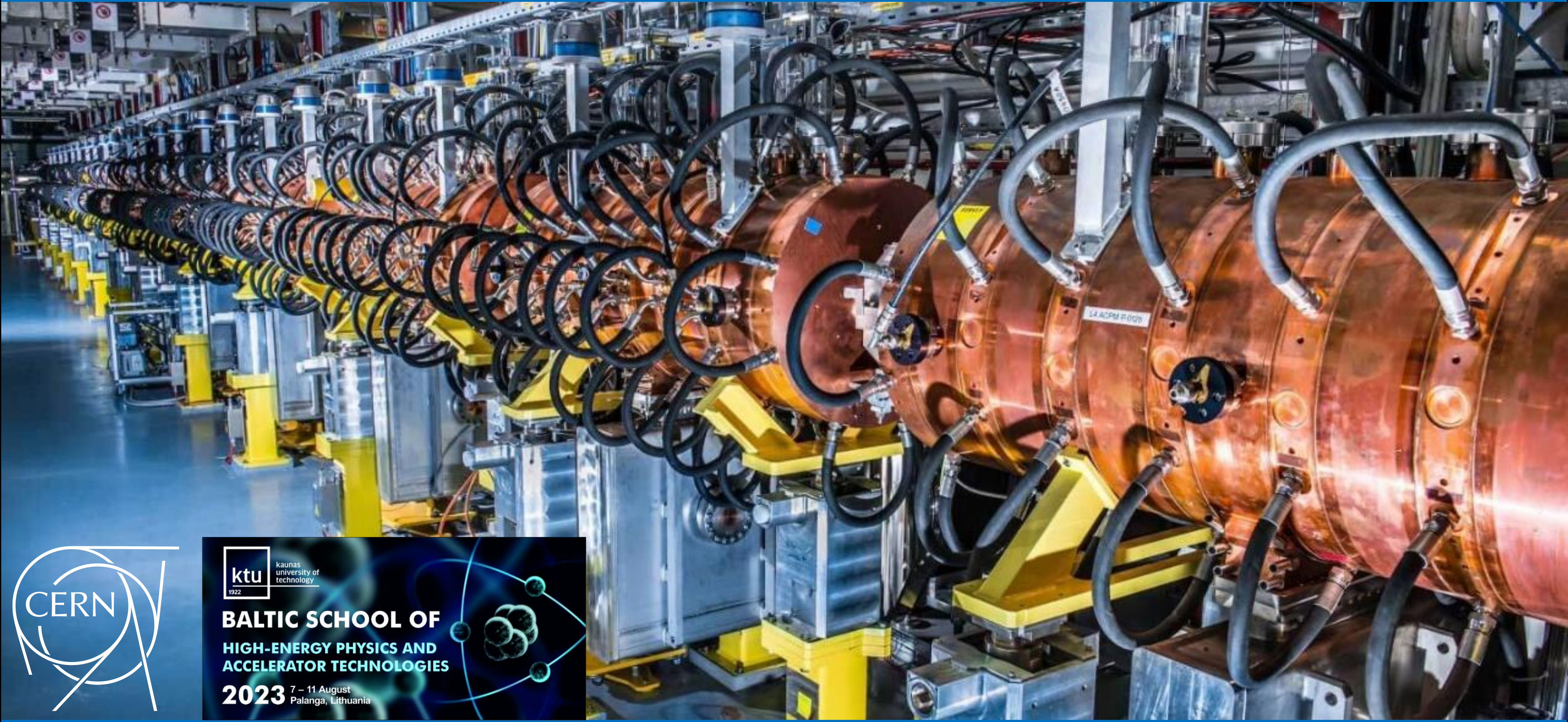
Maurizio Vretenar CERN

3rd Baltic School of High-Energy Physics and Accelerator Technologies



ktu kaunas university of technology 1922

BALTIC SCHOOL OF
HIGH-ENERGY PHYSICS AND
ACCELERATOR TECHNOLOGIES
2023 7 – 11 August
Palanga, Lithuania

2: Accelerators for society: industry, environment, health

Accelerators for Society

More than 35’000 particle accelerators are in operation world-wide.

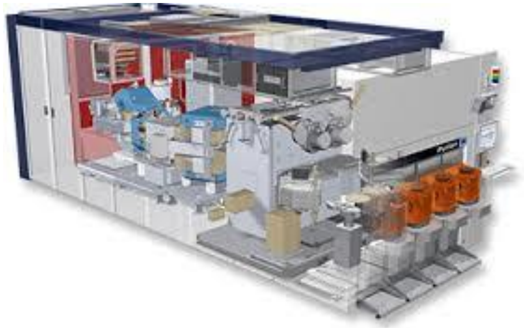
Only ~1% are used for fundamental research.

Medicine is the largest application with more than 1/3 of all accelerators.

Research		**6%**
	Particle Physics	0,5%
	Nuclear Physics, solid state, materials	0,2 - 0,9%
	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 (semiconductors)	34%
	Cutting and welding with electron beams	16%
	Polymerization	7%
	Neutron testing	3.5%
	Non destructive testing	2,3%

Radiotherapy electron linac

Proton cyclotron for radioisotope production



Commercial system for ion implantation

Accelerators for industry

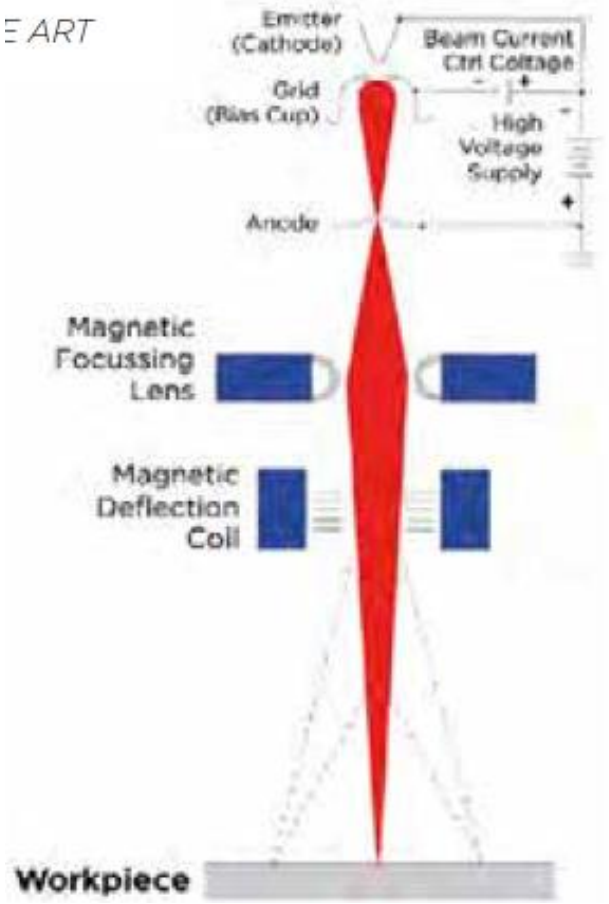
Very low energy electrons

	Energy	Applications
Very low energy electrons	<350 keV	detection, welding, 3D-sintering, sterilisation, seed and grain treatment
Low-energy electrons	<10 MeV	polymer modification, sterilisation, treatment of flue-gas, wastewater, sewage

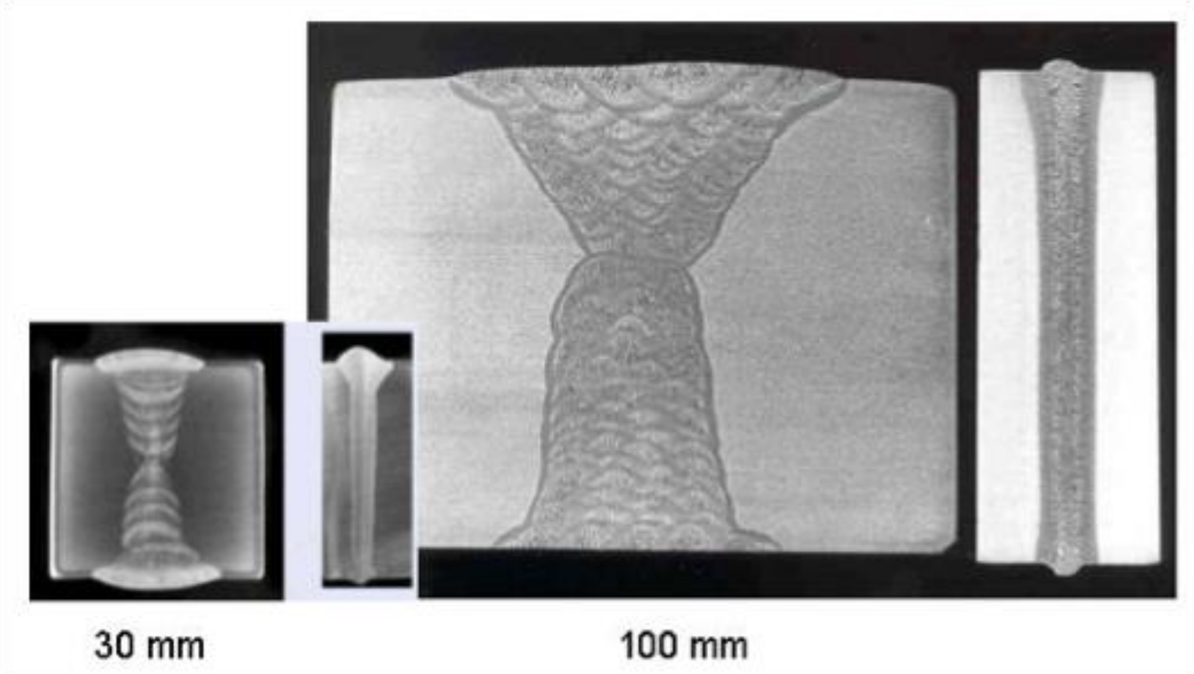
- ➢ Non-thermal: breaking molecular bonds, chemical modifications of organic materials, creation of radicals.
- ➢ Thermal: melting, evaporation, welding, joining, drilling, hardening, sintering,…

Fig. 4.7: An impressive example of an EB-welding application. In a huge vacuum chamber two 70-mm-thick aluminium plates, with a diameter of 6 metres, are joined with a 'single-shot'. It is the basic material used in forging and machining the main stage of Ariane-rocket tanks.

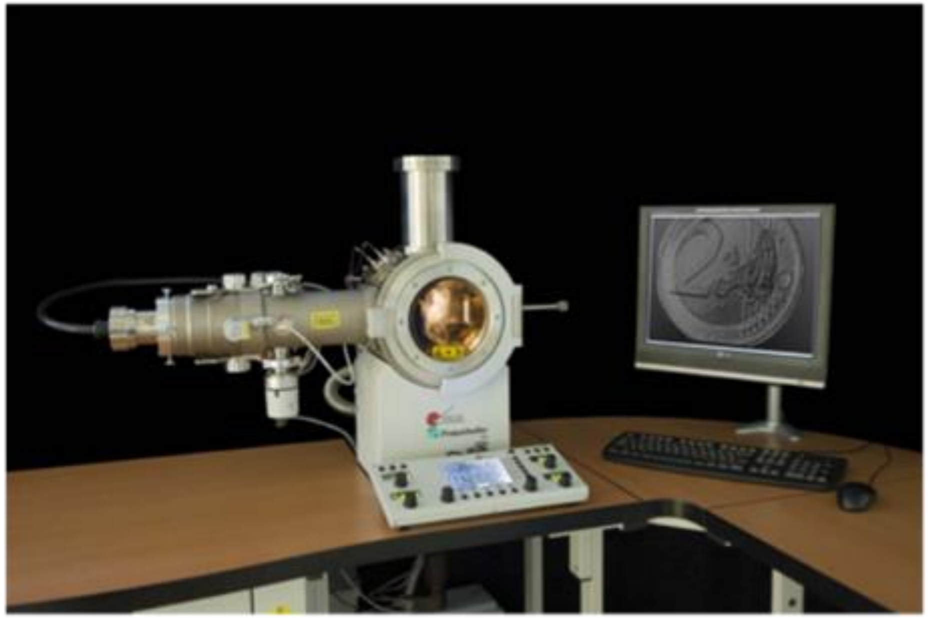
Fig. 4.8: A desk-top e-beam laboratory machine for welding and structuring with a magnified backscattered electron-image.



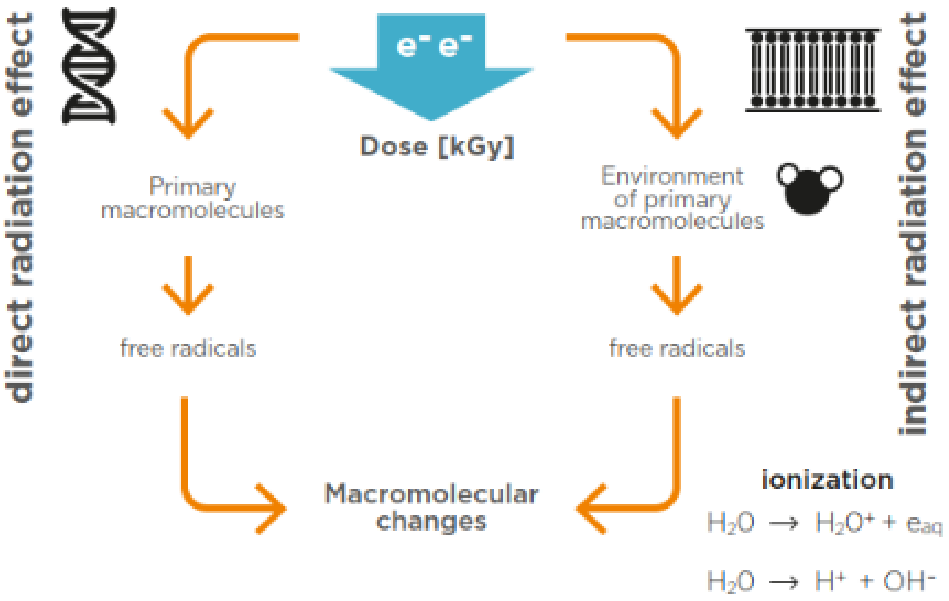
Electron beam welding



Cross-sections - Comparison of extensive TIG-welding with a lot of weld seams with the single-weld seam of EB-welding at the same material thickness



Sterilisation



direct radiation effect

e⁻ e⁻

Dose [kGy]

indirect radiation effect

Primary macromolecules

free radicals

Environment of primary macromolecules

free radicals

Macromolecular changes

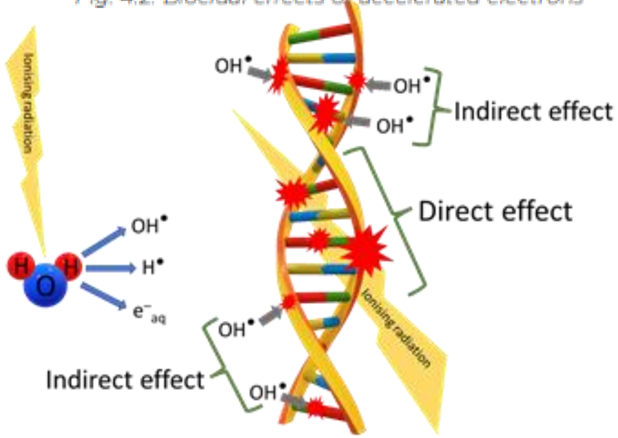
ionization

$H_2O \rightarrow H_2O^+ + e_{aq}$

$H_2O \rightarrow H^+ + OH^-$

- DNA Line-break (single, double)
- Change or damage of bases
- Denaturation
- Cross linking
- Absorption of proteins

Fig. 4.2: Biocidal effects of accelerated electrons



- Sterilisation processes caused by the breaking of molecular bonds associated with the water and DNA in microbial cells.
- Medical products (implants and instruments), food, and pharmaceutical packaging can be sterilised.
- Energy between 1 and 10 MeV, all surfaces must be accessible (small penetration depth).
- The world market-leader in the aseptic carton packaging of liquid foods has installed e-beam sterilisation machines in the majority of its production facilities.

Fig. 4.12: E-beam technology fo sterilising medical products

Fig. 4.13: Tetra Pak has a new generation of automated filling machines that uses e-beams to sterilise packaging.

Food sterilisation and radiophobia

Seed and crop treatment – *20 to 30% of food harvested is lost to rotting and insect infestation*
Crop seeds must be free from pathogens (fungi, bacteria and viruses) that can endanger health and food security. Standard treatment: chemical seed dressing that can result in the contamination of soil and ground water with waste products, drifting of dressing agents across fields, killing of probiotic microorganisms.

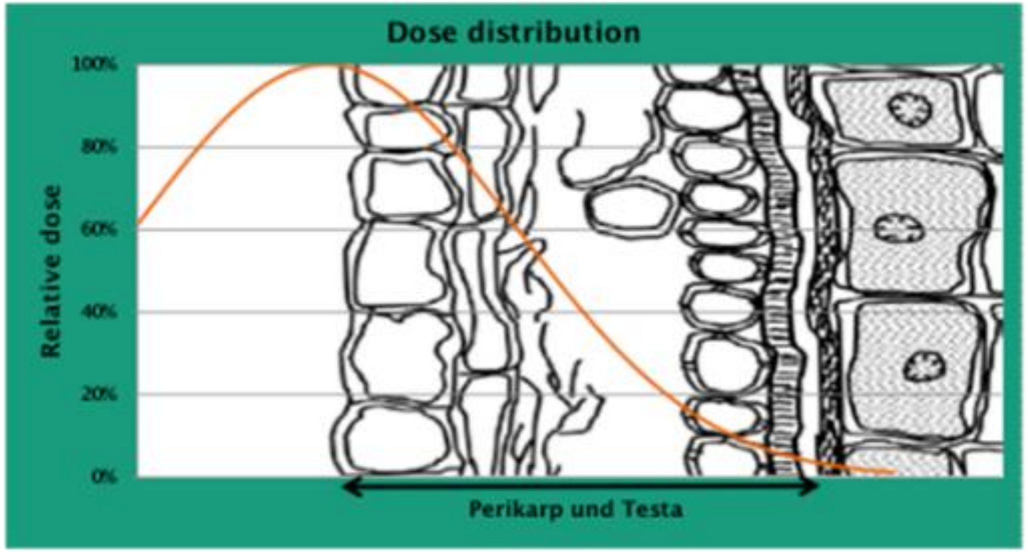
Alternative: physical disinfection of seed using the **biocidal effect of accelerated electrons**. By precisely adjusting the energy of the e-beam, contamination on the seed surface can be treated without damaging the DNA of the seed grain.

