Medical Applications at CERN

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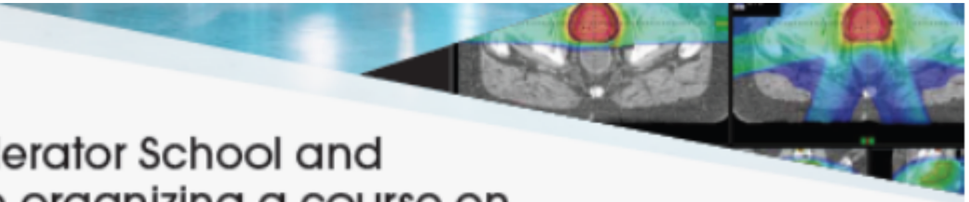
Geneva, Switzerland

20th November 2014



The CERN Accelerator School and MedAustron are organizing a course on

Accelerators for Medical Applications

26 May - 5 June, 2015

Eventhotel Pyramide, Vösendorf, Austria

This course will mainly be of interest to staff in accelerator laboratories, university departments, particle therapy centres and companies manufacturing therapy systems and associated accelerator equipment.

Following introductory lectures on radiobiological and oncological issues, the basic requirements on accelerators and beam delivery will be reviewed. The medical applications of linear accelerators, cyclotrons and synchrotrons will then be treated in some detail, followed by lectures on the production and use of radioisotopes and a look at some of the acceleration techniques for the future.

A full day visit to the MedAustron centre in Wiener Neustadt will provide a practical insight into the field. Participants will also have the opportunity to work on realistic case studies as an integral part of the program.

Contact: CERN Accelerator School
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cern.ch/schools/CAS

MedAustron

Innovation
Education
CERN
uniting people
Research

CERN: Particle Physics and Innovation

- Interfacing between fundamental science and key technological developments

- CERN Technologies and Innovation

Accelerating particle beams

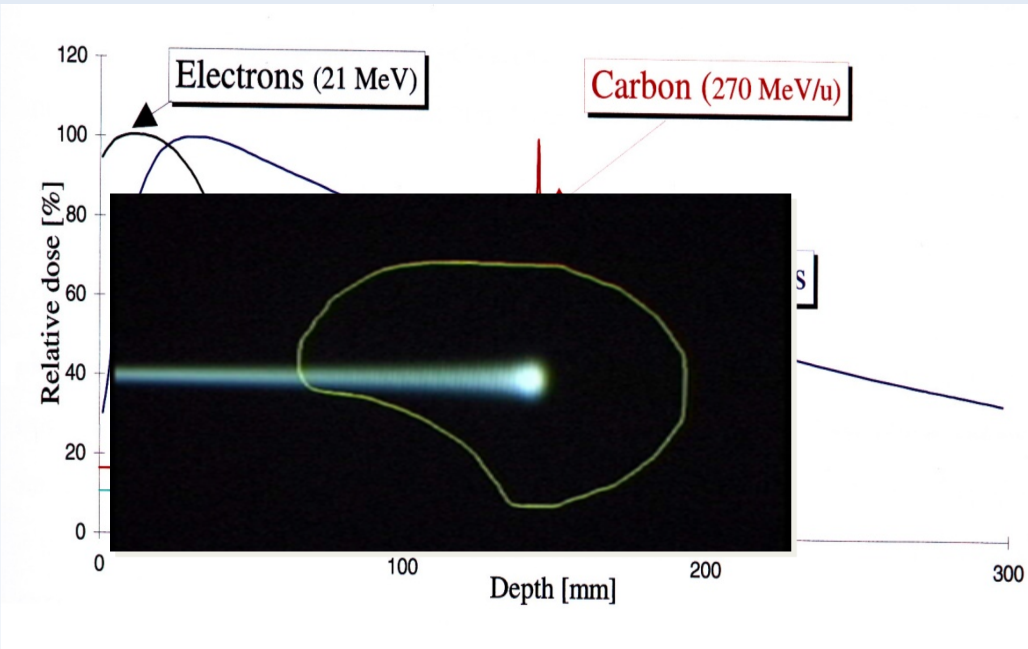
Detecting particles

Large-scale computing (Grid)

CERN

What Everyone Knows

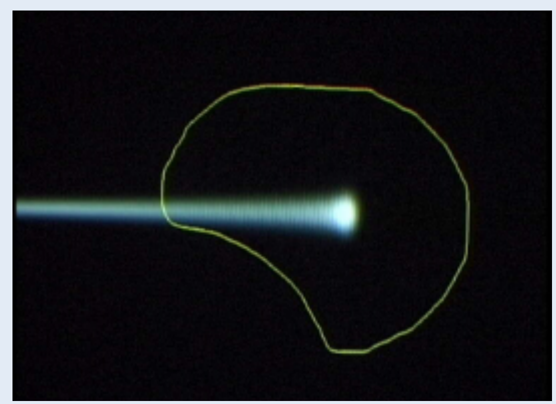
Hadrontherapy vs. radiotherapy



The BRAGG Peak

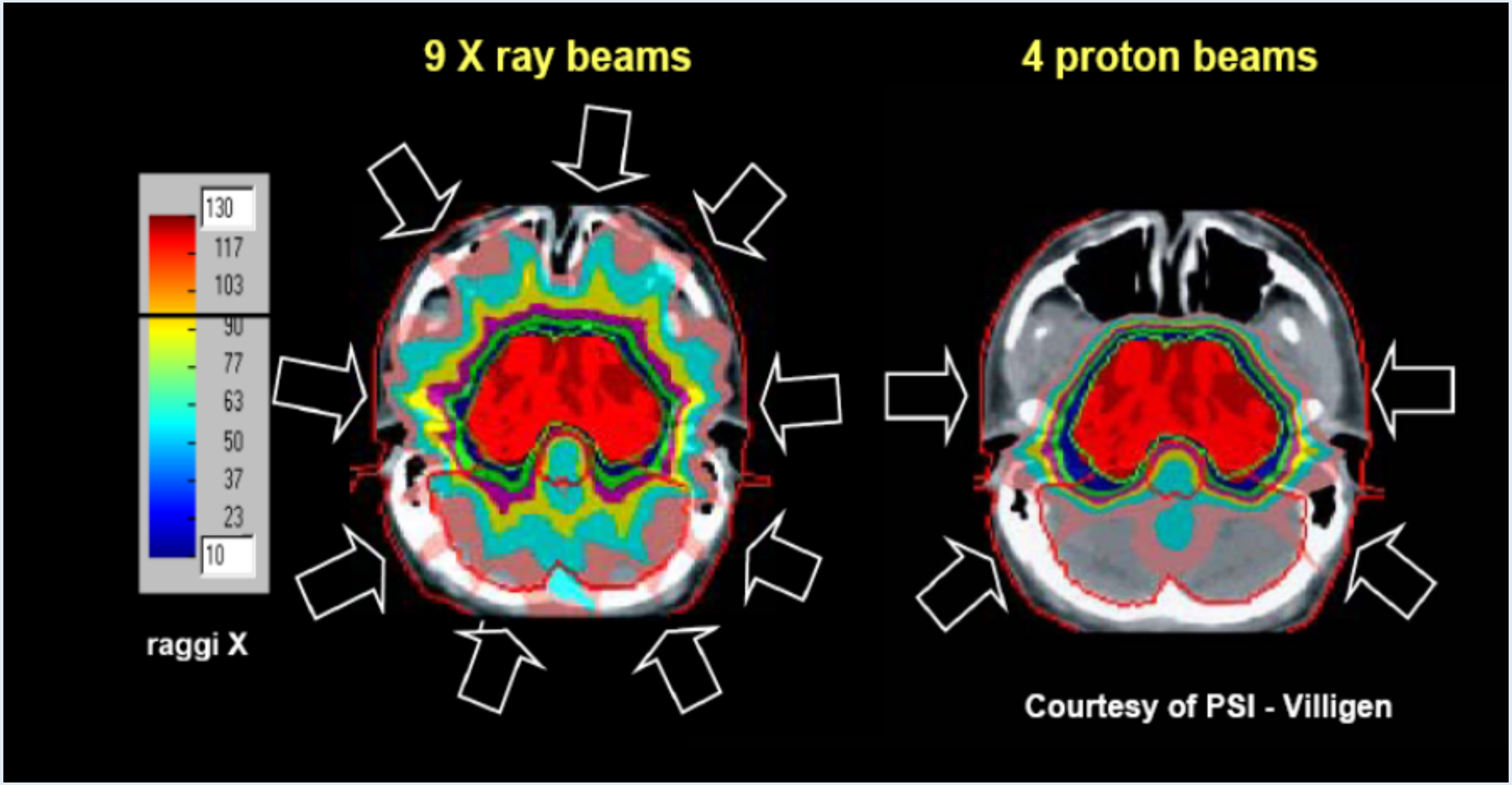
- Tumours close to critical organs
- **Tumours in children**
- Radio-resistant tumours

The physics properties of light ions (Bragg) may make them much more efficient in treating some kinds of tumours



Energy deposition

Comparison of Collateral Damage

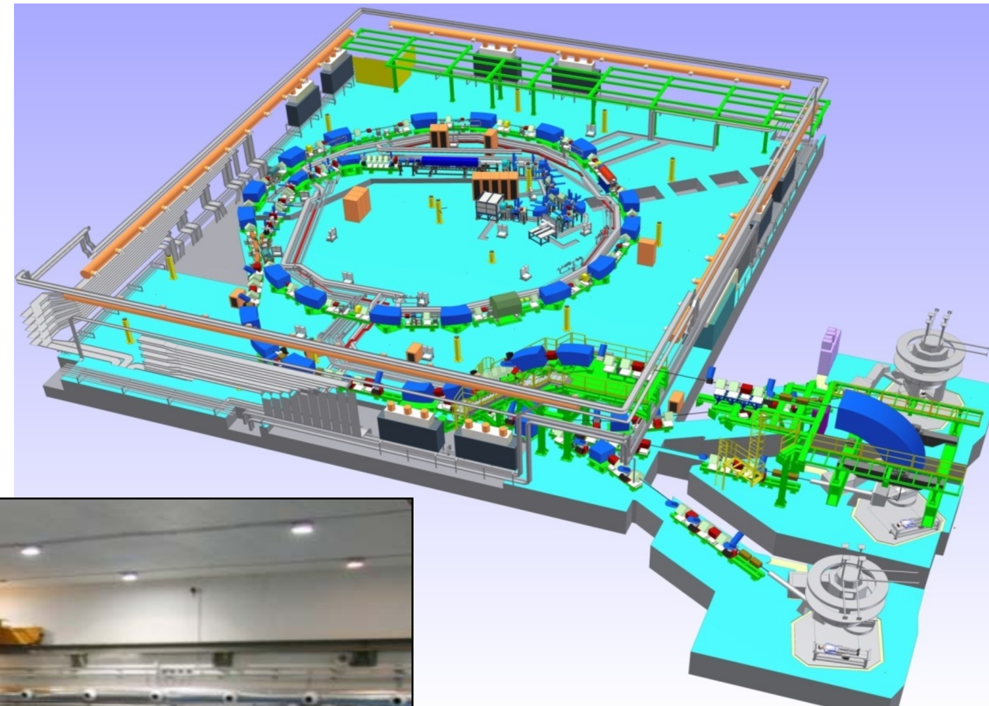


History and Reminders

Initiative: Accelerator reminder PIMMS

"In 1996, CERN initiated the Proton Ion Medical Machine Study (PIMMS), which aimed at designing a synchrotron optimized for the treatment of moving organs with carbon ions (and protons). Together with CERN part-time staff, the study participants were the TERA Foundation (Italy), the MedAustron project (Austria) and Oncology 2000 (Czech Republic). The design was summarized in two reports issued in 2000. The project was adapted by TERA and used as a basis for the CNAO centre, which has just been completed in Pavia by the CNAO Foundation and INFN. The MedAustron facility utilises the same synchrotron design, and is currently being built in Wiener Neustadt (Austria)."

