Radionuclide production and radiation therapy with particle accelerators

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- Brief historical introduction of particle accelerators and their use in medicine
- Radionuclide production:
  - production routes
  - production methods
  - decay equation, decay scheme
  - nuclear reactions, production rate, cross section, targetry
- Radiation therapy:
  - external photon radiation therapy
  - hadron therapy
  - Boron Neutron Capture Therapy

Brief historical introduction of particle accelerators and their use in medicine

The beginnings of modern physics and of medical physics

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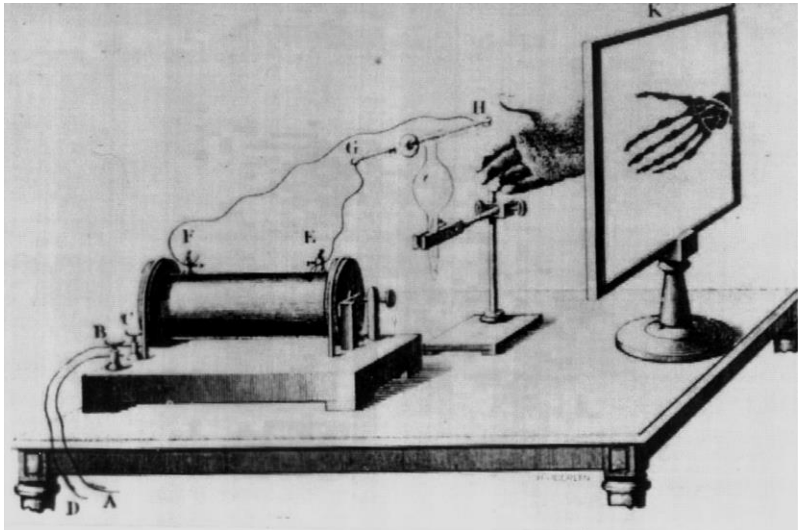
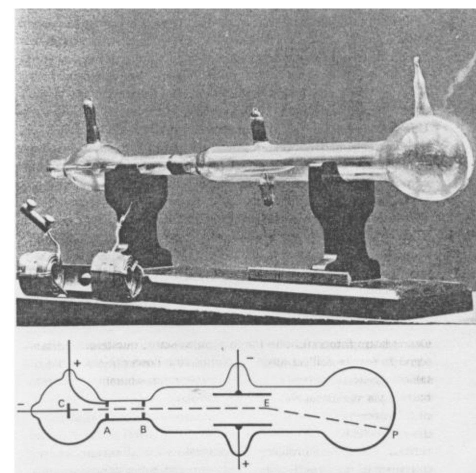


1895
discovery of X rays

Wilhelm Conrad Röntgen

J.J. Thompson

1897
"discovery" of the electron



Courtesy Prof. Ugo Amaldi

Tools for (medical) physics: the cyclotron

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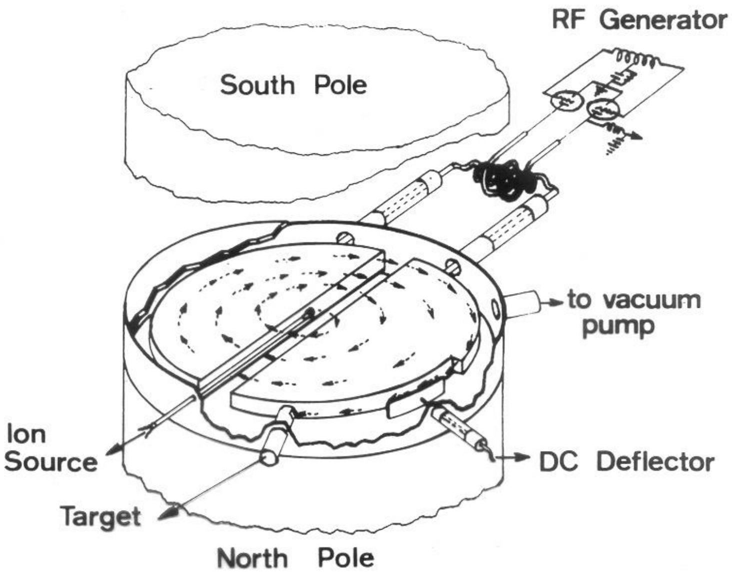
1930
Ernest Lawrence invents the cyclotron



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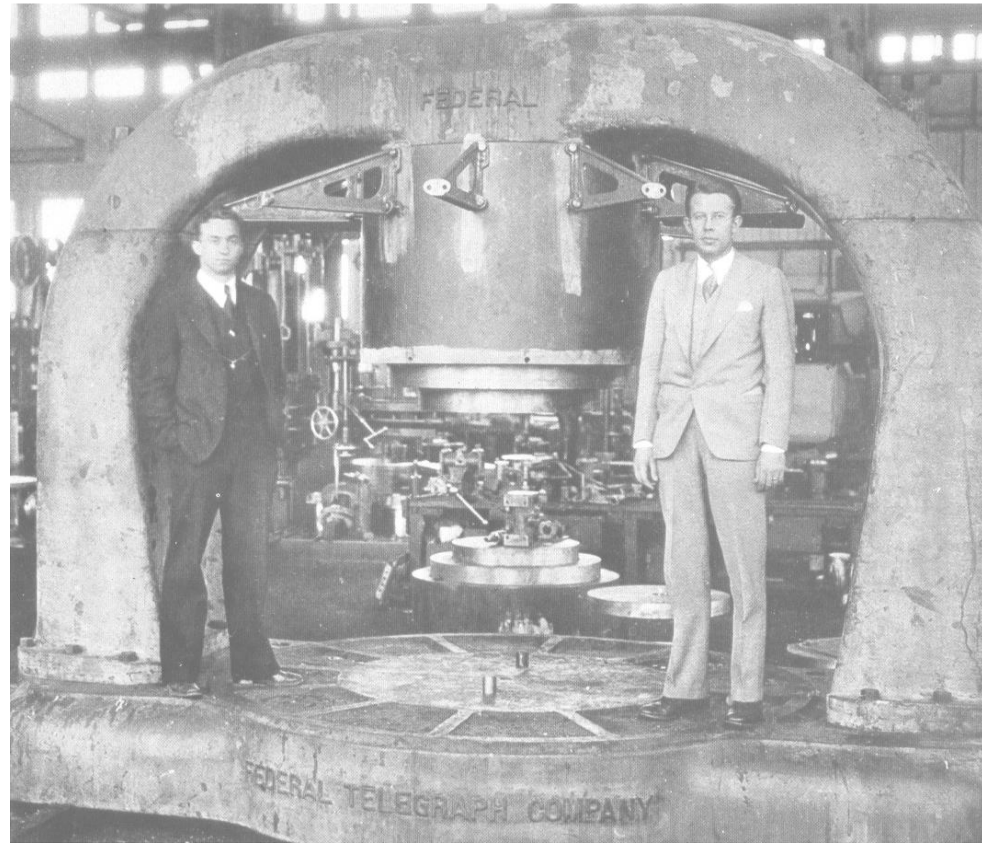


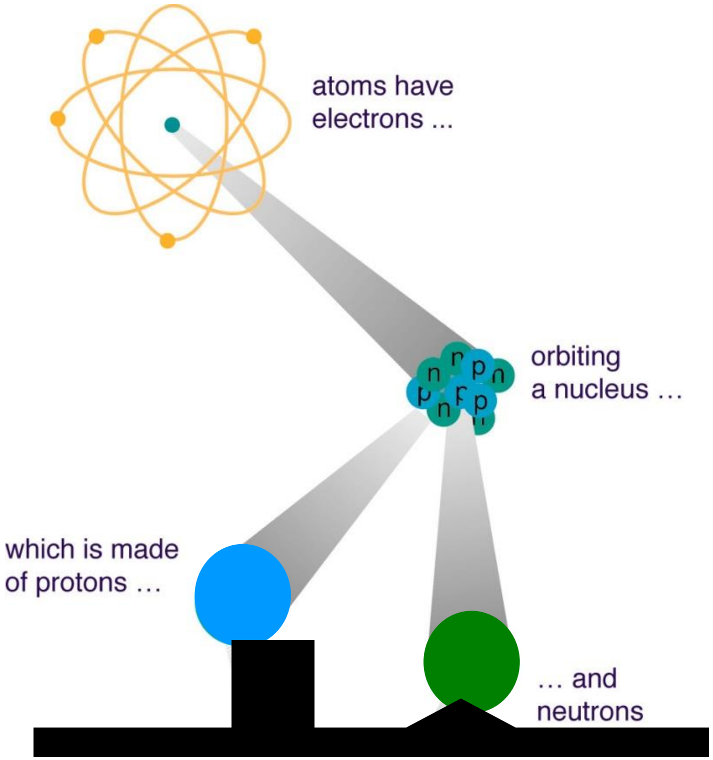
M. S. Livingston and E. Lawrence with the 25 inch cyclotron

James Chadwick
(1891 – 1974)

Courtesy Prof. Ugo Amaldi

1932

Discovery of the neutron



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

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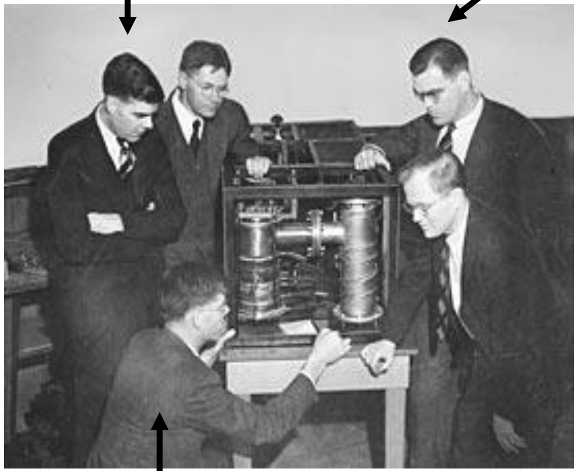
Sigmur Varian

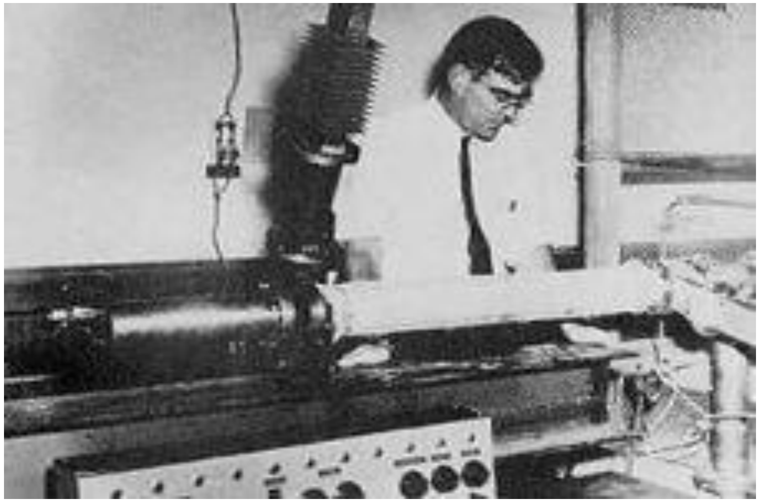
William W. Hansen



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

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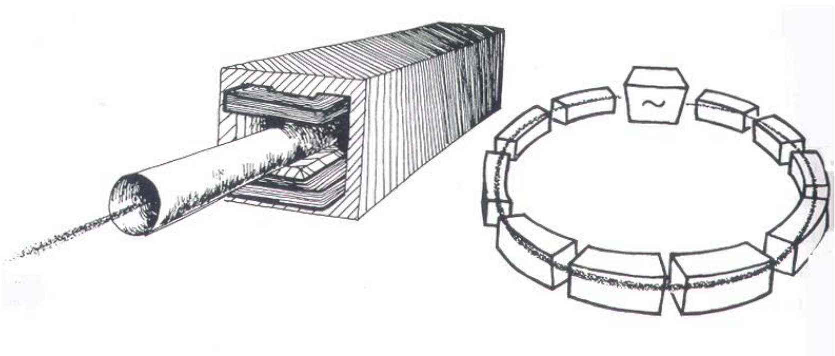
Tools for (medical) physics: the synchrotron

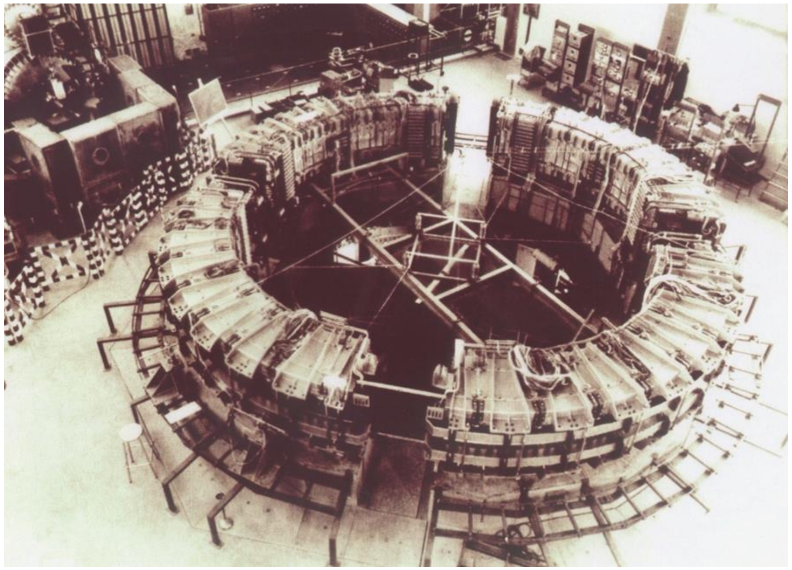
1945: E. McMillan and V.J. Veksler

discover the principle of phase stability



1 GeV electron synchrotron

Frascati - INFN - 1959



6 GeV proton synchrotron

Bevatron - Berkeley - 1954

Courtesy Prof. Ugo Amaldi

Particle accelerators operational in the world

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Three main applications: 1) Scientific research, 2) Medical applications 3) Industrial uses

Accelerators	1968 [1]	1970 [2]	1989 [3]	1994 [4, 5]	1998 [6–8]	2000 [9, 10]	2004 [11, 12]	2007 [13, 14]	2009 [15, 16]	2012 [17, 18]	2014 forecast
Industrial accelerators,	~2000	~2700	>4000	>4500	~7500	~8500	>8500	~17 900	22 500	25 300	27 000
including											
Electron accelerators rated to energies in excess of 300 keV			~650	1500	1500	1500	>1500	2700	2750	~5000	~5000
Electron accelerators rated to energies below 300 keV			>350	>1000				4500	7000	7500	~8000
Ion implanters and accelerators for ion analysis			~3000	>2000	~6000	~7000	>7000	~9700	~10 000	~11 300	~12 000
Neutron generators								~1000	~2000	~2000	~2000
Accelerators in science				~1000	~1200	~1200	~1200	~1200	~1200	~1200	~1200
Accelerators in medcine,		306	>2500	~4200	~4700	~5200	~8500	~9650	~11 600	~13 000	~14 000
including											
Electron accelerators			~2500	~4000	~4500	~5000	~7500	~9000	>11 000	~12 000	~13 000
Proton and ion accelerators (radiotherapy) [19]			11	17	20	20	25	29	32	39	~59
Production of radioisotopes for medicine				~200	~200	~200	~260	>550	>600	~1000	~1100
Total	~2000	~3000	>6500	>9700	>13 500	>15 000	>18 000	~27 500	~30 000	~39 500	41 000

A. P. Chernyaev and S. M. Varzar, Particle Accelerators in Modern World, Physics of Atomic Nuclei, 2014, Vol. 77, No. 10, pp. 1203–1215.

Particle accelerators for medical uses

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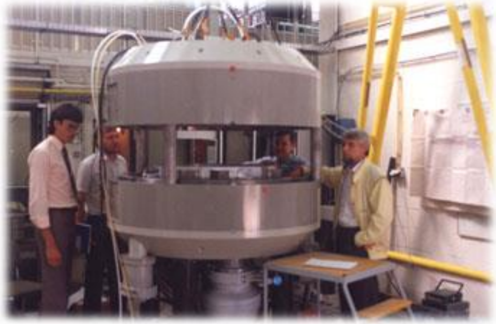
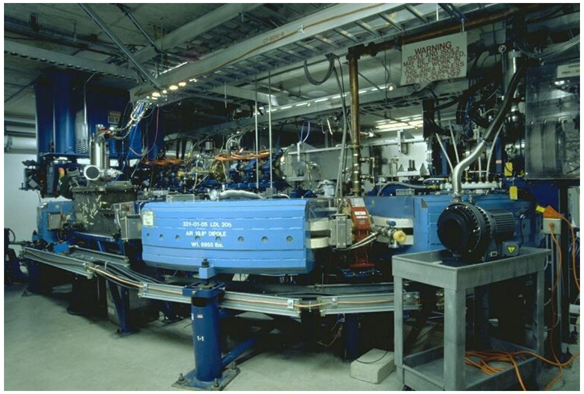
I. Production of radionuclides with (low-energy) cyclotrons
   I. Imaging (PET and SPECT)
   II. Therapy
II. Electron linacs for conventional radiation therapy (including advanced modalities)
III. Medium-energy cyclotrons and synchrotrons for hadron therapy with protons (250 MeV) or light ion beams (400 MeV/u ^{12}C-ions)
IV. Compact proton accelerators for BNCT





Radionuclide production

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The use of radionuclides in the physical and biological sciences can be broken down into three general categories:

- Radiotracers
- Imaging (95% of medical uses)
  SPECT (^{99m}Tc, ^{201}Tl, ^{123}I)
  PET (^{11}C, ^{13}N, ^{15}O, ^{18}F)
- Therapy (5% of medical uses)
  - Brachytherapy (^{103}Pd)
  - Targeted therapy (^{211}At, ^{213}Bi)

Relevant physical parameters (function of the application)

- Type of emission (α, β^+, β^-, γ)
- Energy of emission
- Half-life
- Radiation dose (essentially determined by the parameters above)

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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

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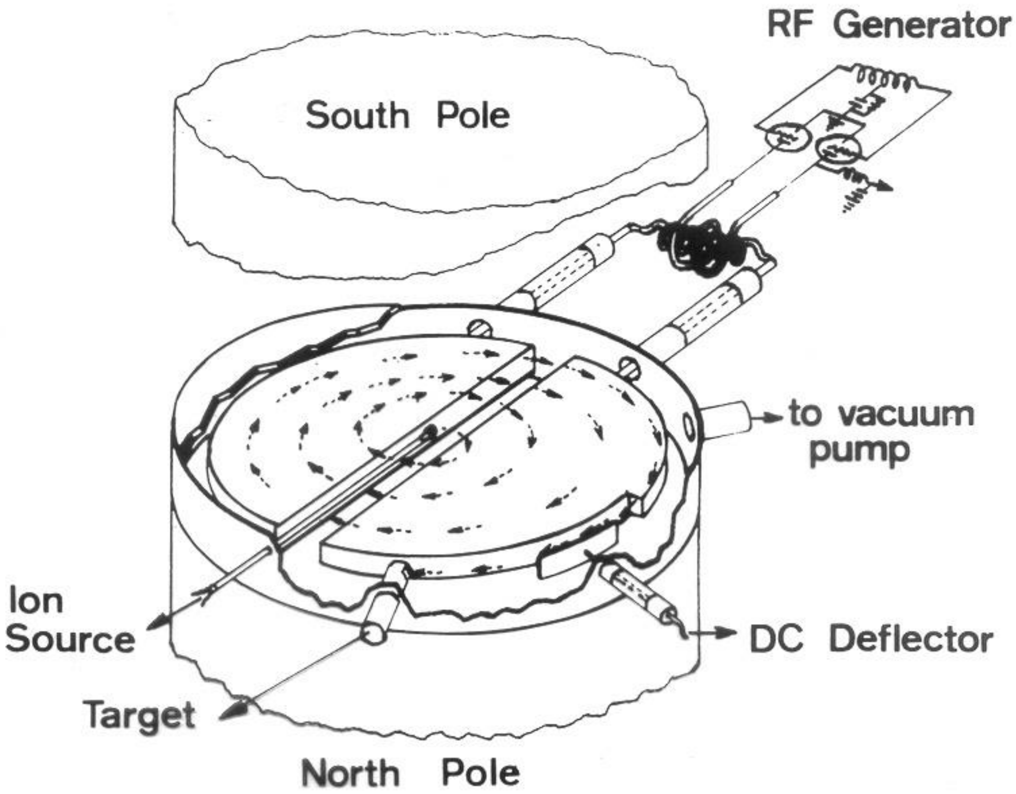

Scanditronix MC40

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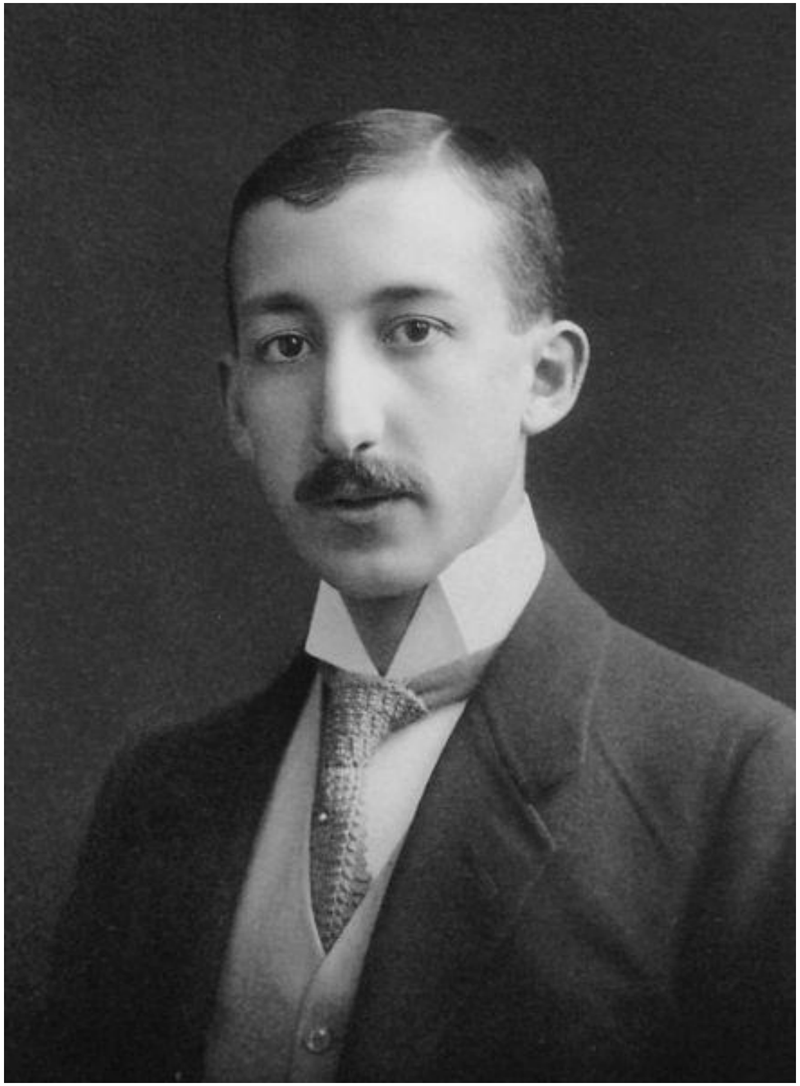
- 1911: **first practical application of a radioisotope** (as *radiotracer*) by G. de Hevesy, a young Hungarian student working with naturally radioactive materials in Manchester

- 1924: de Hevesy, who had become a physician, used radioactive isotopes of lead as tracers in bone studies



Historical development of radioisotopes in medicine

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- 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
- 1955: **first cyclotron installed in a hospital** (Hammersmith, London)
- 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

Emission versus transmission imaging

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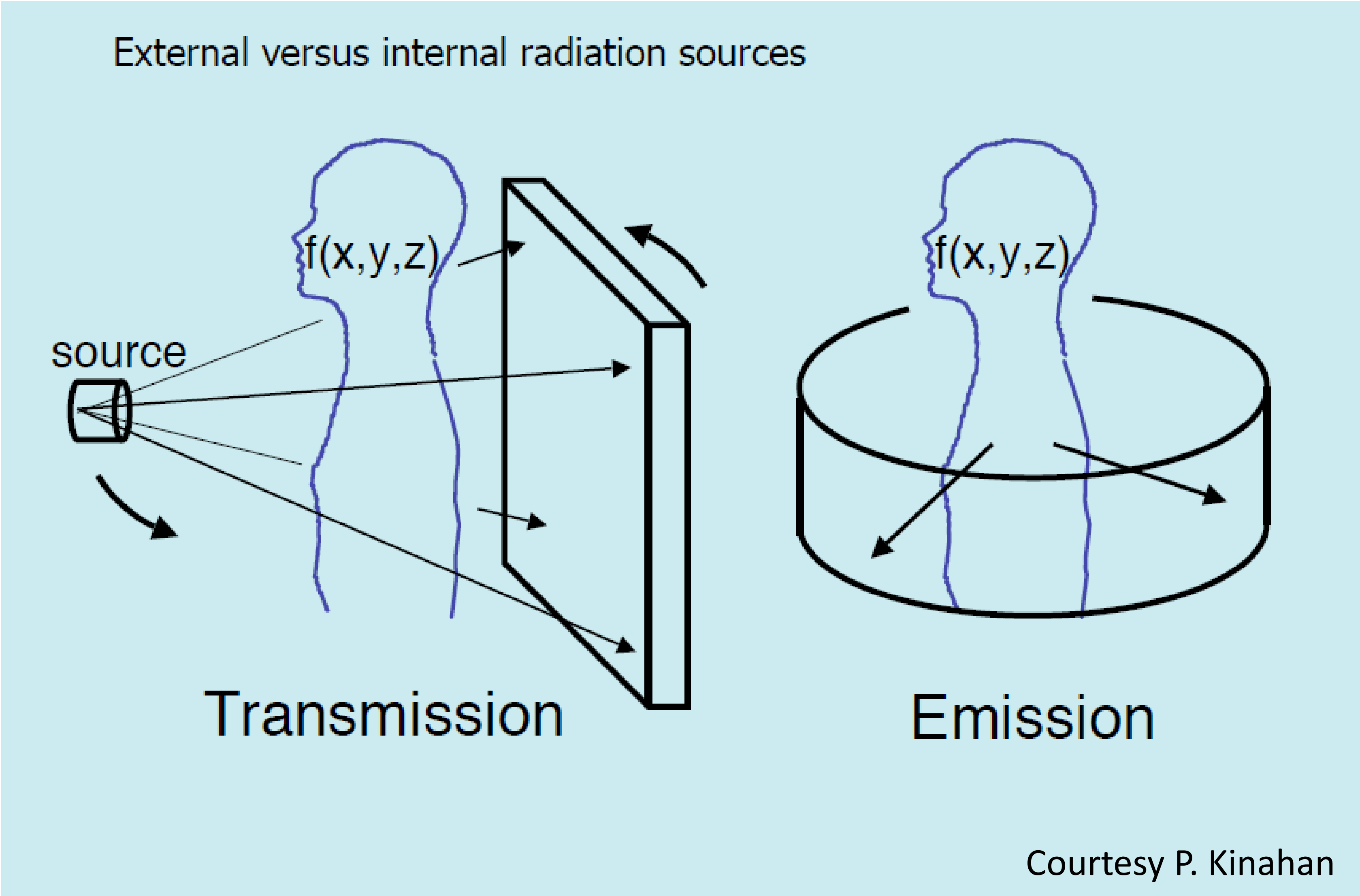

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A conventional X-ray image is basically a shadow: you shine a “light” on one side of the body, and a piece of film or a silicon sensor on the other side registers the silhouette of the bones (to be more precise, organs and tissues of different densities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

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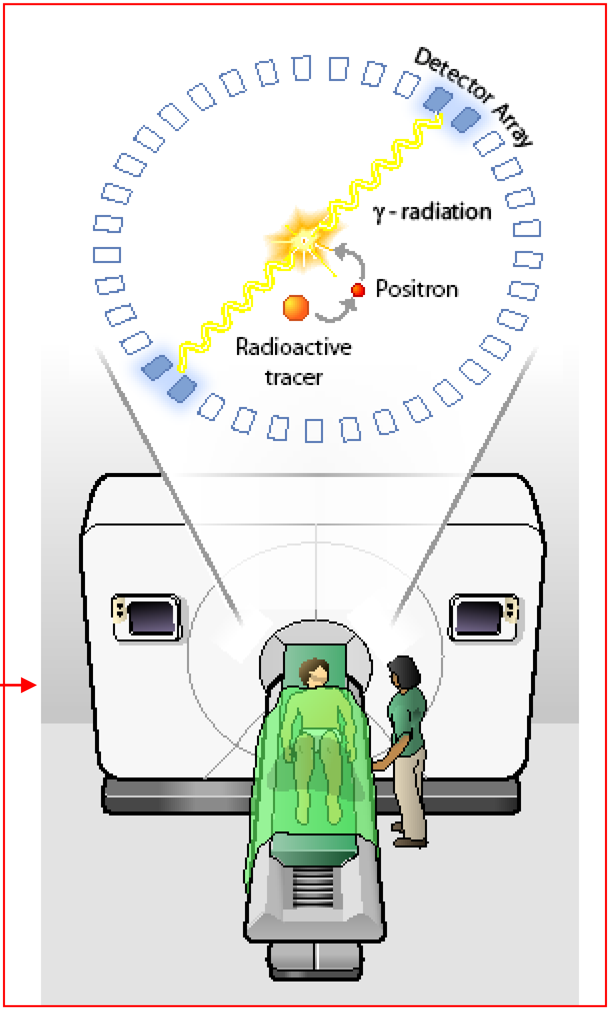
Cyclotron

