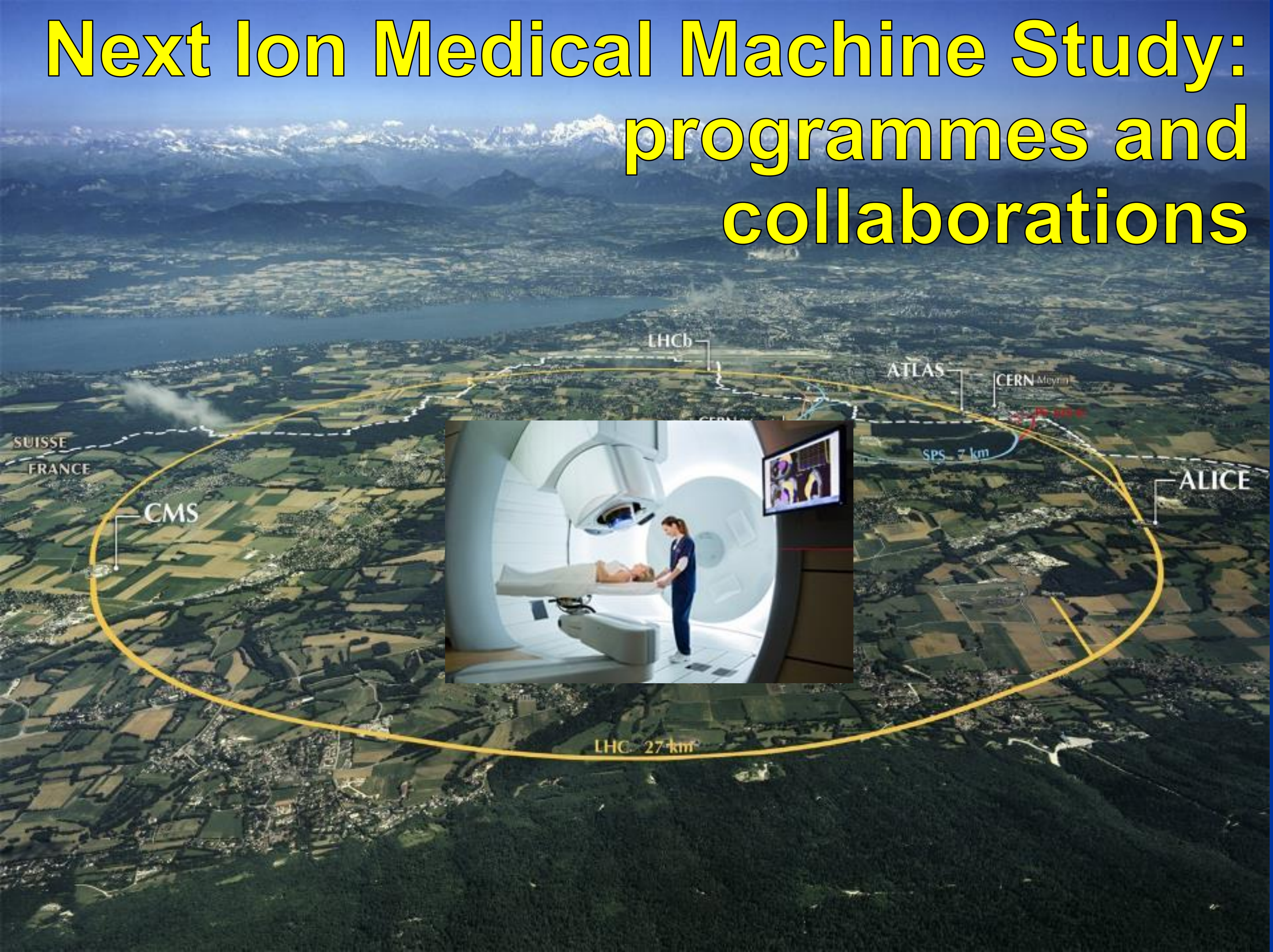
Next Ion Medical Machine Study: programmes and collaborations



Maurizio Vretenar

CERN, ATS/DO
Accelerator and Technology Projects and Studies

CERN

nimms

Symposium for the 30th Anniversary of the TERA Foundation

15 September 2022

The Next Ion Medical Machine Study (NIMMS)

The Next Ion Medical Machine Study is an international collaboration based at CERN, established in 2018 with the support of the CERN KT for Medical Applications, with the goal of developing new technologies for the future generation of accelerators for cancer therapy with ions heavier than protons.

- Building on the experience of the PIMMS (proton-ion medical machine study) of 1996/2000;
- Federating a large number of partners to develop designs and technologies for next-generation ion therapy;
- Concentrating on technologies for ions – protons are covered by commercial companies;
- **Partners** can use the NIMMS technologies to assemble their own optimized facility.

nimms

International partners collaborating with NIMMS:

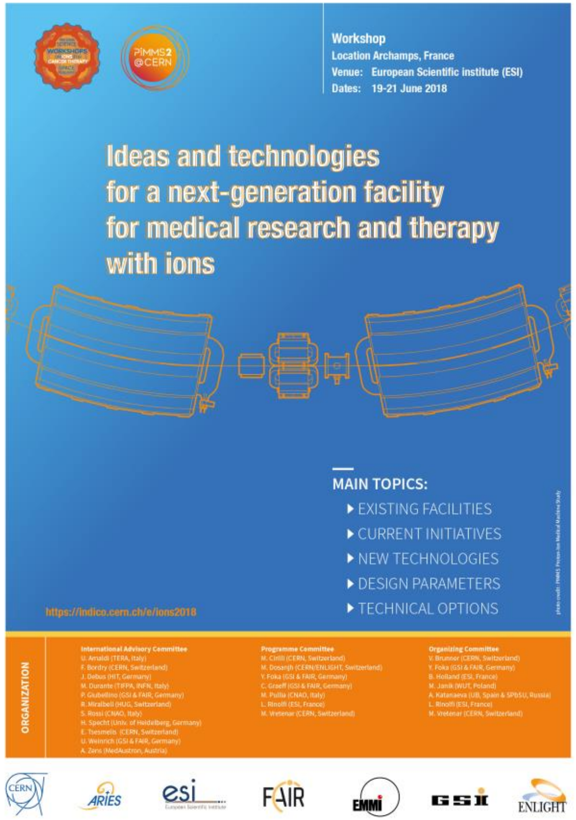
- SEEIIST (South East European International Institute for Sustainable Technologies)
- TERA Foundation (Italy)
- GSI (Germany)
- INFN (Italy)
- CIEMAT (Spain)
- Cockcroft Institute (UK)
- University of Manchester (UK)
- CNAO (Italy)
- Imperial College (UK)
- MedAustron (Austria)
- U. Melbourne (Australia)
- ESS-Bilbao (Spain)
- Riga Technical University (Latvia)
- Sarajevo University (Bosnia &H.)

The origins of NIMMS

TERA is at the origin of the new CERN effort in the field of hadron therapy:

- In 2016 F. Gianotti starts her 1st term as CERN Director-General and Prof. Amaldi asks the CERN Direction to promote a new action for hadron therapy, using some accelerator resources possibly available after the successful completion of LHC construction and commissioning;
- After some discussions in the Directorate, the idea of a “new PIMMS” is enthusiastically endorsed by F. Bordry, at the time Director for Accelerators and Technology;
- After the end of Linac4 project in 2017, I get involved trying to identify and collect ideas and resources to organize a first study group, starting from the recent work carried on by TERA and in contact and consultation with Prof. Amaldi.
- A pivotal Workshop in June 2018 at ESI Archamps was the decisive moment to:
  - collect input from the medical community,
  - review recent activities in the field,
  - establish a first informal collaboration,
  - define a work plan

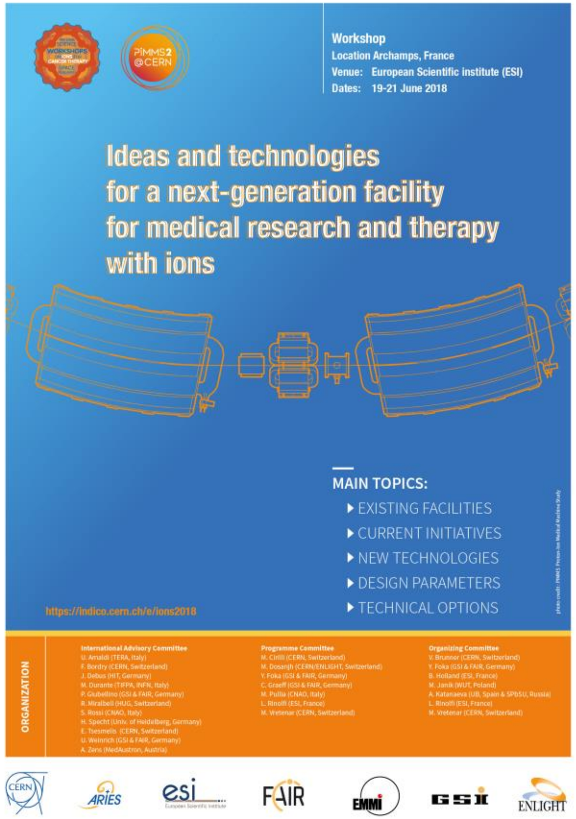
3 days of presentations and discussions
63 participants from EU, US, Asia.
1st idea of supporting the study within an EU project.



Main outcomes of the Archamps Workshop

Basic requirements of a next generation cancer therapy accelerator:

- Operation with multiple ions: protons, helium, carbon, oxygen, etc.
- Lower cost and dimensions, compared to present;
- Faster dose delivery with higher beam intensity and new delivery schemes (FLASH and mini-beams).
- A gantry device to precisely deliver the dose to the tumour is a must.



A strategic consideration (again, thanks to TERA): Cancer ion therapy is still in its early phase: much pre-clinical research is needed, in radiobiology and medical physics with different ions and treatment modalities.

- A new European facility must be able to devote a large fraction of its operation time (≈ 50%) to a wide research programme.

Several accelerator designs are possible: compact superconducting synchrotrons, conventional synchrotrons with higher performance, high-frequency linear accelerators, (cyclotrons), all equipped with superconducting gantries.

A strategy for CERN

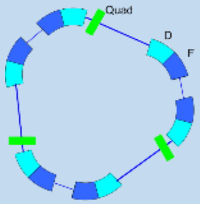
- **Proton** therapy is now commercial, and CERN, as an international organisation, cannot interfere with a mature commercial market.
- **Heavy ion** therapy is still in an early phase despite its advantages. Its diffusion is limited mainly by:
  - ✓ **Size and cost of the accelerator**;
  - ✓ **Lack 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.

