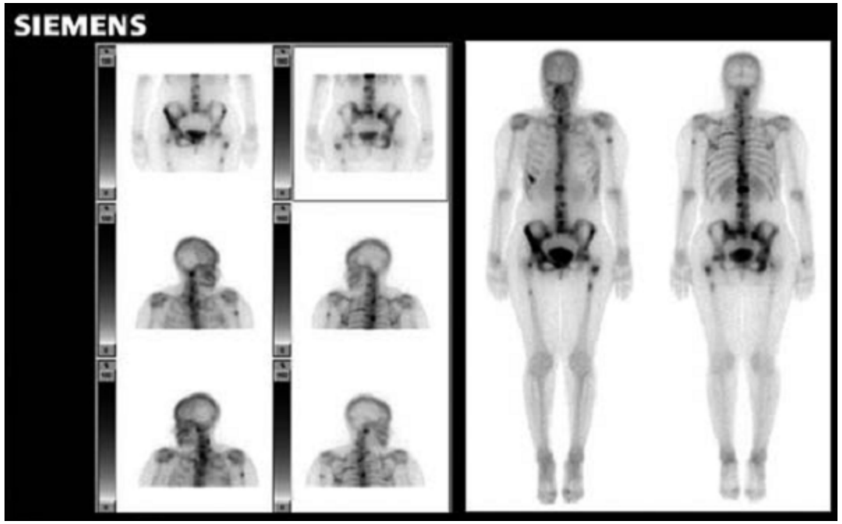
Medicina nuclear ("molecular imaging")

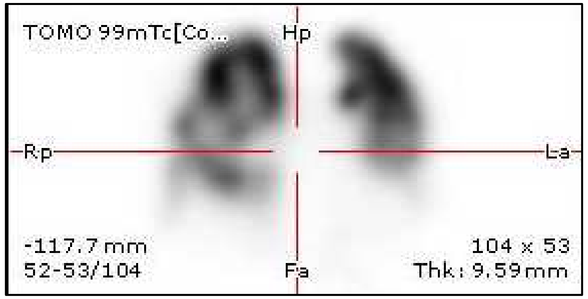
Ideia fundamental: injectar no paciente uma molécula bioactiva e radioactiva

- A molécula vai participar nos processos biológicos para os quais tem afinidade e vai acumular radioactividade nos locais onde esses processos são mais activos
- A detecção exterior da distribuição de actividade no paciente permite revelar a intensidade do processo biológico que se pretende estudar.
- Revela-se a função e não a anatomia.

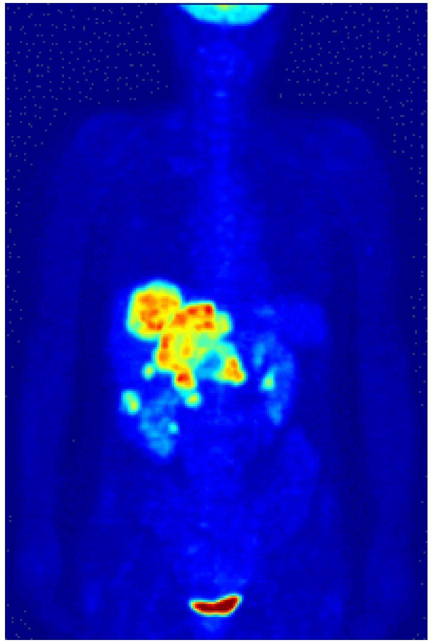
Cintigrafia



SPECT



PET



Imagiologia funcional vs. anatómica

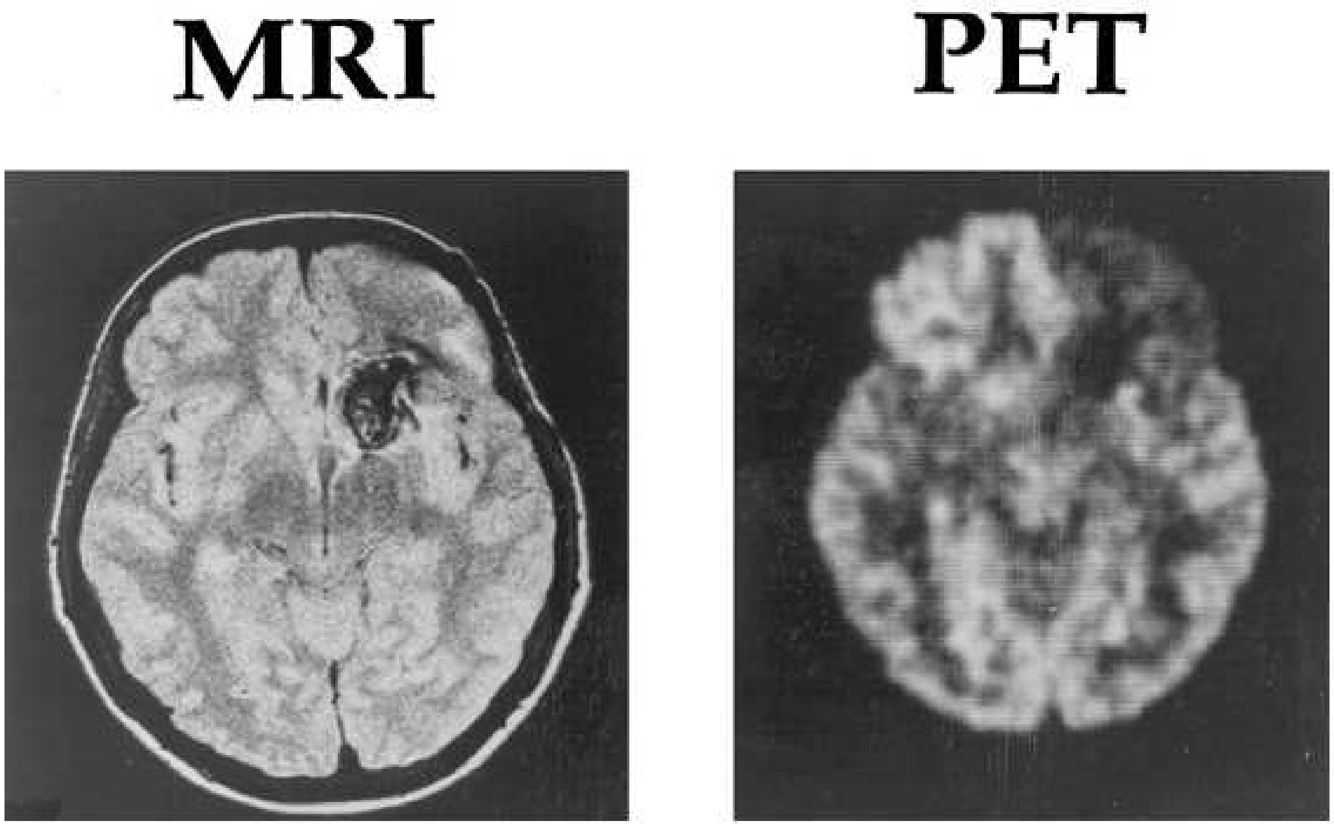


FIGURE 67.4 The MRI image shows the arteriovenous malformation (AVM) as an area of signal loss due to blood flow. The PET image shows the AVM as a region devoid of glucose metabolism and also shows decreased metabolism in the adjacent frontal cortex. This is a metabolic effect of the AVM on the brain and may explain some of the patient's symptoms.

fonte: http://www.iba-cyclotron-solutions.com/products-cyclo

Radioisótopos

Table 10.2 Principal Characteristics of Most Commonly Used Radioisotopes for Emission Imaging

Radioisotope	Half-life	Decay	Gamma energy used for imaging (keV)	Production
^{99m}Tc	6.02 h	IT	140	Generator
^{201}Tl	73 h	EC	70, 169	Cyclotron
^{111}In	68 h	EC	170	Cyclotron
^{131}I	8.04 d	β^-	362	Fission product
^{123}I	13.2 h	EC	158	Fission product
^{133}Xe	5.25 d	β^-	80	Fission product
^{67}Ga	78.3 h	EC	93, 185, 300	Cyclotron
^{81m}Kr	13 s	IT	190	Generator
^{18}F	110 m	β^+	511	Cyclotron
^{15}O	2.1 m	β^+	511	Cyclotron
^{13}N	10 m	β^+	511	Cyclotron
^{11}C	20.4 m	β^+	511	Cyclotron
^{82}Rb	1.3 m	β^+	511	Generator

IT: Isomeric transition; EC: Electron capture. Fonte: ref 6

há muitos mais…

cintigrafia/SPECT

PET

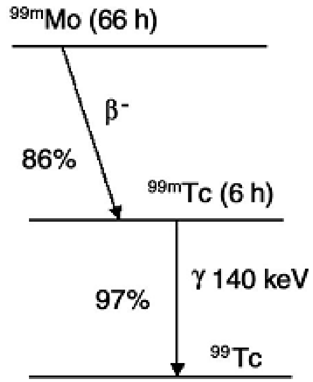
Cintigrafia: imagem planar (projectada)

SPECT: Single Photon Computed Emission Tomography

PET: Positron Emission Tomography

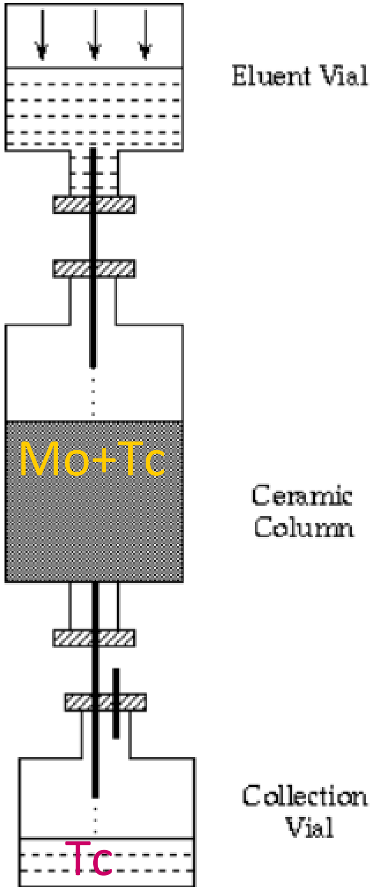
Gerador de ^{99}Mo/ ^{99}Tc (o mais comum em MN – “milking cow”)

