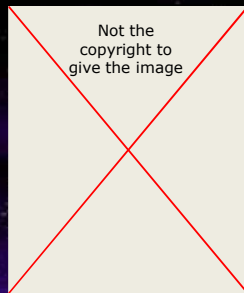




## The carrier



The carrier is associated with a metabolic or physiologic characteristic.  
 ➔ Choice of the carrier according to the organ or the studied metabolism.

## The radiopharmaceuticals

**Radioactivity** : Natural physic phenomenon with a spontaneous emission of radiation, either directly from unstable atomic nuclei or as a consequence of a nuclear reaction. The unstable nuclei can become stable, by emission of particles, usually accompanied by electromagnetic radiation, in the form of a wave as a result of the motion of electric charges.

The radiation produced during radioactivity is predominantly of three types, designated as  $\alpha$ ,  $\gamma$  and  $\beta$  rays. Only two are used in nuclear medicine :

- Emitter of  $\gamma$ -rays (planar scintigraphy, Single photon emission computed tomography (SPECT))
- Emitter of  $\beta^+$ -rays (positron emission tomography (PET))

Radiopharmaceutical characteristics :

- Energy of the radiation (in keV)
- Decay and half-life of the element (from several minutes to several hours). The half-life must be as short as possible, in order to reduce the radiation of the body.
- Injected radioactivity according to the examination and the weight of the patient.

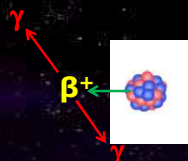
## Choice of the isotope

### Single photo emission



Isotope	Energy (keV)
$^{99m}\text{Tc}$	140
$^{123}\text{I}$	160
$^{111}\text{In}$	170
$^{201}\text{Tl}$	70-80
...	...

### Positron emission

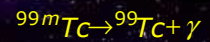


Isotope	Energie (keV)
$^{18}\text{F}$	511
$^{11}\text{C}$	511
$^{13}\text{N}$	511
$^{68}\text{Ga}$	511
...	...

## Example of $\gamma$ emitter Technetium $^{99m}\text{Tc}$

**Technetium-99m** is a metastable nuclear isomer of technetium-99

Pure  $\gamma$  emitter



**Characteristics:**

Ideal for gamma imaging  
 Target the mitochondrion  
 Half-life of 6 hours  
 Energy of 140 keV

## Advantages and disadvantages of a radiopharmaceutical

Radiopharmaceutical with a short half-life

Advantages :

- Reduction of the radiation
- Repetition of the examination with short delays

Disadvantages :

- Short duration of storage (Substance not always available)

Radiopharmaceutical with a long half-life

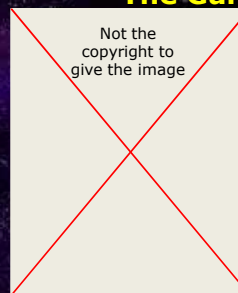
Advantages :

- Long duration of storage

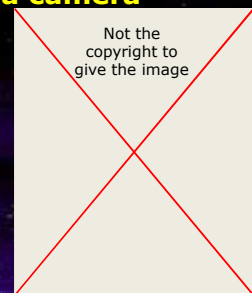
Disadvantages :

- High level of radiation

## Data acquisition system : The Gamma camera



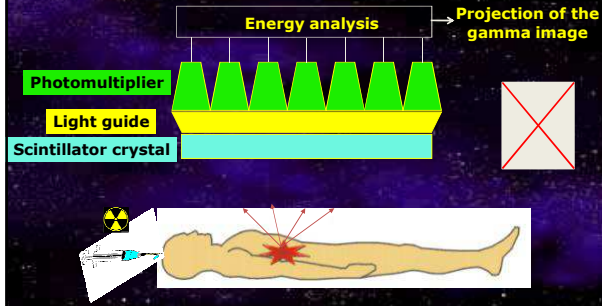
Gamma camera  
Single-head camera



Gamma camera  
Dual-head camera

## Data acquisition system : The Gamma camera

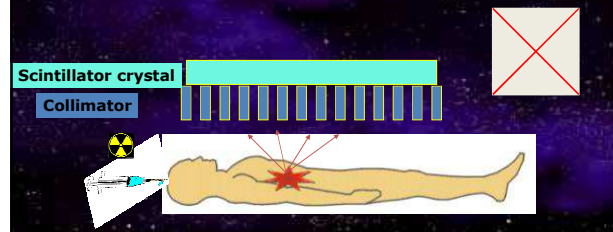
Planar imaging depicting the projection of the radiation due to the emitted photons, i.e. the number of counted photons for each point.



