Medical Applications of Modern Physics

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Medical Physics

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A branch of applied physics concerning the application of physics to medicine

or, in other words

The application of physics techniques to the human health

Outline of the lecture

Physics discoveries

Tools for physics applied to medicine

Medical imaging

X-ray CT

PET and PET/CT

Photon/electron radiation therapy

Hadron therapy

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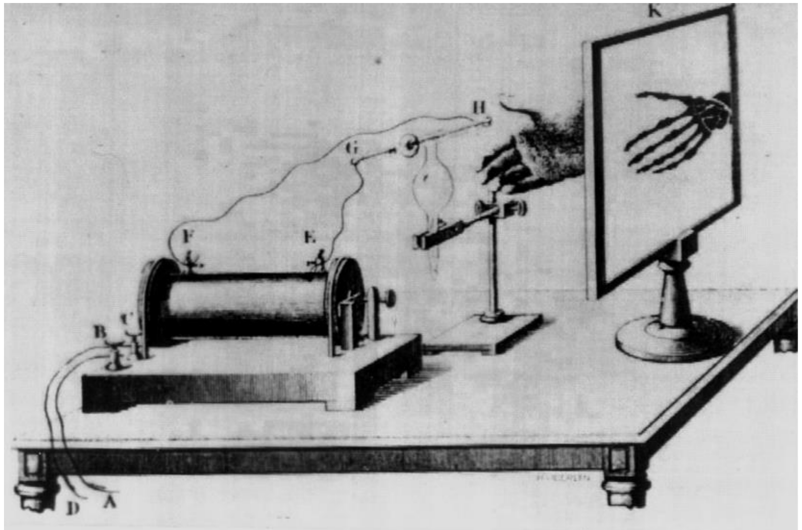
The beginnings of modern physics and of medical physics



1895

Discovery of X rays

Wilhelm C. Röntgen

1897

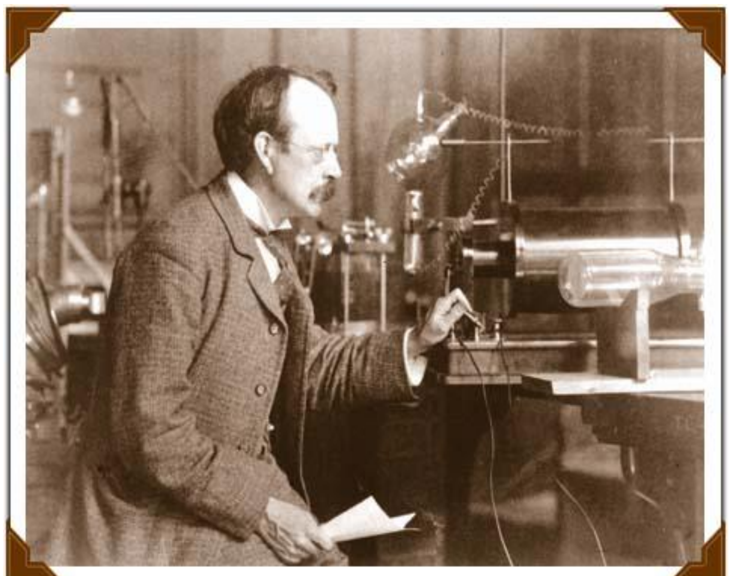
First treatment of tissue with X rays

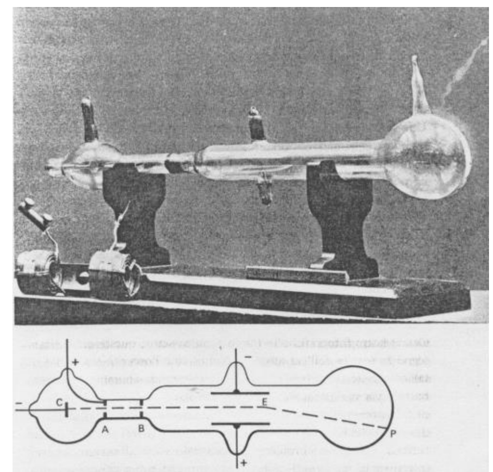
Leopold Freund

J.J. Thompson

1897

"Discovery" of the electron





The beginnings of modern physics and of medical physics

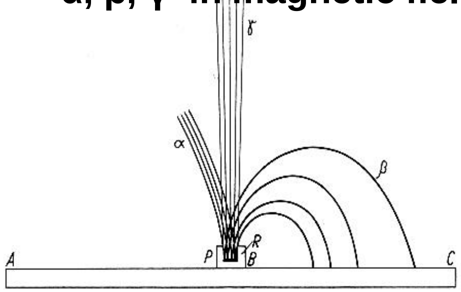
Henri Becquerel (1852-1908)

1896

Discovery of natural radioactivity

Thesis of Mme. Curie – 1904

α, β, γ in magnetic field



Hundred years ago

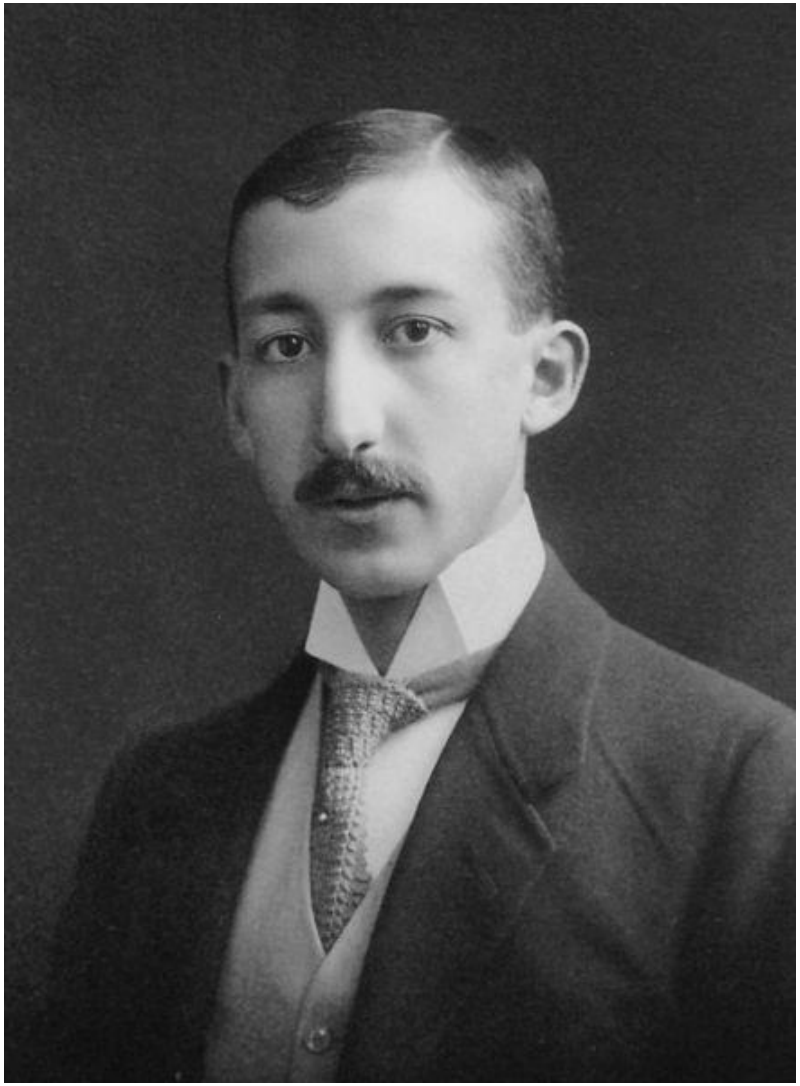
1898

Discovery of polonium and radium

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

First practical application of a radioisotope

- 1911: **first practical application of a radioisotope** (as *radiotracer*) by G. de Hevesy (a young Hungarian student working with naturally radioactive materials) in Manchester
- 1924: de Hevesy, who had become a physician, used radioactive isotopes of lead as tracers in bone studies

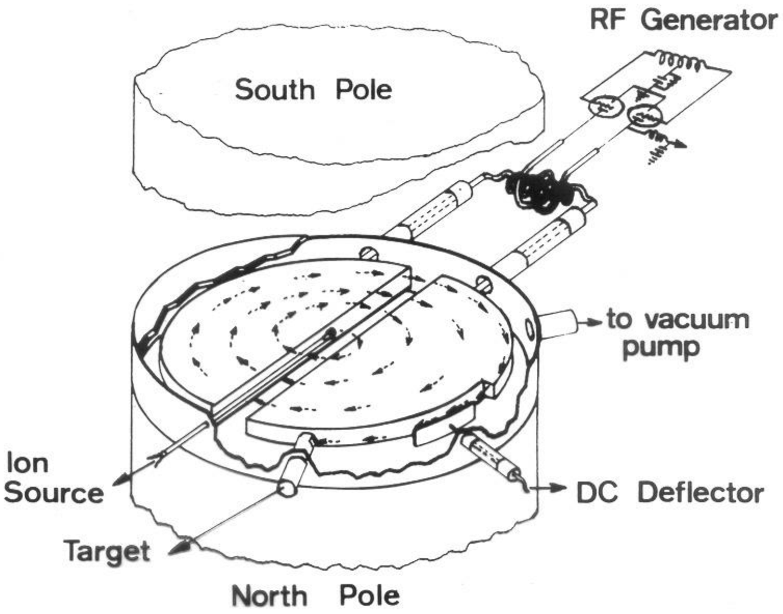


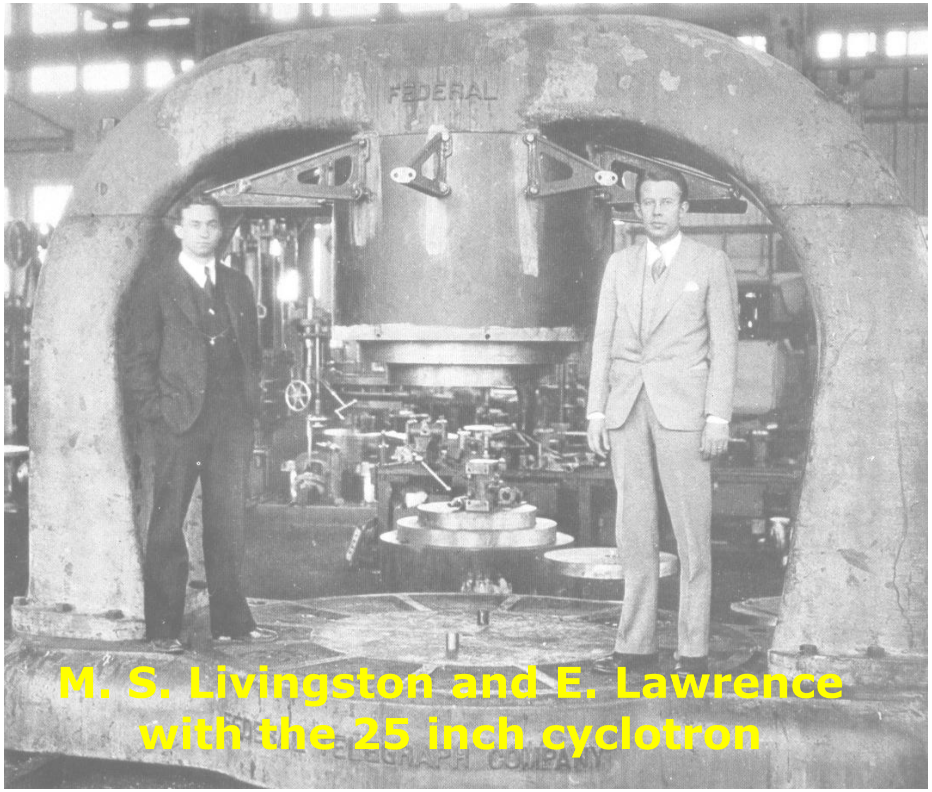
Tools for (medical) physics: the cyclotron

1930

Invention of the cyclotron

Ernest Lawrence



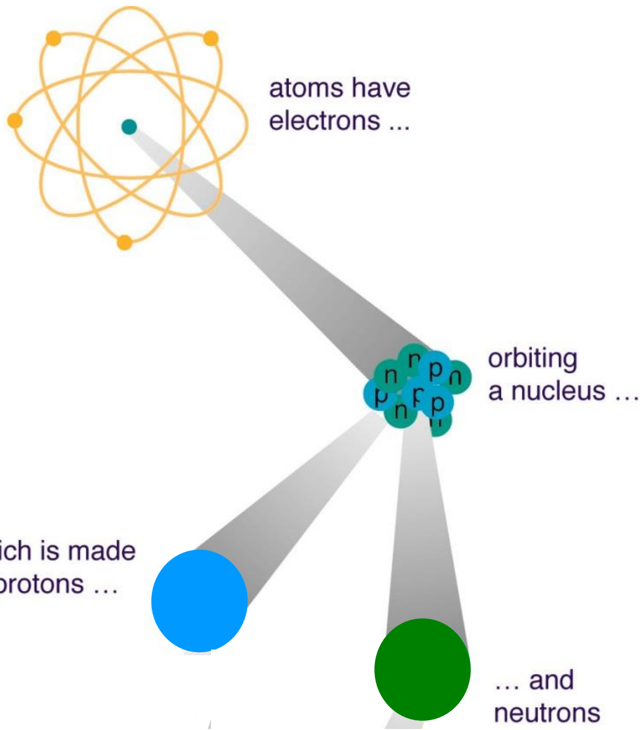


M. S. Livingston and E. Lawrence with the 25 inch cyclotron

The beginnings of modern physics and of medical physics

1932

Discovery of the neutron



James Chadwick

(1891 – 1974)

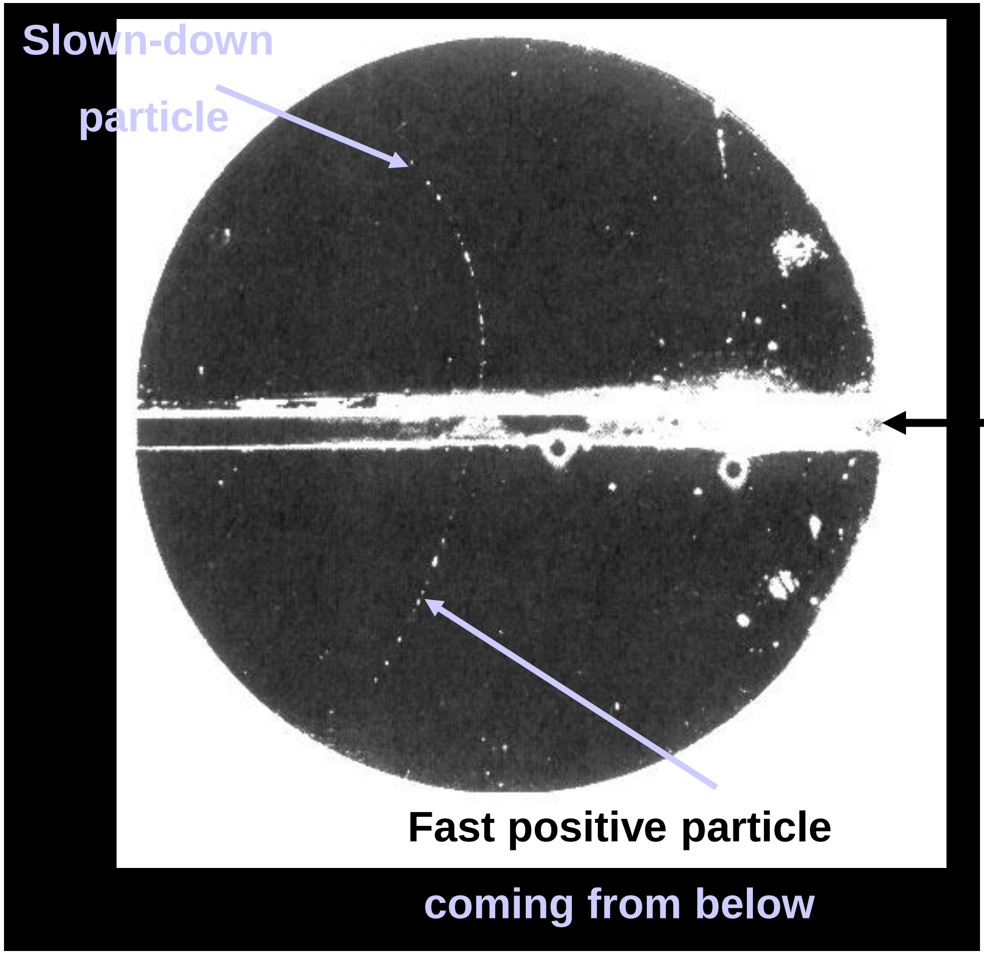
Cyclotron + neutrons = first attempt of radiation therapy with fast neutrons at LBL (R. Stone and J. Lawrence, 1938)

The beginnings of modern physics and of medical physics

1932

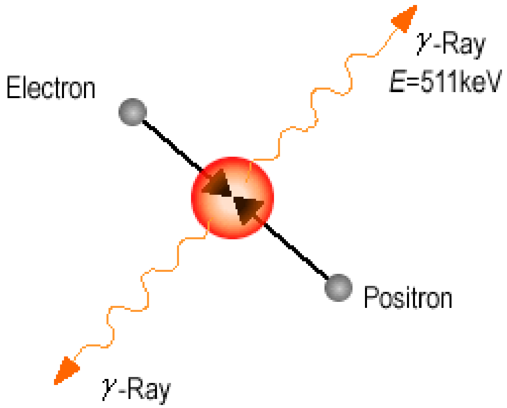
Discovery of the positron

C. D. Anderson



Layer of lead

Inserted in a cloud chamber



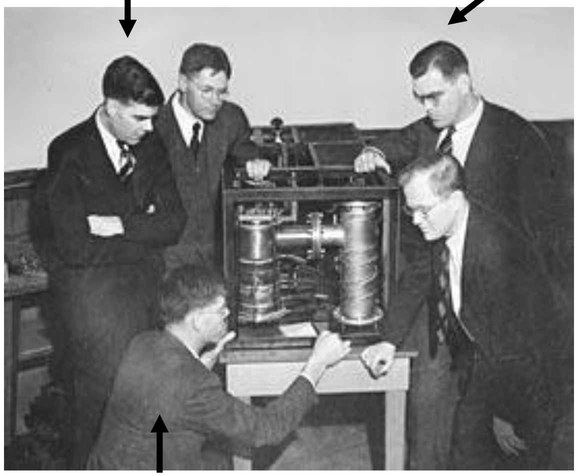
Historical development of radioisotopes for medicine

