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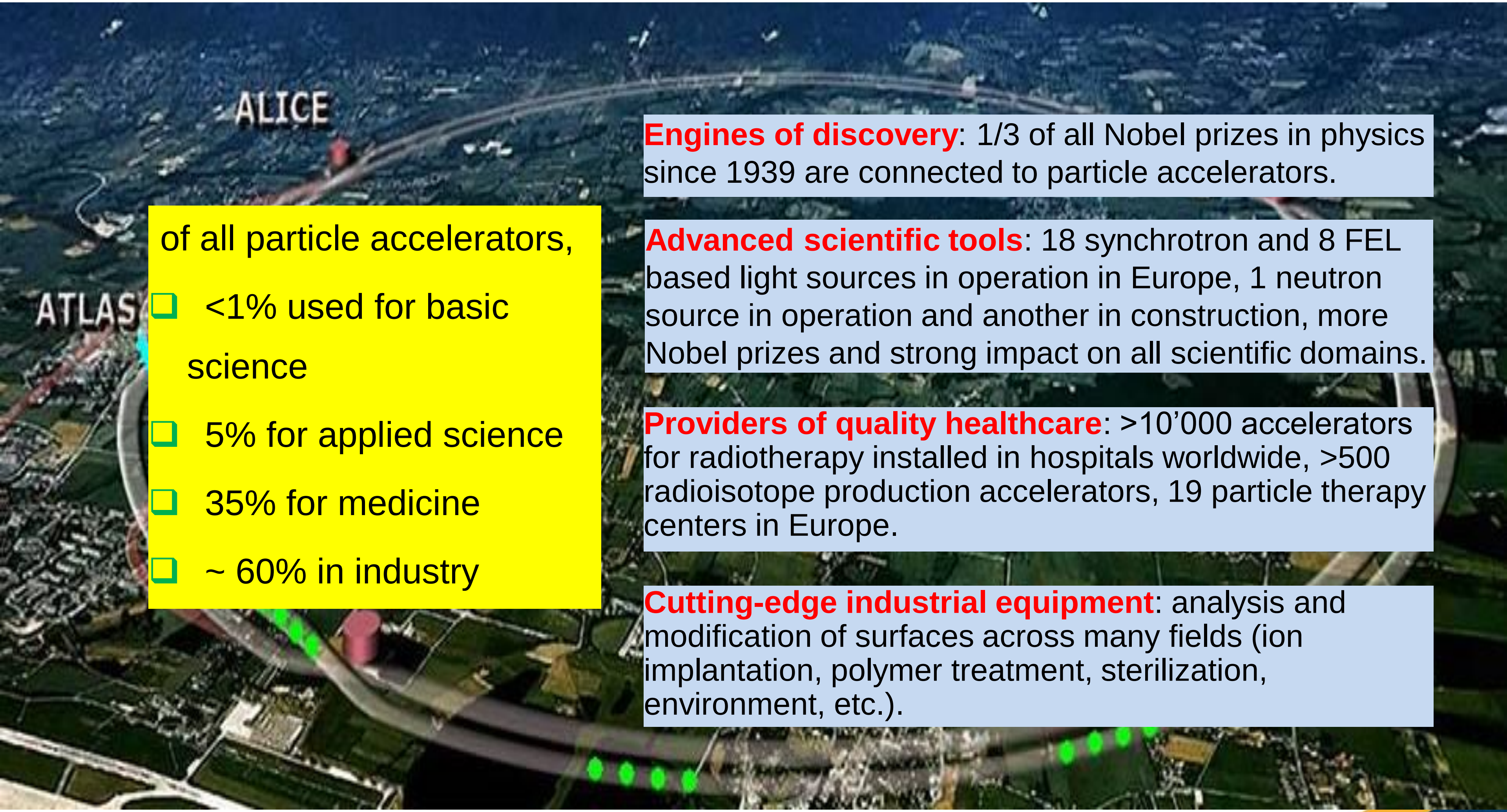
Opportunities for ion accelerators in medicine and industry

Maurizio Vretenar, CERN ATS/DO and ARIES Coordinator

Workshop on Ions for Cancer Therapy, Space Research and Material Science

Chania, August 26-30, 2017

Accelerators in transition



of all particle accelerators,

- <1% used for basic science
- 5% for applied science
- 35% for medicine
- ~ 60% in industry

Engines of discovery: 1/3 of all Nobel prizes in physics since 1939 are connected to particle accelerators.

Advanced scientific tools: 18 synchrotron and 8 FEL based light sources in operation in Europe, 1 neutron source in operation and another in construction, more Nobel prizes and strong impact on all scientific domains.

Providers of quality healthcare: >10’000 accelerators for radiotherapy installed in hospitals worldwide, >500 radioisotope production accelerators, 19 particle therapy centers in Europe.

Cutting-edge industrial equipment: analysis and modification of surfaces across many fields (ion implantation, polymer treatment, sterilization, environment, etc.).

