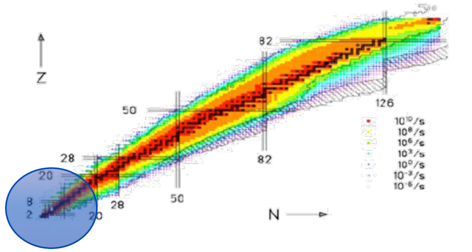
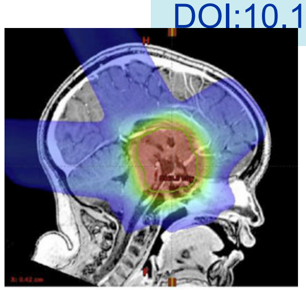
Innovation Aspects in Future Accelerators for Hadron Therapy

Elena Benedetto, SEEIIST Association
Maurizio Vretenar, CERN
29th June 2022, HIAT

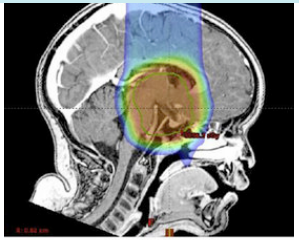
Protons /“Heavy Ions” radiation therapy



DOI:10.1016/j.ijrobp.2016.06.2446

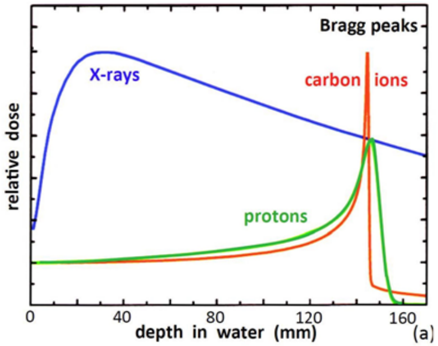


photons IMRT

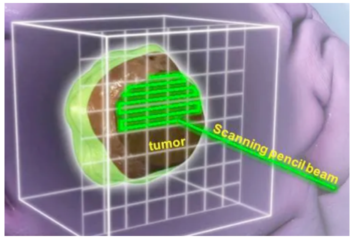


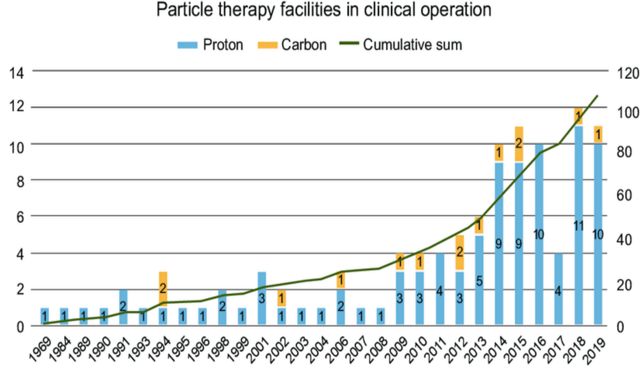
protons

Bragg Peak: charged particles deposit energy @ specific depth, depending on the beam energy



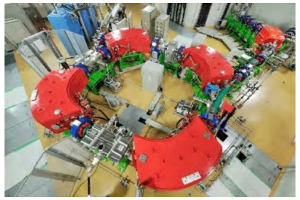
3D beam scanning

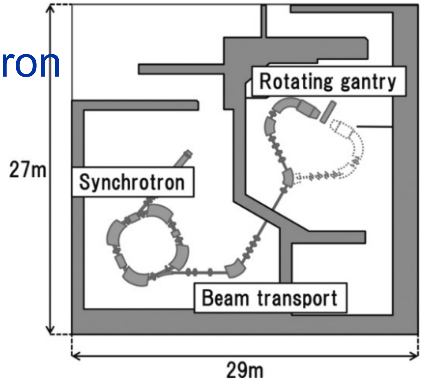




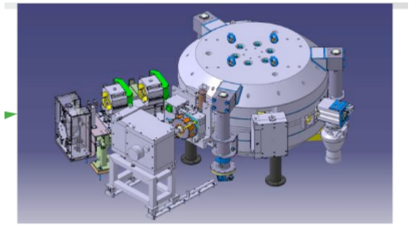
110 particle - proton therapy facilities, 30 in Europe (Vs. 14’000 X-ray facilities)
~40MEur

HITACHI Synchrotron

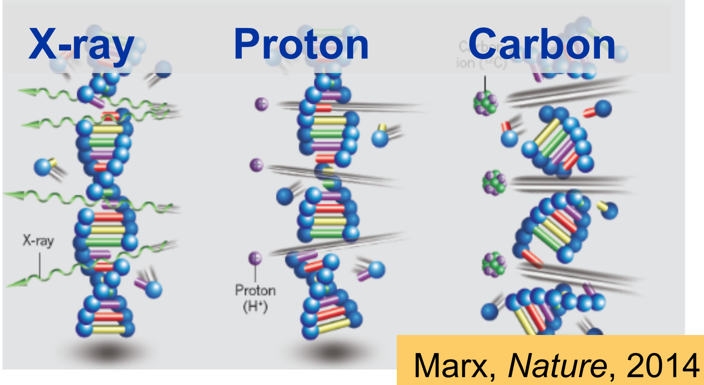




IBA SynchroCyclotron



Carbon (and other) ions therapy



Marx, *Nature*, 2014

Single-strand breaks (easy to repair) vs. double-strand breaks (not reparable)

- ✓**3x more damage (RBE)**
- ✓**also in oxygen-depleted “radioresistant” tumours**

now also Helium and Oxygen of interest for treatment

Range 3 mm to 300 mm in water-equivalent (Bragg Peak)

Protons: 60 - 250 MeV (Bρ = 2.42 Tm)

Carbon: 100 – 430 MeV/u (Bρ = 6.6 Tm)

~2.7x beam rigidity, i.e. more difficult to bend

Facilities become larger and more expensive ~200 MEur

MedAustron, 25 m diameter synchrotron, 3 treatment rooms, proton gantry

HIT C-ion gantry (600 tons)

Innovation Aspects in Future Accelerators for Therapy

- ✧ **Superconducting (SC) magnets to reduce size, weight, cost**
  - compact synchrotron and gantry …and no-gantry solutions
- ✧ **Multi-ions treatment Vs. optimization for a single ion**
  - protons, Helium, Carbon, Oxygen Vs. Helium (and protons) only
- ✧ **Higher (x20) beam intensity for flexible delivery:**
  - deliver full beam at Multi-Energy in one cycle (Vs. limitation of SC magnet ramp)
  - ready for FLASH treatment modalities
- ✧ **Energy efficiency**

The CERN **Next Ion Medical Machine Study (NIMMS)** leverages on CERN expertise to develop a **portfolio of technologies (…a "toolbox")** for a new generation of medical accelerators with ion beams

- HF Linac
- Synchrotron
- Gantry
- Magnets
- AI/ML*
- R-isotopes*

* in preparation

NIMMS launched as a Knowledge Transfer initiative in 2019.

Started ~20y after PIMMS, on which CNAO/MedAustron are based.

