



Radiation Therapy

And some new magnet developments

Eric Forton, I&D Director – System Engineering



Life.
Science.

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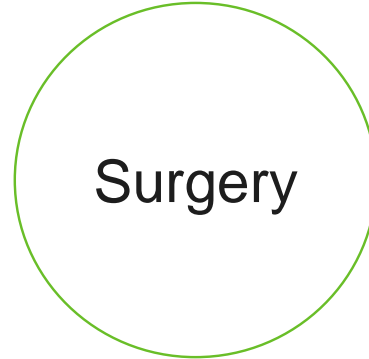
Introduction

Cancer treatments modalities



\$ 85 B*

Drugs
Kills cancer cells
Long and harsh
Lose hair and weight
Lots of new developments
Future: Immunotherapy



\$ 38 B*

Knife
Removes the tumor
Short and radical
Invasive
anesthesia
Future: Robot surgery



\$ 10 B*

Beam
Destroys the tumor
Non disruptive
Non-Invasive
Lots of new developments
Future: Proton Therapy

+ Brachytherapy
+ Theranostics

*US spendings per year in cancer care

Radiation Therapy

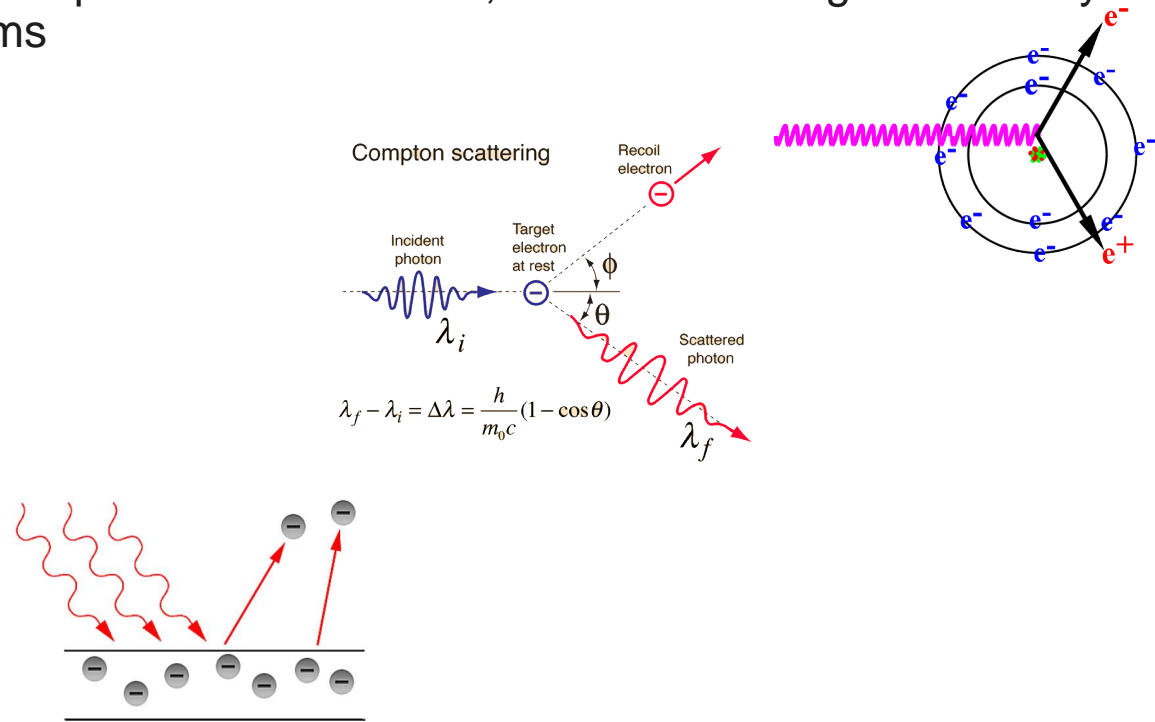
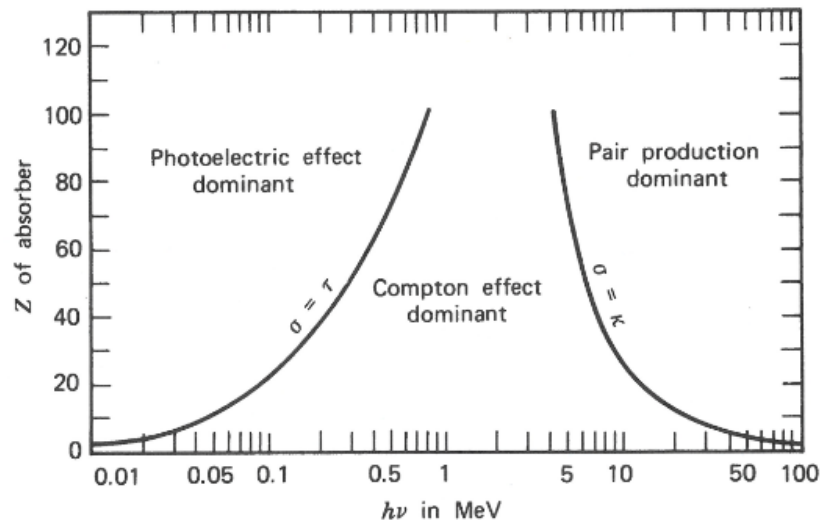
- **Three-dimensional conformal radiotherapy, 3D CRT**
- 3D CRT is a photon-based treatment that uses 3D medical images to precisely define the tumour target. The radiation dose is then shaped to match the shape of the tumour by delivering X-ray beams from many directions.
- **Intensity-modulated radiotherapy, IMRT**
- IMRT is a type of conformal radiotherapy in which not only the shape, but also the intensity profile, of each treatment beam is varied to precisely target the tumour.
- **Volumetric modulated arc therapy, VMAT**
- With VMAT, the linear accelerator that delivers the radiation beam rotates around the patient during treatment. The shape and intensity of the X-ray beam are continuously controlled as it moves around the body.
- **Stereotactic body radiotherapy, SBRT**
- Stereotactic radiotherapy uses high radiation doses to treat tumours in the brain and central nervous system in one or just a few treatments. SBRT is similar but refers to treatment of tumours elsewhere in the body.
- **Intensity-modulated proton therapy, IMPT**
- IMPT is a proton therapy technique in which scanned proton pencil beams of variable energy and intensity are used to precisely paint the radiation dose onto a tumour.
- **Proton arc therapy, PAT**
- With PAT, the proton beams are delivered continuously as the gantry rotates around the patient. During this rotation, the beam energy and intensity are adjusted to match the dose to the target volume

<https://physicsworld.com/a/proton-arc-therapy-do-we-need-it-can-we-deliver-it/>



« Conventional » radiation therapy vs. hadrontherapy

- Most conventional radiation therapy and arc therapy systems use xrays for cancer treatment
 - Dose is not delivered to tissues by the photons themselves, but rather through secondary electrons produced by 3 mechanisms



G.F. Knoll – Radiation detection and measurement, Wiley

« Conventional » radiation therapy vs. hadrontherapy

■ Results in:

- Some electron buildup
- A decrease in photon intensity following a superimposition of decreasing exponentials

=> dose builds-up and then ~exponentially decreases with depth once electron equilibrium is reached

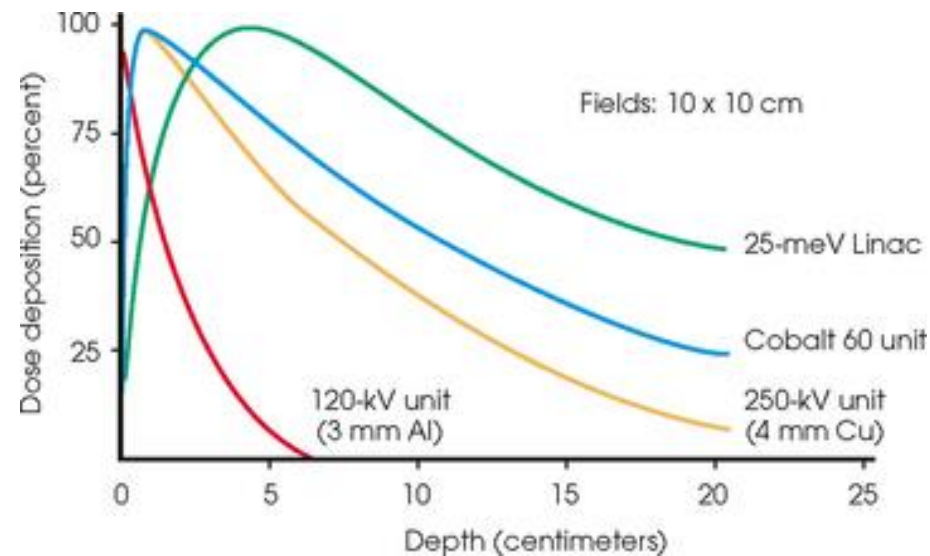


Image: <http://radiologykey.com/radiation-oncology/>



« Conventional » radiation therapy vs. hadrontherapy

- Instead, hadrons lose their energy in matter according to Bethe-Bloch formula:

$$-\frac{dE}{dx} = 2\pi N_A r_e^2 m_e c^2 \rho \frac{Z}{A} \frac{z^2}{\beta^2} \left[\ln \left(\frac{2m_e \gamma^2 v^2 W_{max}}{I^2} \right) - 2\beta^2 - \delta^2 - 2\frac{C}{Z} \right]$$

Shell correction
Density correction

Where

$$W_{max} = \frac{2m_e c^2 \beta^2 \gamma^2}{1 + 2\frac{m_e}{M} \sqrt{1 + \left(\frac{m_e}{M}\right)^2 + \beta^2 \gamma^2}} \approx 2m_e c^2 \beta^2 \gamma^2 \text{ is head-on collision energy transfer}$$

And $I(eV) = Z \left(12 + \frac{7}{Z} \right)$ for $Z < 13$

$I(eV) = Z(9.76 + 58.8Z^{-1.19})$ for $Z \geq 13$ is the average ionization potential of the absorber

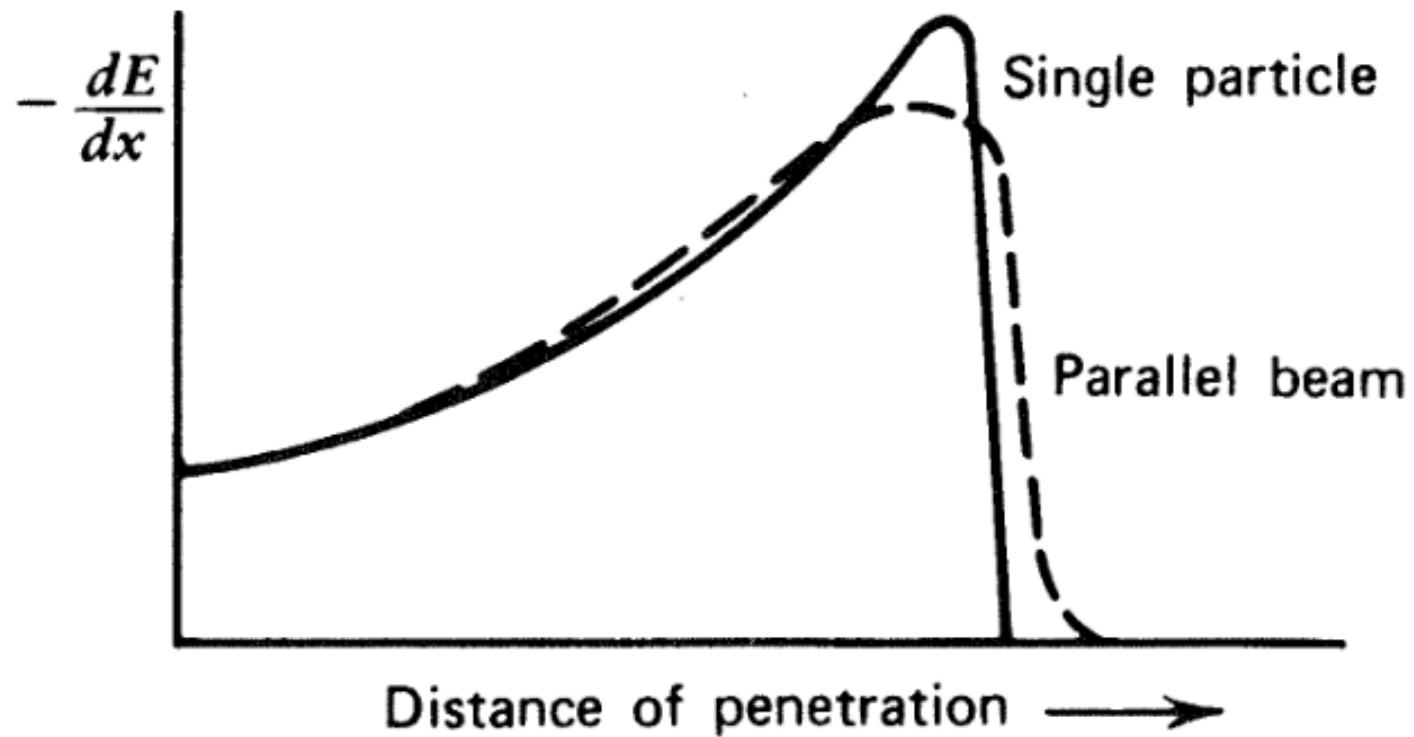
And

$$\begin{aligned} Z &\rightarrow Z_{eff} = \sum a_i Z_i \\ A &\rightarrow A_{eff} = \sum a_i A_i \\ \ln(I) &\rightarrow \ln(I_{eff}) = \sum \frac{a_i Z_i \ln(I_i)}{Z_{eff}} \\ \delta &\rightarrow \delta_{eff} = \sum \frac{a_i Z_i \delta_i}{Z_{eff}} \\ C &\rightarrow C_{eff} = \sum a_i C_i \end{aligned}$$

