History of accelerators in medicine

Tomas Vrba

List of abbreviations

- IR – ionizing radiation
- LINAC – linear accelerator
- LET – linear energy transfer
- RBE – relative biological effectiveness
- RF – radiofrequency
- RT – radiation therapy

Key statement

Basic knowledge of **radiobiology** can explain development of medical accelerators.

It explains why, but not how.

Fundamental principles of RT

- Strategy
  - deliver a sufficiently high dose to eradicate target
  - minimize dose to heathy tissue

- Tactics
  - use of different radiation (physical property of ionizing radiation type)
  - make target more sensitive to IR
  - decrease radio-sensitivity of heathy tissue(s)
  - combine RT with other techniques

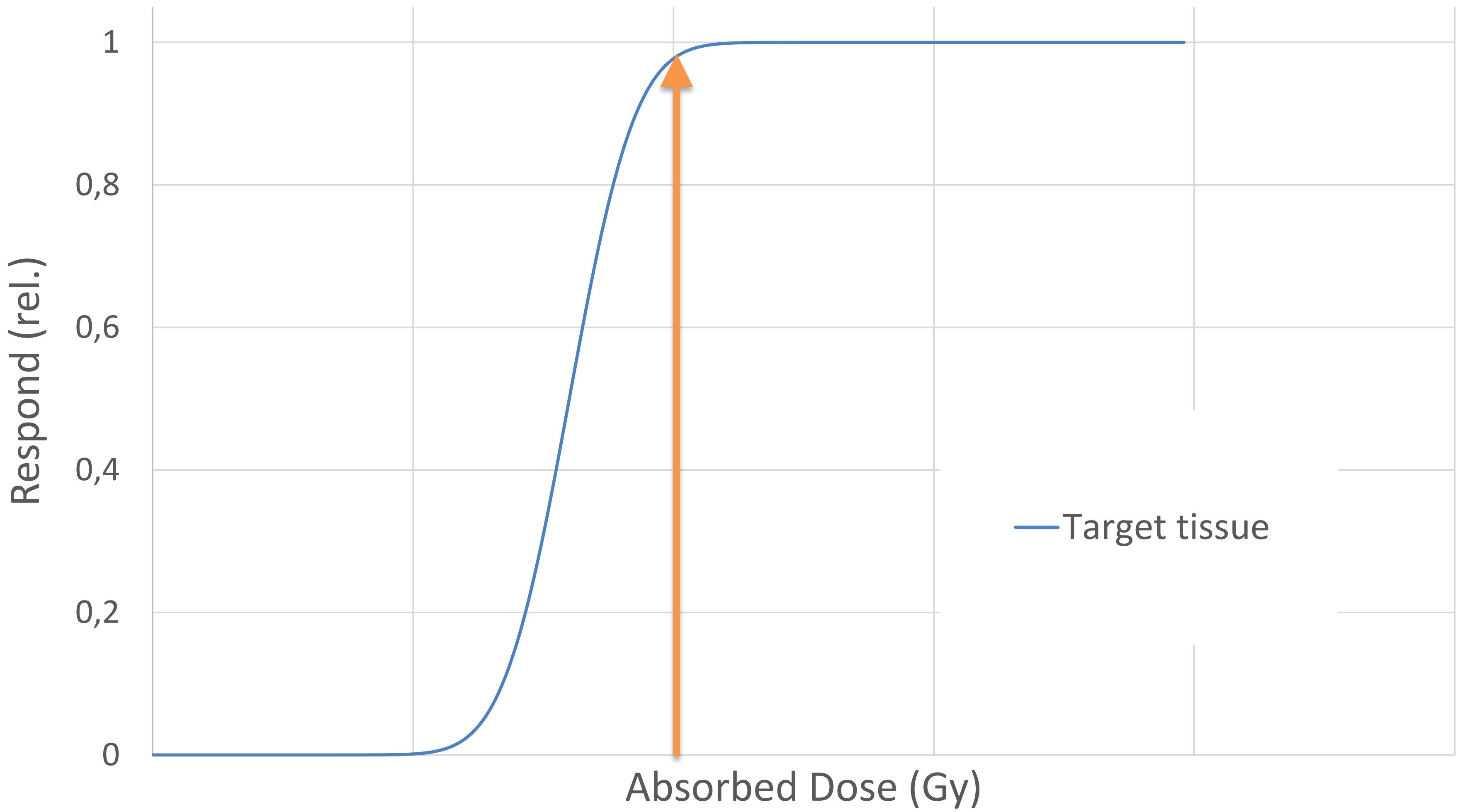
Absorbed dose

- The fundamental quantity given by

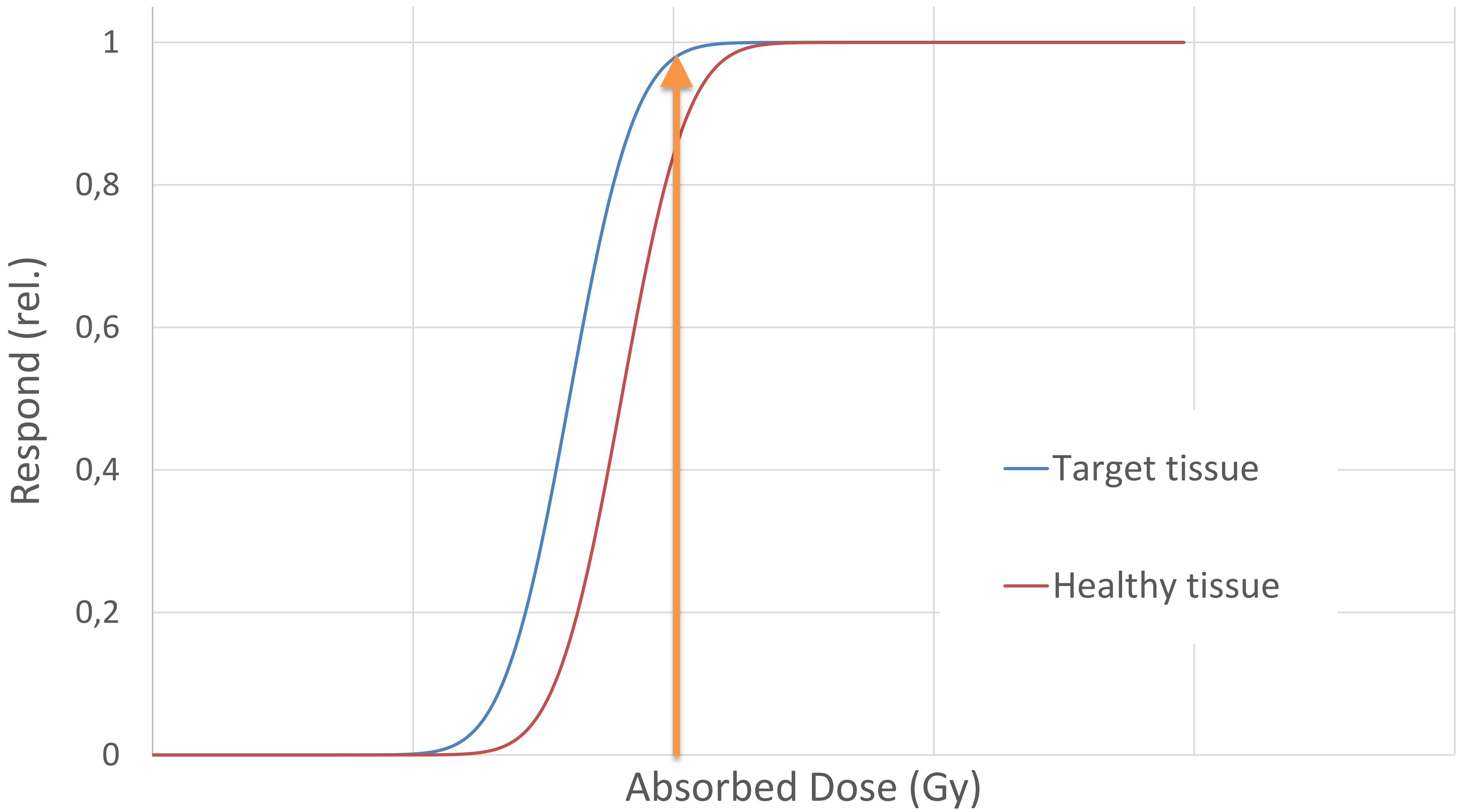
$$D = \frac{\bar{\varepsilon}}{m}$$

- where $\bar{\varepsilon}$ is the mean energy imparted to matter of mass dm by ionizing radiation.
- The SI unit for absorbed dose is joule per kilogram (J kg^{-1}) and its special name is **gray** (Gy)
- Old unit rad (100rad=1Gy)

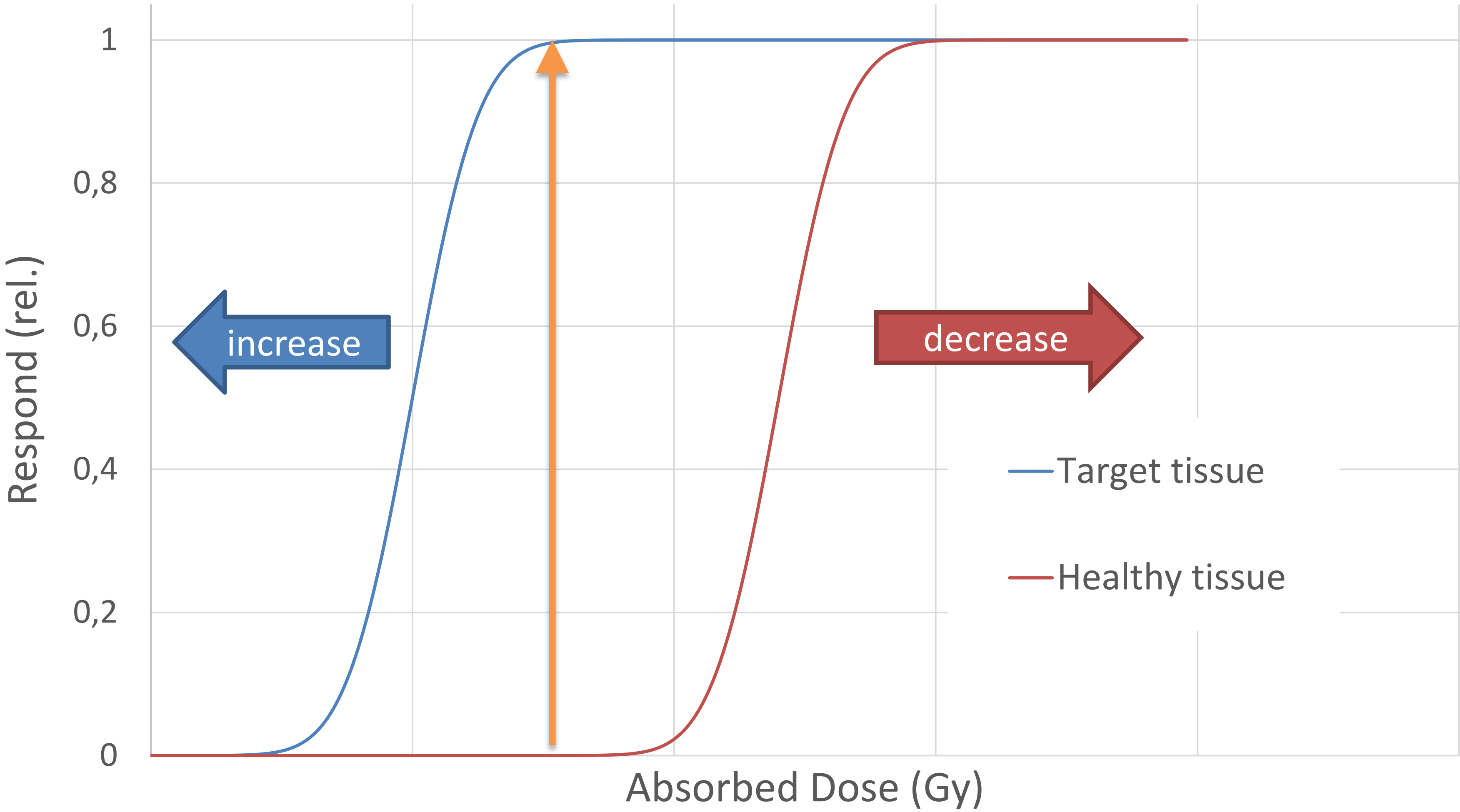
Dose respond curve (tissue reactions)



Dose respond curve (tissue reactions)



