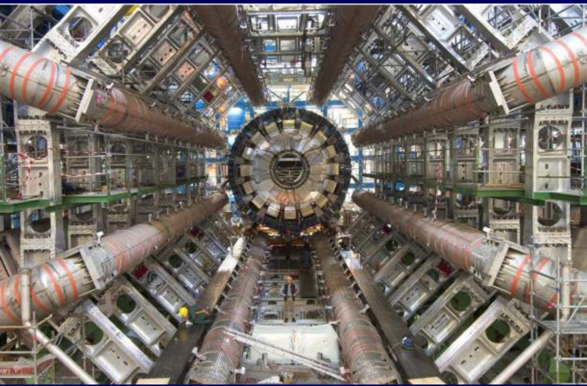
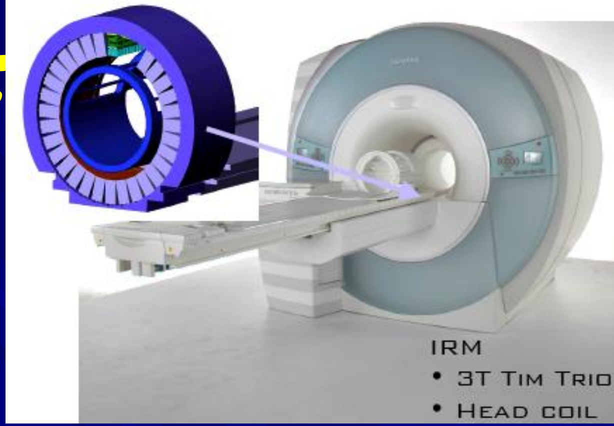
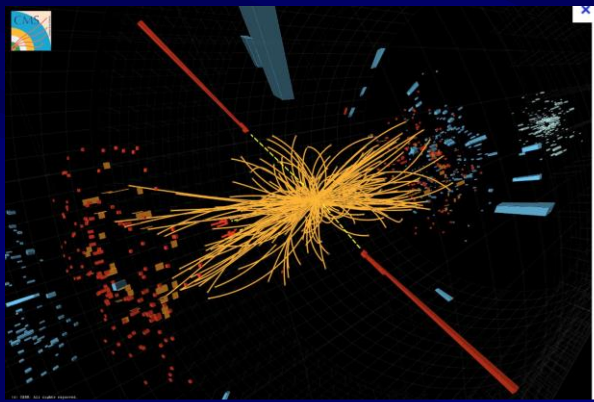


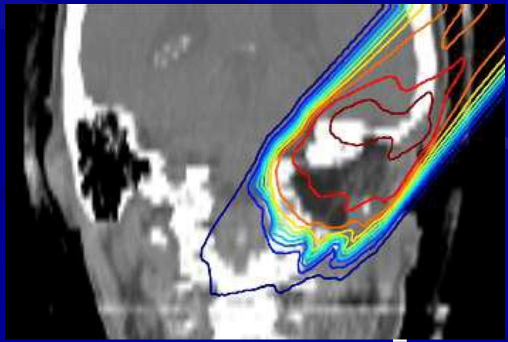
Application of fundamental physics in medicine





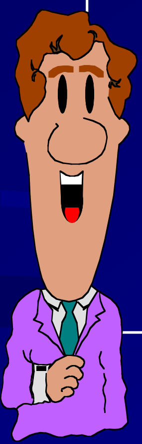
P. Le Dû

patrickledu@me.com



Goals of this presentation

- A flavor of valorisation of Particle Physics
  - Can we use the tools and techniques and state of the art technologies developped for HEP experiments in another field ?
- Illustrate using sucessfull examples in the most challenging and innovative biomedical field for diagnostic and treatment of cancer (PET and particle therapy)
- X Ray Radiography and dose reduction (CT)



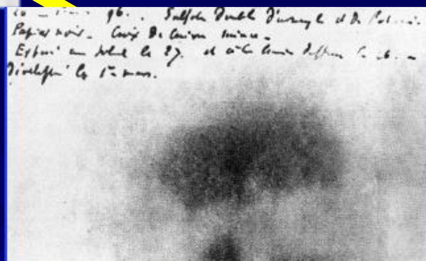
Outlines

- Few words of introduction
- PET Imaging for diagnostic
  - Past ,present and future
- Xray applications
    - New radiography devices
- Particle Therapy for treatment and verification
  - Proton CT→The ultimate dream!

A little bit of history About radiation and its application in medicine

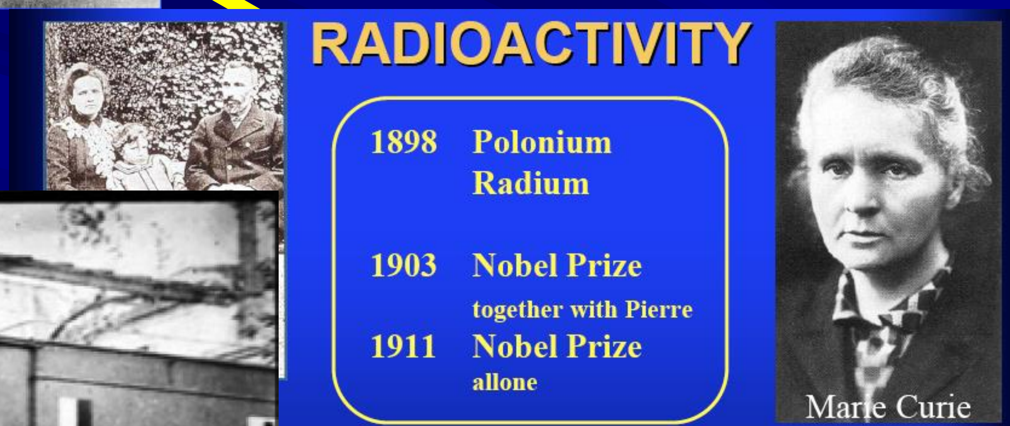
How physics discoveries have impacted our life (1)

1895
W.C. Rontgen
Discovery of X Ray



1896 - Discovery of the natural radioactivity by Henri Becquerel

First image of potassium uranyl disulfide



1898
Pierre and Marie Curie
the Radioactivity
Polonium,Radium

1910

X Ray Radiography

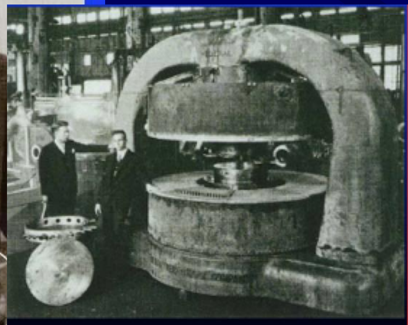
1923 - The Tracer principle
`G.V.Hevesy- the father of nuclear medicine

Tracer

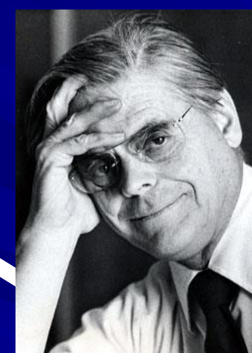
How physics discoveries impact our life (2)

1932 - The Invention of the cyclotron
Production of radioisotopes

Ernest O. Lawrence and his First cyclotron 1932

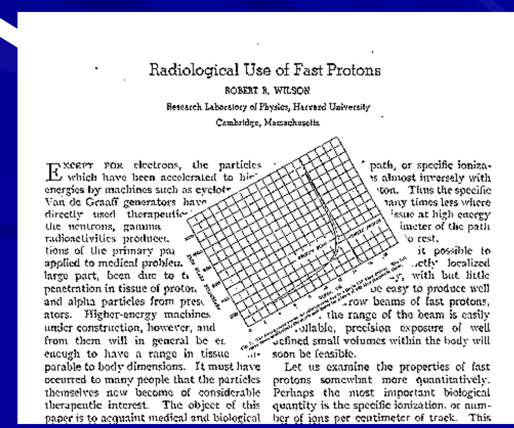


1934 - Artificial radioactivity
Irène and Fréderic Jolio Curie



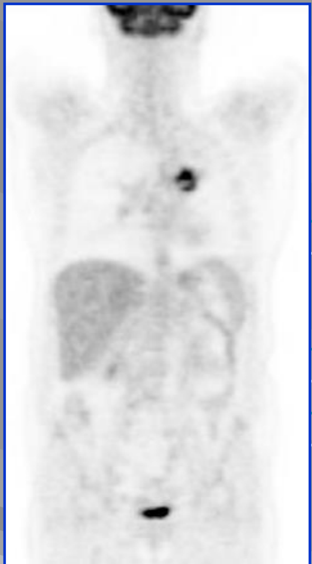
1946 – R.R.Wilson
The origin of particle therapy
Using the Bragg peak discovery (1903)

Proton therapy

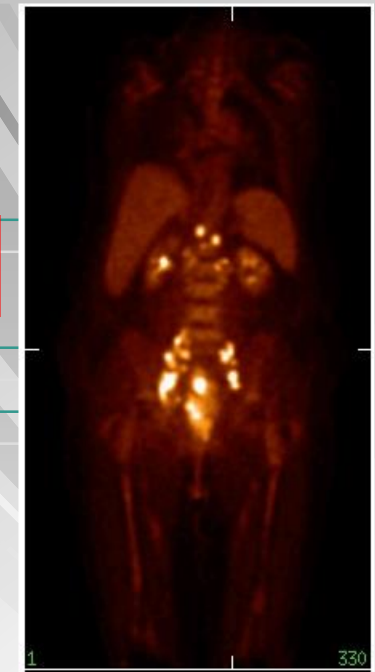


Radiological Use of Fast Protons
ROBERT R. WILSON
Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

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.

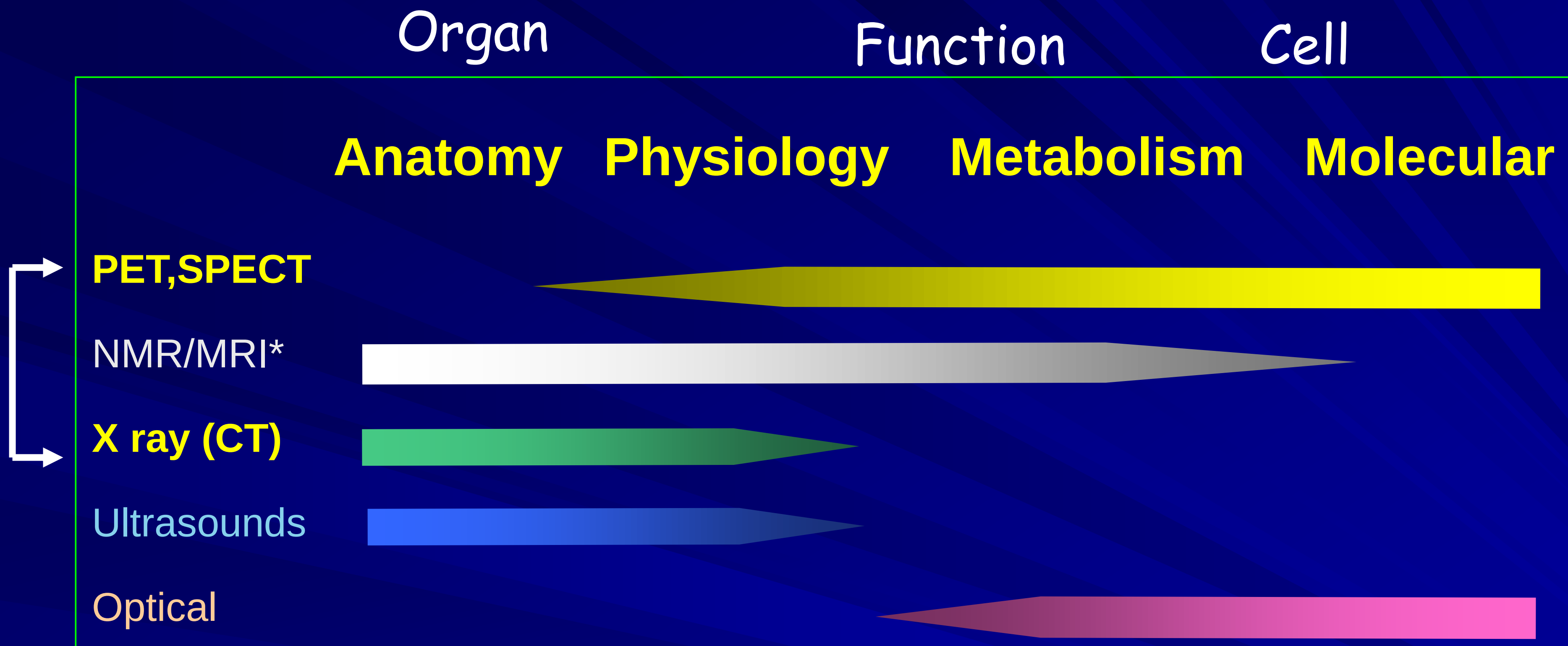


The best 'typical example → The PET



PET imaging
From past,present to future

The various types (modalities) of imaging

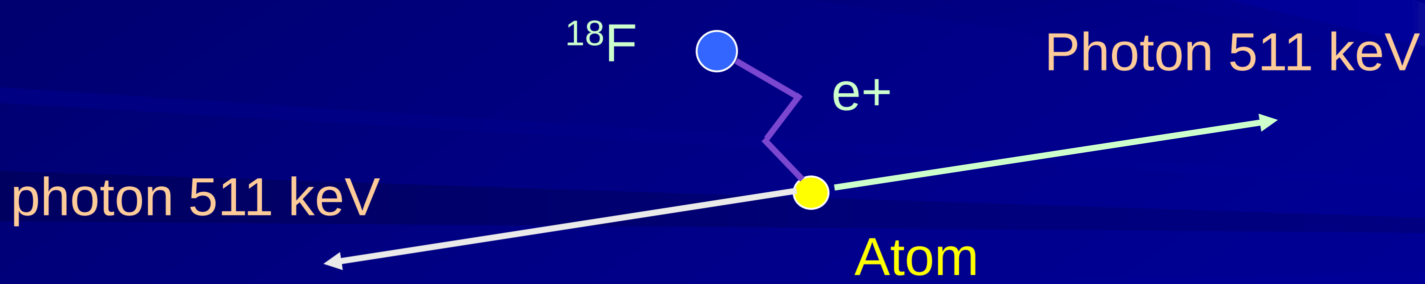


- Complementary !
- Depends on what you want to see

MRI/MMR = Magnetic resonnance*

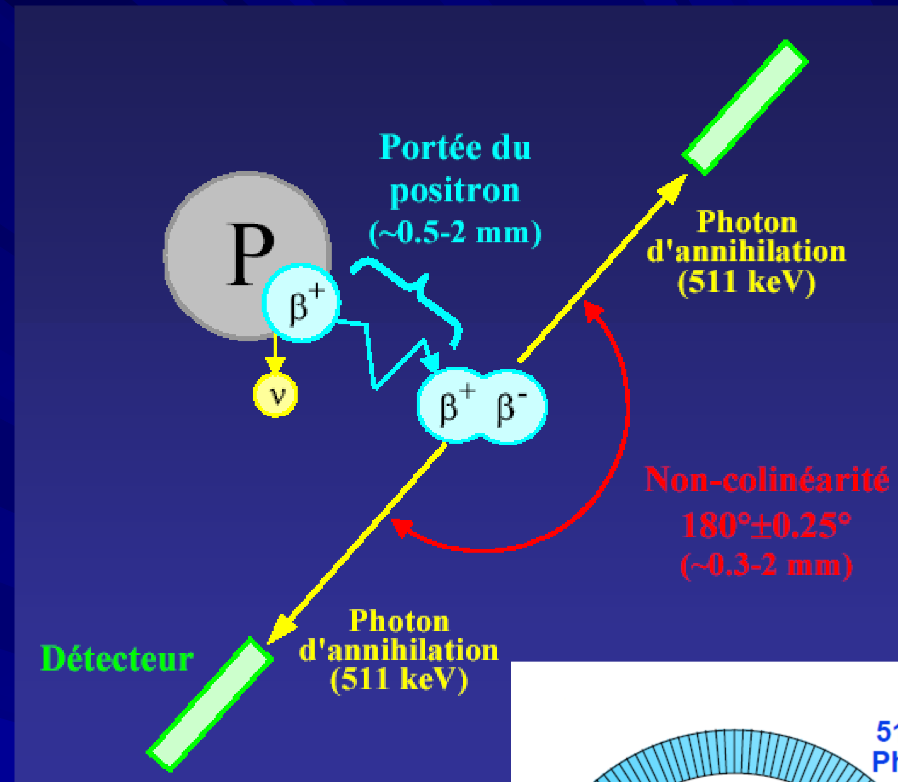
Positron Emission Tomography principle

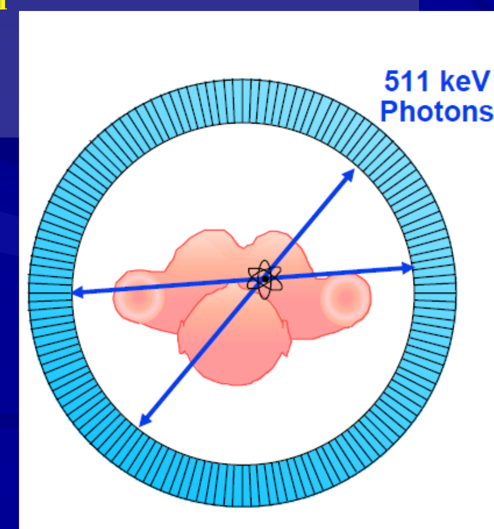
- Functional imaging device
- Molecular tracers with doped beta + emitters
  - ^{11}C(20 min), ^{15}O (2min) , ^{13}N (10 min), ^{18}F (2h)
  - Produced by a 18 Mev Proton cyclotron
  - The most common → ^{18}F => ^{18}FDG fluoro-deoxy-glucose
    - Sign the degree of activity of an organ hungry of glucose
- annihilation positron with an electron
  - emission of two 511 keV photons back to back



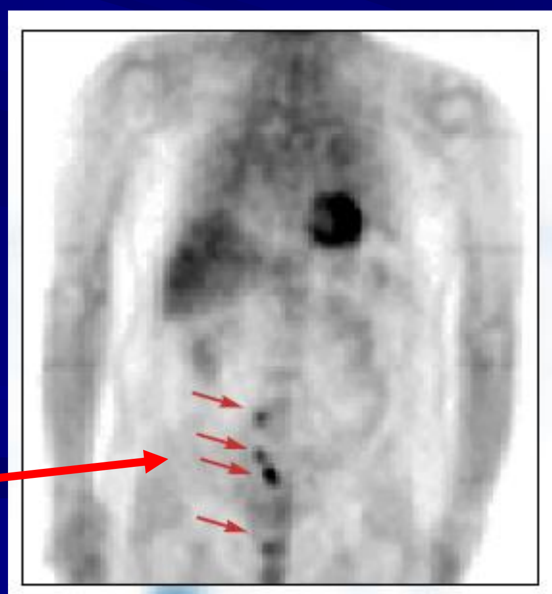
Positron Emission Tomography principle

- Sign the degree of activity of an organ hungry of glucose ---> show abnormal glucose metabolism like cancer tumour cells





Colon cancer spots



The PET sequence

Produce radio-
active sugar (FDG)

Intravenous
injection

10mC

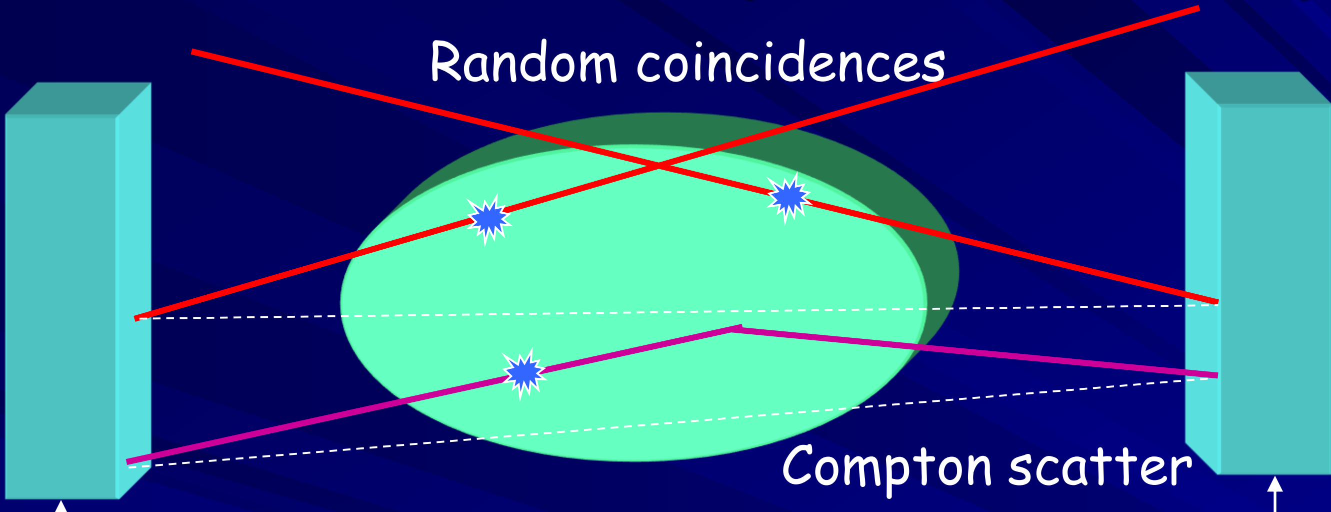
Wait for
accumulation
in target site

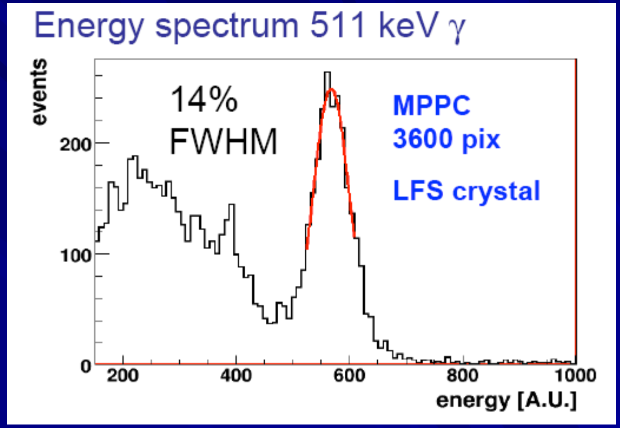
Detect
coincidence
events

Get 2 gamma
events

Reconstruct
image coincidence
events

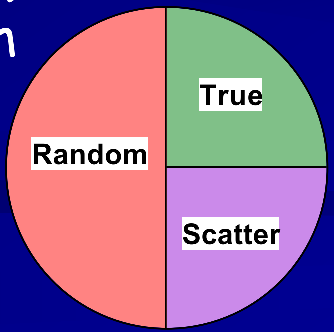
The experimental aspect

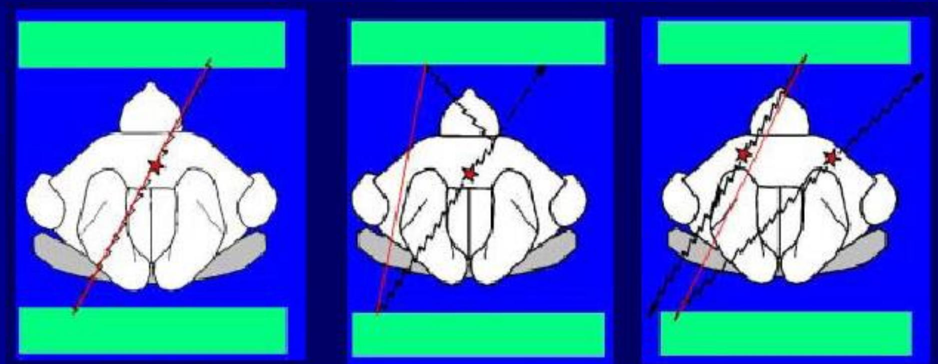




Detector in coincidences
Energy window around 511keV
Time window < ns
Limited Acceptance (Field Of View)

Signal : true concidences (25%)
Background: Compton + Random

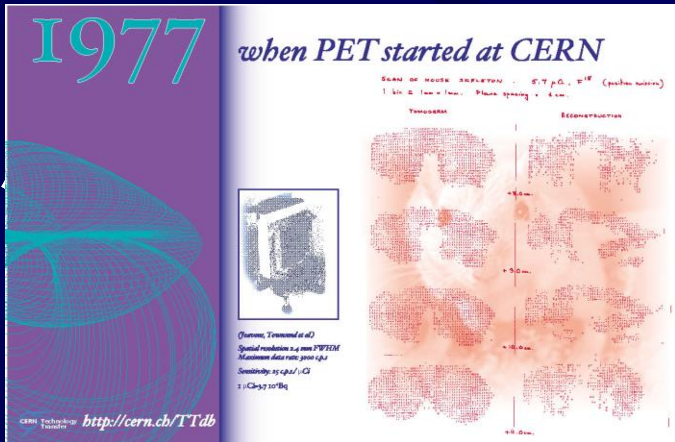




TRUE coincidences | Scattered coincidences | Random coincidences

Efficiency ≈ 0,01 (1 photon / 100)

Historical Evolution of PET



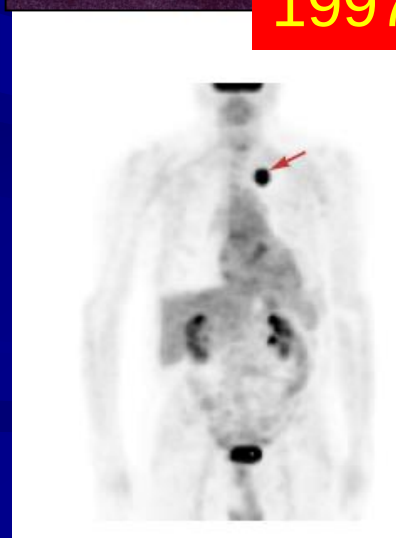
1977

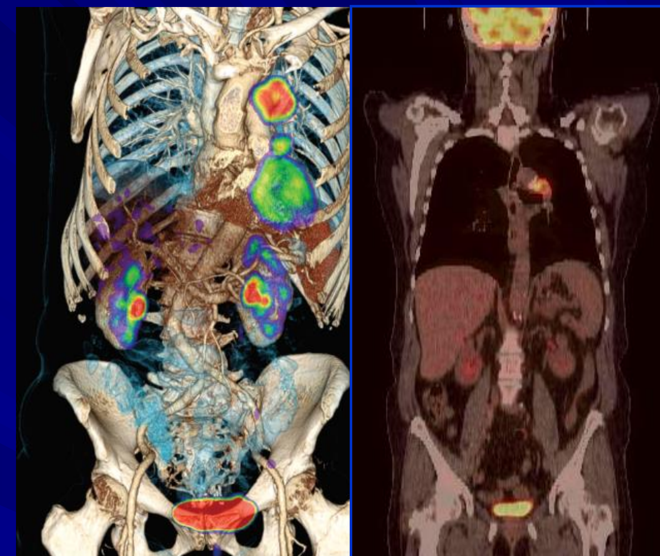
First Steps
Townsend & Jeavons

First mouse imaging with ^{18}F

C-PET Philips

1997





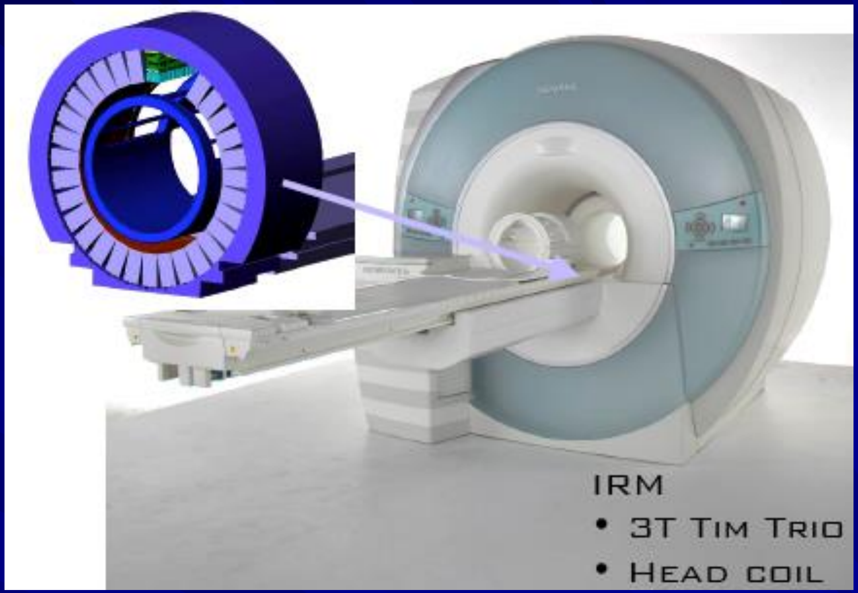
2007

Biograph PET + X ray-CT

From Today ---> Tomorrow Challenge

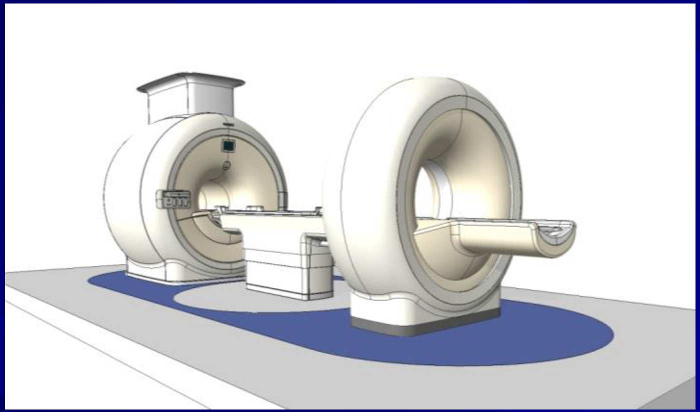
TDM/PET-TOF (500 psec)

Today



Siemens

PET-MRI



Philips

Next ?

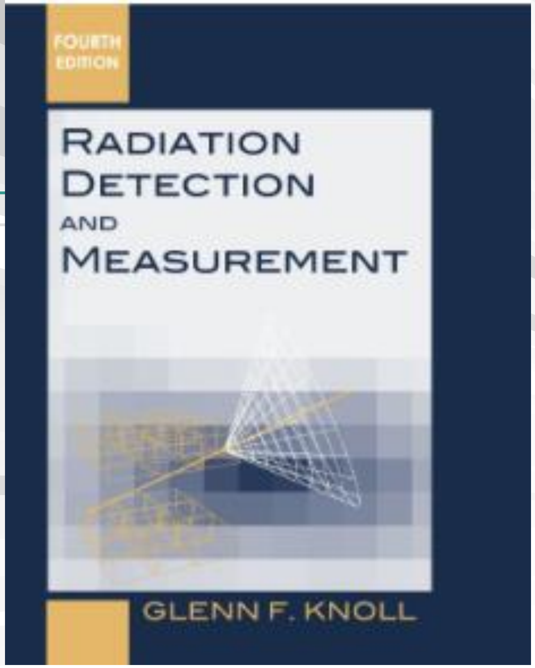
Few words about Particle Physics Detector

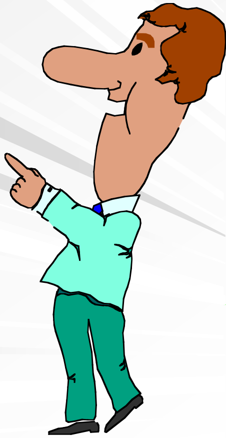
Radiation

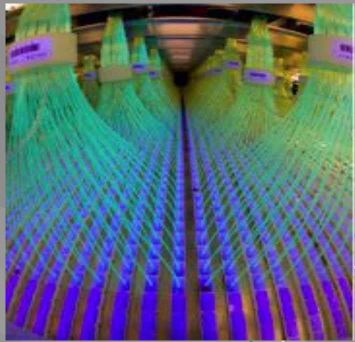
Instrumentation

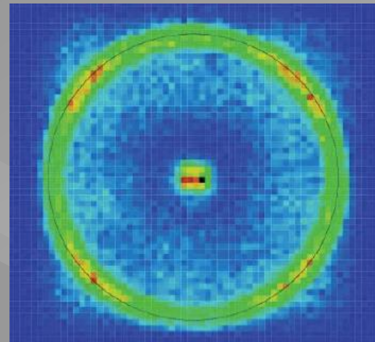
The Bible

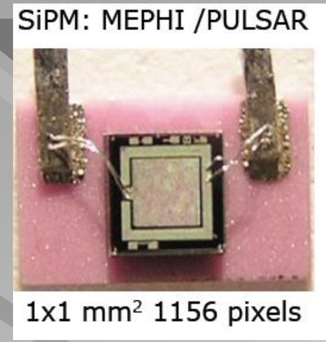
Glenn Knoll









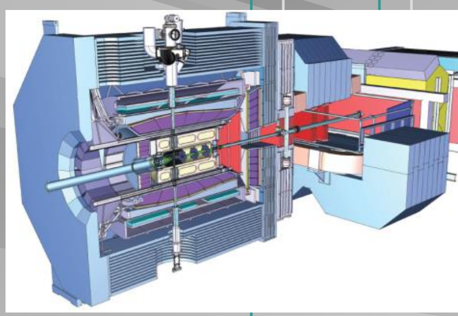


T2K
scintillators
WLS fiber
60000 SiPM

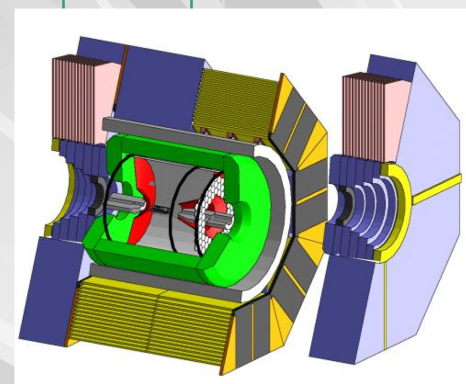
Belle2 RICHs
single γ

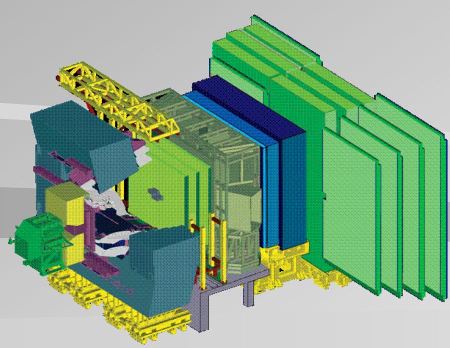
ILC - CALICE
$8x10^6$ SiPM

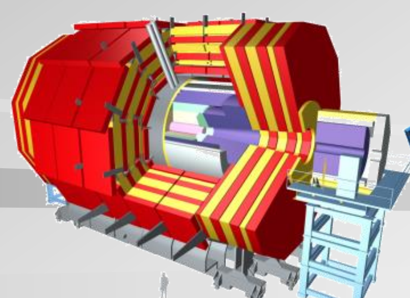
CMS HCAL
$2 x10^3$ SiPM

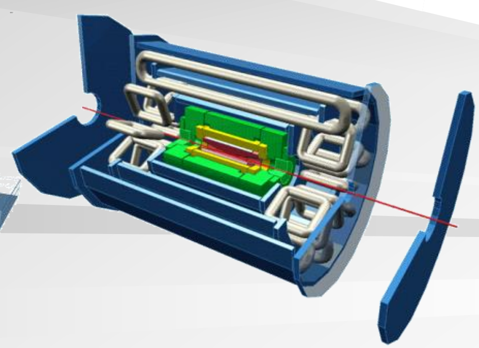


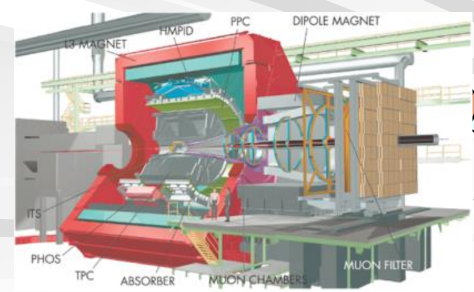
Some technologies that can make a breakthrough

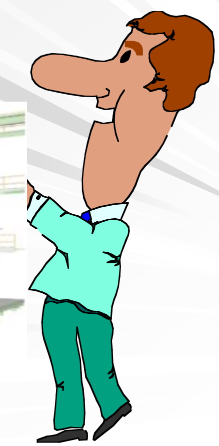










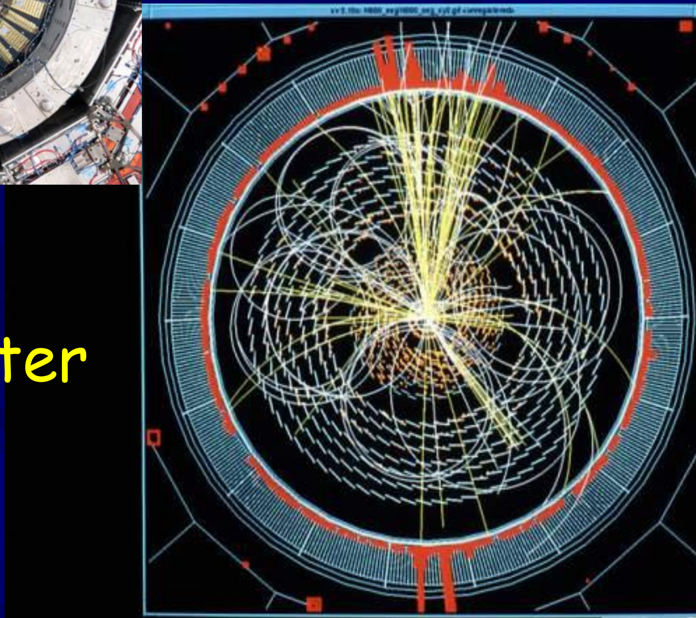


HEP & PET

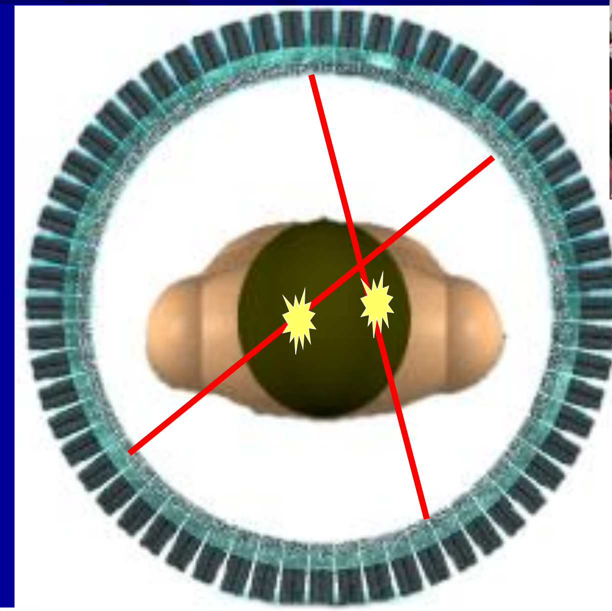
Similarities and differences

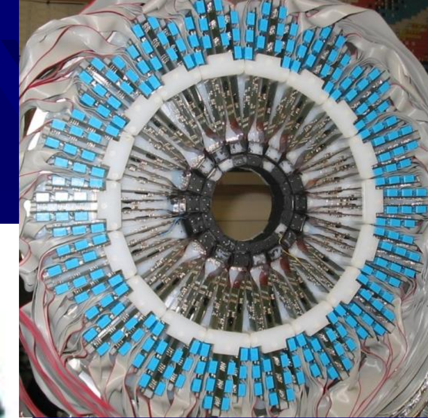
Calorimeter

HEP



M_{Higgs} = 100 GeV



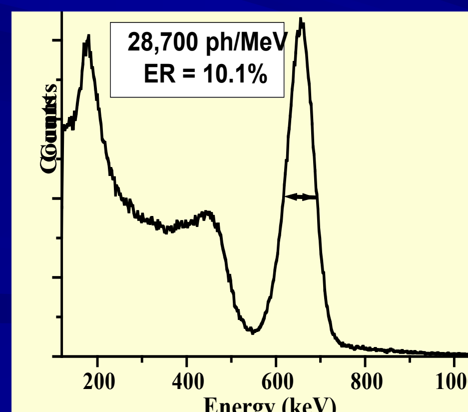


PET Camera

Biomedical Imaging

Similarities

Geometry and granularity
Detector (Crystals & scintillator)
Sensor Photodetectors (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

A survey of common areas

LSO

- Material for photon detection
  - Standard : Crystal
    - From LEP/ L3 BGO ,LHC/ CMS PbO4
    - → Crystal Clear Collaboration.
  - Possible alternatives: LXenon, MG-RPC's … ????

