

Frontiers of Research in Medical and Biological Imaging Systems

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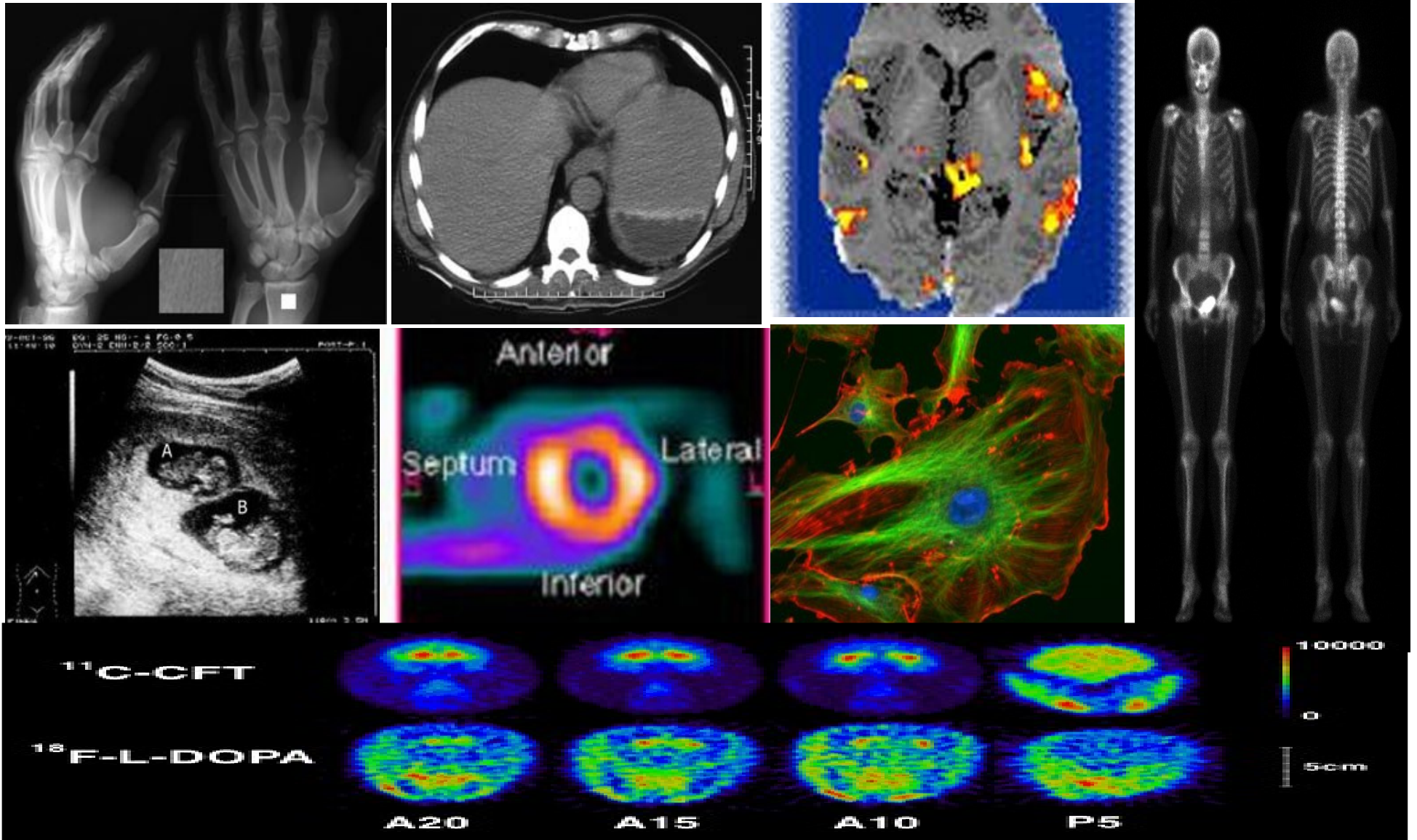
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Examples of Medical and Biological Images



Medical Imaging Modalities

- **Anatomical**

Depicting primarily morphology
(Radiography, MRI, CT, X-ray, Ultrasound Echography)



- **Functional**

Depicting primarily information on the metabolism of the underlying anatomy
(SPECT, PET)



Medical imaging modalities

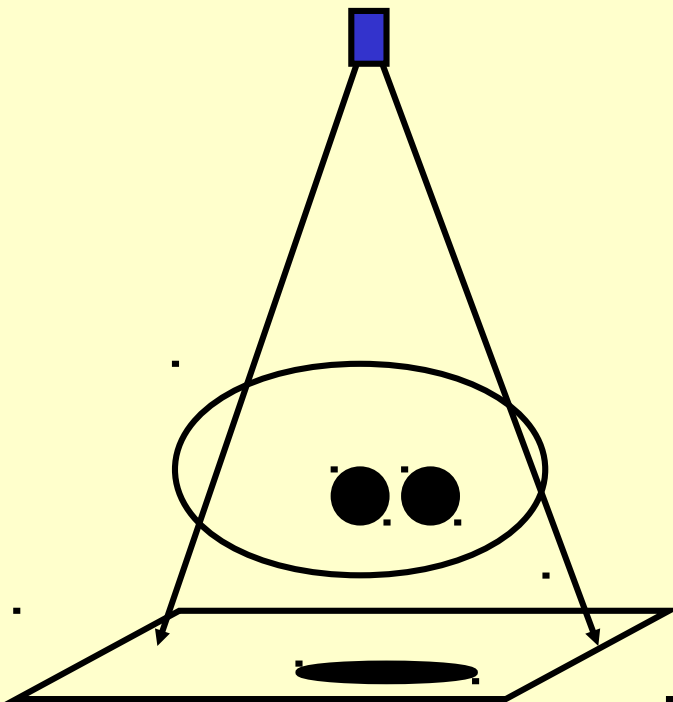
- Analog and Digital Radiography
- Mammography, Angiography
- X-ray Computer Tomography (CT scans)
- Magnetic Resonance Imaging (MRI)
- Ultrasound Echography
- Radioisotope Imaging
 - Positron Emission Tomography (PET)
 - Single Photon Emission Computed Tomography (SPECT)
- Fluorescence imaging
- Magnetoencephalography for Brain imaging
- Electrocardiography for Heart activity imaging
- ...

Analog and Digital Radiography

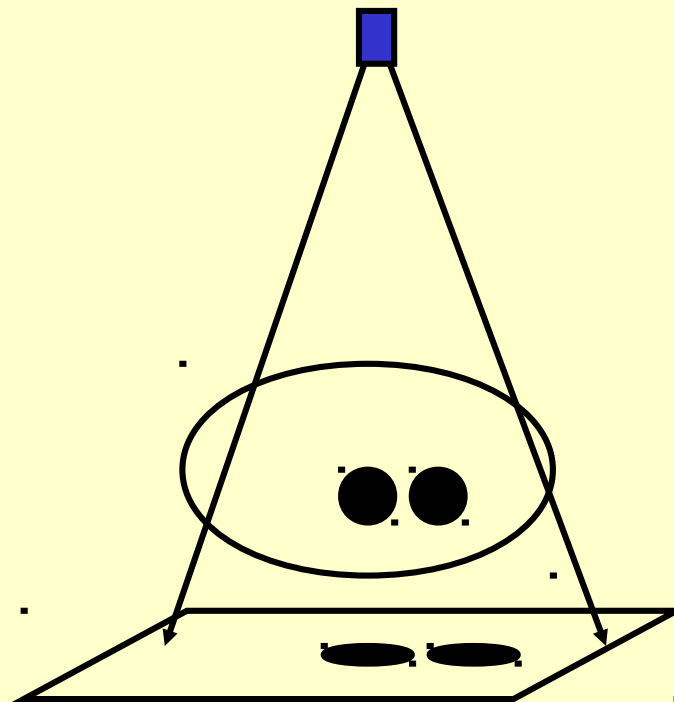
- The transmission and detection of X-rays still lies at the heart of radiography, angiography, fluoroscopy and mammography examinations.
- However, traditional film-based scanners are gradually replaced by digital systems
- In Digital Radiology, the end result is an **image** which can be viewed, moved and stored without a single piece of film ever being exposed.
- All the aspects of **Digital Image Processing** are used to enhance, to increase the resolution, to segment, to detect contours, to recognize shapes and patterns, ...

General Characteristics of Digital Radiology

Resolution: Ability to discern two points close together



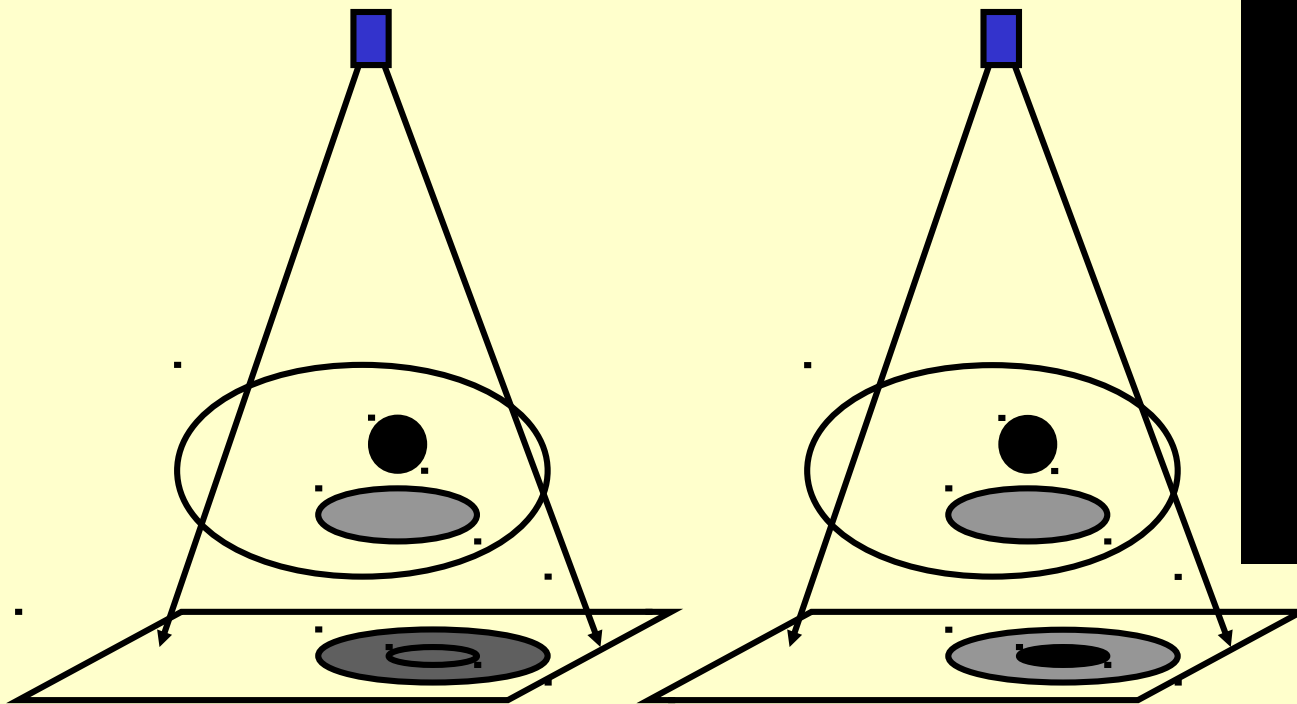
Unresolved



Resolved

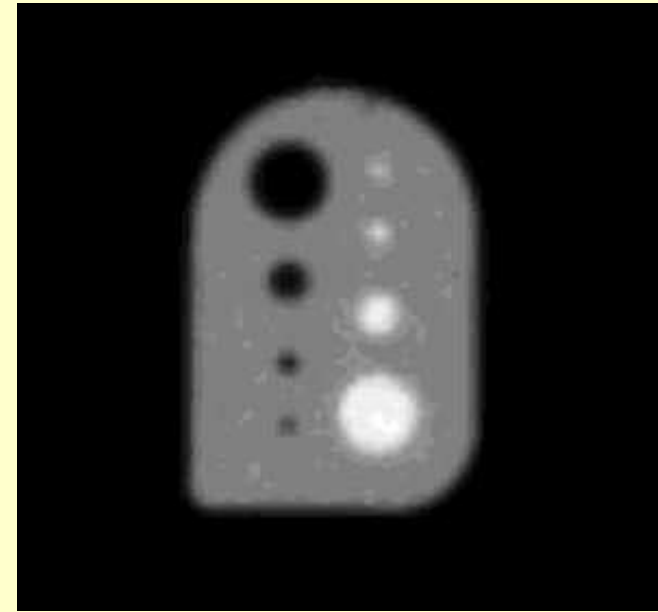
General Characteristics of Digital Radiology

Contrast: Ability to discern interesting object from noise or other tissues



Poor Contrast

Good Contrast



Detectability

Digital Radiography Image Processing

- **Contrast enhancement**
- **Increasing the resolution**
- **Image segmentation**
- **Contour detection**
- **Pattern and shape recognition**
- **Fast compression, progressive transmission and decompression**
- **Multiple access, tagging, commenting, ...**
- **Classification**
- **Archiving**
- **...**



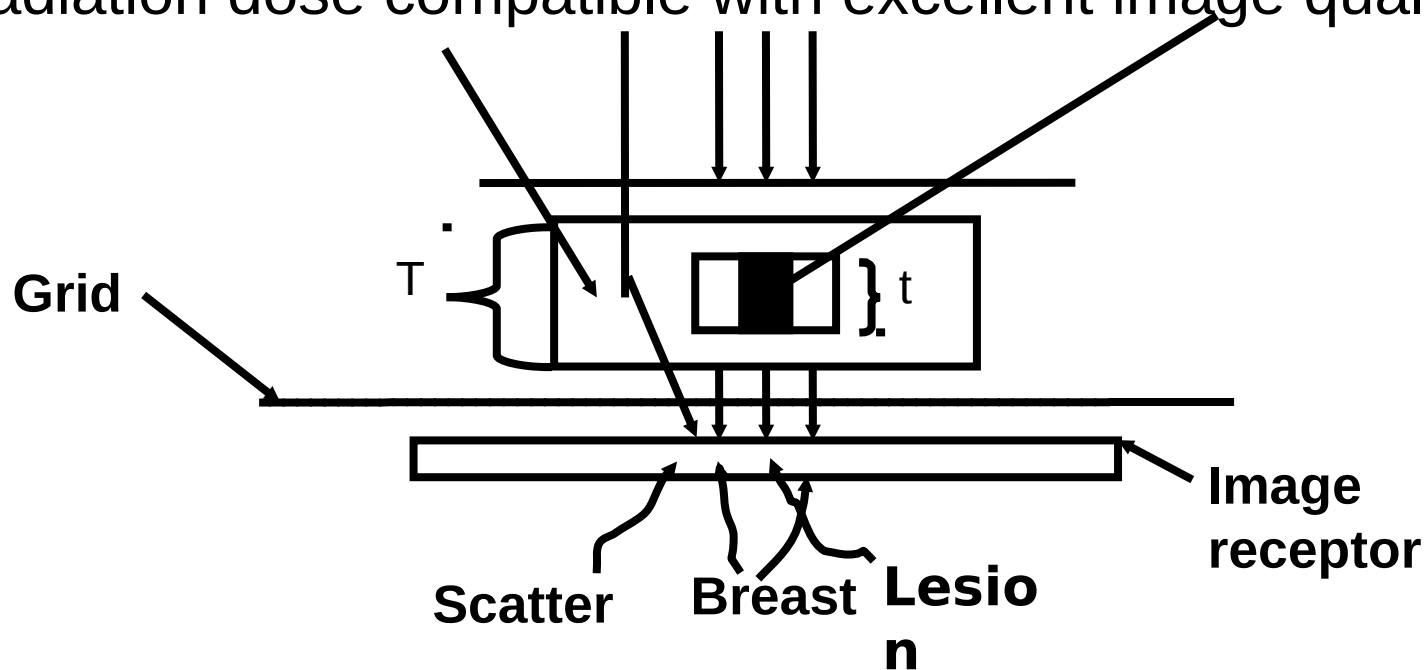
Fluoroscopy (Angiograms)

Fluoroscopy is a technique in which a continuous beam of x-rays is used to produce moving images.

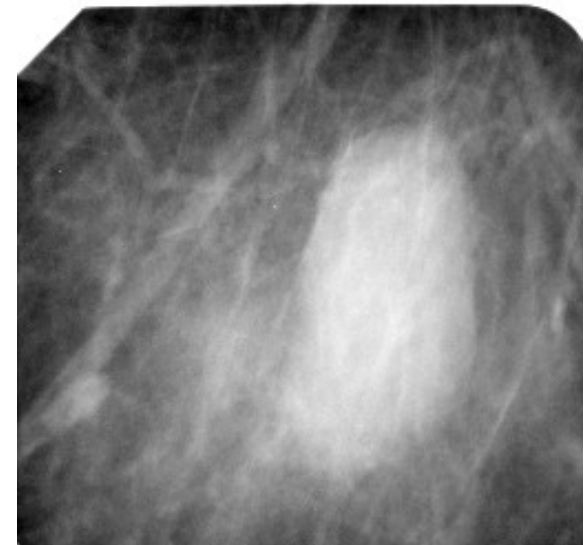
It is used to show movement in the digestive system (which may require ingestion of a high-contrast liquid such as barium) and the circulatory system (angiograms).

Mammography

- The mammogram is an X-ray shadowgram.
- Regions of reduced transmission such as a tumor, a calcification or normal fibro glandular tissue.
- The imaging system must have a sufficient spatial resolution to delineate the edges of fine structures in the breast.
- Structural detail small as $50\text{ }\mu\text{m}$ must be resolved adequately.
- Because the breast is sensitive to ionization radiation, which is known to cause breast cancer, it is desirable to use the lowest radiation dose compatible with excellent image quality.



Mammography



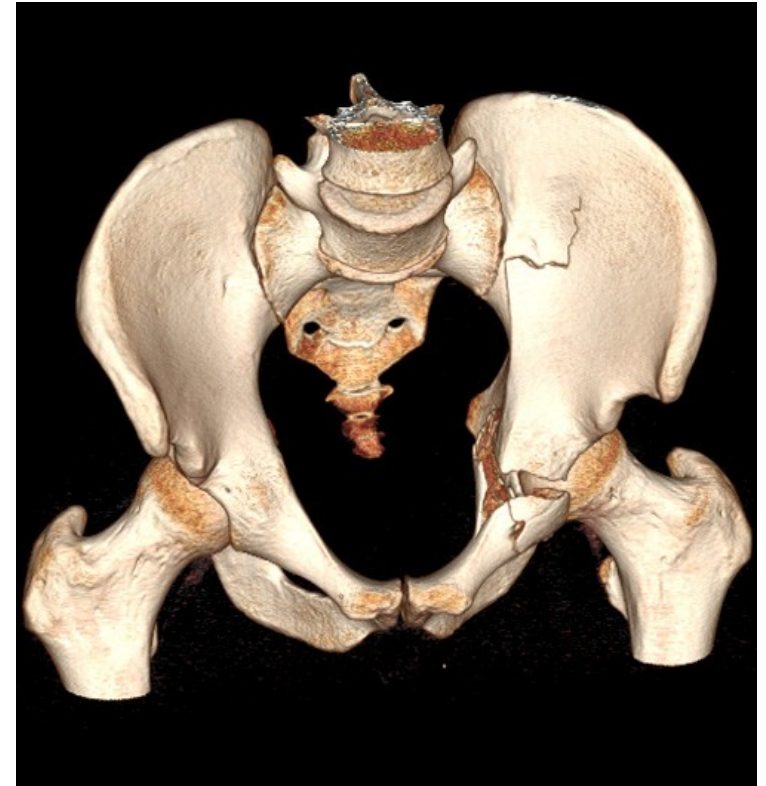
Benign lesion - Fibroadenoma

Computed Tomography

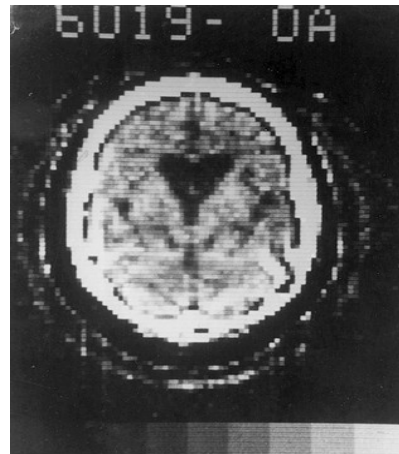
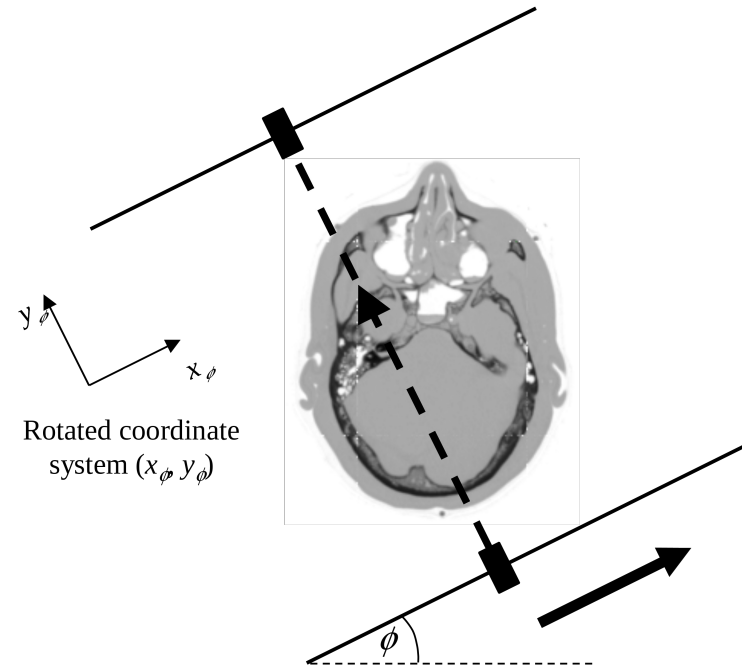
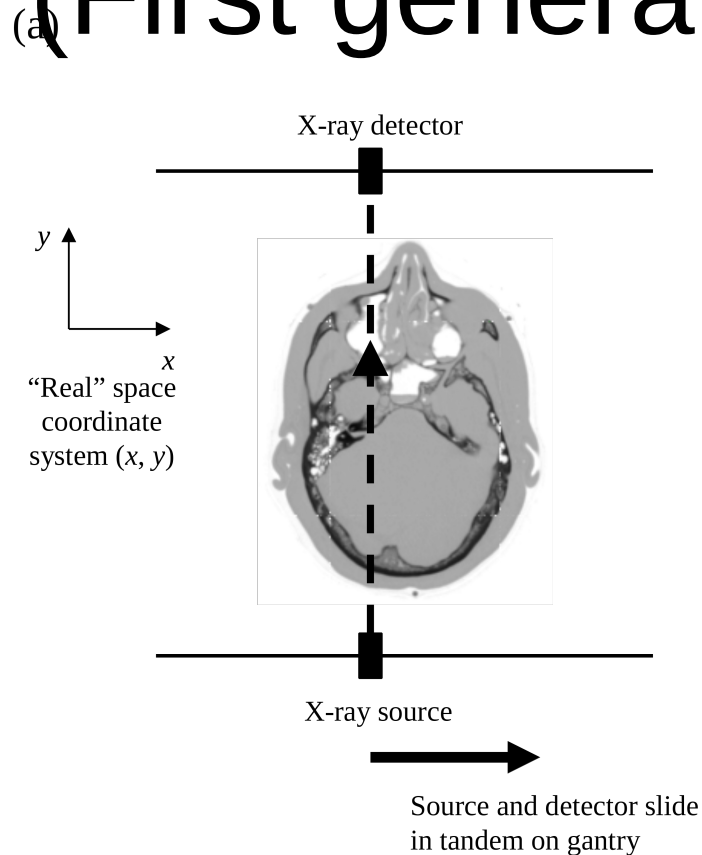
Computed tomography (CT) scans, also called computer-assisted tomography (CAT) scans, use x-rays to produce images at different angles through the body so that a 3D image can be constructed.