CNAO (Pavia) is treating patients



CNAO in Pavia

MedAustron is building a centre in Wiener Neustadt

MedAustron Status – Wiener Neustadt

PIMMS1 design has been a big service to the community

- **2 source branches installed**
- **Beam commissioning**

- **Synchrotron hall installation**

What has happened since 2000 on the technology side?

- LHC accelerator technology development
  - Operation of 8T magnets
  - Testing of 11T magnets for Luminosity upgrade
  - Development of 18-20T magnets for energy upgrade

MRI

- LHC Detectors developments
  - Crystal scintillators improvements
  - Medipix proliferation and enhancements
  - Developments of new vertex detectors for LHC luminosity upgrade
  - Development of TOF resolution for Luminosity Upgrade

Medical Imaging and Diagnostics

- CLIC
  - Accelerating structure frequency reduced from 30GHz to 12GHz
  - Development of room temperature structures for 100MV/m gradient
  - Proposals for structures of 3 and 5.7 GHz with 30 and 50 MV/m for medical applications

Compact Accelerators Protons and Light Ions

- LHC Grid
  - Demonstration of the efficiency and reliability
  - Rapid adoption to new domains; Medicine

Large scale data storage, transfer and analysis

- Developments of medical simulations with FLUKA/GEANT

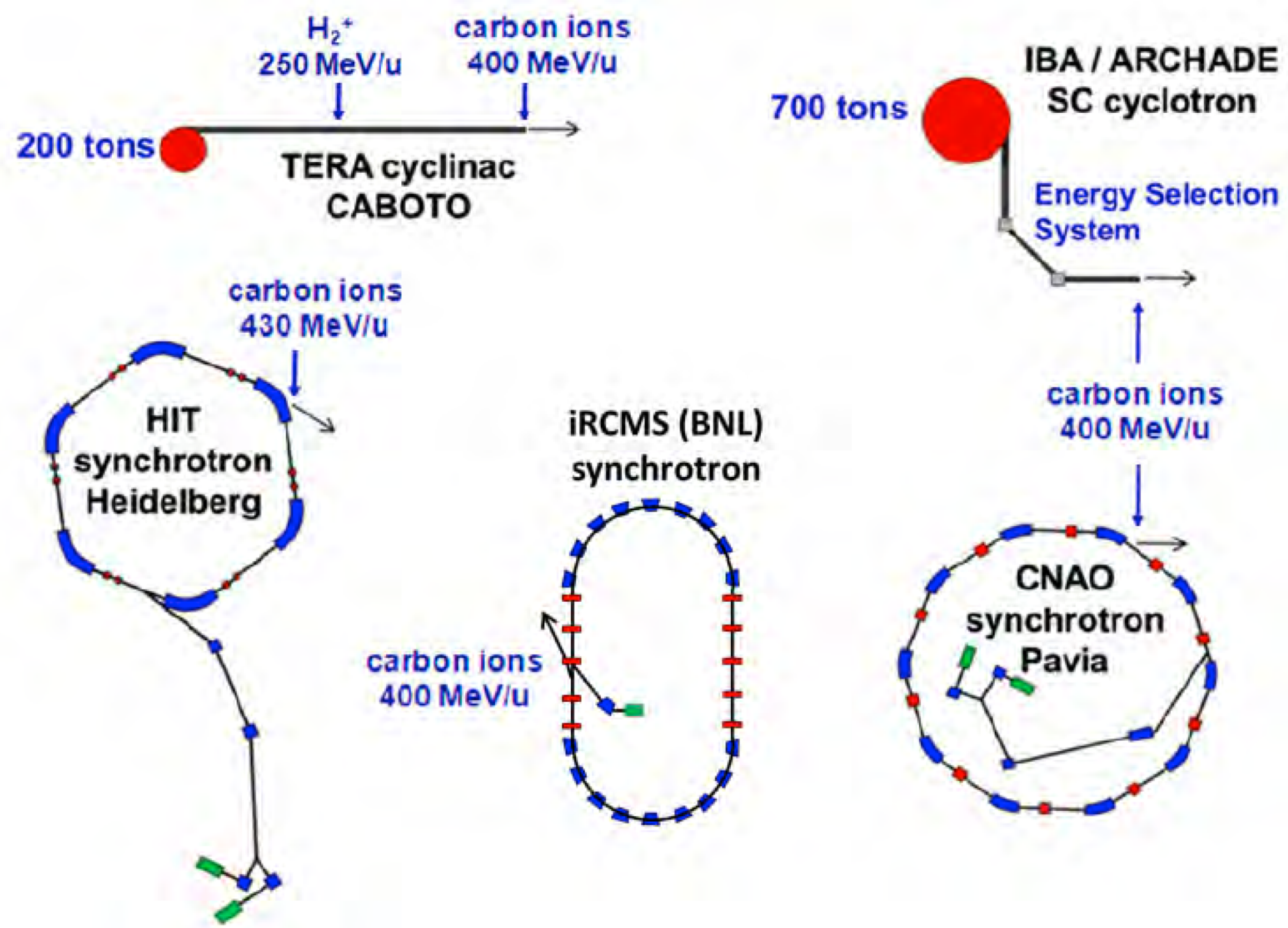
Treatment planning, medical research

Animation of Hadron Cancer Therapy

What should an ideal facility do?

- ❑ Treat the tumour and only the tumour
  - ⇒ monitor and control, the ideal dose to the tumour
  - ⇒ Minimal collateral radiation "outside" the tumour
  - ⇒ Minimal radiation to nearby critical organs
  - ▪ Even if the tumour is moving
- ❑ Be affordable
  - ✓ Capital cost ?
  - ✓ Operating costs ?
  - ✓ Increased number of treated patients per year ?
- ❑ Compact: Fit into a Teaching Hospital ?

Dimensional comparison for carbon ion accelerators



Courtesy U. Amaldi/A.Degiovanni

Cost Questions (user Specs)

- ***Compactness***
  - Specification of “maximum” dimensions…MA
  - Balance of importance of compactness vs cost..MA
- ***Cost Effectiveness .. The Over-riding Parameter***
  - What is a reasonable cost parameter (e.g. relative cost per patient compared with conventional therapy? Survival parameter?)..MA
  - Reduction of capital cost… Acc + MA
    - Number of treatment rooms + number and specs of gantries
  - Reduction of running and operational costs (experts…)..Acc + MA
    - Number of treatment rooms + gantries
  - number of patients treated per year…MA +Acc

Technical/Medical Questions (user Specs)

- ***Beam Specs*** ***(needs R&D)***
  - Type of Light Ion (protons to Carbon or multiple ion capability)…M
  - Central beam energy and energy range (?multiple energies for different functions)….M
  - Beam size (h+v) (emittance)…..M
  - Energy spread of beam….M

- ***Beam Distribution (gantry)***
  - Required angular coverage…..M
  - Allowed rate of change of beam energy…Acc + M
  - Degree of allowed movement of patient…..M

- ***Diagnostics and Imaging*** ***(needs Test bed and simulations)***
  - Dose: requirements and precision deposition….M
  - Beam control devices…..Acc
  - Requirements for imaging (update rate, precision, resolution)… M

Technical/Medical Questions (user Specs)

❑ *Spot Scanning (Needs R&D)*

- Comparison of specs for spot scanning (fast with low dose per shot or large dose per shot)…M
- Optimum spot scanning parameters, rate, dose, etc..M
- Control of dose per deposition….M

❑ *Type of Accelerator …Acc*

- Synchrotron (normal or rapid cycling)
- Linac
- Cyclotron
- Or a combination of the above (SC, Cyclo-Linac, etc)

The agreed specs will influence decision on type of accelerators and design of gantries

Dealing with Organ Movement

- Time gating: apply dose when the organ is in the correct position. E.g. respiration cycle
- Fast rescanning: very rapid multiple painting. Statistically distribute the dose
- **Tumour tracking: diagnostics and imaging**

All methods need high scanning speeds

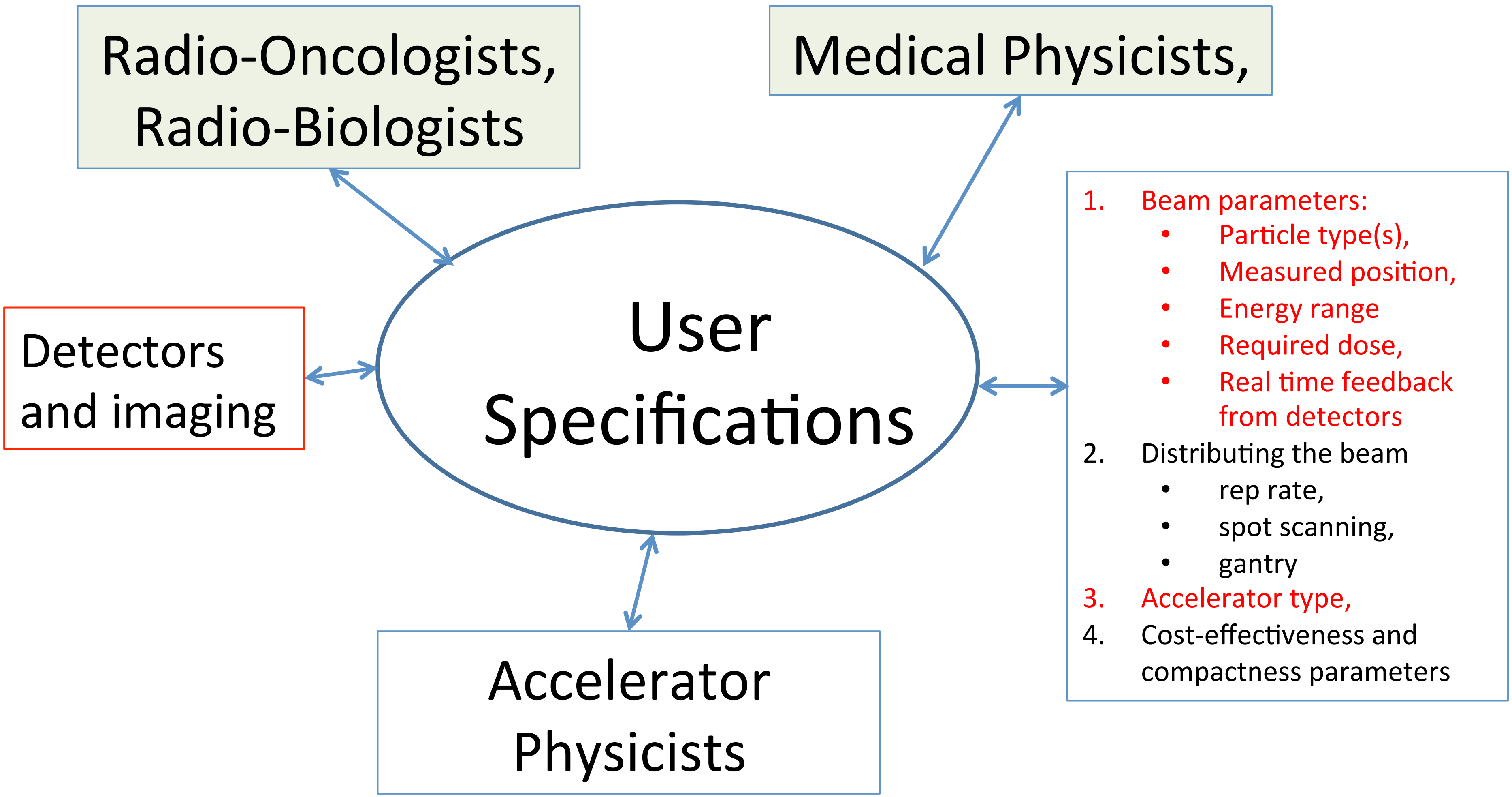
The New CERN Initi… s

Each Initiative is part of a package but also is important as a stand-alone project

