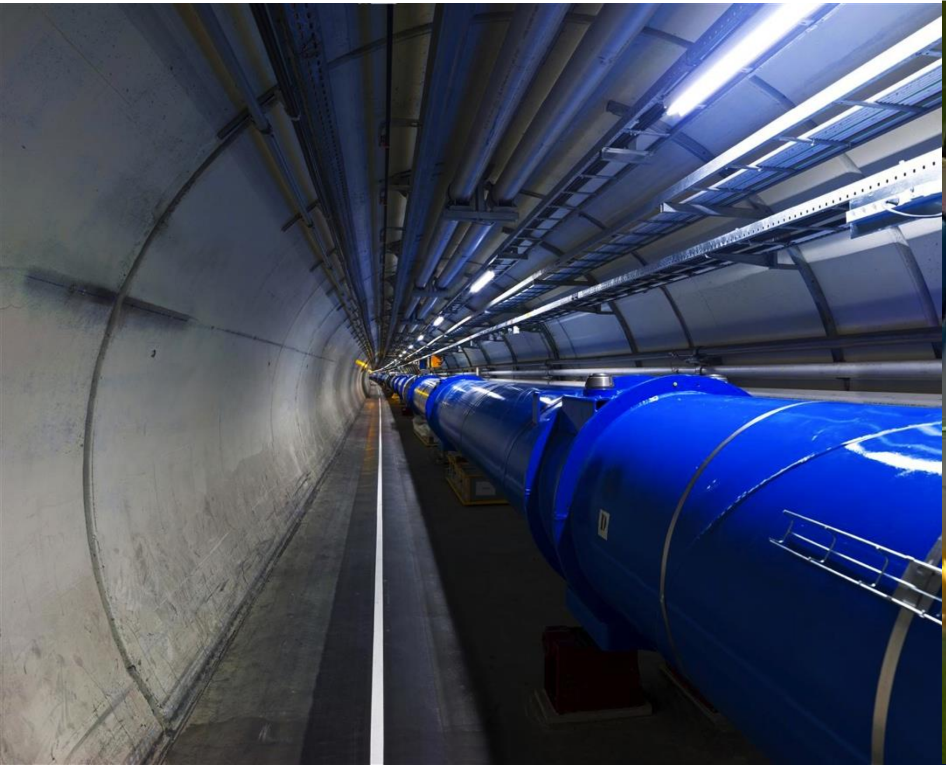
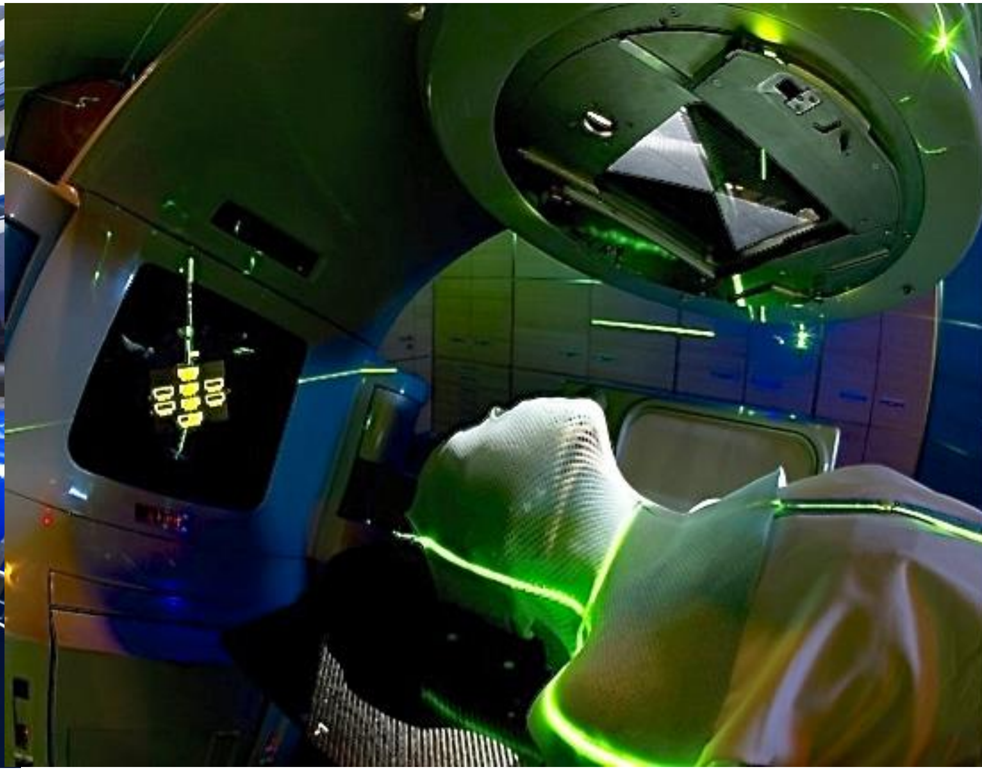
From Accelerator and Particle Physics to Cancer Treatment

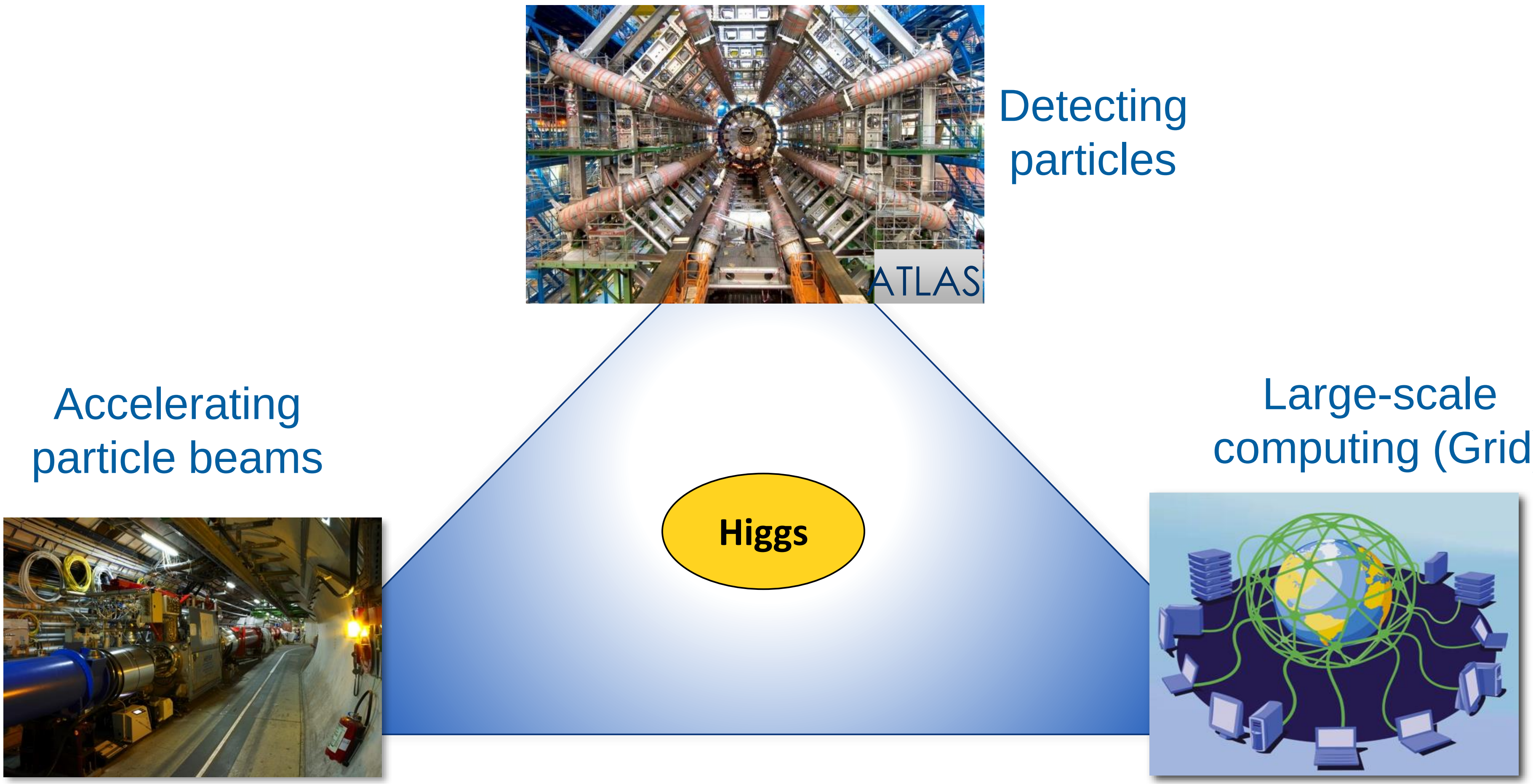


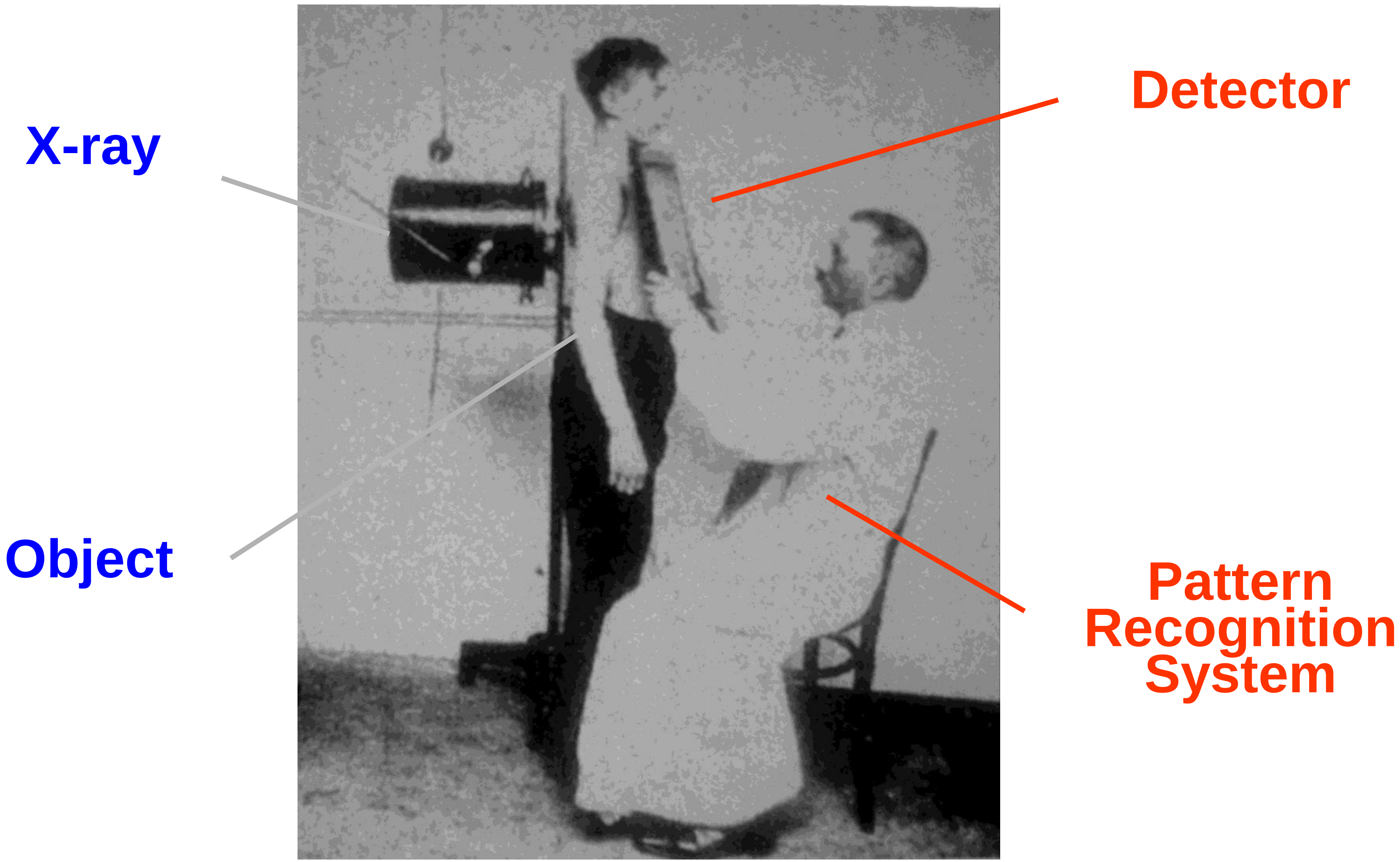


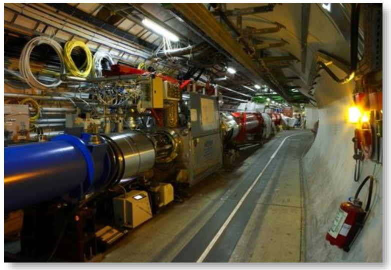
Manjit Dosanjh, CERN

APPEAL, July 2019

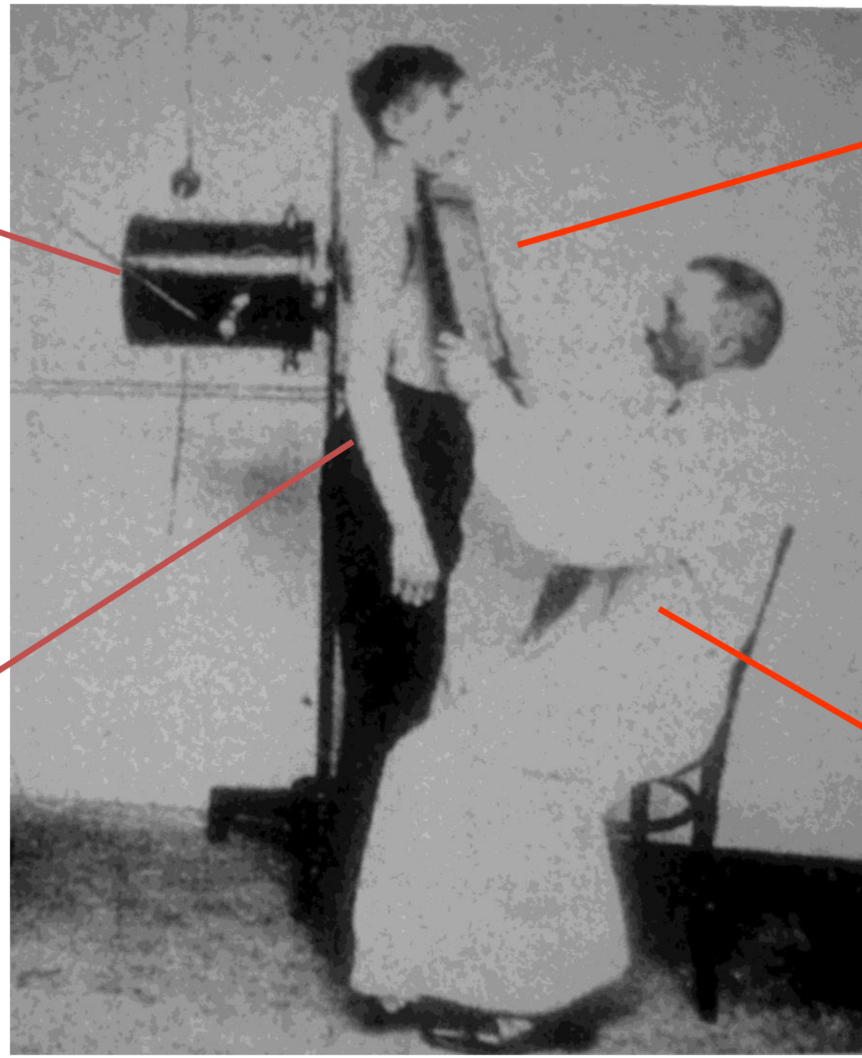
Physics technologies



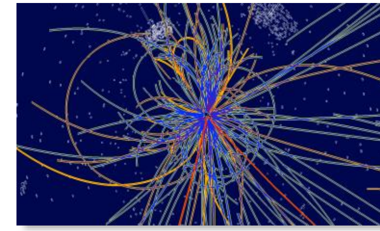

X-ray
Object
Detector
Pattern Recognition System



X-ray source



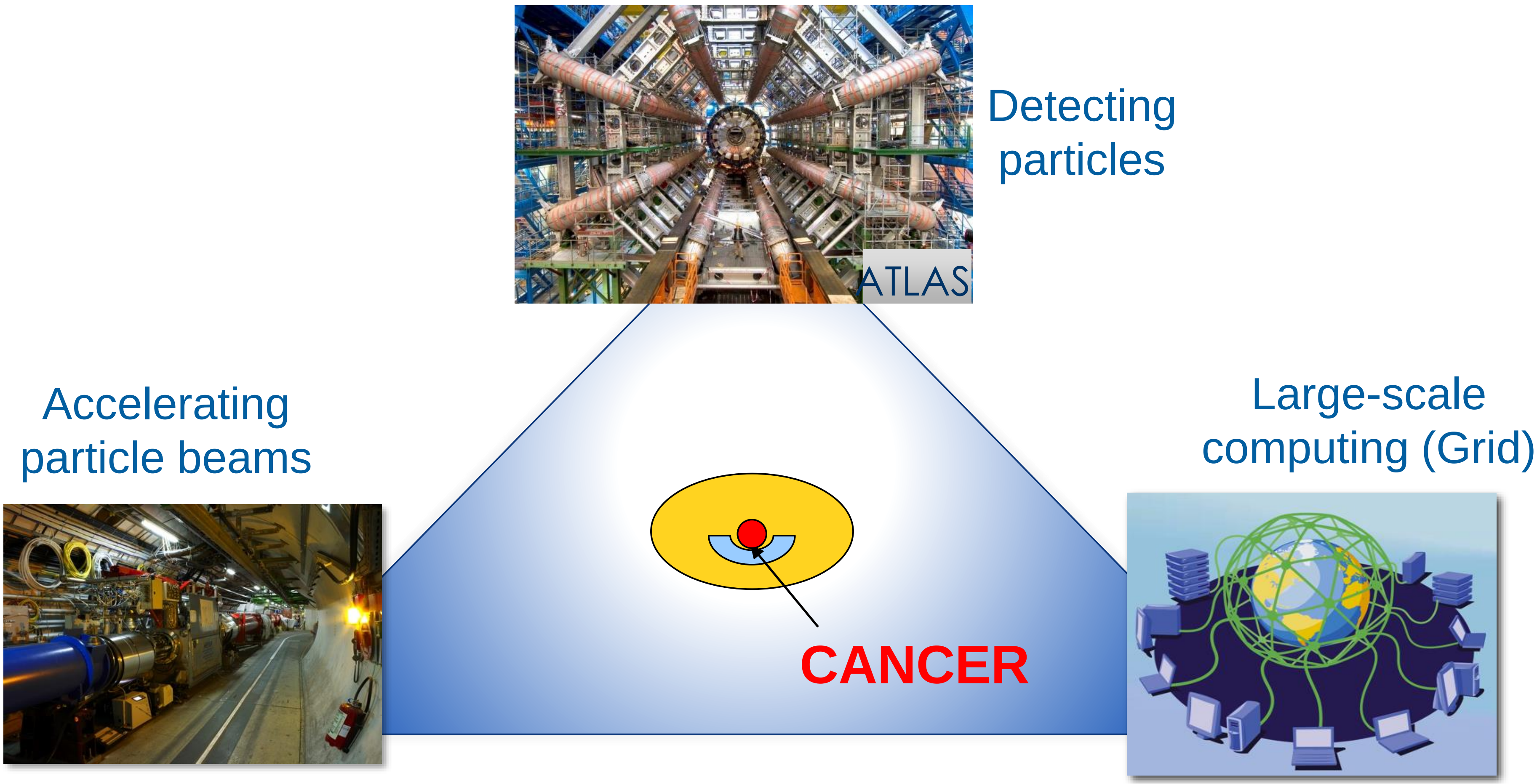
Object (Higgs)



Detector

Pattern Recognition System

Physics technologies for cancer



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?

