Medical Physics Introduction to nuclear medicine

P. Le Dû

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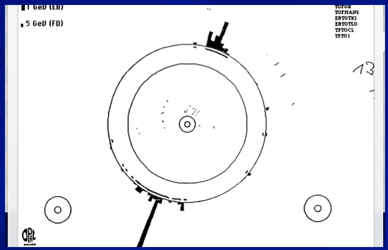
TIPP School Capetown

Who I am ? -

- NA3 @ CERN (Di-Muon Drell Yan) : 1974-1980
  - Large MWPC (4x4 m2)
  - Trigger & DAQ
- LEP - OPAL @ CERN (1980-1990)
  - TOF system
  - Trigger & DAQ → First Z^0
- SSC- SDC @ Dallas/LBL Berkeley (1990-1994)
  - Trigger L2
  - Shower Max Detector electronics (APD & SCA)
- LHC- ATLAS @ CERN (1994-2000)
  - L2 trigger & LARG calorimeter Read Out electronics (SCA)
- D0 @ FNAL (1996-2005)
  - L1 Calormeter trigger and L2 trigger.
- ILC study group (1996-2008)
  - Trigger & DAQ convener → Software triigeer
- 2000→Technology transfer advisor for medical application (PET & Particle therapy)
- Ultra fast (picosecond) timing and TOF



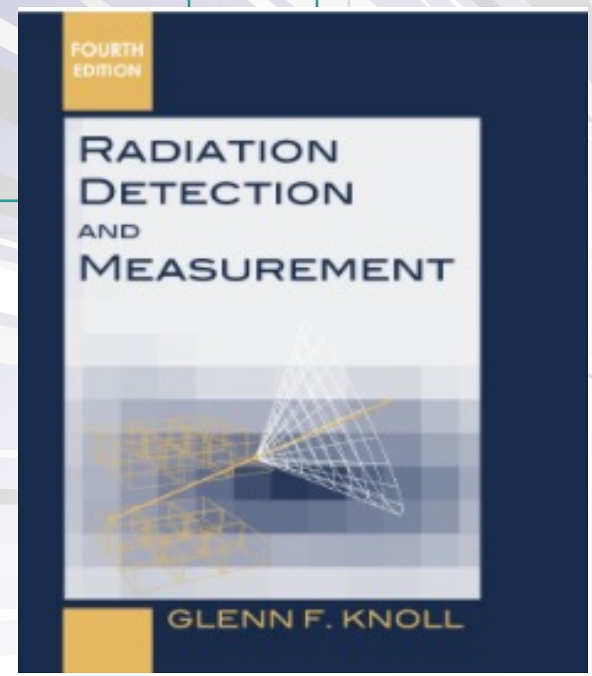
Experimental Physicist
- CEA Saclay (1969-2008)
- IN2P3-IPN Lyon (2009 ..

Goals of this lecture

- A very simple basic introduction of Medical Physics seen from a HEP experimental physicist.
- I will present mainly the radiation instrumentation aspect around the nuclear medicine and its perspectives
- Might be a bit too naive and simple sometime BUT give a broad overview of the medical nuclear domain

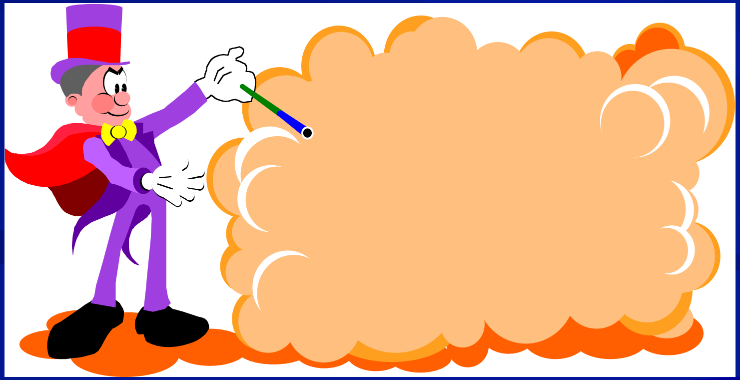
Few words about Radiation Detectors

Radiation Instrumentation THE Book Glenn Knoll



What is medical physics outlines

- A little bit of history
- Radiation effects units
- Basics of Radiology
- From Radiotherapy to Particle Therapy
- Introduction to Nuclear medicine
- Radioactive tracers for diagnosis and treatment
- Short survey of Imaging tools and techniques from diagnostic to therapy and their future



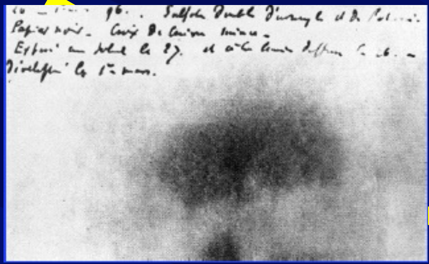
Some history

.. how the development of radiation instrumentation has been crucial for fundamental scientific discoveries and for the improvement of human life...

More in 'back up slides'

How physics discoveries have impacted our life (1)

1895
W.C. Rontgen
Discovery of X Ray



1896 - Discovery of natural radioactivity by H. Becquerel
1897 – J.J. Thomson – electron
1899 – E. Rutherford : Alpha & Beta
1900 – U. Vilars – the Gamma

First image of potassium uranyl disulfide

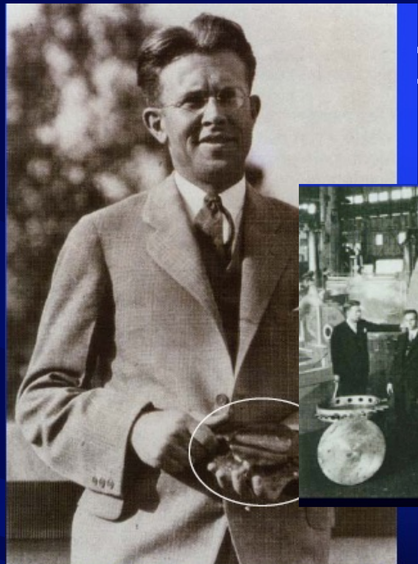
1898
Pierre and Marie Curie
the Radioactivity
Polonium,Radium

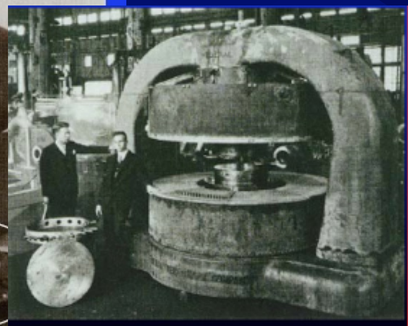
1910

X Ray Radiography

1923 - The Tracer principle
`G.V.Hevesy- the father of nuclear medicine

How physics discoveries impact our life (2)





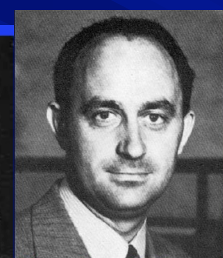
Ernest O. Lawrence and his First cyclotron 1932

1932 - The Invention of the cyclotron
Production of radioisotopes

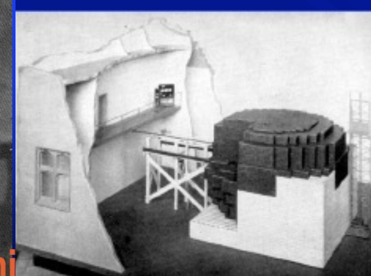
1934 - Artificial radioactivity
Irène and Fréderic Jolio Curie
in combination with the cyclotron open the door to the production of useful radio indicators.

1938-1942 Fission of Uranium

Otto Hahn, 1944 Nobel Prize



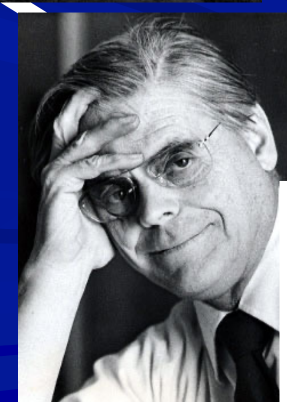
Enrico Fermi

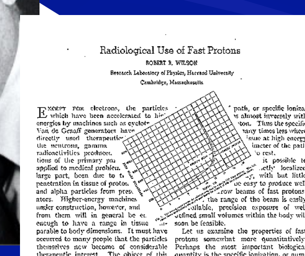


O.Hahn
E. Fermi

From discovery to first graphite miler in Chicago
To the Production of long lived radio-isotopes and nuclear energyproduction

1946 – R.R.Wilson The origin of particle therapy
Using the Bragg peak discovery (1903)





Radiological Use of Fast Protons
ROBERT R. WILSON
Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

Effects of radiation on human body

What is a Curie,Bequerel, Seivert?

From Prof. Aurengo - Hopital de la Salpetriere - Paris

The Units - a bit of definition!

- Activity = Number of decays per second
  - Becquerel Bq : 1 decay / second
  - Curie Ci : 37 x 10^9 Bq (37 GBq)
- Dose : GRAY = amount of radiation absorbed in an material = absorbed energy / mass unit
  - Gy : 1 joule / kilogram = 100 Rad
- Effective dose : SEIVERT Sv = **estimates biological effect from the absorbed radiation**

→ indication of global risc

= absorbed dose x WR* x WT**

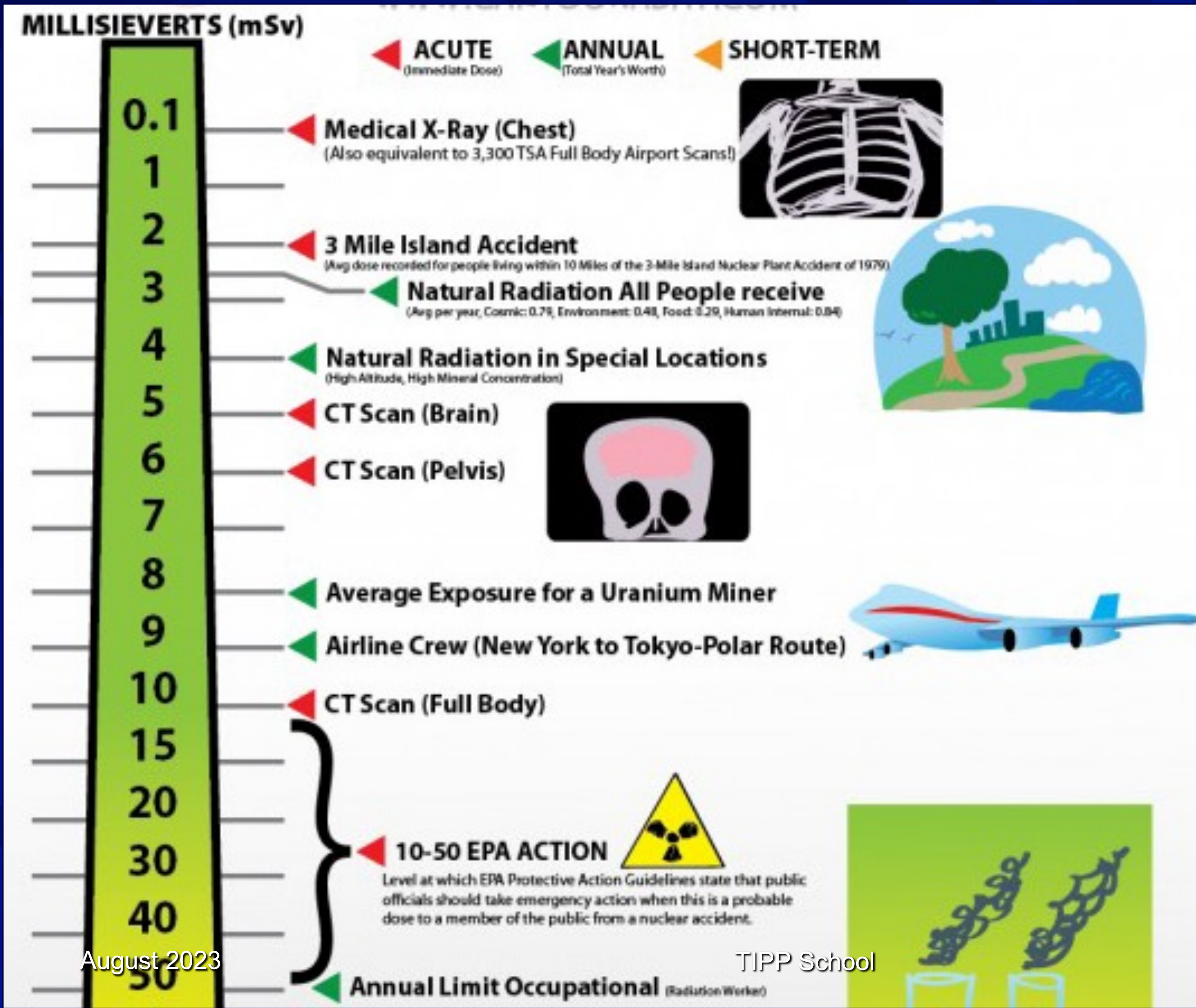
- Particle → WR*= 1 pour RX, beta and gamma, p=5, α=20
- Organ → WT** = 0.05 for thyroïd, 0.01 for skin

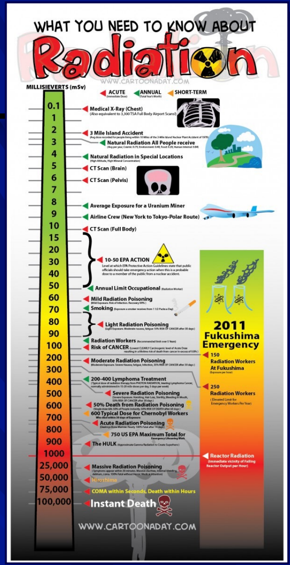
Effective dose values

- 10.000 mSv : high irradiation / rapid death
- 1.000 mSv : moderate irradiation / clinical visible signs (burn…)
- 5 mSv : annual irradiation in Clermont-Ferrand (volcanic soil)
- 2,5 mSv : annual irradiation in Paris
- 1 mSv : legal limit irradiation in France
- 1 mSv : average annual medical irradiation in France

1 Sv = 1 J/kg equivalent 1 Sv = 100 rem


WHAT YOU NEED TO KNOW ABOUT
Radiation


MILLISIEVERTS (mSv)
ACUTE (Immediate Dose)
ANNUAL (Total Year's Worth)
SHORT-TERM
0.1
1
2
3
4
5
6
7
8
9
10
15
20
30
40
50
Medical X-Ray (Chest)
(Also equivalent to 3,300 TSA Full Body Airport Scans!)
3 Mile Island Accident
(Avg dose recorded for people living within 10 Miles of the 3-Mile Island Nuclear Plant Accident of 1979)
Natural Radiation All People receive
(Avg per year, Cosmic: 0.79, Environment: 0.48, Food: 0.29, Human Internal: 0.84)
Natural Radiation in Special Locations
(High Altitude, High Mineral Concentration)
CT Scan (Brain)
CT Scan (Pelvis)
Average Exposure for a Uranium Miner
Airline Crew (New York to Tokyo-Polar Route)
CT Scan (Full Body)
10-50 EPA ACTION
Level at which EPA Protective Action Guidelines state that public officials should take emergency action when this is a probable dose to a member of the public from a nuclear accident.
Annual Limit Occupational (Radiation Worker)




60
70
80
90
100
200
300
400
500
600
700
800
900
1000
25,000
50,000
75,000
100,000
Mild Radiation Poisoning
Smoking
Light Radiation Poisoning
Radiation Workers
Risk of CANCER
Moderate Radiation Poisoning
200-400 Lymphoma Treatment
Severe Radiation Poisoning
50% Death from Radiation Poisoning
600 Typical Dose for Chernobyl Workers
Acute Radiation Poisoning
750 US EPA Maximum Total for
The HULK
Massive Radiation Poisoning
Hiroshima
COMA within Seconds, Death within Hours
Instant Death
WWW.CARTOONADAY.COM
2011
Fukushima
Emergency
150
Radiation Workers
At Fukushima
250
Radiation Workers
Reactor Radiation

Some simple exemple

a 'standard' Scintigraphy exam

	W_R	W_T	%
RX : 100 mGy / 50 cm^2 skin	1	0,01	30 %
^{131}I : 10 mGy / thyroïde	1	0,05	100 %

Effective dose = (100 x 1 x 0,01 x 0,30) + (10 x 1 x 0,05 x 1)

= 0,8 mSv

- Mammogram : 2 view x 2 breasts
- X ray with Q factor WR = 1
- Tissue weighting factor = 0,12
- Absorbed dose: 4 x 1 = 4 mSv
- Effective dose: 4 x 0.12 ≈ 0.5 mSv

- Mammogram exposure equivalent to whole-body dose of 0.5 mSv

Variation of natural radioactivity

- Cosmic rays
  - sea level 0,25 mSv / year
  - Mexico (2240 m) 0,80 mSv / year
  - La Paz (3900 m) 2,00 mSv / year
- External exposure due to earth exposure
  - average 0,9 mSv / year
  - Espirito Santo (Bresil) 35 mSv / year
  - Maximum (Iran) 100 mSv / year
  - Marseille (France) 0,20 mSv / year
  - Limousin (France) 1,20 mSv / year
- Internal exposure due to water
  - Evian water 0,03 mSv / year
  - St Alban water 1,25 mSv / year

Most radioactive place in the world: Ramsar, Iran

Background radiation: 100- mSv / year due to ^{226}Radium

No epidemiological evidence of adverse affects

Residents demonstrate a marked increase in DNA repair capacity

Proposal: to relocate the inhabitants (2000) to a lower radioactive area!

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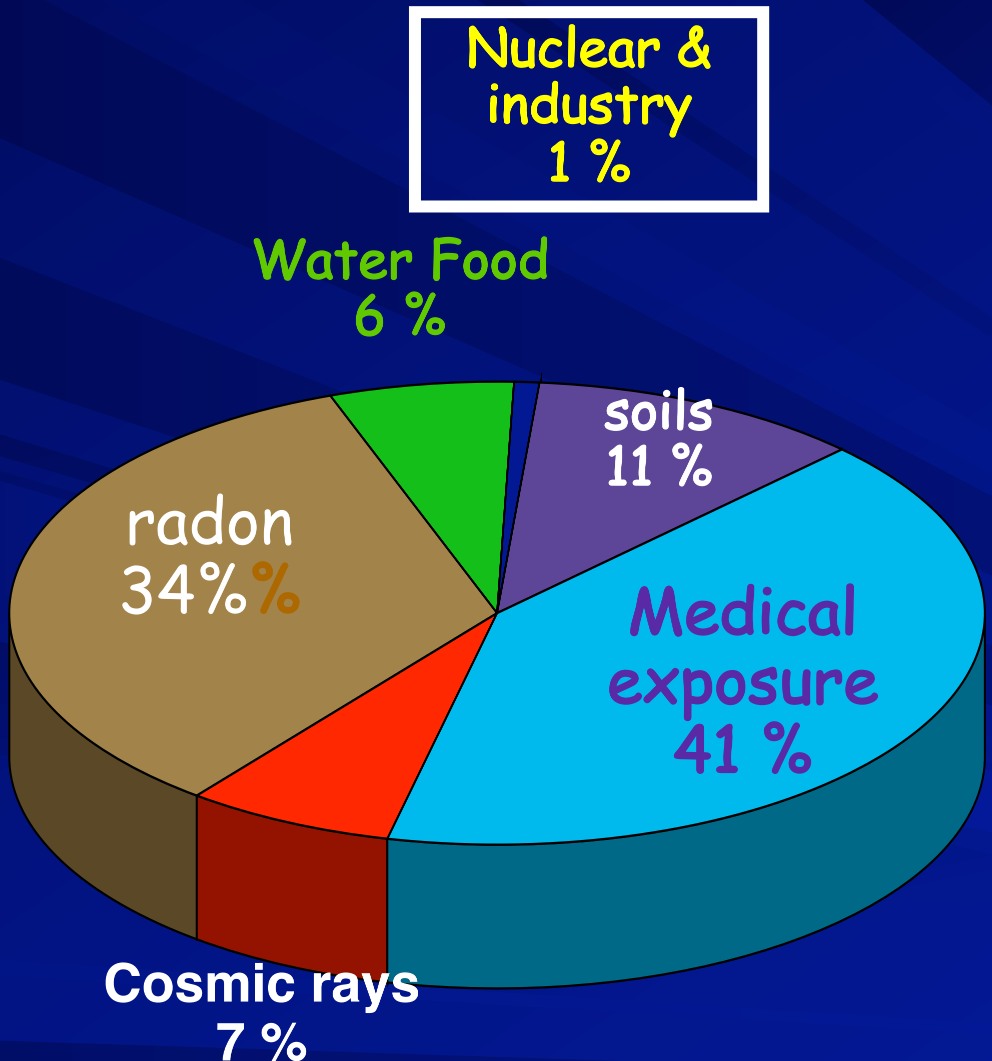
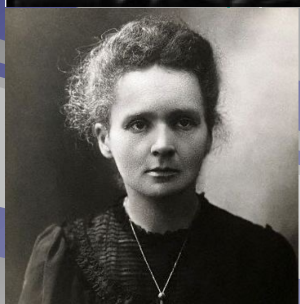
Main sources of ionizing radiation



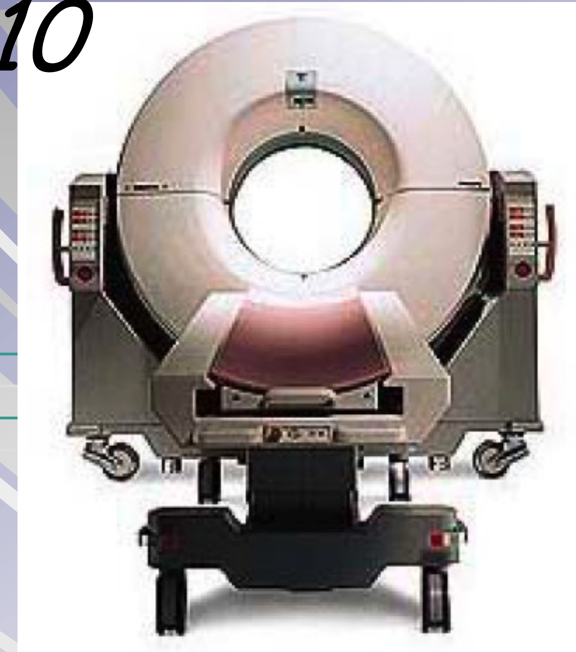
- Earth has been radioactive ever since its formation into a solid mass over 4½ billion years ago. However, we have only known about radiation and radioactivity for just over one hundred years...

Conclusion & question ?

- Sv= Unit well adapted to radioprotection
- However : why this official' limit of 1 mSV/ year is so low ?
  - No sanitary argument : industrial irradiation :10 -15 μSv
  - Interpretation of the 'low' absolute value might be controversial!
- Do not take into account debit and age ..an personal sensitivity, instant vs integrates
- The total radiation accumulates along the full life
  - At 70's I have received certainly 200—300 mSr ?



2010



Radiology

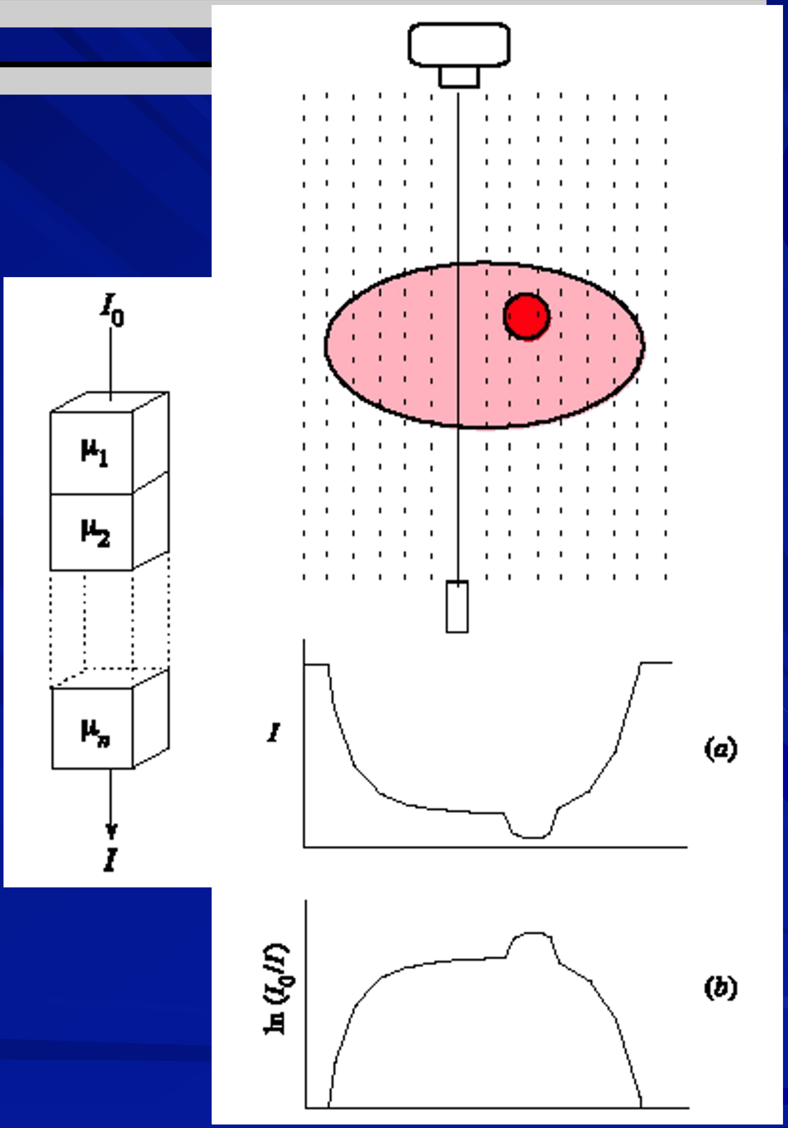
Common tools & techniques

Radiology principle

- The most common exam
- Transmission of X rays through tissue

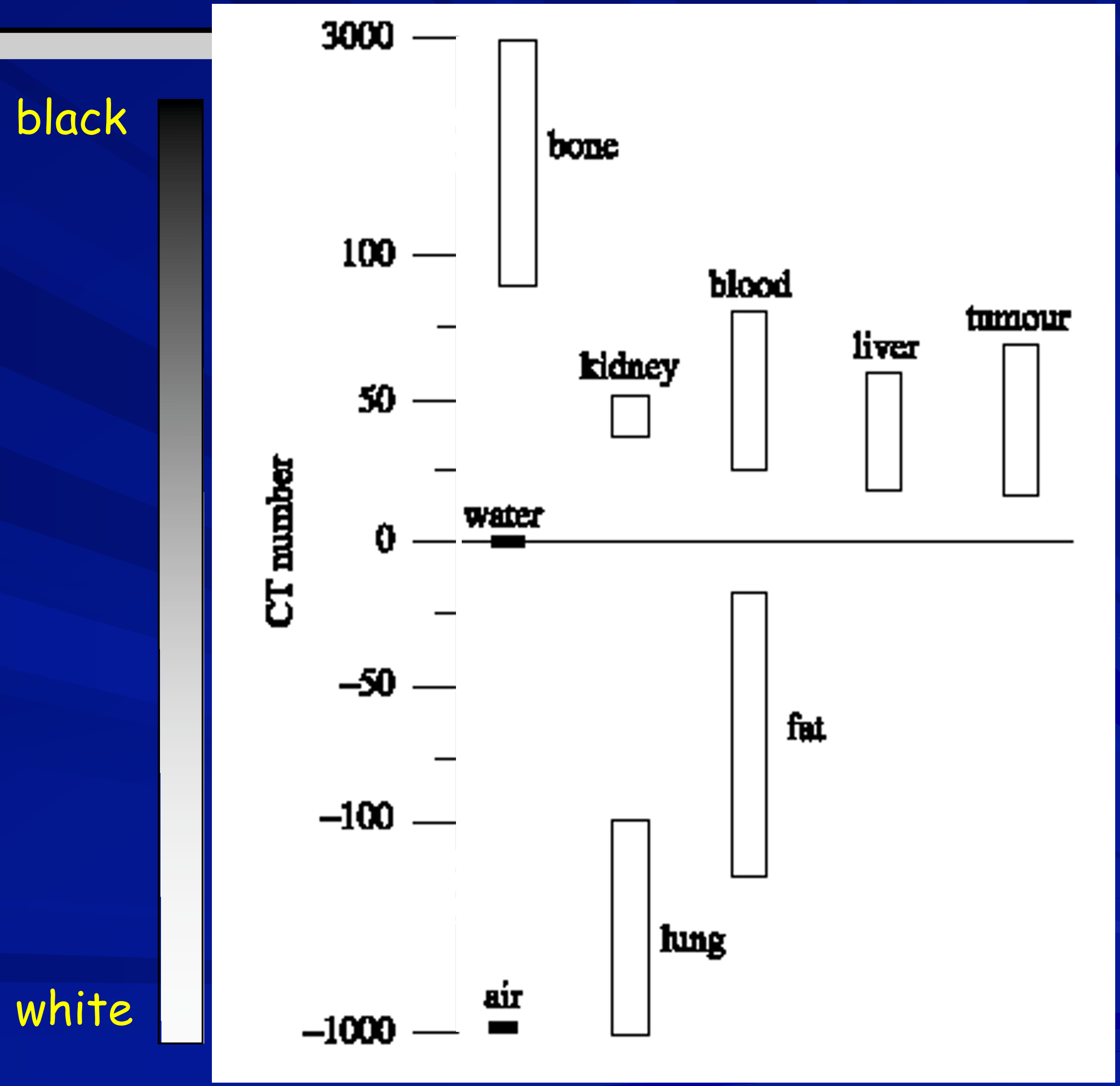
$$I = I_0 \, exp\left(-x \sum_{i=1}^{n} \mu_i\right)$$

$$\ln \frac{I_0}{I} = x \sum_{i=1}^{n} \mu_i$$



Radiology problem = contrast

- How to get the best contrast?

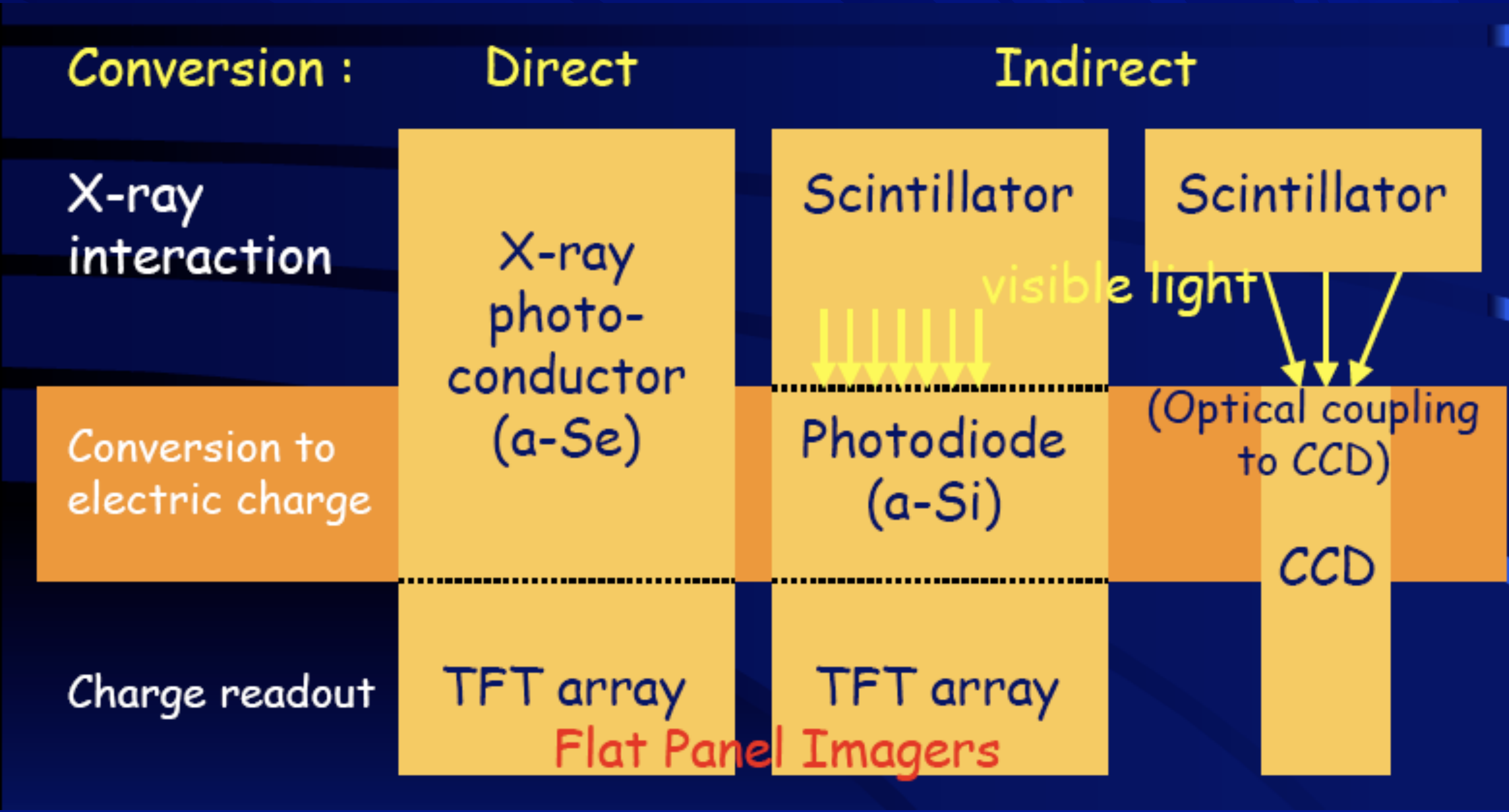


Detection techniques

- The standard : film scren system
- How to replace the film
  - More sensitive --> better contrast
  - Less dose
  - Affordable ?