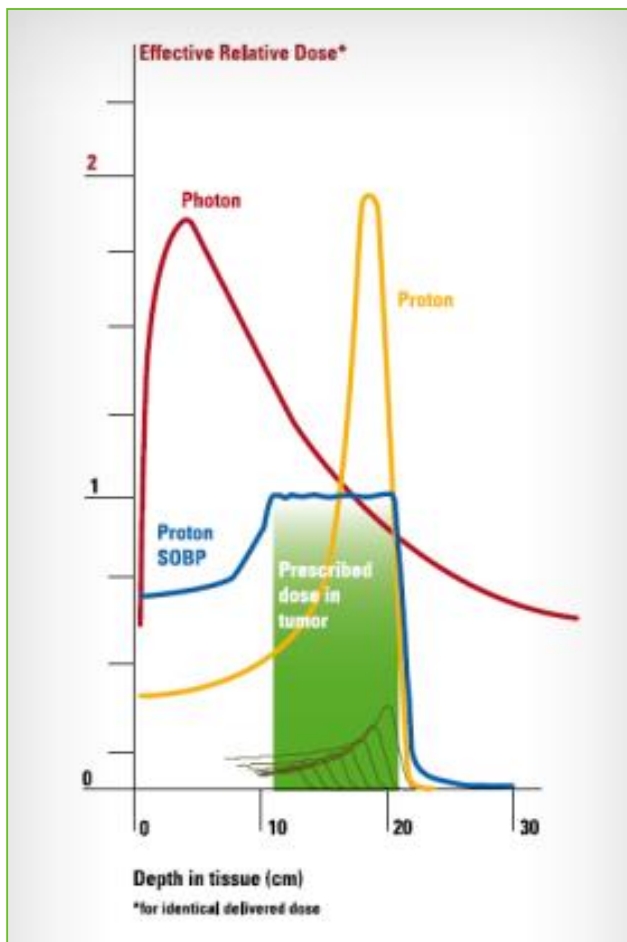
} Compound materials

« Conventional » radiation therapy vs. hadrontherapy

- Resulting in the famous « bragg peak » dose distribution

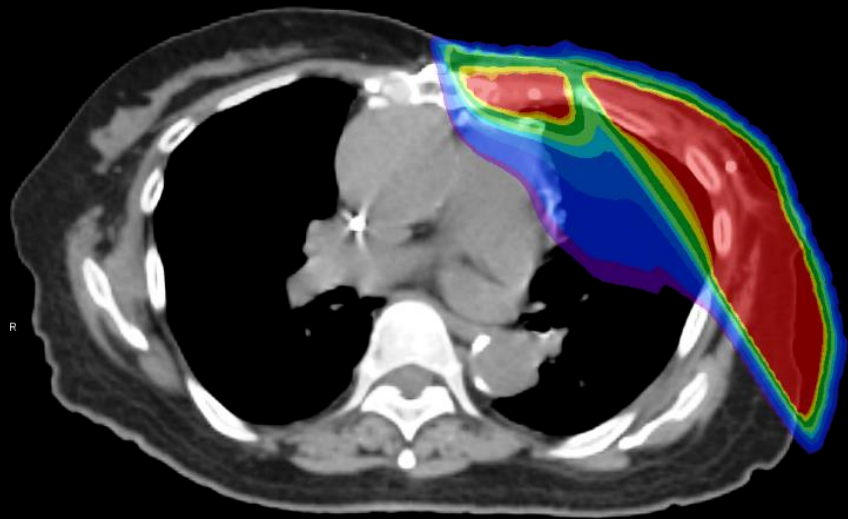


Dose and conformality

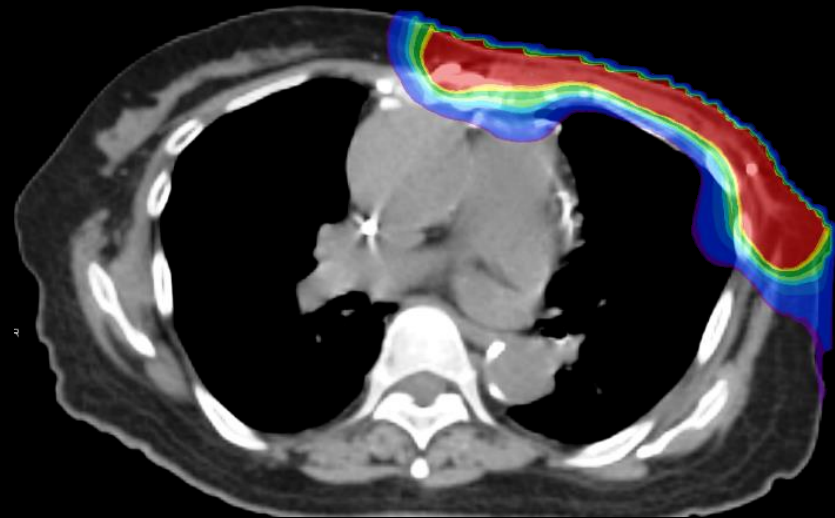


- Hadrons offer the following advantages:
 - Little radiation upfront the tumor
 - No/little radiation at all beyond the tumor
=> Lower integral dose per treatment
- Leading to potential clinical advantages:
 - Up to 50% reduced risk of radiation-induced secondary cancer
 - Drastically lower risk of adverse effects (treatment toxicity, side effects, growth abnormality) – better quality of life

Benefits in practice: **left breast cancer patients**



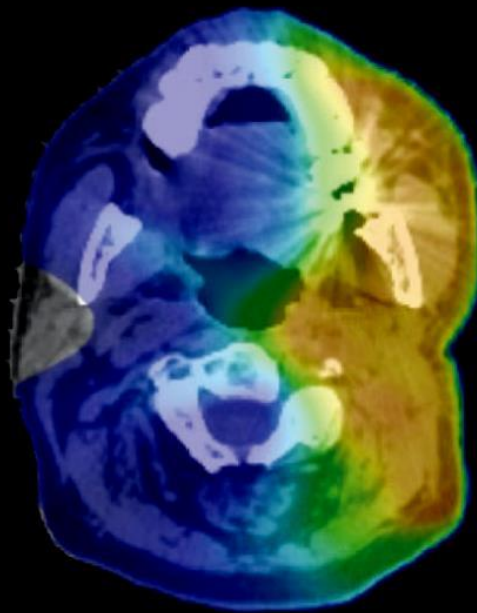
Photons



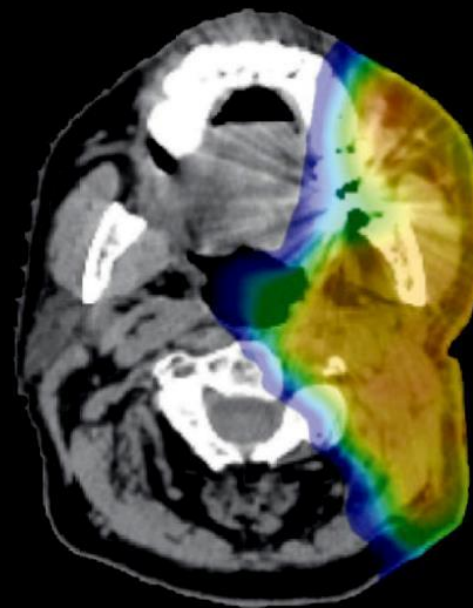
Protons

Courtesy of Seattle Cancer Care Alliance Proton Therapy Center – Locally Advanced Stage III Breast Cancer

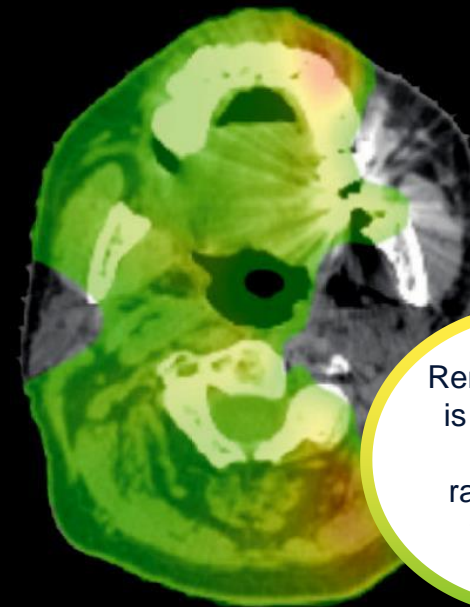
Benefits in practice: head and neck patient



Photons



Protons



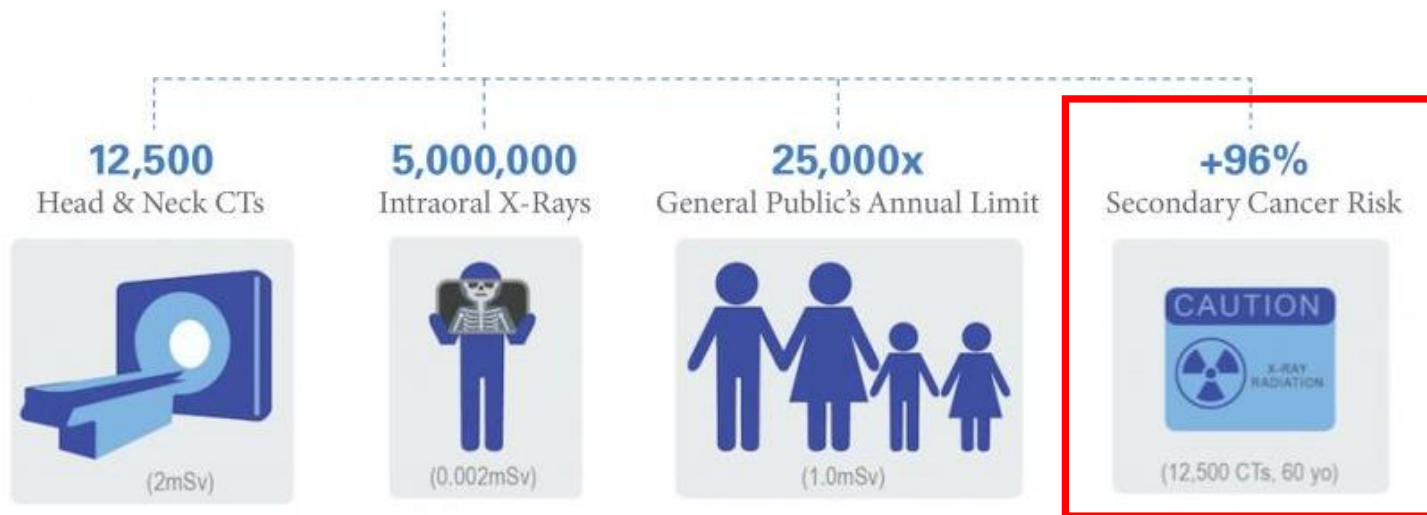
Photons excess
Up to 25 Gy

Reminder: a Gray
is a measure of
absorbed
radiation dose.
 $1\text{Gy} = 1\text{J/kg}$



