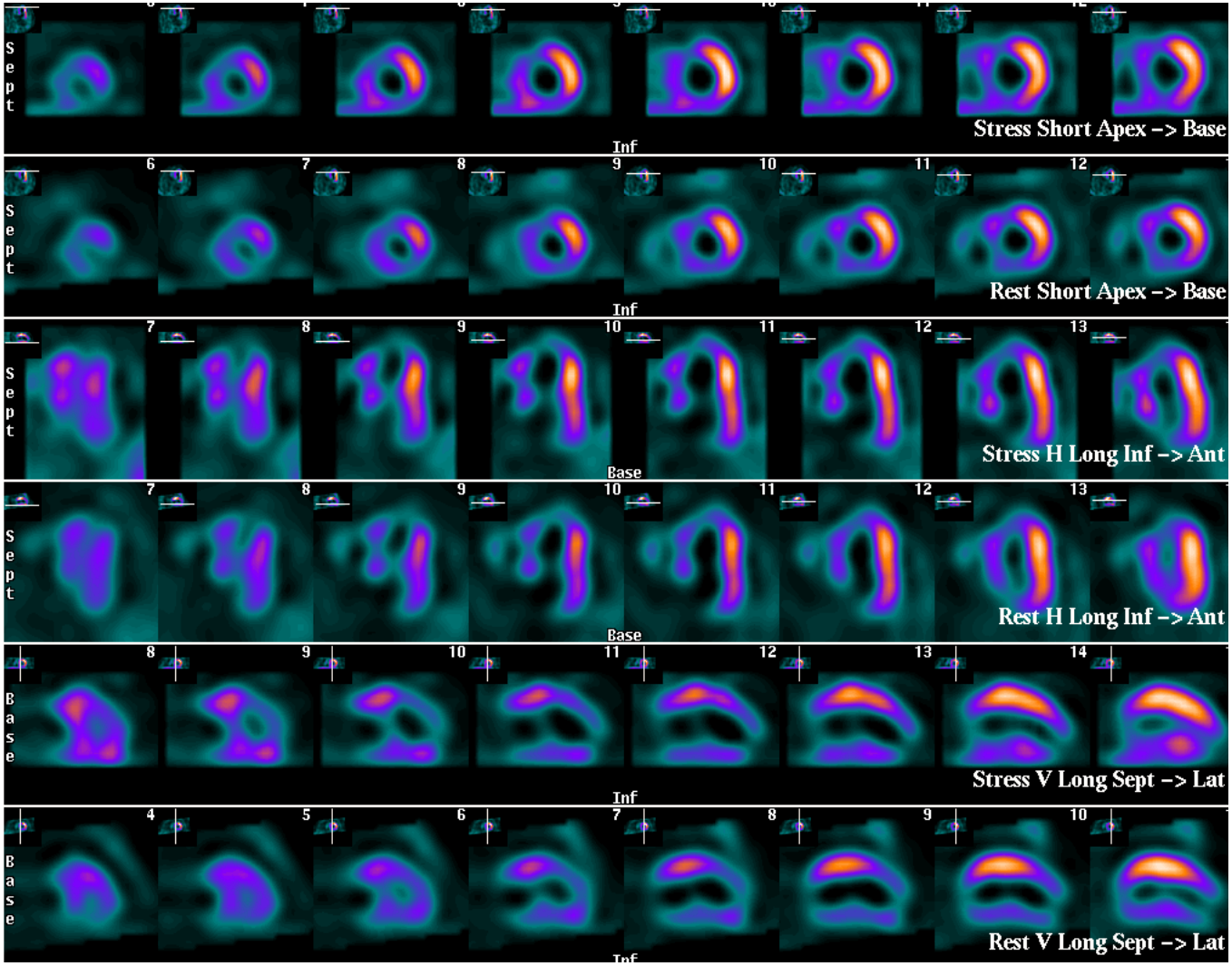
Myocardial Perfusion Scintigraphy

- Coronary artery blood flow
  - proportional to uptake of radiopharmaceutical in heart
- Stress and rest studies performed
- Stress
  - exercise
  - pharmacologic stress
- Gated SPECT (unless in Atrial Fibrillation)
- Radiopharmaceuticals
  - $^{99}Tc^{m}$-MIBI or Tetrofosmin
  - ^{201}Tl (thallous chloride)
- Can be used to look at wall motion, thickening and ejection fraction

