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MEDICAL PHYSICS WORKSHOP

Devoted to PET Developments and Applications

6 - 8 September 2015

	6 Sept	7 Sept	8 Sept
8:15		Session 3: PET and main applications	Session 7: RP in MP applications
9:15	Registration		
10:15	Coffee break	Coffee break	Coffee break
10:30	Opening Session	Session 4: More PET imaging applications	Session 8: PET and HEP transfer to medical physics
11:30			
12:30	Lunch	Lunch	Lunch
14:15	Session 1: Medical physics in NM	Session 5: PET complements	Session 9: Use of PET in hadrontherapy
15:15			
16:15	Coffee break	Coffee break	Coffee break
16:30	Session 2: Medical imaging	Session 6: Hybrids system PET-MRI	Session 10: Open discussions and conclusion END
17:30			
18:30			
19:30	Welcome cocktail (St. Naum Monastery)	Banquet	
23:00			

Ss. Cyril and Methodius University in Skopje

Congress Centre - Ohrid, Ohrid, Macedonia

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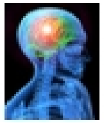
AMBILLY, FRANCE



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Ohrid-Workshop 6-8 September 2015
PET cameras: Principles, use a hospital & ongoing developments

(# is for15 mn)
(= is for 30 mn)
(= = is for 50 mn)

Time –table
31/08/15

Time	SUNDAY 6/9/15 : Introduction & CT, SPECT	MONDAY 7/9/15 : PET, Hybrid & Applications	TUESDAY 8/9/15 : Rad Protection & Developments
08:15 10:15	 *9:30 : Registration* *10:30*	*Session 3 :* PET & Main Applications Chair : S. Petkovska == *PET Principle & History* *I. Rausch, Vienna, A* == *Clinical application of FDG PET/CT* *J-N Talbot , Tenon Hospital., Paris-F*	*Session 7 :* Radiation Protection in MP applications Chair : P. Le Dû, = *General Risks with Radiation* *M. Medvedec, Zagreb, HR* = *Optimisation in Nuclear Medicine* *M. Medvedec, Zagreb, HR* == *Patient, Workers, Public protection & Hospital* *M. Medvedec, Zagreb, HR*
	Coffee Break	Coffee Break	Coffee Break
10:30 12:30	*11:00* *Opening Session* Chair : D. Miladinova # *Welcome (University Rector or Dean)* # *Med. Phys. In MK, S. Petkovska, Skopje* == *Medical Imaging Review* *Y.Lemoigne, IFMP & CERN-CH* = *Interactions of biomedical oscillations* *T. Stankovski, Skopje-MK* *13/00*	*Session 4 :* More PET Imaging Applications Chair : M. Zdraveska == *clinical PET/CT with other tracers* *J-N Talbot, Tenon Hospital, Paris-F* = *Research Example by Small Animal PET* *Y.Lemoigne, IFMP & CERN-CH* = *Opportunities in early diagnosis & treatment* *N. Papapostolou, Varian H A*	*Session 8:* PET and HEP Transfer to Medical Physics Chair : I .Rausch = shielding requirements for PET/CT *J. Haglund , Fredrikstad, NO* == *Transfer from HEP* *P. Le Dû , IEEE & IPN Lyon-F* = *Developments in PET from HEP* *L. Litov, Sofia Uni. BG*
	Lunch	Lunch	Lunch
14:15 16:15	*Session 1 : Medical Physics in NM* Chair : Y. Lemoigne == NM Dosimetry: Diagnostic & Therapy *M. Bardies , Toulouse, F* = *Dose & risks in Iodine 131 treatment* *M. Zdraveska, Skopje-MK* = *CT: Computed Tomography* *J. Haglund , Fredrikstad, NO*	*Session 5 : PET complements* Chair : J-N Talbot == *Pet Quality Control & Quantification* *I. Rausch, Vienna, A* = *Pet in Norway / an example* *J. Haglund , Fredrikstad, NO* = *Imaging for R. Oncology (CT, PET-CT)* *S. Petkovska, Skopje-MK*	*Session 9 : Use of PET in Hadrontherapy* Chair : M. Medvedec == *Hadrontherapy principles* *P.R. Altieri, INFN & Bari Uni, IT* = *On line dose monitoring* *P.R. Altieri, INFN & Bari Uni, IT* = *Particle Therapy - the future* *P. Le Dû, IEEE & IPN Lyon-F*
	Coffee Break	Coffee Break	Coffee Break
16:30 18:30	*Session 2 : Medical Imaging* Chair : M. Bardies == *SPECT/CT Instrument' & Clinical App* *D. Miladinova, Skopje-MK* = *Dose Optimisation in MDCT* *V. Gershan, Skopje-MK*	*Session 6 : Hybrids system:* PET-MRI Chair : P.R. Altieri === *PET-MRI: Principle, Advantages&Problems* *L. Bidaut, Dundee, UK* = *Ecologic Talk* *F. Vosniakos, Thessaloniki-Gr*	*Session 10 : Open Discussion & conclusions* *Chair: D. Miladinova, Y. Lemoigne* *With: P.A, J.H, M.M, P.LD, I.R ,S.P and other persons for very short presentations…* *End of Workshop*
19:30 20:00 23:00	*WELCOME COKTAIL* *@ st Naum Monastery*	*BANQUET*	Possibility of Transport to Skopje by Public Bus (Courtesy bus to SKP Airport Wednesday 8:00)

Ohrid Workshop September 2015 Yves LEMOIGNE / IFMP – Ambilly – France & CERN-Geneva-Switzerland

The (R)EVOLUTION of Hybrid Devices in MEDICAL IMAGING

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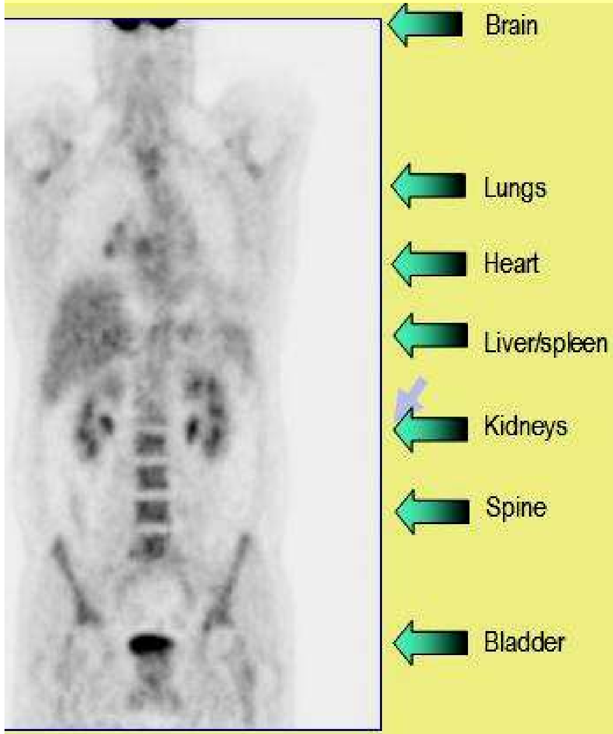
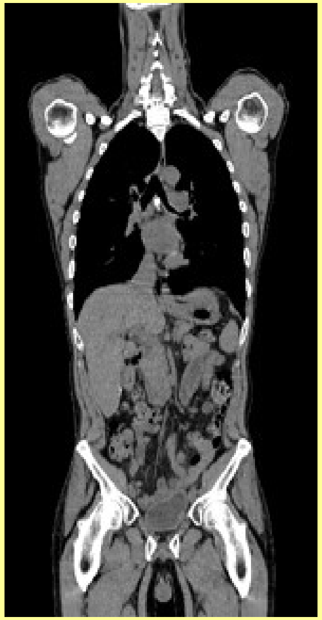
Yves LEMOIGNE, PhD

Institut pour la physique médicale, Ambilly
Archamps Biomedical Centre (ABC) Lab.
France
CERN, Geneva, Switzerland



PET

1. Intro to Medical Imaging
2. CT-scanner (with X-Rays)
3. MRI
4. SPECT
5. PET
6. Quantification
7. Uses in Hospital
8. Improvements
9. Conclusion



CT

1.INTRODUCTION

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Imaging modalities today

Hardware combination ➡ Evolution / Revolution

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^{-11}-10^{-12}	>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	10^3-10^6	10^{-9}-10^{-11}	1-20	Low
MRI	0.025-0.1 (animal) 0.2 (clinical)	0.1-100	10^3-10^6	10^{-3}-10^{-5}	>300	High
US	0.05-0.5 (animal) 0.1-1 (clinical)	0.1-100	10^3-10^6	Not well characterized	1-300	Low
CT	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

EVOLUTION in MEDICAL IMAGING (combination of existing equipment)

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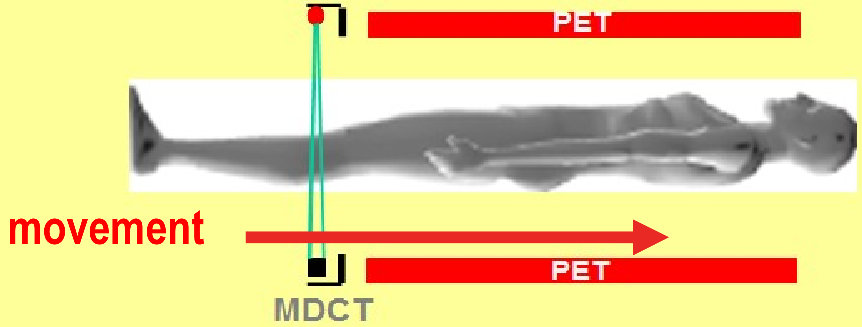
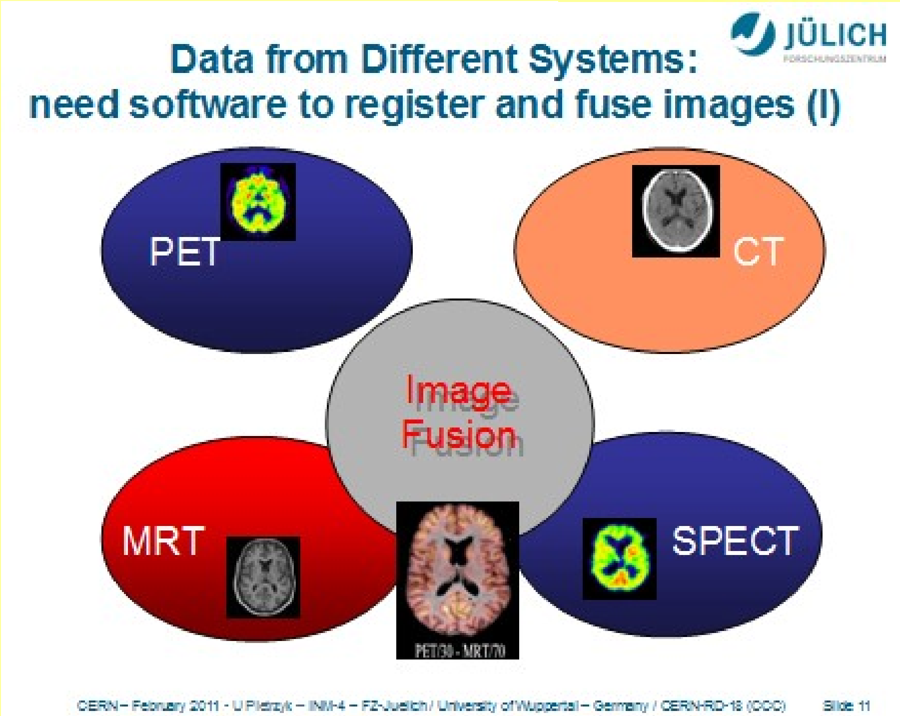
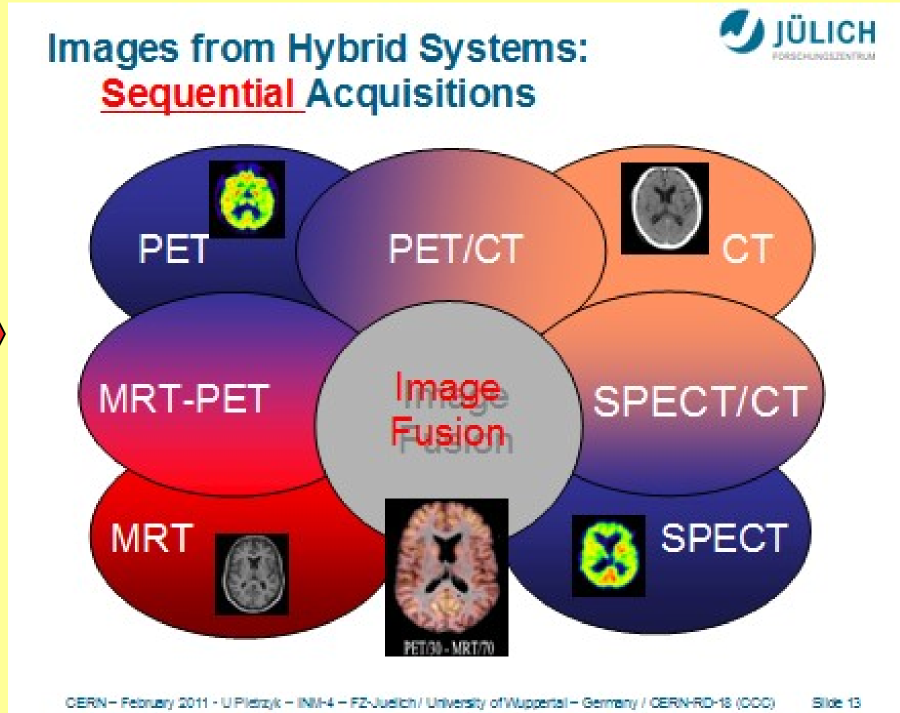
Example: **CT** **PET**







Data taken at different time / in different configuration / in different places…

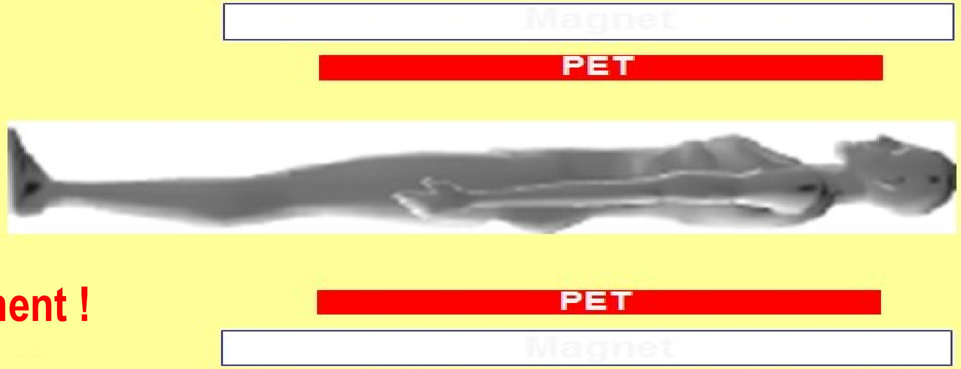
Fusion only by software

Data taken at sequential time / with minimal movement of patient

Fusion by software

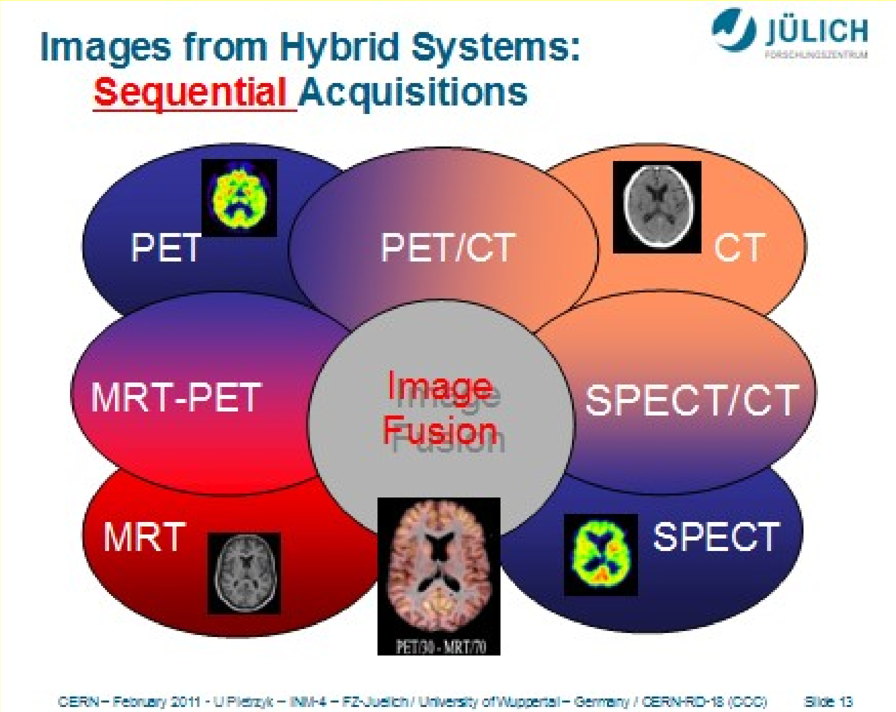
REVOLUTION in MEDICAL IMAGING

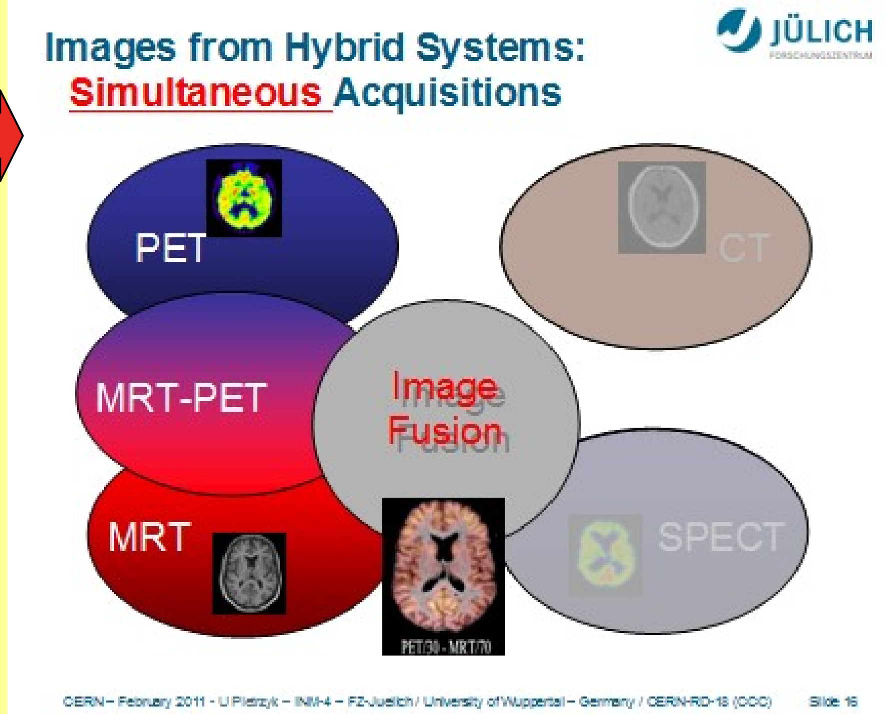
(Integrated devices from technical developments)

Example: **MRT**  **PET**

No movement !

(same hardware)

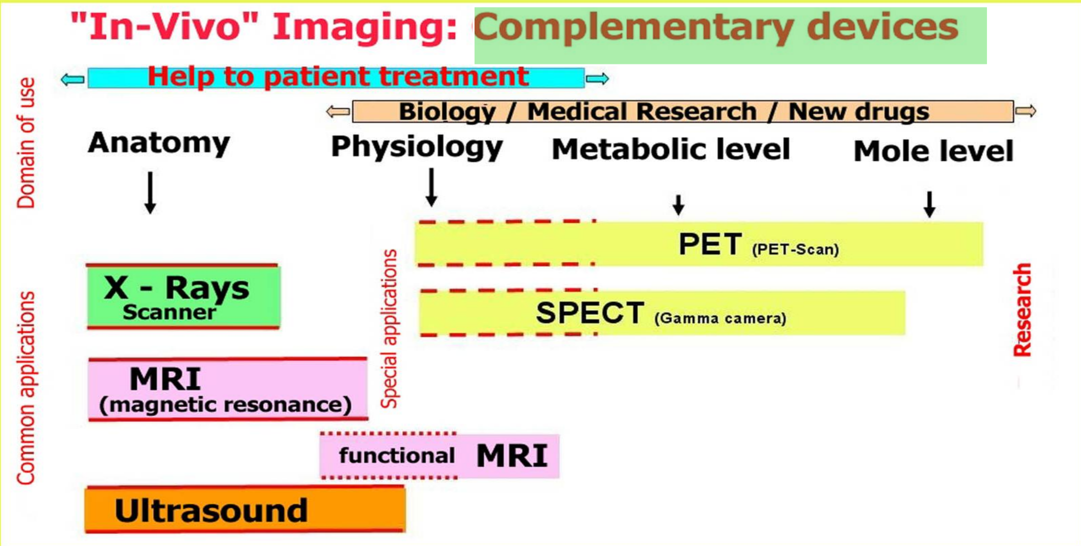


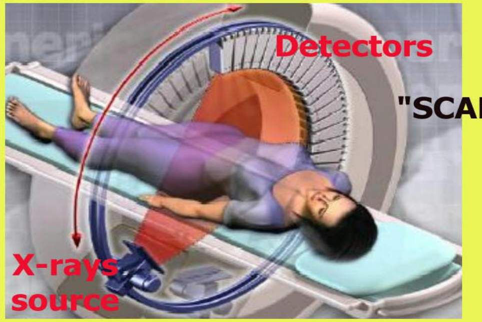


REVOLUTION is simultaneous Acquisitions without patient deplacement !!

HOW PHYSICS HELPS IN ESTABLISHING DIAGNOSIS

Physics has made it possible to create sophisticated devices to "explore" the human body from different perspectives:
- anatomical, to see "inside" the human body at a certain moment;
- functional, to see how the body functions during a given period of time.





"SCANNER" - TDM

CT

"PET-SCAN"

Each technique has its own specificity and thus a particular area of application:

- Scanner: TDM with a good space-resolution; ionising X-rays.

- PET-SCAN: functional analysis can be VERY sensitive; limited space-resolution. Uses ionising rays (radiotracers).

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2. X-Rays CT

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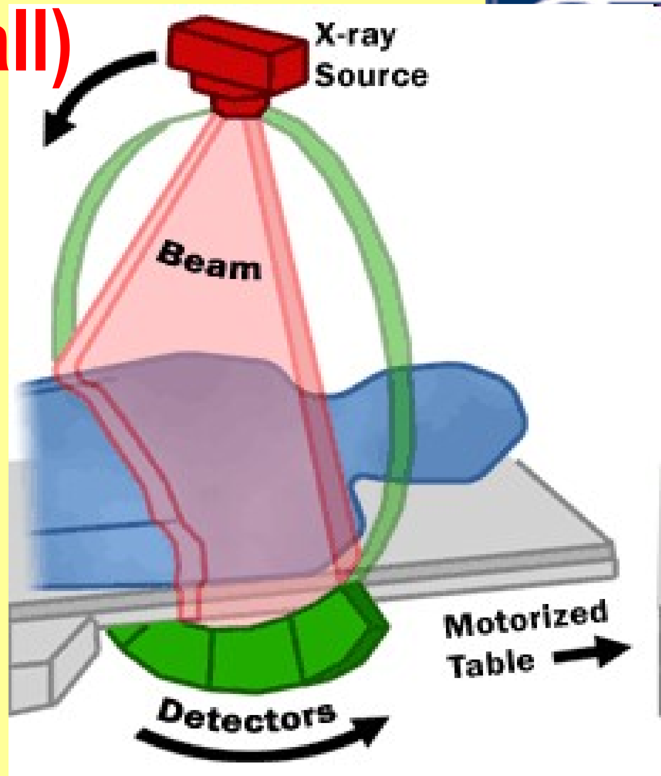
2 - CT Principle (recall)



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)

CT Utility & Definitions

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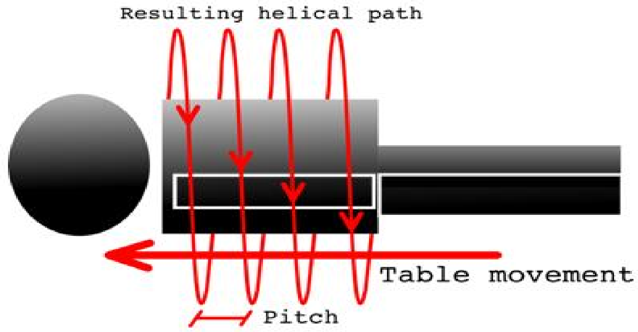

X-Rays-CT has become recognized as a valuable medical tool, for:

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

Beer's Law for one material: $I = I_0 \exp[-\mu x]$

where I_0 and I are the initial and final X-ray intensity, μ is the material's linear attenuation coefficient (units 1/length) and x is the length of the X-ray path.
With multiple materials i, the equation becomes: $I = I_0 \exp\left[\sum_i (-\mu_i x_i)\right]$

But:

Non-negligeable x-ray radiation exposure:

- Typical dose, Computed Tomography (CT)-Body : 10 mSv (=3 years of natural dose)
- Classical Chest Radiography: 0.1 mSv (10 days of natural dose)

$$\text{Hounsfield unit} = \frac{\mu_{tissue/material} - \mu_{water}}{\mu_{water}} \times 1000$$

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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Typical CT Doses :

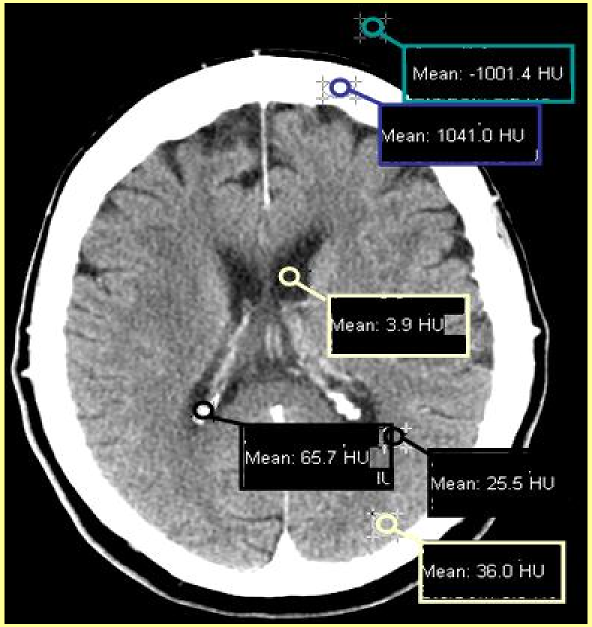
ExaminationTypical	Effective dose (mSv)
Chest X-ray	0.110
Head CT	1.5
Abdomen CT	5.3
Chest CT	5.8
Chest, abdomen and pelvis CT	9.9

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 !!.

CERN

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 %.

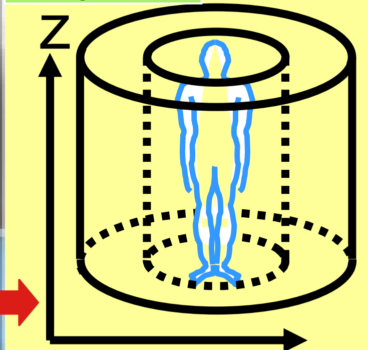
2. Individualize the examination and adjust the radiation dose to the body type and body organ examined. Different body types and organs require different amounts of radiation.

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.

