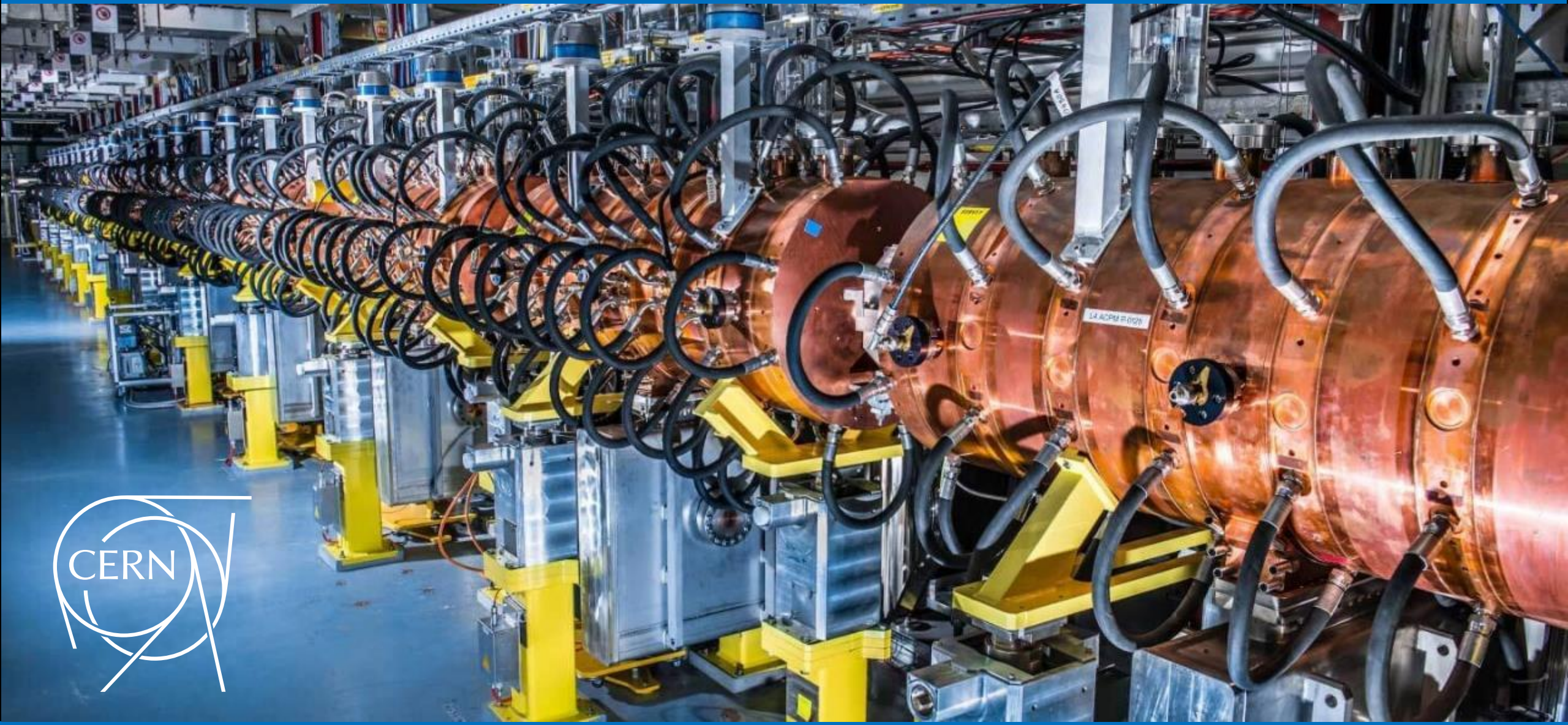
Maurizio Vretenar CERN

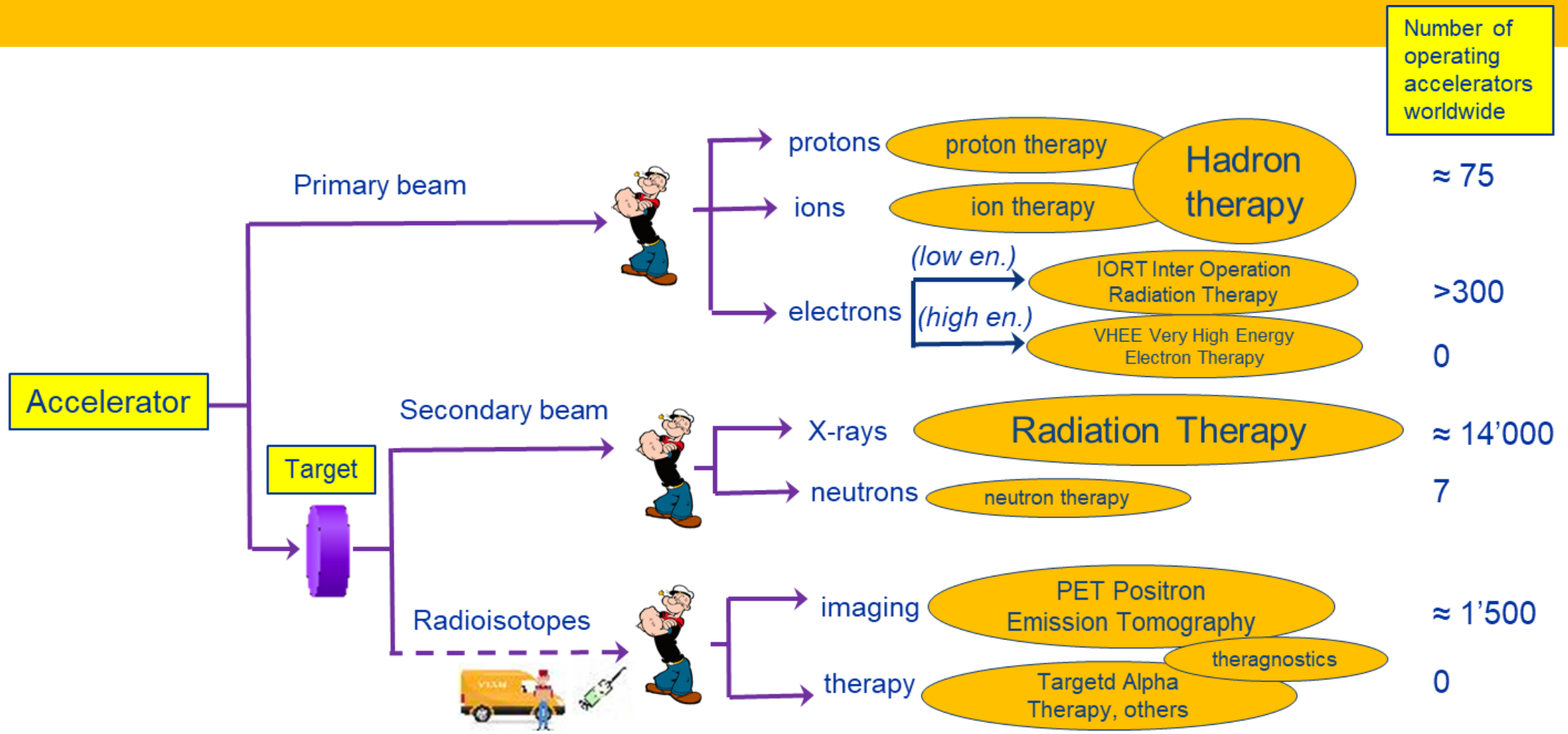
LECTURE 6: Accelerators for Medicine

August 2021



Introduction to Particle Accelerator Science and Technology

Accelerators for medicine



Total: ≈ 16'000 particle accelerators 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.

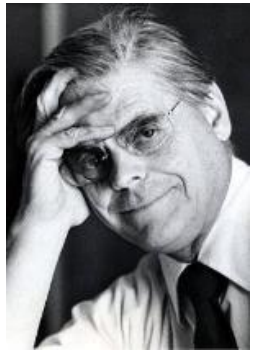
Nuclear medicine:
application of radioactive substances in the diagnosis and treatment of disease

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.
- Starting in 1937, Lawrence's brother John was the pioneer of injecting radioisotopes produced at the cyclotron to cure leukemia and other blood diseases.
- 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 center at Loma Linda (US) in 1990.



Lawrence's priority was to promote his science and to build larger and larger cyclotrons. He considered medical applications as a formidable tool to show the public the potential of this new technology and to raise more funding for his projects.

During the 30's, more than 50% of beam time was devoted to producing isotopes for medicine and other applications, to the disappointment of the physicists that were using the cyclotron beams to lay the ground of modern nuclear physics.

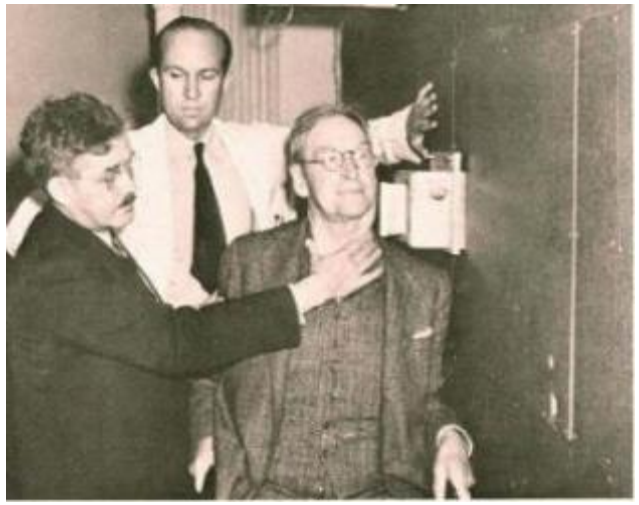
Modern accelerators for cancer treatment and isotope production

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.

Example: factor 4 in the complexity and cost of the control system for a medical accelerator as compared to a scientific one.

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

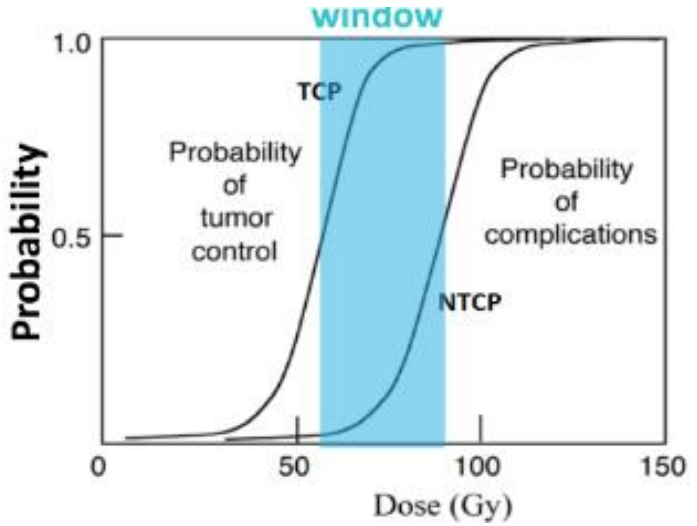


From the early tests at Lawrence’s cyclotron to a modern treatment room at CNAO

Medical exposure – a critical issue

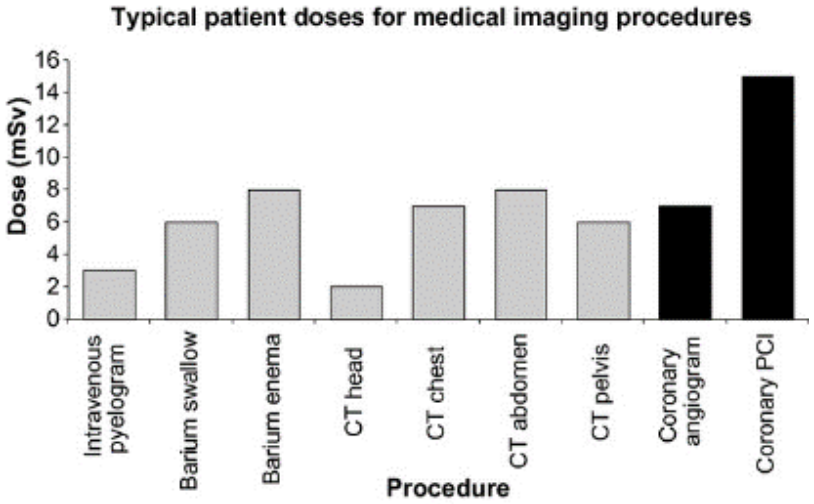
TCP=Tumor control probability
NTCO=normal tissue complication probability

Radiation management and control is a key issue in nuclear medicine.
- important doses are delivered to patients (comparison risk-benefit)
- the dose to medical personnel is subject to strict legal limits.



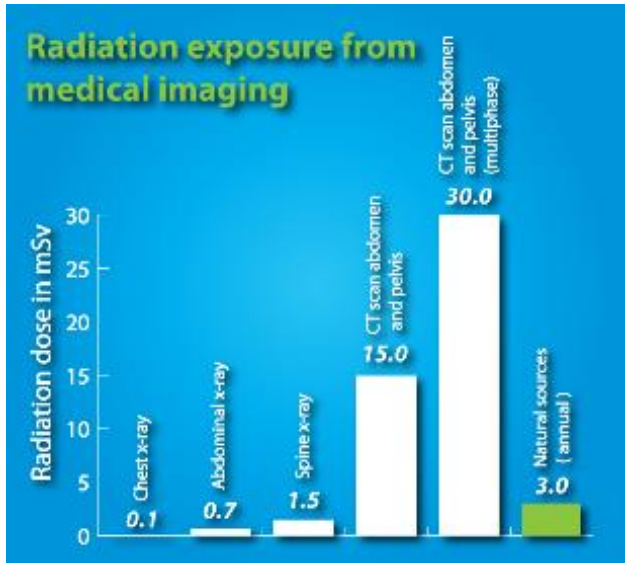
CERN limits

	Area	Dose limit [year]	Ambient dose equivalent rate	
			Work place	Low occupancy
Radiation Area	Non-designated	1 mSv	0.5 µSv/h	2.5 µSv/h
	Supervised	6 mSv	3 µSv/h	15 µSv/h
	Simple	20 mSv	10 µSv/h	50 µSv/h
	Limited Stay	20 mSv		2 mSv/h
	High Radiation	20 mSv		100 mSv/h
	Prohibited	20 mSv		> 100 mSv/h



Up to 2000 mSv highly targeted dose in conventional radiotherapy !