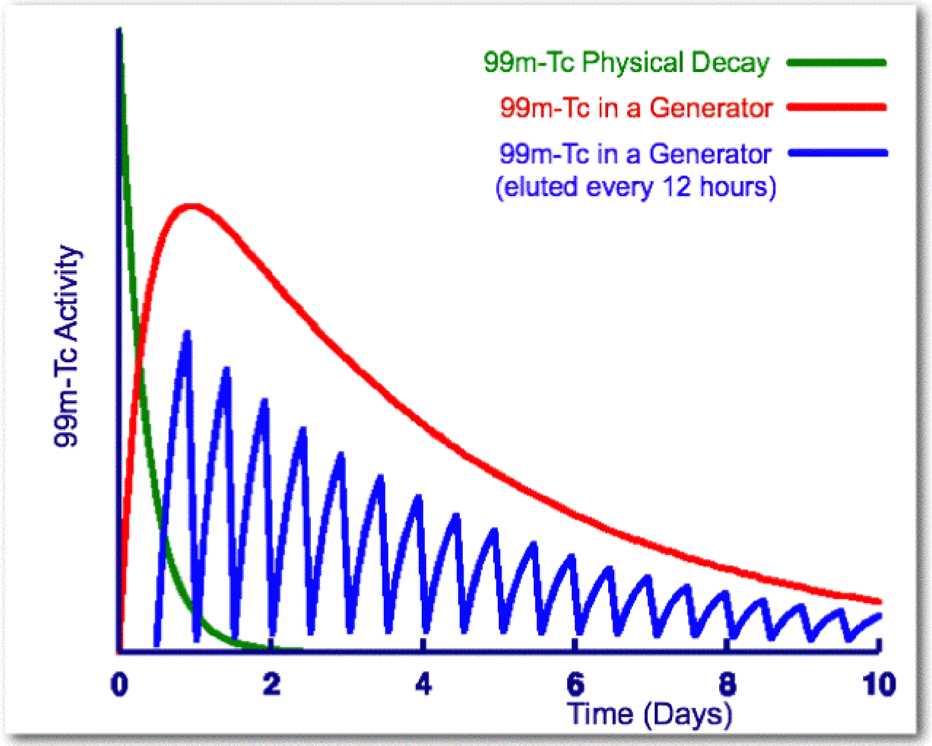
$$ {}^{99}_{42}Mo \xrightarrow{\tau_{1/2}=66h} {}^{99m}_{43}Tc + \beta^- \xrightarrow{\tau_{1/2}=6.0h} {}^{99g}_{43}Tc + \gamma(140keV) $$



O ^{99}Mo é separado quimicamente do combustível usado de centrais nucleares e incorporado num material cerâmico.

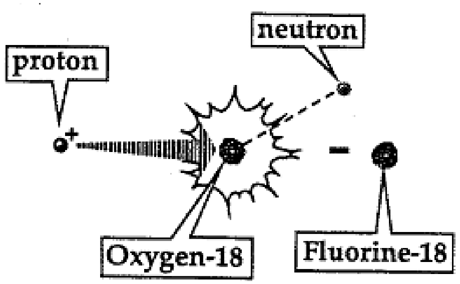
O Tc produzido é separado do Mo por lavagem (eluição).





Aceleradores

Exemplo de acelerador para produção de radioisótopos

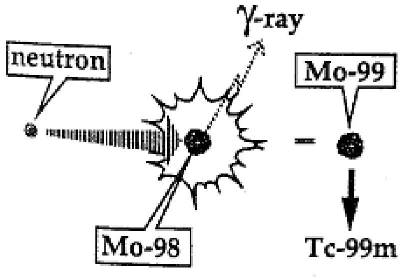


$$^{12}C \xrightarrow{\text{proton}} {}^{11}C + \text{proton} + \text{neutron}$$
$$^{14}N \xrightarrow{\text{proton}} {}^{11}C + {}^{4}_{2}He$$
$$^{16}O \xrightarrow{\text{proton}} {}^{11}N + {}^{4}_{2}He$$
$$^{13}C \xrightarrow{\text{proton}} {}^{13}N + \text{neutron}$$
$$^{15}N \xrightarrow{\text{proton}} {}^{15}O + \text{neutron}$$
$$^{14}N \xrightarrow{\text{deuterium}} {}^{15}O + \text{neutron}$$
$$^{18}O \xrightarrow{\text{deuterium}} {}^{18}F + \text{neutron}$$
$$^{20}Ne \xrightarrow{\text{deuterium}} {}^{18}F + {}^{4}_{2}He$$

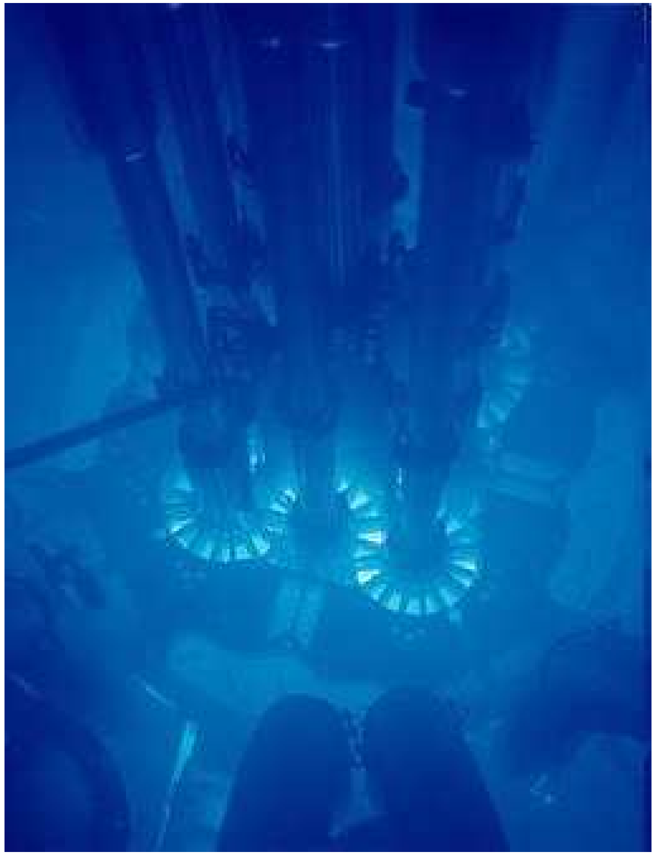
IBA Cyclone 18/10
- iões negativos até 18MeV
- deuterões até 10MeV

fonte: http://www.iba-cyclotron-solutions.com/products-cyclo

Reactores



Exemplo de reactor para produção de radioisótopos



Radiofármacos

TABLE 2.2. ^{99m}Tc **Radiopharmaceuticals and Corresponding Clinical Applications**

Fonte: ref 1

Radiopharmaceutical	Clinical Application
^{99m}Tc-macroaggregated albumin	Pulmonary perfusion
^{99m}Tc-diphosphonate	Skeletal
^{99m}Tc-glucoheptonate	Brain tumors
^{99m}Tc-sulfur colloid	Liver and spleen, sentinel node location
^{99m}Tc-DTPA	Renal, pulmonary ventilation
^{99m}Tc-HMPAO	Brain perfusion
^{99m}Tc-Sestamibi	Myocardial perfusion
^{99m}Tc-MAG_3	Renal

há muitos mais…

Radiofármacos

TABLE 10.3 Radiopharmaceuticals in Nuclear Cardiology Fonte: ref 6

	SPECT (mechanisms)	PET (mechanisms)
Perfusion	^{201}Tl (potassium analogue) ^{99m}Tc-sestamibi (passive diffusion) ^{99m}Tc-tetrofosmin (passive diffusion) ^{99m}Tc-teboroxime (passive diffusion) ^{99m}Tc-furifosmin, Q12 (passive diffusion) ^{99m}Tc-N-NOET (passive diffusion) ^{99m}Tc-albumin microspheres (blood flow)	^{38}K (potassium) ^{15}O water (difusion) ^{82}Rb (potassium analogue) ^{13}N ammonia (metabolic trapping) ^{62}Cu PTSM (lipophilicity)
Viability	^{201}Tl (Na^+-K^+ ATP-ase) ^{99m}Tc-glucarate (cell damage) ^{99m}Tc-nitroimidazole (hypoxia)	^{18}F FDG (fluorodeoxy-D-glucose) ^{13}N L-Glutamate (amino acid metabolism) ^{18}F Misonidazole (hypoxia)
Metabolism	^{99m}Tc-fatty acid ^{123}I-BMIPP (fatty acid) ^{123}I-IPPA, (fatty acid)	^{11}C palmitate (fatty acid metabolism) ^{11}C acetate (oxidative metabolism) ^{11}C (^{13}N) amino acids (metabolism) ^{18}F FDG (fluoro deoxy-D-glucose) ^{15}O oxygen (oxygen consumption)
Sympathetic Innervation	^{123}I MIBG (norepinephrine analogue)	^{18}F metaraminol (adrenergic neuron density) ^{11}C-HED, hydroxyephedrine (adrenergic neuron density)
Other	^{111}In platelets (thrombus) ^{111}In antimyosin (cell damage) ^{99m}Tc red blood cells (blood pool) ^{125}I and ^{123}I fibrinogen (thrombus)	^{11}C (^{13}N) amino acids (protein synthesis)

