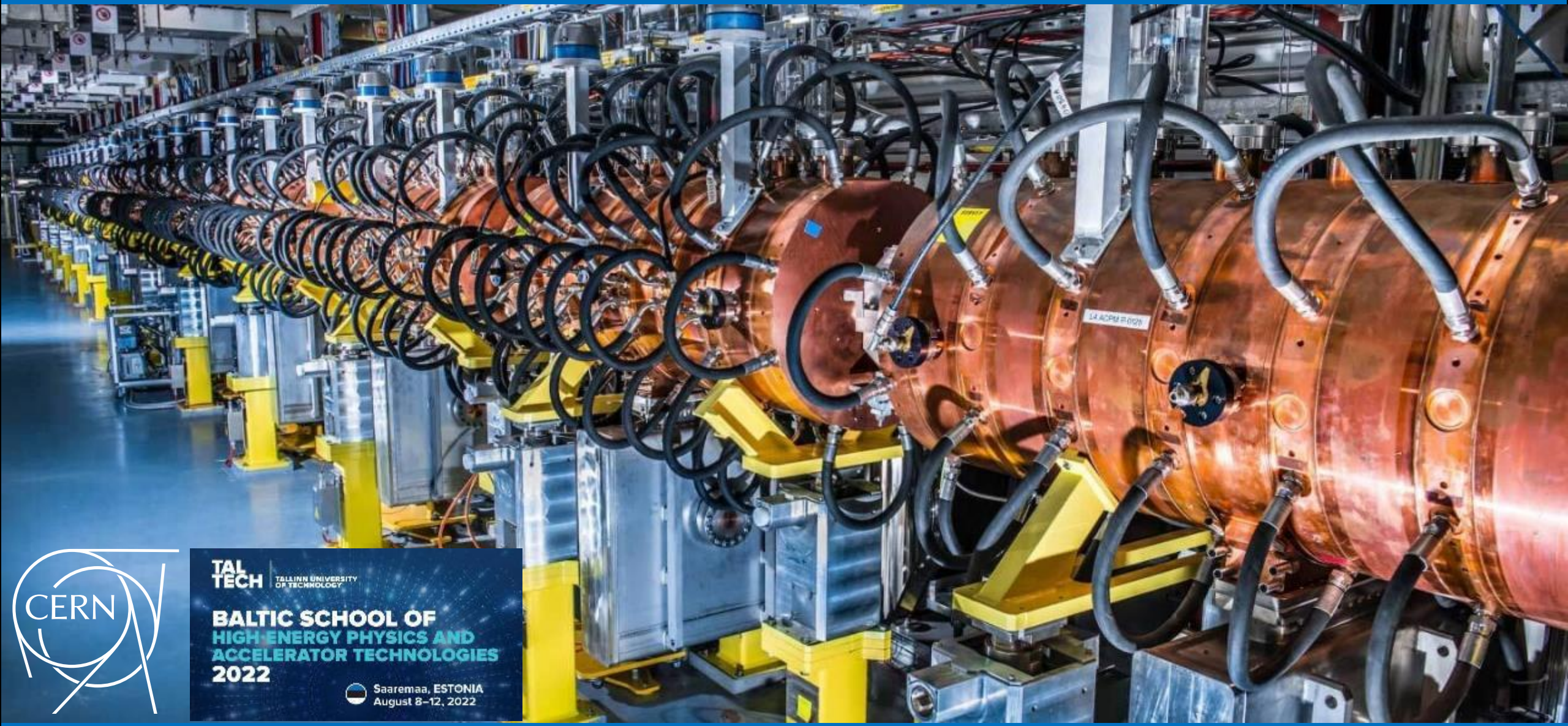
Maurizio Vretenar CERN



Introduction to Particle Accelerators and their Applications – Part 1

Outline of the two lectures

Lecture 1:

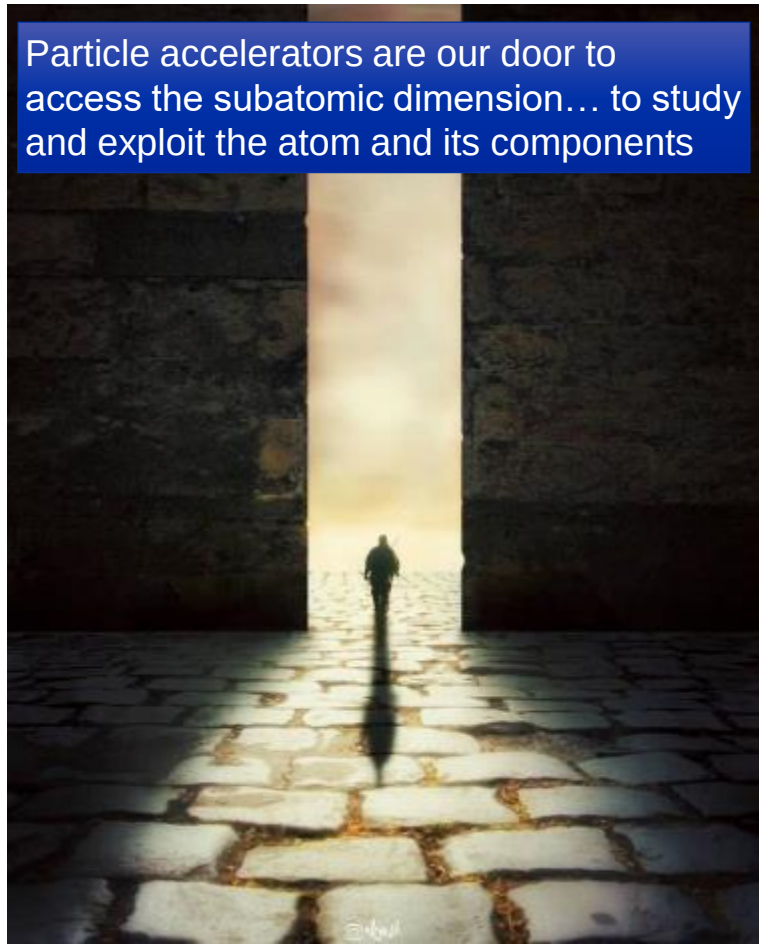
- The accelerator as an instrument to store and deliver energy
- Quick review of particle accelerator types
- Medical applications of accelerators
- The Advanced Particle Therapy Centre for the Baltic States

Lecture 2:

- Innovations in particle accelerators
- Challenges of particle accelerators in the XXIst century
- Accelerators for society
- Miniature accelerators

Particle Accelerators can concentrate energy

A particle accelerator is an instrument capable of concentrating large amounts of energy at subatomic scale, to be used for applications in science, medicine, and industry

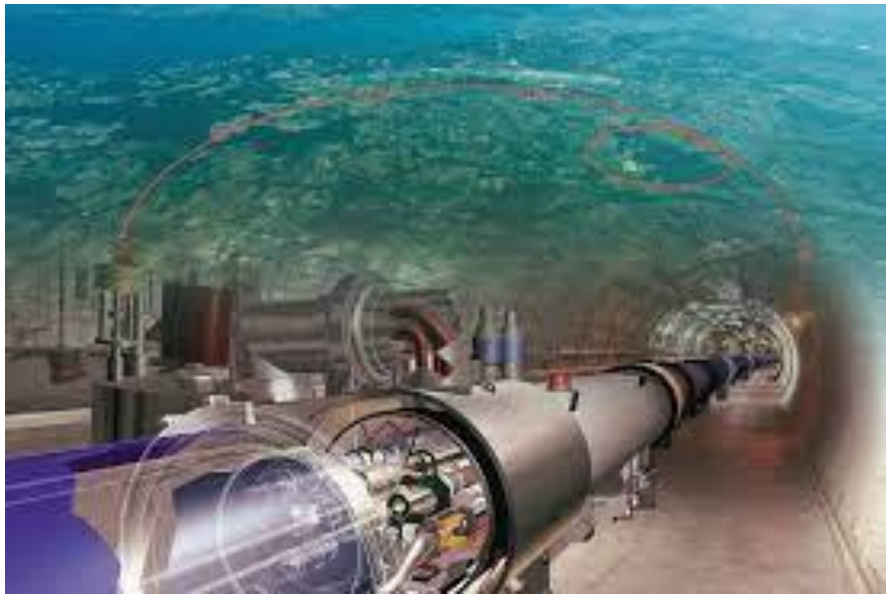


When we extract particles from an atom and we accelerate them, we concentrate **enormous amounts of energy in tiny volumes**

Where will this energy go? An accelerated subatomic particle sent towards an atom will:

1. Deliver some **energy to the electrons**.
2. Deliver some **energy to the nucleus** (if the particle has sufficient energy to penetrate the atom.

How large is the energy of a particle beam?



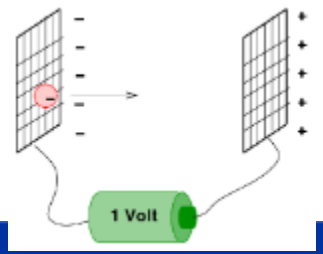
Comparing the energy of a single proton out of the CERN Large Hadron Collider, the largest particle accelerator ever built.

The energy is small, but the energy density is enormous!

	Proton out of LHC	150g Yoghurt	TGV train
	• 7 TeV	 120 cal	
Energy	$1.1\ 10^{-6}$ J	$5\ 10^{2}$ J	$3.6\ 10^{8}$ J
Energy density	$5.3\ 10^{38}$ J/m^3	$3.3\ 10^{6}$ J/m^3	$1.5\ 10^{5}$ J/m^3
Type of energy	Kinetic Subatomic scale	Chemical Macroscopic scale	Kinetic Macroscopic scale

TGV train: 400 tons, 200 m, 150 km/h

Accelerator energies in eV (energy acquired by an electron in a potential of 1V)
1 eV = 1.6 x 10^{-19} Joules



*1 Joule is really tiny: =1 W*s, cost ≈ 10^{-7} €*

Energy in an LHC bunch (1.15 10^{11} protons) is 1.3 10^{5} J, in the full beam (2808 bunches) 3.6 10^{8} J
Energy density of an LHC bunch at interaction point (30 cm, 16x16 μm^2) ≈ ***0.5 10^{12} J/m^3***

Where does the energy go?

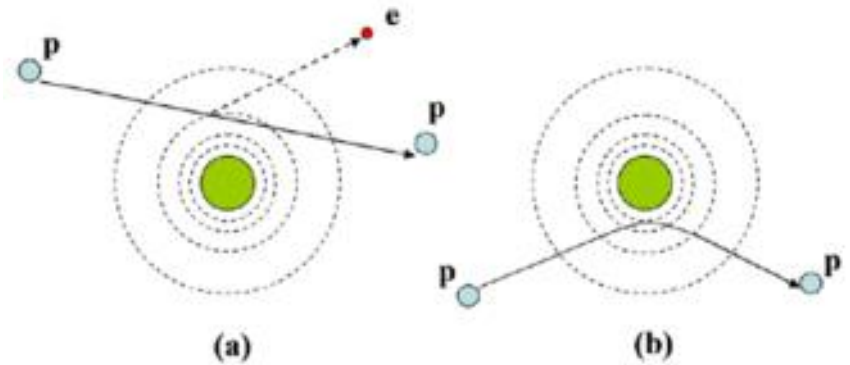
The accelerated particle can:

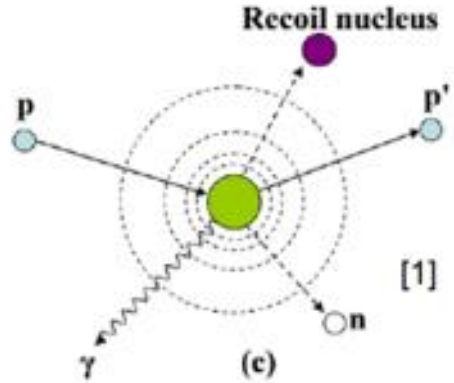
a) kick an electron out of the atom (ionization) or to a higher orbital (excitation) – in the latter case, the electron can come back generating an **X-ray** (photon).

b) be deflected by the nucleus and give energy to the atom - increase of temperature, **breaking of molecular bonds**.

c) be absorbed by the nucleus bringing it to an excited state that can **generate radiation** or secondary particles.

Scattering of an accelerated beam of particles





We can of course accelerate only charged particles:
Protons, Electrons, Ions (=ionised atoms)

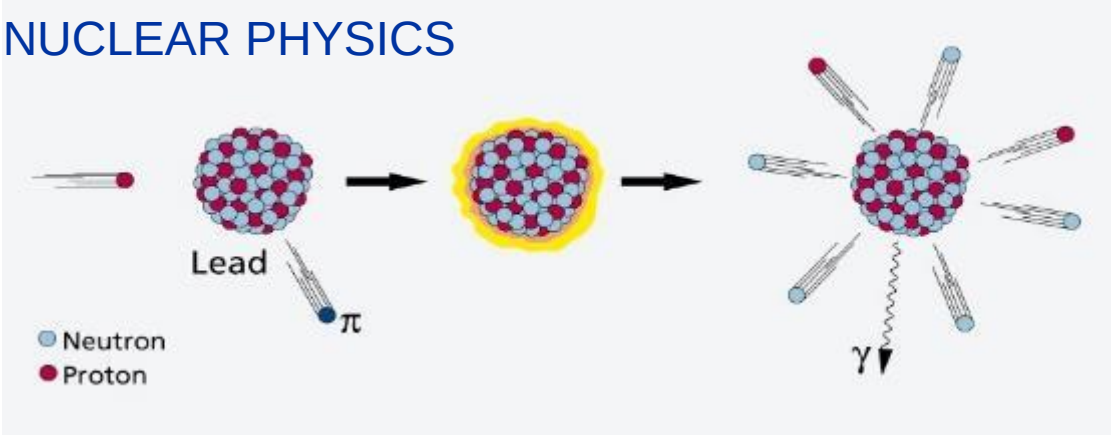
	Charge	Mass
Electrons	-1 e	1 m_e
Protons	+1 e	1 m_p
Ions	+1 / +82 e	1 – 238 m_p

Unit charge 1 e = 1.6×10^{-19} Coulombs
Electron mass 1 m_e = 9.1×10^{-31} kg = 511 keV/c^2
Proton mass 1 m_p = 1.67×10^{-27} kg = 938 MeV/c^2

Accelerators can modify the nuclei and create new particles

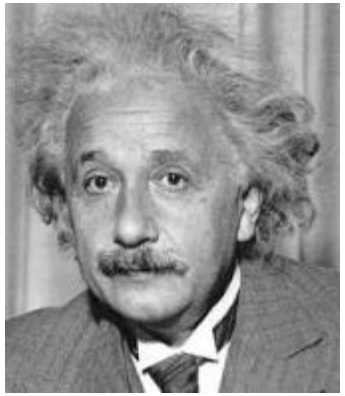
If the energy is sufficiently high, the particles in the beam transfer energy to the nucleus and its components (and are then scattered, reflected or absorbed).

NUCLEAR PHYSICS



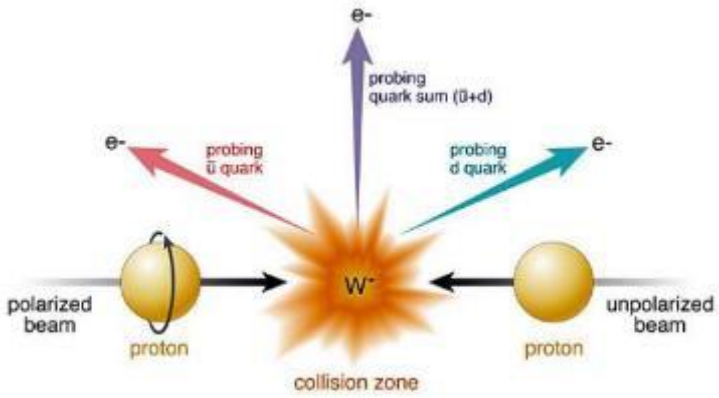
Particles in the beam can break and modify the nucleus (and then generate new elements and transform the matter!)

The dream of the ancient alchemists coming true!

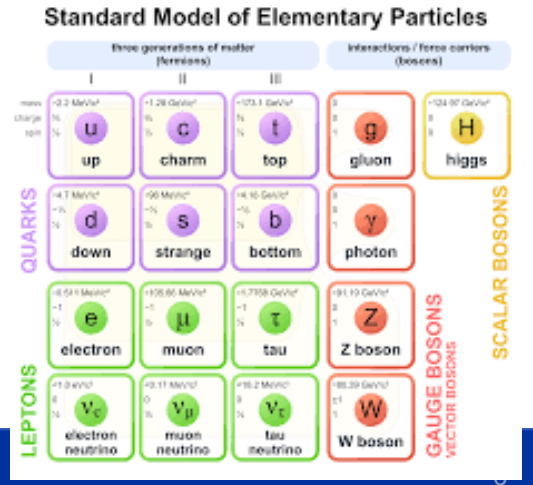


$E = m c^2$

PARTICLE PHYSICS

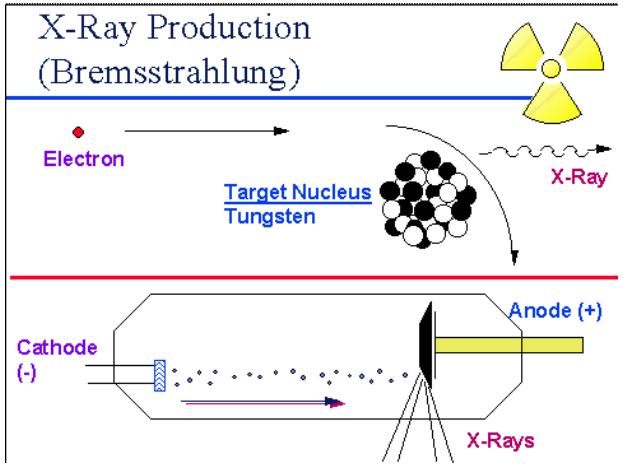


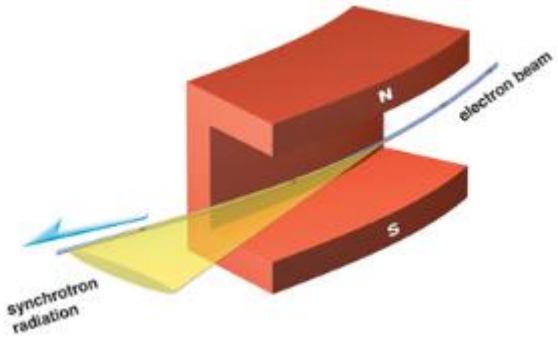
In the collisions can be generated new particles.



