The UK Proton Beam Therapy Programme and Supporting Research

Simon Jolly

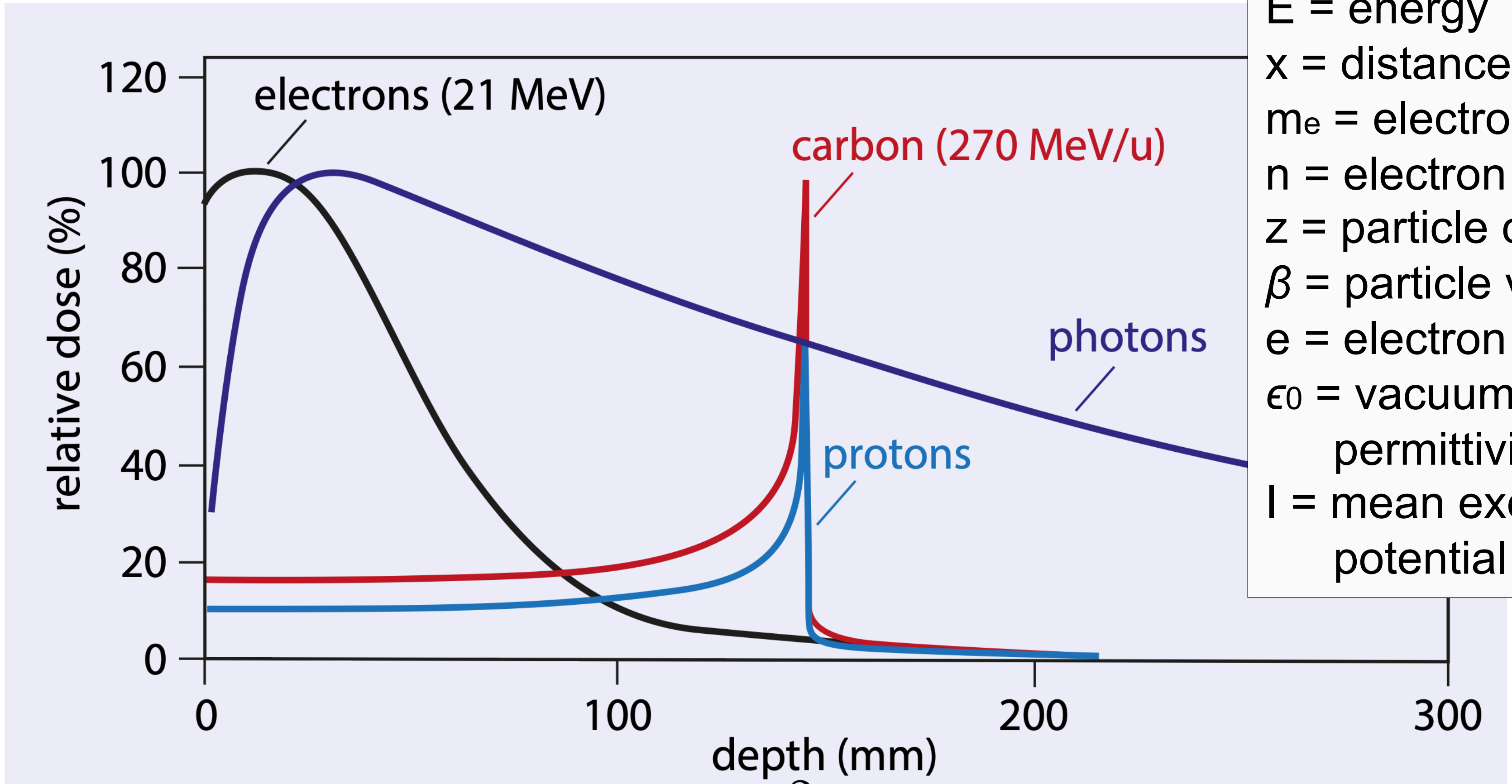
Abstract

Modern cancer treatment is largely a combination of 4 techniques: surgery, chemotherapy, radiotherapy and immunotherapy. Proton Beam Therapy (PBT) is a more targeted version to conventional radiotherapy, where protons in the 60-250 MeV energy range are used to maximise the destructive radiation dose to cancerous tumours whilst minimising the damage to healthy tissue. The advantage of PBT is that dose can be delivered more precisely than conventional radiotherapy due to the way protons lose energy: as a result of the Bragg Peak, most of the energy is deposited in the last few millimetres of the proton path. This has particular significance in the treatment of deep-lying tumours in the head, neck and central nervous system, particularly for children whose bodies are still developing and are particularly susceptible to long-term radiation damage.

In 2018, the NHS opened the first of two high energy PBT centres at The Christie in Manchester to complement the ocular facility at Clatterbridge that has been treating with protons since 1989; this was followed in 2021 by UCLH. The current status of the three clinical facilities will be presented, as well as the ongoing clinical trials to support improvements in patient outcomes and potential expansion of the current indications list. In addition, there will be an overview of some of the research and development in particle therapy accelerator technology.

Particle Dose Distribution

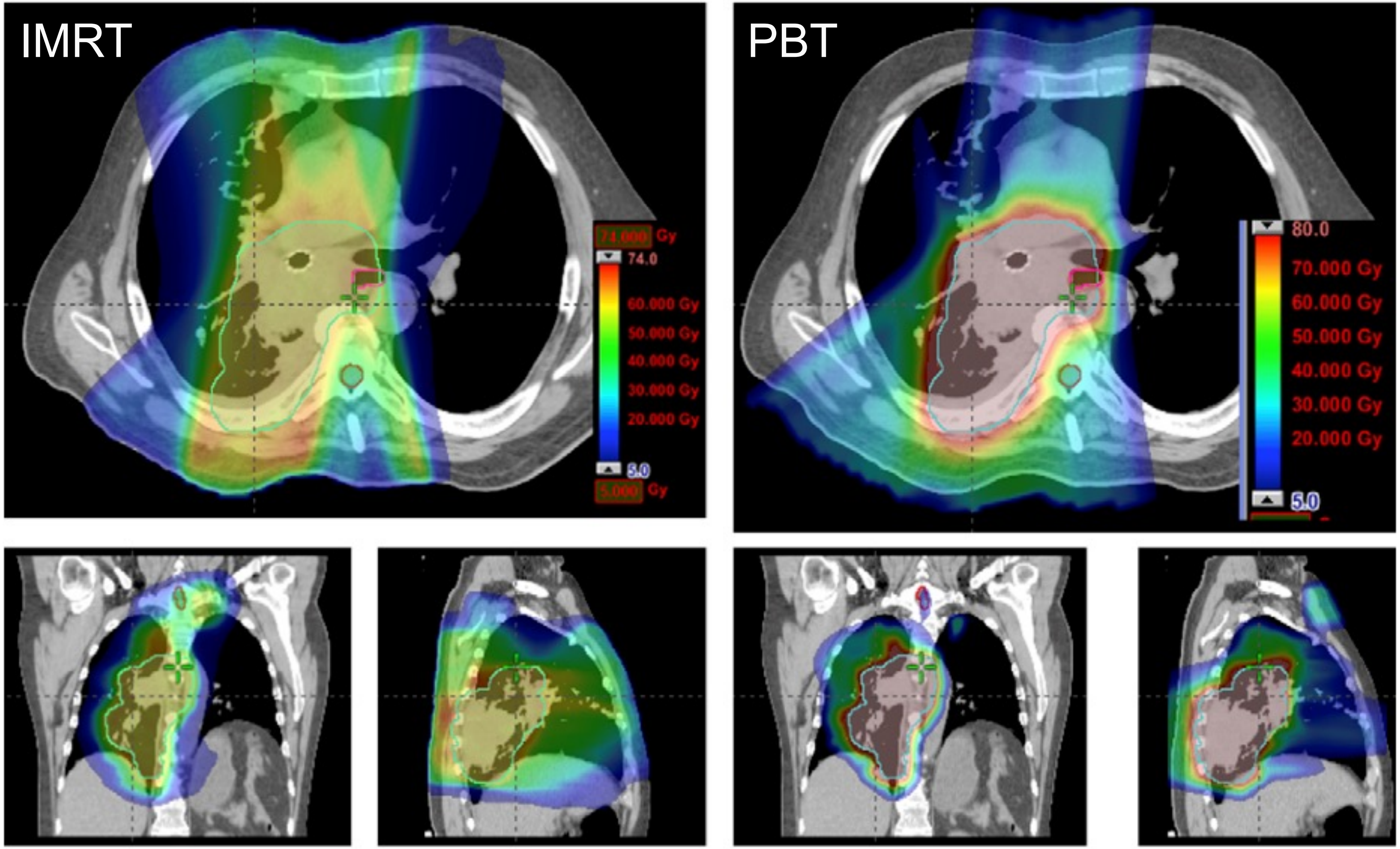
- Unlike X-rays, charged particles stop!
- Electrons, being lighter, scatter and spread out.
- Protons deposit most dose at the *end* of their path: the **Bragg Peak**.



Bethe-Bloch:
E = energy
x = distance
m_e = electron mass
n = electron density
z = particle charge
β = particle velocity
e = electron charge
ϵ_0 = vacuum permittivity
I = mean excitation potential

$$-\frac{dE}{dx} = \frac{4\pi}{m_e c^2}\frac{nz^2}{\beta^2}\left(\frac{e^2}{4\pi\epsilon_0}\right)^2\left[\ln\left(\frac{2m_e c^2\beta^2}{I\left(1-\beta^2\right)}\right)-\beta^2\right]$$

Non Small Cell Lung Cancer Doses



Zhang X, Li Y, Pan X, et al. *Int J Radiat Oncol Biol Phys*. (2010); 77 (2): 357–366 [DOI: 10.1016/j.ijrobp.2009.04.028](https://doi.org/10.1016/j.ijrobp.2009.04.028)

	Indication	Patients
Paediatric	Chordoma/ Chondrosacoma	15
	Rhabdomyosarcoma (Orbit)	5
	Rhabdomyosarcoma (Prameningeal and H&N)	15
	Rhabdomysarcoma (Pelvis)	10
	Osteosarcoma	3
	Ewings Sarcoma	9
	PPNET	5
	Paediatric Ependymoma	25
	Low Grade Glioma	5
	Optic Pathway Glioma	12
	Craniphayngioma	15
	Medulloblastoma (PNET)	70
	Hodgkins	5
	Retinoblastoma	5
	Meningioma	3
	Intracranial germinoma	10
	Nasopharynx (H&N)	15
	Difficult Cases (Esthe/Neuro/Liver)	5
	Very Young Age	20
	Total	**252**
Adult	Choroidial Melanoma	100
	Ocular/Orbital	25
	Chordoma	60
	Chondrosarcoma	30
	Para-Spinal/Spinal Sarcoma	120
	Adult Sacral Chordoma	60
	Meningoma	100
	Acoustic Neuroma	100
	Craniospinal NOS (Pineal)	10
	Head & Neck & Paranasal Sinuses	300
	PNET (medulloblastoma intracranial)	30
	Difficult cases	300
	Total	**1,235**
Grand Total		**1,487**