- Photon detectors :

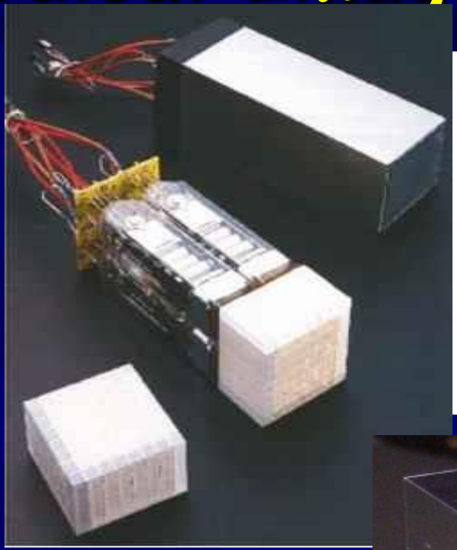
compact, high QE, high gain and stability
  - Standard : PMT ---> MAPMT --> MCP
  - Semiconductor : APD --> SiPM/MPPC,DSiPM

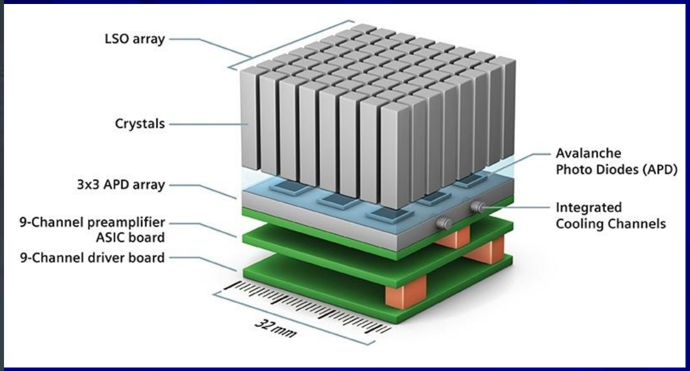
Scintillators for PET

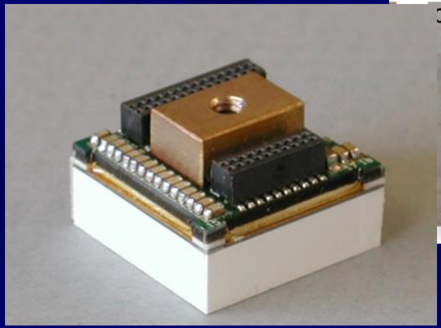
	1962	1977	1995	1999	2001	2003	2007
	NaI	BGO	GSO:Ce	LSO:Ce	LuAP:Ce	$LaBr_3$:Ce	LuAG:Ce
Density (g/cm^3)	3.67	7.13	6.71	7.40	8.34	5.29	6.73
Atomic number	51	75	59	66	65	47	63
Photofraction	0.17	0.35	0.25	0.32	0.30	0.13	0.30
Decay time (ns)	230	300	30-60	35-45	17	18	60
Light output (hν/MeV)	43000	8200	12500	27000	11400	70000	>25000
Peak emission (nm)	415	480	430	420	365	356	535
Refraction index	1.85	2.15	1.85	1.82	1.97	1.88	1.84

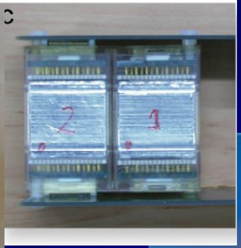
- No Scintillator with Superior Properties in All Aspects

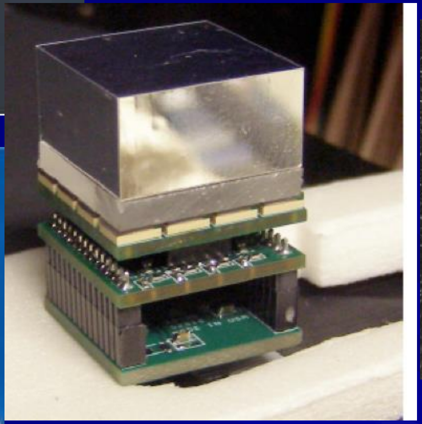
Scintillation Detectors in Nuclear Medical Imaging

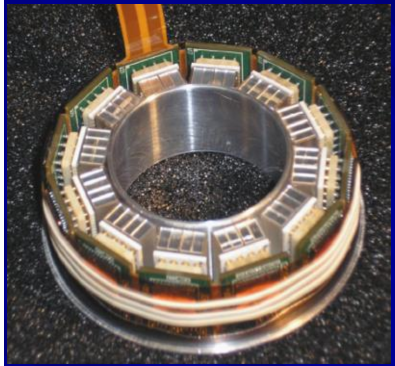


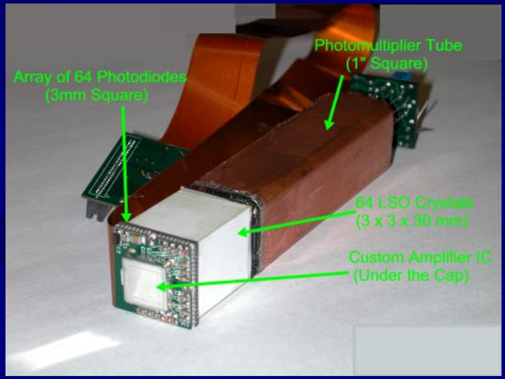


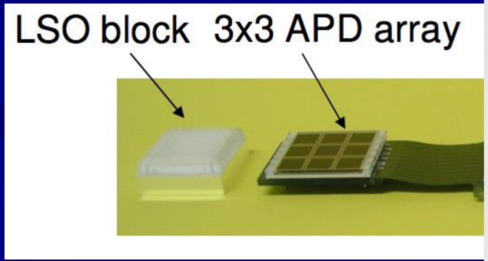




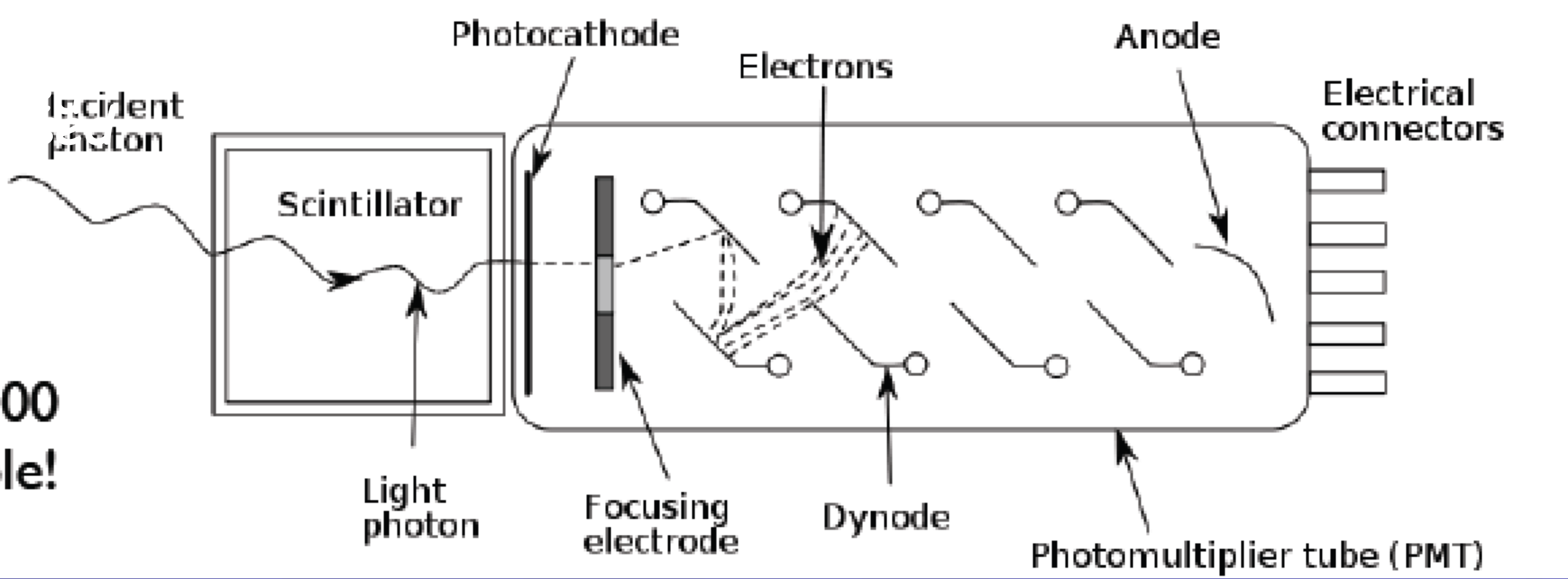








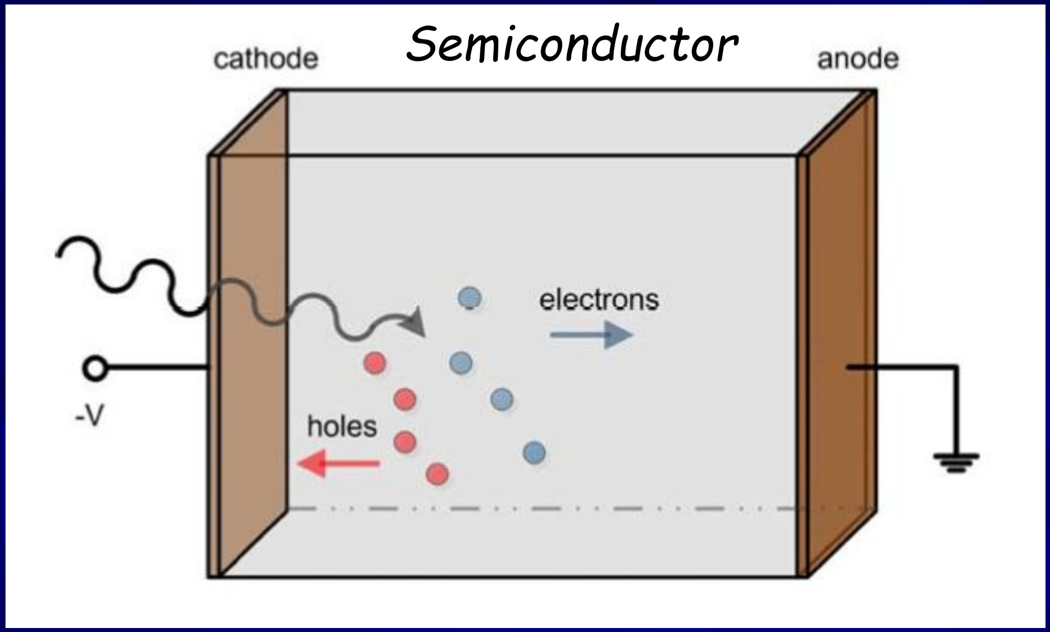
Photomultiplier Tube (PMT)

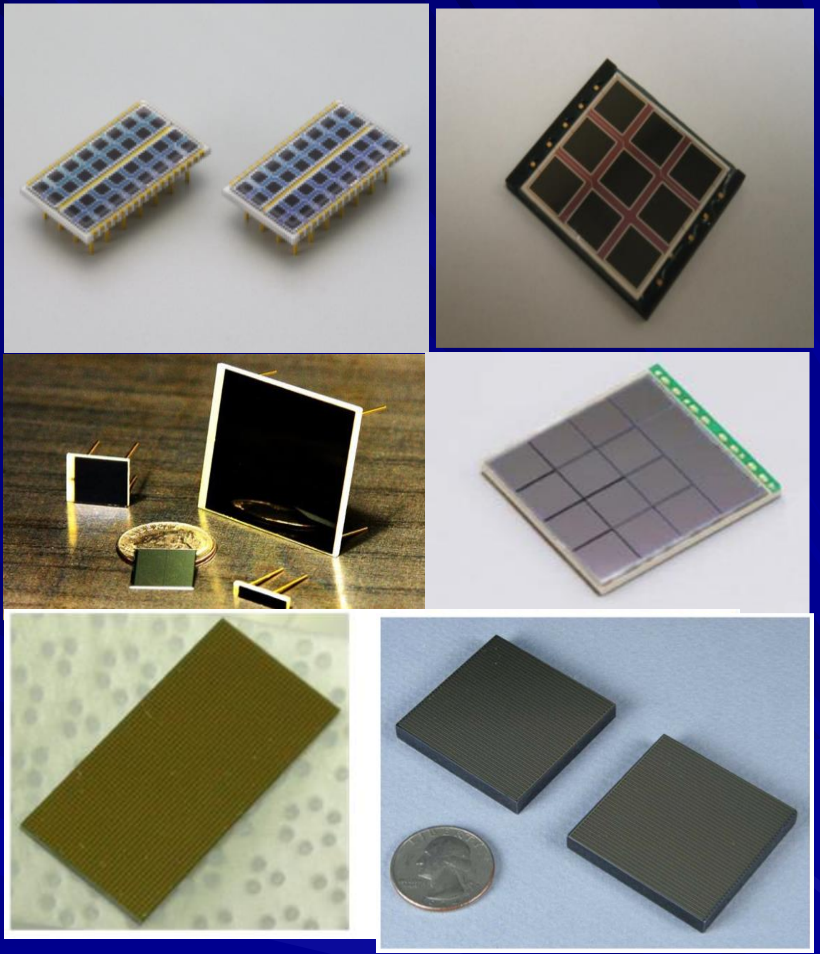


Gains of x100,000,0000 are achievable!

Use since 75 years
Large gain
Bulky
Sensitive to magnetic field

The 'solid state' photodetector





- *Electric field is created by an applied bias voltage*
- *e-h pairs are created by incoming radiation*
- *Electrons move to the anode and holes move to the cathode*
- *Electrical signal is induced on the electrodes by the moving charges*

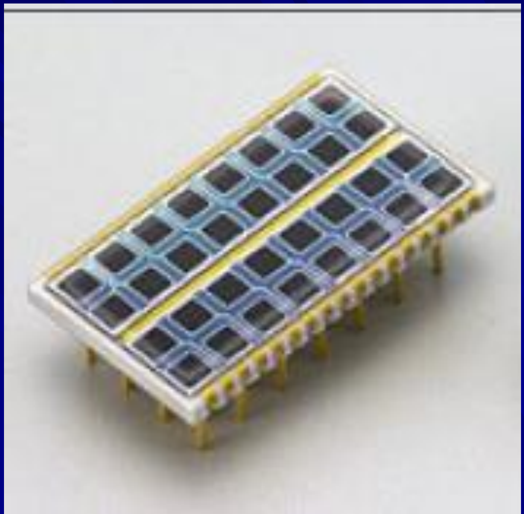
Photodiode (PIN)
Avalanche Photodiode (APD)
Silicon Photomultiplier (SiPM)
CdZnTe
CdTe/

22

Evolution: PMT → Silicon photodetectors : SiPM

Advantages:

- High QE (>70% for 400−600 nm)
- APD operating in Geiger mode
- High internal gain ($10^5 - 10^6$)
- Very fast response (~100 ps rise time)
- Capable of detecting single photoelectron
- Insensitive to magnetic field

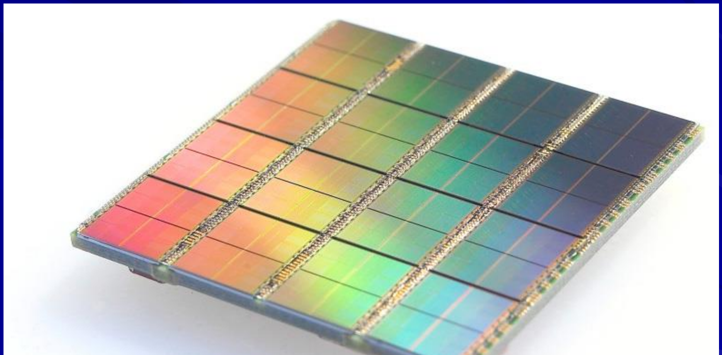


Drawbacks:

- Geometric fill factor
- Limited micro-cell => limited dynamic range

Sensitive to temperature and voltage fluctuations in analog mode, but not in purely digital mode

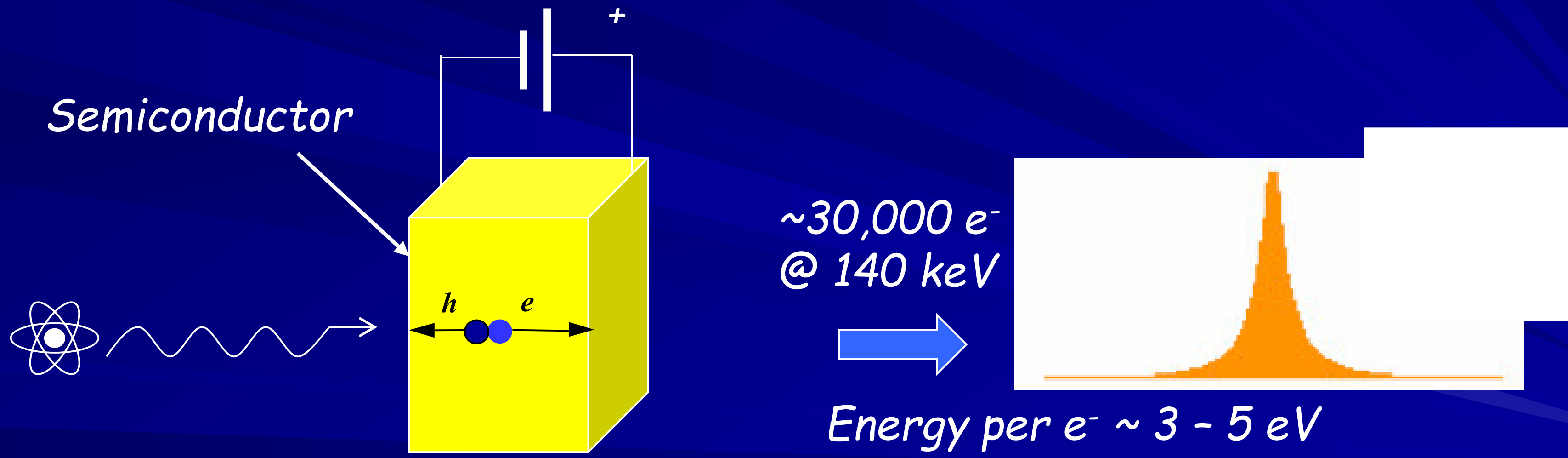
- Cross-talk and after-pulses issues



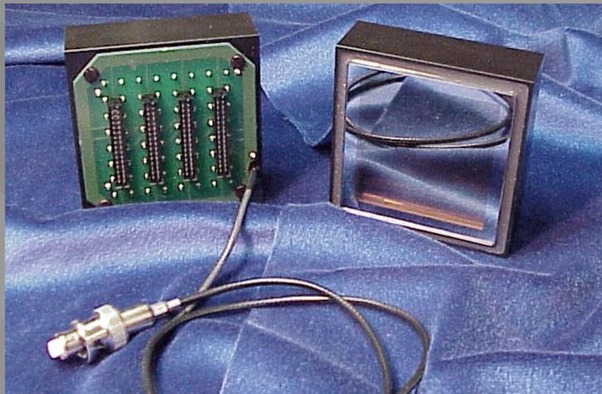
Philips Digital SiPM
32x32 mm2

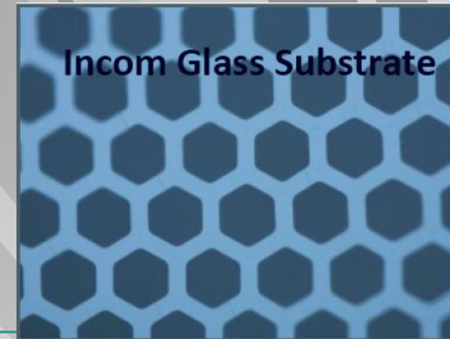
Scintillation Detectors vs Solid-State Detectors

Gamma Ray --> Visible Light --> Electrical Signal (Indirect Detection)



Gamma Ray --> Electrical Signal (Direct Detection)

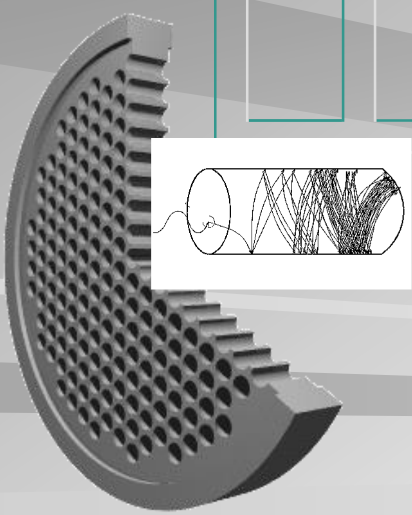




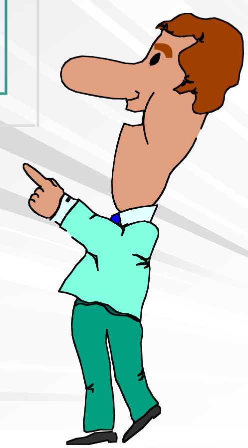
Photek, HPK, Burle-Photonis 2" x 2"

ALD Nanolayer

The large area Micro Channel Plate Coming soon !



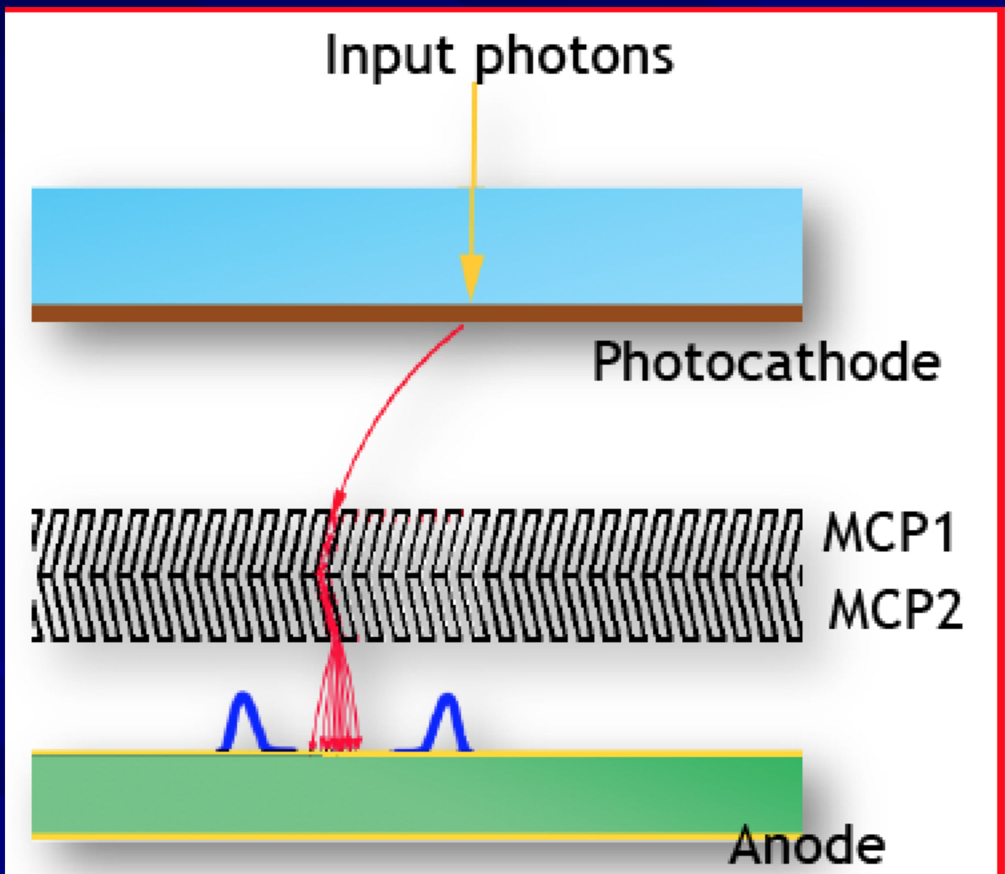
http://psec.uchicago.edu

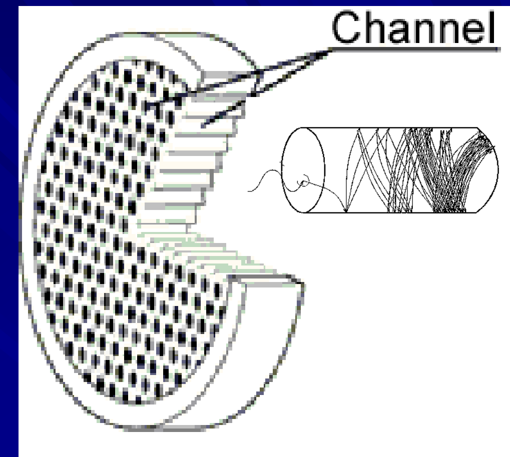


Micro Channel Plate → How does it work ?

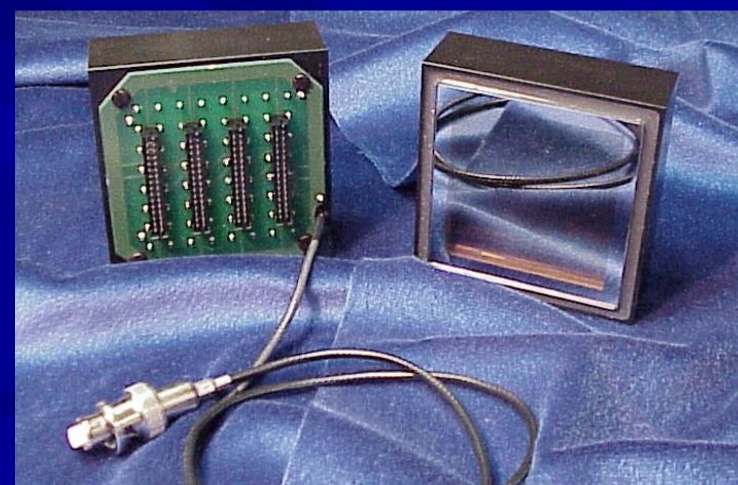
- High, gain > 10^7, low noise, low power, $\sigma(t) < 10$ psec, $\sigma(x) < \$1$mm
- Goal → large area, low cost:

(since intrinsic time and space scales are set by the)



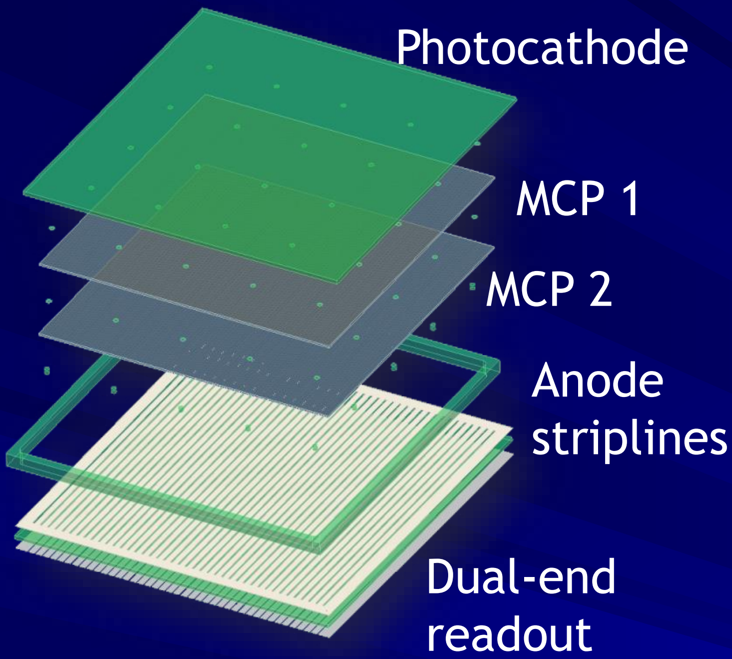


pore sizes 2-20μm



Photonis

Large Area Micro-Channel Plates Devices



LAPPD project : *Chicago-ANL-Hawaii*

Large Area MCP pad ***8" x 8"***

Transmission lines 2D readout:

limits the number of electronic channels compared to pixels

Goal: Both position $\sigma(mm^2)$ *and timing*

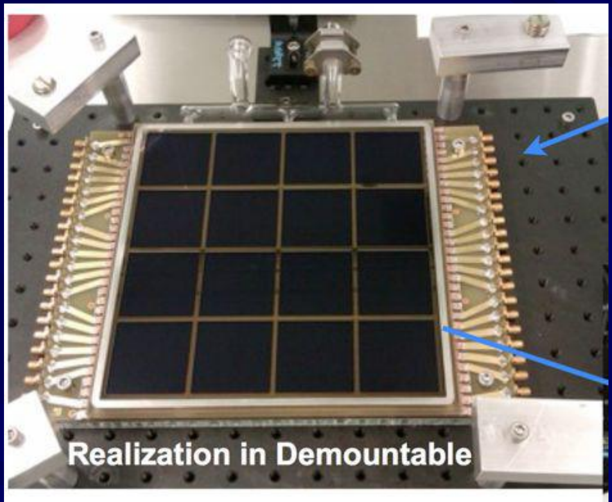
σ*(10-100ps)*

Electronics

PSI, Orsay/Saclay, Chicago-Hawaii

- GigaSample/s Waveform Sampling and Digital Processing

Workshop on Pico-second sensors,
LPC Clermont-Ferrand March 12-14th 2014



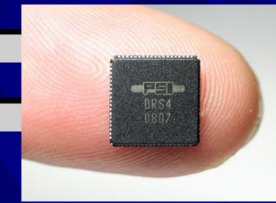
Coming soon

A Super Module holds 12 tiles in 32 rows.15 waveform sampling ASICS on each end of the tray Digitze 90 strips. 2$layers of local Processing (Altera) measuer extract Charge,time,positon,goodnessof fit

- ***Application in tracker sampling calorimeters & PET***

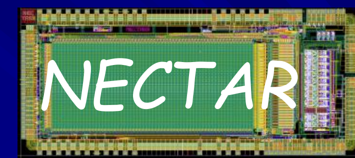
Some words about electronics

A survey of common area (cont't)

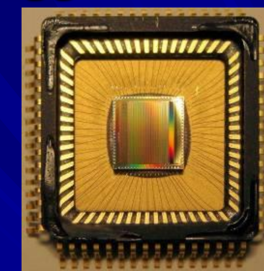


- Front end electronics & signal treatment
  - Fast shaping, integrated, low noise, low power, self trigger
  - Digital filtering and signal analysis

    --> Waveform Digitizer :SCA



Giga sampling chip
LAL-Saclay)

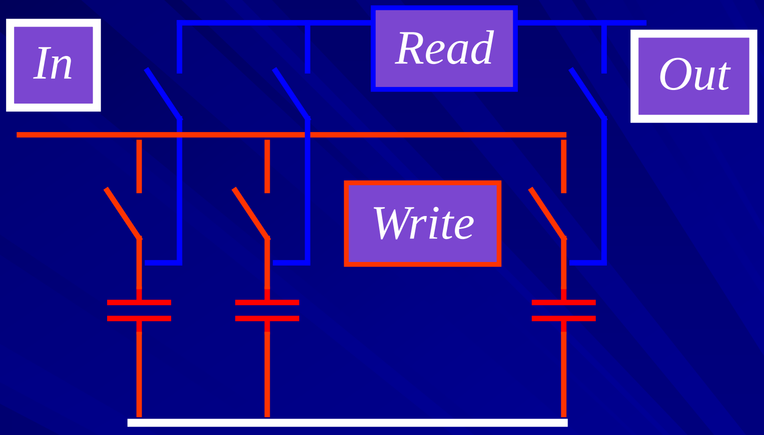


DRS4 (PSI)

- Trigger & DAQ
  - Pipeline and parallel read-out → FPGA
  - Feature extraction techniques →like Time Of Flight (TOF)
  - Real Time selection → GPU's image processing
  - High bandwidth networks → new telecom standard (xTCA)
- Computing & software : handling high quantity of data
  - Reconstruction, simulation & modelling --> GATE
- Global design
  - Compact integration of large number of channels

Analog memories → Waveform digitizers

Switched Capacitor Arrays (SCA)
Store signal on capacitors (~pF)
High speed (up to 5 GHz)
Slower readout (~10MHz)
High channel density
    9 channels on 5x5 mm^2
Dynamic range : 10-13 bits
Depth : 100-2000 cells
Low power (10-40 mW / channel)
Low cost (~ 10€ / channel)



DRS4

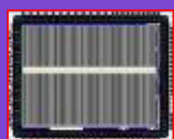
But possible loss of data integrity
    limited deeph
    leakage current,
    non linear timing

Switched Capacitor Arrays for Particle Physics

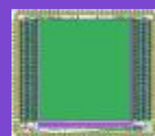
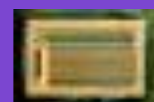
G. Varner, Univ. of Hawaii

E. Delagnes
D. Breton
CEA Saclay

H. Frisch et al., Univ. Chicago

STRAW3  *LABRADOR3*  *TARGET* 

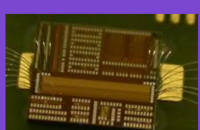
- *Many chips for different projects (Belle, Anita, IceCube …)*
- *Bufferend and unbuffered*
- *Deep arrays (up to 64k)*
- *Wilkinson ADC on chip*

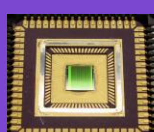
AFTER  *SAM*  *MATACQ* 

- *Buffered (f_{3db}~300 MHz)*
- *Low noise (~12 bits)*
- *Short PLL → good timing*

PSEC1 - PSEC4

- *Goal: Measure 1 ps (!)*
- *130 nm IBM*
- *18 GSPS*
- *256 sampling cells*
- *Influenced by G. Varner*
- *Wilkonson ADC on chip*