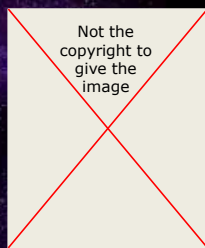
## The collimator

- Lead plate (about 1 cm thick) pierced by an array of many thousands of small holes.
- Obliquely-angled photons are absorbed by the lead between holes.

→ Only photons travelling close to the hole axis can traverse the plate and reach the detectors. The image corresponds to the projection of the object on the detectors' plane.



## The collimator



The collimator is essential but leads to a drastic reduction in the efficiency of photon detection (typically the collimator will transmit less than 0.1 % of the incident photons).

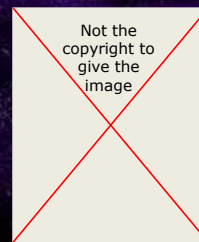
→ The recorded signal is often low, but this is partially compensated by the high sensibility of the crystal and the signal amplification.

## Parallel-Hole Collimator

Image is the same size as the source distribution to the detector

Spatial resolution according to the characteristics of the collimator.

- Hole diameter
- Lead thickness between holes



## Pinhole collimator

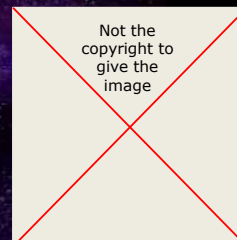
A cone shape lead with a small pinhole of a few millimeter in diameter, about 20-25 cm from the pinhole position to the detector.



- Higher resolution
- Lower sensibility

- Enlarged image
- Inverted image

## Photomultipliers



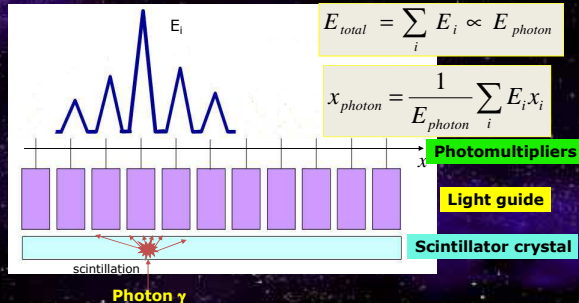
*Scintillator crystal*

*Photomultipliers*



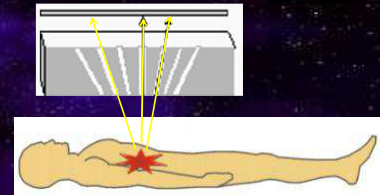
## Spatial localization

Data acquired at the level of the photomultipliers allows :  
 - The spatial localisation  
 - La mesure de l'énergie du photon gamma



## Image acquisition Static planar imaging

Static gamma camera opposite to the organ  
 Acquisition of images during a determined duration

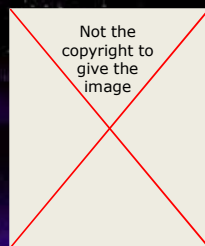


## Ventilation and perfusion Pulmonary scintigraphy

Ventilation scintigraphy by aerosol inhalation  
 → Xenon 127, Xenon 133, Krypton 81<sup>m</sup>, and now aerosols labeled with Tc 99<sup>m</sup>

Perfusion study with intravenous injection of Technetium 99<sup>m</sup>-labeled albumin (that stay in the blood pool).

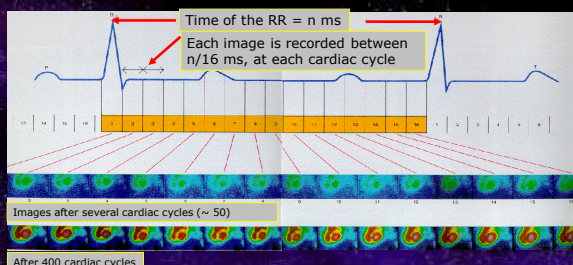
Research of discordance between the two series of images  
 → Pulmonary embolism  
 Blockage of the main artery of the lung or one of its branches by a substance (in general thrombus)  
 → Some areas of the lung are normally ventilated but not perfused with blood