Type of detector	Dynamic range
film-screen system	30:1
image intensifier	100:1
CCD detector	1000:1
flat panel detector	10,000:1
computed radiography	40,000:1

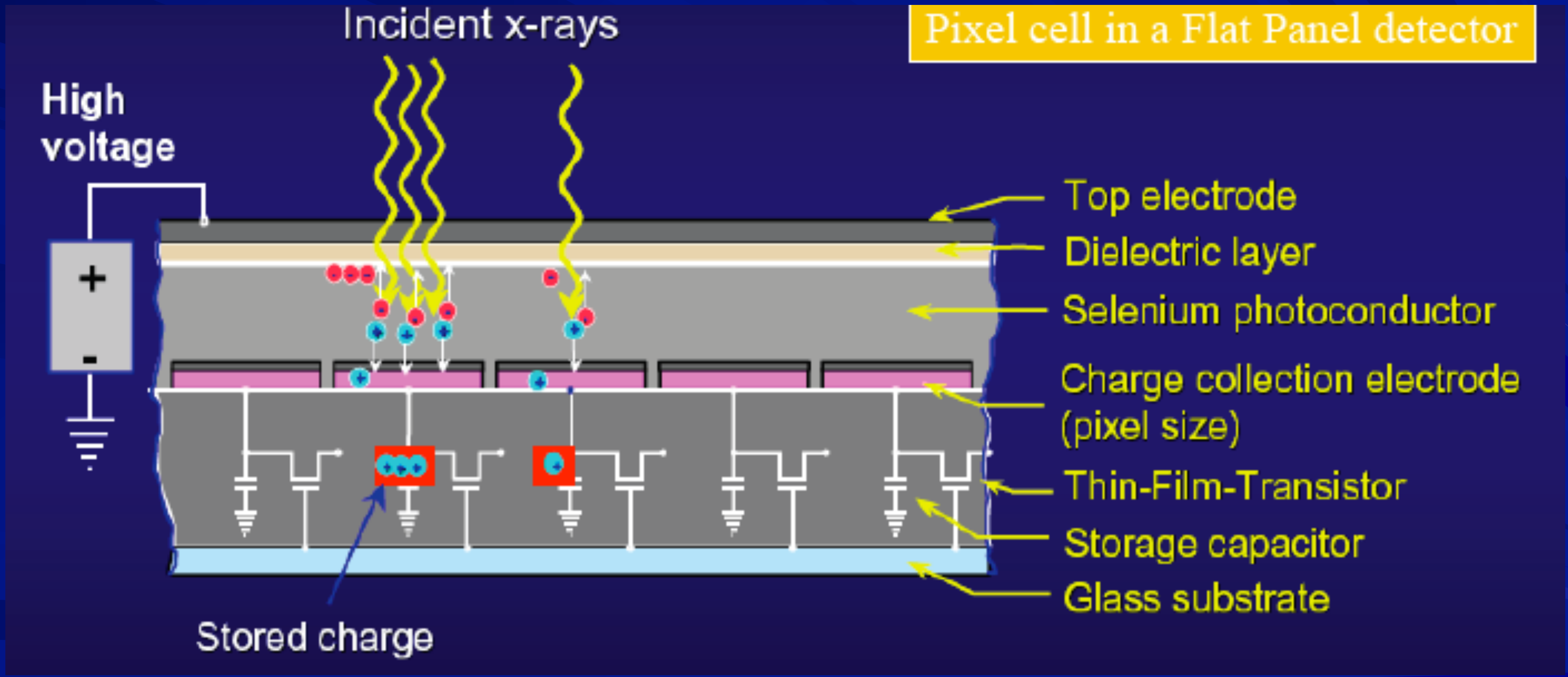
Radiology survey of electronically readable detectors



Radiology: Flat panel direct detection

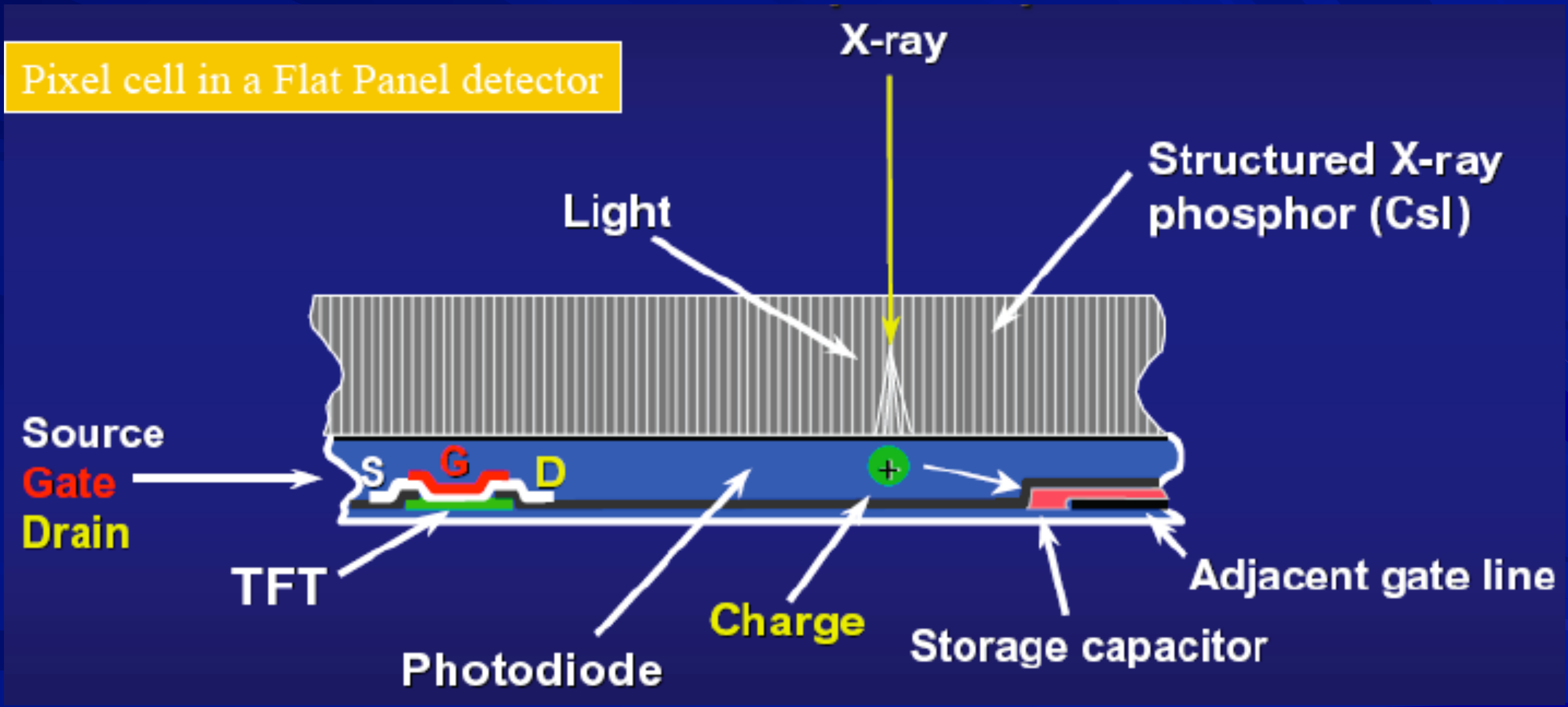
- Xray ---> electron --> electric signal

Selenium



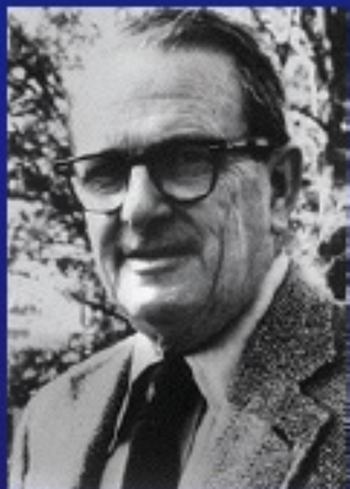
Radiology :Flat panel indirect detection

- Xray -->Light--> electron ---> electronic signal

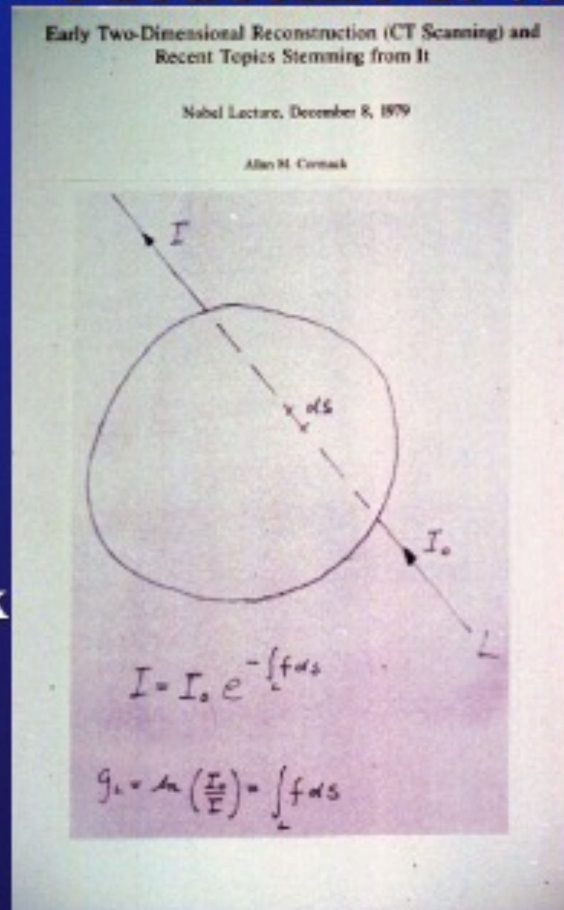


State of the art :Computed Tomography (CT)

Nobel Price Physiologiy and Medecine 1979



Allan MacLeod **Cormack**
Physicien Nucléaire
Cape Town
Harvard University
Tufts University



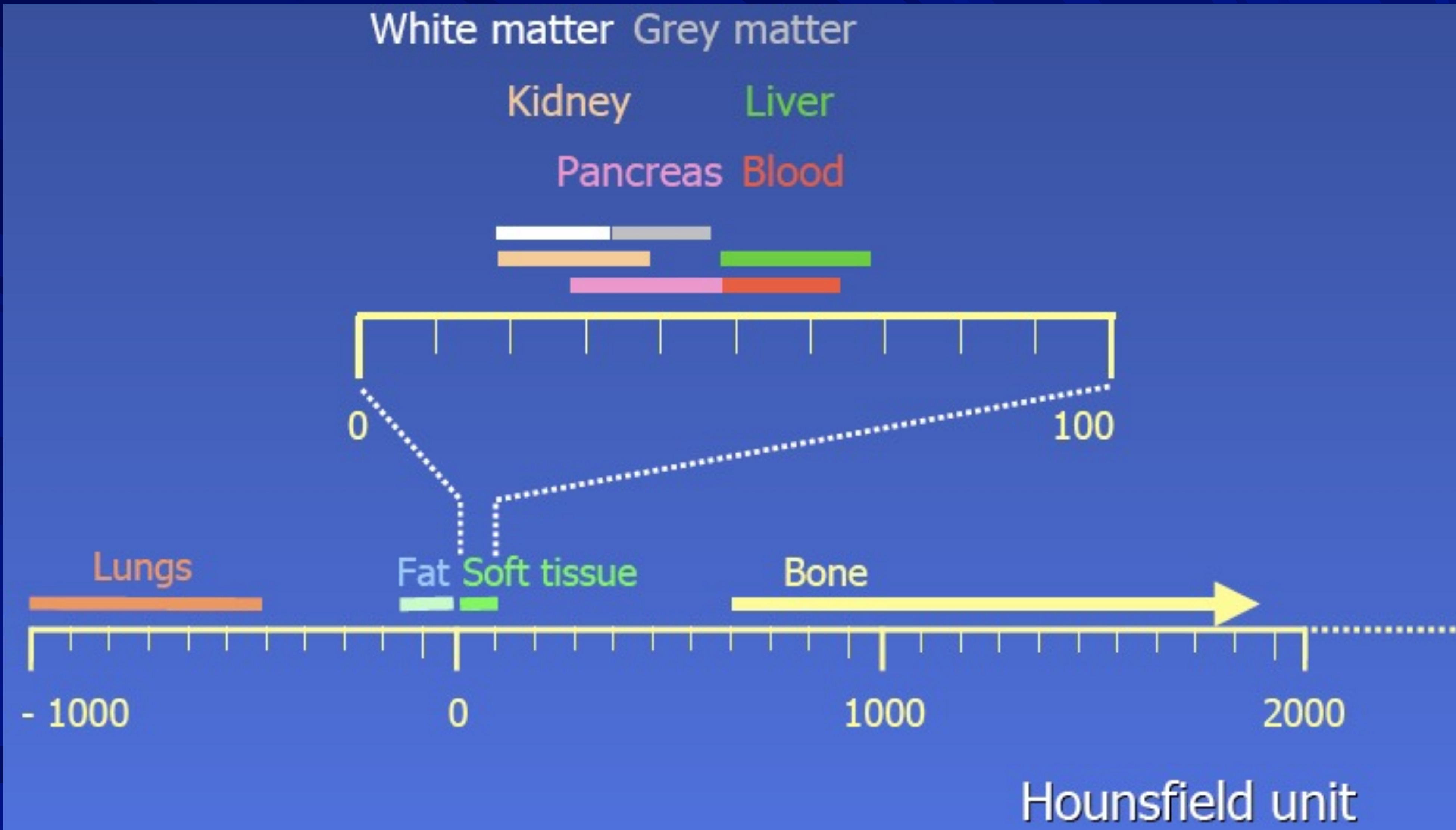
Early Two-Dimensional Reconstruction (CT Scanning) and Recent Topics Stemming from It

Nobel Lecture, December 8, 1979

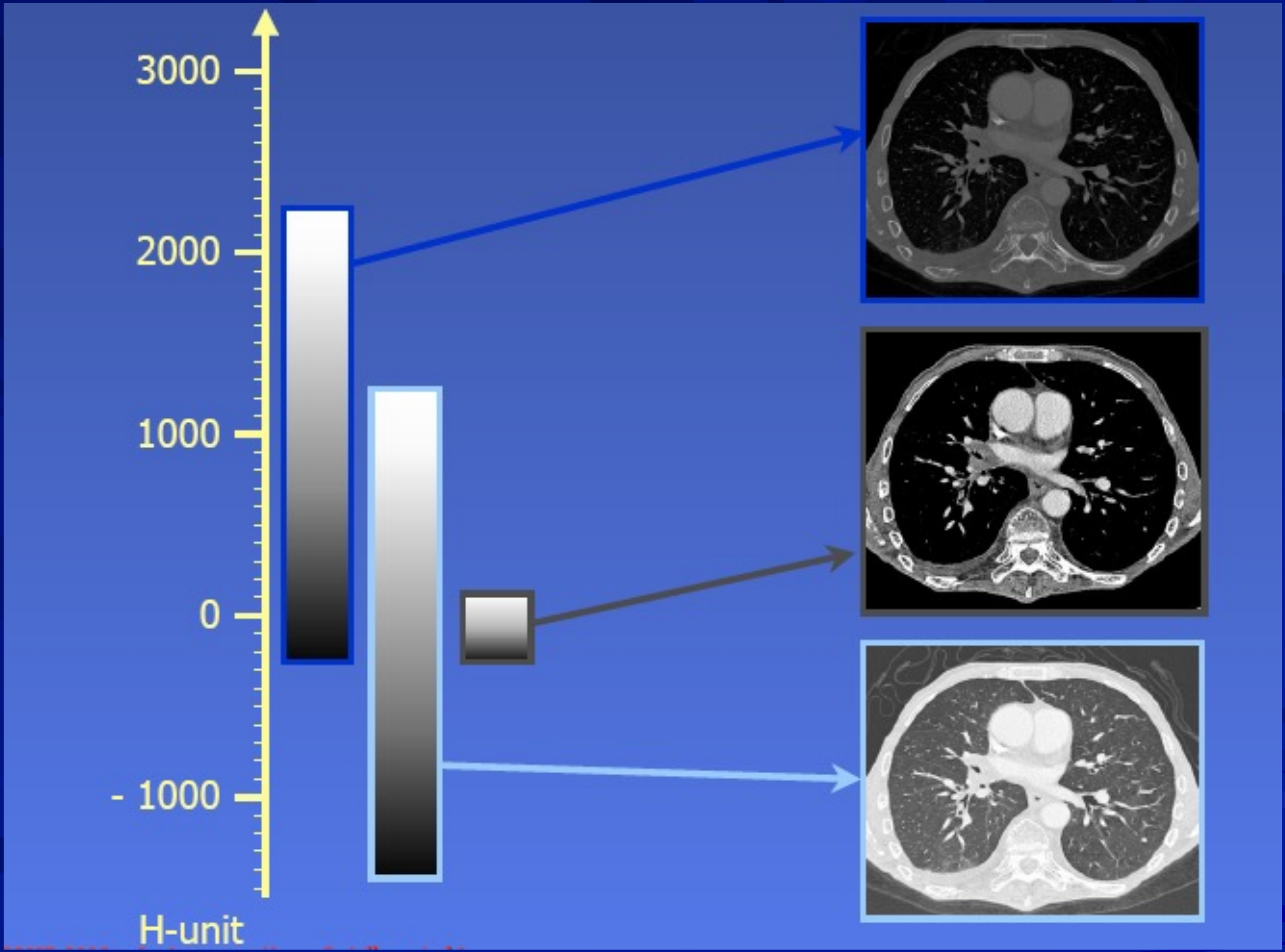
Allan M. Cormack

Sir Godfrey N. **Hounsfield**
Electrical engineer
EMI Research

Contrast (Houndsfield) units

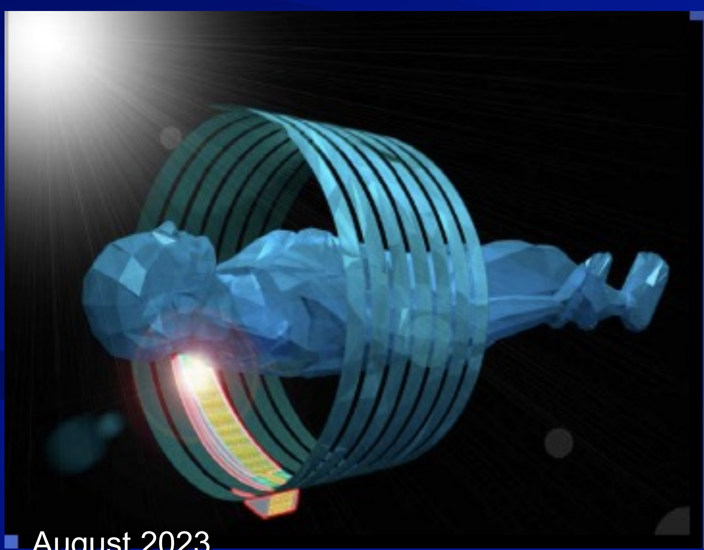


From Hounfield units to image



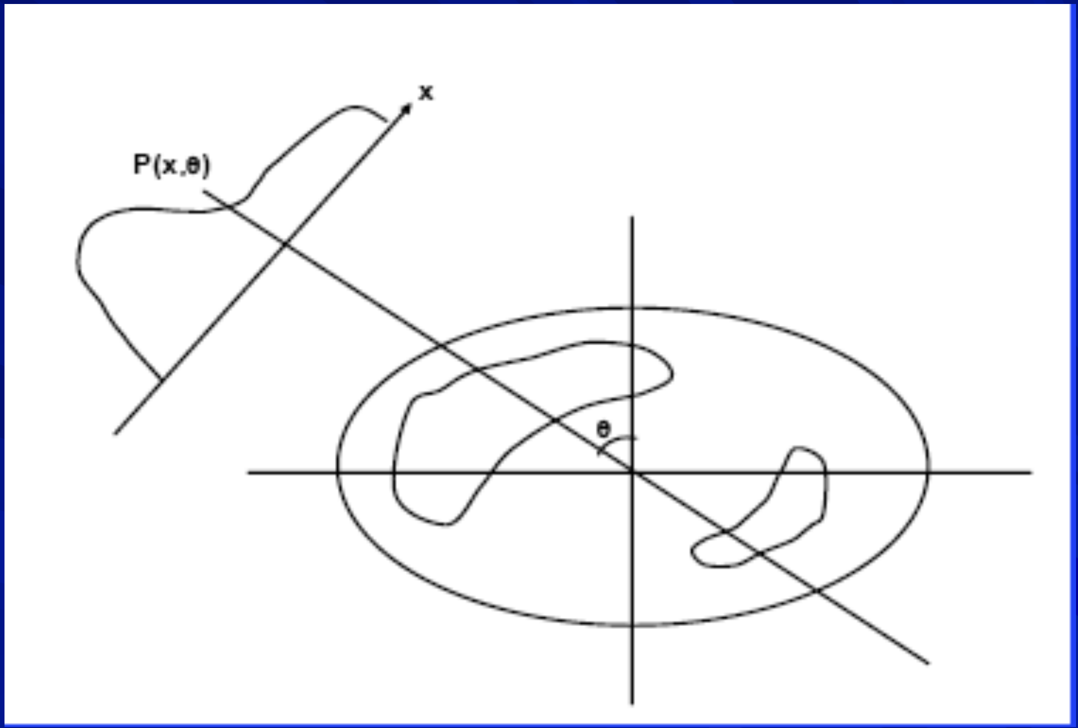
CT Scaner principle

- Spatial resolution and speed
  - 64 … 320 detector rows
  - Slice thickness 0.33 … 0.6 mm
  - Tube rotation time 0.3 s
    - Organ in a sec
    - Whole body < 10 sec
  - dual source (180° → 90°)
  - Volume coverage with one rotation: 4 … 16 cm



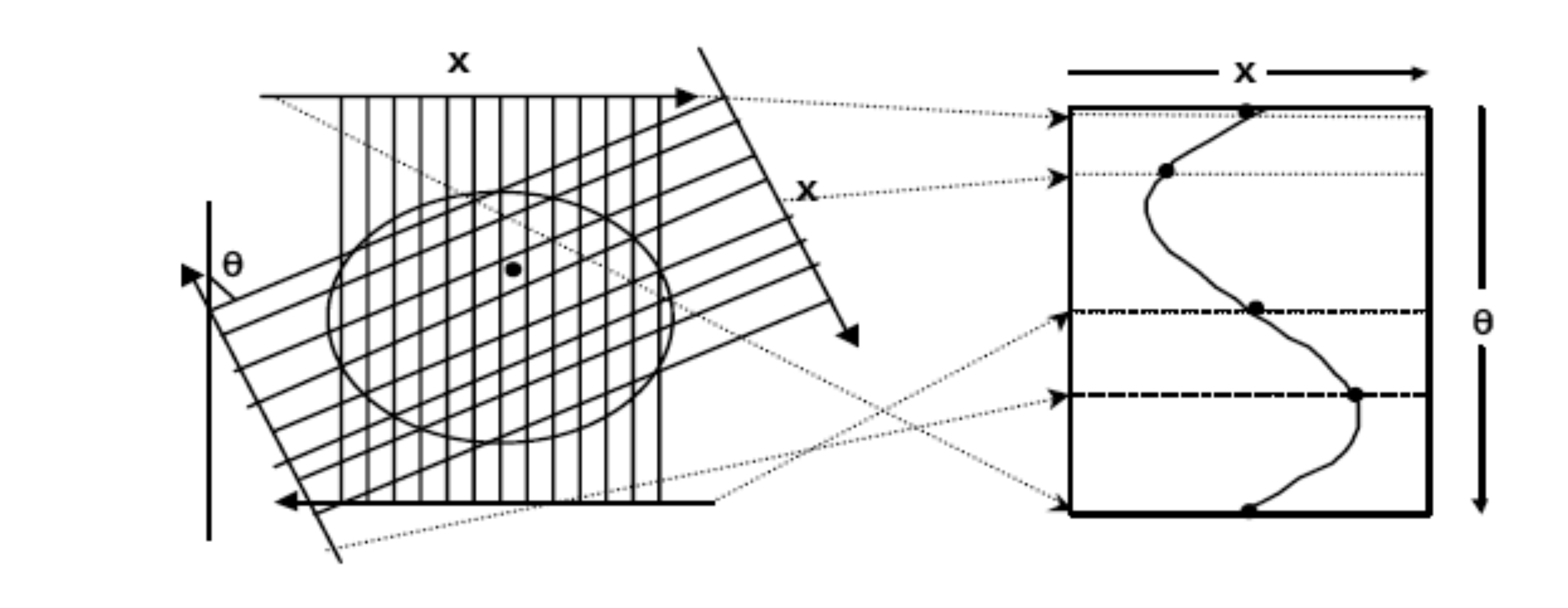
Computed Tomography
Basic method of Image reconstruction

- Take 1D profiles or 2D projection at discrete angle around the object
- Assume that each measured point = sum of actvity elements along the Line of Response (LOR)



Raw data can be displayed as a 'sinogram'

Computed Tomography
Basic method of Image reconstruction



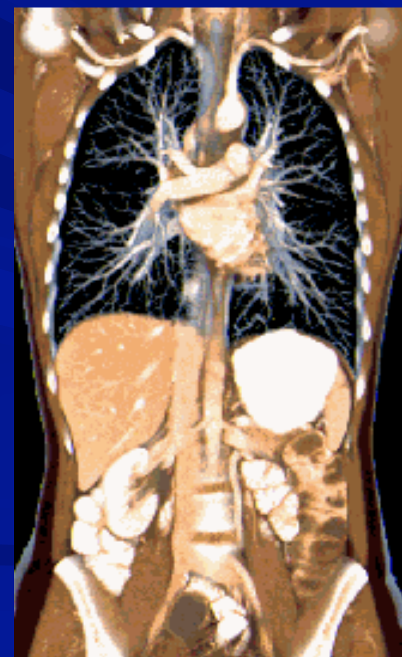
Projection

Sinogram

Raw data can be displayed as a ‘sinogram’
Then a lot of corrections …..

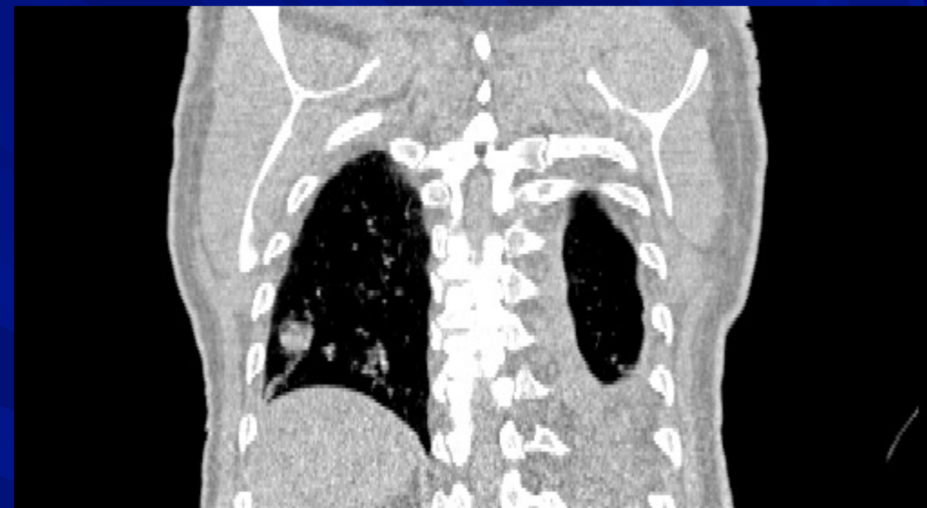
Computed Tomography scaner (CT)

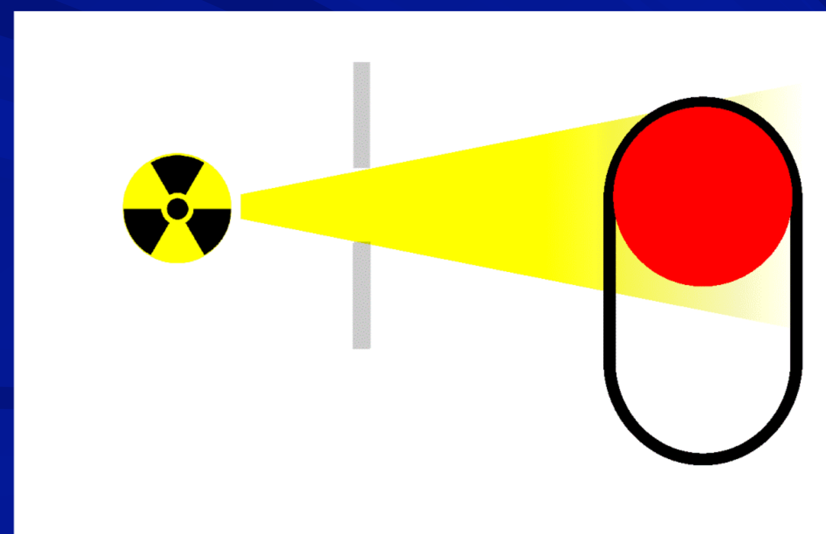
- The best device widely used for precise exam
  - Whole body
  - Cardiology
- Still a lot of radiation full body CT = 4-10 mSv (depending organ)
  - Standard radiography = 0.1 mSv



State o the art : 4D CT

- Position influenced by the breathing motion



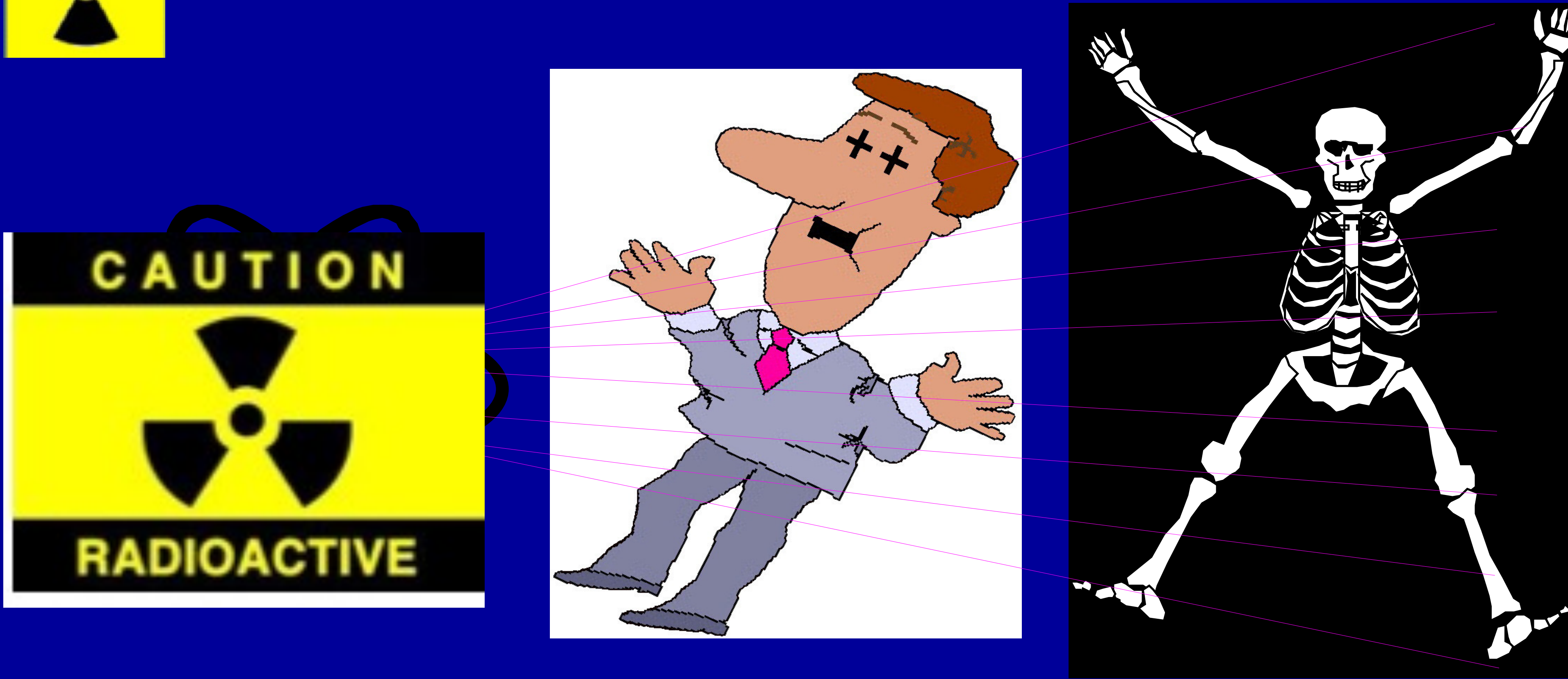


Exposure for radiological exams

- Some examples

organ	dose skin mGy	effective dose mSv
Thorax, face	0,2 - 0,5	0,015 - 0,15
Lumbar region	4 - 28	1,5
Urography	40 - 60	3
Brain scan	7 - 78	1
Whole Body scan	30 - 60	4 - 10
Mammography	7 - 25	0,5 - 1

Patient Radiation Dose is Limited!