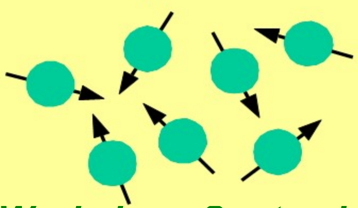
3. MAGNETIC RESONANCE IMAGING

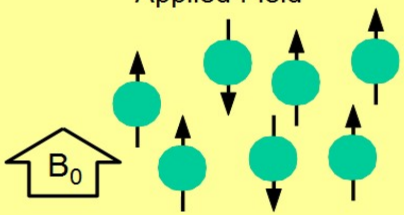
MRI : Overall picture of how it works…

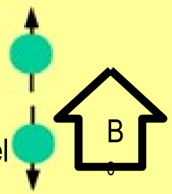
- Our bodies are made up of roughly **63% water**
- MRI machines use hydrogen atoms
- **The hydrogen atoms act like little magnets,** which have a north and south pole (“Spin”).
- The atoms inside our body are aligned in all different directions



- 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







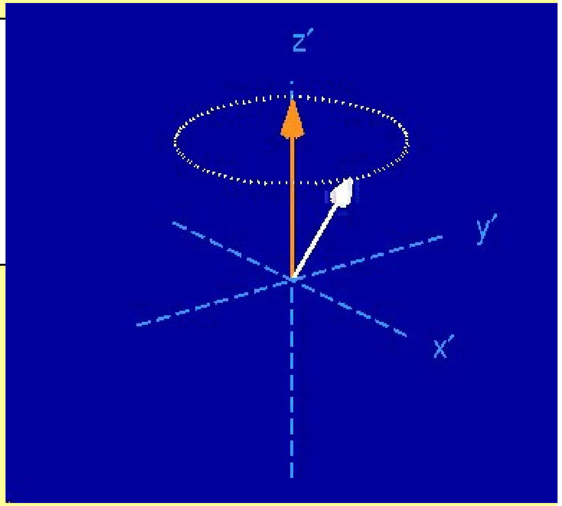
Anti-Parallel have higher Energy than Parallel ones

Radio waves are emitted when coming back to equilibrium

Precession

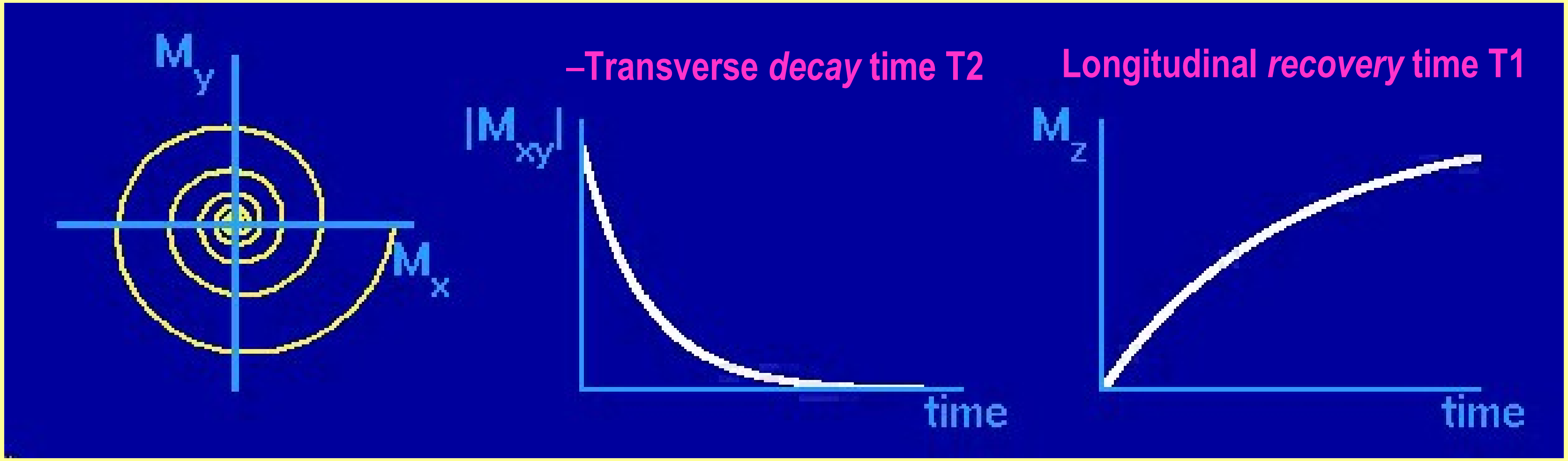
- Spins precess about applied magnetic field, B_0, that is along z axis.
- The frequency of this precession is proportional to the applied field.

Larmor law: $$\omega = \gamma B$$



- Magnetization returns **exponentially** to equilibrium:
  - Longitudinal *recovery* time constant is T_1
  - Transverse *decay* time constant is T_2
- Relaxation and precession are independent.

Relaxation



Precession Decay Recovery

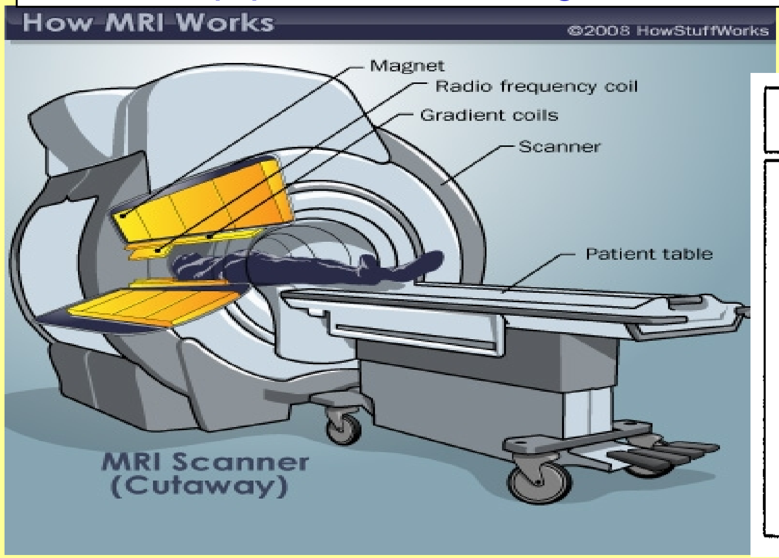
MRI : how it works (Cont'd)...

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 coil: emits the radiofrequency pulse allowing disturbence of the alignment of the protons / also Receiver

Larmor Equation $\omega_o = \gamma.\beta_o$ **For H^1 :** $\gamma = 2.675x10^8$ $\beta_0 = 1.5T$ $\omega_0 = 63.864MHz$

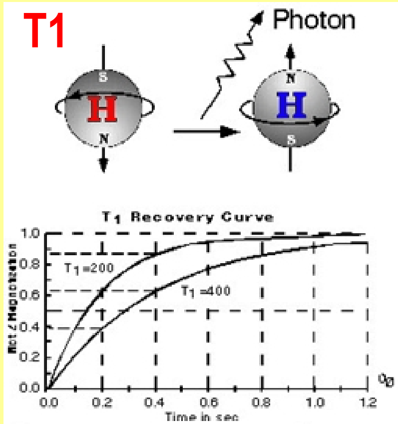
- Protons align parallel or anti-parallel to the magnetic field generated
- Larmor Frequency: magnetic moment of proton within external field
- Protons that are parallel=lower energy
- Protons can oscillate back and forth between states, but majority line up parallel with magnetic field



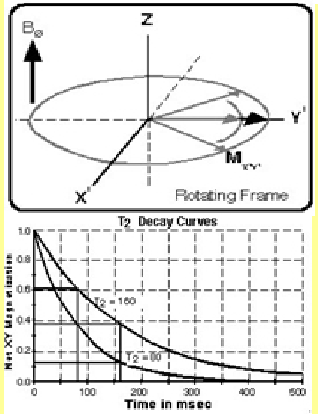
Different relaxation times T1 & T2 help to recognize different matters

Tissue	T_1 (ms)	T_2 (ms)
gray matter (GM)	950	100
white matter (WM)	600	80
muscle	900	50
cerebrospinal fluid (CSF)	4500	2200
fat	250	60
blood	1200	100-200[3]

Relaxation:



T2



MR Image Formation Selective Excitation

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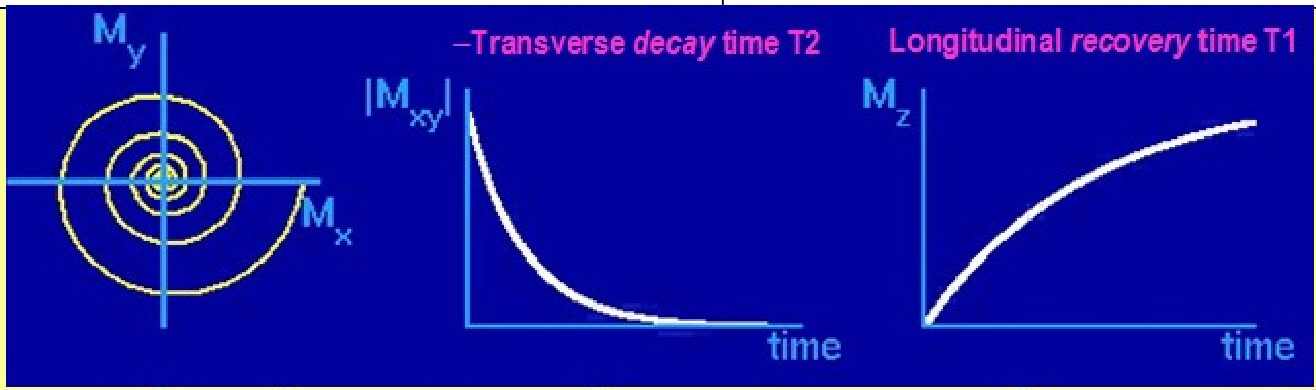
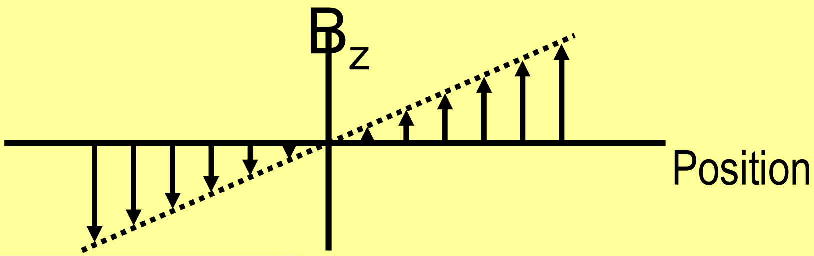
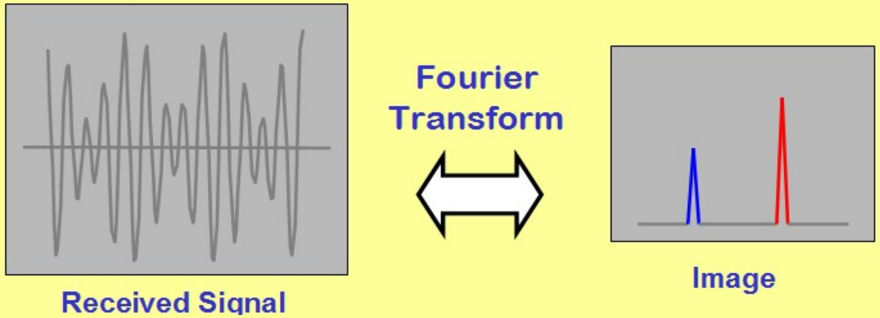
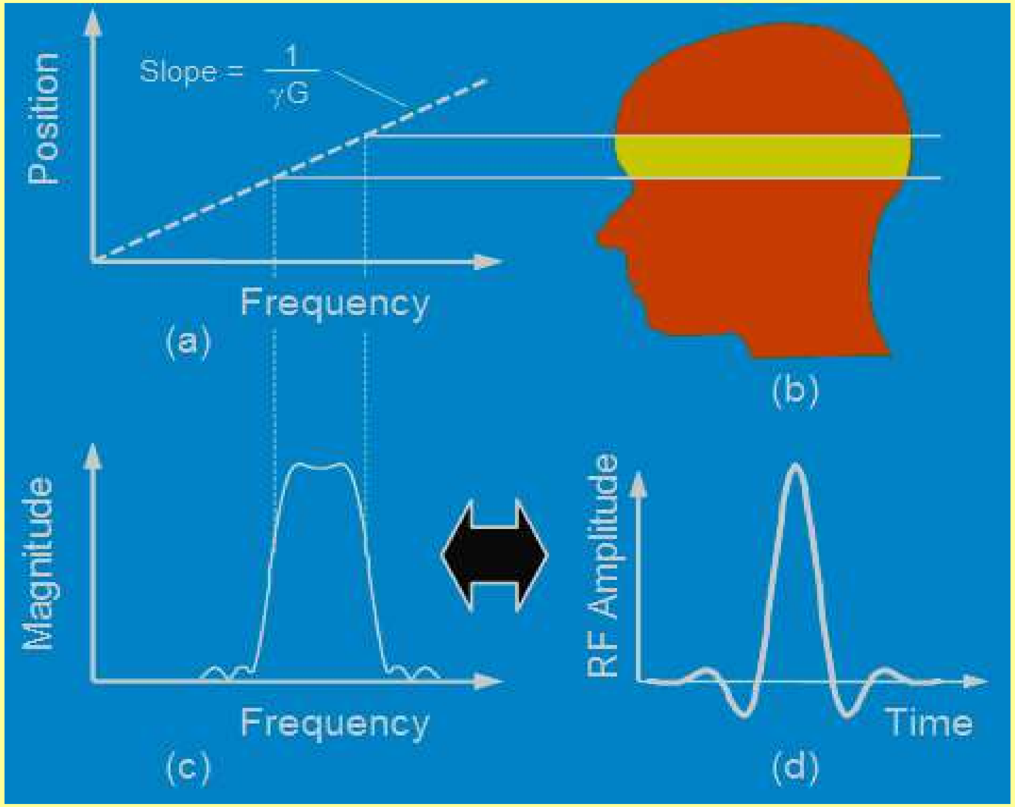


Precession Decay Recovery

- **Gradient coils provide a linear variation in B_z with position.**
- Result is a resonant frequency variation with position.







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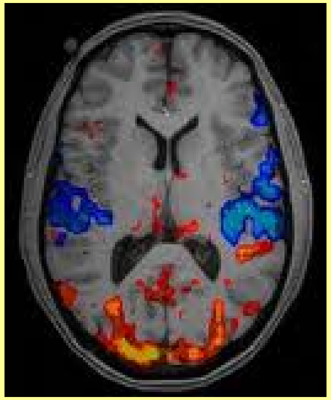
Different types of MRI

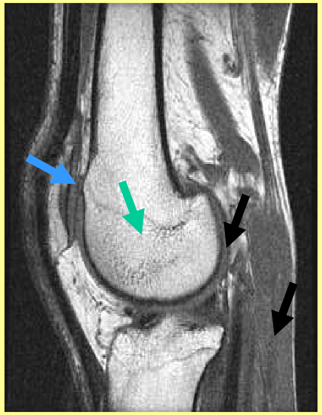
Advantages:
- Excellent / flexible contrast
- Non-invasive
- No ionizing radiation
- Arbitrary scan plane

Challenges:
- New contrast mechanisms
- Faster imaging

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

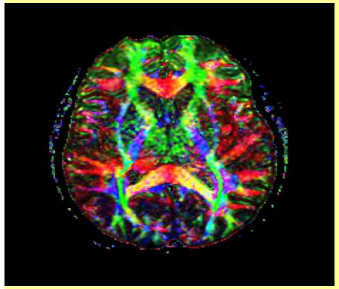
- Interventional MRI :
  Used to guide in some noninvasive procedures
- Real Time MRI
  Continuous filming/ monitoring of objects in real time
- Functional MRI (fMRI)
  Measures signal changes in the brain due to changing neural activity
- MRS (MR spectroscopy)





Resonance frequencies of common nuclei

Nucleus	Resonance Frequency (1.5Tesla) MHz
^{1}H	63.86
^{2}D	9.81
^{13}C	16.05
^{14}N	4.62
^{19}N	6.57
^{23}F	60.07
^{31}Na	16.89
^{31}P	25.86
^{35}Cl	6.27
^{39}K	2.97



MRI showing nerve connections inside the brain.

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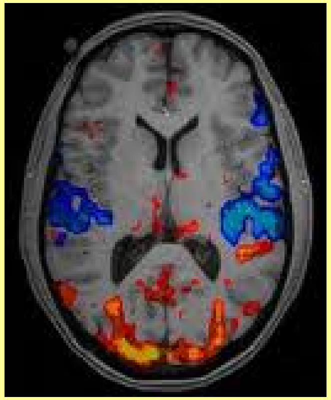

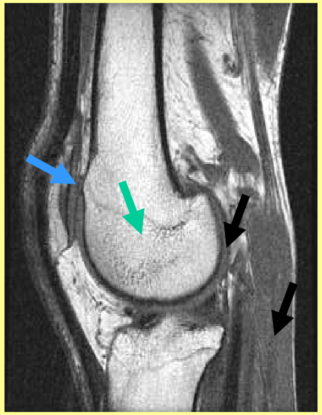

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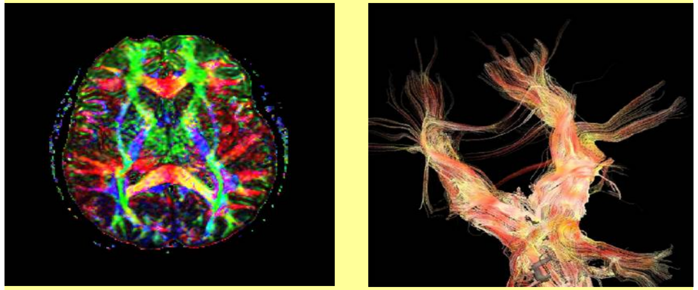

MRI showing nerve connections inside the brain.

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4. SPECT

ISOTOPIC TRACERS AND THEIR USE WITHIN SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

The technique of isotopic tracers consists in the fact that one or more atoms of the molecules at work in the studied reaction are replaced by another isotope of the same chemical element, but radioactive. This isotope, having the same number of protons and electrons as the atom which it substitutes, behaves chemically like the latter and therefore it does not interfere, but it makes it possible to "trace" the molecule to which it links.

Some isotopes uses:

Isotope	Half-life
Technetium-99m	6 hours
Iode-131	8 days
Iode-123	13 hours
Indium-111	2.8 days
Thallium-201	3 days
Fluor-18	2 hours
Carbon-11	20 minutes
Azote-13	10 minutes
Oxygen-15	2 minutes
Gallium-68	68 minutes

In medicine it is necessary that the radioactivity should disappear quickly enough (short half-life) and that the quatity of tracer applied to the patient should be very small (measured in micro-moles and even in pico-moles). The sensivity of the apparatus used is thus crucial.

Some isotopes emit gamma photons, others emit positrons (see PET).

In monophotonic tomography, the patient receives marked molecules whose biological behaviour is known. The detectors will recognise the photons emitted and therefore they will allow to recognstitute one or more images data processing (which is a complex process).

MONOPHOTONIC TOMOGRAPHS or GAMMA CAMERAS / SPECT

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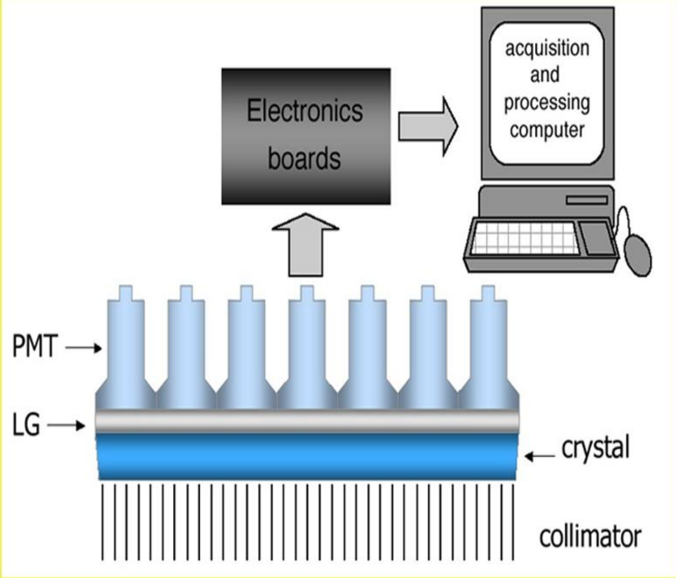
Very popular in Nuclear Medicine because they require only standard radiotracers.



A radiotracer (Technetium-99m, by example) is injected into the patient to depose into the target-organ.

The radiotracer emits gamma photons of 140 KeV energy which are detected by the crystals and the photomultipliers (PM).

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

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

To fight background noise, the device can use only two **Tools :**

- the selection on the energy specific to the detected photon (in this case, 140 KeV);
- the photon origin imposed by the collimator.

The device shows here allows anyway to obtain images of the whole-body of the patient by the succesive translation, as in the photo above.

D. NEAMTU, Y. LEMOIGNE, ESI-Archamps

Emission Computed Tomography

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

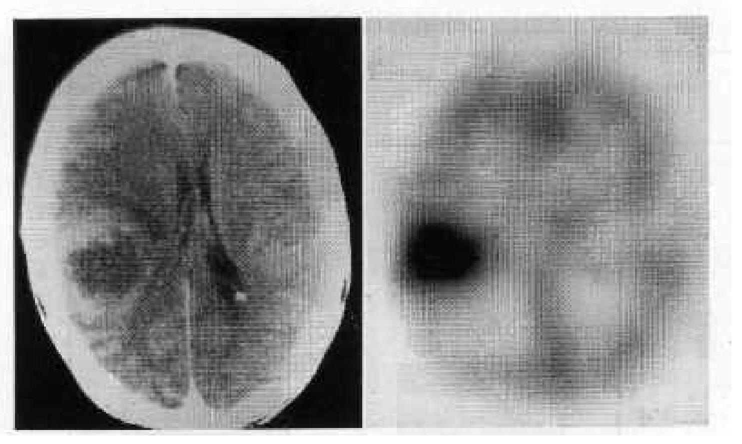
SPECT: Single photon emission computed tomography with tracers such as Tc-99m using either a rotating gamma camera or a dedicated ring camera

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

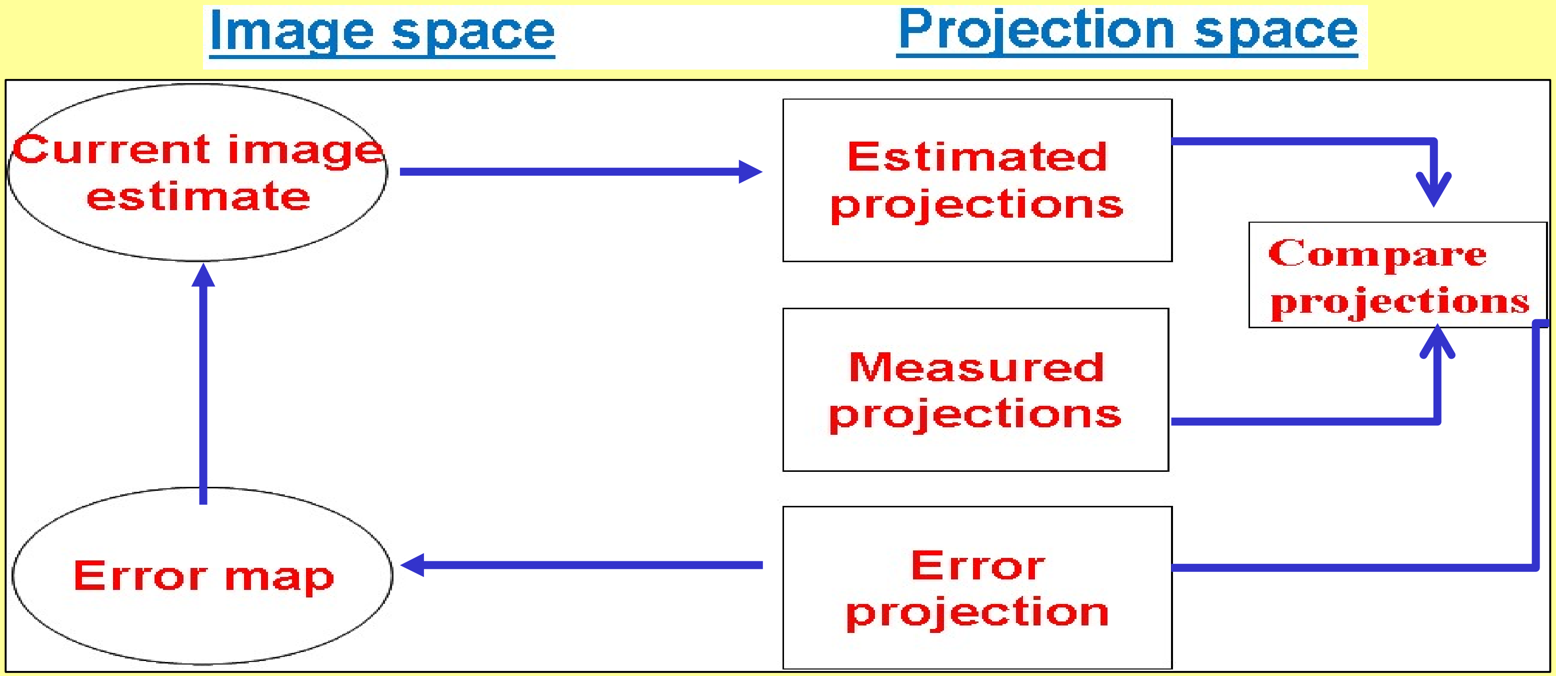


X-ray CT scan *SPECT blood flow scan*

Image reconstructions proceed thru projections:

- Similar to X-ray CT : take 1D profiles or 2D projections at discrete angles around the object
- Assume that each profile/projection point = sum of activity elements along detector LOR

Principles of iterative reconstruction :



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….

