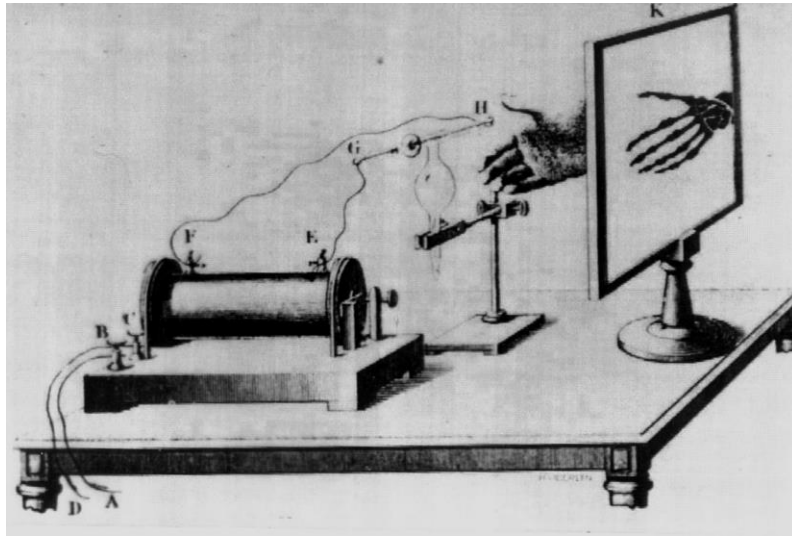

Medical accelerators, radionuclide production and radiation therapy

Marco Silari
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- Brief historical introduction
- Particle accelerators for medical uses
 - Cyclotron
 - Betatron
 - Microtron
 - Electron linac
 - Proton synchrotron
- Radionuclide production
- Radiation therapy



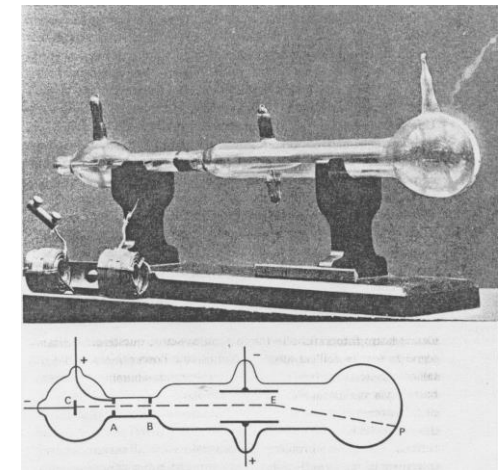
1895
discovery of X rays

**Wilhelm Conrad
Röntgen**



J.J. Thompson

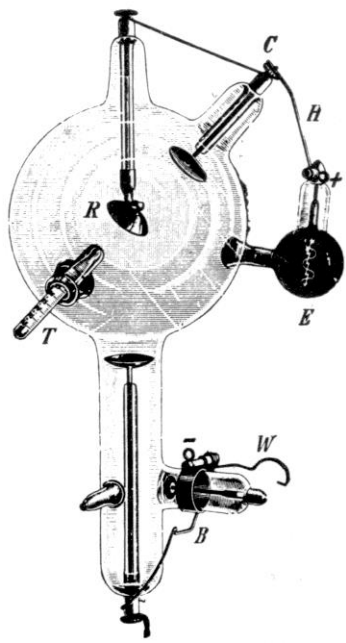
1897
“discovery” of the
electron



Courtesy Prof. Ugo Amaldi

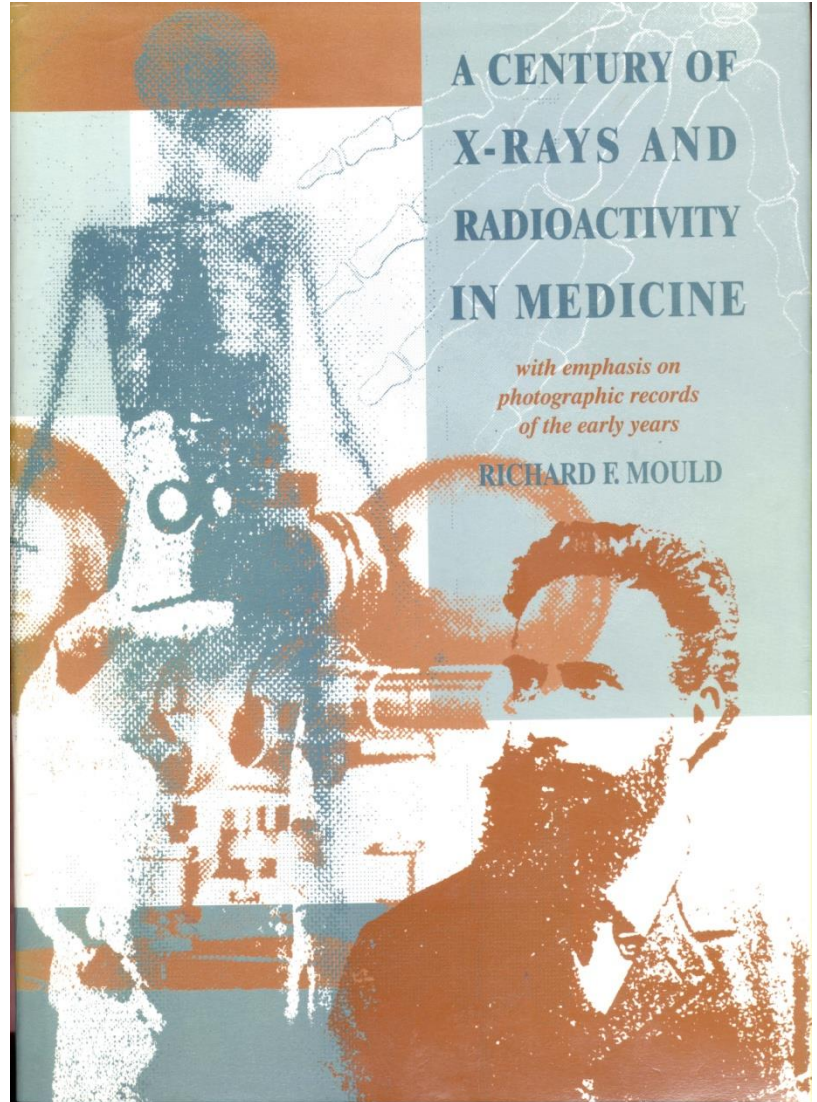
Röhren fremden Fabrikates.

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



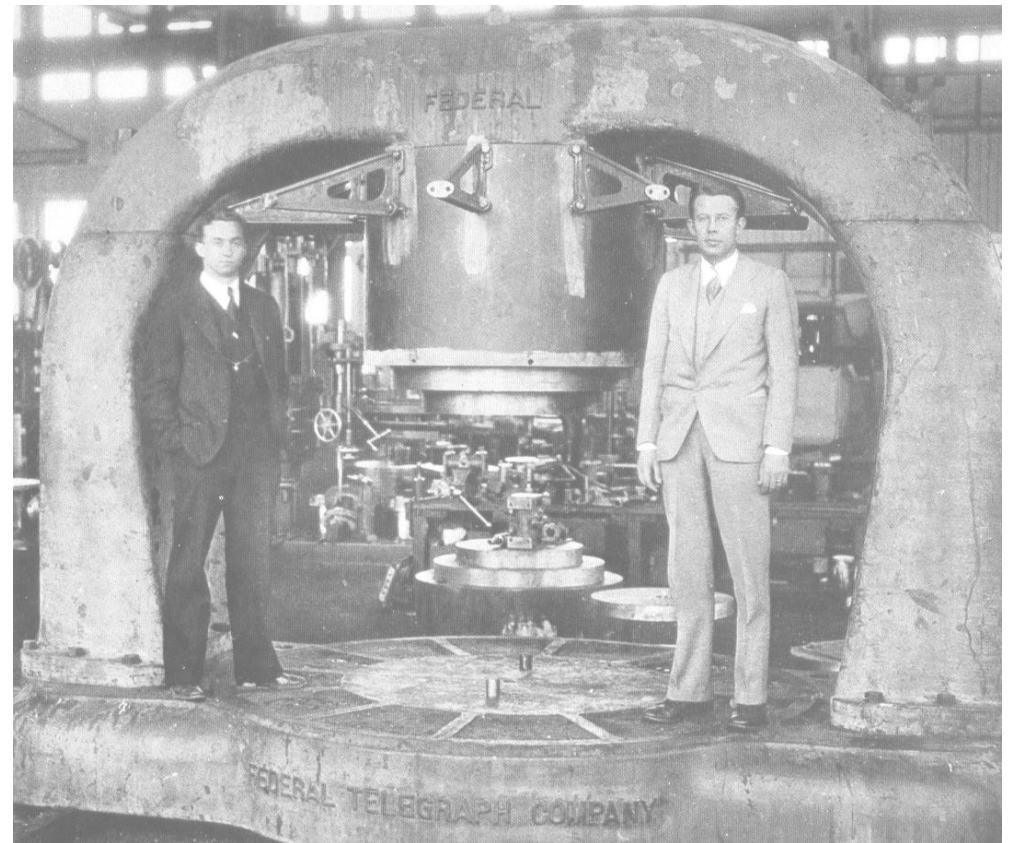
Diese Röhre ist besonders für die Röntgen-Oberflächen-therapie bestimmt. Sie gestattet eine praktisch genügend genaue Verabreichung der für eine Sitzung erforderlichen Strahlenmenge durch bequeme direkte Ablesung an einer Thermometerskala.

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

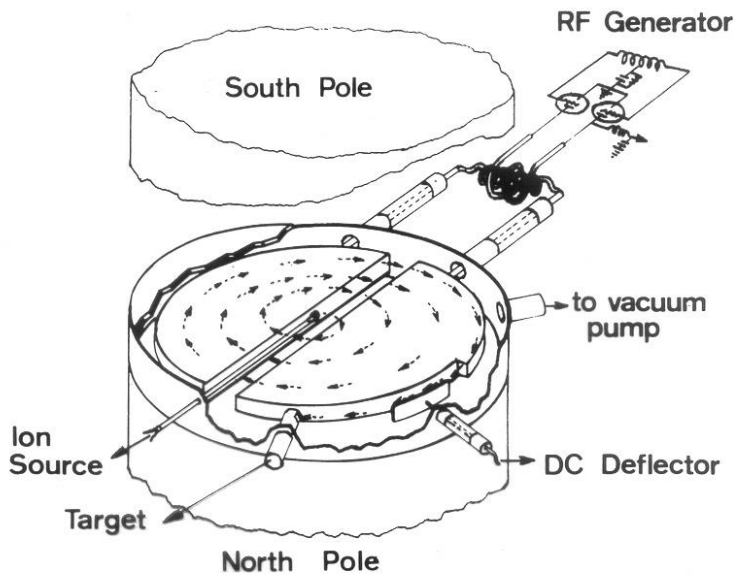




1930 Ernest Lawrence invents the cyclotron



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



Courtesy Prof. Ugo Amaldi

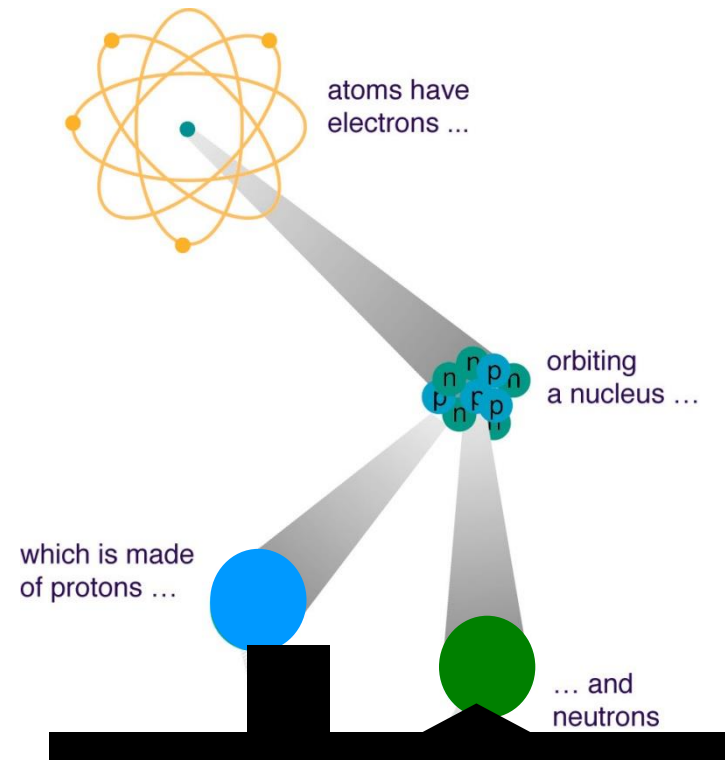


James Chadwick
(1891 – 1974)

Courtesy Prof. Ugo Amaldi

1932

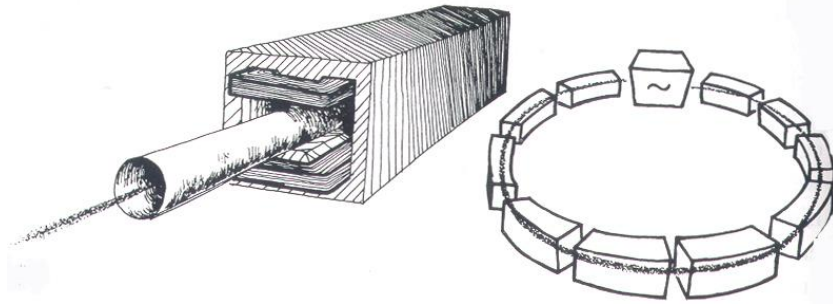
Discovery of the neutron



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

Tools for (medical) physics: the synchrotron

1945: E. McMillan and V.J. Veksler
discover the principle of phase stability

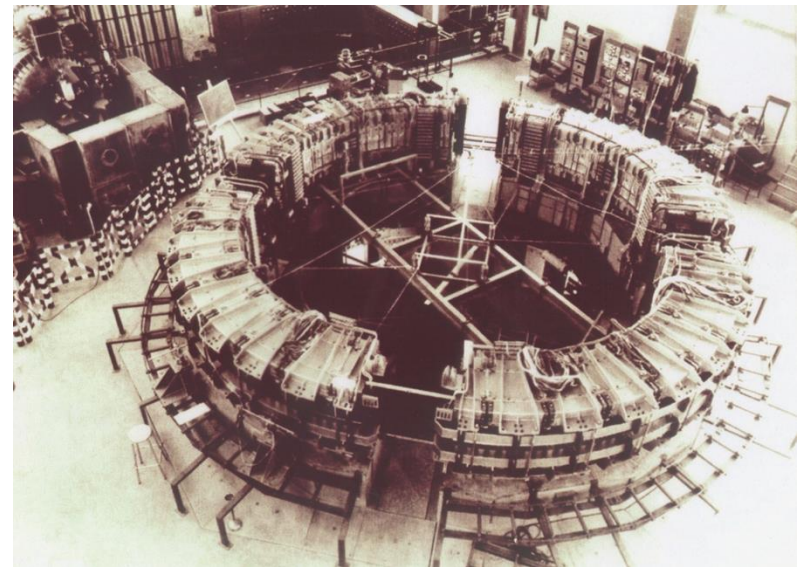


6 GeV proton synchrotron

Bevatron - Berkeley - 1954

1 GeV electron synchrotron

Frascati - INFN - 1959



Courtesy Prof. Ugo Amaldi

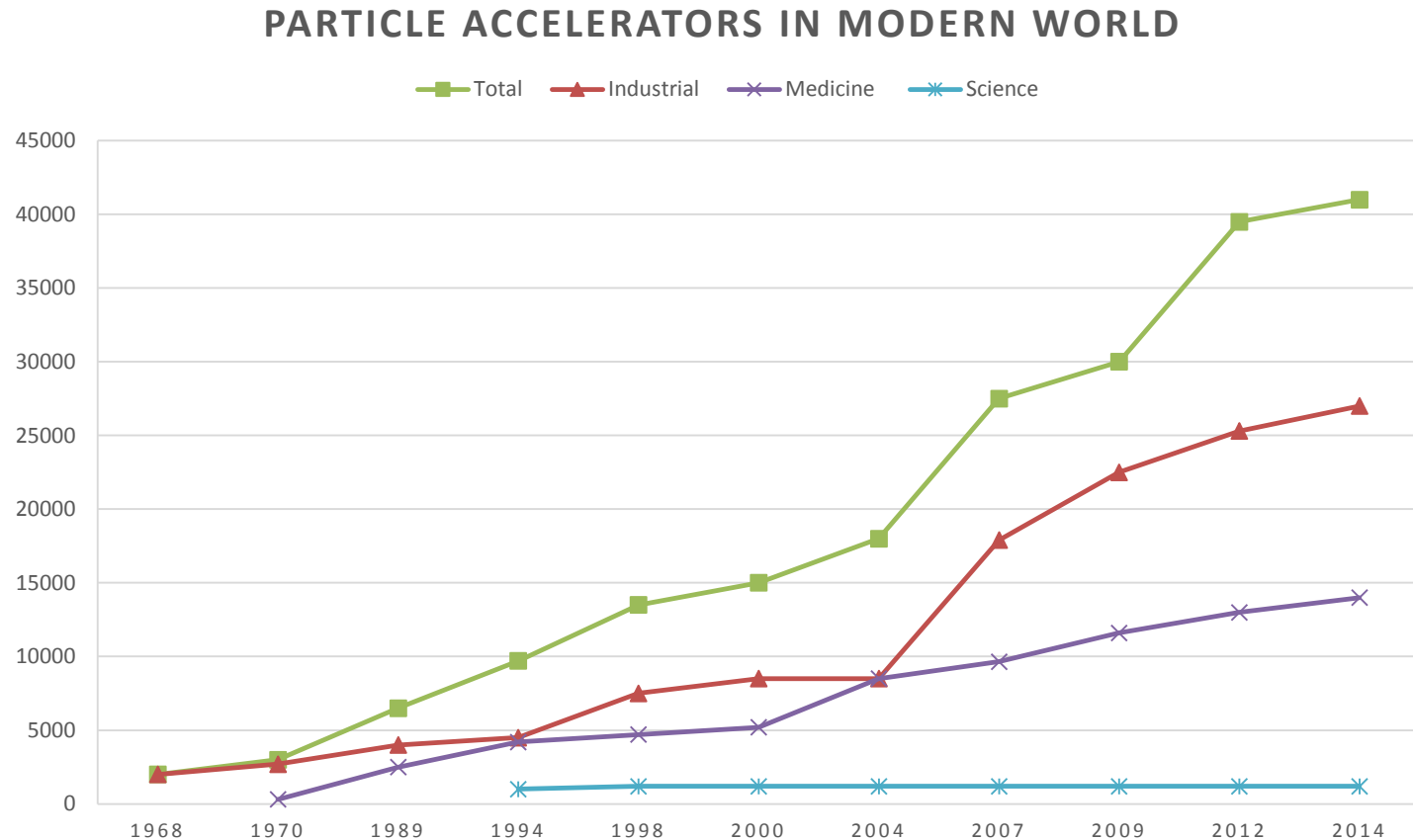
Particle accelerators operational in the world

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, including	~2000	~2700	>4000	>4500	~7500	~8500	>8500	~17 900	22 500	25 300	27 000
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 medicine, including		306	>2500	~4200	~4700	~5200	~8500	~9650	~11 600	~13 000	~14 000
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

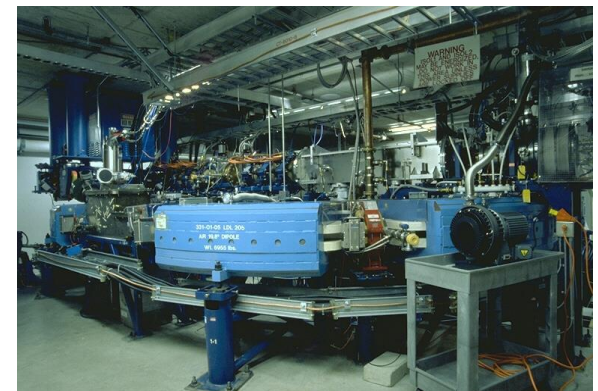
A. P. Chernyaev and S. M. Varzar, Particle Accelerators in Modern World, Physics of Atomic Nuclei, 2014, Vol. 77, No. 10, pp. 1203–1215.

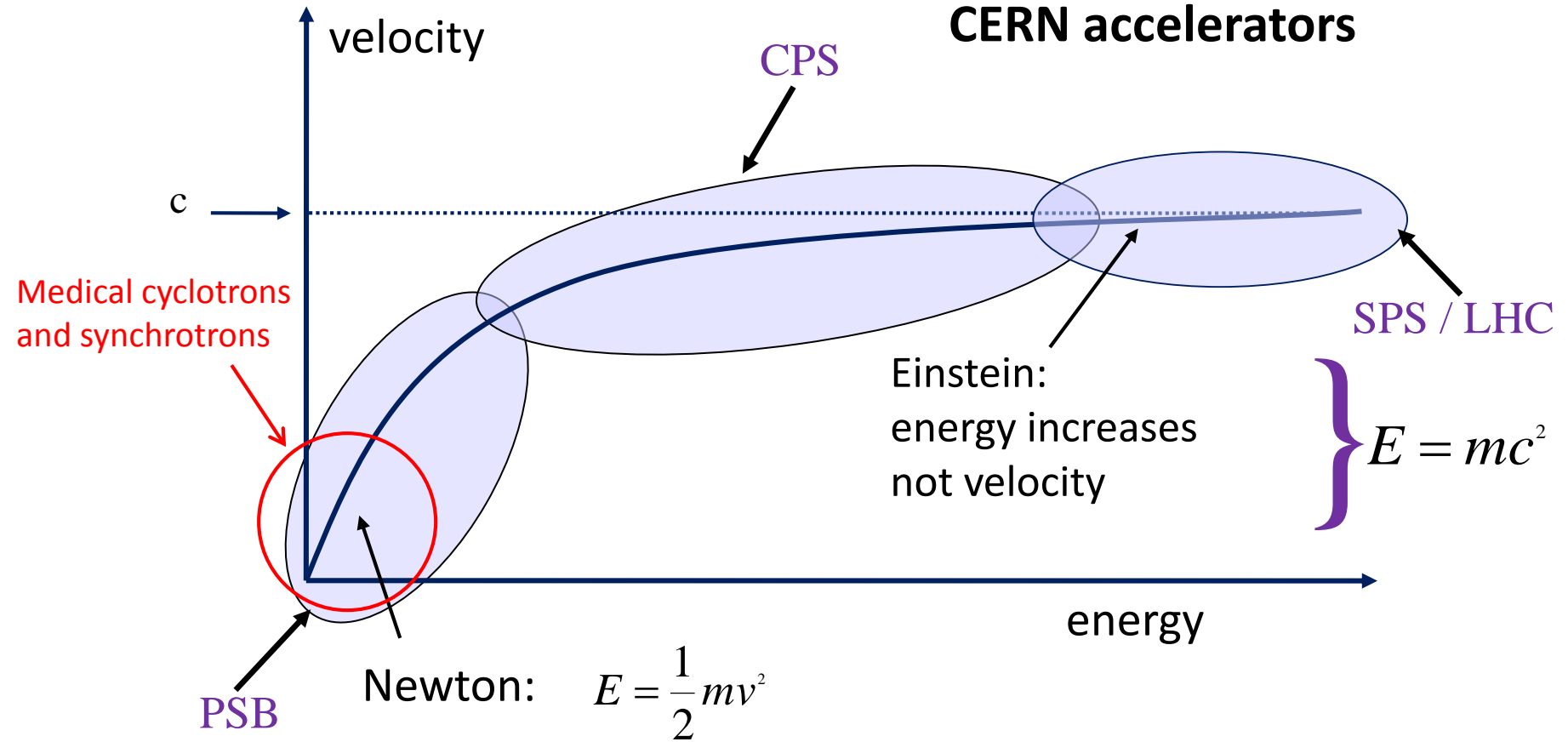
Three main applications: 1) Scientific research, 2) Medical applications 3) Industrial uses



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

- Production of **radionuclides** with (low-energy) cyclotrons
 - Imaging (PET and SPECT)
 - Therapy
- Electron linacs for **conventional radiation therapy**, including advanced modalities
- Medium-energy cyclotrons and synchrotrons for **hadron therapy** with protons (250 MeV) or light ion beams (400 MeV/u ^{12}C -ions)
 - Accelerators and beam delivery
 - New concepts





