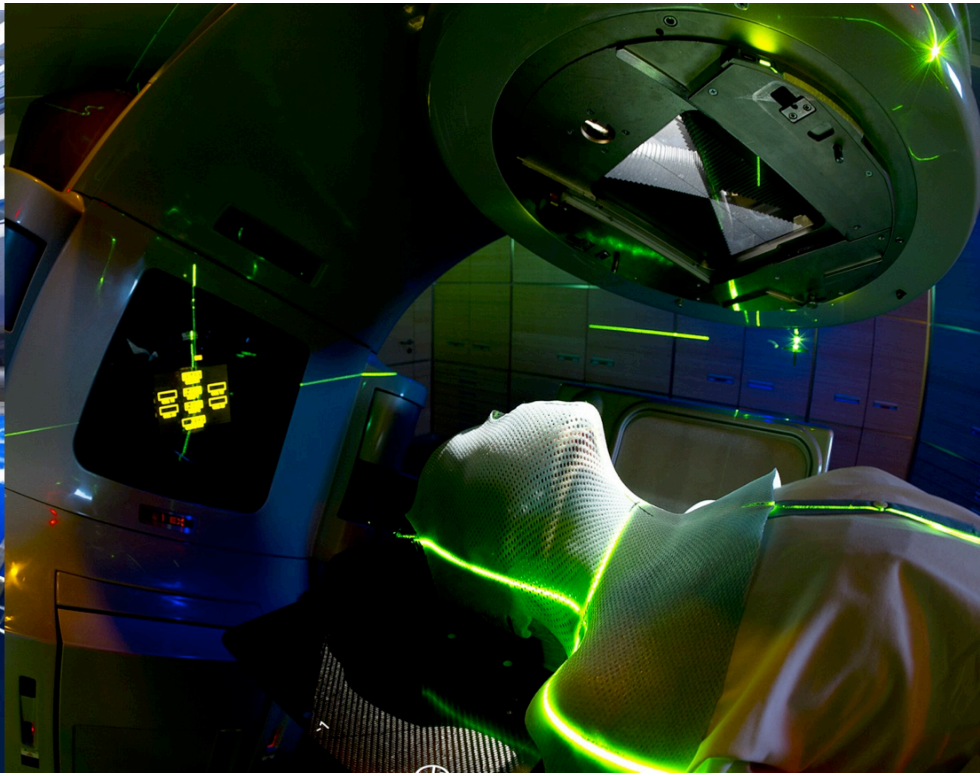
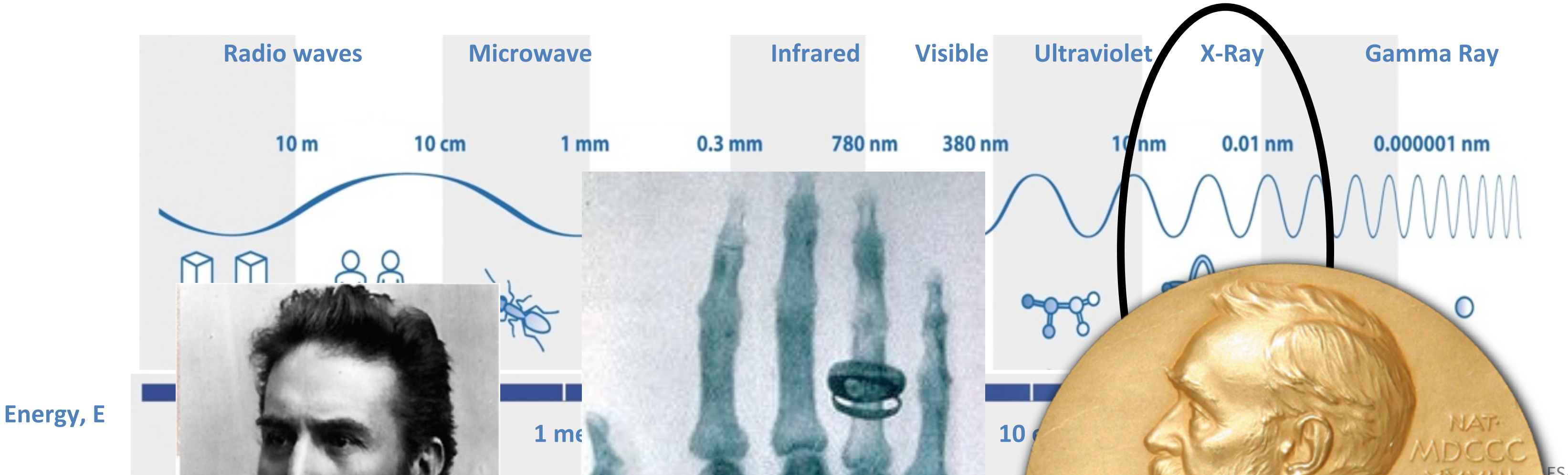
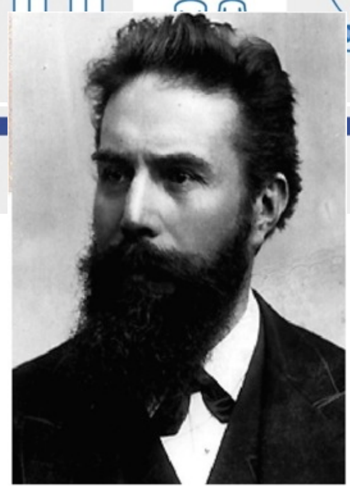
From physics to medical applications



Manjit Dosanjh, CERN 2019
manjit.dosanjh@cern.ch
www.cern.ch/enlight

Modern medical physics– X-rays





Wilhelm Röntgen

8/11/1895

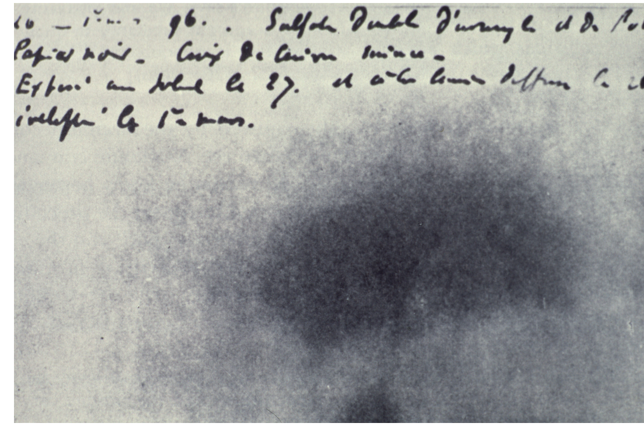
22/12/1895

1901

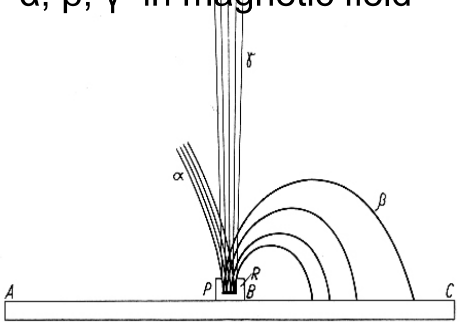
……….beginning of medical physics

Henri Becquerel

1896:
Discovery of natural radioactivity

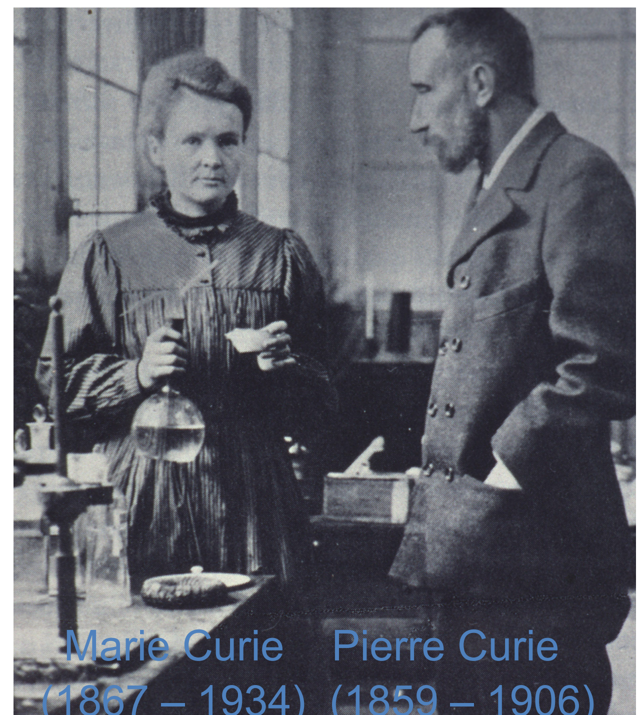


Thesis of Mme. Curie – 1904
α, β, γ in magnetic field



1898: Discovery of radium

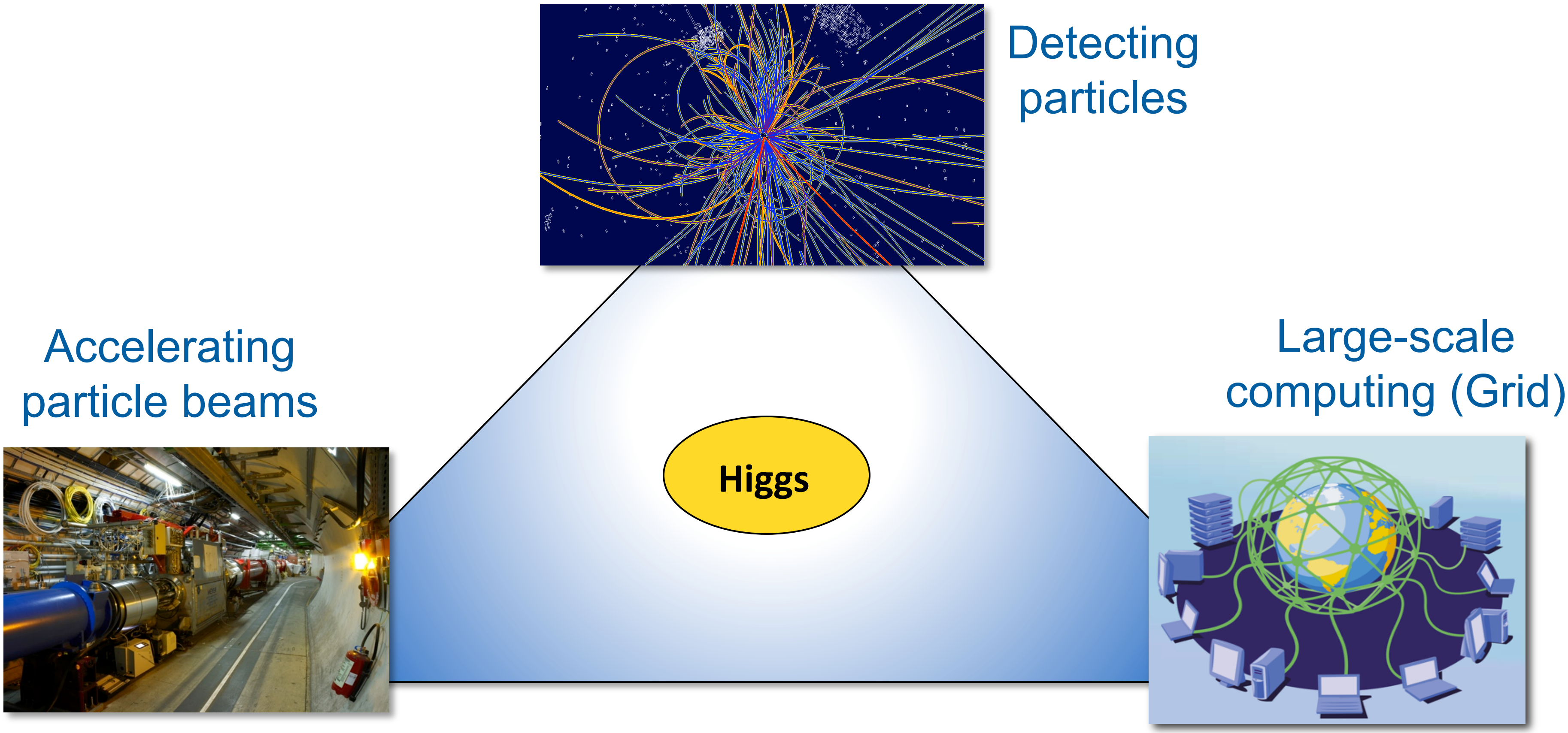
used immediately for “Brachytherapy”



First radiobiology experiment

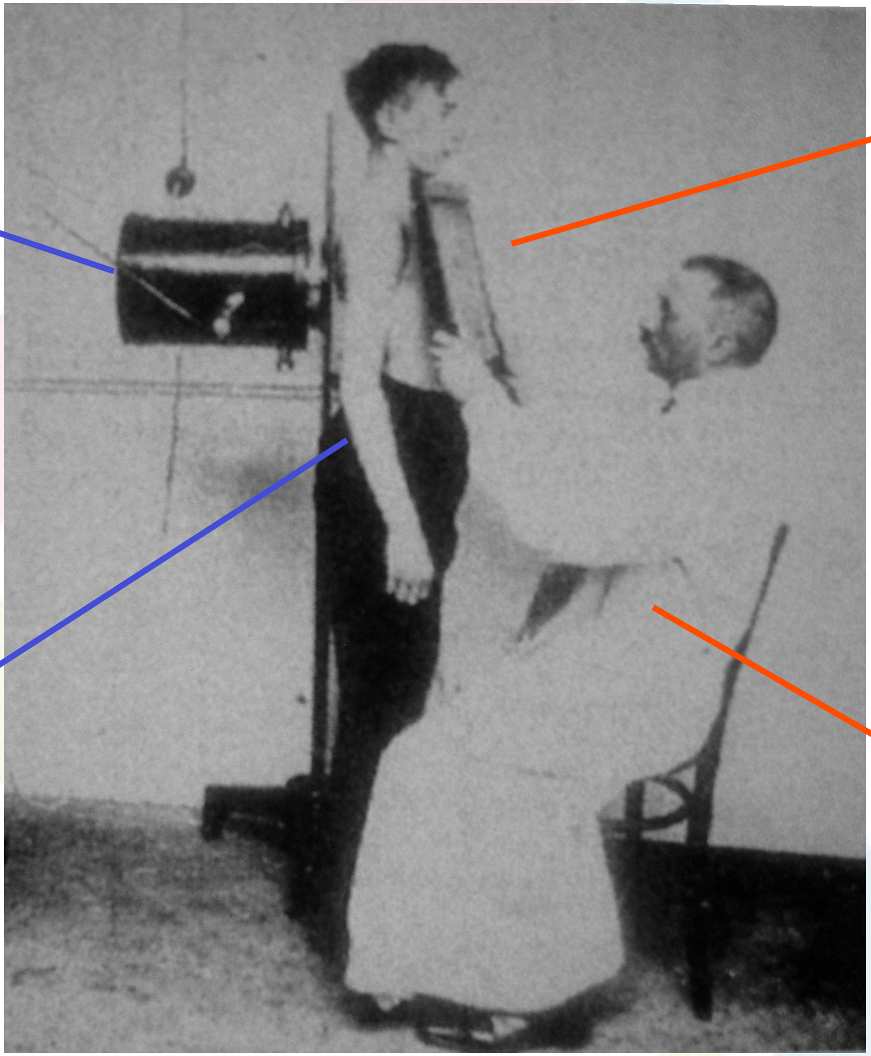
Pierre Curie and Henri Becquerel

CERN and Physics Technologies



Manjit Dosanjh, CERN

X-ray systems



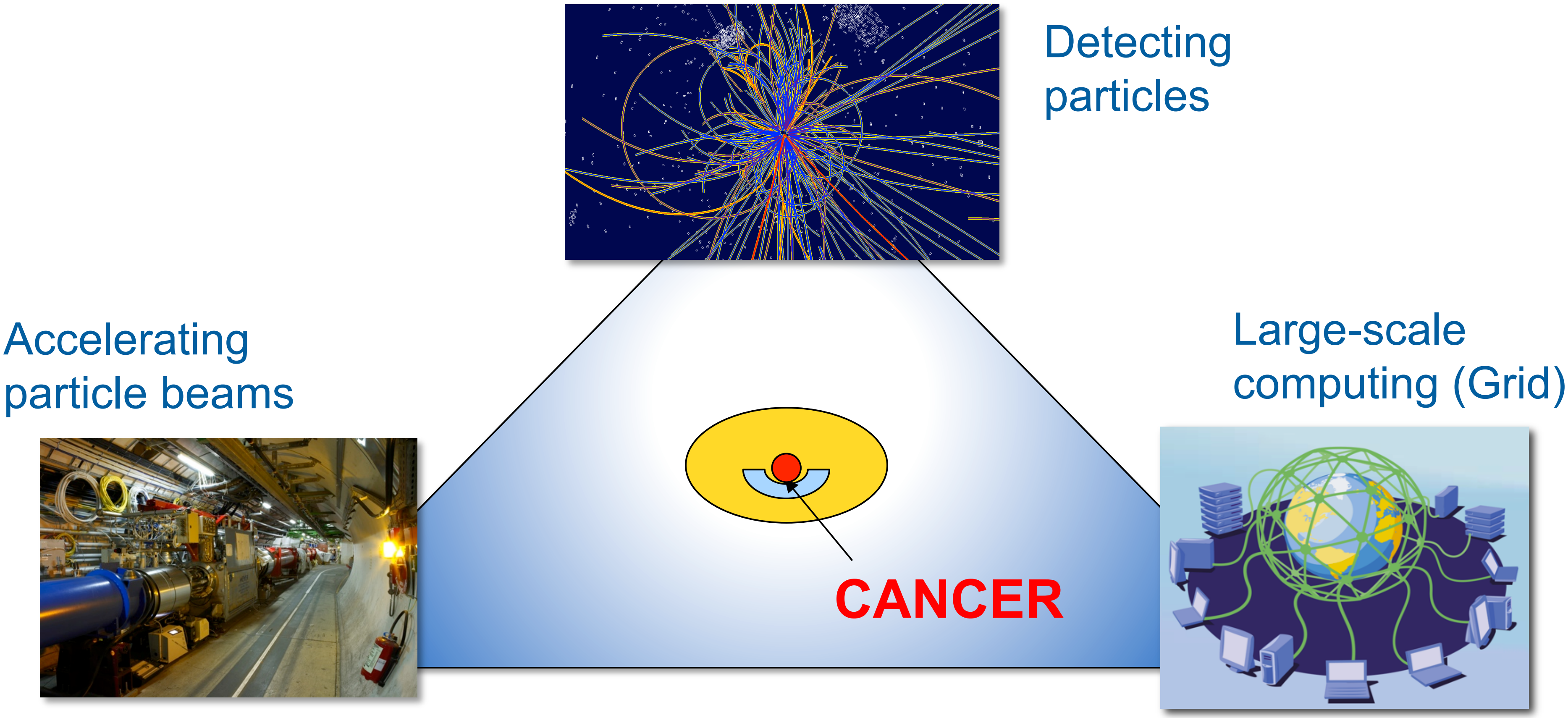
X-ray source

Object

Detector

Pattern Recognition System

How Can Physics Technologies help?



Manjit Dosanjh, CERN

Why Cancer and Physics Technologies?

It is a large and a growing societal challenge:

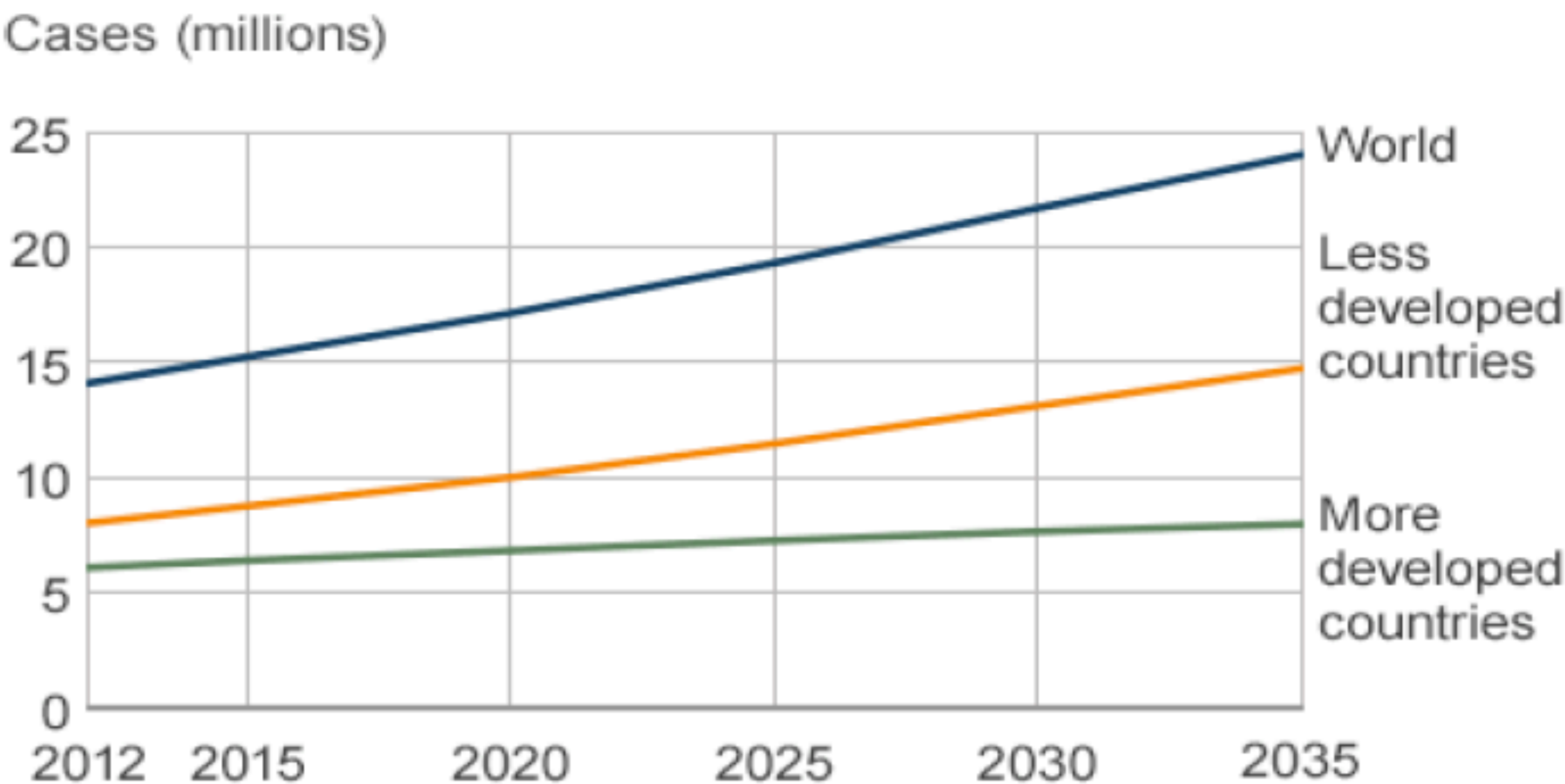
- More than 3 million new cancer cases in Europe in 2015
- Nearly 15 million globally in 2015
- This number will increase to 25 million in 2030
- Currently around 8 million deaths per year

(In Ireland: 4.8 million inhabitants; 40,000 new cancer patients per year; by 2020: 1 in 2 people will develop cancer in their lifetime; around 30% deaths by cancer; skin, prostate, breast, bowel, lung) *National Cancer Registry of Ireland (NCRI)*

How can physics help?