PET camera



Radiochemistry

J. Long, “The Science Creative Quarterly”,scq.ubc.ca

Positron Emission Tomography (PET)

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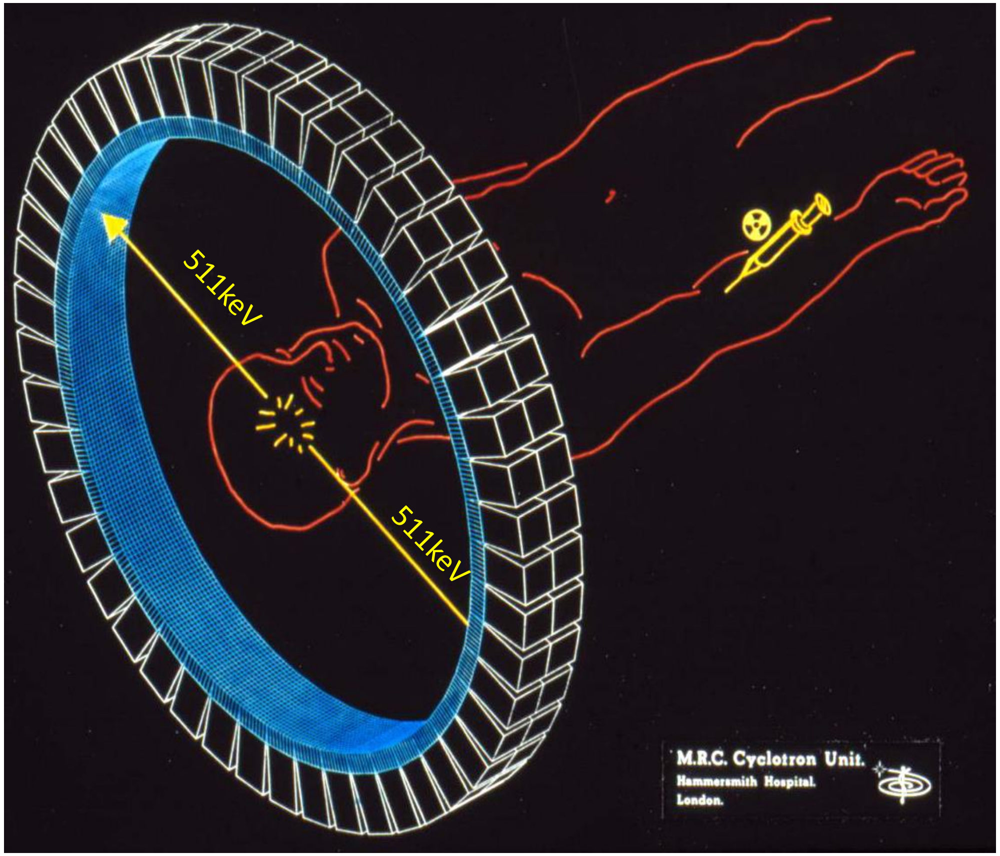

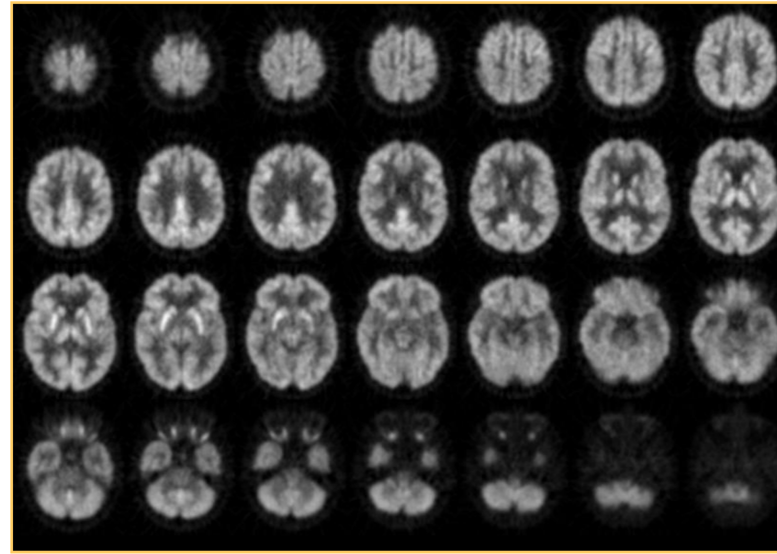

COVERAGE:
~ 15-20 cm
SPATIAL RESOLUTION:
~ 5 mm
SCAN TIME to cover an entire organ:
~ 5 min
CONTRAST RESOLUTION:
depends on the radiotracer

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$$N(t) = N_0 e^{-\lambda t} \text{ or } A(t) = A(0)e^{-\lambda t}$$

where:

- $N(t)$ = number of radioactive atoms at time t
- N_0 = initial number of radioactive atoms at $t = 0$
- $A(t)$ = activity at time t
- $A(0)$ = initial activity at $t = 0$
- e = base of natural logarithm = 2.71828…
- λ = decay constant = $1/\tau = \ln 2/T_{1/2} = 0.693/T_{1/2}$
- t = time

and remembering that:

$$-dN/dt = \lambda N$$

$$A = \lambda N$$

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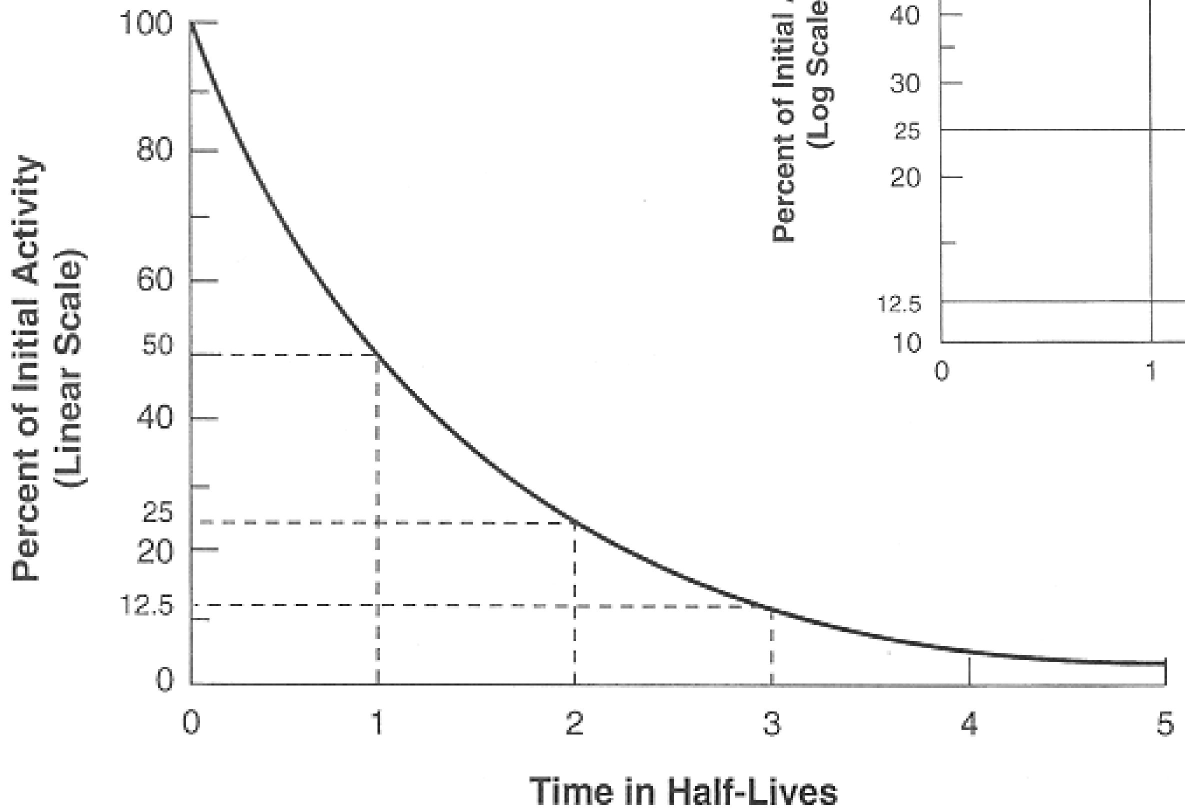
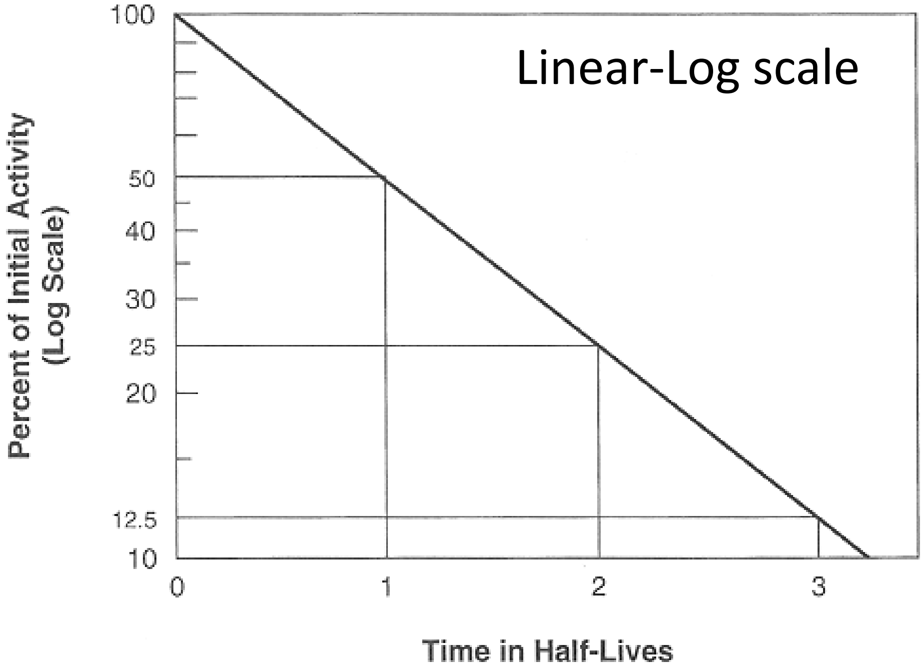
Linear-Linear scale



Linear-Log scale



Generalized decay scheme

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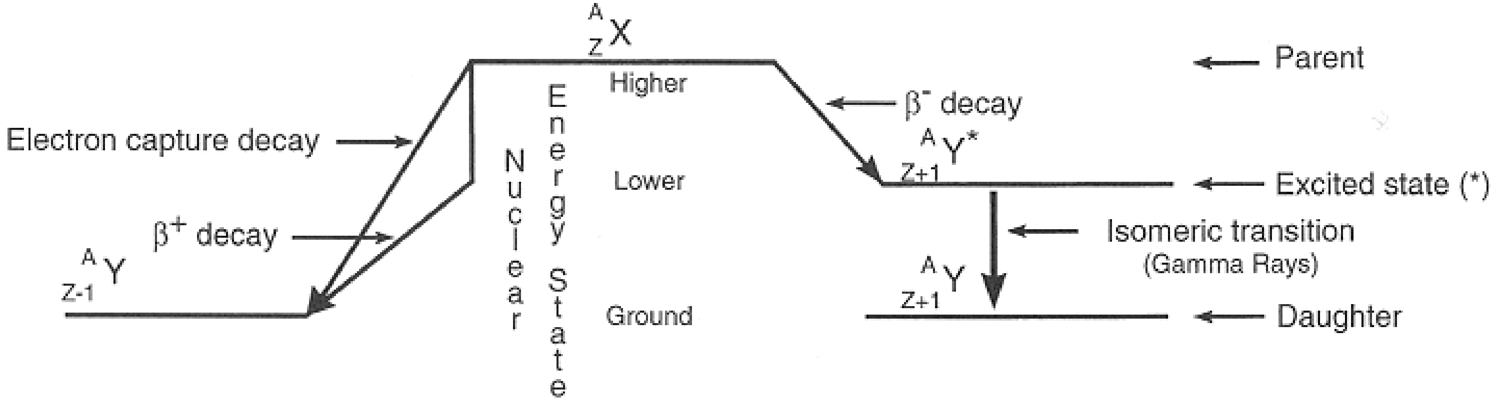

The "ideal" diagnostics radiopharmaceutical

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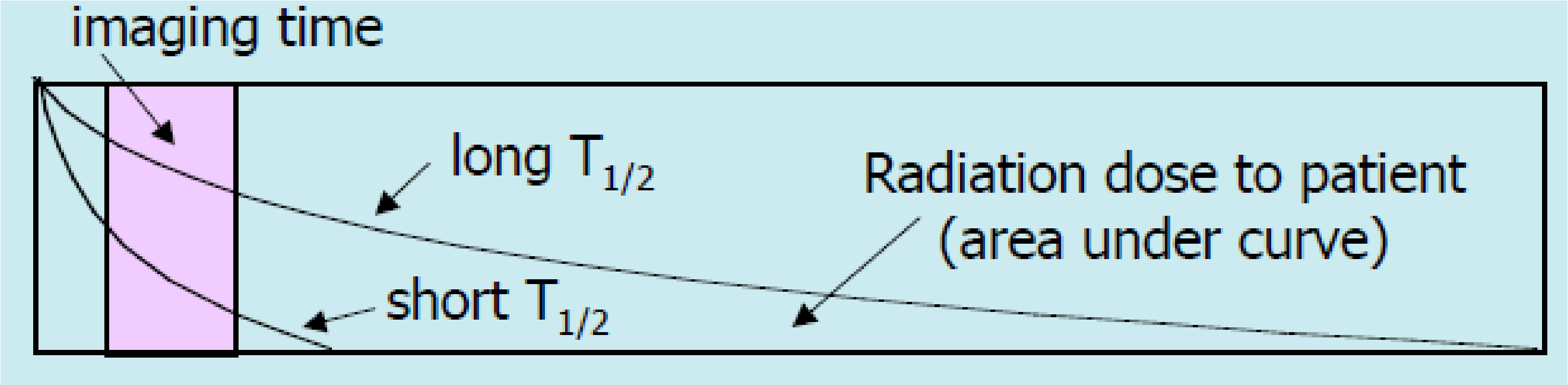
a) Be readily available at a low cost
b) Be a pure gamma emitter, i.e., have no particle emission such as alphas and betas (these particles contribute radiation dose to the patient while not providing any diagnostic information)
c) Have a short effective biological half-life (so that it is eliminated from the body as quickly as possible)
d) Have a high target to non-target ratio so that the resulting image has a high contrast (the object has much more activity than the background)
e) Follow or be trapped by the metabolic process of interest



$$A(t) = A(0)e^{-t(\ln(2)/T_{1/2})}$$

The essential steps in accelerator radionuclide production

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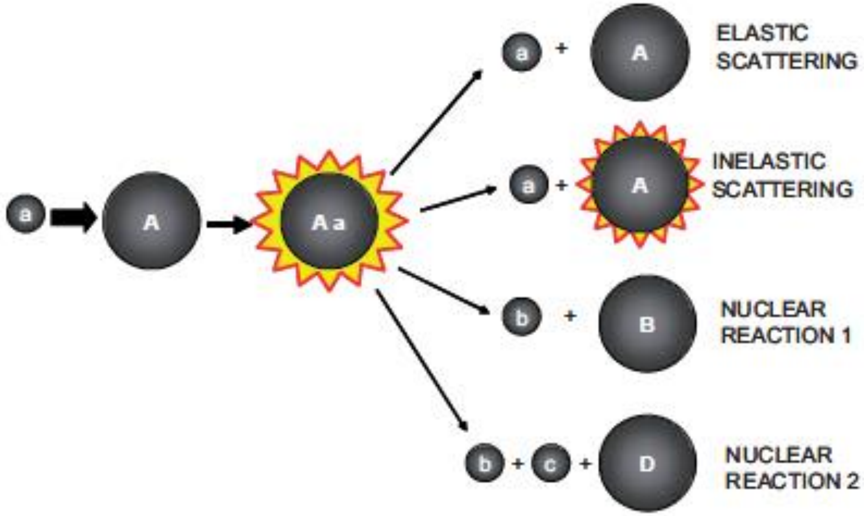
1. Acceleration of charged particles in a cyclotron
2. Beam transport (*or not*) to the irradiation station via a transfer line
3. Irradiation of target (solid, liquid, gas) – *internal or external*
4. Nuclear reaction occurring in the target (e.g. $^{A}X_{Z}(p,n)^{A}y_{Z+1}$)
5. Target processing and material recovering
6. Labeling of radiopharmaceuticals and quality control



a = bombarding particle
b, c = emitted particles
A, B, D = nuclei

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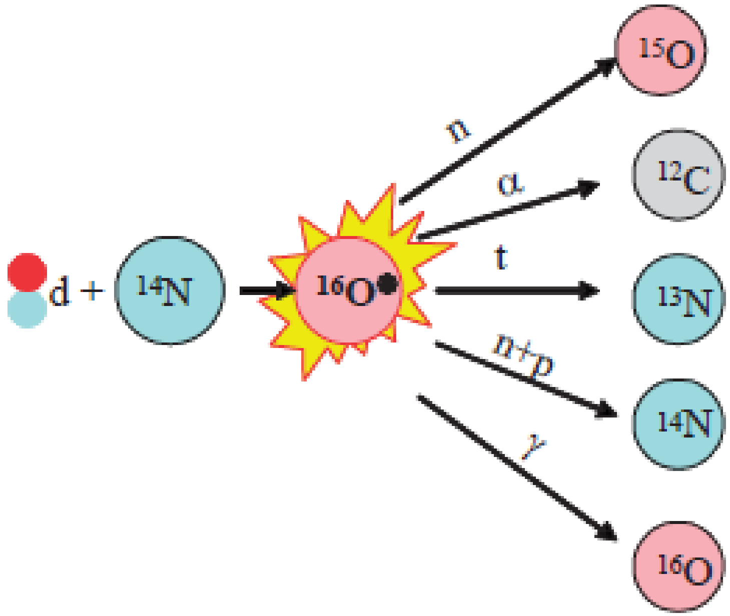
Q values and thresholds of nuclear decomposition for the reaction of a deuteron with a ^{14}N nucleus after forming the compound nucleus ^{16}O



Q value	Threshold
5.1 MeV	0 MeV
13.6 MeV	0 MeV
-4.3 MeV	4.9 MeV
-2.2 MeV	2.5 MeV
20.7 MeV	0 MeV

Q value = **the amount of energy absorbed or released during the nuclear reaction**

$$Q\ (\text{MeV}) = 931.5\ (m_1 + M_2 - m_3 - M_4)$$

Production rate and cross section

$$\frac{dn}{dt} = R = nI(1 - e^{-\lambda t}) \int_{Eth}^{E0} \frac{\sigma(E)}{dE/dx} dE$$

R = the number of nuclei formed per second
n = the target thickness in nuclei per cm^2
I = incident particle flux per second (related to the beam current)
λ = decay constant = (ln 2)/$T_{1/2}$
t = irradiation time in seconds
σ = reaction cross-section, or probability of interaction (cm^2), function of E
E = energy of the incident particles
x = distance travelled by the particle

and the integral is from the initial energy (threshold of reaction) to the final energy of the incident particle along its path

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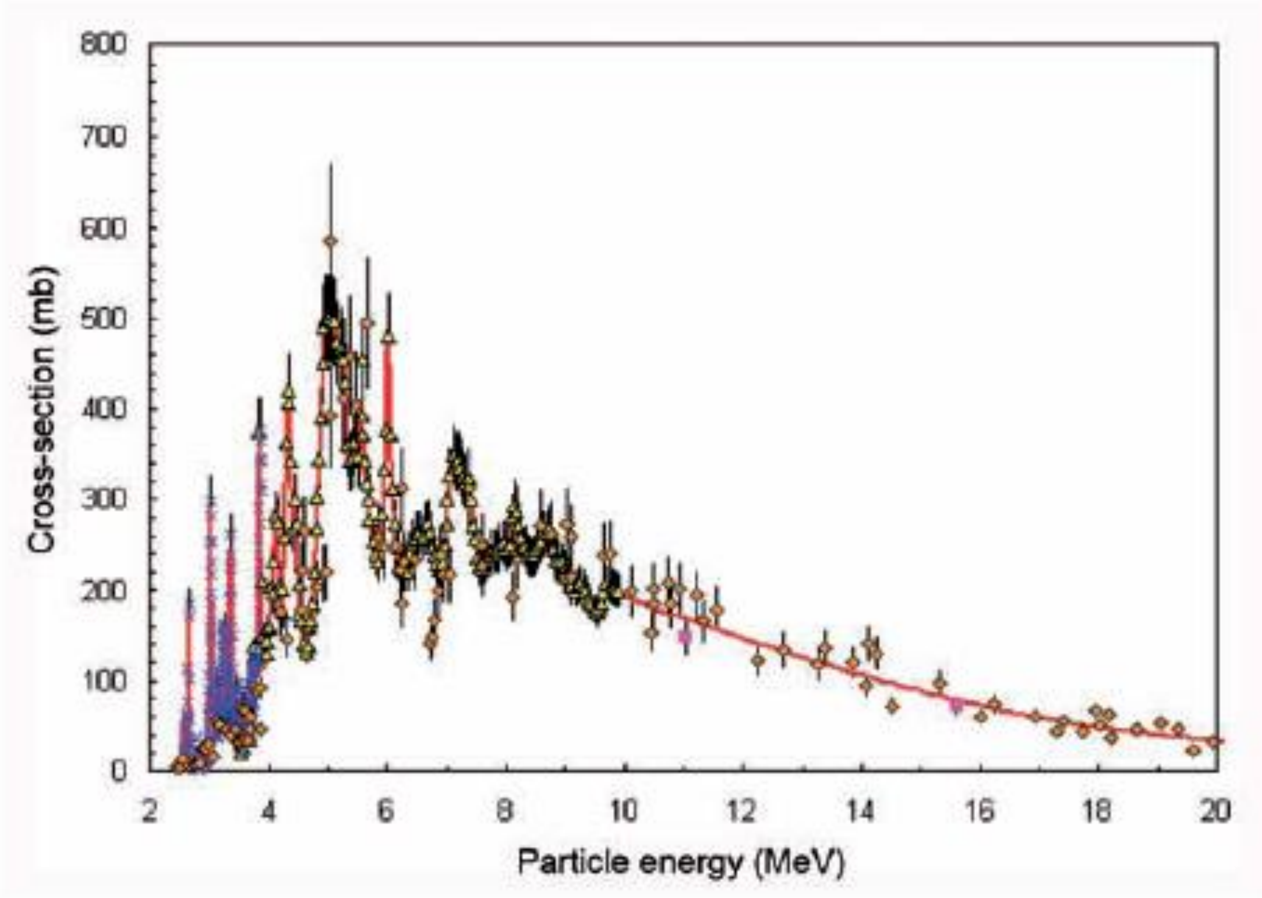
Excitation function of the $^{18}O(p,n)^{18}F$ reaction



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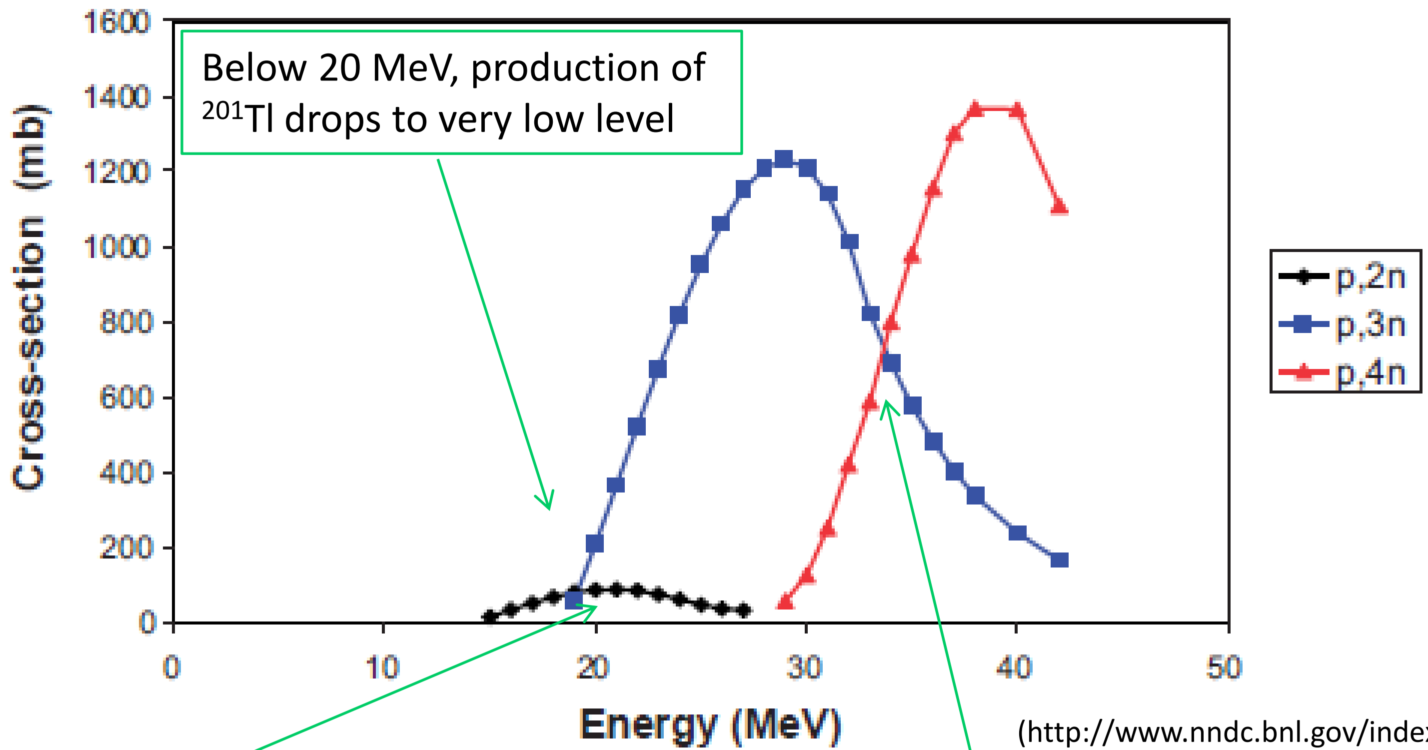
The nuclear reaction used for the production of ^{201}Tl is the $^{203}Tl(p,3n)^{201}Pb$

^{201}Pb ($T_{1/2}$ = 9.33 h) → ^{201}Tl ($T_{1/2}$ = 76.03 h)

Cross-section versus energy plot for the $^{203}Tl(p,2n)^{202}Pb$, $^{203}Tl(p,3n)^{201}Pb$ and $^{203}Tl(p,4n)^{200}Pb$ reactions



(http://www.nndc.bnl.gov/index.jsp)

Around threshold, production of ^{201}Tl is comparable to that of ^{202}Pb

Above 30 MeV, production of ^{200}Pb becomes significant

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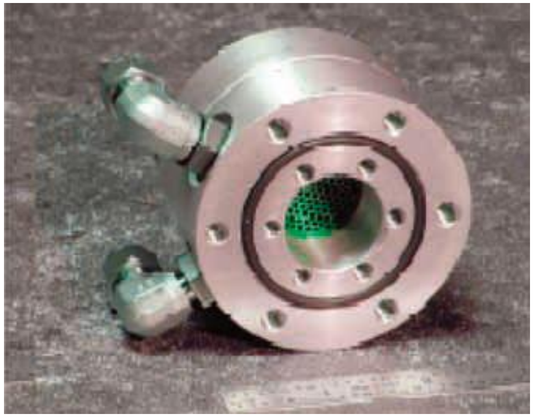
Internal (beam is not extracted from the cyclotron)
External (extracted beam + beam transport to target)

Simultaneous irradiation of more than one target (H^- cyclotrons)

The target can be
- **Solid**
- **Liquid**
- **Gaseous**

^{18}O water target
to produce ^{18}F via $^{18}O(p,n)$



Principal constraints on gas targets
- removal of heat from the gas (gases are not very good heat conductors)
- the targets must be quite large in comparison with solid or liquid targets in order to hold the necessary amount of material.