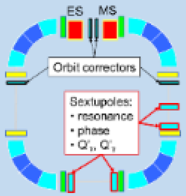
Approval in the frame of the CERN Knowledge Transfer for Medical Applications of the "NIMMS" initiative, with a budget of 250 kCHF/year for 2020/21 and 450 kCHF/year for 2022/23, to be used mainly for personnel and as "seed money" to launch and support collaborations.

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 unique design (NIMMS as a «toolbox»).

Four NIMMS Work Packages

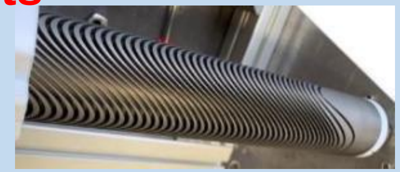
1. Small synchrotrons for particle therapy

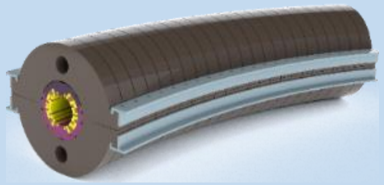




Reduced dimensions with improved performance (injection, extraction)

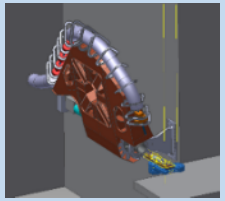
2. Curved superconducting magnets for synchrotrons and gantries

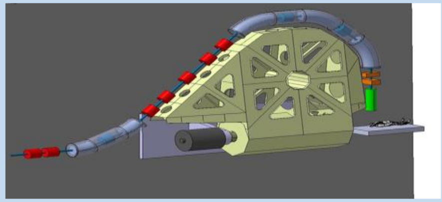




Canted Cosine Theta, NbTi or HTS

3. Superconducting gantries



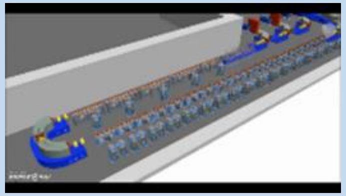


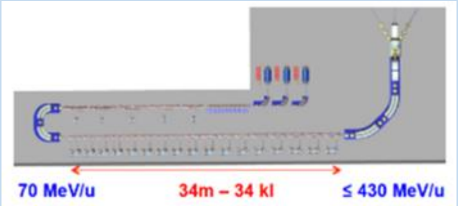
Precise beam delivery on multiple angles

HITRIplus EU project

IFAST EU project

4. High-frequency ion linacs





Compact bent layout

EU supporting initiatives

Superconducting magnets for synchrotrons and gantries

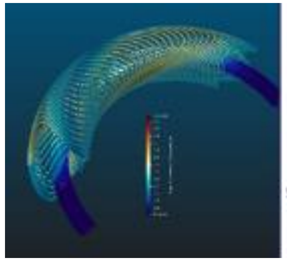
High Energy Physics is promoting a wide international effort in the development of conductors, designs and technologies for SC magnets.

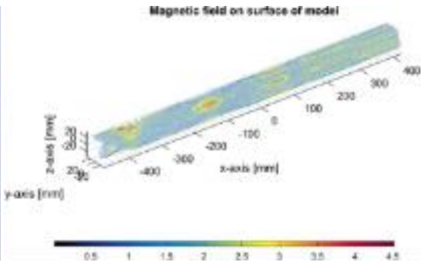
NIMMS aims at profiting of this R&D effort for compact synchrotron and gantry magnets.

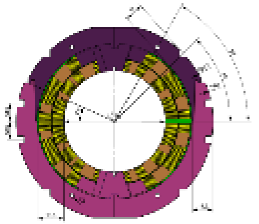
Some of the challenges are common, other are specific for medical accelerator magnets: ramping field, curved shape, quadrupole integration, use of cryocoolers.

A few ideas

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







Curved cos-theta dipole with H-split yoke with assembly clamps - Courtesy Mikko Karppinen, CERN

Magnet Parameters for HITRI+ and IFAST

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)

2 proposals submitted to H2020 calls with Workpackages dedicated to SC magnets for medical accelerators – covering 2021/25

HITRI*plus* – Integrating Activity for Ion Therapy

- **WP8 on Magnet Design:** overview and assessment of various conductors (LTS, HTS, various types of cables) and magnet layouts (costheta, CCT, racetracks – spit coils or flare ends – etc…). Design construction and test of 1 demontrator 500 mm long (either LTS or HTS)

I.FAST – General innovation programme for accelerator R&D

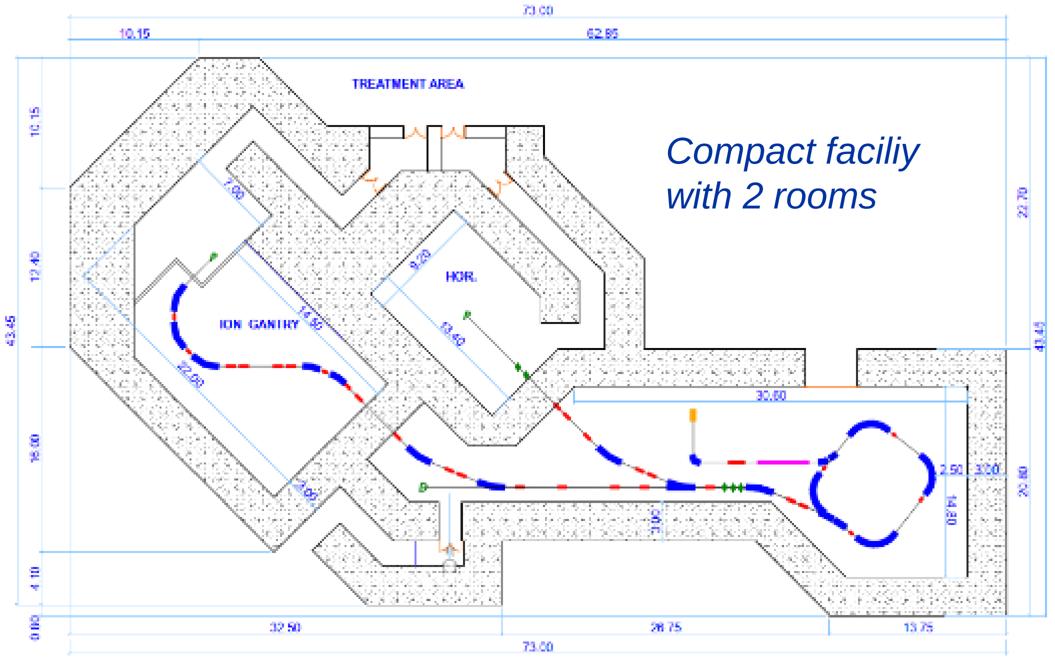
- **WP8 on Innovative Superconducting Magnets:** General consensus to go toward CCT, different conductors. Development of a HTS cable suitable for low losses - large size - fast cycling - synchrotrons (led by GSI)

Both WPs coordinated by L. Rossi (INFN, former CERN)

Participants: CEA, CERN, CIEMAT, INFN, PSI, UU, Wigner, SEEIIST, GSI + BNG, Sigmaphi, Elytt (industrial)

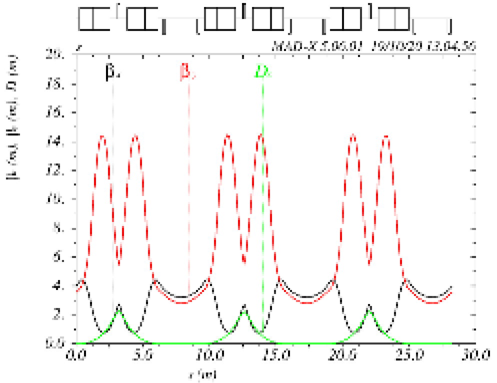
The compact SC synchrotron

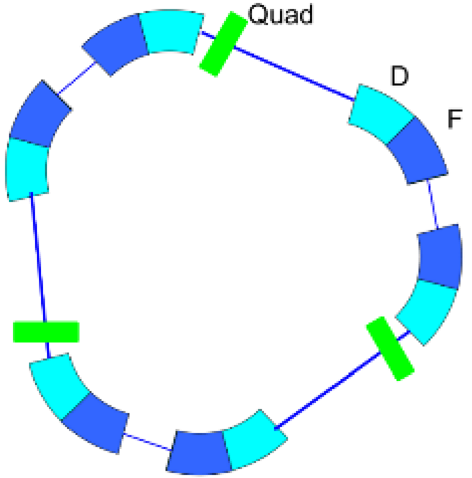
E. Benedetto, M. Sapinski, TERA/SEEIIST
P. Foka, GSI
D. Kaprinis, Kaprinis Architects
M. Vretenar, CERN