Advantages:

- no change in taste, texture of colour;
- no toxic residue;
- less energy consumption than e.g. steaming;

E-beam treatment diffusion is limited by **low social acceptance** of any association between “radiation” and “food”, which results (in Europe) in stringent regulatory constraints.

Crop treatment companies never use the word “radiation”…



Environmental applications of accelerators - 1

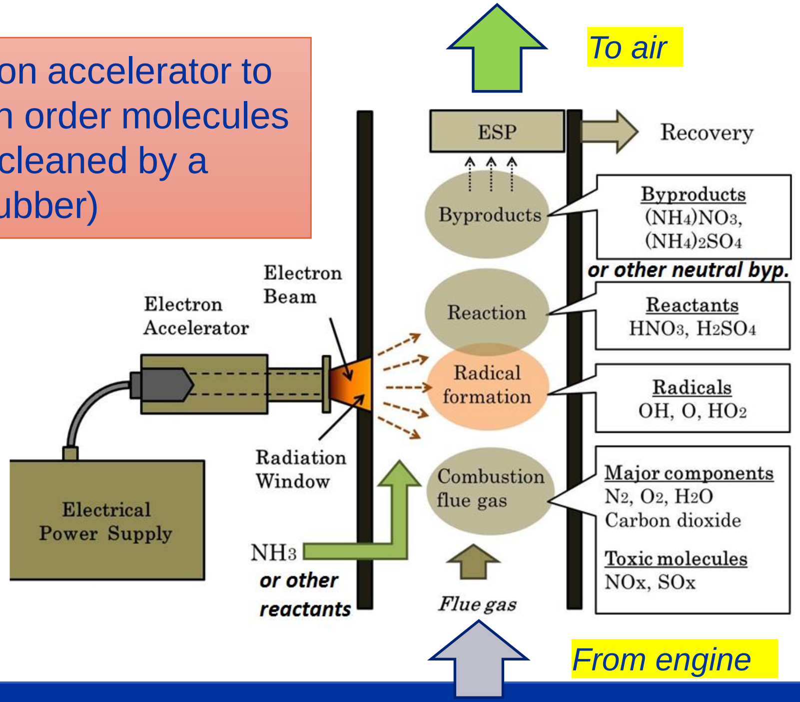
Low-energy electrons can break molecular bonds and be used for:
- Flue gas treatment (cleaning of SOx from smokes of fossil fuel power plants)
- Wastewater and sewage treatment
- Treatment of marine diesel exhaust gases (removal of SOx and NOx).

- **Maritime transport** is the largest contributor to air pollution: a cruise ship emits as much sulphur oxides as 1 million cars!
- Ships burn Heavy Fuel Oil, cheap but rich in Sulphur. Diesels (high efficiency) emit Nitrogen oxides and particulate matter.
- New legislation is going to drastically limit SOx and NOx emissions from shipping, with priority to critical coastal areas.
- So far, technical solutions exist to reduce SOx or NOx, but there is no economically viable solution for both.

Hybrid Exhaust Gas Cleaning Retrofit Technology for International Shipping (HERTIS)

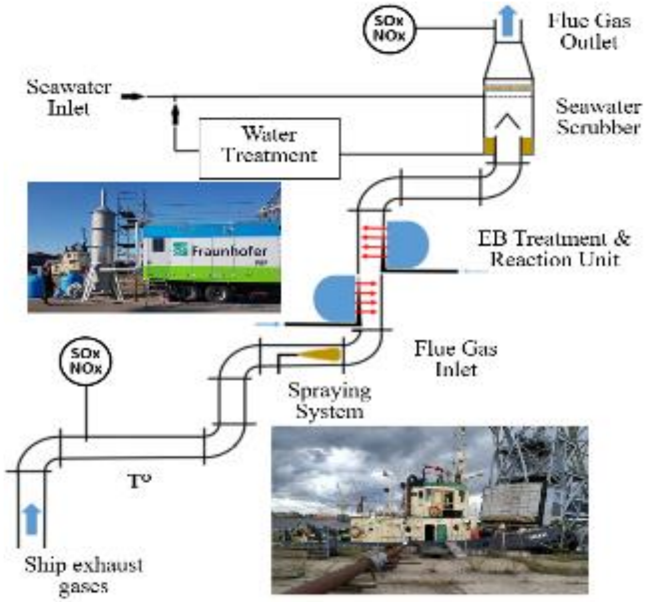
A project based on a patent from INCT Warsaw promoted by a collaboration of research institutions (including CERN), accelerator industry, shipyards, maritime companies, maritime associations (Germany, UK, Switzerland, Poland, Latvia, Italy).

150 kV electron accelerator to break the high order molecules that are then cleaned by a water jet (scrubber)



Test of HERTIS at Riga Shipyard, July 2019

Mobile electron accelerator system from FAP Dresden commonly used to treat crops connected to the exhaust funnel of the Orkāns, an old Soviet-built tugboat. The fumes then passed through a small water scrubber before being released in the air.

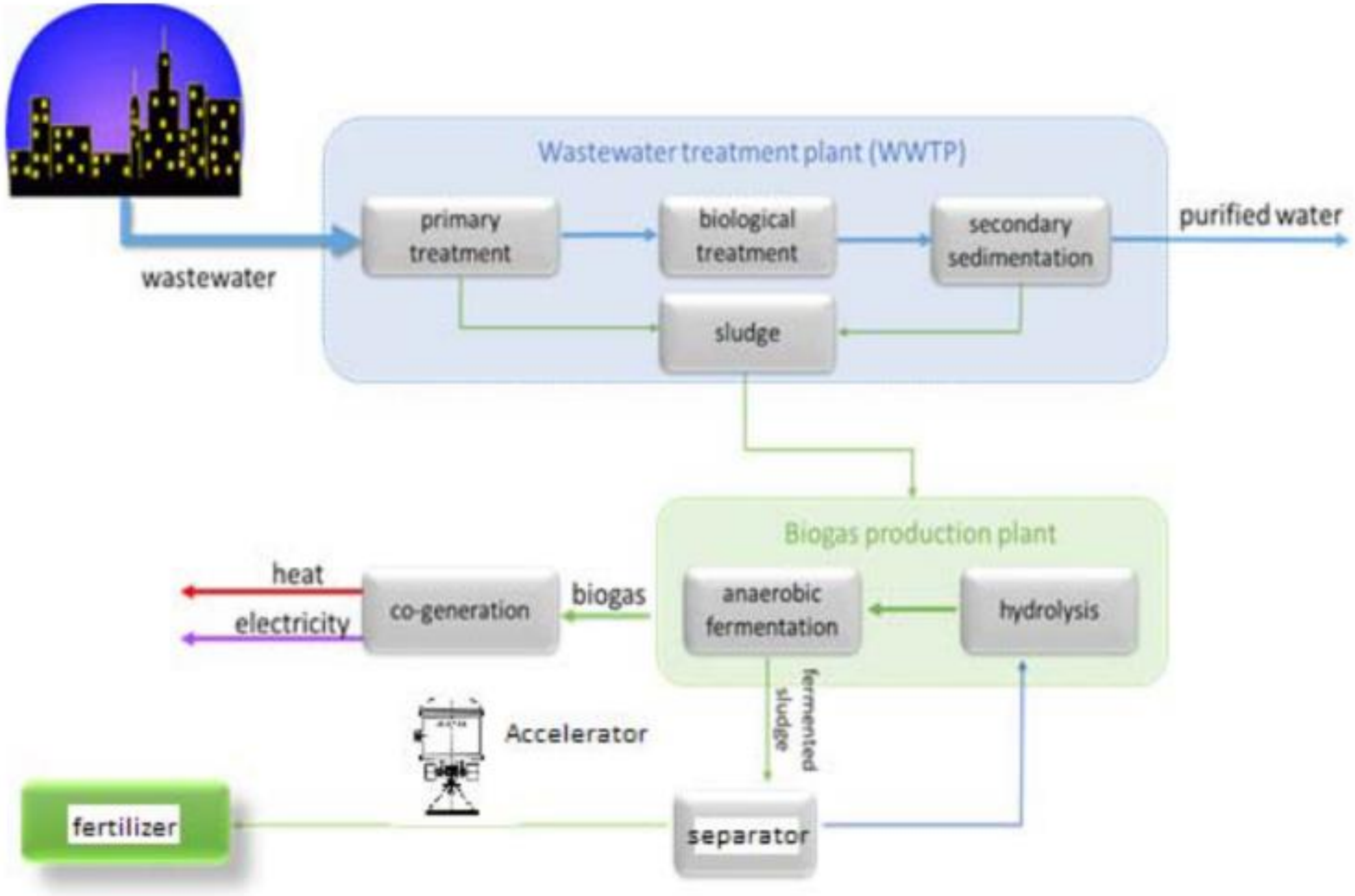


The tests confirmed the laboratory measurements and the overall effectiveness of the system.

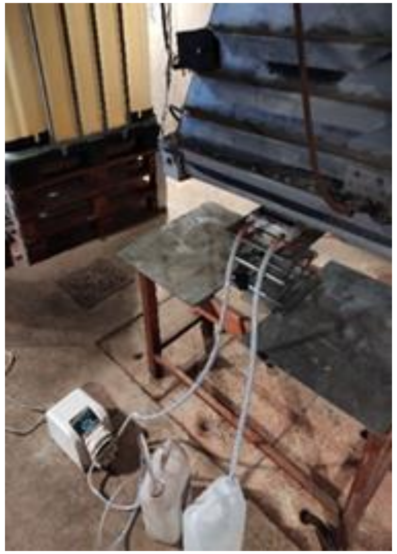
Measured **NOx removal rate 45%** at full engine power with the available scrubber and accelerator.
Estimated removal with optimised scrubber and homogeneous e-beam 98%.
SOx removal only measured in laboratory (no Sulphur allowed in port) with similar removal rates.

Environmental applications of accelerators - 2

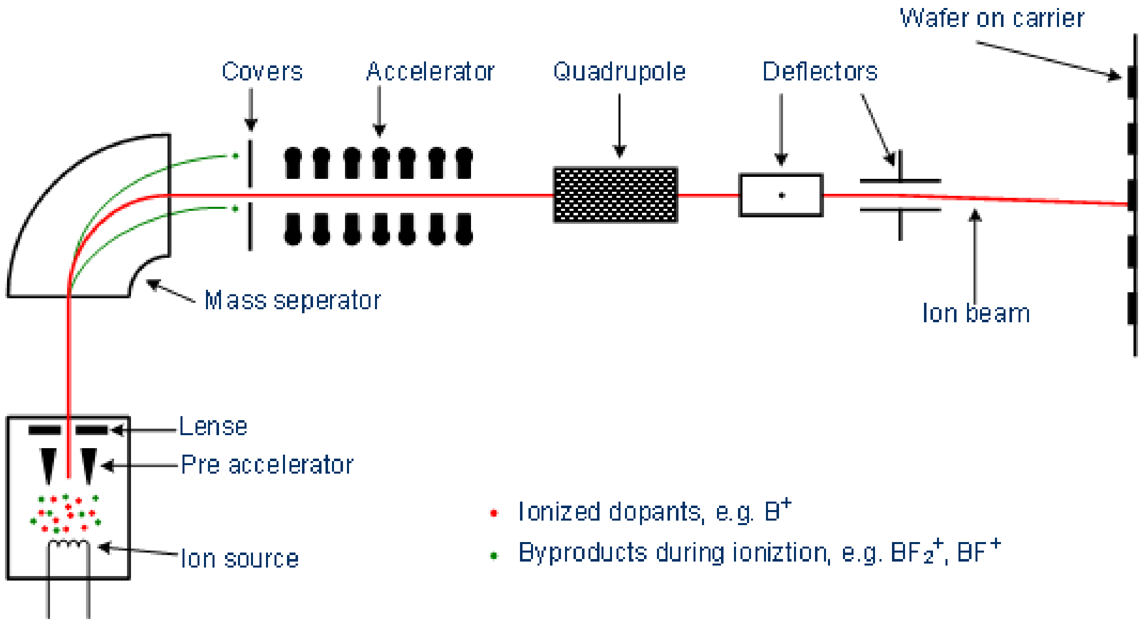
Design of an advanced electron accelerator plant for biohazards treatment



Sludge produced in municipal sewage treatment plants is highly contaminated with parasite eggs.
An expensive hygienization process is needed before agricultural utilization, with the consequence that in most cases the sludge is dumped.
Treatment with an electron accelerators provides a simple and inexpensive way to sanitize sludge and directly convert it into fertiliser, using the energy produced onsite.



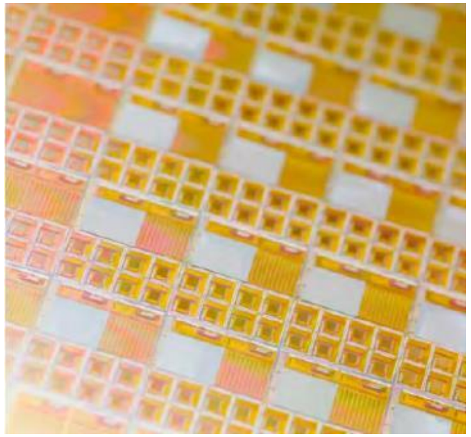
Ion implantation

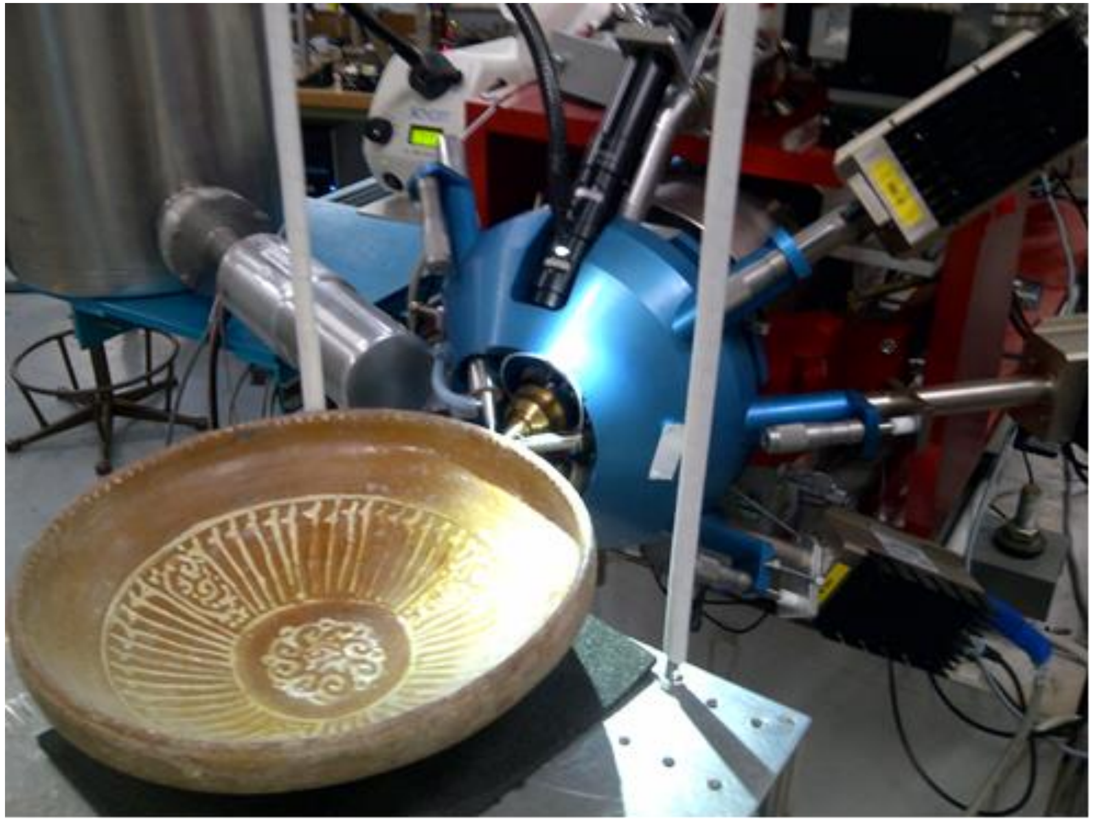


The **semiconductor industry** requires ion implantation to introduce atoms into semiconducting materials to alter their electronic properties (doping).
Huge industry and one of the most important uses of particle accelerators.

Developing into research for quantum computing (single ions with nanometre-scale spatial accuracy) and novel opto-electronic devices (nano-precipitates in silicon-dioxide layers for light-emitting devices).

Commercial system for ion implantation





Surface analysis

Accelerators for art

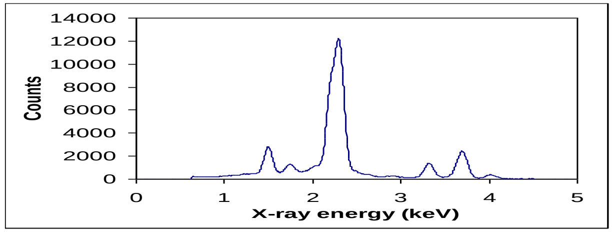
PIXE, Proton Induced X-ray Emission

A beam of particles (protons) from an accelerator is sent on a sample (e.g. a painting)

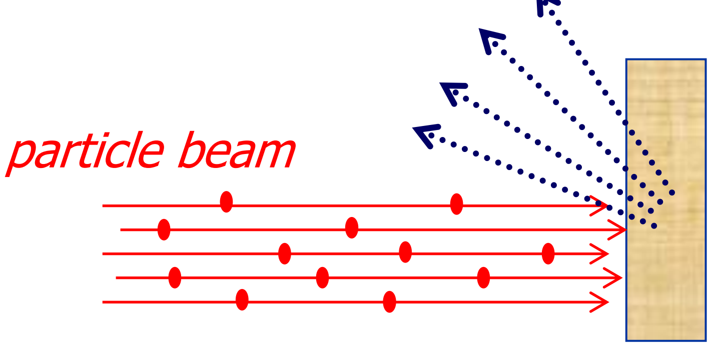
The atoms are excited and emit different types of radiation (X-rays, gammas, etc.)