The Challenge of Treatment

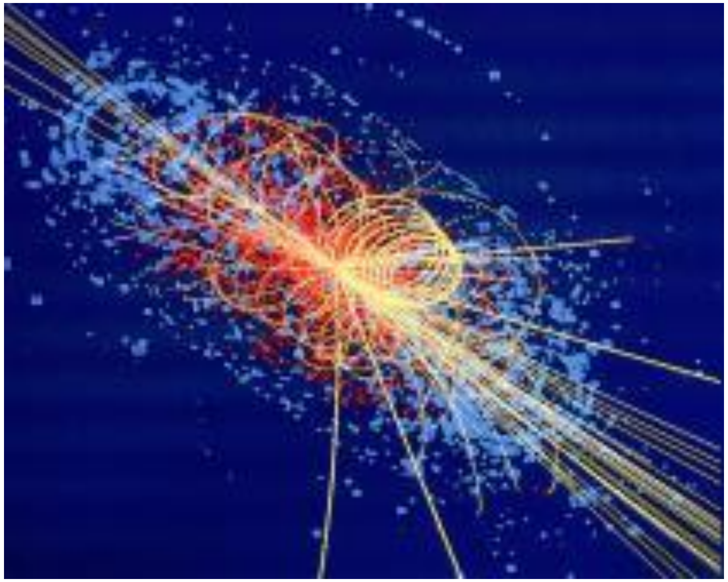
Ideally one needs to treat:

– 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.

Art of seeing………

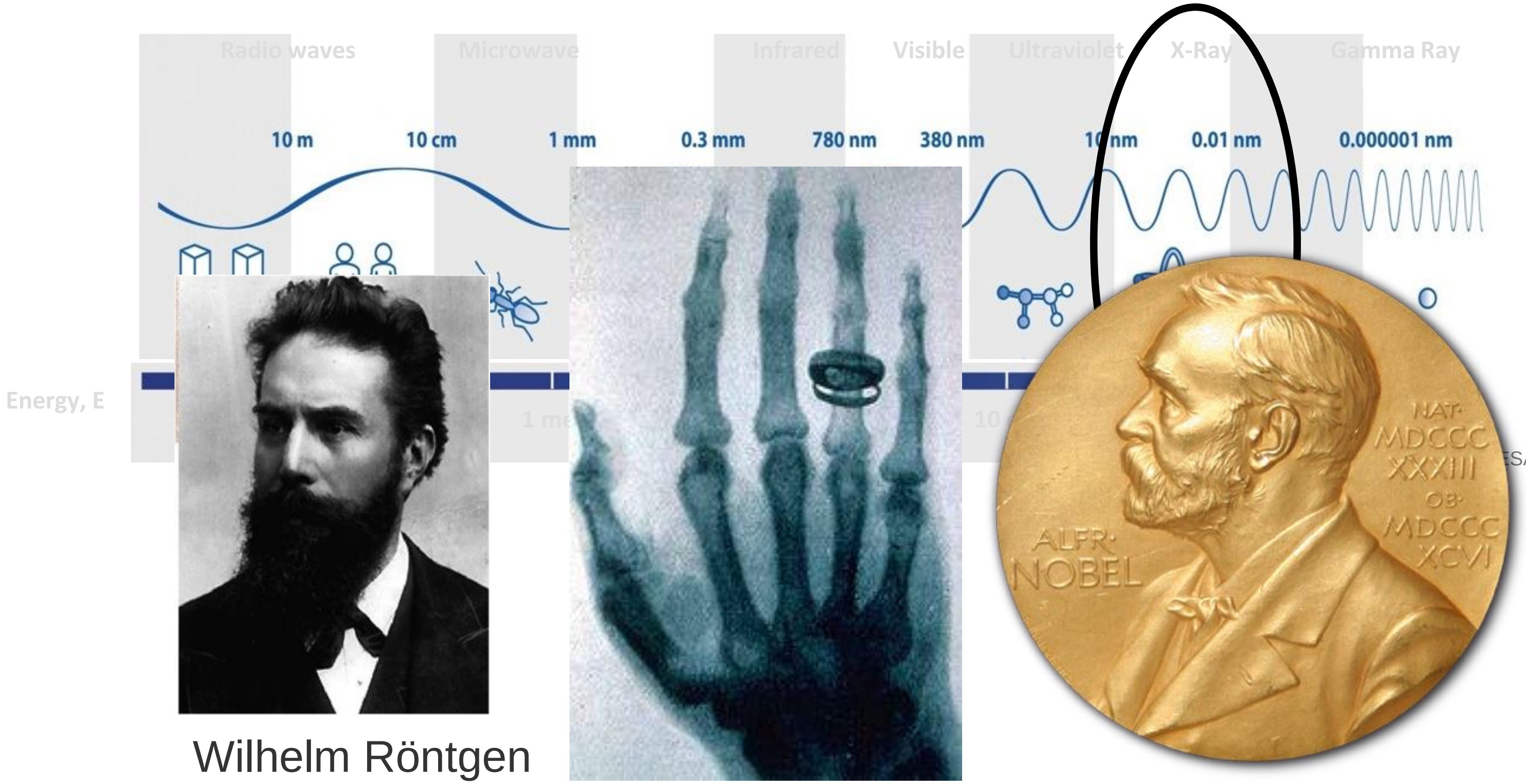
Particle Detection



Imaging

X-ray, CT, PET, MRI

X-ray imaging



Wilhelm Röntgen

8/11/1895

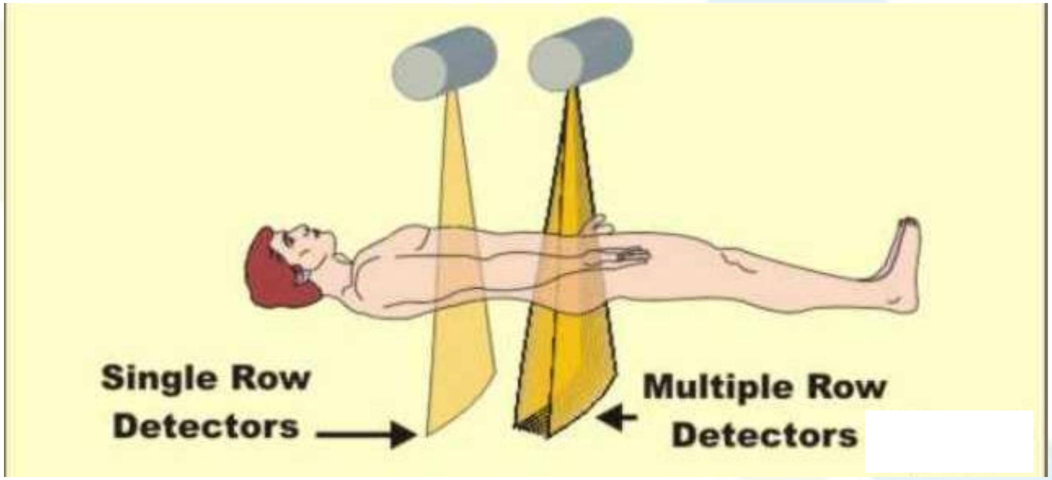
22/12/1895

1901

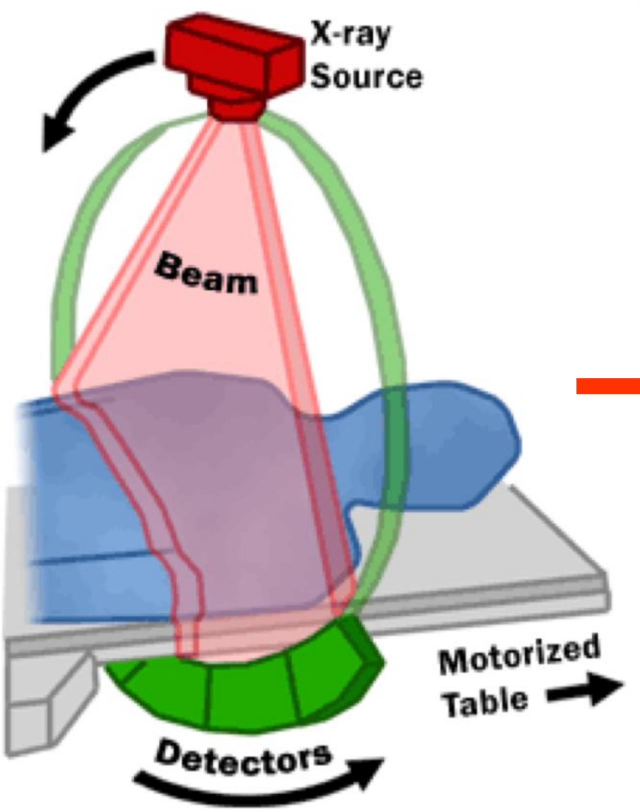
Driver of change: X-ray CT

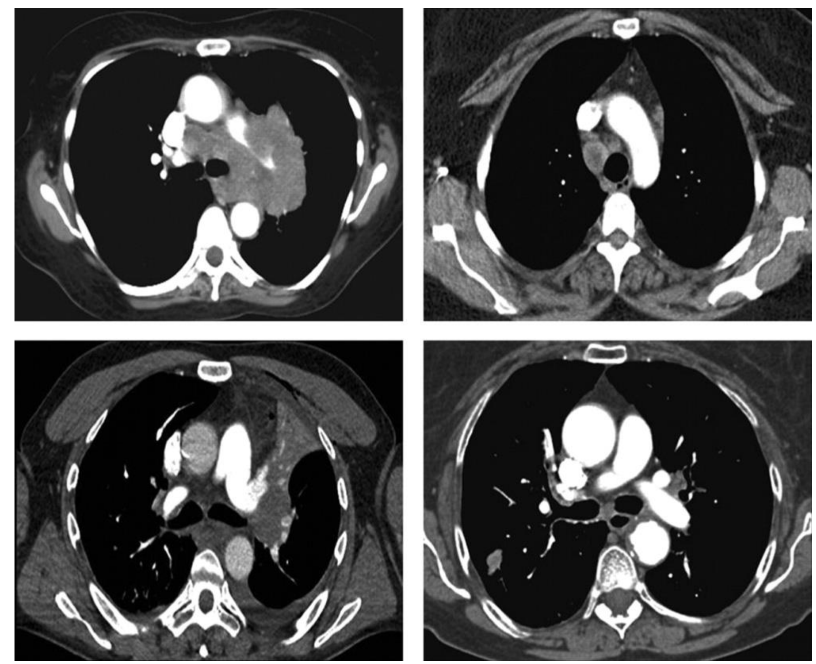
2000-2008 “CT Slice War”

- *CT became very fast with small voxel / pixels*
  - 2000: acquire a single transverse slice per rotation
  - 2012: acquire up to 64-500 slices per rotation



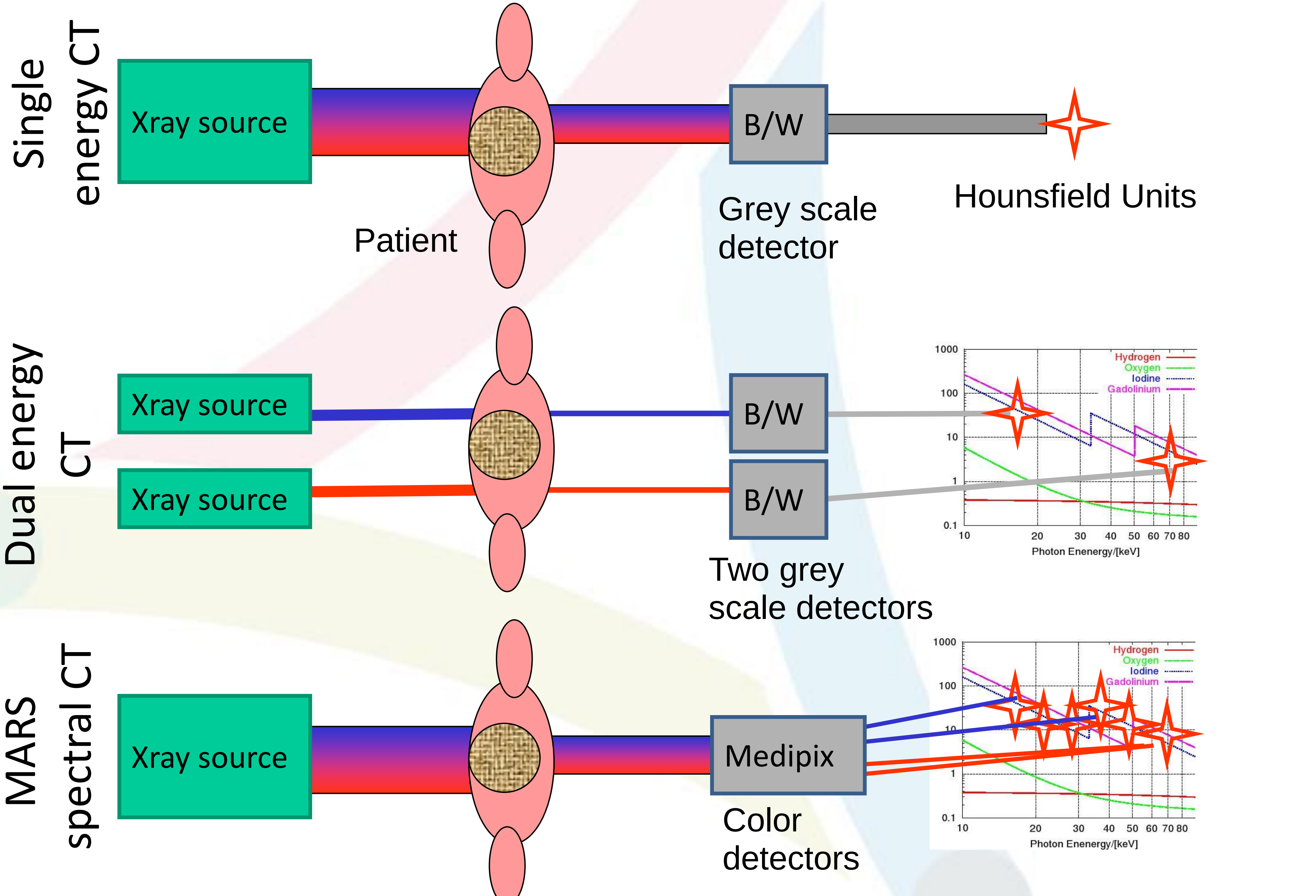
CT – Computed Tomography





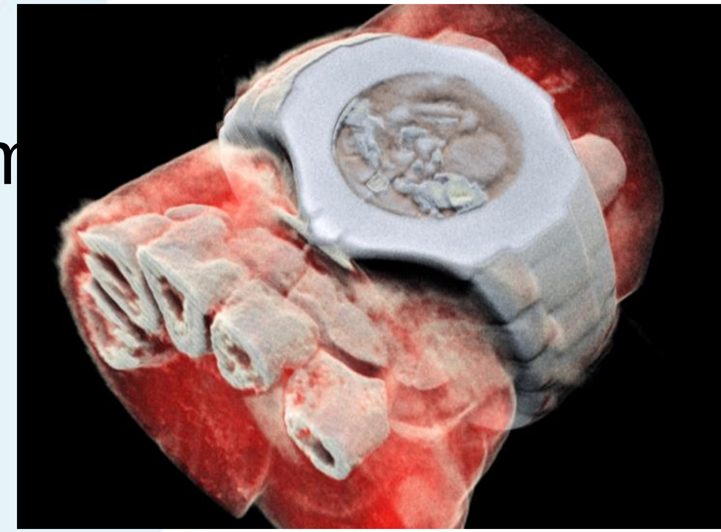
"3D-imaging"