Accelerators can produce intense secondary beams

Accelerated electrons produce X-ray beams by interaction with a metal target (bremsstrahlung) or by synchrotron radiation in accelerator magnets)





Accelerated protons produce neutron beams by spallation reactions in a heavy metal target

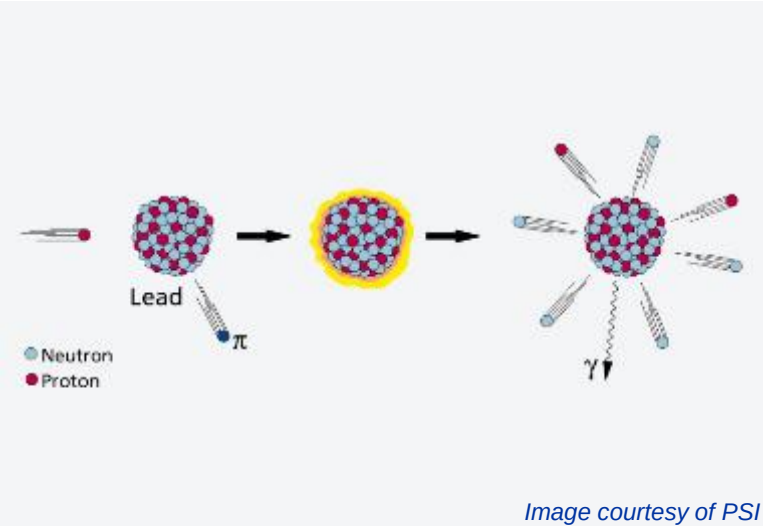
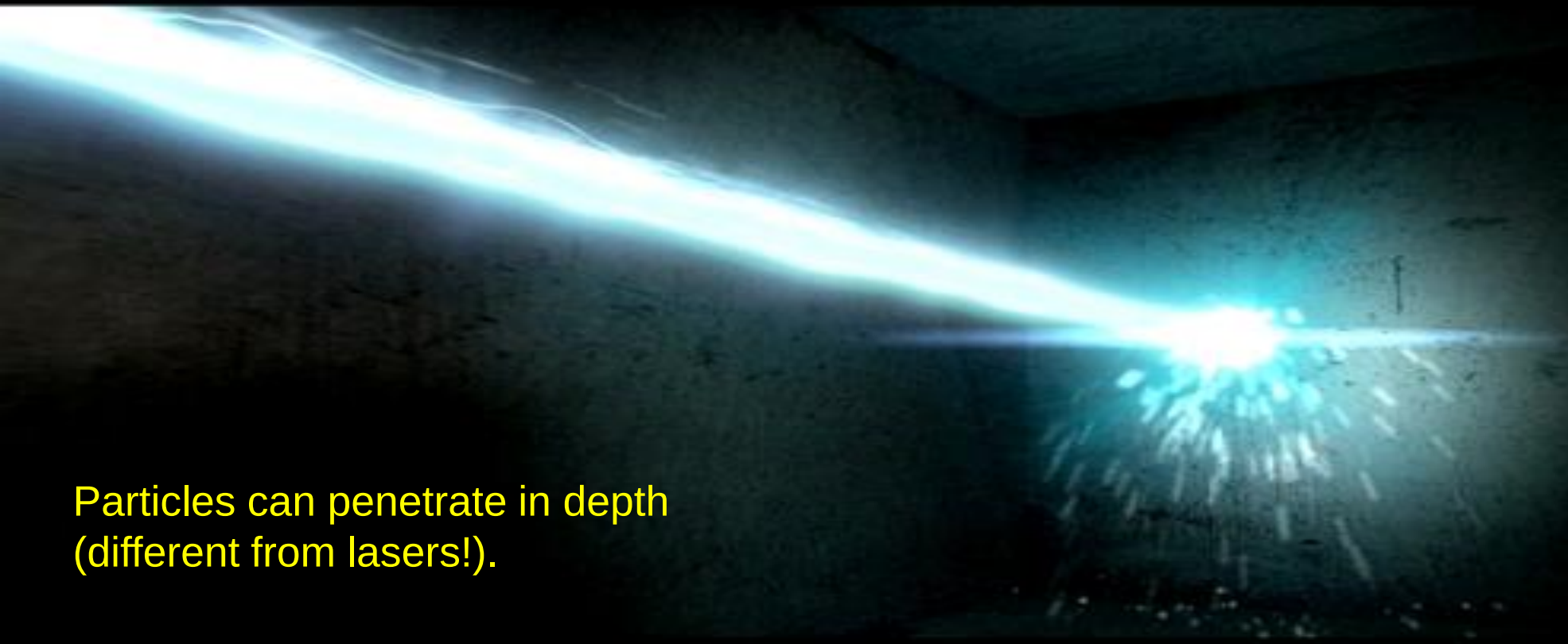


Image courtesy of PSI

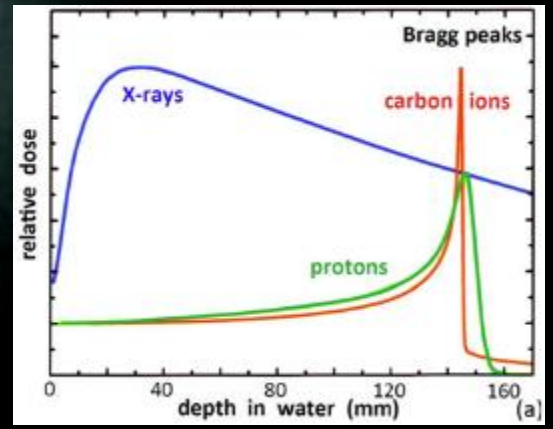
- X-rays generated by accelerators are commonly used in **medicine**
- Both X-rays and neutrons generated from accelerators are used for **advanced imaging** in many fields: life sciences, condensed matter, energy, material science, cultural heritage, life sciences, pharmaceuticals,…
- Additional applications are appearing for other types of secondary beams.

Accelerators can precisely deliver energy

A «beam» of accelerated particles is like a small “knife” penetrating into the matter



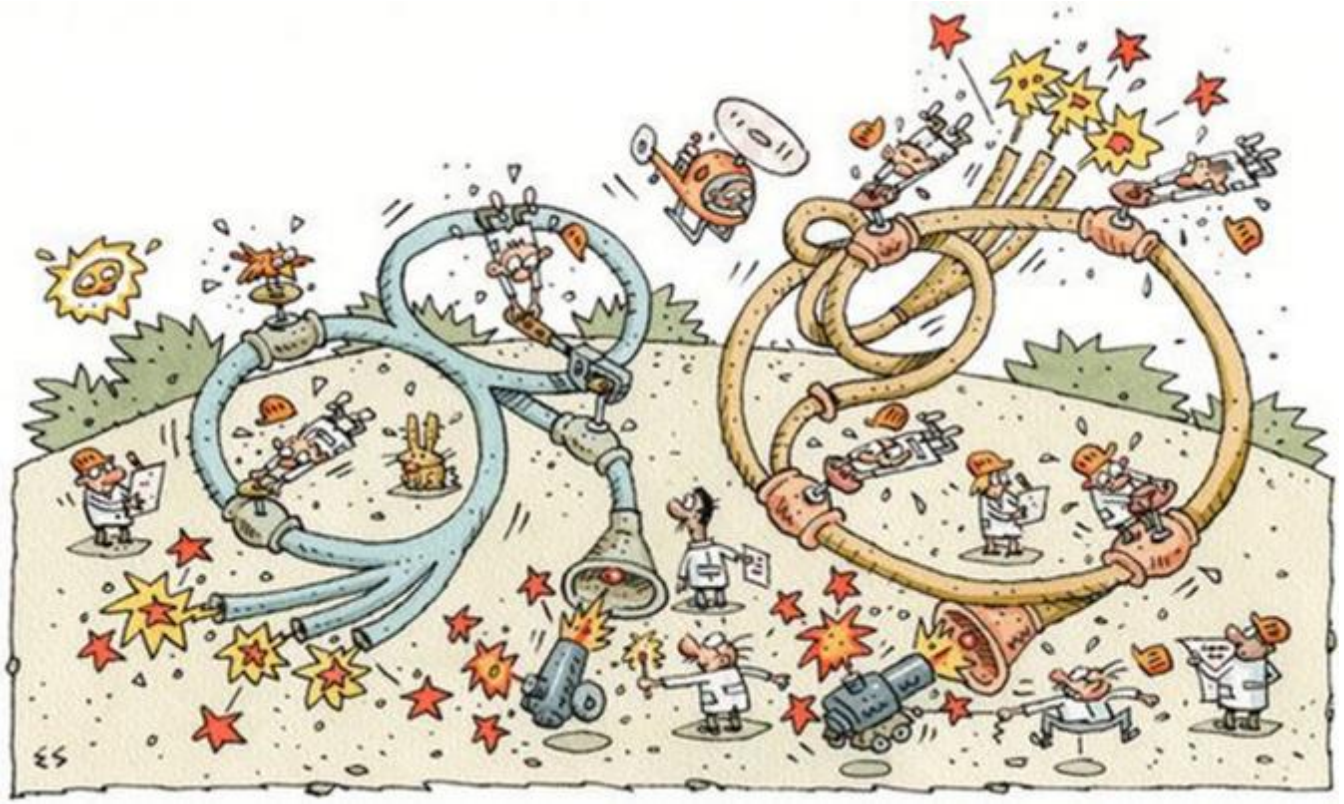
A particle beam can deliver energy to a very precisely defined area, interacting with the electrons and with the nucleus.



Particles can penetrate in depth
(different from lasers!).

Particle beams are used in medical and industrial applications,
e.g. to cure cancer, delivering their energy at a well-defined depth inside the body (Bragg peak)

A quick review of particle accelerator types

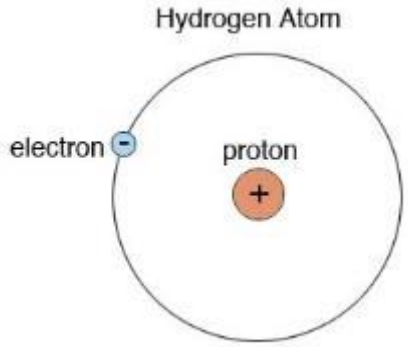


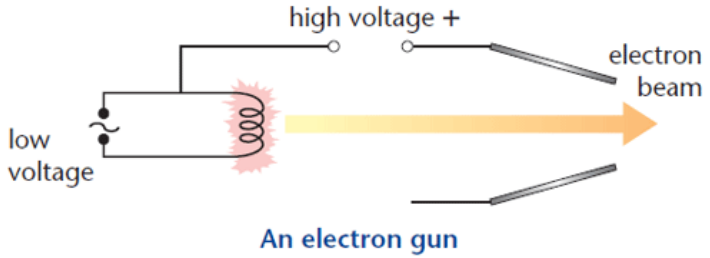
How do we get the particles?

Protons are obtained heating a hydrogen gas (plasma) and extracting the protons with a high voltage

Electrons are obtained by heating of a filament (exactly like an electric bulb)

Ions are obtained in a similar way as protons



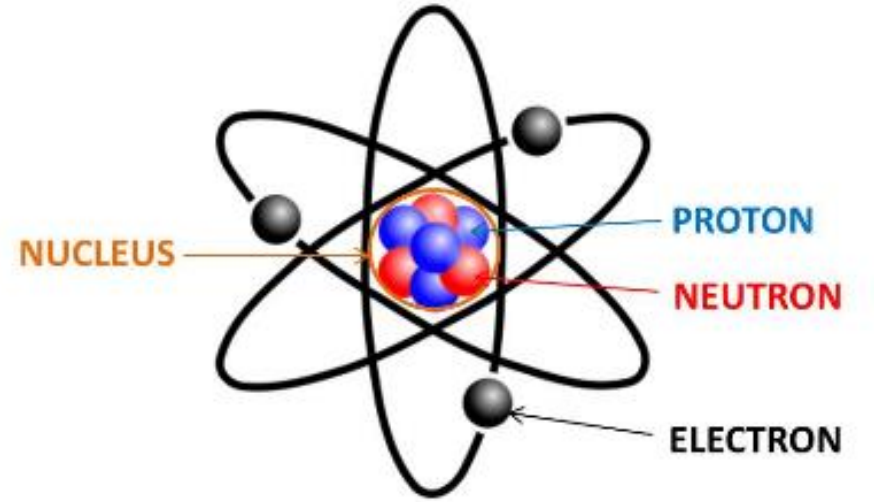


Scheme of the ion source delivering protons to CERN accelerators

The ion source at the CNAO hadron therapy facility

All protons going to the LHC come out of this single bottle of industrial hydrogen (5 kg) that contains 3'000'000'000'000'000'000 billions of protons! The LHC needs only 1'200'000 billions of protons per day.

Combined effect on particles: the Lorentz force



	Charge	Mass
Electrons	-1 e	1 m_e
Protons	+1 e	1 m_p
Ions	+1 / +82 e	1 – 238 m_p

Unit charge 1 e = 1.6×10^{-19} Coulombs
Electron mass 1 m_e = 9.1×10^{-31} kg = 511 keV/c^2
Proton mass 1 m_p = 1.67×10^{-27} kg = 938 MeV/c^2

We extract the particles from the atoms and then:

- give them energy using electric fields,
- guide them using magnetic fields

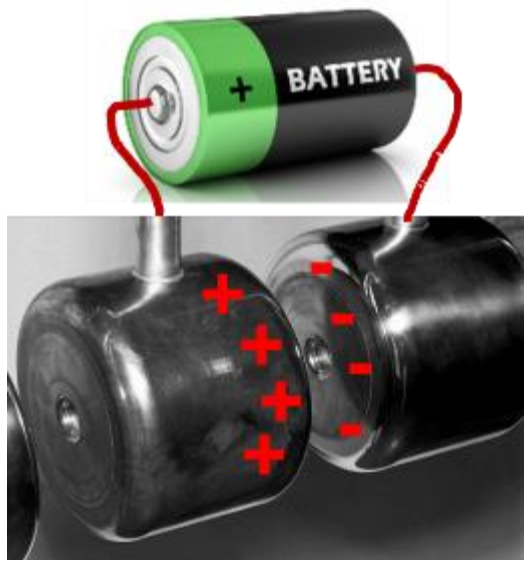
Newton-Lorentz force:

$$\vec{F} = \frac{d\vec{p}}{dt} = e\left(\vec{E} + \vec{v}\,' \ \vec{B}\right)$$

2nd term always perpendicular to motion => no acceleration

Can be accelerated only particles that have an electric charge: electrons, protons, ions (= charged nuclei)

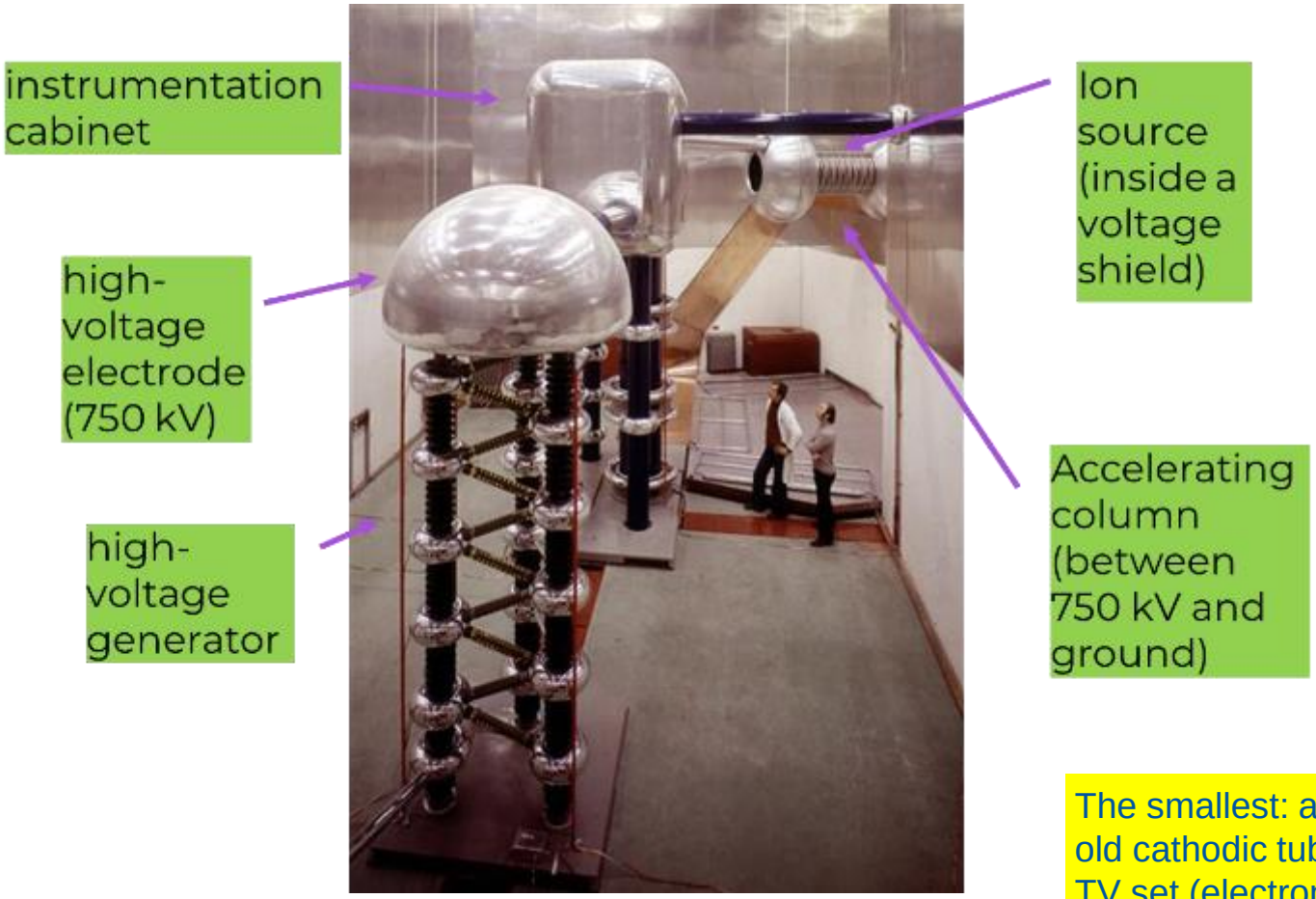
Low energy: electrostatic accelerators



Electrostatic: use a DC voltage between 2 tubes

(A simple capacitor !)