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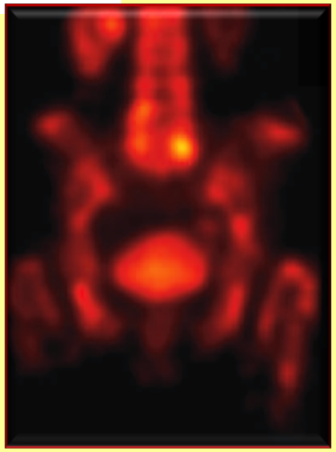
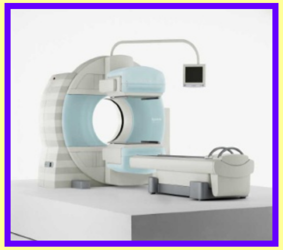
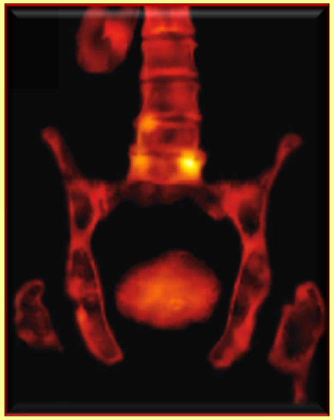
Now: SPECT/CT in the clinic

(From D. Townsend 2014)



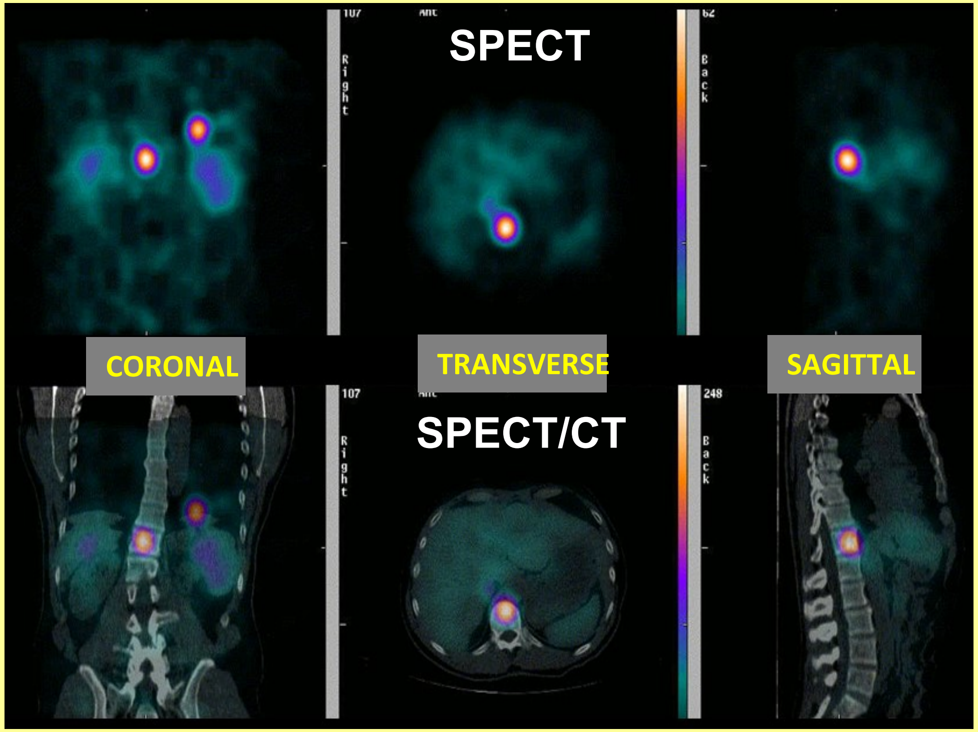
Conventional SPECT





SIEMENS xSPECT

Symbia TX



Discovery NM/CT 670

"CT is potentially more valuable for SPECT than for PET"

Bailey **DL. Eur J Nuc Med & Mol Imag 2003; 30(7):1045-1046**

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5. PET

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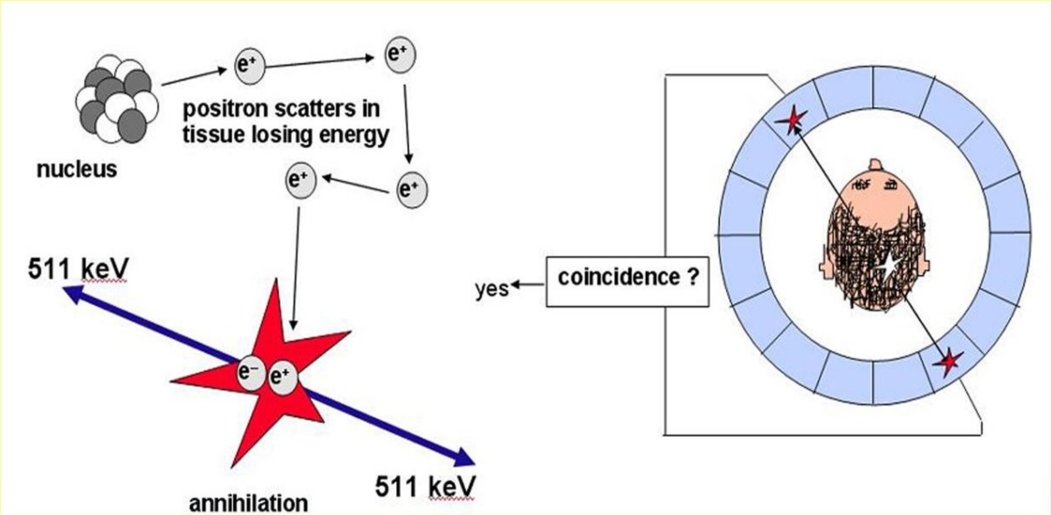
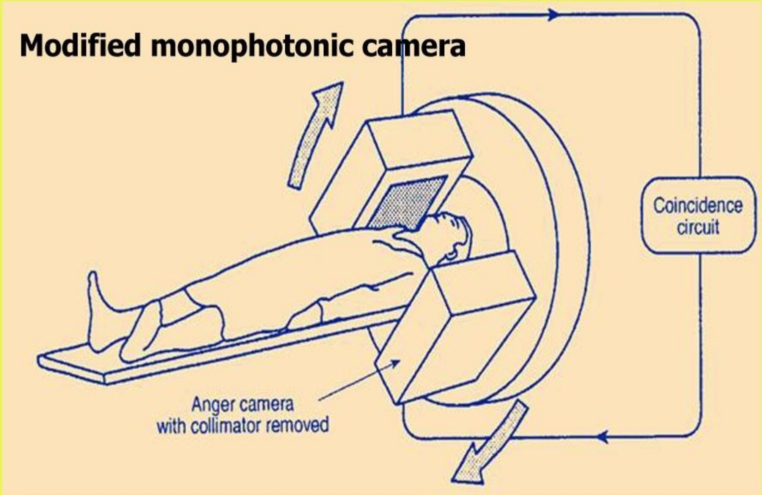
DIPHOTONIC TOMOGRAPH or PET CAMERA

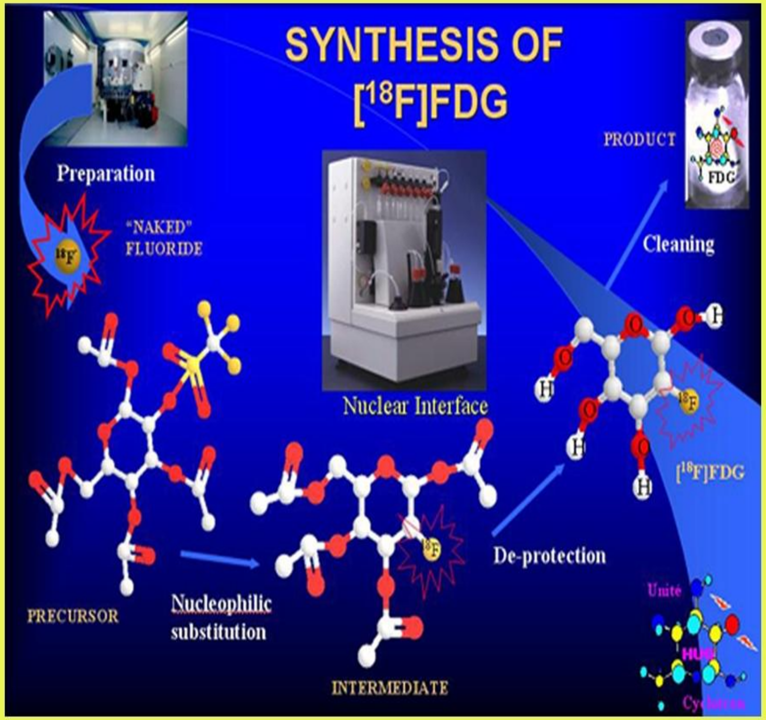
ANTI-MATTER ON CENTER STAGE!

Some isotopes disintegrate by emitting a positron (anti-electron) which, by successive collisions with the matter, will lose its energy and will produce matter-antimatter annihilation with an electron from one of the atoms encountered. This process results in two "back-to-back" photons of well-established energy (511 KeV) and emitted simultaneously. Consequently, we can suggest that two opposed detectors should emit two simultaneous signals (see the diagram). With all this constraints, the PET camera eliminates the background noise much better than the Gamma camera and thus reaches a higer sensitivity.

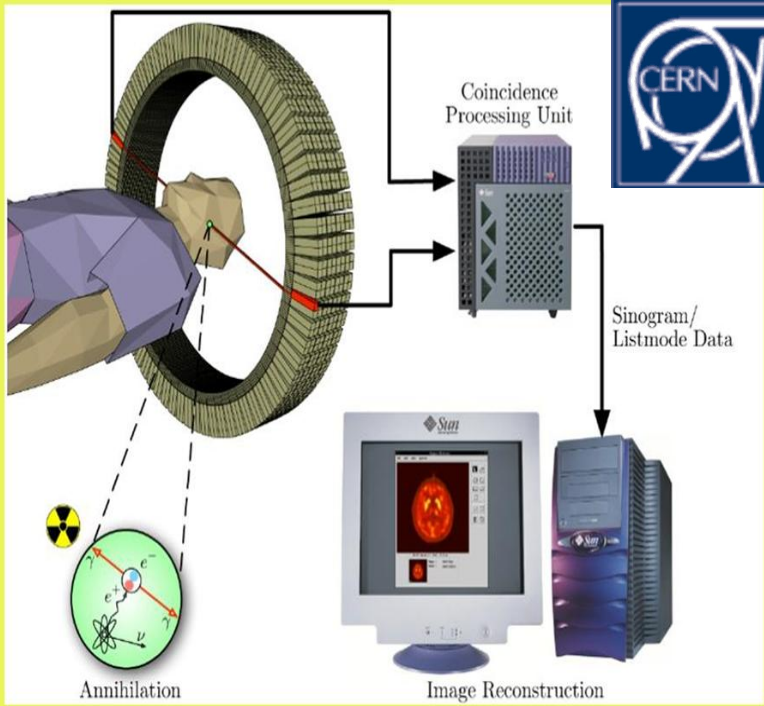




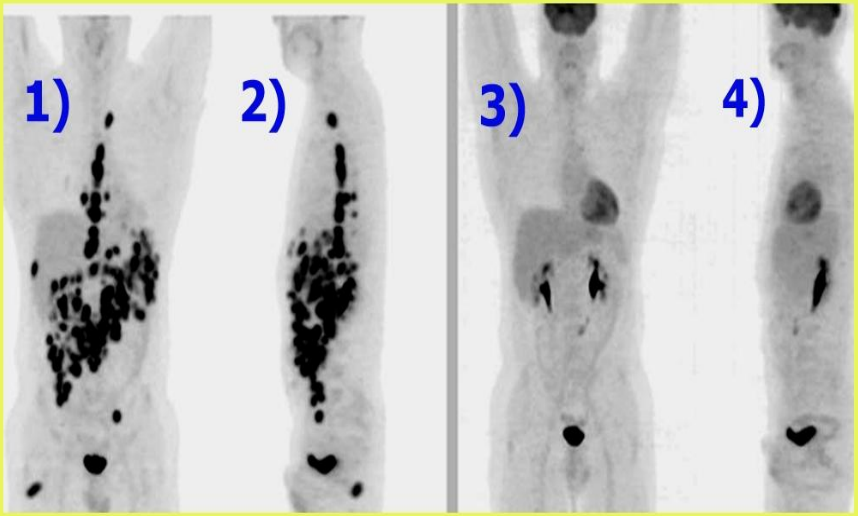
The first PET were simply Gamma cameras, from which the collimators had been removed and coincidence added between opposed detectors. Thereafter, better optimised PET equipments were built. For the human PET, several rings of detectors (crystals and PM) are assembled together.



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 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-PO_4 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!

VEAMTU, Y. LEMOIGNE, ESI-Archamps

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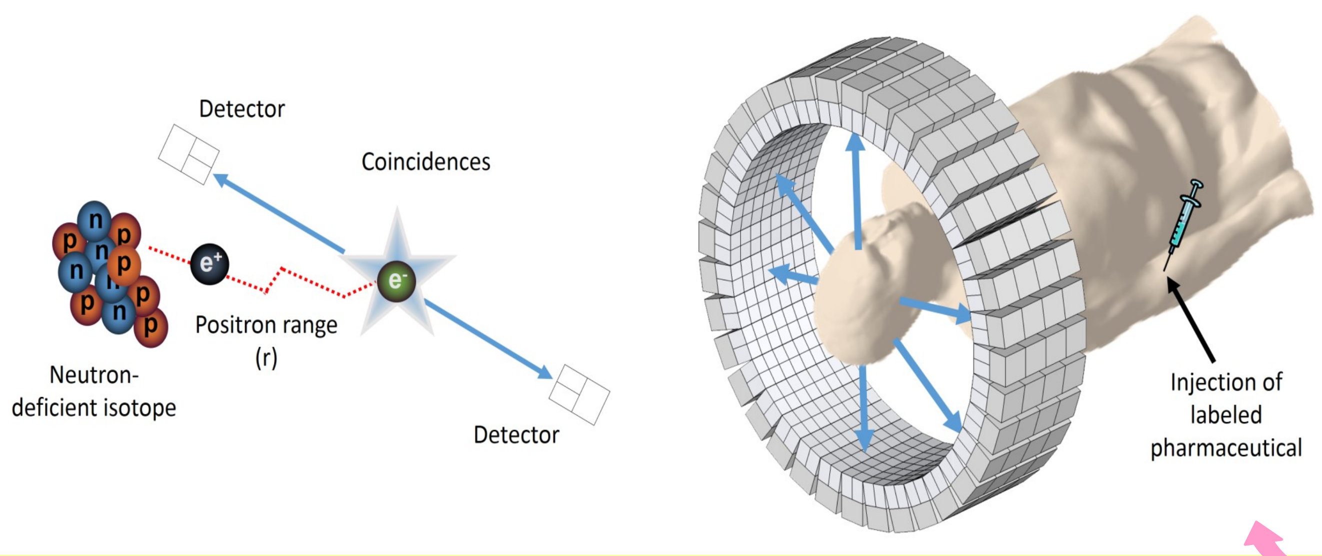
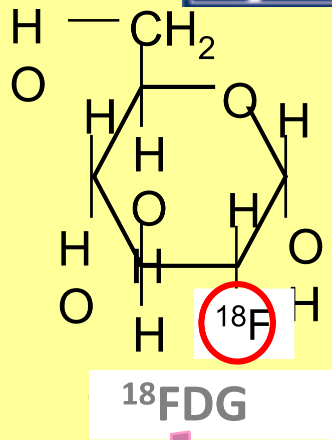
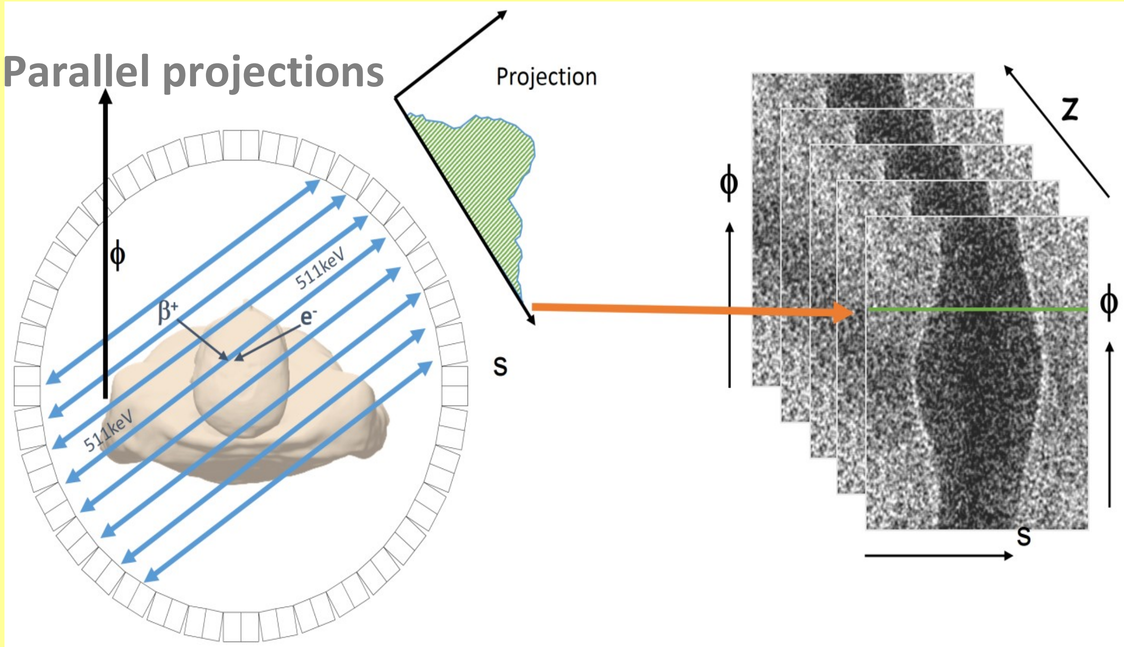
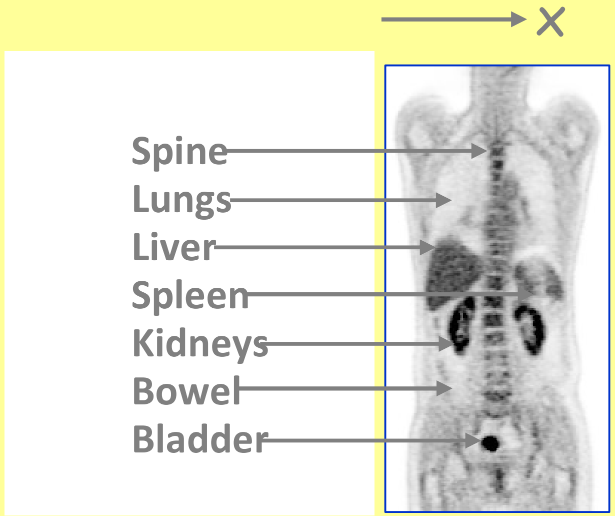
Positron Emission Tomography: how it works
SUMMARY









From D. Townsend 2014

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

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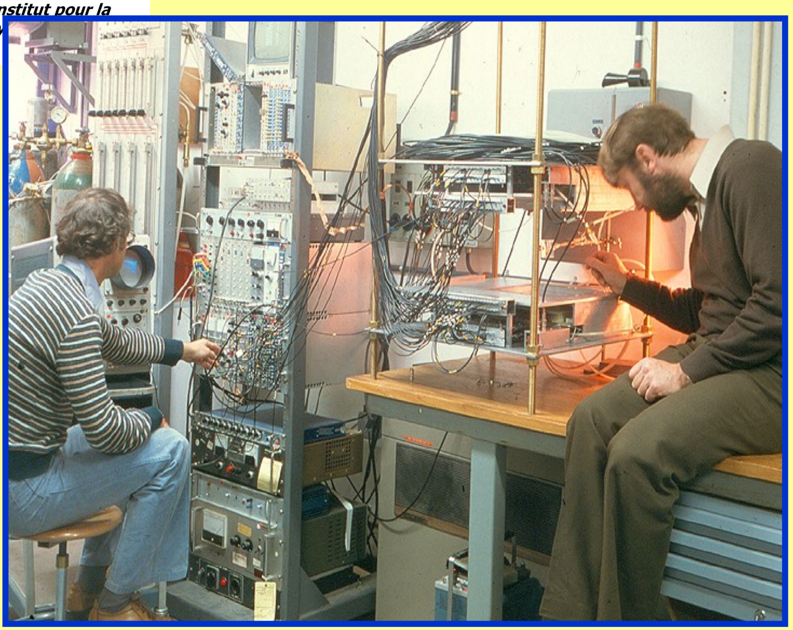
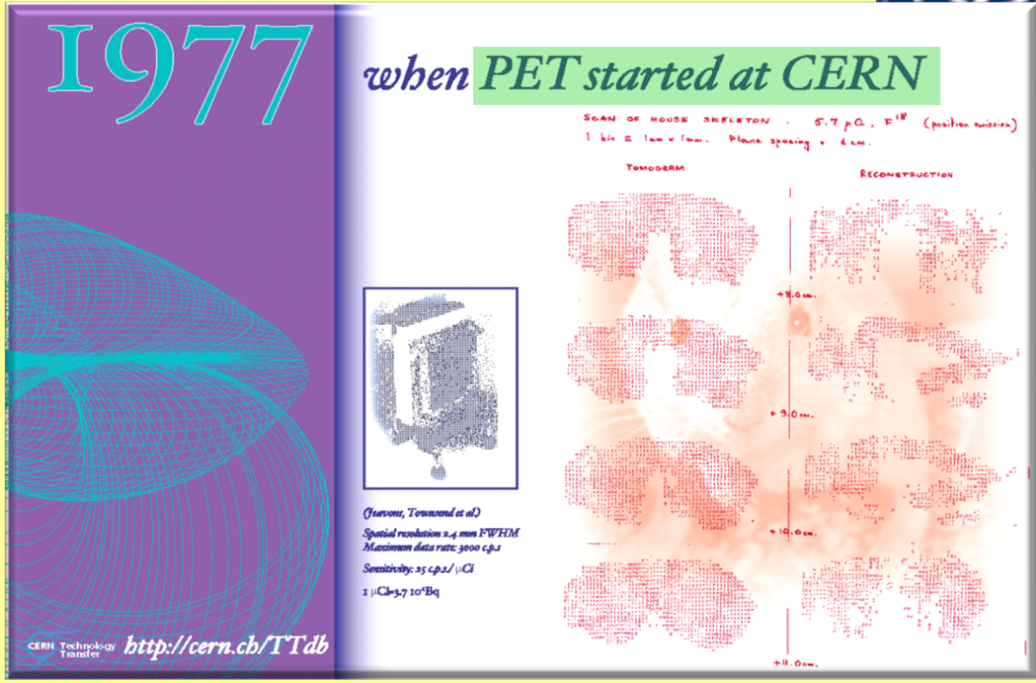
Phy…

From D. Townsend 2014

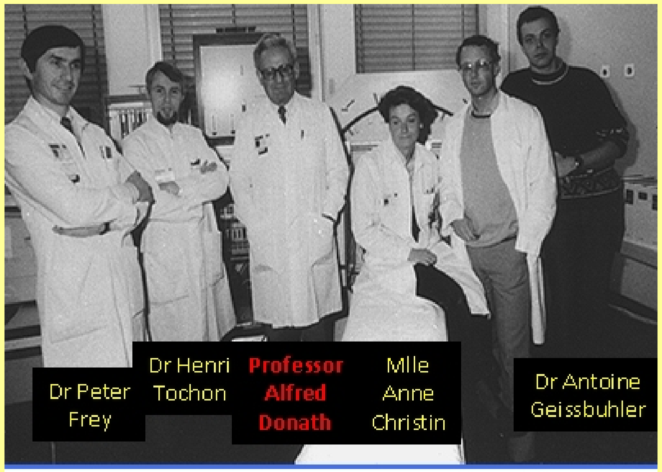




First mouse imaged at CERN with Na-^{18}F in 1978

1978 at CERN

Team & HIDAC PET Camera at HCUGE



Tribune de Genève, January 1988

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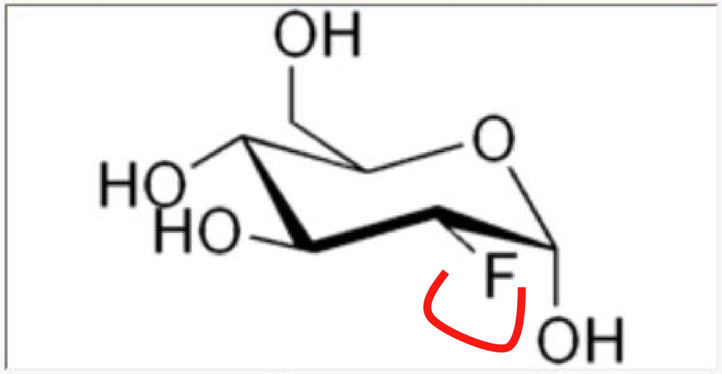
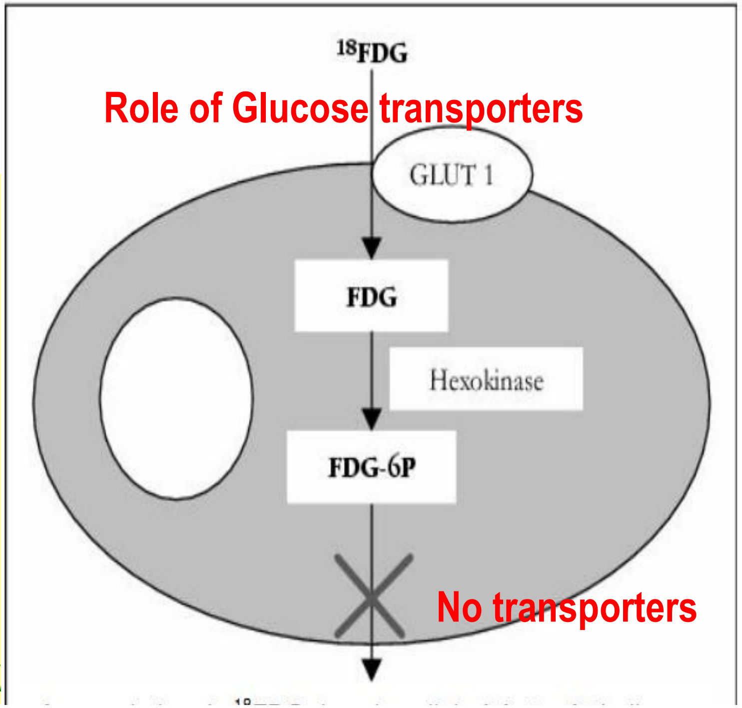
Why FDG Works So well?

$C_6H_{11}FO_5$

Fluorodeoxyglucose is a glucose analog. Its full chemical name is **2-fluoro-2-deoxy-D-glucose**, commonly abbreviated to FDG.

FDG is most commonly used in the medical imaging modality positron emission tomography (PET): the fluorine in the FDG molecule is chosen to be the positron-emitting radioactive isotope fluorine-18, to produce ^{18}F-FDG. After FDG is injected into a patient, a PET scanner can form images of the distribution of FDG around the body. The images can be assessed by a nuclear medicine physician or radiologist to provide

Fluorodeoxyglucose	
	
Chemical name	2-Deoxy-2-fluoro-D-glucose
Other names	2-Fluoro-2-deoxy-D-glucose FDG



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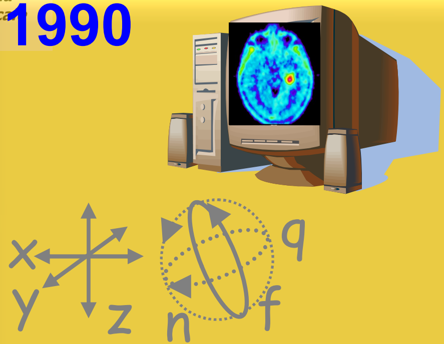
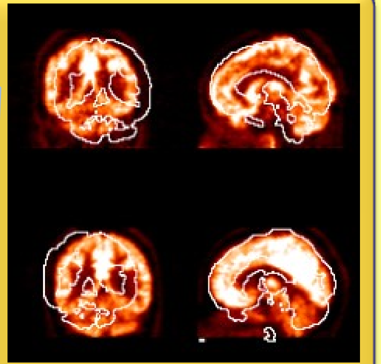
Fusion imaging: from software to hardware

(from D. Townsend 2014)

1990





Software-based fusion (semi-automated)

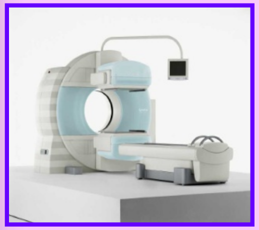
1993 - 1998

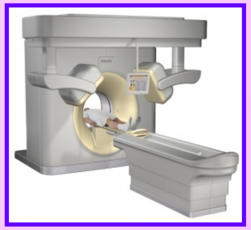
Hardware-adjunction: Prototype designs

2001

Hardware-adjunction: Commercial PET/CT

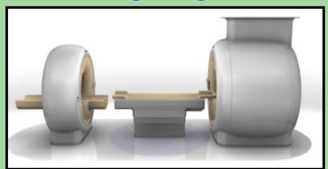
2004

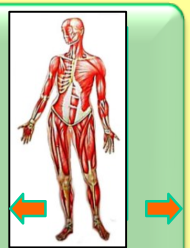




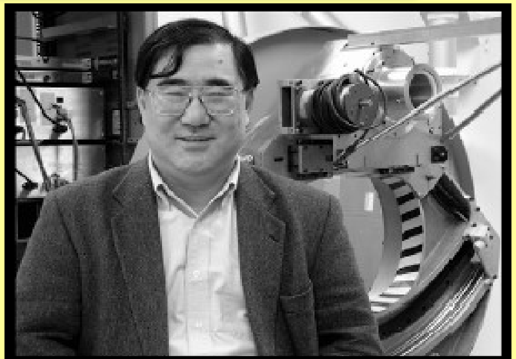
Hardware-adjunction: Commercial SPECT/CT

2010





Hardware-based fusion: Commercial PET/MR



Bruce H Hasegawa, PhD, 1951-2008
Participant ESI, Archamps In 1997

Why Imaging (SPECT, PET..)

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….