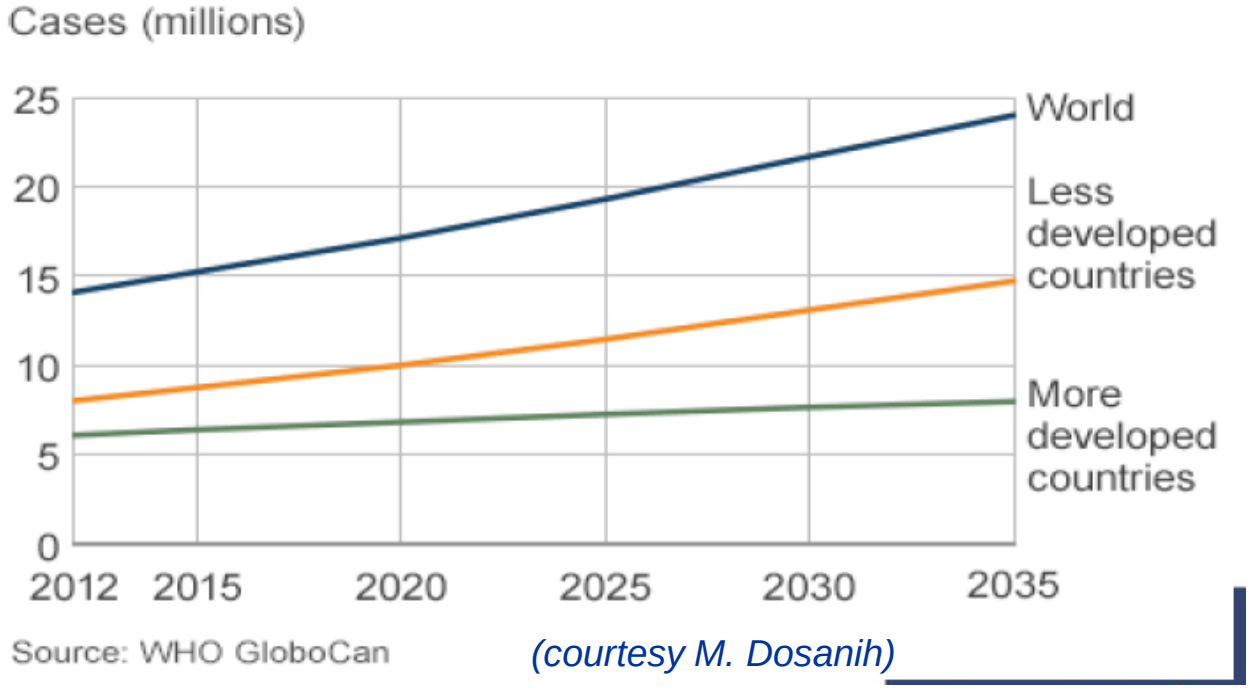
Source: S. Liauw et al., Translational Medicine, 5, 173



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)

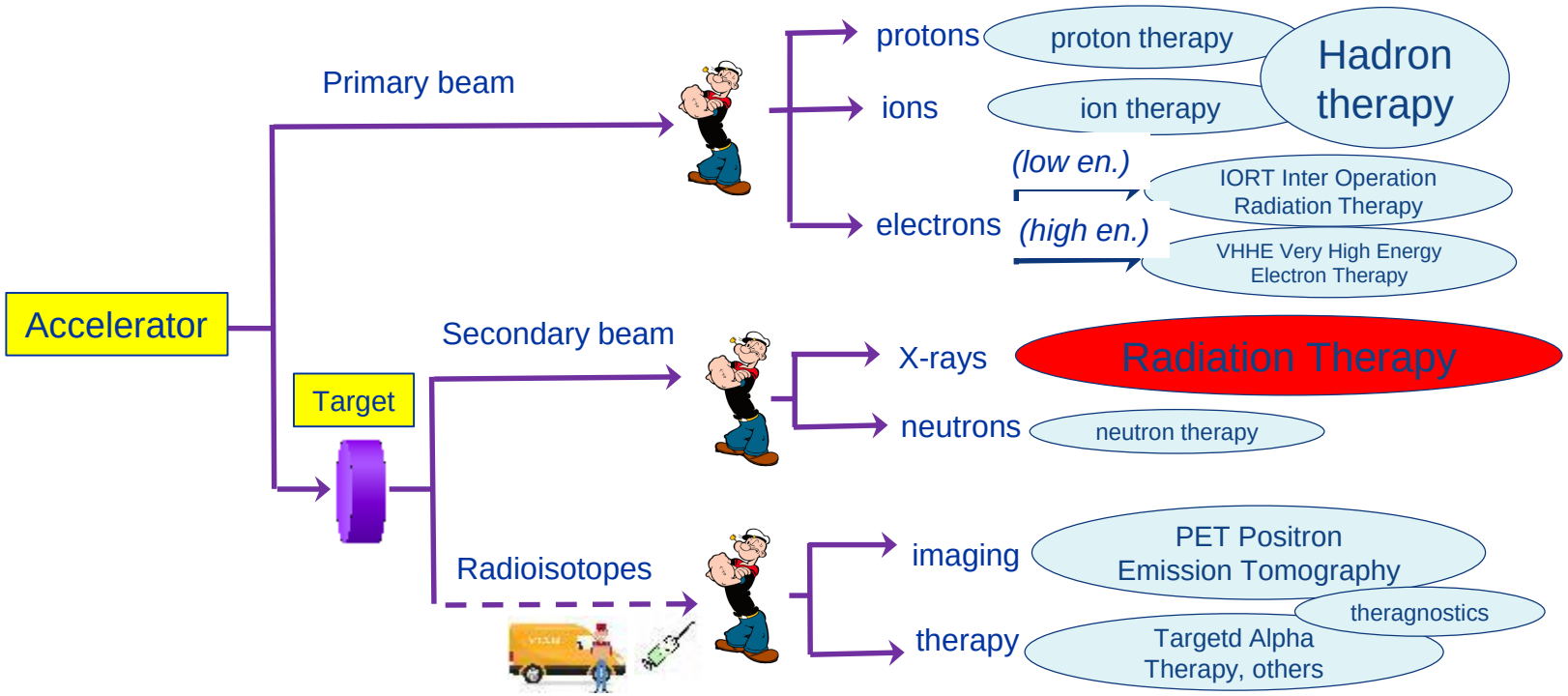
Increase of cancer cases due to:

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

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

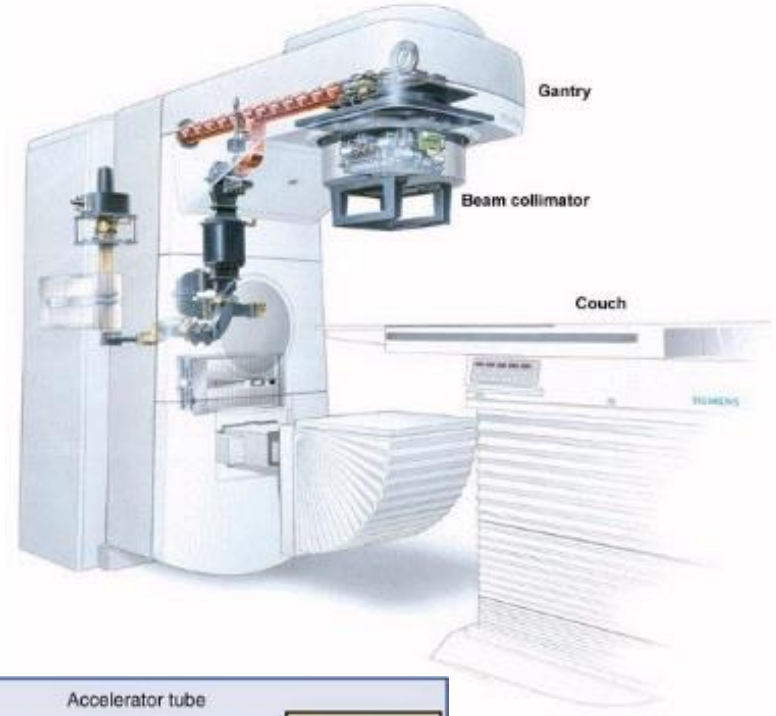
1. Surgery
2. **Radiotherapy** (accelerator-based)
3. Chemiotherapy
4. (Immunotherapy)

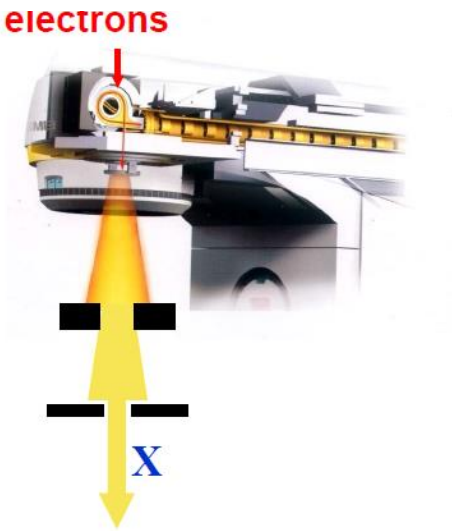
1. Radiation therapy



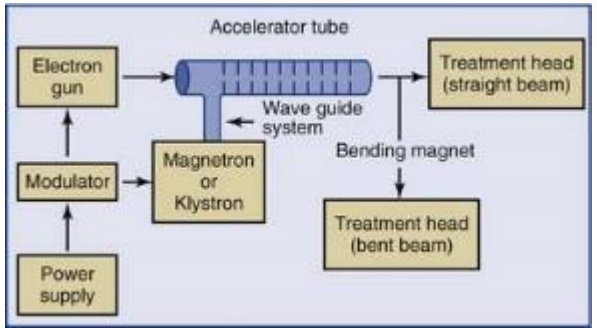
The most successful accelerator

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



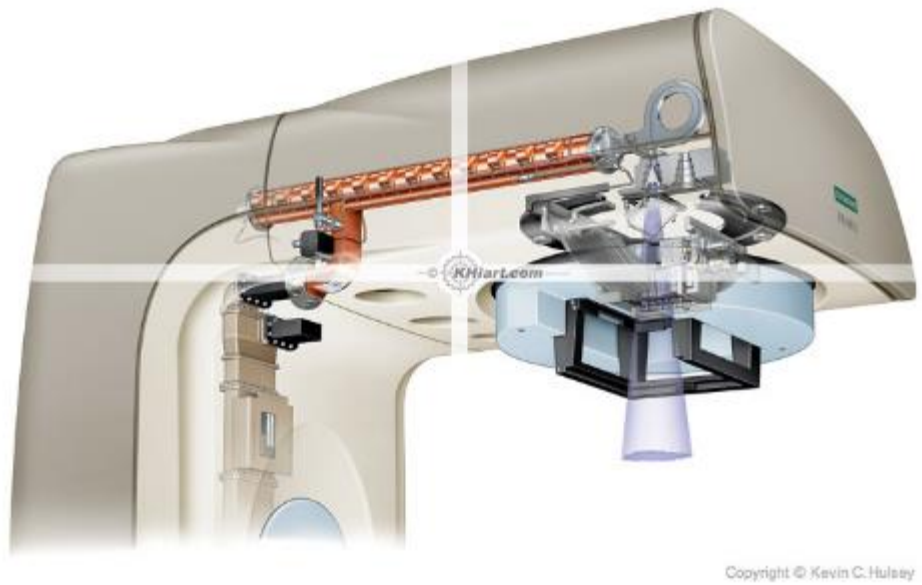


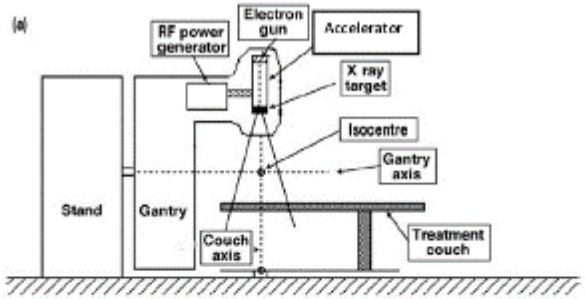
5 – 25 MeV e-beam
Tungsten target

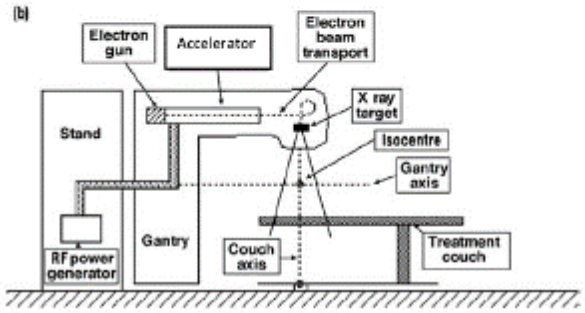


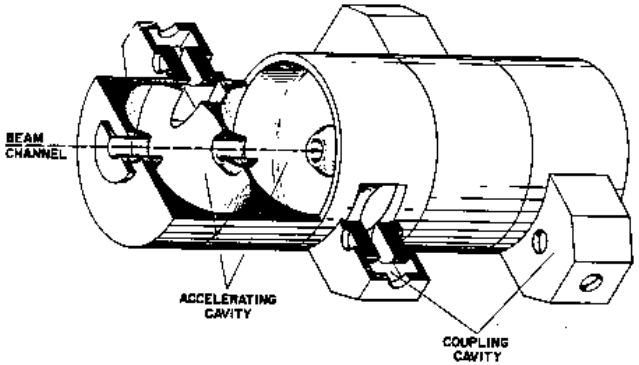
14,000 in operation worldwide!

Inside a radiation therapy linac







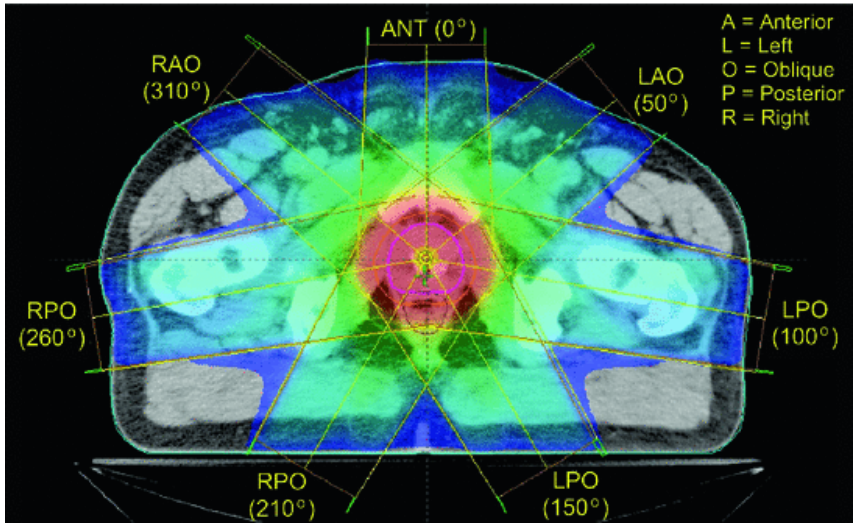


The Side Coupled Linac structure was invented at Los Alamos in the late 60's for the 800 MeV LA meson facility.
Because of its robustness, stability, reliability and low cost since the late 70's it has been used in a 3 GHz version to produce X-rays for radiation therapy

A great example of technology transfer from basic science to society

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

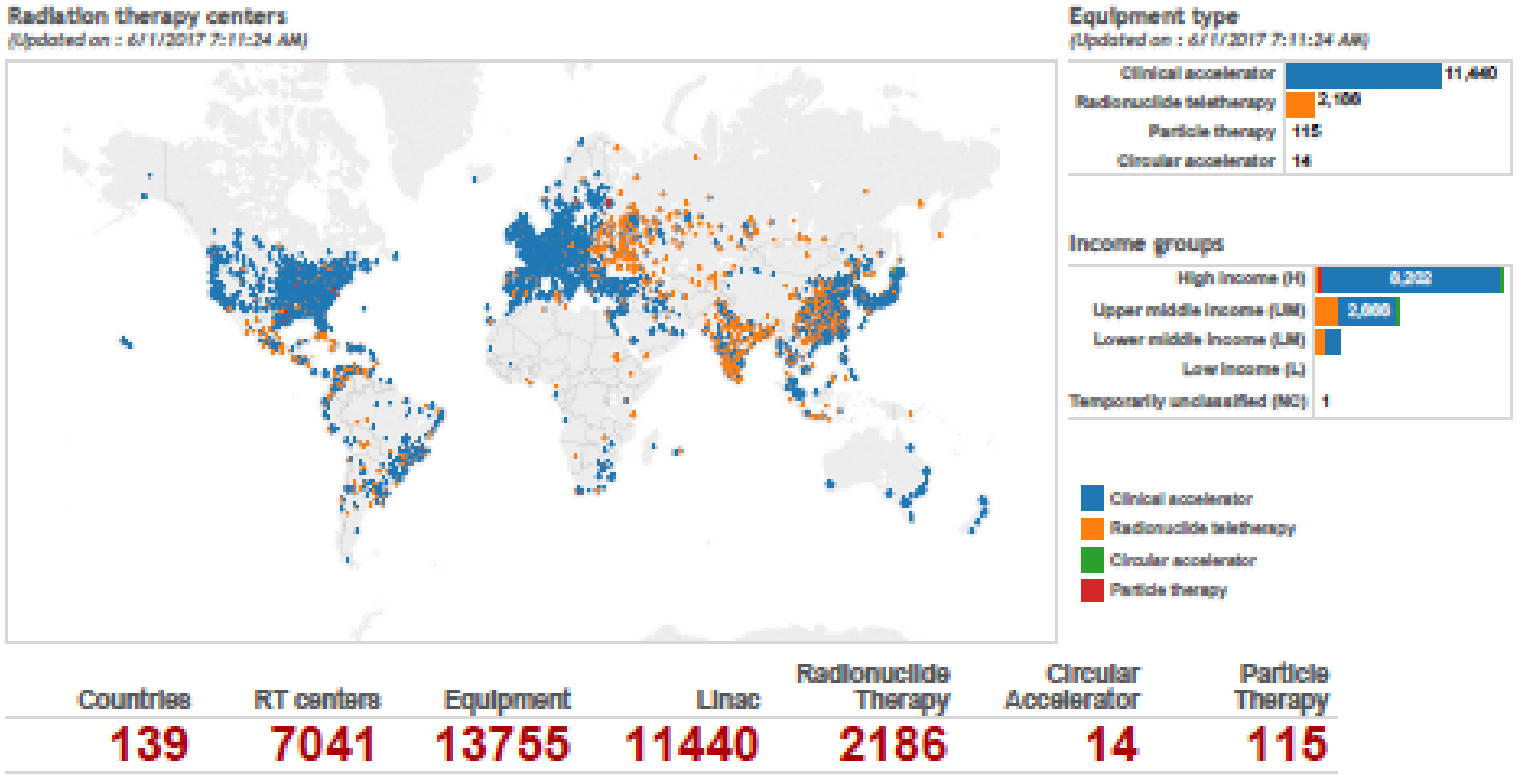
To spare surrounding tissues and organs, computer-controlled treatment methods enable precise volumes of radiation dose to be delivered. The radiation is delivered from several directions and transversally defined by multi-leaf collimators (MLCs).