CT scans may be used to diagnose cancers, skeletal abnormalities and vascular diseases (affecting blood vessels).

But since CT scans use x-rays, they also increase your cancer risk.



X-ray Computer Tomography (First generation CT scans 1970)



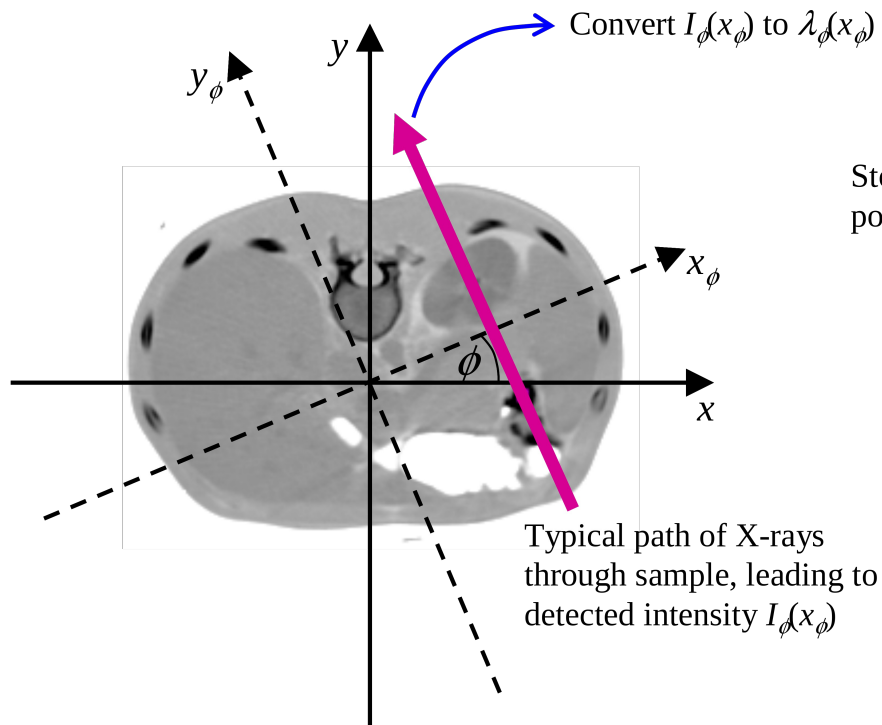
80 x 80-matrix head
CT image obtained with

EMI CT head scanner
(Mayo Clinic, Rochester,
Minn, circa 1973)

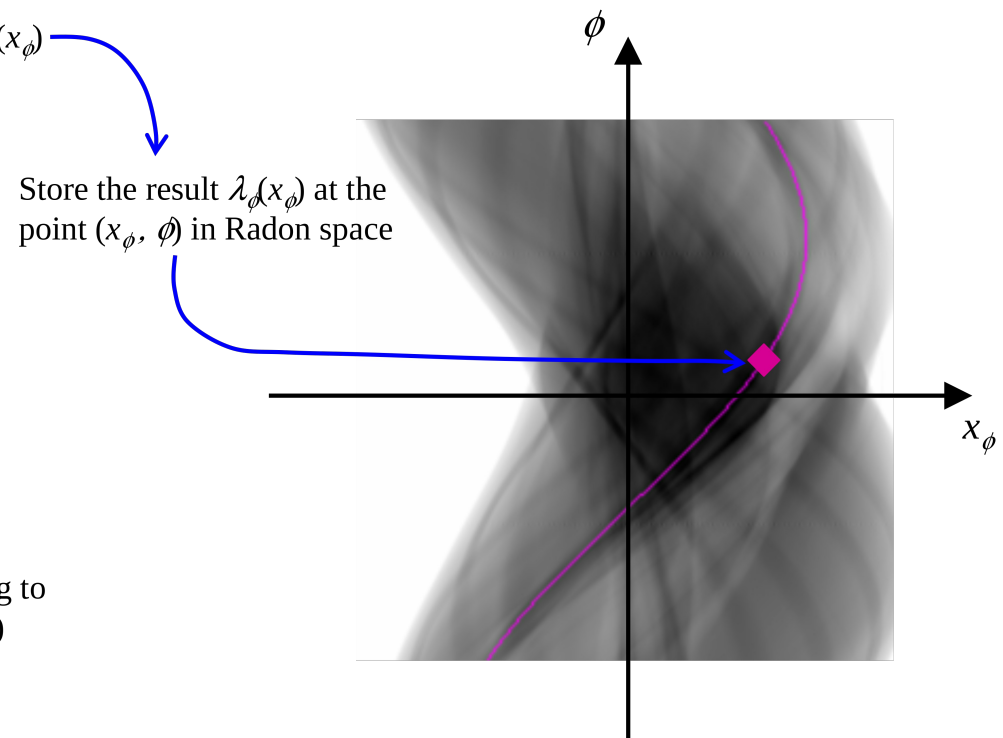
X ray CT and Radon Transform

Parallel rays : $I(x) = I_0 \exp\left\{-\int \mu(x, y) dy\right\}$

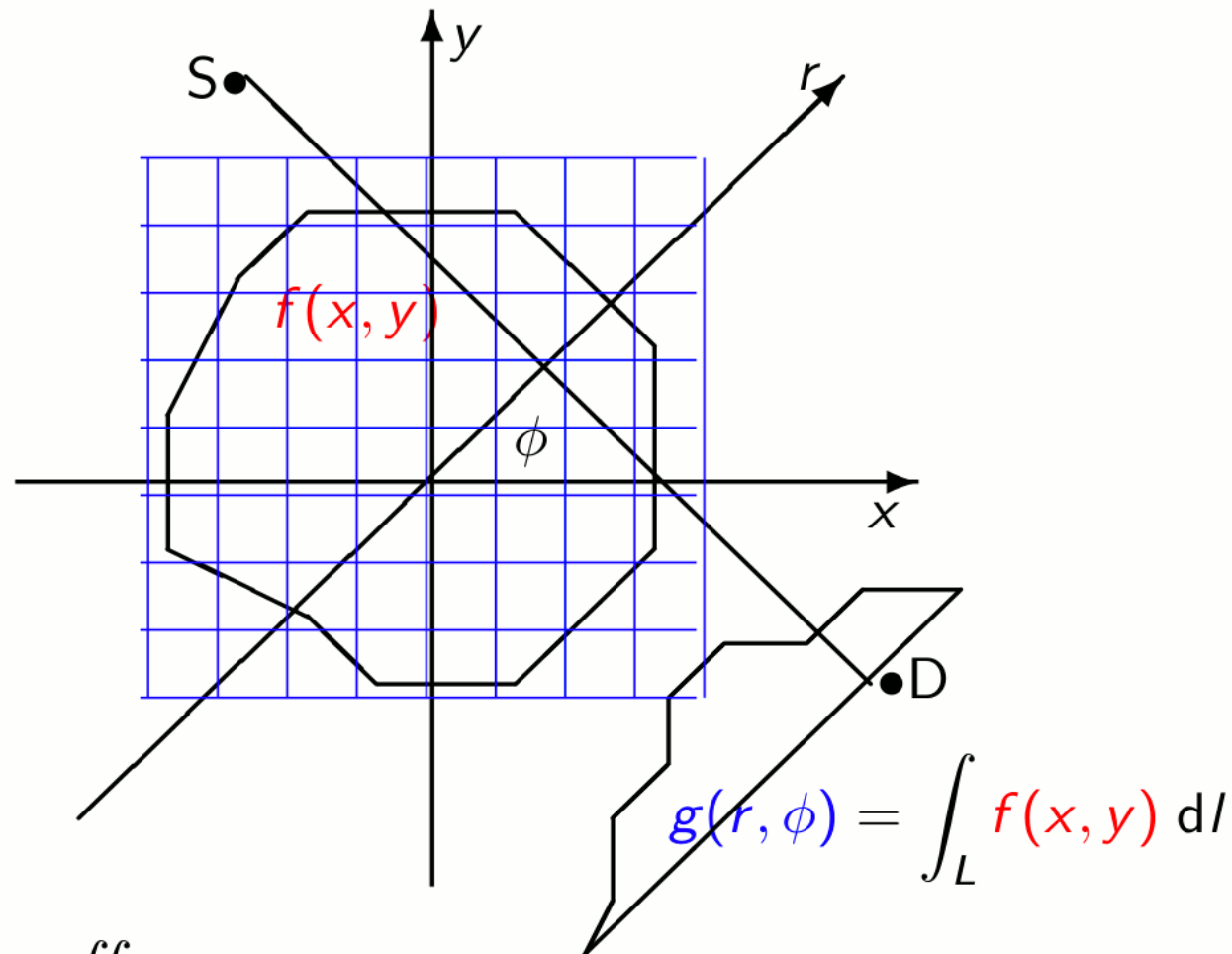
Real (Image) Space



Radon Space



Analytical Inversion methods



Radon:

$$g(r, \phi) = \iint_D f(x, y) \delta(r - x \cos \phi - y \sin \phi) dx dy$$

$$f(x, y) = \left(-\frac{1}{2\pi^2} \right) \int_0^\pi \int_{-\infty}^{+\infty} \frac{\frac{\partial}{\partial r} g(r, \phi)}{(r - x \cos \phi - y \sin \phi)} dr d\phi$$

Filtered Backprojection method

$$f(x, y) = \left(-\frac{1}{2\pi^2} \right) \int_0^\pi \int_{-\infty}^{+\infty} \frac{\frac{\partial}{\partial r} g(r, \phi)}{(r - x \cos \phi - y \sin \phi)} dr d\phi$$

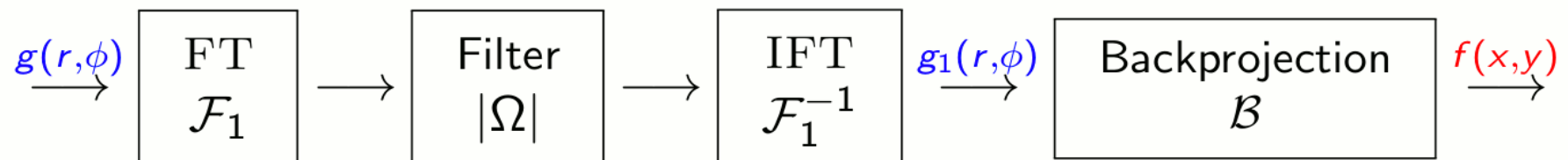
Derivation \mathcal{D} : $\bar{g}(r, \phi) = \frac{\partial g(r, \phi)}{\partial r}$

Hilbert Transform \mathcal{H} : $g_1(r', \phi) = \frac{1}{\pi} \int_0^\infty \frac{\bar{g}(r, \phi)}{(r - r')} dr$

Backprojection \mathcal{B} : $f(x, y) = \frac{1}{2\pi} \int_0^\pi g_1(r' = x \cos \phi + y \sin \phi, \phi) d\phi$

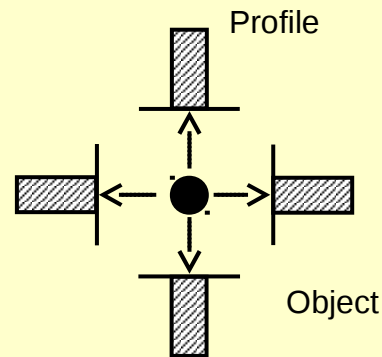
$$f(x, y) = \mathcal{B} \mathcal{H} \mathcal{D} g(r, \phi) = \mathcal{B} \mathcal{F}_1^{-1} |\Omega| \mathcal{F}_1 g(r, \phi)$$

- Backprojection of filtered projections:

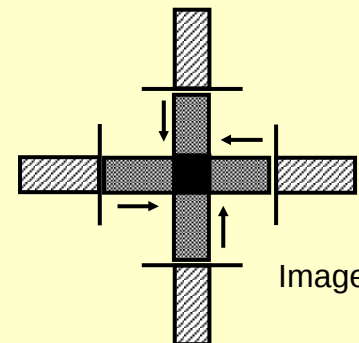


Radon Transform: BackProjection (BP) and Filtered BP

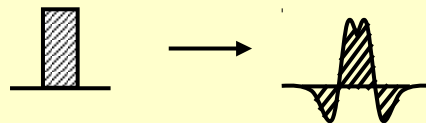
**Forward
Projection**



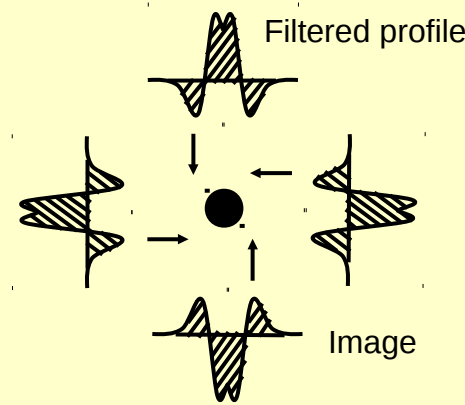
**Back-
Projection**



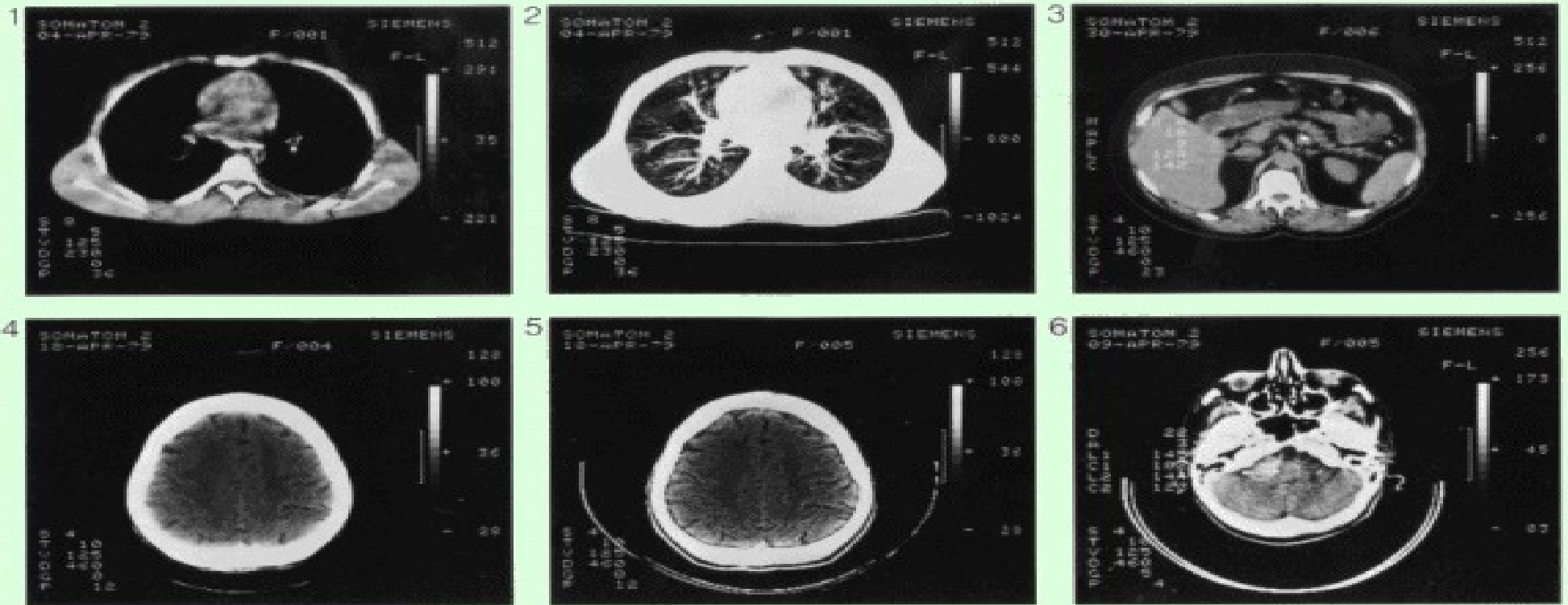
**Filtered
Projection**



**Filtered
Back-
Projection**

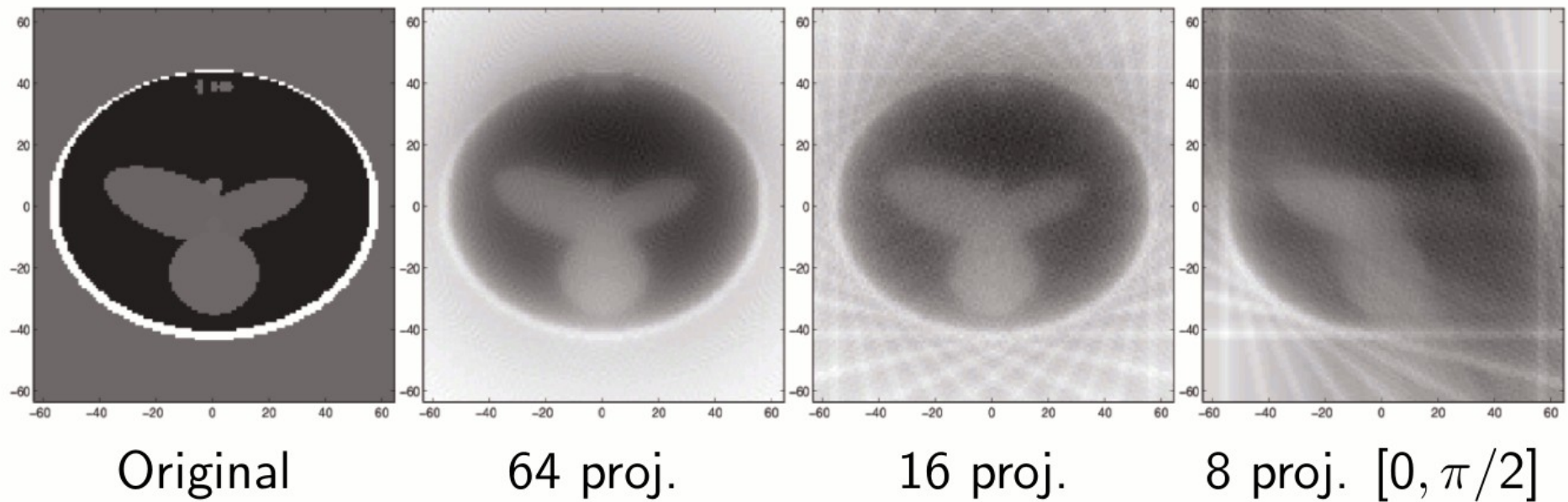


Example of cross-sections through several parts of the body:
skull, thorax, and abdomen, obtained by computed tomography.