Production reactions (1)

Radionuclide	Use	Half-life	Reaction	Energy (MeV)
^{99m}Tc	SPECT imaging	6 h	$^{100}Mo(p,2n)$	30
^{123}I	SPECT imaging	13.1 h	$^{124}Xe(p,n)^{123}Cs$ $^{124}Xe(p,pn)^{123}Xe$ $^{124}Xe(p,2pn)^{123}I$ $^{123}Te(p,n)^{123}I$ $^{124}Te(p,2n)^{123}I$	27 15 25
^{201}Tl	SPECT imaging	73.1 h	$^{203}Tl(p,3n)^{201}Pb \rightarrow ^{201}Tl$	29
^{11}C	PET imaging	20.3 min	$^{14}N(p,\alpha)$ $^{11}B(p,n)$	11–19 10
^{13}N	PET imaging	9.97 min	$^{16}O(p,\alpha)$ $^{13}C(p,n)$	19 11

Production reactions (2)

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Radionuclide	Use	Half-life	Reaction	Energy (MeV)
^{15}O	PET imaging	2.03 min	$^{15}N(p,n)$ $^{14}N(d,2n)$ $^{16}O(p,pn)$	11 6 > 26
^{18}F	PET imaging	110 min	$^{18}O(p,n)$ $^{20}Ne(d,\alpha)$ $^{nat}Ne(p,X)$	11-17 8-14 40
^{64}Cu	PET imaging and radiotherapy	12.7 h	$^{64}Ni(p,n)$ $^{68}Zn(p,\alpha n)$ $^{nat}Zn(d,\alpha xn)$ $^{nat}Zn(d,2pxn)$	15 30 19 19
^{124}I	PET imaging and radiotherapy	4.14 d	$^{124}Te(p,n)$ $^{125}Te(p,2n)$	13 25

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- High LET decay products (Auger electrons, β-particles or α-particles)
- Radionuclide linked to a biologically active molecule that can be directed to a tumour site
- Beta emitting radionuclides are neutron rich ⟶ they are in general produced in reactors
- Some of the radionuclides that have been proposed as possible radiotoxic tracers are:

Sc-47	Cu-64	Cu-67	Br-77	Y-90
Rh-105	Pd-103	Ag-111	I-124	Pr-142
Pm-149	Sm-153	Gd-159	Ho-166	Lu-177
Re-186/188	Ir-194	Pt-199	At-211	Bi-213

Click here to learn about radionuclide generators

Radiation therapy

Treatment planning and dose delivery to tumour volume

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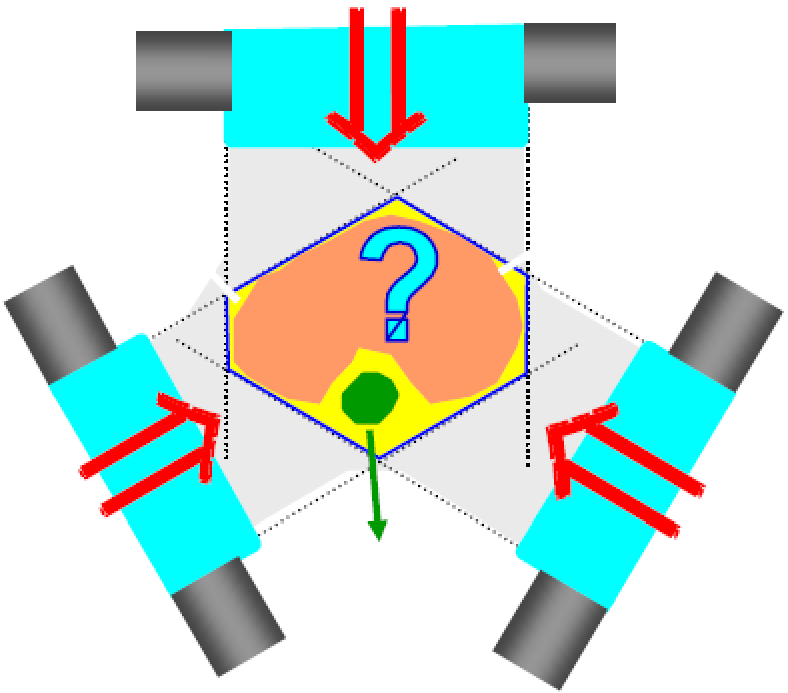

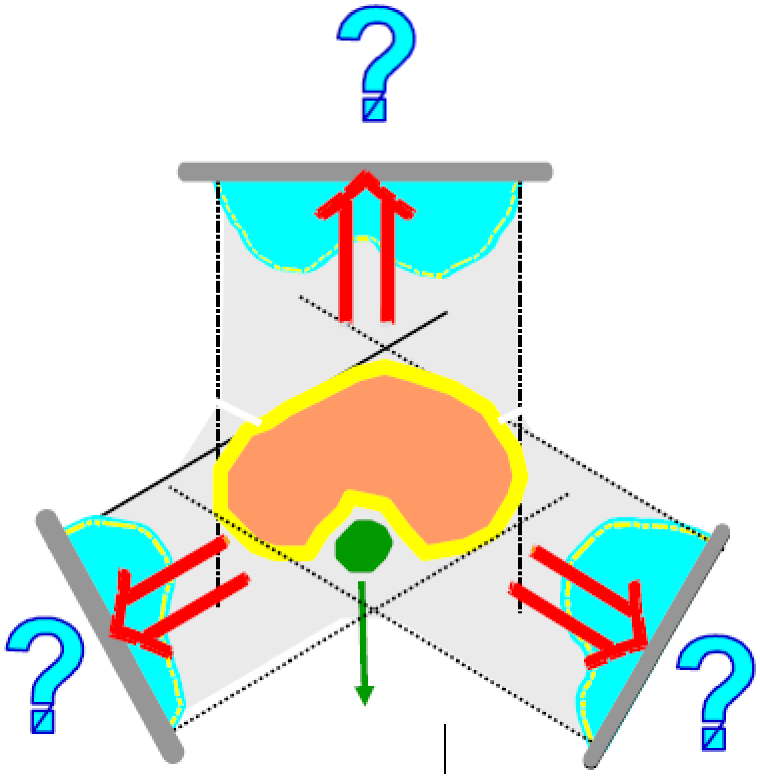

Tumour control and therapeutic window

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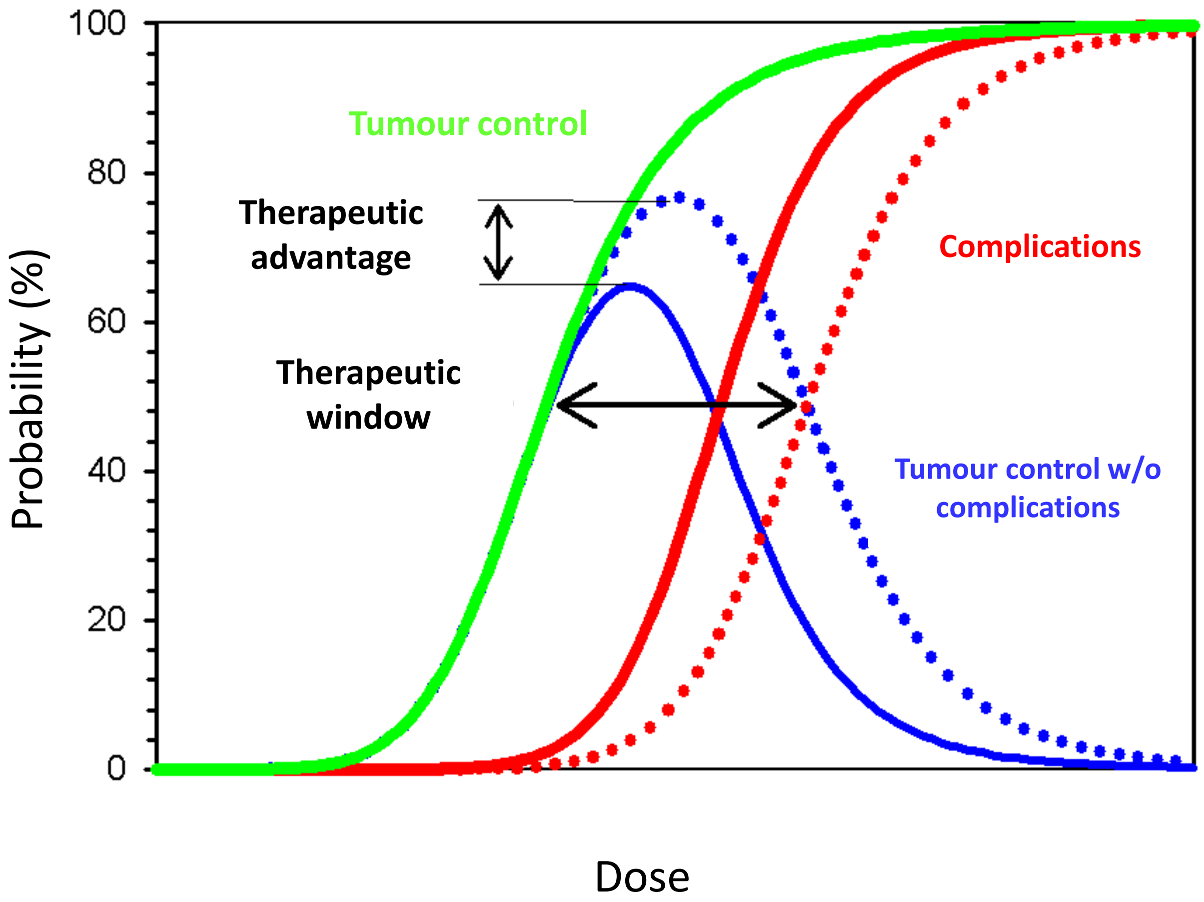

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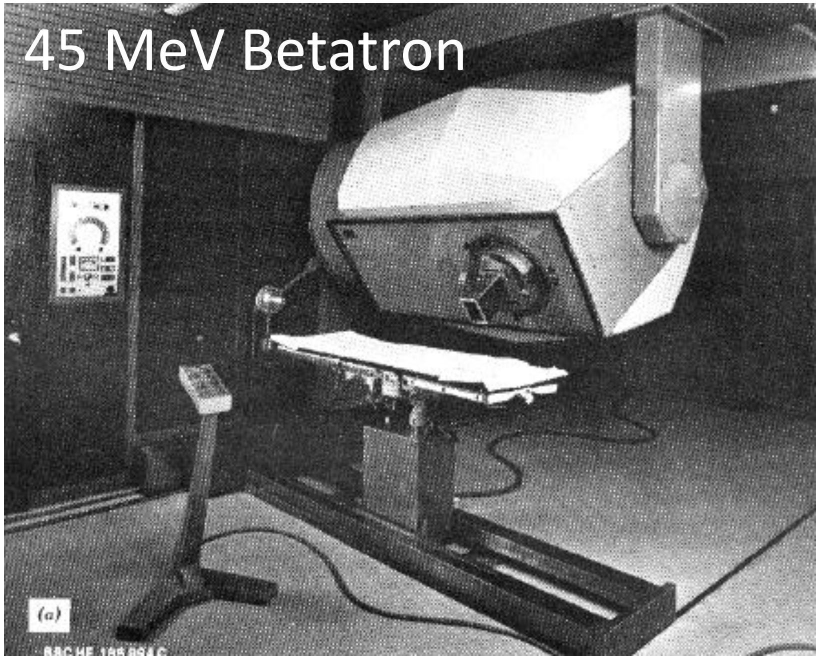


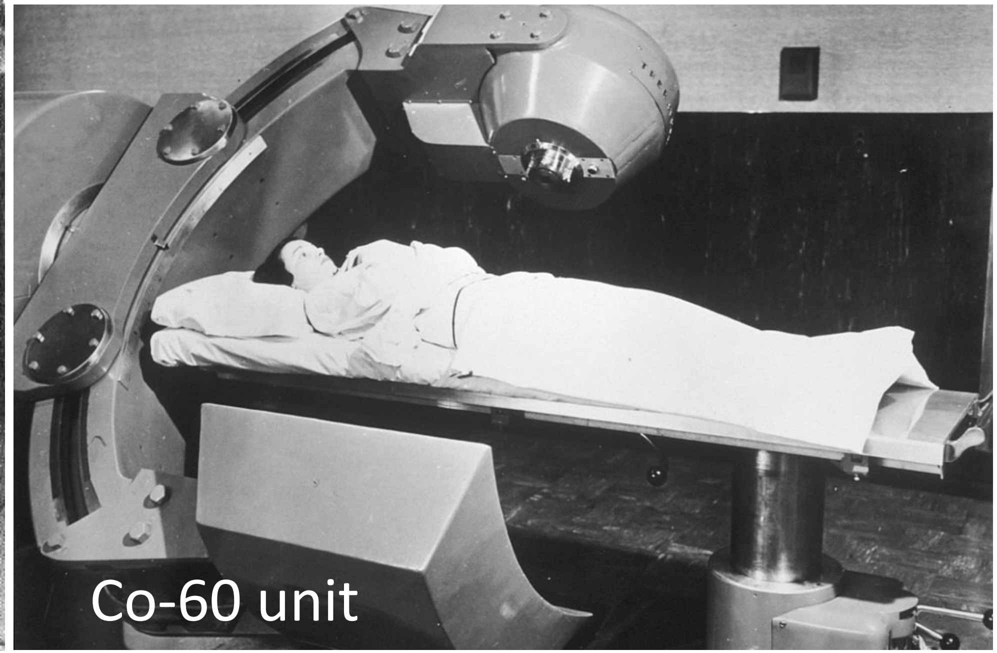
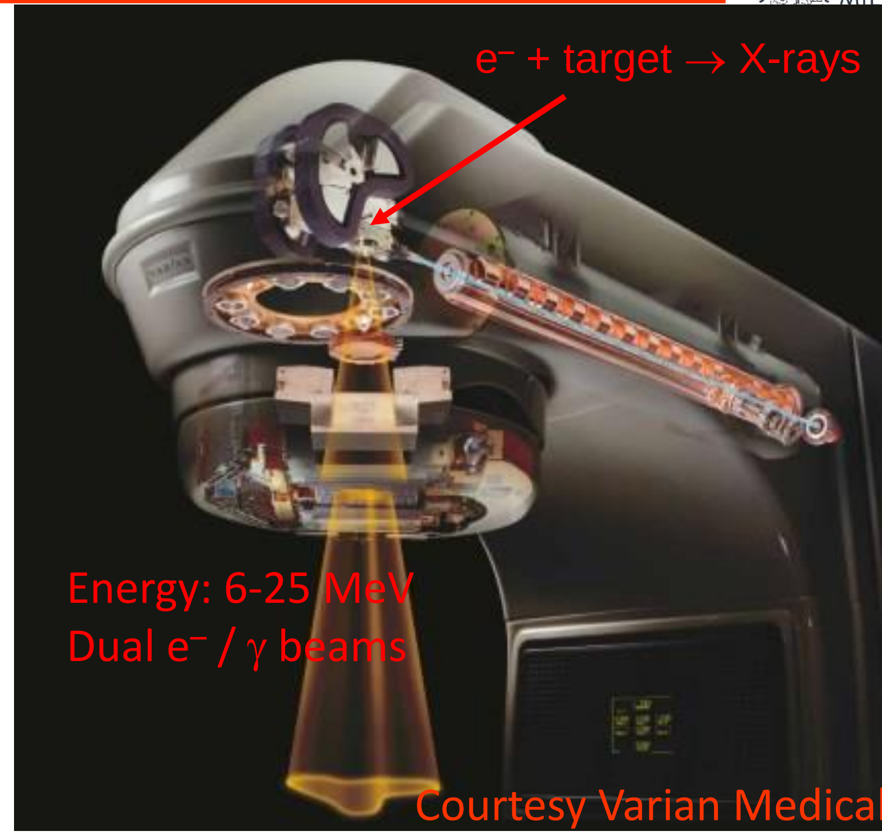


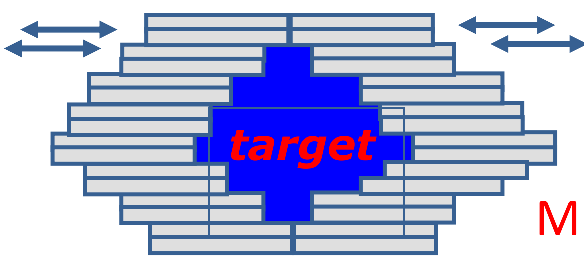
Photo: Wikipedia

Radiation therapy is much more than the radiation source. One also needs:

- diagnostic equipment, CT scanners
- treatment planning software
- patient set-up devices
- computers
- a broad range of professional figures

Betatron and microtron





Multi-leaf collimator

Cyber-knife robotic surgery system

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
- Dose rate @ 80 cm = 400 cGy/min

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

Intra-operative radiation therapy (IORT)

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- Small electron linac
- Energy 6 – 12 MeV
- Treatment with electrons only
- Single irradiation

Courtesy: myself!

Intensity modulated radiation therapy (IMRT)

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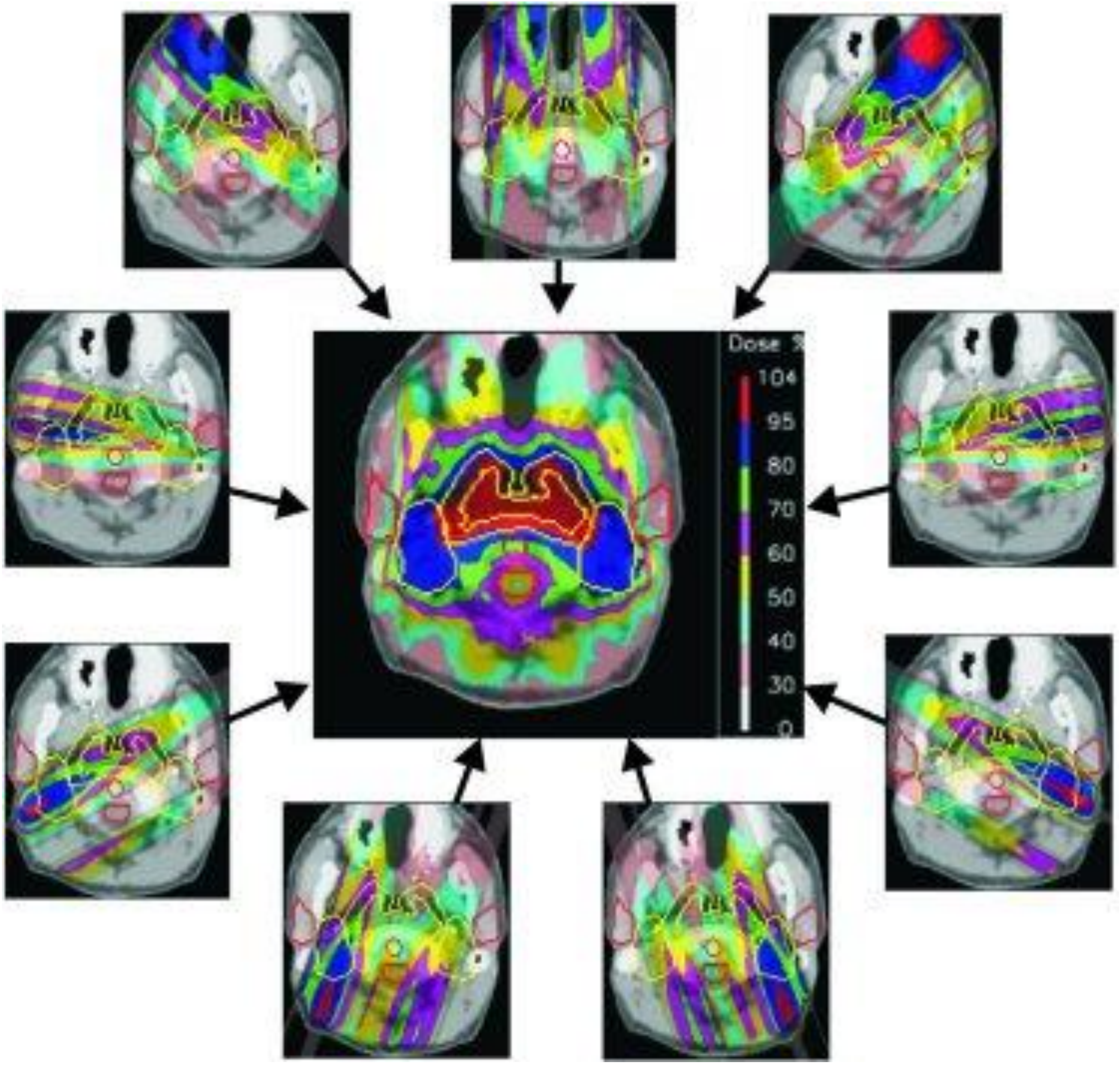

An example of intensity modulated treatment planning with photons. Through the addition of 9 fields it is possible to construct a highly conformal dose distribution with good dose sparing in the region of the brain stem (courtesy of T. Lomax, PSI).

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

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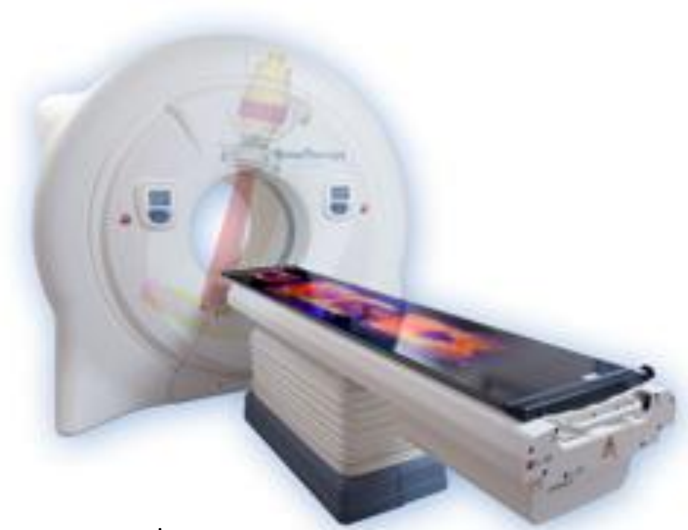
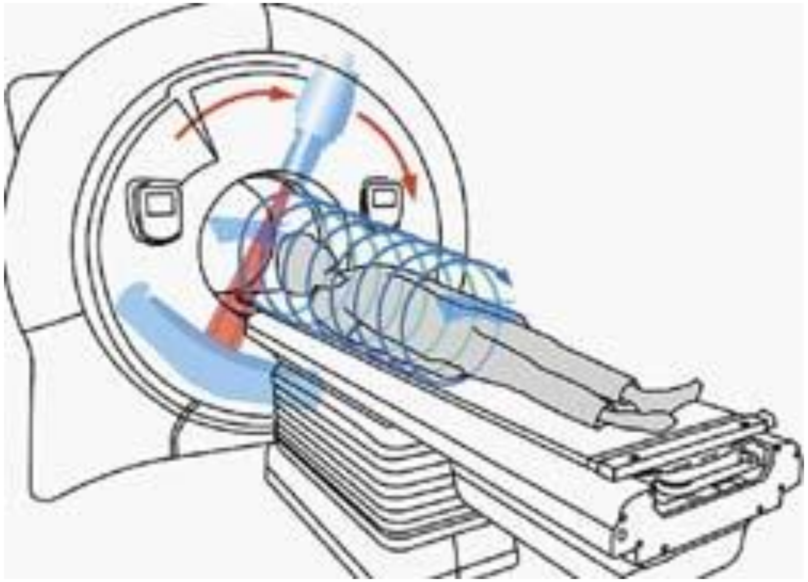
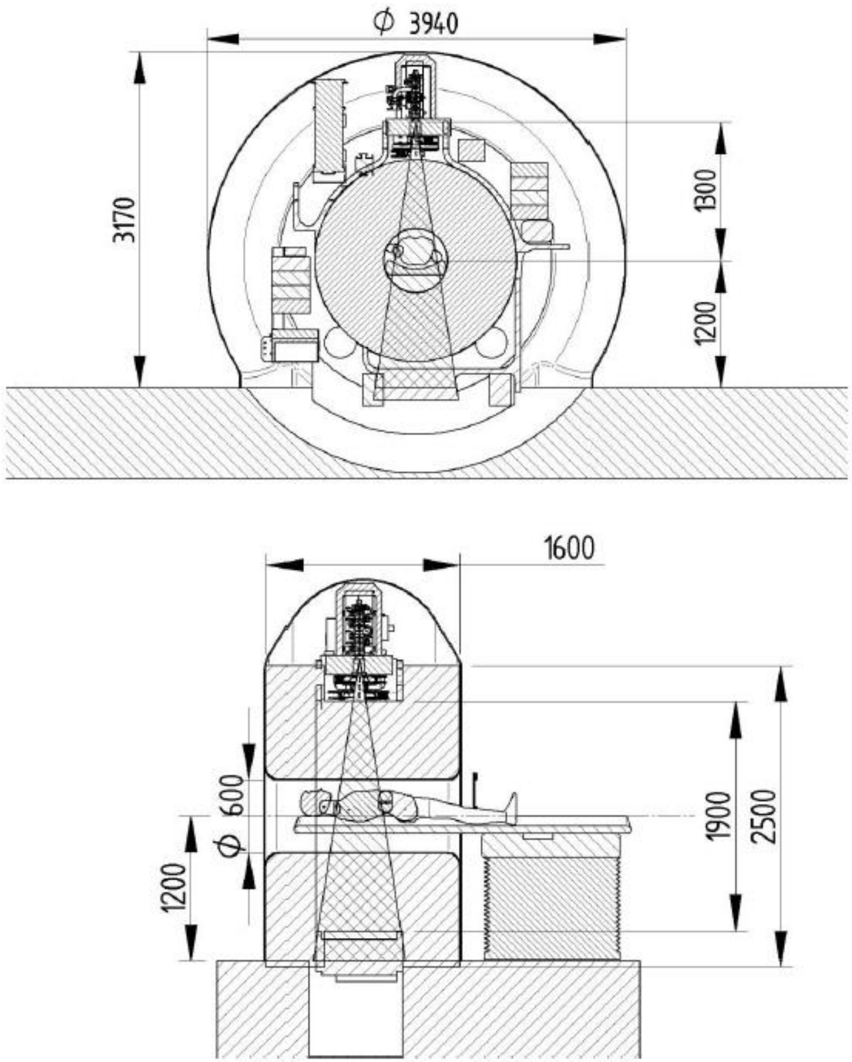


www.tomotherapy.com

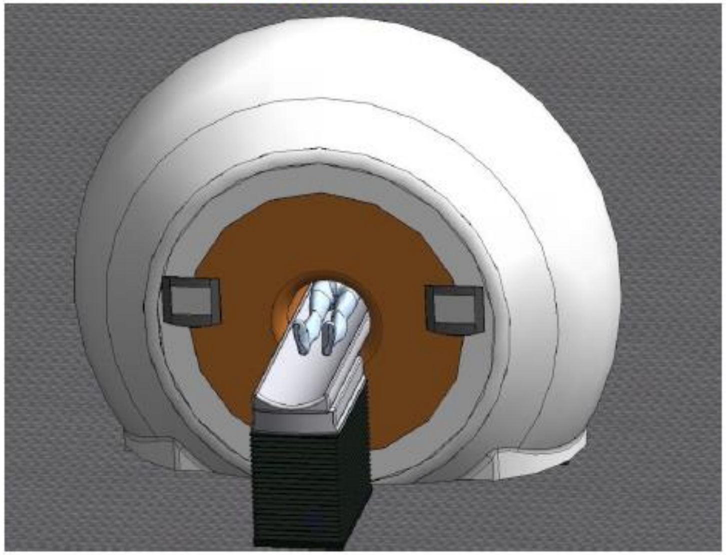


- Integrated CT guidance
  - Integrated CT scanner allowing efficient 3D CT imaging for ensuring the accuracy of treatment
- A binary multi-leaf collimator (MLC) for beam shaping and modulation
- A ring gantry design enabling TomoHelical delivery
  - As the ring gantry rotates in simultaneous motion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



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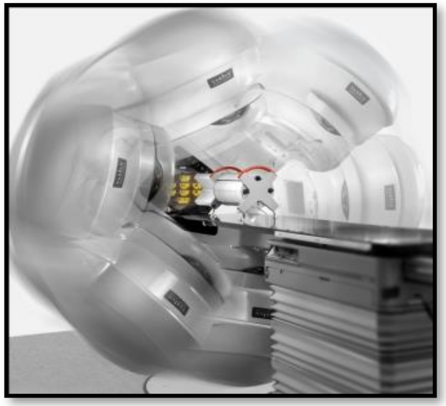
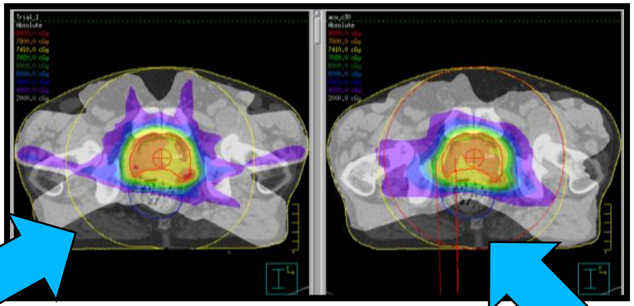
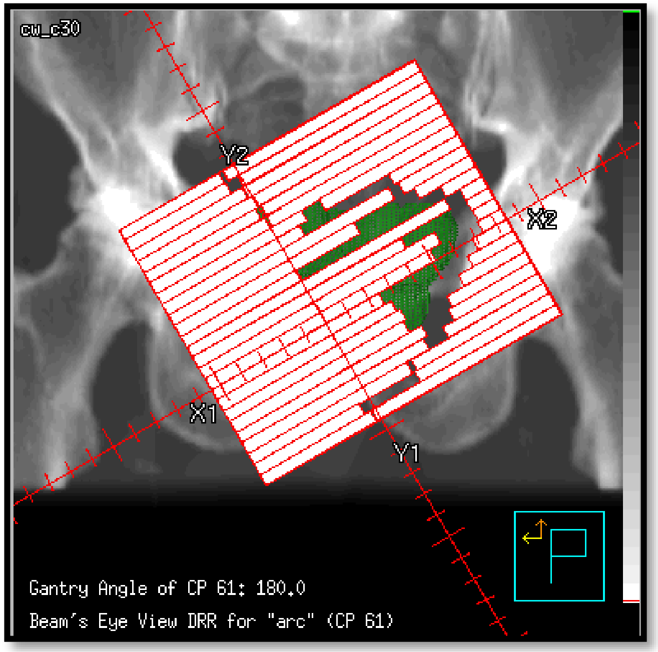
Rotate linac gantry while modulating the beam





