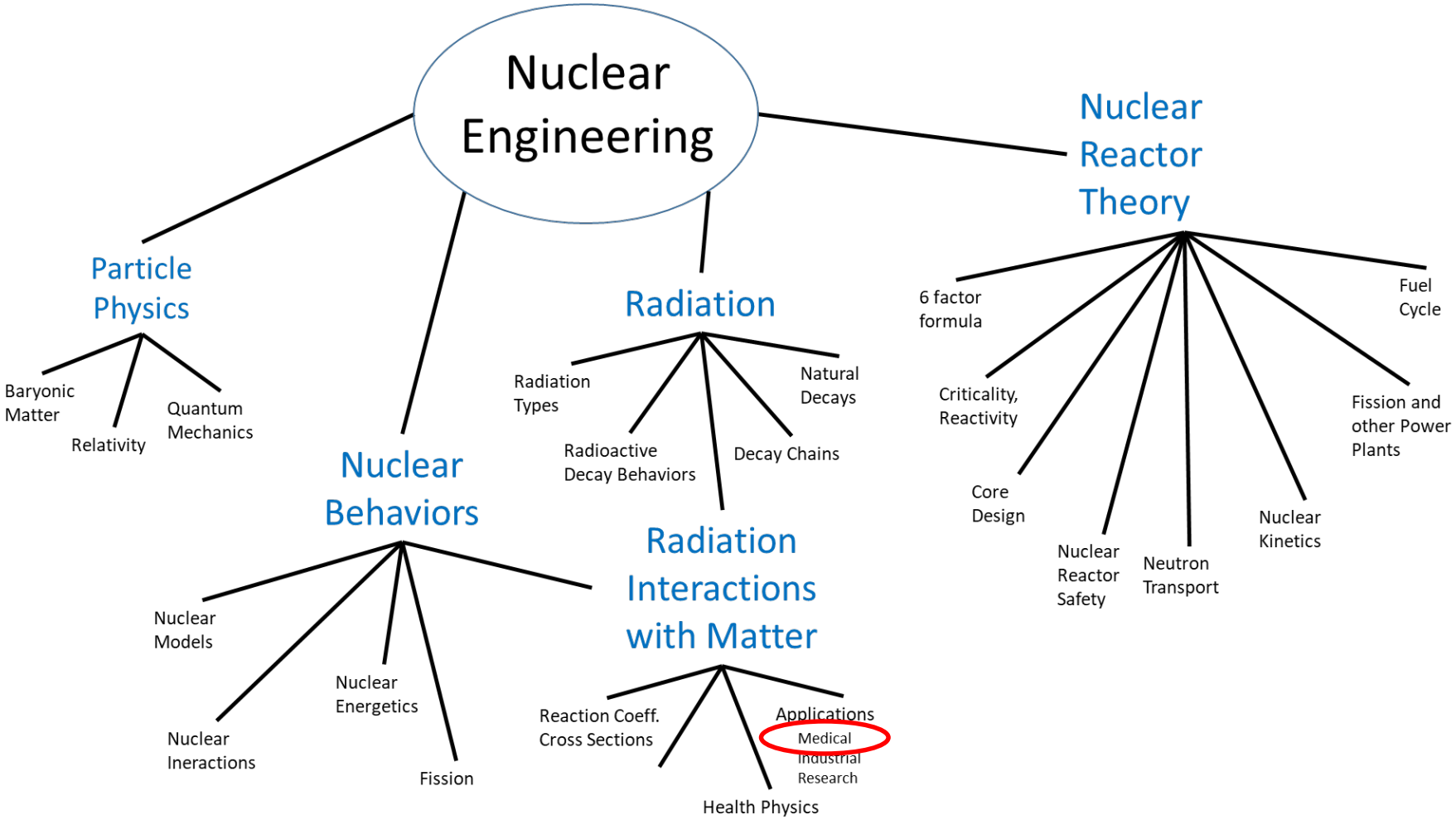
Chemical Engineering 412

Introductory Nuclear Engineering

Lecture 30

Medical Applications

The BIG Picture



Spiritual Thought

Brethren, there may be times in our lives when rising up and continuing on may seem beyond our own ability... Even when we think we cannot rise up, there is still hope…

Brethren, our destiny is not determined by the number of times we stumble but by the number of times we rise up, dust ourselves off, and move forward.

Elder Dieter F. Uchtdorf

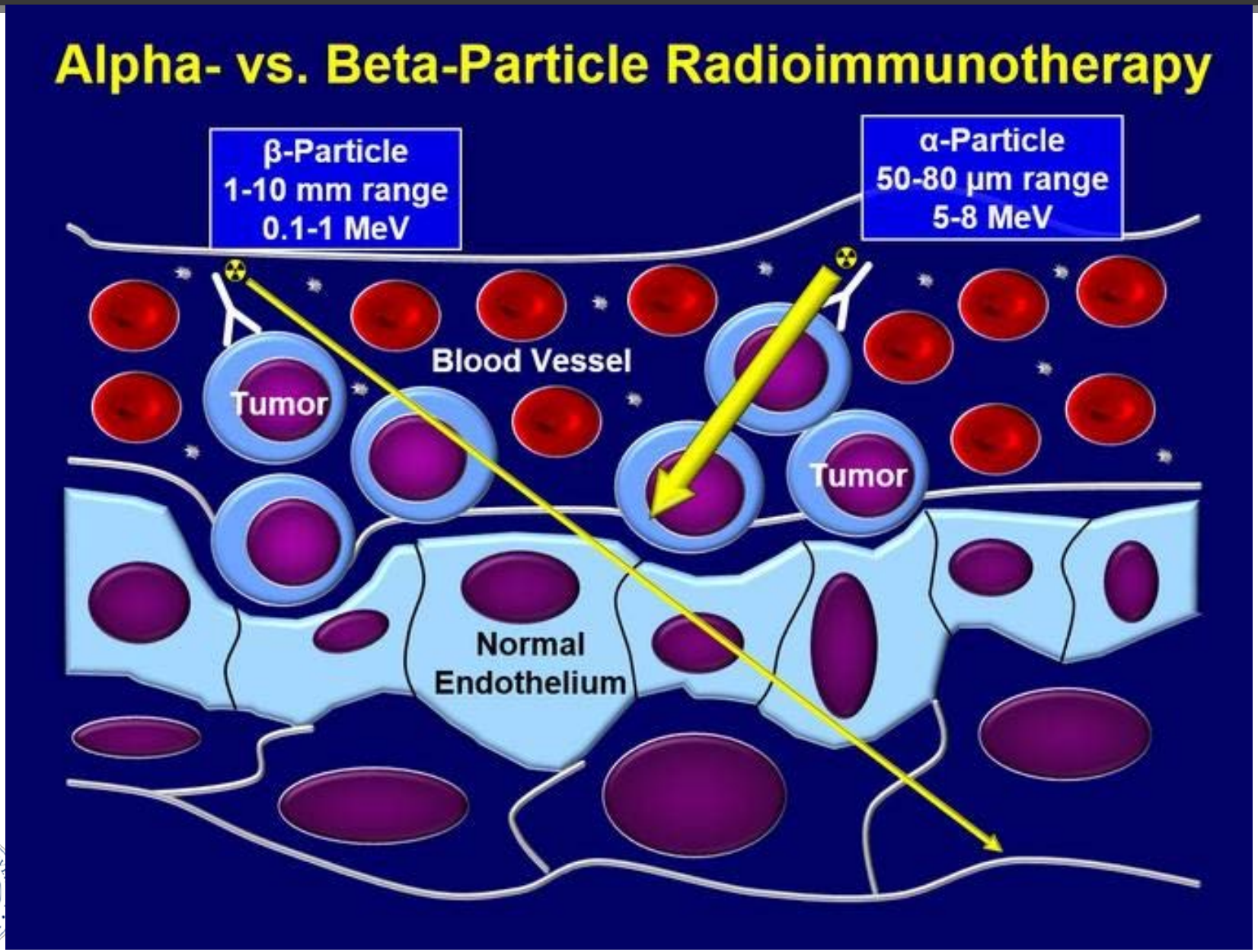
Beneficial Uses of Radiation

- Imaging
  - X-Ray Projection Imaging
  - Fluoroscopy
  - Mammography
  - Bone Densitometry
  - X-Ray Computed Tomography (CT)
  - CT Detector Technology
  - Single Photon Emission Computed Tomography (SPECT)
  - Positron Emission Tomography (PET)
  - Magnetic Resonance Imaging (MRI)
- Radioimmunoassay
- Radiotracers
- Radioimmunoscintigraphy
- Radio Therapy