Single- , dual-, and spectral CT



Spectral CT is now possible

Medipix **A**ll **R**esolution **S**ystem



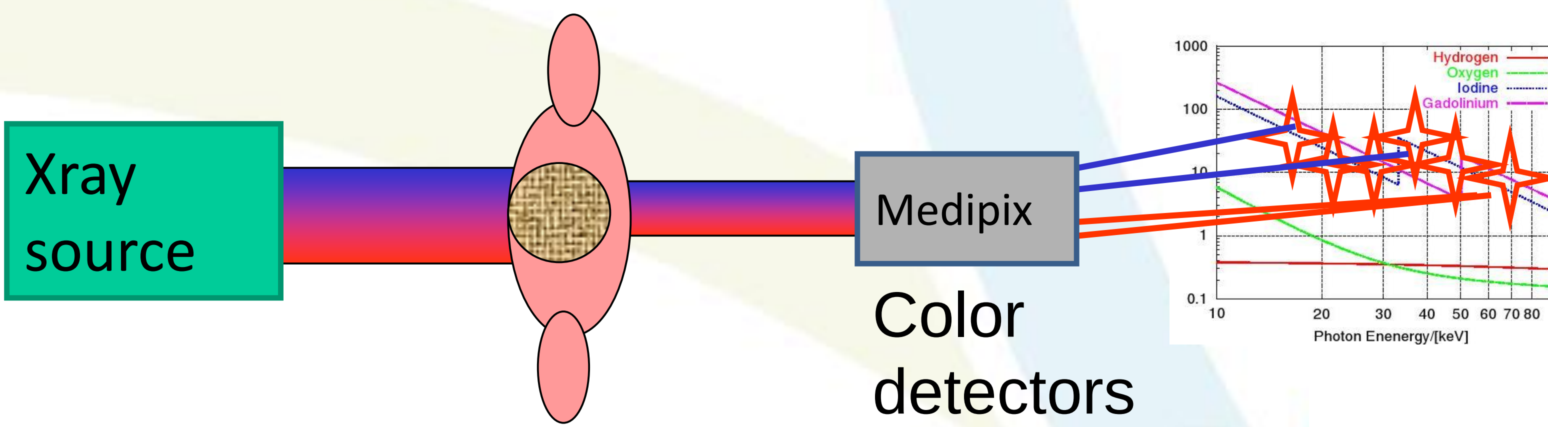
First 3D colour x-ray human image

Energy resolution

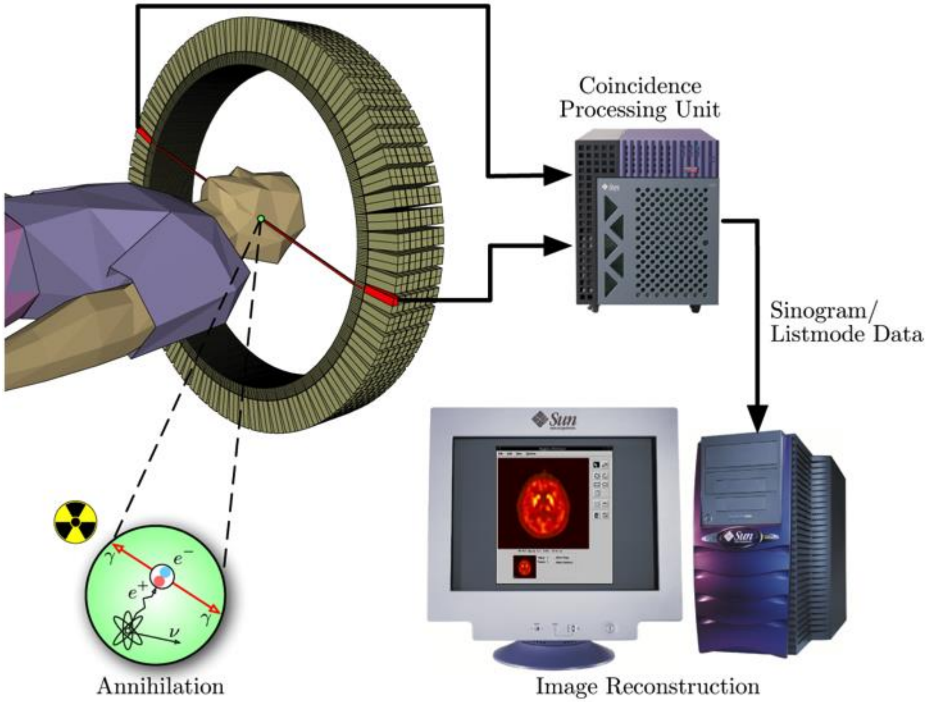
Spatial resolution

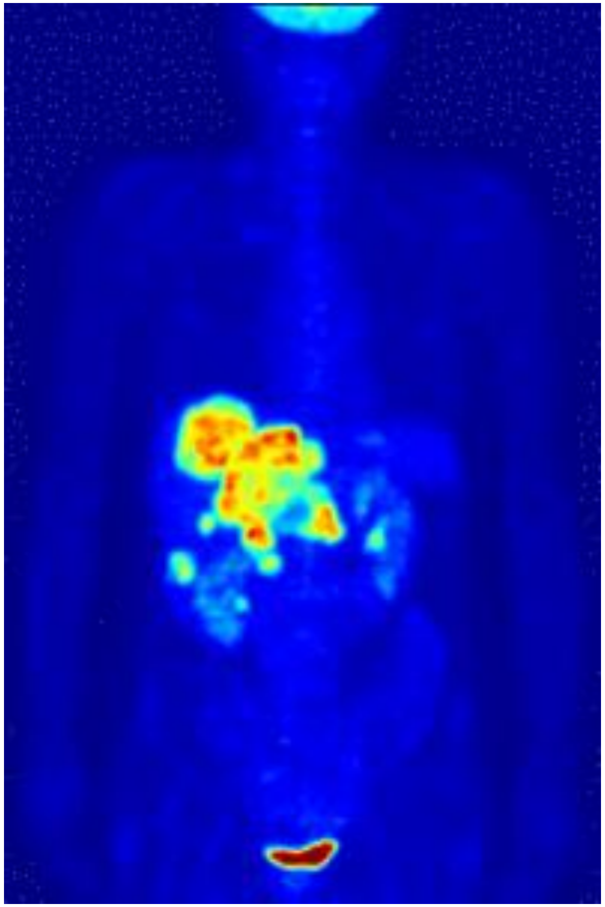
Temporal resolution

MARS
spectral CT



Positron Emission Tomography



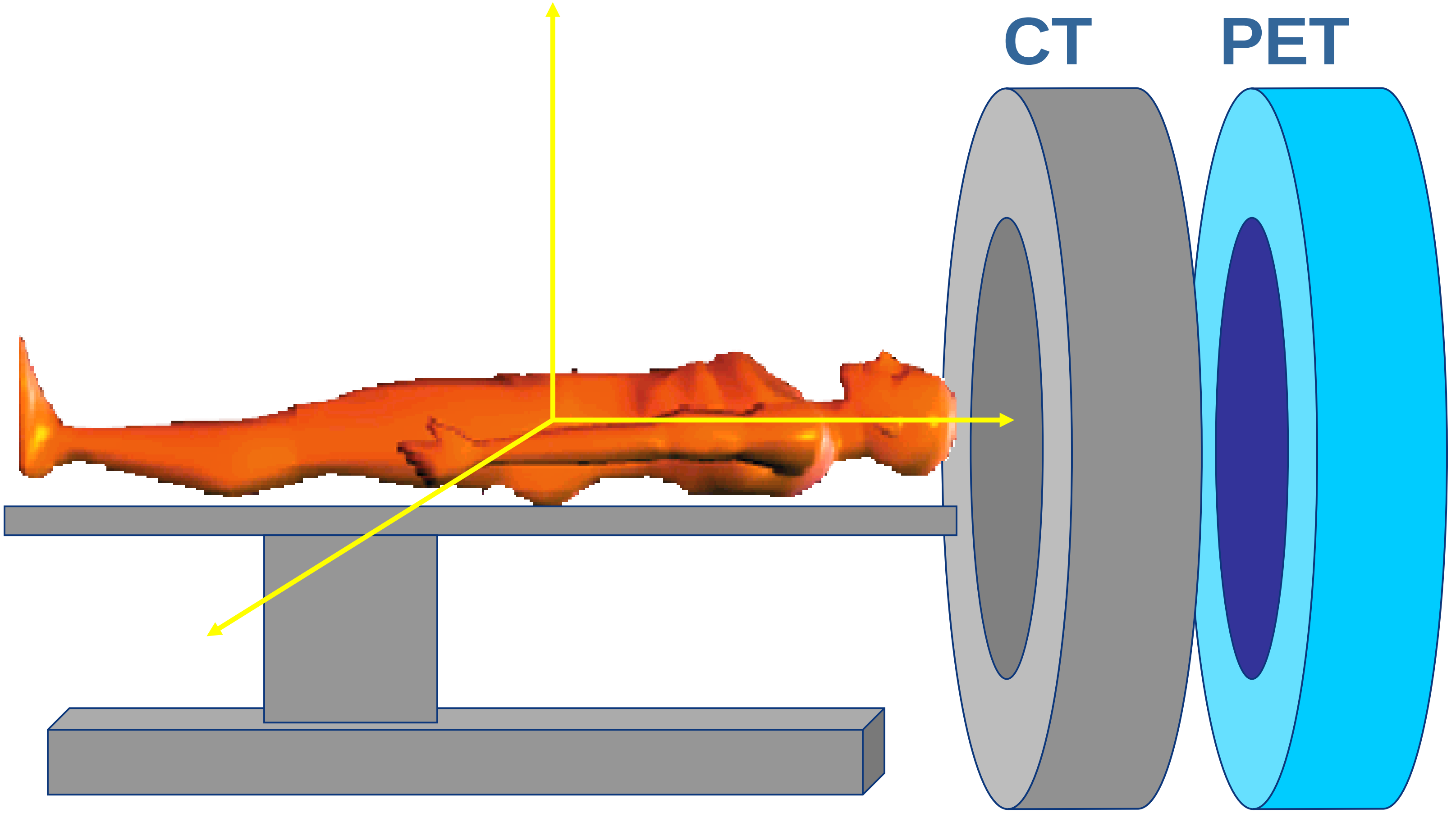


- ^{18}FDG carries the ^{18}F to areas of high metabolic activity
- 90% of PET scans are in clinical oncology

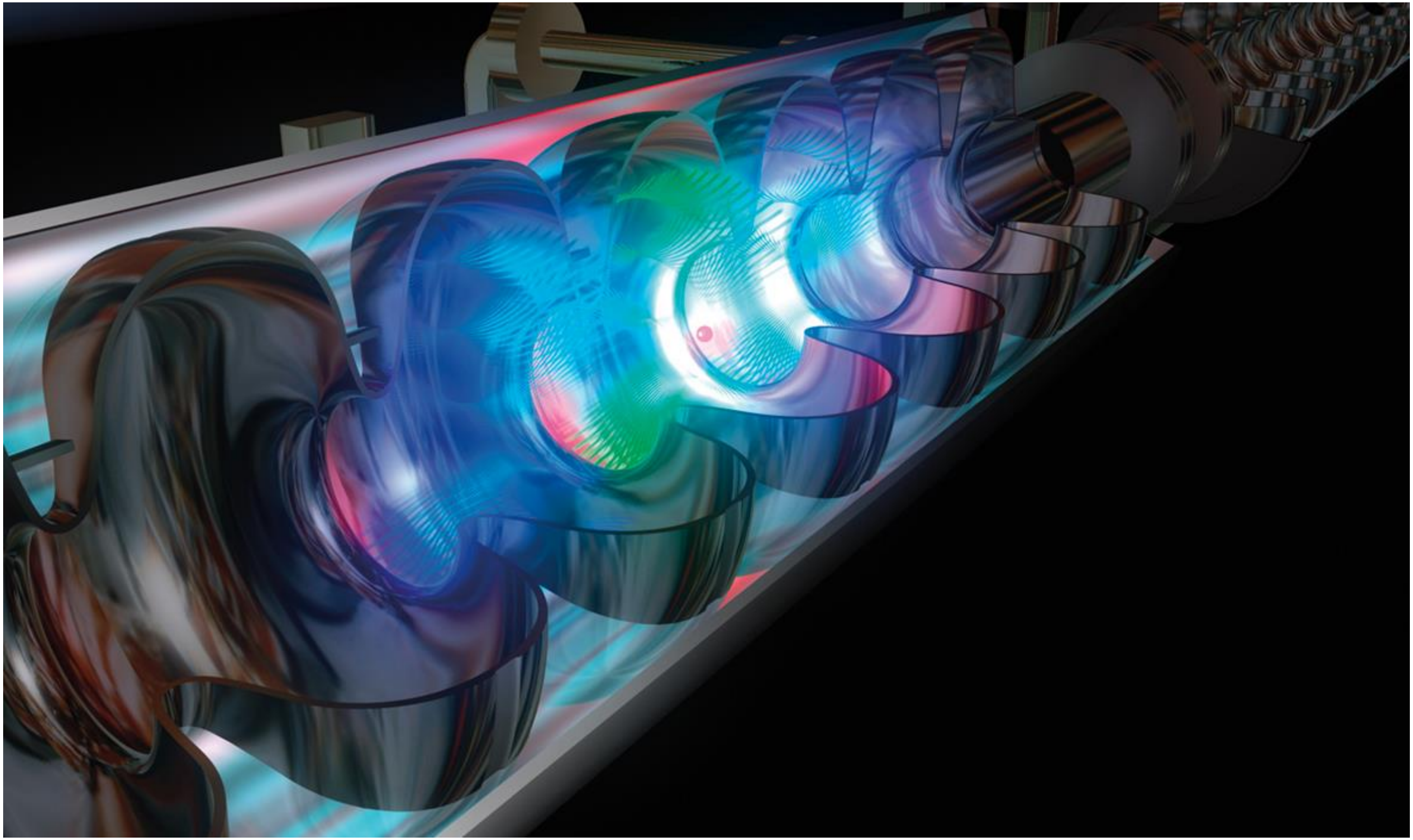
1974 the first human positron emission tomography

Multimodality Imaging: PET-CT

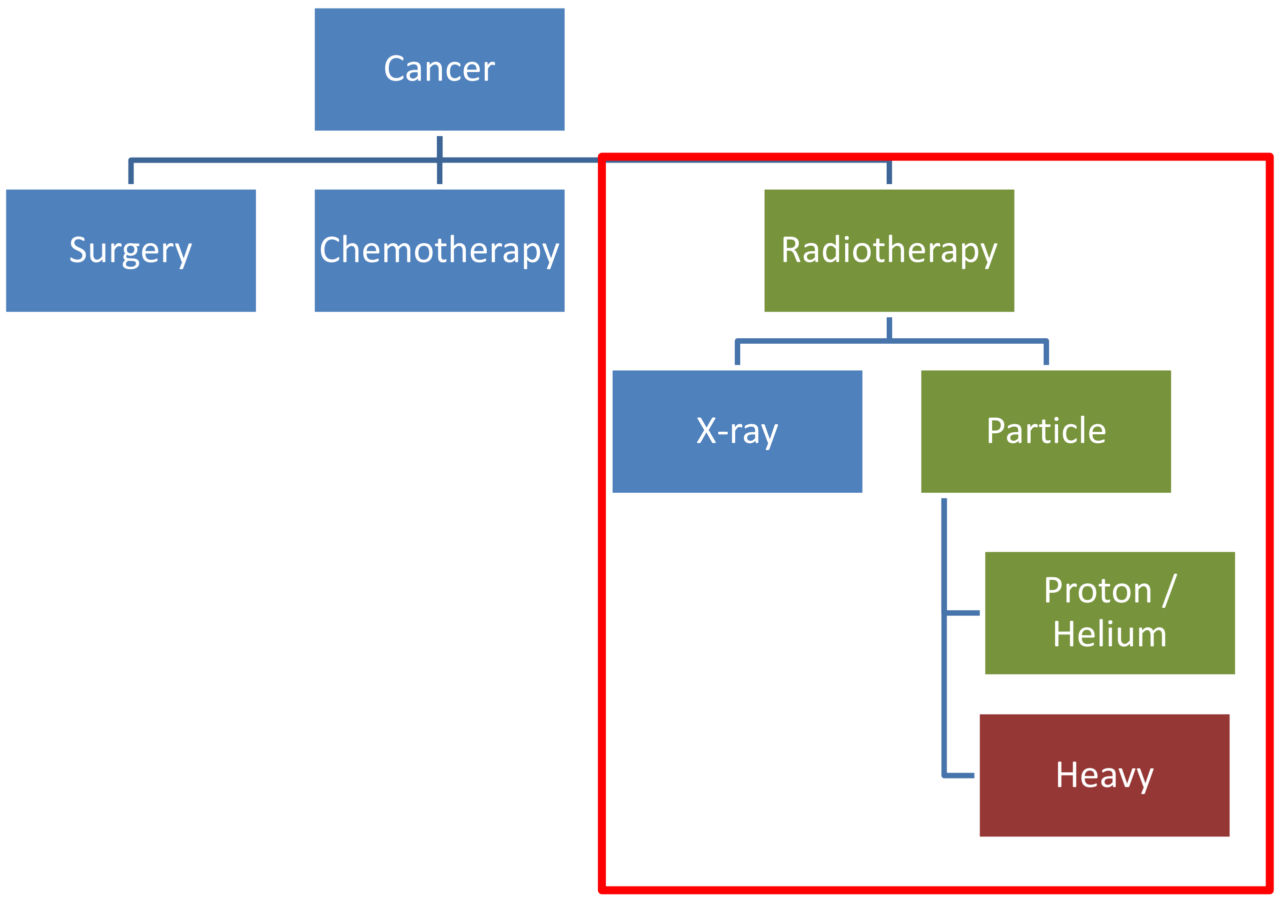
David Townsend



Accelerators For Treatment



Cancer treatment



Radiotherapy in 21st Century

3 "Cs" of Radiation

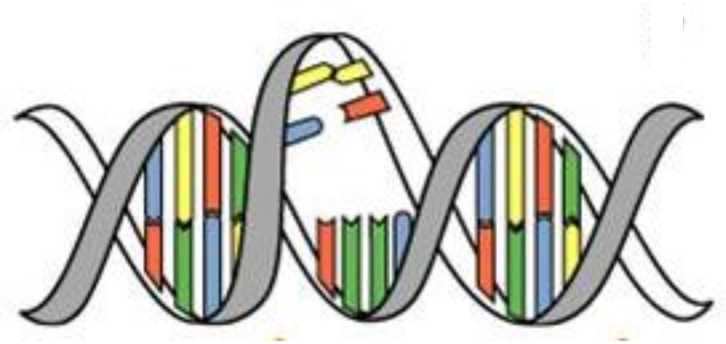
Cure (about 50% cancer cases are cured)

Conservative (non-invasive, fewer side effects)