DRS1  *2002*

DRS2  *2004*

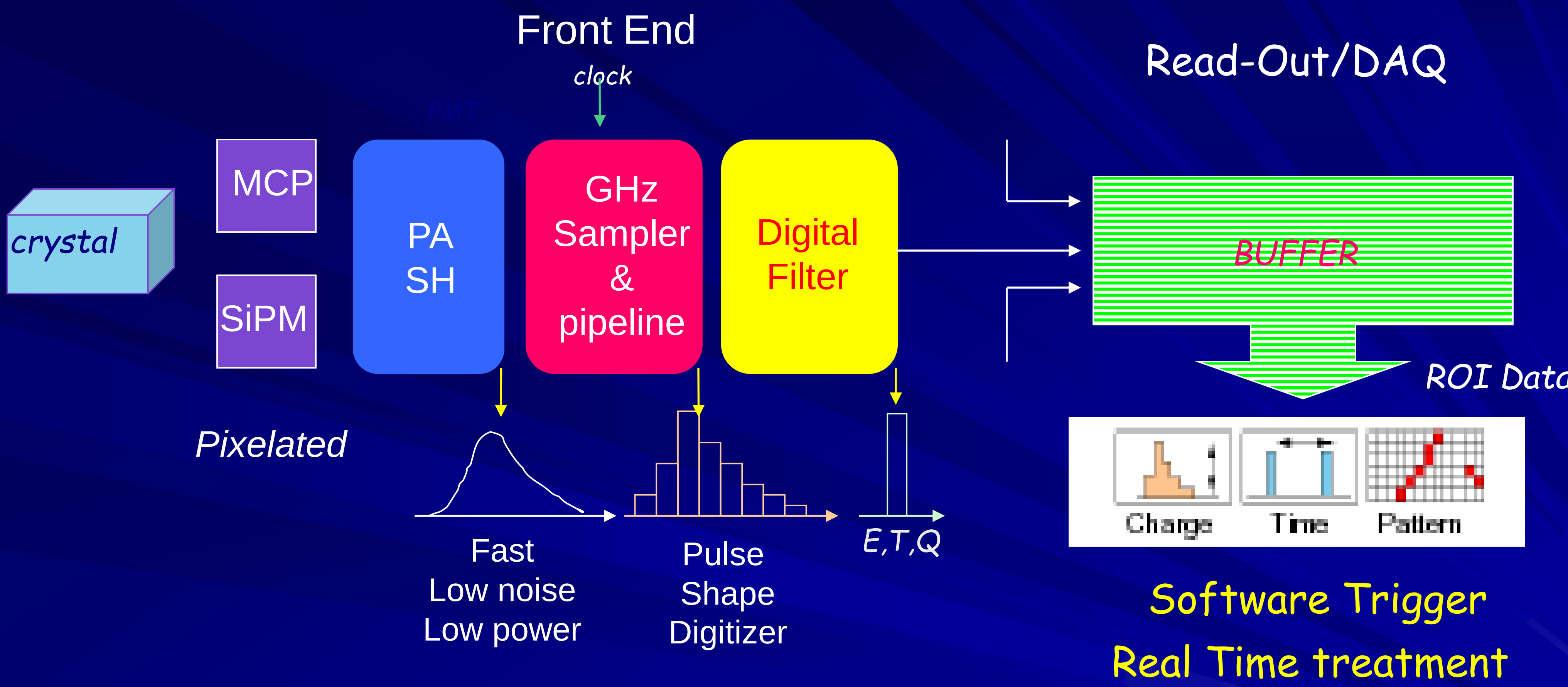
DRS3  *2007*

DRS4  *2008*

- *Universal chip for many applications*
- *8+1 channels 1024 sampling cells*
- *5 GSPS, 950 MHz analog BW*
- *1 μs readout time for short pulses*

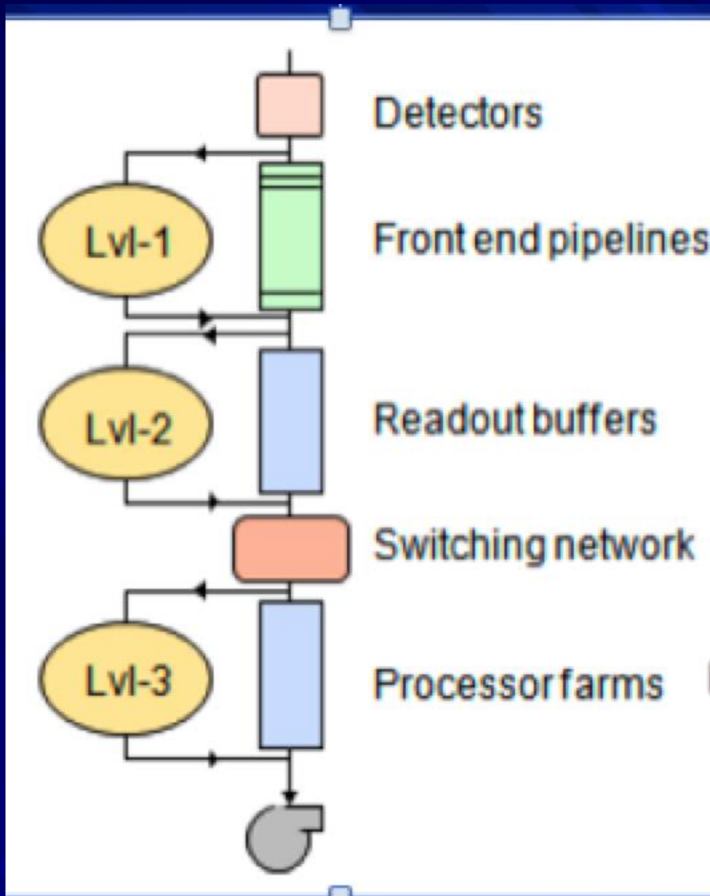
SR
R. Dinapoli
PSI, Switzerland

Exemple of Conceptual TOF-PET architecture model

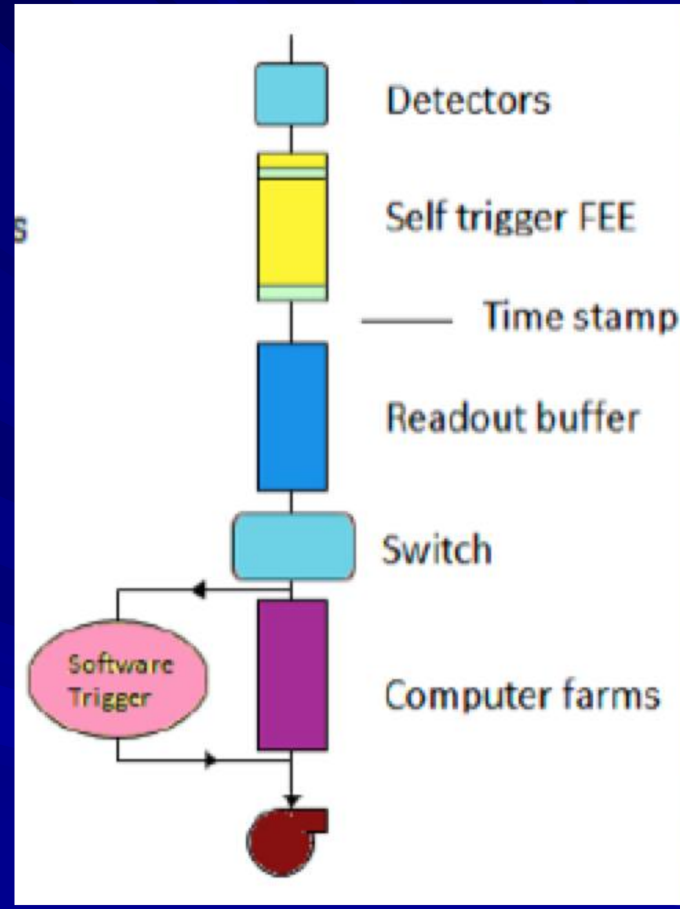


- ♦Free-running analog waveform sampling and digitizer (SCA)
- ♦ Digital filter used to extract pulse amplitude and high resolution timing (FPGA)
- ♦ Pipelined processing architecture to avoid deadtimes (GPU's)
- ♦Parallel digital read out
- ♦Terabit network for communication and processing (xTCA)

Evolution of HEP architecture

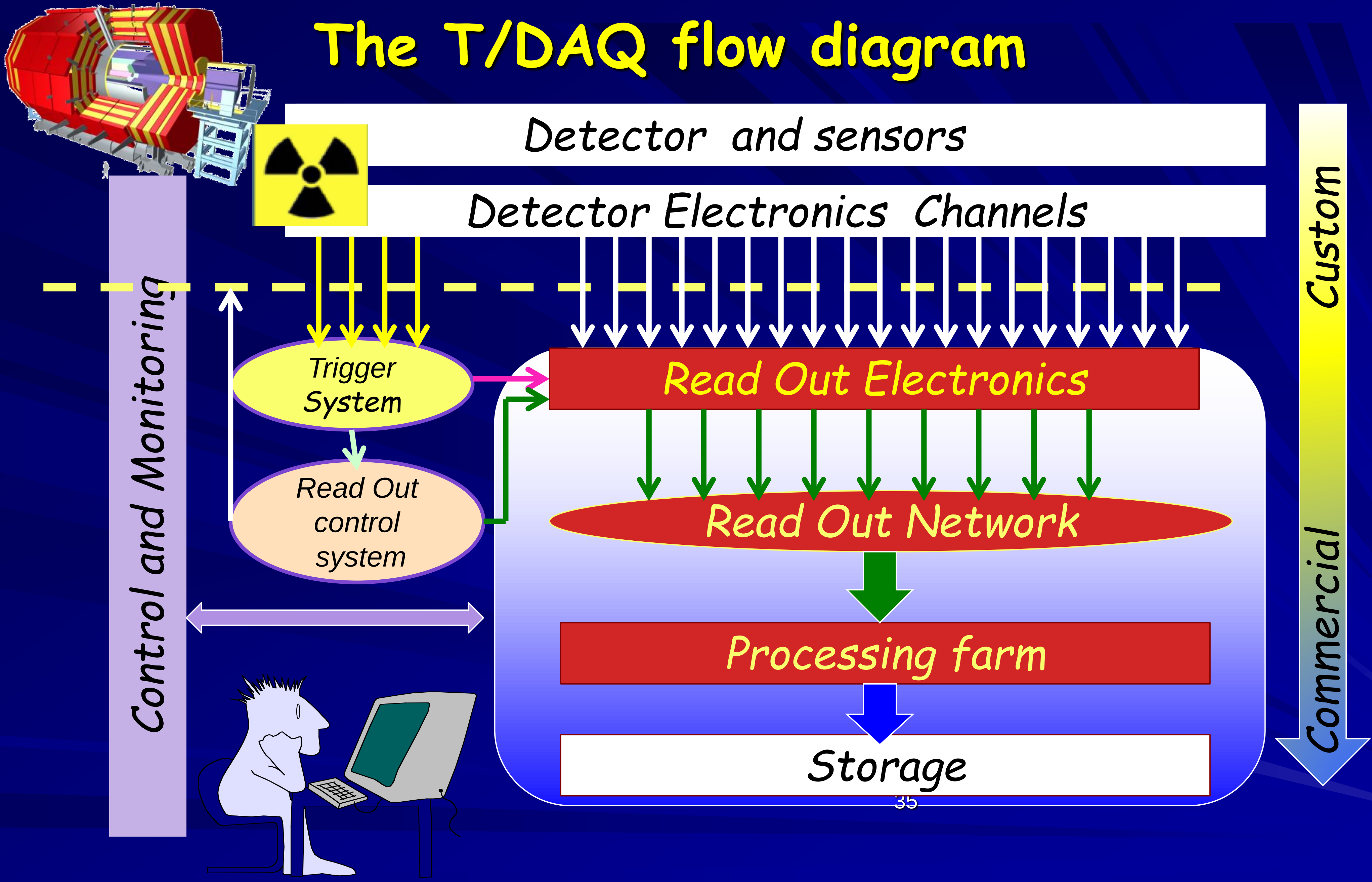


ATLAS present scheme
Multilevels trigger

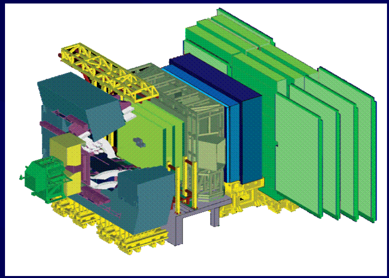


Self trigger
Deadtimeless

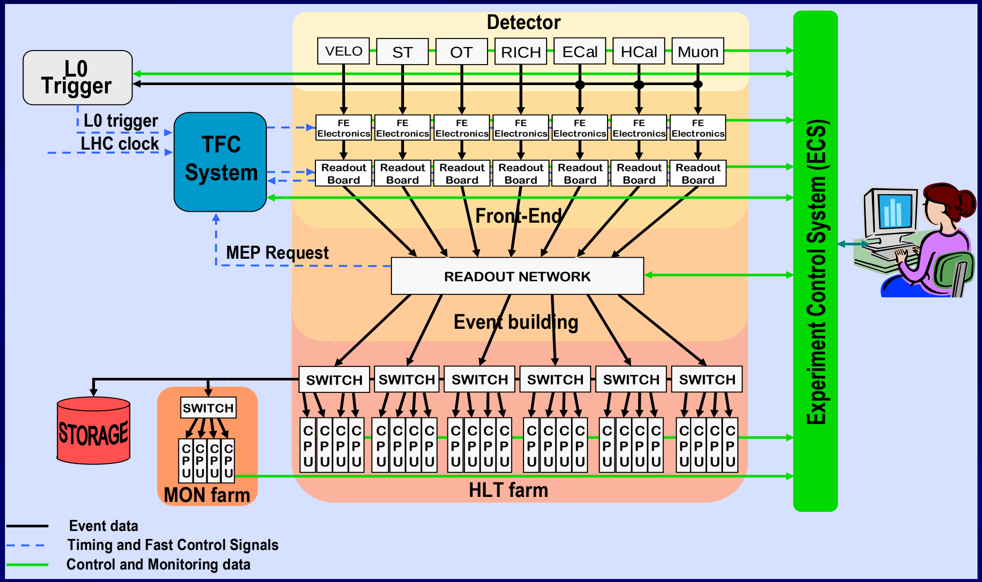
The T/DAQ flow diagram



DAQ = The evolution of architecture

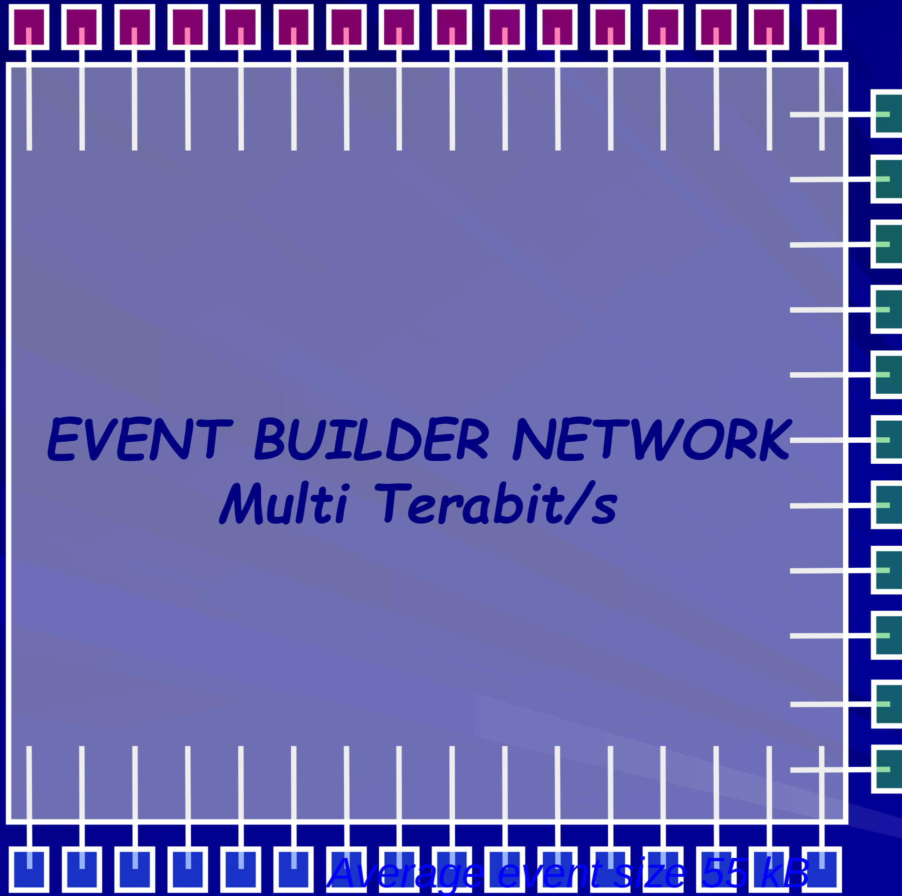


LHCb



Average event size 55 kB
Average rate into farm 1 MHz
Average rate to tape 4 – 5 kHz

Direct network access From Detectors and Machine



Controls & Storage servers

Average event size 55 kB
Average rate into farm 1 MHz
Average rate to tape 4 – 5 kHz

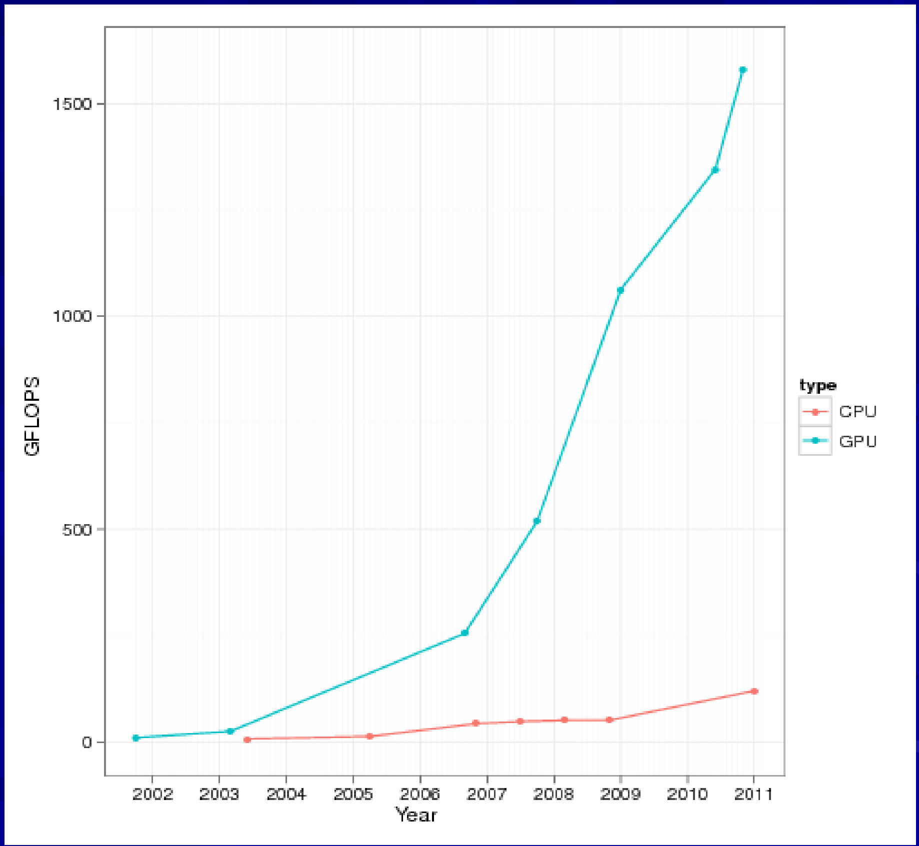
Trigger Farms & Analysis

Computer farm evolution → GPU's

- GPUs: Graphical Processor Units :

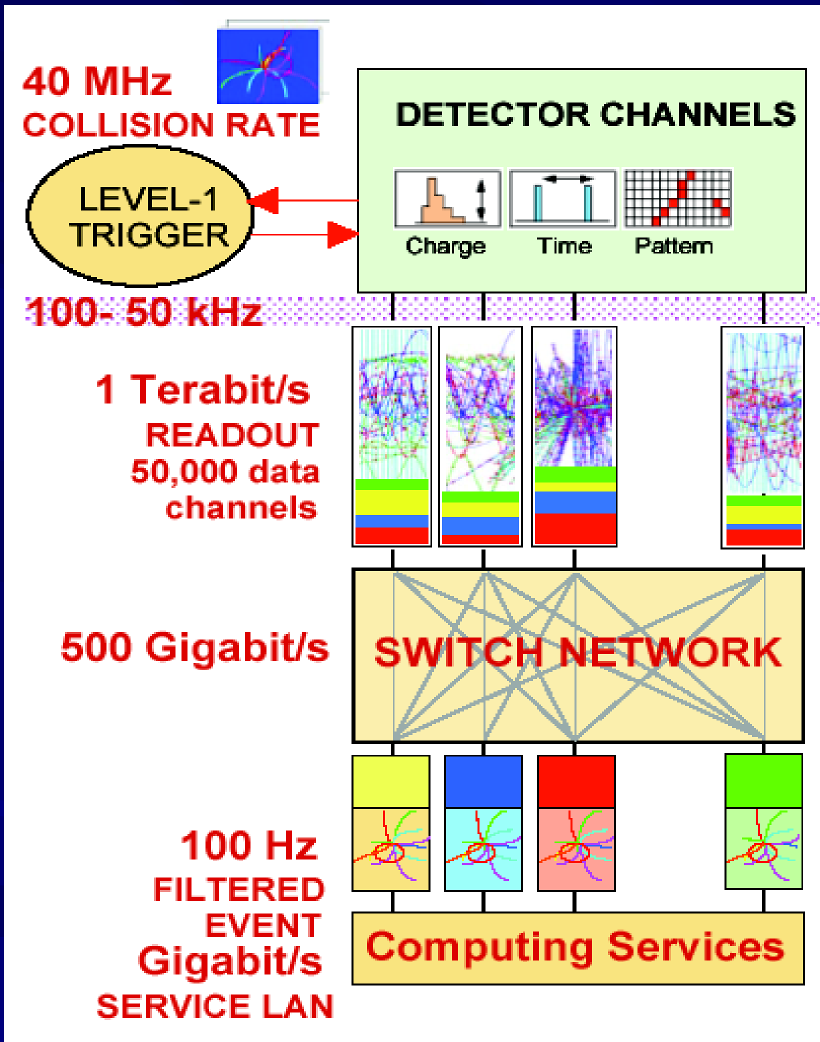
highly parallel, multi-threaded, multicore processors with remarkable computational power and high memory bandwidth: promising candidate for fast track fitting at high luminosity

From the video game world



DAQ = Pipeline Architectures

LHC

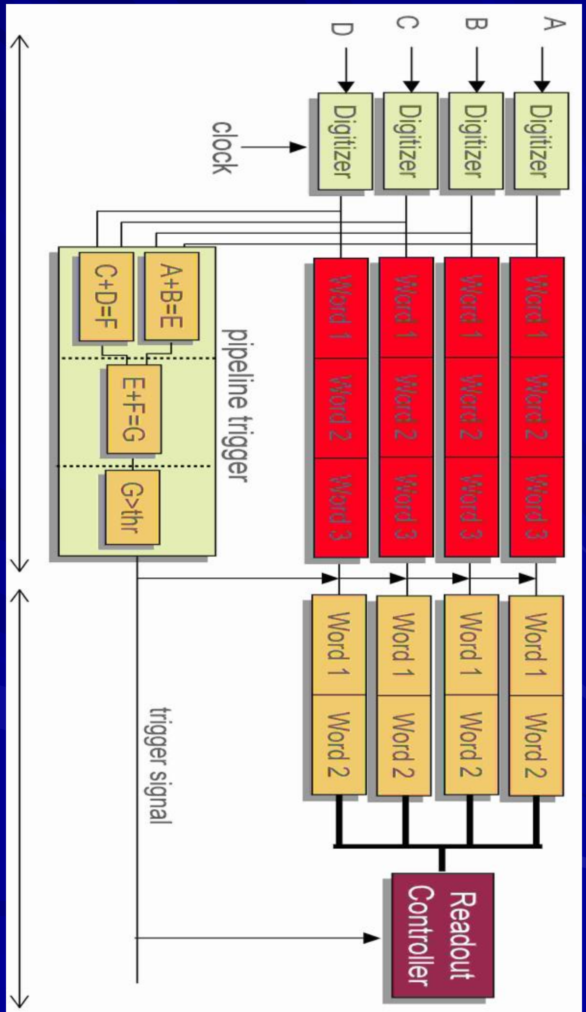


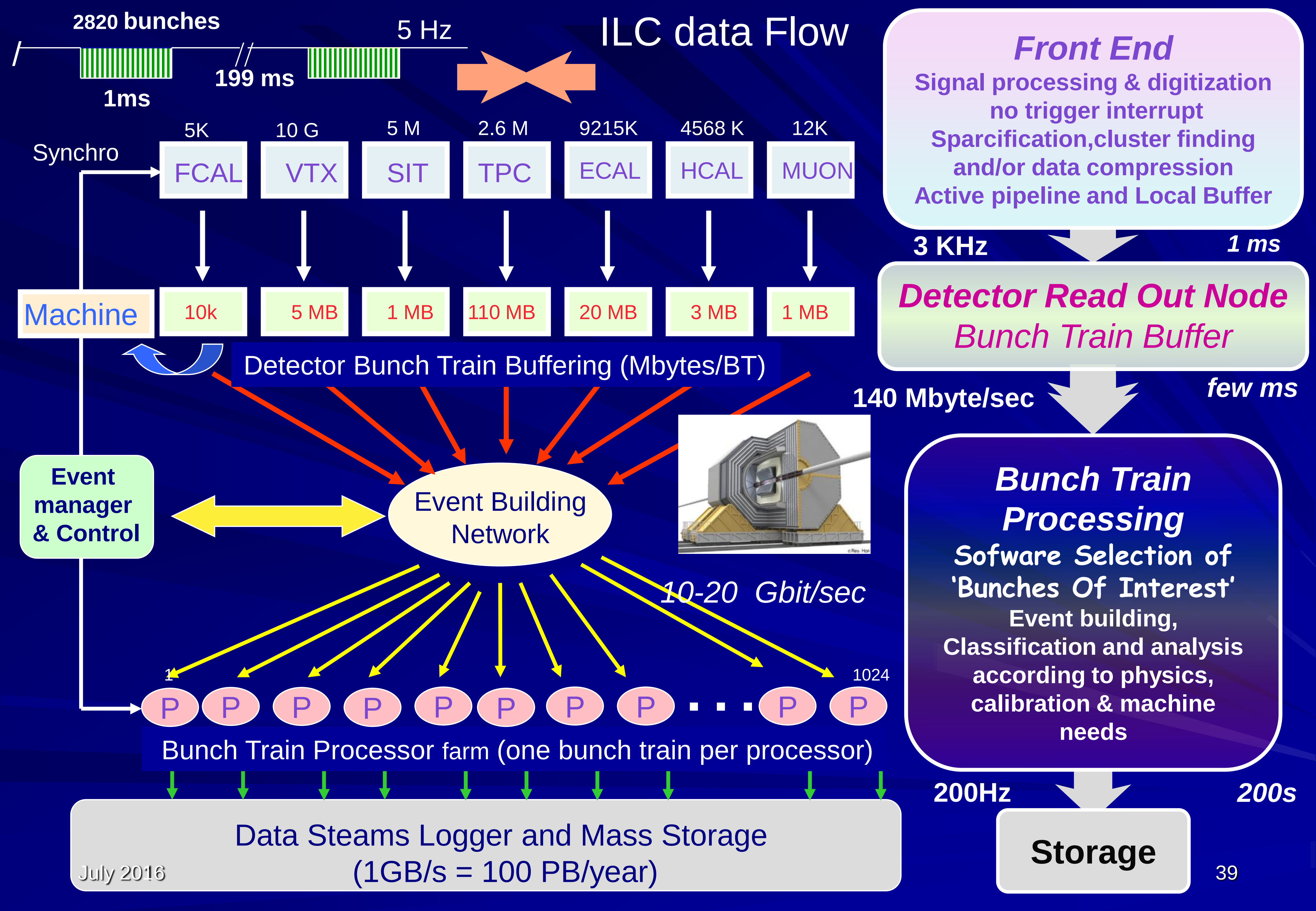
Future PET

Digitisation

Pipeline

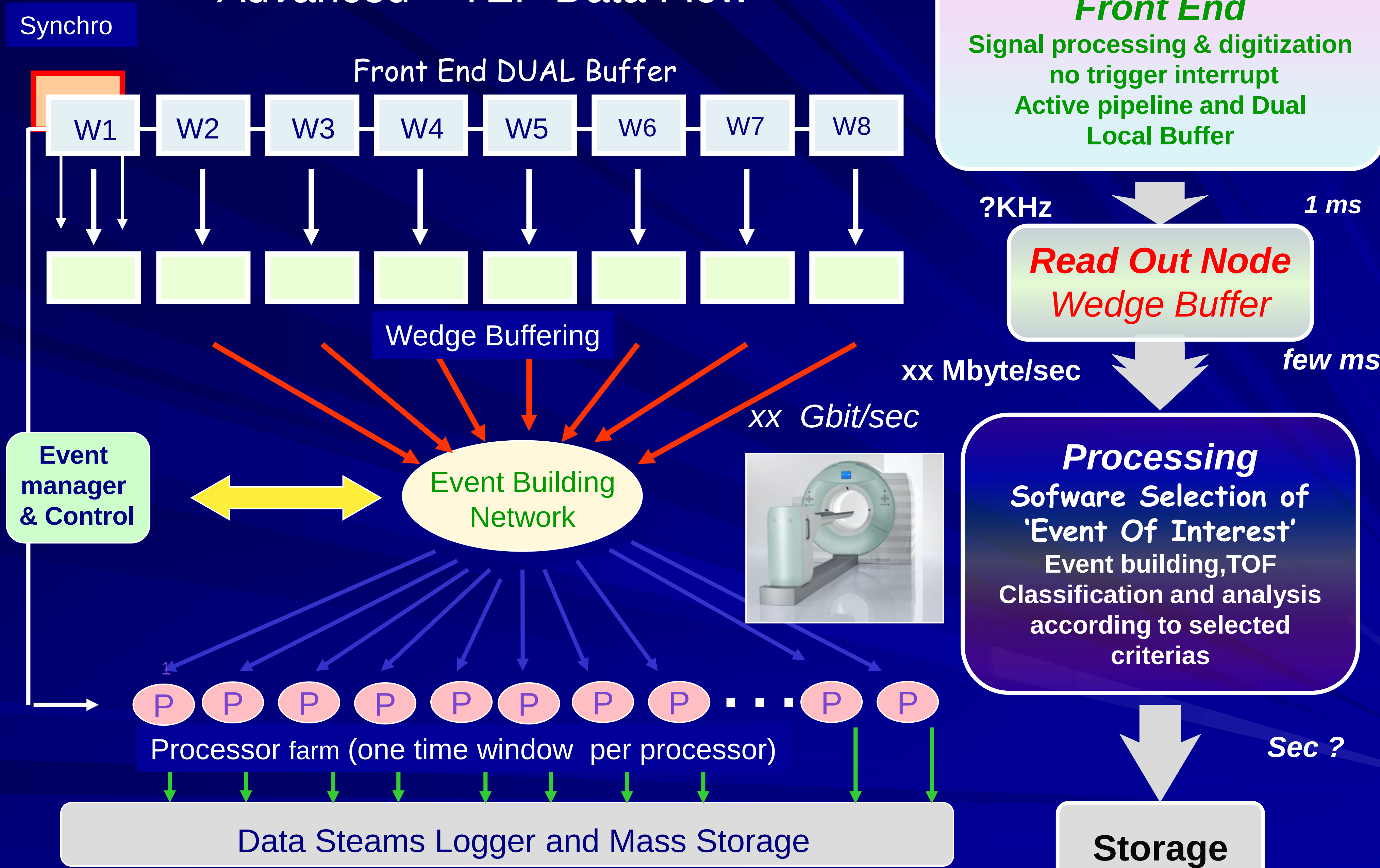
Event builder





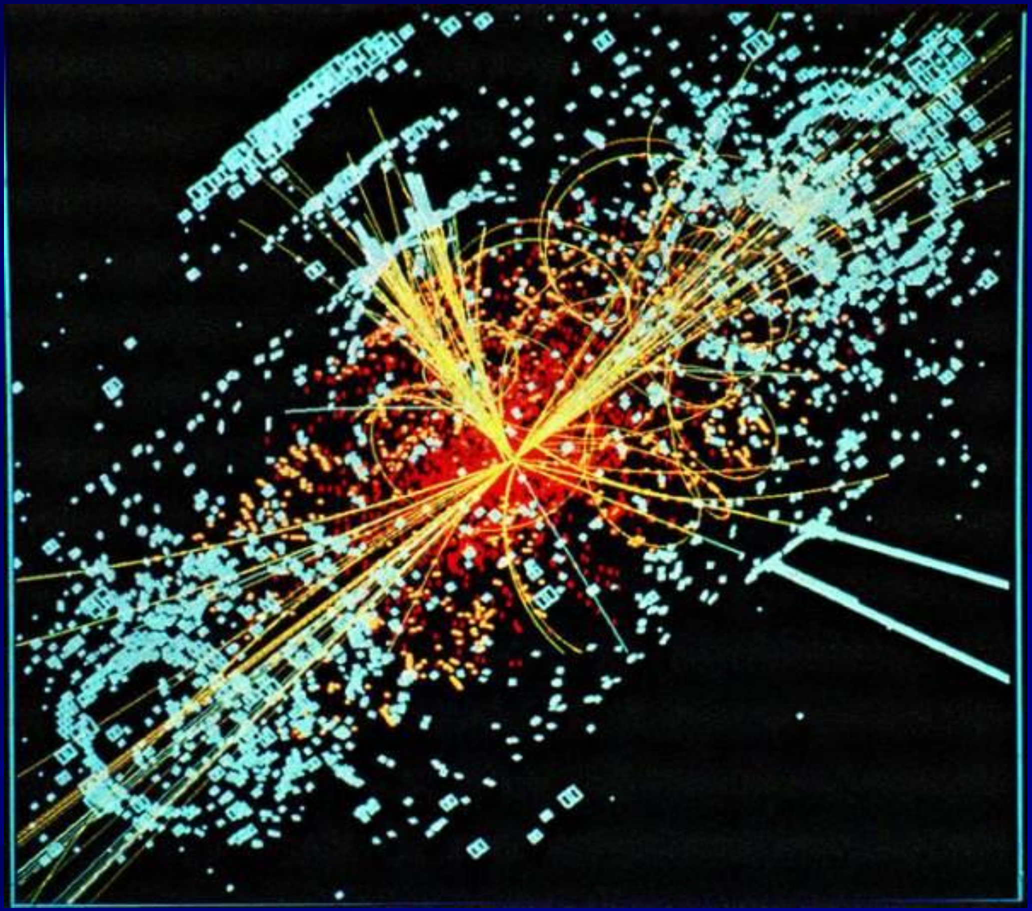
ILC data Flow
2820 bunches
5 Hz
1ms
199 ms
Synchro
5K
10 G
5 M
2.6 M
9215K
4568 K
12K
FCAL
VTX
SIT
TPC
ECAL
HCAL
MUON
Machine
10k
5 MB
1 MB
110 MB
20 MB
3 MB
1 MB
Detector Bunch Train Buffering (Mbytes/BT)
Event manager & Control
Event Building Network
10-20 Gbit/sec
1
1024
P P P P P P P P . . . P P
Bunch Train Processor farm (one bunch train per processor)
Data Steams Logger and Mass Storage
(1GB/s = 100 PB/year)
Front End
Signal processing & digitization
no trigger interrupt
Sparcification,cluster finding
and/or data compression
Active pipeline and Local Buffer
3 KHz
1 ms
Detector Read Out Node
Bunch Train Buffer
140 Mbyte/sec
few ms
Bunch Train Processing
Sofware Selection of 'Bunches Of Interest'
Event building,
Classification and analysis
according to physics,
calibration & machine
needs
200Hz
200s
Storage

« Advanced » TEP Data Flow

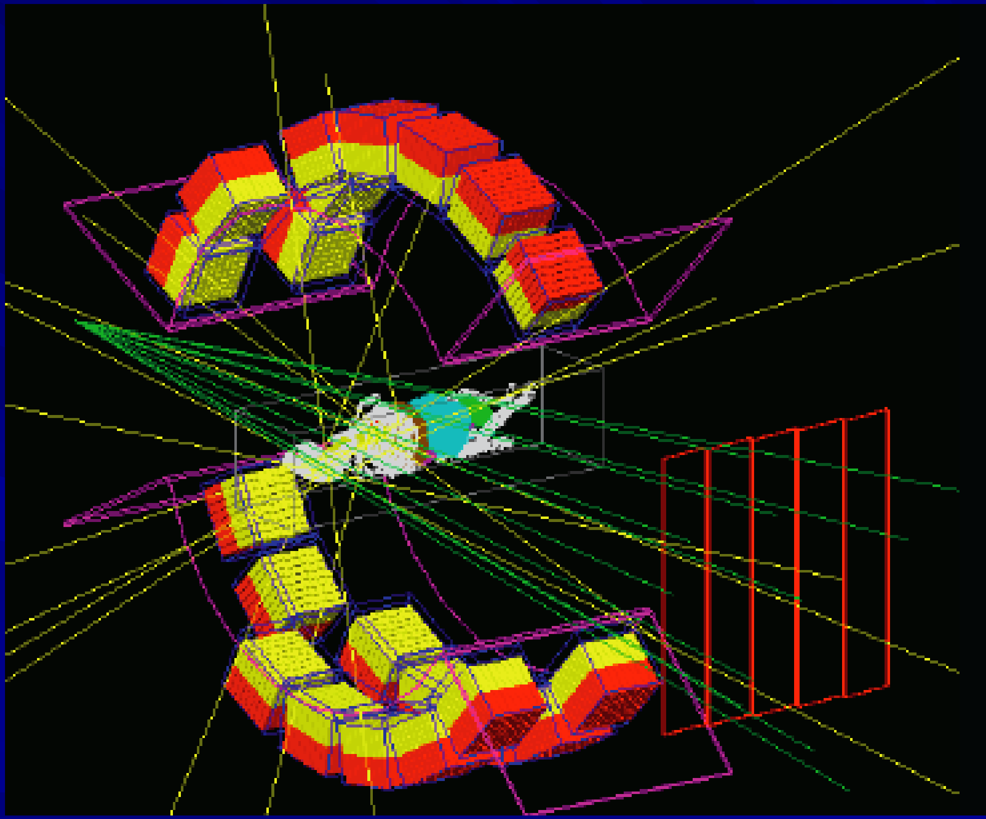


Simulation

Higgs event at LHC (*CMS*) with Geant4



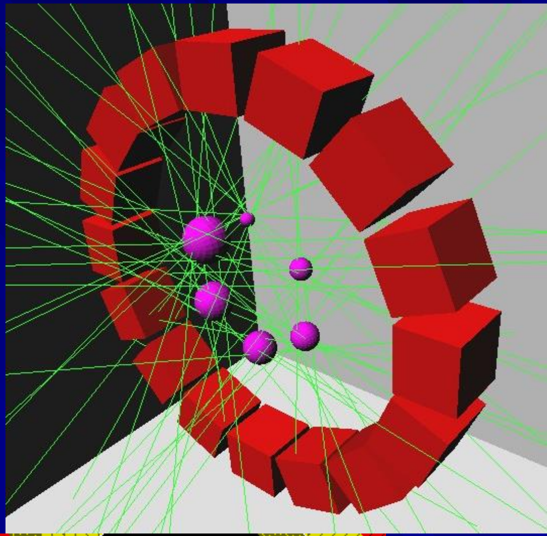
PET with GATE: Geant4 Application for Tomographic Emission

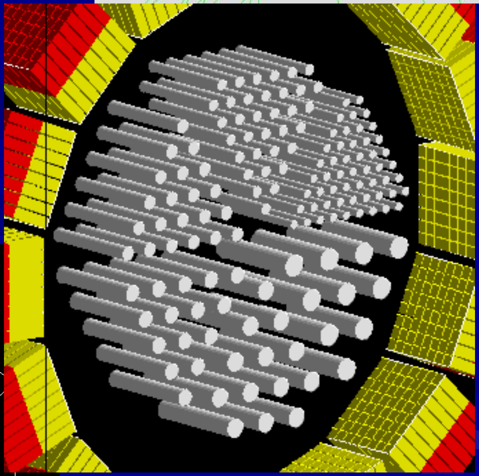


GATE : Geant4 Application for Tomographic Emission

Monte-Carlo simulation allowing to :

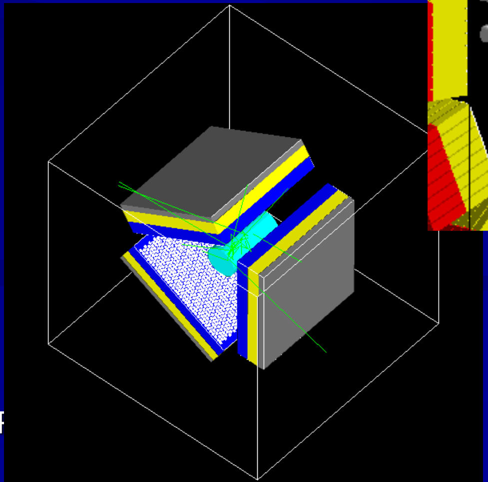
✓define geometries
(size, materials,…)
✓ define sources
(geometry, nature, activity)
✓ choice of physical process
(low energy package of G4)
✓ follow track point by point

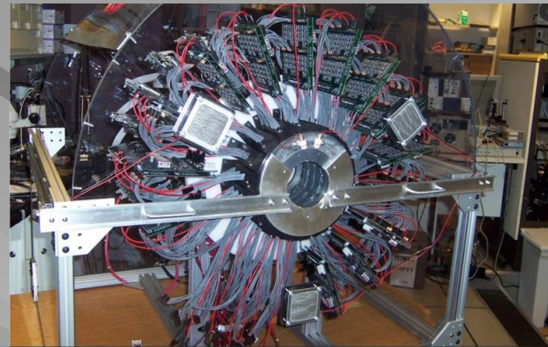




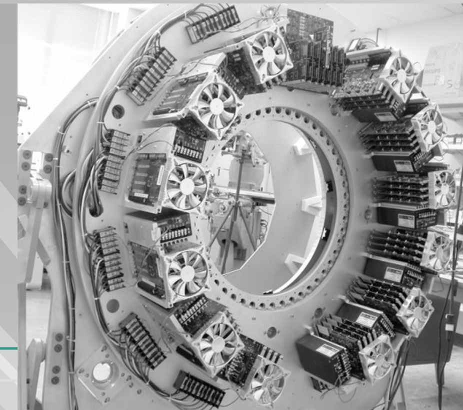
GATE specificities:

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

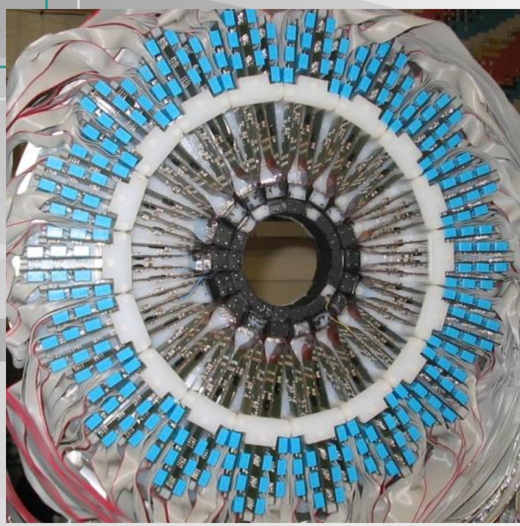


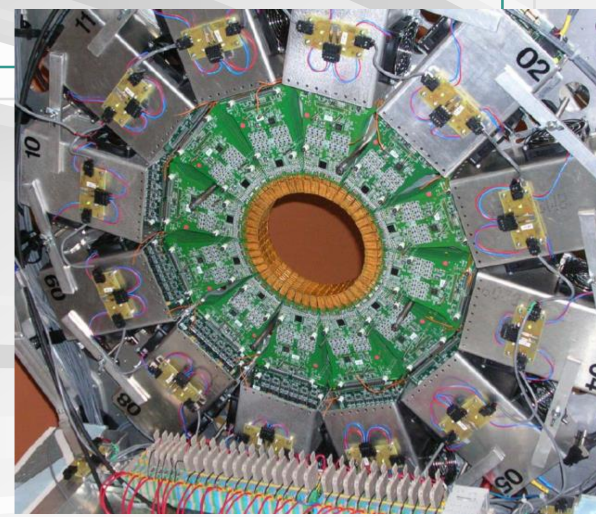


The MiCES PET scanner, with 72 detector modules and 700-micron resolution, was designed entirely on the Mac and runs on an 8-core Mac Pro.
It provides nearly twice the resolution of commercial systems.