Limitations: few 100 kV are possible but difficult, few MeV possible but require huge installations



The largest: the old (1975-92) CERN 750 keV proton pre-accelerator

The smallest: an old cathodic tube TV set (electrons, max. 30 keV)

Acceleration using oscillating electric fields

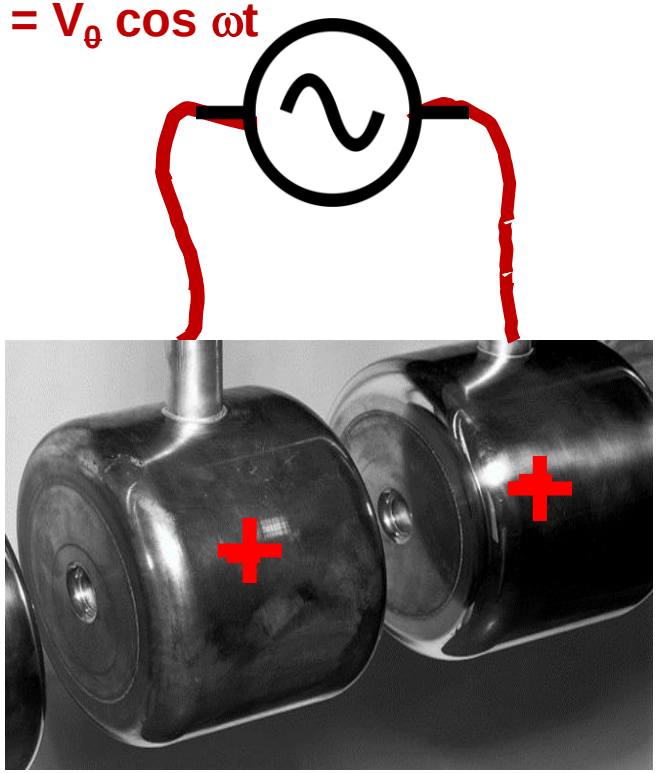
In 1928 a PhD Thesis introduced the basic concept of modern particle accelerators:

Periodic acceleration provided by electric field at Radio-Frequency (RF).

Rolf Wideröe, inventor of Radio-Frequency acceleration

Innovation by cross-fertilization: use the radio transmission technology that was rapidly developing in the 20's and connect a radio transmitter to a system of tubes to obtain incremental acceleration.

$V = V_0 \cos \omega t$



Ion Source
Ionised potassium atoms

Drift tube
2 gaps, one on each side

Spectrometer
Transverse electric field

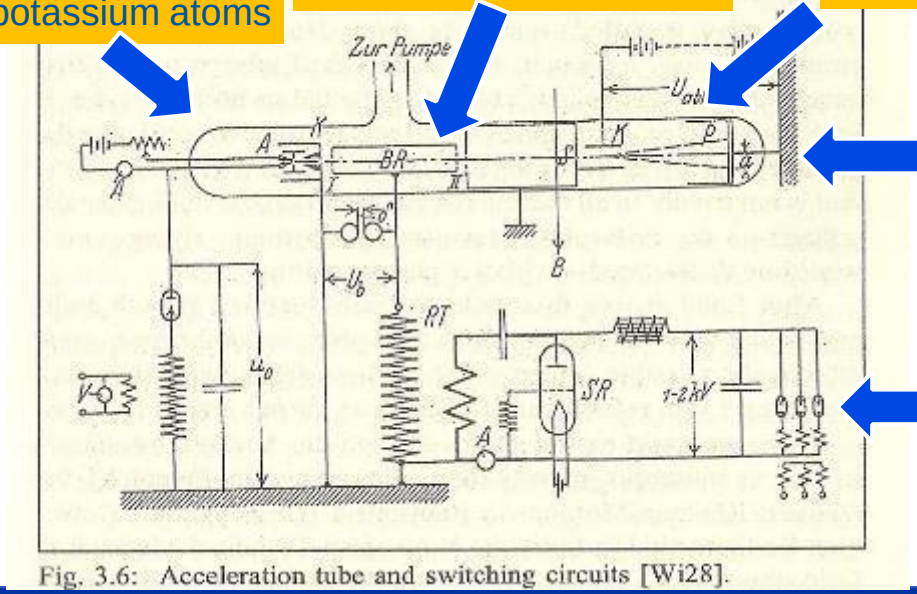
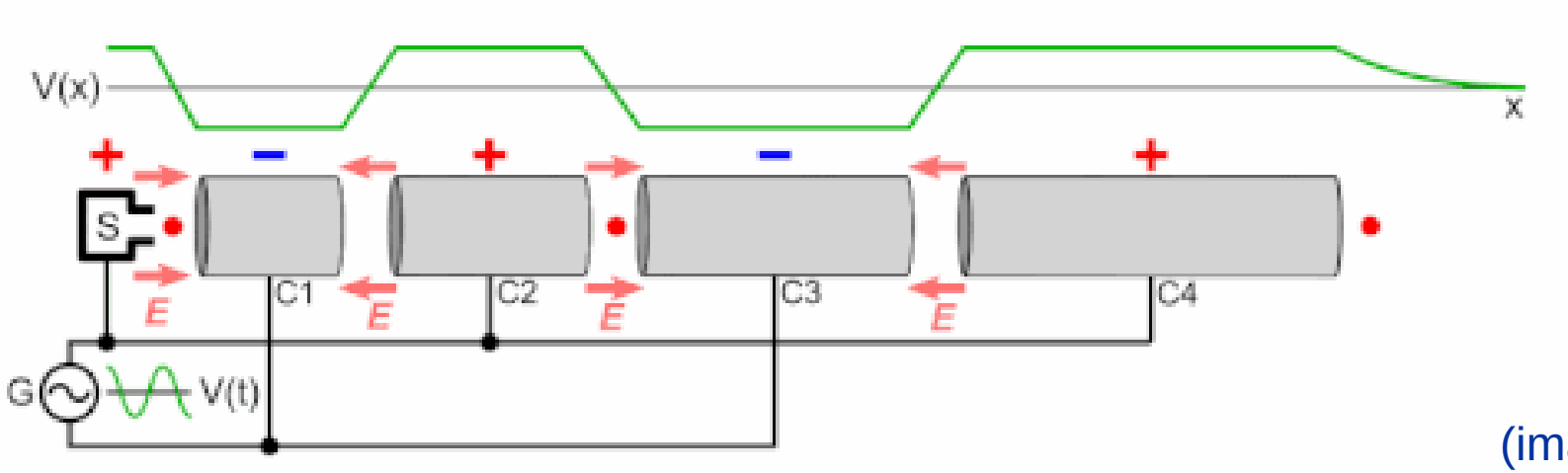


Fig. 3.6: Acceleration tube and switching circuits [Wi28].

System in vacuum
To avoid losing particles on air molecules

Radio generator
1 MHz, 25 kV

The linear particle accelerator (linac)

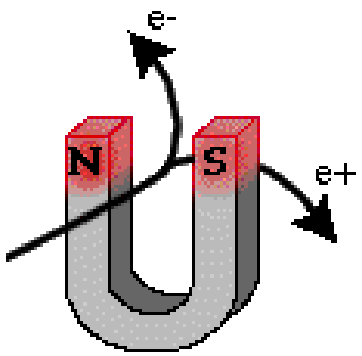


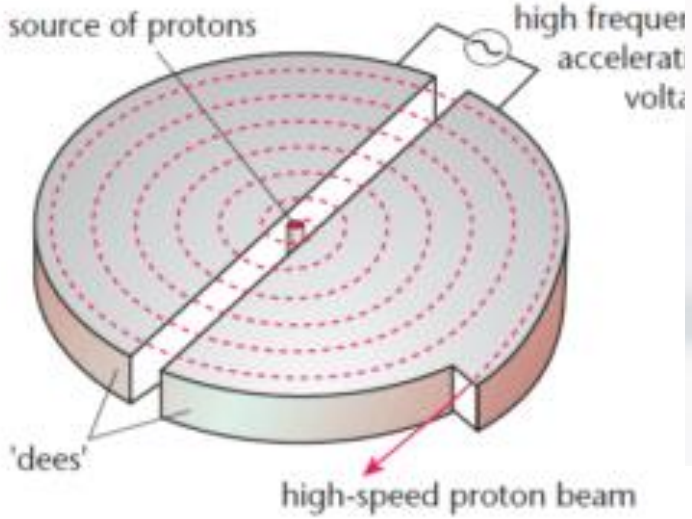
(image from Wikipedia)

Note that tubes become longer and longer as energy and velocity increase, to keep constant (equal to half RF period) the time to go from one accelerating gap to the next.

Linear accelerators for protons can reach 100's MeV energies but become expensive at high energy. Accelerating gradients of 2 – 5 MeV/m (protons).

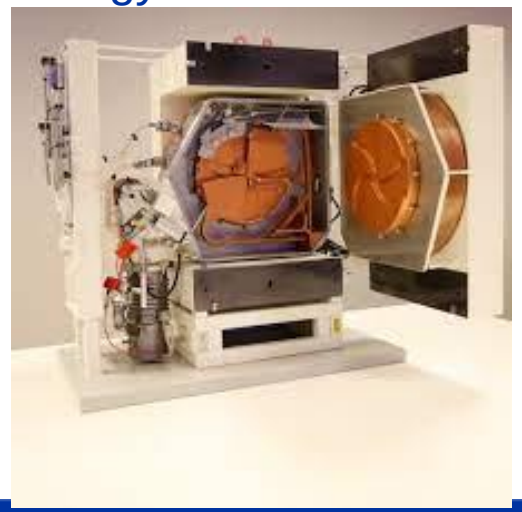
Bending particles: the cyclotron





The range of BEST cyclotrons, from 15 to 70 MeV output energy

- The device is between the poles of a large magnet
- Protons are produced by an ion source in the centre
- They are accelerated in the gap between 2 electrodes fed with radio-frequency
- The protons go in larger and larger spirals, and their velocity increases proportionally to the spiral radius, keeping their revolution frequency constant.

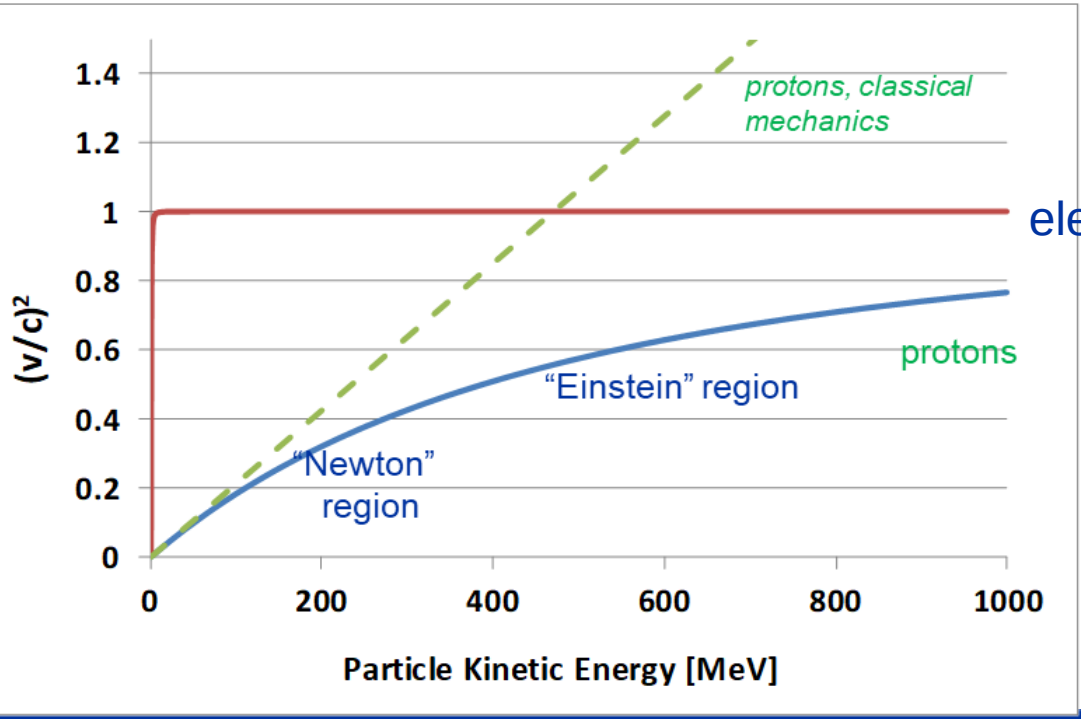


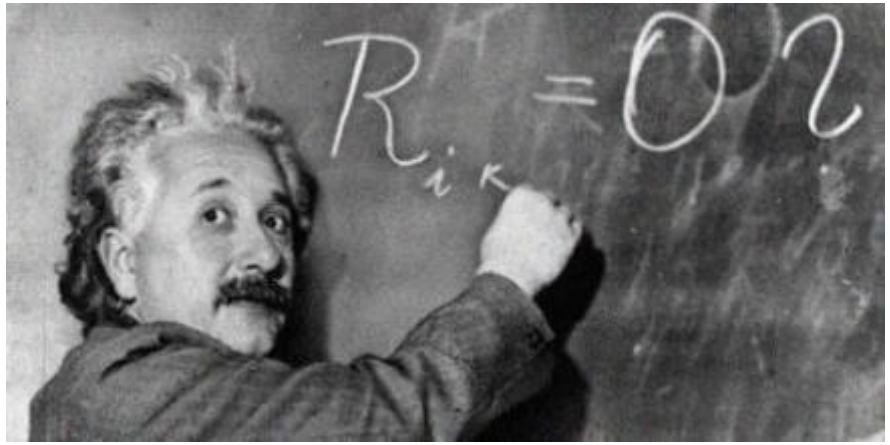
A compact cyclotron for production of PET radioisotopes (GE Healthcare)

Relativity

When we accelerate, we give energy to the particles that become faster and faster.
But a hard limitation is given by special relativity: we cannot exceed the speed of light.
Before reaching the speed of light, the energy goes to increasing the mass and not the velocity!