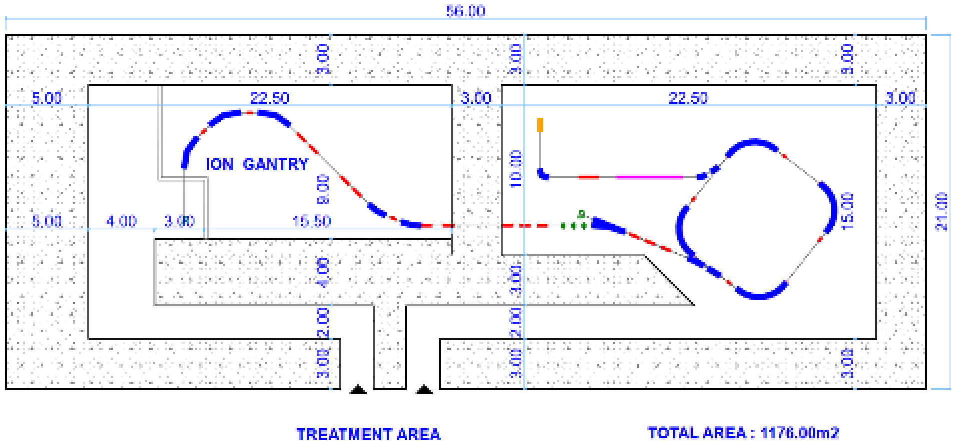
Compact faciliy with 2 rooms

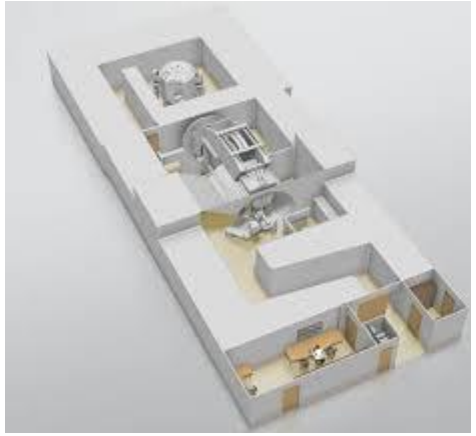
Alternative lattice with 60^0 magnets





A compact single-room ion therapy facility in about 1,000 m^2

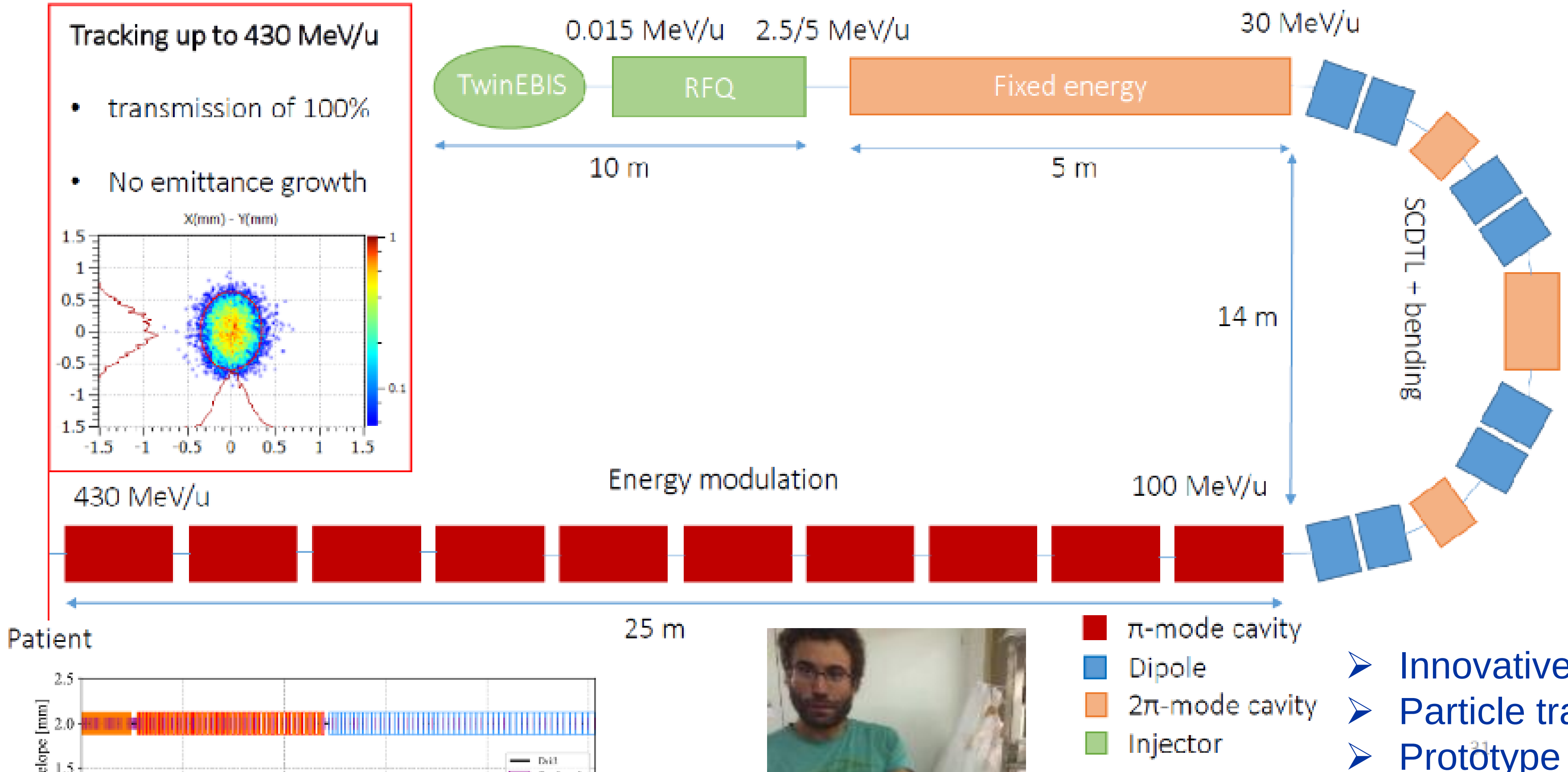




Comparable in size with proton therapy systems – here the single-room proton facility ProteusOne, from IBA)

The linac

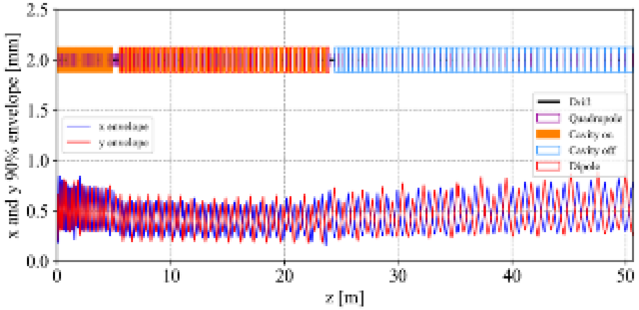
A. Lombardi, V. Bencini, D. Gibellieri, F. Wenander, BE/ABP
A. Grudiev, H. Pommerenke, S. Ramberger, M. Khalvati, BE/RF
J. Navarro, C. Oliver, D. Perez, CIEMAT



High repetition frequency (360 Hz) with pulse-to-pulse energy modulation allow fast and accurate dose delivery to the tumour

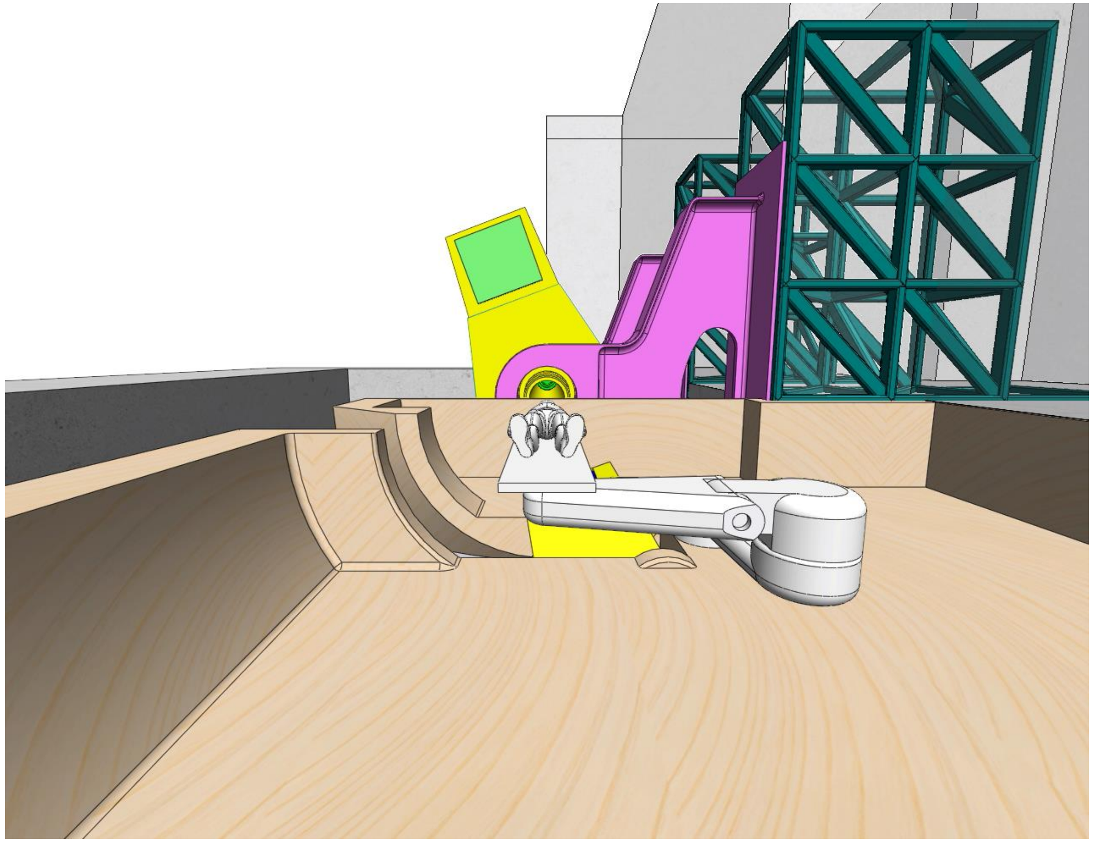
Parameter	Value
Frequency	750 MHz/3 GHz
Species	$^{12}C^{6+}$
Final energy	100-430 MeV/u
Repetition rate	200 (400) Hz
Pulse length	5 µs

Acceleration of fully stripped Carbon with 750MHz/3GHz structures



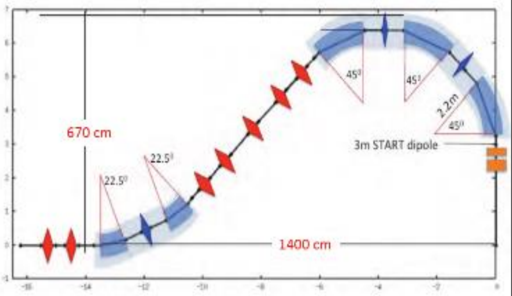
- Innovative «folded» version to save space
- Particle tracking completed
- Prototype EBIS source under commissioning
- RFQ designed
- **Agreement with CIEMAT** for construction of pre-injector in collaboration with Spanish industry

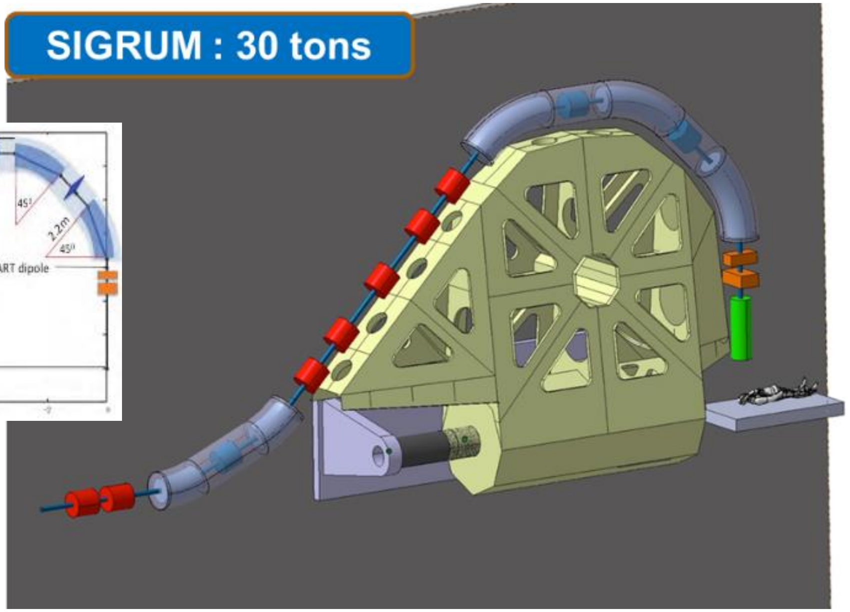
The superconducting ion gantry



Development of a rotating Superconducting Gantry for Carbon ions (SIGRUM), Supported by 2 collaborations:

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





7 m

“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-ACC-NOTE-2021-0014 ; NIMMS-Note-002

NIMMS and HITRIplus

Three of the four NIMMS Work Packages are now part of the HITRIplus EU project, that provides additional resources, collaborations, and connections.