1. Medical Accelerator Design
   - coordinate an international collabora… new compact, cost-effective accelerator facility, using … ced technologies
2. Biomedical Facility
   - creation of a facility at CE… particle beams of different types and energies to extern… biology and detector development
   - Iterative experimen… r simulation results
3. Detectors fo… trol and medical imaging
4. Diagnost… metry (pot) for control of radiation
5. Radi… (imaging and possibly treatment)
6. L… omputing and data (simulations, treatment … elemedicine etc)

… ations other than cancer therapy

User Specs for Hadron Therapy



- Many of these questions can only be answered with
  - experimental verifications
  - significant simulations
  - Development of diagnostics (imaging, dosimetry)
- $\Rightarrow$ We need a dedicated test facility

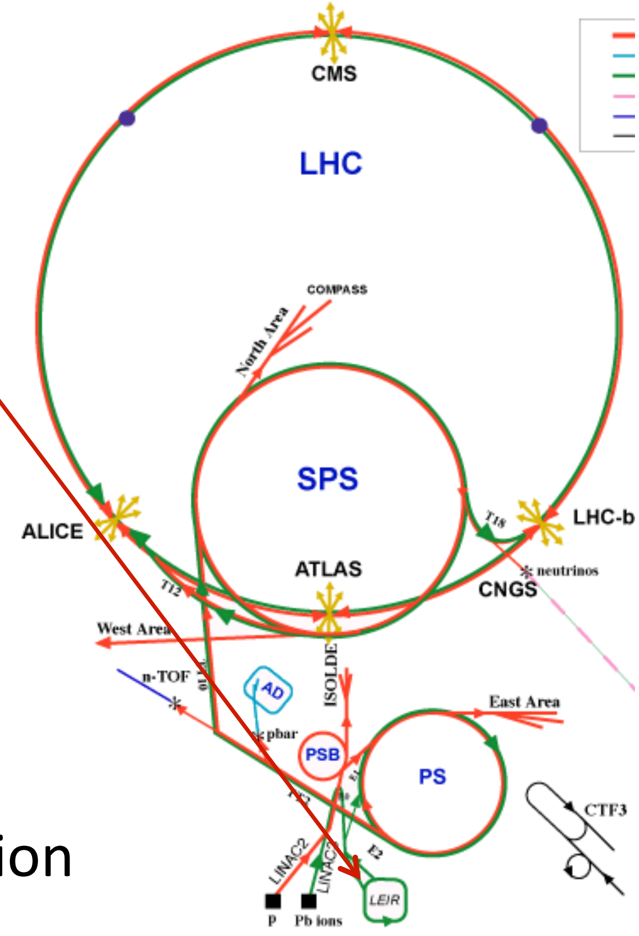
We have many accelerators at CERN

But, one is a perfect test-bed, LEIR

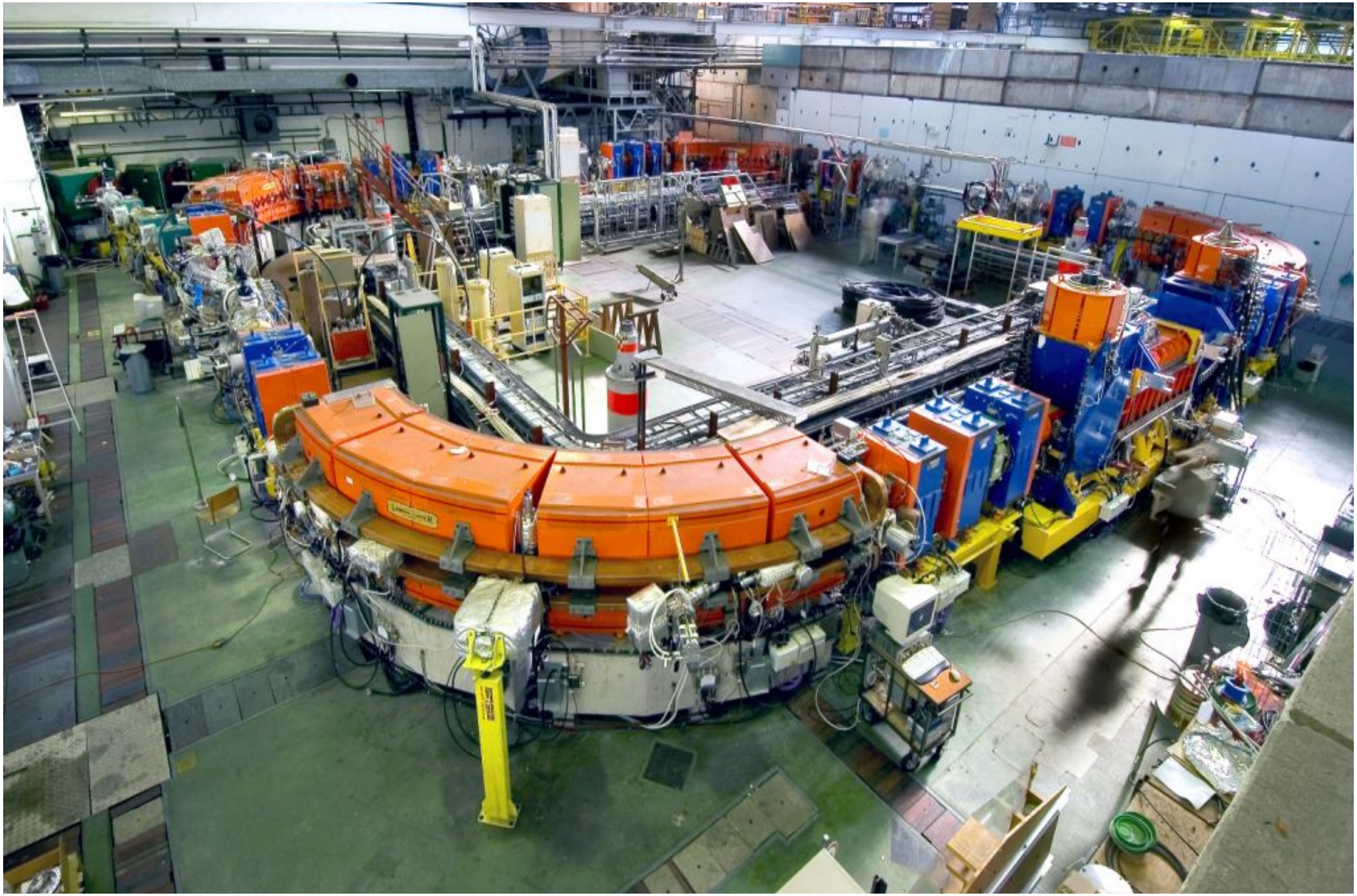
LEIR (Low Energy Ion Ring)

- part of LHC injection chain
- accumulator for LHC ion programme (lead ions)
  - only used for several weeks / year

- Plan to **establish facility** for
  - Test-bed for medical instrumentation
  - Diagnostics and dosimetry
  - **radiobiology**
  - basic physics studies such as fragmentation of ion beams