Fixed 6 or so gantry angles

VMAT



Centre for Medical Radiation Physics
Name-Prof Peter Metcalfe
BSOC lecture 08
University of Wollongong

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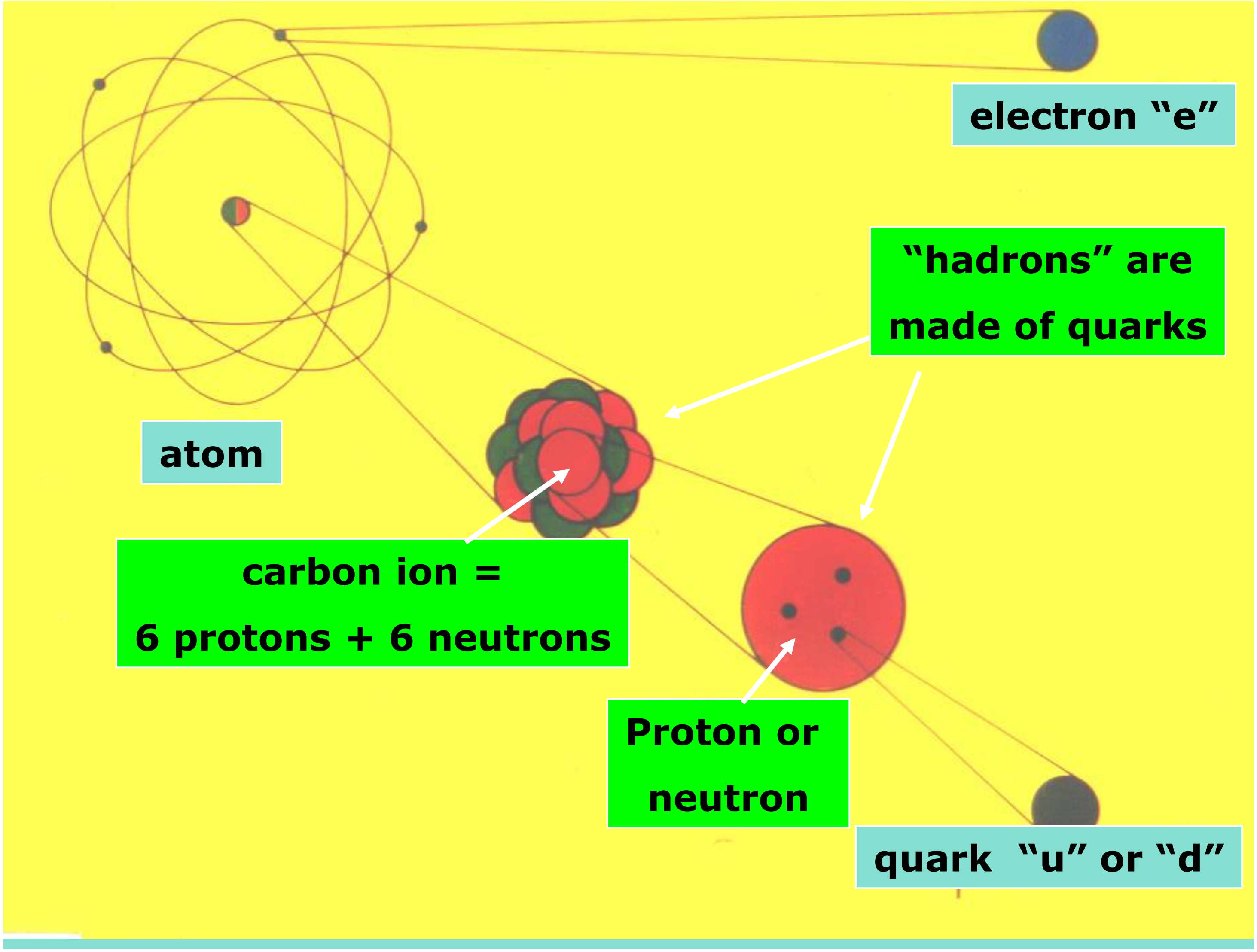

Particle therapy (hadron therapy)

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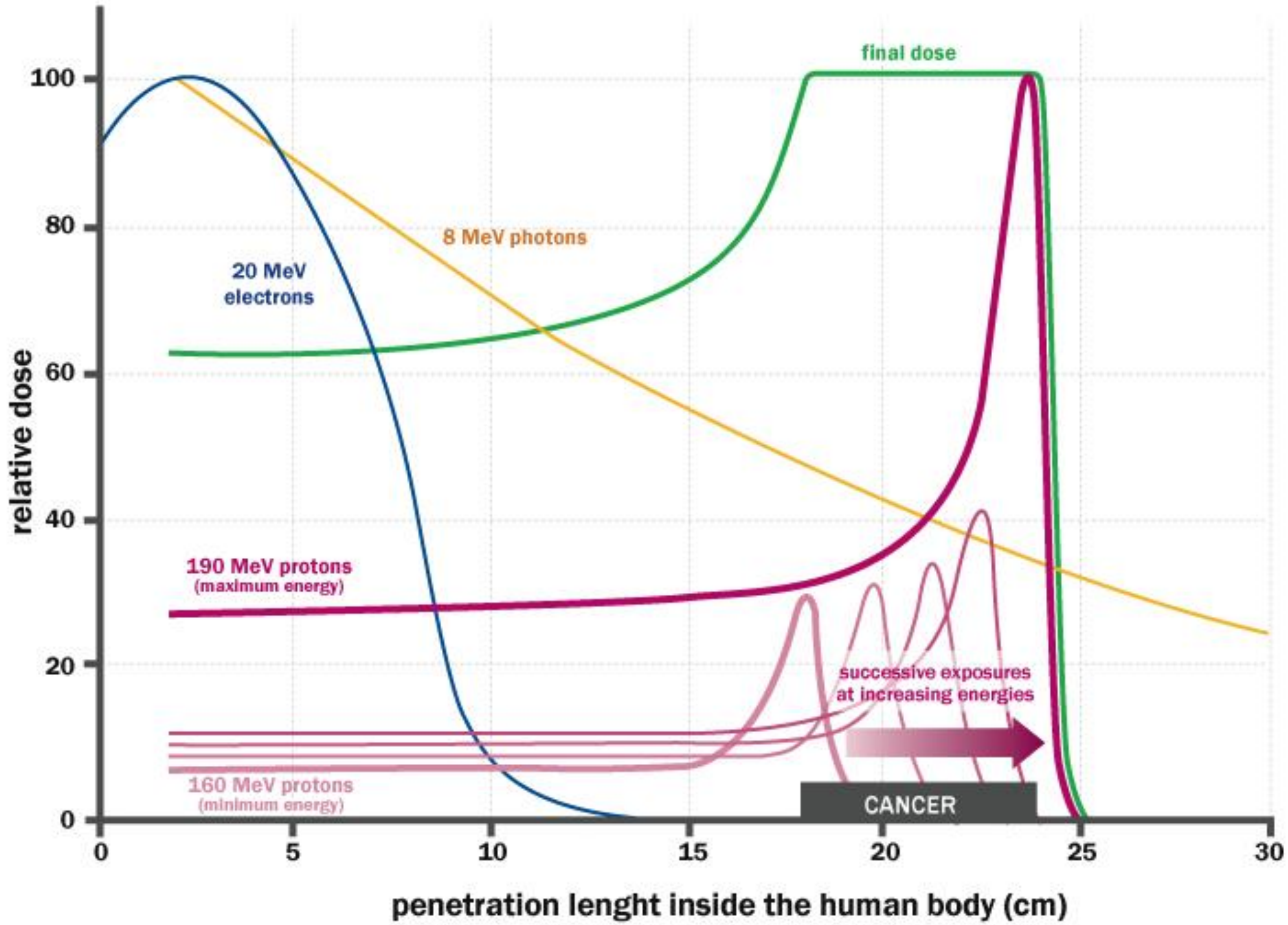

Courtesy INFN, Italy

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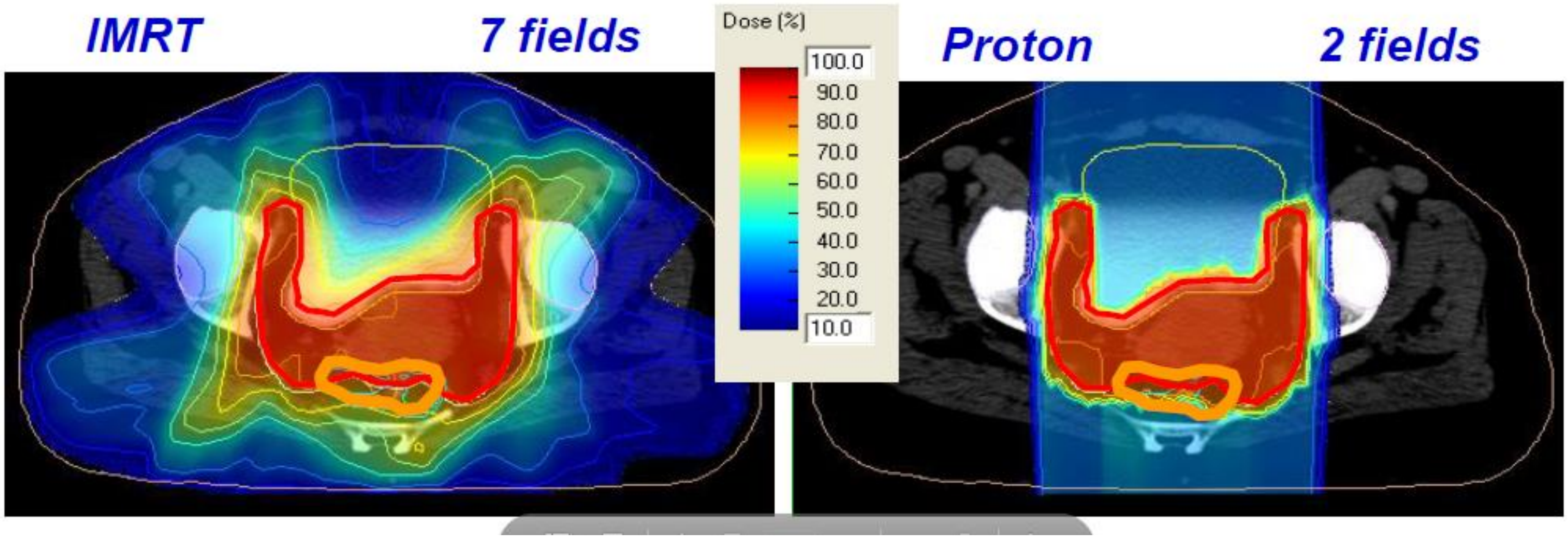
- *Ion beam therapy is more conformal than photon beam RT*
- *Sharper dose fall off*
- *Range of ions much more influenced by tissue heterogeneities than photon beams with direct impact on TCP and NTCP*
- *Image guidance is necessary for ion beam therapy*



Particle therapy (hadron therapy)

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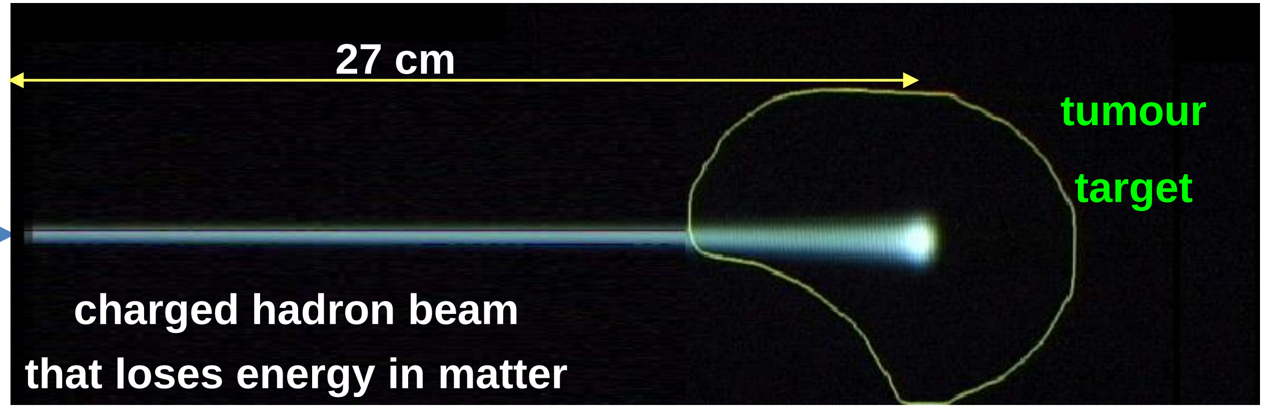
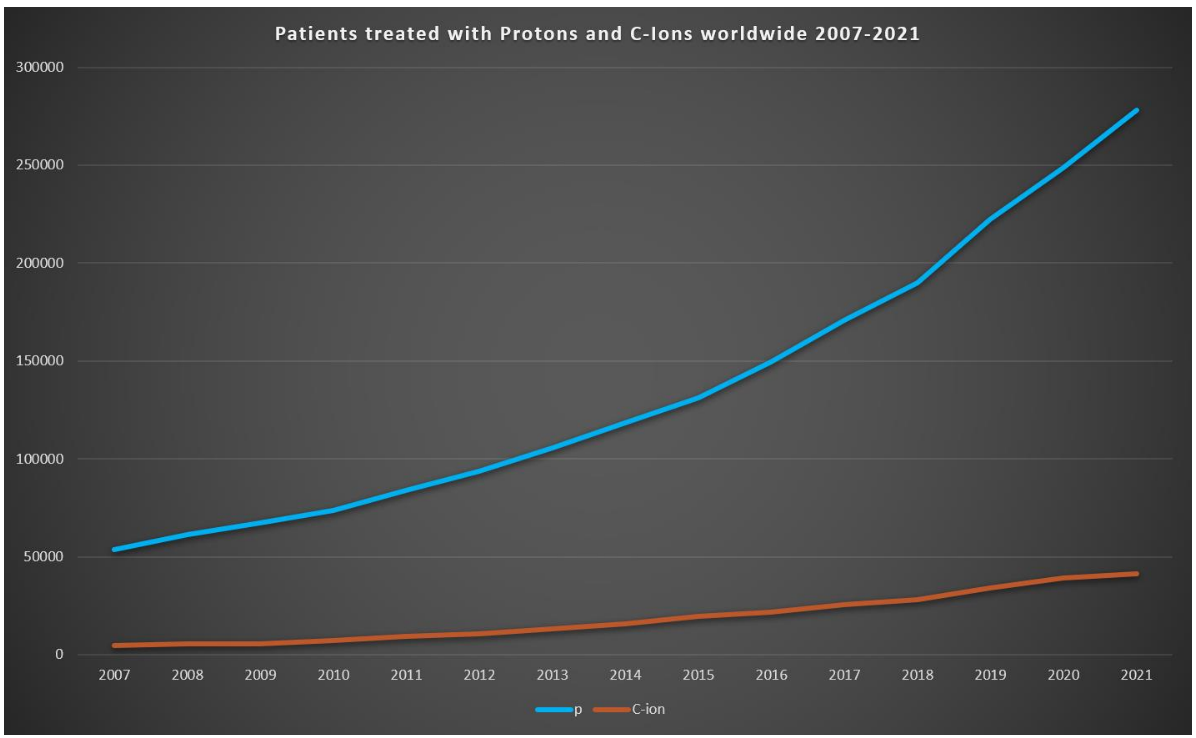
200 MeV protons

4800 MeV carbon ions





www.ptcog.ch

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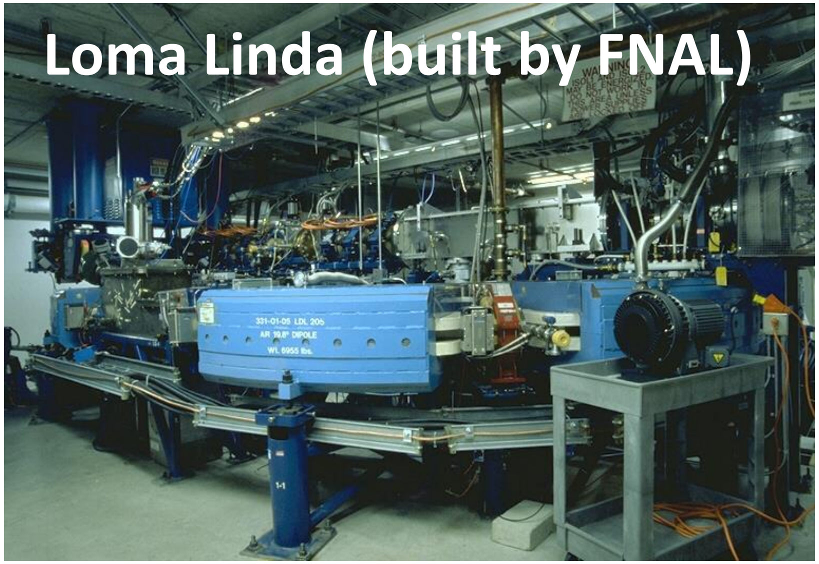
Accel-Varian (superconducting)



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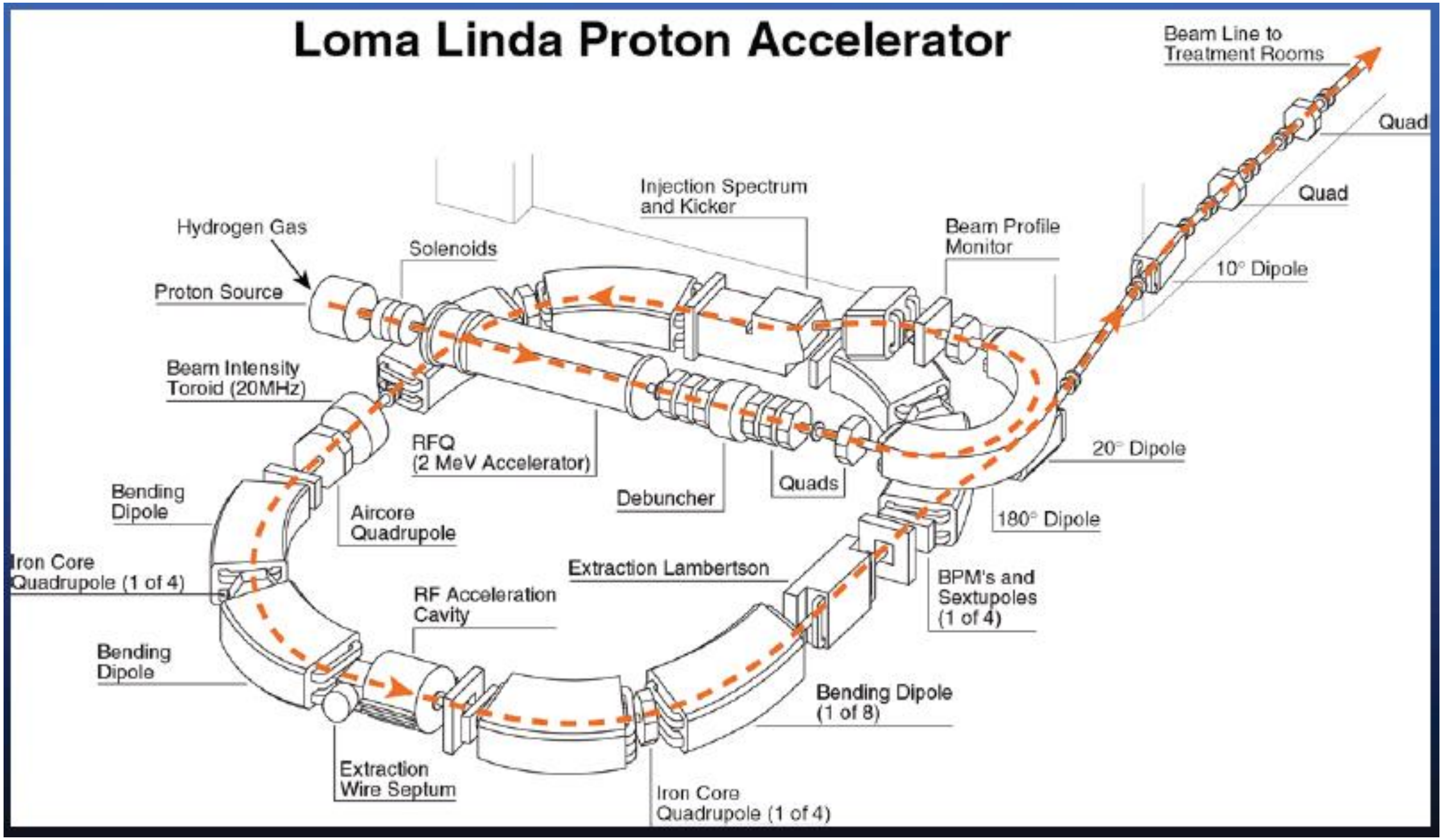
Loma Linda University Medical Center



Beam delivery: passive vs active

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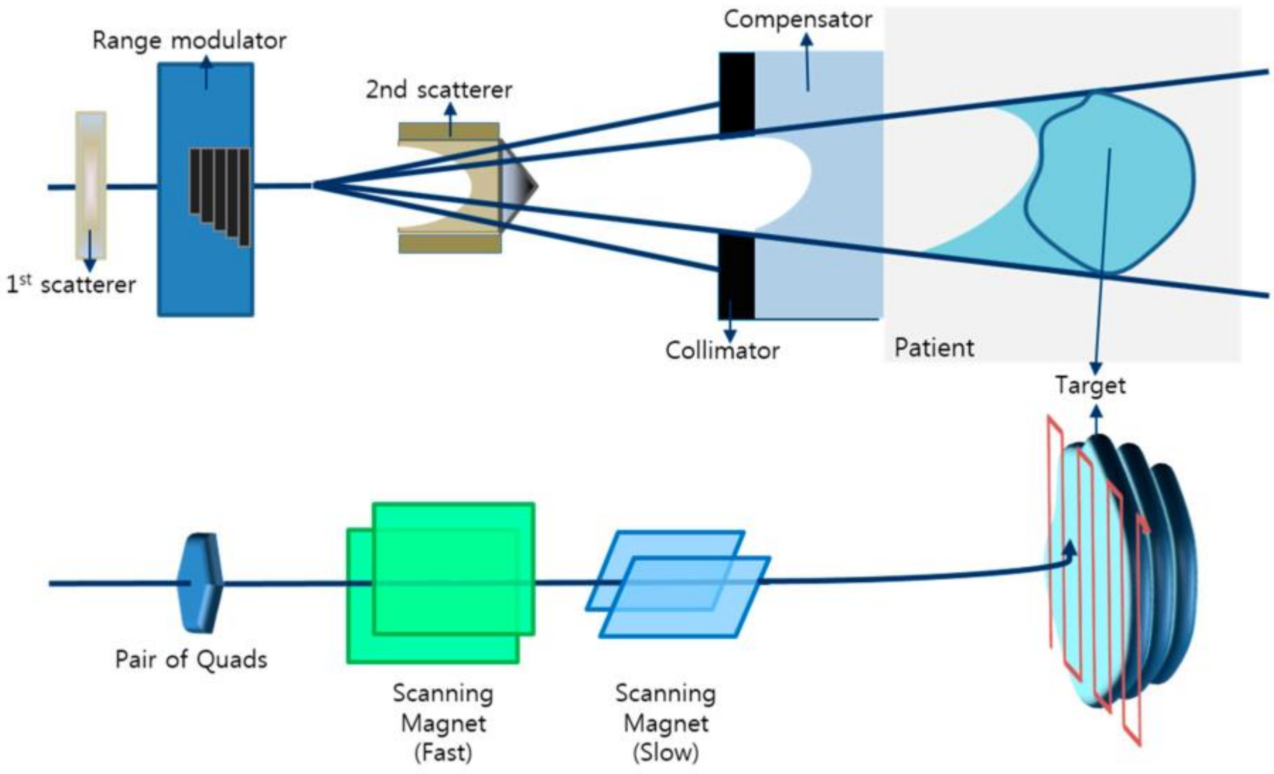

A. C. Kraan and A. Del Guerra, Technological Developments and Future Perspectives in Particle Therapy: A Topical Review, IEEE Transactions on Radiation and Plasma Medical Sciences 8, 453-480, 2024

This recent review provides an overview of technological advances in particle therapy hardware (accelerators, gantries and treatment verification techniques), software (Monte Carlo simulations, treatment planning calculations), and studies toward clinical applications

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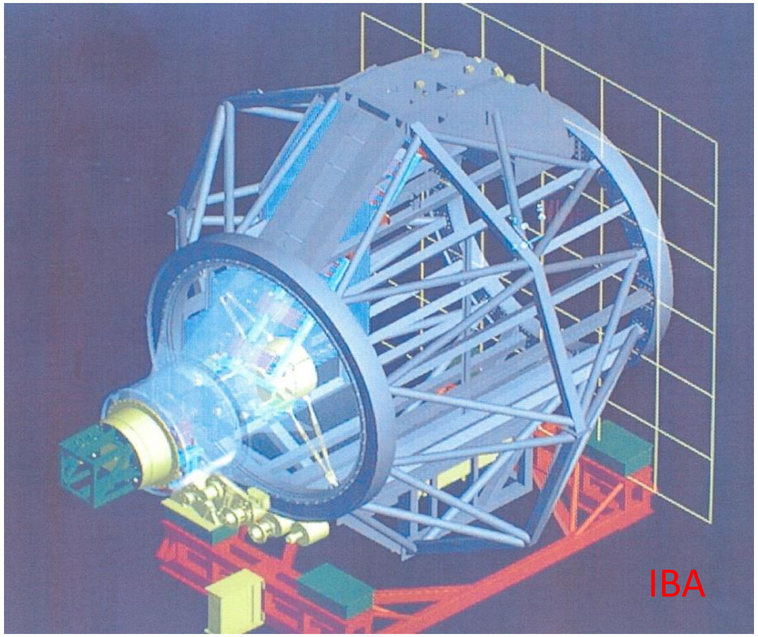
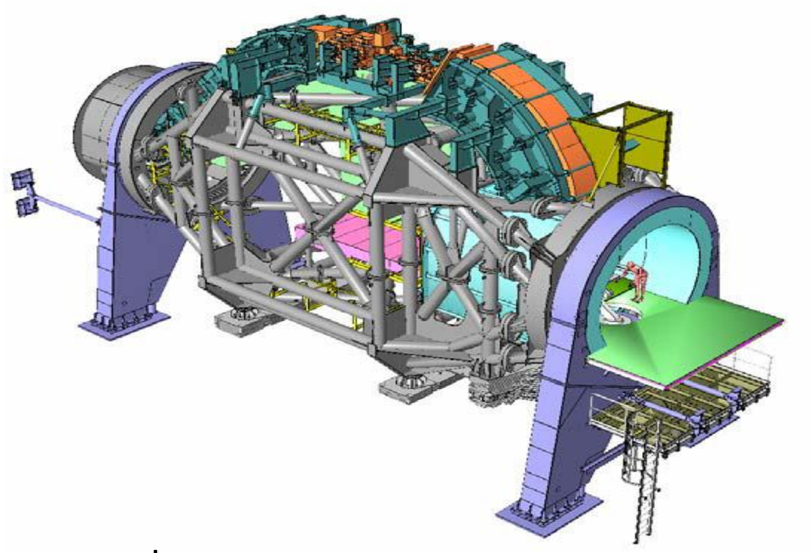
ISOCENTRIC GANTRIES