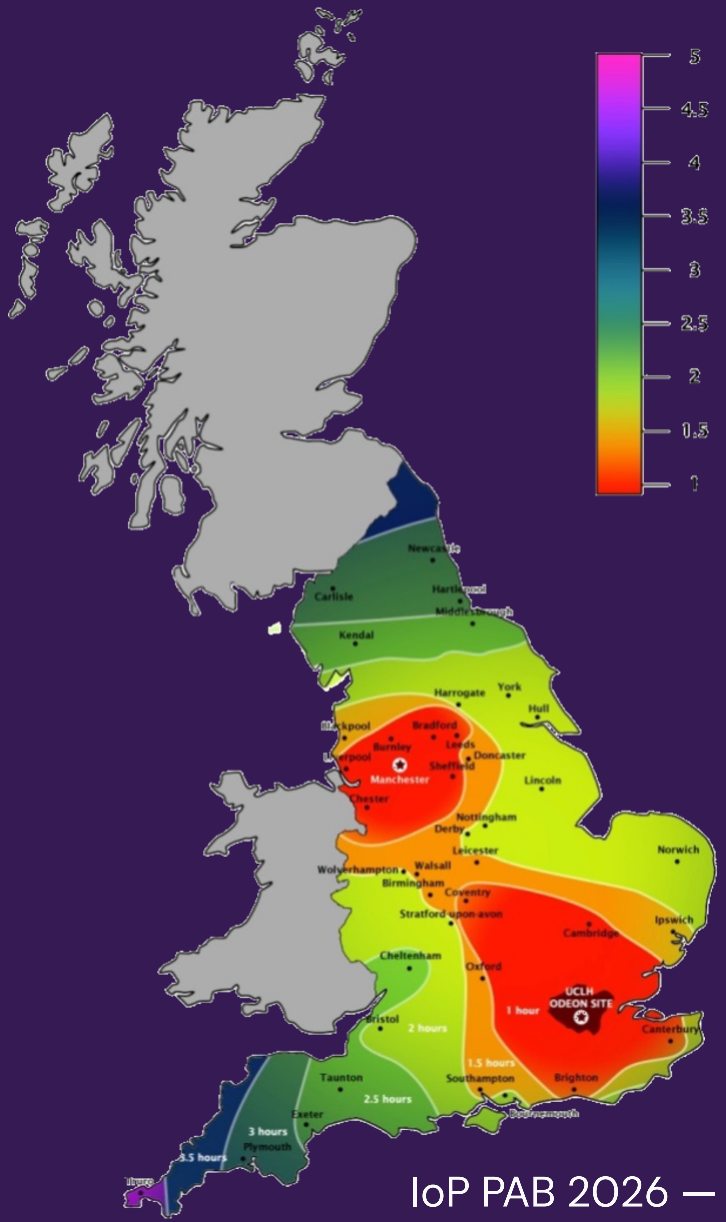
National Proton Beam Therapy Service Development Programme

https://www.gov.uk/government/publications/national-proton-beam-therapy-service-development-programme

The strategic outline case and accompanying value for money addendum published in October 2012.

Provided suggested list of indications to fill maximum capacity of 2 centres (1,500 patients).

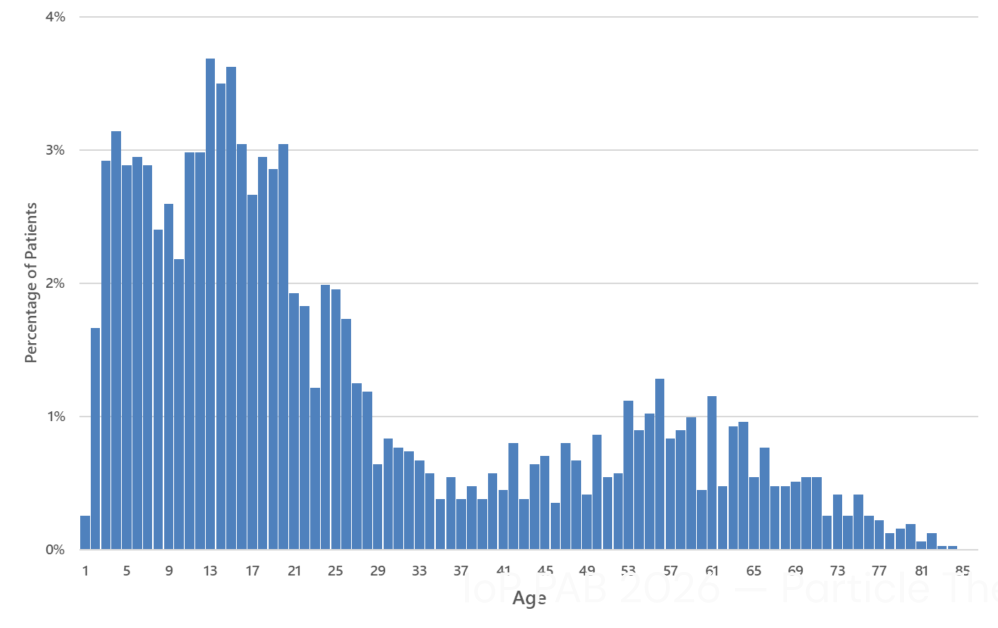
NHS PBT Patient Access



- Two high energy facilities to complement 60 MeV Clatterbridge ocular facility:
  - The Christie (Manchester)
  - UCLH (London)
- Sites partially chosen for geographic location.
- National referral pathway:
  - Patients referred by primary care teams to central panel.
  - Those deemed appropriate for PBT passed to nearest centre.

NHS PBT Clinical Service Status

- The Christie opened late 2018.
- UCLH followed early 2022.
- Current status:
  - ~12 hour treatment days.
  - 300 patients per year per centre.
- Current case mix:
  - ~40% CNS spine
  - ~20% Sarcoma
  - ~13% Head & Neck



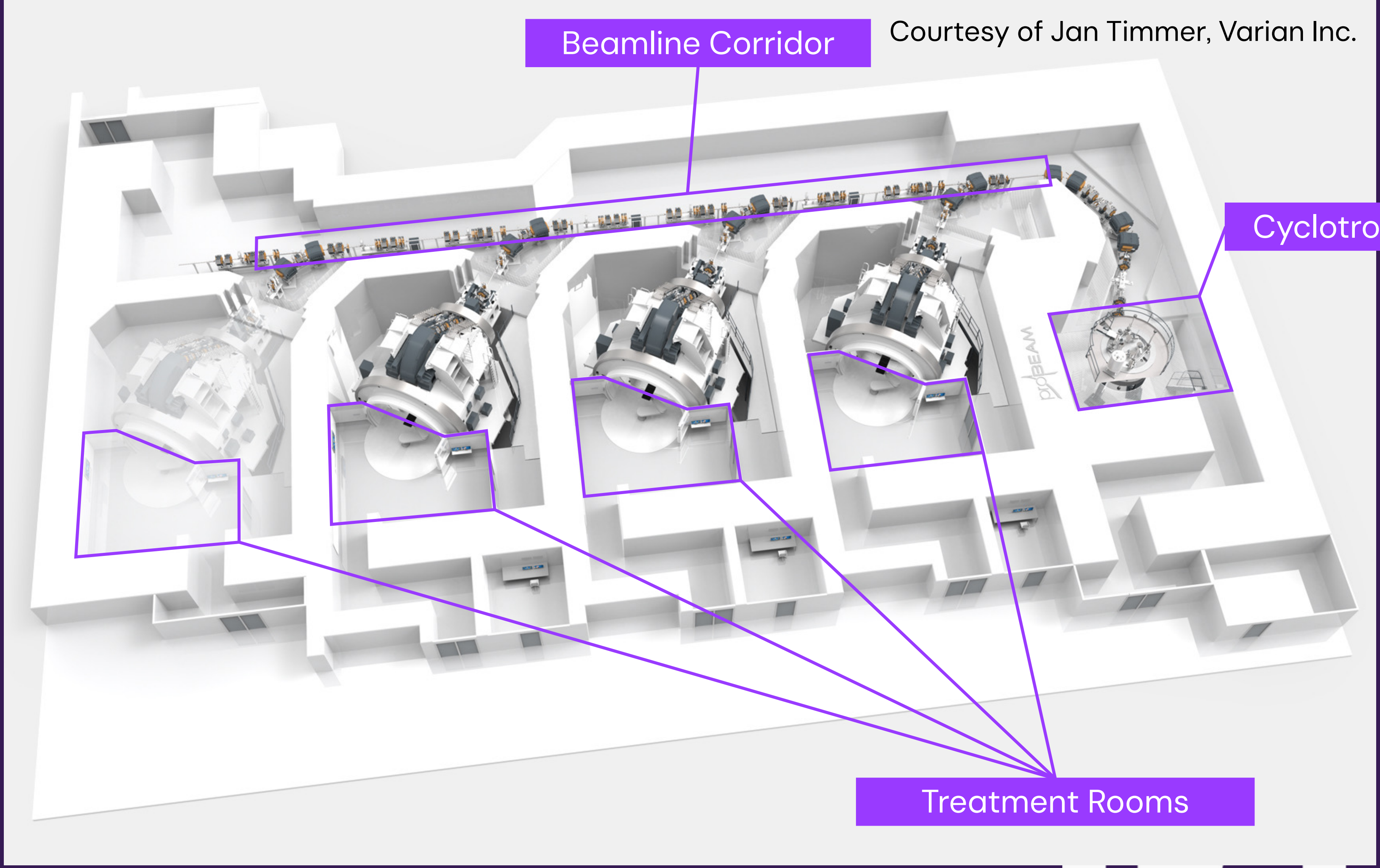
Many trials in progress:

- SIOP – Ependymoma II
- FaR-RMS – rhabdomyosarcoma
- HR-MB – medulloblastoma
- HRNBL2 – neuroblastoma
- INTER EWING1 – ewings sarcoma
- PARABLE (now closed to recruitment) – breast
- APPROACH (recruitment for G3 LGG on hold / G2 open) – oligodendroglioma
- HIT-Meso – mesothelioma
- PROTIEUS – oesophagus
- PROTIS –sinonasal

Evaluative commissioning

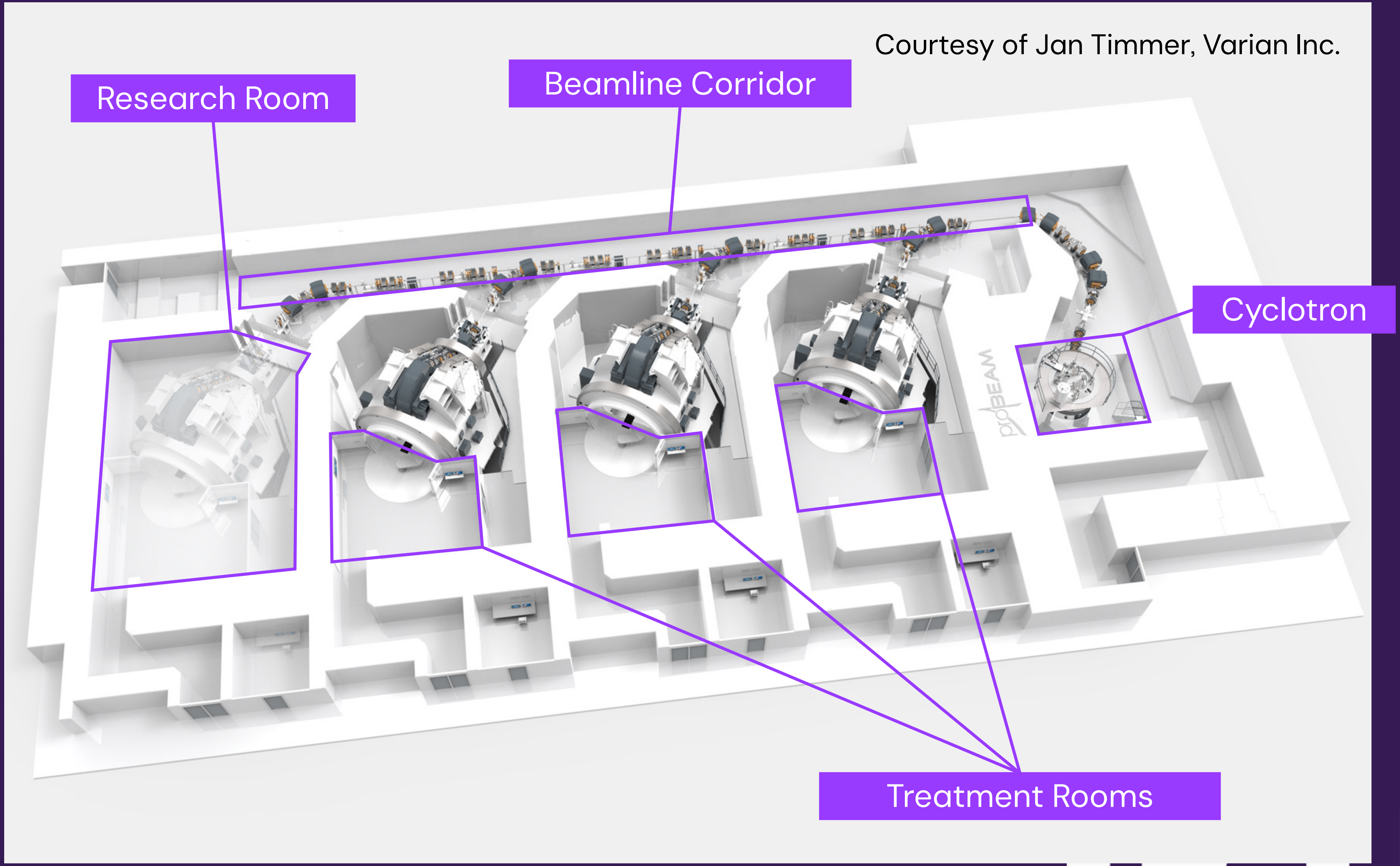
- SUPERMAN (neuroblastoma)
- EMPHATIC (liver)
- PRONTO (parotid)

