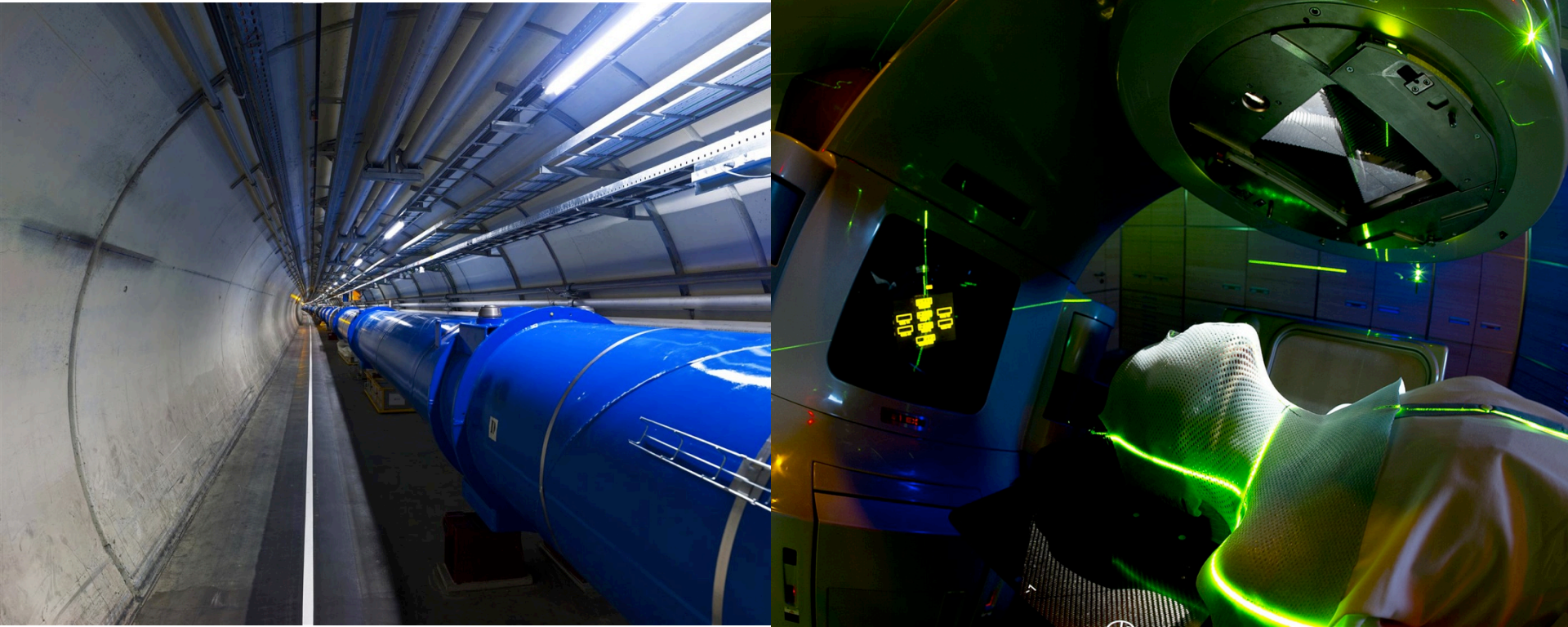
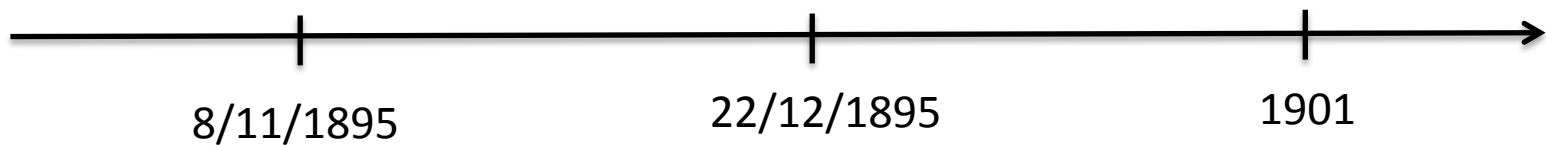


# From Physics to Medical Applications



Manjit Dosanjh, CERN  
[manjit.dosanjh@cern.ch](mailto:manjit.dosanjh@cern.ch)

# Modern medical physics– X-rays

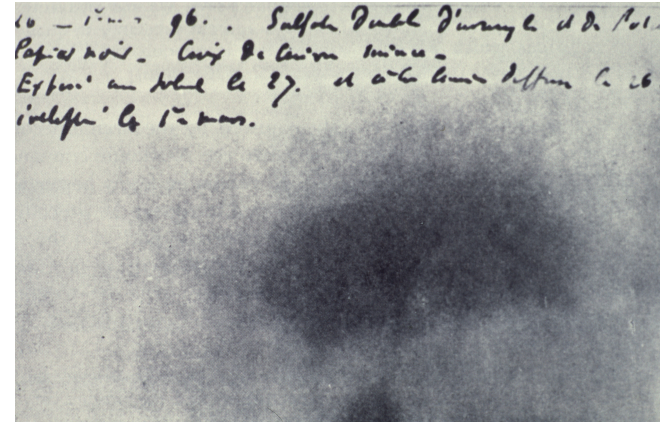


.....beginning of medical physics

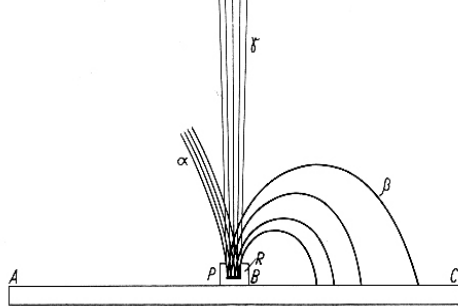


Henri Becquerel

**1896:**  
**Discovery of natural radioactivity**

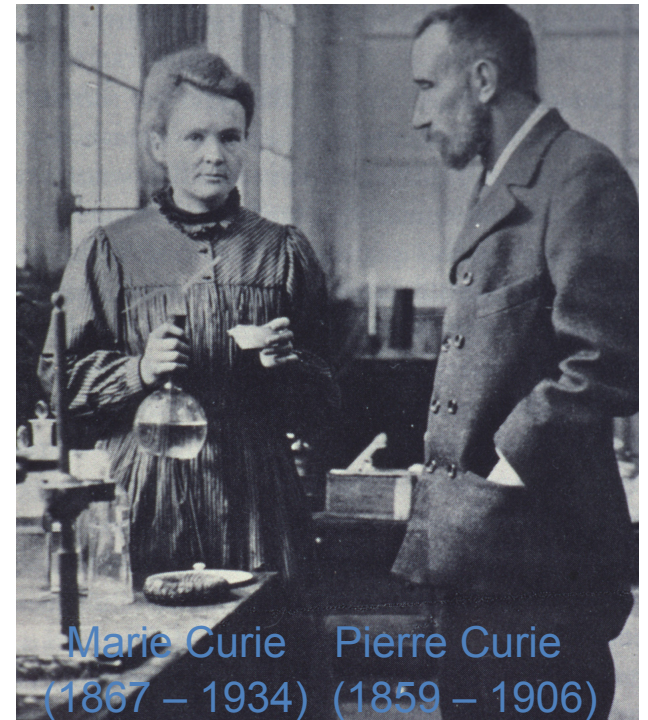


Thesis of Mme. Curie – 1904  
 $\alpha$ ,  $\beta$ ,  $\gamma$  in magnetic field



**1898: Discovery of radium**

**used immediately for “Brachytherapy”**



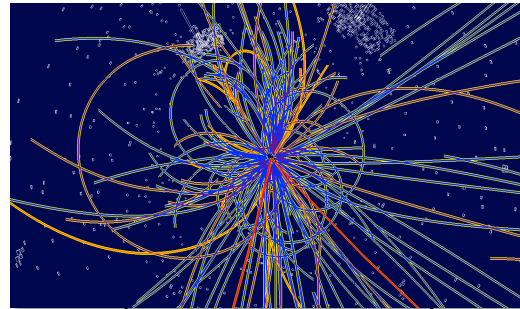
Marie Curie (1867 – 1934) Pierre Curie (1859 – 1906)

# First radiobiology experiment



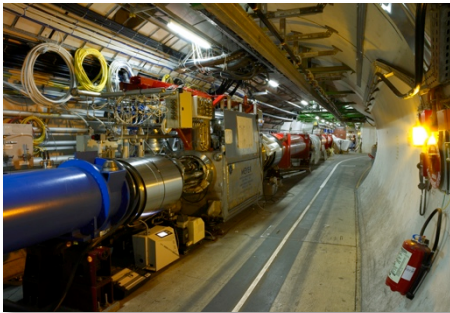
Pierre Curie and Henri Becquerel

# CERN Technologies and innovation



Detecting particles

Accelerating particle beams



Higgs

Large-scale computing (Grid)



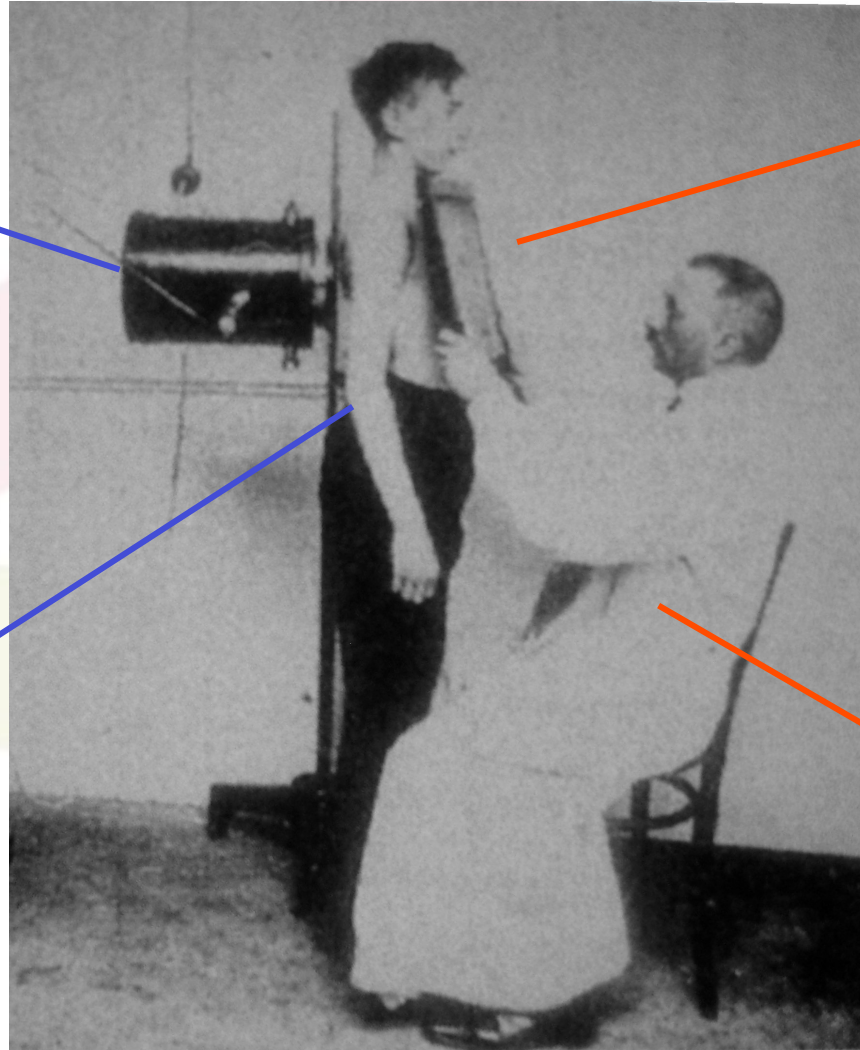
# X-ray systems

X-ray source

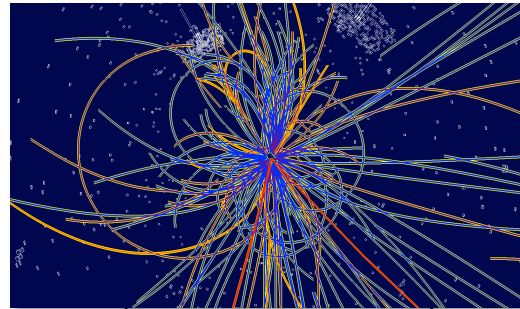
Object

Detector

Pattern Recognition System

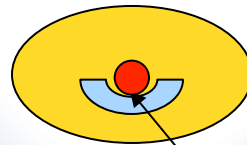
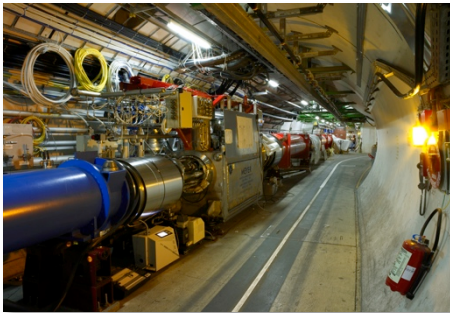


# CERN Technologies and innovation



Detecting particles

Accelerating particle beams



**CANCER**

Large-scale computing (Grid)



# Why Cancer and physics technologies?

It is a large and a growing societal challenge:

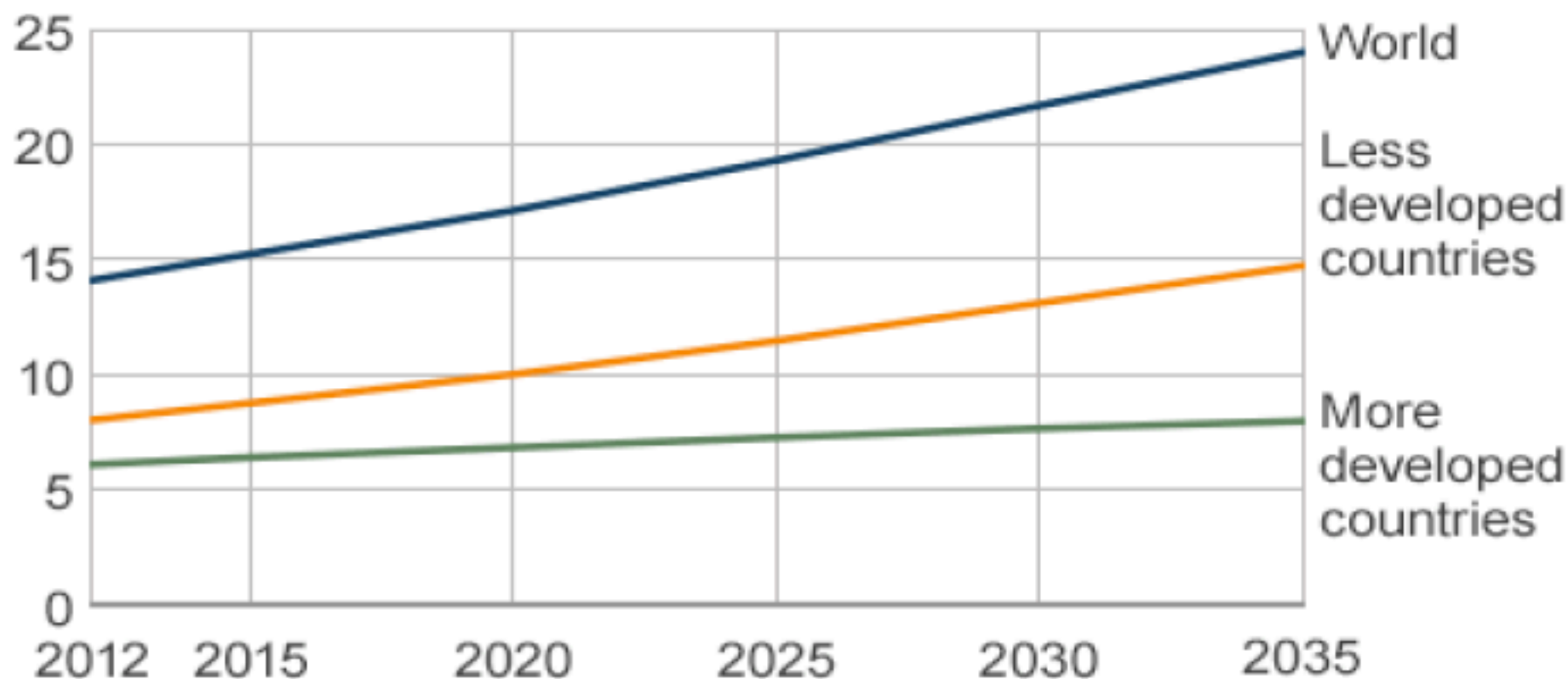
- More than 3 million new cancer cases in Europe in 2015
- Nearly 15 million globally in 2015
- This number will increase to 25 million in 2030
- Currently around 8 million deaths per year

## How can physics help?



## Predicted Global Cancer Cases

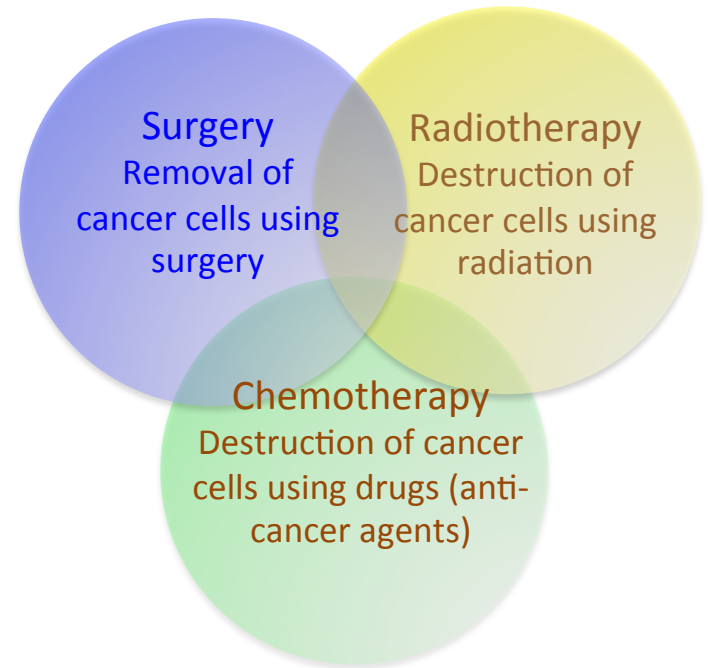
Cases (millions)