10 - 12 m



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

PROSCAN at Paul Scherrer Institut (PSI), Switzerland

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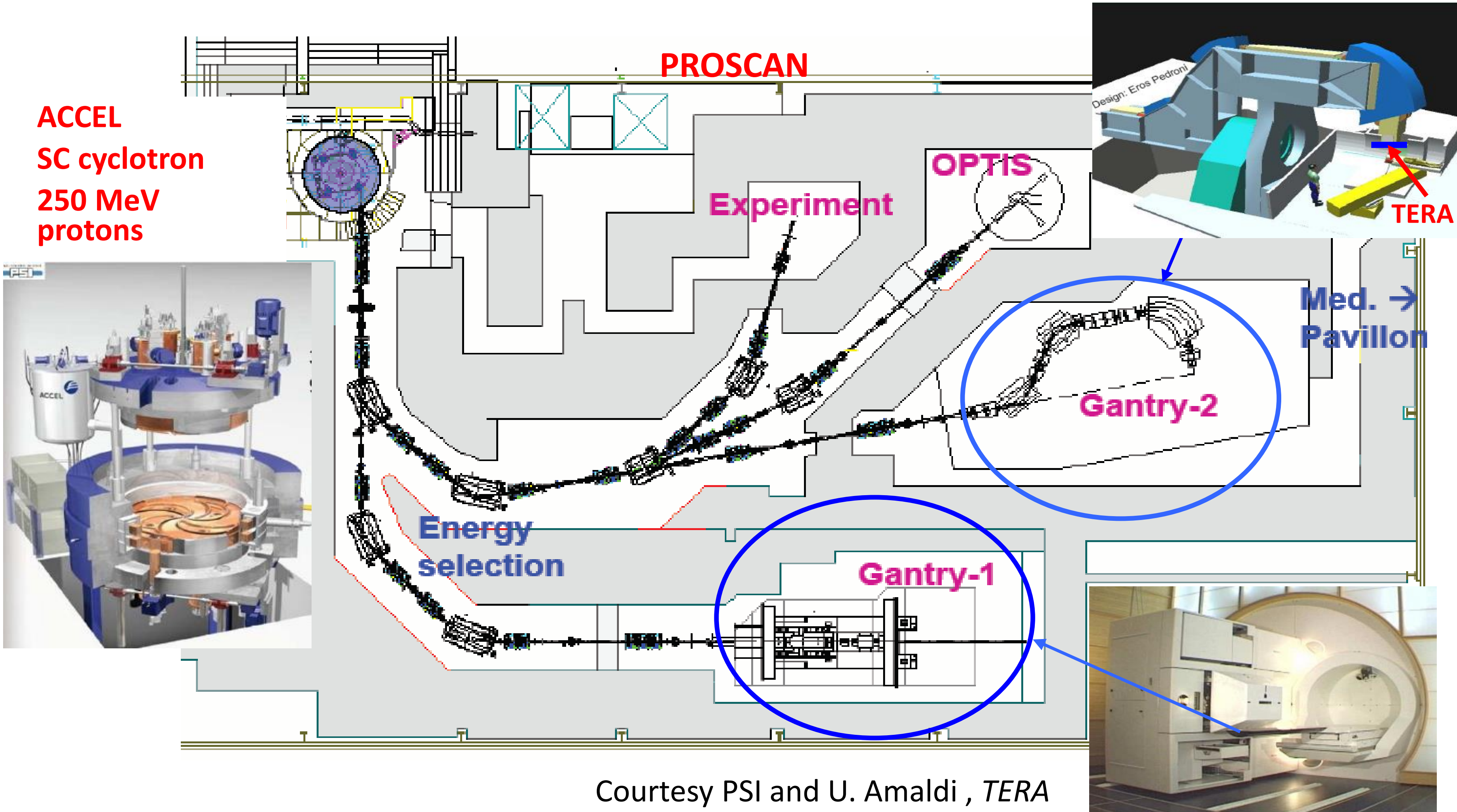
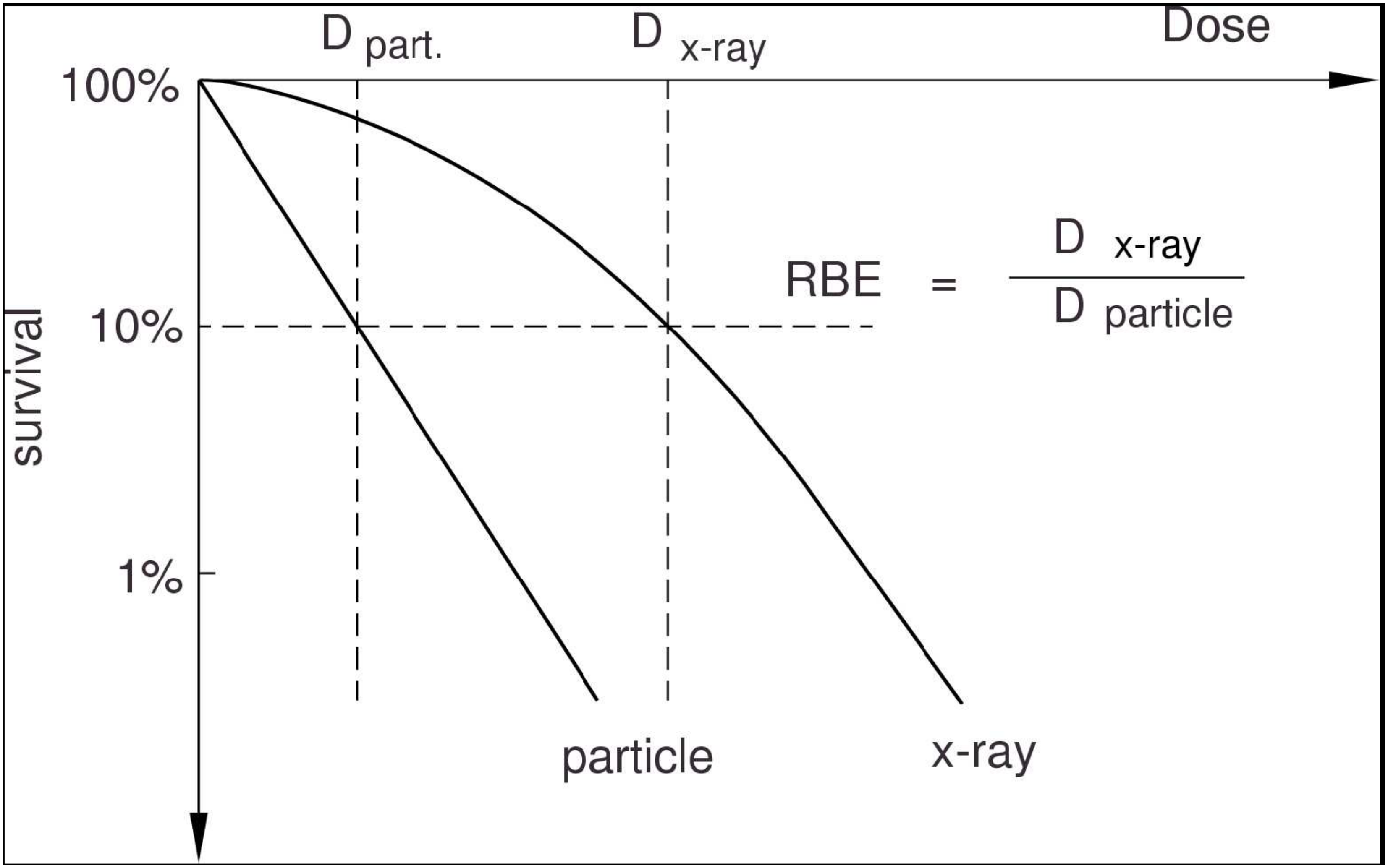


Courtesy PSI and U. Amaldi , *TERA*

J.M. Schippers et al., NIM BB 261 (2007) 773–776

Protons vs carbon: radiobiological effectiveness RBE of radiation



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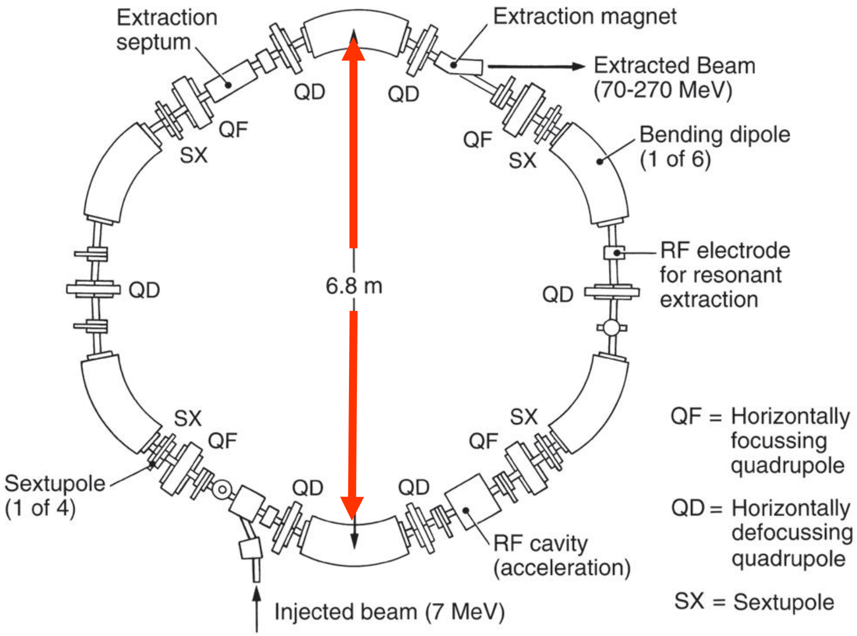
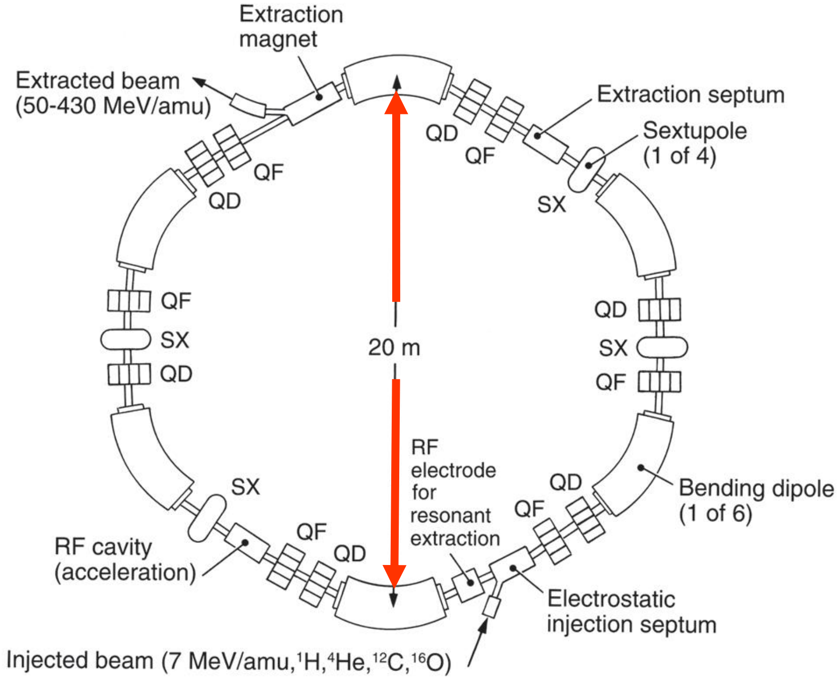
Do you see the difference between the two?

Hitachi proton synchrotron

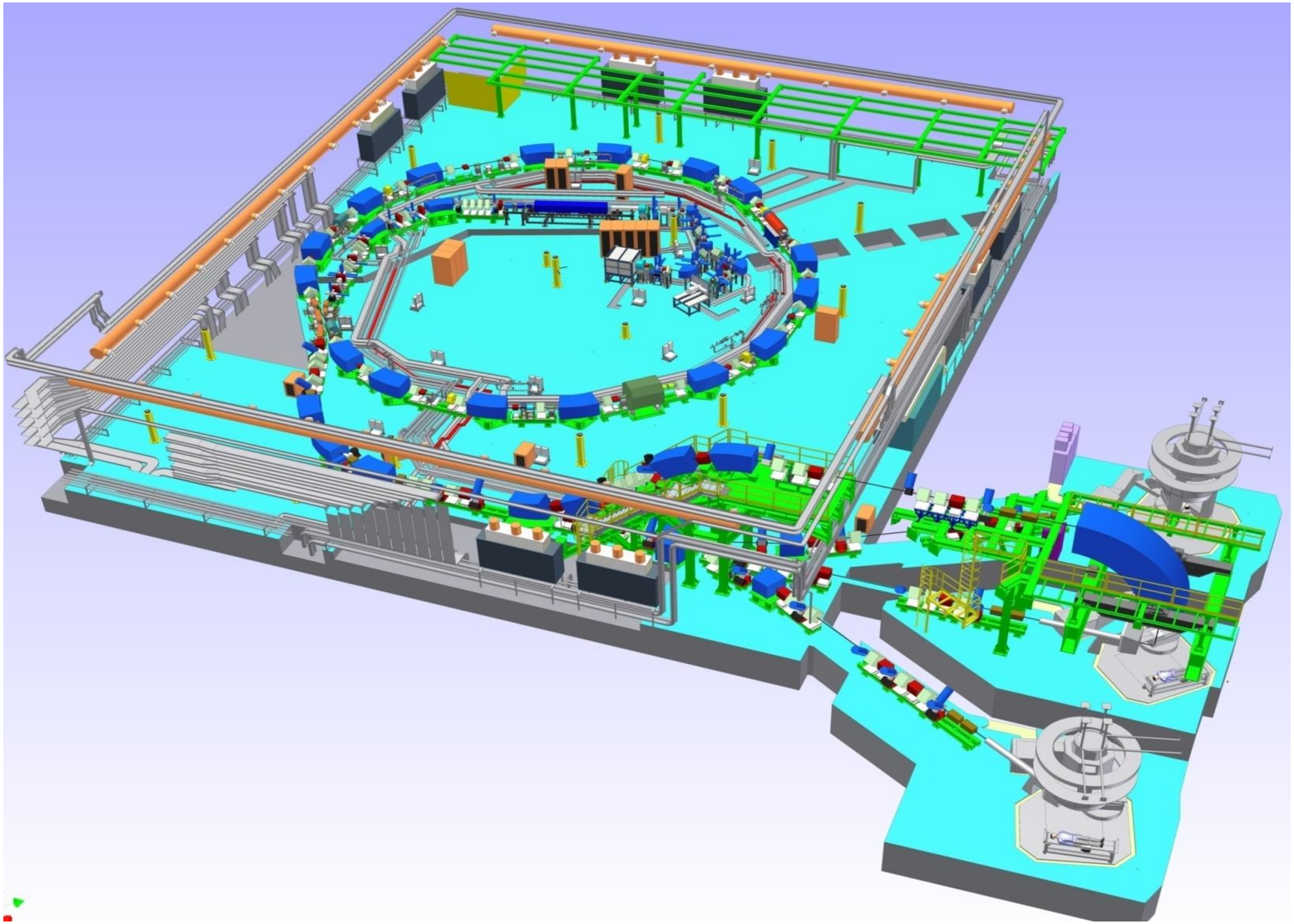


Siemens ion synchrotron



G. Coutrakon, Accelerators for Heavy-charged-particle Radiation Therapy, *Technology in Cancer Research & Treatment, Volume 6, Number 4 Supplement, August 2007*

National Centre for Oncological Hadrontherapy, CNAO, Italy



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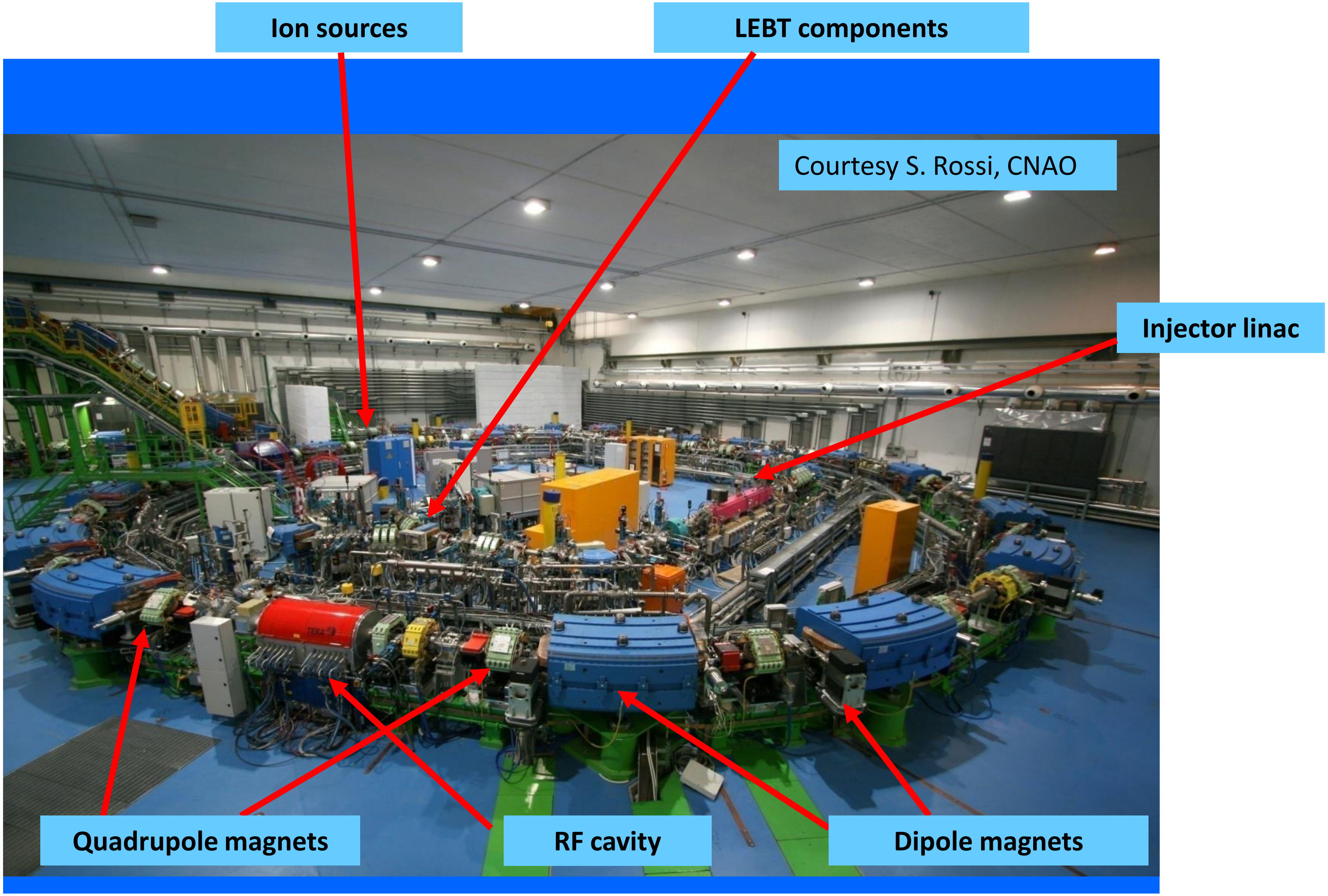

National Centre for Oncological Hadrontherapy, CNAO, Italy

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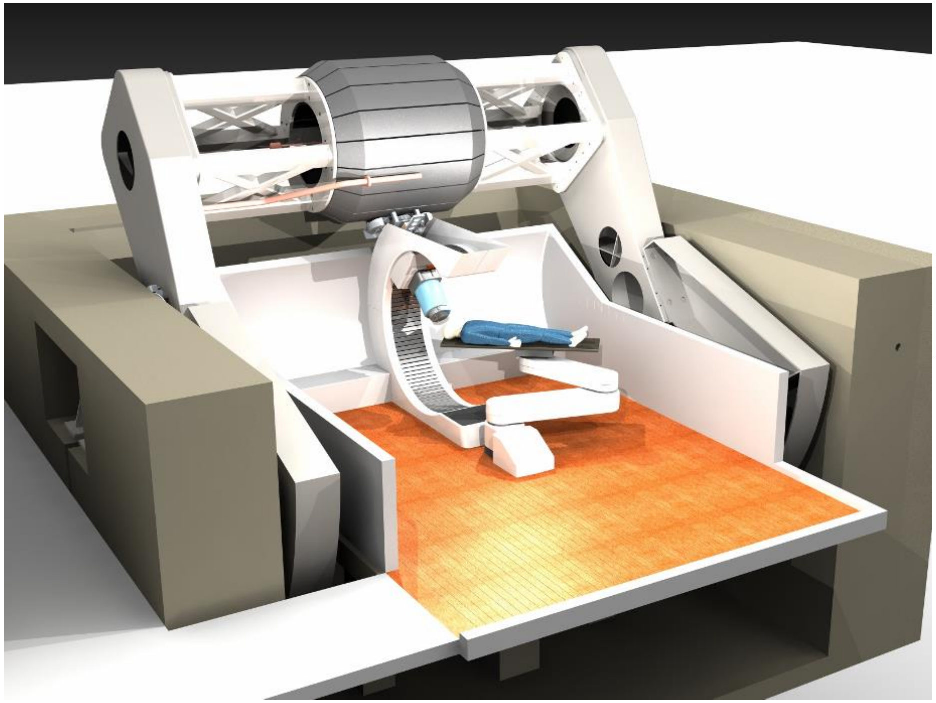
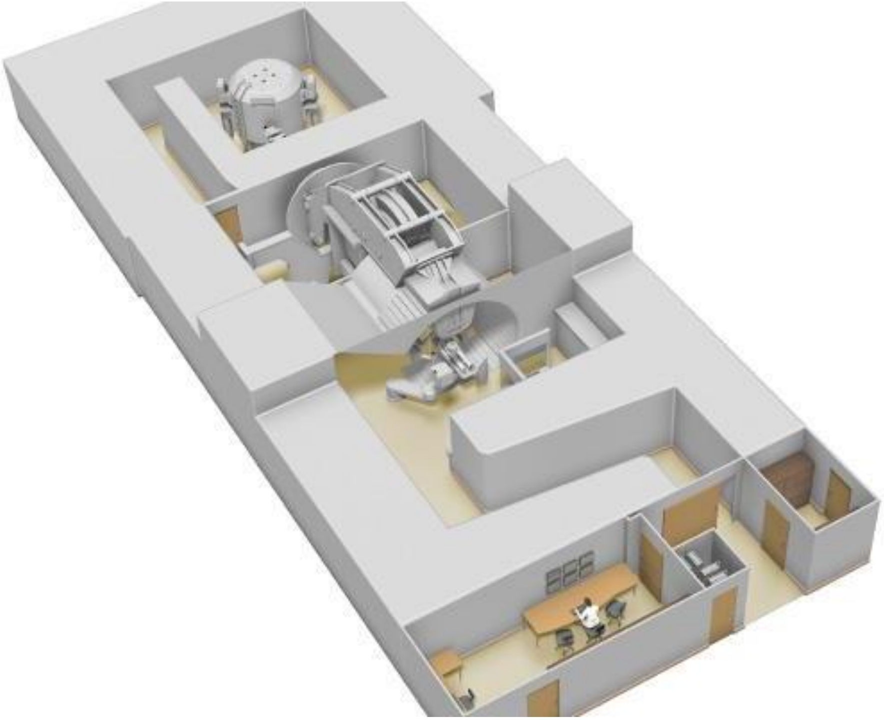


Mevion Medical Systems

IBA Proteus Nano



Multi-room versus single-room facilities

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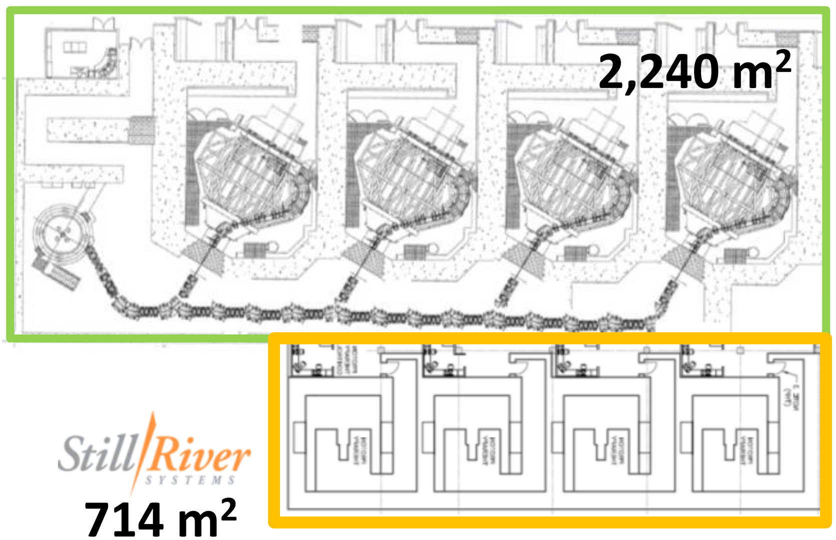

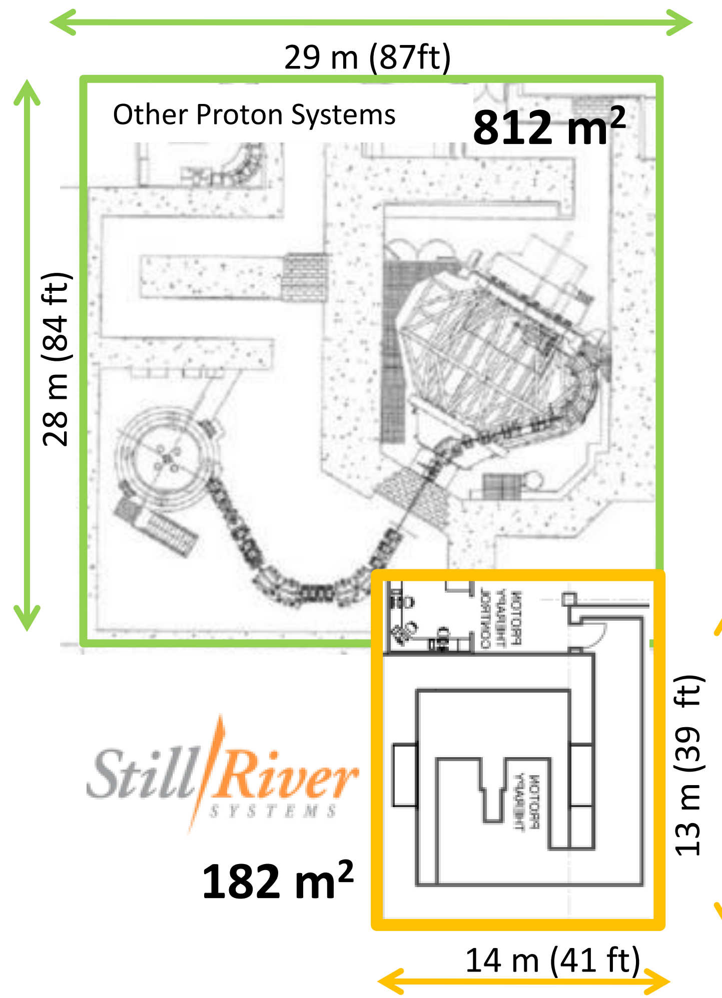

Advantages of single-room facility:

- ✓ **Modularity**
- ✓ **Reliability / back-up**
- ✓ **PT treatment available at more hospitals**
- ✓ **(Hopefully) cost**

Courtesy L. Bouchet, *Still River Systems*

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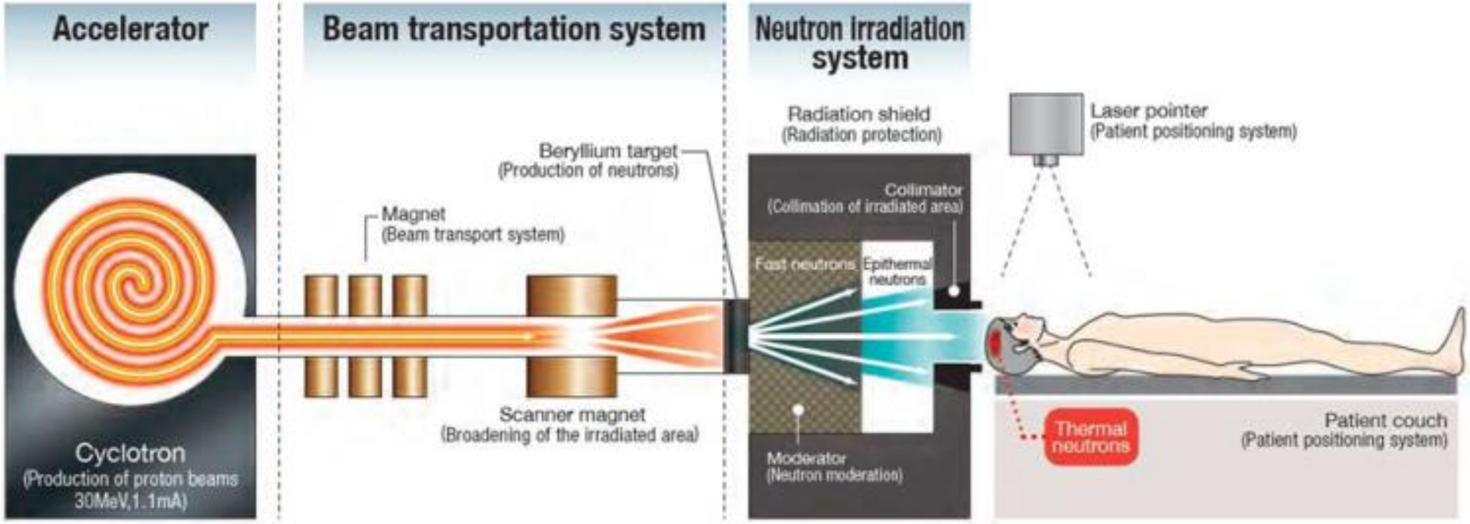
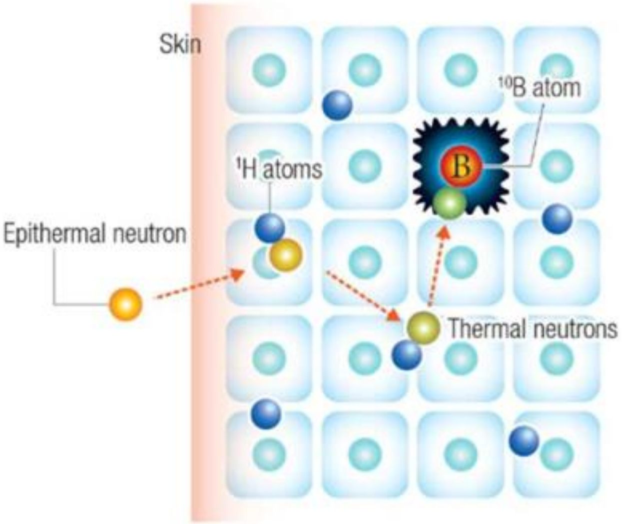
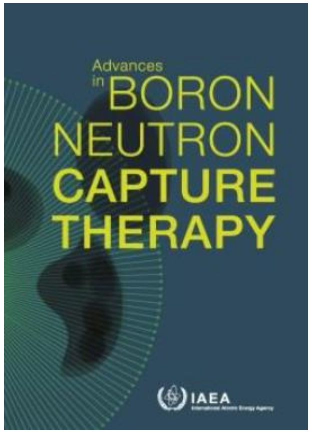