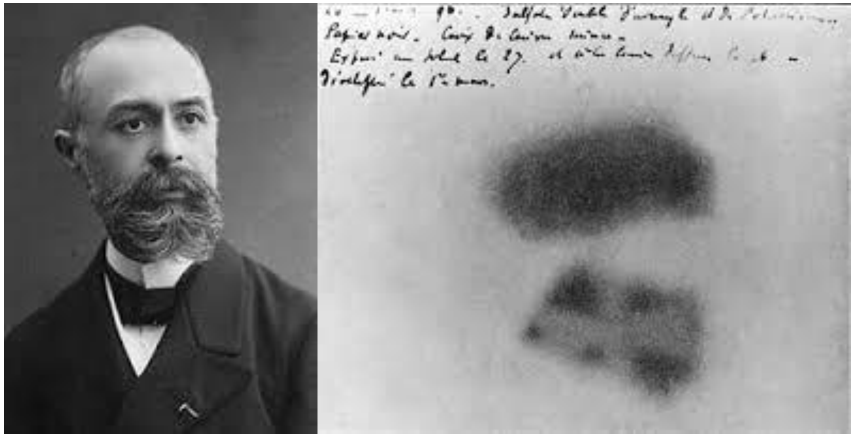
Ideal state for RT



At the beginning

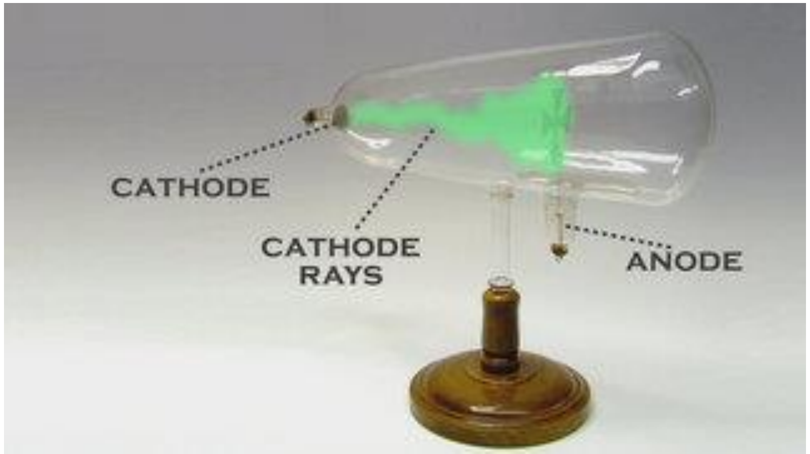
- Wilhelm Conrad Roentgen
  - 8th of November 1895
  - X-ray discovery

- Antoine Henry Becquerel
  - February 1896
  - discover of (natural) radioactivity



X-ray tube development

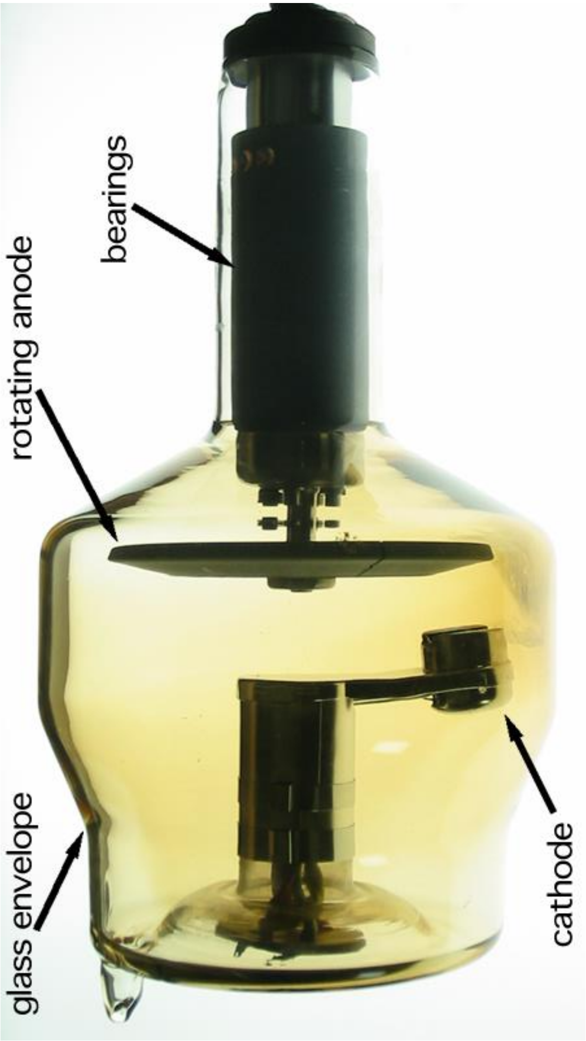
- Crookes–Hittorf tube
  - William Crookes, 1869
  - no shielding
  - gas filed (~ 0.1 Pa)
  - cold aluminum cathode
- Coolidge tube
  - William Coolidge, 1913
  - hot cathode, tungsten
  - evacuated to about 10^{-4} Pa



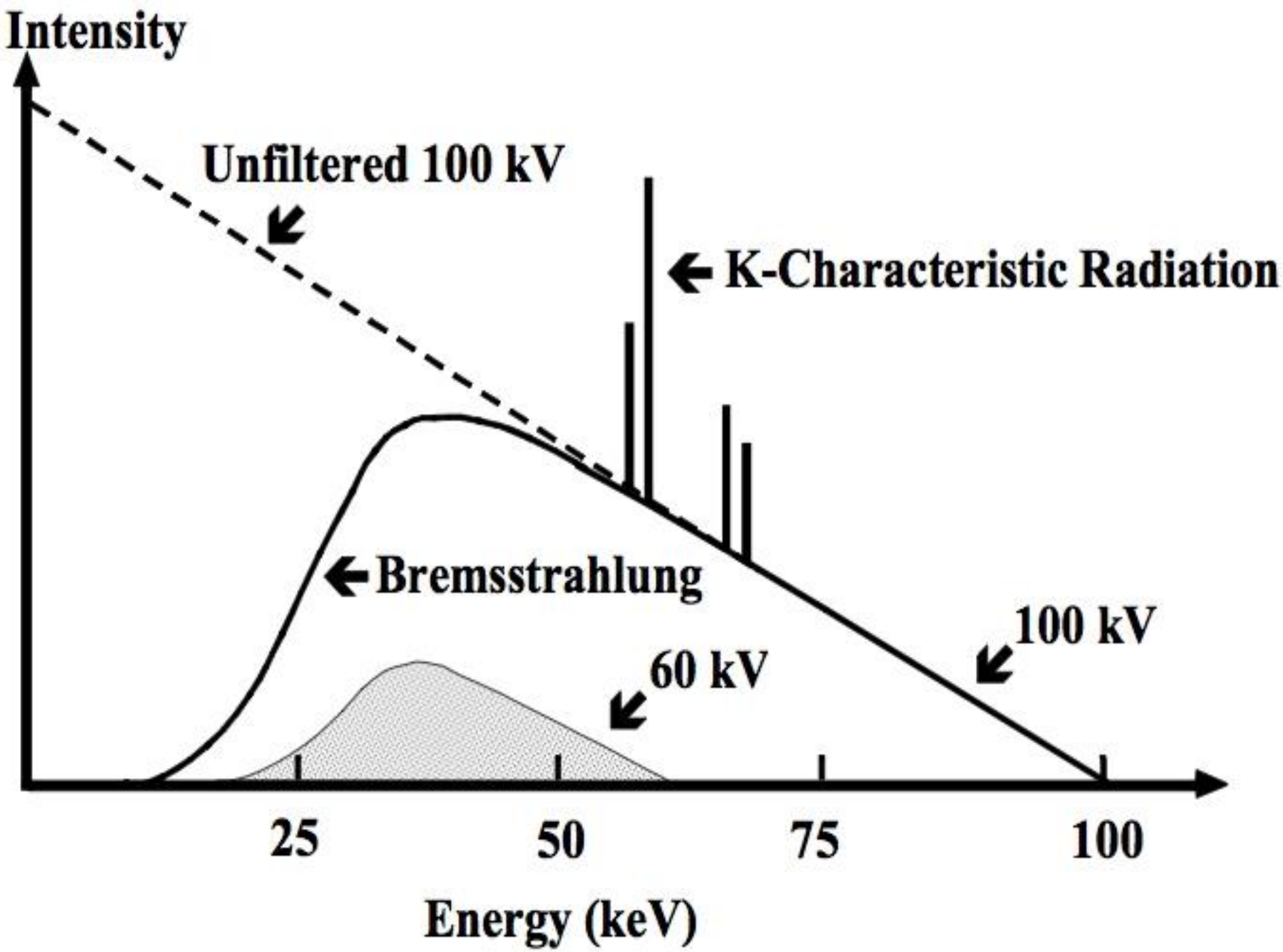
More tweaks and perks

- Rotational anode
  - heat dispersion, longer operational time
  - need for CT or therapy
  - higher current (up to 1 A)

- Different anode materials
  - production of characteristic radiation (e.g. Molybdenum)



X-ray spectrum

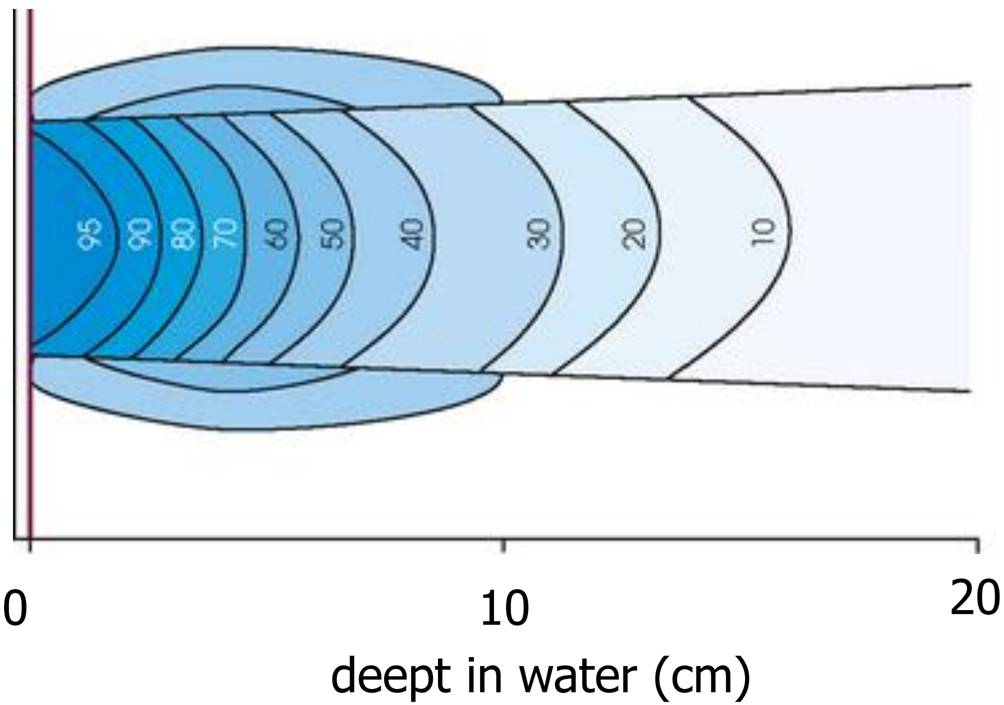


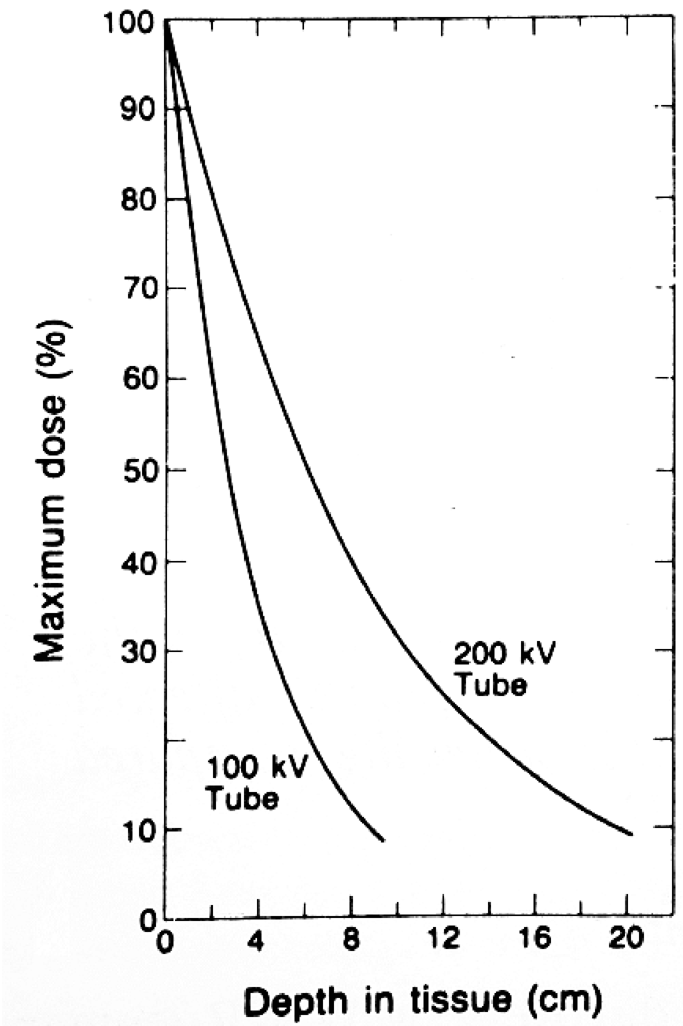
X-ray therapy - orthovoltage

- 1896 – 1st therapy of skin lesions
- 1898 – 1st successful treatment (lupus erythematosus)
- Not known mechanism of X-ray radiation effects
  - they do experiments on patients … and guess
  - ozone production, charge
- 1900 – 1st proposal that effect is due to X-ray