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).

Radiation therapy worldwide



Countries	RT centers	Equipment	Linac	Radionuclide Therapy	Circular Accelerator	Particle Therapy
139	7041	13755	11440	2186	14	115

(courtesy ENLIGHT Network)

Radiation therapy nowadays relies mostly on linear accelerators, which in developed countries have replaced the old «cobalt bombs».
Many countries with an expected increasing cancer rate are not covered.

The ICEC Initiative for a new linac design

Today the radiation therapy linac market is in the hands of 2 large companies – and two smaller «niche» producers.
Equipment is expensive, requires maintenance and a stable operating environment (electricity, humidity, dust, etc.) → this has reduced the access of low and middle income countries to radiation therapy.

A collaboration led by the NGO International Cancer Expert Corps with the participation of STFC and CERN has started the development of a new radiotherapy linac specifically aimed at low and medium income countries.

International Cancer Expert Corps

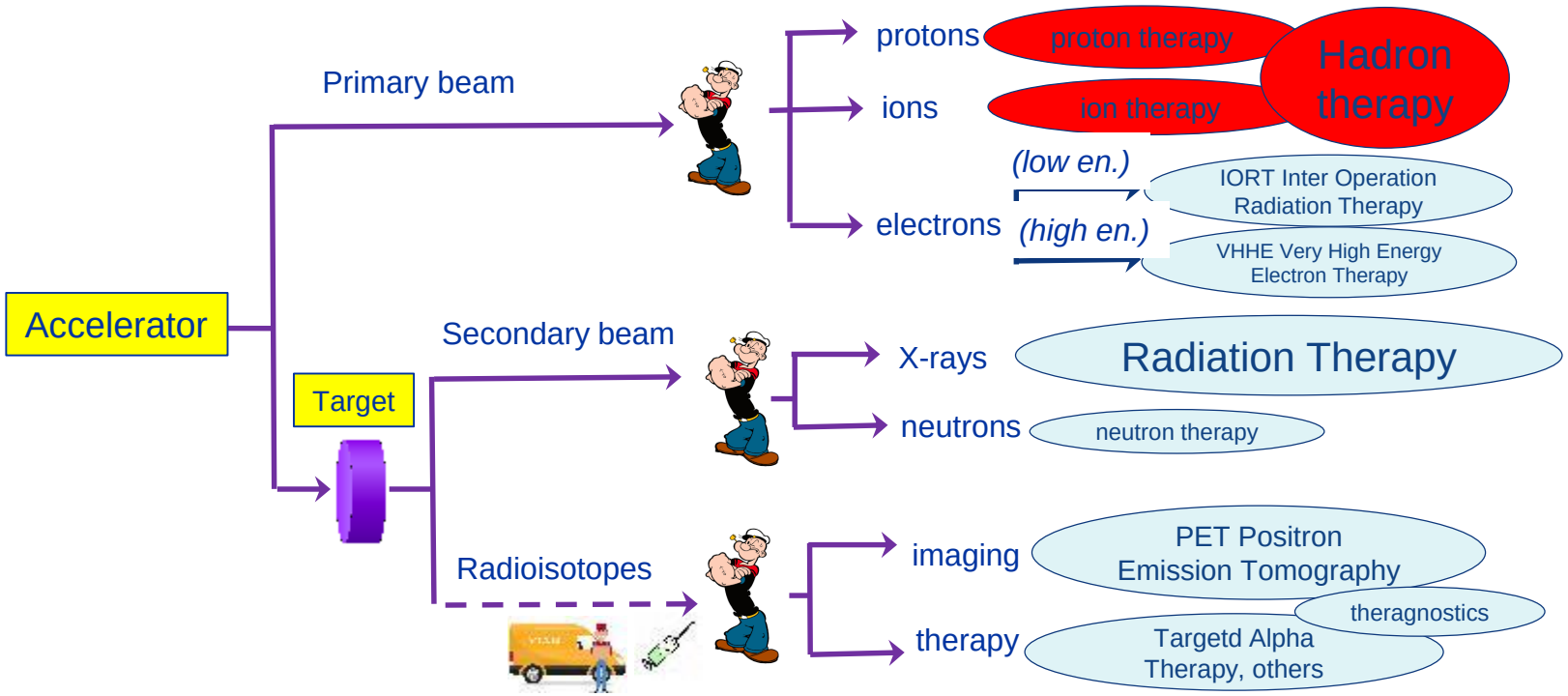
Partnering to transform global cancer care

CERN hosted workshop on:
"Design Characteristics of a Novel Linear Accelerator for Challenging Environments"

Norman Coleman, David Pistenmaa (ICEC) Manjit Dosanjh (CERN)
International Cancer Expert Corps &CERN

European Organization for Nuclear Research (CERN)
International Atomic Energy Agency (IAEA)
James Martin Center for Nonproliferation Studies (CNS)
National Aeronautics and Space Administration (NASA)
National Nuclear Security Administration (NNSA)

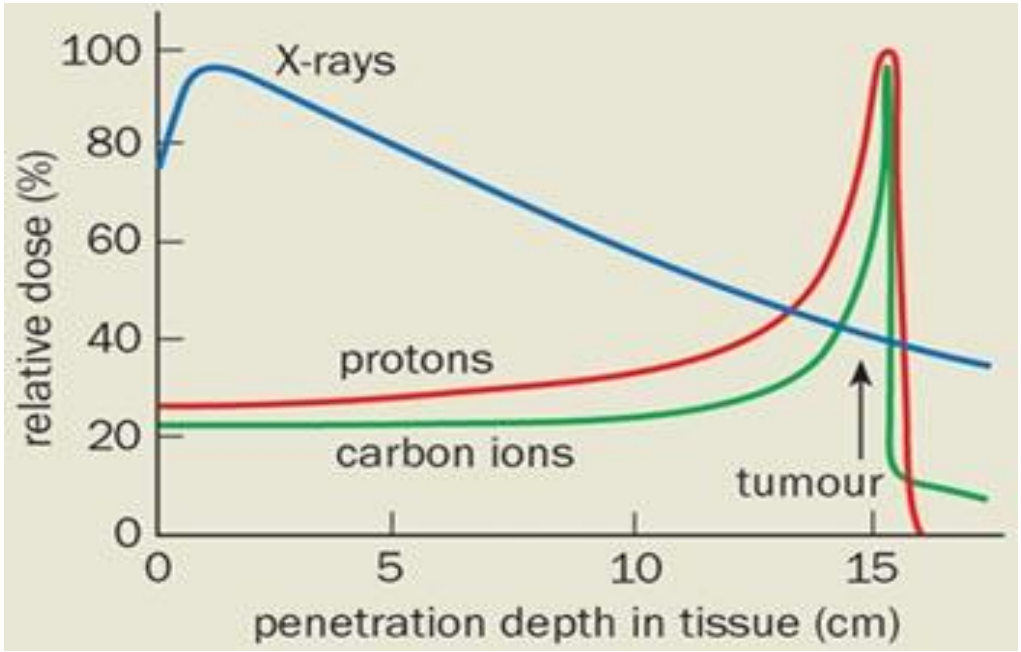
2 – Hadron therapy



The Bragg peak

Bethe-Bloch equation of ionisation energy loss by charged particles

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



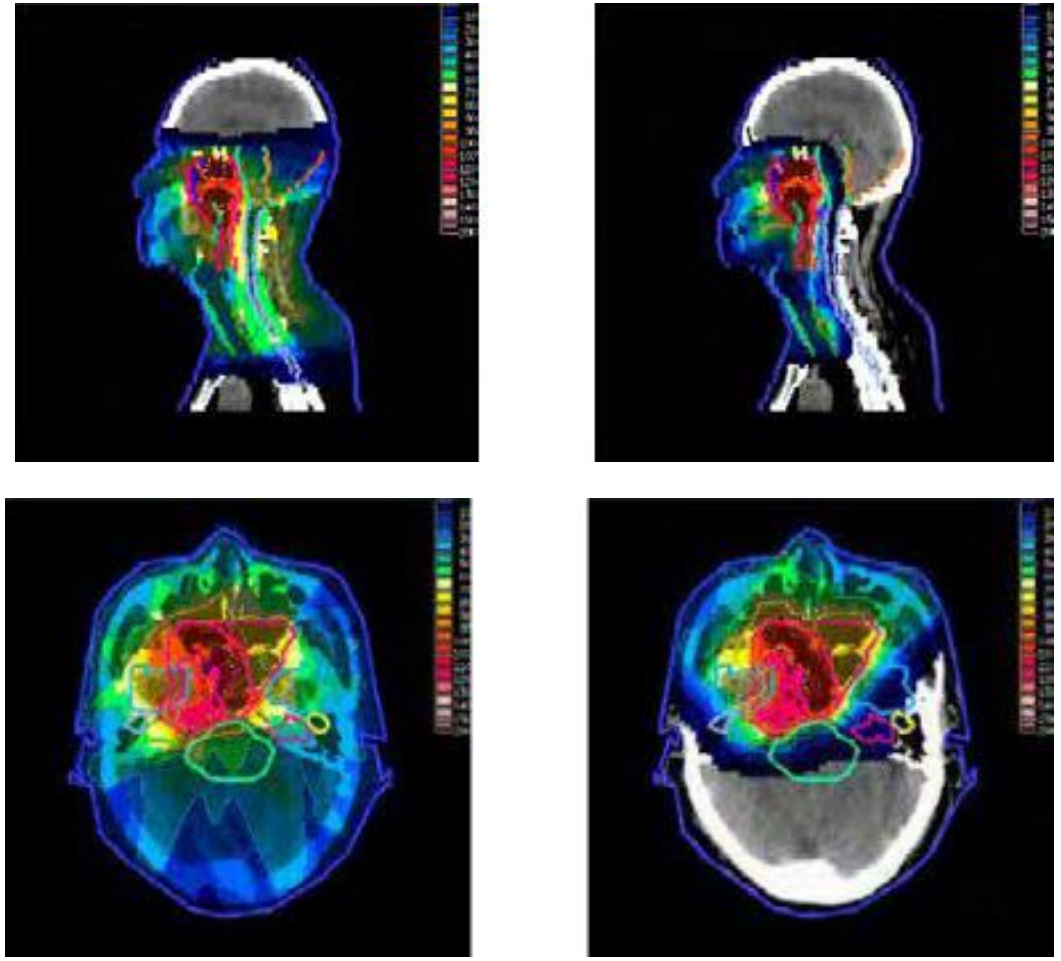
«Bragg» peak

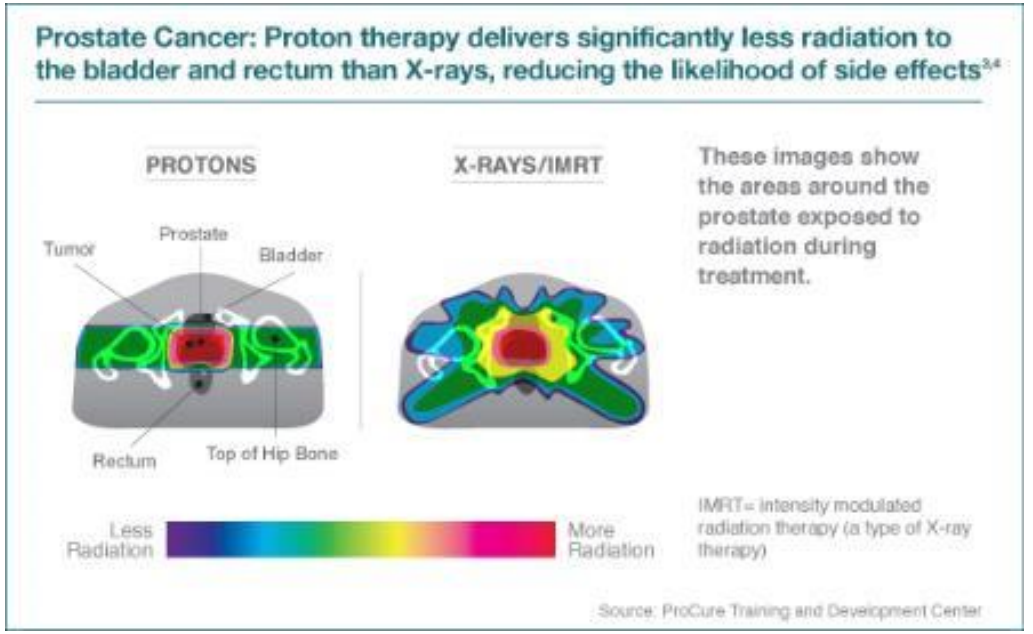
Different from X-rays or electrons, protons and ions deposit their energy at a given depth inside the tissues, **minimising the dose to the organs close to the tumour**.

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.

accelerators-for-society.org

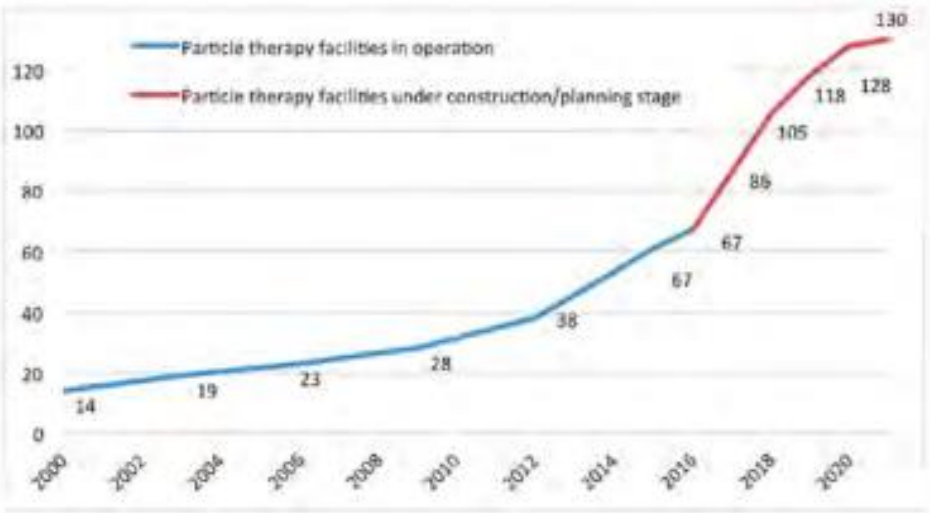
Comparing proton and X-ray therapy





The results of irradiating a nasopharyngeal carcinoma by X-ray therapy (left) and proton therapy (right), showing the potential reduction in dose outside the tumour volume that is possible with proton treatment. (Z. Taheri-Kadkhoda et al., Rad. Onc., 2008, 3:4 – from APAE Report, 2017).

The rise of particle therapy



First experimental treatment in 1954 at Berkeley.

First hospital-based proton treatment facility in 1993 (Loma Linda, US).

First treatment facility with carbon ions in 1994 (HIMAC, Japan).

Treatments in Europe at physics facilities from end of ‘90s.

First dedicated European facility for proton-carbon ions in 2009 (Heidelberg).

From 2006, commercial proton therapy cyclotrons appear on the market (but Siemens gets out of proton/carbon synchrotrons market in 2011).

