The introduction into principles of nuclear medicine

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What is Nuclear Medicine?

- Nuclear medicine is a medical specialty that uses radioactive materials to both diagnose the body and treat disease.

- Nuclear medicine imaging documents organ function and structure.

Nuclear Medicine Procedures

- Nuclear medicine procedures may be:
  - diagnostic studies, which are tests of body function
  - therapeutic procedures in which the radiation is used to treat disease.
- Radionuclide therapy is used in the treatment of both benign disease (eg hyperthyroidism and arthritis) and malignant disease (eg thyroid cancer and hepatocellular carcinoma)

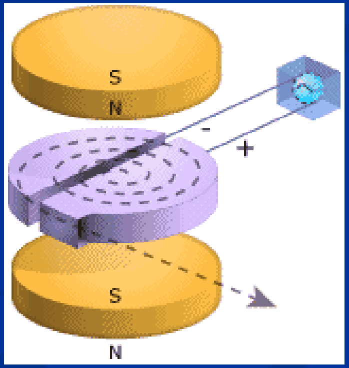
What is radiopharmaceutical

- The radioactive materials administered to patients are known as radiopharmaceuticals.
- These consist of :
  - a chemical molecule which determines the behaviour of the radiopharmaceutical in the body
  - a radionuclide. The radiation emitted by the radionuclide may be detected from outside the body by a radionuclide imaging device (a gamma camera) or may be detected in a sample of a body fluid (eg plasma or urine)

Výroba radionuklidů pro RF

- Nuclear reactor
  - Fission of nuclear fuel
  - ^{131}I, ^{99}Mo, ^{97}Y, (^{137}Cs, ^{60}Co)

- Accelerators
  - Cyclotron – accelerated particle enters into nucleus
  - Gamma emmiters: ^{67}Ga, ^{123}I, ^{111}In, ^{57}Co
  - Positron emmiters: ^{18}F



- Radionuclide generators
  - Radionuclides are transformed into doughter radioactive elements
  - ^{99m}Tc, ^{81m}Kr

Preparation of radiopharmaceuticals

- RF provided prepared (eventually necessary to be diluted)

- RF prepared at department of NM by radiopharmacist
  - provided non-radioactive kits
  - adjunction of radionuclide (at room temperature, by heating in water bath) (all ^{99m}Tc preparations)

Types of radiopharmaceuticals (kits)

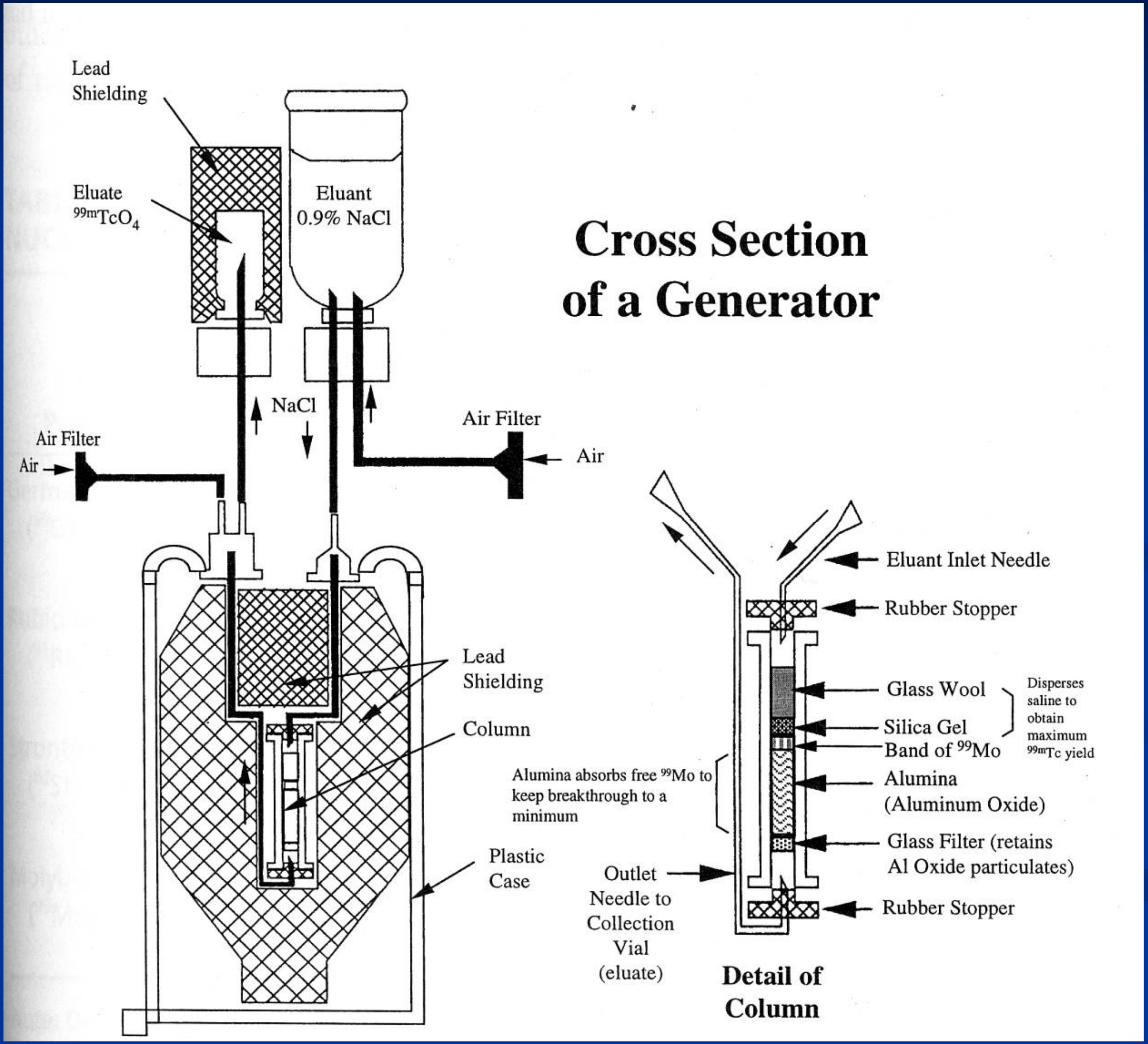
^{99m}Tc

- MDP - bones
- MAG3 - kidney
- DMSA - kidney
- DTPA - kidney
- HIBIDA - liver, glad bladder
- CARDIO-SPECT – myocardium, parathyroid glands, tumors
- MACRO-ALBUMON - lungs
- SENTI-SCINT - sentinel lymph nodes, brest cancer, melanoma
- NEUROLITE - brain
- ANTI-GRANULOCYTE - inflammations, marrow
- LEUKO-SCINT – leukocytes labelled 99mTc- HM-PAO, nflammations

^{111}In

- OCTREOSCAN – neuroendocrine tumors , and carcinoids

Generator ^{99}Mo - ^{99m}Tc



SAFEFLOW
MANIPULATION CELLS
Tema
CAUTION

Radiopharmaceuticals

- Diagnostic radiopharmaceuticals must deliver the minimum possible radiation dose to the patient while still obtaining the required diagnostic information.
- Therapy radiopharmaceuticals must deliver the maximum radiation dose to the diseased organ or tumour, while minimising the radiation dose to non-target tissues such as the bone marrow. ensure minimal irradiation of other parts in patient's body .

The ideal radionuclide for diagnostics in-vivo imaging

- It must emit photons in high abundance in energies which can be efficiently detected by the gamma camera (100 keV - 300 keV)
- It should not emit charged particles as these are absorbed within a few millimetres of tissue. These can not be detected outside of the body and greatly increase the radiation dose to the patient.
- It should have a short half-life, again to keep the radiation dose as low as possible

The ideal radionuclide for therapy

- Must emit energetic charged particles. These are usually beta particles but may be Auger electrons, internal conversion electrons or even alpha particles.
- A low abundance gamma photon is an advantage, allowing the activity distribution to be imaged.
- A fairly short half-life, typically several days.

Radiopharmaceutical Administration

Depending on the requirements for a particular study, the radiopharmaceutical may be :

- injected intravenously or occasionally arterially
- inhaled as a gas or aerosol
- ingested as a liquid or as a solid meal

Targeting the Right Tissue or Organ

The metabolism of the radiopharmaceutical in the body will depend on its chemical properties.

- Some are simple ions, such as ^{67}Ga citrate and sodium ^{131}Iodide
- Some are particles or aggregates of molecules labelled with a radionuclide
- Some are radio-labelled blood cells (red cells or white cells)
- The remainder are labelled complex molecules, such as phosphonates, peptides and antibodies.

Radionuclides used in diagnostics

Diagnostic γ radiators

radionuclid	E[keV]	$T_{1/2}$
^{99m}Tc	140	6,03 h
^{111}In	172, 247	2,83 d
^{67}Ga	93, 185, 300	78,3 h
^{123}I	159	13,2 h
^{131}I	364	8,04 d
^{81m}Kr	190	13 s
^{201}Tl	75, 167	73,2 h

Diagnostic β^+ radiators

radionuclid	E_γ[keV]	$T_{1/2}$
^{18}F	511	110 min
^{11}C	511	20,4 min
^{15}O	511	2,07 min
^{13}N	511	10 min

Radionuclides in Therapy

Therapy using β^-emitters

Radionuclide	E_{max}[keV]	$T_{1/2}$
^{131}I	606	8,04 d
^{153}Sm	635, 705, 808	46,7 h
^{186}Re	940, 1077	3,7 d
^{89}Sr	1495	50,5 d
^{90}Y	2280	64 h

Palliative radionuclide´s therapy of metastases (^{131}I, ^{153}Sm, ^{186}Re)

Chronic articular diseases (^{89}Sr, ^{90}Y)

Examinations are performed using gamma cameras

Scintiallation camera or Gamma Camera

- The first scintilation camera was developed by Hal Anger in 1958.
- The principles of the Anger camera are still used in modern gamma cameras.

Gamma kamera

- Hal Anger
- 1958 - first prototype of gamma camera (NaI(Tl) + photographic plate, low sensitivity, long time of aquisition)
- 1962 – first comercial Anger camera, Ohio (USA)
- Principle of Anger camera is still used even in modern gamma cameras

Principle of operation of a scintillation detector

- A radionuclide emits discrete energy photons which can either be totally absorbed, partially absorbed, or completely missed by a scintillation detector.
- If the gamma ray is absorbed, the scintillation detector converts the energy of the photon into a flash

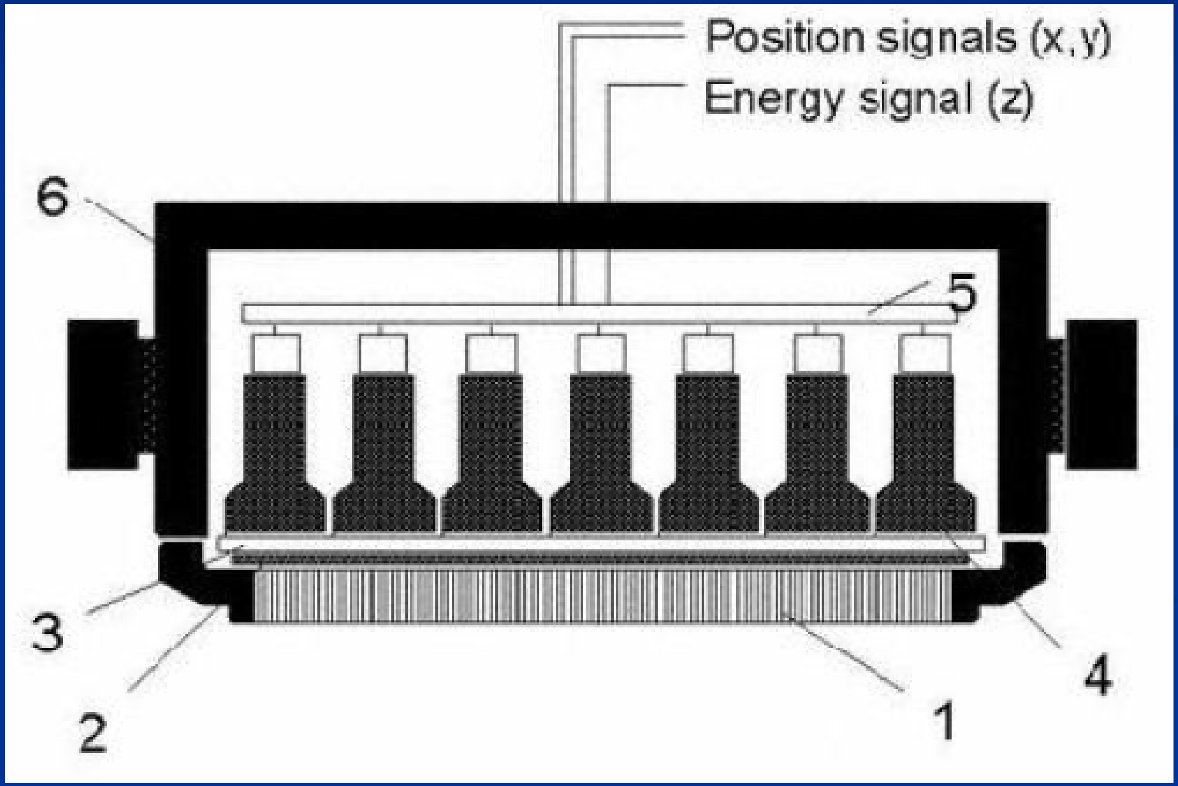
Principle of operation of a scintillation detector (continued):

- A flash of light is converted into an electrical pulse which is amplified in the system and is subsequently analyzed.
- Depending on the energy initially absorbed and depending on how the operator sets up the scintillation detector, the photon is either counted or rejected

Scintillation detector components:

- Crystal
- Photomultiplier tube
- High voltage supply
- Preamplifier
- Amplifier
- Pulse height analyzer
- Display device
  - Scaler
  - Ratemeter