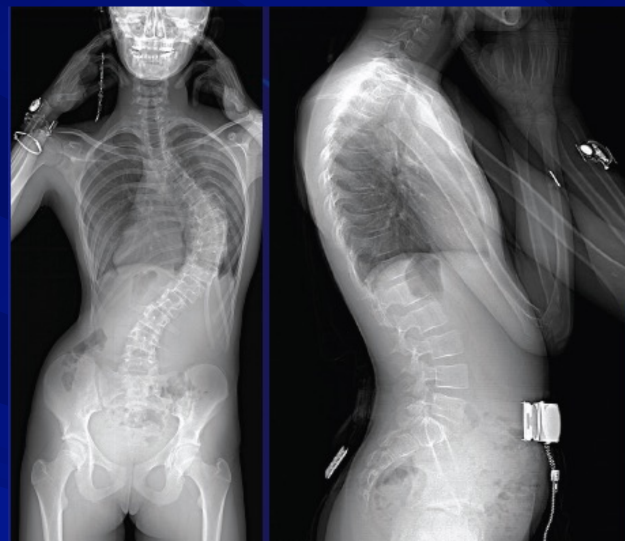


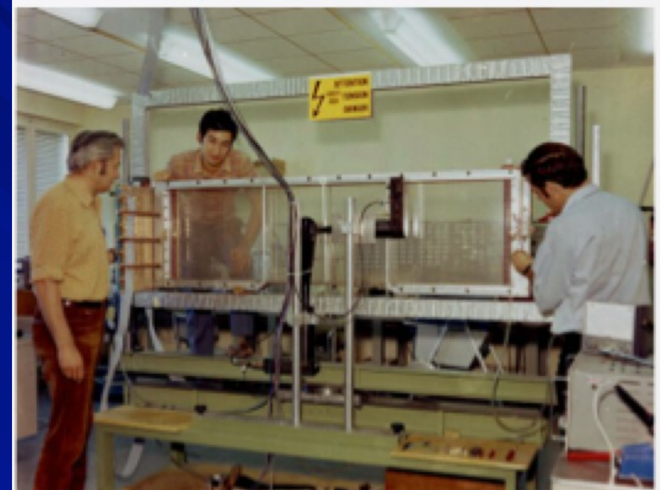
- Image Noise Is Limited by Counting Statistics
- Cannot Increase too much Source Strength
- See the BU slides about how to decrease the dose using gaseous detetors

Deacreasing the dose with HEP Gazeous detector

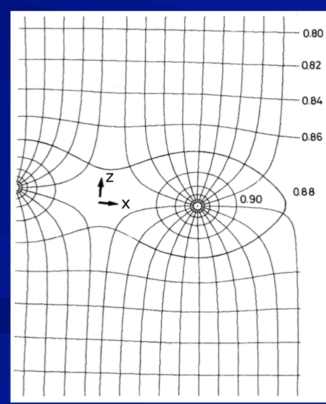
The 1970's dream : Digital radiography with MWPC
A tribute to George Charpak

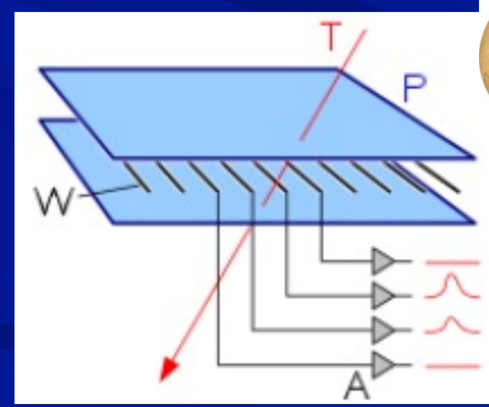
- With 10 time less dose





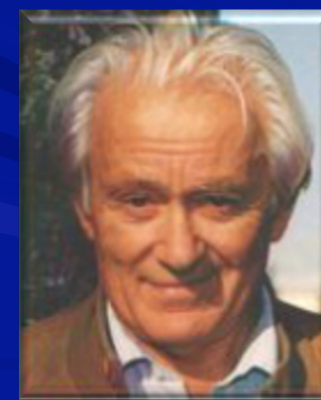
G. Charpak, F. Sauli and J.C. Santiard





Multiwire Proportional Chamber
1968

1992

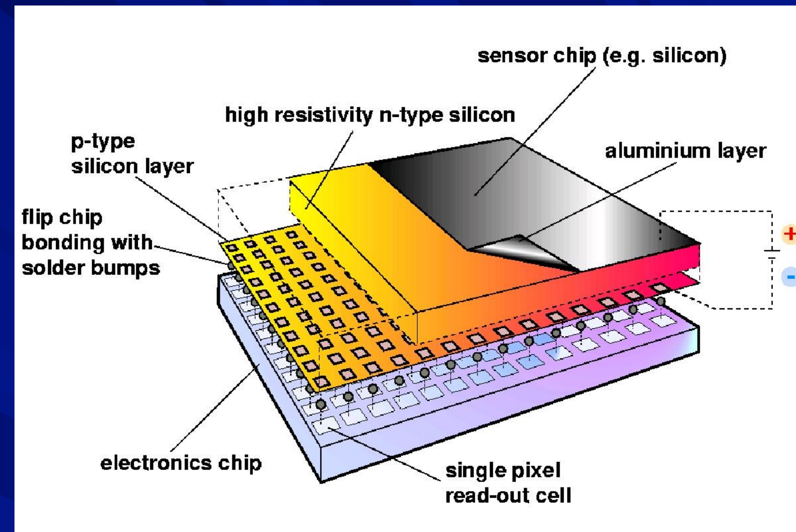


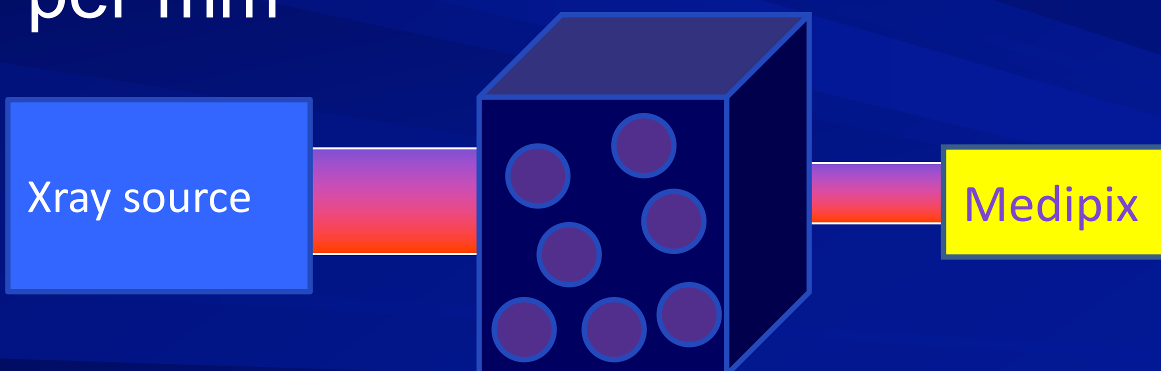
Georges Charpak
1924 - 2010

The Future ?: New Si detector and signal processing On the way to photon counting?

Medipix3

- 8 simultaneous energies
- 55 µm isometric resolution
- Excellent energy resolution
- 10^8 photons per second per mm^2



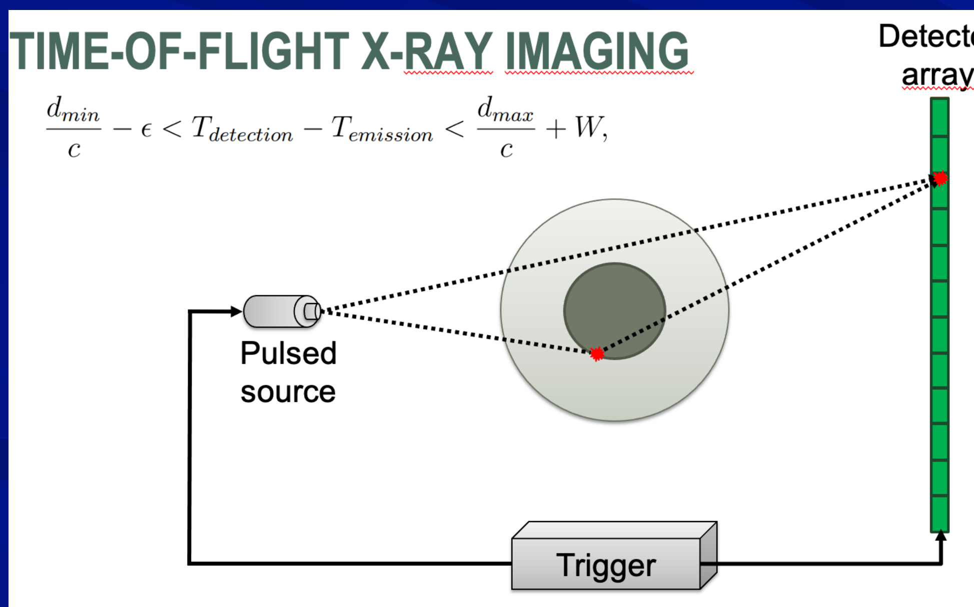


Jacubek & al. Prague University

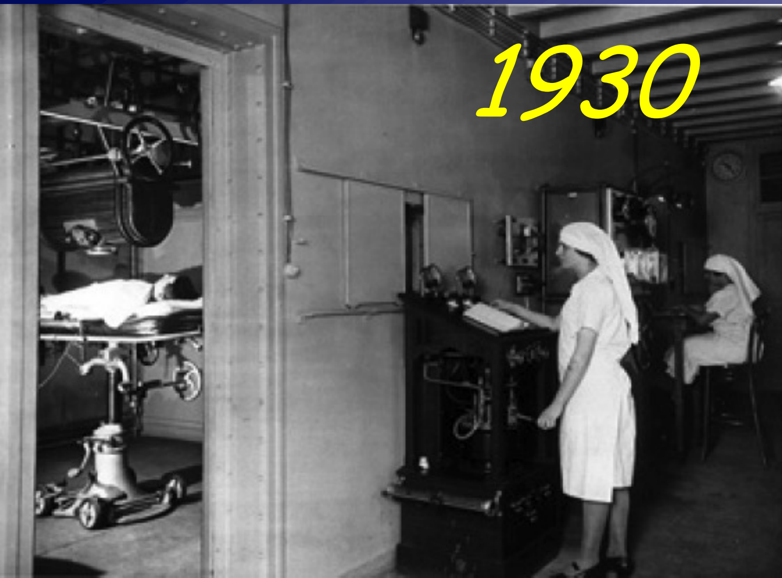
See presentation of Stanislav Pospisil about Timepix

Time Of Flight X ray imaging

- Time-of-flight gives significant insight on scattered photons in x-ray imaging
- 10 ps total timing (source + detector) required for optimal performance.
- Potential to reduce the radiation dose in X-ray imaging

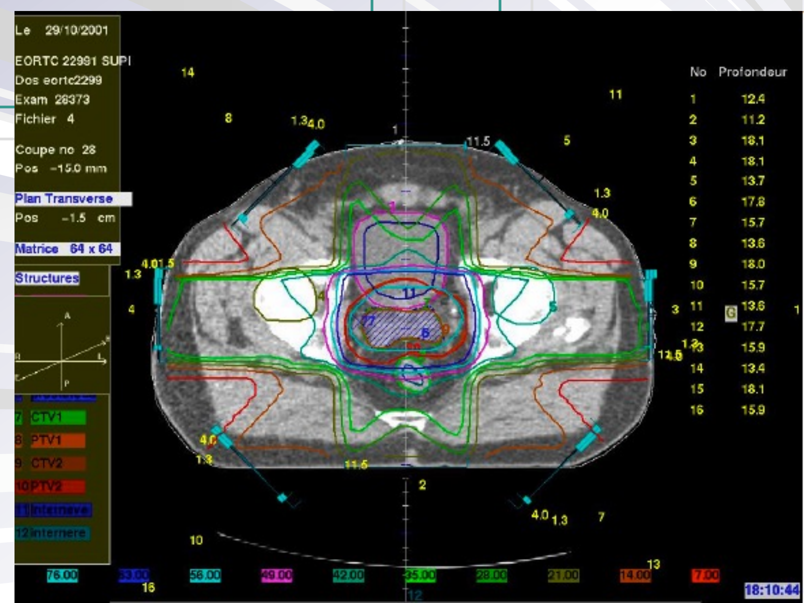


Very Preliminary
Courtesy of Sherbrooke University



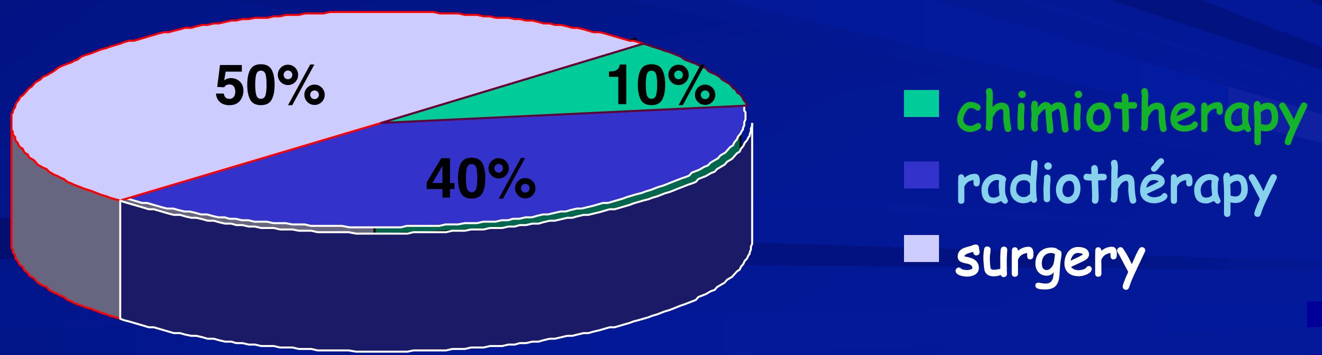
Radiotherapy

Common tools & techniques



Fight again cancer - Radiotherapy

- Local irradiation to kill tumour → 100 Gy = 90 % of sterilization
- Frequent treatment (2/3 of cases).
- Efficient treatment: cure → 40 to 50% of recovery
- Allow good quality of life and tolerance
- non invasive, itinerant and without important physical effects.
- Cheap (< 10%) of the cancer budget (France)
- Essentially X rays
  - (Linear accelerators) & photons (curietherapy)



RT modern techniques

- Conformal RT
- Intensity Modulated (IMRT)
- Image guided (IGRT)
- Robotic Stereotactic

PORTAL IMAGING

VERY HIGH RATE GAMMA RAYS DETECTION and measurement

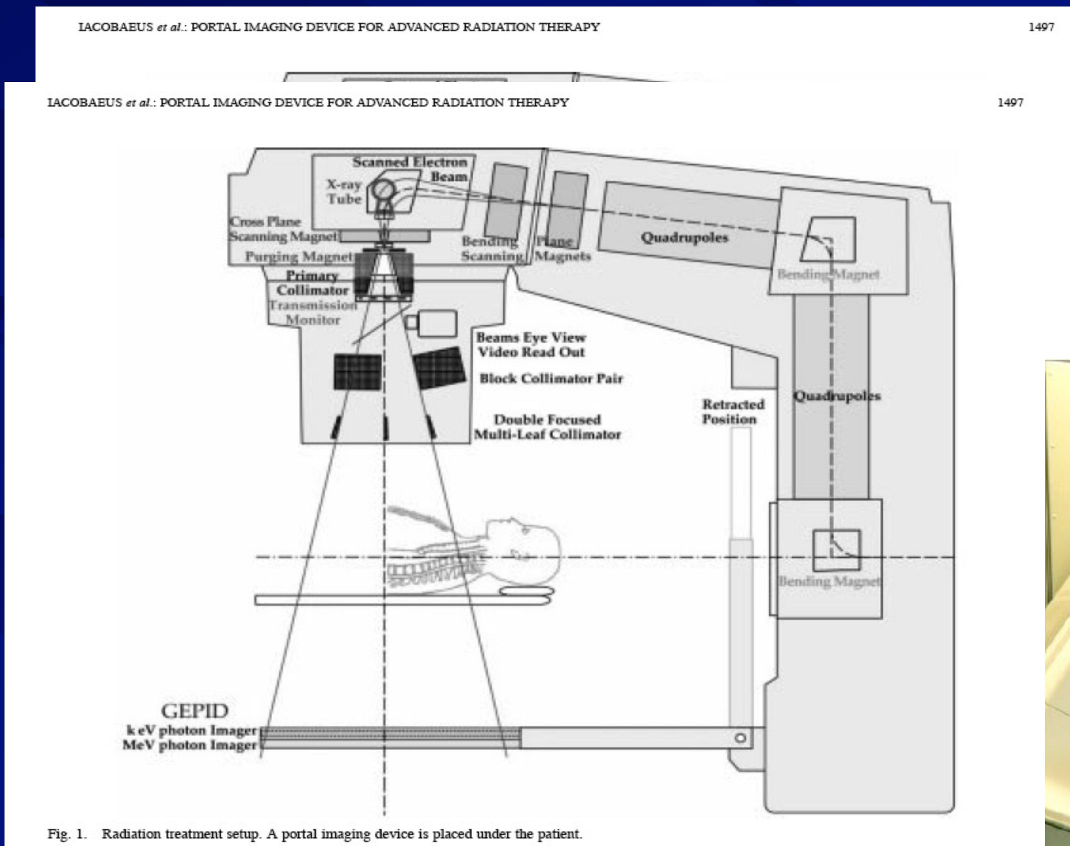

IACOBAEUS *et al.*: PORTAL IMAGING DEVICE FOR ADVANCED RADIATION THERAPY 1497

Fig. 1. Radiation treatment setup. A portal imaging device is placed under the patient.

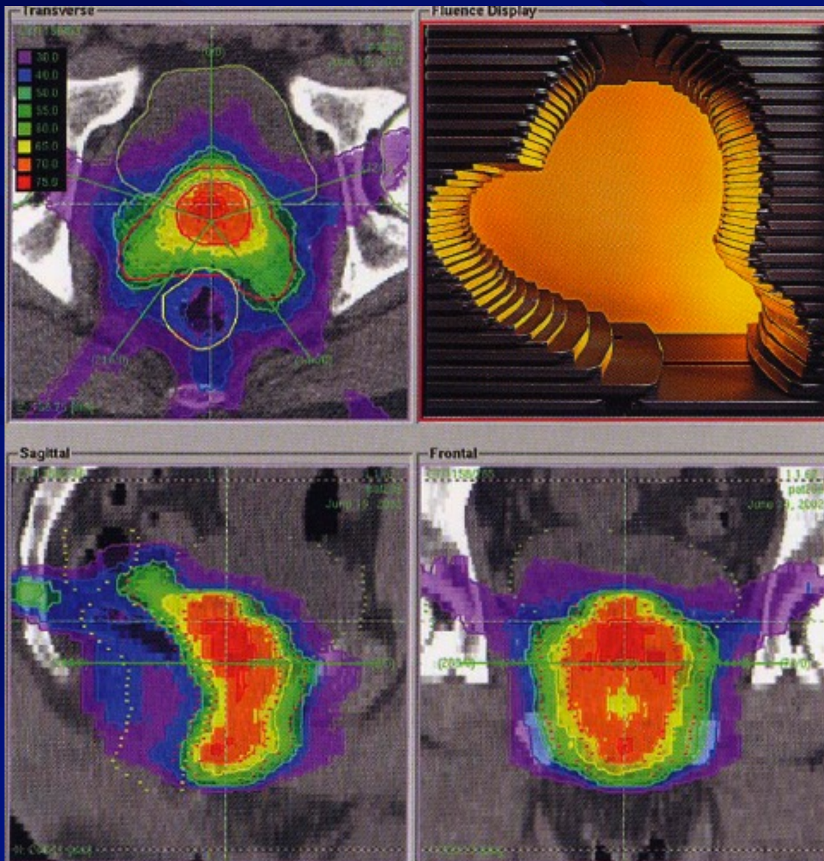
Real Time Imaging
and Dosimetry

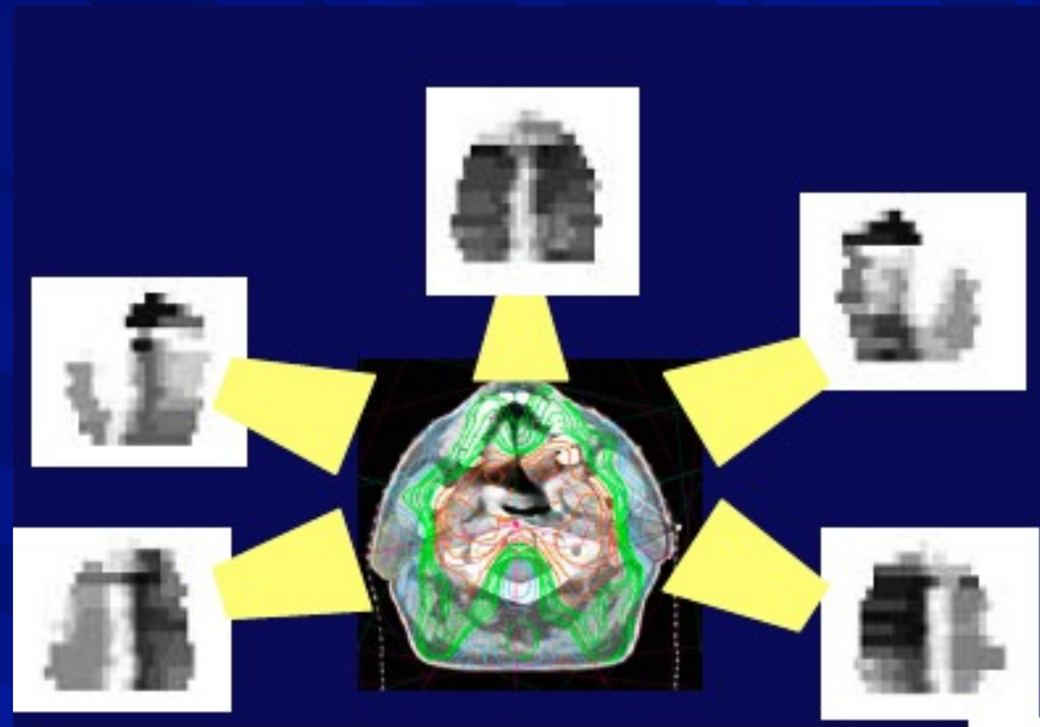
GEM-BASED PIXEL DETECTOR

ROYAL INSTITUTE OF TECHNOLOGY AND KAROLINSKA HOAPITAL (STOKHOLM)

C. Iacobaeus et al, IEEE Trans. Nucl*. Sci. NS-48 (2001)1496*

'standard' RT devices

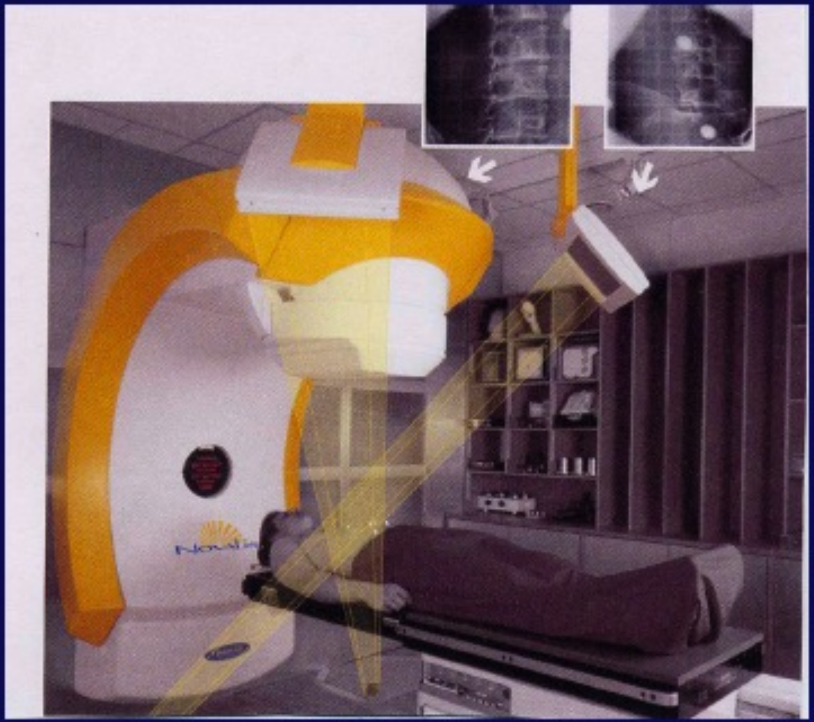


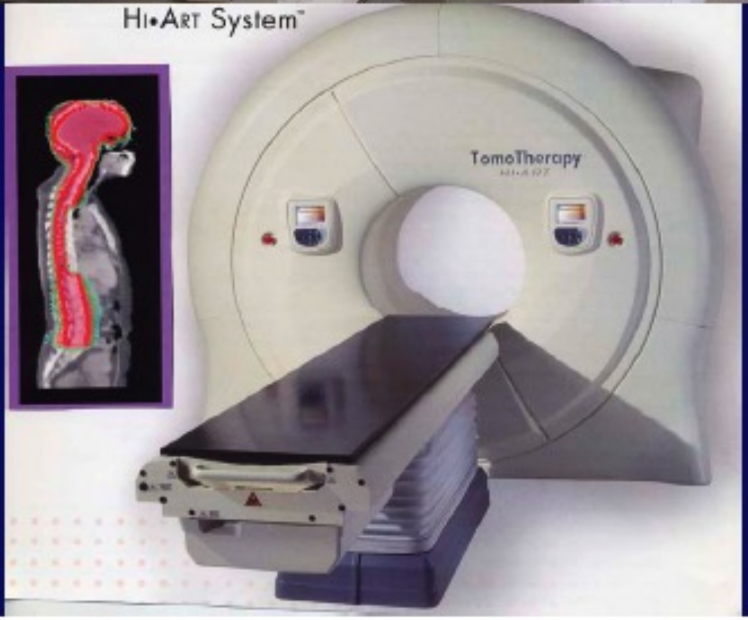


Intensity Modulated (IMRT)

Conformal 3D radiotherapy

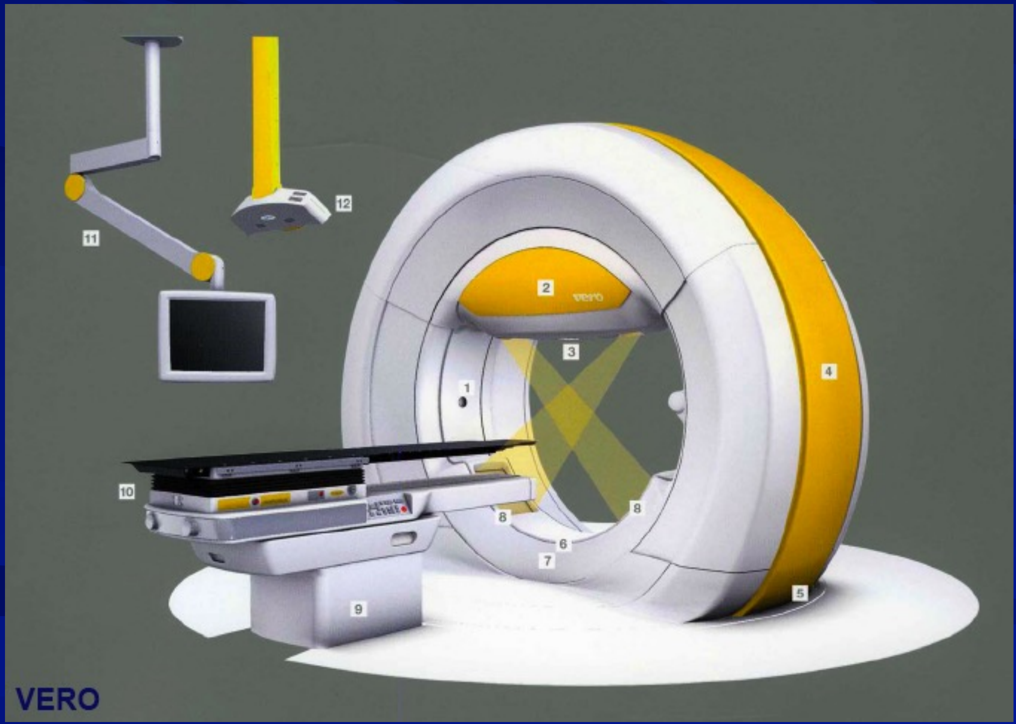
IGRT : Image guided

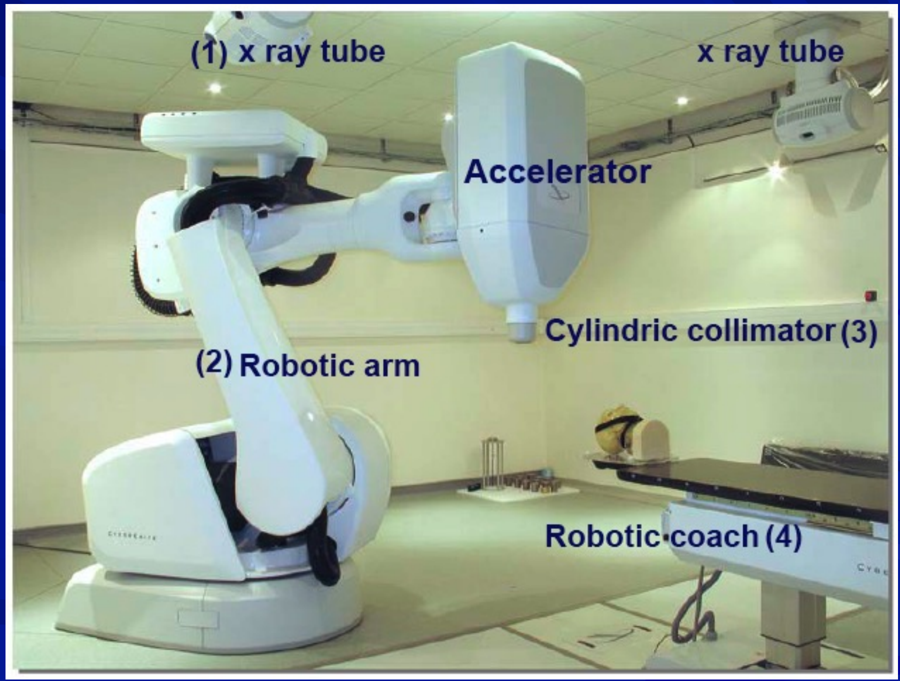




State of the art: Robotic Stereostatic RT

- Multiple beams and radiation sources (Co^{60})
- High Precision 1 mm
- Dedicated & invasive (radiochirurgy with Co^{60})