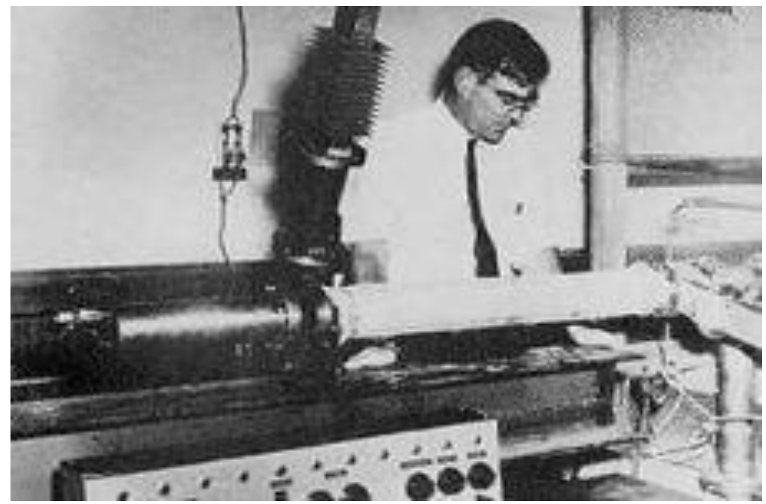
- 1932: the invention of the cyclotron by E. Lawrence makes it possible to produce radioactive isotopes of a number of biologically important elements
- 1941: first medical cyclotron installed at Washington University, St Louis, for the production of radioactive isotopes of phosphorus, iron, arsenic and sulphur
- After WWII: following the development of the fission process, most radioisotopes of medical interest begin to be produced in nuclear reactors
- 1951: Cassen et al. develop the concept of the rectilinear scanner
- 1957: the ^{99}Mo/^{99m}Tc generator system is developed by the Brookhaven National Laboratory
- 1958: production of the first gamma camera by Anger, later modified to what is now known as the Anger scintillation camera, still in use today

Tools for (medical) physics: the electron linac

Sigmur Varian

William W. Hansen





Russell Varian

1939

Invention of the klystron

1947
first linac for electrons
4.5 MeV and 3 GHz

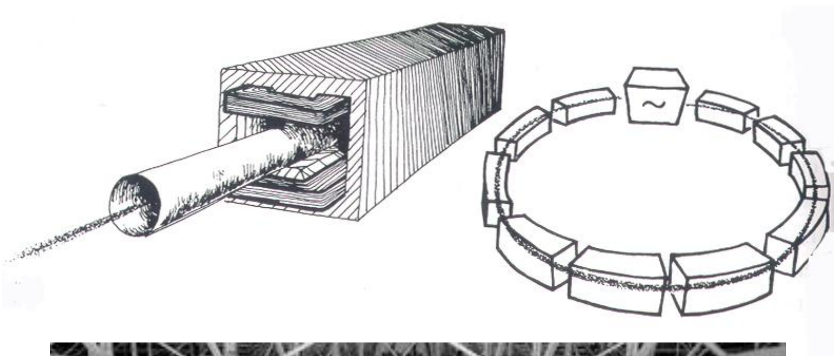
1950's: development of compact linear electron accelerators by various companies

Tools for (medical) physics: the synchrotron

1945: E. McMillan and V.J.Veksler

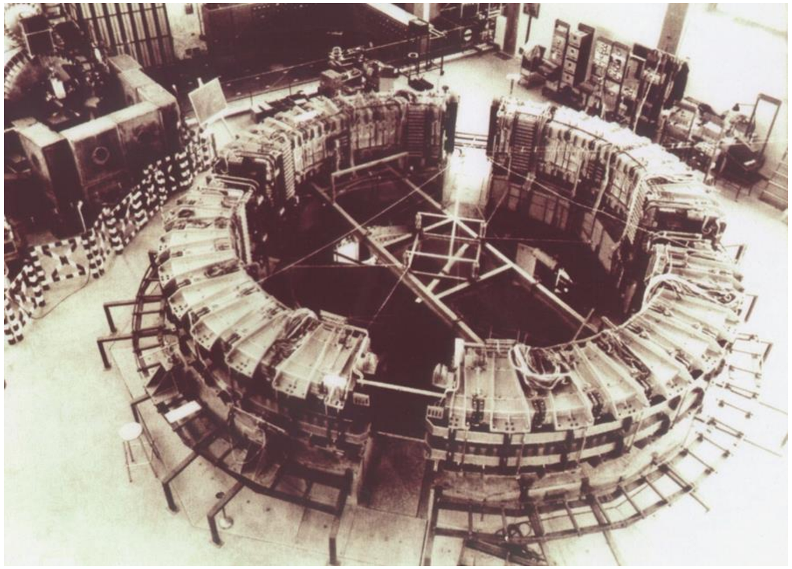
discover the

principle of phase stability



1 GeV electron synchrotron

Frascati - INFN - 1959

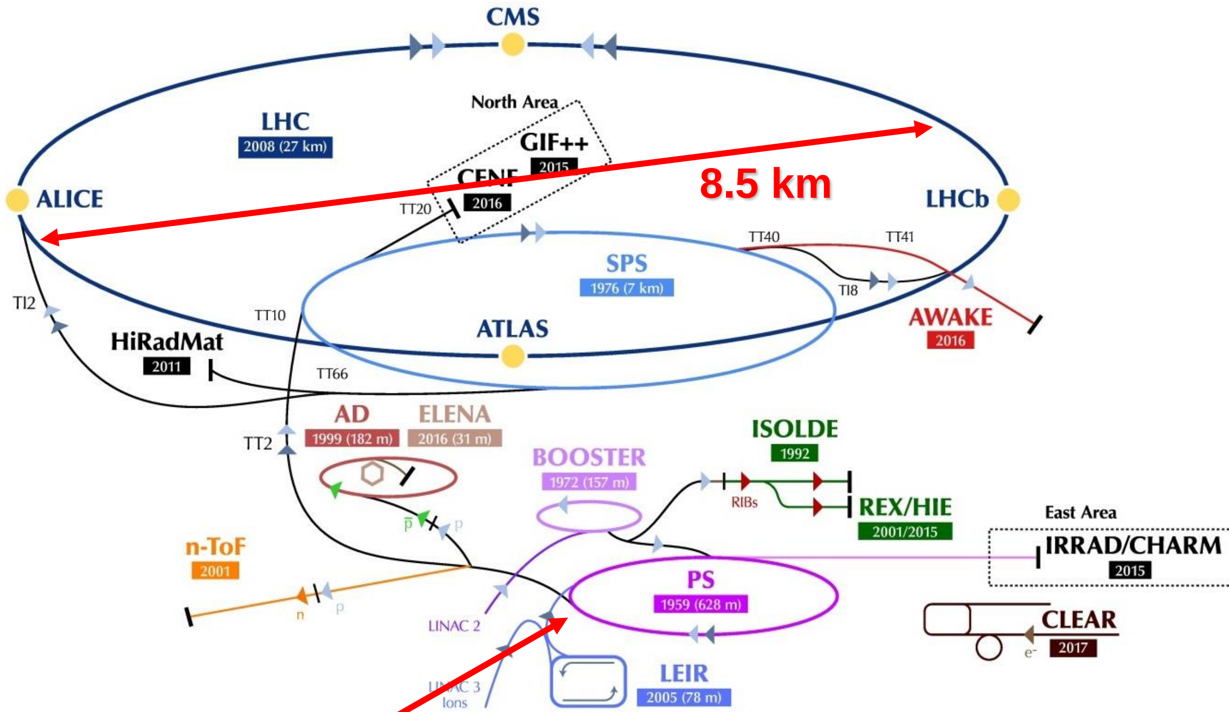


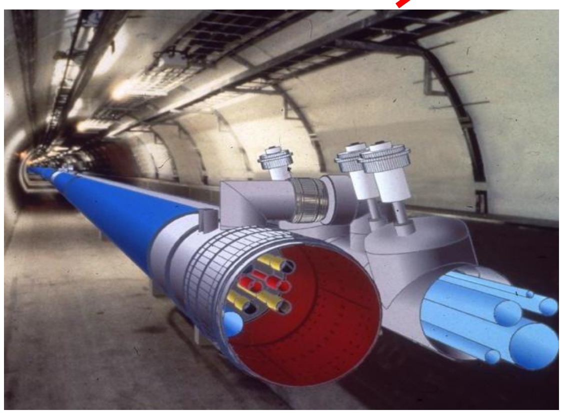
6 GeV proton synchrotron

Bevatron - Berkeley - 1954

CERN accelerators

Large Hadron Collider
7 TeV + 7 TeV
Start in 2008





The PS in 1959

In 1952 the “strong-focusing” method
invented at BNL (USA)
was chosen for the CERN PS

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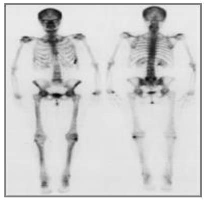
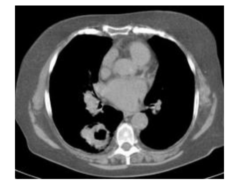
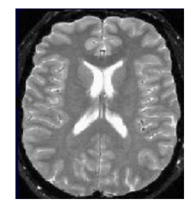
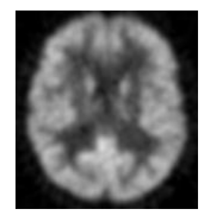
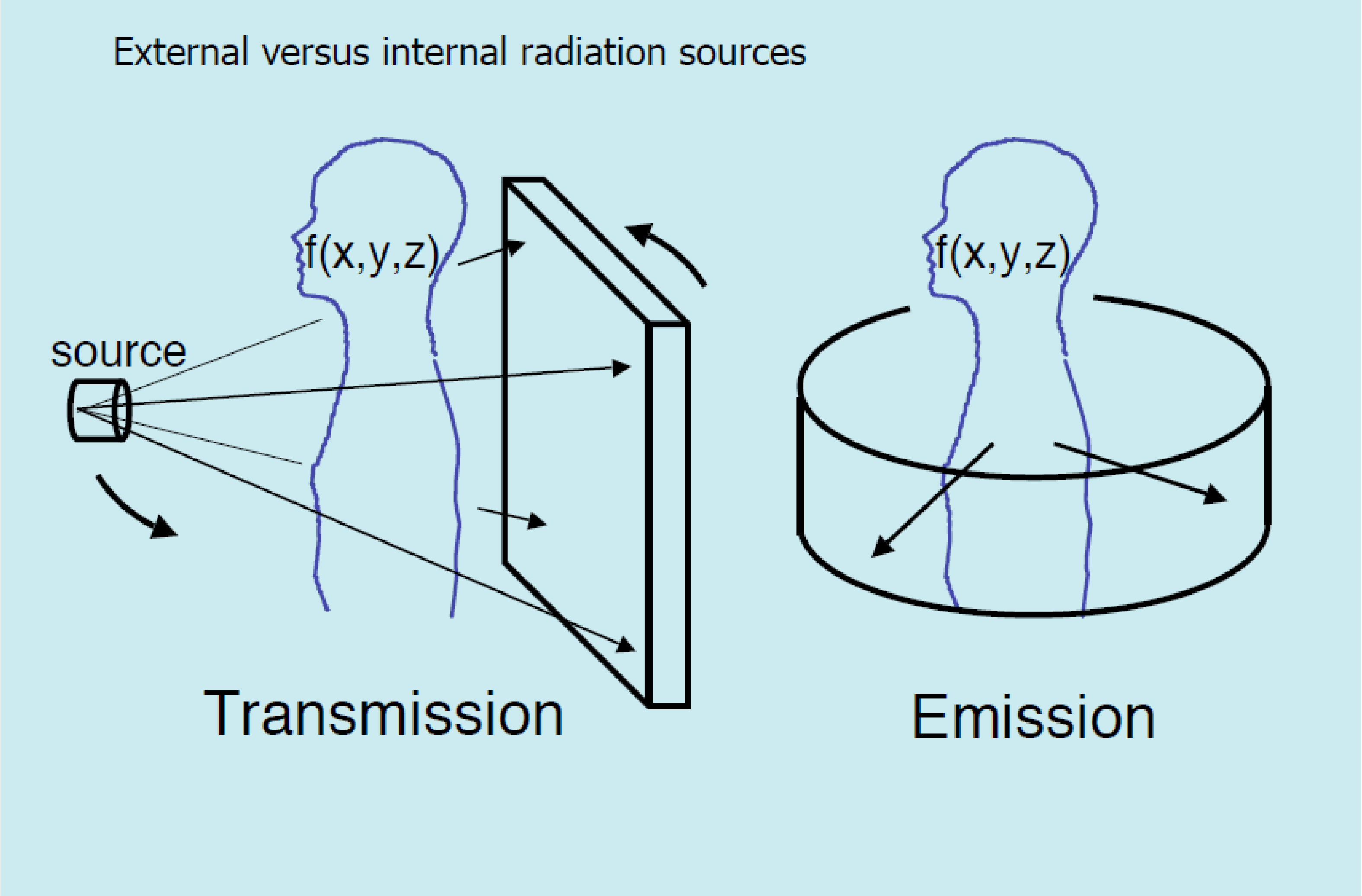
Medical imaging

TECHNIQUE		YEAR	ENERGY	PHYSICAL PROPERTY	IMAGING
RADIOLOGY	X RAYS IMAGING	**1895**	X RAYS	ABSORPTION	
ECHOGRAPHY	ULTRASOUND IMAGING	1950	US	REFLECTION TRANSMISSION	
NUCLEAR MEDICINE	RADIOISOTOPE IMAGING	1950	γ RAYS	RADIATION EMISSION	

Medical imaging

TECHNIQUE		YEAR	ENERGY	PHYSICAL PROPERTY	IMAGING	
X RAYS COMPUTERIZED TOMOGRAPHY	**CT**	**1971**	X RAYS	ABSORPTION		MORPHOLOGY
MAGNETIC RESONANCE IMAGING	MRI	1980	RADIO WAVES	MAGNETIC RESONANCE		MORPHOLOGY /FUNCTION
POSITRON EMISSION TOMOGRAPHY	PET	1973	γ RAYS	RADIATION EMISSION		FUNCTION

Emission versus transmission imaging



X-ray image versus CT scan

A conventional X-ray image is basically a shadow: you shine a "light" on one side of the body, and a piece of film on the other side registers the silhouette of the bones (to be more precise, organs and tissues of different densities show up differently on the radiographic film).

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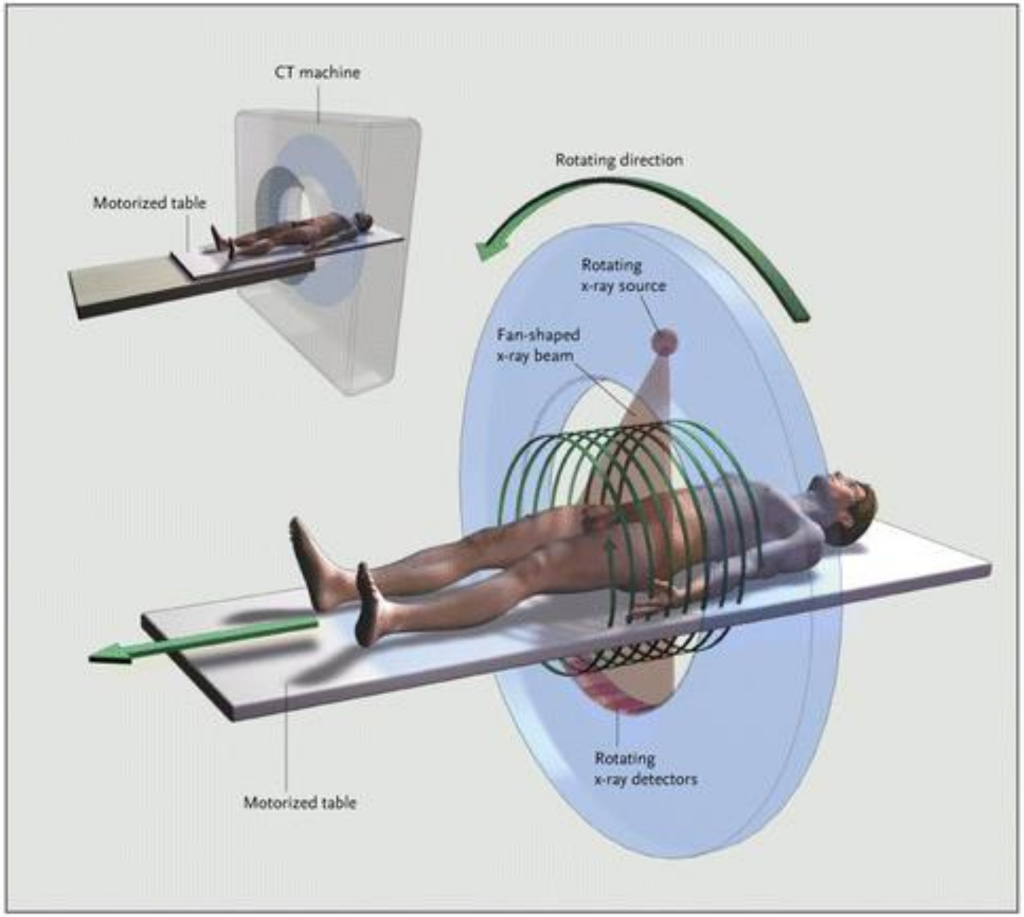
Shadows give an incomplete picture of an object's shape.

Look at the wall, not at the person. If there's a lamp in front of the person, you see the silhouette holding the banana, but not the pineapple as the shadow of the torso blocks the pineapple. If the lamp is to the left, you see the outline of the pineapple, but not the banana.

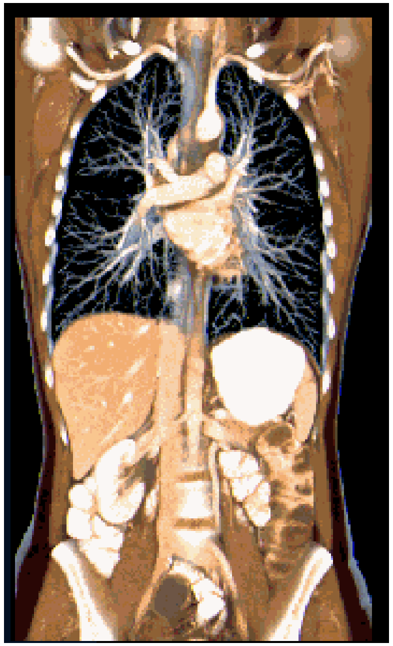
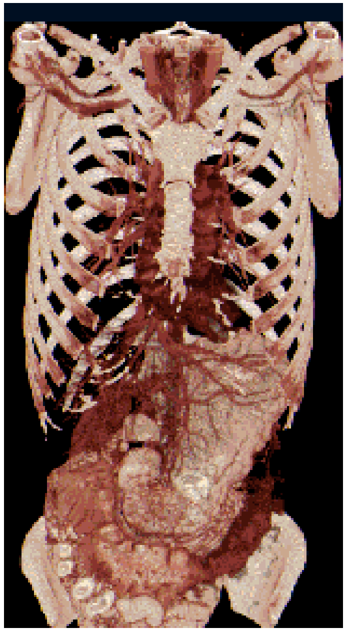
Computed tomography

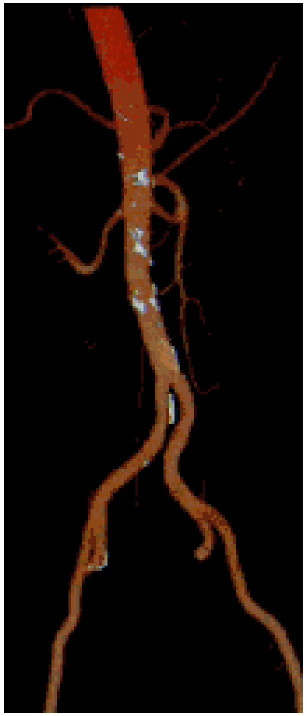


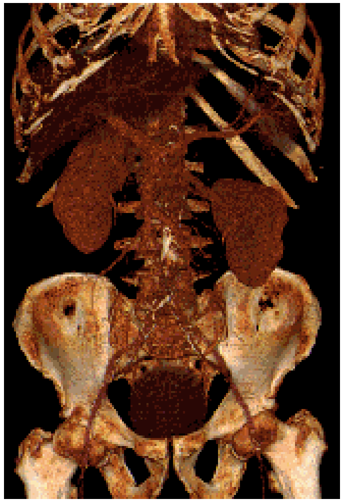
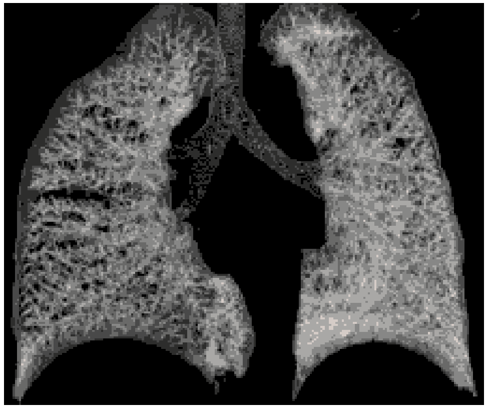
- The X-rays source rotates around the longitudinal axis of the body: it moves 360° around the patient, scanning from hundreds of different angles
- Opposite to the x-ray source, a series of detectors measure the radiation emerging from the body
- Each rotation scans a different body slice
- The couch moves to scan the next slice
- A computer analyses the data and reconstructs the **3D image** through mathematical algorithms.