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

(J.P.Gérard)

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

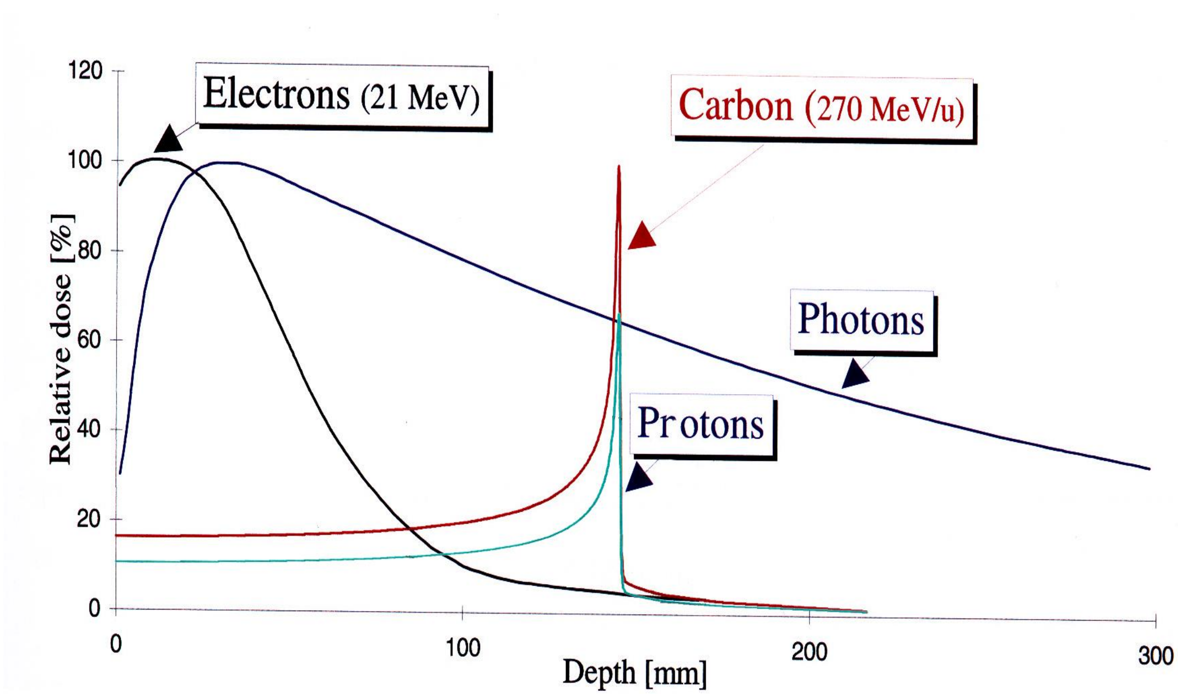


Aims of Radiotherapy:

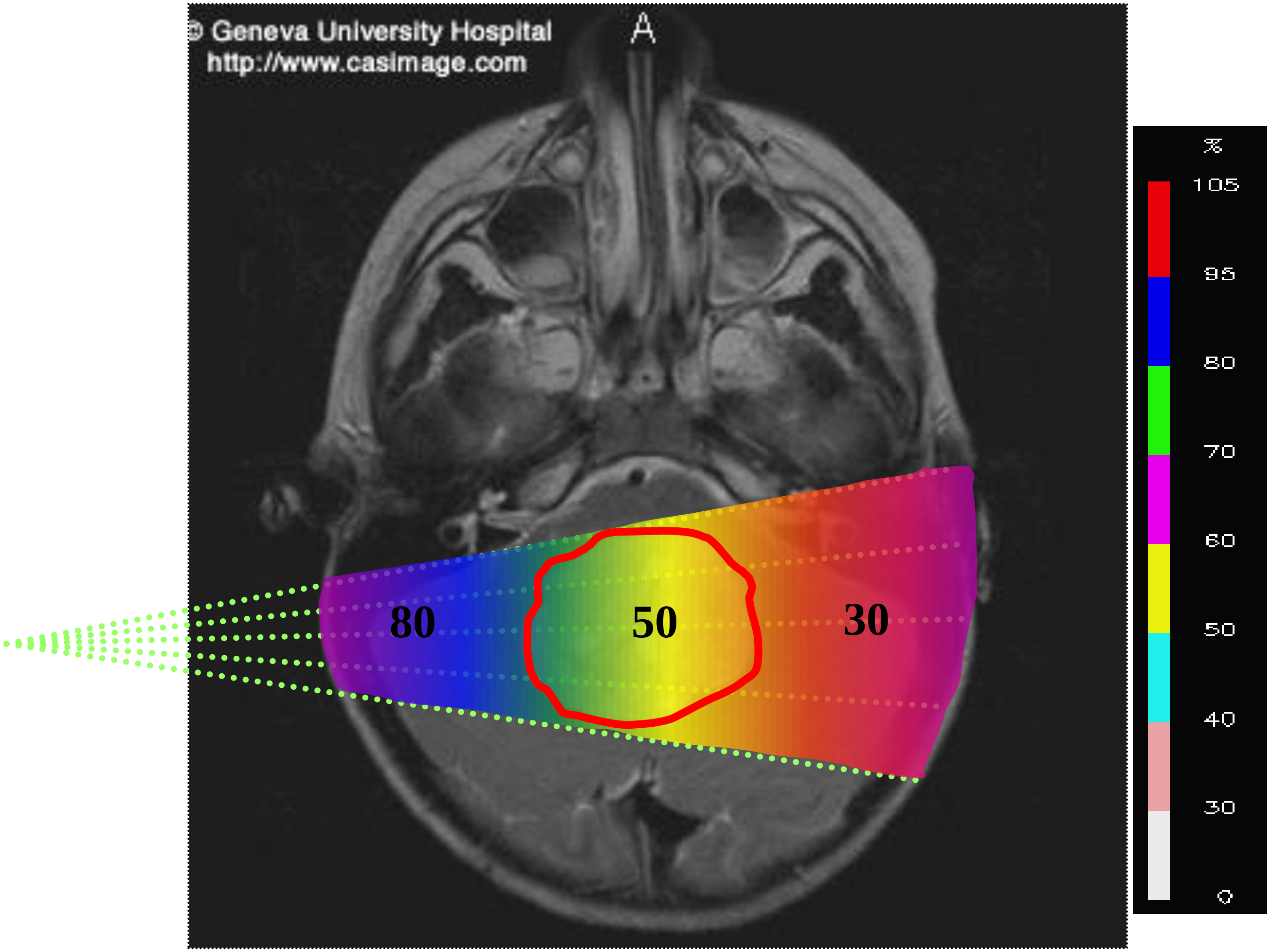
- Irradiate tumour with sufficient dose to **stop cancer growth**
- **Avoid complications** and **minimise** damage to surrounding tissue

Current radiotherapy methods:

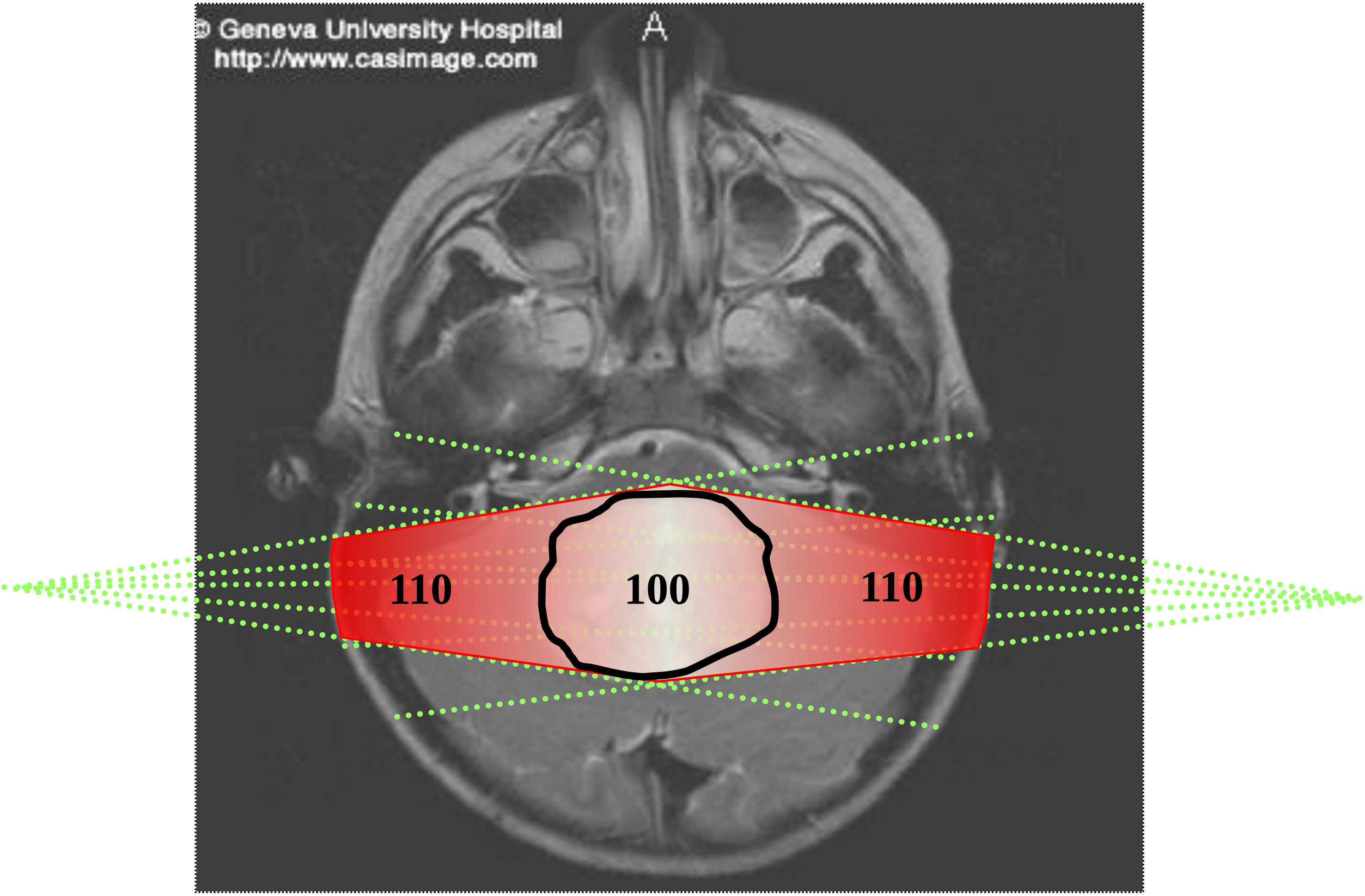
- MV photons
- 5 - 25 MeV electrons
- 50 - 300 MeV/u hadrons