Case 1: Reversible Ischemia



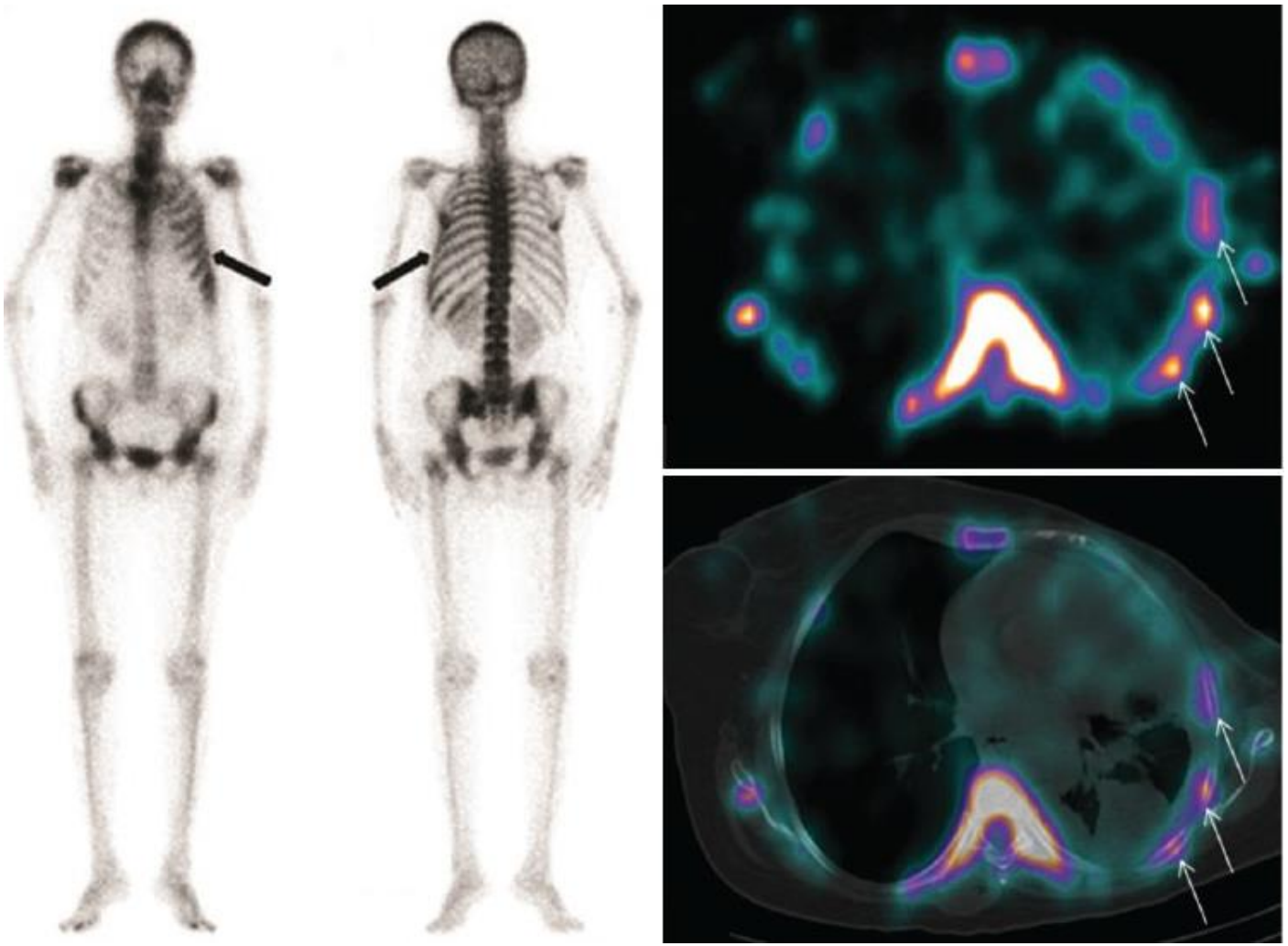
Case 2: Infarct



SPECT Applications

SPECT Applications Oncology

Bone SPECT

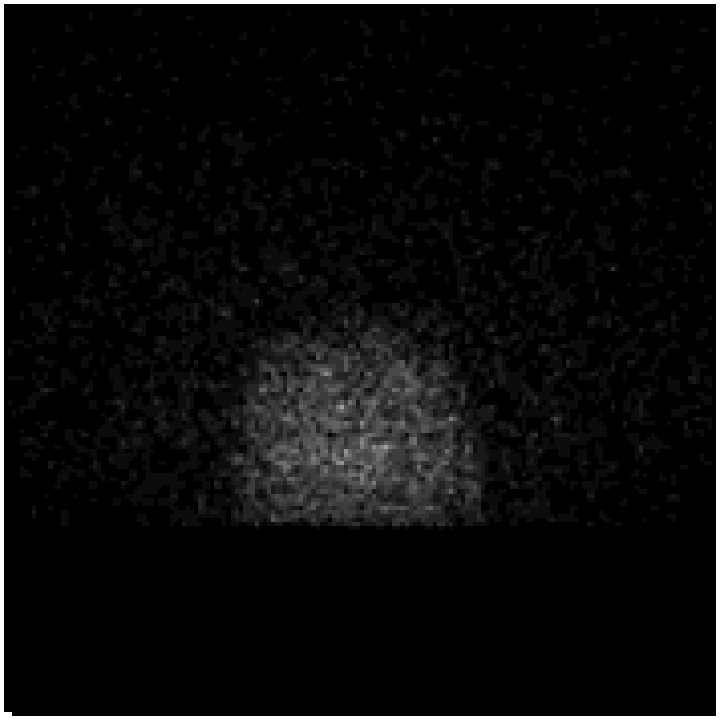


SPECT Applications

SPECT Applications Neurology