X-ray limitation

- X-ray @ 200 KV not good for deeper organ
- Lateral spread



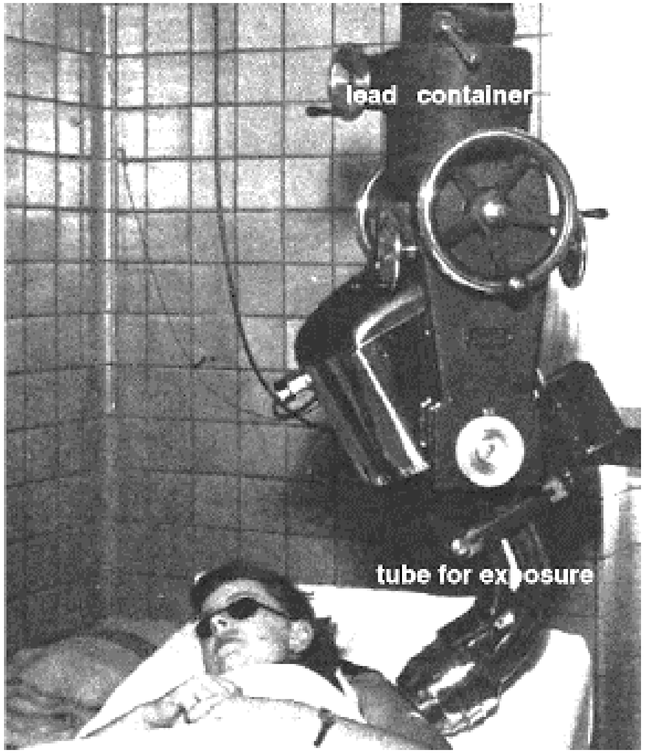


Move forward

- Use radionuclide source with discrete photon energy
  - ^{226}Ra in equilibrium, photons up to 2.5 MeV
  - Radium cannon, circa 1912
    - 2 – 10 grams of radium
  - Base for future radionuclide irradiators
    - ^{60}Co, ^{137}Cs irradiators
      - Goiânia accident (1985)
    - Leksell gamma knife (^{60}Co)
      - Not dead yet
      - Leksell Gamma Knife® Perfexion™ - Elekta

Radium cannon – drawbacks

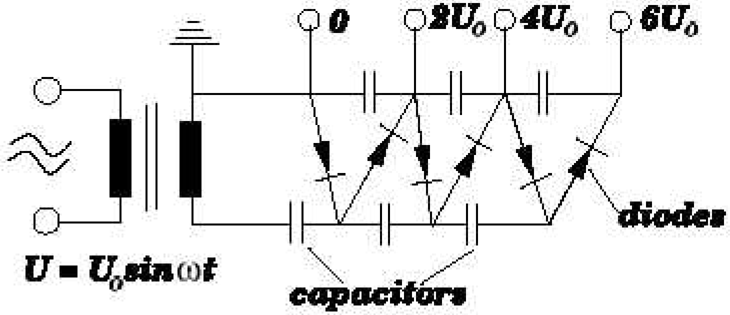
- Dose rate
  - 45 min per 2 Gy
- Price
  - Circa $50000 per gram (1935)
- Dose depth curve far from prefect
- Need another RN, higher HV or apply different accelerator methods



Norwegian Radium Hospital

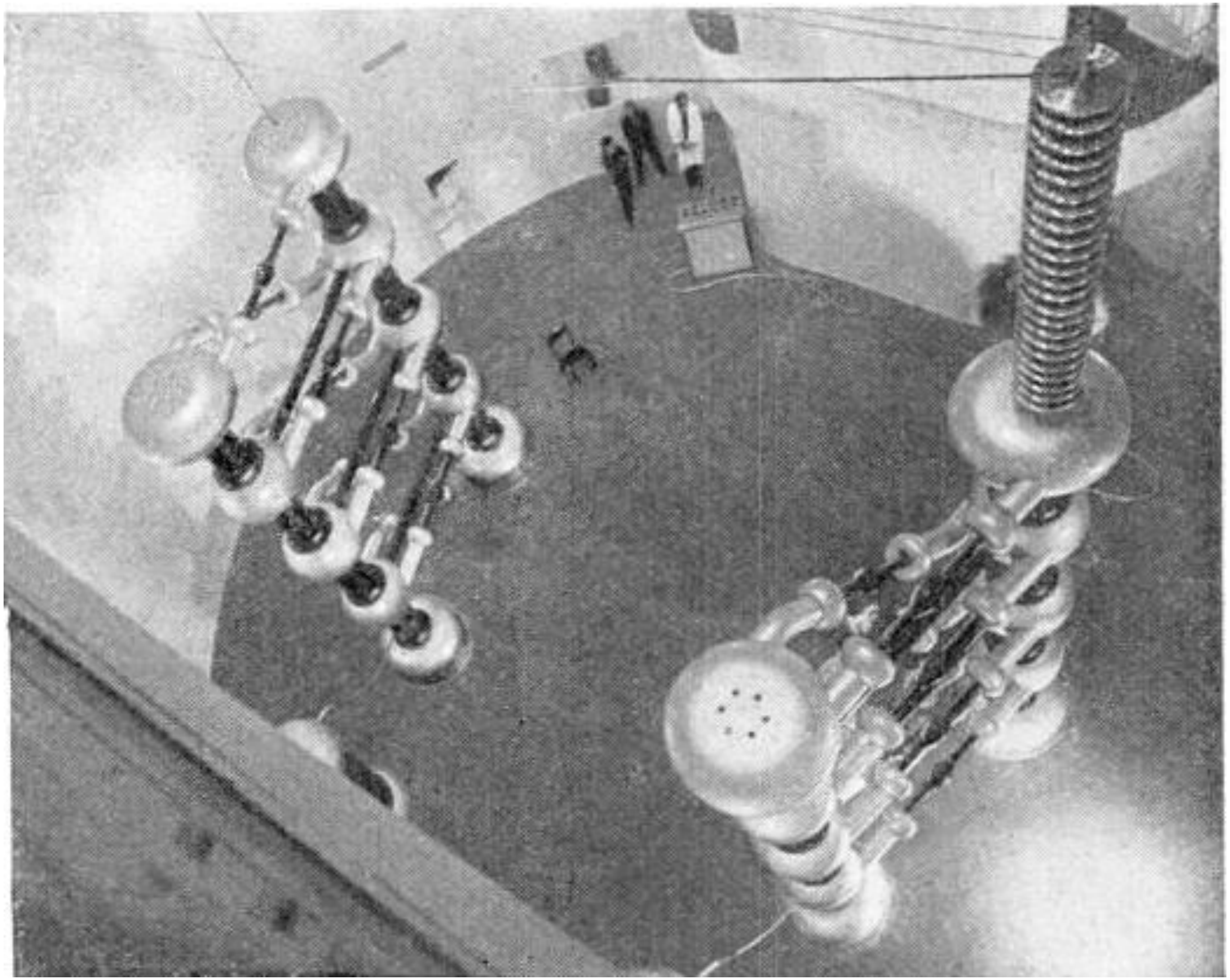
Rectifier accelerators

- 1932 Cockcroft and Walton
- Cascade generator
  - High DC voltage from a low-voltage AC input



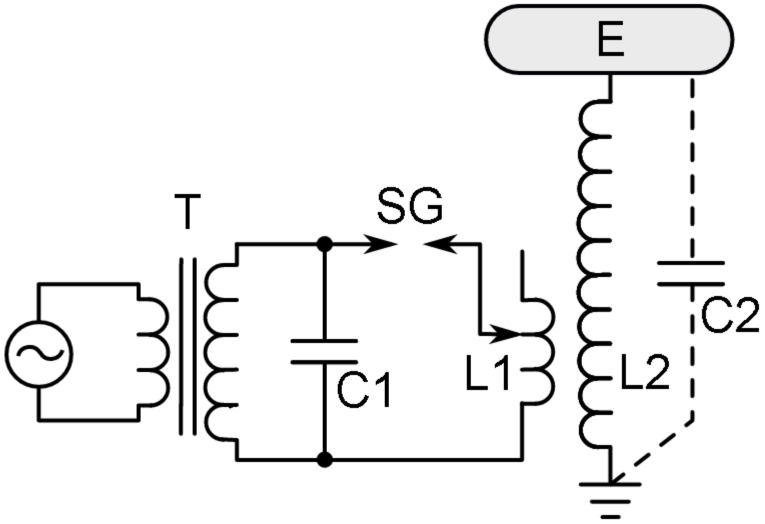
John Cockcroft, Ernest Rutherford, and Ernest Walton

CW accelerator

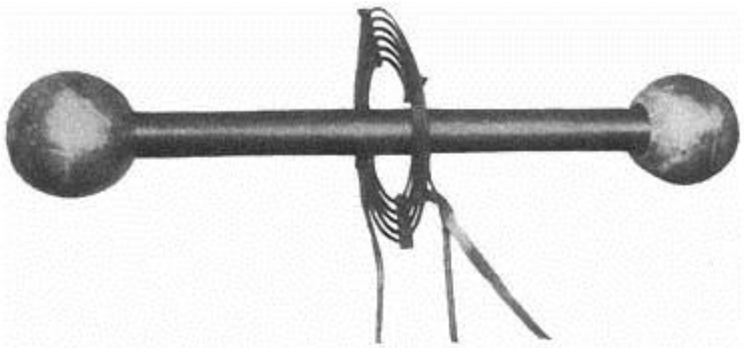


Resonant transformers

- Merle Tuve and Gregory Breit (1928)
  - 5 MV Tesla coil as a linear particle accelerator
- No wide impact on radiation therapy