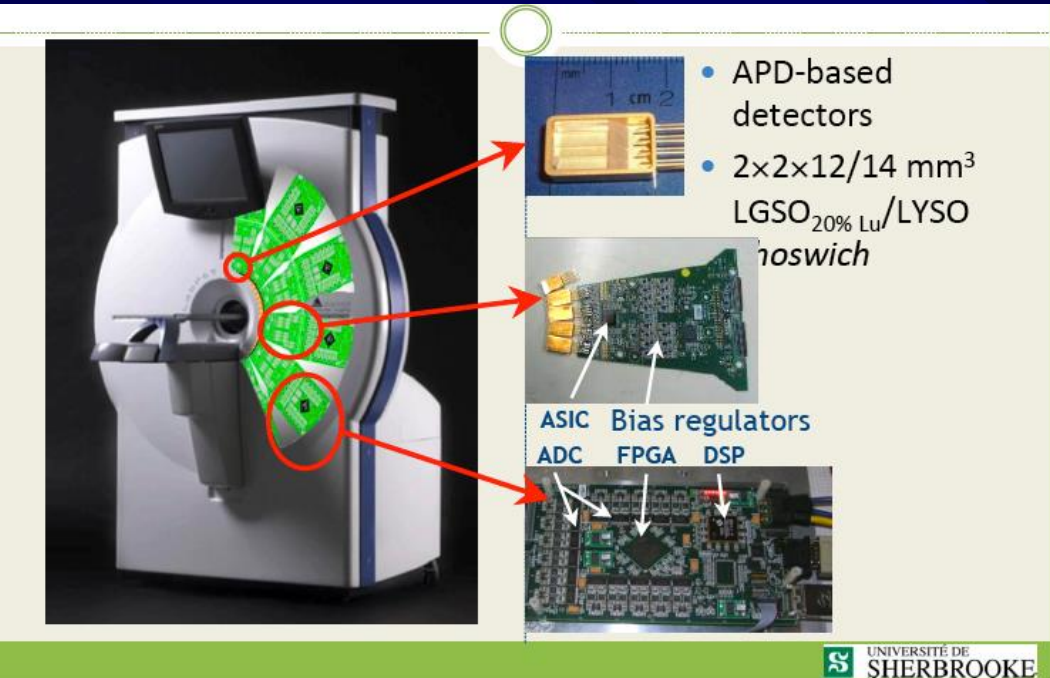


Some 'dedicated PET examples



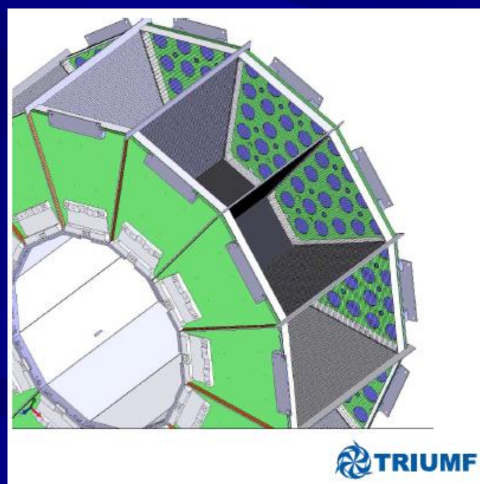


MicroPET for small animals

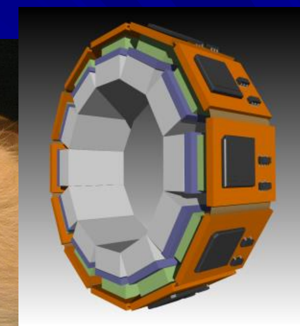


- Φ=20cm
- FOV few cm
- Development
  - Radio pharmacology
  - Tracer development

Crystal Clear Col.



Liquid Xenon



RatCap
BNL

The Rat Conscious Animal PET scanner

Small animal PET images

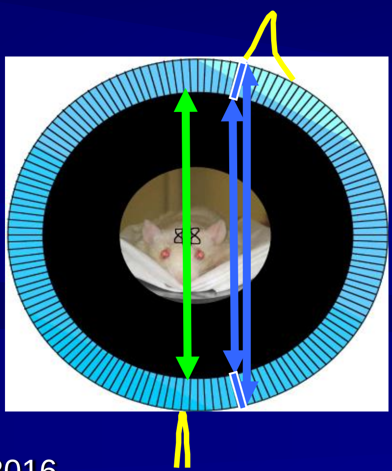
31 g mouse
1 mCi $^{18}F^-$

Whole-body
FDG-PET scan
250 g rat
(Sherbrooke APD)

μPET vs whole body PET → different requirements

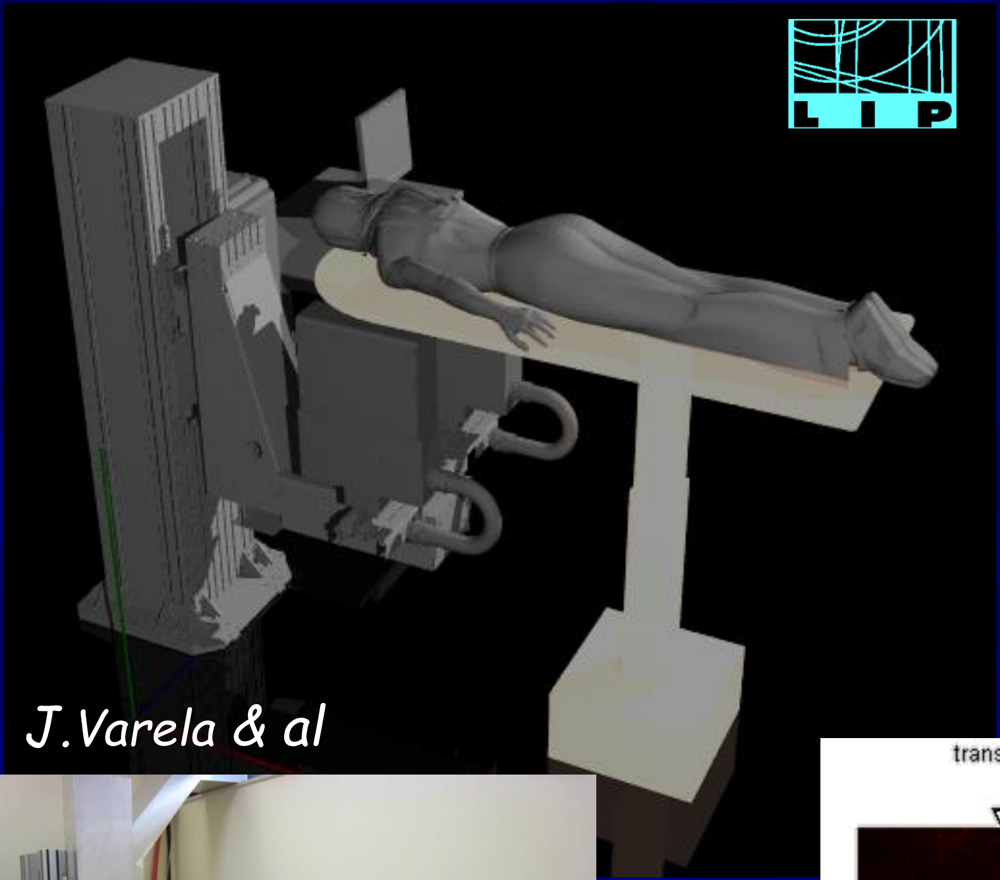
- **High Spatial resolution →fundamental**
  - Objective ~ 1mm or less
  - Today → 1,2 mm
- **High sensitivity**
  - Less Compton event
  - Small dose
- **Paralax correction**

  → Deph Of Interaction Technique



- High Efficiency (>85%)
- Good Spatial Resolution (<5 mm)
- Low Cost (<$100/cm2)
- Short Dead Time (<1 μs)
- High Timing Resolution (< ns fwhm)
- Good Energy Resolution (<100 keV fwhm)

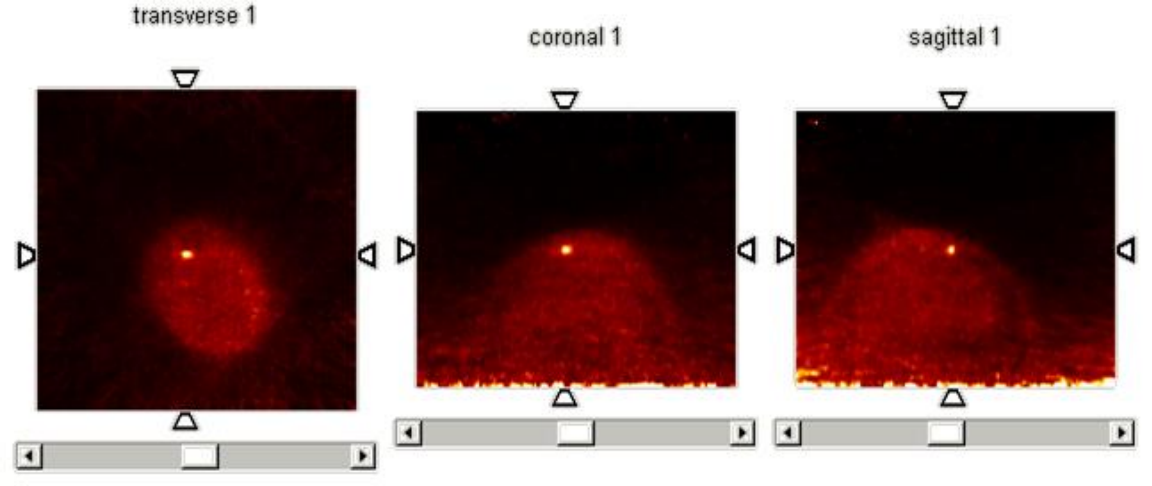
The ClearPEM Breast Imaging Scanner



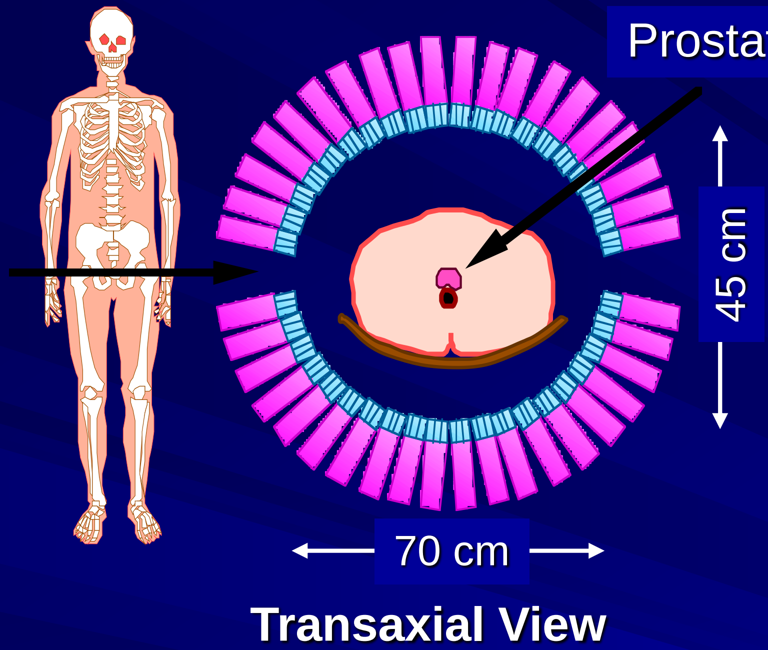
J.Varela & al

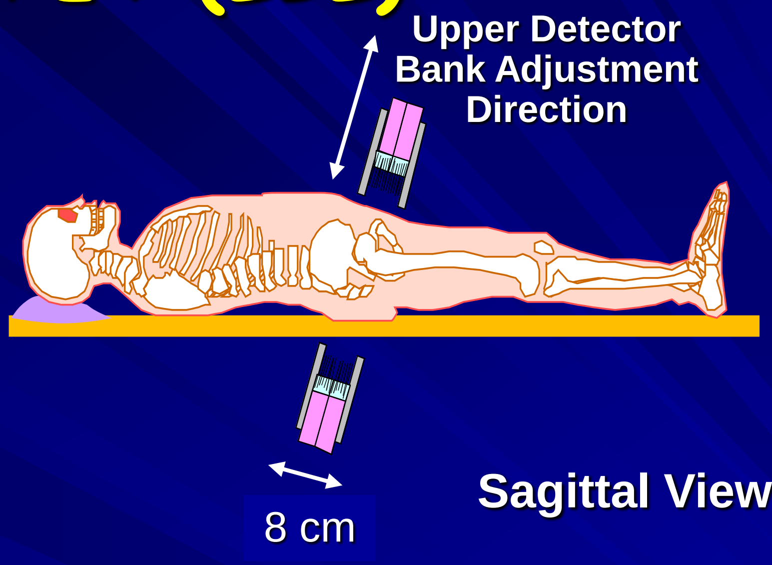
- *160 x 180 mm2 active area*
- *6144 scintillation crystals LYSO:Ce*
- *12288 APD pixel channels*
- *Double readout of crystal pixels for Depth-of-Interaction measurent (to minimize parallax effect)*

--> Reach 1,2 mm patial resolution

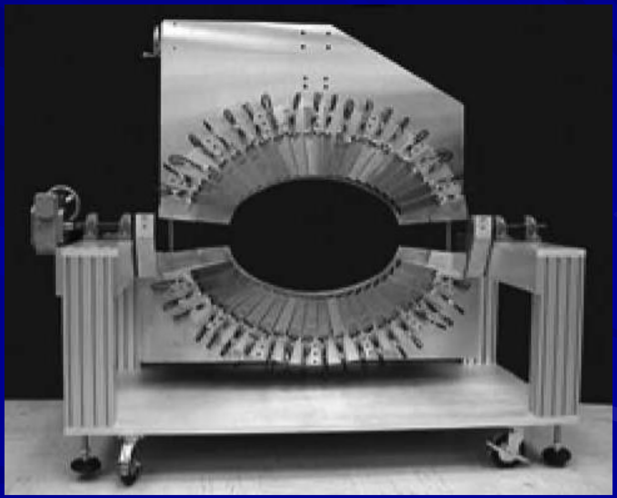


Prostate PET (LBL)





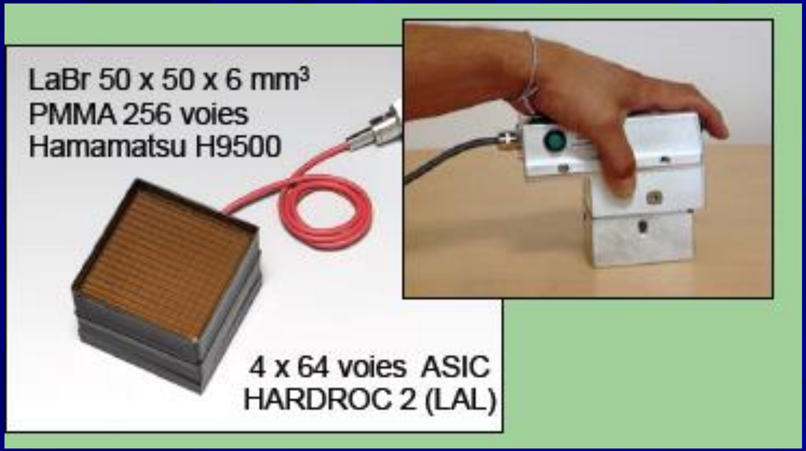
Lower cost and higher performance
than conventional commercial PET camera

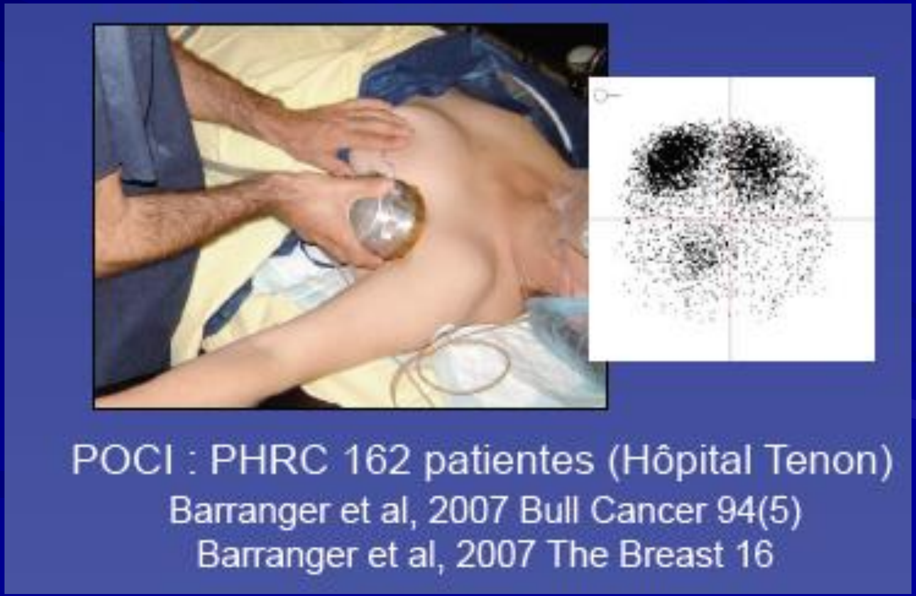


W.Moses & al.

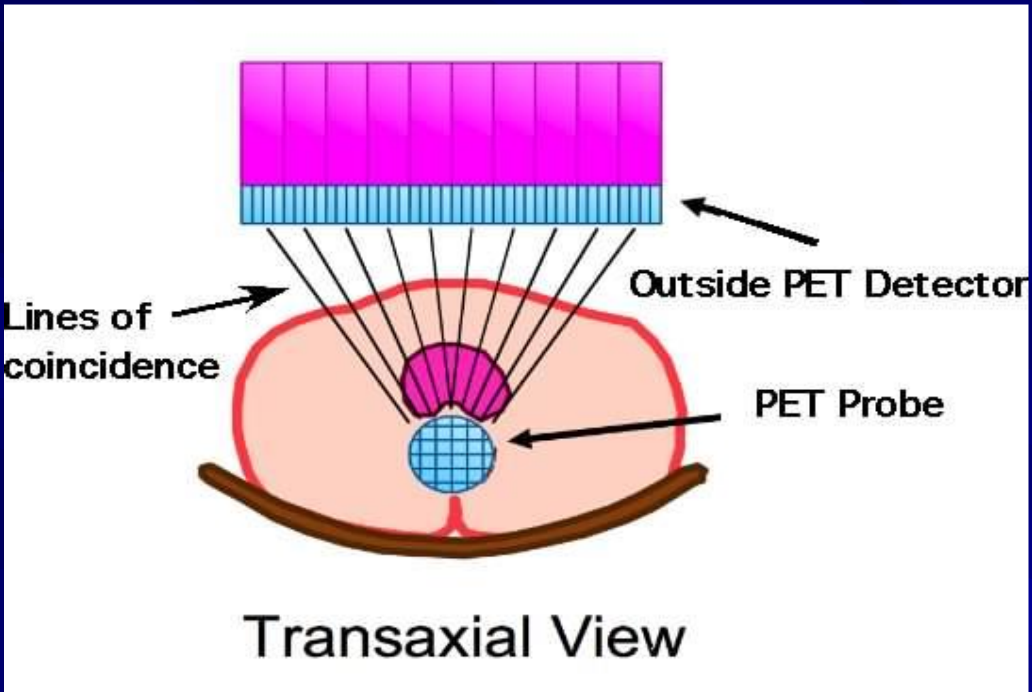
Surgical portable probes

- Developent of very sensitive detectors, miniaturized and ergonimics with a great capability of rejecting noise and background
  - Based on SiPM,CMOS pixels,Scintillating cristals LaBr3:Ce, LuI3:Ce, …, and integrated electronics
- Objectives : portable small imaging systems for beta/gamma probes adapted to new tumor tracers





High resolution PET Imaging probes



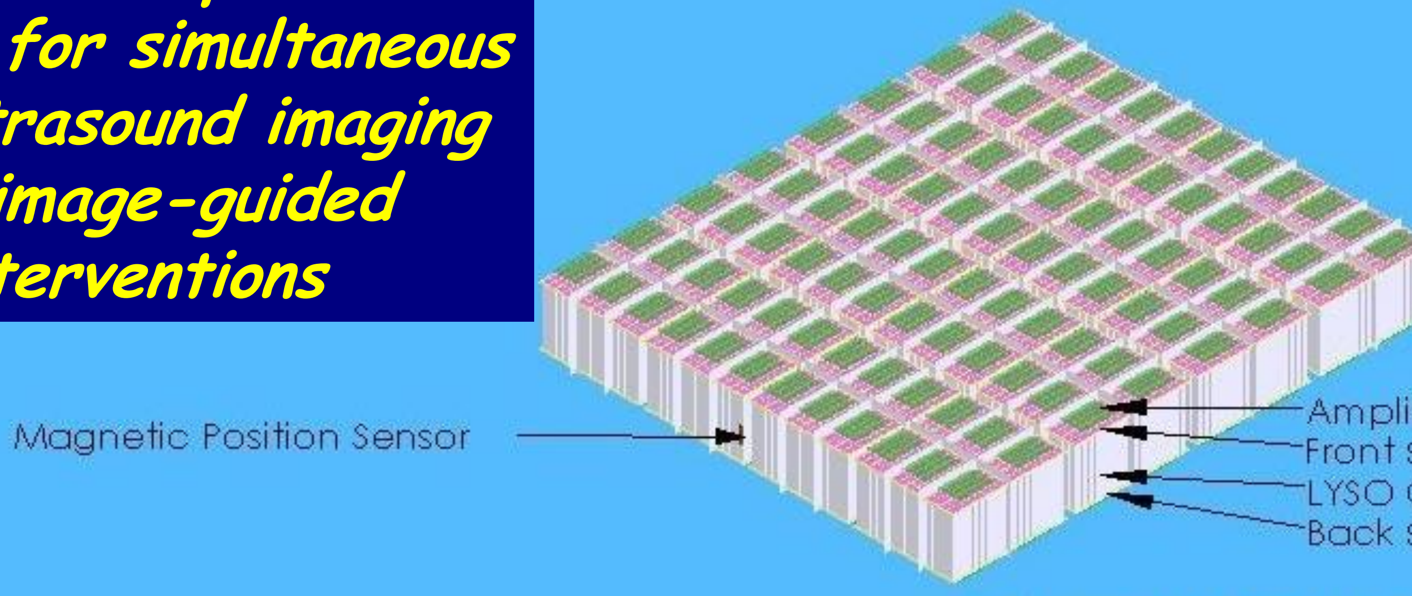
Prostate PET probe principle

- *Non-conventional PET configuration*
- *Assymetric: one PET head in near contact to ROI*
- *Endoscopic: one PET head inside the body*
- *Miniaturization*
- *High background from other organs (heart, bladder,…)*
- *Variable geometry*
- *Reconstruction problems*

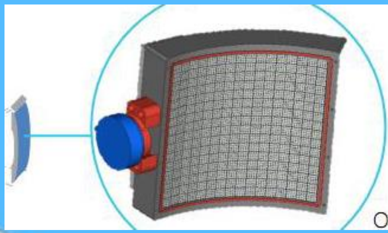
TOFPET-US

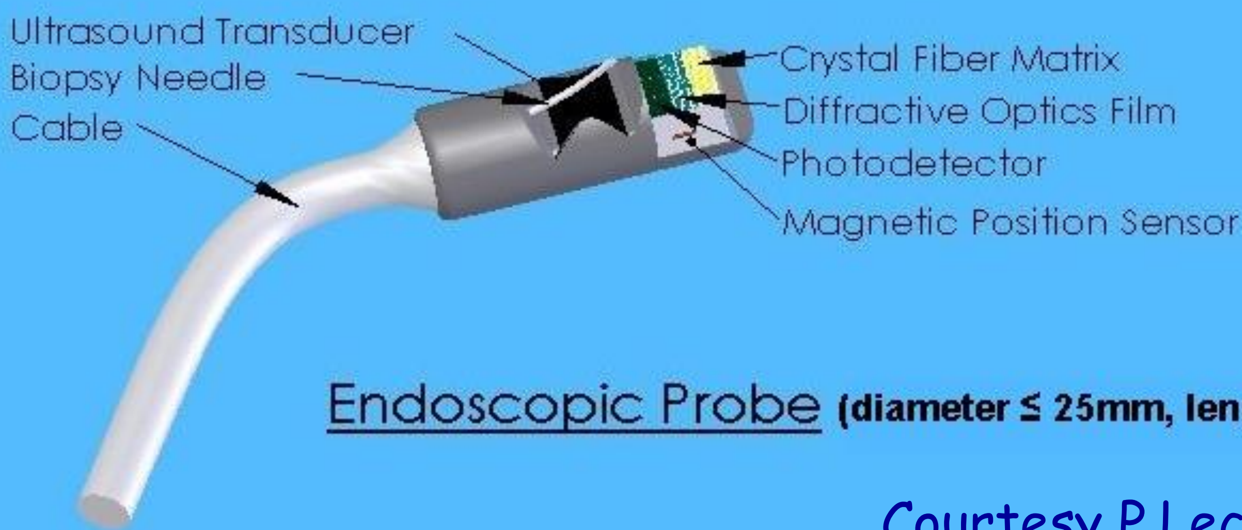
Novel multimodal endoscopic probes for simultaneous PET/ultrasound imaging for image-guided interventions

EU FP7 project, call Health 2010



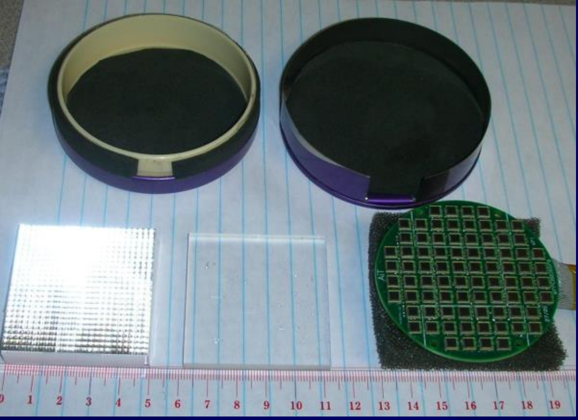
External PET Plate (16cm X 16cm)



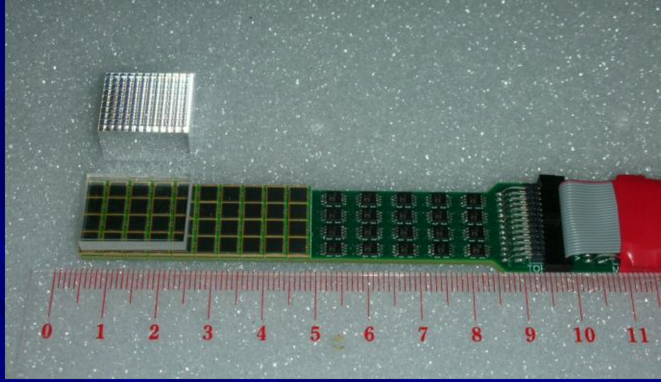


Endoscopic Probe (diameter ≤ 25mm, length ≤ 5

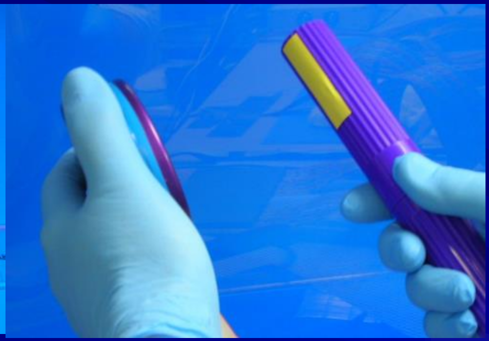
Courtesy P.Lecoq et al.