Radionuclide production

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)

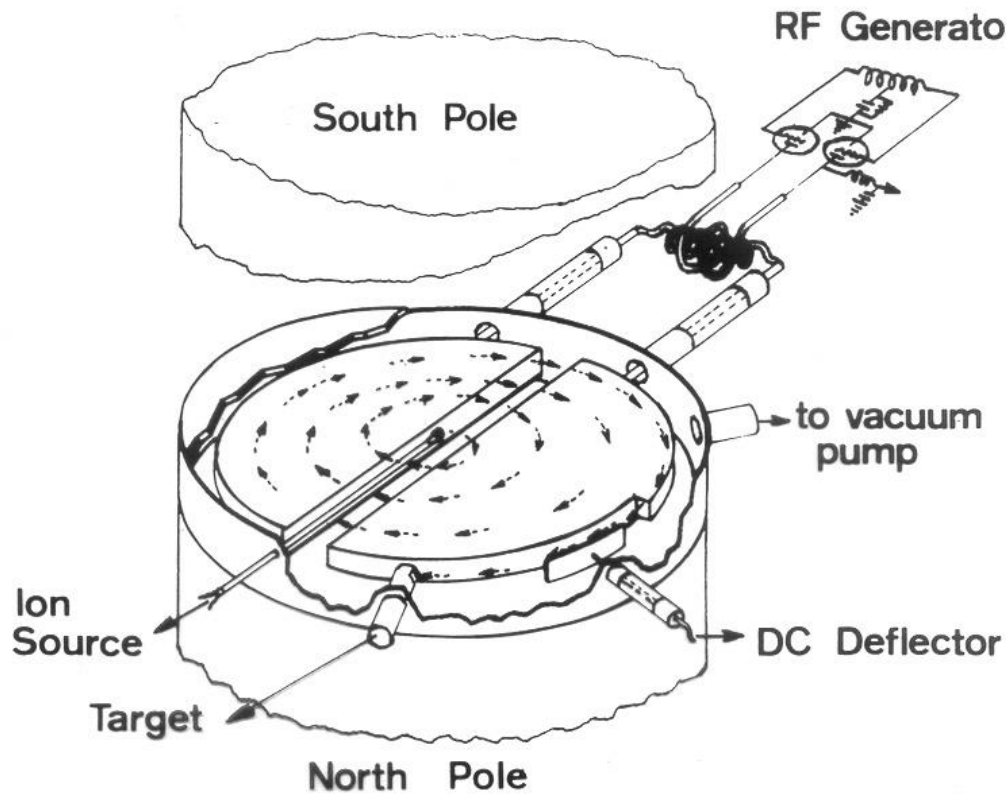
- Type of emission (α , β^+ , β^- , γ)
- Energy of emission
- Half-life
- Radiation dose (essentially determined by the parameters above)

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

The cyclotron – The work horse for radionuclide production

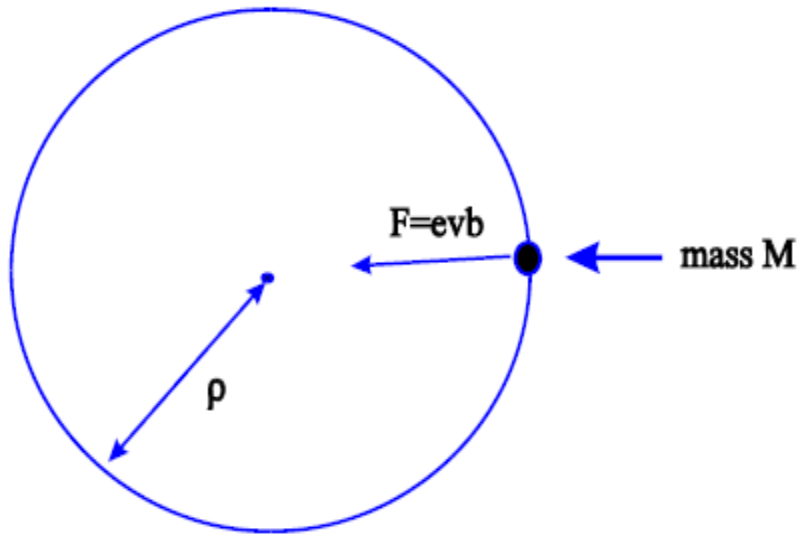


Scanditronix MC40



Motion of a particle in a dipole magnetic field

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



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

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

($p = \text{momentum} = mv$)

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

$$B\rho = 33.356 \cdot p \text{ [kG}\cdot\text{m]} = 3.3356 \cdot p \text{ [T}\cdot\text{m]} \text{ (if } p \text{ is in GeV/c)}$$

$B\rho$ 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

The cyclotron

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

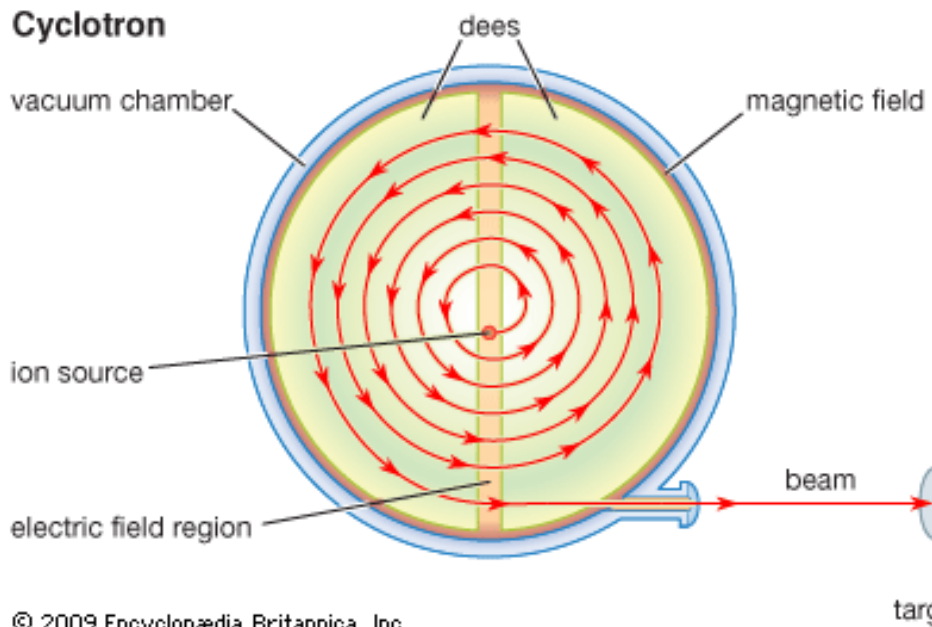
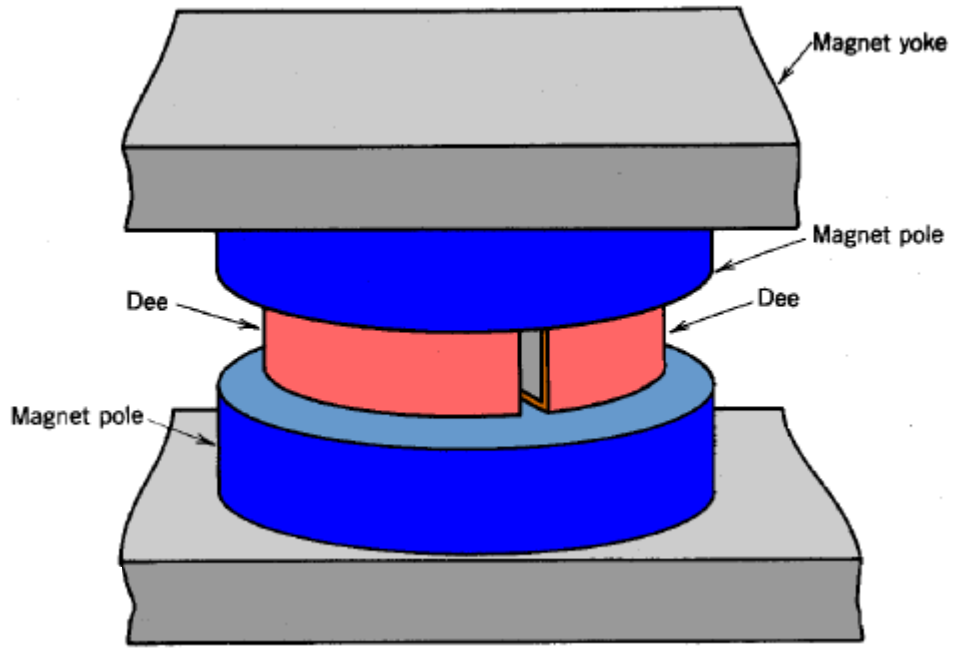
$$mv^2 / \rho = qvB \quad \omega = 2\pi f = v / \rho$$

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

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

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

 Isochronism



Maximum energy/nucleon:

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

$$\text{with } k = e^2 / 2m_p$$

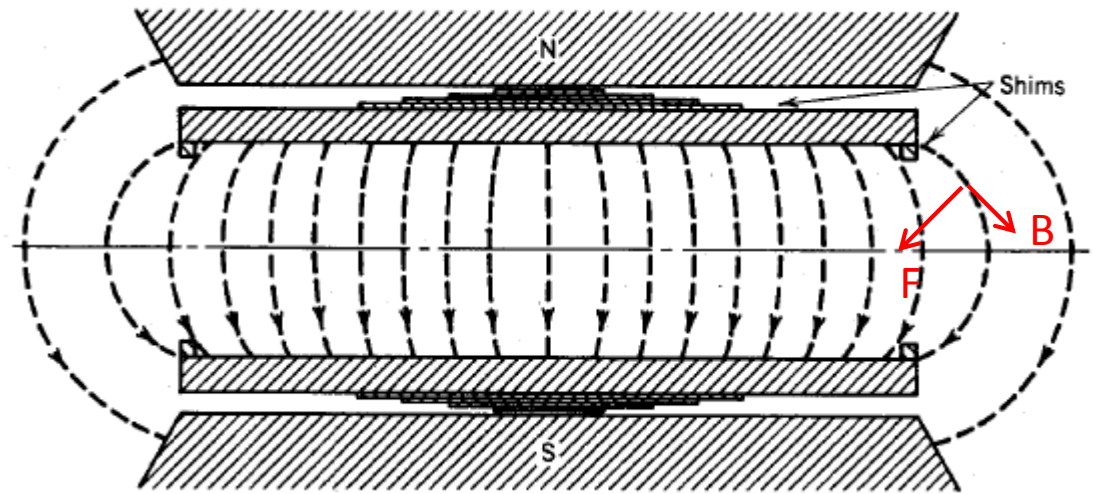
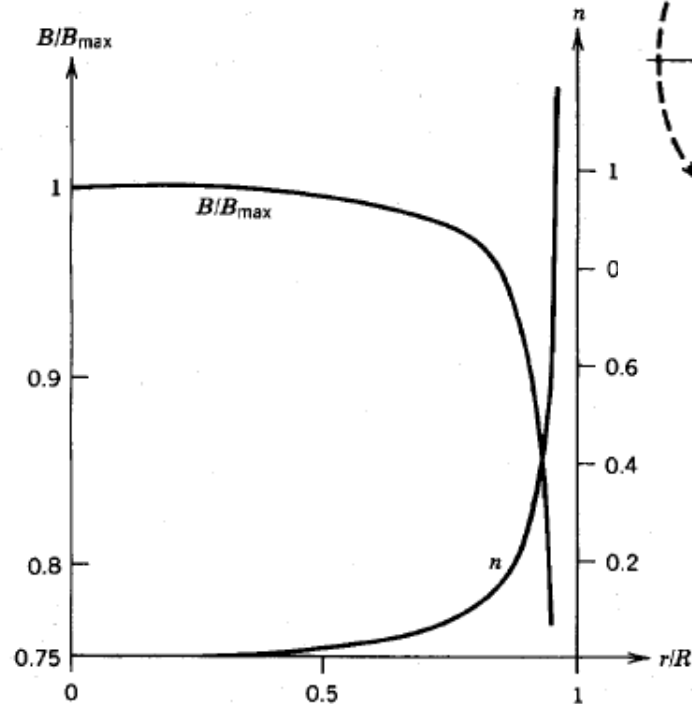
$K = k (B\rho)^2$ is called "bending limit"

$$K = 48 (B\rho)^2 \quad (\text{MeV})$$

if B is in teslas and m in metres

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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

AVF = azimuthally varying field

$$B(r, \theta) = \langle B(r) \rangle + \text{Mod}(r, \theta)$$

- RF constant
- $\langle B \rangle$ 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

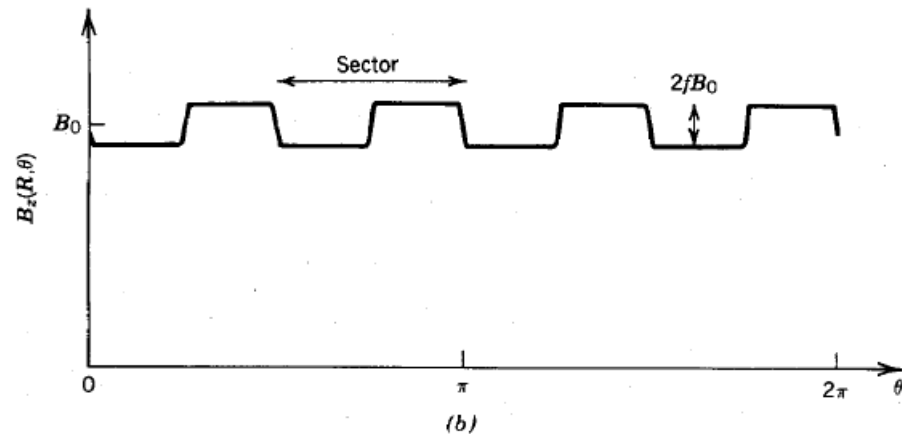
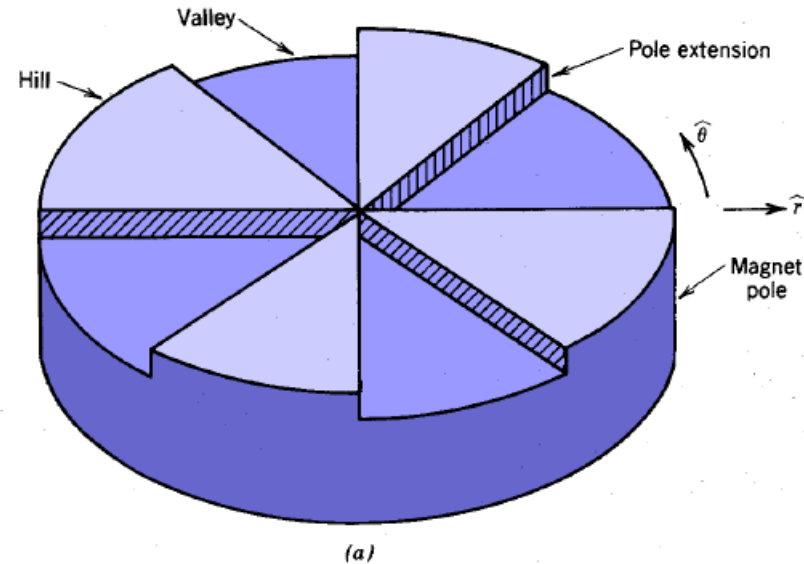
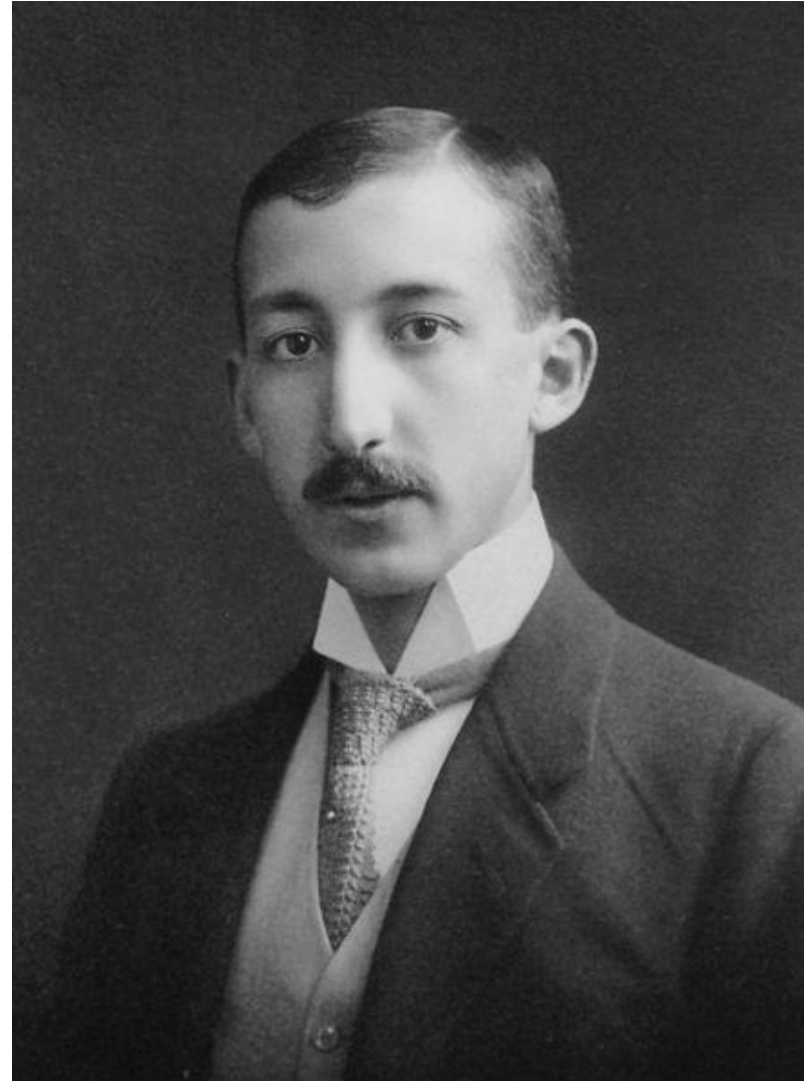


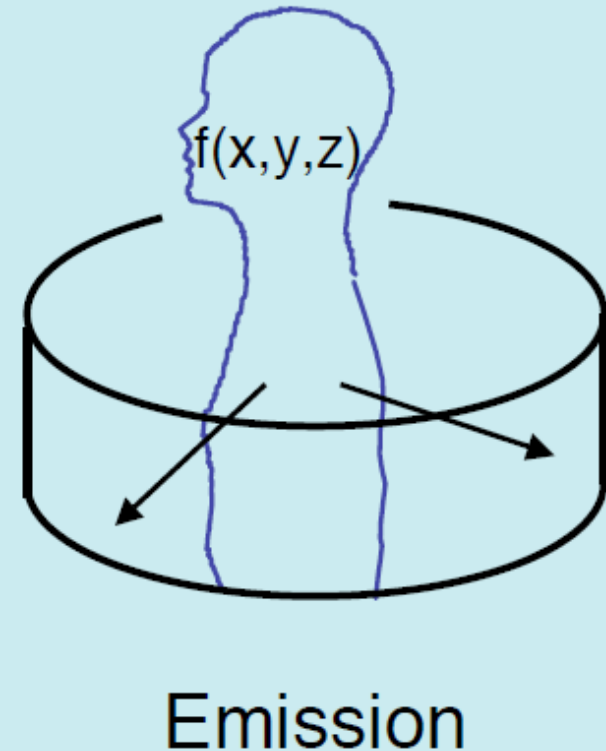
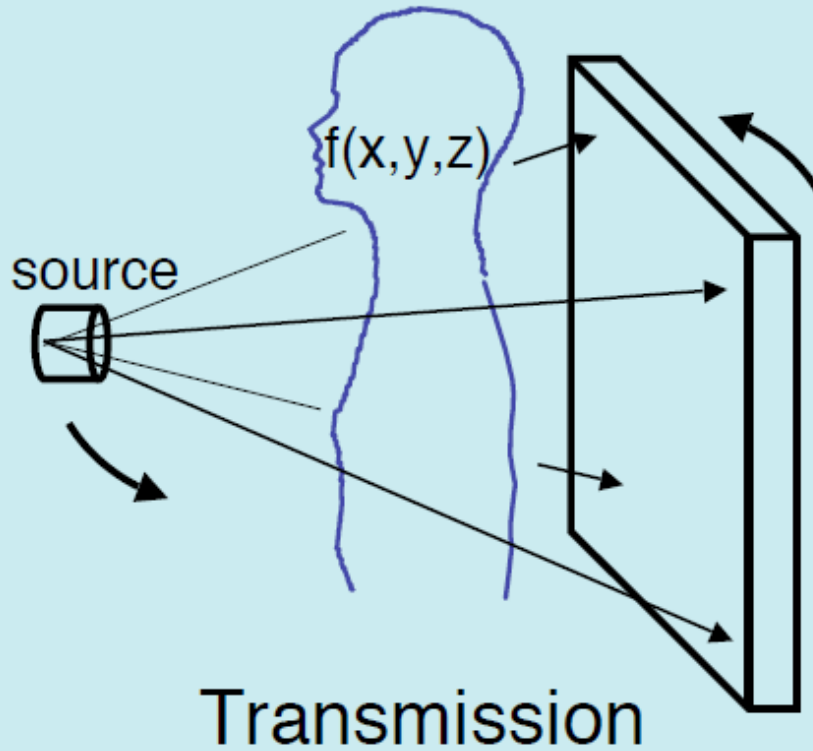
Figure 15.6 Magnetic fields in AVF cyclotron. (a) Magnet pole of AVF cyclotron, no spiral angle. (b) Vertical field amplitude as function of azimuth at constant radius.