Volumetric CT

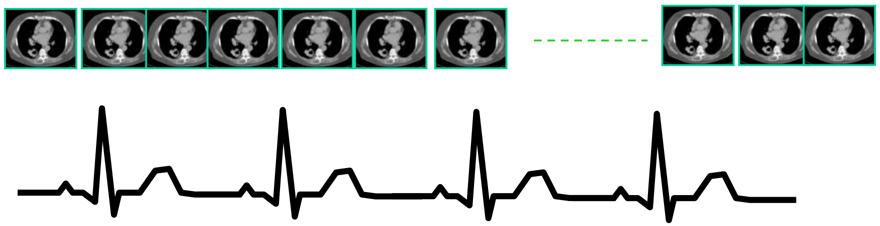
< 0.4 sec/rotation
Organ in a sec (17 cm/sec)
Whole body < 10 sec



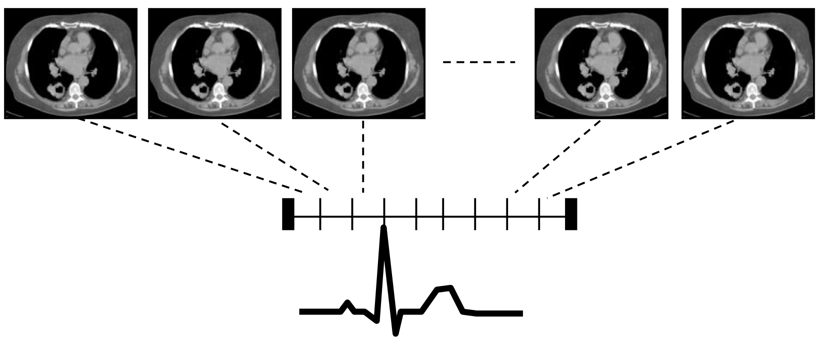



Cardiac CT



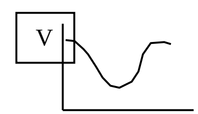
DYNAMIC CT ACQUISITION

ECG

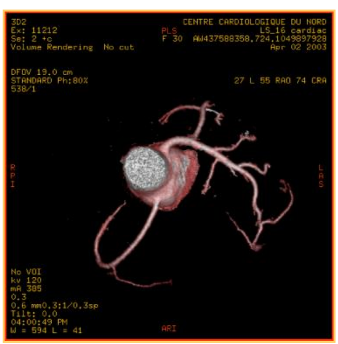


PHASES OF A CARDIAC CYCLE

- EJECTION FRACTION
- CARDIAC OUTPUT
- REGIONAL WALL MOTION
- ..



FUNCTIONAL PARAMETERS



VOLUME RENDERED IMAGE OF HEART AND VESSELS

All radionuclides commonly administered to patients in nuclear medicine are *artificially* produced

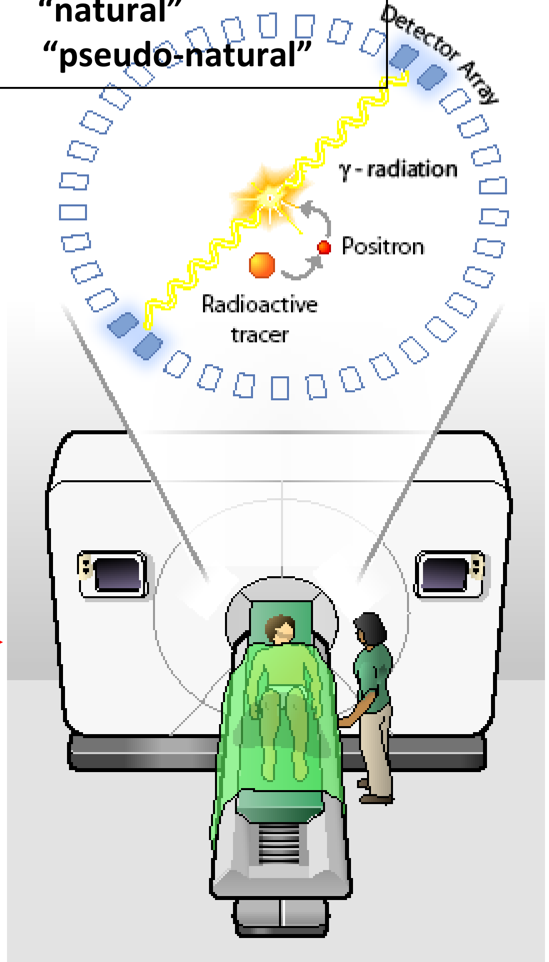
Three production routes:

- (n, γ) reactions (**nuclear reactor**): the resulting nuclide has the same chemical properties as those of the target nuclide
- Fission (**nuclear reactor**) followed by separation
- Charged particle induced reaction (**cyclotron**): the resulting nucleus is usually that of a different element

Positron Emission Tomography (PET)

Cyclotron

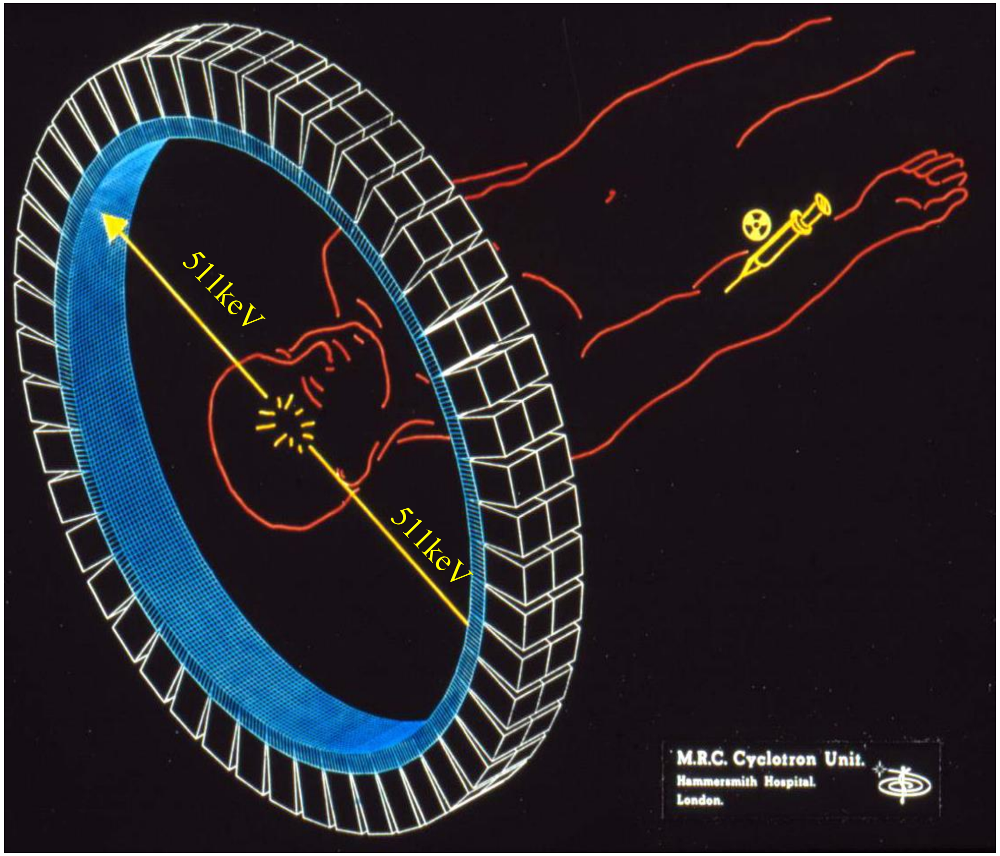
ISOTOPES	Half-Life	
11-C	20.4 min,	“natural”
13-N	10.0 min	“natural”
15-O	2.0 min	“natural”
18-F	109.8 min	“pseudo-natural”

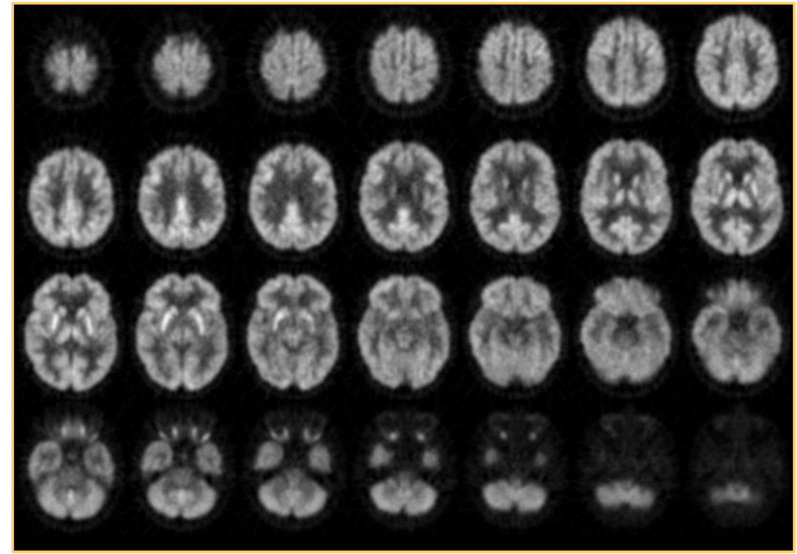


Radiochemistry

PET camera

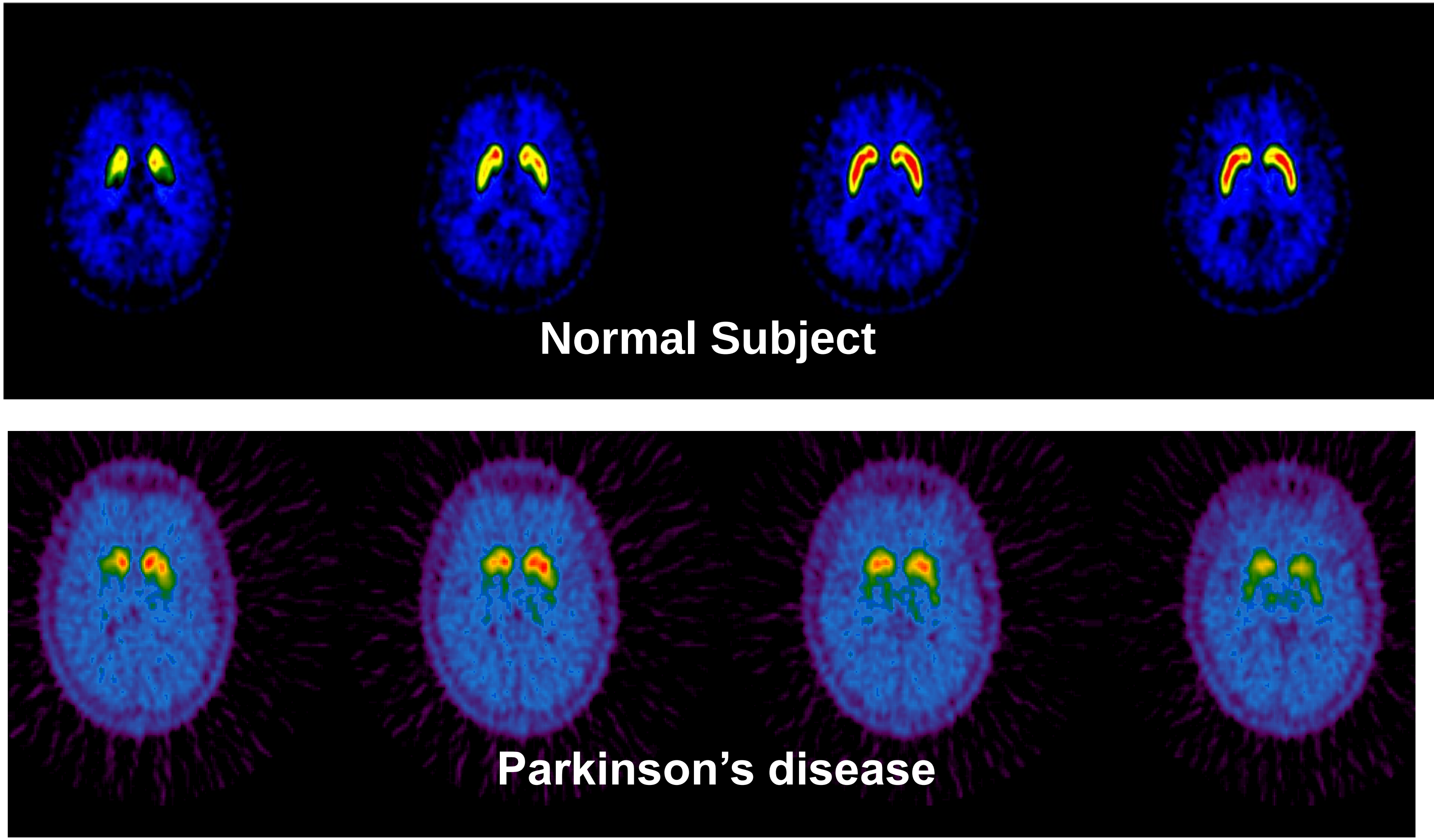
Positron Emission Tomography (PET)





COVERAGE:
~ 15-20 cm
SPATIAL RESOLUTION:
~ 5 mm
SCAN TIME to cover an entire organ:
~ 5 min
CONTRAST RESOLUTION:
depends on the radiotracer

