Medical Applications of Modern Physics

Marco Silari
CERN, Geneva, Switzerland
marco.silari@cern.ch

Medical Physics

=

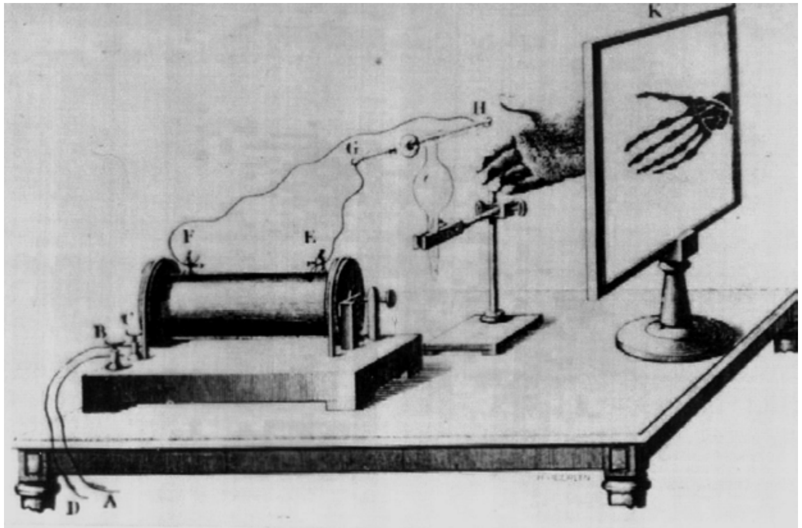
A branch of applied physics concerning the application of physics to medicine

or, in other words

The application of physics techniques to the human health

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

The beginnings of modern physics and of medical physics



1895

Discovery of X rays

Wilhelm C. Röntgen

1897

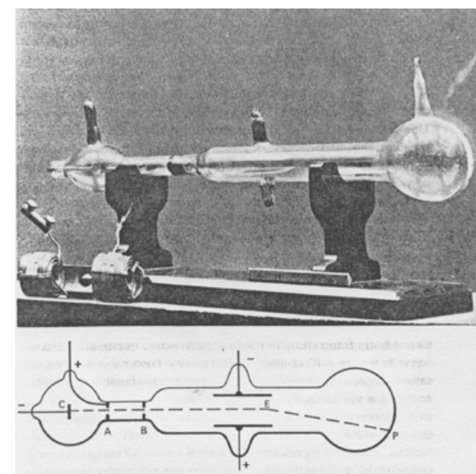
First treatment of tissue with X rays

Leopold Freund

J.J. Thompson

1897

"Discovery" of the electron



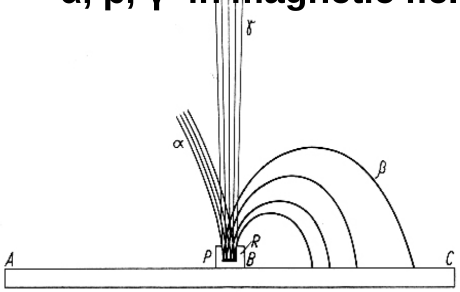
Henri Becquerel (1852-1908)

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)**

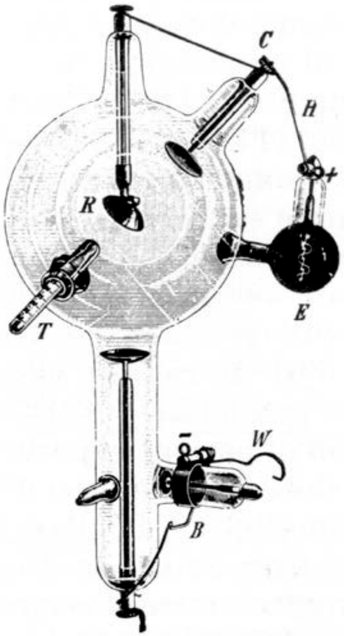
First practical application of a radioisotope

- 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

1920's – Industrially manufactured x-ray apparatus

Röhren fremden Fabrikates.

„Monopol"-Oberflächen-Therapie-Röntgenröhre mit Vorrichtung zur therapeutischen Dosierung der Röntgenstrahlen nach Prof. Dr. A. Köhler, Wiesbaden.

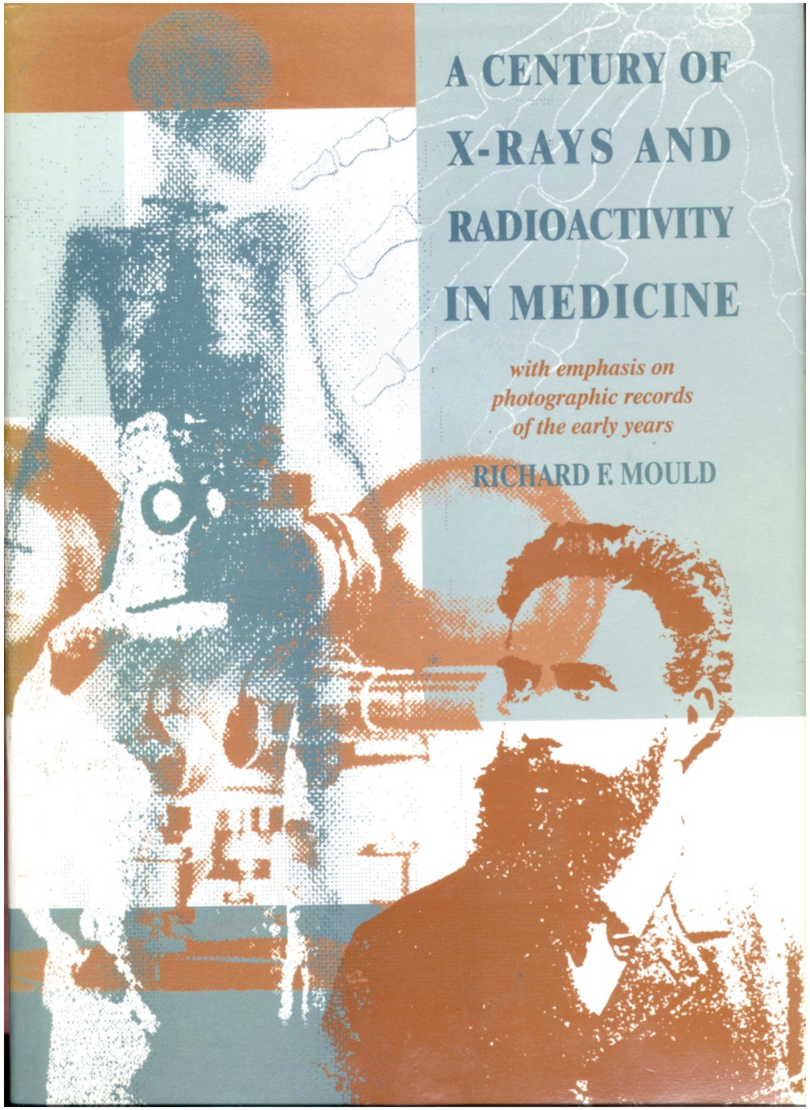


MONOPOL

Schutzmarke.

Diese Röhre ist besonders für die Röntgen-Oberflächentherapie bestimmt. Sie gestattet eine praktisch genügend genaue Verabreichung der für eine Sitzung erforderlichen Strahlenmenge durch bequeme direkte Ablesung an einer Thermometerskala.

[22.5] Monopol X-ray tubes were available in 1907 and some were modified to Kohler's specification by 1914. (Courtesy: Siemens AG, Erlangen.)

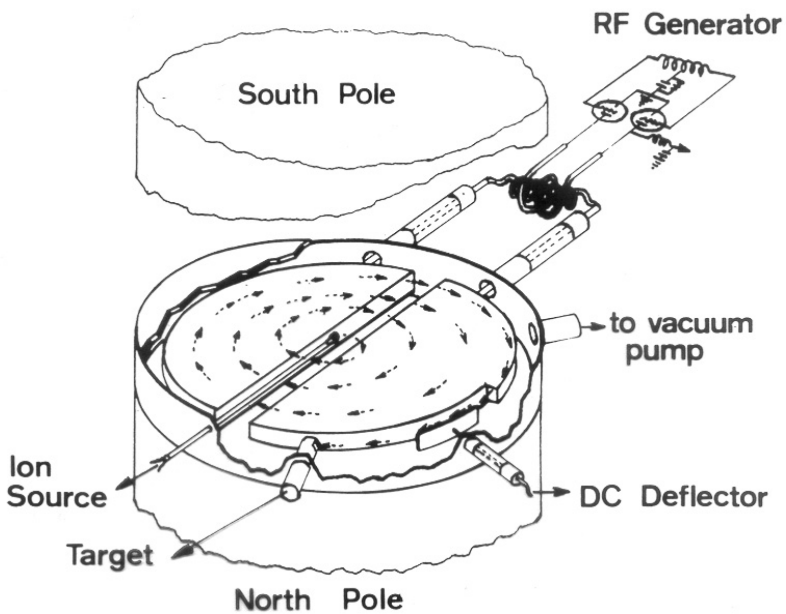


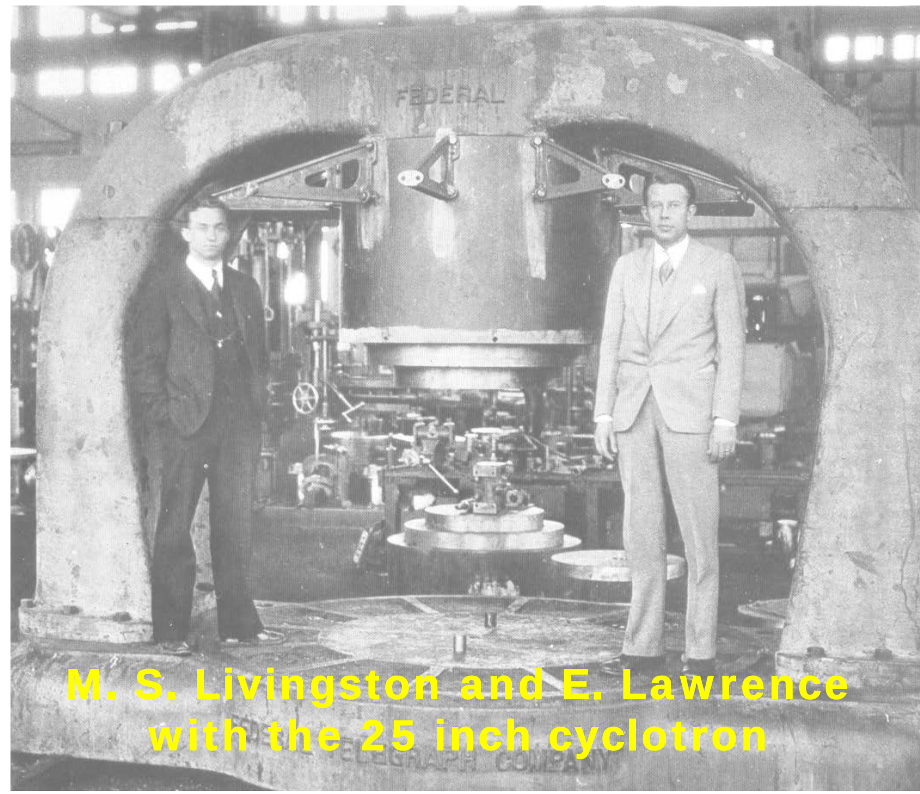
Tools for (medical) physics: the cyclotron

1930

Invention of the cyclotron

Ernest Lawrence





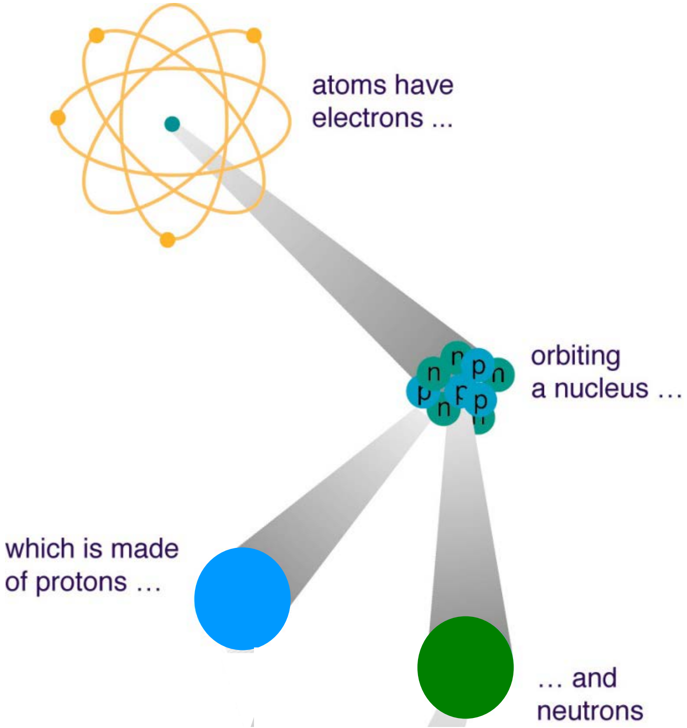
M. S. Livingston and E. Lawrence with the 25 inch cyclotron

James Chadwick

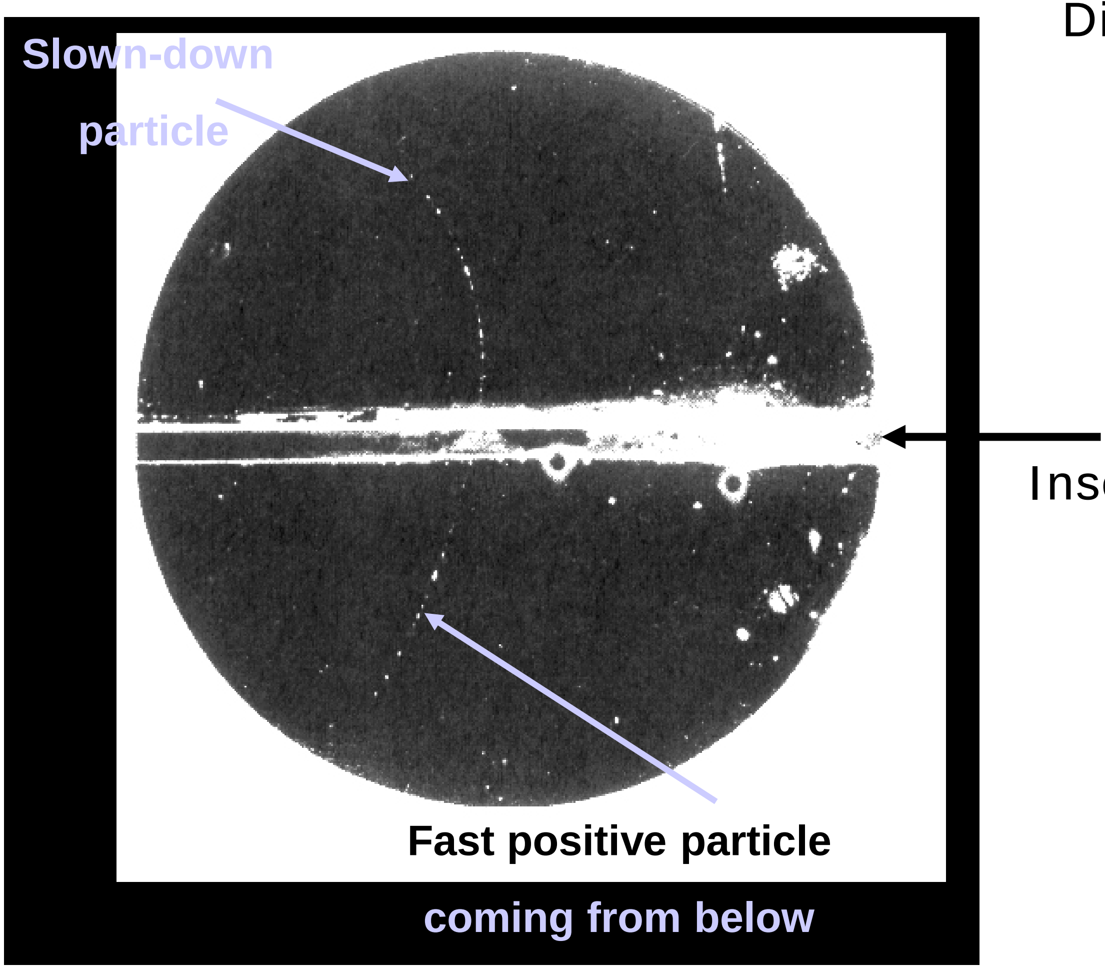
(1891 – 1974)

1932

Discovery of the neutron



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



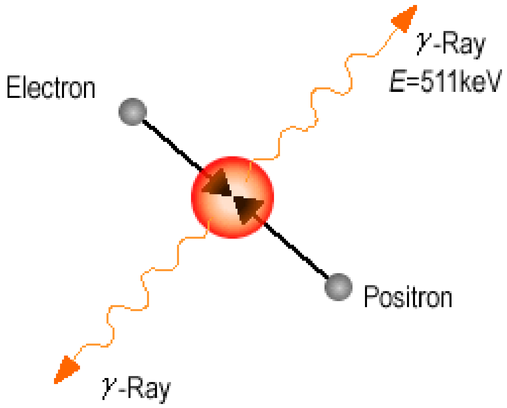
1932

Discovery of the positron

C. D. Anderson

Layer of lead

Inserted in a cloud chamber



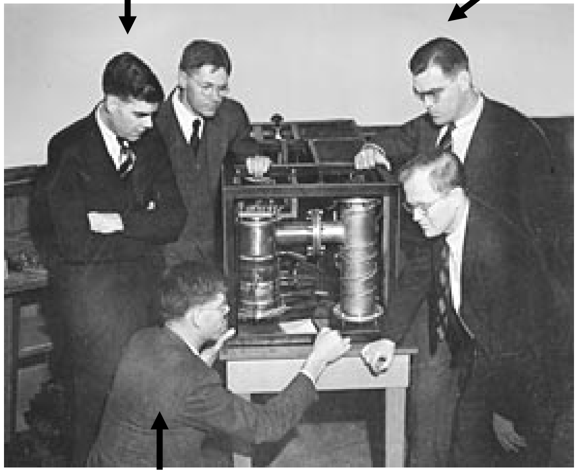
Historical development of radioisotopes for medicine

- 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

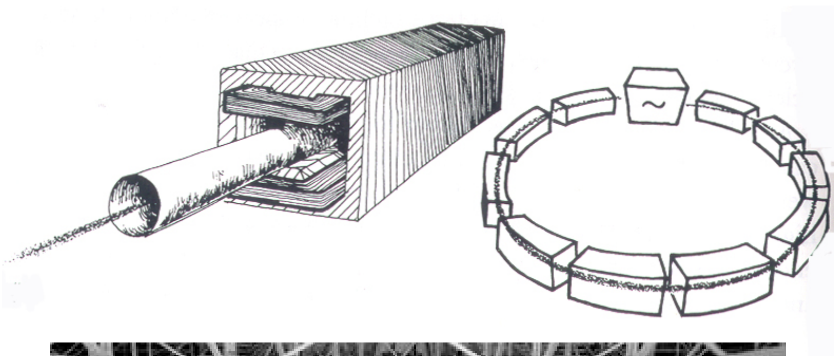
1950's: development of compact linear electron accelerators by various companies