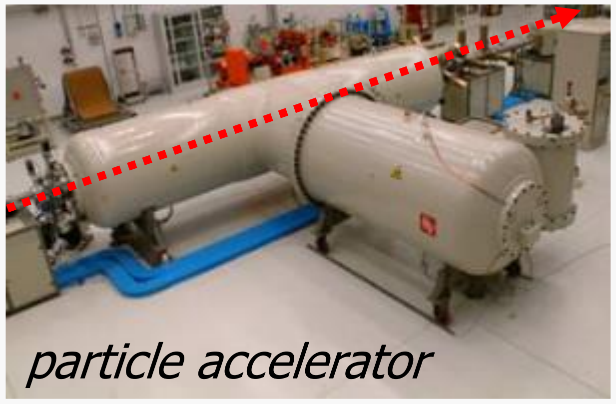
Different atomic elements emit X-rays at different energies – Spectral analysis from one or more detectors allows determination of the chemical composition (e.g. of the pigments).

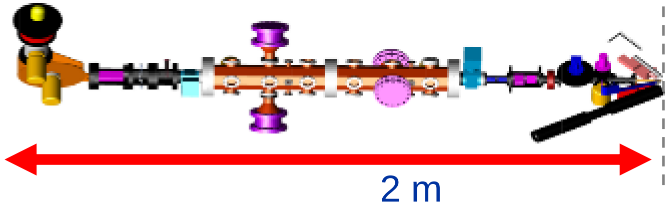
Radiation detection and spectral analysis



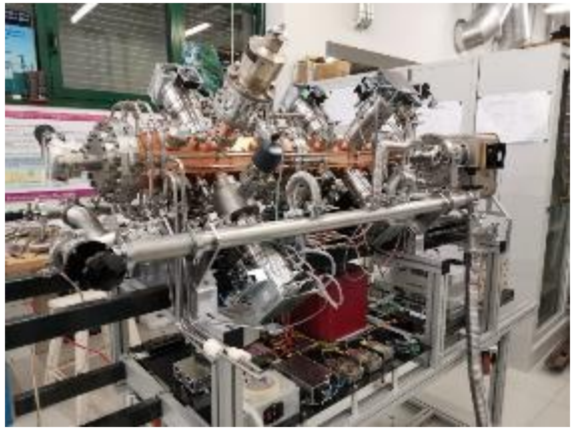
Emission of radiation of __characteristic energies__ (X-rays, γ, particles…)





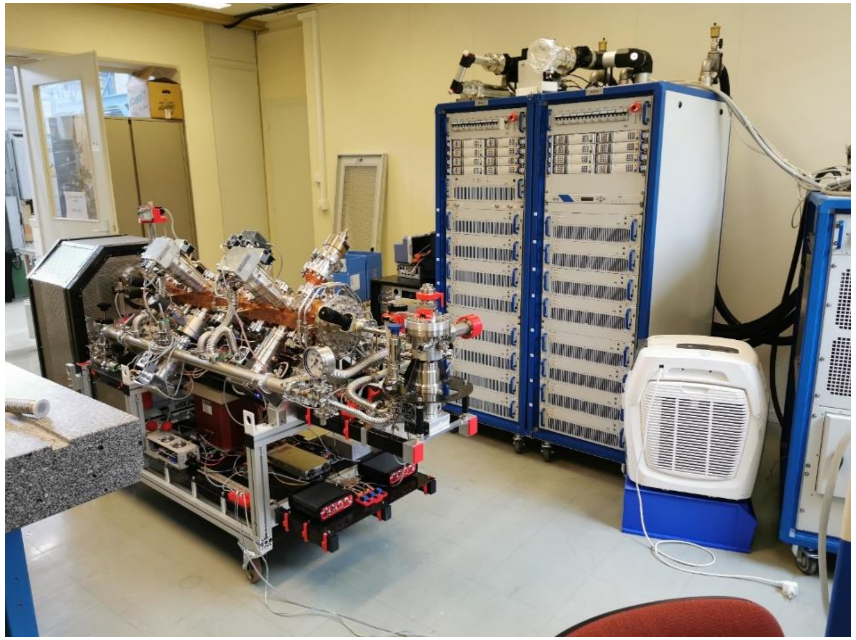


Ritratto Trivulzio by Antonello da Messina, 1476 – analysis at INFN-LABEC (Florence)



Portable PIXE system based on an RFQ linac built by CERN and LABEC

The MACHINA project



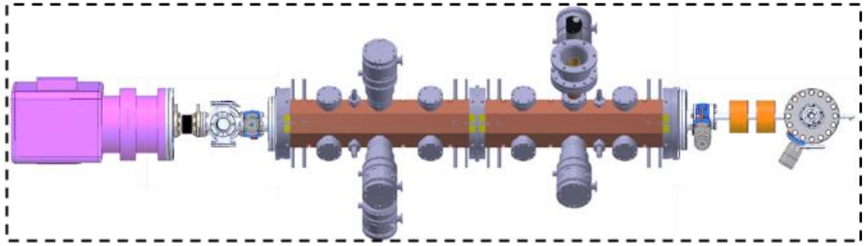
MACHINA (Movable Accelerator for Cultural Heritage In situ Analysis) project of CERN and INFN.

Construction of a transportable RFQ (PIXE-RFQ) optimized for the analysis of material with a 2 MeV proton beam.

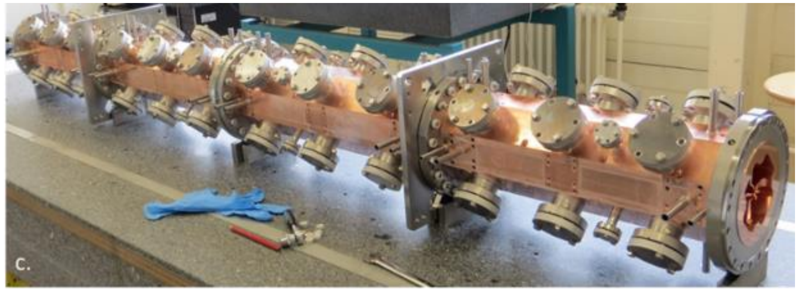
Will be installed in the Opificio delle Pietre Dure in Florence (Italian central institution for artwork analysis)

RF Frequency (MHz)	749.48
Length (mm)	1072.938
Input Energy (MeV)	0.02
Output Energy (MeV)	2

Average Current (nA)	5
Peak Current (nA)	200
Repetion Rate (Hz)	200
Pulse Duration (ms)	0.125
Duty Cycle (%)	2.5
Vane Voltage (kV)	35



Accelerator: ≈ 2.35 x 0.6 = 1.4 m^2



Towards the miniature accelerator?

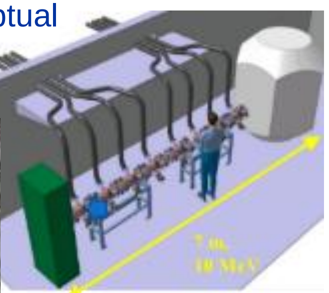
Important trend towards miniaturization of accelerators, for use in medicine and industry

Here are presented only three examples of recent developments at CERN:

The mini-RFQ

750 MHz
92 mm diameter
2.5 MeV/m

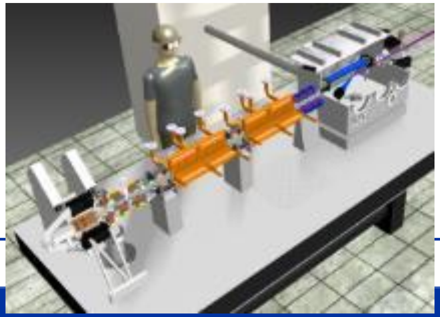
Proton therapy injector (in operation)
Artwork PIXE analysis (in construction, transportable)
Isotope production (design)
Neutron radiography (conceptual stage)



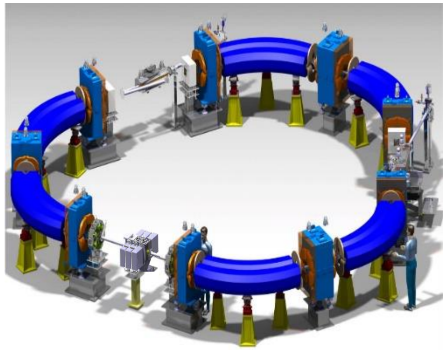
X-band structures

12 GHz
100 MeV/m

Developed for CLIC, in operation at CLIC test stand
- Compact XFEL (CompactLight Design Study)
- VHEE and FLASH therapy linac (design)
- SmartLight (table top inverse Compton scattering light source, design)

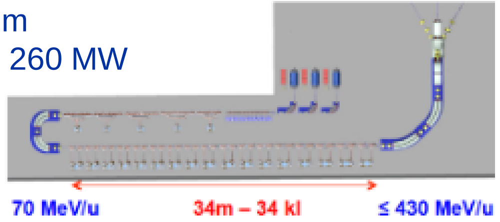


Compact accelerators for ion therapy



Superconducting C-ion synchrotron
Bmax 3.5 T
27m circumference

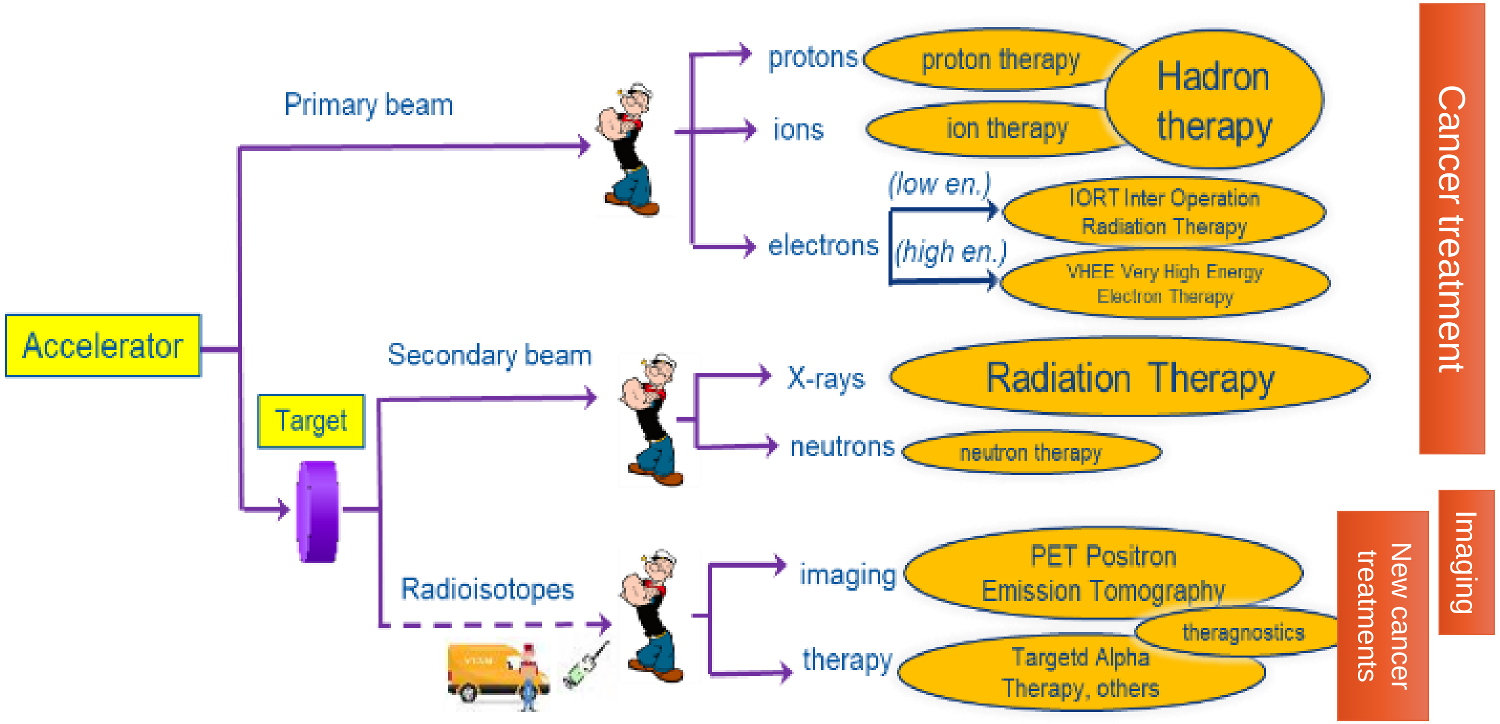
Folded C-ion linac,
Tot. length 53 m
Tot. RF power 260 MW



Medical applications of accelerators

Particle accelerators: a formidable tool for medicine

Accelerators are the way to realise the old dream of a **bloodless surgery and imaging**: penetrate into the human body to treat diseases and to observe internal organs without using surgical tools.



Accelerator

Primary beam

protons – proton therapy

ions – ion therapy

Hadron therapy

electrons

(low en.) – IORT Inter Operation Radiation Therapy

(high en.) – VHEE Very High Energy Electron Therapy

Target

Secondary beam

X-rays – Radiation Therapy

neutrons – neutron therapy

Radioisotopes

imaging – PET Positron Emission Tomography

theragnostics

therapy – Targetd Alpha Therapy, others

Cancer treatment

Imaging

New cancer treatments

Operating facilities

> 150

12

>300

0

≈ 14’000

7

≈ 1’500

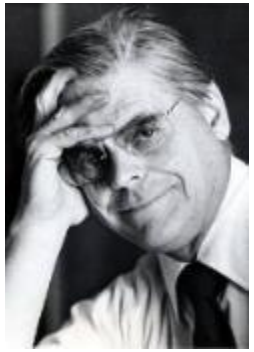
0

≈ 16’000 particle accelerators operating for medicine worldwide, in cancer therapy and imaging

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.

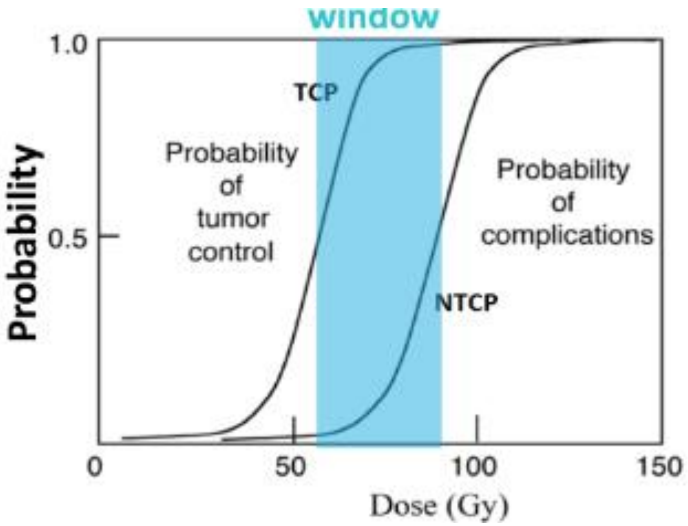


Modern accelerators for cancer treatment and isotope production

There are today about 16'000 accelerators in hospitals or working for hospitals, complex devices that have specific requirements, somehow different from a scientific accelerator:

- The beam must be perfectly known, stable and reliable.
- The accelerator (as the radiopharmaceutical unit in case of production of isotopes) have to follow strict Quality Assurance procedures.

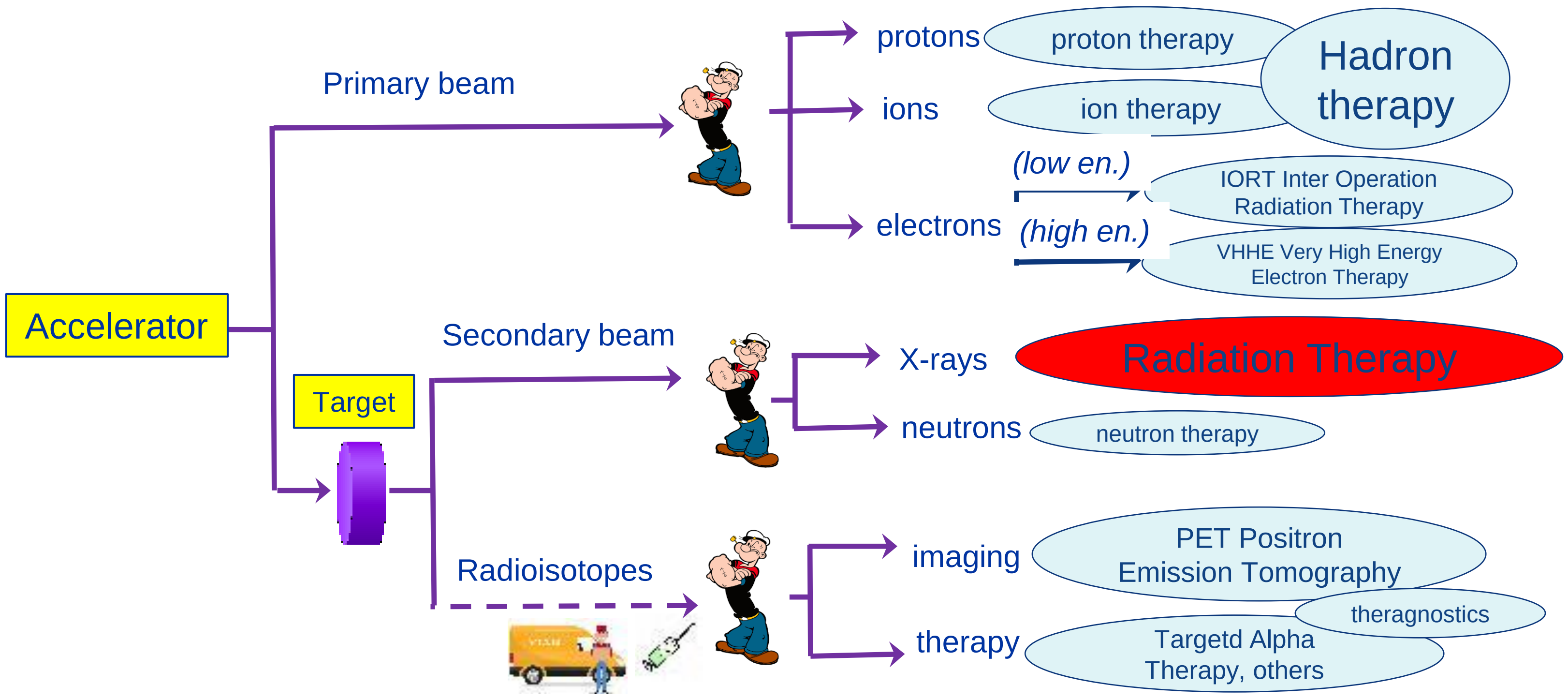
The role of the medical physicist is essential in planning the treatment and in guaranteeing the delivered dose.