Visualization of the values of the attenuation coefficients by way of gray values produces an anatomic image.

Limitations : Limited angle or noisy data



- ▶ Limited angle or noisy data
- ▶ Accounting for detector size
- ▶ Other measurement geometries: fan beam, ...

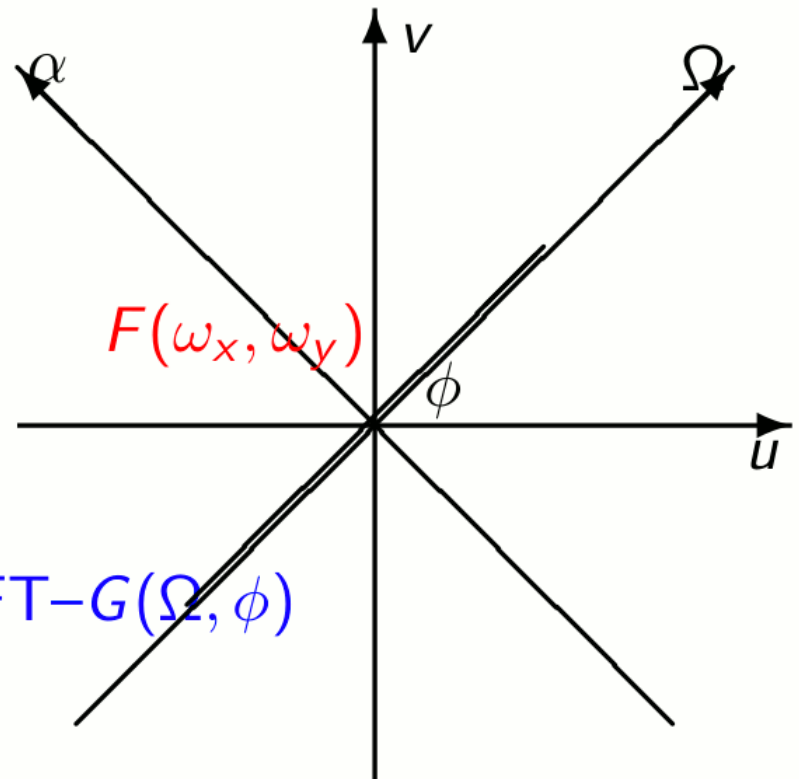
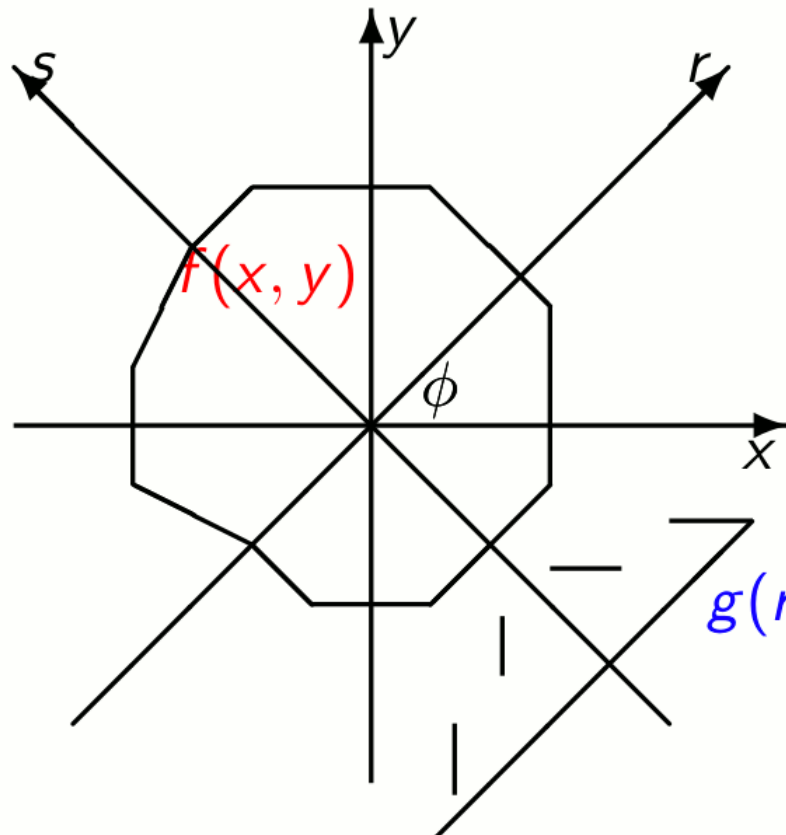
Fourier Synthesis in X ray Tomography

$$g(r, \phi) = \iint f(x, y) \delta(r - x \cos \phi - y \sin \phi) dx dy$$

$$G(\Omega, \phi) = \int g(r, \phi) \exp[-j\Omega r] dr$$

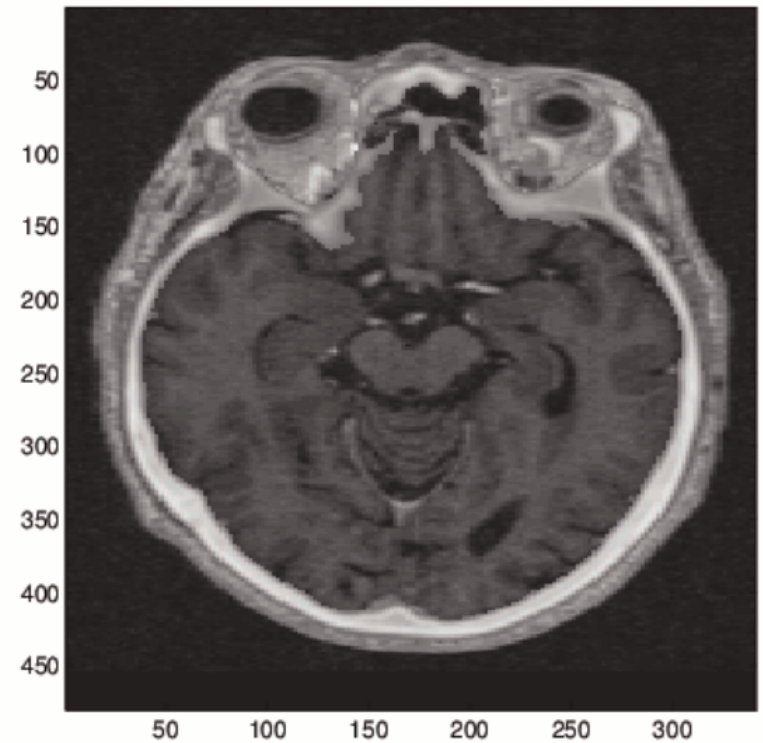
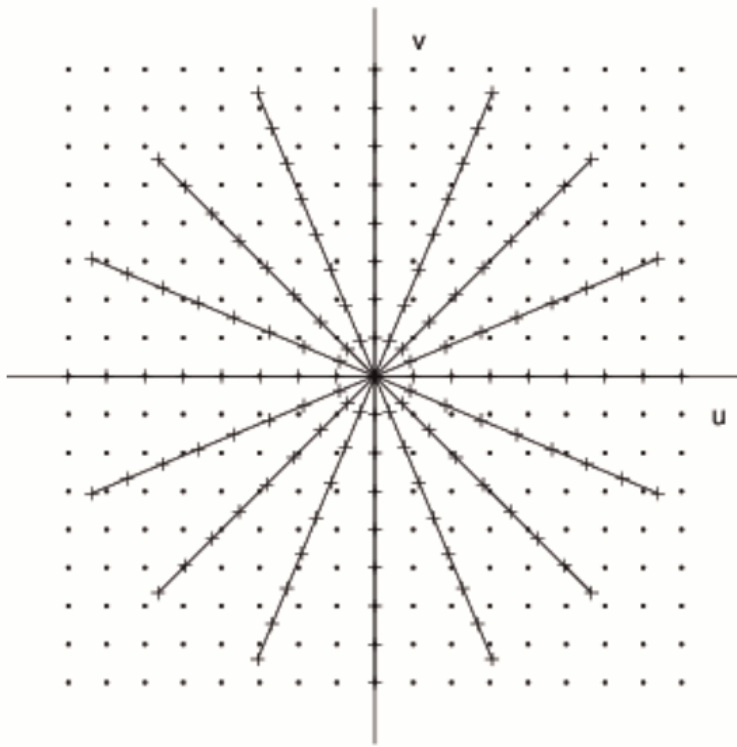
$$F(\omega_x, \omega_y) = \iint f(x, y) \exp[-j\omega_x x, \omega_y y] dx dy$$

$$F(\omega_x, \omega_y) = G(\Omega, \phi) \quad \text{for} \quad \omega_x = \Omega \cos \phi \quad \text{and} \quad \omega_y = \Omega \sin \phi$$



Fourier Synthesis in X ray tomography

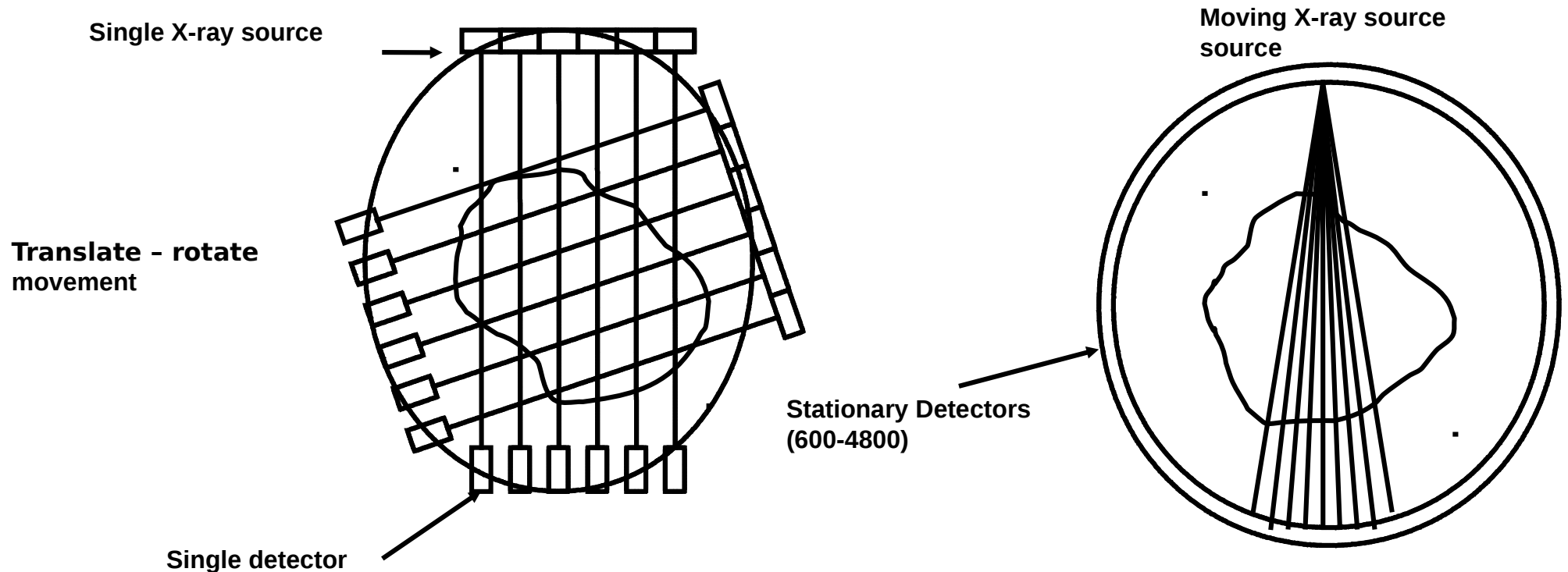
$$G(\omega_x, \omega_y) = \iint f(x, y) \exp[-j(\omega_x x + \omega_y y)] dx dy$$



Forward problem: Given $f(x, y)$ compute $G(\omega_x, \omega_y)$

Inverse problem: Given $G(\omega_x, \omega_y)$ on those lines
estimate $f(x, y)$

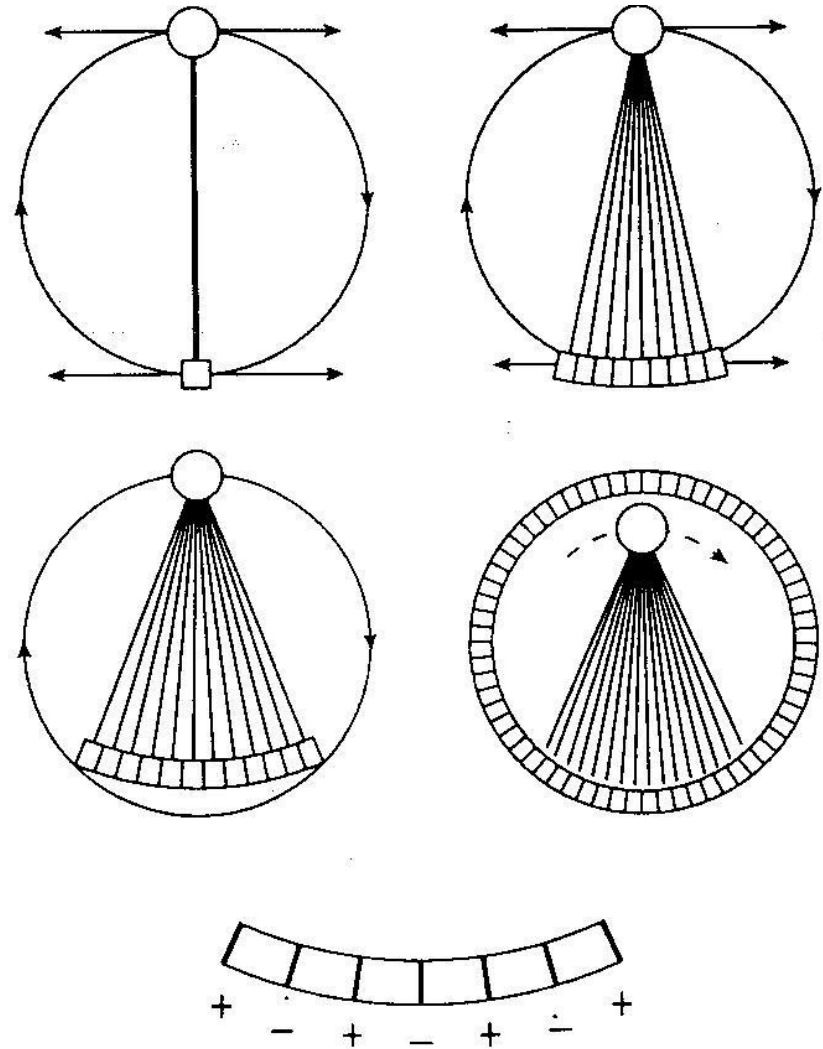
Different X ray tomography systems



- Parallel and fan beam geometry
- Helical acquisition for whole body

Different generations of X rays CT

- Single source/Single detector
- Single source/multi detectors
- Parallel/Fan Beam/Helical
- Single/Multi slice
- Wide angle source
- Rotation speed
- Electron beam
- FBP
- Iterative methods



X rays CT different generations

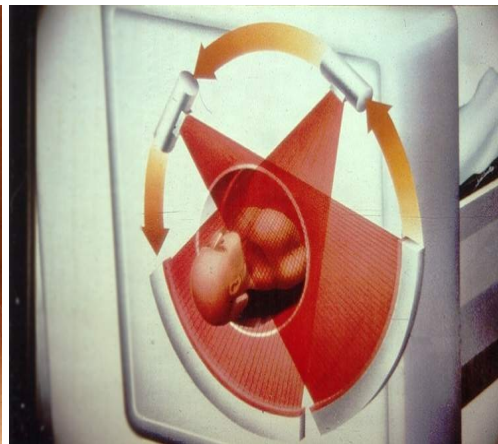
1975

Translation / Rotation



1980

Rotation / Rotation



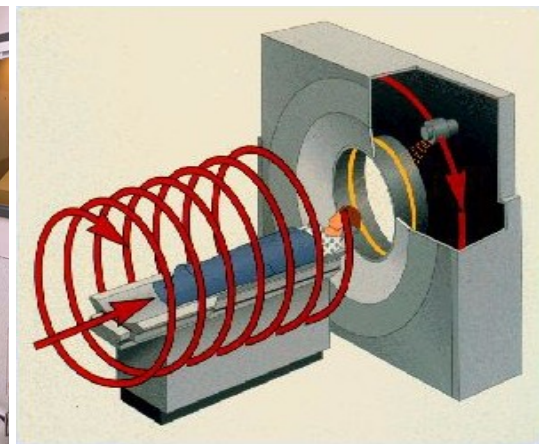
1990

Rotation / Stationary



2000

Rotation / Helical



- 2010 : Fifth generation
Electron Beam (EBCT)
Helical, multi slice,
high performance detectors,
3D, Low dose, ...



Low Dose X rays CT

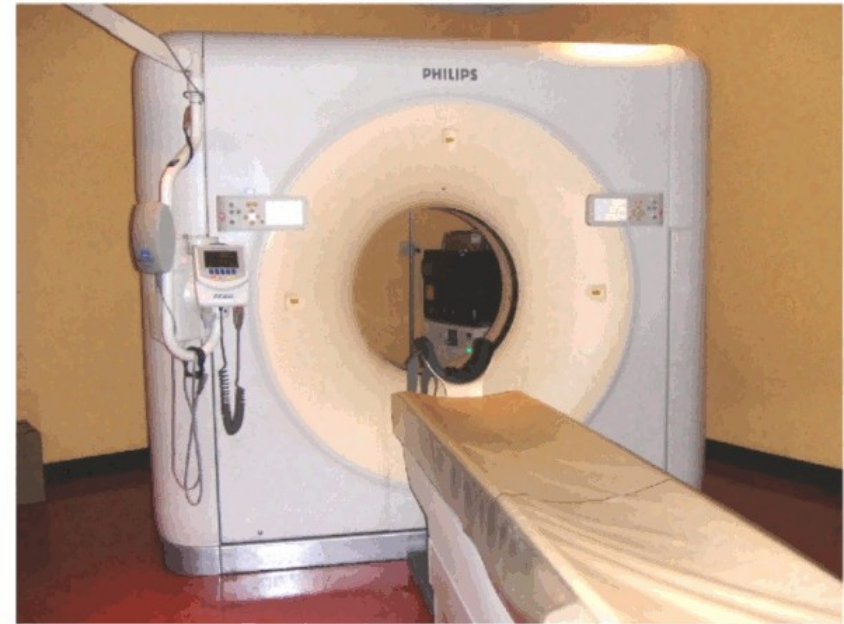
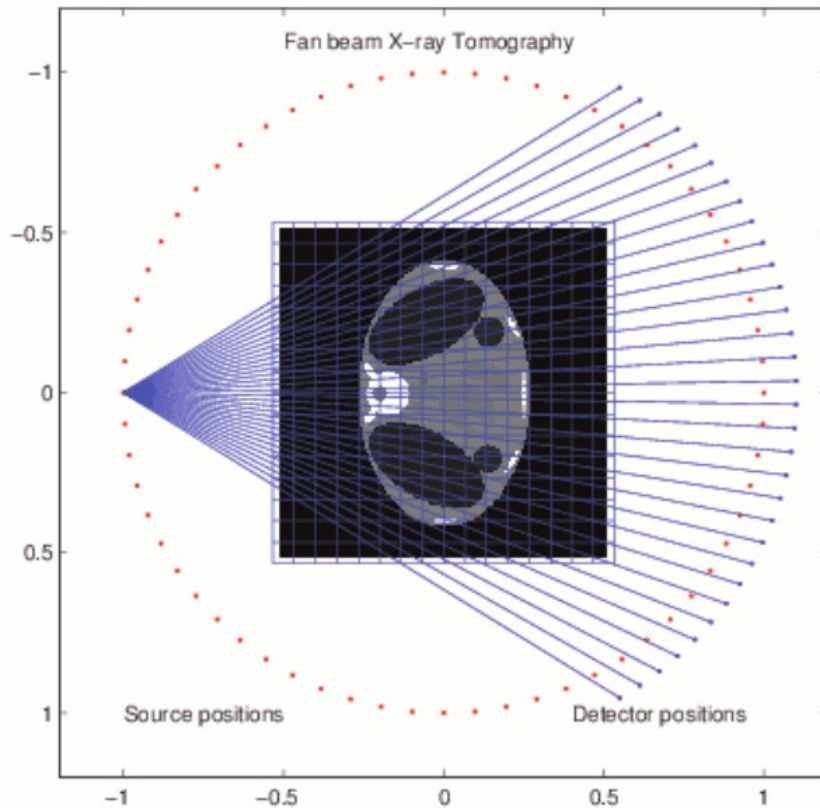
Dose = $1 / (\text{Slice thickness} \times \text{relative noise}^2 \times \text{pixel size}^3)$

Risk of fatal cancer - 1 in 20,000 per mSv per year

- Reducing exposure energy and time
- Poisson likelihood
- Bayesian approach with more appropriate prior models depending on application
- Reducing the number of projections
- Using both attenuation and diffusion
- Iterative Reconstruction methods

Computed tomography (CT)

A Multislice CT Scanner



$$g(s_i) = \int_{L_i} f(r) \, dl_i + \epsilon(s_i)$$

Discretization

$$\mathbf{g} = \mathbf{H} \mathbf{f} + \epsilon$$

$$\mathcal{M} : \quad \mathbf{g} = \mathbf{H} \mathbf{f} + \epsilon$$

- ▶ Observation model \mathcal{M} + Hypothesis on the noise $\epsilon \rightarrow$ Likelihood

$$p(\mathbf{g} | \mathbf{f}; \mathcal{M}) = p_{\epsilon}(\mathbf{g} - \mathbf{H} \mathbf{f})$$

- ▶ A priori information $p(\mathbf{f} | \mathcal{M})$

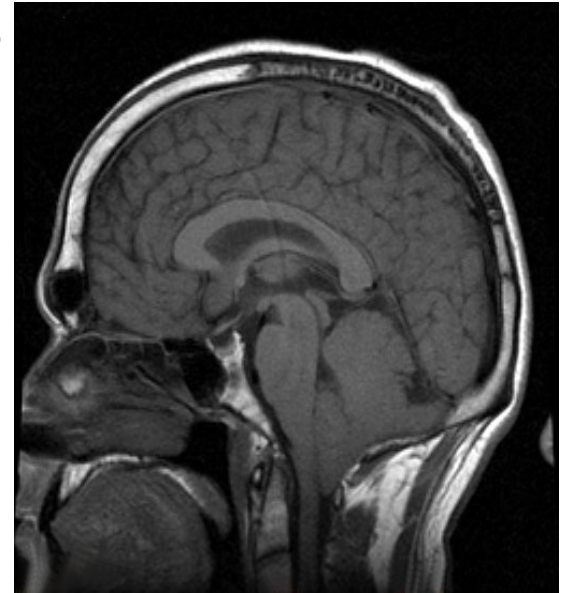
- ▶ Bayes :
$$p(\mathbf{f} | \mathbf{g}; \mathcal{M}) = \frac{p(\mathbf{g} | \mathbf{f}; \mathcal{M}) p(\mathbf{f} | \mathcal{M})}{p(\mathbf{g} | \mathcal{M})}$$

Main steps:

- ▶ Expression of Likelihood:
Gaussian, Poisson, ...
- ▶ Expression of prior law:
Gaussian, Generalized Gaussian, Student, Gauss-Markov,
Gauss-Markov-Potts
- ▶ Choice of estimators and Computational aspects: MAP, EAP,
MCMC, VBA, ABC

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) is a technique that uses strong magnets and radio waves that interact with the hydrogen atoms in your body (esp. in water). A computer is used to construct an image from the signal received from the atoms.