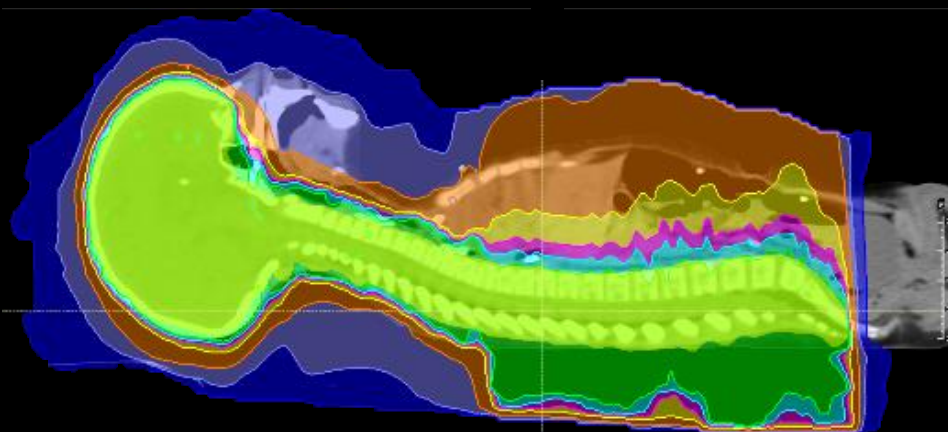
What unnecessary radiation means for the patient

25 Gy

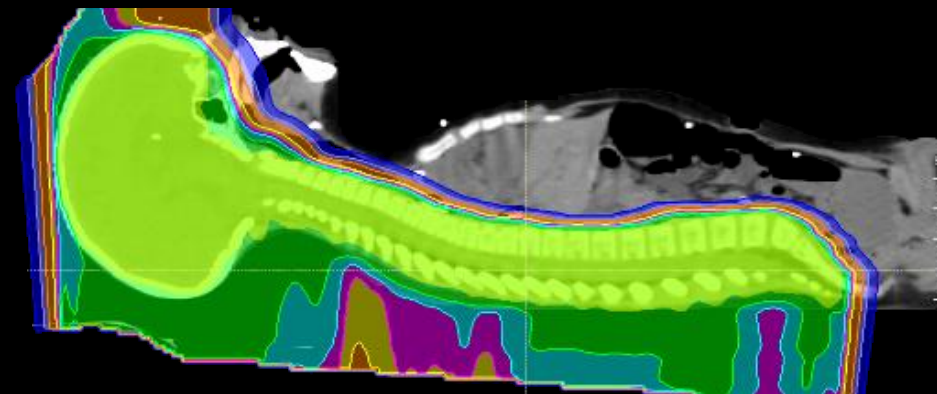


Courtesy of Dr Steven Frank, MD Anderson Cancer Center

Benefits in practice: **pediatric patient**



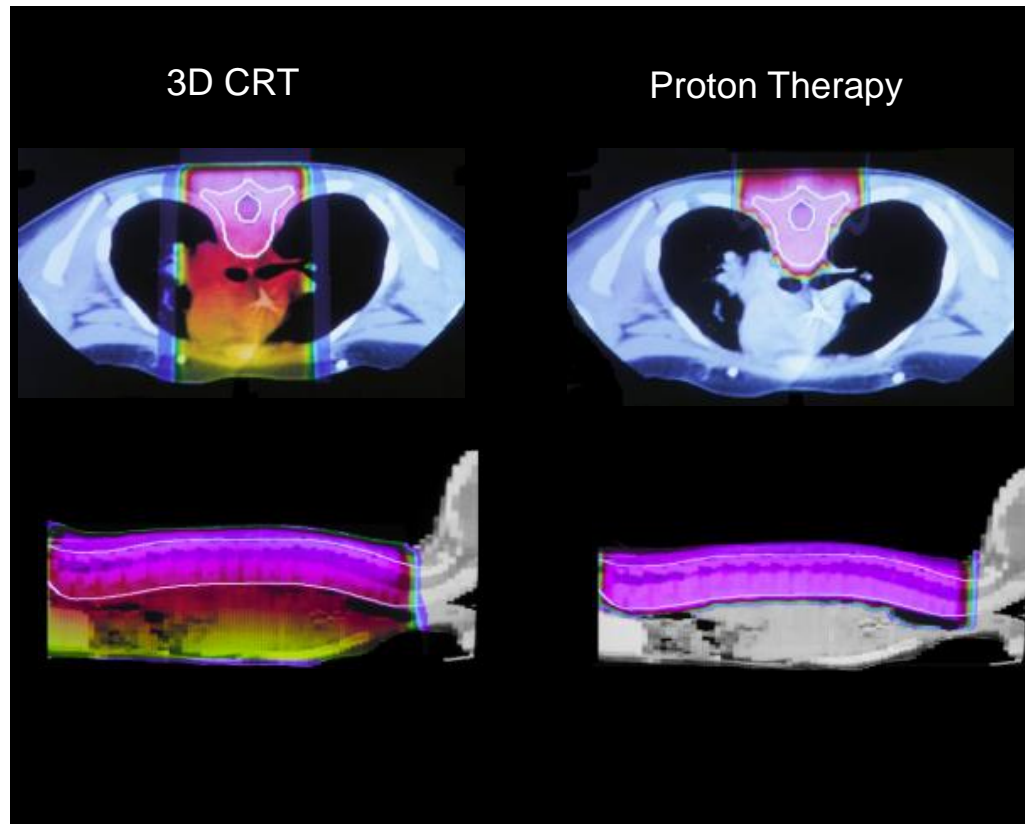
Photons



Protons

Courtesy of Seattle Cancer Care Alliance Proton Therapy Center - Medulloblastoma

Pediatric medduloblastoma – Side effects



Side Effects	Protons	Photons
Restrictive Lung Disease	0%	60%
Reduced exercise capability	0%	75%
Abnormal EKGs	0%	31%
Growth abnormality	20%	100%
IQ drop of 10 points at 6 yrs	1.6%	28.5%
Risk of IQ score < 90	15%	25%

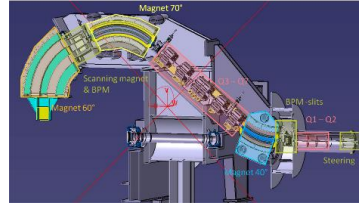


Proton equipment example: IBA ProteusONE (360 m²)

Compact super-conducting accelerator for producing the energetic proton beam

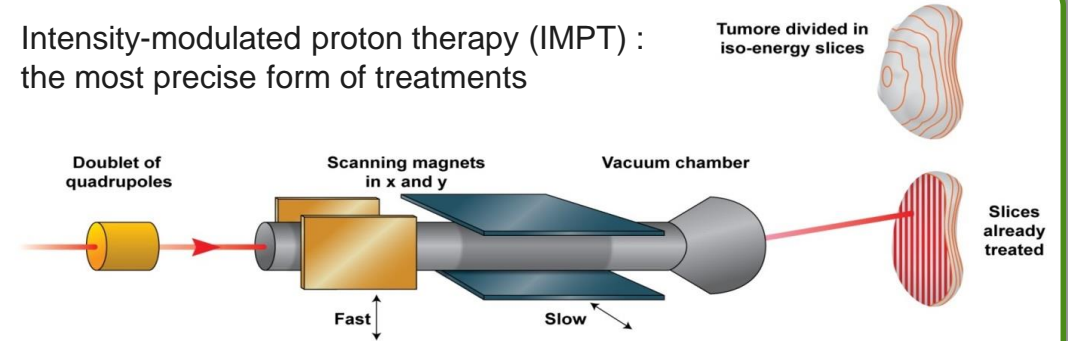


A rotating gantry to set the beam at the right angle



(3.6 m radius)

Intensity-modulated proton therapy (IMPT) :
the most precise form of treatments



Stereoscopic imaging and CBCT at isocentre:
accurate patient setup,
quality images for adaptive treatments



Efficient software integration,
enabling easy & flexible workflows

Proton Therapy is growing but remains a small fraction of RT

Centers treating from
2000 to 2020 per region*
Without carbon centres



2020: **39 (+18)**

2015: **21 (+11)**

2010: **10**

2005: **4**

2000: **3**

2020: **34 (+14)**

2015: **20 (+7)**

2010: **13**

2005: **11**

2000: **10**

2020: **25 (+10)**

2015: **15 (+8)**

2010: **7**

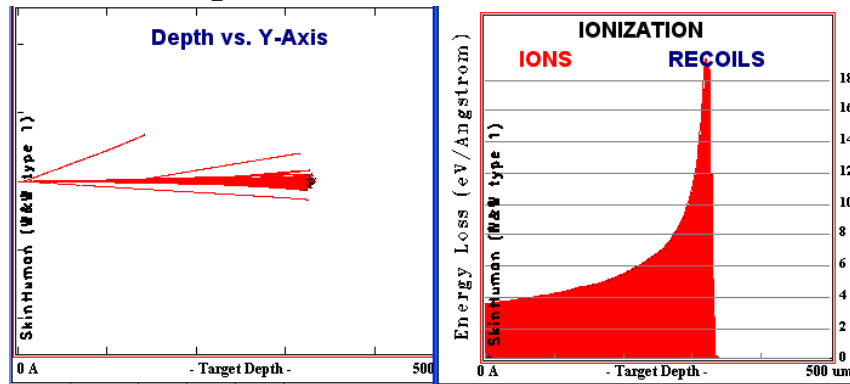
2005: **5**

2000: **1**

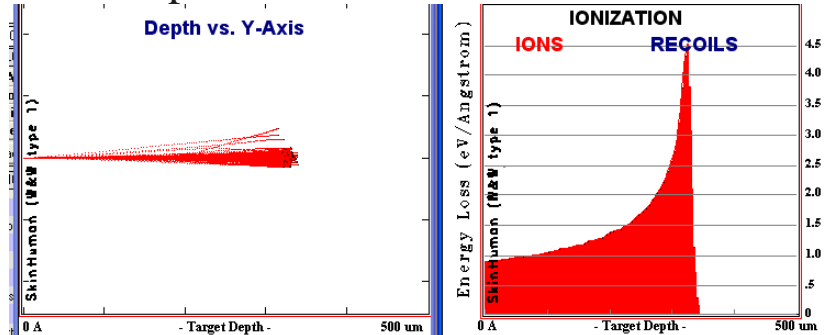
* PTCOG 2020 Data including centers with eye treatments only

Protons are good - How heavy should we go?