*The "**therapeutic window**":*
TCP=Tumor control probability
NTCO=normal tissue complication probability

From the early tests at Lawrence's cyclotron to a modern treatment room at CNAO

1. Radiation therapy



Accelerator

Primary beam

protons

proton therapy

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ion therapy

Hadron therapy

electrons

(low en.)

IORT Inter Operation Radiation Therapy

(high en.)

VHHE Very High Energy Electron Therapy

Target

Secondary beam

X-rays

Radiation Therapy

neutrons

neutron therapy

Radioisotopes

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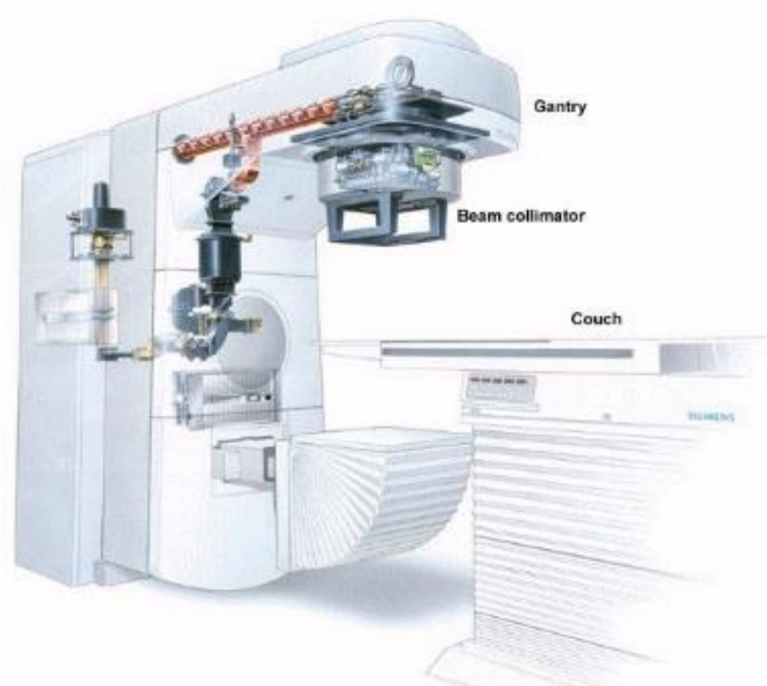
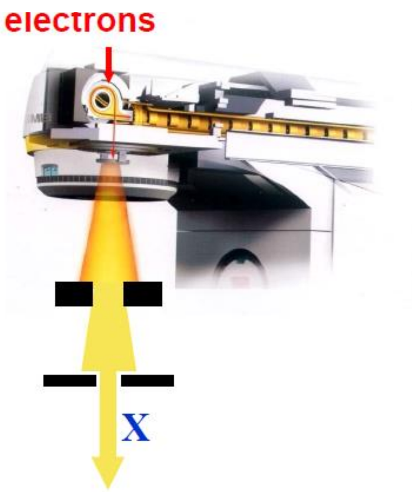
Targetd Alpha Therapy, others

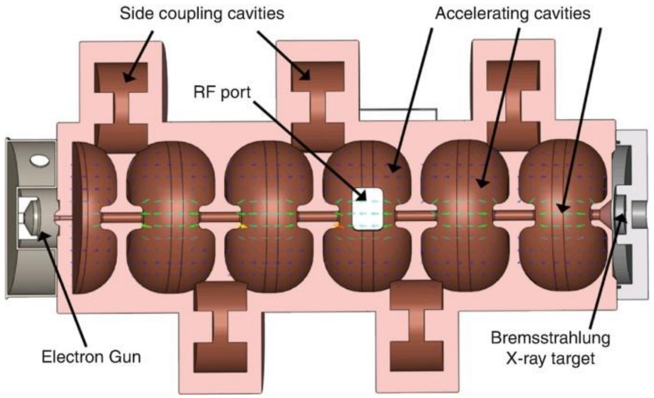
The most successful accelerator

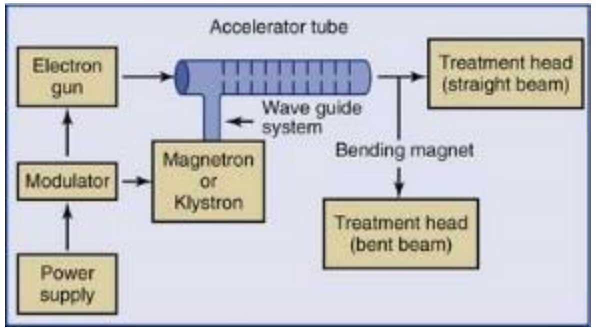
Electron Linac (linear accelerator) for radiotherapy (X-ray treatment of cancer)





5 – 25 MeV
e-beam
Tungsten
target

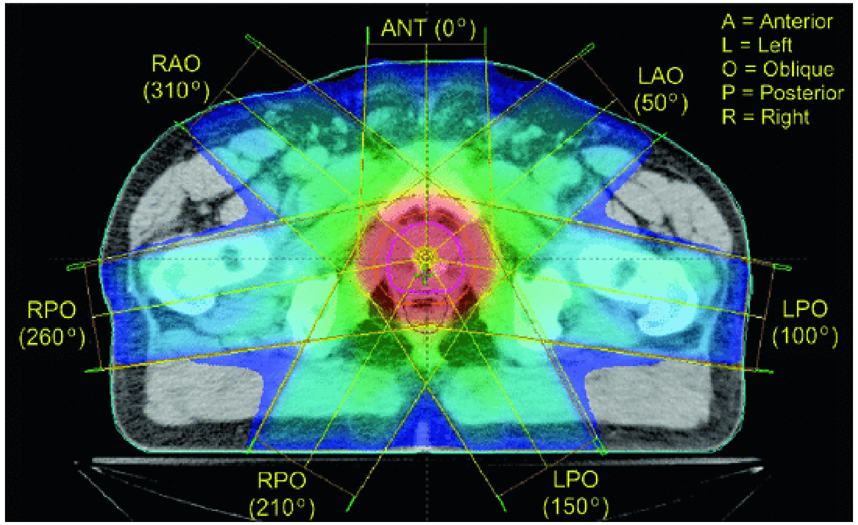




14,000 in operation worldwide!

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.

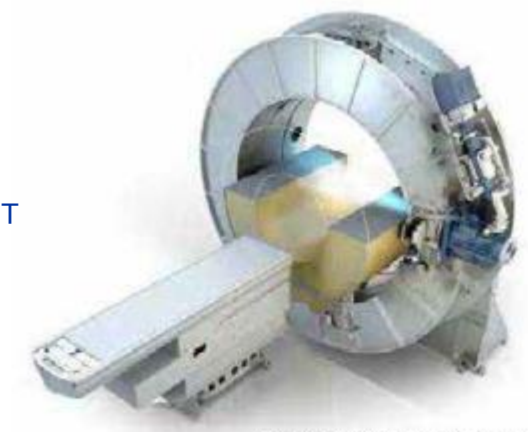
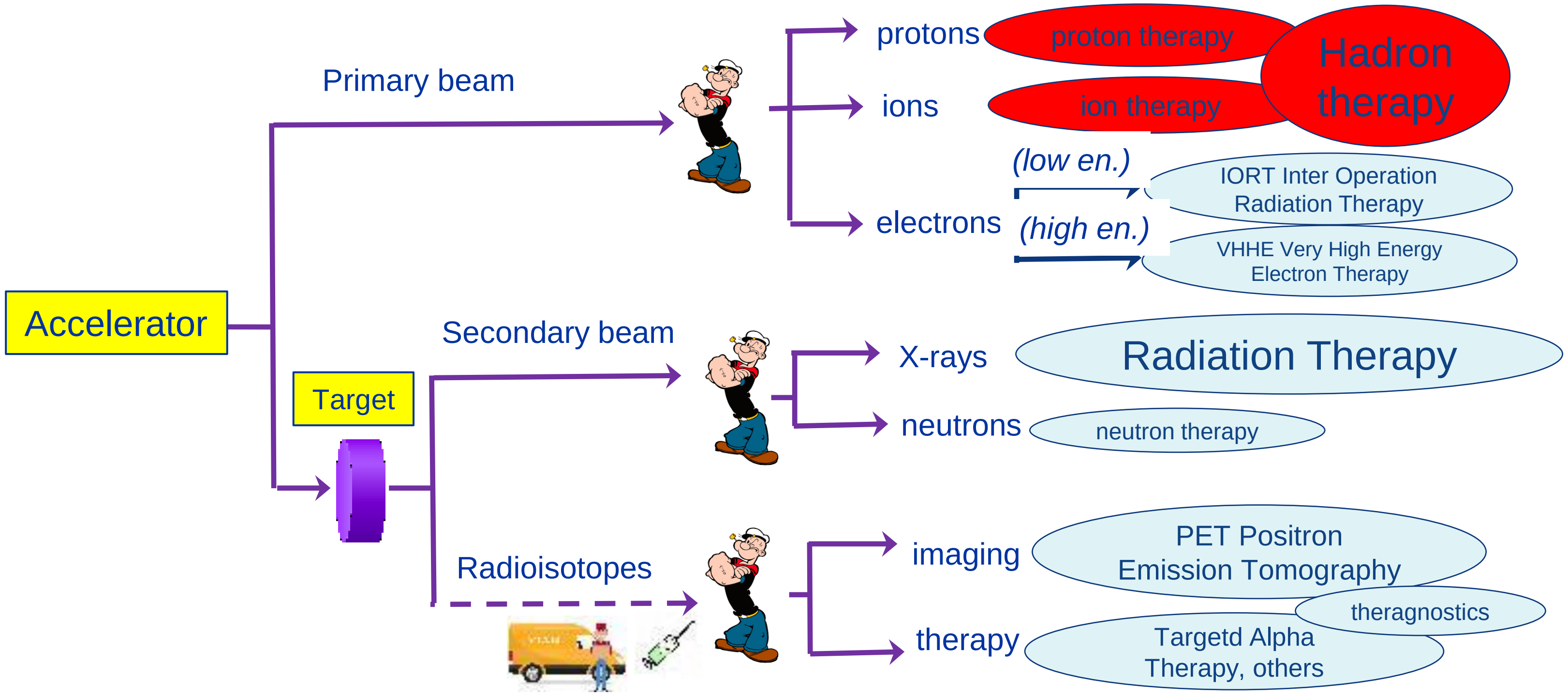


Fig. 3.4: The MR-linac, developed by Elekta, consists of a linear accelerator equipped with multi-leaf collimator technology for accurate radiotherapy dosage, combined with a high-field MR imaging system. The MR-linac is work in progress and is not available for sale or distribution (courtesy of Elekta).

2 – Hadron therapy (protons and ions)



Accelerator

Primary beam

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Secondary beam

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neutrons

neutron therapy

Radioisotopes

imaging

PET Positron Emission Tomography

theragnostics

therapy

Targetd Alpha Therapy, others

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

Treating cancer with proton and ion beams

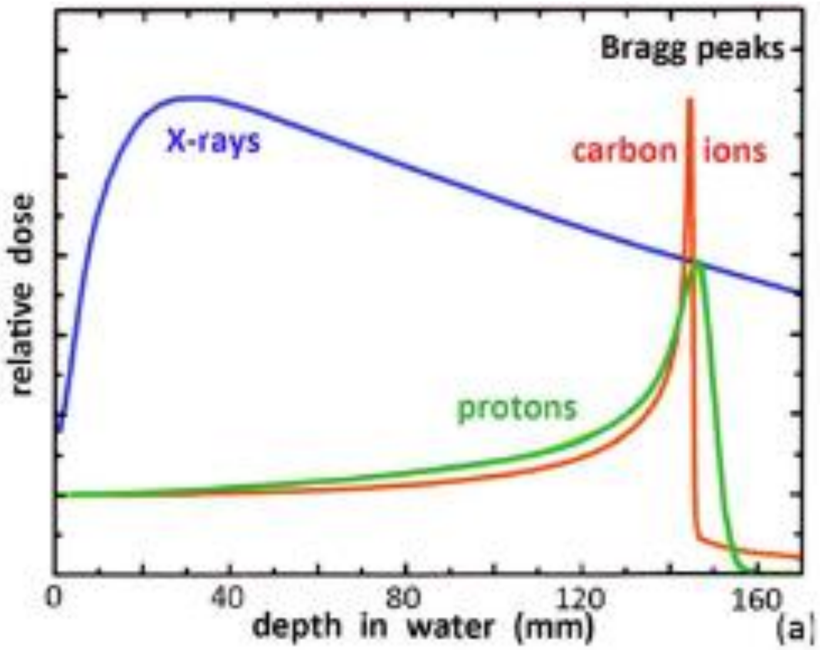
Cancer today: ~ 65% of cancers are curable; ~ 35% of cancer treatments fail, 2/3 because of metastasis, 1/3 in the primary site.

- **Priority of cancer research** is treating the >10% “not curable” cancers, usually large, deep seated, radioresistant.
- **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».

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

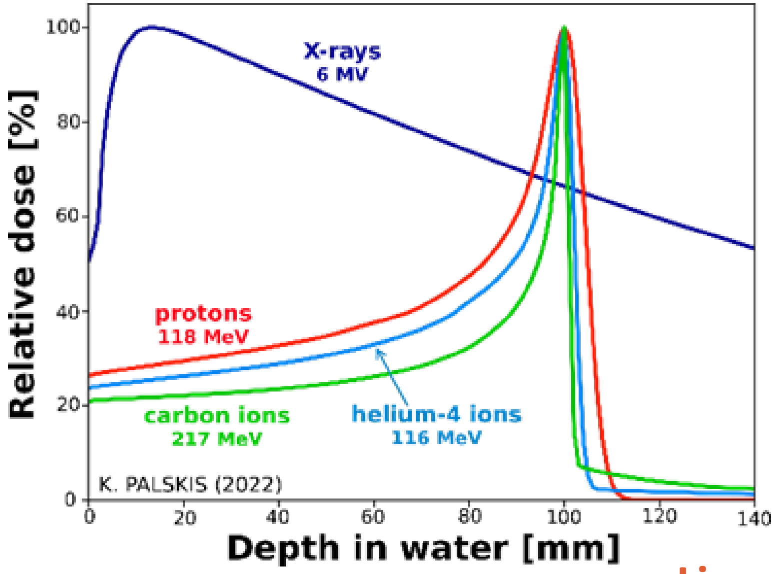
Bethe-Bloch equation of ionization energy loss by charged particles (~1/β²)



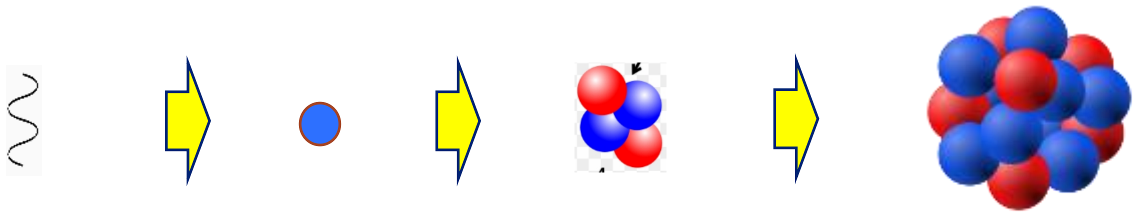
Required **energy** to penetrate the full body (about 33 cm): 230 MeV protons, 430 MeV/u carbon ions.

Required **beam current**: generally small, 10 nA for a typical dose of 1 Gy to 1 liter in 1 minute.

Comparing photons, protons, and ions



m_0= 1.67 × 10^{-27} kilograms

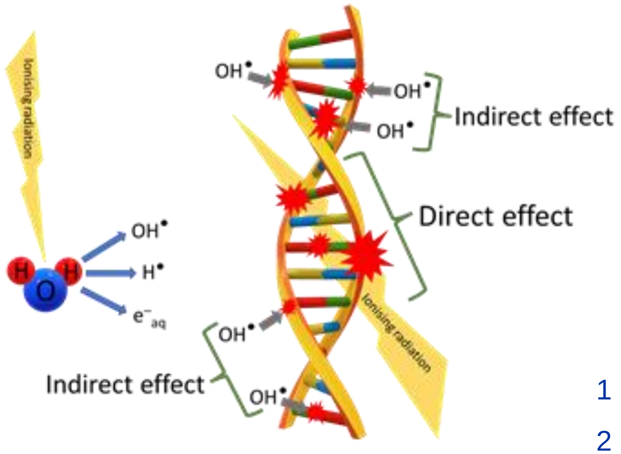


Photon (X-ray)
no mass

Proton
mass: 1 m_0

Helium ion
mass: 4 m_0

Carbon ion
mass: 12 m_0



Linear Energy Transfer low → high

Effect on DNA[1] indirect (via ROS) → direct (SSB and DSB)

Conformality low → high → high + fragm.