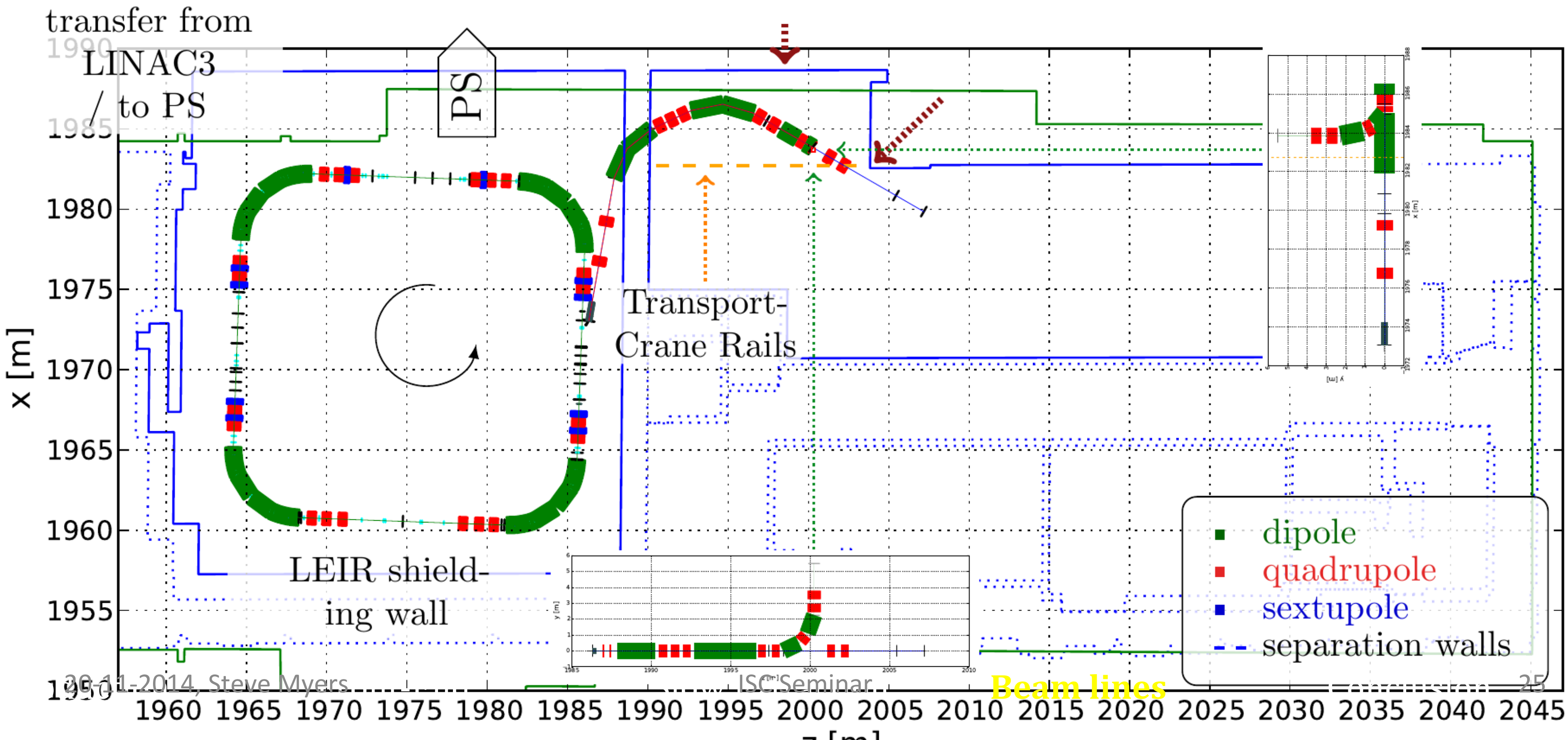
Biomedical Research Facility at LEIR



Adriano Garonna

Two experimental beamlines are foreseen

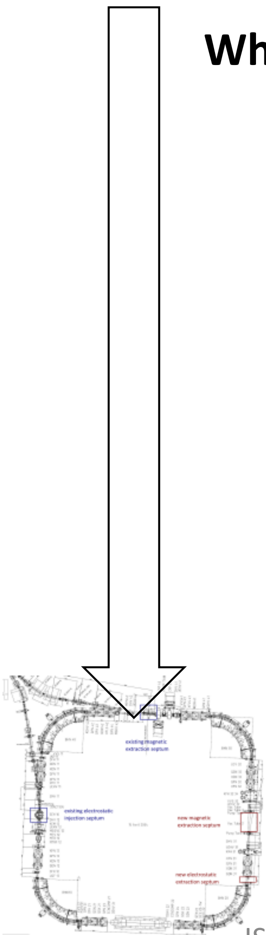
- Horizontal beamline up to maximum energy
- and Vertical beamline up to 2.6 Tm (75 MeV/u C)
- Pencil beam 5-10 mm FWHM and broad beam 5x5 cm^2 considered
- 4 bending magnets (max 1.6 T, ± 40 mm gap) and 12 quadrupoles (max 23 T/m, max 40 mm radius) in total



Radiobiological Facility @ CERN

Ions	Priority Rating /5	Why
Protons	5	Clinical
(molecular ion) H_2	2	Correlated particle experiments Experiments -Spatial distribution Variation in response
Helium $_2^3$	5	Possibly clinical
Helium $_2^4$	4	Stable and possibly clinically relevant
D	4 (if clean), 0 (if not)	Radiobiologically interesting, not clinically useful
Li $^6_3$	4	RBE greater than P Fragmentation tail shorter, less dose deposited past the distal edge
B $_5^{10}$	2	Potentially clinical Fragmentations more than Li, better than C
C $_6^{12}$	5	Clinical
N $_7^{14}$	3	Radiobiological Studies
O $_8^{16}$	4	Possibly clinically relevant Radiobiological Studies
Ne $_{10}^{20}$	3-4	Comparison to present radiobiological studies
Ne-Fe	1	To analyse radiobiological trends across the ions
Ca $_{20}^{40}$	1	Intermediate Biologically important trace element
Fe $_{26}^{56}$	3	Radiobiological interpolation

Collection of requirements for Radiobiology Facility



What radiobiological experiments are of interest?

What are the desired beam properties?

- ion species & energies
- beam intensities & duration
- beam size
  (micro vs. broad beam)
- beam homogeneity

How could an end-station for radiobiological experiments be designed

- Precision of beam-cell positioning
- Setup and Tooling

Also a test bed for diagnostics

OPENMED Facility Summary

- With a new Front End (Source)
  - LEIR can provide ions of interest for biomedical studies up to <430 MeV for fully stripped ^{12}C or ^{16}O ions
  - Facility can also be used to test detectors and diagnostics as well as test the results of medical simulations
  - Study well under way:
    - (Re-)implemention of slow ejection with longitudinal and/or transverse excitation
    - New extraction channel (septa) and transfer line to experiment
- Need the Funding for Implementation

Detectors

- Continuous development on particle physics detectors at CERN
- Scintillating crystals
- Medipix
- Diamond detectors

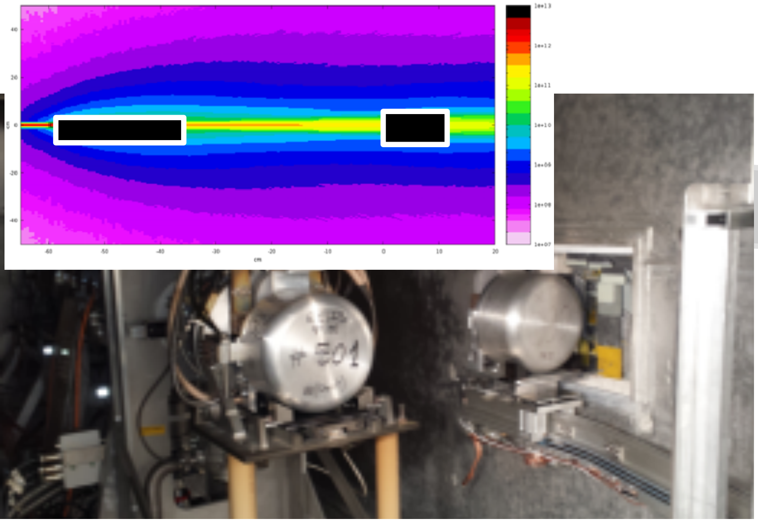
Radio-Isotopes (1)

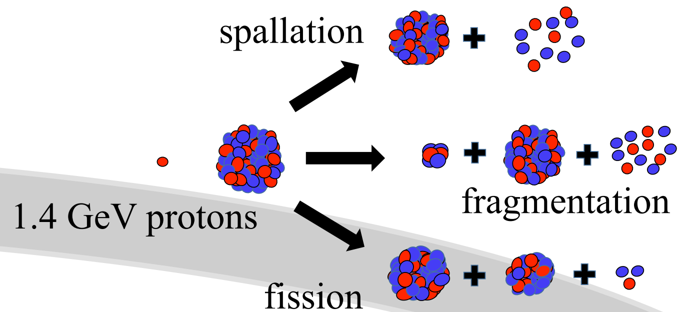
- Radioisotopes are used in medicine for applications ranging from imaging to treatment.
- The most used tracers are 99mTechnecium, often locally made available in hospitals from so-called generators created at nuclear reactors, for SPECT imaging.
- The most popular PET tracer 18F, is produced either in hospitals or in distributed cyclotron centres .
- Novel isotopes are emerging, either as imaging or treatment isotopes, exhibiting a range of chemical and decay properties.
- CERN has been hosting the Isolde facility for about 50 years.
- Over 1000 radioisotopes of more than 70 chemical elements have become available for fundamental and applied research.
- The technique of isotope mass-separation for medical isotope production will now be taken one step further with the construction of the CERN-MEDICIS facility.

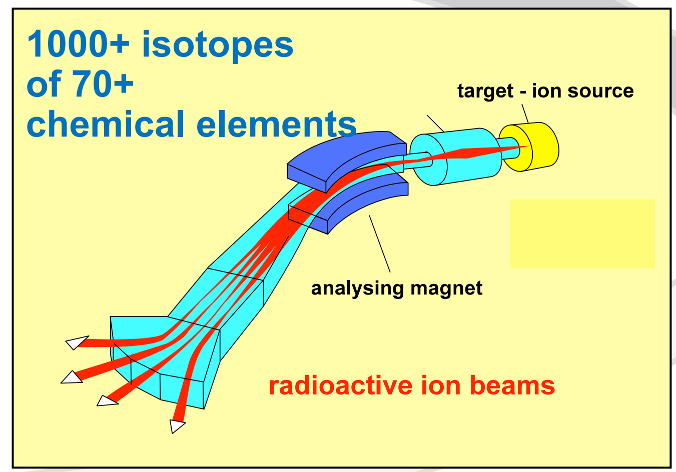
Key Points : Radio-Isotopes

- Securing an adequate supply of radioisotopes is a big challenge, (not only for $^{99}Mo/^{99m}Tc$) but even more for promising "new" radioisotopes such as alpha emitters for radio-immunotherapy.
- A European user facility to be created to supply innovative radioisotopes (produced at ISOLDE-CERN, ILL, PSI, Arronax,...) for R&D in life sciences (preclinical and clinical studies).
- Medicis on ISOLDE

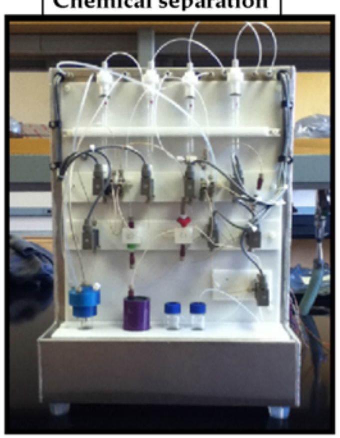
Isotope production in the dump and mass separation in the lab







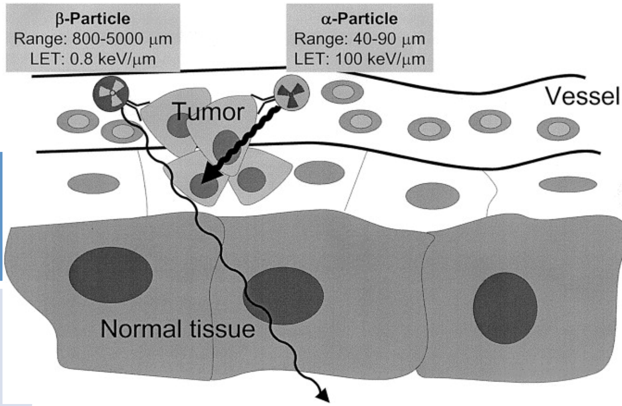
Chemical separation



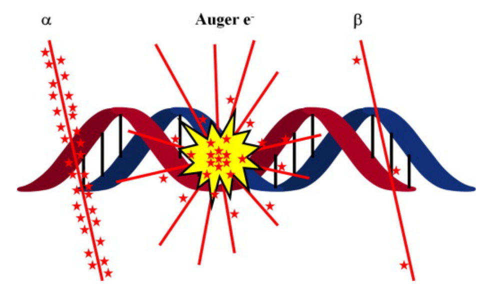
Pure isotope batch

The scope

- Scope : Life sciences, Medicine
- Innovative protocols (Surgery/brachytherapy/combination)
- Innovative isotopes