Basic gamma camera components



1 – colimator

2 – scintilation crystal

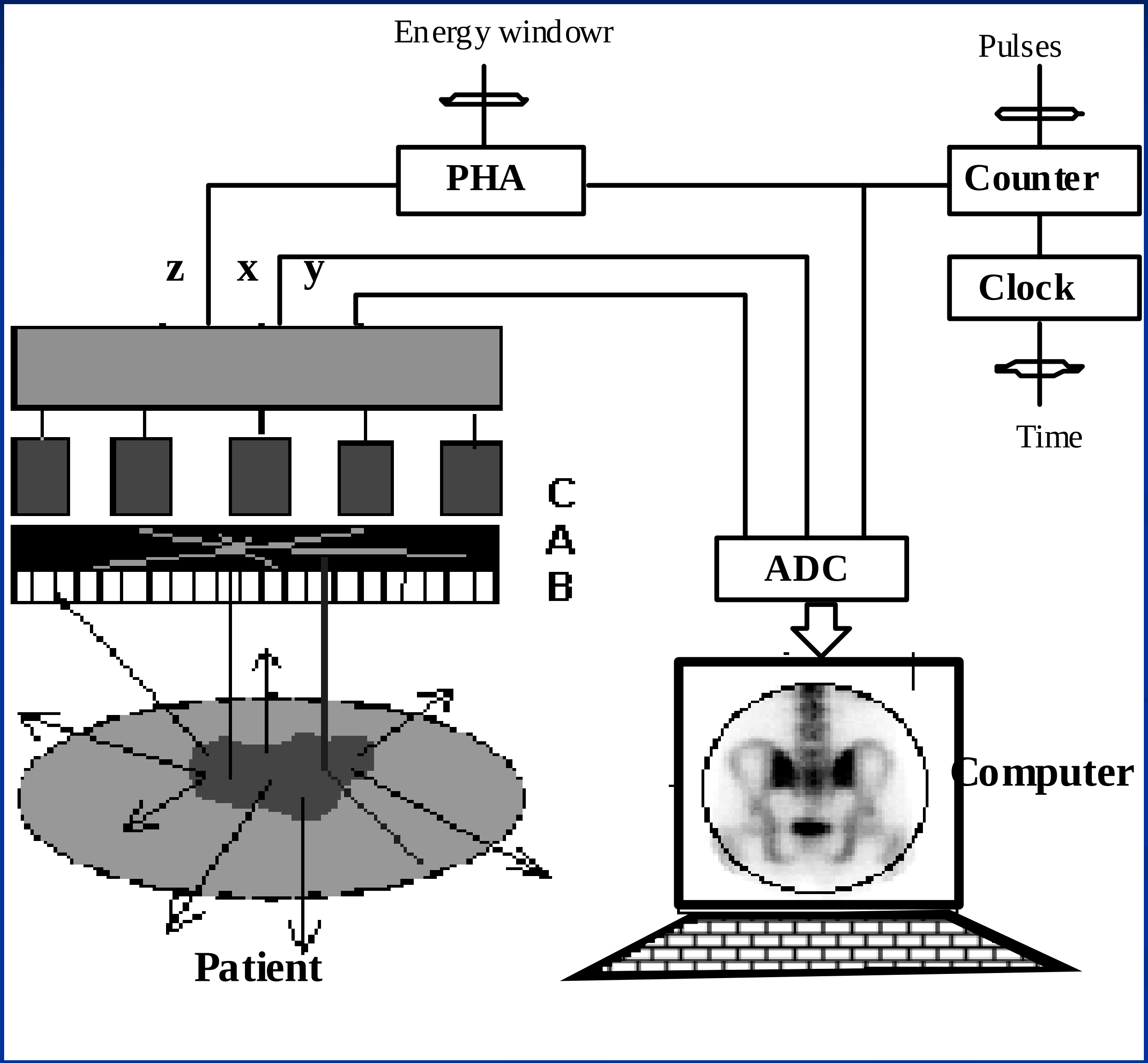
3 – light guide

4 – photomultiplier

5 – circuitry

6 - shielding

Basic gamma camera components



PHA
Puls high
analyser

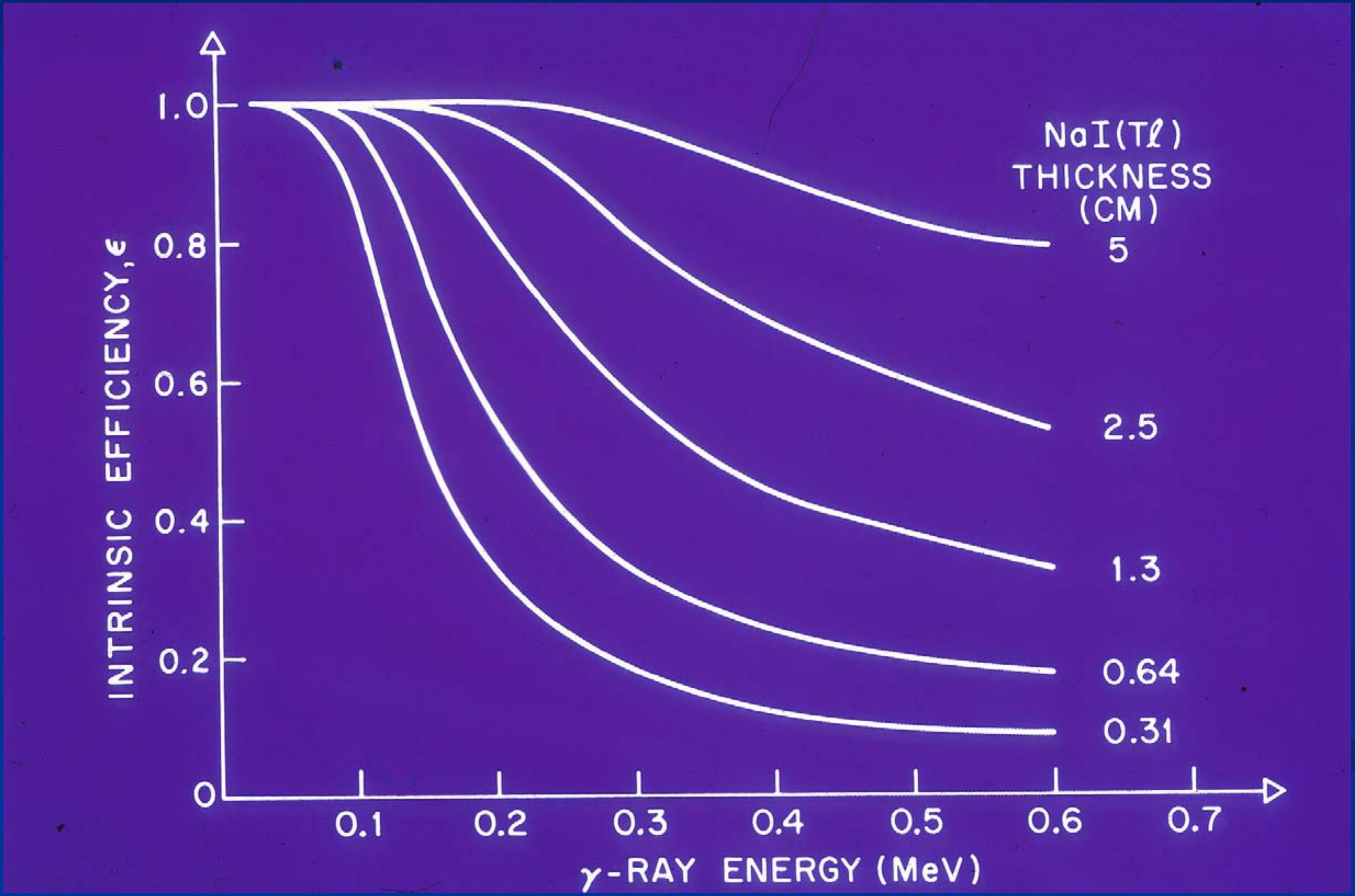
Counter =
Impulse
counter

ADC
Analog-digital
converter

Scintillation crystal

- Thallium activated sodium iodide NaI(Tl) has a high density (3.67 g/cm^3) and a high atomic number.
- The efficiency of detection increases with increasing crystal thicknesses and decreases with increasing photon energy.
- Most gamma cameras use a crystal thickness of 9.5 mm (3/8 inch)

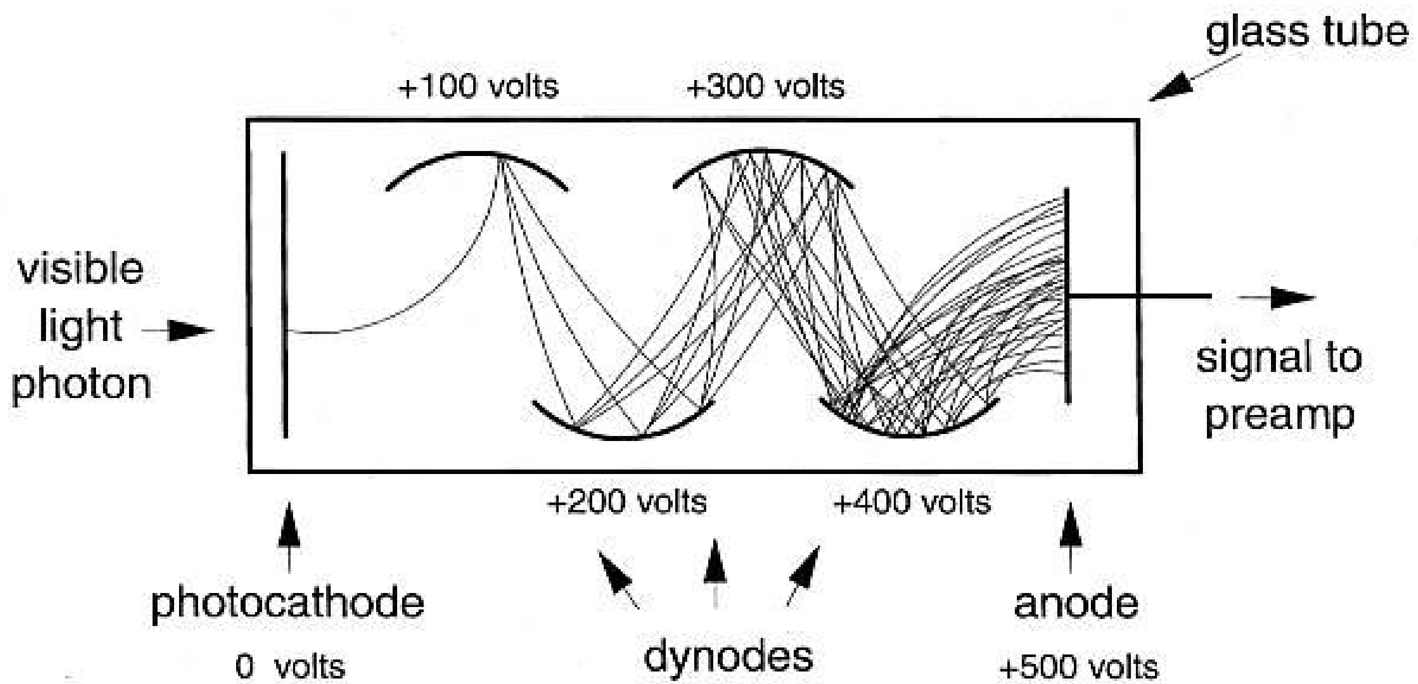
Variation of Detector Efficiency with Crystal Thickness and Photon Energy



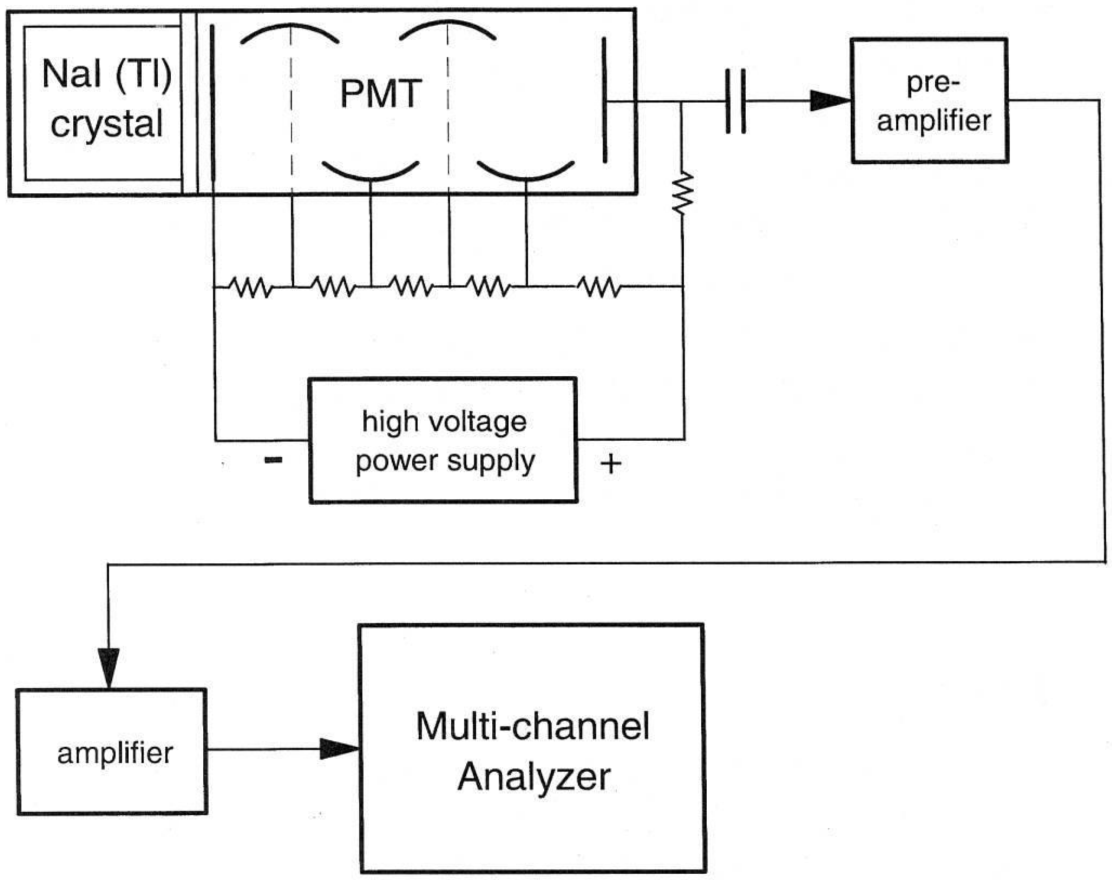
Photomultipliers

- Fotokatoda + vakuová trubice se soustavou elektrod (dynody, cca 10)
- Opticky spojeny s krystalem (vlnovod)
- Původní Angerova kamera používala 7 fotonásobičů. Moderní kamery mají až 90 fotonásobičů (gamakamera Sopha má 87 fotonásobičů).
- Kruhové (∅ 5cm), hexagonální, čtvercové

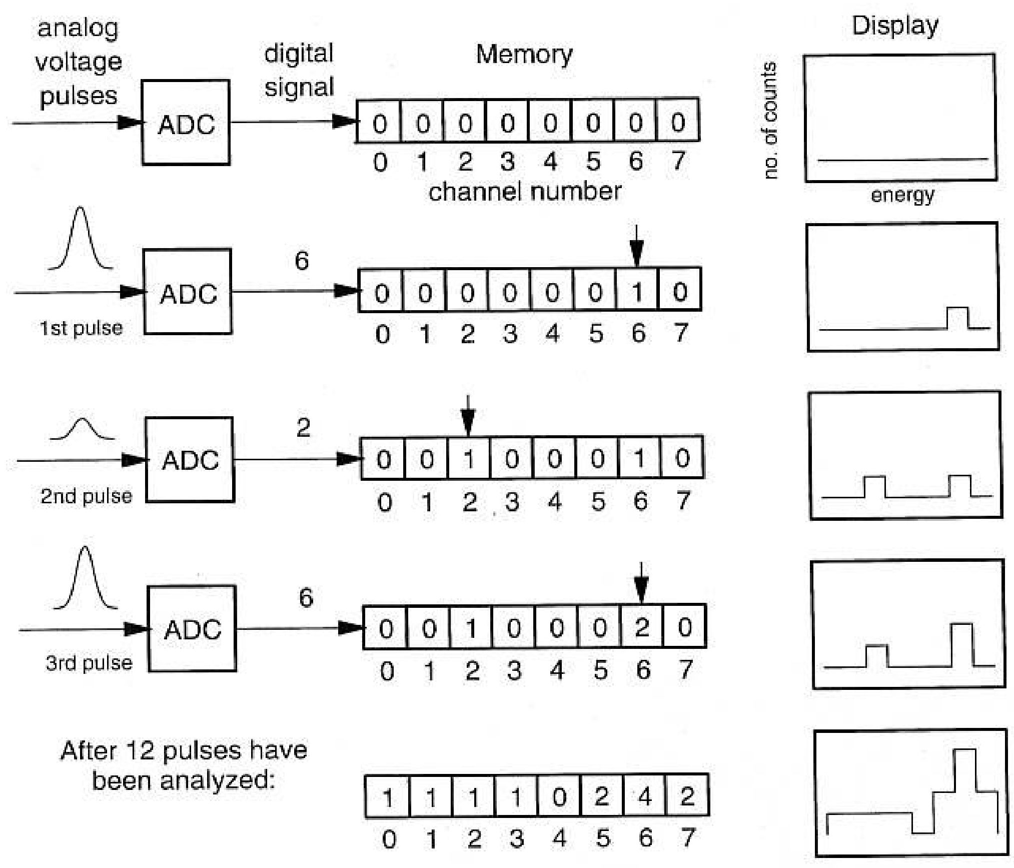
Photomultipliers



Photomultiplier tube. Actual photomultiplier tubes typically have 10 to 12 dynodes.

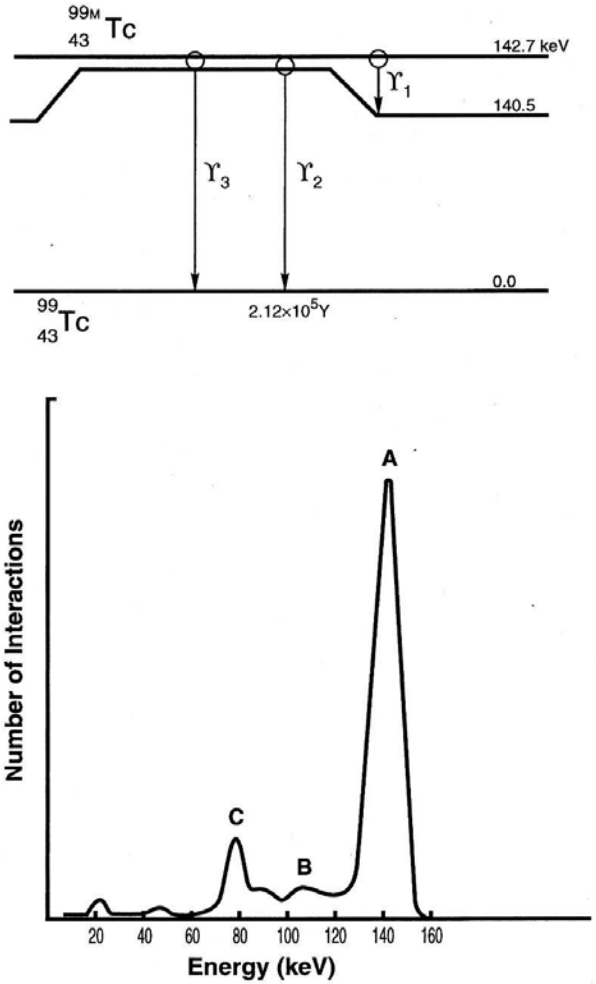


Multichannel analyzer system with NaI(Tl) detector.



Acquisition of a spectrum by a multichannel analyzer (MCA). The digital signal produced by the analog-to-digital converter (ADC) is a set of binary pulses, as described in Chapter 4. After the analog pulses are digitized by the ADC, they are sorted into bins (channels) by height, forming an energy spectrum. Although this figure depicts an MCA with 8 channels, actual MCAs have as many as 8,192 channels.

TECHNETIUM 99M
Isomeric Transition Decay

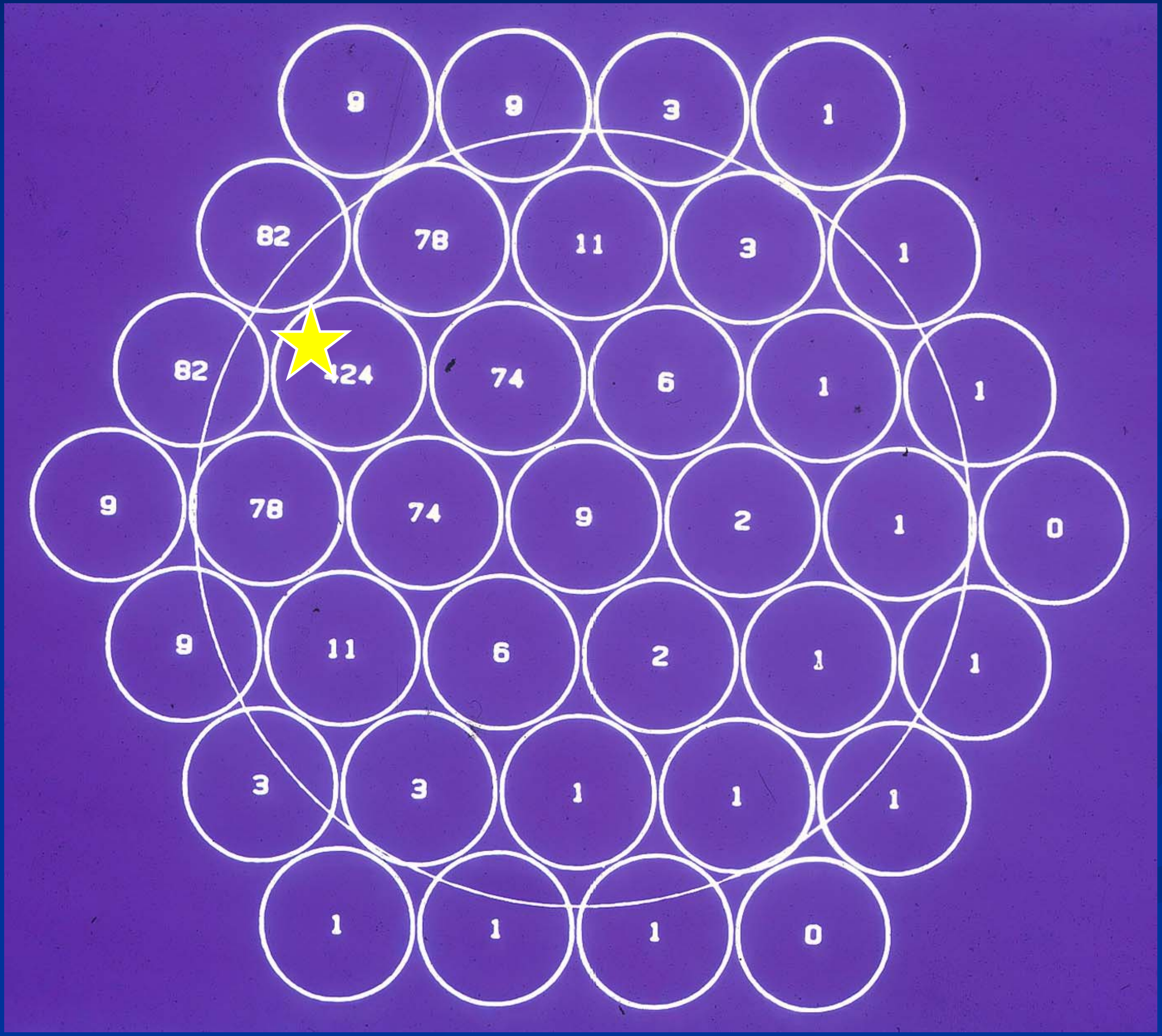


Decay scheme of technetium 99m *(top)* and its pulse height spectrum on an NaI(Tl) scintillation detector *(bottom)*. See text for details.