Cyberknife ™

Radiatherapy X

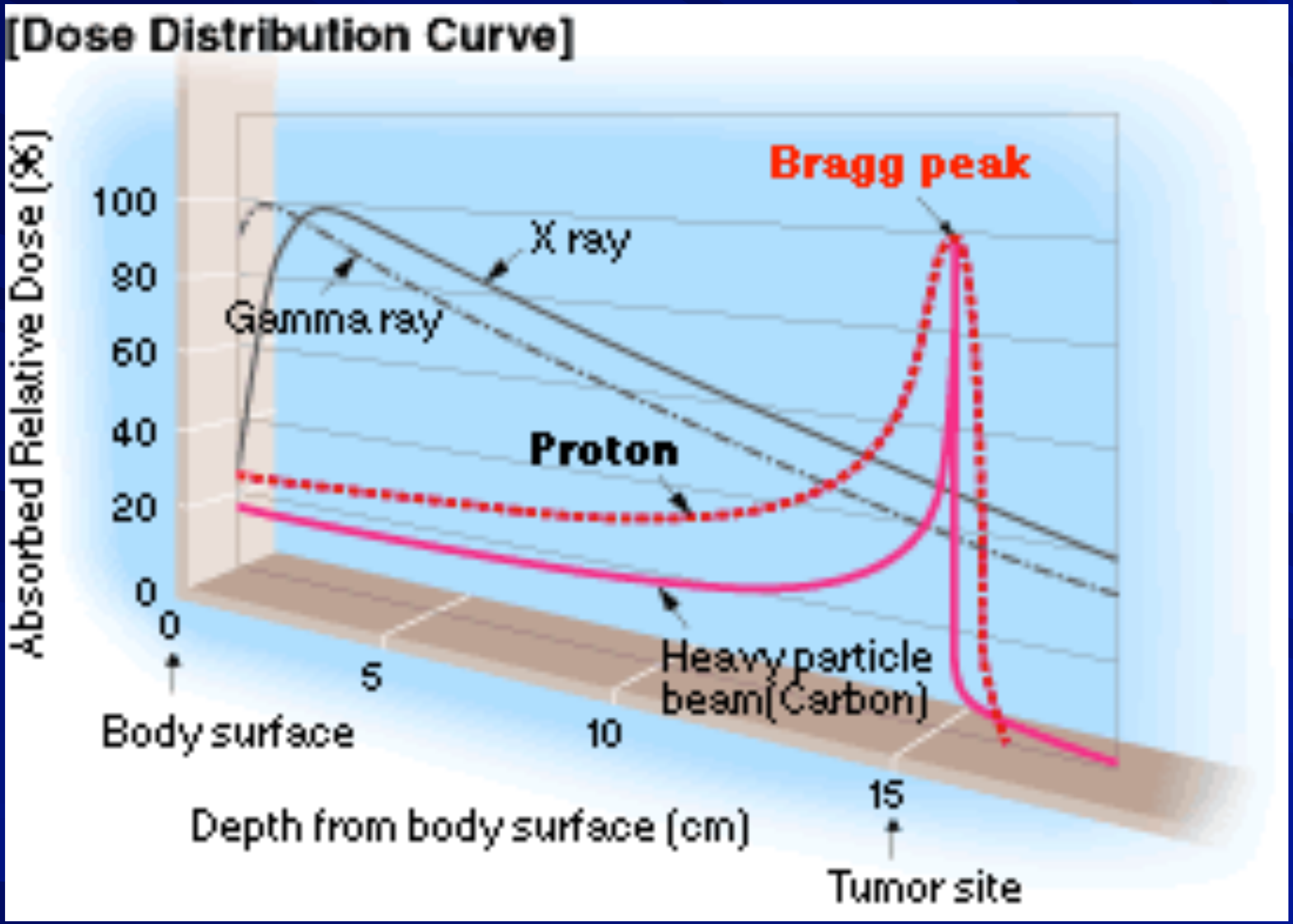
- No substitute for RT in the near future
- Number of patient increasing
- Present limitation of RT→ 30 % of patients recurs
- Why Radiotherapy X is NOT 100 % efficient?
  - Complication < 5 %
  - Tolerance of saine tissue is the limiting factor
    - Close to Organ at Risk
  - Failures due to radioresistant tumors!
  - Second cancer 30 years after Radio Therapy (from recent statistics)
    - Adult : 1.1
    - Chidren : 6

→Particle therapy
→Around 25% of the case

Today

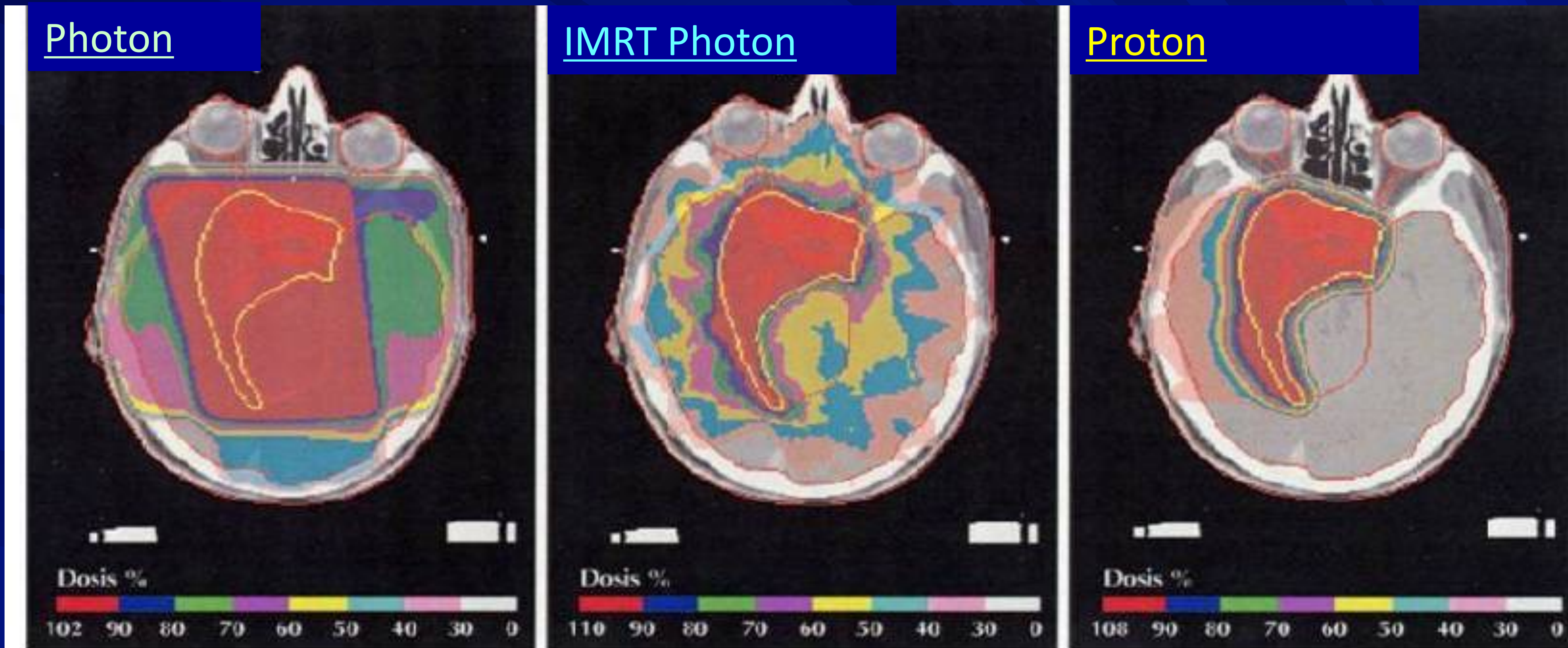
From radiotherapy to Particle therapy

Why use Hadrons for Therapy?



- Most dose is deposited in the sharp "Bragg Peak", with no dose beyond
- Escalate the dose in the tumor
- Reduction of dose in surrounding normal tissue

Comparing Proton and conventional RT

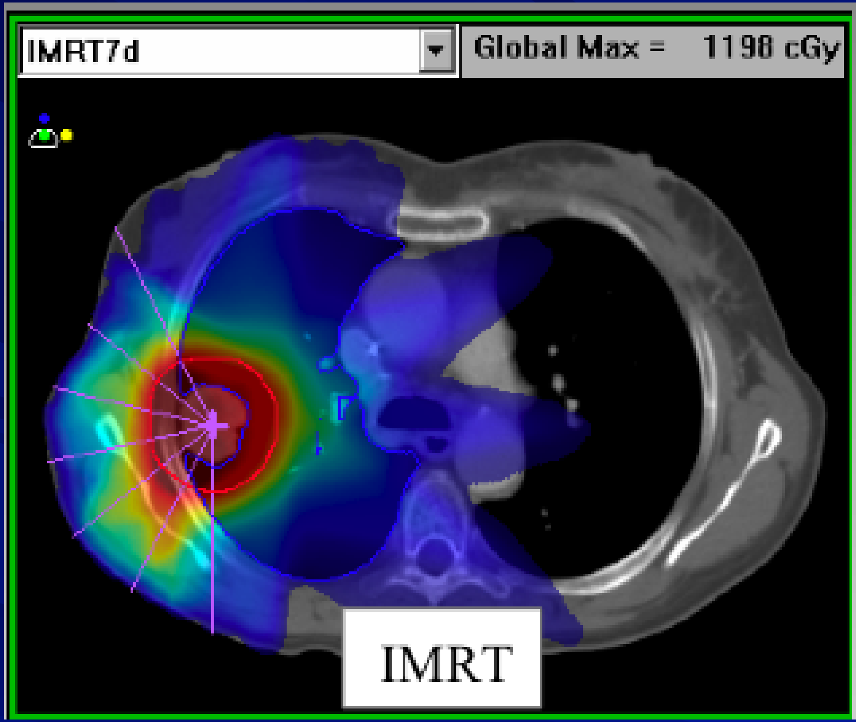


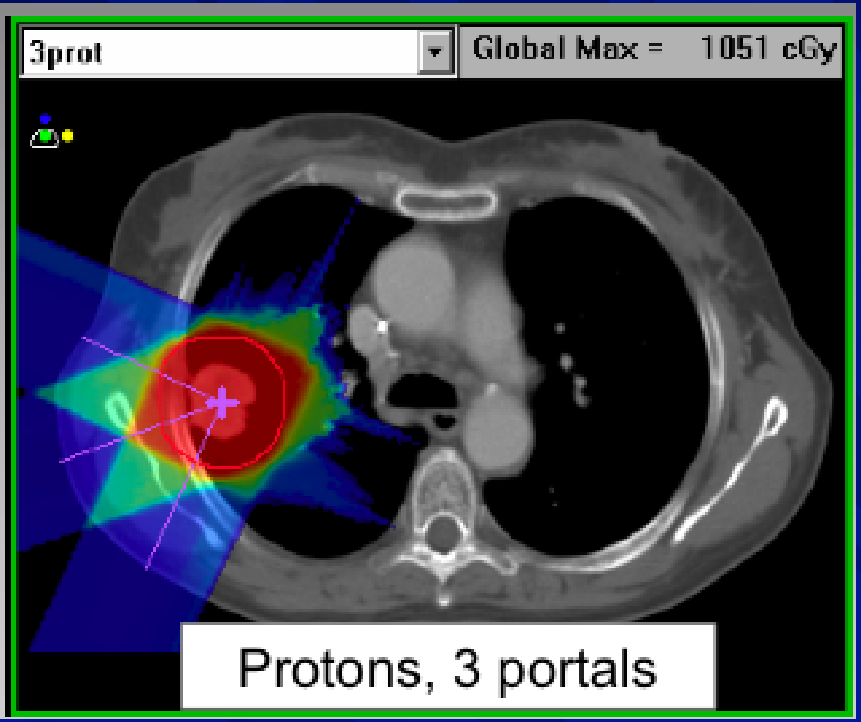
Conventional Radiotherapy:
Important dose outside the tumor

IMRT = Intensity Modulated Radio Therapy:
still non negligable dose outside the tumor

Scattering technique :
Low dose outside

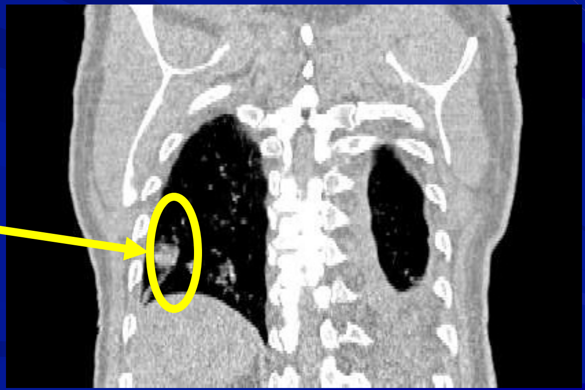
Comparison IMRT-Protons





What are the critical issues & challenges?

- This is NOT a 'simple target' but a human body
  - Treatment and quality assurance techniques of conventional radiotherapy not adequat for particle therapy
    - A complex procedure for the 'treatment planning'
- How to be sure that the dose is delivered at the right place (tumour) ?
  - Particle beam are error sensitive
    - Displaced organ & overdose
    - Moving organ in some case



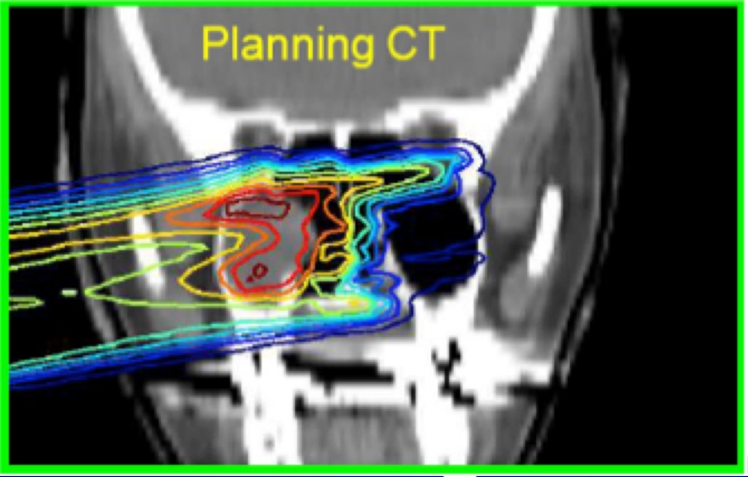
What is the dose deposited ?
How to verify the treatment?

The two 'simultaneous' challenges

- Reducing error means → Real Time imaging
  - 3D in vivo dosimetry and tomography
    - *Use fragments of beam projectile reactions in the biological matter emerging from the tumor target volume*
- Verification using Computed Tomography/Radiography:
  - CT imaging in charged Particle therapy is needed for:
    - Target volume definition (anatomical boundaries with additional information from multimodality imaging (CT/MRI/PET studies)
    - Dose and range calculation
    - Patient alignment verification

But today these process are made at different moment and place

Particle therapy workflow

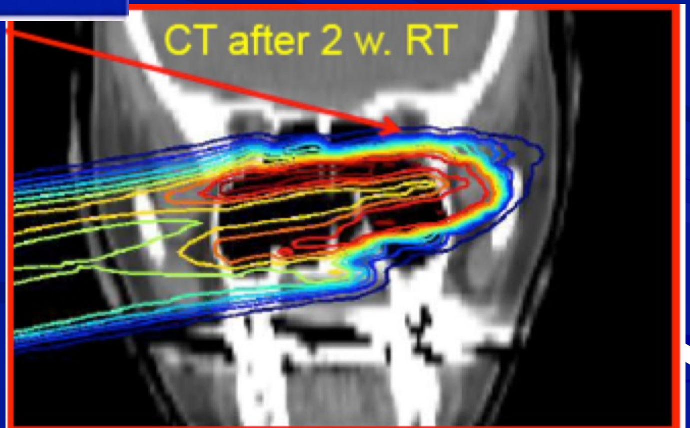


- Step 1 → Treatment planning after CT scan
  - Dose to be distributed
  - MC simulation
  - Give information to the machine

Step 2 → Treatment
- 10-20 fractions (tumour irradiation)

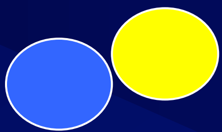
- *Step 3 →* verification *using CT scan*

Overdosage in normal tissue

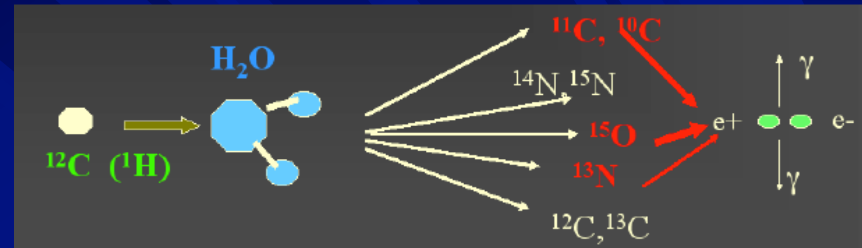


W. Enghardt et al.: Radiother. Oncol 73 (2004) S96

In-beam nuclear method principle for 'in vivo' dosimetry



Nucleons & projectile/target fragments



10^{-21} 10^{-18} 10^{-15} 10^{-12} 10^{-9} 10^{-6} 10^{-3} 10^{0} 10^{3}

Time (s) after collision

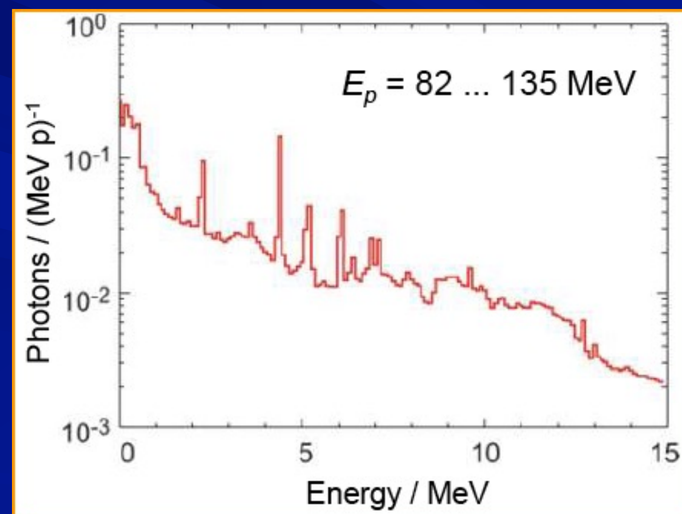
Particles

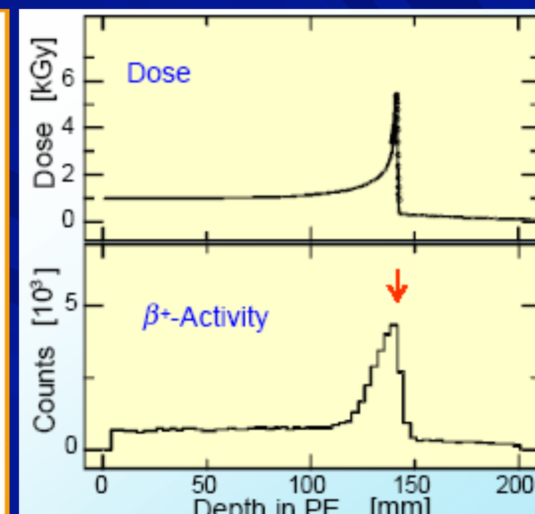
β^+ - emitter decay

Prompt γ-rays

Balance of promptly emitted particles outside the target:

Incident protons:	1.0	($\sim 10^{10}$)
γ-rays:	0.3	($3 \cdot 10^{9}$)
Neutrons:	0.09	($9 \cdot 10^{8}$)
Protons:	0.001	($1 \cdot 10^{7}$)
a-particles:	$2 \cdot 10^{-5}$	($2 \cdot 10^{5}$)



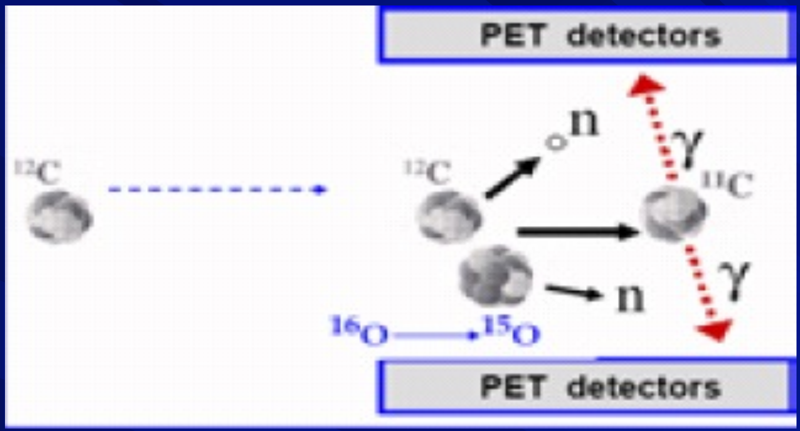


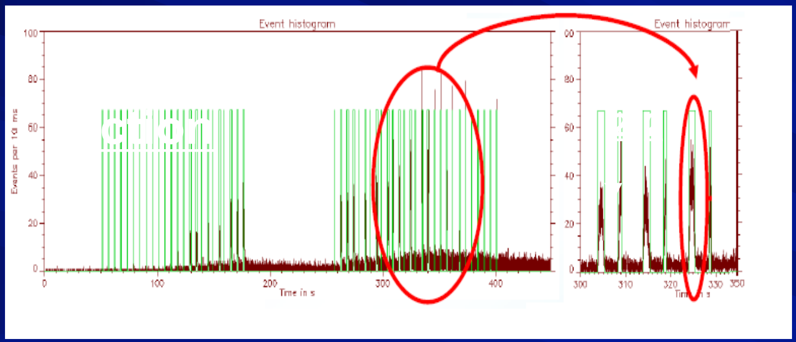
- *However the photon energy different from standard medical (Anger) SPECT camera*

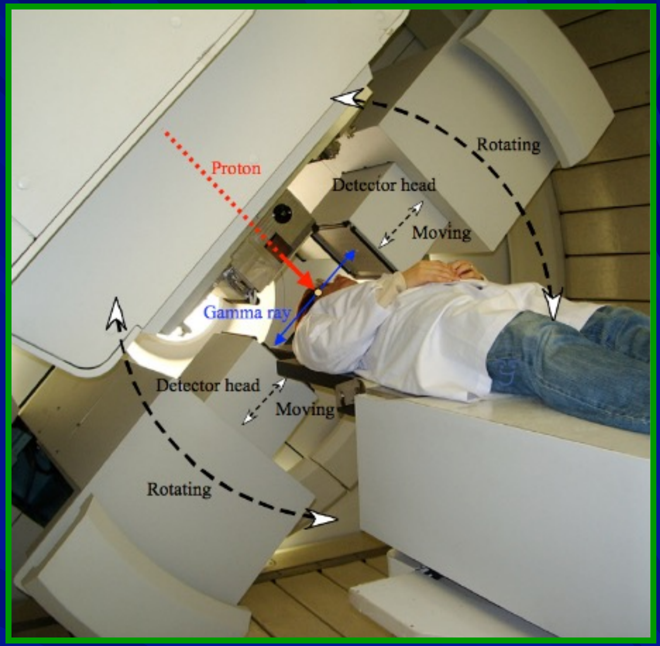
Relation between dose and β+ activities

Present examples: in beam PET

In-beam PET scanner at ^{12}C-therapy unit at GSI







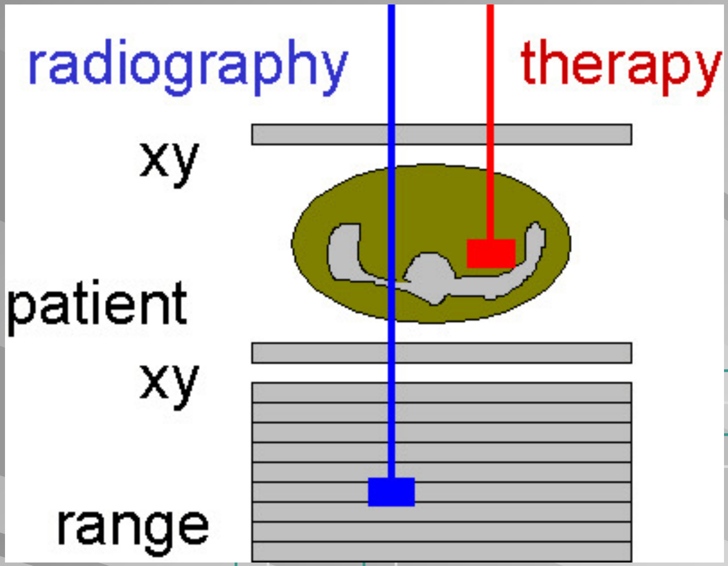
^{1}H-therapy at the National Cancer Center, Kashiwa, Japan

- Large beam background
- No Real time capability
- Low signal to noise ratio

More topics on Particle therapy

(another presentation)

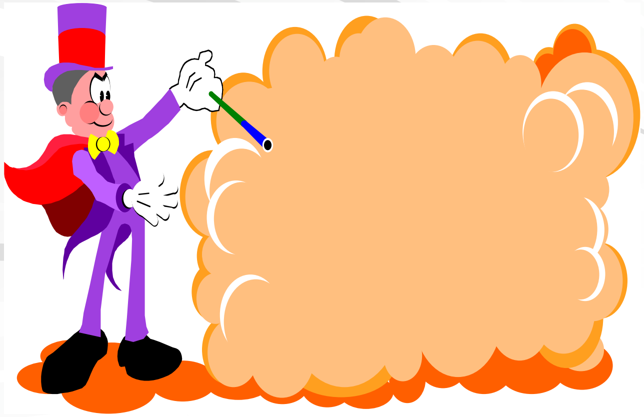
- 1946 : R. Wilson propose to use protons in radiotherapy
- 1954->1970 : first clinical trials (Boston, Uppsala, Berkeley)
- 1970 : first clinical programmes (Boston, Berkeley)
- 1990-1991 : new centers (CPO Orsay, Nice, GSI,PSI,NAC South Africa). First dedicated center : Loma Linda (cost per patient for treating prostate cancer → 120 K$
- Today more than around 130 Facilities are running or planned: that increase very rapidly (>10/year) over the world !
- Becoming Commercial market now (IBA,Siemens,Hitachi ….)
- Proton versus ion (use cyclotron and synchrotron ..Linear?)
- NEW: FLASH THERAPY with Minibeam projects → deliver Very High dose (40/GY/sec) → Machine?
- Big annual conference (PTCOG)

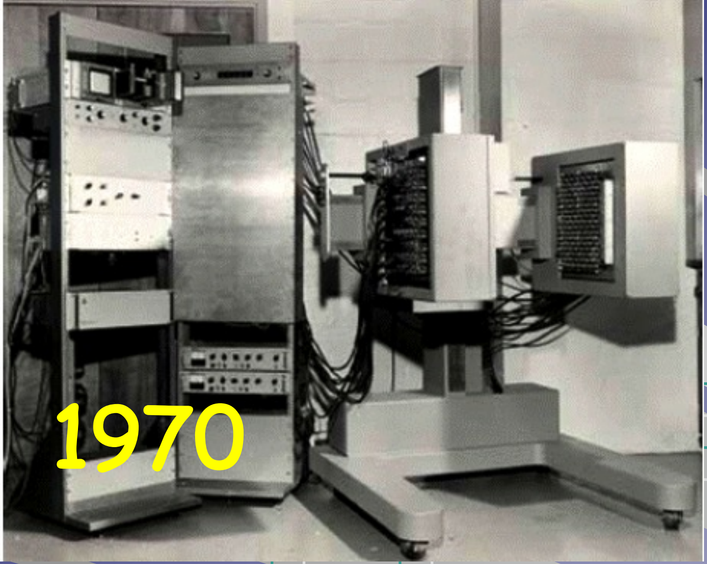


Radiograph of a phantom
Uwe Schneider PhD thesis
(1978,PSI)

Another dream
The Proton CT

A tribute to G.Charpak





Nuclear medicine

What is Nuclear medicine ? Definition

- Use in vivo of radioactive elements (tracers) injected to the patient orally or by blood injection to image the function of the body
- Functional and metabolic (scintigraphy)
- In vivo biochemistry
- Study of a radioactive molecule in a living organism
  - Images are Static 2D/3D (x,y,z)
  - Or 4D (+time) --> dynamic
  - Or 5D (+ Energy) --> Multisotopes /multitracers

What about tracers ?

George Hevesy

1855-1966

Isotopes in medicine

DIAGNOSIS		THERAPY		
in vitro	in vivo	internal		external
		systemic	sources	tele radio
^{14}C ^{3}H ^{125}I others	^{99}Mo-^{99m}Tc ^{201}Tl ^{123}I ^{111}In ^{67}Ga ^{81}Rb-^{81m}Kr others ß$^{+}$ emitters for PET ^{18}F, ^{11}C, ^{13}N, ^{15}O ^{86}Y, ^{124}I ^{68}Ge-^{68}Ga ^{82}Sr-^{82}Rb	^{131}I, ^{90}Y ^{153}Sm, ^{186}Re ^{188}W-^{188}Re ^{166}Ho, ^{177}Lu, others α-emitters: ^{225}Ac-^{213}Bi ^{211}At, ^{223}Ra ^{149}Tb e^{-}-emitters: ^{125}I	sealed sources ^{192}Ir, ^{182}Ta, ^{137}Cs many others needles for brachytherapy: ^{103}Pd, ^{125}I many others stands ^{32}P and others seeds ^{90}Sr or ^{90}Y, others applicators ^{137}Cs, others	^{60}Co gamma knife ^{137}Cs blood cell irradi-ation

Common Diagnosis Tracers

Application	Requirement	Isotope
DIAGNOSIS In vivo SPECT	single photons no particles biogenic behavior $T_{½}$ = moderate	^{99m}Tc, ^{123}I, ^{111}In, ^{201}Tl,
DIAGNOSIS in vivo PET	$ß^{+}$-decay mode biogenic elements $T_{½}$ = short	^{11}C, ^{13}N, ^{15}O, ^{18}F

MTR = Material Testing Reactors

There are different solutions available worldwide to produce artificial radioisotope, i.e. by accelerators, nuclear reactors or research reactors such as the JHR Material Test Reactor.

Cyclotrons

EU tracer production situation

Pays	Réacteur	Puissance (MWth)	Age en 2022 (ans)
Rep. tchèque	LVR15	10	66
Norvège	HBWR	19	62 (arrêté en 2018)
Pays Bas	HFR	45	62
Belgique	BR2	100	62
Pologne	MARIA	30	46
France	OSIRIS	70	(arrêté fin 15)
France	RJH	100	En cours

Very worry about the future this why we are building the RJH

RJH Producing radioisotope for nuclear medicine

- The JHR Material Test Reactor (70MWh) has been designed to produce artificial radioisotope by way of fission or neutron capture, The need for artificial radioisotope has been increasing year after year, especially for nuclear medicine where radioisotopes are used for examinations (diagnostics) and cancer treatment (therapy).
- Producing between 25% (representing about 2 millions patients diagnosed) and 50% of European yearly requirements
- Diagnostic radioelement
  - ^{99}Mo/^{99m}Tc • ^{125}I ^{131}I• ^{133}Xe produced by ^{235}U fission
- Therapeutic radioelement
  - ^{89}Tc, ^{90}Y, ^{153}Sm, ^{166}Ho, ^{169}Er, ^{177}Lu, ^{186}Re, ^{192}Ir, ^{103}Pd, ^{125}I
  - ^{192}Ir, ^{60}Co, ^{75}Se ....

The Jules Horowitz MTR Reactor

Cadarache France

2025?