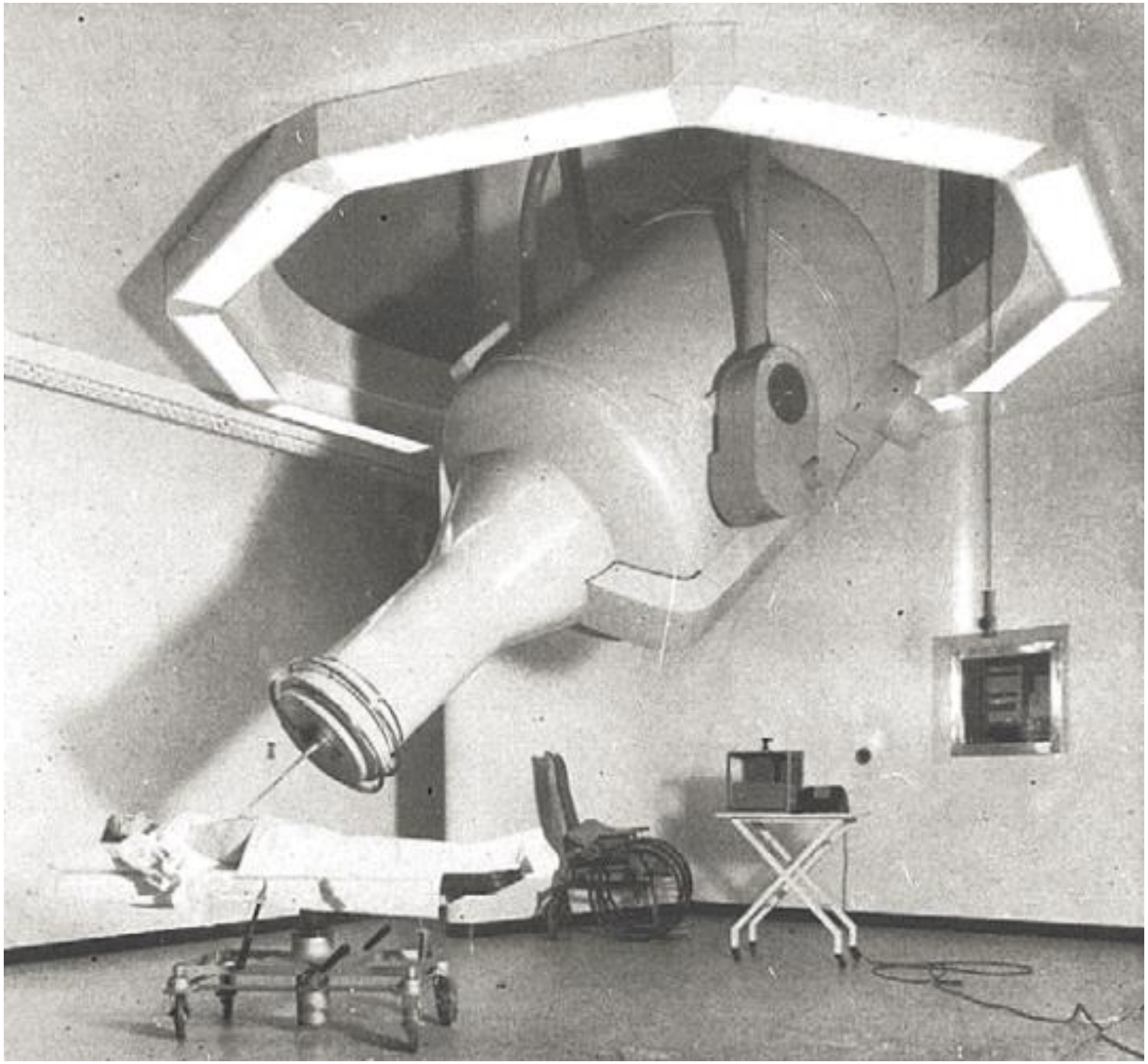


Unipolar tesla coil



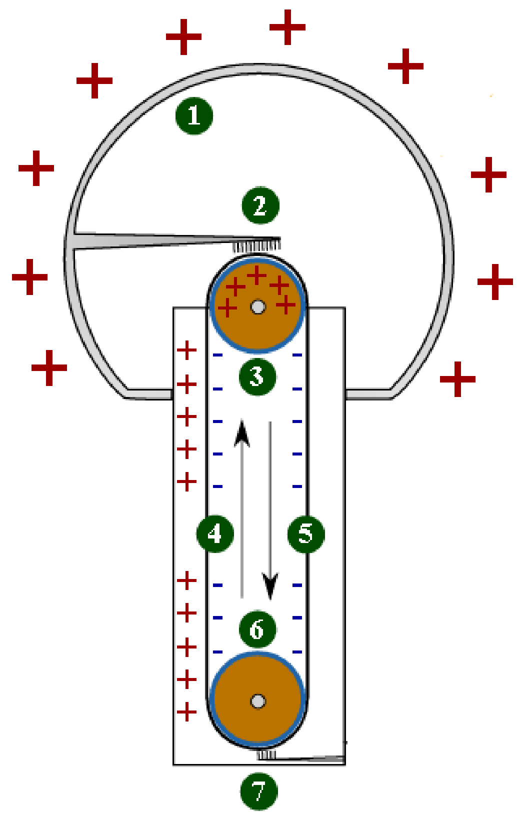
Resonance particle accelerator

Resonant transformer (4 MeV)



Van de Graaff accelerator

- Electro-static generator
- triboelectric effect
- 1st apparatus in 1929
  - Princeton university
- Made of:
  - tin can
  - small motor
  - silk ribbon
- Inexpensive device



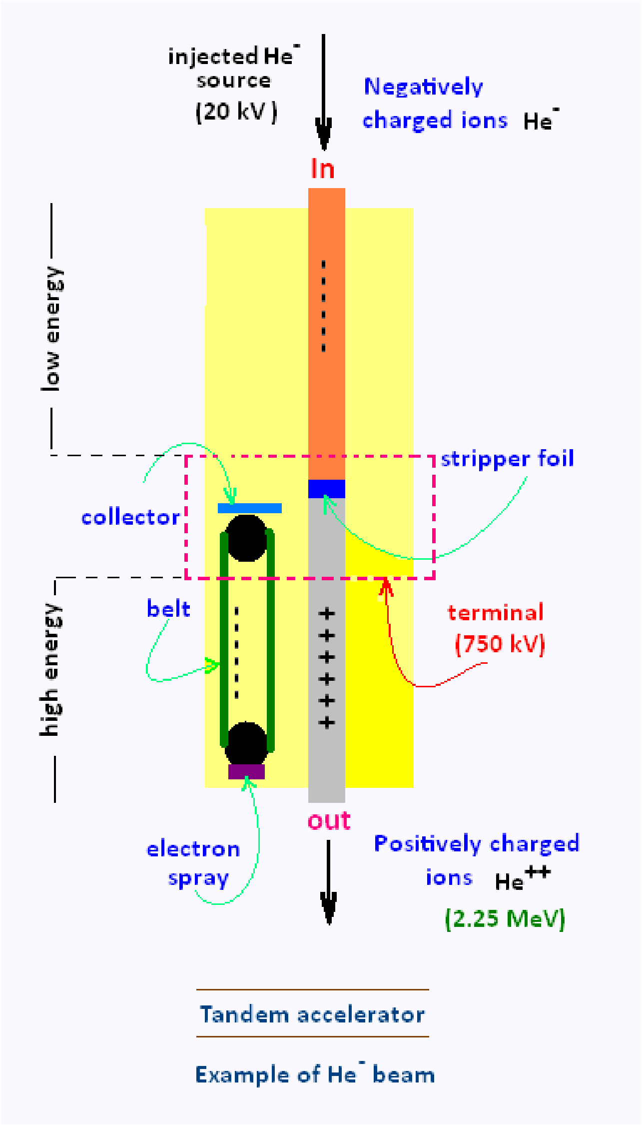
1. hollow metal sphere
2. upper electrode
3. upper roller
4. belt (+ charges) , 5. belt (- charge)
6. lower roller
7. lower electrode – ground

Improving initial concept

- 1931 - 1.5 MV accelerator (for $100)
- 1937 - 5 MV accelerator in Forest Hills
  - Westinghouse Electric
- 1937 - 1st medical air insulated VdGA in Boston (1 MeV)
- 1946 - Commercial production (2 – 2.5 MV) for medical application (totally about 40)
  - 12 of them operated till 1959

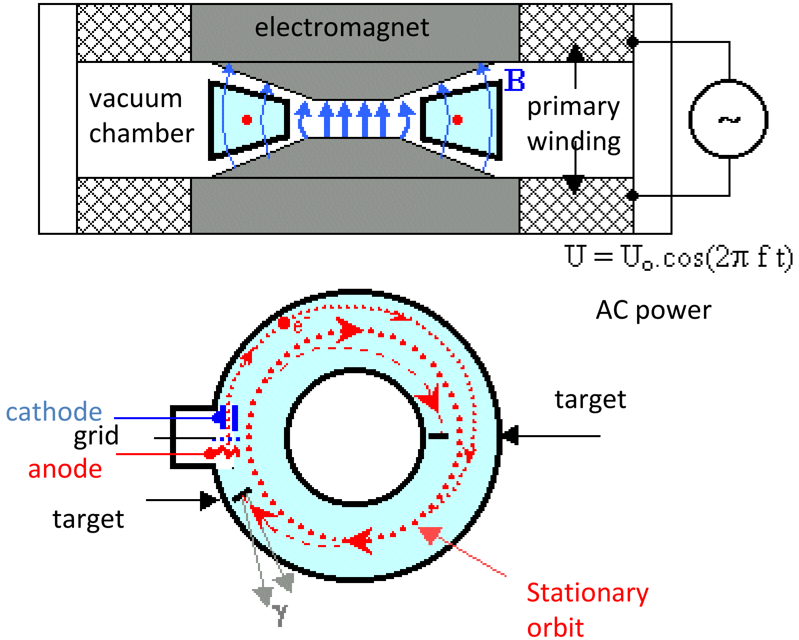
Tweaks and disadvantage

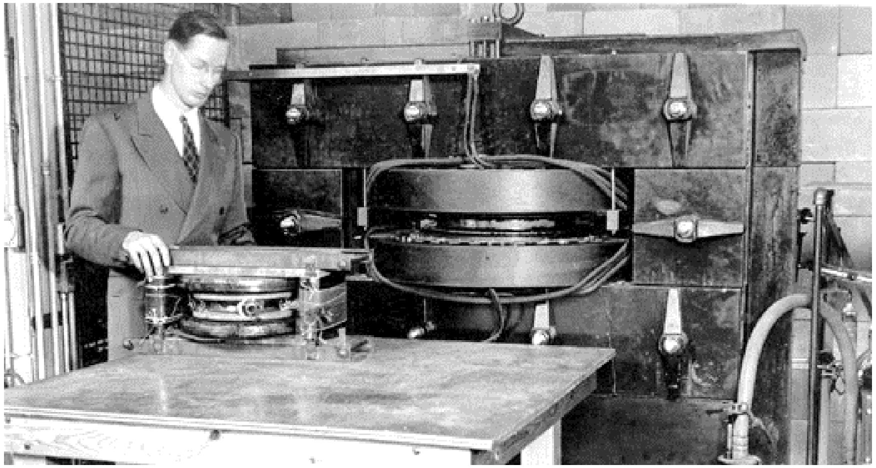
- Dielectric strength of air is limited to 3 MV m^{-1}
  →pressure air insulation
- Insulation gases freon and SF_6
- Belt durability
  - Ruberized materials, Chains
- Multistage accelerators (tandem)
- Bulky design – a lot of space needed



Betatron

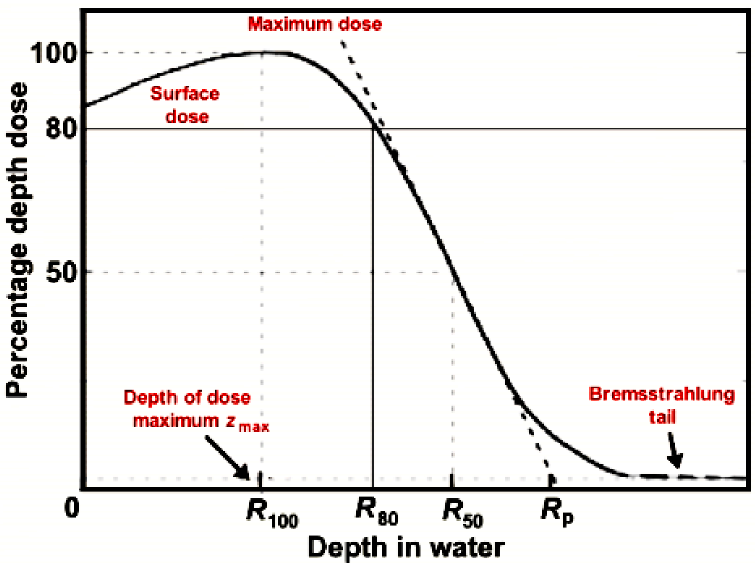
- Initial Concept of Rolf Widerøe build in 1935 by Max Steenbeck ??
- subsequently developed by D. W. Kerst in 1940s
- 1949 – 1st patient irradiated with X-ray from 20 MV electrons