The Photomultiplier Tube Array

- The scintillation photons produced within the crystal are detected by an array of photomultiplier tubes (PMTs) which are optically coupled to the crystal.
- The original Anger camera used 7 PMTs. Most modern cameras use tens of PMTs.

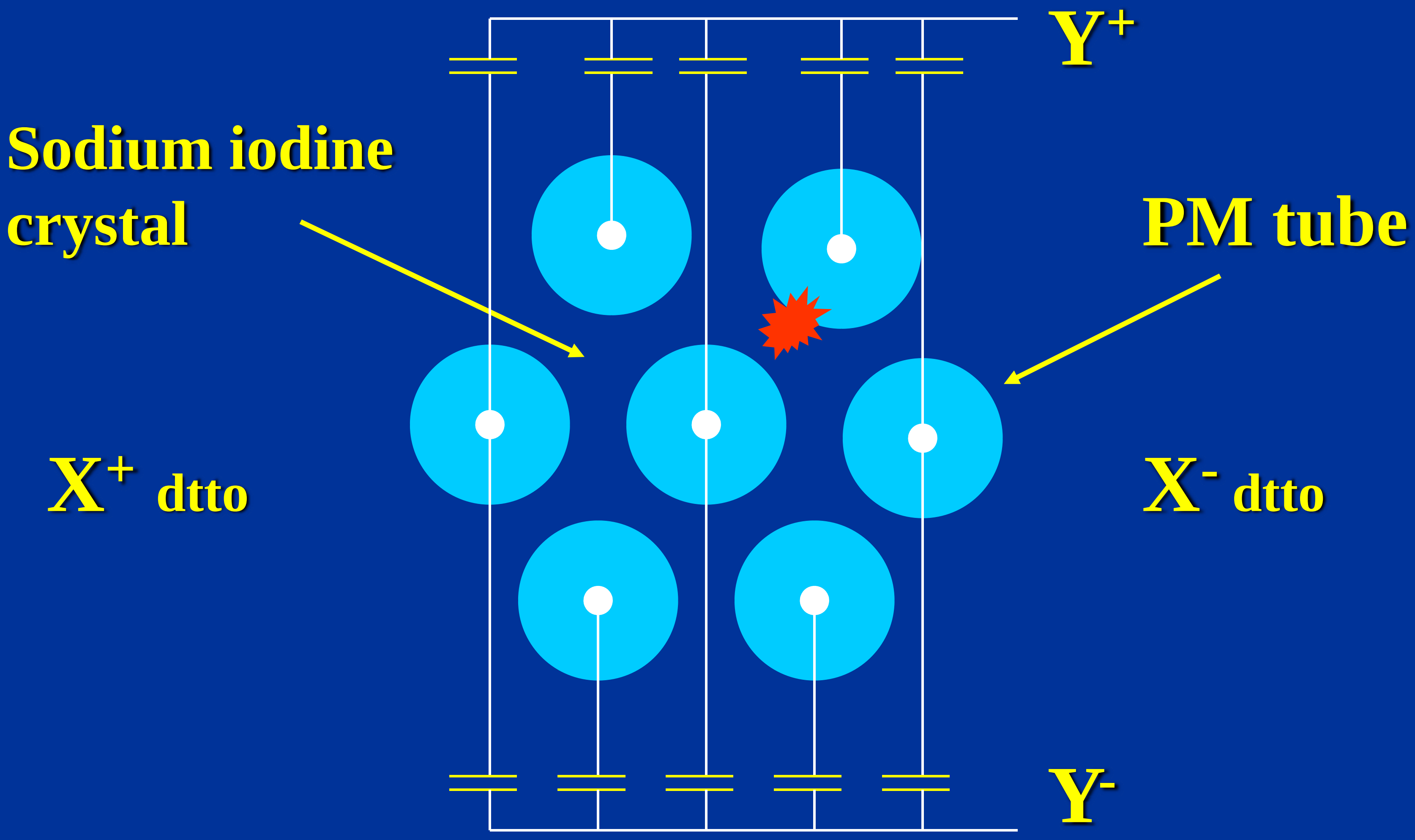
Signal from PMTs from an interaction in the Crystal



The Photomultiplier Tube Array

- The output from the PMTs will be a function of their distance from the location of the scintillation in the crystal.
- The X and Y signals are the weighted sum of the outputs from the PMT array.
- The combined output from all the PMTs together gives a signal known as the Z pulse which will be proportional to the total amount of energy deposited in the crystal.

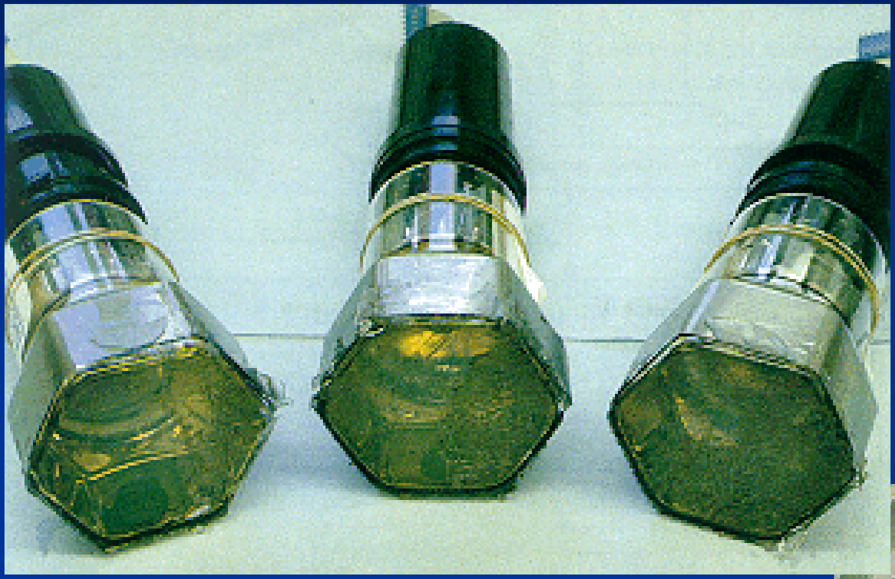
Principal of Gamma Camera

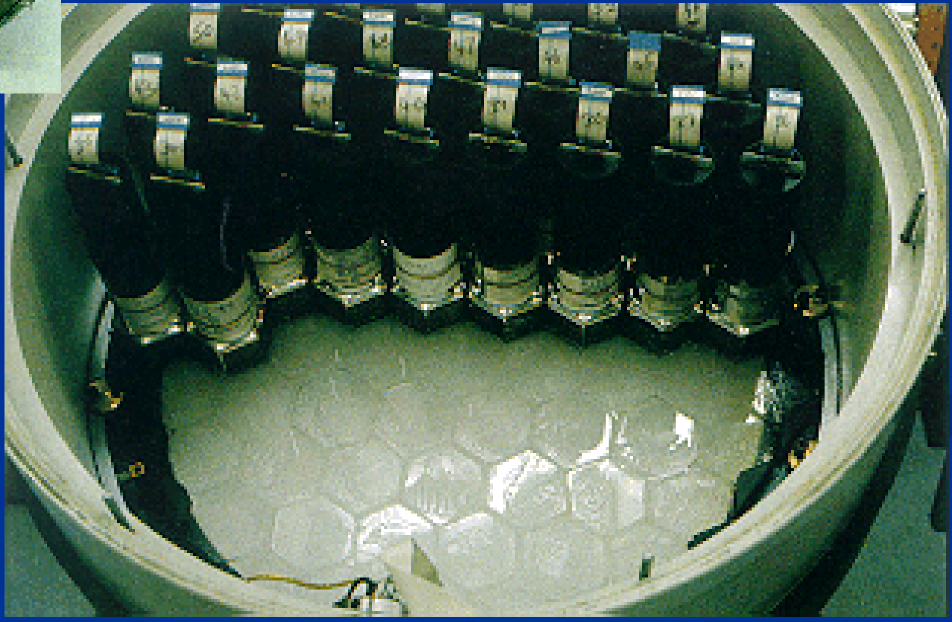


Capacitors sum up γ impulses detected by PM tubes

Photomultipliers

Photomultipliers





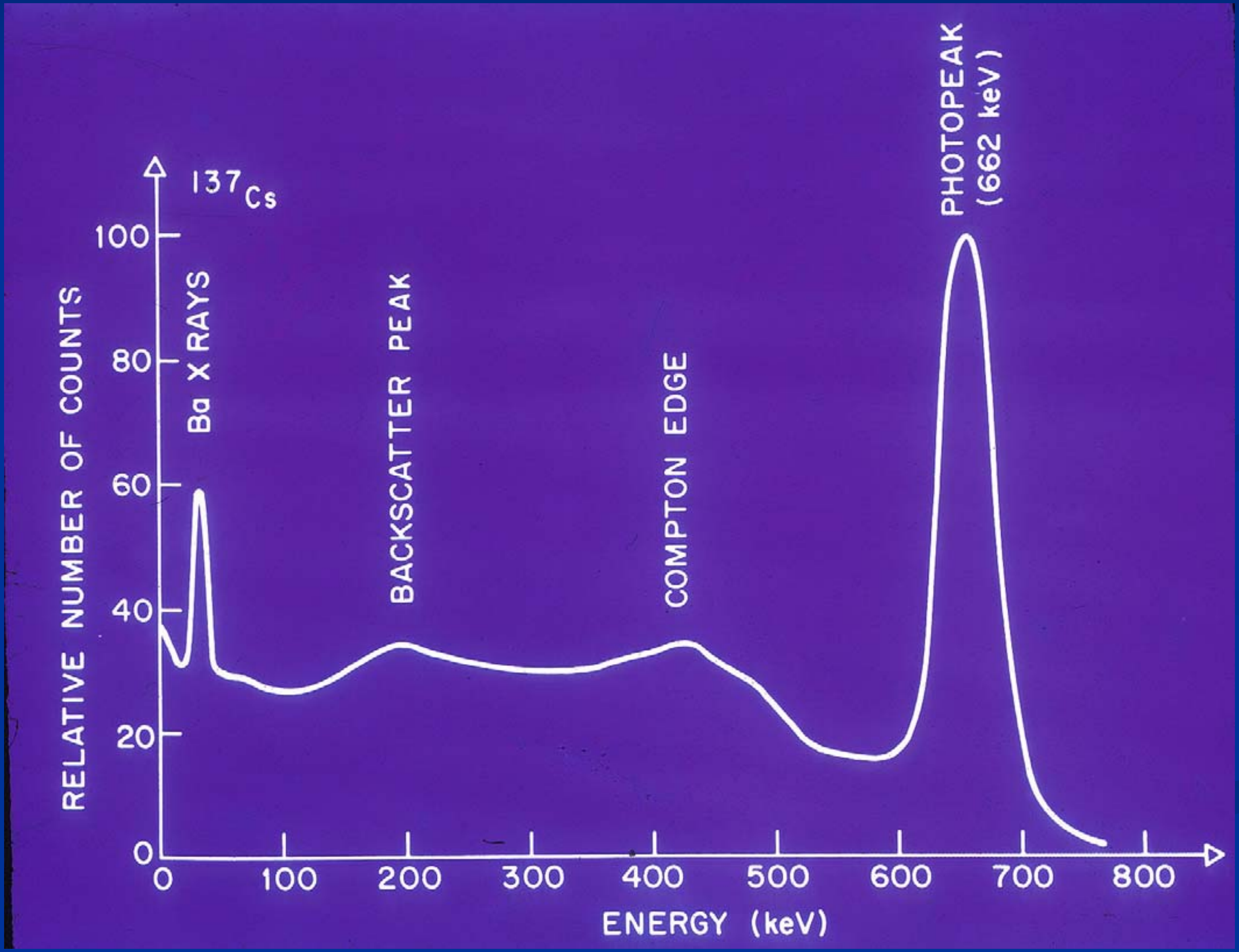
Photomultipliers

Pulse Height Analysis

Analysis of the spectrum of Z pulses (the energy spectrum) is used to:

- limit the inclusion of scattered photons in the images
- allow dual-isotope imaging
- allow efficient detection of radionuclides with 2 or more primary photons (eg ^{67}Ga and ^{111}In)

Energy Spectrum of ^{137}Cs showing Photopeak and Compton Distribution



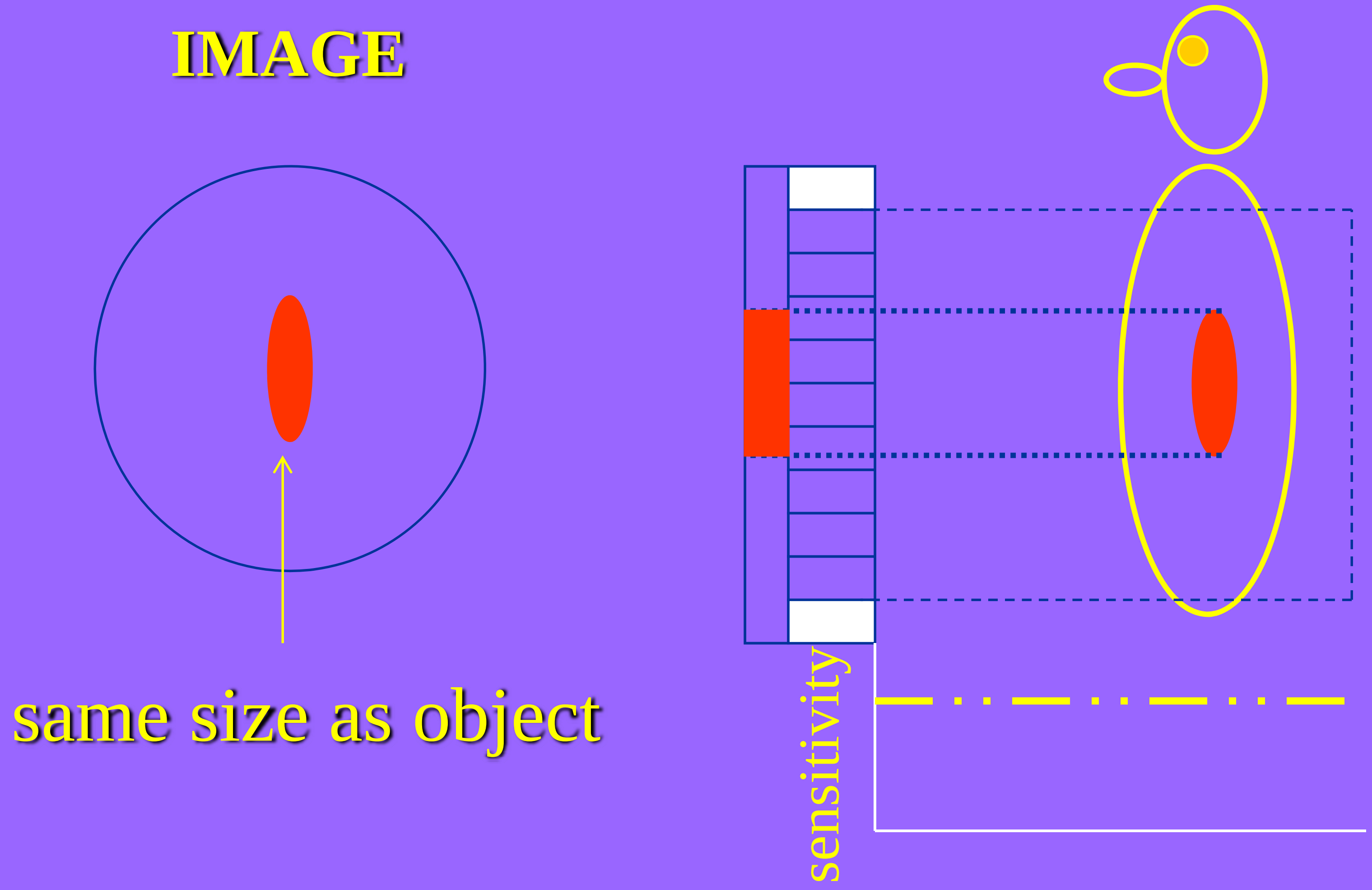
The Collimator

- The collimator projects an image of the source distribution on to the crystal by absorbing all the gamma rays outside of a narrow angle of acceptance.
- Early collimators used glued corrugated sheets of lead.
- Most modern collimators are made as a single casting with hexagonal holes.