Required Energy[2] low → medium → high

Size of accelerator small → medium → large

Number of op. units ~15,000 108 0 14

---

[1] ROS = Reactive Oxygen Species, SSB = Single Strand Breaking, DSB = Double Strand Breaking

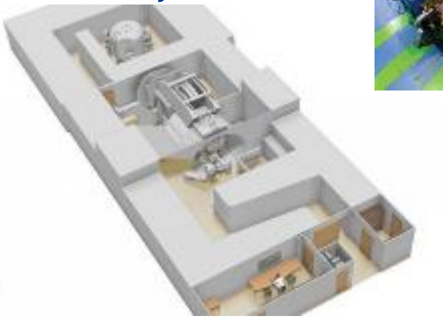
[2] Energy required for full body penetration (30-35 cm)

Comparing accelerator designs

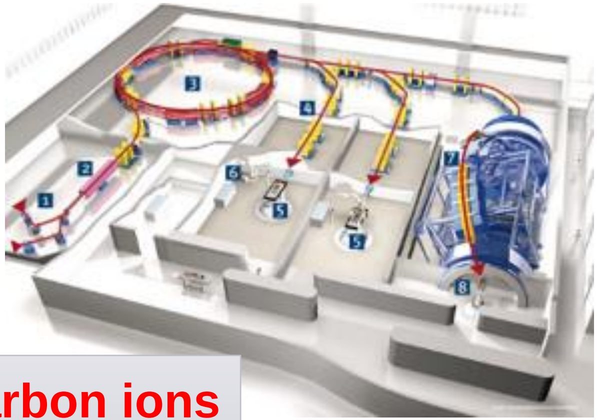
Ions deliver more energy to the tissues but need more energy to enter the body → factor 2.8 in accelerator diameter going from protons to carbon

Linac, X-rays
~50 m^2
~few M€

courtesy IBA



Cyclotron, protons
~500 m^2
~few 10 M€

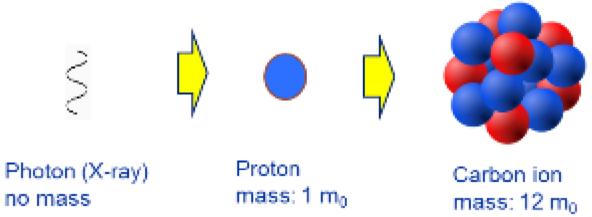


Synchrotron, carbon ions
~5,000 m^2
>200 M€

Commercially available

Specially designed and built

Space for translational R&D



Range: max. 300 mm (Bragg Peak)

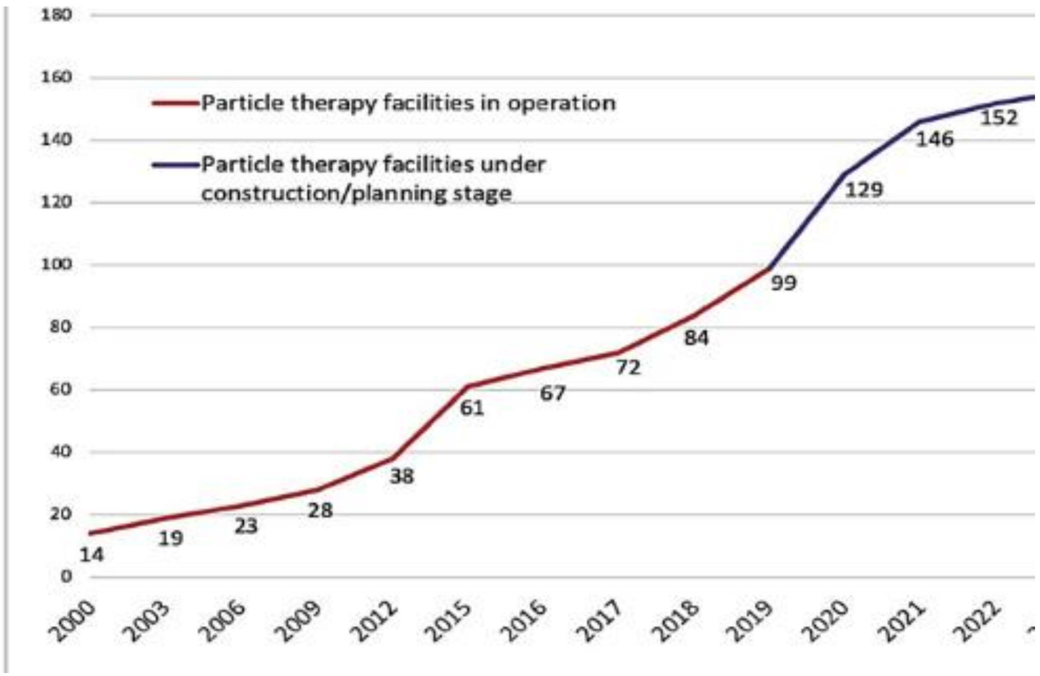
Protons: 220 MeV (max. $B\rho$ = 2.4 Tm)

Helium: 220 MeV/u (max. $B\rho$ = 4.5 Tm)

Carbon: 400 MeV/u (max. $B\rho$ = 6.3 Tm)

The rise of particle therapy

- After the first facilities built in the 90's (1993 US, 1994 Japan, 1997 Germany), a constant increase of operational facilities worldwide.
- From 2006, proton therapy becomes commercial. There are today 5 vendors on the market.
- Total today >140 facilities for protons, 15 for carbon ions.



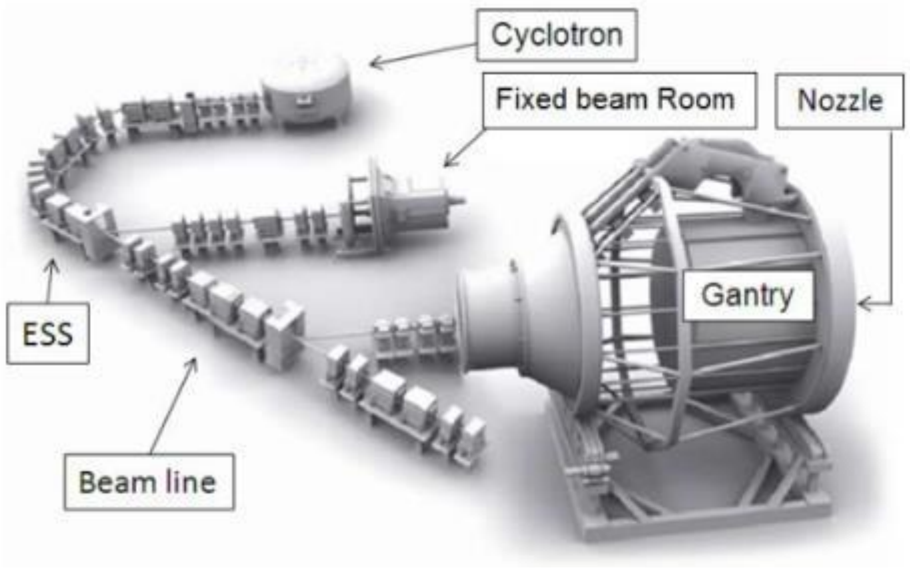
ptcog.com

Particle therapy centres in Europe. Courtesy of ENLIGHT, 2020

Only 2 regions in Europe without particle therapy:

- South East Europe
- Baltics

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).

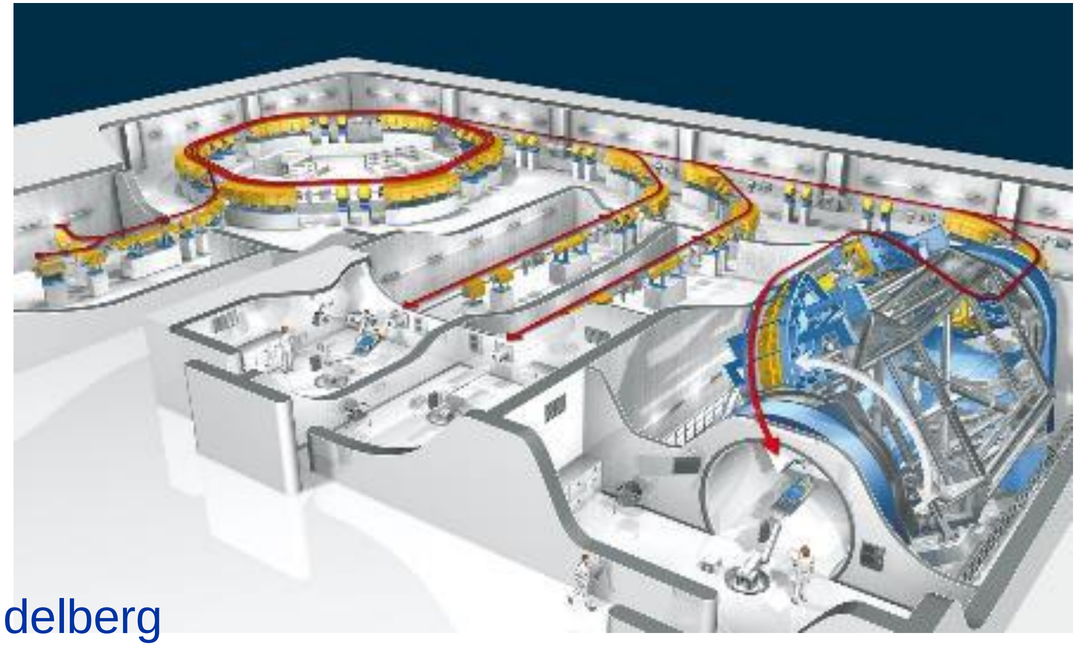
Critical issues with cyclotrons:

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. Beam loss indices activation requiring large shielding

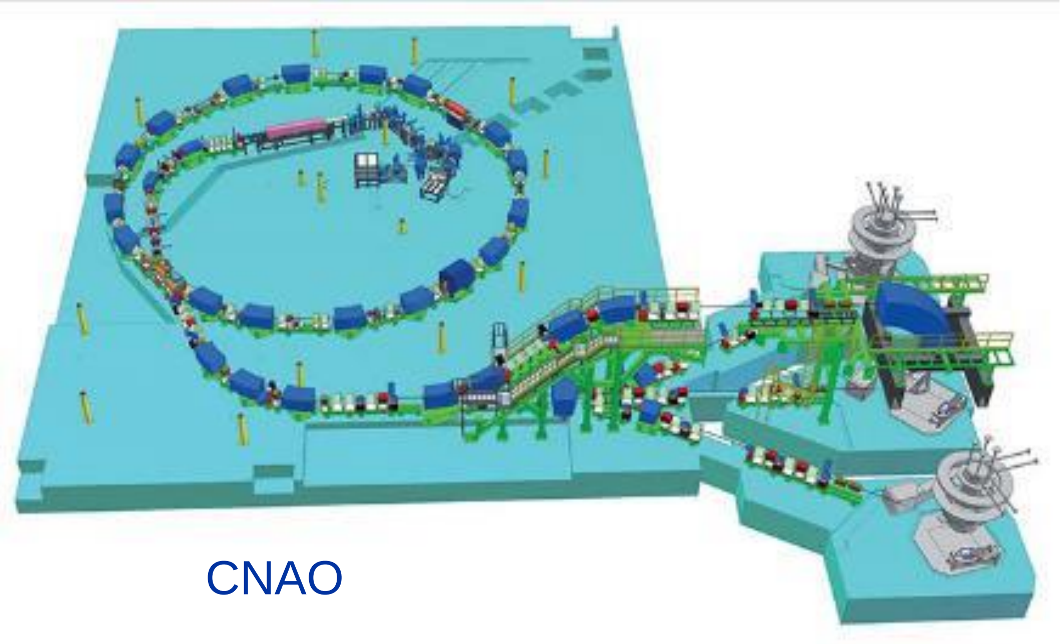
ProteusOne and ProteusPlus turn-key proton therapy solutions from IBA (Belgium)

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

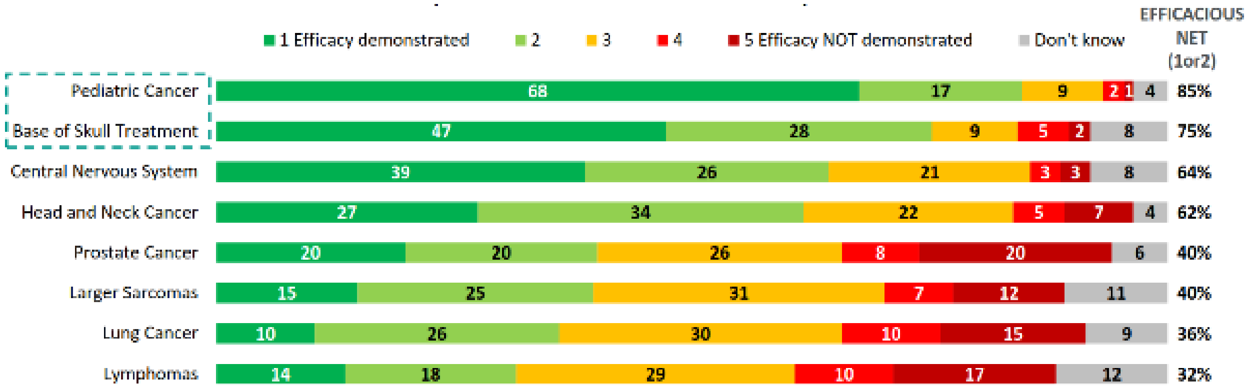


CNAO

The advantages of particle therapy

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 more **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!

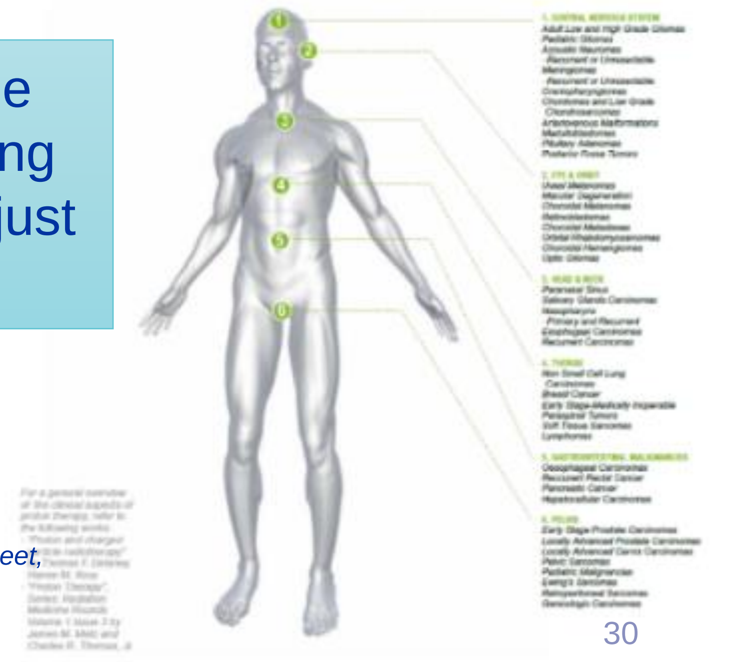
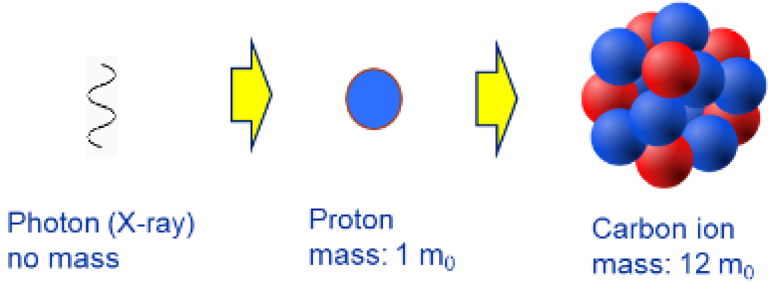


Image: IBA proton therapy fact-sheet,

Advantages of heavier ions

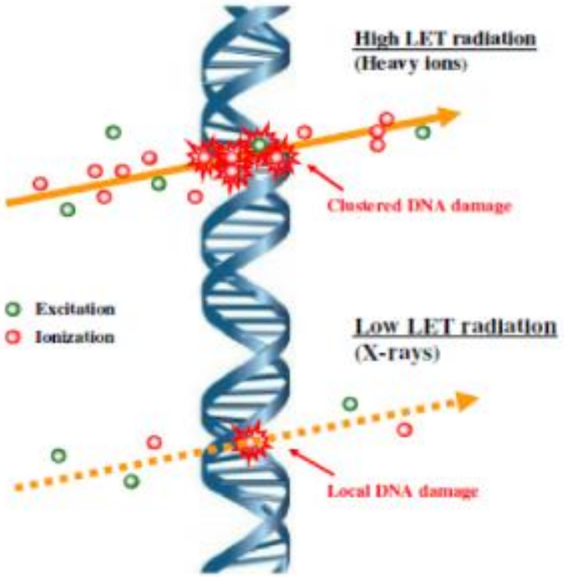
High LET radiation (ions) generates denser ionisations inducing clustered DNA lesions difficult for the cell to repair.

→ **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.