## Dynamic planar imaging

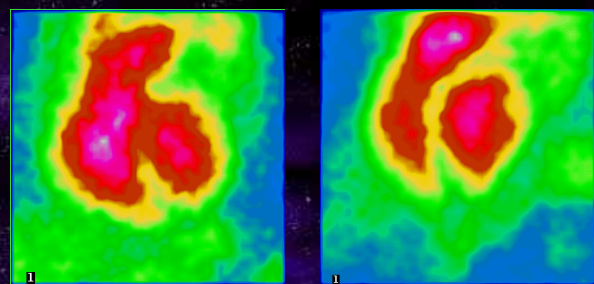


## Gated imaging with ECG Angiocardi-scintigraphy



Tracer intravenously injected and that stay in the blood pool (for example Technetium 99<sup>m</sup>-labelled human serum albumin). Acquisition after equilibrium of the tracer in the blood pool.

## Angiocardi-scintigraphy



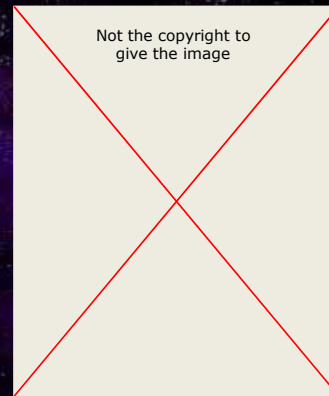
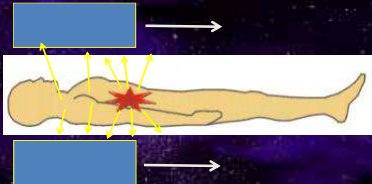
Normal subject

Pathological case

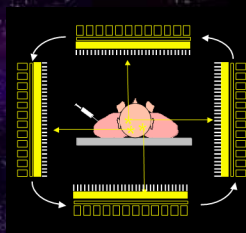
The intensity variation in a region of interest (for example, the left ventricular cavity) corresponds to the variation of the blood pool volume.

## Image acquisition Whole body scanning

The camera move with a constant speed above and below the patient. Whole body imaging of the anterior and posterior sides of the patient.



## Tomographic images

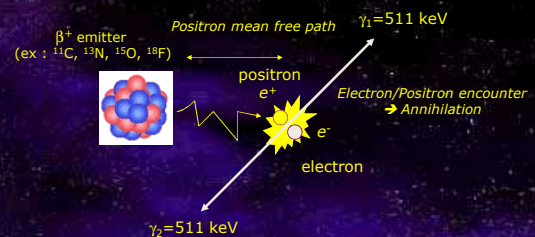


The position of the camera between two acquisition depends on the number of orientations and the number of heads:

$$\theta = \frac{360^\circ}{N_{\text{images}} N_{\text{Heads}}}$$

Image reconstruction with backprojection (same principle as for computed tomography)

## Positron Emission tomography (PET)



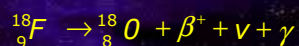
⇒ Simultaneous emission of 2  $\gamma$  photons in opposite directions  
⇒ Conversion of the combined electron/positron rest mass into photon energy

## Example of $\beta^+$ emitter Fluorine

$^{18}\text{F}$ FDG : Fluorodesoxyglucose

Carrier : Glucose

Radionuclide =  $^{18}\text{F}$  (Fluorine 18)



### Characteristics :

FDG is a glucose analog

→ Assessment of glucose metabolism

FDG is taken up by cells, and retained by tissues with high metabolic activity, such as most types of malignant tumours

→ Tumour imaging in oncology

Half-life of 109 minutes (short duration)

Energy of 511 keV

## Other $\beta^+$ emitters

$^{15}\text{O}$  : Half life = 2 minutes

-  $\text{C}^{15}\text{O}_2$  :  $\text{O}_2$ ,  $\text{CO}_2$ ,  $\text{H}_2\text{O}$  (cerebral blood flow studies, myocardial oxygen consumption, oxygen extraction etc)

$^{13}\text{N}$  : Half life = 10 minutes

- Ammonia  $\text{NH}_3$  (blood flow)

$^{11}\text{C}$  : Half life = 20 minutes

- Acetate (oxidative metabolism)

- Cocaine (drug binding sites)

## Positron Emission tomography (PET) Coincidence detection

The simultaneous emission of the 2 photons in opposite directions is the basis of coincidence detection and coincidence imaging.