- **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



- **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 $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ 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

External versus internal radiation sources



Courtesy P. Kinahan

Positron Emission Tomography (PET)

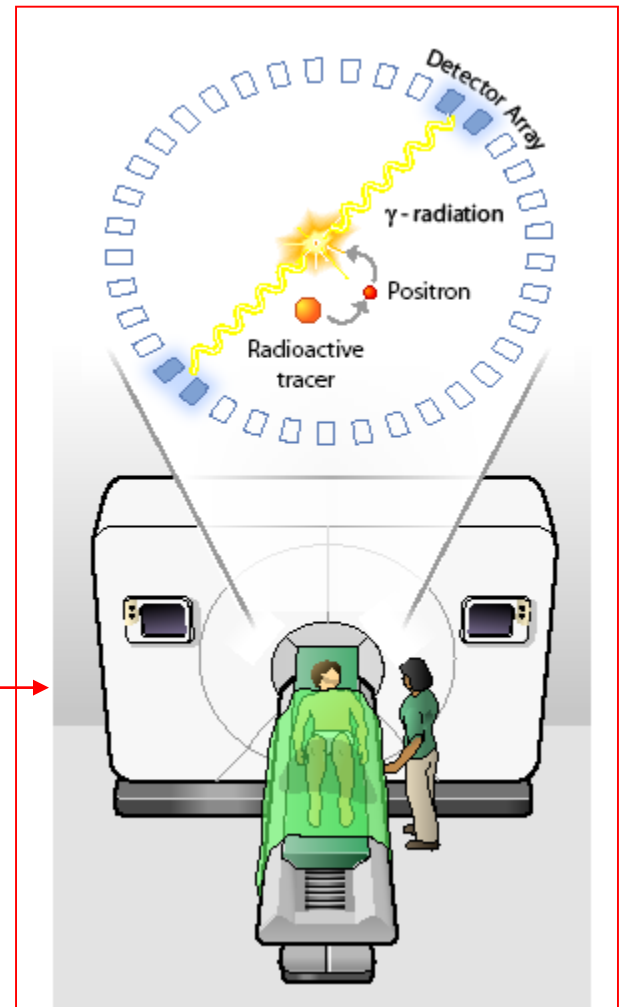


Cyclotron

Radiochemistry



PET camera



J. Long, "The Science Creative Quarterly", scq.ubc.ca

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

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

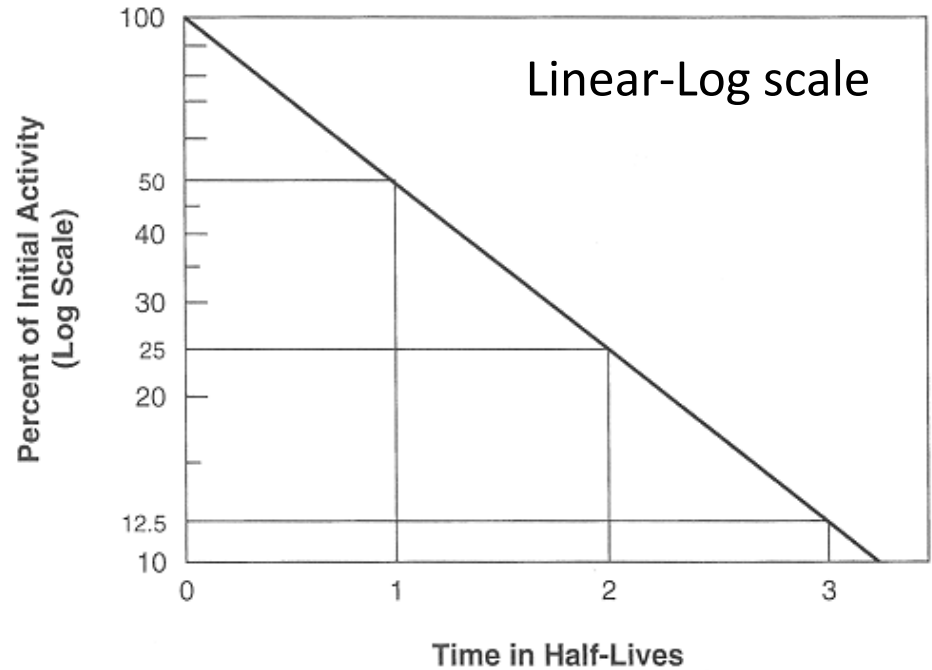
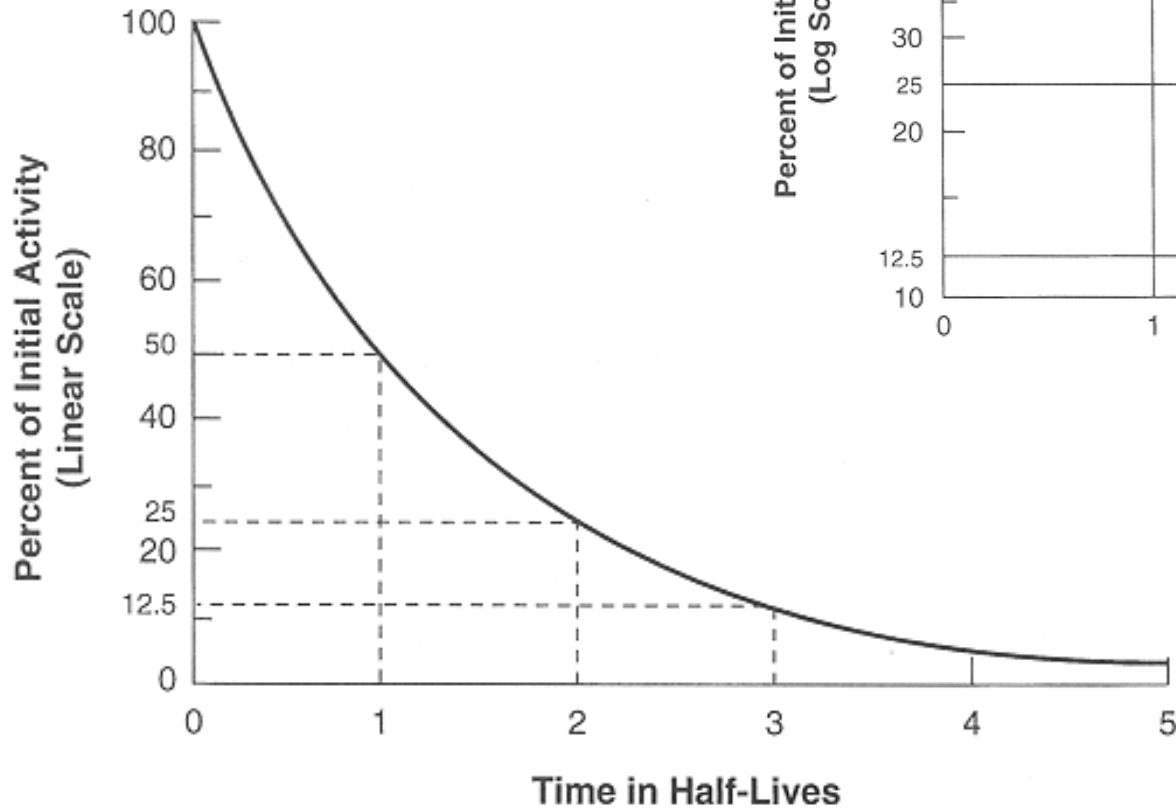
and remembering that:

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

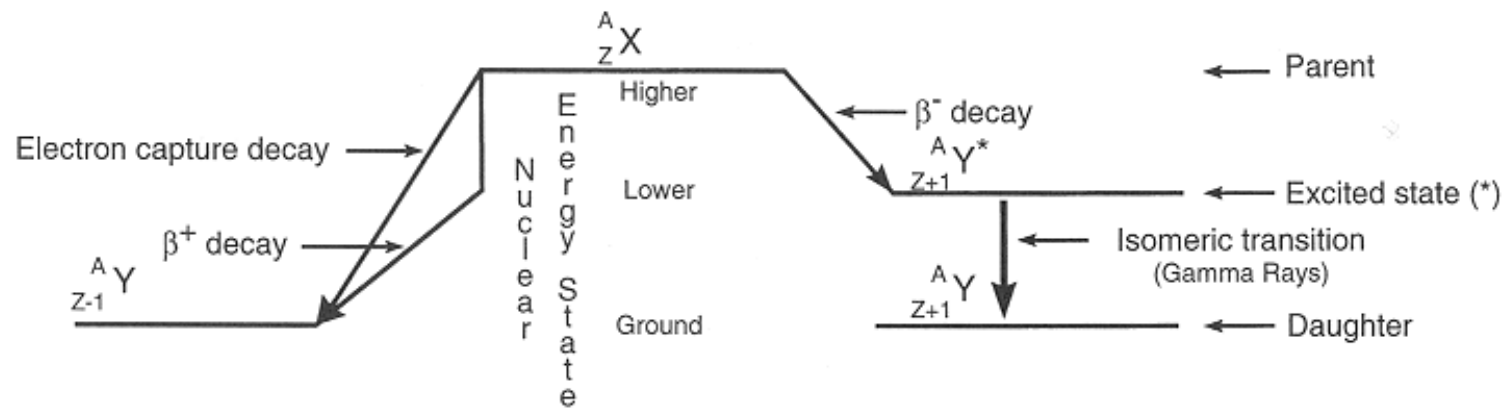
$$A = \lambda N$$

Radionuclide production: fundamental decay equation

Linear-Linear scale

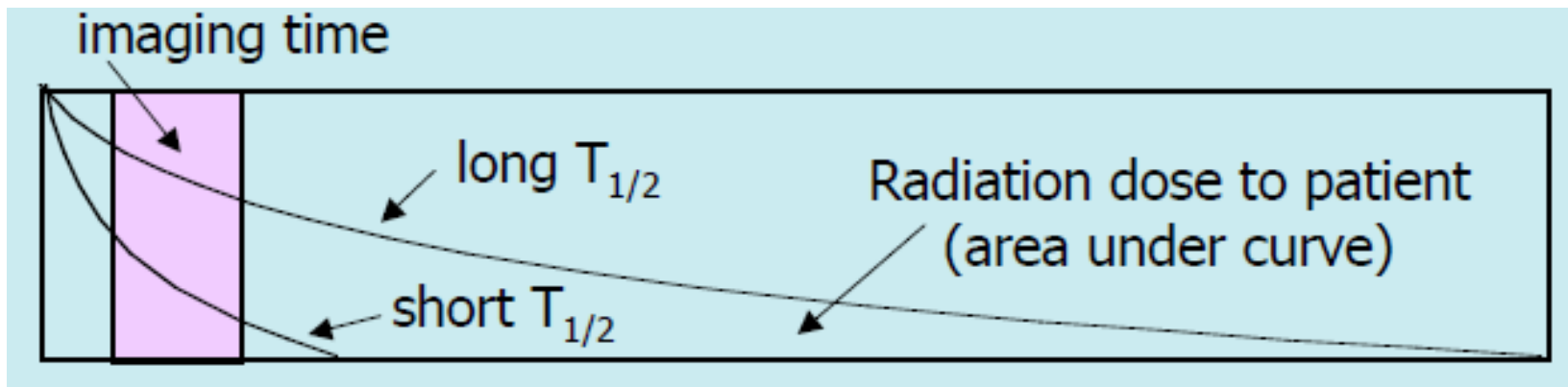


Generalized decay scheme



The "ideal" diagnostics radiopharmaceutical

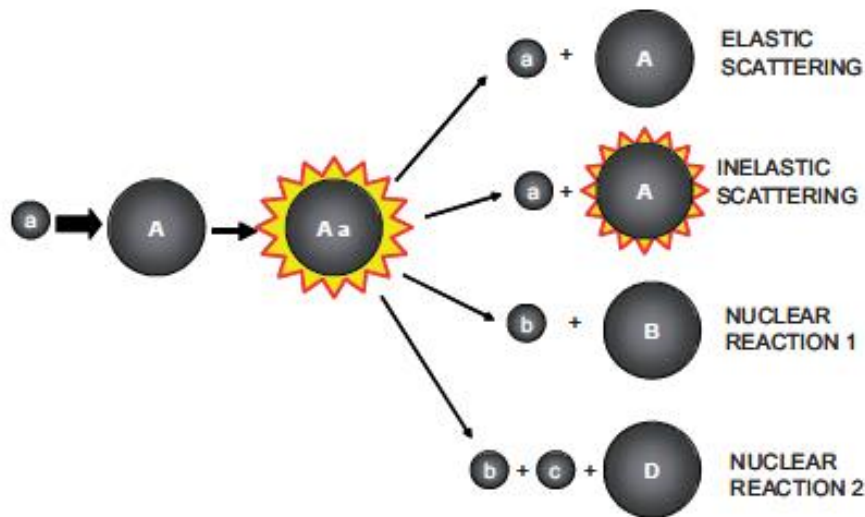
- Be readily available at a low cost
- Be a pure gamma emitter, i.e. have no particle emission such as alphas and betas (these particles contribute radiation dose to the patient while not providing any diagnostic information)
- Have a short effective biological half-life (so that it is eliminated from the body as quickly as possible)
- 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)
- Follow or be trapped by the metabolic process of interest



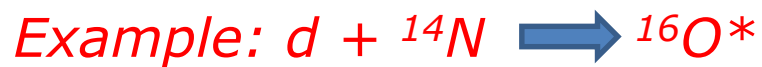
$$A(t) = A(0)e^{-t(\ln(2)/T_{1/2})}$$

The essential steps in accelerator radionuclide production

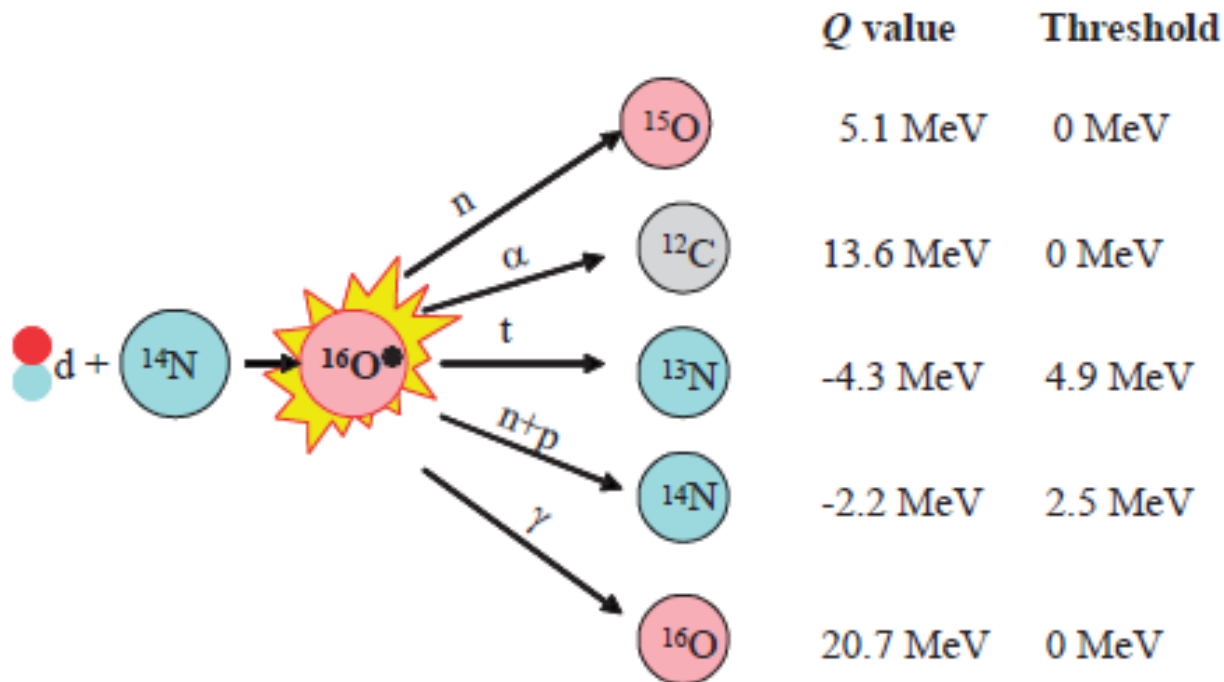
1. Acceleration of charged particles in a cyclotron
2. Beam transport (*or not*) to the irradiation station via a transfer line
3. Irradiation of target (solid, liquid, gas) – *internal or external*
4. Nuclear reaction occurring in the target (e.g. ${}^A X_Z(p,n){}^A Y_{Z+1}$)
5. Target processing and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



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



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



$$\frac{dn}{dt} = R = nI(1 - e^{-\lambda t}) \int_{E_{th}}^{E_0} \frac{\sigma(E)}{dE/dx} dE$$

R = the number of nuclei formed per second

n = the target thickness in nuclei per cm²

I = incident particle flux per second (related to the beam current)

λ = decay constant = (ln 2)/T_{1/2}

t = irradiation time in seconds

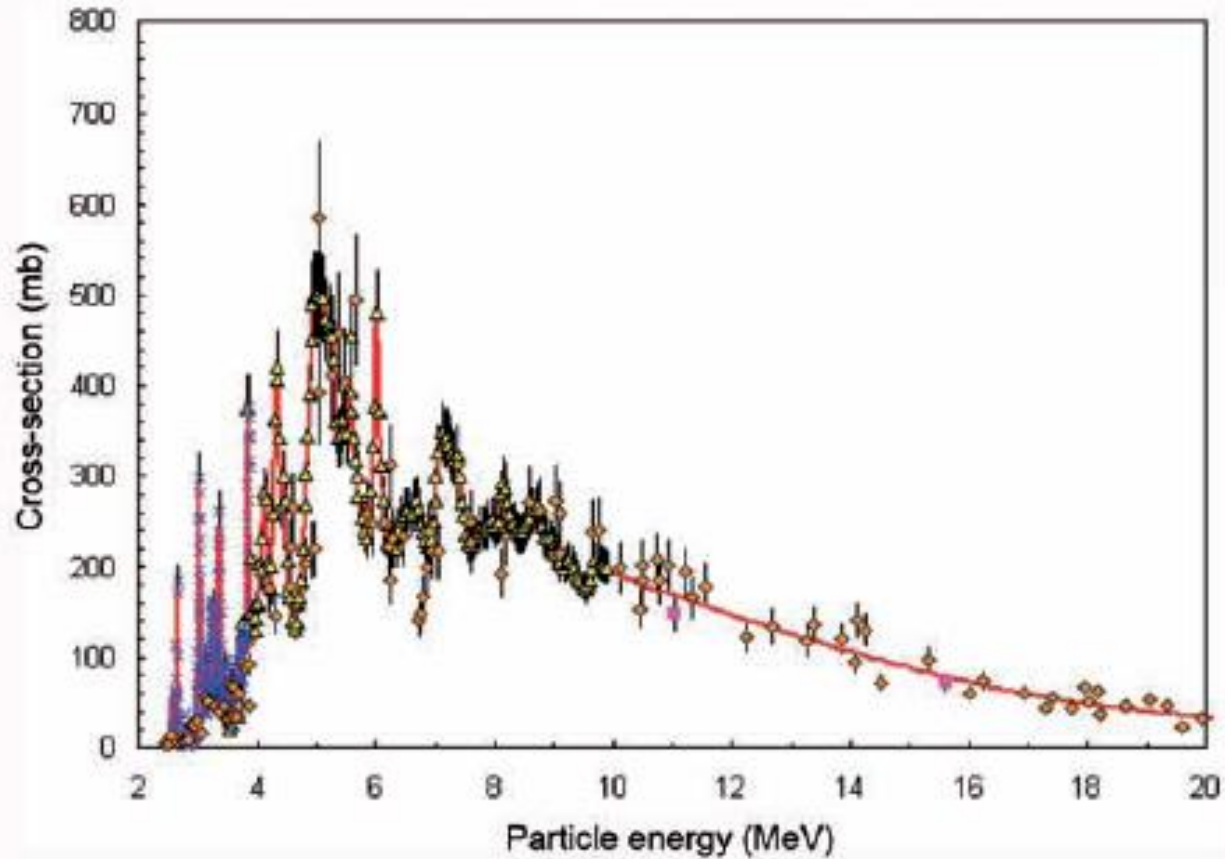
σ = reaction cross-section, or probability of interaction (cm²), function of E

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

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



$$R_i = I n x \sigma_i$$

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

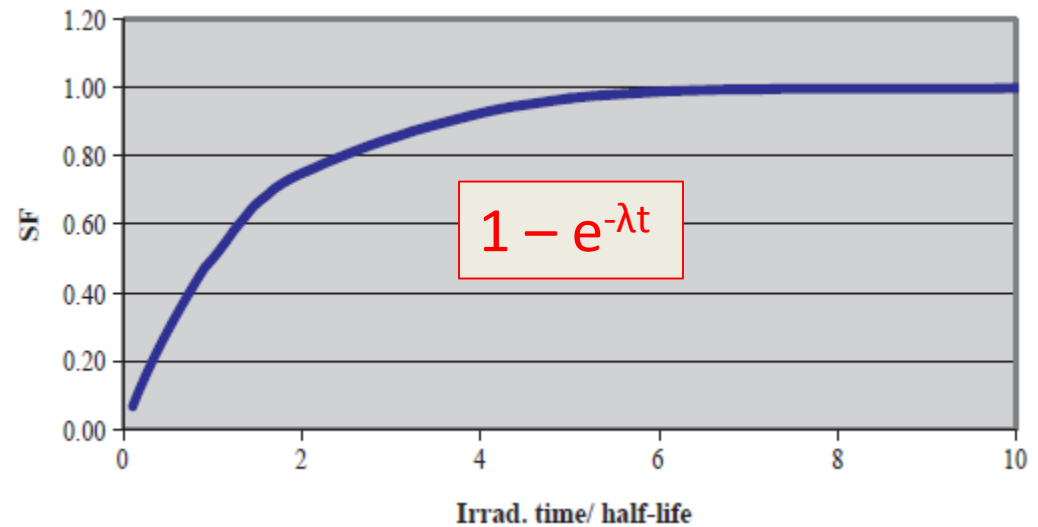
1. The beam current is constant over the course of the irradiation
2. The target nuclei are uniformly distributed in the target material
3. The cross-section is independent of energy over the energy range used

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

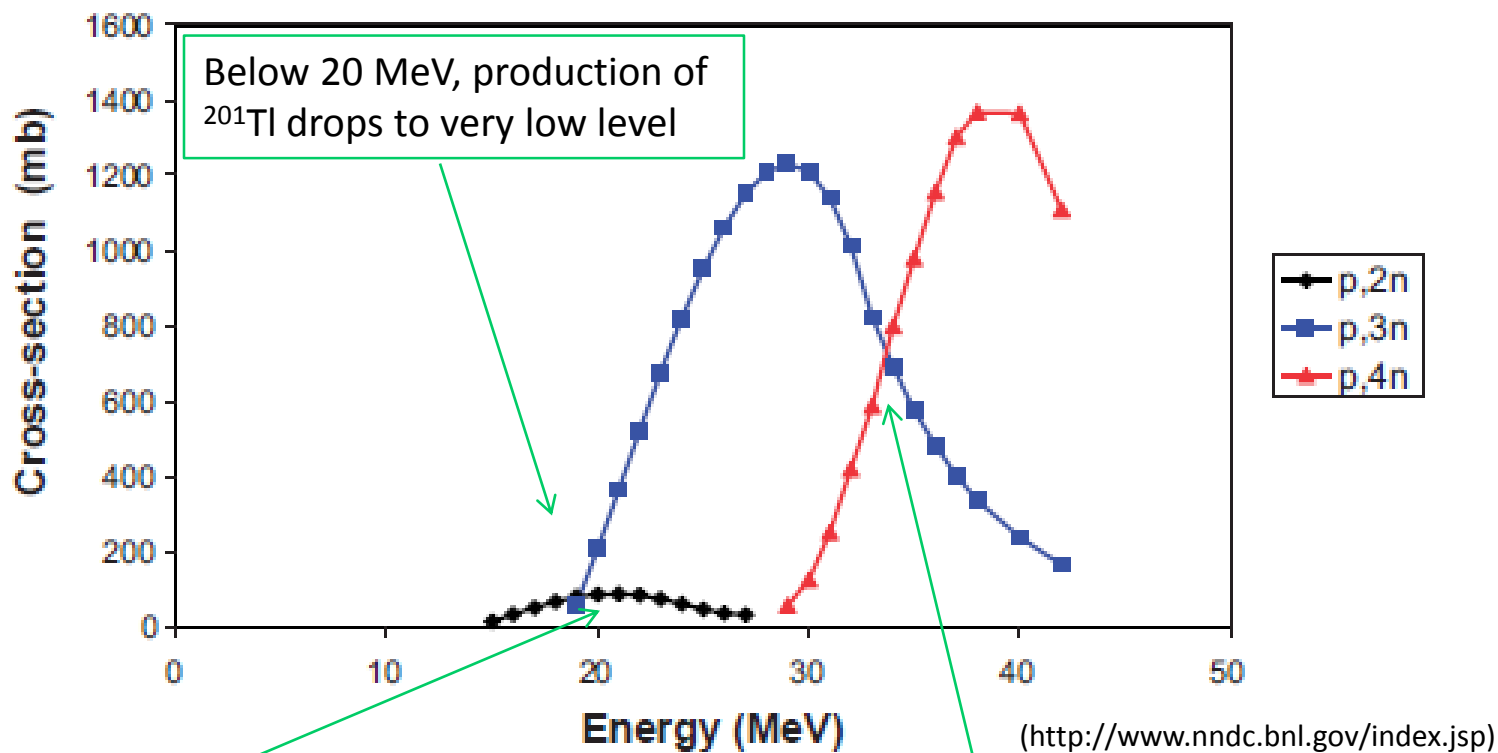


For **long lived species**, the production rates are usually expressed in terms of integrated dose or total beam flux ($\mu\text{A}\cdot\text{h}$)

Competing nuclear reactions, example of ^{201}Tl

The nuclear reaction used for the production of ^{201}Tl is the $^{203}\text{Tl}(p,3n)^{201}\text{Pb}$
 ^{201}Pb ($T_{1/2} = 9.33 \text{ h}$) \rightarrow ^{201}Tl ($T_{1/2} = 76.03 \text{ h}$)

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



Below 20 MeV, production of ^{201}Tl drops to very low level

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

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

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



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

Production reactions (2)