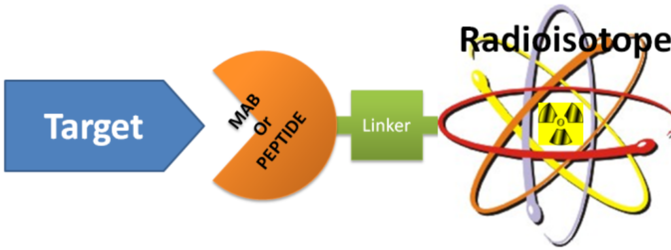


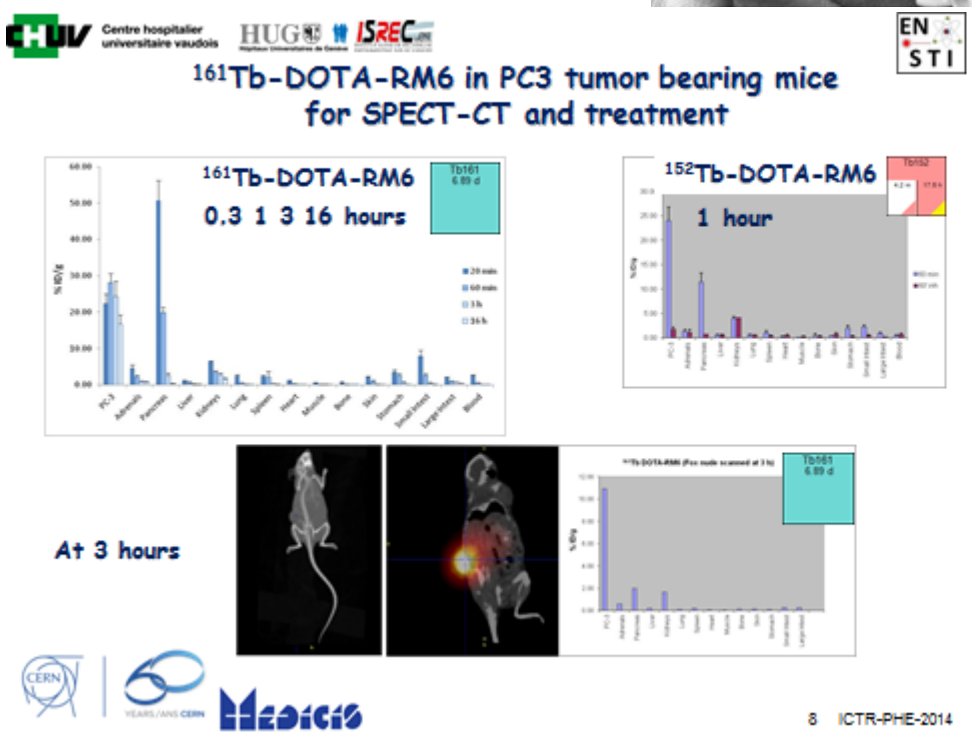
Field of Application	Radiation	Chemical elements	Half lives
PET	β^+	Alkaline earth	10's min.
SPECT	γ	Halogen	Hours
TAT	α	Lanthanide	Days
Beta therapy	β^-	Transition metals	Months
Auger therapy	e^-	…	



- Studies on cells, animals (« preclinical »)
  possibly extended to clinical phases

The scope


Target
MAB
Or
PEPTIDE
Linker
Radioisotope


Centre hospitalier universitaire vaudois
HUG
ISREC
EN STI
^{161}Tb-DOTA-RM6 in PC3 tumor bearing mice
for SPECT-CT and treatment
^{161}Tb-DOTA-RM6
0.3 1 3 16 hours
^{152}Tb-DOTA-RM6
1 hour
At 3 hours
8 ICTR-PHE-2014

Civil Engineering is on track

September 4th 2013

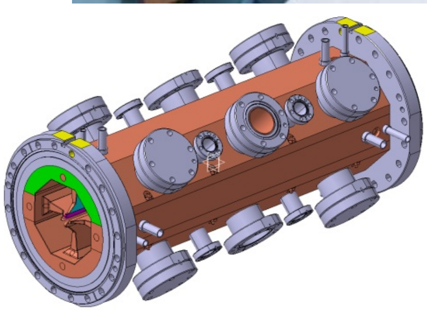
Planning …

	Construction	2013-2015
PHASE I	Commissioning : No beam	end 2015
PHASE II	Commissioning with beam and light targets to gain operational experience	2016
PHASE II B	Isotope production with light targets	mid 2016
PHASE III	Extending to heavy targets up to Tantalum	end 2016
PHASE IV	Collection of short lived alpha emitters (e.g. 149Tb)	2017
PHASE IVB	Operation with Lasers	
PHASE V	Operation with Uranium targets/possible proton beam upgrade	2018

The CERN HF-RFQ for Medical Applications

A few Images

- First prototype under construction @ CERN



Injector for Protontherapy Linac:

→ Compact : 5 MeV in only 2 meters

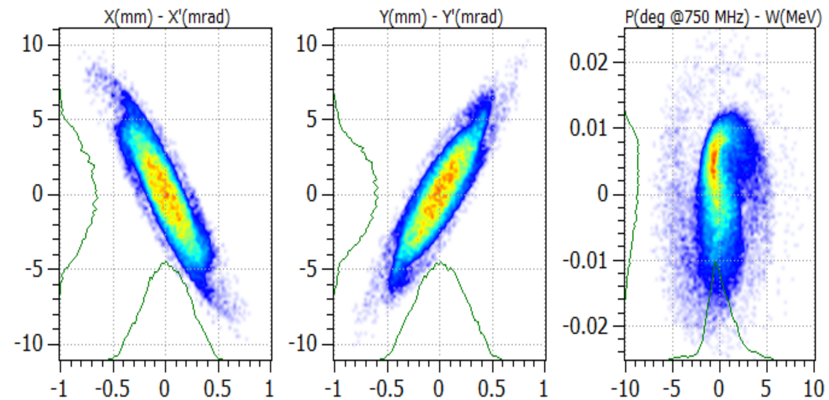
→ High Frequency: 750 MHz

→ For injection into 3 GHz structures

● RFQ Main Parameters

Input/Output Energy	40 keV / 5 MeV
Length	1.964 m
Vane voltage	67.6 KV
Min aperture radius	1 mm
Maximum modulation	3
Final synchronous phase	-15 deg
Output current (max.)	300 μA
Beam transmission	30 %
Output transv. rms emit.	0.027 p.mm.mrad
Output phase spread	± 2 deg
Output energy spread	± 20 KeV
RF Frequency	750 MHz

(M. Vretenar et al, Linac14, Geneva, 2014)



Output phase spaces

Highest lost particle energy = 500 KeV.
99.5% of the lost particles @ E < 100 KeV → No activation of the structure.

Overall peak RF power = 399 KW.
4 IOT-based amplifiers, one per module.

Cooling for max. 5% duty cycle.

HF-RFQ Advantages

- Compactness and shielding limited to the target
- Reduced weight
- Highly reduced activation of the accelerating structure
- Highly reliable and very simple to use with limited maintenance
- Modular: addition of modules to change the energy
- Compatible with proton, deuteron and alpha particles
- Safe: Immediate cut-off in case of beam loss
- No power consumption in beam off mode
- No conditioning time

HF-RFQ Medical Applications

→ Protontherapy Injector: 1 RFQ

~2 meters – 5 MeV p^+ – low current – low duty cycle

→ PET Isotope Production: 2 RFQ

~4 meters – 10 MeV p^+ - 20 µA average current – 4% duty cycle

==> Production of ^{18}F AND short lived isotopes (^{15}O, ^{11}C, ^{13}N, …)

→ High energy proton source for ^{99m}Tc Production: 2 RFQ + 1 DTL

~10 meters – 18 MeV p^+ - 2 mA average current – 10% duty cycle

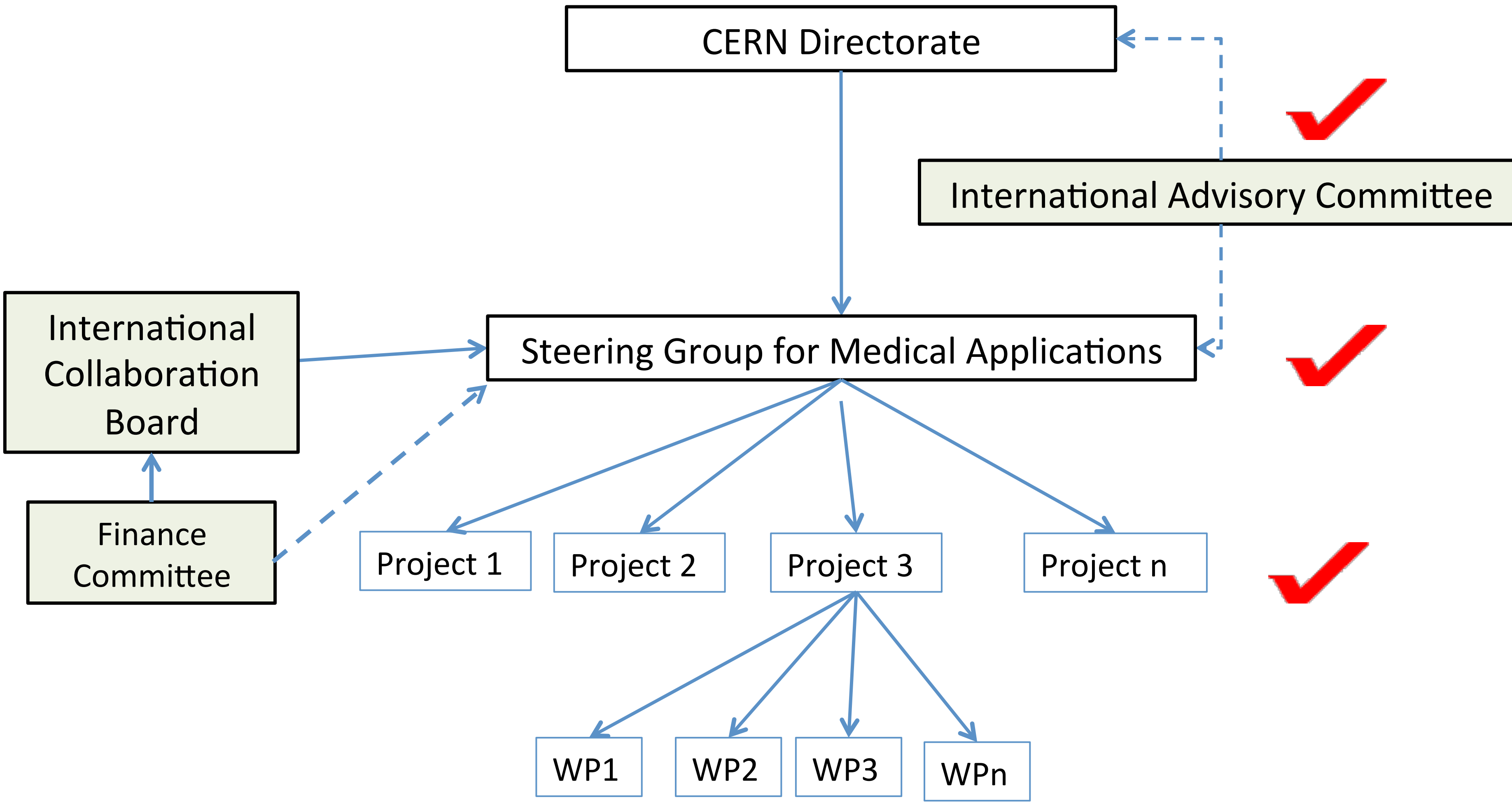
Low cost – Direct production by $^{100}Mo(p,2n)^{99m}Tc$

Reduce Nuclear Wastes - No need of ^{235}U

CMA Initiatives: Where are we?