PET functional receptor imaging

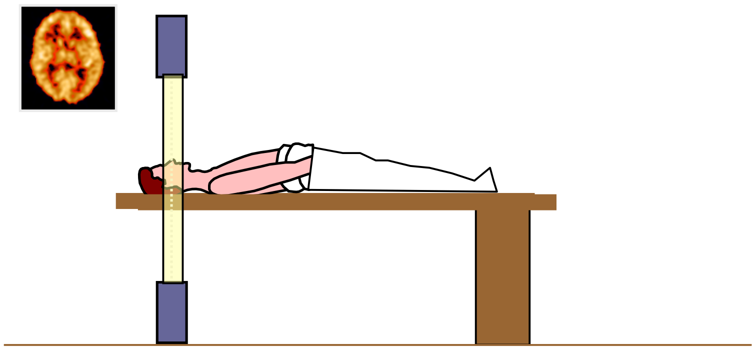


[^{11}C] FE-CIT

Courtesy HSR MILANO

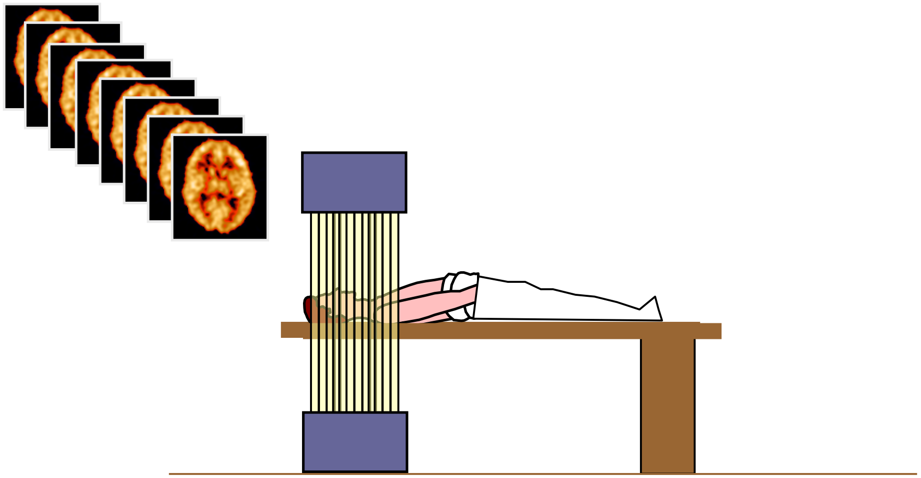
PET coverage and axial sampling

FIRST GENERATION PET



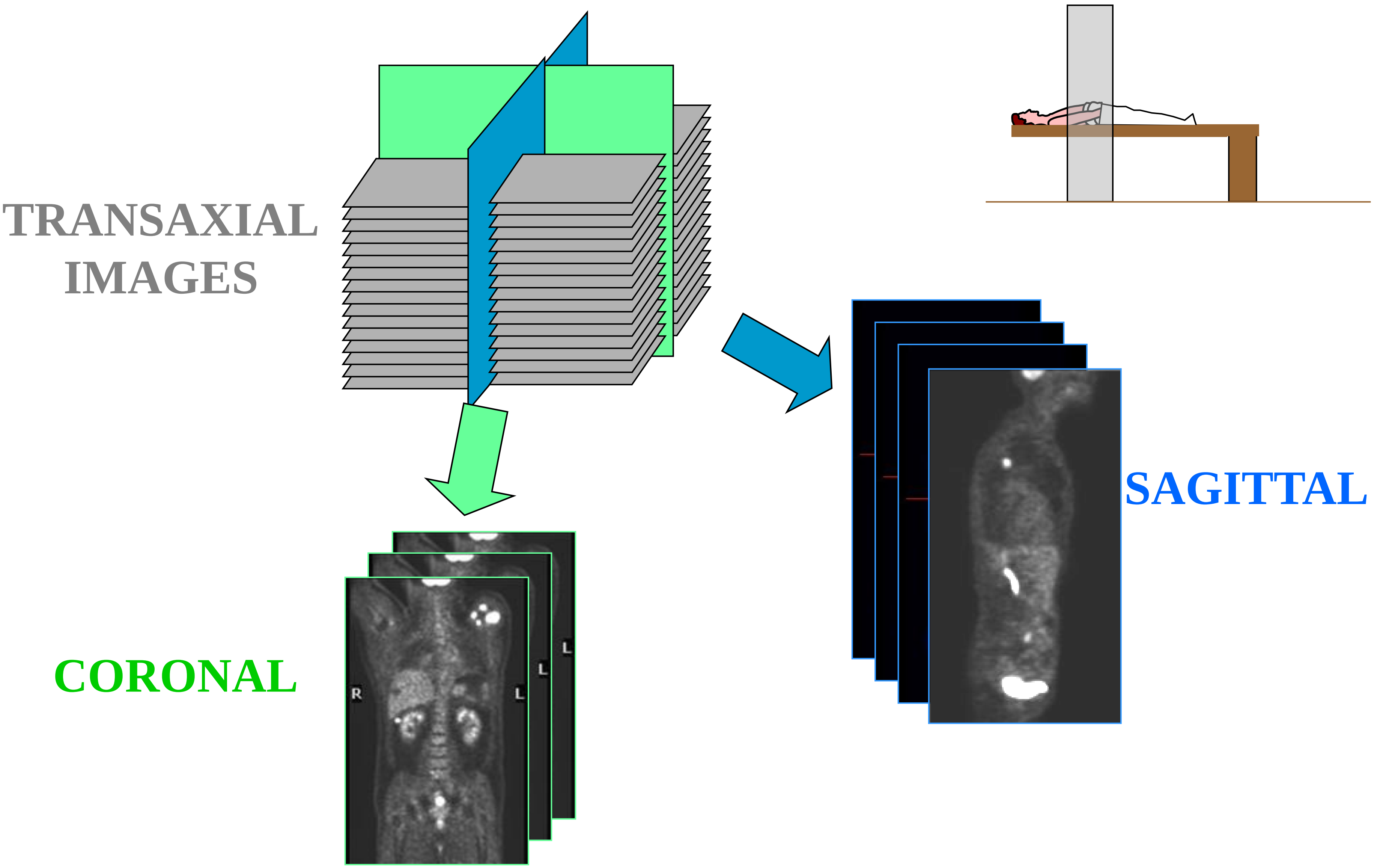
1 SLICE – 2 cm

CURRENT GENERATION PET

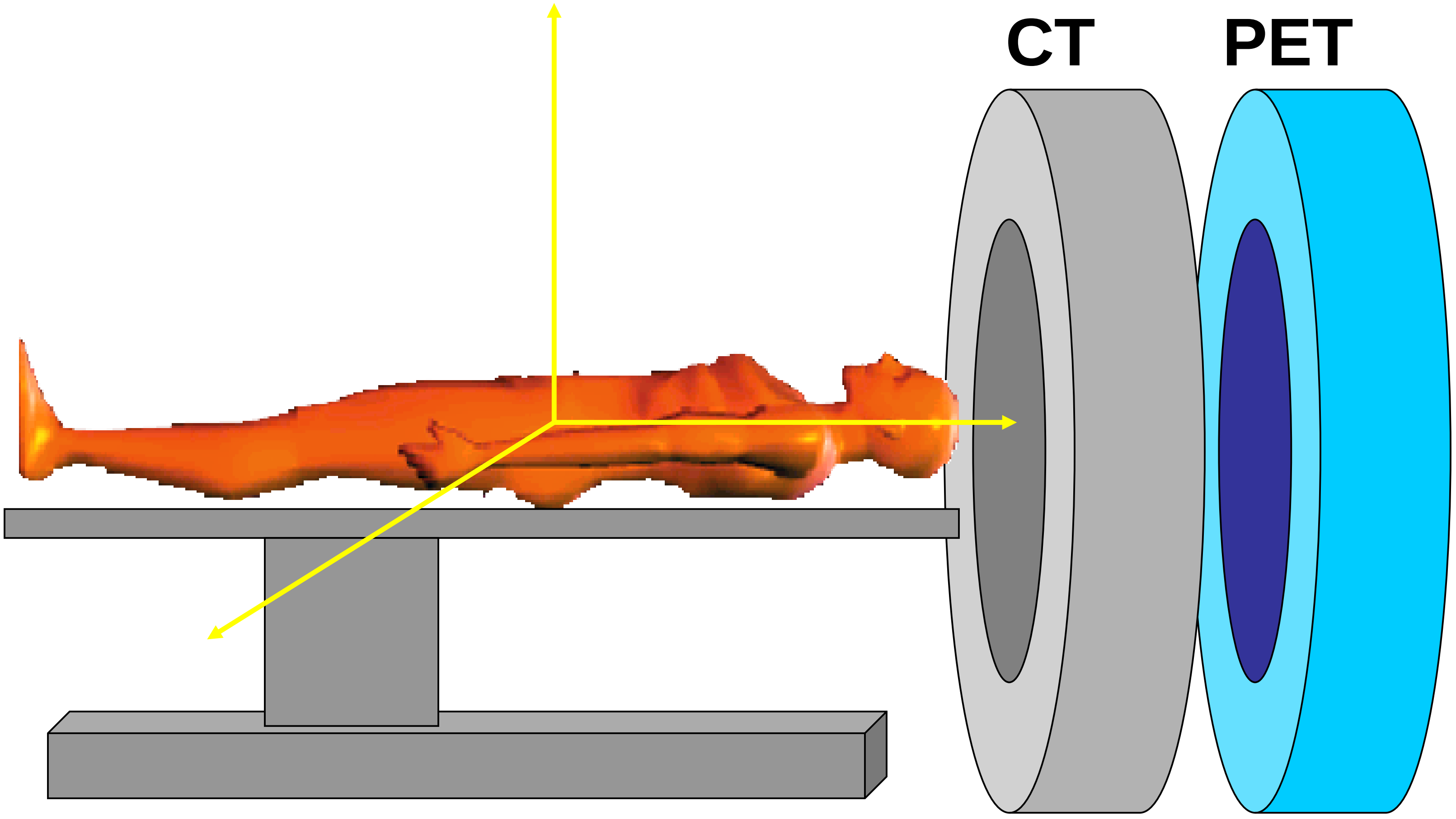


> 40 SLICES – 6 mm
Axial FOV: 15 –20 cm

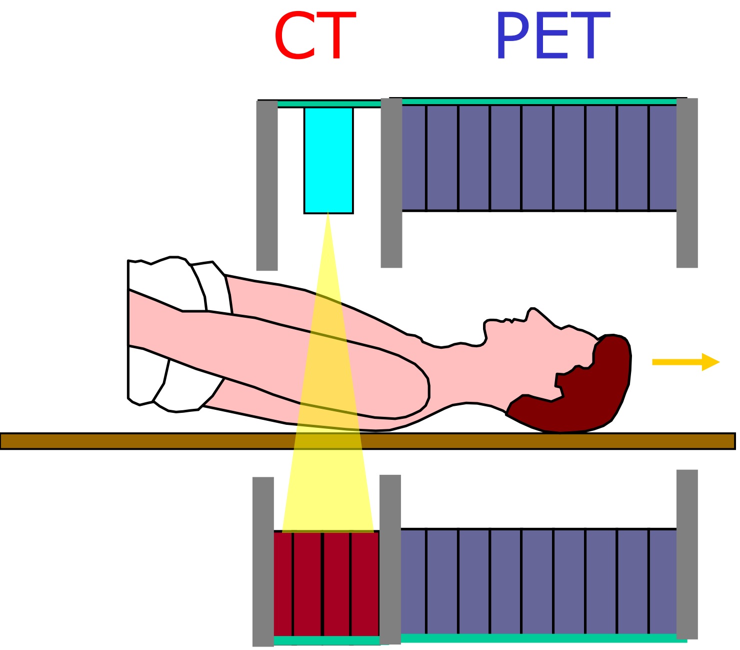
PET: total body studies

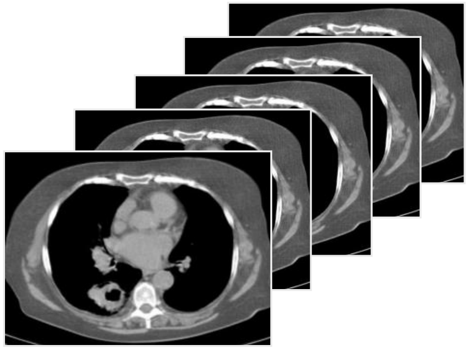


PET/CT scanner



PET/CT scanner





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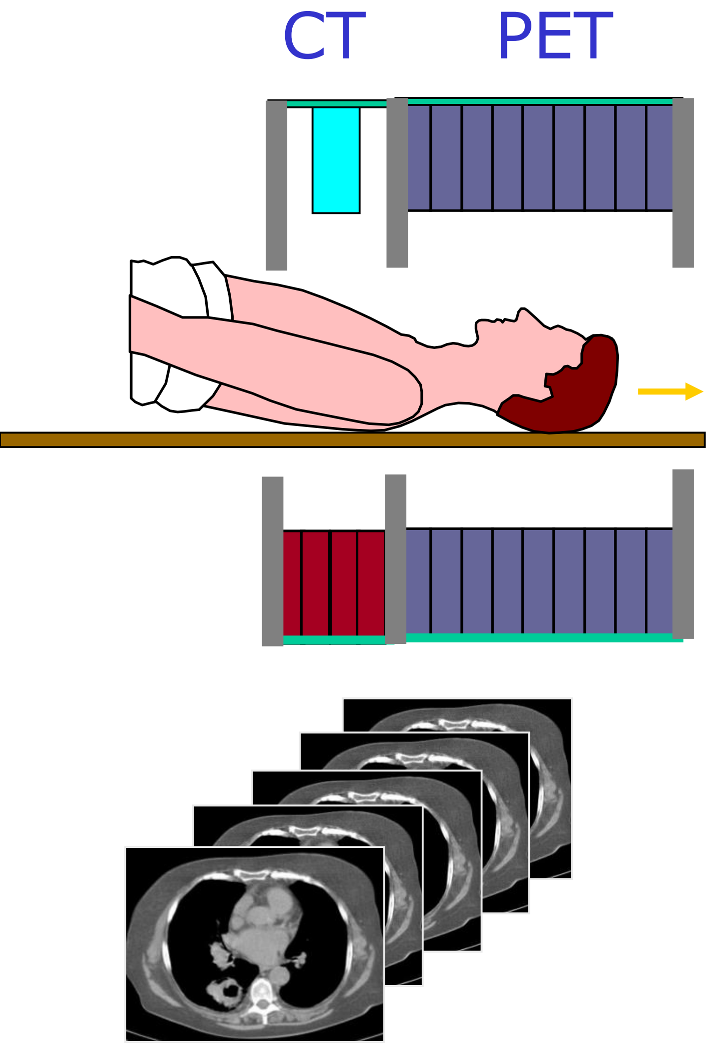
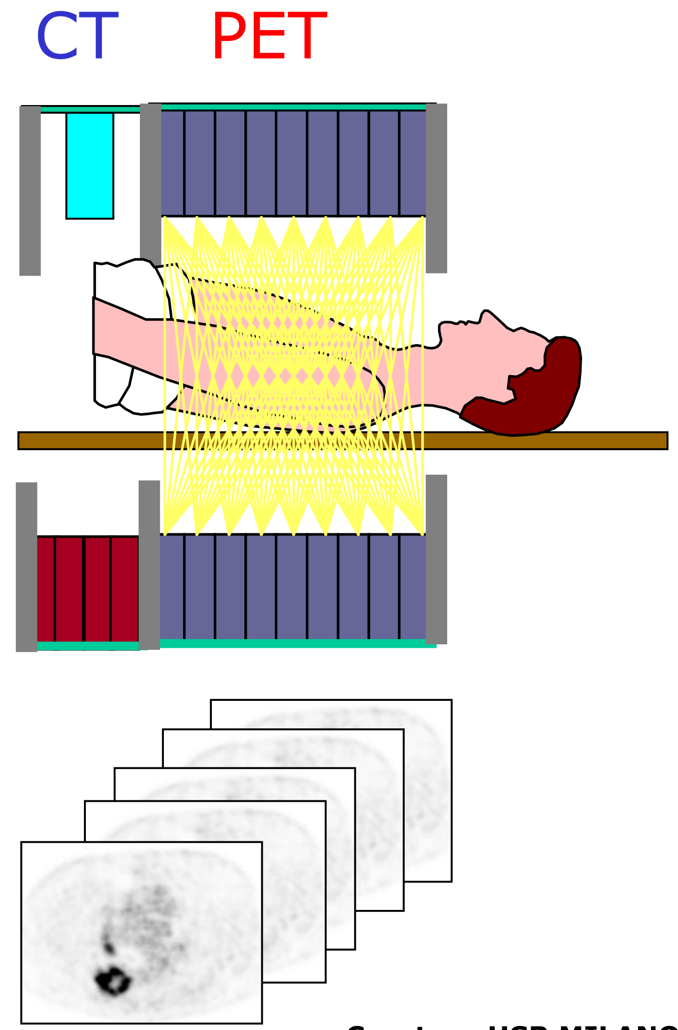
PET/CT scanner





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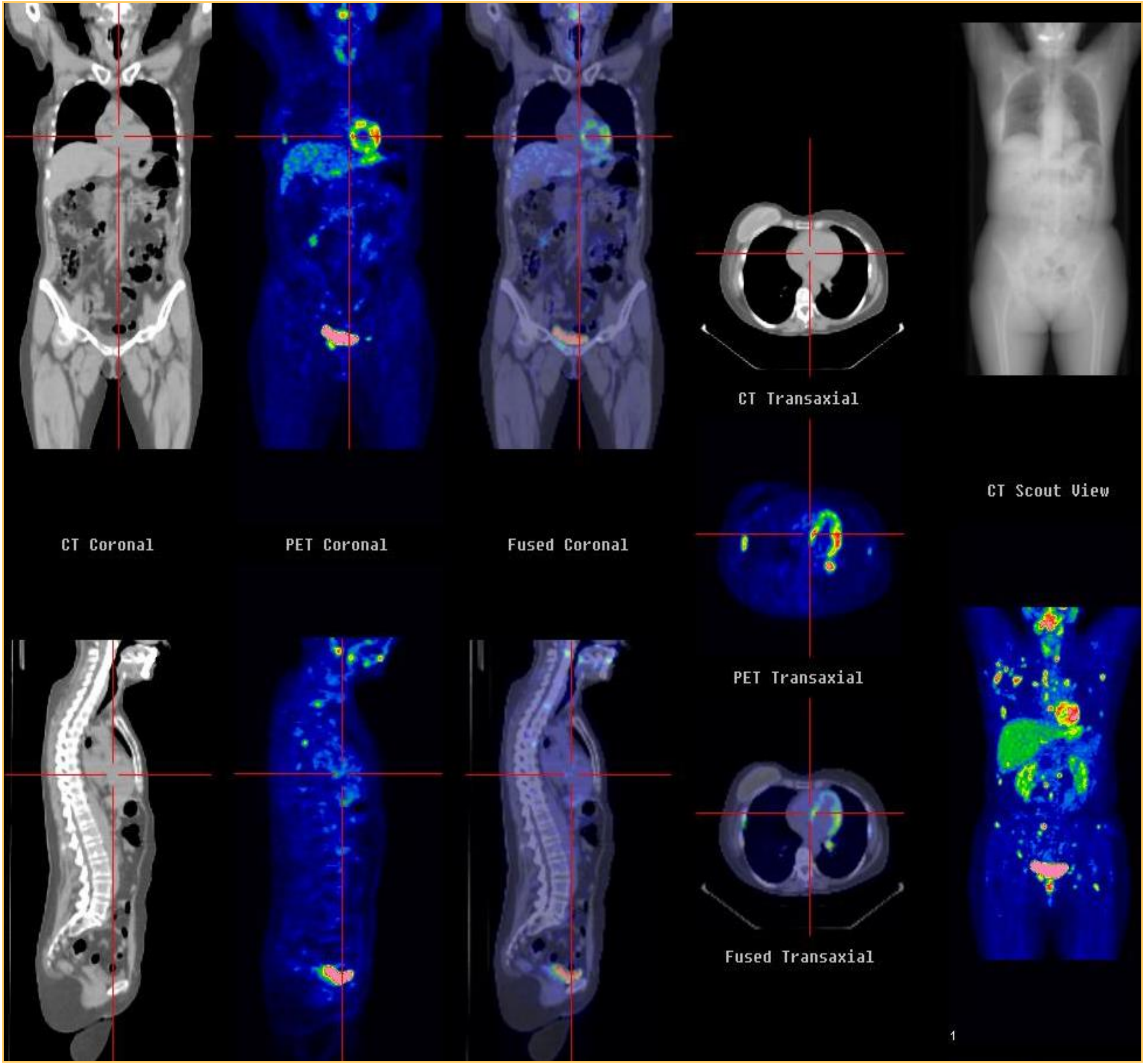
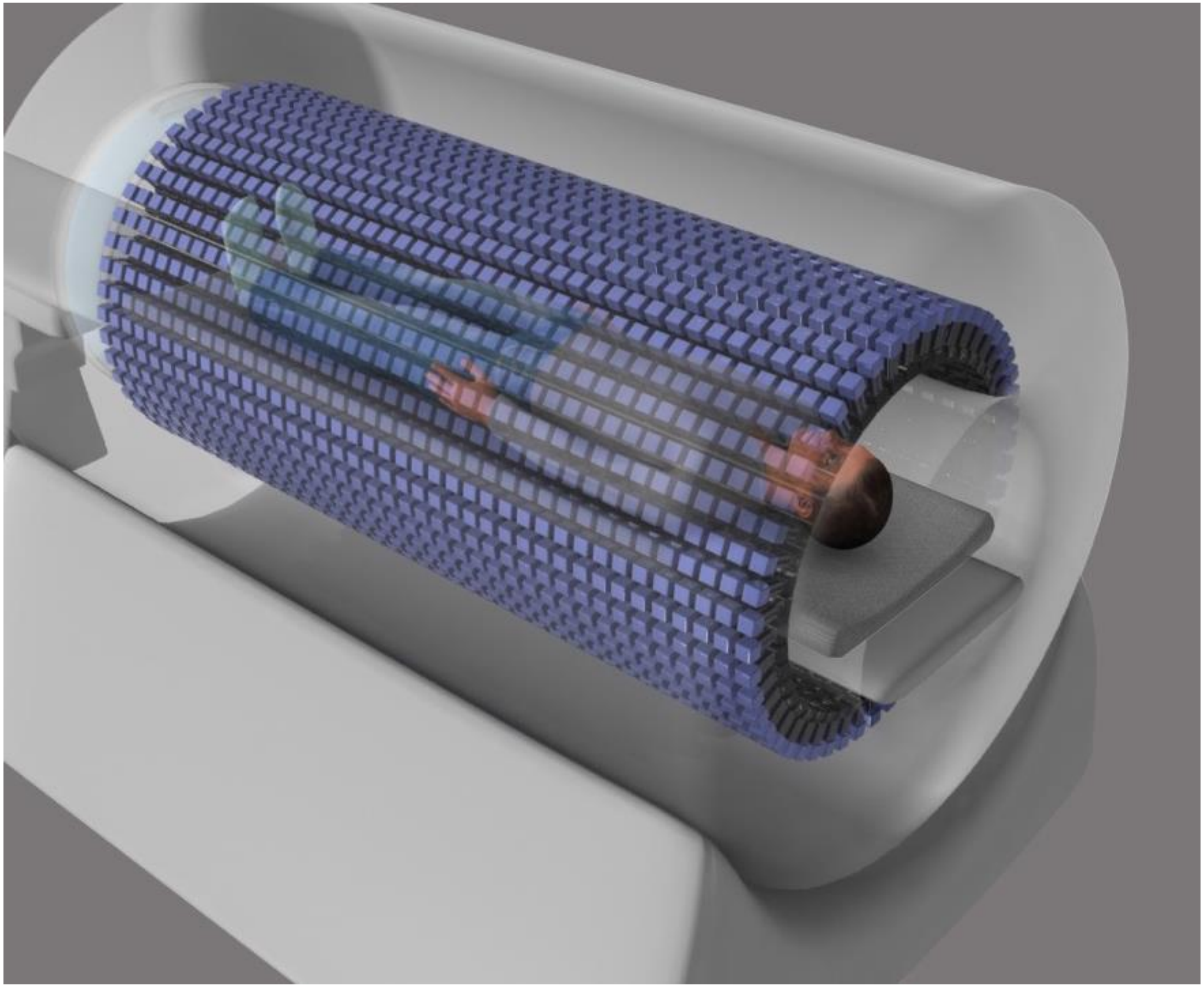
^{18}F-FDG PET/CT