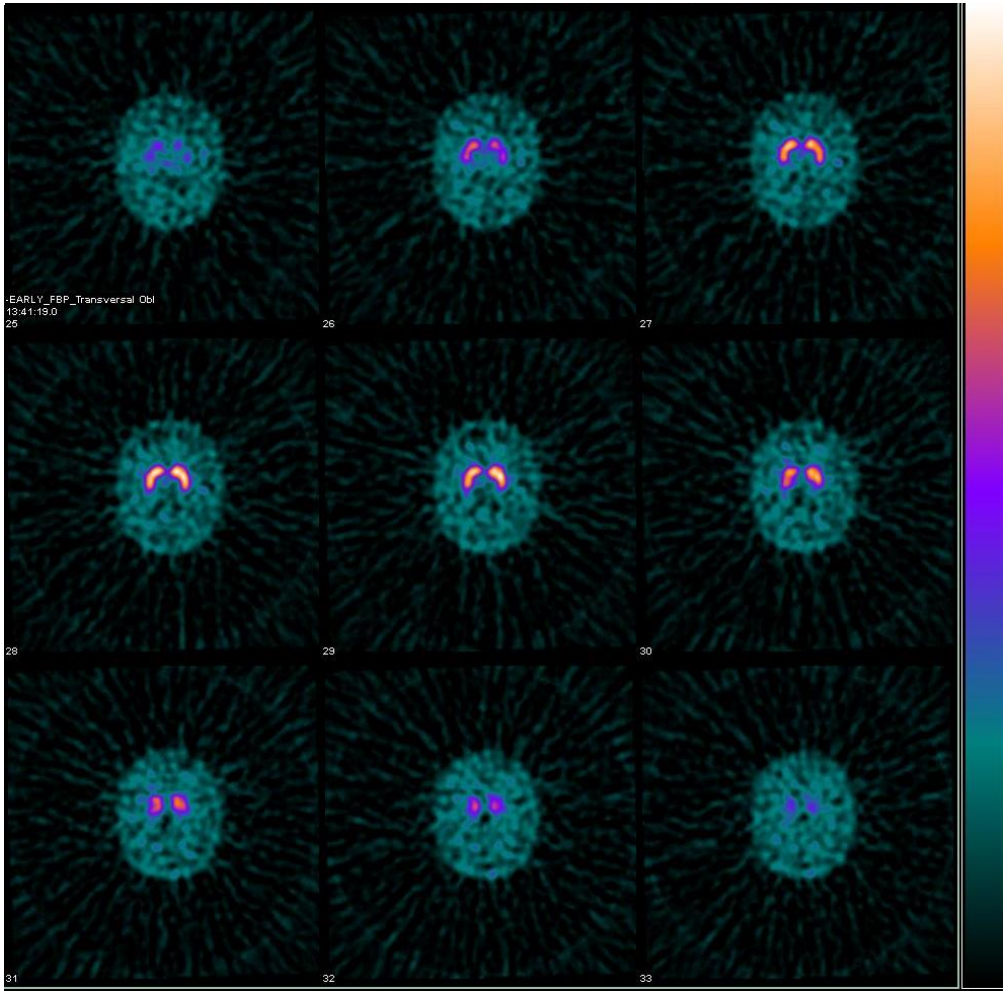
DaTSCAN Brain Imaging

- Radiopharmaceutical
  - ^{123}I-Ioflupane
- Imaged at 3-6 hours
- Effective dose 4.4 mSv
- Differentiates between
  - ET, Drug-induced parkinson's and Parkinsonian syndromes