Source: WHO GloboCan

# Some facts about Cancer

- Tumour: why?
  - Abnormal growth of cells
  - Malignant: uncontrolled, can spread → cancer
- Treatment: how?
  - Surgery
  - Radiation
  - Chemotherapy



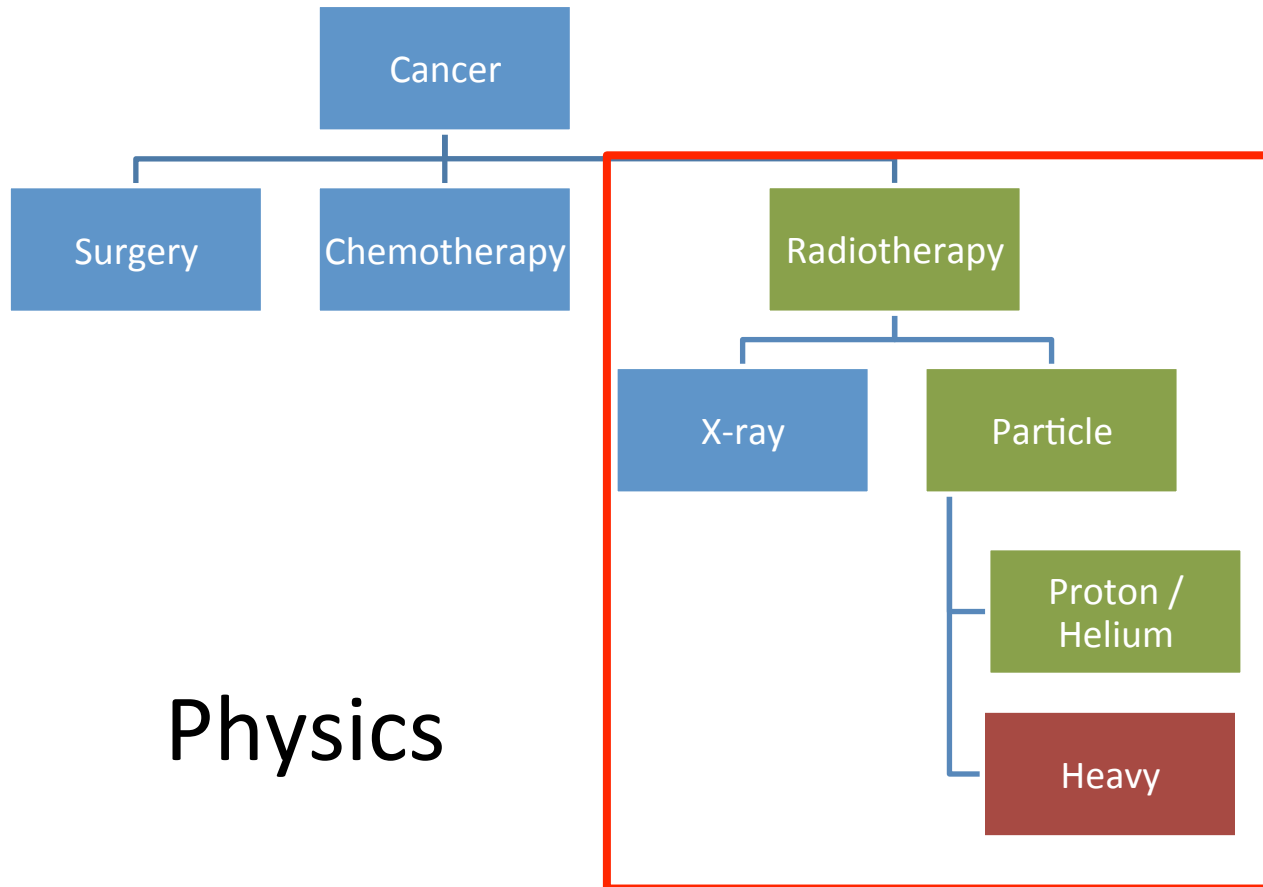
# The Challenge of Treatment

Ideally one needs to treat:

- The tumour
- The whole tumour
- And nothing BUT the tumour”

Treatment has **two equally important goals** to **destroy** the tumour and **protect** the surrounding normal tissue. Therefore **“seeing”** in order to know where and precise **“delivery”** to make sure it goes where it should are **key**.

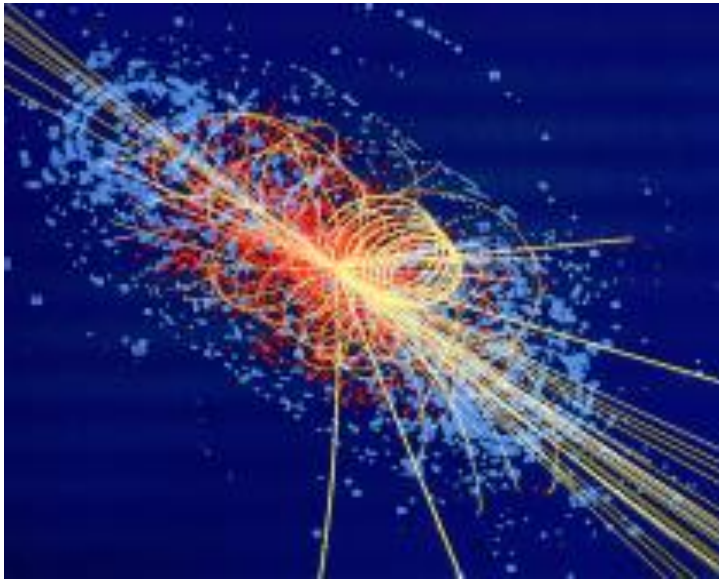
# Cancer treatment



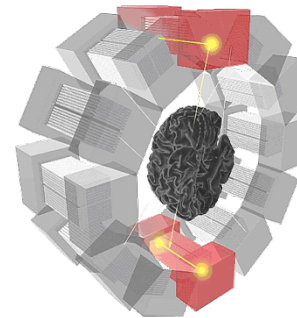
Physics

# No treatment without detection!

## Particle Detection

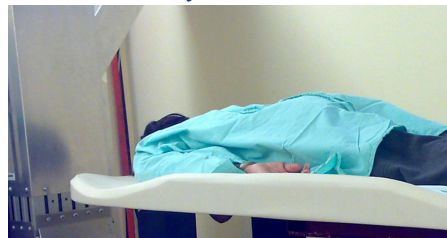


## Imaging

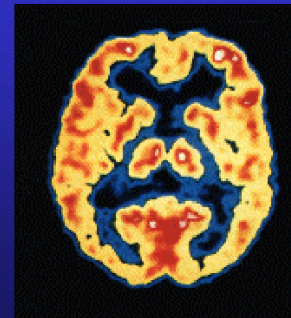


PET Scanner

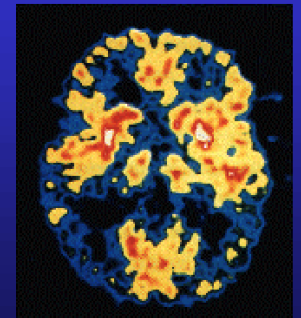
Breast imaging  
(ClearPEM)



Brain Metabolism in Alzheimer's  
Disease: PET Scan



Normal Brain



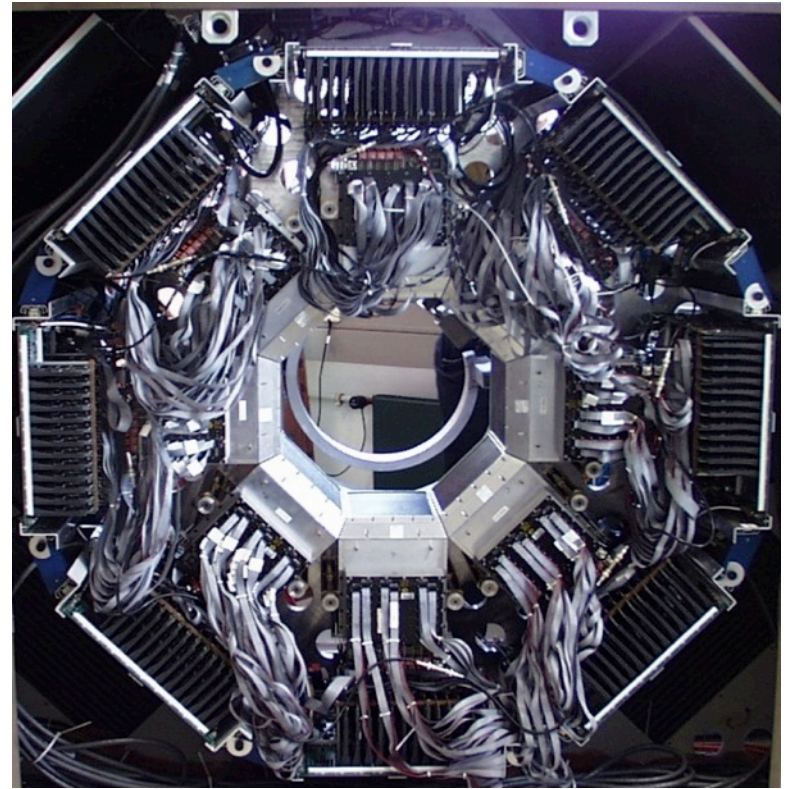
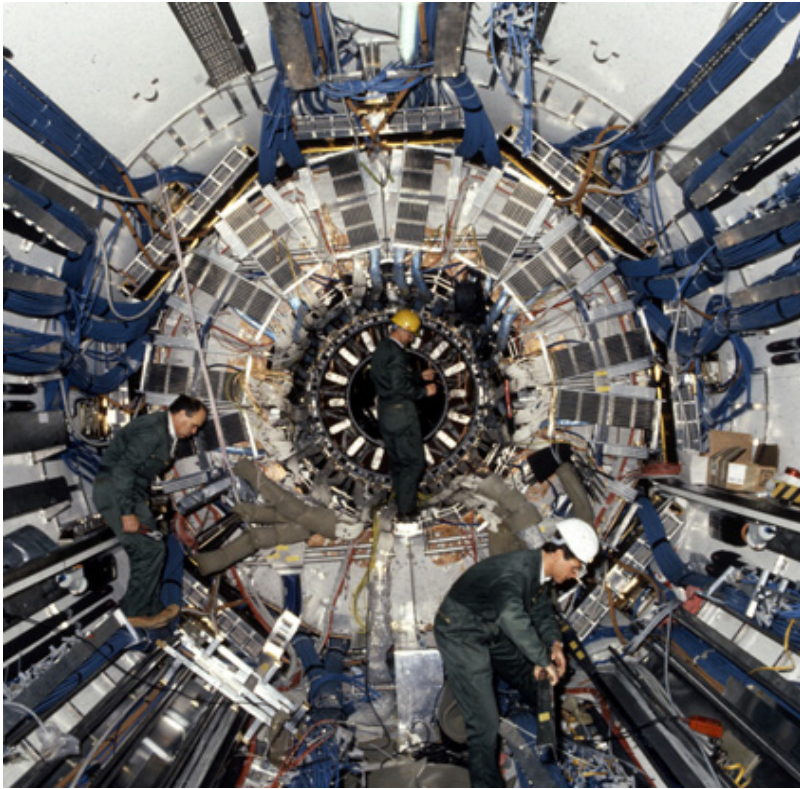
Alzheimer's Disease

[cds.cern.ch/record/1611721](https://cds.cern.ch/record/1611721)



European NoVel Imaging Systems  
for ION therapy

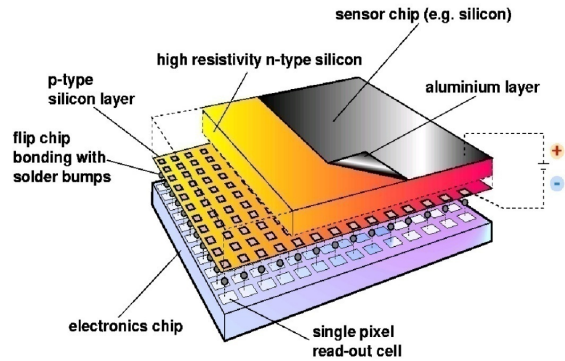
# The detector challenge



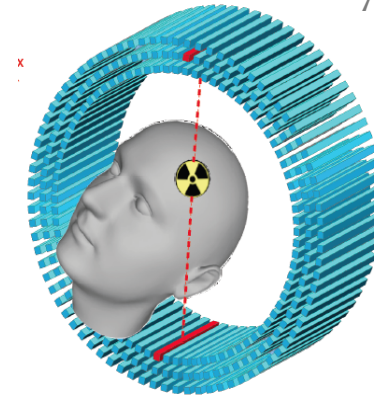
# CERN is contributing to imaging for decades

## CERN-coordinated international collaborative projects

### MEDIPIX

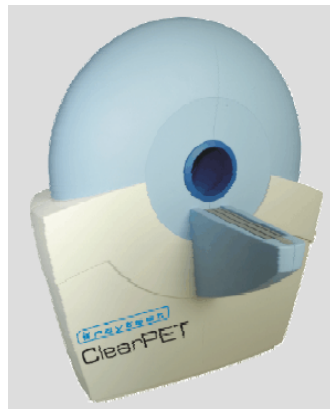


### AXPET

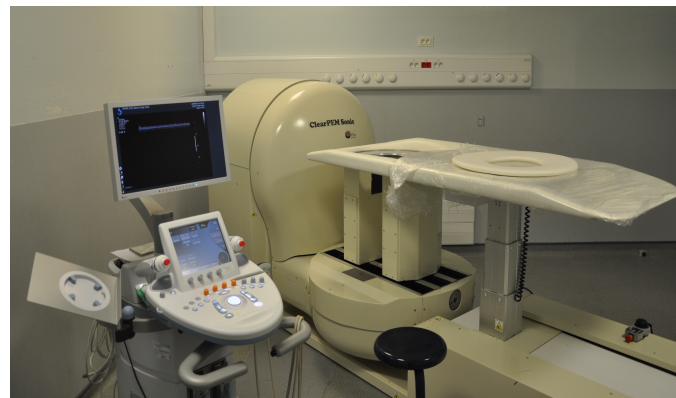


## Crystal Clear projects

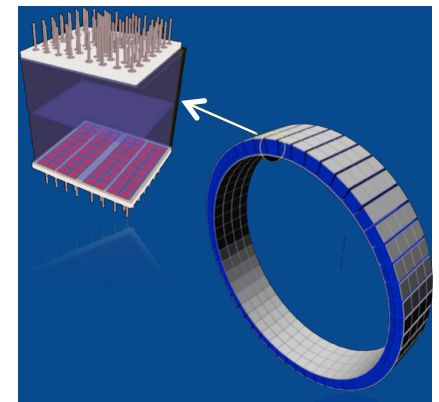
Courtesy of Paul Lecoq



ClearPET



ClearPEM & ClearPEM-Sonic



BrainPET



# CERN's role in detection and imaging...

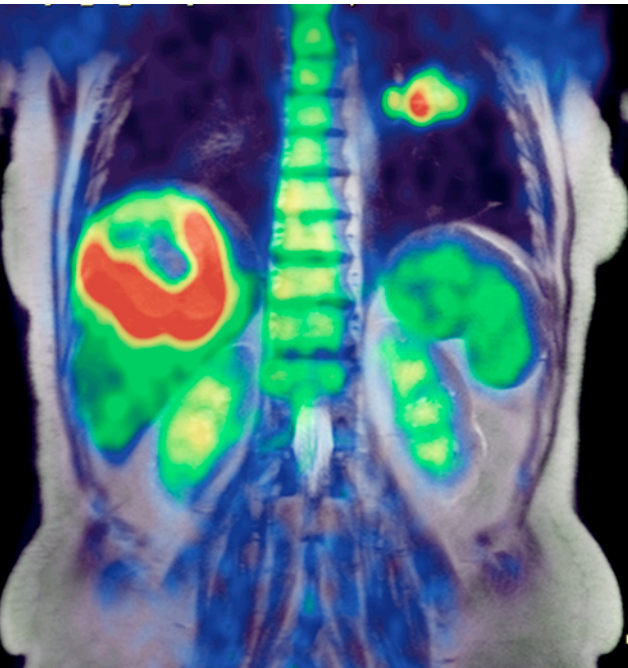
## Continuous development in particle physics:

- Scintillating crystals (David Townsend .....
- Pixel detectors (Medipix collaboration)
- Diamond detectors
- Multi-wire proportional chambers/ GEMS (Charpak...)
- Resistive Plate Chambers for imaging

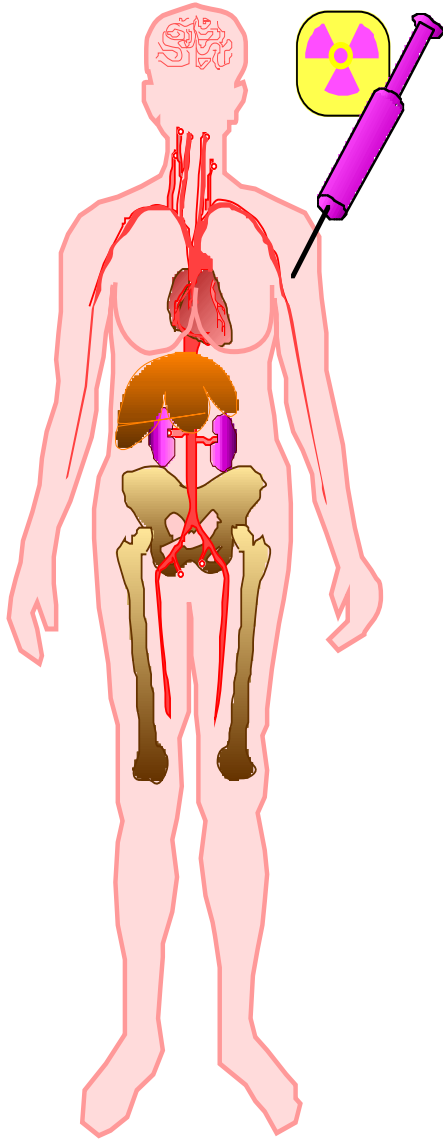
# Antimatter – ~~science fiction?~~



**PET**



# PET: how it works

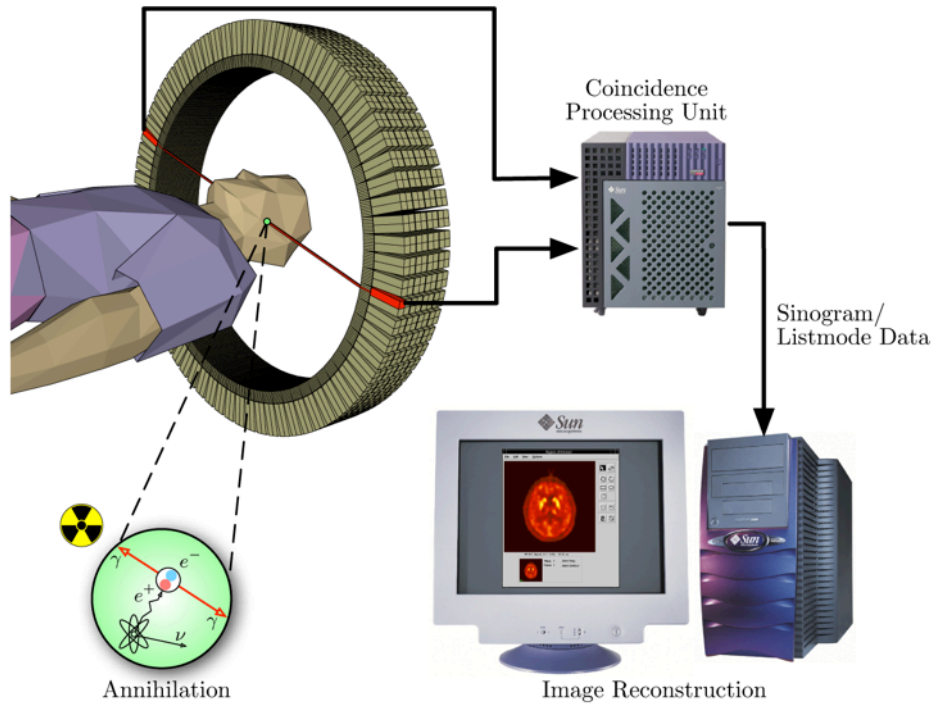


- Drug is labeled with positron ( $\beta^+$ ) emitting radionuclide.
- Drug localizes in patient according to metabolic properties of that drug.
- Trace (pico-molar) quantities of drug are sufficient.
- Radiation dose fairly small (<1 rem = 0.01 Sv).