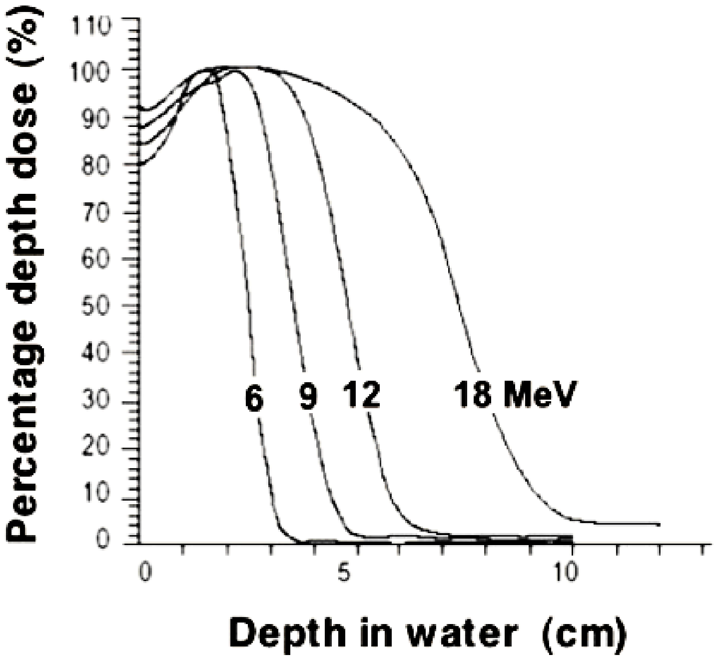




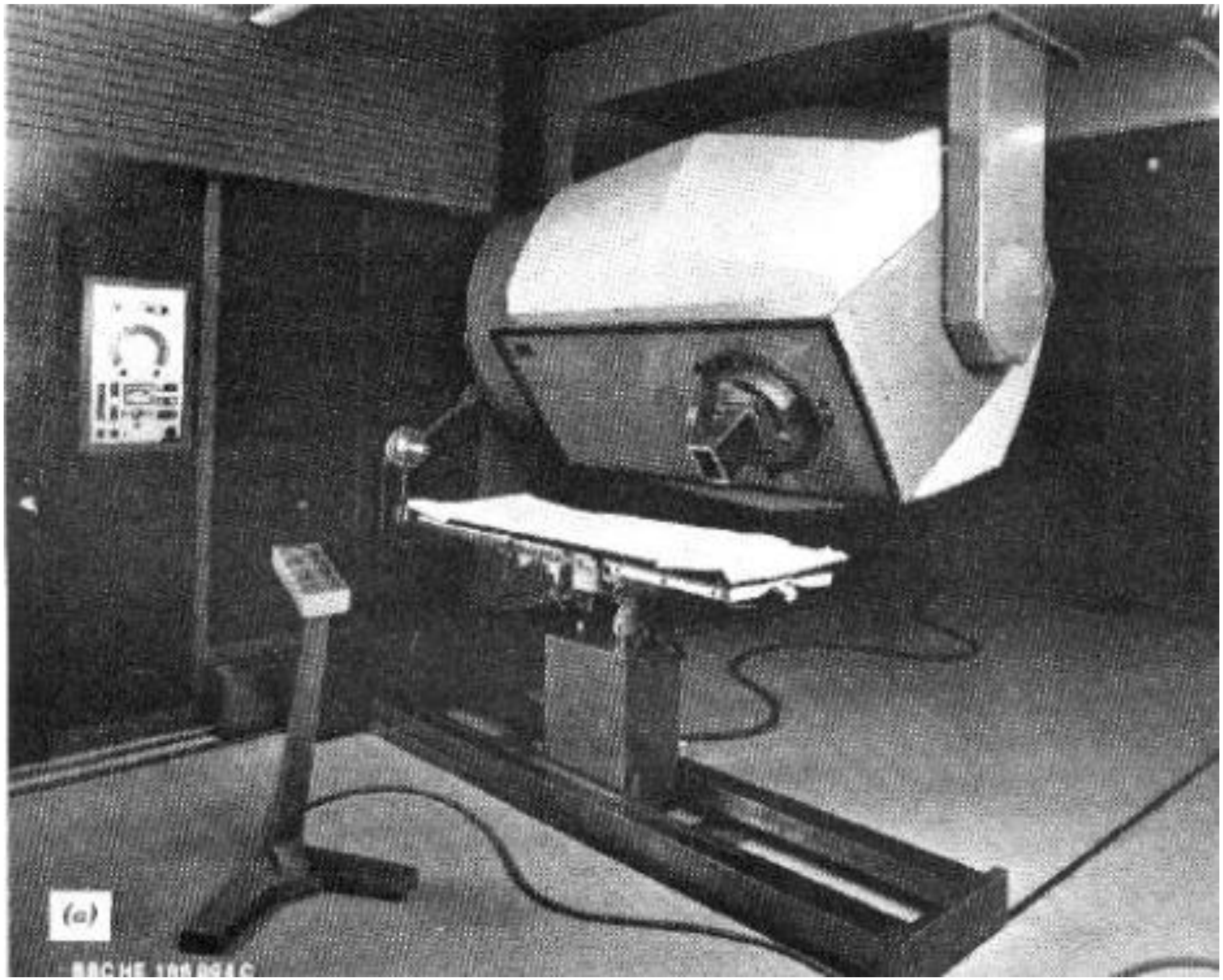
Betatron in medicine

- 1951 – 31 MeV betatron operated in Cantonal Hospital in Zurich (radiation therapy)
- Siemens, Brown Boveri, and Allis Chalmers
- Electron therapy



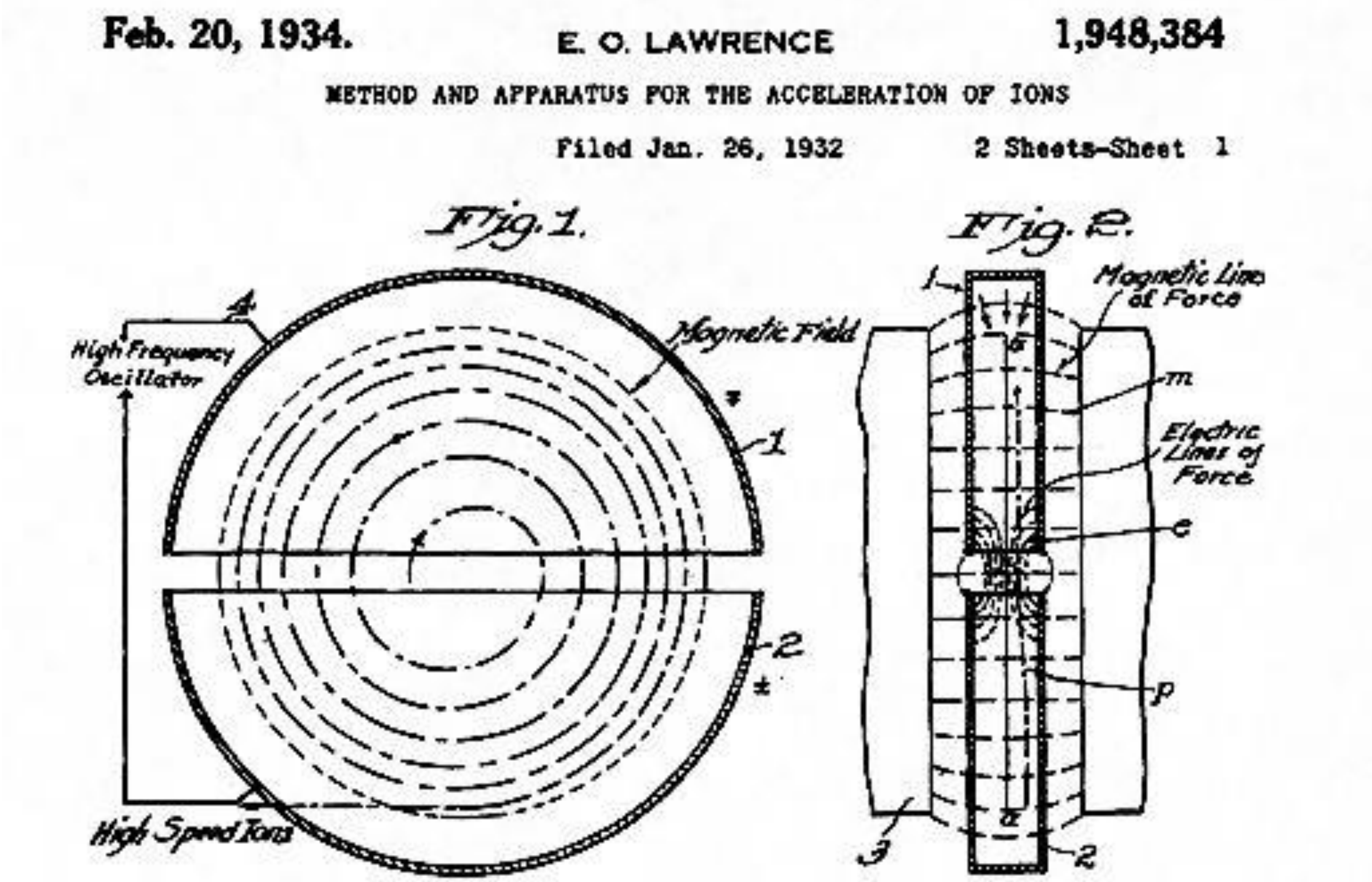


Betatron - 45 MeV



Cyclotron

- Ernest Lawrence and Stanley Livingston



First device - proof of concept

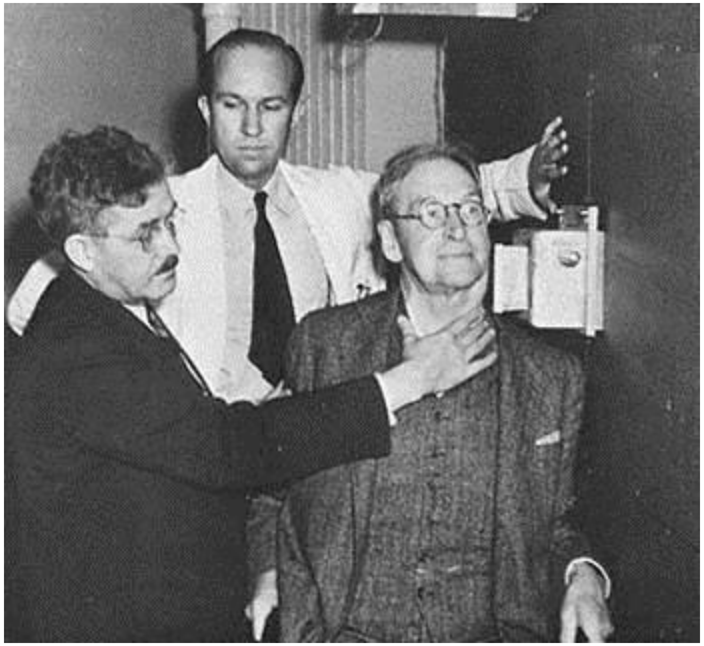
- 4-5 inch ~ 12 cm
  - brass, wire
  - sealing wax
  - about $25
  - HV = 1.8 KV
  - 80 keV proton
- 11 inch ~ 28 cm
  - 1.2 kV
  - 1MeV proton

Medical use of cyclotron

- Tele-therapy
  - possilbe photon therapy (megavolt X-ray)
  - fast neutron therapy
  - proton therapy
- Production of radionuclides
  - Diagnostic radionuclides
  - Therapy radionuclides

Fast neutron therapy

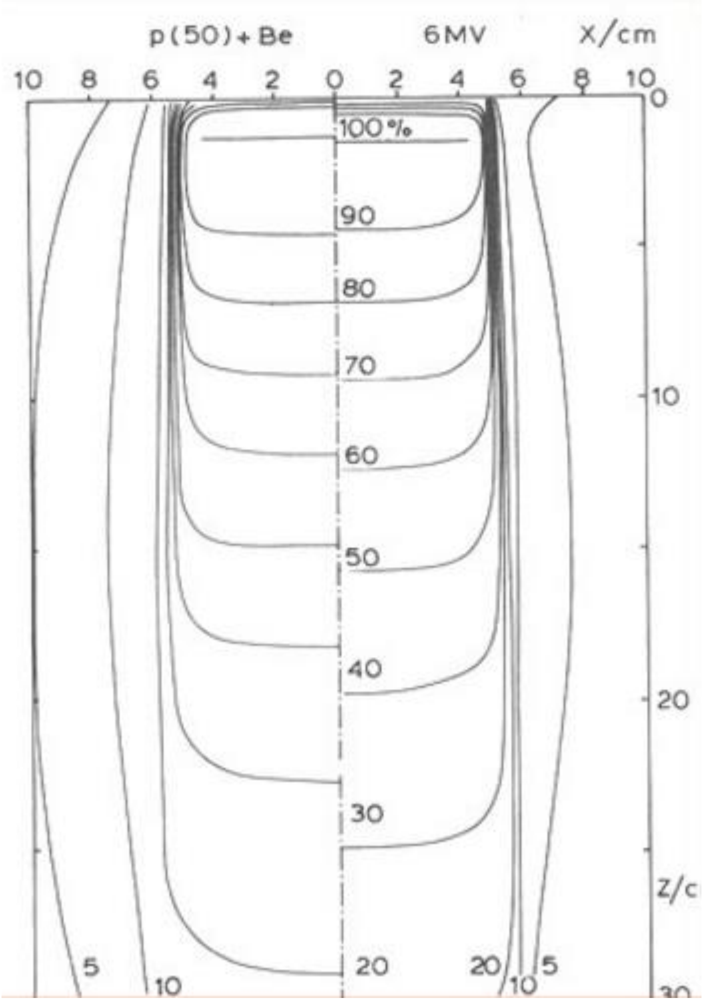
- 1932 – J. Chadwick discovered neutron
- 1938 – R. Stone proposed neutron therapy and performed 24 treatments till 1339
- Neutron production
  - $^{9}Be + p \rightarrow {}^{9}B + n$
  - $^{9}Be + d \rightarrow {}^{10}B + n$
- 1939 - John Lawrence →