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What particle accelerators can do for you

Accelerators are our only tool to access the atomic and subatomic world

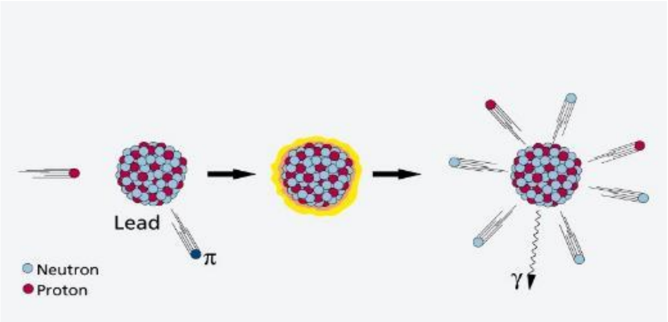
A particle beam can deliver large amounts of energy to a precisely defined volume, situated deeply in the matter (deeper than lasers!).

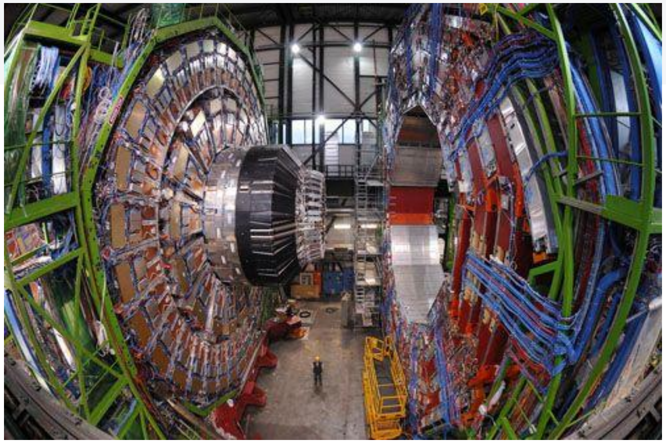
This energy can:

- Precisely break chemical bonds, as for the DNA of cancer cells;
- Modify or break the atomic nuclei, creating new isotopes or elements;
- Generate new particles: $E = mc^2$
- Be converted into intense streams of photons (x-rays) or neutrons, to be used as probes to study the structure of matter.

Accelerators are the tools of modern alchemy

Alchemist Heating a Pot, by David Teniers the Younger (1610 - 1690), oil on canvas.





Definition of alchemy (Merriam-Webster)

a medieval chemical science and speculative philosophy aiming to achieve the transmutation of the base metals into gold, the discovery of a universal cure for disease, and the discovery of a means of indefinitely prolonging life

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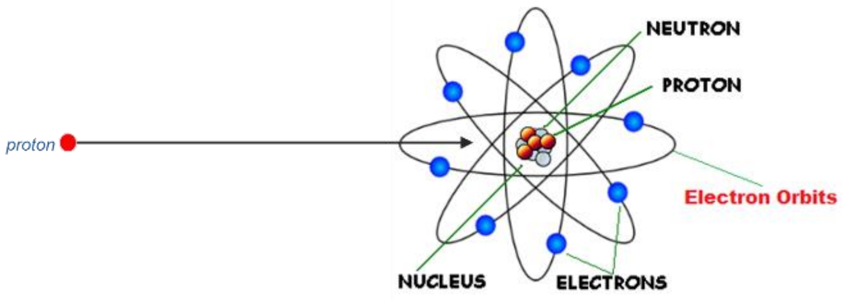
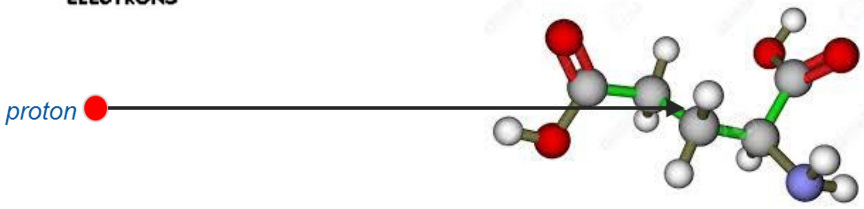
Accelerators can realise an old human dream

From chemistry to physics

- Most of the processes used in medicine and industry are based on altering the chemical bonds.
- Accelerators give us an extremely precise and selective knife to act on the chemical bonds, and go one step beyond by altering the atomic and nuclear bonds.
- There is a huge potential for new societal applications based on acting at the atomic level in a controlled way.