$\beta^2=(v/c)^2$ as function of kinetic energy T for protons





Relation kinetic energy / velocity:

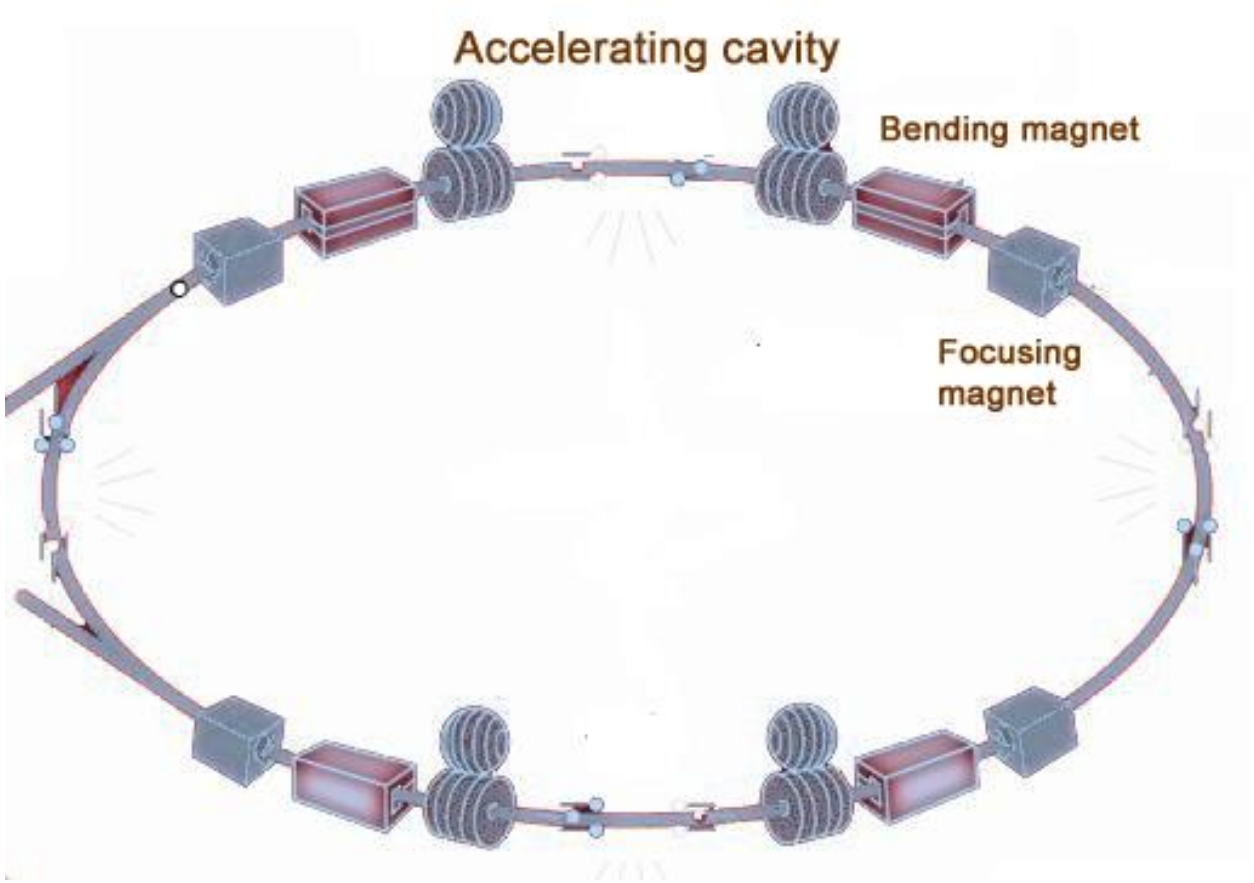
Classic (Newton) relation

$$T = m_0 \frac{v^2}{2}, \quad \frac{v^2}{c^2} = \frac{2T}{m_0 c^2}$$

Relativistic (Einstein) relation

$$\frac{v^2}{c^2} = 1 - \frac{1}{\sqrt{1 + T/m_0 c^2}}$$

Higher energies: the synchrotron



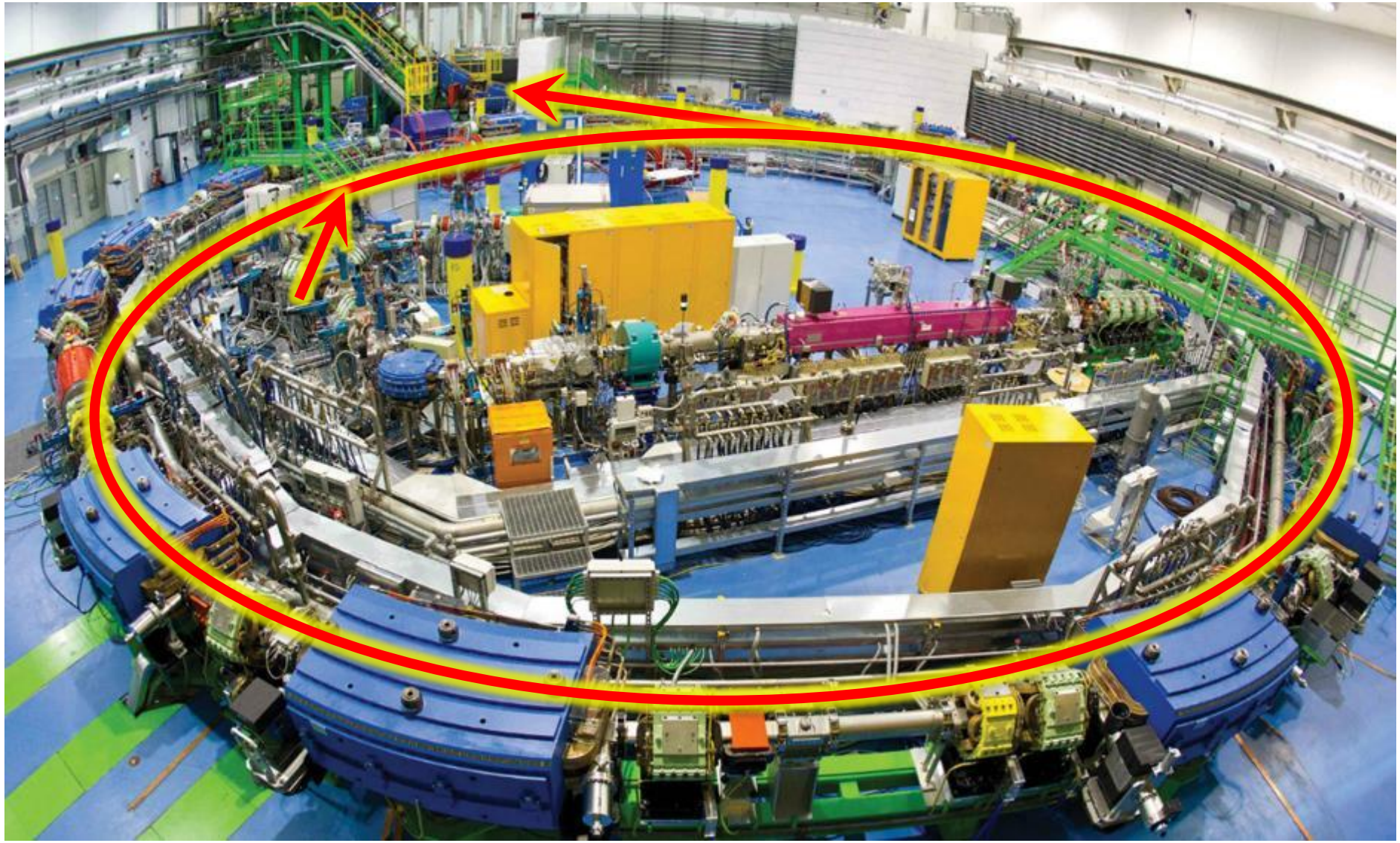
(Proton) linacs and cyclotrons operate in the energy range where the velocity of particles increases with energy.

When particles become relativistic (increasing the energy the velocity is nearly constant, very close to the speed of light) we need to use a **synchrotron**.

Acceleration is provided by some **gaps and tubes** placed in one or more positions on the ring. The revolution period is constant, and the bunches of particles will always find an accelerating field between the tubes.

Magnets cover (almost) the entire circumference, to keep the particle on a closed orbit.

The CNAO synchrotron for carbon ion therapy of cancer



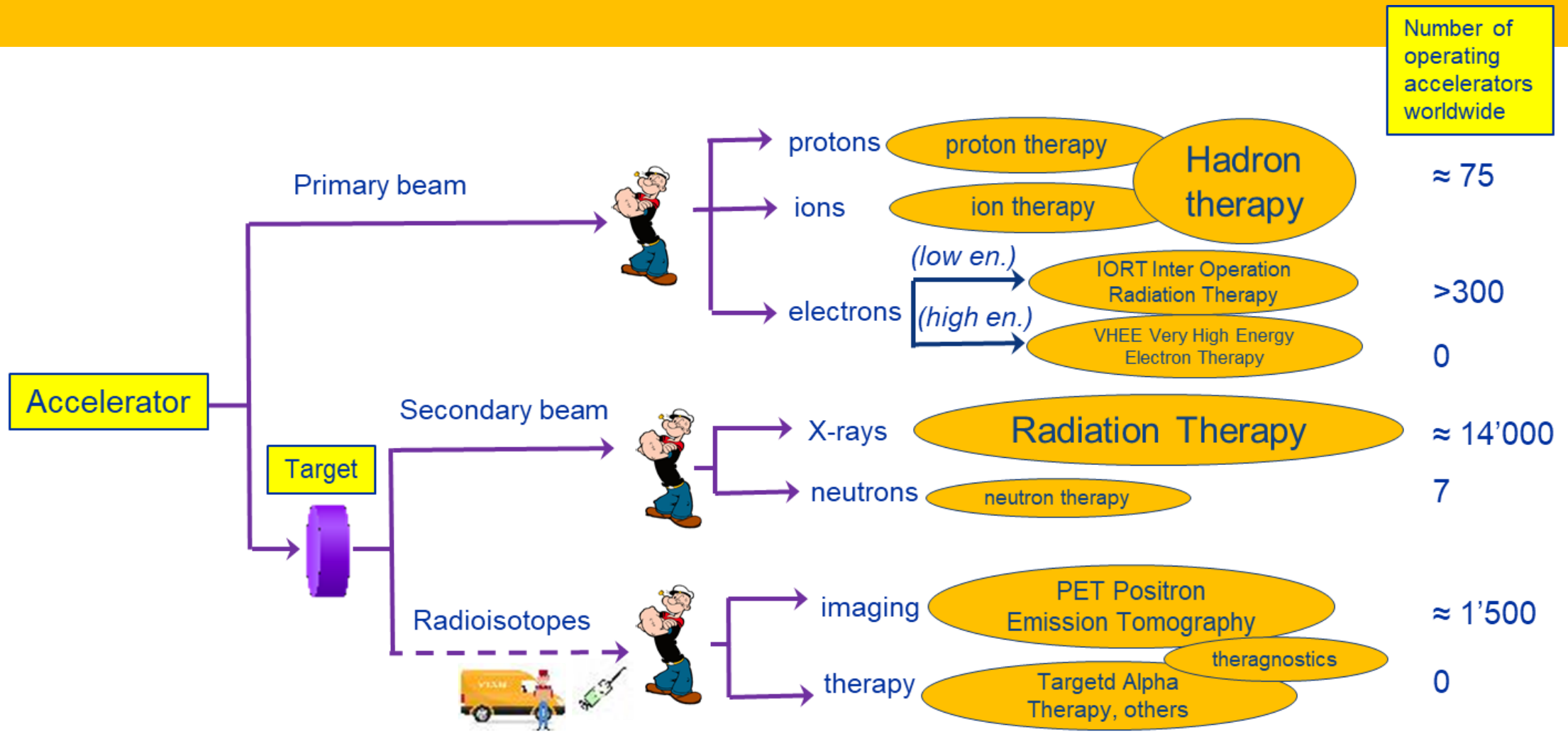
Medical applications of accelerators

Multiple challenges for accelerator science

There are more than 35’000 particle accelerators in operation around the world:

Research		**6%**
	Particle Physics	0,5%
	Nuclear Physics, solid state, materials	0,5%
	Biology	5%
Medical Applications		**35%**
	Diagnostics/treatment with X-ray or electrons	33%
	Radio-isotope production	2%
	Proton or ion treatment	0,1%
Industrial Applications		**60%**
	Ion implantation	34%
	Cutting and welding with electron beams	16%
	Polymerization	7%
	Neutron testing	3.5%
	Non destructive testing	2,3%

Accelerators for medicine



Total: ≈ 16'000 particle accelerators worldwide operating for medicine

The healthcare potential of accelerators

- All these systems share the vision of a **bloodless surgery and imaging**: penetrate into the human body to treat diseases and to observe internal organs without using surgical tools.
- Particle beams (primary and secondary) precisely deliver large amounts of energy to small volumes, penetrate in depth (**different from lasers**) and interact with cells, molecules, and atoms (electrons and nuclei).
- Particles beams can activate the nuclei generating radiation that can destroy cancerous cells or can be detected from outside.

For a U.S. population of over 300 million people, there are some 16 million nuclear medicine procedures per year.

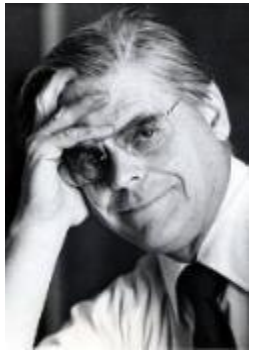
Nuclear medicine:
application of radioactive substances in the diagnosis and treatment of disease

Radiation therapy:
therapy using ionizing radiation, generally as part of cancer treatment to control or kill malignant cells

Medicine at the first accelerators

The idea of using accelerators for treating diseases is almost as old as accelerators

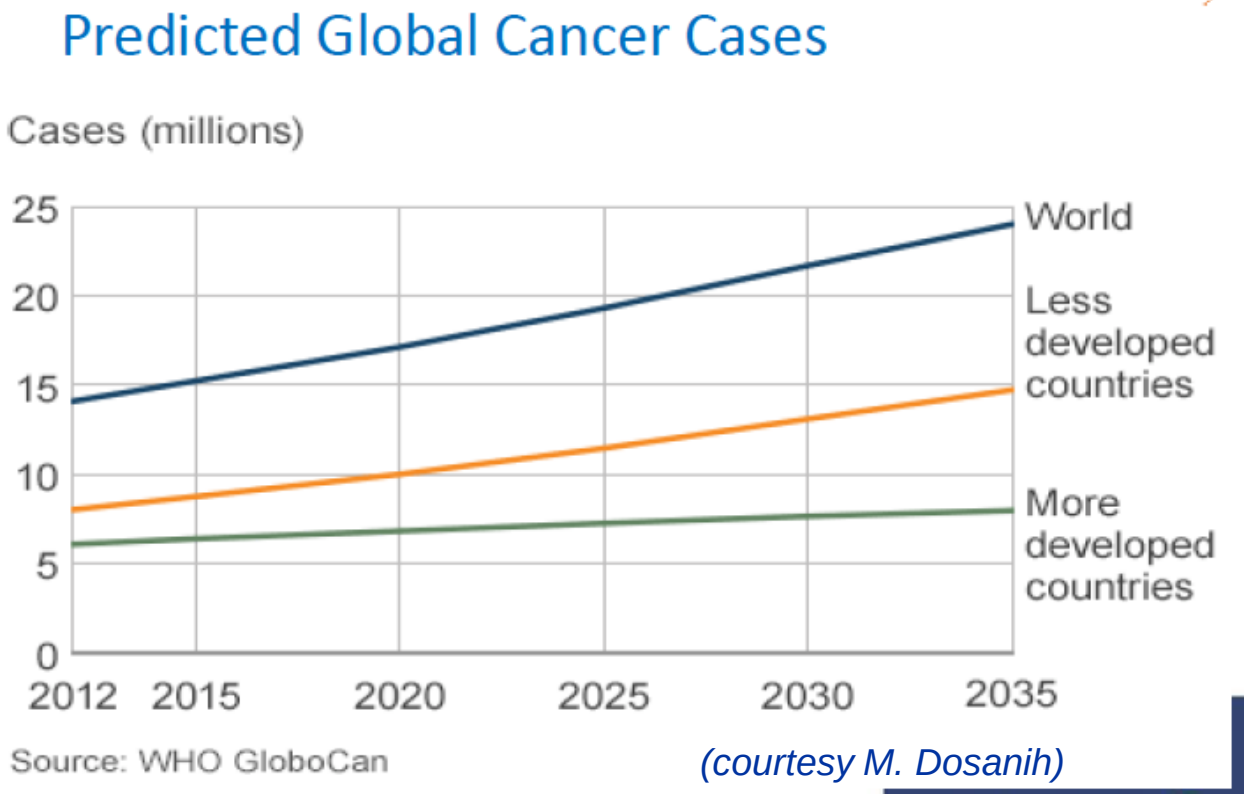
- After the cyclotron invention in 1936, the new Berkeley 37-inch cyclotron was producing isotopes for physics, biology and medicine – in parallel to the time devoted to discoveries in nuclear physics.
- In 1938 starts direct irradiation of patients with neutrons from the new 60-inch cyclotron.
- In 1946, Robert Wilson proposed to use protons to treat cancer, profiting of the Bragg peak to deliver a precise dose to the tumour.
- First treatment of pituitary tumours took place at Berkeley in 1956.
- First hospital-based proton treatment centre at Loma Linda (US) in 1990.



Impact of cancer on world population

Cancer is the second leading cause of death globally, and was responsible for 8.8 million deaths in 2015. Globally, nearly 1 in 6 deaths is due to cancer (WHO).

GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012



(courtesy M. Dosanih)

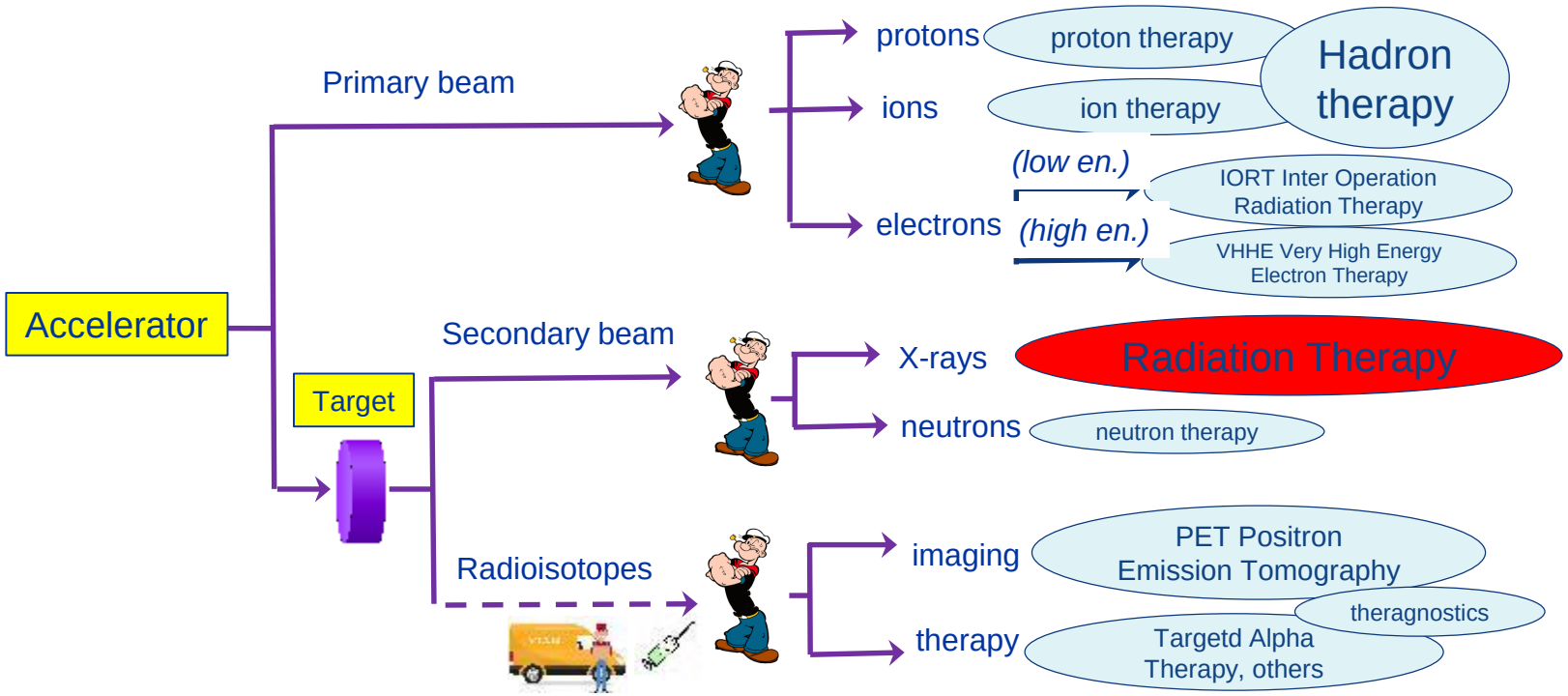
Increase of cancer cases due to:

- Increasing age of population
- Aggressive environmental and living conditions in developing countries.