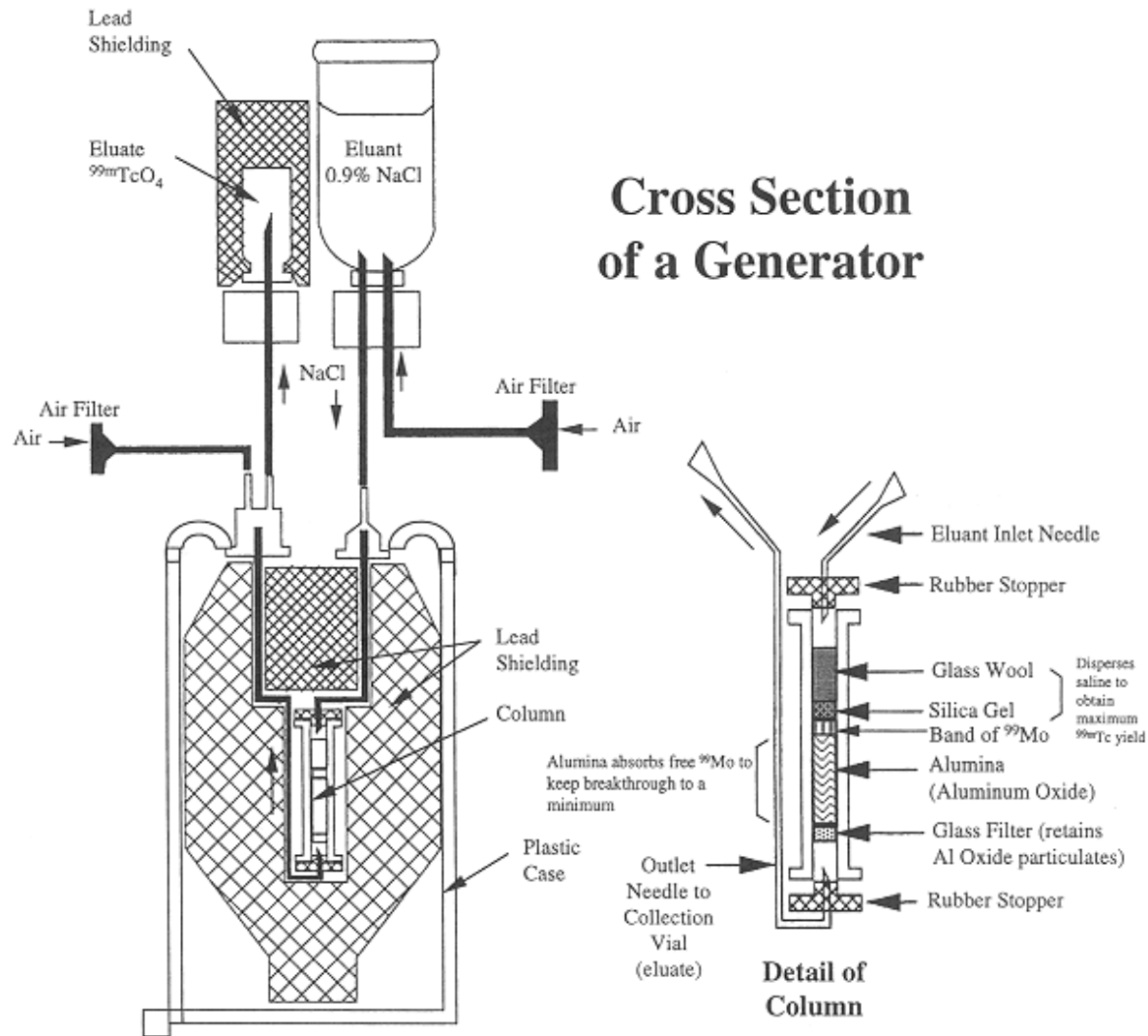
Radionuclide	Use	Half-life	Reaction	Energy (MeV)
^{15}O	PET imaging	2.03 min	$^{15}\text{N}(p,n)$ $^{14}\text{N}(d,2n)$ $^{16}\text{O}(p,pn)$	11 6 > 26
^{18}F	PET imaging	110 min	$^{18}\text{O}(p,n)$ $^{20}\text{Ne}(d,\alpha)$ $^{\text{nat}}\text{Ne}(p,X)$	11-17 8-14 40
^{64}Cu	PET imaging and radiotherapy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

- **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 \longrightarrow 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

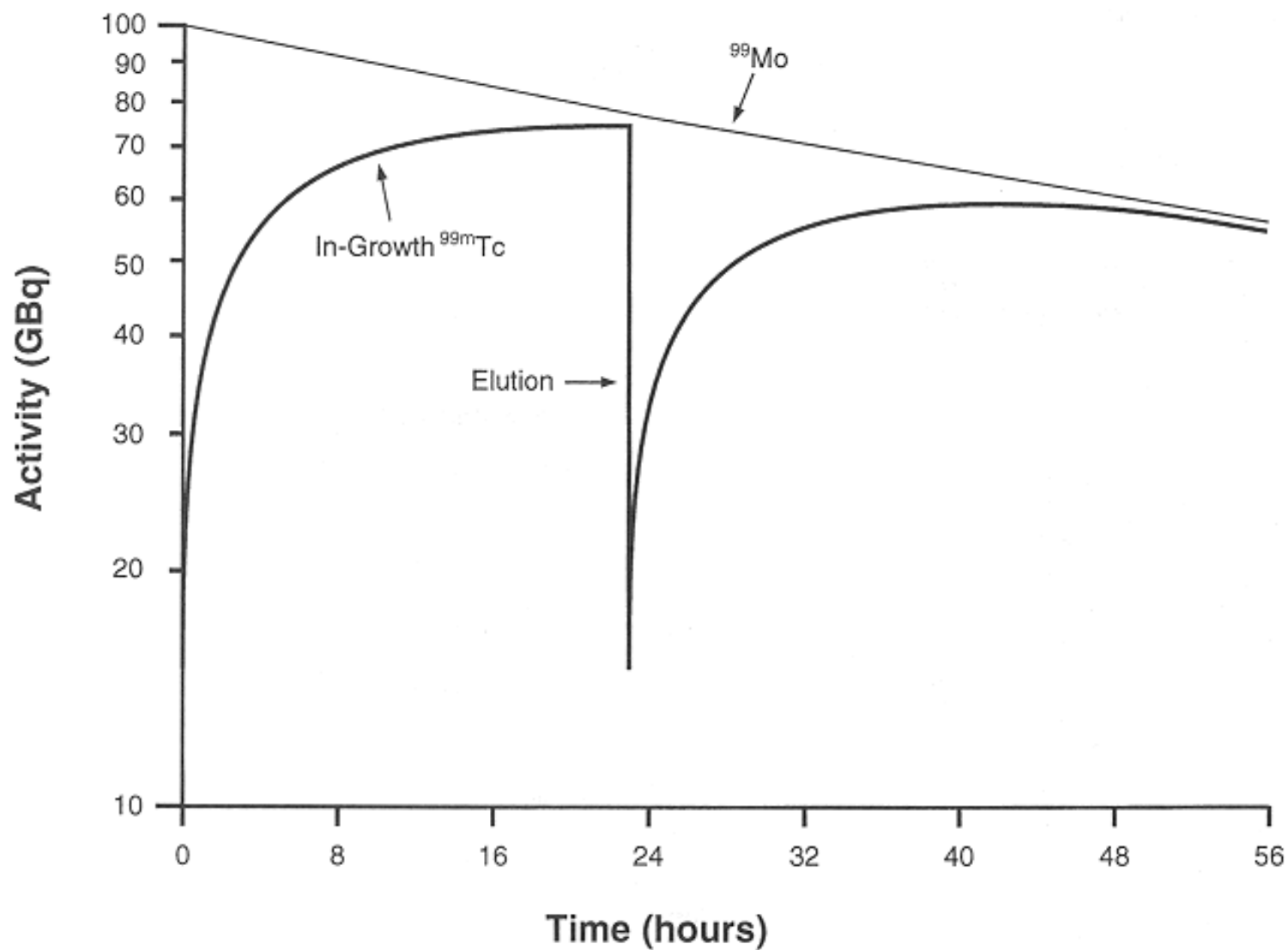
- Technetium-99m (^{99m}Tc) has been the most important radionuclide used in nuclear medicine
- Short half-life (6 hours) makes it impractical to store even a weekly supply
- Supply problem overcome by obtaining parent ^{99}Mo , which has a longer half-life (67 hours) and continually produces ^{99m}Tc
- 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*

Radionuclide generators



- 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

Transient equilibrium

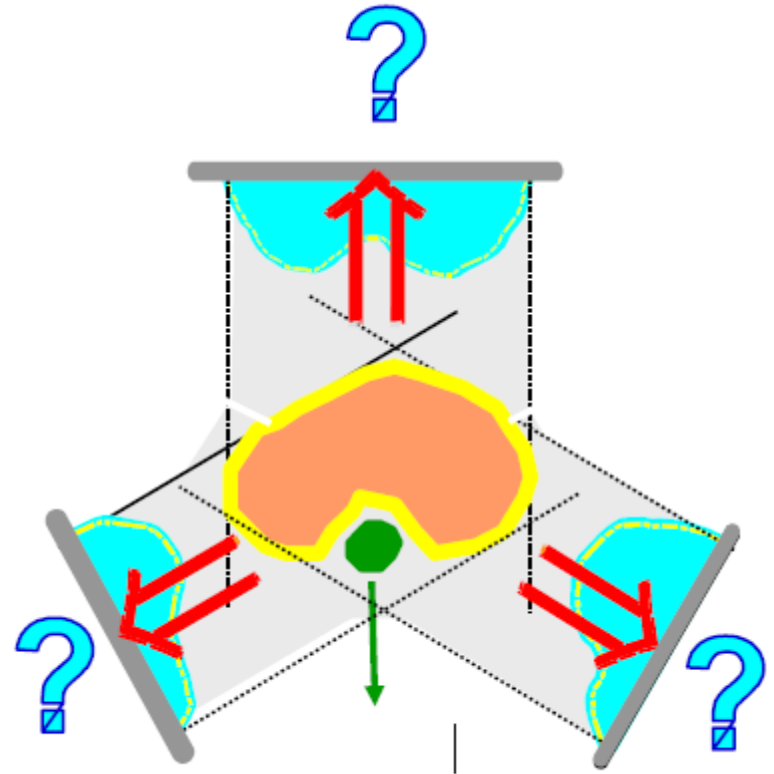
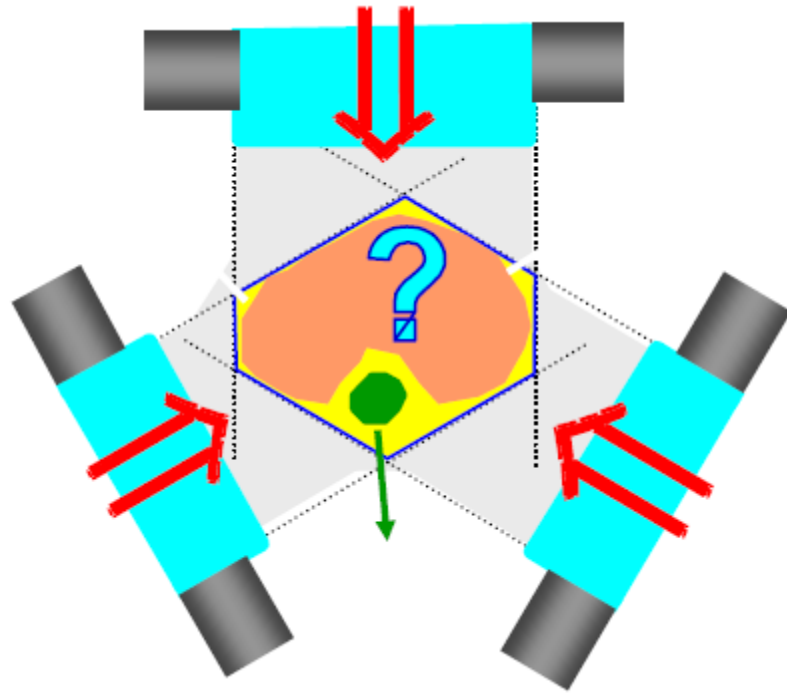


Radionuclide generators

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

Radiation therapy

Treatment planning and dose delivery to tumour volume



Past radiation therapy equipment

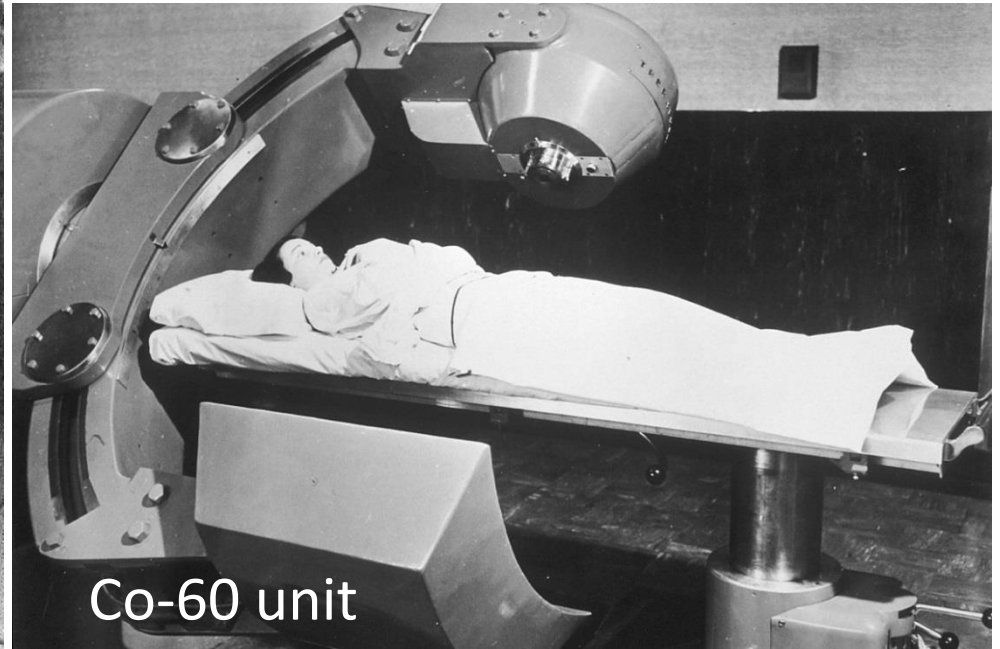
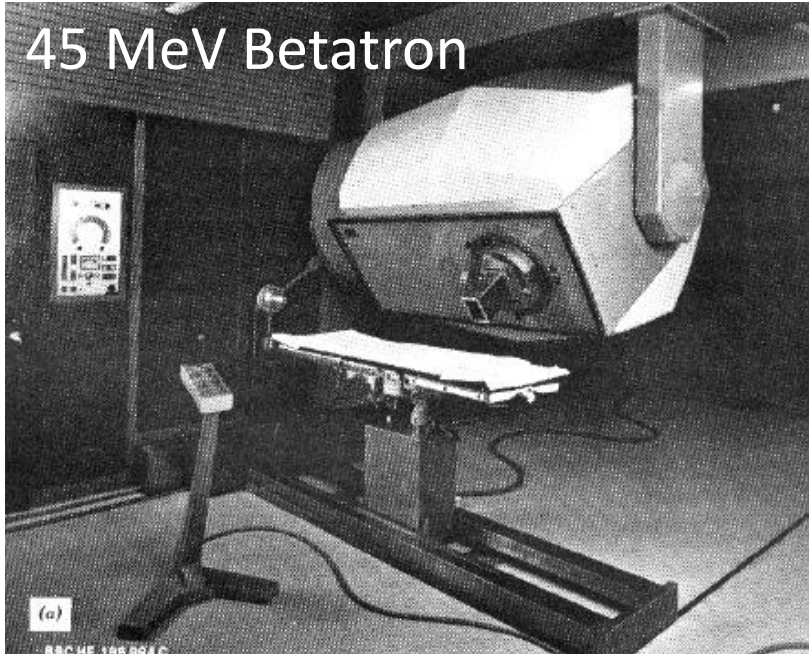
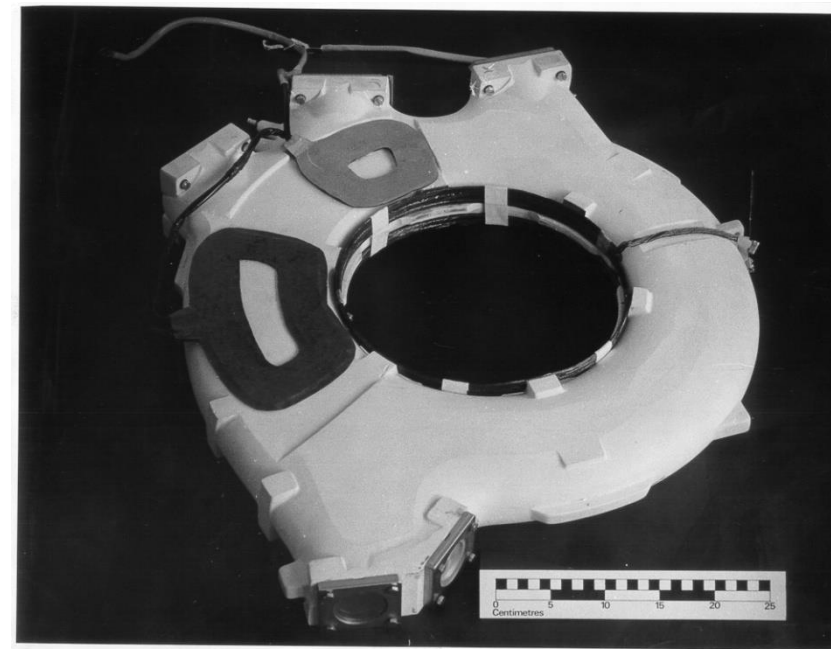
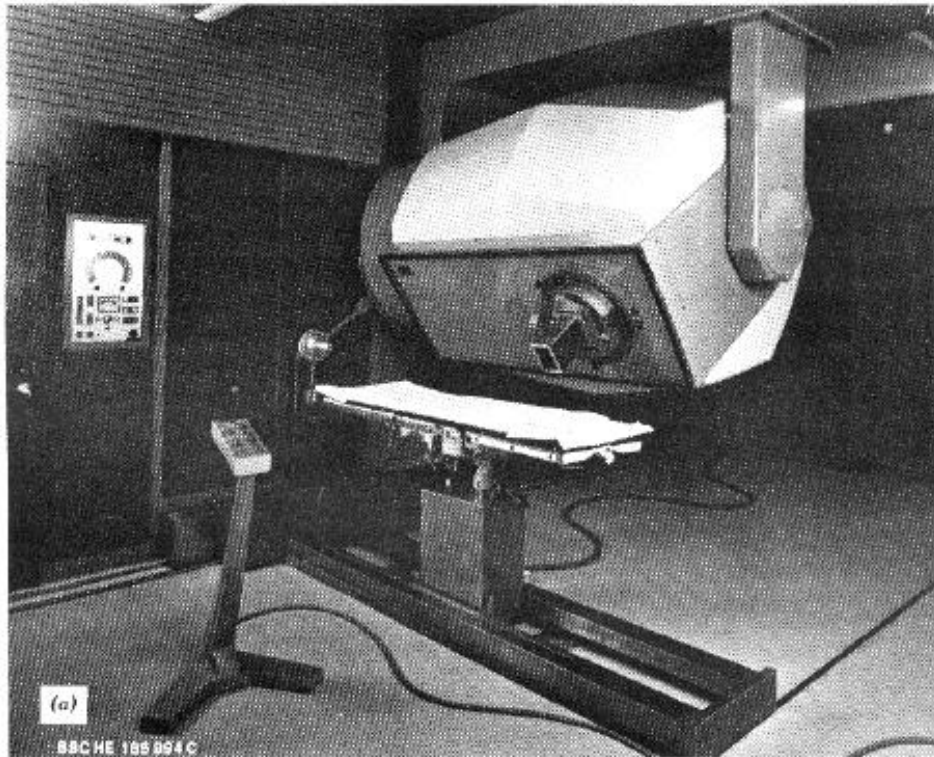


Photo: Wikipedia

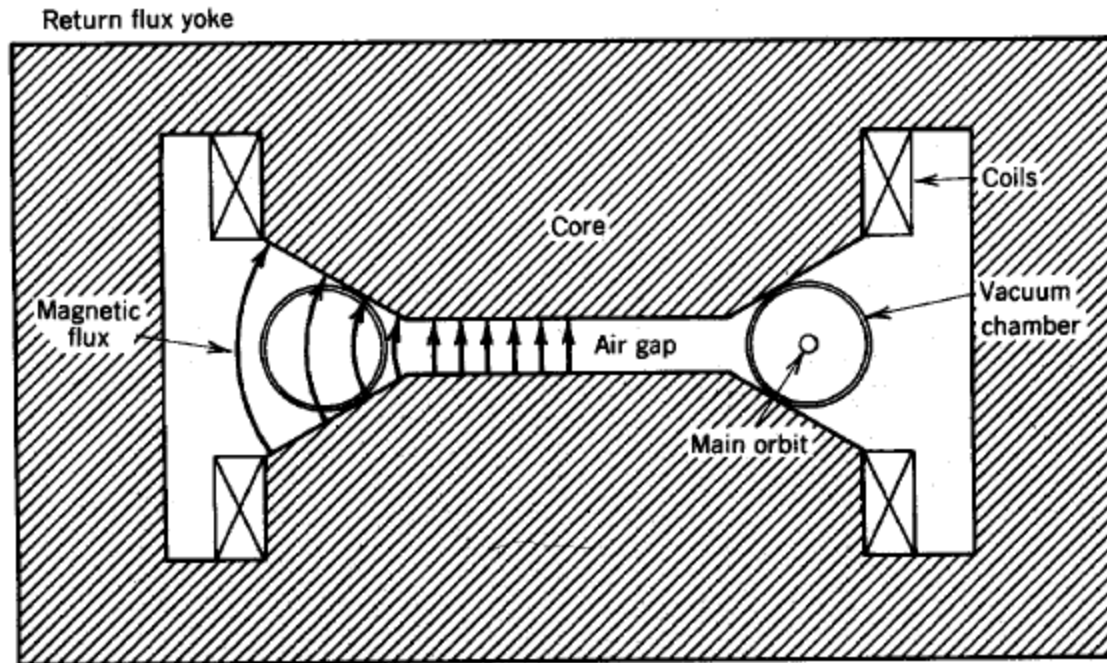
Radiation therapy is much more than the radiation source. One also needs:

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

An old 45 MeV betatron for radiation therapy



Schematic diagram of betatron with air gap

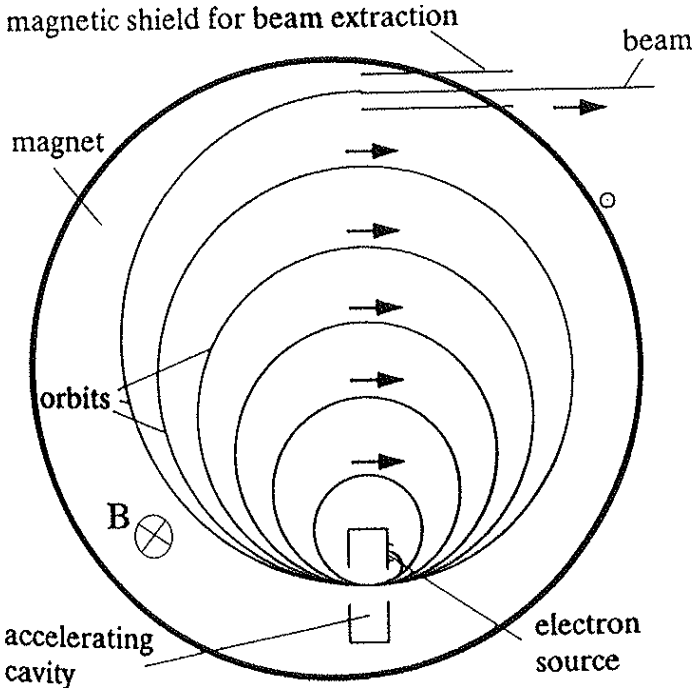


$$B(R) = \frac{1}{2} \bar{B}(R)$$

$B(R)$ = field at the orbit

$\bar{B}(R)$ = 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



An “electron cyclotron”