Tools for (medical) physics: the synchrotron

1945: E. McMillan and V.J.Veksler

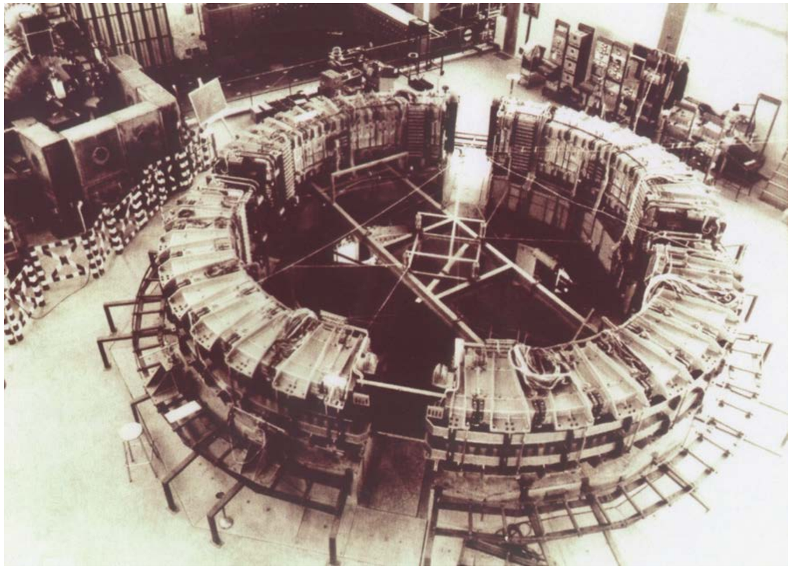
discover the

principle of phase stability



1 GeV electron synchrotron

Frascati - INFN - 1959

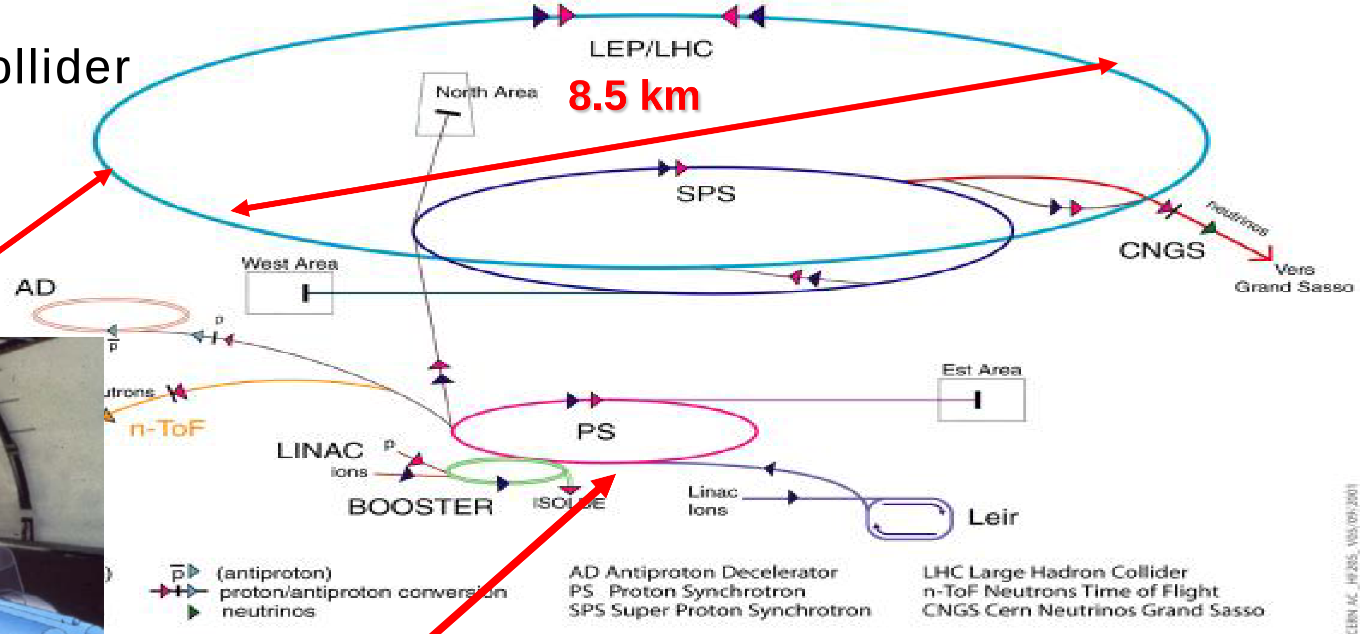


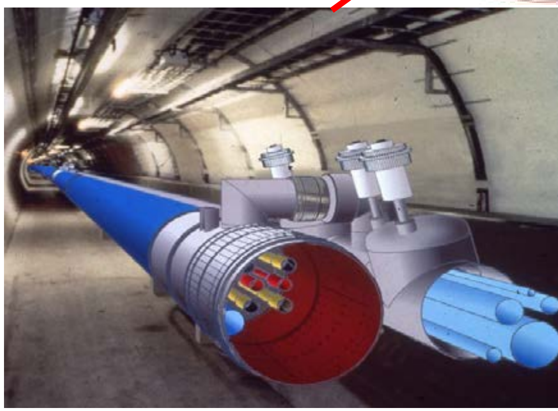
6 GeV proton synchrotron

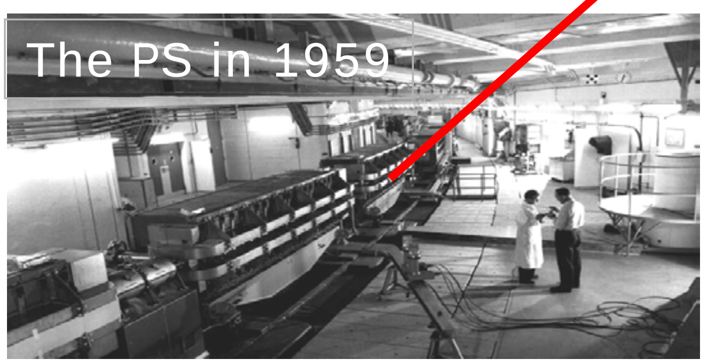
Bevatron - Berkeley - 1954

CERN accelerators

Large Hadron Collider
7 TeV + 7 TeV
Start in 2008

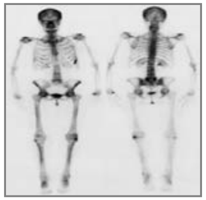




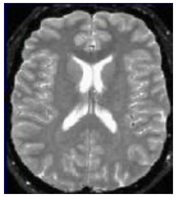
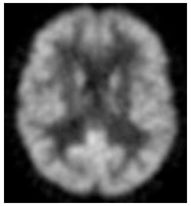


In 1952 the “strong-focusing” method invented at BNL (USA) was chosen for the CERN PS

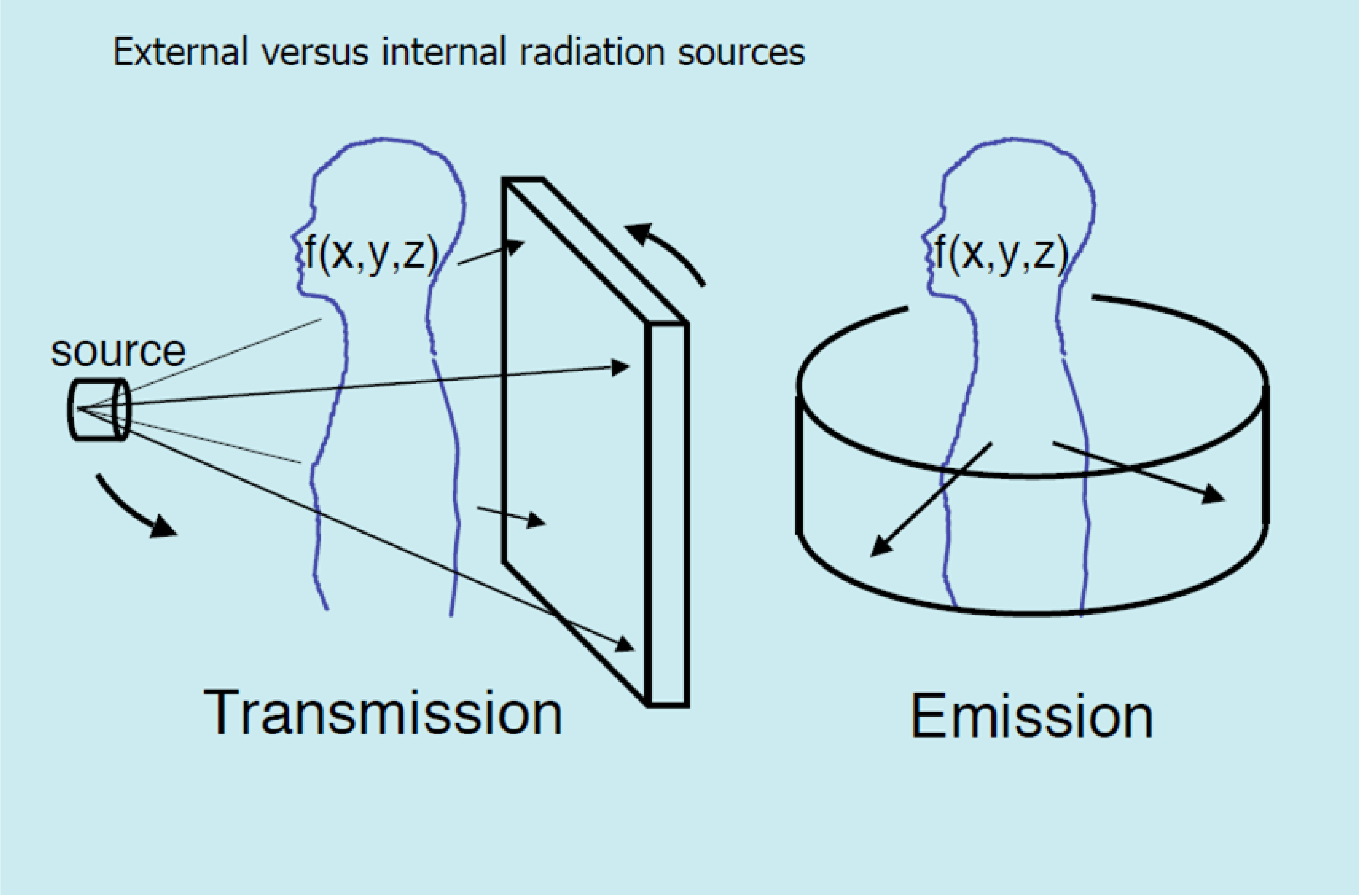
Medical imaging

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	

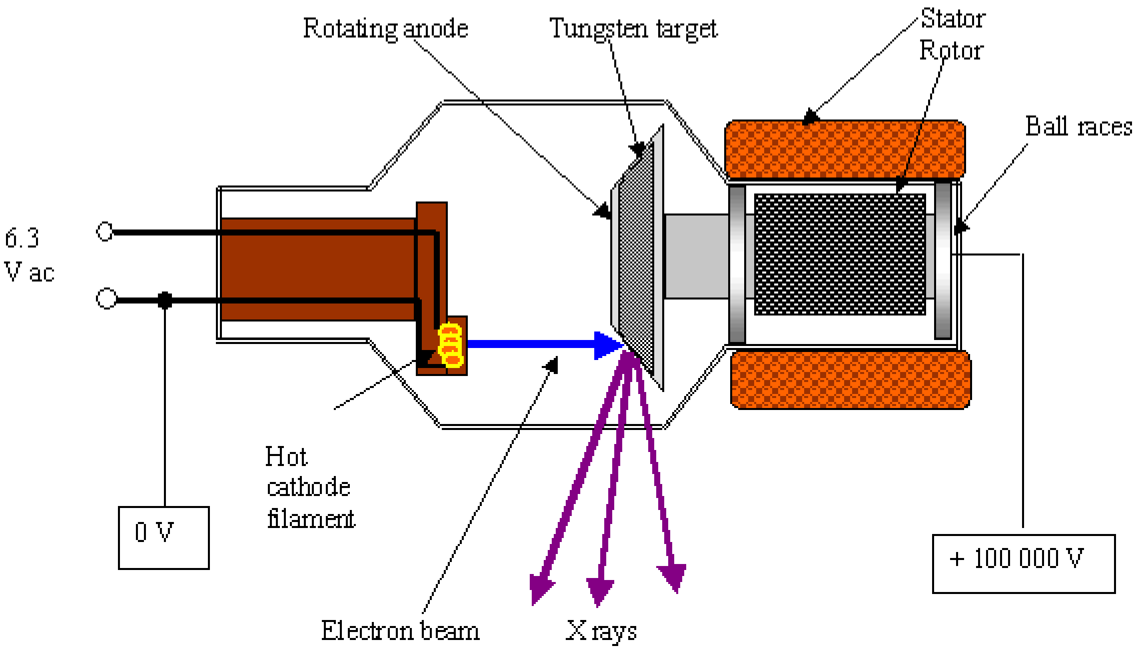
Medical imaging

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



Medical imaging: x-ray generator and image intensifier



X-ray tube

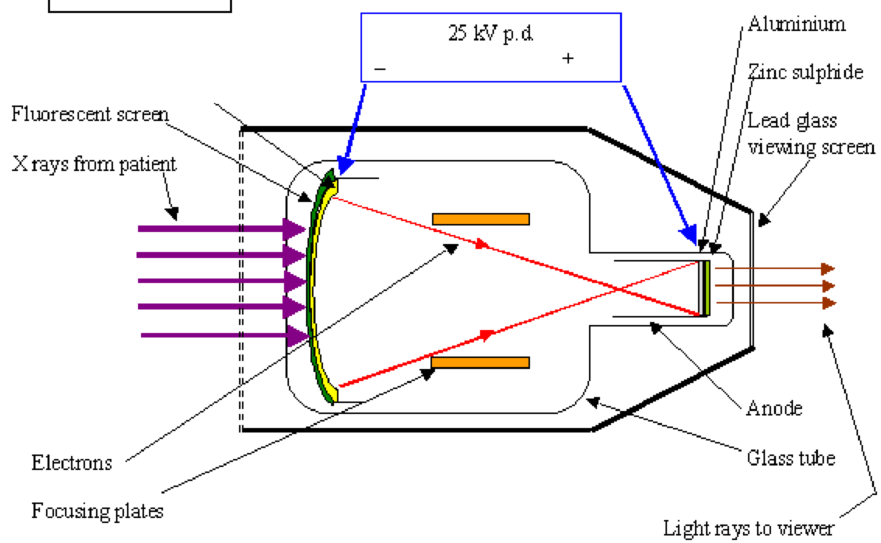
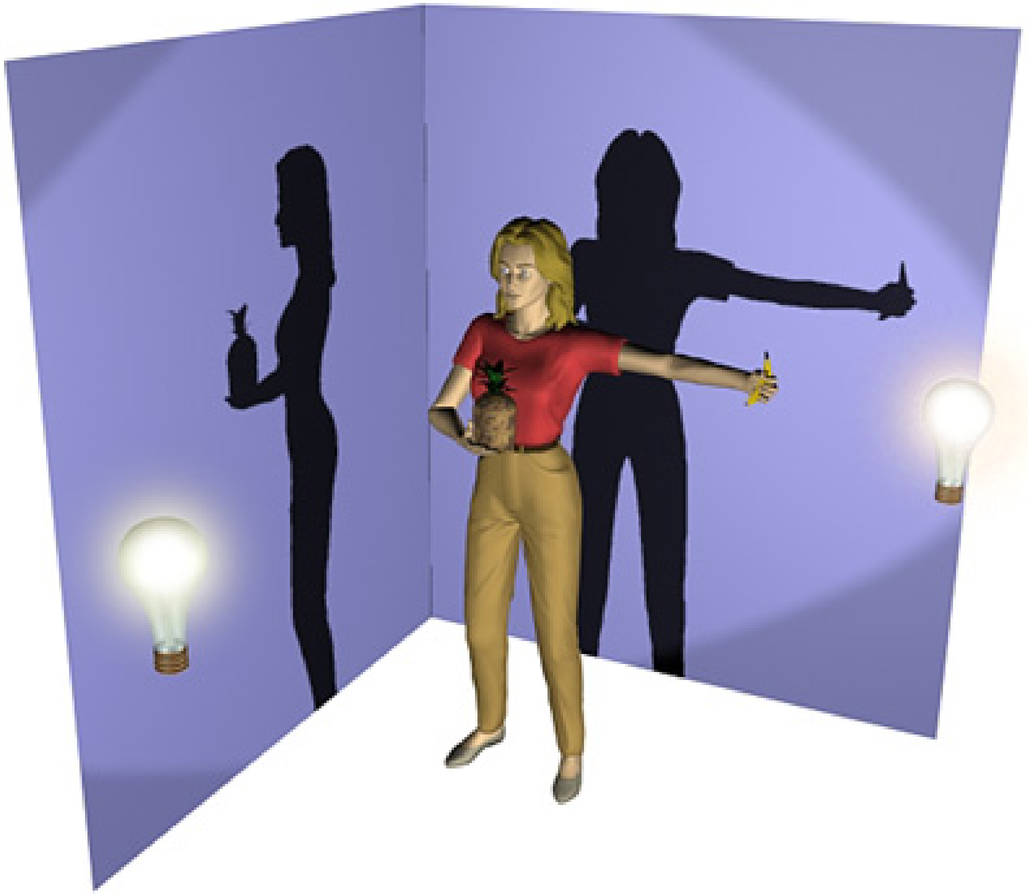


Image intensifier

X-ray image versus CT scan

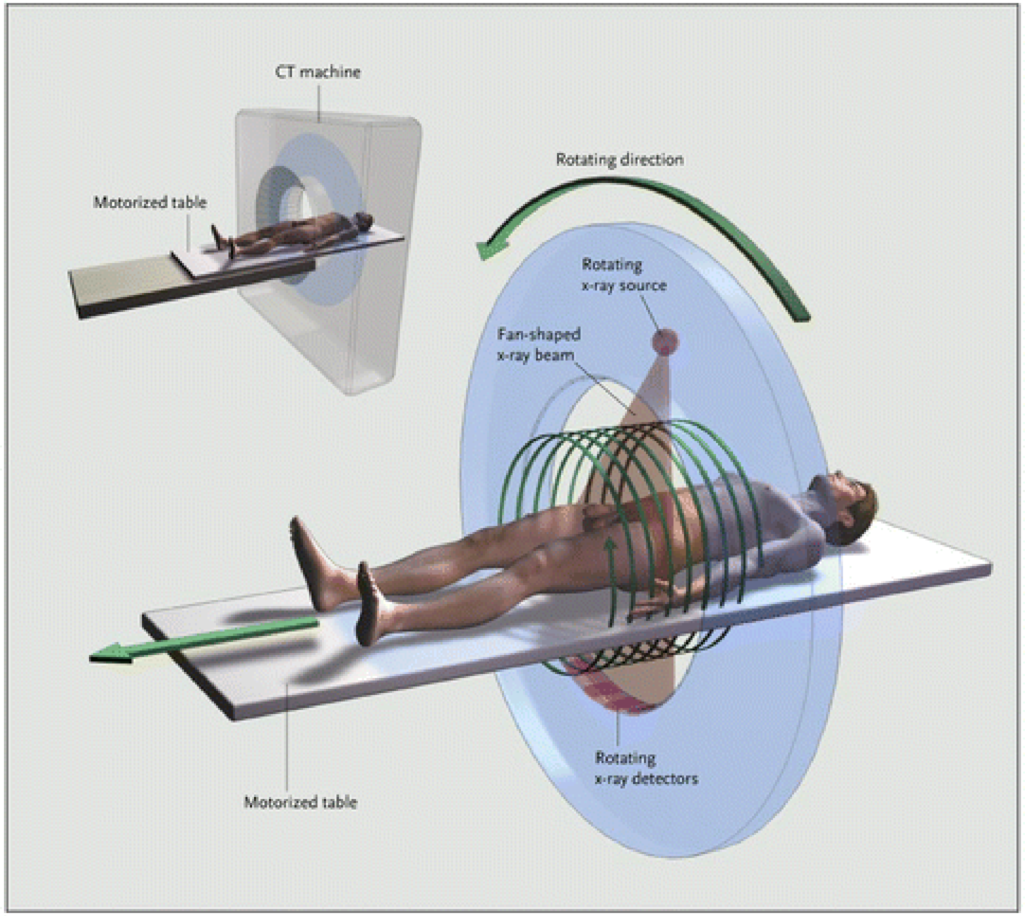
A conventional X-ray image is basically a shadow: you shine a “light” on one side of the body, and a piece of film on the other side registers the silhouette of the bones (to be more precise, organs and tissues of different densities show up differently on the radiographic film).



