





# **1.INTRODUCTION**

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## Hardware combination **Evolution** / Revolution

Ŵ	Imaging Modality	Spatial Resolution (mm)	Acquisition time per frame(s)	Molecular probe mass required (ng)	Molecular sensitivity (mol/L)	Tissue penetration depth (mm)	Signal quantification capabilities
	PET	1-2 (animal) 6-10 (clinical)	1-300	1-100	10 <sup>-11</sup> -10 <sup>-12</sup>	>300	High
	SPECT	0.5-2 (animal) 7-15 (clinical)	60-2000	1-100	10-10-10-11	>300	Medium-High
	Optical	2-5 (visible to IR)	10-2000	10 <sup>3</sup> -10 <sup>6</sup>	10 <sup>-9</sup> -10 <sup>-11</sup>	1-20	Low
	MRI	0.025-0.1 (animal) 0.2 (clinical)	0.1-100	10 <sup>3</sup> -10 <sup>6</sup>	10-3-10-5	>300	High
	US	0.05-0.5 (animal) 0.1-1 (clinical)	0.1-100	10 <sup>3</sup> -10 <sup>6</sup>	Not well characterized	1-300	Low
	СТ	0.03-0.4 (animal) 0.5-1 (clinical)	1-300	NA	Not well characterized	>300	Medium-High

From Craig S Levin. Eur J Nucl Med & Mol Imag. 2005, 32(14), S-325-45

(Thru D. Townsend and modifiied by YL)





**REVOLUTION is simultaneous Acquisitions without patient deplacement !!** SSHEMP 19-24 May 2014 - Yves LEMOIGNE / IFMP – Ambilly – France & CERN-Geneva-Switzerland



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#### EUROPEAN SCIENTIFIC INSTITUTE (ESI) ARCHAMPS, FRANCE EUROPEAN SCHOOL OF MEDICAL PHYSICS (ESMP)



## HOW PHYSICS HELPS IN ESTABLISHING DIAGNOSIS



onising rays (radiotracers).





# 2. X-Rays CT



# **2 - CT Principle** (recall)

#### Description

**Computed tomography (CT)** scanning is a medical imaging procedure that uses x-rays to show cross-sectional images of the body.

These cross-sectional images are used for a variety of diagnostic and therapeutic preparation purposes.

#### How a CT system works:



A motorized table moves the patient through a circular opening in the CT system. While the patient is inside the CT, a x-ray source and detector within the housing rotate around the patient. The x-ray source produces a narrow beam of x-rays that passes through a section of the patient's body.

A detector opposite from the x-ray source records the x-rays passing thru the patient's body as a "snapshot" image. Many different "snapshots" (at many angles through the patient) are collected during one complete rotation and are sent to a computer to reconstruct all individual "snapshots" into one or multiple cross-sectional images (slices) of the internal organs and tissues. (3-D Imaging) SSHEMP 19-24 May 2014 - Yves LEMOIGNE / IFMP – Ambilly – France & CERN-Geneva-Switzerland



## **CT Utility & Definitions**

# X-Rays-CT has become recognized as a valuable medical tool, for:

- 1. Diagnosis of disease, trauma, or abnormality (Anatomy imaging)
- 2. Planning, guiding, and monitoring therapy (Ex: Treatment Planning preparation)

But:

- Non-negligeable x-ray radiation exposure:
  - Typical dose, Computed Tomography (CT)-Body : 10 mSv (=3 years of natural dose)

• Clássical Chest Radiography: 0.1 mSv (10 days of natural dose)

An important issue within CT radiology today is how to reduce the radiation dose during CT examinations without compromising the image quality (Target CTA protocol, Adaptive Iterative Dose Reduction ...) in some case hopefully 1 mSv can be reached...