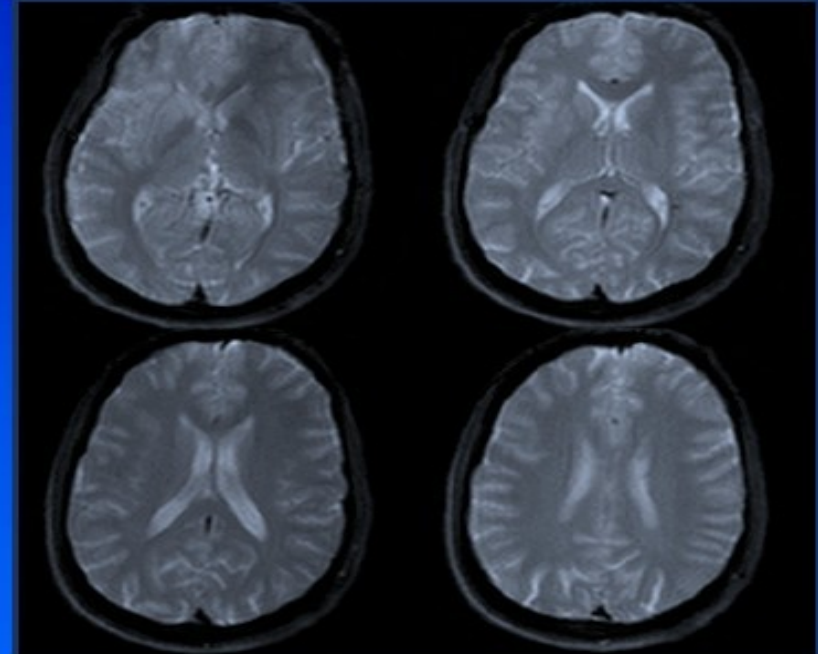
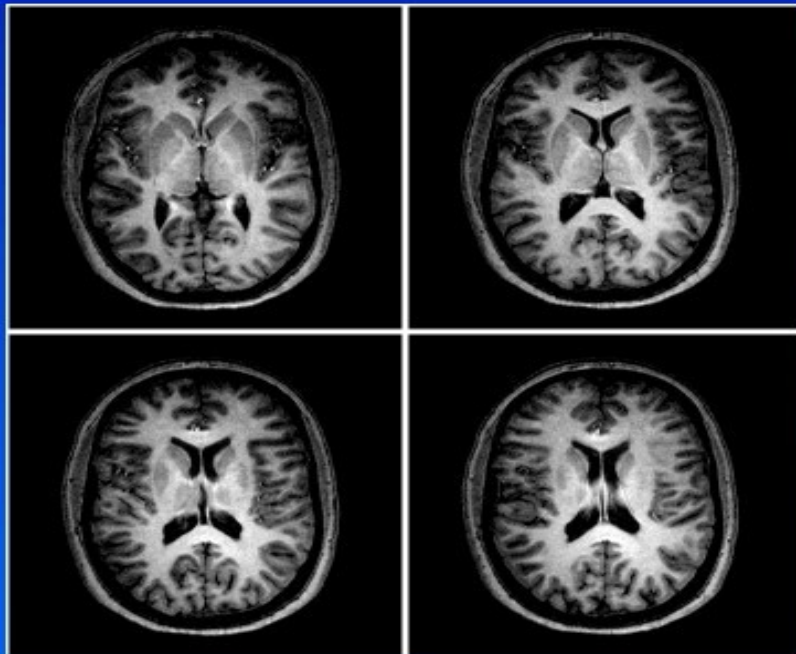
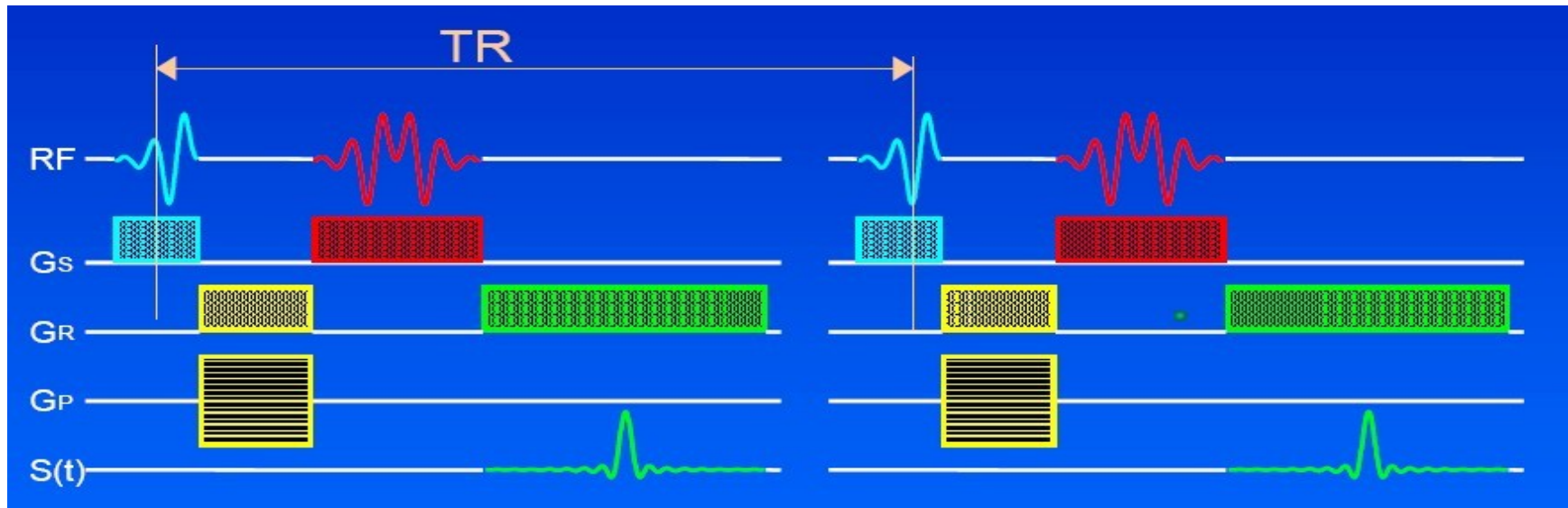


MRI is used to image the structure and function of the brain, heart, soft tissue, and the inside of bones; to diagnose cancers, brain diseases, and problems with the circulatory system.

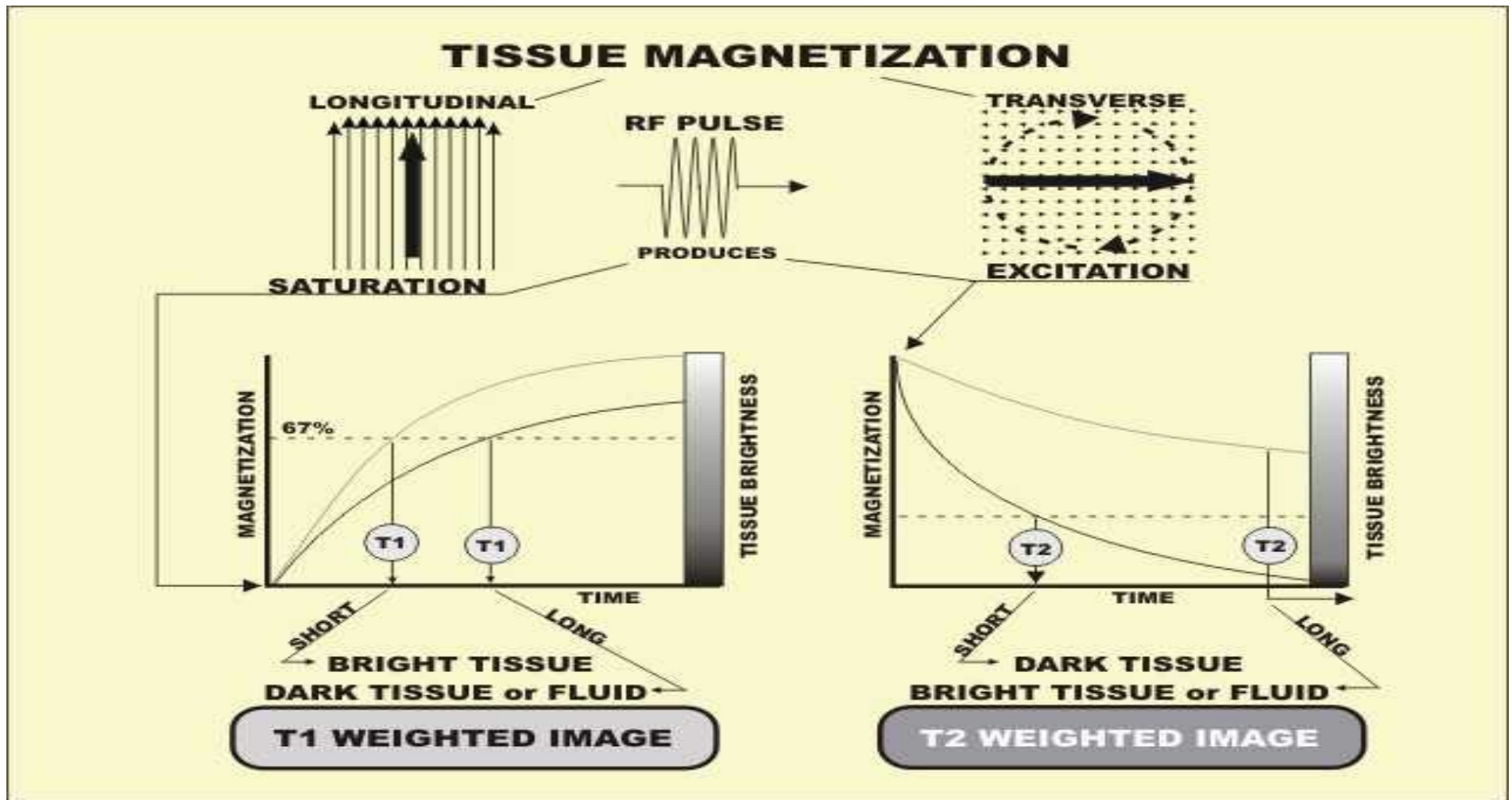
Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI)

- 1970: Lauterbur introduced concept of magnetic field gradients, leading to images based on magnetic resonance.
- 1980: whole body magnets produced in UK, permitting first *in vivo* images of human anatomy.
- Nowadays 20 million scans performed worldwide annually.
- Provides excellent soft-tissue contrast; can be acquired in any imaging plane;
- Unlike CT, does not involve ionising radiation.
- Imaging modality of choice in **brain** and **spinal cord**

Magnetic Resonance Imaging (MRI)



Two modes (T1, T2) of MRI Imaging



MRI Brain images

T_2 -weighting requires long TE, long TR

T_1 -weighting requires short TE, short TR

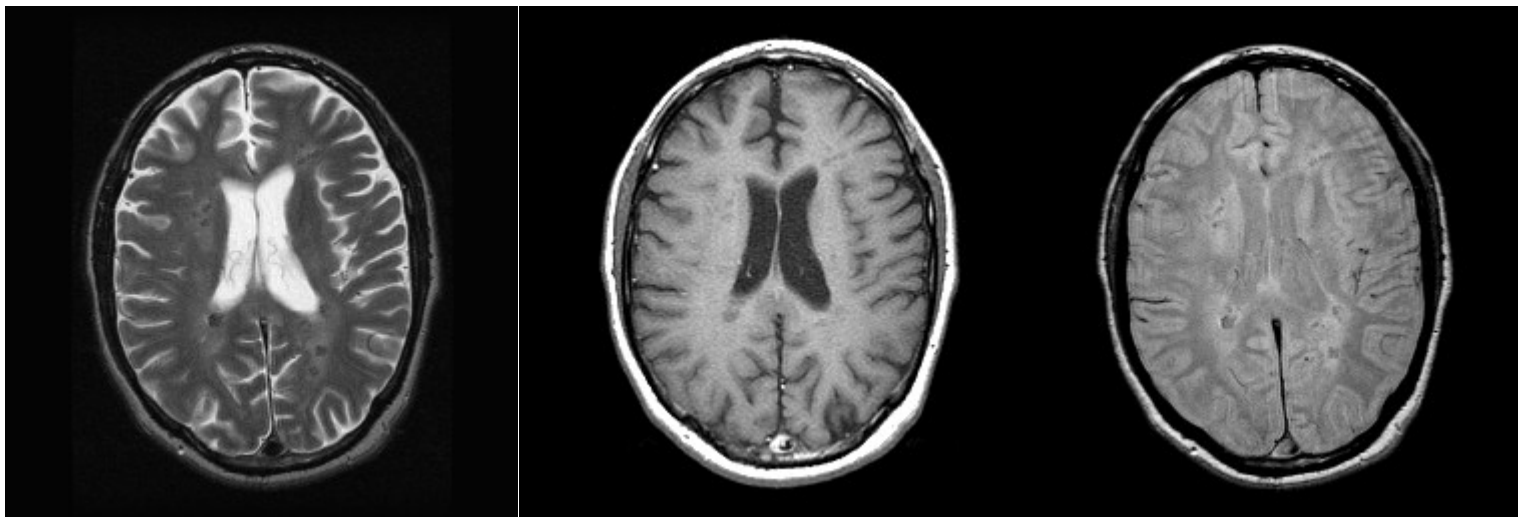
PD-weighting requires short TE, long TR

MRI brain examples with

T_2

T_1

and proton density.



Functional MRI (fMRI)

- 1992: Early development of functional MRI (fMRI)
- Allows the mapping of the function of the various regions of the human brain.
- Five years earlier many clinicians thought echo-planar imaging's primary applications was to be in real-time cardiac imaging.
- The development of fMRI opened up a new application for EPI in mapping the regions of the brain responsible for thought and motor control.
- In 1994, researchers at the State University of New York at Stony Brook and Princeton University demonstrated the imaging of hyperpolarized ^{129}Xe gas for respiration studies.

Different MRI imaging systems

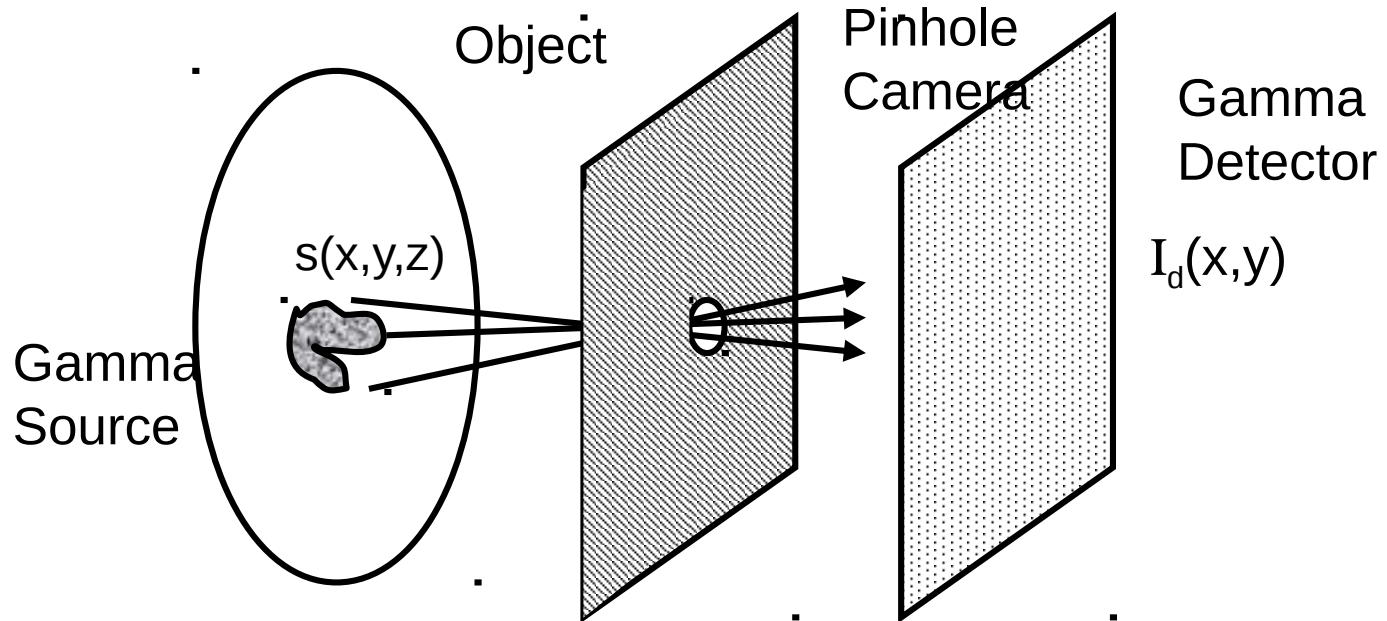


Open MRI



**Main
Mathematical problem :
Fourier Synthesis**

Nuclear Medicine (Scintigraphy)



- Detector records *emission* of gamma photons from radioisotopes introduced into the body
- The integral is a line-integral or a “projection” through obj
- Source $s(x,y,z)$ usually represents a selective uptake of a radio-labeled pharmaceutical

Nuclear Medicine (Scintigraphy)

- Pinhole Size
 - Large pinhole – more photons, better SNR
 - Large pinhole – more blur, reduced resolution
- Half-life
 - Long half lives are easier to handle, but continue to irradiate patient after imaging is done
- Functional Specificity
 - Pharmaceuticals must be specific to function of interest
 - Thallium, Technicium
- No depth info
 - Nuclear Medicine Computed Tomography (SPECT, PET)

Nuclear Imaging systems: Gamma Camera, PET, SPECT



SPECT

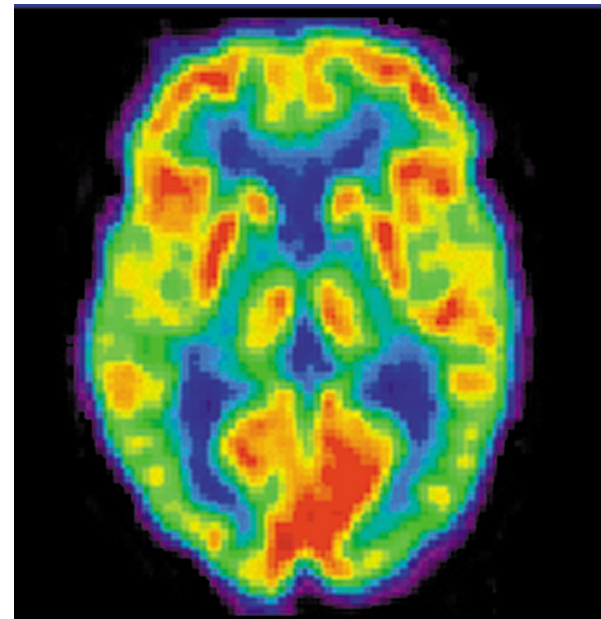


Whole body PET

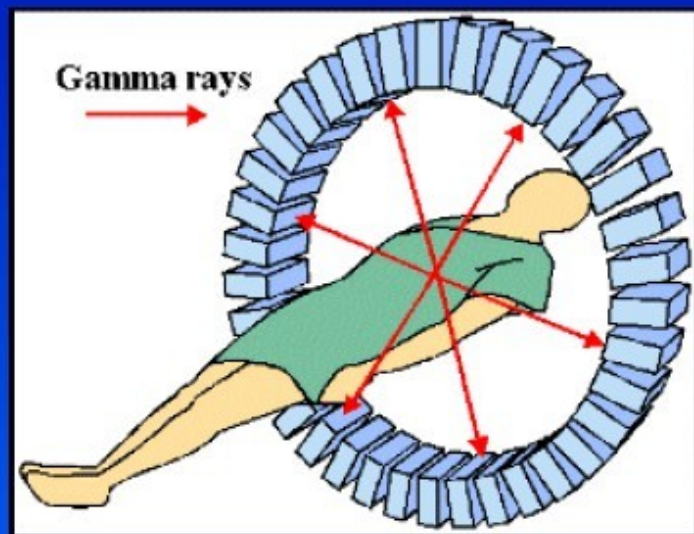
Positron Emission Tomography (PET)

PET scans are a type of nuclear medicine in which a patient is given a radioisotope that emits positron radiation; the radioisotope is attached to a chemical absorbed by certain tissues or organs.