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

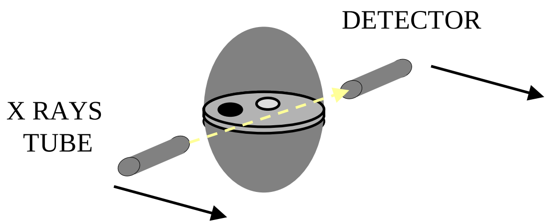
Look at the wall, not at the person. If there's a lamp in front of the person, you see the silhouette holding the banana, but not the pineapple as the shadow of the torso blocks the pineapple. If the lamp is to the left, you see the outline of the pineapple, but not the banana.

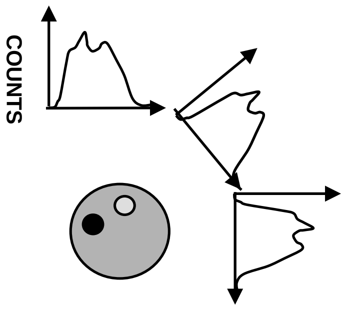
Computed tomography

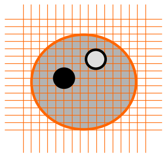


- The X-rays source rotates around the longitudinal axis of the body: it moves 360° around the patient, scanning from hundreds of different angles
- Opposite to the x-ray source, a series of detectors measure the radiation emerging from the body
- Each rotation scans a different body slice
- The couch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

X-ray computerized tomography (CT)



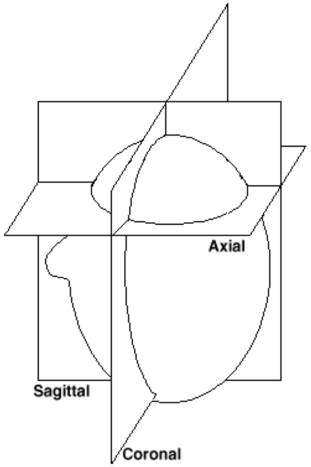


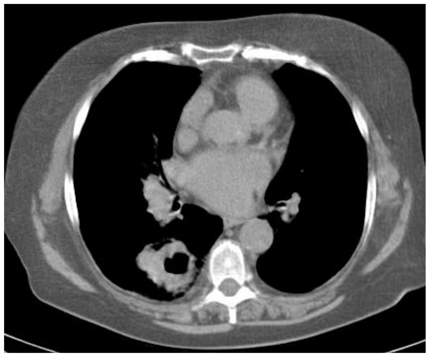


A – LINEAR SAMPLING

B – ANGULAR SAMPLING

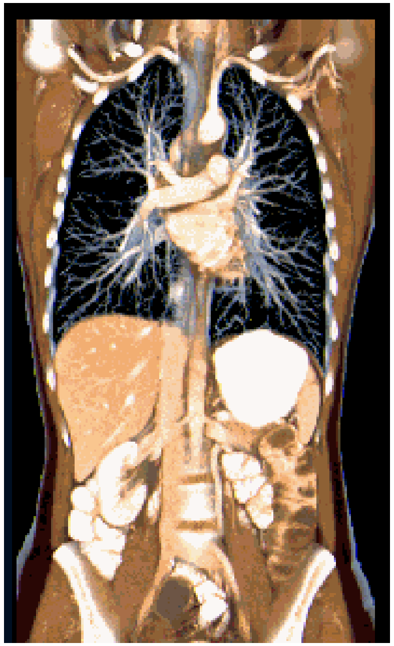
C - RECONSTRUCTION

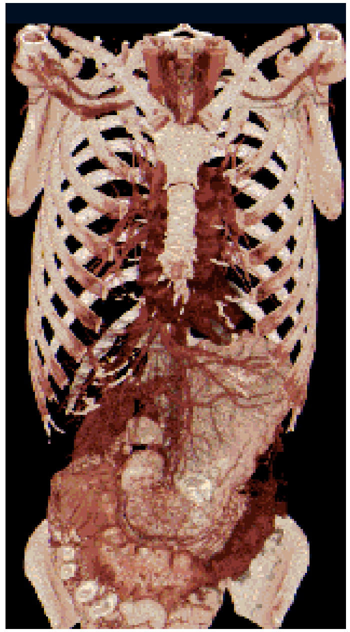




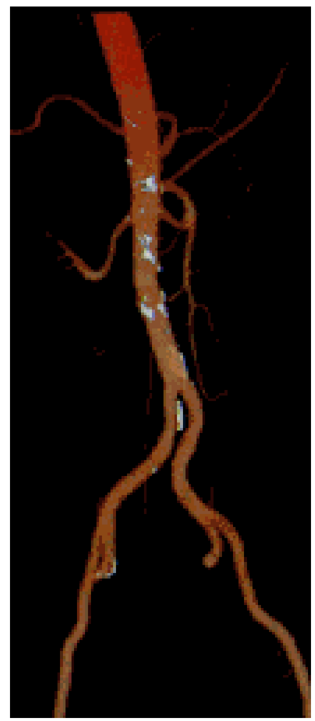
X RAYS
COMPUTERIZED TOMOGRAPHY

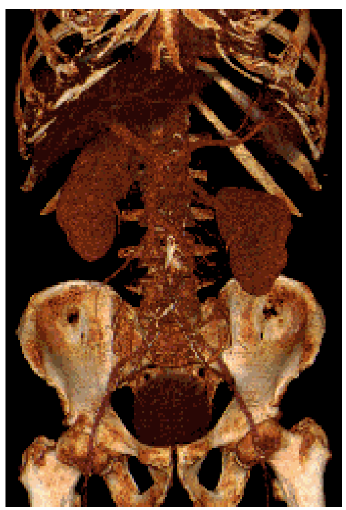
Volumetric CT

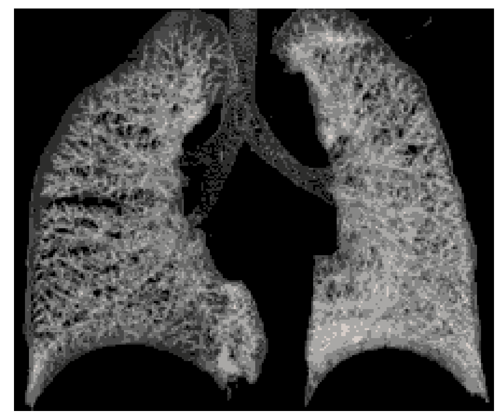




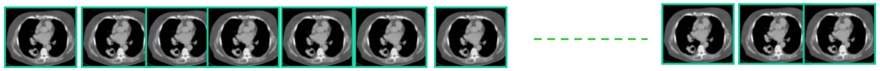
< 0.4 sec/rotation
Organ in a sec (17 cm/sec)
Whole body < 10 sec



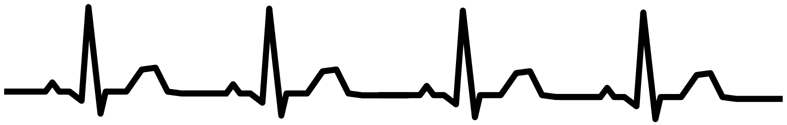




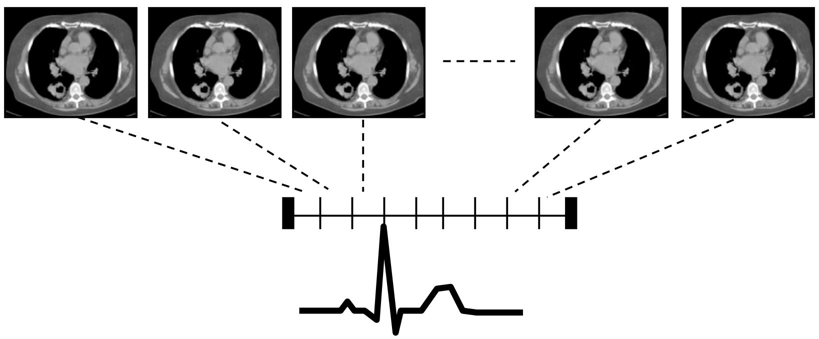
Cardiac CT



DYNAMIC CT ACQUISITION

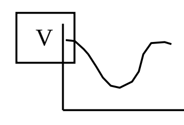


ECG

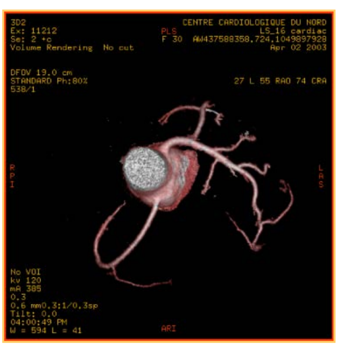


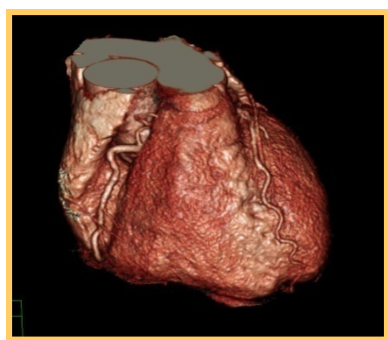
PHASES OF A CARDIAC CYCLE

- 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

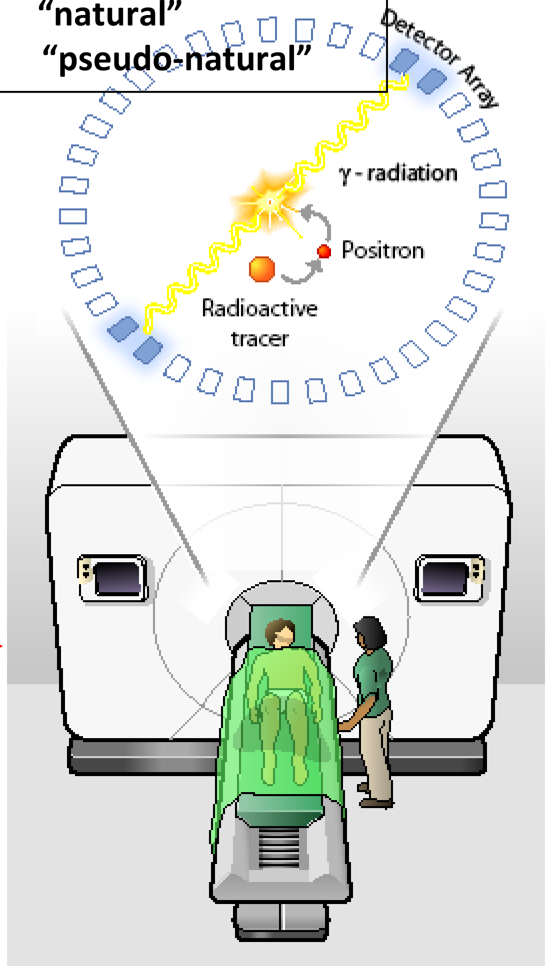
Positron Emission Tomography (PET)

Cyclotron

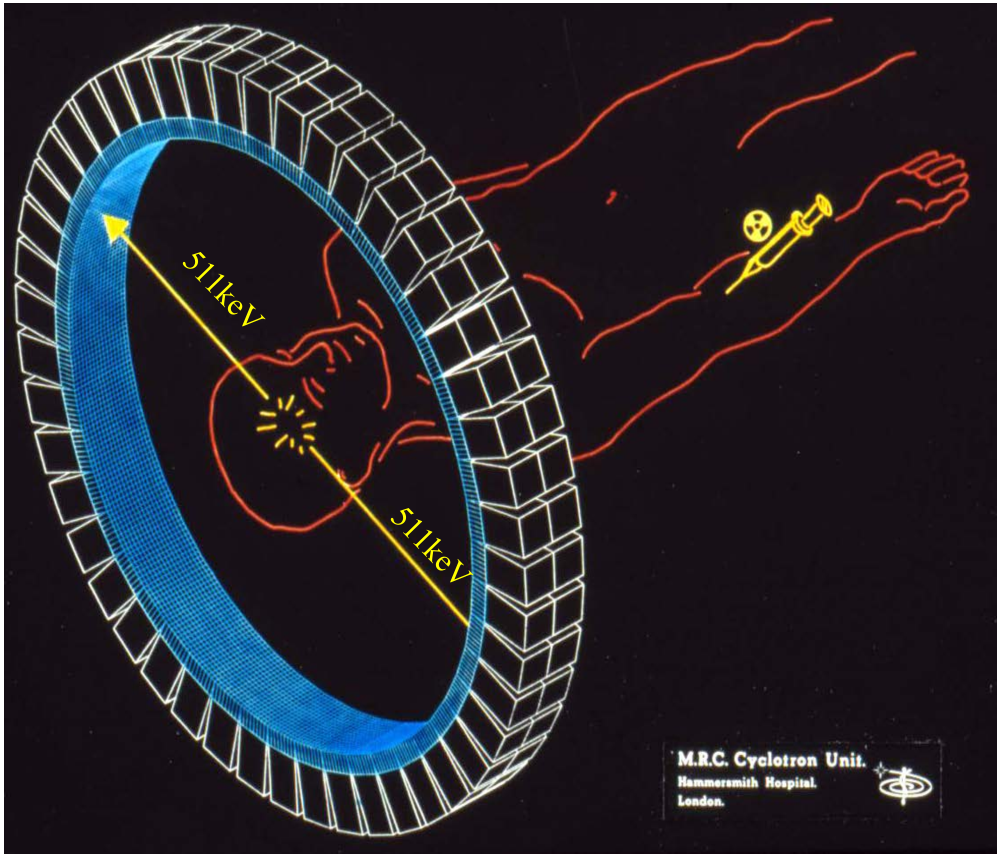
ISOTOPES	Half-Life	
11-C	20.4 min,	"natural"
13-N	10.0 min	"natural"
15-O	2.0 min	"natural"
18-F	109.8 min	"pseudo-natural"

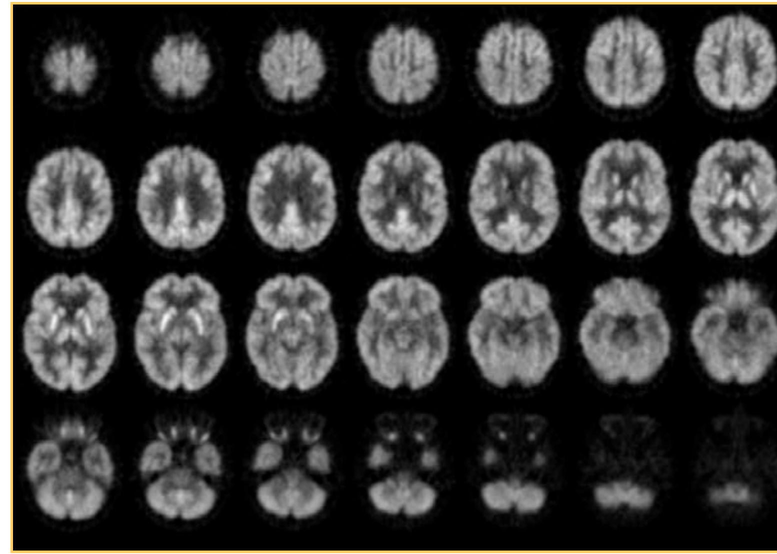
Radiochemistry

PET camera



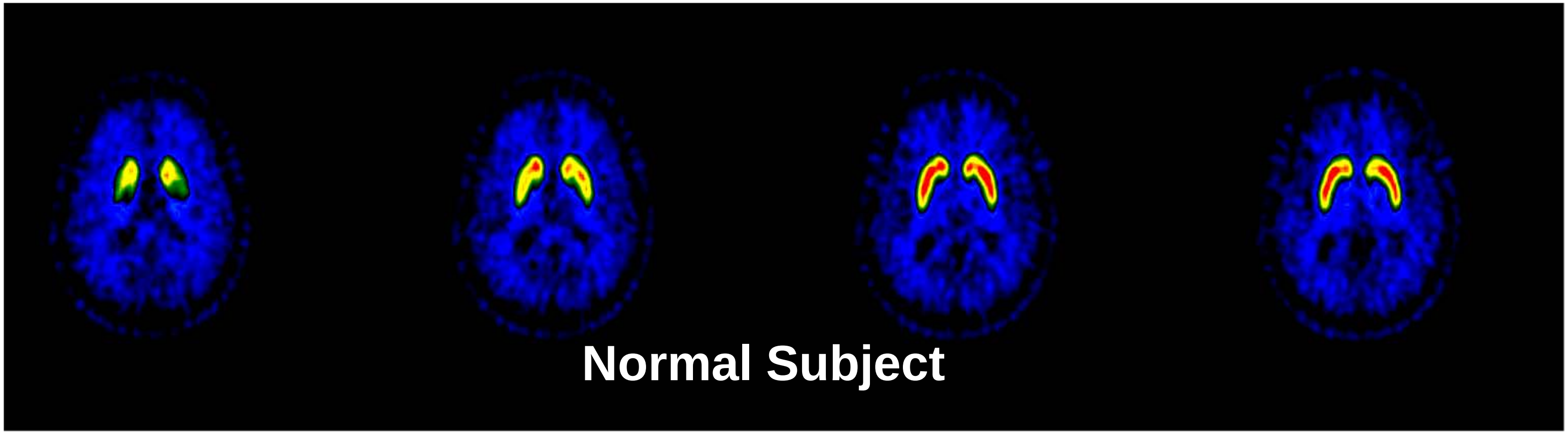
Positron Emission Tomography (PET)