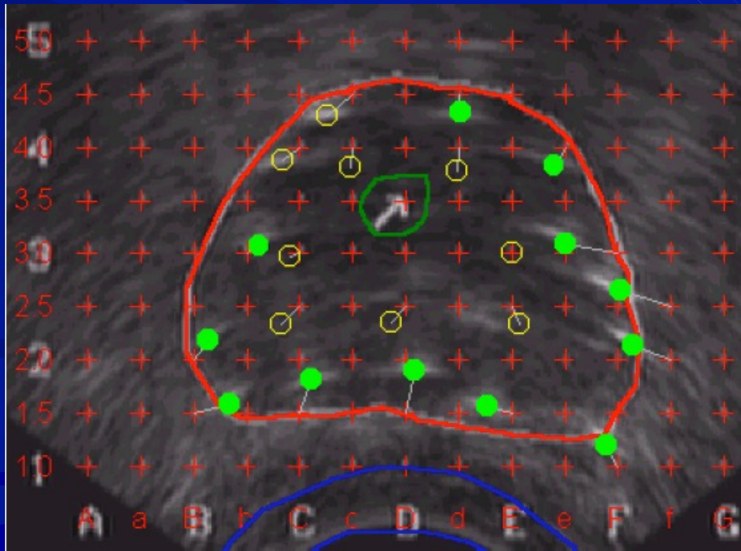
WEB site: **https://jhrreactor.com/**

Therapy with radioelement

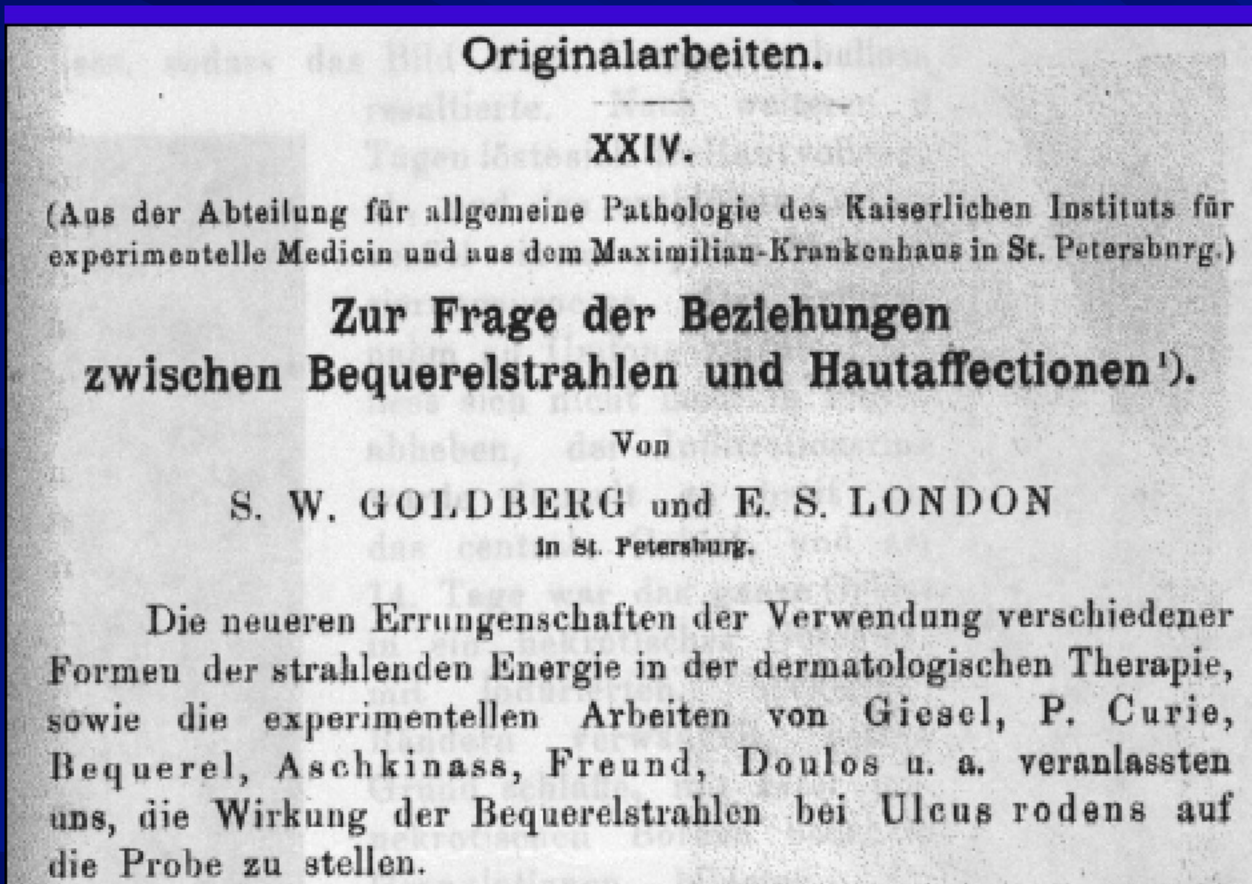
Curietherapy/Brachytherapy

1910 *Today*

- Local (contact) deposit of the dose by needles or implants



First cancer cure by brachy (ulcus rodens, basal cell carcinoma): Goldberg and London in Moscow, 1903



Originalarbeiten.

XXIV.

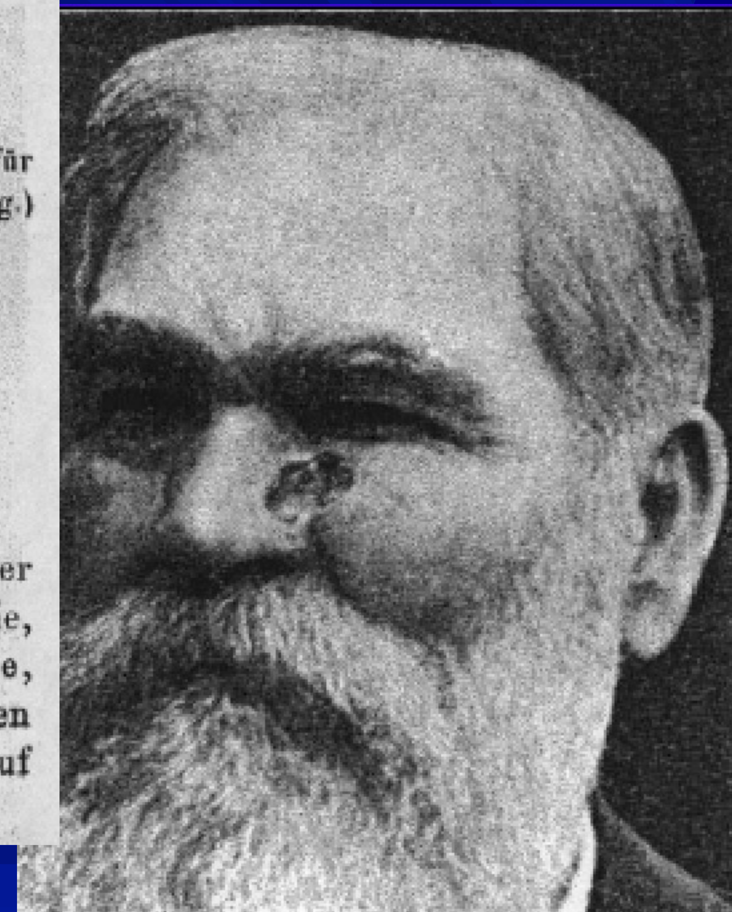
(Aus der Abteilung für allgemeine Pathologie des Kaiserlichen Instituts für experimentelle Medicin und aus dem Maximilian-Krankenhaus in St. Petersburg.)

Zur Frage der Beziehungen zwischen Bequerelstrahlen und Hautaffectionen[1].

Von

S. W. GOLDBERG und E. S. LONDON
in St. Petersburg.

Die neueren Errungenschaften der Verwendung verschiedener Formen der strahlenden Energie in der dermatologischen Therapie, sowie die experimentellen Arbeiten von Giesel, P. Curie, Bequerel, Aschkinass, Freund, Doulos u. a. veranlassten uns, die Wirkung der Bequerelstrahlen bei Ulcus rodens auf die Probe zu stellen.



First brachy treatment, any disease, generally credited t

- Henri Alexandre Danlos,
- Parisian dermatologist,
- exhibiting a woman who he
- successfully treated for
- *lupus vulgaris* of the
- face. Pierre Curie loaned
- him the source and he

Note sur le traitement du lupus érythémateux par des applications de radium.

Par MM. Danlos et P. Bloch.

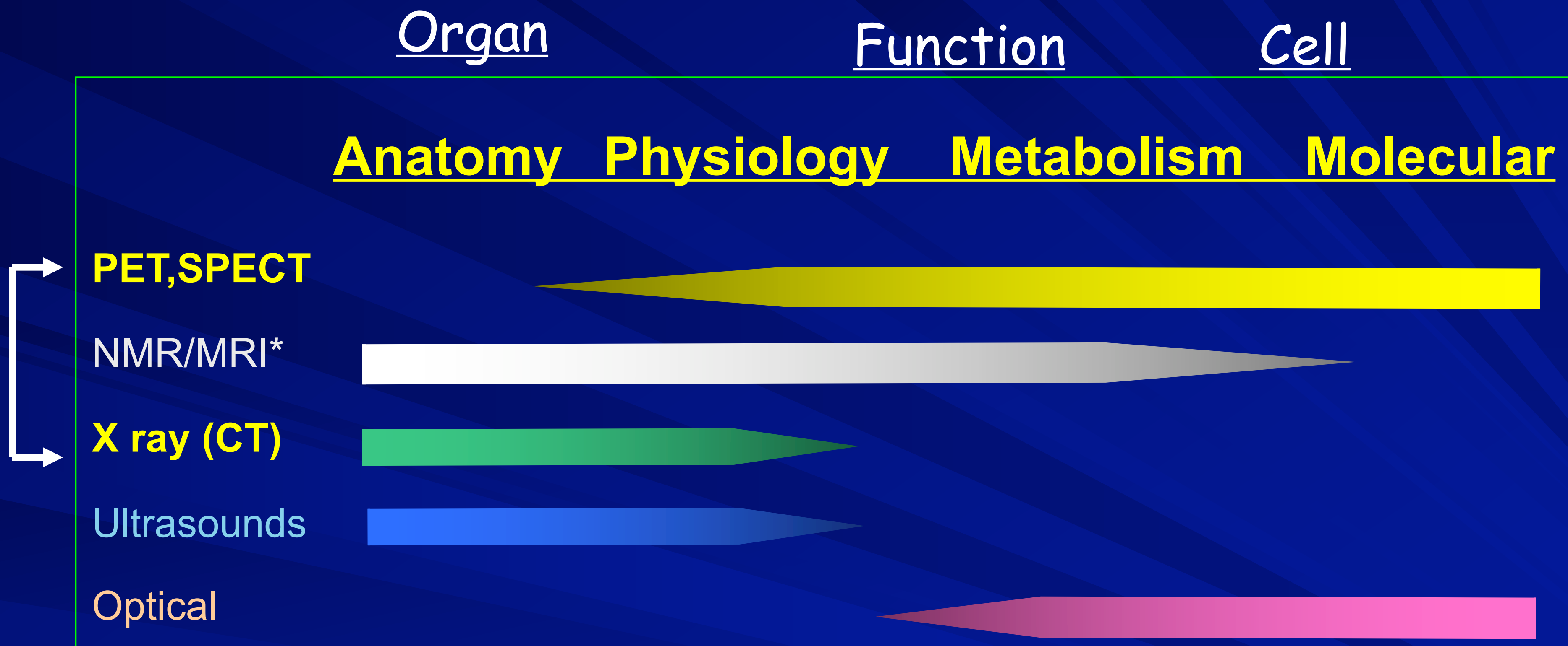
Le 2 mars 1896, M. H. Becquerel, dans une communication à l'Institut, indiquait que tous les sels d'uranium et l'uranium métallique émettent, sans cause excitatrice et d'une manière incessante, un rayonnement qui traverse les corps opaques pour la lumière et impressionne les plaques photographiques. L'étude de ces rayons, dits aussi rayons uraniques ou rayons de Becquerel, a été l'origine

BRT (typically 10-20% of patients)

- 1) Radiation sources placed in the tumor, ergo less toxicity
- 2) Dose homogeneity in the target not an issue
- 3) Conformal treatment without complicated technological
- tools
- 4) Generally invasive (except intracavitary)
- 5) In BRT timing is critical
- 6) Overall risk of a second cancer is claimed to be lower for
- brachy
- *A. The actual dose delivered can be precisely known* (a
- double-edged sword…)
- *B. Full QC* (operator-independent treatment)
- *C. Ideal for focal therapy* (radiobiology not needed)

Modern imaging

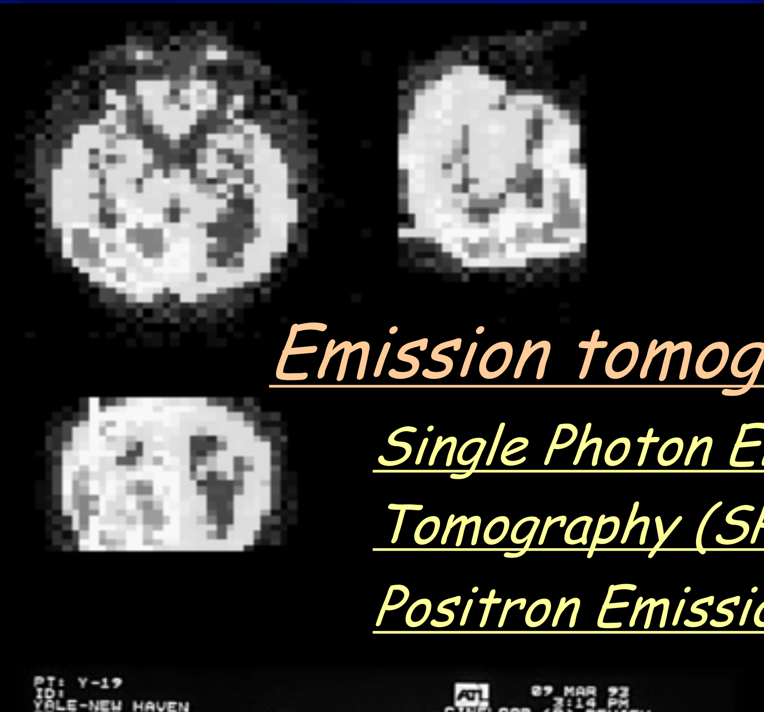
The various types (modalities) of imaging

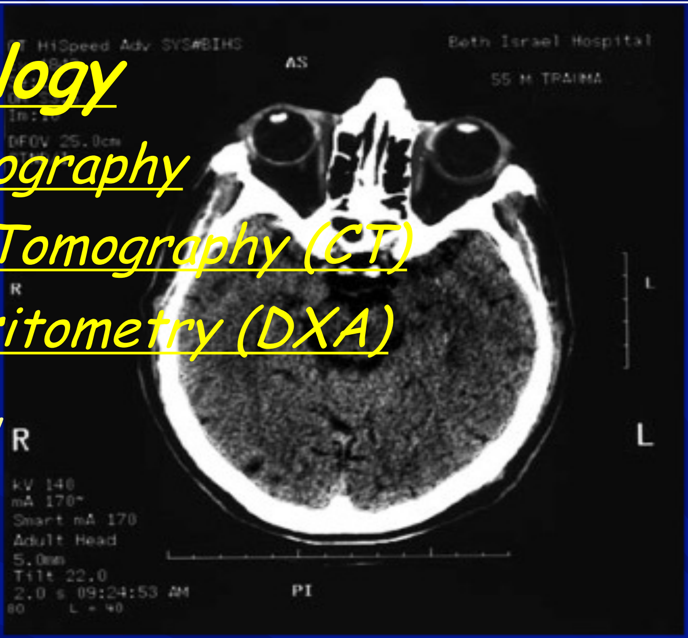


- Complementary !
- Depends on what you want to see

MRI/MMR = Magnetic resonnance*

Medical Imaging Modalities





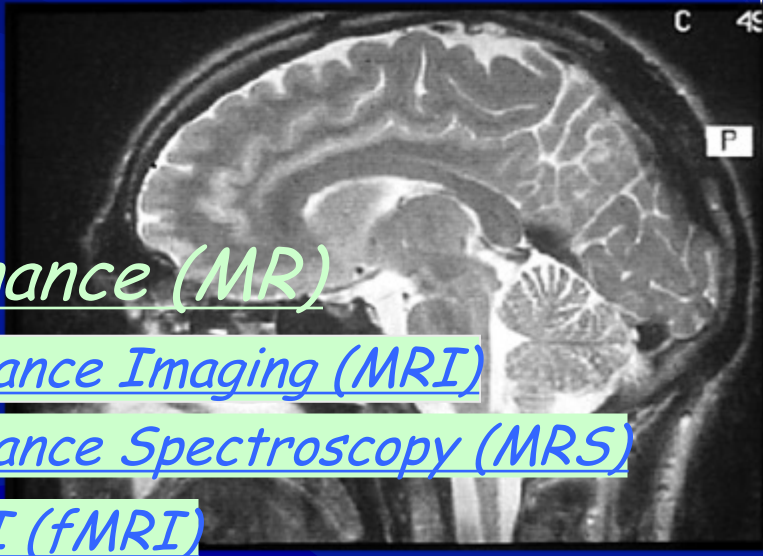
X-ray radiology

- X-ray Radiography
- Computed Tomography (CT)
- Tomo-Densitometry (DXA)

Emission tomography

- Single Photon Emission Computerized Tomography (SPECT)
- Positron Emission Tomography (PET)

Ultrasonic imaging

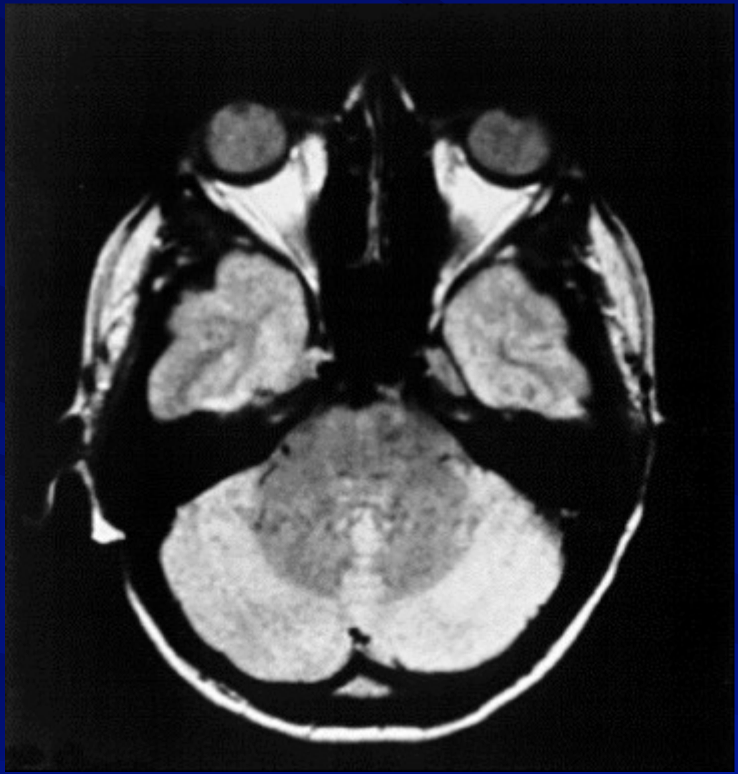


Magnetic Resonance (MR)

- Magnetic Resonance Imaging (MRI)
- Magnetic Resonance Spectroscopy (MRS)
- Functionnal MRI (fMRI)

NMR & PET Images of Epilepsy

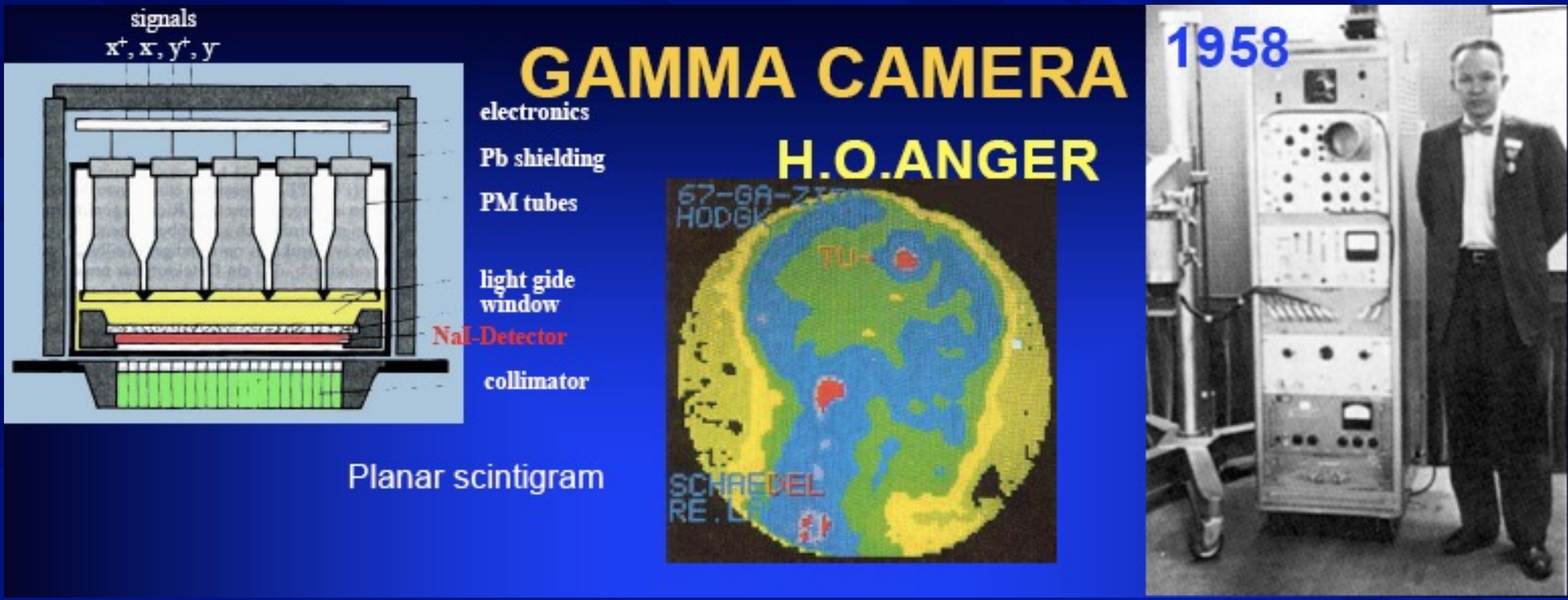
NMR



PET

- NMR "Sees" Structure with 0.5 mm Resolution
- PET "Sees" Metabolism with Few mm Resolution but with very high sensitivity (picomolar level)

The first gamma camera (Hanger,1956)



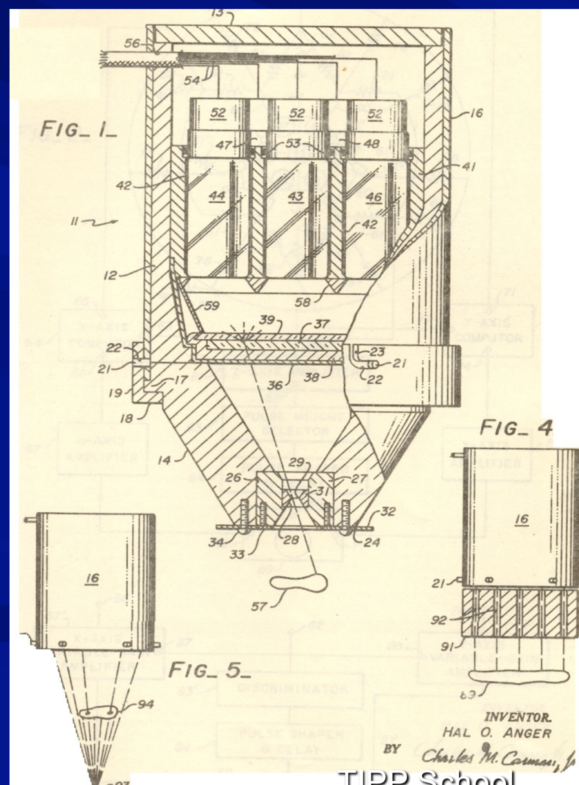
SPECT Gamma camera components

- Collimator
  - Ability to localize the photon sourse in the patient (6-12 mm)
- Detection system
  - Ability of the large NaI scintillator and photomultiplier to localize the photon interaction in the crystal
- Problem :
  - only few useful photons
  - 1:100 000

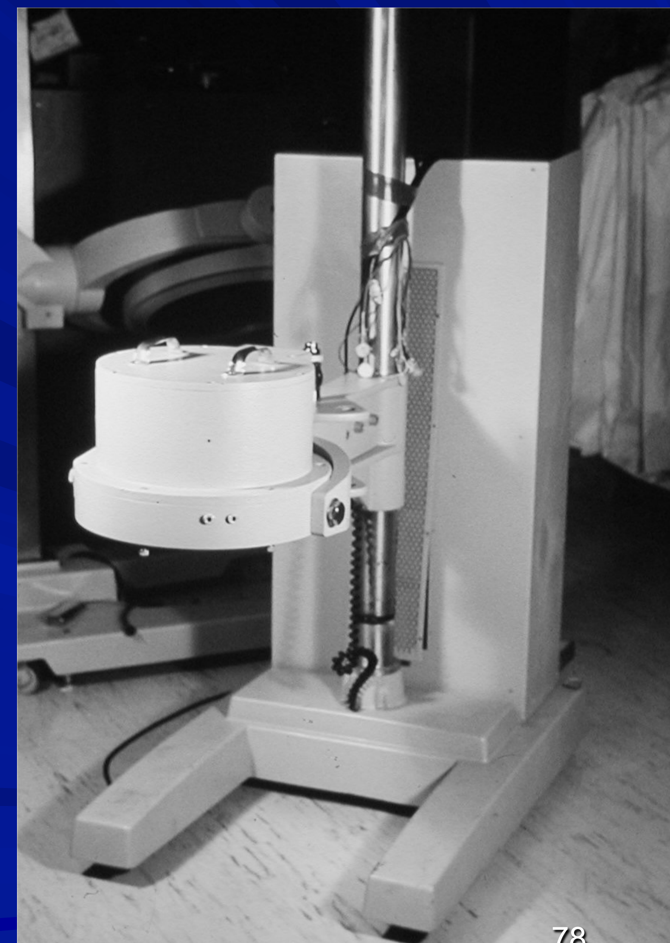
Anger Camera

Anger camera invented in 1957

First camera had 7 PMTs

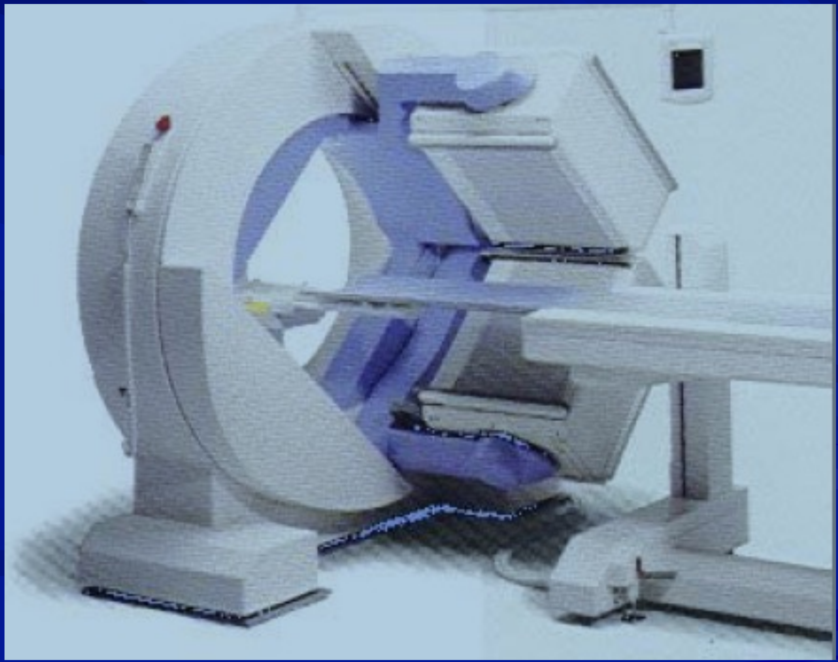


First commercial Anger camera was delivered by Nuclear Chicago to W. Myers, Ohio State 1962

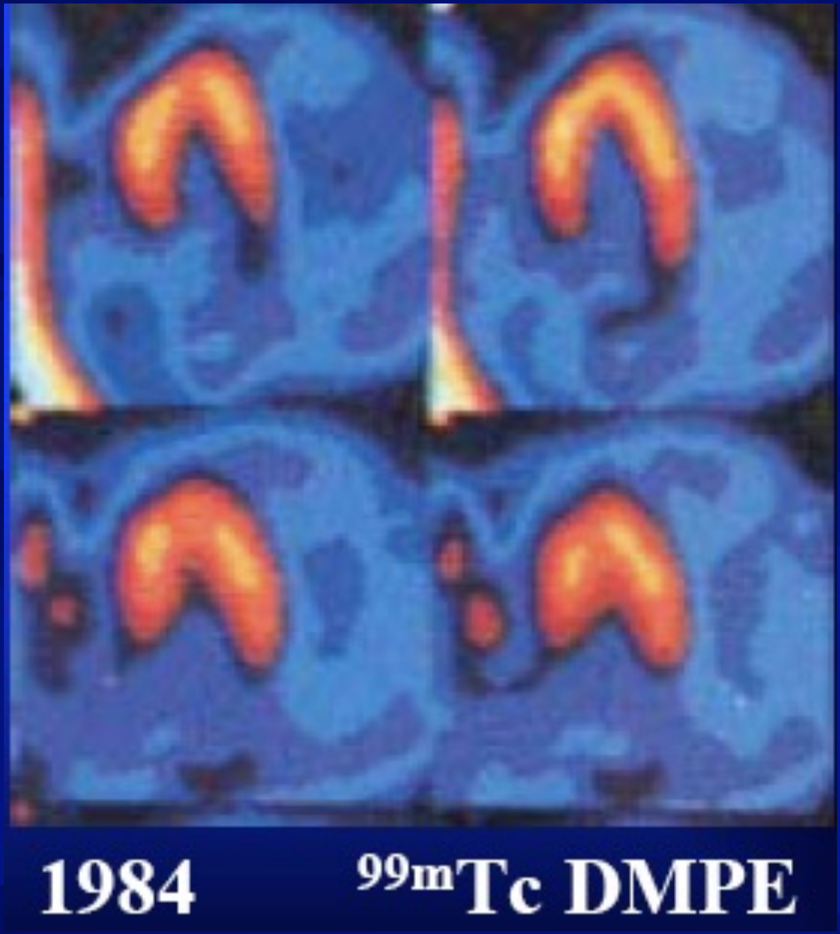


Single Photon Emission Computed Tomography (SPECT)

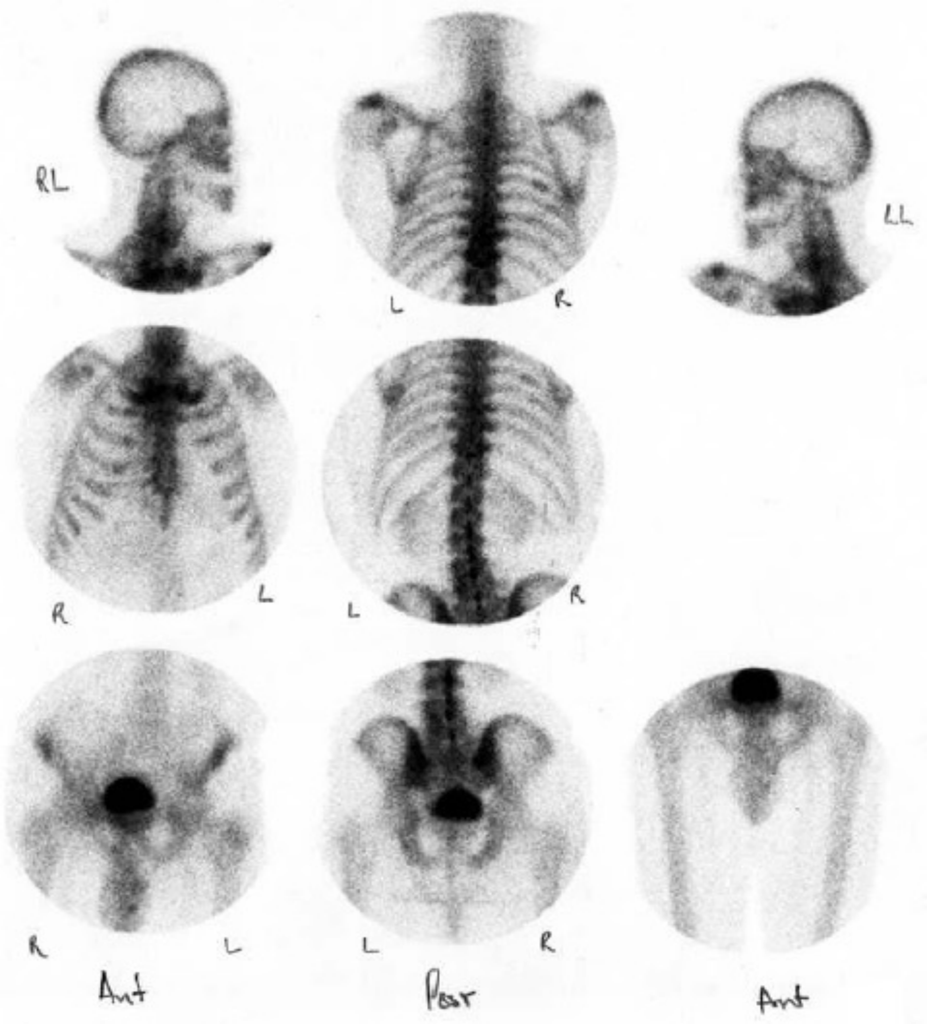
- Two ways
  - Tc ^{99} tracer and a gamma camera
  - Positron emitting tracers with positron camera