Environment to develop, exchange, …innovate

Collaborations internal and worldwide:

> **SEEIIST**, TERA Foundation, GSI, INFN, STFC, Imperial College, U. Manchester, U. Melbourne, CIEMAT, CNAO, MedAustron, Riga University, DKFZ, U.Thessaloniki,…

Support from EU programs: **HITRI*plus*** and **iFAST**.

Input from medical/scientific community via ENLIGHT and the International Biophysics Collaboration.

SEEIIST advanced design

South **E**ast **E**urope **I**nternational **I**nstitute for **S**ustainable **T**echnologies, consortium of 10 countries, facility for cancer in South East Europe.

- ✓ Science for peace
- ✓ Scientific excellence
- ✓ Education & Training

Strategic partner of NIMMS and part of HITRIplus iFAST

- Research and therapy with ions: p, He, C, O,… up to Ar
- Synchrotron baseline is PIMMS layout, option of a compact SC-magnet machine
- Flexible extraction (multi-energy slow-ex and FLASH)
- Intensity x20(*) EU facilities

(*)To deliver 2 Gy Carbon ions to 1 liter in one cycle

	p	He	C
Intensity	2.6 e11	8.2 e10	2.0 e10
Inj. Energy (MeV/u)	7-10	5	5
Extr. Energy (MeV/u)	60-250	60-250	100-430
Beam rigidity max (Tm)	2.42	4.85	6.62

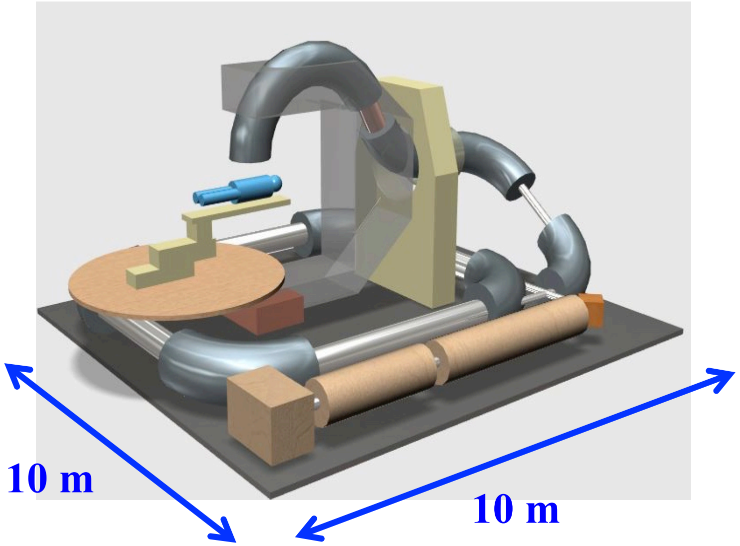
✧ SC-magnet for Carbon therapy (and multi ions)

First SC gantry, HIMAC, NIRS

300 tons “only”
(compared to HIT ~600 t, warm magnets)

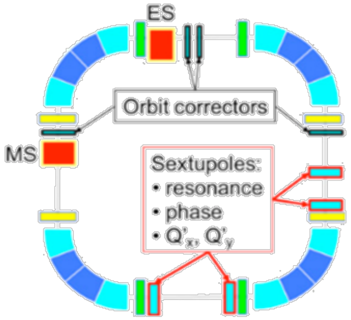
A new one 3.5T instead of 2.9T installed and currently under commissioning at Yamagata

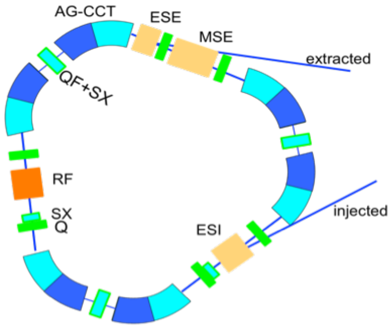
Quantum Scalpel project, QST-NIRS



- same size as proton accelerator
- HTS magnets
- Laser acceleration

SC-magnet compact ring for C-ions

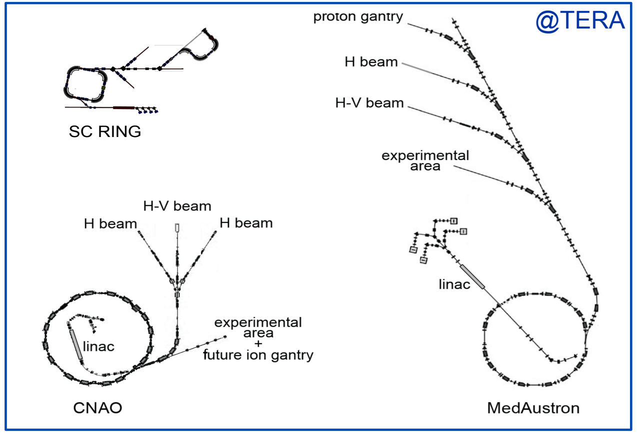




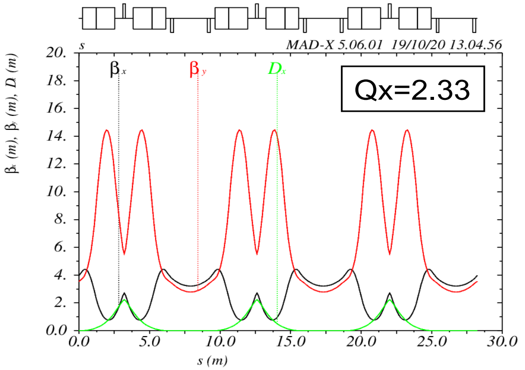
Developed within HITRI*plus* (E. Benedetto)
Evolved to triangular, with 3.5 T 60^0 magnets and a SC quadrupole in between.
No-dispersion in straight sections (inj, extr, RF)

TERA E.Benedetto et al. 2018

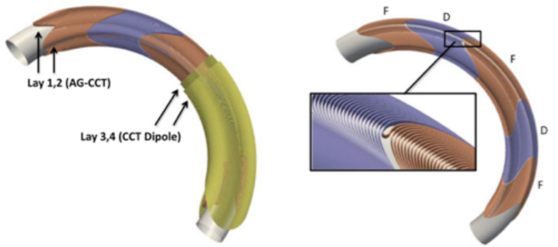
https://arxiv.org/abs/2105.04205



~30m length. Optics is flexible with small quads for tune adjustment, carring sextupole + orbit correctors



AG-CCT magnets allow periodic focusing while bending, reducing beta function (and beam size)