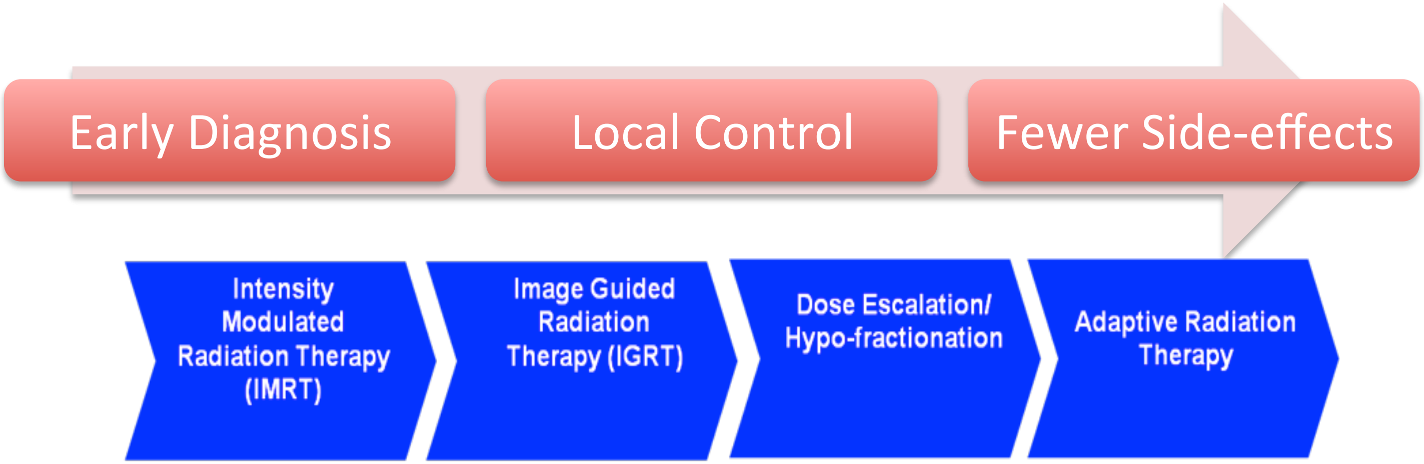
GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012

Predicted Global Cancer Cases



Source: WHO GloboCan

Improving Cancer Outcomes



- New Technologies
- Advanced radiotherapy
- Radiobiology, Biology, Clinical
- Multi-disciplinary collaboration

The Challenge of Treatment

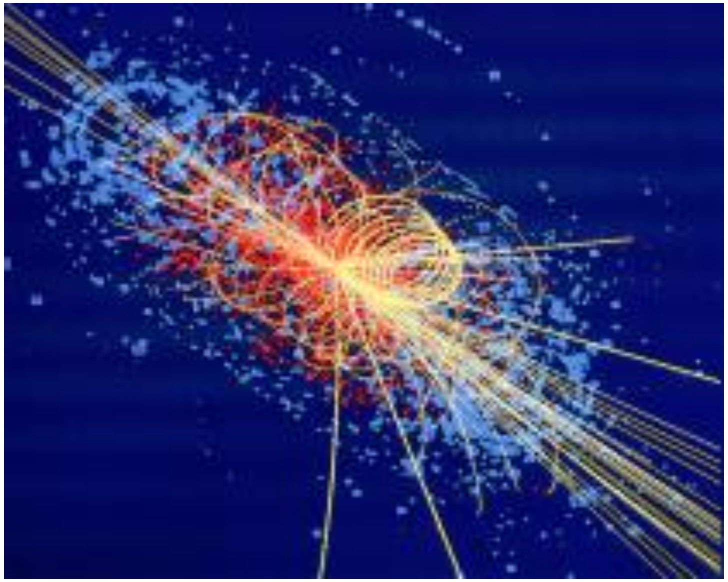
Ideally one needs to treat:

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

Treatment has two important goals to kill 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.

No treatment without detection!

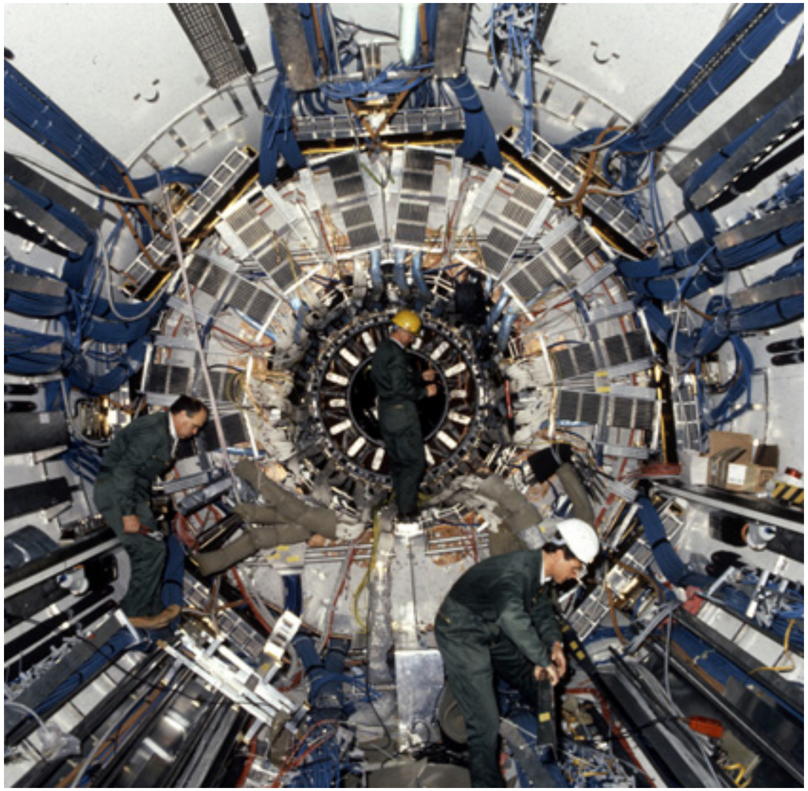
Particle Detection

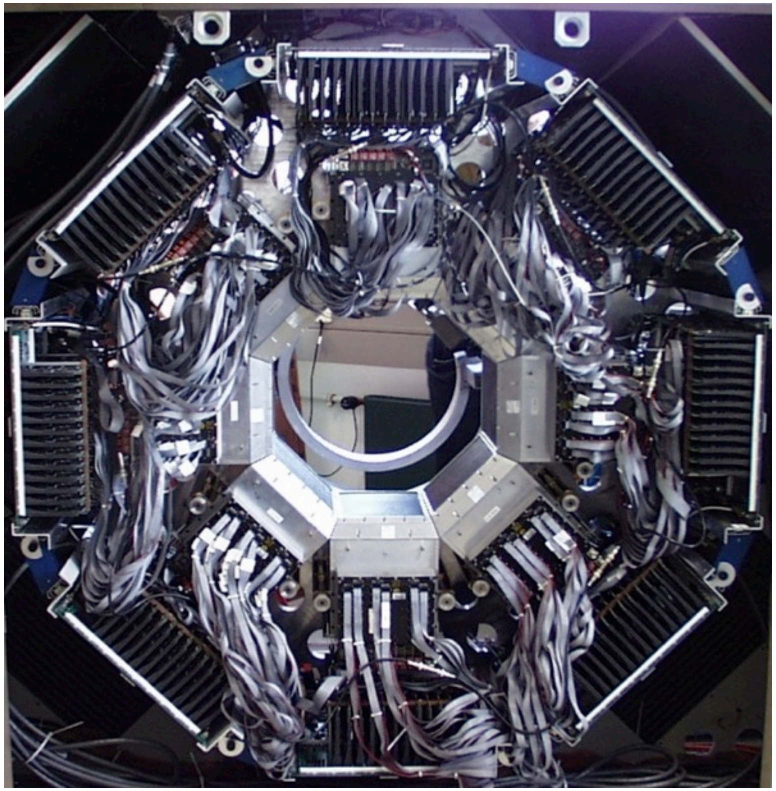


Imaging

X-ray, CT, PET, MRI

The detector challenge

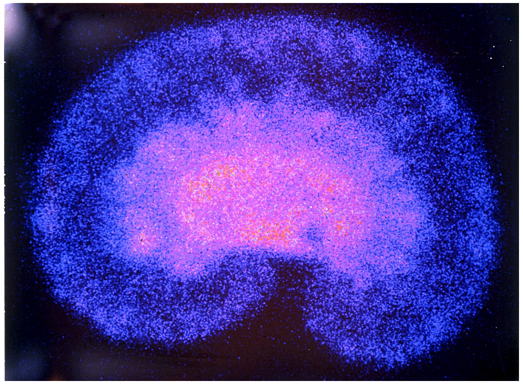


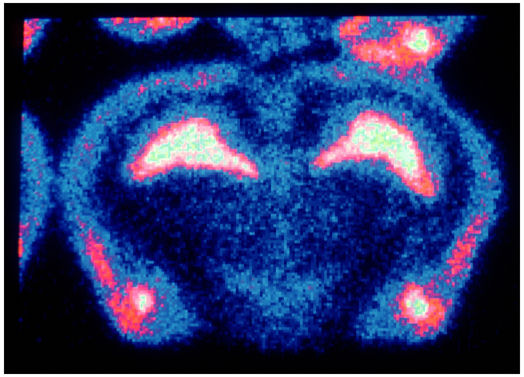


Low dose digital X-Ray Imaging

Physics Nobel Prize 1992

Georges Charpak

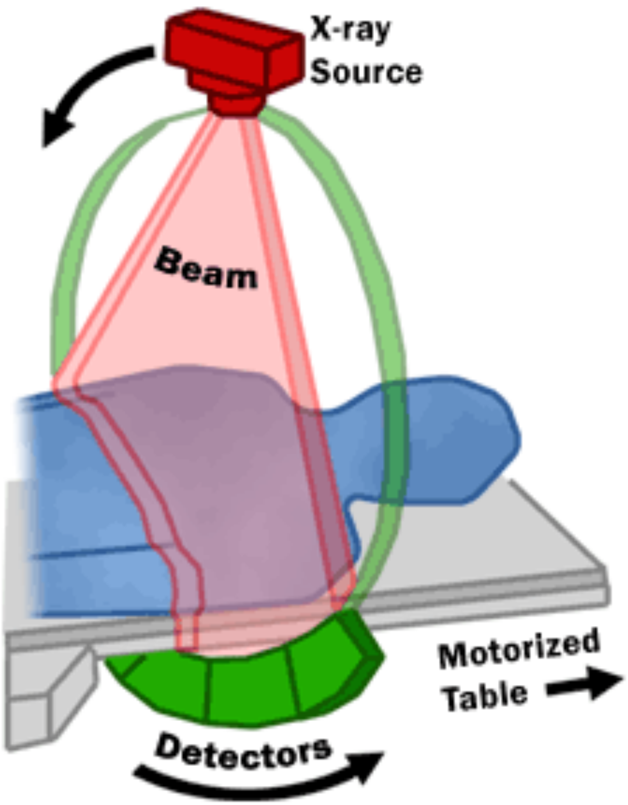




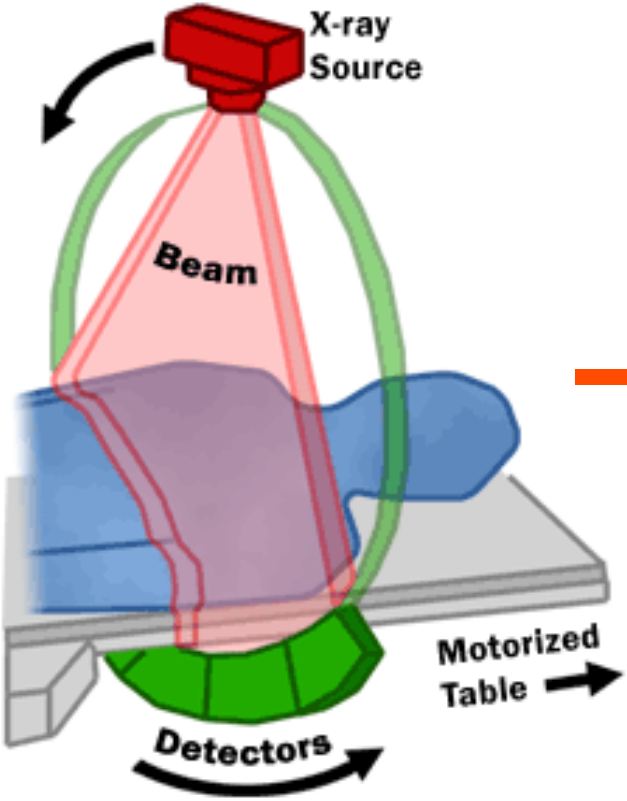
Low dose X-ray image of rat brain and kidney the use of MWPC

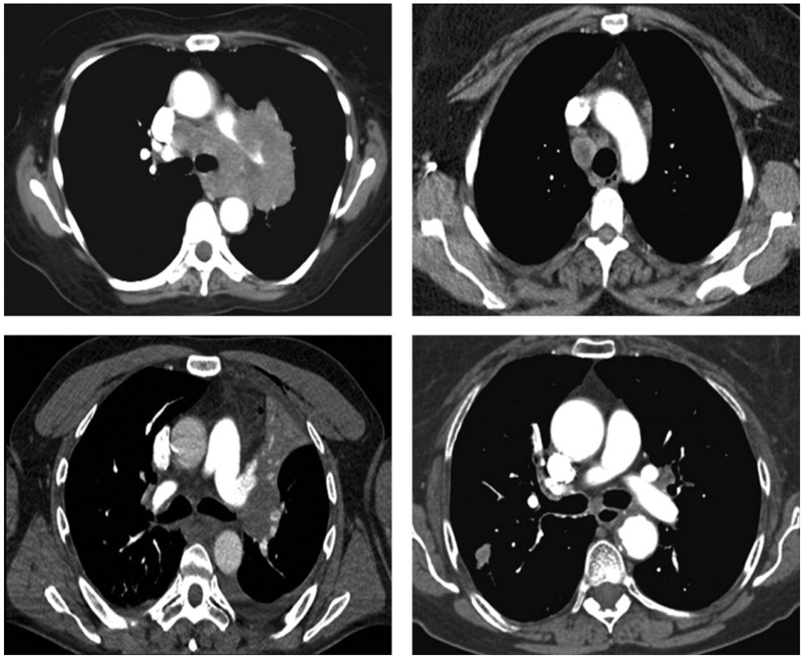
CT – Computed Tomography

"3d X-rays"



CT – Computed Tomography



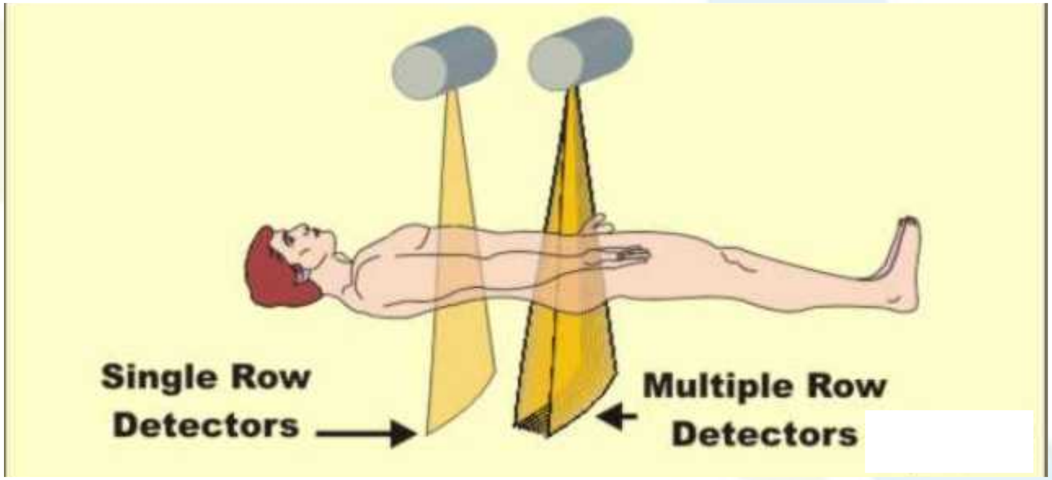


“3D-imaging”

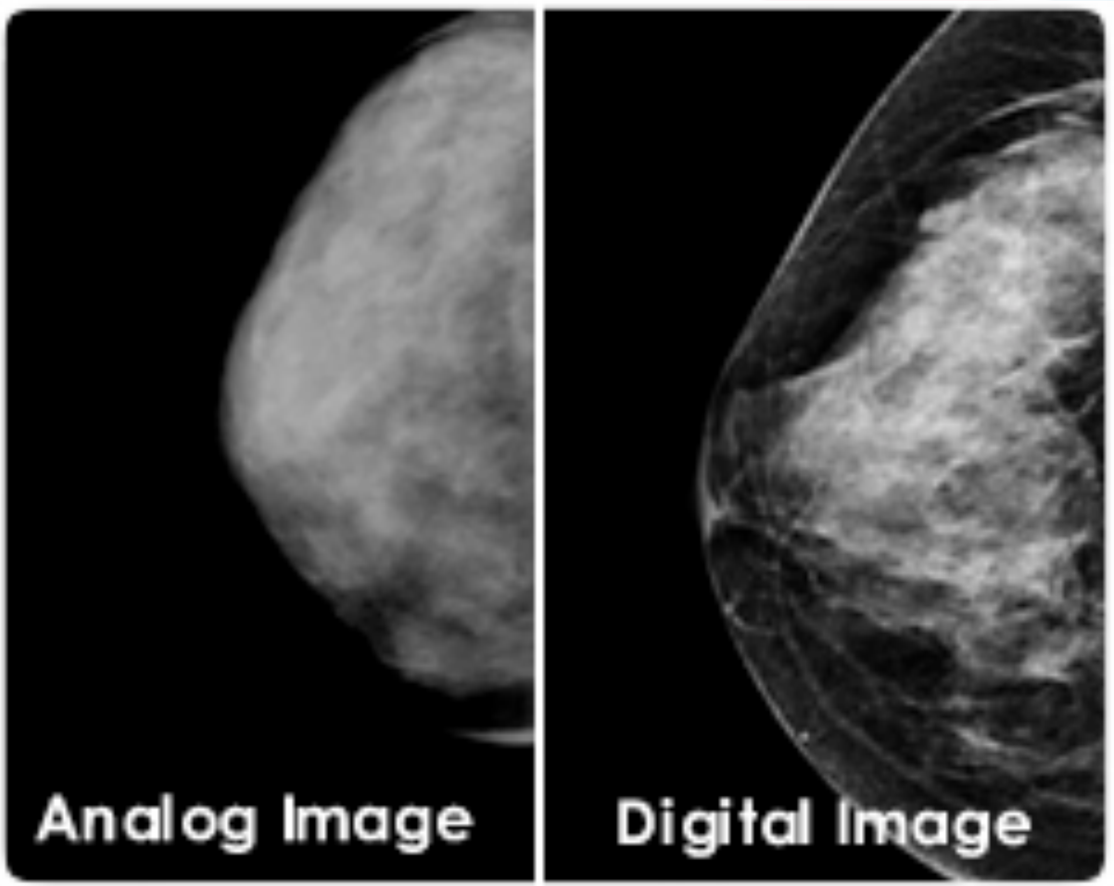
X-ray CT is a key driver of change in medical imaging