It is used to detect cancers, heart disease, and some brain disorders (such as Alzheimer's).



PET imaging

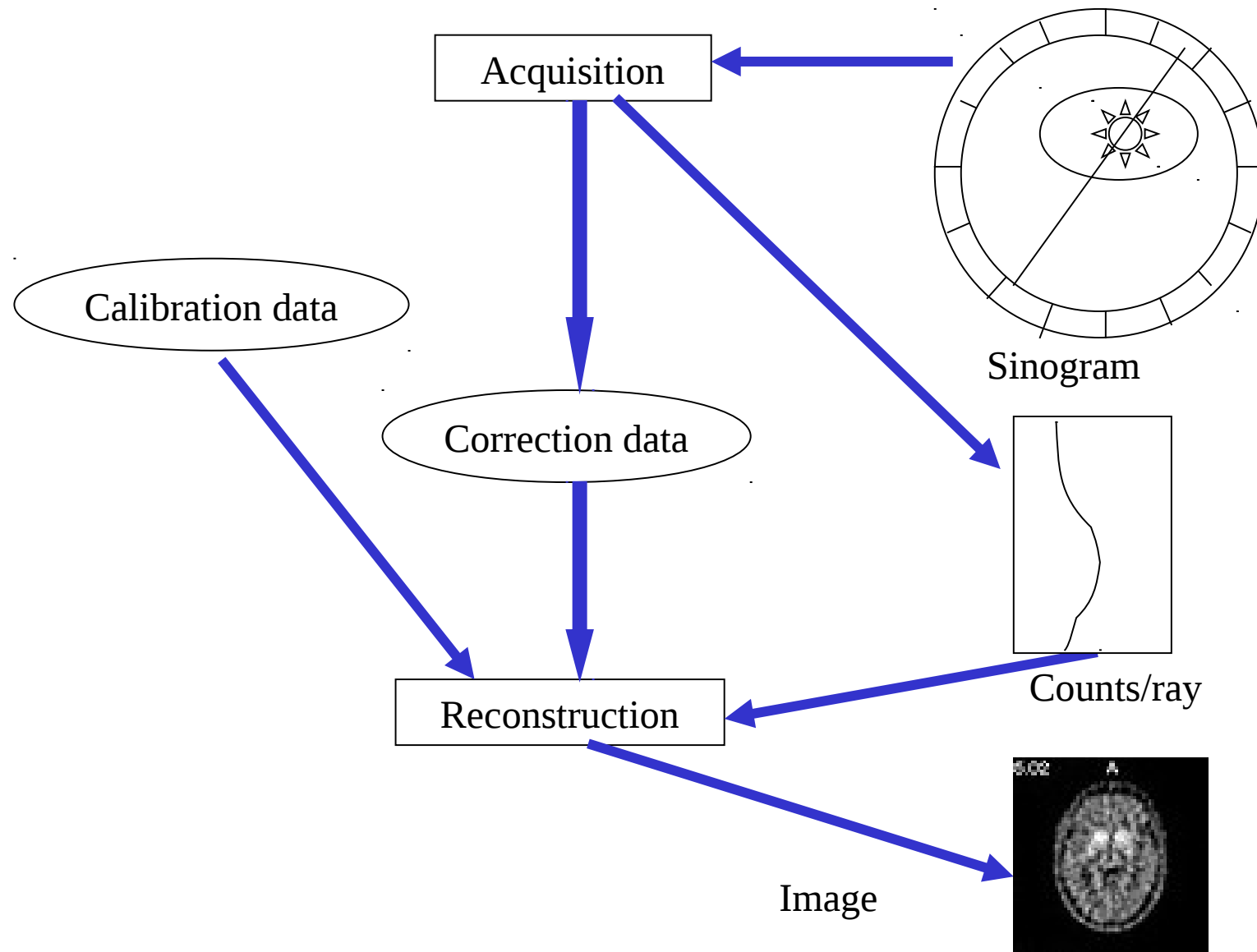


Inject (short-lived) positron emitting isotope.

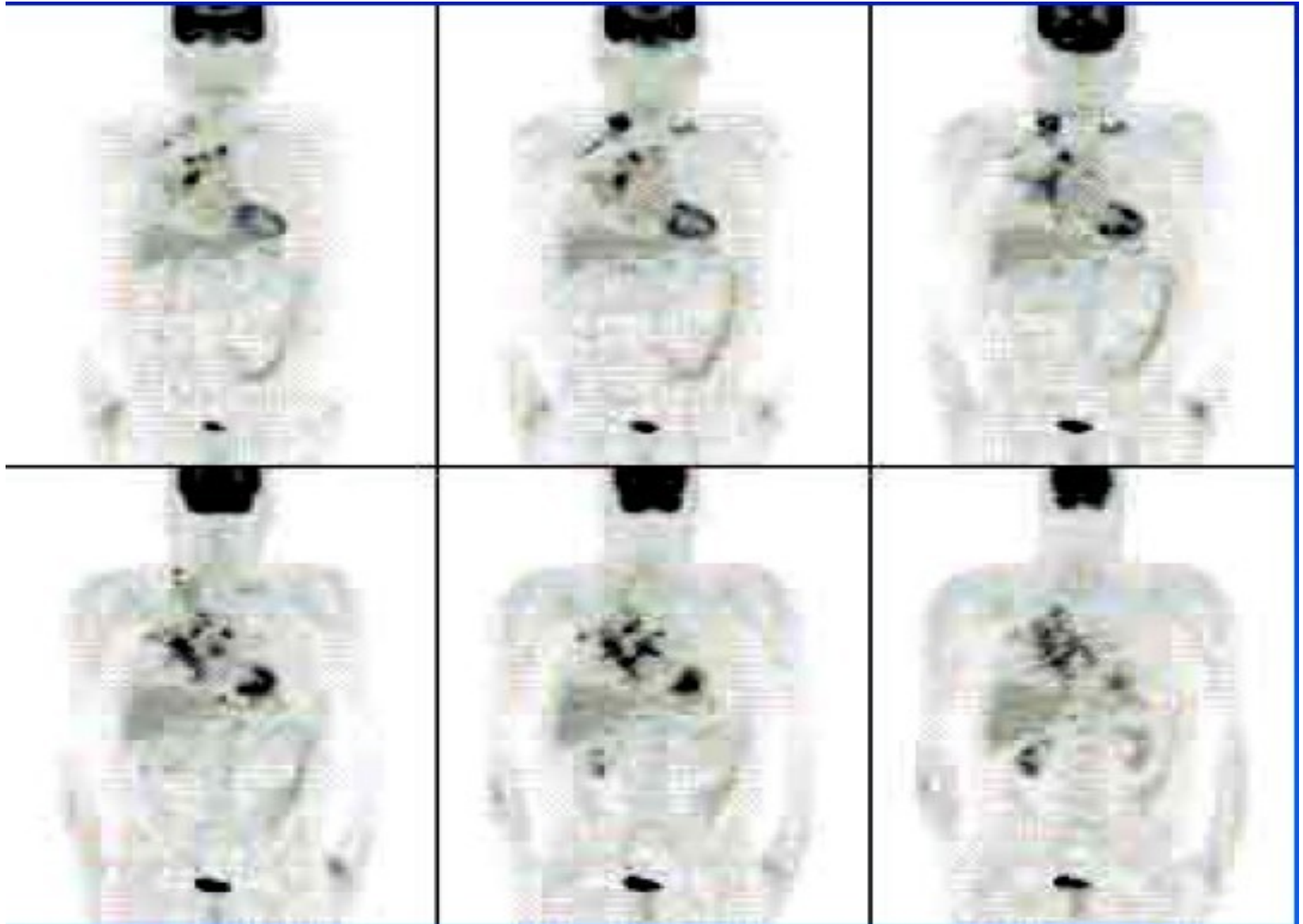
Positron annihilates with electron giving pair of back to back 0.511 MeV gamma rays.

Detect both gammas using fast (5ns) coincidences, get “Line of Response” (LOR). Reconstruction of tracer distribution similar to CT – Radon Transform again.

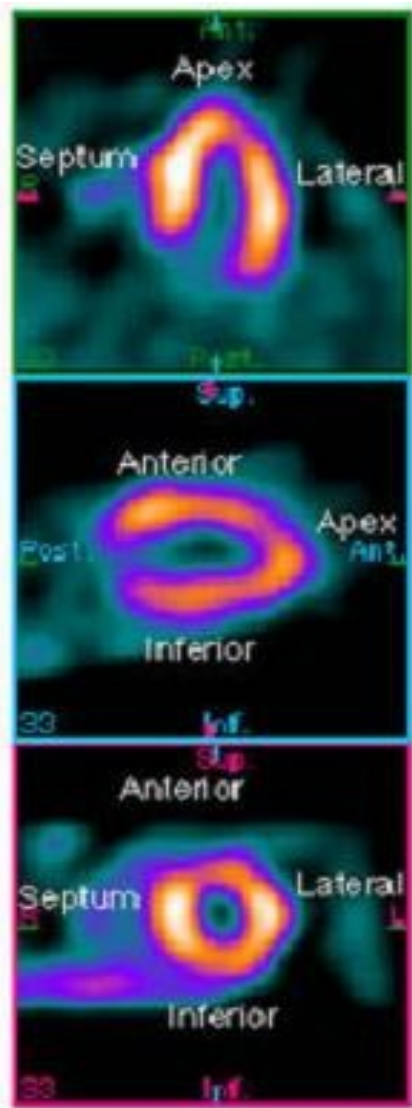
PET Acquisition and processing



Whole body PET images



Single Photon Emission Computed Tomography (SPECT)



Vertical long axis

Horizontal long axis

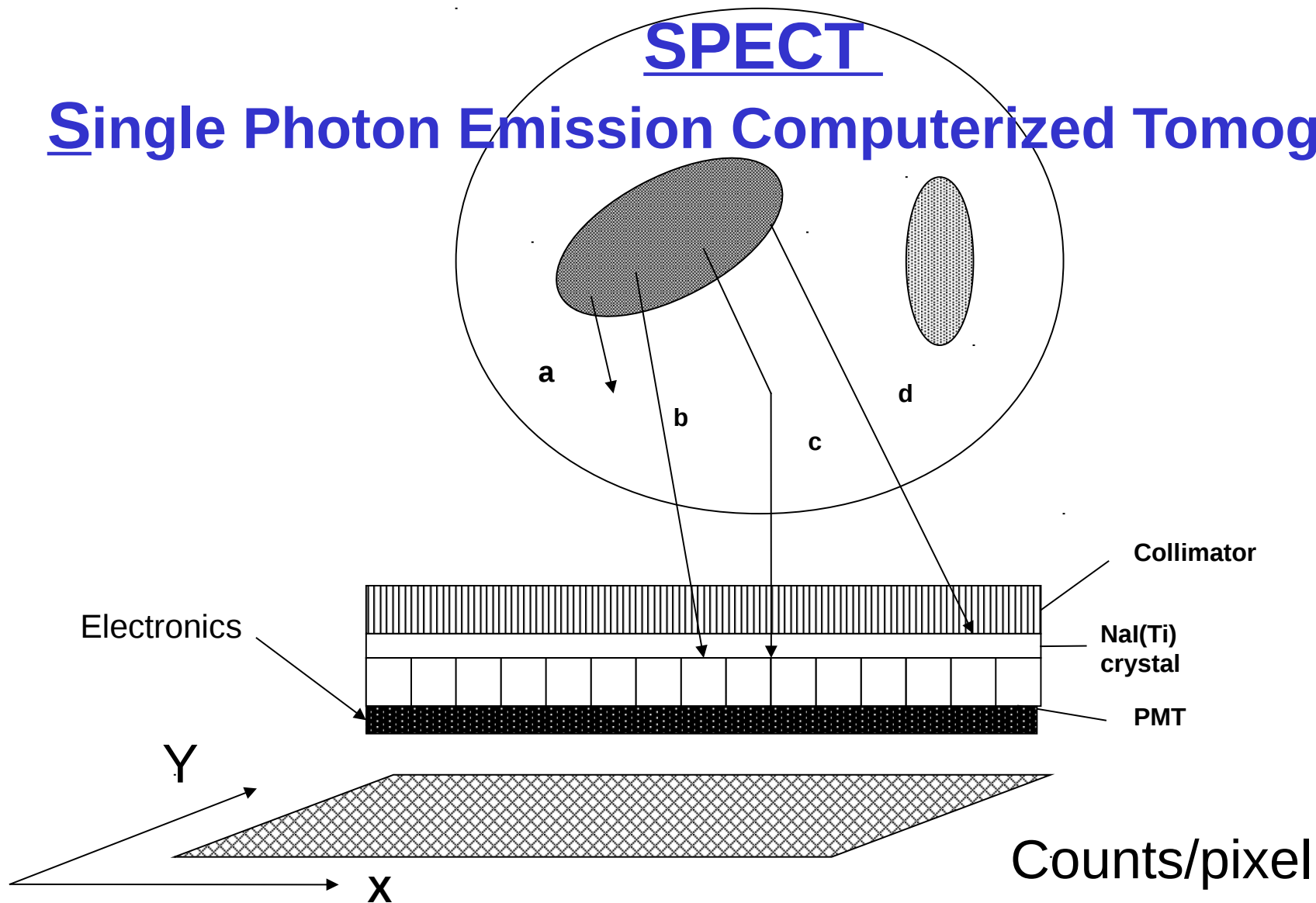
Short axis



- Images on left show three sections through the heart.
- A radioactive tracer, Tc99m MIBI (2-methoxy isobutyl isonitride) is injected

SPECT

Single Photon Emission Computerized Tomography

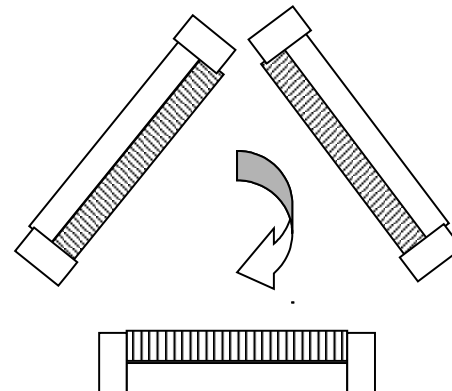
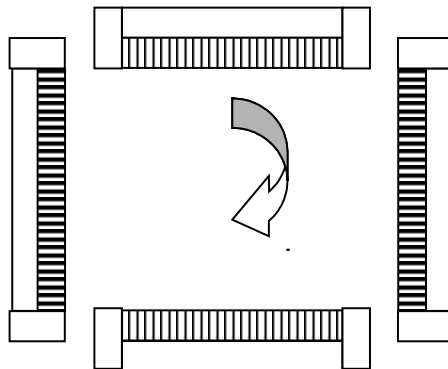
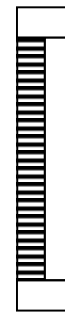


The most important tool in nuclear medicine is the scintillation camera (angier camera) based on a large area (~40 cm in diameter) NaI(Tl) crystal. When a photon hits and interact with the crystal, the scintillation generated and detected by the area of PMTs. An electronic circuit evaluates the relative signals from the PMTs and determines the location of the signal.

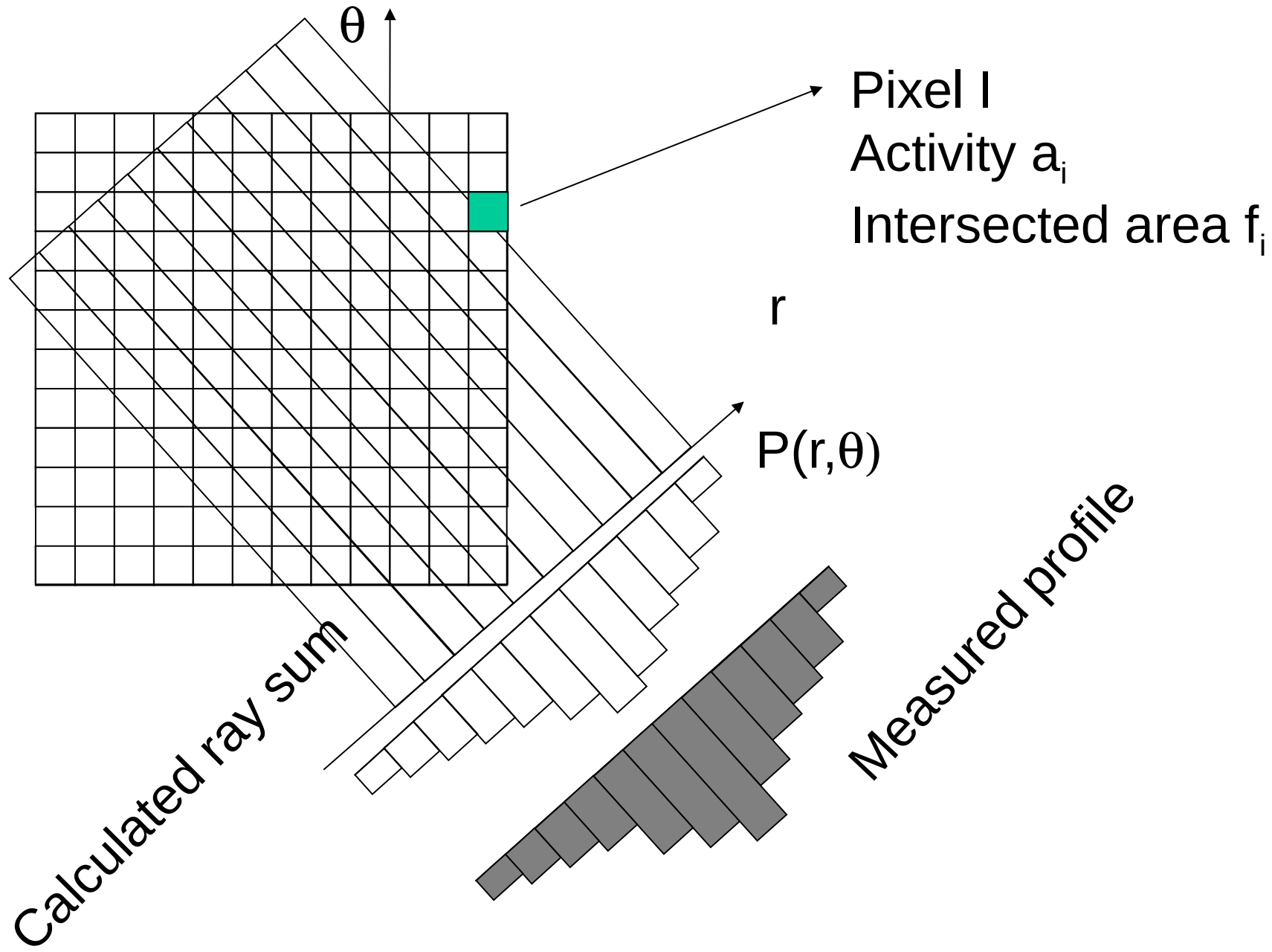
SPECT Machine



Camera based SPECT systems can be one of the configurations below:



Discrete geometry used for iterative reconstruction methods



Whole body nuclear image



PET TRACER PRODUCTION SYSTEMS



PET scanning uses artificial radioactive tracers and radionuclides. Their lifetime is usually rather short, thus they need to be produced on site.