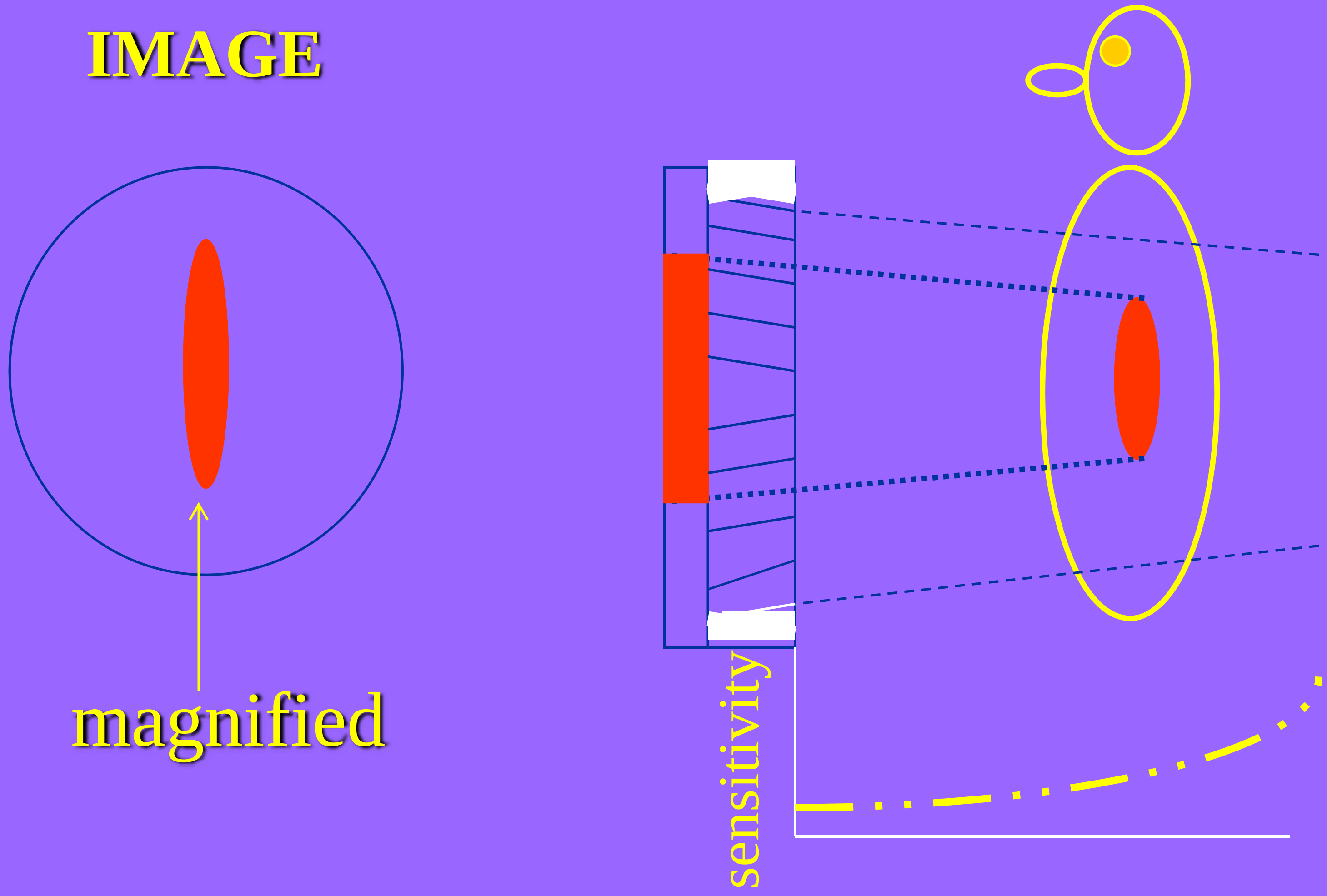
The Collimator

- The sensitivity and resolution of a collimator are a function of :
  - the hole diameter
  - the length of the hole
  - the septal thickness between each hole
  - the distance of the object away from the front of the collimator
- Collimators are therefore designed for different photon energies and resolutions (eg LEHR, MEAP)
- Collimators may use parallel holes, converging holes, diverging holes or a pinhole.

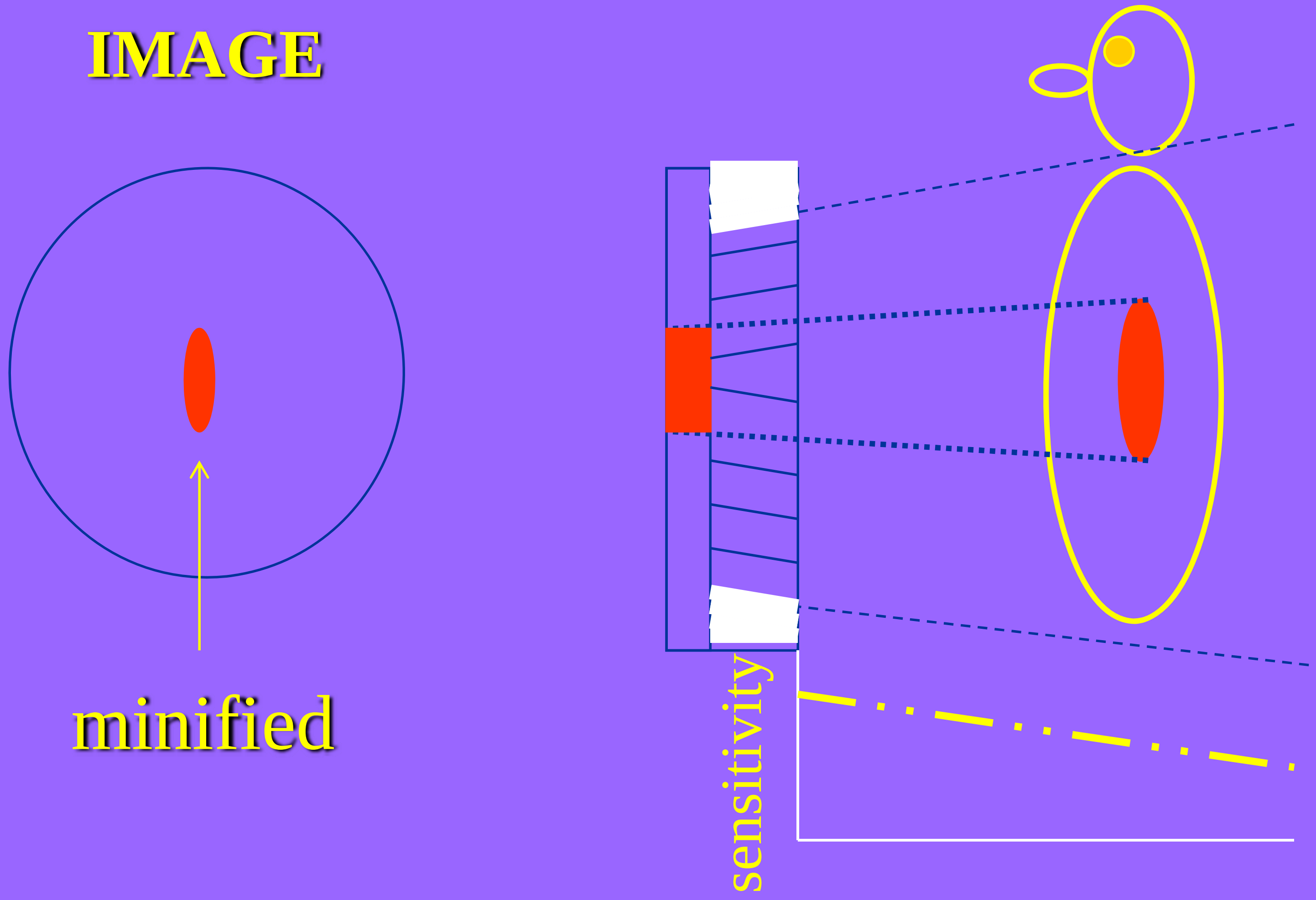
Parallel-Hole Collimator



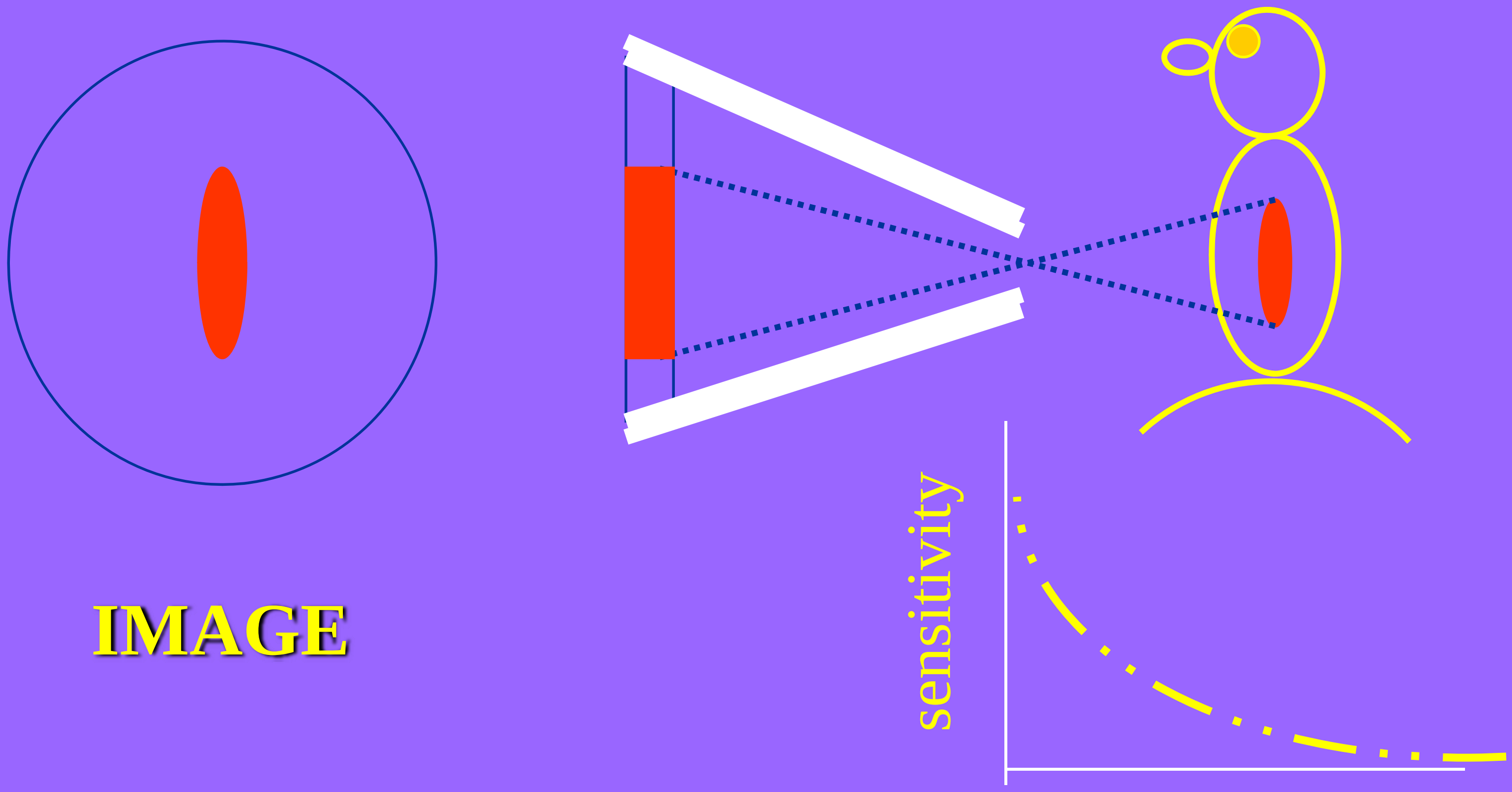
Converging Collimator



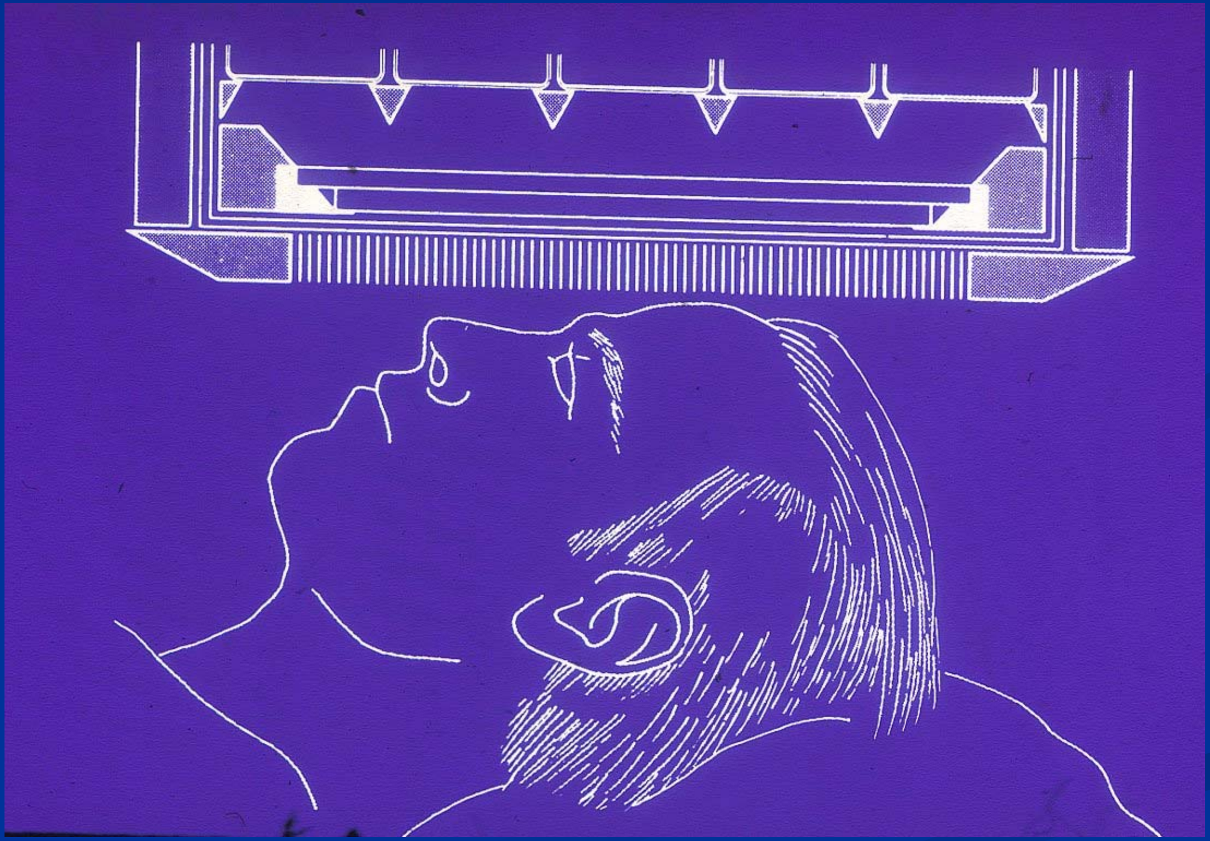
Diverging Collimator



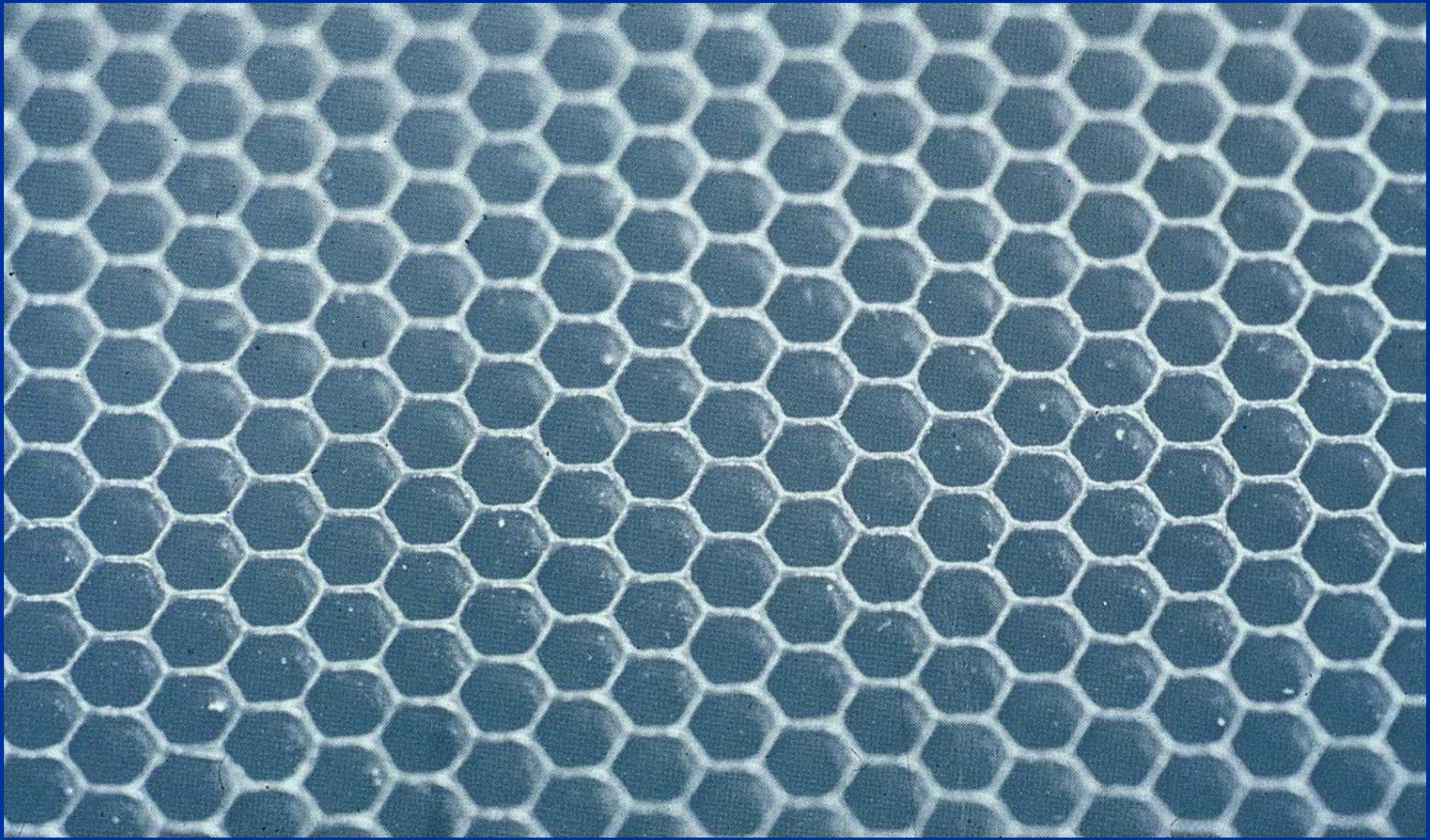
Pin-Hole Collimator



Example of the Use of a Parallel Hole Collimator



Internal Structure of a Microcast Parallel Hole Collimator



Limitations of the Gamma Camera

Unfortunately the basic Anger camera has a number of imperfections that limit the final image quality. To overcome these limitations, all manufacturers now provide:

- on-line energy correction
- on-line linearity correction
- automatic gain adjustment
- improved count rate performance

Gamma Camera Quality Control

- Daily Procedures
  - Image Uniformity
  - Background count rate (to detect possible contamination)
  - System sensitivity
- Weekly or Monthly (depending on the camera)
  - Resolution and Linearity

Gamma Camera Quality Control

Image Uniformity

- must be performed daily before starting patient studies
- can be performed with or without a collimator
- gross changes can be detected visually
- gradual changes may only be observed by computer quantitation of the uniformity

Gamma camera imperfetions

- Basic Anger´s camera has some imperfections, which limit final image quality. Todays cameras are provided by
  - on-line energy corection
  - on-line linearity corection
  - automatic setting of gain
  - Recofiding of higher

Gamma camera imperfetions

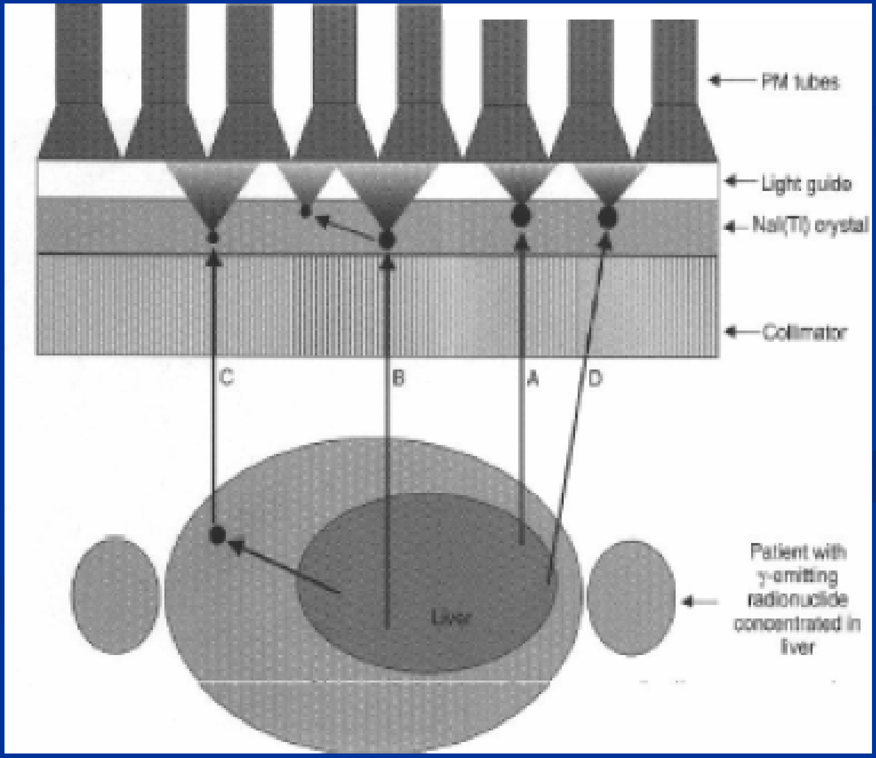
- Events which that may be detected by a gamma camera

A…valid event

B… detector scatter event

C… object scatter event (in patient´s body)

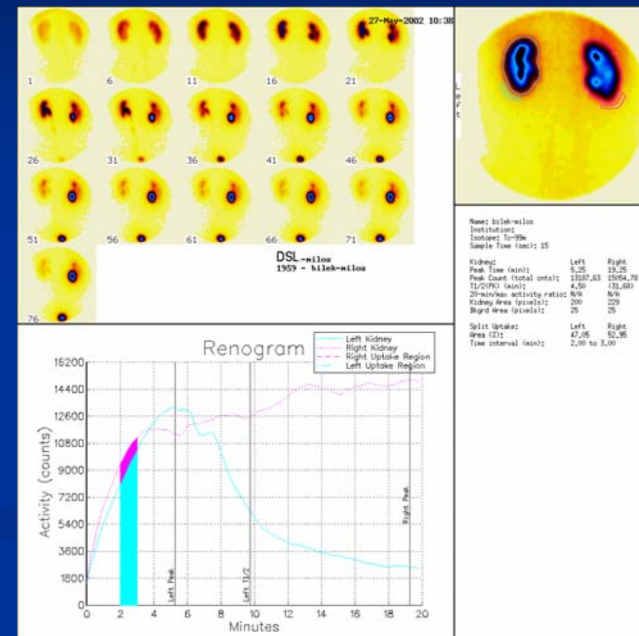
D… septal penetration



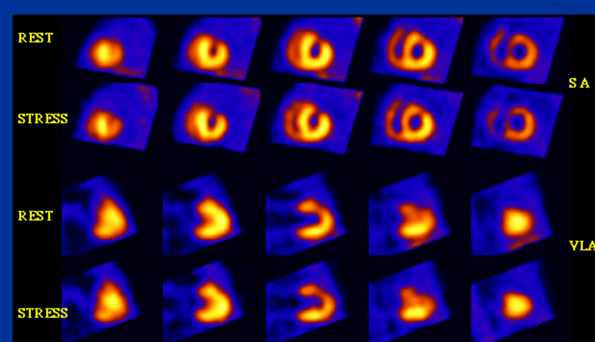
Types of gamma camera´s examinations

- Static st.
  - wholebody
  - targeted
- Dynamic st.
  - dynamic
  - gated
- Tomographic st.
  - SPECT

Dynamic renography

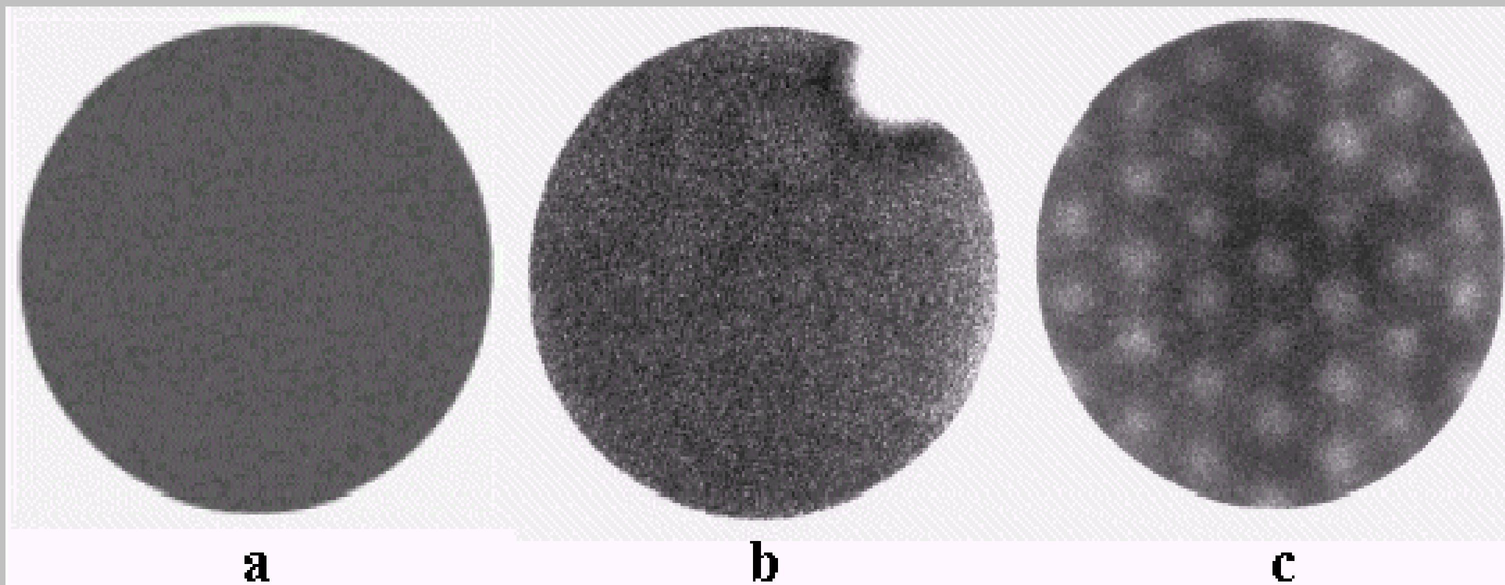


Gated study



Bone scinti

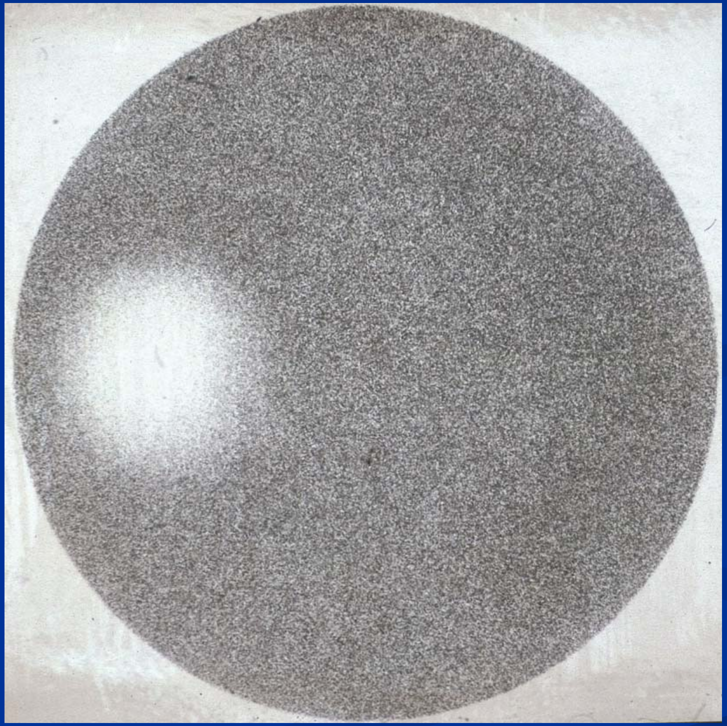
Homogenita na gama kameře



Některé typické obrazy homogenity s plošným zdrojem či bodovým zářičem.
a) Normální obraz homogenity. b) Výpadek periferního fotonásobiče.
c) Celkově rozladěné fotonásobiče či fotopík nastavený mimo okénko analyzátoru.

Defekt krystalu způsobený nárazem nebo proražením

Gamma Camera Flood Images



Faulty PMT

SPECT Imaging

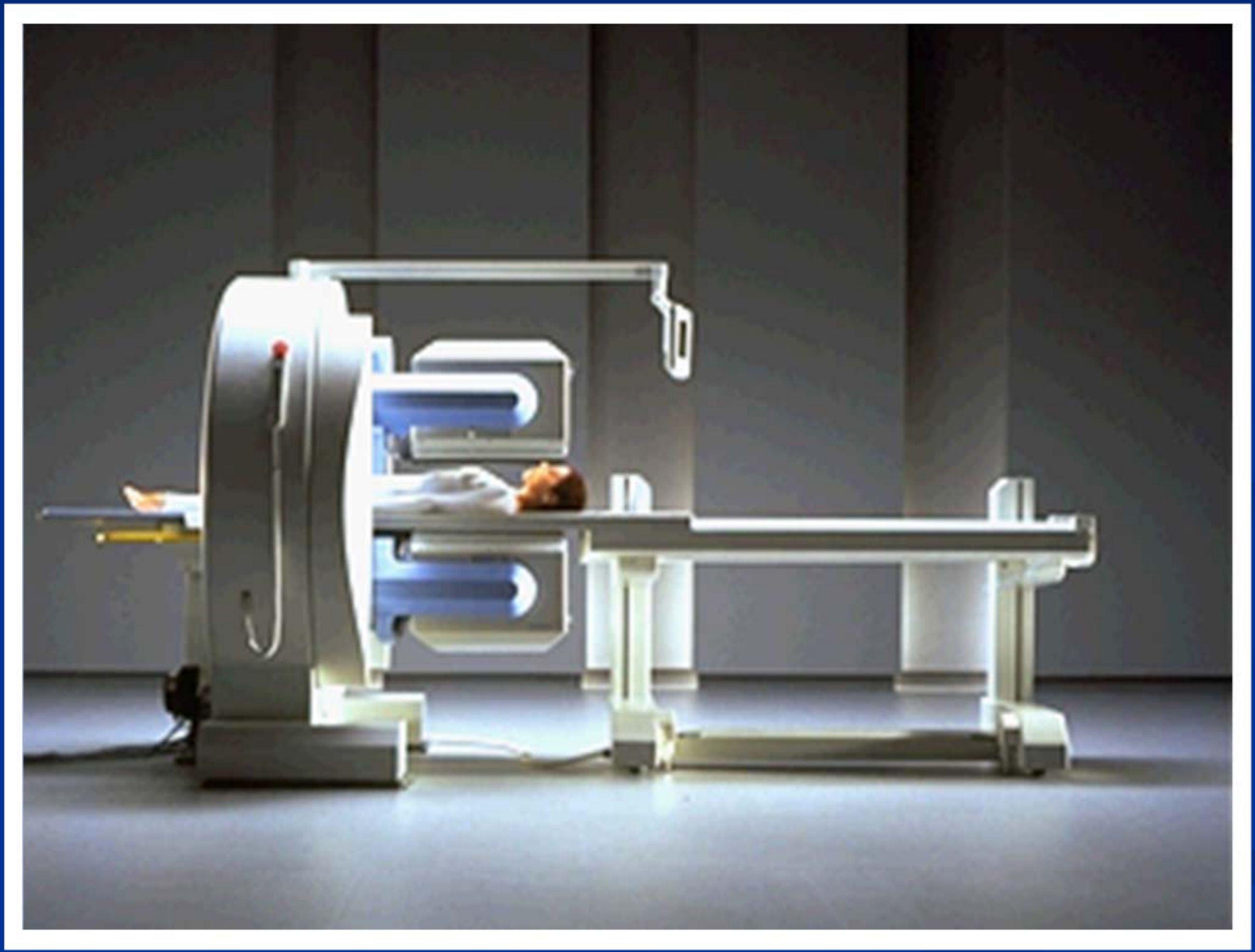
- Single Photon Emission Computed Tomography provides:
  - improved image contrast
  - 3 dimensional information
- SPECT requires additional quality control procedures

Gamma Cameras at the Department of Nuclear Medicine and Endocrinology

- Two single-headed SPECT, 86 photomultipliers
- Dual-headed SPECT, 86 photomultipliers per head
- Hybrid SPECT/CT