UCLH PBT Facility

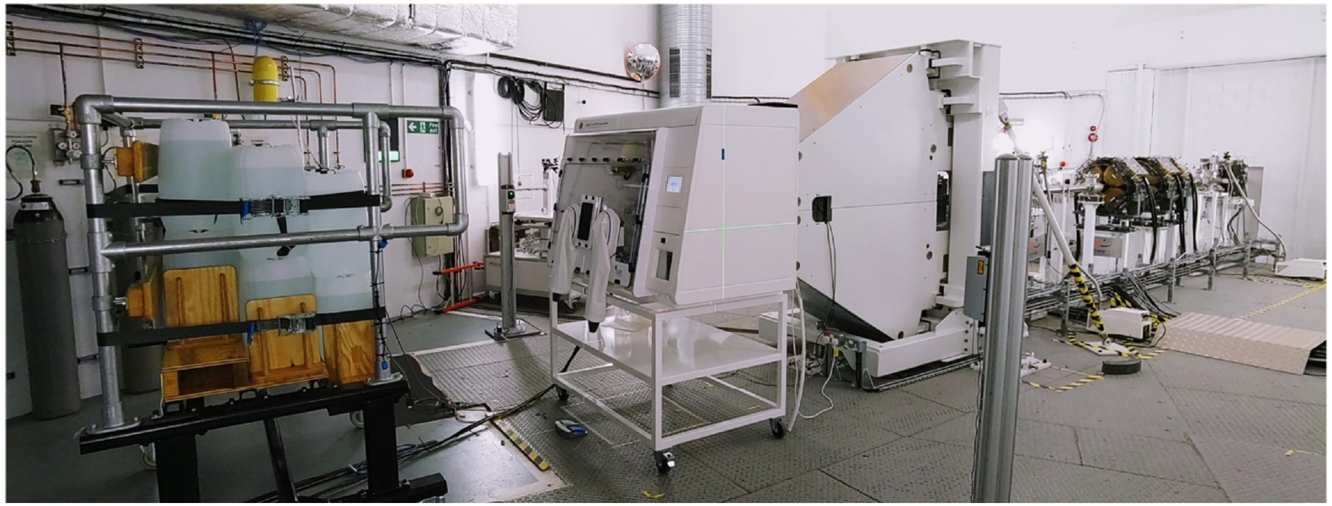


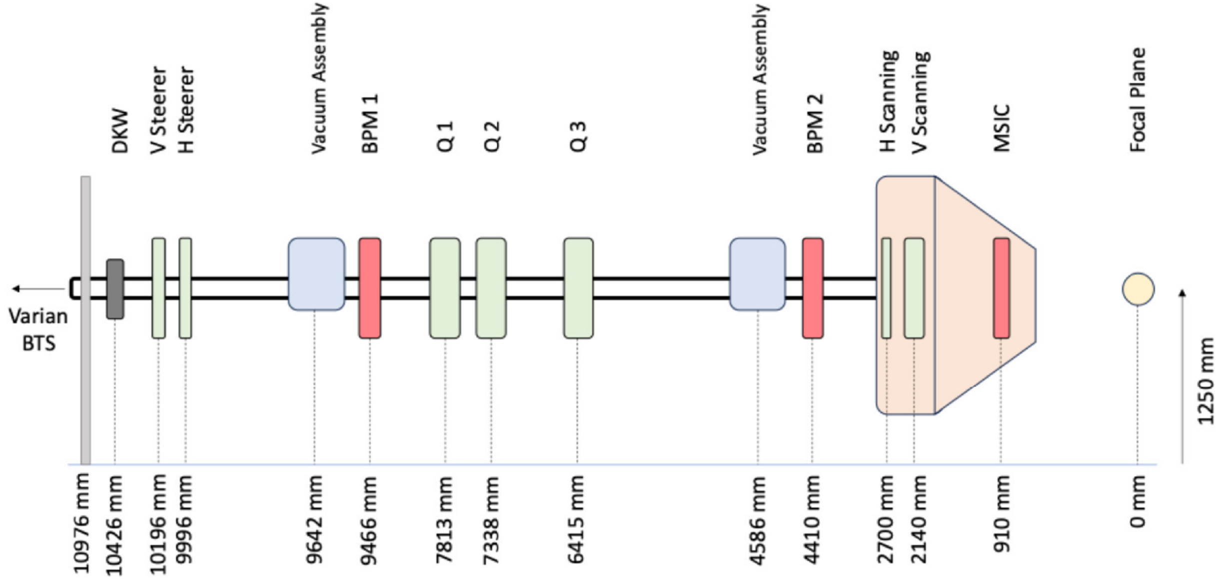
Courtesy of Jan Timmer, Varian Inc.

The Christie PBT Facility



The Christie Research Room (M. Taylor)

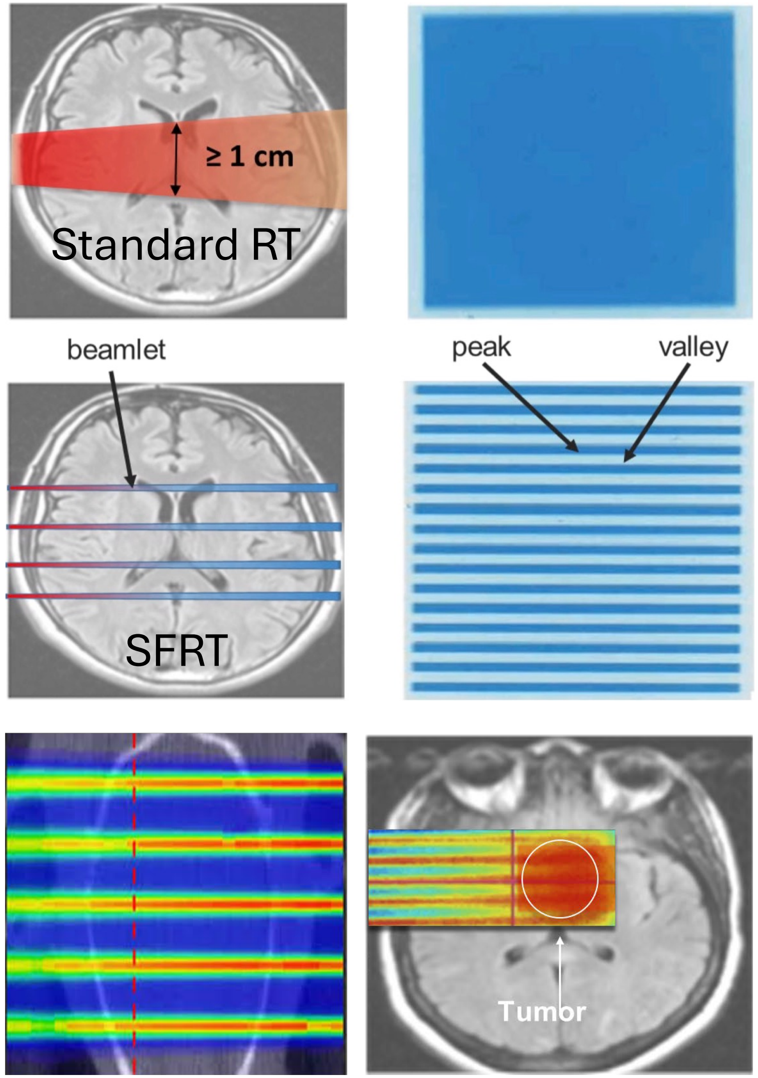




- The Christie 4th gantry vault equipped with research beamline:
  - Air-gapped from clinical facility.
  - Clinical nozzle.
- Radiobiology end station; extending capability with second beamline.
- Multiple physics projects:
  - Range and dose verification
  - Proton CT
  - Proton-SFRT
  - FLASH (Bragg peak and shoot through)

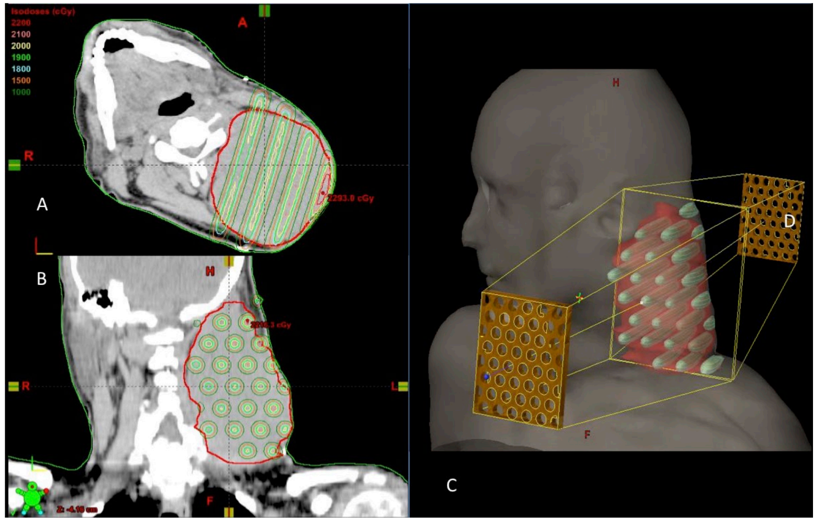
https://doi.org/10.1088/2057-1976/addbe8
Henthorn *et al* (2025)

Spacially Fractioned Radiotherapy (SFRT)

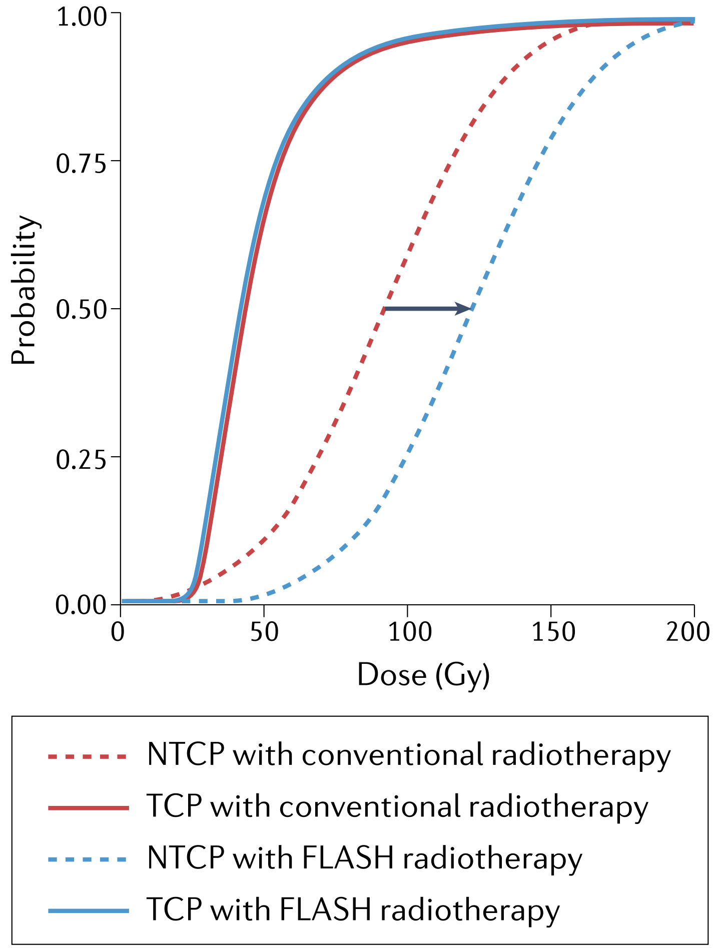


- Separate field into smaller beamlets
- Maximium lateral **heterogeneous** dose distributions (*peaks* and *valleys*)
- **Increase** of **normal tissue tolerance**.
- A **high** peak-to-valley dose ratio (PVDR) combined with **low valley doses** improves normal tissue **preservation**.