Medical Uses

- Diagnostic
  - Generally low doses
  - Short-time exposures
- Therapeutic
  - Generally high doses
  - Short to long time exposures
- New Therapeutic – Targeted Alpha Treatment

Targeted Alpha Therapy (TAT)



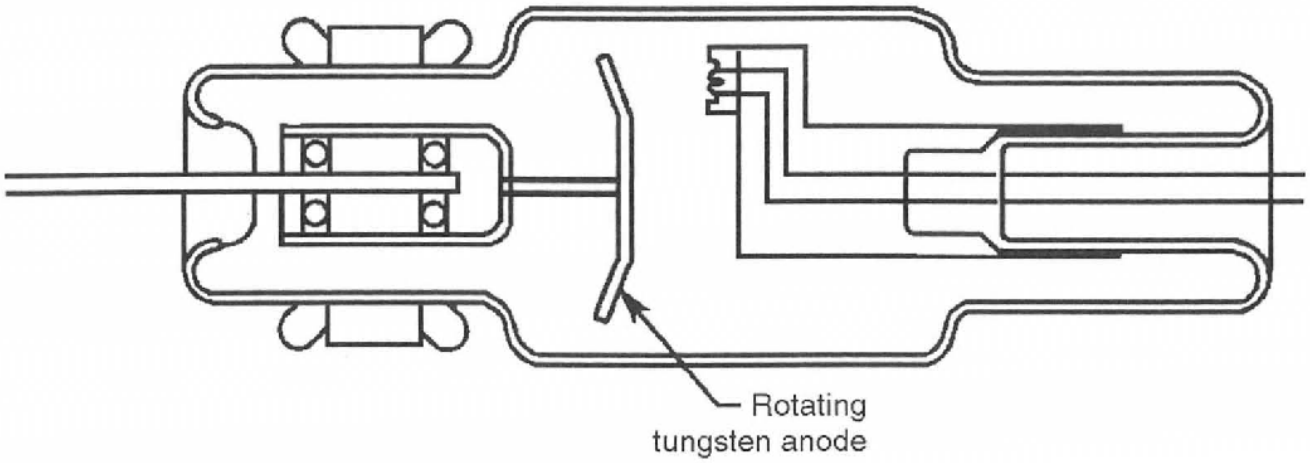
- X-ray imaging (medical & dental) dominates all radiology
  - 130 million people/yr in US
  - 250 million procedures/yr)

Quantity		No. per 10^6 population	
		Level I[a]	Global
Physicians			
All physicians		2800	1100
Radiological physicians		110	80
X-ray Imaging			
Equipment:	medical	290	110
	dental	440	150
	mammography	24	7
	CT	17	6
Exams per year:	medical	920,000	330,000
	dental	310,000	90,000
Radionuclide Imaging			
Equipment:	gamma cameras	7.2	2.1
	rectilinear scanners	0.9	0.4
	PET scanners	0.2	0.05
Exams per year		19,000	5600
Radionuclide Therapy			
Patients per year:		170	65
Teletherapy			
Equipment:	x ray	2.8	0.9
	radionuclide	1.6	0.7
	LINAC	3.0	0.9
Patients per year		1500	820
Brachytherapy			
Afterloading units		1.7	0.7
Patient per year		200	70

[a] Level I represents countries with one or more physicians per 1000 population.

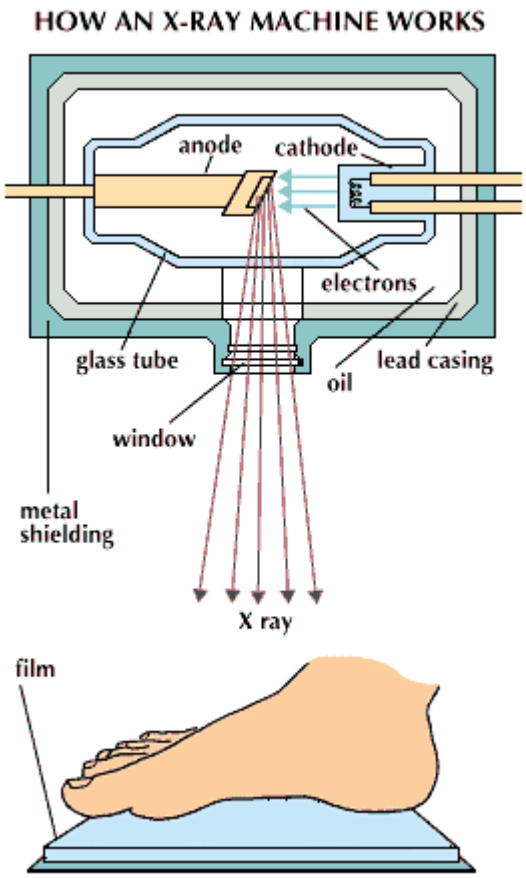
X-Ray Generation

- X-Ray Source/Tube for Projection Analysis



- x-rays generated by bremsstrahlung and fluorescence
- Cathode emits electrons that accelerate and impact rotating anode (rotation helps dissipate heat)
- Small fraction of electrons produce x-rays and small fraction of x-rays are energetic enough

X-ray Machine (snapshot)



- X-ray source called a Stanton tube
- Target is usually tungsten (high Z, melting pt. and thermal conductivity, low vapor pressure), sometimes molybdenum or rhodium.
- Acceleration voltages:
  - 40-150 kV (dental)
  - 6-150 kV (superficial medical)
  - 180 – 50,000 kV (deeply penetrating medical).
- Windows and collimation shape beam and filter low energy rays.