scintibed™

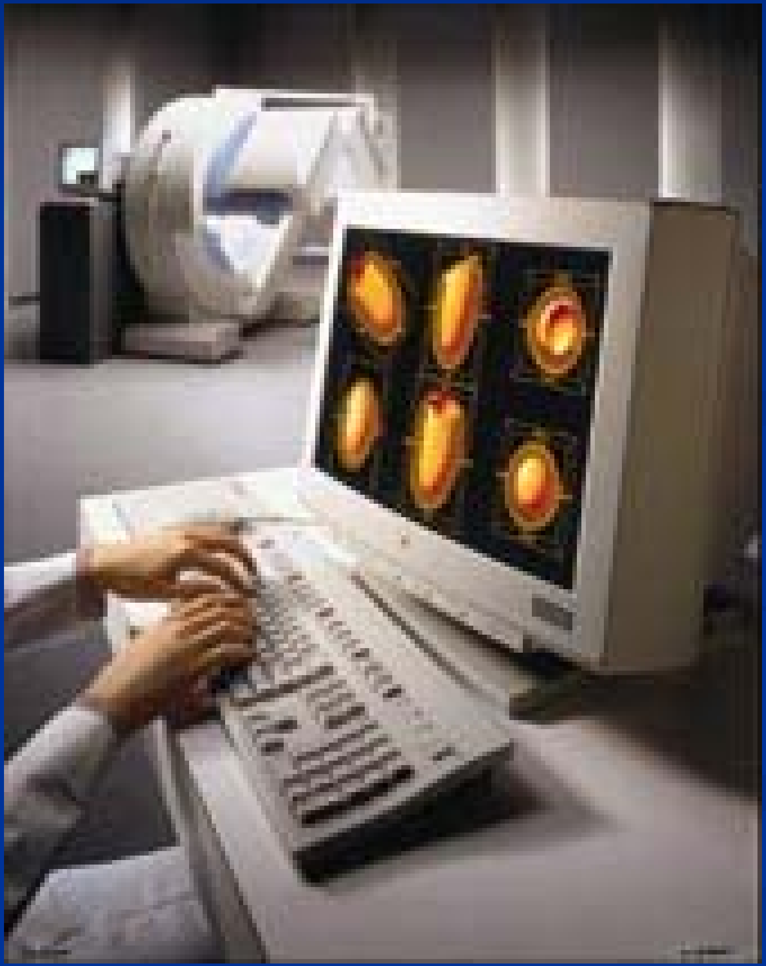
SPECT

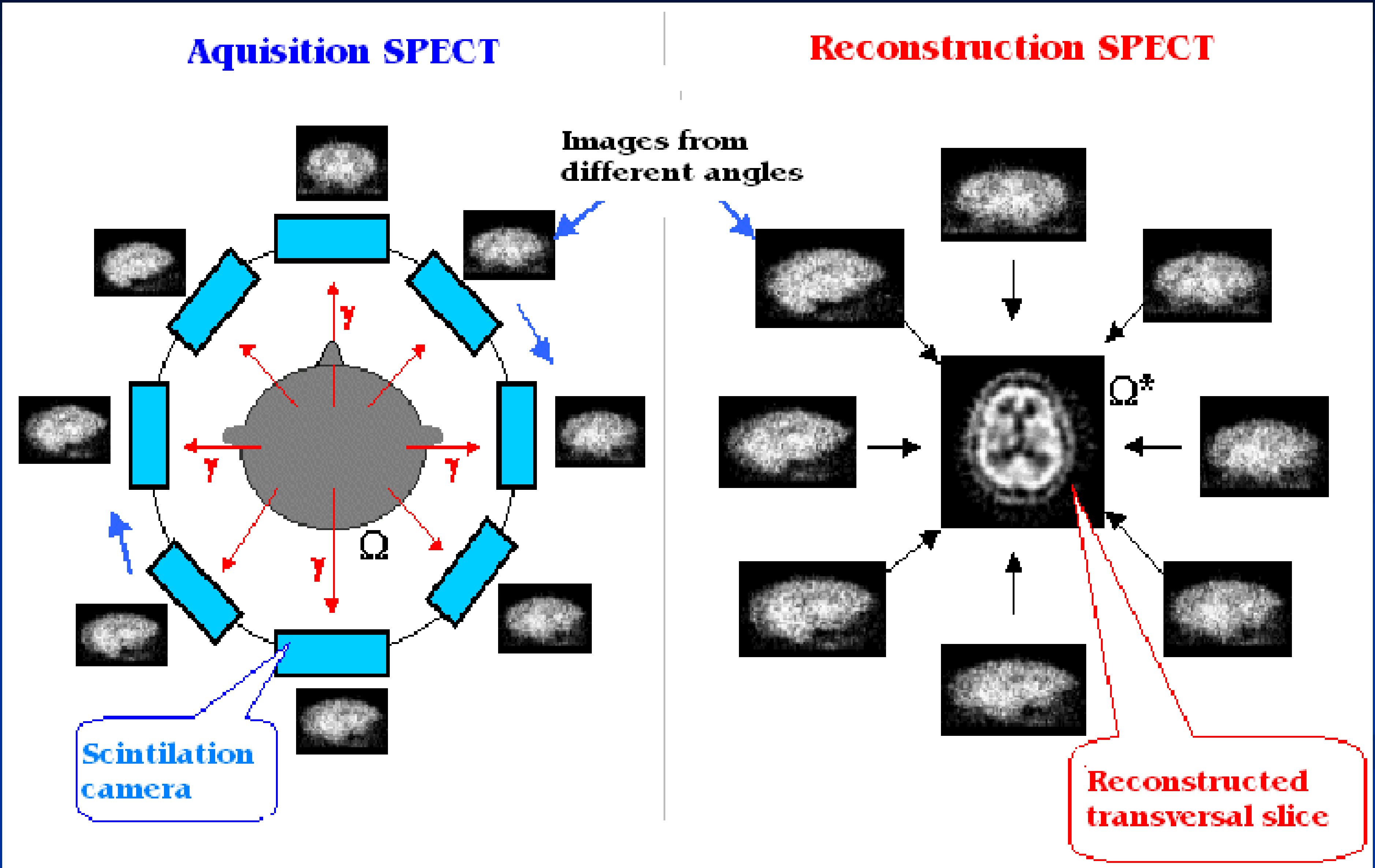


SPECT Image Acquisition and Reconstruction

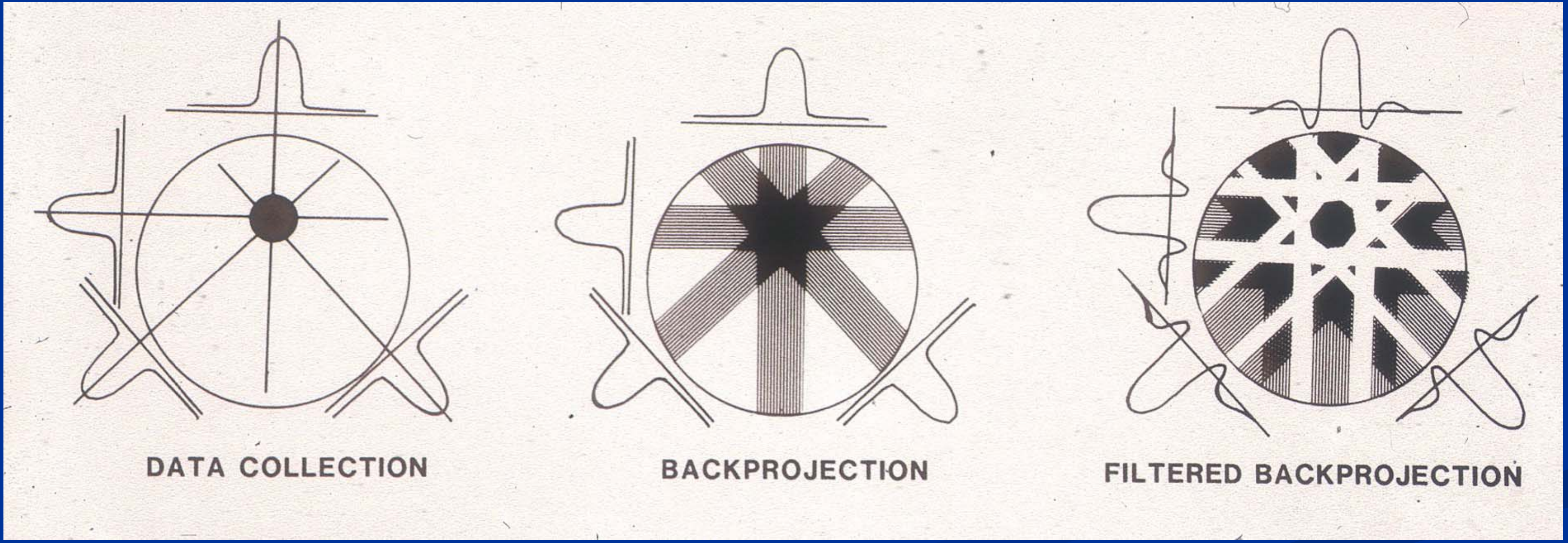
- A series of gamma camera images is acquired as the camera rotates around the patient.
- Typically 60 or 120 images will be obtained in 20 to 30 minutes
- Image reconstruction is usually performed using a technique known as *Filtered Backprojection* to produce a series of transaxial slices.
- Coronal and/or sagittal slices can be computed from the transaxial slices.

Data Analysis is Performed with Computer System

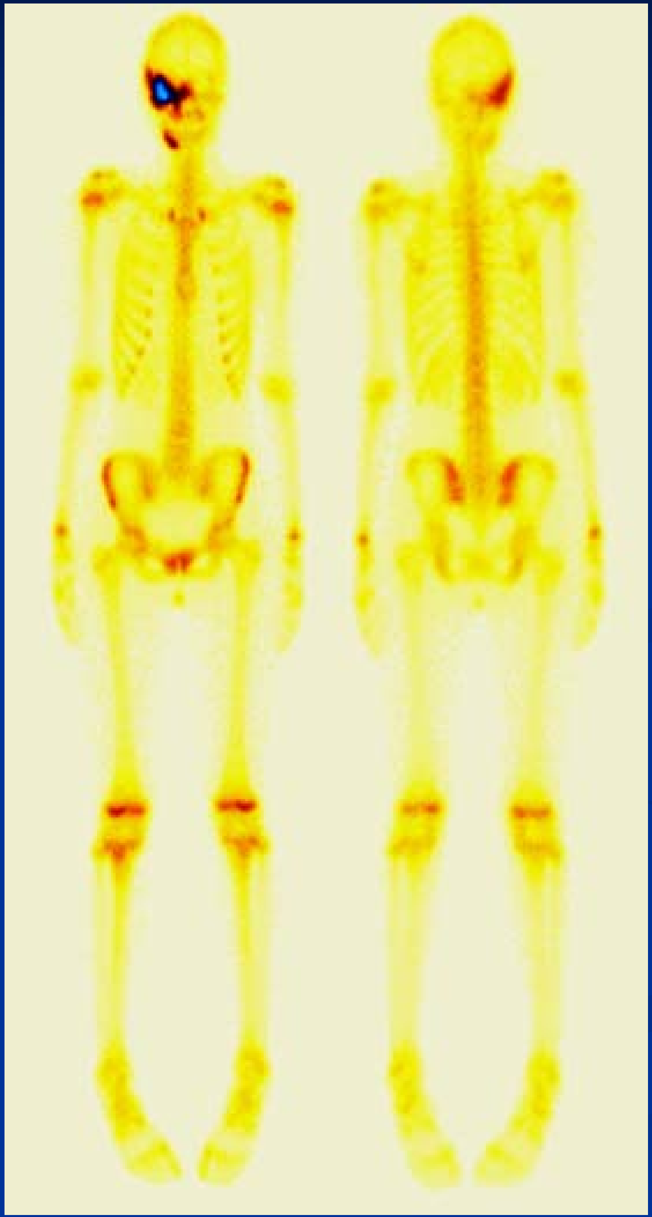



Aquisition SPECT
Reconstruction SPECT
Images from
different angles
γ
Ω
Ω*
Scintilation
camera
Reconstructed
transversal slice

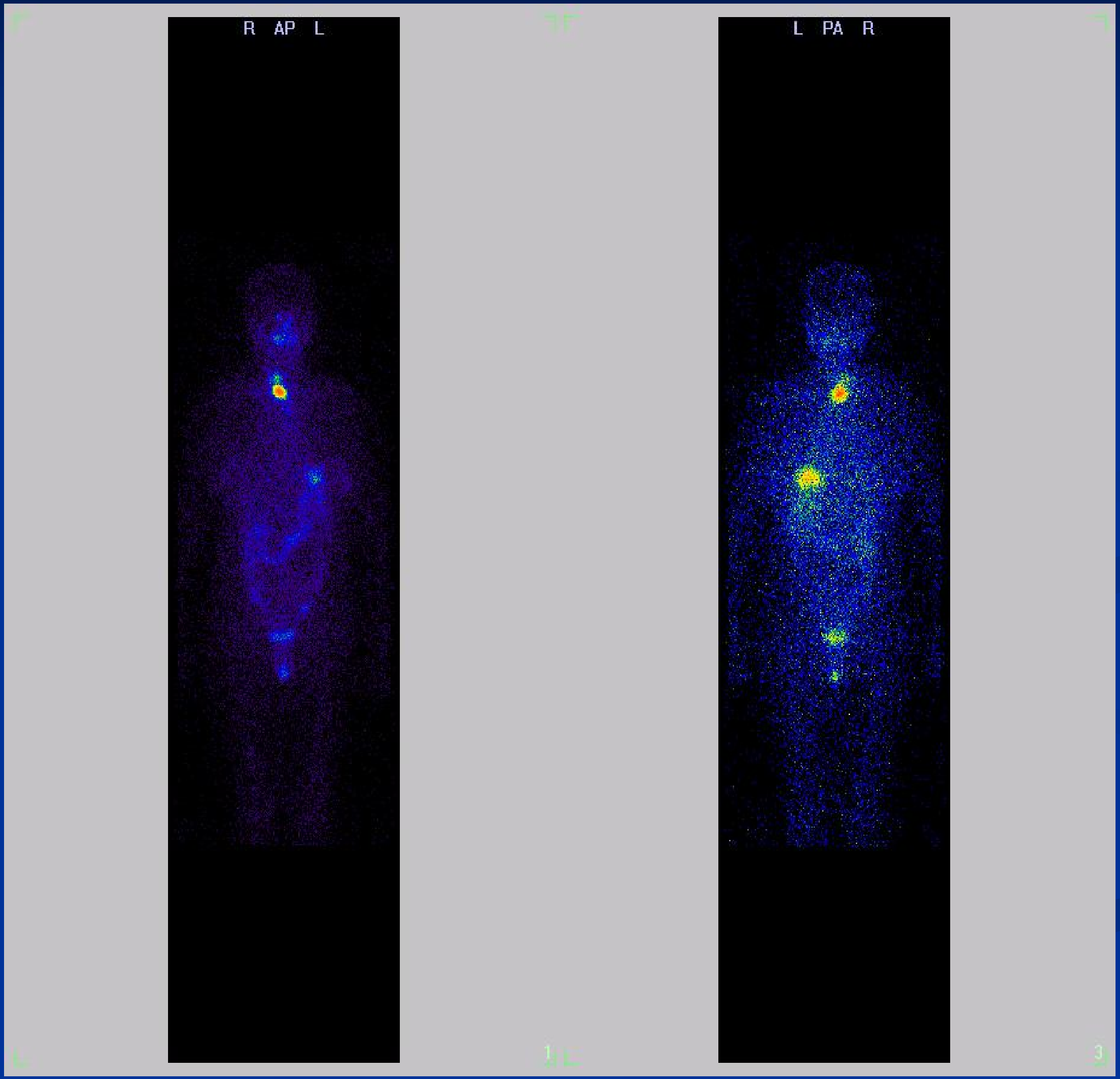
Principle of SPECT Image Reconstruction using Filtered Back Projection



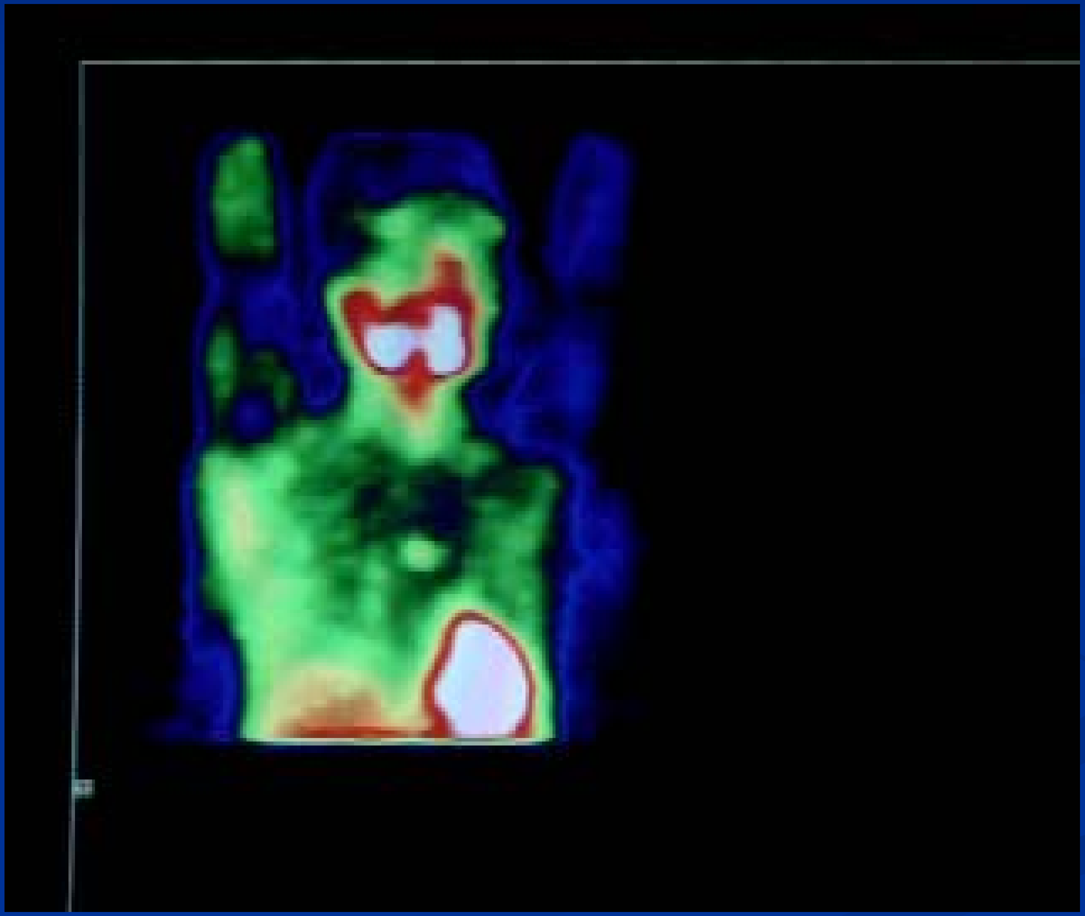
Wholebody SPECT



Wholebody SPECT



SPECT 3D imaging

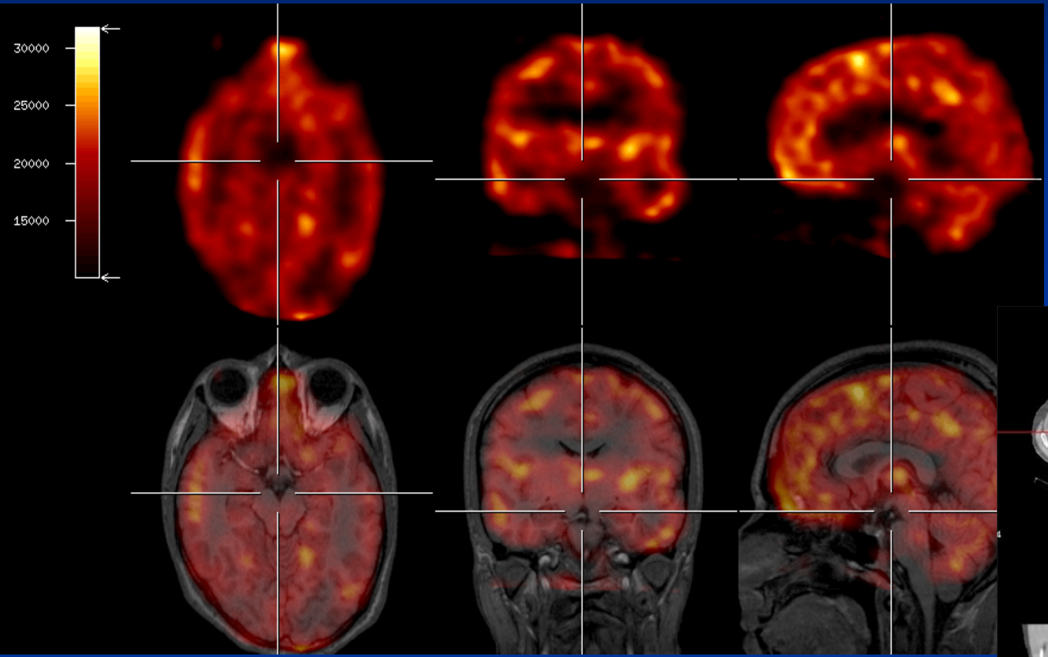


SPECT Quality Control

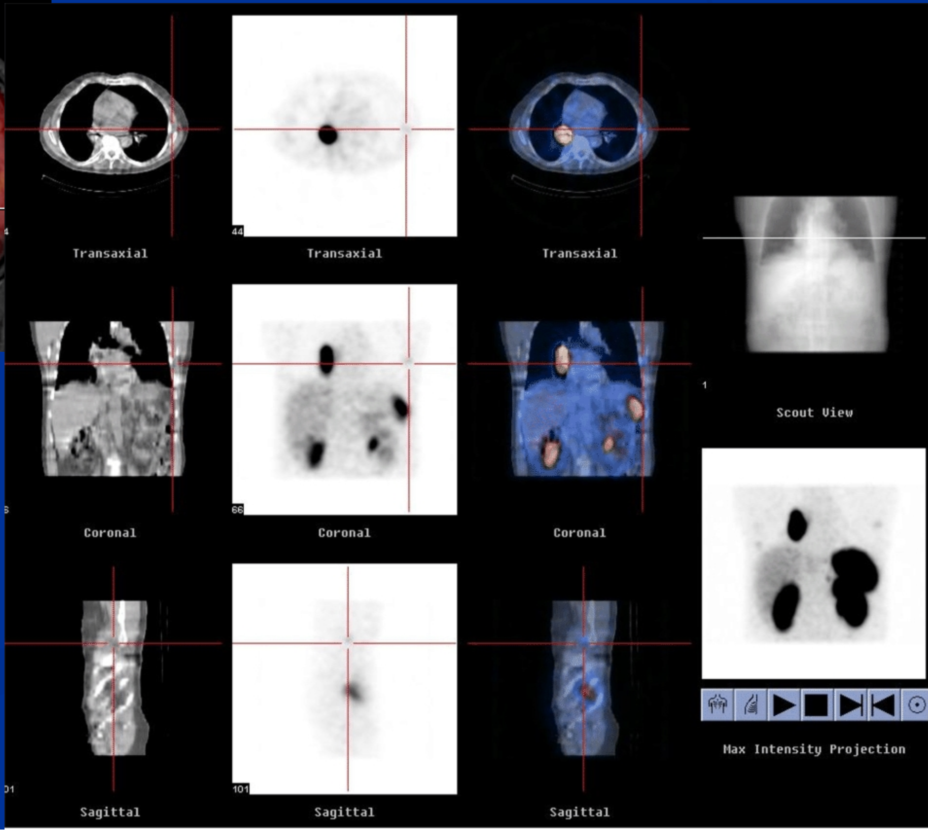
- Strict quality control is essential or significant image artefacts will be produced.
- Planar gamma camera QC must be acceptable, particularly uniformity
- Centre of Rotation (COR) calibration must be performed for each collimator used for SPECT.
- On older SPECT systems checks must be performed for rotational stability
- Overall SPECT performance should be determined, using a SPECT phantom, on acceptance of the camera and after any major service.