Some examples of such materials are:

Radionuclide	Half life	Application
Carbon-11	20.3 min	Positron emitter for metabolism studies
Copper –64	12.8 hours	clinical diagnostic agent for cancer and metabolic disorder
Iodine –122	3.76 min	Positron emitter for blood flow study
Iodine –131	8.1 days	Diagnose thyroid disorders including cancer
Iron - 52	8.2 hours	Iron tracer for PET bone marrow imaging
Nitrogen – 13	9.9 min	Positron emitter used as ¹³ NH for heart perfusion studies
Strontium – 85	64 days	Study of bone formation metabolism
Oxygen – 15	123 sec	Positron emitter used for blood flow
Technetium – 99m	6 hours	The most widely used radiopharmaceutical In nuclear medicine

Ultrasound

Ultrasound is high-frequency sound waves produced by a device called a transducer that are reflected back to the transducer by internal body structures.

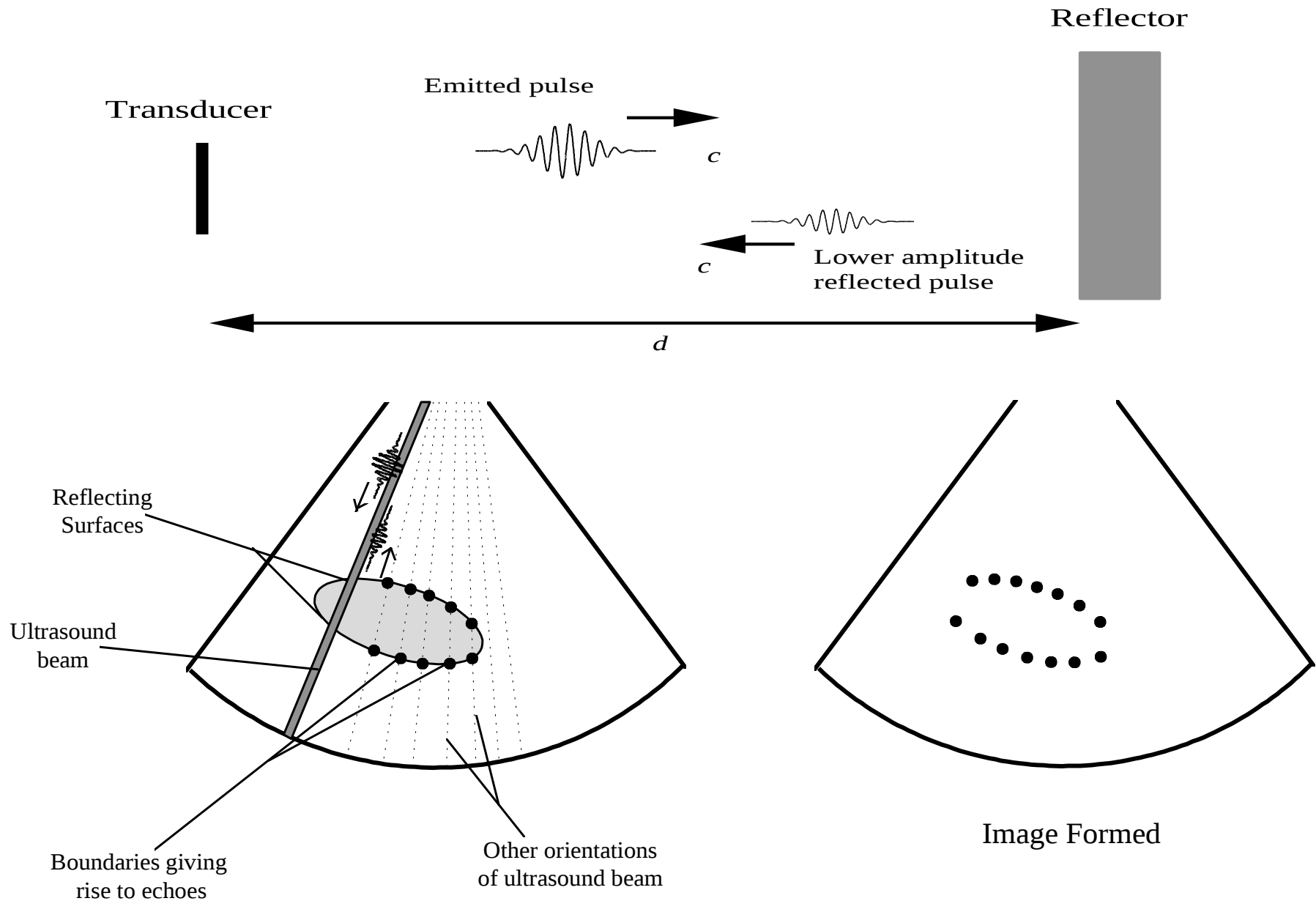


Ultrasound

Ultrasound is used to study soft tissues and organs, especially the heart (echocardiograms) and especially during pregnancy.

Because the presence of gas can distort images, ultrasound is not often used for imaging the respiratory or digestive systems.

Ultrasound Echography



Two basic equations used in ultrasonic imaging:

$$d = \frac{1}{2}tc$$

Where:

d = the one way distance of an object that cause the echo

t = time delay (for the round trip)

c - speed of sound in tissue (between 1450 and 1520 m/s)

The other equation:

$$S(t) = T(t) \otimes B(t) \otimes A(t) \otimes \eta(t)$$

Where:

S(t) - Received signal strength.

T(t) - Transmitted signal

B(t) - transducer properties

A(t) - The attenuation of signal path to and from the scatterer

$\eta(t)$ - The strength of the scatterer

In the frequency domain it turns to be:

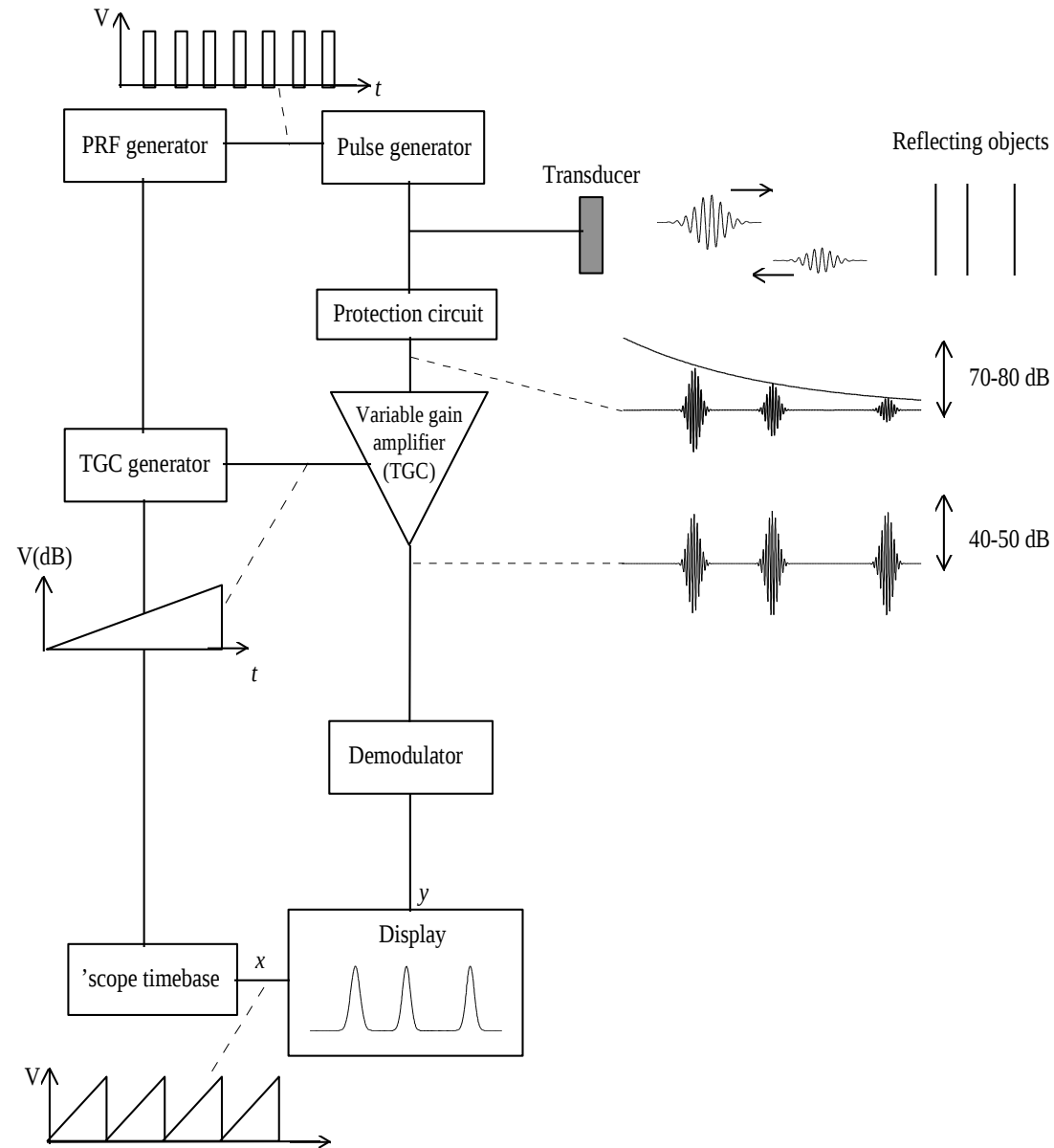
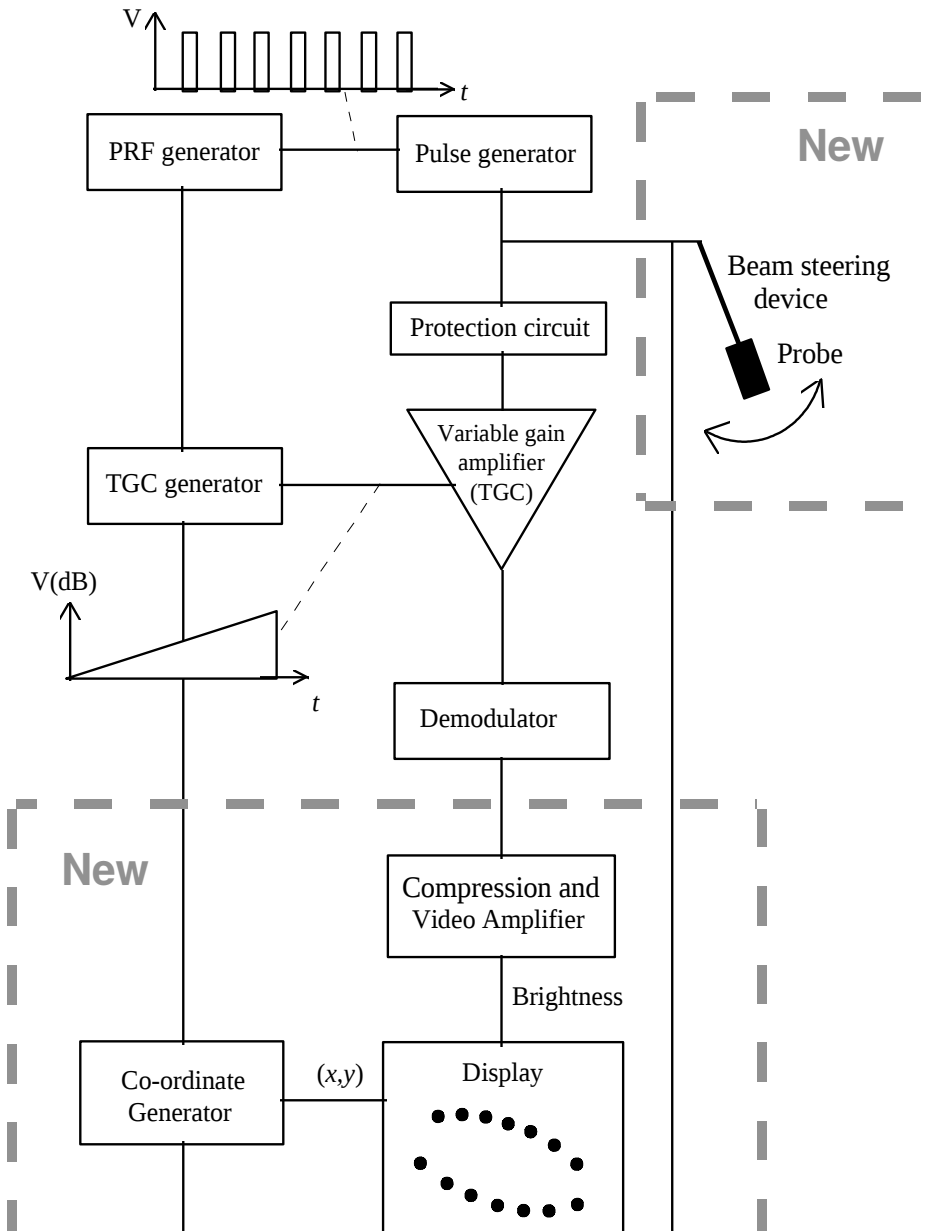
$$S(f) = T(f)B(f)A(f)\eta(f)$$

A-mode - The original display mode of ultrasound measurements, in which the amplitude of the returned echoes along a single line is displayed on an oscilloscope.

B-mode (2-D) - The current display mode of choice. This is produced by sweeping the transducer from side to side and displaying the strength of the returned echoes as bright spots in their geometrically correct direction and distance.

M-mode - Followed A mode by recording the strength of the echoes as dark spots on moving light sensitive paper. Object that move, such as the heart cause standard patterns of motion to be displayed. A lot of diagnostic information such as valve closure rates, whether valves opened and closed completely, and wall thickness could be obtained from this mode.

Ultrasound Echography : A and B modes

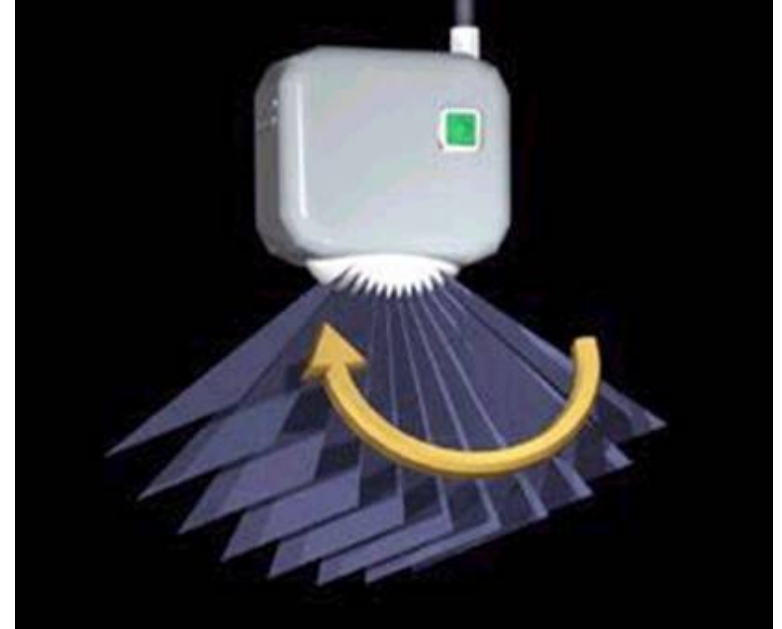
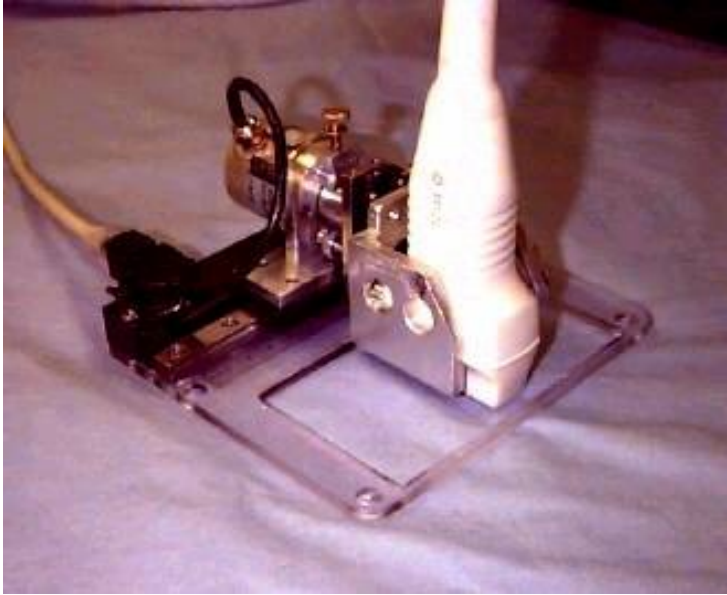


Ultrasound Echography

- by far least expensive
- very safe
- very noisy
- 1D, 2D, 3D scanners
- irregular sampling - reconstruction problems



Ultrasound Positioning





Ultrasound machine

Ultrasound examination

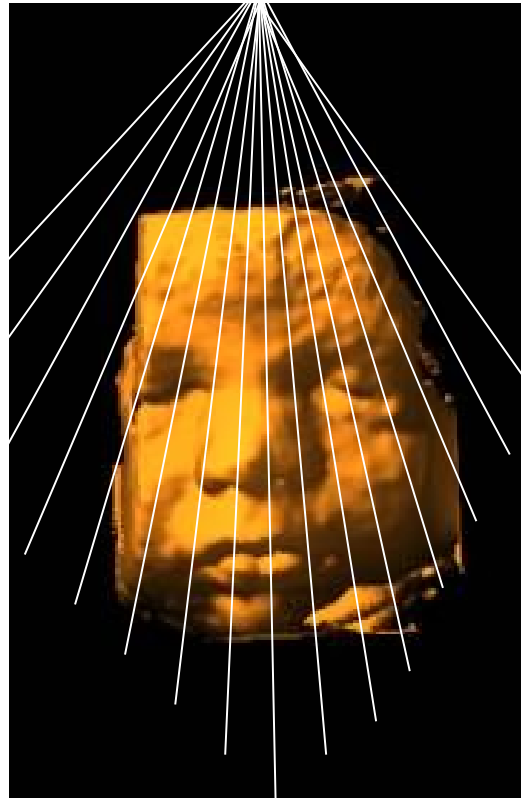


Convex 3.5 MHz
For abdominal
and
OB/GYN studies

Micro-convex: 6.5MHz
For transvaginal and
transrectal studies



Ultrasound Scan Modes



Ultrasound 2D-3D+time

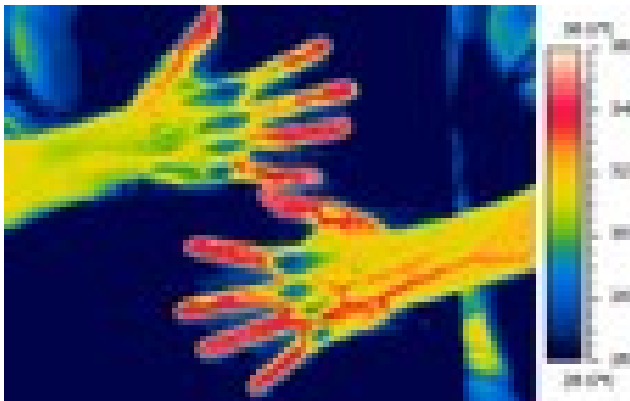
Ultrasound is high-frequency sound waves produced by a device called a transducer that are reflected back to the transducer by internal body structures.



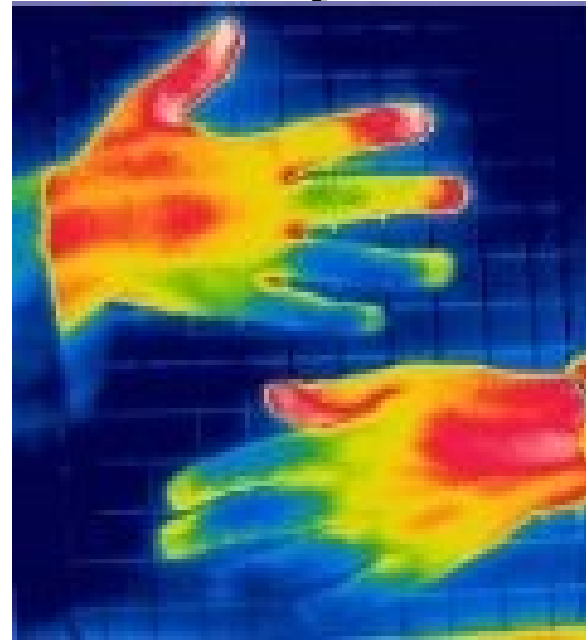
Thermography

In thermograms, infrared light cameras are used to diagnose problems with circulation.