SiPM hand-held PET probe



- The 'Central' part
  - 64 MPPC
  - LYSO crystals
- The photosensor 'stick' part
  - 4x10 array of Hamamatsu MPPC
  - Amplifier and connector banks are in the handle region of the probe



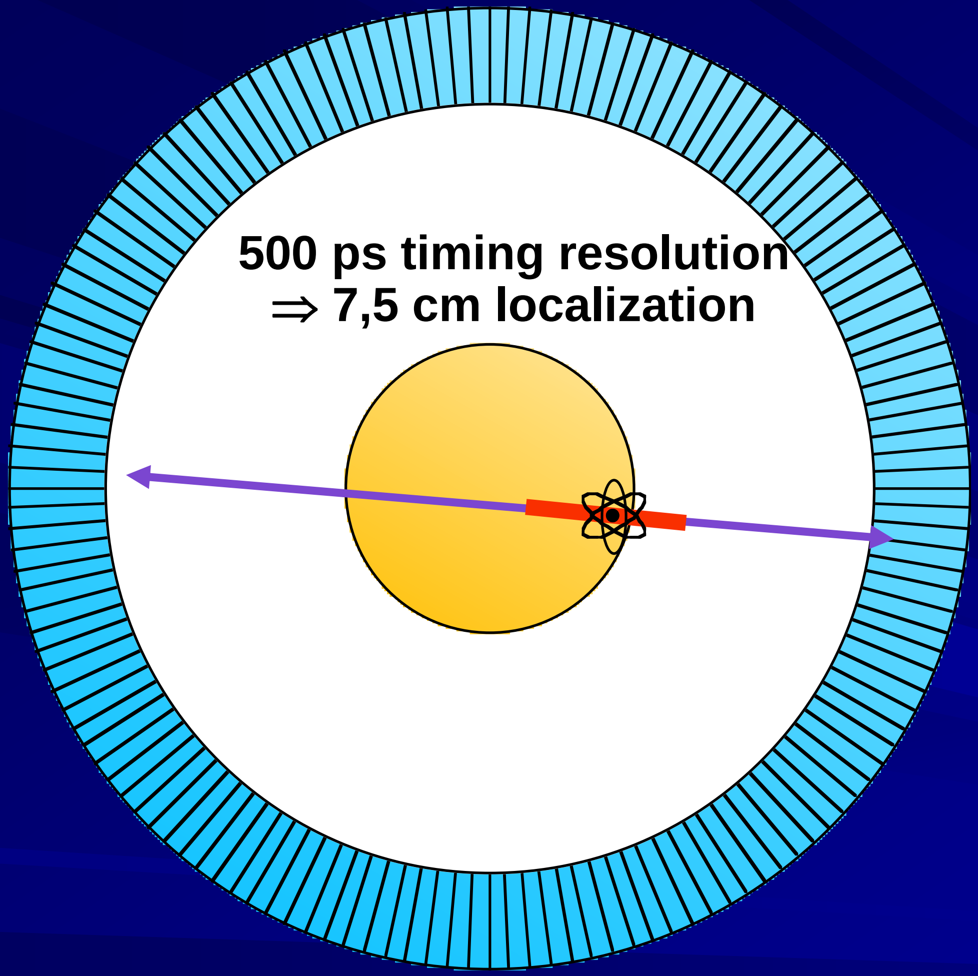
S. Majewski et al. (WVU)

- Biopsy guidance
- Surgical imaging with radio-guided surgery procedures in breast, melanoma, head and neck, pulmonary, pancreas and prostate cancer cases

A succesfull transfer

the TOF technique

Time-of-Flight in medical PET



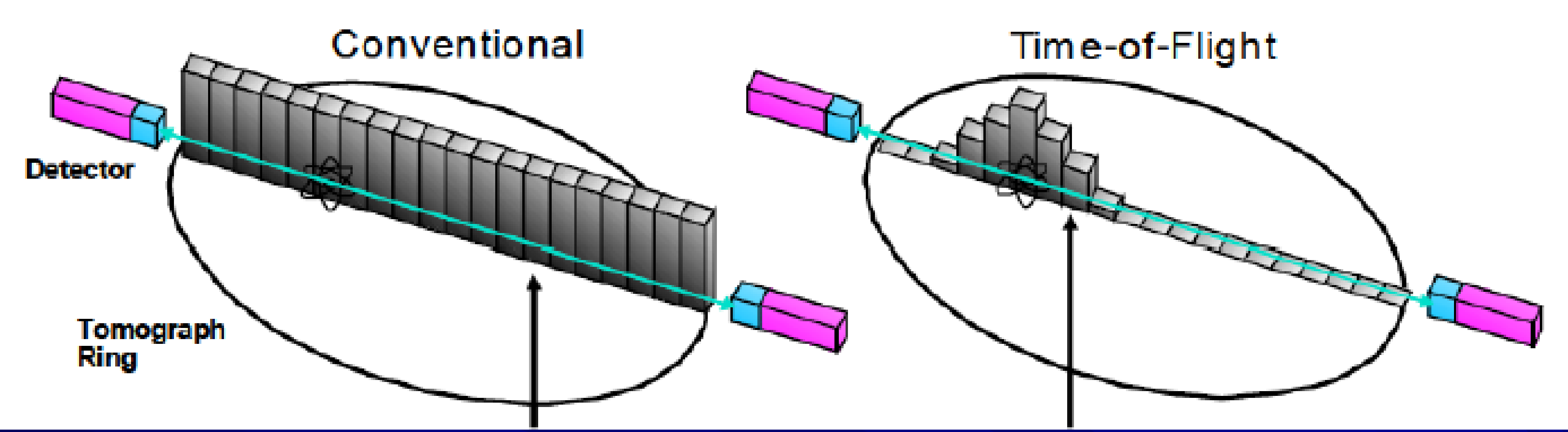
- Can localize source along line of flight.
- Time of flight information reduces **noise** in images.
- **Line Of Response ---> list mode**

	δt (ps)	Δd (cm)	SNR*
	100	1.5	5.2
	300	4.5	3.0
Today	500	7.5	2.3
	600	9.0	2.1

** SNR gain for 40 cm phantom*
$= SNR_{TOF} / SNR_{non\text{-}TOF}$

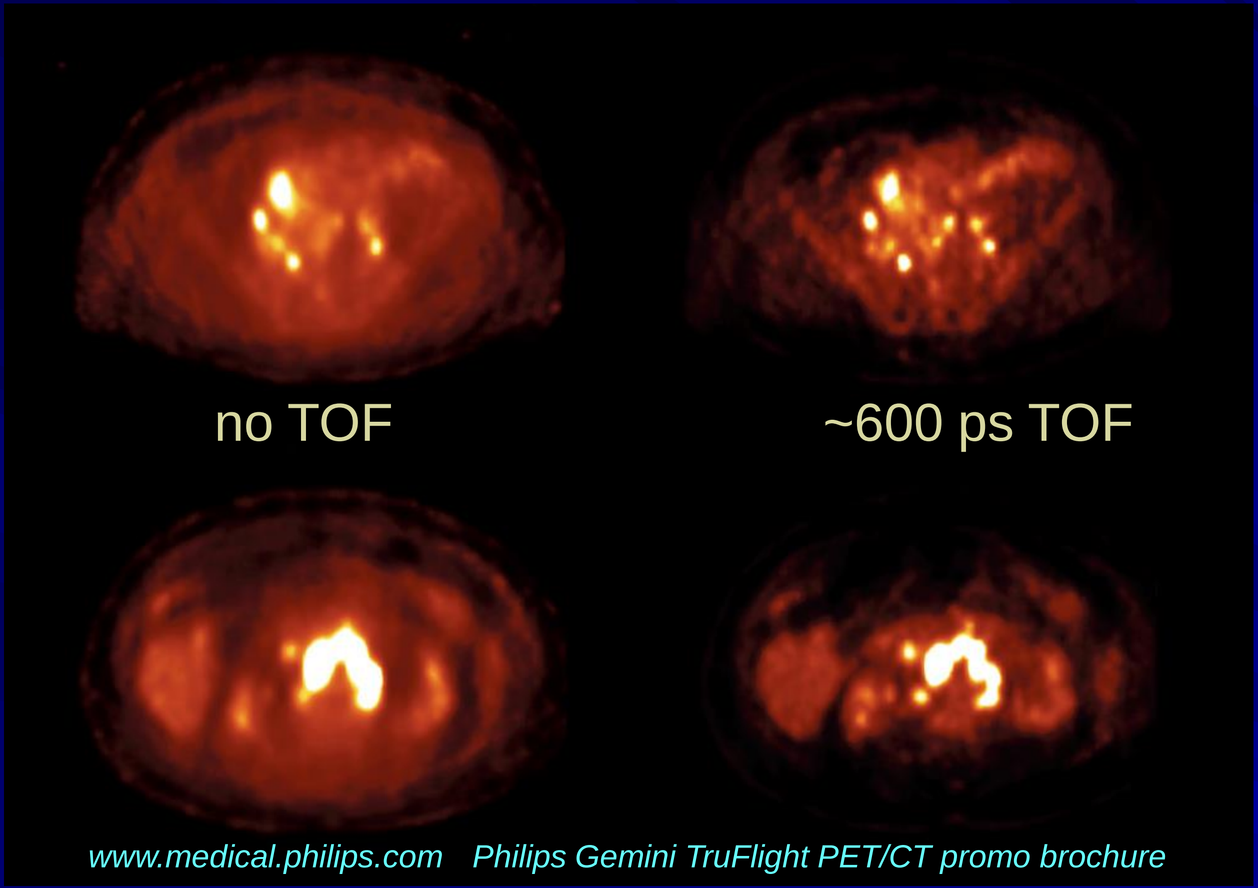
W.Moses courtesy

TOF technique (Con't)



- But need to use list mode data
- More complex data analysis and computing power

TOF PET example

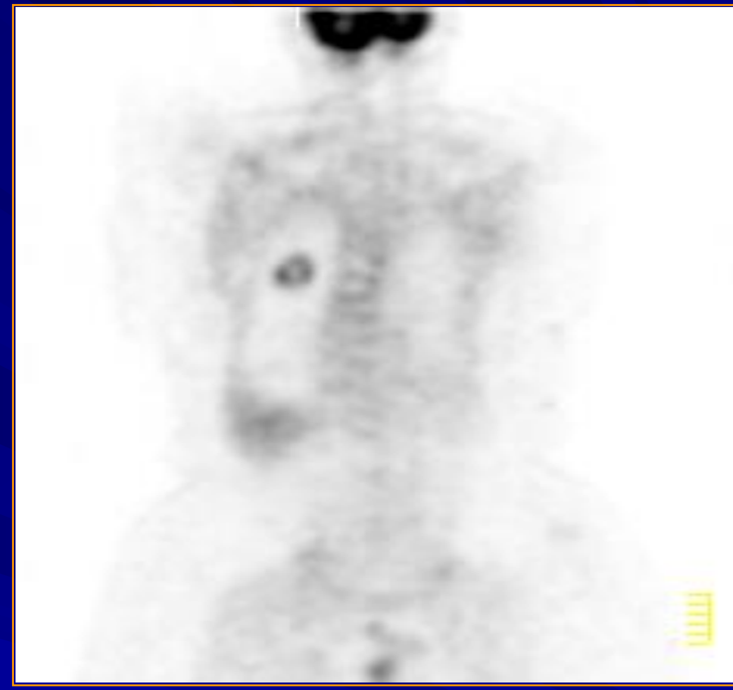


TOF-PET allows

- better images
- shorter scans
- smaller radiation dose to patients

- Time of Flight provides a Huge performance increase
- Largest improvment for large patients

However: Impaired Image Quality in Larger Patients

Slim Patient	Large Patient
	

For an equivalent data signal to noise ratio, a 120 kg person would have to be scanned 2.3 times longer than a 60 kg person

Courtesy

PHILIPS

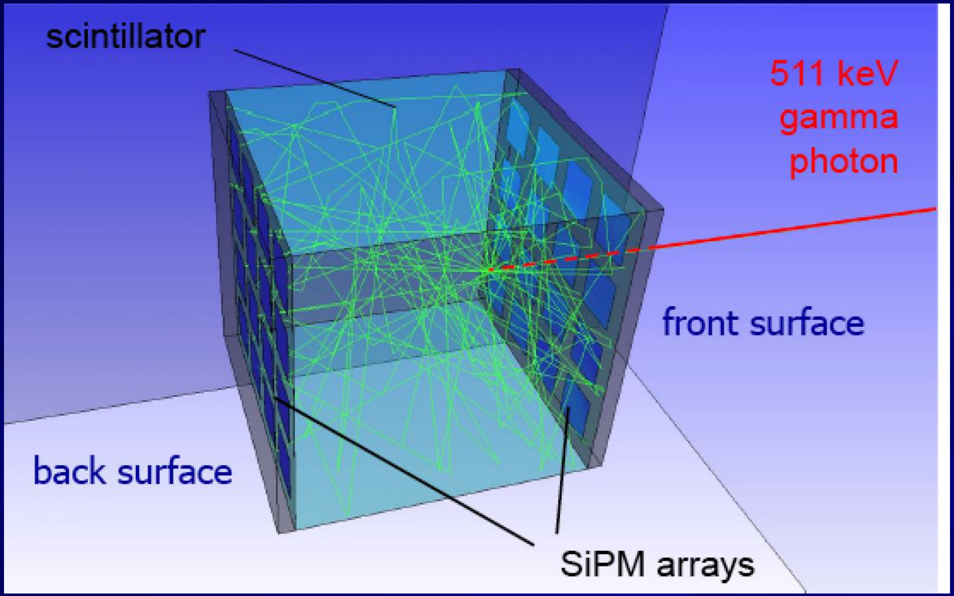
What is the limit ?

Hardware	Δt (ps)	TOF Gain
BGO Block Detector	3000	0.8
LSO Block (non-TOF)	1400	1.7
LSO Block (TOF)	550	4.2
$LaBr_3$ Block	350	6.7
LSO Single Crystal	210	11.1
LuI_3 Single Crystal	125	18.7
$LaBr_3$ Single Crystal	70	33.3

Research $LaBr_3$ Camera Built by U. Penn
- ~350 ps Intrinsic Detector Resolution
- 420–500 ps Camera Resolution (Electronics Limited)

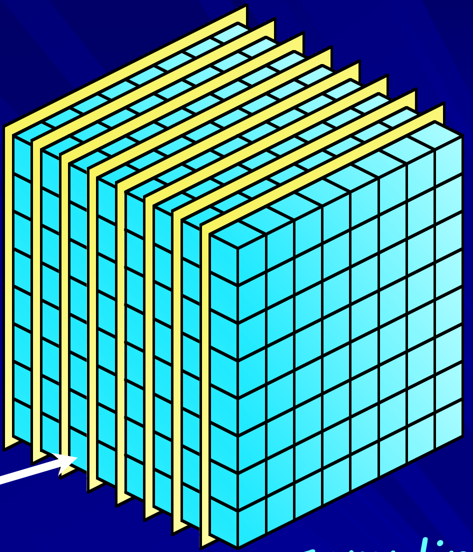
New 'picosecond development → 100 psec goal

On going TOF-PET module development



Monolithic scintillator

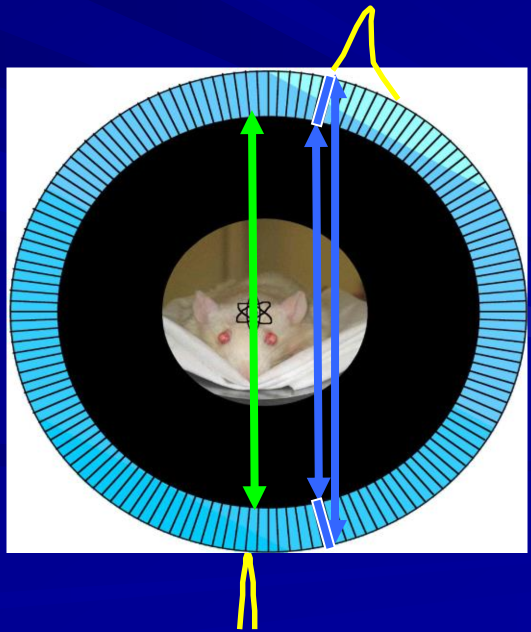
Photodetector
Array
(SiPM/LAMCP)



Scintillator
Array

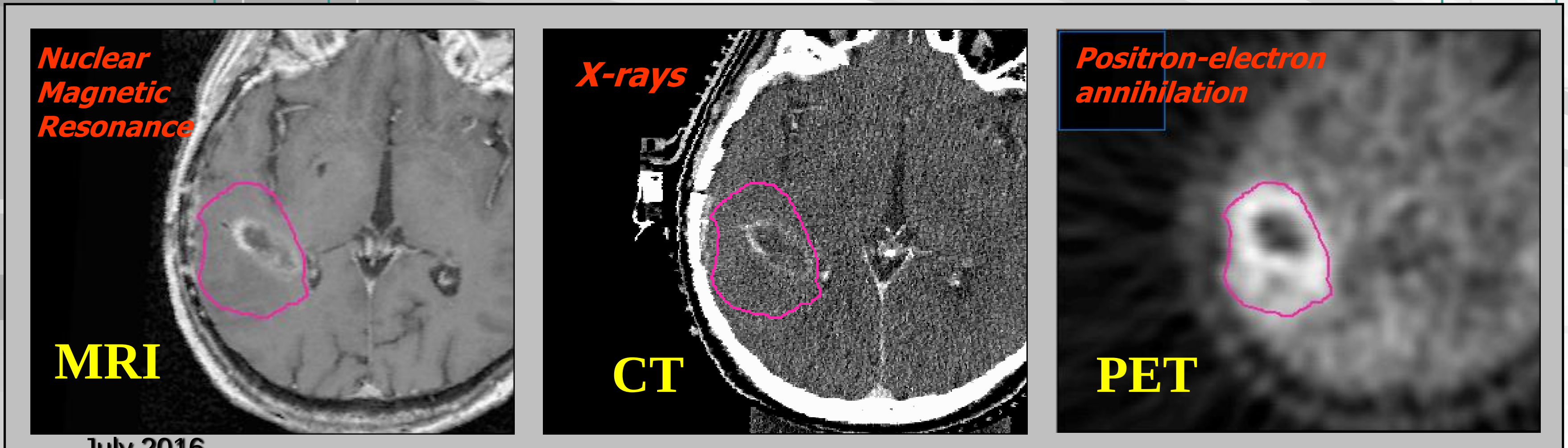
sampling

- Goal
  - TOF: 100 psec resolution
  - Position : 1 mm
  - DOI* capability

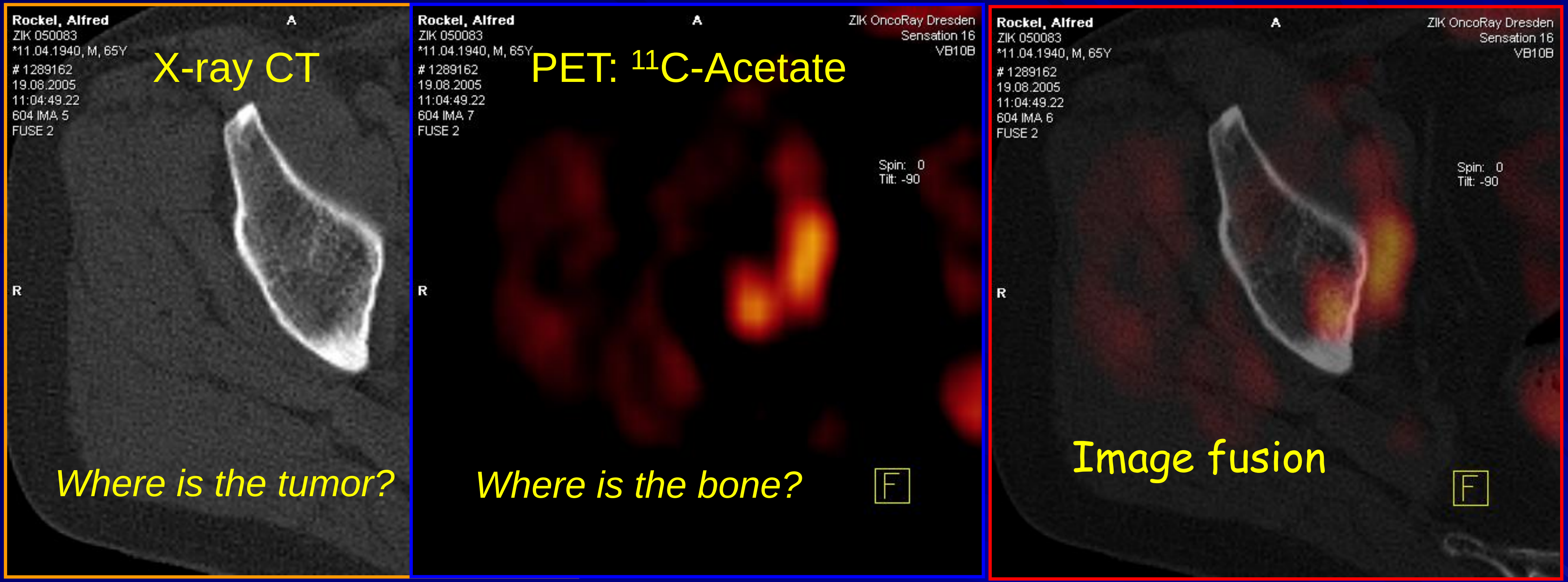


*Depth
Of
Interaction

Multimodality



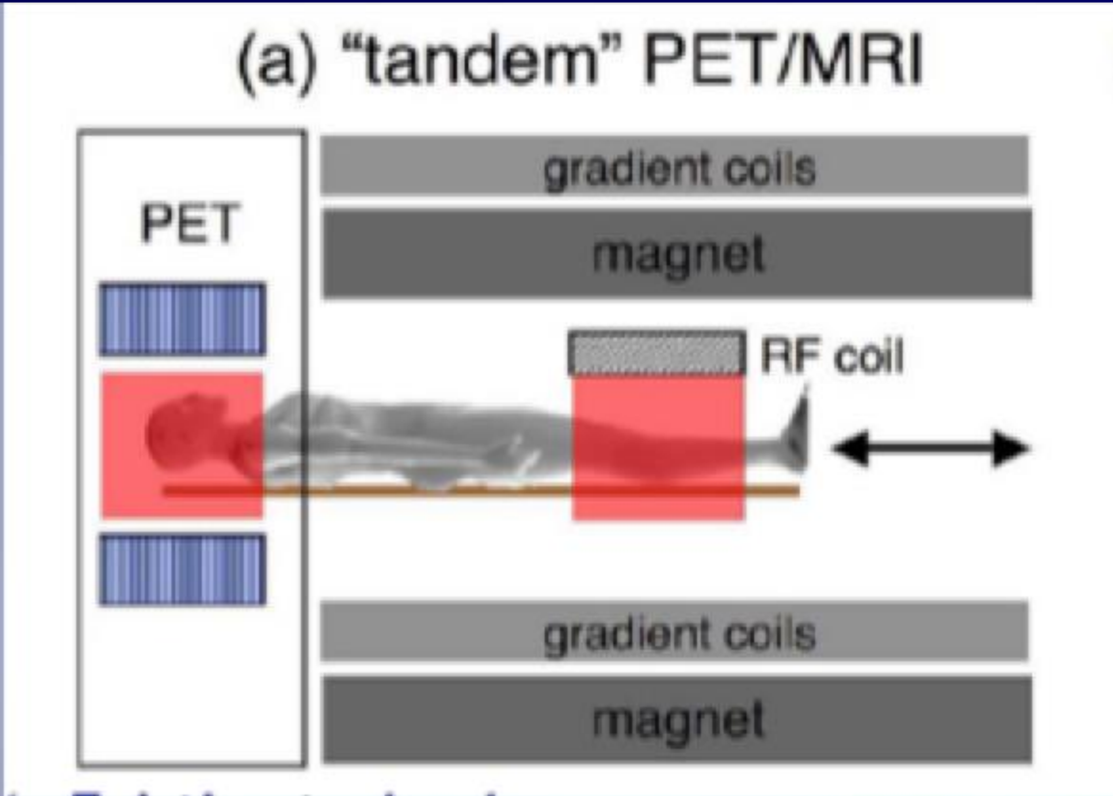
Multimodalities issues --> Image fusion

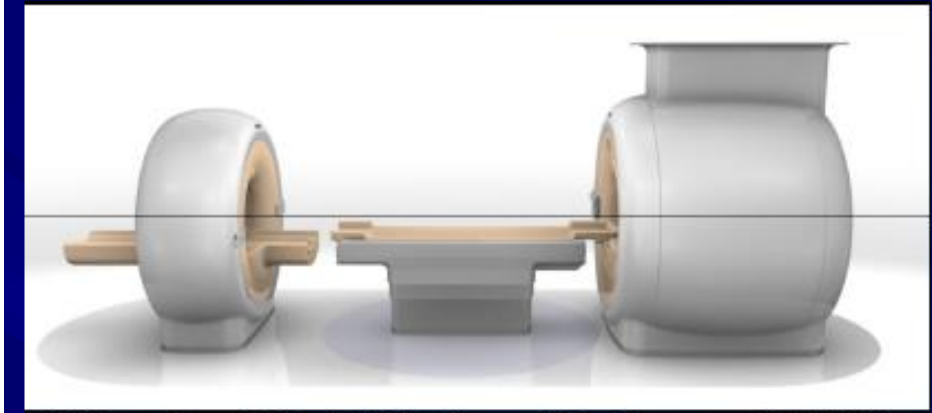


Metastases of a prostate carcinoma

Courtesy: N. Abolmaali, OncoRay Dresden

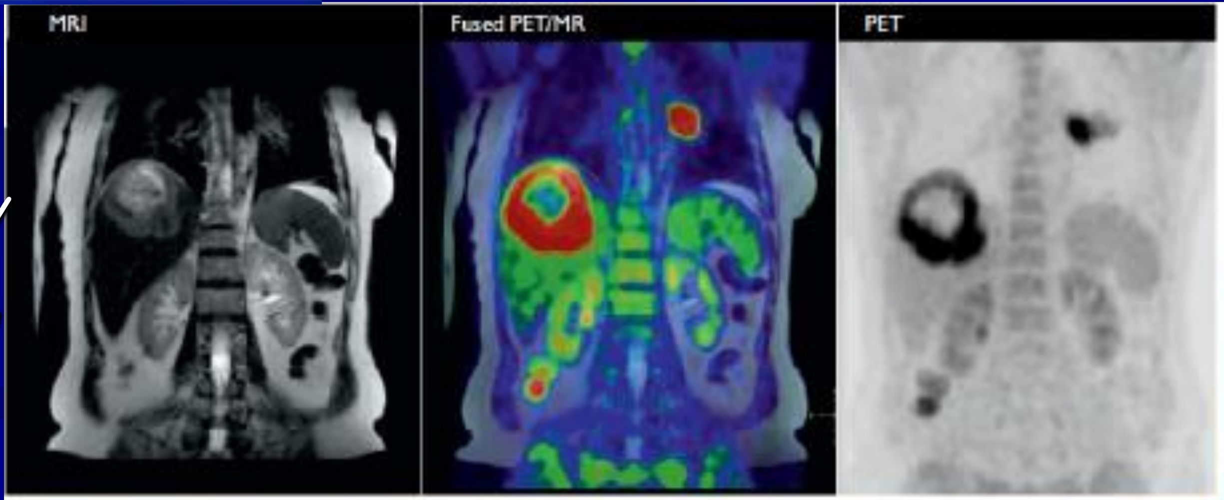
PET-MRI



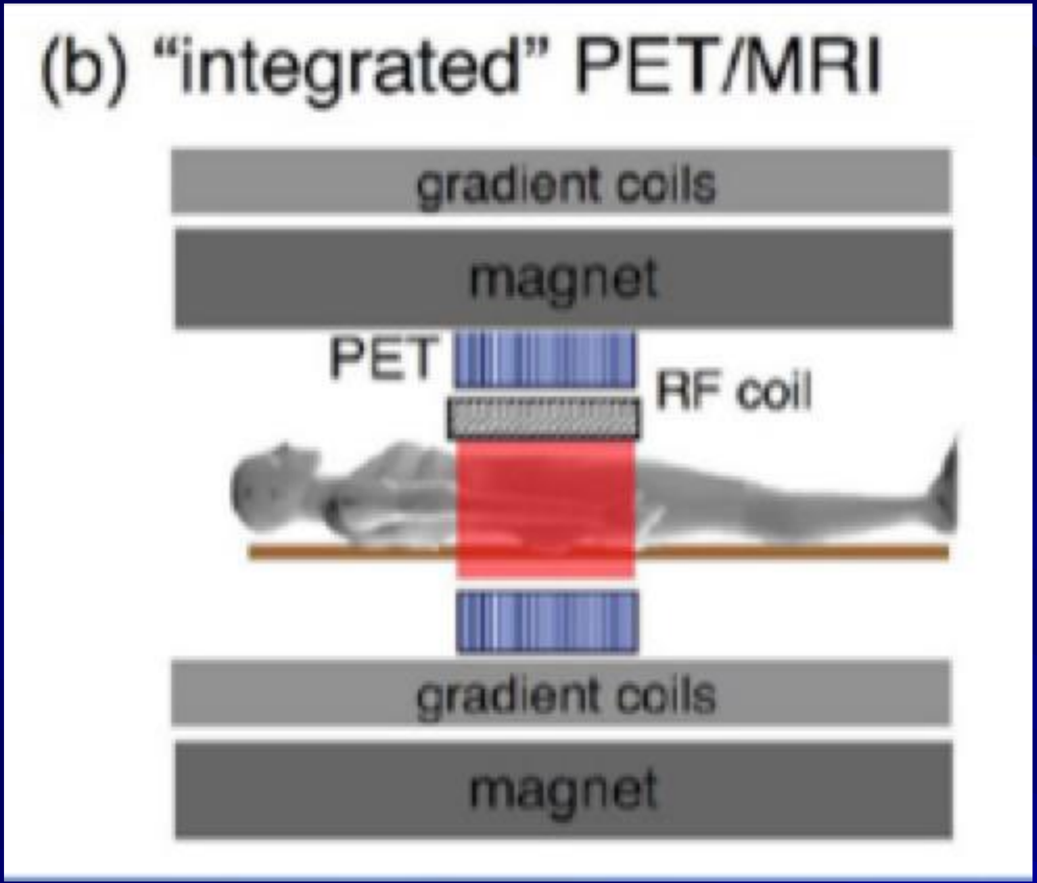


Philips Gemini TF (PET) and Achieva 3T (MRI)

- *Standard 'old' approach*
  - *Existing technologies*
  - *PET design not limited by geometrical constraints*
  - *Interferences minimized*
  - *Require image fusion*
  - *Not simultaneous*

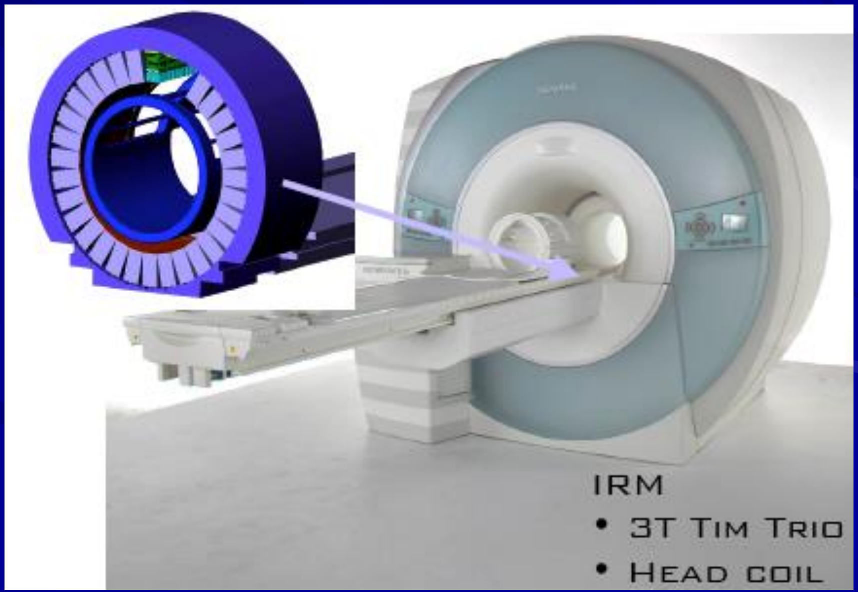


Courtesy Philips and University Hospital of Geneva



PET/MRI

- New approach
  - Simultaneous image acquisition
  - Shorter acquisition time geometrical constraints
  - Some geometrical constraints
  - System interference

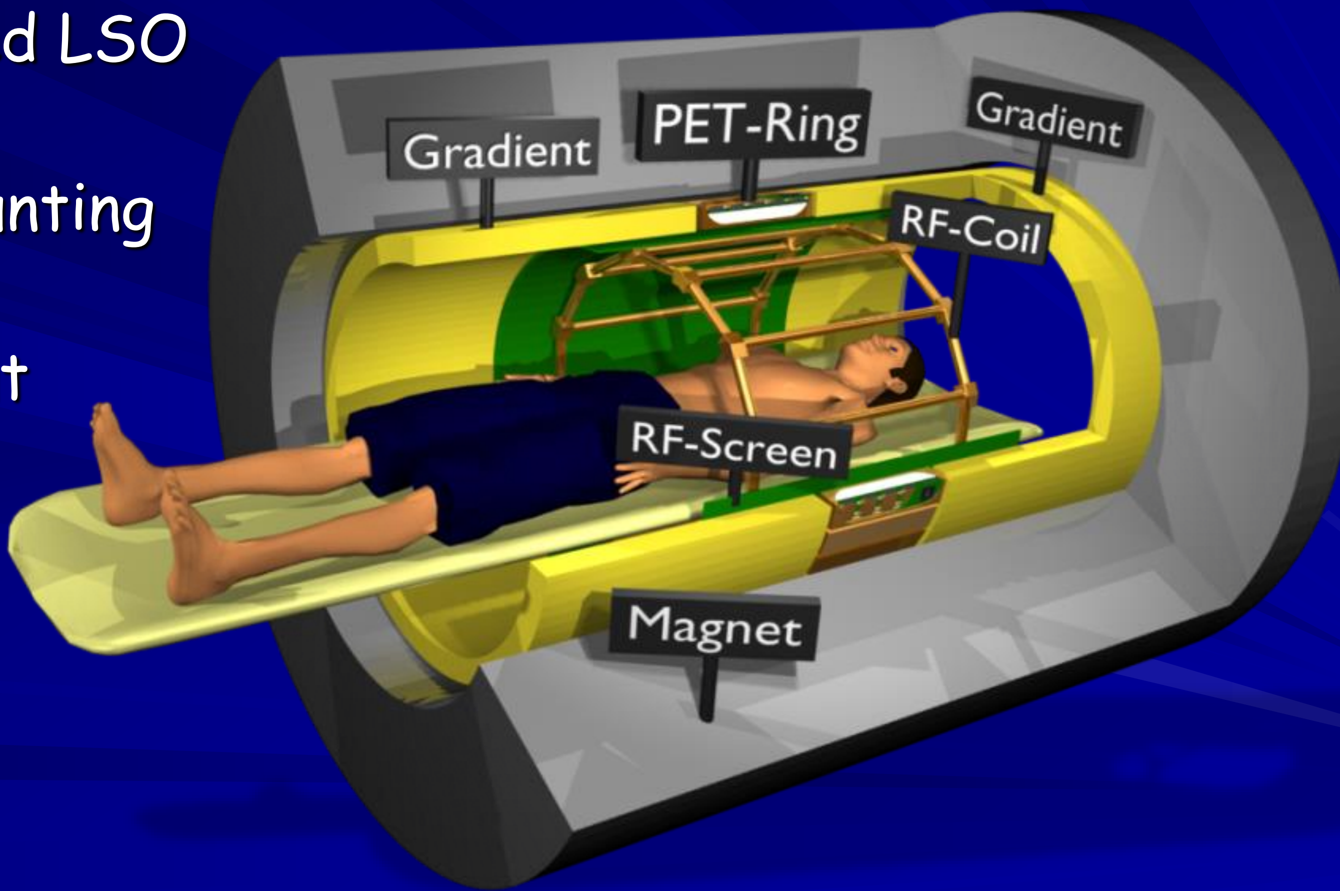


A lot of developments Since SiPM availablility

The SUBLIMA project: High resolution TOF-PET / MRI

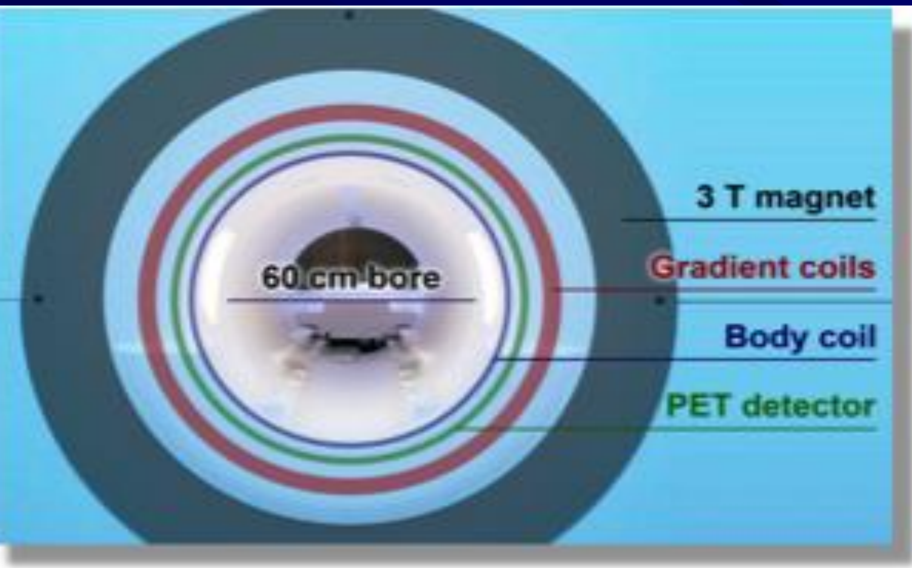
www.sublima-pet-mr.eu

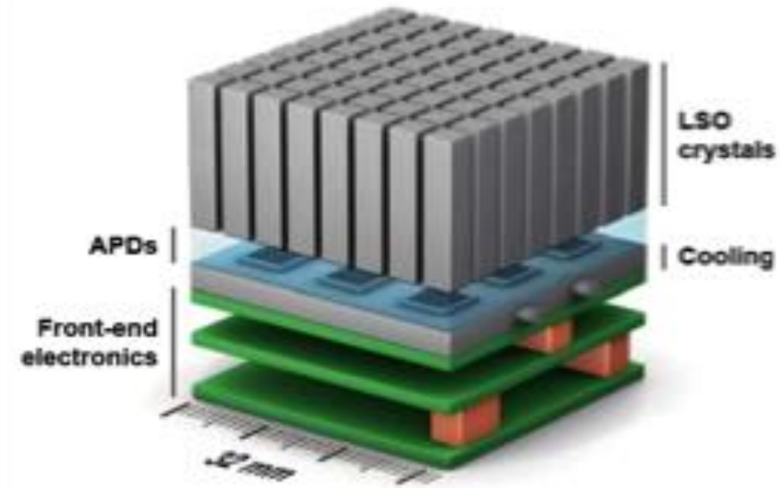
- Monolithic TOF/DOI detector
- Improved performance due to Ca co-doped LSO scintillator,
- Digital photon counting (dSiPM)
- Optimized readout algorithms



APD detectors in human PET/MRI

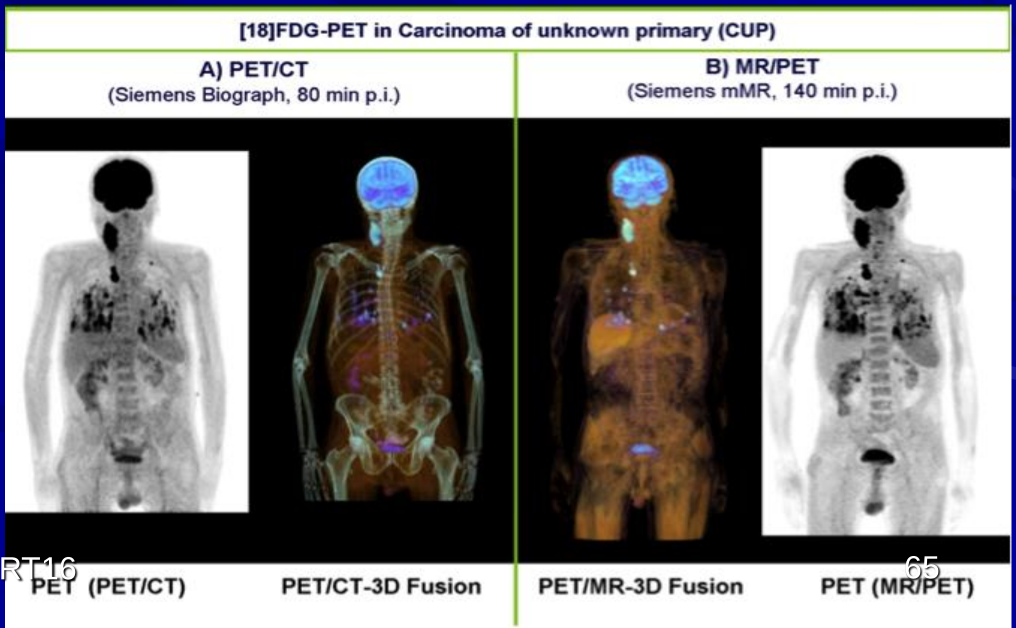
Siemens Biograph mMR



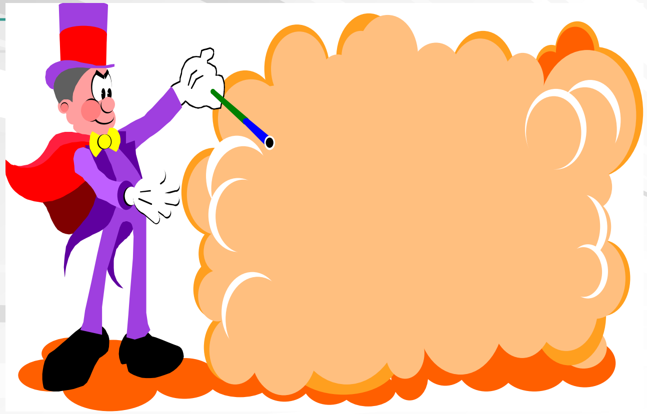


Drzezga SNM 2011

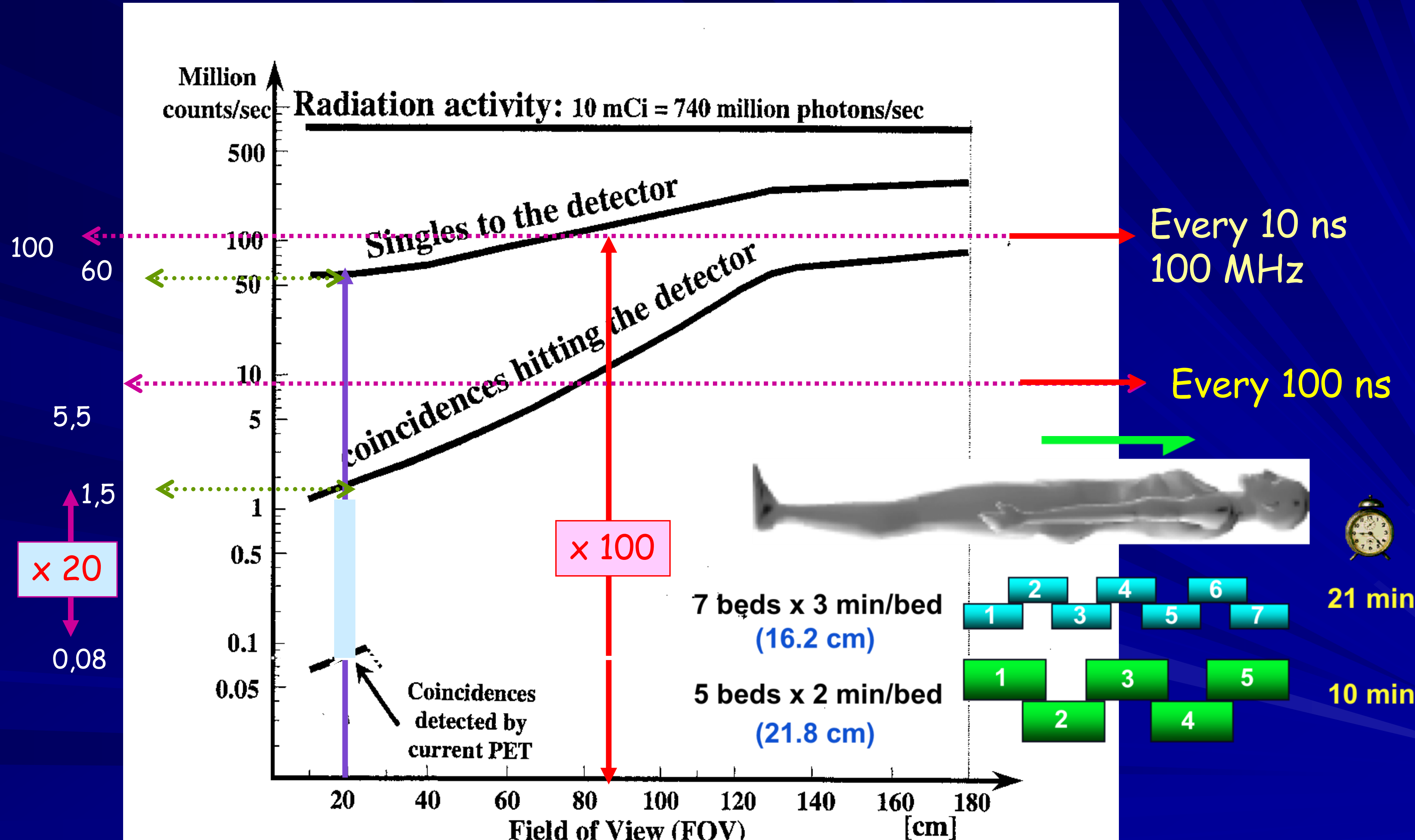
	Biograph mMR
Ring diameter	65.6 cm
Axial FOV	25.8 cm
Energy window	430 – 610 keV
Sensitivity (0 cm)	1.47 % (1.47 %)
(10 cm)	1.38 % (1.38 %)
Scatter fraction[1]	36.7 %
Spatial resolution[2]	4.3 mm (4.3 mm)



The Physician dream
' the minute PET'



Counting rate estimate



The Physician Dream

Courtesy of D.Townsend

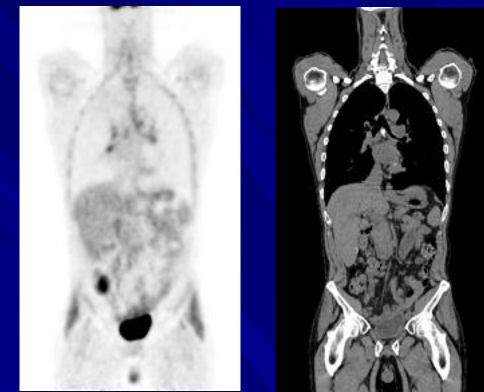
Combined whole-body PET/CT or PET/MR…..