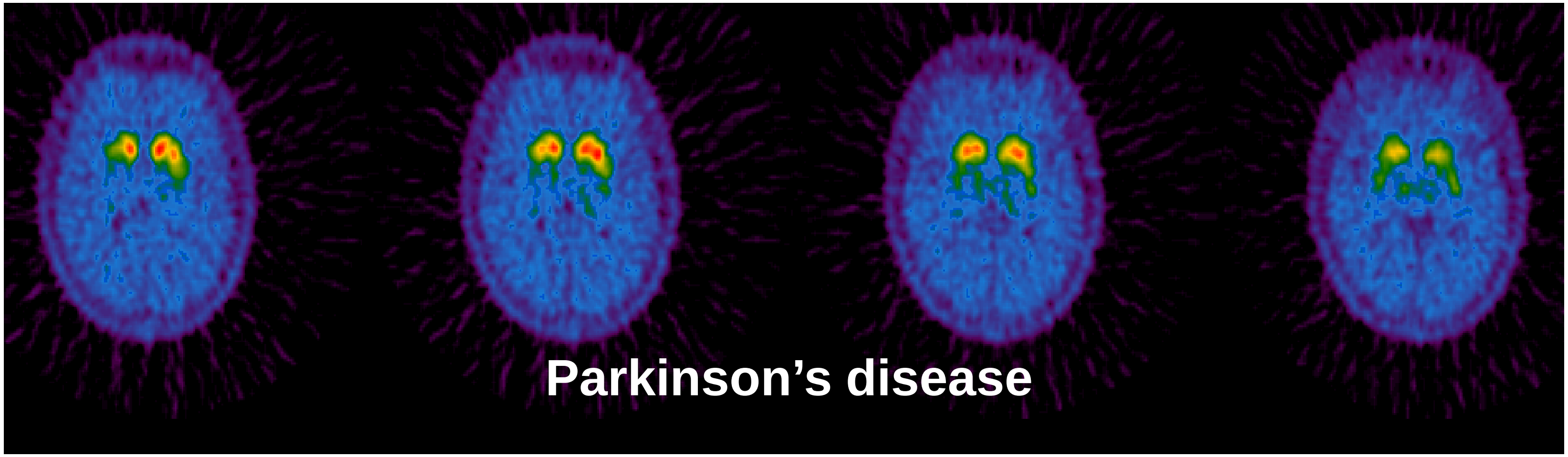




COVERAGE:
~ 15-20 cm
SPATIAL RESOLUTION:
~ 5 mm
SCAN TIME to cover an entire organ:
~ 5 min
CONTRAST RESOLUTION:
depends on the radiotracer