Nowadays, the standard protocol for treatment of most cancers is based on:

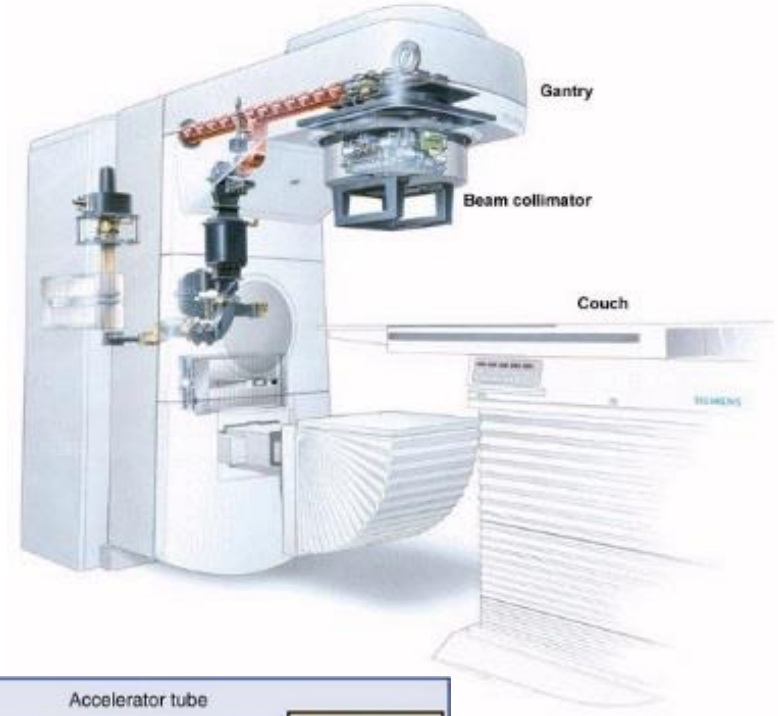
1. Surgery
2. **Radiotherapy** (accelerator-based)
3. Chemiotherapy
4. (Immunotherapy)

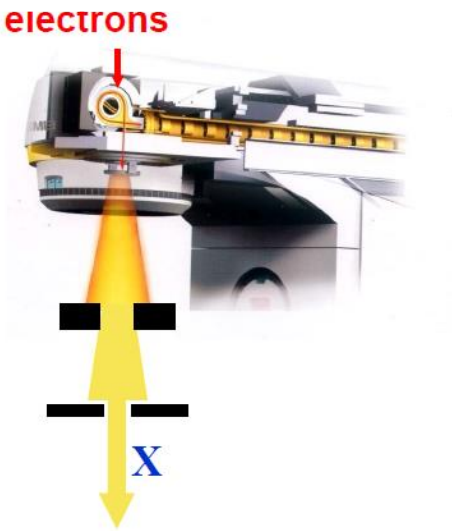
1. Radiation therapy



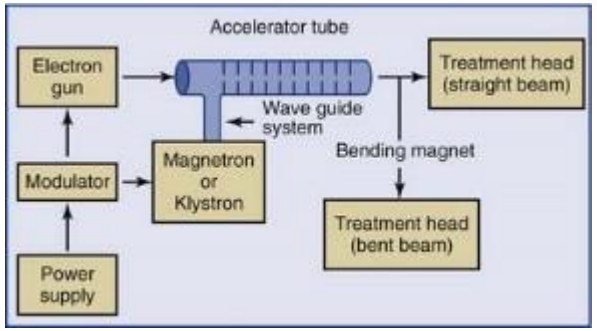
The most successful accelerator

Electron Linac (linear accelerator) for radiotherapy (X-ray treatment of cancer)





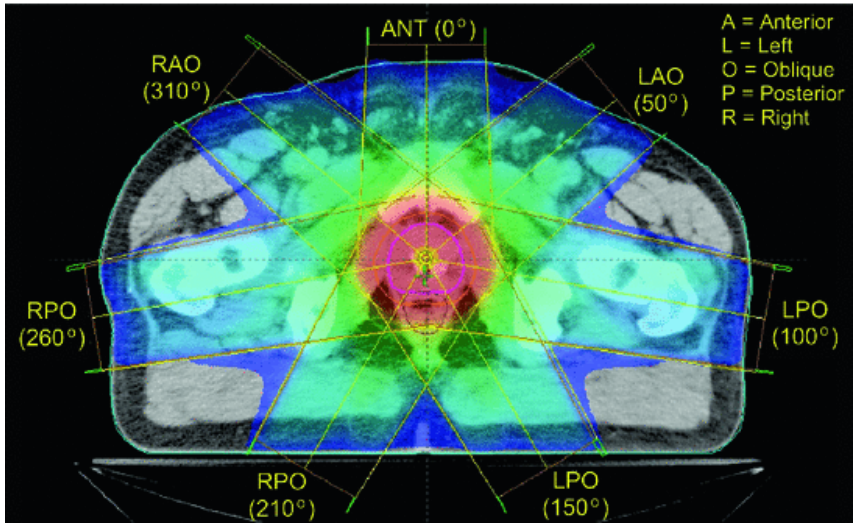
5 – 25 MeV e-beam
Tungsten target



14,000 in operation worldwide!

Modern radiotherapy

X-rays are used to treat cancer since last century. The introduction of the electron linac has made a huge development possible, and new developments are now further extending the reach of this treatment.



Accurate delivery of X-rays to tumours

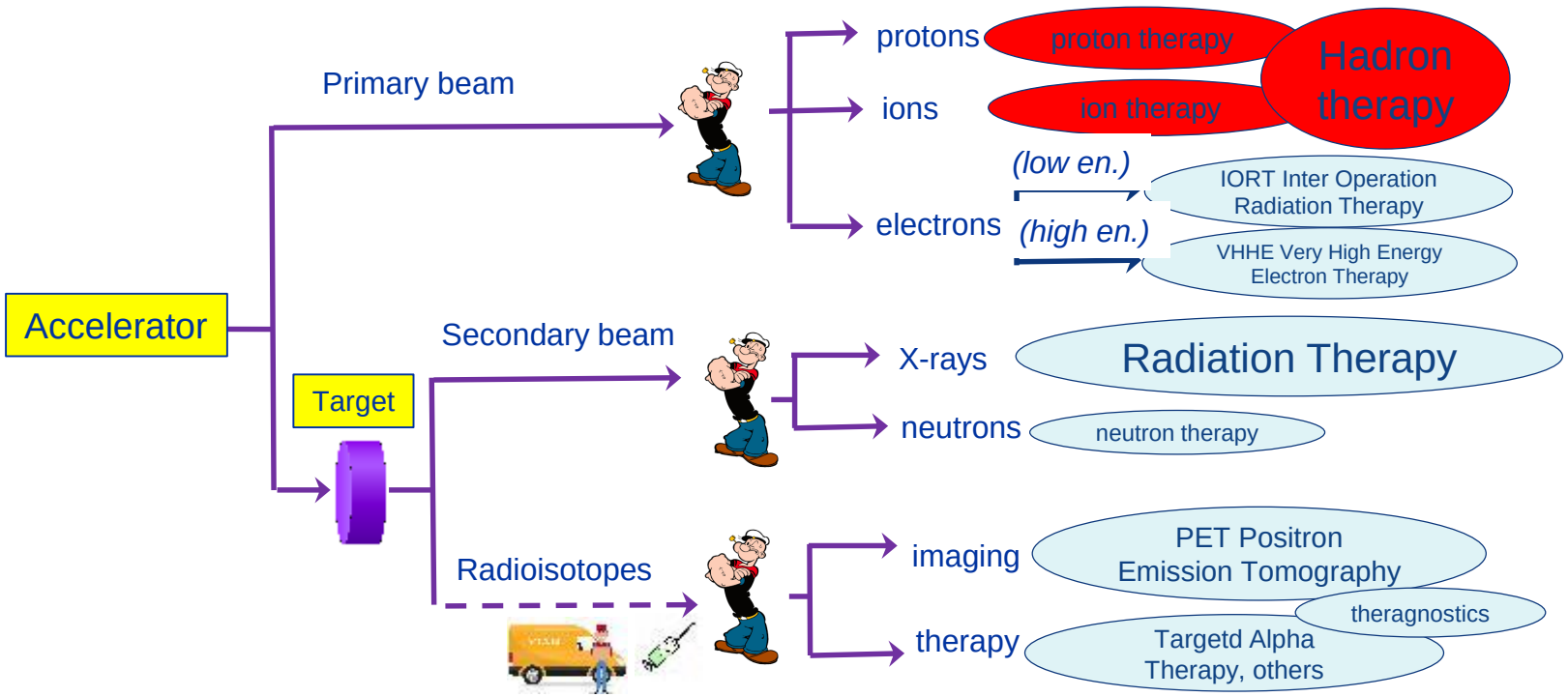
To spare surrounding tissues and organs, computer-controlled treatment methods enable precise volumes of radiation dose to be delivered. The radiation is delivered from several directions and transversally defined by multi-leaf collimators (MLCs).

Combined imaging and therapy

Modern imaging techniques (CT computed tomography, MRI magnetic resonance imaging, PET positron emission tomography) allow an excellent 3D (and 4D, including time) modelling of the region to be treated.
The next challenge is to combine imaging and treatment in the same device.

Fig. 3.4: The MR-linac, developed by Elekta, consists of a linear accelerator equipped with multi-leaf collimator technology for accurate radiotherapy dosage, combined with a high-field MR imaging system. The MR-linac is work in progress and is not available for sale or distribution (courtesy of Elekta).

2 – Hadron therapy (protons and ions)



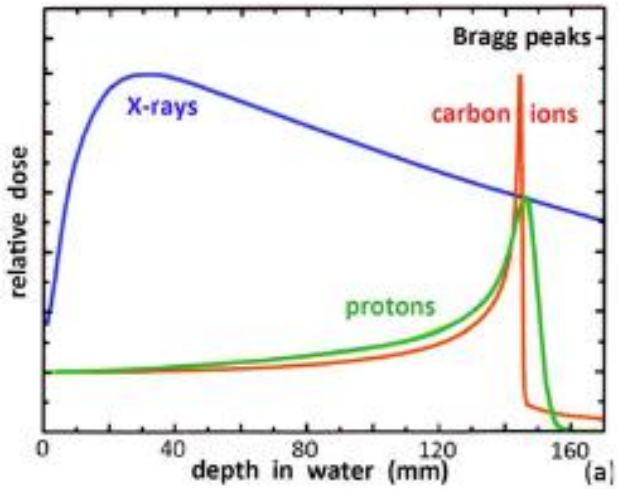
Note:
Therapy with electrons will be left for the last lecture by W. Wünsch

Treating cancer with particle beams

Cancer today: ~ 65% of cancers are curable; ~ 35% of cancer treatments fail, 2/3 because of metastasis, 1/3 in the primary site.

- **Priority of cancer research** is treating the >10% “not curable” cancers, usually large, deep seated, radioresistant.
- **Techniques**: Advanced Radiation Therapy (e.g. IMRT), or **Hadron Therapy** (protons or ions).
- **Challenge**: Deposit enough dose on the cancer, sparing the surrounding tissues (secondary cancers, quality of life).

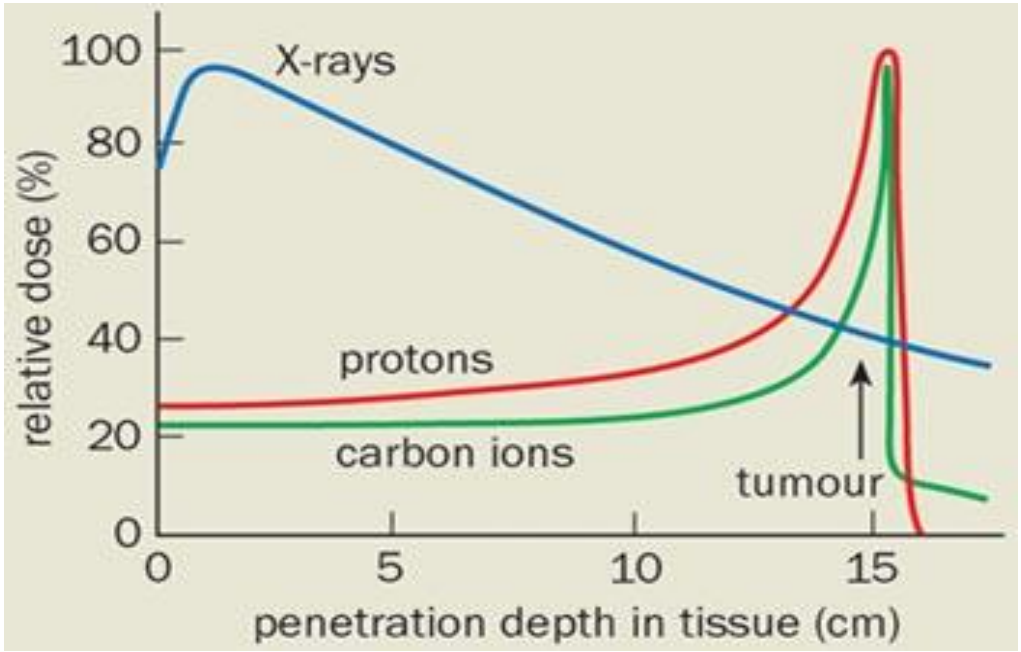
Hadron Therapy (or **Particle Therapy**) allows concentrating the radiation dose on the tumour, thanks to the «Bragg peak».
More **expensive** than X-ray therapy, is rapidly growing thanks to new compact industry-made accelerators.



The Bragg peak

Bethe-Bloch equation of ionisation energy loss by charged particles

$$-\frac{dE}{dx} = \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0}\right)^2 \cdot \left[\ln\left(\frac{2m_e c^2 \beta^2}{I.(1-\beta^2)}\right) - \beta^2\right]$$



«Bragg» peak

accelerators-for-society.org

Different from X-rays or electrons, protons and ions deposit their energy at a given depth inside the tissues, **minimising the dose to the organs close to the tumour**.

Required energy (protons) about 230 MeV, corresponding to 33 cm in water.

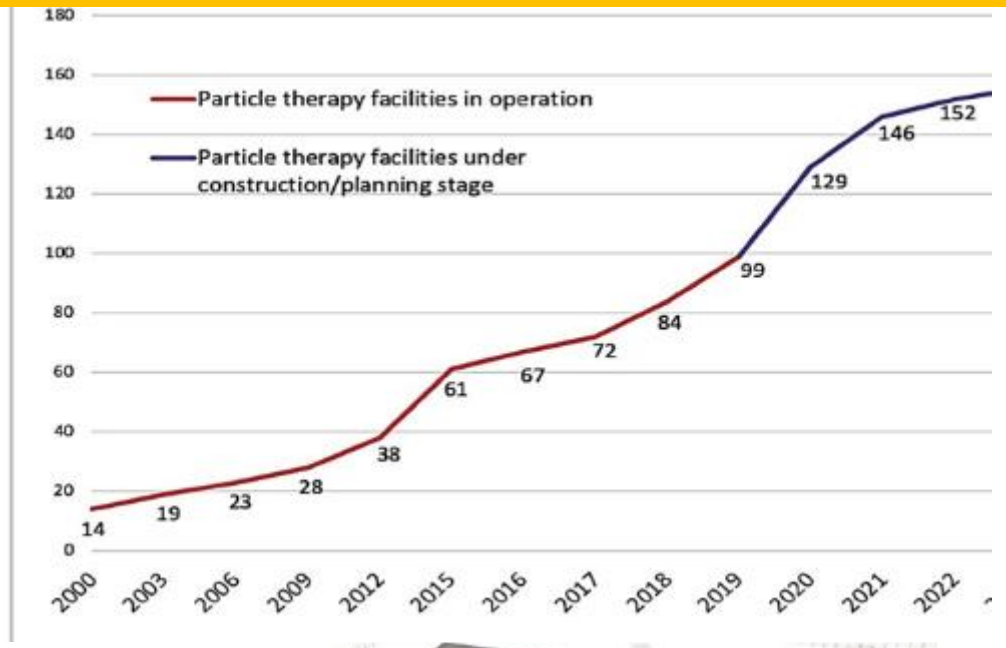
Small currents: 10 nA for a typical dose of 1 Gy to 1 liter in 1 minute.