HITRI plus
Heavy Ion Therapy Research Integration

Starting Community Integrating Activity

Coordinator: S. Rossi, CNAO
Deputy Coordinator.: M. Vretenar, CERN

EC Contribution: 5 M€
Total budget: 8.25 M€ (40% cofunding)
4 years duration (April 2020 – March 2024)

Participant No *	Participant organisation name	Country
1 (Coordinator)	Fondazione Centro Nazionale di Adroterapia Oncologica (CNAO)	IT
2	Bevatech GmbH (BEVA)	DE
3	Commissariat à l'énergie atomique et aux énergies alternatives (CEA)	FR
4	European Organisation for Nuclear Research (CERN)	IEIO
5	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	ES
6	Cosylab Laboratorij za kontrolne systeme dd (CSL)	SI
7	GSI Helmholtzzentrum für Schwerionenforschung GmbH (GSI)	DE
8	Universitätsklinikum Heidelberg (UKHD/HIT)	DE
9	Istituto Nazionale di Fisica Nucleare (INFN)	IT
10	EBG MedAustron GmbH (MEDA)	AT
11	Marburger Ionenstrahl-Therapie Betreibergesellschaft mbH (MIT)	DE
12	Paul Scherrer Institut (PSI)	CH
13	South East European International Institute for Sustainable Technologies (SEEIIST)	CH
14	Universita ta Malta (UM)	MT
15	Philipps-University Marburg (UMR)	DE
16	Uppsala University (UU)	SE
17	Wigner Research Centre for Physics (Wigner RCP)	HU
18	Riga Technical University (RTU)	LV

Third party participation linked to SEEIIST		
Participant No *	Participant organisation name	Country
19	Ss, Cyril and Methodius University in Skopje, Republic of North Macedonia (UKIM)	MK
20	Clinical Centre of Montenegro (CMSM)	ME
21	Sentronis a.d. (SEN)	RS
22	Jožef Stefan Institute (IJS)	SI

Wider Objectives:
Not only design an accelerator facility, but integrate, coordinate and strengthen the research on cancer treatment with ions, starting from the 4 existing ion therapy centres. Develop a set of new technologies to progress ion therapy. Define technical aspects and scientific programme of a future research and therapy facility.

For CERN, being part of HITRIplus is a way to support our medical accelerator research and to connect it to a larger European effort that includes the medical and biophysics parts, where we are traditionally weak.

NIMMS Impact on Ion Therapy Accelerator Research

Service Contract for SEEIIST support, total budget 1.3 M€, 0.5 M€ to CERN
2019/2021
- development RT synchrotron design
- design Quasi-Alvarez option for bent linac
- design SC gantry optics
- design transfer lines for therapy and experiment
- facility integration
- comparison of 3 accelerator designs

SEEIIST, TERA, CERN, GSI, SAE

Gantry collaboration for new SC gantry design
2019/…
- Design and prototyping of a novel SC ion gantry

CERN, CNAO, MedA, INFN, TERA

Bent-linac pre-injector collaboration
2021/…
- Engineering design and construction by Spanish industry

CERN, CIEMAT

Synchrotron design collaboration
2020/…
U. Melbourne, UKRI/STFC

NIMMS

Starting from a CERN investment of 500 k€ for 2019/21, NIMMS has launched collaborations that have collected funding for ~4 M€ (factor 8 leverage factor)

HITRI+, H2020, 1.2 M€ for accelerator studies (total budget 5 M€ for all ion therapy
2021-2024
- synchrotron injection and extraction
- synchrotron beam optics and operational modes
- SC synchrotron lattice
- injector linac design
- gantry integration
- engineering design of SC magnets
- small SC magnet demonstrator

SEEIIST, CERN, CNAO, MedA, INFN, CEA, CIEMAT, PSI, UU, Wigner

IFAST, H2020, 1.41 M€ for accelerator studies (total budget 10 M€ for accelerator Research & Innovation)
2021-2025
- Improvement of slow extraction spill quality (with FAIR)
- Engineering design of curvet CCT magnet
- Engineering design of HTS CCT magnet
- Construction of curved CCT magnet demonstrator
- Construction of HTS magnet demonstrator
- Development of ReBCO HTS nuclotron cable (with FAIR)

GSI, BI, BT, CERN, HIT, CERN, CEA, INFN, CIEMAT, Wigner, UU, PSI, Scanditronix, Elytt, SigmaPhi

NIMMS-sponsored accelerator designs

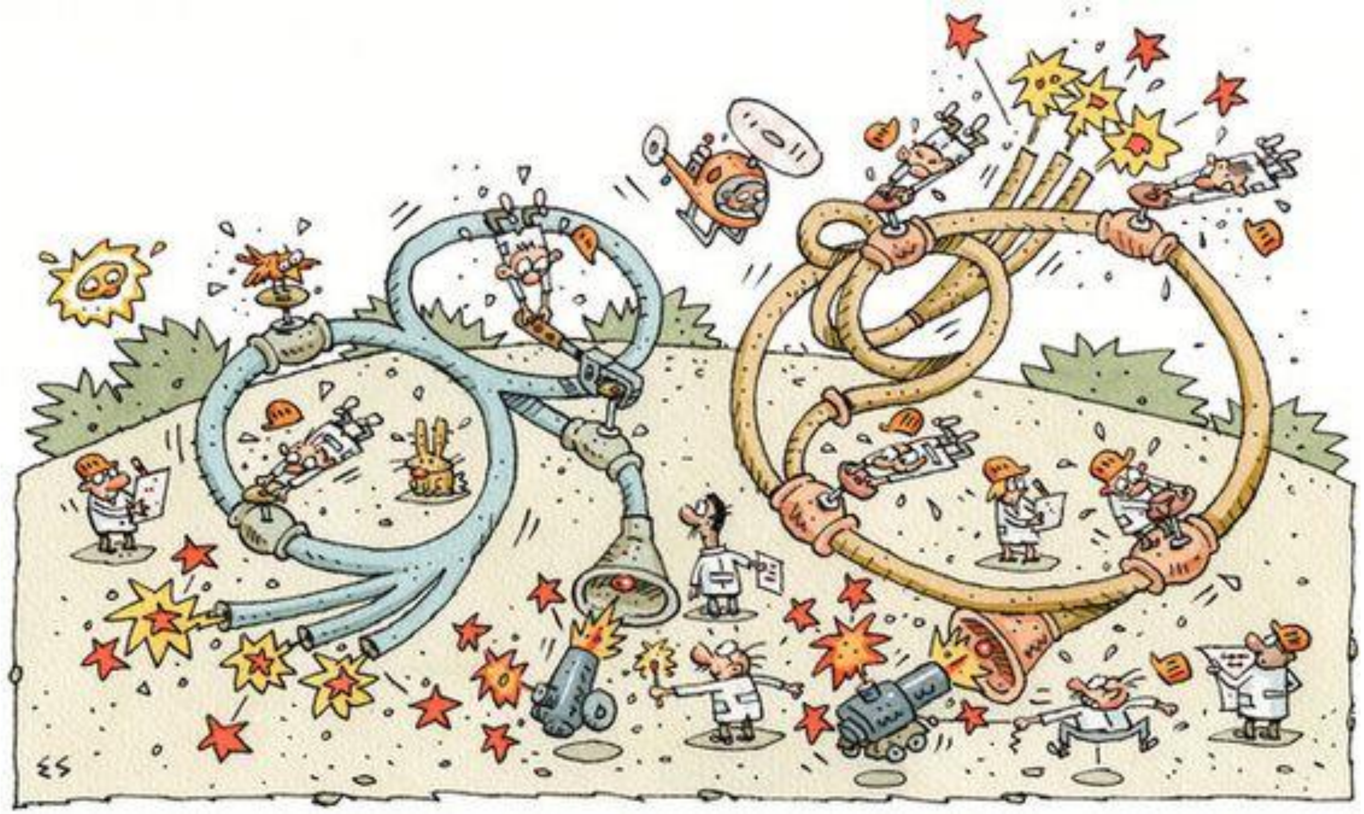


Image credit: Elwood H. Smith, The New York Times

The SEEIIST initiative

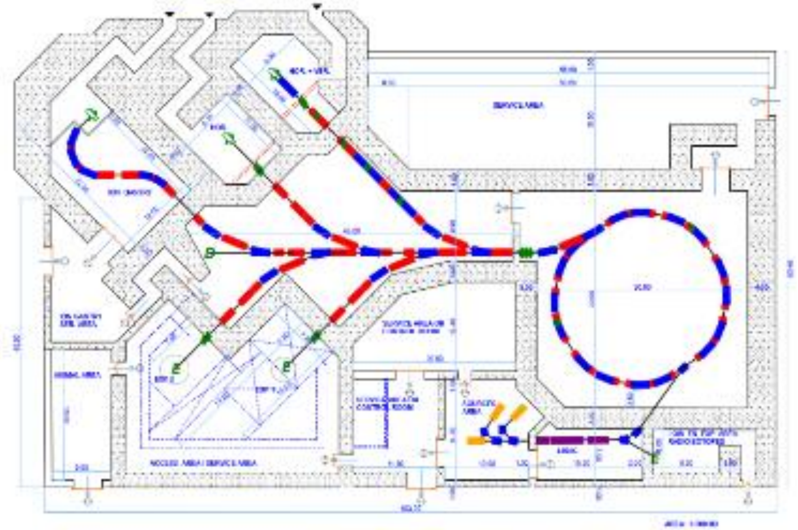
- **SEEIIST** (South East Europe International Institute for Sustainable Technologies): a new international partnership aiming at the construction of a new Research Infrastructure for cancer research and therapy in South East Europe (11 member countries)
- SEEIIST is supported by the European Commission, 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 still divided, in the line of “science for peace”.