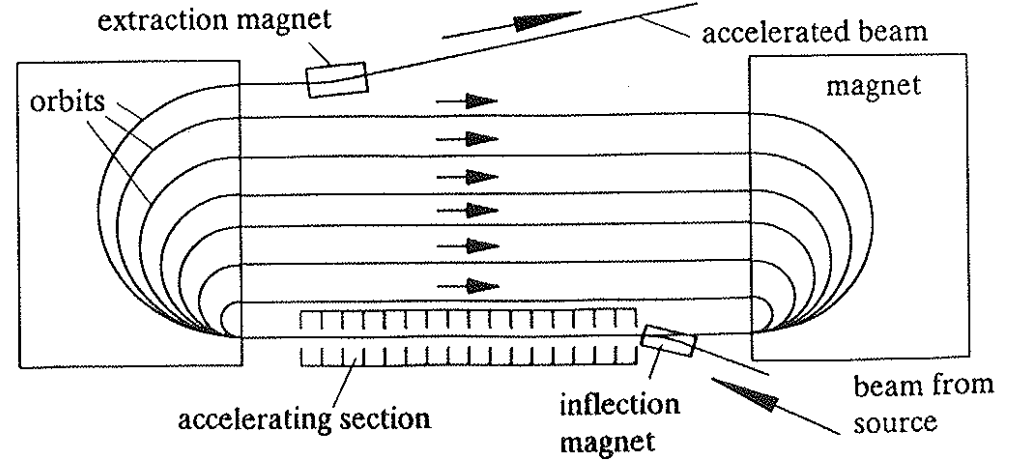
- Uniform magnetic field
- Fixed-frequency RF system
- Well-separated orbits

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

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

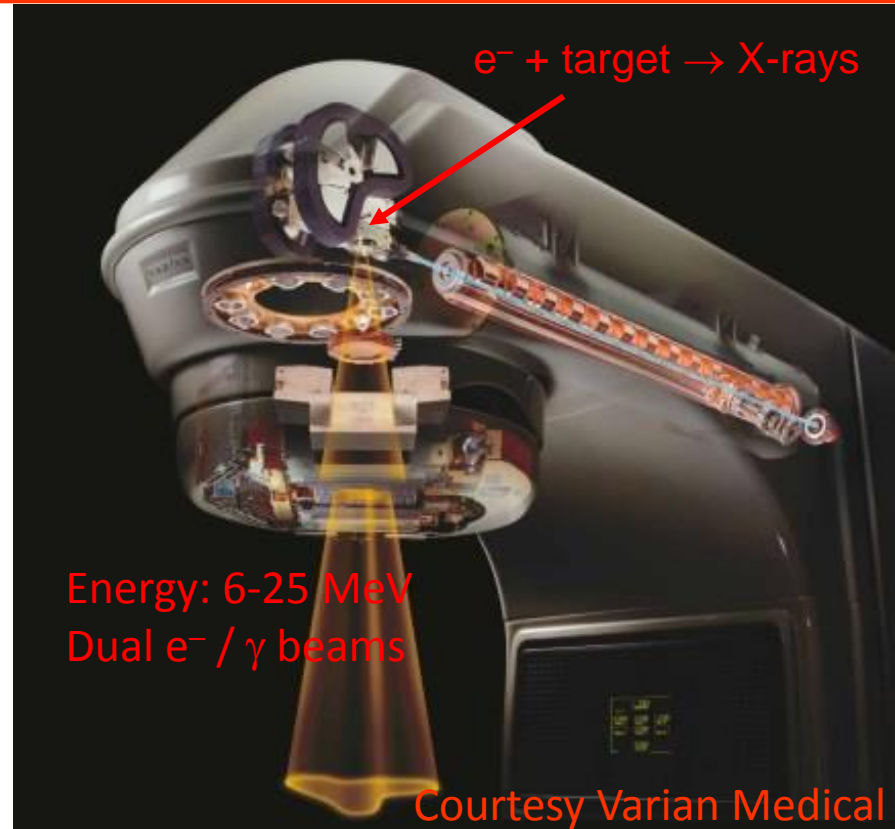
- Isocronism only if $\gamma \approx 1$
- If $\gamma > 1$, $\Delta\tau$ per turn = $\Delta\gamma$
- To have isochronism it must be $\Delta\tau$ per turn = $h\tau_{RF}$
- Required energy gain per passage
 - for electrons $\Delta E_e = 511 \text{ keV}$
 - for protons $\Delta E_p = 938 \text{ MeV}$

Racetrack microtron



Magnet weight $\approx (\text{energy})^3$

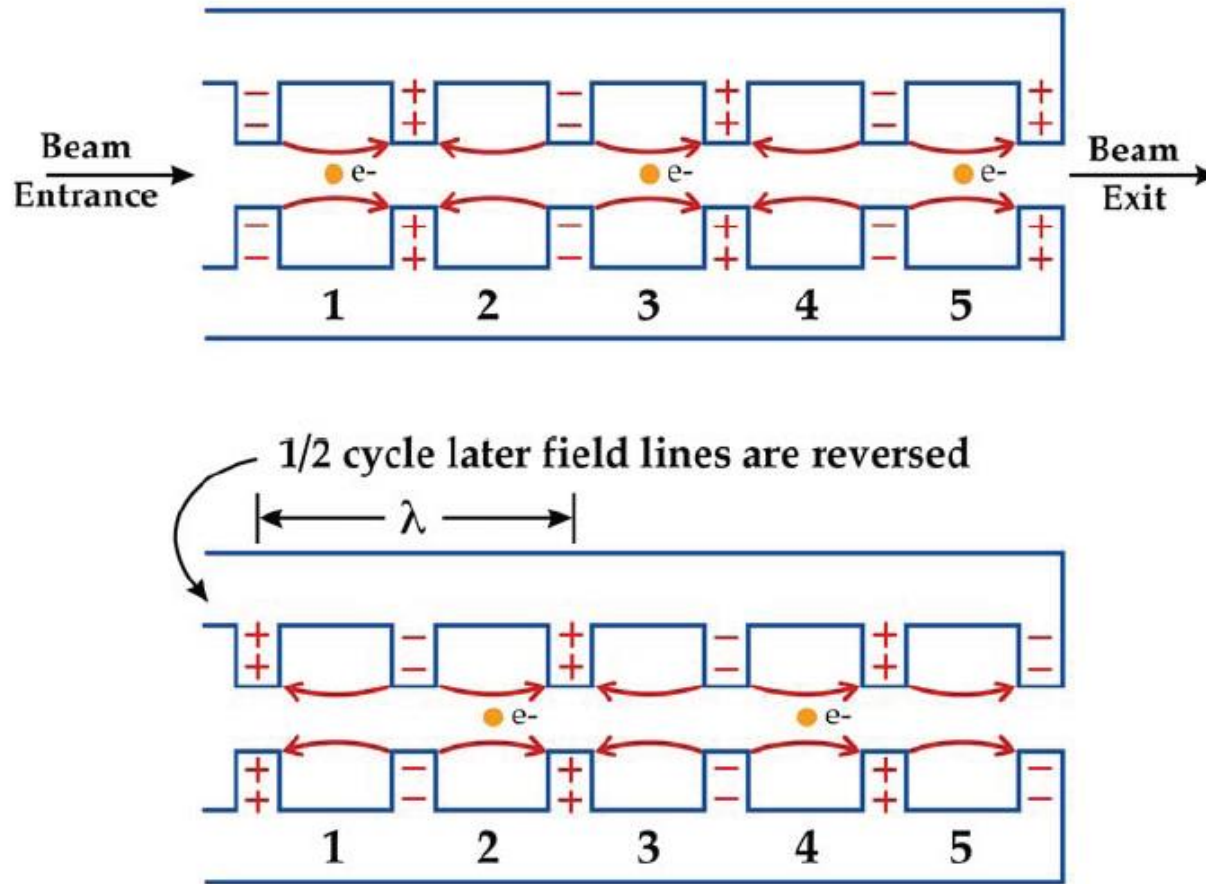
Medical electron linacs



Multi-leaf collimator



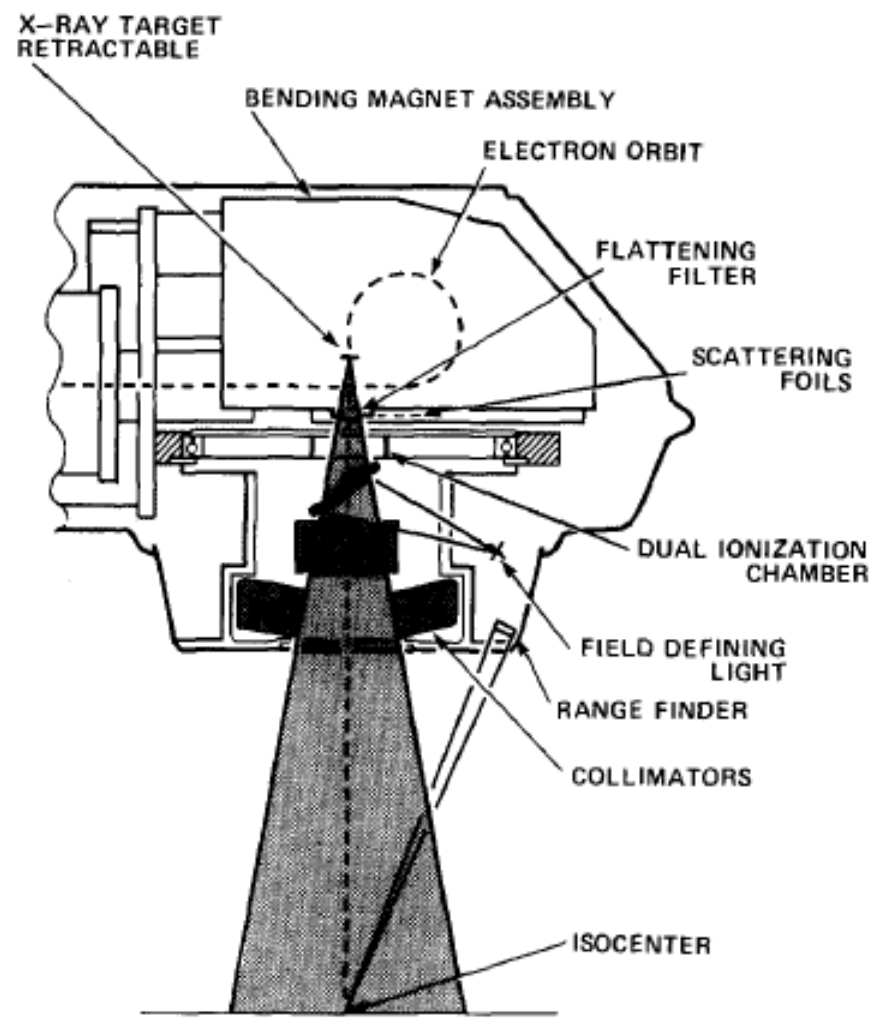
Operation of Linear Accelerators



Particles initially in cell 1 arrive in cell 2 to get further accelerating kick. Frequency must match particles velocity and cell periodicity = $\frac{1}{2} \lambda$:

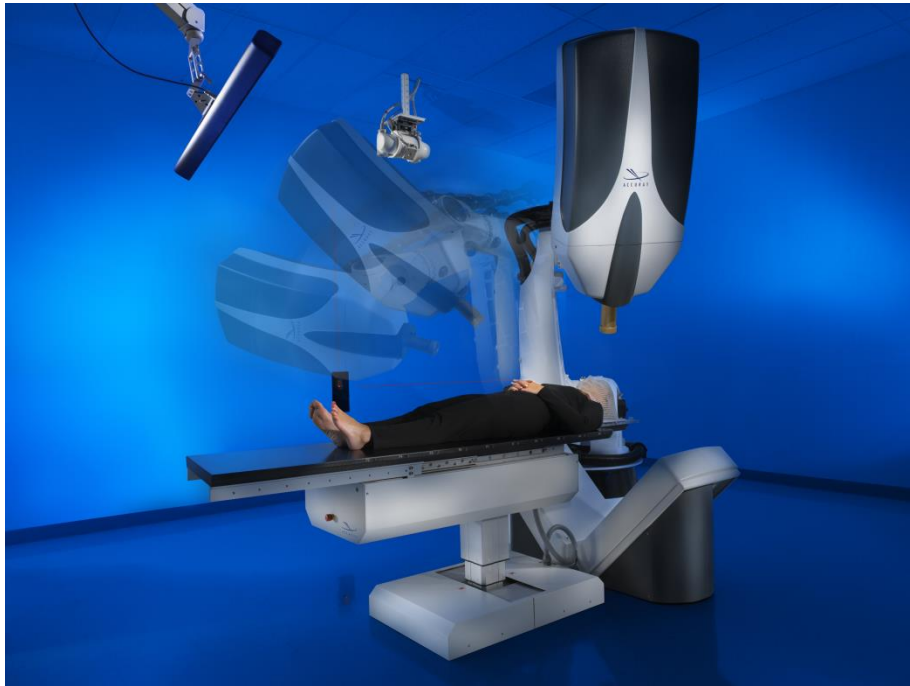
$$f = \frac{v}{\lambda}$$

Schematics of a treatment head of a medical electron linac



Cyber-knife robotic surgery system

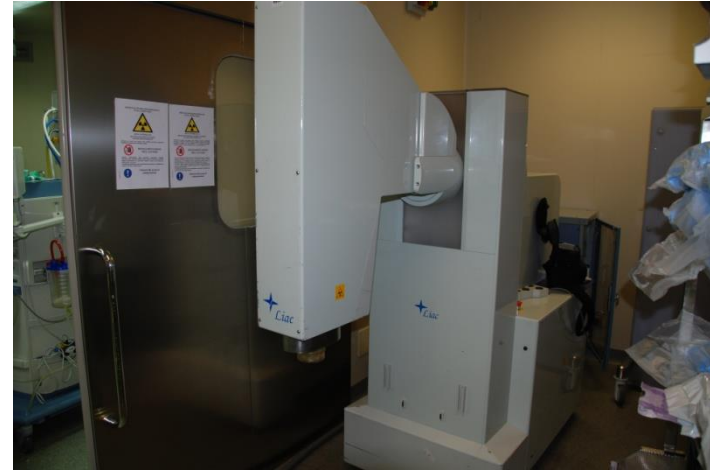
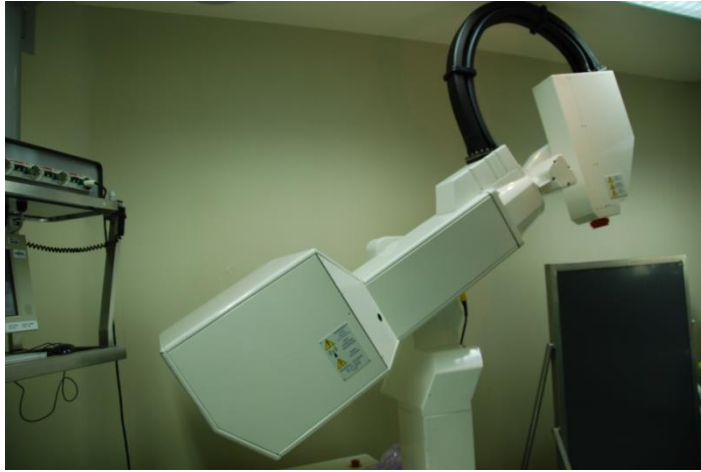
6 MV Linac mounted on a robotic arm



- 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>

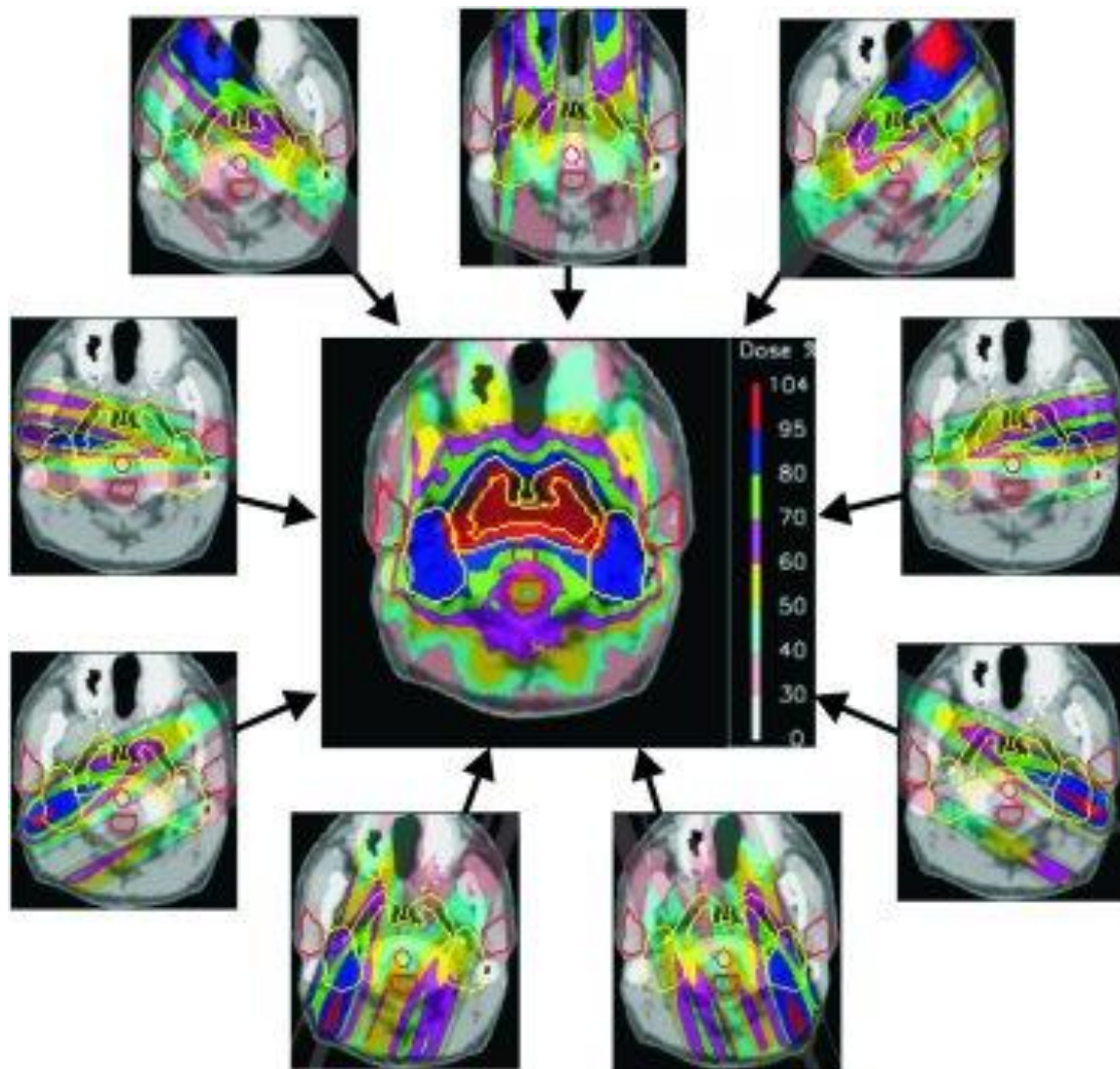
Intra-operative radiation therapy (IORT)



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



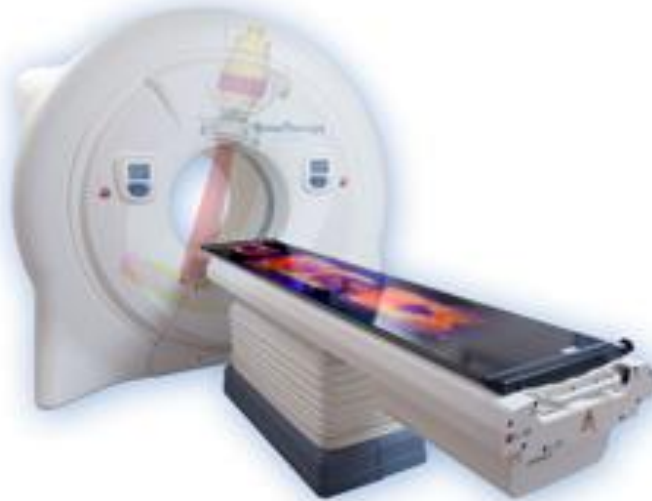
Intensity modulated radiation therapy (IMRT)



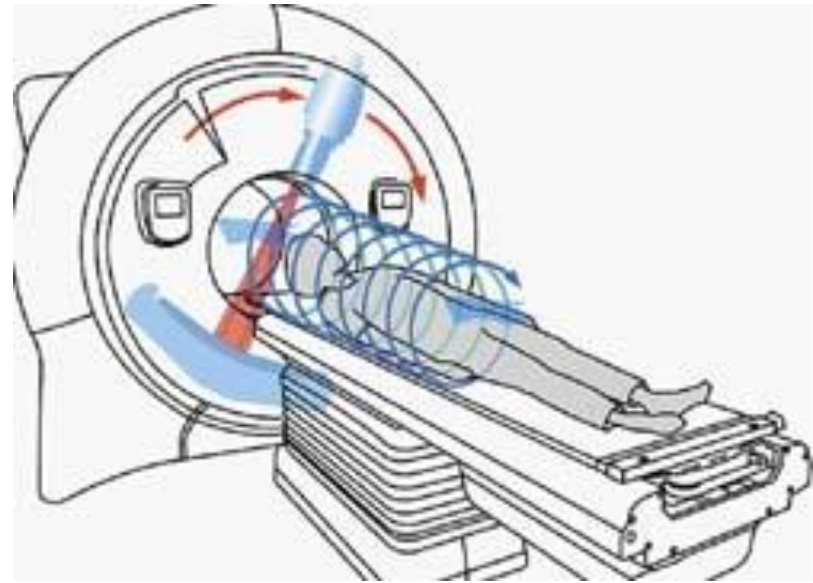
An example of intensity modulated treatment planning with photons. Through the addition of 9 fields it is possible to construct a highly conformal dose distribution with good dose sparing in the region of the brain stem (courtesy of T. Lomax, PSI).