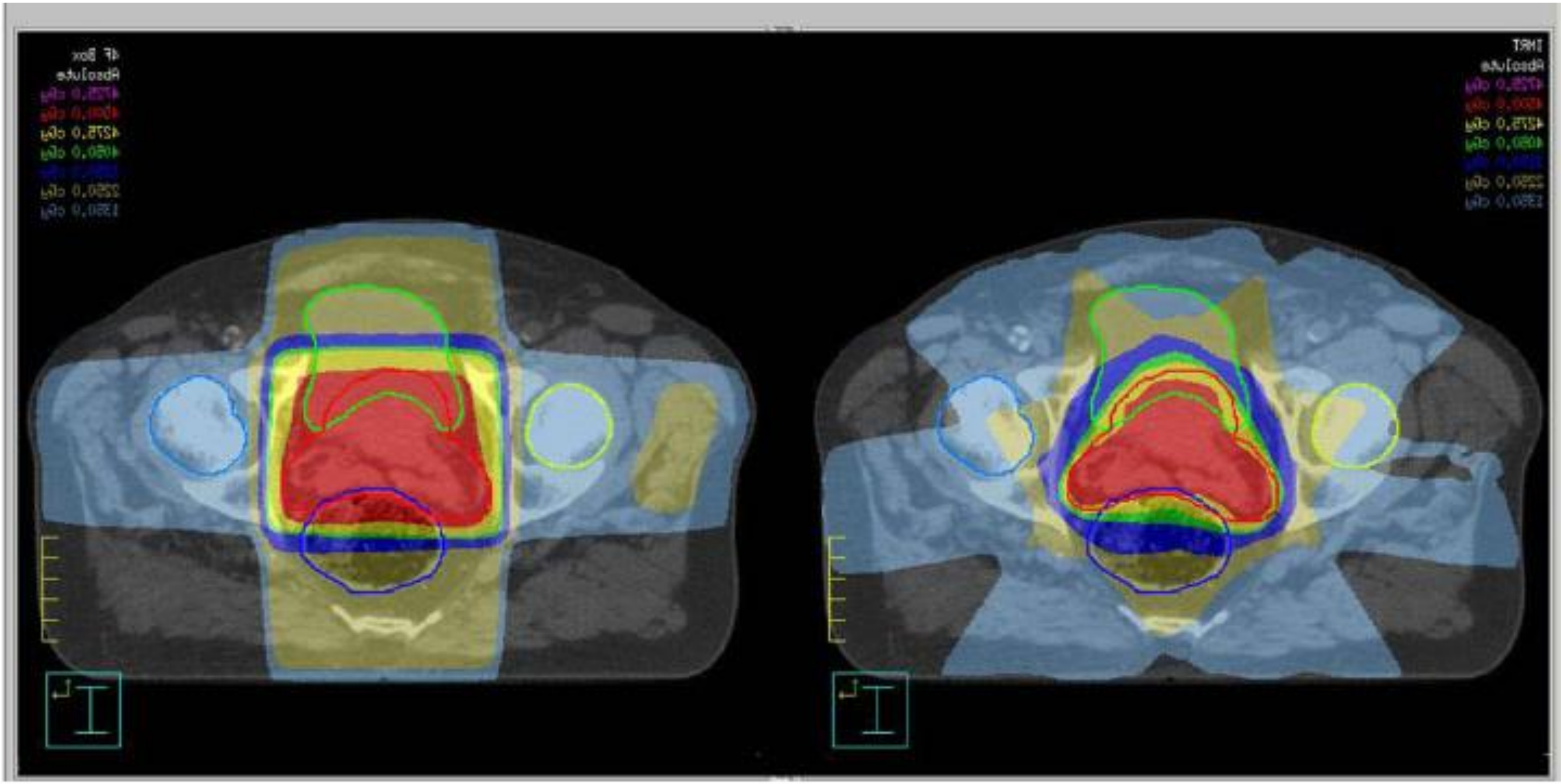
Single beam of photons



2 opposite photon beams



Improved Delivery

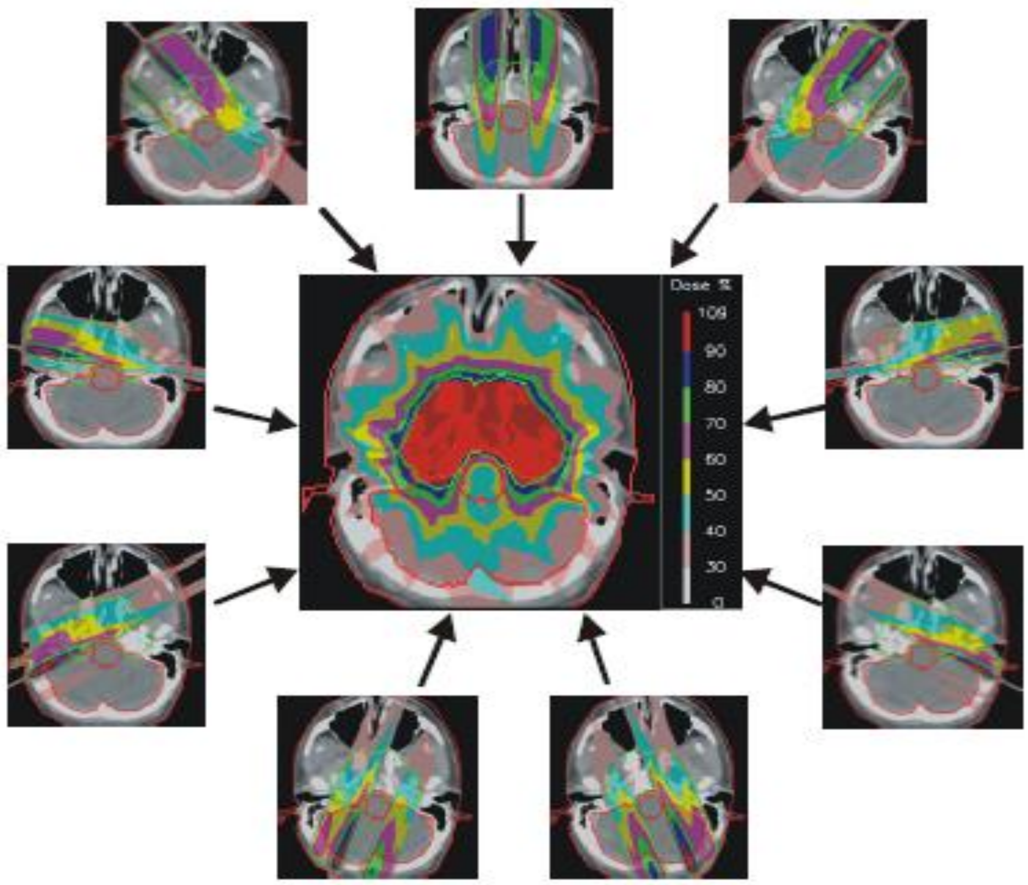


1990s: 4 constant intensity fields

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

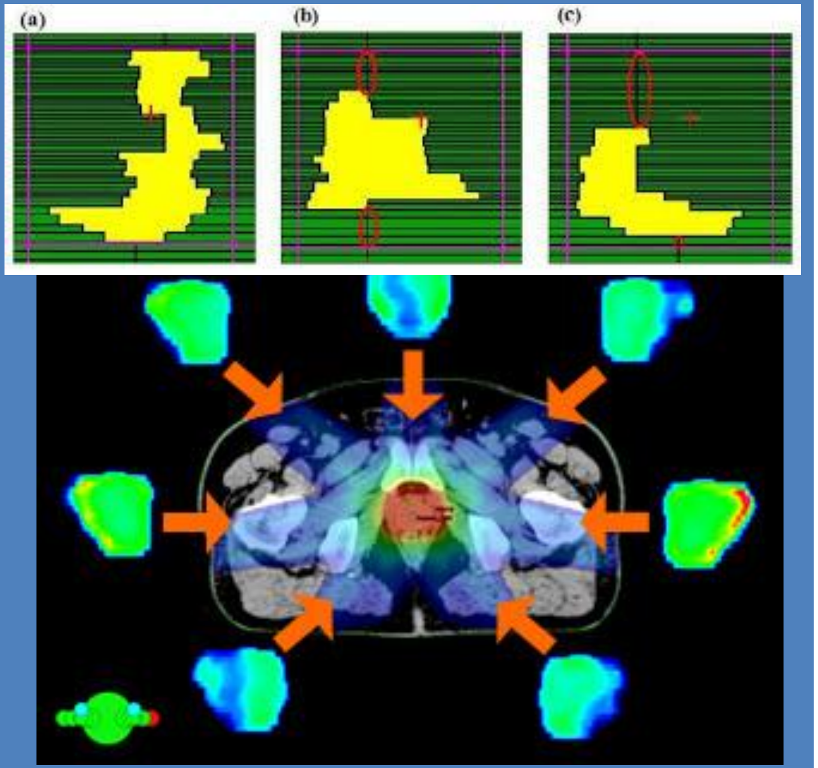
Intensity Modulated Radiation Therapy

9 NON-UNIFORM FIELDS



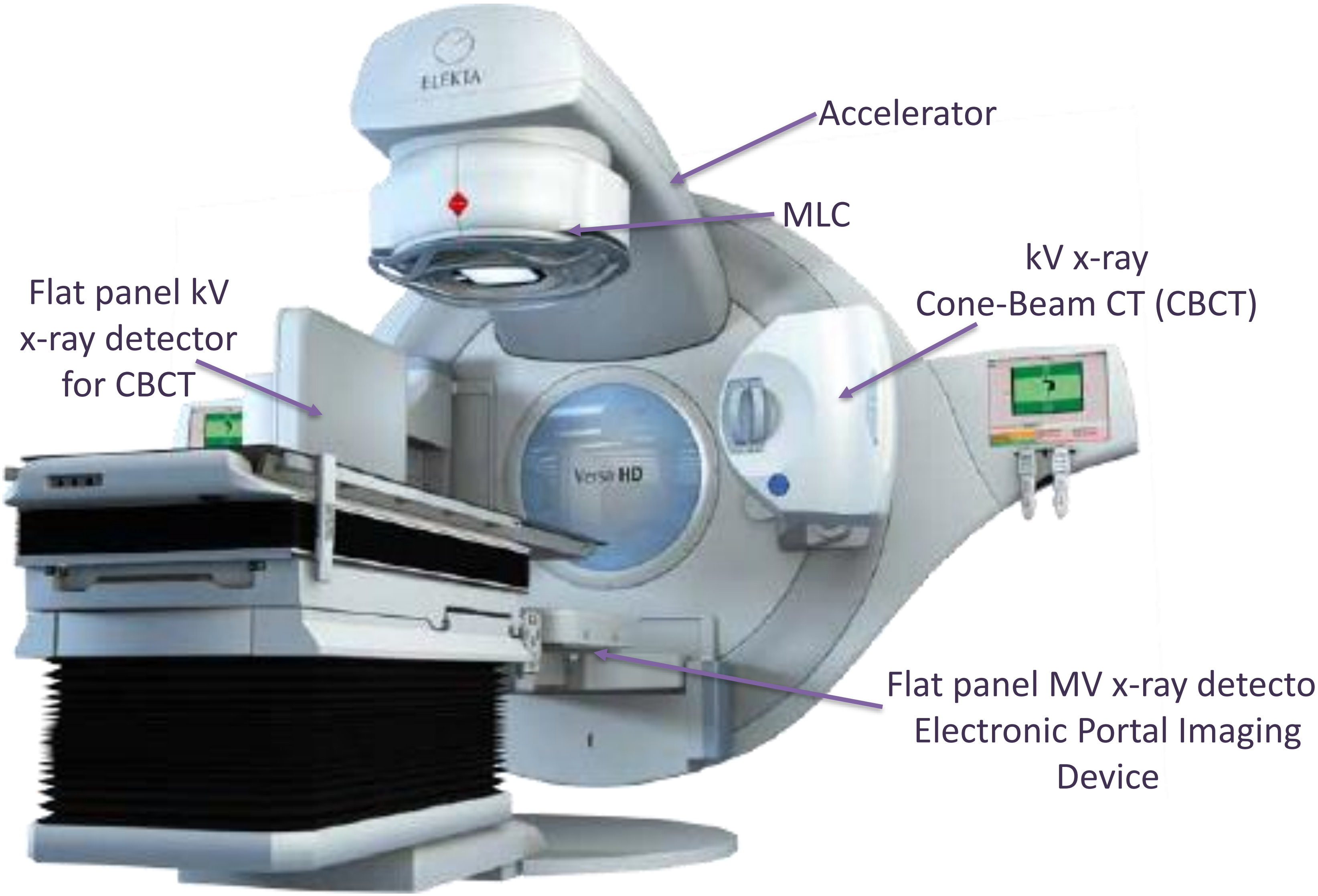
PSI

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.

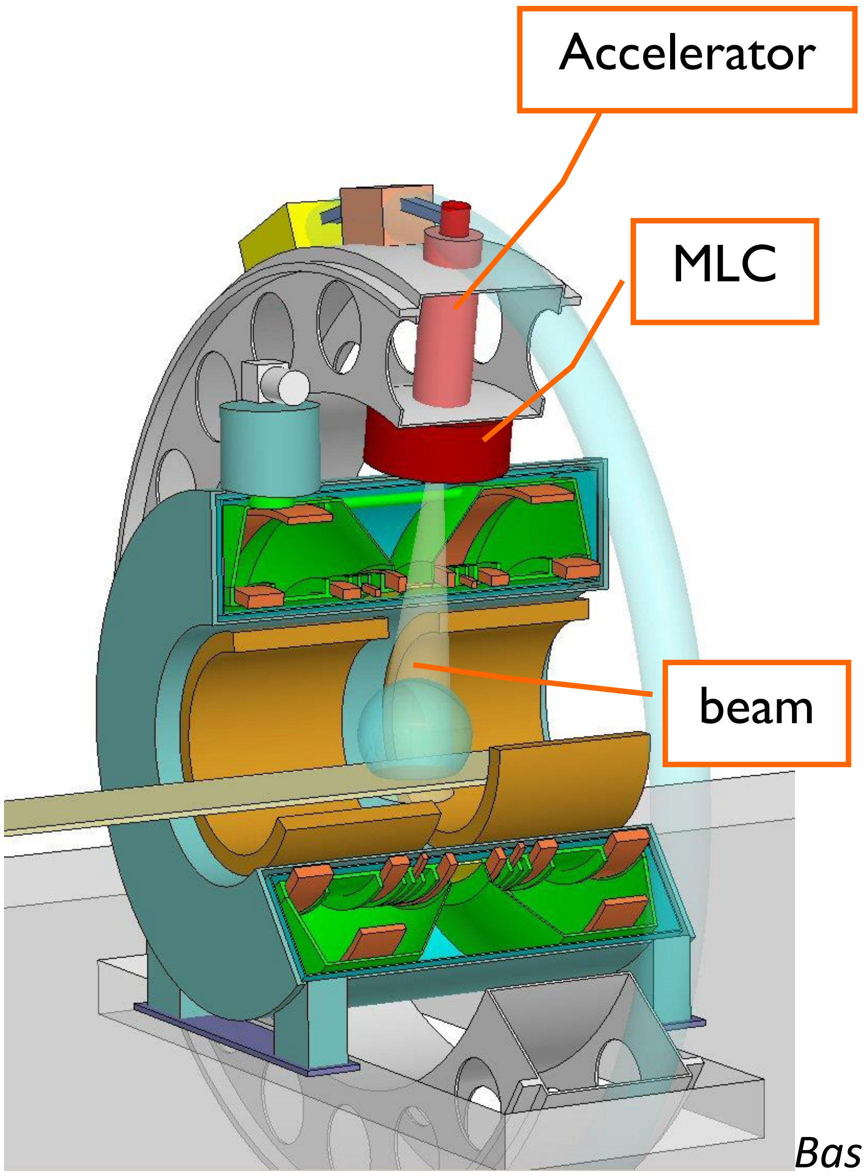
The most widespread accelerator



New Advances are here

The tumour and only the tumour.....

Concept of MRI guided accelerator



Seeing what you treat at the moment of treatment

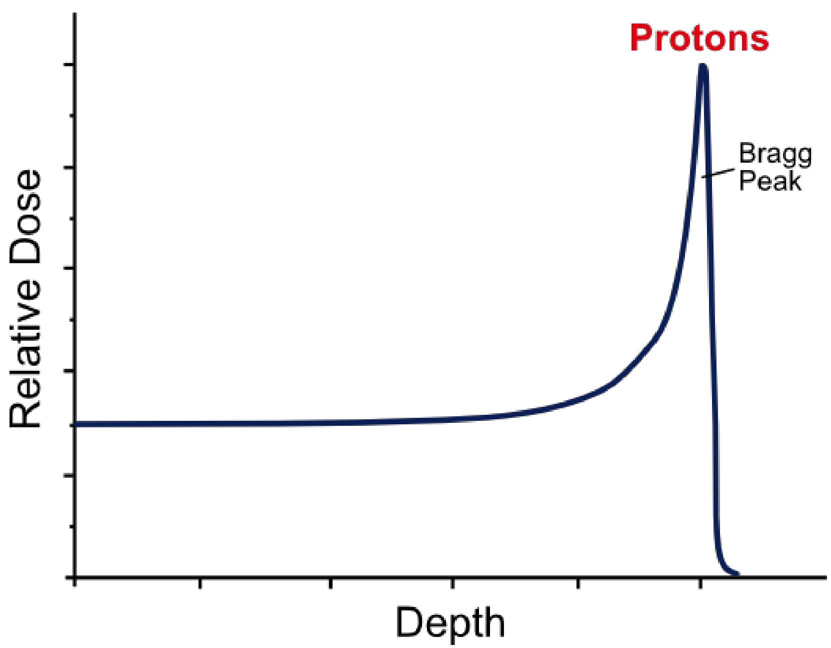
Bringing certainty in the actual treatment

Bas Raaymakers, Utrecht, UMC, ENLIGHT

Hadron Therapy

- 1946: Robert Wilson

  Protons can be used clinically

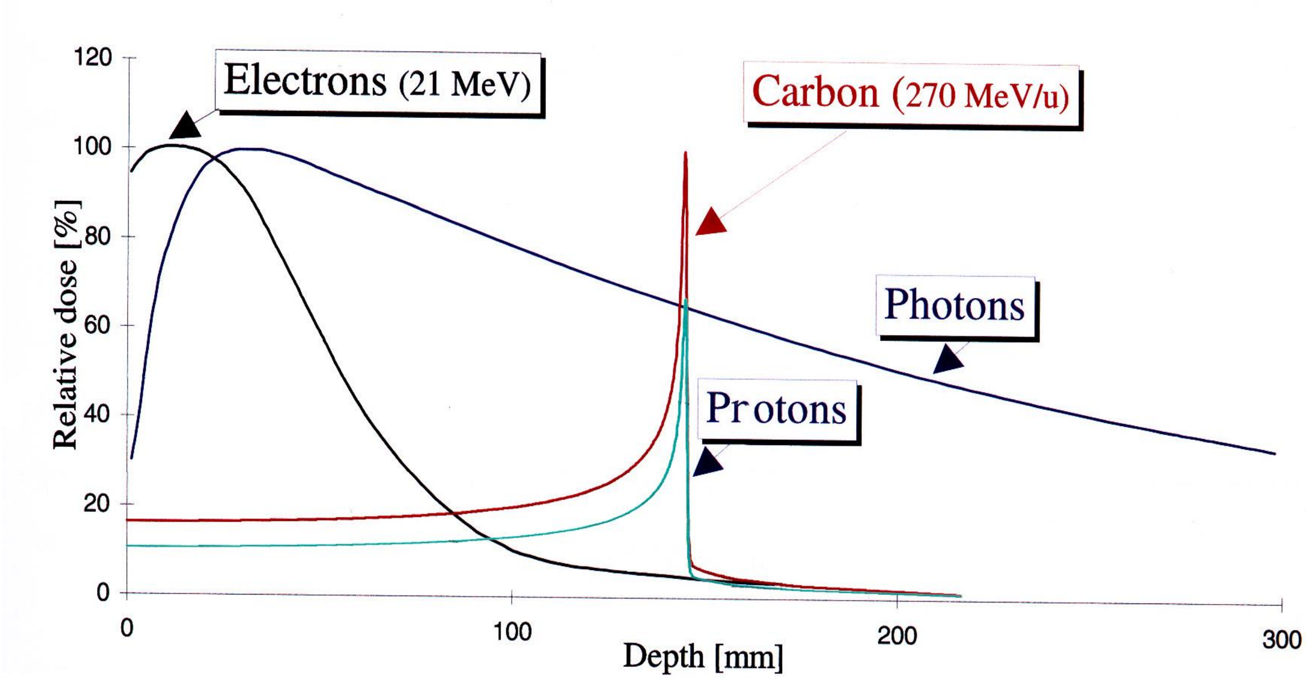


Robert Wilson

Why Hadron Therapy?

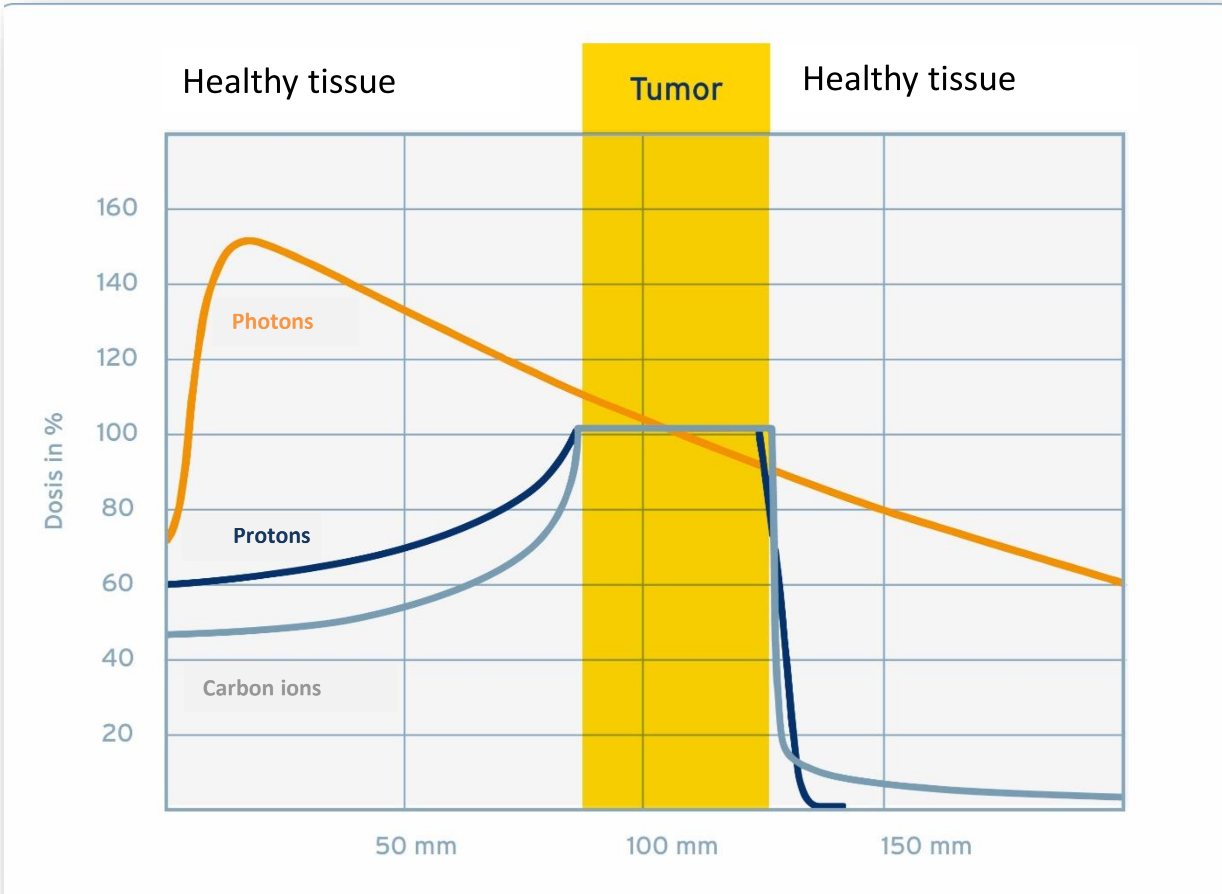
In 1946 Robert Wilson:

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



Depth in the body (mm)

Ion therapy



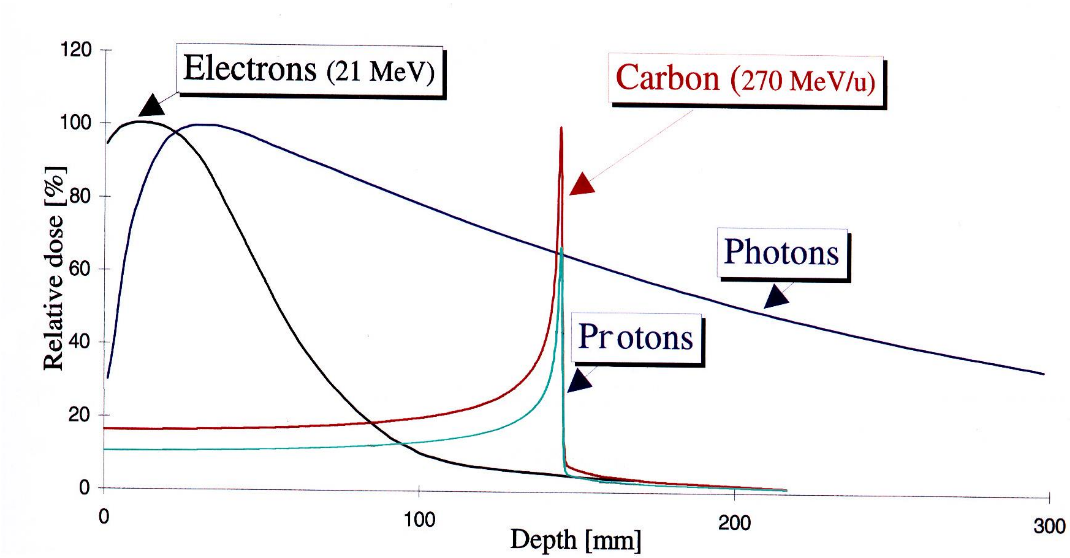
- Less impact on surrounding tissue
- Reduction of negative side effects