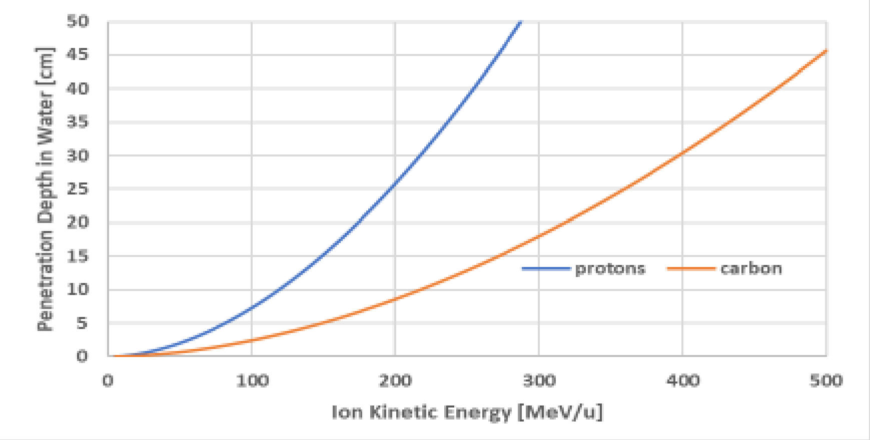
Helm A, Ebner DK, Tinganelli W, Simoniello P, Bisio A, Marchesano V, et al. Combining heavy-ion therapy with immunotherapy: an update on recent developments. Int J Part Ther. (2018) 5:84–93.
Durante M, Formenti S. Harnessing radiation to improve immunotherapy: better with particles? Br J Radiol. (2019)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



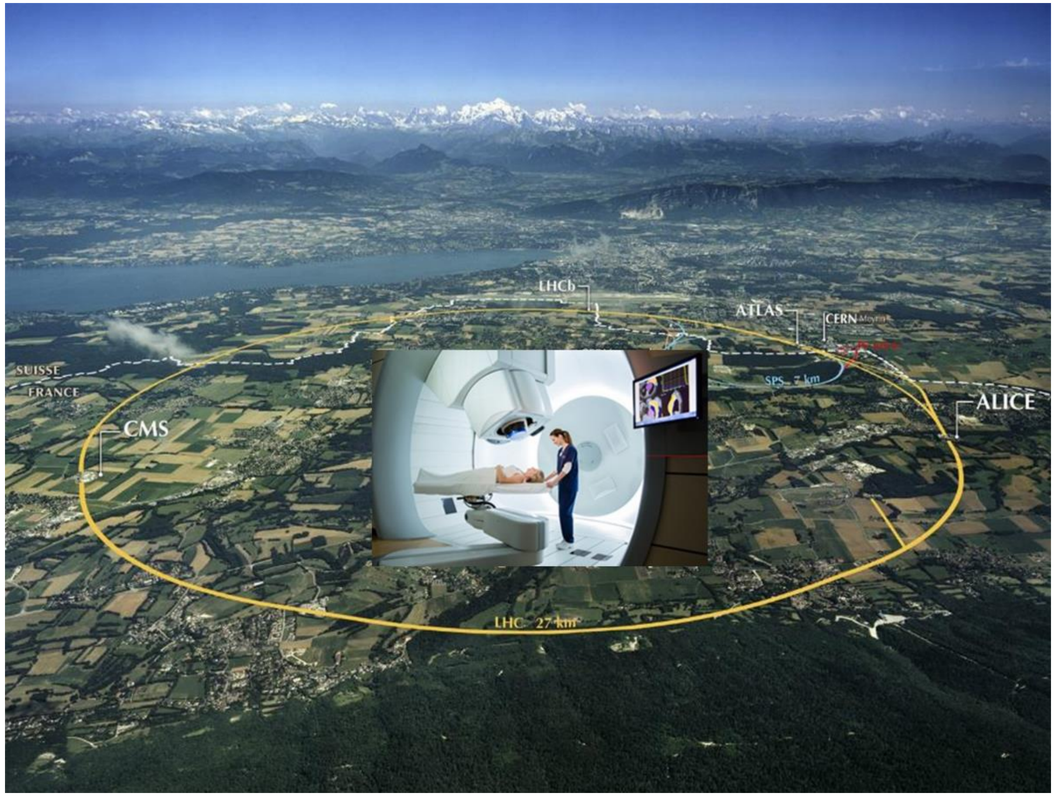
$$Br\,[T.m] = 3.3356 \times pc[GeV]$$

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.



Medical accelerator activities at CERN

A strategy for CERN: the Next Ion Medical Machine Study

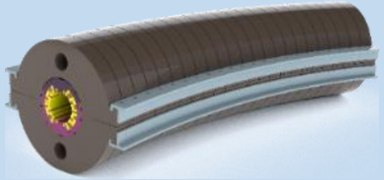
- **Proton** therapy is now commercial, and CERN, as an international organisation, cannot interfere with a mature commercial market.
- Therapy with **heavier ions** is still in an early phase despite its advantages. Its diffusion is limited mainly by:
  - ✓ **Size and cost of the accelerator**;
  - ✓ **Lack of experimental data**.
- New demands from the medical community and new opportunities from recent research can be integrated in a newly designed ion therapy facility.

Approval in 2019 of the **Next Ion Medical Machine Study (NIMMS)** in the frame of the CERN Knowledge Transfer for Medical Applications.

In line with CERN mission, the goal of NIMMS is to build on CERN expertise to develop a portfolio of technologies that can be used in a next generation facility, more than developing a single design (NIMMS as a «toolbox»).

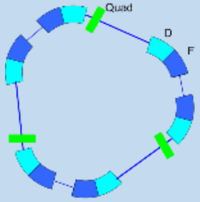
Four avenues to future ion therapy: the NIMMS Work Packages

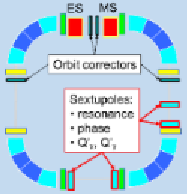
Curved superconducting magnets for synchrotrons and gantries



Superconductivity to reach higher magnetic field and small dimensions

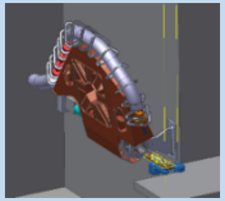
Small synchrotrons for particle therapy

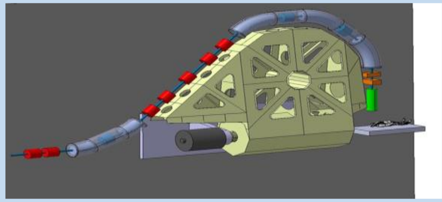




Reduced dimensions with improved performance (injection, extraction)

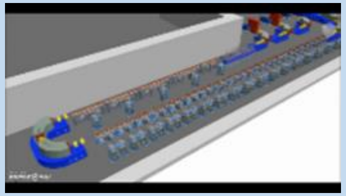
Superconducting gantries

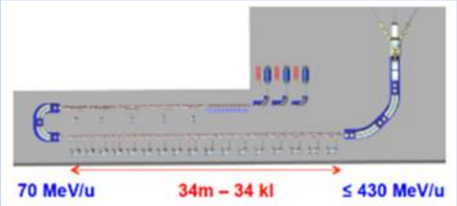




Precise beam delivery on multiple angles

High-frequency ion linacs





Compact bent layout

HITRIplus EU project

IFAST EU project

EU supporting initiatives

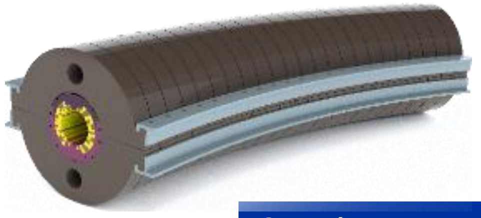
Superconducting magnets for synchrotrons and gantries

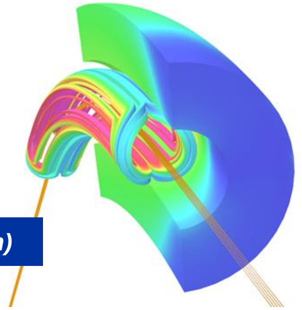
The main avenue to reducing the dimensions of a magnetic system is **superconductivity**.
But medical accelerator magnets have specific challenges: ramped field, curved shape, integrated focusing

4 projects launched for the construction of 5 **demonstrator magnets** (short length, pre-prototypes) supported by 3 collaborations:

1. **Cos-theta** (**2** demonstrators, thermal and curved) for **gantry**
   4 T, 0.4 T/s, 80 mm ø, r=1.65 m (430 MeV/u)
   collaboration INFN-CERN-CNAO-MedAustron
2. **Canted Cosine Theta (CCT)** curved demonstrator
   4 T, 0.4 T/s, 80 mm ø, r=1.65 m (430 MeV/u), 30^0
   EU Project HITRIplus (2021-25)
3. **Combined-functions CCT** straight demonstrator
   4 T + 5 T/m quadrupole, 80 mm ø, L=0.73 m
4. **Combined-functions HTS CCT** straight demonstrator
   4 T @ 10 K, ReBCO tapes, 80 mm ø, L=1 m
   EU Project I.FAST (2021-25)

Timeline: mid-2025 for experimental results!





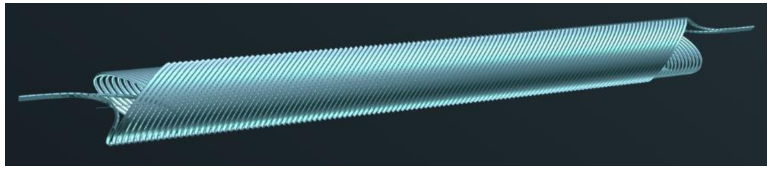
CERN (courtesy M. Karppinen)

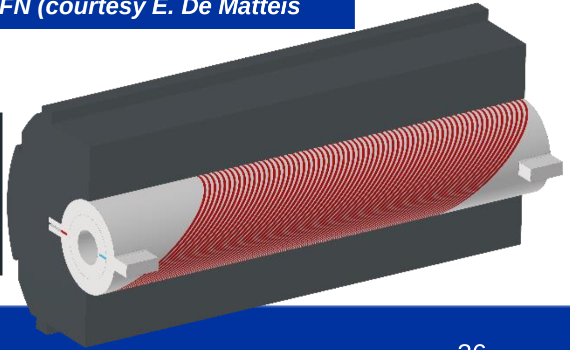
Curved Canted Cosine Theta

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

INFN (courtesy E. De Matteis)

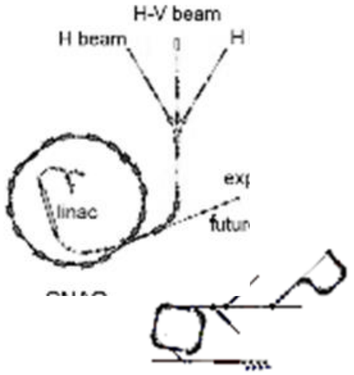
HTS=High Temperature Superconductor

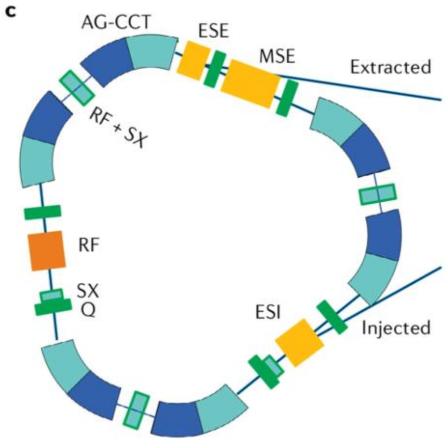


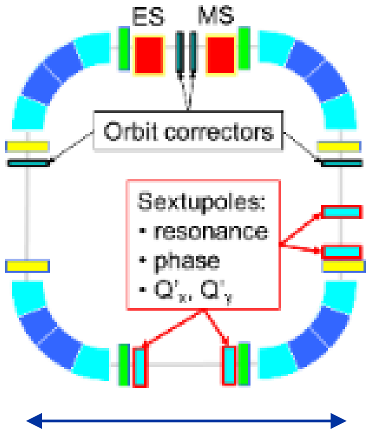


The compact superconducting synchrotron

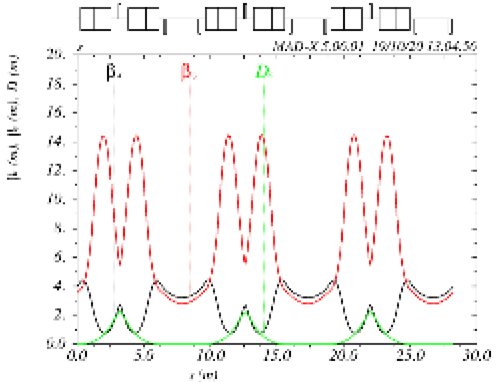
Considerable gain in dimensions thanks to superconductivity







Lattice with 60^0 magnets

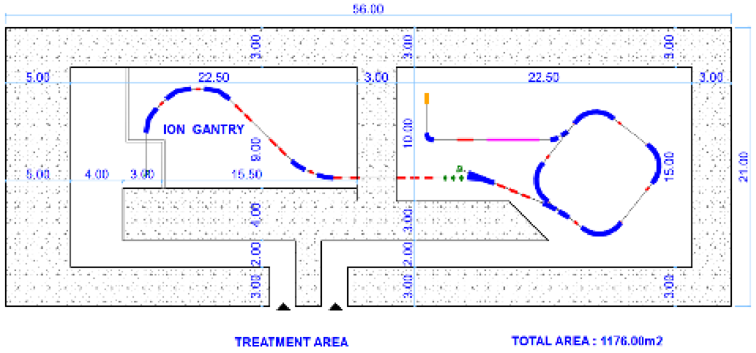


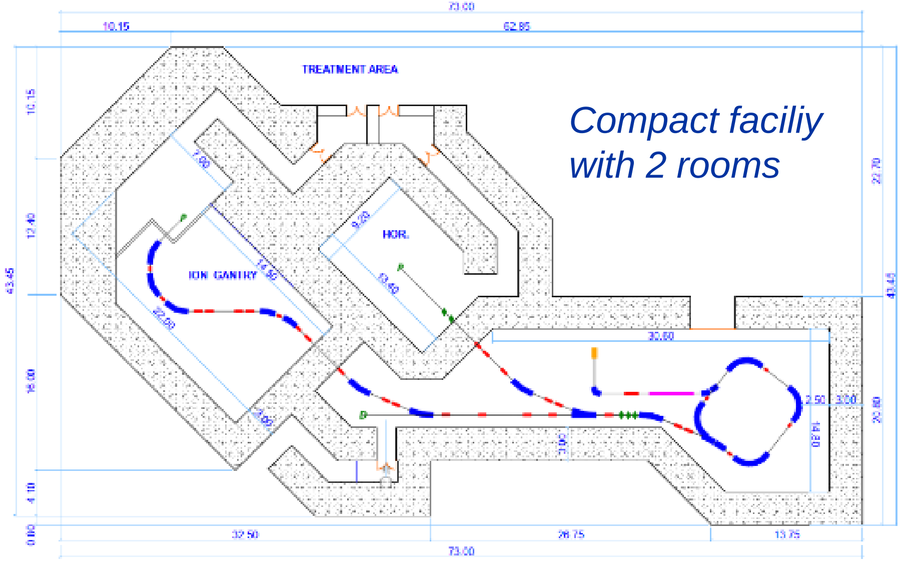
Additional features

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

Goal: a compact single-room C-ion therapy facility in about 1,000 m^2

Alternative synchrotron layouts





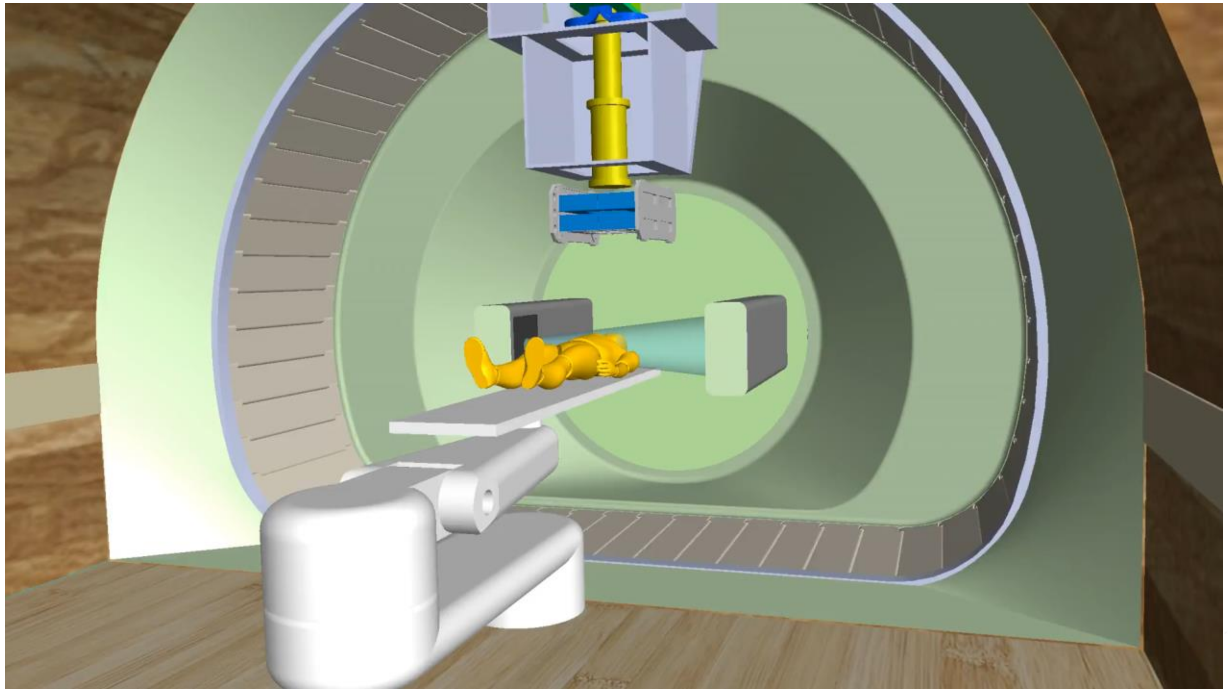
Compact faciliy with 2 rooms

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

Gantries: superconducting ion gantry, gatoroid

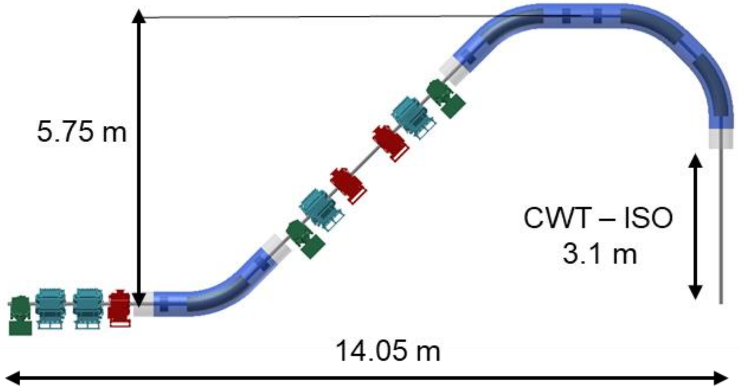
Development of a rotating SC gantry for Carbon ions:

- CERN-INFN-CNAO-MedAustron: magnets, dose delivery, range verification, scanning system.
- HITRIplus EU project (CNAO, RTU, SEEIIST, CERN: optics and mechanics design.