Courtesy HSR MILANO

A look into the future: whole-body PET



Outline of the lecture

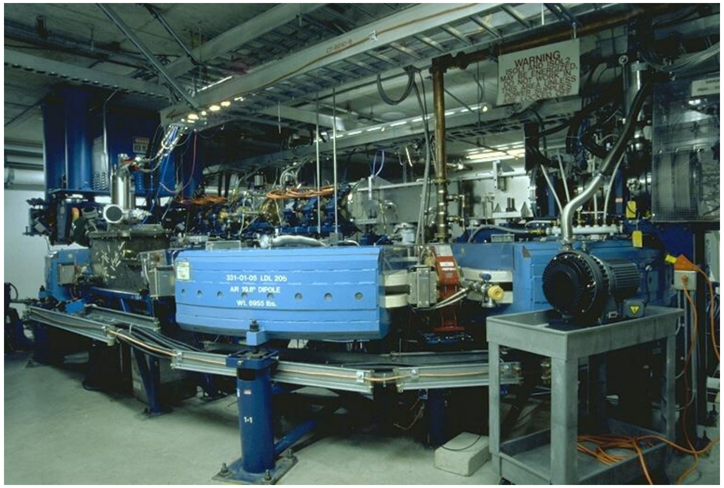
- Physics discoveries
- Tools for physics applied to medicine
- Medical imaging
- X-ray CT
- PET and PET/CT
- Photon/electron radiation therapy
- Hadron therapy

Three classes of medical accelerators

Electron linacs for conventional radiation therapy, including advanced modalities:

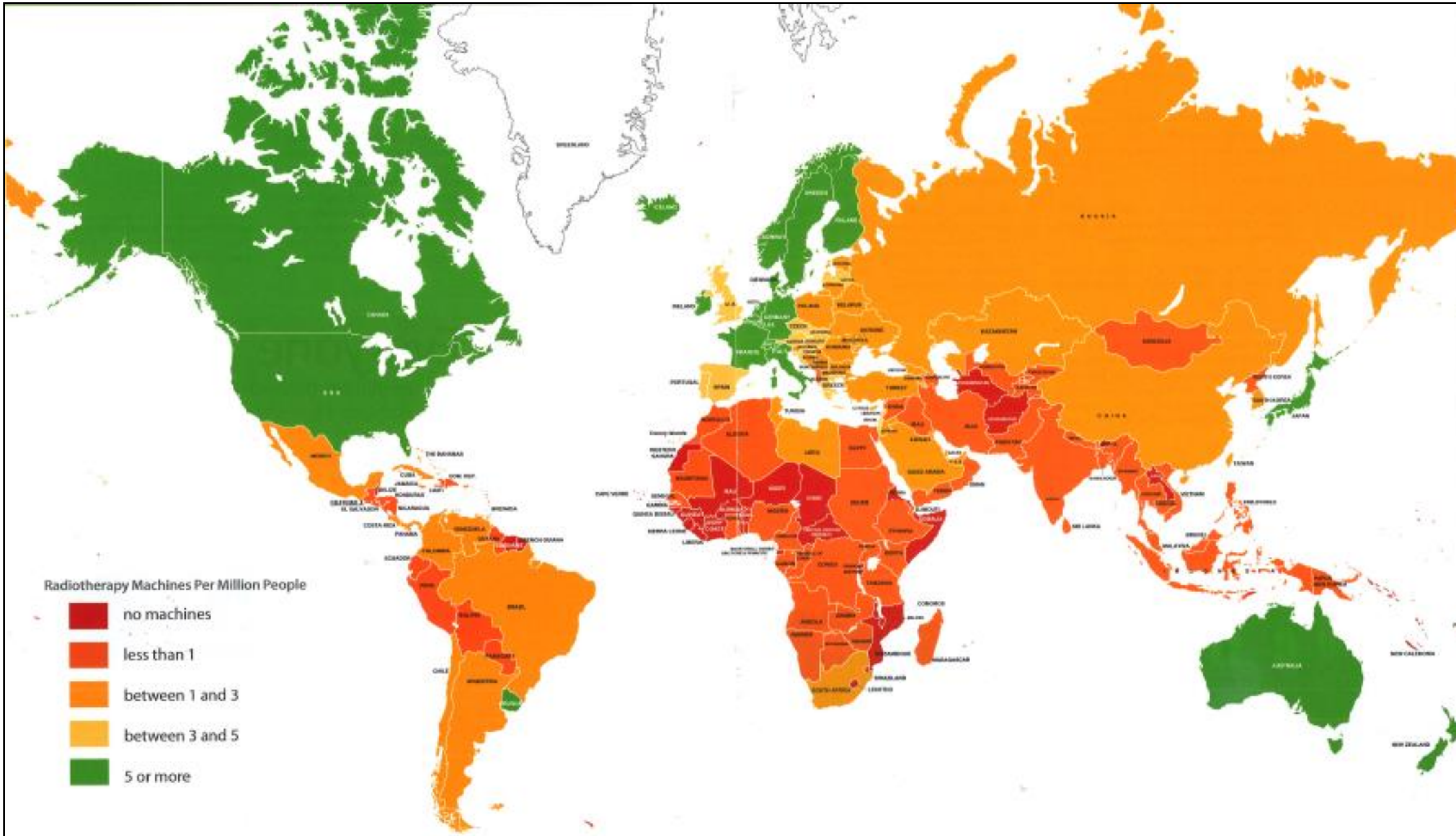
- Cyberknife
- IntraOperative RT (IORT)
- Intensity Modulated RT

Low-energy cyclotrons for production of radionuclides for medical diagnostics



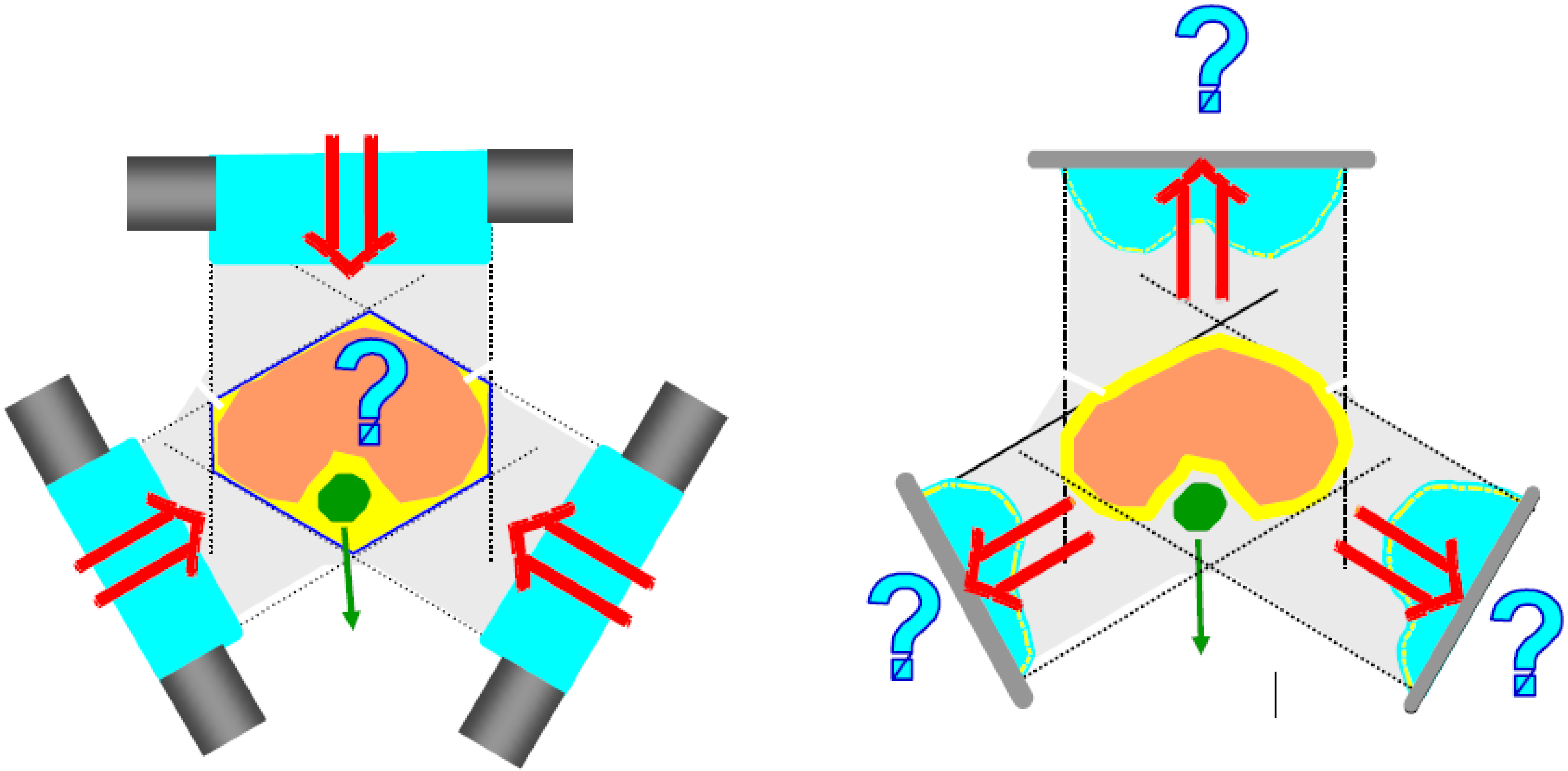
Medium-energy cyclotrons and synchrotrons for hadron therapy with protons (250 MeV) or light ion beams (400 MeV/u ^{12}C-ions)

Availability of radiation therapy worldwide

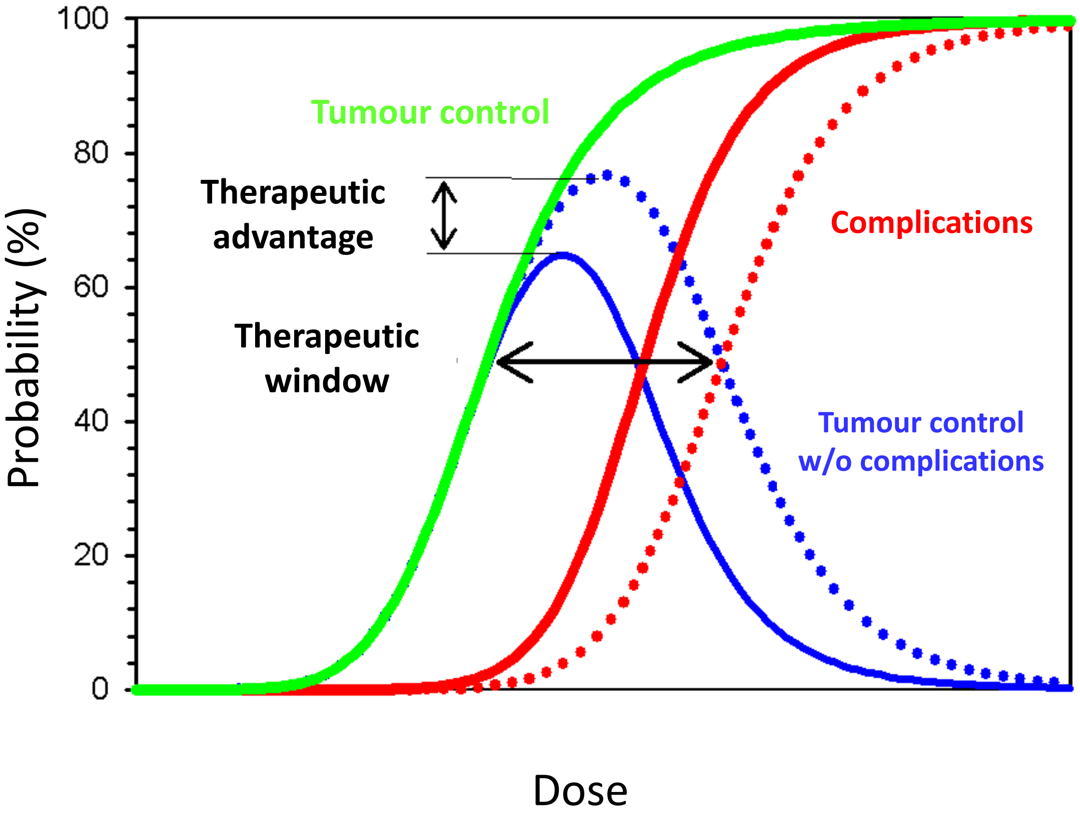


Number of radiation therapy machines per million people

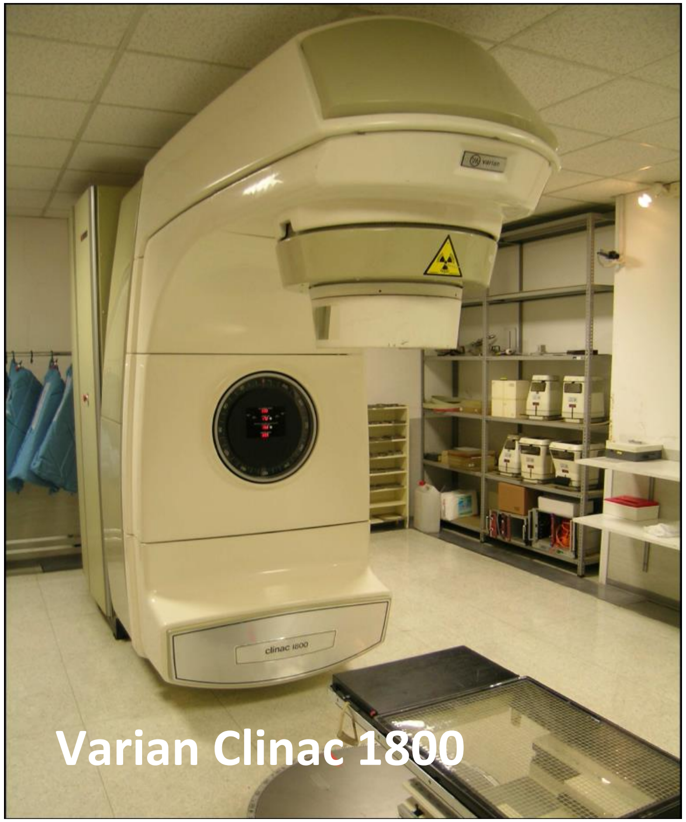
Treatment planning and dose delivery to tumour volume

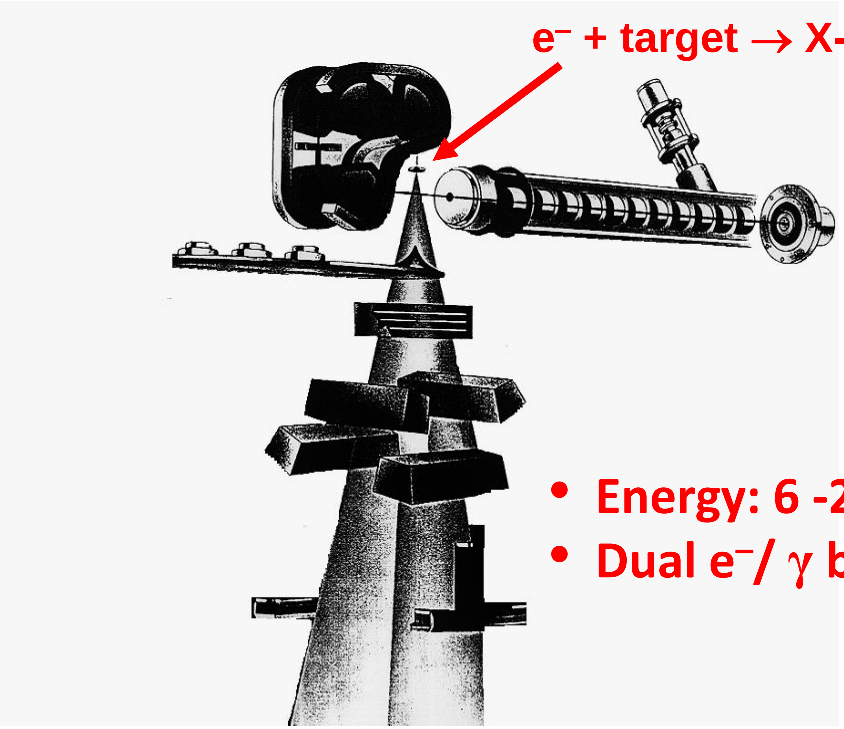


Tumour control and therapeutic window

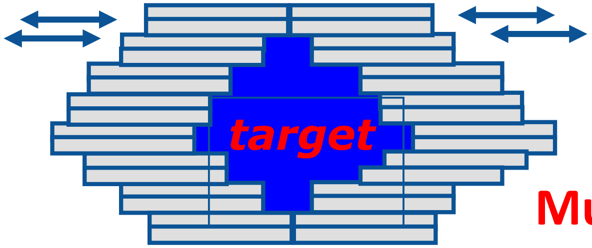


X-rays in radiation therapy: medical electron linacs

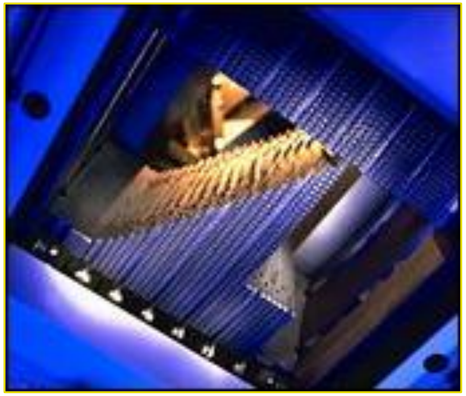




- **Energy: 6 -25 MeV**
- **Dual e^-/γ beams**



Multi-leaf collimator



Intra-Operative Radiation Therapy (IORT)

- Small electron linac
- Energy 6 – 12 MeV
- Treatment with electrons only
- Single irradiation
- Three models of linac produced by three manufacturers (two in Italy)