SEE ST
South East European
International Institute
for Sustainable Technologies

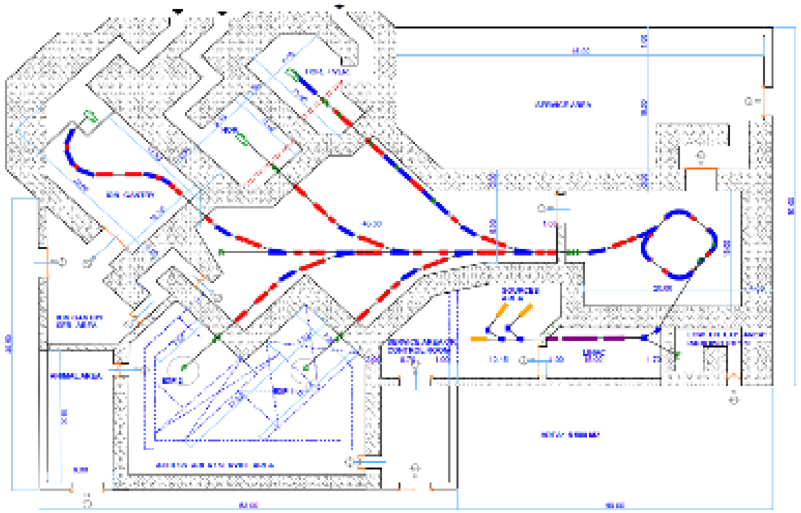
After an initial competition between a 3rd generation synchrotron light facility and a hadron therapy facility as main SEEIIST initiative, the hadron therapy option has been selected by the SEEIIST Steering Committee based on a study coordinated by TERA and published as a Yellow Report:
U. Amaldi et al., A facility for tumour therapy and biomedical research in South-Eastern Europe, CERN-2019-002

Comparing the three options for SEEIIST

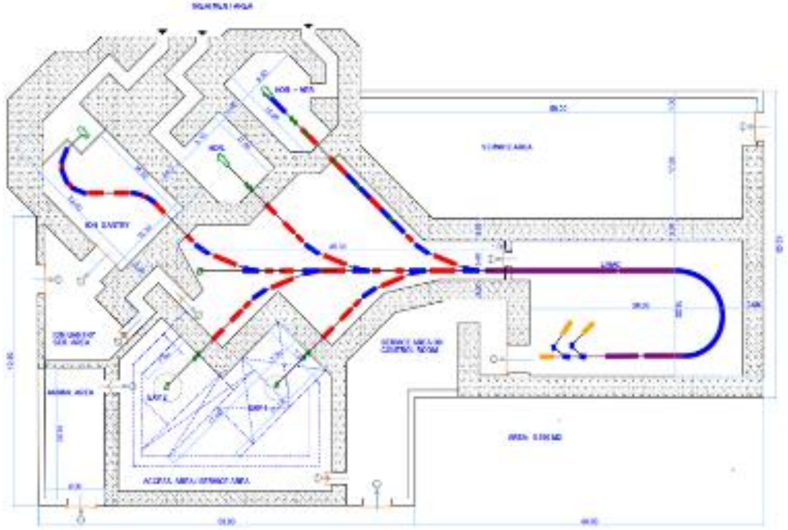
SEEIIST requirements: a facility to be built in 10 years, for 50% research and 50% treatment



RT synchrotron:
accelerator 1,200 m^2, facility 6,500 m^2



SC synchrotron:
accelerator 600 m^2, facility 5,500 m^2



Full linac:
accelerator 600 m^2, facility 5,500 m^2

SC synchrotron or linac: 50% reduction in accelerator dimensions, 15% in overall facility dimensions, and 20% in cost with respect to conventional synchrotron, but both require substantial R&D (5 years for SC magnets, similar for linac)

	Construction Cost	Operation cost	Footprint	Performance	Time to development	Risk of development	Treatment protocols	Gantry
Warm (new) synchrotron	Medium	Medium	Large	Good	Low	Low	Existing	Simple design
Superconducting synchrotron	Lower	Lower	Small	Good	Medium	Medium	Existing	Simple design
Linear accelerator	Lower	Lower	Small	Better	Long	Medium	To be developed	Complex design

The SEEIIST has selected as baseline a **room-temperature synchrotron design of PIMMS type with advanced features**.

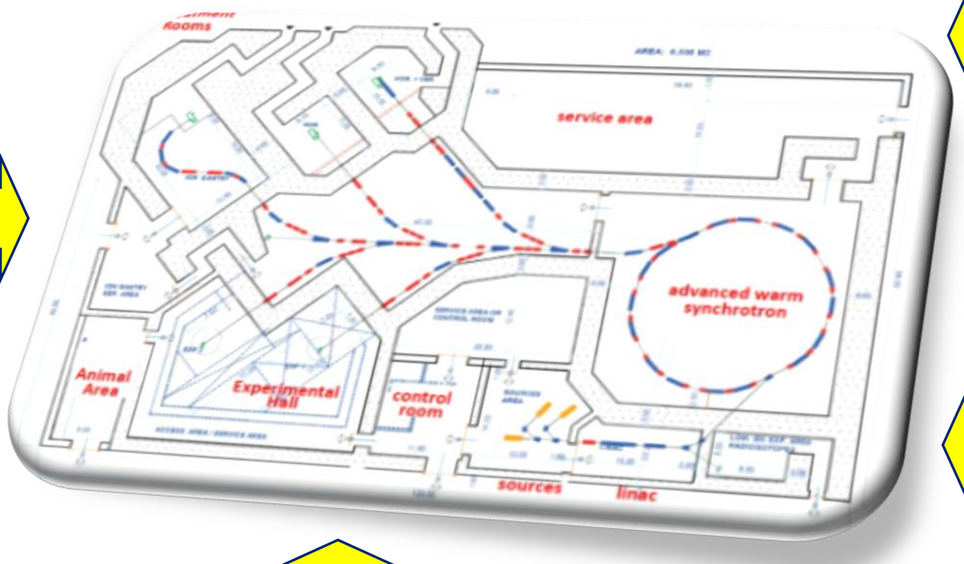
The decision might be revised after the results of the SC magnet R&D foreseen in HITRI+ and IFAST (~4/5 years)

The unique 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.



C. Conservative SEEIIST feature:

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

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.

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.

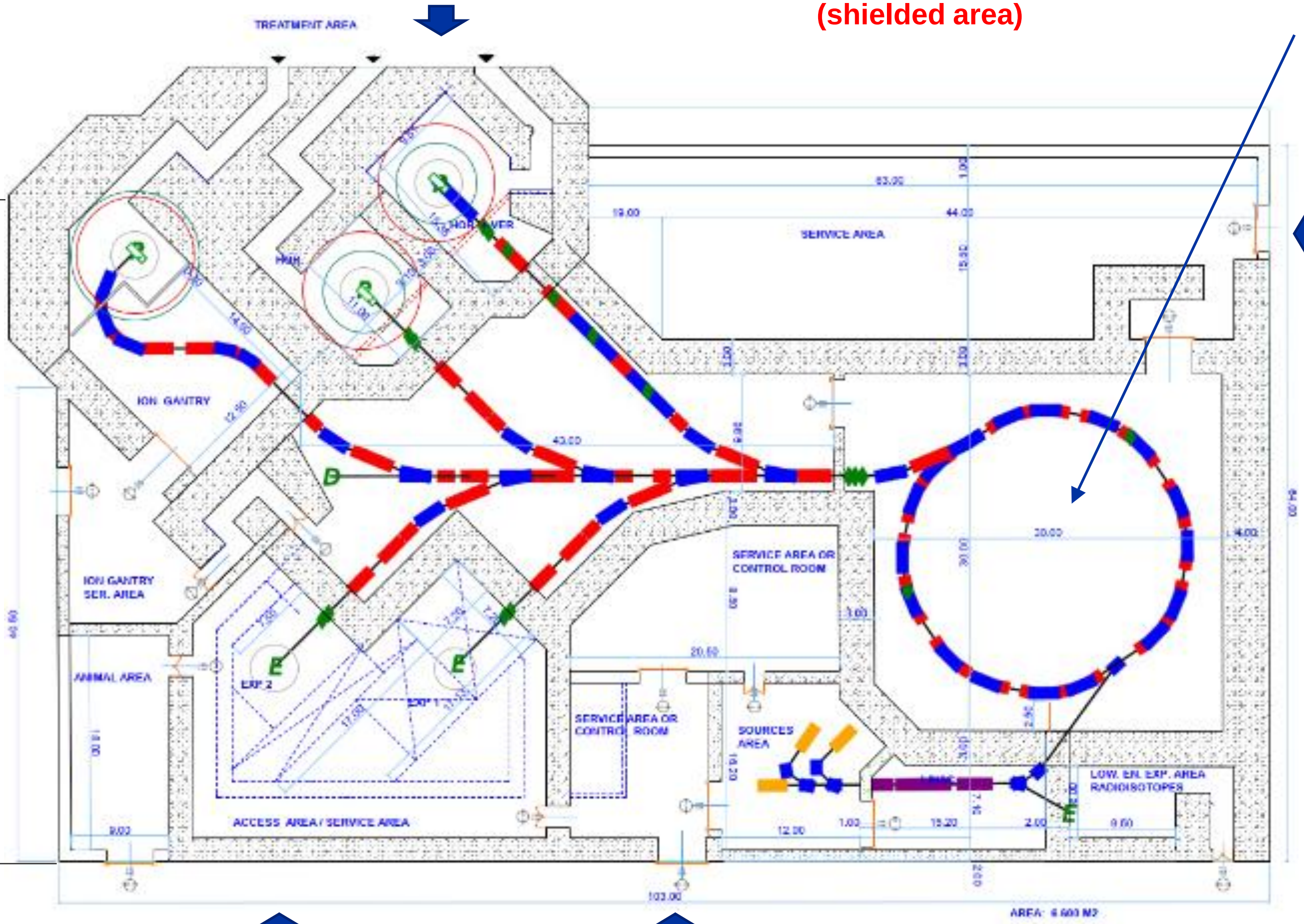
Layout of the complete SEEIIST-type facility

Design to be presented in a CERN Yellow Report in preparation

Access for therapy

Total 5,400 m²
(shielded area)

The synchrotron can be replaced by an SC version if R&D successful



Equipment room and access to synchrotron

Area for future expansion

Target for isotope production

Access for animal testing

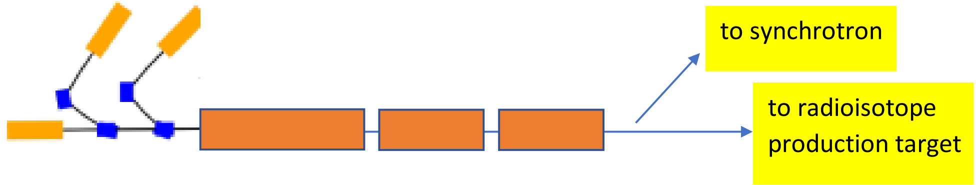
Reconfigurable experimental room

Access to experimental room and linac

Dual-mode injector linac for production of radioisotopes

The advanced NIMMS synchrotron needs a **new injector linear accelerator** (linac) designed for higher energy (5-10 MeV/u), with lower cost, higher efficiency and higher intensity.