PET functional receptor imaging



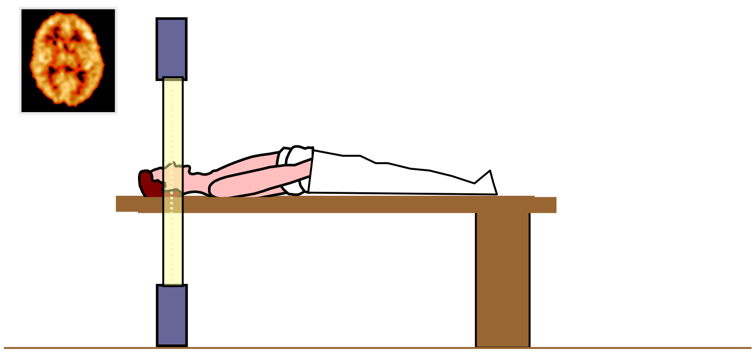


[^{11}C] FE-CIT

Courtesy HSR MILANO

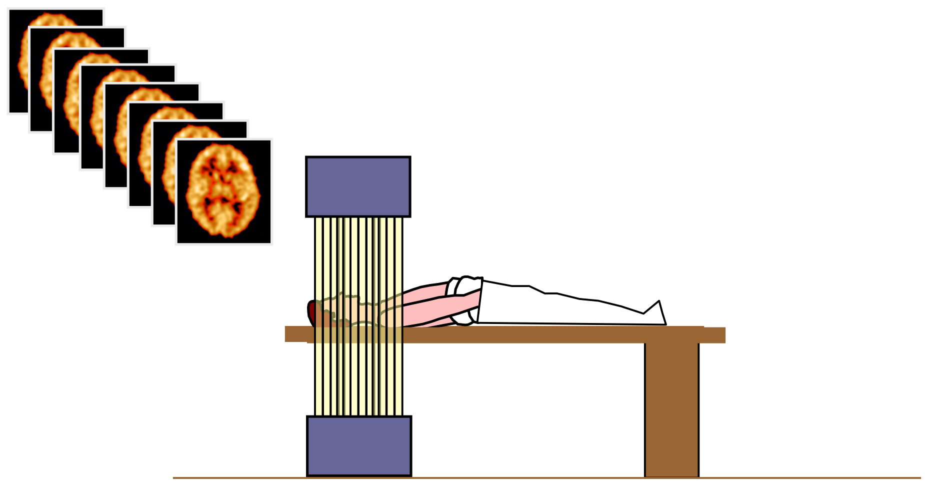
PET coverage and axial sampling

FIRST GENERATION PET



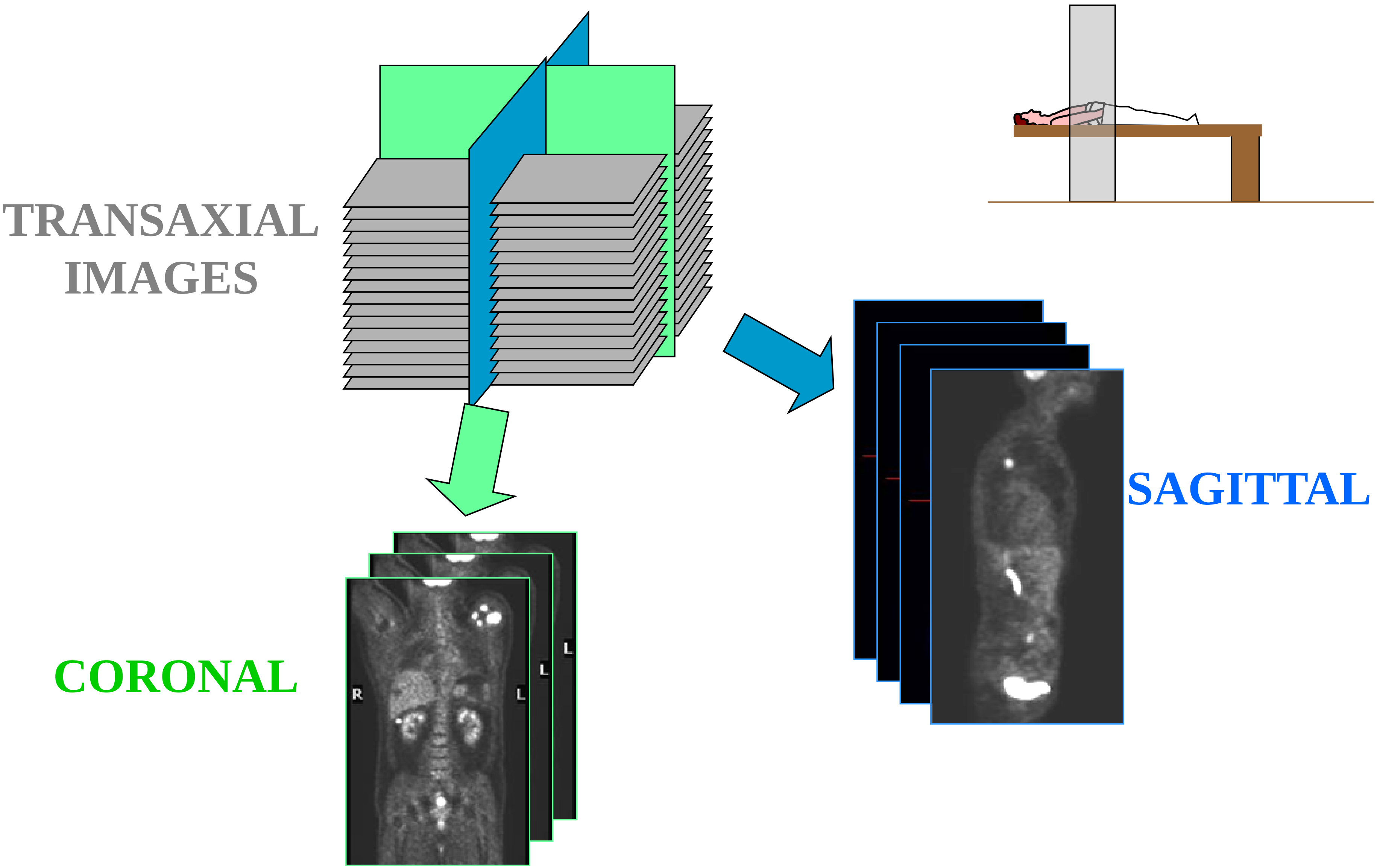
1 SLICE – 2 cm

CURRENT GENERATION PET

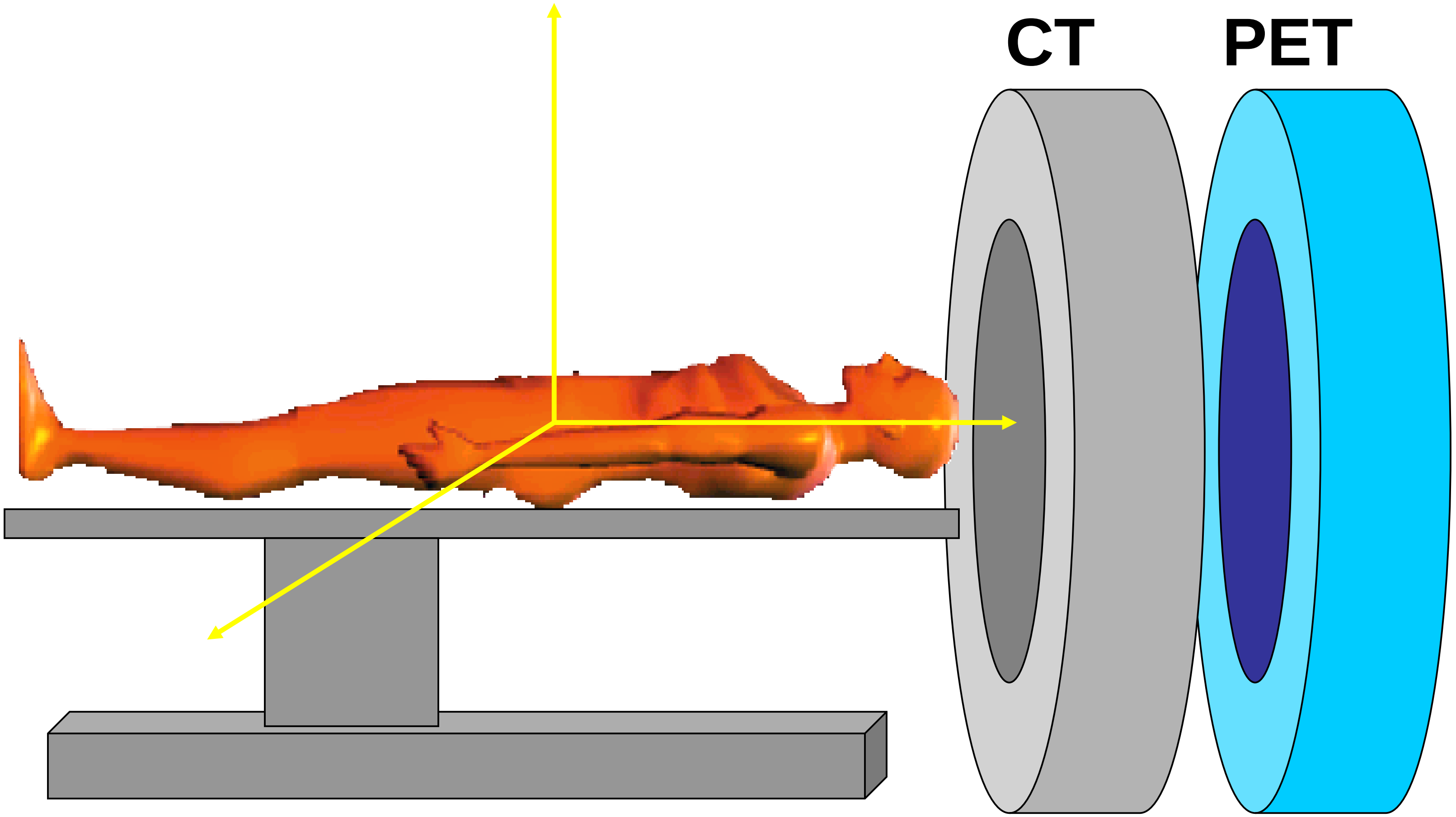


> 40 SLICES – 6 mm
Axial FOV: 15 –20 cm

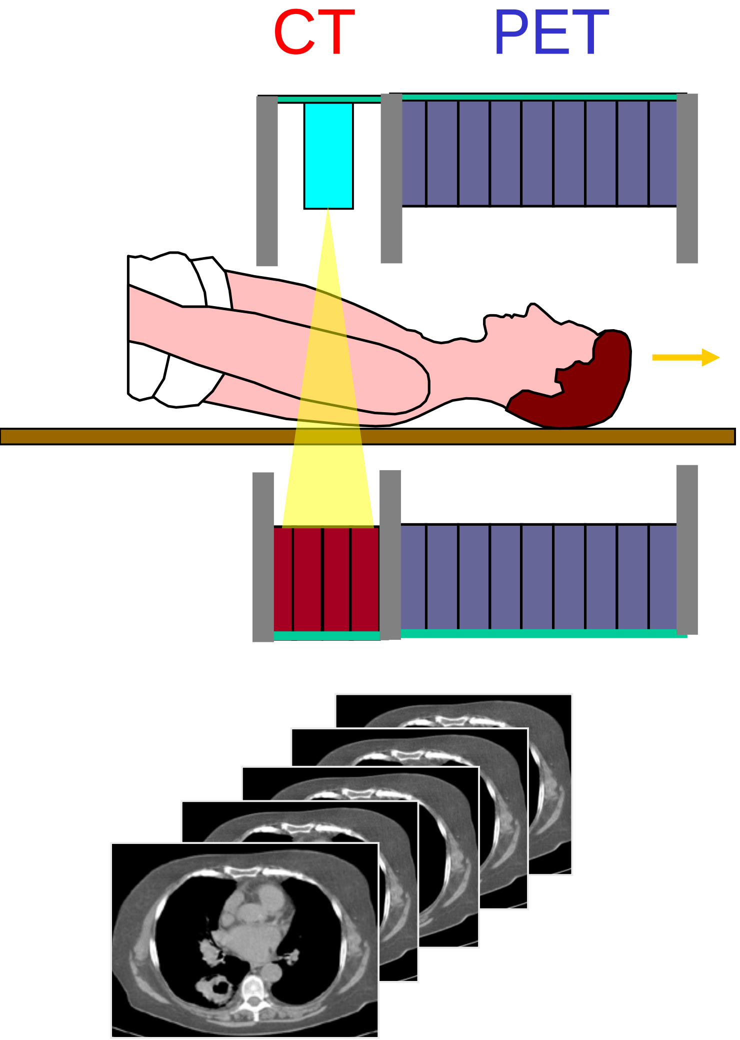
PET: total body studies



PET/CT scanner

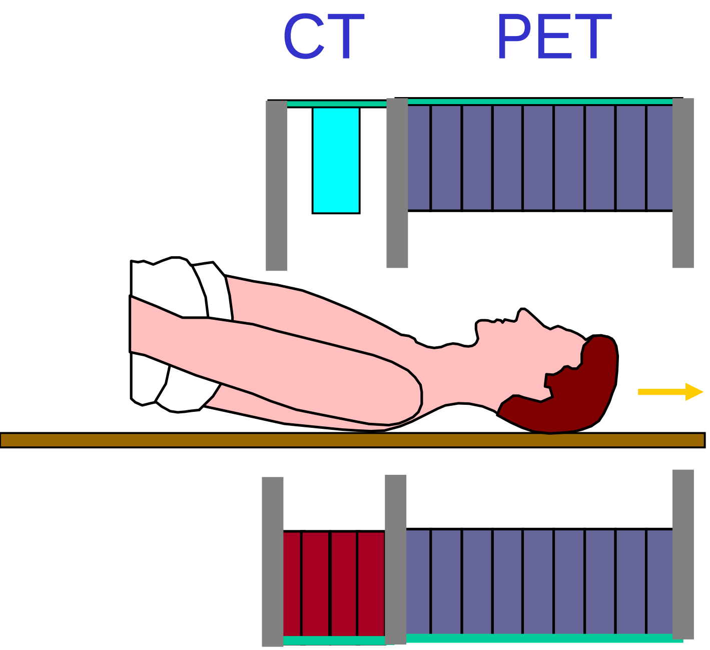


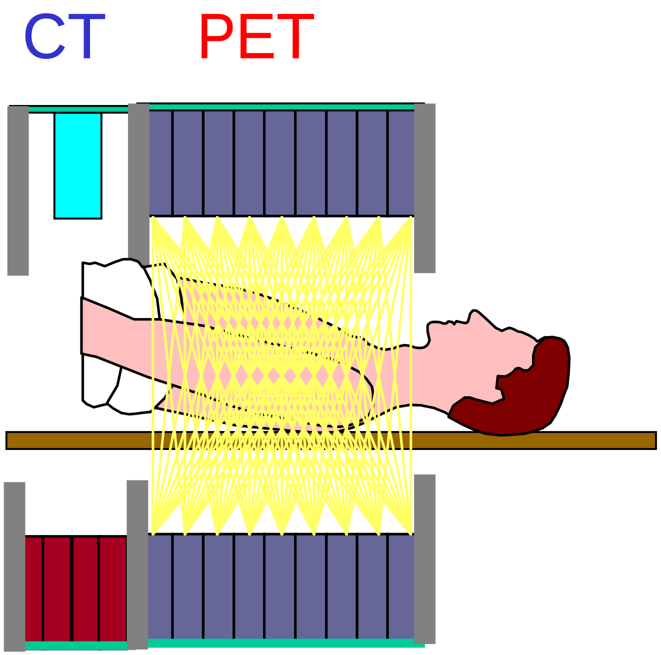
PET/CT scanner

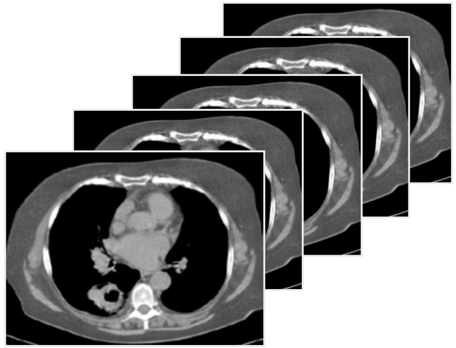


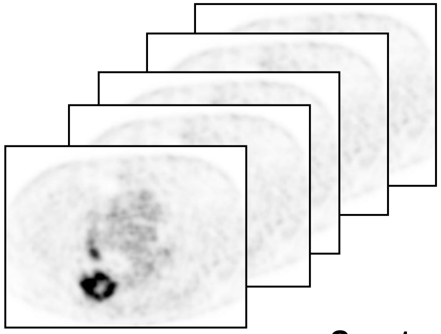
Courtesy HSR MILANO

PET/CT scanner



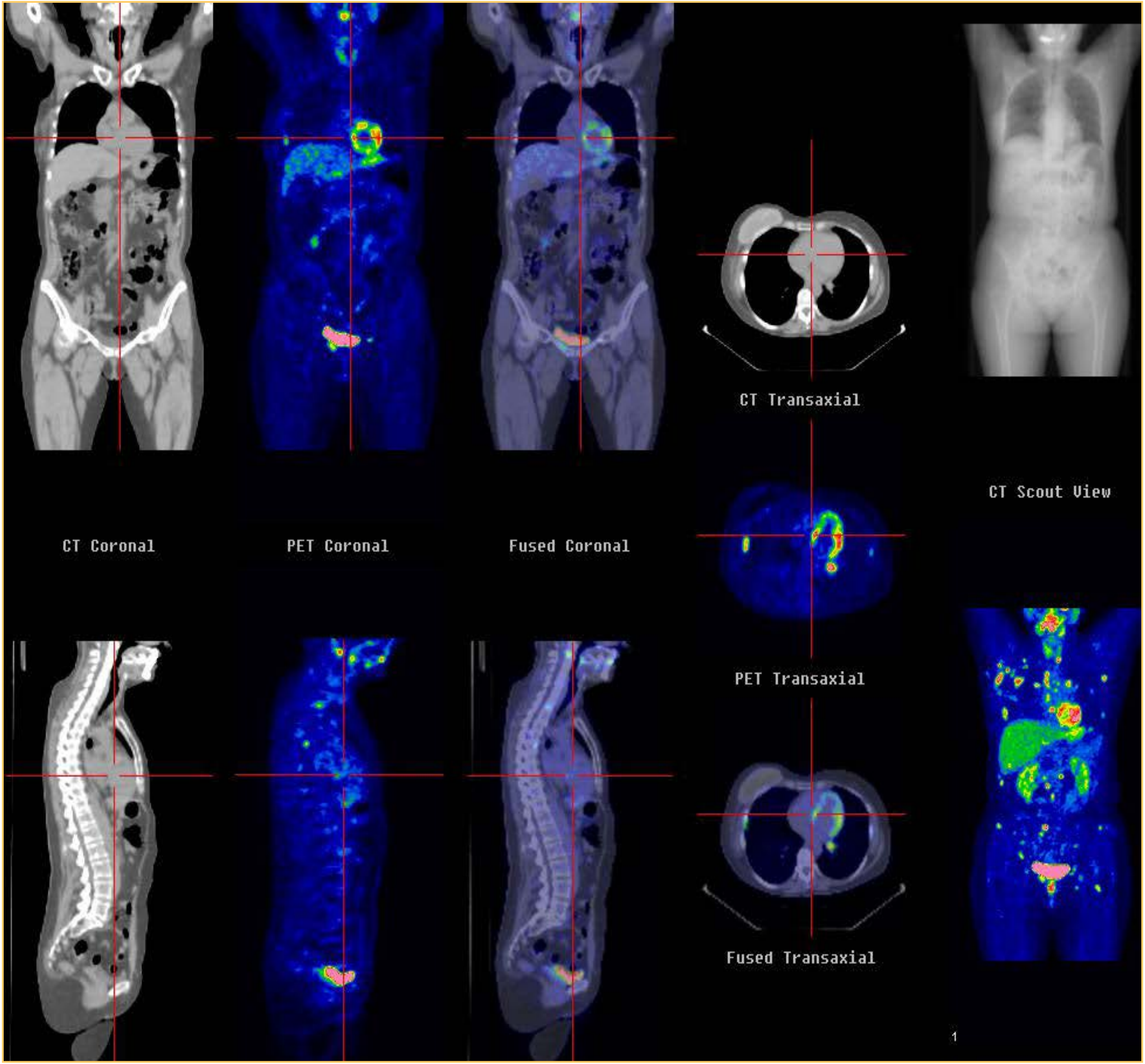






Courtesy HSR MILANO

^{18}F-FDG PET/CT



Courtesy HSR MILANO

Summary of accelerators running in the world

Three main applications

1) **Scientific research**
2) **Medical applications**
3) **Industrial uses**

CATEGORY OF ACCELERATORS	NUMBER IN USE (*)	
High-energy accelerators (E >1 GeV)	~ 120	
Synchrotron radiation sources	> 100	
Medical radioisotope production	~ 1,000	10,000
Accelerators for radiation therapy	> 7,500	
Research accelerators including biomedical research	~ 1,000	
Industrial processing and research	~ 1,500	
Ion implanters, surface modification	> 7,000	
TOTAL	> 18,000	

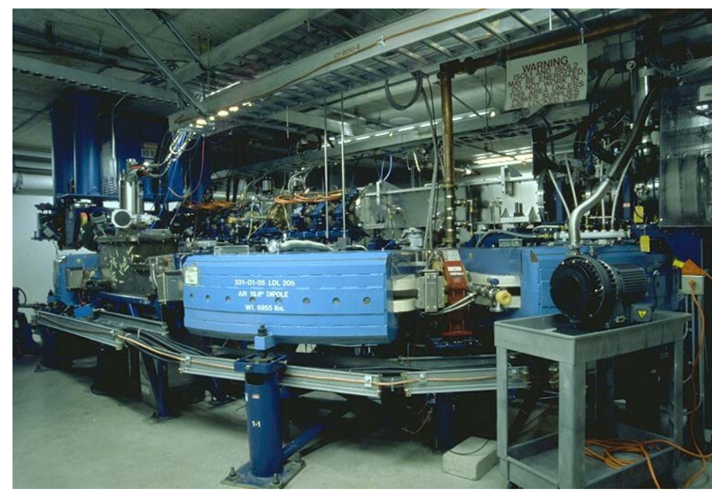
Adapted from "Maciszewski, W. and Scharf, W., *Particle accelerators for radiotherapy, Present status and future*, Physica Medica XX, 137-145 (2004)"

Three classes of medical accelerators

Electron linacs for conventional radiation therapy, including advanced modalities:

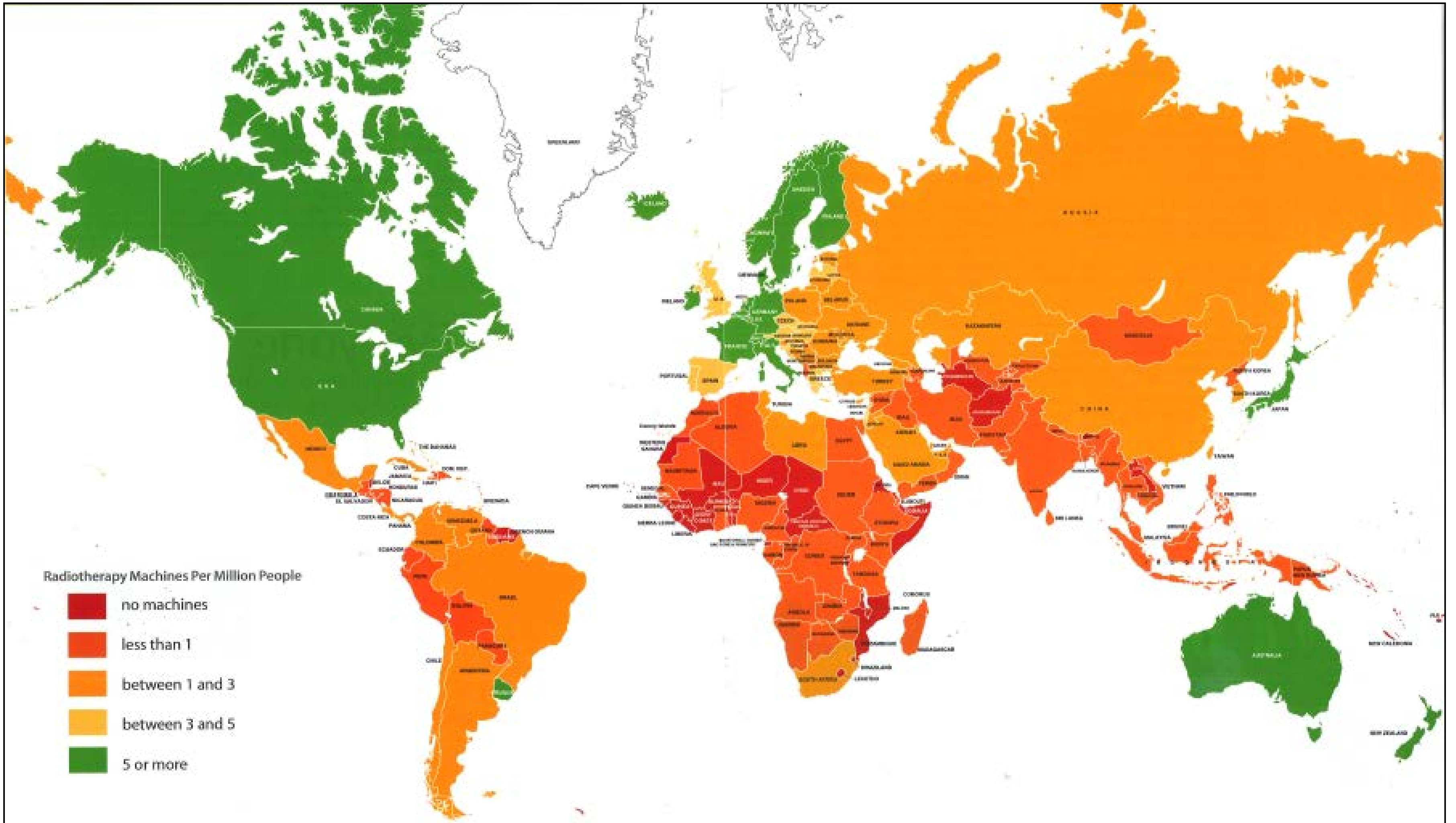
- Cyberknife
- IntraOperative RT (IORT)
- Intensity Modulated RT

Low-energy cyclotrons for production of radionuclides for medical diagnostics



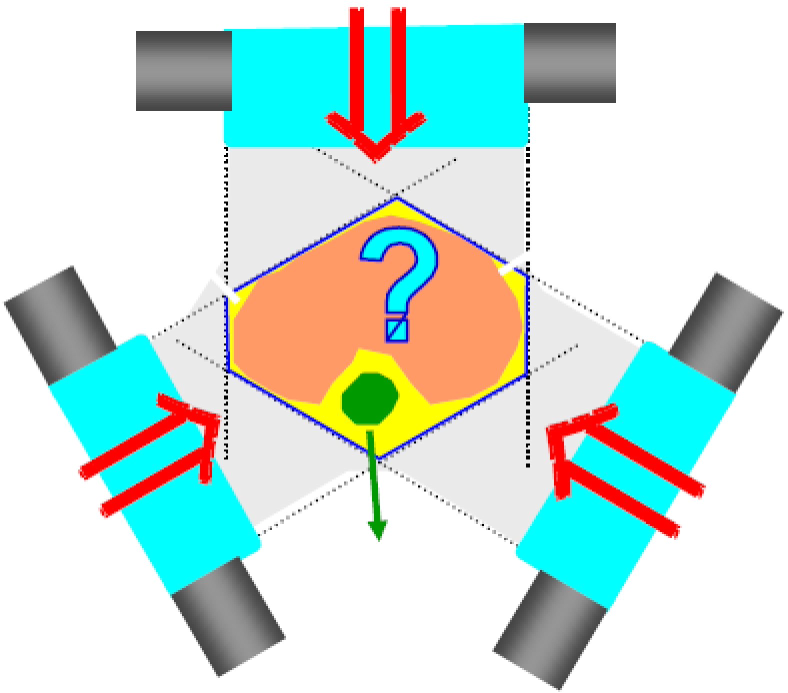
Medium-energy cyclotrons and synchrotrons for hadron therapy with protons (250 MeV) or light ion beams (400 MeV/u ^{12}C-ions)

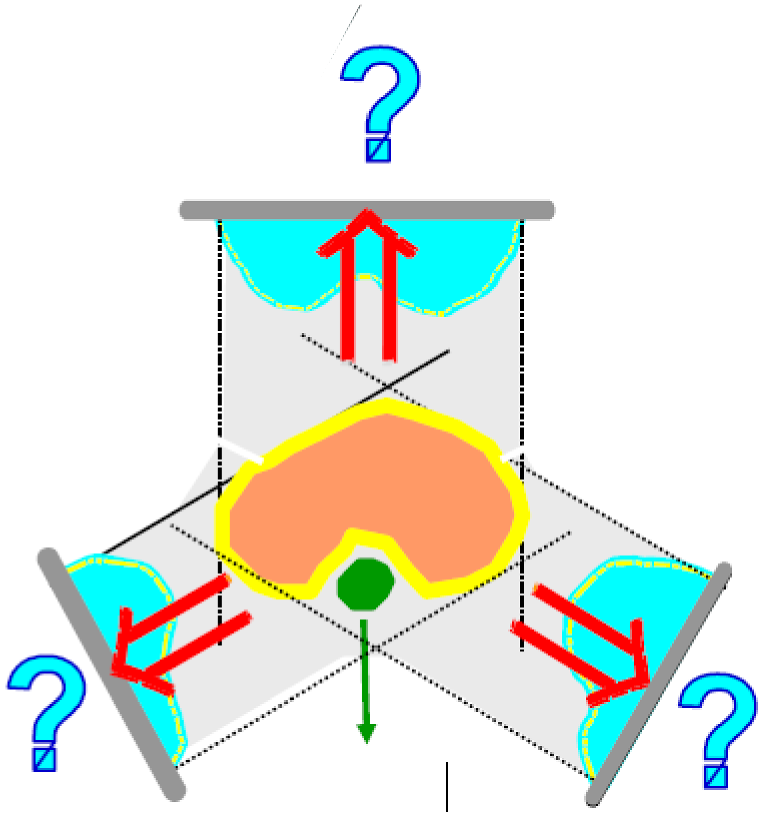
Availability of radiation therapy worldwide