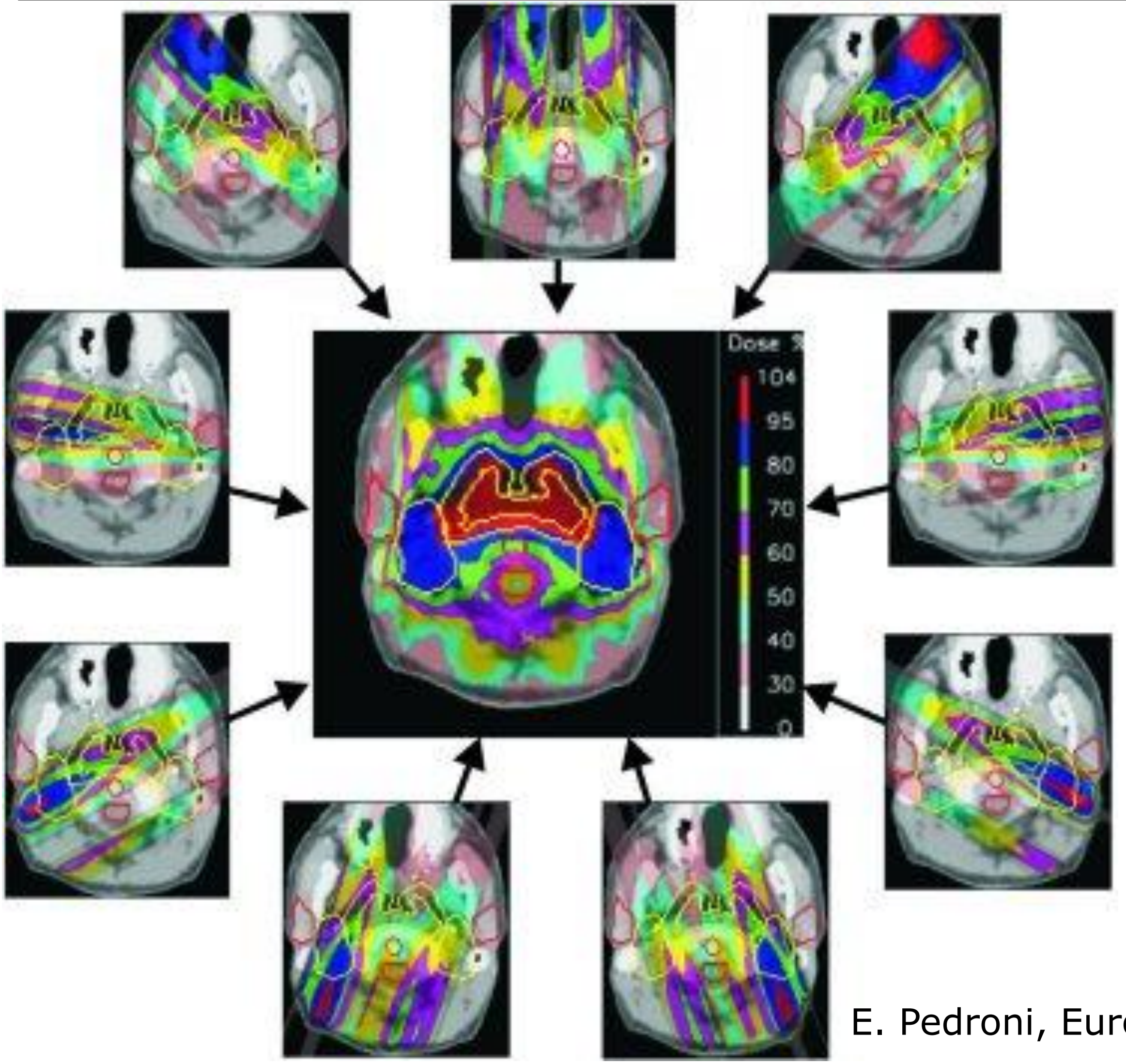
CyberKnife (CK) Robotic Surgery System

6 MV Linac mounted on a robotic arm

- Non-Isocentric
- Average dose delivered per session is 12.5 Gy
- 6 sessions/day
- Dose rate @ 80 cm = 400 cGy/min

http://www.accuray.com/Products/Cyberknife/index.aspx

Intensity Modulated Radiation Therapy

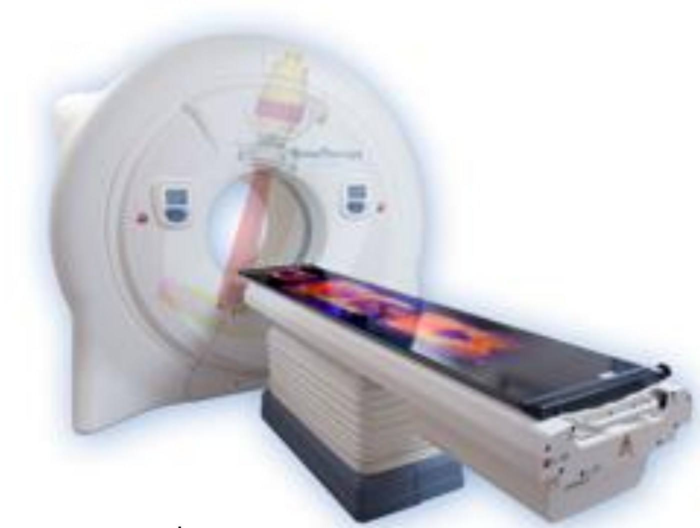


An example of intensity modulated treatment planning with photons. Through the addition of 9 fields it is possible to construct a highly conformal dose distribution with good dose sparing in the region of the brain stem (courtesy of T. Lomax, PSI).

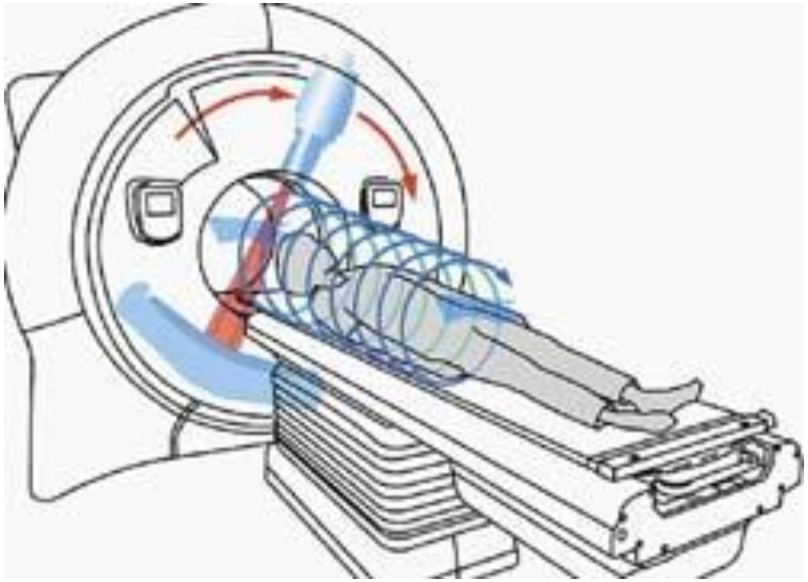
E. Pedroni, Europhysics News (2000) Vol. 31 No. 6

Yet X-rays have a comparatively poor energy deposition as compared to protons and carbon ions

Helical tomotherapy

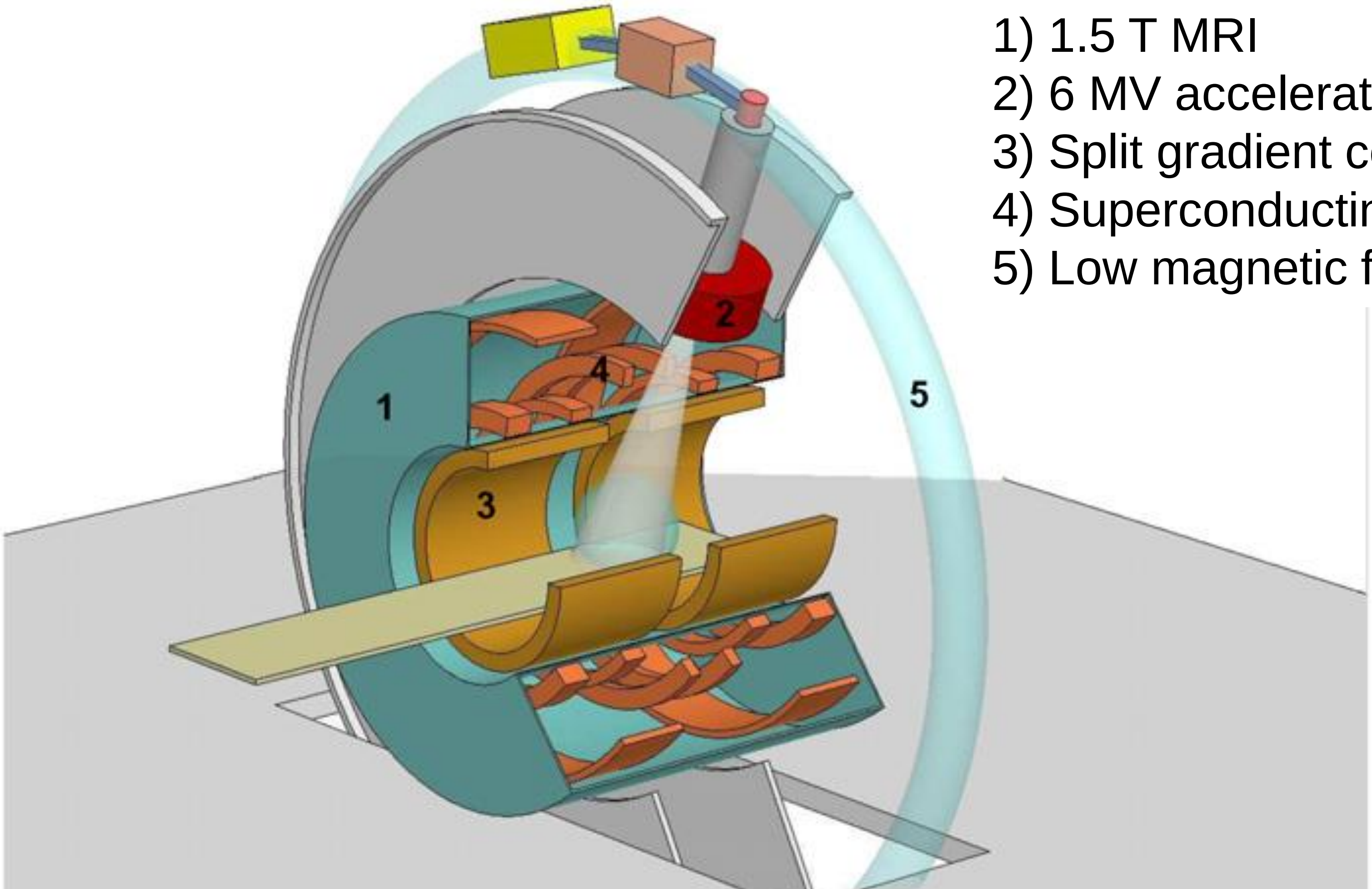


www.tomotherapy.com



- Integrated CT guidance
  - Integrated CT scanner allowing efficient 3D CT imaging for ensuring the accuracy of treatment
- A binary multi-leaf collimator (MLC) for beam shaping and modulation
- A ring gantry design enabling TomoHelical delivery
  - As the ring gantry rotates in simultaneous motion to the couch, **helical fan-beam IMRT** is continuously delivered from all angles around the patient
- Very large volumes can be treated in a single set-up

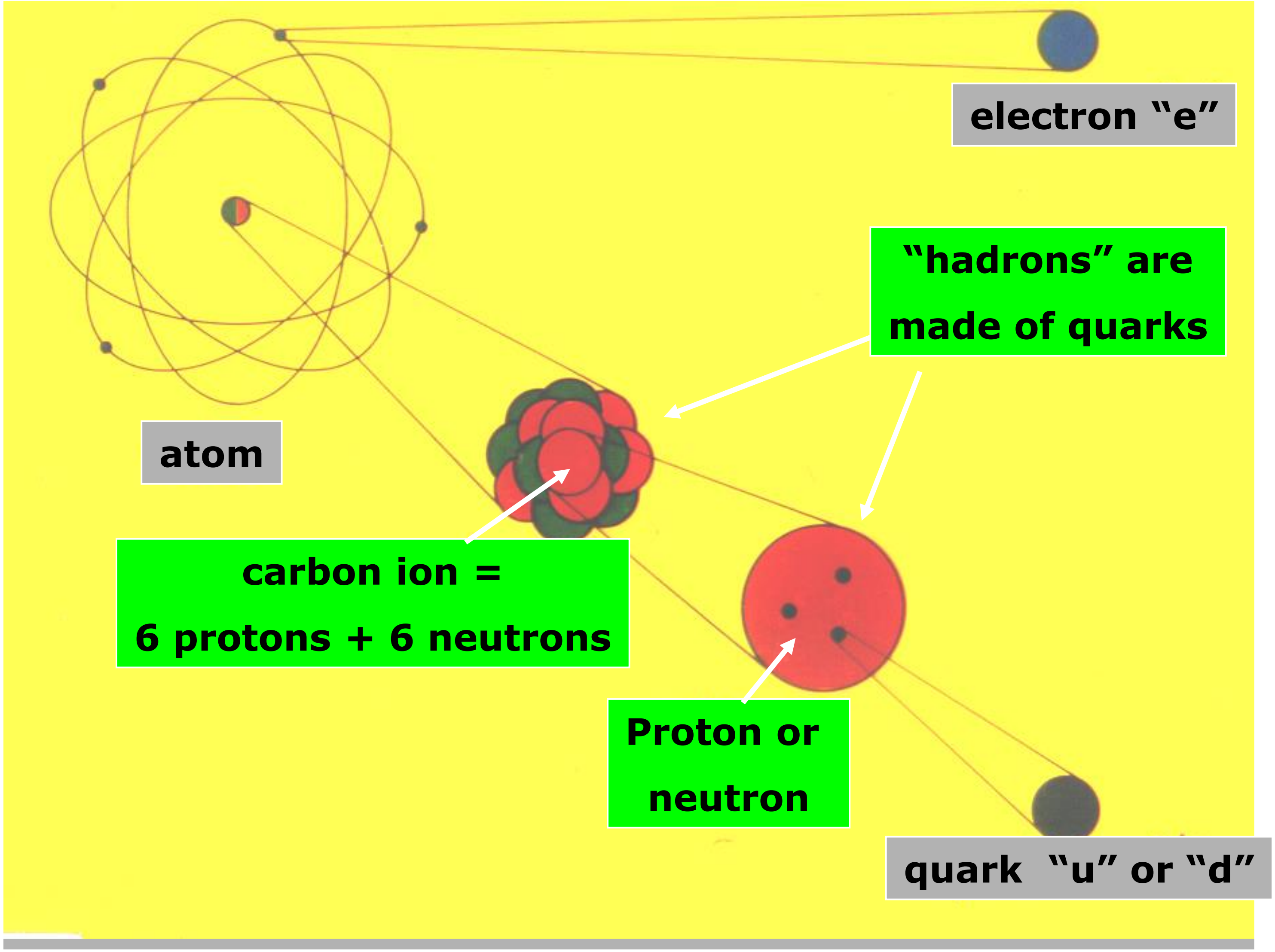
Dedicated sequences for MRI guided radiotherapy treatments



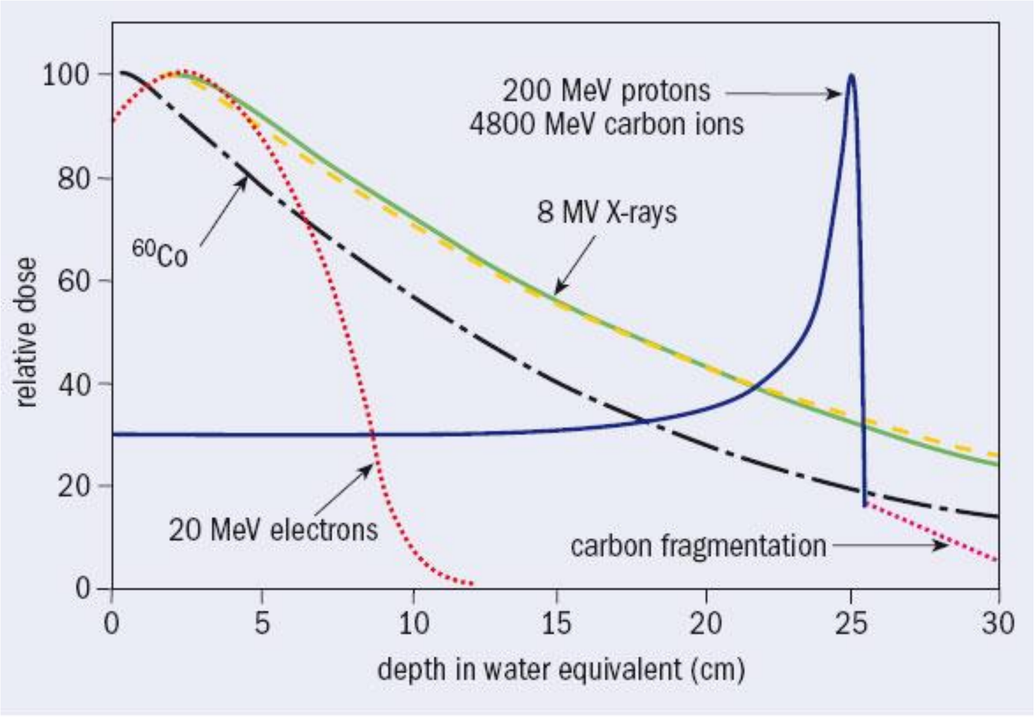
1) 1.5 T MRI
2) 6 MV accelerator
3) Split gradient coil
4) Superconducting coils
5) Low magnetic field toroid

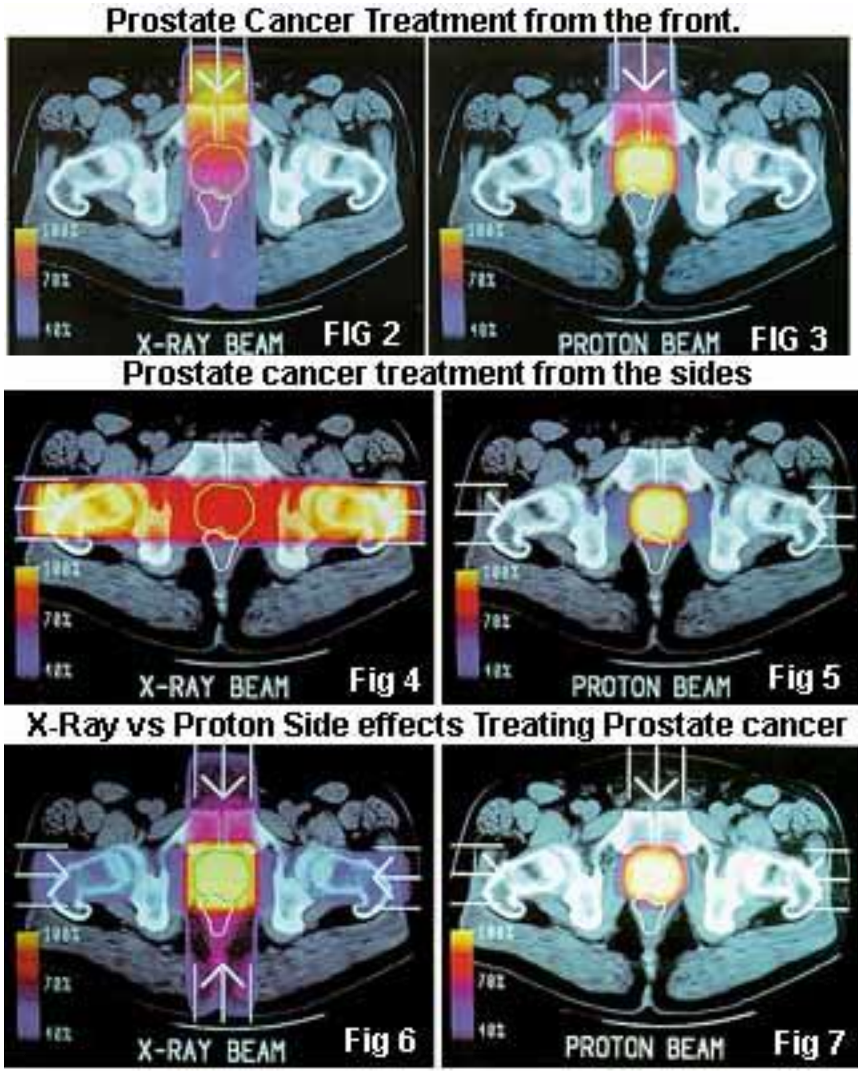
Raaymakers et al, Phys. Med. Biol. **54** (2009) N229–N237