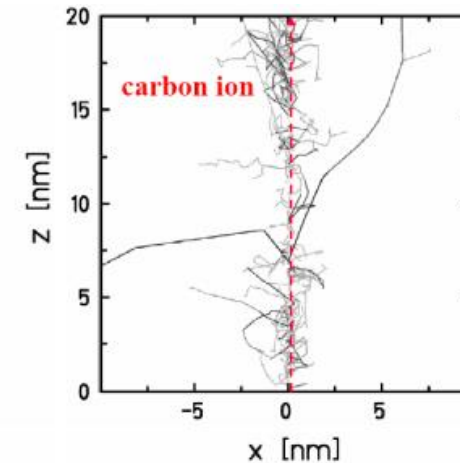
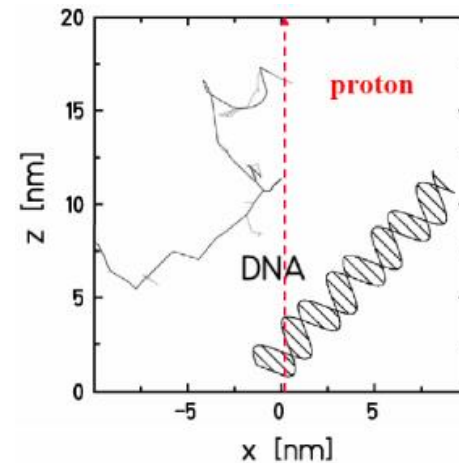
20 MeV alphas



5 MeV protons



- For the same range, heavier and/or more charged particles need higher entrance energy
 - Straggling is reduced => sharper knife
 - LET is higher => Biological effect is usually enhanced

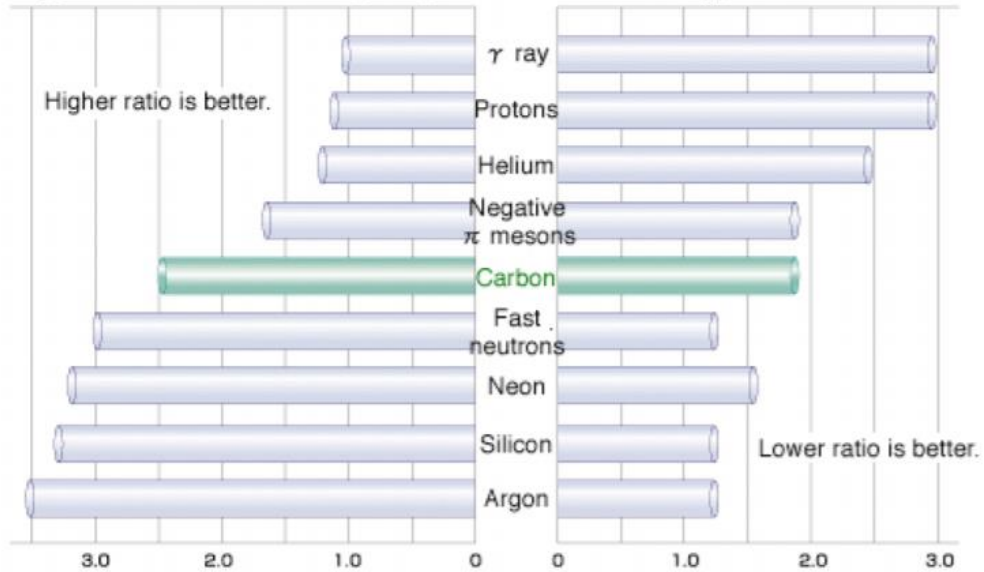


Ugo Amaldi and Gerhard Kraft - Radiotherapy with beams of carbon ions [Reports on Progress in Physics, Volume 68, Number 8](#)
Published 11 July 2005 • 2005 IOP Publishing Ltd

How heavy should we go?

RBE and OER

Relative biological effectiveness (RBE) and oxygen enhancement ratio (OER) of various radiation types

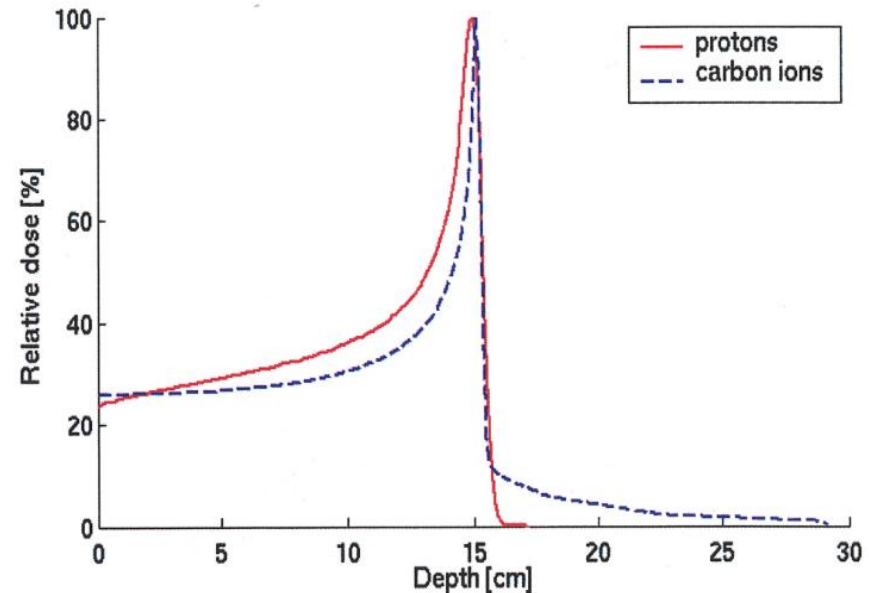


RBE represents the biological effectiveness of radiation in the living body. The larger the RBE, the greater the therapeutic effect on the cancer lesion.

OER represents the degree of sensitivity of hypoxic cancer cells to radiation. The smaller the OER, the more effective the therapy for intractable cancer cells with low oxygen concentration.

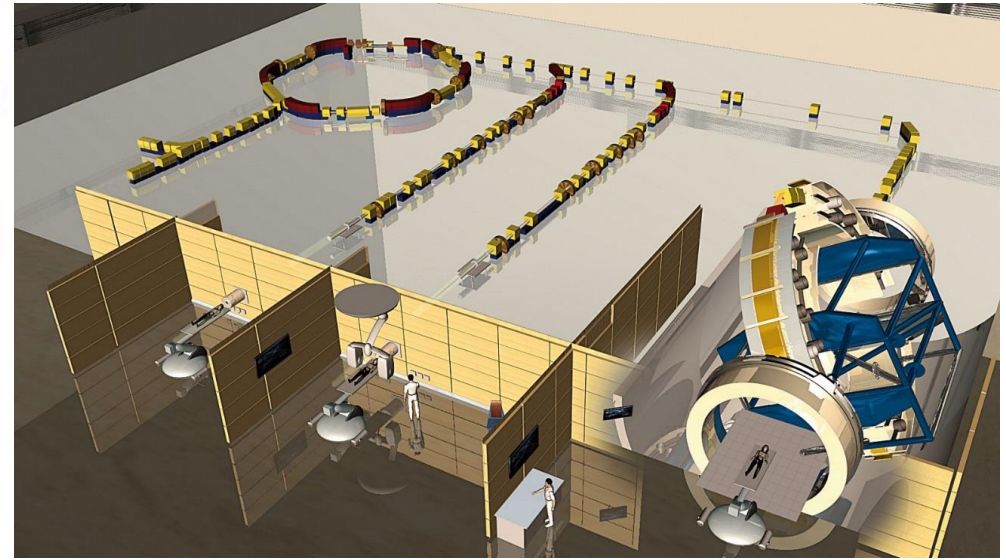
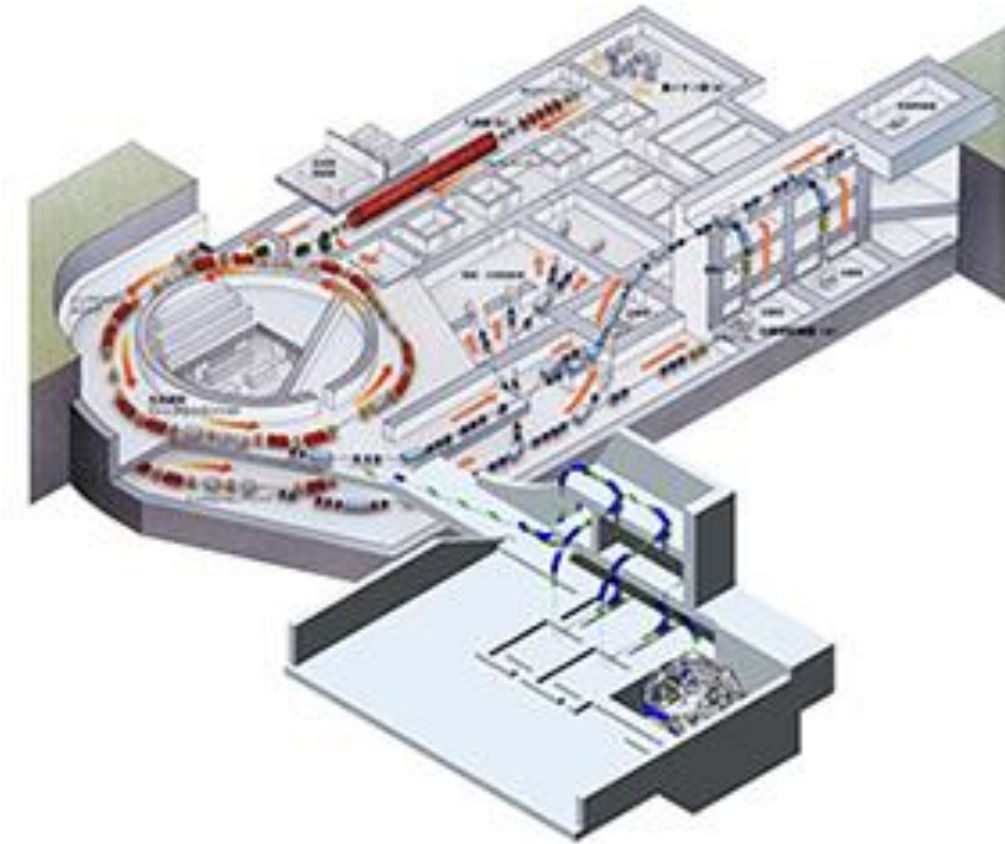
■ But

- You want to avoid killing upstream cells
- Fractionation problem

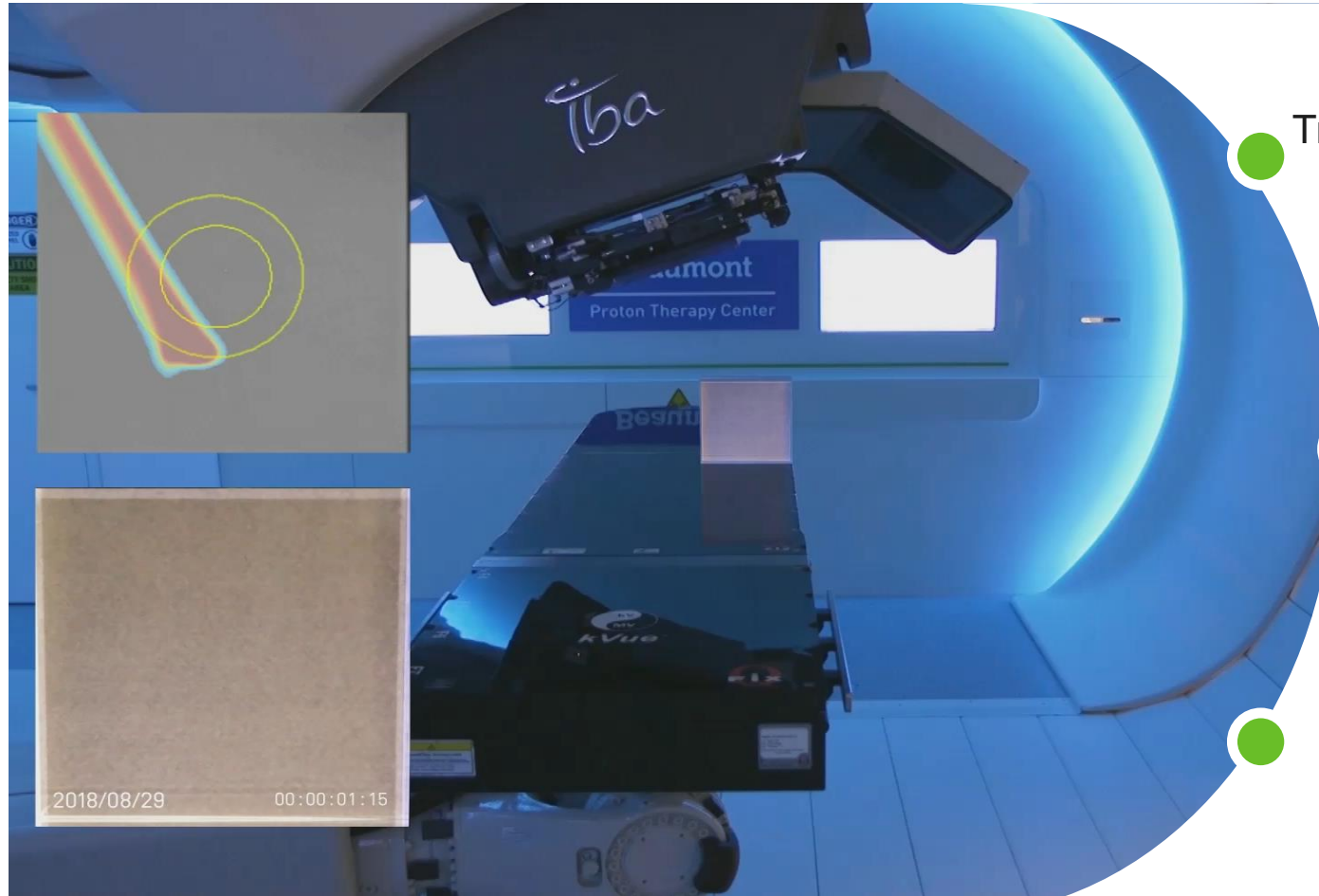


Ugo Amaldi and Gerhard Kraft - Radiotherapy with beams of carbon ions
[Reports on Progress in Physics, Volume 68, Number 8](#)
Published 11 July 2005 • 2005 IOP Publishing Ltd

Carbon & Heavy Ion examples: HIMAC and HIT (CNAO ring 25m dia.)