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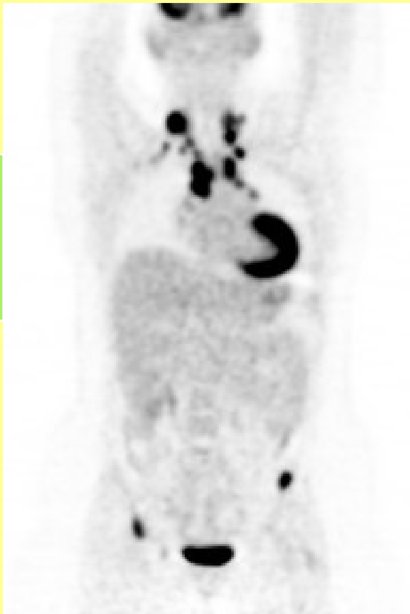
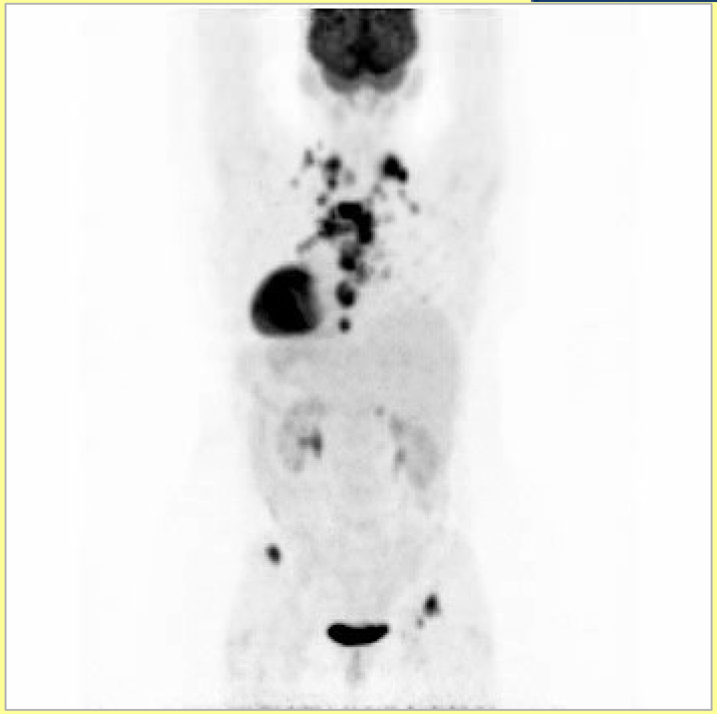
disease progression SURVEY(ex: Breast cancer)

CERN

*

Two imagings at a 9 months interval :





28 min (8/05)

10.6 mCi, 115 min pi
4 min/bed, 7 beds
3i / 8s; 6f

15 min 9 months later (5/06)

10.5 mCi, 104 min pi
3 min/bed, 5 beds
3i / 8s; 6f

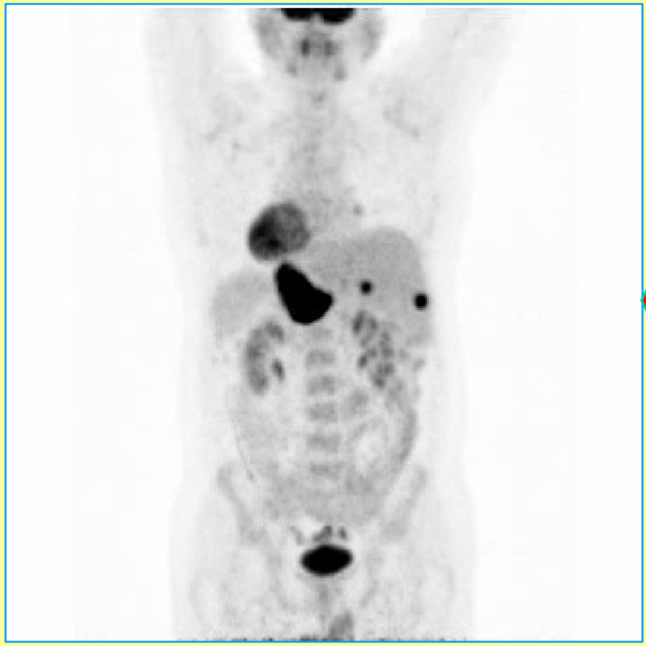
Scan duration: 15 min

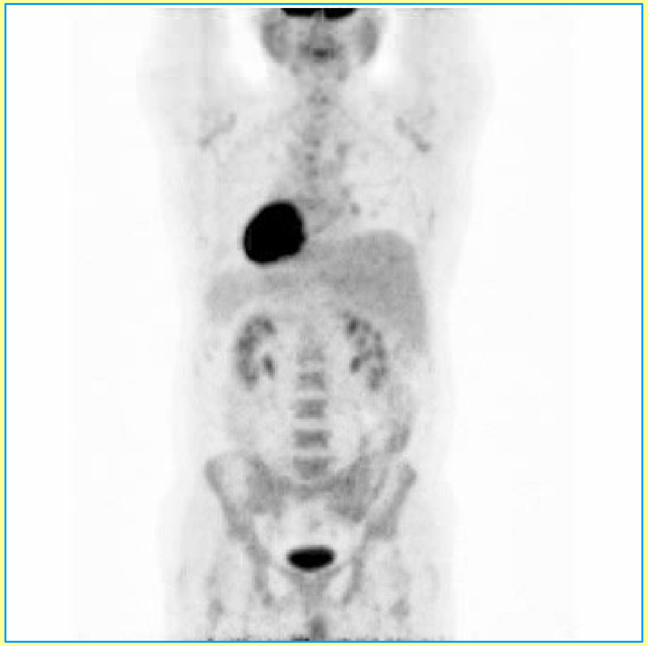
Biograph

48 year-old female (200 lbs) with history of breast cancer. First PET showed intense uptake in bilateral supraclavicular, mediastinal and right parasternal nodes and the thyroid. 9 months later PET showed significant disease progression including sternum and pelvic region

½ year Post / Pre treatment Survey

Restaging gastric cancer





Pre-therapy

Post-therapy

Pre-therapy (4/06)

With Biograph

Post-therapy (10/06)

6 months later

Pre-therapy	Post-therapy
Scan duration: 15 min	Scan duration: 15 min
5 beds; 3 min/bed; 8s/3i/6F	5 beds; 3 min/bed; 8s/3i/6F
10.6 mCi; 90 min post-injection	9.8 mCi; 90 min post-injection

A 52 year-old male patient with history of gastric cancer imaged pre- and post-therapy (after ½ year)

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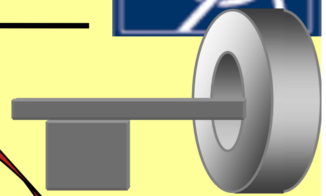
TREATMENT PLANNINGS

(Will be explained later by Alex Rijnders)

Treatment plannings are compulsory for correct treatment

The Software start from Images



CT-SCAN ↔ MRI or / and PET

- external contours
- densities
- anatomical structures
- beam data library

- anatomical structures

BEAM DEFINITION

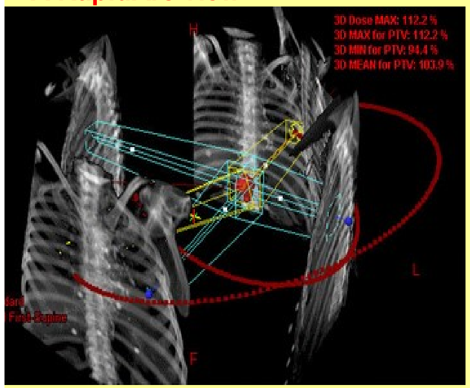
TREATMENT PLANNING SYSTEM

OPTIMISATION

Most Popular systems:

Pinnacle (Philips Medical systems)
ADAC -> Pinnacle3(Philips)
Monaco (CMS/Elekta)
Eclipse (Varian Medical Systems)
RapidArc: see(varian.com/us/oncology/treatments/treatment_techniques/rapidarc/resources.html
…..

A RapidArc view



- Reconstructed radiographs (DRR)

SIMULATOR and/or ELECTRONIC PORTAL IMAGING

- Field shape
or
- Position of leaves

BLOCK CUTTING DEVICE or MLC

- Dose distribution
- Dose-Volume Histograms
- Biological indices

- Treatment parameters
- Treatment time (monitor units)

ACCELERATOR

VERIFIY AND RECORD SYSTEM

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6. QUANTIFICATION

(SPECT & PET)

Definition of SUV (Standardized Uptake Value):

Coeficient used in Oncology for semiquantitative analysis

The percent injected dose per gram of tissue:

$$SUV = CT.Ws / d_T.Dinj$$

Where: C_T (in mCi/cc) is obtained from counts/pixel/time from PET ROI.

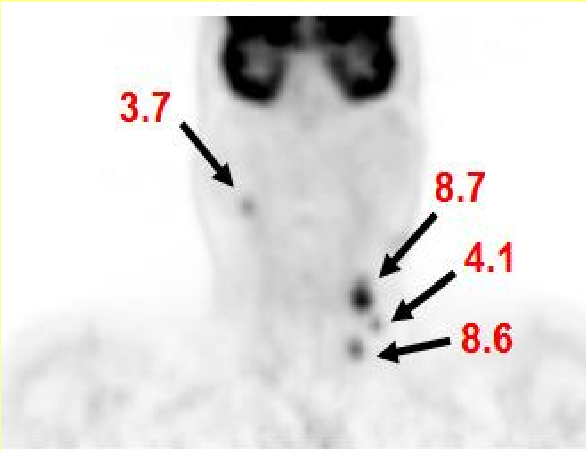
$d_T=W_T/V_T$ (weigth to volume of studied tissue) is the density in the region (often 1 g/cc)

D_{inj} being the injected dose

Ws is the total weight of the patient)

SUV=unitless parameter (from 1 to about 10)

Example of SUV



11.2 mCi; 90 min uptake

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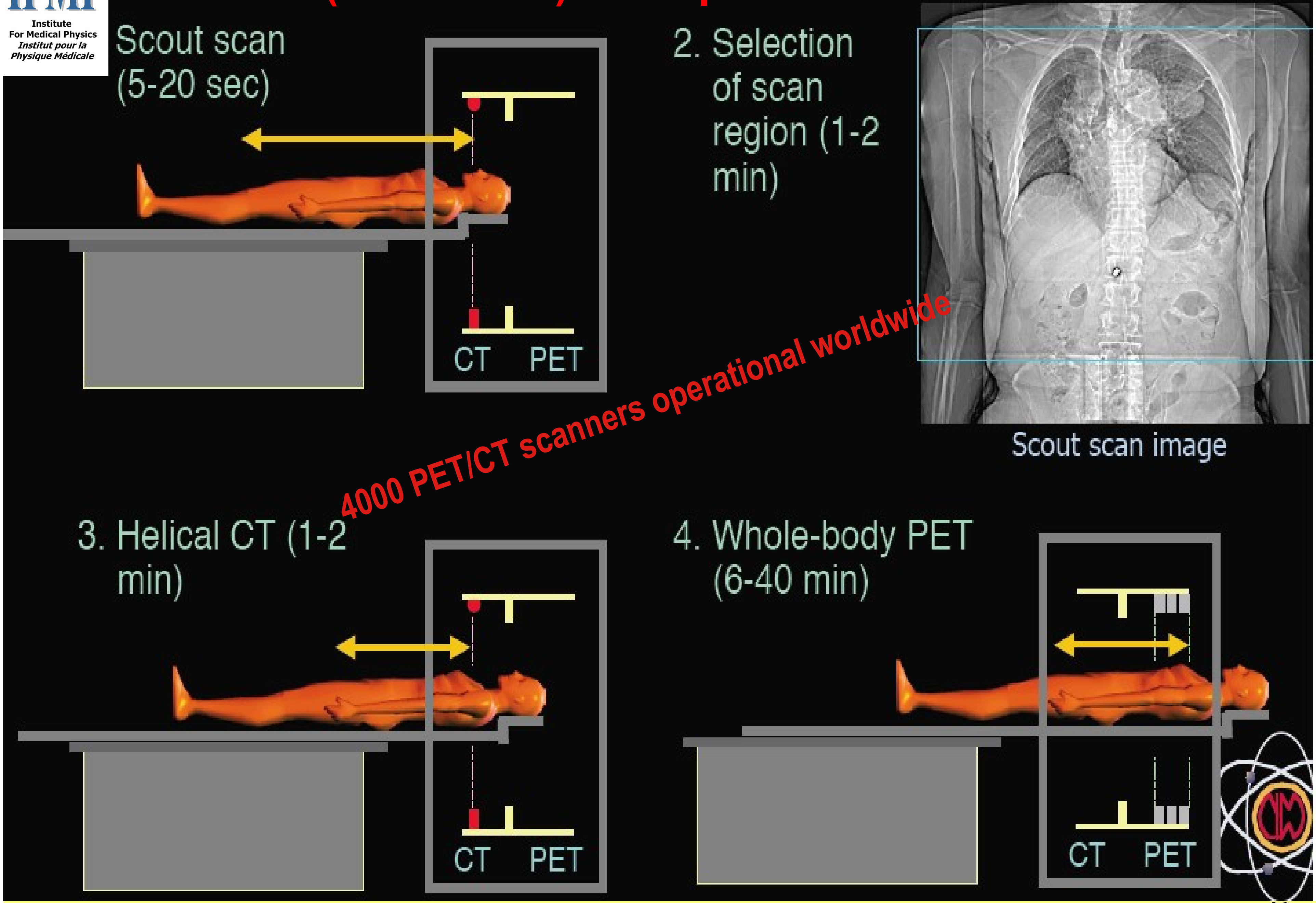
7. EXAMPLES OF USES @ HOSPITAL

PET/CT (SPECT/CT) Scan protocol



SURVEY : Vaginal cancer

PET-CT is more powerful than PET alone….

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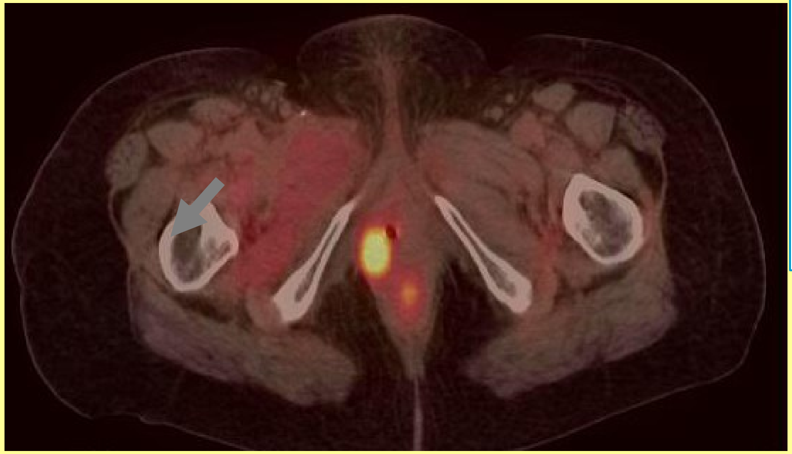
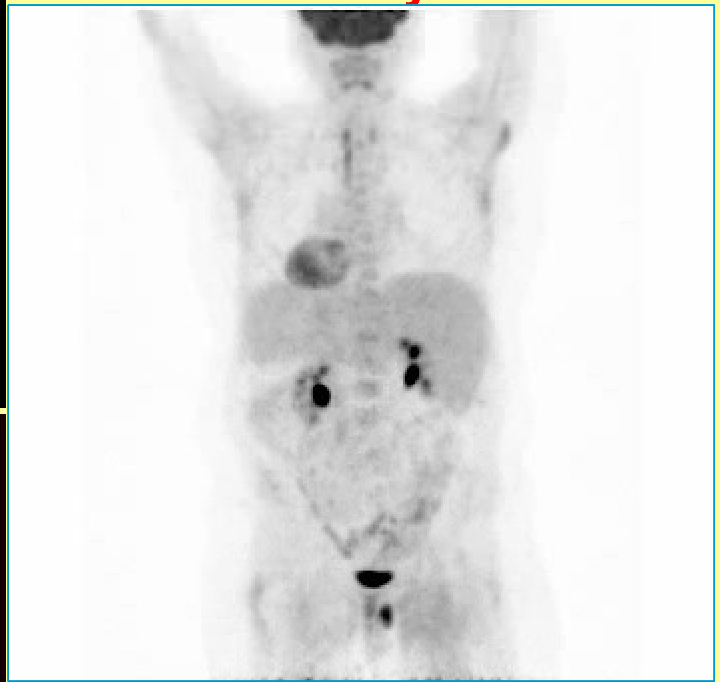
CT only

PET+CT



*** PET only**



Biograph Scan duration: 15 min

5 beds; 3 min/bed; 8s/3i/6F

10.6 mCi; 90 min post-injection

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!

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8. IMPROVEMENTS

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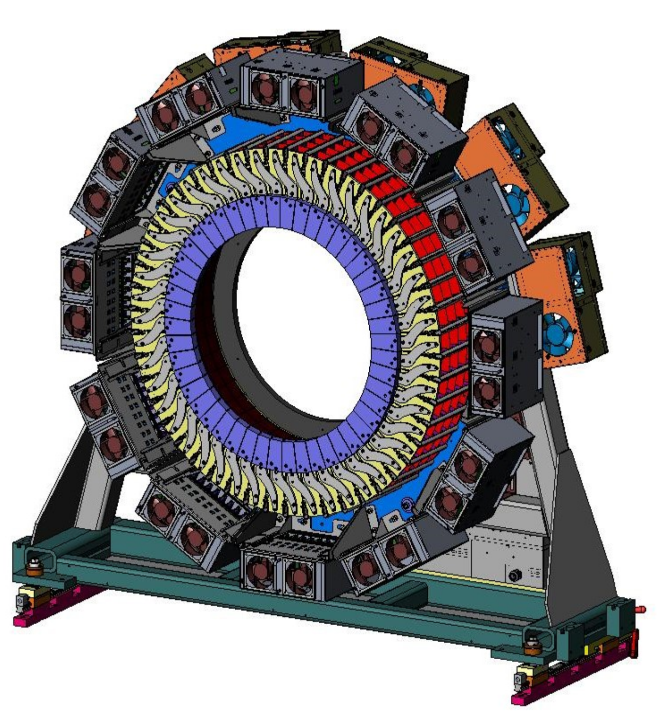
Last years Improvements in PET cameras

- **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**



Ex: Biograph TruePoint PET•CT (Biograph TP)

Time-of-Flight (TOF)

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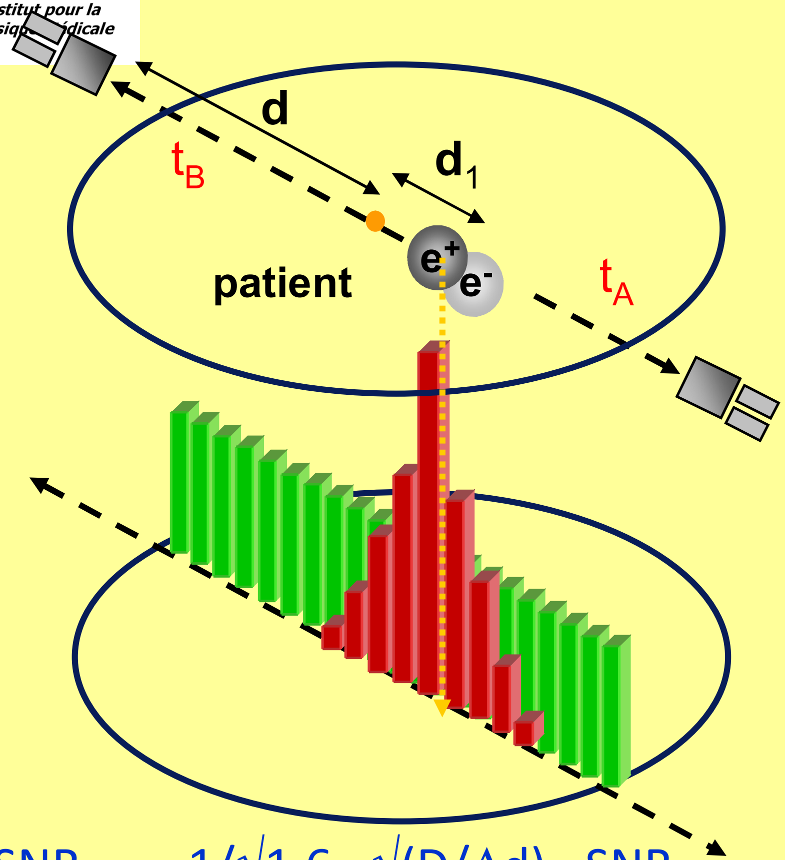
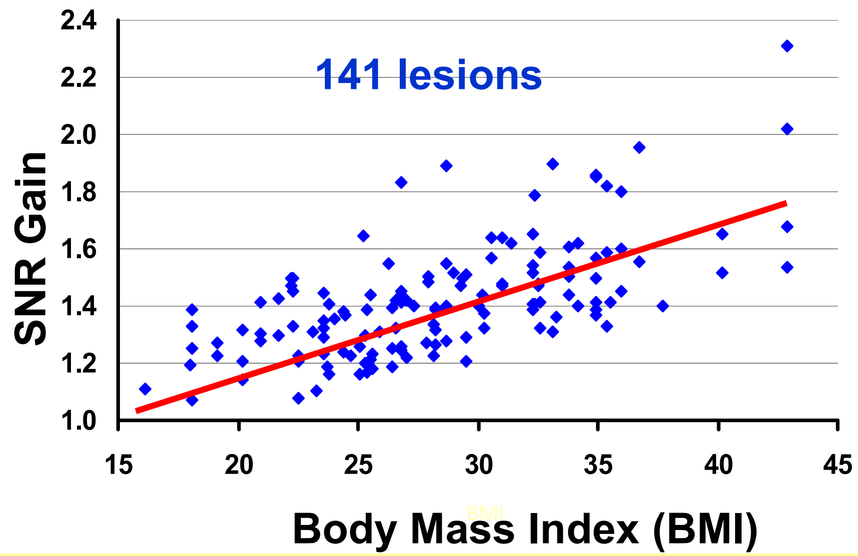
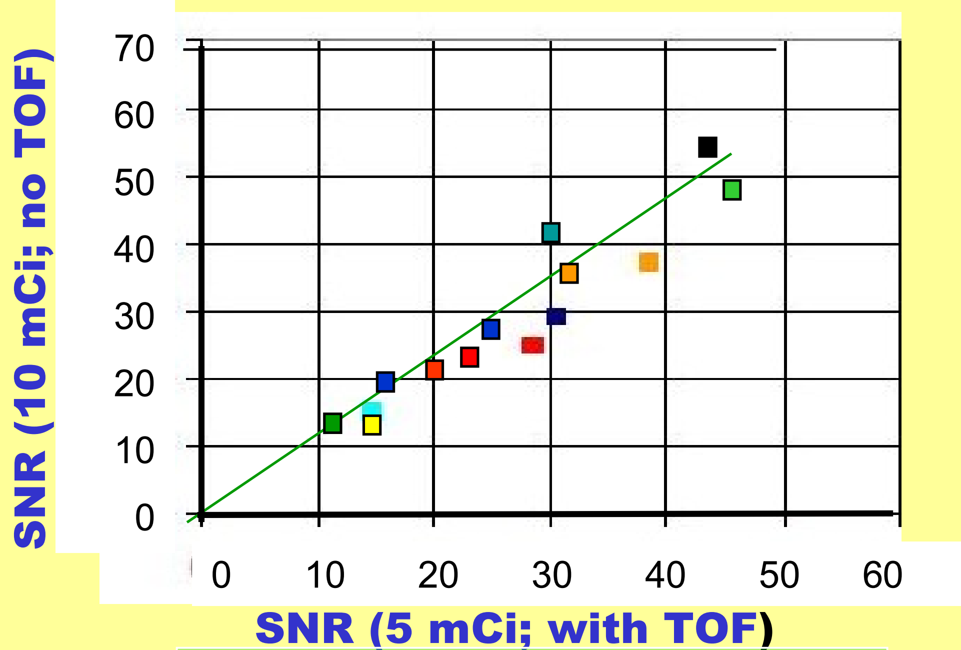


$$SNR_{TOF} = 1/\sqrt{1.6} \cdot \sqrt{(D/\Delta d)} \cdot SNR_{conv}$$

Ds (ps)	Dx (cm)	SNR gain
100	1.5	5.2
300	4.5	3.0
500	7.5	2.3
1200	18.0	1.5



✓ Improved signal-to-noise



✓ Reduced radiation dose

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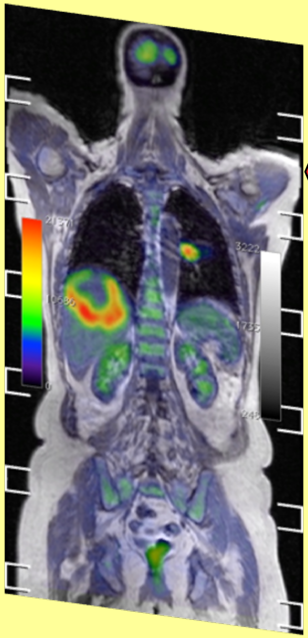
2010: PET/MR in the clinic

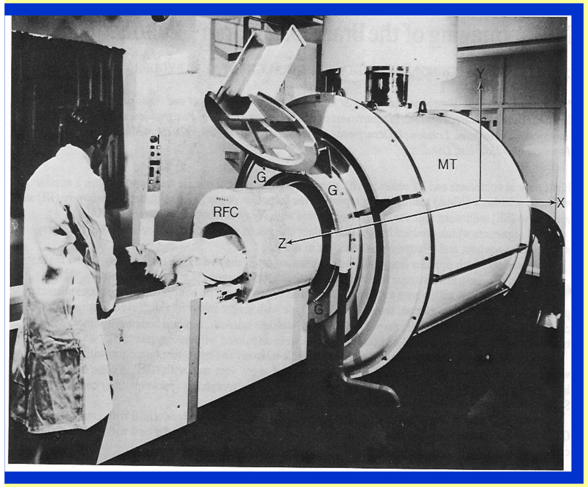


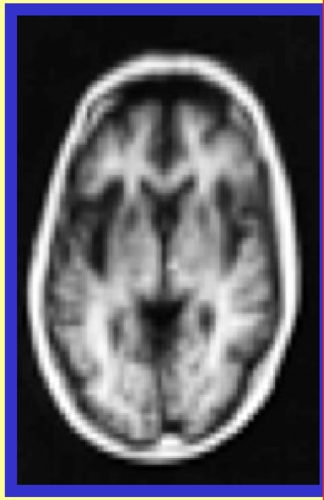
Over 30+ years of development

(1980)

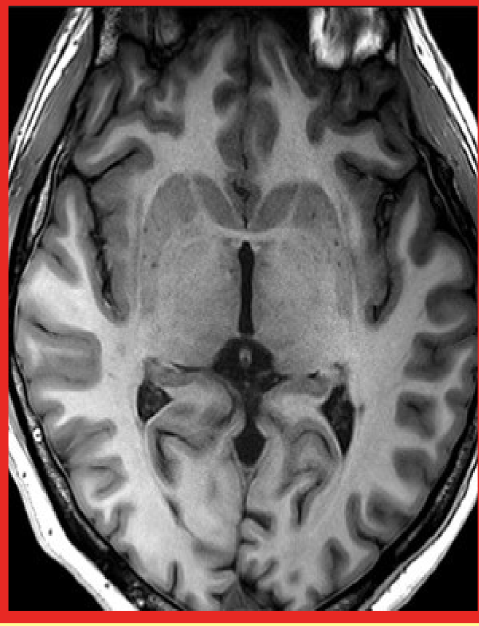
Image Quality

SIEMENS Skyra MRI scanner (2013)





First patient on Aberdeen MRI (1980)



Solid state photodetectors for integrated PET/MR

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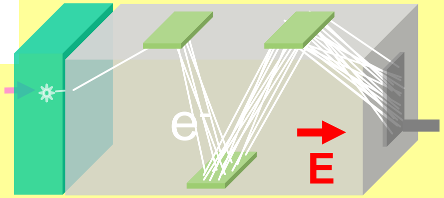
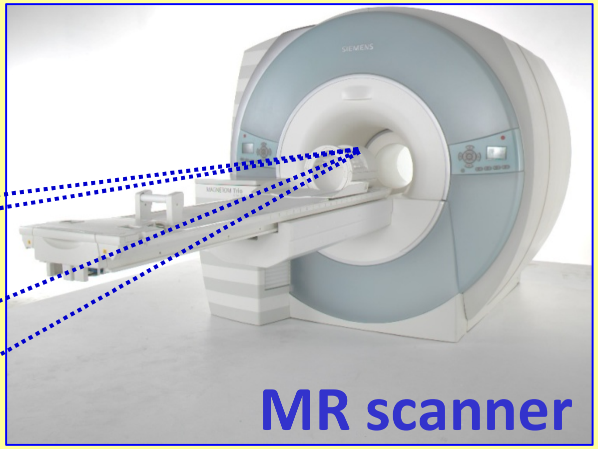
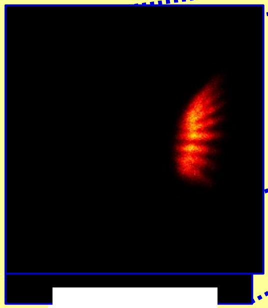
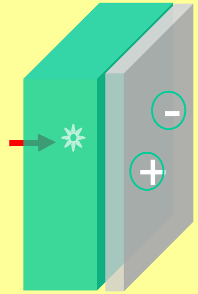


Block detector

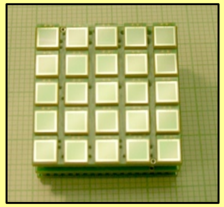




B = 1.5 T



APD-based PET detector



SiPM-based PET detector

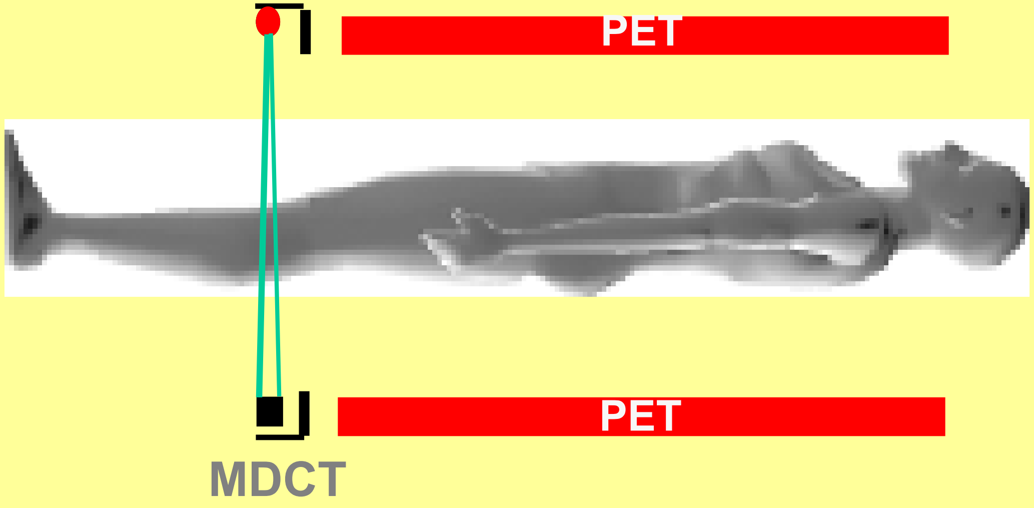
Photodetectors

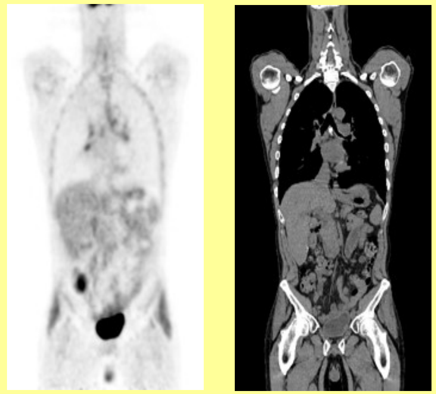
	PMT	APD	SiPM	dSiPM
MR compatible	No	Yes	Yes	Yes
TOF capability	Yes	No	Yes	Yes
Stability	Good	Good	Unknown	Unknown
Amplification	High (10^6)	Low (10^3)	High (10^6)	N/A
Compactness	Bulky	Compact	Compact	Very compact
Power Readout	HV, ASIC Analog	HV, ASIC Analog	LV, ASIC Analog	LV, simple Digital

PHILIPS VEREOS PET/CT

Combined whole-body PET/CT to PET/MR..