SPETCT images

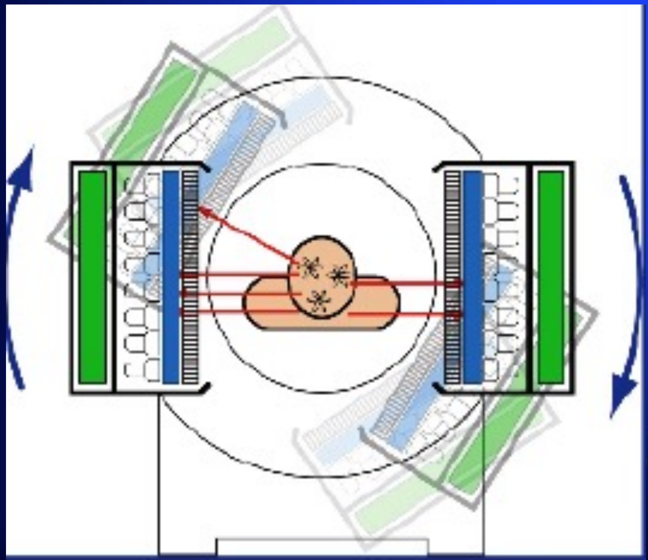


Hearth



Multiview skeleton with Tc^{99}

Modern SPECT camera



Few word about PET

The PET sequence

Produce radio-active sugar (FDG)

Cyclotron

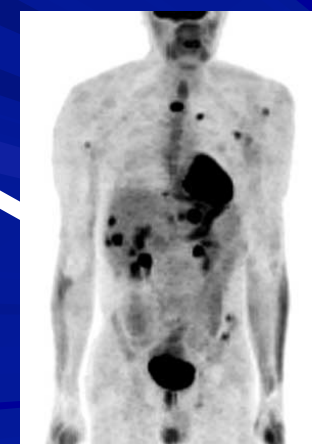
Intravenous injection

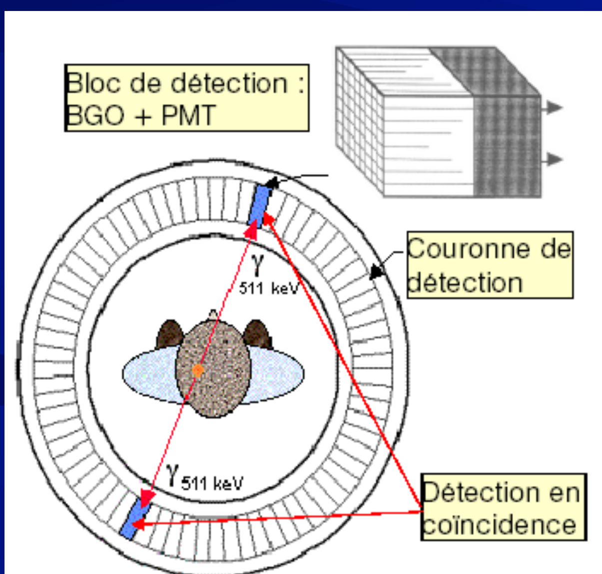
10mC

Wait for accumulation in target site

Get 2 gamma events

Reconstruct image coincidence events

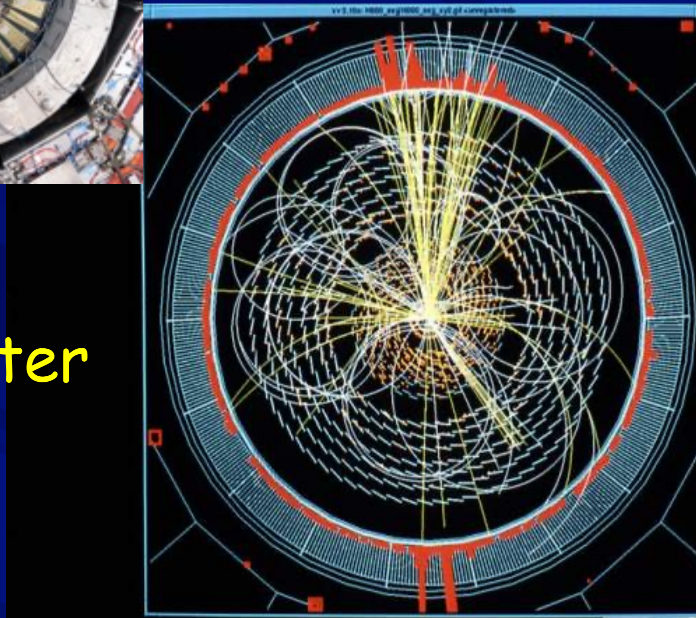




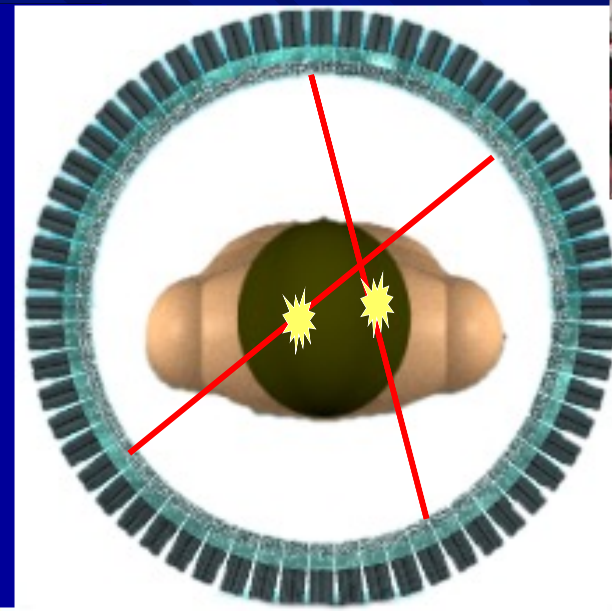
Detect coincidence events

HEP & PET

Similarities and differences



M_{Higgs} = 100 GeV



Calorimeter

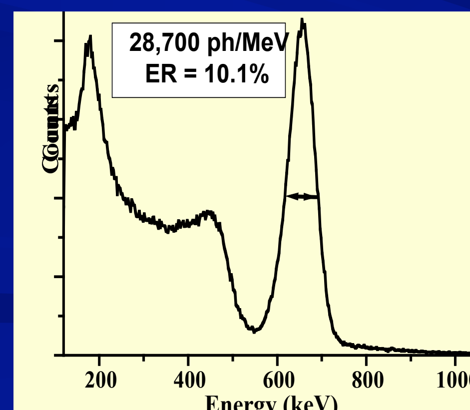
HEP

PET Camera

Biomedical Imaging

Similarities

Geometry and granularity
Detector (Crystals & scintillator)
Sensor (PMT,APD)
Digitizers: ADC,TDC,
Data volume (Gbytes)



Differences

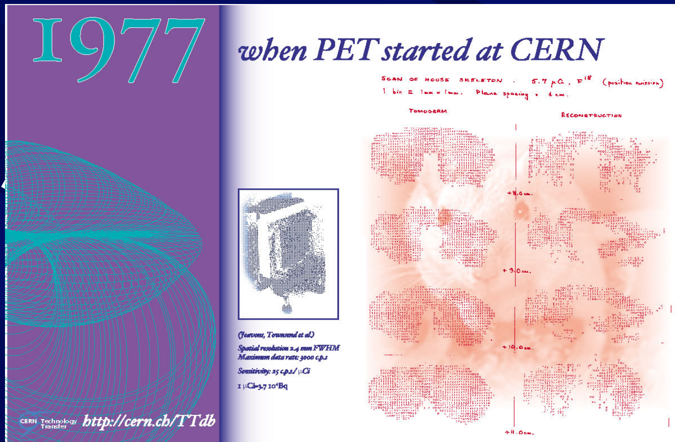
Energy range
(10GeV → -511keV)
Event Rate 40 → 10 MHz

No synchronization
Self triggered elrctronics
Multiple vertices

Survey of common area with HEP

- Energy
  - From Kev to Tev with very good resolution
- Scintillator & crystal
- Photodetector
  - *compact, high QE, high gain and stability*
  - *Standard : PMT ---> SiPM/MPPC,DSiPM*
- Fast Electronics devices
  - We are speaking today to achieve the PICOSECOND
- # Channels
  - Billions due to 'pixellated & high granularity detectors

Historical Evolution of PET

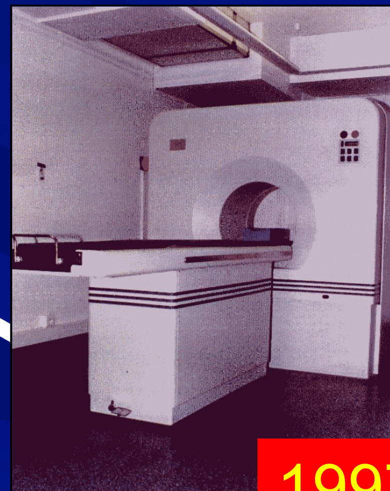


1977

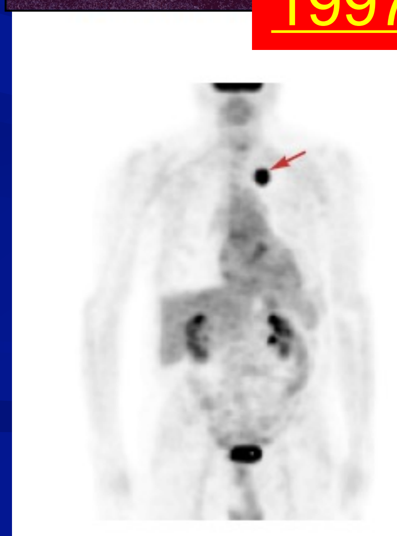
First Steps
Townsend & Jeavons

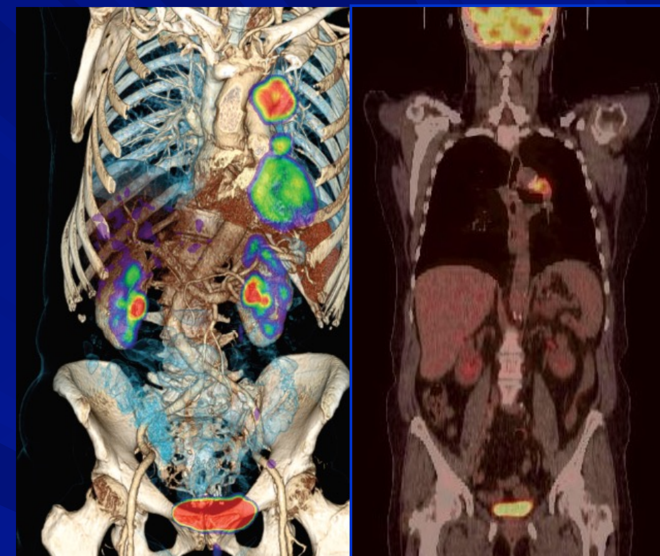
First mouse imaging with ^{18}F

C-PET Philips



1997



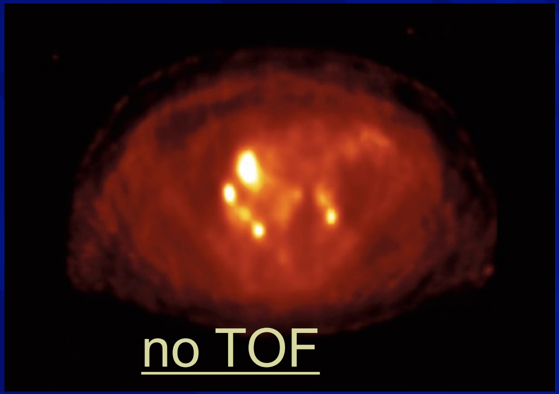


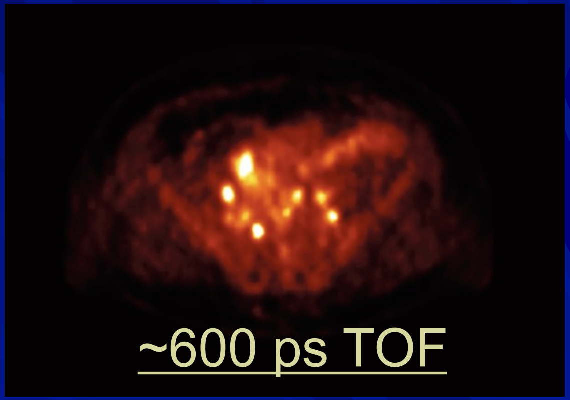
2007

Biograph PET + X ray-CT

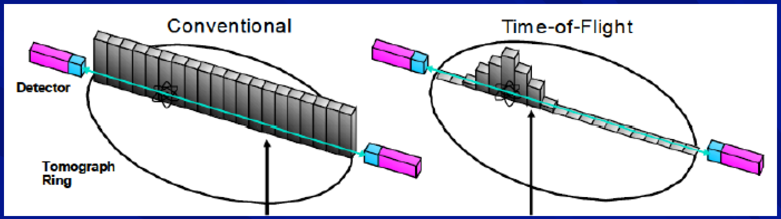
From Today ---> Tomorrow Challenge

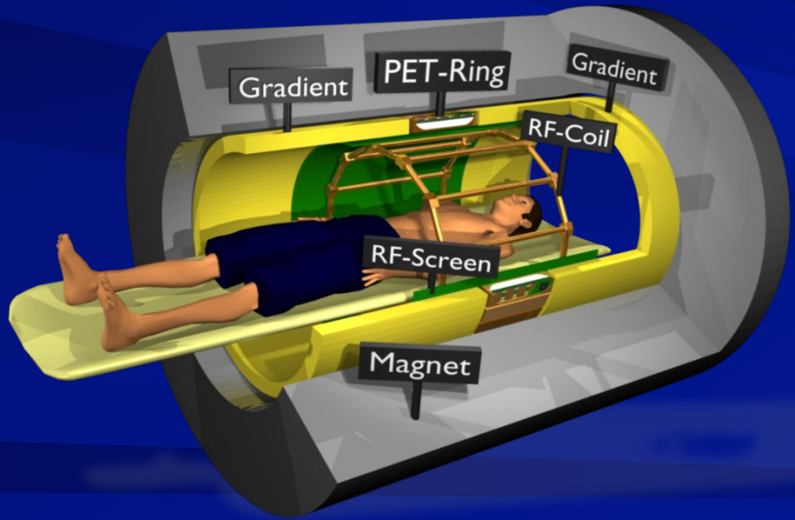
2017





TDM/PET-TOF (250 psec)





Sucima PET-MRI EU project

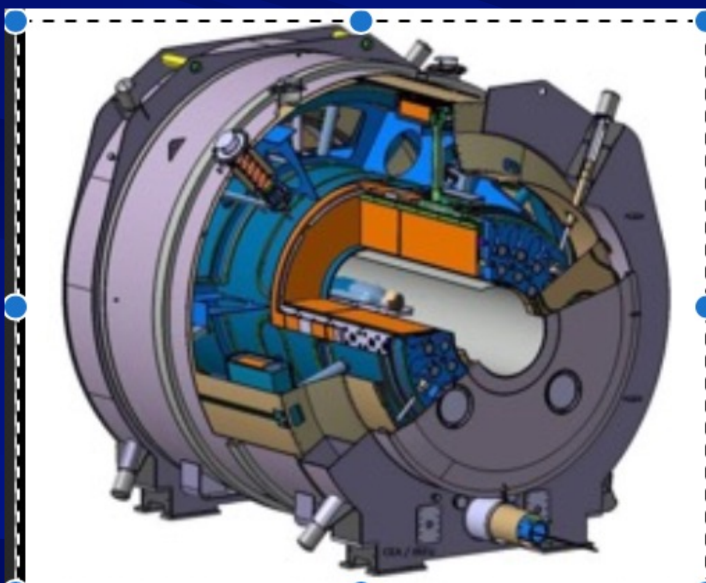
2022

~200-ps TOF PET Siemens Biograph Vision 600

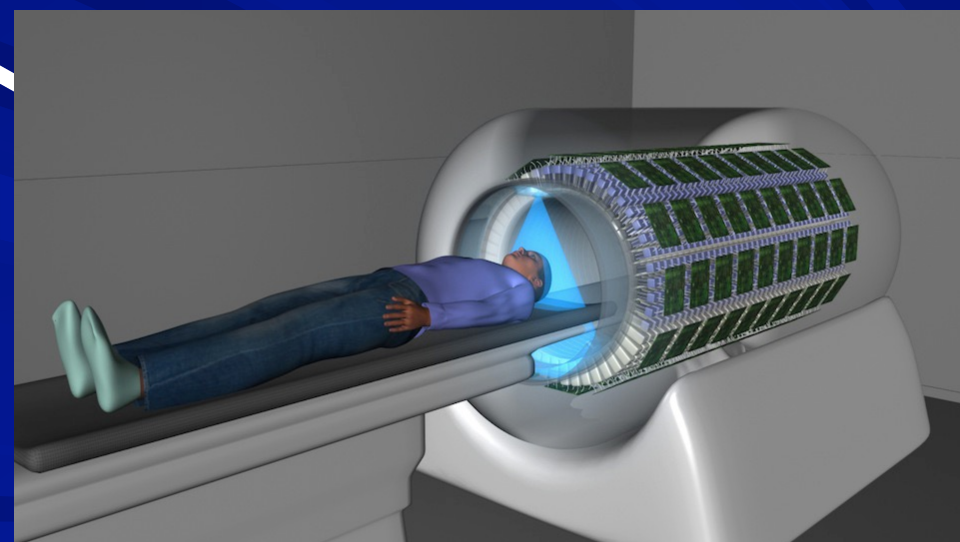
From Today ---> Tomorrow Challenge

2022

CRT = Laboratory 30ps
→ 10 to 1 psec 3 min scan
SNR, Direct imaging Multi-photon imaging, Positronium imaging
Scintillation, Cerenkov,
Metascintillators, Photonics
AI vs TOF, Cost?



2027 ?

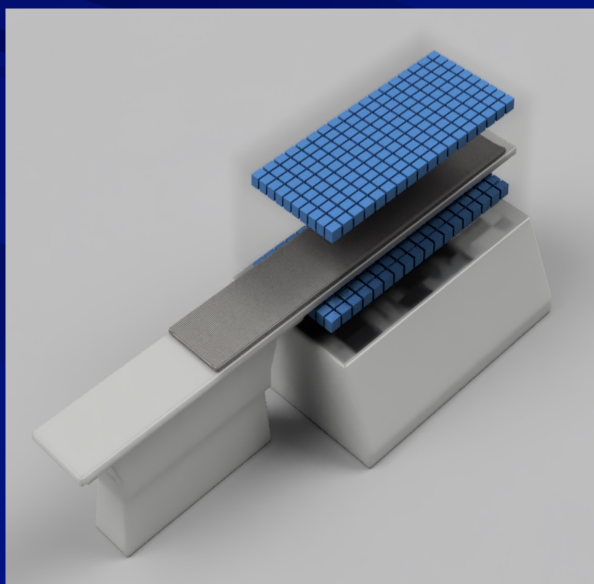


Iseult Project: 11.7T Whole-Body MRI

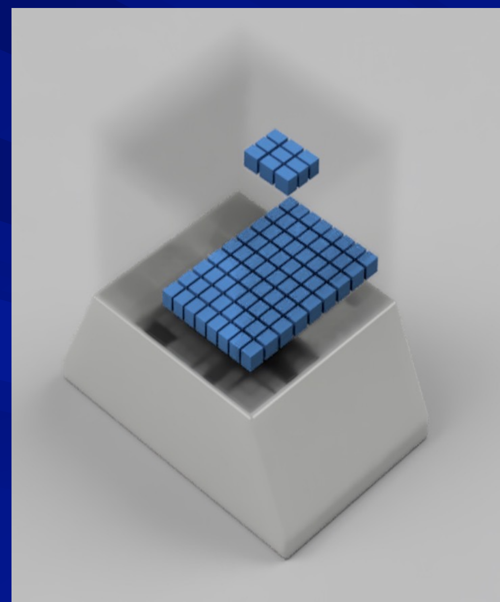
Explorer total body project

Non conventional ideas

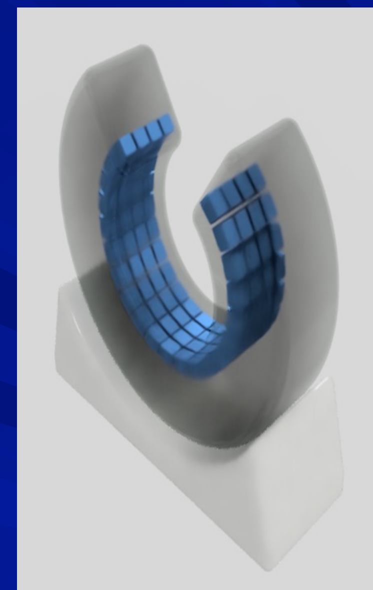
- Free of geometric constraints for tomography
  High solid angle coverage with smaller detector area



Total-Body System

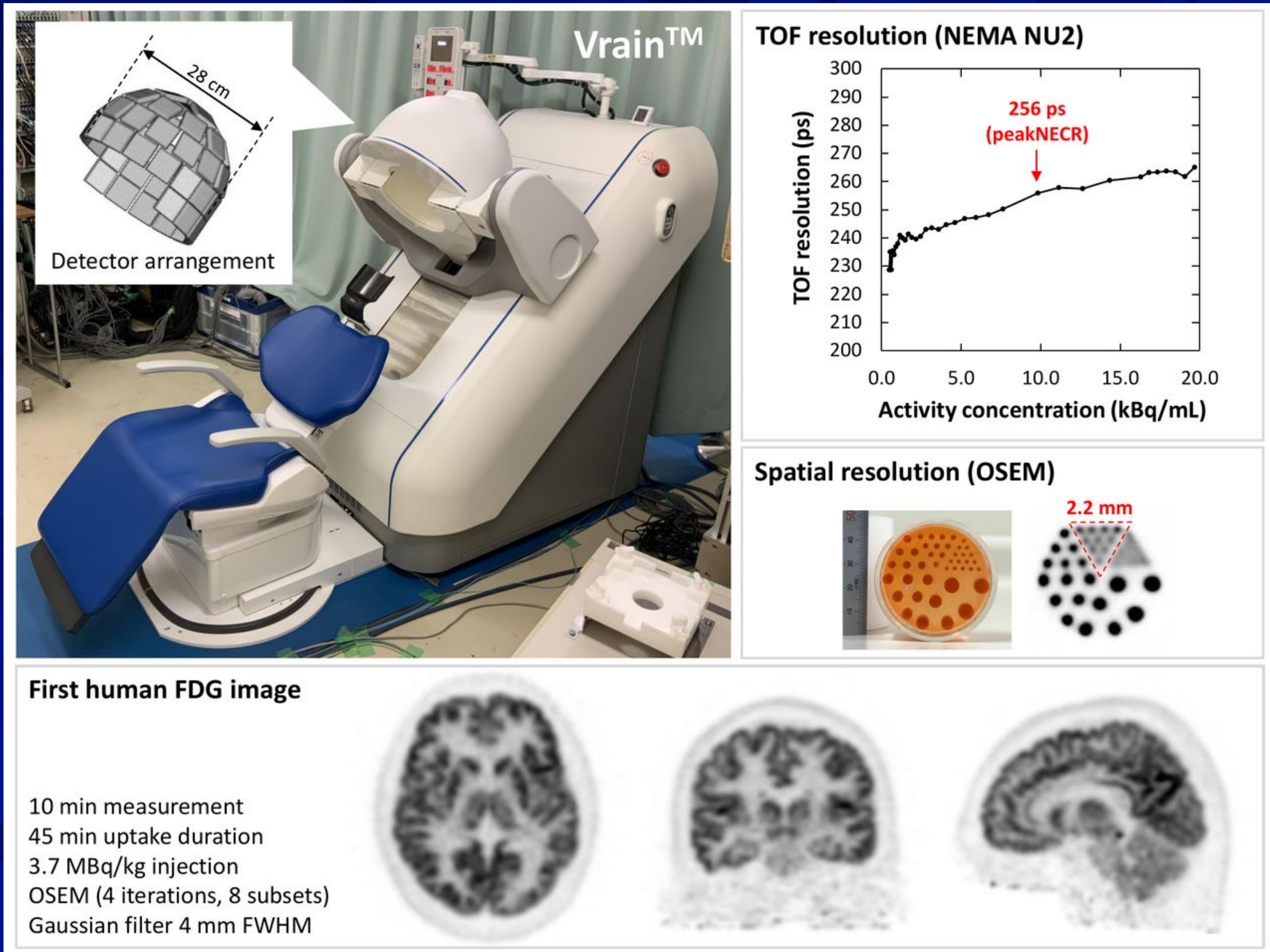


Brain Imaging System

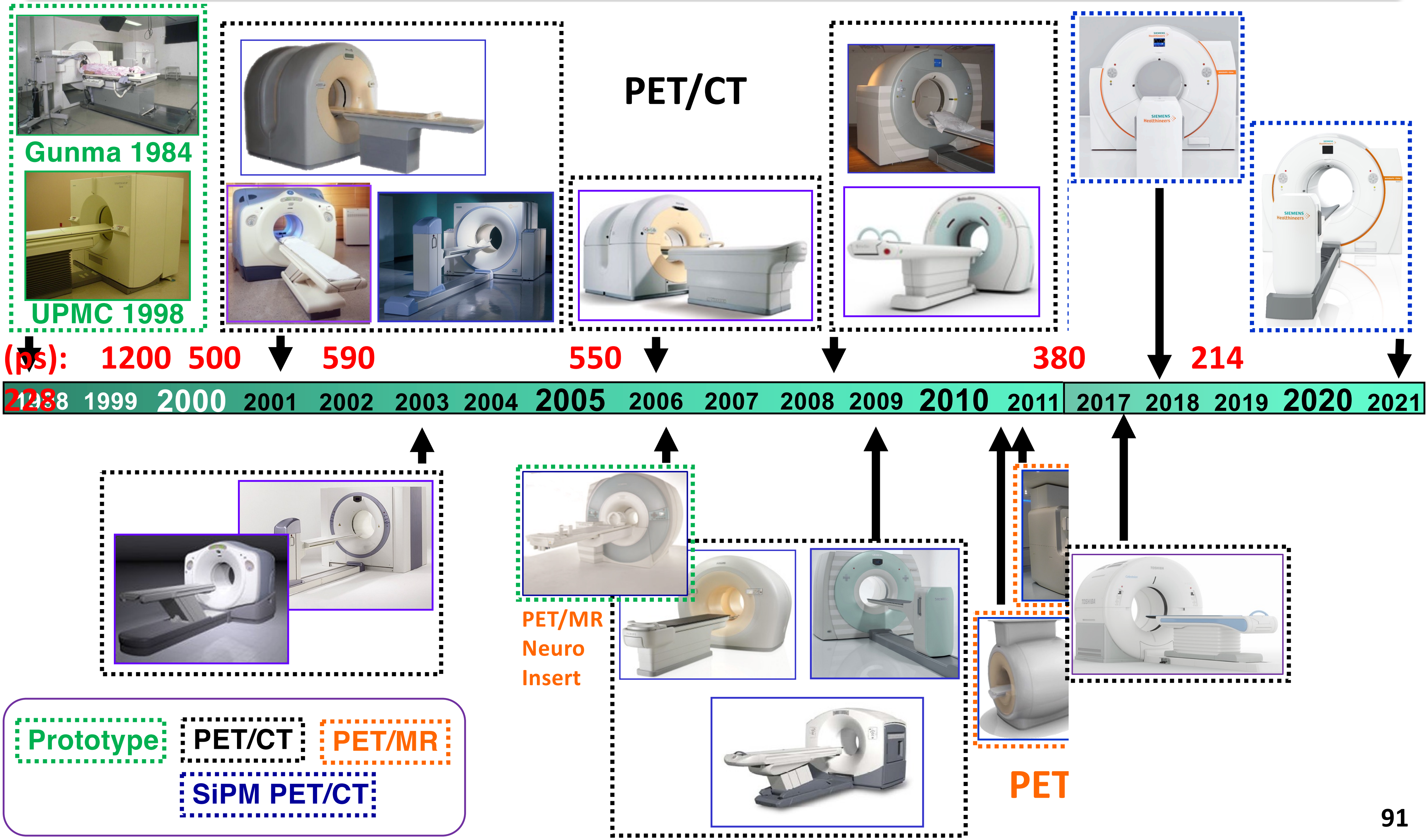


Cardiac or Breast Imaging System

Example : the VRAIN head PET (Japan)



Imaging technology: PET/CT and PET/MR **1984 - Today**

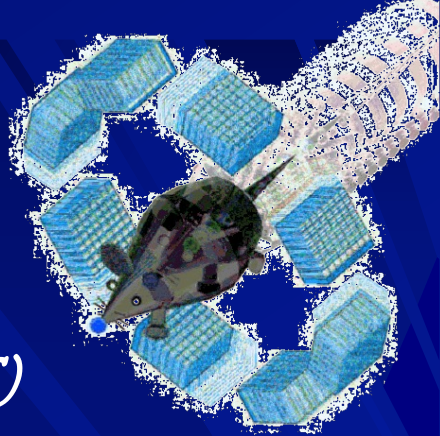


Summary of PET evolution

- Began with Scintillators - one crystal per photosensor (PMTs for most systems to date) → SiPMT
- As we moved to smaller crystals, started doing many on one (crystals to photosensors) designs to reduce cost and allow for physical size of the photosensors
- Added time-of-flight to the mix in the 2000's
- Looked at alternatives, including plastic Scintillators and fibers, various solid state devices
- Recent advances in photosensors, crystals, and solid state materials have opened up the field for many new designs to move the capabilities of PET scanners forward.