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



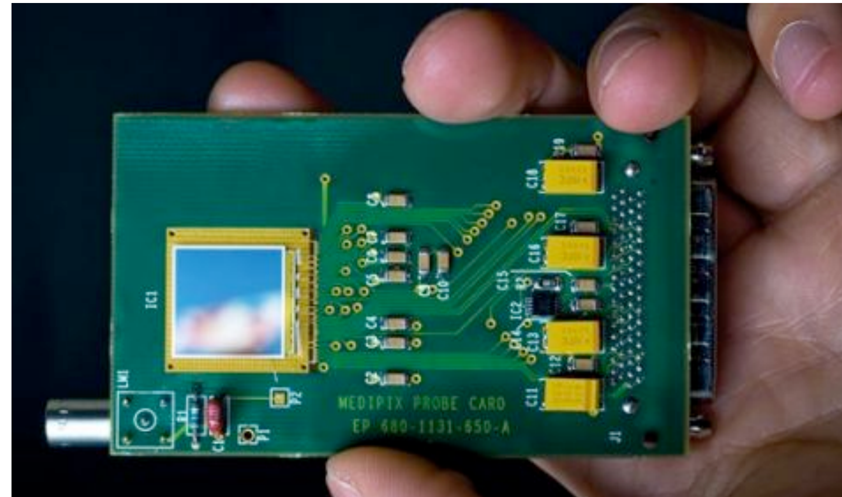
Towards digital colour x-ray imaging



mars
Medipix All Resolution System

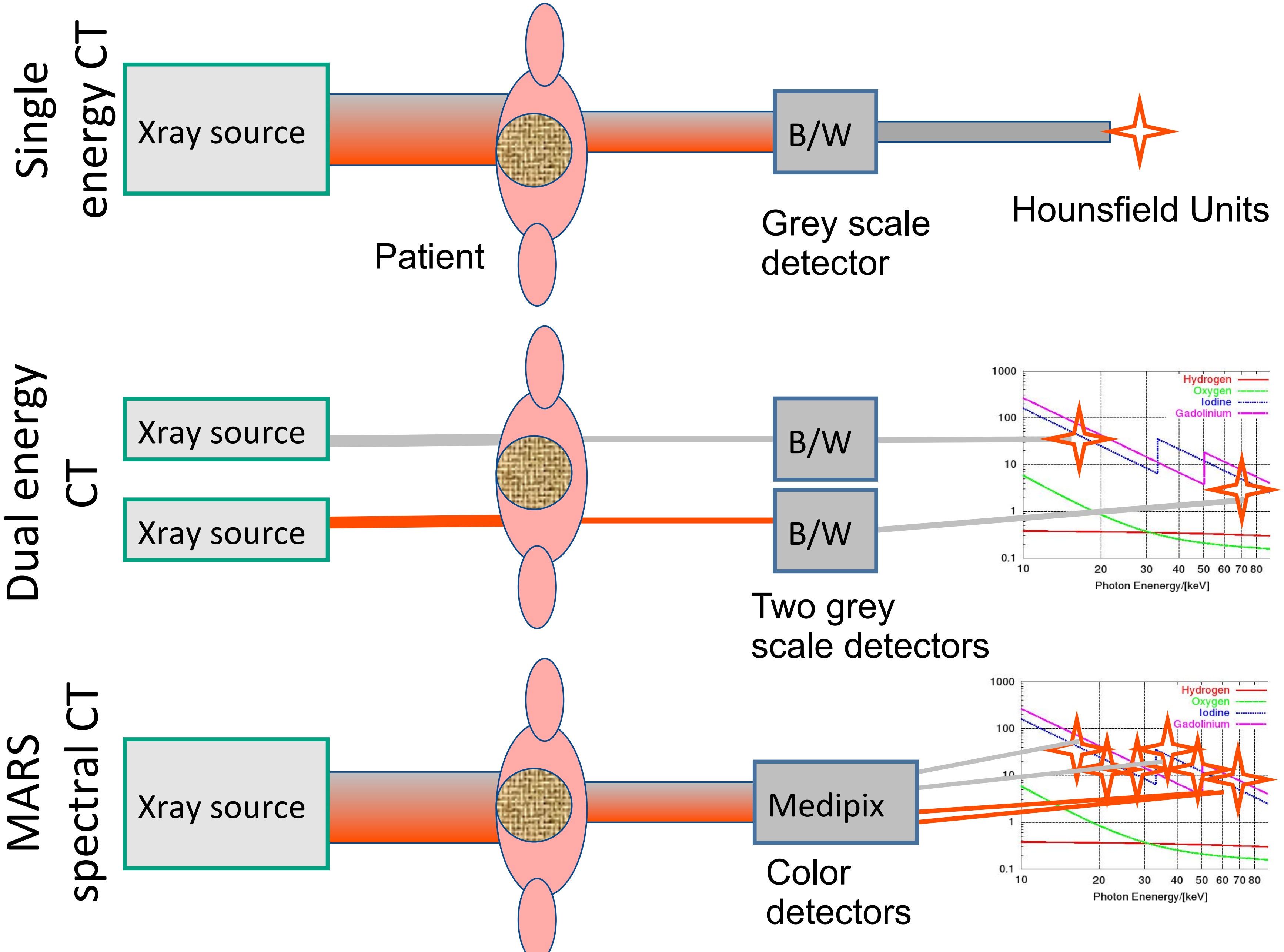
Medipix

- 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

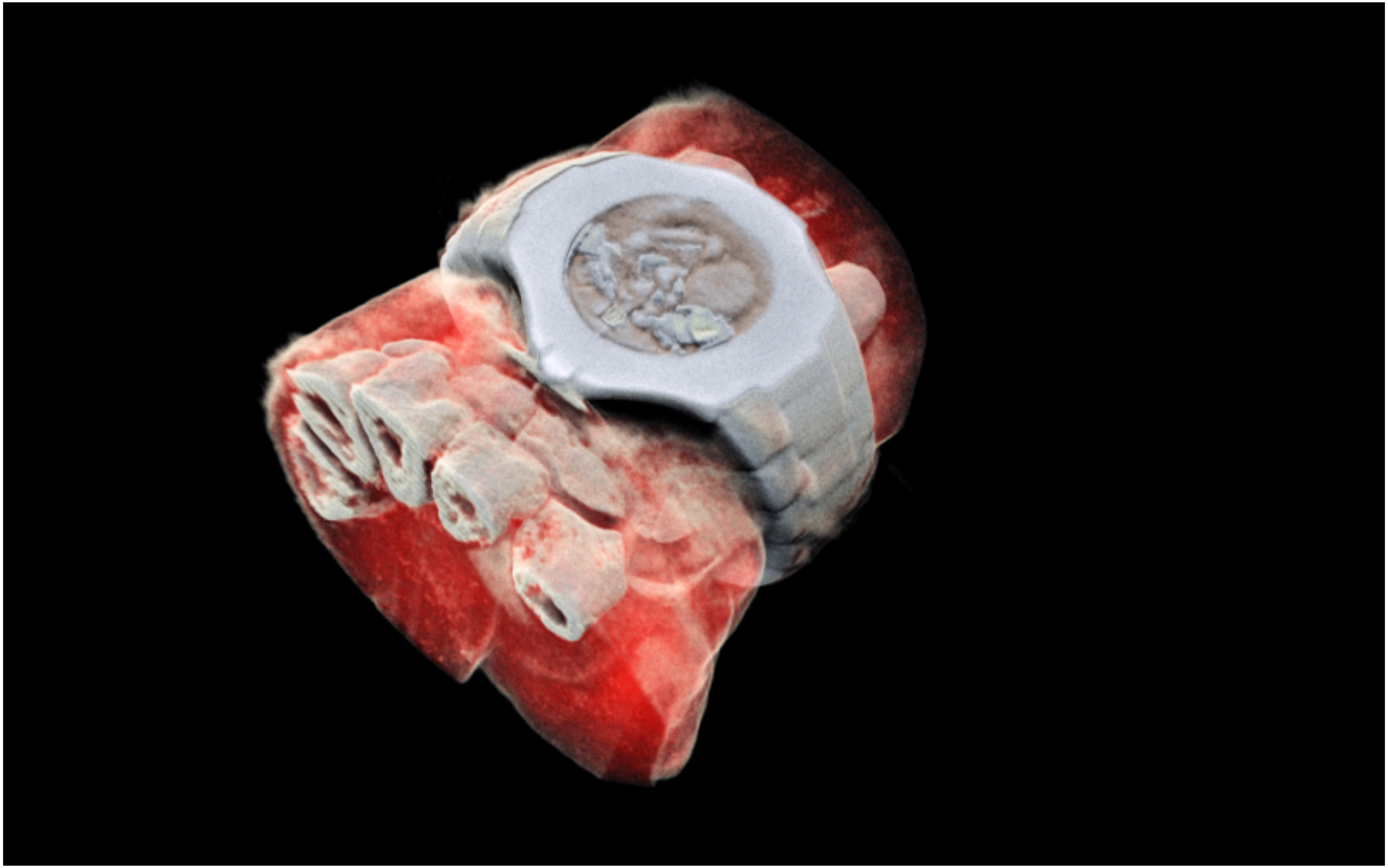


Credits: Simon Procz, University of Freiburg

Single- , dual-, and spectral CT



First 3D colour x-ray image of human



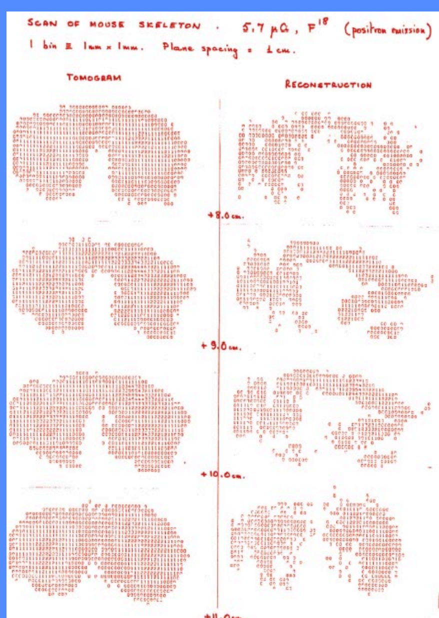
A 3D image of a wrist with a watch showing part of the finger bones in white and soft tissue in red. couples the spectroscopic information generated by the Medipix3 with powerful algorithms to generate 3D images (Image: MARS Bioimaging Ltd)

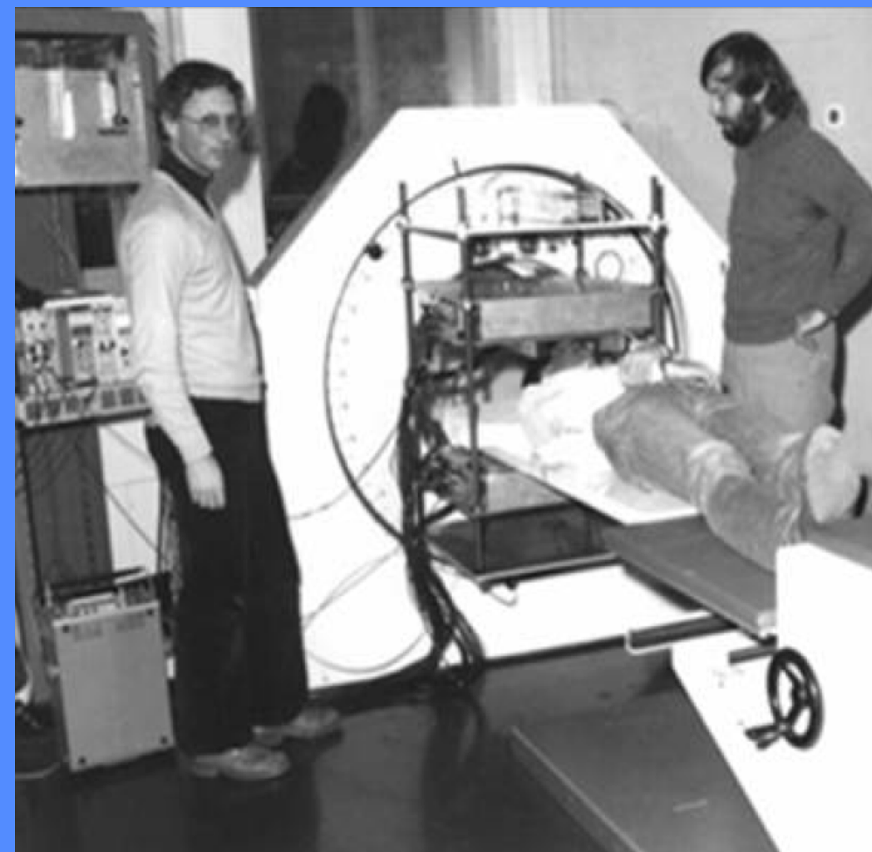
PET Imaging activities at CERN

Alan Jeavons and David Townsend

built and used in Geneva Hospital

a PET system based on high-density avalanche gas chambers HIDACs

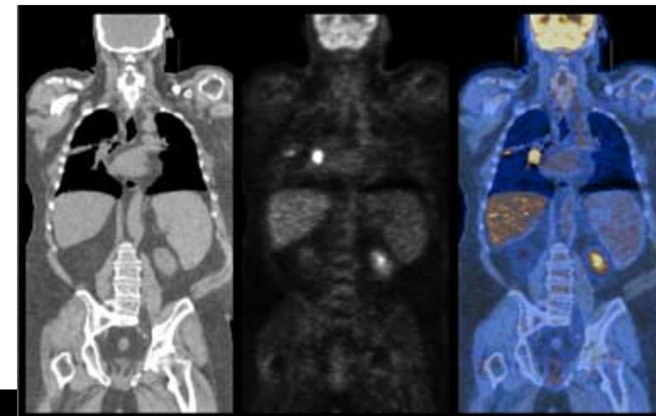




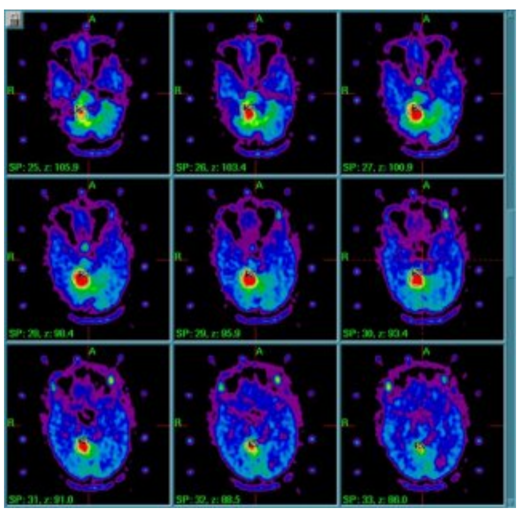
Paul Lecoq,

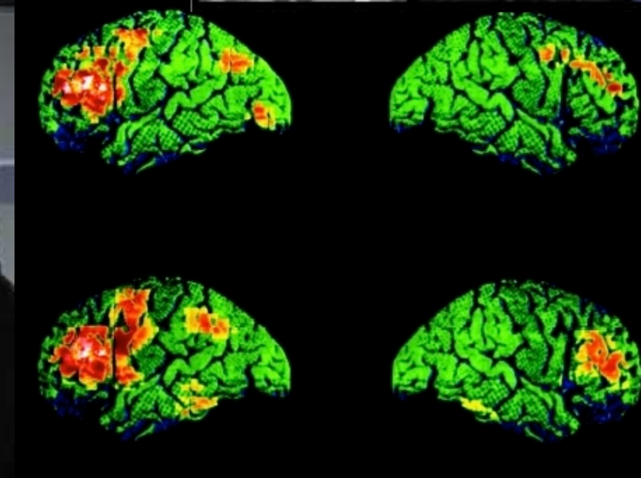
PET: antimatter for clinical use

- Not only science-fiction

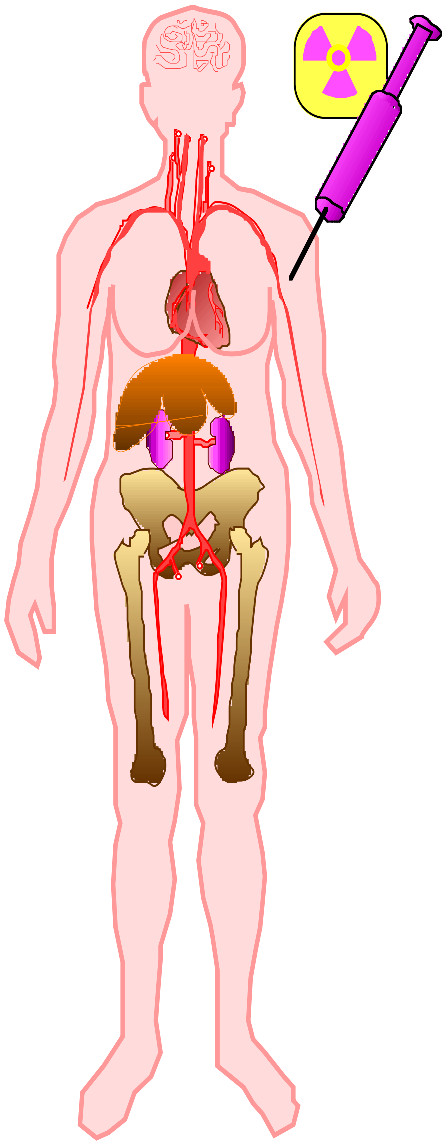


- Positrons are used in PET:
- PET = Positron Emission Tomography





PET: how it works

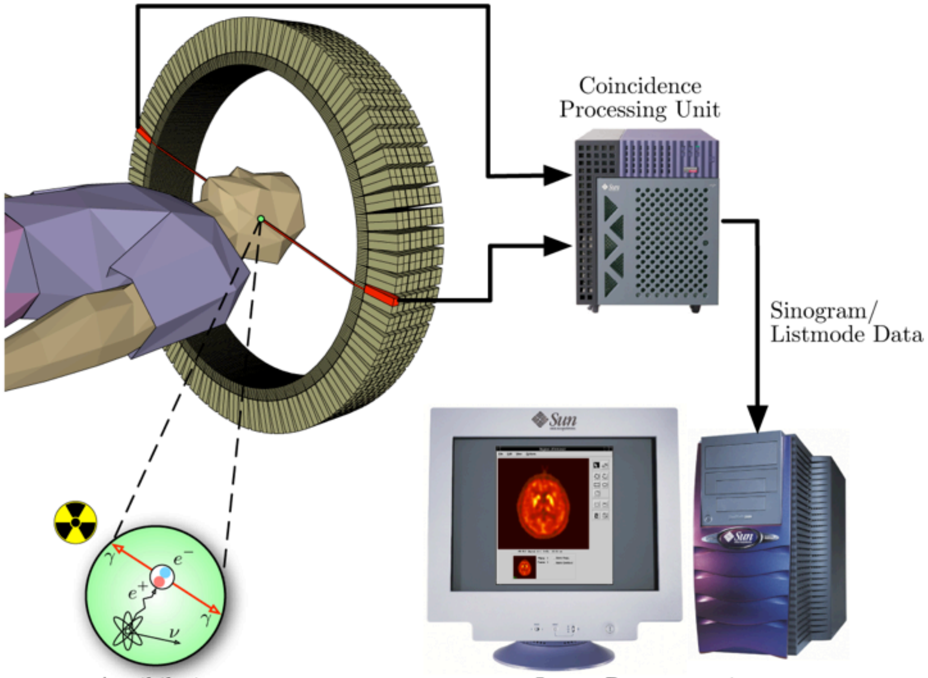


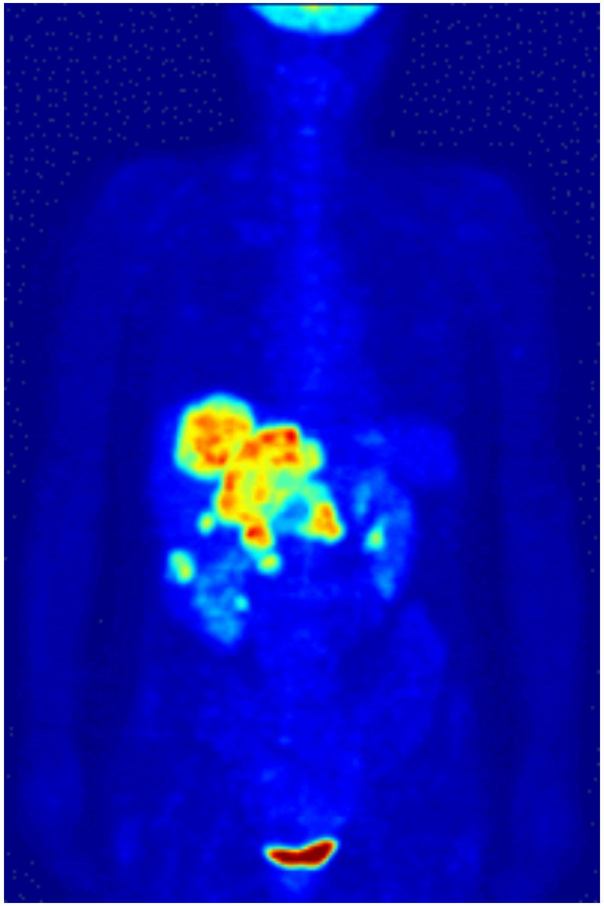
- Drug is labeled with positron (β+) emitting radionuclide.
- Drug localizes in patient according to metabolic properties of that drug.
- Trace (pico-molar) quantities of drug are sufficient.
- Radiation dose fairly small (<1 rem = 0.01 Sv).