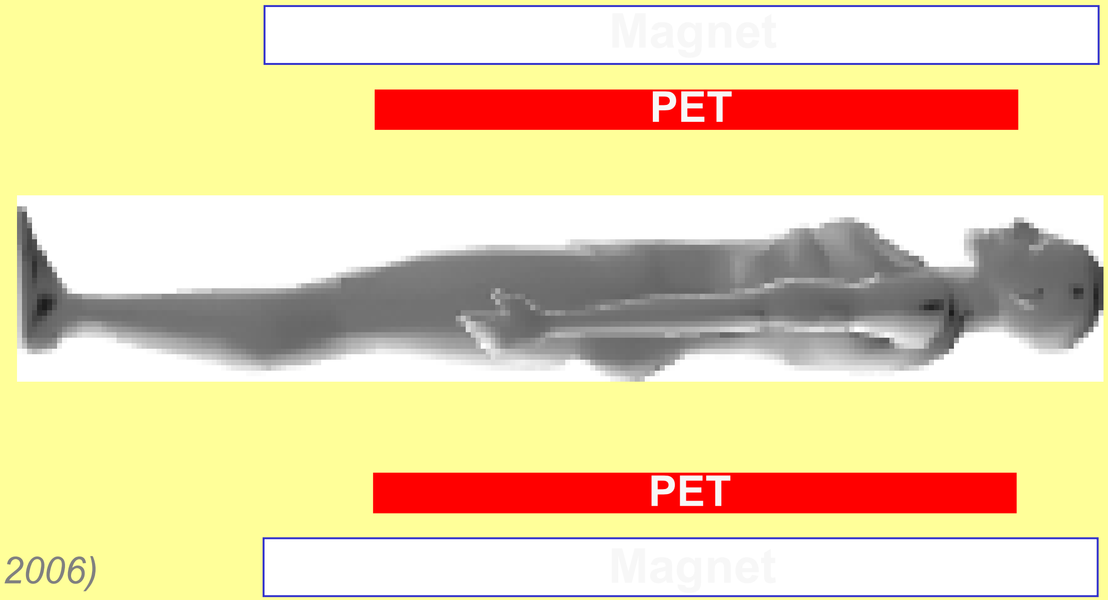
PET/CT

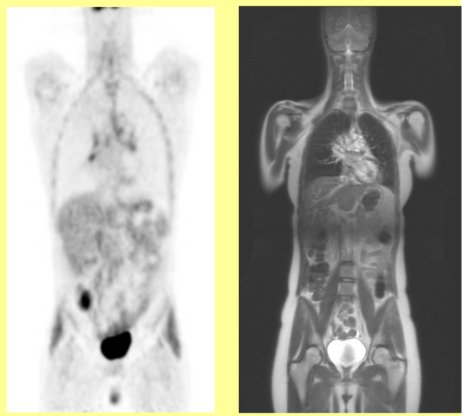




PET *CT*

PET/MR





PET *MR*

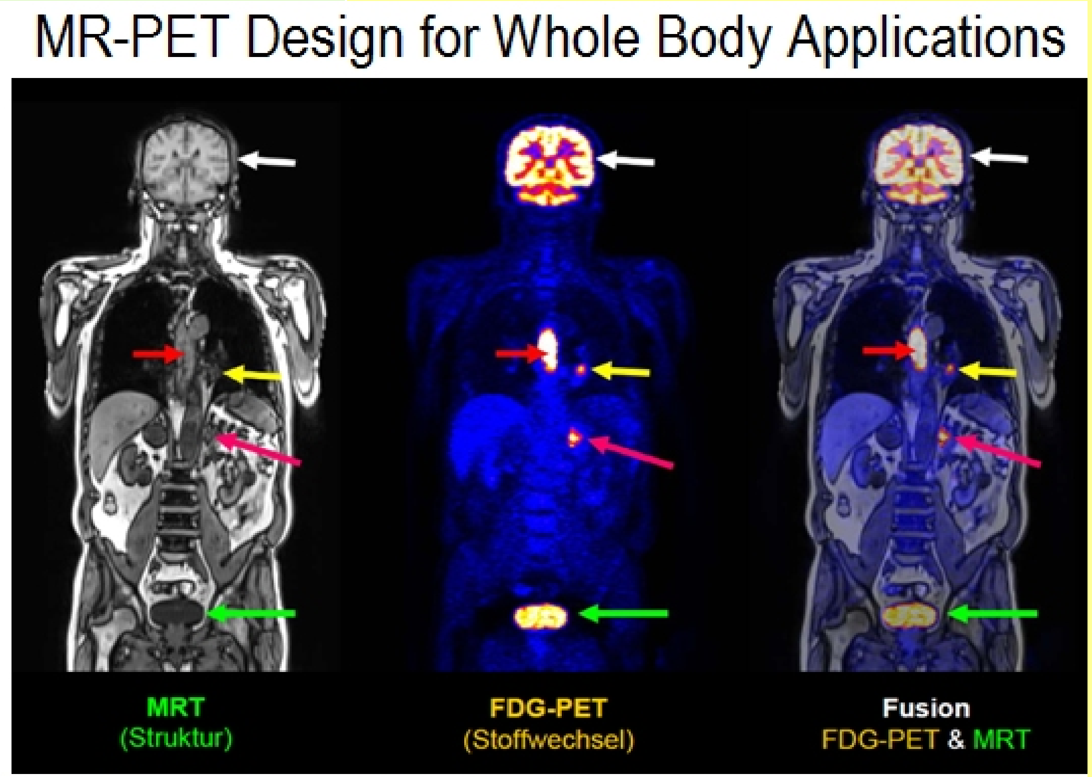
(S.R. Cherry, 2006)

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 then for patientd (L. Bidaut)

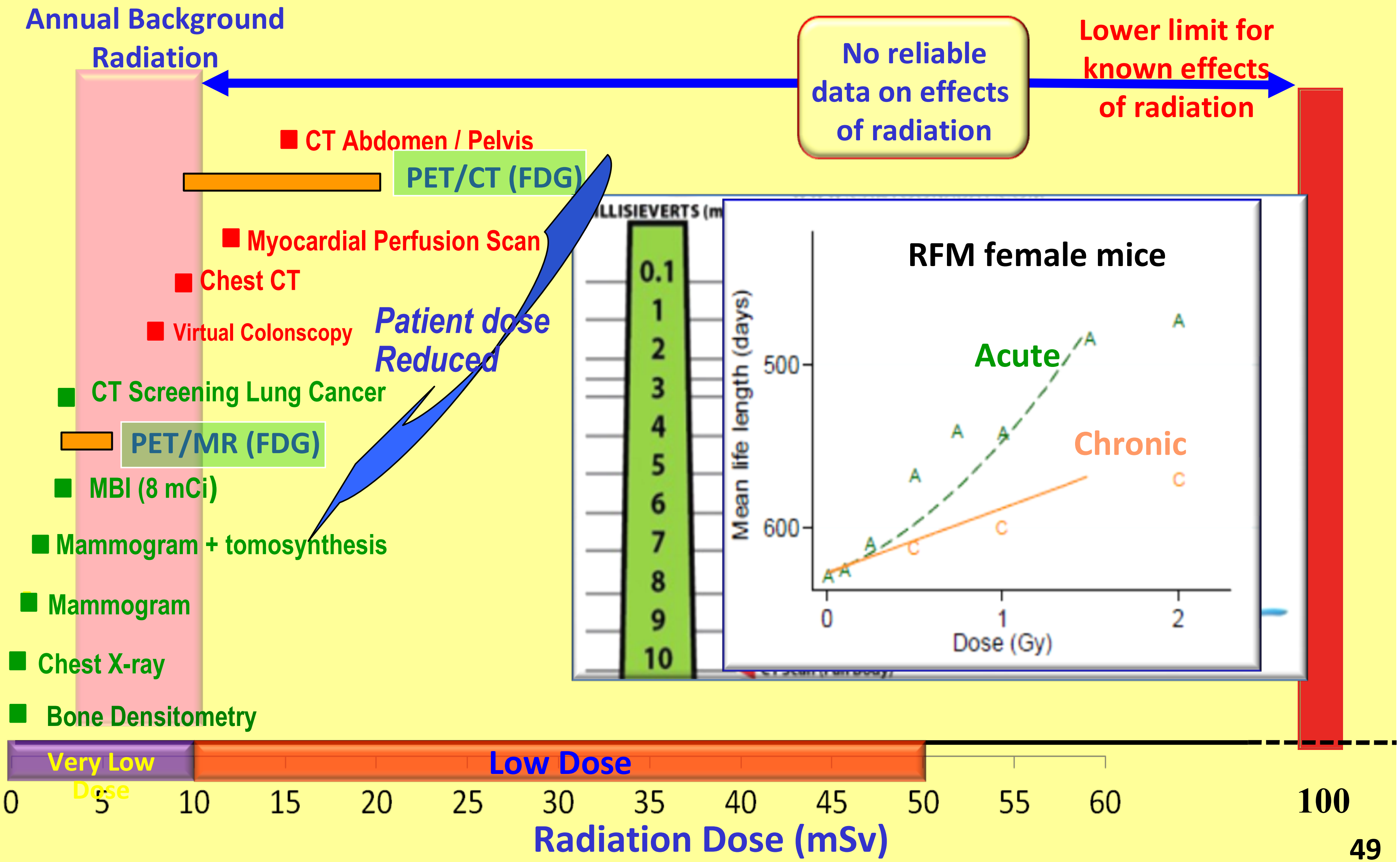
But already exceptionnal images …

See Luc BIDAUT talks tomorrow…



Courtesy: Sibylle Ziegler, TU Munich, Fall 2010)

As conclusion:
Radiation doses for clinical imaging procedures



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

All that is for the main benefit of patients….

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CERN

Thanks a lot for the gentle attention!

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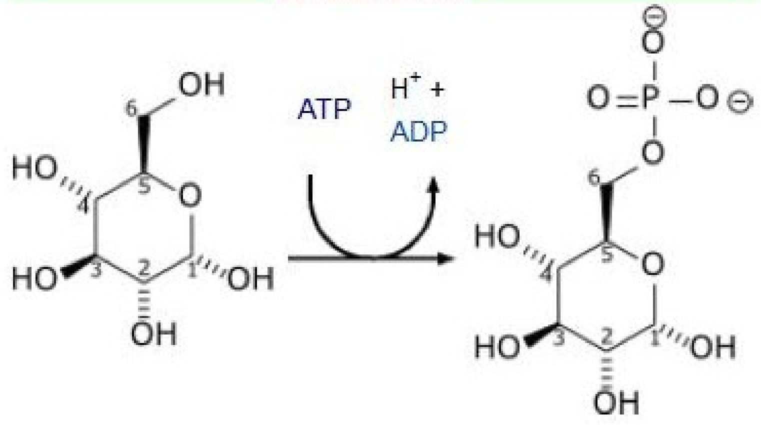
The first step in glycolysis is phosphorylation of glucose by a family of enzymes called hexokinases to form glucose 6-phosphate (G6P). This reaction consumes ATP, but it acts to keep the glucose concentration low, promoting continuous transport of glucose into the cell through the plasma membrane transporters. In addition, it blocks the glucose from leaking out - the cell lacks transporters for G6P, and free diffusion out of the cell is prevented due to the charged nature of G6P.

D-Glucose (**Glc**)	Hexokinase (**HK**) *a transferase*	α-D-Glucose-6-phosphate (**G6P**)



Adenosine-5'-triphosphate (ATP) is a multifunctional nucleoside triphosphate used in cells. It is often called the "molecular unit of currency" of intracellular energy transfer. ATP transports chemical energy within cells for metabolism.

Idem if F^{18} added

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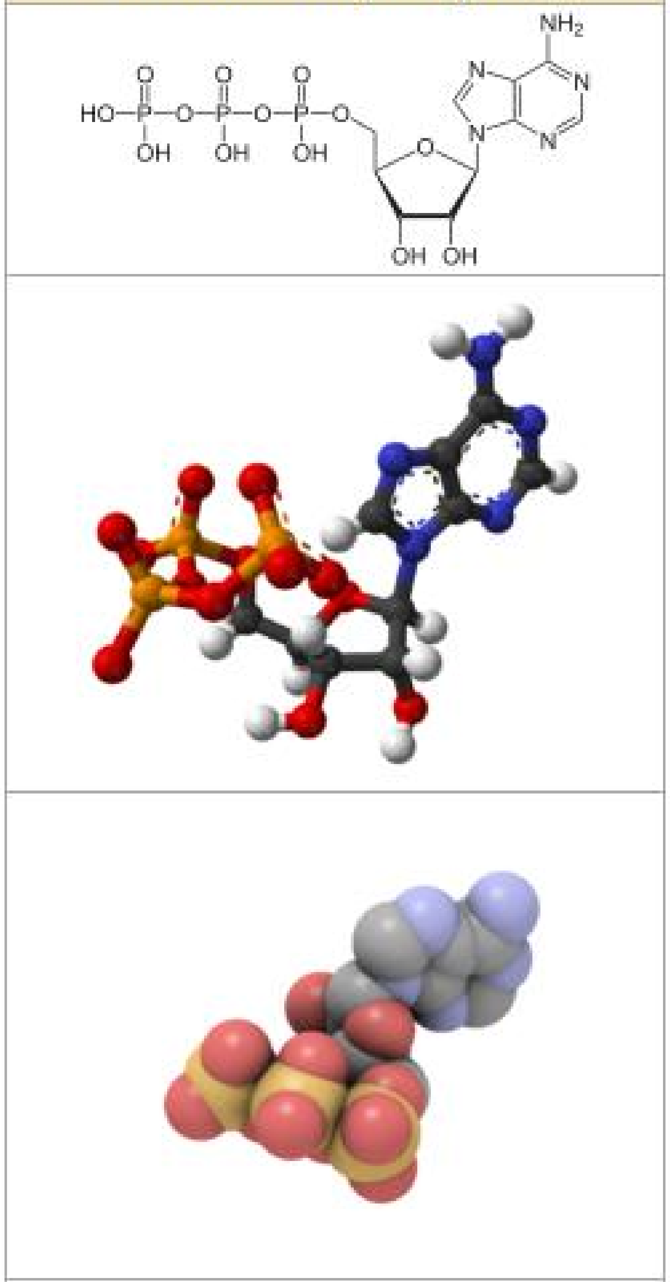
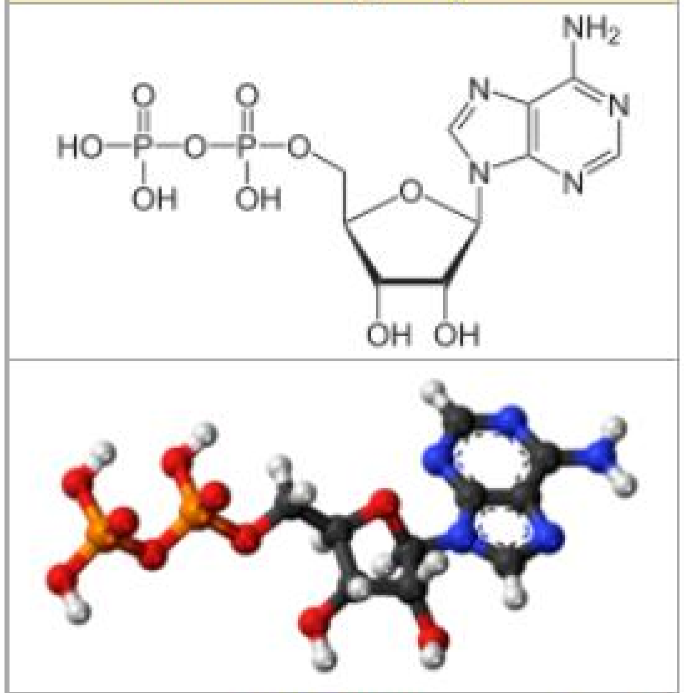
Adenosine triphosphate



Adenosine diphosphate



IUPAC name [hide]

adenosine 5'-(trihydrogen diphosphate)

Other names [hide]

adenosine 5'-diphosphate

Adenosine-5'-triphosphate (ATP) is a multifunctional nucleoside triphosphate used in cells. It is often called the "molecular unit of currency" of intracellular energy transfer. ATP transports chemical energy within cells for metabolism.

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Combining complementa

PET can be combined with other device:

- **X-ray-CT**
- **MRI**
- **SPECT**
- **Opt**
- **US**

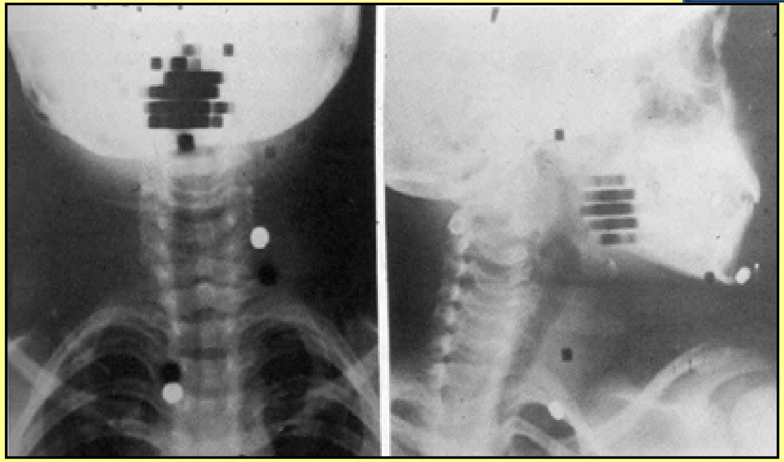
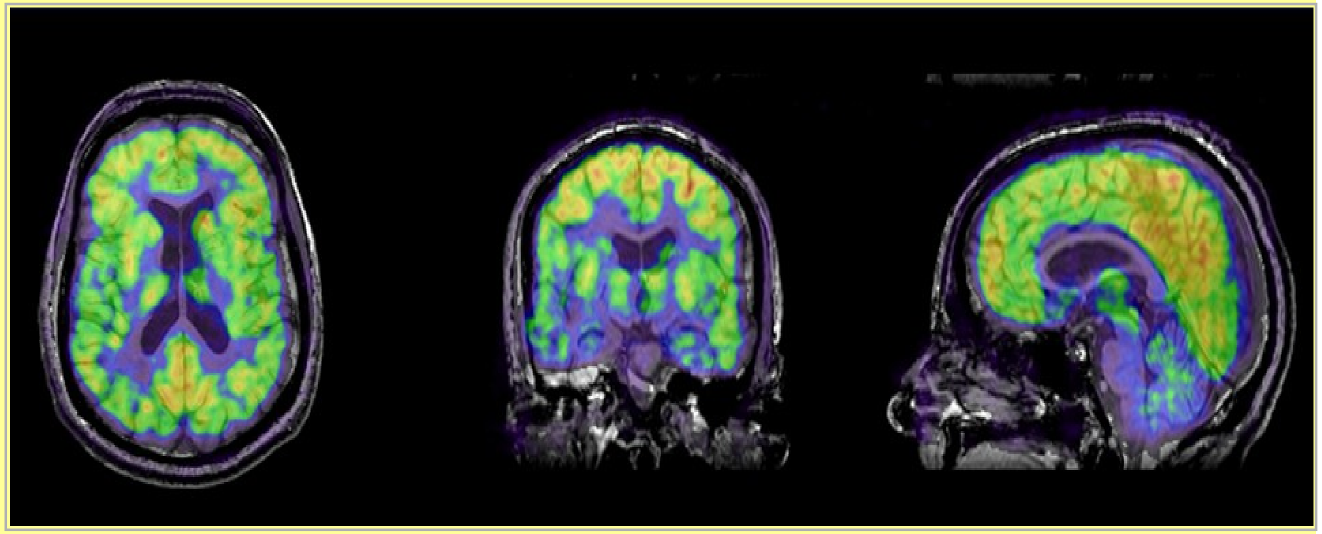


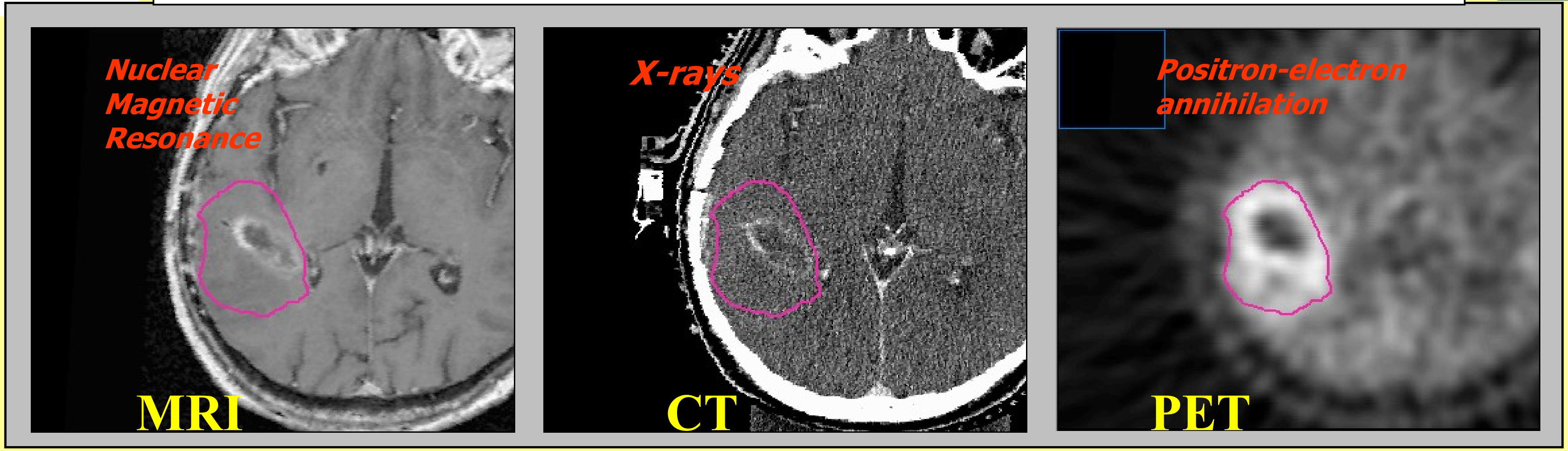
Image fusion in 1961 (*HN Wagner, MD)*

PET/CT now



PET/MRI Now

What about the imaging method for Tumor Volume definition ?