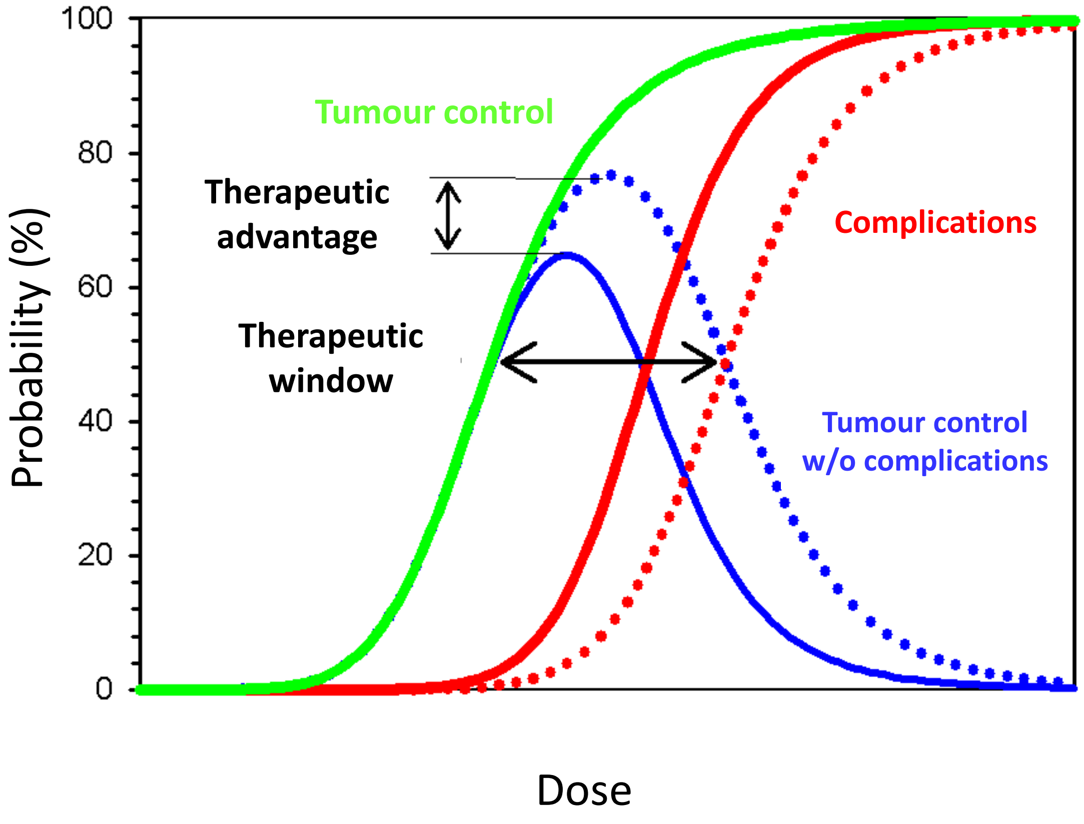


Number of radiation therapy machines per million people

Treatment planning and dose delivery to tumour volume

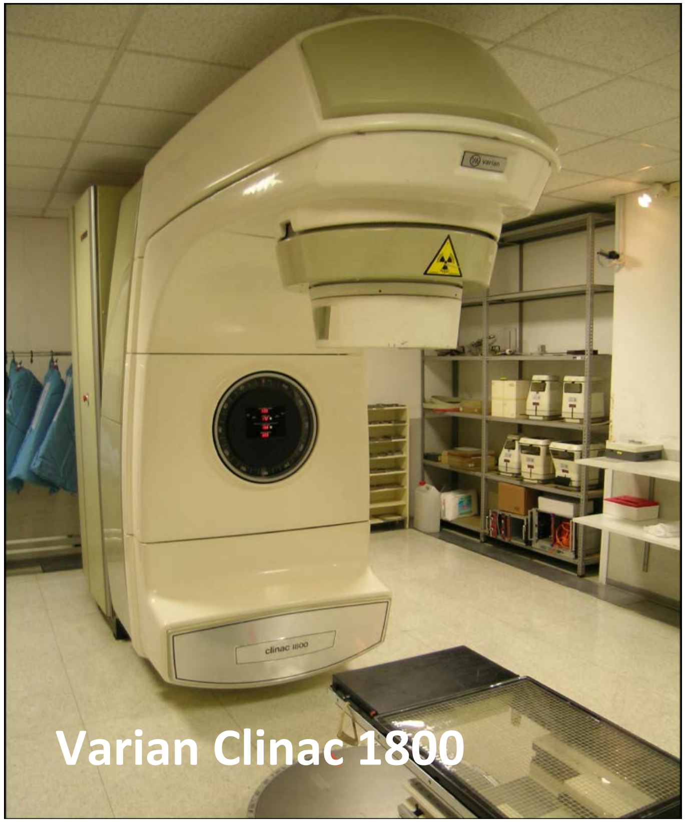


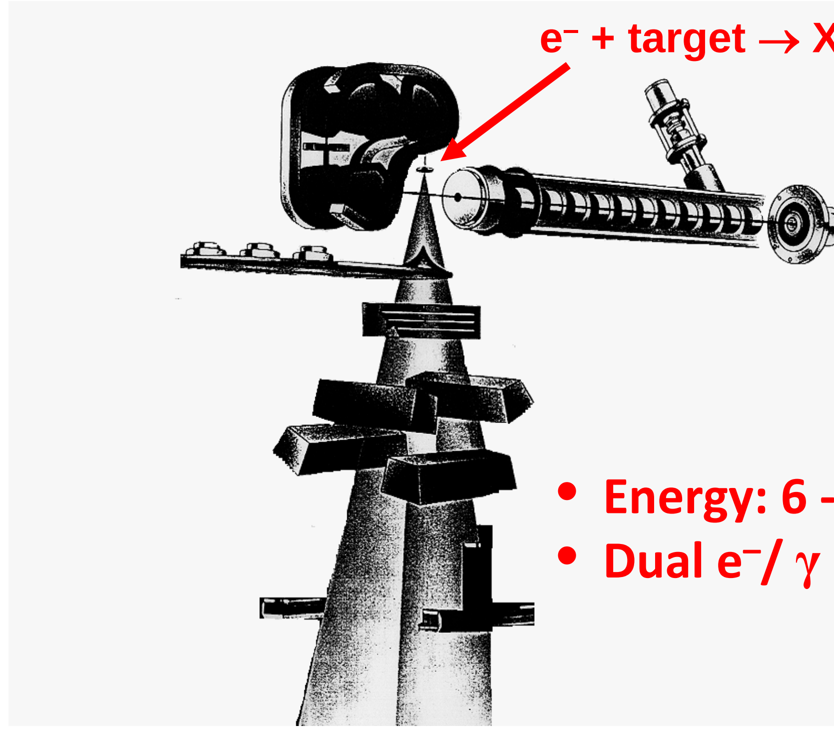




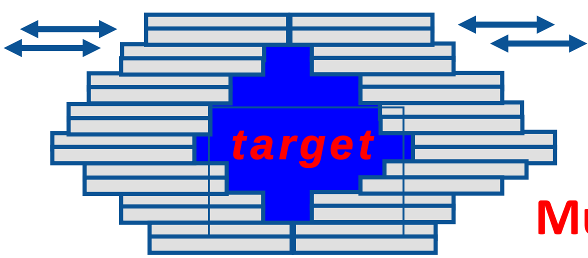
100
80
60
40
20
0
Probability (%)
Dose
Tumour control
Therapeutic advantage
Therapeutic window
Complications
Tumour control w/o complications

X-rays in radiation therapy: medical electron linacs



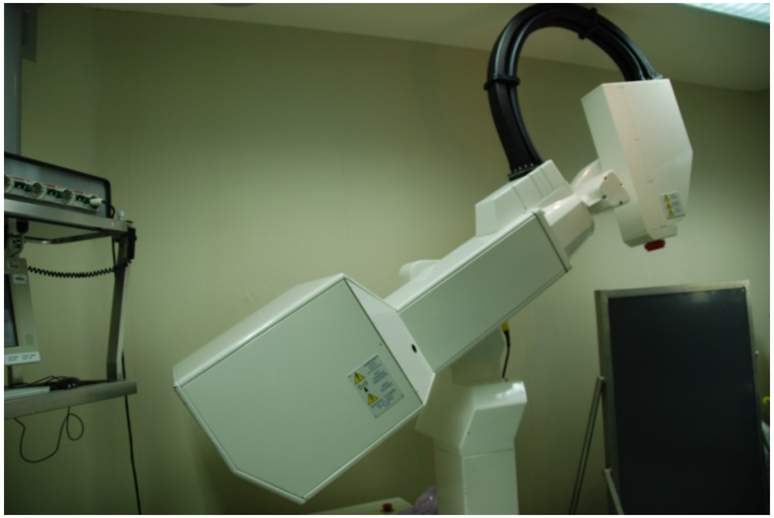


- **Energy: 6 -25 MeV**
- **Dual e⁻/ γ beams**



Multi-leaf collimator

Intra-Operative Radiation Therapy (IORT)



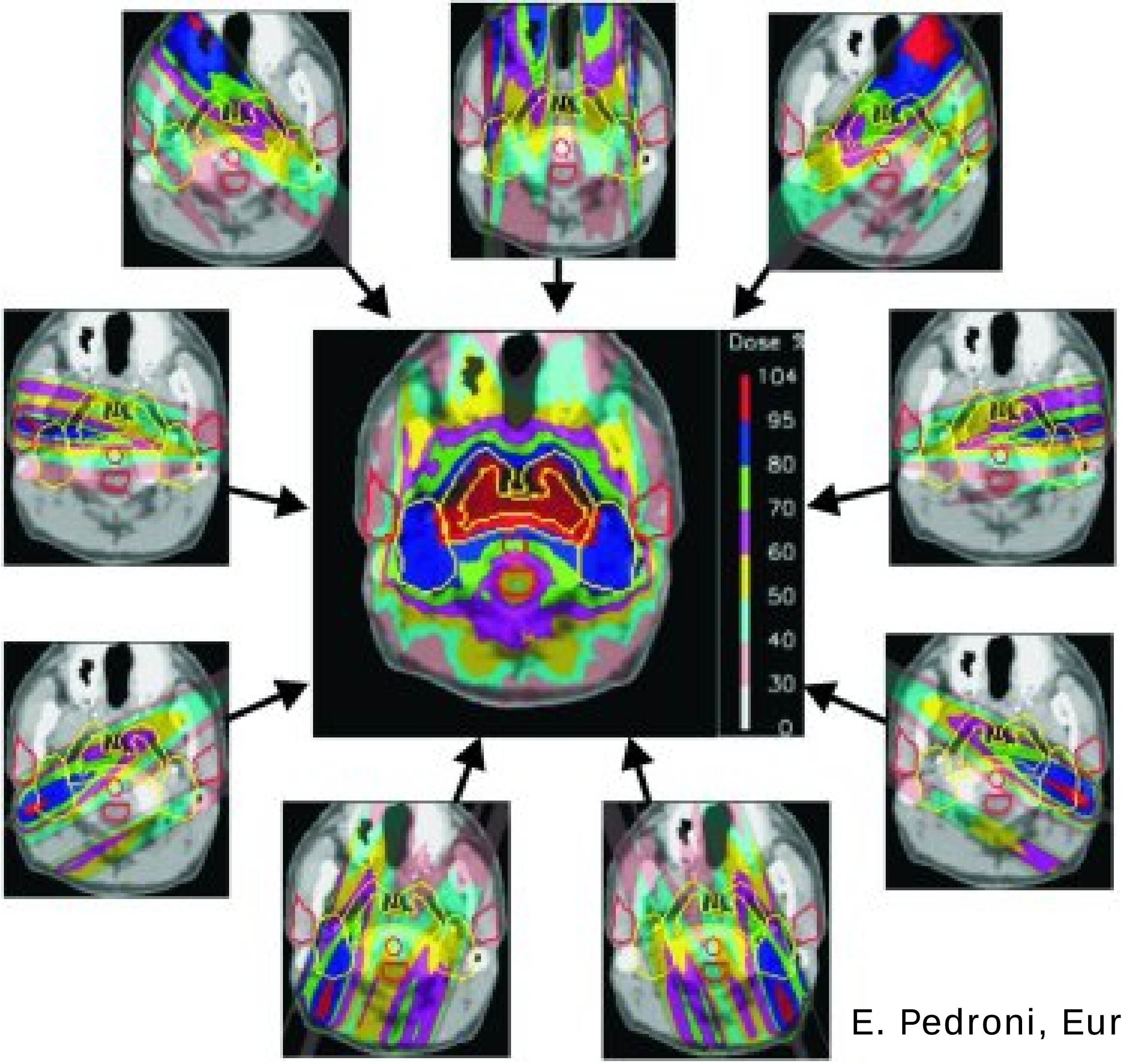
- Small electron linac
- Energy 6 – 12 MeV
- Treatment with electrons only
- Single irradiation
- Three models of linac produced by three manufacturers (two in Italy)

6 MV Linac mounted on a robotic arm

- No flattening filter
- Uses circular cones of diameter 0.5 to 6 cm
- 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

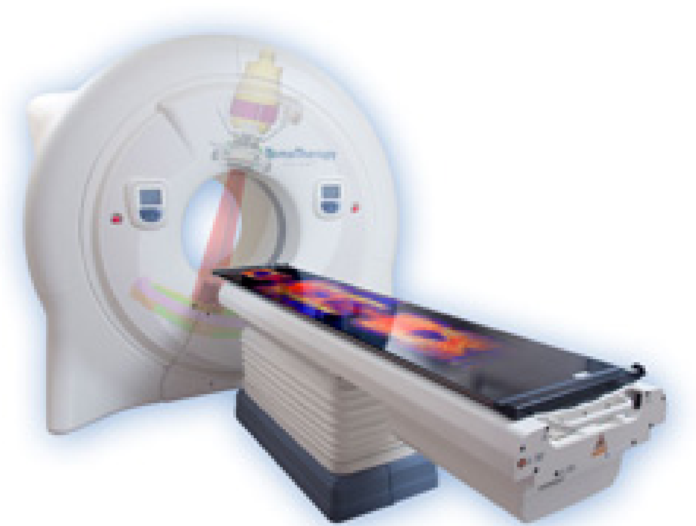


An example of intensity modulated treatment planning with photons. Through the addition of 9 fields it is possible to construct a highly conformal dose distribution with good dose sparing in the region of the brain stem (courtesy of T. Lomax, PSI).

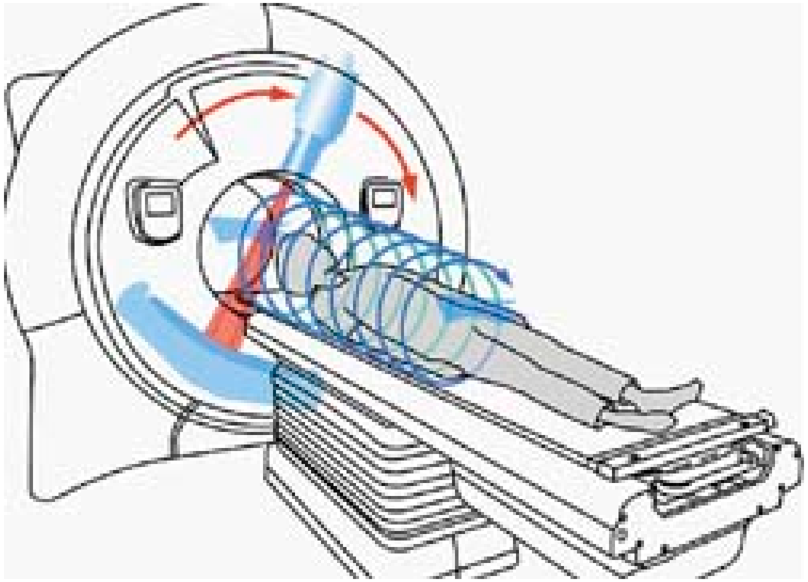
E. Pedroni, Europhysics News (2000) Vol. 31 No. 6

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

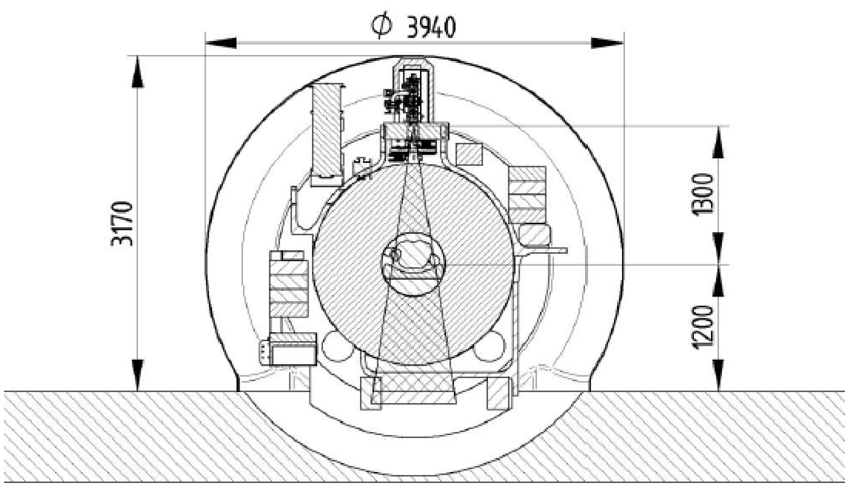
Helical tomotherapy

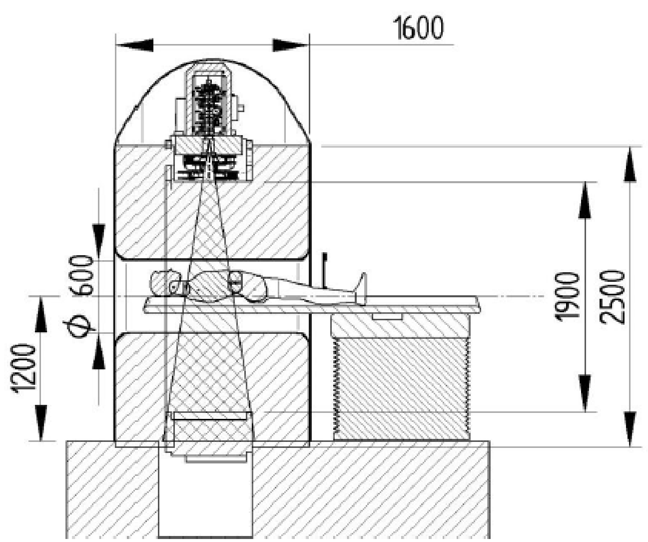


www.tomotherapy.com



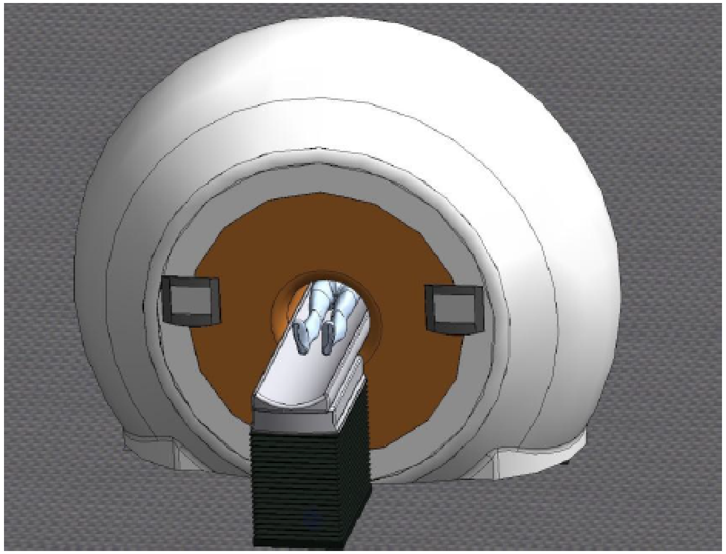
- Integrated CT guidance
    - Integrated CT scanner allowing efficient 3D CT imaging for ensuring the accuracy of treatment
- A binary multi-leaf collimator (MLC) for beam shaping and modulation
- A ring gantry design enabling TomoHelical delivery
    - As the ring gantry rotates in simultaneous motion 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



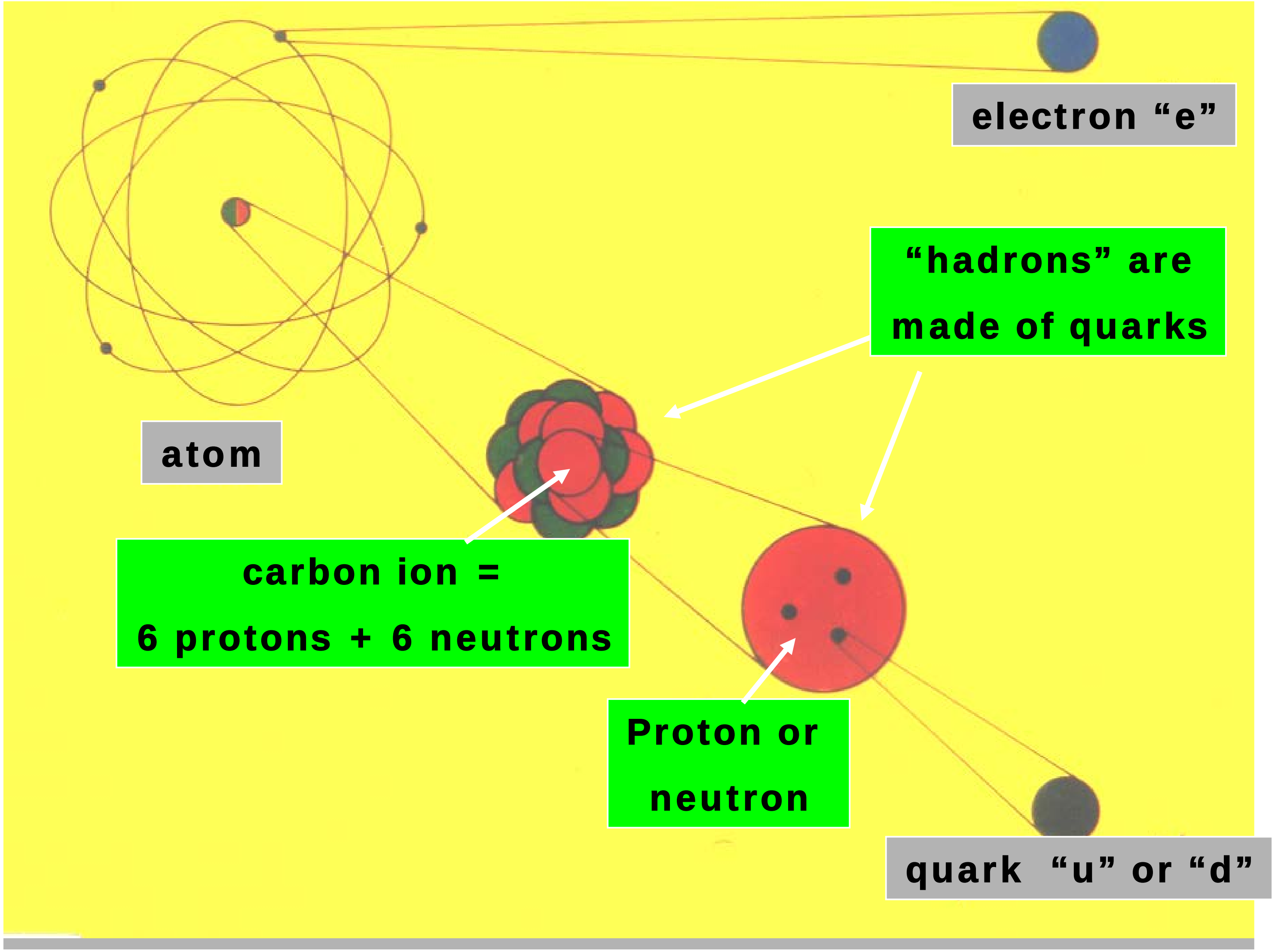


- *Closed bore high field MRI*
- *Gantry ring based 6 MV accelerator with MLC*
  - ➔ *accelerator and MRI system have to operate simultaneously and independently*