Tungsten most common anode

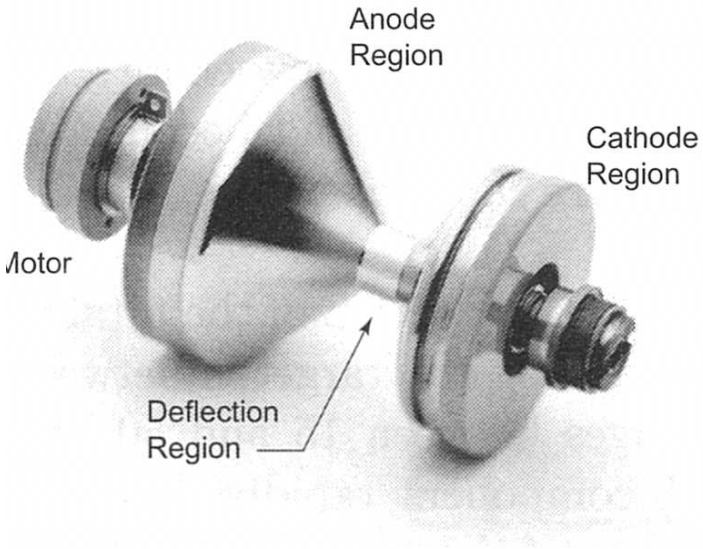
Element	X-ray line	Wavelength (10^{-10} m)	Energy (keV)	Excitation voltage (kV)
Tungsten	$K_{\alpha 1}$	0.2090	59.3182	69.525
	$K_{\beta 1}$	0.1844	67.2443	69.525
	$L_{\alpha 1}$	1.4764	8.3976	10.207
	$L_{\beta 1}$	1.2818	9.6724	11.514
Molybdenum	$K_{\alpha 1}$	0.7093	17.4793	20.000
	$K_{\beta 1}$	0.6323	19.6083	20.000
	$L_{\alpha 1}$	5.4066	2.2932	2.520
Rhodium	$K_{\alpha 1}$	0.6134	20.2158	23.230
	$K_{\beta 1}$	0.5456	22.7236	23.230
	$L_{\alpha 1}$	4.5971	2.6973	3.014

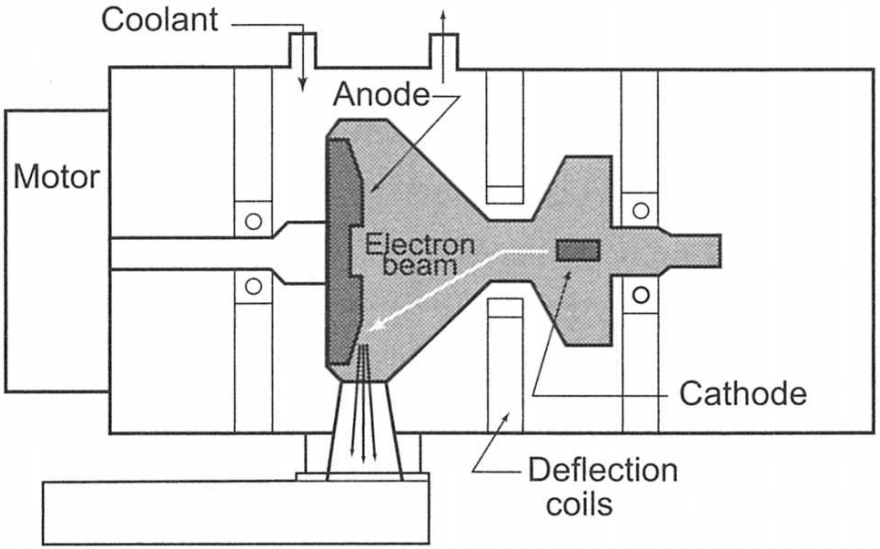
Heat dissipation typically limiting

40-150 kV needed for superficial applications

0.18-50 MV needed for deep penetration

Typical Source





Windows and shielding absorb low energy rays

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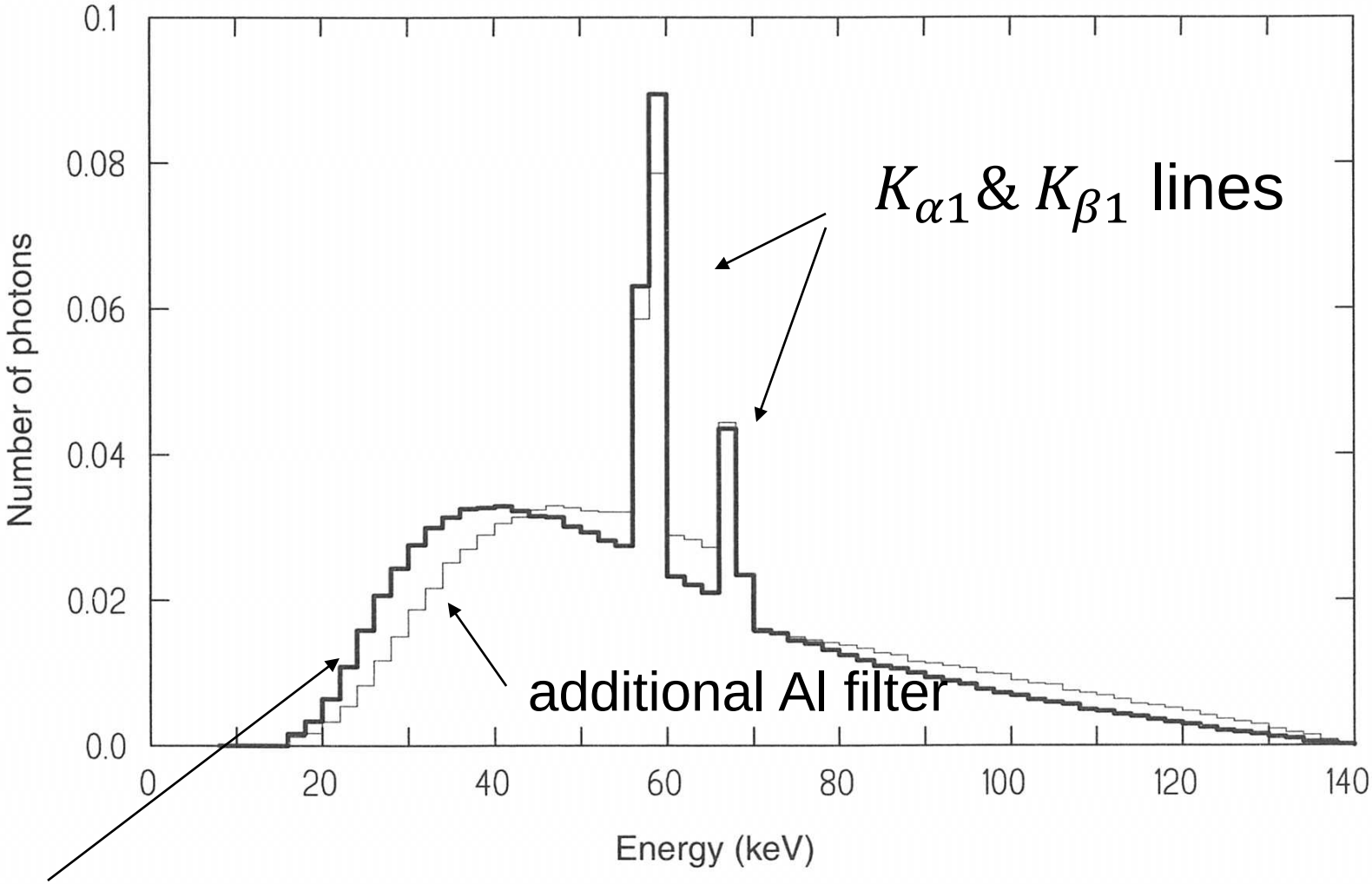
Energy Spectrum (typical)



How does it work?