"It's a brave new world of applications," project leader M. Vretenar told Reuters in Linac 4's tunnel 12 meters under Geneva.
T. Miles, Reuters #Innovation and Intellectual Property, May 9, 2017



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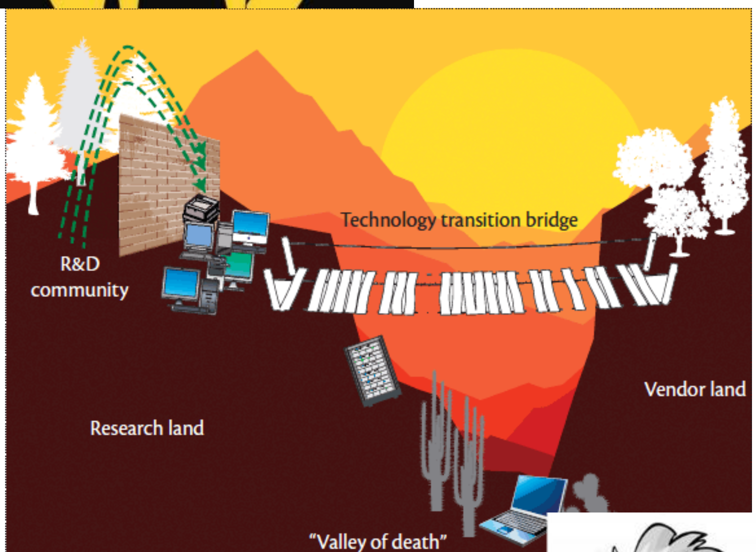
Our challenges



- Win the suspicions of the people for technologies related to radiation (the widely spread «radiophobia»).
- Bring our technologies out of scientific laboratories towards commercial exploitation (i.e. cross the «valley of death»).
- Create structures and collaborations to promote innovation and absorb the financial risk related to new technologies.
- Produce new compact, affordable and reliable accelerator designs for societal use.

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Common innovative accelerator R&D

The new **ARIES Integrating Activity** project for particle accelerator R&D has started in May 2017.

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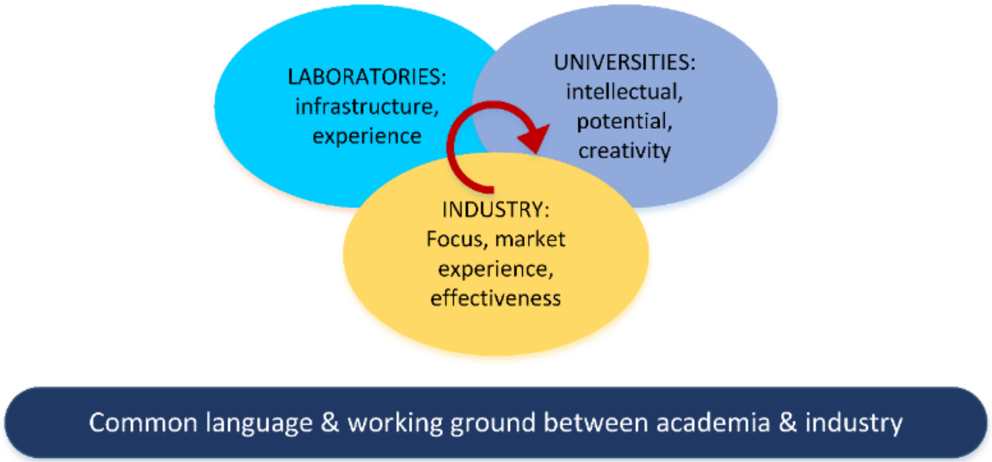
Accelerator
Research and
Innovation for
European
Science and
Society

EC funding 10 M€, total budget 24 M€.

Duration of **4 years (May 2017-April 2021**)

41 partners from **18 EU countries,** coordinated by CERN.

18 Workpackages, covering R&D topics for the future generation of particle accelerators.

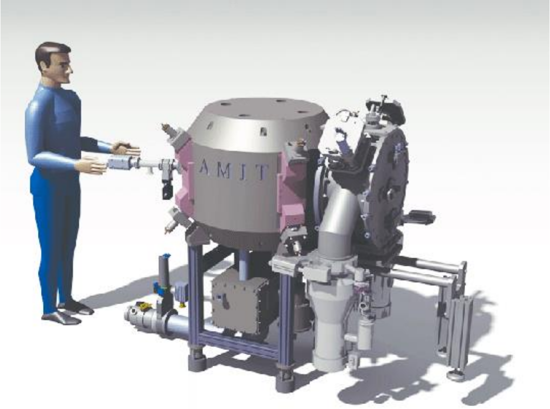


You can register to ARIES at https://aries.web.cern.ch/

The ARIES Accelerator Application Network

After the exploratory work of EuCARD2, the «Accelerator Applications» Network concentrates on 2 specific applications:

1. Technology of compact low-energy electron accelerators and their applications for **environment and industry** (treatment of water and flue gases, treatment of agricultural waste, etc.)
2. Radioisotope production with accelerators: compact accelerators for **PET isotope production in hospitals**, accelerator production of Tc for SPECT tomography and of **therapeutic isotopes**.



The compact AMIT superconducting cyclotron for isotope production in hospitals.