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

Helical tomotherapy



www.tomotherapy.com



- **Integrated CT guidance**

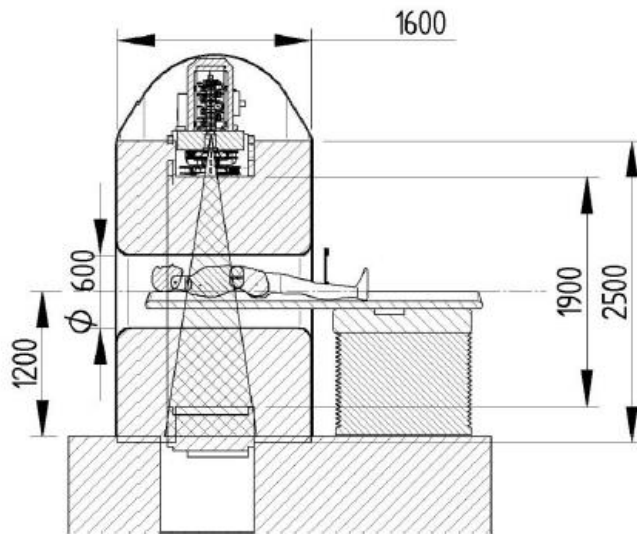
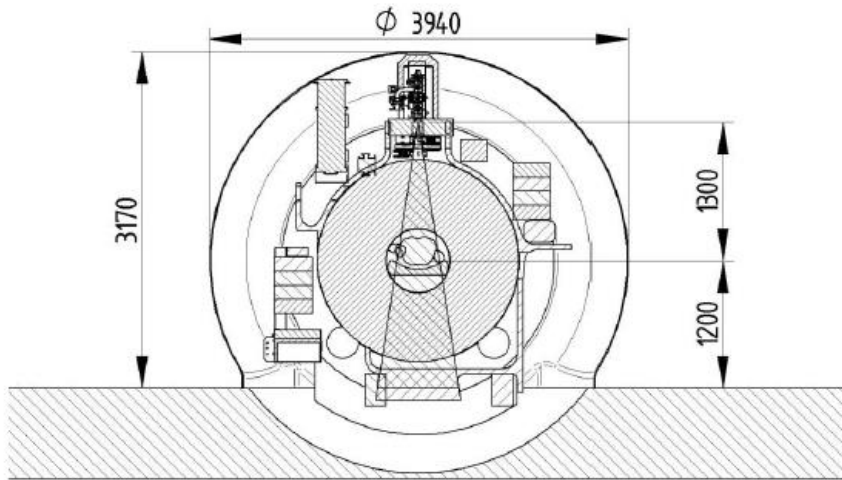
- Integrated CT scanner allowing efficient 3D CT imaging for ensuring the accuracy of treatment

- **A binary multi-leaf collimator (MLC)** for beam shaping and modulation

- **A ring gantry design** enabling TomoHelical delivery

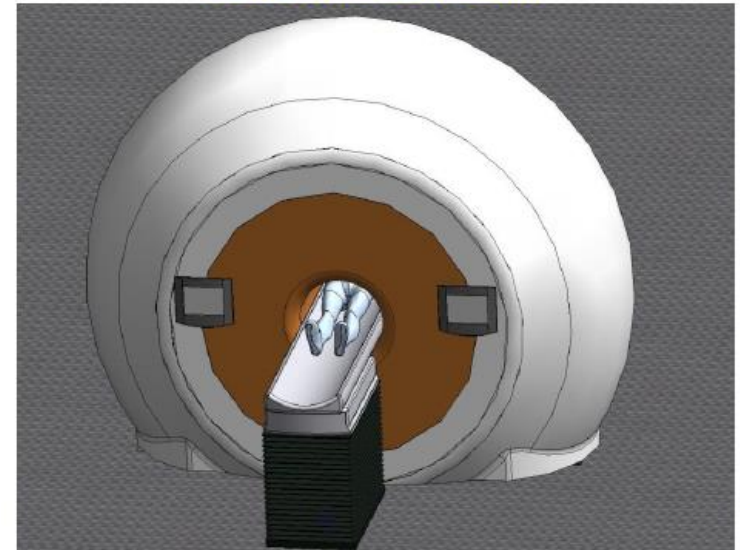
- As the ring gantry rotates in simultaneous motion to the couch, **helical fan-beam IMRT** is continuously delivered from all angles around the patient
- Very large volumes can be treated in a single set-up

Hybrid MRI linac

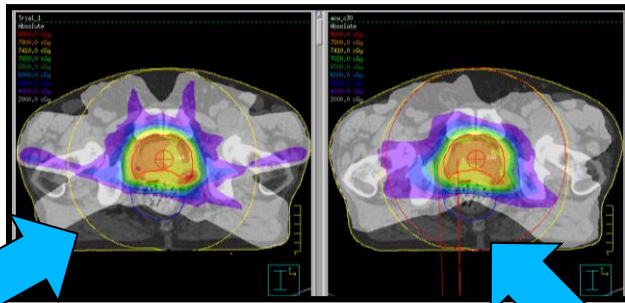
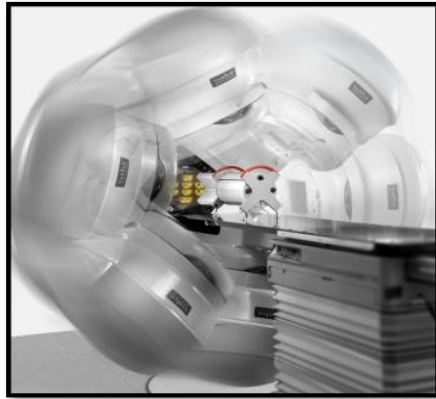


- Closed bore high field MRI
 - Gantry ring based 6 MV accelerator with MLC
- accelerator and MRI system have to operate simultaneously and independently

Courtesy J. Lagendijk

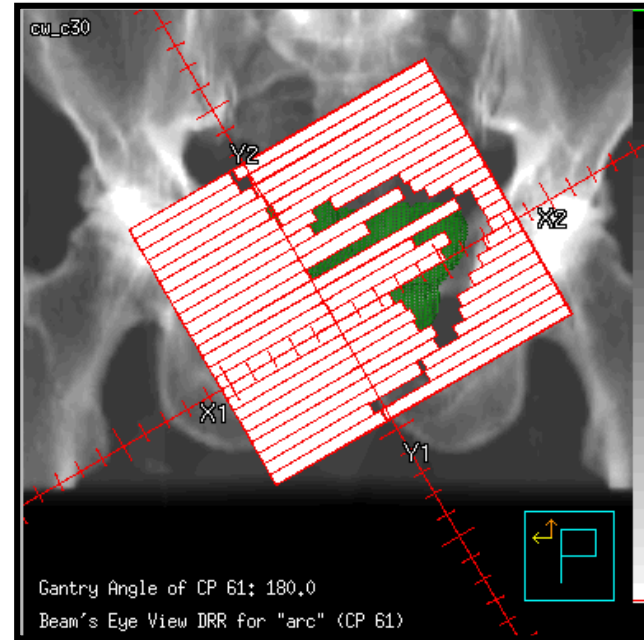


Rotate linac gantry while modulating the beam



Fixed 6 or so gantry angles

VMAT

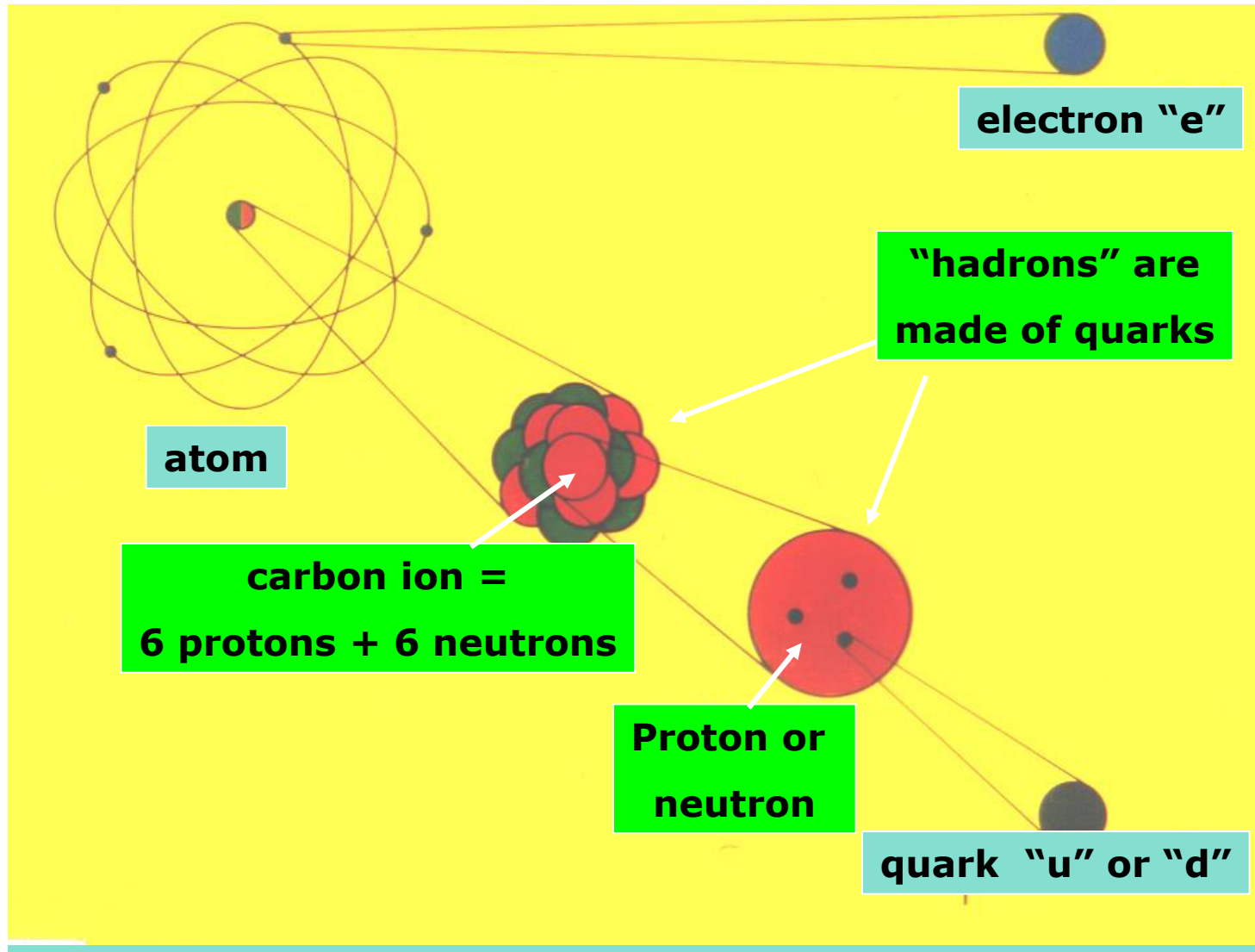


Name-Prof Peter Metcalfe
BSOC lecture 08

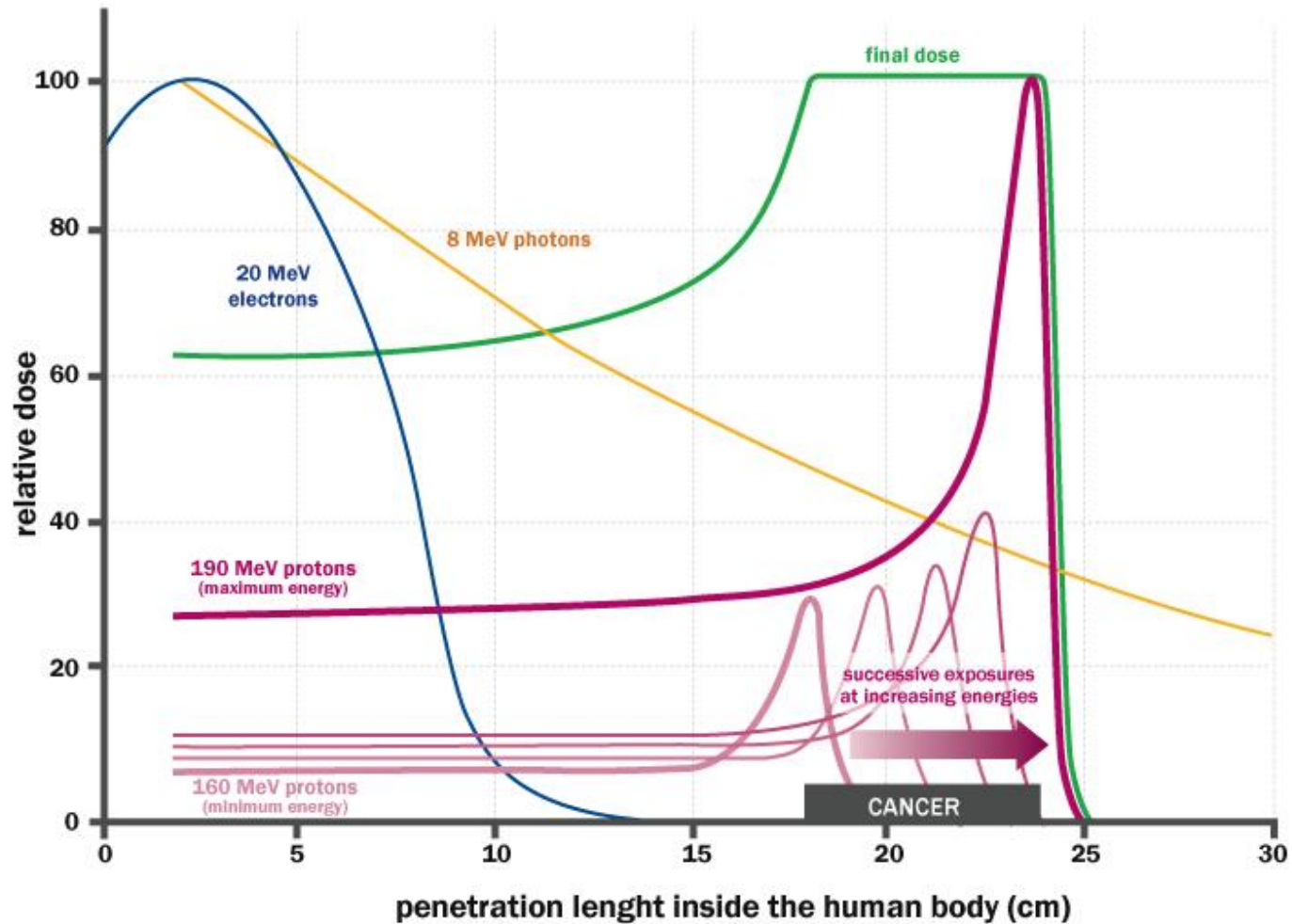
University of Wollongong



Particle therapy (hadron therapy)



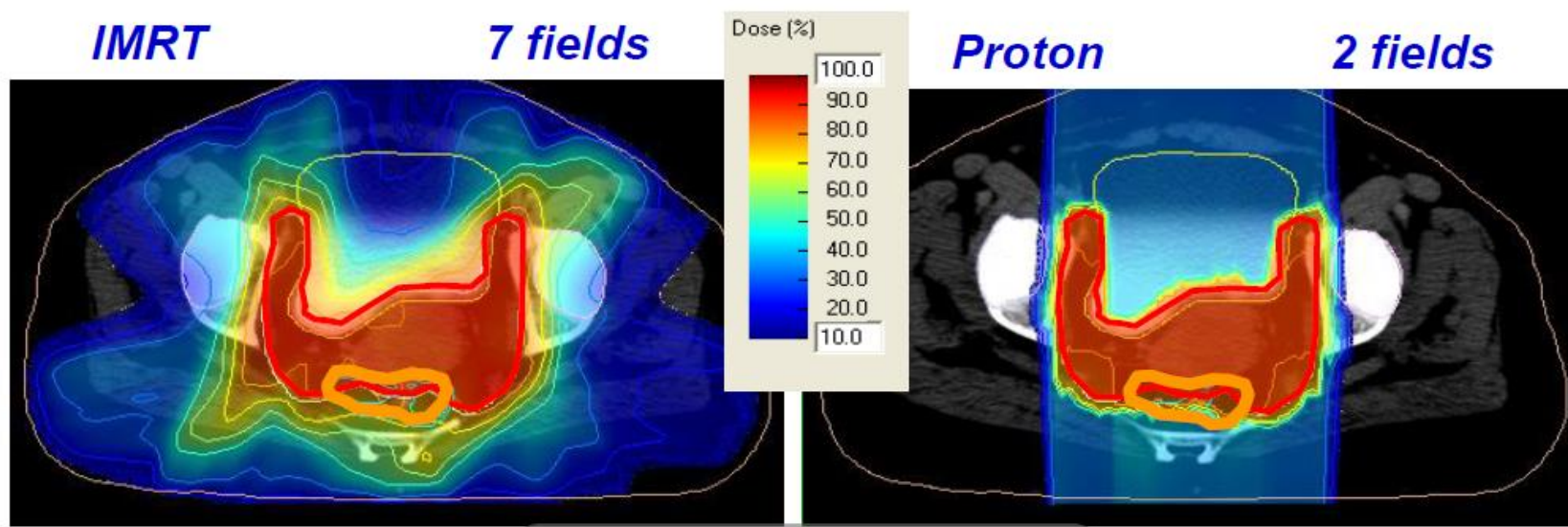
Particle therapy (hadron therapy)



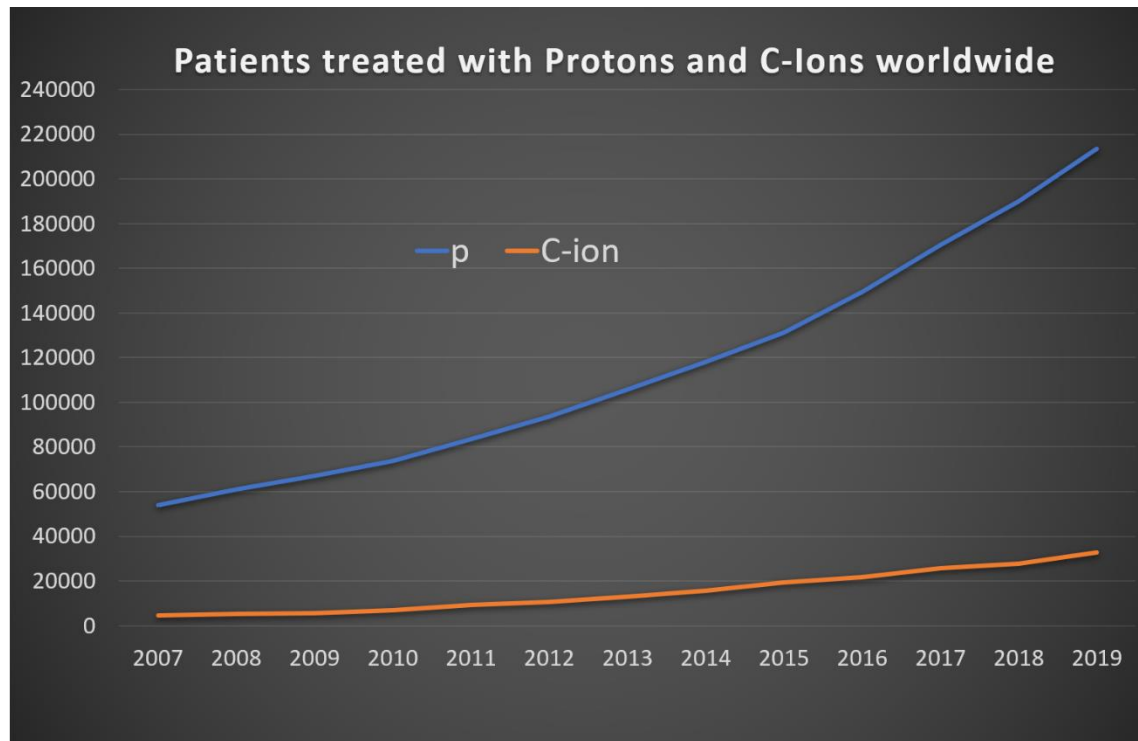
Courtesy INFN, Italy

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*

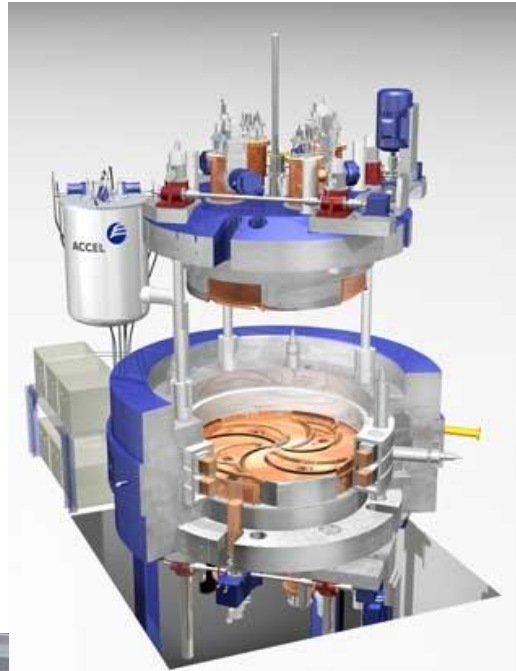


Particle therapy (hadron therapy)

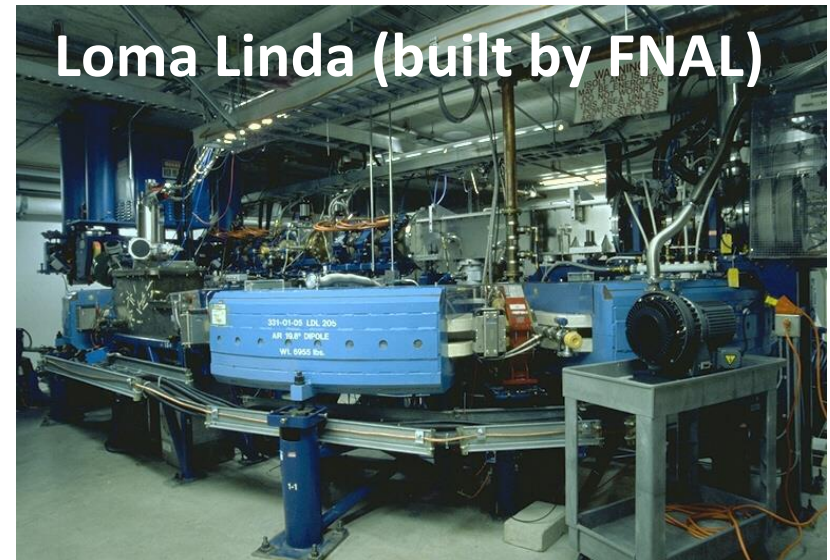


www.ptcog.ch

Cyclotrons and synchrotrons for proton therapy

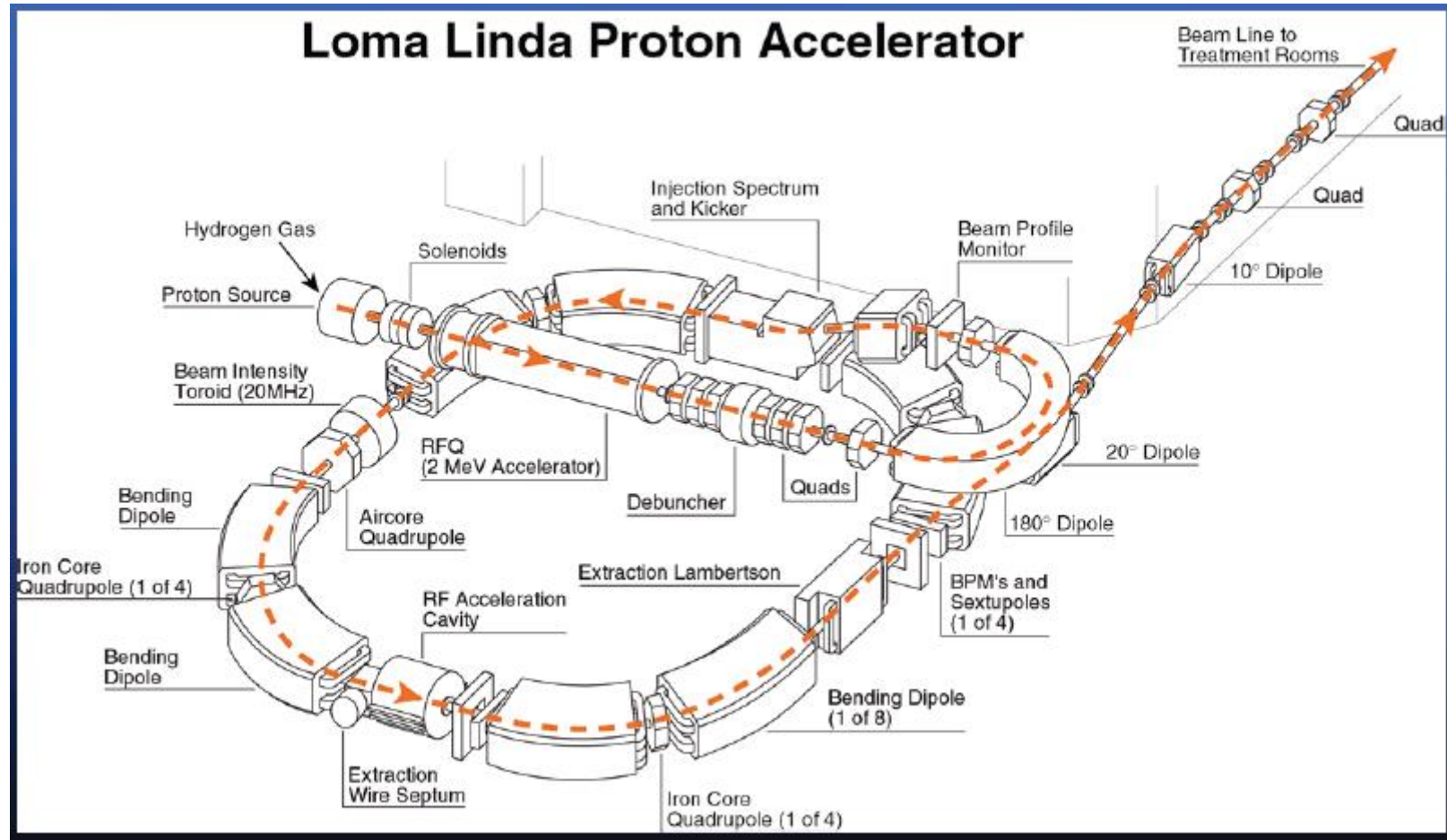


**Accel-Varian
(superconducting)**



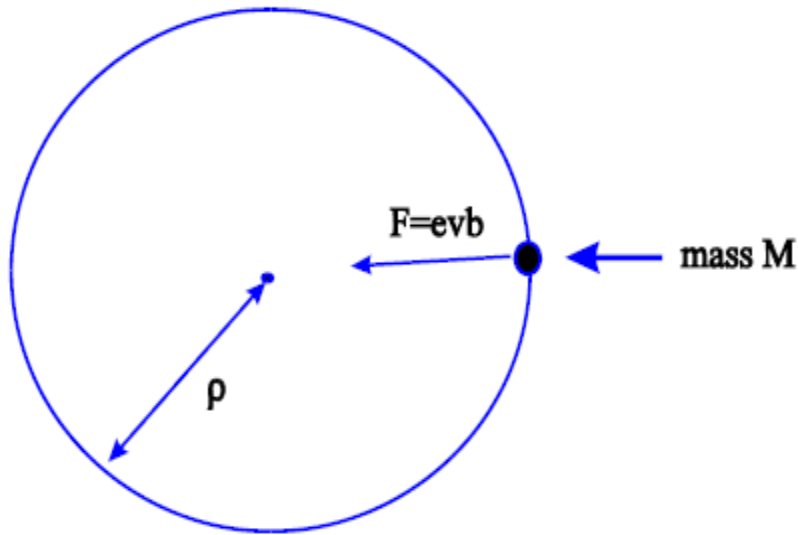
Loma Linda (built by FNAL)

Loma Linda University Medical Center



We have already seen the motion of a particle in a dipole field...