- How can we “image” an object (body part) with x-rays?
- μ
- Higher density = higher N
- Higher N = higher μ
- Higher μ = more interactions
- Less uncollided x-rays reach detector

Detectors and Exposure

- Until recently, film shadowgraphs
- Digital receivers now common
- Short time exposures (much less than a second)
- Low doses
  - Dental: 0.08 - 0.10 mSv (8 - 10 mrem)
  - Chest: 0.06 - 0.10 mSv (6 - 10 mrem)
  - Mammogram: 0.3 - 0.5 mSv (30 - 50 mrem)
  - Hip: 0.4-0.8 mSv (40-80 mrem)

X-Radiation: Fluoroscopy (real time)

- Coat stomach and upper intestine (upper GI) or colon (barium enema) with barium to provide contrast for X-rays
- Double contrast procedures inject air to inflate organs and provide more detailed analysis
- Long time exposures (minute or longer)
- Higher doses
  - Barium Enema: 6 - 9 mSv (600 - 900 mrem)
  - Upper GI: 3.5 - 5.5 mSv (350 - 550 mrem)

Mammography & Densitometry

- Much higher resolution (micro-calification) and contrast (tumors) required
- Mo or Rh filters absorb all but narrow window of x-rays
- Compression improves resolution and reduces required dose
- Low energy, monoenergetic x-rays ideal
- Digital imaging and anti-scatter films improve contrast and resolution

Bone Densitometry

- Uses two beams (dual x-ray absorptiometry – DEXA).
- Alternative methods use ultrasound and quantitative computed tomography.
- Largely replaced technology is dual photon absorptiometry (DPA), which emits 44 and 100 keV gamma rays from ^{153}Gd.

$$I_1 = I_{1o}\ \exp\left[-\left(\frac{\mu_1}{\rho}\right)_b \rho_b x_b - \left(\frac{\mu_1}{\rho}\right)_s \rho_s x_s\right]$$

$$I_2 = I_{2o}\ \exp\left[-\left(\frac{\mu_2}{\rho}\right)_b \rho_b x_b - \left(\frac{\mu_2}{\rho}\right)_s \rho_s x_s\right]$$

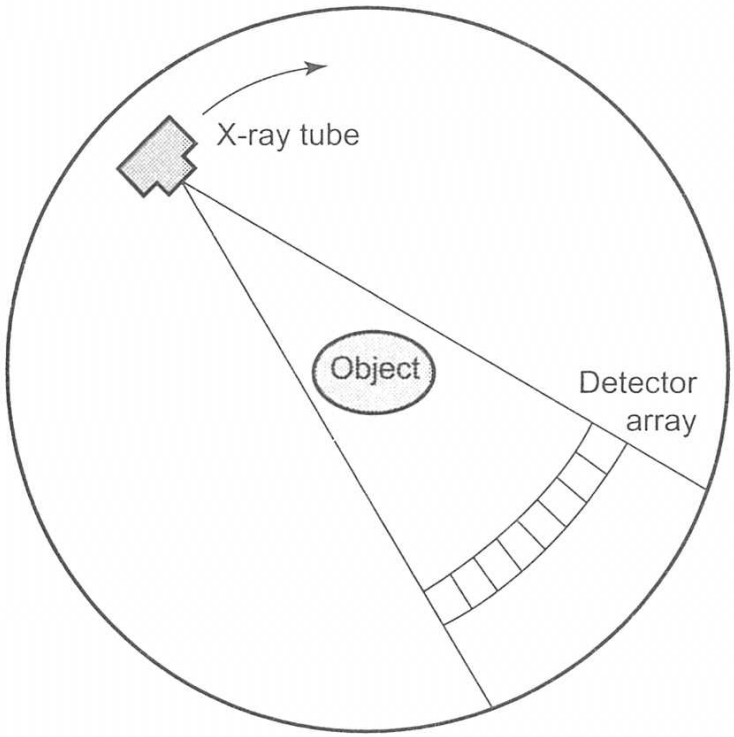
$$\rho_b x_b = \frac{\mathcal{R}\ln\left(\frac{I_1}{I_{1o}}\right) - \ln\left(\frac{I_2}{I_{2o}}\right)}{\left(\frac{\mu_2}{\rho}\right)_b - \mathcal{R}\left(\frac{\mu_1}{\rho}\right)_s}$$

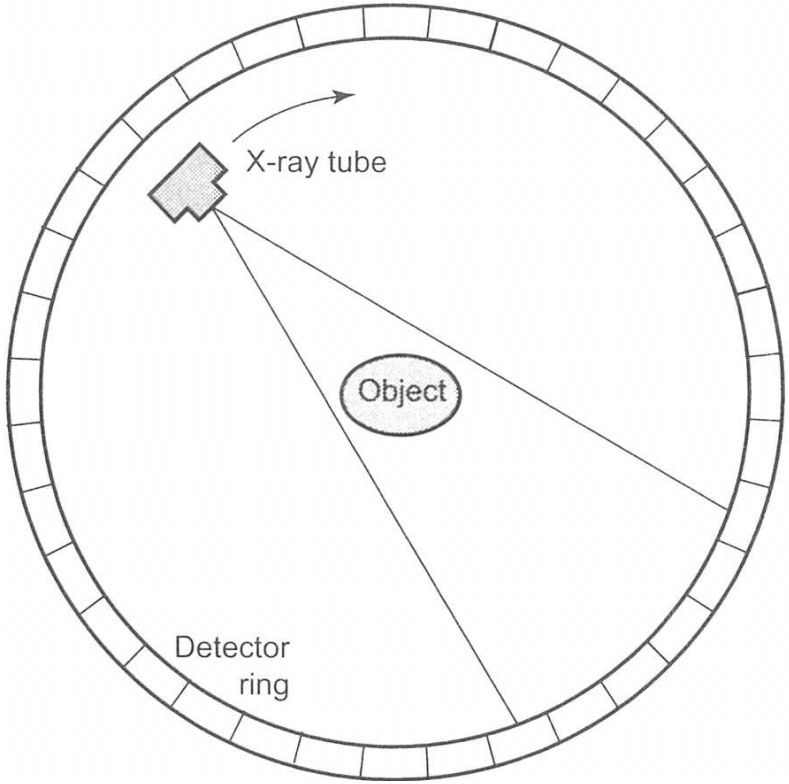
$$\mathcal{R} \equiv \frac{\left(\frac{\mu_2}{\rho}\right)_s}{\left(\frac{\mu_1}{\rho}\right)_s} \neq 1$$

X-Radiation: CT-Scan (cat scan)

- X-Ray Computed Tomography
- Series of short exposures at different angles
- Computer analysis and display
- Gives cross-section view of anatomy
- Medium doses:
  - Head: 2 - 3 mSv (200 - 300 mrem)
  - Body: 3 - 4 mSv (300 - 400 mrem)
- Estimates of cancer caused by CT scans range from 1/1800 to 0.4%, possibly rising to 1.5%.

X-Ray Computed Tomography (CT)





Commercial System

Applications

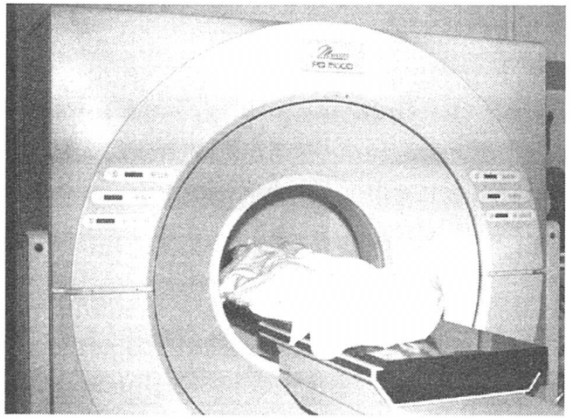


Figure 14.11. Marconi Medical System PQ5000 continuous spiral CT scanner.

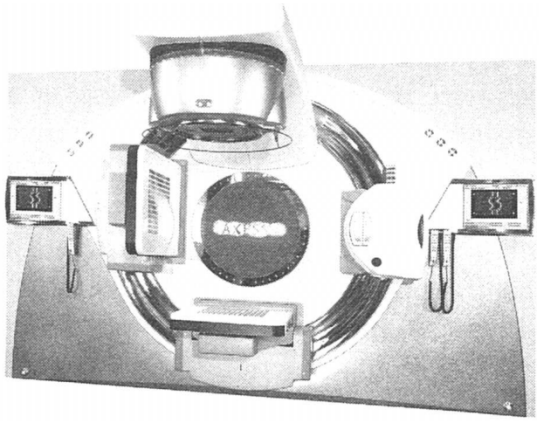


Figure 14.12. Elekta Axesse image guided stereotactic radiosurgery accelerator. Image courtesy of Elekta AB; all rights reserved.