DynamicARC[®] maximises conformal delivery



Treatment is delivered while **rotating the gantry**

Advantages of PBS

i.e. no exit dose with the Bragg peak
SAD becomes irrelevant

Conformal delivery

With partial Arc



What is FLASH Radiation and why is it Important in Radiation Oncology ?

1

FLASH radiation is dose delivery at ultrahigh dose-rate **above 40Gy/s** (>1000 fold faster than Conv. RT)

2

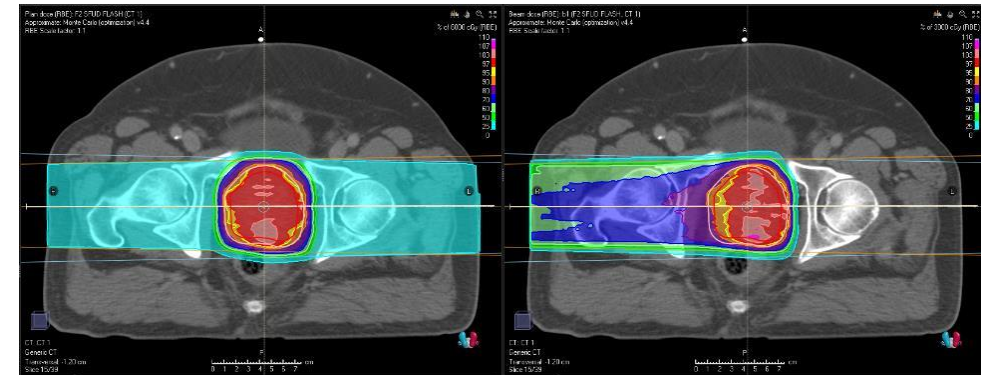
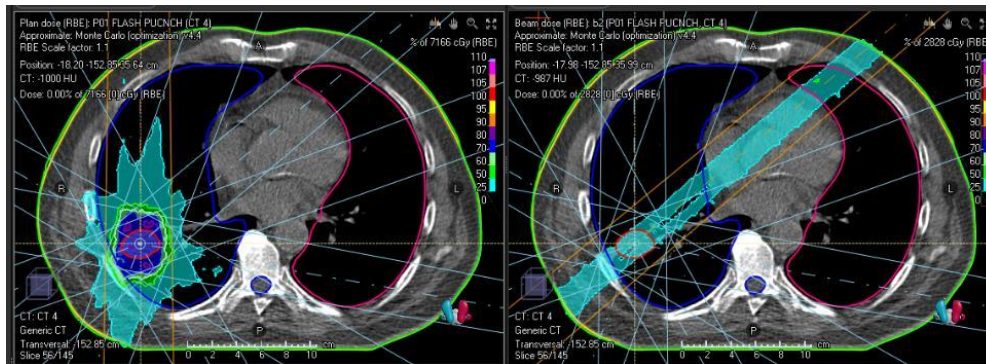
FLASH RT is **less toxic to normal tissues** while being as effective (or, more effective) to tumor tissue.

3

Clinical Proton machines already enable FLASH studies! Substantial technical challenges to overcome for photon machines.

ConformalFLASH® is the next evolution in FLASH Therapy: Combines the biological tissue sparing effects of FLASH with physics sparing effects of Proton Bragg Peak.

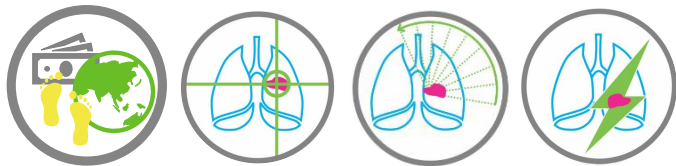
Shoot Through FLASH



ConformalFLASH® is a registered brand of the IBA Proton Therapy solutions currently under research and development phase.

Some current challenges, in a nutshell

- Adoption and reimbursement: Cost challenge
 - Treatment cost (planification, number of fraction, positioning)
 - Equipment cost (initial equipment cost + operation and maintenance + dismantling + sustainability and CSR)
- Make it even better / deal with uncertainties
 - Motion management
 - Arc-flash: improve speed and dose rate



How to tackle

- Clinical side
 - NTCP model-based clinical decisions
- Equipment design
 - Improve imaging capabilities (to enable new functionalities)
 - Decrease footprint
 - Integrate Arc
 - Enable Flash (energy degradation vs. transmission vs. duty cycle)

Keep in mind: small series vs. cost

On the clinical side



NTCP and model-based approach

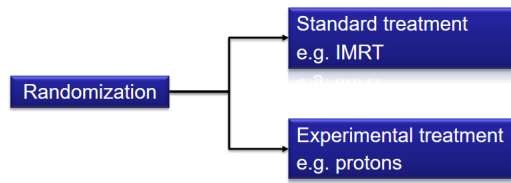


Clinical Evidence Generation

Gold standard
Evidence-based medicine

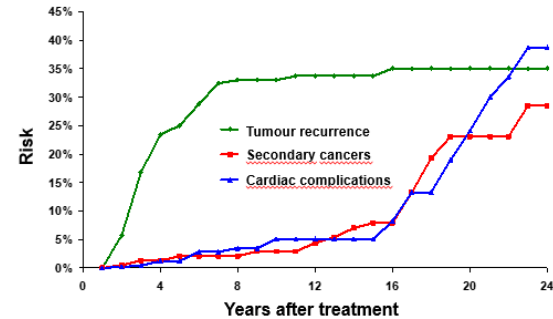


- Randomised controlled trials are considered the “holy grail” of evidence-based medicine



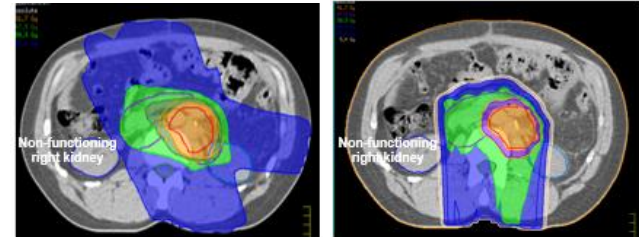
Courtesy Prof J. Langendijk UMCG

- Problem with RCT
 - Long latency times



Courtesy Prof J. Langendijk UMCG

- Problem of Equipose

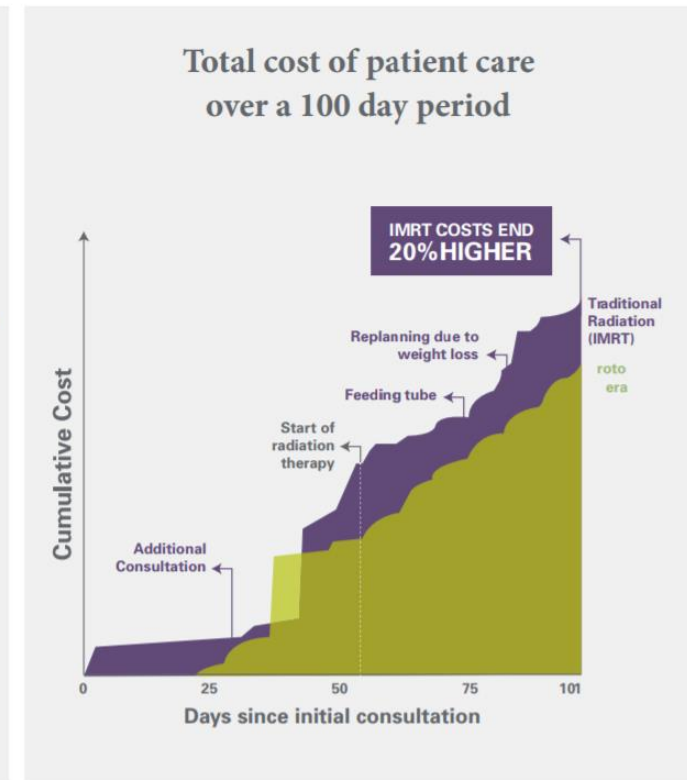
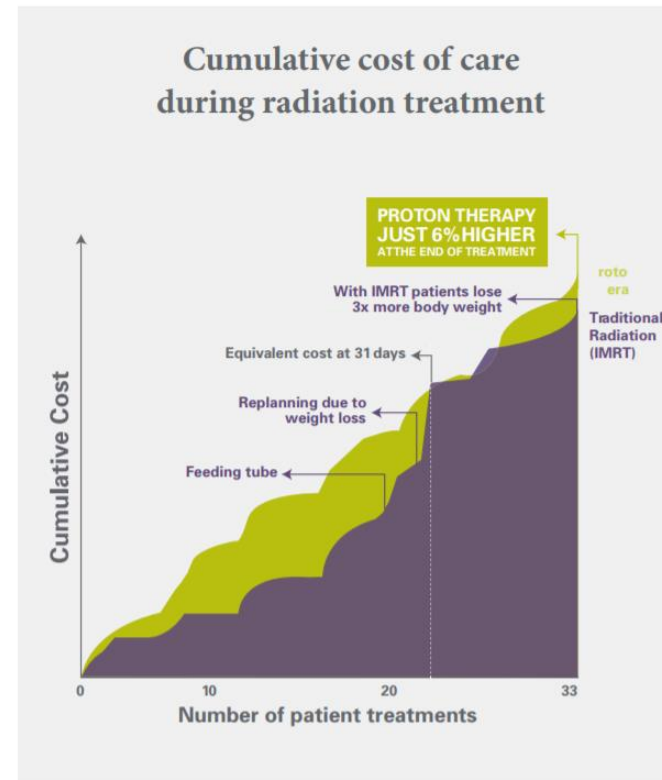


- No reimbursement for experimental arms
- Total costs for well powered study > M€ 7-10
- Most new radiation techniques aiming at reduction of side effects clinically introduced without RCT's
- Fast evolving technology

And then, there's the cost


MD Anderson pilot study:

- 25 patients with IMPT (2011-2012)
- 25 patients with IMRT (2000-2009)
- Case matched based on:
 - Unilateral vs bilateral
 - Tonsil vs base of tongue
 - T and N stage
 - Concurrent and induction chemo
 - Smoking status
 - Sex
 - Age