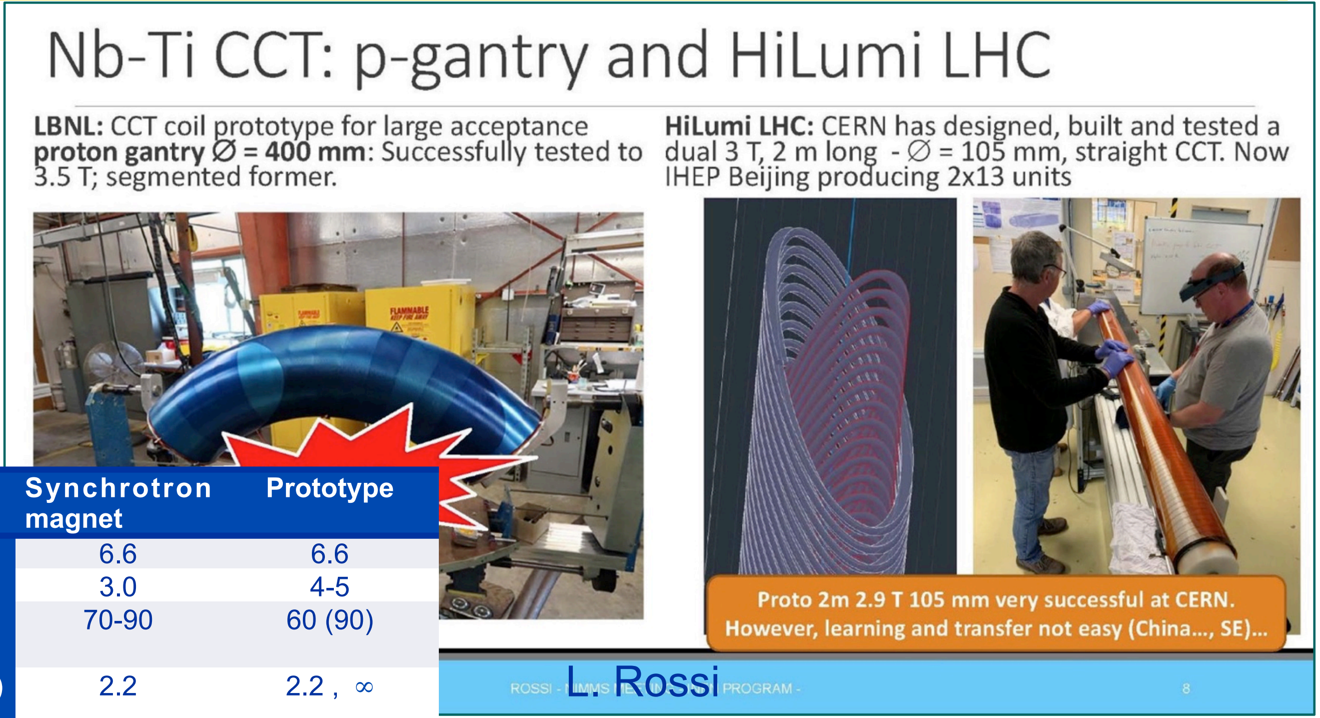


IEEE TRANSACTIONS ON APPLIED SUPERCONDUCTIVITY, VOL. 27, NO. 4, JUNE 2017 4400106

Design of an Achromatic Superconducting Magnet for a Proton Therapy Gantry

L. Brouwer, S. Caspi, R. Hafalia, A. Hodgkinson, S. Prestemon, D. Robin, and W. Wan

SC Strongly-Curved CCT magnets



Nb-Ti CCT: p-gantry and HiLumi LHC

LBNL: CCT coil prototype for large acceptance **proton gantry ∅ = 400 mm**: Successfully tested to 3.5 T; segmented former.

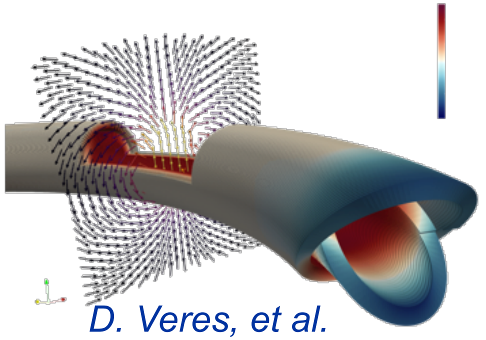
HiLumi LHC: CERN has designed, built and tested a dual 3 T, 2 m long - ∅ = 105 mm, straight CCT. Now IHEP Beijing producing 2x13 units

Proto 2m 2.9 T 105 mm very successful at CERN. However, learning and transfer not easy (China..., SE)...

L. Rossi

see L. Rossi's talk

Parameter	Synchrotron magnet	Prototype
$B\rho$ (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



D. Veres, et al.

Several prototypes will be built in ~3y from now

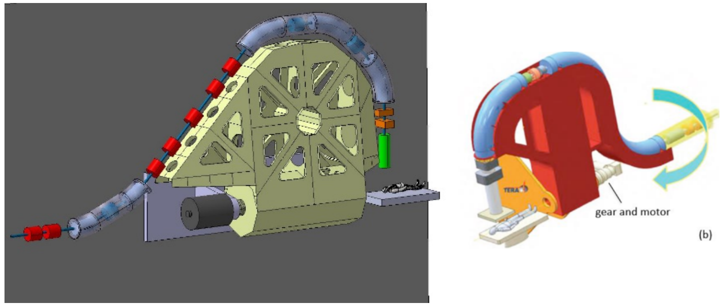
Field Quality in strongly curved magnets (& modeling challenges)

Study group HITRI*plus* E.Benedetto, D.Barna

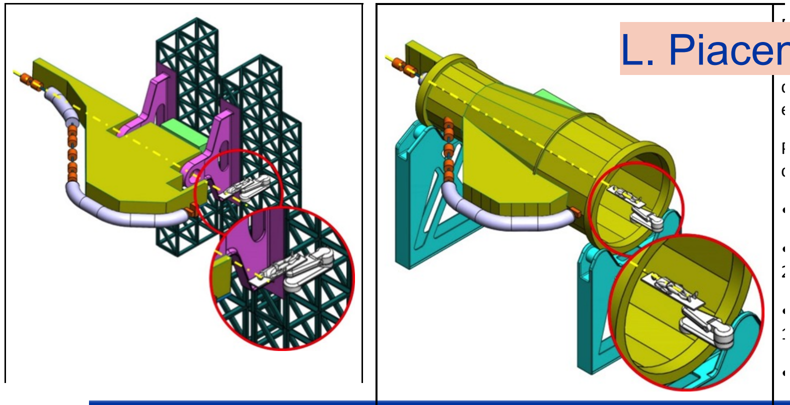
→ use generalized gradients Vs. multipoles

SC-magnet compact gantry

- Gantries for Carbon ions are huge, two SC gantry in Japan, studies in Europe.
- Objective: Develop a superconducting gantry with weight lower than 100 tons and length below 16 metres.
- Subject: a «SIGRUM» type gantry selected by an expert committee in Dec. 2020.
- Development ongoing within HITRI*plus* (M.Pullia)



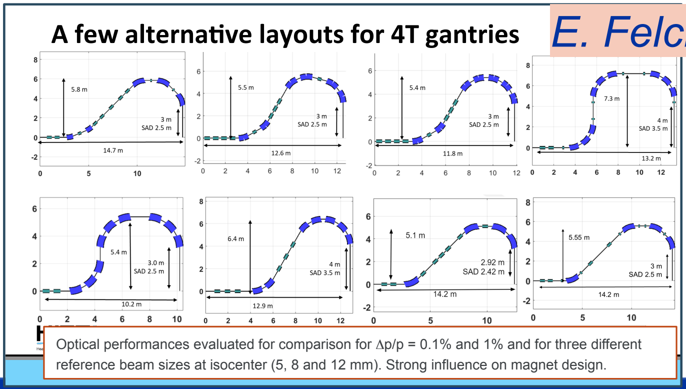
E.B. et al, TERA,
https://arxiv.org/abs/2105.04205
U. Amaldi, et. al, TERA + CERN, NIMMS-Note-002