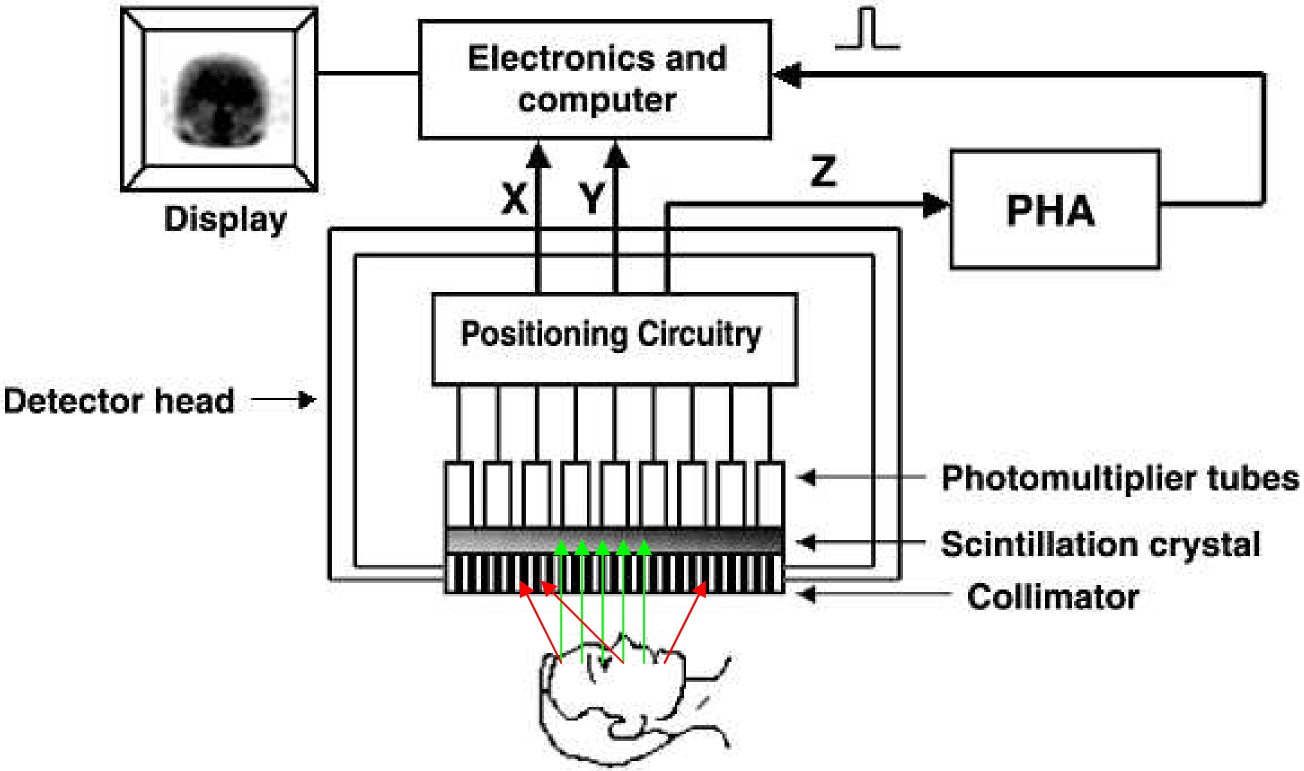
Síntese de radiofármacos

Os radiofármacos são sintetizados em laboratórios automáticos.

Estes devem ser alojados em “células quentes”: contentores isolados que contêm a radioactividade no seu interior.

fonte: http://www.iba-cyclotron-solutions.com/products-cyclo

Princípio da câmara gama



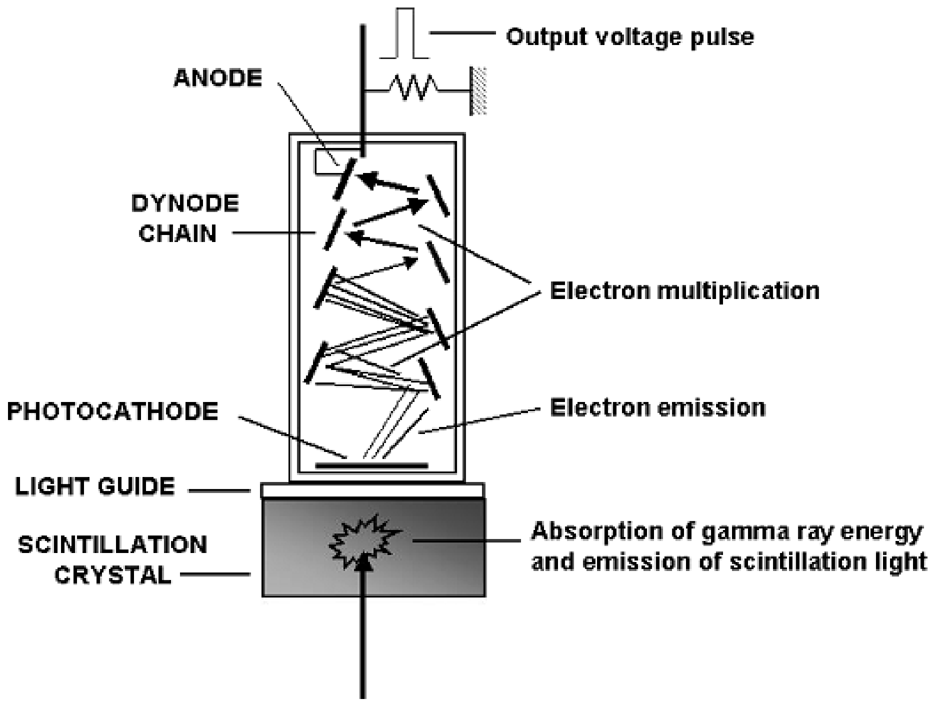
11 Simplified diagram of a gamma camera and its major components.

Fonte: ref 6

O colimador constitui um sistema óptico para raios-X, permitindo a formação de imagem.

Eficiência ~10^{-4}!
Muito ineficaz: a imensa maioria dos fotões são perdidos.

Detecção dos fotões



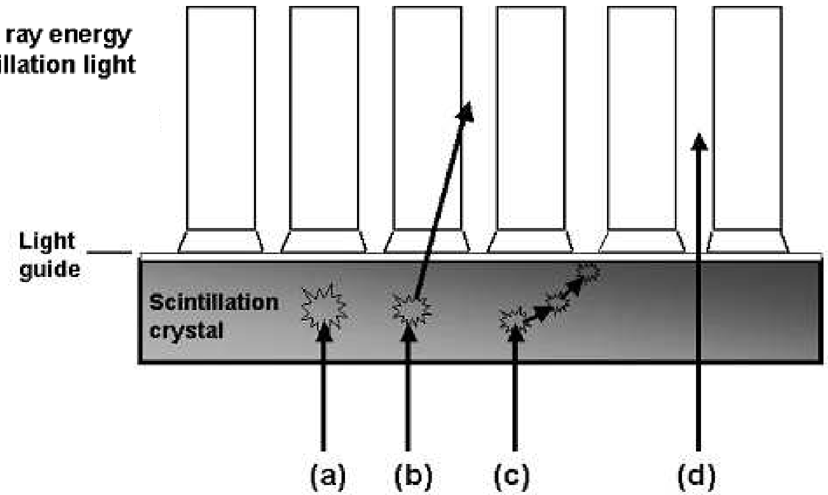
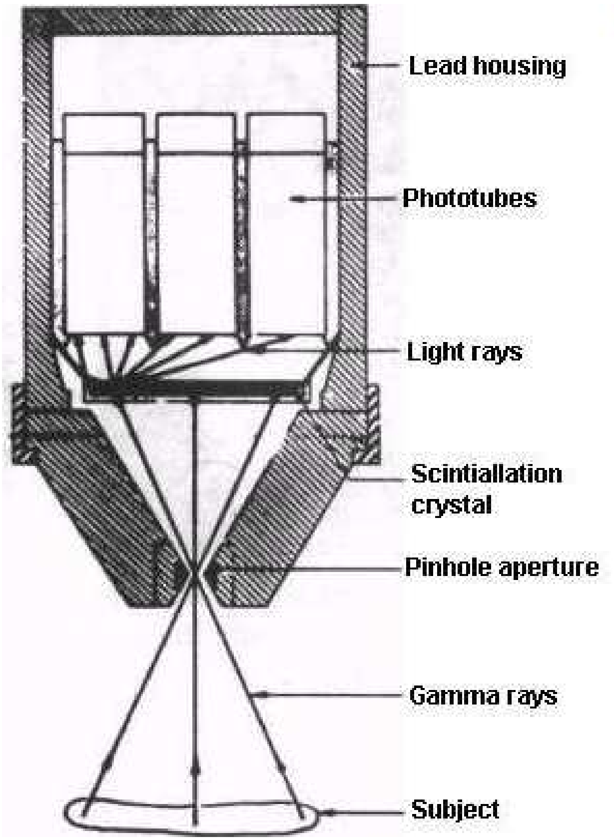
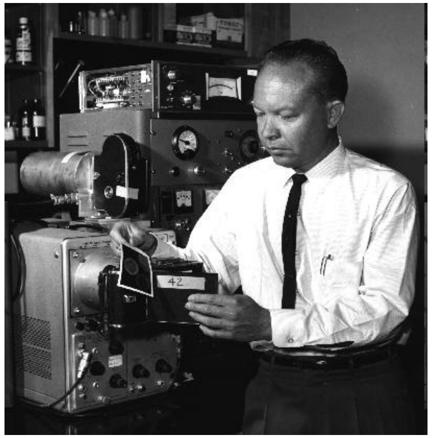


FIGURE 10.15 Probable events during the interaction of a gamma ray with a scintillation crystal: (a) photoelectric absorption, (b) Compton scattering, (c) multiple Compton and a final photoelectric absorption and (d) escape of the gamma ray.