ARIES meets industry workshop 1.12.17
Electron beam treatment of ship exhausts to eliminate polluting Sox and NOx

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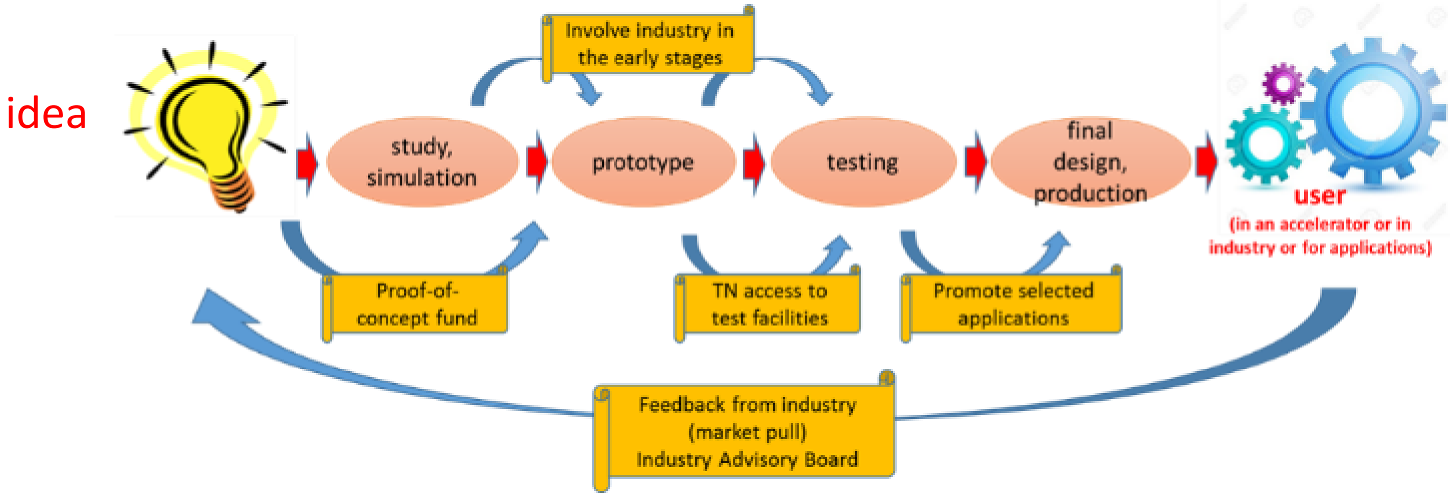
ARIES Innovation Strategy



Support to all stages of the innovation process:

- **Proof-of-concept innovation fund**: for Business Plan preparation, market assessment, demonstration in connection with industry of the technological viability of new ideas.
- **Industrial Advisory Board**: provide business consultation (eg. business plans) and support market assessments (“market pull”).
- **ARIES meets industry events**
- **3 co-innovation programmes with industry**

Proof of Concept Fund

Academia meets Industry events

Projects co-run with industry

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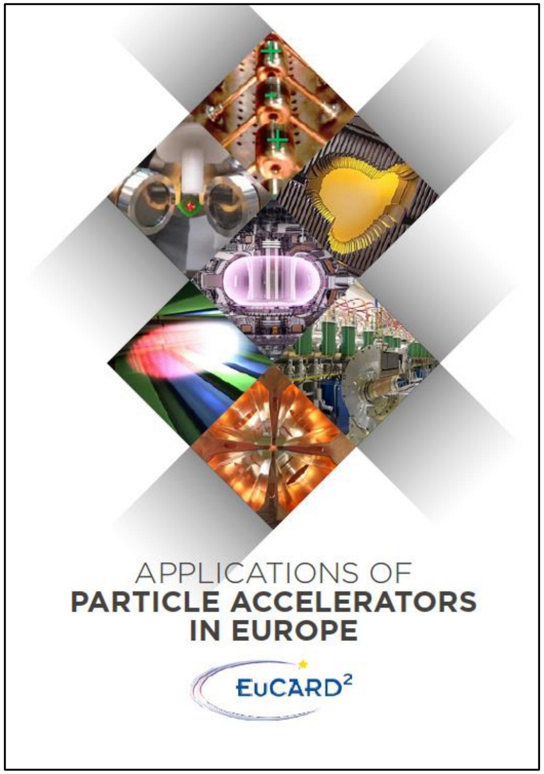
The APAE Document



Accessible at http://apae.ific.uv.es/apae/

113 page document highlighting applications of accelerators, their extent in Europe and directions for future work