Combination SPECT/CT

Imaging SPECT/CT



- Lokalizační diagnostika
- Korekce na atenuaci (při průchodu záření tkání dochází k zeslabení)



Centrum of rotation SPECT/CT

PET Scanning

PET Scanning

POSITRON EMISSION TOMOGRAPHY (PET)

- is an imaging technique, which tracks biochemical and physiological processes in vivo with the aid of tracer compounds labelled with positron-emitting radionuclides intravenously injected to the patient
- belongs to the larger family of functional imaging techniques, complementary in their results to the conventional anatomical ones

The necessary components to perform a PET scan are the following:

- the **SCANNER** - to perform the clinical examination
- the **CYCLOTRON** - to produce the positron-emitter
- the **STANDARD CHEMISTRY SYSTEM** - to create the chemical precursor which will be further processed by
- the **DEDICATED SYNTHESIS UNIT** and the **TRACER LAB EQUIPMENT** - to produce the tracer

PET Scanning

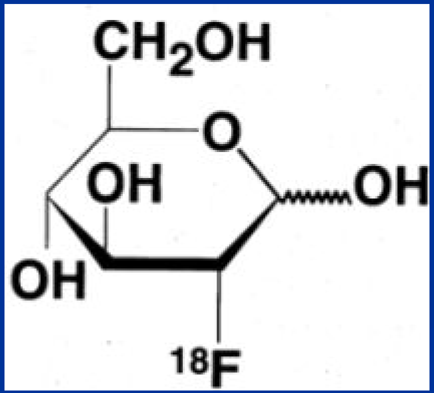
- Used to study physiologic and biochemical processes within the body.
- Processes studies are blood flow, oxygen, glucose and fatty acid metabolism, amino acid transport, pH and neuroreceptor densities.

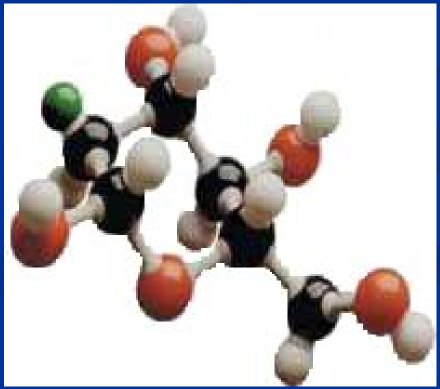
PET Scanning

- PET imaging was based initially on the use of ^{15}O ion labelled to O_2, CO and CO_2. This preference for the ^{15}O ion was mainly due to the fact that the main applications were related to the brain regional oxygen metabolism and blood volume.

PET Scanning

- PET acceptance was boosted by the development of *18F* labelled 2-fluorodeoxy-D-glucose (shortly called FDG) with an optimal half-life of almost 2 hours and its ideal property of giving precise values of energy metabolism not only for the brain or heart but also for other organs.





PET Scanning

- An onsite cyclotron is required to produce the very short lived PET radiopharmaceuticals (Řež, PET Centre Na Homolce).

- PET scanning is, however, in very limited usage because of the high cost of setting up a PET department.

PET

Pozitronové zářiče

^{18}F	109.8 min	$^{18}O(p,n)^{18}F$ $^{20}Ne(d,\alpha)^{18}F$
^{11}C	20.3 min	$^{14}N(n, \alpha)^{11}C$
^{15}O	122 s	$^{14}N(d,n)^{15}O$ $^{16}O(p,pn)^{15}O$
^{13}N	9.96 min	$^{16}O(p,\alpha)^{13}N$ $^{13}C(p,n)^{13}N$

Production of ^{18}F

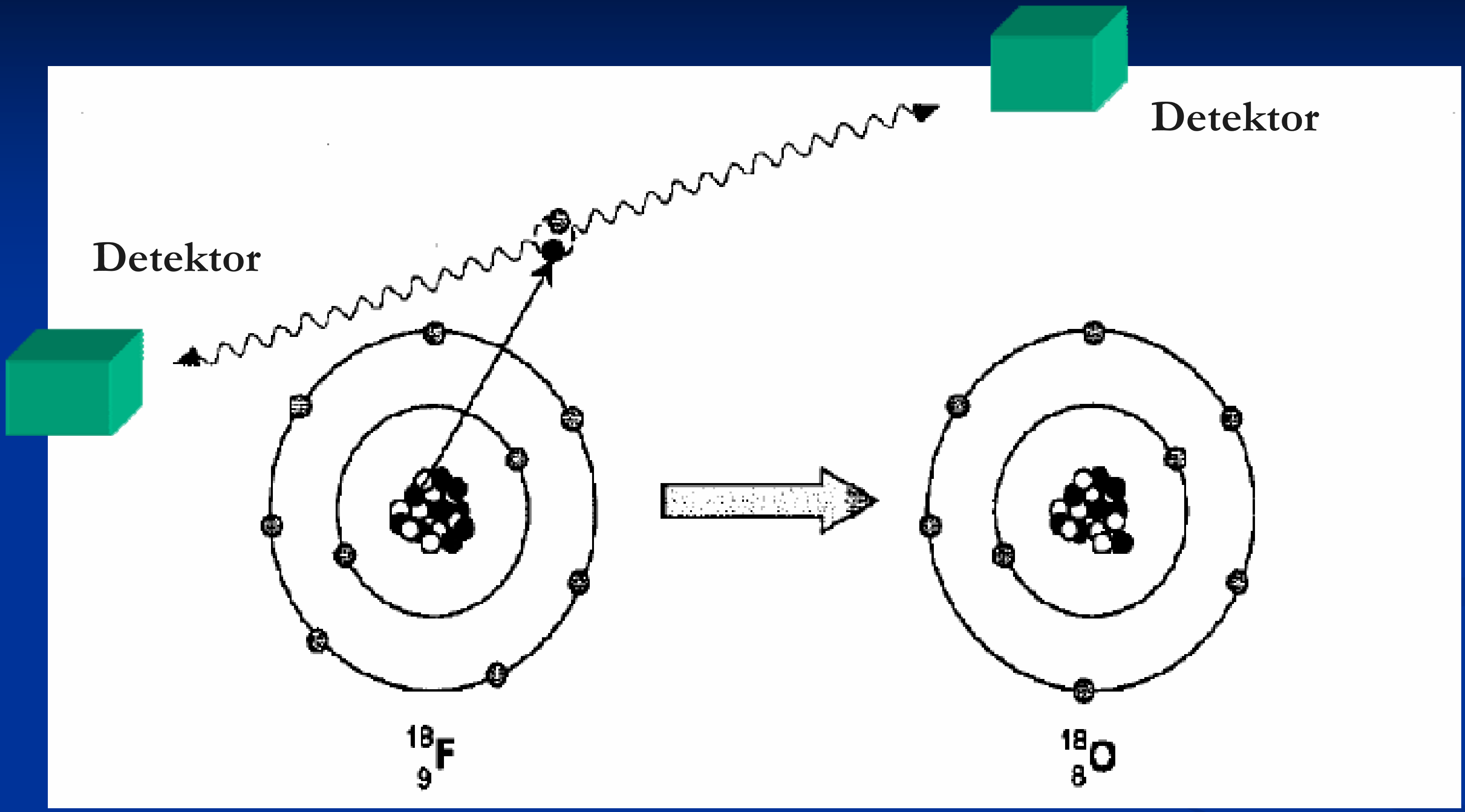
- proton is accelerated in cyclotron
- falls on targed ^{18}O
- p is connected with nucleus of ^{18}O
- from nucleus is catapulted neutron
- oxygen is transformed to ^{18}F

$$^{18}_{8}O + ^{1}_{1}p \rightarrow ^{18}_{9}F + ^{1}_{0}n$$

Cyclotron ÚJF Řež

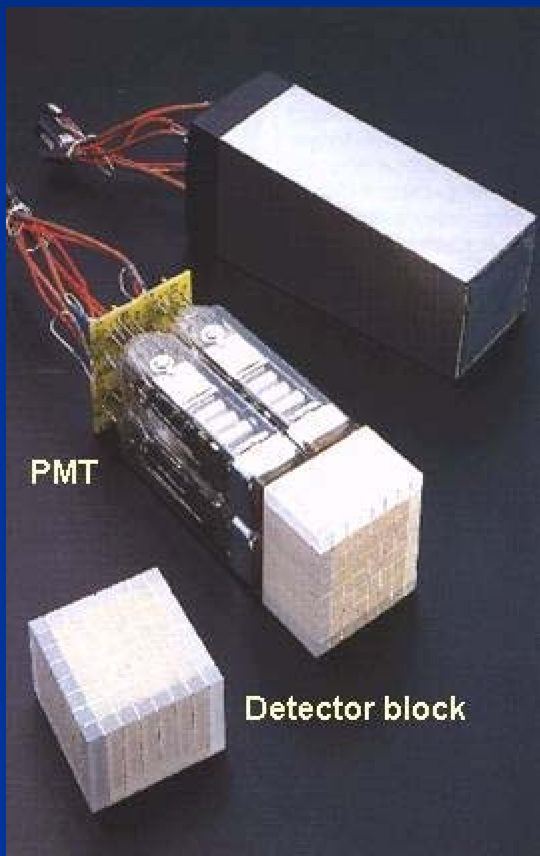
Cyclotron ÚJV Homolka

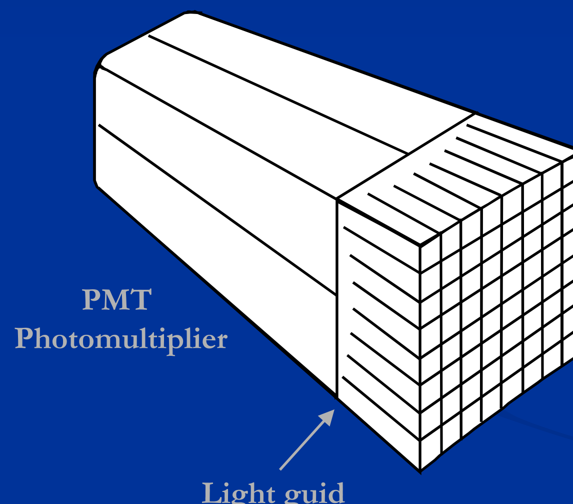
PET – anihilation radiation



$$ {}^{18}_{9}F \rightarrow {}^{18}_{8}O + {}^{0}_{1}\beta^{+} + \upsilon $$

PET – scintilation detectors



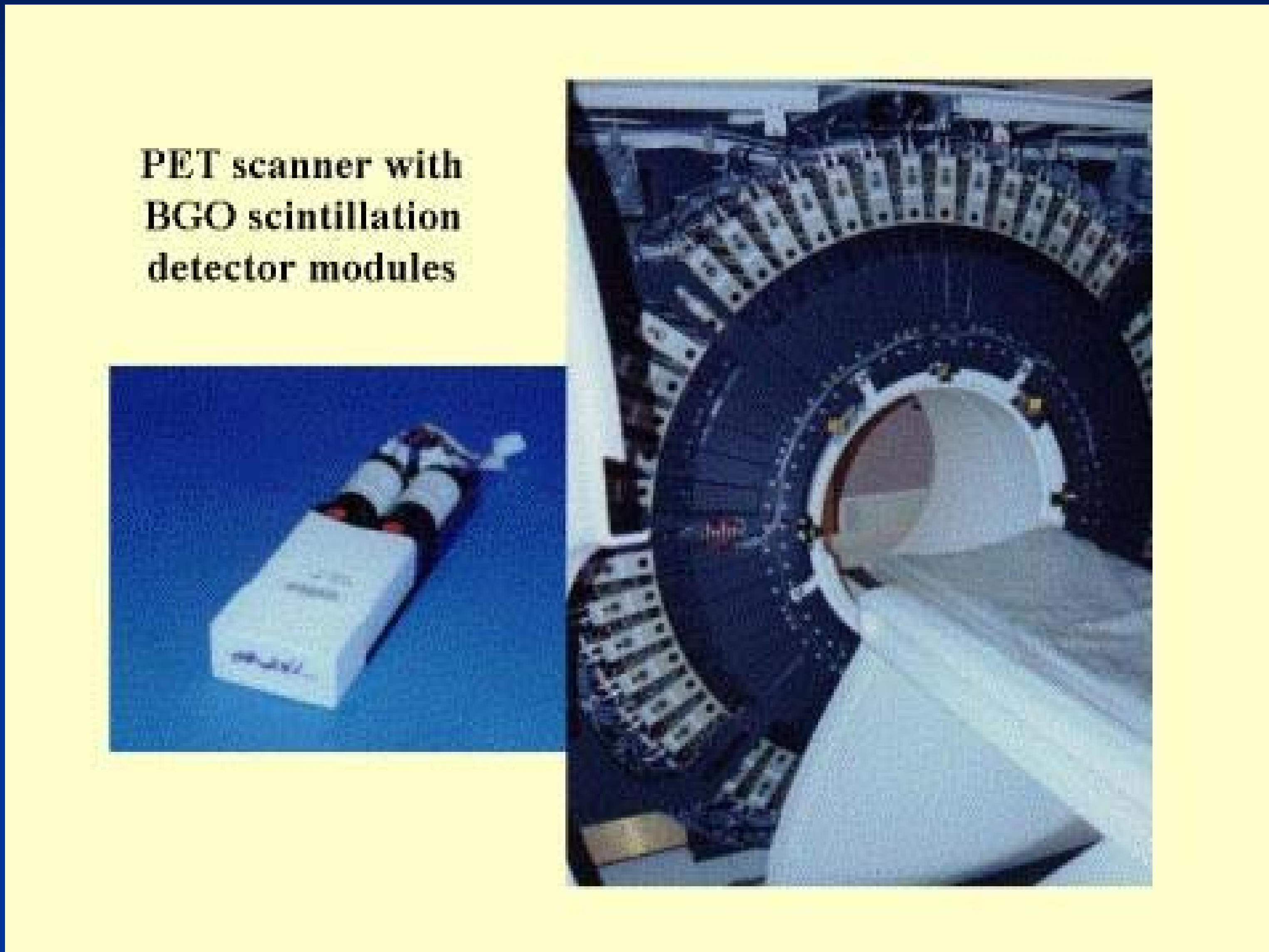


PET Physics:
Used Crystals

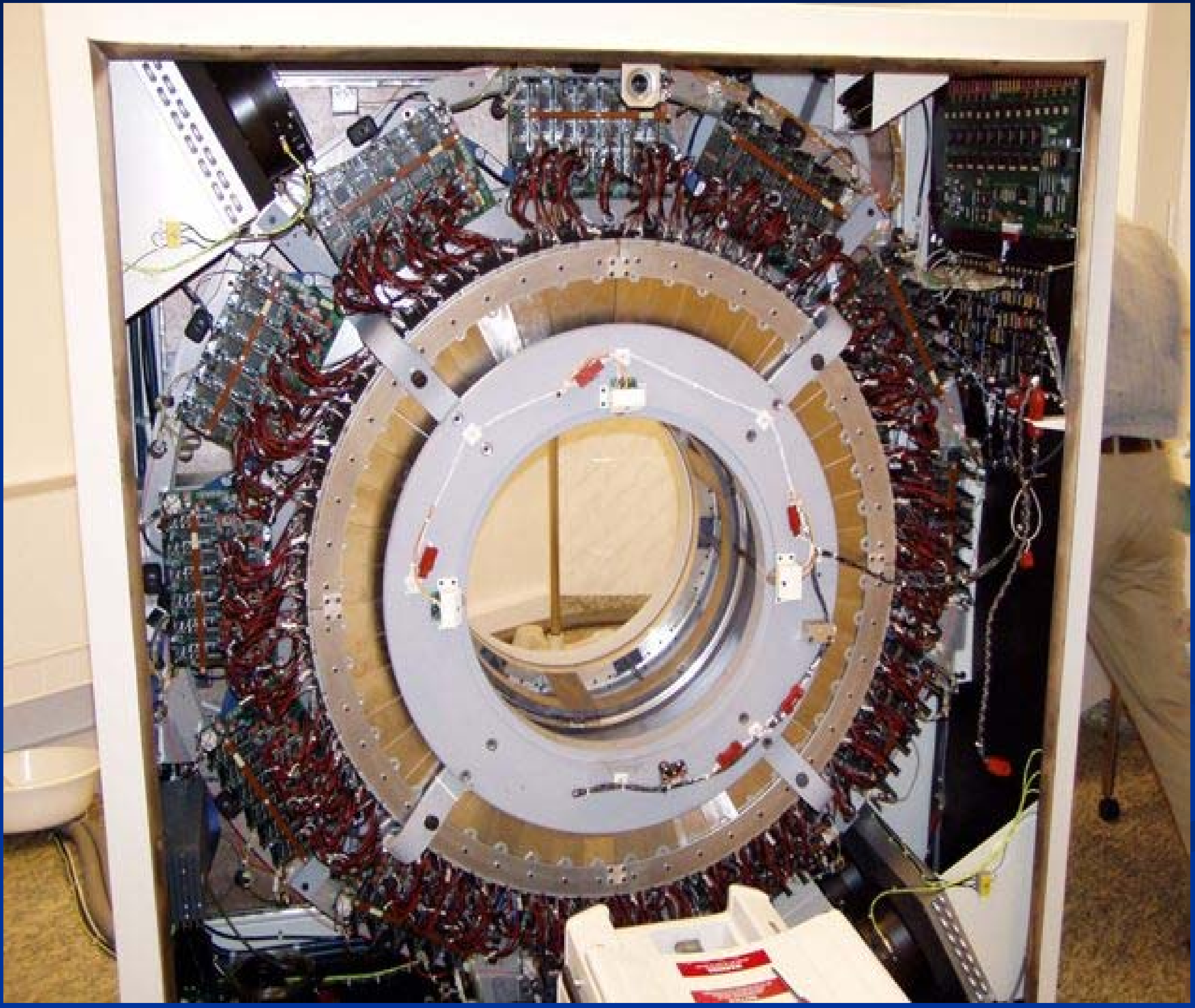
Crystals used in PET are BGO, LSO, GSO, NaI(Tl).