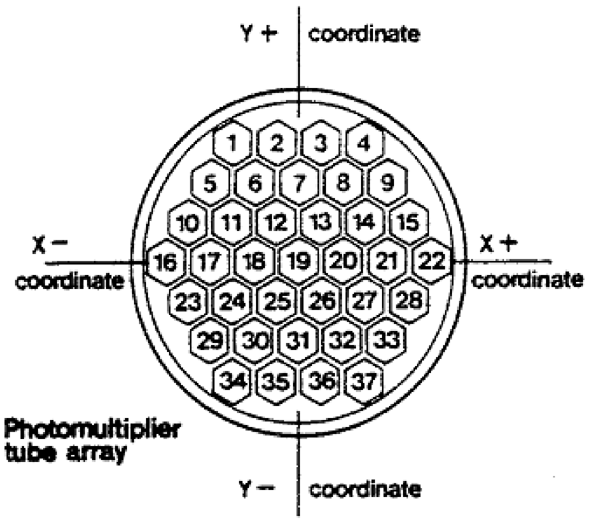
Apontamento histórico: a "câmara Anger"

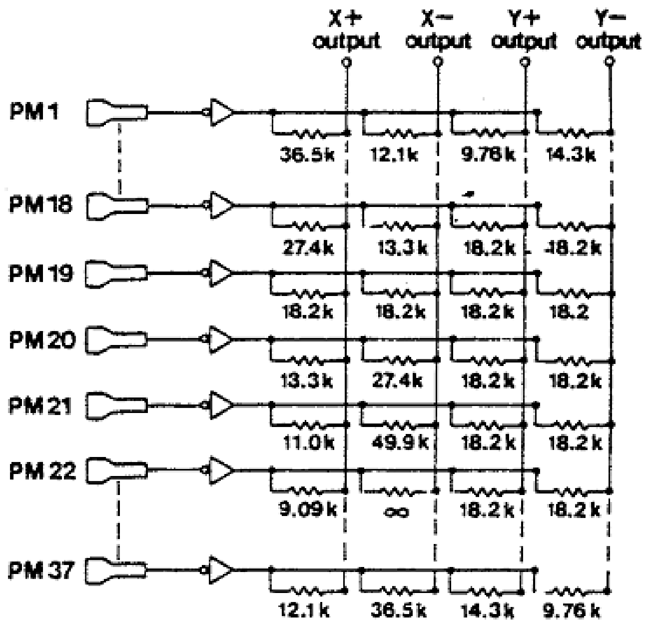
Esquema
da câmara
original de
Harold Anger





Esquema da "lógica de Anger": um esquema simples (ainda usado hoje!) de codificação da posição do sinal de luz na diferença entre dois sinais eléctricos

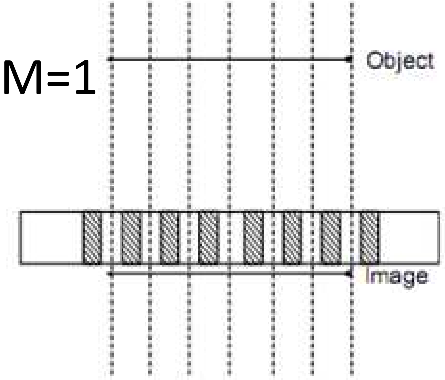




O colimador

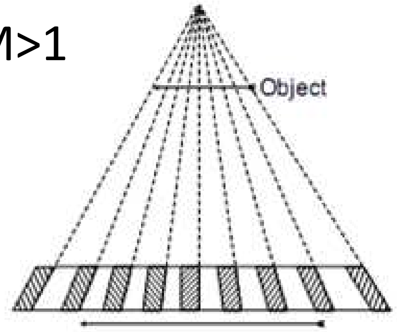
M = ampliação = tamanho da imagem/ tamanho do objecto

M=1



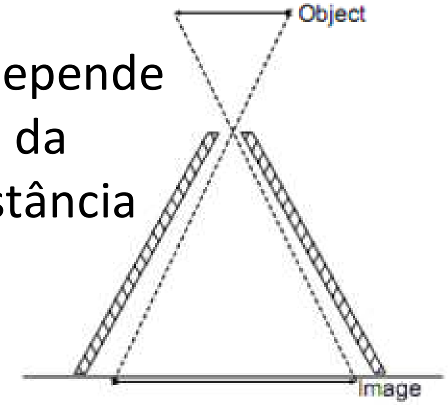
A

M>1



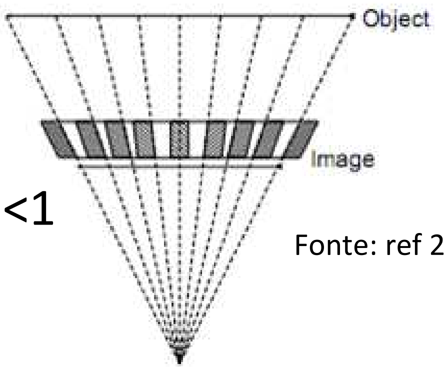
C

M depende da distância



D

M<1



B

Fonte: ref 2

Espectro visível em cristais de NaI

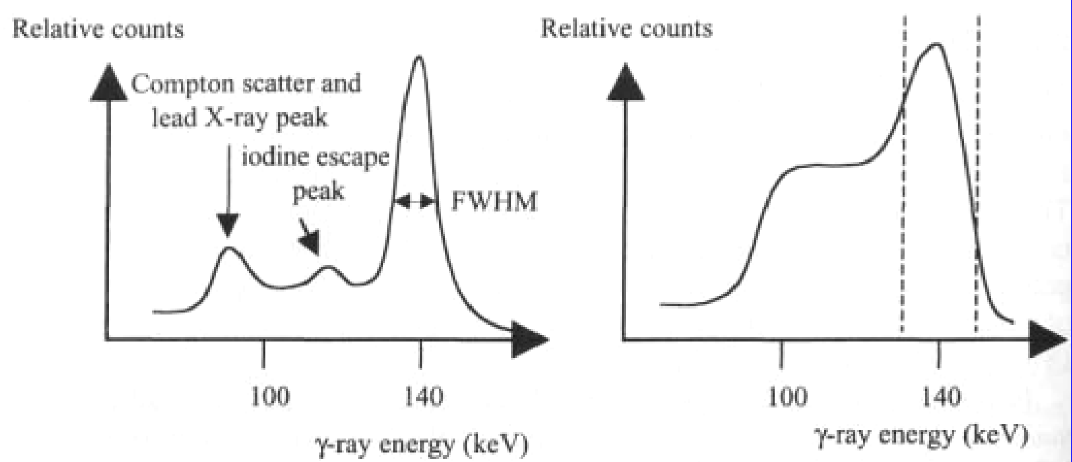
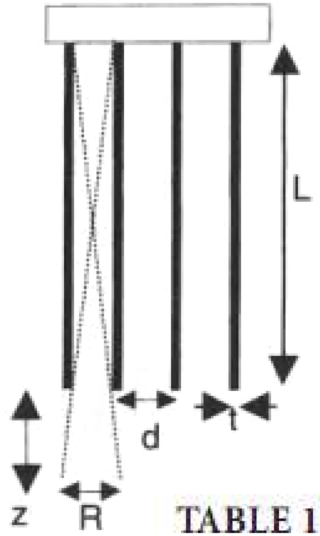


FIGURE 2.9. Energy spectra of ^{99m}Tc γ-rays detected by the scintillation crystal. (Left) The situation when only the gamma camera is used, with no patient. (Right) A broadened spectrum is obtained with the patient in place. The dashed vertical lines represent the range of values accepted by the pulse height analyzer. Fonte: ref 1

O colimador paralelo

Fonte: ref 1



Resolução (separação entre pontos)

$$R = \frac{d(L+z)}{L} \underset{(z \gg L)}{\simeq} \frac{d}{L} z$$

Eficiência geométrica

$$G = k\left(\frac{d^2}{L(d+t)}\right)^2 = k \underbrace{\left(\frac{d}{L}\right)^2}_{\substack{\text{fracção aceite} \\ \text{do ângulo sólido}}} \underbrace{\left(\frac{d}{d+t}\right)^2}_{\approx 1}$$

$$\simeq k\left(\frac{R}{z}\right)^2 \underbrace{\left(\frac{d}{d+t}\right)^2}_{\approx 1}$$

TABLE 10.7 Performance Characteristics of some Typical Parallel Hole Collimators used in Emission Imaging with Gamma Cameras   Fonte: ref 6

Collimator Type	Septa FWHM at 10 cm (mm) From the Collimator	Number of Holes	Maximum Energy (keV)	Geometric Sensitivity (%)
LEHR 7.4 mm	0.15	90,000	140	0.019
LEGP 8.8 mm	0.18	86,000	140	0.024
LEHS 13.4 mm	0.18	82,000	140	0.055
MEGP 12.3 mm	1.14	13,000	300	0.018
HEGP 12.5 mm	1.73	7,000	400	0.017

Note: LEHR: low energy high resolution; LEGP: low energy general purpose; LEHS: low energy high sensitivity; MEGP: medium energy general purpose; HEGP: high energy general purpose.

Cintigrafia

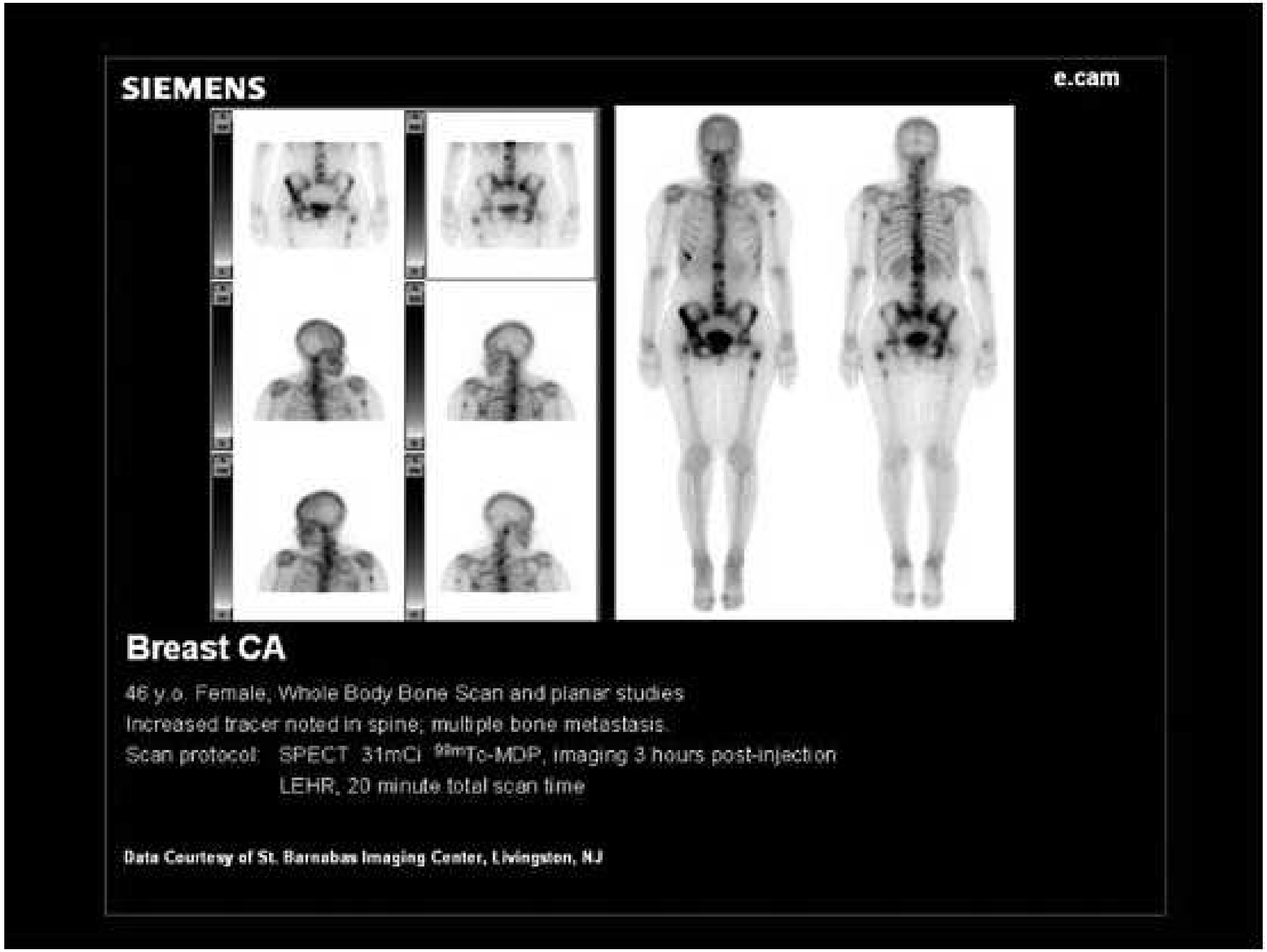


Figure 8. Whole-body image of a bone scan patient using translation of the gamma camera from head to foot. A sample of 20 mCi of ^{99m}Tc-MDP was used as the radiotracer for this image taken at 4 h postinjection.