Hadron Therapy

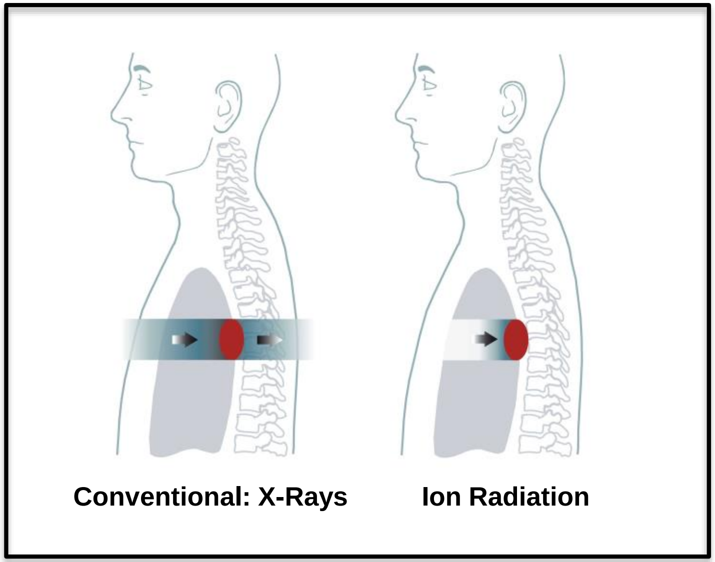
In 1946 Robert Wilson:

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

- Tumours near critical organs
- Tumours in children
- Radio-resistant tumours

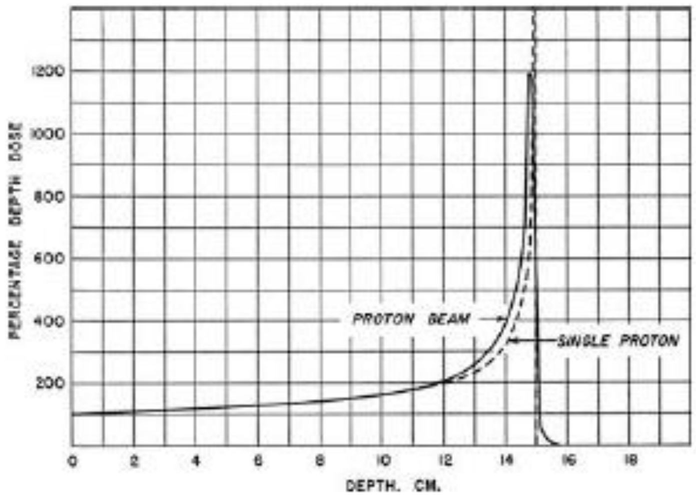


Depth in the body (mm)



1932 - E. Lawrence First cyclotron

1946 – proton therapy proposed by R. Wilson



1954 – Berkeley treats the first patient

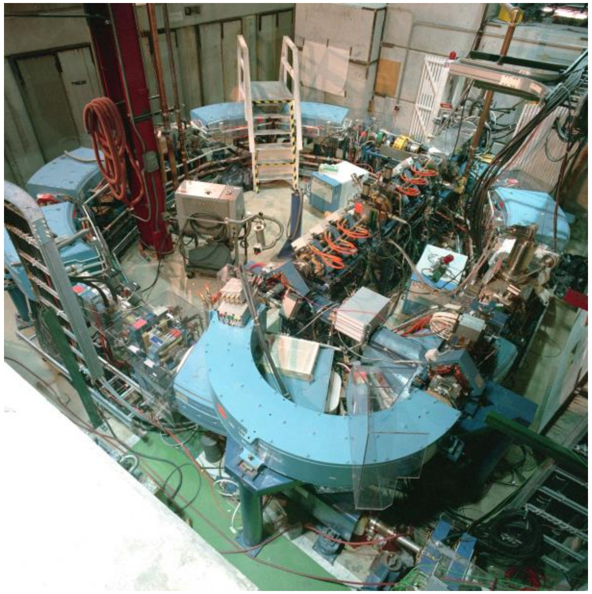
From physics…

Knowledge Transfer

1993- Loma Linda USA (proton)

1994 – HIMAC/NIRS Japan (carbon)

1997 – GSI Germany (carbon)



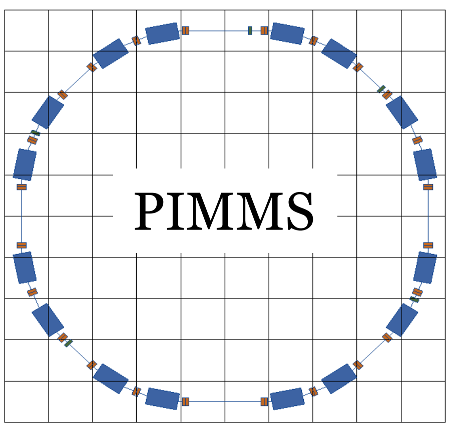
First dedicated clinical facility

Three crucial years ………to clinics

PIMMS study at CERN (1996-2000)

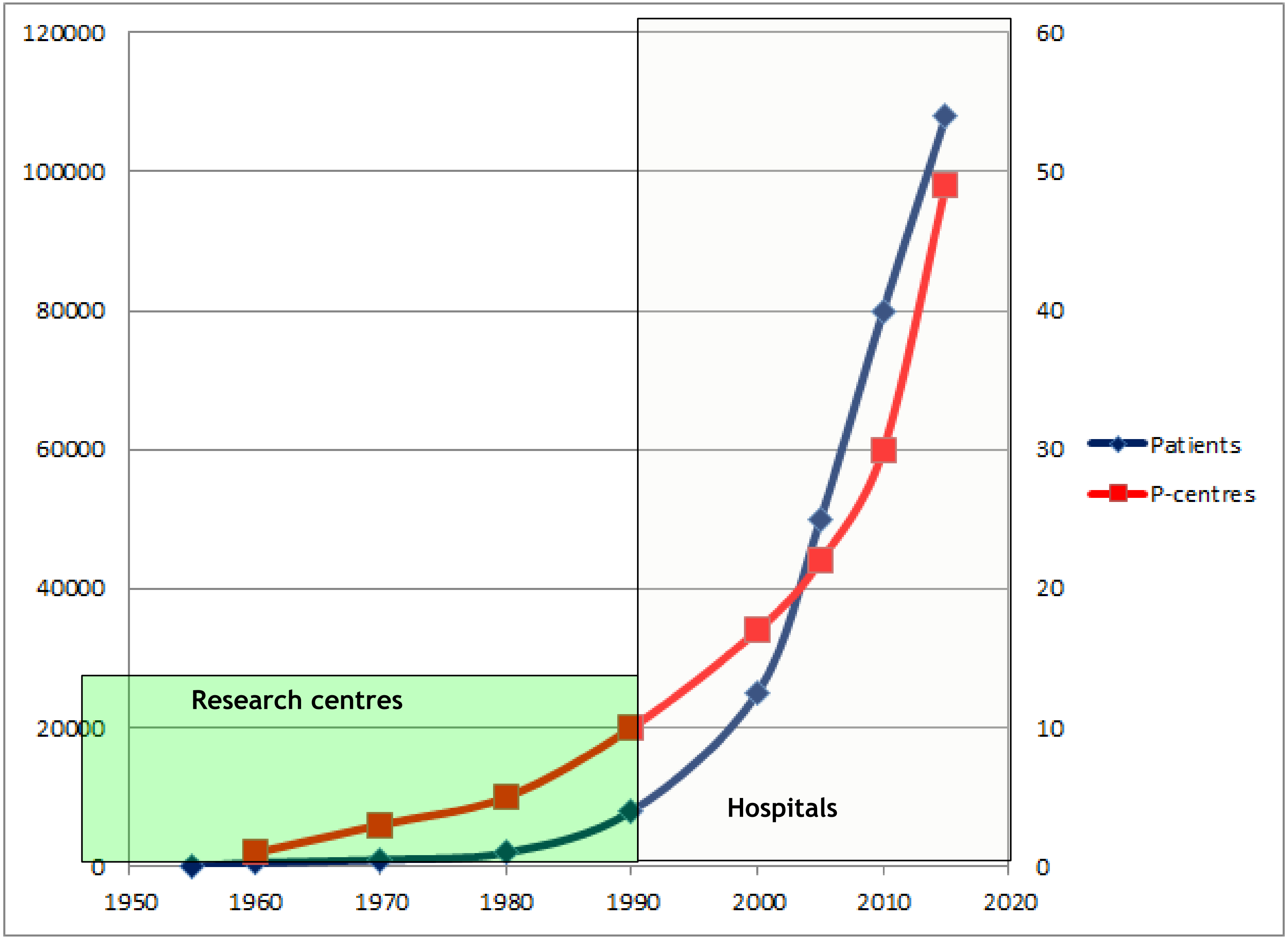
Treatment , CNAO, Italy
2011

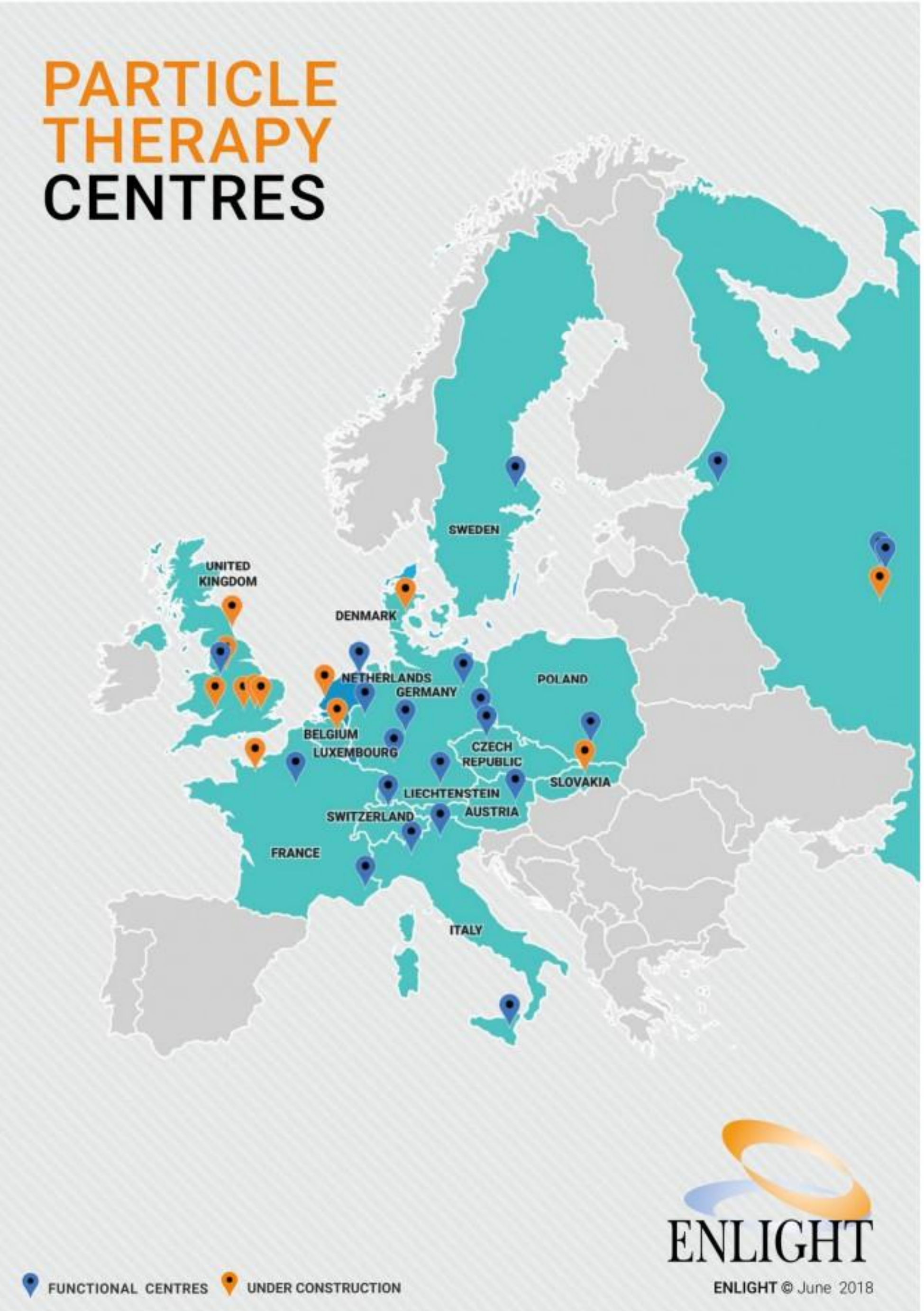
1996-2000
PIMMS study



MedAustron, Austria
Ist carbon patient this week

[Data from www.ptcog.ch]

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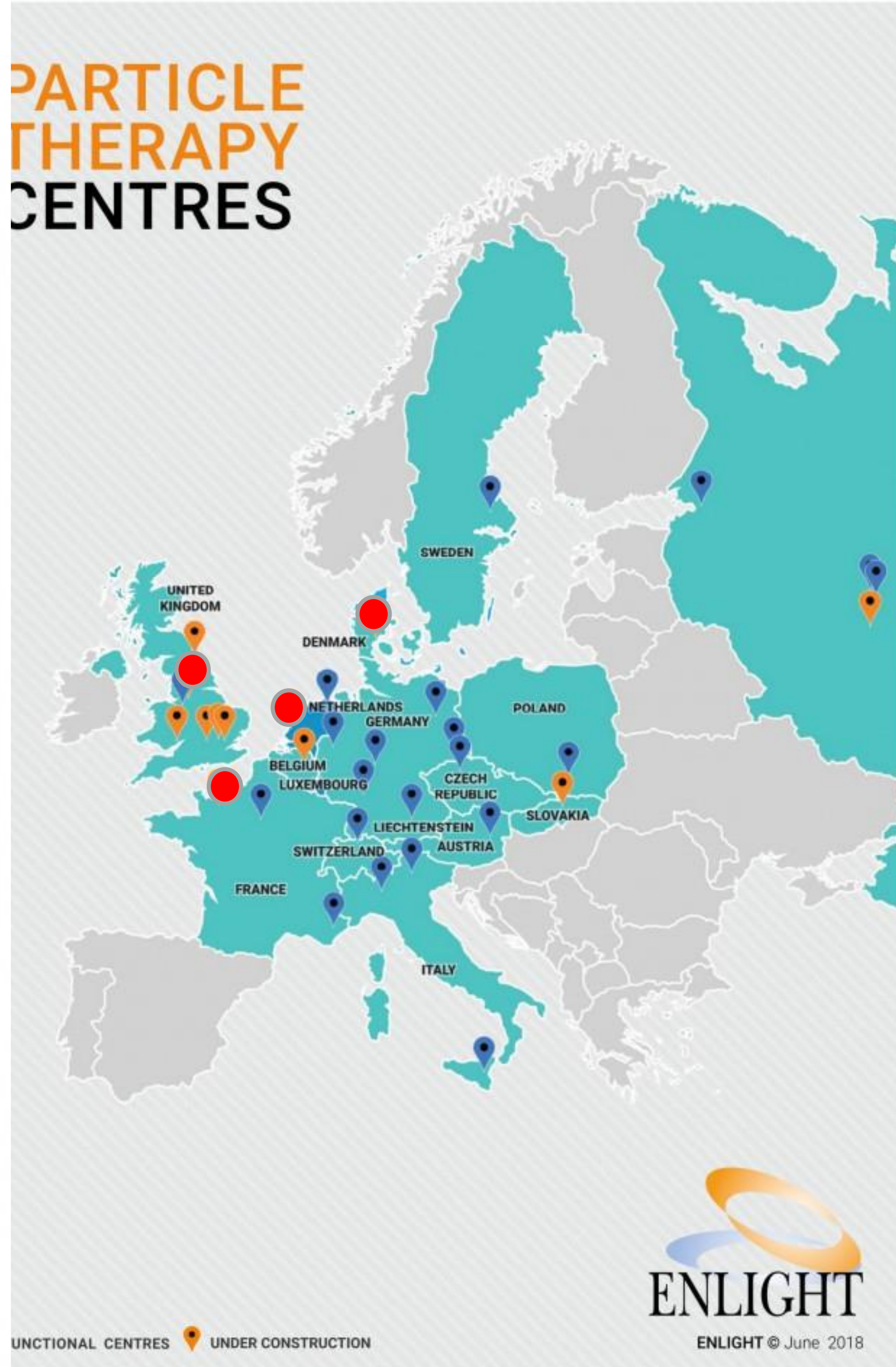
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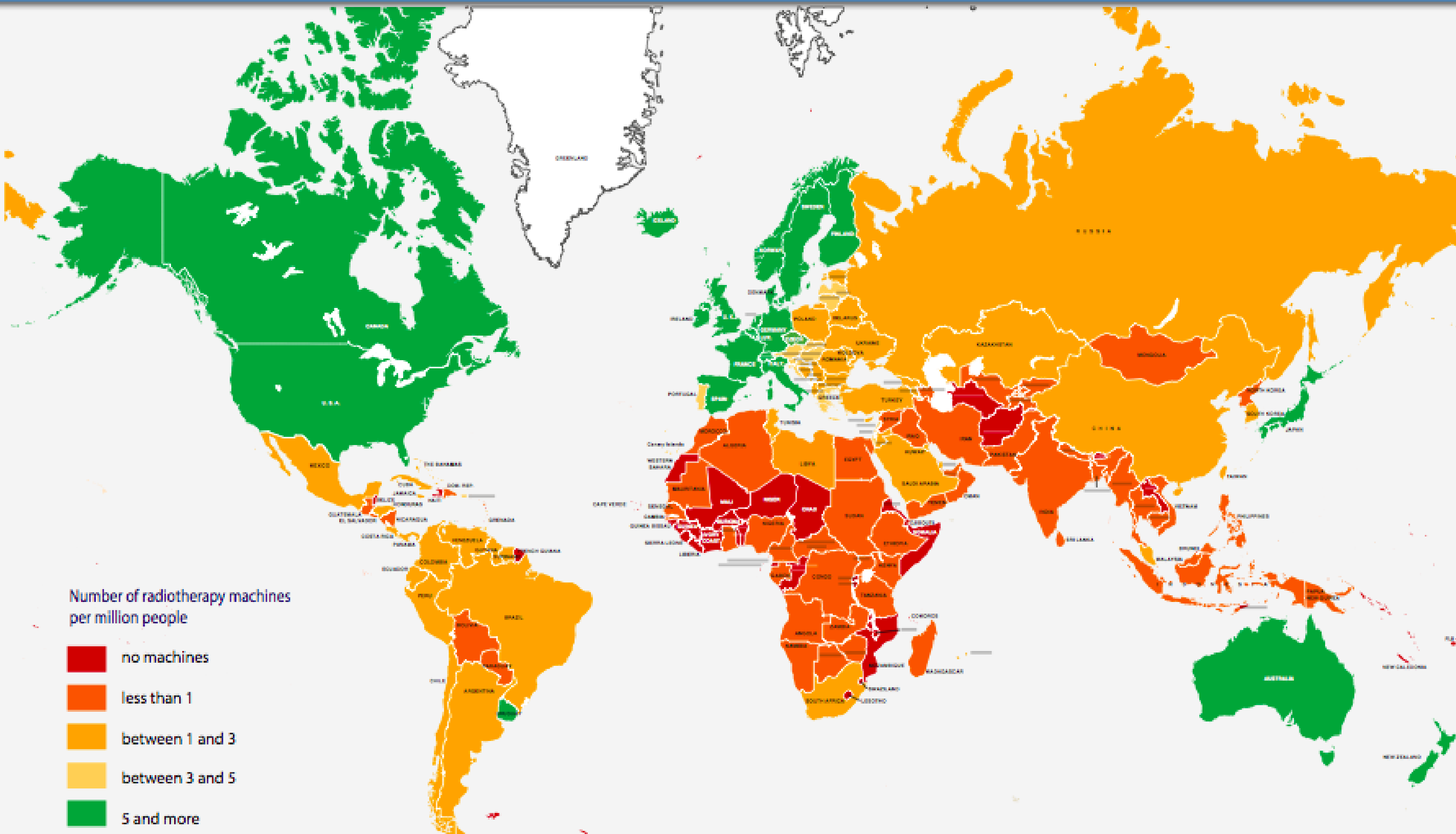
Much remains to be done ……..