L. Piacentini et al.

HITRI*plus*
Heavy Ion Therapy Research Integration

E. Felcini et al



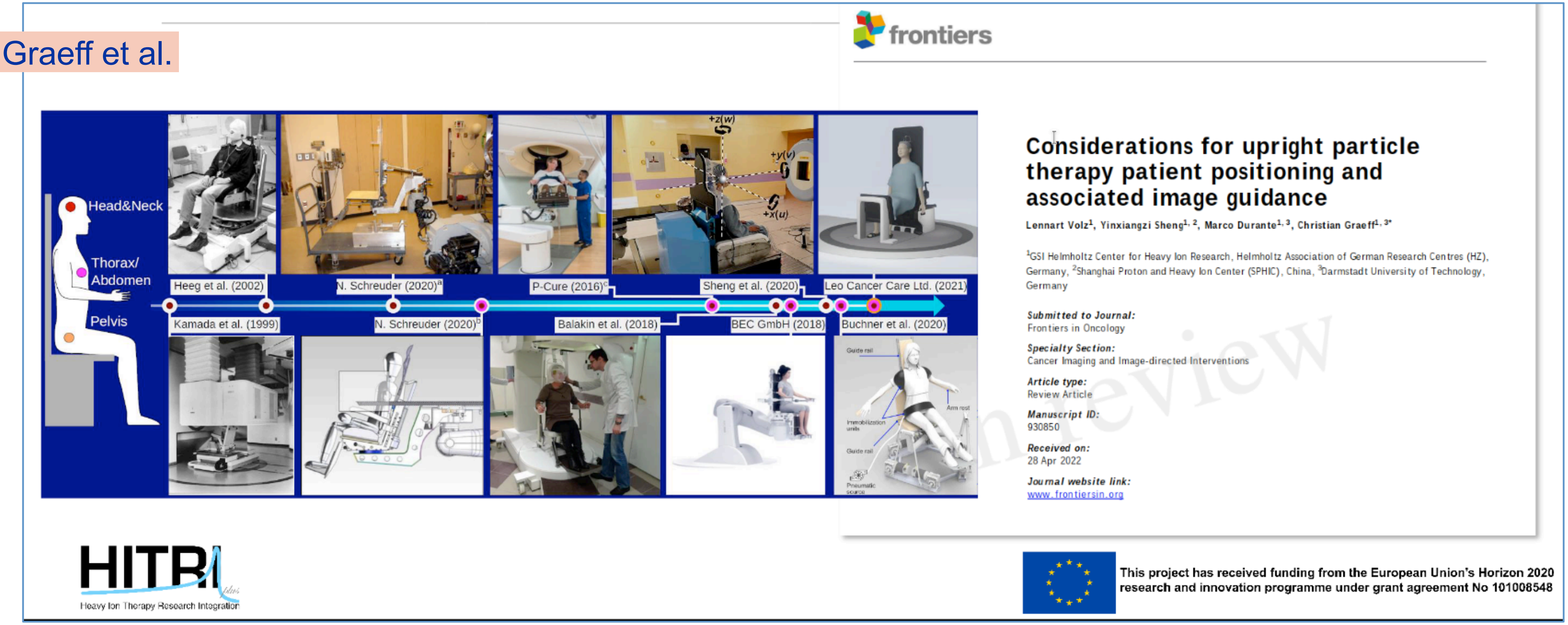
A few alternative layouts for 4T gantries

Optical performances evaluated for comparison for $\Delta p/p = 0.1\%$ and 1% and for three different reference beam sizes at isocenter (5, 8 and 12 mm). Strong influence on magnet design.

…or no-gantry at all?

Chair becomes interesting (again!) because availability of vertical imaging system

C. Graeff et al.



Considerations for upright particle therapy patient positioning and associated image guidance

Lennart Volz[1], Yinxiangzi Sheng[1, 2], Marco Durante[1, 3], Christian Graeff[1, 3*]

[1]GSI Helmholtz Center for Heavy Ion Research, Helmholtz Association of German Research Centres (HZ), Germany, [2]Shanghai Proton and Heavy Ion Center (SPHIC), China, [3]Darmstadt University of Technology, Germany