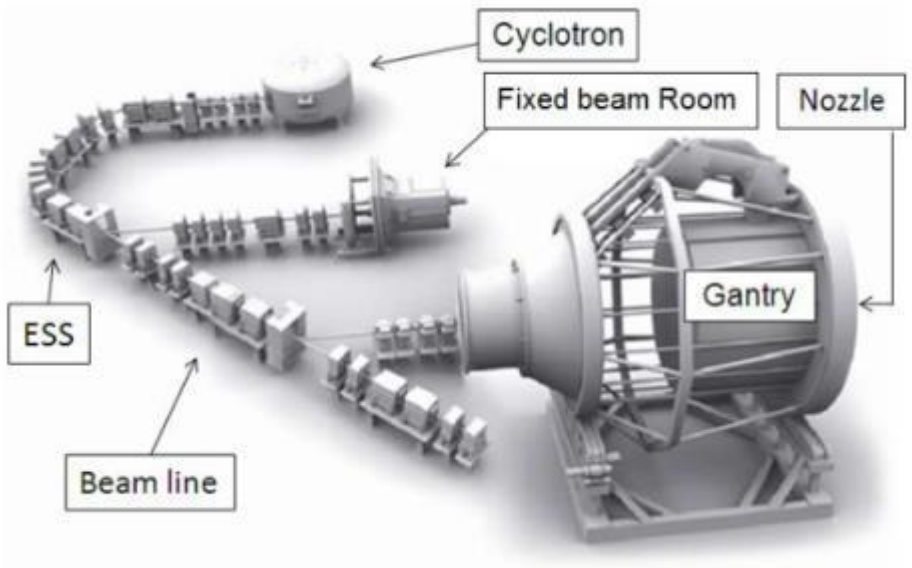
Nowadays 3 competing vendors for cyclotrons, one for synchrotrons (all protons).

More centres are planned in the near future.

A success story, but …

many ongoing discussion on effectivness, cost and benefits.

Proton therapy accelerators: cyclotrons



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

Critical issues with cyclotrons:

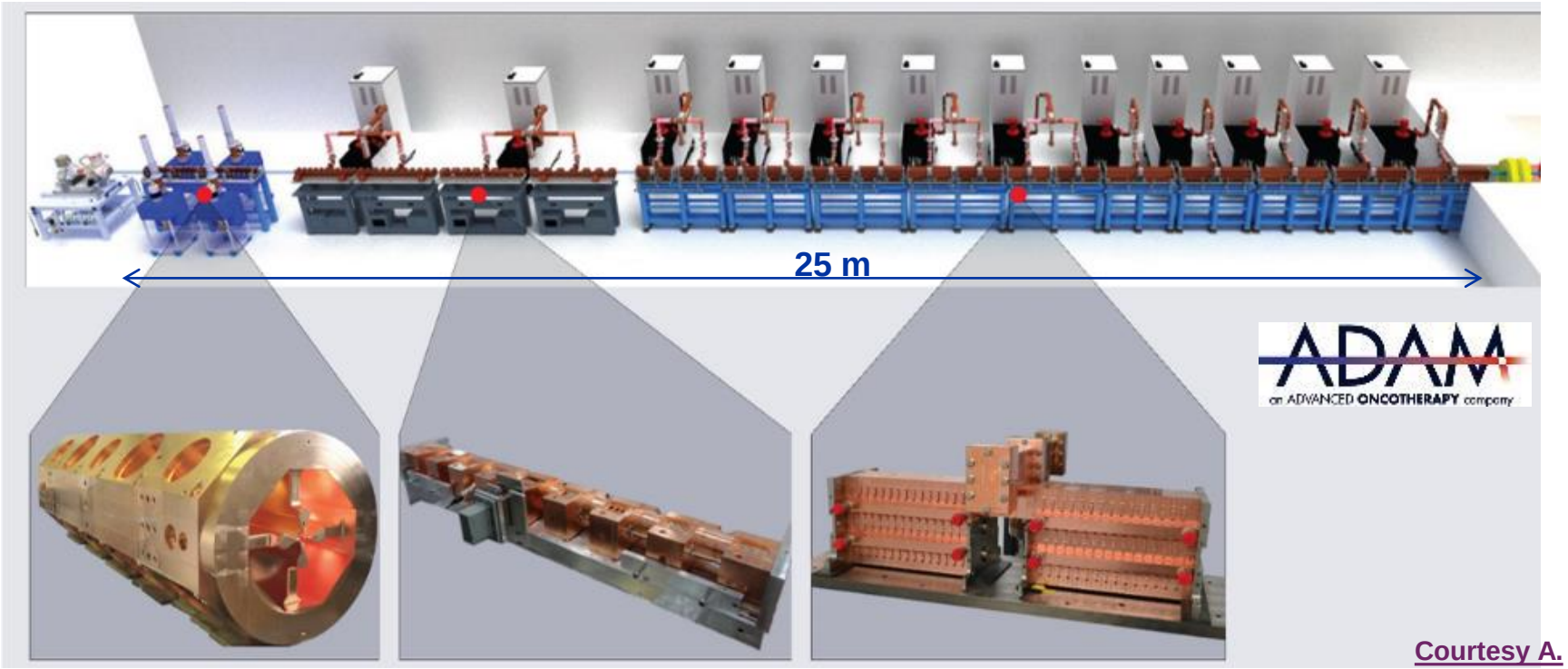
1. Energy modulation (required to adjust the depth and scan the tumour) is obtained with degraders (sliding plates) that are slow and remain activated.
2. Large shielding

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

A linac alternative: LIGHT (Linac for Image Guided Hadron Therapy)

The LIBO prototype structure and accelerating cells (CERN)

Advantages of a LINAC:
- High repetition frequency with pulse-to-pulse energy variability
- Small emittance, no beam loss.



Courtesy A. Degiovanni,

750 MHz Radio Frequency Quadrupole (RFQ)

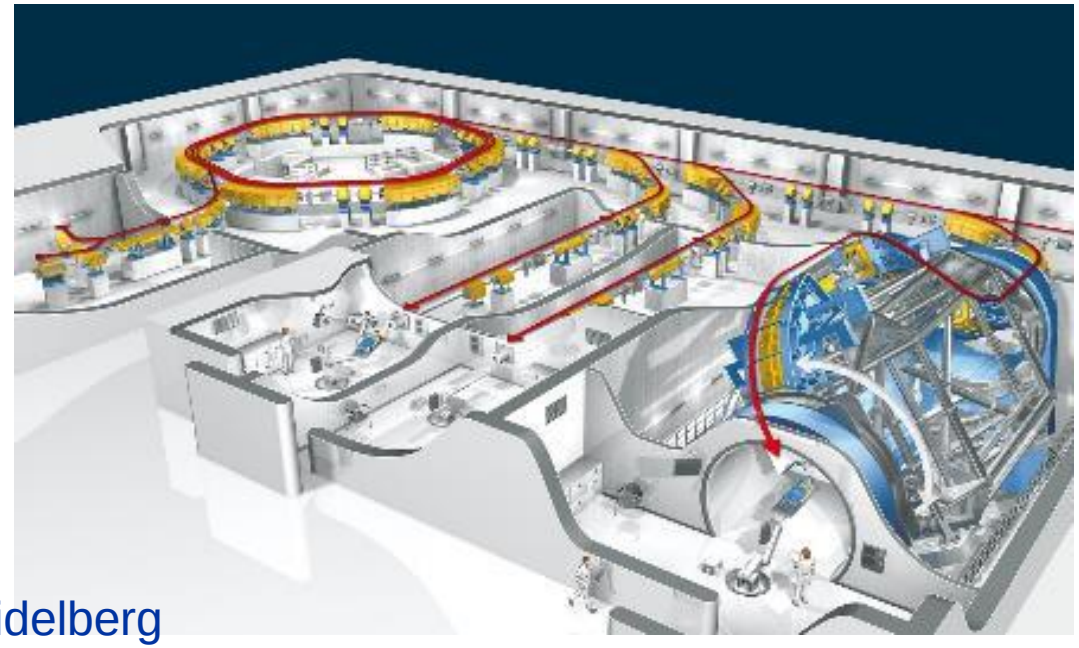
3 GHz Side Coupled Drift Tube Linac (SCDTL)

3 GHz Coupled Cavity Linac (CCL)

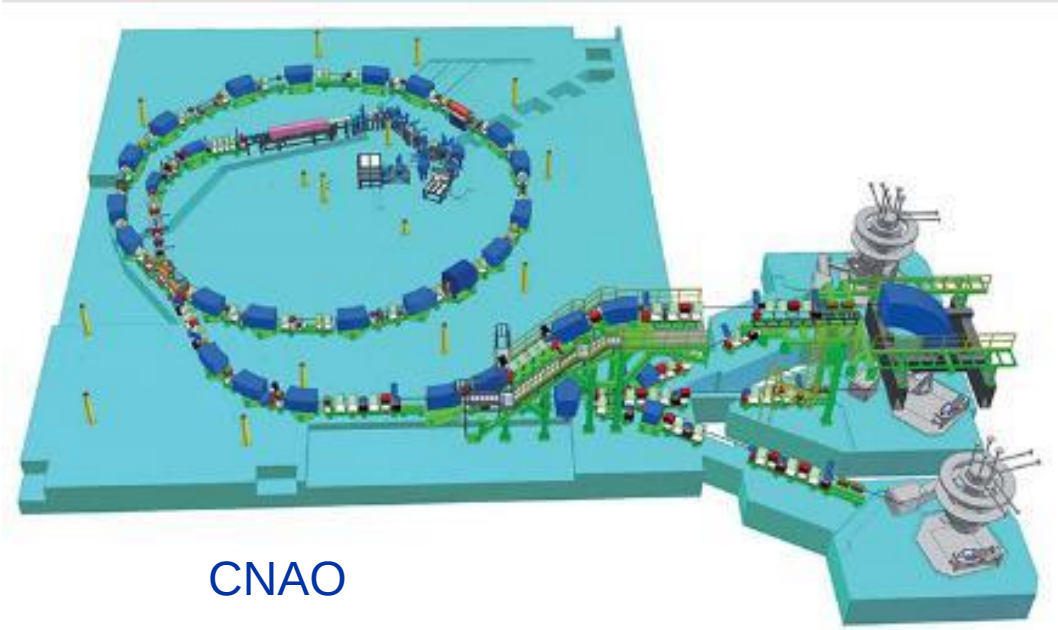
ADAM is an old CERN spin-off now part of the UK company AVO (Advanced Oncotherapy). They reported acceleration to 52 MeV in September 2018. From end 2019, the development will continue at Daresbury Laboratory (UK). The first LIGHT unit will be installed at the Harley Street Hospital in London.

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.



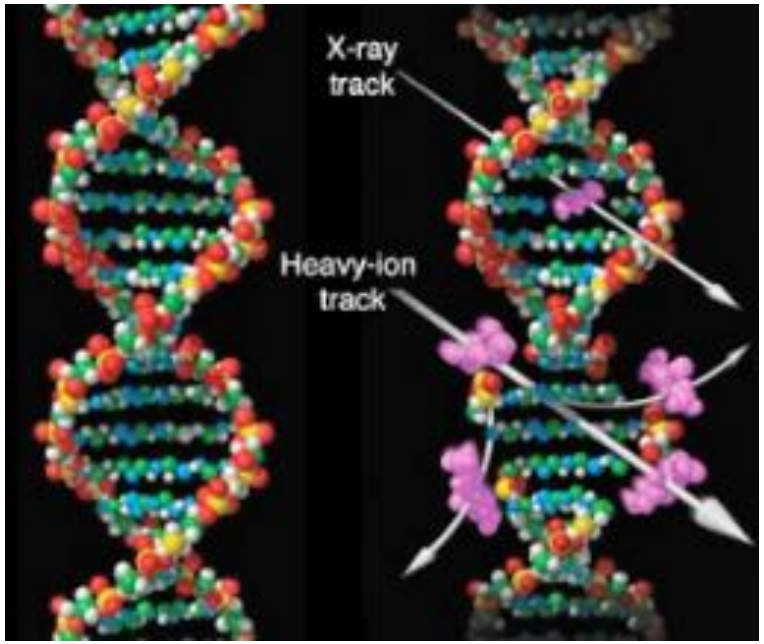
HIT Heidelberg



CNAO

Advantages of therapy with ions (Carbon and others)

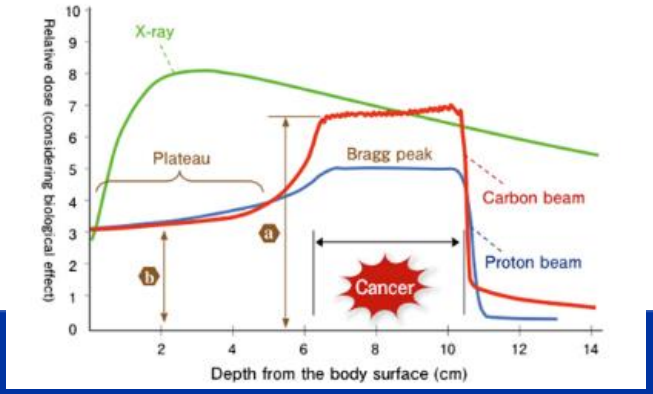
Ions (e.g. Carbon) are different from X-rays or protons!



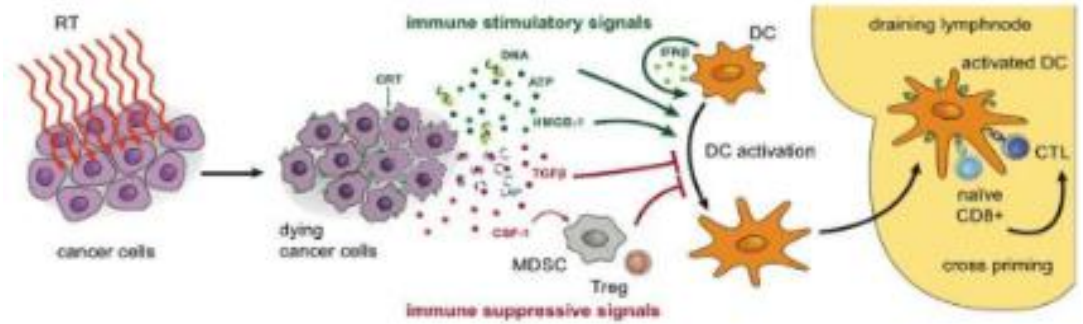
Heavy ions are **more effective than protons or X-rays** in attacking cancer:

1. The higher energy deposition (and ionisation) per length generates a large number of double-strand DNA breakings that are not reparable by the cell itself.
2. The different damage mechanism makes them effective on hypoxic radioresistant tumours (while protons or X-rays act via generation of Reactive Oxygen Species) – 1 to 3% of all RT cases.
3. Are more precise, with lower straggling and scattering.
4. Recent studies show that ion therapy combined with immunotherapy may be successful in treating diffused cancers and metastasis.

So far, 2/3 of cases at the mixed facilities like CNAO are treated with carbon.



Radio Biological Effectiveness (RBE) is higher for Carbon than for protons.
1.1 for protons
3 for C ions
(reference 1 for Co X-rays)



Ion therapy: cost and perspectives

For practical and historical reasons, all ion accelerators operate with fully stripped **Carbon ions**.

Bethe energy loss goes as z^2, z=charge of the incident particle → the energy loss is higher for ions → we need a higher energy (per atomic mass unit) to fully penetrate inside the body → around **440 MeV/u**.

The accelerator is more complex than for protons: magnetic rigidity at full energy is **2.76 times** that of proton at full treatement energy.

$$B\mathrm{r}\,[T.m] = 3.3356 \times pc[GeV]$$

For a given magnet field, in a medical ion synchrotron with respect to a proton one accelerator and gantries have to be almost 3 times larger.

The HIT gantry has a mass of 600 tons for a dipole bending radius of 3.65 m.

Particle	H^+		C^{6+}		
Ring 1	inj	ext	inj	ext	
Ring 2				inj	ext
Energy [MeV/u]	31 MeV	250	7.9	68.8	440
$B\rho$ [T·m]	0.811	2.432	0.811	2.432	6.716

All existing ion therapy accelerators are large synchrotrons.

Cyclotrons cannot be easily used because of the dimensions and complexity (needs superconductivity) and because of the difficult ion extraction.