Courtesy of Dr Steven Frank, MD Anderson Cancer Center

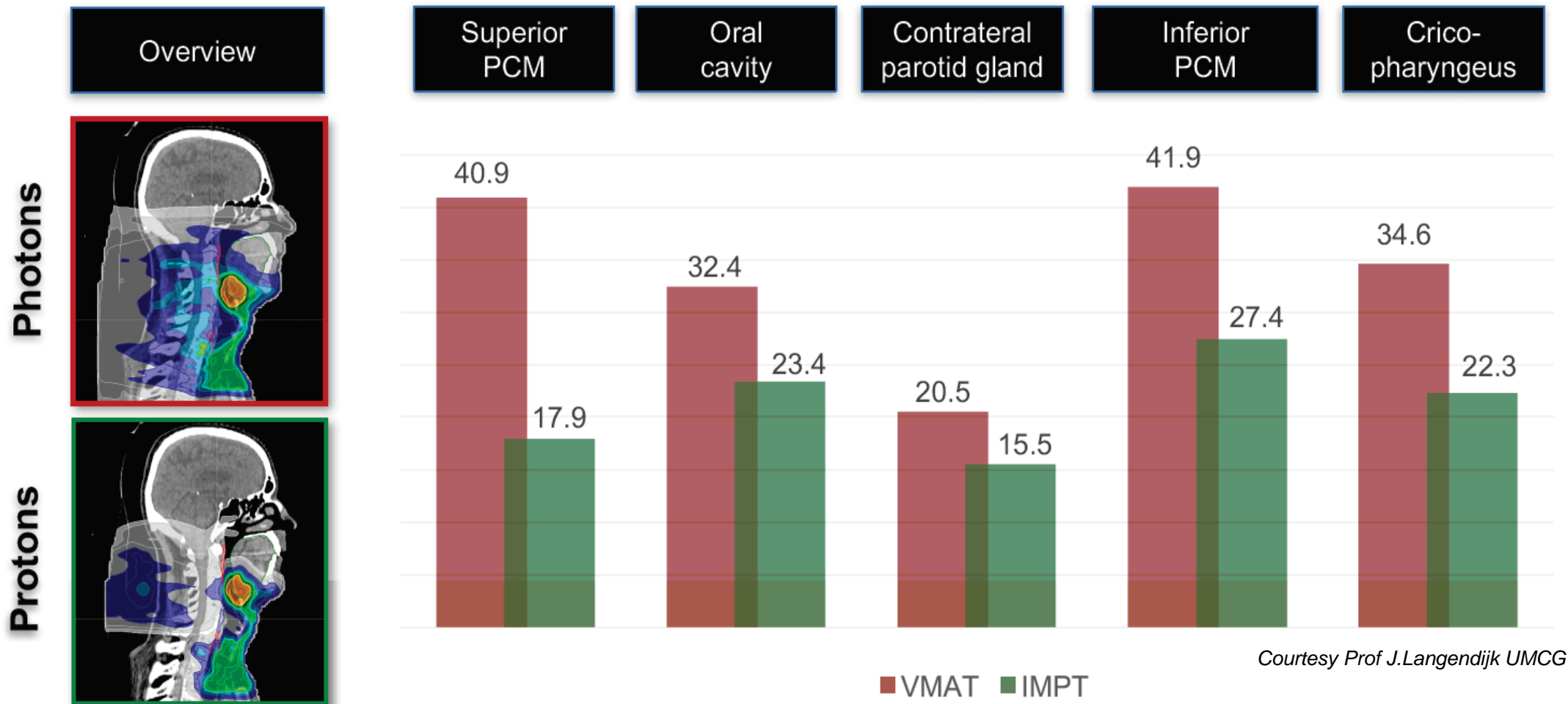
Model-based approach: 4 steps (3+1)

1. Development and validation of Normal Tissue Complication Probability (NTCP) models
 2. Individual planning comparative studies
 - Using DVH parameters of NTCP models
 3. Estimation of the potential benefit and treatment selection
 - integrating step 1 and 2
 4. *Clinical validation:*
 - (RCT's) **Not required for selection**
 - *Sequential prospective cohort studies with standard follow up programs*
- 

Courtesy Prof J.Langendijk UMCG

Model-based selection

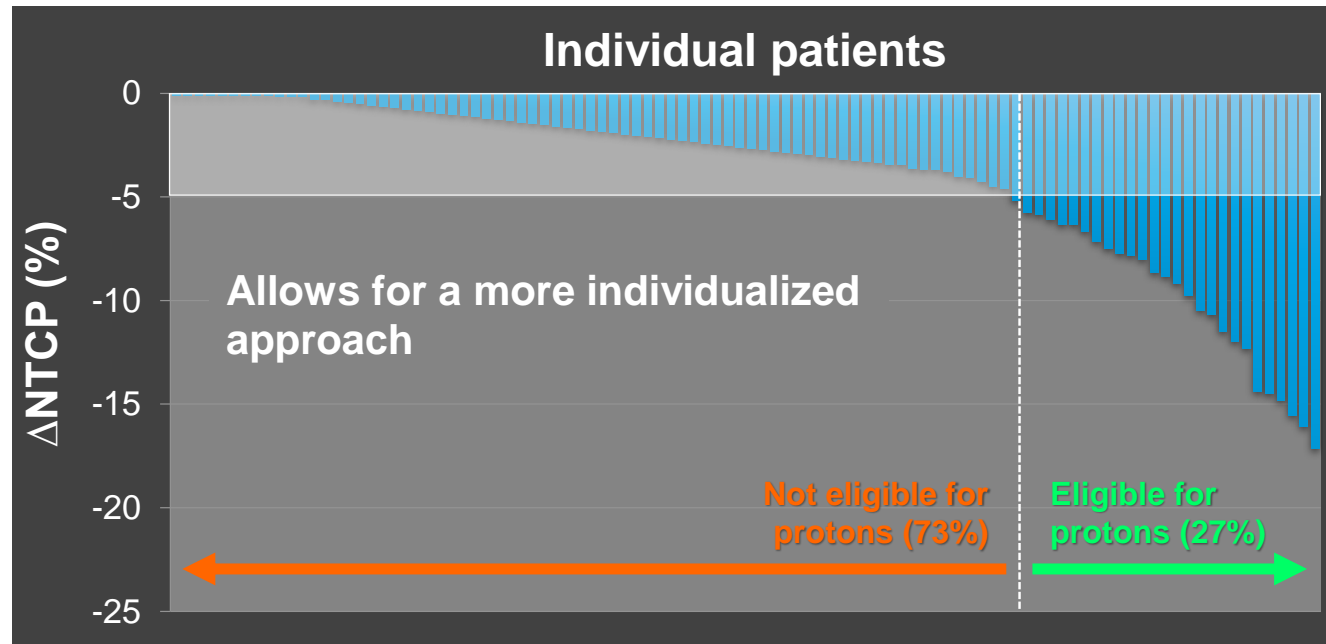
Step 2: Plan comparison to determine Δ Dose



Δ NTCP variation

Translate Δ DOSE in to Δ NTCP-model




50 patients wit OPC comparing IMRT versus IMPT

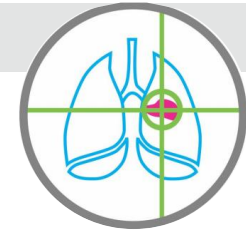


Threshold for selection for proton therapy:

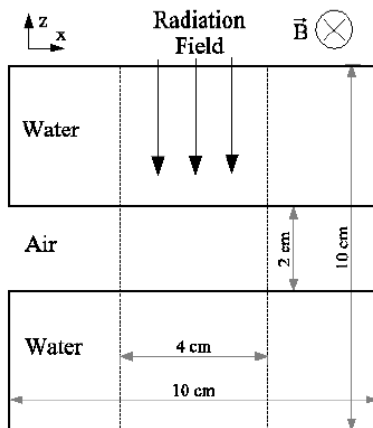
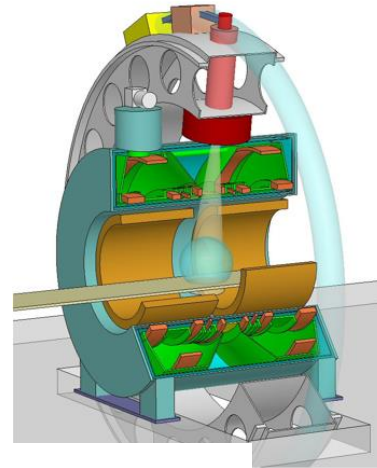
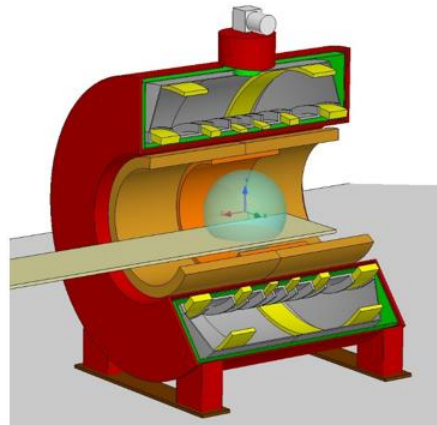
- Grade III or higher side effects: 5%

Non-exhaustive review of projects where magnets play an essential role

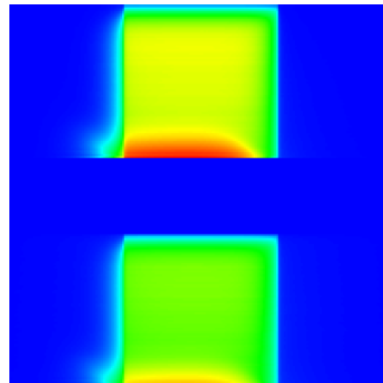
-  Improve imaging capabilities
-  Decrease footprint and Total cost of ownership
-  Enable Arc and Flash



Imaging: About MR-Linac (Xrays)



(a) Simulation Setup.



(b) Central x-z plane

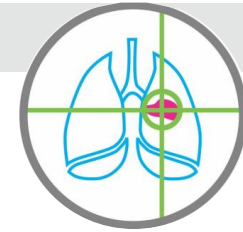
Technical complexity

- MRI magnet stray field
(+interaction with vault => linac disturbance)
- Linac RF power, presence of magnets, pulsed beam
- Radiation window

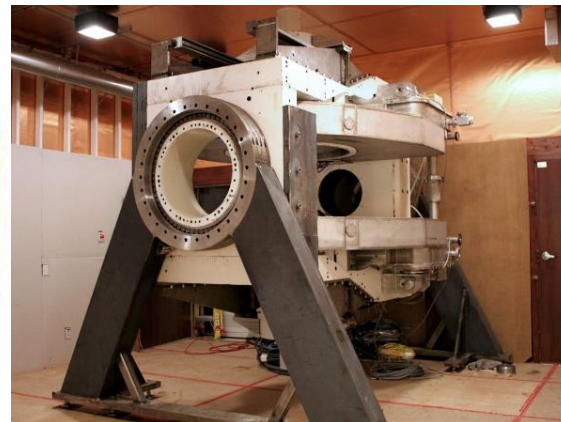
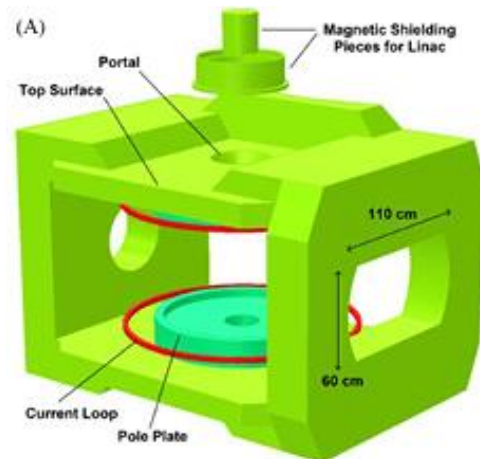
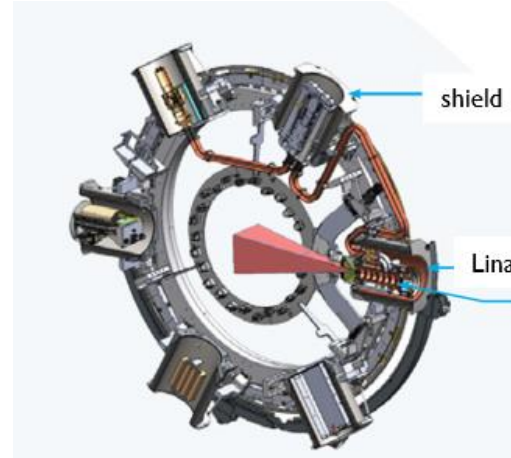
Solutions in Philips+Elekta Unity

- Magnetic shields
- Move MRI service turret
- Standard of care 1.5 T MRI (NbTi)

J. Overweg – ISMRM Virtual Study Group 20190926



MR-Linac: other systems



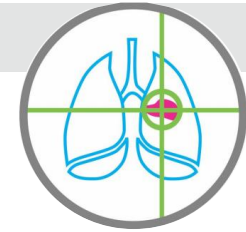
Viewray:

- fully split (radiation window), 0.35 T, optimized shielding

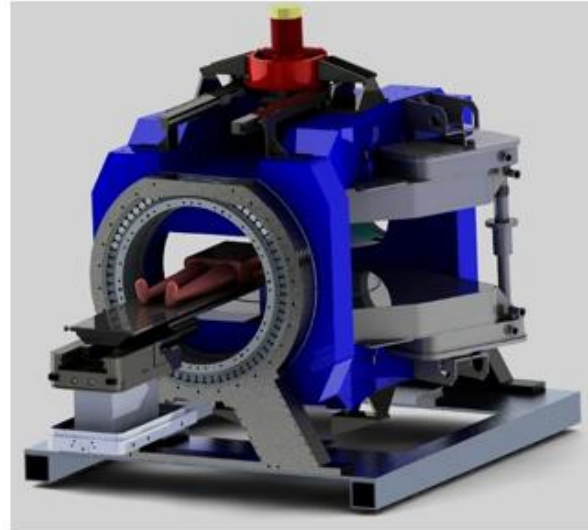
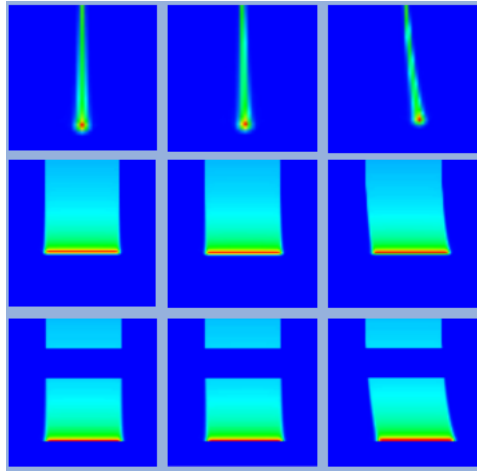
MagnetX

- 0.5 T magnet by ASG/Paramed
- based on MROpen MgB2 design

J. Overweg – ISMRM Virtual Study Group 20190926



Imaging: towards MR-PT



Issues with MR-Linac even more complicated

- Higher field beam line magnets
- Need for more transparent radiation window
- Beam deflection in MR field

Advantages vs. RT

- No electron equilibrium dose distribution impact

Game-changer

- Did one actually see the beam?