- Obtained some "seed" funding from CERN, as well as donations from outside
- "CERN Medical Applications Workshop" followed the ICTR-PHE (15-16 February)
- Attracted ~80 top experts from all over the globe
- Funding, governance,… "institute or.."
- International Strategy Committee (Nov 2014)
- CERN as a medical data repository (HUG, EPFL, CHUV, NCI)
- Radio-isotopes project well under way
- White paper well under way
- RFQ development

DRAFT Structure (to be decided)



Large Scale Computing and Data

- Clinical data
- Simulations
- Medical data storage, transfer and analysis

Hadron Therapy

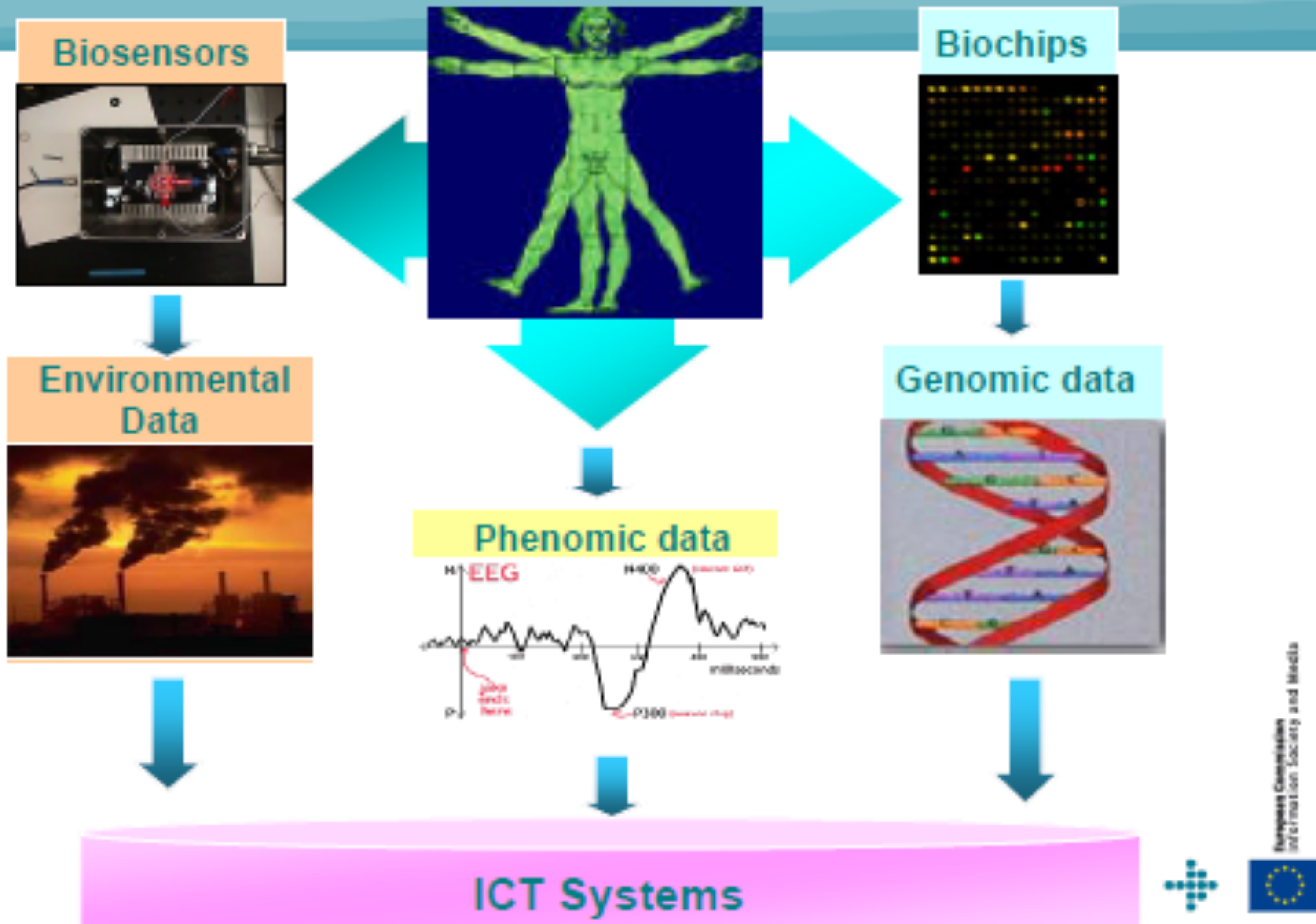
- Bioinformatics has become an increasingly important domain of life and health sciences, as technological progress and data handling go hand-in-hand.
- The requirements are well beyond the current state-of-the-art and the applicability of developments from basic research, including solutions implemented for CERN's Large Hadron Collider, is being explored.
- Standard information-processing tools need to be adapted to the complexity of medical data, which are more heterogeneous than physics data, and hence present new challenges for data mining. The confidentiality of patient information is also a major issue in medical data sharing.

Hadron Therapy

- We are investigating the application of grid computing and analytical software tools in data storage, handling, sharing and analysis, as well as the use of modern Monte Carlo (MC) calculation techniques.

- The high-level software systems will be effectively complemented by a user-friendly MC-based TPS capable of handling photon and ion therapy in various configurations, and by the MC modelling of the physical and biological behaviours of alternative ion species as well as of protons and carbon ions (followed by experimental verification).

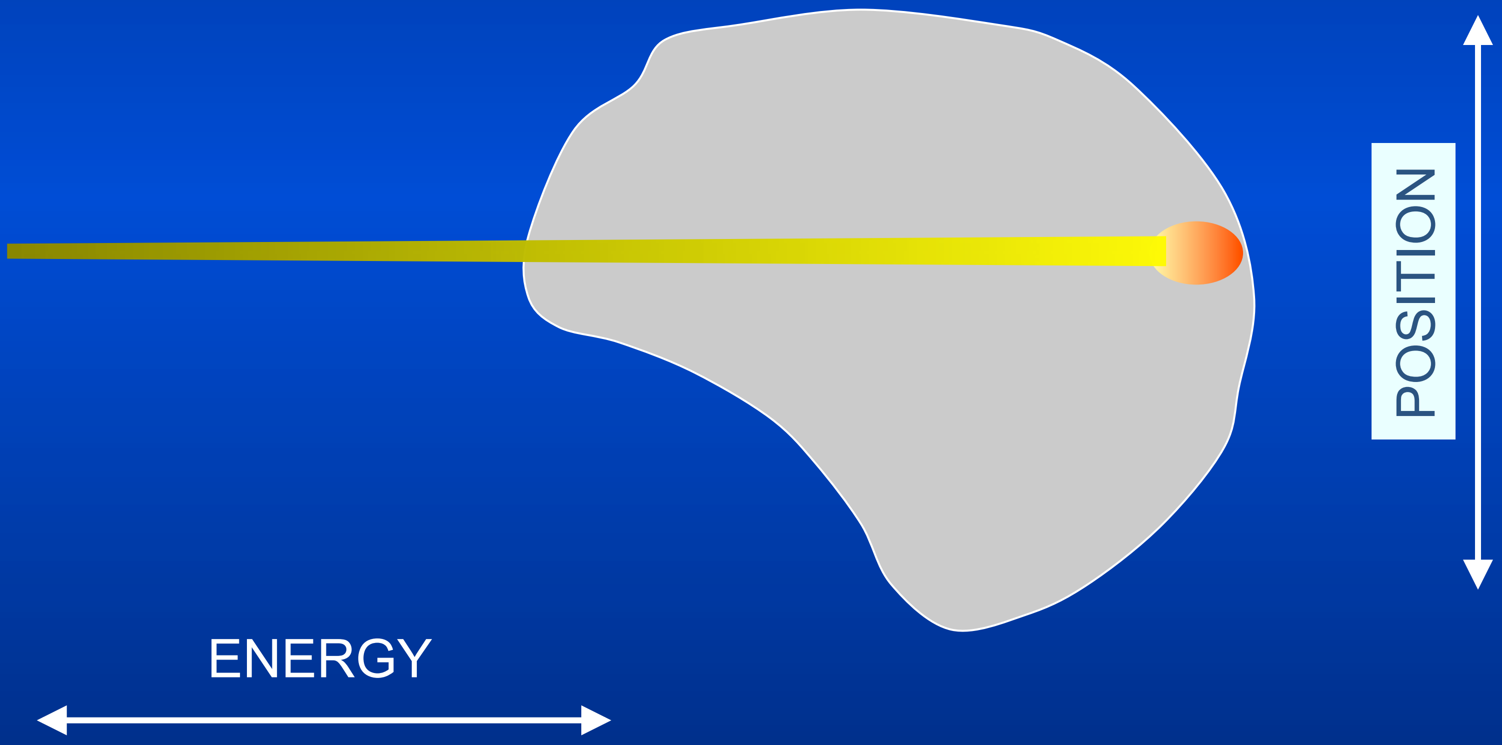
Towards full picture of individual's health status



Courtesy Marco Manca

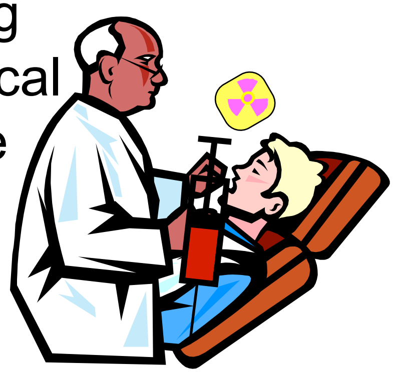
Thank you for your attention

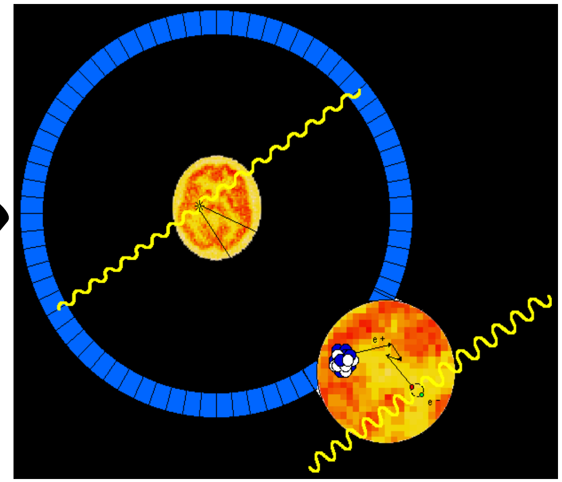
SPOT SCANNING



PET Principle

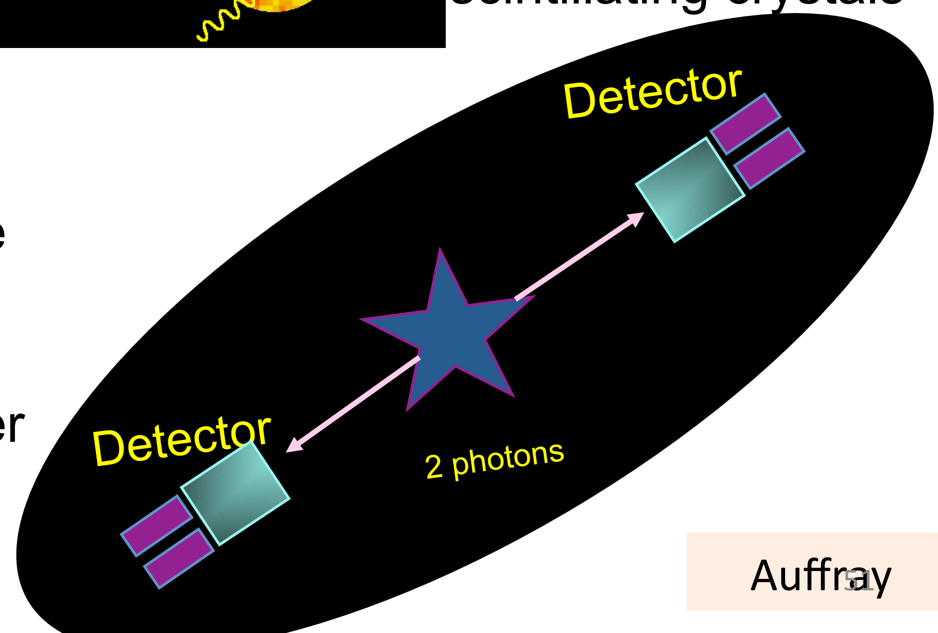
A positron emitting radiopharmaceutical is injected into the patient: the distribution