Mohiuddin *et al* (2022)
[DOI: 10.7759/cureus.417](https://doi.org/10.7759/cureus.417)



FLASH

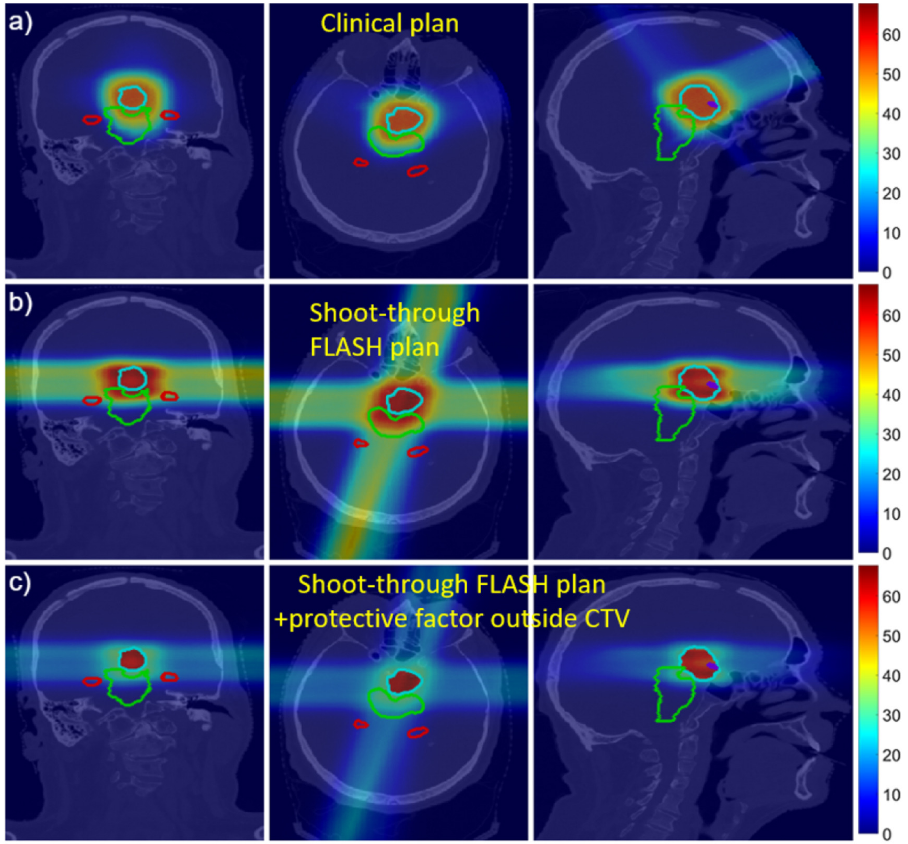


Vozenin, Bourhis, Durante (2022)
DOI: 10.1038/s41571-022-00697-z

- "Therapeutic Window" is gap between:
  - Tumour Control Probability (TCP)
  - Normal Tissue Complication Probability (NTCP)
- CONV delivery:
  - 2–8 Gy per fraction
  - 0.5–20 Gy/min
  - ~30 s per field
- FLASH delivery **improves healthy tissue sparing**:
  - 40 Gy/s.
  - <200 ms per field.
- Beam delivery is challenging!

Jolly, Owen, Schippers, Welsch (2022)
DOI: 10.1016/j.ejmp.2020.08.005

FLASH with Shoot-Through Protons (Varian)

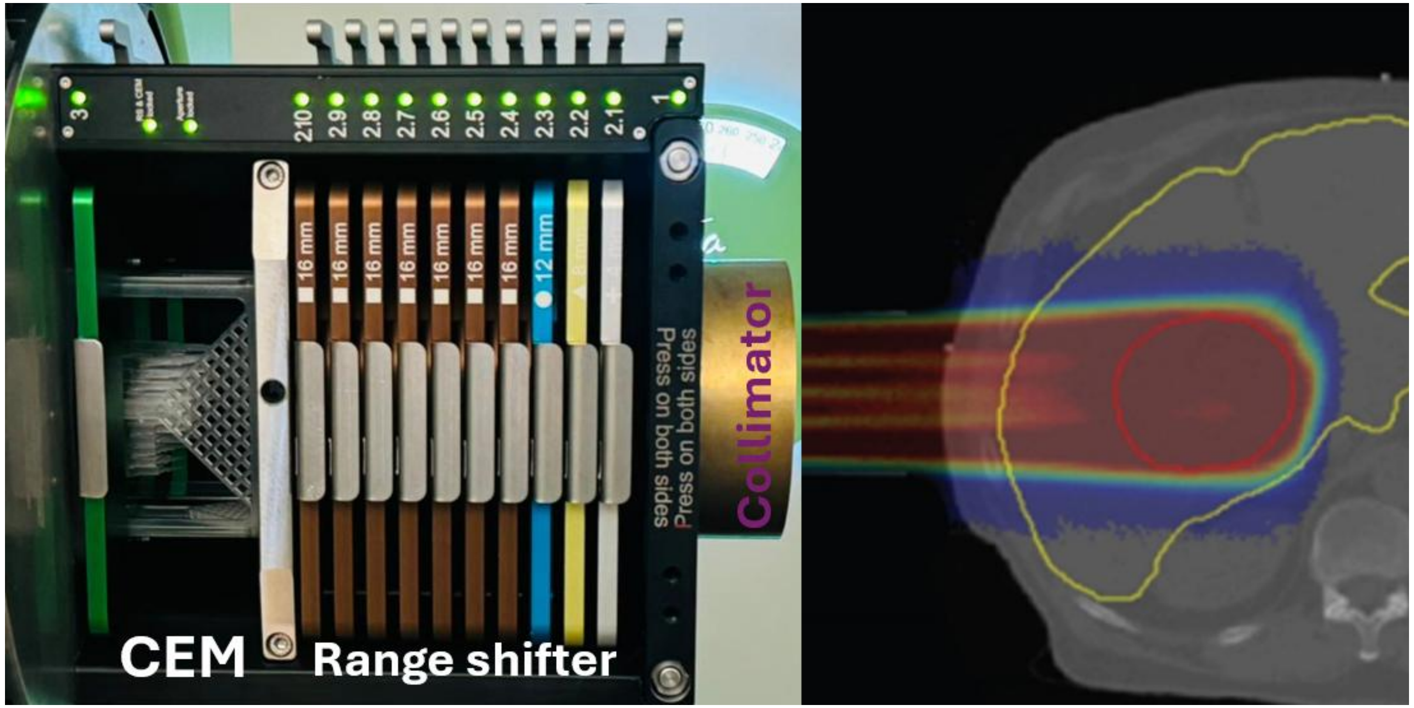


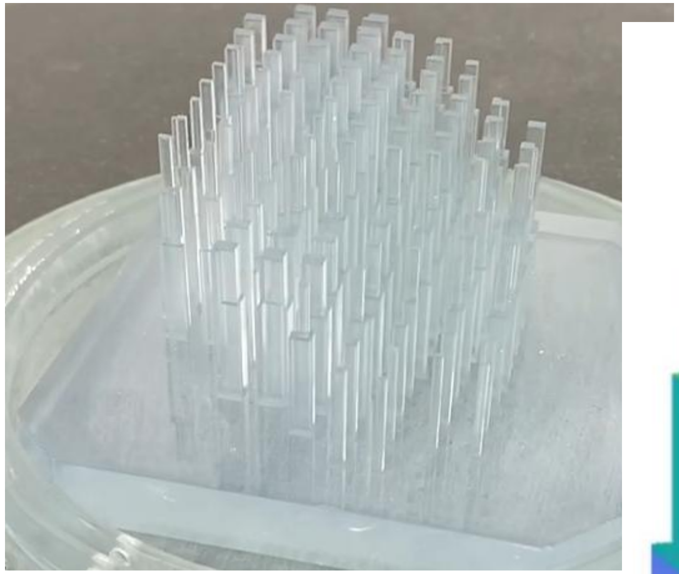
Verhaegen, Wanders, Wolfs, Eekers (2021)
DOI: 10.1088/1361-6560/abe55a

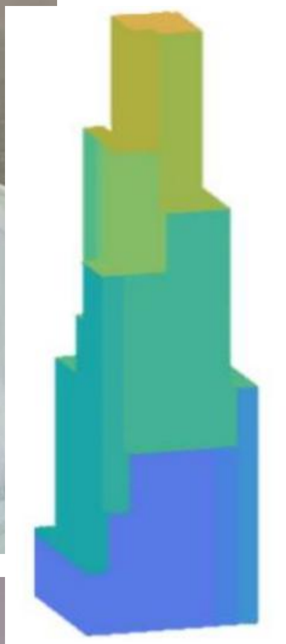
- Treating with highest energy protons (<250 MeV) avoids two issues:
  - Energy layer switching time.
  - Beam current reduction from degraders (Varian 600x reduction 250→70 MeV).
- Improves lateral penumbra.
- Similar to photon planning.
- But…
  - Relies on FLASH to minimise impact of dose to healthy tissue.
  - No longer conformal.

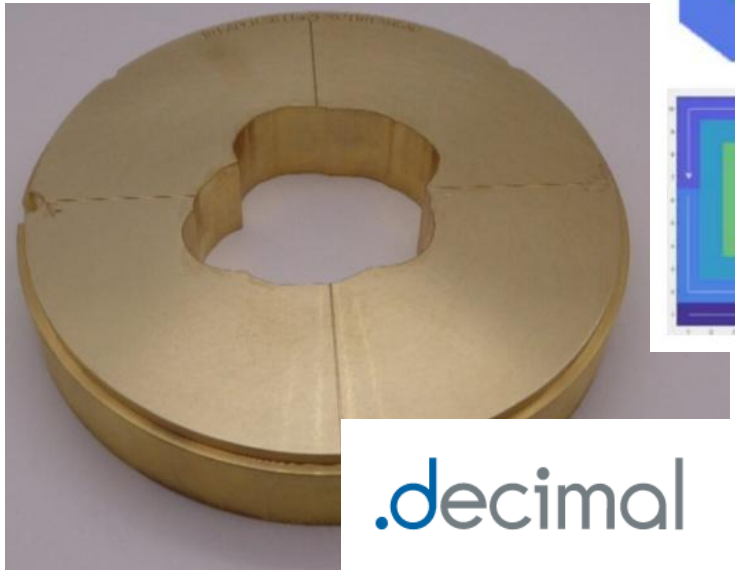
Bragg Peak FLASH (IBA)

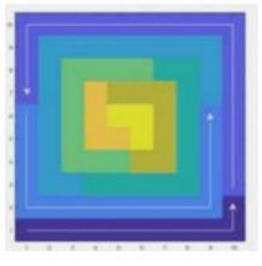
Courtesy of Nicolas Gerard, IBA









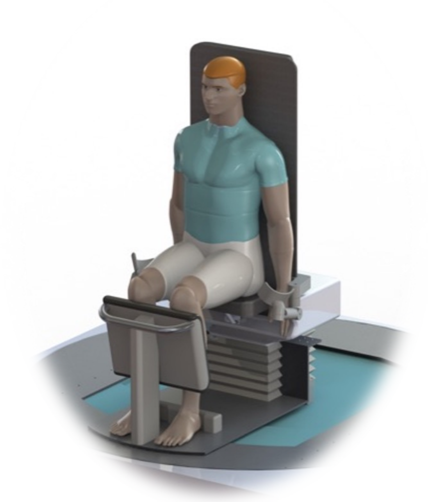


Pin ridge “hedgehog” patient specific filter enables conformal dose without modulating energy at the accelerator.