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



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

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

($p = \text{momentum} = mv$)

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

$$B\rho = 33.356 \cdot p \text{ [kG}\cdot\text{m]} = 3.3356 \cdot p \text{ [T}\cdot\text{m]} \text{ (if } p \text{ is in GeV/c)}$$

$B\rho$ 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

Trajectory of particles in a dipole field

Trajectory of a particle in a bending magnet

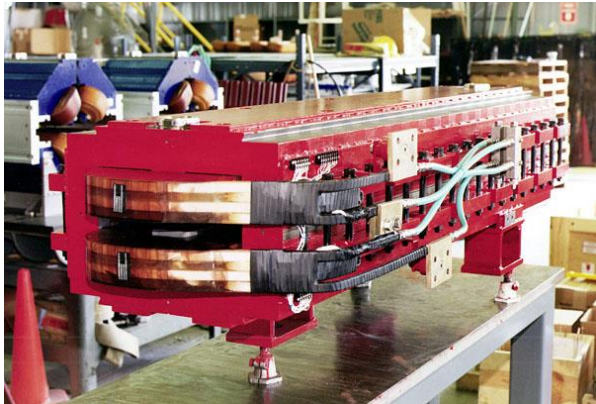
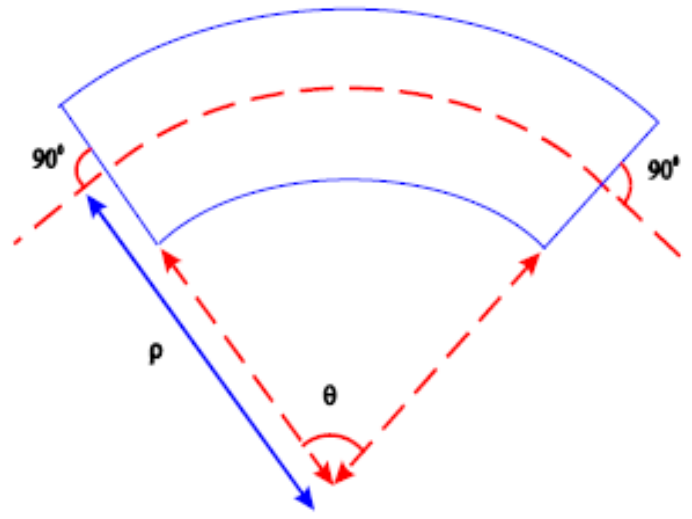
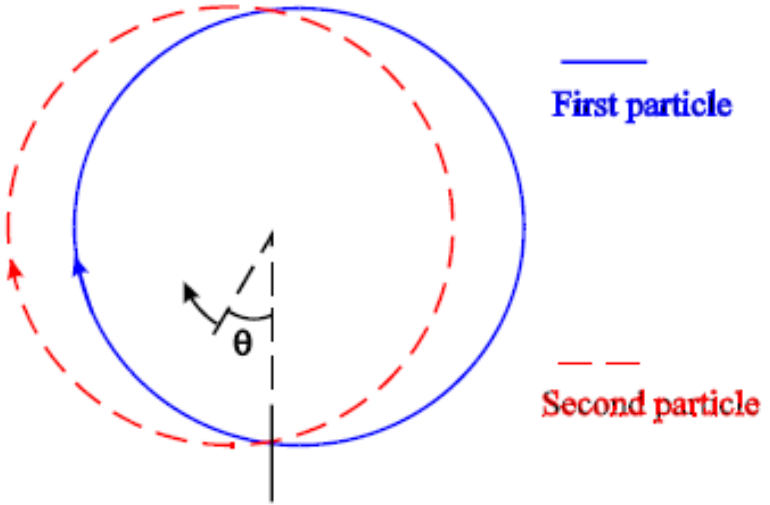
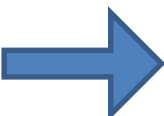


Photo: courtesy ANL

Unfortunately an accelerator contains more than one particle!

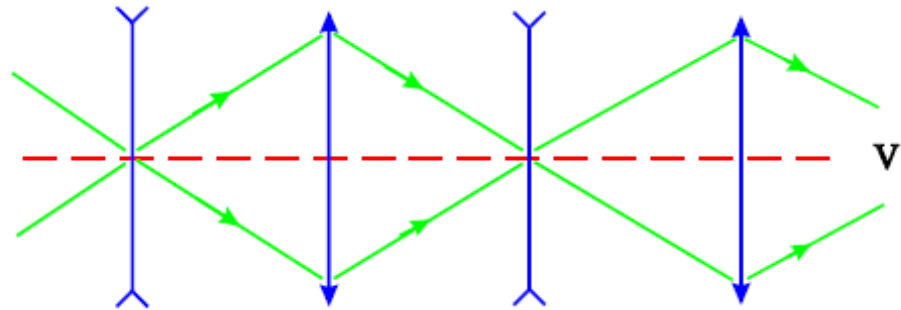
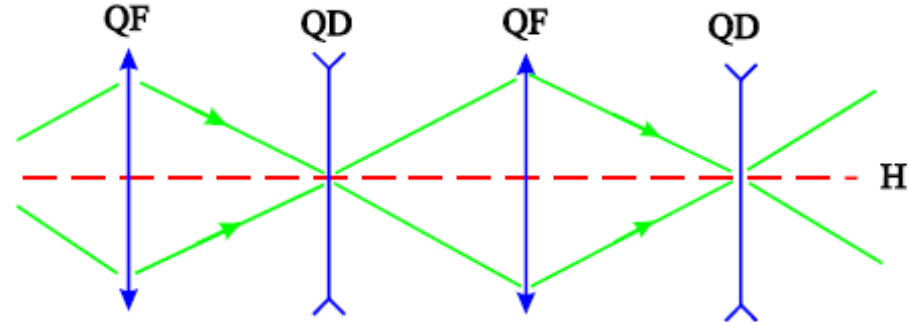
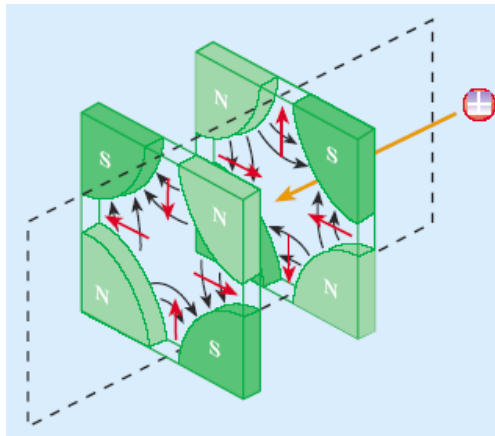
Number of circulating particles in a synchrotron is typically in the order of 10^{10} - 10^{12} or more



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

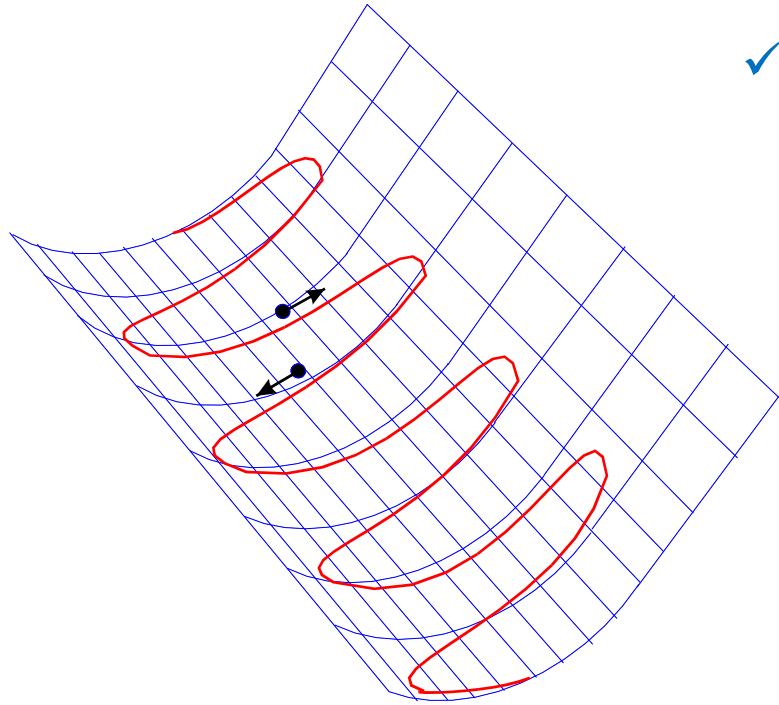
Light rays passing through a series of focusing and defocusing lenses

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

- ✓ 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.

Beam “envelope” defined by the β function

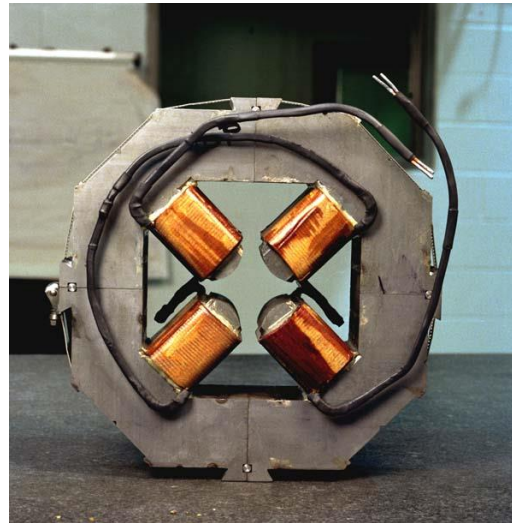
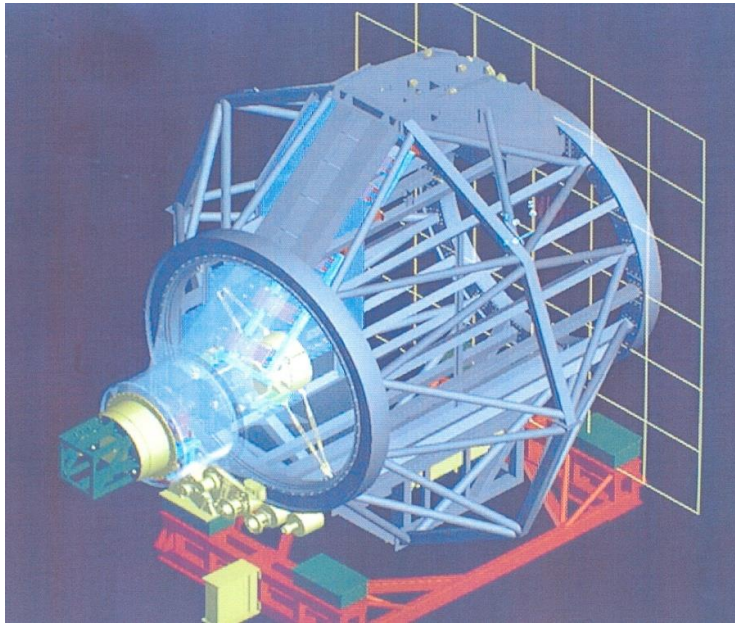


Photo courtesy Fermilab Visual Media Services



The IBA proton 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

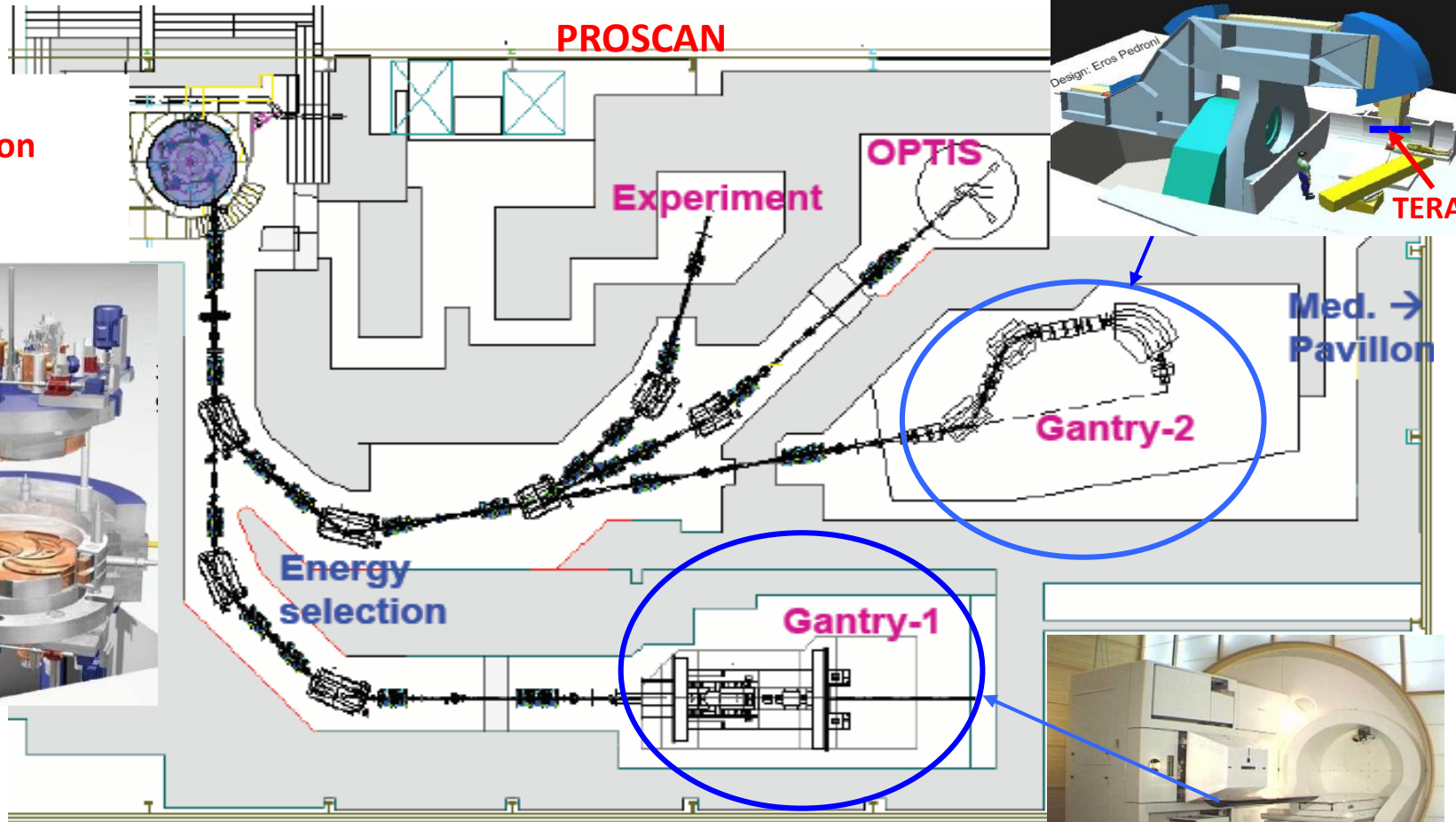


**What it looks like to the patient:
gantry room at the Midwest Proton
Radiotherapy Institute (MPRI)
(modified IBA gantry)**

Adapted from B. Gottschalk

PROSCAN at Paul Scherrer Institut (PSI), Switzerland

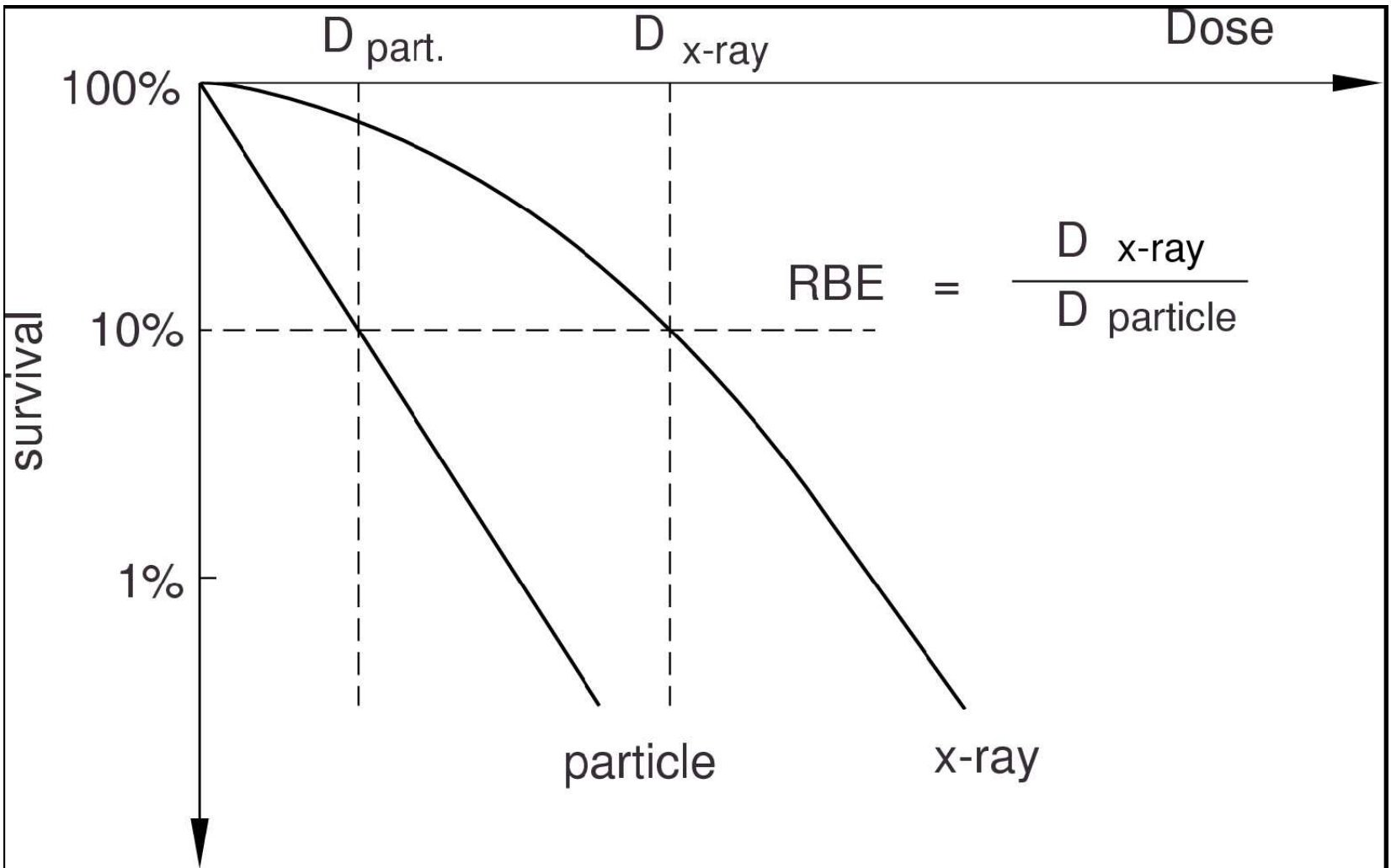
ACCEL
SC cyclotron
250 MeV
protons



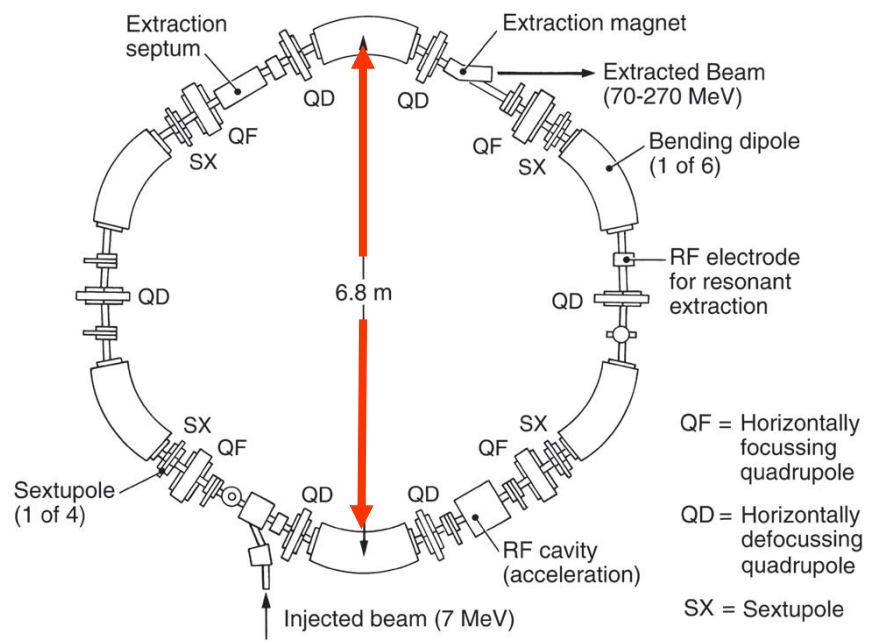
Courtesy PSI and U. Amaldi , TERA

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

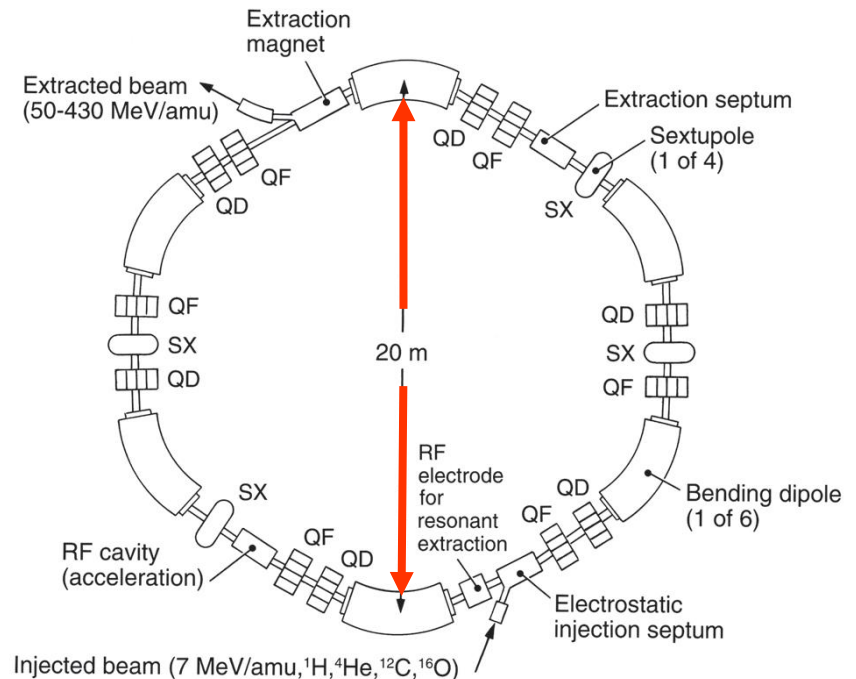
Protons vs carbon: radiobiological effectiveness (RBE) of radiation