The rise of particle therapy (hadrontherapy)

Hadrons = protons and heavier atomic nuclei (ions)

- Proposed 1946, first experimental treatment Berkeley 1954.
- First hospital-based proton treatment facility in 1993 (Loma Linda, US).
- First treatment facility with carbon ions in 1994 (HIMAC, Japan).
- Treatment in Europe at physics facilities from end of '90s.
- First dedicated European facility for proton-carbon ions in 2009 (HIT).
- From 2006, commercial proton therapy accelerators (mostly cyclotrons) come to market.
- In 2022, 6 competing vendors for protons, 1 for carbon ions. A total of 152 centres worldwide.

A success story, but … many ongoing discussions on **effectiveness, costs and benefits**.



ptcog.com

The Heidelberg Ion Therapy (HIT) facility (protons and carbon ions)

Particle therapy in Europe

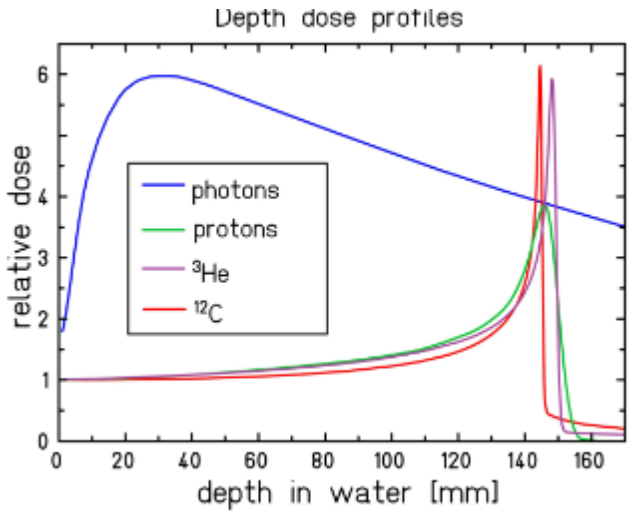
Particle therapy centres in Europe. Courtesy of ENLIGHT, 2020

Only 2 regions in Europe without particle therapy facilities:

- South East Europe
- Baltics

The Bragg peak is not all…

The Bragg peak is very simple physics concept: distribution of energy deposition inside the tissue, leading to *atomic ionisations* (**LET = Linear Energy Transfer**, energy loss per unit mass)



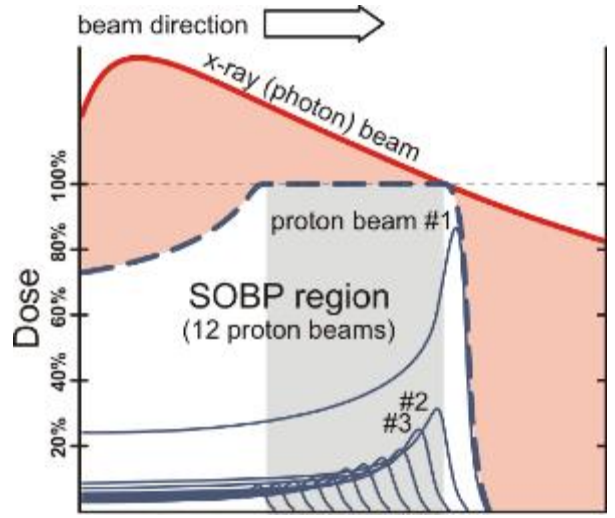
Durante, Debus & Loeffler, *Nat. Rev. Phys.* 2021

Biology is more complex than physics:

- Radiobiological effect **RBE** has a complex dependence on LET and particle type: need of experimental work, complex models and sophisticated treatment plans.

Practical dose delivery reduces effectiveness:

- **Longitudinal** scan of tumour leads to higher dose in the penetration zone (Spread Out Bragg Peak, SOBP),
- The precise dose distribution requires **comparable accuracy** in imaging of tumours and in compensation of organ motion.



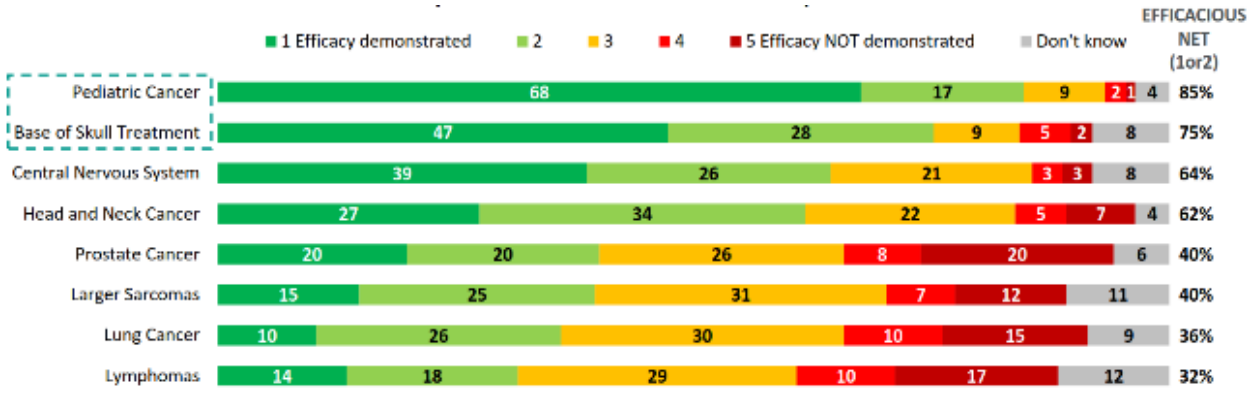
Levin et al., Br J Cancer (2005) 93:849–54

Particle therapy: an ongoing debate

Particle therapy comes with a cost: ≈40 M€ for single-room proton therapy, compared with ≈3 M€ of a modern X-ray radiotherapy system. A complex carbon facility costs ≈200 M€.

Reduced toxicity to organs adjacent to the tumour is the main advantage of particle beams. Using particles reduces the risk of secondary cancers and other diseases after treatment, and in general improves **quality of life** after treatment. Particle treatment is particularly indicated for **paediatric tumours** and tumours **close to vital organs**.

There is still much space for further **improving particle therapy** (organs in motion, dose optimisation, type of particle,…) and **research** is essential: pre-clinical research, optimisation of treatment modalities, long-term clinical trials, etc.

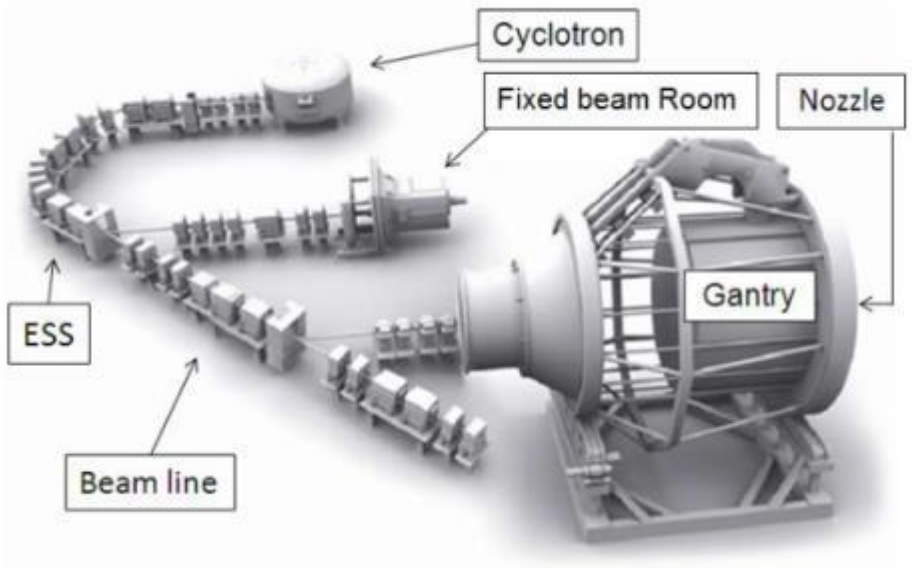


Source: IBA, state of proton therapy market entering 2017

The goal of particle therapy is improving health more than just treating cancer!

Image: IBA proton therapy fact-sheet,

Proton therapy accelerators: cyclotrons



At present, the cyclotron is the one of the best accelerators to provide proton therapy reliably and at low cost (4 vendors on the market).

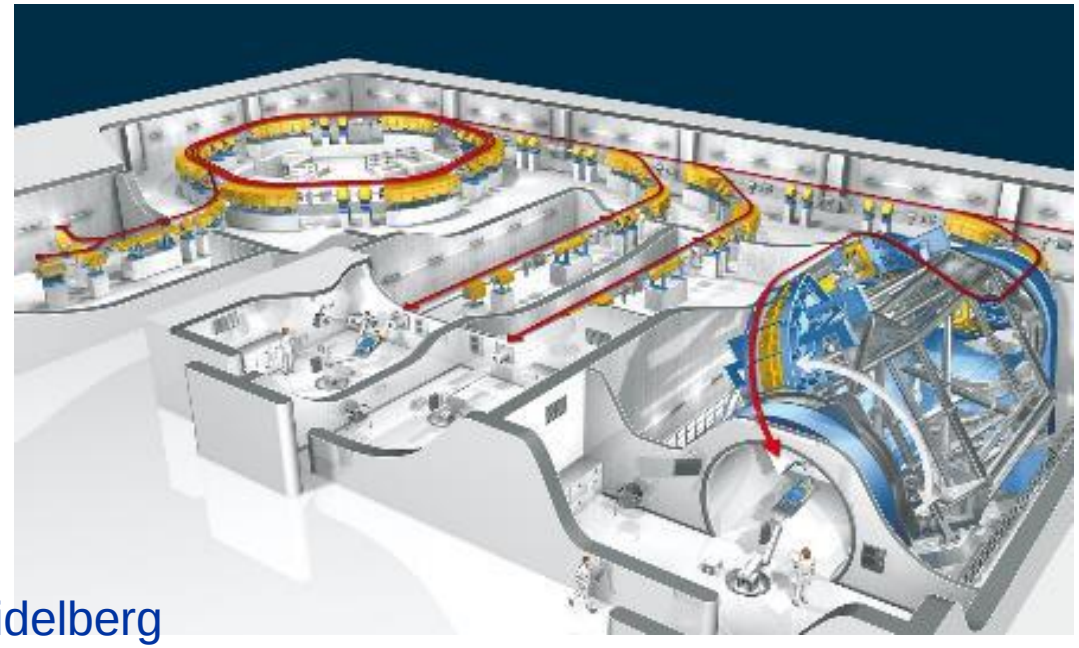
Critical issues with cyclotrons:

1. Energy modulation (required to adjust the depth and scan the tumour) is obtained with degraders (sliding plates) that are slow and remain activated.
2. Large shielding

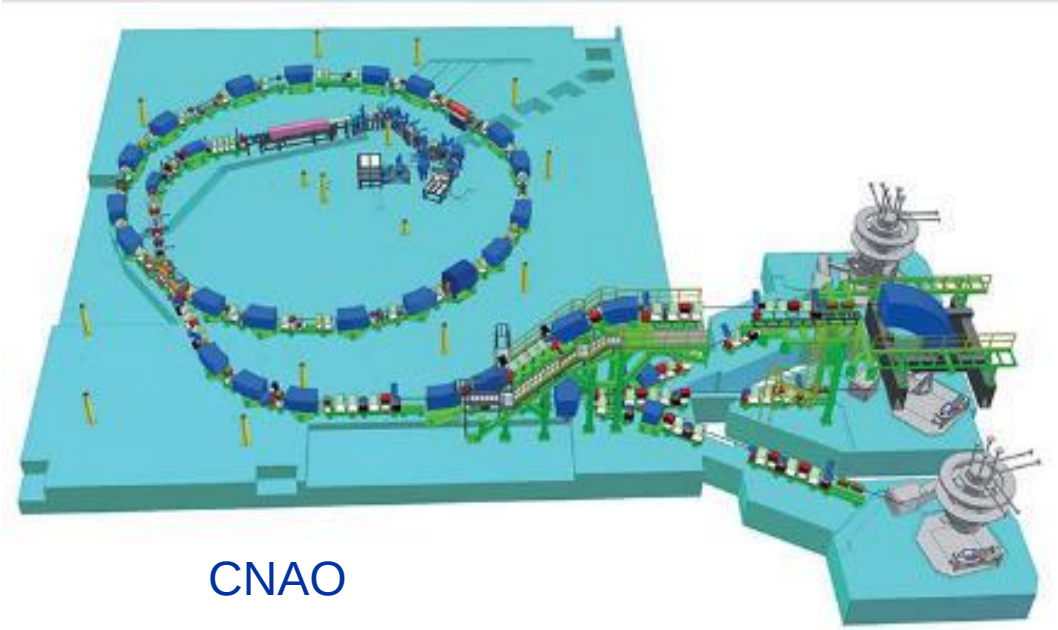
ProteusOne and ProteusPlus turn-key proton therapy solutions from IBA (Belgium)

Synchrotrons for proton and ion therapy

- The Loma Linda Medical Centre in US (only protons) and the ion therapy centres in Japan have paved the way for the use of synchrotrons for combined proton and ion (carbon) therapy).
- 2 pioneering initiatives in Europe (ion therapy at GSI and the Proton-Ion Medical Machine Study PIMMS at CERN) have established the basis for the construction of **4 proton-ion therapy centres**: Heidelberg and Marburg Ion Therapy (HIT and MIT) based on the GSI design, Centro Nazionale di Terapia Oncologica (CNAO) and Med-AUSTRON based on the PIMMS design.



HIT Heidelberg

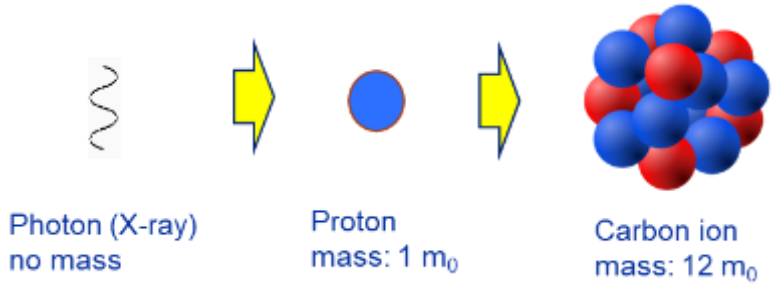


CNAO

Ion therapy: from photons to protons to ions

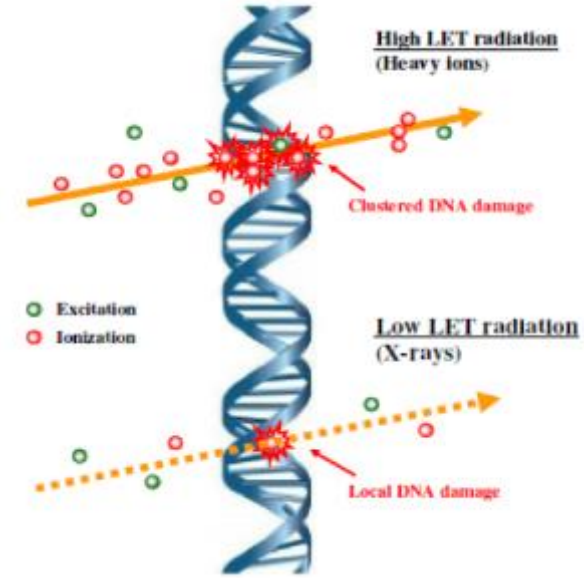
High LET radiation (ions) generates denser ionisations inducing clustered DNA lesions difficult for the cell to repair.

→ **RBE(carbon)=2.0-2.4**



Advantages of heavier ions (compared to protons or X-rays)

- **Higher LET and RBE** generate non-reparable double-strand DNA breakings that are effective on **hypoxic radioresistant tumours**.
- Energy deposition is more precise, with lower straggling and scattering
- Emerging opportunities from combination with immunotherapy to treat diffused cancers and metastasis.



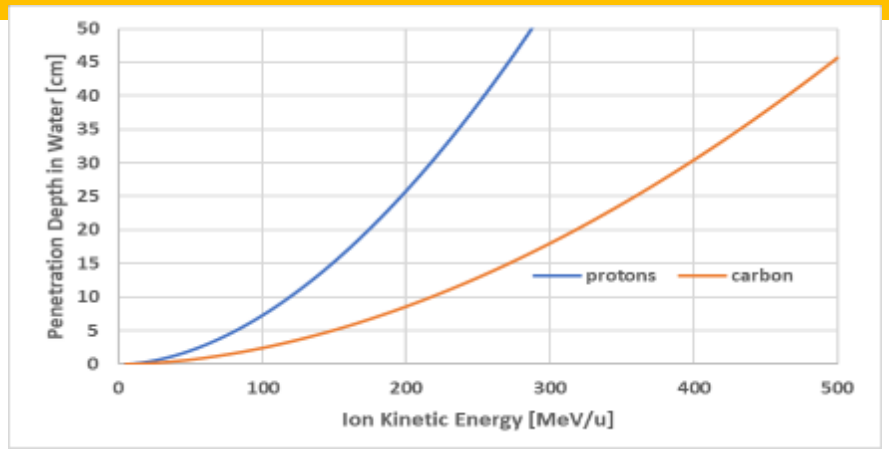
Helm A, Ebner DK, Tinganelli W, Simoniello P, Bisio A, Marchesano V, et al. Combining heavy-ion therapy with immunotherapy: an update on recent developments. Int J Part Ther. (2018) 5:84–93.
Durante M, Formenti S. Harnessing radiation to improve immunotherapy: better with particles? Br J Radiol. (2019) 192:20190224.