- Assesses the severity of Parkinsonian syndromes



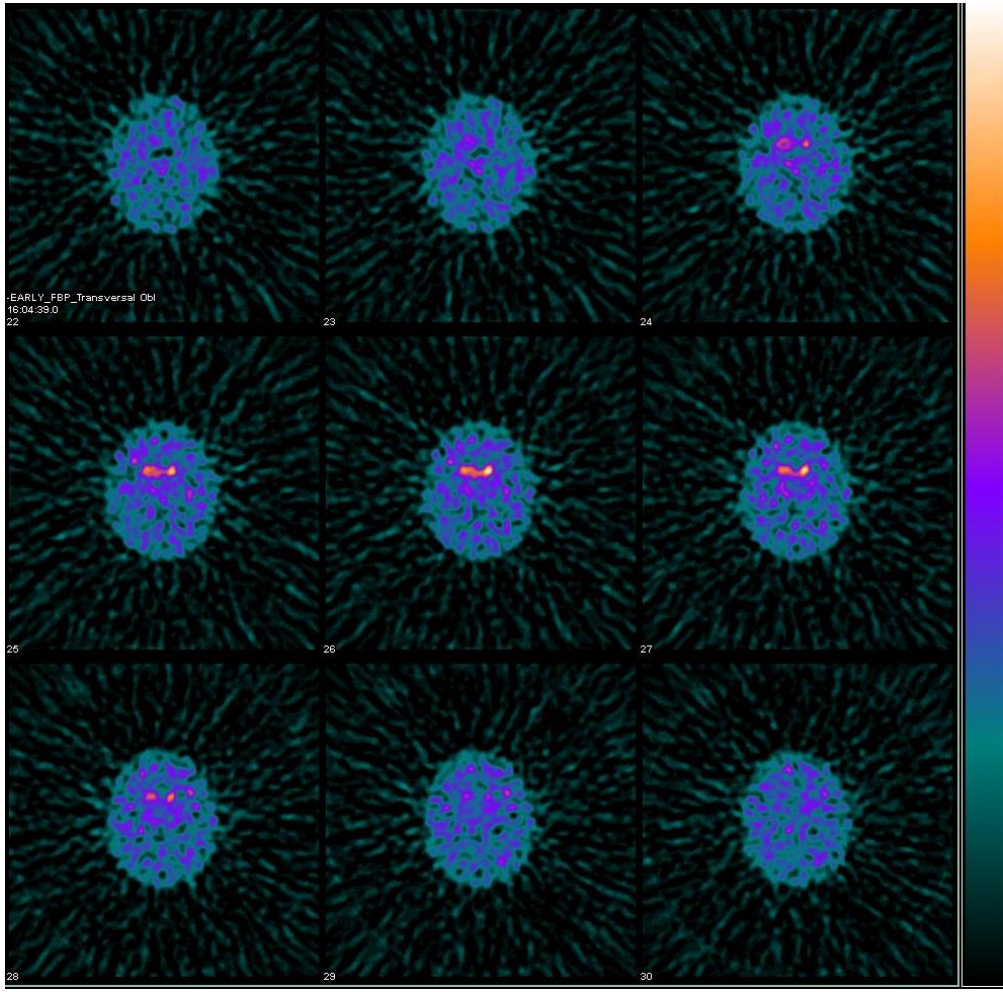
Case 1: Normal Scan

- Ioflupane binds to
  - pre-synaptic dopamine transporters
- Normal appearance is
  - comma shaped putamen
- Abnormal
  - “full stop” shape of one or both putamen