Simulation & Sofware

GATE 'early 'Collaboration 2004)



Uni Louis Pasteur (IRES) Strasbourg
Uni Joseph Fourier (LPSC) Grenoble
Forschungszentrum-Jülich (IME)
Uni. Massachusetts, Worcester
CHU Morvan (LATIM) Brest
Uni California (CRUMP) Los Angeles
Uni Toronto (CAMH)
CEA (DAPNIA) Saclay
MSKCC New York
Uni Athens (IASA)

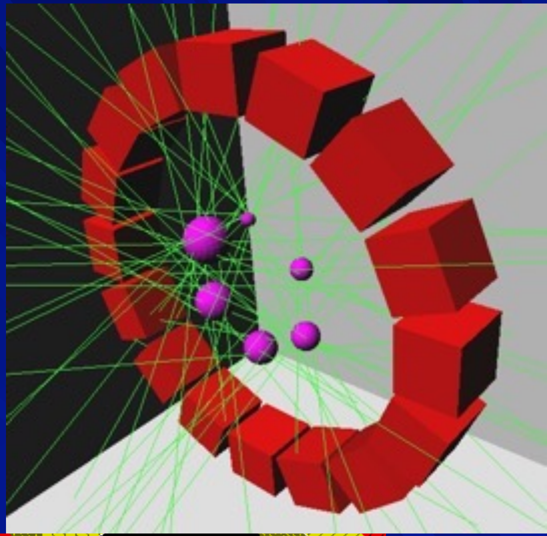
- Irène Buvat CEA SHFJF – Orsay-F)
- Technical Coordinator: S. Jan (CEA - Orsay, F)

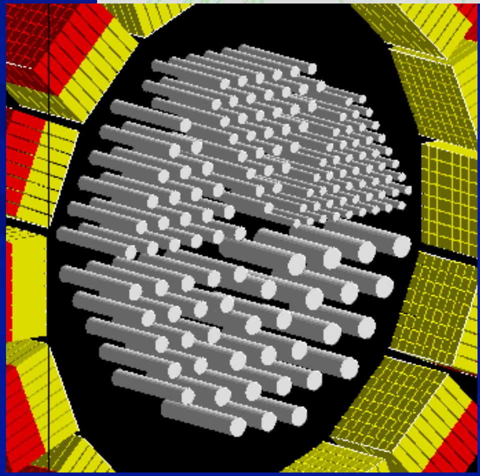
Uni Lausanne (IPHE)
Uni Clermont-Ferrand (LPC)
Uni Ghent (ELIS)
CHU Pitié-Salpêtrière (U494 INSERM) Paris
Vrije Uni Brussel (IIHE)
CERMEP, Lyon
CEA (SHFJ) Orsay
CHU Nantes (U463 INSERM)
Sungkyunkwan Uni. Seoul
Uni Claude Bernard (IPNL) Lyon

GATE : Geant4 Application for Tomographic Emission

Monte-Carlo simulation allowing to :

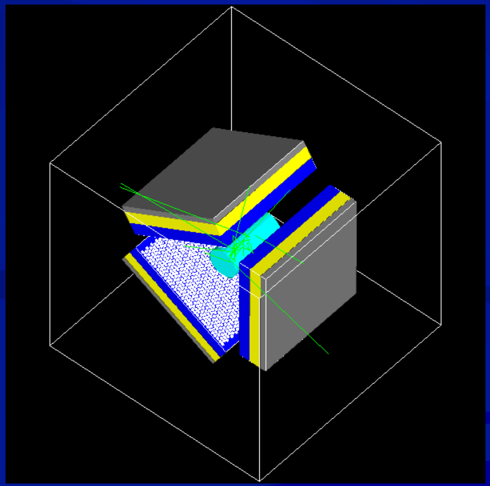
- ✓define geometries
  (size, materials,…)
- ✓ define sources
  (geometry, nature, activity)
- ✓ choice of physical process
  (low energy package of G4)
- ✓ follow track point by point





GATE specificities:

- ✓CERN GEANT4 libraries
- ✓Time modellign
  (sources , movement,random…)
- ✓Script language(avoid C++)
- ✓Code interactivity
- ✓Sharing development



AI in GATE (EGEEE)
Enabling GRID for EsciencE

GEANT4 Application to Tomography Emission

- ## Scientific objectives

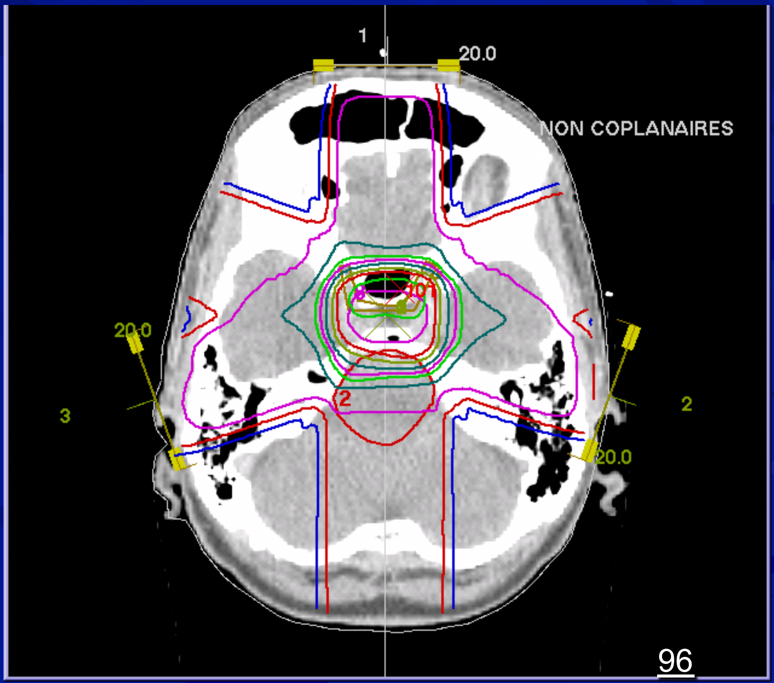
  Radiotherapy planning for improving the treatment of cancer by ionizing radiations of the tumours.

  Therapy planning is computed from pre-treatment MR scans by accurately locating tumours in 3D and computing radiation doses applied to the patients.

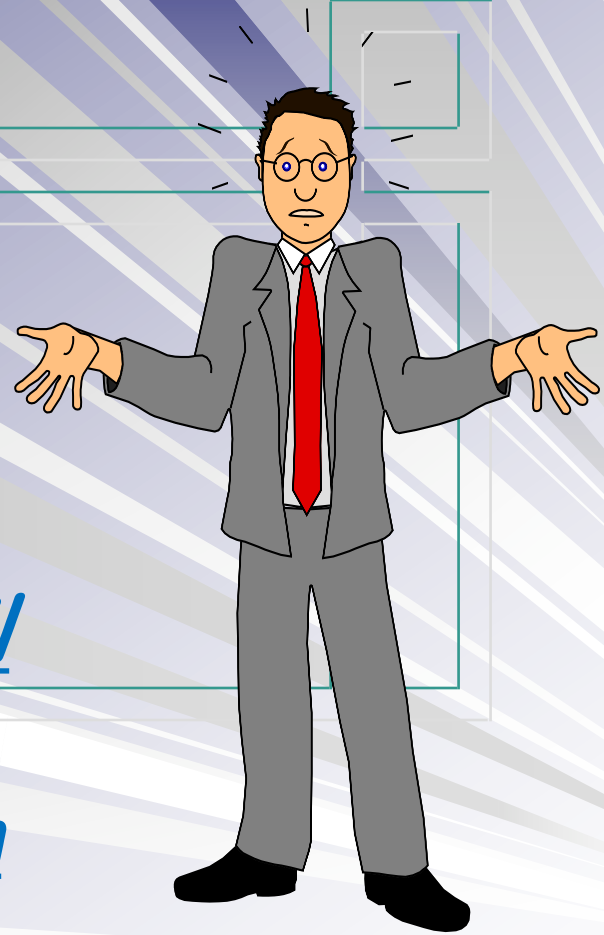
- ## Method

  GEANT4 base software to model physics of nuclear medicine.

  Use **Monte Carlo simulation** to improve accuracy of computations (as compared to the deterministic classical approach)



Thank you for your attention



Questions?

Or send me an email

patrickledu@me.com

Instrumentation schools References

- IRSTS 14 Osaka

http://rt2014.rcnp.osaka-u.ac.jp/rt2014-school/index.html

- IRTS 16 HoChiMinh City

http://ntlab.hcmus.edu.vn/en/rt2016-school/

- Le Cap South Africa.18
  https://indico.cern.ch/event/661919/overview
- ICISE July 19
  https://indico.in2p3.fr/event/19513/
- IRSTS Kuala Lumpur (Malaysia) Nov 2019
  https://indico.cern.ch/event/854879/surveys/1178
- IEEE NPSS Workshop on Radiation Instrumentation – Dec 2021
  Dakar Senegal

https://indico.cern.ch/event/954194/

- IEEE NPSS Workshop on Radiation Instrumentation – Nov 2020
  Jakarta Indonesia

https://indico.cern.ch/event/954199/

Thank you
for your attention

Lecture-Review references

- CERN SiPM Workshop 2011, State of the art in SiPM's, Y. Musienko
- RICH 2013, Status and Perspectives of Solid State Photo-Detectors, G. Collazuol
- New Developments in Photodetection 2014, Tutorial SiPMs, V. Puill
- https://www.hamamatsu.com/resources/pdf/etd/PMT_handbook_ v3aE.pdf
- PHOTOMULTIPLIER TUBES. Principles & applications. S-O Flyckt* and Carole Marmonier**,Photonis, Brive, France
- Large Area Picosecond Photo-Detectors Project http://psec.uchicago.edu/Papers

Acknowledgements and References

- Slides
  - ,Bill Moses, Steve.Derenzo, P.Lecoq, Veronique Puill, Dieter Renker, Kanai Shah, and many others

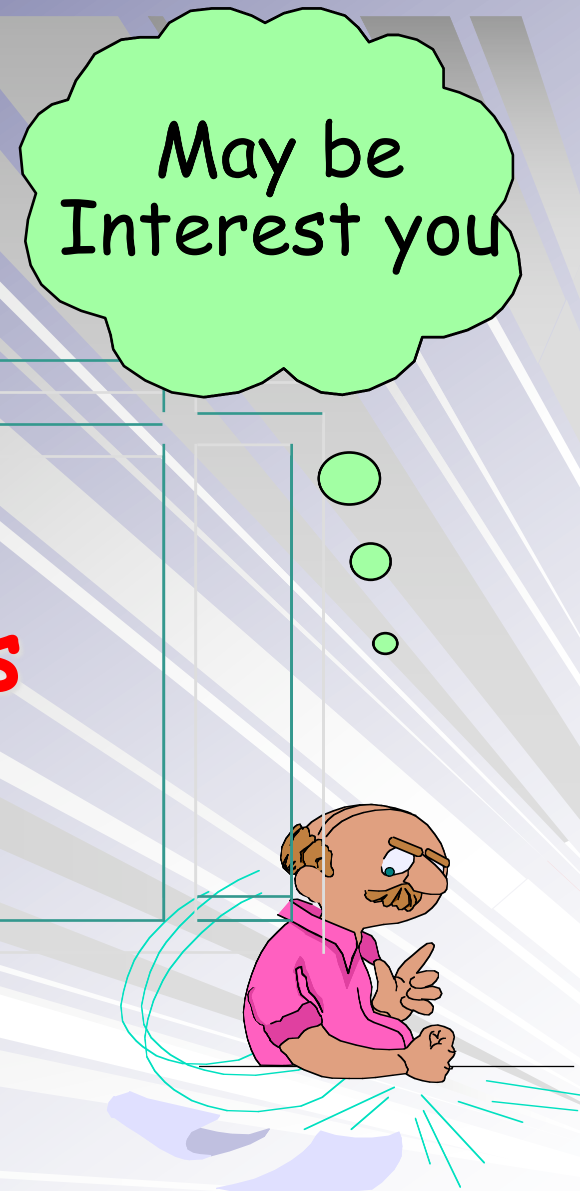
- Books/References
  - G. F. Knoll, □Radiation Detection and Measurement, 3rd Edition, New York, Wiley, 2000
  - Hamamatsu Photonics K. K., “Opto-Semiconductor Handbook”

Thanks to

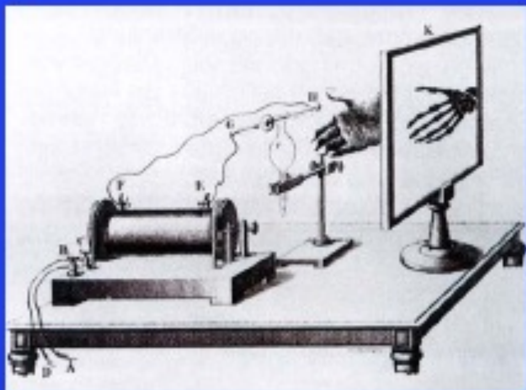
- C. DaVia (Manchester).
- D.Townsend (U. Singuapor)
- H. Frisch (U. Chicago)
- P. Lecoq (CERN)
- R. Lecomte (Sherbrook)
- W. Moses (LBL)
- S. Cherry (Davis)
- K. Parodi (HIT)
- Pr. J.N. Talbot (Hopital Tenon - Paris)
- … and many others

Thank you for your attention

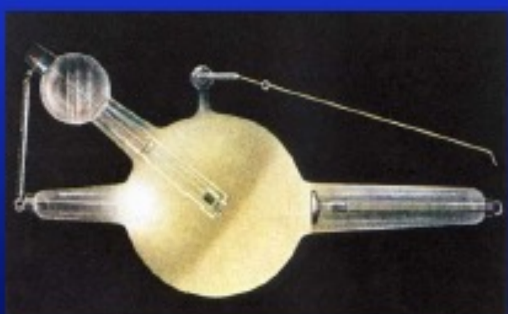
Back up & extra slides



18 Nov, 1895 W.C. Rontgen discovers Xrays



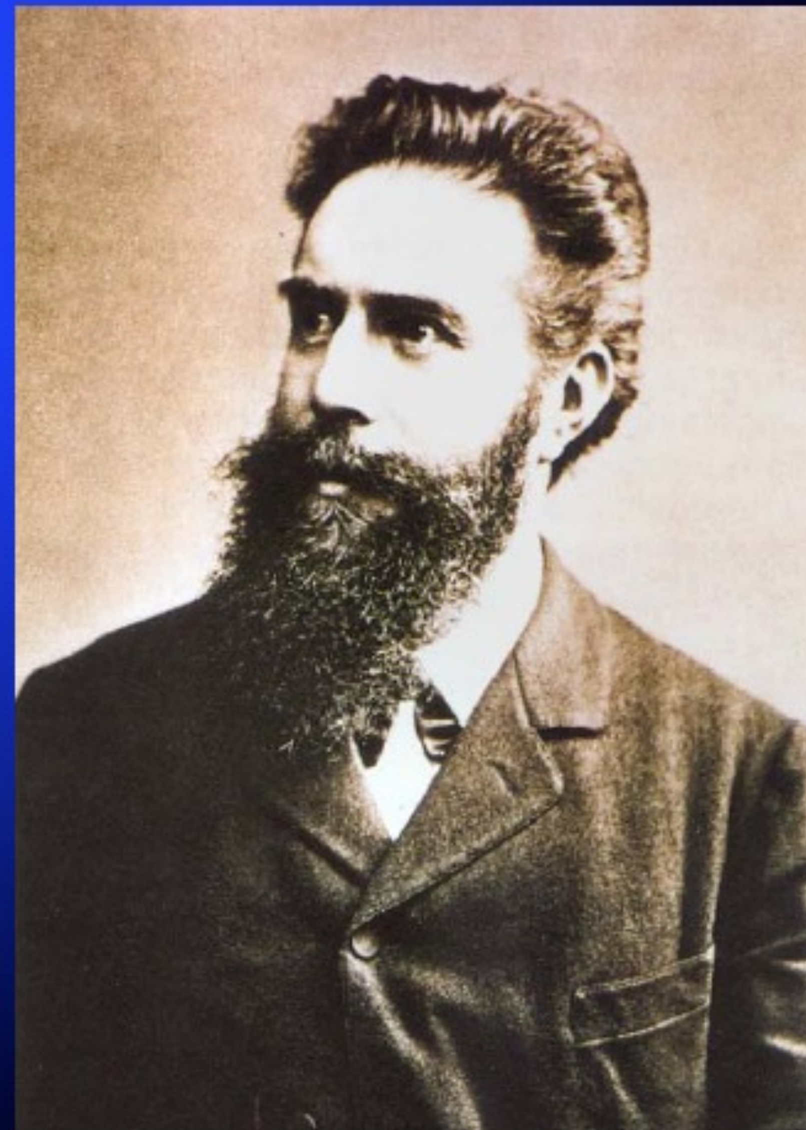
W.C.Röntgens experiment in Würzburg



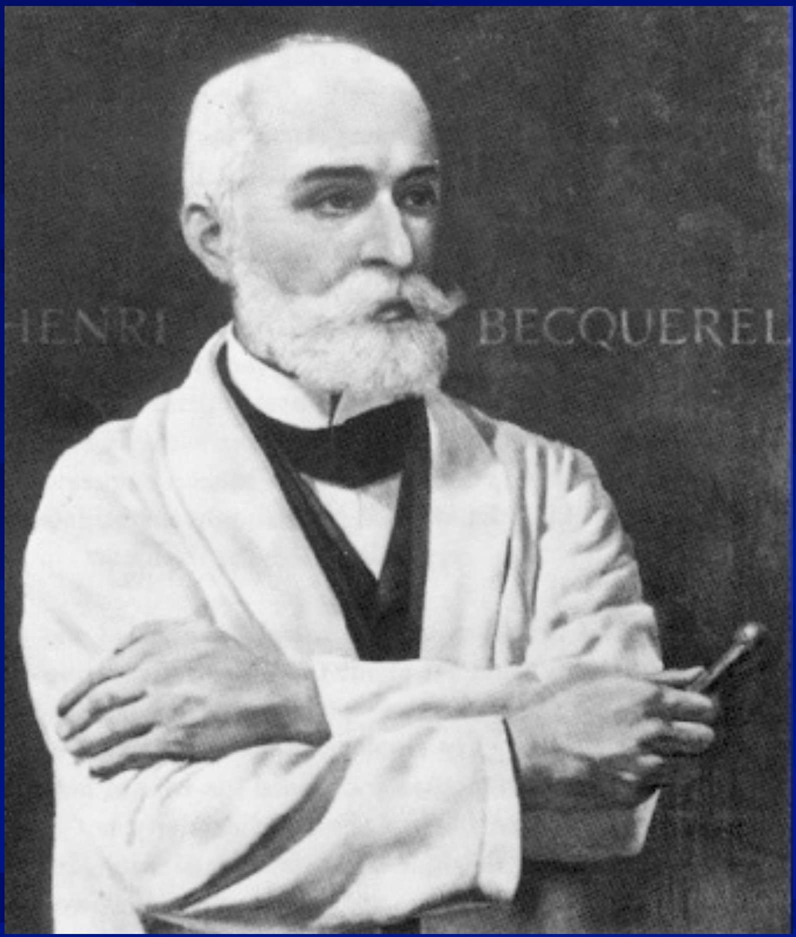
An early XXth century

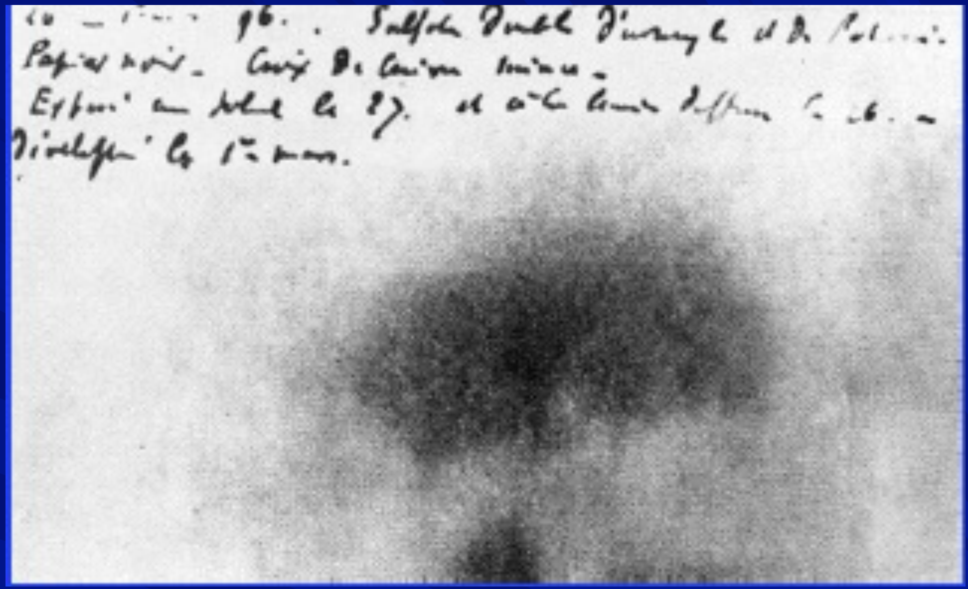
X-ray tube

Radiograph of Mrs.Röntgens hand, the first x-ray image ever taken, 22.Dec.1895, published in The New York Times January 16, 1896



1996 - Discovery of the natural radioactivity by Henri Becquerel



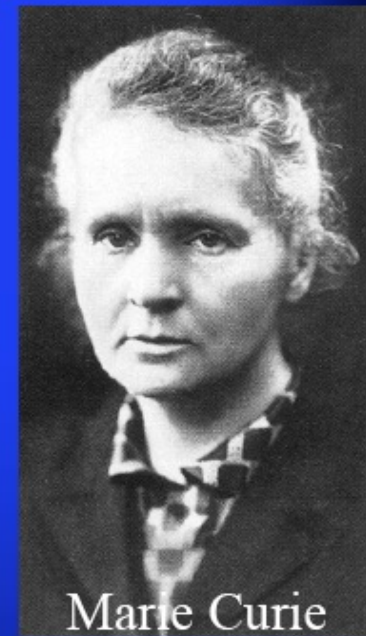


- First image of potassium uranyl disulfide

1898 the Radioactivity

RADIOACTIVITY

1898	**Polonium**
	Radium
1903	**Nobel Prize**
	together with Pierre
1911	**Nobel Prize**
	allone



1897 Becquerels friend, Pierre Curie, also Prof. of physics in Paris suggested to his young bride, Marie, that she study the phenomena discovered by H.Becquerel for her thesis. She found soon that some components of Uranium minerals were much more radioactive than Uranium itself. "**We shall call the mysterious rays 'radioactivity'**," she told to her husband Pierre, and the substances that produce the rays "**radioelements**".

1898 Pierre started to join Marie in the study of the mysterious rays. In **July** that year they reported the discovery of **Polonium** (^{210}Po) and in **December** they announced the discovery of the **Radium** (^{226}Ra)

1923 - The Tracer principle

G.V.Hevesy:
The Absorption and Translocation of Lead (ThB) by Plants [ThB = ^{212}Pb]
Biochem.J. **17**, 439 (1923)

Measurements of the tracer's Radioactivity provided thousand fold increases in sensitivity and accuracy over existing chemical assays. The foundation and basic rationale of much of Hevesy visualized that **a radioactive atom might be used as a "representative" tracer of stable atoms of the same element** whenever and wherever it accompanied them in biological systems.

1943 Nobel Prize Chemistry

the father of Nuclear Medicine

1934 - Artificial radioactivity

Irène & Frederic Joliot-Curie

1934 Nature, February 10
1935 Nobel Prize

"Our latest experiments have shown a very striking fact: when aluminum foil is irradiated on a polonium preparation, the emission of positrons does not cease immideatly when the active preparation is removed. The foil remains radioactive and the emission of radiation decays exponentially as for an ordinary radioelement. We observed the same phenomena with boron and magnesium."

$^{27}Al\ (\alpha,n)\ ^{30}P$ and $^{10}B\ (\alpha,n)\ ^{13}N$

- The discovery of artificial radioactivity in combination with the cyclotron open the door to the production of useful radio indicators. Practically any element could be bombarded in the cyclotron to generate radioactive isotopes.

1935 Nature **136**, 754 O.Chievitz and G.V.Hevesy
Radioactive indicators in the study of phosphorus metabolism in rats (^{32}P)

1937 Radiology **28**, 178 J.G.Hamilton, R.S.Stone:
The administration of radio-sodium (^{24}Na)

1938 Proc.Soc.Exp.Biol.Med. **38**, 510 S.Hertz, A.Roberts, R.D.Evans
Radioactive iodine (^{128}I) – Study of thyroid physiology

1939 Proc.Soc.Exp.Biol.Med. **40**, 694, J.H.Lawrence, K.G.Scott:
Metabolism of phosphorus (^{32}P) in normal and lymphomatous animals

1940 Am.J.Physiol. **131**, 135 J.G.Hamilton, M.H.Soley:
Studies of **iodine** metabolism by thyroid in situ

1940 J.Biol.Chem. **134**, 543 J.F.Volker, H.C.Hodge, H.J.Wilson
The adsorption of fluoride (^{18}F) by enamel, dentine, bone and hydroxyapatite

1945 Am.J.Physiol. 145, 253 C.A.Tobias, J.H.Lawrence, F.Roughton
The elimnation of 11-C-Carbon monoxide from the human body

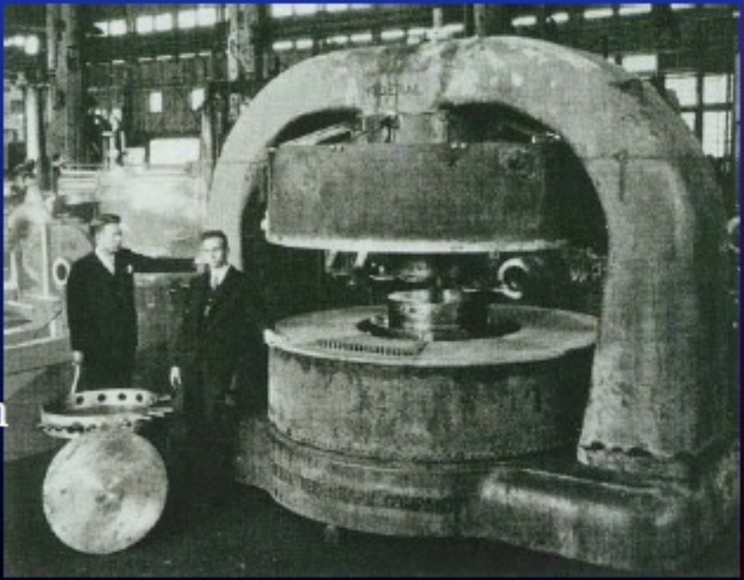
1932 - The Invention of the cyclotron

Ernest O. Lawrence and his First cyclotron 1932

E.O.Lawrence and M.S. Livingston "The production of high speed Light ions without the use of high voltages",

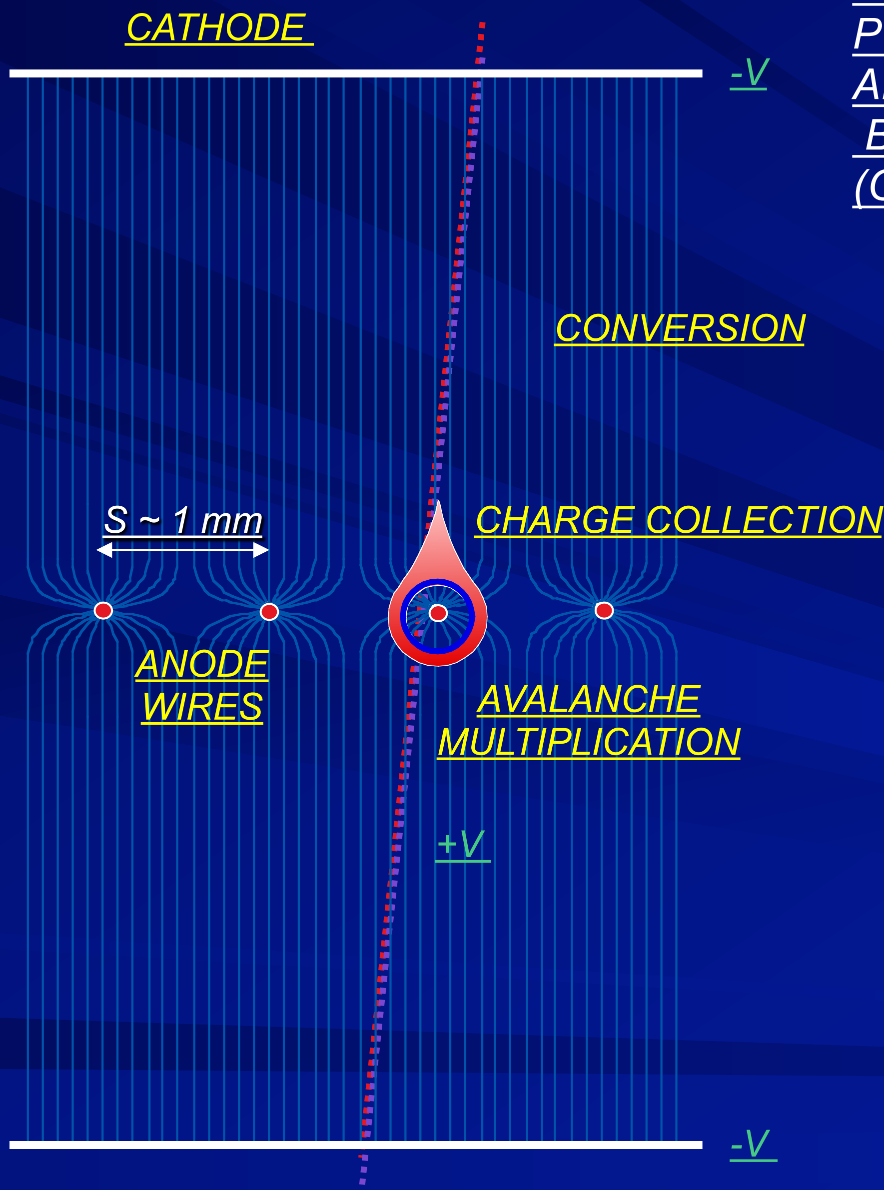
A milestone in the production of usable quantities of radionuclides.