+ 8-page foldable brochure to be translated in main EU languages

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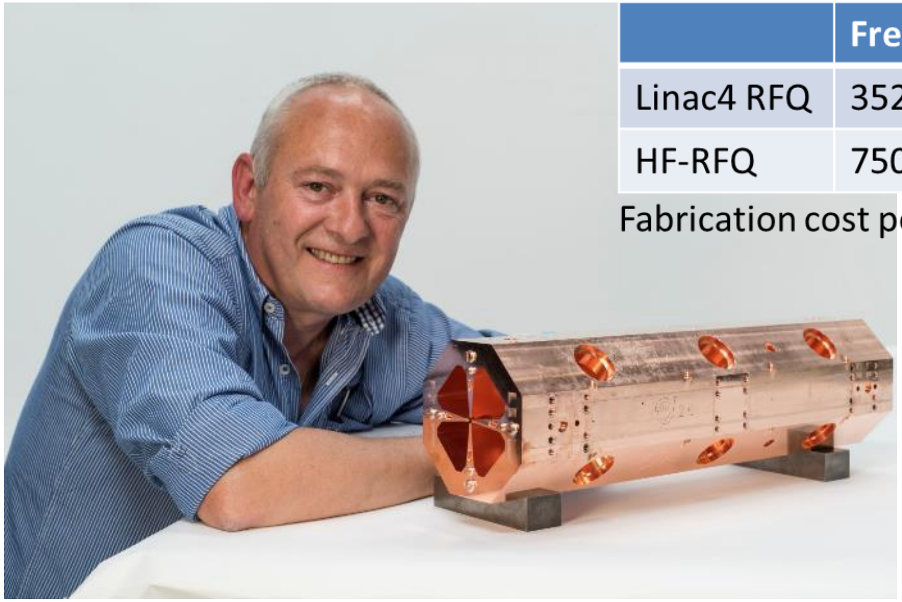
An example of accelerator for applications

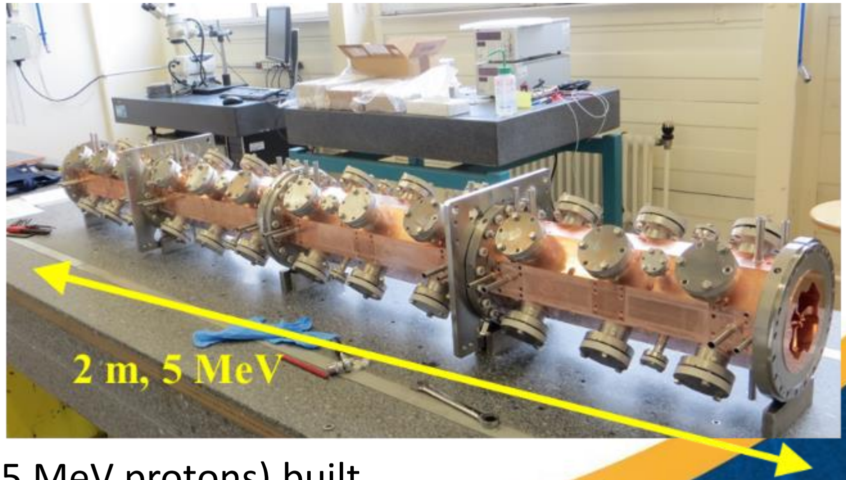
The CERN «mini-RFQ» development (High-Frequency RFQ)

Radio Frequency Quadrupole (the first element of any ion acceleration chain) at high frequency – targeted at low current applications requiring small dimensions, low cost, low radiation emissions, up to portability



	Frequency	Energy	Length	Gradient	Current
Linac4 RFQ	352 MHz	3 MeV	3 m	1 MeV/m	90 mA
HF-RFQ	750 MHz	5 MeV	2 m	2.5 MeV/m	400 μA

Fabrication cost per meter about 50% for HF-RFQ



The first unit (5 MeV protons) built at CERN for the ADAM company

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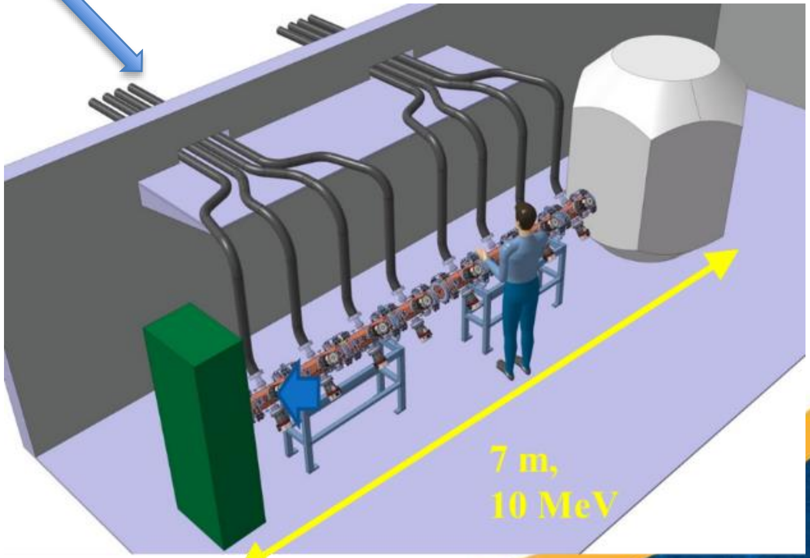
Applications of the «mini-RFQ»

The modular design allows using the same structure for different energies and particles