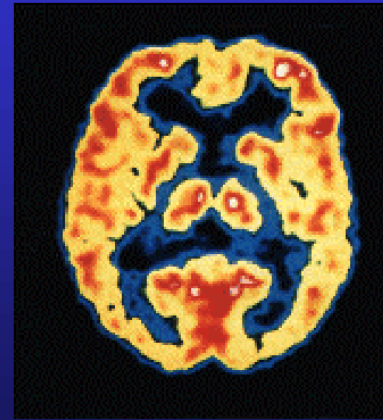
# PET – How it works

<http://www.nymus3d.nl/portfolio/animation/55>

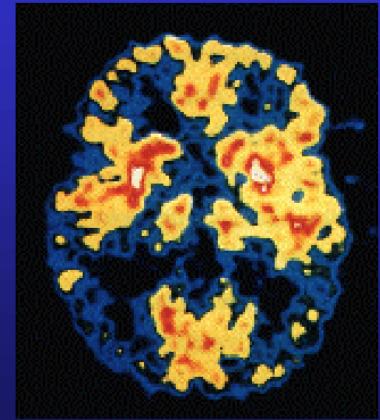
# PET Scan



## Brain Metabolism in Alzheimer's Disease: PET Scan



Normal Brain



Alzheimer's Disease

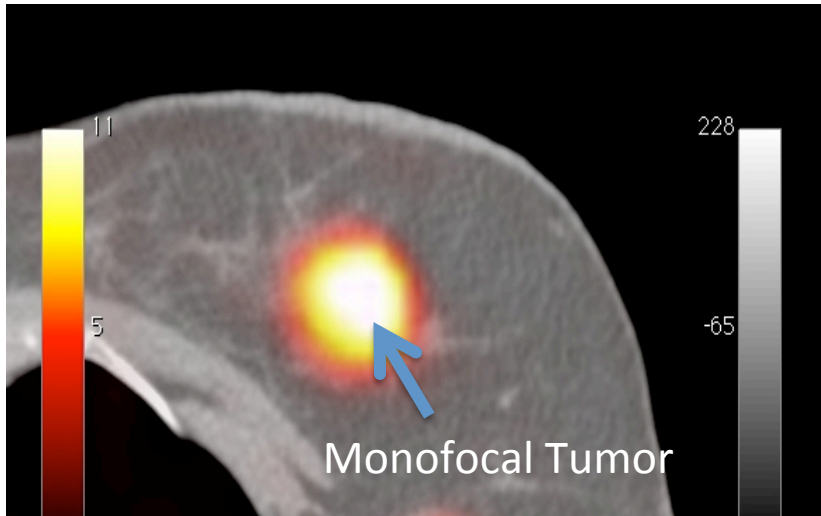
# ClearPEM



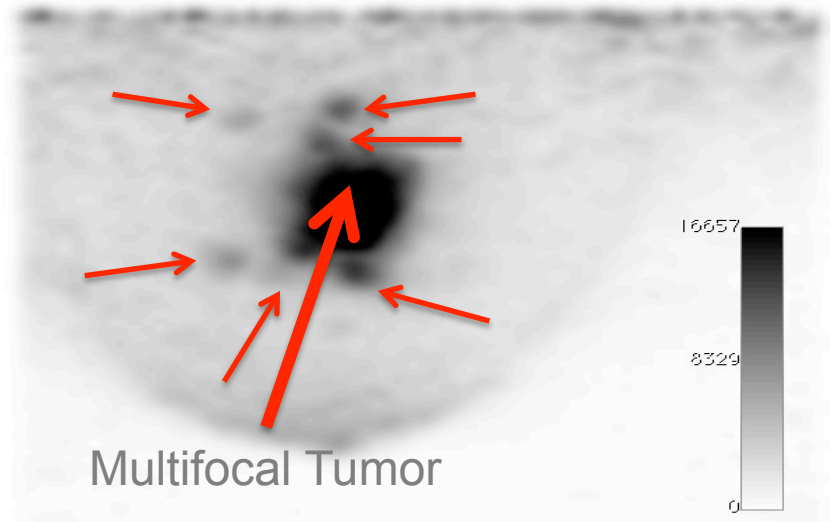
Photos: Crystal Clear Colaboration

PET for mammography: Crystal Clear Collaboration

# Breast Cancer Detection



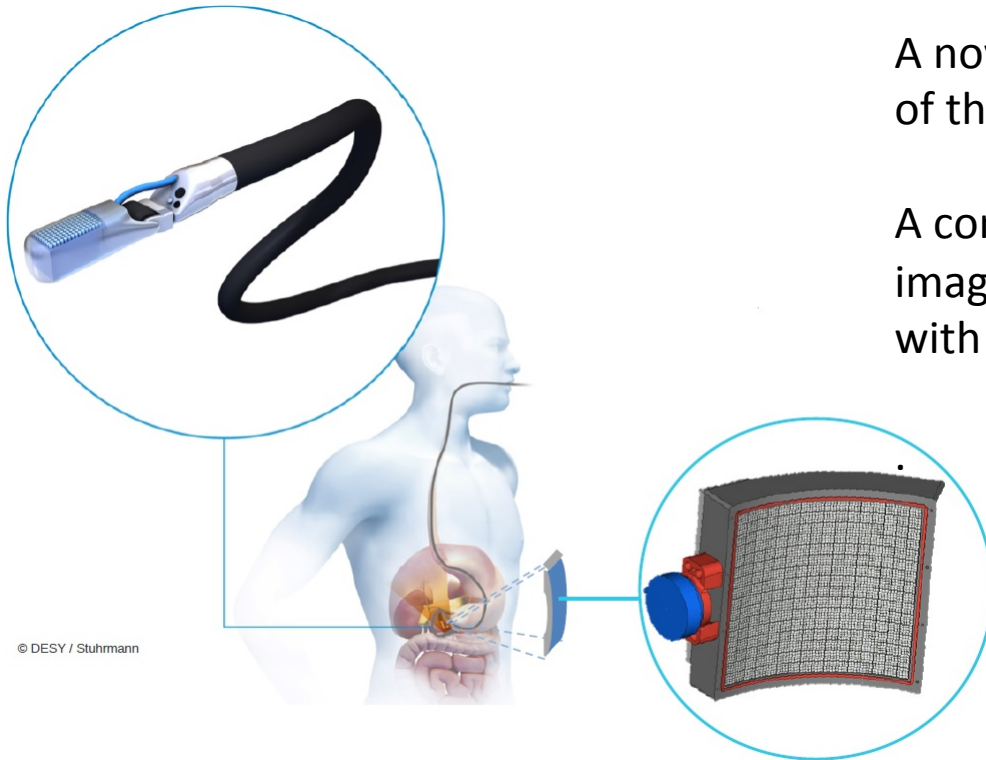
**PET Wholebody**



**ClearPEM dedicated Breast imaging**

# Endo TOFPET-US

a novel multimodal tool for endoscopy and positron emission tomography



A novel imaging system for endoscopic exams of the pancreas or the prostate.

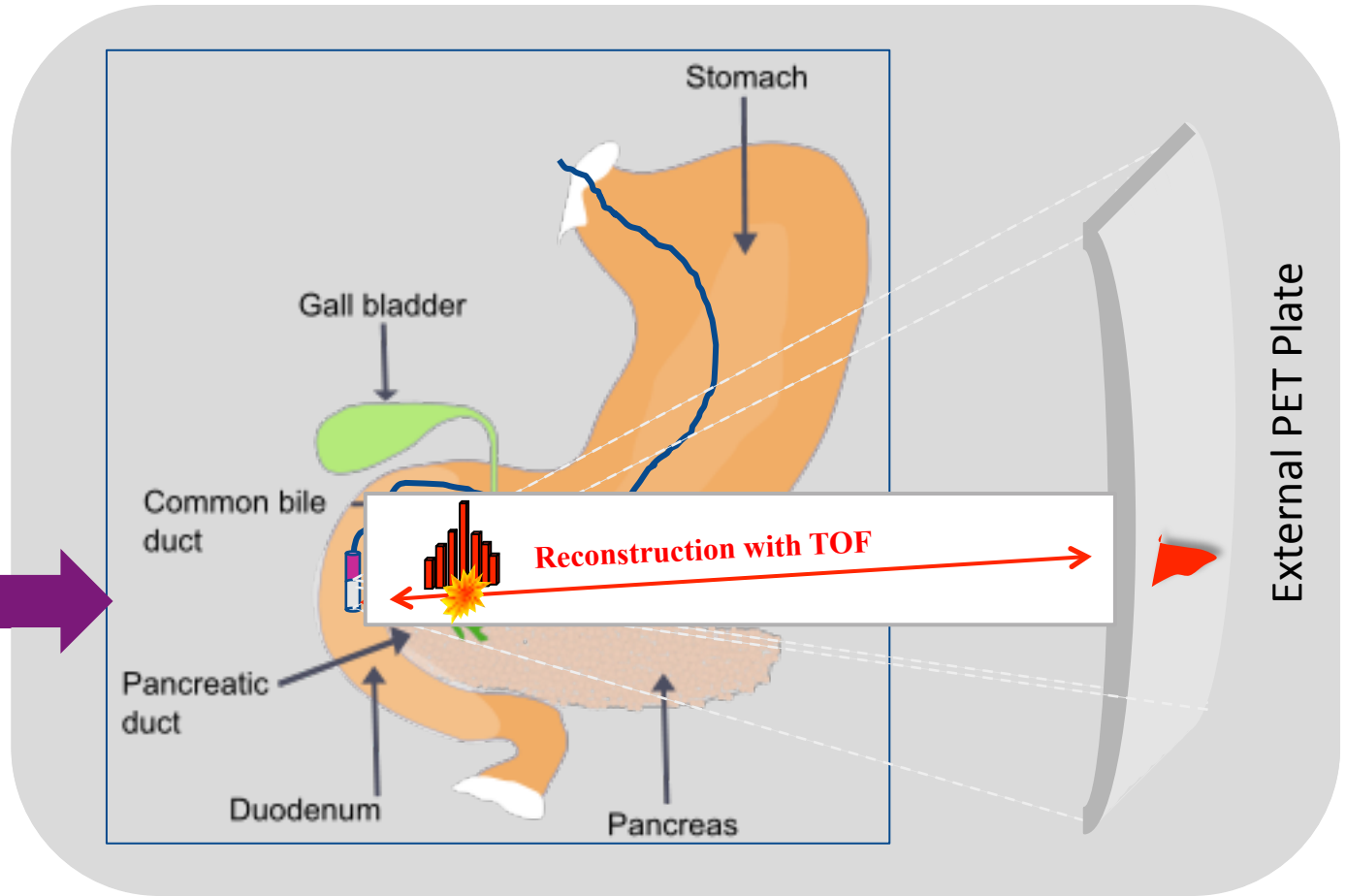
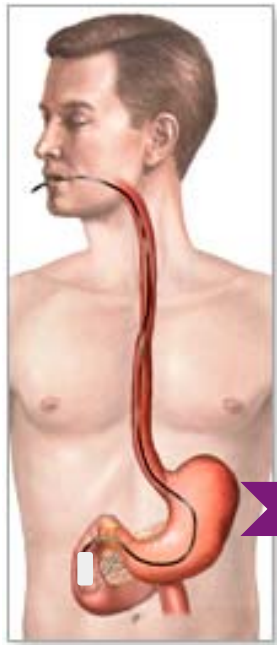
A combination of high resolution metabolic imaging with TOFPET and anatomical imaging with ultrasound.

Endo = Endoscopic  
TOF = Time of Flight PET  
US = Ultrasound

© DESY / Stuhmann



# The Principle



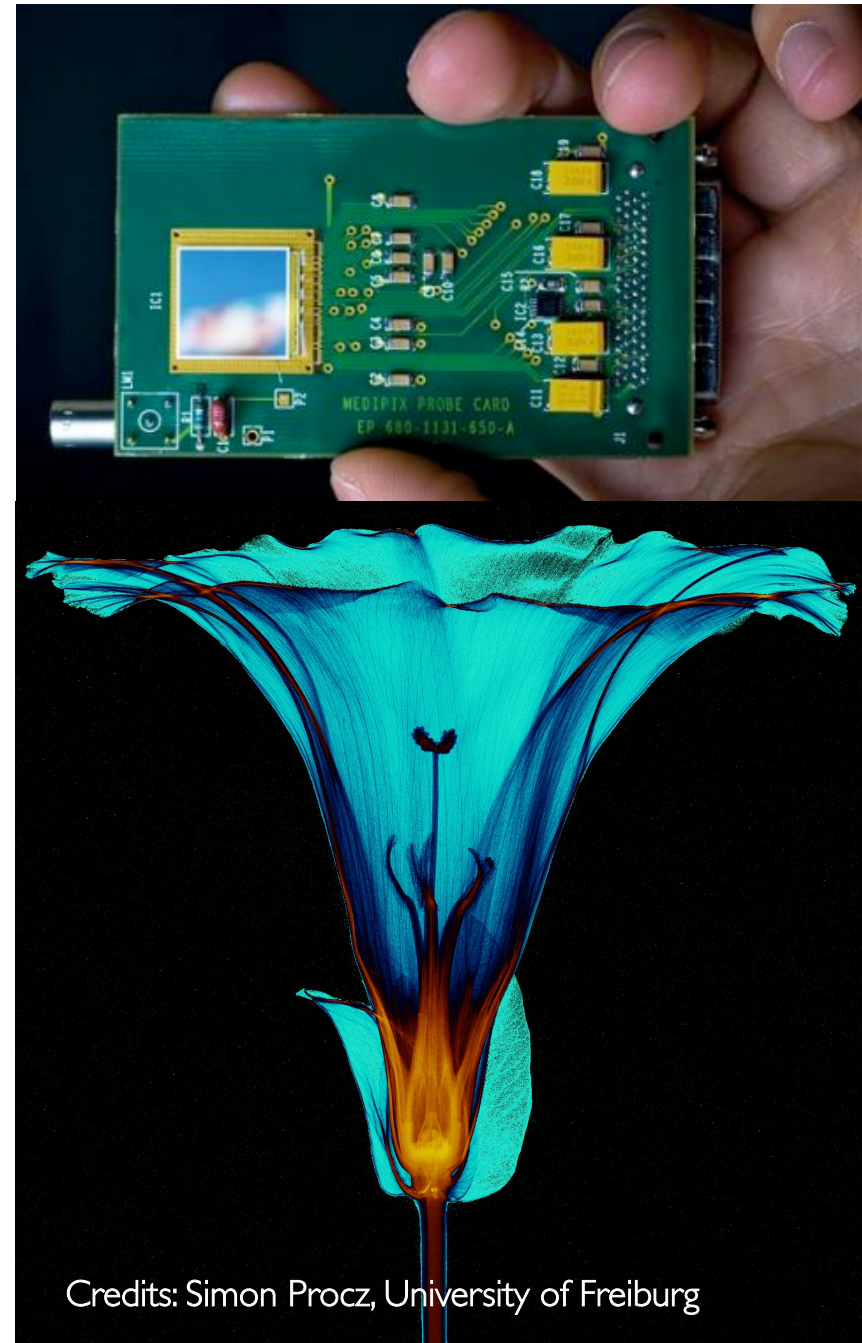
# Medipix

- High Energy Physics original development:

- Particle track detectors
- Allows counting of single photons in contrast to traditional charge integrating devices like film or CCD