In-beam MRI scanner in RF cabin

B. Raaijmakers et al. *Phys med Biol* 53-20 p5615

A. Hoffmann et al. - *Radiation Oncology*, 2020 (DOI: [10.1186/s13014-020-01571-x](https://doi.org/10.1186/s13014-020-01571-x))

S. Gantz et al. - *Physics in Medicine & Biology*, 2020 (DOI: [10.1088/1361-6560/abb16f](https://doi.org/10.1088/1361-6560/abb16f))

S. M. Schellhammer et al. - *Physics in Medicine and Biology*, 2018 (DOI: [10.1088/1361-6560/aaece8](https://doi.org/10.1088/1361-6560/aaece8))

B. G. Fallone: The rotating biplanar linac-magnetic resonance imaging system, in *Seminars in Radiation Oncology*, 2014 (DOI: [10.1016/j.semradonc.2014.02.011](https://doi.org/10.1016/j.semradonc.2014.02.011))



Scanning magnets (and gantry)



Interesting announcement from Bdot medical (QST/NIRS startup targeting very compact system)

- Combined XY magnet (what about power)
- Gantry to come

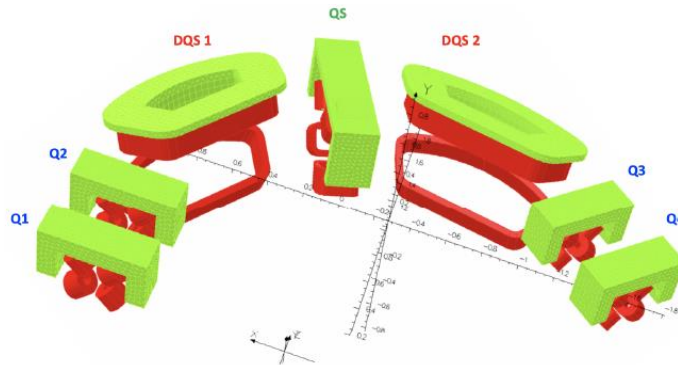
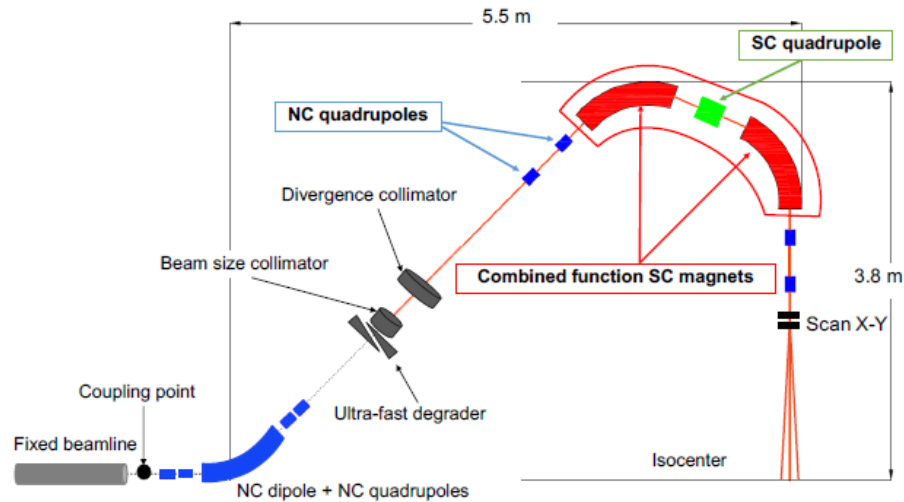
But keep SAD in mind

	Conventional systems	Proposed systems
Scanning magnet	2 independent units (in horizontal and vertical directions)	1 combined unit (in both directions)
Distance from irradiation system to irradiation position	about 3 meters	about 1 meter
Size of the treatment system	Height: about 10 meters Weight: about 200 tons	Height: about 4 meters Weight: about 20 tons

<https://www.businesswire.com/news/home/20211024005051/en/Sumitomo-Heavy-Industries-Succeeds-in-Developing-a-Superconducting-Cyclotron-for-Proton-Therapy>



Gantry and beam line - PSI



Increasing the field with SC magnets does not result in dramatic deduction in gantry size. But benefits can be found elsewhere:

- Changing the energy quickly is an enabler for flash. If the gantry is achromatic over a wide momentum range, then the beam line is no bottleneck anymore for speed

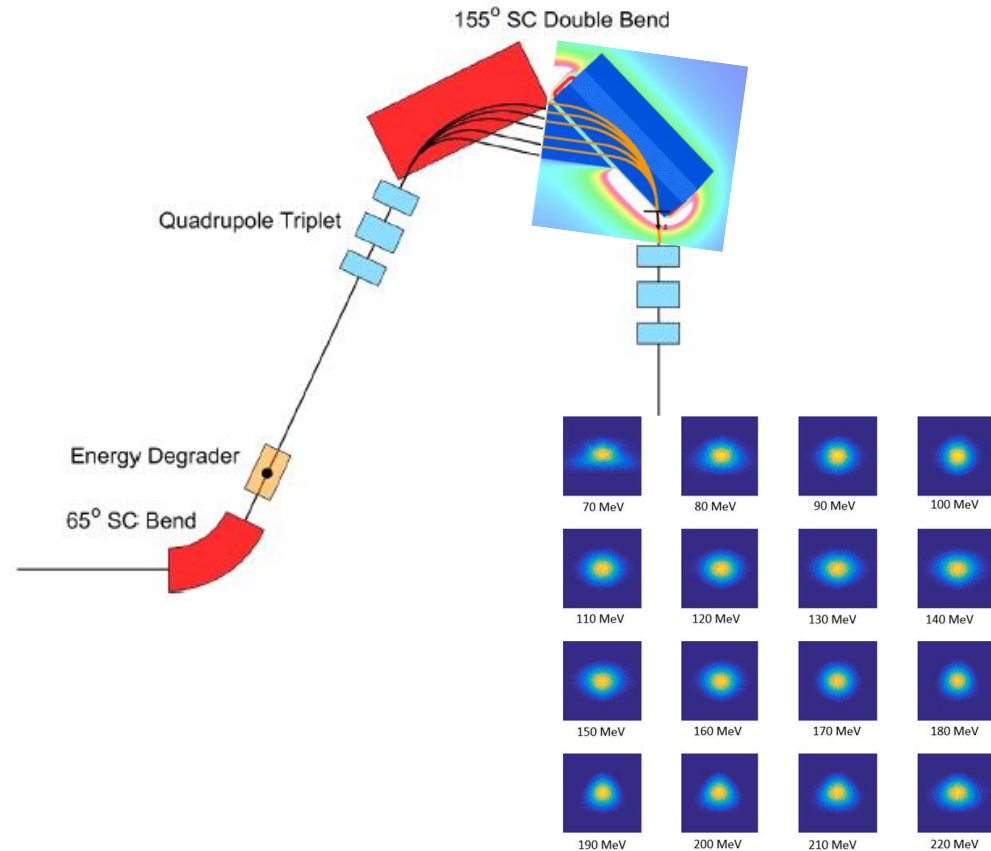
Main features

- Degrader in the gantry
- Nb3Sn achromatic magnet structure
 - +/-15% momentum acceptance
 - lighter, some size reduction
- Multipole-optimized magnets

K. P. Nesteruk et al. - arXiv:1901.01821v1 [physics.med-ph] 7 Jan 2019



Gantry and beam line - LBNL



Similar concept to PSI

- SC dipoles at 3-3.5 T to keep size
- A compromise: fixed field dipoles, ramped quads
- About 3.5 m radius => similar to current commercial gantries
- Compact size along axis (3.4m)

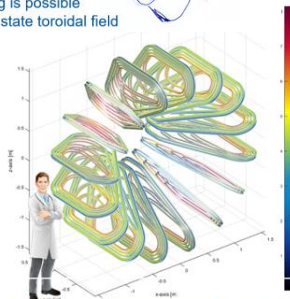
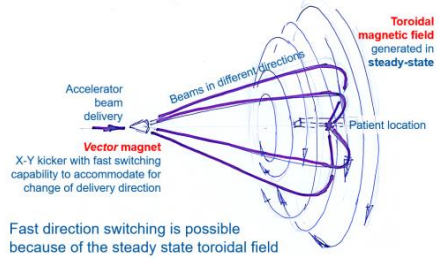
Bear in mind:

- In an IBA Proteus One, the last magnet is a large gap (20 cm GFR) 60° bending magnet that has about 100 kW of installed power, but uses only 5 kW on average
- Distal fall-off is a key clinical parameter, so is SAD too
- All in all, size does not change much anymore for proton gantries, so it is about total cost vs. functionality

L. Brouwer et al. - International Journal of Modern Physics A Vol. 34, No. 36 (2019) 1942023

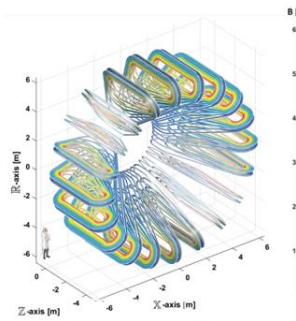


What if we get rid of the rotation? CERN's GaToroid



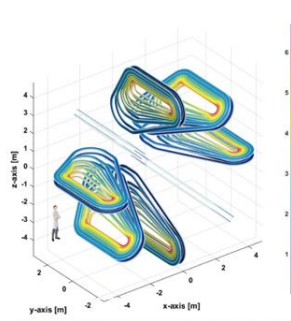
Torus dimension	1.5 m x 3 m
Bore size	0.8 m
Estimated total mass	25 tons

For ions (the largest possible size)

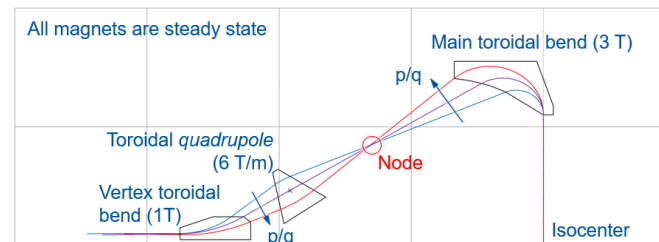
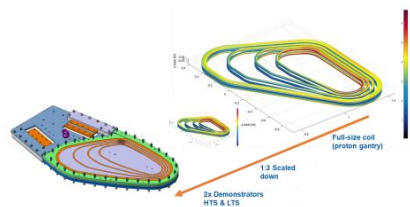


Torus dimension	5.8 m x 12.8 m
Bore size	3.7 m
Estimated total mass	300 tons

For ions (medium size)



Torus dimension	5.6 m x 9.7 m
Bore size	2.25 m
Estimated total mass	130 tons



Toroidal magnet structures are developed for various applications (HEP, fusion, SMES...) and could also be used in radiotherapy, as proposed by L. Bottura

- Various toroid sizes and models are proposed
- Optics is being studied and shows
 - scanning (vector) magnet must be very accurate
 - Pseudo-achromatic beam line concept (constant field in toroid but matching optics at the entrance)
- Prototype coil under construction

NB: toroid bending magnets also proposed by MIT, but used in a different way

Courtesy L. Bottura – EP 3 573 075 A1



Cyclotrons – SHI announcement (Oct. 25, 2021)



Table 1: Main Design Parameters of the SC Cyclotron

Description	Parameter	Unit
Particle species	Proton	
Energy	>230	MeV
Beam current (max.)	1000	nA
RMS emittance	~ 1	π mm.mrad
RMS momentum spread	<0.1%	
Extraction efficiency	>70%	
Extraction radius	0.6	m
Average magnetic field	3.1–3.9	T
Yoke size	$\phi 2.8 \text{ m} \times 1.7$	m
Yoke weight	65 t	t
Coil material	NbTi/Cu	
Stored energy	5.1	MJ
Magnetic induction	9.7×10^5	AT/coil
Main coil current	442	A
Coil cooling time	14	days
Field ramp up time	<1.5	h
Quench recovery time	<24	h
RF frequency	95.2	MHz
Harmonic number	2	
Dee voltage	50–75	kV
RF wall loss	<120	kW

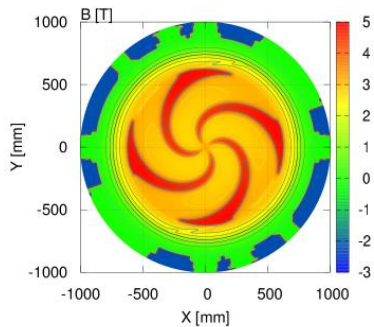


Figure 5: Magnetic field map. R < 630 mm region was measured by Hall probes [5]. The outside region was obtained by 3D calculation [6].