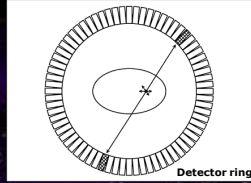
Light speed:  $3 \cdot 10^8 \text{ m.s}^{-1}$   
Time to travel 1 m :  $3.3 \cdot 10^{-9} \text{ s}$   
Diameter of the ring  $\sim 80 \text{ cm}$   
Time to cross the ring  $\sim 2.6 \text{ ns}$

If 2 photons are detected in a time lapse less than 10 ns, we consider that they come from the same annihilation.

The annihilation occurred somewhere along the path between the detectors.

Image reconstruction with backprojection.

Spatial resolution can not be lower than the positron mean free path.

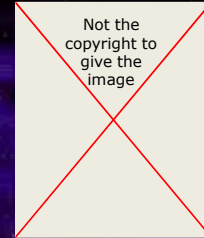


Detector ring

PET shows radiographically occult but highly metabolically active bone and soft tissue metastases



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Not the copyright to give the image

Multiple metastases ( $^{18}\text{F}$ FDG)

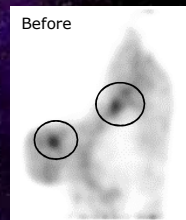
## Planar imaging with single photon emission vs TEP



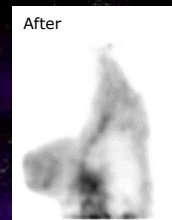
Not the copyright to give the image

## Example in chemotherapy

Purpose : To evaluate, in breast cancer patients treated by neoadjuvant chemotherapy, the predictive value of reduction in FDG uptake with regard to complete pathological response (PR).



Before



After

The relative decrease in FDG uptake after the first course of neoadjuvant chemotherapy was significantly greater in the PR group than in the non-PR group.  
→ FDG-PET predicts complete pathological response of breast cancer to neoadjuvant chemotherapy.

Berriolo-Riedinger et al, Eur J Nucl Med Mol Imaging ;1915-1924; 2007

## Multimodal imaging approaches

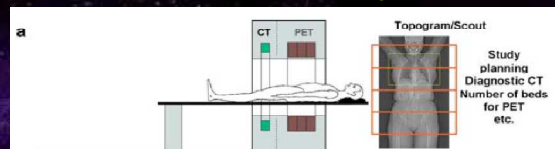
Often combination of anatomical structures, revealed from CT (or MRI), and the functional information from PET into one image.

Both imaging modalities are fully integrated into one device  
→ fixed and known transformation matrix

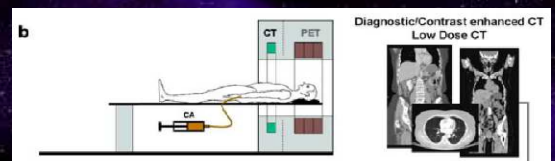
The inclusion of the CT images provides anatomical reference and helps in understanding the metabolic information present in the PET images.

The CT images can also be used to correct the PET images for scatter and attenuation effects, creating images that are quantitative for estimating uptake and metabolic rates *in vivo*.

## Schematic workflow of the PET/CT examination



A fast scout scan is used to determine examination regions for PET and diagnostic CT

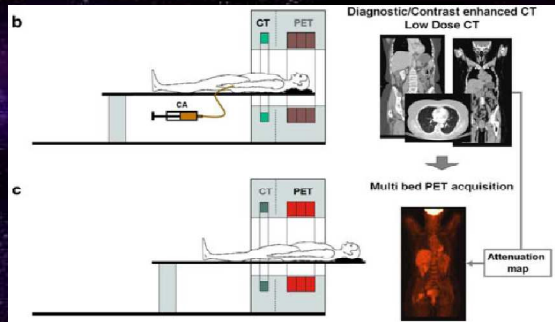


Acquisition of either a diagnostic or low-dose contrast enhanced CT scan.

Pichler et al, Handb Exp Pharmacol. ;109-132;2008



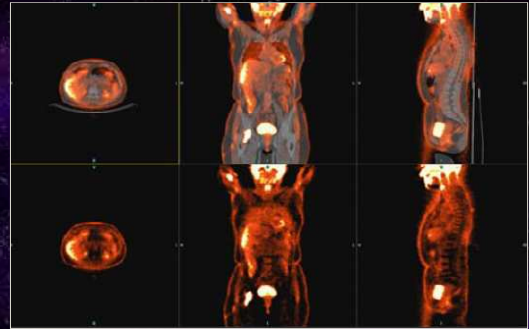
### Schematic workflow of the PET/CT examination



PET data are acquired at multiple bed positions, reconstructed and corrected for attenuation using the previously acquired CT data.