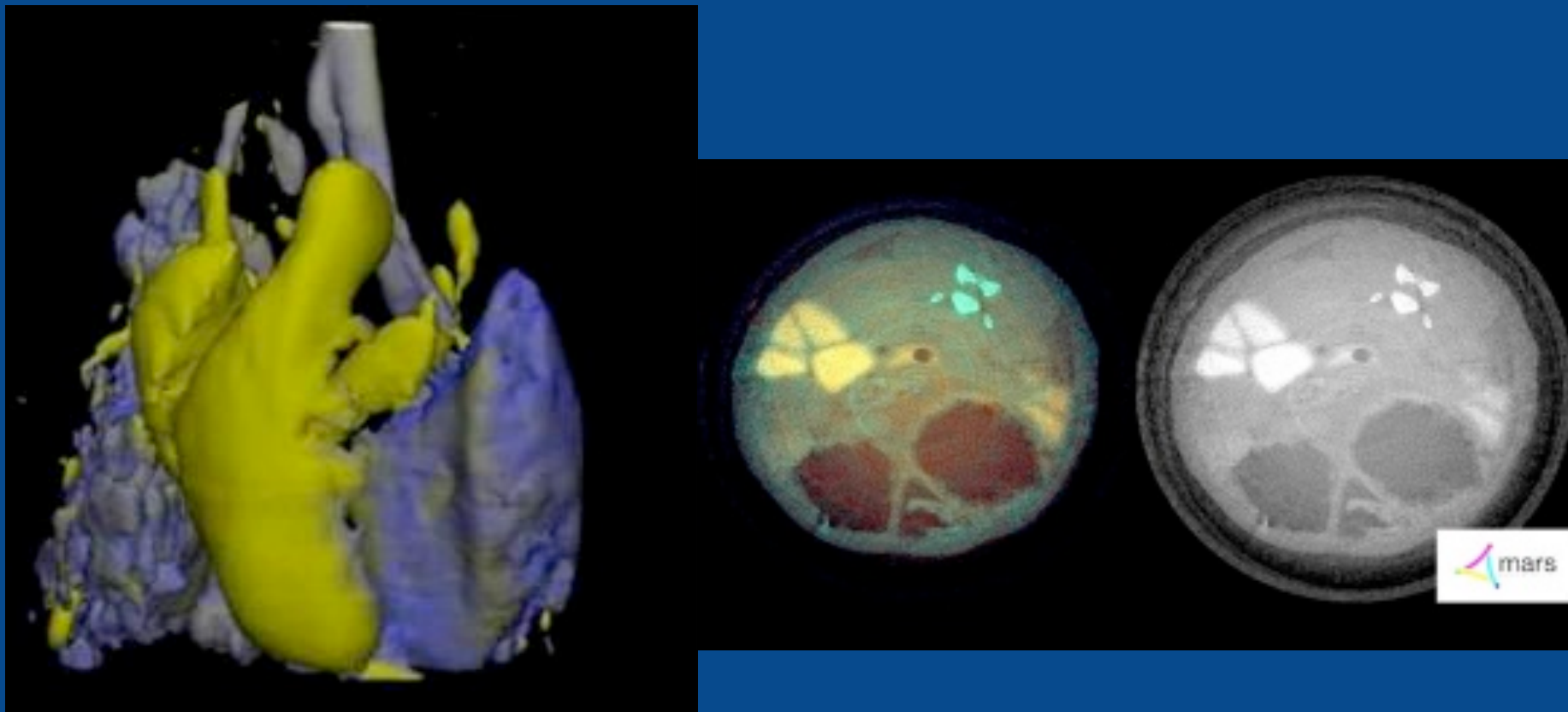
- Main properties:

- Fully digital device
- Very high space resolution
- Very fast photon counting
- Good conversion efficiency of low energy X-rays



Credits: Simon Procz, University of Freiburg

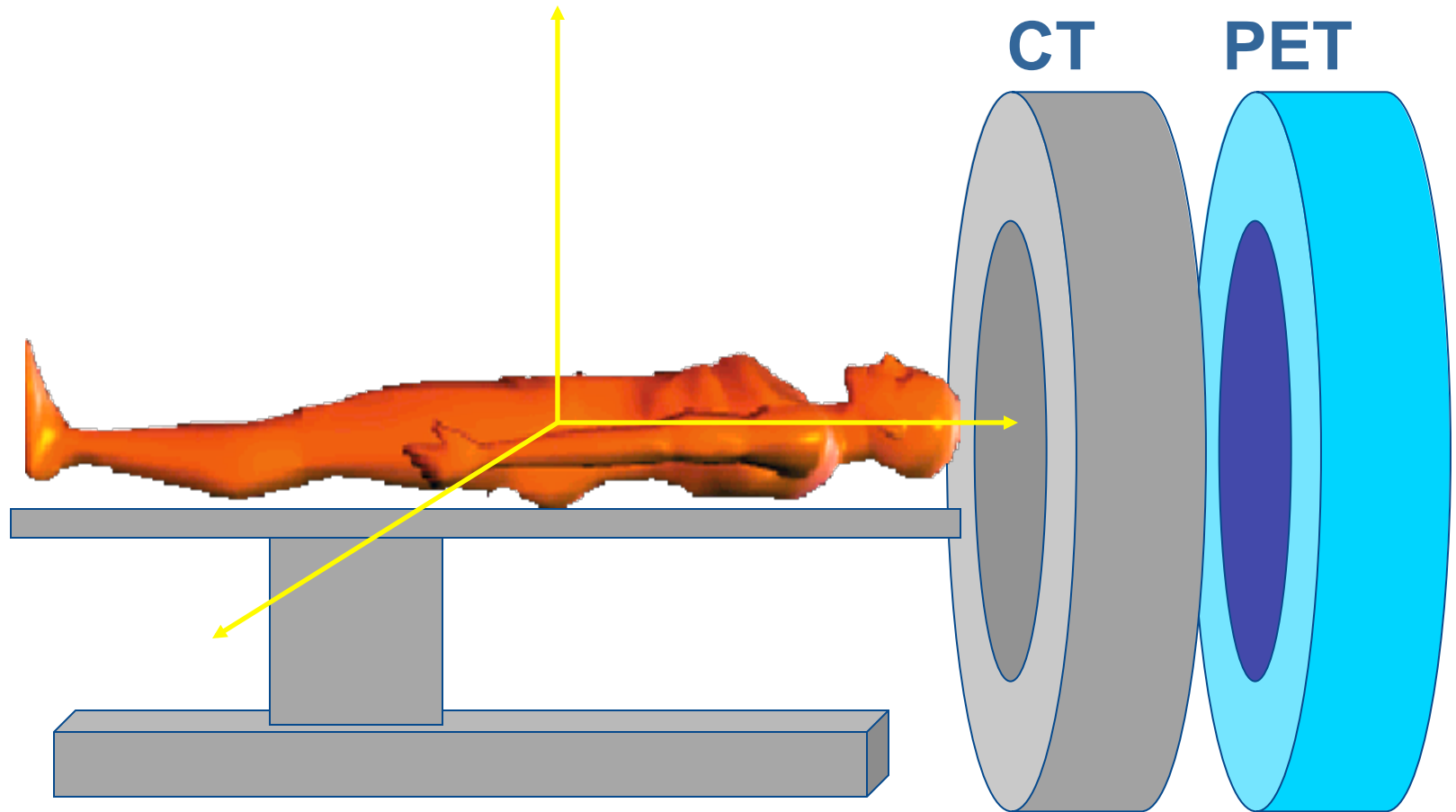
# MARS – MEDIPIX ALL RESOLUTION SYSTEM



courtesy of MARS Bioimaging Ltd)

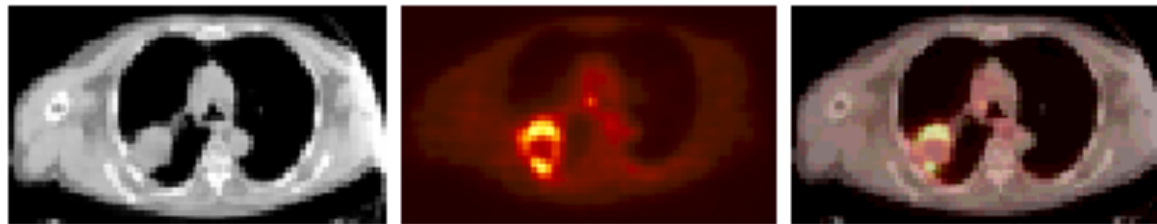
# Concept of PET-CT

*David Townsend*



# Multi-modality imaging

Primary lung cancer imaged with the Dual/Commercial scanner. A large lung tumor, which appears on CT as a uniformly attenuating hypodense mass, has a rim of FDG activity and a necrotic center revealed by PET.



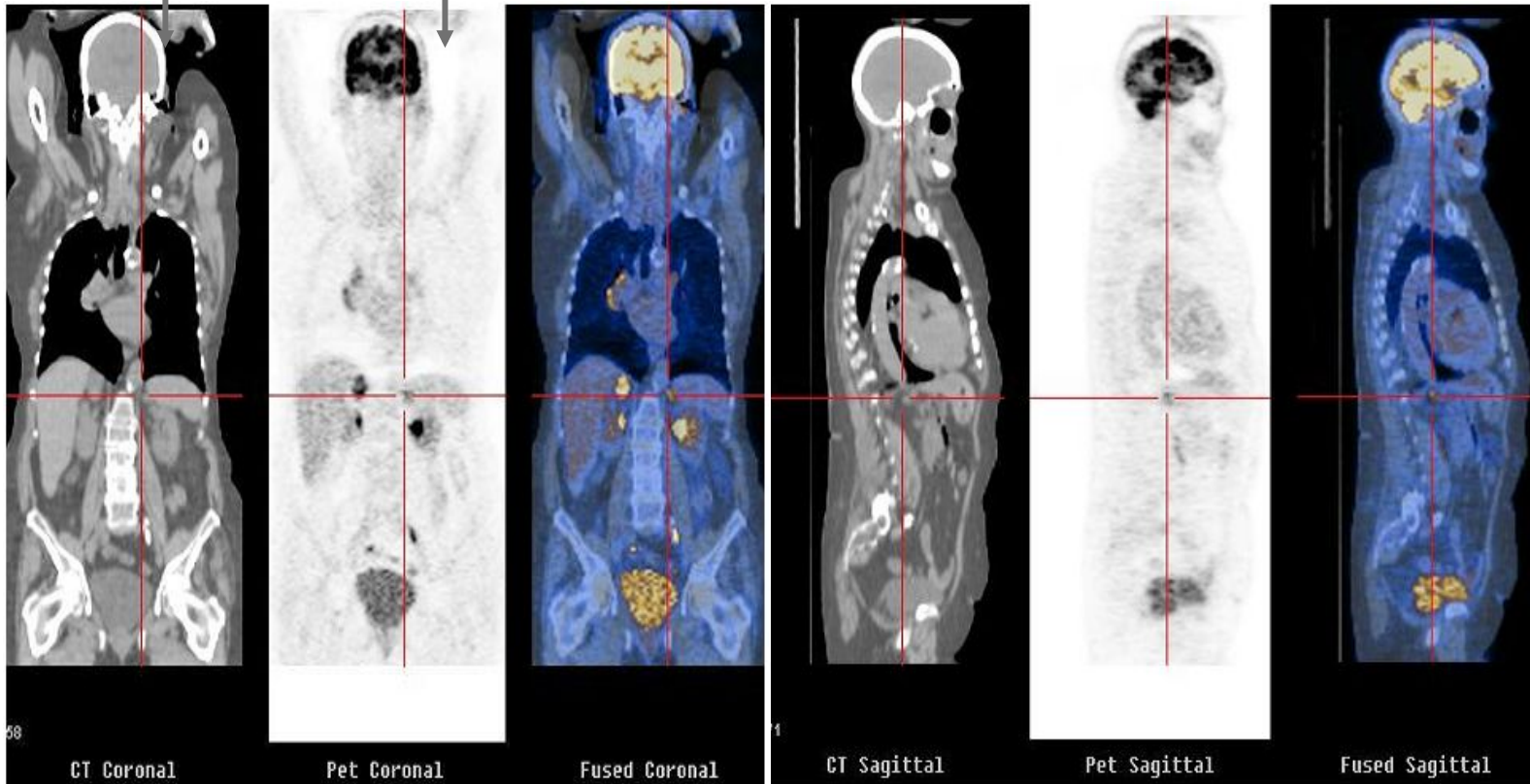
*Courtesy of David Townsend*

# Multimodality imaging: CT with PET

## Combining anatomic and functional imaging

morphology

metabolism



David Townsend, Former CERN Physicist

# Radiotherapy in 21st Century

## 3 "Cs" of Radiation

**Cure** (40-50% cancer cases are cured)

**Conservative** (non-invasive, fewer side effects)

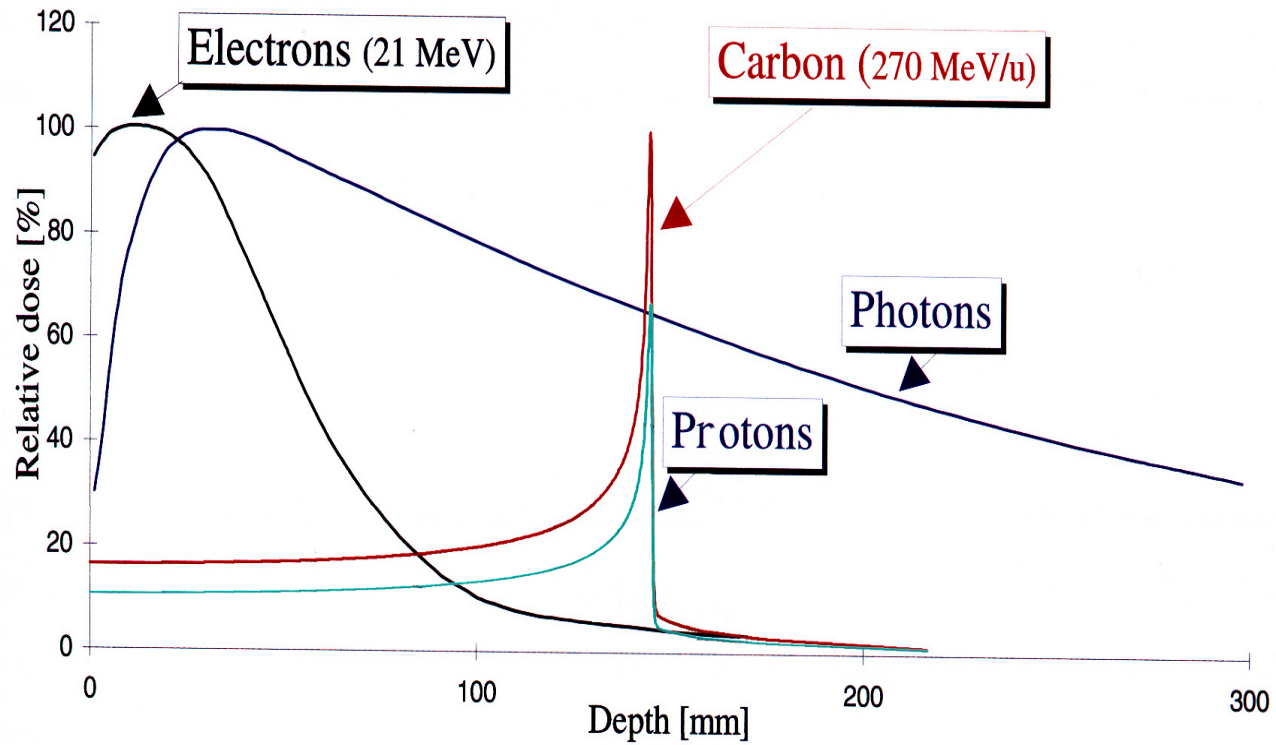
**Cheap** (about 10% of total cost of cancer on radiation)

*(J.P.Gérard)*

- About 50% patients are treated with RT
- No substitute for RT in the near future
- No of patients is increasing