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



3 ion sources	Linac section1	Linac section2	Linac section3	Maximum duty cycle:
$^{12}C^{4+}$, 600 μA, 0.2-0.3 π mm mrad	q/m=1/3	q/m=1/2	q/m=1/2 or 1	10%
$^{4}He^{2+}$, 2-5 mA, 0.2-0.4 π mm mrad	W_{in}=20 keV/u	W_{in}= 5 MeV/u	W_{in}= 7.1 MeV/u	
P or H_2^+, 5 mA, 0.2-0.3 π mm mrad	W_{out}= 5 MeV/u	W_{out}= 7.1 MeV/u	W_{out}= 10 MeV/u	

Version 1 : 217 MHz

Version 2 : 352 MHz

Main target isotopes for the linac:

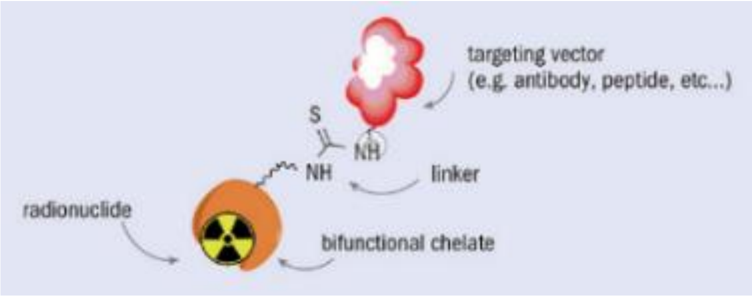
- 211At for Targeted Alpha Therapy
- 117mSn, for theranostic, artherial plaque and bone malignancies
- 11C and 18F for PET imaging

Targeted Alpha Therapy (211At)

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

Advanced experimentation in several medical centres, very promising for solid or diffused cancers (leukaemia). Potential to become a powerful and selective tool for personalised cancer treatment.

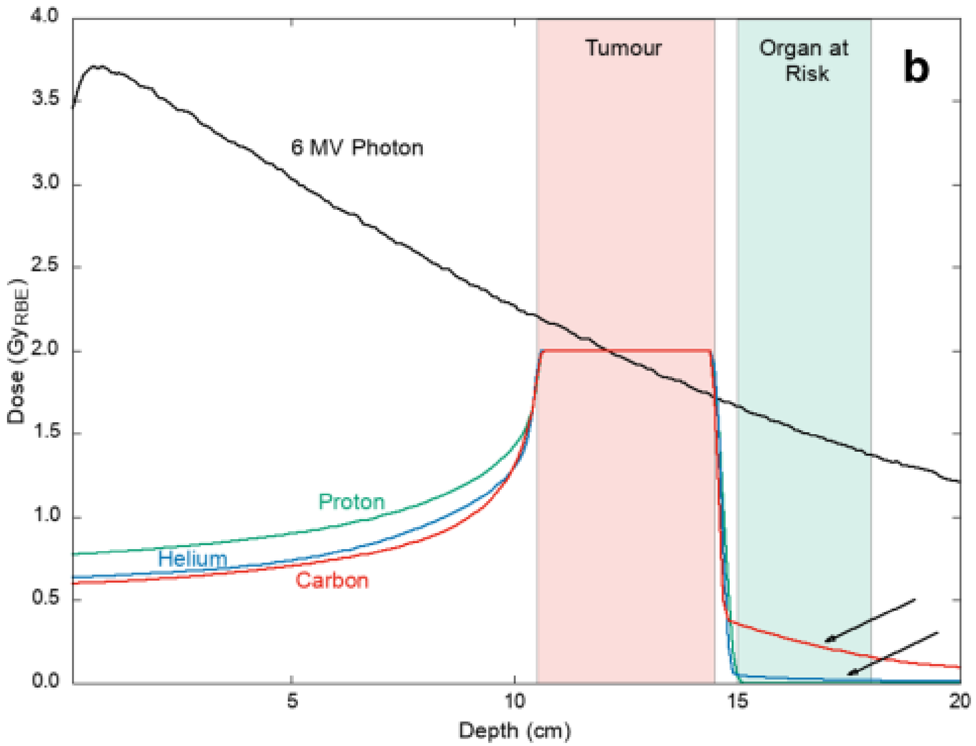
If the radioisotope is also a gamma or beta emitter, can be coupled to diagnostics tools to optimise the dose (theranostics)



The proposed SEEIIST facility

Roof of accelerator building is removed to show accelerator components

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)*

- ➢ Treatment with helium is under advanced study at carbon therapy centres.
- ➢ First patient treated in September 2021 at the Heidelberg Ion Therapy (D).
- ➢ Clinical trials starting, will be soon licensed for treatment.
- ➢ An accelerator designed for helium treatment can easily produce protons for standard treatment, and be used for research with helium and heavier ions.

- ➢ reduced lateral scattering w.r.t. protons,
- ➢ lower fragmentations than carbon,
- ➢ lower neutron dose than protons or carbon, reducing risks in paediatric patients,
- ➢ could treat some radioresistant tumours at lower cost than carbon.

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Physics in Medicine & Biology

IPEM Institute of Physics and Engineering in Medicine

TOPICAL REVIEW

Roadmap: helium ion therapy

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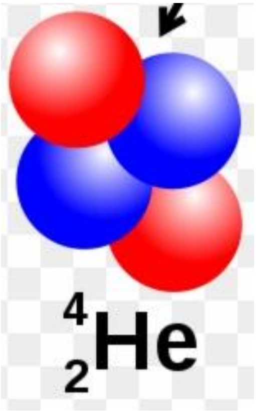
Recently published (August 2022) helium ion therapy Roadmap (63 pages)

Main features of an accelerator for helium therapy

Synchrotron because of size, flexibility and cost:

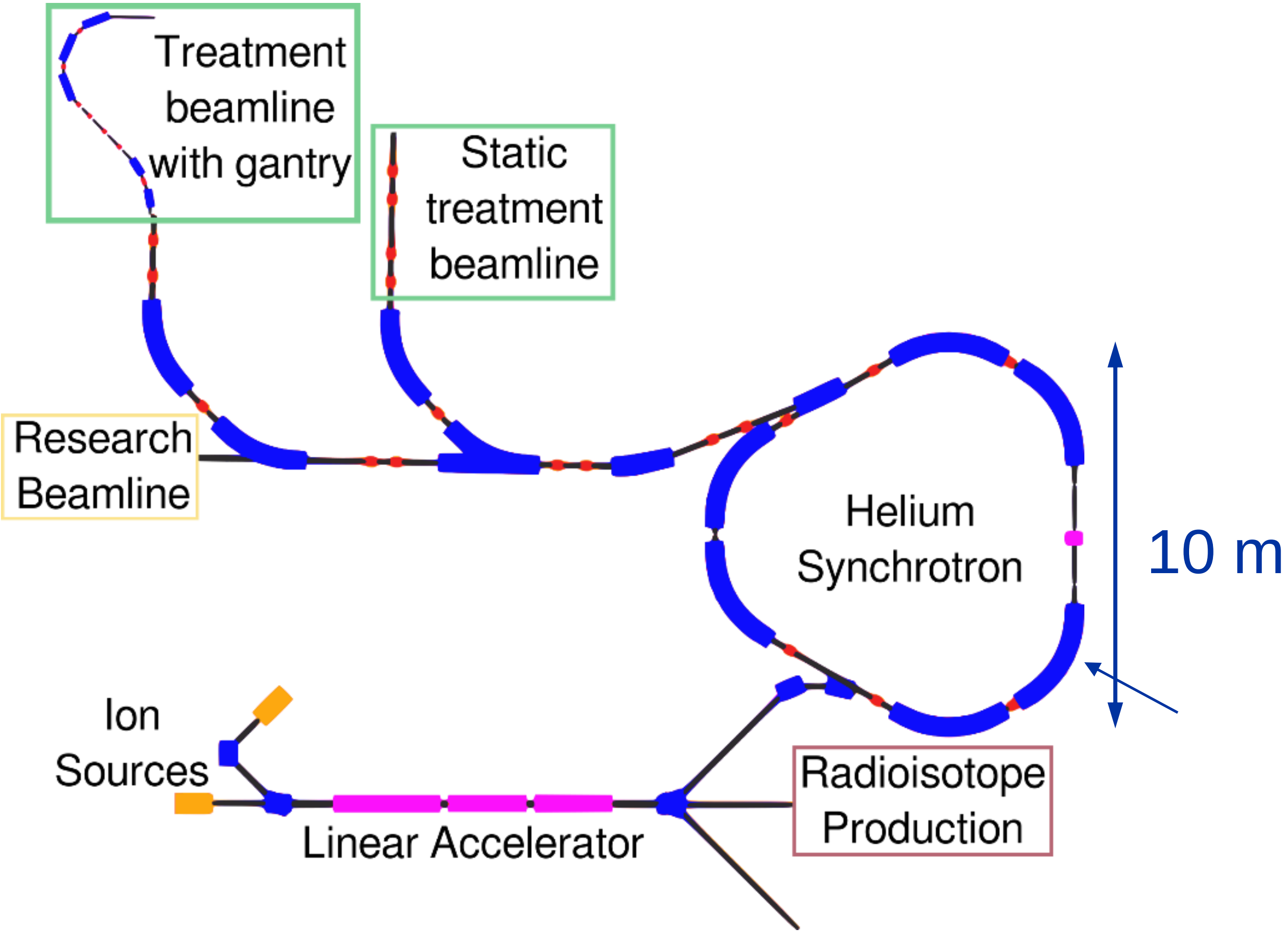
1. Can accelerate protons at treatment energy;
2. Can use protons at higher energy for full body on-line radiography;
3. Can accelerate other ions (carbon, oxygen) for biophysics experiments.
4. Can be equipped with modern FLASH extraction and can produce mini-beams.
5. The linac injector can be used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



Main synchrotron parameters:

- maximum magnetic rigidity 4.5 T/m (**220 MeV/u** for 4He, penetration 30 cm in water).
- Source current 2 mA for **8 x 10^{10} ions injected**, to irradiate a 1 litre tumour with 2 Gy with a factor 2 margin for losses.
- Helium injection energy **5 MeV/u**. Additional linac tank to accelerate only **protons to 10 MeV**.