Minute PET/CT

PET

PET

MDCT



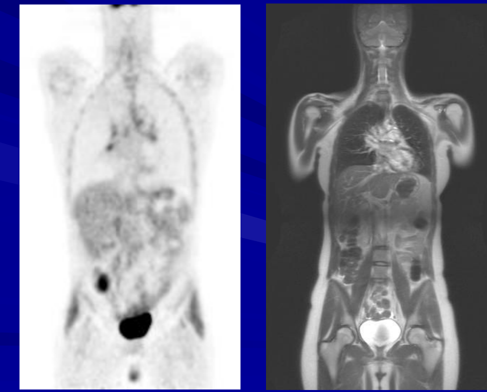
Less dose
Less movment correction
Screaning capability

Image In Real Time !

PET/MRI

Magnet

PET



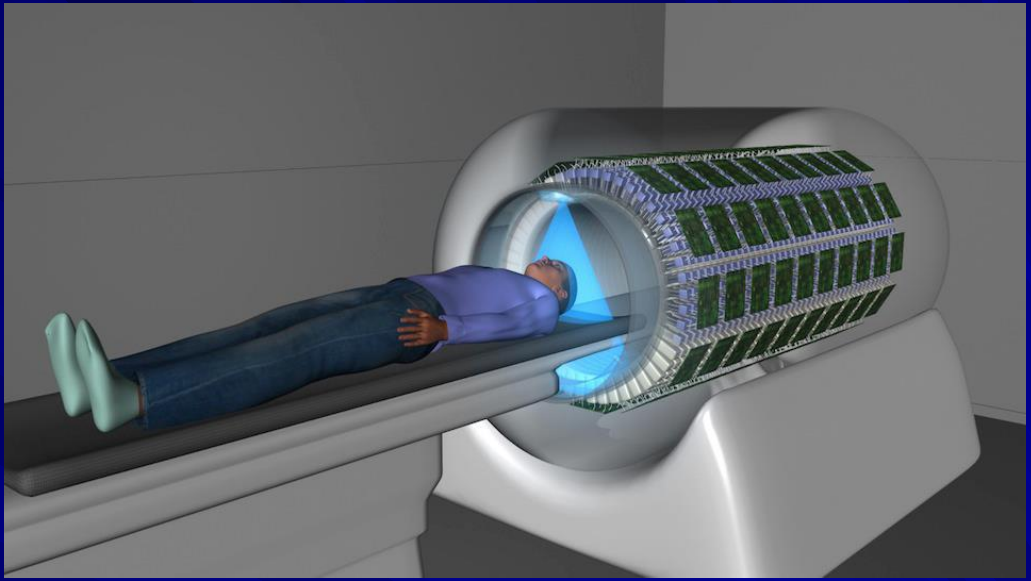
PET Insert with
Semiconductor photodetectors

PET

Magnet

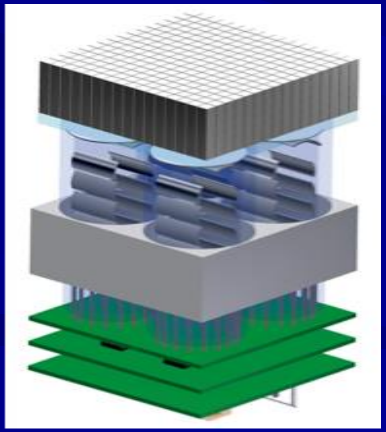
The total body 'explorer' project

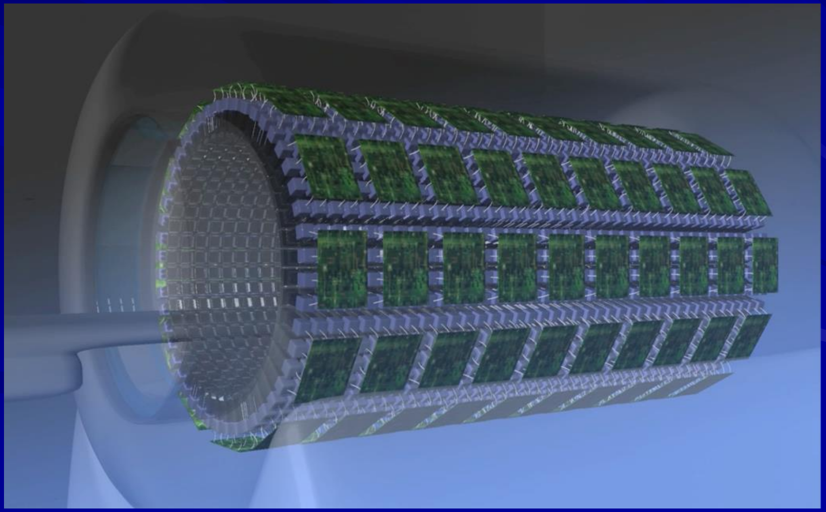
Davis,LBL,Upenn



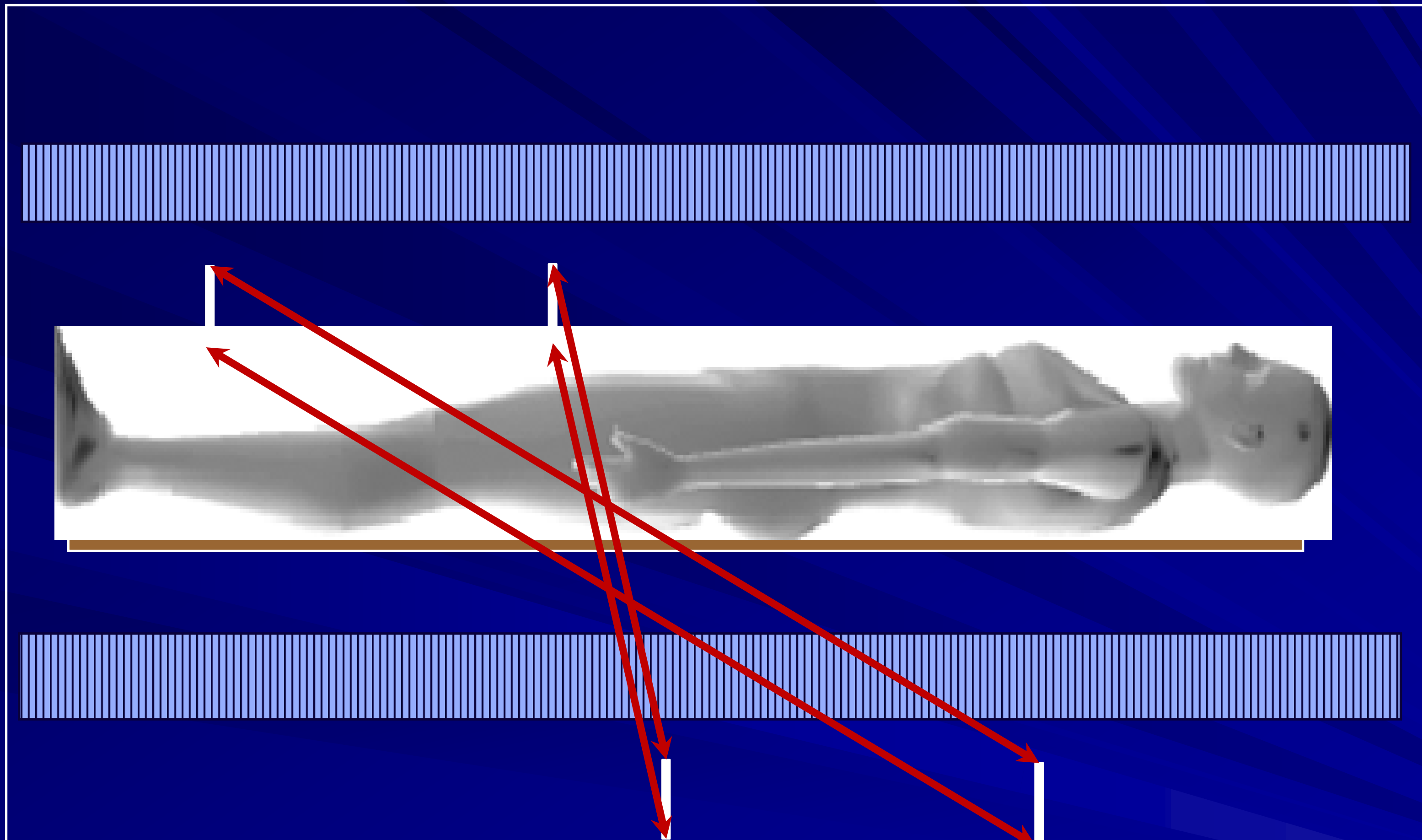
- Modular "Block" Detectors
- ~3.1 x 3.1 x 20 mm L(Y)SO
  - 880 kg of L(Y)SO!
- PMT (possibly SiPM) readout
- Time of flight and 1-bit DOI
- 40 rings, 48 detectors/ring
- ~78.6 cm ring diameter
- 215 cm axial FOV
- OpenPET electronics

S. Cherry, J3-7
NSS-MIC 2013 Seoul





Estimated data production

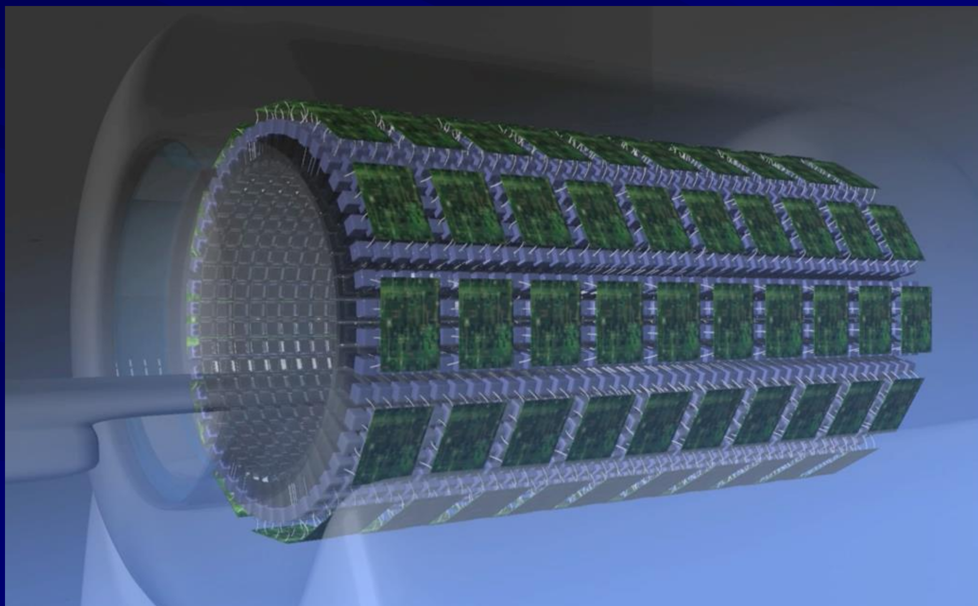


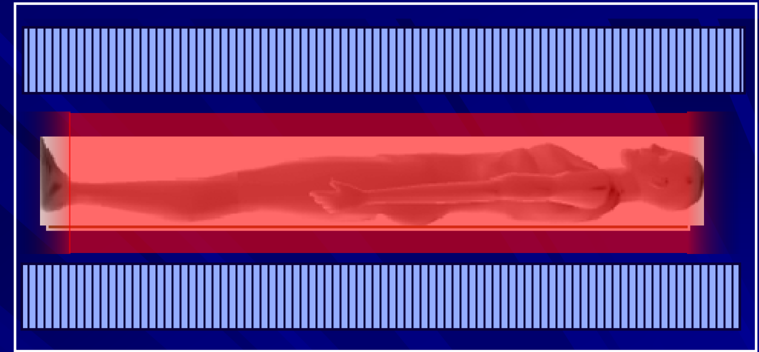
Singles: *164 MHz*
Prompts: *47 MHz*
Randoms: *34 MHz*

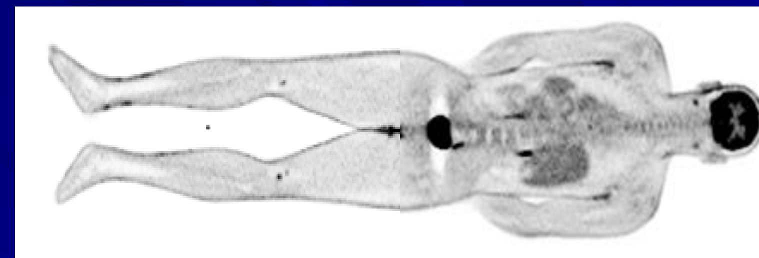
A very interesting subject for T/DAQ experts

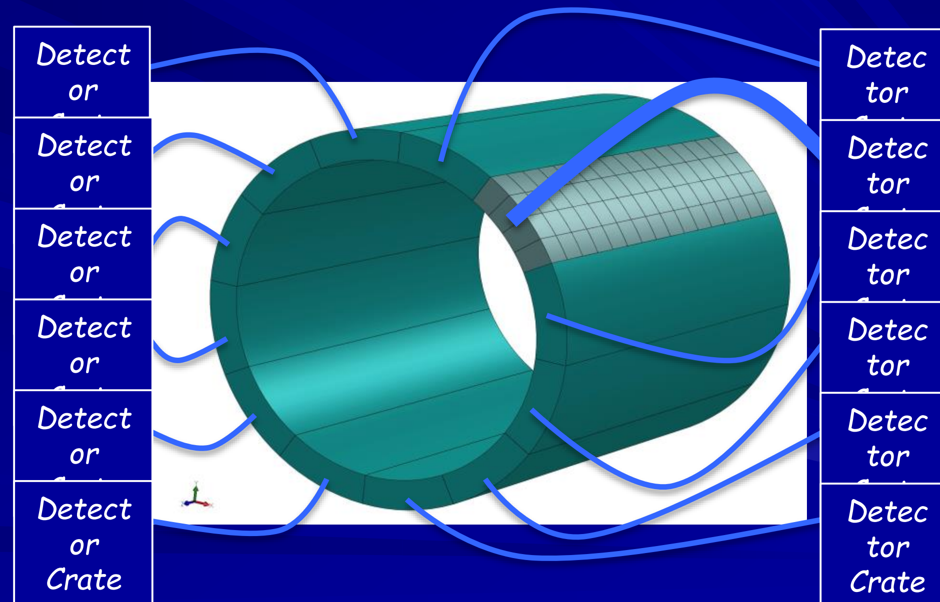
This idea is coming …..

- The Total body PET







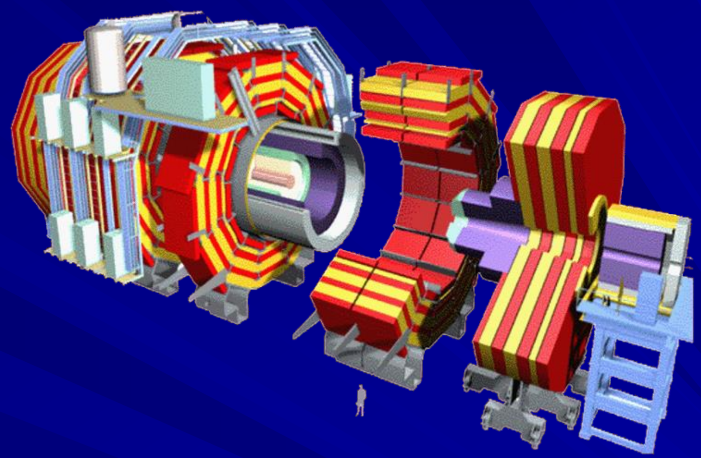


The Challenge

Total-Body "Explorer" Project

- Very large number of channels (20 → 2m FOV)
  ~ 500 k channels (2x2 mm2 pixels)
- High trigger rate ~ 10 MHz
  (10 mCi, 20% sensitivity)
- High data rate
  ~ 10 Gbyte/s (1 kbyte event size)
- Large number of events
  - *160 x 160 x 1000 image matrix*
  - Large data volume per image
  - 1 billion events

  Real Time analysis
- Simultaneous merging of multimodality data
  - CT- MRI



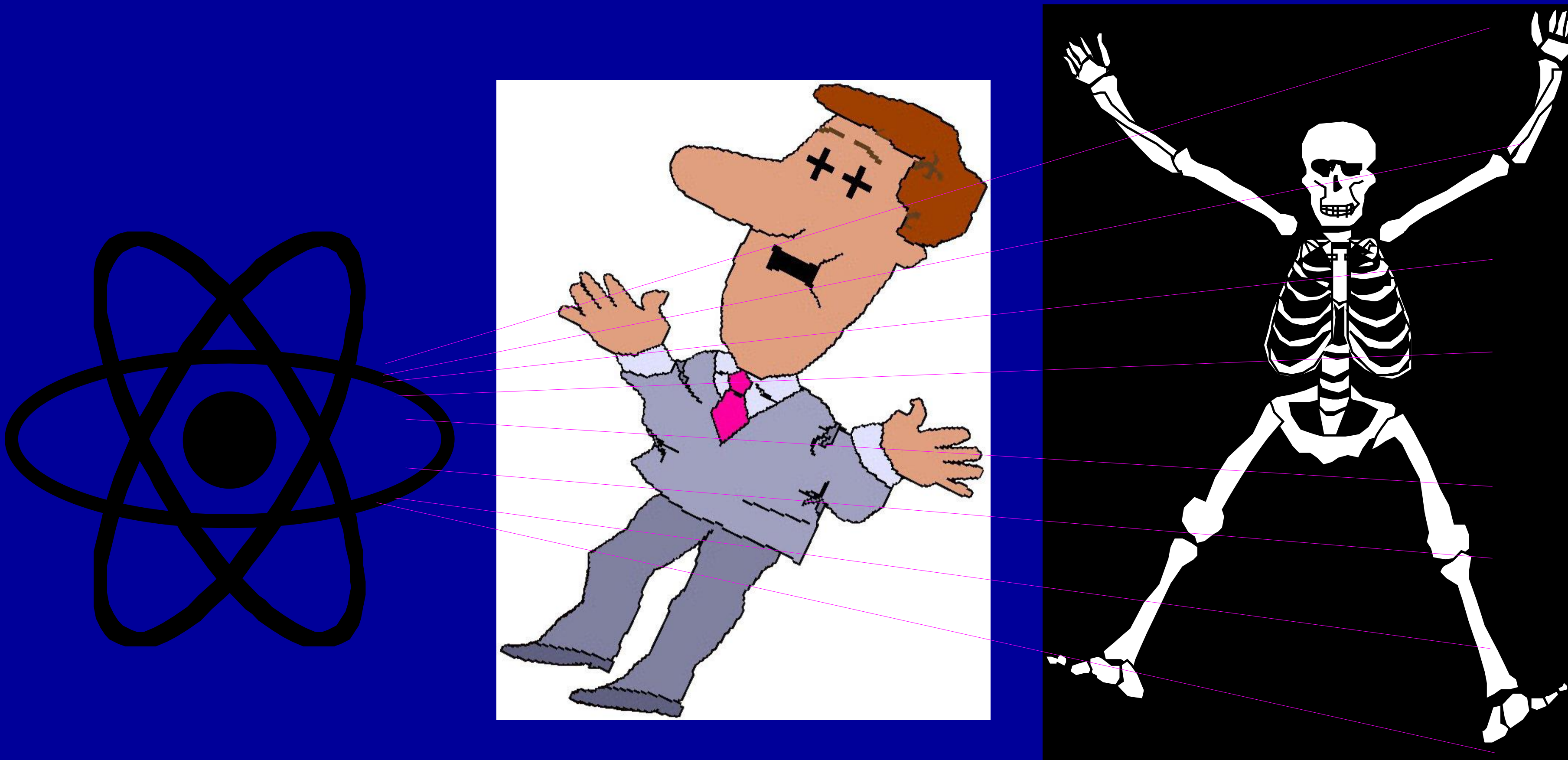
Looks like

2010

Radiography
X Ray imaging

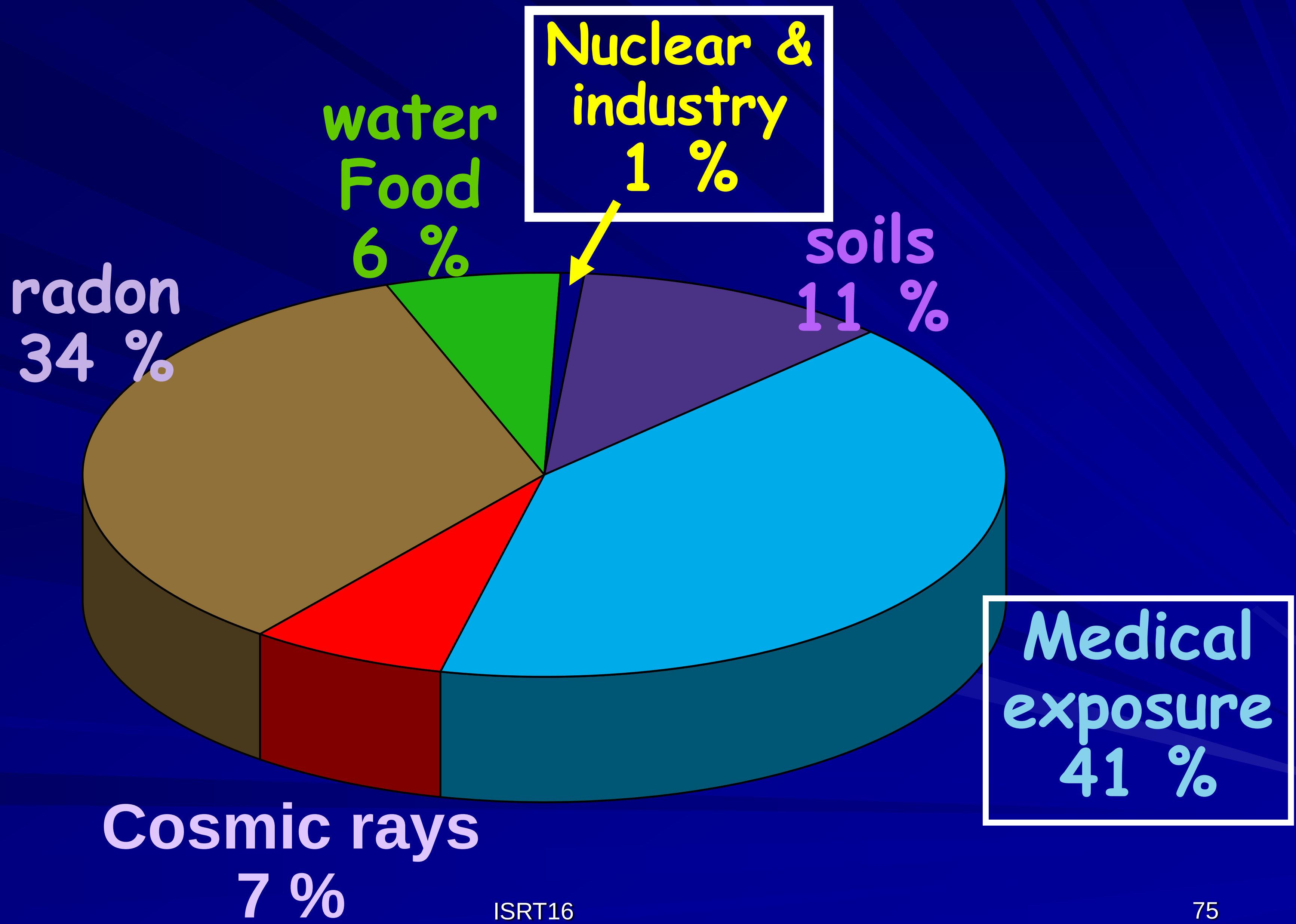
CT

Patient Radiation Dose is Limited!



- Image Noise Is Limited by Counting Statistics
- Cannot Increase too much Source Strength

Natural versus medical irradiation



Exposure for radiological exams

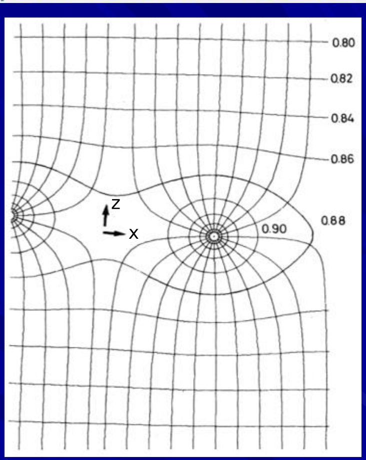
- Some examples

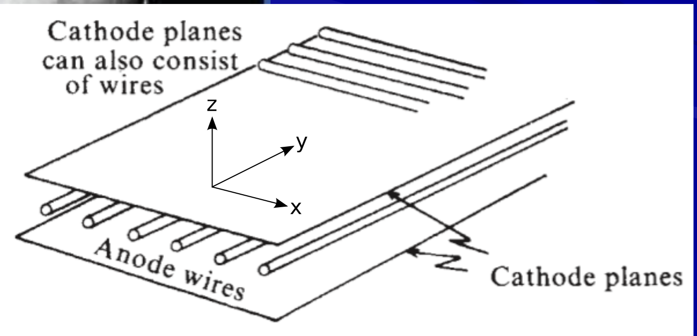
organ	dose skin mGy	effective dose mSv
Thorax, face	0,2 - 0,5	0,015 - 0,15
Lumbar region	4 - 28	1,5
Urography	40 - 60	3
Brain scan	7 - 78	1
Whole Body scan	30 - 60	4 - 10
Mammography	7 - 25	0,5 - 1

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



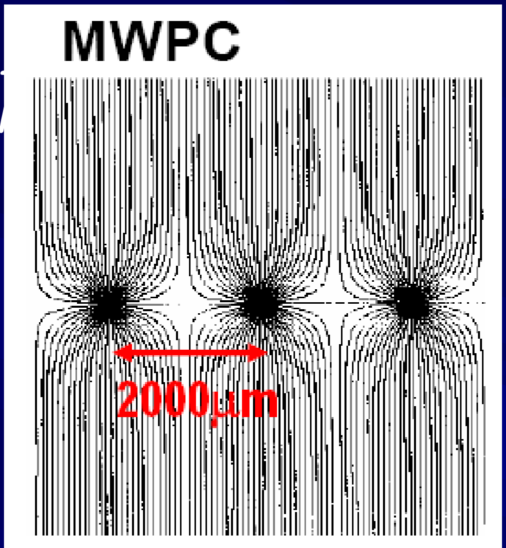


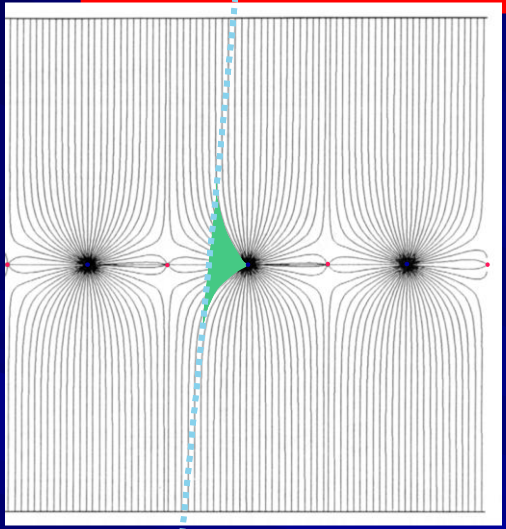
From MWPC's to MGPD's

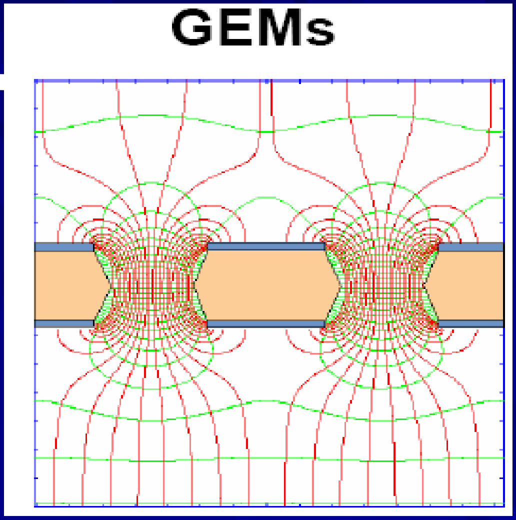
MGPD

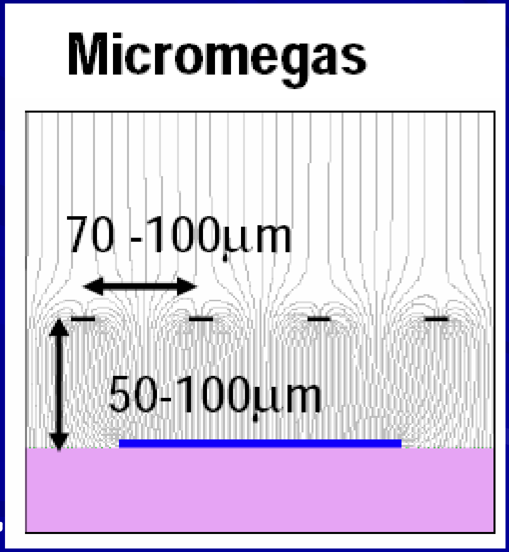
MWPC

Drift Chamber









1975 - 1995

UA2-LEP

1990 -

Multiwire Proportional Chamber

Georges Charpak 1968

GEM F.Sauli)

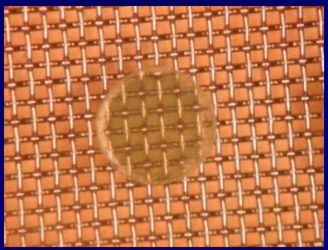
Micromegas Y. Giomataris

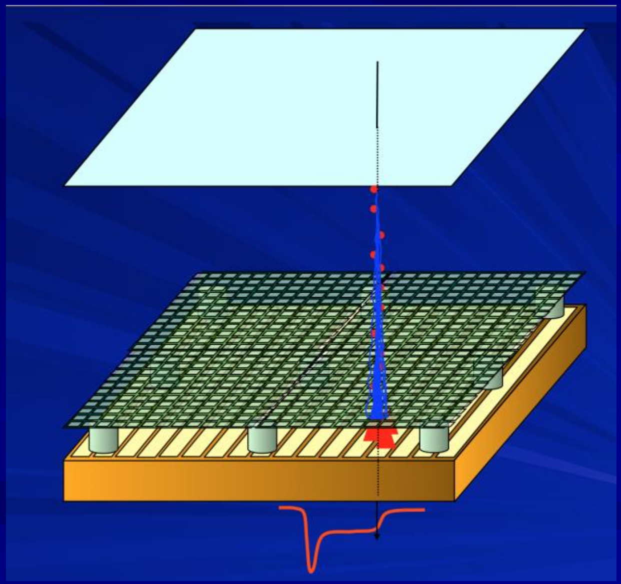
MPGD

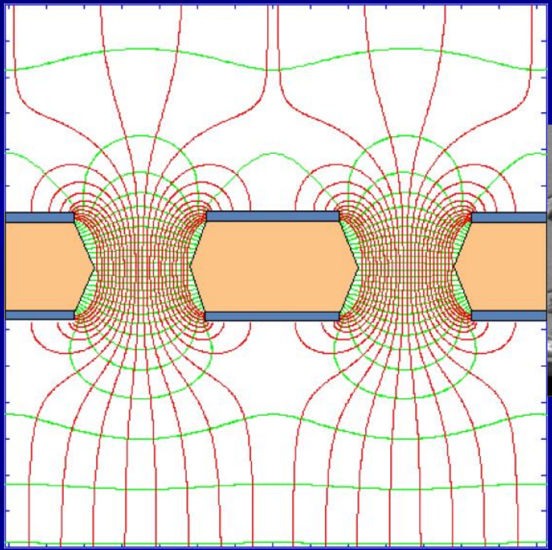
- From 1988-1998 Micro-technologies and etching techniques allowed development of Micro Patter Gaseous Detectors

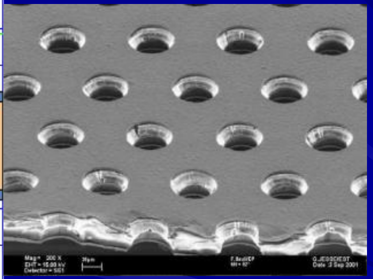
- MICROMEsh GAseous Structure
  - Thin gap Parallel Plate Chamber: micromesh stretched over readout electrode.

- Gas Electron Multiplier
  - Thin, metal-coated polymer foil with high density of holes, each hole acting as an individual proportional counter.