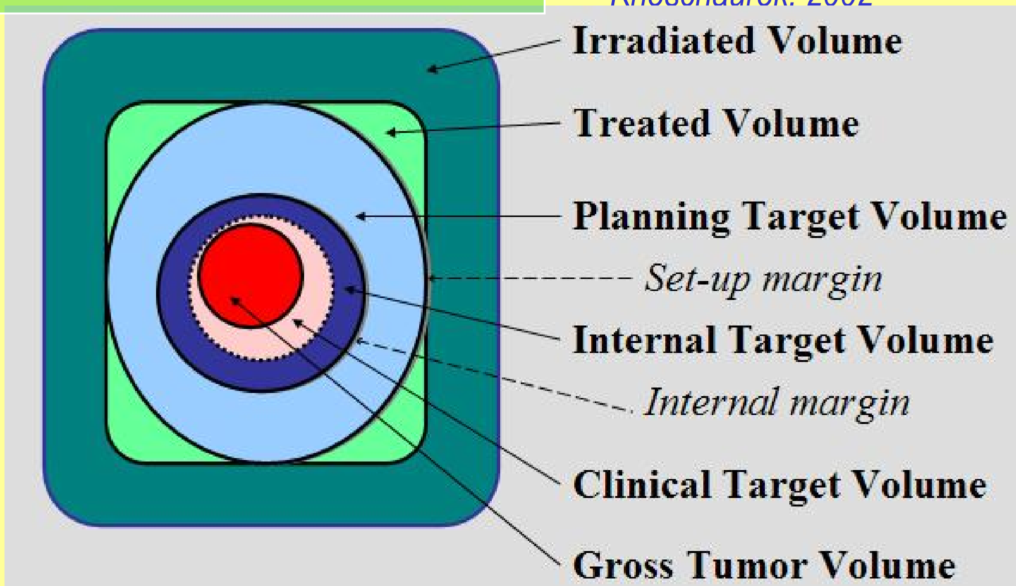


Only PET is giving the real size of the tumour

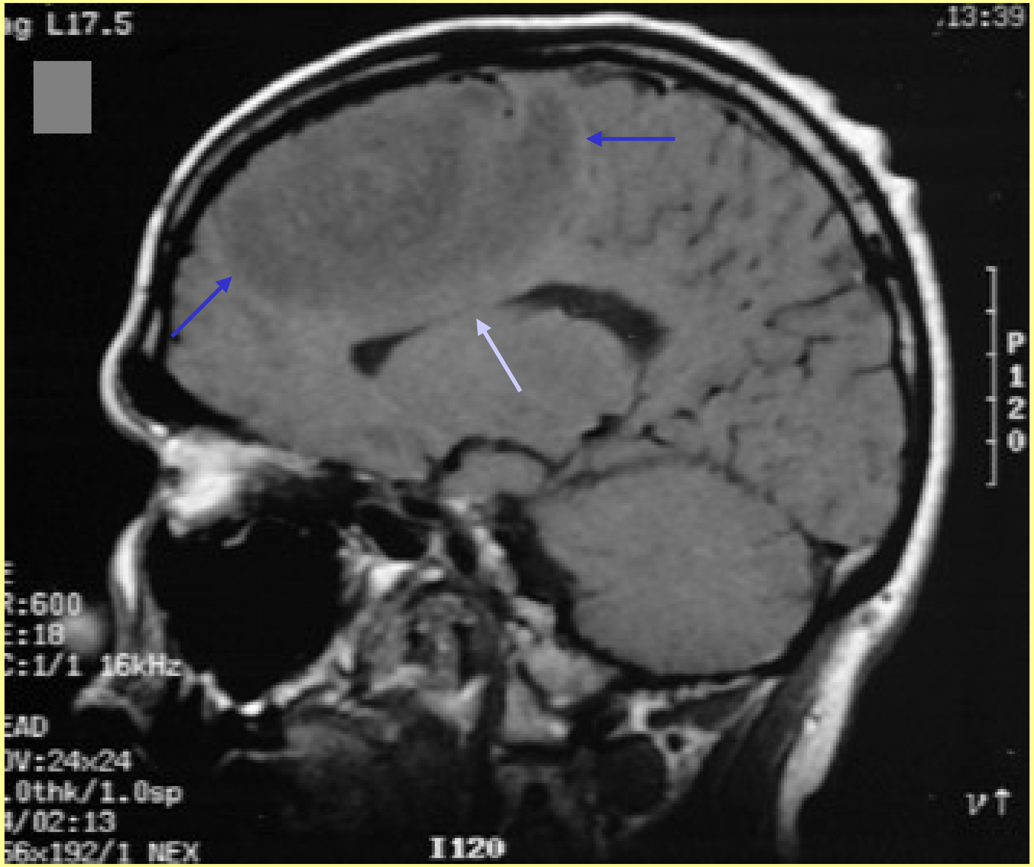
Kneschaurek. 2002

Recall
Summary Volumes and Margins
[ICRU-50 Supplement of rules definitions]

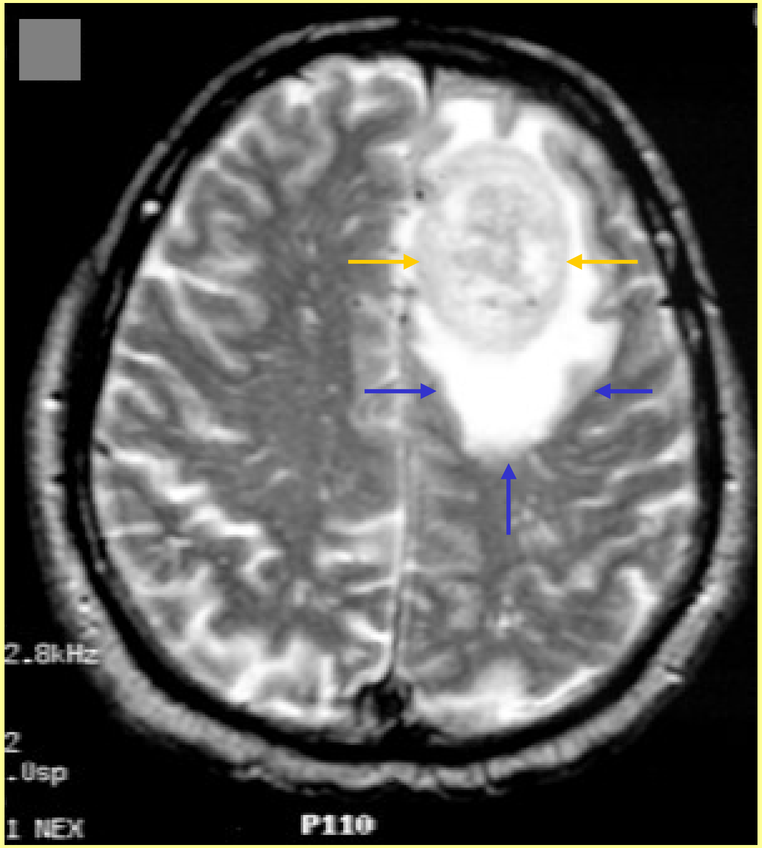
PTV ⇒
ITV ⇒
CTV ⇒
GTV ⇒



Glioblastoma Multiforme



T1-Weighted



T2-Weighted

TOF result example: Gemini TF

Courtesy Joel Karp PhD, University of Pennsylvania

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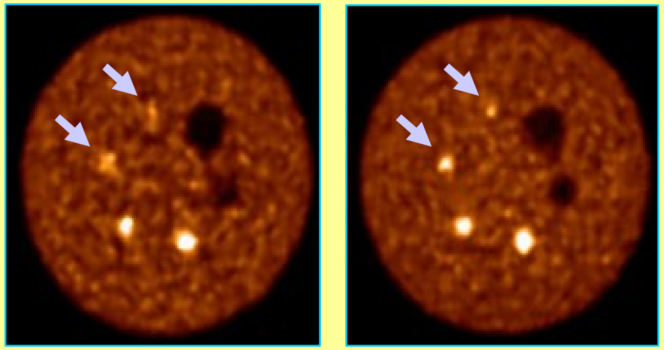
LYSO

4 x 4 x 22 mm^3 (LYSO)
3D only (no septa)
Brilliance 16 CT
70 cm port
18 cm axial FOV
585 ps timing

Mainly for large volume patients…



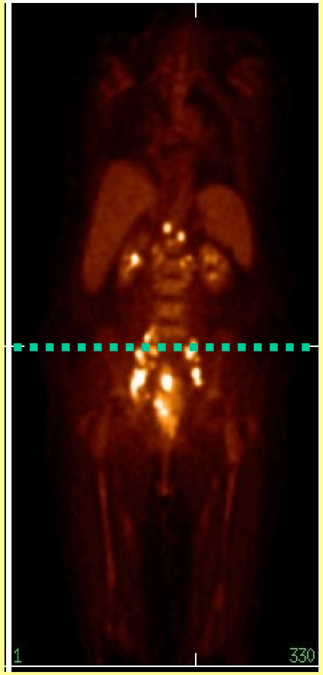
Non-TOF **TOF**

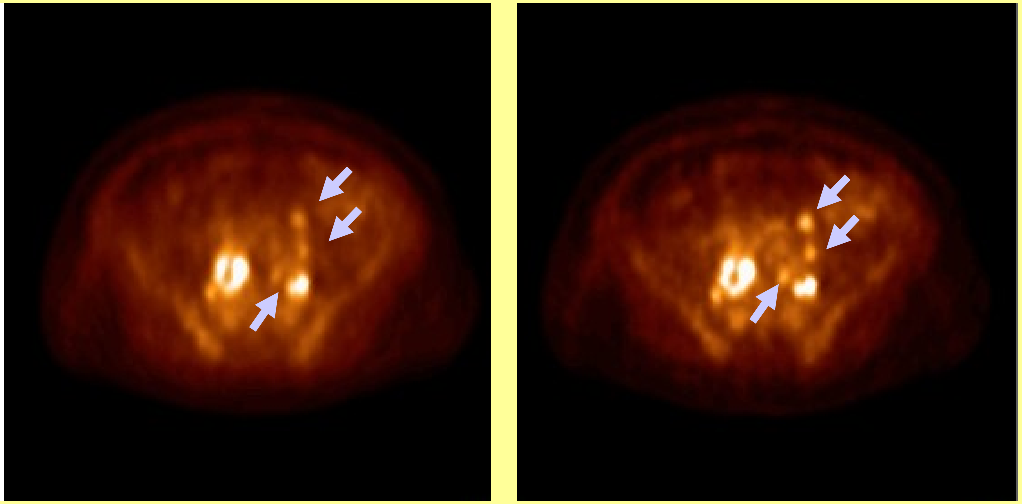
60 s scan duration

Better signifiance with TOF

Rectal carcinoma, with metastases located in the mesentery and bilateral iliac chains more clearly seen with TOF.

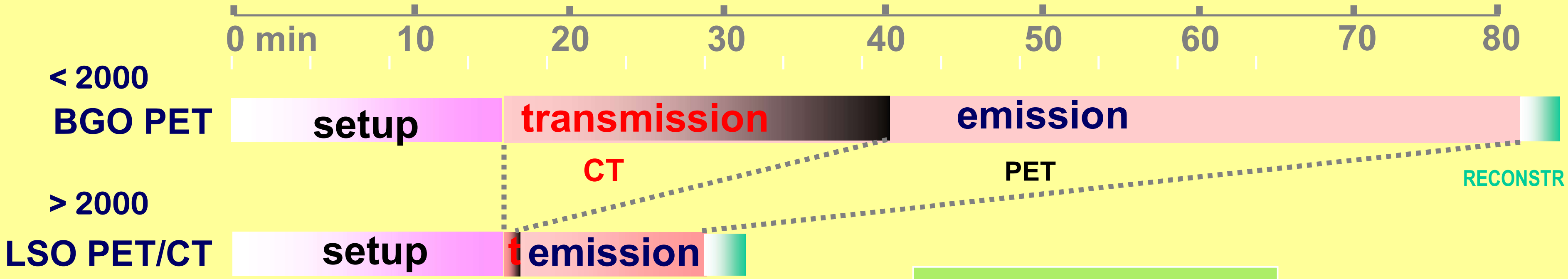
114 kg; BMI = 38.1
12 mCi; 2 hr pi
3min/bed position





Non-TOF **TOF**

Advances in clinical workflow



FASTER IMAGING

- injection of 10 mCi FDG
- wait 90 min uptake period
- acquire CT scan over range
- acquire PET scan (2-3 min/bed)
- images available within ~3 min

Setup and patient positioning

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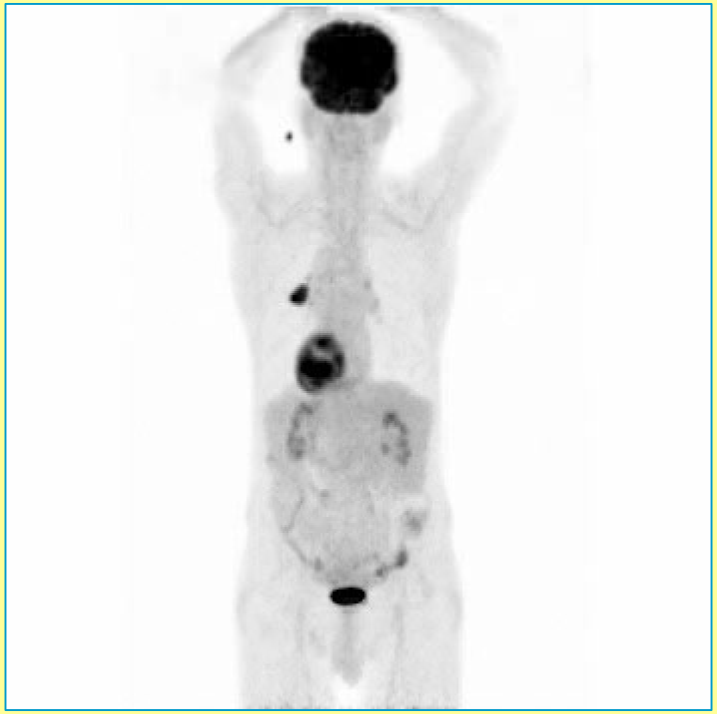
Decreasing scan duration: several benefic consequences

FAST

Same

Biograph 6 TrueV



Total PET scan duration: 3 min	**Total PET scan duration: 12 min**
6 beds; 0.5 min/bed; 8s/3i/5F	**6 beds; 2 min/bed; 8s/3i/5F**
10.5 mCi; 105 min post-injection	**10.5 mCi; 93 min post-injection**

84 year-old male, 109 lb,
with lung Ca cancer;
restaged with PET/CT

- **possible reduce dose**
- better patient tolerance
- less movement
- claustrophobia
- flexible protocols
- max throughput

Advances in reconstruction techniques

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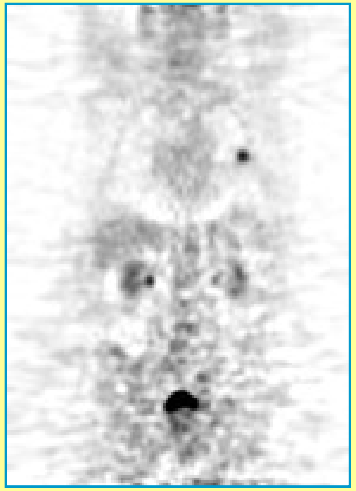
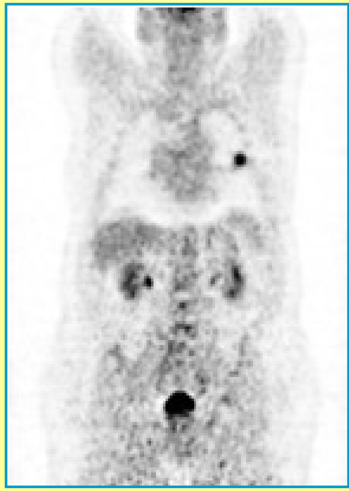
Software Algorithms:

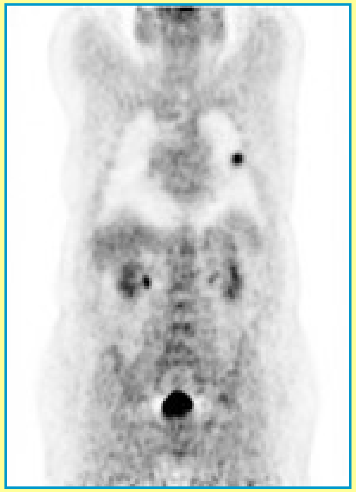
144 kg (317 lbs),
Scan duration: 15 min
5 beds; 3 min/bed
10.6 mCi; 90 min post-injection
168 x 168



3DRP
(Re Projection)



2D iterative

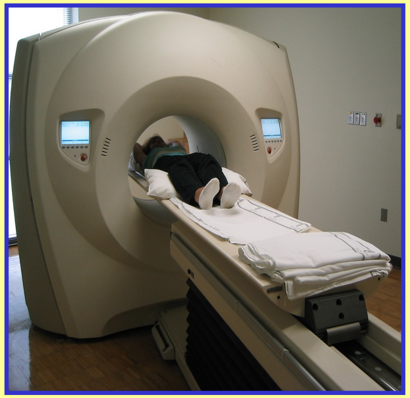


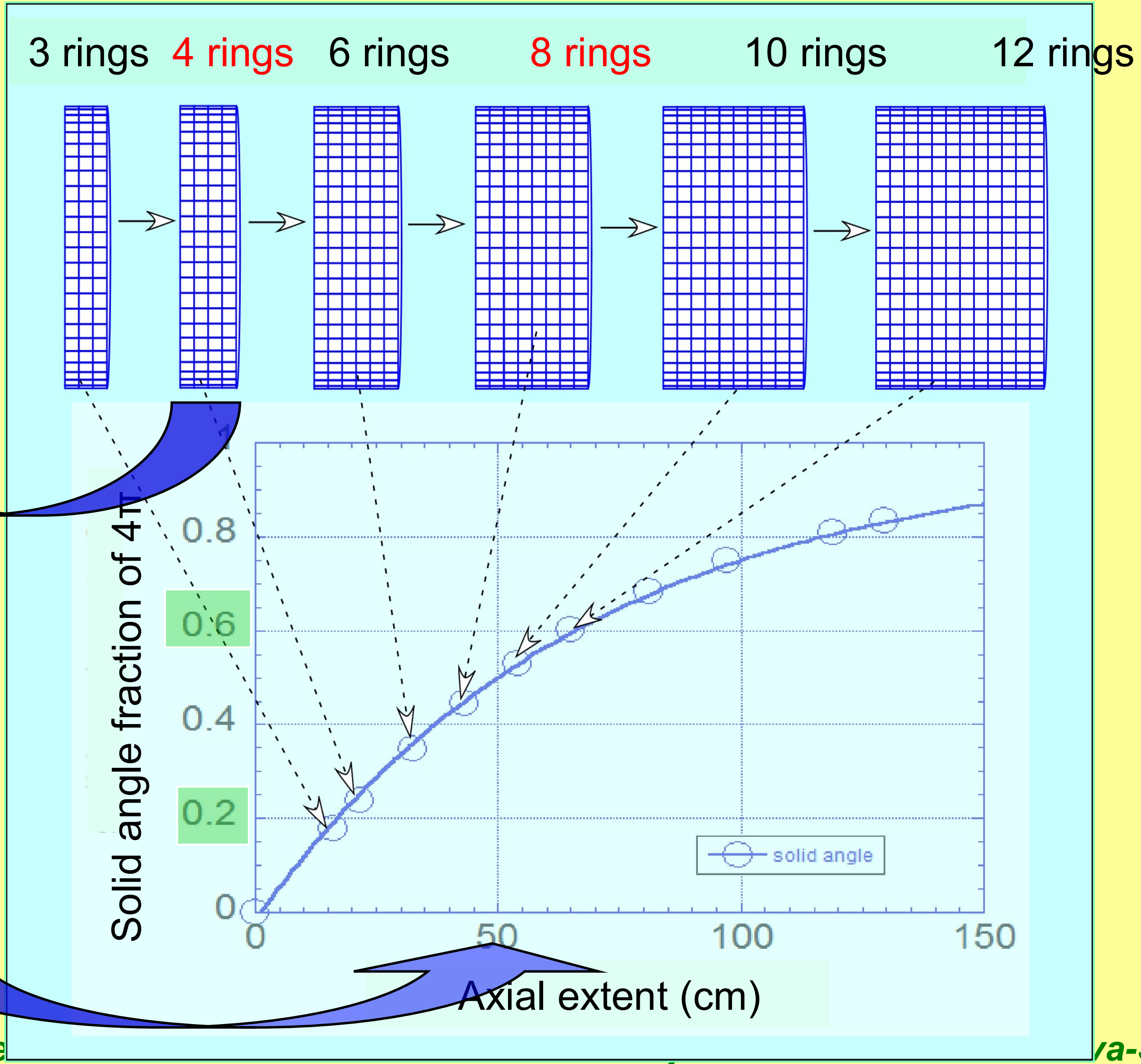
3D OSEM
Ordered **S**ubset **E**xpec-tation **M**aximization

3D PSF (WIP)
Point Spread Function….

The way of Improving Sensitivity

Present **Future?**





Whole body PET imaging: the future

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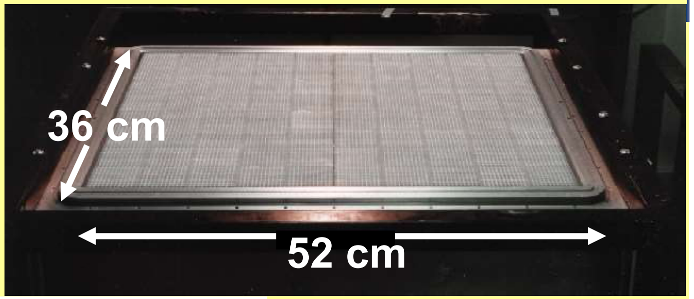
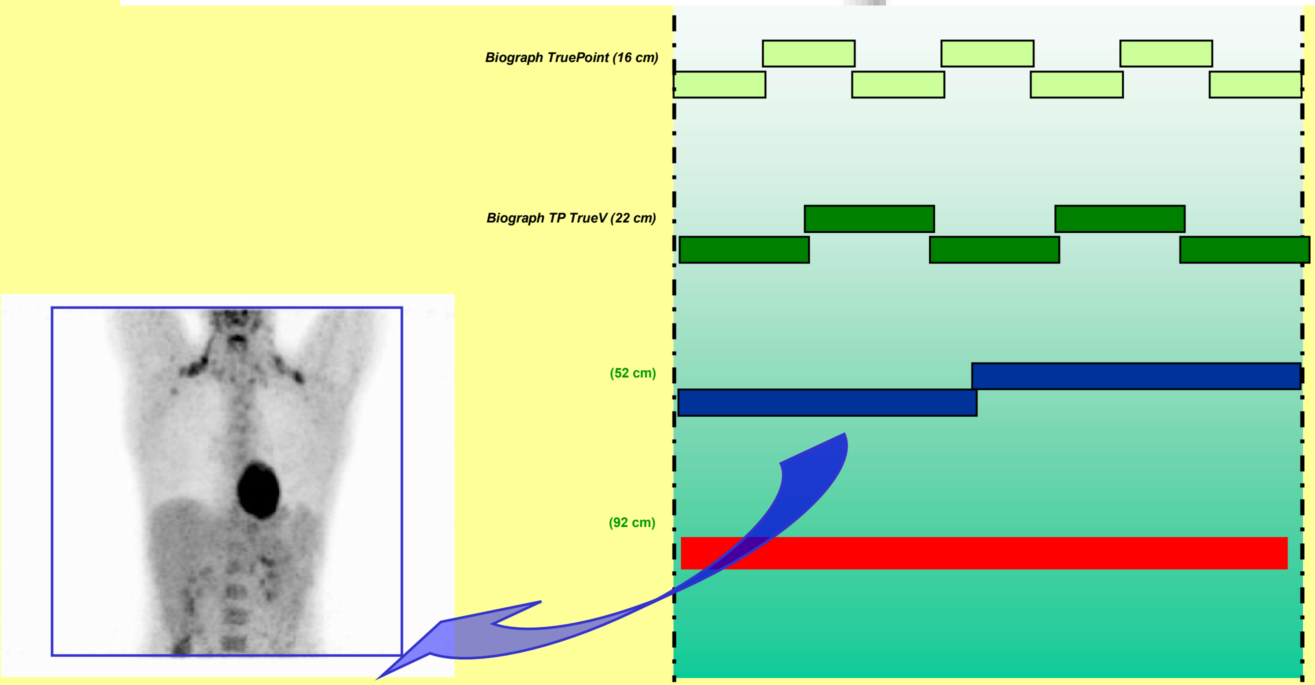
Average whole-body coverage of 80 cm

= Faster Data Taking (7 Beds => 1 Bed?)





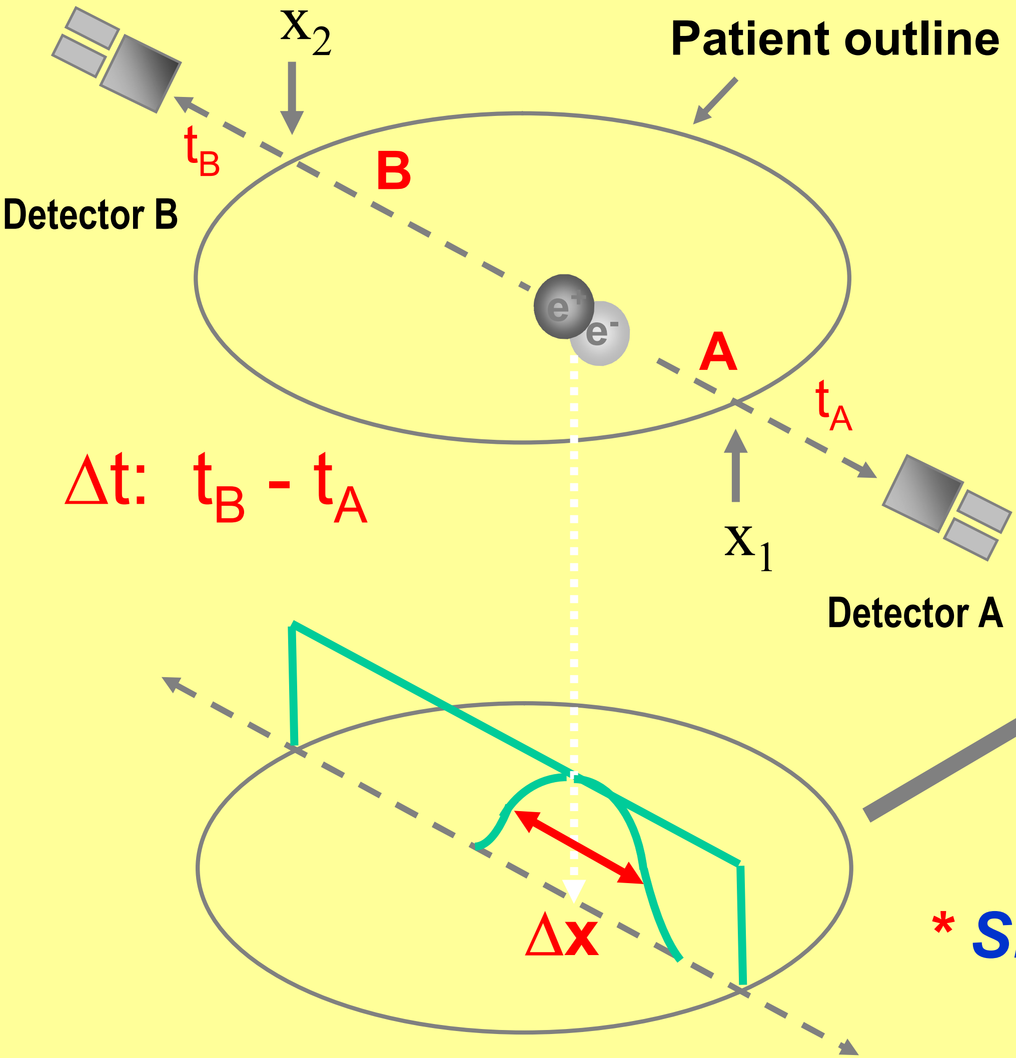
7 x 3 min = 21 min

5 x 2 min = 10 min

2 x 1 min = 2 min

1 x 1 min = 1 min

Improving signal-to-noise: *time-of-flight (TOF)*

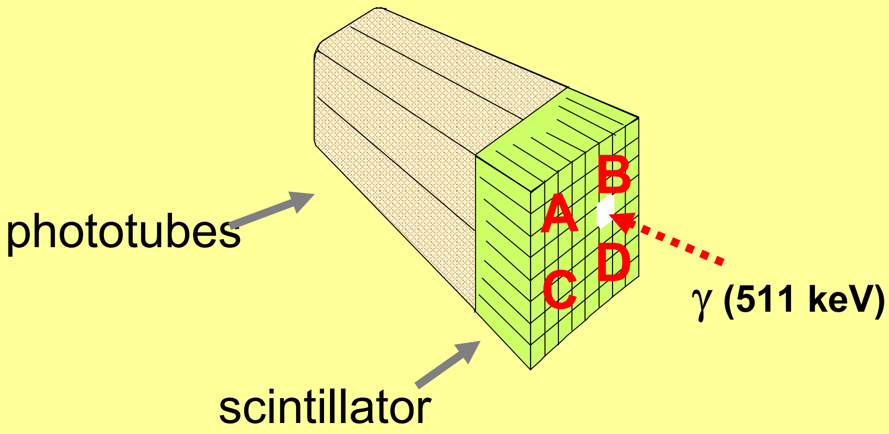


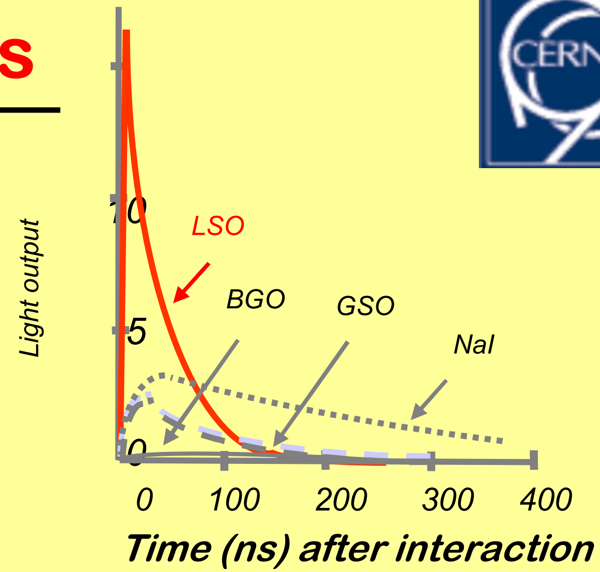
$$\Delta x = \frac{\Delta t}{2} c \qquad SNR_{TOF} \cong \sqrt{\frac{D}{\Delta x}} \cdot SNR_{conv}$$