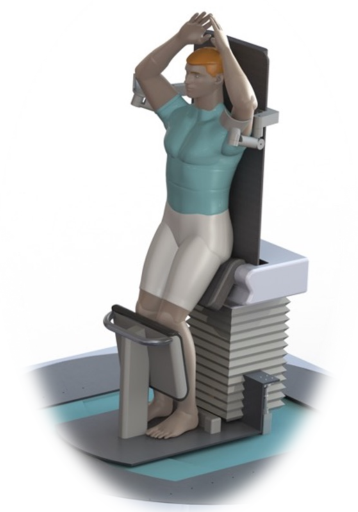
Upright Radiotherapy (Leo)

510K CLEARED IN SEPT 2024

UPRIGHT PATIENT POSITIONER



Seated Position

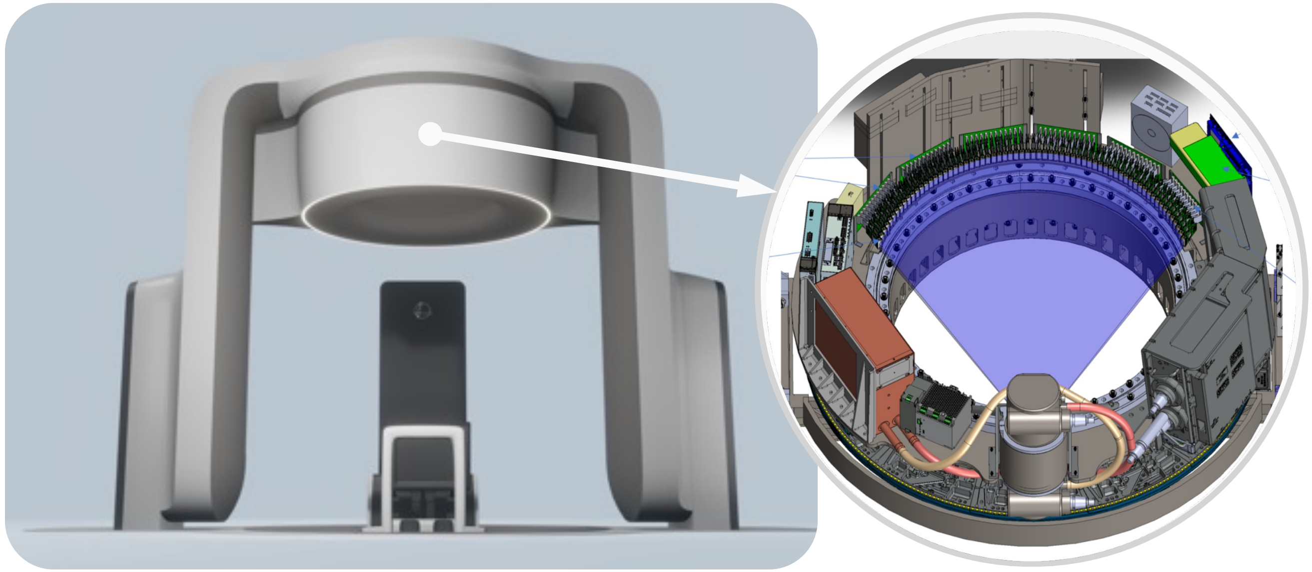


Perched Position

Courtesy of Niek Schreuder, Leo Cancer Care

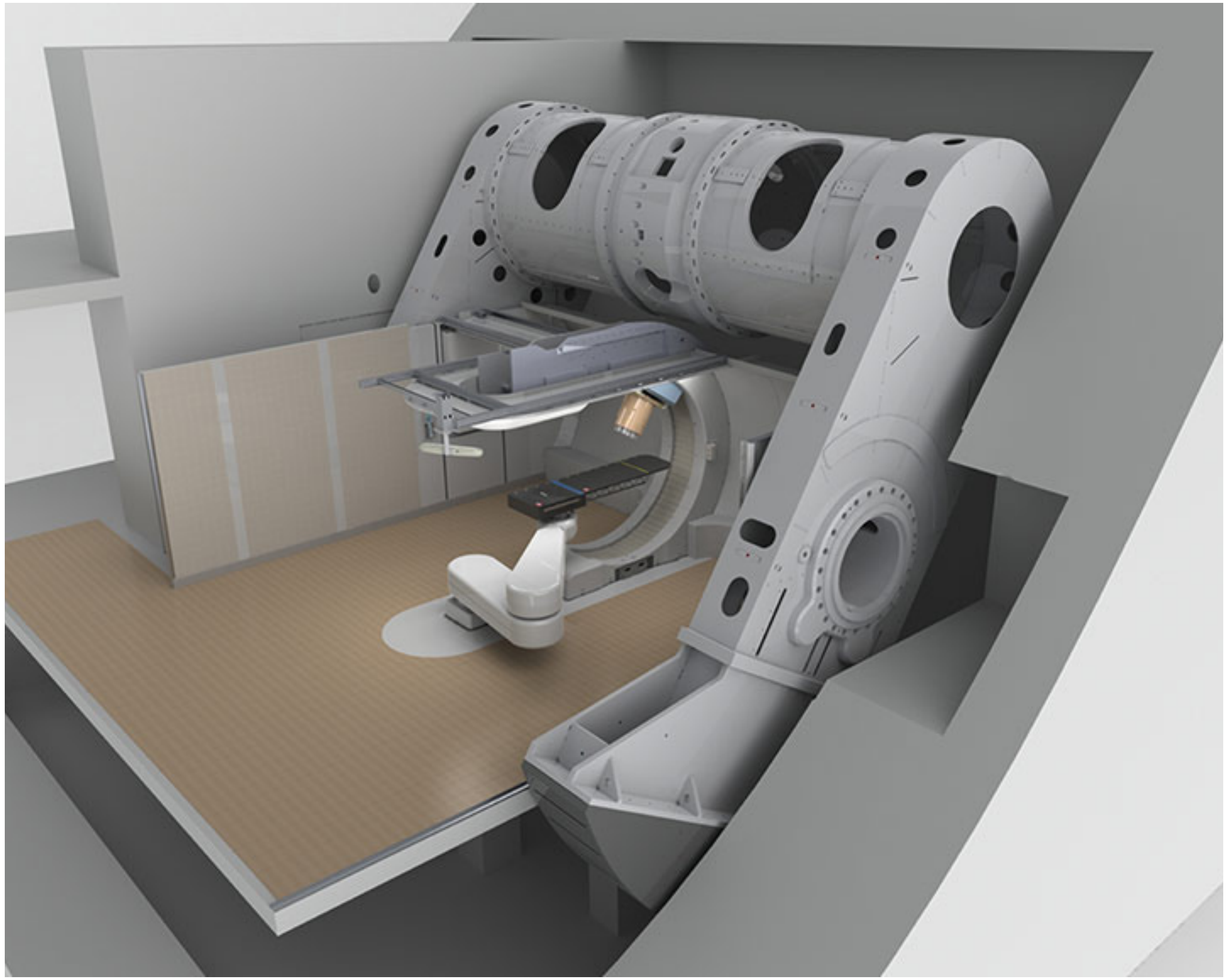
510K CLEARED IN JULY 2025

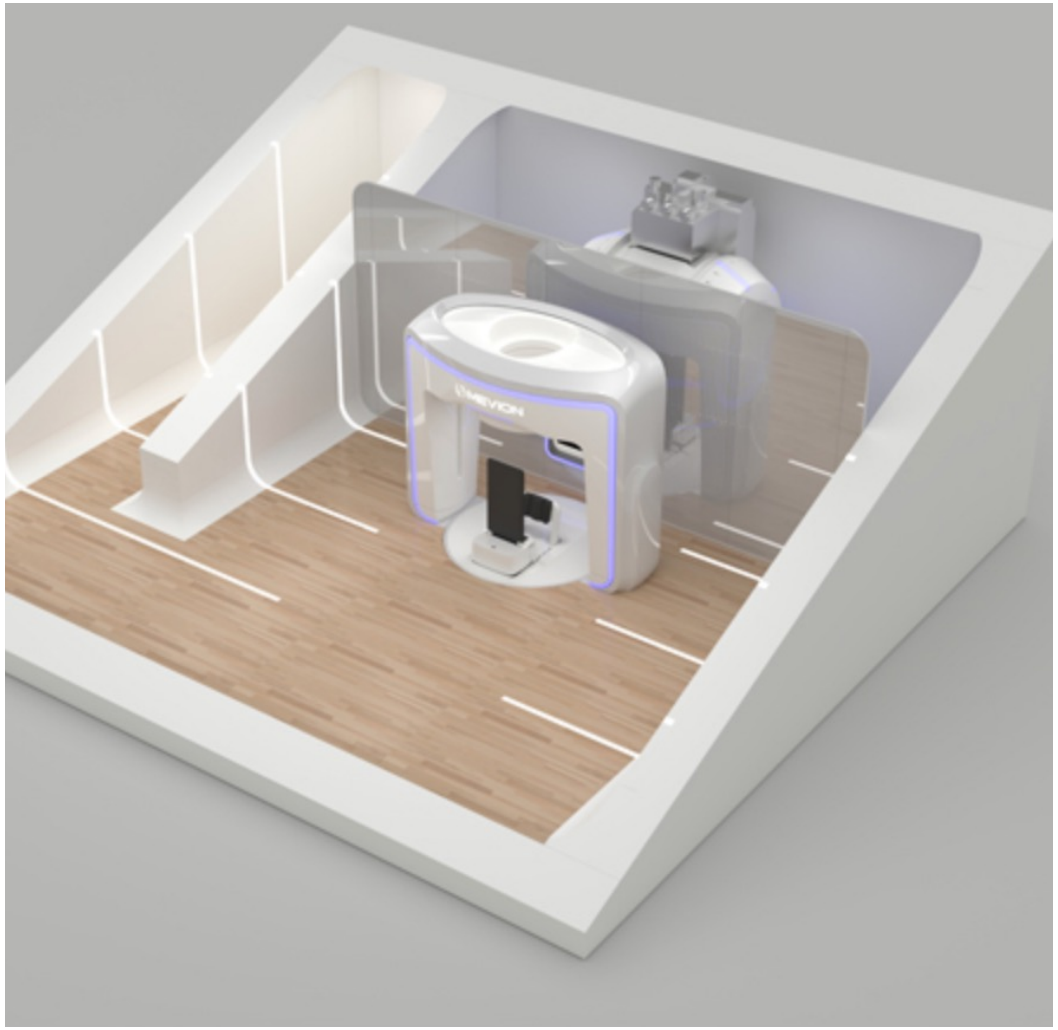
UPRIGHT AXIAL CT SCANNER



This system can be placed in front of any external radiation therapy beam. **Standardizing** radiation therapy among Ext Beam RT modalities.

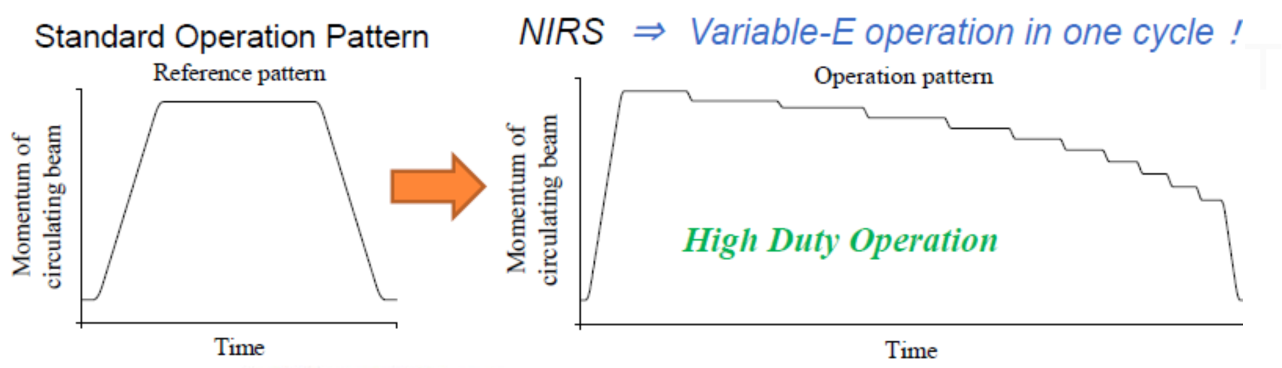
Compact Proton Therapy (Mevion S250-FIT)