1. Injector for a proton therapy linac (5 MeV) — Built
2. Production of PET isotopes in hospitals (10 MeV) — Designed
3. PIXE analysis of artwork (2 MeV) — In construction
4. Testing cellular response to proton beams (2 MeV) — Proposal Preparation
5. Acceleration of q/m=1/2 particles (deuterons for neutron production, carbon 6+ for beam therapy, alpha particles for targeted therapy. — Under study



Analysing art and molecules…

The PIXE RFQ (Proton Induced X-ray Emission)

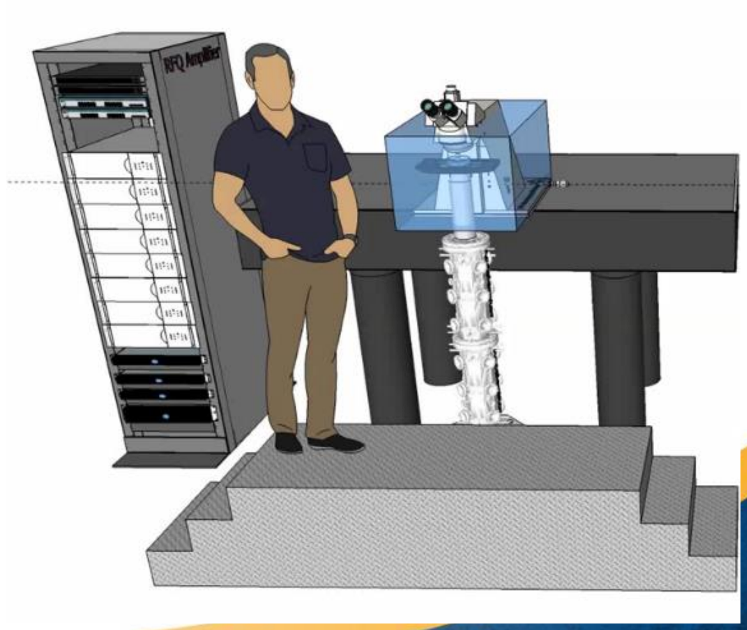
A transportable system of only 1m and 100 kg to test artwork in situ (chemical composition of outer layer). Can allow dating (from composition of paint) or finding the origin of jewelry.

In construction at CERN (collaboration with INFN Florence)

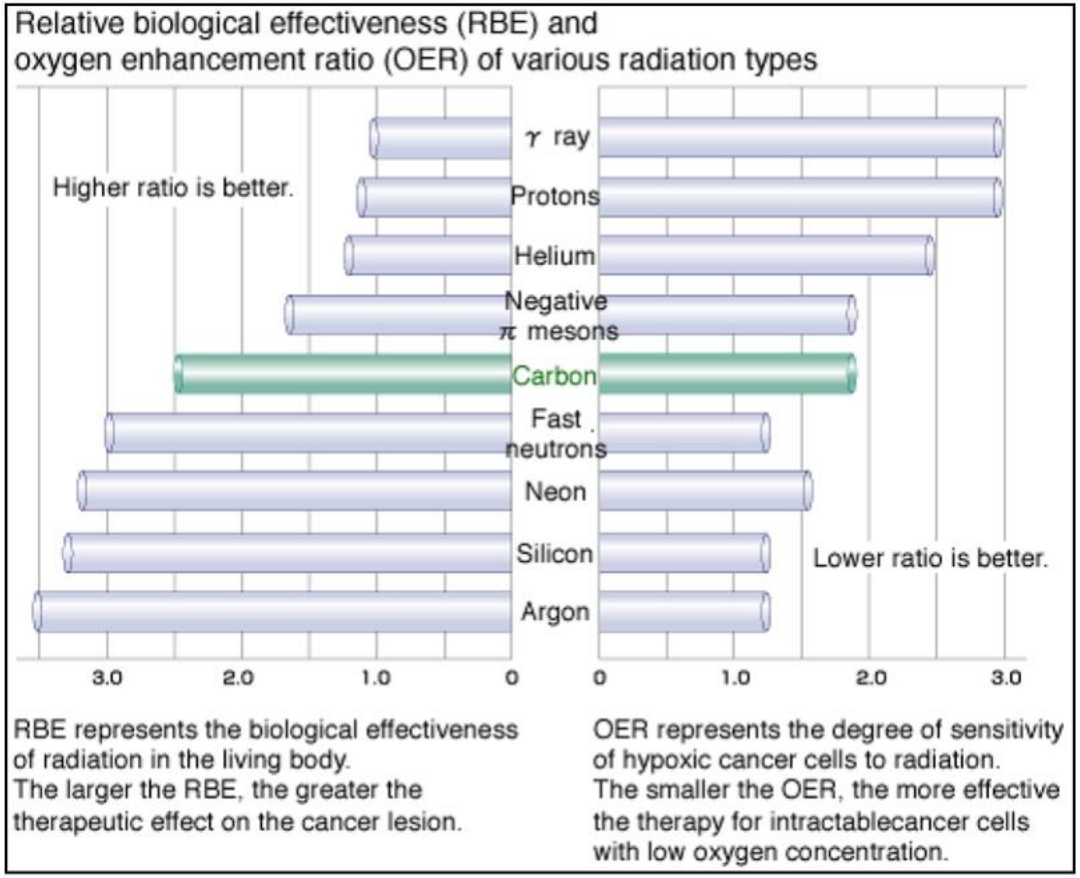
The COMPASS RFQ for proton radiobiology

Collaboration Amsterdam Medical Centre – Eindhoven University – CERN (request for funding in preparation)

The PIXE RFQ installed in vertical position in a system to measure cell response (DNA damage and repair) to a proton beam, to collect data for proton therapy.