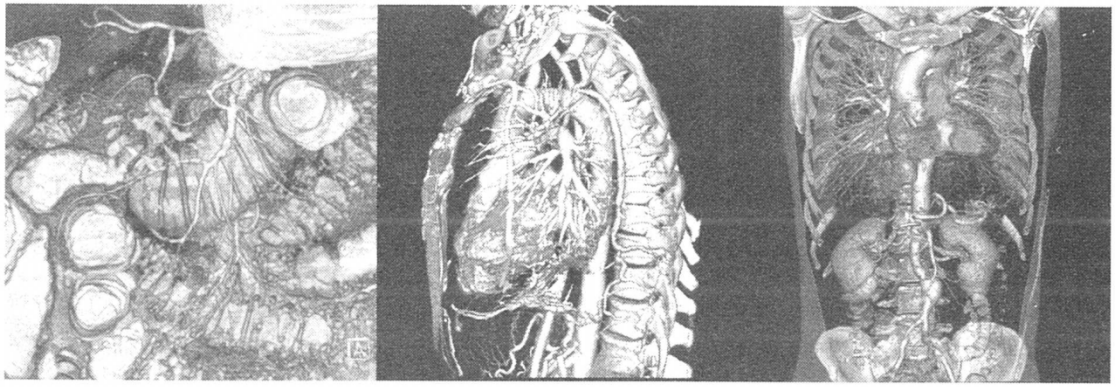


Figure 14.13. Abdominal, thoracic, and vascular CT images obtained using the Somatom Sensation multi-slice scanner. Images courtesy of Siemens Medical Systems.

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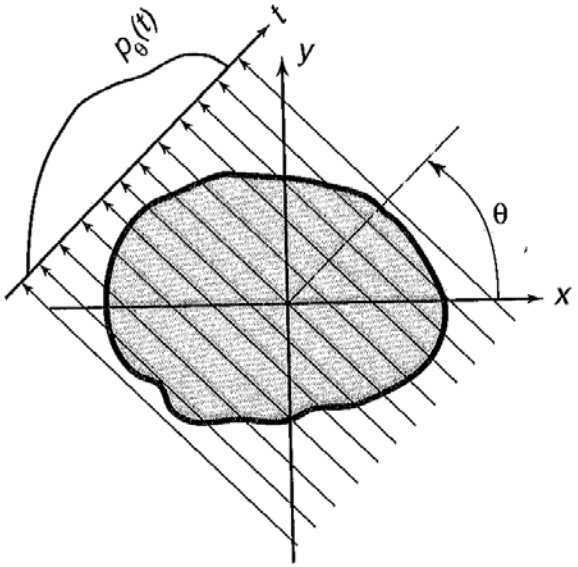
CT scan math

rotated coordinate system

$$t = x\cos\theta + y\sin\theta$$

$$s = -x\sin\theta + y\cos\theta$$



$$I_\theta(t) = I_0 \exp\left[\oint f\big(x(s), y(s)\big)ds\right]$$

The objective is to determine $f(x, y)$ from the measured $p_\theta(t)$.

$$p_\theta(t) \equiv -\ln\frac{I_\theta(t)}{I_0} = \oint f\big(x(s), y(s)\big)ds$$

$$= \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} f(x, y)\delta(x\cos\theta + y\sin\theta - t)$$

CT Scan

- Challenge is to reconstruct $f(x,y)$ from $p_\theta(t)$.
- 1972 Nobel prize awarded to Hounsfield and Cormack, who independently developed a Fourier-transform-based approach.
- One-dimensional FT (just a definition)

$$F(\omega) = \mathcal{F}_1|f(x)| = \int_{-\infty}^{\infty} f(x)\exp[j2\pi\omega x]dx$$

$$f(x) = \mathcal{F}_1^{-1}|F(\omega)| = \int_{-\infty}^{\infty} F(\omega)\exp[-j2\pi\omega x]d\omega$$

- Two-dimensional FT (a related definition)

$$F(u,v) = \mathcal{F}_2|f(x,y)| = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} f(x,y)\exp[j2\pi(ux+vy)]dy\,dx$$

$$f(x,y) = \mathcal{F}_2^{-1}|F(u,v)| = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} F(u,v)\exp\left[-j2\pi(ux+vy)\right]dv\,du$$

Convolution backprojection algorithm

$$P_\theta(\omega) = \mathcal{F}_1[p_\theta(t)] = \int_{-\infty}^{\infty} p_\theta(t)\exp(j2\pi\omega t)dt$$

$$= \int_{-\infty}^{\infty} \exp(j2\pi\omega t)dt \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} f(x,y)\delta(x\cos\theta + y\sin\theta - t)dy\,dx$$

$$= \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} f(x,y)\exp[2\pi j(x\,\omega\cos\theta + y\,\omega\sin\theta)]\,dy\,dx$$

$$= F(u,v)\Big|_\theta = F(\omega,\theta)$$

u and v are called spatial frequencies

$$u = \omega\cos\theta \qquad v = \omega\sin\theta$$

$$f(x,y) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} F(u,v)\exp[2\pi j(ux+vy)]\,du\,dv$$

$$f(x,y) = \int_0^{2\pi}\int_{-\infty}^{\infty} |\omega|F(\omega,\theta)\exp[-2\pi j\omega(x\cos\theta + y\sin\theta)]\,d\omega\,d\theta$$

Finite and Continuous forms

$$f(x,y) = \frac{2\pi}{K}\sum_{i=1}^{K}\mathcal{F}^{-1}\left(|\omega|F(\omega,\theta_i)\right)$$

$$f(x,y) = \int_0^{2\pi}\int_{-\infty}^{\infty}|\omega|F(\omega,\theta)\left\{\int_{-\infty}^{\infty}p_\theta(t')\exp(j2\pi\omega t')\,dt'\right\}\exp[-2\pi j\omega(x\cos\theta + y\sin\theta)]\,d\omega\,d\theta$$

$$f(x,y) = \int_0^{2\pi}\int_{-\infty}^{\infty}p_\theta(t')g(t-t')dt'\,d\theta$$

$$g(t-t') = g(\tau) = \int_{-\infty}^{\infty}|\omega|\exp(-j2\pi\omega\tau)\,dt' = \mathcal{F}_1^{-1}(|\omega|)$$

Since $p_\theta(t) = p_{\theta+\pi}(t)$ and with $\hat{p}_\theta(t') = \left(p_\theta(t) + p_{\theta+\pi}(t)\right)$

$$f(x,y) = \int_0^{\pi}\int_{-\infty}^{\infty}\hat{p}_\theta(t')g(t-t')dt'\,d\theta$$

Gamma-ray Techniques

- Single-Photon Emission Computed Tomography (SPECT) creates 3-D images from gamma rays emitted by radionuclides injected for this purpose in the body
- Most commonly the radionuclides are bound via ligands to chemical compounds that concentrate in places of medical interest
- Occasionally, ionic forms of radionuclides with no specific biological or physiological binding are used
- Images collected with gamma cameras