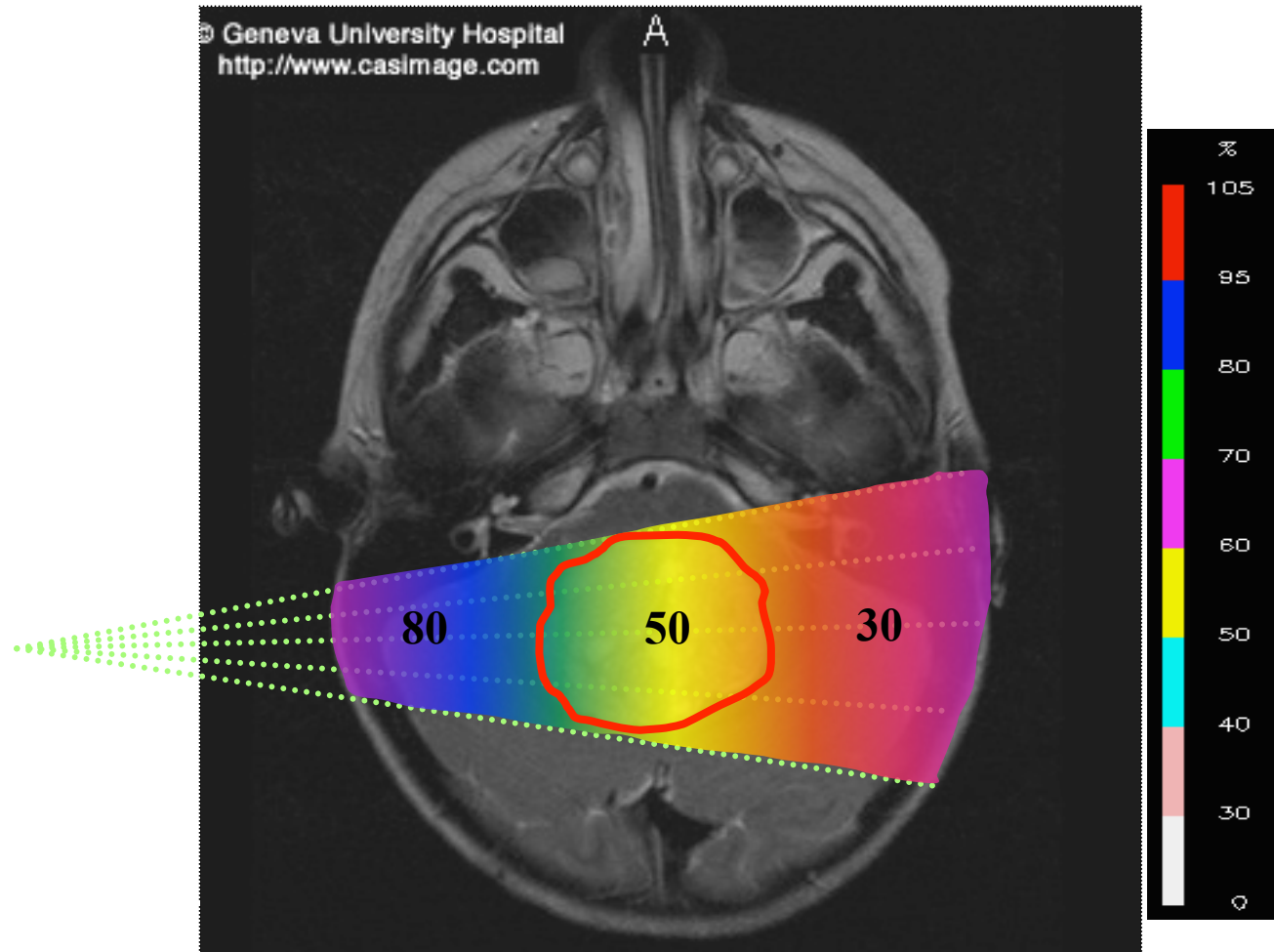
# Radiation therapy



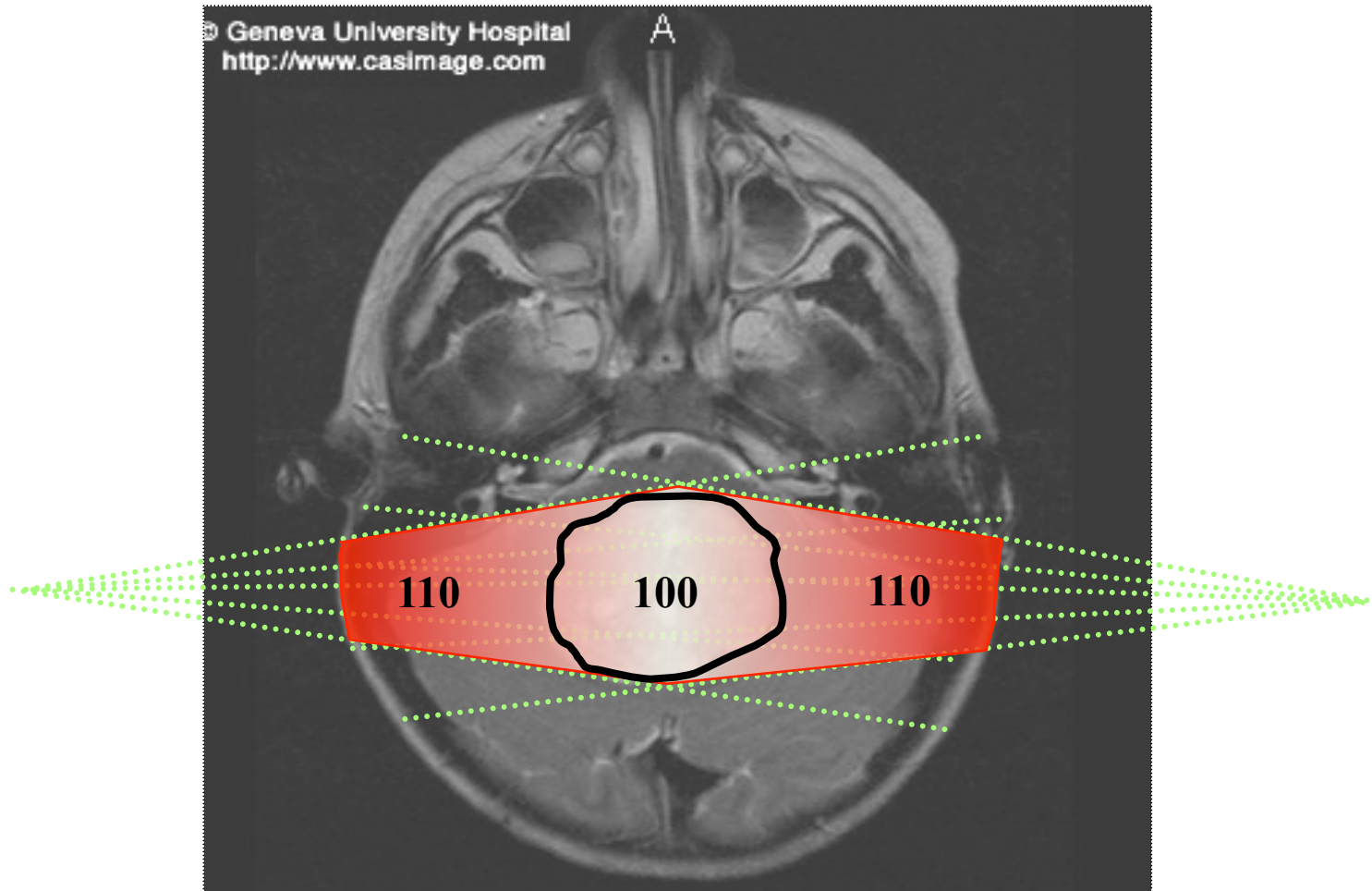
Depth in the body (mm)



# Single beam of photons



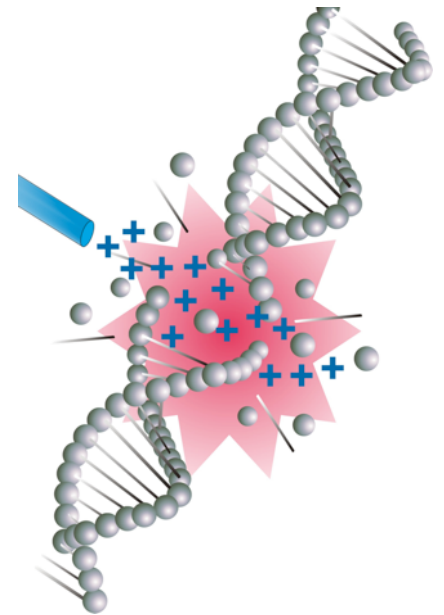
# 2 opposite photon beams



# Conventional external radiotherapy

- least expensive cancer treatment method
- most effective
- no substitute for RT in the near future
- rate of patients treated with RT is increasing

**In many patients cancer comes back in the same location after RT**

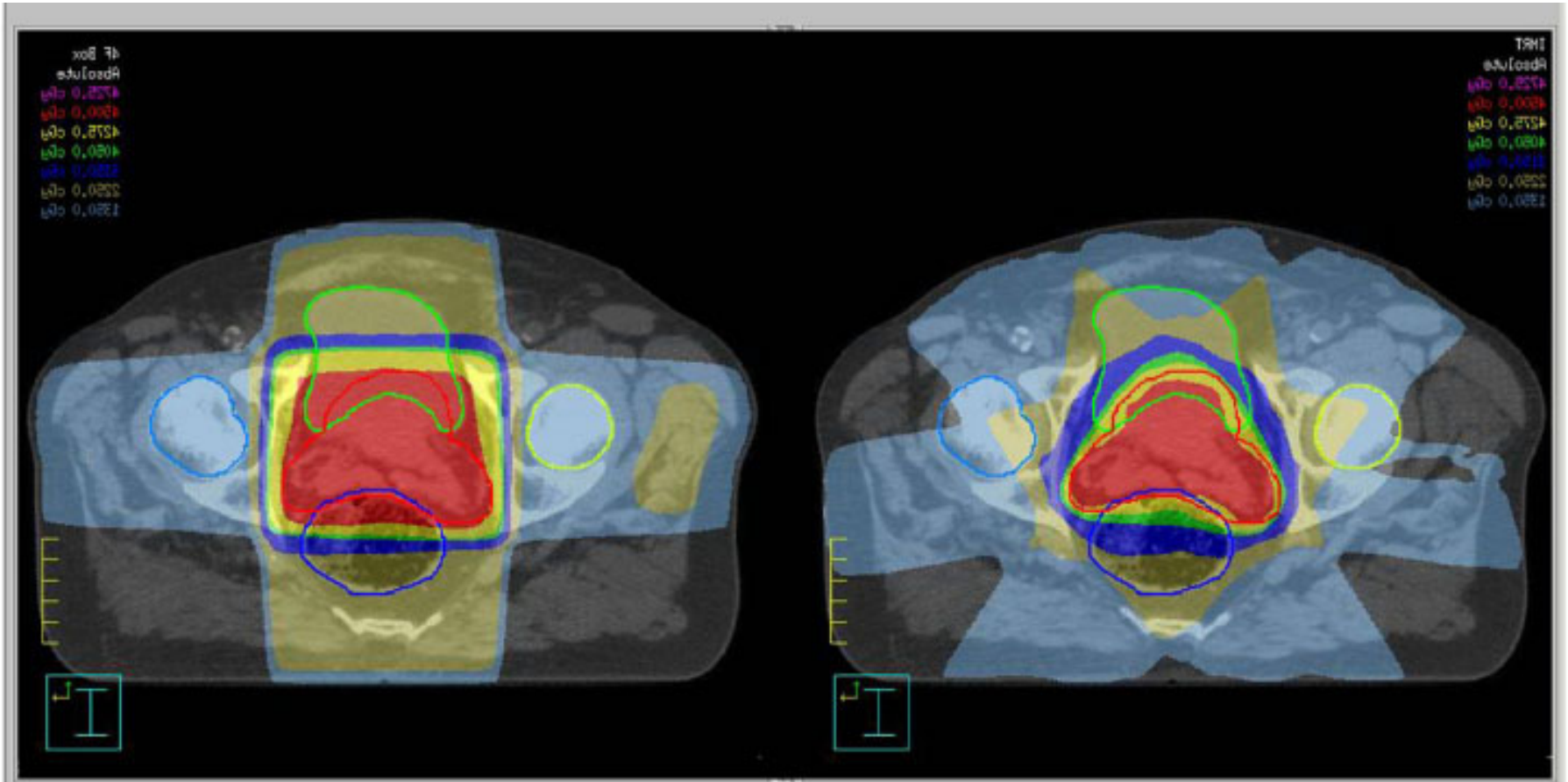


# Improving Cancer Outcome

*Earlier diagnosis, better tumour control, fewer side-effects*

- **Imaging**: accuracy, multimodality, real-time, organ motion
- **Accelerator technologies**: higher dose, more localised, real time targeting
- **Data**: analysis, image fusion/reconstruction, treatment planning, sharing, screening, follow-up patient ....
- **Biology**: basic research, fractionation, radio-resistance, radio-sensitization

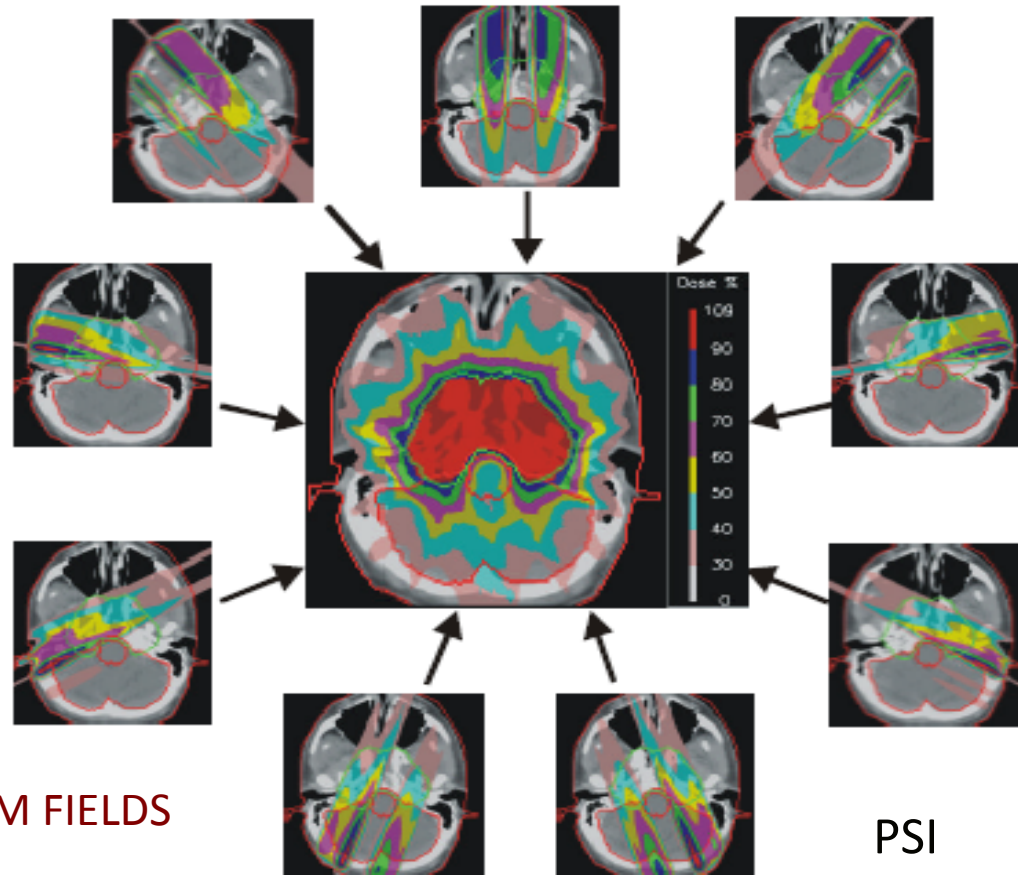
# Improved Delivery



1990s: 4 constant intensity fields

Current state of RT: **Intensity Modulated Radiotherapy (IMRT)** – Multiple converging field with planar (2D) intensity variations

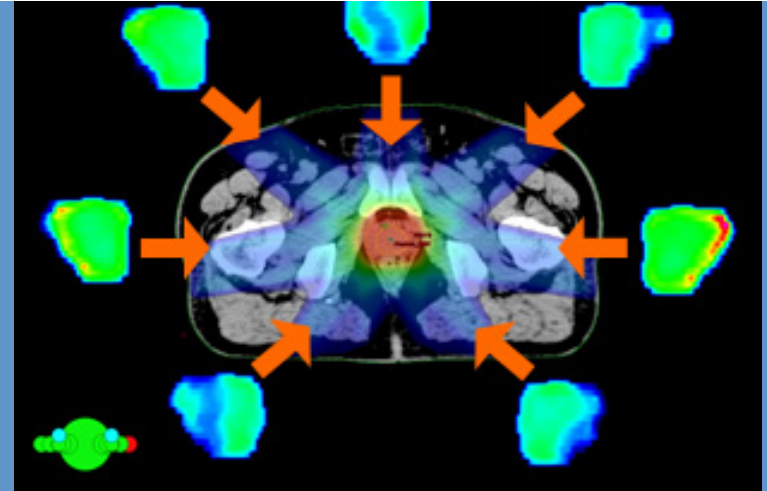
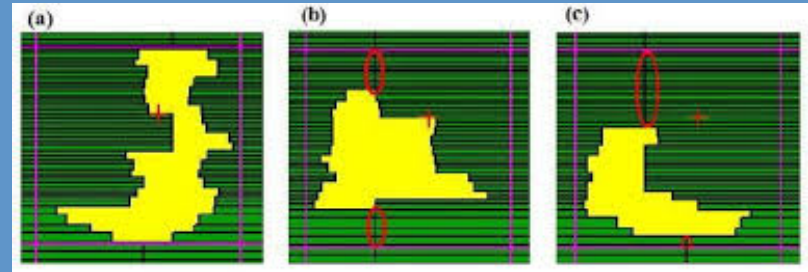
# Intensity Modulated Radiation Therapy



9 NON-UNIFORM FIELDS

PSI

# Modern X-ray Therapy

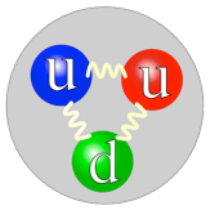


Current accelerator system with gantry, patient positioner and X-ray panels to acquire CBCT and planar X-rays.

Intensity modulation is achieved by changing the multi-leaf collimator (MLC) patterns (right), gantry rotation and dose rate. Thus, intensity modulation is achieved through mechanical (slow) means.

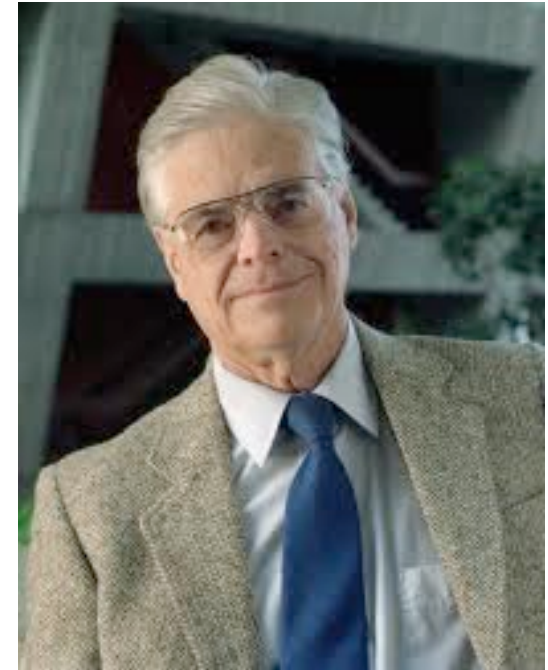
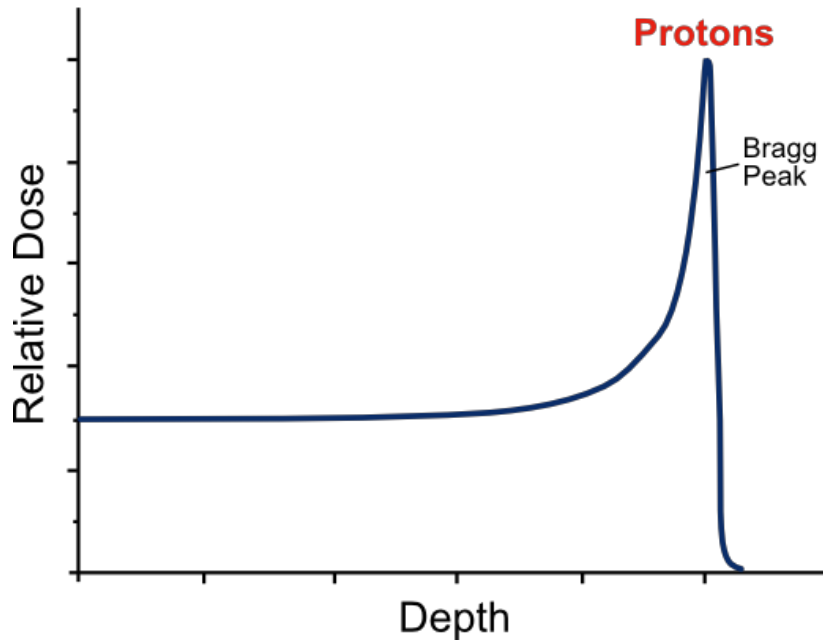
Could Hadron Therapy be the future?