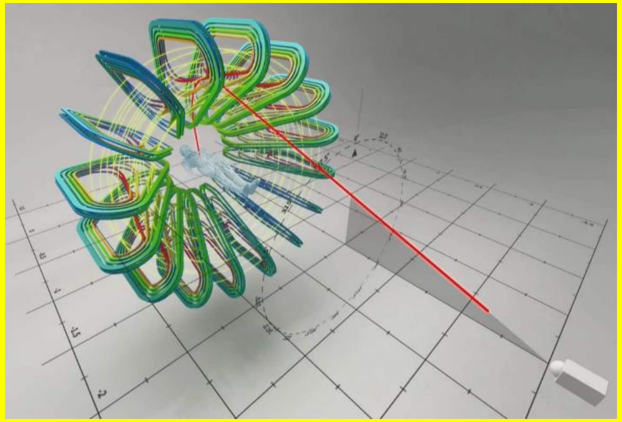
Courtesy L. Piacentini (CERN, RTU), E. Felcini, M. Pullia (CNAO)

4 magnets 45^0, 360^0 rotation



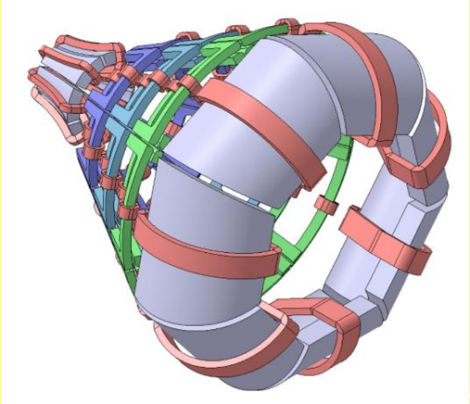
Development of a toroidal gantry (Gatoroid) at CERN.

- Explored proton and carbon versions, now concentrates on a non-superconducting version for electrons, to be tested with low-energy protons.



VHEE version of the Gatoroid gantry, based on normal conducting magnets.
Inherent FLASH capability with multidirectional treatment.
Being designed at CERN.

(image courtesy T. Lehtinen, L. Bottura)

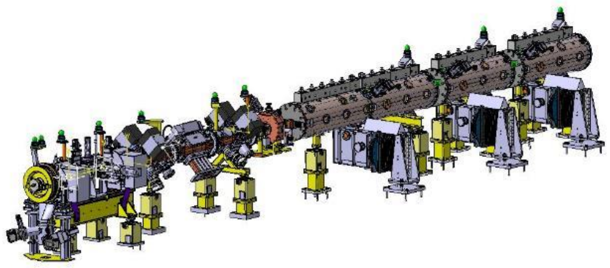


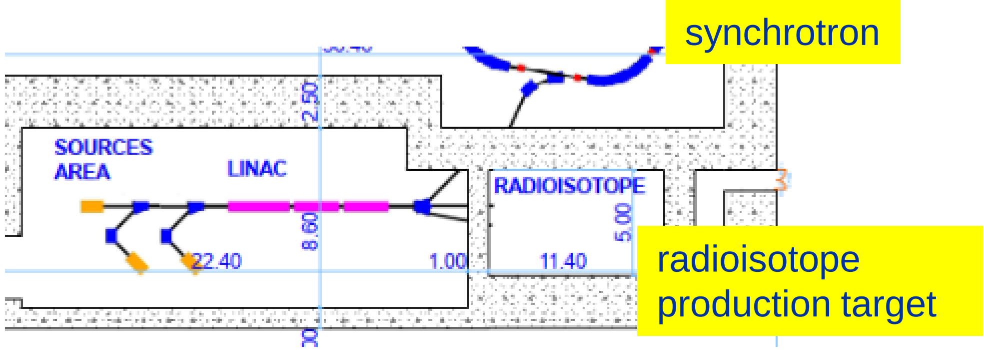
Linear accelerator for radioisotope production

Coupling particle therapy with nuclear medicine

The linear injector of a helium therapy synchrotron can be used to produce radioisotopes for imaging and therapy, in parallel to operation for therapy.

Linear accelerators are more efficient and less demanding than conventional cyclotrons for operation with helium ions.





synchrotron

radioisotope production target

Radioisotope	Usage
Scandium-43, 44	Diagnostic – PET
Cobalt-57	Diagnostic – SPECT
Copper-64	Theranostic (β^-)
Copper-67	Theranostic (β^-)
Indium-111	Diagnostic – SPECT
Tin-117m	Theranostic (β^-)
Samarium-153	Theranostic (β^-)
Rhenium-186	Theranostic (β^-)
Astatine-211	Therapeutic (α)

Courtesy K. Palskis, RTU/CERN

Example: Targeted Alpha Therapy with Astatine 211

Alpha particles = Helium ions (2 protons, 2 neutrons) are the most dangerous radiation, short range and high toxicity!

The linear injector produces alpha-emitting therapeutic isotopes like 211At that are attached to antibodies and injected to the patient. The targeting vector accumulates the isotopes in the cancerous tissues where they selectively deliver their dose.

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

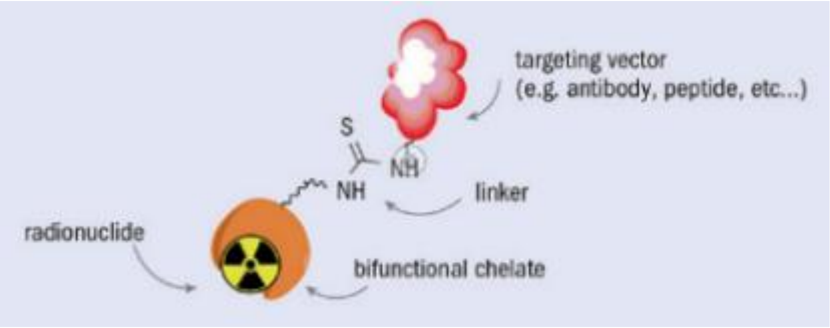


Image credit: Caterina F Ramogida, CERN Courier

Outside NIMMS: FLASH with high energy electrons

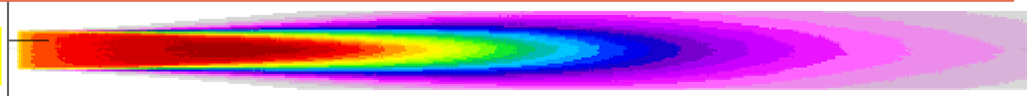
- Treating tumours delivering radiation in short pulses at ultra-high dose rates appears to reduce toxicity to healthy tissue while maintaining tumour control.
- Dose delivered in **fractions of a second instead of several minutes**.
- First observed in the 70's, rediscovered in 2014 (Favaudon and Vozenin), 1st treatments 2014-18, 1st clinical trial in 2020.

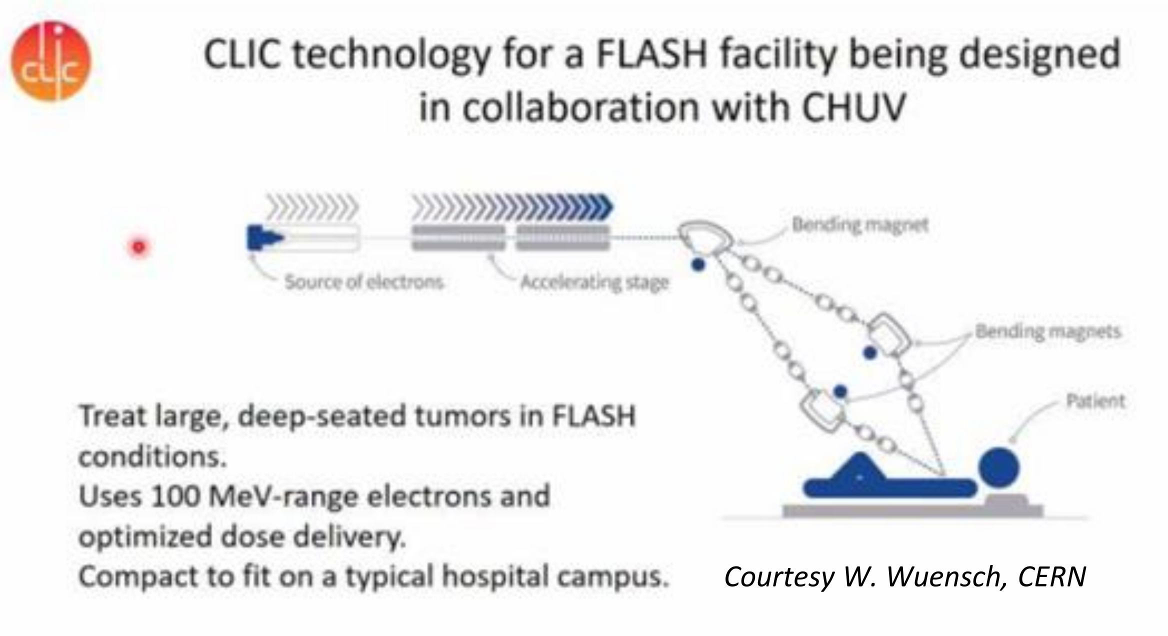
Balloon debate at FLASH conference 2022:
Photon, electrons or protons, what has the best long-term potential for FLASH for clinical application?

- 1st vote: 37% protons, 33% electrons, 30% photons.
- 2nd vote: 53% electrons, 47% protons.

New interest in cancer treatment with very high energy electrons (VHEE) !

Dose distribution for high-energy electron beam





CLIC technology for a FLASH facility being designed in collaboration with CHUV

Treat large, deep-seated tumors in FLASH conditions.
Uses 100 MeV-range electrons and optimized dose delivery.
Compact to fit on a typical hospital campus.

Courtesy W. Wuensch, CERN

Three collaborations are starting construction of the first accelerator for treating deep seated tumours with 100 MeV **FLASH electron beams,** using technology from particle physics:

- CERN-CHUV-THERYQ, 12 GHz
- Curie Institute-THALES, 6 GHz
- Rome University-INFN-(?), 6 GHz

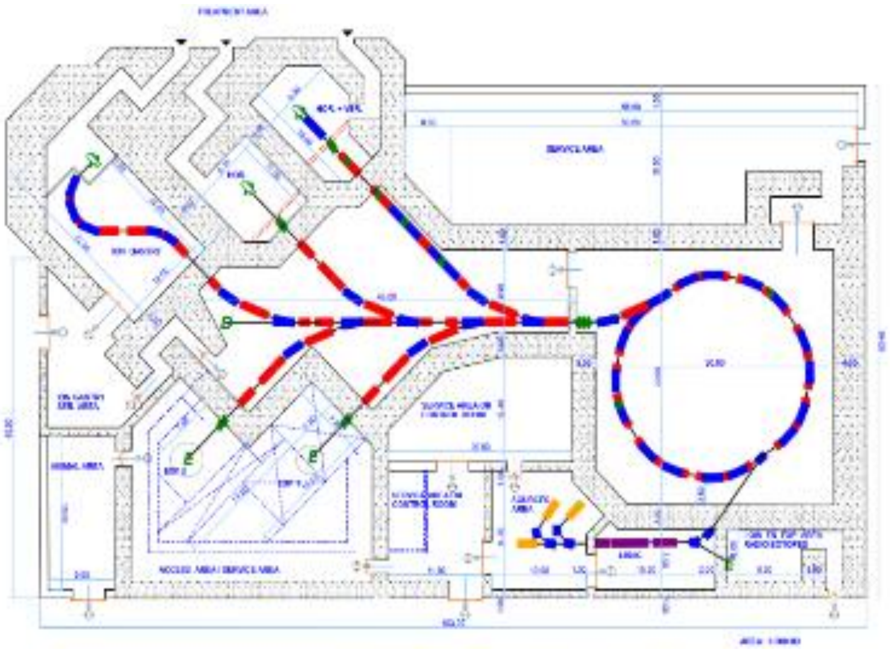
+ experimentation for **proton FLASH**

New proposed facilities for cancer therapy with particle beams

The construction site of Saint-Denis, "Les Grandes Chroniques de France", XIV c., Wikimedia commons

The SEEIIST initiative

- **SEEIIST** (South East Europe International Institute for Sustainable Technologies): a new international partnership aiming at the construction of a new Research Infrastructure for cancer research and therapy in South East Europe (11 member countries).
- SEEIIST is supported by the European Commission, to develop the facility design in collaboration with CERN and other partners.
- Goals are to develop a new advanced design and to build international cooperation and scientific capacity in a region that will join EU but is less develop and divided, in the line of “science for peace”.



- All ions up to carbon and oxygen
- Conventional synchrotron, PIMMS design
- 3 treatment rooms (H, V, SC gantry)
- Large experimental room.
- Estimated cost (2021): 240 M€

The SEEIIST ion therapy and research facility

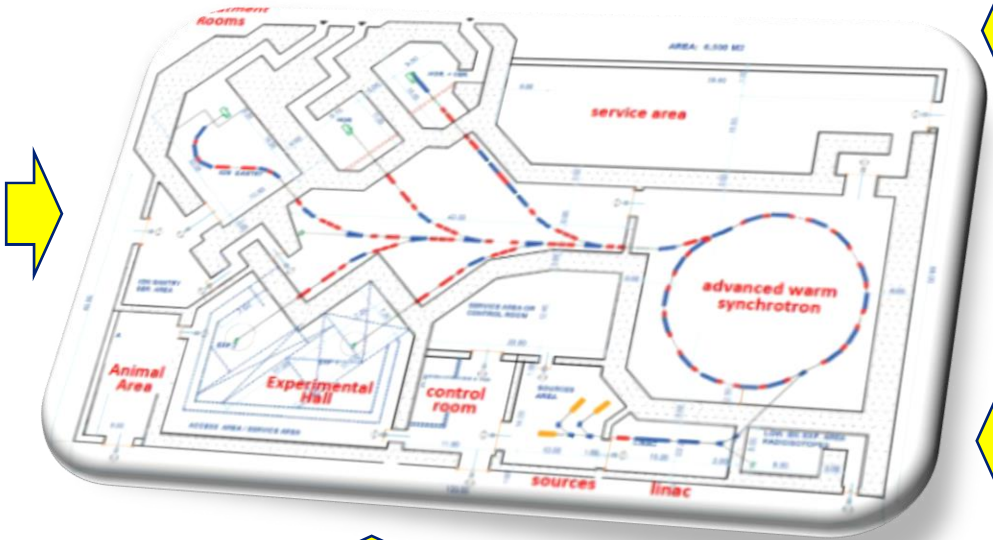
Intensive design work in 2019/20 in collaboration between CERN and SEEIIST, with the contribution of TERA and other NIMMS partners, and of the European ion therapy centres

A. Innovative SEEIIST features:

1. Optimised for 50% research and 50% patient treatment (~400 patients/year);
2. Providing 20 times higher beam intensity for carbon ions than present facilities;
3. Equipped with flexible extraction for operation in FLASH mode;
4. Equipped with dual mode linear injector capable of producing radioisotopes for cancer imaging and therapy.

B. Advanced SEEIIST features (common to other advanced facilities):

1. Operation with multiple ions: protons, Helium, Carbon, Oxygen, Argon;
2. Multiple energy extraction (multiple flat-tops) for faster treatment;
3. Equipped with a compact superconducting gantry of novel design.



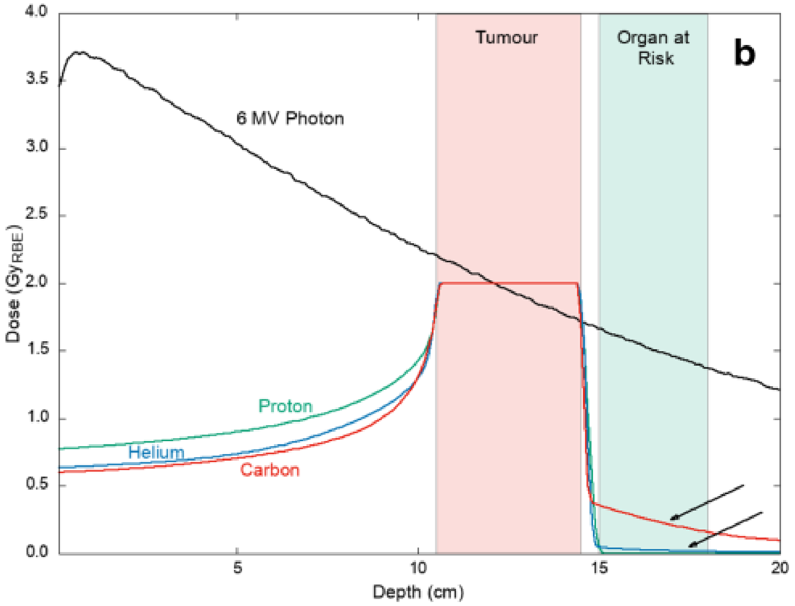
C. Conservative SEEIIST feature:

The synchrotron adopts the well-established PIMMS design (known and available components, flexible layout for research);

D. Specific SEEIIST features:

1. Environmental strategy: minimise energy consumption, strategy for energy generation;
2. Conceived as a multiple-hub facility, to federate partners in different countries.

Helium beams for cancer treatment



Spread-out Bragg peak for proton, helium, carbon compared to X-rays

(K. Kirkby et al., Heavy Charged Particle Beam Therapy and related new radiotherapy technologies, https://doi.org/10.1259/bjr.20200247)

- ➢ Helium ions: treatment started at Berkeley in the 70's then stopped.
- ➢ Recent years have seen a surge of interest for He in the European ion centres, first patient treated in September 2021 at HIT Heidelberg.
- ➢ An accelerator designed for helium treatment can easily produce protons for standard treatment, and be used for research with helium and heavier ions.

Advantages:

- ➢ reduced lateral scattering w.r.t. protons, better conformality.
- ➢ lower fragmentations than carbon, lower dose after tumour.
- ➢ lower neutron dose than protons or carbon, less risks in paediatric patients,
- ➢ could treat some radioresistant tumours at lower cost than carbon.
- ➢ might be better suited for FLASH than other ions.