- Only carbon ions licensed for treatment, after the pioneering developments at HIMAC (Japan) from the 90's
- First patient treatments with carbon ions only in 1994: ion therapy is still in an early stage of its development !

Ion therapy: accelerator challenges

Particle accelerators for heavy ions are large and complex:

1. The high energy deposition means that to reach deep seated tumours ions must be accelerated to **higher energies** than protons: ion energy loss goes as (charge of the incident particle)^2. → around 440 MeV/u for carbon, compared to 240 MeV for protons.



$$B\rho\,[T.m] = 3.3356 \times pc[GeV]$$

Magnetic rigidity Bρ for carbon ions at full energy is **2.76 times higher** than protons.

→ For cyclotrons and synchrotrons, accelerator diameter scales with rigidity

2. The required energies fall into a **transition range between accelerator technologies**: cyclotrons and linacs are better at low energies, synchrotrons at high energies. In the intermediate region, there is not an **ideal accelerator** configuration → need to compare options, characterised by **complexity, cost, and R&D requirements**.

For a given magnet field, in an ion synchrotron or cyclotron accelerator and gantry are almost 3 times larger than for protons. The HIT gantry has a mass of 600 tons for a dipole bending radius of 3.65 m.

New technologies for ion therapy accelerators

Ions deliver more energy to the tissues but need more energy to enter the body → the required diameter of the accelerator increases with energy, accelerator dimensions increase by a factor 2.8 going from protons to carbon

The main limitation to the diffusion of ion therapy is the cost and size of the accelerator

Only 4 ion therapy facilities operating in Europe (+ 6 in Japan, 3 in China, 1 planned in US)

- CNAO and MedAustron based on a design started at CERN in 1996. 1st patient at CNAO in 2011.
- HIT and MIT based on a design started at GSI (Germany) in 1998 . 1st patient at HIT in 2009.

The ion gantry of the Heidelberg Ion Therapy facility: 600 tons

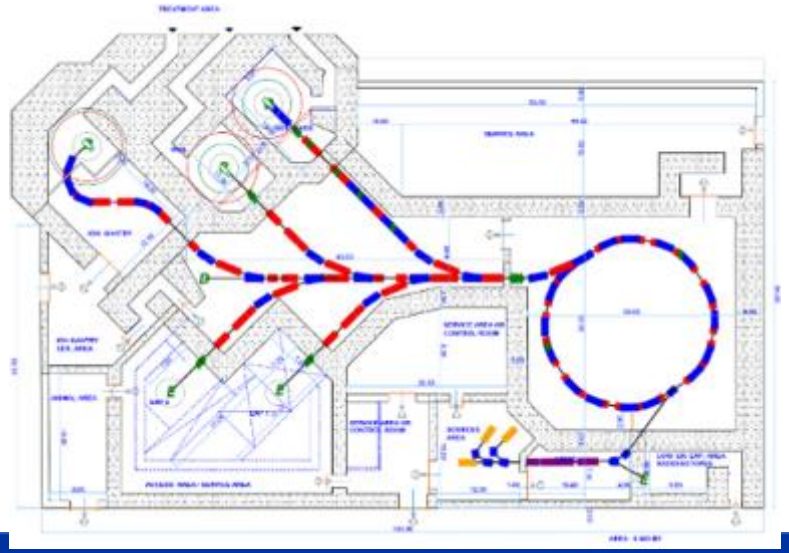
Particle accelerator technology has made a huge progress in the last 20 years, towards more compact and performant accelerator designs.

We can today explore new accelerator designs profiting of the latest advances in accelerator technologies.

A conventional synchrotron for carbon ions

New design developed at CERN in 2018-2021

- Higher beam intensity for faster treatment ($2x10^{10}$, 20 times higher than CNAO or HIT)
- Multiple energy extraction (**multiple flat-tops**)
- Additional **fast extraction for FLASH operation**
- Redesigned **linac** at higher frequency, for lower cost and parallel isotope production
- Multiple particles: p, He, C, O
- Optimised layout of beam transport, for both research and therapy



Optimised layout recently developed for the SEEIIST initiative

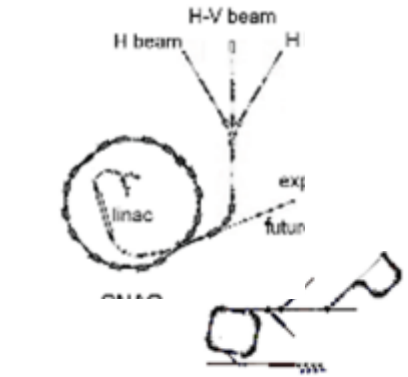
Room temperature magnets at 1.6 T field

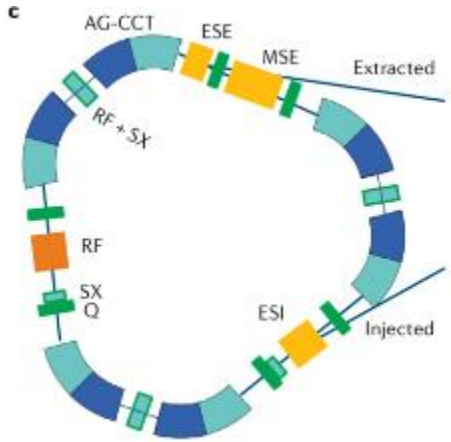
Injection/Acceleration	Unit					
Particle after stripping		p	$^{4}He^{2+}$	$^{12}C^{6+}$	$^{16}O^{8+}$	$^{36}Ar^{16+}$
Energy	MeV/u	7				
Magnetic rigidity at injection	Tm	0.38	0.76	0.76	0.76	0.86
Extraction energy range (**)	MeV/u	60 – 250 (1000)	60 – 250 (430)	100 - 430	100 - 430	200 – 350
Magnetic rigidity at highest energy (for therapy)	Tm	2.42	4.85	6.62	6.62	6.62
Maximum nominal field	T	1.5				
Maximum number of particles per cycle		$2.6 \cdot 10^{11}$	$8.2 \cdot 10^{10}$	$2 \cdot 10^{10}$	$1.4 \cdot 10^{10}$	$5 \cdot 10^{9}$
Ramp-up rate	Tm/s	<10				
Ramp-down time of magnets	s	1				
Spill ripple, intensity ratio I_{max}/I_{mean} (average on 1 ms)		< 1.5				
Slow extraction spill duration with multi-energy	s	0.1 – 60				
Fast extraction	s	$< 0.3\ 10^{-6}$				

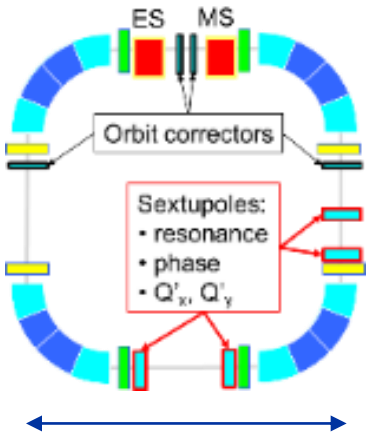
The SEEIIST facility

The compact superconducting synchrotron

Considerable gain in dimensions thanks to superconductivity







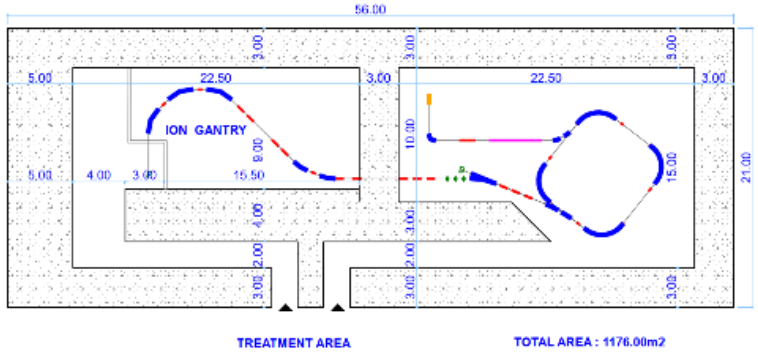
6.5 m

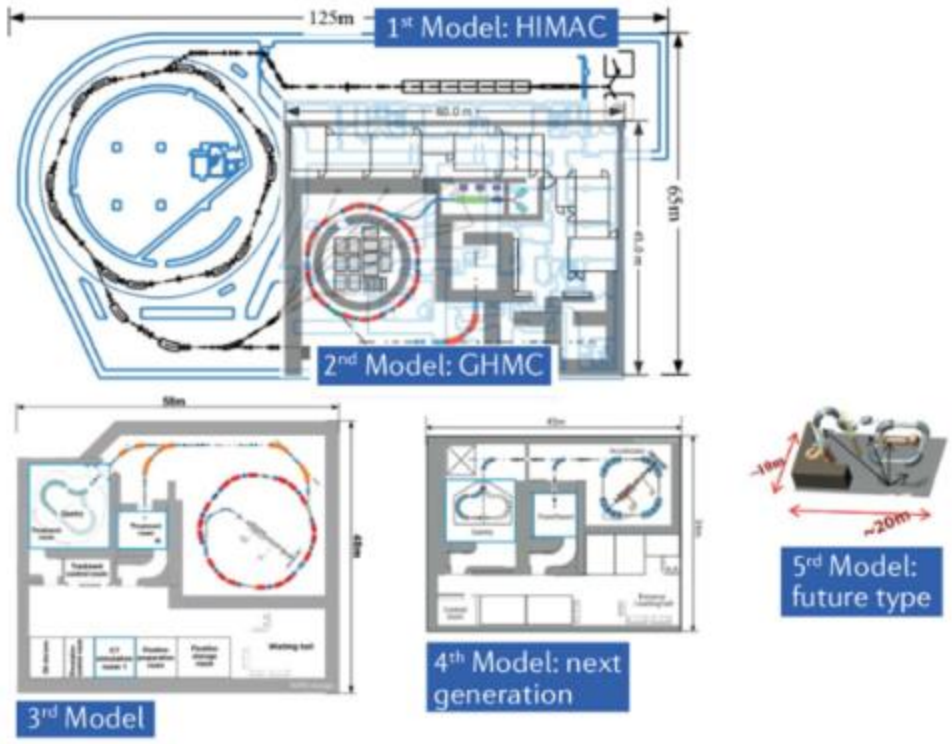
Additional features

- High intensity (2 x 10^{10} C ions per pulse
- Slow and FLASH extraction
- Multiple ion operation

Goal: a compact single-room ion therapy facility in about 1,000 m²

Alternative synchrotron layouts





Japan: the roadmap of the National Institutes for Quantum and Radiological Science and Technology (NIRS-QST, Chiba) for reducing the footprint of heavy ion centres. Form the large HIMAC (1994) to 3rd and next generation (courtesy of K. Noda, NIRS-QST).

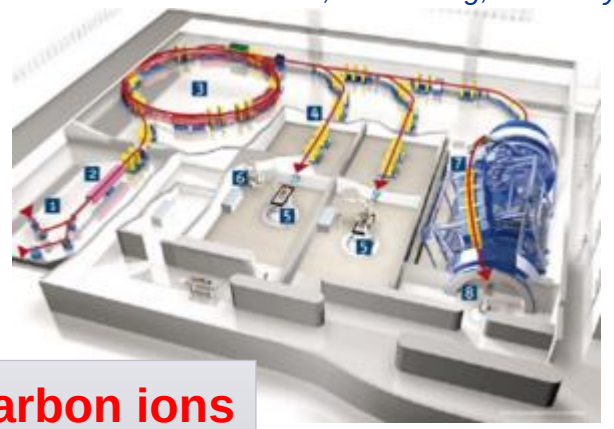
E. Benedetto et al., Comparison of accelerator designs for an ion therapy and research facility, CERN-ACC-NOTE-2020-0068, http://cds.cern.ch/record/2748083?ln=en

Accelerators for cancer therapy

Ions deliver more energy to the tissues but need more energy to enter the body → need larger accelerators

Cnao , Pavia, Italy

HIT, Heidelberg, Germany



courtesy IBA

Synchrotron, Carbon ions
~5,000 m^2
~200 M€

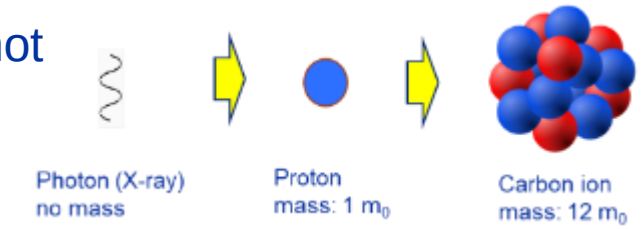
Cyclotron, protons
~500 m^2
~40 M€

Linac, X-rays
~50 m^2
~5 M€

Commercially available

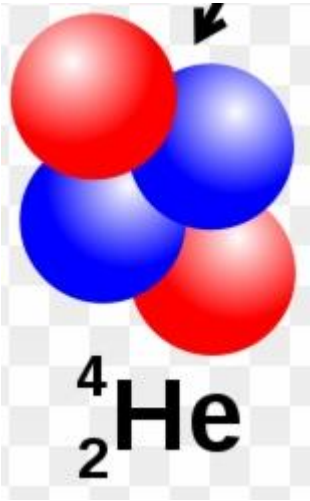
Specially designed and built

The population in the Baltics (6.2M) does not justify a large carbon therapy centre.
Can we imagine something in between protons and carbon?



Helium beams for cancer treatment

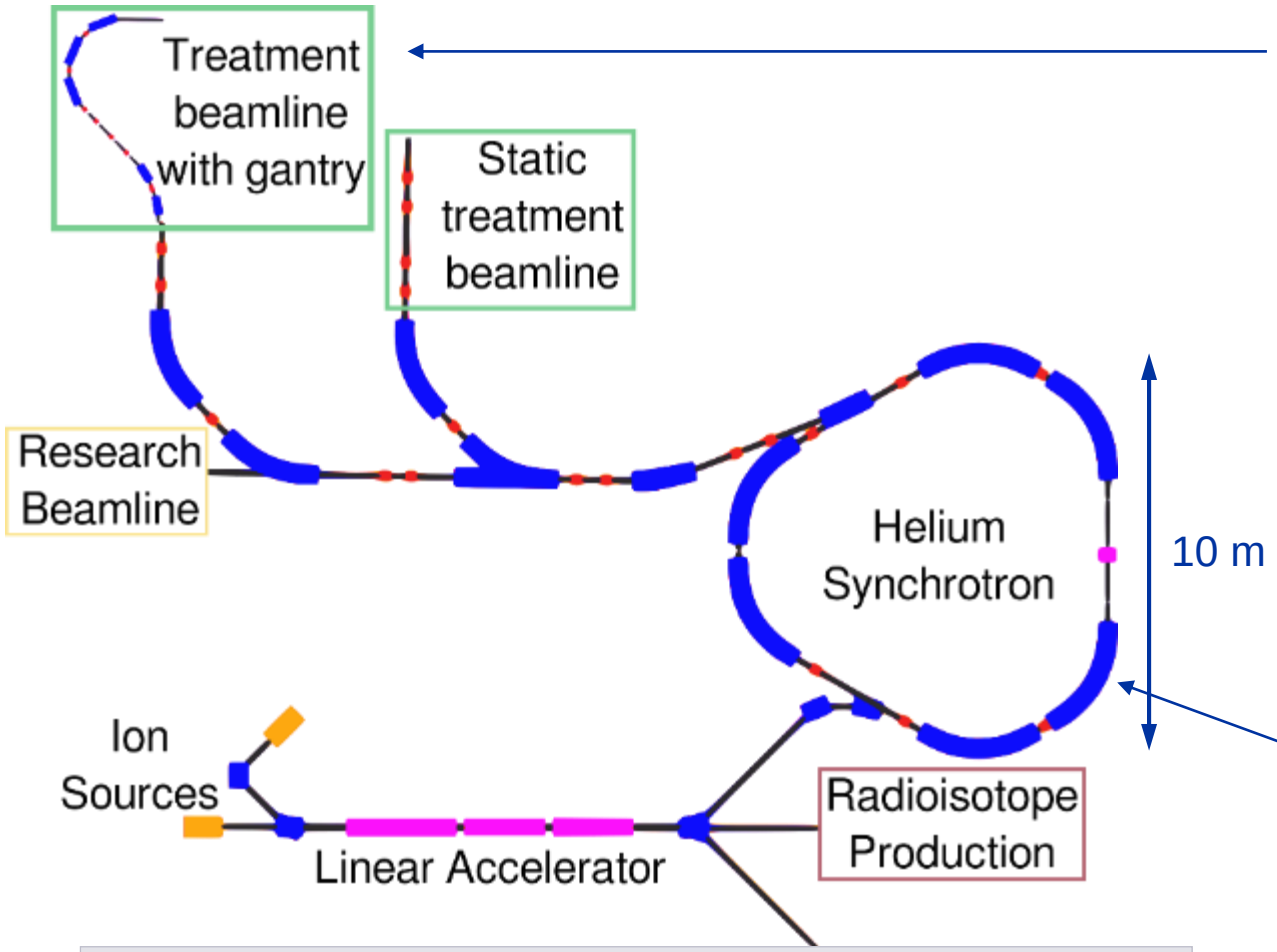
- Treatment with helium ions (2 proton + 2 neutrons) is under advanced study at the EU carbon therapy centres.
- First patient treated in September 2021 at the Heidelberg Ion Therapy centre (D).
- Clinical trials ongoing, will be soon licensed for treatment.
- An accelerator designed for helium treatment can easily produce protons for standardised treatment, and be used for research with helium and heavier ions.
- Possible parallel production of radioisotopes for diagnostics, therapy, and research

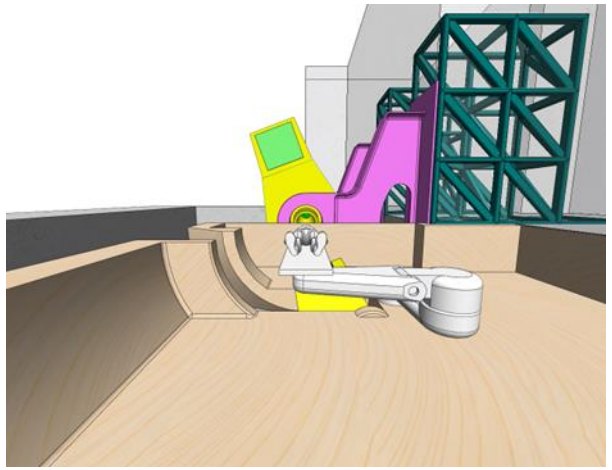


Helium has many advantages:
- reduced lateral scattering than protons,
- lower fragmentations than carbon,
- lower neutron dose than protons or carbon, reducing risks in paediatric patients,
- could treat some radioresistant tumours at lower cost than carbon.