Submitted to Journal:
Frontiers in Oncology

Specialty Section:
Cancer Imaging and Image-directed Interventions

Article type:
Review Article

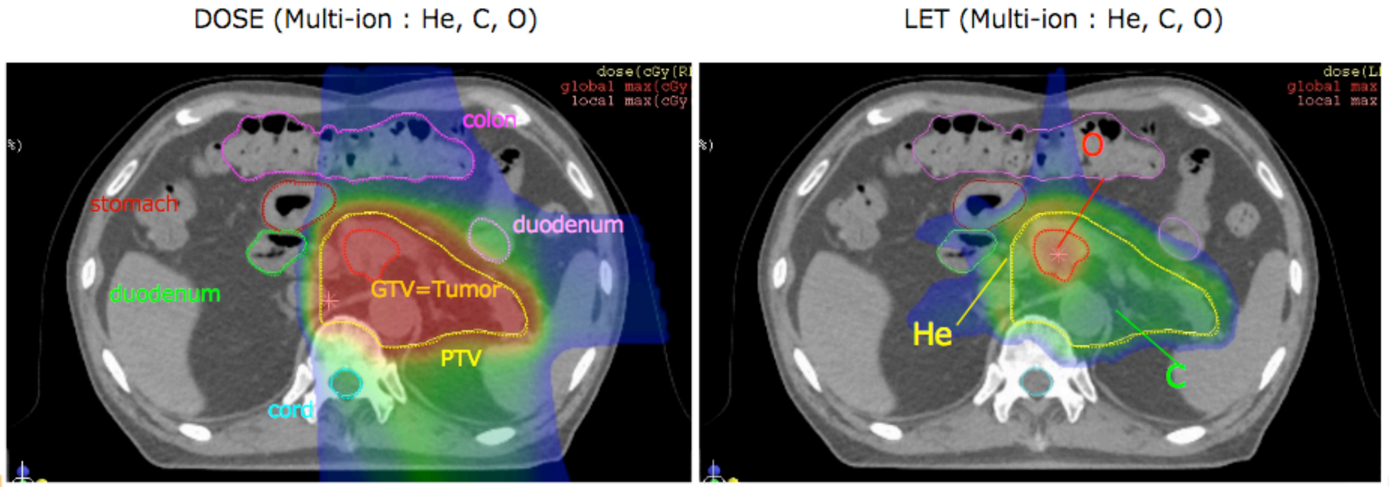
Manuscript ID:
930850

Received on:
28 Apr 2022

Journal website link:
www.frontiersin.org

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

✧ Multi-ions treatment Vs. Optimization for single ion



Inaniwa et al., Phys. Med. Biol. 2021

O, C (high LET) at Tumour,

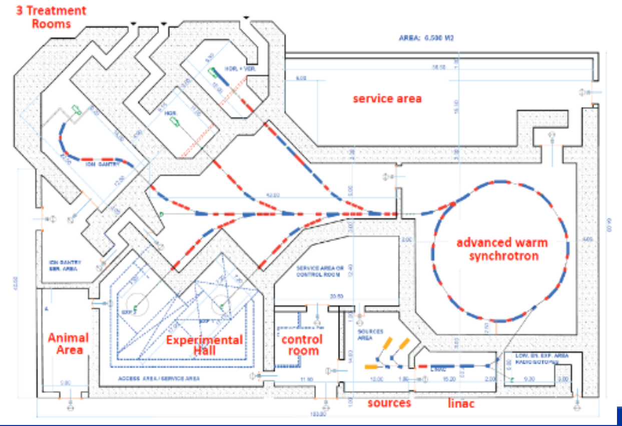
He and p near Organs At Risks

Requires fast switching between ion species (multiple ion source)

SEEIIST facility, being designed for it – hardware & control - :

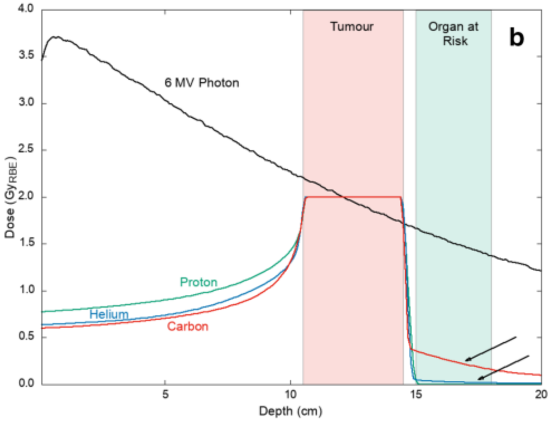
- between ions species (treatment)
- between treatment/experimental rooms

HITRIplus
Heavy Ion Therapy Research Integration

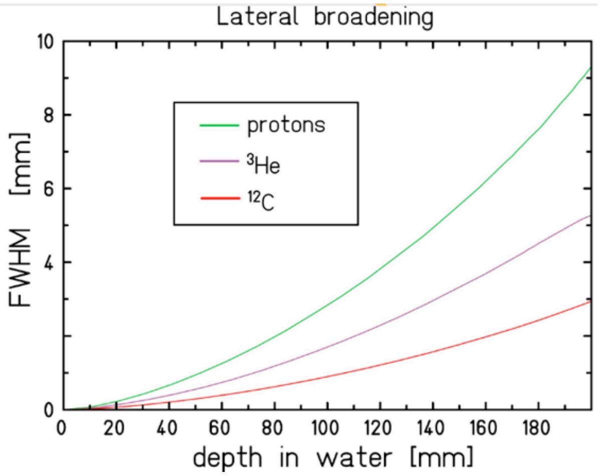


✧ …Optimization for Helium Vs. Multiple-ions

M. Vretenar et al., IPAC22



K. Kirkby et al., https://doi.org/10.1259/bjr.20200247



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

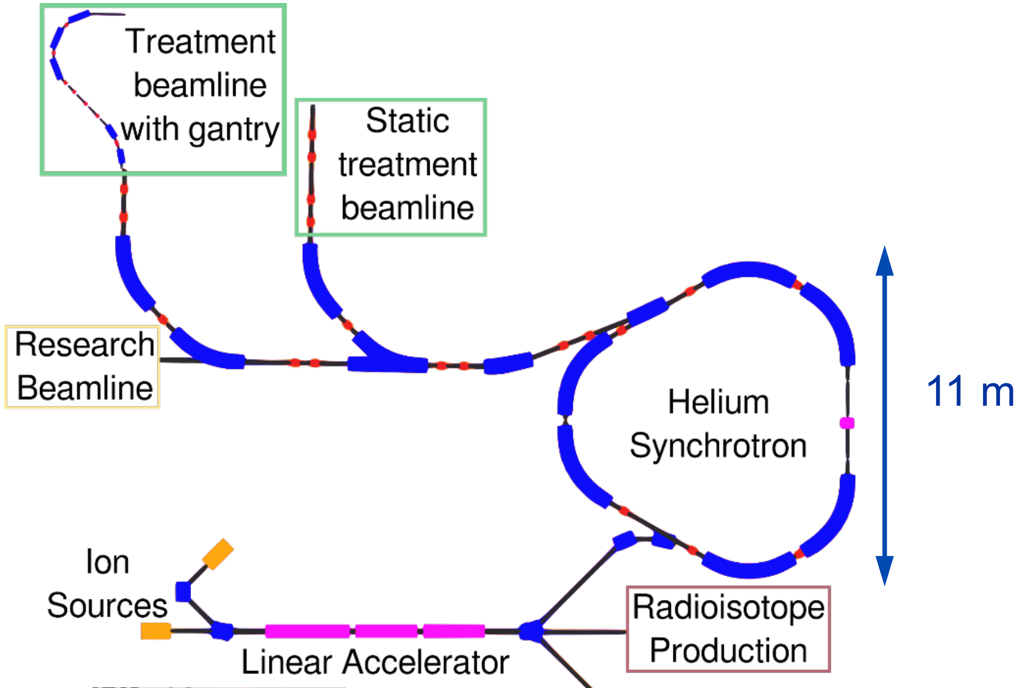
Why Helium?

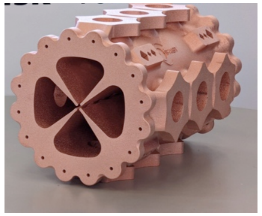
- ➢ reduced lateral scattering than p
- ➢ lower fragmentations than C
- ➢ lower neutron dose than p or C
- ➢ could treat some radioresistent tumours

- ➢ Max. beam rigidity Brho = 4.5 Tm
  (~intermediate between p and C)

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

Helium facility





…possibly with AM → *see talk T. Torims*
(baseline is 325 MHz as CERN L4)

Considered for a recently proposed Advanced Particle Therapy Centre for the Baltic States.