Pichler et al, Handb Exp Pharmacol. ;109-132; 2008

### Schematic workflow of the PET/CT examination

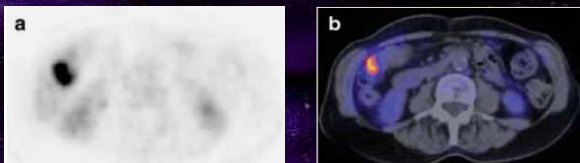


PET and CT images are registered and displayed as fused images.

Pichler et al, Handb Exp Pharmacol. ;109-132; 2008

### Example of CT/PET images

Example of the localization of pathological FDG uptake in a 60-year-old patient with melanoma.

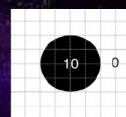


Axial PET image

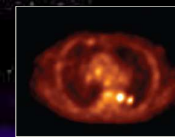
The fusion of PET image with the CT show a focal spot of FDG uptake in the lower right abdomen, which corresponds to the colon ascendens.

Pichler et al, Handb Exp Pharmacol. ;109-132; 2008

### Example of partial volume effect



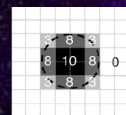
Object with pixel grid overlapped



PET image



CT image



Measured image



The contours seen on the CT image do not delineate the metabolically active part of the tumor.

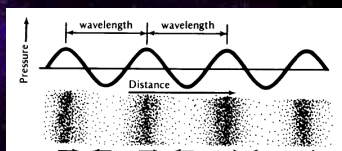
Soret et al, J Nucl Med, 48; 932-945; 2007

### Ultrasound

Sound : Propagation of mechanical wave corresponding to an oscillation of pressure transmitted through a solid, liquid or gas.

Propagation of the sound only in the matter (cannot propagate through a vacuum).

Oscillatory disturbance is passed along from one group of atom to the next along the direction of travel of the wave.



The wave consists of an alternating pattern of compression and rarefaction in the medium

Velocity (speed of propagation of the sound) depends on the matter.

Mean velocity in the soft tissues = 1540 m/sec

### Ultrasound

Ultrasounds: frequency (sound) > 20 000 Hz (20 KHz)

Humans cannot hear ultrasounds (frequency higher than for the audible sound)

Echography : frequency from 2 to 40 MHz

Piezoelectric effect (discover in 1880)

Conversion of energy by applying pressure to a crystal.

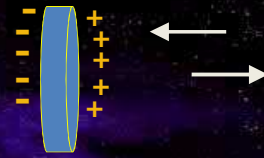
The reverse of piezoelectric effect converts the energy back to its original form.

Ultrasound transducers convert electricity into sound (pulse) and sound into electricity (echo).

## Ultrasound probes

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give the image

## Piezoelectric effect



When an electric field is placed across a slice of piezoelectric material, the material contracts or expands. So a rapidly alternating electric field causes the crystal to vibrate.

The vibrations are then passed through any adjacent materials, or into the air as a longitudinal wave i.e. a sound wave is produced.

The frequency of the sound depends on the characteristics of the crystal.

## Piezoelectric effect



The ultrasound transducer intermittently generates an ultrasound wave at a predefined rate  
→ Pulse repetition frequency

Between each pulse of emitted ultrasound, the transducer acts as a receiver for the reflecting waves.

The piezoelectric effect also works in reverse. If the crystal is squeezed or stretched, an electric field is produced across it. So if ultrasound hits the crystal from outside, it will cause the crystal to vibrate in and out, and this will produce an alternating electric field.

## Attenuation of the ultrasound

As the X-rays, the ultrasound are absorbed by the matter

Intensity  $I$  of the wave (having initial intensity of  $I_0$ ) after crossing a matter with a thickness  $x$  :

$$I = I_0 e^{-\mu x}$$

$\mu$  : Attenuation coefficient

$$\mu = \mu_{\text{scatter}} + \mu_{\text{absorption}}$$

$\mu$  in dB (according to the frequency)

For example, for a frequency of 10MHz, the attenuation coefficient is equal approximatively to 10 dB per cm in the soft tissues (by comparison, it is around 0,8 dB.cm<sup>-1</sup> for the X-rays)

## Boundary of two materials

$$\text{Acoustic impedance } Z : \rho \times v$$

Density of the matter

Acoustic velocity

Acoustic impedance : This is a measure of how ultrasound traverses a tissue. This is the opposition of a tissue to the passage of sound waves.