# Future: Hadron Therapy?

- 1946: Robert Wilson  
Protons can be used clinically

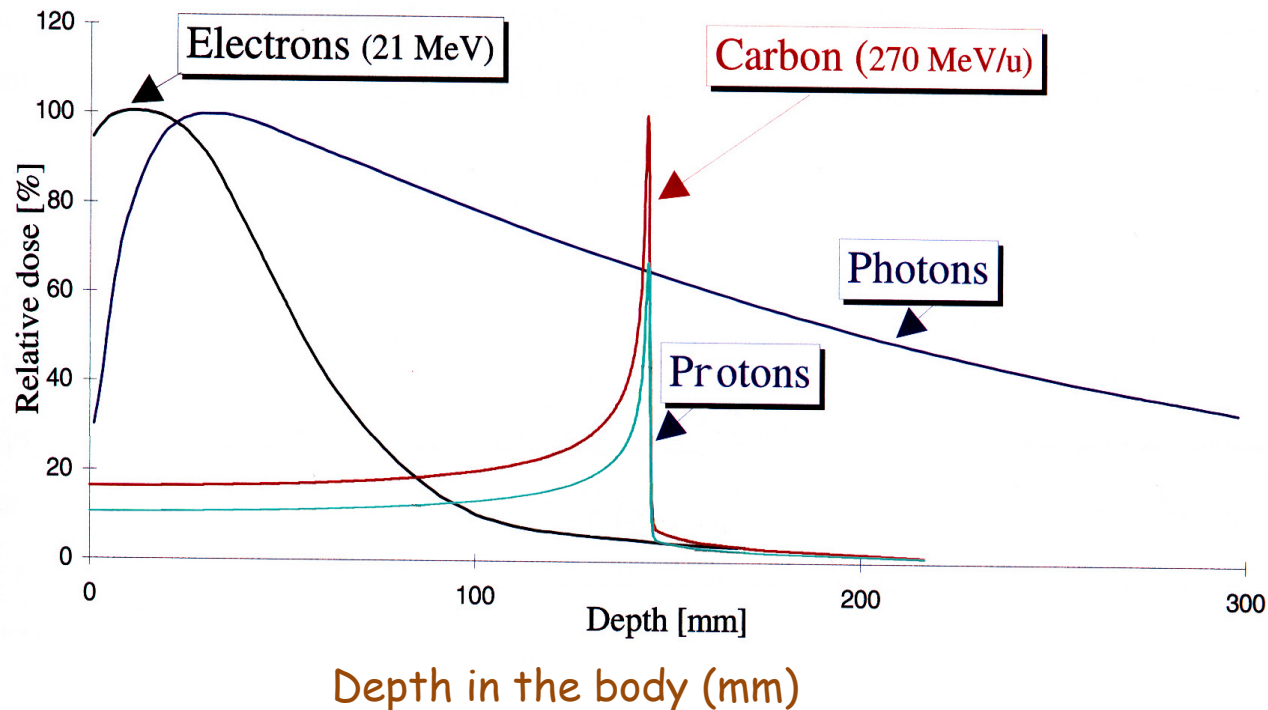


Robert Wilson

# Why Hadron Therapy?

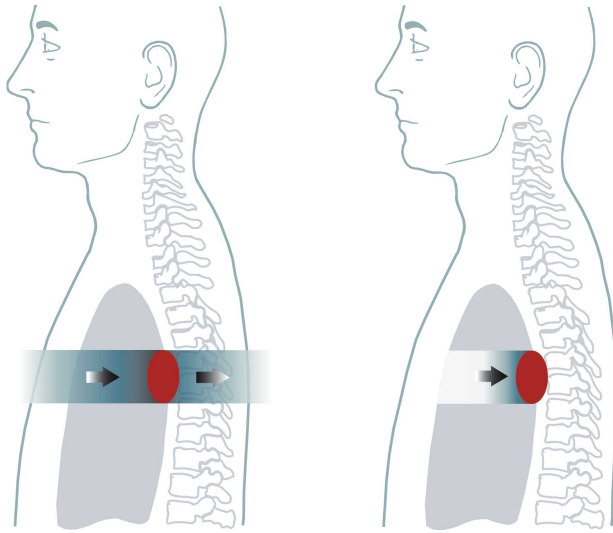
In 1946 Robert Wilson:

- Hadrons can be used clinically
- Accelerators are available
- Maximum radiation dose can be placed into the tumour
- Particle therapy provides sparing of normal tissues



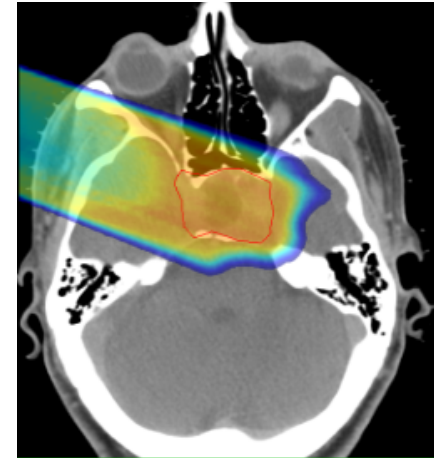
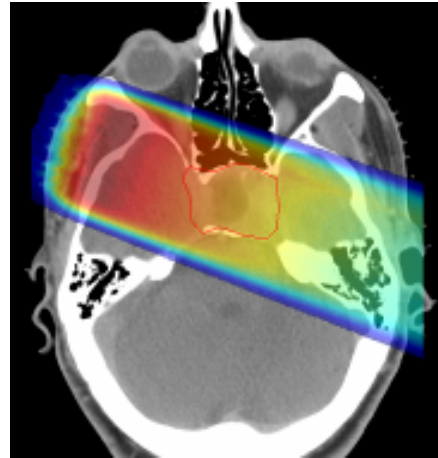
# Why hadrontherapy?

Image courtesy  
MedAustron



Conventional: X-Rays

Ion Radiation

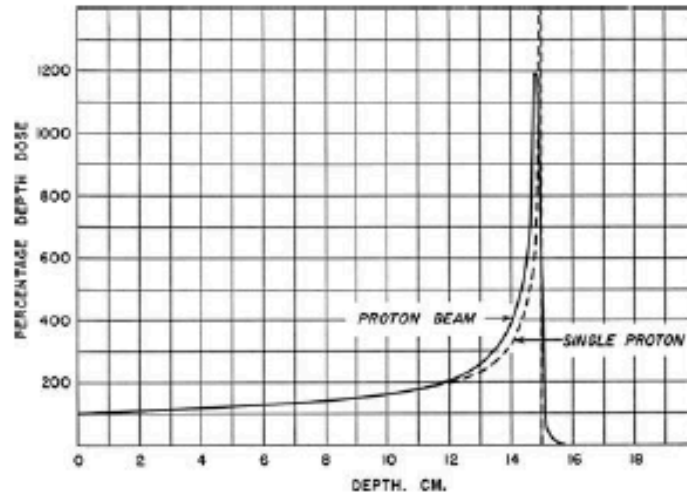


Spares normal healthy tissue

1932 - E. Lawrence  
First cyclotron



1946 – proton therapy  
proposed by R. Wilson

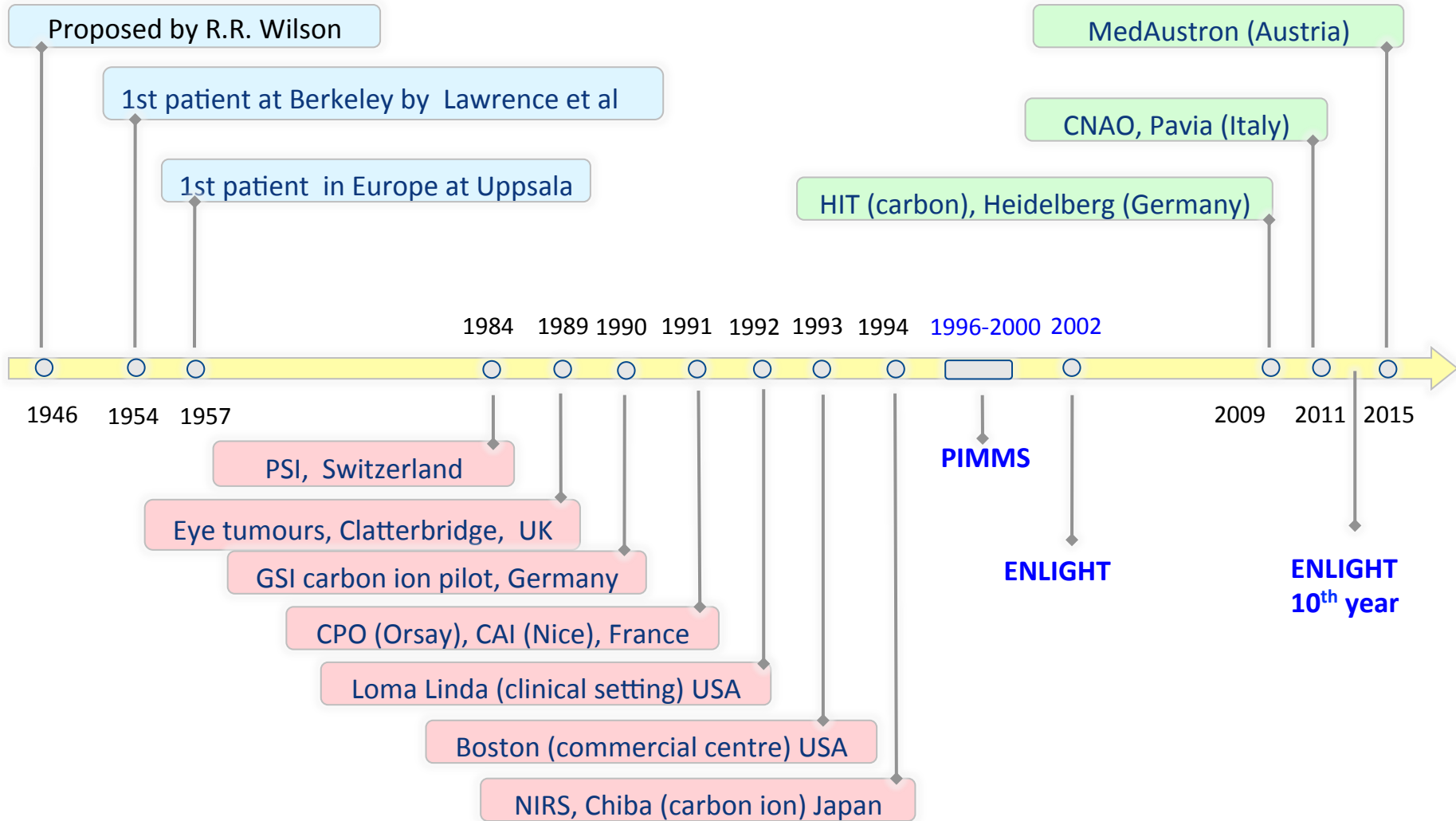


1954 – Berkeley treats  
the first patient

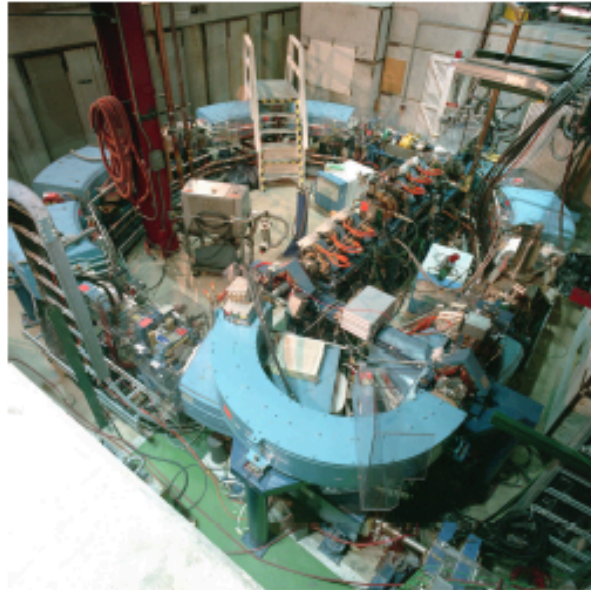


From physics...