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Beer's Law for one material: where  $I_0$  and I are the initial and final Xray intensity,  $\mu$  is the material's linear attenuation coefficient (units 1/length) and x is the length of the X-ray path. With multiple materials  $\hat{\iota}$ , the equation

**becomes:** 
$$I = I_0 \exp\left[\sum_i (-\mu_i x_i)\right].$$

Hounsfield unit = 
$$\frac{\mu_{iissue | material} - \mu_{water}}{\mu_{water}} \times 1000$$

IFMP	Typical CT	ExaminationTypical Effective dose (mSv)			
Institute		Chest X-ray	0.110		
For Medical Physics Institut pour la Physique Médicale	Doses :	Head CT	1.5		
		Abdomen CT	5.3		
		Chest CT	5.8		
		Chest, abdomen and pelvis CT	9.9		

The annual per capita exposure to medical radiation in the U.S. increased from 0.54 mSv in 1980 to 3.2 mSv in 2006 !!.



## Low-dose CT scan :

- Aim is : Reduce the radiation dose during CT examinations without compromising image quality.
- Higher radiation doses => higher-resolution images,
- Lower doses => higher image noise => unsharp images.
- An abdominal CT gives = 300 chest x-rays (for dose).
- Several methods exist to reduce exposure dose :

1- New software technologies: some filters reduce random noise and enhance structures => to get higher quality images and at the same time lower the dose by 30% to 70 %.

Mean: -1001.4 Ht lean: 1041.0 HU ean: 25.5 HU

2. Individualize the examination and adjust the radiation dose to the body type and body organ examined. Different body types and organs require different amounts of radiation.

3. Prior to every CT examination, evaluate the appropriateness of the exam whether it is motivated or if another type of examination is more suitable. Higher resolution is not always suitable for any given scenario, such as detection of small pulmonary masses.





# 3. MAGNETIC RESONANCE IMAGING

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## MRI : Overall picture of how it works...



- Our bodies are made up of roughly 63% water
- MRI machines use hydrogen atoms
- The hydrogen atoms act like little magnets, which have a north and south pole ("Spin").
- The atoms inside our body are aligned in all different directions
- The MRI is basically a large magnet
- Patient lies within scanner where magnetic field is created
- Magnetic force causes nuclei with hydrogen (proton) to line with the field-referred to as parallel, there is also antiparallel
- Electromagnetic radiation (radio waves) are emitted from machine









## Precession



z

- Spins precess about applied magnetic field,  $B_0$ , that is along z axis. - The frequency of this precession is proportional to the applied field. Larmor law:  $\omega = \gamma B$ 
  - Magnetization returns exponentially to equilibrium:
    - Longitudinal recovery time constant is T<sub>1</sub>
    - Transverse *decay* time constant is  $T_2$
  - Relaxation and precession are independent.







How MRI Works



Photon

#### An MRI consists of

- a big magnet creates the magnetic field by coiling electrical wire and running a current through the wire
- gradient magnets: to alter precisely the magnetic field and allow image slices of the body to be created.
- a coll: emits the radiofrequency pulse allowing disturbence of the alignment of the protons / also Receiver.

Tissue

gray matter (GM)

white matter (WM)

muscle

cerebrospinal fluid (CSF)

recognize different matters

 $T_1$  (ms)

950

600

900

4500

 $T_2$  (ms)

100

80

50

2200

Larmor Equation  $\omega_o = \gamma \beta_o$  For H<sup>1</sup>:  $\gamma = 2.675 x_{10}^{8}$  $\beta_0 = 1.5T \quad \omega_0 = 63.864 MHz$ 

- Protons align parallel or anti-parallel to the magnetic field generated
- Larmor Frequency: magnetic moment of proton within external field
- Protons that are parallel=lower energy

Magnet

Radio frequency coil

Scanner

Gradient coils

Protons can oscillate back and forth between states, but majority line up parallel with magnetic field Different relaxation times T1 & T2 help to

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Patient table



**Relaxation:** 

**T1** 



# MRI and Radio Frequencies

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the magnetic moments of protons within a person are not cohesive. They are pointing and moving in all different directions.







The radio frequency pulse manipulates the fact that you are now magnetized making your net magnetic moment flip in a particular area. This generates an electric current in a receiver of the MRI.



The MRI is a giant solenoid magnet providing a magnetic field which aligns the protons magnetic moments.

The MRI scanners extend the frequency along a plane creating a slice that can be imaged.