PET – How it works

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

Positron Emission Tomography



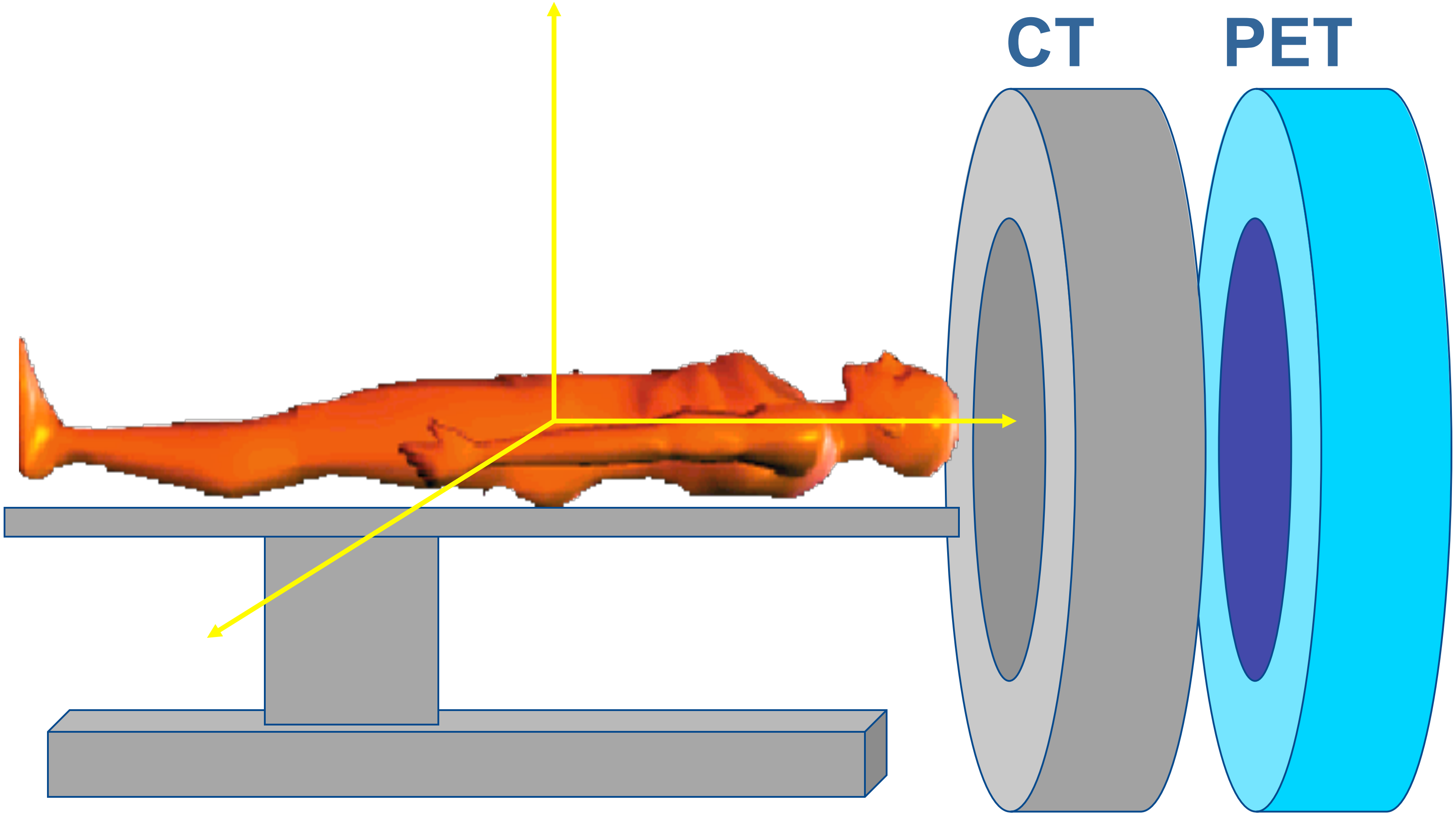


- ^{18}FDG carries the ^{18}F to areas of high metabolic activity
- 90% of PET scans are in clinical oncology

1974 the first human positron emission tomography

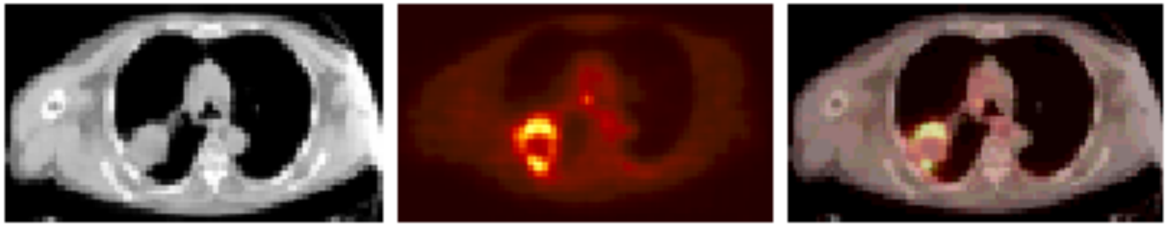
Concept of PET-CT

David Townsend



Multi-modality imaging

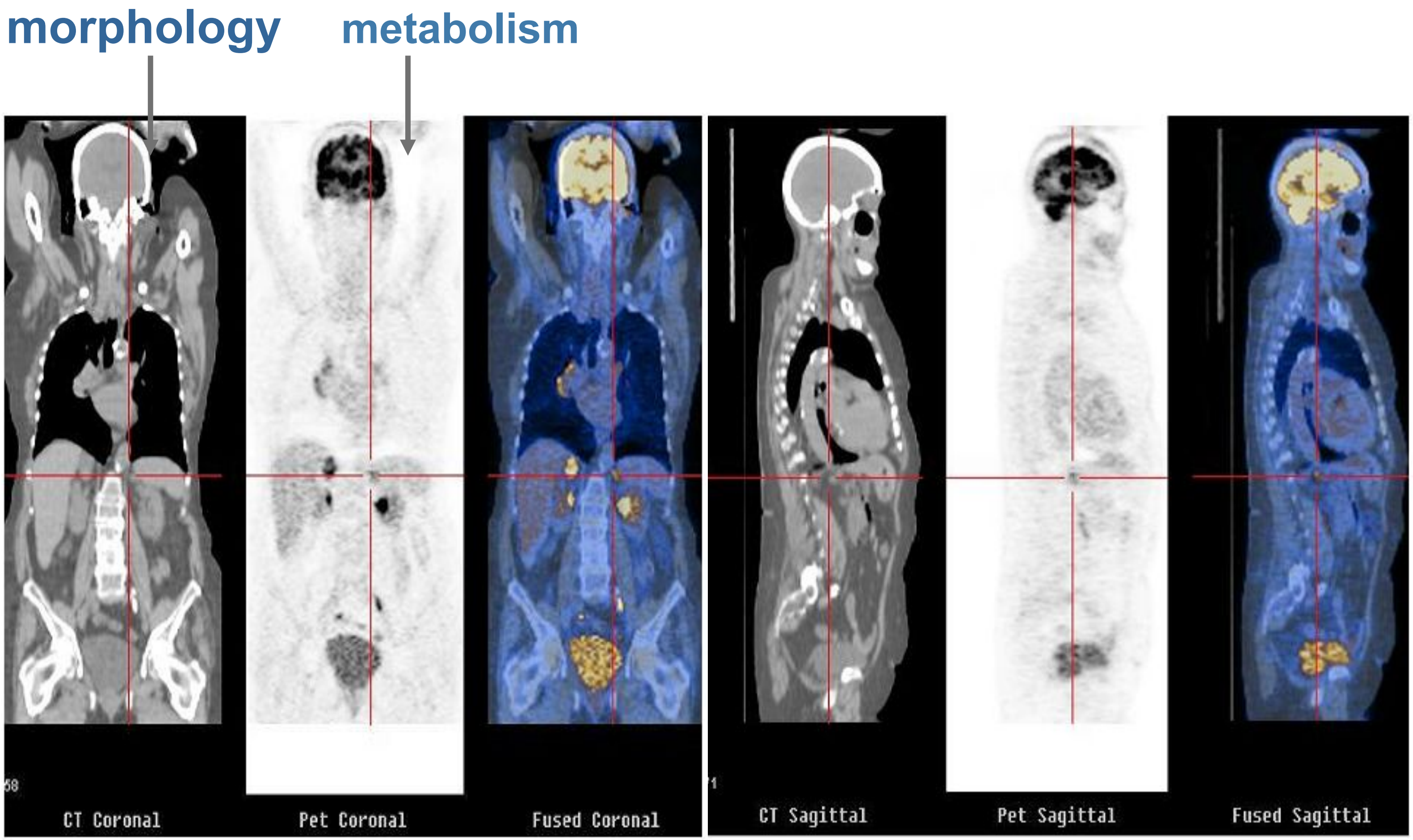
Primary lung cancer imaged with the Dual/Commercial scanner. A large lung tumor, which appears on CT as a uniformly attenuating hypodense mass, has a rim of FDG activity and a necrotic center revealed by PET.



Courtesy of David Townsend

Multimodality imaging: CT with PET

Combining anatomic and functional imaging



David Townsend, UK Physicist

Multimodal imaging

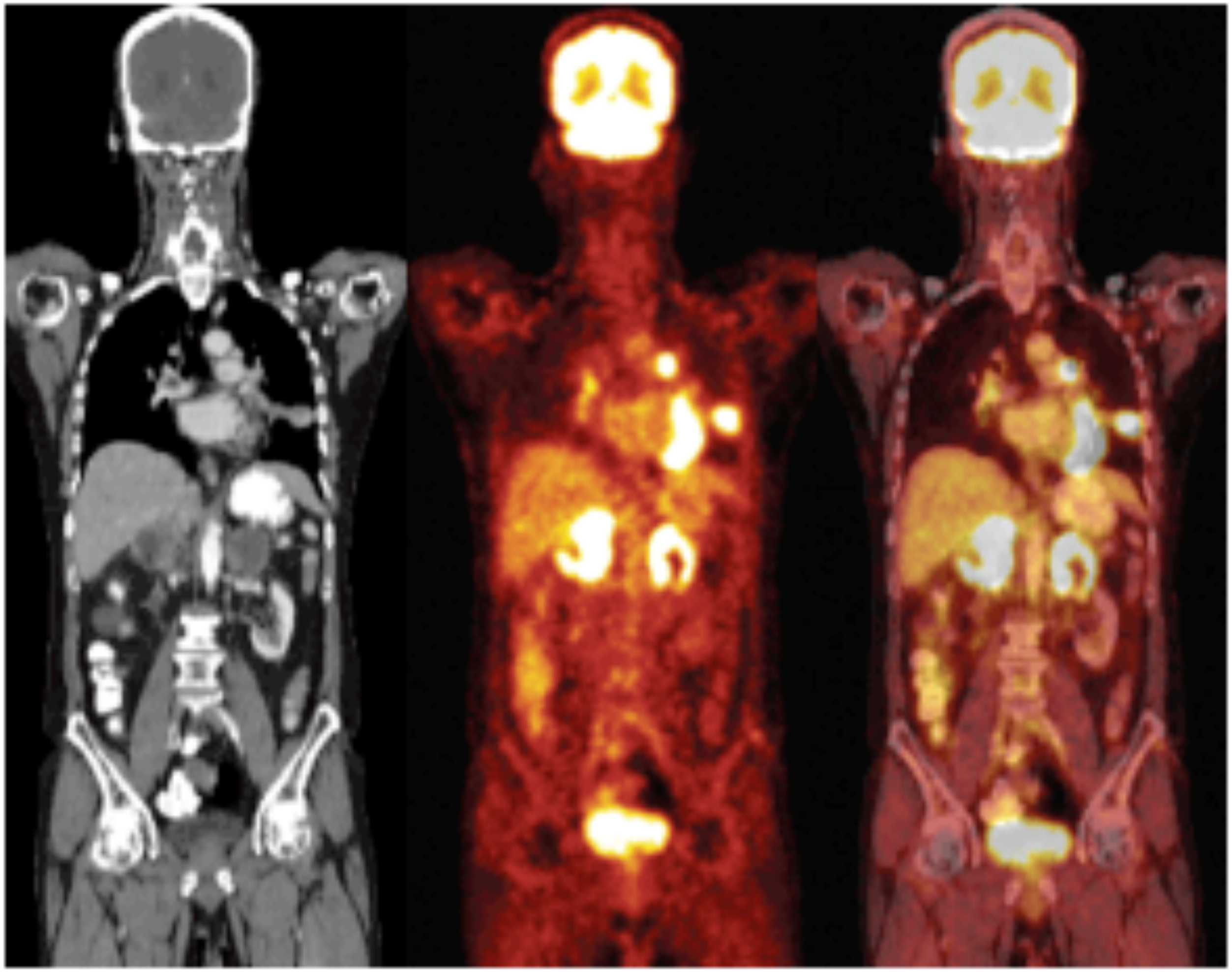
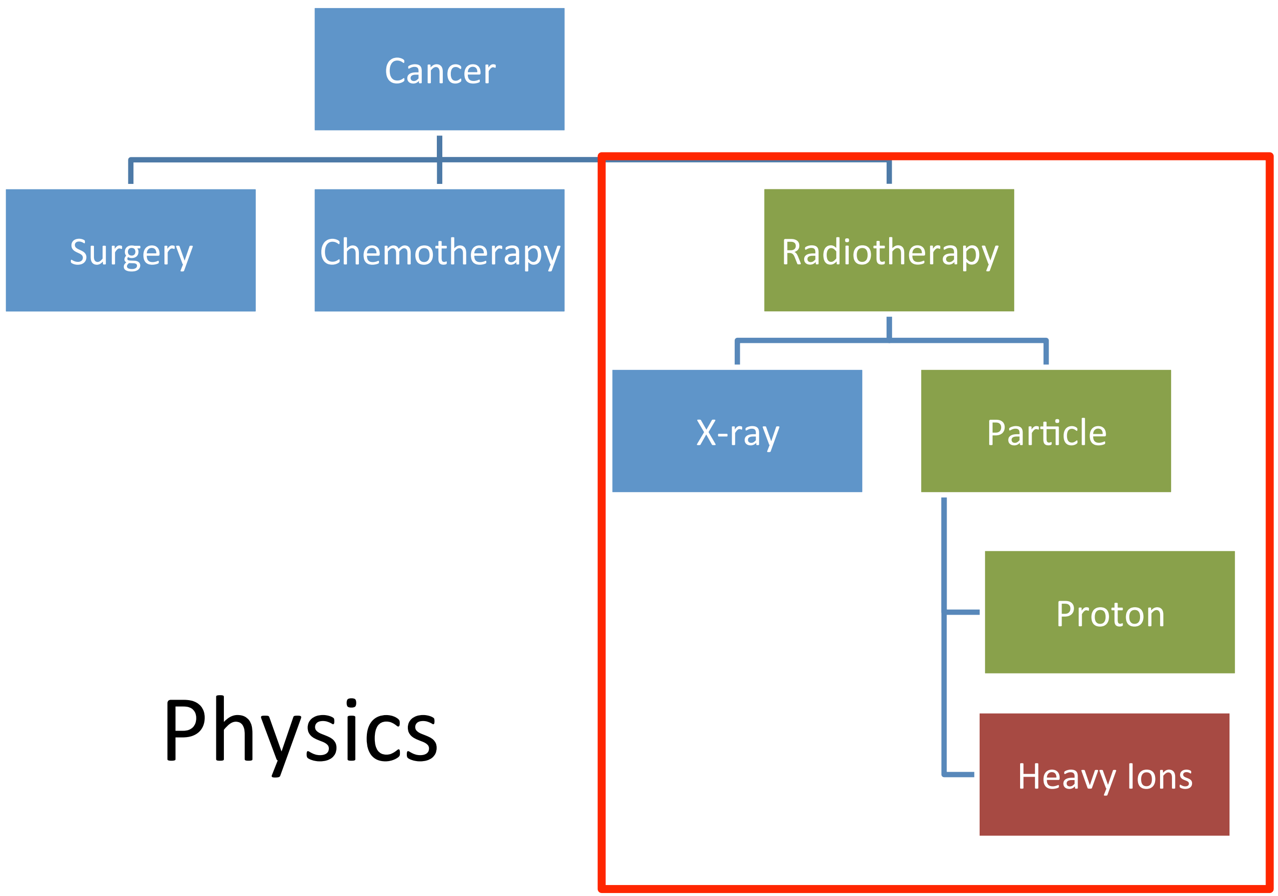


FIGURE 1. CT, PET, and PET/CT of lung cancer with adrenal metastases.

Proposed by David Townsend

Cancer treatment options

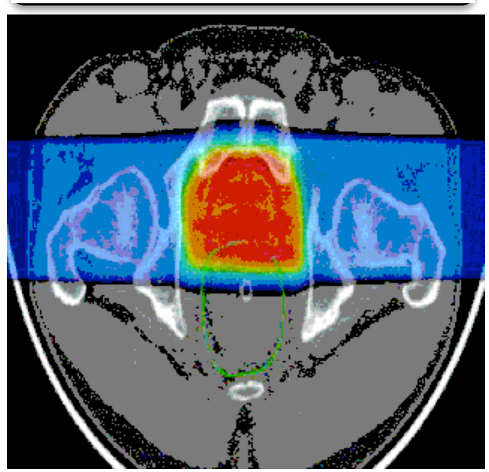


Physics

Treatment options

Surgery

Radiotherapy



X-ray, IMRT, Brachytherapy, Hadrontherapy

Chemotherapy (+ others)

Hormones; Immunotherapy;
Cell therapy; Genetic treatments; Novel specific targets (genetics..)

AIM:
Survival, Quality of life

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)

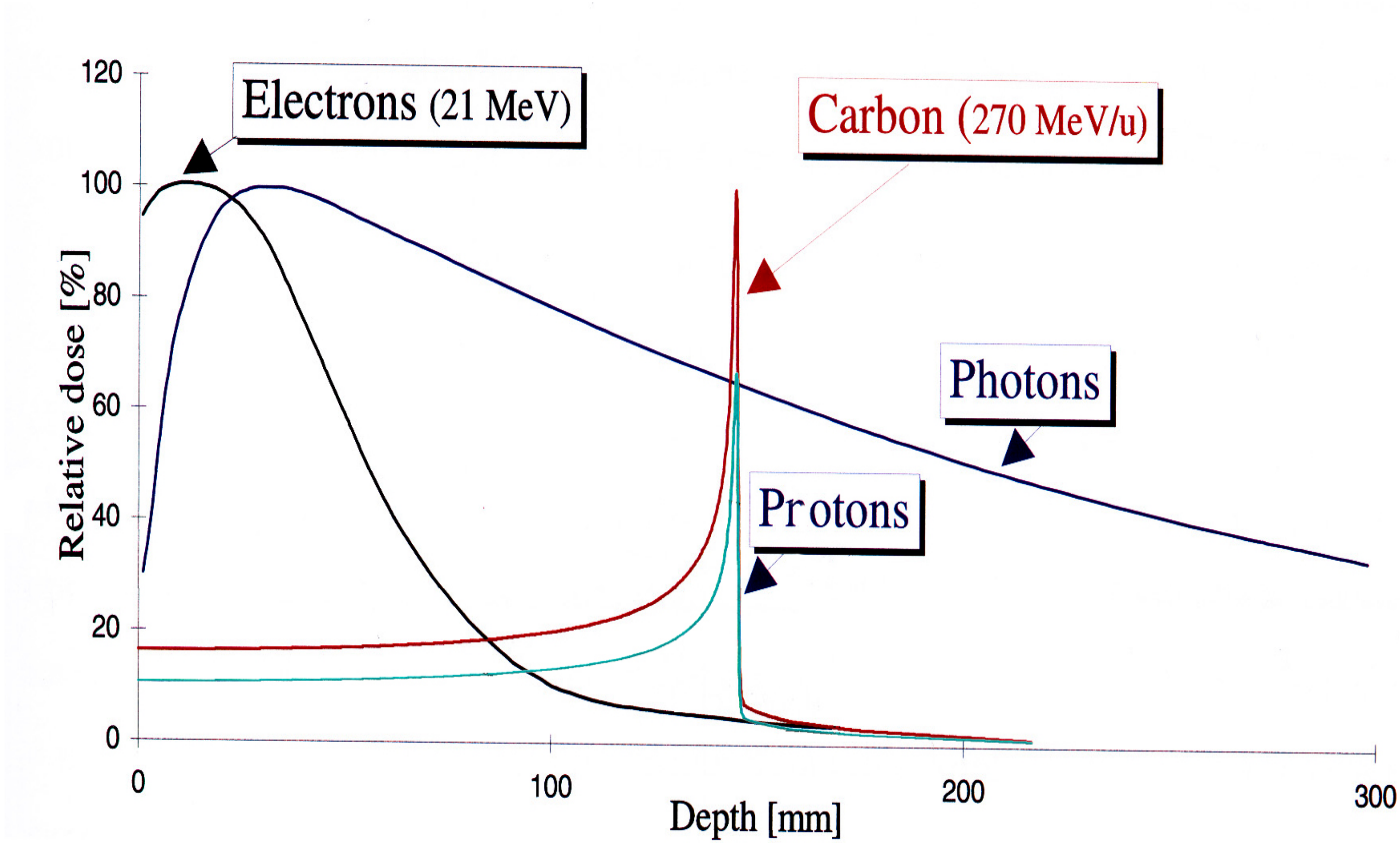
(J.P.Gérard)

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

Improving outcomes …..