# Particle therapy: a short history



1993- Loma Linda  
USA



1994 – HIMAC  
Japan



1997 – GSI  
Germany

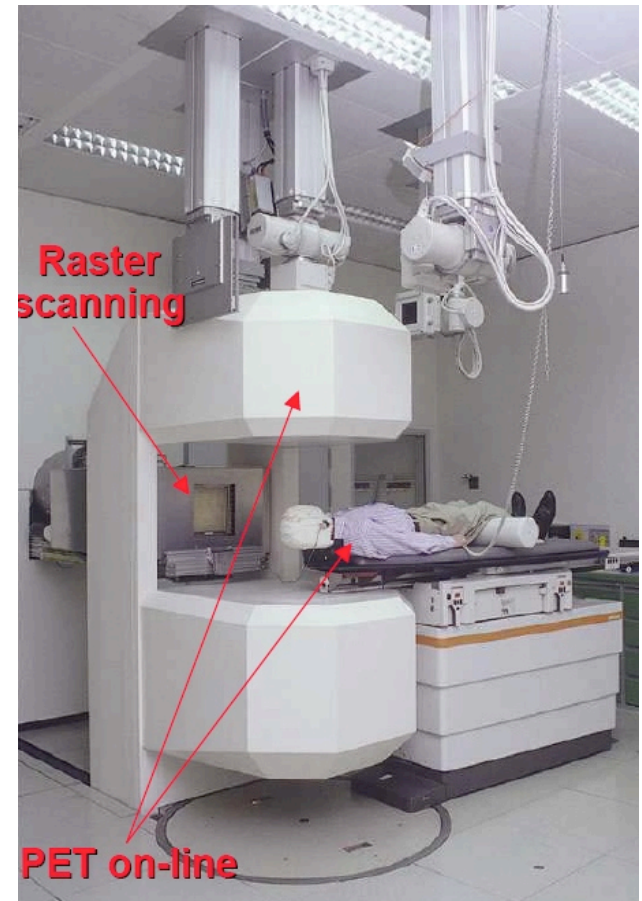


...to clinics

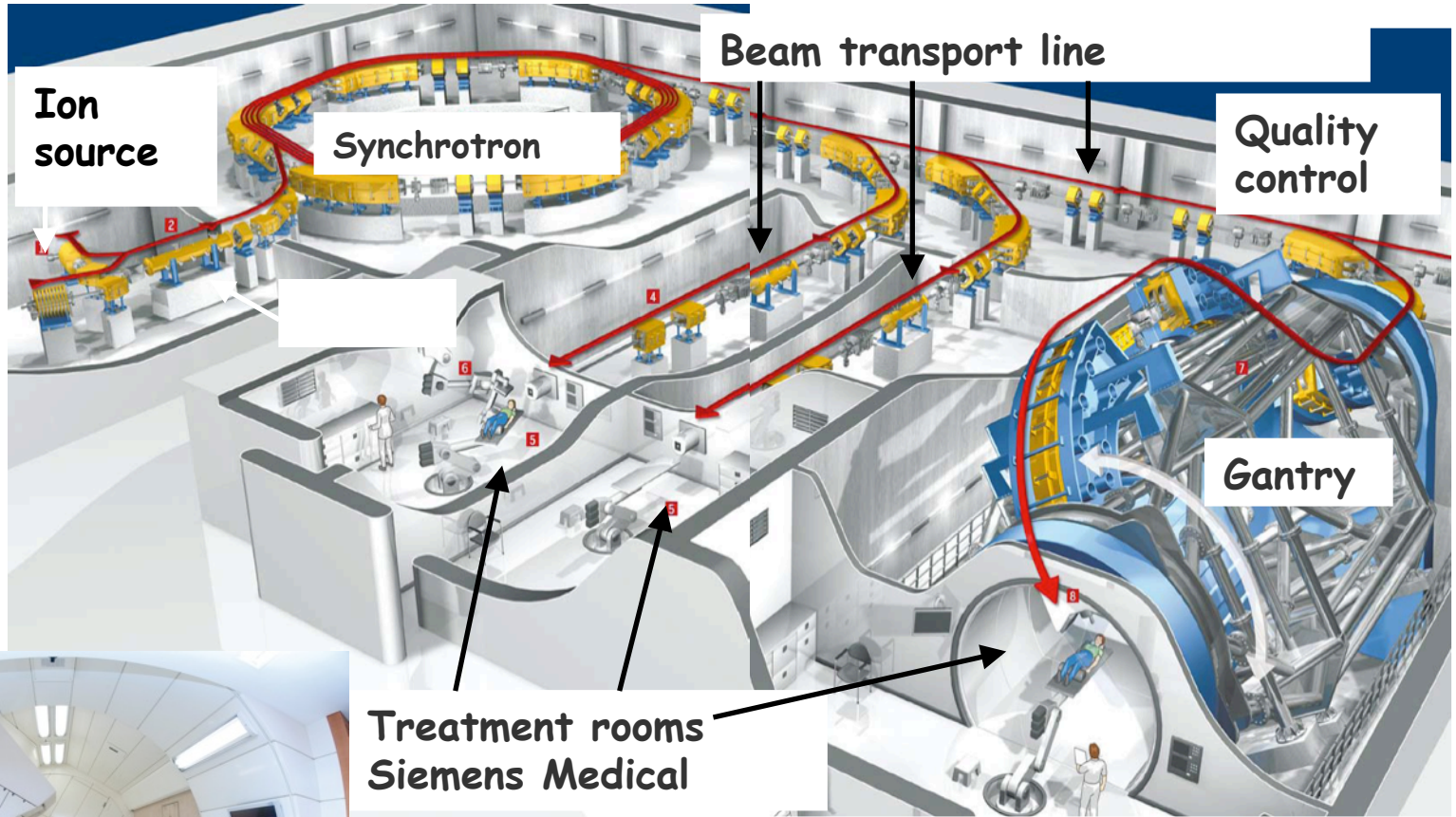
# Carbon ions: pilot project in Europe

GSI & Heidelberg

– 450 patients treated

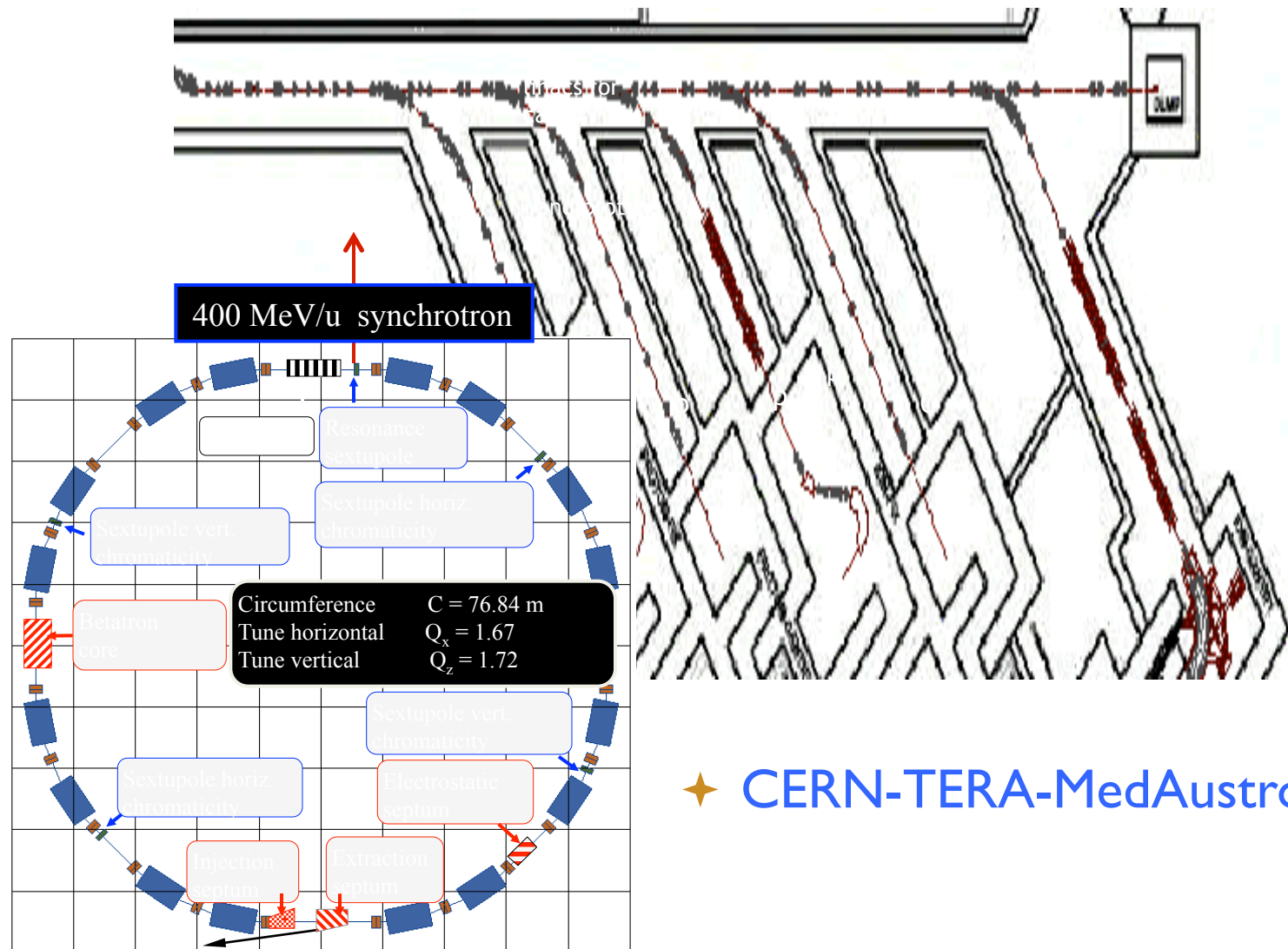


# HIT - Heidelberg





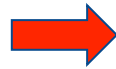
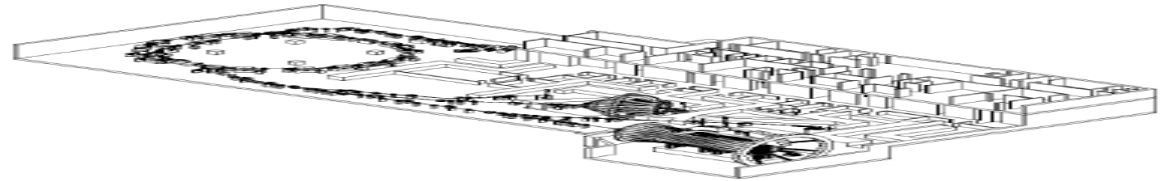
# PIMMS at CERN (1996-2000)



✦ CERN-TERA-MedAustron

# Accelerator Technologies

PIMMS 2000  
(coordinated by  
CERN) has led to:



fondazione CNAO

Treatment centre in Pavia, Italy.

**First patient treated with in 2011**

ebg MedAustron

Treatment centre in Wiener Neustadt, Austria,  
foundation stone in 2011, installation moved to  
MedAustron at beginning of 2012, first patient treated  
in 2016

# From PIMMS study to clinical reality



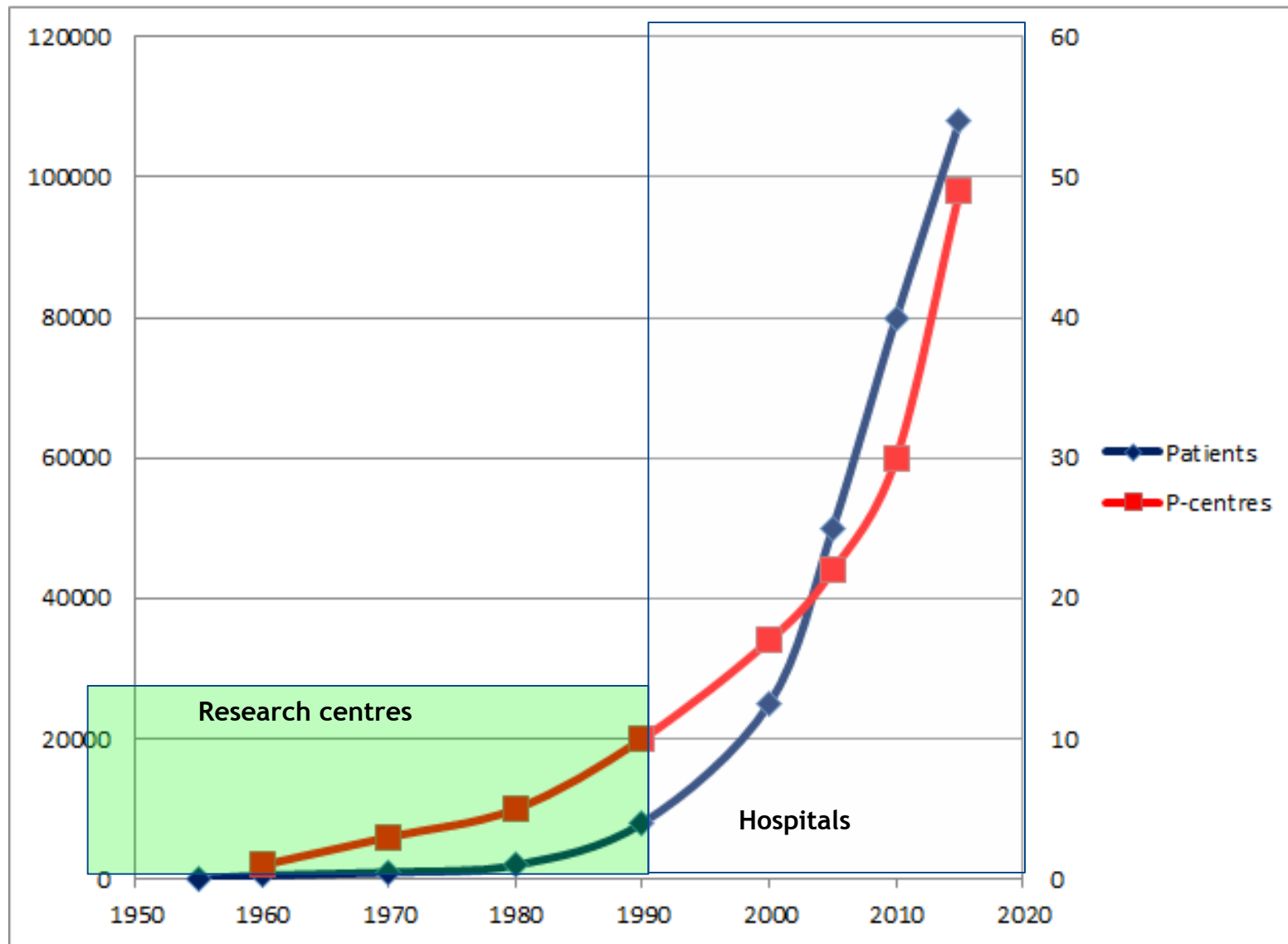
First patient with carbon ions Nov 2012



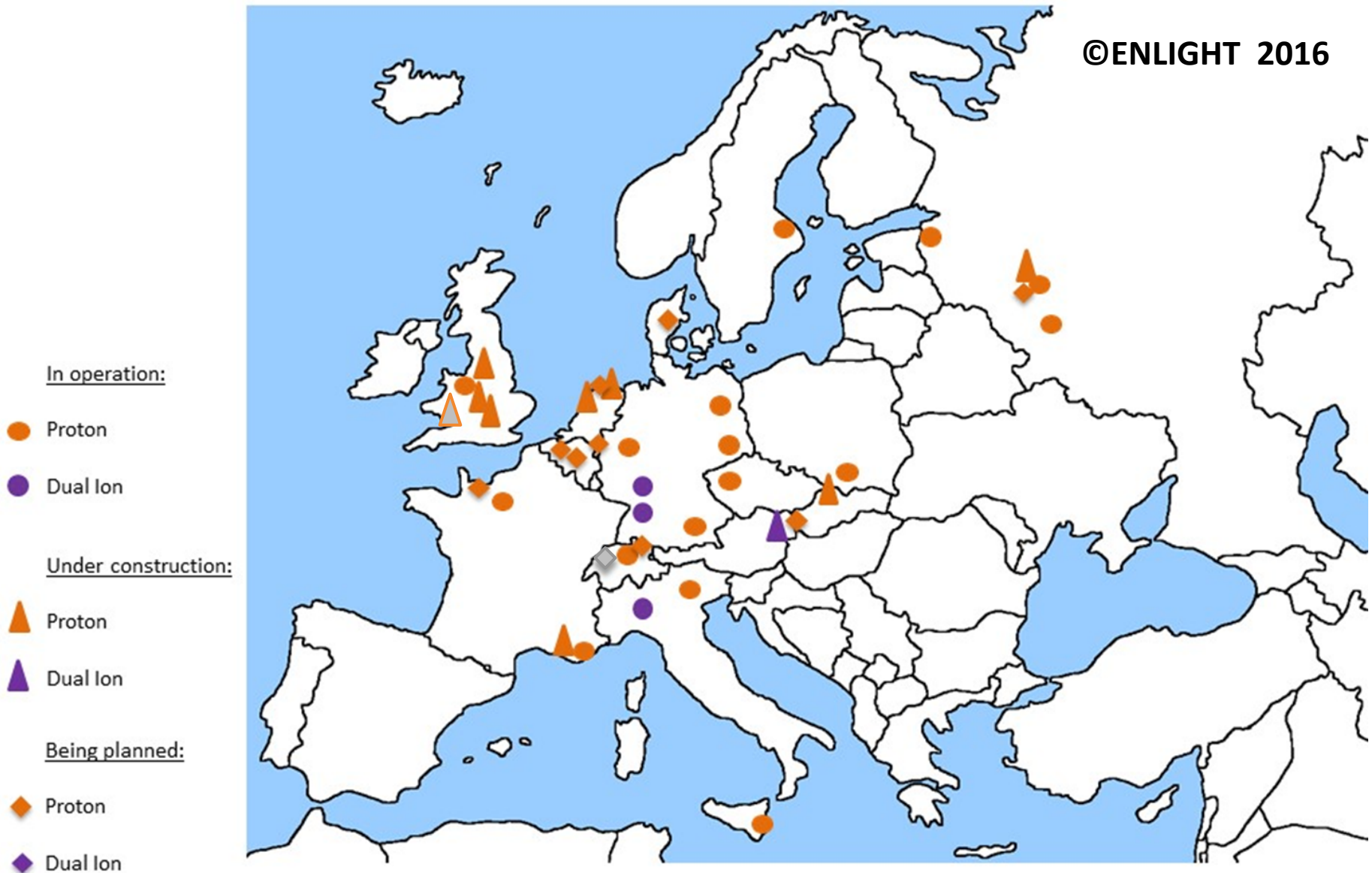
Treatment started in 2016



[Data from [www.ptcog.ch](http://www.ptcog.ch)]



# Particle therapy centres in Europe - 2016

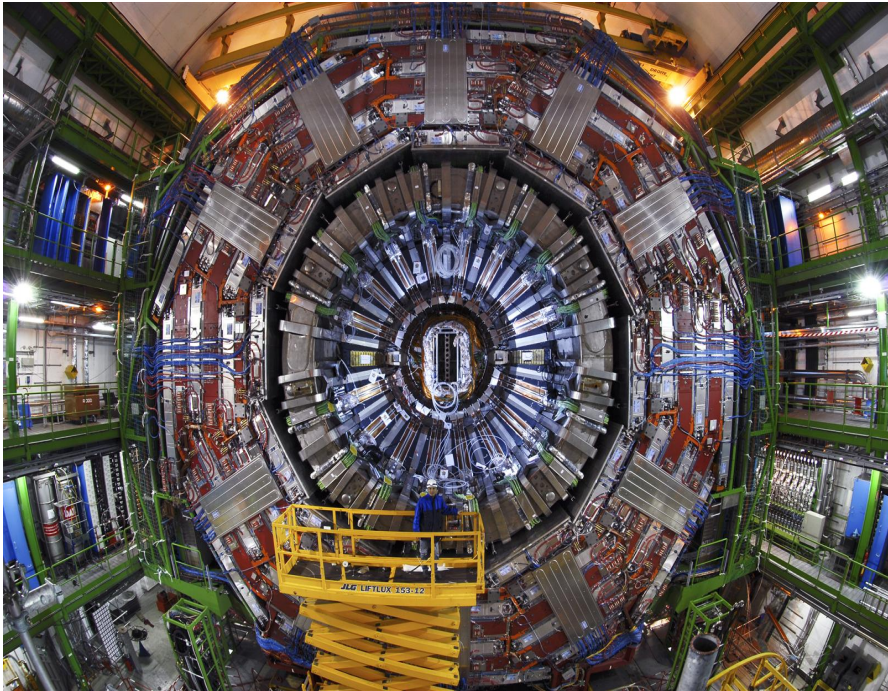


Manjit Dosanjh, CERN

**New Advances are on their way**

The tumour and only the tumour.....

# The next challenge: PET + MRI



**Detectors in magnetic field**



# Advances in Radiation Therapy

In the past two decades due to:

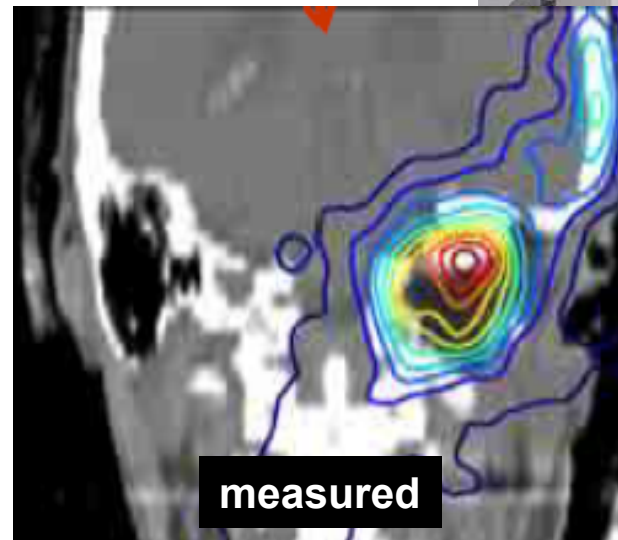
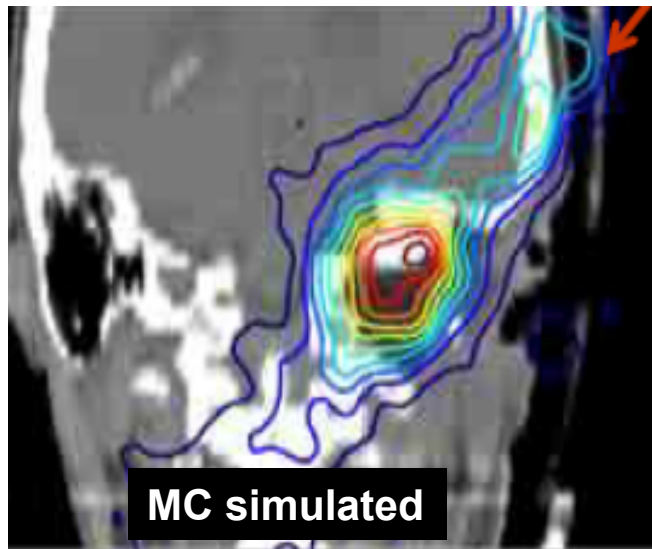
- improvements in imaging modalities,
- powerful computers and software and delivery systems have enabled:
  - Intensity Modulated Radiotherapy (IMRT),
  - Image Guided Radiotherapy (IGRT),
  - Volumetric Arc Therapy (VMAT) and
  - Stereotactic Body Radiotherapy (SBRT)
- Is Particle Therapy the future since the physics of X-rays cannot be changed?