-The RF coil produces a radio frequency simultaneously to the magnetic field -This radio frequency vibrates at the perfect frequency (resonance frequency) which helps align the atoms in the same direction

-The radio frequency coil sent out a signal that resonates with the protons.

-The radiowaves are then shut off. The protons continue to vibrate sending signals back to the radio frequency coils that receive these signals.







- The signals are then ran through a computer and go through a Fourier equation to produce an image.
- Tissues can be distinguished in function of nature (atoms) and densities.





Used to image a large variety of tissues and substances.

- Brain imaging: to define anatomy, identify bleeding, swelling, tumors, or the presence of a stroke
- To locate glands, organs, joint structures, muscles and bone
- Some diseases manifest themselves in having an increase in water content
- The MRI can detect inflammation (tumors) in many tissues
- Helpful in diagnosing problems with eyes, ears, heart, circulatory system, lungs, pelvis, spinal cord, etc.

Uses for an MRI

Creates a 2D (3D) image that comes from the information of the radio waves of the protons









For Medical Physics Institut pour la Physique Médicale Different types of MRI

#### Advantages:

- Excellent / flexible contrast
- Non-invasive
- No ionizing radiation
- Arbitrary scan plane Challenges:
- New contrast mechanisms
- Faster imaging

#### Advantages:

- Various acquisition sequences
- Large range of contrast
- Excellent space resolution: 25 µm (animal research ) 200 µm (@clinic)





#### - Interventional MRI :

Used to guide in some noninvasive procedures

- Real Time MRI

Continuous filming/ monitoring of objects in real time

- Functional MRI (fMRI)

Measures signal changes in the brain due to changing neural activity - MRS (MR spectroscopy)

Resonance frequencies of common nuclei

Resonance Frequency (1.5Tesla) MHz Nucleus <sup>1</sup>H 63.86 2 D 9.81 13 C 16.05 14N 4.62 <sup>19</sup>N 6.57 23F 60.07 <sup>31</sup>Na 16.89 31P 25.86 35CI 6.27 <sup>39</sup>K 2.97









MRI showing nerve connections inside the brain.

# Image: Status points with the private status points with the p

Α

в

Time MR antenna AC current (Larmor frequency) Precessing net magnetic moment Time

Volts

• **. A)** The falling water rotates a wheel to which a magnet is attached. When this magnet rotates it induces an alternating current in a coil of wire which can be detected. **B)** A magnetic field (spin of a proton) rotating near a coil of MR antenna induces a similar current in the loop which can be detected.





"Protons resonate or wobble at a certain frequency and when you excite them they relax and emit energy in the form of electromagnetic radiation. The body has different numbers and location of protons in various tissues. When you receive the emitted energy you can map the data onto a matrix. Then you can extrapolate using sine and cosine waves what the body looks like based on the mapped RF pulses emitted by different numbers of protons residing in various tissues (kind of like picturing the music arrangement by looking only at the sound signal on your audio receiver!)."

- It is not simple to understand exactly how MRI works....
- But MRI has so many Possibilities (many acquisition modes for instance) that it is very exciting... It is worth working hard to master the MRI...
- MRI has a great future....





# 4. SPECT



**MONOPHOTONIC TOMOGRAPHS** or GAMMA CAMERAS/ SPECT

Very popular in Nuclear Medicine because they require only standard radiotracers.



The radiotracer emits gamma photons of

110 KoV anoray which are detected by the

and the photomultipliers (PM).

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IS

Electronics boards Description Computer Compu

The collimator removes the photons not directly emitted by the organ targeted.

The signals are collected by the electronic components and sloo by the computer to reconstitute the images.

 Methods
 Construction
 Tools :

 specific to the detected photon (in this case, 140 KeV);
 Tools :

 by the Commuter.
 Tools :

is anyway to obtain images of the whole-body of the patient by the the photo above.