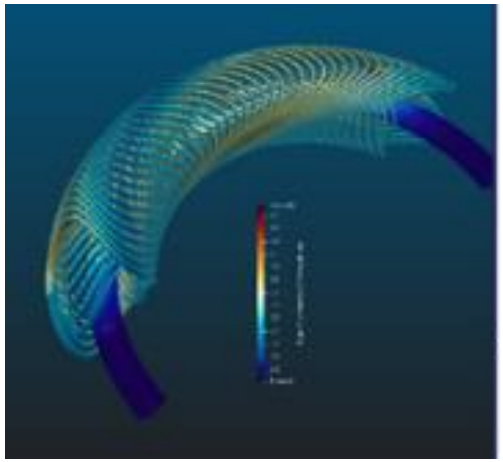
Development of superconducting magnets for ion therapy

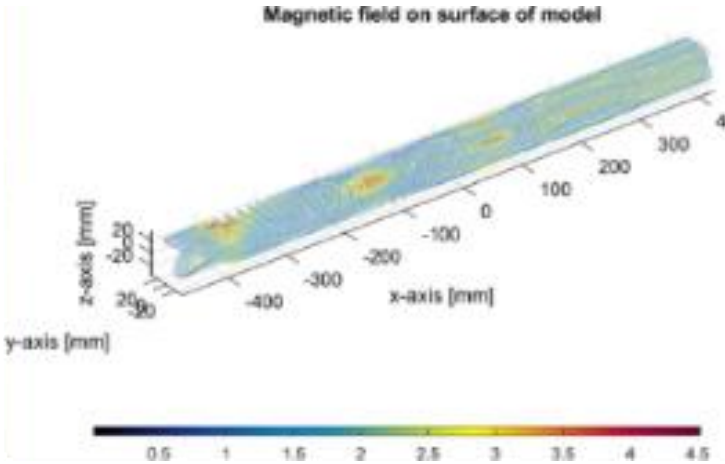
Wide international effort towards the development of a new generation of superconducting magnets for small synchrotrons.

Some of the challenges are common with magnets for scientific applications, other specific for medical accelerator magnets: ramping field, curved shape, quadrupole integration, use of cryocoolers.

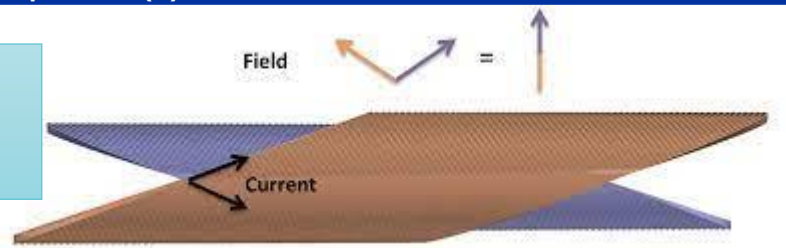
Magnet Parameters

Parameter	Synchrotron magnet	Prototype Magnet
Bρ (Tm)	6.6	6.6
B_0 dipole (T)	3.0	4-5
Coil apert. (mm)	70-90	60 (90)
Curvature radius (m)	2.2	2.2 , ∞
Ramp Rate (T/s)	1	0.15-1
Field Quality (10^{-4})	1-2	10-20
Deflecting angle	90°	0 - 45°
Alternating-Gradient	yes (triplet)	N/A
Quad gradient (T/m)	40	40
B_{quad} peak (T)	1.54- 1.98	1.2
B_{peak} coil (T)	4.6 - 5	5.6-7
Operating current (kA)	< 6	< 5
Type of Superconductor	NbTi (Nb_3Sn)	NbTi (curved), HTS (straight)
Operating temperature (K)	5 (8)	5 (20)





Canted Cosine Theta magnets
(drawing: E. Oponowicz)



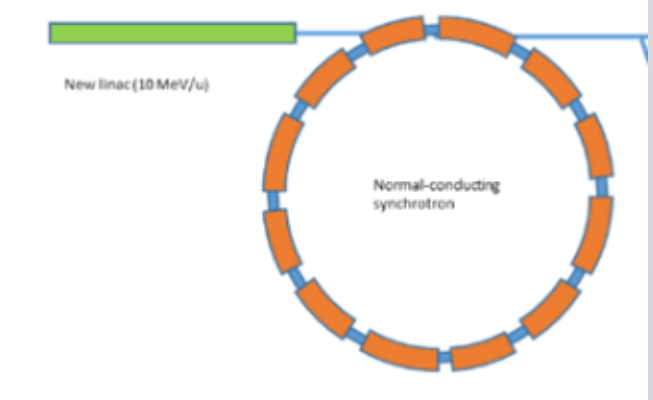
Solution for curved and straight CCT coils combining dipole and quadrupole in the same winding - Courtesy G. Kirby and J. van Nugteren, CERN

Advanced ion therapy: 3 alternative accelerator designs

Improved synchrotron (warm)

Equipped with several innovative features: multi-turn injection for higher beam intensity, new injector at higher gradient and energy, multiple extraction schemes, multi-ion.

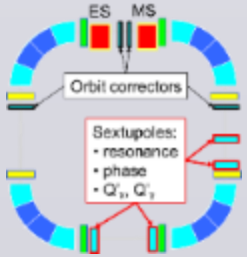
Circumference ~ 75 m

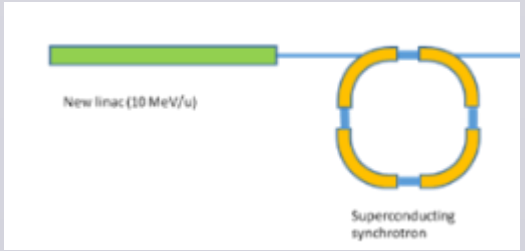


Improved synchrotron (superconducting)

Equipped with the same innovative features as warm, but additionally 90^0 superconducting magnets.

Circumference ~ 27 m

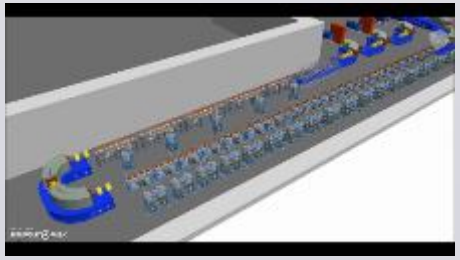


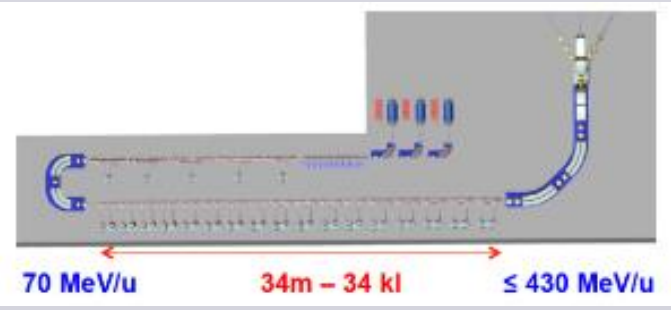


Linear accelerator

Linear sequence of accelerating cells, high pulse frequency.

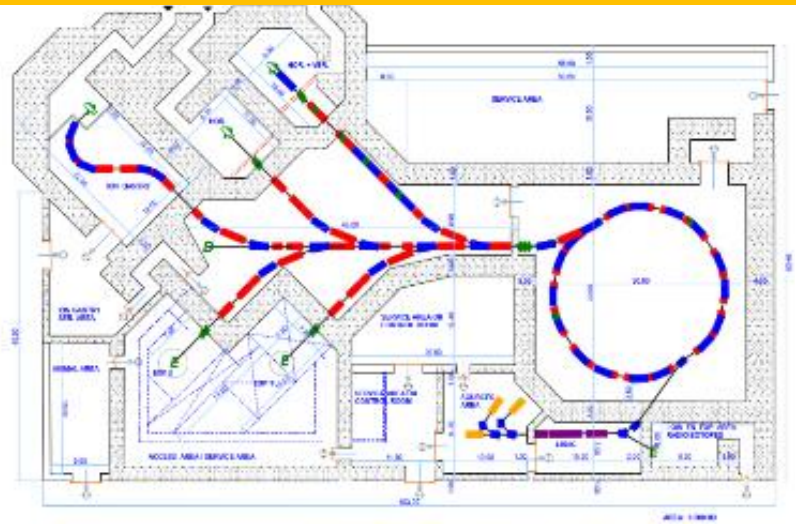
Length ~ 53 m



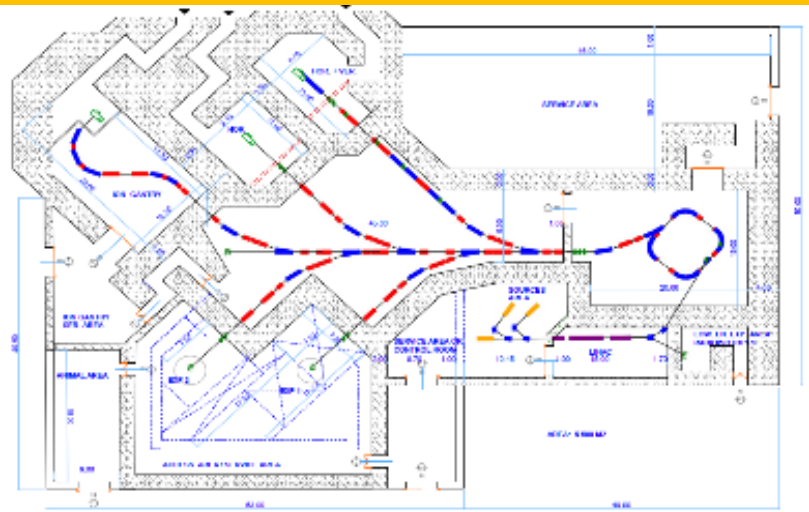


Other options considered as less interesting because of cost and/or required R&D: **RC synchrotron**, **FFAG**, **SC cyclotron**, **PWFA**

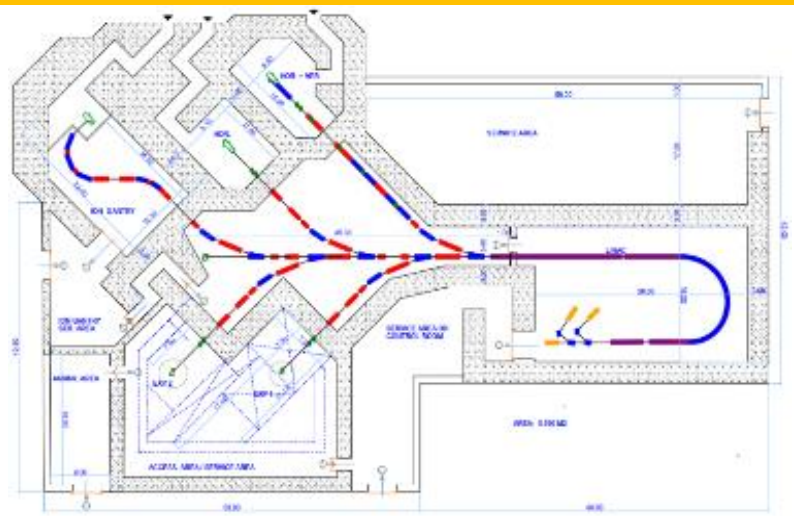
Comparing three accelerator options for SEEIIST



RT synchrotron:
accelerator 1,200 m^2, facility 6,500 m^2
Reference for cost calculation



SC synchrotron:
accelerator 600 m^2, facility 5,500 m^2
estimated cost (acc. only): 20% lower



Full linac:
accelerator 600 m^2, facility 5,500 m^2
estimated cost (acc. only): 20% lower

SC synchrotron or linac allow 50% reduction in accelerator dimensions, 15% in overall facility dimensions, and 20% reduction in cost.

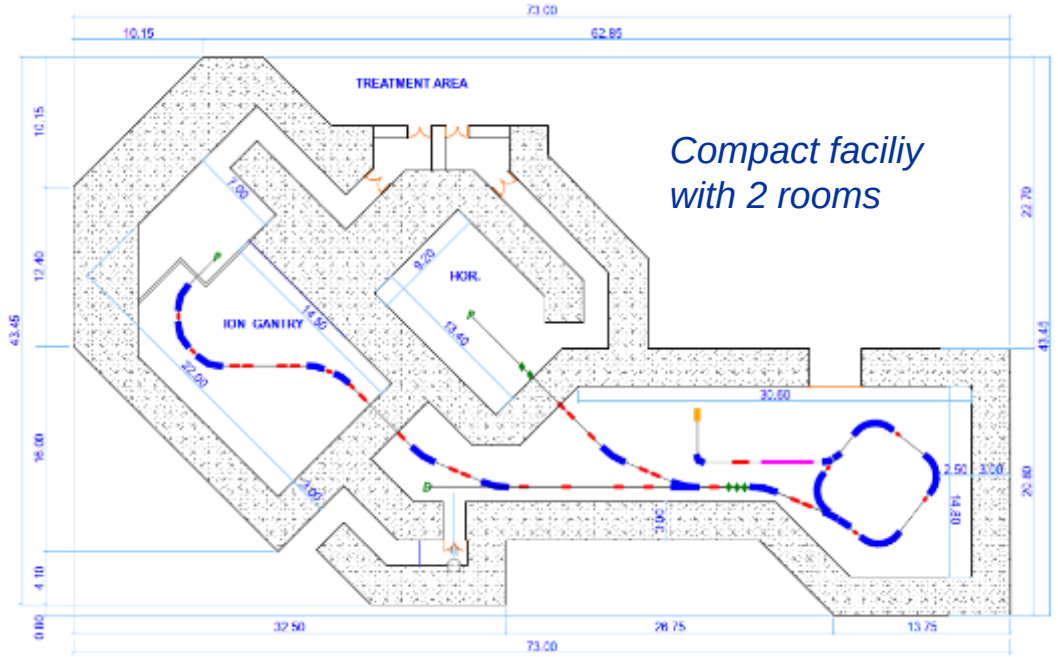
- The **SEEIIST** (South East Europe International Institute for Sustainable Technologies) is a new international partnership aiming at the construction of a new Research Infrastructure for cancer research and therapy in South East Europe (9 member countries).
- Supported by the European Commission, to develop the facility design in collaboration with CERN.

SEE IIST
South East European International Institute for Sustainable Technologies

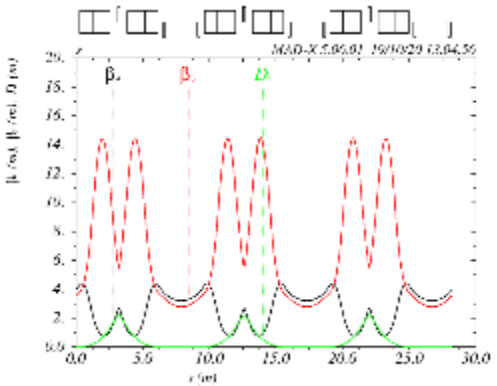
The SEEIIST facility

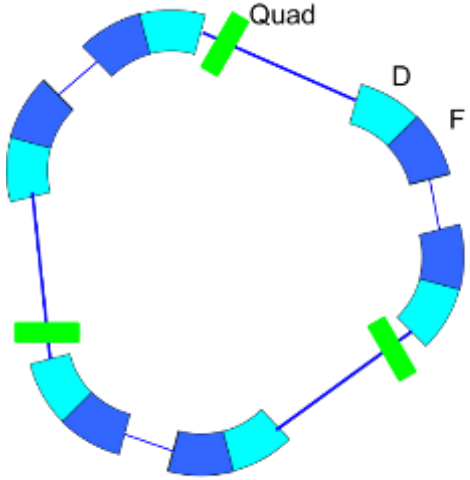
The compact SC synchrotron

E. Benedetto, M. Sapinski, TERA/SEEIIST
P. Foka, GSI
D. Kaprinis, Kaprinis Architects
M. Vretenar, CERN

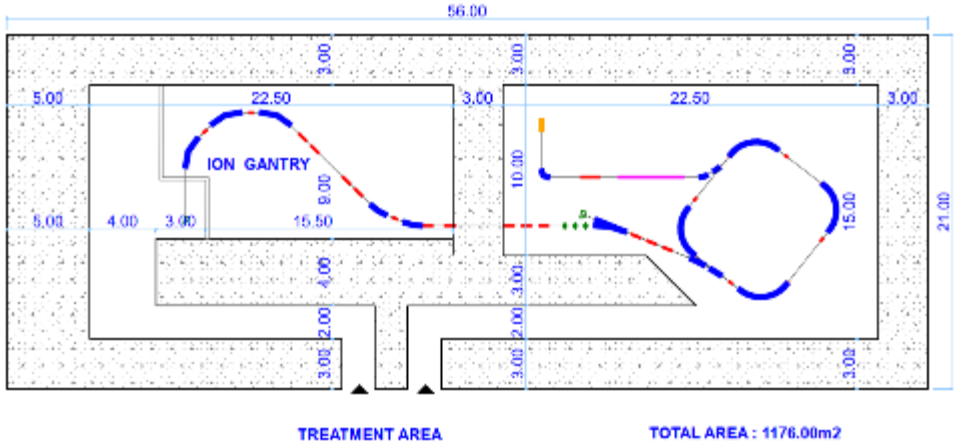


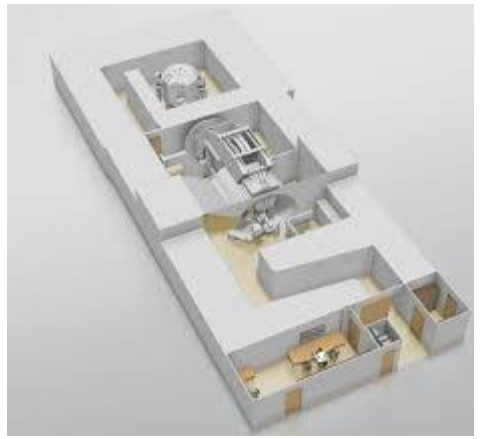
Alternative lattice with 60⁰ magnets





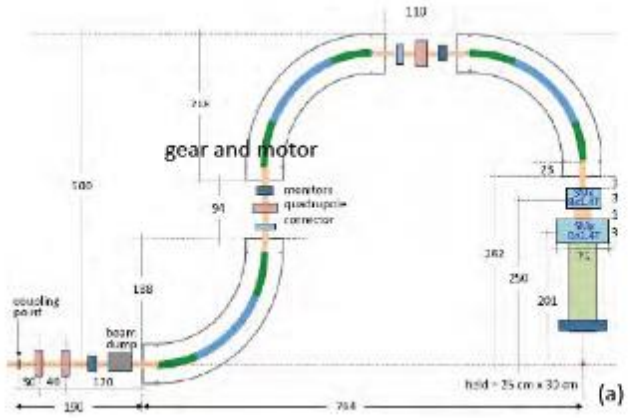
A compact single-room ion therapy facility in about 1,000 m²