Cintigrafia

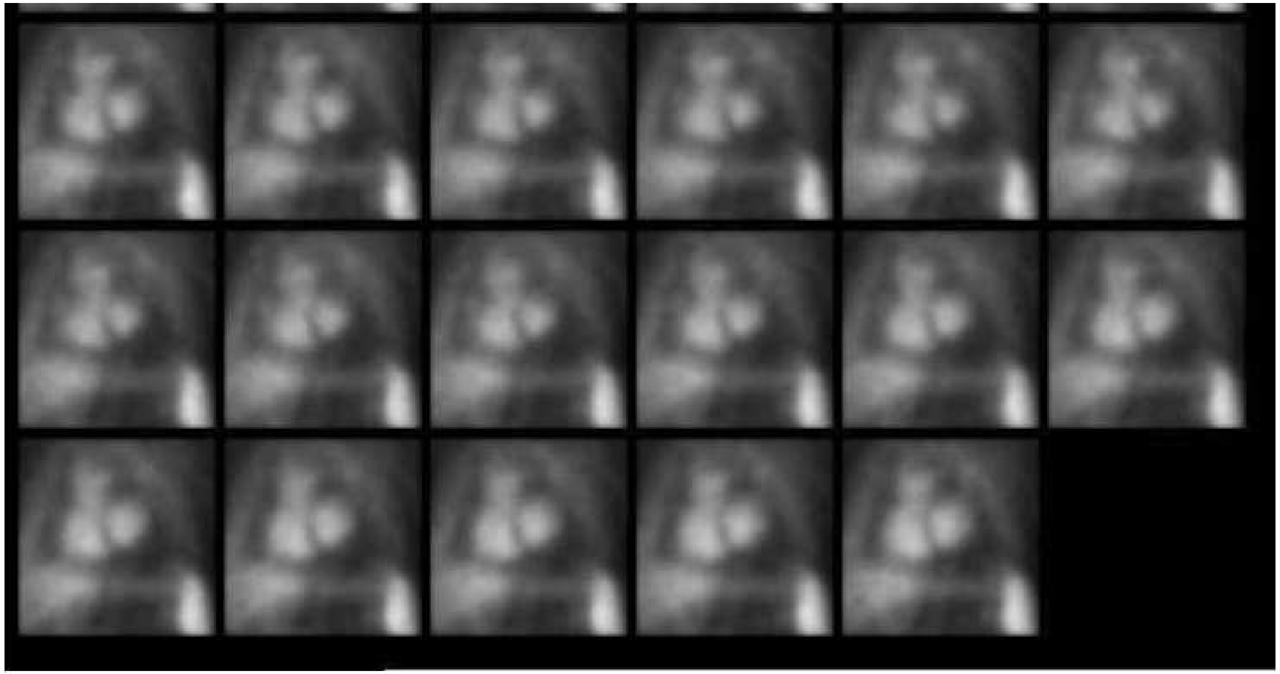


Figure 9. A multiple gated (MUGA) study of the left ventricle. The 16 images acquired over a heartbeat are uniformly assigned in time to the R wave-to-R wave cardiac interval. An ejection fraction of 69% was calculated.

Table 3. Representative Gamma Camera Imaging Studies Done in Nuclear Medicine

Fonte: ref 2

Study	Agent	Label	Device	Results
Renogram	DTPA and MAG3	^{99m}Tc	Camera	Kinetic values
MUGA	Red cells	^{99m}Tc	Camera with EKG gating	Ejection fraction of LV
Myocardium	Sestamibi	^{99m}Tc	Camera	Bulls eye image of LV
Bone scan	MDP	^{99m}Tc	Camera	Fracture location. Tumor location
Lung scan	Aggregated albumin	^{99m}Tc	Camera	Regions of reduced perfusion
Lung scan	Aerosolized albumin	^{99m}Tc	Camera	Regions of reduced ventilation
Lung scan	Xenon gas	^{133}Xe	Camera	Regions of reduced ventilation
Thyroid imaging	Iodine	^{123}I	Camera	Uniformity of uptake in gland

SPECT Single Photon Emission Computed Tomography

Multiplas cintigrafias
+
reconstrução

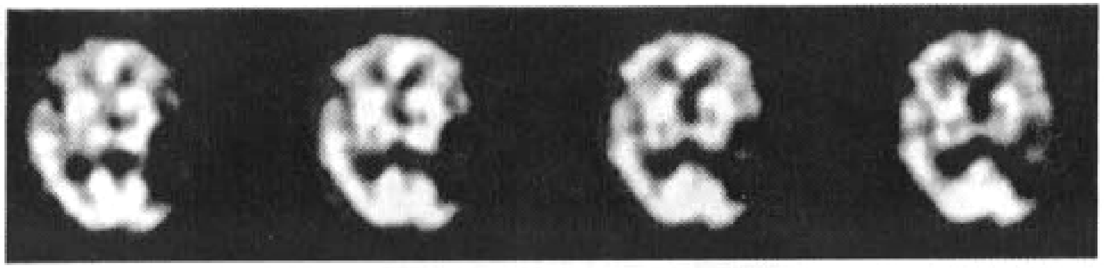


FIGURE 2.15. Multislice SPECT brain perfusion images of a patient who has extensive brain damage from a stroke. A striking perfusion deficit can be seen in the lower right side of the brain

Fonte: ref 1

Fonte: ref 6

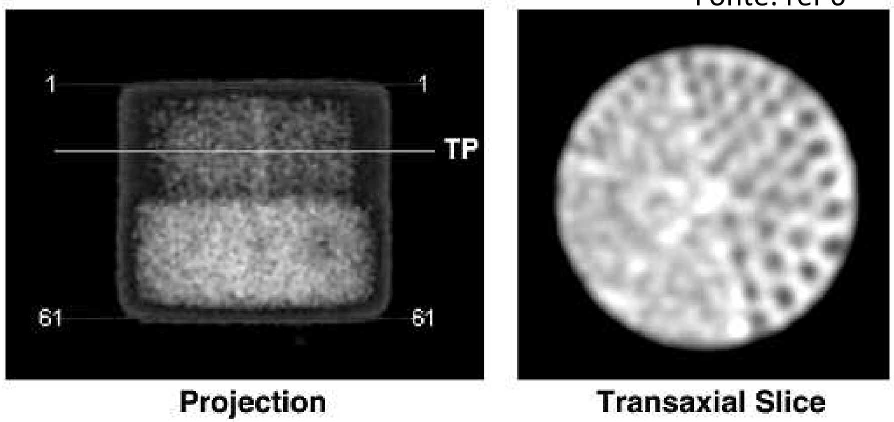
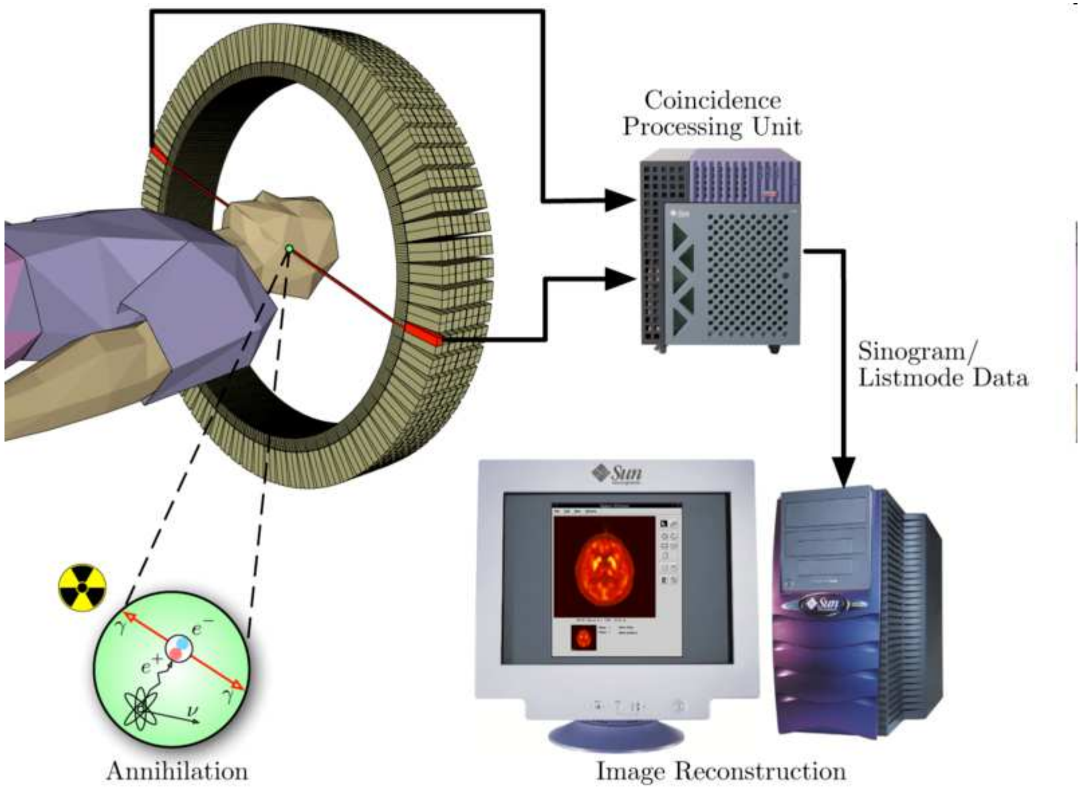


FIGURE 10.18 Projection of a Jaszczak phantom and reconstructed transaxial slice of the plane TP.