(bismuth germanate, lutetium orthosilicate, gadolinium silicate, GaSiO5, thallium-doped sodium iodine)

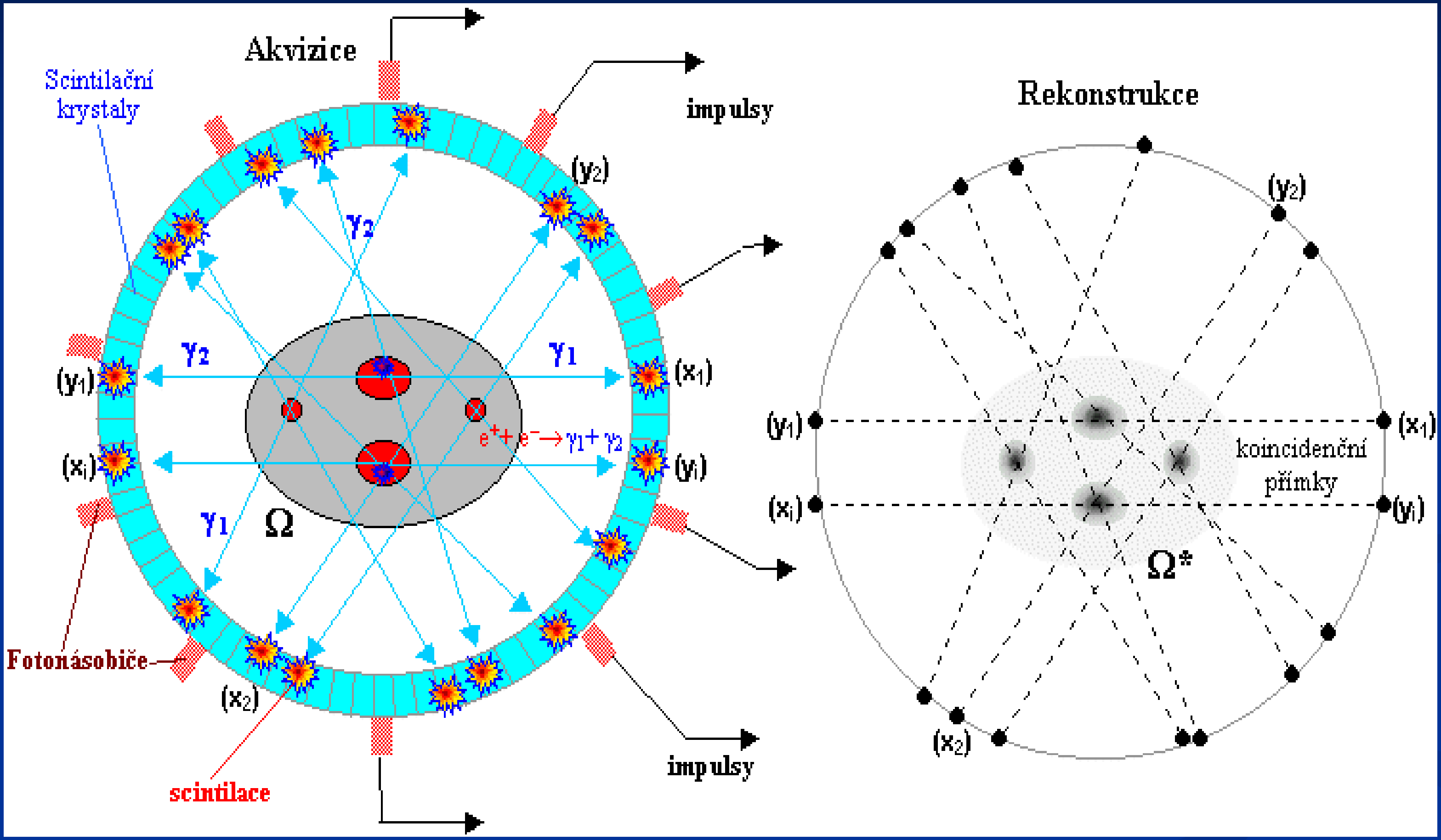
PET – scintilation detectors



PET – scintilation detectors



PET – aquisition and reconstraction



Scintilační krystaly = Scintilation crystals

Akvizice = Aquisition

Rekonstrukce = Reconstraction

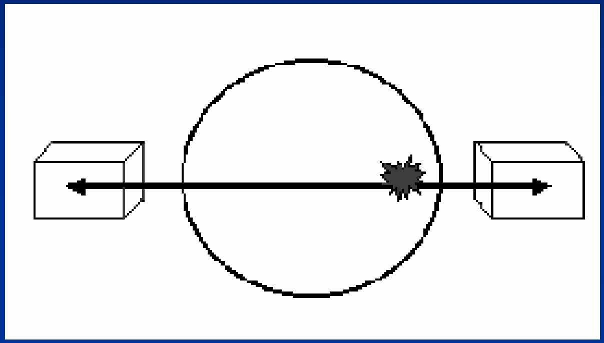
Fotonásobiče = Photomultipliers

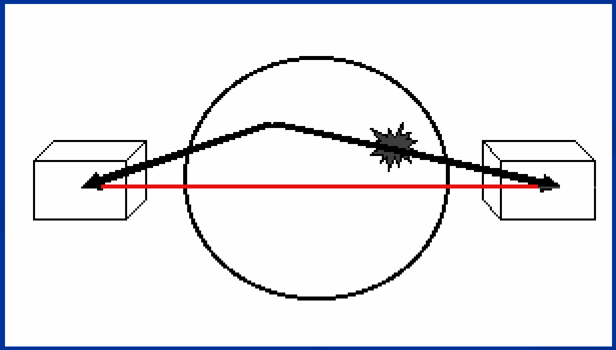
Scintilace = Scintilation

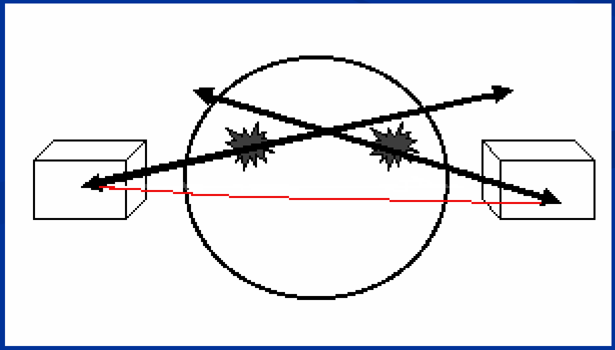
Impulsy = impulses

PET Physics: Coincidence Events

- True Events
- Scatter Events
- Random Events



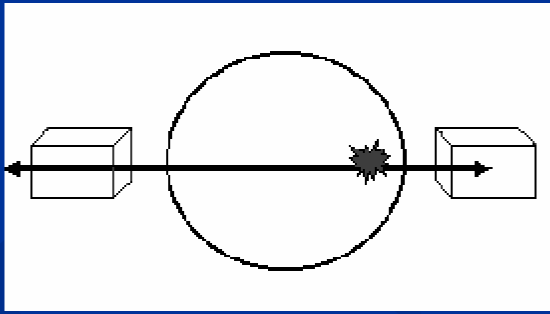




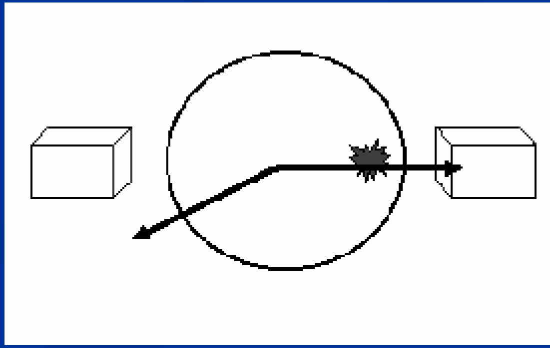
PET Physics:
Single Events

Singles are coincidence events which are lost due to:

Deadtime and sensitivity



Tissue attenuation

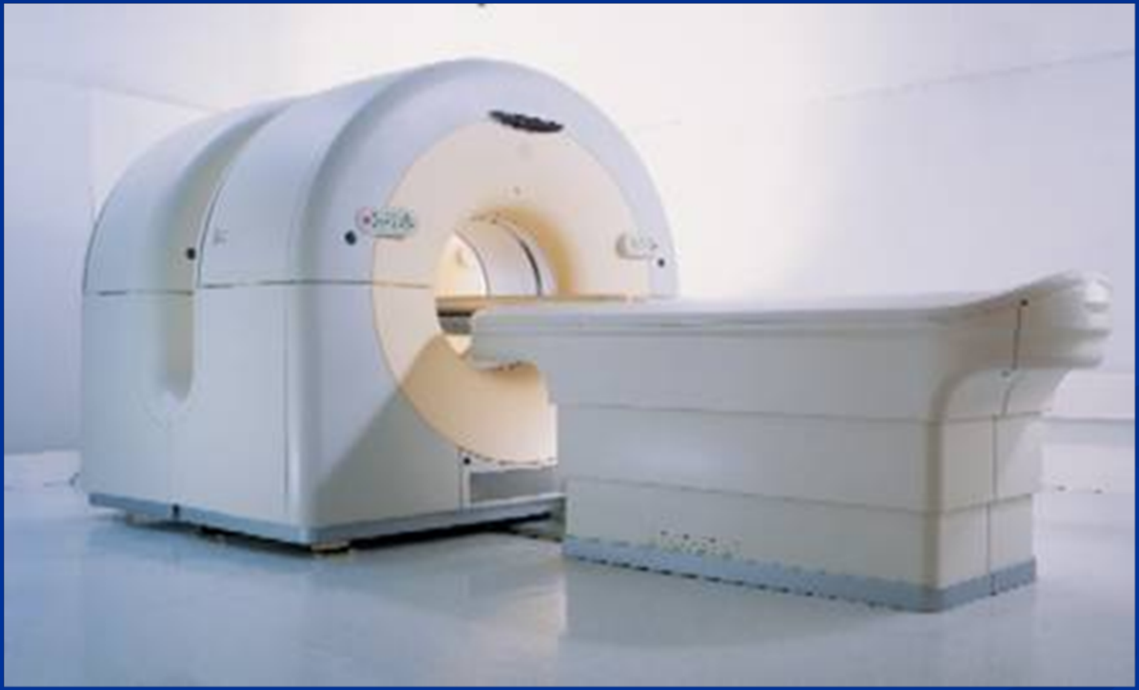


Whole Body PET Imaging

Whole body PET scan of patient with metastatic disease

3D PET Imaging

Combination PET/CT



Whole Body PET/CT Imaging

The limiting spatial resolutions of various medical imaging modilities

Modality	Δ (mm)	Comments
Screen film radiography	0,08	Limited by focal spot and detector resolution
Digital radiography	0,17	Limited by size of detector elements
Fluoroscopy	0,125	Limited by detector and focal spot
Screen film mammography	**0,03**	Highest resolution modality in radiology
Digital mammography	0,05 – 0,1	Limited by size of detector elements
Computed tomography	**0,4**	About 1/2 mm pixels
NM planar imaging	7	Spatial resolution degrades substantially with distance from detector
SPECT	7	Spatial. resolution. worst toward the center of cross-sectional image slice
PET	**5**	Better sp. res. than with other nuclear imag. mod.
Magnetic resonance imaging	**1**	Resolution can improve at higher magnetic fields
Ultrasound imaging 5 MHz	0,3	Limited by wavelength of sound

European Association of Nuclear Medicine - Windows Internet Explorer

https://www.eanm.org/

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eLearning in Nuclear Cardiology

European Association of Nuclear medicine

http://www.cbvcp.com/nmrc/

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Welcome to the Nuclear Medicine Research Council website! Spend a few minutes gathering information that can benefit someone's health – maybe even save a life. Your time will be well spent.

The Nuclear Medicine Research Council (NMRC) is a nonprofit organization promoting the beneficial uses of radioisotopes to prevent, diagnose, and treat disease. Radioisotopes are the centerpieces for recent advances in the treatment of cancer. Medical research in nuclear medicine is rapidly discovering improved strategies for fighting many varieties of cancers along with heart disease, arthritis, and other diseases. We are dedicated to raising awareness about these exciting medical treatments.

The NMRC brings together professionals and citizens from government, education, and industry. It provides opportunities for growing understanding and partnership so that the most promising nuclear medicine technologies can be effectively delivered to the people who need it most.

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Last Updated - September 21, 1999
Send questions and comments to:
Robert E. Schenter at re_schenter@webtv.net

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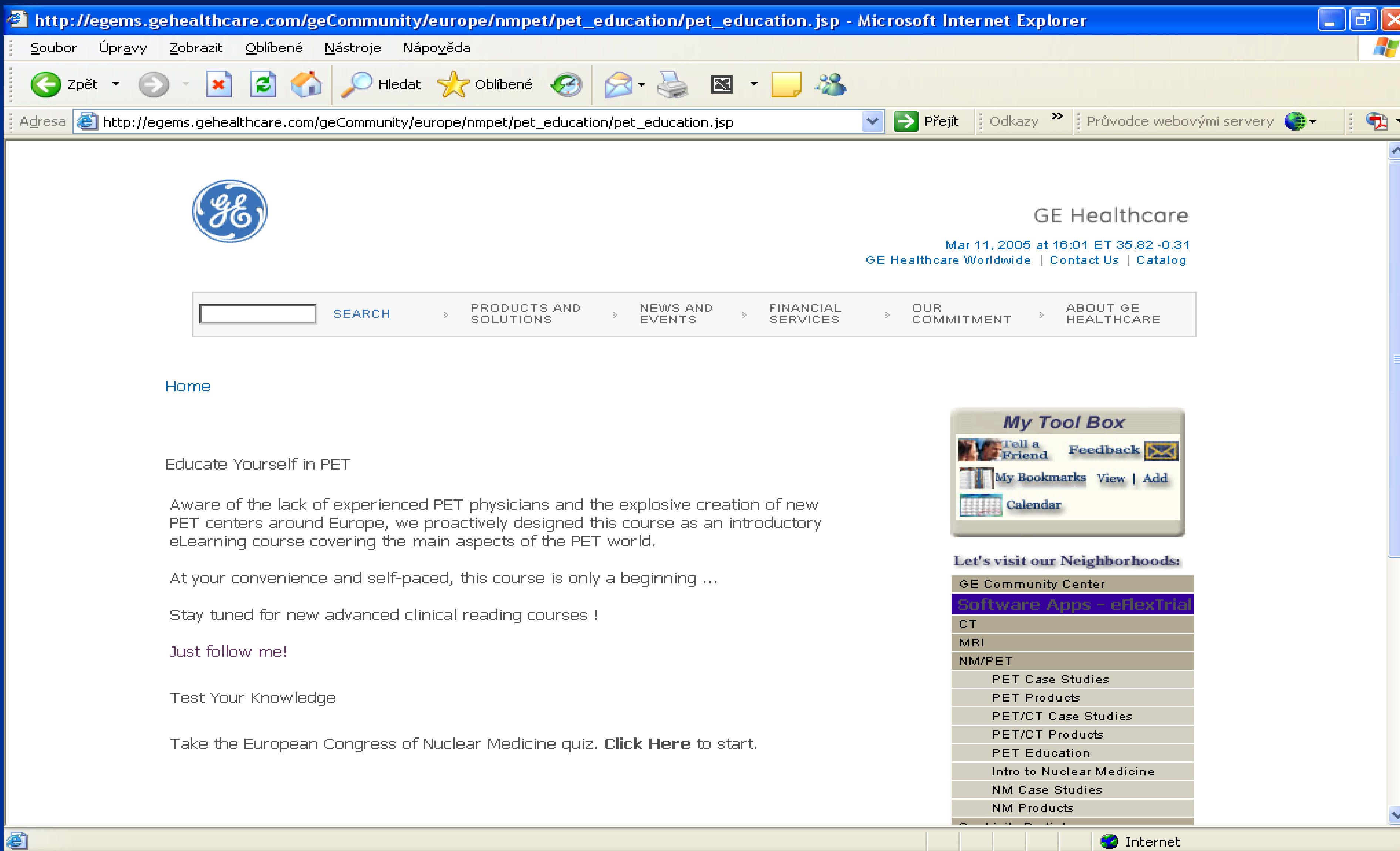

The End