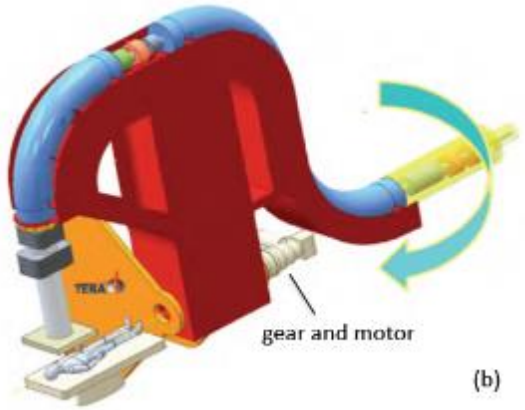




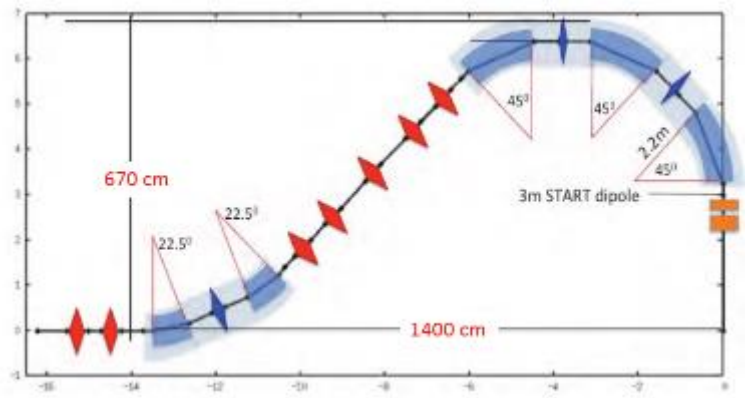
Comparable in size with proton therapy systems – here the single-room proton facility ProteusOne, from IBA)

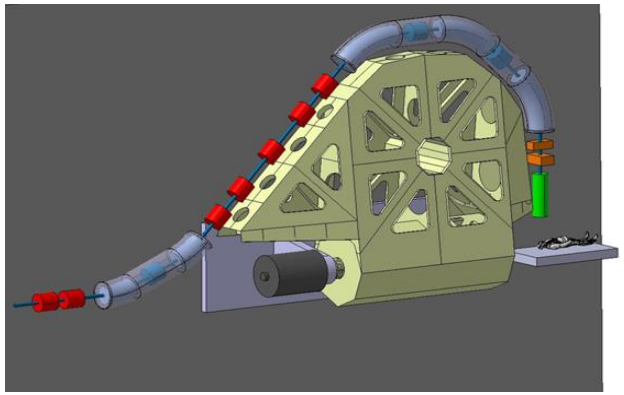
A superconducting ion gantry



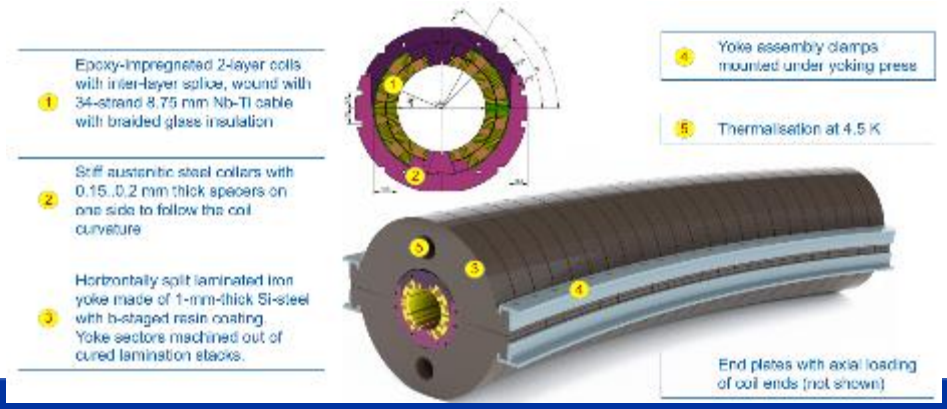


2018 design of a 4 T gantry equipped with Canted Cosine Theta (CCT) dipole magnets of 90^0 with nested-quadrupoles. The cables are in NbTi and the magnets weight 4 tons.



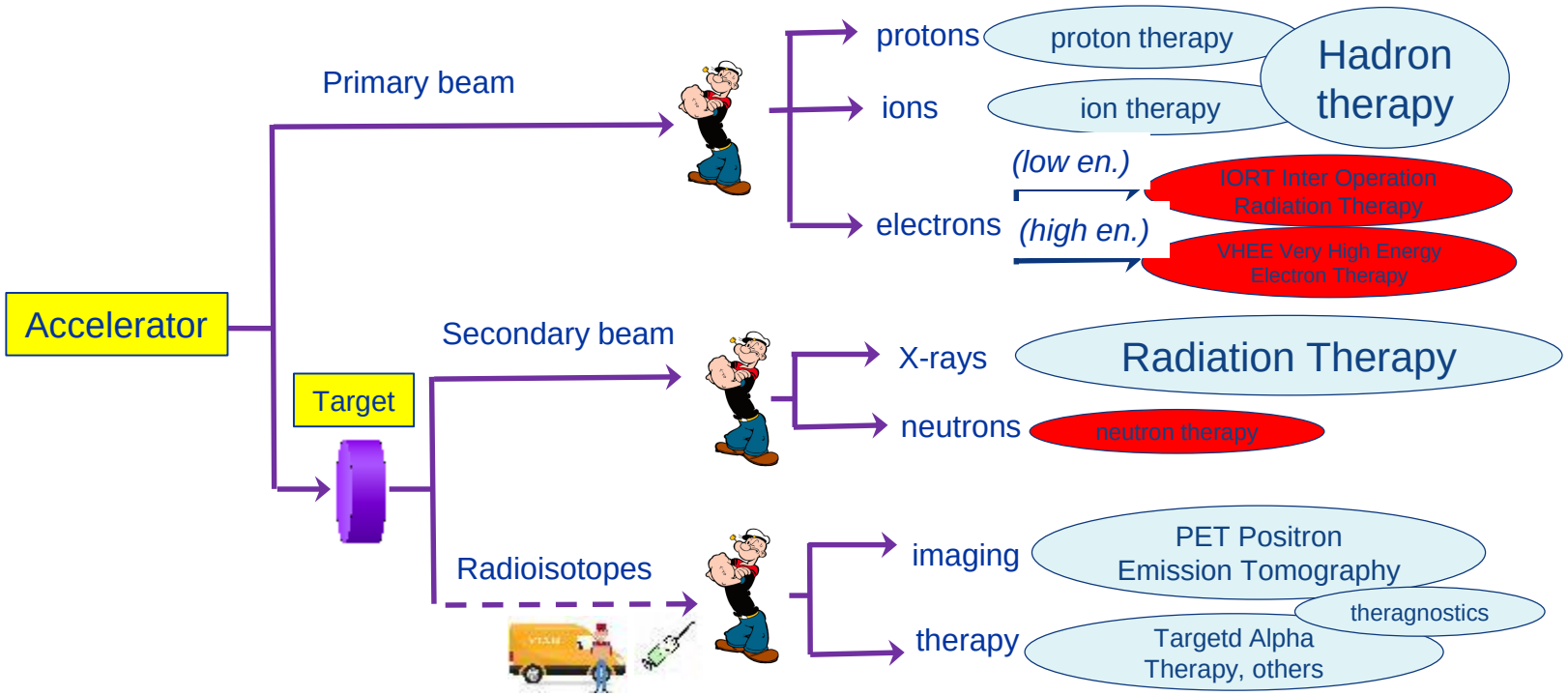


2020 design of a 3 T gantry equipped with cos-theta dipole magnets.
Collaboration for prototyping being formed (CERN, INFN, INFN, MedAustron).
Time to construction: 10 years



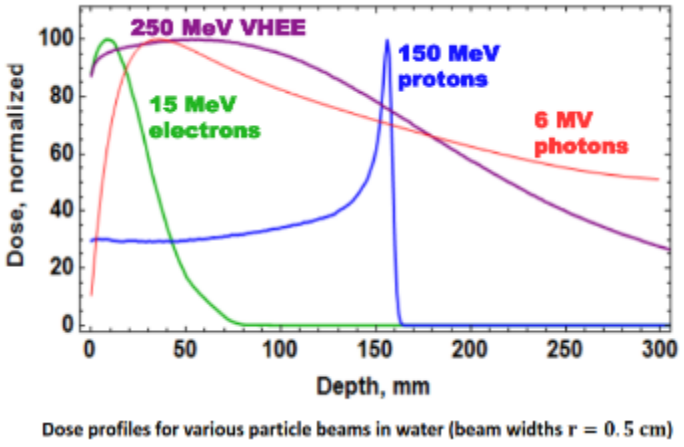
From “SIGRUM, A Superconducting Ion Gantry with Riboni’s Unconventional Mechanics”
U. Amaldi, N. Alharbi, E. Benedetto, P.L. Riboni and M. Vaziri, TERA Foundation
D. Aguglia, V.Ferrentino, G. Le Godec, M.Karppinen, D. Perini, E.Ravaioli and D. Tommasini, CERN
CERN-NIMMS-Note-2

3 – electrons and neutrons

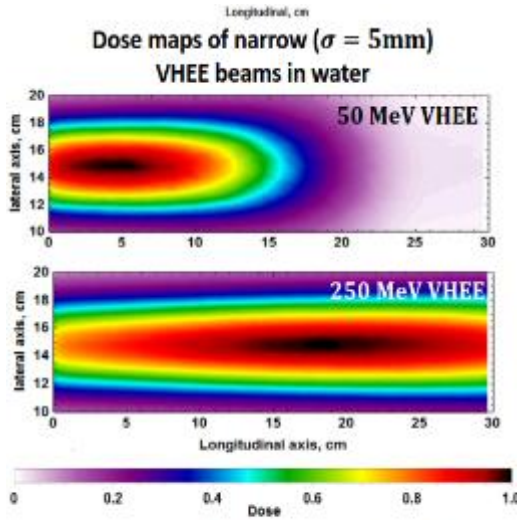


Electrons: IORT and VHEE

Inter Operational Radiation Therapy (IORT) – (5-20 MeV):
Technique derived from radiation therapy, where a compact electron linac is not used to produce X-rays, but to send the electrons directly on the tissues.
It delivers a concentrated dose of radiation therapy to a tumour bed during surgery. This technology may help kill microscopic diseases, reduce radiation treatment times, preserve more healthy tissue.



Dose profiles for various particle beams in water (beam widths r = 0.5 cm)

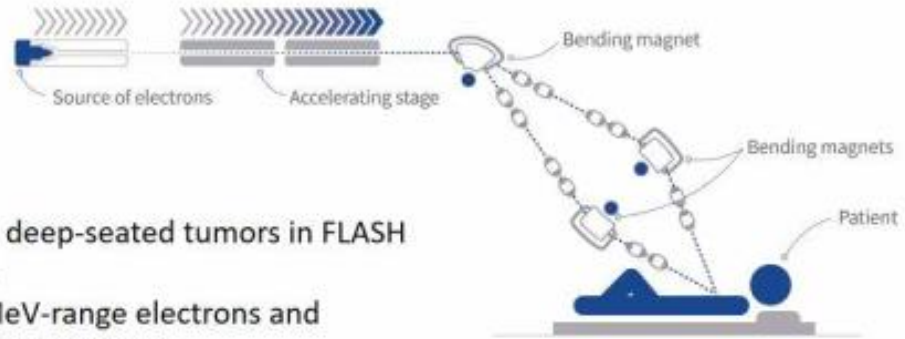


Dose maps of wide (σ = 20mm)
VHEE beams in water

Very High Energy Electrons (50-250 MeV) for radiotherapy:
Proposed as a lower-cost alternative to hadron therapy, treat deep seated tumours with high-energy electron beams. High dose deposition, less sensitive to errors, good sparing of healthy tissues.
Made possible by recent advances in high-gradient NC linac technology (CLIC, etc.).

FLASH with electrons – a new avenue to radiation therapy

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.

Construction of the prototype

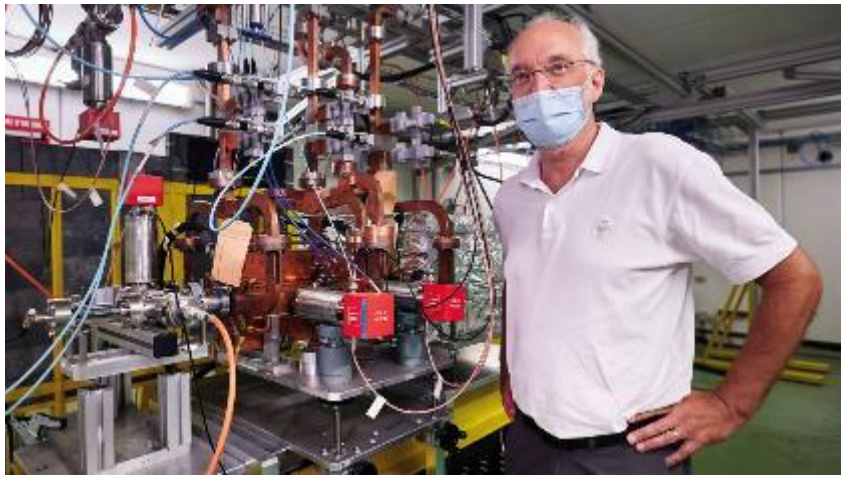
Installation 2023

First patient
2024-25

Lausanne University Hospital and CERN collaborate together on a pioneering new cancer radiotherapy facility

Lausanne University Hospital (CHUV) and CERN, in Switzerland, are collaborating to develop the conceptual design of an innovative radiotherapy facility, used for cancer treatment. The facility will capitalise on CERN breakthrough accelerator technology applied to a technique called FLASH radiotherapy, which delivers high-energy electrons to treat tumours. The result is a cutting-edge form of cancer treatment, highly targeted and capable of reaching deep into the patient's body, with less side-effects. The first phase of the study comes to a conclusion this September.

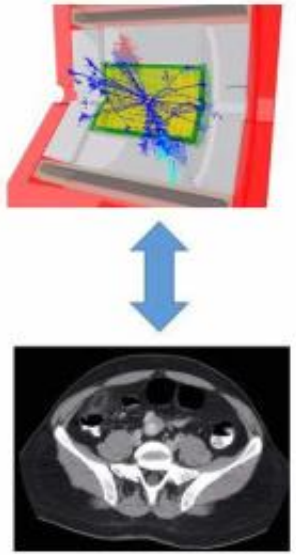
In radiotherapy, the FLASH effect appears when a high dose of radiation is administered almost instantaneously - in milliseconds instead of minutes. In this case, the tumour tissue is damaged in the same manner as with conventional radiotherapy, whereas the healthy tissue appears to be less affected, meaning that less side effects are expected.