Current Challenge: how to ensure high quality radiotherapy globally: Challenging Environments

Availability of **RADIATION THERAPY**

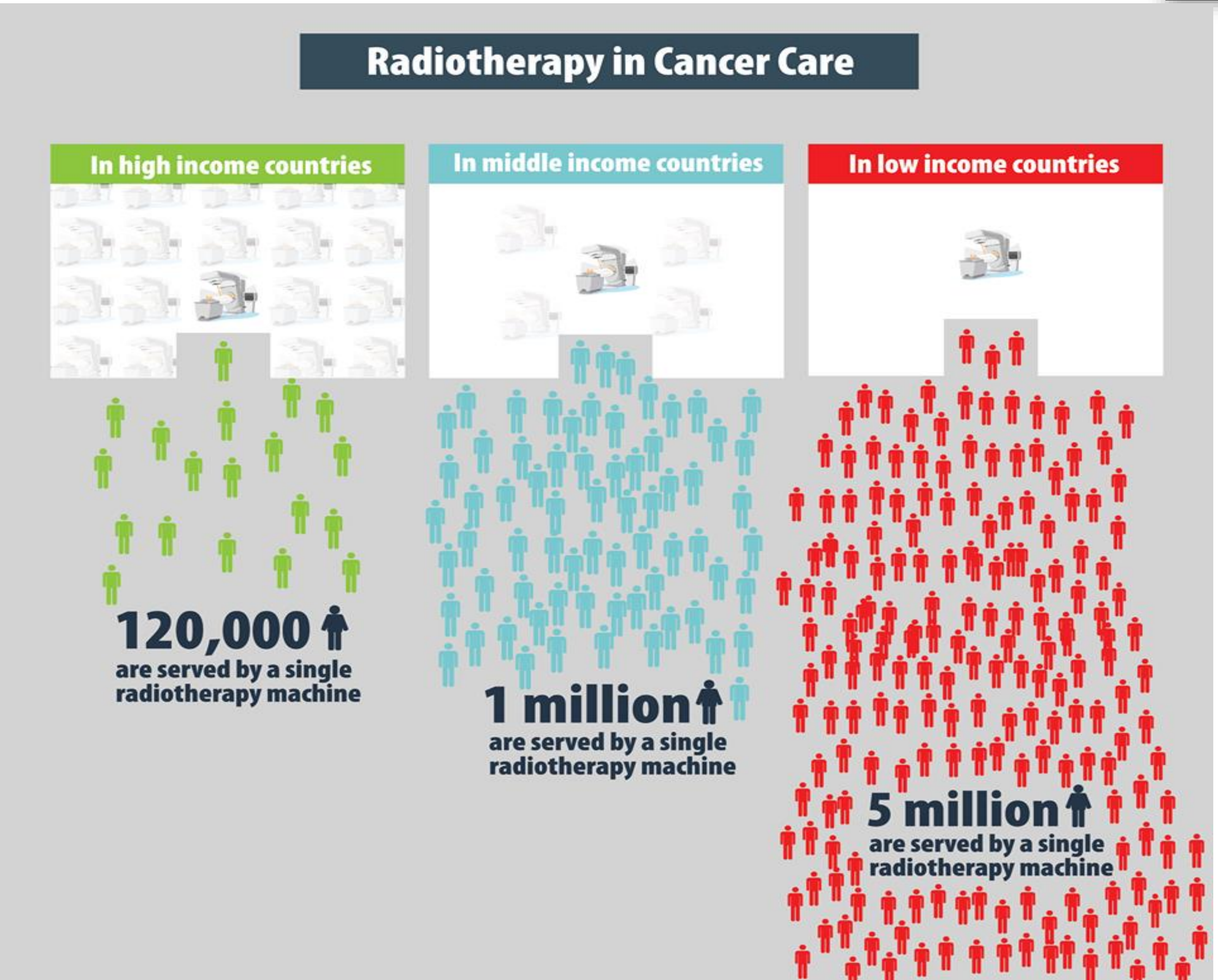
Number of Radiotherapy Machines per Million People 2012



Source: *DIRAC (Directory of Radiotherapy Centres), 2012 / IAEA*

For more information: *http://www-naweb.iaea.org/nahu/dirac/*
dirac@iaea.org

25 MILLION CASES PREDICTED IN 2035, 65–70% WILL OCCUR IN LOW-AND MIDDLE- INCOME COUNTRIES



Radiotherapy in Cancer Care
In high income countries
In middle income countries
In low income countries
120,000 are served by a single radiotherapy machine
1 million are served by a single radiotherapy machine
5 million are served by a single radiotherapy machine

Desirable features regarding LINACs designed for LICs

(Pomper MA et al. The Stanley Foundation, CNS, February 2016)

- A developing-world LINAC with modular enhancements,
- Costs could be phased in by starting with a basic unit, and options could be provided for:
  - new technology,
  - remote diagnosis and adjustment,
  - a long-term maintenance contract with the vendor.

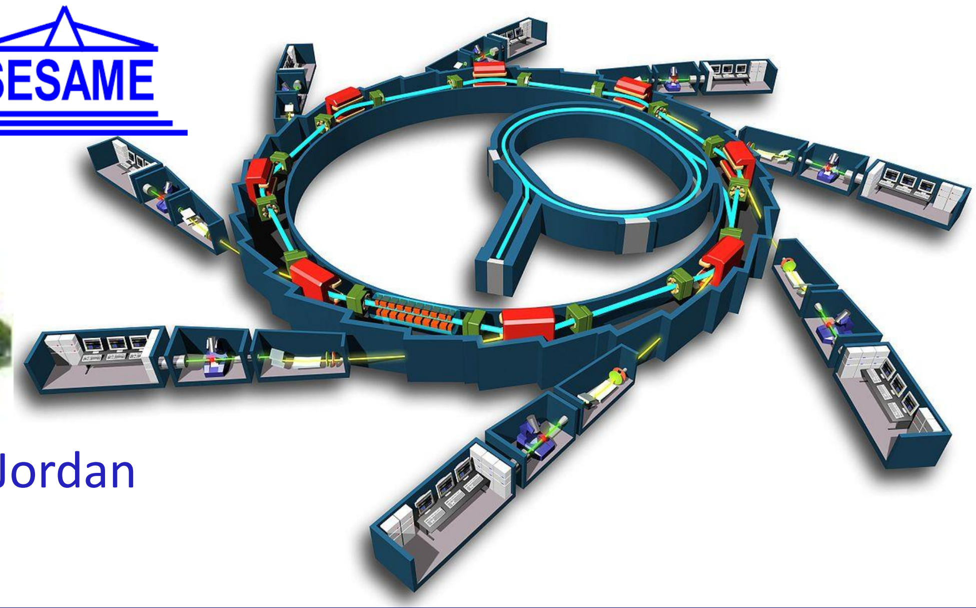
Accelerators for "Peace and medical applications"

Initiated and Championed by Prof. Herwig Schopper, former Director General of CERN

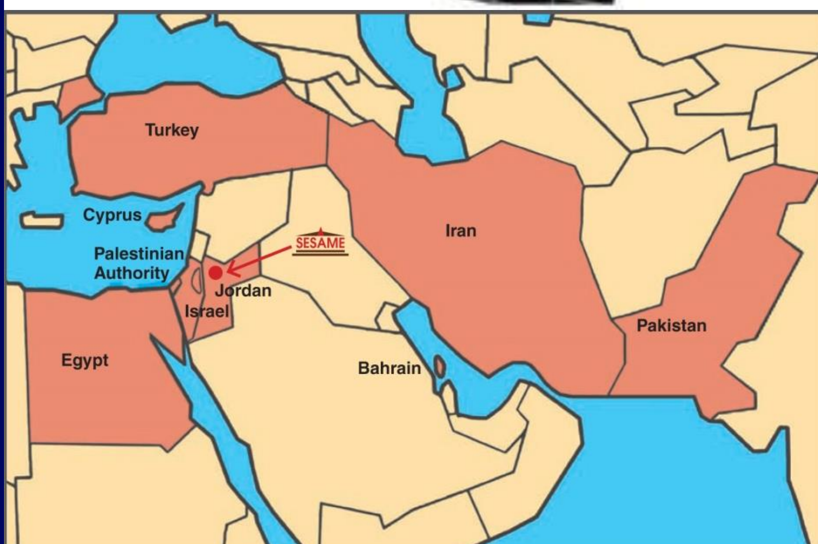
UNESCO CERN IAEA

SESAME project: 'Synchrotron Light for Experimental Science and Applications in the Middle East'

SESAME



Jordan



The success of such an initiative is being demonstrated by the SESAME project:

built in Jordan, unifies nine member states of different political systems and religions in the Middle East: Bahrain, Cyprus, Egypt, Israel, Iran, Jordan, Pakistan, Palestinian Authority, Turkey; has achieved all of them to peacefully work together

The founding father of the SESAME project is also Prof. Herwig Schopper

Candidate Members for the South-East European International Institute for Sustainable Technologies

Signed a Declaration of Intent

Agreed 'ad referendum'

Observer

Republic of Albania

Bosnia and Herzegovina

Republic of Bulgaria

Republic of Croatia

Hellenic Republic

Kosovo*

FYR of Macedonia

Montenegro

Republic of Serbia

Republic of Slovenia

Main objectives

- To promote collaboration between science, technology and industry, but also to provide platforms for the development of the education of young scientists and engineers based on knowledge and technology transfer from European laboratories like CERN and others
- To mitigate tensions between countries in the region
- Bringing people from different countries to work together

'CERN model' for SESAME in the Middle East and for South East Europe

What do we need in the future?

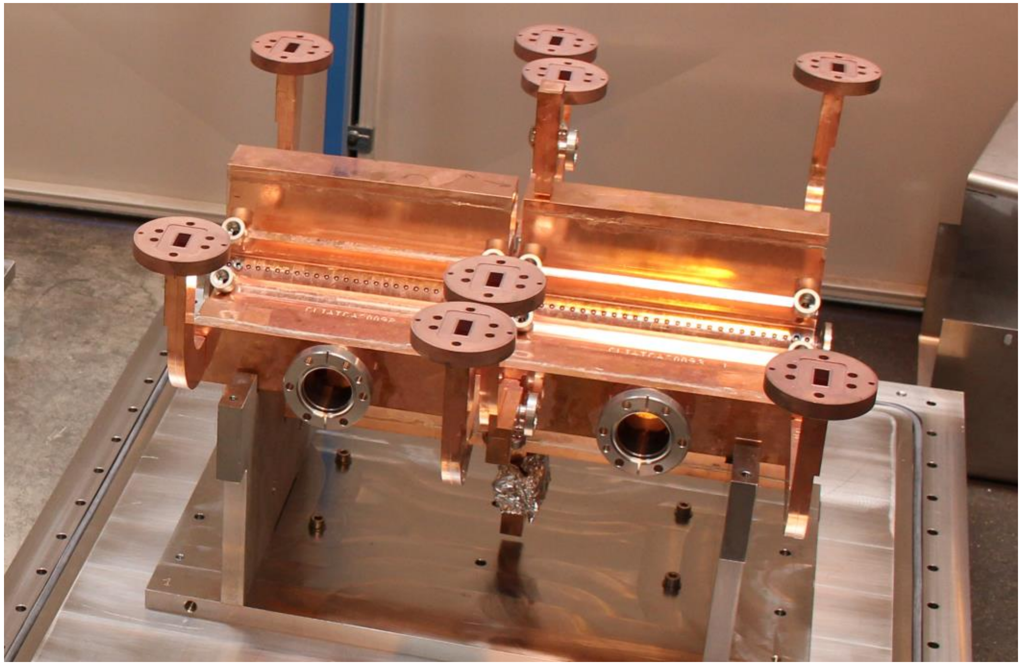
- Treat the tumour and only the tumour
  - ⇒ Control and monitor the ideal dose to the tumour
  - ⇒ Minimal collateral radiation "outside" the tumour
  - ⇒ Minimal radiation to nearby critical organs
  - ➢ Even if the tumour is moving
- Be affordable
  - ✓ Capital cost ?
  - ✓ Operating costs ?
  - ✓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

- Improve patient through-put
- Increase effectiveness
- Decrease cost

Current Hot topics: VHEE, FLASH, Compact Machine ……….

New State of the art?

With recent High-Gradient linac technology developments,
Very High Energy Electrons (VHEE) in the range 100–250 MeV
offer the promise to be a cost-effective option for Radiation Therapy

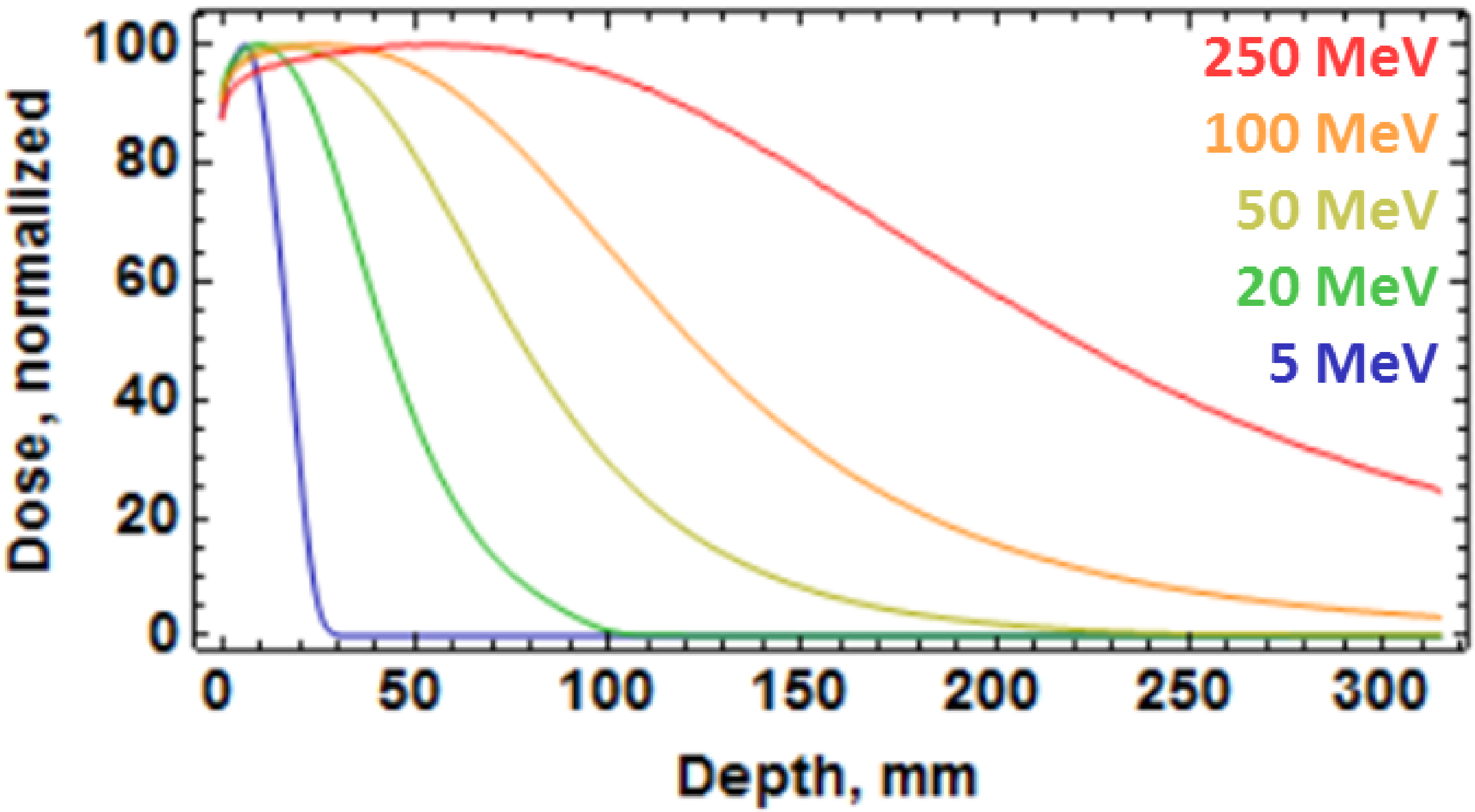


CLIC RF X-band cavity prototype (12 Ghz, 100 MV/m)