Normal

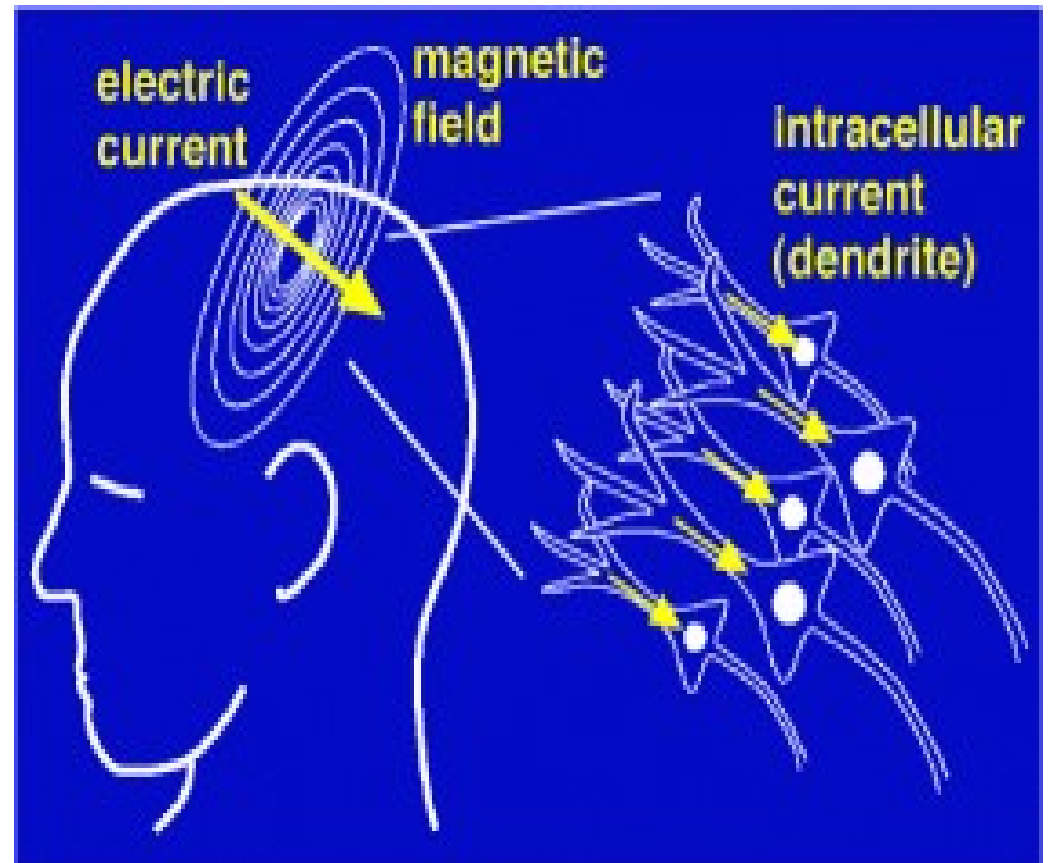
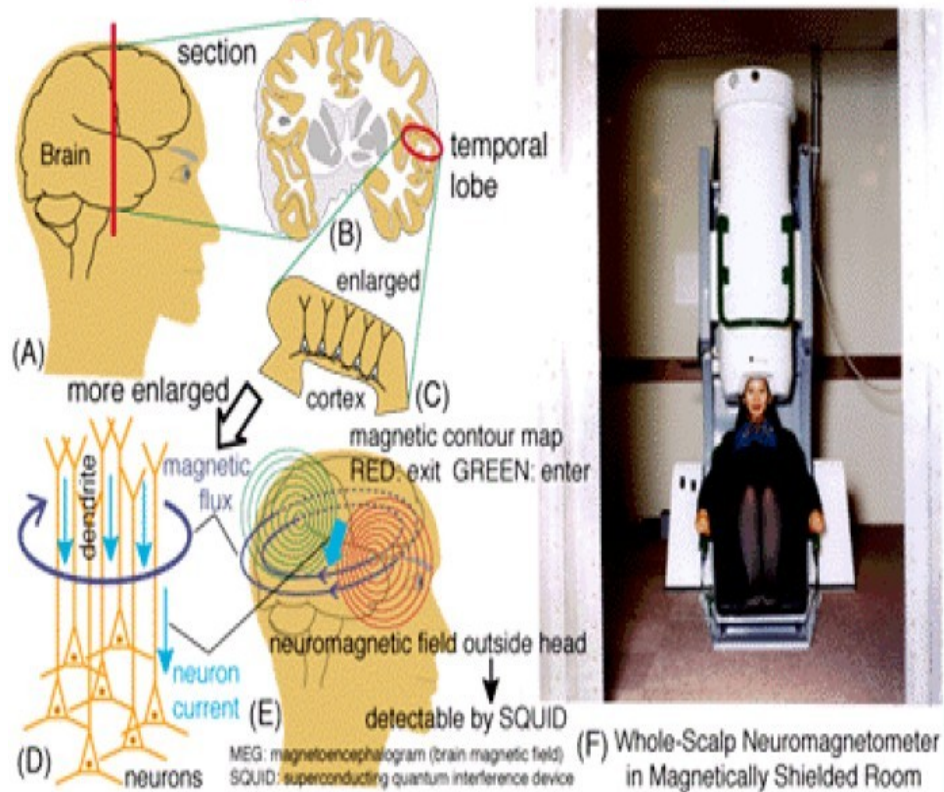


Raynaud's syndrome

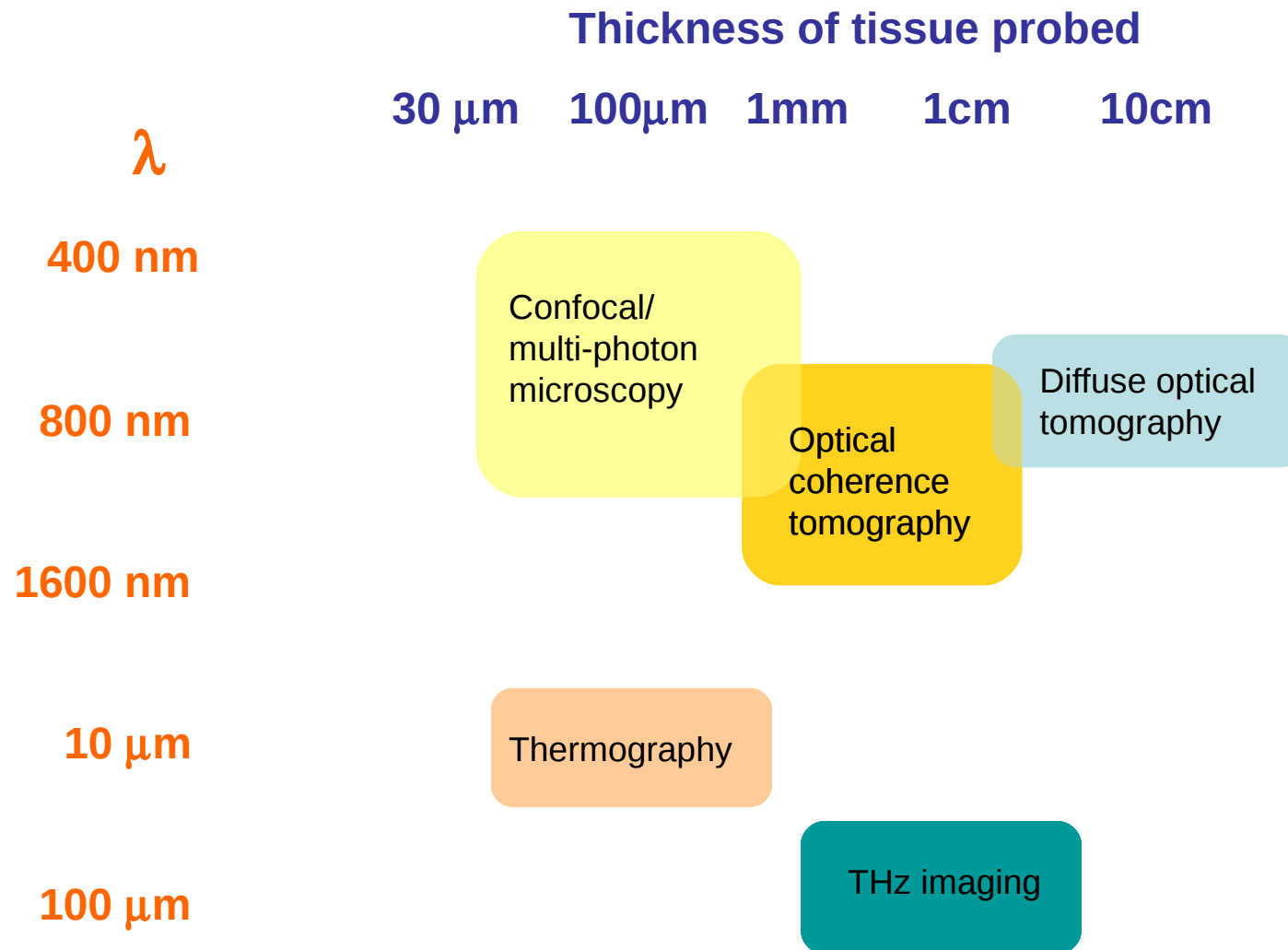


Magnetoencephalography

Revealing Brain Mechanisms by MEG



Optical, Infra Red, THZ imaging



Fluorescence Microscopy

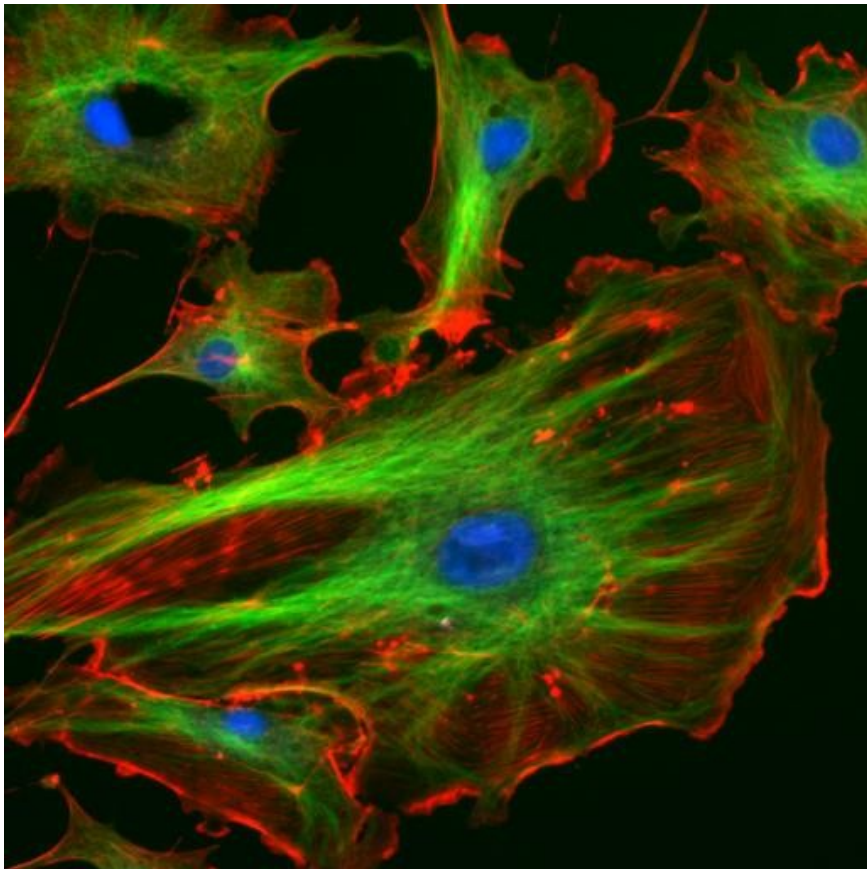


Image of living tissue culture cells.

Three agents are used to form this image.

They bond to the nucleus (blue), cytoskeleton (green) and membrane (red).

Summary of Medical Imaging systems

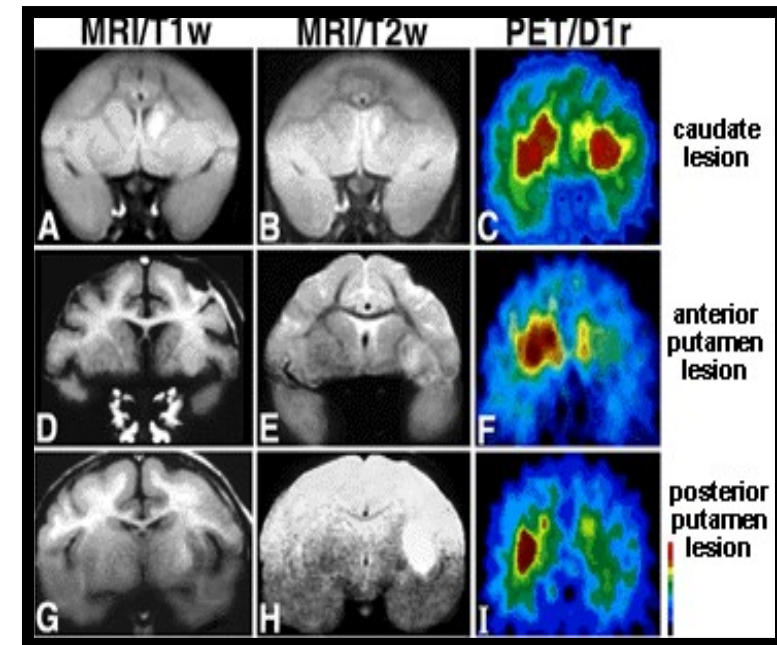
- Digital Radiography, Fluoroscopy, Angiography, Mammography
- X rays CT scan
- MRI
- PET
- SPECT
- Ultrasound
- MagnetoEncephaliGraphy (MEG)
- Infra Red or Thermography
- Optical (Microscopic imaging)
- Micriwave Imaging
- THZ Tomography

Medical Imaging Modality Comparison

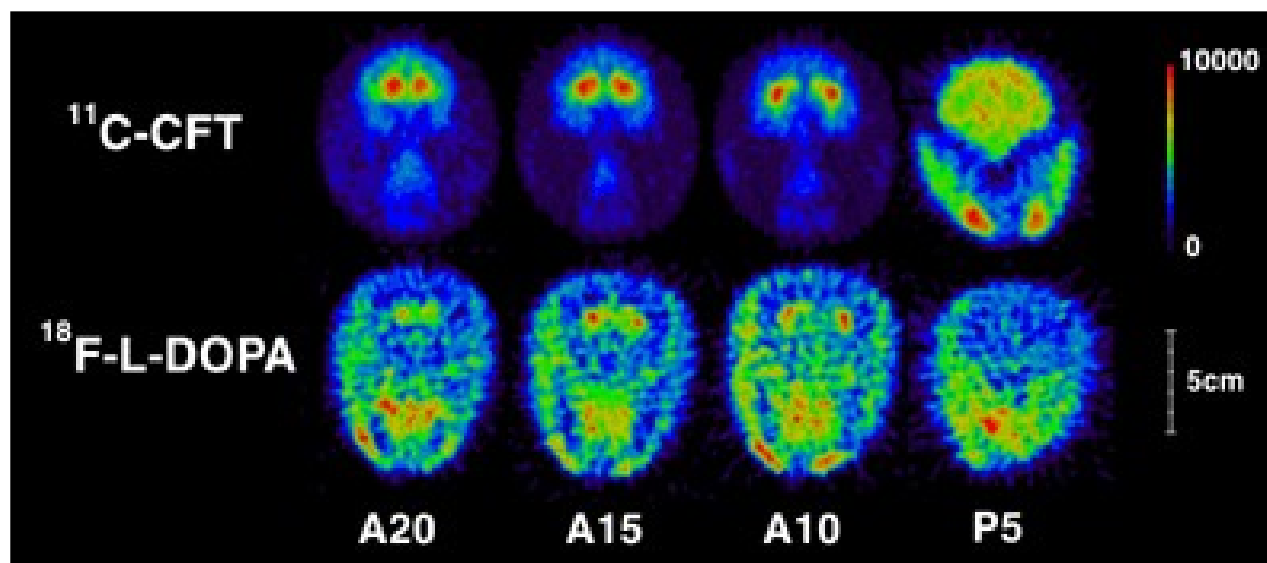
Modality	Strength	Weakness	Safety
X-Ray	Simple, versatile	Only Air-Tissue-Bone	Ionizing
CT	Sectional Images	Low Resolution	Ionizing
MRI	Can see many properties	Slow	Safe
Ultrasound	Real time	Only abdomen, limbs	Safe
Isotope	Functional	Slow, low resolution	Ionizing
Fluorescence	Can see many properties	Low penetration	Not applicable

Applications & Types of Tomography

Medical Applications	Type of Tomography
Full body scan	X-ray
Respiratory, digestive systems, brain scanning	PET Positron Emission Tomography
Respiratory, digestive systems.	Radio-isotopes
Mammography	Ultrasound
Whole Body	Magnetic Resonance (MRI, NMR)



MRI and PET showing lesions in the brain.

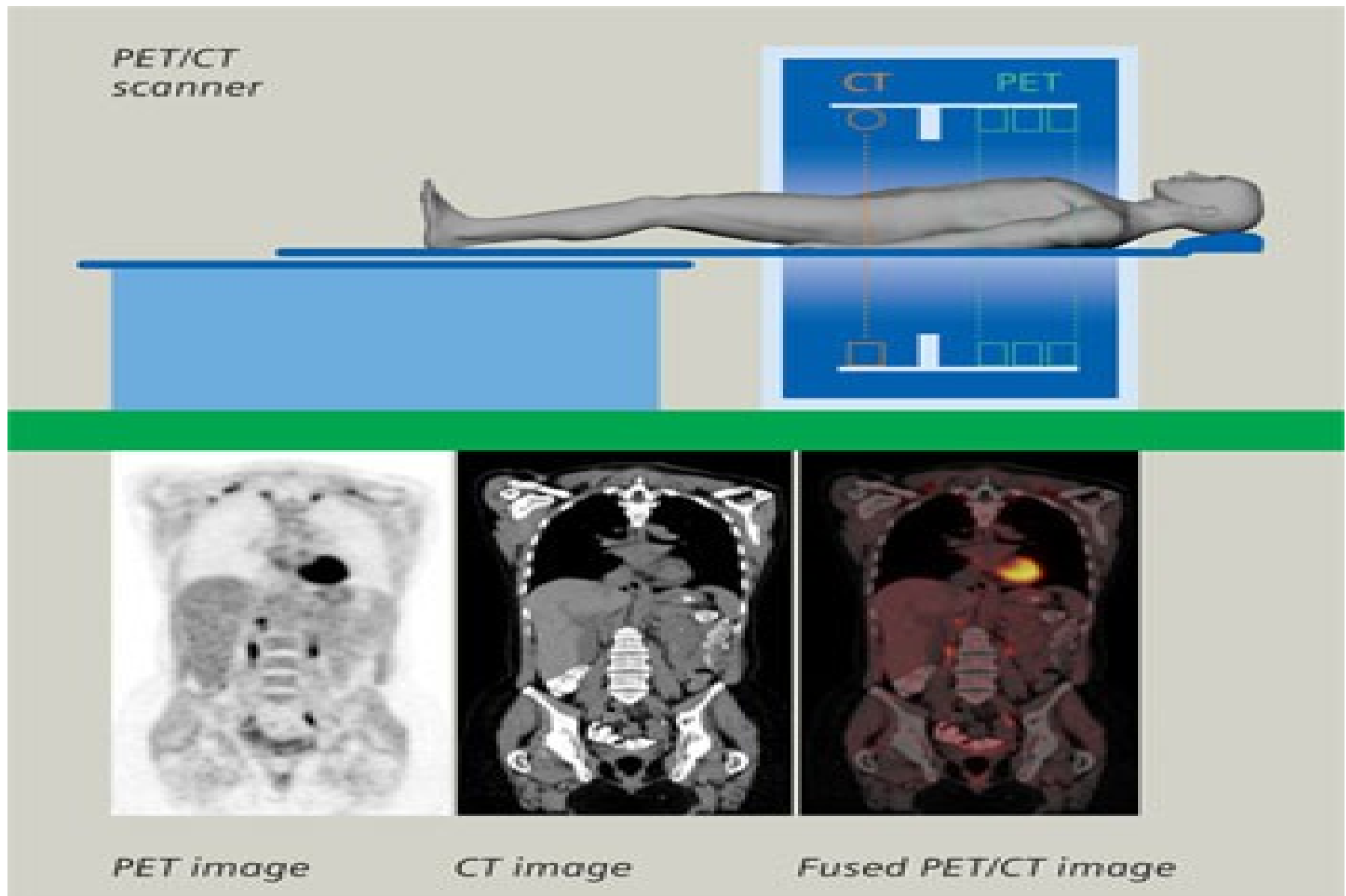


PET scan on the brain showing **Parkinson's Disease**

New Imaging Systems

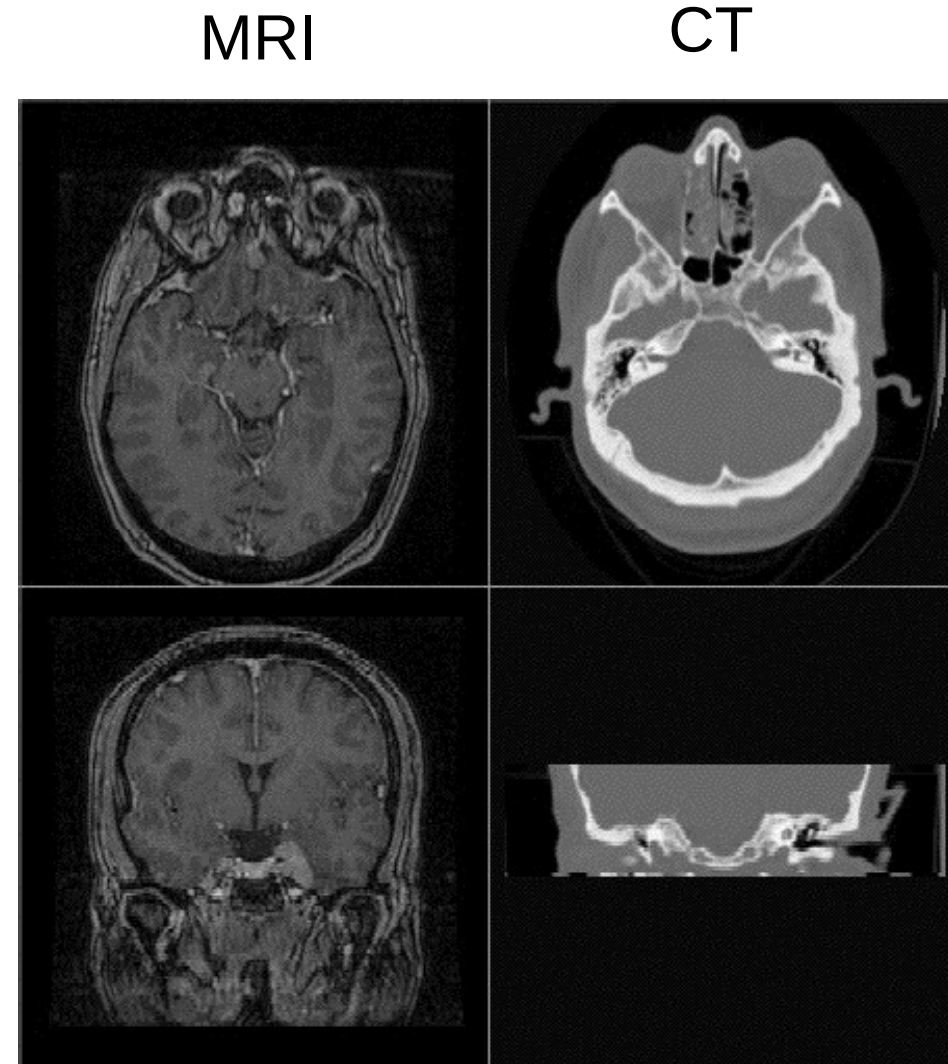
- Optical imaging: Visible, Infrared
- Molecular imaging: PET, fMRI
- Time of Flight (ToF) PET
- Hybrid (Multi modal) imaging systems: PET-CT, MRI-CT, ...
- Electric Impedance Tomography (EIT)
- Proton Computed Tomography
- Neutron imaging
- Microwave Tera Hertz (THz) Imaging
- Infrared (IR) emission imaging (Thermography)
- Optical Diffusion
- Multi-Energy, Multi-Frequency, Multi-Spectral, Hyper-Spectral
- All the microscopic imaging techniques for biological imaging
- New detector technology