E.O Lawrence and M.S.Livingston with the 27-inch cyclotron at Berkeley 1933, the first cyclotron that produced radioisotopes



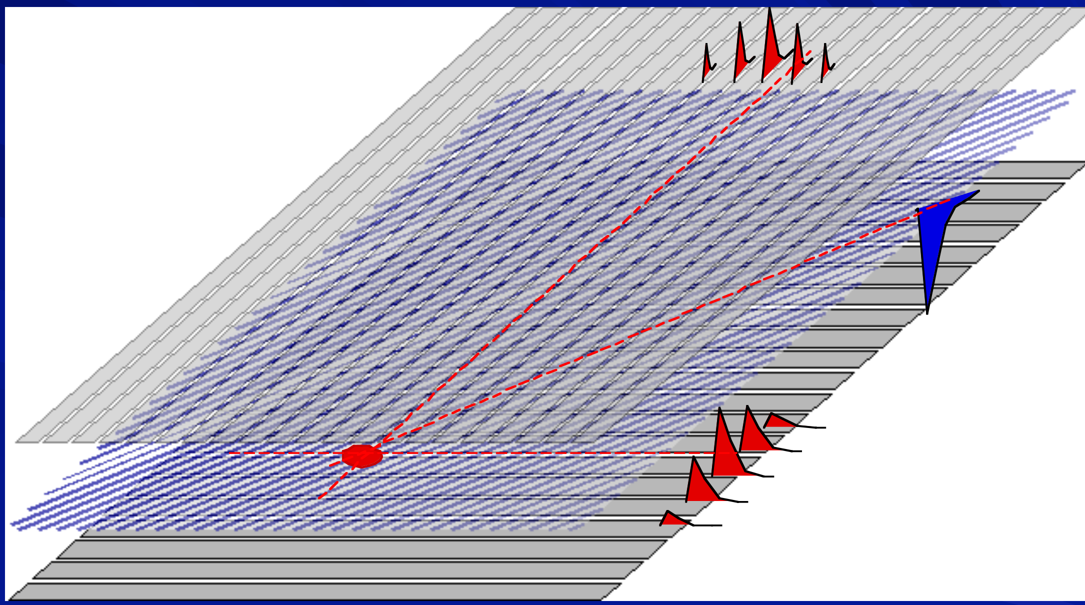
Deacreasing the dose with HEP Gazeous detector

Multi Wires Proportional chambers MWPC



MODERN GASEOUS DETECTORS:
POWERFUL TOOLS FOR RADIATION DETECTION
AND LOCALIZATION IN PARTICLE PHYSICS,
BASED ON THE MULTIWIRE PROPORTIONAL CHAMBER
(Georges Charpak, 1967)

TWO-DIMENSIONAL MWPC READOUT CATHODE
INDUCED CHARGE (Charpak and Sauli, 1973)

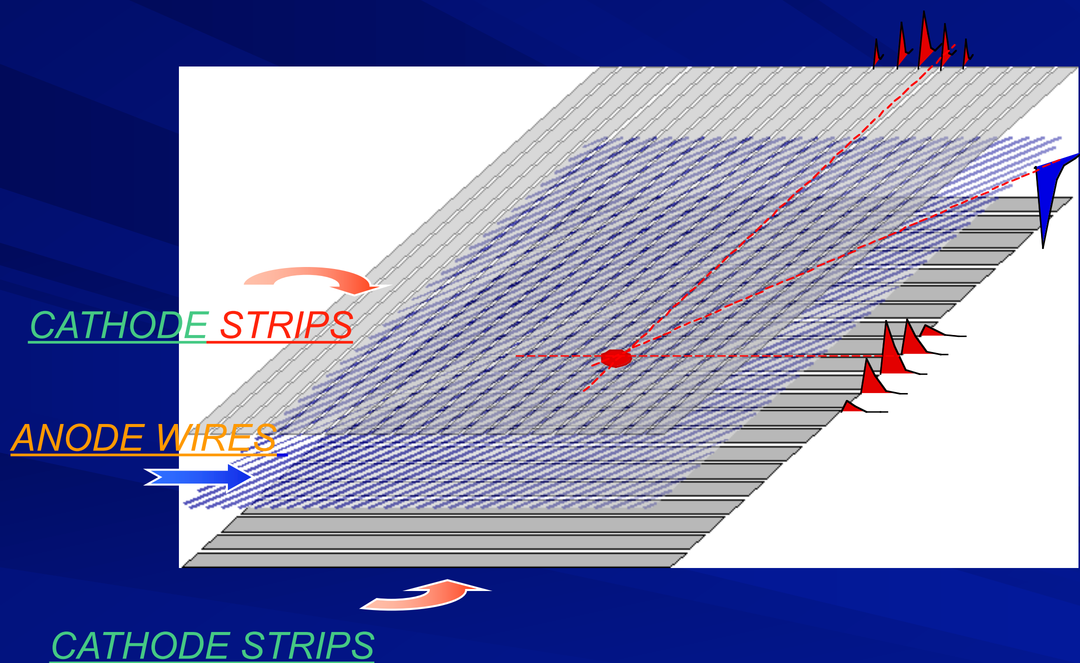


Spatial resolution determined by: Signal / Noise Ratio
Typical (i.e. 'very good') values: S ~ 20000 e: noise ~ 1000e
Space resolution < 100 μm

E. Gatti et al, Optimum geometry for strip cathodes … , Nucl. Instr. and Meth. 163(1979)83

TWO-DIMENSIONAL LOCALIZATION

TWO-DIMENSIONAL LOCALIZATION FROM SIGNALS INDUCED ON CATHODE PLANES (Charpak & Fabio Sauli, ~1973)



LOW-DOSE DIGITAL RADIOGRAPHY
WITH MWPC:
CHARPAK'S HAND (2002):

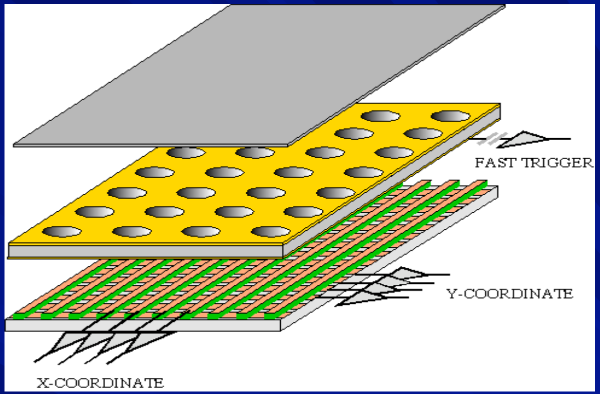
X Ray imaging

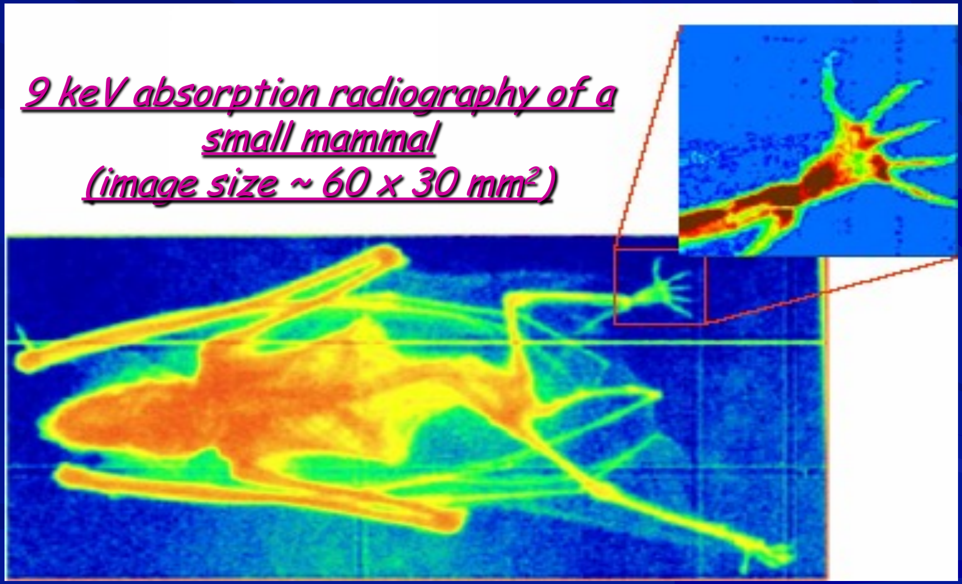
Wire Chamber Radiography:

Position resolution ~ 250 μm

GEM for 2D Imaging:

Using the lower GEM signal, the readout can be self-triggered with energy discrimination:





Position resolution ~ 100 μm
(limited by photoelectron range in the gas)

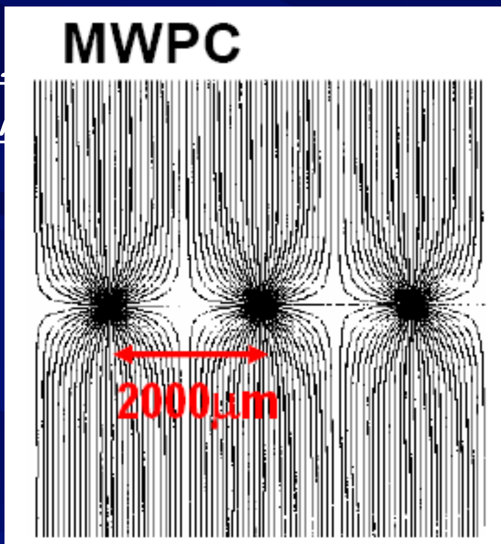
A. Bressan et al, Nucl. Instr. and Meth. A 425(1999)254
F. Sauli, Nucl. Instr. and Meth.A 461(2001)47
G. Charpak, Eur. Phys. J. C 34, 77-83 (2004)
F. Sauli, http://www.cern.ch/GDD

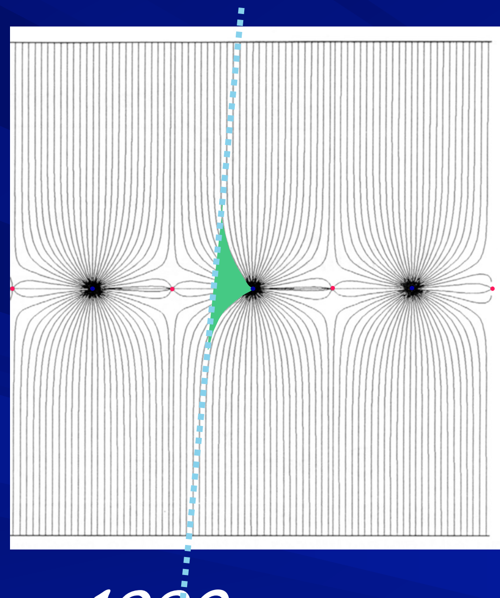
From MWPC's to MGPD's

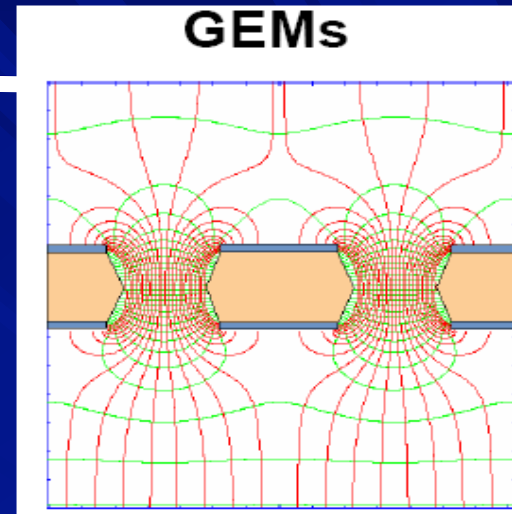
MGPD

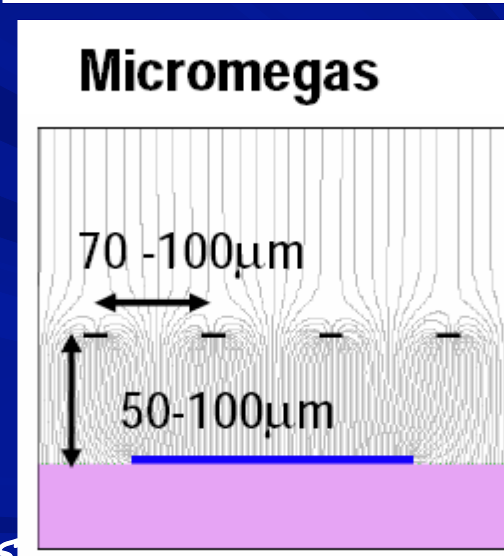
MWPC

Drift Chamber









1975 - 1995

UA2-LEP

Multiwire Proportional Chamber

Georges Charpak 1968

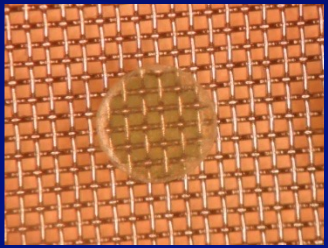
1990 -

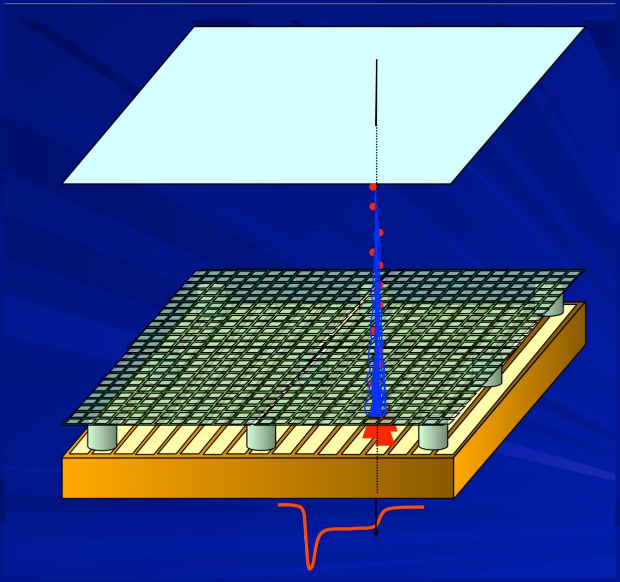
GEM F.Sauli)

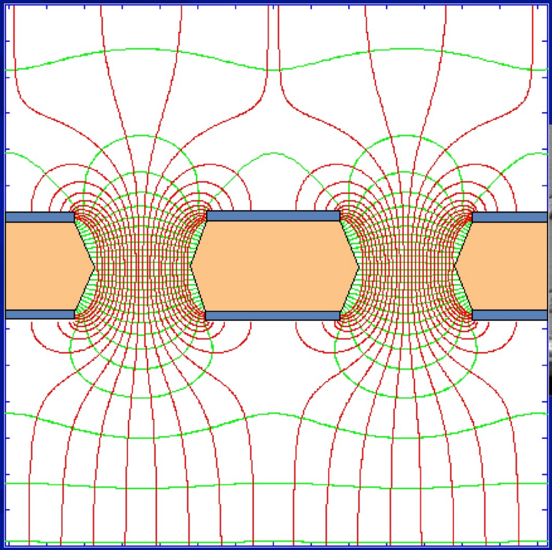
Micromegas Y. Giomataris

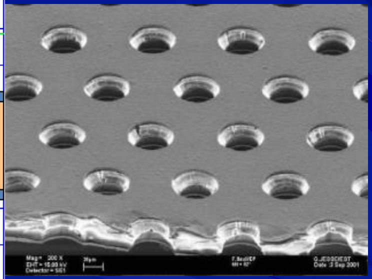
MPGD

- From 1988-1998 Micro-technologies and etching techniques allowed development of Micro Patter Gaseous Detectors
  - MICROMEsh GAseous Structure
    - Thin gap Parallel Plate Chamber: micromesh stretched over readout electrode.
  - Gas Electron Multiplier
    - Thin, metal-coated polymer foil with high density of holes, each hole acting as an individual proportional counter.



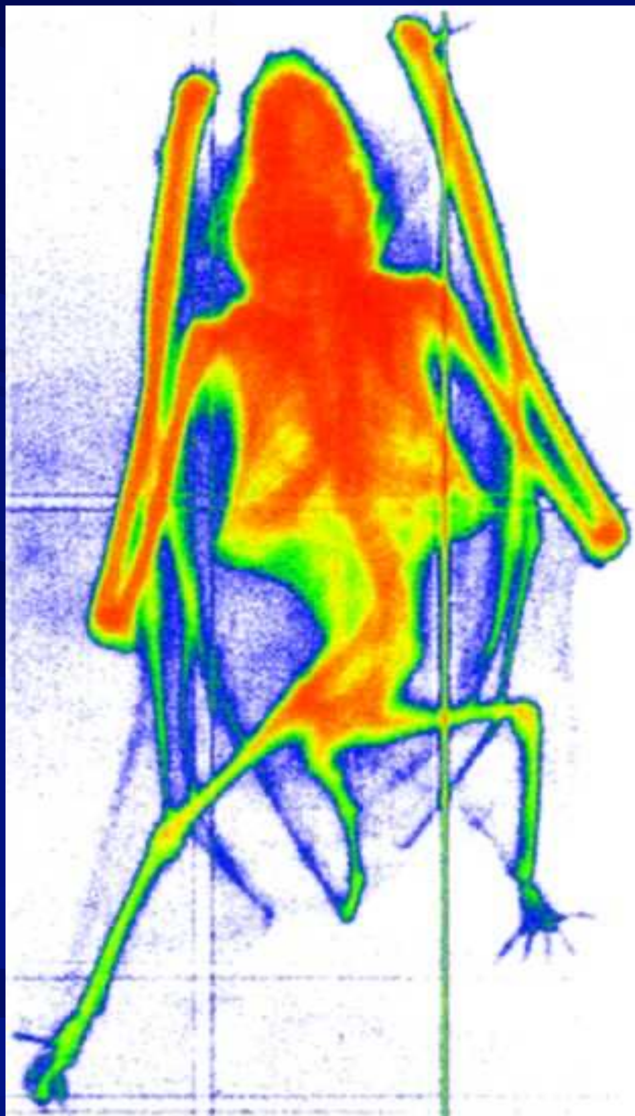




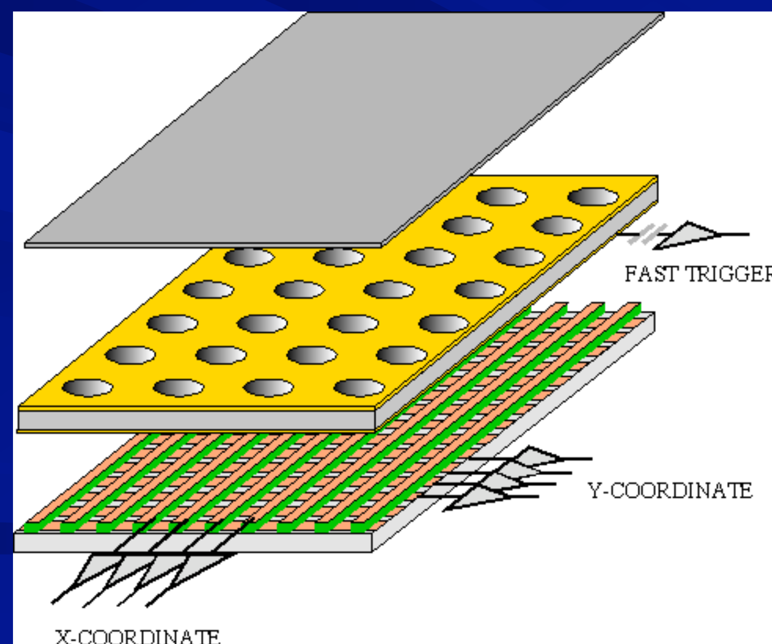


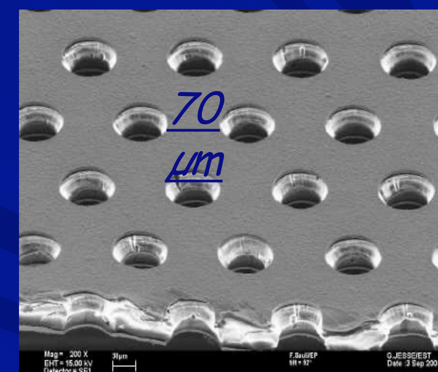
Exemple with GEM Detector

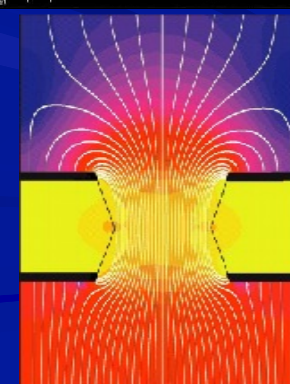
- Thin, metal-clad polymer foil, chemically pierced by a high density of holes (70-80 μm diameter).
- On application of a difference of potential between the two electrodes, electrons released by radiation in the gas on one side of the structure drift into the holes, multiply and transfer to a collection region.
- Cascading several foils results in high multiplication factors.



F.Sauli & al.

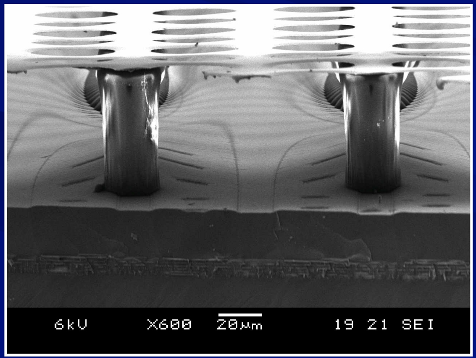




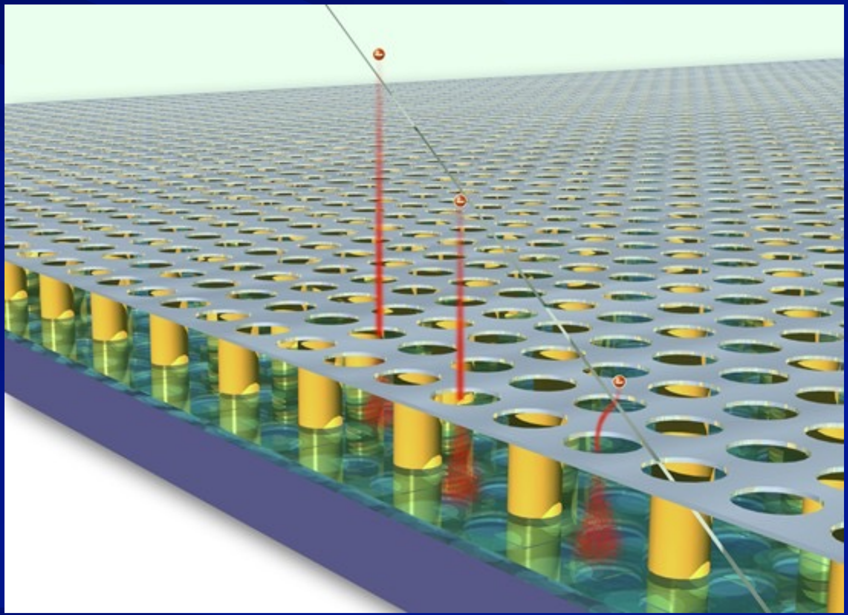


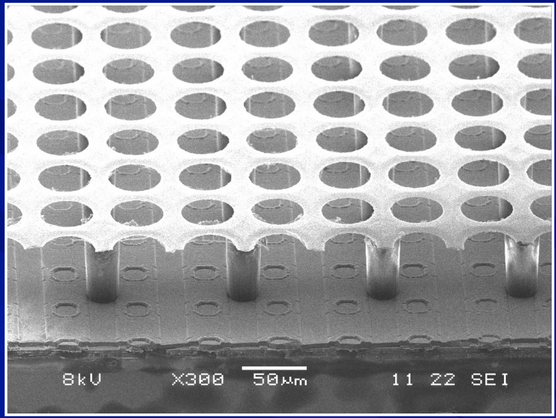
Next → INGRID

- InGrid :integrate the Micromegas/GEM concept on top of a MediPix pixel CMOS chip (Timepix)
  - pixel size: 55 x 55 μm^2
  - per pixel: preamp – shaper – 2 discr. –
  - Thresh. DAQ - 14 bit counter



metalized foil
~100 μm ~1mm





117Cmos Medipix chip

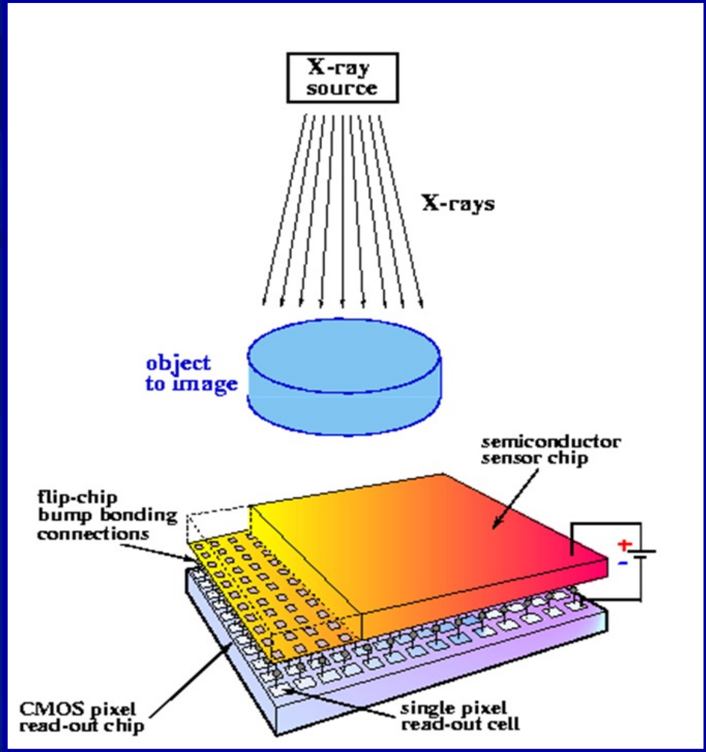
- Use → Large Trackers & Calorimeters

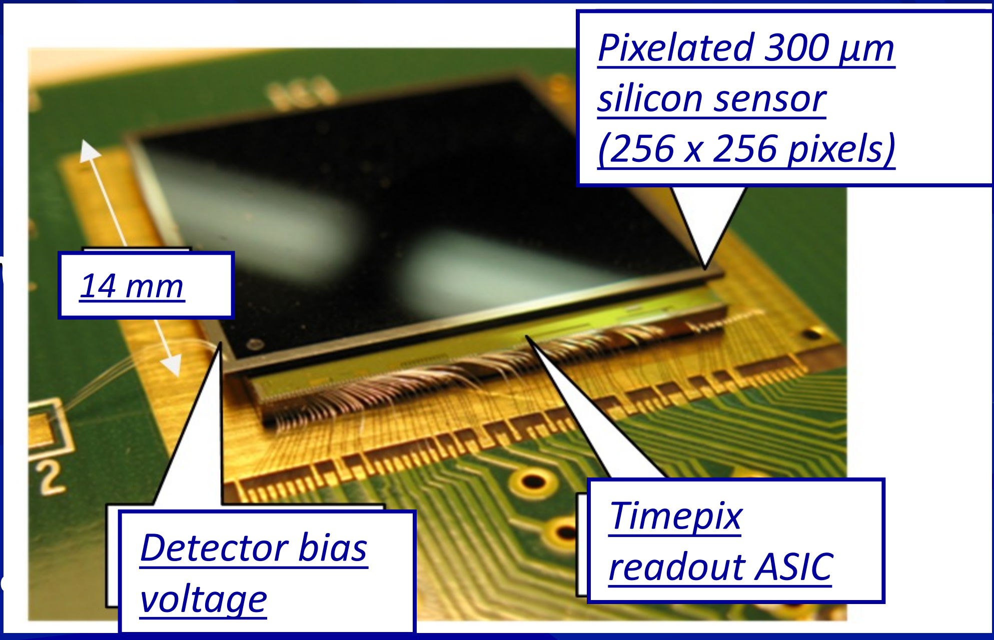
Timepix Hybrid detector

On the way of photon counting

- Medipix is a Silicon pixel-based detector technology AND signal processing that can be employed to measure charged particles,photons, and neutrons.
- It is based on a read-out chip that embeds the electronics for each pixel within the pixel's footprint!
- Detector and electronics readout are optimized separately
- developed for use in the CERN LHC Central Trackers
- Medipix 3/TimePix This technology is an extension of designs originally
  - Integrate a TDC ....

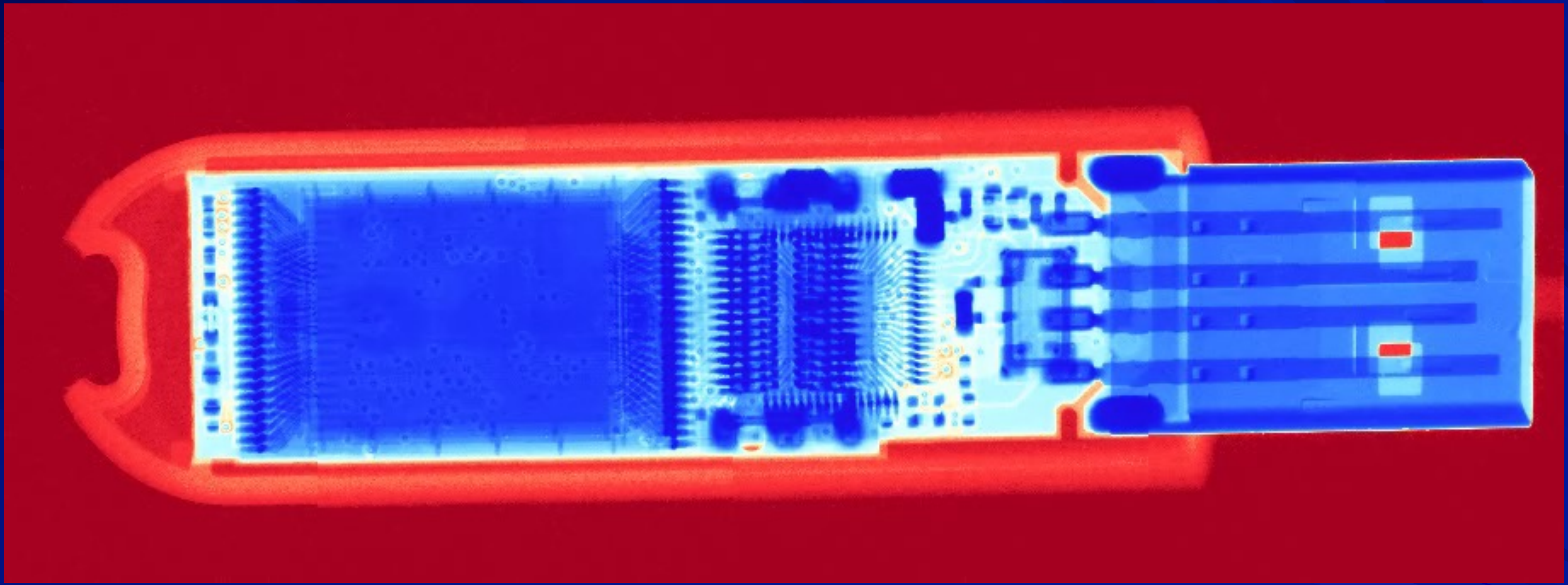
TU Prague - J. Jakubec
NSS-MIC 2013 Seoul J4-3





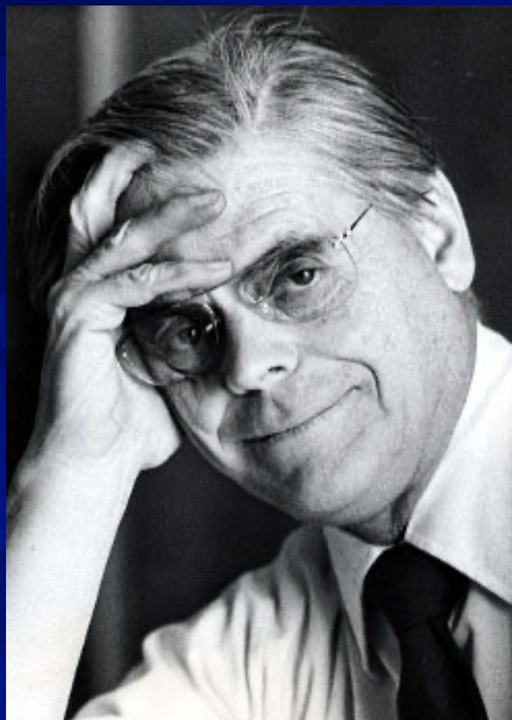
Medipix-CT setup for detector investigations & material analysis

Example → USB flash drive



TPX 110µm + CdTe 2mm
8x2 tiles / mag. 1.5x
65kV / 200µA

1946 - The origin of particle therapy



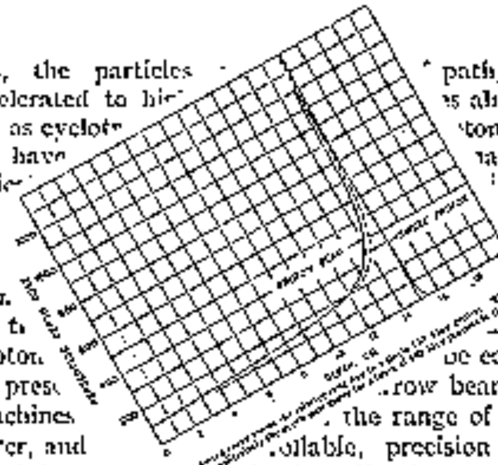
R.R. Wilson, Radiology 47(1946), 487-491

Radiological Use of Fast Protons

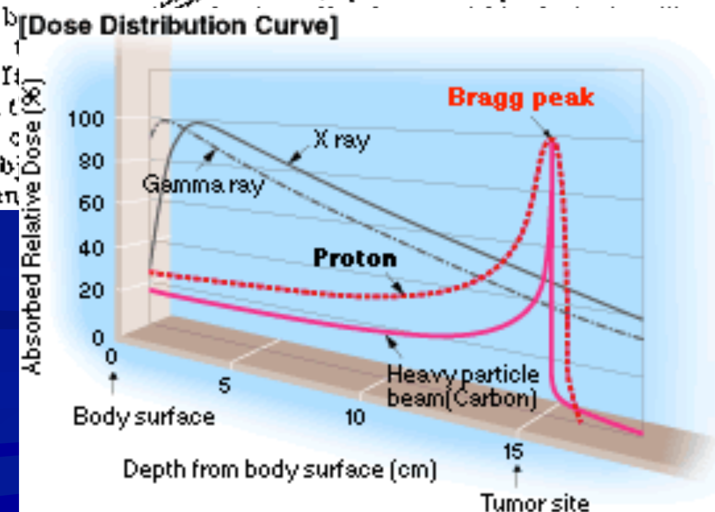
ROBERT R. WILSON

Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

EXCEPT FOR electrons, the particles which have been accelerated to hi… energies by machines such as cyclot… Van de Graaff generators have … directly used therapeutic… the neutrons, gamma … radioactivities produce… tions of the primary pa… applied to medical problem… large part, been due to t… penetration in tissue of proton… and alpha particles from pres… ators. Higher-energy machines … under construction, however, and … from them will in general b… enough to have a range in t… parable to body dimensions. It … occurred to many people that t… …lves now become of … …eutic interest. The obj… …s to acquaint medical an…



… path, or specific ioniza… …s almost inversely with …ton. Thus the specific …any times less where …issue at high energy …imeter of the path …o rest. … it possible to …actly localized …y, with but little …be easy to produce well …row beams of fast protons, … the range of the beam is easily …ollable, precision exposure of well



- The origin of particle therapy using the Bragg peak discovery (1903)

Basics of particle imaging

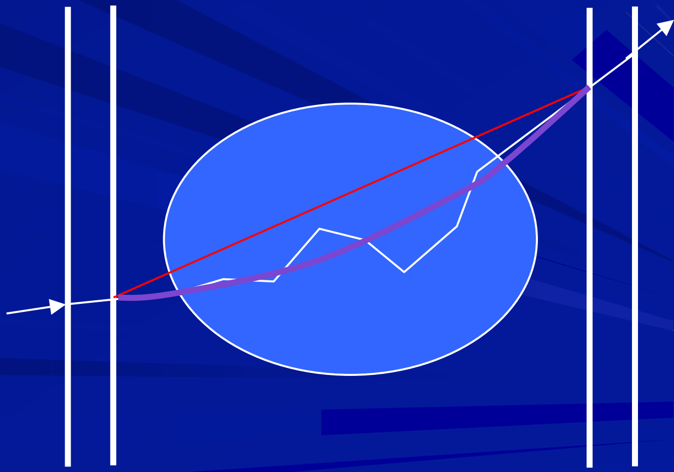
- *The particle (proton/ion) go through the patient at high energy*
- *Advantages:*
  - *Decrease the uncertainties → better dose accuracy*
  - *Reduce the dose delivered to the patient*
- *Challenge → the data reconstruction*
  - *correctly reconstruct the path of the proton*

Radiograph of a phantom
Uwe Schneider PhD thesis
(1978,PSI)

Proton CT:

1) replaces X-ray absorption with proton energy loss

2) reconstruct mass density distribution instead of electron distribution



A tribute to G.Charpak