Layout of a facility for treatment and research with helium and protons



- Two beamlines for treatment, one for research.
- Rotating superconducting gantry (HITRIplus/SIG collaborations).
- Linac for parallel radioisotope production (211At for targeted alpha therapy)
- Surface ~1,600 m2

The synchrotron

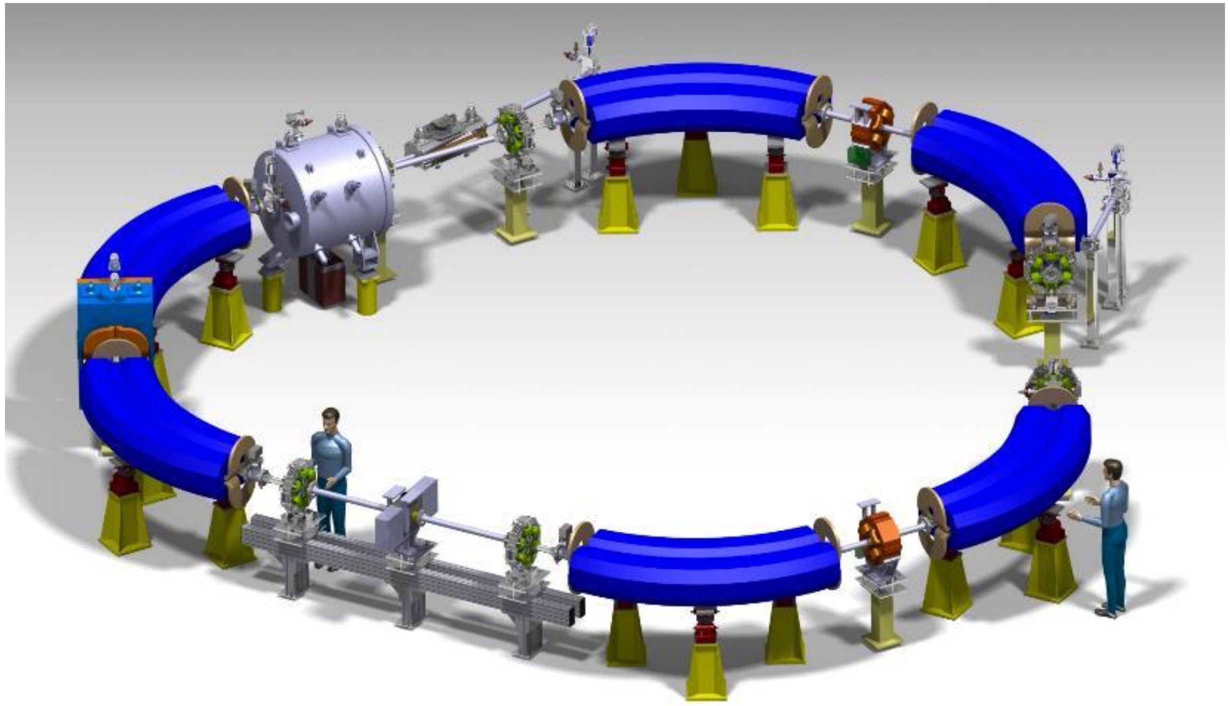
Design based on CERN experience in small synchrotrons (LEAR, LEIR, ELENA)

Three straight sections (injection, extraction, RF)

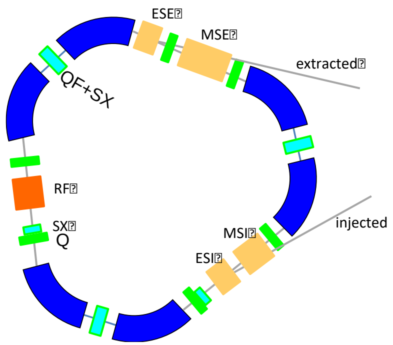
Conservative dipole field of 1.65 T (minor impact on ring size).

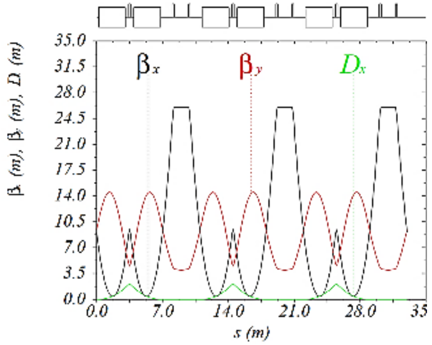
Estimated energy consumption ~430 kW (to be optimized).

Injector linac at 352.2 MHz, based on CERN Linac4 design



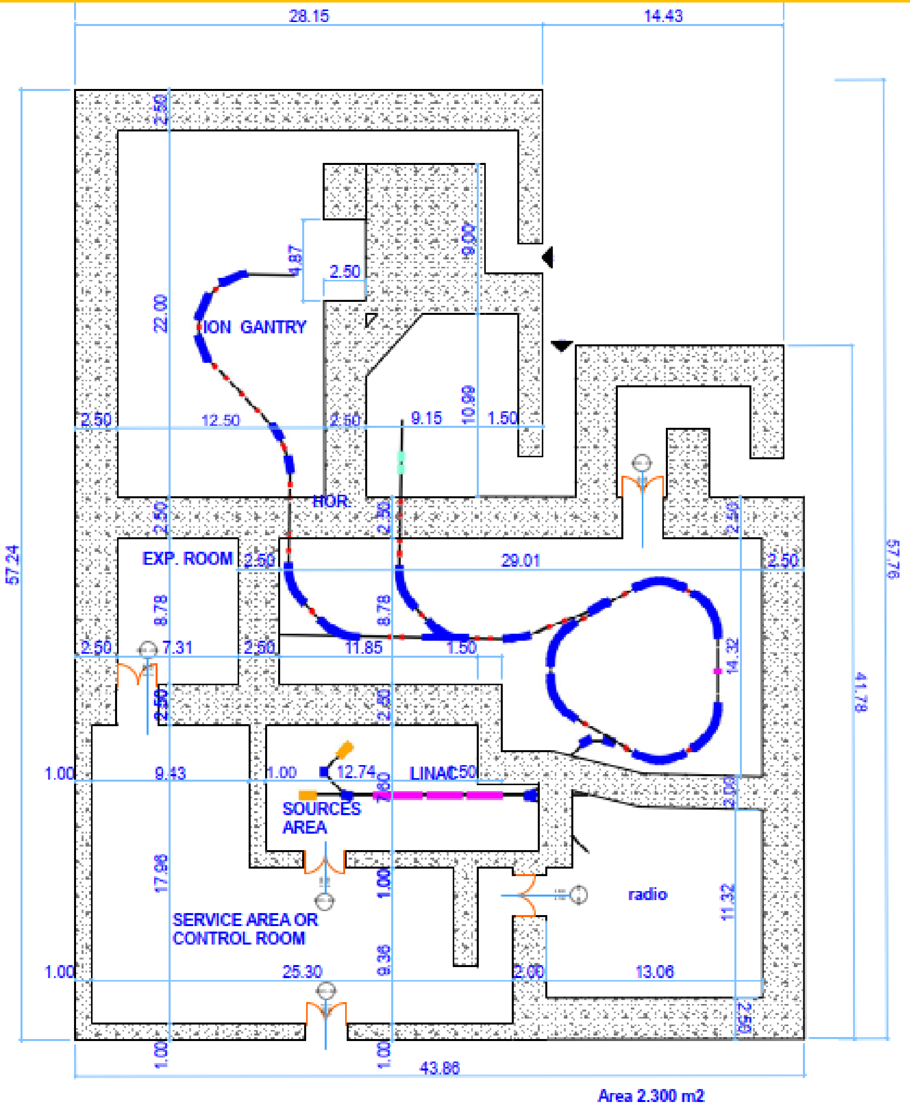
Preliminary design, circumference 33 m





Same design of straight sections can be used for a superconducting synchrotron for carbon ions

The Advanced Particle Therapy Centre for the Baltic States



CERN Baltic Group

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

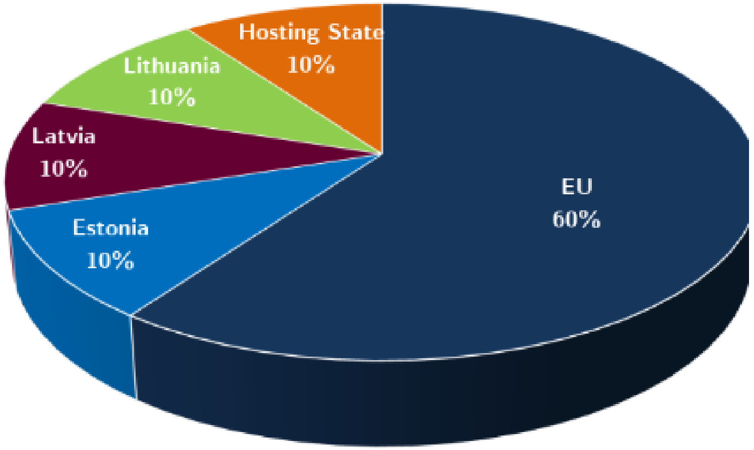
Concept developed in collaboration between CERN (NIMMS study) and the CERN Baltic Group: a combined facility for research and therapy with proton and helium beams and alpha emitters.