Features

- 40% reduction in magnet power from heir previous NC cyclo
- 65 tons isochronous cyclotron
- Iron-dominated

NB:

Magnetic field in isochronous cyclotrons has two main features: It follows the relativistic mass increase with radius and it uses strong focusing.

This combination prevents building cyclotrons much more compact than this machine, if one keeps a traditional iron-dominated structure: Iron pole would not generate enough “flutter” and pole spiralization becomes impractical

H. Tsutsui et al. doi:10.18429/JACoW-Cyclotrons2019-FRA02

<https://www.businesswire.com/news/home/20211024005051/en/Sumitomo-Heavy-Industries-Succeeds-in-Developing-a-Superconducting-Cyclotron-for-Proton-Therapy>



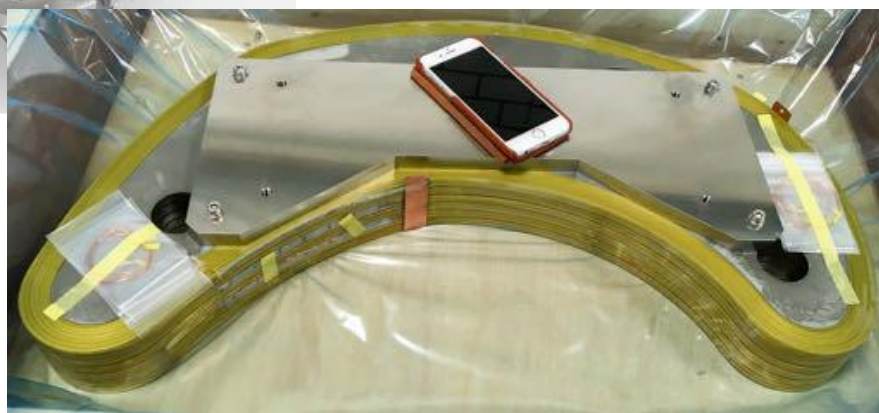
Cyclotrons – Varian



In order to circumvent this, one can introduce “Flutter coils” which enhance the magnetic field difference between “hills” and “valleys”.

Several patents on flutter coil exist and Varian conducted collaborations to propose such a design

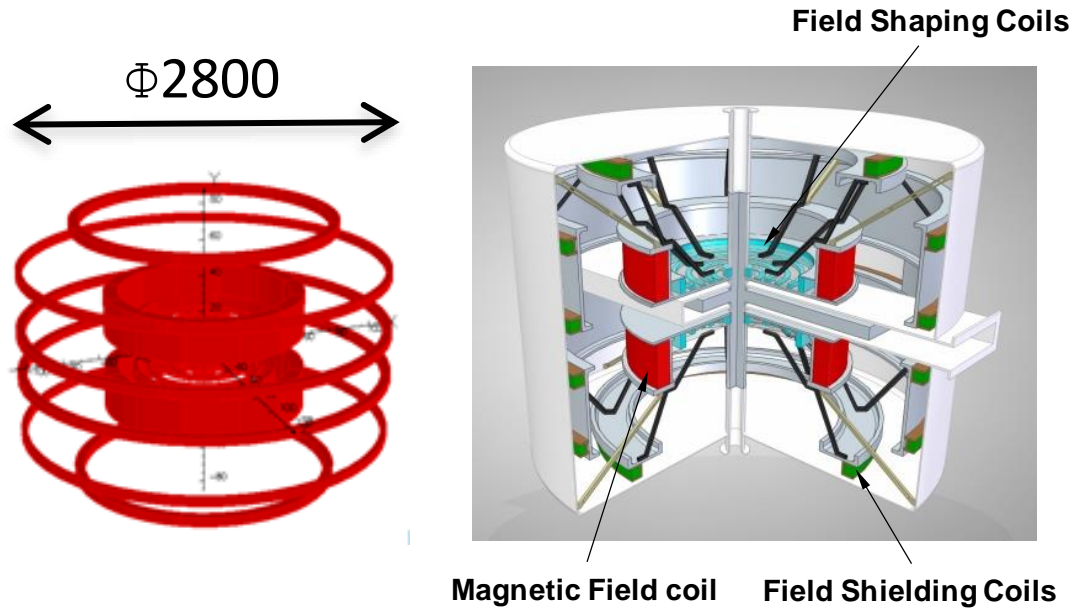
- HTS main coil (Bi-2223)
- Flutter coils made out of BiSCCO tapes from Sumitomo



A Godeke et al 2020 Supercond. Sci. Technol. **33** 064001



Cyclotrons - Ironless



High field isochronous cyclotrons offer little opportunities to scale the field, accelerating RF frequency or extract at various radii to change the energy

Synchrocyclotrons, on the other hand, use weak focusing and give up on isochronism. They therefore offer the opportunity to scale the field and vary the extracted energy

(this doesn't make them free of challenge)

The ironless synchrocyclotron concept:

- Up to 250 MeV
- Sealed NbTi CICC for improved ramp rate



More compact Carbon systems – NIRS synchrotron

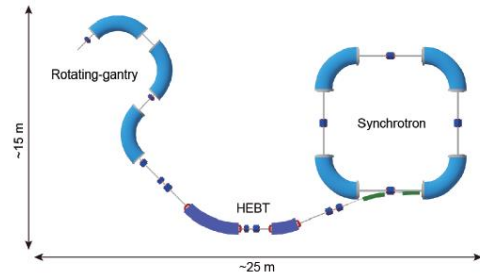


Figure 8: Schematic layout of the quantum scalpel (4th generation). An ion-source and an injector are omitted in this figure.

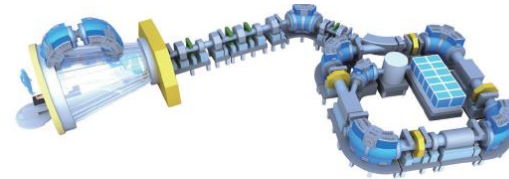


Figure 1: Schematic view of the quantum scalpel (5th generation). It consists of a laser-driven injector, a compact synchrotron and a rotating-gantry with superconducting magnets.

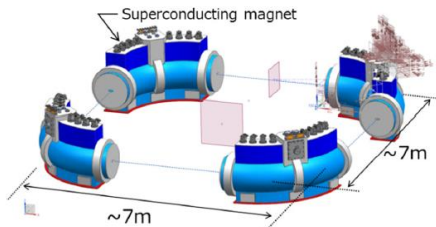


Figure 1: Layout of the

Table 1: Main Parameters of the Superconducting Magnet

Bending angle	[deg]	90 (45×2)
Bending radius	[m]	1.66
Field ramp speed	[T/s]	0.8
Maximum dipole field	[T]	4
Maximum field gradient	[T/m]	2
Effective magnetic field (Hori., Vert.)	[mm]	(±55, ±25)
Field uniformity (dipole)		$< 1 \times 10^{-4}$
Field uniformity (quadrupole)		$< 1 \times 10^{-3}$

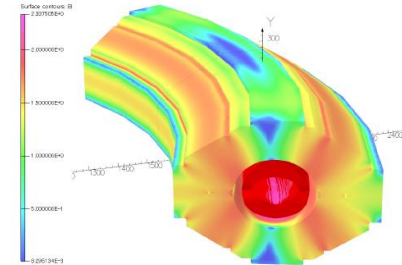


Figure 5: 3D image of the magnetic field distribution for the synchrotron superconducting magnet. A central dipole magnetic field is 3.5 T.

Growing experience in building gantry magnets, used to develop compact synchrotron concept

Several interesting features:

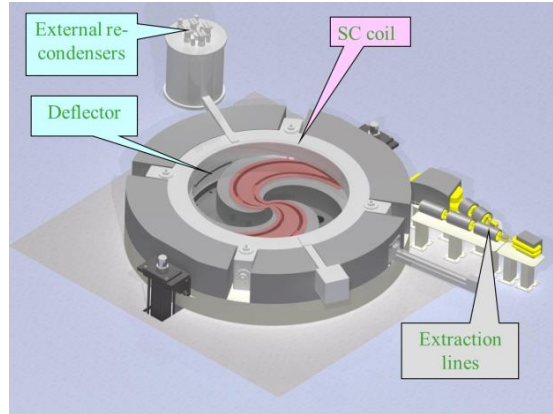
- Compact multipole magnets
- As efficient use of cryogenics as possible (reduction from gantry V1 to gantry V2)
- Reduction in size, carbon is now almost at the size of proton
- Multi-ions treatments are considered

Refer to the numerous articles and presentations made

Y. Abe et al. Proceedings of the 17th Annual Meeting of Particle Accelerator Society of Japan - September 2-4, 2020,
 T. Fujimoto et al. Proceedings of the 16th Annual Meeting of Particle Accelerator Society of Japan - July 31-August 3, 2019, Kyoto, Japan
 Takayama et al. Proceedings of the 15th Annual Meeting of Particle Accelerator Society of Japan - August 7-10, 2018, Nagaoka, Japan
 T. Fujimoto et al. Proceedings of the 17th Annual Meeting of Particle Accelerator Society of Japan - September 2-4, 2020



More compact Carbon systems – NHa cyclotron



Parameters	Value
Overall diameter (m)	6.6
Overall height (m)	3.4
Yoke weight (tons)	694
Coil type	Superconducting, NbTi



Please note

- No flutter coils (3.5 T average field at extraction)
- Ease of operation
- High current expected

Current status

- Yoke being machined
- SCC manufacturing

Next steps

- Magnet commissioning
- Field mapping

Pictures courtesy of Normandy Hadrontherapy and Sigmaphi

Conclusions

- Radiation therapy and especially proton therapy, is a moving field with several challenges
- Magnet technologies play a key role and there are several ongoing developments and novel concepts being explored
- These novel concepts are worth investigating...
 - ... Because some may provide solutions to the current challenges
 - ... But all of them must be assessed bearing constraints in mind
- These constraints and challenges are, for instance,
 - clinical environment (physical - e.g. rotation, stray field - and non-physical - e.g. workflow, safety etc.)
 - integration of imaging and patient-related equipment
 - treatment quality (novel concepts must bring something new)
 - constraints of commercial systems (cost and ease of installation and operation, etc.)
 - CSR and environmental considerations (overall power consumption, dismantling, material of conflicts...)

To go further during this MT and learn about LBNL's achromatic gantry concept of CERN's

- plenary WED-PL2-02
- Oral session on medical applications THU-OR4-401
- Posters TUE-PO1-LN1-02

To learn about protontherapy

- <https://www.campus-iba.com/>



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- H. Rocken, Varian
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* National Institute for Quantum and Radiological Science and technology, former NIRS



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