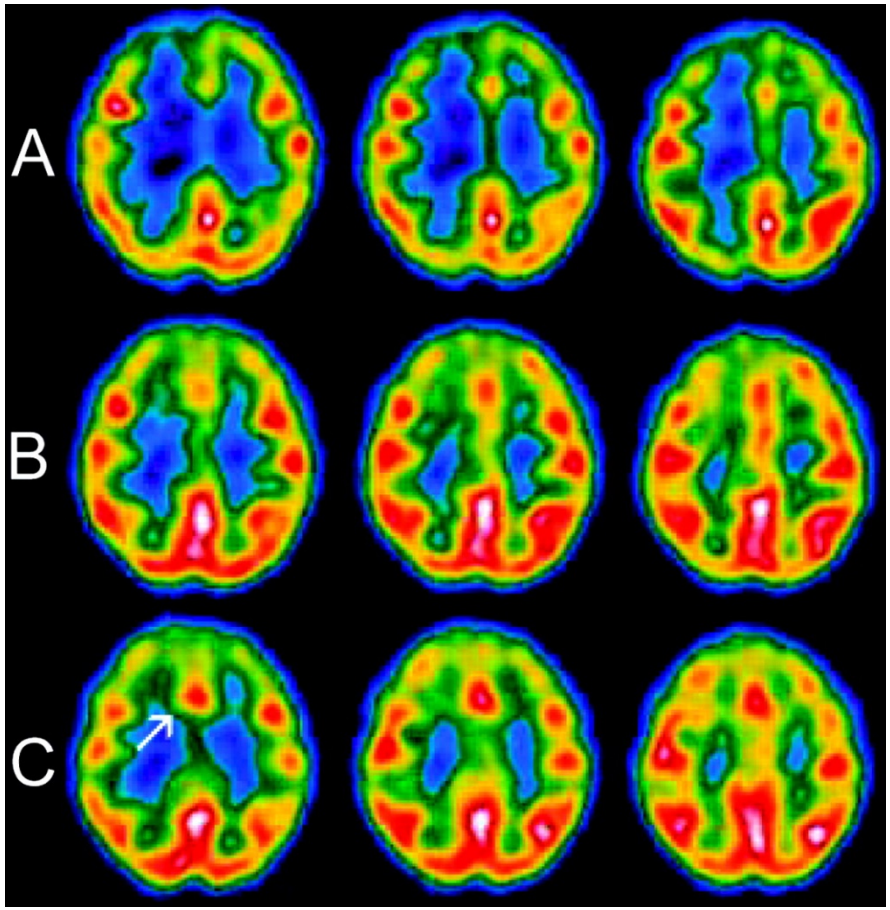
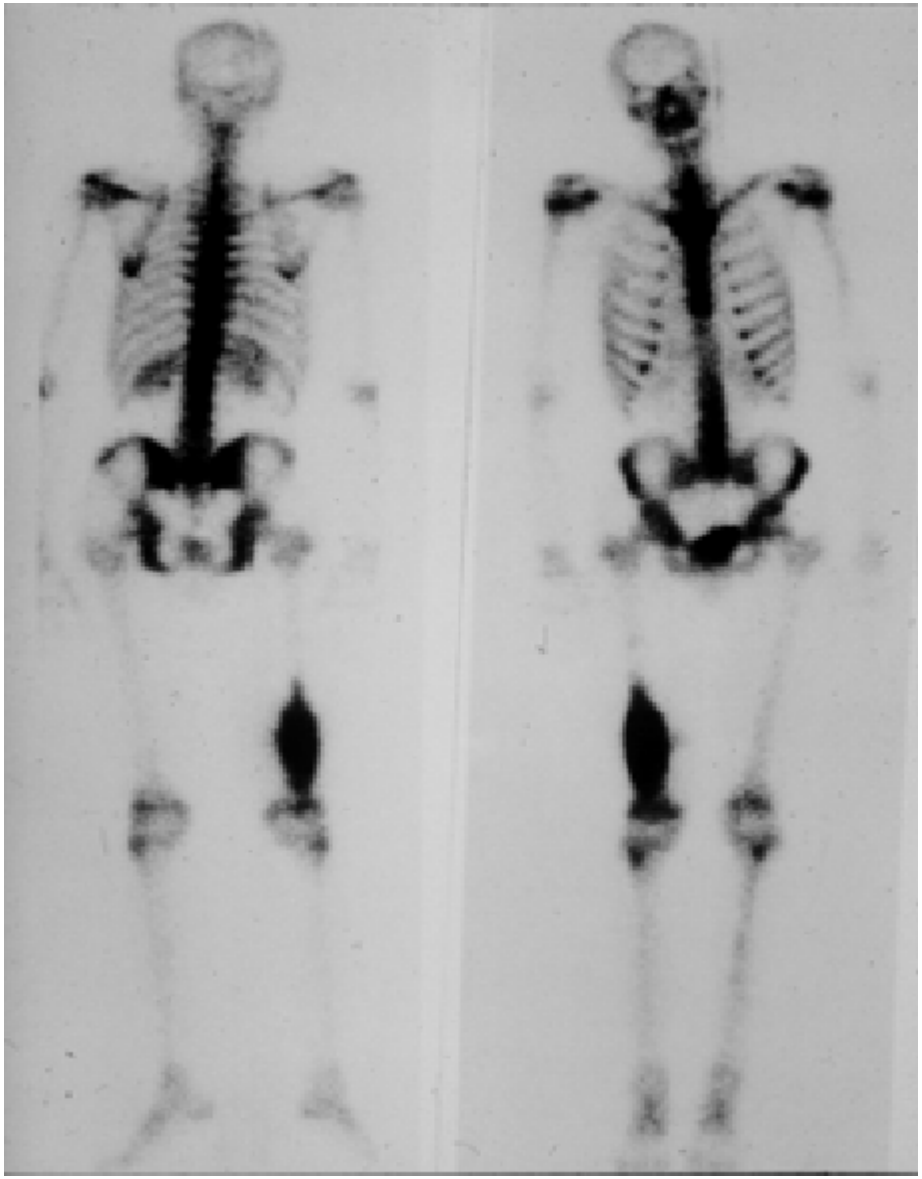


Image: Han et al., *Neurology October 26, 2004 vol. 63 no. 8 1519-1521*

SPECT

- Produces 3-D image based on gamma emission of a radiopharmaceutical (typically ^{99m}Tc, ^{125}I or ^{123}I).
- Developed prior to CT-scan but now uses similar mathematical tomography techniques.
- Unlike CT-scan, which primarily measures material density, SPECT can quantitatively indicate biological or metabolic activity based on biological concentration of radiopharmaceuticals used in the analysis.
- Typically use NaI(Tl) cameras with photomultiplier tubes.

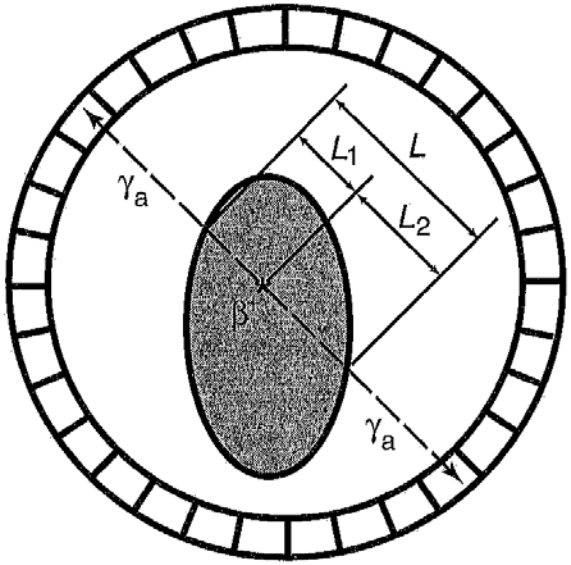
Skeletal Scan of Person After a Tc-99m nuclear medicine injection



PET

- Positron Emission Tomography
- Similar to SPECT but uses positron annihilation reactions, which produce two simultaneous and essentially oppositely directed photons.
- Two opposing camera arrays collect signals.
- The fact that the emission is simultaneous and opposite allows substantial increase in S/N ratio by filtering spurious signals and hence much better resolution.
- Positron path length prior to annihilation is 1-4 mm (0.25-1 MeV positrons). They generally do not react until they thermalize.
- ^{18}F, ^{15}O, ^{13}N, and ^{11}C are commonly used for PET.