Boundary : Limit between two materials having different acoustic impedances.

A large difference in acoustic impedances between two materials is referred as acoustic impedance mismatch. The greater the acoustic mismatch the greater the percentage of ultrasound reflected and the less transmitted.

## Reflection

Echo : Reflected ultrasound that is recorded after latency period.

In an idealised situation, an ultrasound wave is directed normally at a flat boundary between two media.

→ Some of the pulse is reflected and return to the transducer. The distance from the transducer to the boundary can be found by recording the time between the pulse and its echo.

→ Some of the pulse is carry on into the next region without changing its direction

Reflect coefficient (or transmission coefficient) : The fraction of the incident wave intensity that is reflected (or is transmitted).

→ Proportionnal to the difference of acoustic impedances.

↗ Difference of acoustic impedances → ↗ Reflection

Boundaries with a lot of reflection : soft tissues/ air  
soft tissues / bones or stones (kidney stones)



## Reflection and the acoustic impedance

Z : Acoustic impedance of the matter  
Z in  $\text{kg} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$        $Z \times 10^6$  for .....

Water : 1,5

Muscle : 1,65 – 1,74

Bone : 3,8 – 7,4

Air : 0,0004

Soft tissues : 1,3 – 1,7

Liver : 1,7

Lung : 0,26

Reflection coefficient at the level of a boundary between two matters :

$$R = (Z_1 - Z_2)^2 / (Z_1 + Z_2)^2$$

Reflection between a bone and a soft tissue :

$$R = \frac{(Z_1 - Z_2)^2}{(Z_1 + Z_2)^2} = \frac{(1,4 \times 10^6 - 7 \times 10^6)^2}{(1,4 \times 10^6 + 7 \times 10^6)^2} = 0,67$$

## Reflection at the level of the skin



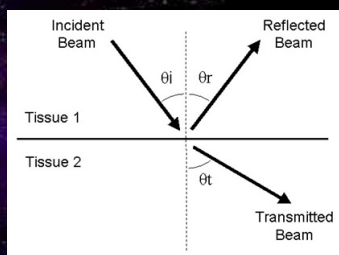
More than 99% of the ultrasounds are reflected !

The degree of reflection is high for air because air has an extremely low acoustic impedance relative to other body tissues.

For this reason, it is clinically important to apply sufficient conducting gel on the transducer surface to eliminate any air pockets between the transducer and skin surface.

It is impossible to study hollow organs, such as the lung.

## The angle of the incidence



Angle < 90°

→ Reflection is move forward to the probe

→  $\theta_i = \theta_r$

→ The signal of the returning echo is weakened and a darker image is displayed.

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give the image

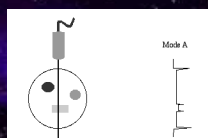
## Ultrasound echo imaging systems

Hypotheses :

- The direction of the ultrasound wave is single
- Only one reflection
- The position of the boundary (distance between the transducer and the location of the reflection) according to the time between the pulse and its echo.

### A-Mode measurements

- A transducer scans a line through the body with the echoes plotted on screen as a function of depth.
- Records are relative amplitude of the echoes
- Only one direction
- Old technique used in neurology or ophthalmology.

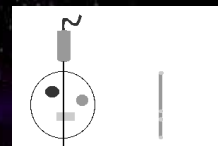


<http://www2.vet-lyon.fr/ens/imagerie/D2/Echo/E-notes.html>

## B-Mode Imaging (Brightness mode)

Each component scan line is plotted with trace brightness modulated by the variation in signal amplitude along the scan direction.

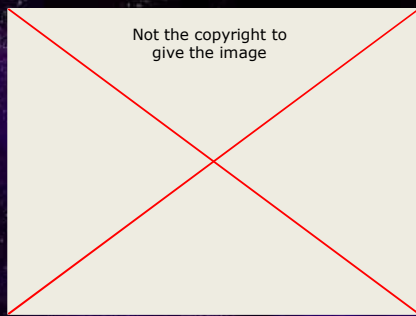
Signal intensity of each point correspond to the degree of reflection.



The development from A-mode to B-mode is that the ultrasound signal is used to produce various points whose brightness depends on the amplitude instead of the spiking vertical movements in the A-mode.