I'o right background noise,
 the selection on the energy
 the photon origin impose
 The device shows here allo
 succesive translation, as in







**Aim: -** to measure and display the concentration of a gamma rayemitting radioisotope within individual slices of the body

SPECT: Single photon emission computed tomography with tracers such as Tc-99m using either a rotating gamma camera or a dedicated ring camera

## **Advantages over planar imaging:**

- improved image contrast
- better localisation
- improved detection rates
- quantification (see later)

## **Example**

SPECT brain scan using a 99mTc labelled blood flow tracer showing high perfusion in the tumour



X-ray CT scan SPECT blood flow scan





#### A very popular algorithm: Ordered Subset Expectation Maximisation (OSEM)

A fast variation of the ML-EM algorithm using subsets of the projections For example 64 projections used 8 at a time for 8 separate image production procedures (requires substantial data storage space). Thanks to Progress in Computers....



"CT is potentially more valuable for SPECT than for PET" Bailey DL. Eur J Nuc Med & Mol Imag 2003; 30(7):1045-1046





# **5. PET**



The first PET were simply Gamma cameras, from which the collimators had been removed and coincidence added between opposed detectors. Thereafter, better optimised PET equipments were built. For the human PET, several rings of detectors (crystals and PM) are assembled together.



The tracers for PET are more difficult to use because their half-life is shorter. A cyclotron and a synthesis laboratory are necessary.



The most used isotopic tracer is **FluoroDeoxyGlucose** (FDG), which has the Fluor atom replaced by Fluor-18 1) which disintegrates by positron emision. The FDG accumulates in the cells with abnormal metabolism, i.e. cancer cells. It is phosphorylated (then trapped in cell) By hexokinase to FDG-6-PO4 not metabolised further in the Glycolitic pathway



PET and cancer:

1) & 2): front and side view before treatment;

3) & 4): front and side view after chemotherapy.

FDG accumulates naturally in the brain, kidneys, bladder and the heart; in this case chemotherapy was very effective. Only the PET can do that!



#### The HIDAC Camera Project, 1977-1988 CERN & HCU, Geneva



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1977 when PET started at CERN Some of House Saturd of CERN I bit is line from the Starty of the Normal Start (in the Starty of the Normal Start)

First mouse imaged at CERN with Na-<sup>18</sup>F in 1978





Why **FDG Works** So well?



## Fusion imaging: from software to hardware

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is useful in Oncology for

- Help in Diagnosis
- Help in Treatment plannings
- Help Post-treatment survey

SPECT-CT & PET-CT are better than SPECT & PET alone....



and the thyroid. 9 months later PET showed significant disease progression

including sternum and pelvic region

(From D. Townsend)



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# 6. QUANTIFICATION

(SPECT & PET)

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• Qua	Intification is a measurement !
= Nu	Imerical value extracted from an image, to get concentration of radiotracer (KBq /
	hen estimate physiological parameters in Nuclear Medicine
• Majo	or problems affecting the quantification
in S	SPECT & PET: problem, consequences,
me	thods, correction, results:
- Att	enuation
- SCa - Fff	attering fect of partial volume
- Mo	ovement N : signal intensity in a C concentration of radiotracer
- Va	riation of spatial resolution in SPECT region (pixel value) (kBq / ml ) in the region
• Two	o types of quantification: Absolute or Relative quantification:
-1- A	Absolute quantification needs:
- a of pa	arameter derived from this concentration
b -	- Measurement of a volume (Ex:glucose metabolism in mouse brain : µmol/100 g
min)	Ensure that N = k C then Determine k
-2-	Relative quantification
- 60 or h	botwoon two instants: Evolution of the tracer untake
The	e measured quantity is dimensionless
	Ensure $N = k C$ Needless to know k (only k constant over time)
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#### **Barriers to quantification**



- Intrinsic Barriers:
  - Matter and radiation interactions in SPECT and PET

. Attenuation \*\*\* . Compton scattering\*

To be studied carefully

- Limits of the imaging device . limited and non-stationary spatial resolution \*\*
- . random coincidences in PET
- . measurement noise

#### Potential Obstacles

- Patient movement
- . Physiological : heartbeat, breathing
- . fortuitous because relatively long exams
- Defects in the detector
- . Non uniformity
- . dead time
- . mechanical stability

# **Attenuation in SPECT & PET**

 In SPECT Attenuation depends on the place of issue on the projection line. When an event is detected, it is not

known how deep it comes: we do not know how much it has been attenuated making it difficult to correct the attenuation.  $\Rightarrow$ Use medium density :  $\mu$  for lungs=0.04 cm<sup>-1</sup>  $\mu$  for soft tissue=0.15 cm<sup>-1</sup>  $\mu$  for cortical bone=0.30 cm<sup>-1</sup>. Attenuation is of course function of  $\gamma$  energy.