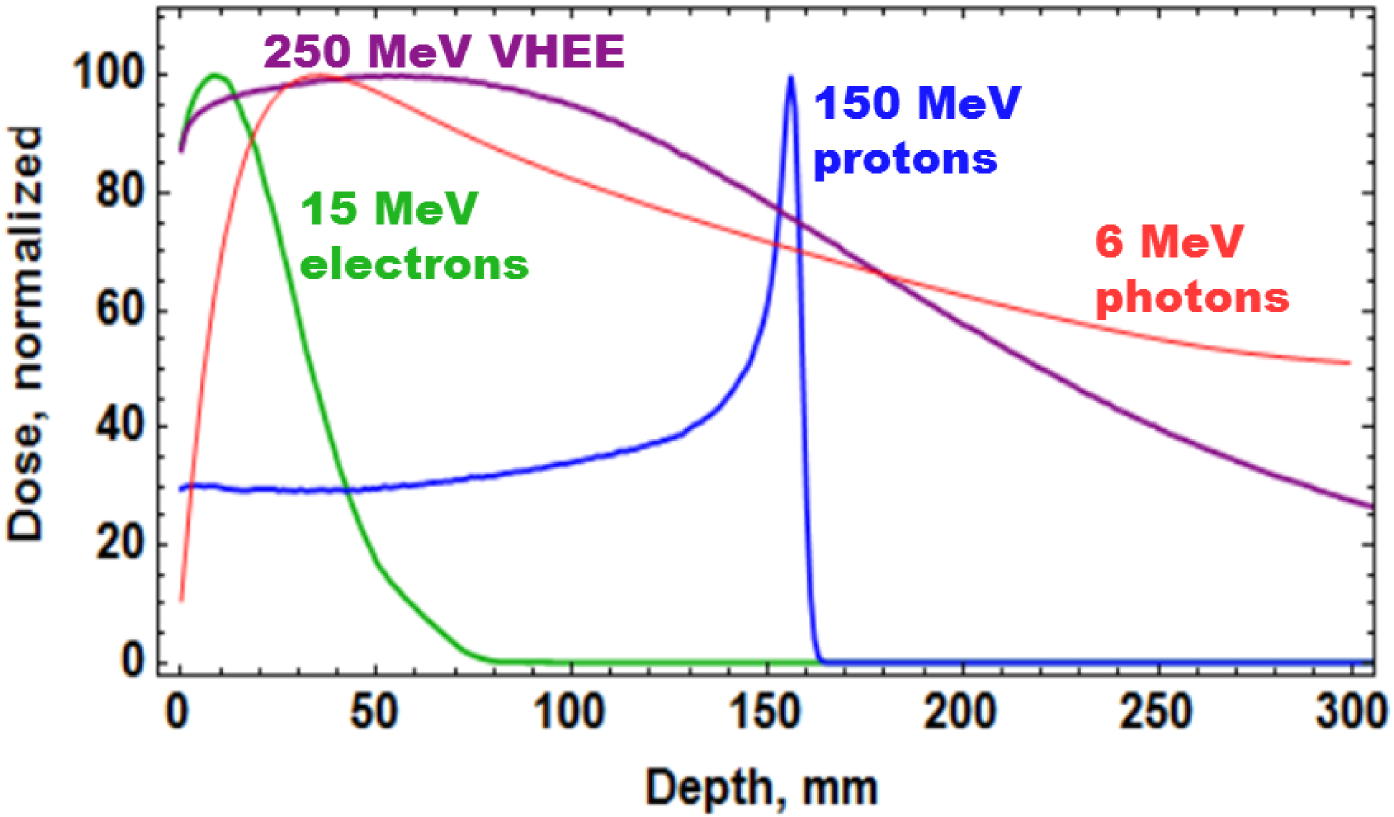
Compact Linear Collider

Acknowledge Lagzda

$\sigma = 5$ mm, various energies

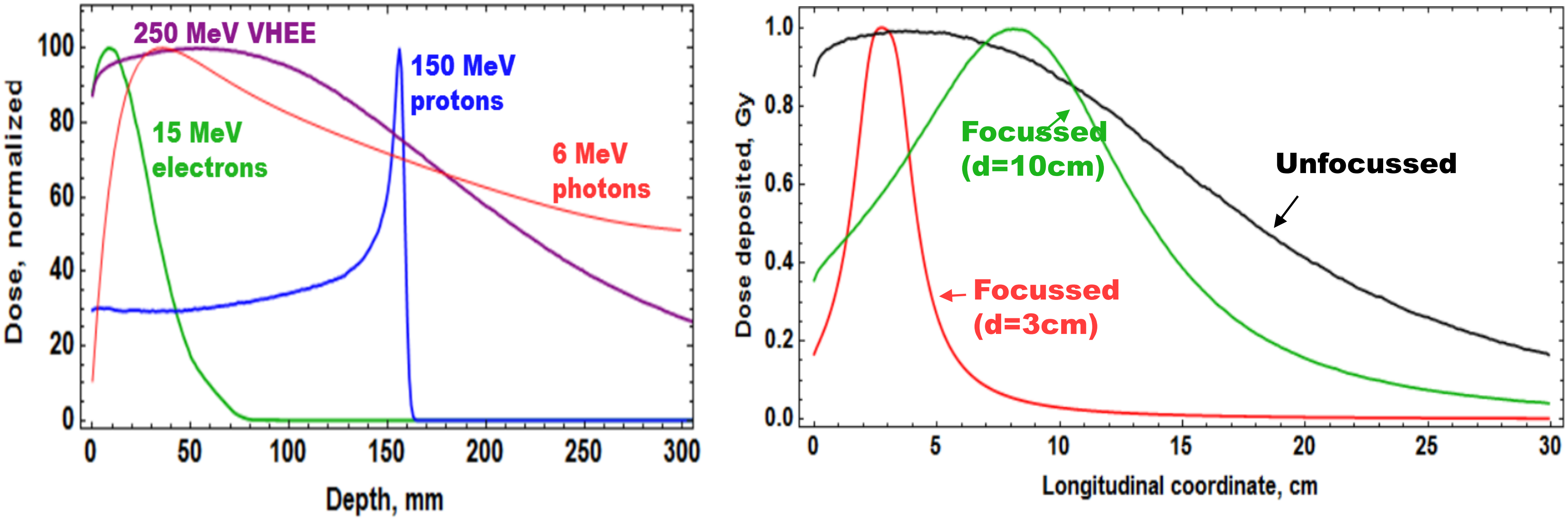


Courtesy of A. Lagzda



Dose profiles for various particle beams in water (beam widths $r = 0.5$ cm)

Courtesy of A. Lagzda



Depth Dose curve for various particle beams in water (beam widths r=0.5 cm)

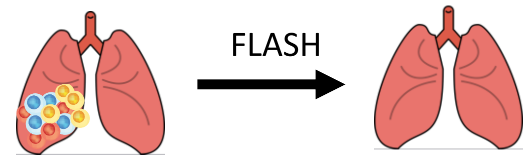
FLASH radiotherapy is based on the observation that healthy tissue is less damaged if treatment occurs very fast

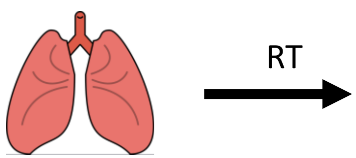
RESEARCH ARTICLE

RADIATION TOXICITY

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

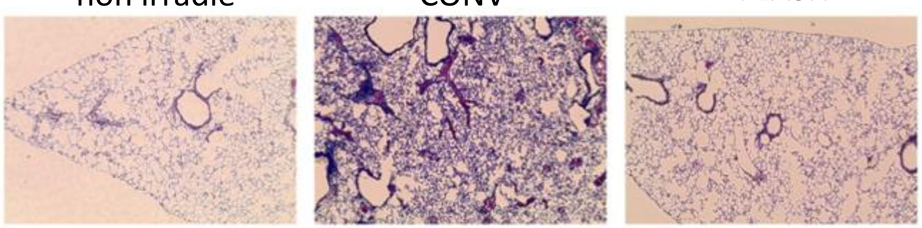
Vincent Favaudon,[1,2*] Laura Caplier,[3†] Virginie Monceau,[4,5‡] Frédéric Pouzoulet,[1,2§] Mano Sayarath,[1,2¶] Charles Fouillade,[1,2] Marie-France Poupon,[1,2||] Isabel Brito,[6,7] Philippe Hupé,[6,7,8,9] Jean Bourhis,[4,5,10] Janet Hall,[1,2] Jean-Jacques Fontaine,[3] Marie-Catherine Vozenin[4,5,10,11]





Toxicity evaluation

Contrôle non irradié | 17 Gy CONV | 17 Gy FLASH



HEALTHY | FIBROTIC | HEALTHY

Anti-tumor efficacy

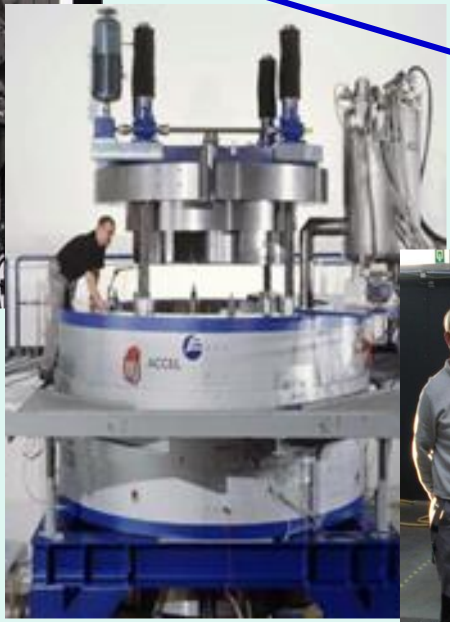
FLASH EFFECT

Absence of radiation-induced toxicity in the Normal lung

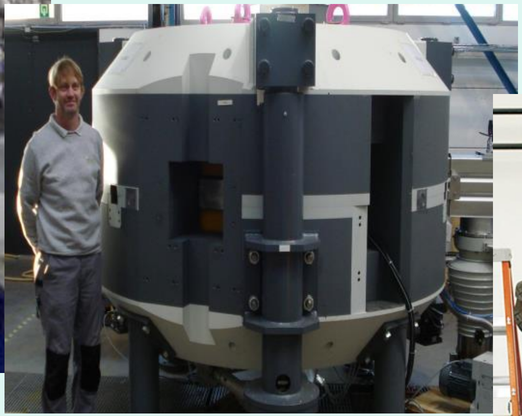
Cyclotrons for proton therapy

Superconducting Coils

IBA (1996) , SHI
250 Tons
Isochronous
Cyclotron



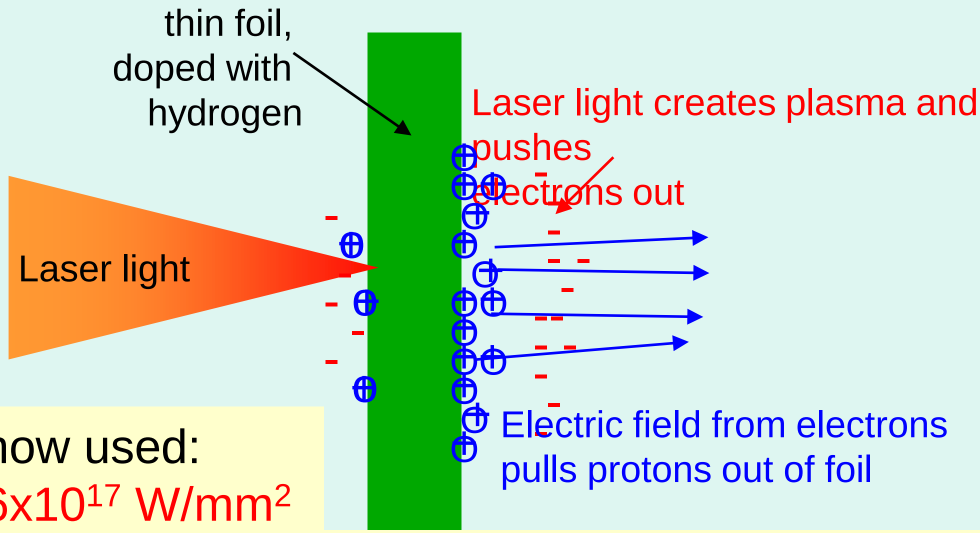
Varian (2005)
90 Tons
Isochronous
Cyclotron



IBA (2018)
60 Tons
Synchrocyclotron

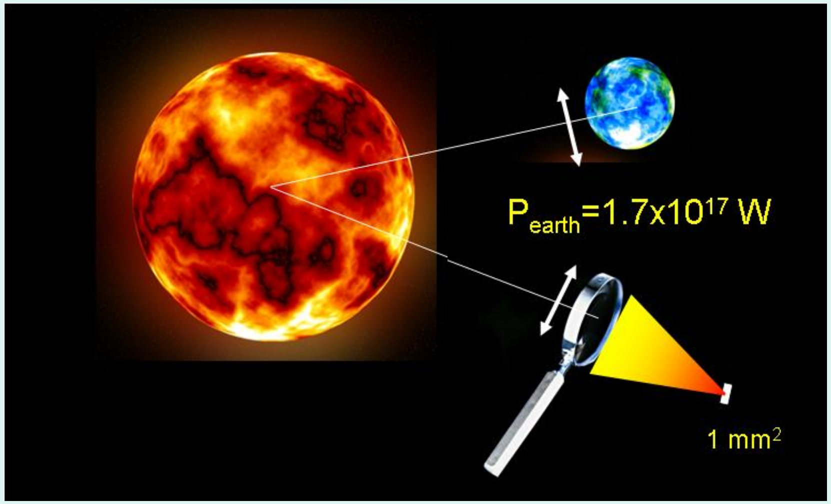
MEVION (2013)
15 Tons
Synchrocyclotron

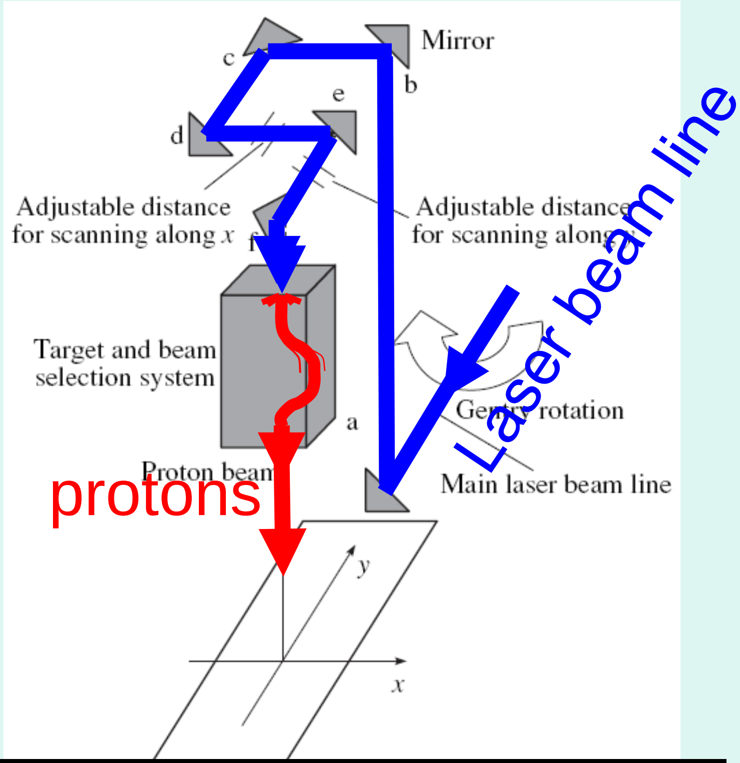
Laser driven proton accelerator



now used:
6×10^{17} W/mm^2

≈ total solar power on earth, focused at 1 mm^2

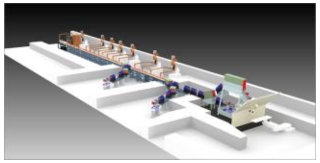


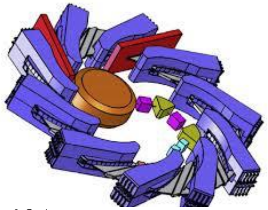


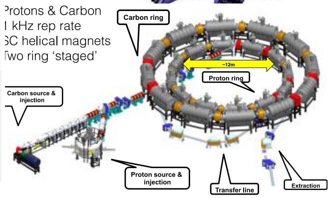
But:
- 100x more power is needed
- Energy spectrum: not homog.
→ takes time!!

Ion acceleration - options

	Pros	Cons	Status
Synchrotron	proven	size, complexity	4 operating
Linac	high rep. frequency, energy modulation, size	unproven	under development (TERA/ADAM/CERN)
Cyclotron	size	low flexibility (ions, energy), unproven	under development (IBA et al.)
FFAG	high rep. frequency	complexity (2 rings), unproven	under development (STFC)
New techniques (lasers, plasmas, etc.)	size	stability, long lead time	conceptual design







This workshop concentrates on the first two options, improved synchrotron and linac, which are more advanced (less development time needed), are within the CERN competences and are not in competition with commercial companies.

Treating moving targets

Courtesy of Christian Graeff, GSI, Germany