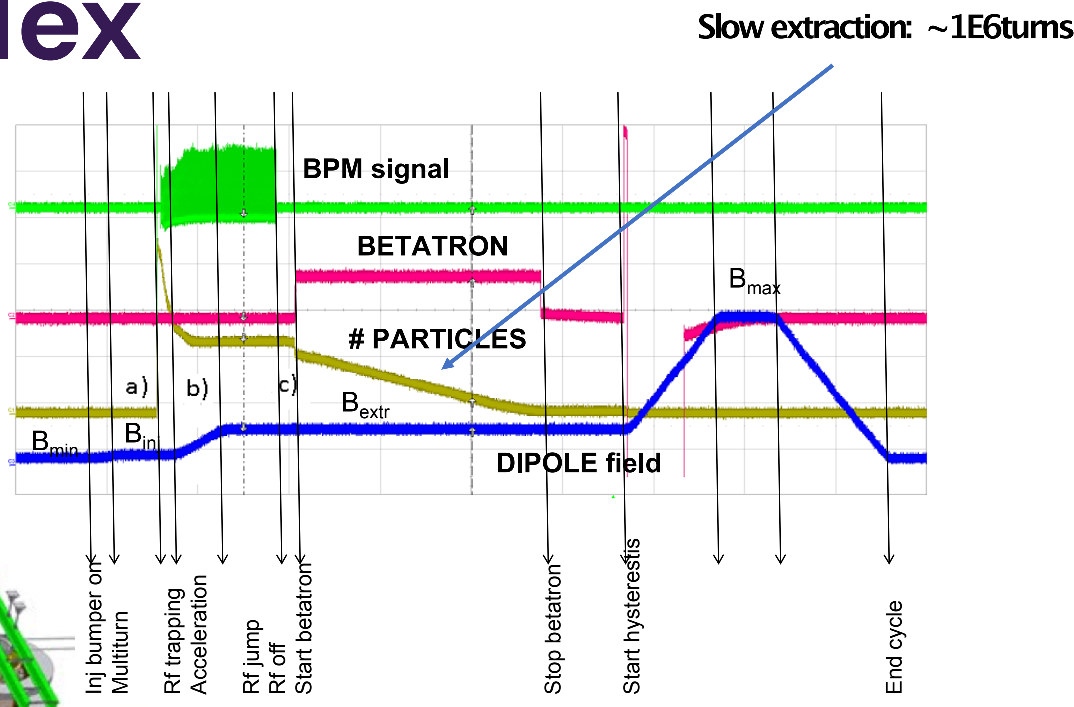




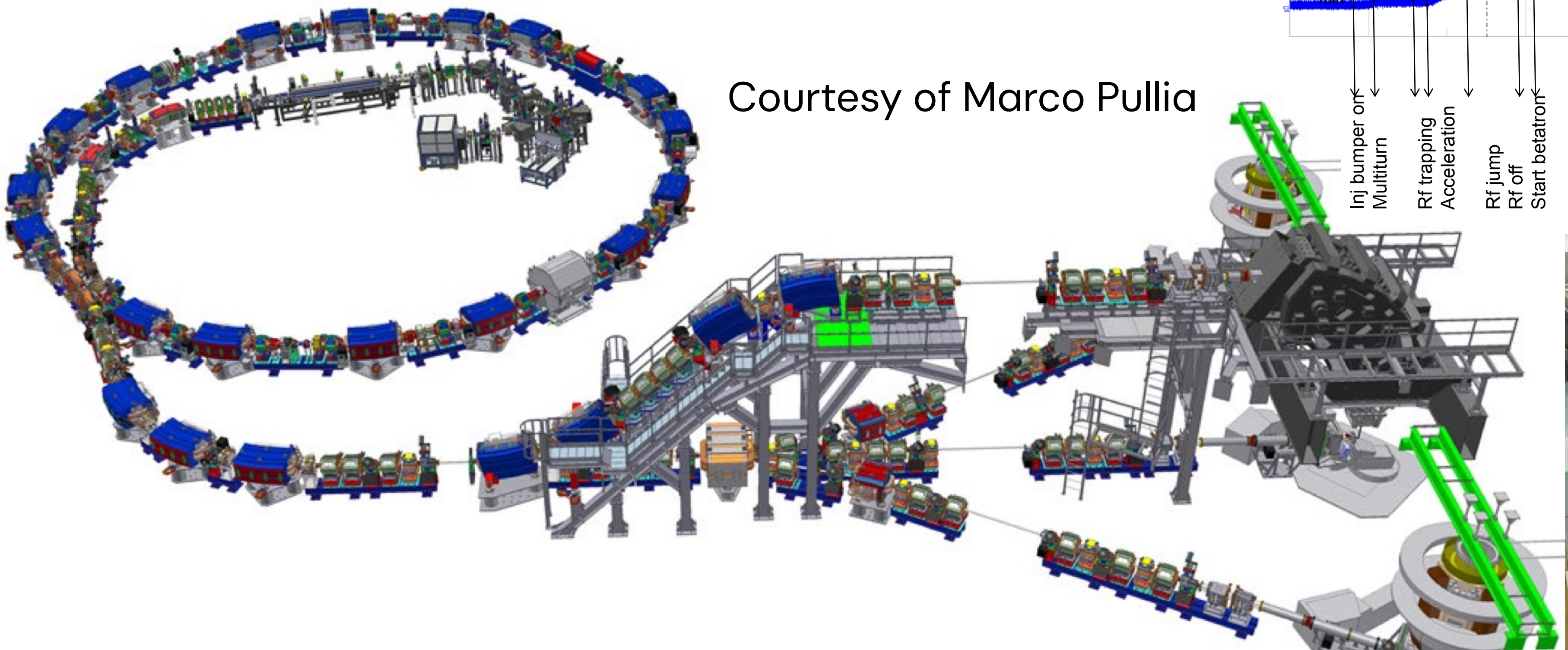
Courtesy of Niek Schreuder, Leo Cancer Care

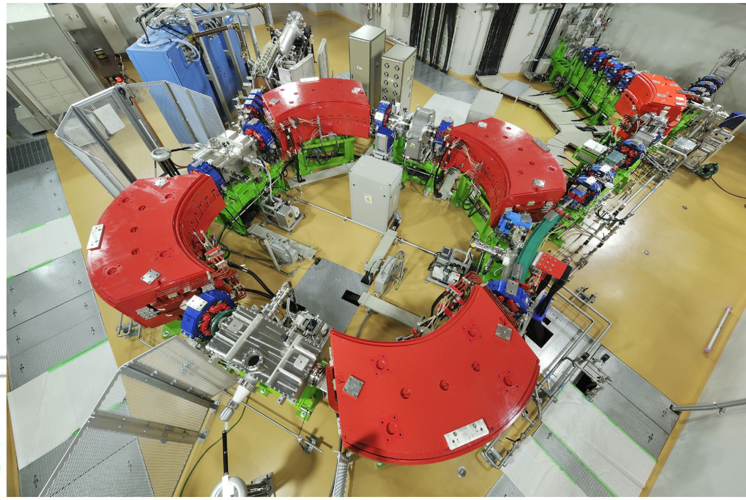
CNAO Accelerator Complex





Courtesy of Marco Pullia

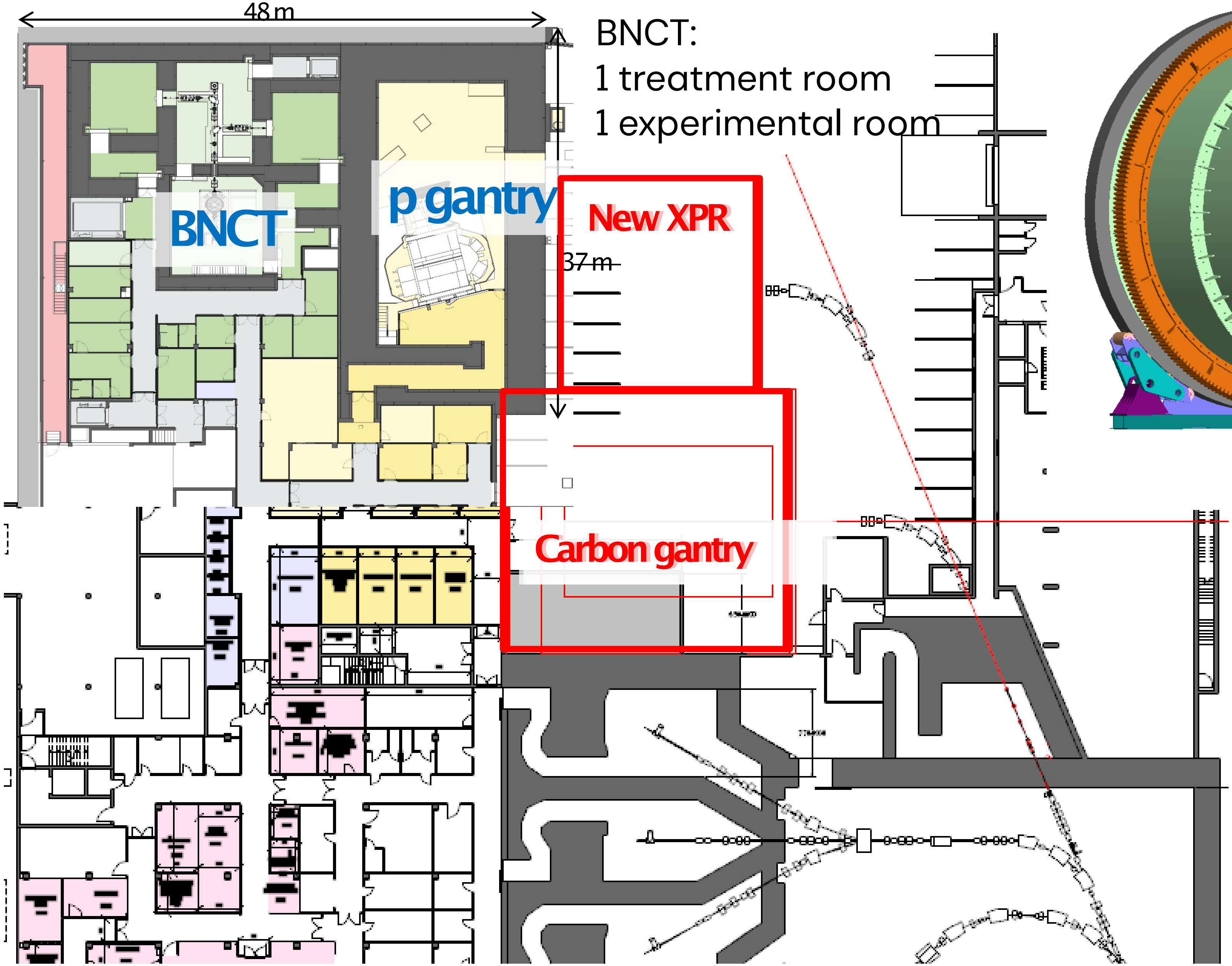


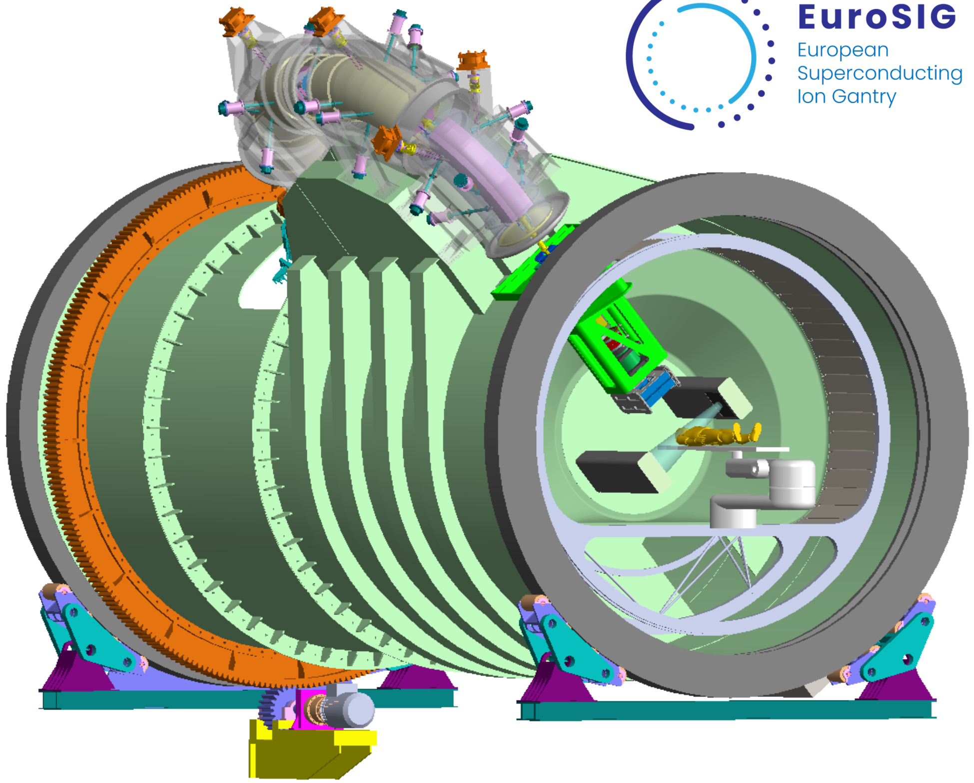


Energy range (MeV/u): 60–227 (250) (p) (30-320mm)
115–400 (C) (30-270mm)