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Physics in Medicine & Biology

IPEM

TOPICAL REVIEW

Roadmap: helium ion therapy

Andrea Mairani, Stewart Mein, Eleanor Blakely, Jürgen Debus, Marco Durante, Alfredo Ferrari, Hermann Fuchs, Dietmar Georg, David R Grosshans, Fada Guan, Thomas Haberer, Semi Harrabi, Felix Horst, Taku Inaniwa, Christian P Karger, Radhe Mohan, Harald Paganetti, Katia Parodi, Paola Sala, Christoph Schuy, Thomas Tessonnier, Uwe Titt and Ulrich Weber

Main features of a helium therapy facility

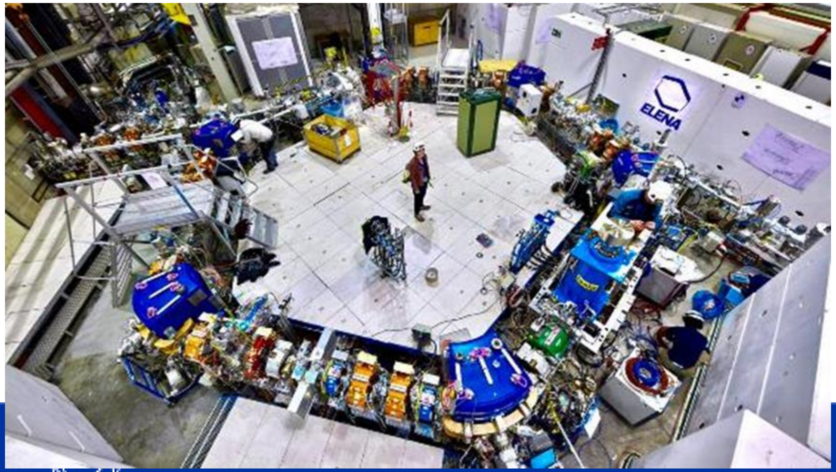
An advanced accelerator capable of cancer treatment with modern techniques in parallel with a robust experimental programme (in-vitro and in-vivo).

Synchrotron because of size, flexibility, cost, available expertise at CERN and elsewhere:

1. Designed for helium ions, can accelerate protons at treatment energy;
2. Can use protons at higher energy for full body on-line radiography;
3. Can accelerate other ions (e.g. carbon) for biophysics experiments.
4. Can be equipped with modern FLASH extraction and can produce mini-beams.
5. The linac injector can be used in parallel for production of radioisotopes (e.g. 211At) using helium ions or protons.

Main synchrotron parameters:

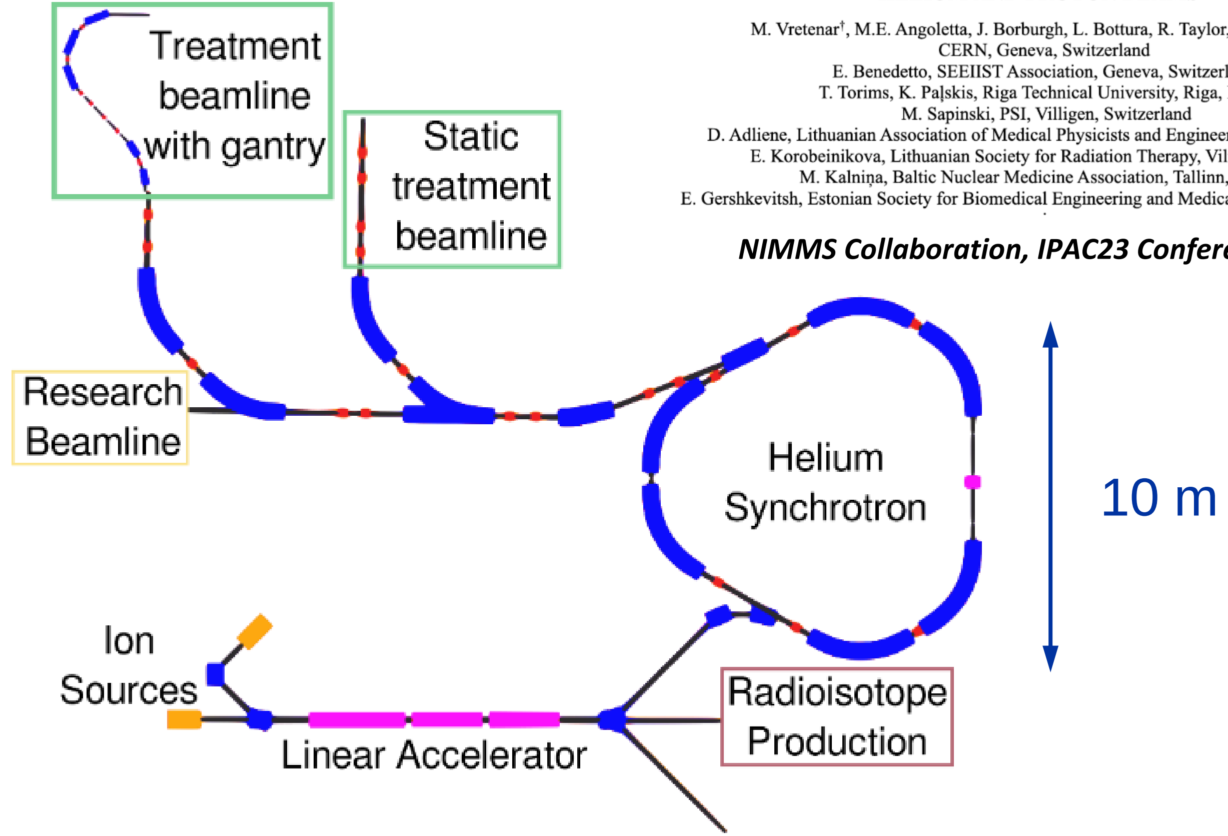
- ☐ maximum magnetic rigidity 4.5 T/m (**220 MeV/u** for 4He, penetration 30 cm in water).
- ☐ **4 x 10^{10} ions extracted**, to irradiate a 1 litre tumour with 2 Gy.



- Based on CERN experience in small synchrotrons (LEAR, LEIR, ELENA)
- Preliminary circumference 33 m

The recently (2011-17) built ELENA antiproton decelerator synchrotron at CERN, 30 m circumference, 6 magnets

Helium facility layout



CONCEPTUAL DESIGN OF A COMPACT SYNCHROTRON-BASED FACILITY FOR CANCER THERAPY AND BIOMEDICAL RESEARCH WITH HELIUM AND PROTON BEAMS*

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E. Gershkevitsh, Estonian Society for Biomedical Engineering and Medical Physics, Tallinn, Esto-

NIMMS Collaboration, IPAC23 Conference

- Two beamlines for treatment, one for research.
- Rotating superconducting gantry.
- Injector with parallel radioisotope production
- Surface ~2,000 m2

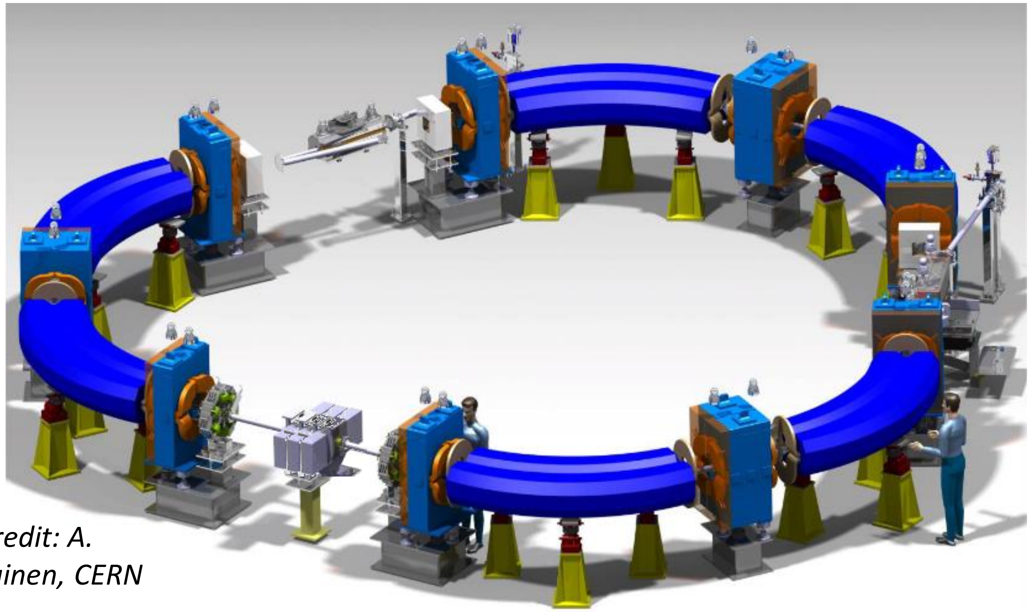
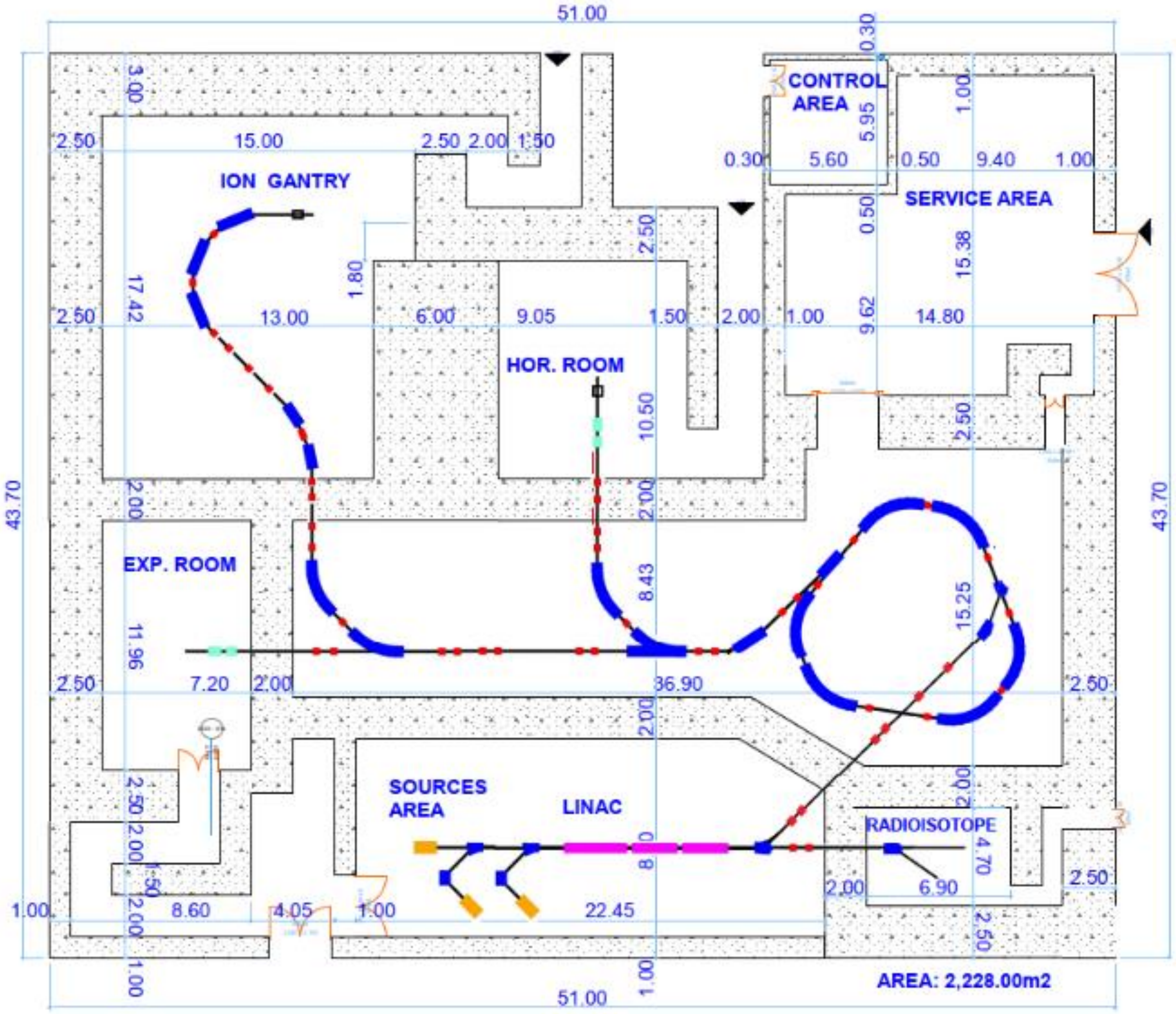


Image credit: A. Kolehmainen, CERN

NIMMS goal: from the present CDR to a complete Technical Design Report (TDR) in June 2025, to be used by anyone willing to build the facility.

FLASH extraction being studied: high-voltage RF KO for 100 ms pulses, RF phase displacement ramp for ms pulses.

The proposed helium facility for the Baltic States



- **Multiple use**, patient treatment, research, isotopes.
- **Modular design**, options can be added/removed (radioisotopes, gantry, treatment rooms, experimental rooms).
- **Flexible operation** with protons and/or helium. Operation (and medical certification) can be adapted to future medical requirements.
- **Upgradable** to future needs (ions, intensities, etc.).

CERN Baltic Group

Draft concept-paper
Advanced Particle Therapy Center for the Baltic States

Where are we going? A look into the future

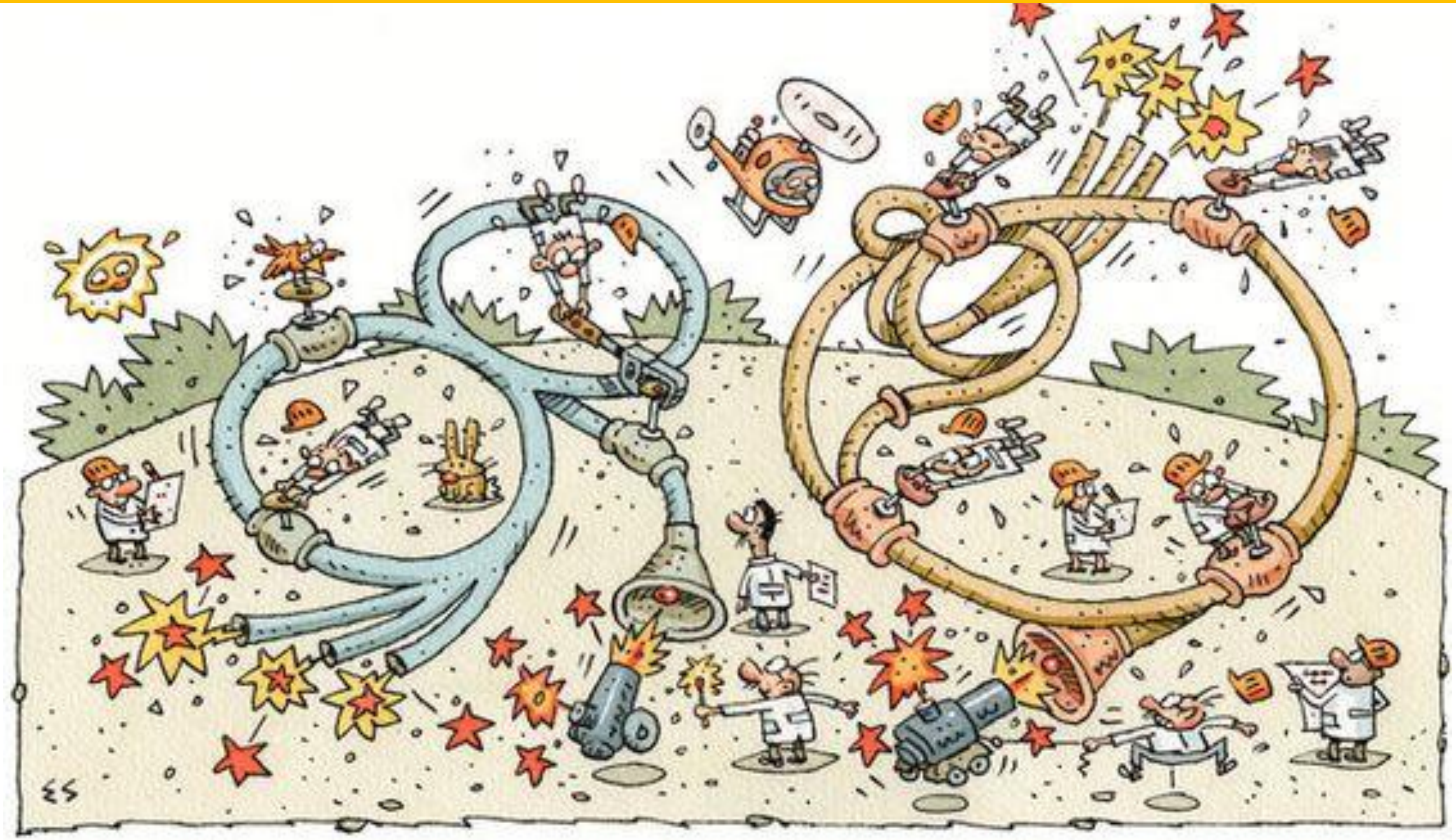
Proton Therapy, carbon therapy, helium therapy, VHEE, FLASH, radioisotopes, theragnostics, targeted alpha therapy, superconductivity, linacs, lasers… What is going to be the future landscape of our tools to fight cancer ?

A few key concepts:

- Medicine is one of the main **technology drivers of XXIst century**. The development of sophisticated medical tools is generating a fantastic progress in all technologies, and this trend is going to continue (think of the progress over the last 50 years!).
- Research in accelerators has the potential to provide new **breakthroughs in cancer therapy** based on new techniques that are **complementary**, with different cost and range of applications. They are going to provide oncologists with an arsenal of instruments to fight different types of cancer.
- The trend is towards **compact systems**, controlled by **artificial intelligence** algorithms, that can act at the **atomic and molecular** level. **Therapy and diagnostics** are going to be more and more integrated, in the device or via “theragnostic” approaches.

Particle accelerators will be crucial actors in this technological evolution – what is advanced medicine and technology today will be standard clinical practice tomorrow!

Thank you for your attention !



Elwood Smith, NYT