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

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

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

The Baltic particle therapy centre: financing and siting



Criteria for site selection:

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

Source: T. Torims, RTU and CERN Baltic Group

Filling the empty areas in the EU hadrontherapy landscape

Particle therapy centres in Europe. Courtesy of ENLIGHT, 2020

The Baltic gap (Estonia, Latvia, Lithuania)

The SEEIIST gap (Slovenia, Croatia, BosniaH., Serbia, Kosovo*, Montenegro, North Macedonia, Albania, Bulgaria, Greece)

Some Conclusions

30 years is still a young age… but TERA has achieved an impressive number of **accomplishments in hadron therapy**, supported by its continuous partnership with CERN and its close connection with medicine and society.

30 years later, research in accelerators has still the potential to provide **breakthroughs in particle therapy** (multiple ions, FLASH, medium and high LET beams,…), in conjunction with a robust **experimental programme** in new facilities that can devote a large fraction of their time to research.

It is thanks to the impulse of TERA that CERN has started the NIMMS adventure, and TERA remains a remarkable partner and source of inspiration.

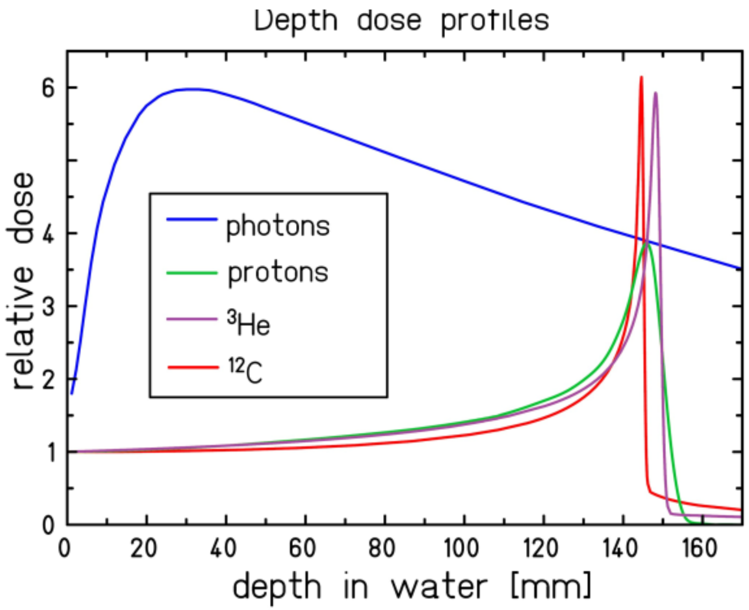
The NIMMS initiative aims at continuing the TERA tradition not only in **striving for innovation in the field of hadron therapy**, but as well in **supporting researchers** in the early phase of their career and in being an **aggregation point** for wide international and multidisciplinary collaborations.

TERA
Fondazione per Adroterapia Oncologica

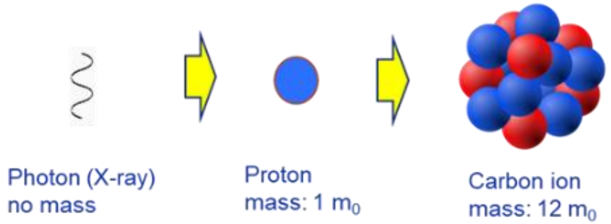
Backup slides

Modern particle therapy

Particle therapy aims at curing deep solid tumours with minimum damage to surrounding organs – promote health by improving quality of life after treatment



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

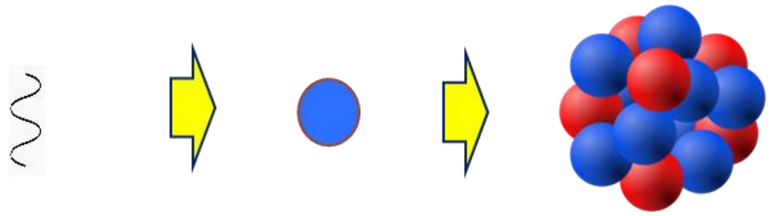


The Bragg peak gives a clear advantage to particles w.r.t. X-rays, but Bragg is not all: *biology is more complex than physics*

- Radiobiological effect **RBE** has a complex dependence on energy transfer and particle type: need of experimental work, complex models and sophisticated treatment plans.
- Practical dose delivery reduces **effectiveness:** longitudinal scan of tumour leads to higher dose in the penetration zone (Spread Out Bragg Peak),
- The precise dose distribution requires **comparable accuracy** in imaging of tumours and in compensation of organ motion.

Need for more **research**, with the two particles presently licensed for treatment (protons and carbon) and with other ions.

Ion therapy: from photons to protons to ions



Photon (X-ray)
no mass

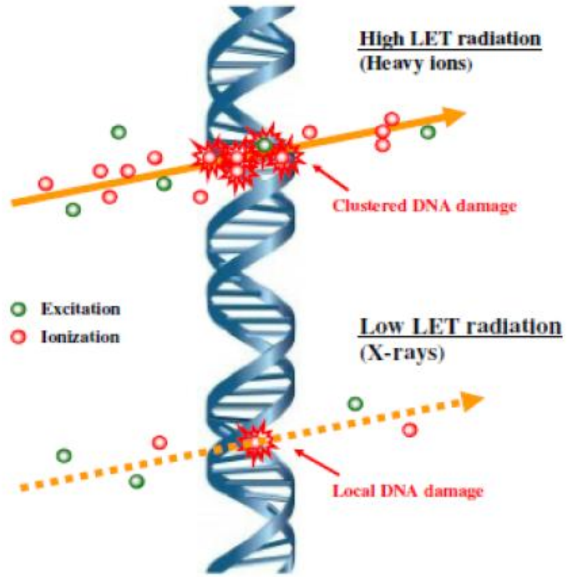
Proton
mass: 1 m_0

Carbon ion
mass: 12 m_0

Ions are heavier, and deliver more energy to the tissues: generate dense ionisations that damage DNA beyond repair. A different and more effective biological action than X-rays or protons.

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

- **G**enerate non-reparable double-strand DNA breakings that are effective on hypoxic radioresistant tumours.
- Energy deposition more precise, with lower straggling and scattering
- Opportunities from combination with immunotherapy to treat diffused cancers and metastasis.

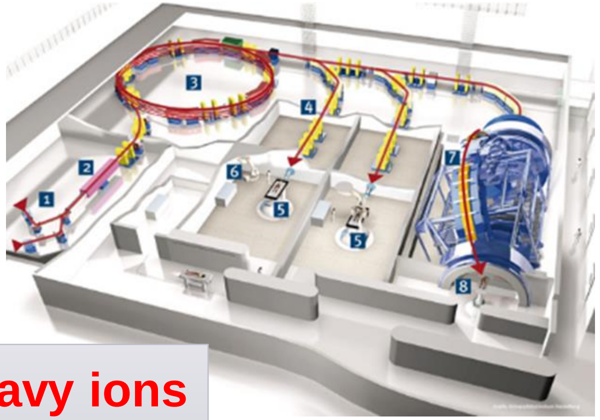


- Only carbon ions licensed for treatment, after the pioneering developments at HIMAC (Japan) from the 90's
- First patient treatments with carbon ions only in 1994: ion therapy is still in its infancy !

What accelerator for what particle

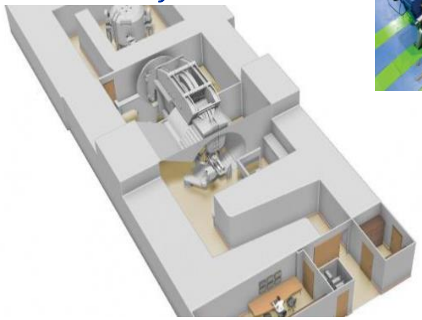
Ions deliver more energy to the tissues but need more energy to enter the body → higher energy accelerator, factor 2.8 in diameter with respect to protons

The CNAO and HIT facilities



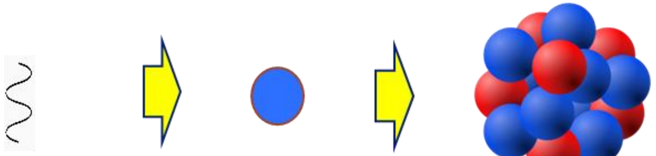
Synchrotron, heavy ions
~5,000 m^2
~200 M€

courtesy IBA



Cyclotron, protons
~500 m^2
~40 M€

Linac, X-rays
~50 m^2
~5 M€



Photon (X-ray)
no mass

Proton
mass: 1 m_0

Carbon ion
mass: 12 m_0

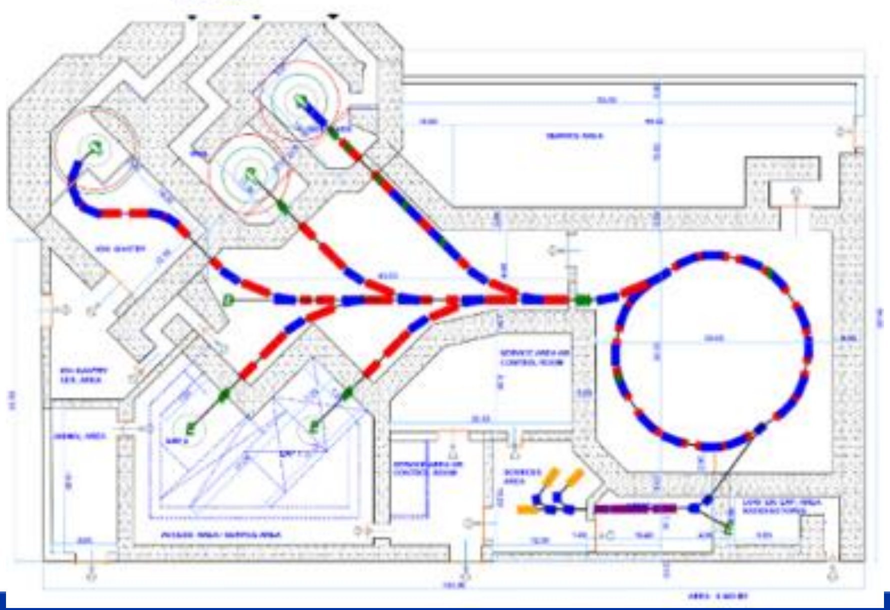
A conventional carbon ion synchrotron for SEEIIST

Design developed in 2018-2021, based on the PIMMS lattice

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

Room temperature magnets at 1.6 T field

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



Optimised layout for the SEEIIST initiative