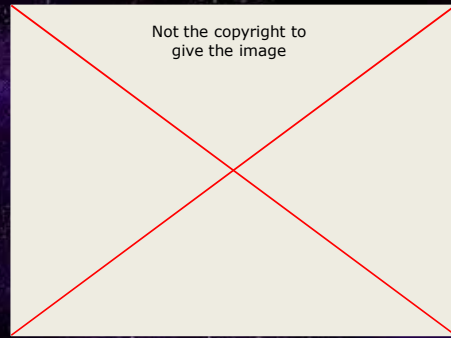


### Linear array



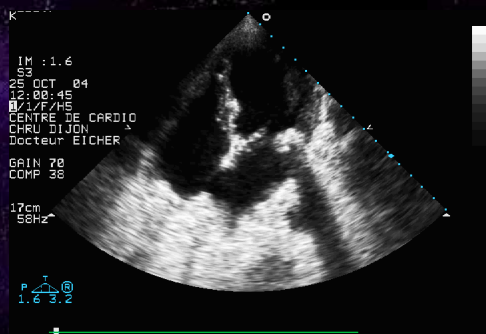
The probe movement is represented as a shift along the axis.  
Production of rectangular image.

### Sector array



Ultrasound beam. Production of a fan like image that is narrow near the transducer and increases in width with deeper penetration.

### Real time imaging



Acoustic shadowing: Marked reduction in the intensity of ultrasound deep due to a strong reflector (or attenuator)

### Distance measurement



$$1540 \text{ m/sec} \times 0.145 \text{ ms} = 0.2233 \text{ m}$$

$$\text{Distance: } 0.2233 \text{ m} / 2$$

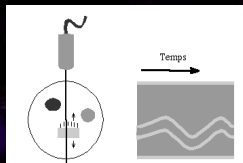
$$\text{Distance: } 11.165 \text{ cm}$$

### M-Scan (Time position plot)

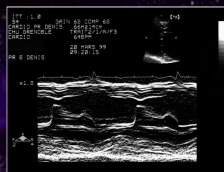
Display of moving structures along a single line.

Movement of a structure, such as heart valve, can be depicted in a wavelike manner.

High sampling frequency : Useful in evaluation of motion



Mitral valve stenosis



<http://www.sante.ujf-grenoble.fr/sante/CardioCD/cardio/chapitre/401a.htm>

### 3D echography

#### Manual scanning

- Conventional probe (2D acquisition)
- Use of sensors to detect the position of the probe
- As the sweep is done the position information is detected and used to calculate a 3D data set.

#### Automatic acquisition

- Probe allowing 3D acquisition
- The ultrasound system drive the movement of the acoustic array.
- Automatic scanning of the different planes due to an automatic displacement of the transducer.



Second trimester

## Doppler effect

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give the image

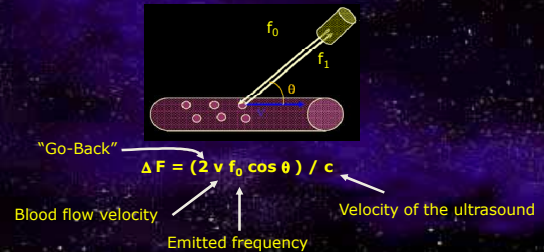
The sound is different if the receiver is inside the car (the position of emitter is fixed against the position of the receiver), if the car come closer to the receiver (the sound becomes more treble) or if the car move away from the receiver (the sound becomes more bass).

## Doppler ultrasound

Reflection of ultrasound wave by the blood cells in motion (slight modification of the ultrasound frequency).

The modification of the ultrasound frequency is according to the velocity of the blood flow against the emitter (i.e. the receiver).

- Longest wavelength if the blood cell move away from the probe.
- Shortest wavelength if the blood cell come closer to the probe.