Particle therapy in Europe. ENLIGHT, 2020

- 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

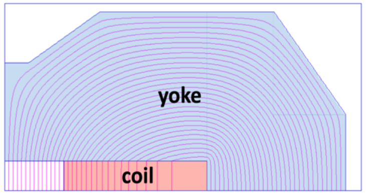
The Helium synchrotron

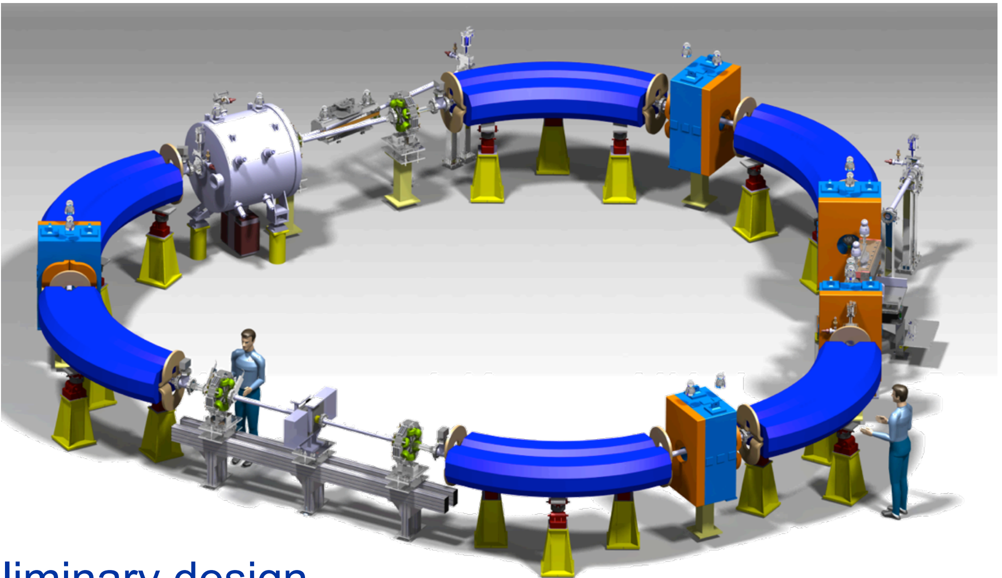
M. Vretenar et al., IPAC22

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

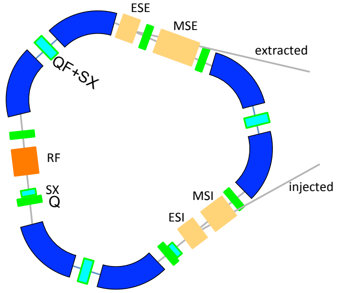
Proven technology, compact & upgradable

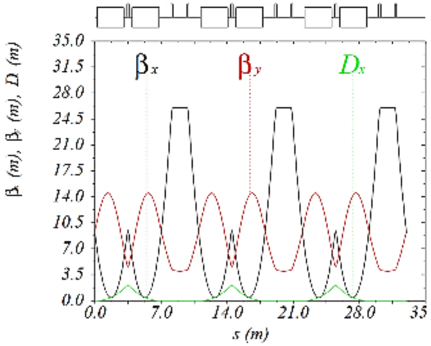
Conservative dipole field of 1.65 T (minor impact on ring size), with window-frame magnets.





Preliminary design, circumference 33 m



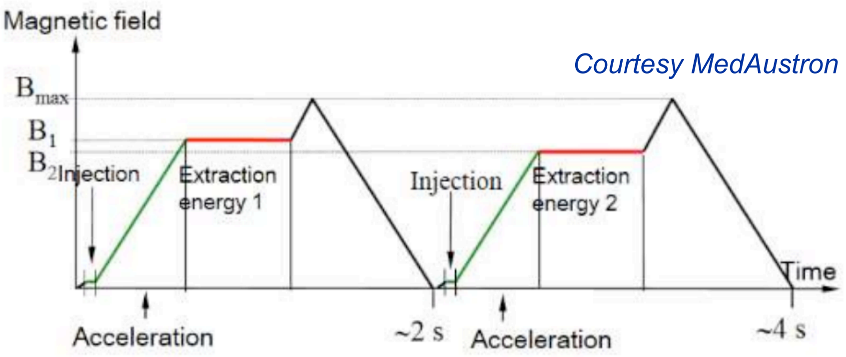


Injector linac at 352.2 MHz, based on CERN Linac4 design.

Three straight sections (injection, extraction, RF)

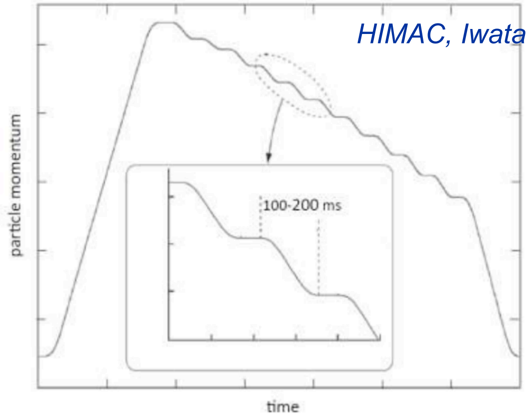
Similarities with SC synchrotron for C- ions, e.g. in the straight sections

✧ Flexible beam delivery requires x20 higher intensity



Courtesy MedAustron

TODAY: Every change of energy → A different cycle



HIMAC, Iwata et al, NIM-A

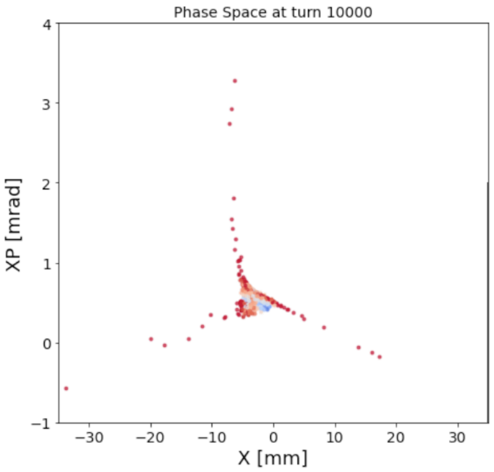
TODAY in Japan (studies at HIT): Multi-Energy Extraction going down (up) within same cycle

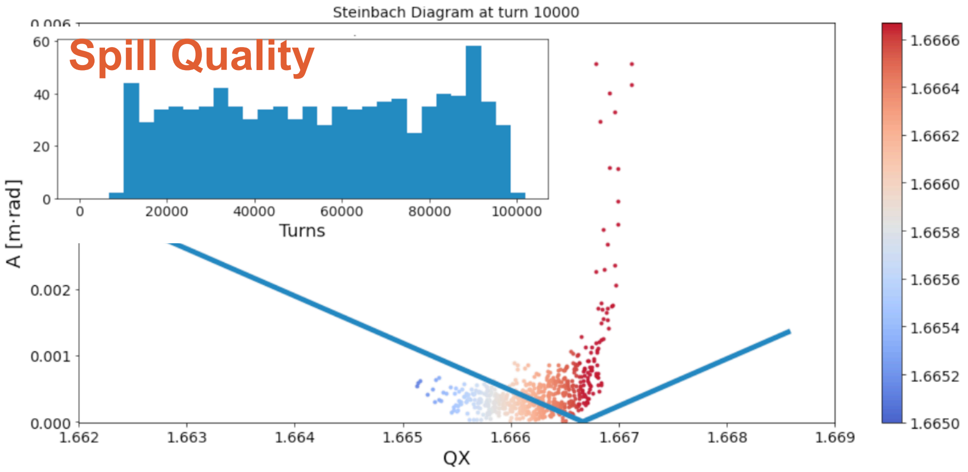
TOMORROW(?) … deliver the entire *high intensity* beam in <500 ms