Interaction of an individual epithermal neutron being moderated by the hydrogenous tissue to thermal energies and thereafter being captured by a ^{10}B atom, triggering the therapeutic α decay



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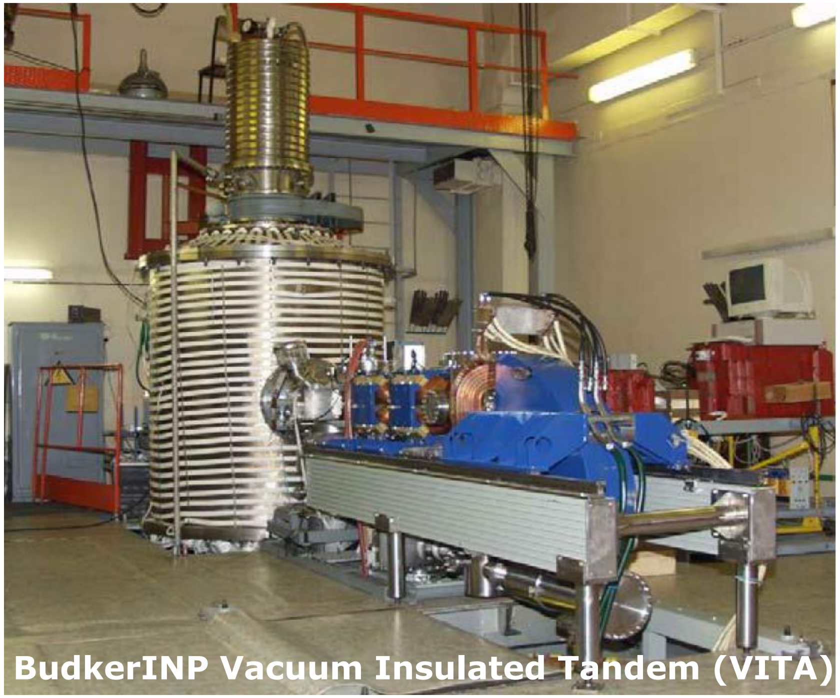
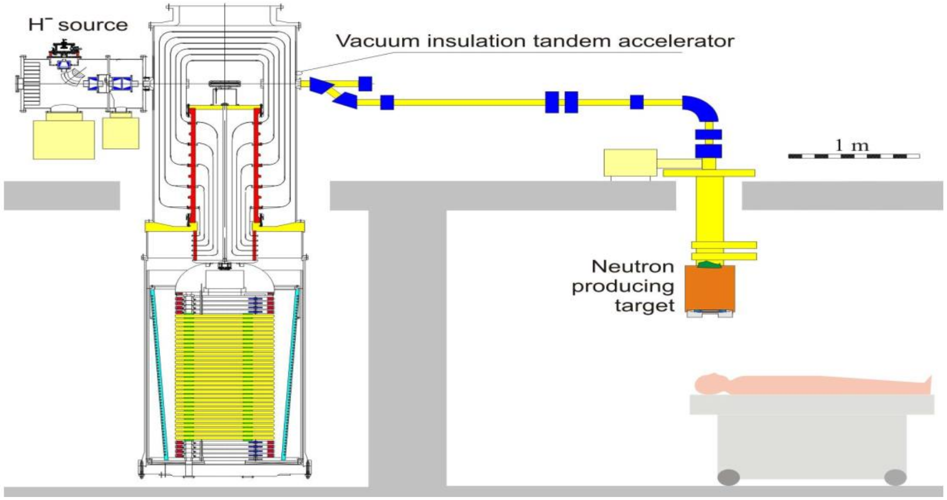
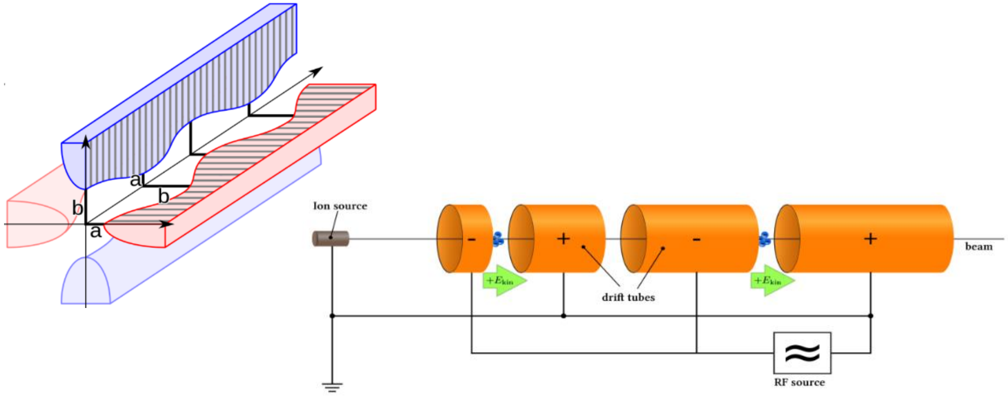
DIPARTIMENTO DI ENERGIA







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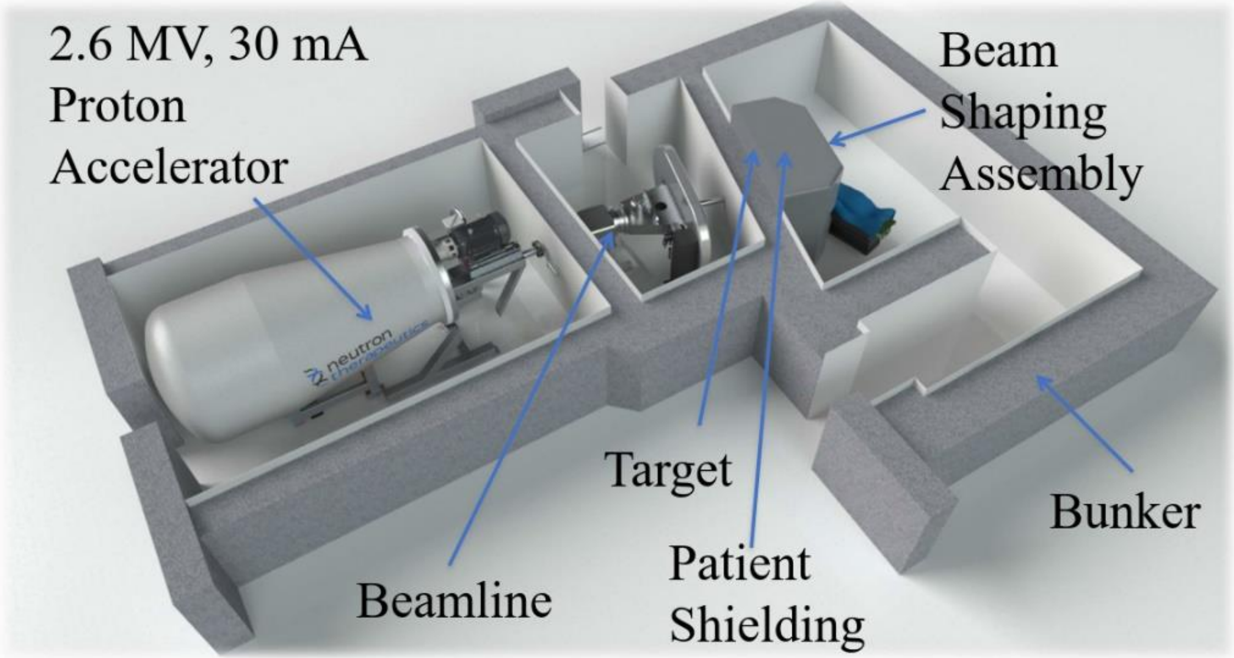

The NT neutron therapy system has not been approved by the FDA.

Bunker size: 20 m x 15 m

Peeter Karihtala (Helsinki University CCC and University of Helsinki)

Accelerator-based BNCT @ CNAO, Italy

Sandro Rossi, CNAO, Italy

E_{proton} 2.5 MeV
Intensity 10-15 mA
Target p-Li

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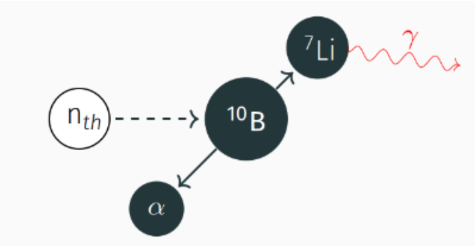
Four separate radiation components with different biological characteristics and spatial distributions

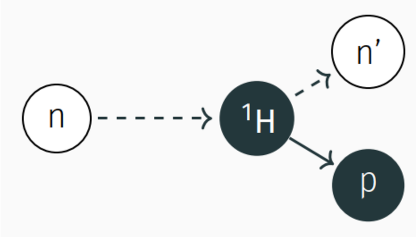
Boron dose (D_B)

- From $^{10}B(n,\alpha)^{7}Li$ reactions



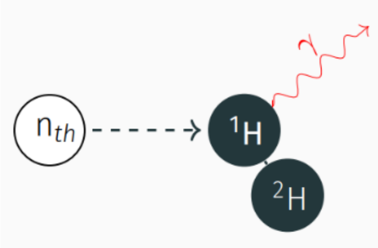
Incident neutrons ($D_{n,}$ D_H)

- Leading to dose deposition mainly via (n,p) reactions



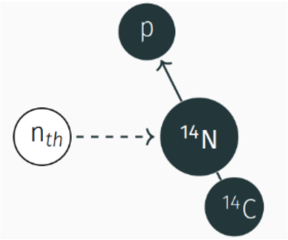
Photons (D_γ)

- Incident with the n beam and internally generated – mainly 2.2 MeV from $^{1}H(n,\gamma)^{2}H$ reactions (radioactive capture)



Thermal neutrons (D_N or D_{Th})

- Mainly from $^{14}N(n,p)^{14}C$ reactions



Availability of radiation therapy worldwide

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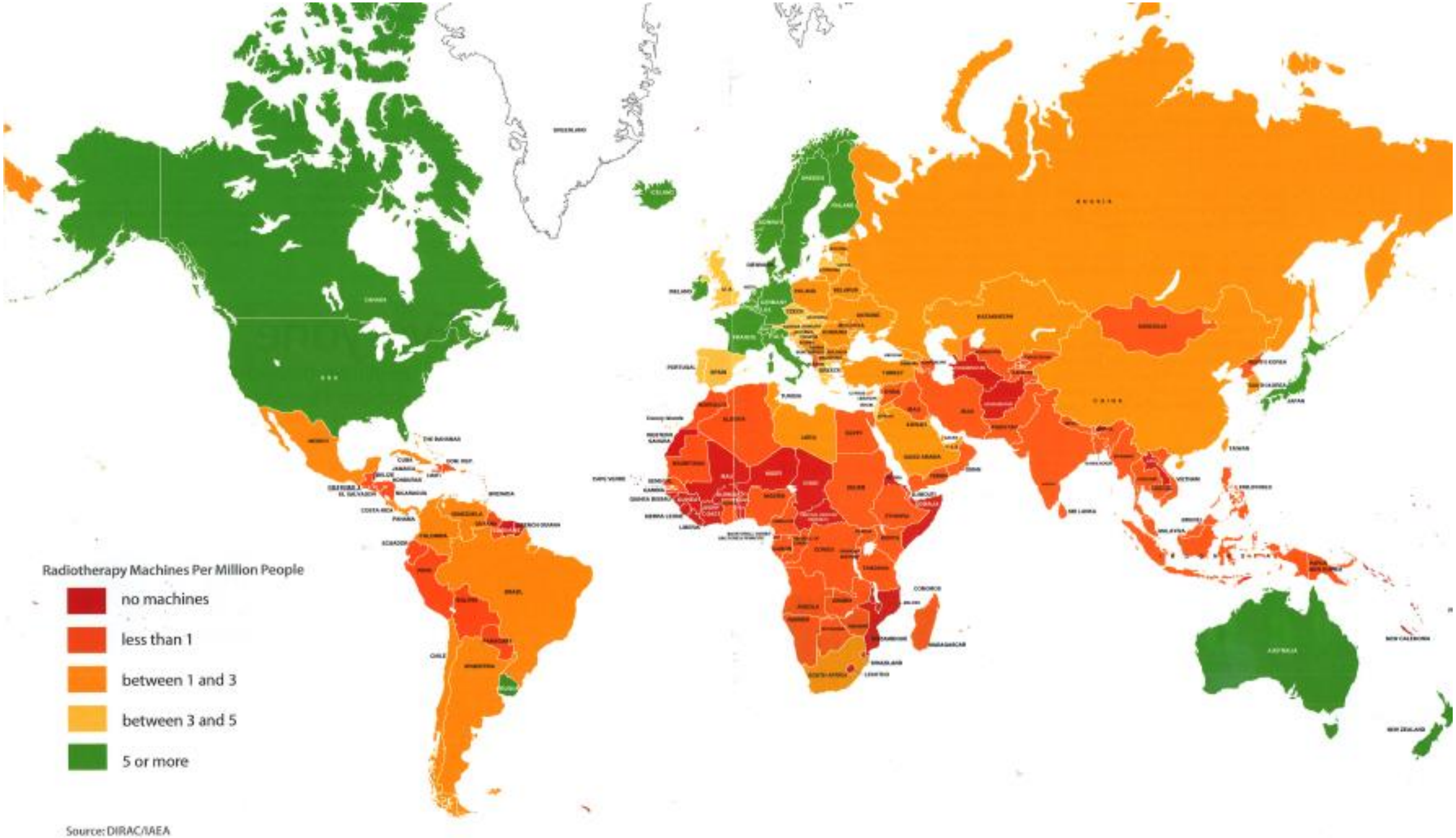

Availability of radiation therapy in African countries

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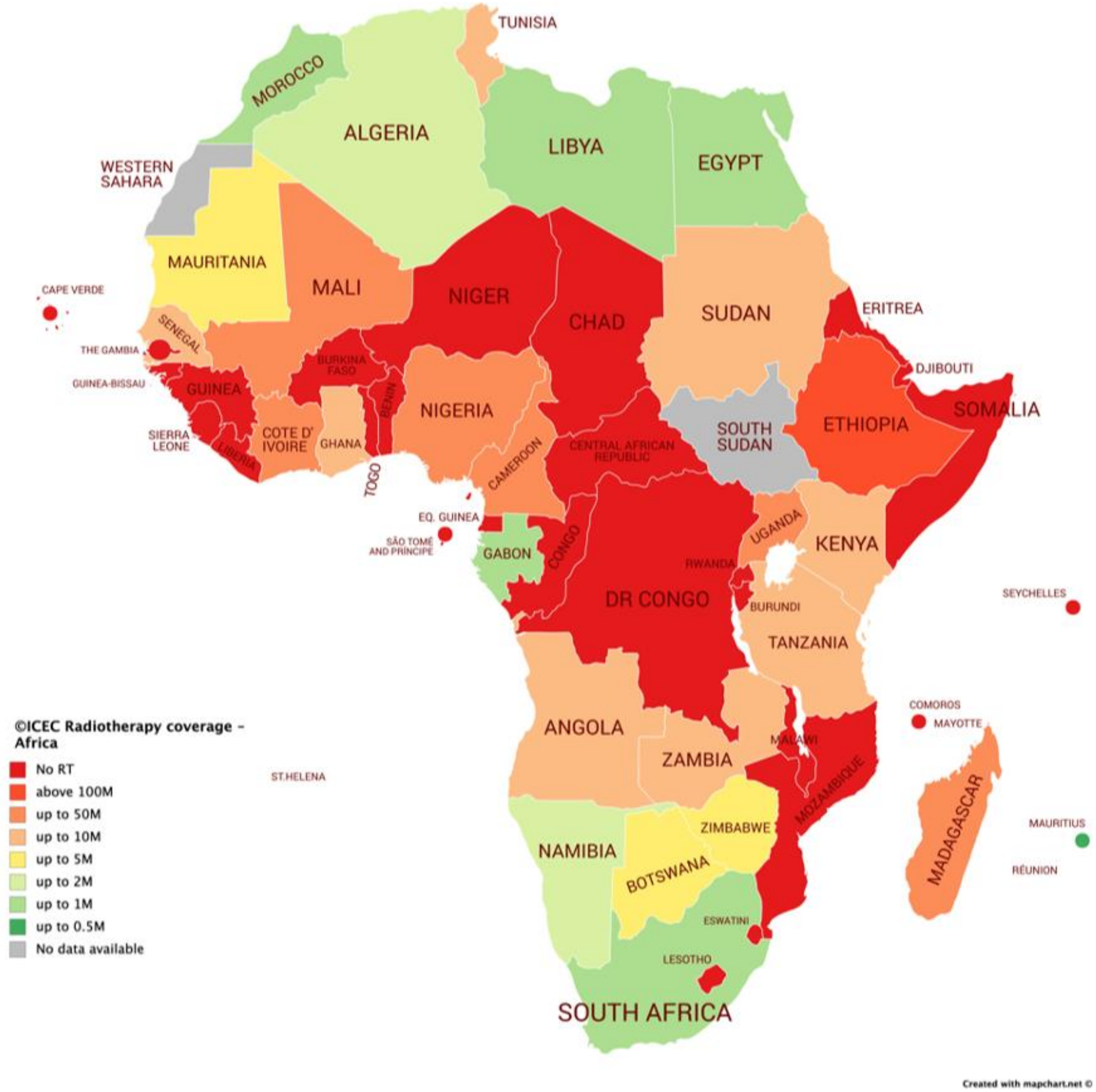
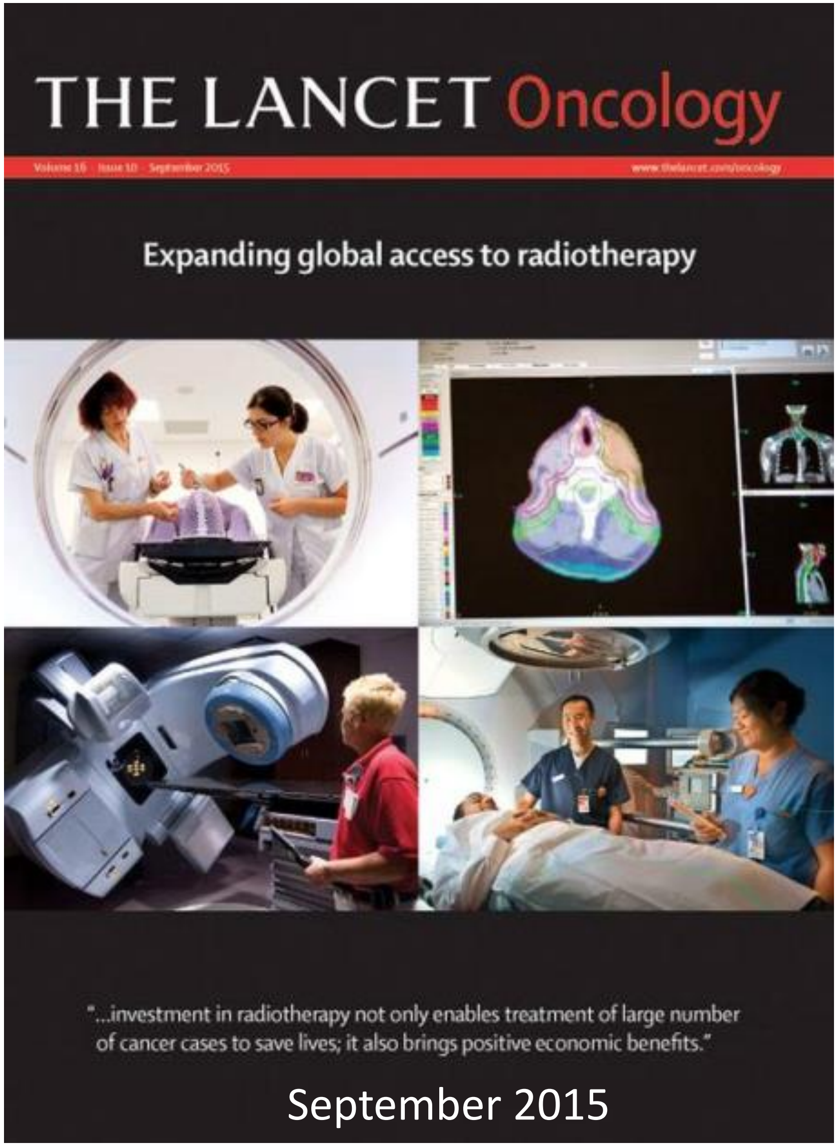
A partnership in pursuit of innovative radiation therapy technology for use in challenging environments - ICEC (icecancer.org)





September 2015

International Cancer Expert Corps
Partnering to transform global cancer care

CERN-ICEC workshop, CERN, November 2016

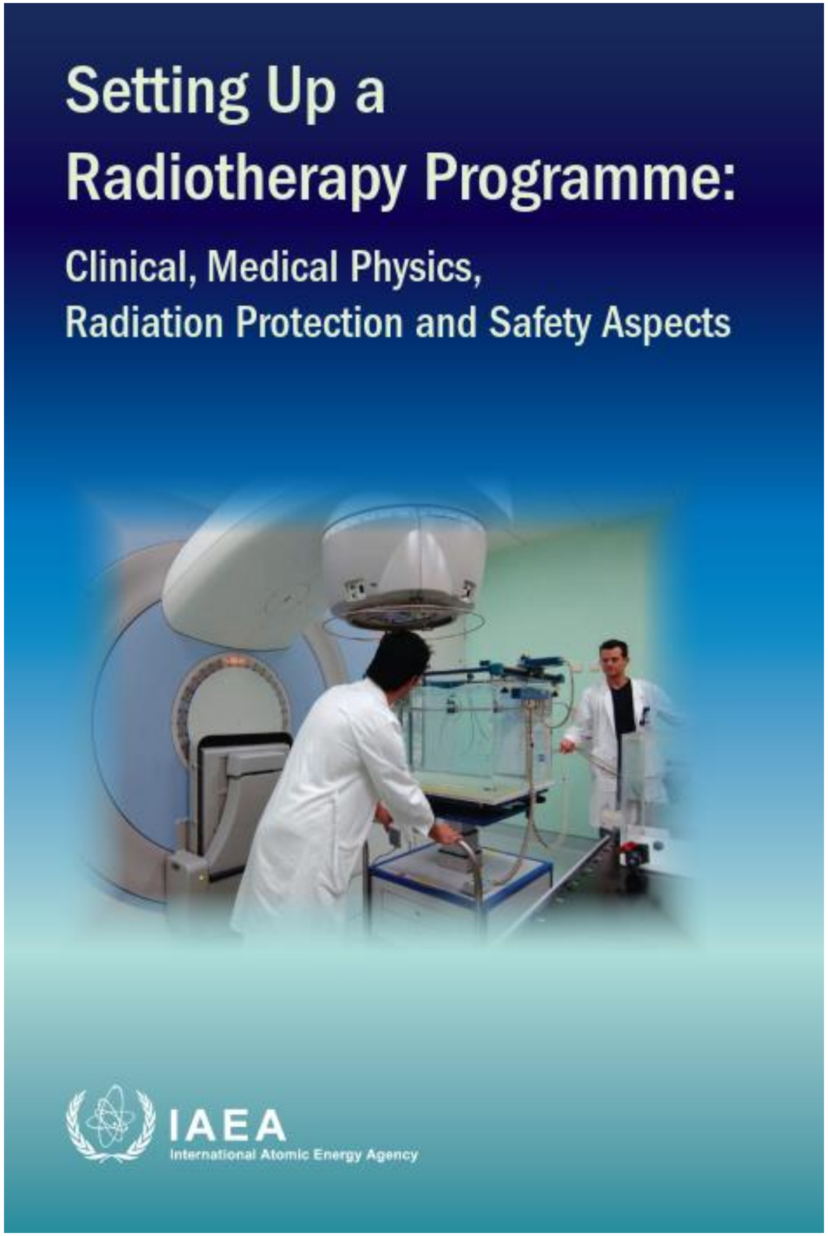
https://indico.cern.ch/event/560969/

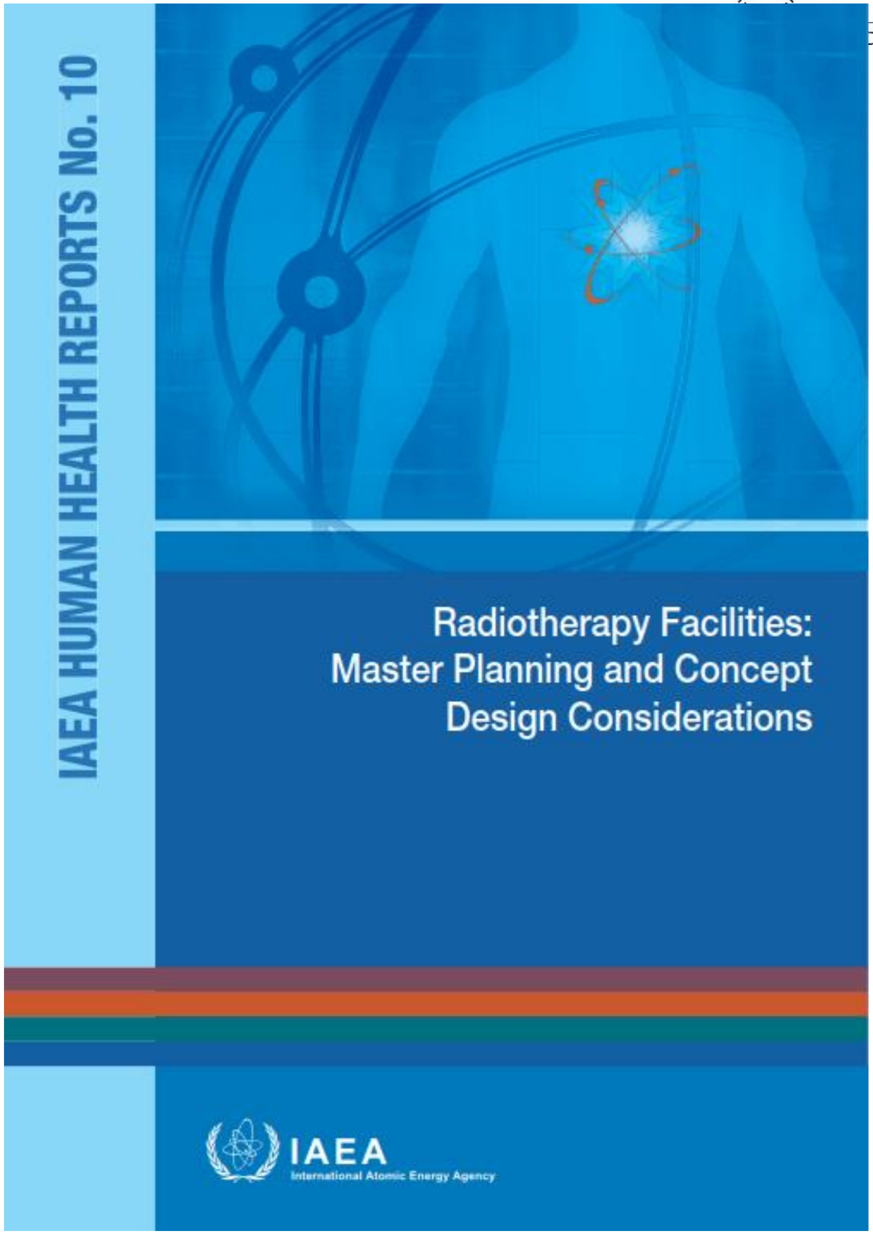
CERN | International Cancer Expert Corps – Partnering to transform global cancer care | 10 Science & Technology Facilities Council – 10 Years of Impact and Inspiration