Hadrontherapy: n, p and C-ion beams



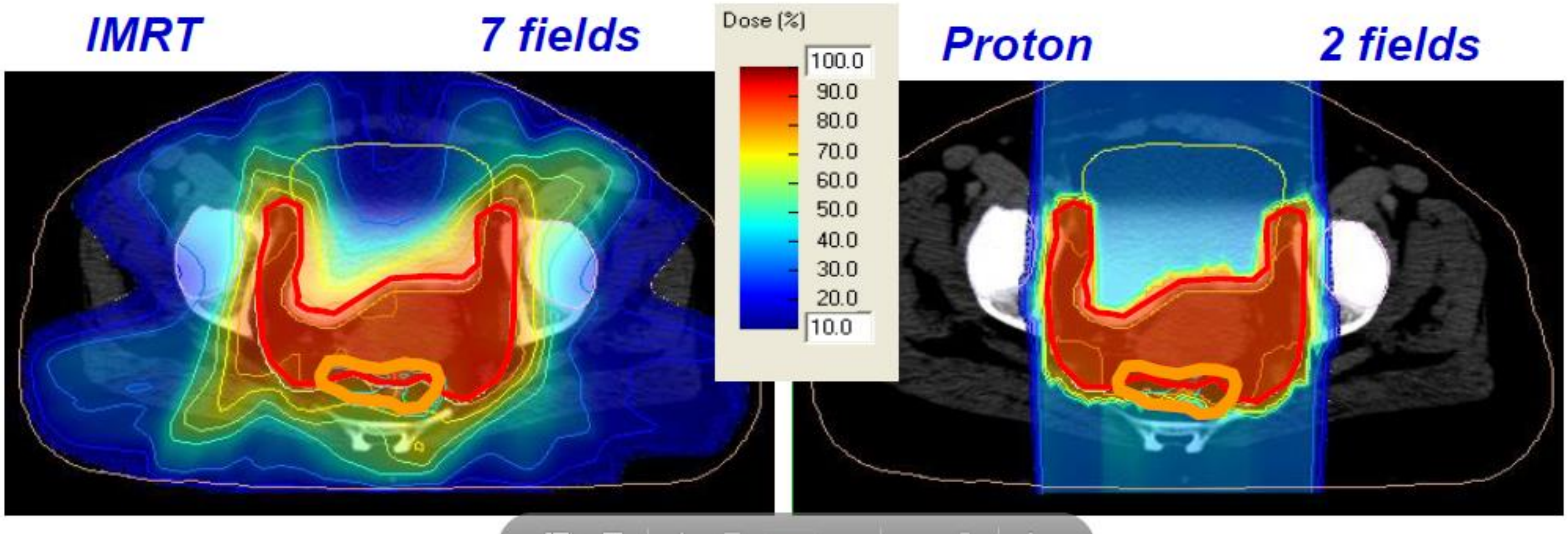
Proton radiation therapy



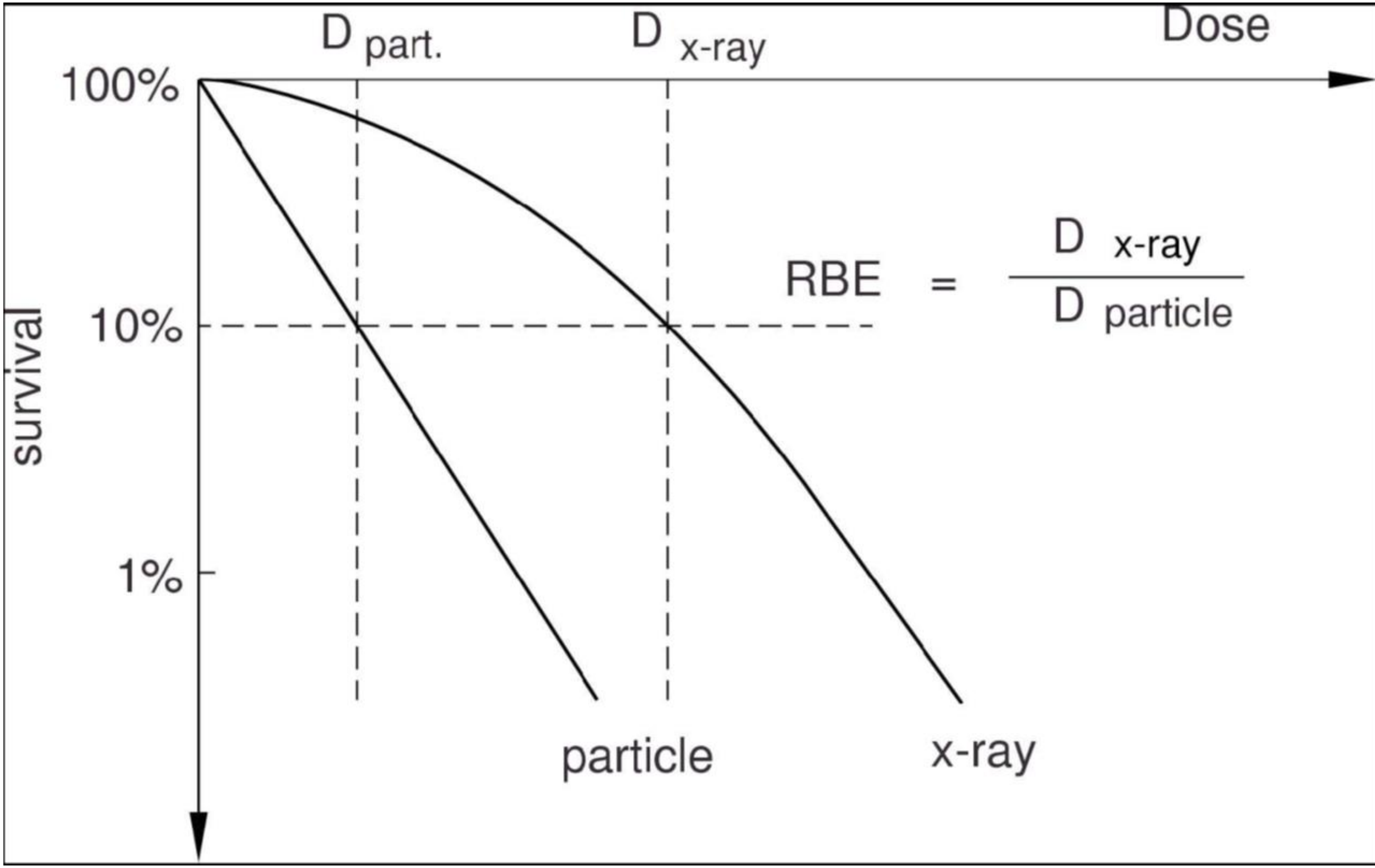


Treatment planning

- *Ion beam therapy is more conformal than photon beam RT*
- *Sharper dose fall off*
- *Range of ions much more influenced by tissue heterogeneities than photon beams with direct impact on TCP and NTCP*
- *Image guidance is necessary for ion beam therapy*



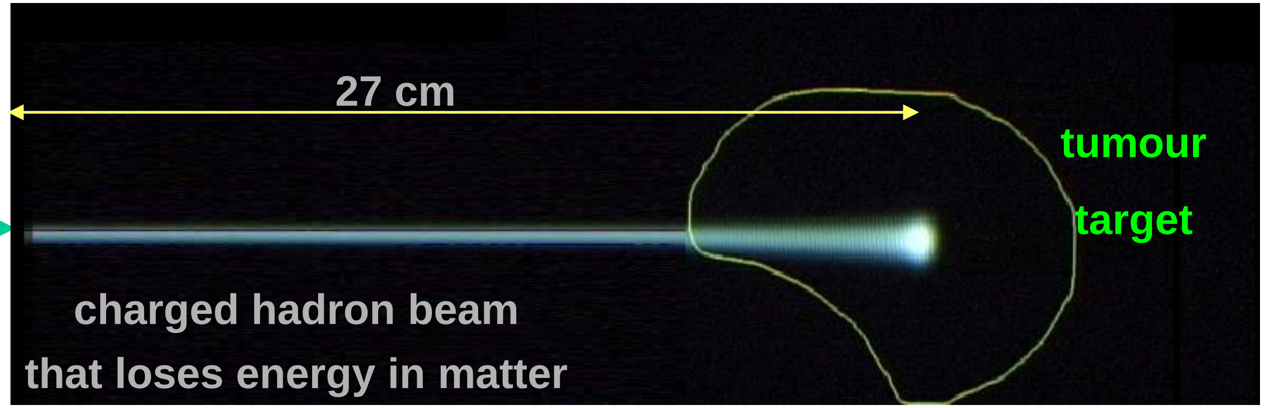
Radiobiological effectiveness (RBE)

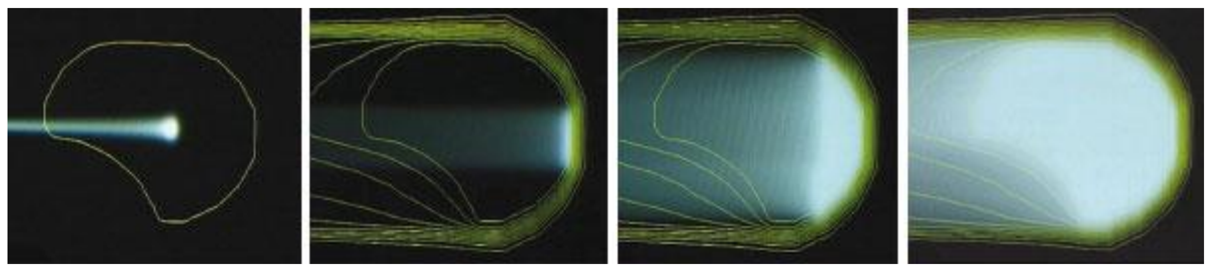


Hadrontherapy

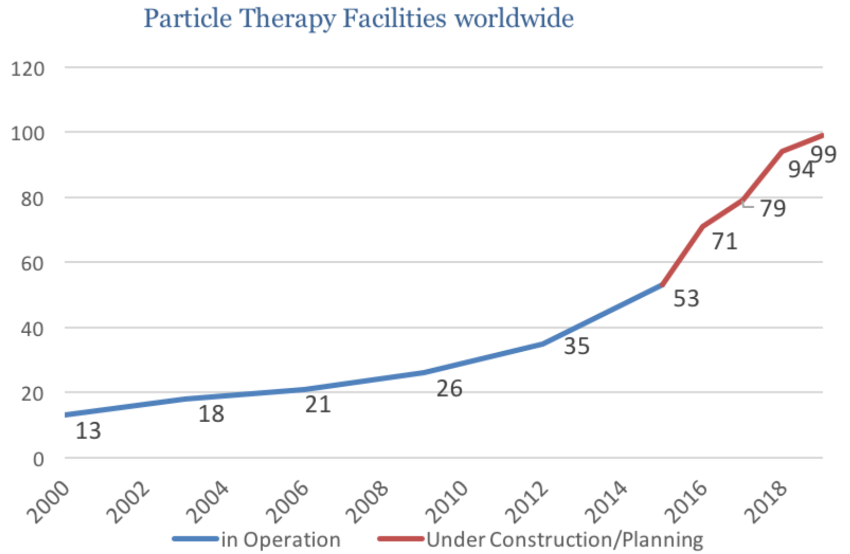
200 MeV protons

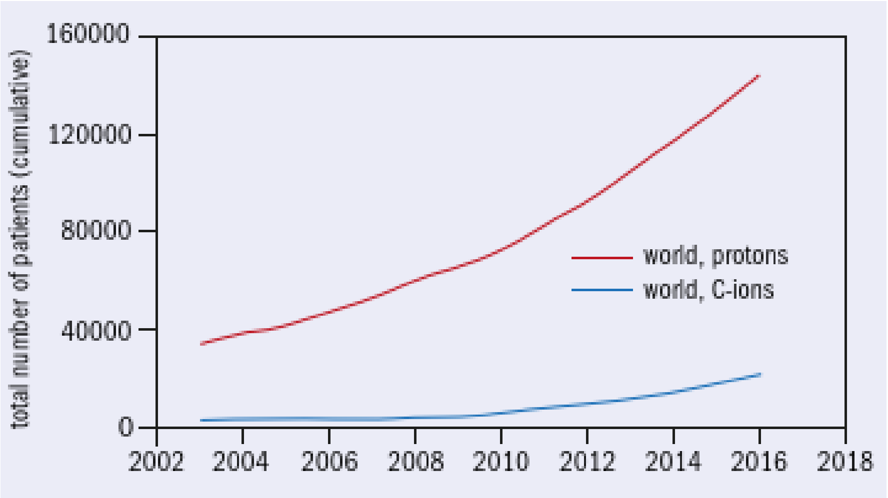
4800 MeV carbon ions

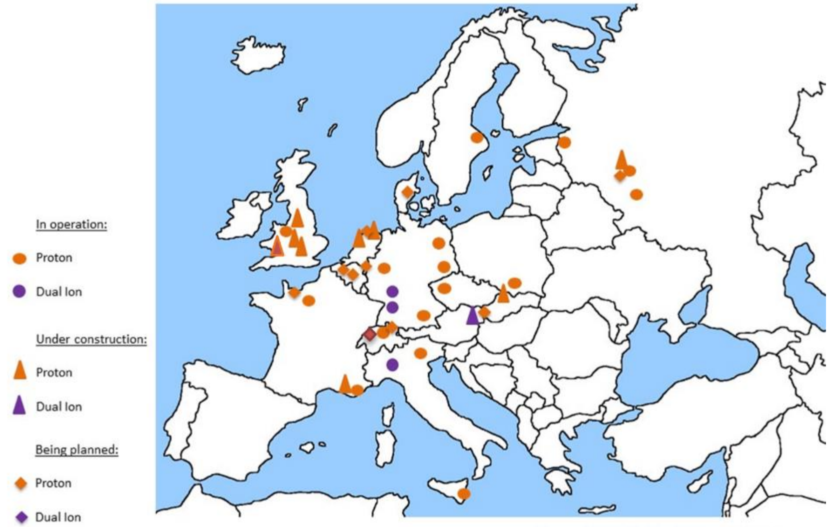




Hadrontherapy in Europe and worldwide





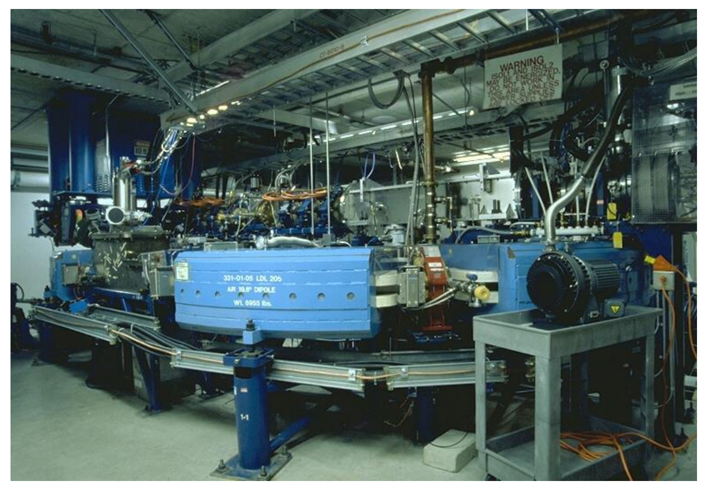


CERN Courier Jan/Feb 2018

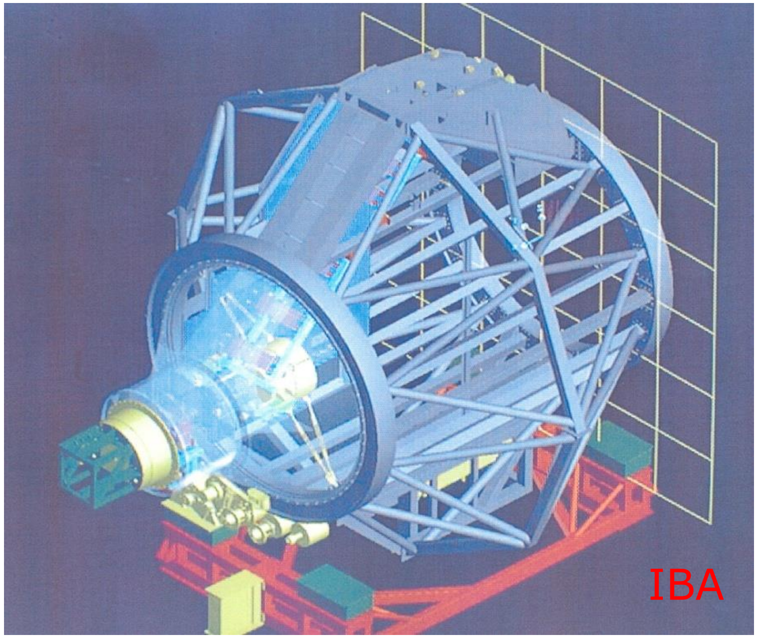
Proton radiation therapy

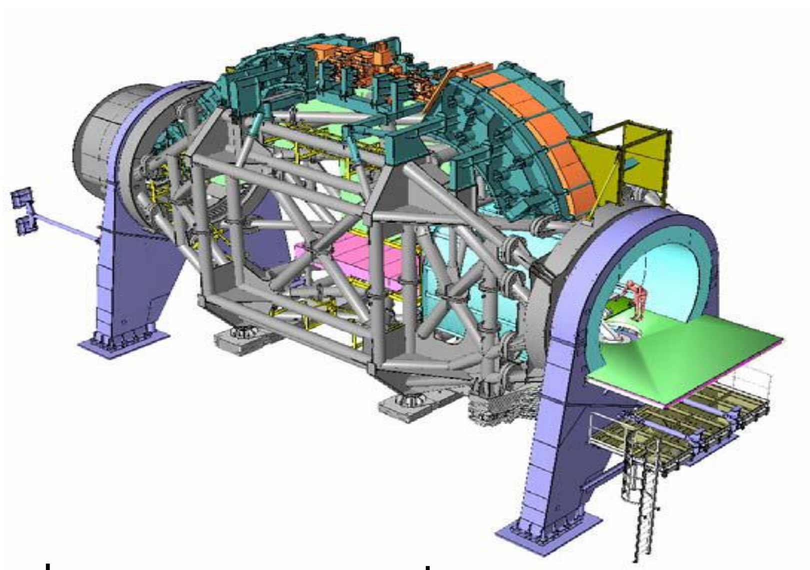
Accel-Varian

Loma Linda
(built by FNAL)