Slow extraction on the 3rd order resonance

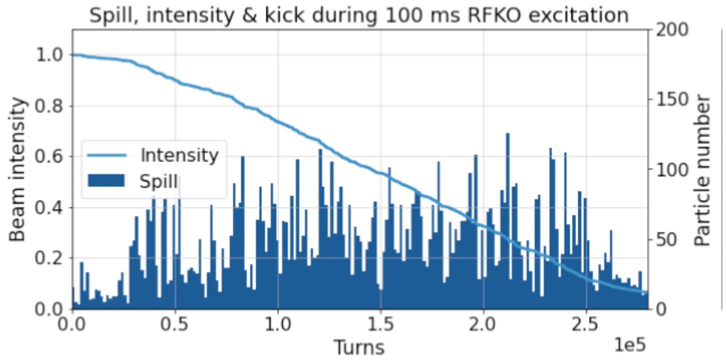
Simulations for benchmark with PIMMS (CNAO, MedAustron)

Rebecca Taylor, CERN/Imperial College





pyNAFF allows fast & precise tune computation



FLASH regime, RF-KO extraction

Preliminary simulations foresee exciter voltage ~1kW for 10urad (10x beyond hardware capability)

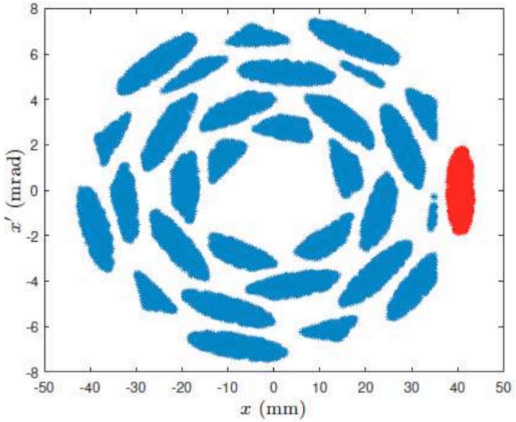
✧ Higher (x20) intensity: MT inj of 2e10 C-ions

Commercially available ECR source ~200 uA C+4

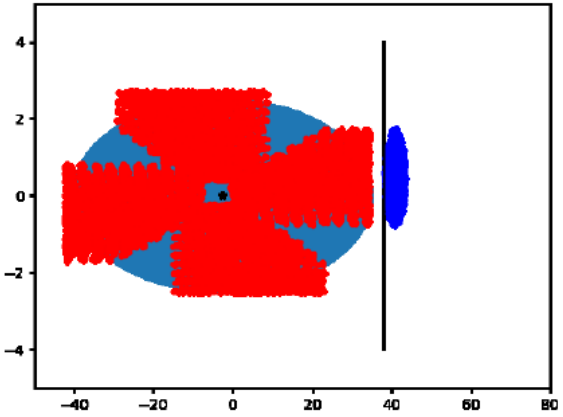
~similar #turns
for He-ions
(source 1mA)

Next generation ECR (e.g. AISHA, Catania) ~600 uA C+4 (in 0.3 mm mrad rms)

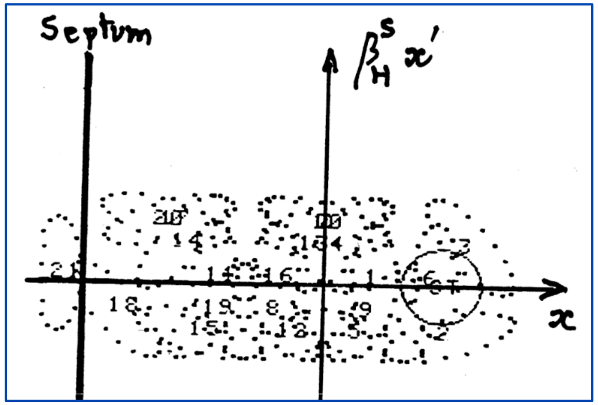
Injecting @ 5 MeV/u in a 70 m circumference
With 90% (high!) efficiency from source to injection → 13 “effective turns” needed (x2 for the compact)
Final emittance of ~5mm mrad (rms normalized)



A. Advic, U. Sarajevo (2019)



EB, playing to increase brightness

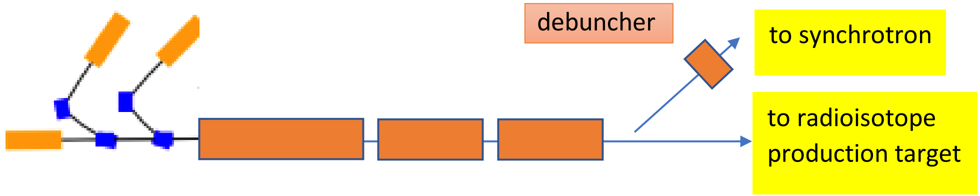


LEIR injection (S.Maury, C.Carli, D. Mohl)

New Linac Design

Bevatec + CERN

- ➢ New injector linac (than the EU facilities) for lower cost, higher intensity, higher transmission
- ➢ Optimal injection energy to the synchrotron
  - 5 MeV/u for C, He ions
  - 10 MeV/u for p



3 ion sources

$^{12}C^{4+}$, 600 μA, 0.2-0.3 π mm mrad (AISHA)

$^{4}He^{2+}$, 0.5 mA, 0.3 π mm mrad (Supernanogun)

P or H_2^+, 5 mA, 0.2-0.3 π mm mrad

(emittances rms normalised)

Linac section1	Linac section2	Linac section3
q/m=1/3	q/m=1/2	q/m=1/2 or 1
W_{in}=15 keV/u	W_{in}= 5 MeV/u	W_{in}= 7.1 MeV/u
W_{out}= 5 MeV/u	W_{out}= 7.1 MeV/u	W_{out}= 10 MeV/u

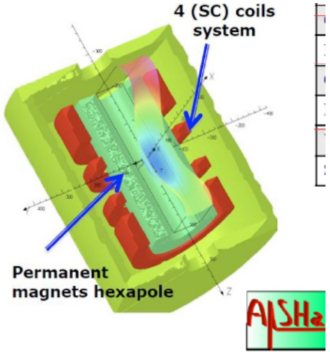
Maximum duty cycle:

10%

Version 1 : 217 MHz

Version 2 : 352 MHz

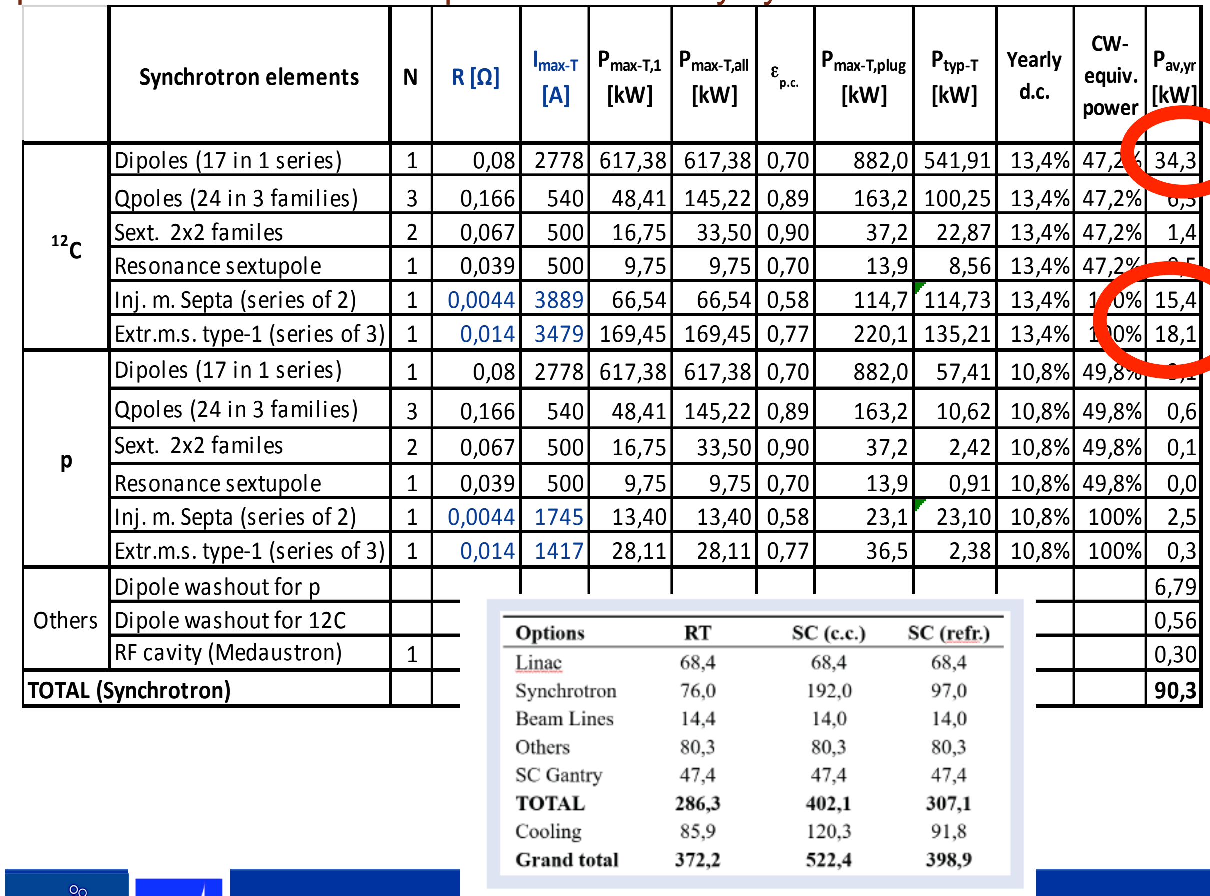
- ➢ Advanced source ~600 uA
- ➢ Radioisotopes production: feasible with small changes in the baselines
  - duty cycle 10%
  - staged Linac



✧ Energy efficiency

G. Bisoffi et al, IPAC22

Table 2: calculation of the CNAO synchrotron average power from the electrical specs and the duty cycle



	Synchrotron elements	N	R [Ω]	I_{max-T} [A]	$P_{max-T,1}$ [kW]	$P_{max-T,all}$ [kW]	$\varepsilon_{p.c.}$	$P_{max-T,plug}$ [kW]	P_{typ-T} [kW]	Yearly d.c.	CW-equiv. power	$P_{av,yr}$ [kW]
^{12}C	Dipoles (17 in 1 series)	1	0,08	2778	617,38	617,38	0,70	882,0	541,91	13,4%	47,2[illegible]	34,3
	Qpoles (24 in 3 families)	3	0,166	540	48,41	145,22	0,89	163,2	100,25	13,4%	47,2%	[illegible]
	Sext. 2x2 familes	2	0,067	500	16,75	33,50	0,90	37,2	22,87	13,4%	47,2%	1,4
	Resonance sextupole	1	0,039	500	9,75	9,75	0,70	13,9	8,56	13,4%	47,2%	[illegible]
	Inj. m. Septa (series of 2)	1	0,0044	3889	66,54	66,54	0,58	114,7	114,73	13,4%	1[illegible]0%	15,4
	Extr.m.s. type-1 (series of 3)	1	0,014	3479	169,45	169,45	0,77	220,1	135,21	13,4%	1[illegible]0%	18,1
p	Dipoles (17 in 1 series)	1	0,08	2778	617,38	617,38	0,70	882,0	57,41	10,8%	49,8[illegible]	[illegible]
	Qpoles (24 in 3 families)	3	0,166	540	48,41	145,22	0,89	163,2	10,62	10,8%	49,8%	0,6
	Sext. 2x2 familes	2	0,067	500	16,75	33,50	0,90	37,2	2,42	10,8%	49,8%	0,1
	Resonance sextupole	1	0,039	500	9,75	9,75	0,70	13,9	0,91	10,8%	49,8%	0,0
	Inj. m. Septa (series of 2)	1	0,0044	1745	13,40	13,40	0,58	23,1	23,10	10,8%	100%	2,5
	Extr.m.s. type-1 (series of 3)	1	0,014	1417	28,11	28,11	0,77	36,5	2,38	10,8%	100%	0,3
Others	Dipole washout for p											6,79
	Dipole washout for 12C											0,56
	RF cavity (Medaustron)	1										0,30
TOTAL (Synchrotron)												**90,3**

Options	RT	SC (c.c.)	SC (refr.)
Linac	68,4	68,4	68,4
Synchrotron	76,0	192,0	97,0
Beam Lines	14,4	14,0	14,0
Others	80,3	80,3	80,3
SC Gantry	47,4	47,4	47,4
TOTAL	**286,3**	**402,1**	**307,1**
Cooling	85,9	120,3	91,8
Grand total	**372,2**	**522,4**	**398,9**

In PIMMS machines, **Inj/extr elements consume as much as all dipoles**
→ new pulsed septa design

SC-magnet accelerator consumes ~as much as warm

→ cryocoolers: development of energy-efficient solutions (power required while ramping up/down)

→ refrigerator: development SC septa, will use the 130 W refrigerator (45 kW @ plug)

Final considerations

What about the users?

Innovations need to keep users (patients, doctors, med. physicists) at the center of the process. What do they need want? what do they need?

(…but sometimes they do not know what they can afford, as they don’t know it is possible!)

Innovation Aspects in Future Accelerators for Hadron Therapy

1) **Developments:** increased intensity, improved inj/extr, multi-ion treatment, fast switch, optimized workflow, energy efficient solutions, Full Linac HF (A.Lombardi et al., within NIMMS, not covered today)
2) **Disruption:** SC-magnets compact ring (in HITRIplus), Innovative gantry support (TERA), Laser acceleration, FLASH dose delivery, Addictive Manufacturing, AI/ML, ...
3) **“Low tech” innovation** to democratize access to hadron therapy: e.g. no-gantry, chair solution, robustness, proven technology (He-ring), easy to operate, industrialize, maintain

In our “toolbox” we need all the three !