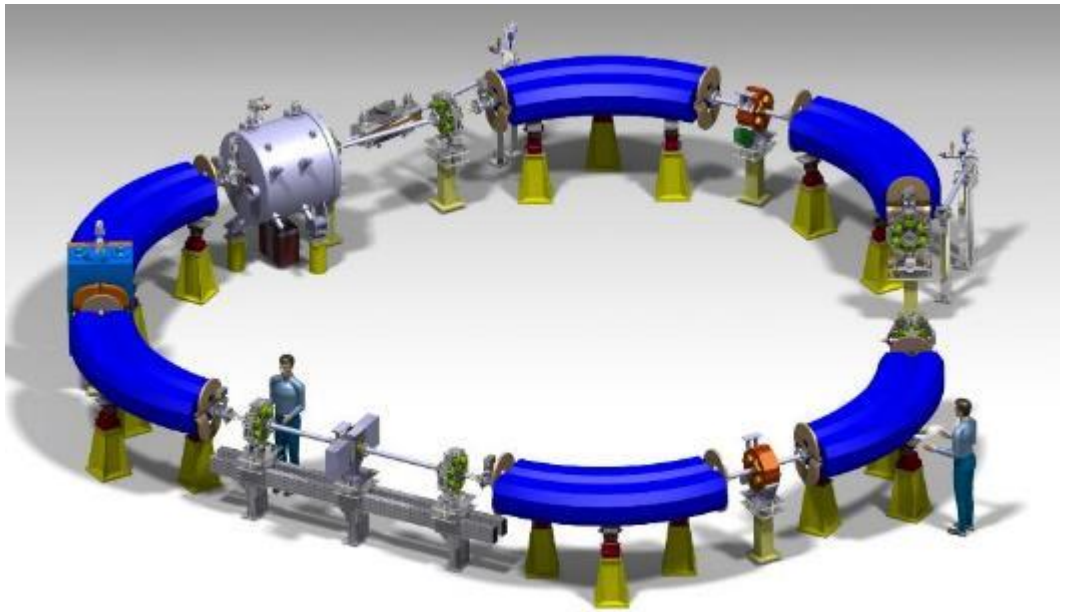
Would be the first accelerator worldwide designed for helium (today helium can be produced only by more expensive carbon accelerators)

An advanced centre for particle therapy and research with proton and helium beams



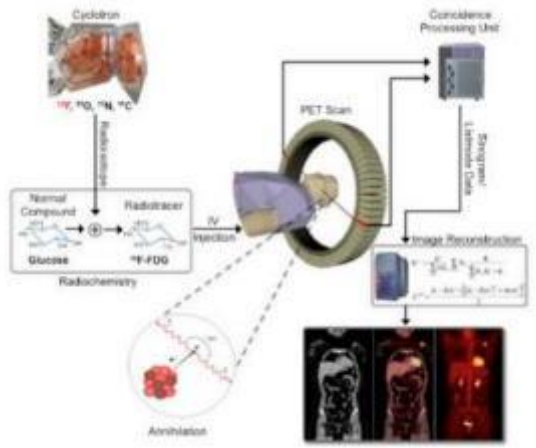


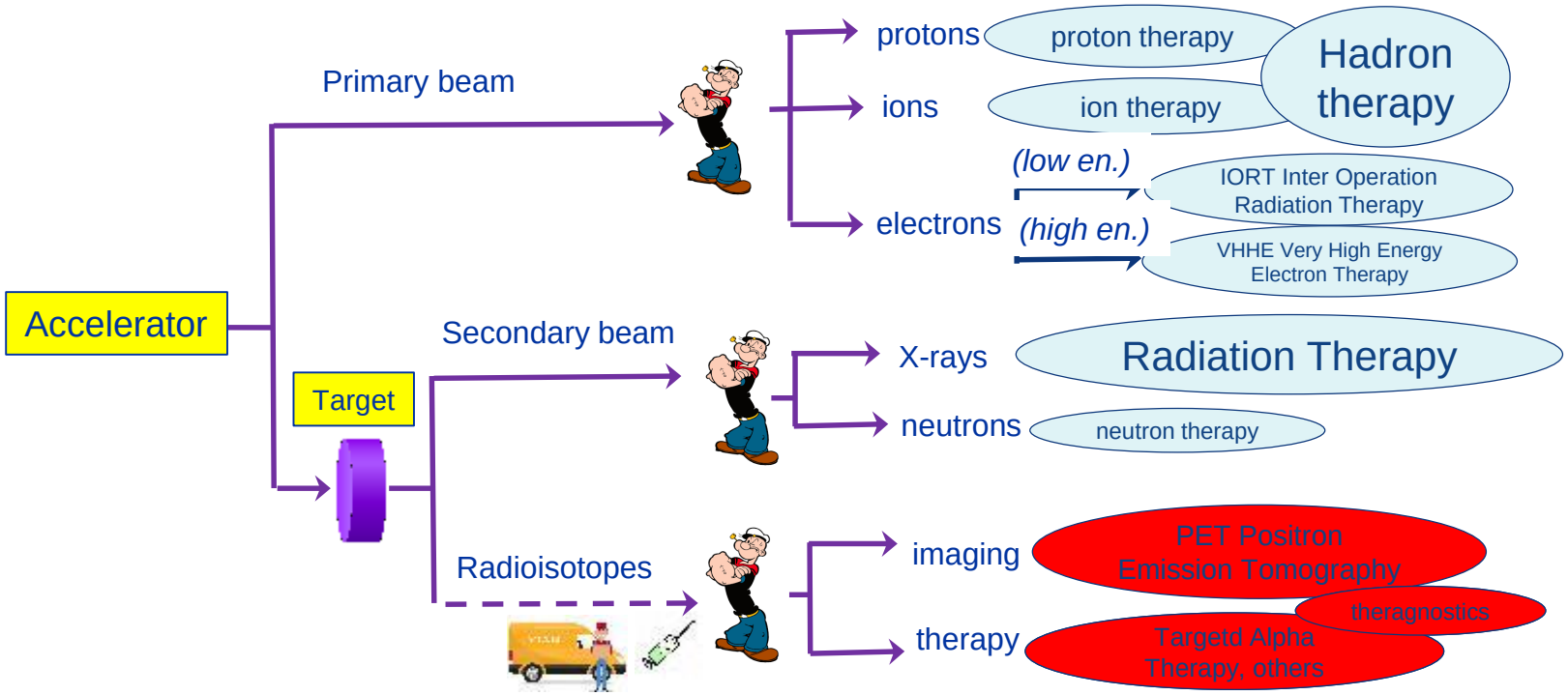
- Rotating superconducting gantry
- FLASH and mini-beams
- Online imaging with protons
- Parallel production of radioisotopes



Known and reliable technologies, based on recent CERN constructions of scientific synchrotrons

4- Radioisotopes – imaging and therapy





PET and SPECT scanning

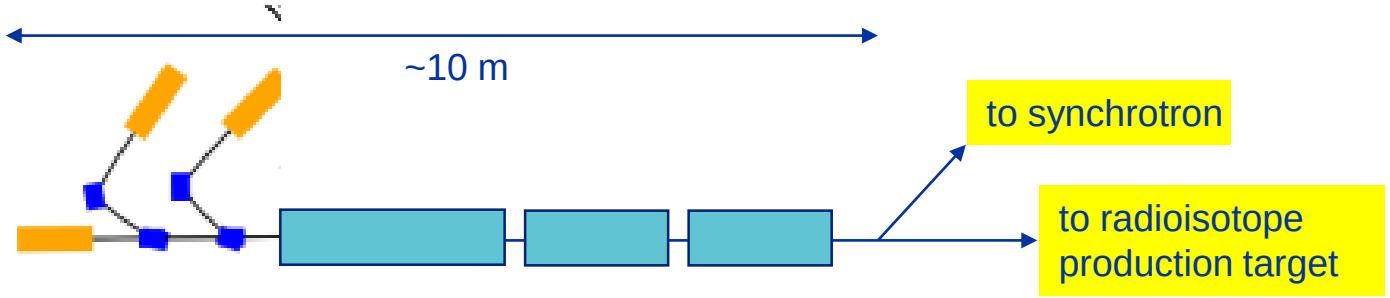
- A **radioisotope** (radiotracer) produced by an accelerator (usually cyclotron) is attached to a chemical compound (glucose).
- The compound is injected to the patient and accumulates in tissues with high metabolic activity, (usually tumours).
- The radioisotope decays emitting particles detected by a scanner.
- **PET** (Positron Emission Tomography) is using Fluorine-18 (1h50' half-life) attached to Fludeoxyglucose (FDG)

Linac for production of therapeutical radioisotopes

A new ion therapy facility should include a **new injector linear accelerator** designed for lower cost, higher efficiency, and higher beam current.

With a minor additional investment, the linac will have 2 modes of operation: for injection in the synchrotron, and for sending the beam to a target for production of medical radioisotopes.

Two frequencies being explored: 216 MHz and 325 MHz.



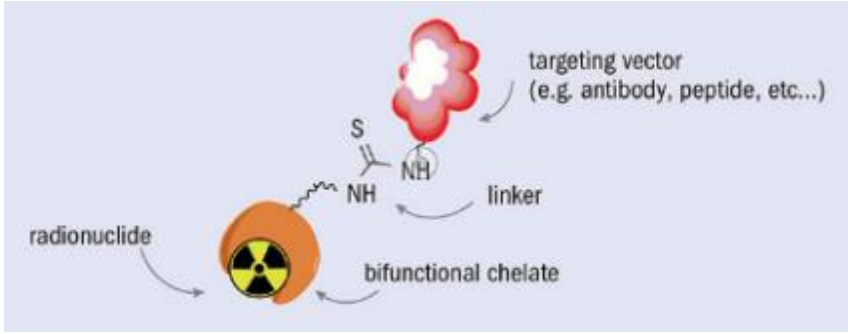
3 ion sources	Linac section1	Linac section2	Linac section3
$^{12}C^{4+}$, 600 μA $^{4}He^{2+}$, 2-5 mA p, 10 mA	q/m=1/3 or 1/2 W_{in}=45 keV/u W_{out}= 5 MeV/u	q/m=1/2 W_{in}= 5 MeV/u W_{out}= 7 MeV/u	q/m=1/2 or 1 W_{in}= 7 MeV/u W_{out}= 10 MeV/u

Maximum duty cycle: 10%

Preliminary linac layout, courtesy of G. Bisoffi and A. Mamaras
To be developed in the HITRI+ EU project

Isotopes being considered:

1. **211 At** for Targeted Alpha Therapy, with alpha particles.
2. 117 mSn for theragnostic and bone metastasis, with alpha particles.
3. 11 C for PET scanning, with protons.

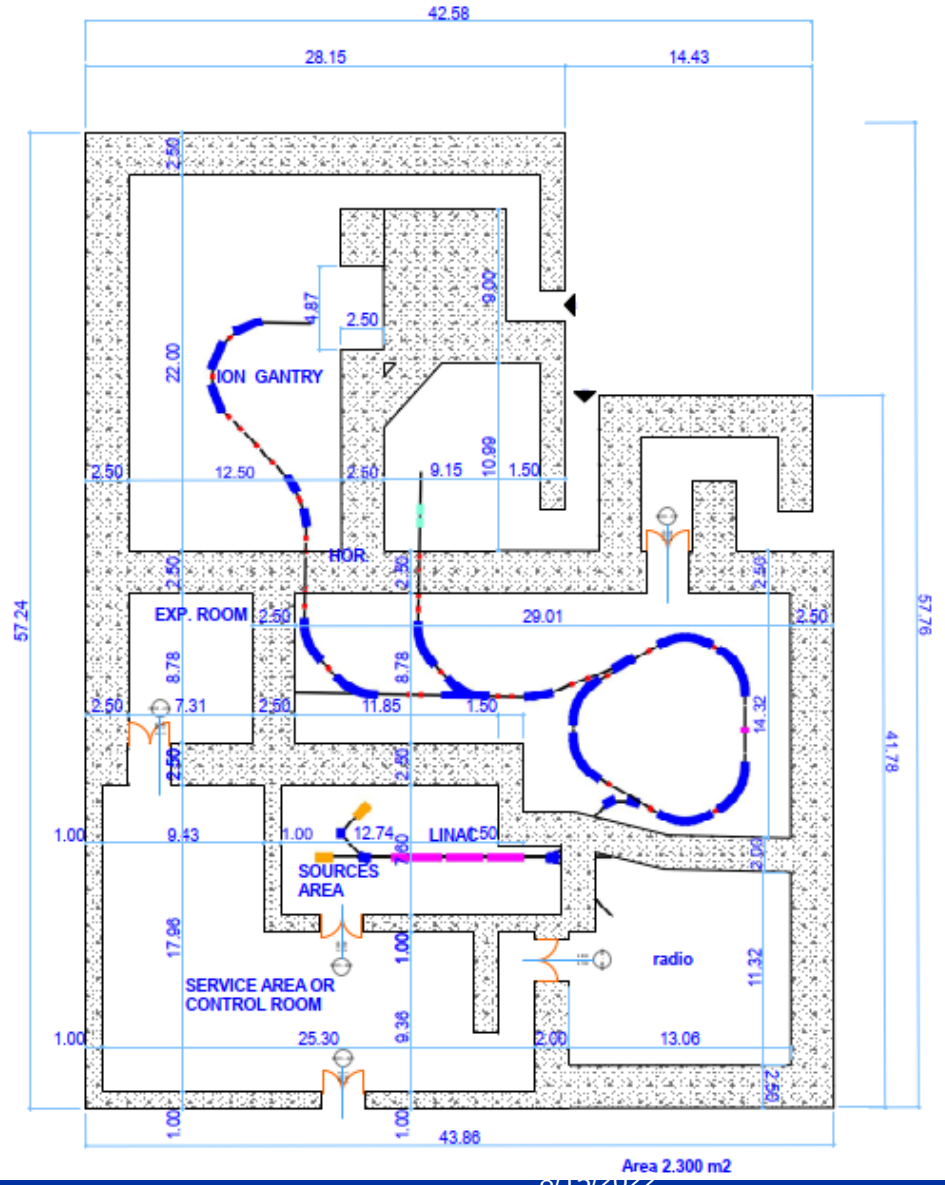


Targeted Alpha Therapy with 211 At

Alpha-emitting therapeutic isotopes attached to antibodies and injected to the patient: accumulate in cancer tissues and selectively deliver their dose.

Advanced experimentation, very promising for solid or diffused cancers (leukaemia).

A combined facility for research and therapy with proton beams, helium beams, and alpha emitters



Concept developed in collaboration between CERN (NIMMS study) and the CERN Baltic Group.

Proposal presented in June 2022 to the Health, Welfare and Family Committee of the Baltic Assembly that has expressed its support and invited the Baltic states to analyse the feasibility and cost of the project.

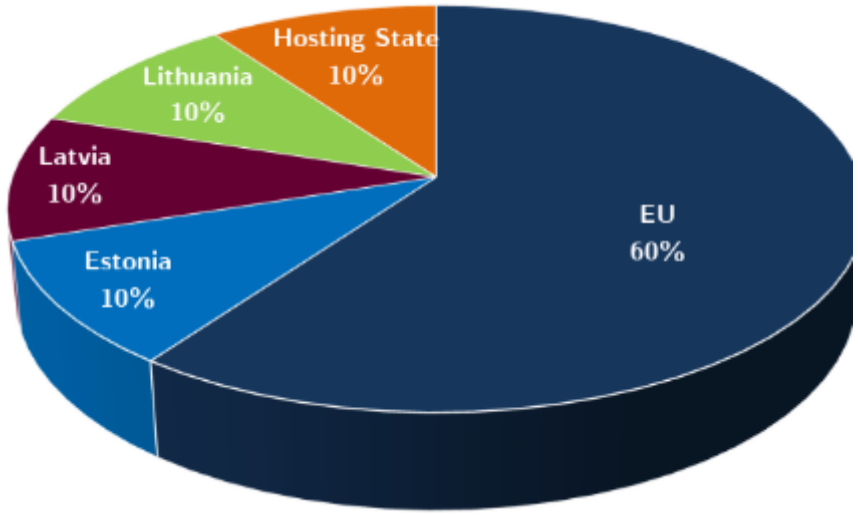
Facility for cancer treatment and research with protons and helium beams:

- 2 treatment rooms (one equipped with rotating gantry)
- 1 experimental room
- Radioisotope production area (with helium beams)

Draft concept-paper

Advanced Particle Therapy Center for the Baltic States

Possible financing and siting



Source: T. Torims, RTU and CERN Baltic Group

Criteria for site selection:

- Medical, local and political support
- Proximity of a large oncology hospital
- Accessibility: airport, railway, hosting facilities
- EC support

Thank you for your attention

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HITRI
Heavy Ion Therapy Research Integration

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