Ions for cancer – ion beam treatment



- Ions have higher Relative Biological Effectiveness than X-rays or protons → higher DNA damage
- Ions have as well a lower Oxygen Enhancement Ratio → more effective for cancer cells with low oxygen concentration (some 5% of tumours, not treatable with X-rays).
- New research focusing on interaction of ions with the immune system, showing enhanced immunological response.

Critical points:

- Choice of ion type
- Cost (in comparison to protons)

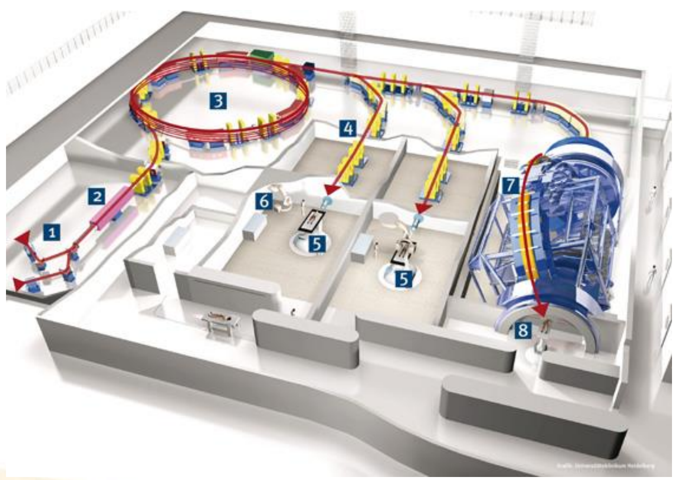
Carbon as «workhorse» of ion therapy

Other options: - go higher (Ar, Ne, Si, traditional RBE/OER approach)

- go lower (He, same immunological response but easier acceleration)

Challenges of ion accelerators

- Dramatic need of clinical data on Carbon and other ions.
- The 1st generation of proton and ion synchrotrons (CNAO-MedAustron, HIT) is very successful but construction and operation costs are high; moving patients to large centres can be an issue.
- Demand for 2nd generation carbon (or other ions) therapy accelerators is strong and being explored in Europe (TERA, CERN, STFC) and USA (BNL, ANL).
- Features: optimised for ions, energy variability, compact and «low-cost».
- Alternatives: cyclotron, compact synchrotron, FFAG or linear accelerator.
- Ion cyclotrons are bulky, limited by extraction losses, and have very limited energy variability.
- FFAG's are still in the development phase.
- Most of the development work concentrated on synchrotrons and linacs.



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PIMMS2 at CERN

The **PIMMS** (Proton-Ion Medical Machine Study) design at CERN in 1996-2000 has made a fundamental contribution to the development of synchrotron-based accelerator systems for multi-ion cancer therapy.

- PIMMS was particularly successful because it was a *wide and open European collaboration with CERN contributing with its expertise*.

The need for future *compact and cost-effective ion therapy accelerators* could be addressed by a new collaborative design study coordinated by CERN: **PIMMS2**.

- PIMMS2 must be *open*, relying on the expertise of *several partners*, and capitalising on the *CERN expertise* and portfolio of technologies (RF systems, advanced magnet design, superconducting materials, beam optics, …).

The CERN Management supports this initiative and asked to **prepare a proposal** (partners, contributions and funding) to be submitted to the CERN Medical Application structure (indicatively at *end 2017 – early 2018*).

- A preliminary technical analysis indicates that there is little to gain from a new RC synchrotron design – there is more space for improvement going to *innovative high-frequency linac based* solutions, the direction opened by TERA (CABOTO) and followed by ANL and RadiaBeam in the US.