- 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

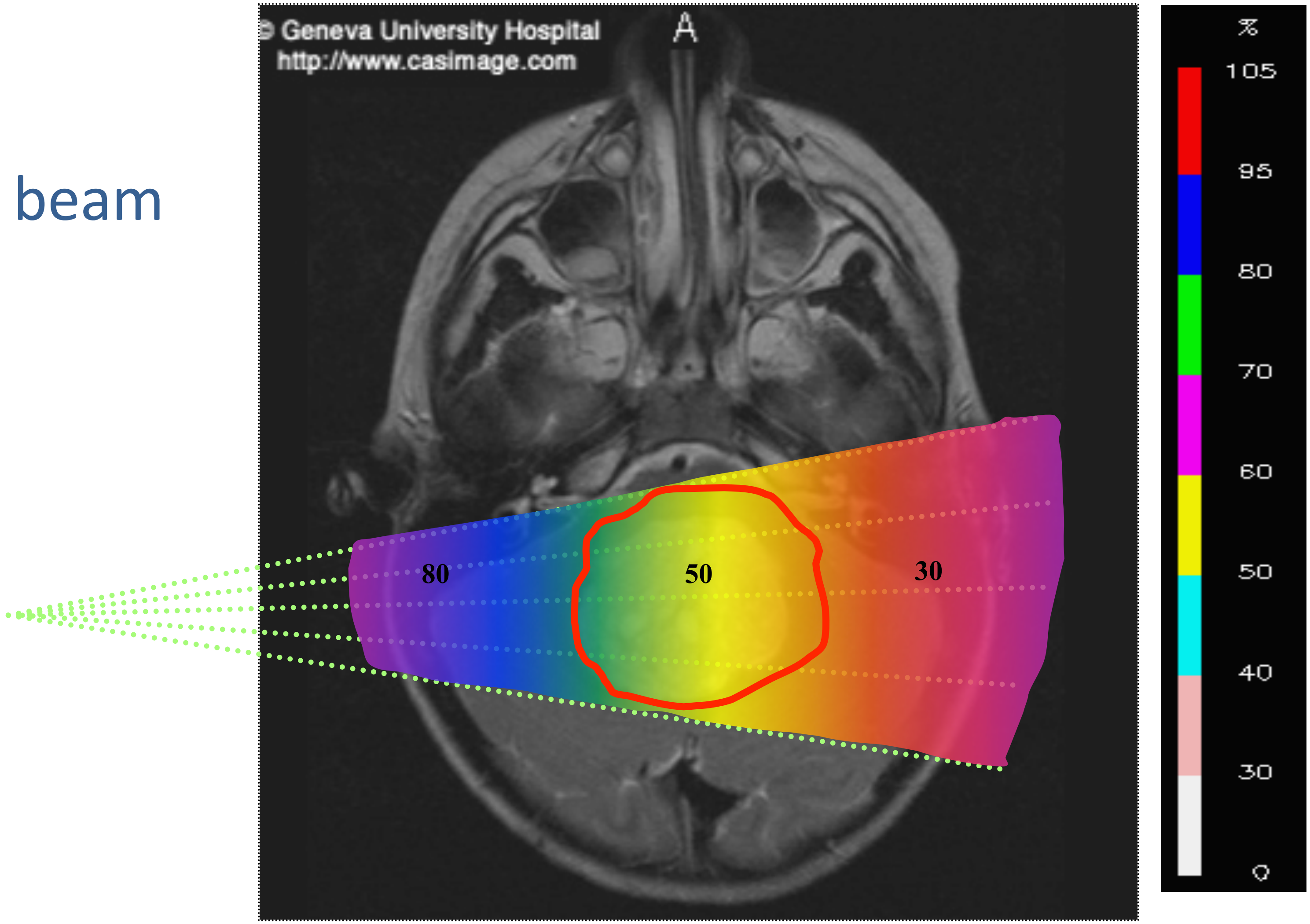
Radiation therapy



Depth in the body (mm)

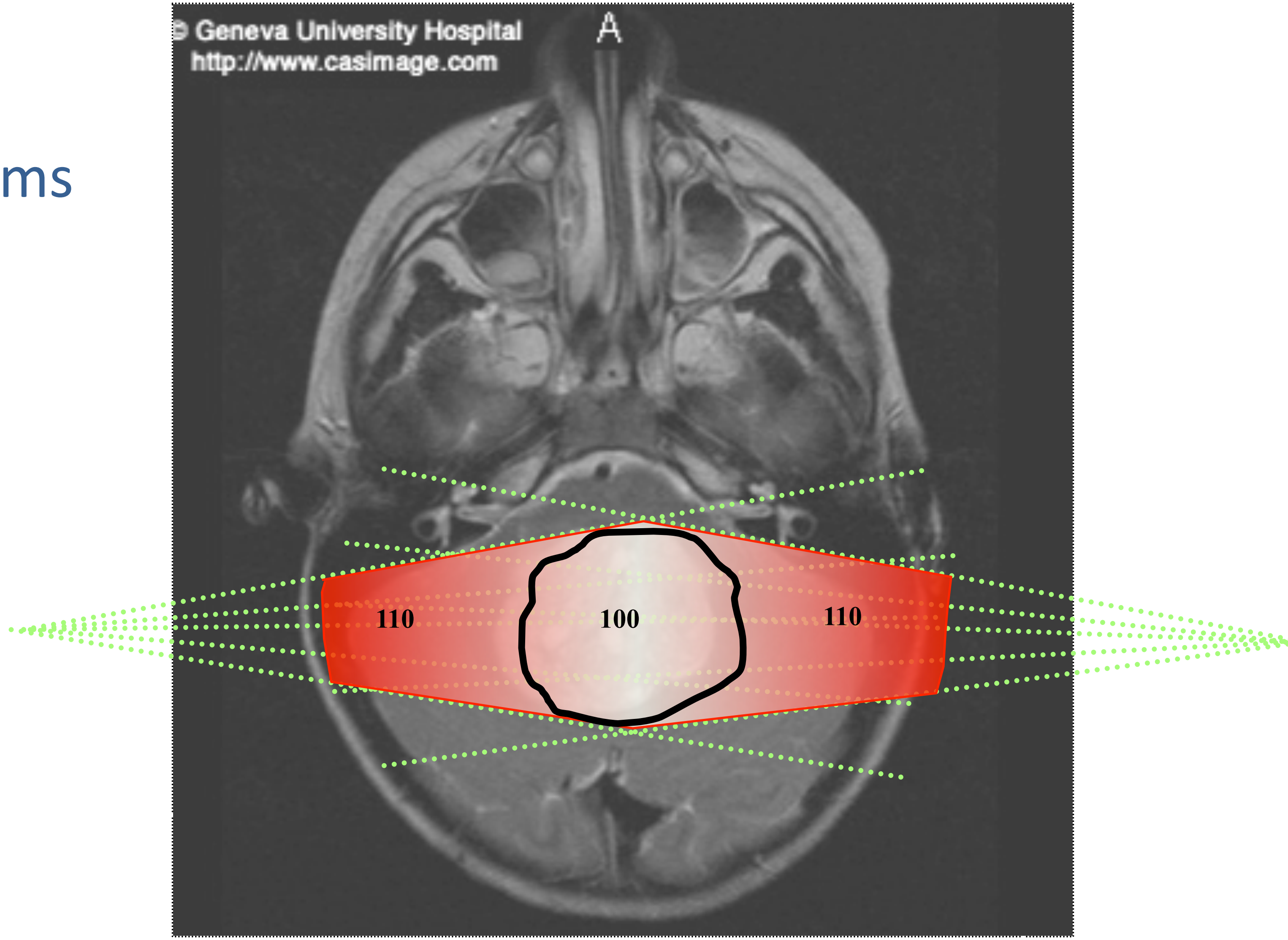
Classical Radiotherapy with X-rays

single beam

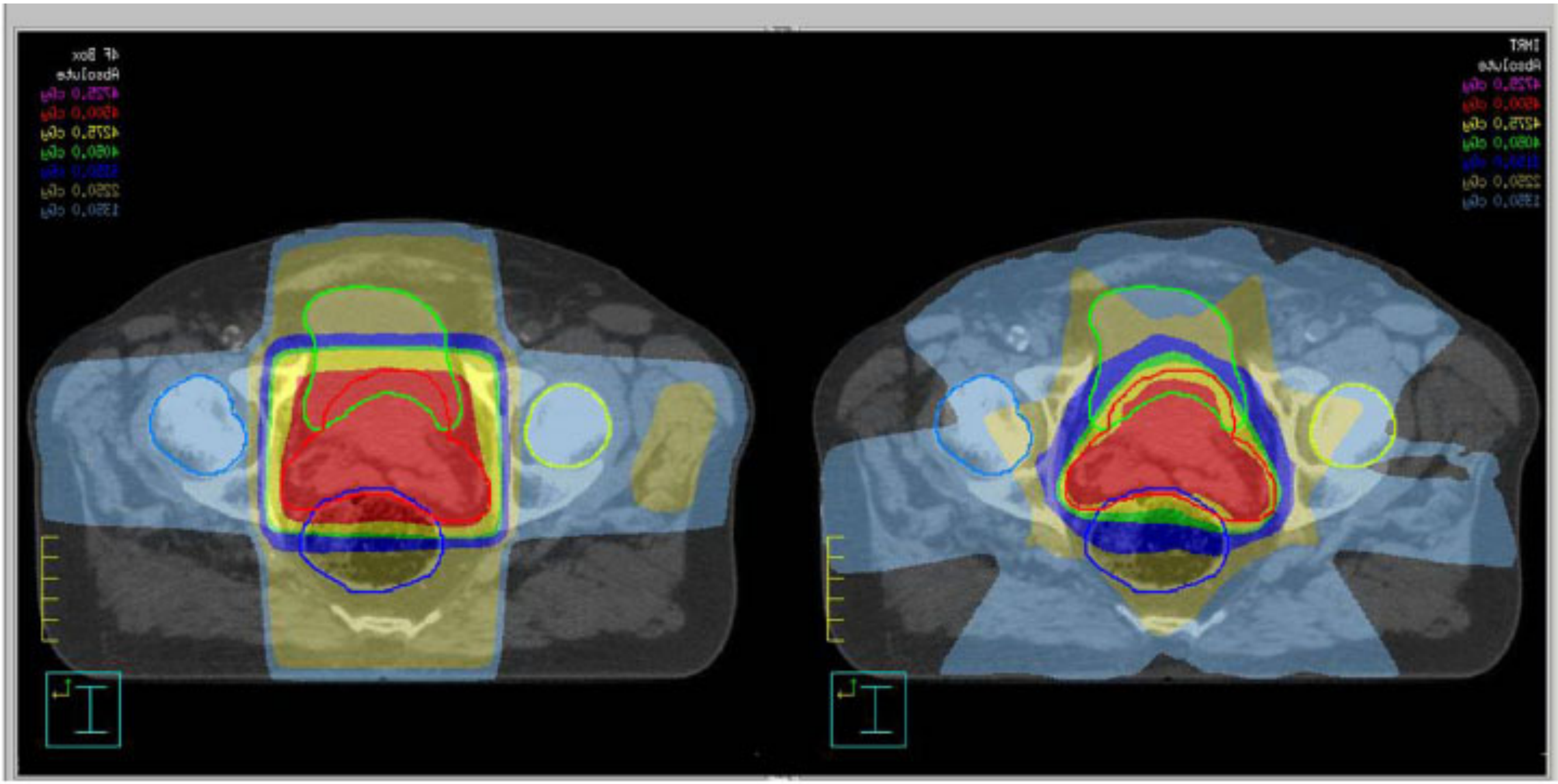


Radiotherapy with X-rays

two beams



Improved Delivery

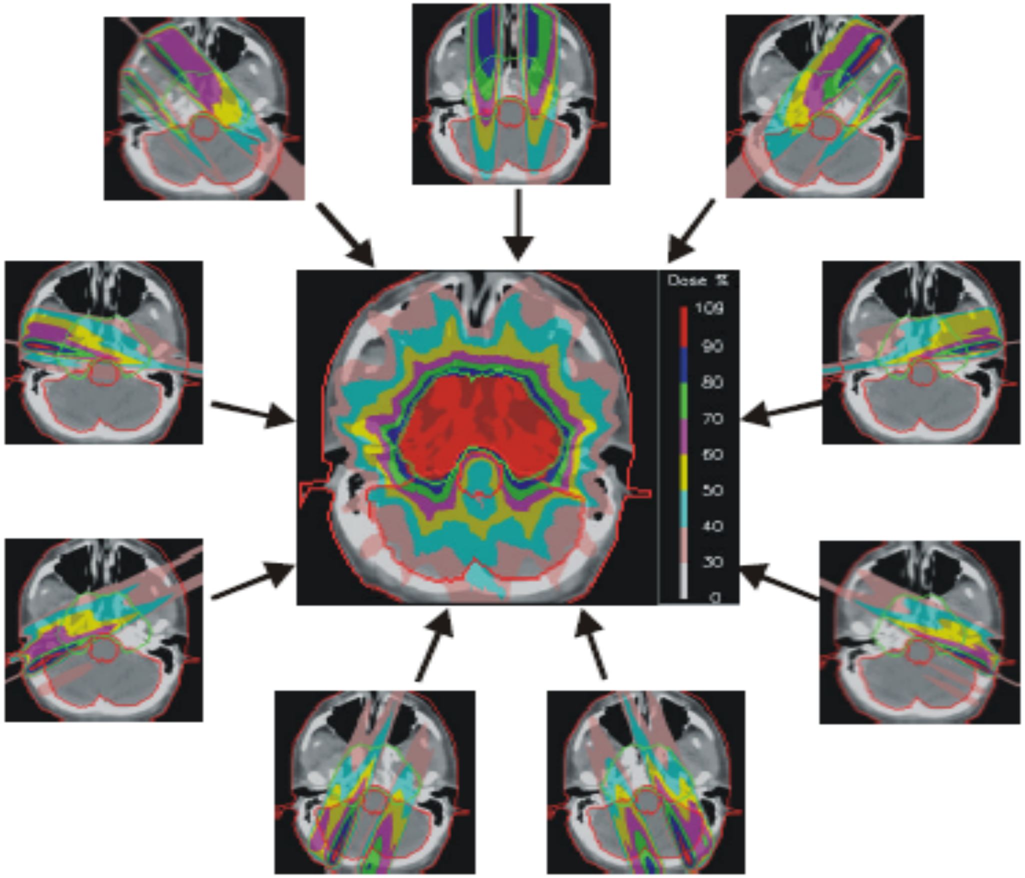


1990s: 4 constant intensity fields

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

Intensity Modulated Radiation Therapy

9 NON-UNIFORM FIELDS



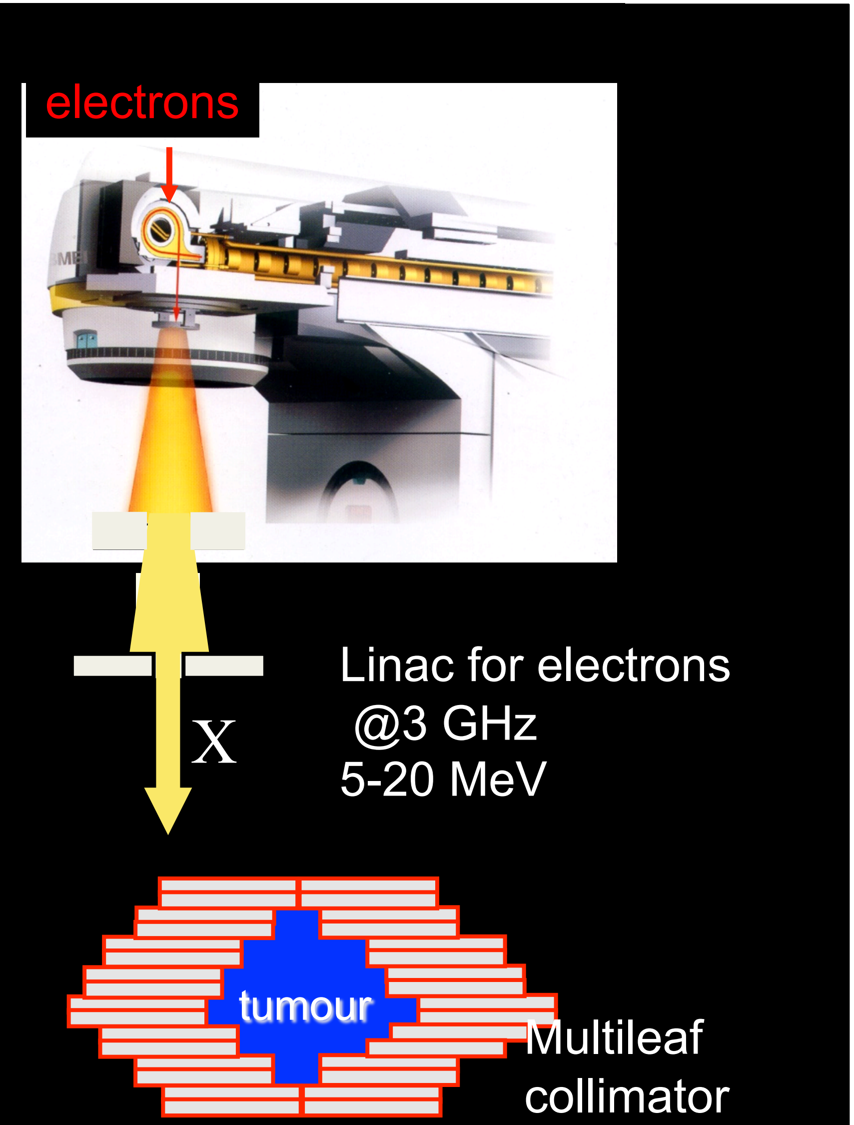
RSI

60-75 grays (joule/kg) given in 30-35 fractions (6-7weeks)

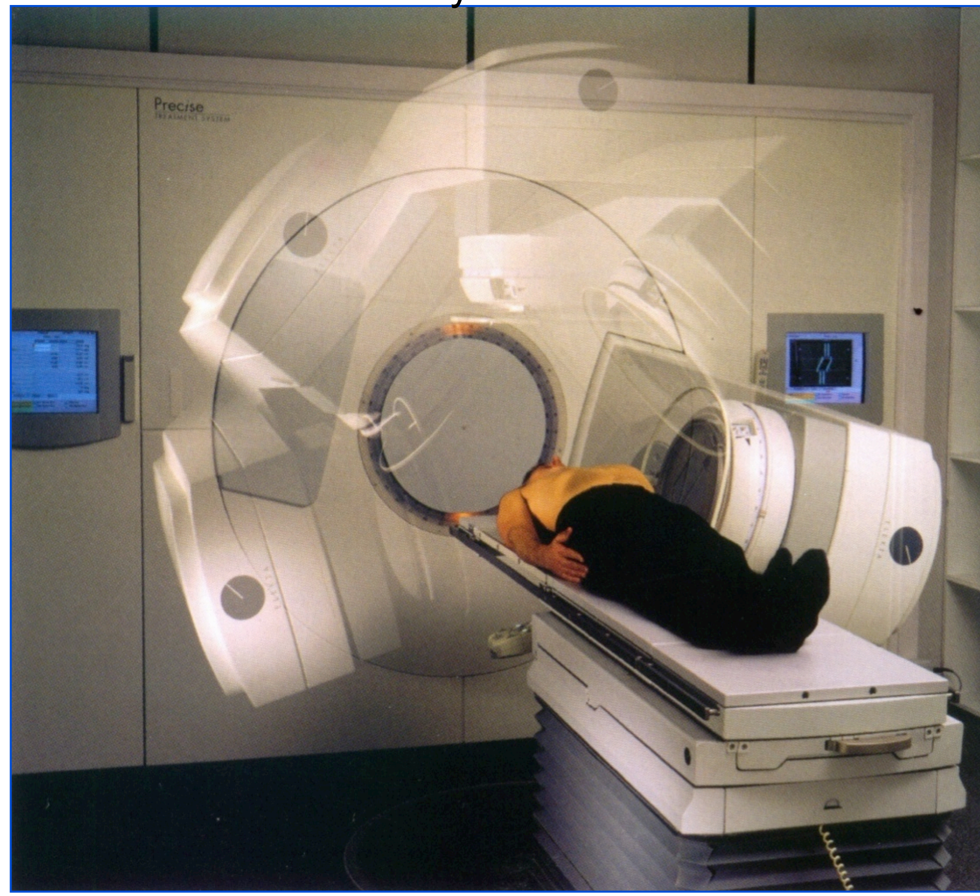
to allow healthy tissues to repair:

90% of the tumours are radiosensitive

‘Conventional’ radiotherapy: LINACS (linear accelerators) dominate

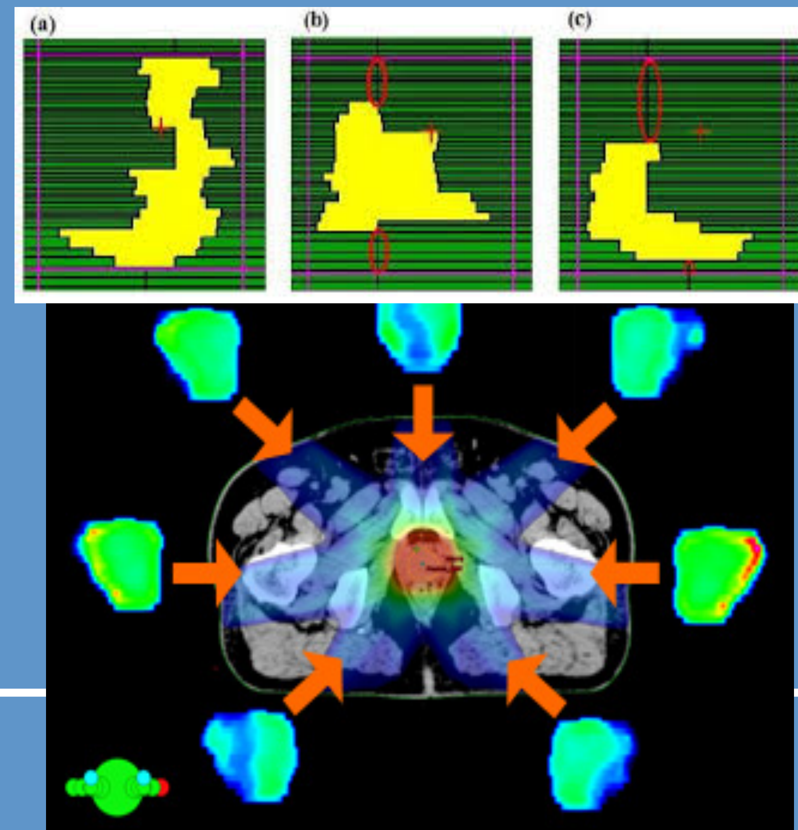


Courtesy of Elekta



5 linacs for 1 million inhabitants needed

Current state of the art X-ray Therapy

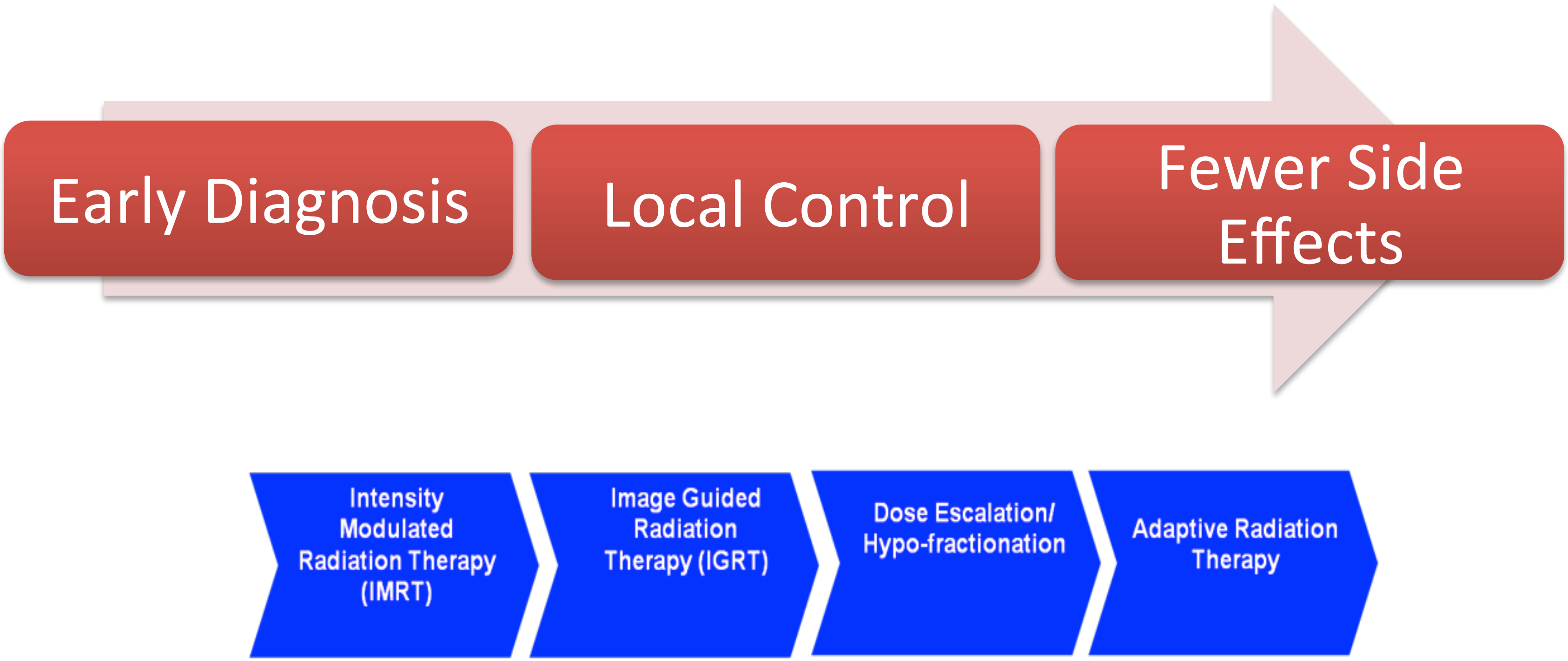


Advances in Radiation Therapy

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?