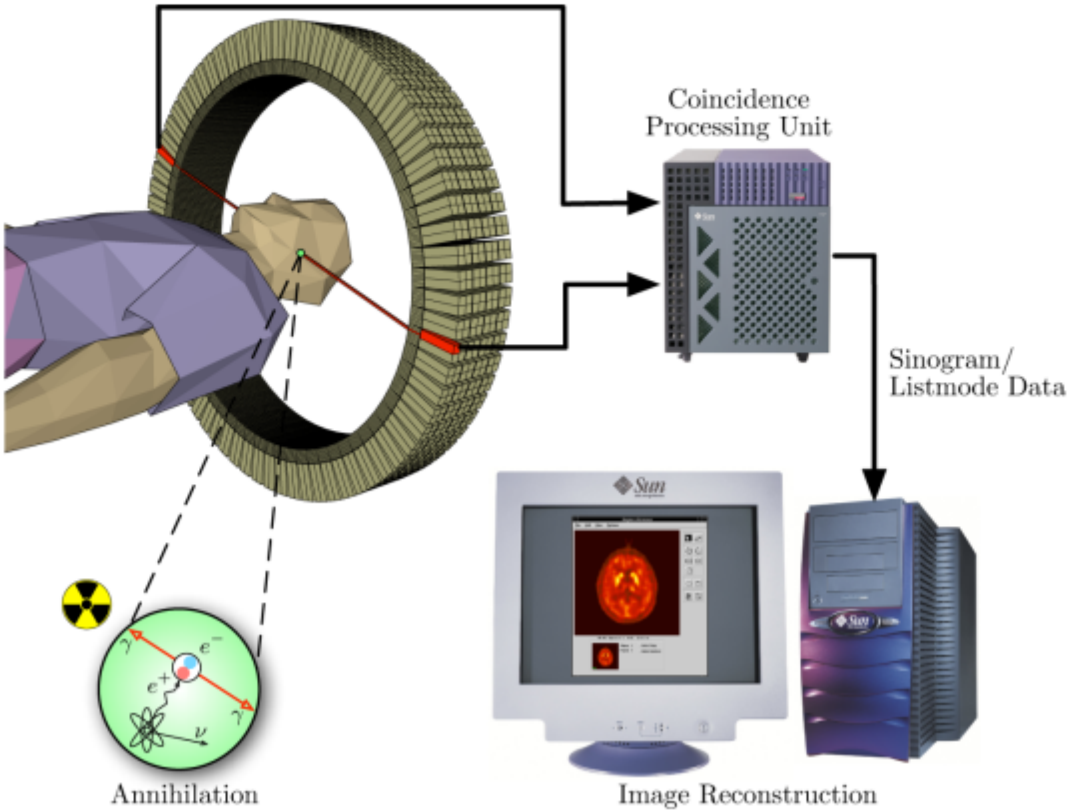
The emitted positrons annihilate with electrons in the tissue producing back-to-back photons detected by scintillating crystals

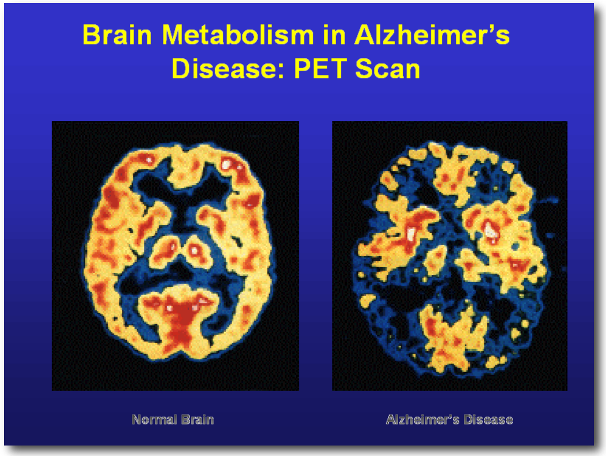
After some time the patient is placed in the imaging scanner

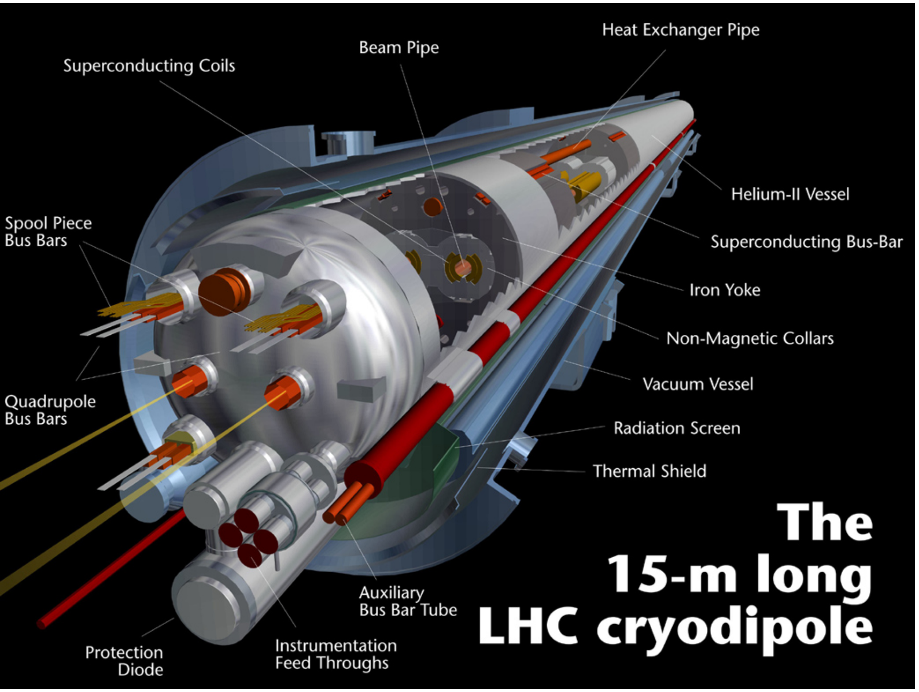


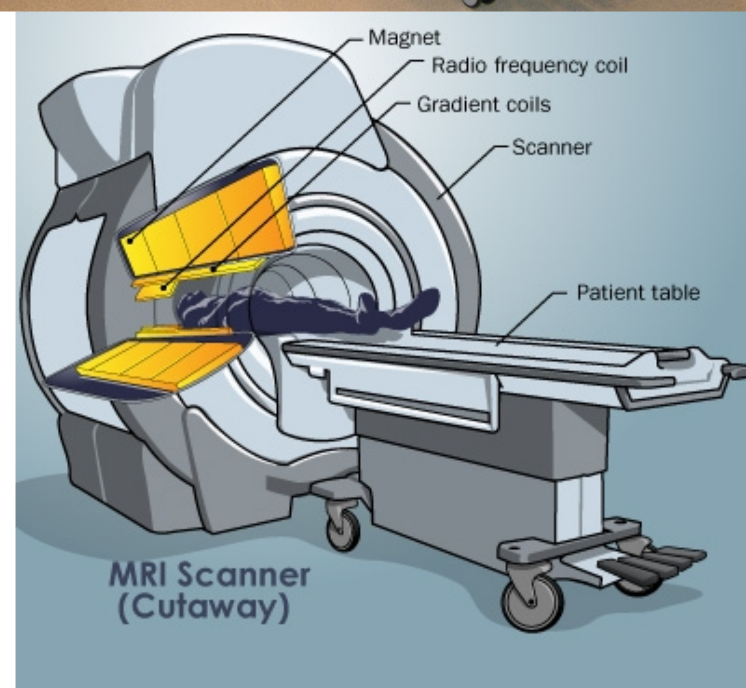
Auffray

PET (Positron Emission Tomography) Imaging





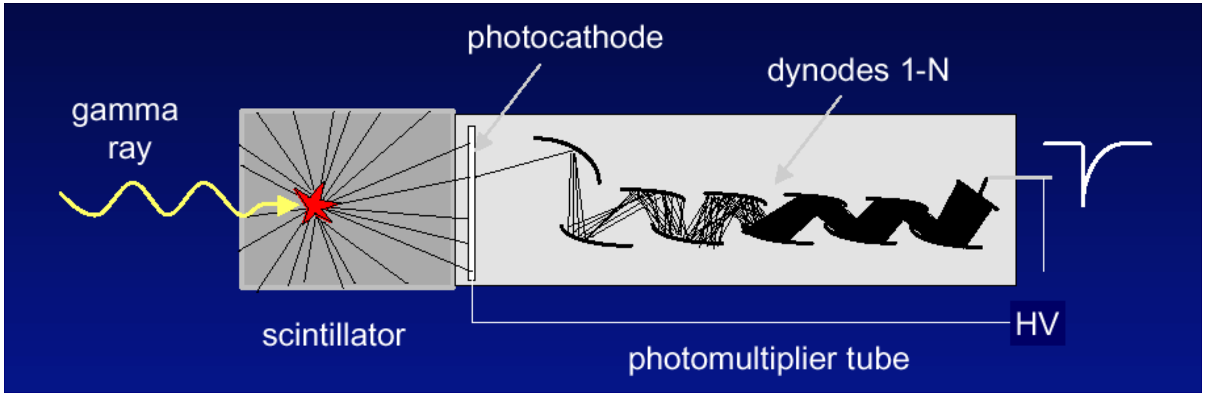




Superconducting magnet technology developments at CERN can be applied to improve MRI scanners

Scintillating crystals in Physics?

Scintillators are used in High Energy Physics to detect electromagnetic particles and measure their energy.