CERN-ICEC-STFC workshop, CERN, October 2017

https://indico.cern.ch/event/661597/

Guidelines


Setting Up a
Radiotherapy Programme:
Clinical, Medical Physics,
Radiation Protection and Safety Aspects
IAEA
International Atomic Energy Agency


IAEA HUMAN HEALTH REPORTS No. 10
Radiotherapy Facilities:
Master Planning and Concept
Design Considerations
IAEA
International Atomic Energy Agency

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Technology

- 23 of 54 countries have teletherapy services
- 20 had high- or low-dose brachytherapy resources
- 293 radiotherapy machines serving 1 billion individuals
- 1 machine per 3.6 million people

Abdel-Waheb et al, Lancet Oncology, 2013 / Grover et al, Front in Oncology, Jan 2015 / Balogun et al, Radiation Oncology, Aug 2016

Taken from Surbhi Grover's lecture at the CERN-ICEC-STFC workshop, CERN, October 2017

Human resources

- a gap of 7,500 oncologists, 6,000 physicists and 20,000 technicians in LMICs (in Africa: 1600 medical oncologists, 1000 medical physicists and 4000 technicians)

Taken from Andras Fehervary's lecture at the CERN-ICEC workshop, CERN, November 2016

RT resources needed in 20 years from now

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	High Income Countries	LMICS
Megavoltage Machines	9200	12600
Radiation Oncologists	1550	30000
Medical Physicists	17200	22100
Radiation Technologists	51900	78300

LMICS = Low Medium Income Countries

Taken from Mary Gospodarowicz's lecture at the CERN-ICEC workshop, CERN, November 2016

Atun et al., Lancet Oncology 2015

Union for International Cancer Control
www.uicc.org

Developing RT for challenging environments

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Linacs

- Ability to operate in a difficult environment
  - Interruptions in electricity / power supply
  - Heat / problem with temperature control
  - Dust and humidity
- Highly modular, so that faulty parts can easily be replaced
- Self-diagnosing, in case of accelerator malfunctioning
- Low power consumption
- …

Screening

- Improve screening and early diagnosis to make RT more effective

Need for

- Qualified professionals: radiation oncologists, medical radiotherapy physicists, radiotherapy technicians, radiation protection officers, maintenance engineers, etc.
- Related training programmes
- Development of medical infrastructure

On accelerators & radiation therapy:

- C.K. Karzmark, Advances in linear accelerator design for radiotherapy, Medical Physics 11, 105- 128 (1984)
- S. Humphries, Principles of charged particle acceleration, John Wiley and Sons
- H. Wiedemann, Particle accelerator physics, Springer- Werlag
- S. Baird, Accelerators for pedestrians, CERN AB-note-2007-014
- PTCOG: Particle Therapy Co-Operative Group (http://ptcog.web.psi.ch/)

On radionuclide production:

- Cyclotron Produced Radionuclides: Principles and Practice, IAEA Technical Reports Series No. 465 (2008)
  (Downloadable from IAEA web site)
- Targetry and Target Chemistry, Proceedings Publications, TRIUMF, Vancouver
  (http://trshare.triumf.ca/~buckley/wttc/proceedings.html)
- CLARK, J.C., BUCKINGHAM, P.D., Short-Lived Radioactive Gases for Clinical Use, Butterworths, London (1975

Supplementary material

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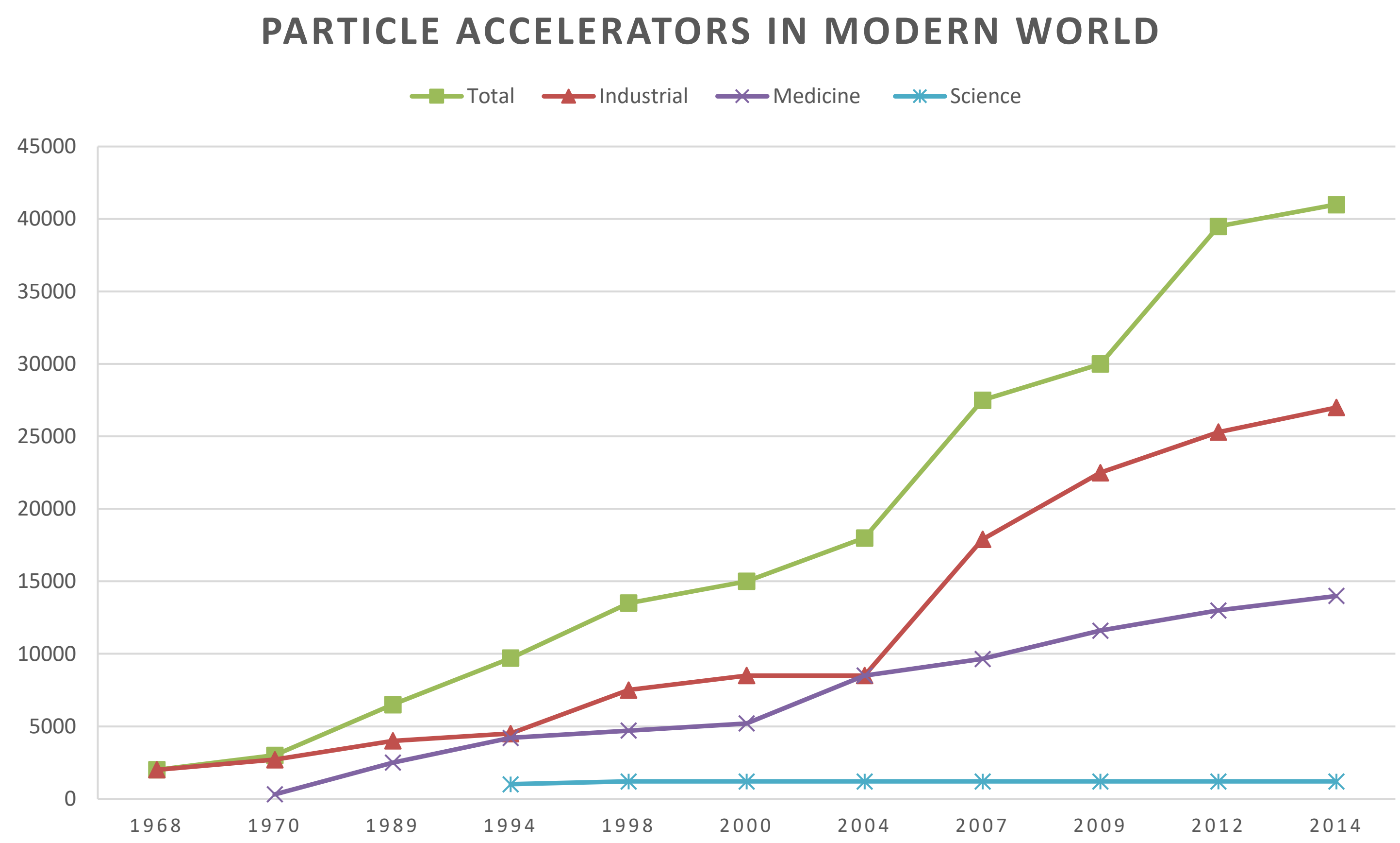
Three main applications: 1) Scientific research, 2) Medical applications 3) Industrial uses



A. P. Chernyaev and S. M. Varzar, Particle Accelerators in Modern World, Physics of Atomic Nuclei, 2014, Vol. 77, No. 10, pp. 1203–1215.

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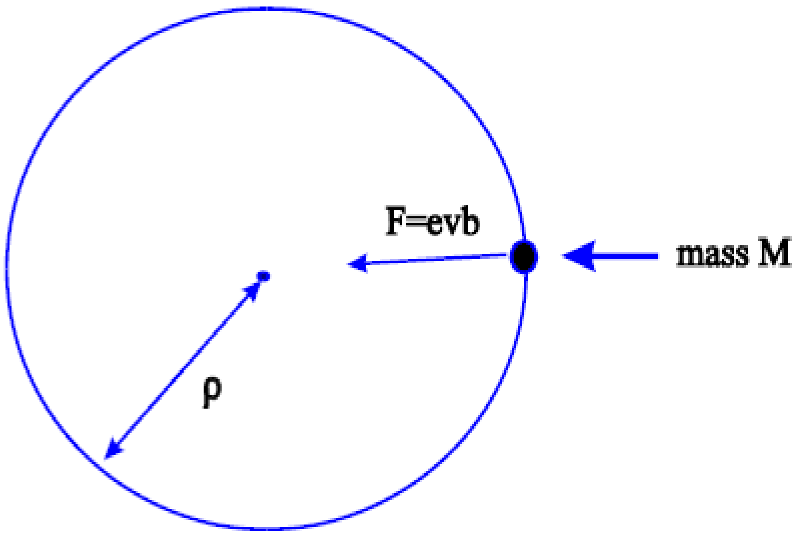
(the field is in/out of the plane of this slide)



$$F = \frac{mv^2}{\rho},$$ where ρ = radius of curvature of the path

$$F = evB = \frac{mv^2}{\rho}$$

$$B\rho = \frac{mv}{e} = \frac{p}{e}$$

(p = momentum = mv)

Bρ = 33.356·p [kG·m] = 3.3356·p [T·m] (if p is in GeV/c)

Bρ is called "magnetic rigidity" of the particle and is an index of how difficult is to bend the motion of a charged particle by a magnetic field

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$F = q(\mathbf{E} + \mathbf{v} \times \mathbf{B})$

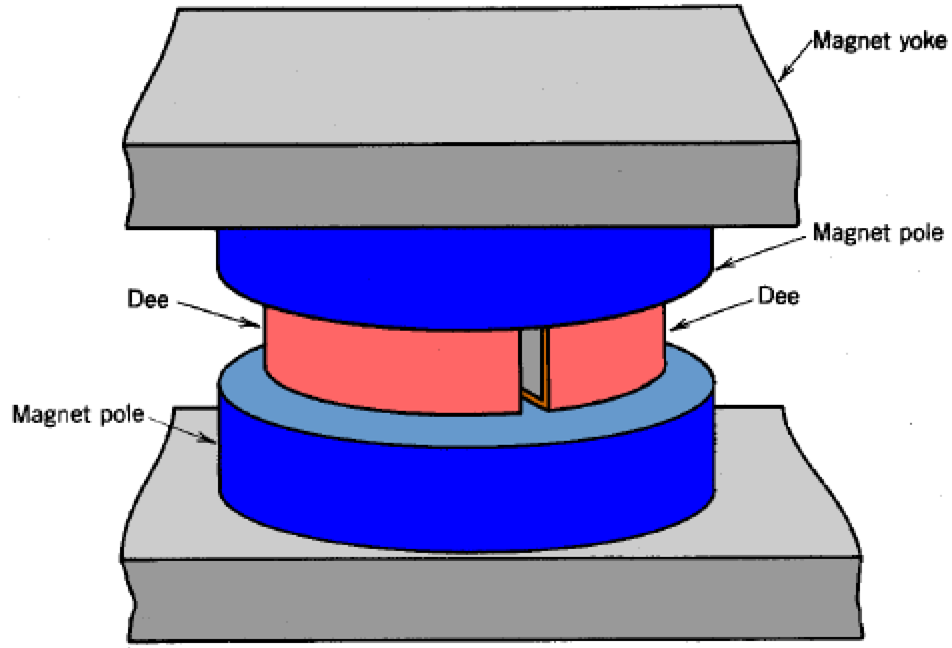
$mv^2 / \rho = qvB \qquad \omega = 2\pi f = v / \rho$

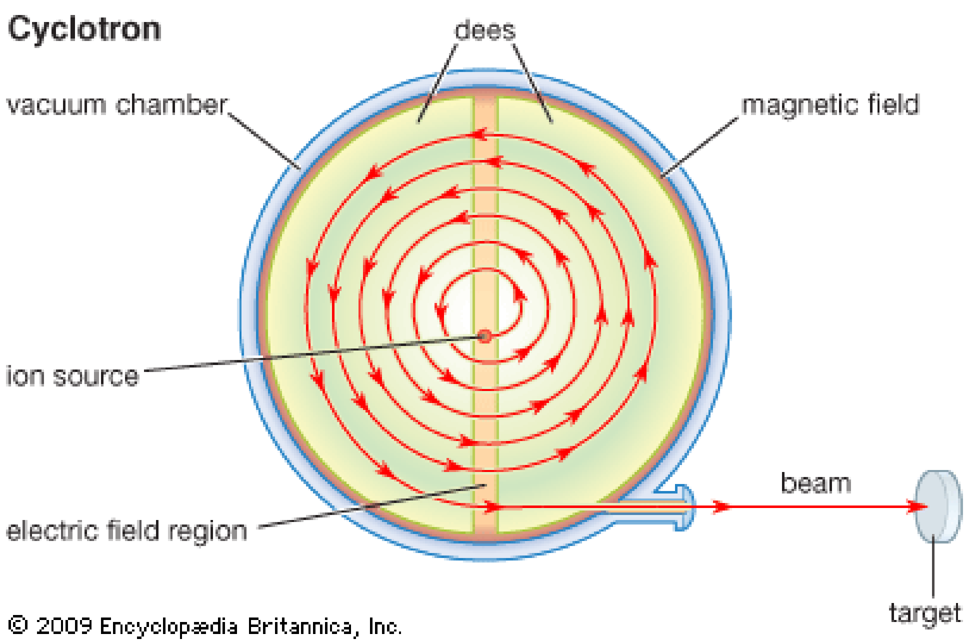
Rev. frequency $f = qB/2\pi m$

Rev. period $\tau = 1/f$ is independent of v

Resonant acceleration with $f_{RF} = h \cdot f$

→ Isochronism





Maximum energy/nucleon:

$T/A = k\,(B\rho)^2\,(Z/A)^2$

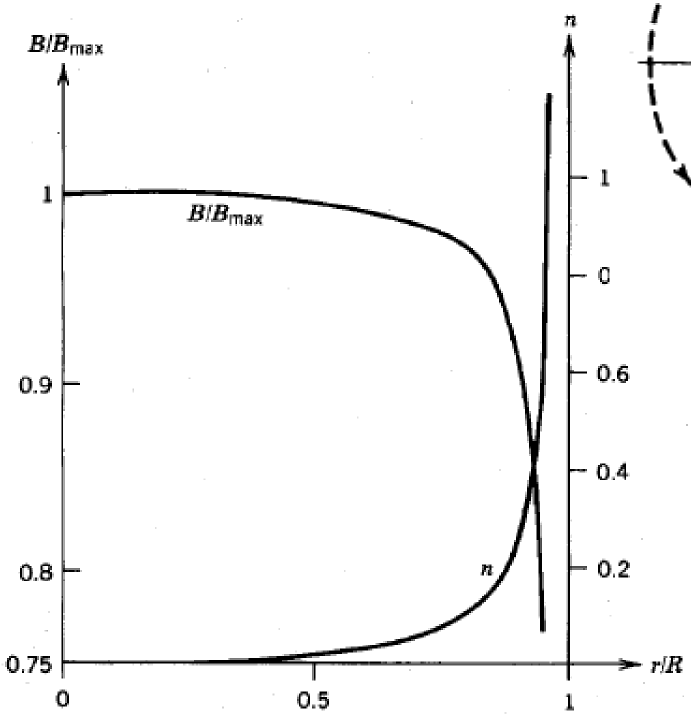
with $k = e^2 / 2m_p$

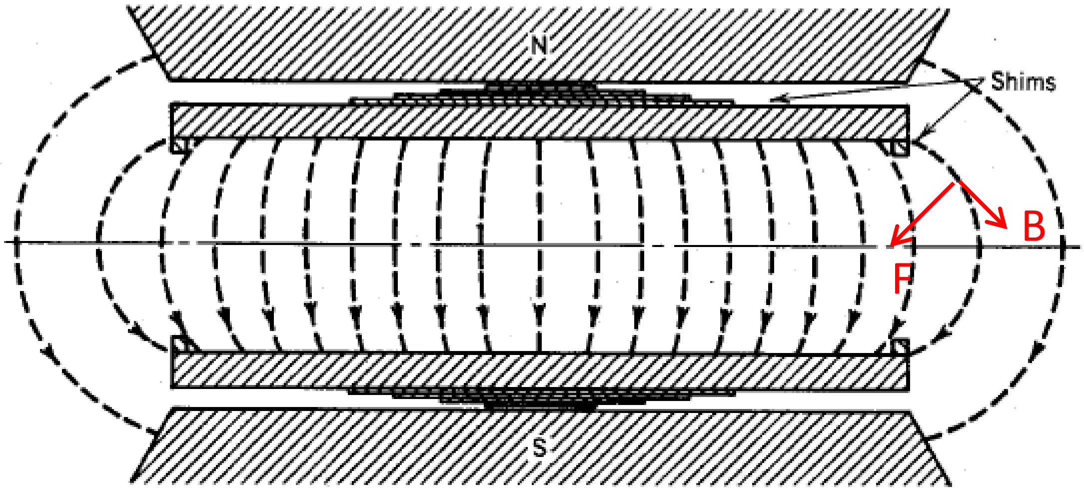
$K = k\,(B\rho)^2$ is called "bending limit"

$K = 48\,(B\rho)^2$ (MeV)

if B is in teslas and m in metres

The classical (non relativistic) cyclotron





Magnetic fields of uniform-field cyclotron: (top) Sectional view of cyclotron magnetic poles showing shims for optimizing field distribution. (left) Radial variation of vertical field magnitude and field index.

- Weak focusing
- Decrease of rev. frequency f with r
- Loss of isochronism

➢ Two solutions to achieve higher energies:
  - synchrocyclotron
  - AVF cyclotron

The AVF (isochronous) cyclotron

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AVF = azimuthally varying field

B(r,θ) = <B(r)> + Mod(r, θ)

- RF constant
- <B> rises with radius r to compensate for the relativistic increase of the particle mass

$f = q\langle B\rangle/2\pi m\gamma$

Vertical focusing achieved by the azimuthal variation of B

A further component of the axial focusing force is obtained by giving the sectors a spiral shape

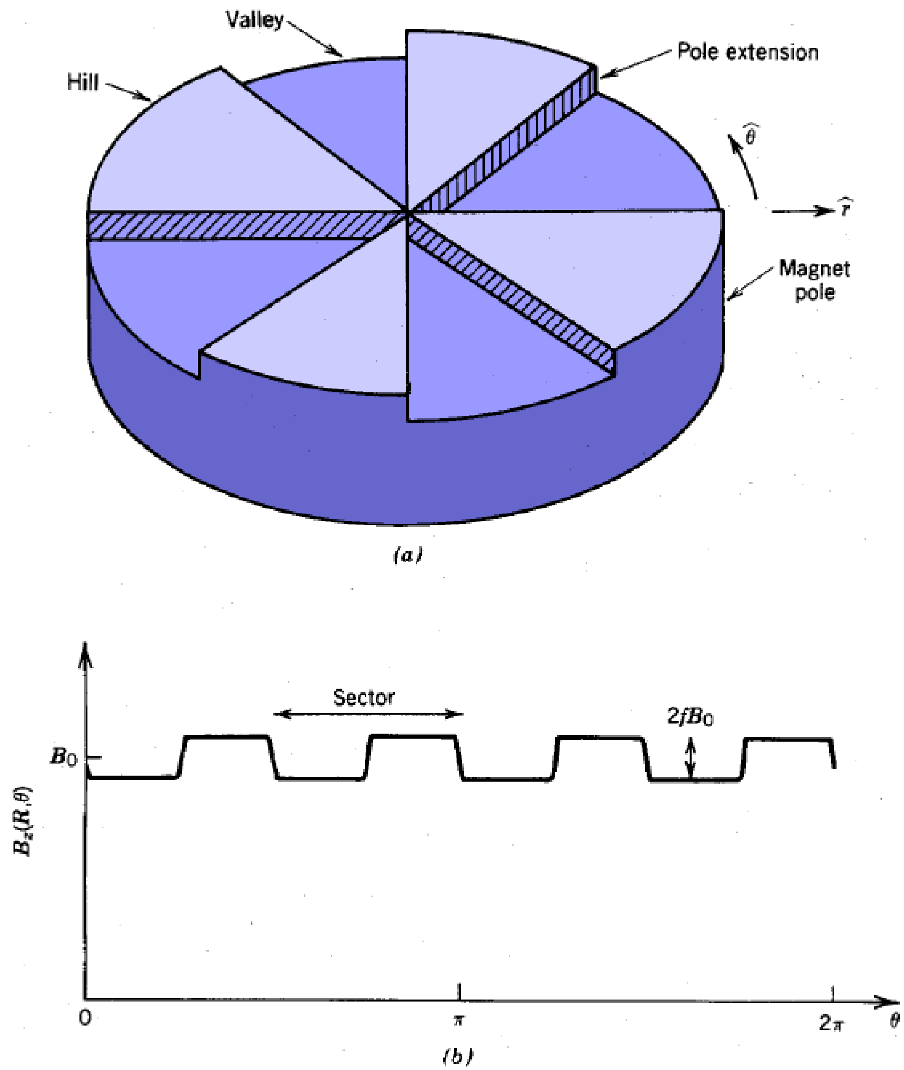

Figure 15.6 Magnetic fields in AVF cyclotron. (*a*) Magnet pole of AVF cyclotron, no spiral angle. (*b*) Vertical field amplitude as function of azimuth at constant radius.

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$$R_i = Inx\sigma_i$$

where

R_i = number of processes of type i in the target per unit time
I = number of incident particles per unit time
n = number of target nuclei per cm^3 of target = **$\rho N_A/A$**
σ_i = cross-section for the specified process in cm^2
x = the target thickness in cm

and assuming that

1. The beam current is constant over the course of the irradiation
2. The target nuclei are uniformly distributed in the target material
3. The cross-section is independent of energy over the energy range used

Saturation factor, SF = $1 - e^{-\lambda t}$

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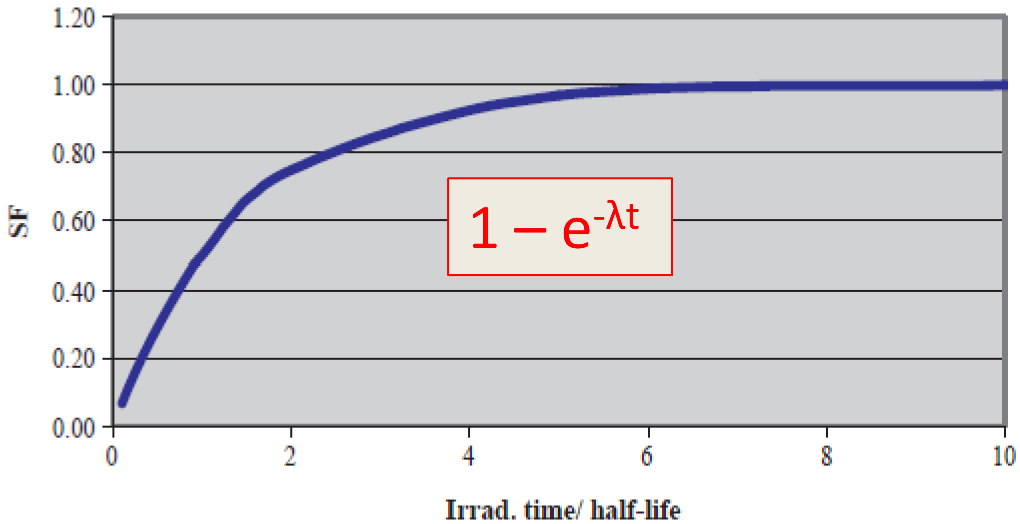
T_{irr} = 1 half-life results in an activity of 50% of the saturation (max) activity
2 half-lives → 75%
3 half-lives → 90%

The practical production limits of a given radionuclide are determined by the half-life of the isotope, e.g.

^{15}O, $T_{1/2}$ = 2 minutes
^{18}F, $T_{1/2}$ = almost 2 hours



For ***long lived species***, the production rates are usually expressed in terms of integrated dose or total beam flux (*μA·h)*

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- Technetium-99m (^{99m}Tc) has been the most important radionuclide used in nuclear medicine
- Short half-life (6 hours) makes it impractical to store even a weekly supply
- Supply problem overcome by obtaining parent ^{99}Mo, which has a longer half-life (67 hours) and continually produces ^{99m}Tc
- A system for holding the parent in such a way that the daughter can be easily separated for clinical use is called a *radionuclide generator*

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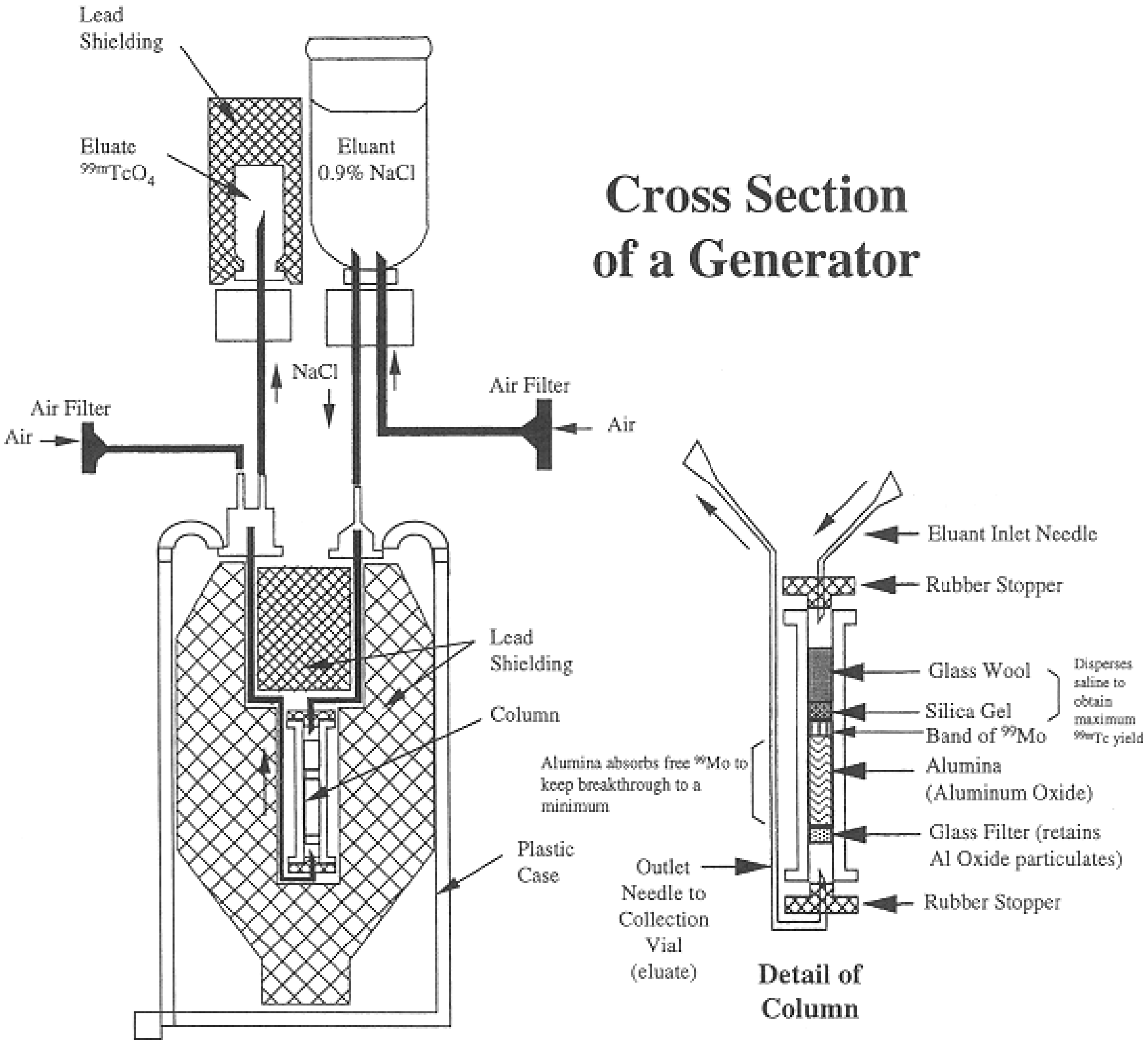

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- Between elutions, the daughter (^{99m}Tc) builds up as the parent (^{99}Mo) continues to decay
- After approximately 23 hours the ^{99m}Tc activity reaches a maximum, at which time the production rate and the decay rate are equal and the parent and daughter are said to be in *transient equilibrium*
- Once transient equilibrium has been reached, the daughter activity decreases, with an apparent half-life equal to the half-life of the parent
- Transient equilibrium occurs when the half-life of the parent is greater than that of the daughter by a factor of about 10