CNAO Facility Expansion

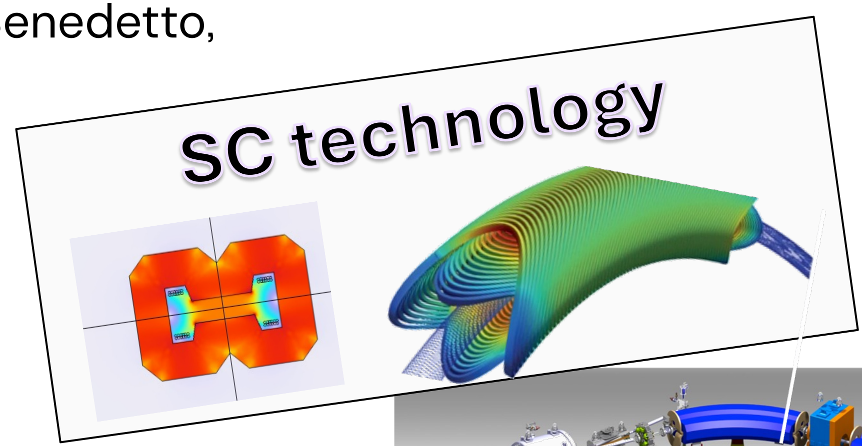
BNCT:
1 treatment room
1 experimental room

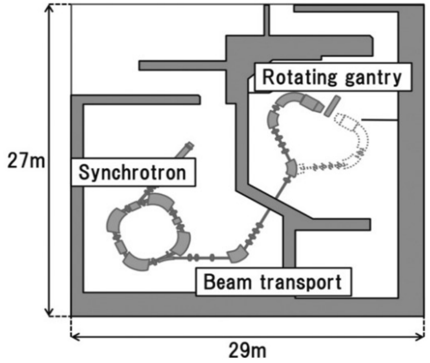




Compact medical synchrotrons

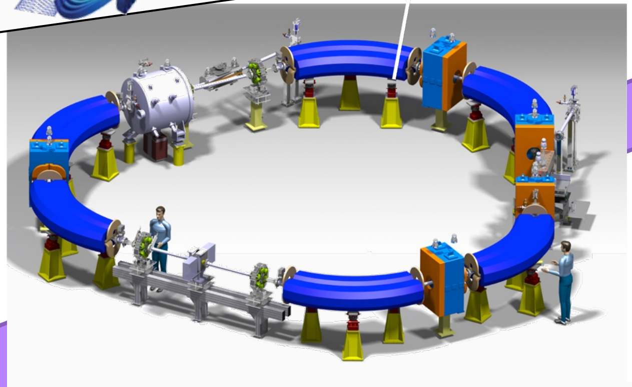
Courtesy of Elena Benedetto,
Heli Huttunen





HITACHI Synchrotron, ~6m

Protons @230
MeV
(Bρ = 2.42 Tm)



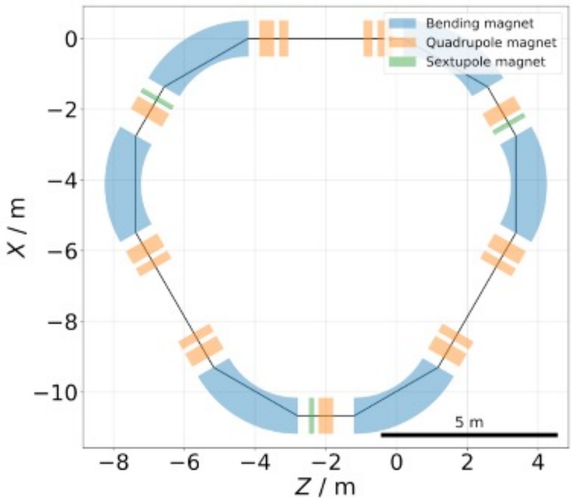
NIMMS He-ions design, ~11m

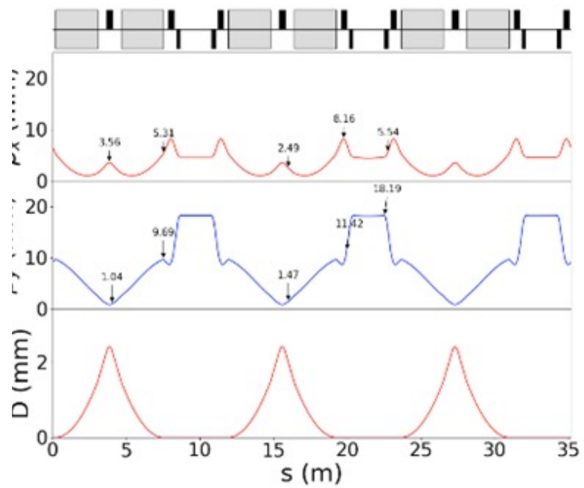
Helium @ 220 MeV/u
(Bρ = 4.5 Tm)

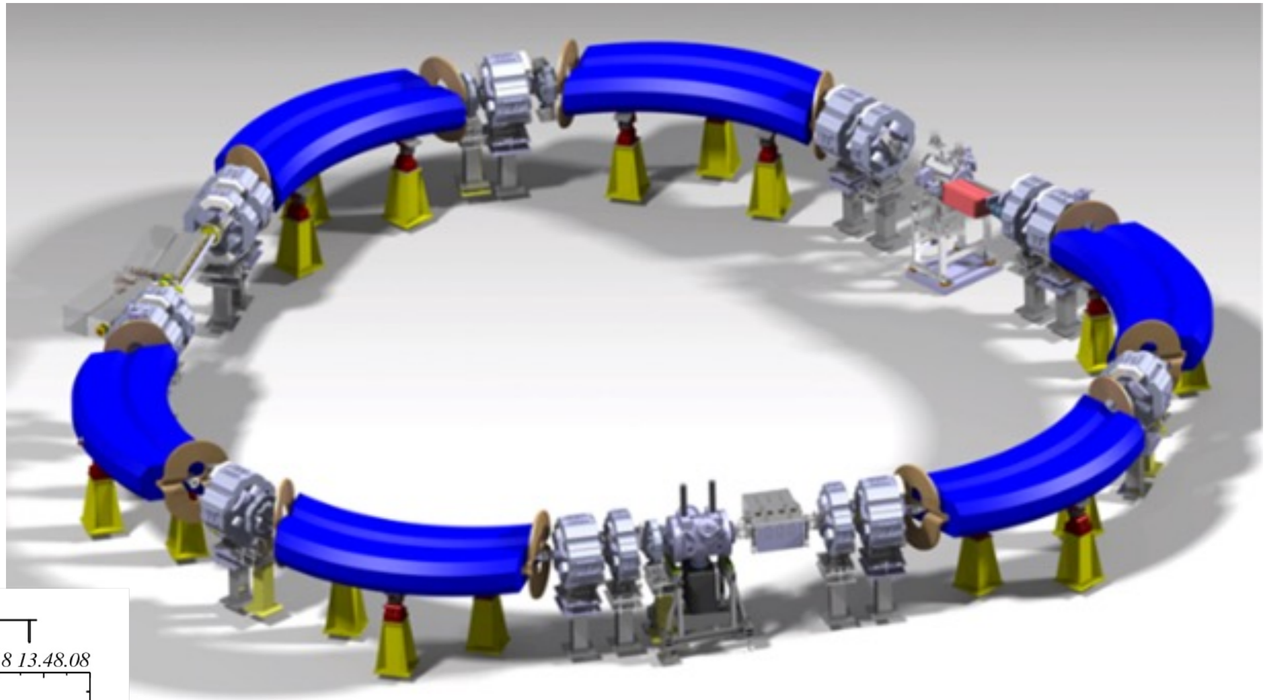
PIMMS (CNAO & MedAustron) ~25m
HIT (Heidelberg) ~ 20m diameter

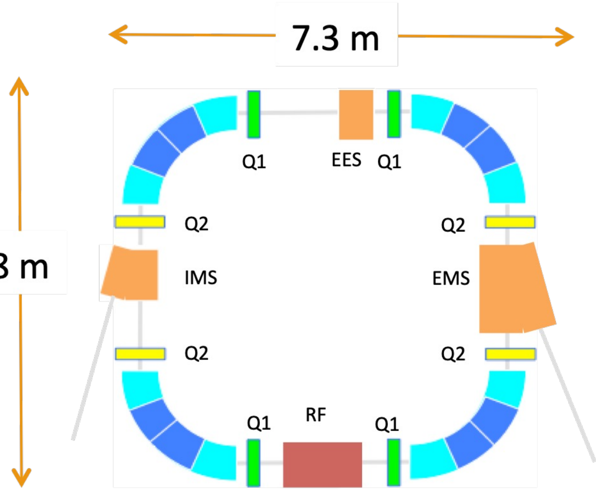
Carbon @430 MeV/u
(Bρ = 6.6 Tm)

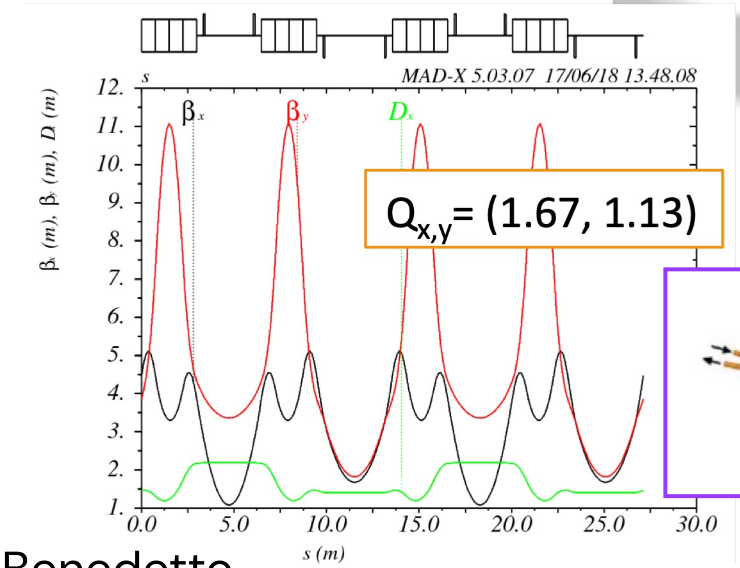
Helium & Light Ion Compact Synchrotron (HeLICS)