Scintillators convert incident energy to light, which is then detected by photo detectors, e.g. photomultiplier tubes (PMTs)

The intensity of the measured light is proportional to the energy of the incident particle

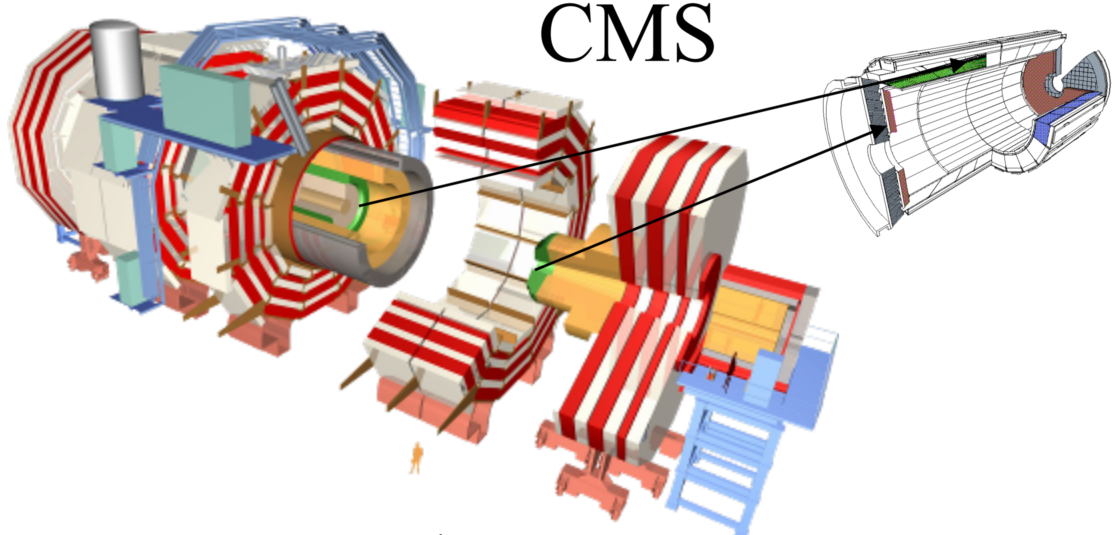
The detectors are called Electromagnetic calorimeters

Auffray

In the CERN Large Hadron Collider (LHC) 2 experiments use scintillating crystals : Lead tungstate crystals : $PbWO_4$

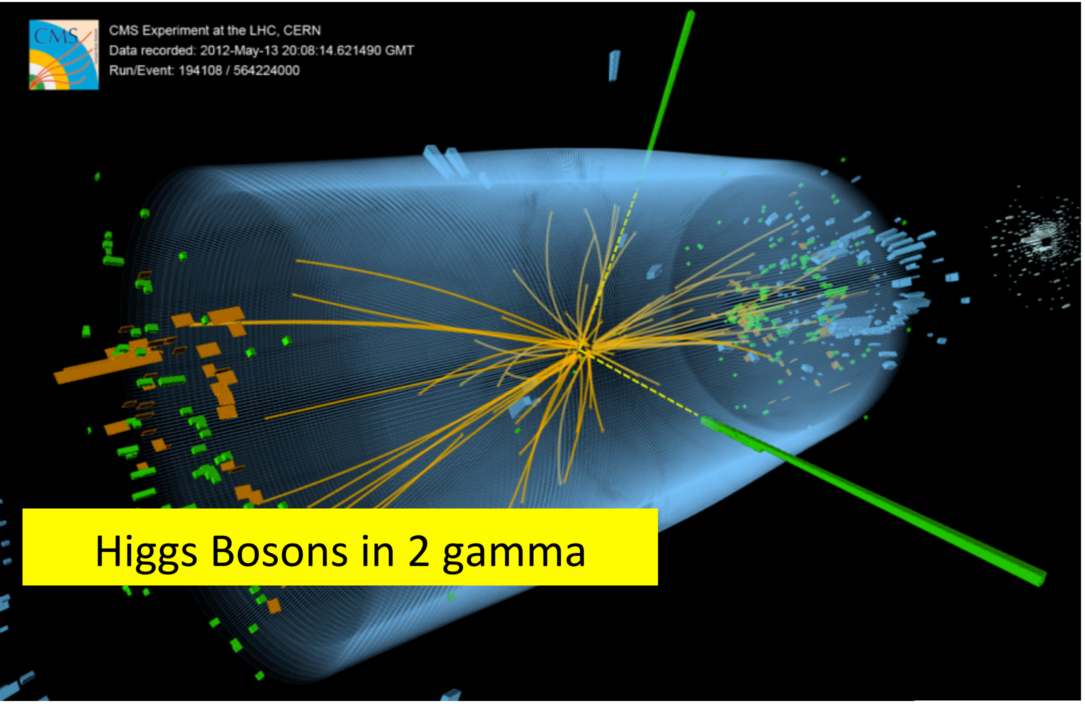
Alice :18000 crystals

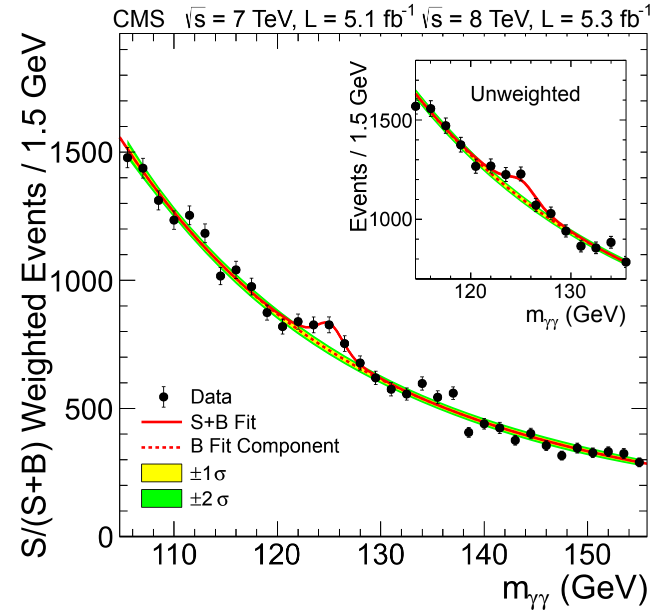
CMS



75000 crystals = 100 tons

Auffray

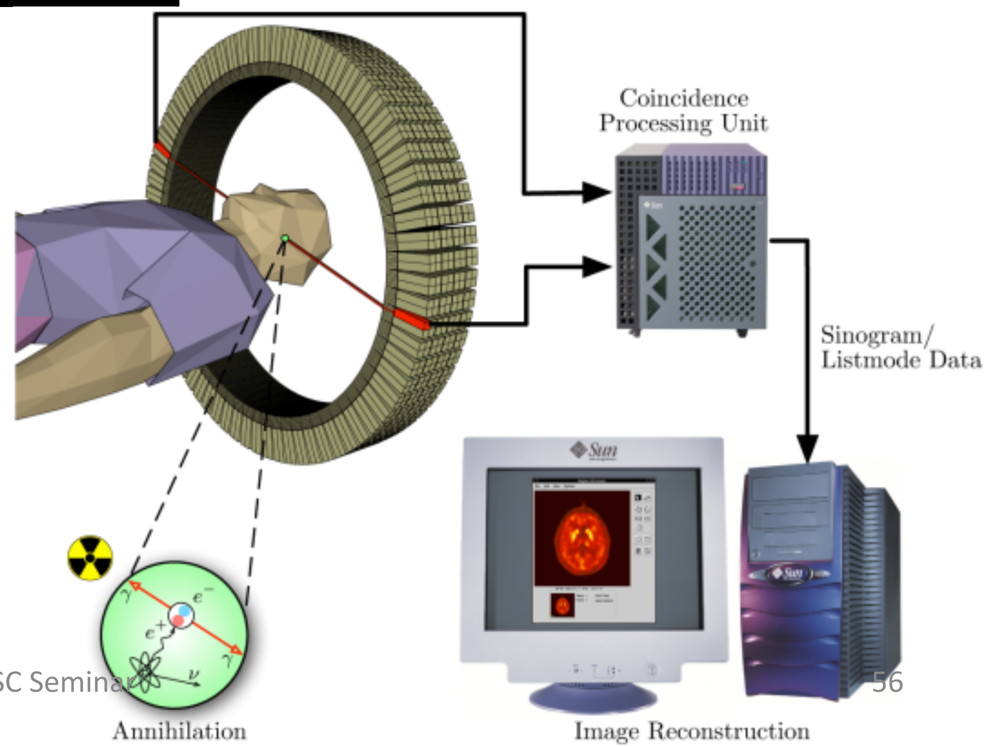




Particle Physics

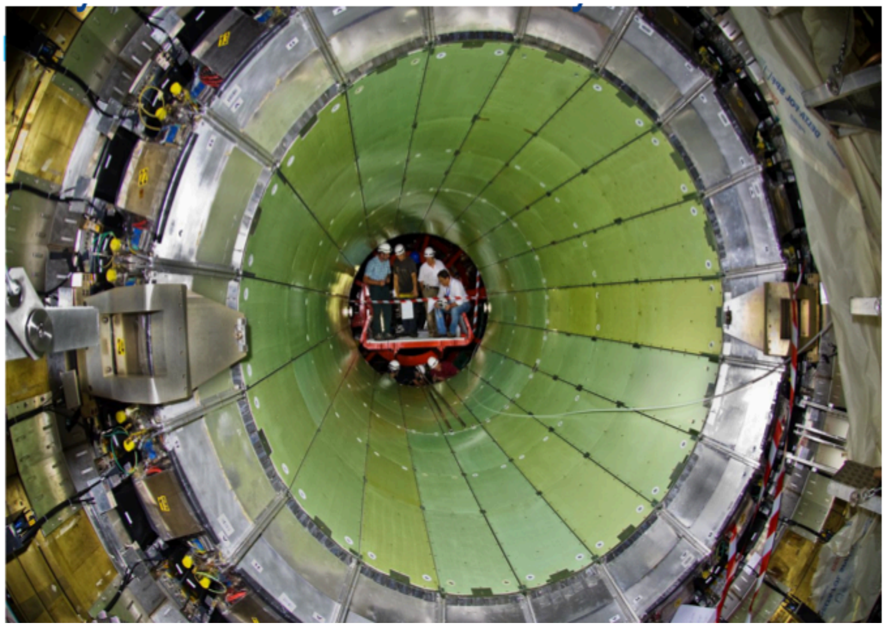
Medical Physics

Slightly lower energy photons!!

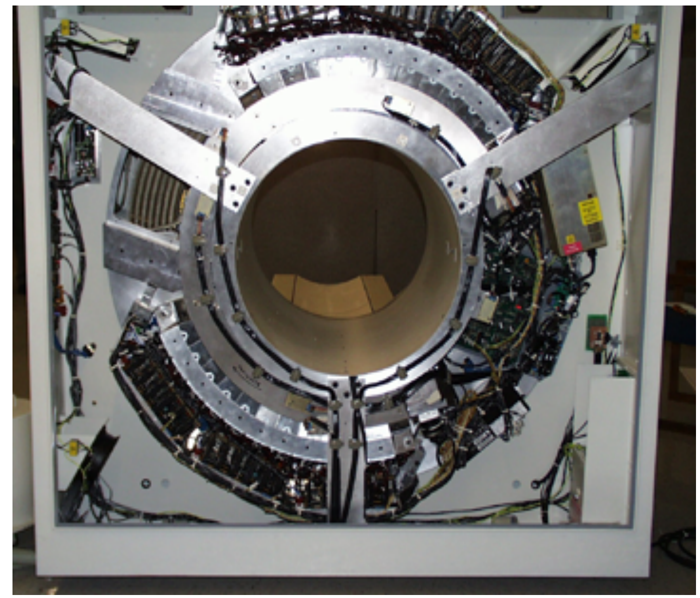


Similar Challenges in HEP and medical imaging

CMS Electromagnetic calorimeter



Positron Emission Tomograph (PET)



Scale is the difference