To summarize X Ray imaging

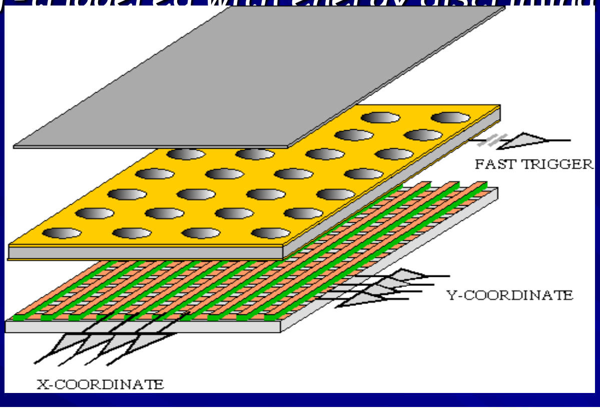
Wire Chamber Radiography:

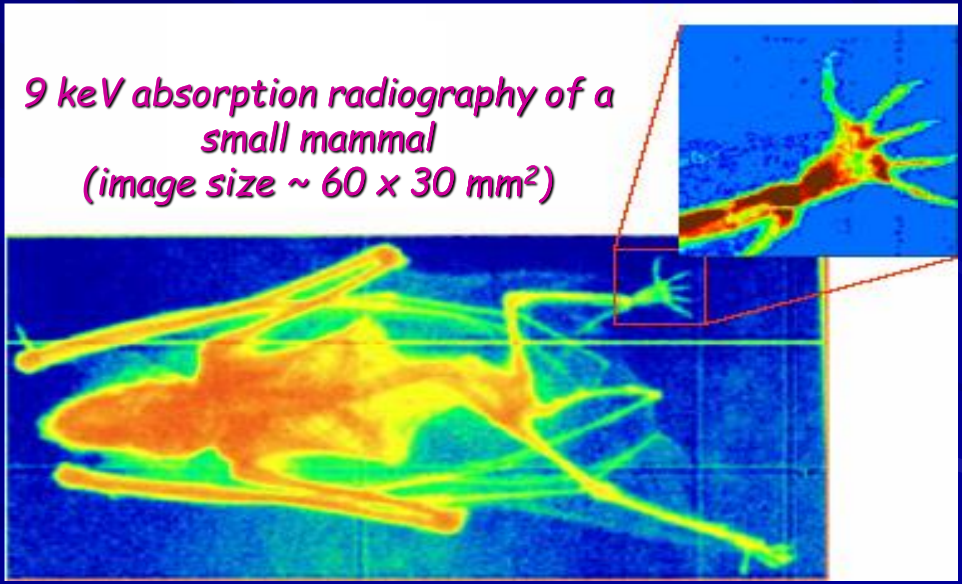
Position resolution ~ 250 μm

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

GEM for 2D Imaging:

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

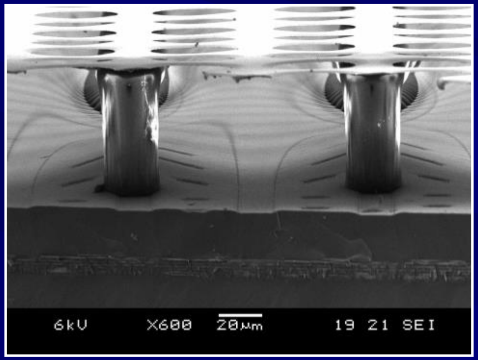




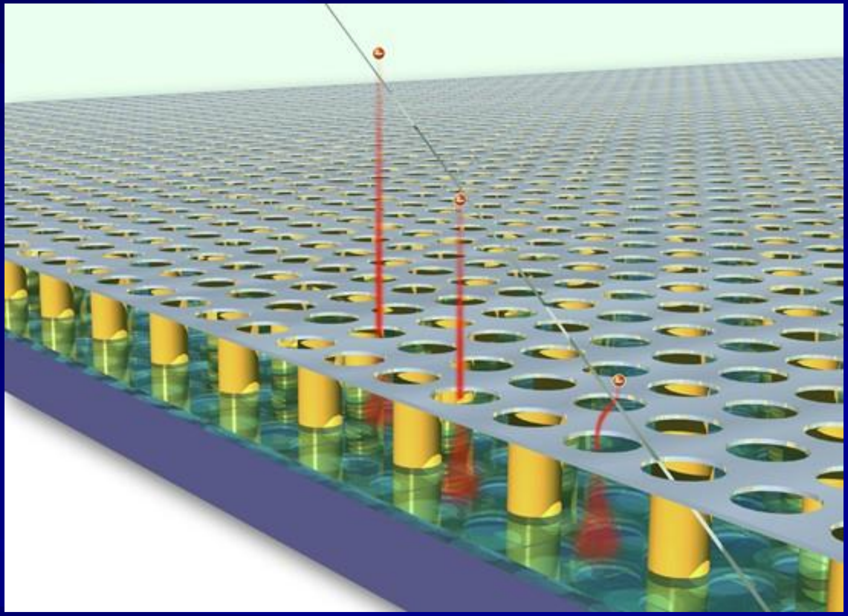
Position resolution ~ 100 μm
(limited by photoelectron range in the gas)

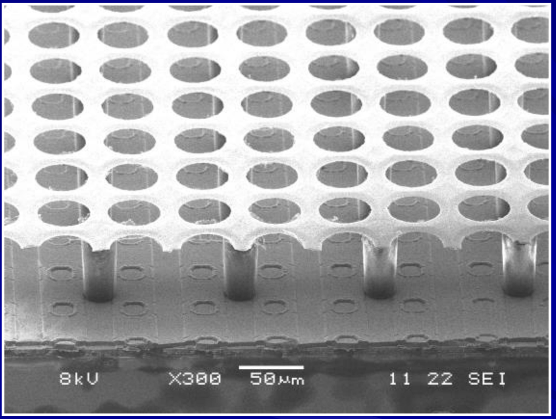
Next → INGRID

- 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



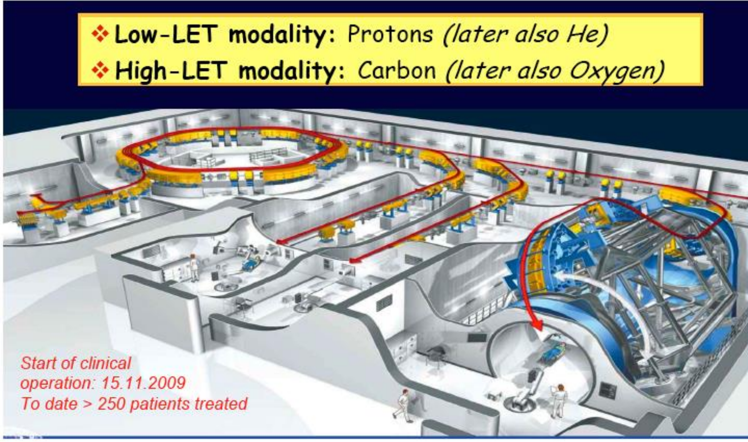
metalized foil
~100 μm ~1mm

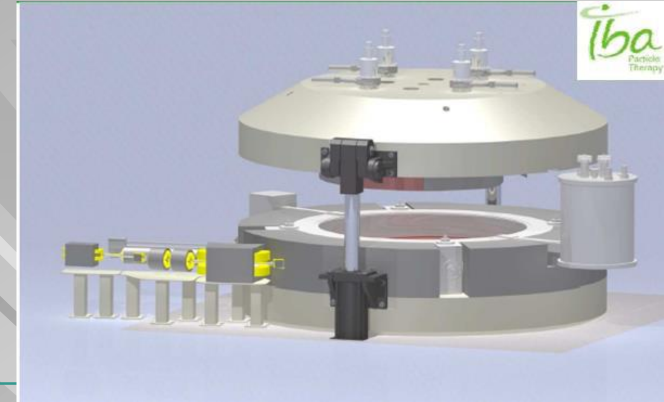




81Cmos Medipix chip

- Use → Large Trackers & Calorimeters

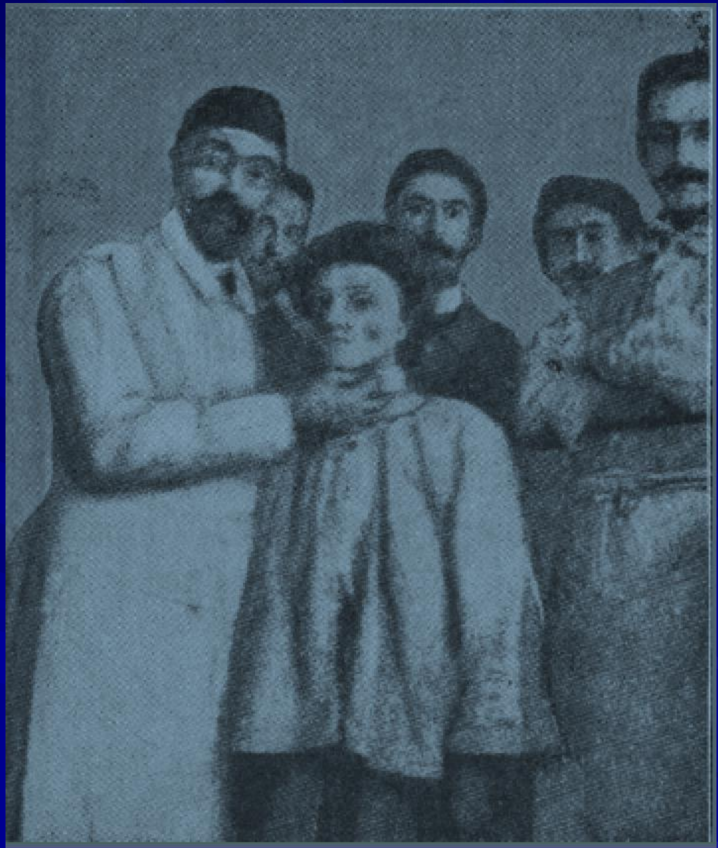




Particle Therapy

First cancer treatment by brachy therapy

- Henri Alexandre Danlos, a Parisian dermatologist, exhibiting a woman who he successfully treated for *lupus vulgaris* of the face. Pierre Curie loaned him the source and hetreated her in 1901.



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

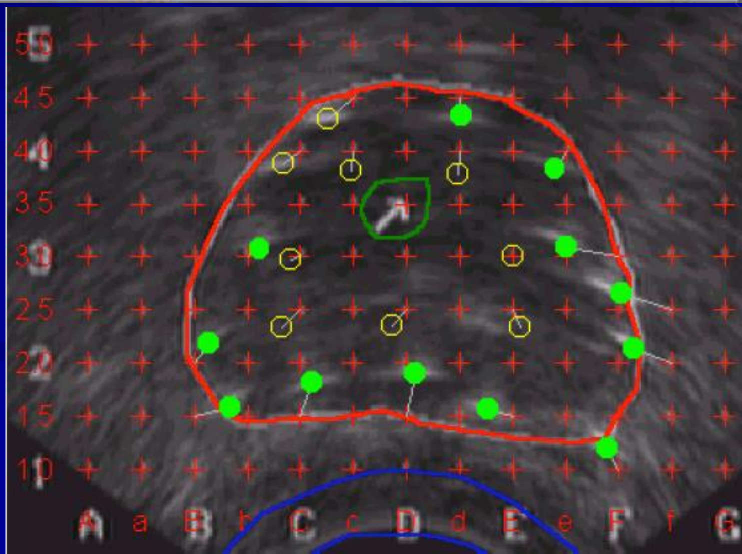
Par MM. Danlos et P. Bloch.

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

Curietherapy/Brachytherapy

1910

Today



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

Treating Cancer

- Radiotherapy X
  - Local irradiation → 100 Gy = 90 % of sterilization
  - Frequent treatment (2/3 of cases).
  - 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)
  - Efficient treatment but ….

Particle therapy: The Context

- *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

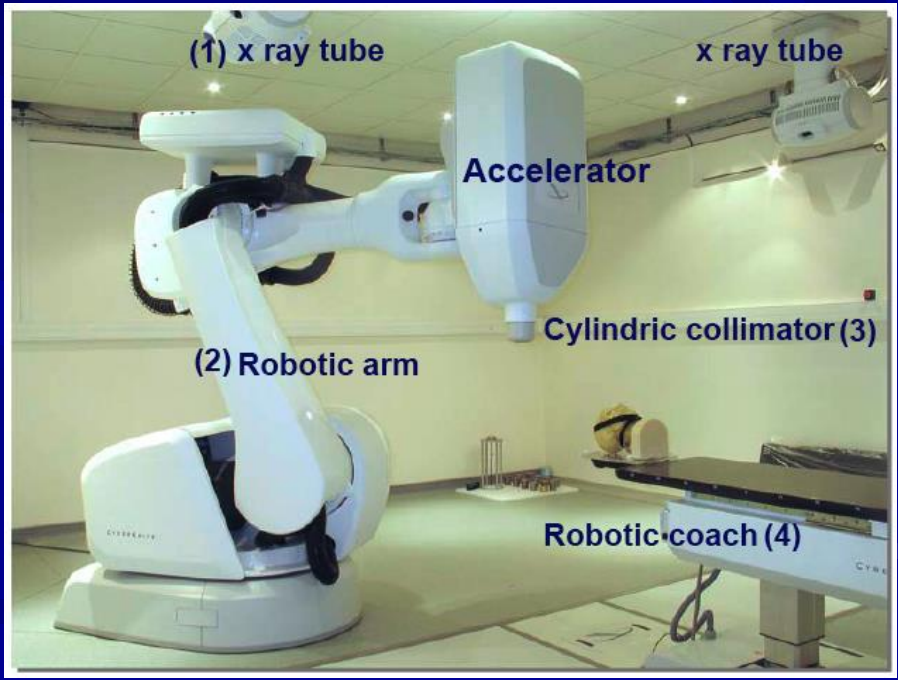
→Particle therapy around 15%of the cases

RT modern techniques

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

Sate of the art: Robotic Stereostatic RT

- Multiple beams
- High Precision 1 mm
- Dedicated & invasive (radiochirurgy)

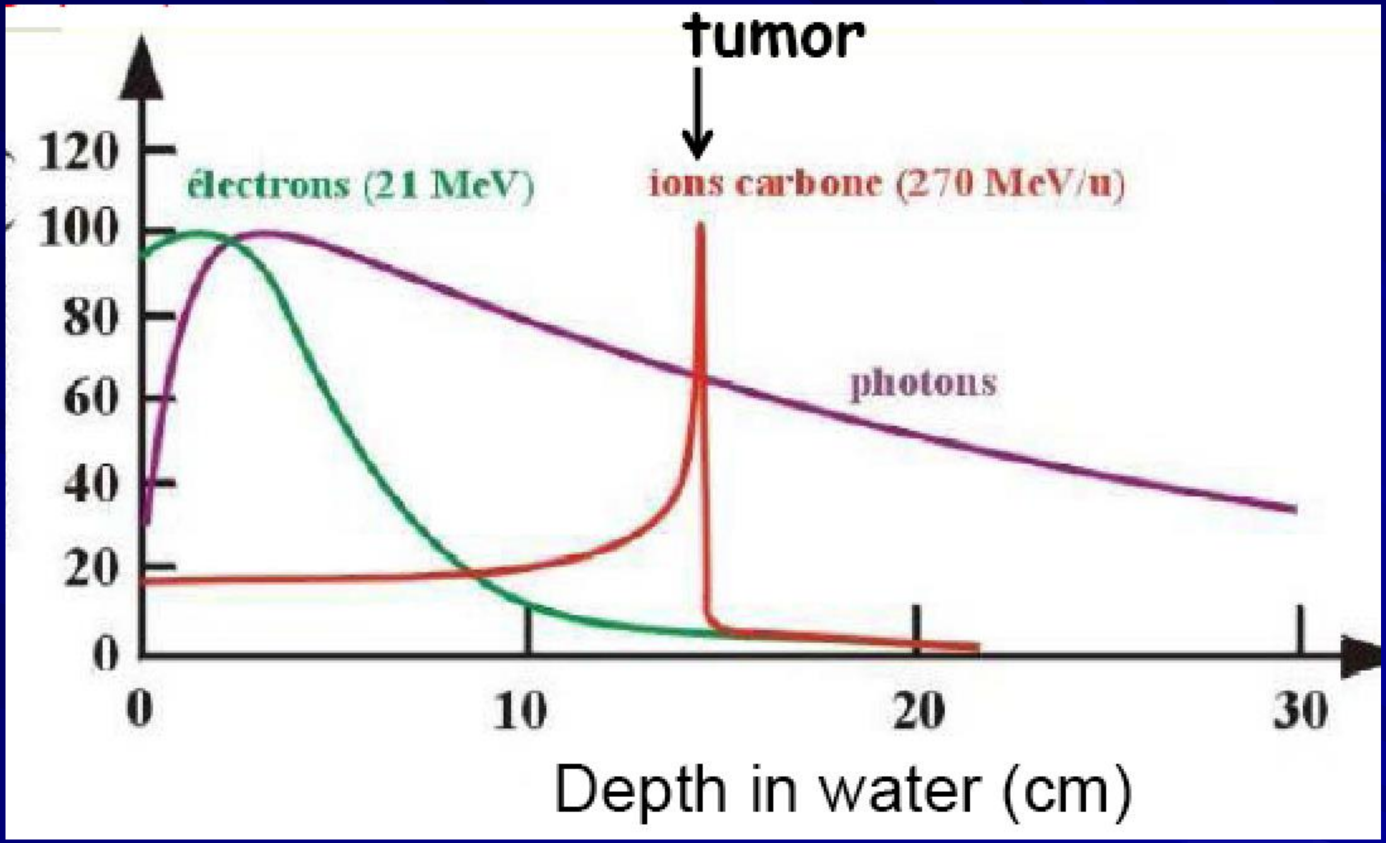


Cyberknife TM

Estimated absolute yearly rate (%) of 2nd cancer

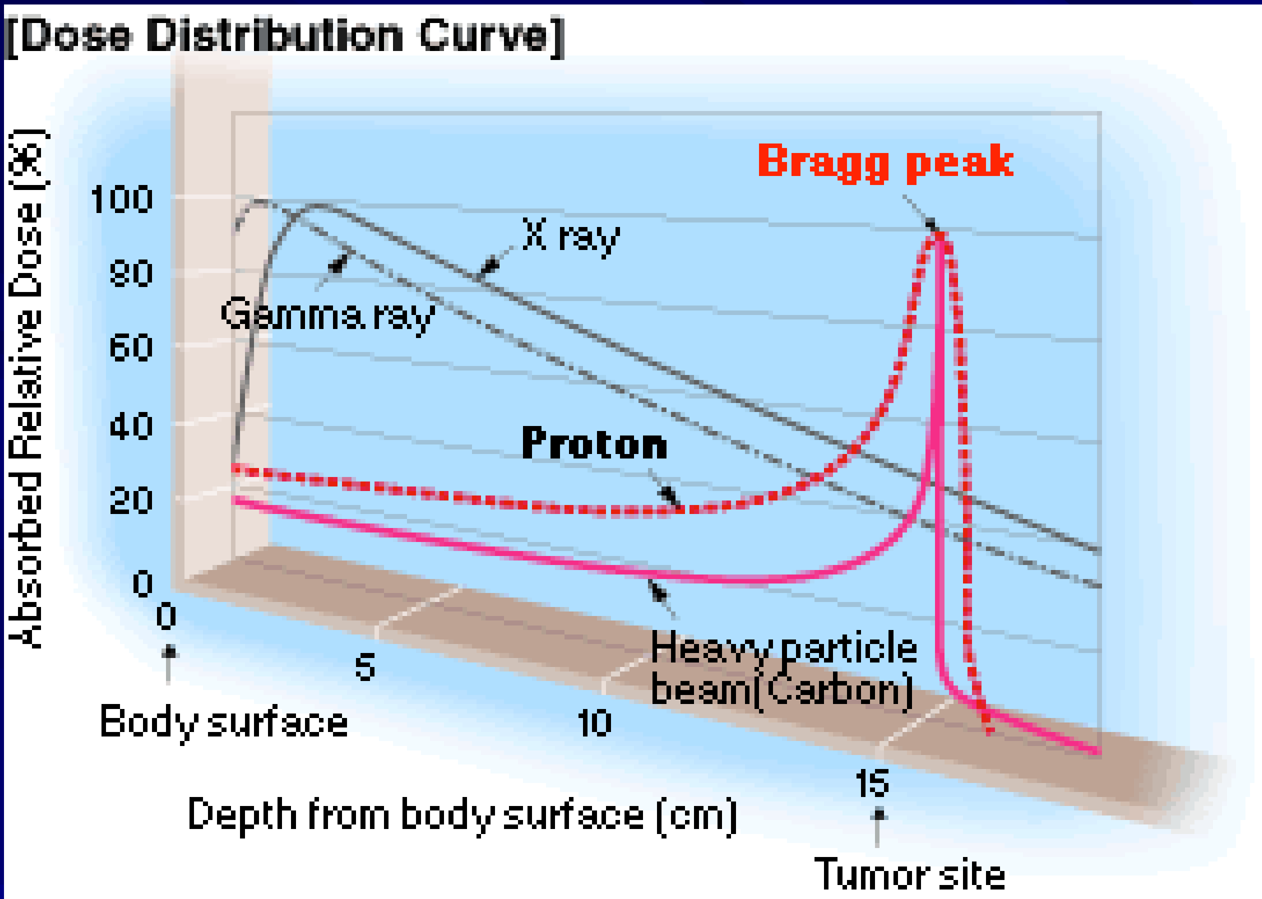
Tumor site	X-rays	IMXT	Protons
Oesoph. & stomach	0.15	0.11	0.00
Colon	0.15	0.07	0.00
Breast	0.00	0.00	0.00
Lung	0.07	0.07	0.01
Thyroid	0.18	0.06	0.00
Bone & soft tissue	0.03	0.02	0.01
Leukemia	0.07	0.05	0.03
All	0.75	0.43	0.05
Compared to X-rays	1	0.6	0.07

Hadrontherapy principle



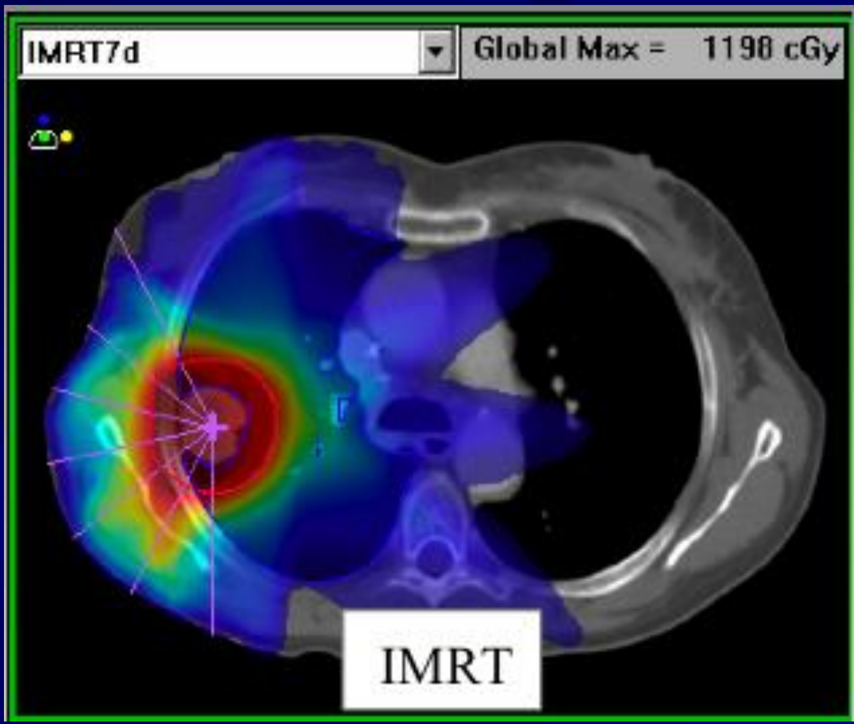
Electron : most of the energy released in first cm
Photon : Large energy loss all over the path (X rays therapy)
C ions : heavy charged particle : most of the energy lost at the end of path (Braggs peak)

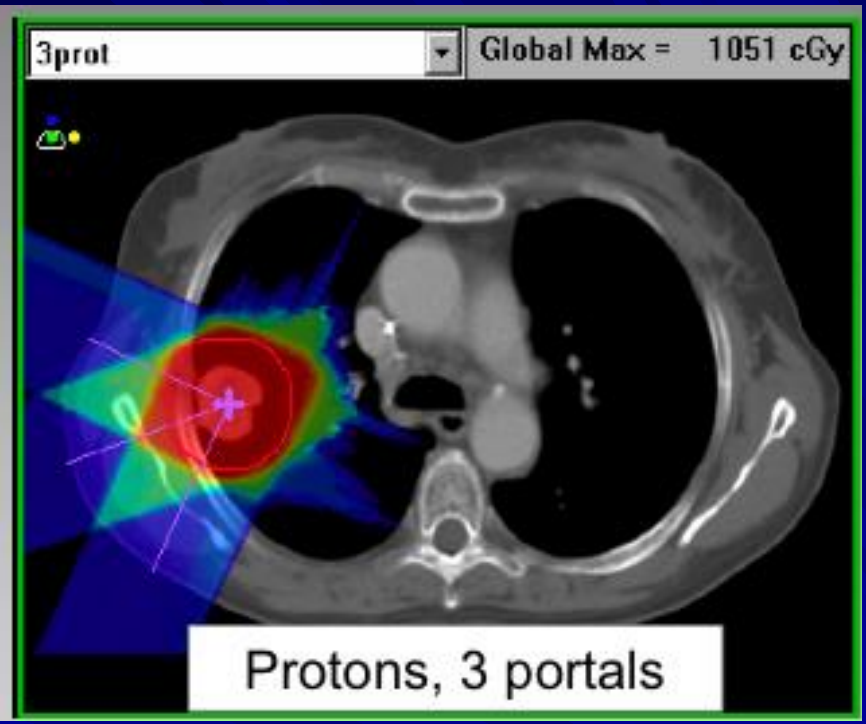
Why use Hadrons for Therapy?



- 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

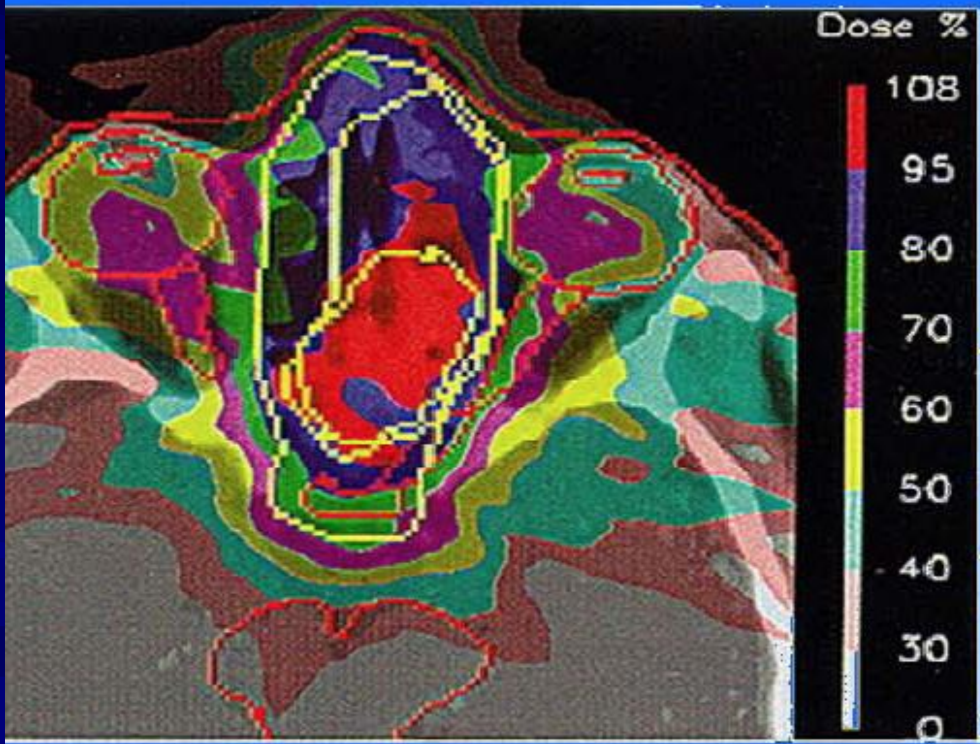
Comparison IMRT-Protons



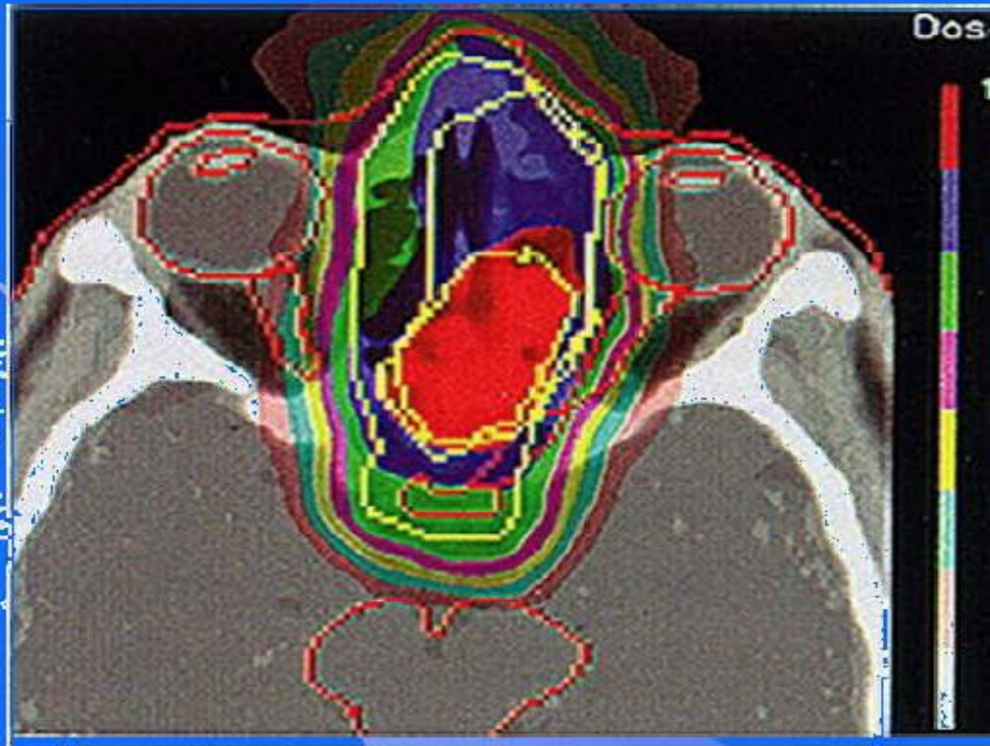


Tumour between the eyes

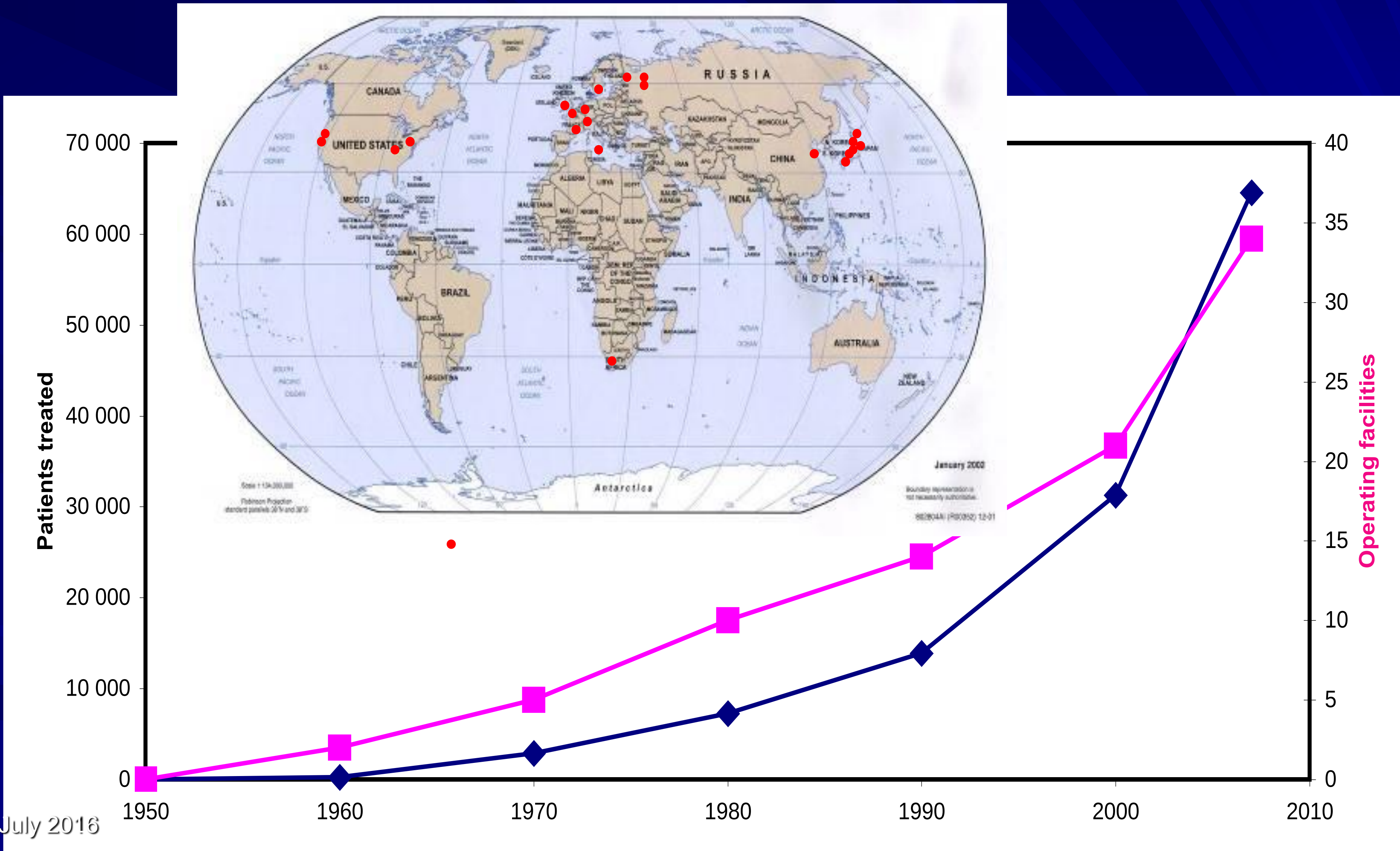
IMRT - 9 X –ray beams

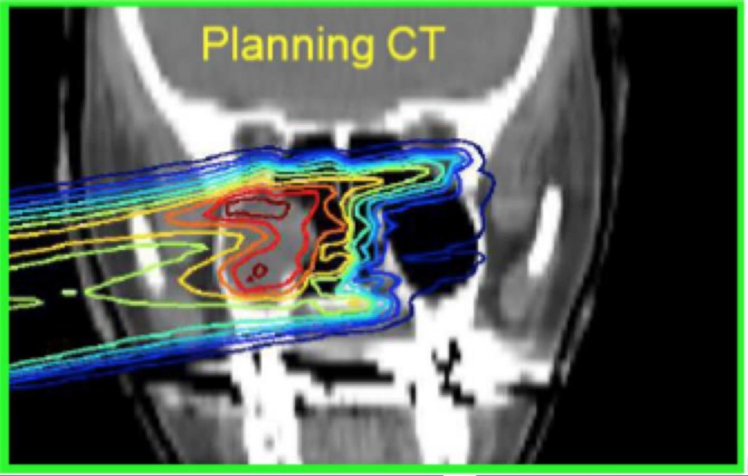


1 proton beam



Proton Therapy is growing rapidly!





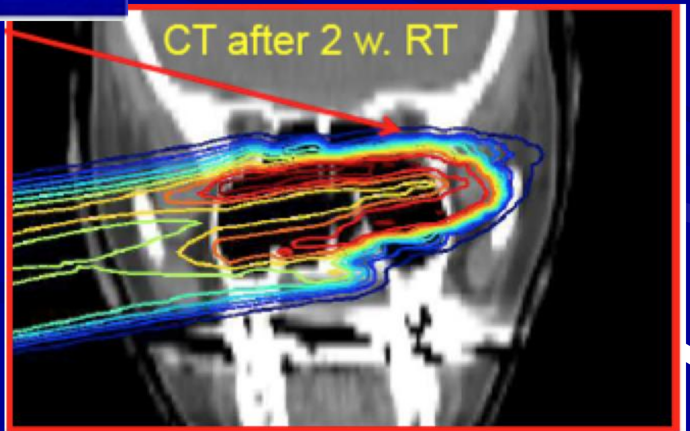
Particle therapy workflow

- 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)

Overdosage in normal tissue

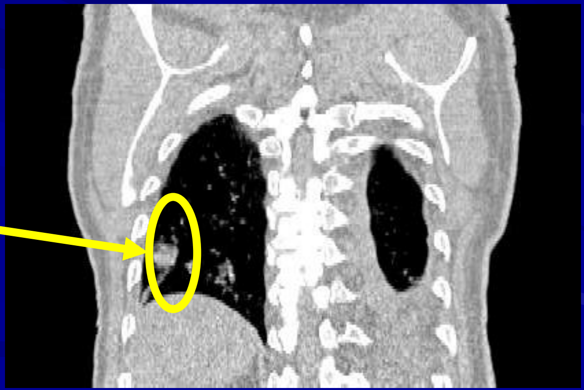
- *Step 3* → verification *using CT scan*



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

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



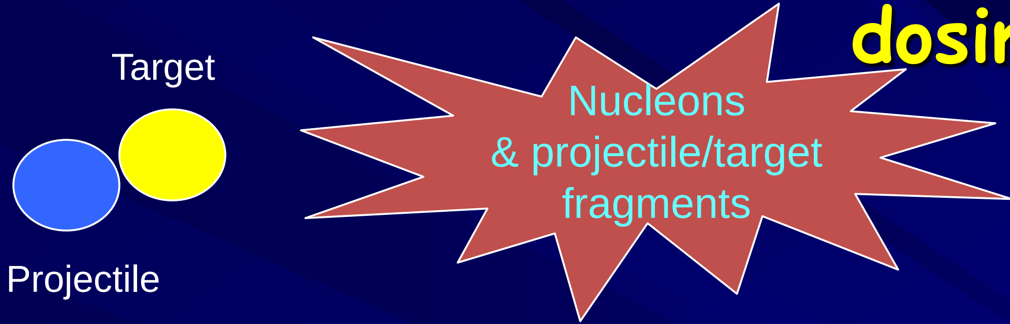
What is the dose deposited ?
How to verify the treatment?