PET Schematic and Isotopes



Nuclide	E_{max} (MeV)	E_{av} (MeV)	Frequency	Half-life	Production Reaction
^{11}C	0.960	0.386	0.998	20.5 m	$^{14}N(p,\alpha)$
^{13}N	1.199	0.492	0.998	9.97 m	$^{16}O(p,\alpha)$,$^{13}C(p,n)$
^{15}O	1.732	0.735	0.999	122 s	$^{15}N(p,n)$
^{18}F	0.634	0.250	1.000	110 m	$^{18}O(p,n)$

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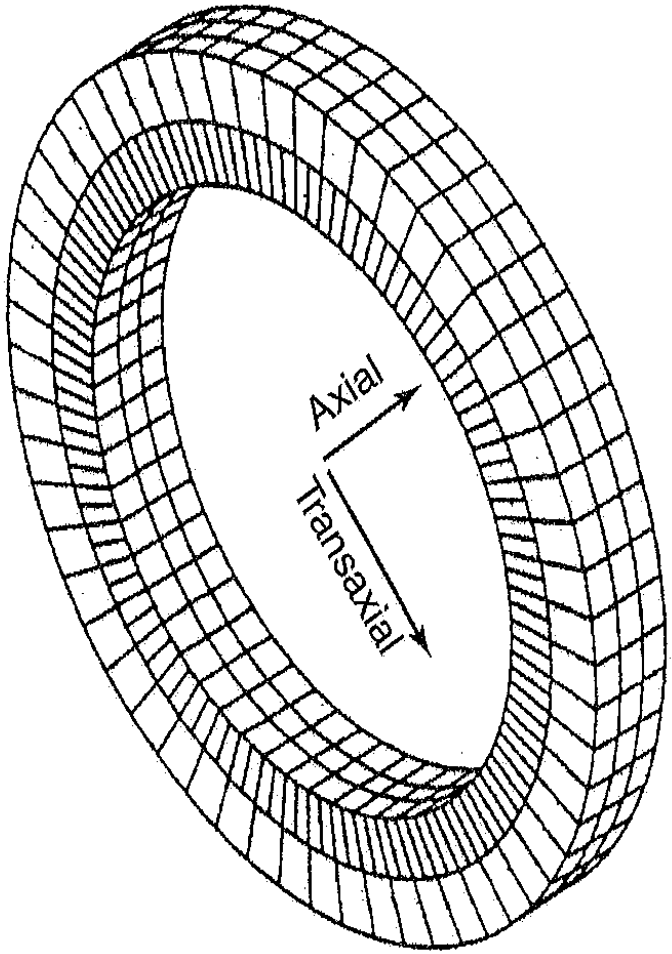
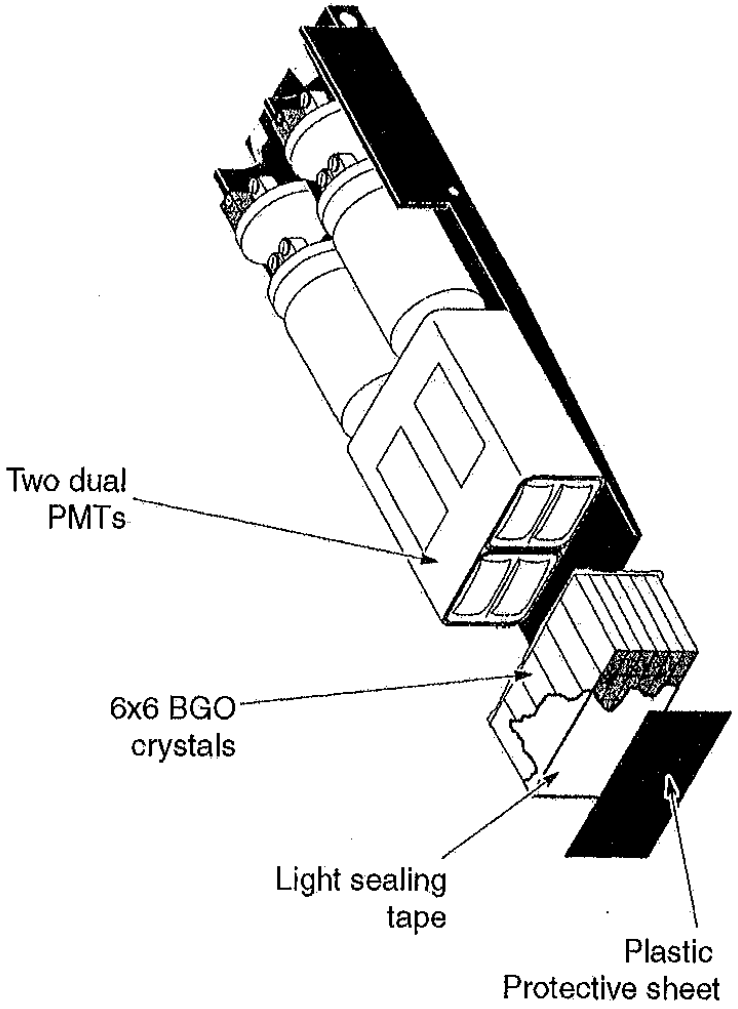
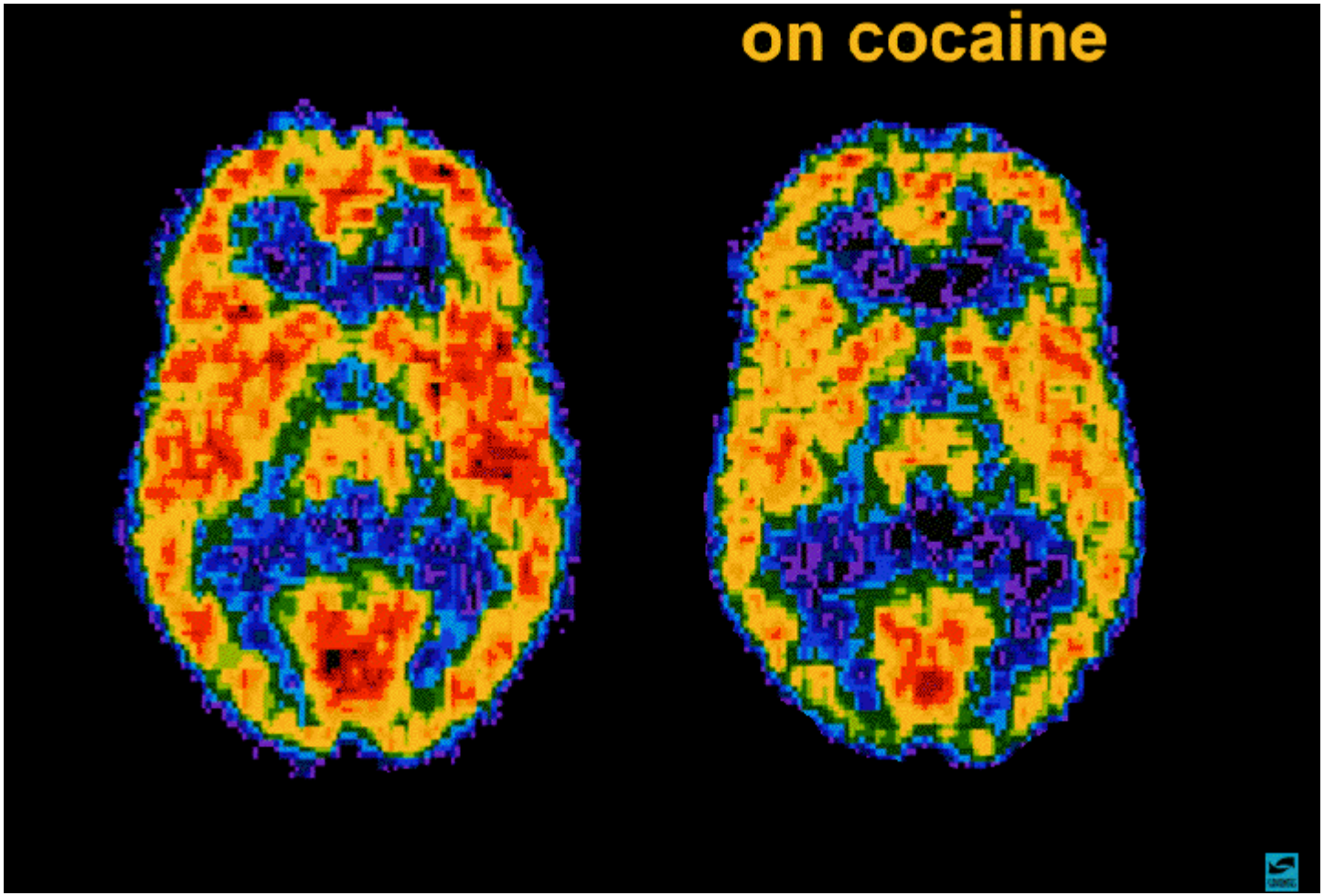
PET Cameras/detectors