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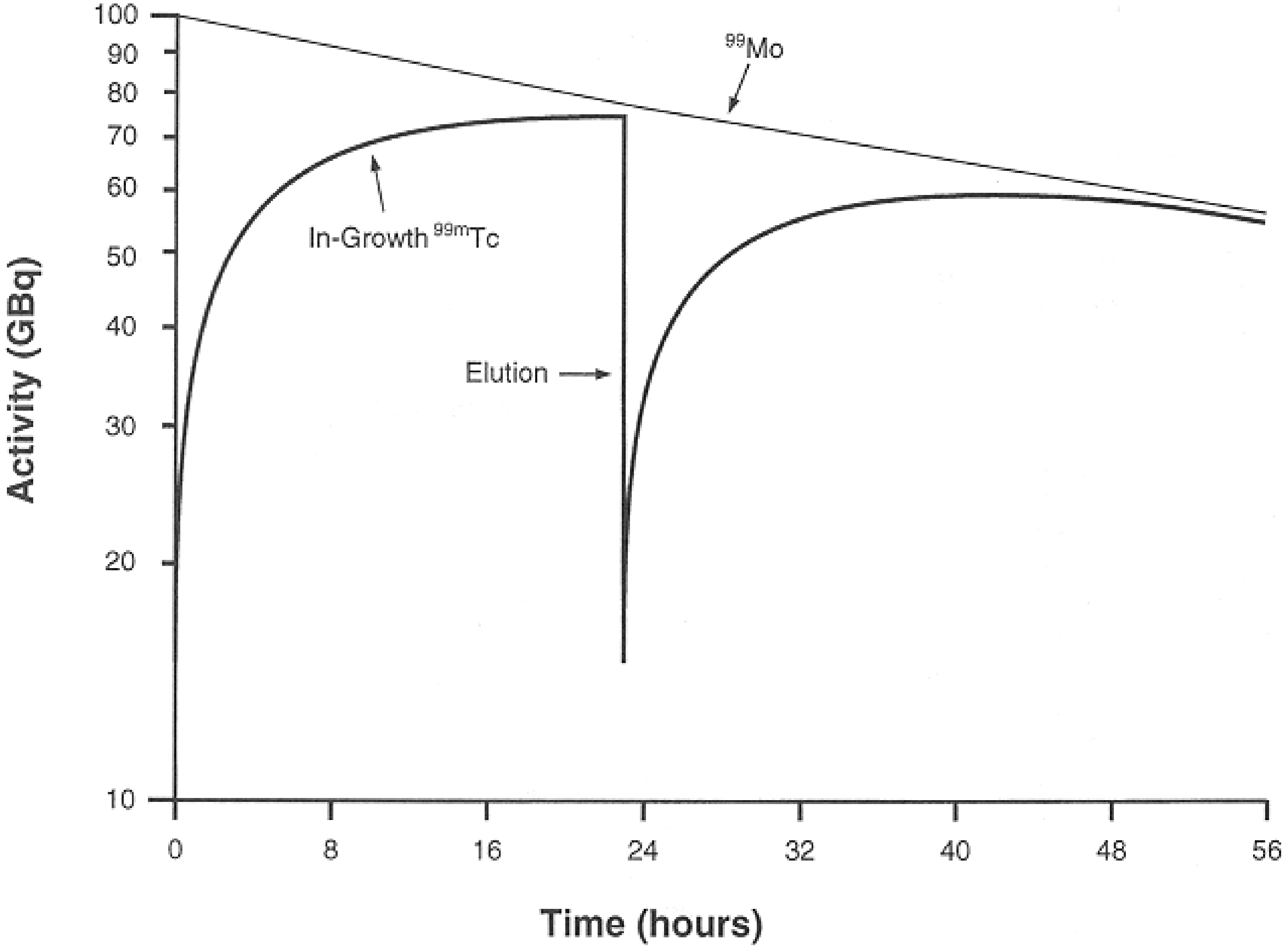

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Parent	Decay mode → Half-life	Daughter	Time of maximal ingrowth (equilibrium)	Decay mode → Half-life	Decay product
Germanium 69 (^{69}Ge)	EC → 271 days	Gallium 68 (^{68}Ga)	~6.5 hr (S)	β^+, EC → 68 min	Zinc 68 (^{68}Zn), stable
Rubidium 81 (^{81}Rb)	β^+, EC → 4.5 hr	Krypton 81m (^{81m}Kr)	~80 sec (S)	IT → 13.5 sec	Krypton 81 $^{81}Kr^{a}$
Strontium 82 (^{82}St)	EC → 25.5 days	Rubidium 82 (^{82}Rb)	~7.5 min (S)	β^+ → 75 sec	Krypton 82 (^{82} Kr), stable
Molybdenum 99 (^{99}Mo)	β^- → 67 hr	Technetium 99m (^{99m}Tc)	~24 hr (T)	IT → 6 hr	Technetium 99 (^{99}Tc)^{a}

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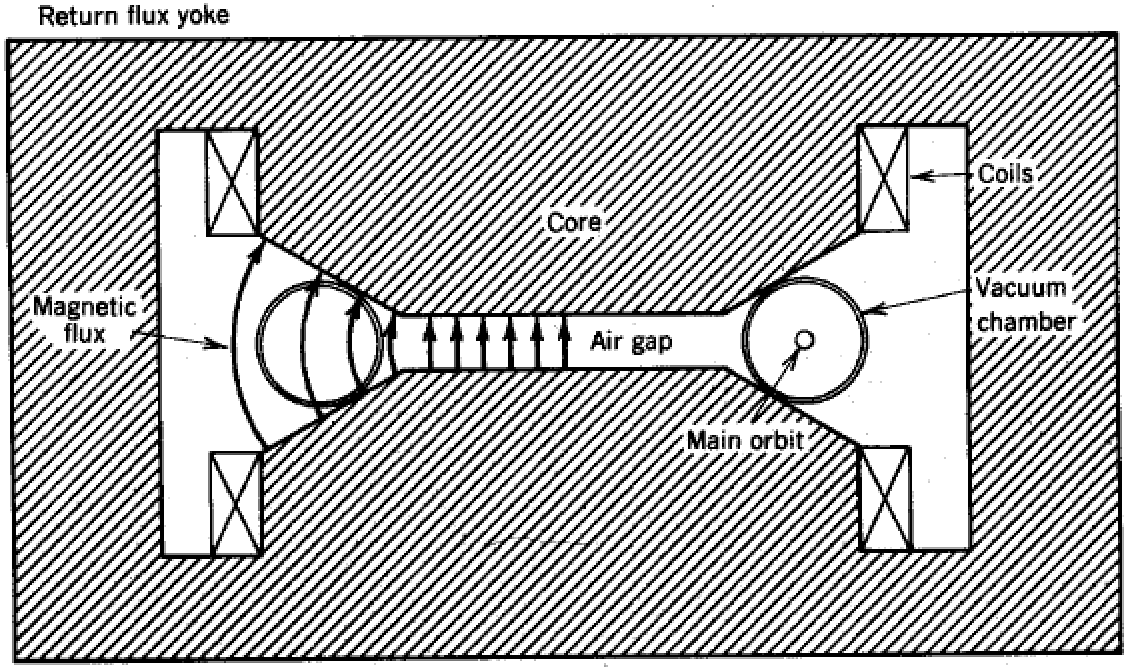
Schematic diagram of betatron with air gap



$$B(R) = \frac{1}{2}\overline{B}(R)$$

$B(R)$ = field at the orbit

$\overline{B}(R)$ = average flux density through the orbit

- Magnetic field produced by pulsed coils
- The magnetic flux inside the radius of the vacuum chamber changes with time
- Increasing flux generates an azimuthal electric field which accelerates electrons in the chamber

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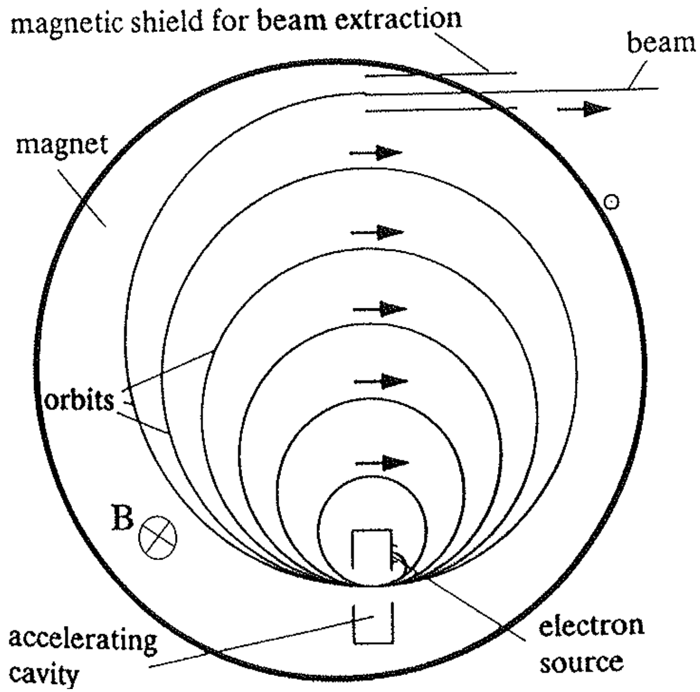


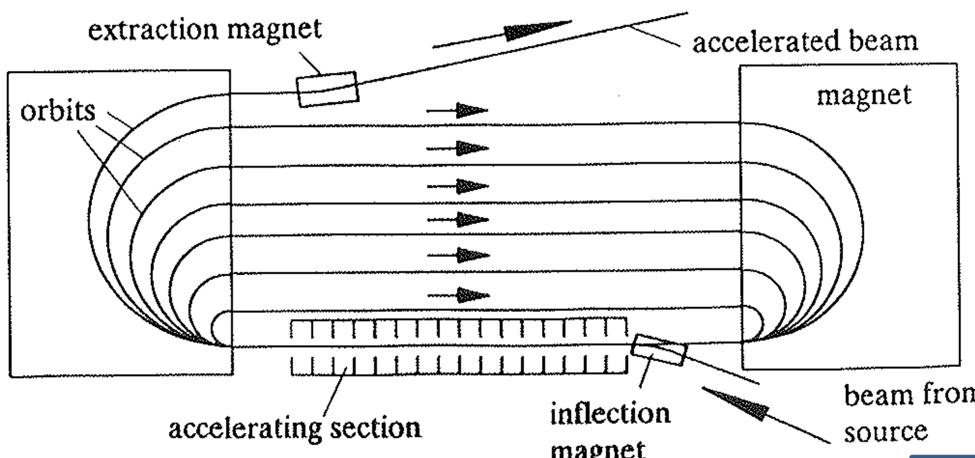
An "electron cyclotron"
- **Uniform magnetic field**
- **Fixed-frequency RF system**
- **Well-separated orbits**

Bending radius $$\frac{1}{r} = \frac{eB}{cp} = \frac{eB}{mc^2\gamma\beta}$$

Revolution time $$\tau = \frac{2\pi r}{v} = \frac{2\pi mc}{e}\frac{\gamma}{B}$$

- Isocronism only if $\gamma \approx 1$
- If $\gamma > 1$, $\Delta\tau$ per turn = $\Delta\gamma$
- To have isochronism it must be $\Delta\tau$ per turn = $h\tau_{RF}$
- Required energy gain per passage
  - for electrons ΔE_e= 511 keV
  - for protons ΔE_p= 938 MeV

Racetrack microtron



Magnet weight ≈ (energy)^3

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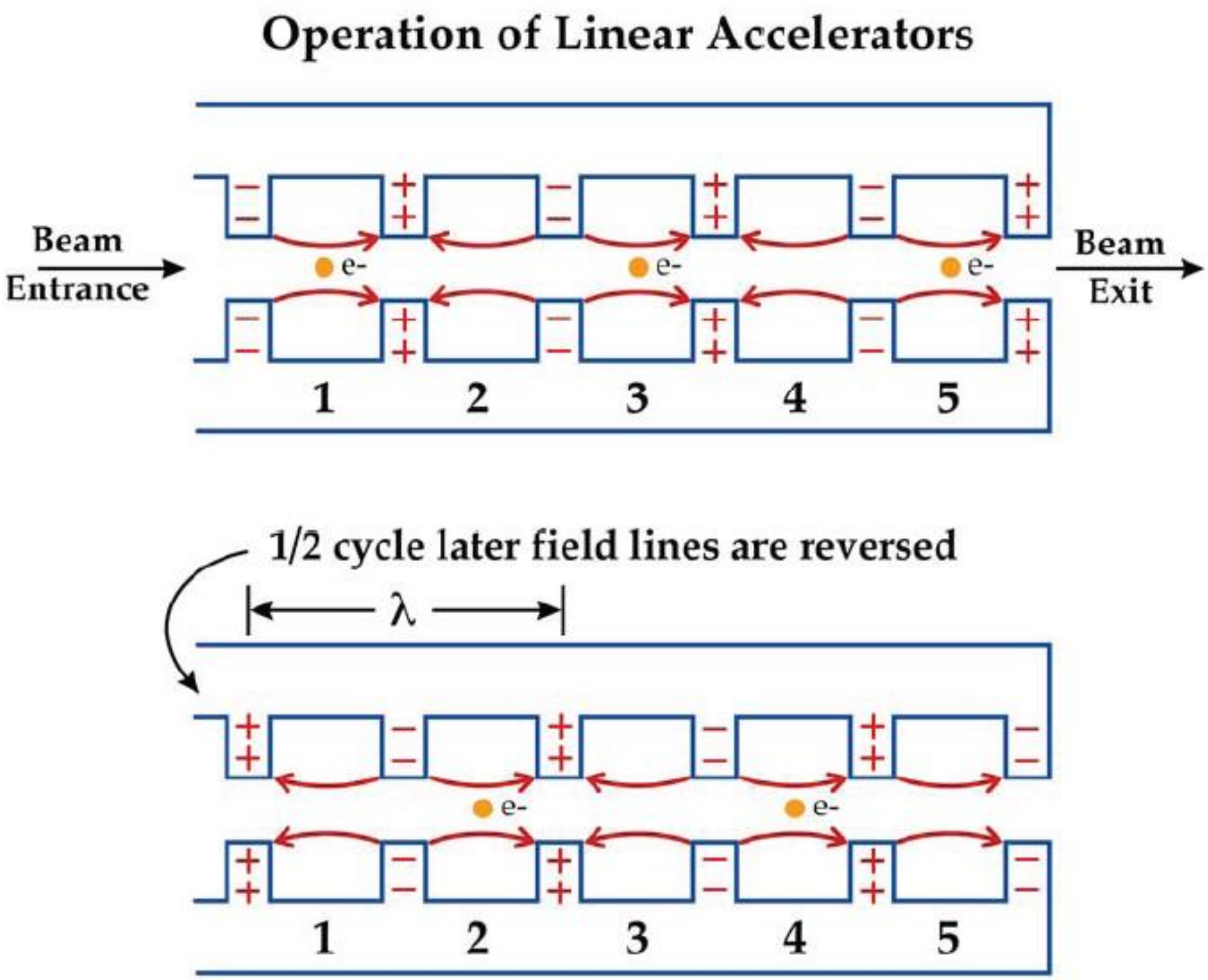

Particles initially in cell 1 arrive in cell 2 to get further accelerating kick. Frequency must match particles velocity and cell periodicity = ½ λ:

$$f = \frac{v}{\lambda}$$

Schematics of a treatment head of a medical electron linac

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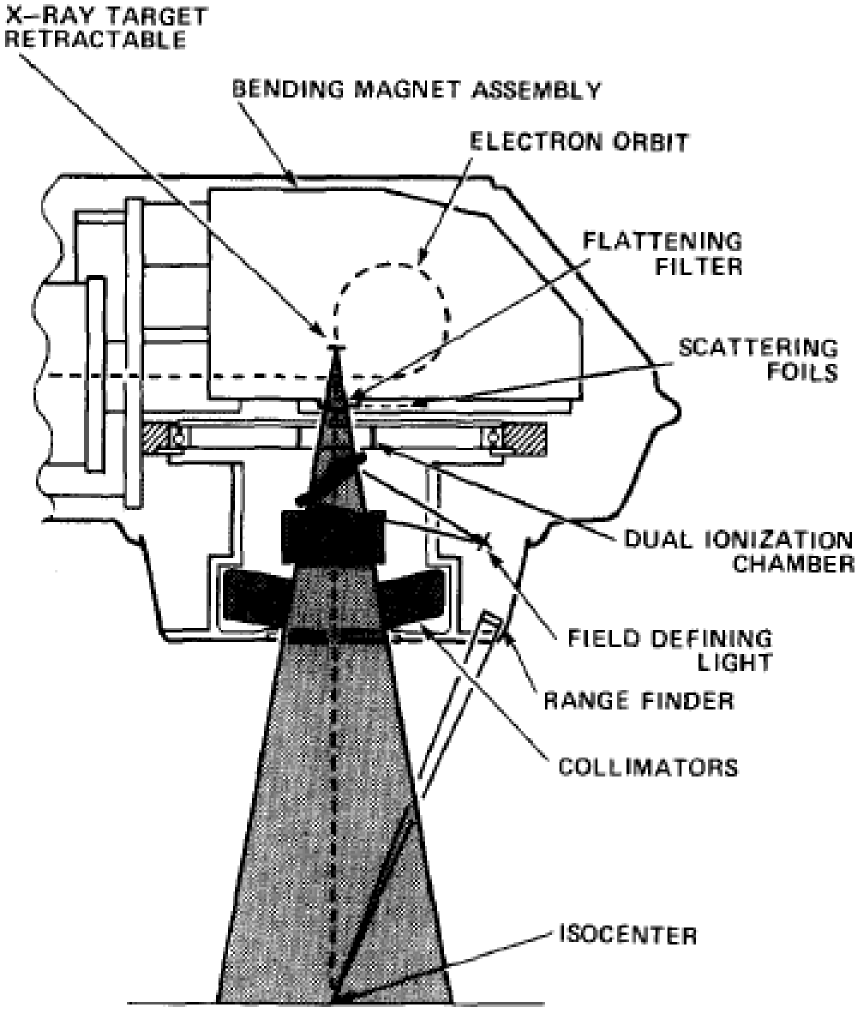

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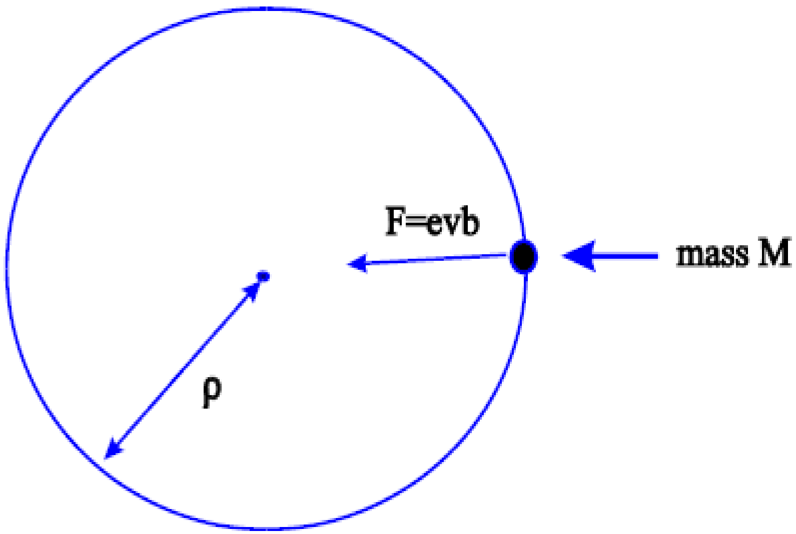
(the field is in/out of the plane of this slide)



$$F = \frac{mv^2}{\rho},$$ where ρ = radius of curvature of the path

$$F = evB = \frac{mv^2}{\rho}$$

(p = momentum = mv)

$$B\rho = \frac{mv}{e} = \frac{p}{e}$$

Bρ = 33.356·p [kG·m] = 3.3356·p [T·m] (if p is in GeV/c)

Bρ is called “magnetic rigidity” of the particle and is an index of how difficult is to bend the motion of a charged particle by a magnetic field

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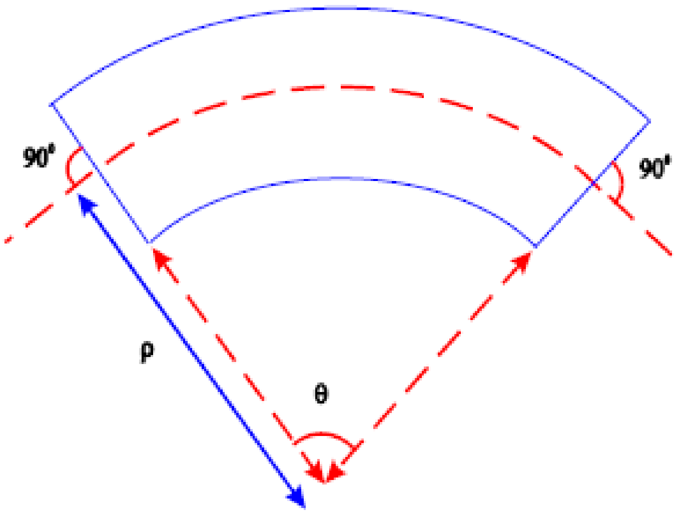


Trajectory of a particle in a bending magnet

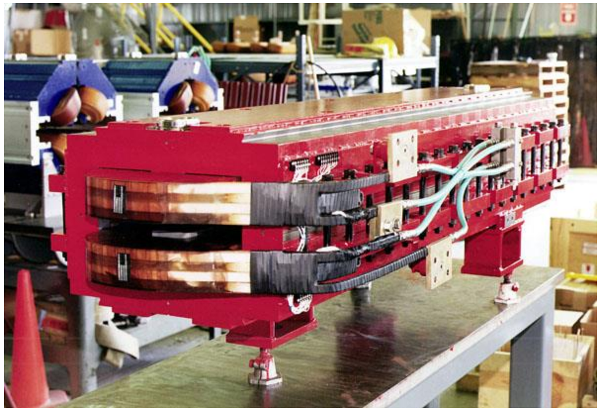
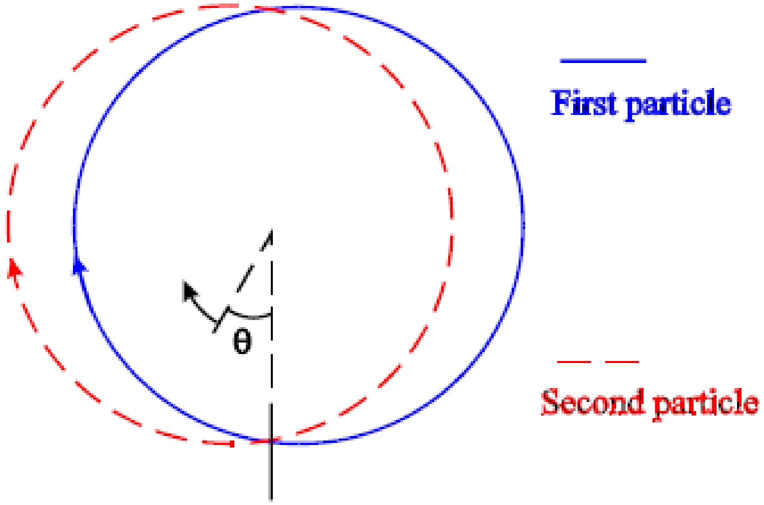


Photo: courtesy ANL

Unfortunately an accelerator contains more than one particle!

Number of circulating particles in a synchrotron is typically in the order of 10^{10} - 10^{12} or more



Two particles in a dipole field, with same momentum but different initial angles

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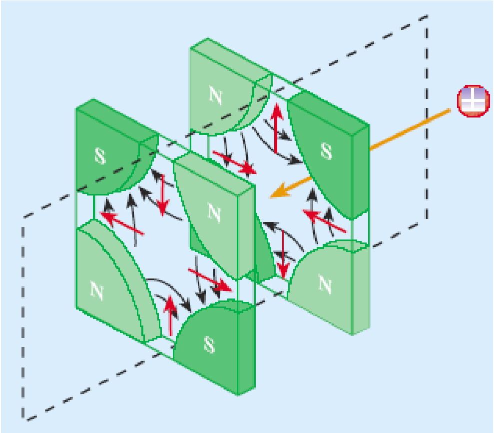
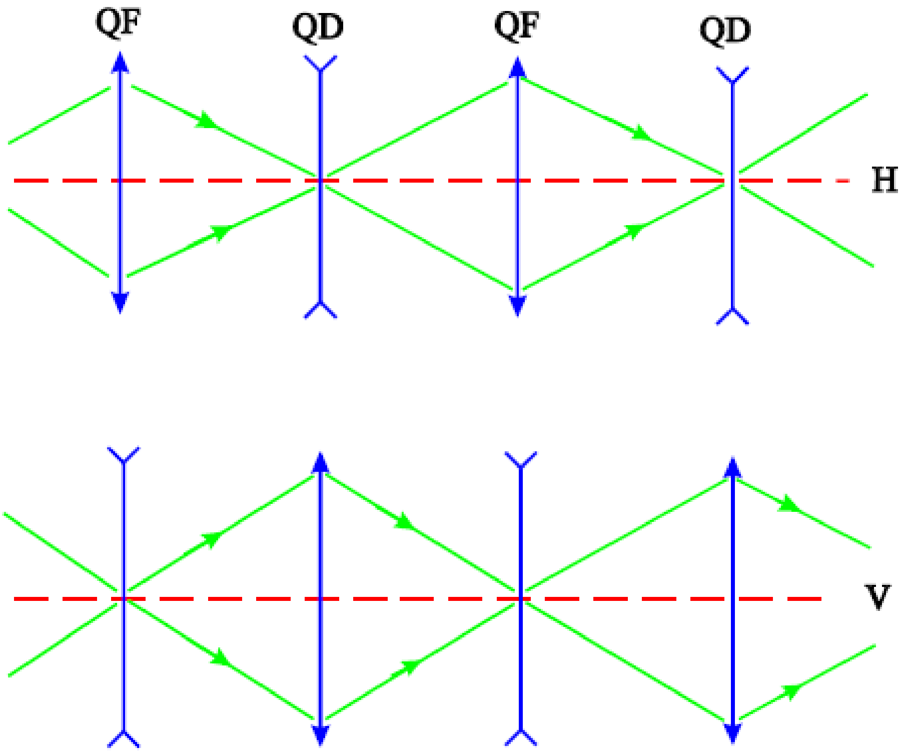
Light rays passing through a series of focusing and defocusing lenses

The lenses, which are concave in one plane, are convex in the other





In both cases the concave lenses will have little effect as the light passes very close to their centre, and the net result is that the light rays are focused in both planes

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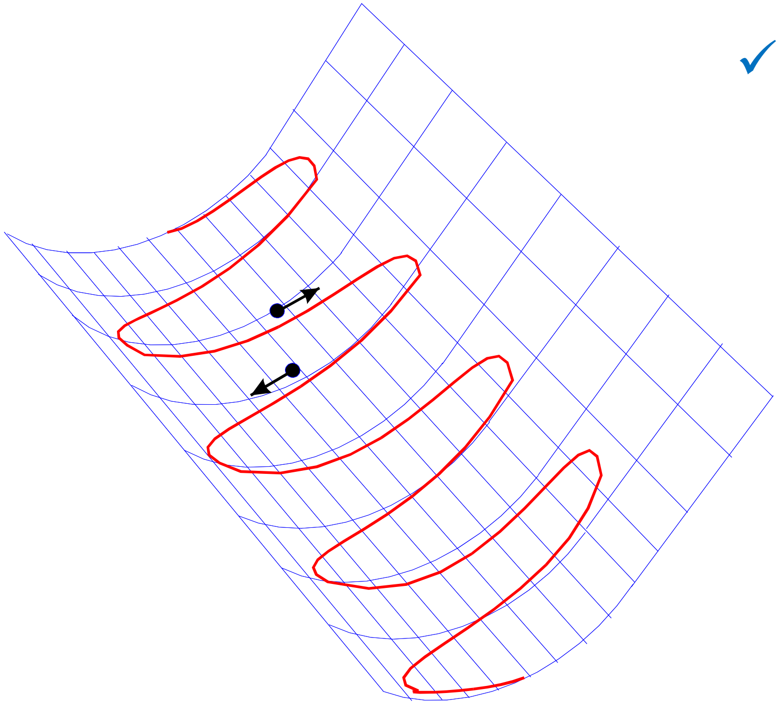
- ✓ **The gutter below illustrates how the particles in a synchrotron behave due to the quadrupole fields.**



- ✓ **Whenever a particle beam diverges too far away from the central orbit the quadrupoles focus them back towards the central orbit.**

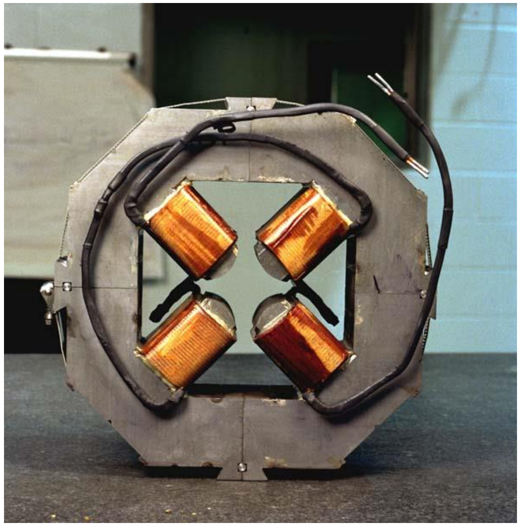


Photo courtesy Fermilab Visual Media Services

Beam “envelope” defined by the β function