Fight Against Cancer

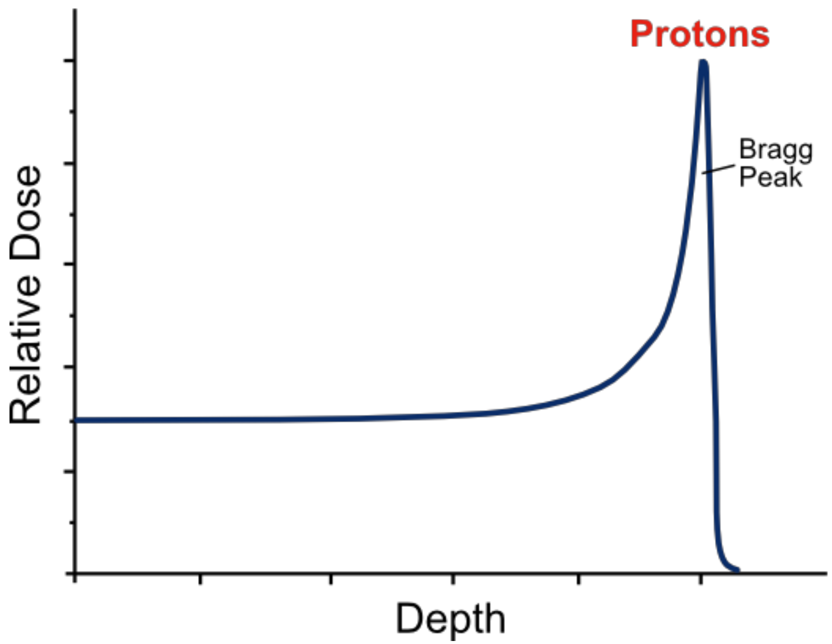


Could Hadron Therapy be the future?

Future: Hadron Therapy?

- 1946: Robert Wilson

  Protons can be used clinically

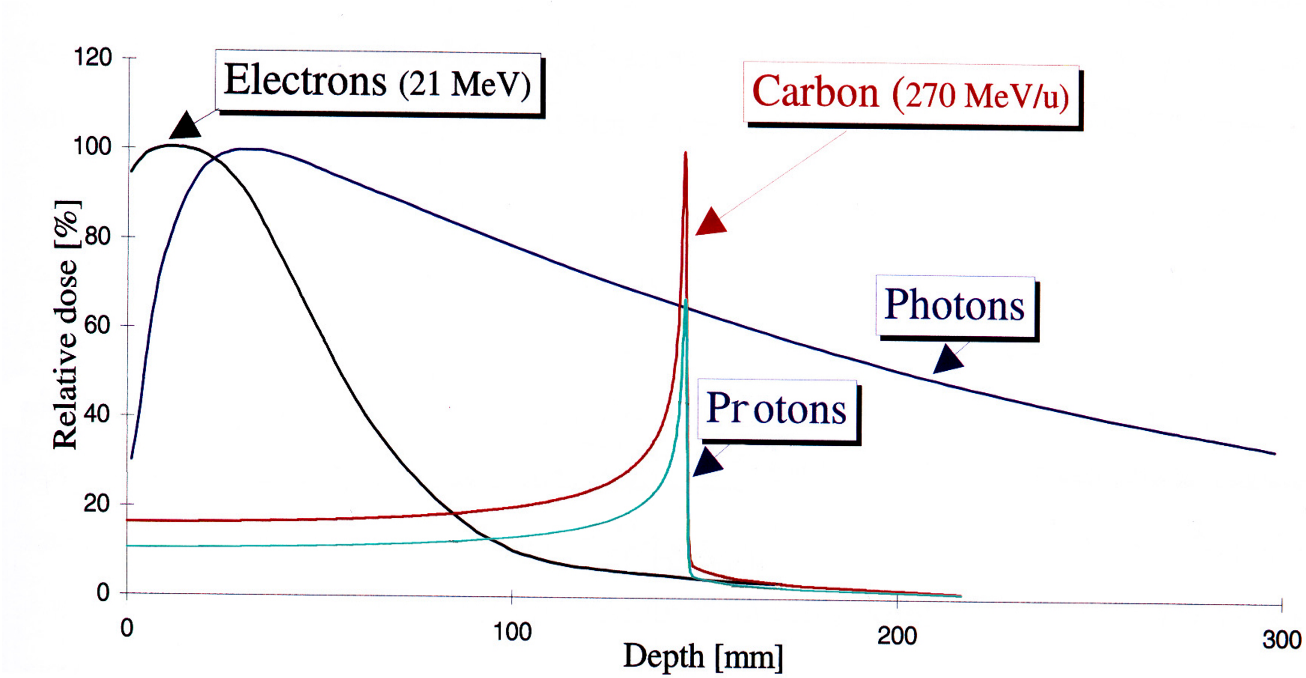


Robert Wilson

Why Hadron Therapy?

In 1946 Robert Wilson:

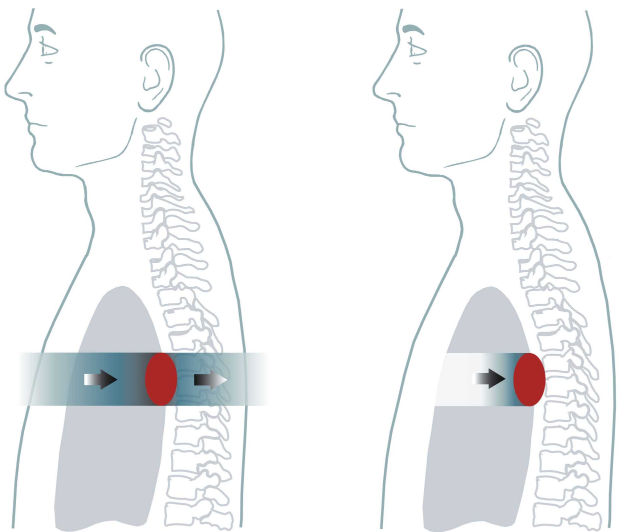
- Hadrons can be used clinically
- Accelerators are available
- Maximum radiation dose can be placed into the tumour
- Particle therapy provides sparing of normal tissues



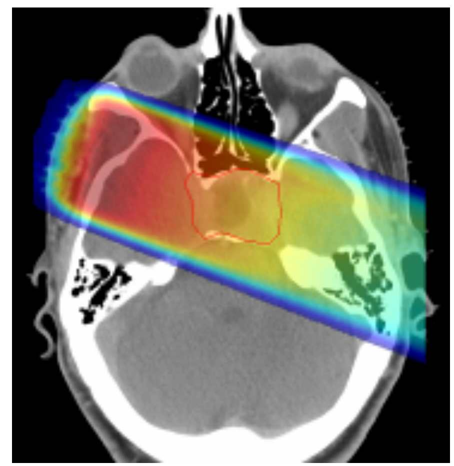
Depth in the body (mm)

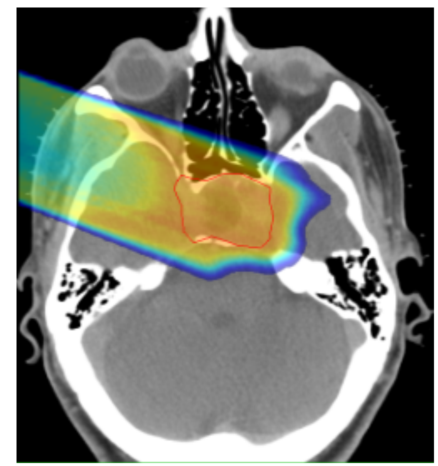
Why hadron therapy?

Image courtesy MedAustron



Conventional: X-Rays Ion Radiation



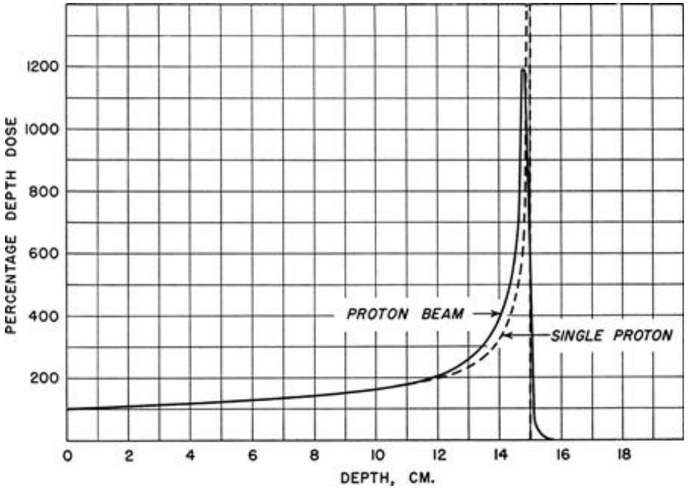


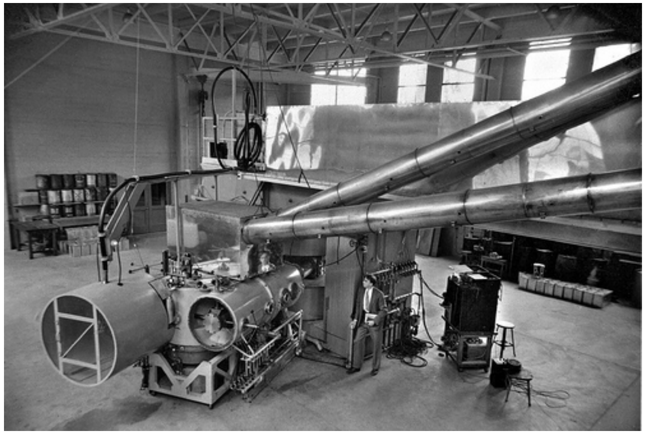
Spares normal healthy tissue

1932 - E. Lawrence First cyclotron

1946 – proton therapy proposed by R. Wilson

1954 – Berkeley treats the first patient



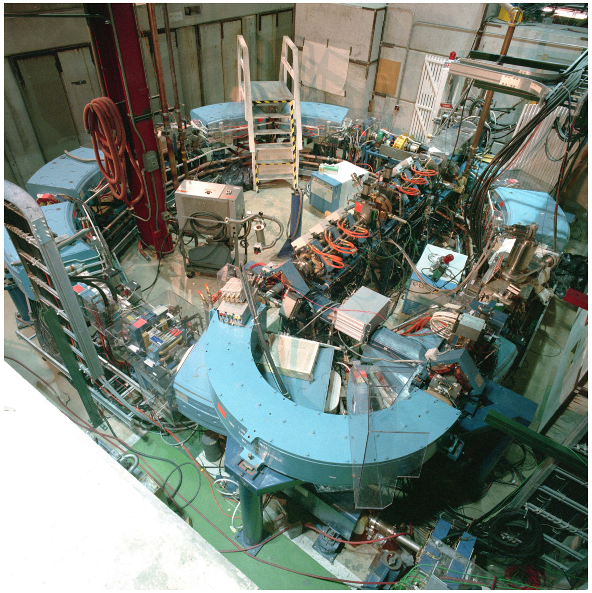


From physics……..

1993- Loma Linda USA (proton)

1994 – HIMAC Japan (carbon)

1997 – GSI Germany (carbon)



First dedicated clinical facility

........to clinics

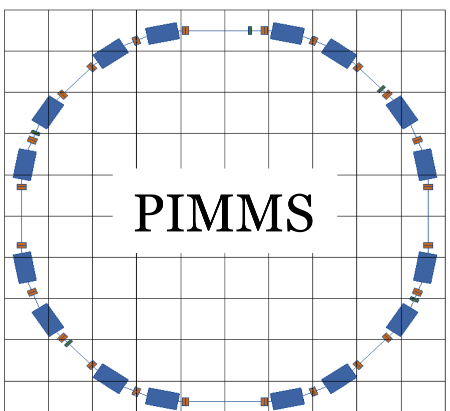
Latest generation of carbon facilities in Europe:

first was HIT in Heidelberg – started treating patients in 2009

PIMMS study at CERN (1996-2000)