The remarkable connection between CLIC and FLASH

Both need:

- Very intense electron beams
  - CLIC – to provide luminosity for experiments
  - FLASH – to provide dose fast for biological FLASH effect
- Very precisely controlled electron beams
  - CLIC – to reduce the power consumption of the facility
  - FLASH – to provide reliable treatment in a clinical setting
- High accelerating gradient
  - CLIC – fit facility in the Geneva area and limit cost
  - FLASH – fit facility on a typical hospital campus and limit cost of treatment



Neutrons: Boron Neutron Capture Therapy (BNCT)

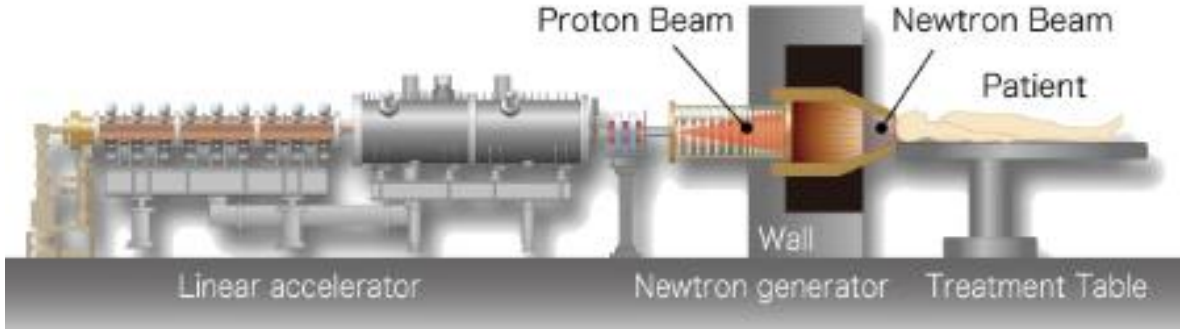
Boron Neutron Capture Therapy

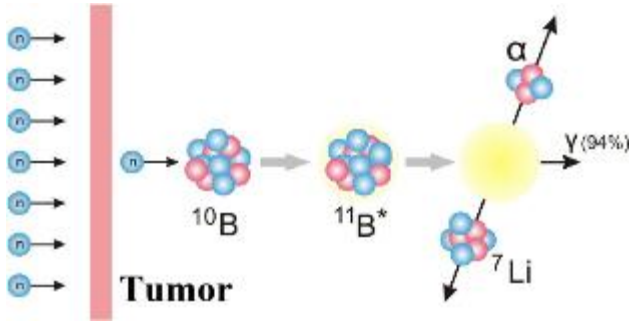
The (normal) stable version of boron, boron-10, captures slow neutrons to give boron-11. This then decays into lithium-7 and alpha particles, which kill any surrounding malignant tissue.

A boron-containing drug designed to localise in cancerous cells is injected into the patient, and a beam of low-energy neutrons shaped to optimise capture by the injected boron is directed at the cancerous sites.

Two-stage creation of the delivered dose, particularly effective with some difficult-to-treat cancers such as brain tumours or malignant melanoma.

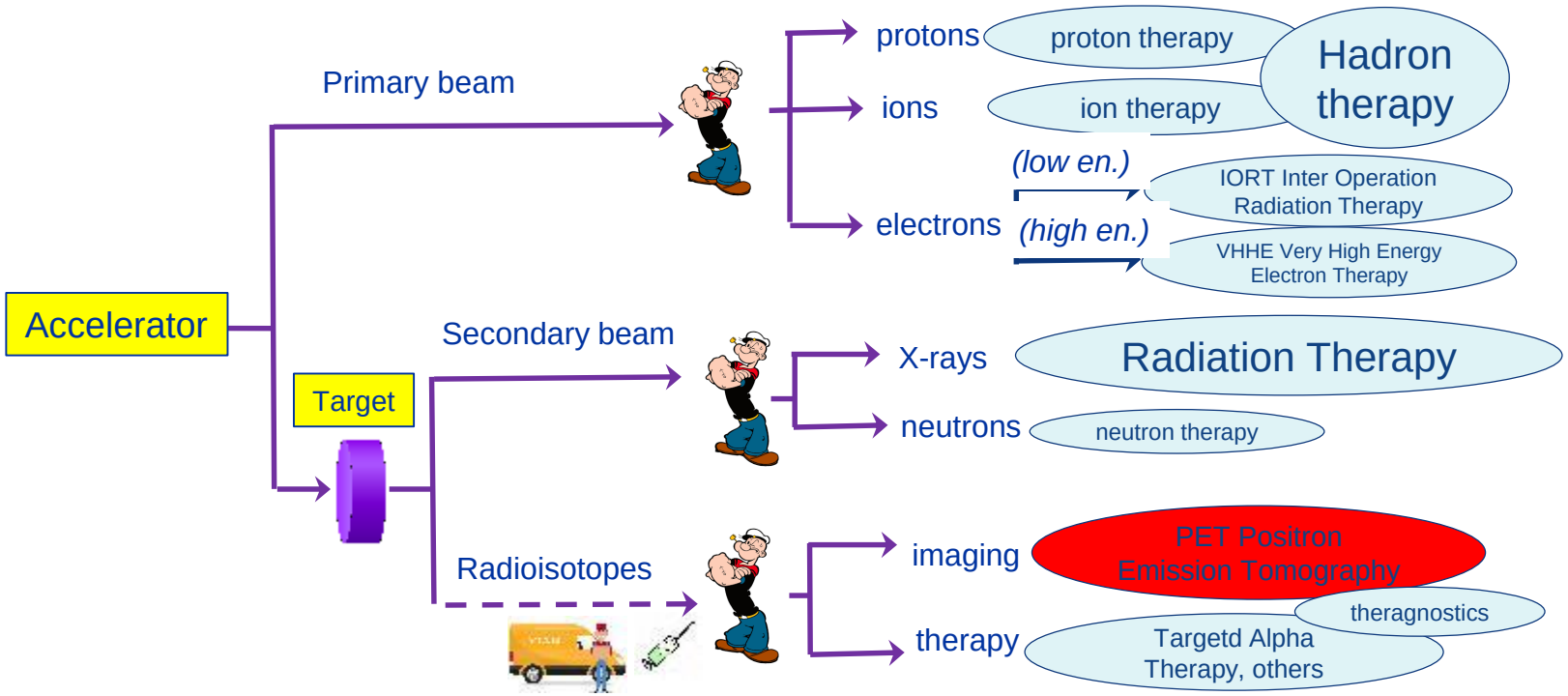
Neutron production requires intense proton beams (e.g. 3 MeV, >1 mA CW) with problems of heat load, activation, target (usually solid lithium).



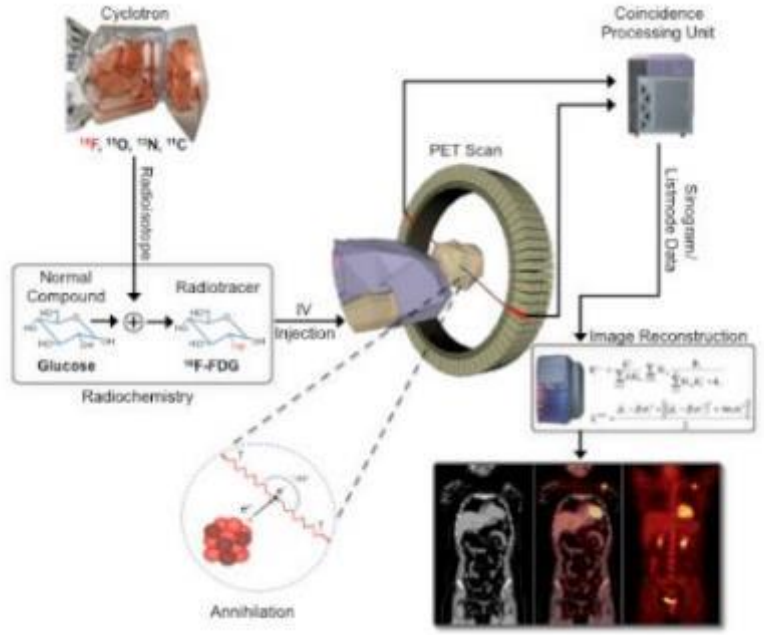


A BNCT centre is in operation in Tokyo, a first commercial unit installed at Helsinki, experimentation progressing in several centres.

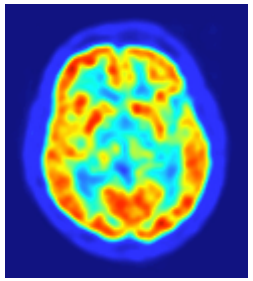
4- Radioisotopes - imaging



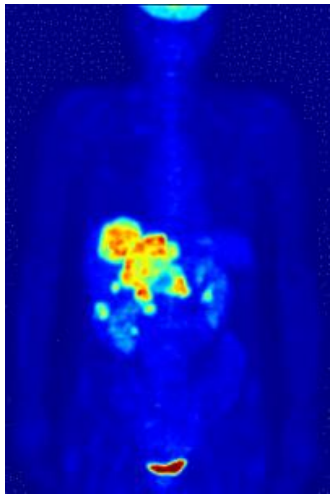
Radioisotope-based tomographies



(source: Huntsman Cancer Institute)

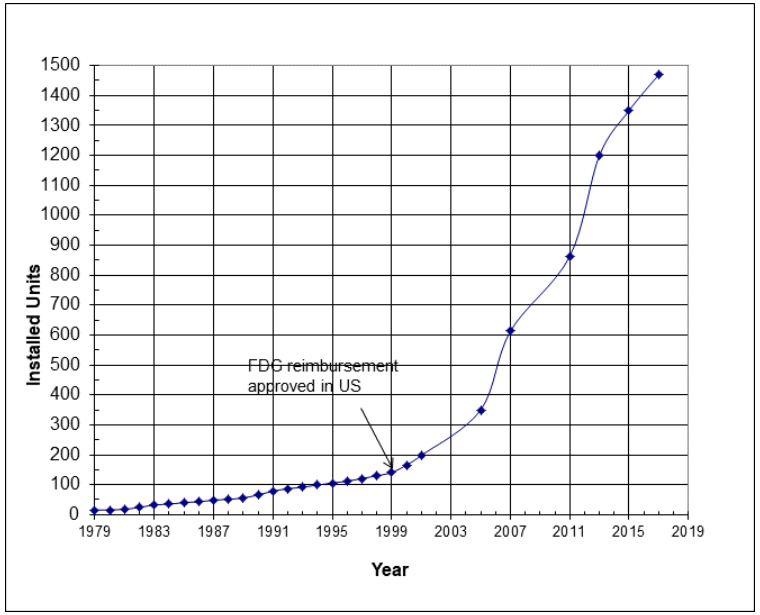


90% of PET scans are in clinical oncology



- A **radioisotope** (radiotracer) is produced by an accelerator (usually a cyclotron) and attached to a normal chemical compound, usually a glucose, in a radiopharmaceutical unit.
- The compound is injected to the patient and accumulates in tissues with high metabolic activity, as tumours – and metastasis.
- When the radioisotope decays, the emitted particles are detected by a scanner allowing a precise mapping of the emitting areas.
- In **SPECT** (single photon emission computed tomography) is used Technetium-99 (6 hours half-life) that emits a photon. 99-Te is generated in the hospital by Molybdenum-99 (66 hours half-life) produced at a nuclear plant.
- In the much more precise **PET** (Positron Emission Tomography) is used Fluorine-18 (1h50' half-life) attached to Fludeoxyglucose (FDG) molecules, which emits positrons that annihilates with electrons producing 2 gamma rays in opposite directions.

The isotope production and distribution scheme

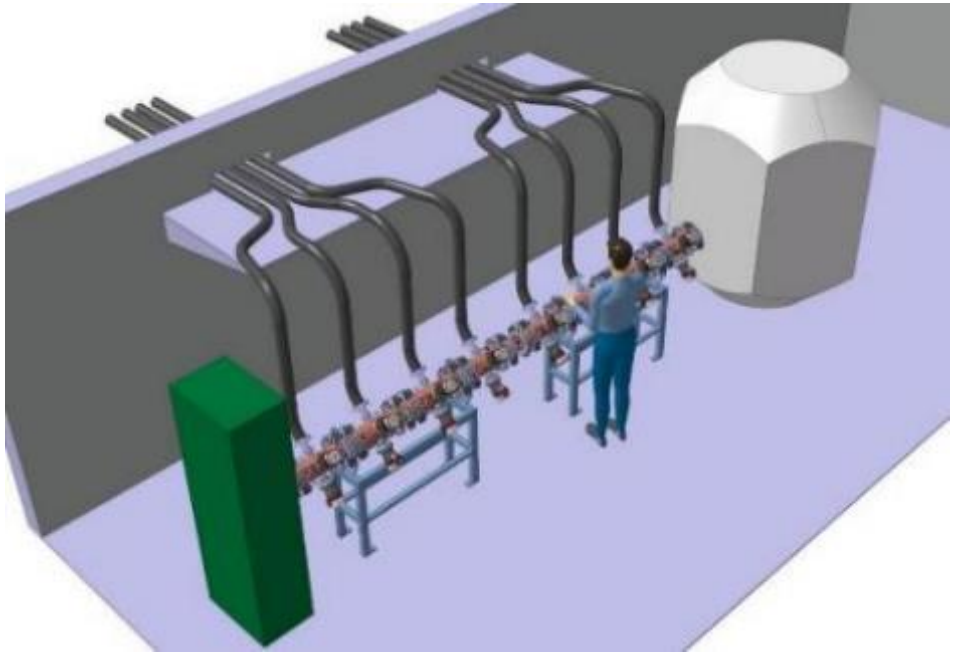


(courtesy Robert Hamm)

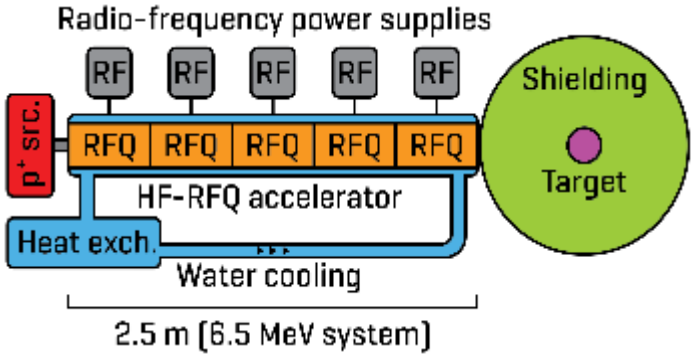
Isotopes and radiochemical drugs are produced in large centres equipped with a commercial cyclotron. After production, the drugs are shipped by road or air to the hospital (FDG half-life 1h50').
This scheme works well in Europe and US (good transport networks, shows limits in Asia and rest of world).

- Sales in 2015 - US$165M (~ 60 units sold per year).
- Top 5 manufacturers sell more than 50 units per year.
- PET sales dominate market (> 95% of all PET procedures use FDG.
- Sales flat (saturated?) in North America and Europe due to FDG distribution model.
- Sales increasing in Asia and rest of the world.