• In PET, attenuation do not depend on the place of emission on line projection. It depends only of the full attenuation d1 + d2 = D. When an event is detected on a line of response, suffered attenuation is known. We can therefore more easily compensate attenuation than in SPECT (identical for all radiotracer giving 511 Kev pair).

• In SPECT (and PET also), attenuation leads underestimates of activity generally greater than 70%. (Cardiac example)

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 Attenuation problem is better solved now by SPECT/CT and PET/CT hybrid machines. Fortunately acquisition in transmission is very fast. If attenuation coefficients are measured at different energies than the radiotracer energy (Spect or PET), adaptation is necessary. SSHEMP 19-24 May 2014 - Yves LEMOIGNE / IFMP – Ambilly – France & CERN-Geneva-Switzerland



 $N = N_0 \exp[-(\mu_1/2 + \mu_2 + \mu_3)] \ell$ 











No attenuation With attenuation



## **Compton scattering**



Scattering can happen:

- In the patient
- In the collimator septa
- In Crystals

#### Consequences of Scattering:

- Photons lose energy
- Photons change direction so they will be poorly localized in images
- Bluring pictures
- Contrast decreases



Importance of scattering in SPECT



acquisition picture window

=





primary photons scatter

scattered photons ( 37 % )

With Tc- 99m, about 30% of detected photons in the conventional acquisition window are scattered photons (thus bad positioned in the image)

Scattering cross section Increases when energy decreases :



images from TI -201 (70 KeV) are more affected by scattering than Tc- 99m images (140 KeV)









# 7. EXAMPLES OF USES @ HOSPITAL







A 50 year-old female patient restaged for vulvar cancer with history of NHL (Non-Hodgkin lymphoma),. The PET/CT scan shows focal uptake in right aspect of the vulva (SUV: 10.3). Adjacent focal anorectal uptake (SUV: 5.5). CT is negative with no abnormality seen. Only combination of CT and PET can show that! SSHEMP 19-24 May 2014 - Yves LEMOIGNE / IFMP – Ambilly – France & CERN-Geneva-Switzerland





# 8. IMPROVEMENTS





- Better Crystals (Ex: more ph/MeV with LSO, LYSO, LuBr3...)
- **Spatial resolution** (Ex : Crystal size 4 x 4 mm or smaller)
- New reconstruction algorithms
- Efficiency (Septa removed in PET)
- Time-of-Flight (Tof)
- MRI-PET Devices:

#### Complementary nature of MRI & PET

Parameter	MRI	PET
Anatomical Detail	Excellent	Poor
Spatial Resolution	Excellent	Compromised
Clinical Penetration	Excellent	Limited
Sensitivity	Poor	Excellent
Molecular imaging	Limited	Excellent



Hence: The Sum of PET and MRI should be excellent and even better **MRI + PET << MRI-PET** 













## **Challenges** for PET/MR



- MR-compatible PET detectors from technics (APD,Si-PM..)
- PET attenuation correction factors from MR images
- role for simultaneous MR and PET acquisition?
- financial cost (eventually) of the PET/MR system
- Used routinely for Small Animal PET ("Medical Imaging Ideas")
   In biomedical research... MR-PET Design for Whole Body Applications

#### But already exceptionnal images ...









# 9. CONCLUSION

#### During last decade: Impressive progress in Medical Imaging

Due to **enormous** work on the technical front:

- New detectors
- Software
- Training
- Radiation Protection

About 4000 PET/CT scanners operational worldwide (start in 2000')

PET/MR scanners are beginning now (2014)

All that is for the main benefit of patients....