Brain on Drugs



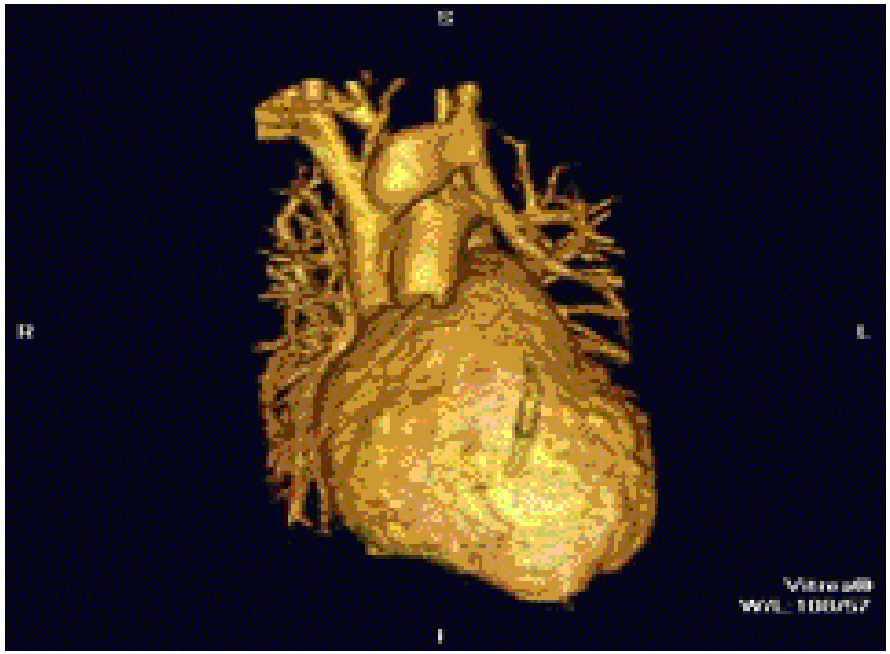
http://www.drugabuse.gov/publications/teaching-packets/brain-actions-cocaine-opiates-marijuana/section-iii-introduction-to-drugs-abuse-cocaine-opiat-5

MRI

- Magnetic Resonance Imaging
- No longer a tomographic technique, but can produce high-quality slice or 3-D images, including time-resolved images, of soft tissue.
- Uses no radioactive isotopes or radiation, but depends on properties of nuclei (not electrons).
- All odd-numbered N or Z nuclei (H, for example) have an intrinsic nuclear spin – not a spin in the physical sense but a finite net spin number – and hence a (very small) magnetic moment.
- Strong magnetic field aligns nuclei and causes them to precess, with precession frequency/speed proportional to mag field strength.

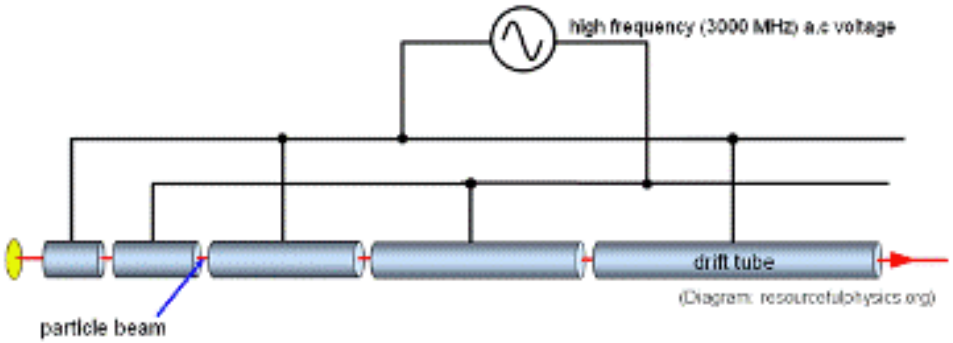
MRI cont'd

- Precessing nuclei can be oriented in the direction of the field (parallel - lowest energy) or the opposite direction (anti-parallel - slightly higher energy).
- Energy difference is $\boldsymbol{2\mu H_0}$, where $\boldsymbol{\mu}$ is the nuclear magnetic moment. This is 2-85 MHz



Teletherapy

- Also called external-beam radiotherapy (EBRT), uses an external source of radiation to treat body tissue
- By far the most common form of radiotherapy
- Nearly always uses x-rays or electron beams – some heavy particle/charged particle treatments under development (more localized energy deposition)
- Modern system use linear accelerator to generate x-rays, replacing cobalt-60 sources of earlier times or in less developed regions.



Source: atomic.lindahall.org

Source: Varian Medical Systems

Brachytherapy Radionuclides

- Source is placed inside or next to the area requiring treatment
- Common for skin, breast, cervical and prostate cancers
- Contrasts with unsealed source radiotherapy, where nuclides are injected directly in the body in forms that concentrate in target tissues.
- Half-life should not cause extended stay in hospital
- Radioisotope should emit alpha or beta radiation
- Radioisotope should also emit gamma rays to ensure targeted area is treated

Unsealed Source Radiotherapy

- Iodine-131 most common for treatment of thyroid (both benign conditions like thyrotoxicosis and malignant conditions like papillary thyroid cancer)
- Other, less common, treatments include phosphorous-32 for overactive bone marrow, radium-223/strontium-89/samarium-153 for secondary cancer in the bones, and yttrium-90 for synovial membrane removal in the knee
- In most cases, beta emission kills the cells while gamma emission escapes the body (but can be used to confirm location of the radionuclide)

Research Use

- Biological and Genetic research
- Agricultural research
- Space research
- Pharmaceutical research