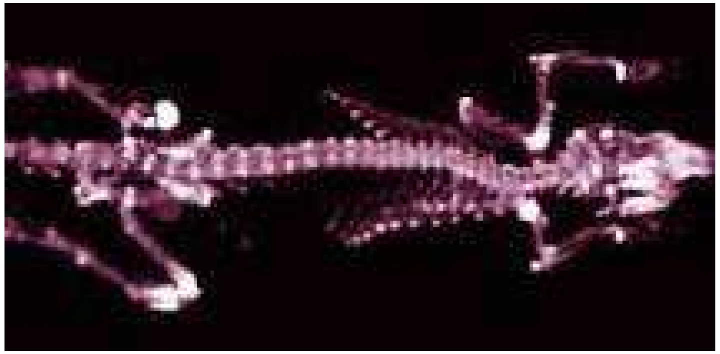
Princípio do PET

Positron Emission Tomography



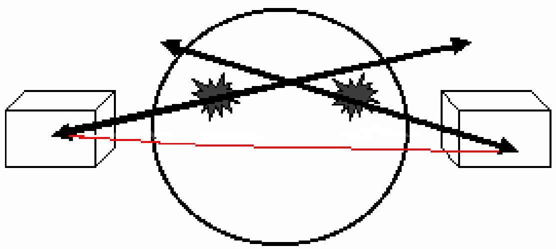
Colectando muitas coincidências (linhas) pode-se reconstruir a distribuição de actividade no objecto de forma semelhantes ao que se faz em TAC.

Óptima resolução <1mm

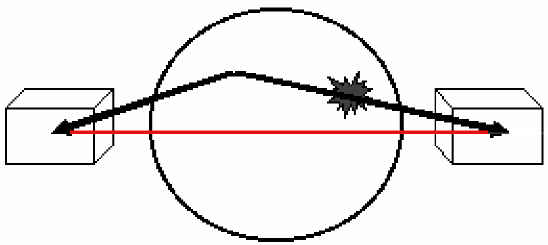


Linhas falsas (criam ruído na imagem)

“Randoms”

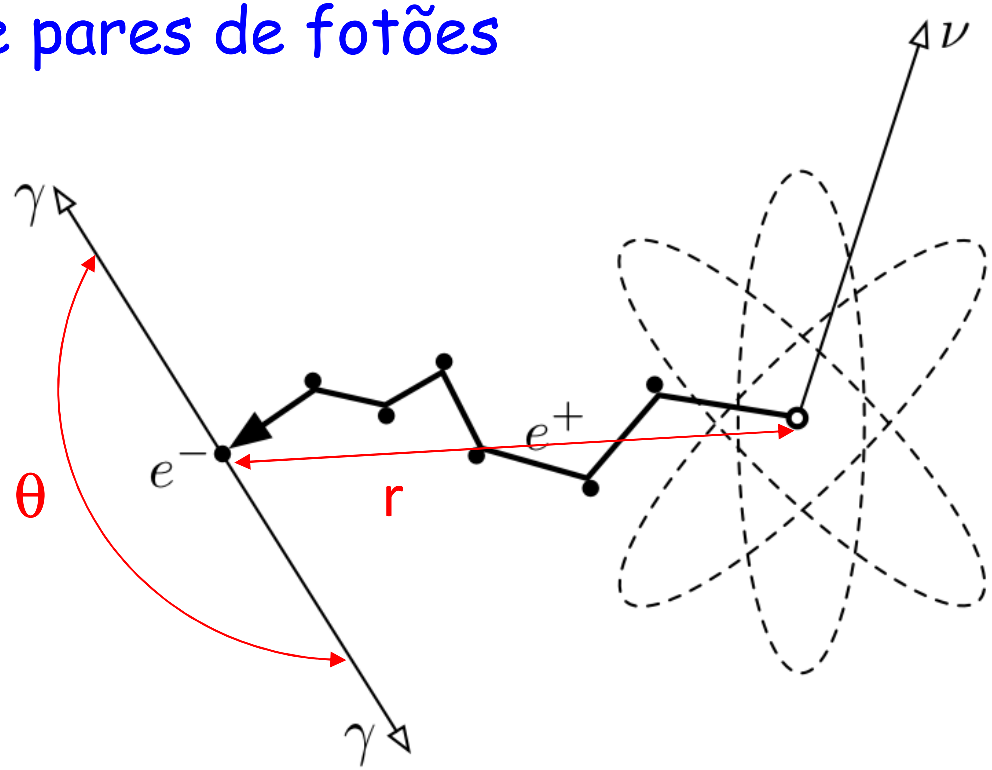


“Scatters”



Sensibilidade ~100x superior ao SPECT (não há colimador)

Geração de pares de fotões



Decaimento β^+

e^+ positron

e^- electron

ν neutrino

γ gamma/photon (511keV)

Erros físicos na localização da actividade

- alcance do positrão: <r>≈1mm
- não-colinearidade: θ=180º±0.25º HWHM

$\Rightarrow$ 2.2 mm por metro de diâmetro do tomógrafo

Detecção dos fotões

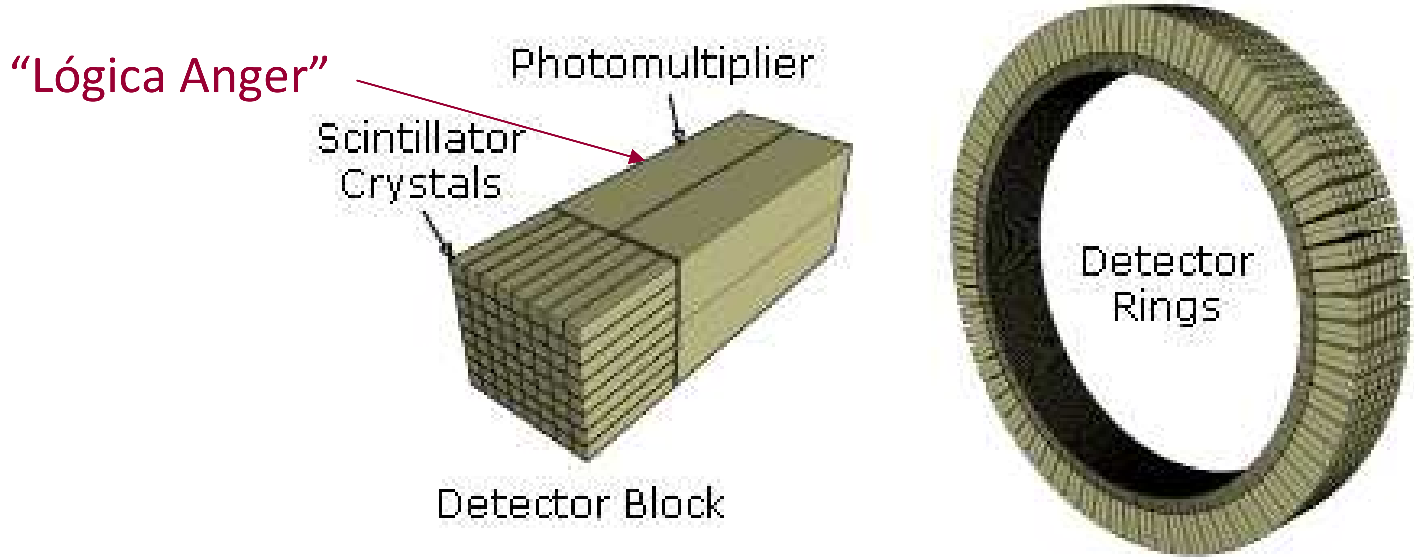


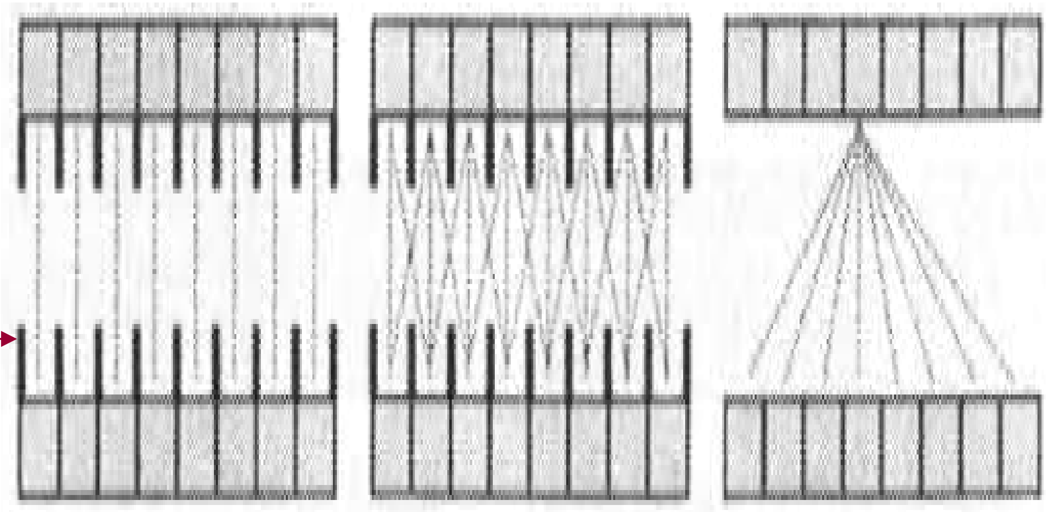
TABLE 2.4. Properties of Various Detectors Employed in PET[a]

Fonte: ref 1

Material	Decay Time (ns)	Emission Intensity	Density (g/cm^3)	$\lambda_{emitted}$ (nm)	η	A_{eff}	Hygroscopic
BGO	300	0.15	7.13	480	2.15	75	No
GSO(Ce)	60_{prim}, 600_{sec}	0.3	6.71	430	1.85	59	No
BaF_2	0.8_{prim}, 600_{sec}	0.12	4.88	220, 310	1.49	53	No
CsF	4	0.05	4.64	390	1.48	53	Yes
CaF_2(Eu)	900	0.4	3.18	435	1.44	17	No
LSO(Ce)	40	0.75	7.40	420	1.82	65	Yes
NaI(Tl)	230_{prim}, 1000_{sec}	1	3.67	410	1.85	51	Yes

[a] A_{eff} is the effective atomic number, η is the refractive index, and decay times are expressed as primary and secondary decays. The emission intensity is reported relative to a value of 1.0 for NaI(Tl). GSO(Ce) is cerium-doped gadolinium orthosilicate (Gd_2SiO_5), and LSO(Ce) is cerium-doped lutetium orthosilicate (Lu_2SiO_5).