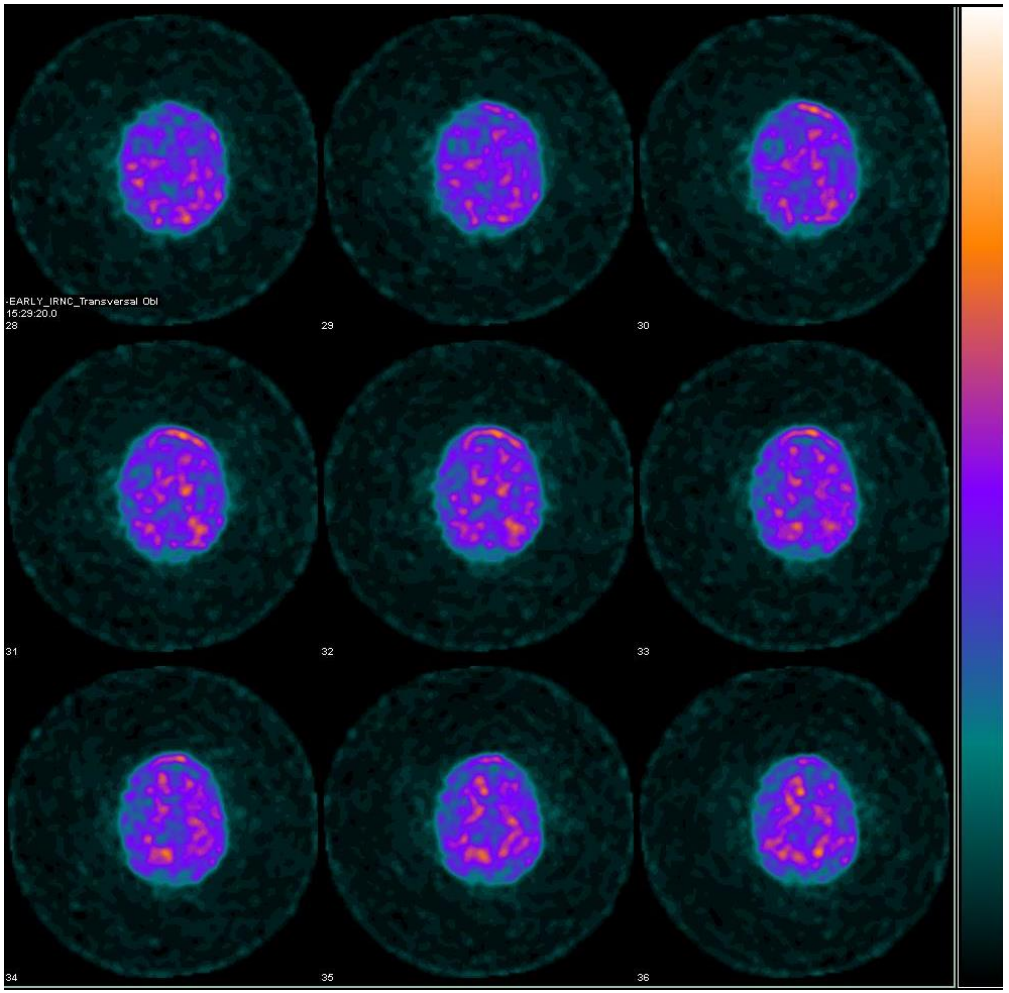
Case 2: Abnormal Scan

- Ioflupane binds to
  - pre-synaptic dopamine transporters
- Normal appearance is
  - comma shaped putamen
- Abnormal
  - “full stop” shape of one or both putamen



Case 3: Abnormal Scan

- Ioflupane binds to
  - pre-synaptic dopamine transporters
- Normal appearance is
  - comma shaped putamen
- Abnormal
  - “full stop” shape of one or both putamen



End of Part 1: Thank you for listening!