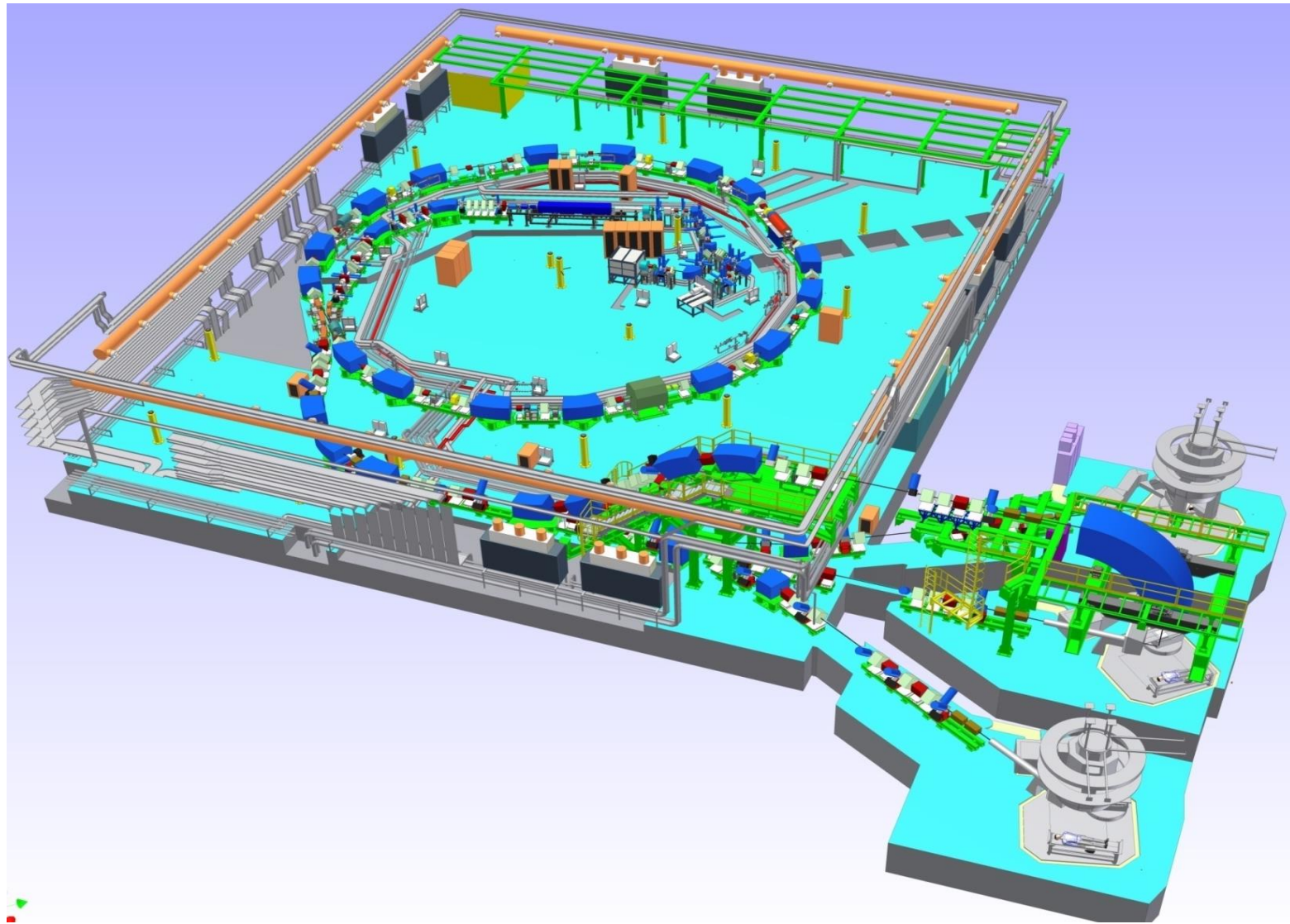
Hitachi proton synchrotron

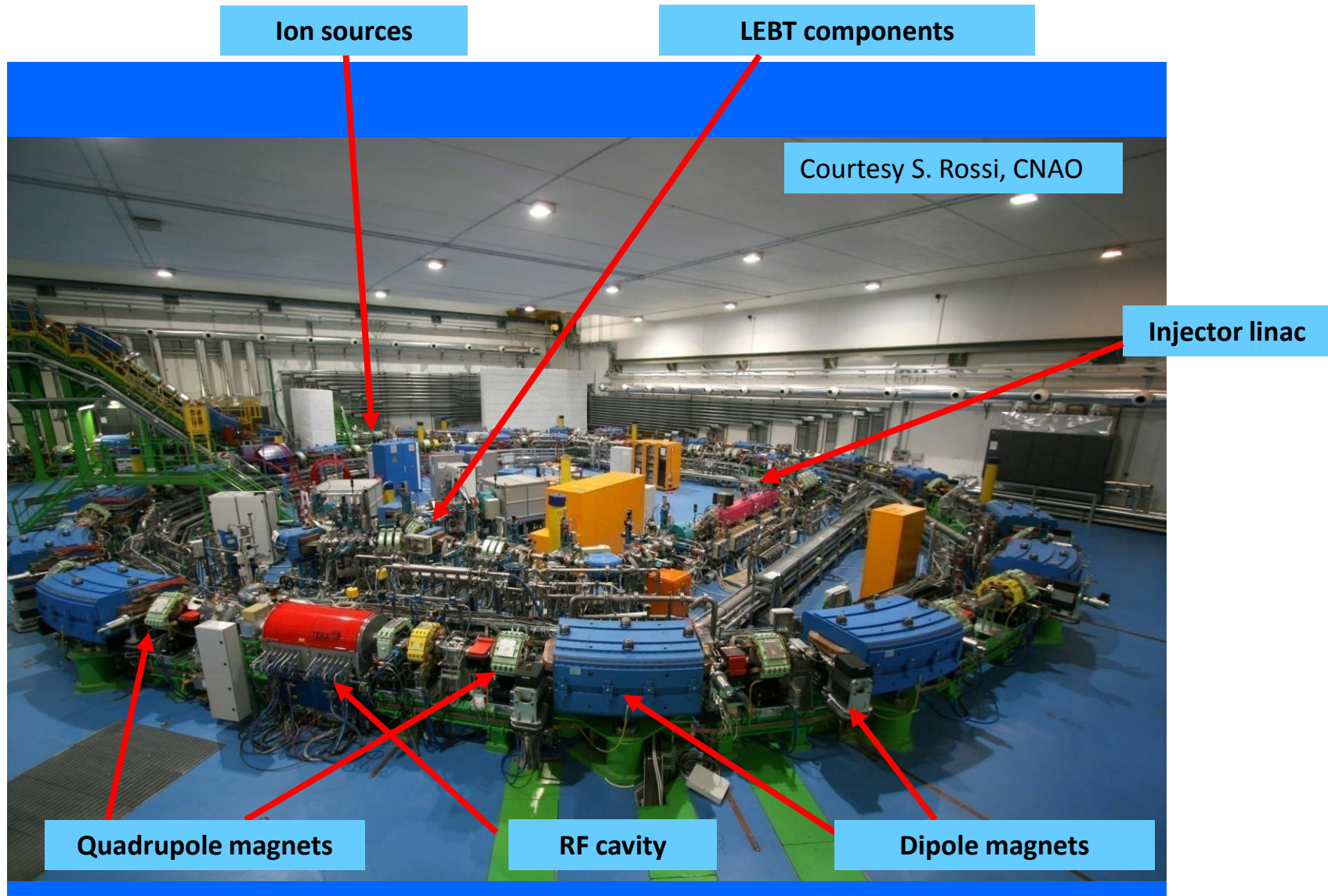


Siemens ion synchrotron



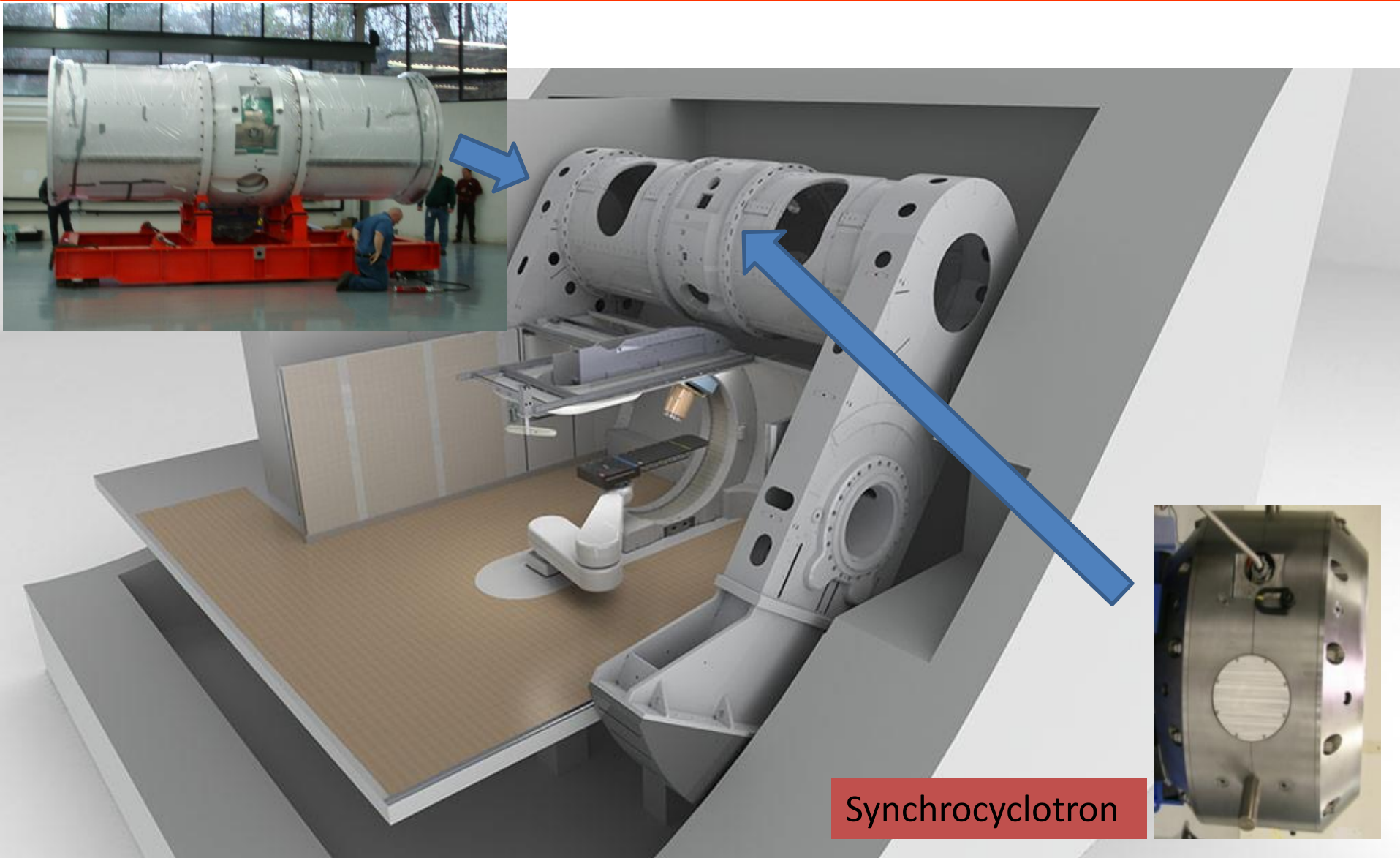
G. Coutrakon, Accelerators for Heavy-charged-particle Radiation Therapy, *Technology in Cancer Research & Treatment*, Volume 6, Number 4 Supplement, August 2007







Mevion Medical Systems – single room facility



Synchrocyclotron operating with 10 Tesla magnetic field

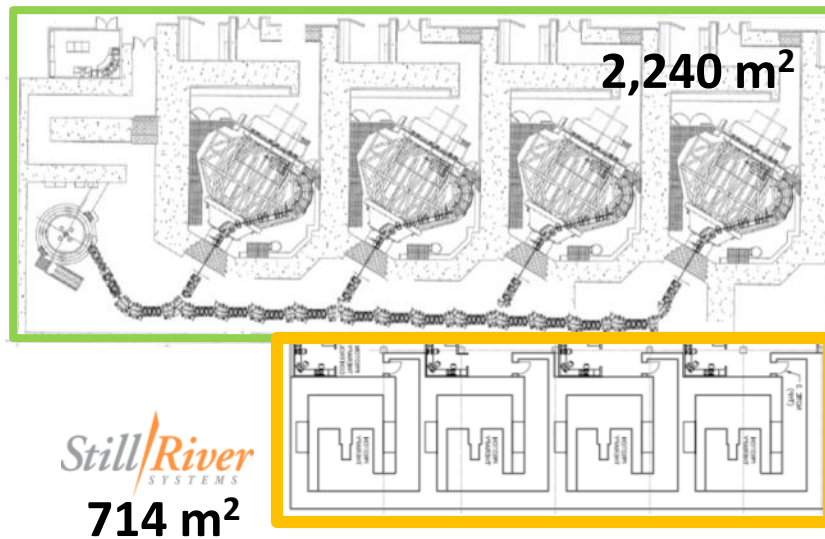
Proton energy: 250 MeV

Cooling is through cryo-compressors (NO liquid Helium)

Low maintenance requirements – quarterly only

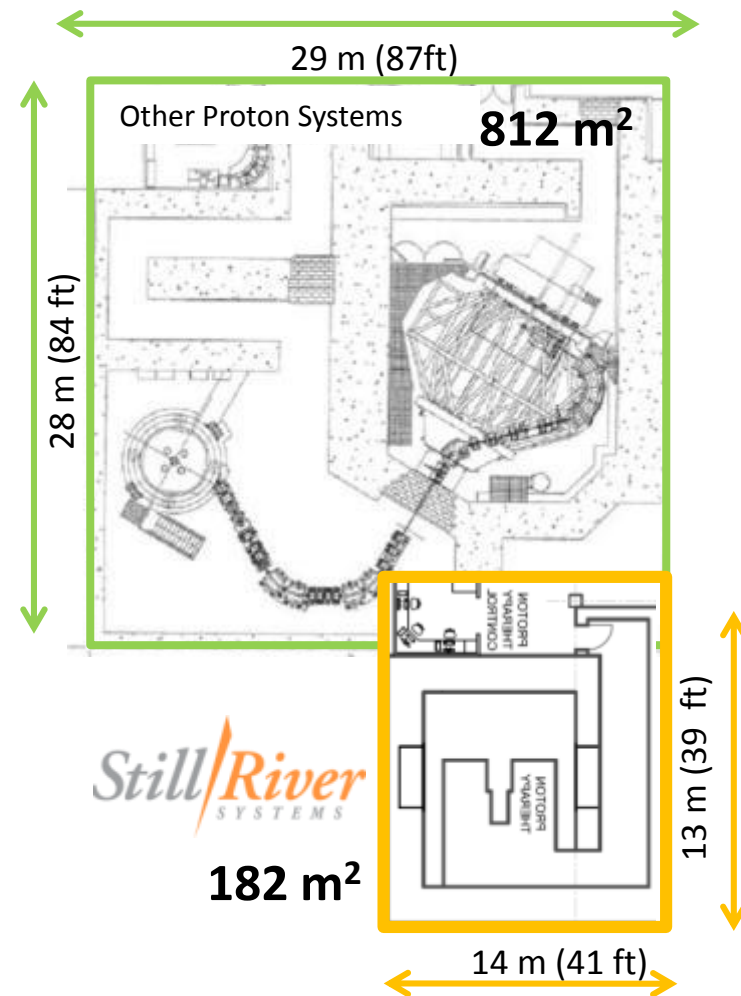


Multi-room versus single-room facilities



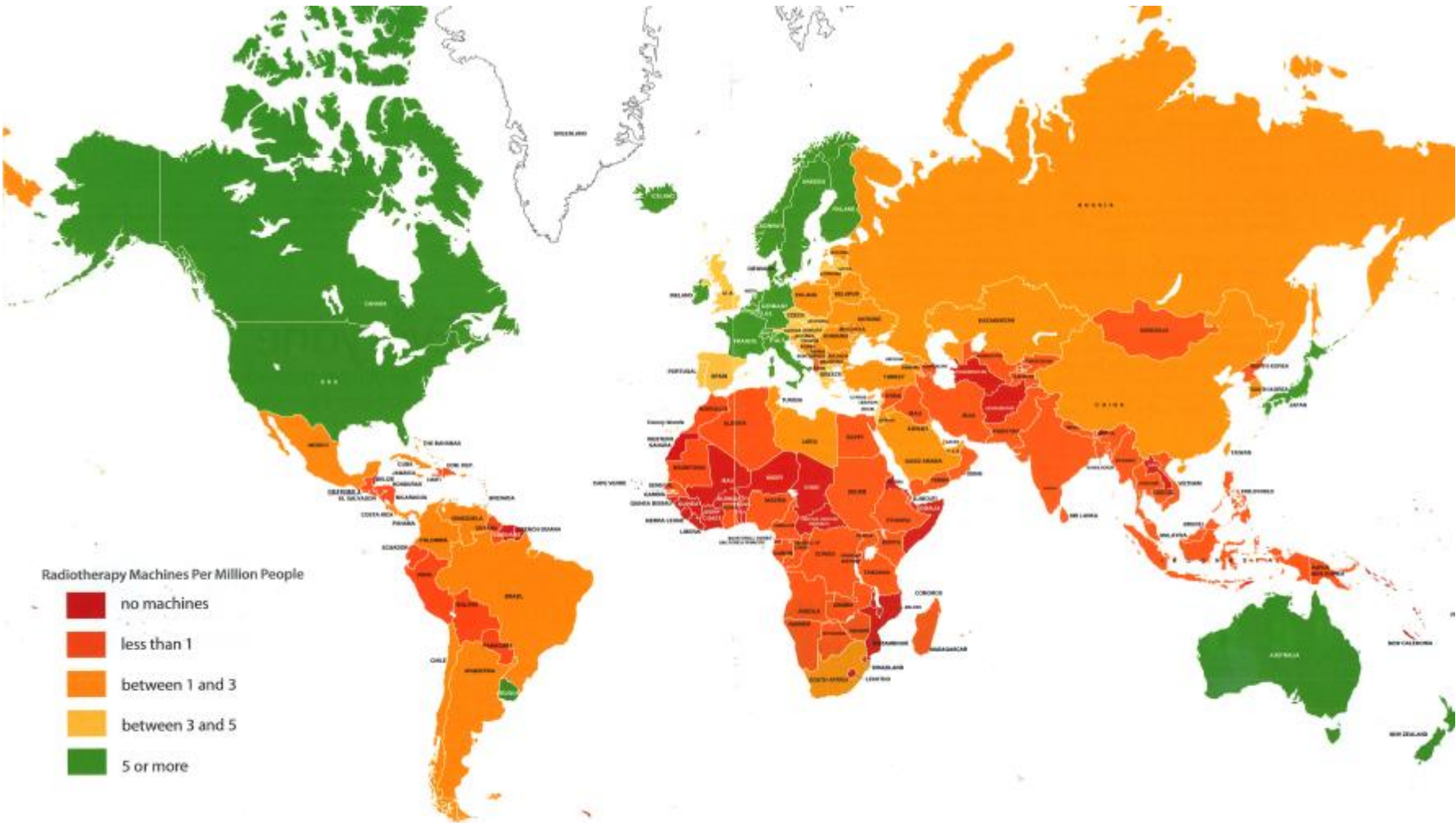
Advantages of single-room facility:

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

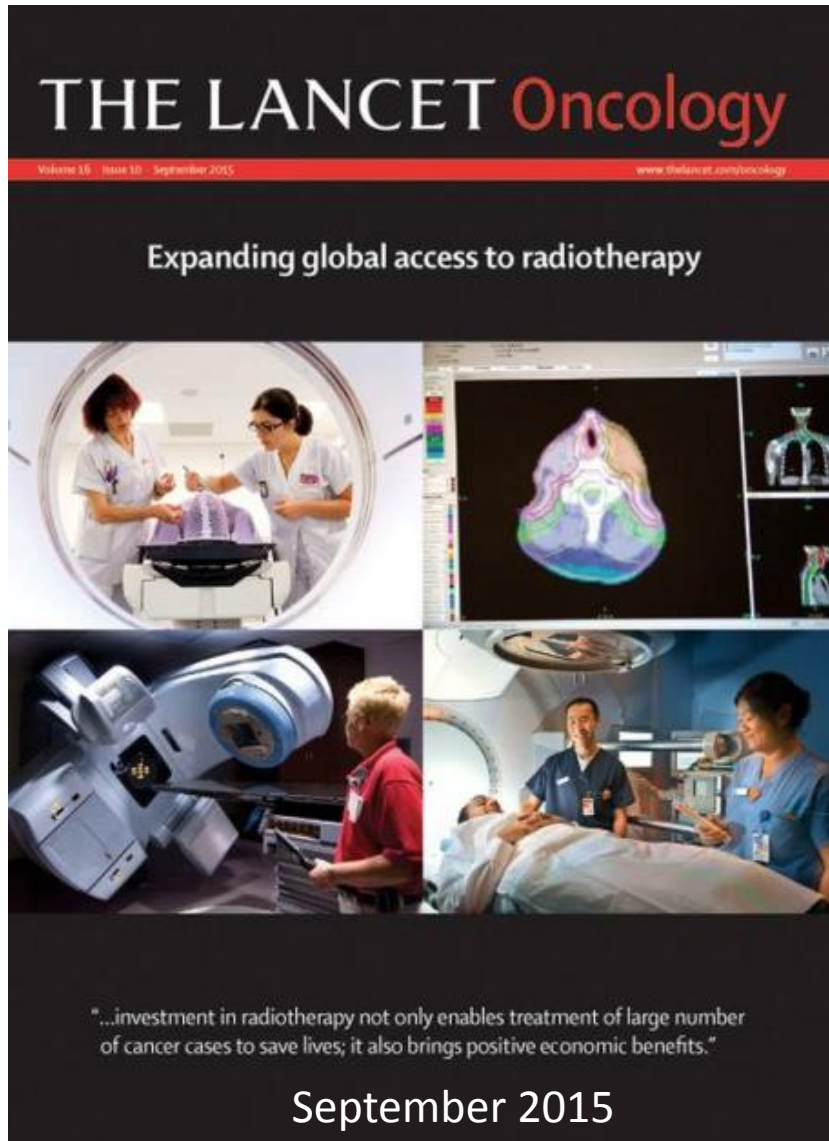


Courtesy L. Bouchet, *Still River Systems*

Availability of radiation therapy worldwide



Source: DIRAC/AEA



International
Cancer
Expert Corps

Partnering to transform global cancer care

CERN-ICEC workshop, CERN, November 2016

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



International
Cancer
Expert Corps

Partnering to transform global cancer care



Science & Technology
Facilities Council
10 Years of Impact and Inspiration

CERN-ICEC-STFC workshop, CERN, October 2017

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

According to estimates made by the International Agency for Research on Cancer (IARC), there are about 15 million new cancer cases per year worldwide, of which two thirds occur in developing countries.

The age distributions of cancer are, however, quite different between developed and developing countries; **there are significantly more cancer cases in childhood, adolescence and young adults in developing countries**, while cancer in the elderly dominates in developed countries

IAEA, Setting up a radiotherapy program, 2008

Need for

- qualified professionals (radiation oncologists, medical radiotherapy physicists, radiotherapy technicians, radiation protection officers, maintenance engineers, etc.)
- development of medical infrastructure for cancer treatment

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

	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

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

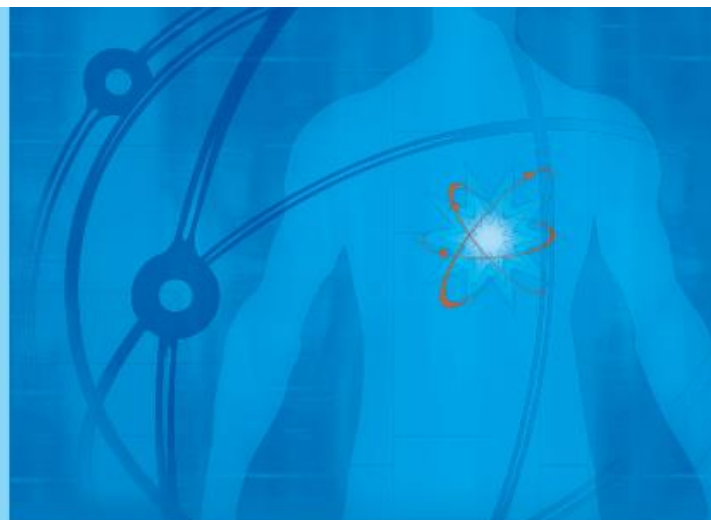
- Qualified professionals: radiation oncologists, medical radiotherapy physicists, radiotherapy technicians, radiation protection officers, maintenance engineers, etc.
- Related training programmes
- Development of medical infrastructure

Setting Up a Radiotherapy Programme:

Clinical, Medical Physics,
Radiation Protection and Safety Aspects



IAEA HUMAN HEALTH REPORTS No. 10



Radiotherapy Facilities:
Master Planning and Concept
Design Considerations

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)