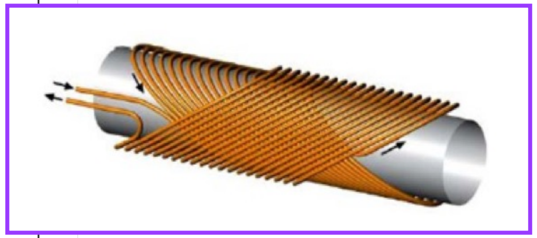


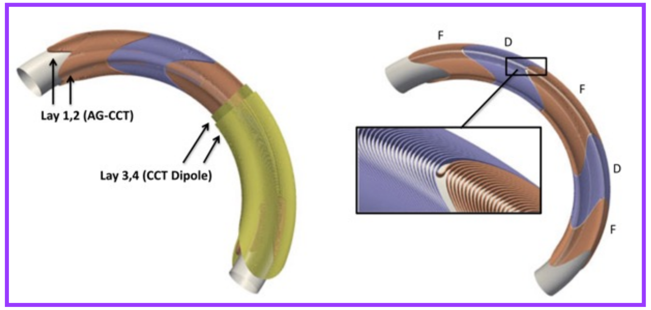






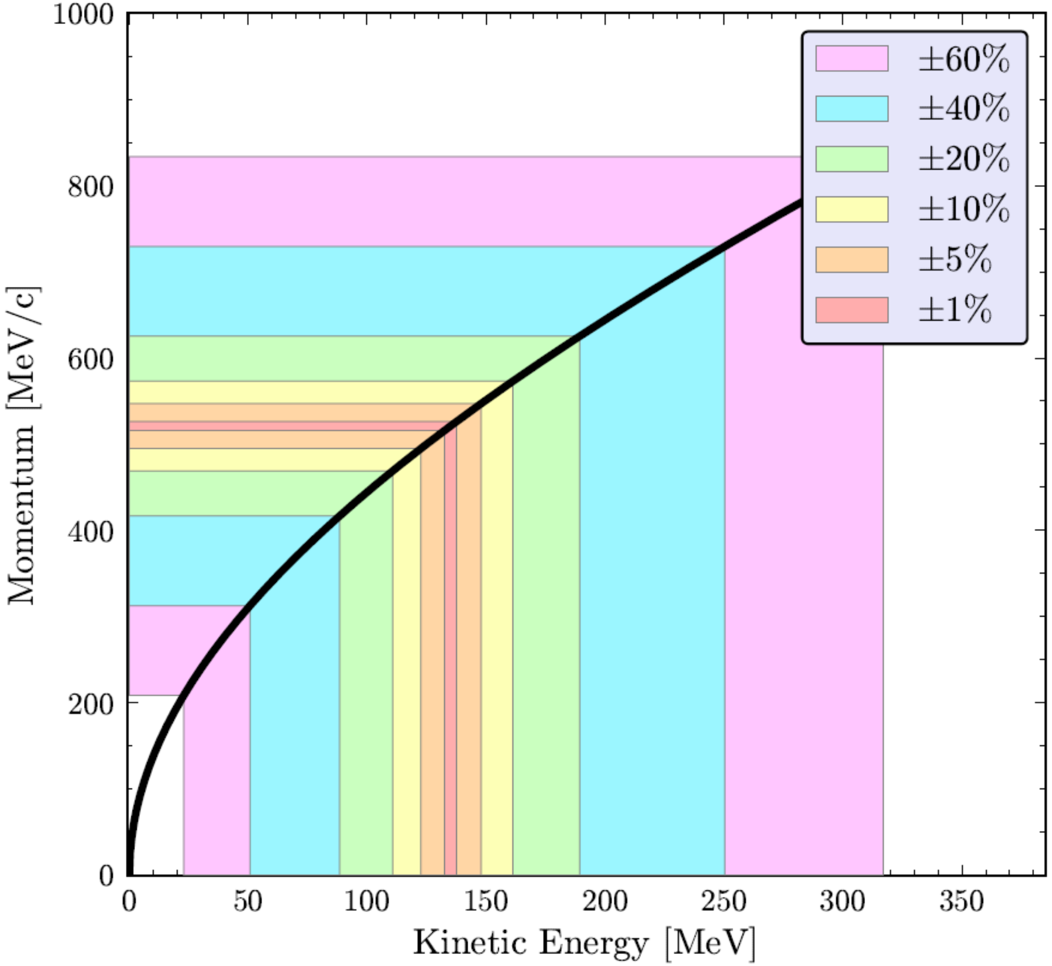




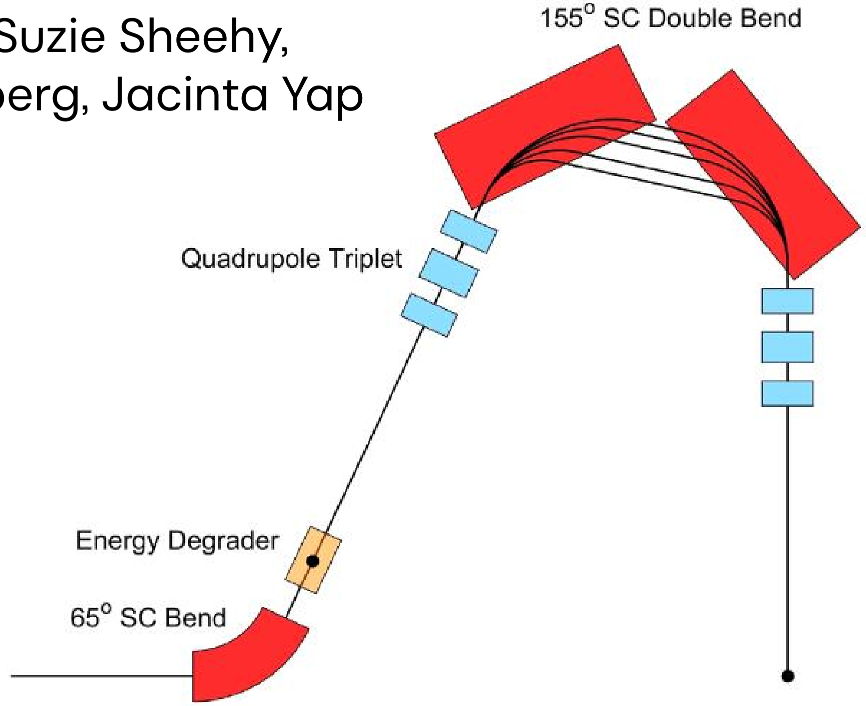


Courtesy of Elena Benedetto,
Heli Huttunen

Large Momentum Acceptance Beamlines

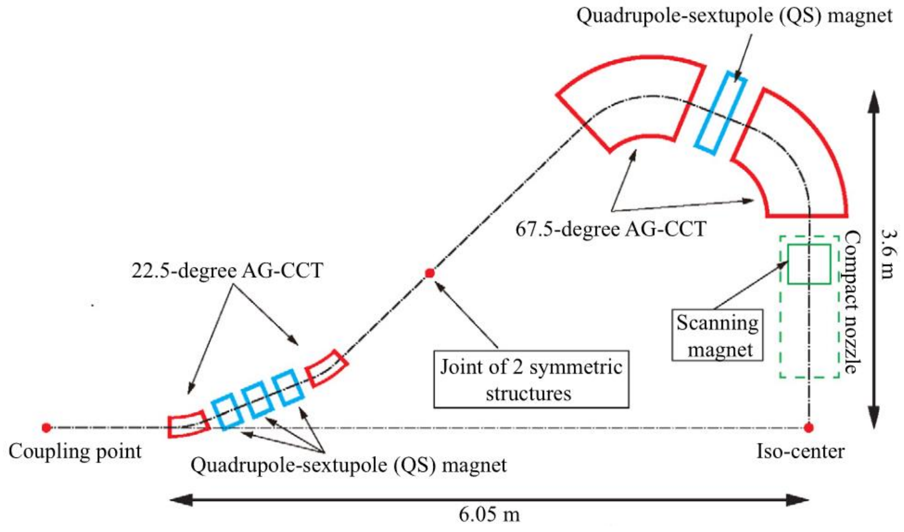


Courtesy of Suzie Sheehy, Adam Steinberg, Jacinta Yap



Achromatic bending with constant-field superconducting dipoles, with matching quadrupoles that vary with energy.

Static Field Gantries: FFAG/TURBO/GaToroid



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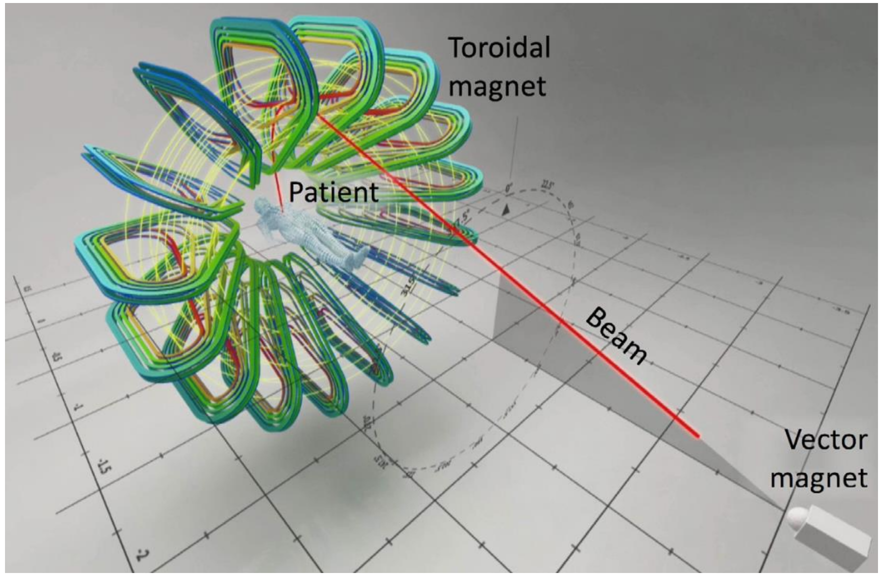

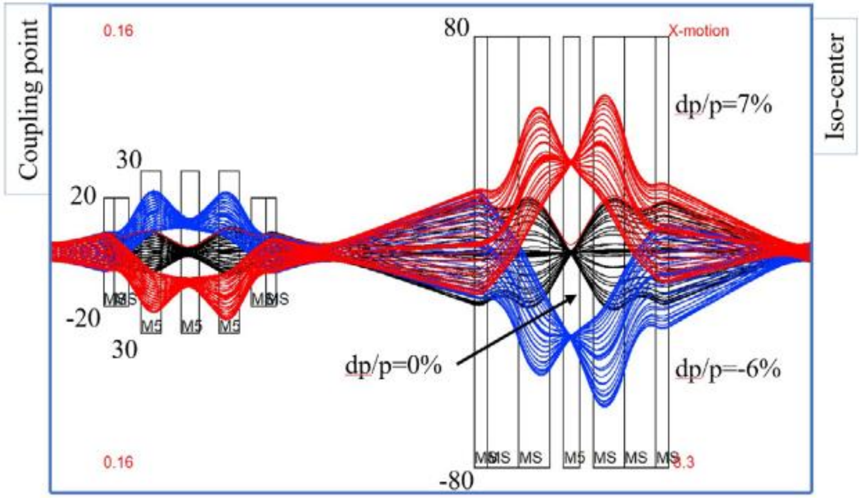

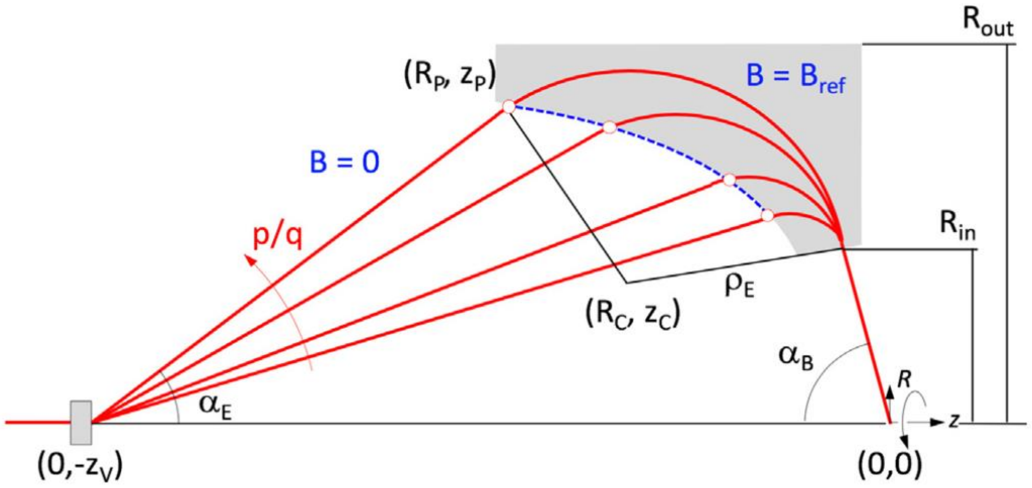

Conclusions

- Exciting time to be in particle therapy!
- FLASH not realised clinically, but developments in delivery speed valuable.
- SFRT continues to grow, with small but increasing clinical validation.
- Compact/upright facilities make ion therapy more feasible.
- Immuno-radiotherapy is the future! Radiation stimulates immune response to eradicate cancer: potentially systemic (abscopal).
- Dose conformality may not be the only metric…