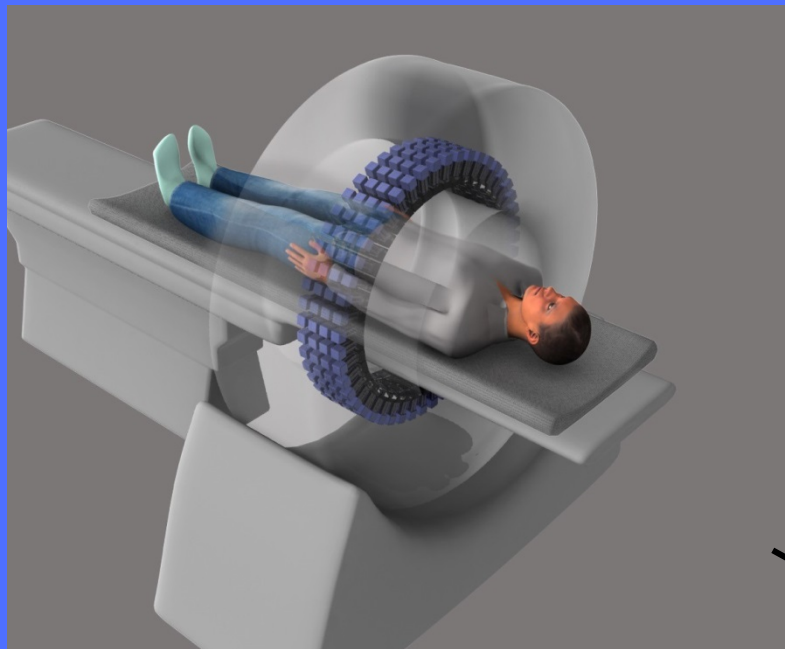
# The Bragg Peak

- Allows more precise allocation of the dose to the tumour
- BUT makes dosimetry and diagnostics more difficult because the energy is deposited preferentially inside the patient
- To take full advantage, we need improved diagnostics
  - To steer the beam spot by measurement of the location of the energy deposition
  - To control the dose (dosimetry)

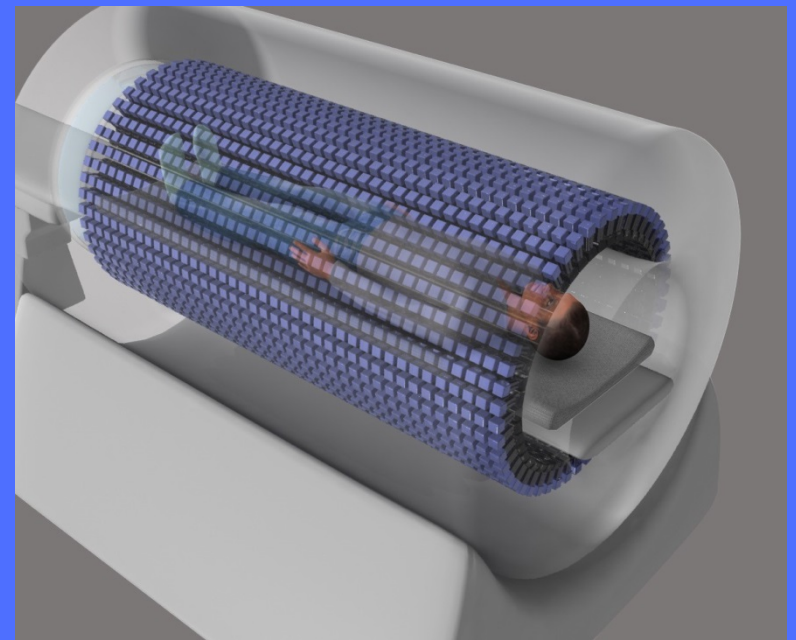
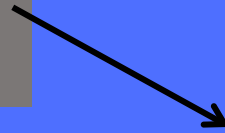
# Real-time monitoring

- In-beam PET @ GSI (Germany)
- MonteCarlo simulations
- Organ motion





**Conventional  
PET Scanner  
(2016)**



**EXPLORER  
Total Body PET Scanner  
(coming)**

“PET Is the most specific and sensitive means for imaging molecular pathways and molecular interactions in humans”.

<http://virtual-hadron-therapy-centre.web.cern.ch/virtual-hadron-therapy-centre/>

[cern.ch/virtual-hadron-therapy-centre](http://cern.ch/virtual-hadron-therapy-centre)



[cern.ch/virtual-hadron-therapy-centre](https://cern.ch/virtual-hadron-therapy-centre)

**How to go from no radiotherapy to high quality radiotherapy globally: Challenging Environments**

# Reality in numbers.....

- No radiotherapy in 36 countries
- HIC have over 60% of all teletherapy machines and 16% of the world population
- LIC and LMIC have less than 10% of teletherapy machines which serve 50% of the world

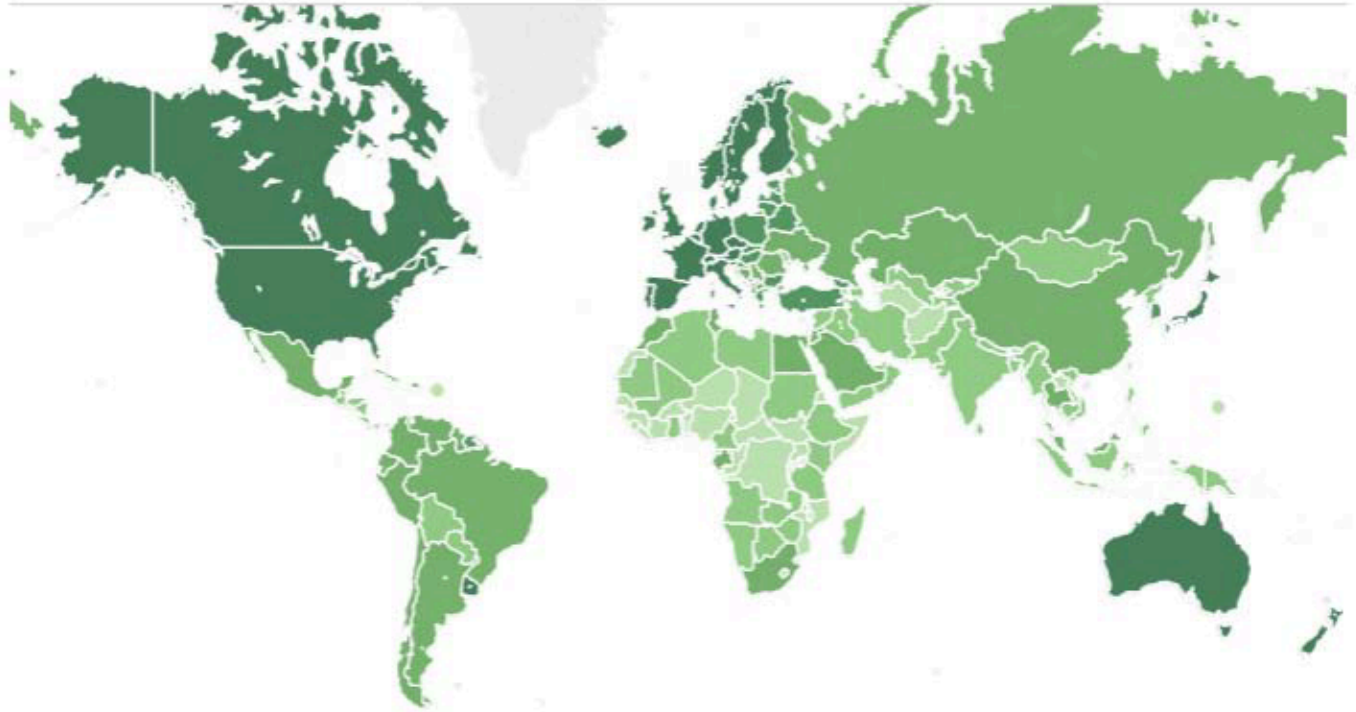


# RT is an essential part of the cancer treatment

## Globally: no of machines per 1 million inhabitants

Number of Radiotherapy Machines Per Million People

(Updated on : 01/06/2017 07:17:12)



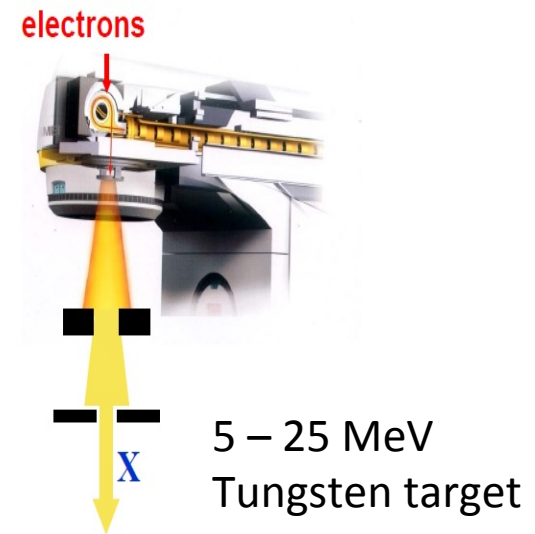
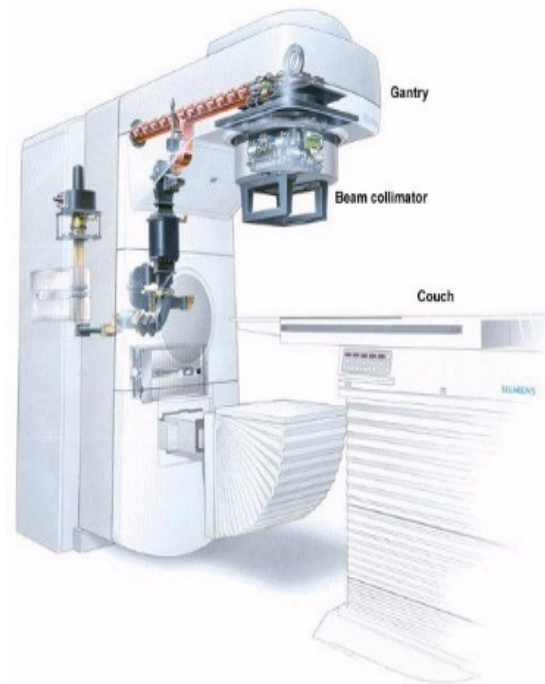
© OpenStreetMap contributors

no reported machi... less than 1 between 1 and 3 between 3 and 5 5 and more

# The most widespread accelerator

Electron Linac (linear accelerator) for radiotherapy (X-ray treatment of cancer)

More than 10'000 in use

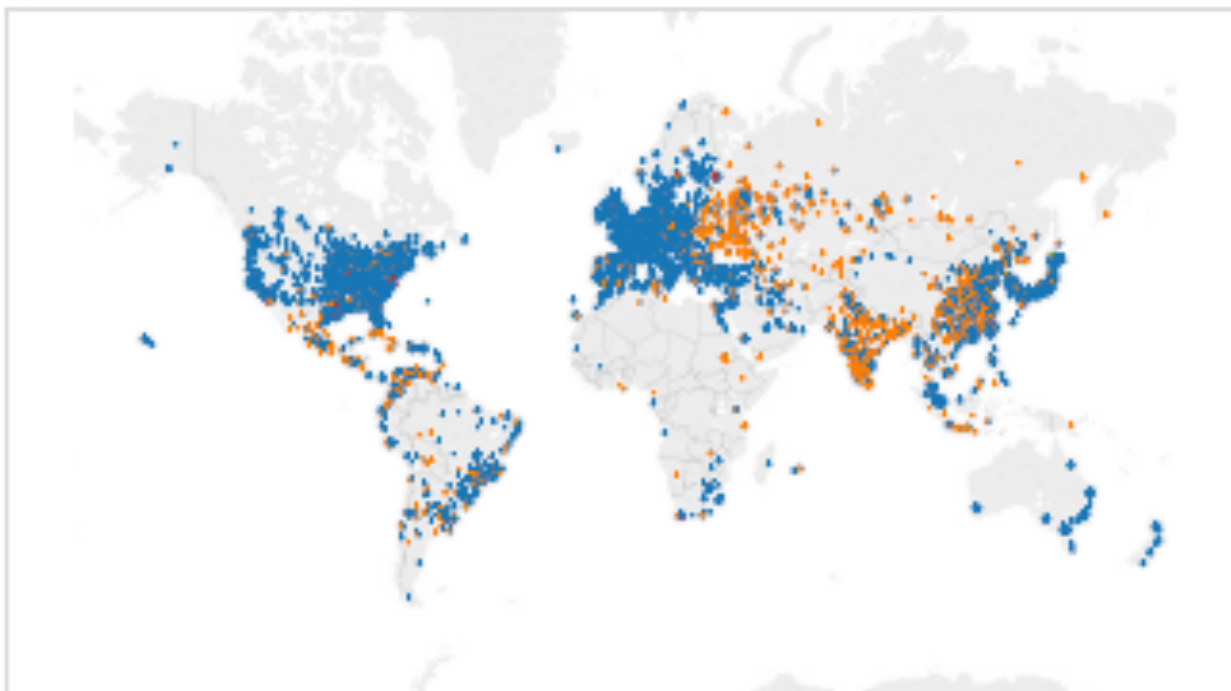


2000 patients/year every  
in 1 million inhabitants

Commercially, widely available in all major hospitals

# World wide radiotherapy coverage

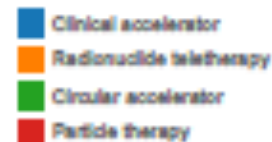
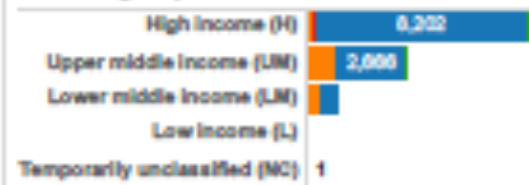
Radiation therapy centers  
(Updated on : 6/1/2017 7:11:24 AM)



Equipment type  
(Updated on : 6/1/2017 7:11:24 AM)



Income groups



Countries	RT centers	Equipment	Linac	Radionuclide Therapy	Circular Accelerator	Particle Therapy
<b>139</b>	<b>7041</b>	<b>13755</b>	<b>11440</b>	<b>2186</b>	<b>14</b>	<b>115</b>

## Thanks to:

- U. Amaldi, CERN & TERA
- E. Blakely, LBNL, USA
- M Durante, Trento, Italy; Kevin Prise, Queens, UK
- HIT, CNAO, MedAustron, PSI, ENLIGHT colleagues
- KT. Medipix, Crytal Clear, Fluka, GEANT
- [E-Book: From Particle Physics to Medical Applications](http://iopscience.iop.org/book/978-0-7503-1444-2)  
<http://iopscience.iop.org/book/978-0-7503-1444-2>

## Useful links

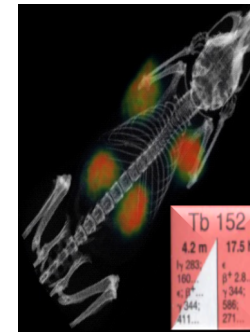
- [cern.ch/crystalclear](http://cern.ch/crystalclear)
- [cern.ch/enlight](http://cern.ch/enlight)
- [cern.ch/virtual-hadron-therapy-centre](http://cern.ch/virtual-hadron-therapy-centre)
- <https://cds.cern.ch/record/2002120?ln=en>
- <http://cds.cern.ch/record/1611721>
- [cern.ch/knowledgetransfer](http://cern.ch/knowledgetransfer)
- [cern.ch/medipix](http://cern.ch/medipix)
- [cern.ch/twiki/bin/view/AXIALPET](http://cern.ch/twiki/bin/view/AXIALPET)
- [cern.ch/medauston](http://cern.ch/medauston)
- [www.fluka.org/fluka.php](http://www.fluka.org/fluka.php)
- <http://geant4.cern.ch/>

# Terbium: Swiss Army Knife of Nuclear Medicine

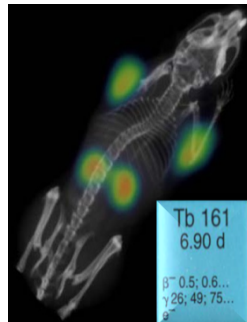
**$^{149}\text{Tb}$ -therapy**



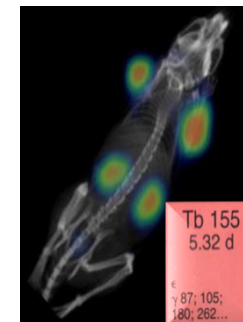
**$^{152}\text{Tb}$ -PET**



**$^{161}\text{Tb}$ -therapy  
& SPECT**



**$^{155}\text{Tb}$ -SPECT**



ISOLDE



NEUTRONS FOR SCIENCE

Müller et al., JNM 2012

# Use of Accelerators Today

## General industrial use:

Sterilisation, imaging

## Research Accelerators:

Particles, synchrotron light used in biomedical, physics, chemistry, biology, medical research.

## Radiotherapy:

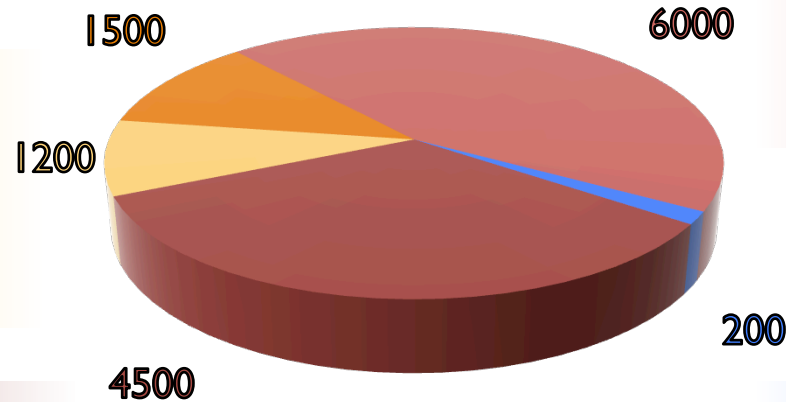
Cancer treatment with X-rays, protons and other particles.

## Ion implantation, surface modifications:

Controlled semiconductor doping; Changing properties of surfaces

## Radioisotope production:

Cancer treatment; imaging organs for medical use.



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~ 9000 of the 17000 accelerators operating in the World today are used for medicine.