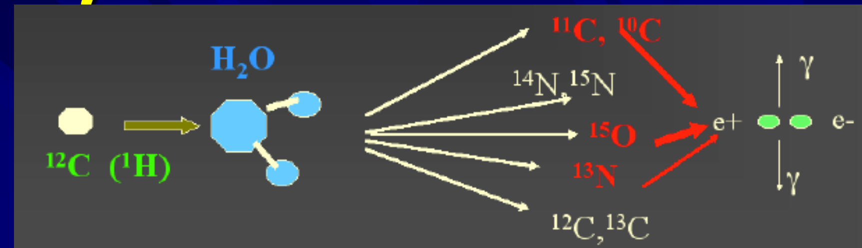
The two 'simultaneous' challenges

- 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

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





10^{-21} 10^{-18} 10^{-15} 10^{-12} 10^{-9} 10^{-6} 10^{-3} 10^{0} 10^{3} Time (s) after collision

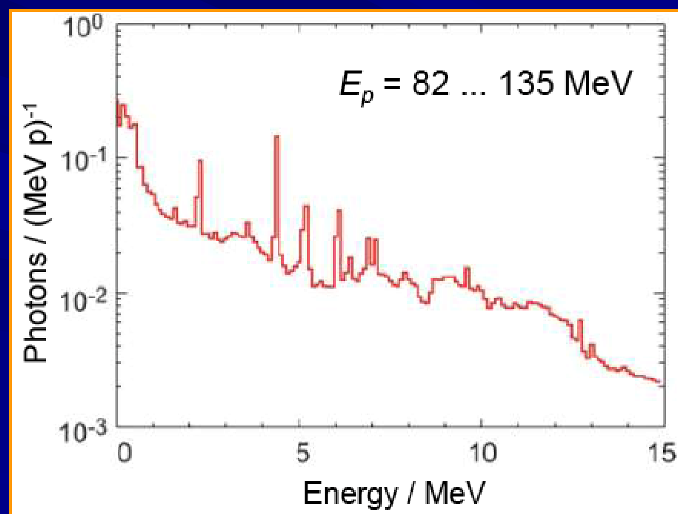
Particles

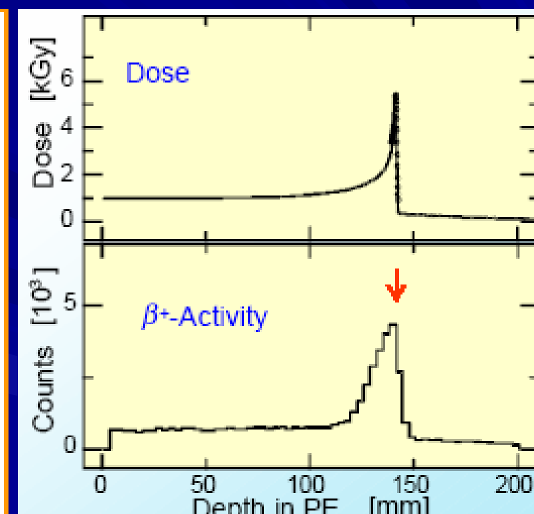
Prompt γ-rays

β^+ - emitter decay

Balance of promptly emitted particles outside the target:

Incident protons:	1.0	(~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:	$2 \cdot 10^{-5}$	($2 \cdot 10^{5}$)



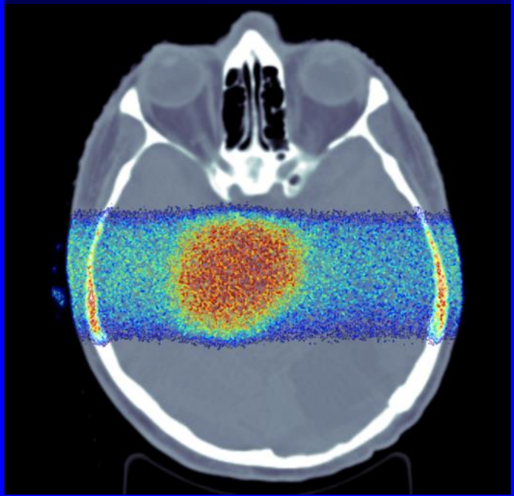


- *However the photon energy different from standard medical (Anger) SPECT camera*

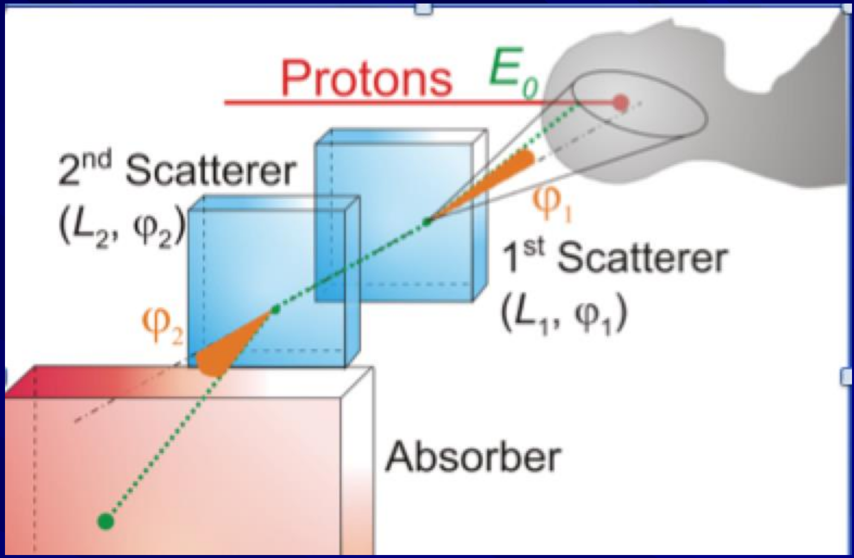
Relation between dose and β+ activities

Single photon: in vivo Compton Camera

γ-rays MC simulation

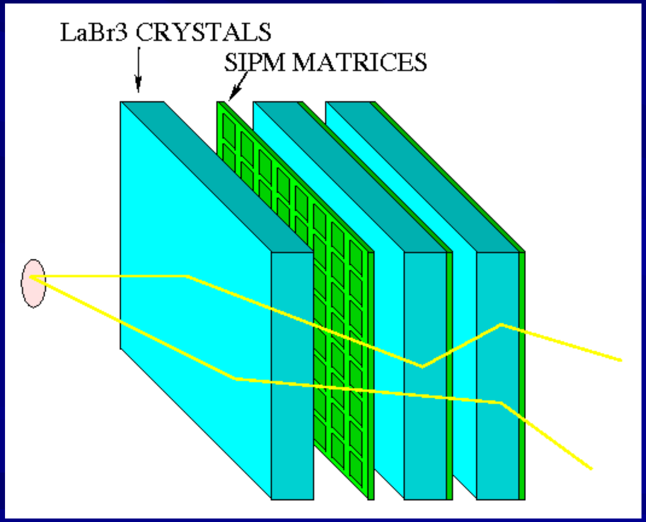


(A.Muller,TU Dresden)

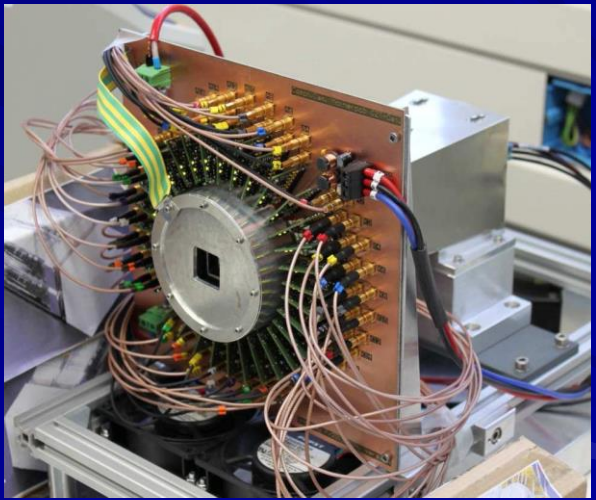


- Required devices:
  - Hodoscope (x,y,t)
  - Scatterer (x,y,E)
  - Absorber (x,y,z,E,t)

Scintillating-fibre Hodoscope + MA PMT Ray et al. IPN Lyon



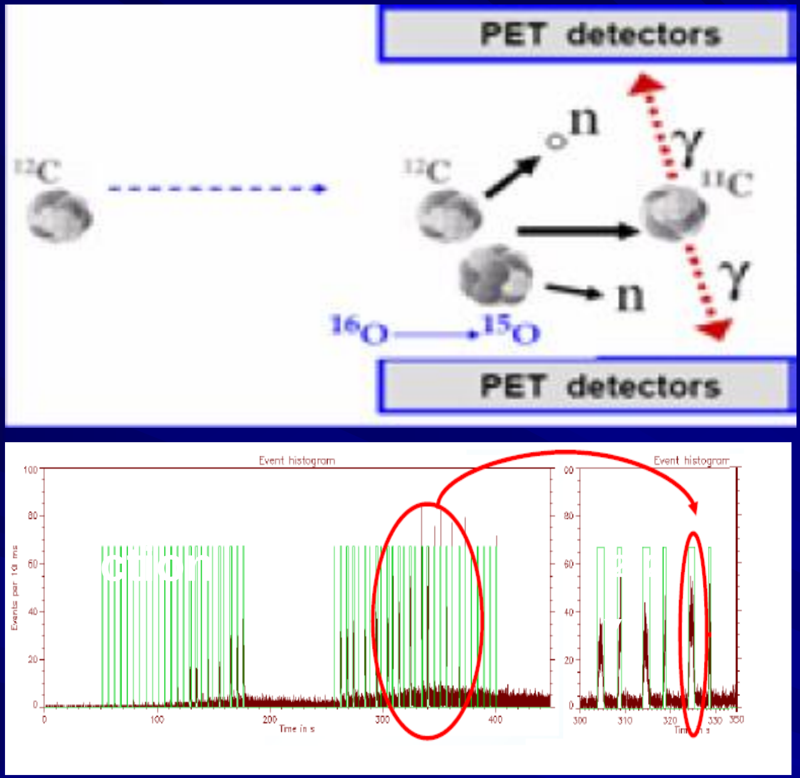
C.Llosa, IFIC

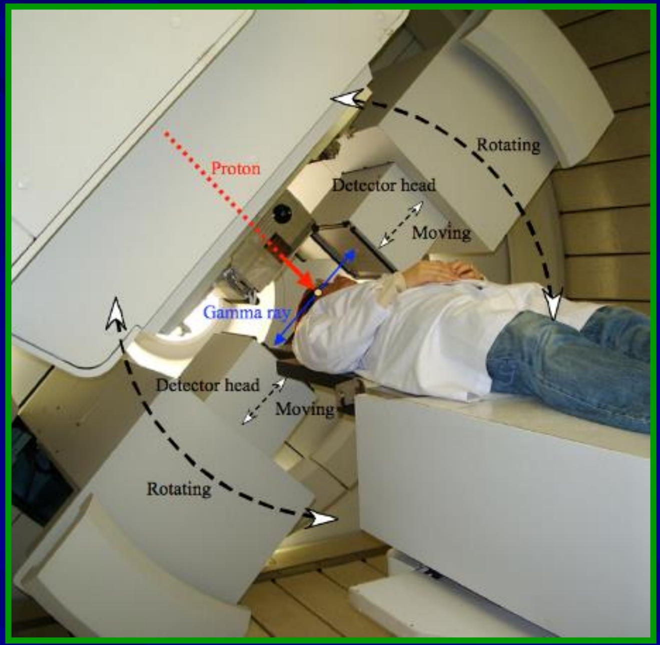


CZT-strip+LYSO-block Detector F.Fiedler et al. Dresden

Present examples: in beam PET

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



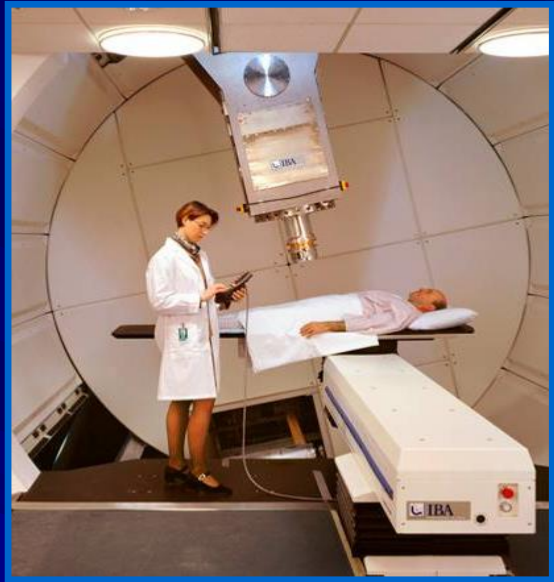


^{1}H-therapy at the National Cancer Center, Kashiwa, Japan

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

Positron Emission Tomograph …some Hardware

In-beam: GSI Darmstadt *Off-line: MGH Boston, HIT Heidelberg*



more…
- *HIMAC, Chiba*
- *NCC, Kashiwa*
- *HIBMC, Hyogo*
- *MDACC, Houston*
- *Univ. of Florida*

☺ *In-vivo range measurements*

☹ *In-vivo dosimetry & real-time image guidance*

- *Ongoing developments (TOF-PET, PET+CT)*
  reduce unfavorable in-beam random coincidences/background (by 20-30%)

Mature technology

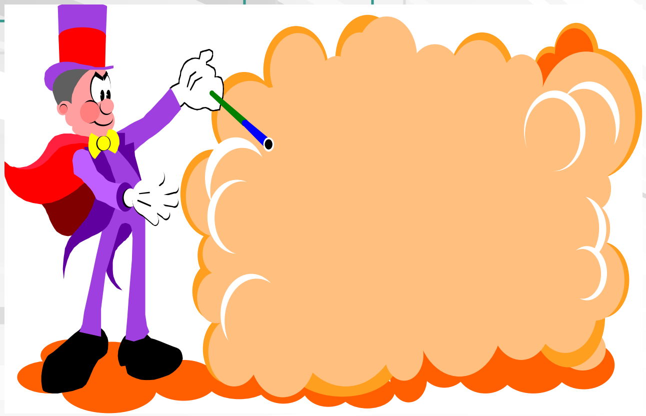
Courtesy W. Enghardt / OncoRay

Conclusion from a pioner
Prof. W. Enghardt Oncoray, Dresden

Particle thearapy units should be equipped with the most advanced imaging and motion tracking devices available

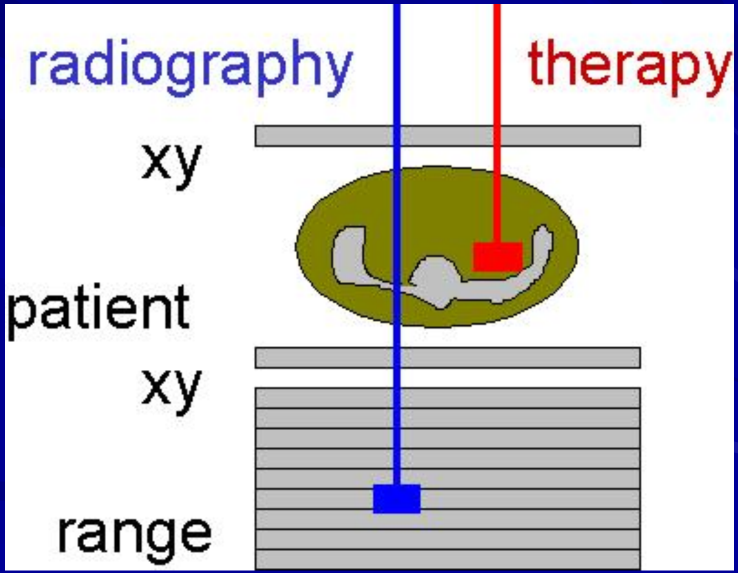
And Not with the ***technology*** of the last century

Another dream
The Proton CT



Why particle CT ?

- *The role of CT imaging in charged Particle therapy is needed for:*
  - *Target volume definition (anatomical boundaries with additional information from fused MRI and PET studies*
  - *Dose and range calculation*
  - *Patient alignment verification*



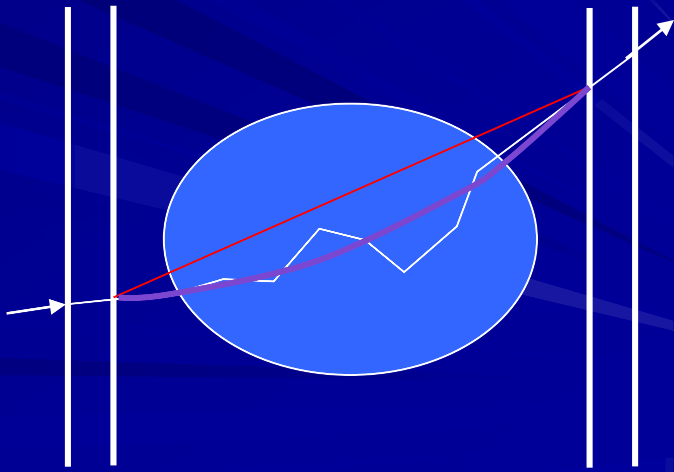
The protons go through the patient
Higher energy, small dose

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

X ray & CT after each fraction ?

- X ray is agressive --> see table below about estimated absolute rate of (%) of 2nd cancer
  - 30-50 mGy/scan
  - 30 fraction daily --> Total : 0,6 -3 Gy

Tumor site	X-rays	IMXT	Protons
Oesoph. & stomach	0.15	0.11	0.00
Colon	0.15	0.07	0.00
Breast	0.00	0.00	0.00
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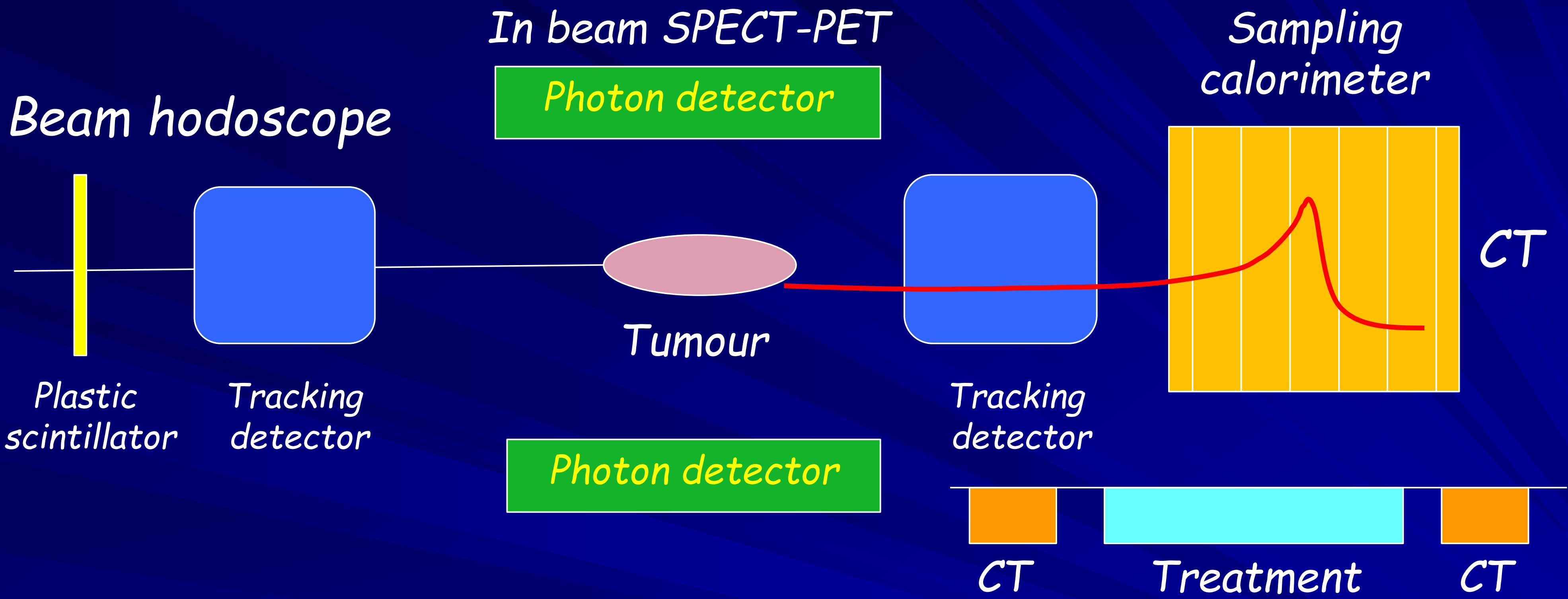
Bone & soft tissue	0.03	0.02	0.01
Leukemia	0.07	0.05	0.03
All	0.75	0.43	0.05
Compared to X-rays	1	0.6	0.07

The Basics Ingredients

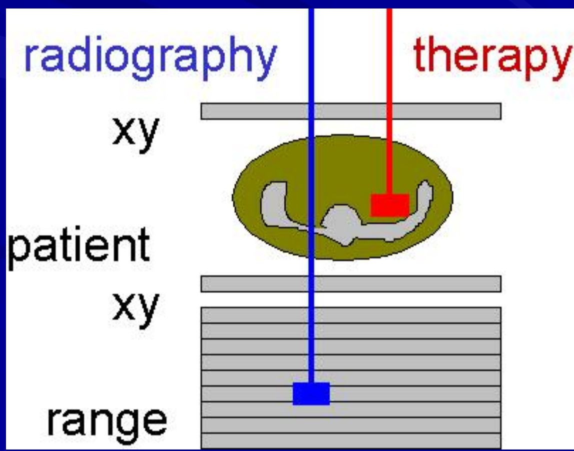
- Beam
  - Measurement (position and direction) particle per particle
- Photon detectors
  - In beam selection of
    - single photon → compton camera (SPECT)
    - two photons → in Beam TOF-PET
- Proton (ion) CT
  - Measure the energy (position, energy and time) of the diffracted particle in an imaging calorimeter
- The Global aspect!
  - Event by event selection particle like in a nuclear & HEP physics experiment.
  - Deatimeless electronics
  - Real time acquisition and reconstruction

Need all HEP modern instrumentation tools & technique

Schematic block diagram of an integrated concept of radiography / therapy system



- *Identify tracks and energy deposition of individual protons*
- *Scintillators for trigger to read-out detectors*
- *Tracking detectors for 3D tracks*
- *Sampling Calorimeter for energy determination*
- *High rate integrated DAQ*



Present examples : PCT

- Different prototypes are proposed based on the same "philosophy" (Reinhard Schulte et Al.)
  - BNL, Santa Cruz, Loma Linda, Stony Brook layout (2003)

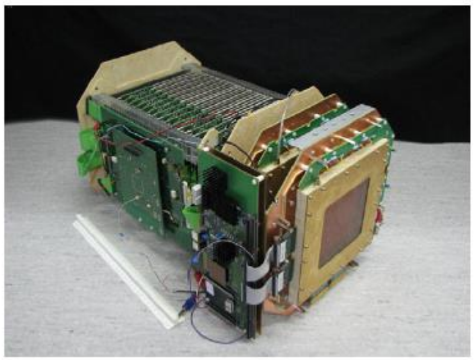
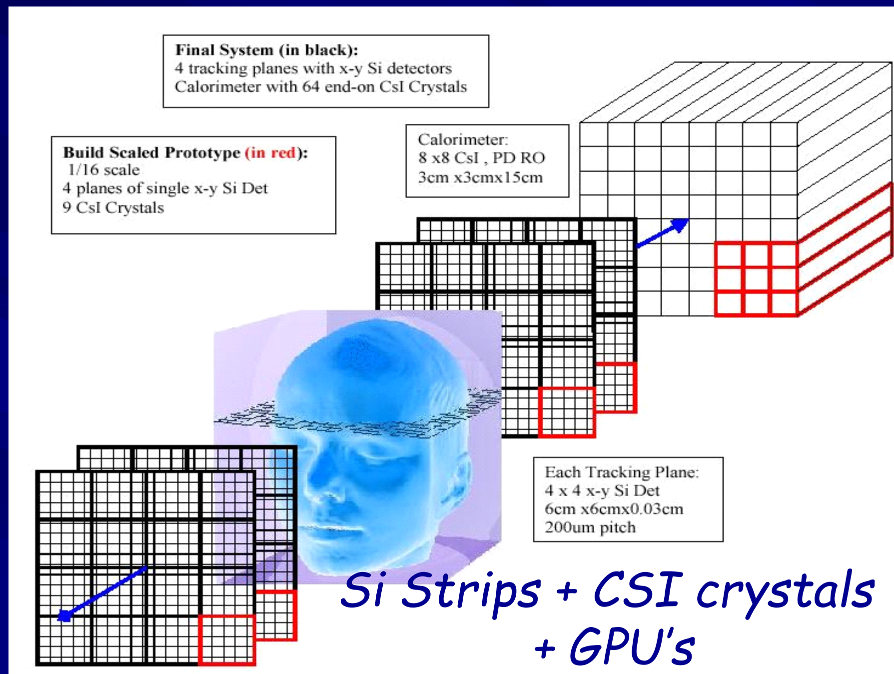
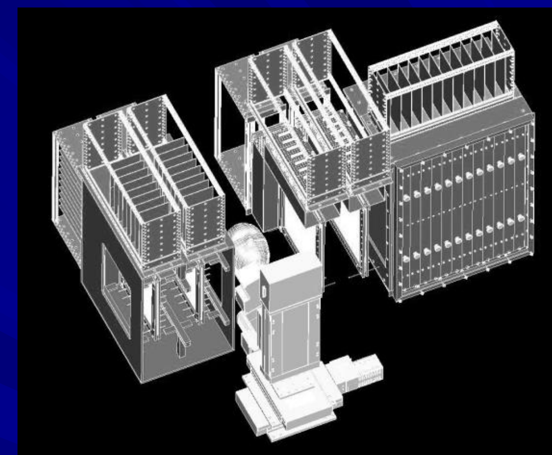


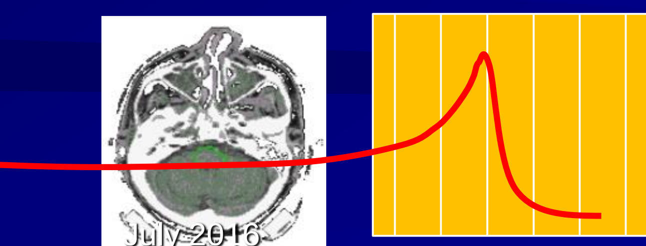
Fig. 1. The Proton Range Radiography setup.

AQUA-CNAO
Scint/MPPC/GEM



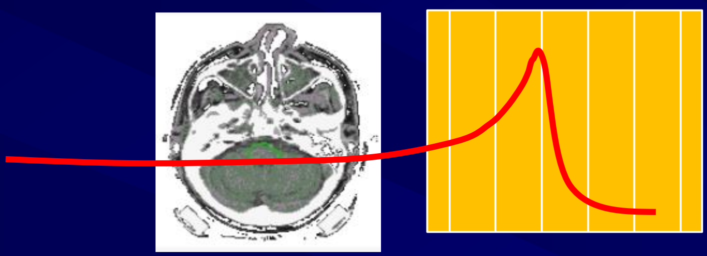


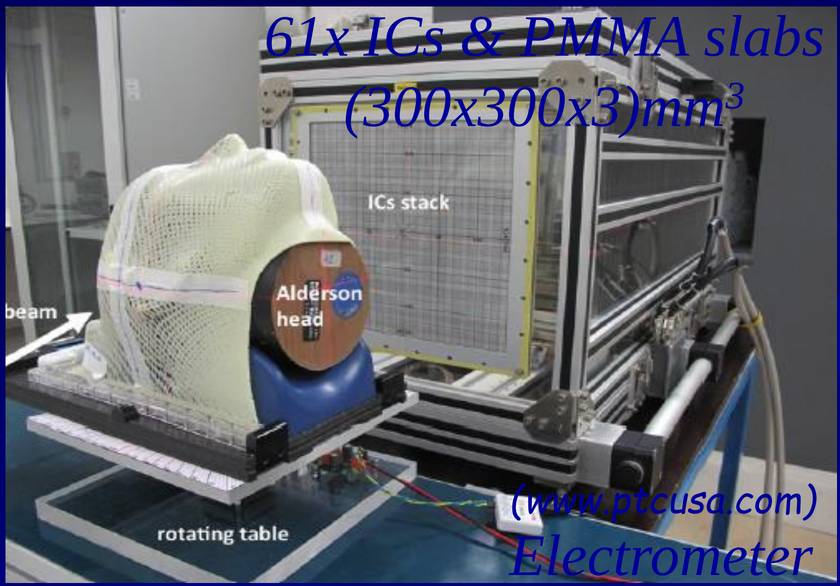
NIU/FNAL
Scint/WLS+SiPM
GPU farm

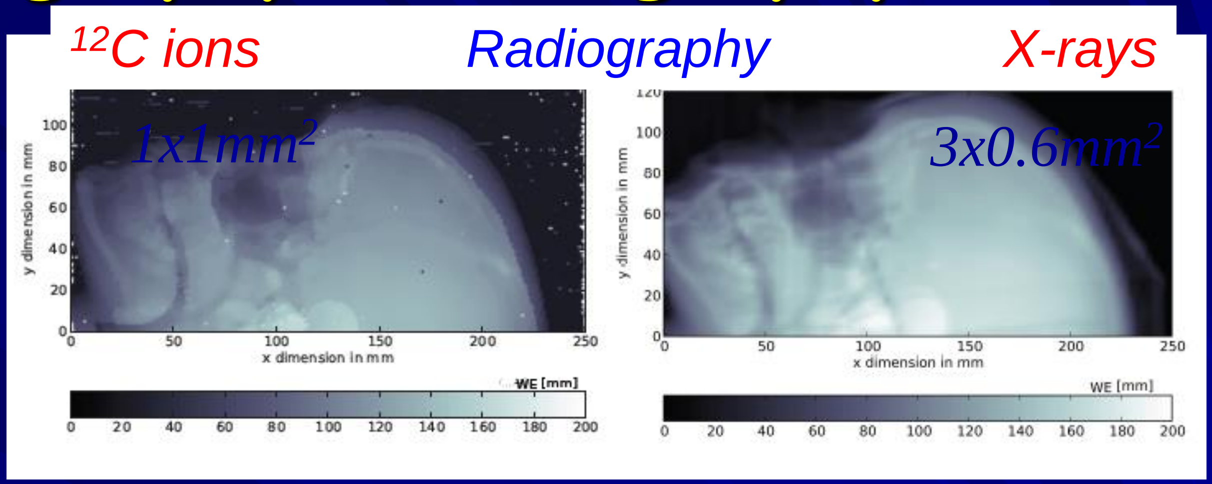


- *Ion Transmission Imaging*
  → See talk from B.Voss

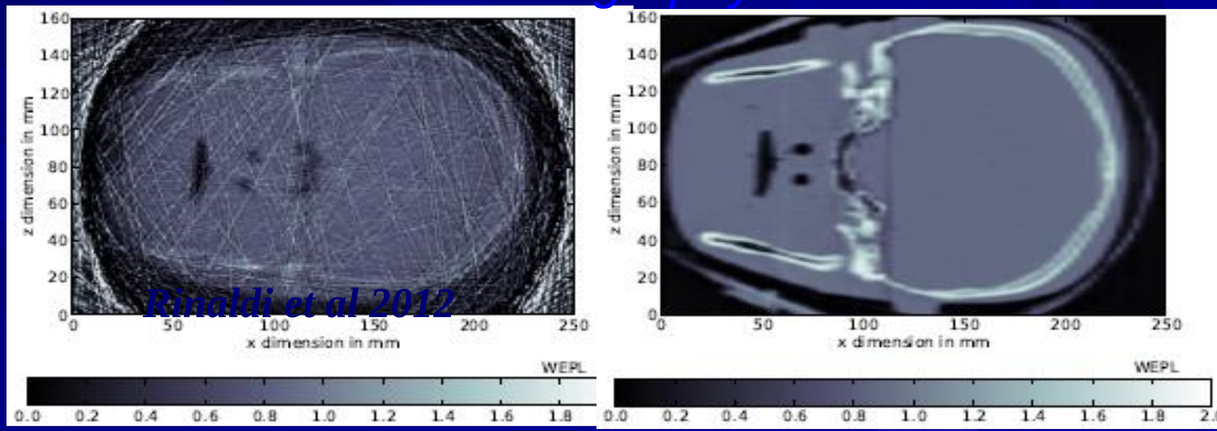
Primary-Ion Radiography / Tomography







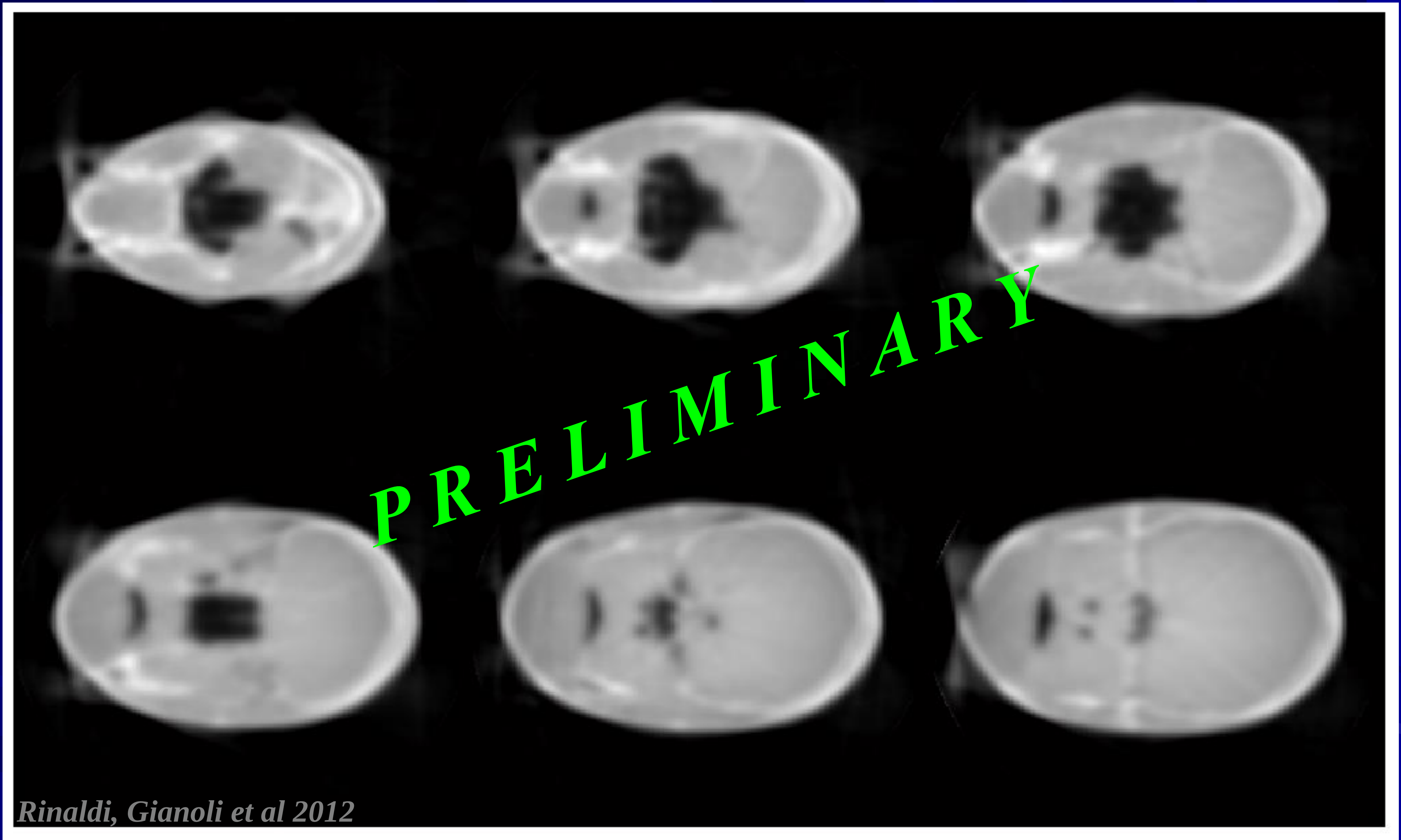
Water equivalent thickness



Water equivalent path length

Transmission ion imaging prior to or in-between RT is feasible

^{12}C Ion Tomography



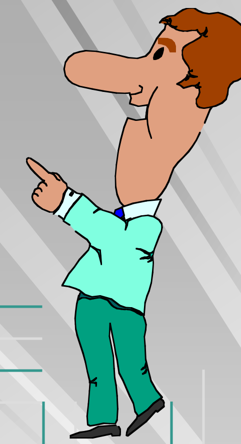
Summary & Conclusions (1)

- HEP has considerable acquired knowledge, expertise and resources that can, when transferred properly, significantly impact the practice of medical imaging and therapy
- A lot of exciting ideas and developments!
  - Should attrack young 'experimentalists'
- Activity that need to be 'promoted' actively outside our community for the benefit of us…in these hard time !
  - HEP is not only hunting the Higgs !

Summary & Conclusions (2)

- It take sometime between the discovery and initial ideas.
- But when the technology is mature, it can make a gigantic breakthrough in the development of a technical device or system
- Collaboration between various scientists and expert is fundamental and the key factor for success.
- Building a community (network) about a specific subjects is the way to integrate students and experts

Final Conclusions



There is a lot to do
Particularly
for students

References
Proceedings
of NSS-MIC
conferences
Transaction on Nuclear Sciences (TNS)
http://www.nss-mic.org/2015/NSSMain.asp

Thanks to

- D.Townsend (U. Singuapor)
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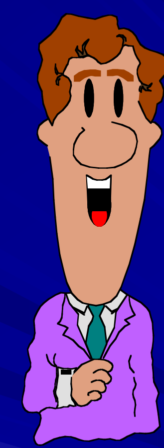
- Pr. J.P. Gerard (Nice)
- … and many others



Thank you
for your attention