Δt (ps)	Δx (cm)	SNR *
100	1.5	5.2
300	4.5	3.0
500	7.5	2.3
1200	18.0	1.5

** SNR gain for 40 cm phantom*

Technical Improvements





	BGO	GSO	LSO	LYSO
Density (g/ml)	7.13	6.7	7.4	7.1
Effective Z	74	61	66.4	65.4
Decay (ns)	300	30-60	**35-45**	41
Timing **(ps)**			**500** ps	585
Light (ph/MeV)	8,200	10,000	30,000	30,000
% NaI	15	25	80	80

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Importance of Spatial resolution

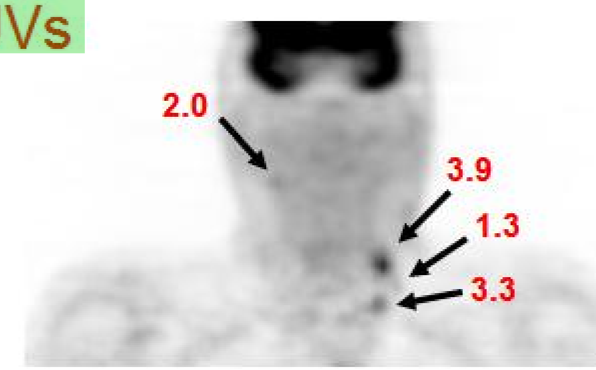
CERN

Spatial resolution: clinical significance

SUVs

8 x 8 elements/block
6.4 mm x 6.4 mm

Biograph

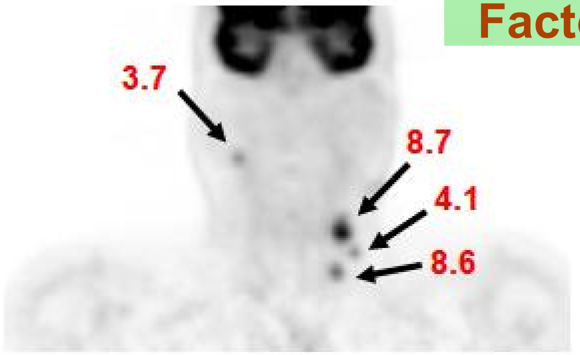


8.6 mCi; 60 min uptake

Factor 2

13 x 13 elements/block
4.0 mm x 4.0 mm

Biograph HI-REZ



11.2 mCi; 90 min uptake

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PET-CT is Better: Non-Small Cell Lung Cancer

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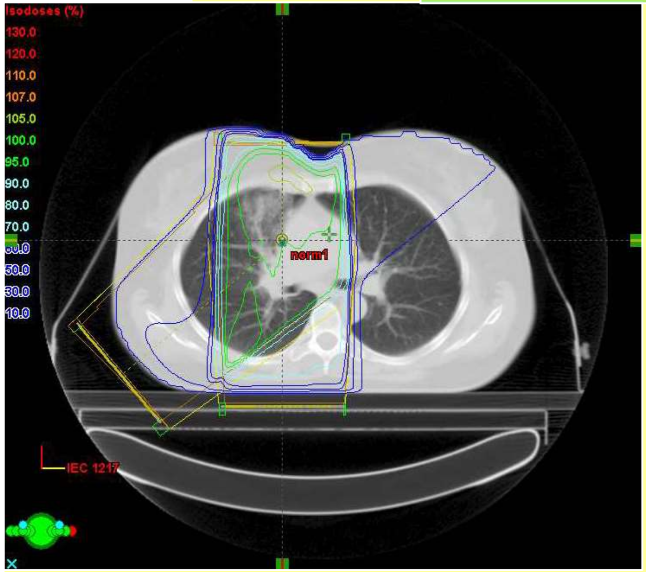
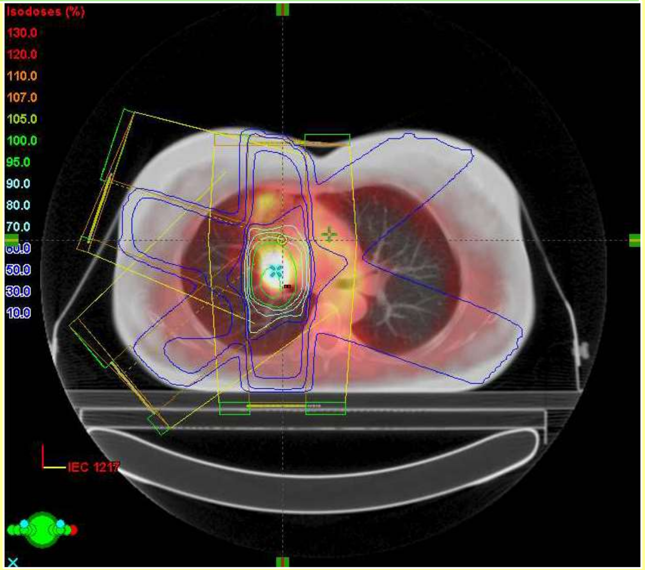
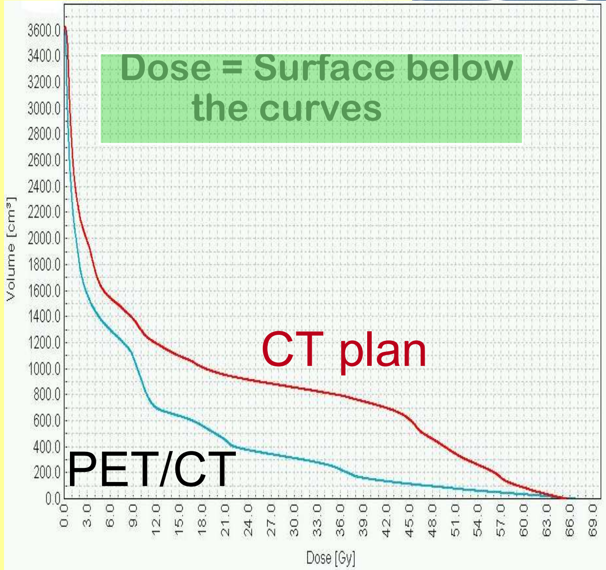
University Hospital Essen, Germany

Treat. Plan from PET/CT = lower dose







CT plan | PET/CT plan | Dose-Volume Histogram

46 year-old female with NSCLC: cT2pN2 diagnosed 01/04 post 3 x CTX; PET/CT for RTP.

Compared to pre-CTX, the bronchial tumor is reduced both in size and metabolic activity (SUV_{max} reduced from 14 to 4.6). PET/CT-based conformal treatment plan yields a cumulative mean lung dose of 8 Gy compared to 15 Gy with an assumed CT-based conventional treatment plan. Thus, **PET/CT allowed for dose escalated treatment of this NSCLC**.

BGO-PET: 320 MBq ^{18}F-FDG, 80 min pi, 3.5 min per bed, 3 beds *(about 15 mSv)*

Dual-row CT: 110 mAs, 130 kVp, IV, water-based oral contrast, 4 mm slices

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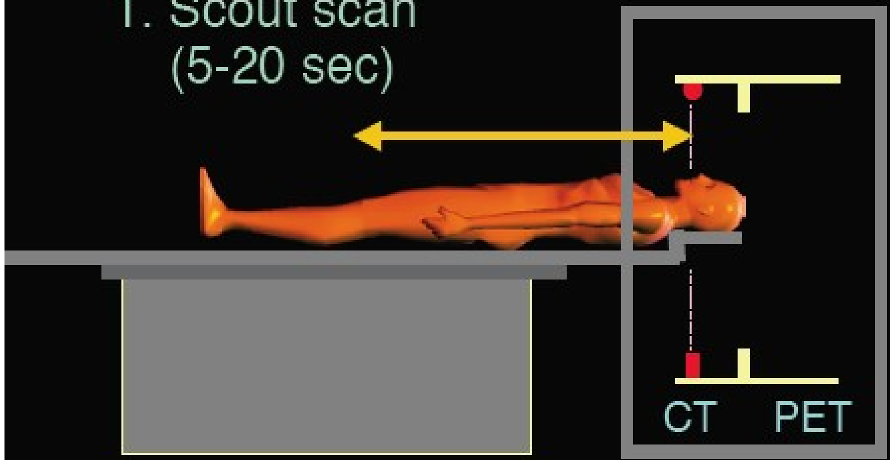
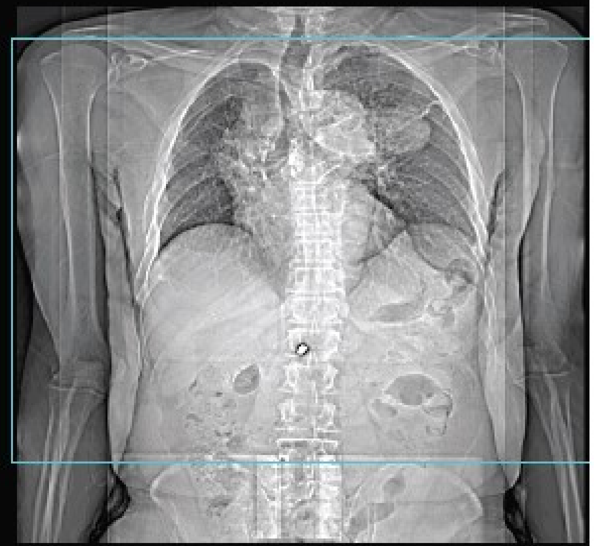
PET/CT scan protocol

1. Scout scan (5-20 sec)

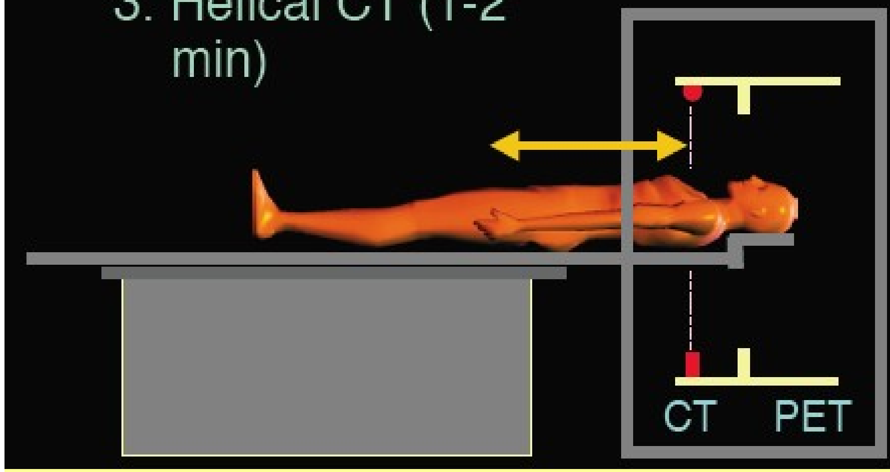


2. Selection of scan region (1-2 min)

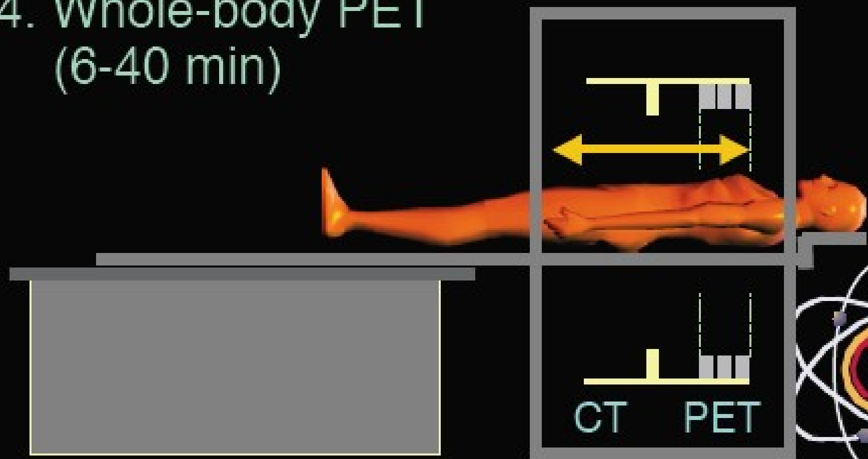


Scout scan image

3. Helical CT (1-2 min)



4. Whole-body PET (6-40 min)



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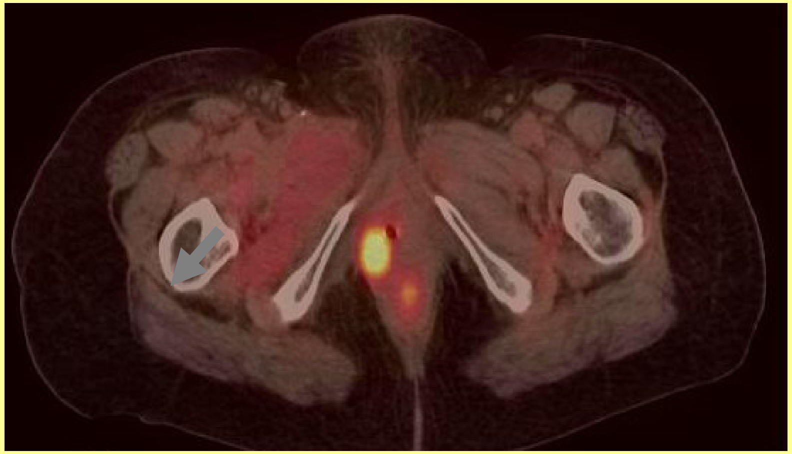
SURVEY : Vaginal cancer

CT only

PET+CT



PET only

Biograph Scan duration: 15 min

5 beds; 3 min/bed; 8s/3i/6F

10.6 mCi; 90 min post-injection

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.

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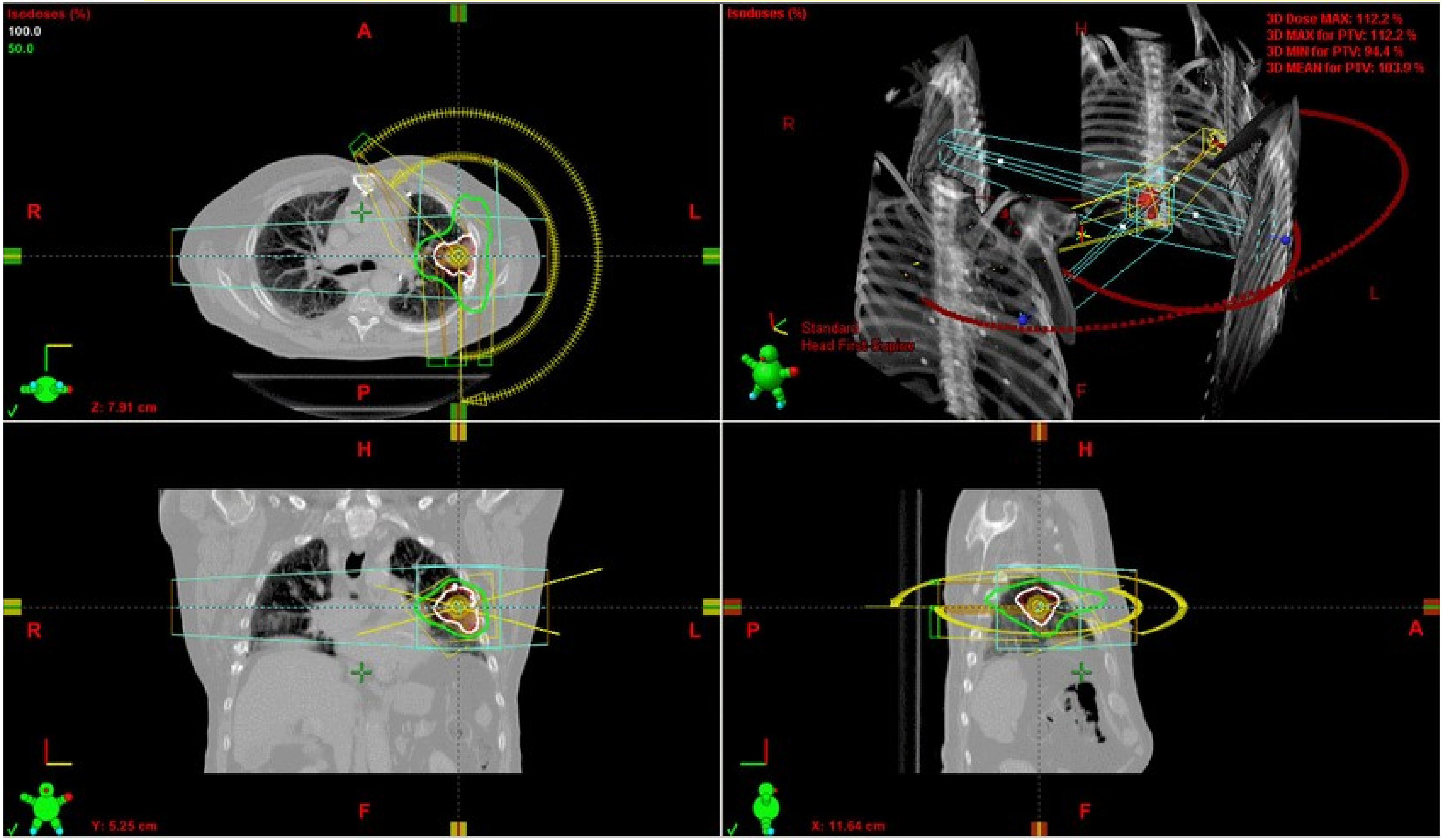

Recurrent stage I-A NSCLC of the left lung (MIMA)

close or Esc Key

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Larmor Equation

$$\omega = \gamma * B$$

Rate of precession

Gyromagnetic Constant

Magnetic field

Resonance frequencies of common nuclei

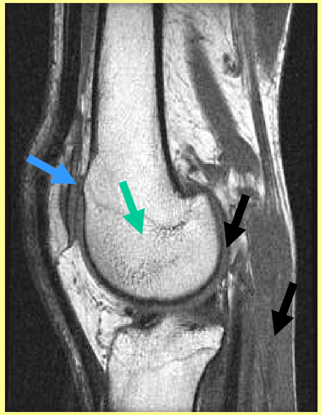
Nucleus	Resonance Frequency (1.5Tesla) MHz
^{1}H	63.86
^{2}D	9.81
^{13}C	16.05
^{14}N	4.62
^{19}N	6.57
^{23}F	60.07
^{31}Na	16.89
^{31}P	25.86
^{35}Cl	6.27
^{39}K	2.97

Magnetic Resonance Imaging

- Magnetic Resonance
- MR Image Formation
- Contrast
- Applications of MRI

Advantages:
- Excellent / flexible contrast
- Non-invasive
- No ionizing radiation
- Arbitrary scan plane

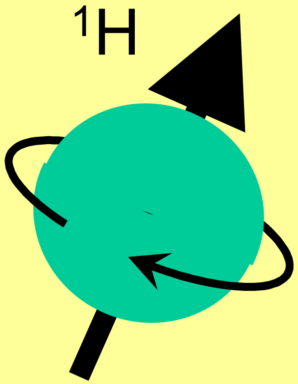
Challenges:
- New contrast mechanisms
- Faster imaging

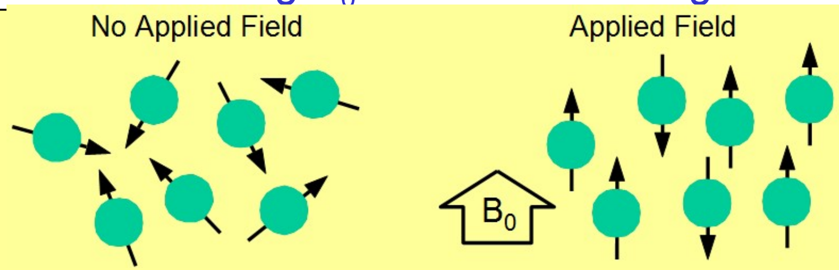


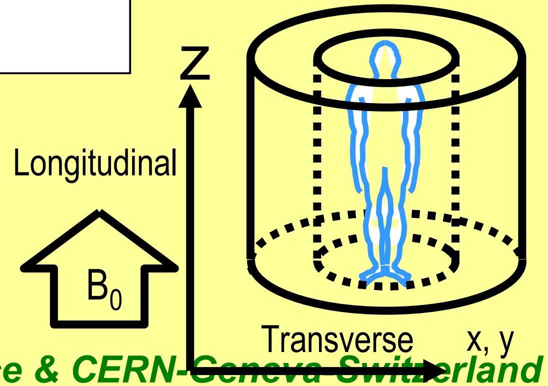
Basic MRI Principles

- Certain atomic nuclei including ^1H exhibit nuclear magnetic resonance.
- Nuclear "spins" are like magnetic dipoles.

- Spins are normally oriented randomly.
- In an applied magnetic field, the spins align with the applied field in their equilibrium state.
- Excess along B_0 results in net magnetization.

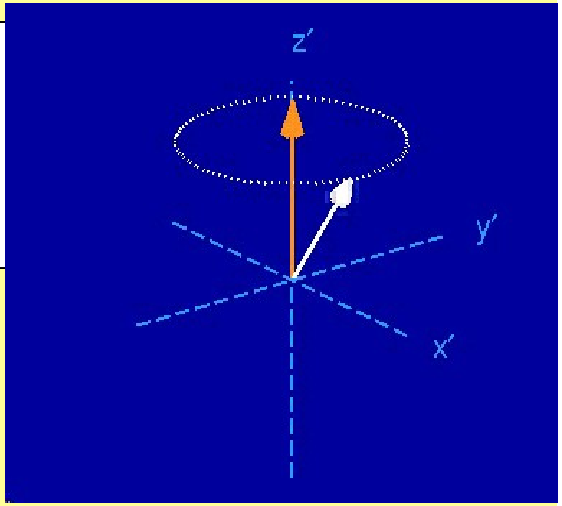






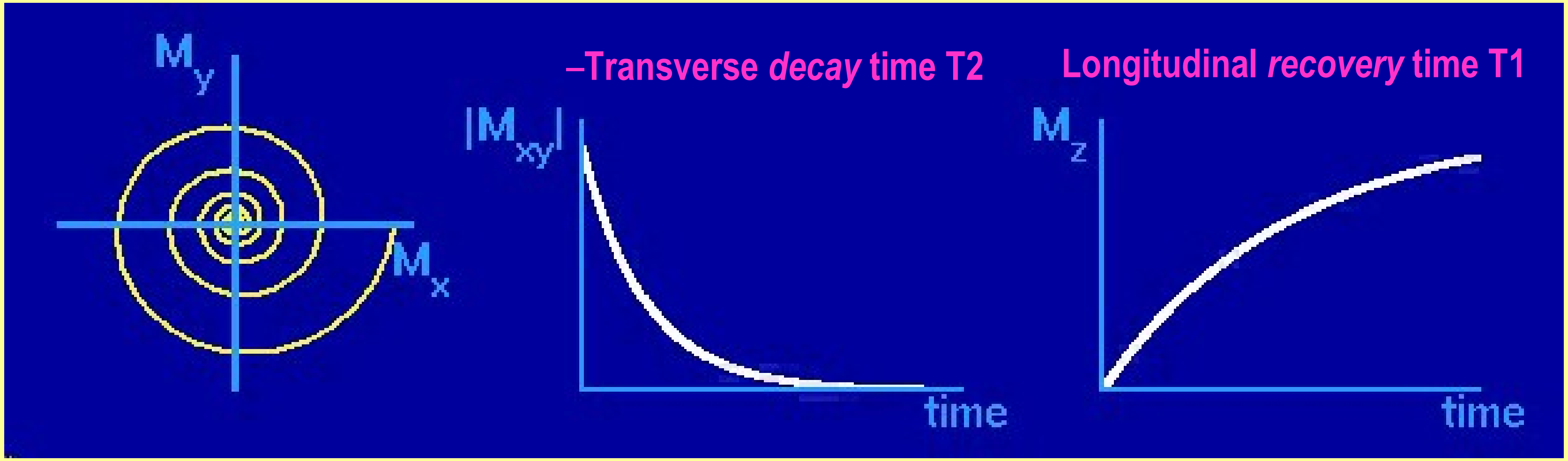
Precession

- 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_1
  - Transverse *decay* time constant is T_2
- Relaxation and precession are independent.

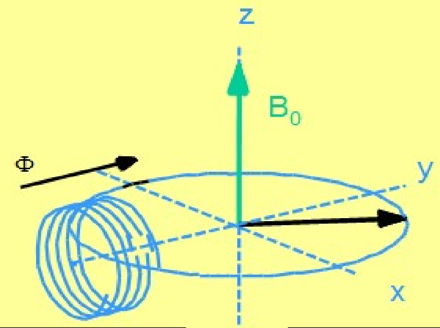
Relaxation

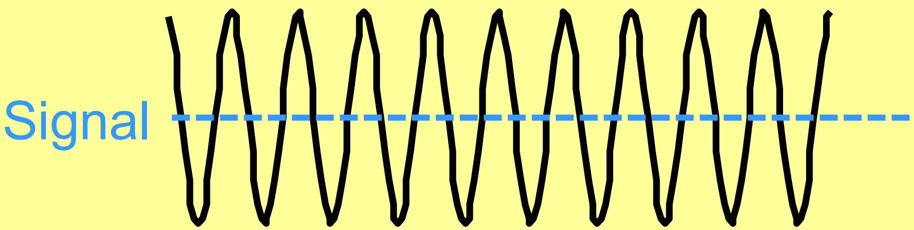


Precession Decay Recovery

Signal Reception

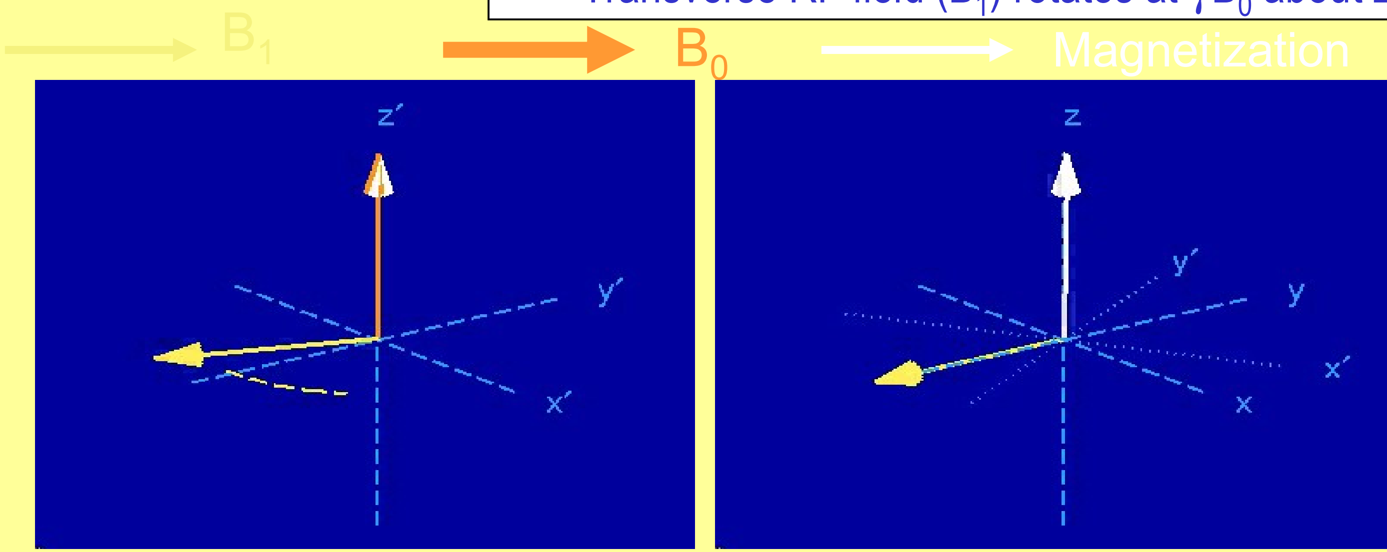
- Precessing spins cause a change in flux (F) in a transverse receive coil.
- Flux change induces a voltage across the coil.