Neutron beam

- Dose depth function similar to 6 MV photon beam
- But LET and thus RBE is different

Radiation	LET (keV/μm)
Cobalt-60 γ-rays	2
250 kV X-rays	3
Protons	3
α-particles	5
π-mesons	10
Carbon ions	15
Neon ions	50
Fast neutrons	75
Argon ions	150
Boron neutron capture	150



Linear Energy Transfer

- The **average** linear rate of energy loss of charged particle radiation in a medium

$$L_\Delta = \frac{dE_\Delta}{dl}$$

- where dE_Δ is the mean energy lost by a charged particle owing to collisions with electrons in traversing a distance dl in matter minus sum of the kinetic energies of all the electrons released with kinetic energy exceeding Δ
- the unit of L is J m^{-1}, often given in keV μm^{-1}

LET

- restricted LET
  - restriction in eV
  - cut off limit range of electrons (100 eV ~ nm)
- unrestricted LET is equivalent to collision stopping power

$$L = \frac{dE}{dl}$$

- describes energy loss along the path of the particle averaged **over many trials**

Relative biological effectiveness, RBE

- the ratio of a dose of a low-LET reference radiation to a dose of the radiation considered that gives an identical biological effect

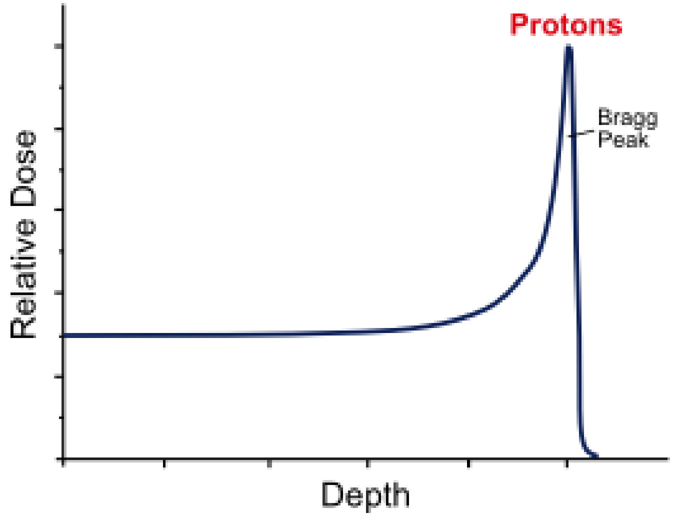
$$RBE = \frac{D_r}{D_i}$$

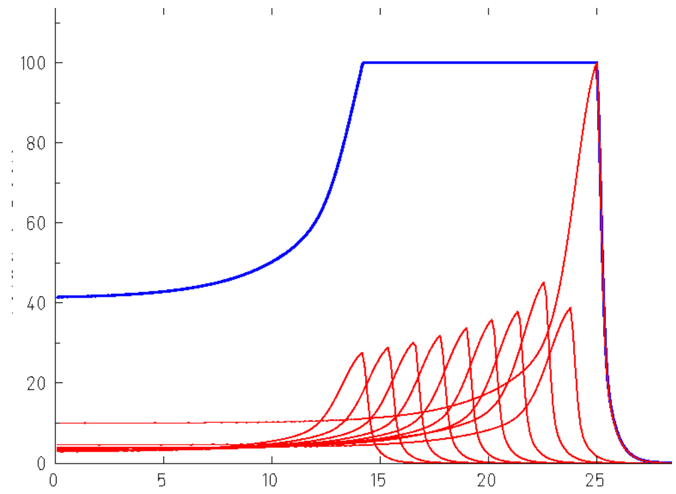
reference radiation (^{60}Co, X (250 kV)

- values vary with the dose, dose rate, and **biological endpoint** considered

Medical use of proton

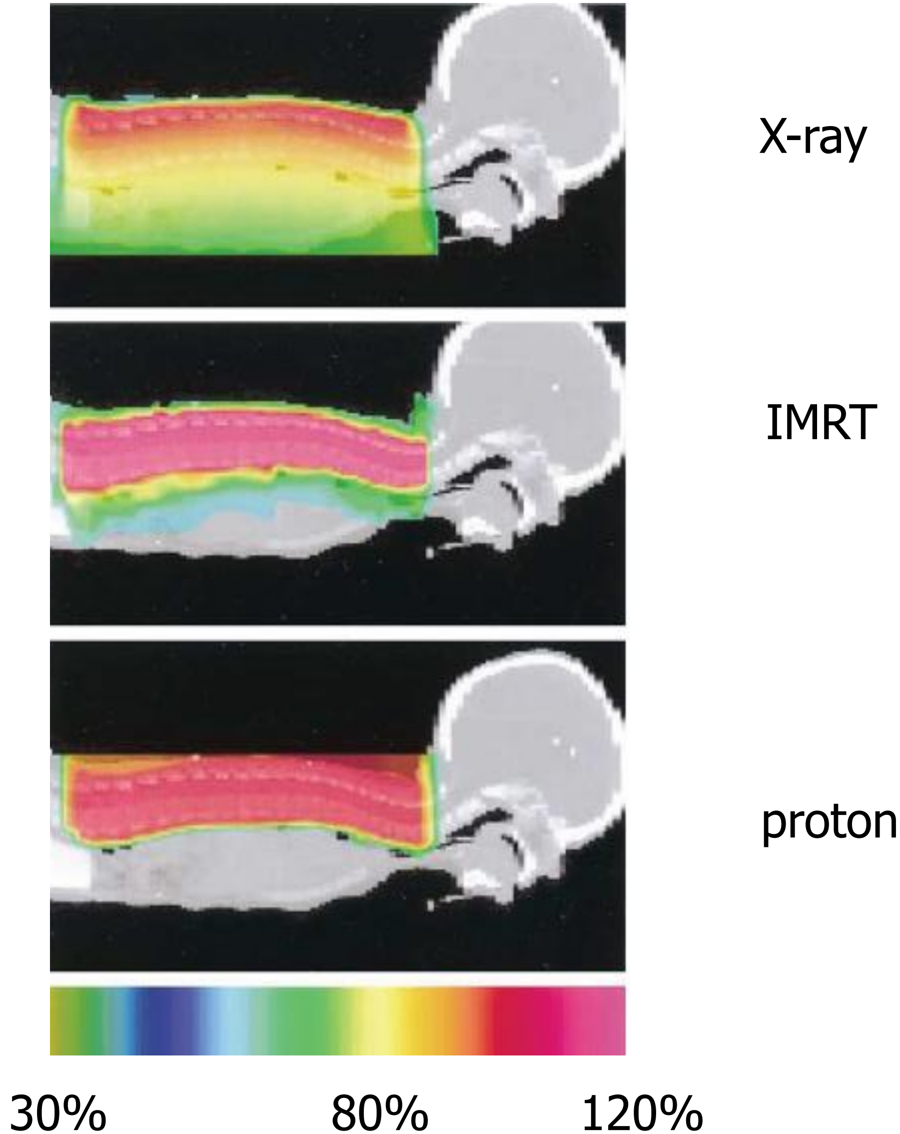
- 1946 Robert R. Wilson
- 1954 John Lawrence was the first to treat cancer with a cyclotron (proton therapy)
  - 30 patients
- Uppsala
  - 1957 p@ 200 MeV patient treatment
  - 1958 brain tumor





Proton therapy gains and drawbacks

- Slightly higher RBE (~ 1.2)
- Skin sparing (for thin targets)
- Sparing of tissue beyond Bragg peak
- Neutron production

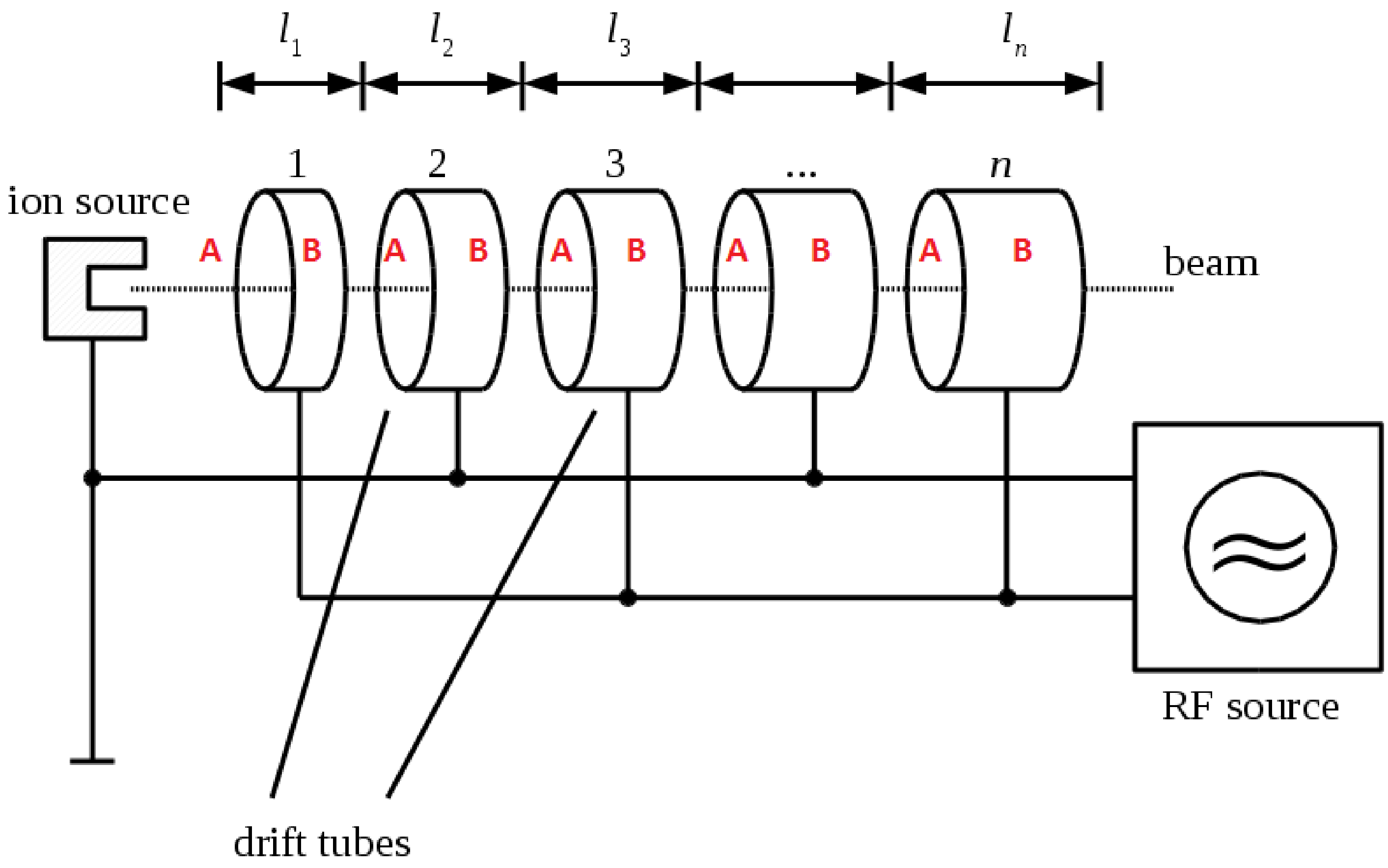


Radionuclide production

- Diagnostic
  - Non - PET radiopharmaceuticals
    - ^{99m}Tc (also by nuclear reactor)
    - ^{67}Cu, ^{201}Tl, ^{123}I
  - Positron emitters
    - ^{18}F, ^{11}C, ^{13}N, ^{15}O, …
- Therapy
  - ^{67}Cu , ^{103}Pd, ^{186}Re, …