Modos de aquisição



"Septa"

Anel

"2D"
(cada plano individualmente)

"3D"
limitado

"3D"
total

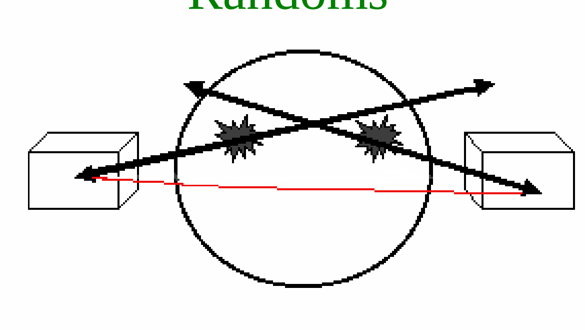
Maior sensibilidade

Reconstrução mais exigente
Mais "scatter"

Ruído de fundo

Linhas falsas (criam ruído na imagem)

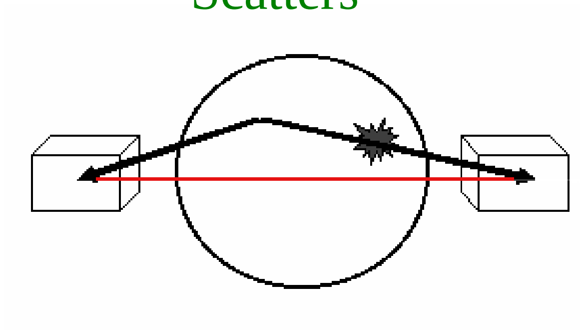
“Randoms”



$$f_{randoms} = 2\tau f^2$$

f = taxa de “randoms”
τ = janela de coincidências no tempo
f = taxa total de detecções
(todos os detectores)

“Scatters”

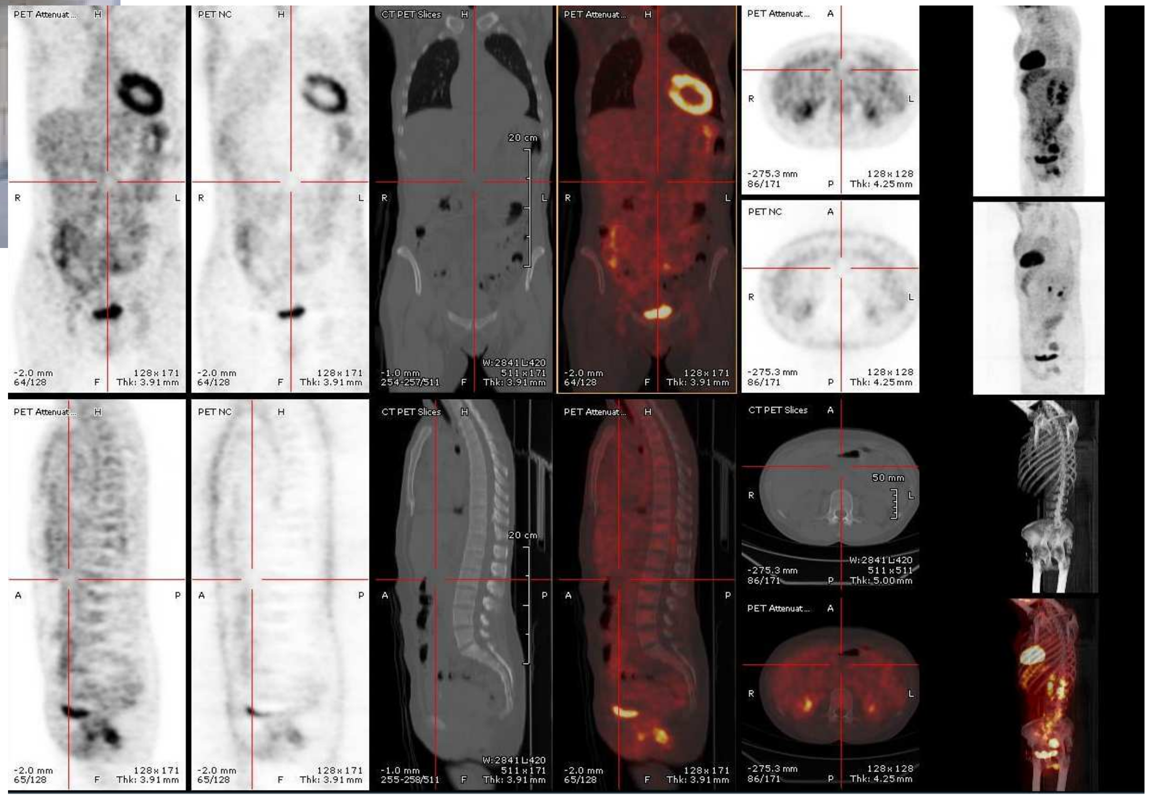


Semi-camada = 7cm $\Rightarrow$ a maioria dos fotões interagem no objecto (~90%).

Reduz-se este efeito por discriminação em energia (os fotões difundidos perdem energia).

Tomógrafos

PET-CT: a combinação moderna



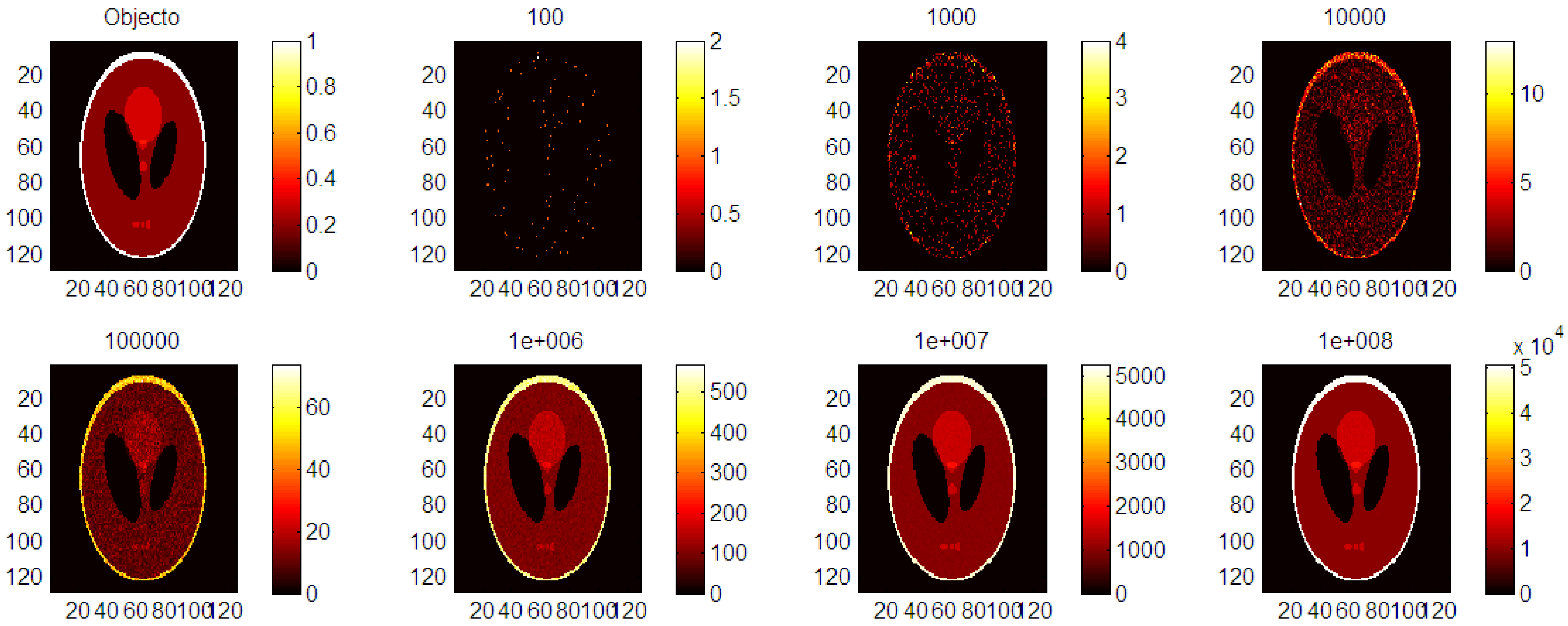
Ruído de contagem

Em Imagiologia de emissão são detectados relativamente poucos fotões (~10000x menos que em TAC).

Numa região de intensidade uniforme no objecto o numero de fotões *N* em cada pixel não é constante: segue uma estatística de Poisson ⇒ ruído de contagem

$$P(N)=\frac{\mu^{N}e^{-\mu}}{N!}; \qquad SNR=\frac{\mu}{\sigma}=\frac{\mu}{\sqrt{\mu}}=\sqrt{\mu}$$

A relação sinal/ruído (SNR) melhora com √média



Comportamento da reconstrução FBP com ruído de contagem

O filtro de Ram-Lak amplifica muito as altas frequências onde o sinal é menor e a relação sinal-ruído (SNR) pior.