Excitation

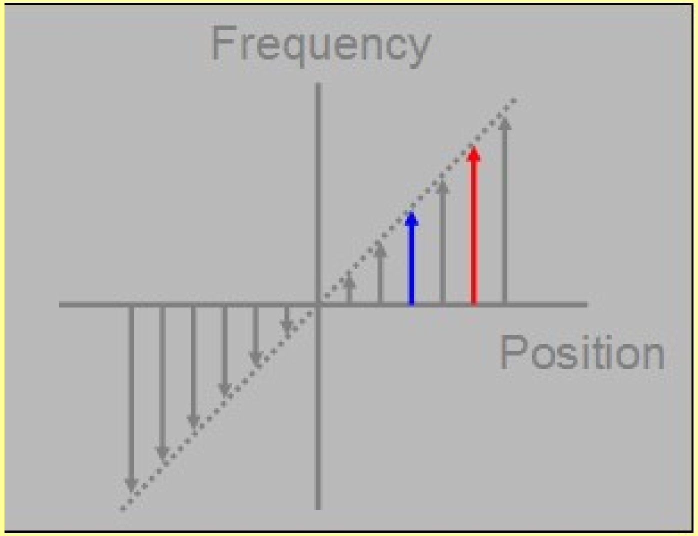
- "Excite" spins out of their equilibrium state.
- Transverse RF field (B_1) rotates at γB_0 about z-axis.

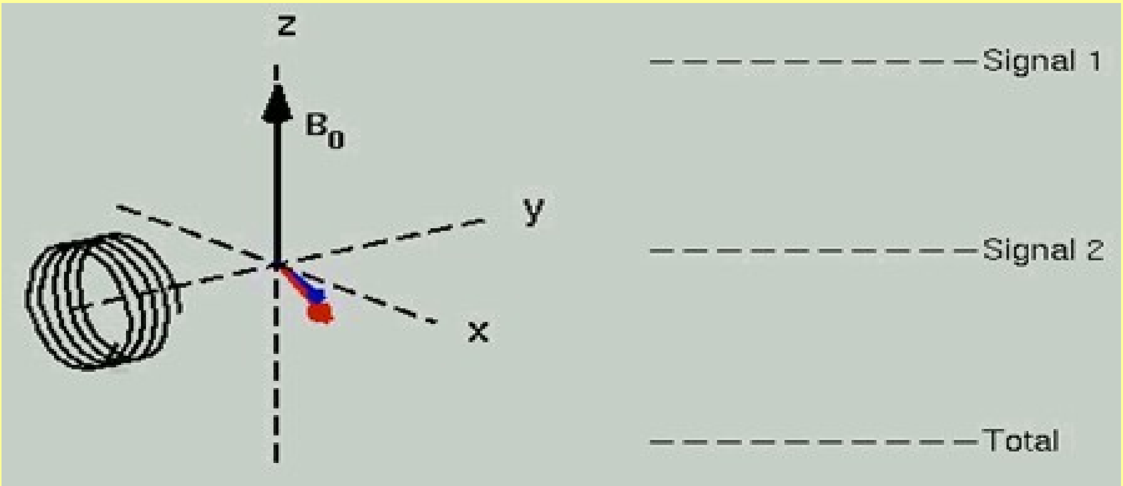


Rotating Frame

Image Acquisition

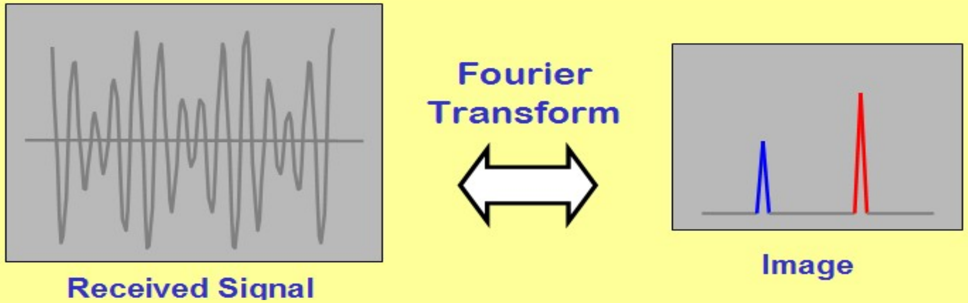
- Gradient causes resonant frequency to vary with position.
- Receive sum of signals from each spin.





- Received signal is a sum of “tones.”
- The “tones” of the signal are the image.
- This also applies to 2D and 3D images.

Image Reconstruction



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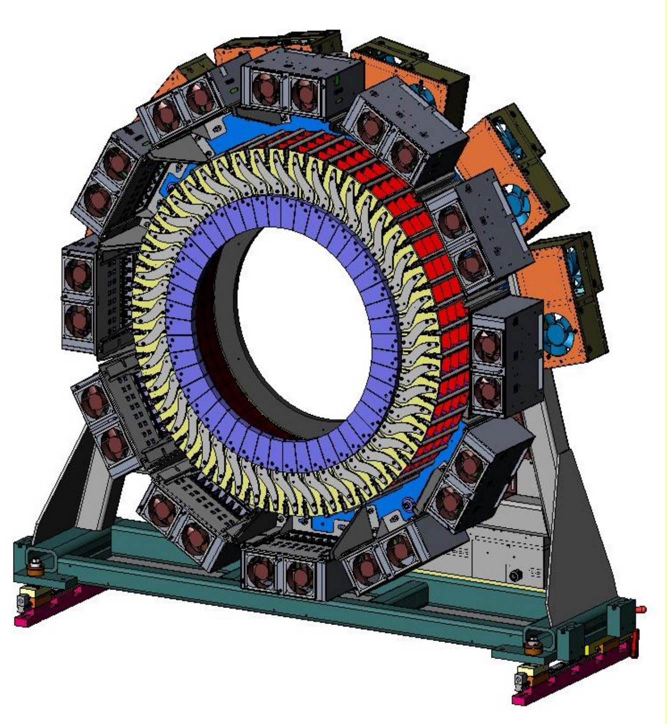
PET IMPROVEMENTS

Last years Improvements in PET cameras

- Better Crystals (Ex: more ph/MeV with LSO, LYSO)
- Spatial resolution (Ex : Crystal size 4 x 4 mm)
- New reconstruction algorithms
- Efficiency (Septa removed)
- Time-of-Flight (Tof)



Ex: Biograph TruePoint PET•CT (Biograph TP)

Going digital……..

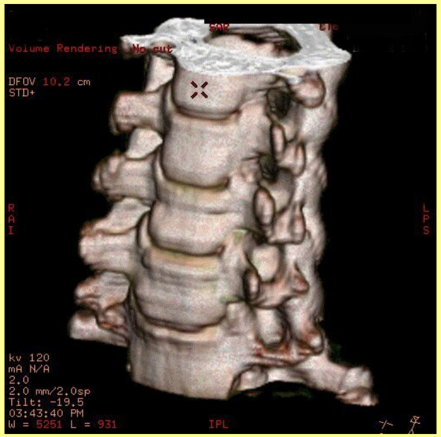
A paradigm shift: current to counting mode thanks to fast electronics developed for LHC detectors (CERN)

Current

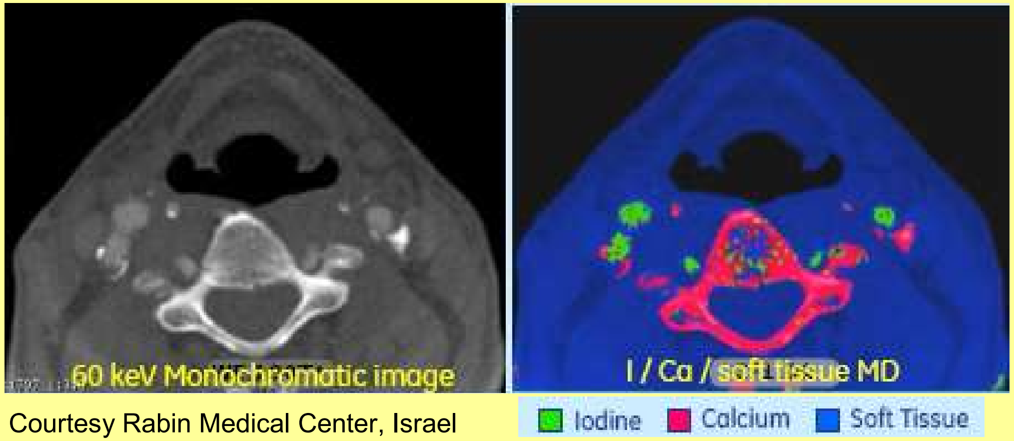
- Limited contrast
- High dose
  - Restricted use for screening

Counting

- High contrast
- Colour mode possible
- Lower dose (factor of 10)
  - Opportunity for screening

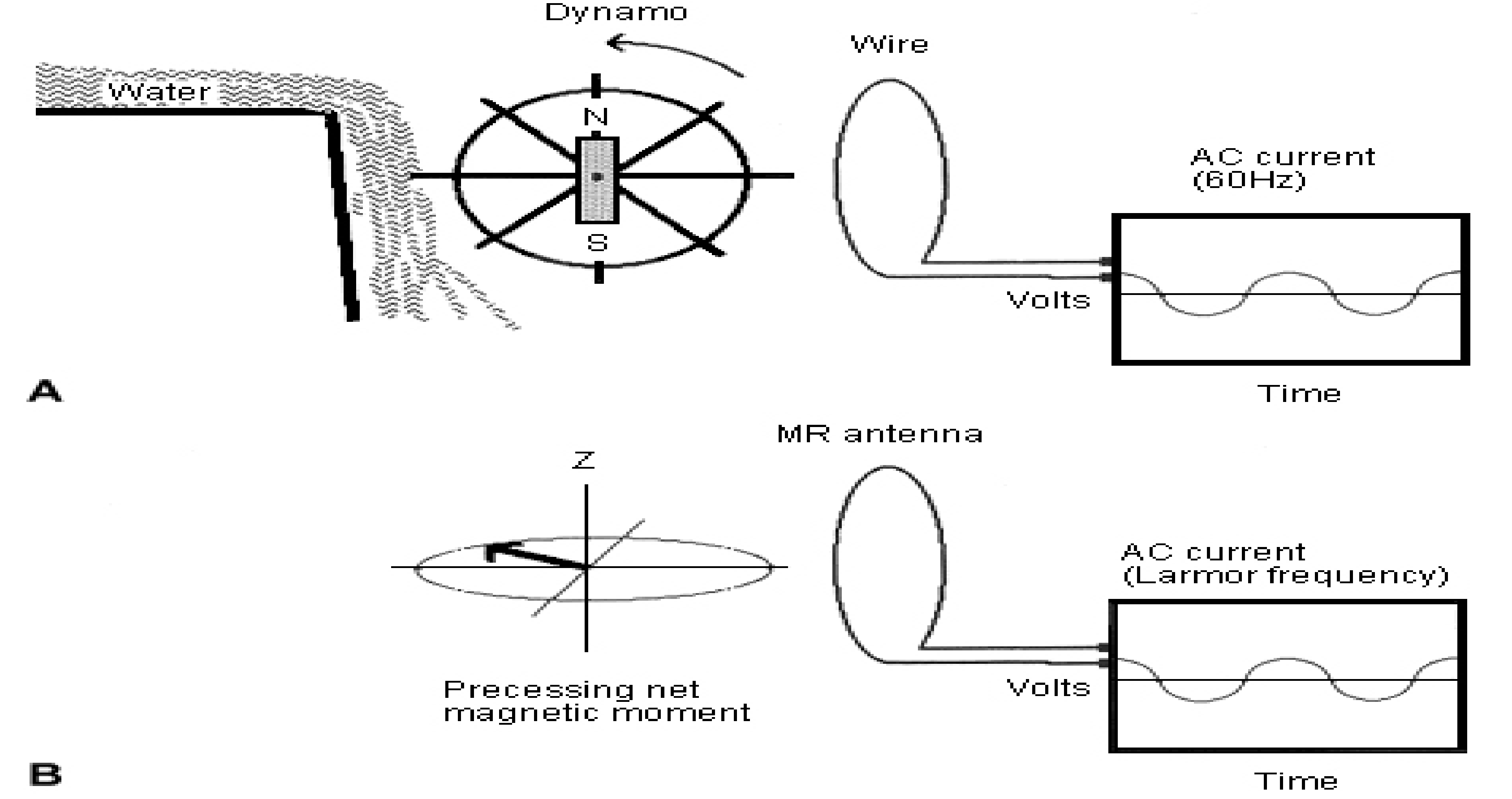


Courtesy GE



Courtesy Rabin Medical Center, Israel

IMAGE (comparison is sometimes treason, but..)



- . **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.

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Introduction: why the quantification ?

Objective characterization observations, may improve :

IN :	EXAMPLE:
• **The differential diagnosis**	Density of dopamine transporters / type of dementia
• **Prognosis**	Cardiac prognosis : cardiac death rates stratified by LV volume and EF . Patients with LVEF of> 45 % or end-systolic volume (ESV) of <70 mL -have low mortality rate, Regardless of severity of perfusion defects.
• **Therapeutic management**	Measurement is potentially richer than visual interpretation
• **Radiotherapy**	Irradiation from a volume defined from SPECT or PET considering all the pixel values > 40% SUVmax

The problem of quantification: Establish the relationship between the value of a pixel and concentration of radiotracer in the corresponding region : N = C k (N kBq / ml)

Take care: Without multiple precautions , N is not proportional to C , and there is no simple relationship between the two quantities…

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

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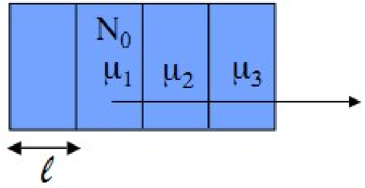
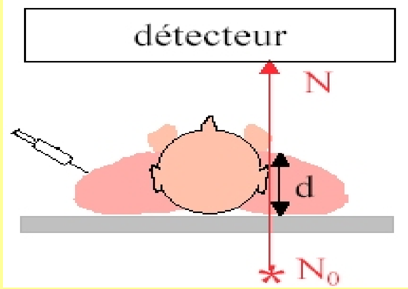
Attenuation in SPECT & PET



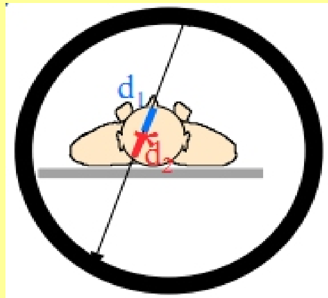
$N = N_0 \exp[-(\mu_1/2+\mu_2+\mu_3)]\,\ell$



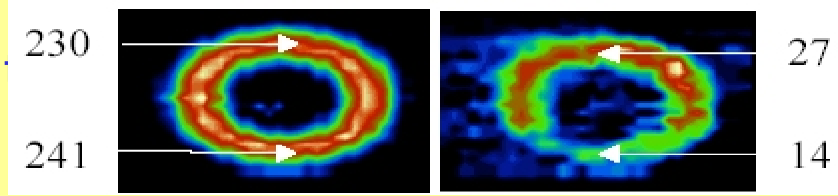
- **In SPECT** Attenuation depends on the place of issue on the projection line. When an event is detected, it is not known how deep it comes: we do not know how much it has been attenuated making it difficult to correct the attenuation.

⇒Use medium density : μ for lungs=0.04 cm^{-1} μ for soft tissue=0.15 cm^{-1} μ for cortical bone=0.30 cm^{-1}. Attenuation is of course function of γ 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).

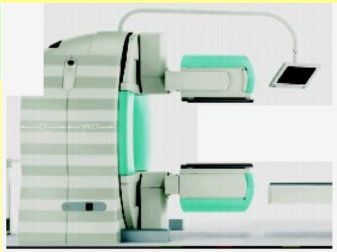


- In SPECT (and PET also), attenuation leads t underestimates of activity generally greater than 70%. (Cardiac example)



No attenuation **With attenuation**

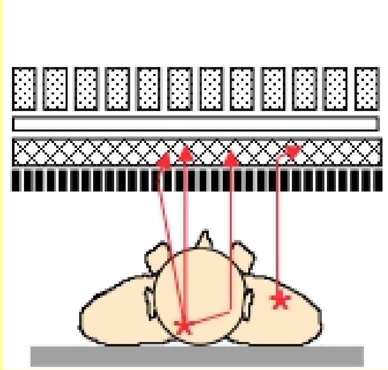
- Attenuation problem is **better solved now by SPECT/CT and PET/CT hybrid** machines. Fortunately acquisition in transmission is very fast. If attenuation coefficients are measured at different energies than the radiotracer energy (Spect or PET), adaptation is necessary.

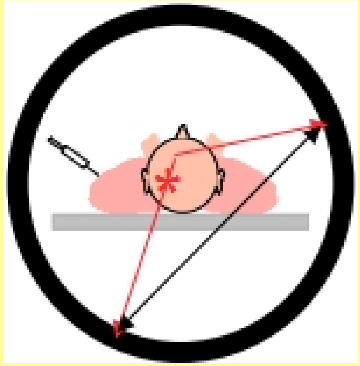


Compton scattering

Scattering can happen:

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



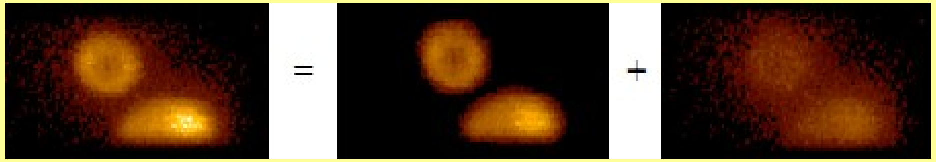


Consequences of Scattering:

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

SPECT

Importance of scattering in SPECT



acquisition picture window — *primary photons* — *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 :

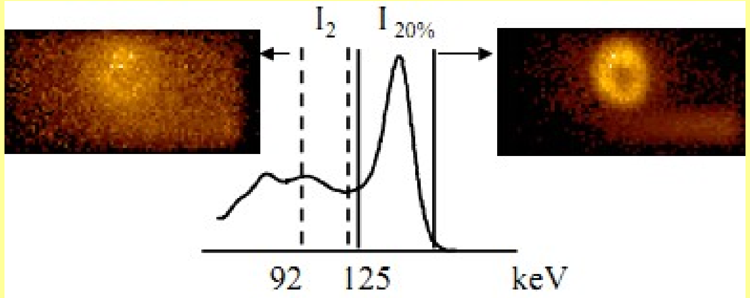
SPECT

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

Different correction methods in SPECT

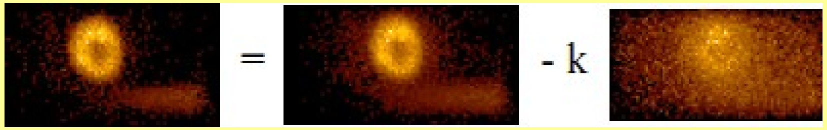
-1 From reduction of acquisition spectrometric windows : Reduction of scattered photons (Importance of having a good energy resolution tomograph)

-2 Jaszczak Subtraction in SPECT



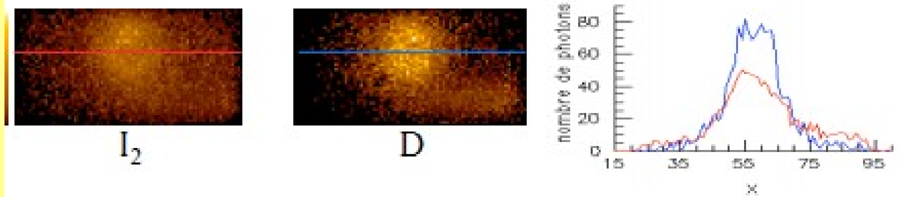
$$\hat{D}(i) = k.I_2(i)$$

Correction very simple to implement (hence its success)



But neglects the dependence of angle deviation θ and wasted energy

$$E' = \frac{E}{1 + E(1 - \cos\theta)/m_0c^2}$$



• overcorrection if away from sources and undercorrection near sources.

• Artificial enhancement giving pleasant contrast for eye.

Approximate on quantitative point of view but overall performant

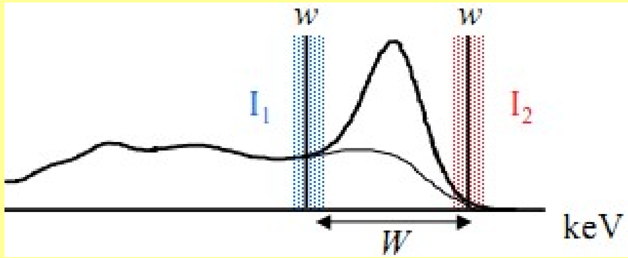
-3 Method 3 energy windows (TEW)

- Data acquisition in 3 windows I20 % , I1 and I2
- Estimation of D (i) for each pixel i :

$$\hat{D}(i) = W\,[I_1(i)+I_2(i)]\,/\,2w$$

- Estimation of P

$$\hat{P}(i) = I_{20\%}(i) - \hat{D}(i)$$



Repositioning of scattered photons / Modeling of scattering

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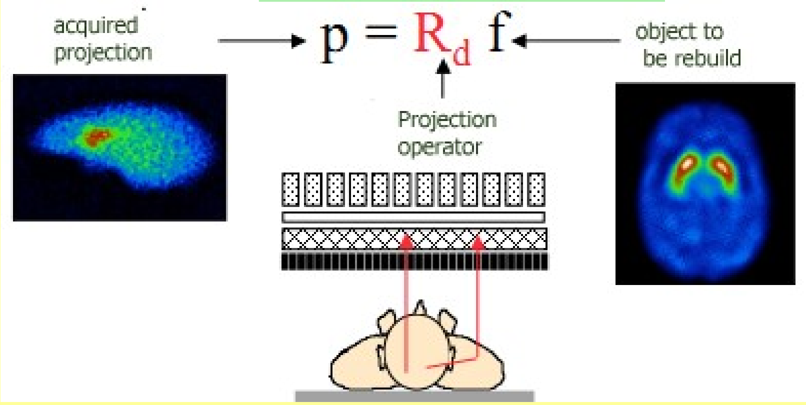
- Iterative Reconstruction with scattering modeling

Illustration in SPECT



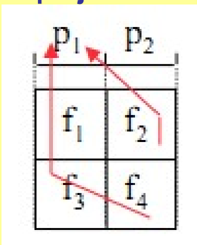
without modeling of scattering:

$p_1 = r_{11} f_1 + r_{13} f_3$

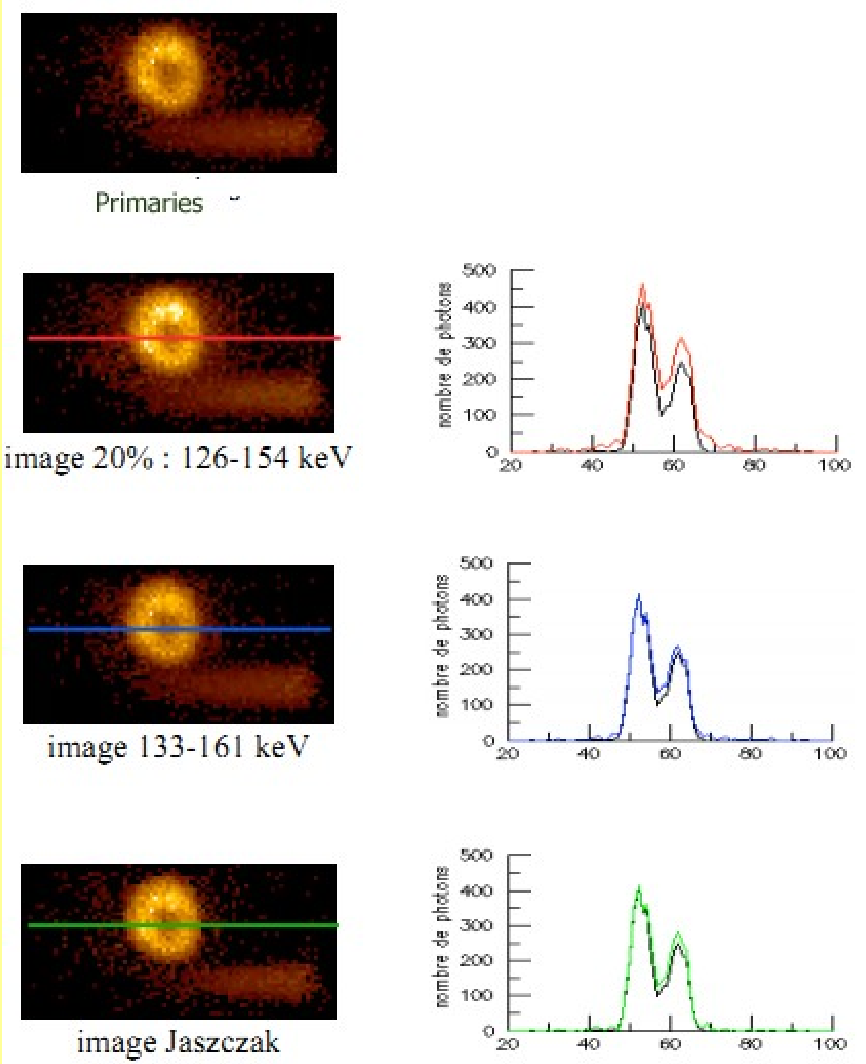
with modeling of scattering :

$p_1 = r_{11} f_1 + r_{12} f_2 + r_{13} f_3 + r_{14} f_4$

projections



- Approximate analytical modeling
- Monte Carlo modeling



- Iterative Reconstruction with scattering modeling

- very general approach suitable for all Iterative reconstruction algorithms
- expensive storage space and computing time

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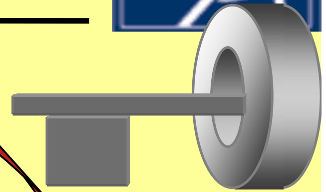
TREATMENT PLANNINGS

(Will be explained later by Alex Rijnders)

The Software start from Images

CT-SCAN ↔ MRI or / and PET



Treatment plannings are compulsory for correct treatment

- external contours
- densities
- anatomical structures
- beam data library

- anatomical structures

BEAM DEFINITION

TREATMENT PLANNING SYSTEM

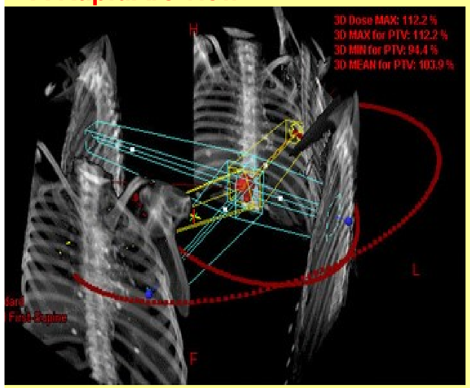
OPTIMISATION

Most Popular systems:

Pinnacle (Philips Medical systems)
ADAC -> Pinnacle3(Philips)
Monaco (CMS/Elekta)
Eclipse (Varian Medical Systems)
RapidArc: see(varian.com/us/oncology/treatments/treatment_techniques/rapidarc/resources.html
…..

- Dose distribution
- Dose-Volume Histograms
- Biological indices

A RapidArc view



- Reconstructed radiographs (DRR)

- Field shape
or
- Position of leaves

- Treatment parameters
- Treatment time (monitor units)

SIMULATOR and/or ELECTRONIC PORTAL IMAGING

BLOCK CUTTING DEVICE or MLC

ACCELERATOR

VERIFIY AND RECORD SYSTEM