Radio Frequency Quadrupole for isotope production



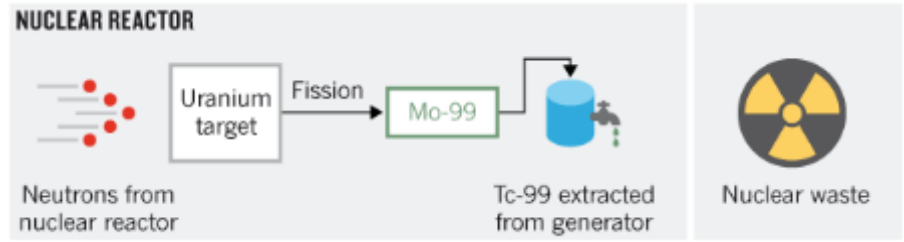
CERN has developed and built a «mini-RFQ» (Radio Frequency Quadrupole) at 750 MHz, extending to higher frequencies and applications outside science the experience of the RFQ for Linac4, the new LHC injector



Thanks to its small dimensions, simple operation, and minimum radiation to the environment, this compact RFQ design can be used for production of isotopes for PET diagnostics (18F, 11C) directly in hospitals (no need for long-distance shipping of isotopes)

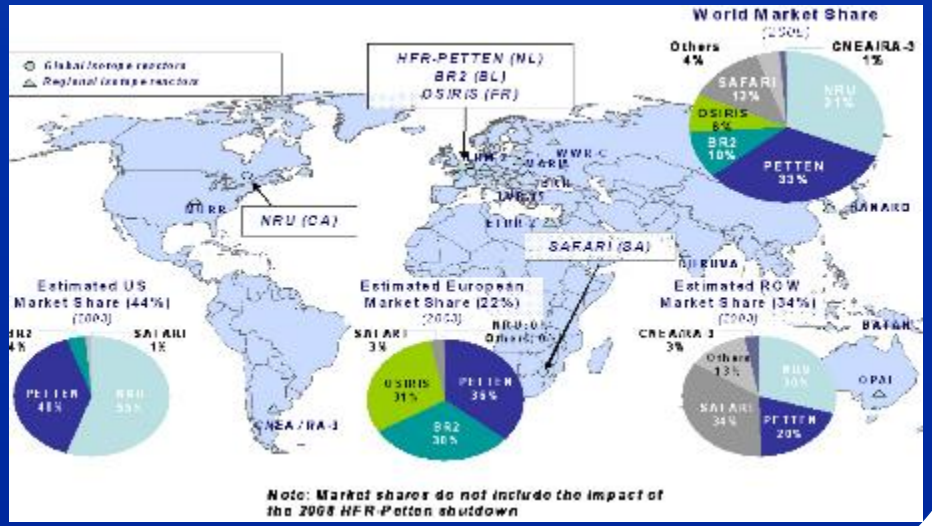
Production rate: >30 average patient doses of ^{18}F per hour

SPECT isotopes from accelerators



Source: Nature, 2013

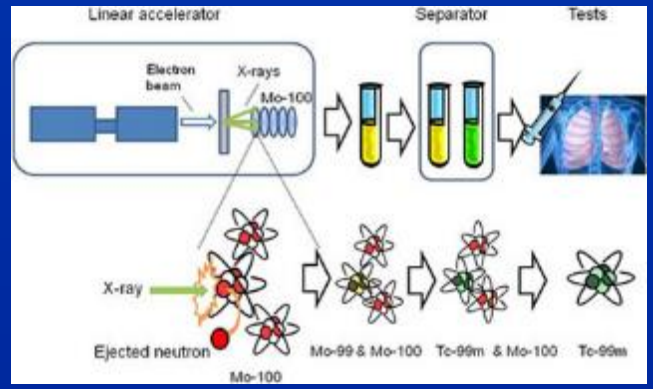
SPECT isotopes are now produced in nuclear reactors (Molybdenum-99 generators, 66 hrs., converted to Technetium-99 in the hospital).



Source: Government of Canada

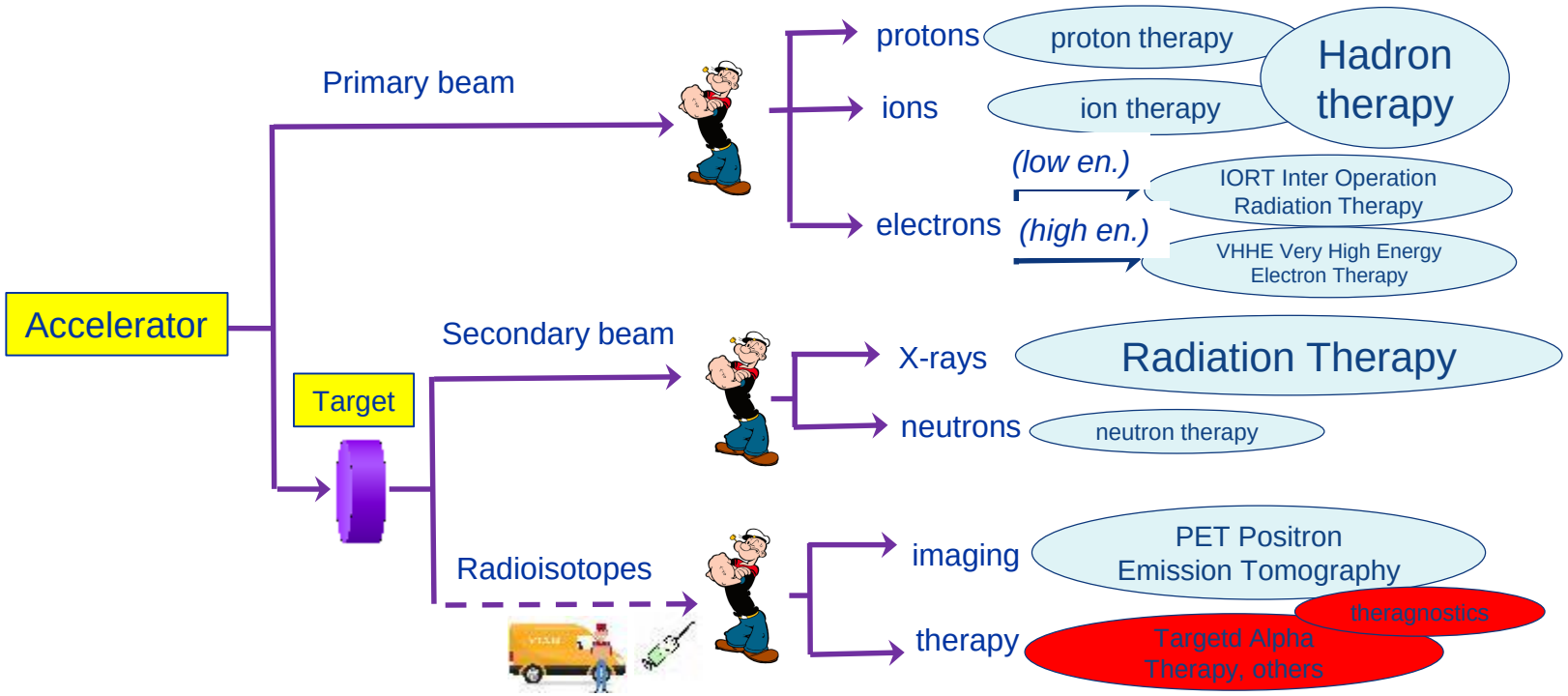
Accelerator Production of Technetium-99 (half-life 6 h)

- 30 MeV cyclotron
- Photo-fission of U
- Neutron-spallation of Mo



2009 shortage crisis

5 – Radioisotopes, treatment

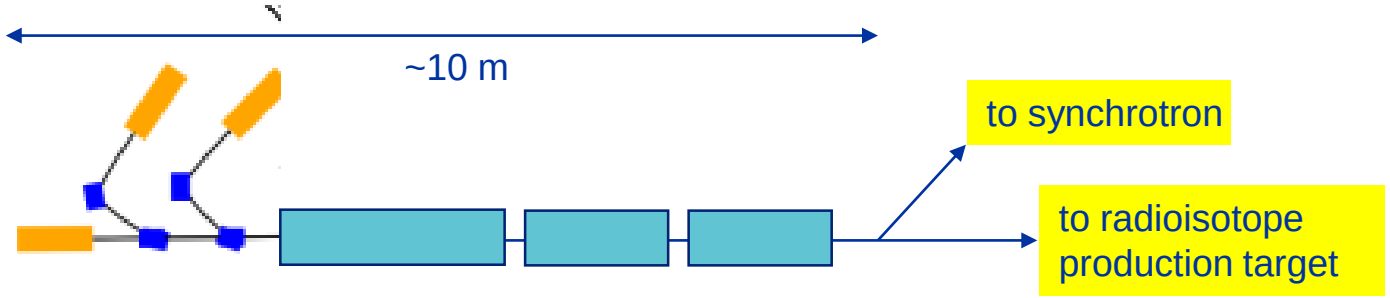


Linac for production of therapeutical radioisotopes

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.



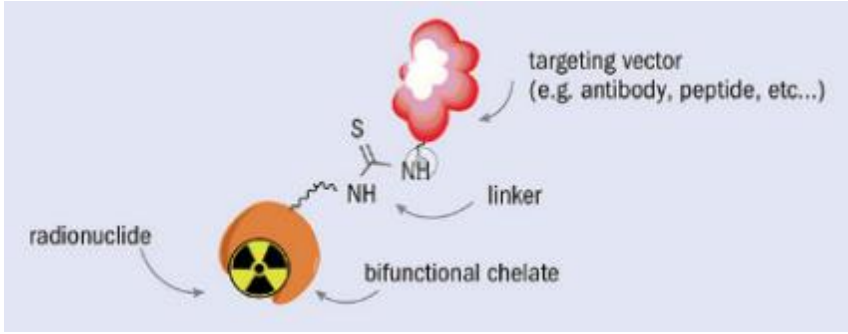
3 ion sources	Linac section1	Linac section2	Linac section3
$^{12}C^{4+}$, 600 μA $^{4}He^{2+}$, 2-5 mA p, 10 mA	q/m=1/3 W_{in}=45 keV/u W_{out}= 5 MeV/u	q/m=1/2 W_{in}= 5 MeV/u W_{out}= 7 MeV/u	q/m=1/2 or 1 W_{in}= 7 MeV/u W_{out}= 10 MeV/u

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

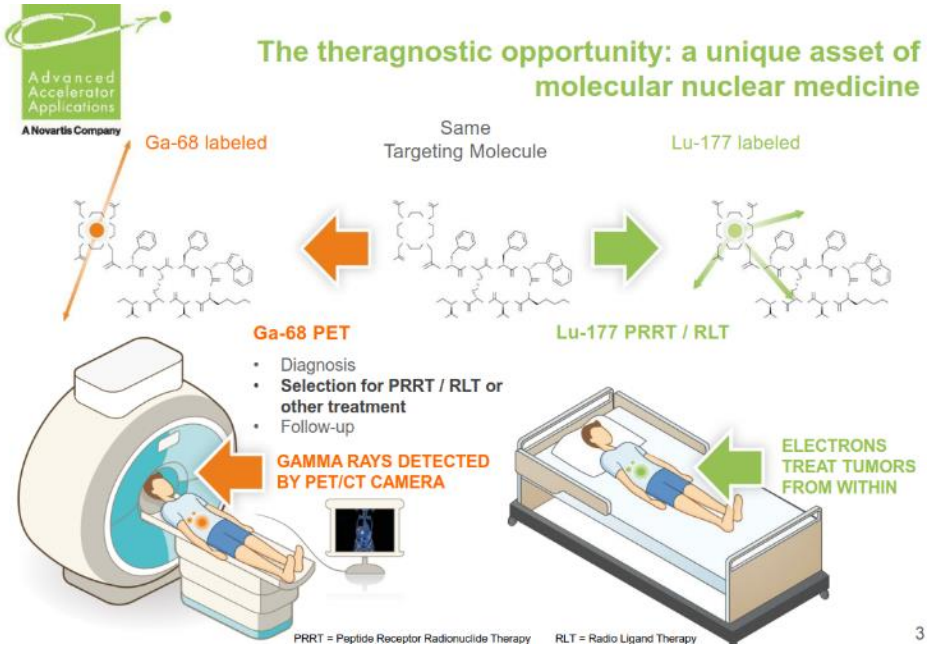
Alpha-emitting therapeutic isotopes attached to antibodies and injected to the patient: accumulate in cancer tissues and selectively deliver their dose.

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

Theragnostics

Theragnostics = integration of diagnostics and therapeutics. Disease identification, targeting, treatment and monitoring opens a new chapter in precision medicine.

In Molecular Nuclear Medicine, theragnostics consists in using targeting molecules labeled either with diagnostic radionuclides (e.g., positron or gamma emitters), or with therapeutic radionuclides (e.g., beta emitters) for diagnosis and therapy of a particular disease. Molecular imaging and diagnosis can be followed by personalised treatment utilizing the same targeting molecules. Example: gallium 68 (Ga-68) labeled tracers for diagnosis, followed by therapy using lutetium Lu-177 to radiolabel the same targeting molecule for personalized radionuclide therapy.



A recent success story:
Lutathera developed by AAA (company with old relations to CERN, based in St. Genis, near CERN).
AAA acquired by Novartis in 2018 for 3.9 billion $

The final words…

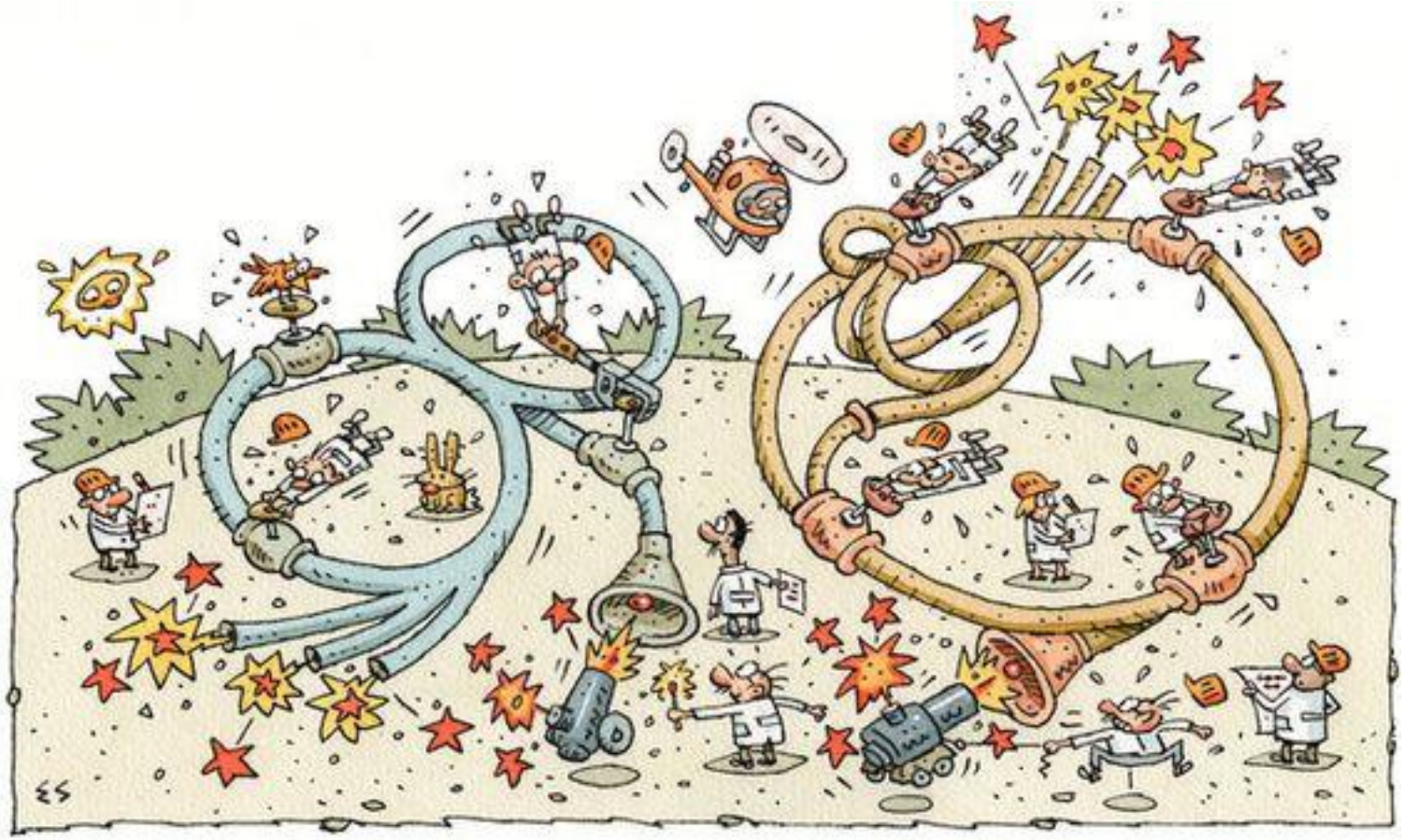
Particle accelerators are a vibrant and growing field, searching for new ideas to support basic science and extending to applied science and to wider societal applications.

But to drive this transition and to push further the frontiers of accelerators we need fresh ideas, technology jumps, dialogue between communities, and (why not!), some change in paradigm…

The secret for the success are novel ideas by young people developed in a collaborative environment, jumping across borders between different scientific fields.

To achieve this we need multinational research programmes with wide support from governments and scientific communities, but above all…

Don't forget… modern particle accelerators have been invented by a PhD student!



End of Lecture 6

Thank you for your attention!

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