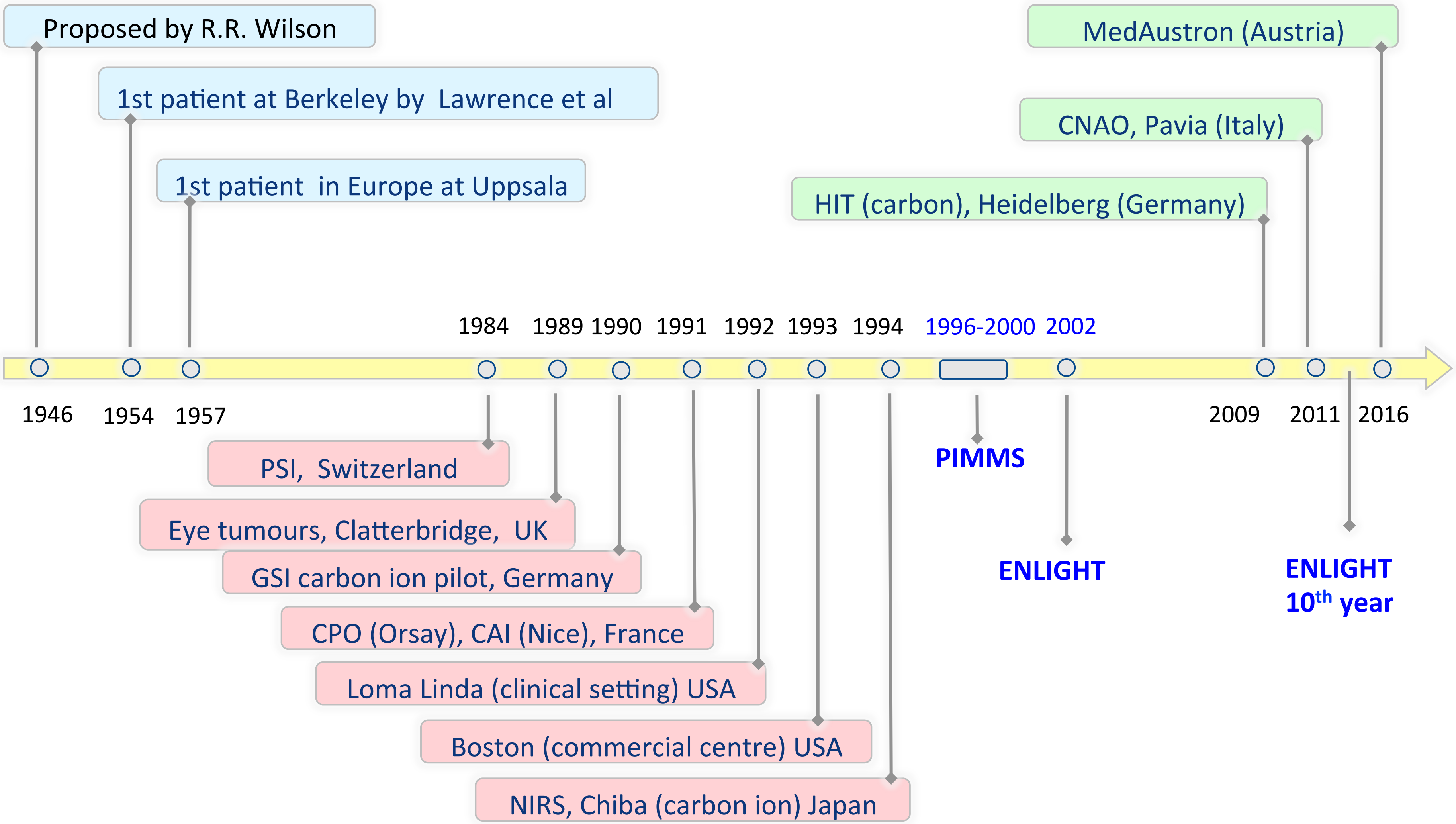
Treatment , CNAO, Italy
2011

1996-2000
PIMMS study

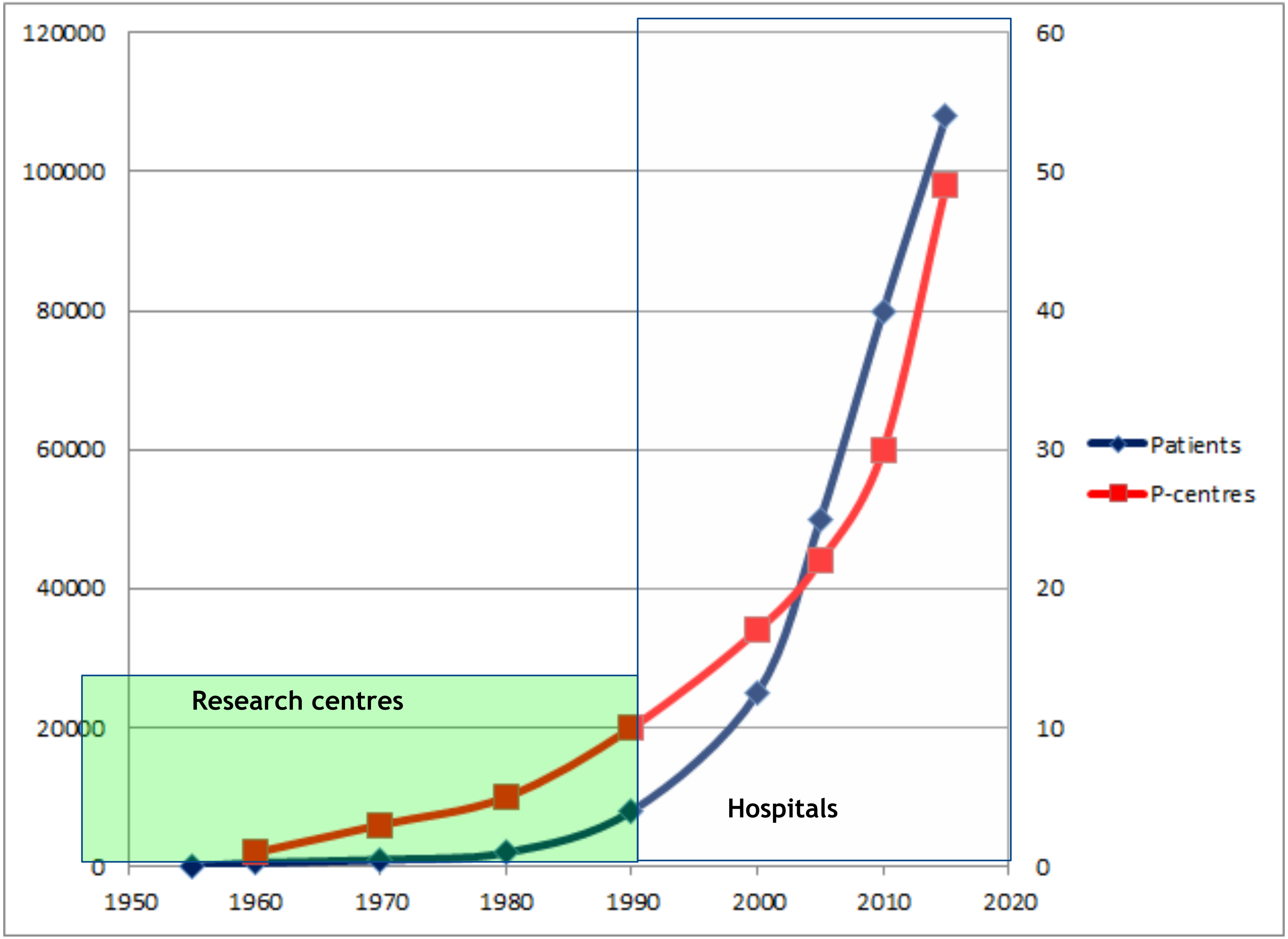


MedAustron, Austria 2016

Particle therapy: a short history

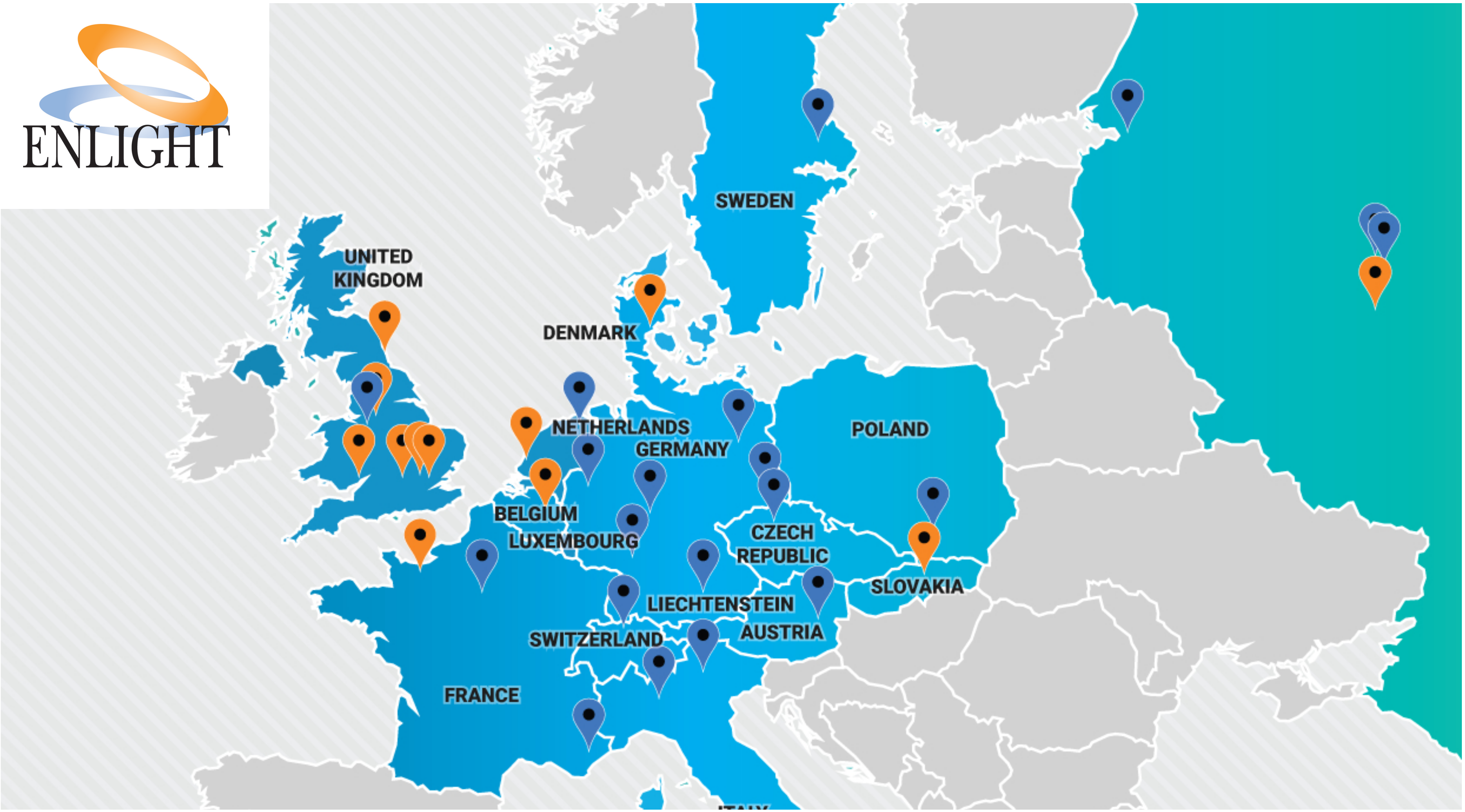


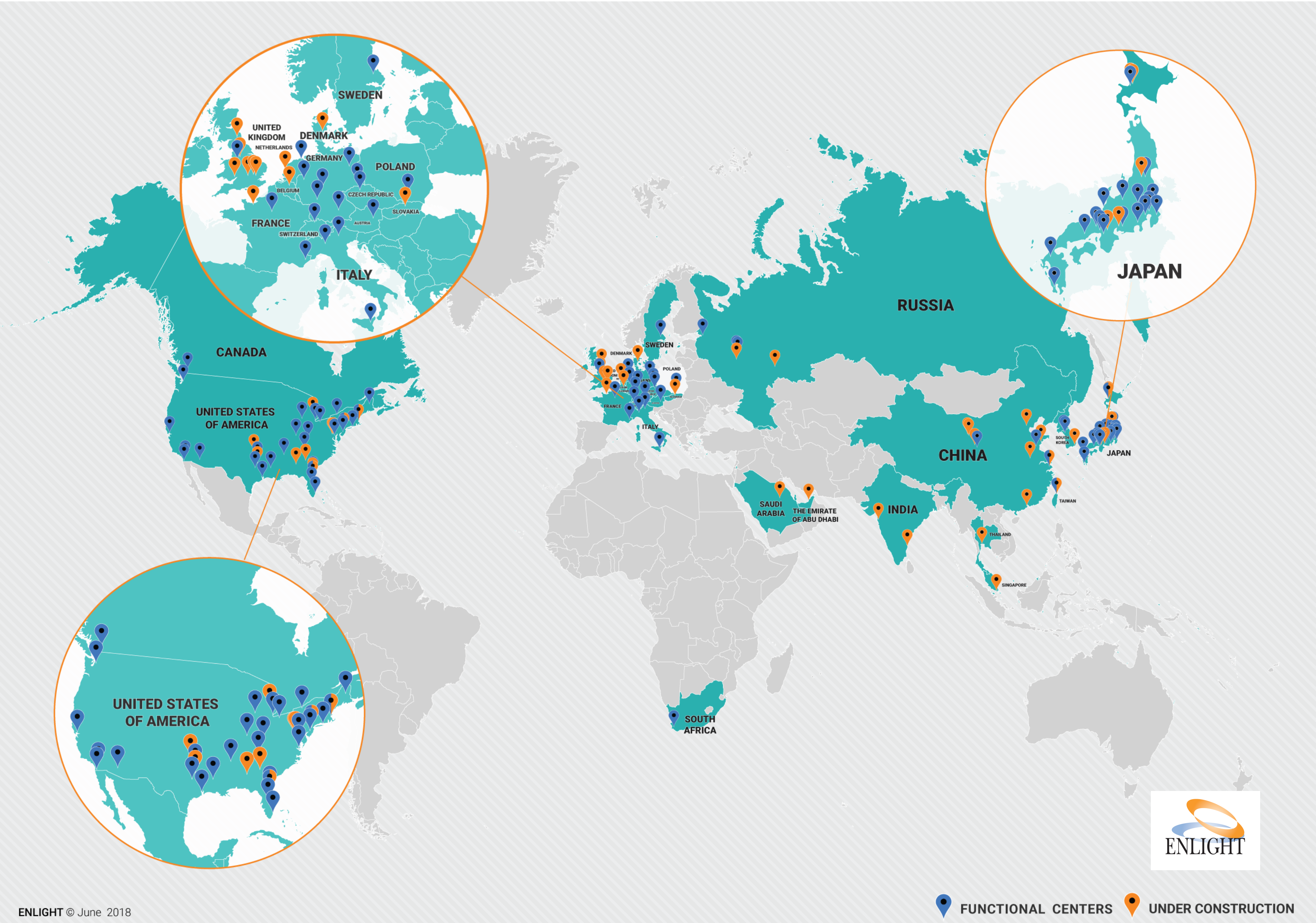
[Data from www.ptcog.ch]



Facilities in operation now – Europe (2018)

ENLIGHT




SWEDEN
UNITED KINGDOM
DENMARK
NETHERLANDS
GERMANY
POLAND
BELGIUM
CZECH REPUBLIC
SLOVAKIA
FRANCE
AUSTRIA
SWITZERLAND
ITALY
JAPAN
RUSSIA
CANADA
UNITED STATES OF AMERICA
SWEDEN
DENMARK
POLAND
FRANCE
ITALY
CHINA
SOUTH KOREA
JAPAN
TAIWAN
SAUDI ARABIA
THE EMIRATE OF ABU DHABI
INDIA
THAILAND
SINGAPORE
SOUTH AFRICA
UNITED STATES OF AMERICA
ENLIGHT
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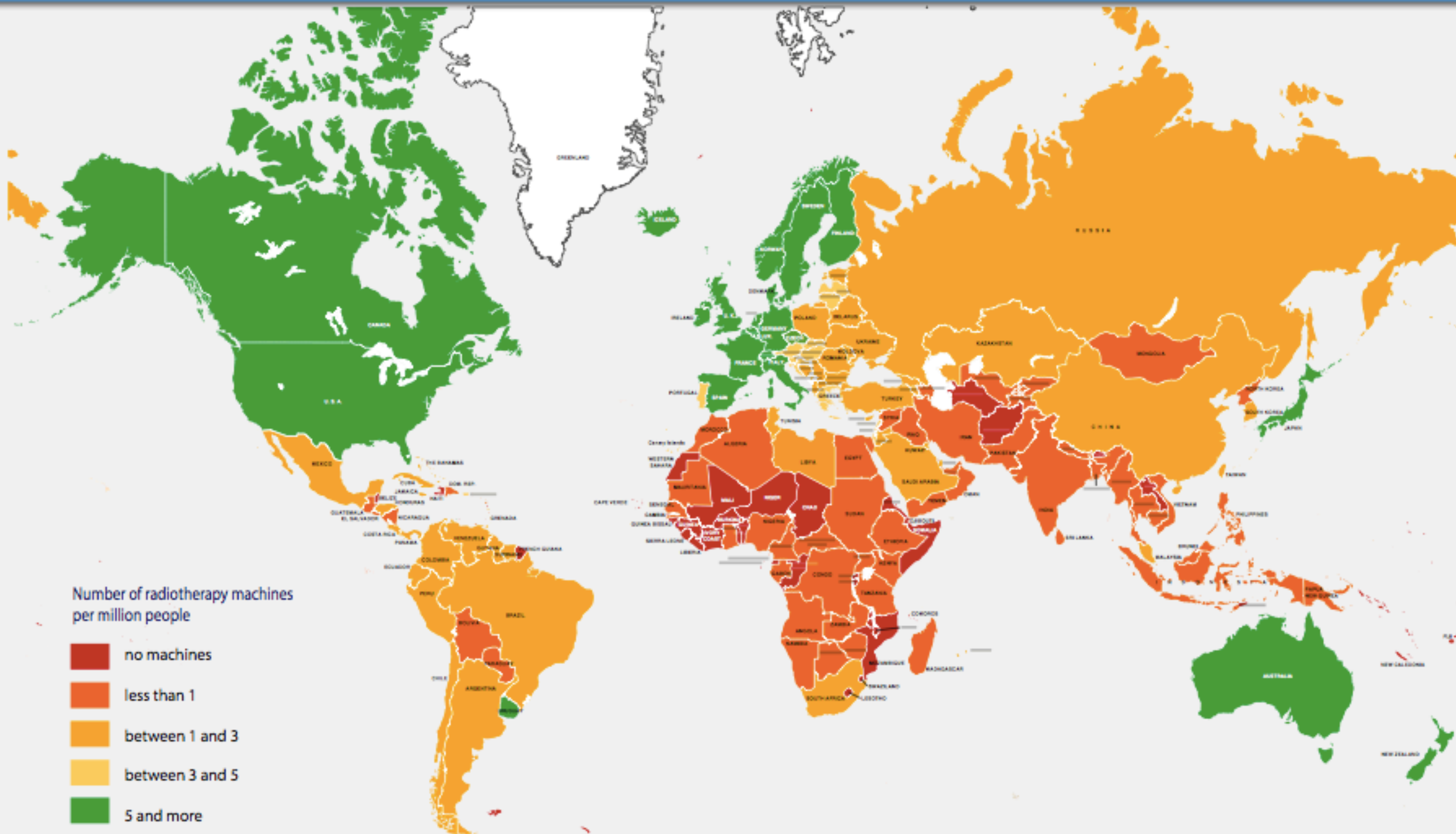
FUNCTIONAL CENTERS
UNDER CONSTRUCTION

Current Challenge: how to go from no radiotherapy to high quality radiotherapy globally: Challenging Environments

Availability of **RADIATION THERAPY**

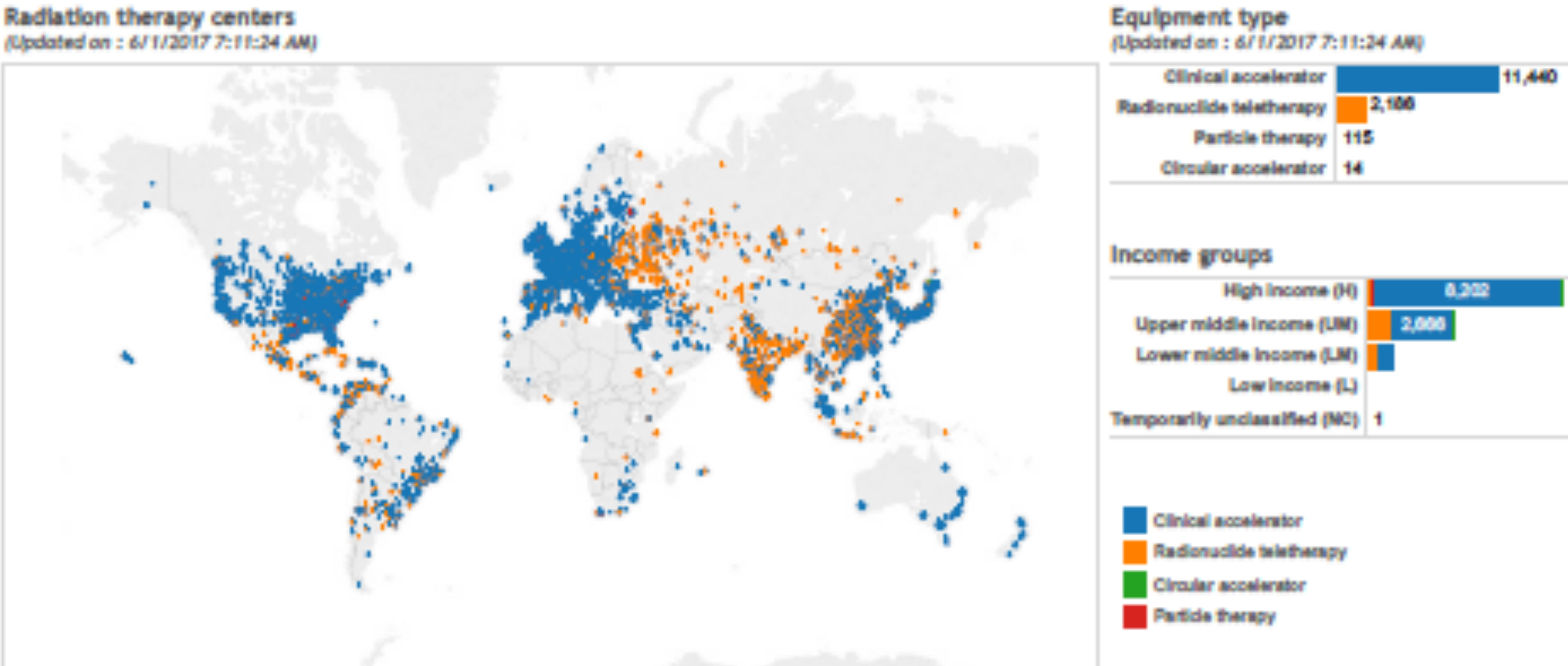
Number of Radiotherapy Machines per Million People 2012



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

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

World wide radiotherapy coverage



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

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

Needs by 2035 in LMIC

Globally 15 million (2015) to 25 million in (2035):

- 12,600 megavolt-class treatment machines
- 30,000 radiation oncologists
- 22,000 medical physicists
- 80,000 radiation technologists

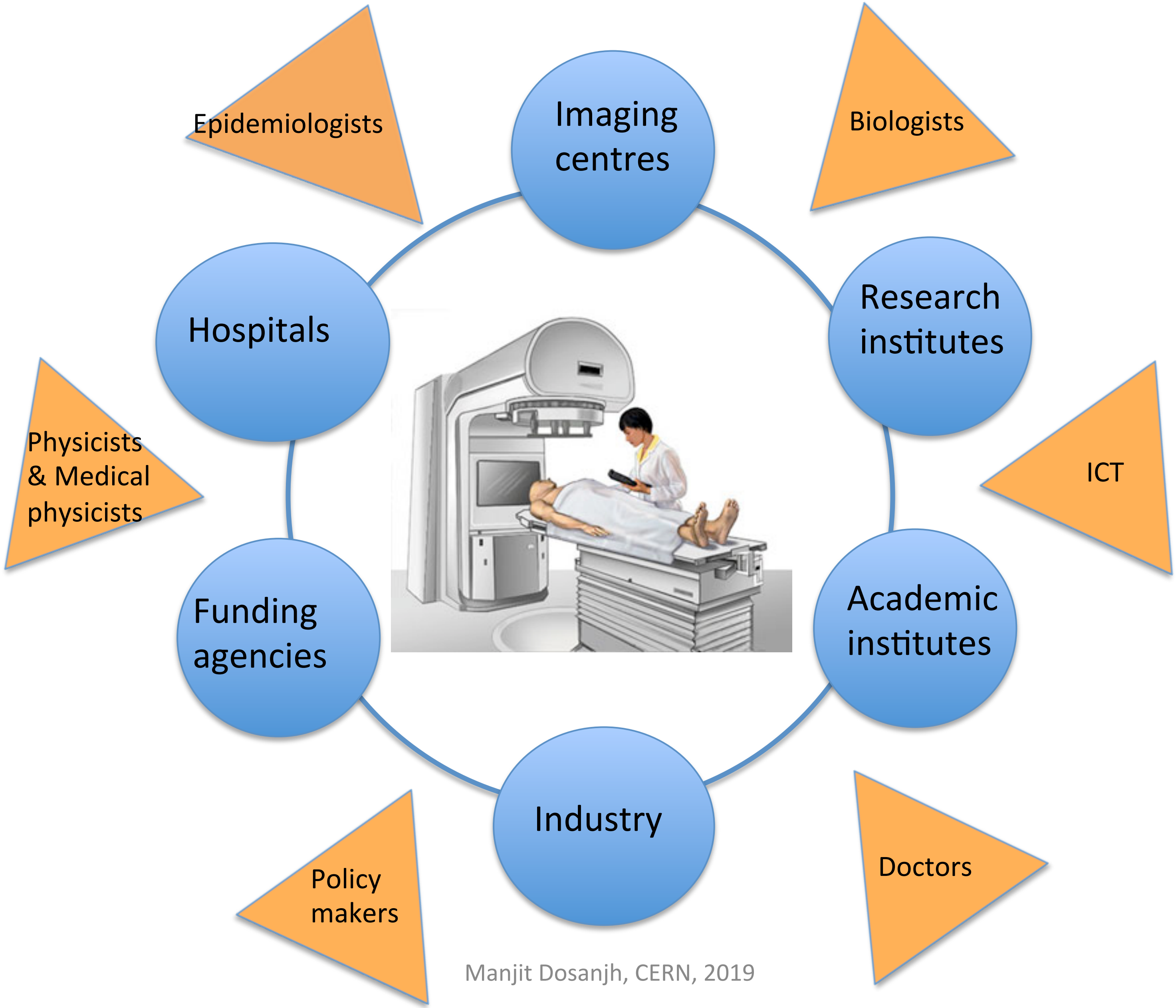
What do we need in the future?

- 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 every large hospital ?

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

Courtesy D. Townsend

Need for collaboration



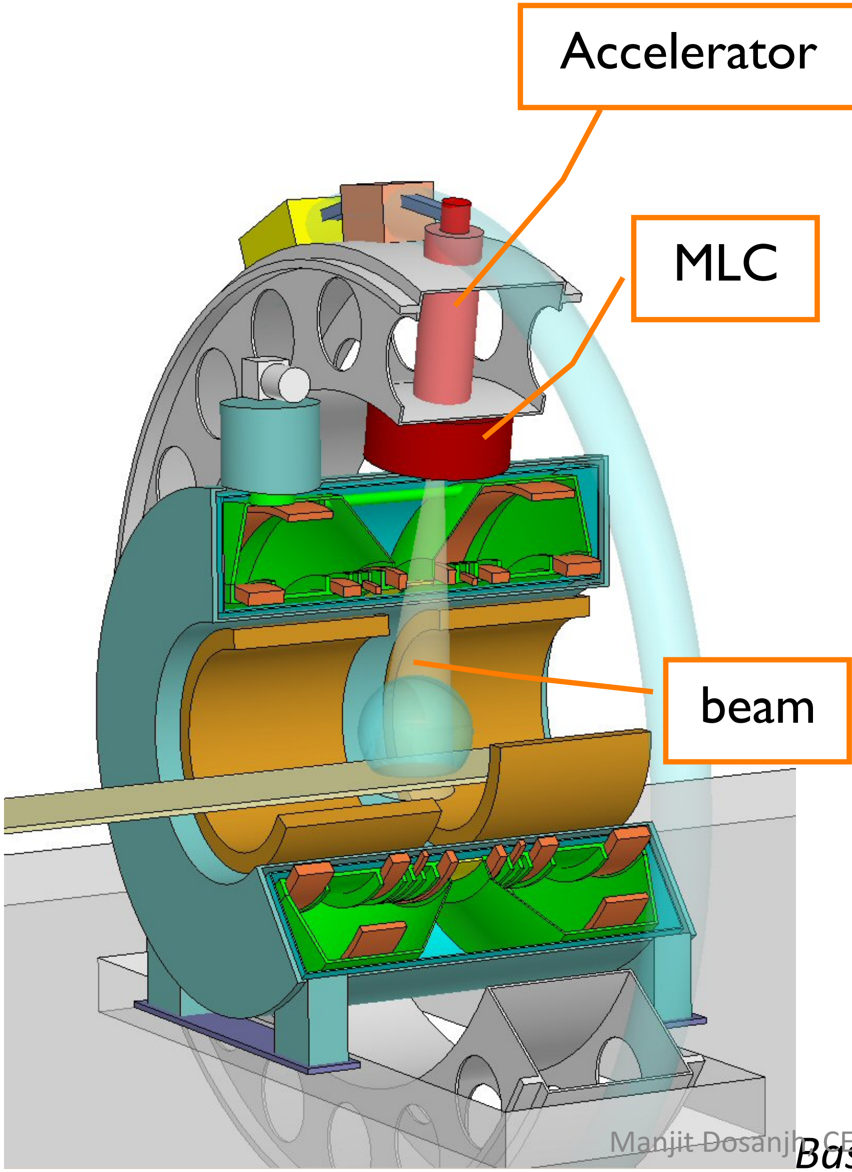
Manjit Dosanjh, CERN, 2019

cern.ch/virtual-hadron-therapy-centre

New Advances are on their way

The tumour and only the tumour…..