Outros filtros dão melhores resultados:

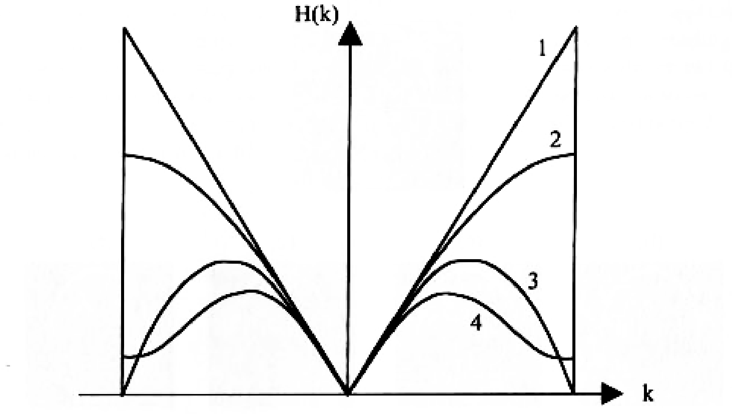
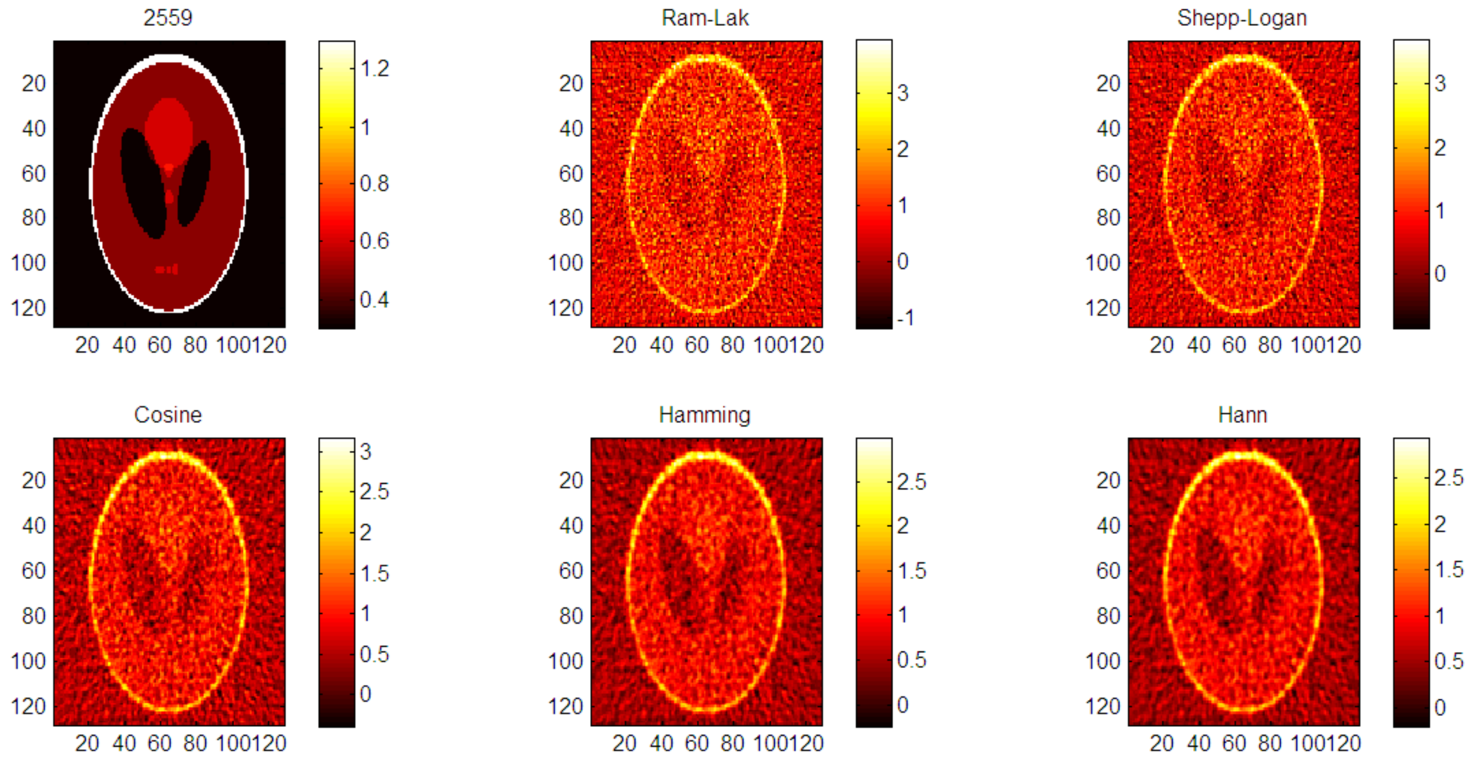
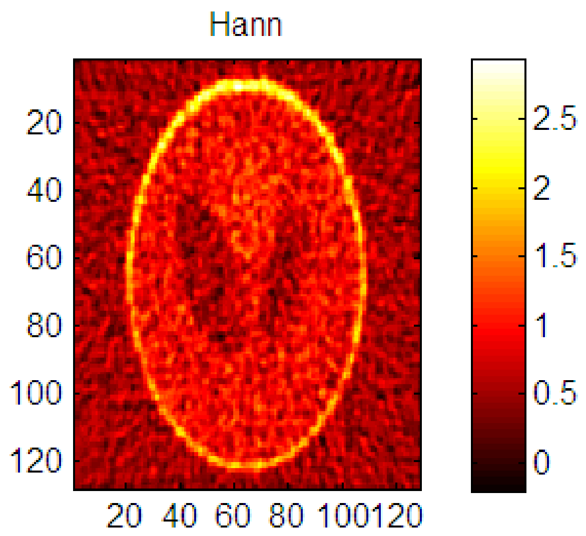


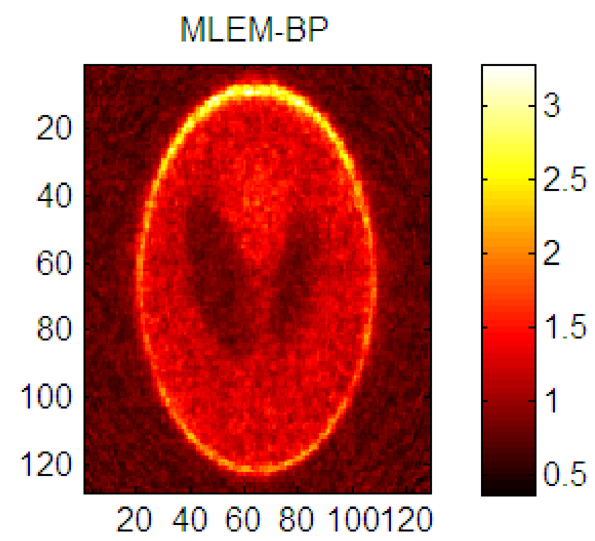
FIGURE B.5. Some common filter functions used for backprojection. 1, Ram–Lak; 2, Shepp Logan; 3, low-pass cosine; and 4, generalized Hamming.



Algoritmo iterativo MLEM (Maximum Likelihood – Expectation Maximization)

```
Imagem=1;                                               % estimativa inicial da imagem
CICLO
Sinograma'=Projecção(Imagem);                           % projecção da estimativa da imagem
ErroRelSinograma=Sinograma/Sinograma';                  % comparação com o Sinograma medido
ErroRelImagem=Retroprojecção(ErroRelSinograma);         % reconstrução grosseira do erro na imagem
Imagem=Imagem*ErroRelImagem;                            % correcção da imagem pixel-a-pixel
REPETIR
```





Exemplo MLEM em SPECT

Mas incorporando as características específicas do detector nas funções

Projecção()
RetroProjecção()

O algoritmo corrige parcialmente as imperfeições do detector

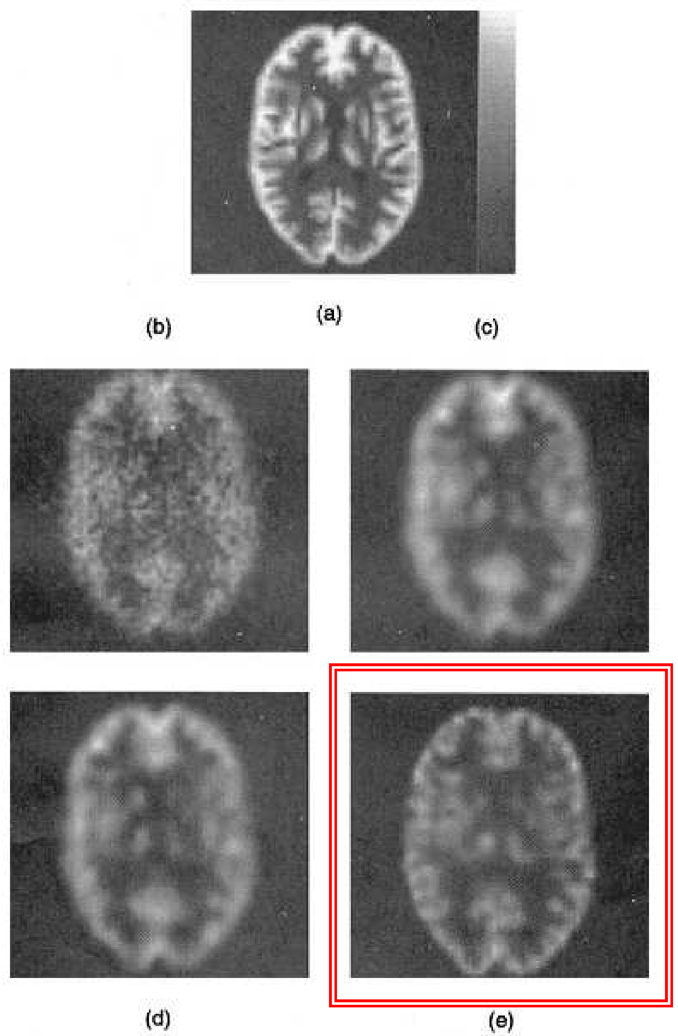


FIGURE 64.12 Sample images from a phantom SPECT study. (*a*) Radioactivity distribution from a selected slice of a 3D brain phantom. (*b*) Reconstructed image obtained from the FBP algorithm without any compensation. (*c*) Reconstructed image obtained with the application of noise-smoothing filter and compensation for uniform attenuation and scatter. (*d*) Similar to (*c*) except for an additional application of a Metz filter to partially compensate for the collimator-detector blurring. (*e*) Reconstructed image similar to that obtained from the iterative ML-EM algorithm that accurately models the attenuation and spatially variant detector response. (From Tsui BMW, Frey EC, Zhao X-D, et al. 1994. Reprinted with permission.)

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