## Doppler ultrasound

Example of the calculation of the blood flow velocity:  
Considering a probe with an initial frequency of 3 MHz, with an angle of 15° between the ultrasound wave and the artery. If the frequency difference between the emitted and the received wave is around 1880 Hz, what is the blood flow velocity ?

$$\Delta F = (2 v f_0 \cos \theta) / c$$

$$v = \Delta F * c / (2 * F_0 \cos \theta)$$

$$= (1880 * 1600) / (2 * 3 \cdot 10^6 * 0.97)$$

$$\sim 3.008 \cdot 10^6 / 2 * 3 \cdot 10^6 \sim 0.5 \text{ m.s}^{-1}$$

$$= 50 \text{ cm.s}^{-1}$$

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give the image

Transoesophageal echography  
Mitral valve regurgitation

## LE2I – Groupe Imagerie Médicale Medical imaging team

Group leader : Pr Brunotte

Localization: Dijon

→ Faculté de Médecine / Médecine

→ Service d'IRM - CHU de Dijon

/ MRI department - University Hospital of Dijon

→ Service de Médecine Nucléaire – CGFL Dijon (Centre anti-cancéreux)

/ Nuclear Medicine department – Anti-cancer centre

Main topics :

→ Fonctionnal study of the heart and the aorta from MRI

→ MRI / MRS of prostate cancer

→ PET in oncology (follow up of patients and use of innovative tracers)

Strength / Available facilities :

→ Clinical 3T and 1.5 T MRI

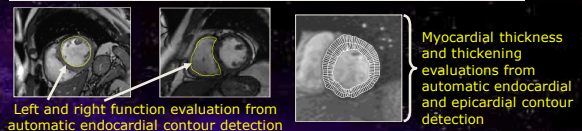
→ Clinical PET

→ Experimental PET / MRI system (pre-clinical experimentation)

→ Close contact with physicists, medical doctors and computing engineers

## Cardio-vascular MRI

### • Automatic evaluation of the cardiac function from cine-MRI



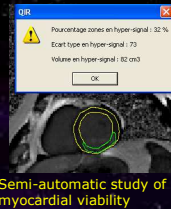
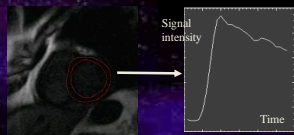
### • Automatic evaluation of cardiac asynchronism from cine-MRI





## Cardio-vascular MRI

### • Automatic evaluation of the myocardial perfusion from cine-MRI



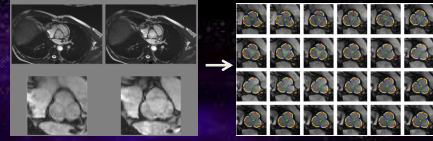
### • 3D/4D representation of the aortic stress area from MRI

3D/4D representation of the aorta from cine-MRI

Stress distribution from multiples parameters along the aorta (morphological and functional parameters from MRI, associated with biological parameters), in order to detect areas with high level of rupture risk

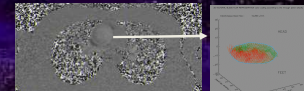
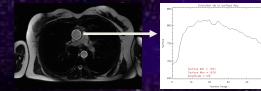
## Cardio-vascular MRI

### • Automatic evaluations of Valsalva sinuses from cine-MRI



Automatic segmentation of the Valsalva sinuses, and automatic detection of the centre, the cusps and the commissures

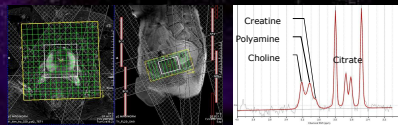
### • Automatic evaluations of the aortic elasticity and of the aortic flow from MRI



## MRI-MRS of prostate cancer

Novel methods using MR technique avoiding the use of endorectal coil

### • Morphological and metabolic study of prostate cancer



### • Segmentation and reconstruction of high resolution MR images

Development of robot-assisted radical prostatectomy

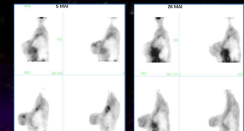
3D high resolution representation from MRI with exquisite contrast of the entire prostate, its internal structure and its adjacent anatomy

Coupling of this representation with the robot in order to offer a greater accuracy to the surgical procedure

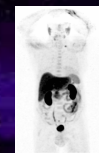
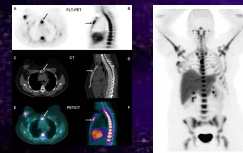
## PET in oncology

### • Follow up of patients with chemotherapy

Patients treated by neoadjuvant chemotherapy  
PET before and after treatment, and evaluation of the FDG uptake



### • Development of innovative tracers



## IMAPPI project (Integrated Magnetic resonance And Positron emission tomography in Preclinical Imaging)

Development of an emerging technology that combine in the same imaging camera both MRI and Positron emission tomography (PET) detection techniques

Development of bimodal molecular MRI-PET imaging probes

Combined PET/MRI system for in-vivo animal imaging applications