Isocentric gantry

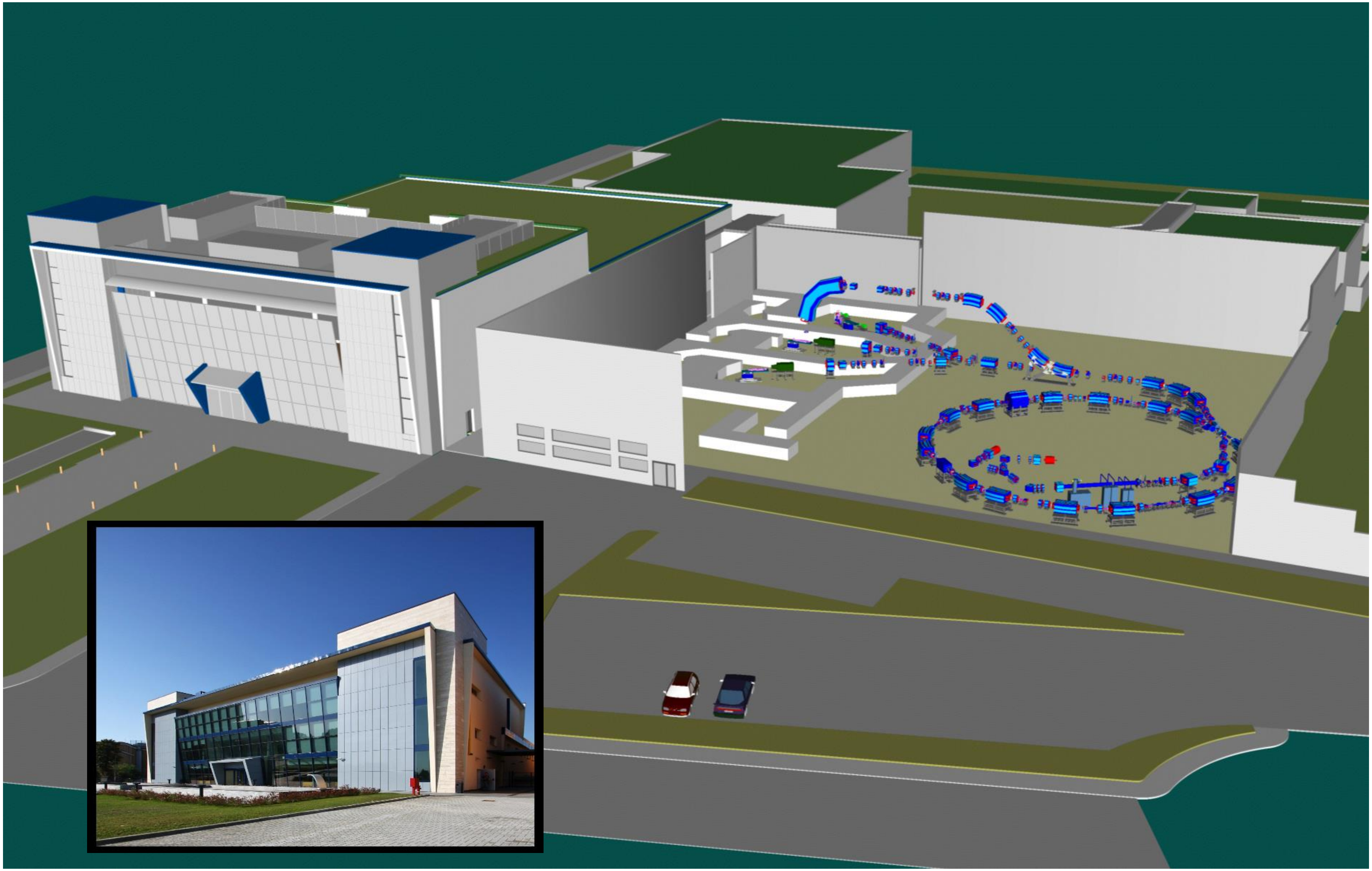




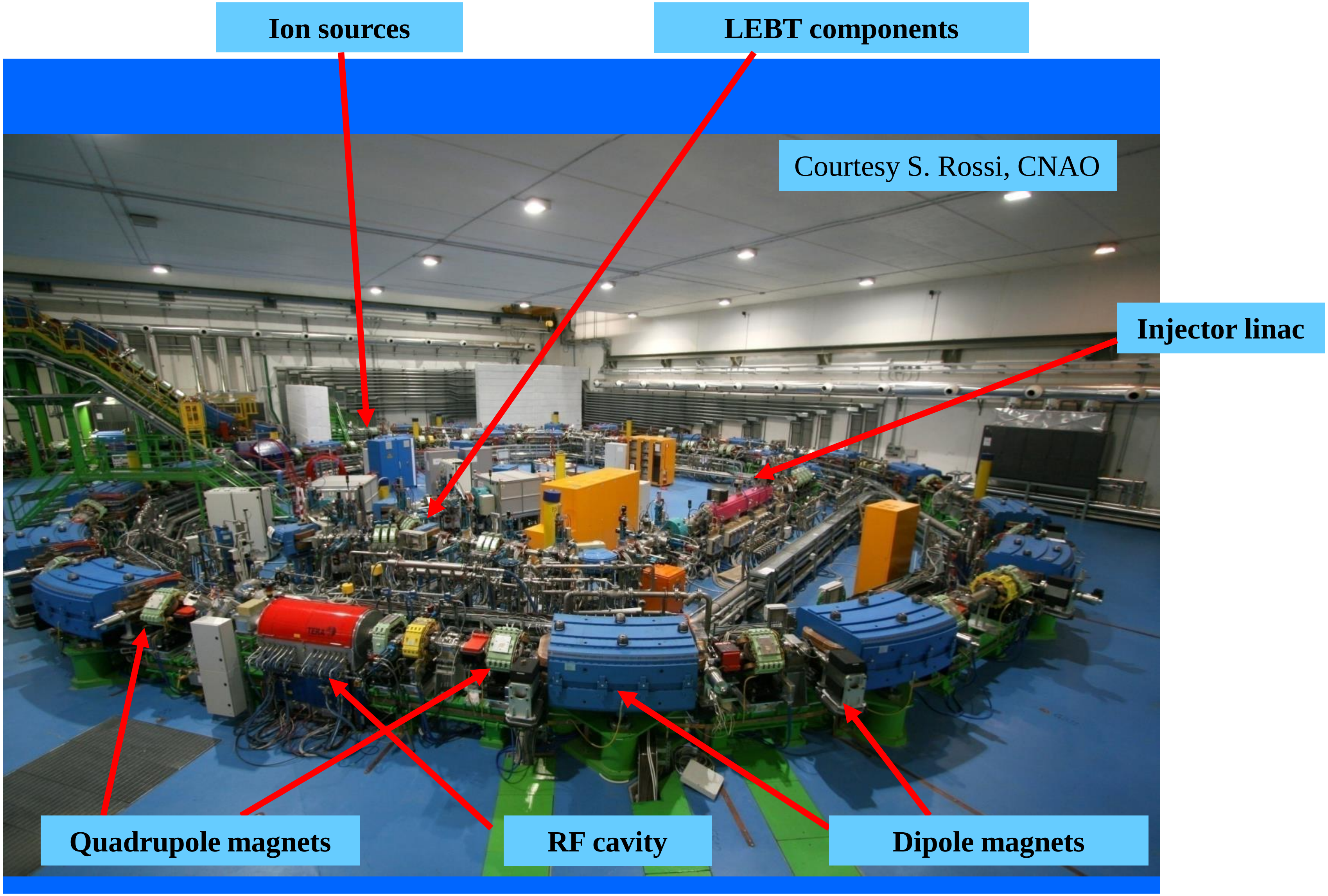
A gantry is a massive structure that allows directing the beam to the tumour from any direction. It carries:

- the final section of the beam line
- the beam spreading 'nozzle'
- the proton 'snout' which carries the aperture and range compensator

National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy

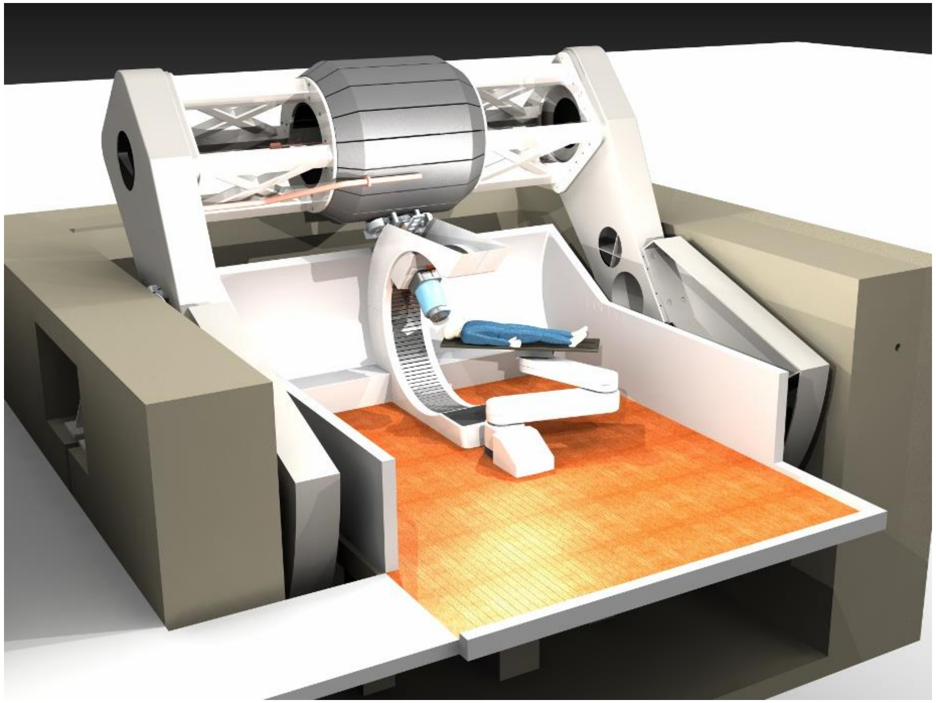


National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy



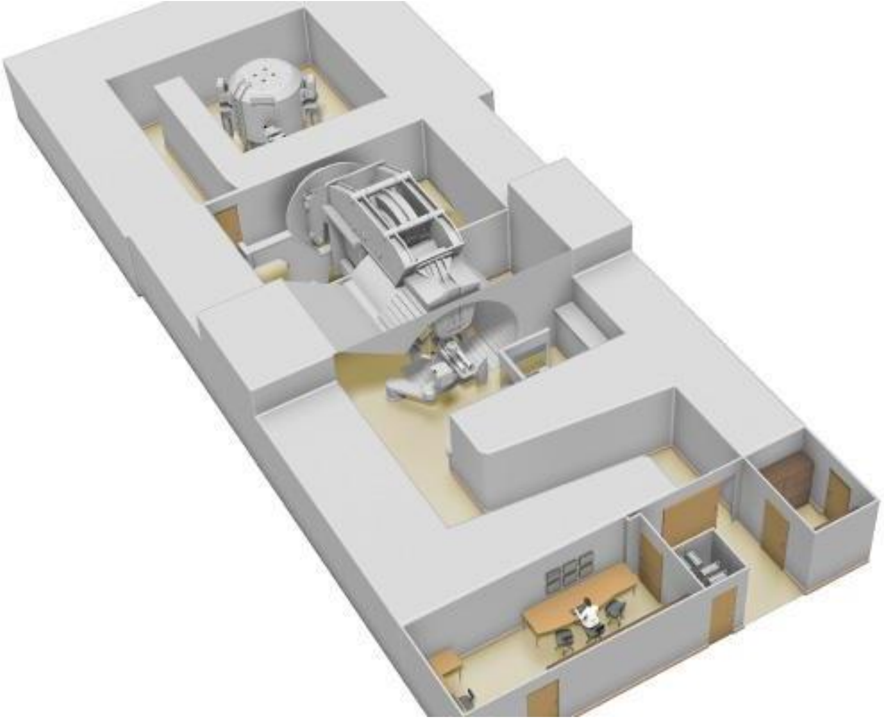
National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy

The future of hadrontherapy: single room facilities ?



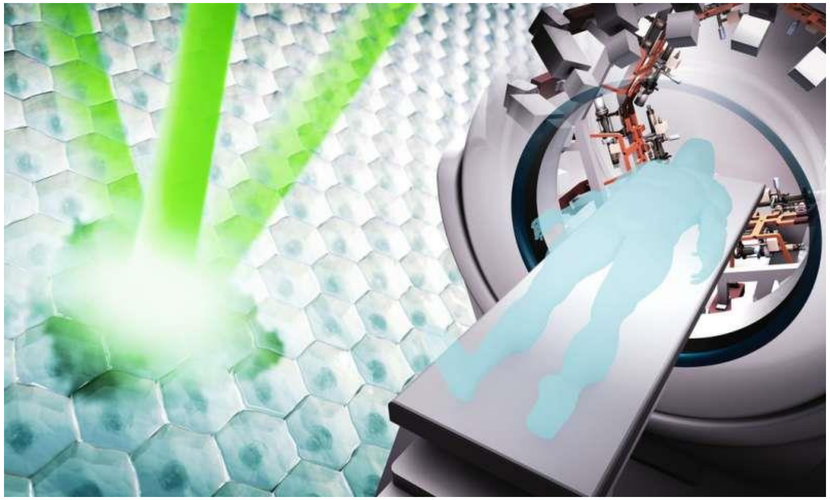
Mevion Medical Systems

IBA Proteus Nano

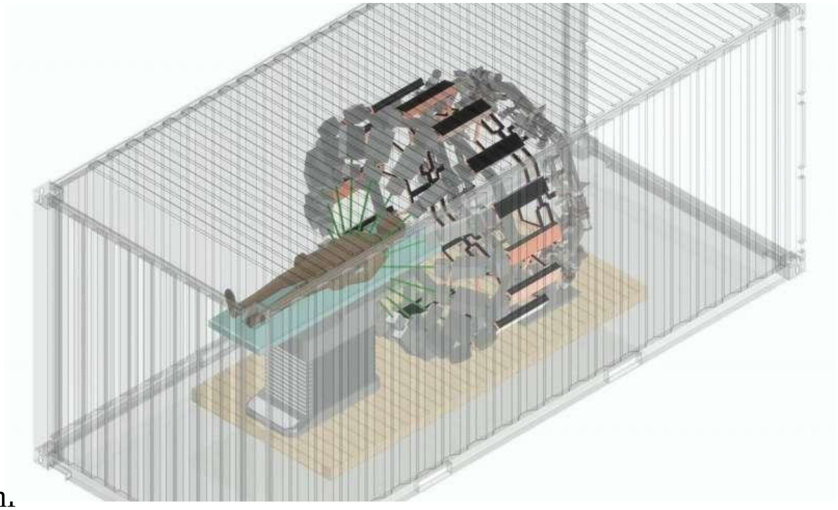


A look into the future: flash irradiation

- New accelerator-based technology being developed by the Department of Energy's SLAC National Accelerator Laboratory and Stanford University



- Irradiation time reduced from minutes to under a second
- Tumour position "frozen"
- Technology for X-rays and protons
- Need accelerator structures that are hundreds of times more powerful than today's technology



- PHASER: flash delivery system for X-rays
- PHASER version for protons

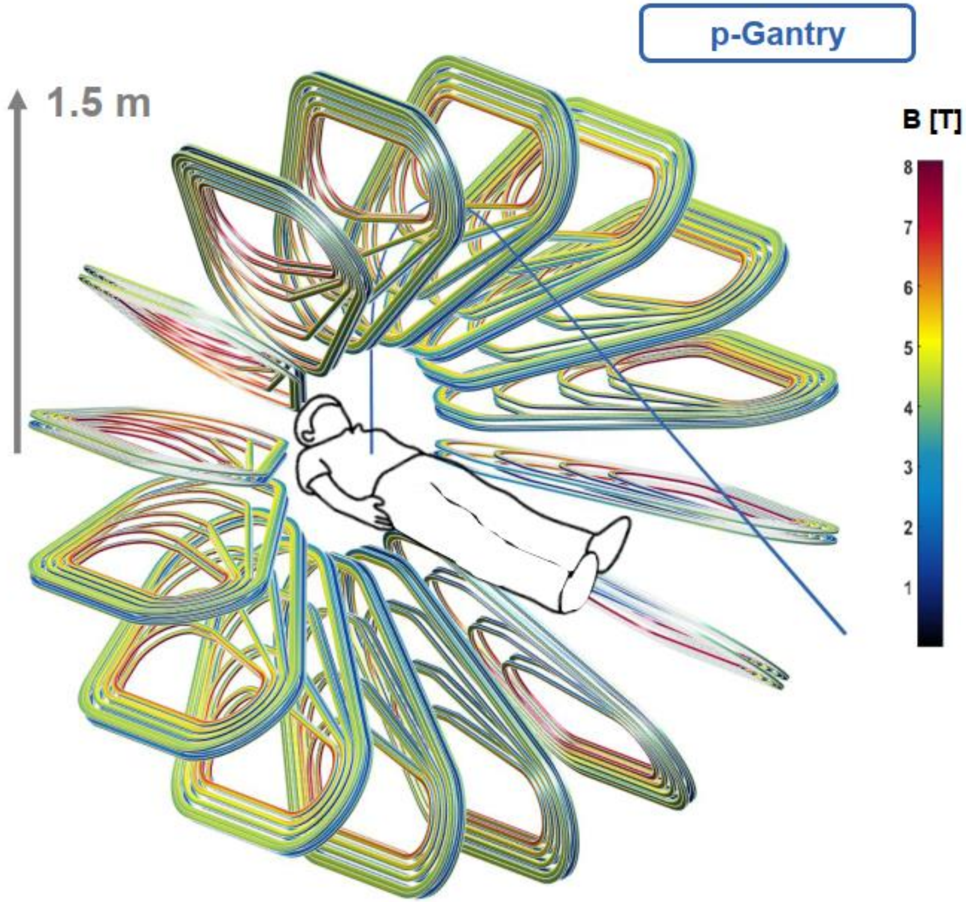
- In mice healthy cells suffer less damage when radiation dose is applied very quickly, with same tumour-killing effect

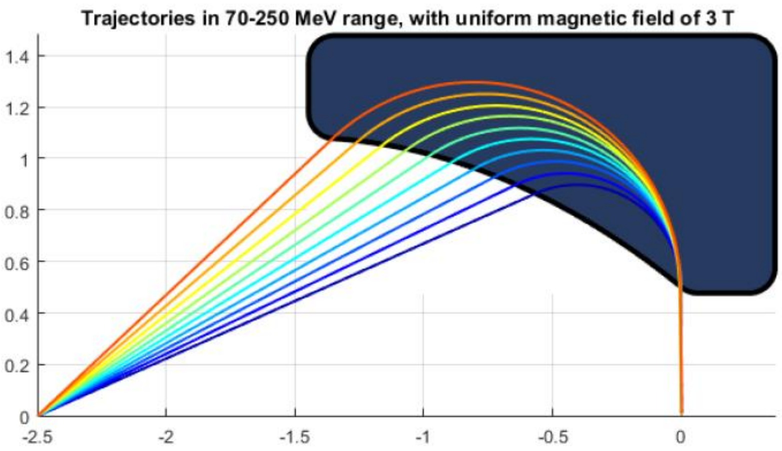
- Make radiation therapy more accessible for patients worldwide

https://phys.org/news/2018-11-future-cancer-zapping-tumors.htm.

A look into the future: CERN's compact gantry

Gantry + Toroid = GaToroid → *GaTo*





L. Bottura, E. Felcini et al, TE-MSC

Acknowledgements

I am indebted to Prof. Ugo Amaldi (TERA Foundation and University of Milano Bicocca, Italy) and Prof. Maria Carla Gilardi (University of Milano Bicocca, Italy) for providing me with some of the slides that I have shown you today.