Concept of MRI guided accelerator



Seeing what you treat at the moment of treatment

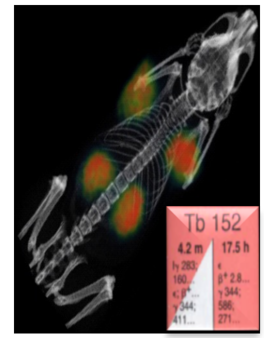
Bringing certainty in the actual treatment

Bas Raaymakers, Utrecht, UMC, ENLIGHT

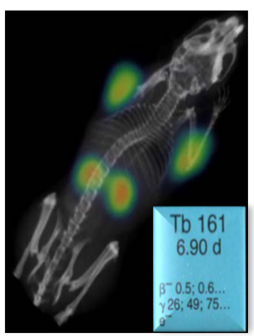
Terbium: Swiss Army Knife of Nuclear Medicine

^{149}Tb-therapy

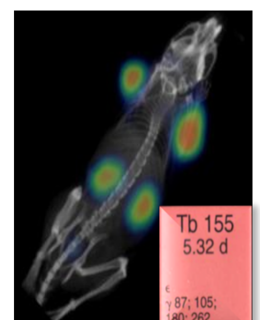
^{152}Tb-PET



^{161}Tb-therapy & SPECT

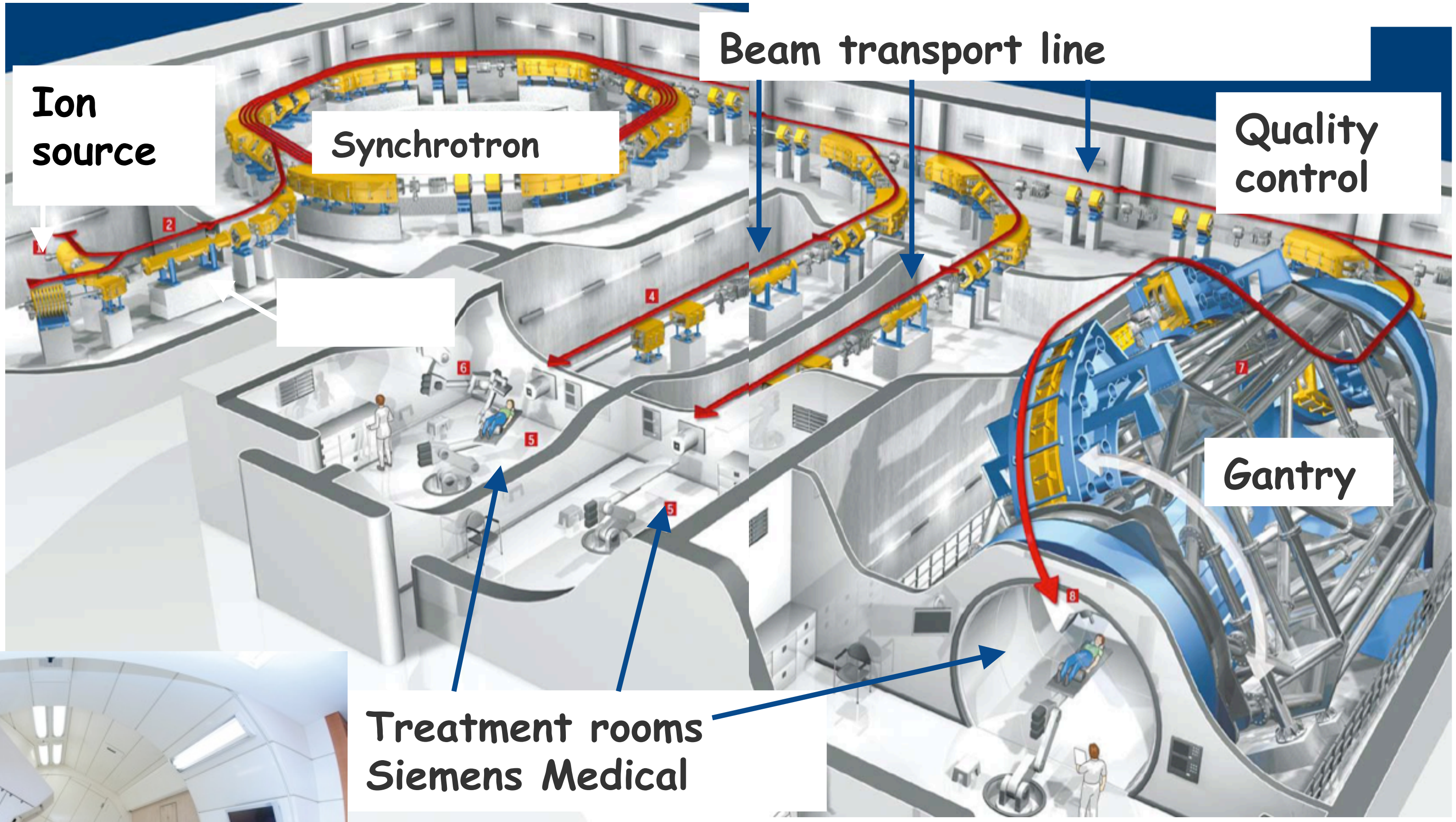


^{155}Tb-SPECT

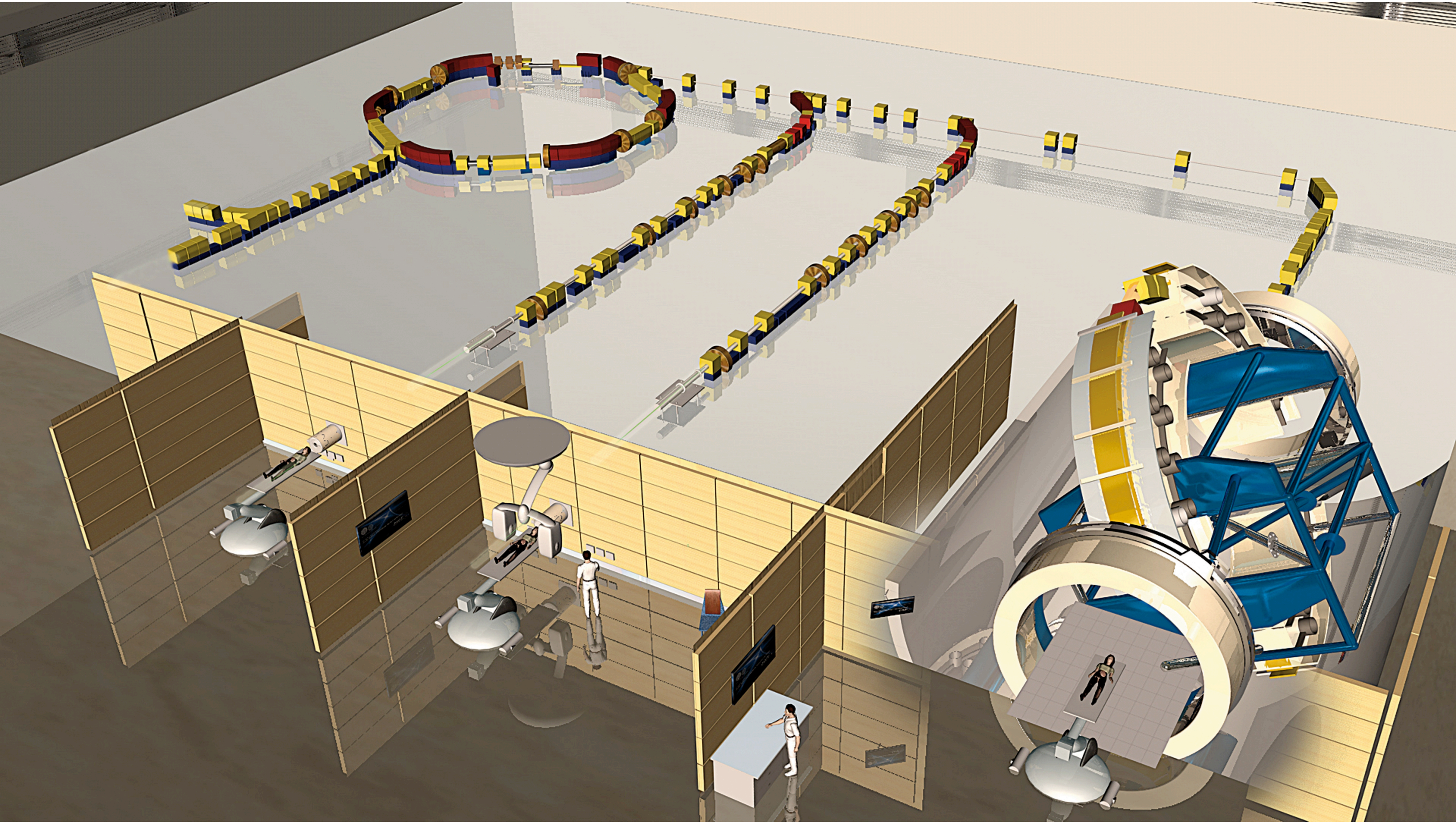


Müller et al., JNM 2012

HIT - Heidelberg

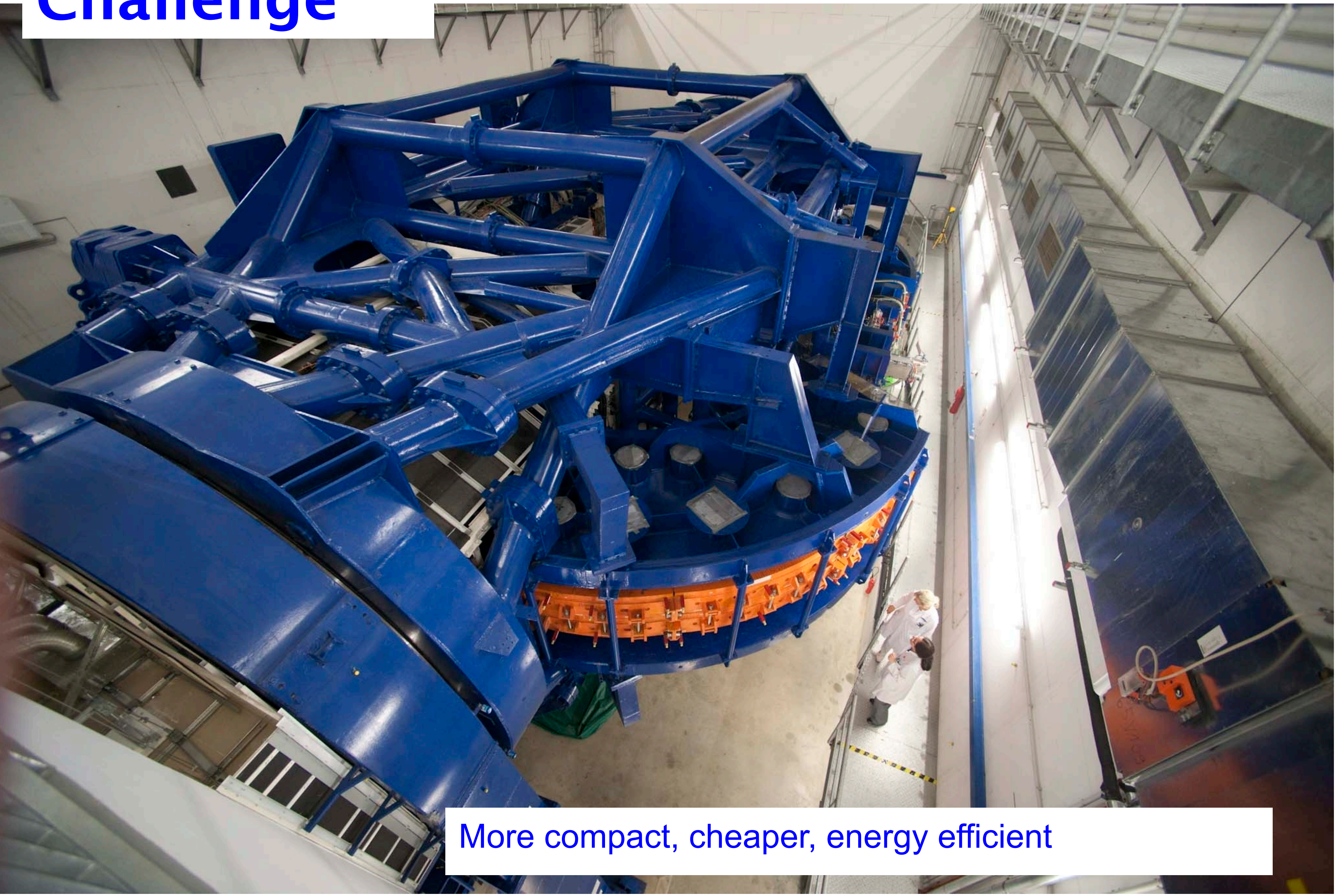


Challenge



Smaller, simpler, cheaper

Challenge

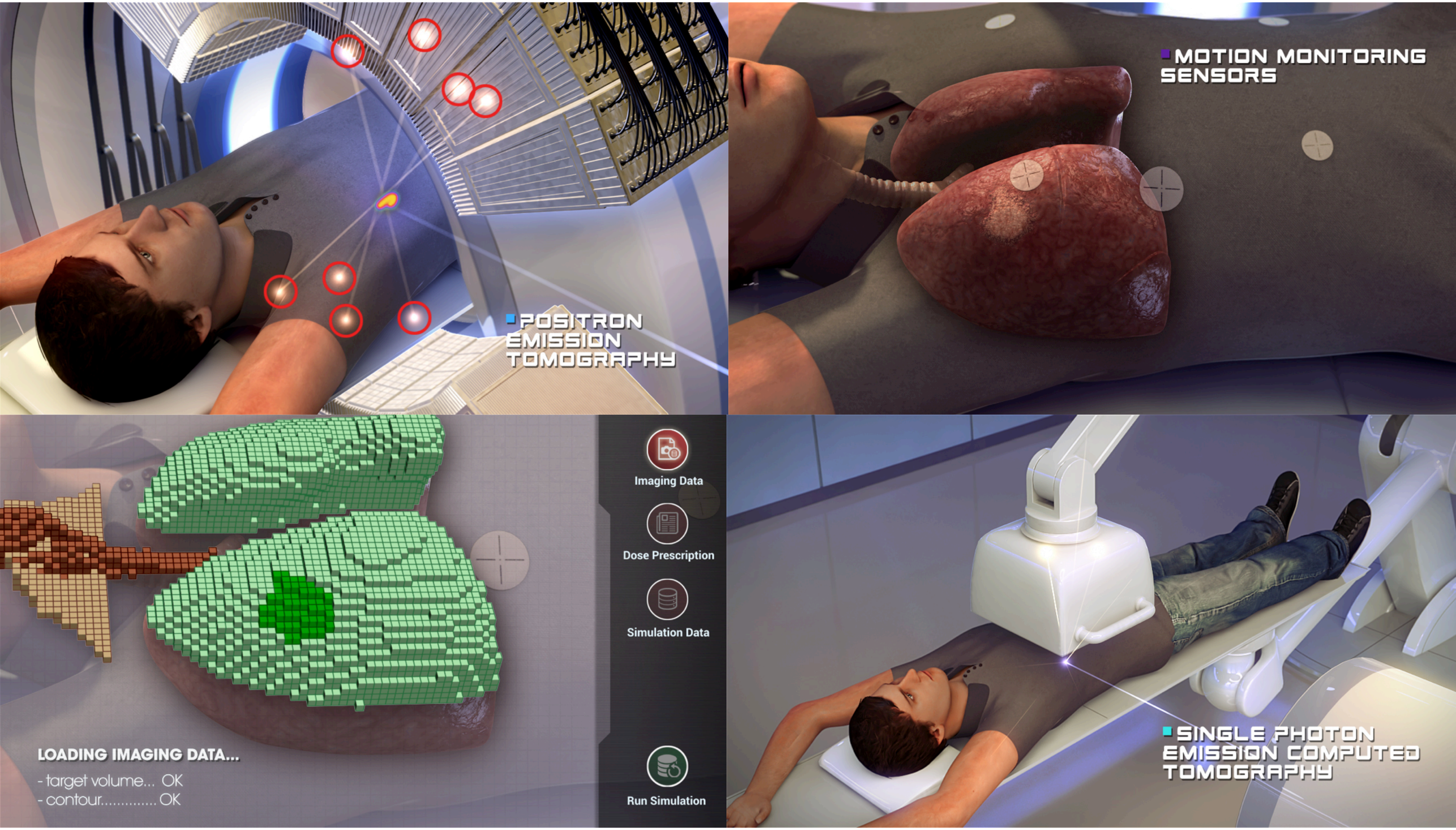


More compact, cheaper, energy efficient

Challenge

precision

Challenge



Safer and more effective therapy

Challenge

Clinical trials: protons, carbon, ions, multi-centric

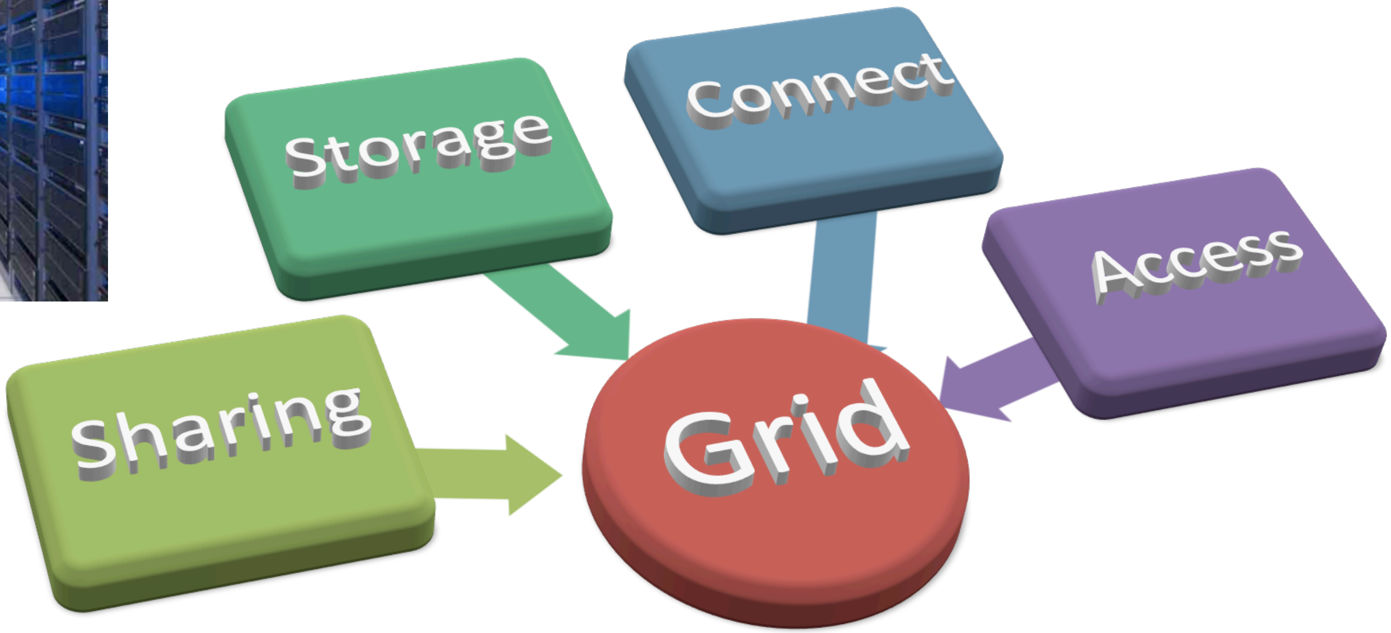
Challenge

RBE – the weakest link

Must be clarified to secure optimal particle therapy

Jens Overgaard, Divonne Brainstorming, 2016

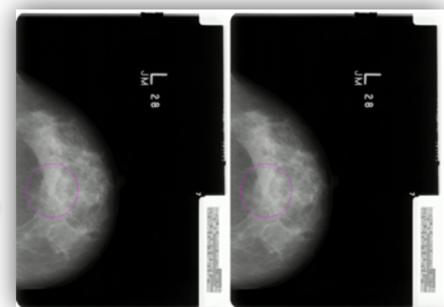
The Grid

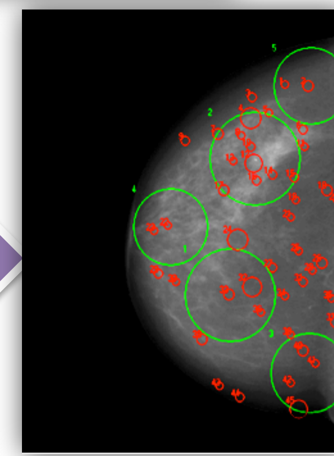


Data and Resources

Mammogrid - a grid mammography database

- Second Opinion
- Cancer Screening
- Education and Training
- Reference Database / Repository





From: David MANSET, CEO MAAT France, www.maat-g.com

What next?

- Learn from - integrate experience from existing projects:
  - Mammogrid