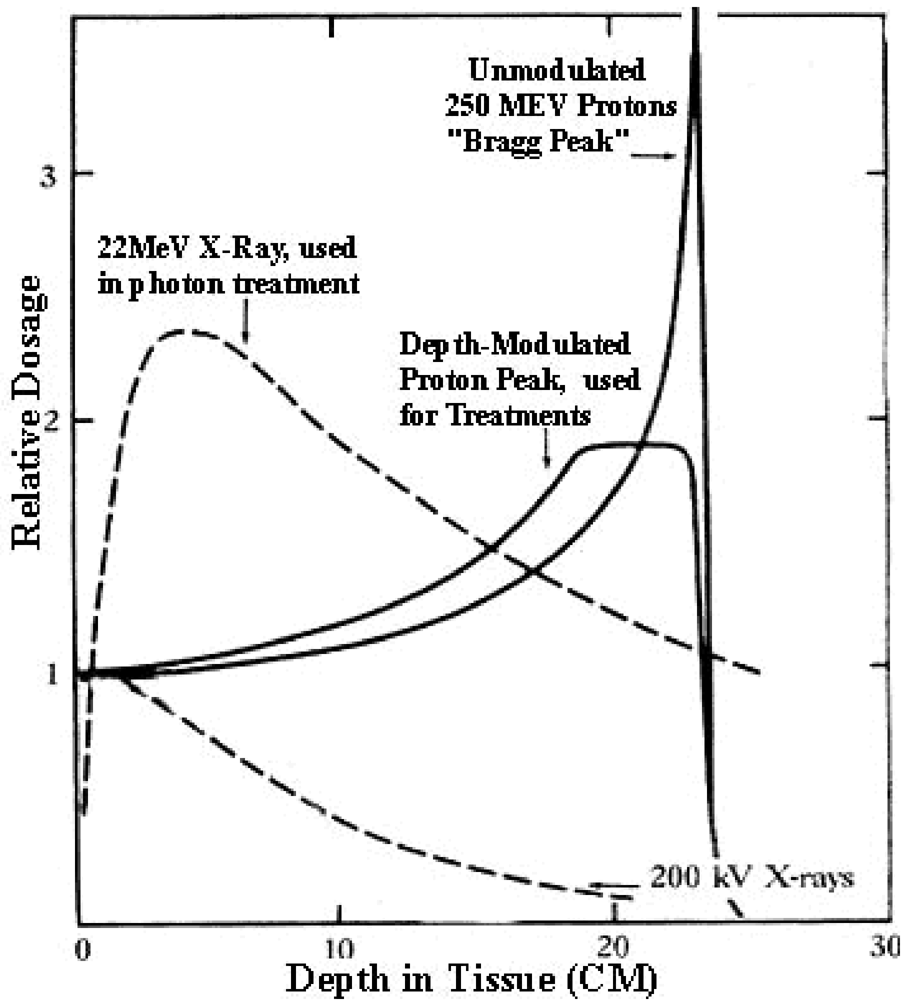
Courtesy J. Lagendijk

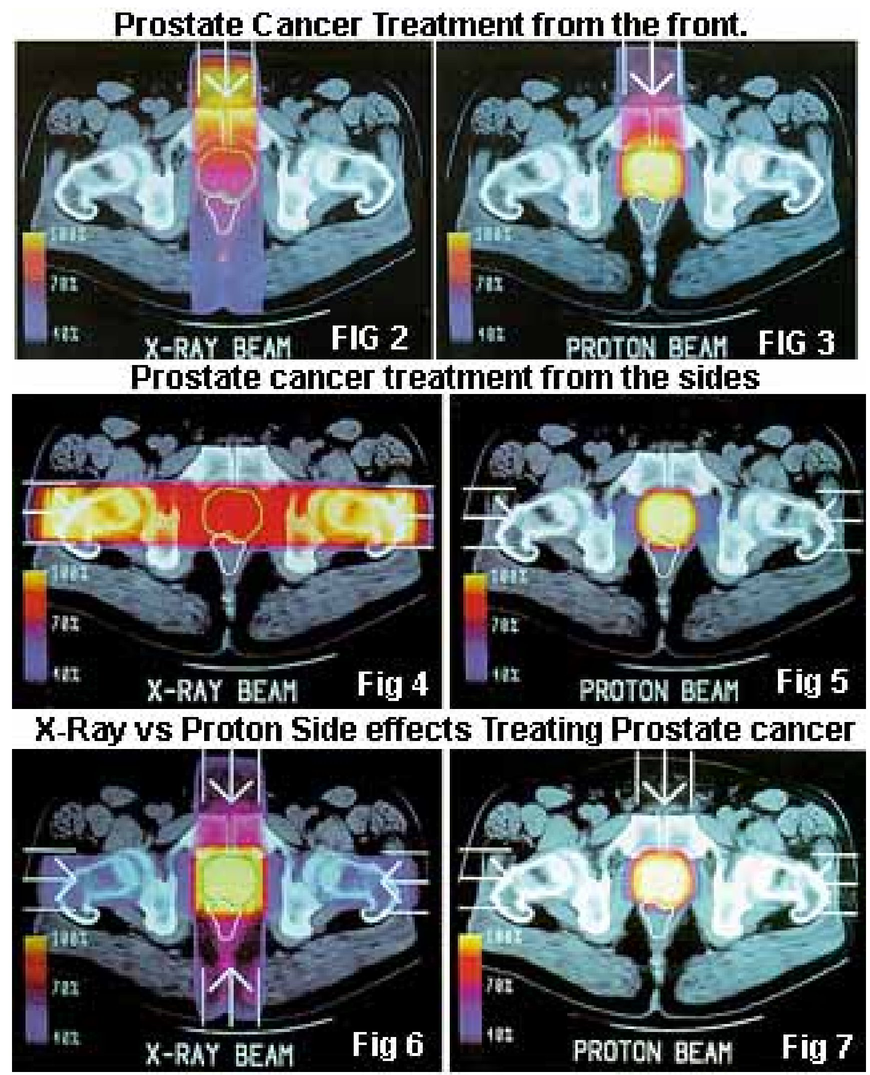


Hadrontherapy: n, p and C-ion beams



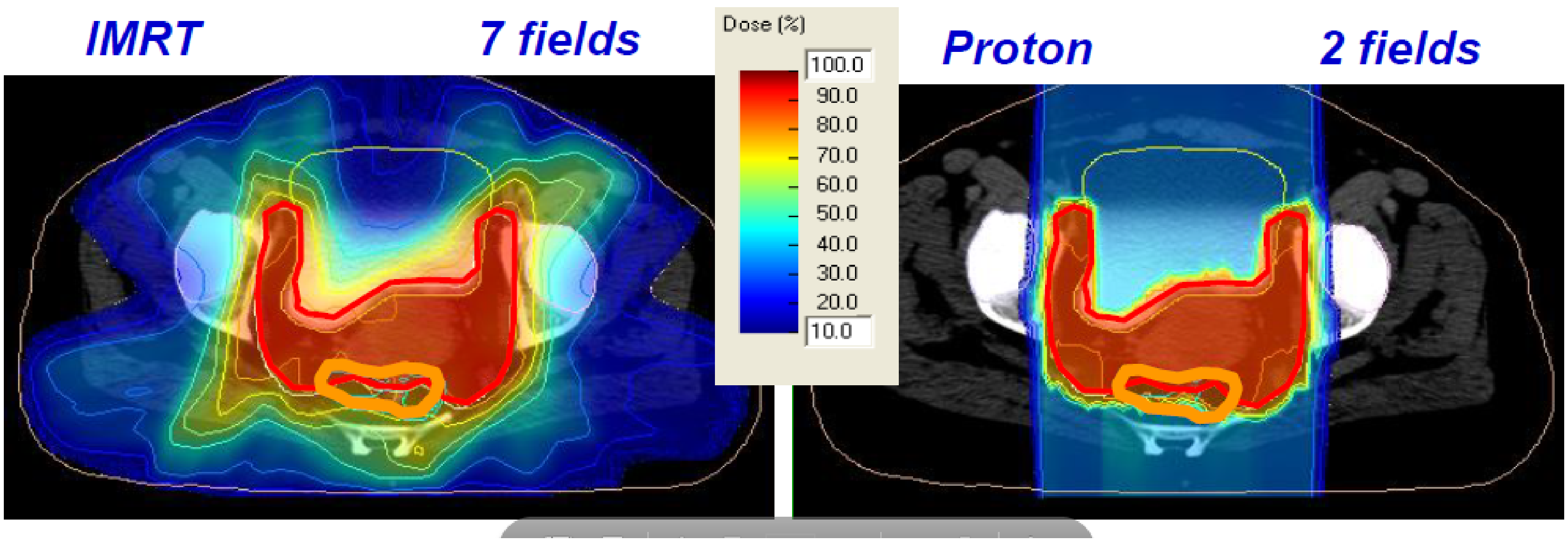
Proton radiation therapy



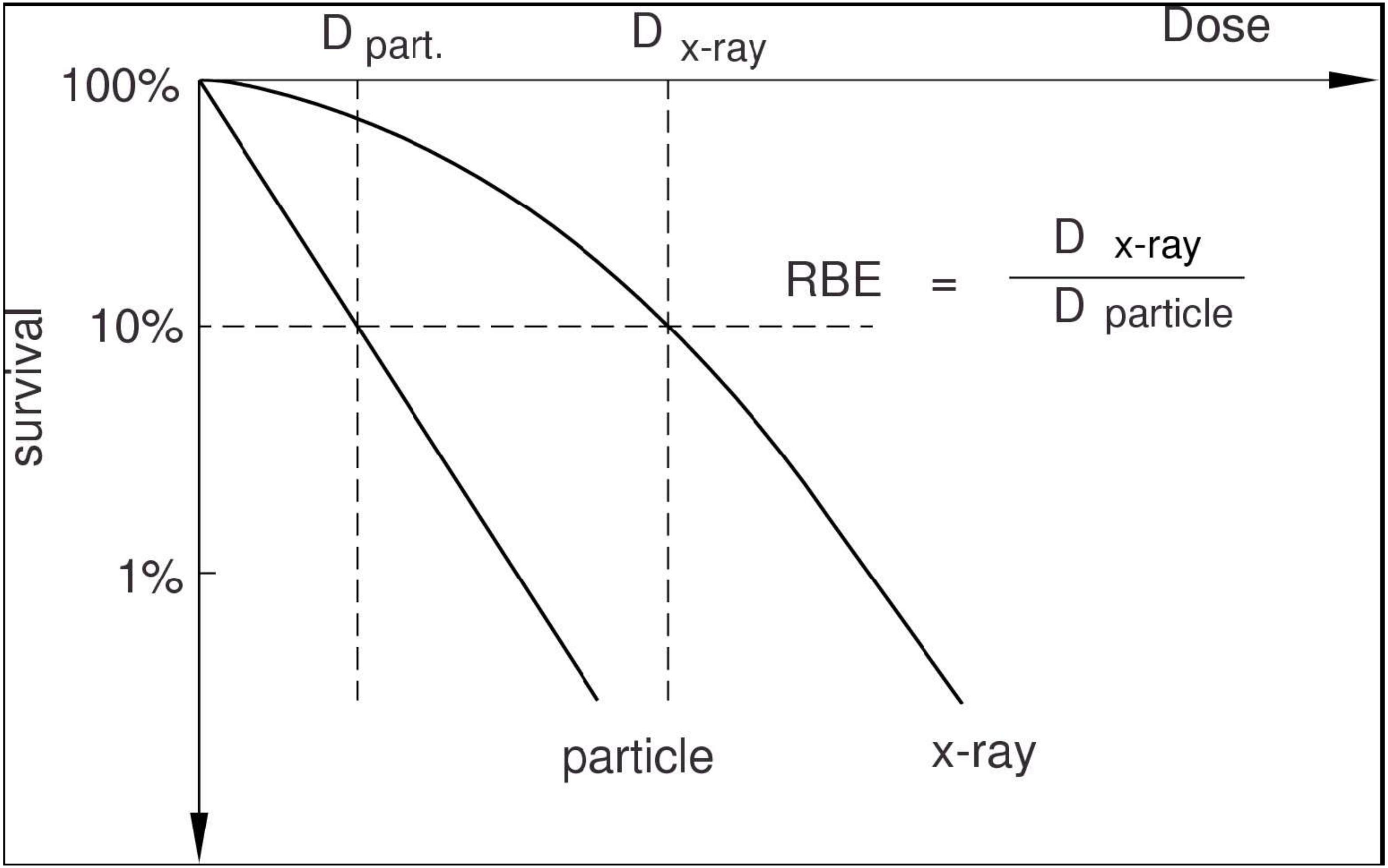


Treatment planning

- *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)



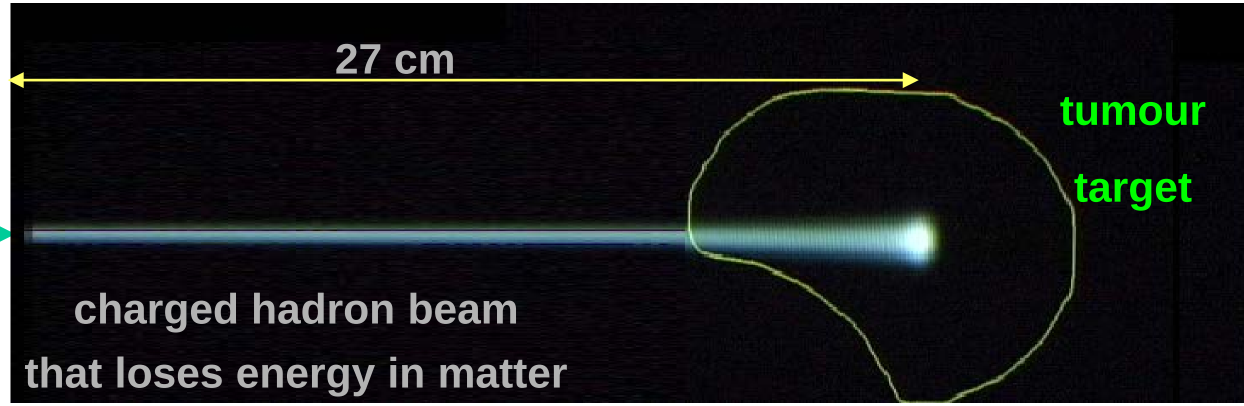
G. Kraft, 2007 - Results for C ions

Indication	End point	Results photons	Results carbon HIMAC-NIRS	Results carbon GSI
Chordoma	local control rate	30 – 50 %	65 %	70 %
Chondrosarcoma	local control rate	33 %	88 %	89 %
Nasopharynx carcinoma	5 year survival	40 -50 %	63 %	
Glioblastoma	av. survival time	12 months	16 months	
Choroid melanoma	local control rate	95 %	96 % (*)	
Paranasal sinuses tumours	local control rate	21 %	63 %	
Pancreatic carcinoma	av. survival time	6.5 months	7.8 months	
Liver tumours	5 year survival	23 %	100 %	
Salivary gland tumours	local control rate	24-28 %	61 %	77 %
Soft-tissue carcinoma	5 year survival	31 – 75 %	52 -83 %	

Hadrontherapy

200 MeV protons

4800 MeV carbon ions

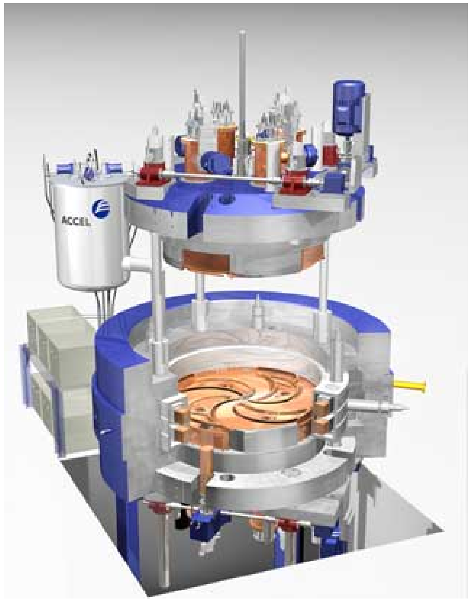


As of August 2015: 55 particle therapy facilities operation worldwide (mostly protons), 36 under construction, 14 at the planning stage

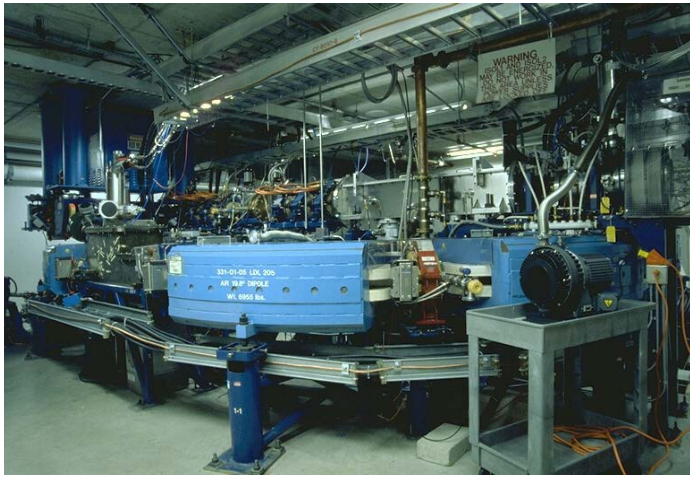
Number of patient treated until end of 2013