Linear accelerator

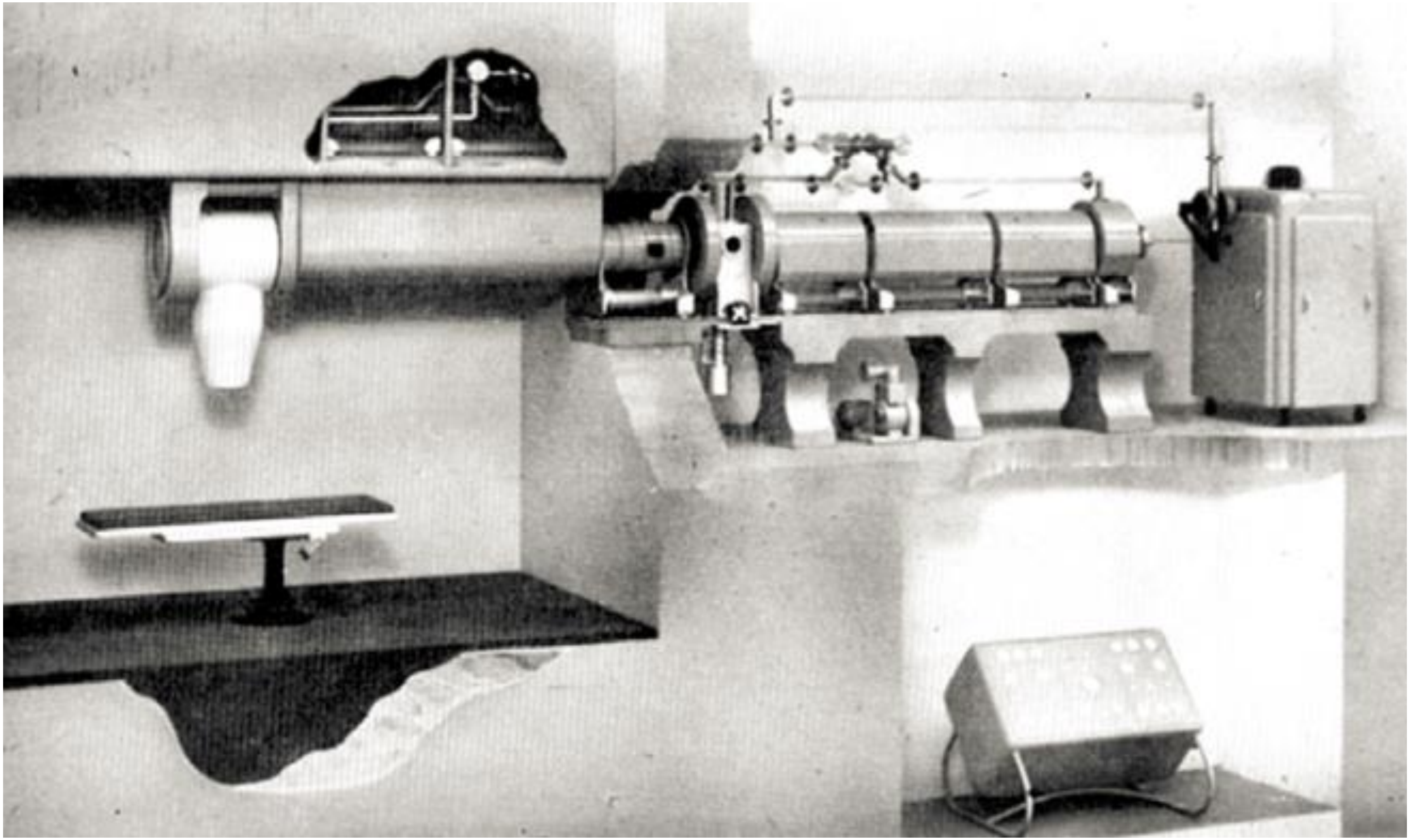
- G. Ising 1924/5 → R. Widerøe 1928



Linac development and use I.

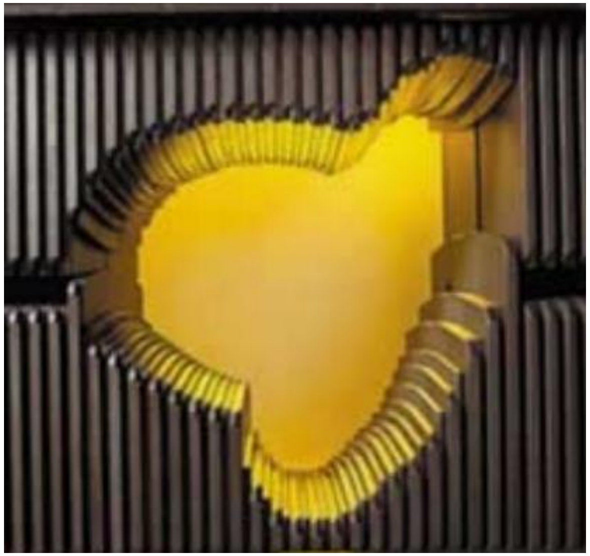
- 1937 klystron (W. W. Hasen , S. & R. Varian)
  - RF to ~100 MHz to > 10 Ghz
- Alvarez – metallic tubing of Widerøe (1946-7)
  - reduced loss at high frequency
- 1947 1st linac (electron, 4.5 MeV @ 3 Ghz)
- 1953 1st patient treated with LINAC

Hammershmit hospital 8 MeV@3m

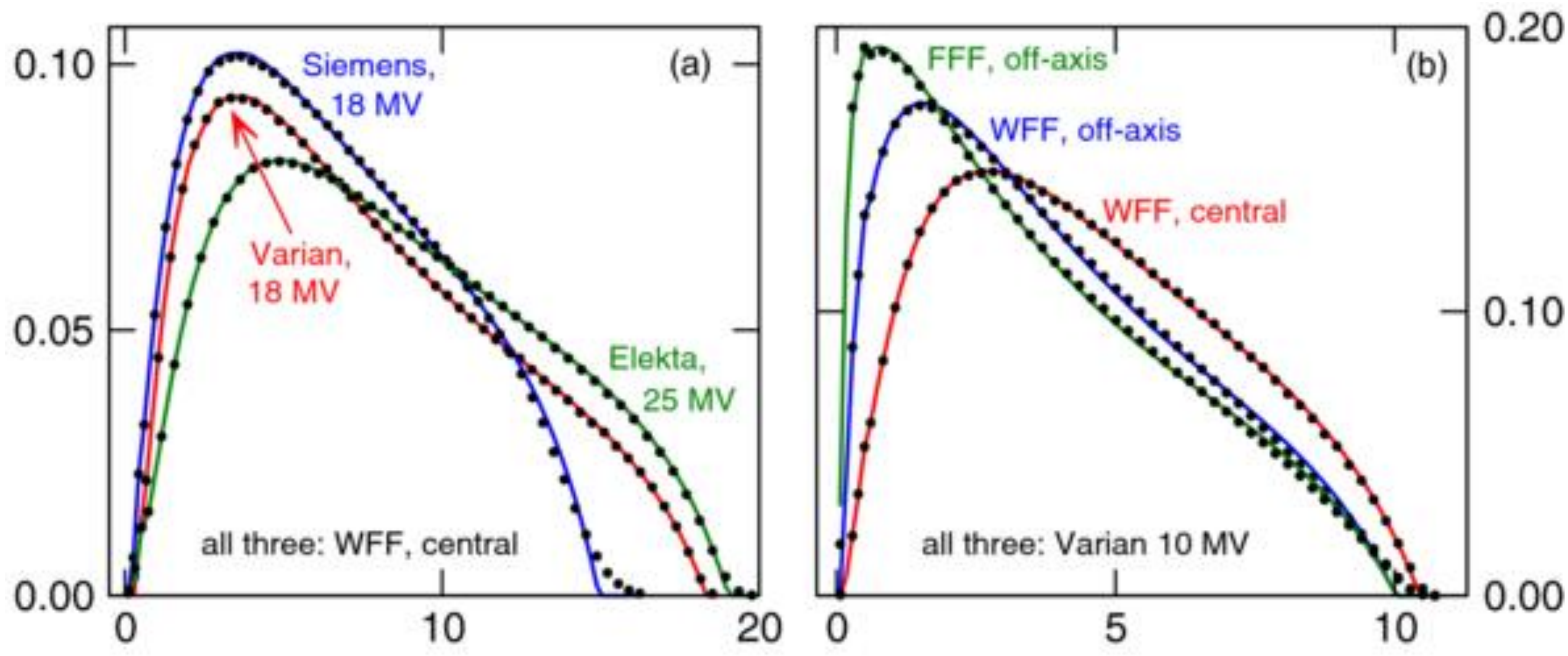


Linac development and use

- ~1952 Microwave electron linac
- 1960s isocentric rotation
- 1968 standing wave
- 1970* Multi-leaf collimator
- 1972 dual particle irradiation
- Dual beam energy
  - e.g. 6 & 22 MeV
- 1982 IMRT
  - Intensity modulated radio terapy