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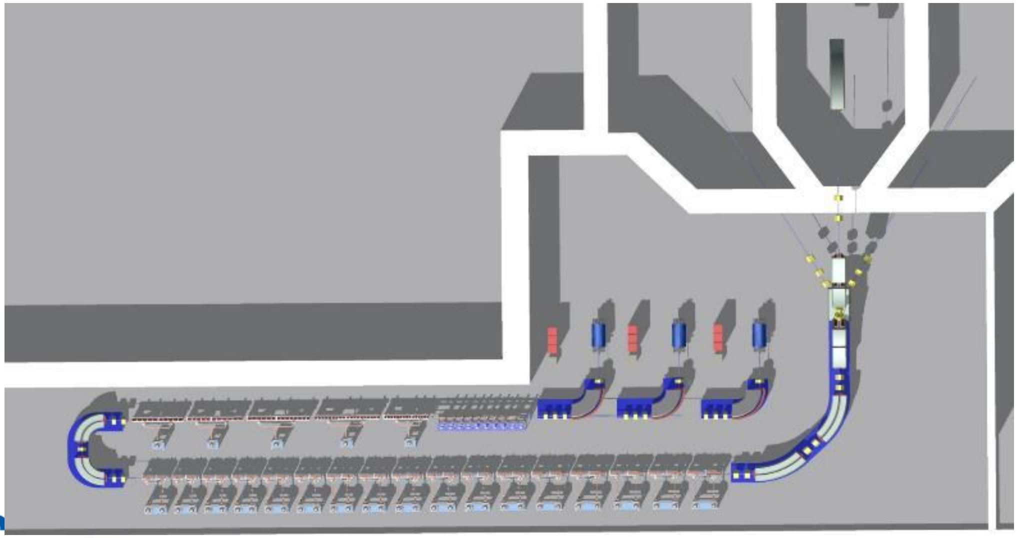
Key features of a linac-based facility

- Acceleration of Carbon 6+ (charge-to-mass ratio ½) requires a special ion source or stripping after the RFQ.
- The new high-frequency RFQ developed at CERN provides an efficient 750 MHz. injector – avoids the limitations of old designs with a cyclotron as injector.
- The linac requires extremely high gradients (length in the 50 m range, or 20 MV/m real estate gradient)
- High gradient means high RF power: needs efficient low-cost RF power sources.
- The linac offers the advantage of pulse-to-pulse energy modulation at high repetition frequency.
- But requires a sophisticated gantry with large energy acceptance.



Top view of CABOTO (TERA Foundation)

Targeted Alpha Therapy (or Targeted Immunotherapy) The road of tomorrow?

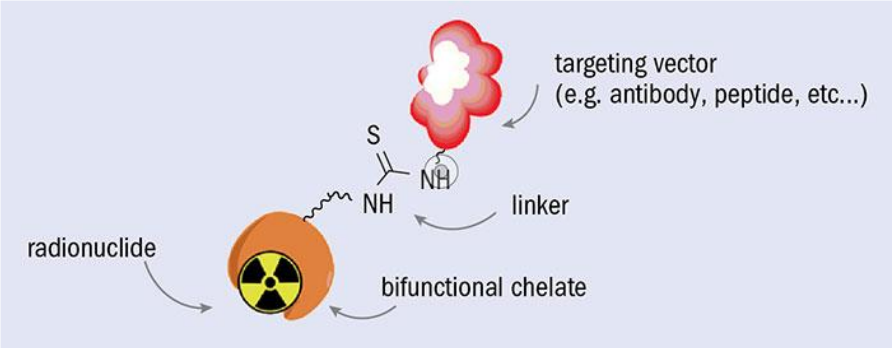
Delivering the dose to the tumour cells from inside; old technique (brachytherapy) now revived thanks to new carriers and new radioisotopes.

Injected radiolabeled antibodies accumulate in cancer tissues and selectively deliver their dose. Particularly effective with alpha-emitting radionuclides (minimum dose on surrounding tissues).

Advanced experimentation going on in several medical centres, very promising for solid or diffused cancers (leukaemia).

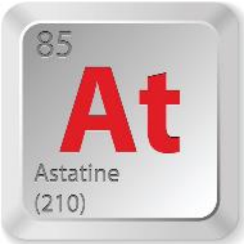
Potential to become a powerful and selective tool for personalised cancer treatment.

If the radioisotope is also a gamma or beta emitter, can be coupled to diagnostics tools to optimise the dose (theragnostics)



Accelerators for Alpha Emitters - Astatine

- In the trial phase, only small quantities of a-emitting radionuclides are needed, provided by research cyclotrons.
- If this technique is successful, there will be a strong demand of α-emitters that the accelerator community has to satisfy.
- One of the most promising α-emitters is Astatine-211, obtained by α bombarding a natural Bismuth target (209Bi(α,2n) 211At nuclear reaction).
- At production needs α (q/m=1/2) accelerator; optimum energy 28 MeV (sufficient yield but below threshold for 210Po), current >10 mA.
- The use of α's in cyclotrons is limited by extraction losses; linacs have a strong potential.
- Synergy with low-energy section of carbon therapy linacs (q/m=1/2), but At requires much higher intensities (and probably low frequencies).



Astatine, the dream of the medieval alchemist.
The rarest element on earth (only 25 g at any given time)
The less stable element in the periodic table (<100)
Half life (210At): 7.2 hours

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Conclusions

The future is in our hands!

Accelerators have a huge potential in the fields of industrial production, environment and medicine but it is up to us to apply what we have learned building the large accelerators for science to develop new *reliable, compact, low-cost and low-radiation* accelerators that can be installed and operated outside of our scientific laboratories.

In collaboration with industry and with the support of the European Commission!

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Thank you for your attention!