2054	He ions
1100	pions
13119	Carbon ions
433	other ions
105743	protons
122449	**Grand Total**

Proton radiation therapy

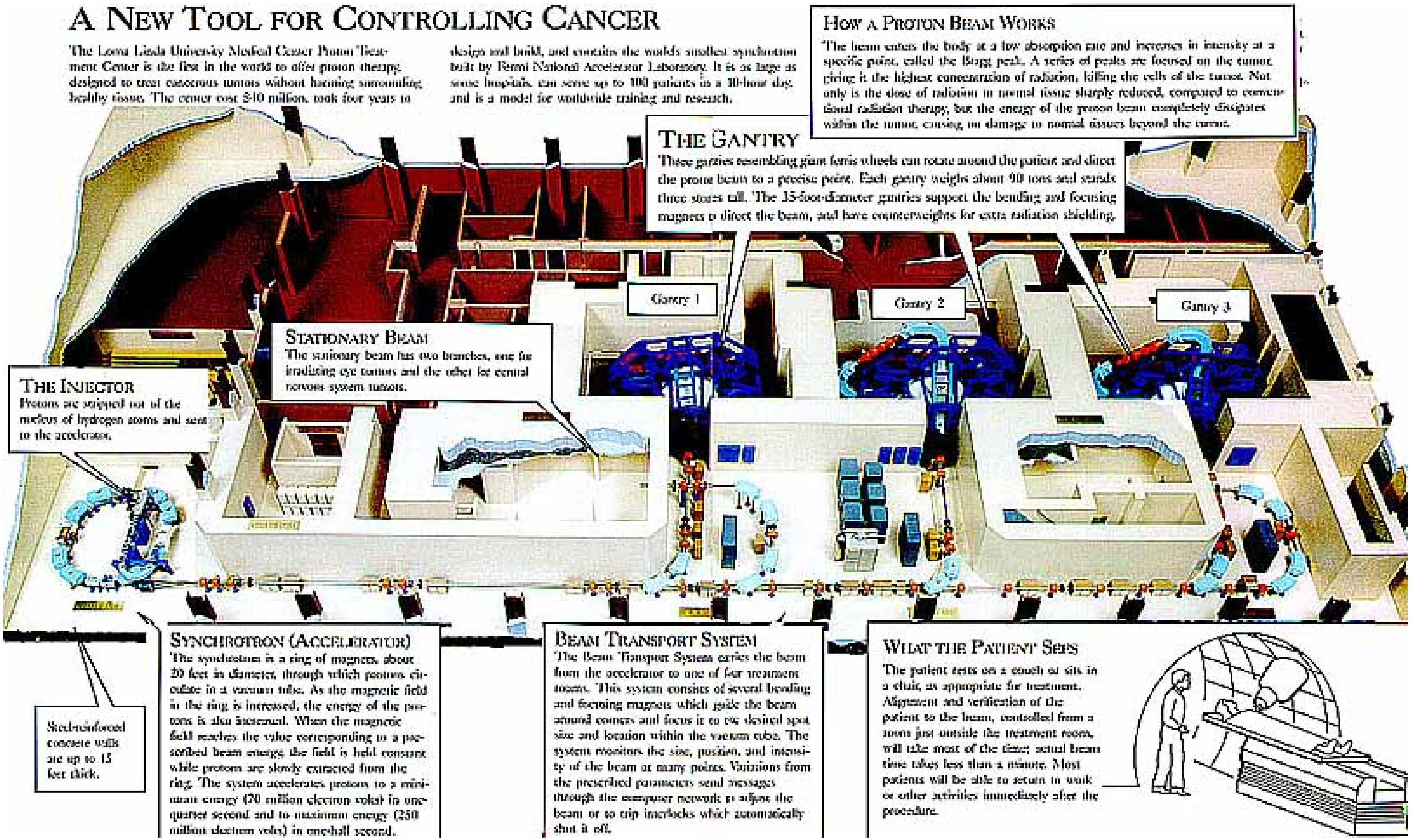


Accel-Varian

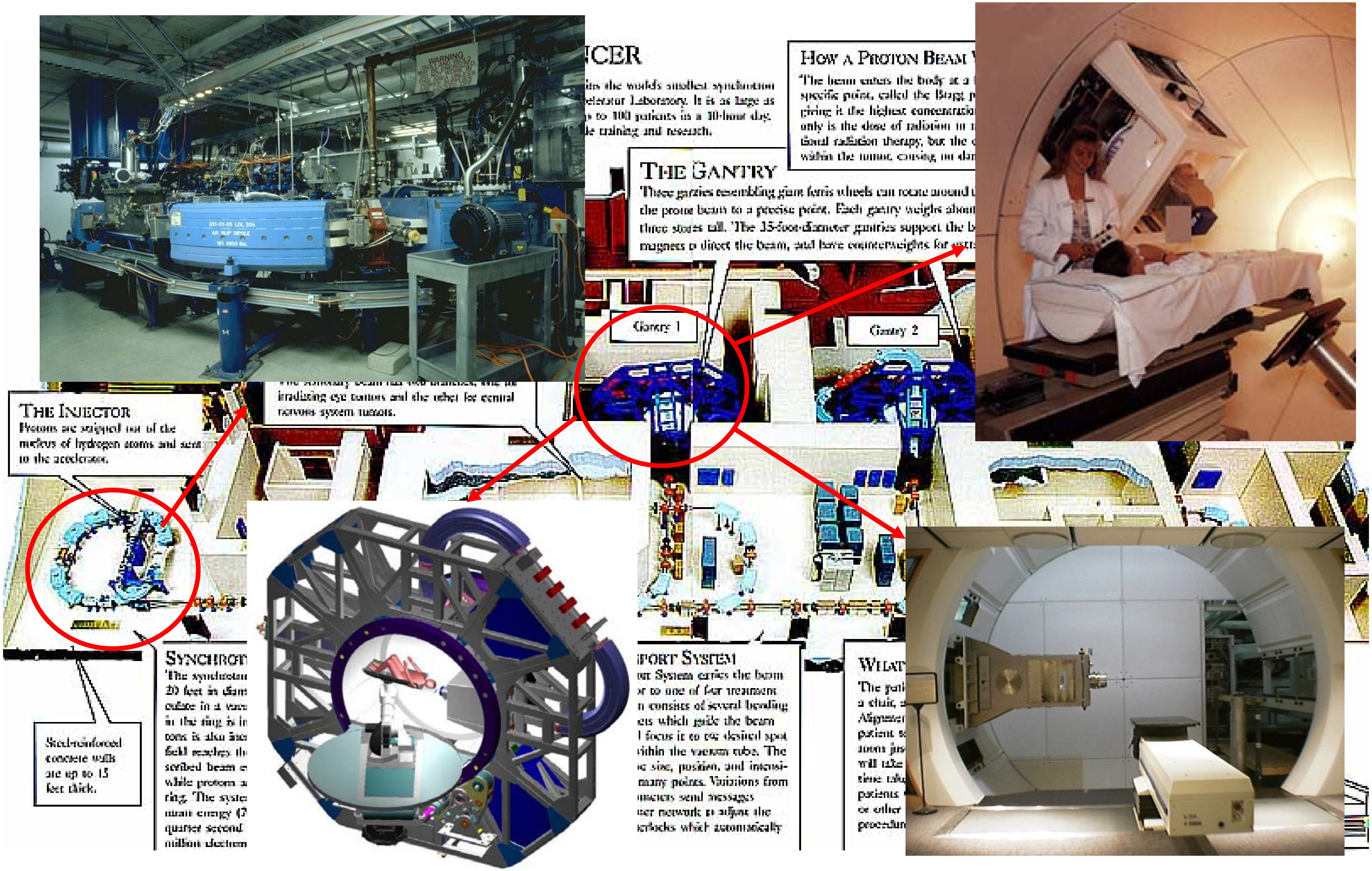


Loma Linda
(built by FNAL)

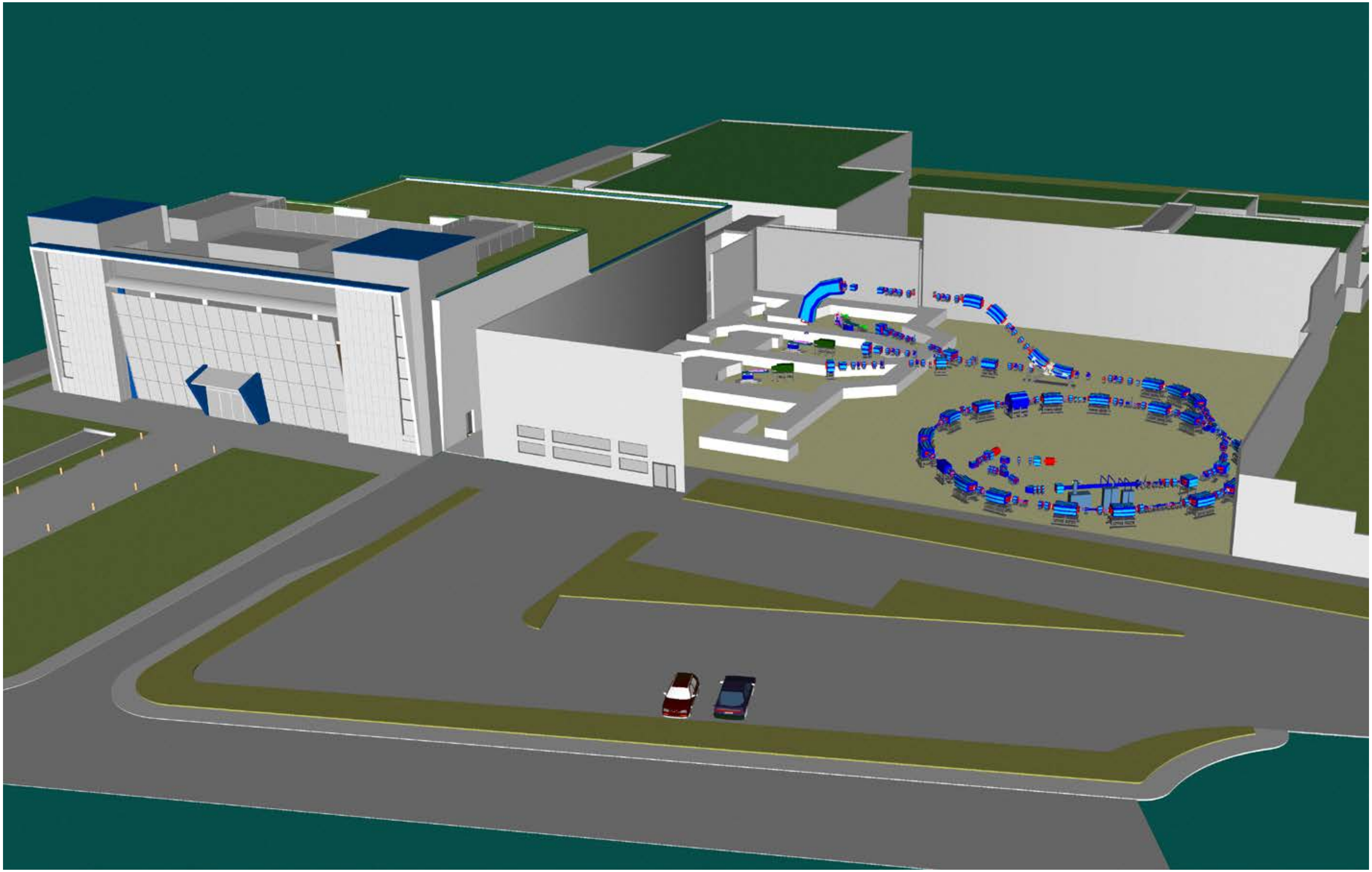
Loma Linda University Medical Center (LLUMC)



Loma Linda University Medical Center (LLUMC)

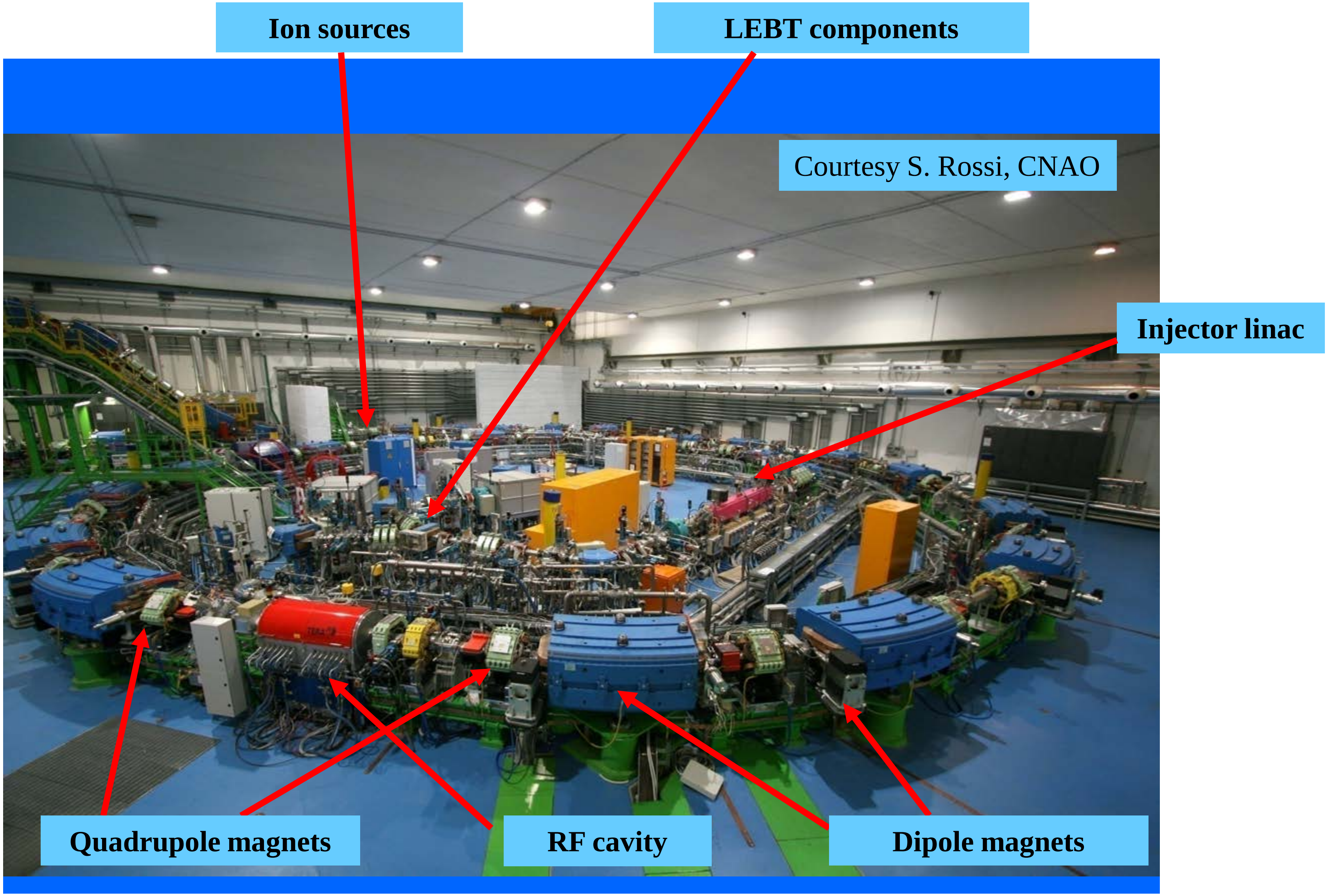


National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy



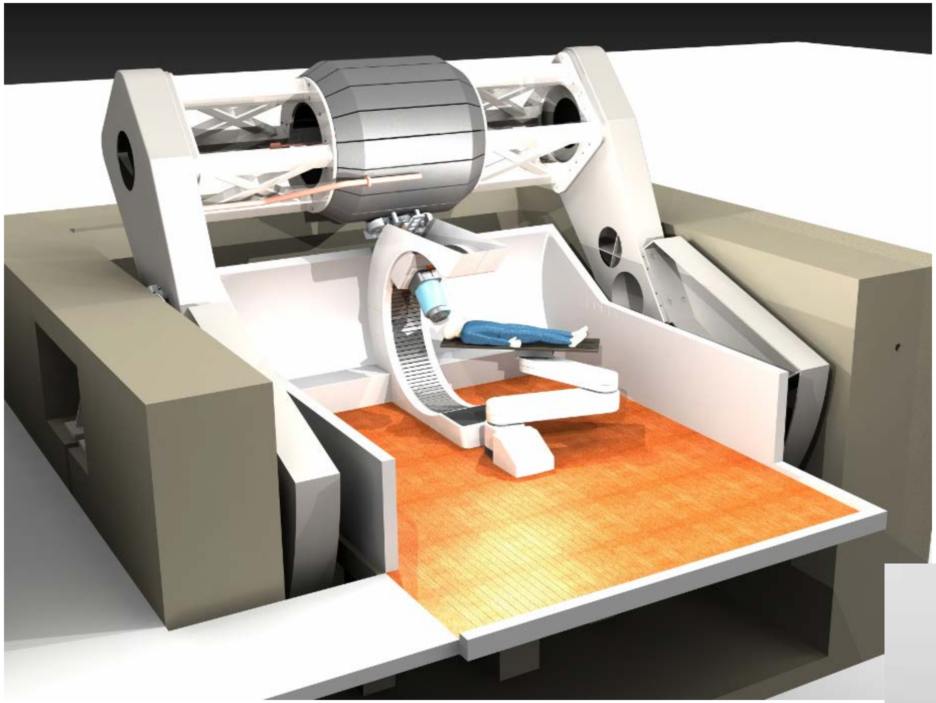
National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy

National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy

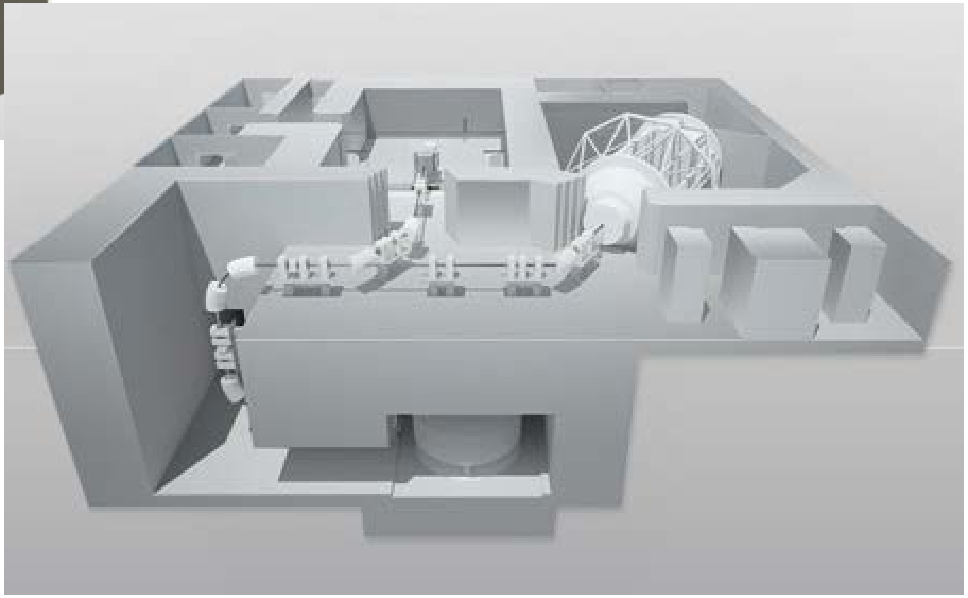


National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy

The future of hadrontherapy: single room facilities ?



IBA Proteus Nano



Mevion Medical Systems

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.