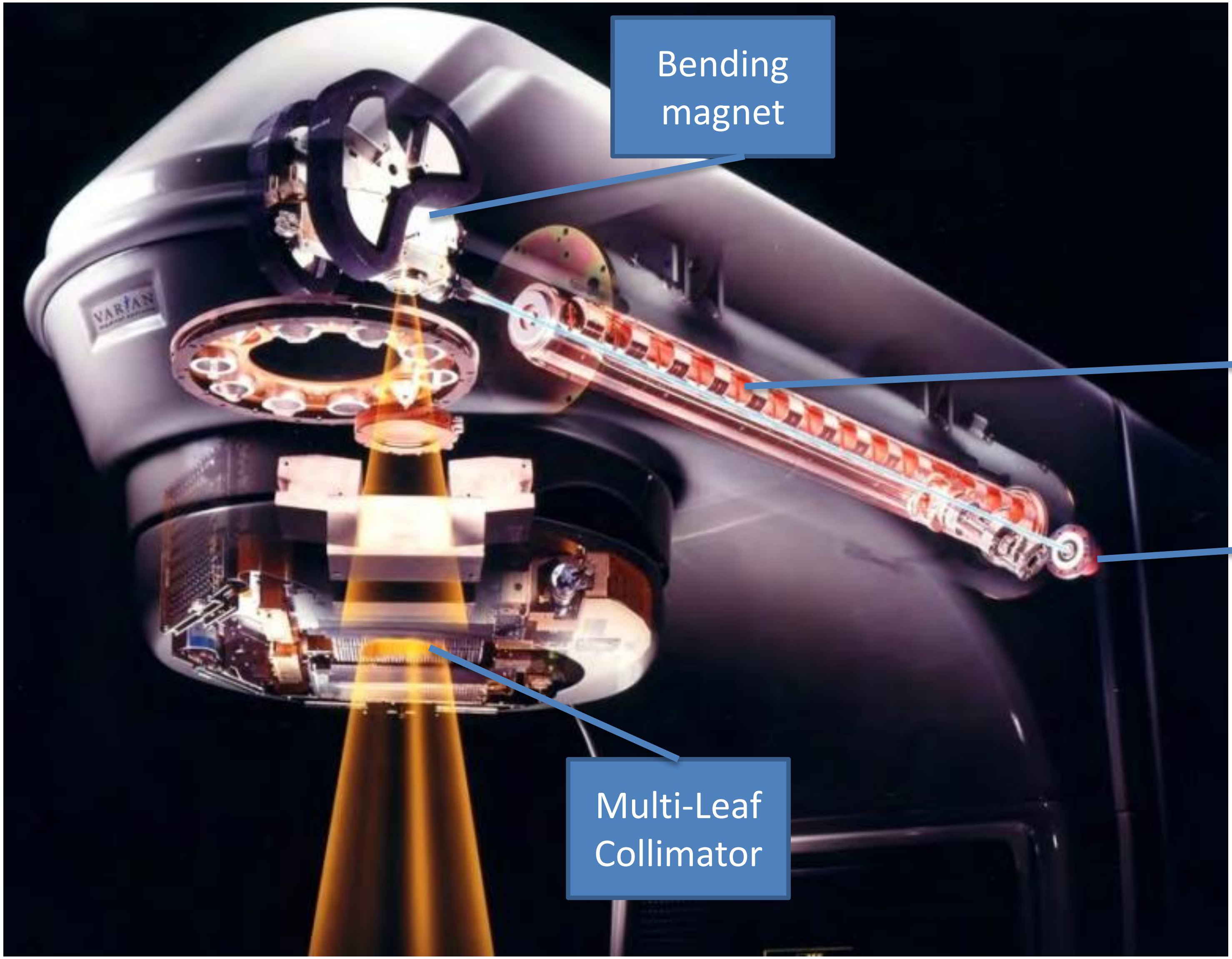


Spectra shape

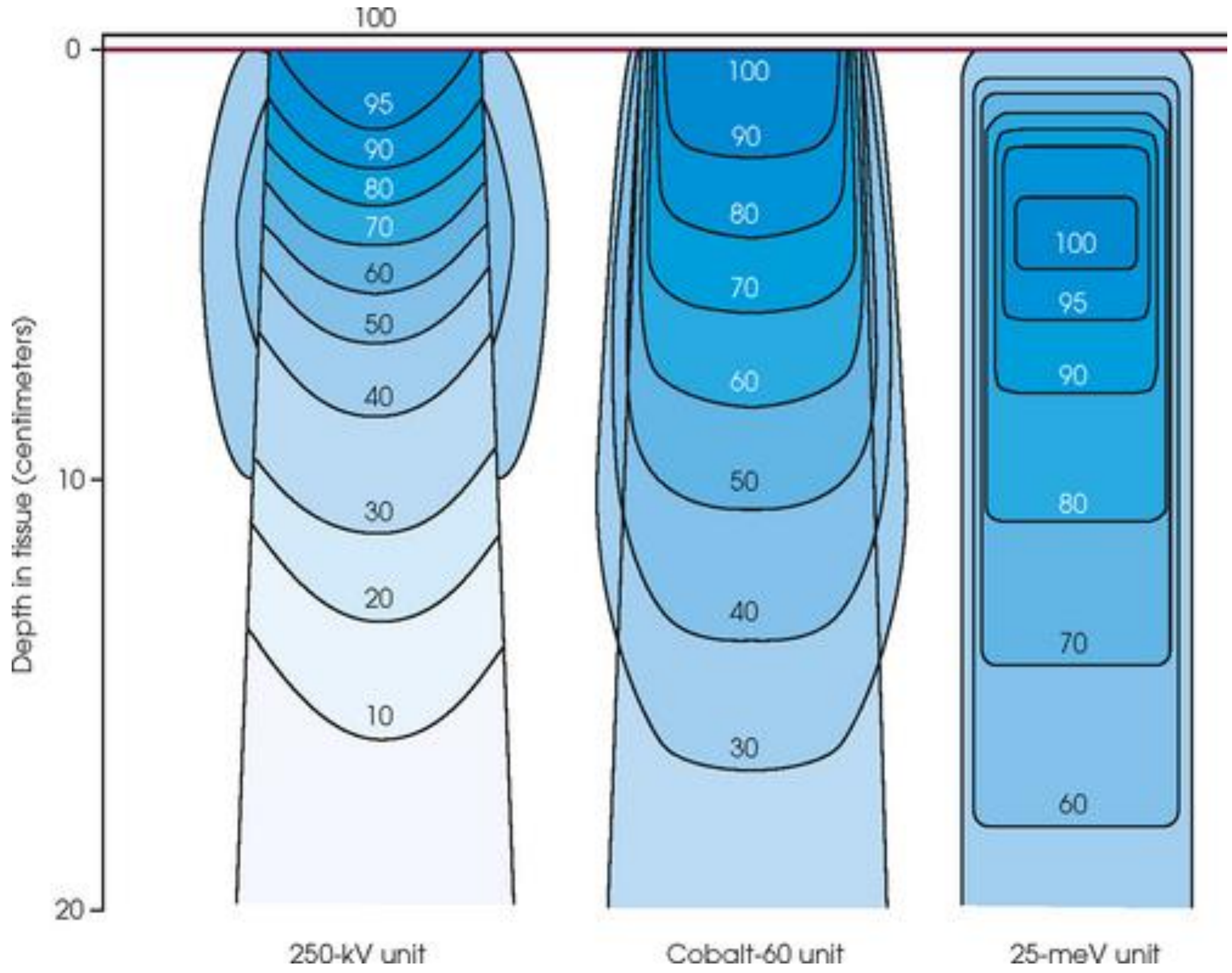


photon energy (MeV)

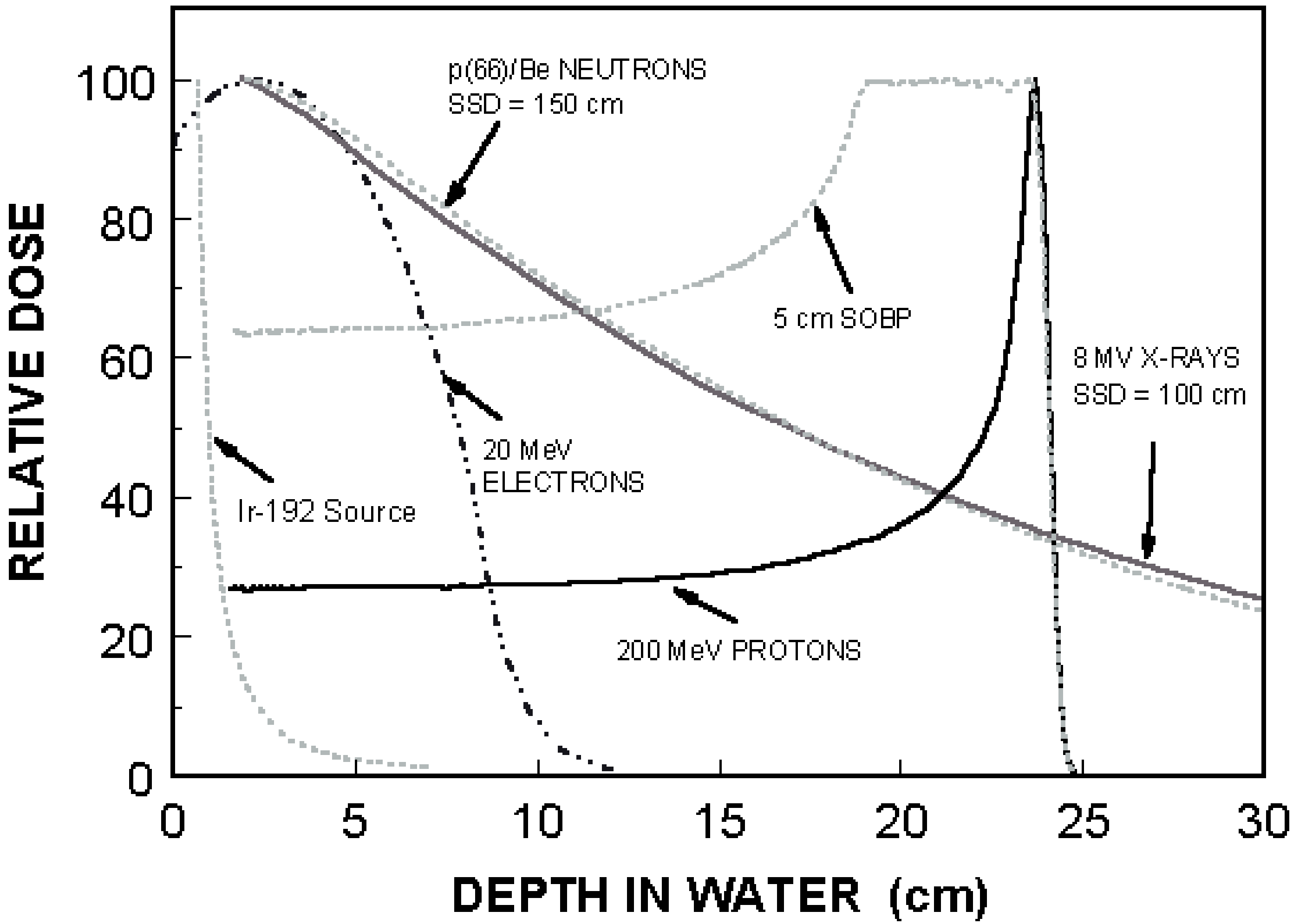
Modern linear accelerator



Isodose depth curves

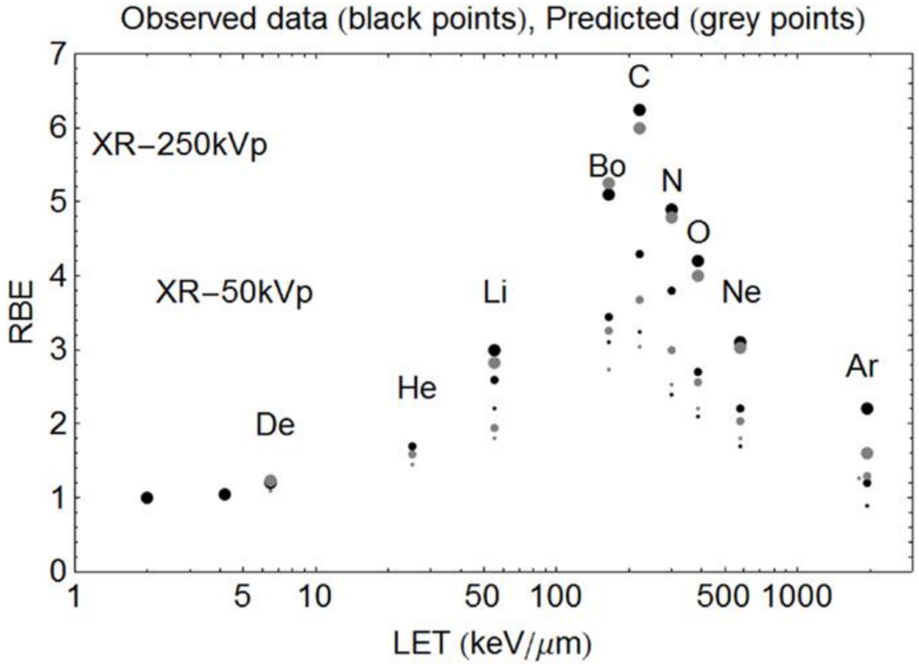


Depth dose function

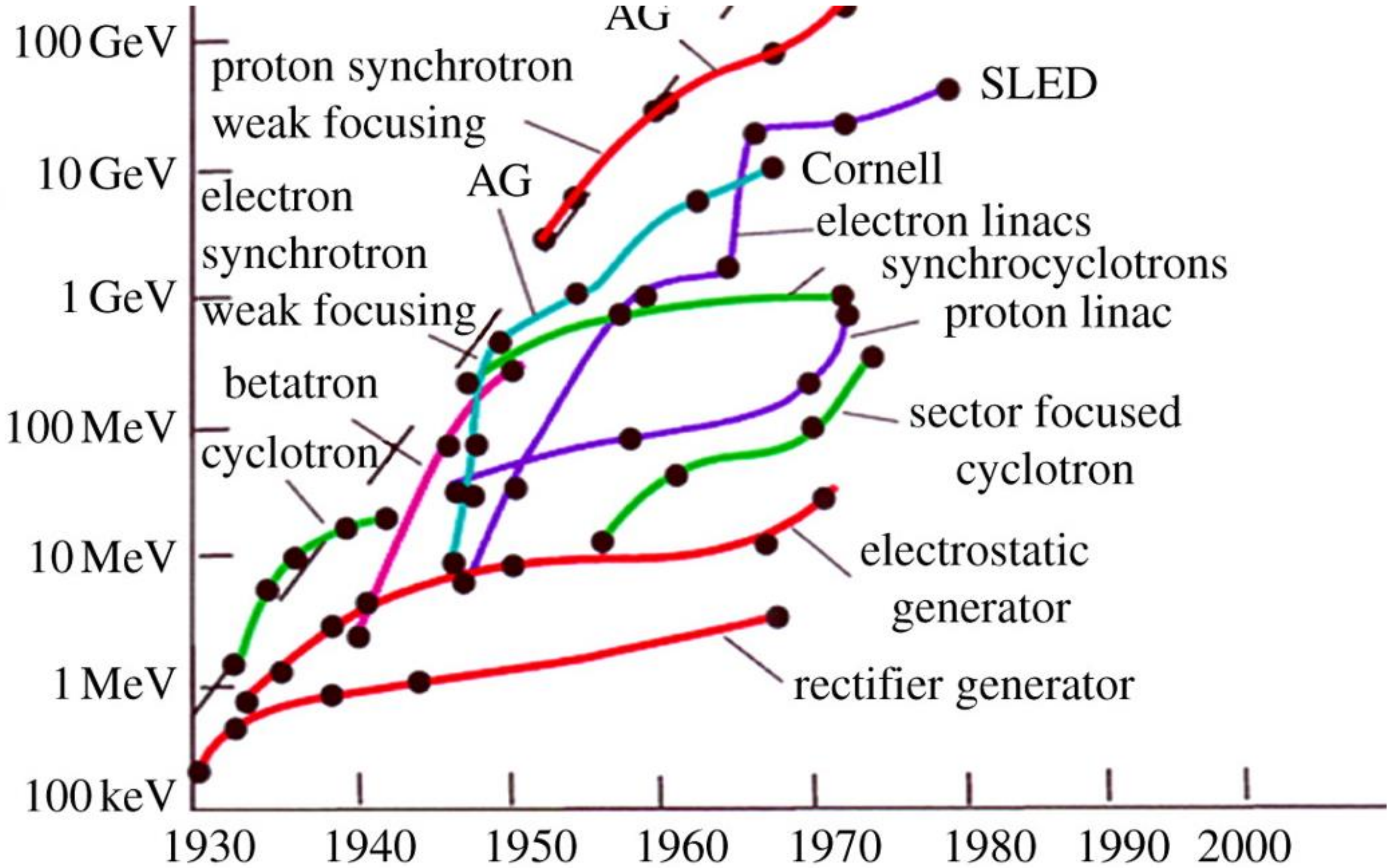


Hadron therapy with carbon ions

- Synchrotrons
- E.g. GUHIM, CNAO, HIMAC, HIT, ….
  - up to 400 MeV/u
- Better beam conformity
- Higher RBE then protons
- Sparing heathy tissue



Development of accelerators



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