PET-CT multimodality



MRI-CT Brain Registration

- MRI (magnetic resonance) measures water content
- CT measures x-ray absorption
- Bone is brightest in CT and darkest in MRI
- Both images are 3d volumes

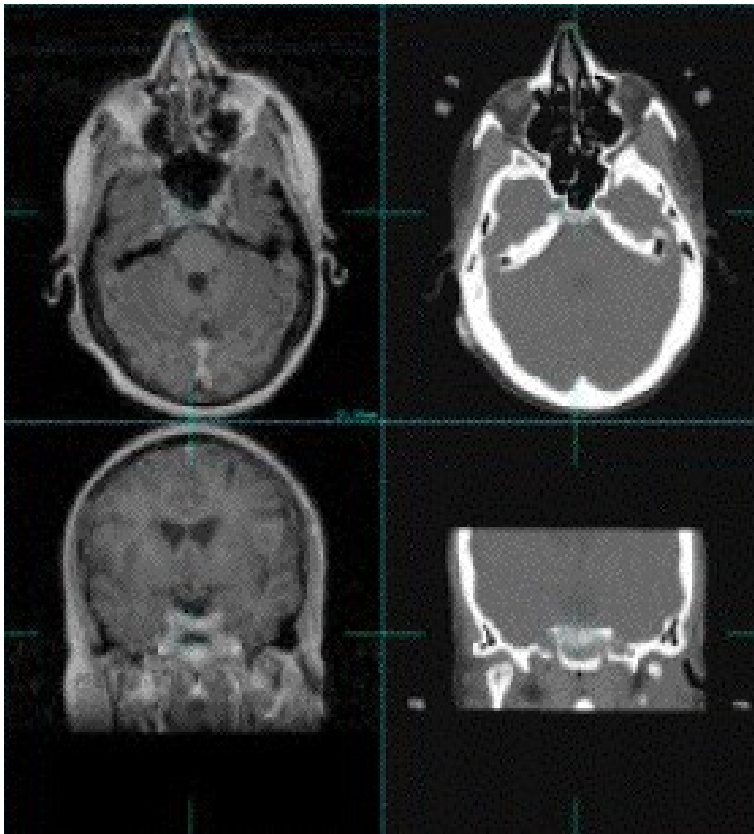


MRI-CT Brain Registration

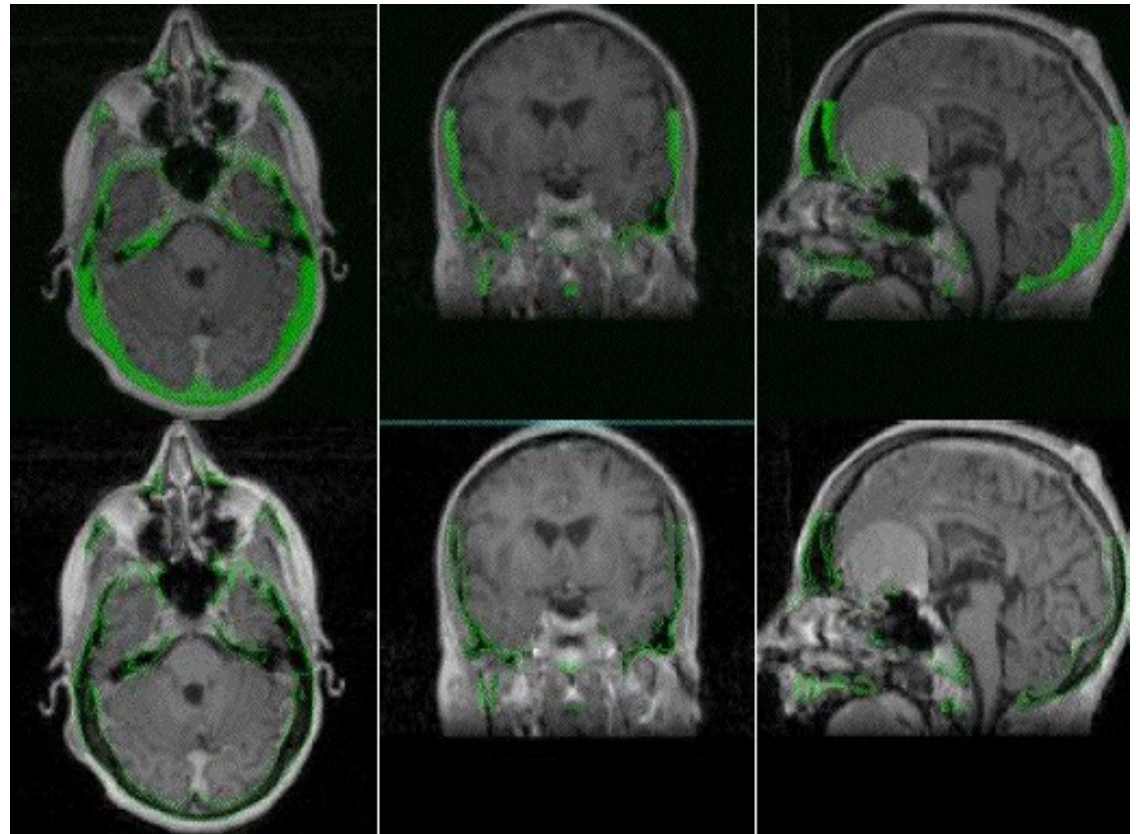
Aligned images

MRI

CT



Super imposed images with bone structures from CT in green



New Challenges

Multimodality Imaging

PET and SPECT combined to MRI

Take advantage of TOF PET in MRI

Detector Design

Detector module component
scintillators, photodetector,
front-end electronics

Photon Counting: Towards Spectral CT

Detector design

Introduction to spectral X-ray

Prospects: detector and application (K-edge imaging...)

Software: Reconstruction and Simulation

Image Reconstruction (system matrix, TOF...)

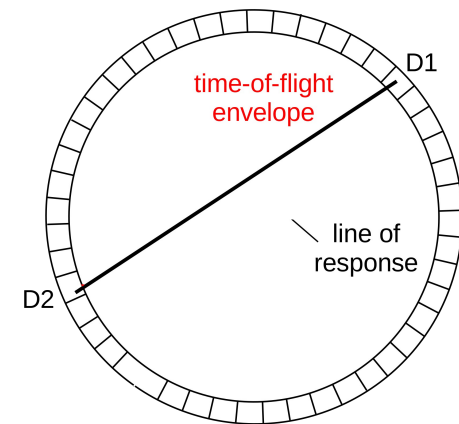
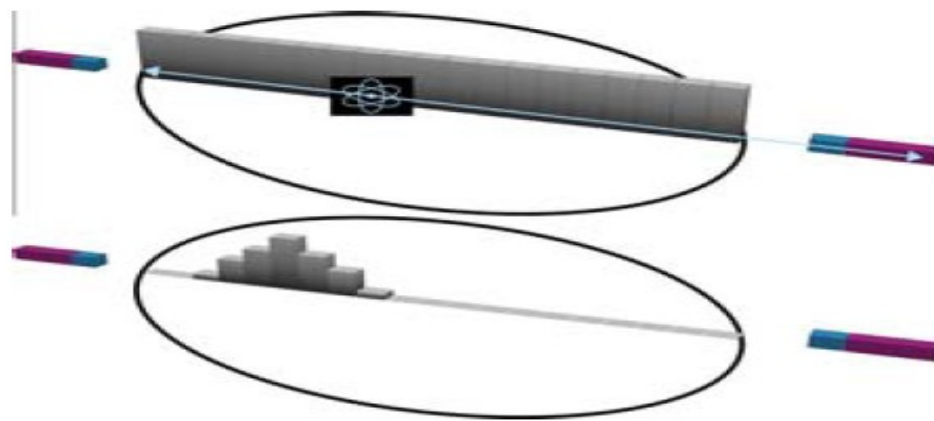
Acceleration procedure
(algorithm, hardware GPU, FPGU,...)

Quantification

Simulation

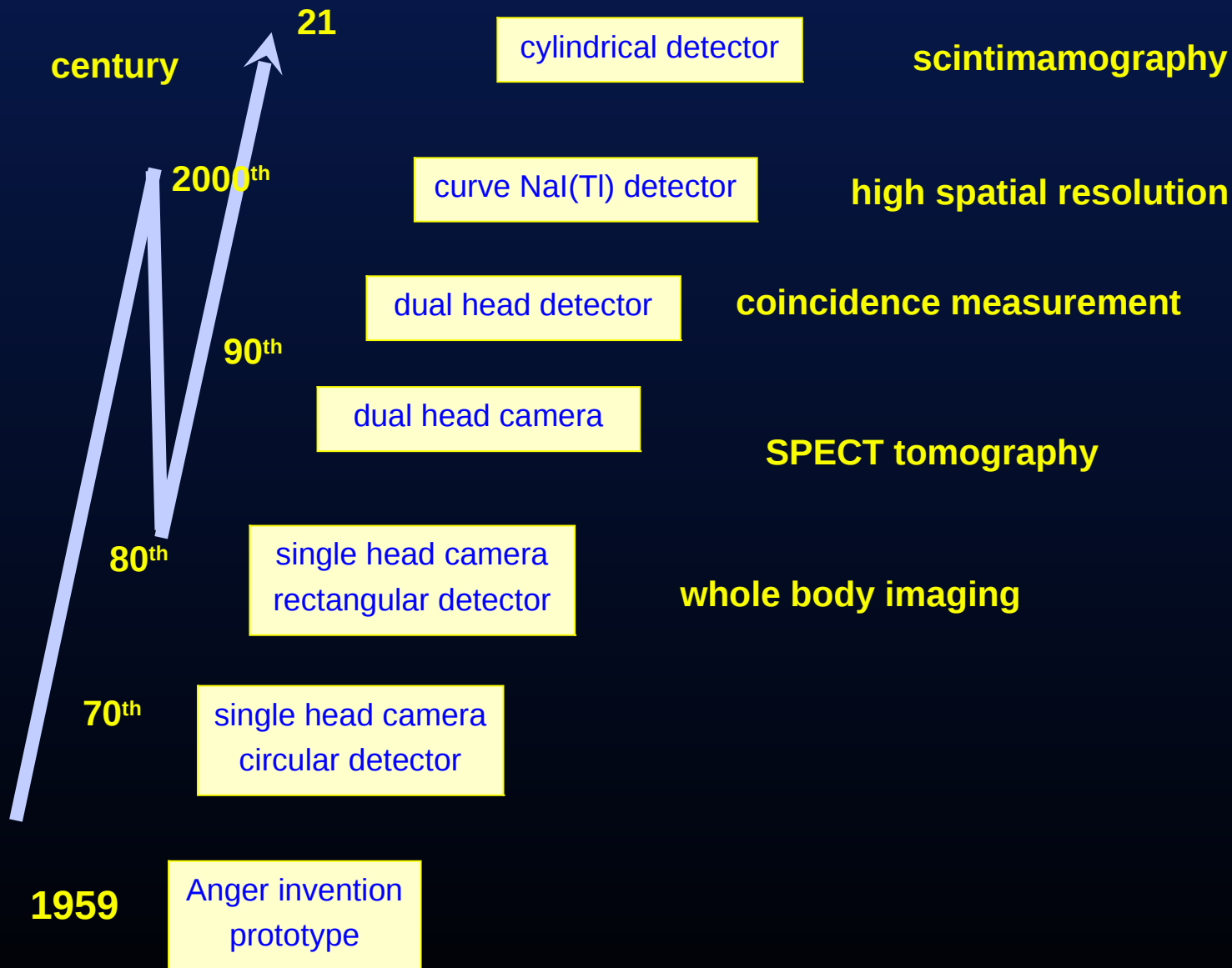
Time-Of-Flight PET (TOF-PET)

- TOF-PET scanner:
 1. Time difference between signals from two crystals measured
 2. Annihilation point along line-of-response directly calculated



- Goal: 100 ps timing resolution (ideally 30 ps and below) = 3 cm spatial resolution (ideally sub-cm)
- Advantages: higher sensitivity and specificity, improved S/N
- Technology needed: fast scintillating materials and fast photon detectors

Nal(Tl) gamma cameras history



Single head camera



Dual head camera

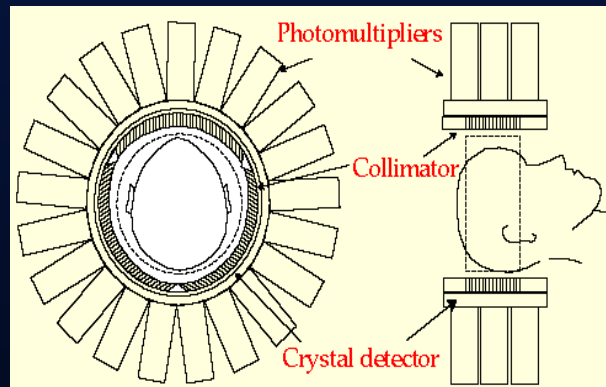


Last years SPECT upgrades

**“Curve Plate”
technology**

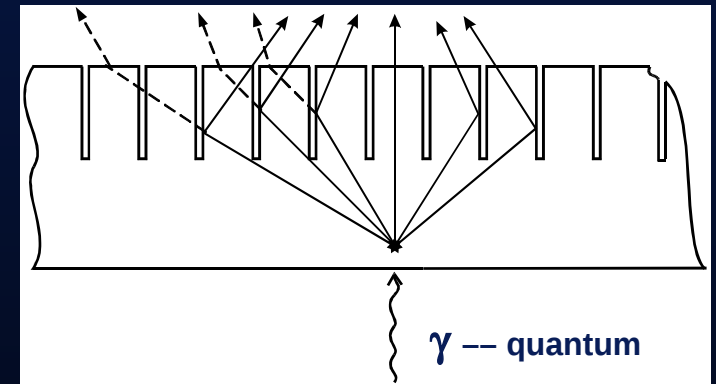


Cylindrical detector technique

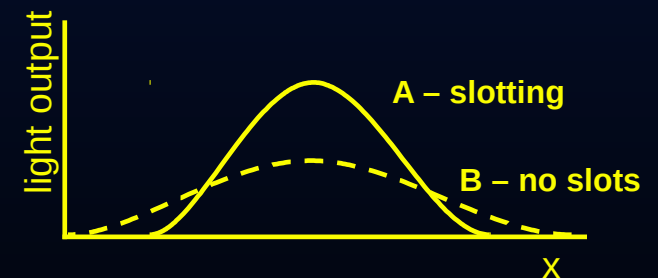


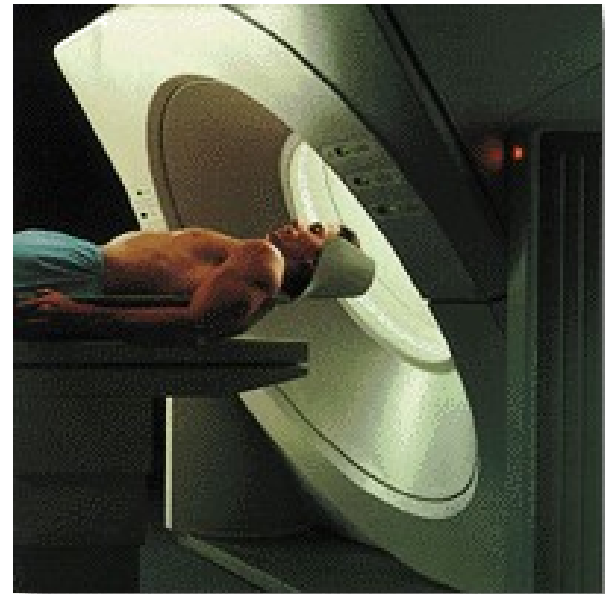
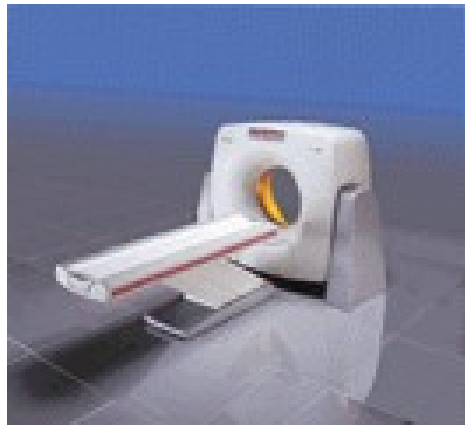
Coincidence mode detector

Slotted scintillator

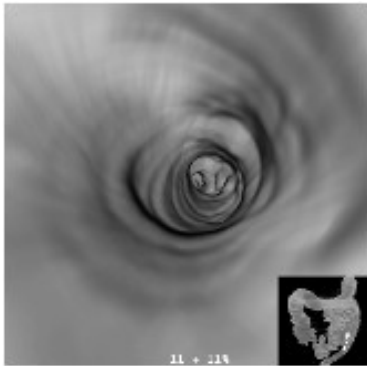


***From conventional to dedicated and dual
mode SPECT systems***

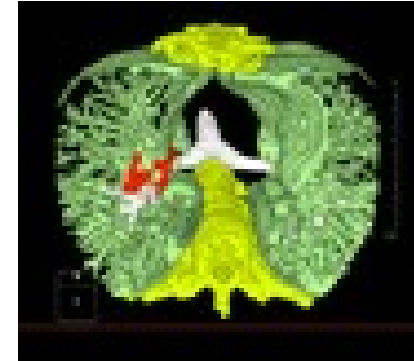




CT (by Picker)



Colonoscopy with spiral CT



Spiral scan

International Symposium on Biomedical Imaging (ISBI) 2015 Challenges

- 1. White Matter Modeling
- 2. Cell Tracking Challenge
- 3. Segmentation of Overlapping Cervical Cells from Multi-layer Cytology Preparation Volumes
- 4. Grand Challenges in Dental X-ray Image Analysis
- 5. Longitudinal Multiple Sclerosis Lesion Segmentation
- 6. MR Brain Image Segmentation in Neonates versus Adults (NEATBrainS15)
- 7. Automatic Polyp Detection Challenge in Colonoscopy Videos
- 8. VISCERAL Anatomy for Grand Challenge

<http://biomedicalimaging.org/2015/program/isbi-challenges/>

Medical imaging constructors

- GE
- Siemens
- Toshiba
- Philips
<http://www.healthcare.philips.com>
- CareStream
<http://www.carestream.com/drmain.html>
- Fuji Medical
<http://digital-radiology.fujimed.com/>
- <http://www.imagingdynamics.com/content/view/419/176/>
-

Thanks for Your Attention

- Questions
- Comments
- Five minutes to talk about the

Universal
Medical and Biomedical
Imaging Center
(UMBIC)