September 2019

Advancements in Particle Therapy Systems - Acceleration and Delivery

Assoc. Prof. Jonathan Farr

ADVANCED ONCOTHERAPY

ADAM an ADVANCED ONCOTHERAPY company

CERN spin-off

The following presentation of the AVO's LIGHT® Proton Therapy Solution is part of our Development roadmap and is subject to conformity assessment(s) by AVO's Notified Body as well as 510(k) clearance by the USA-FDA

COI disclosure: Jonathan Farr is a shareholder of AVO and holds a senior leadership position in the company

CERTIFIED ISO 13485 UKAS MANAGEMENT SYSTEMS 001

Proton Therapy System New Developments

New horizons in particle therapy systems

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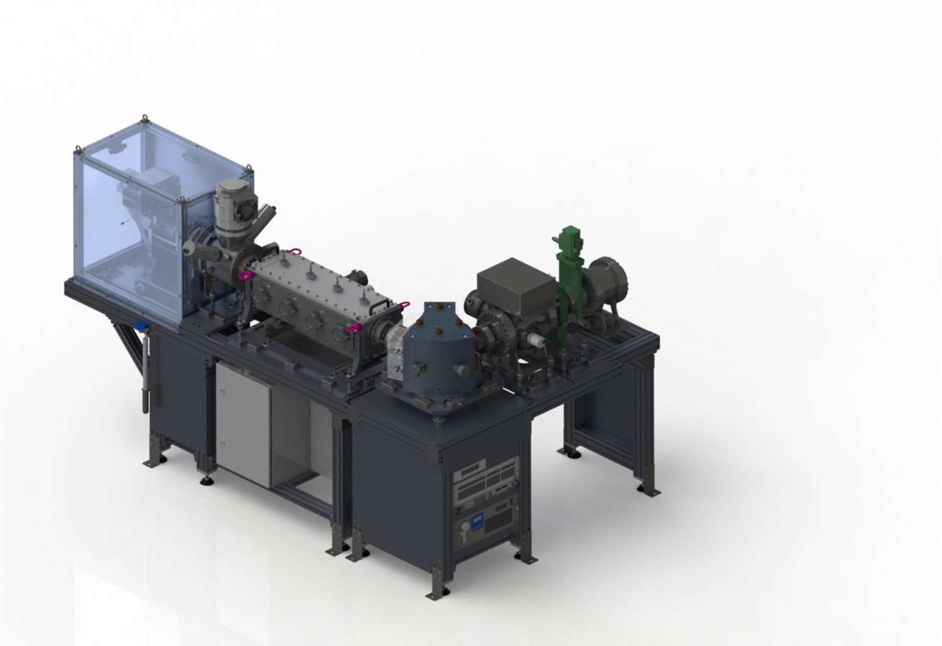
TABLE III. Desirable characteristics of new ion therapy systems compared to current systems.

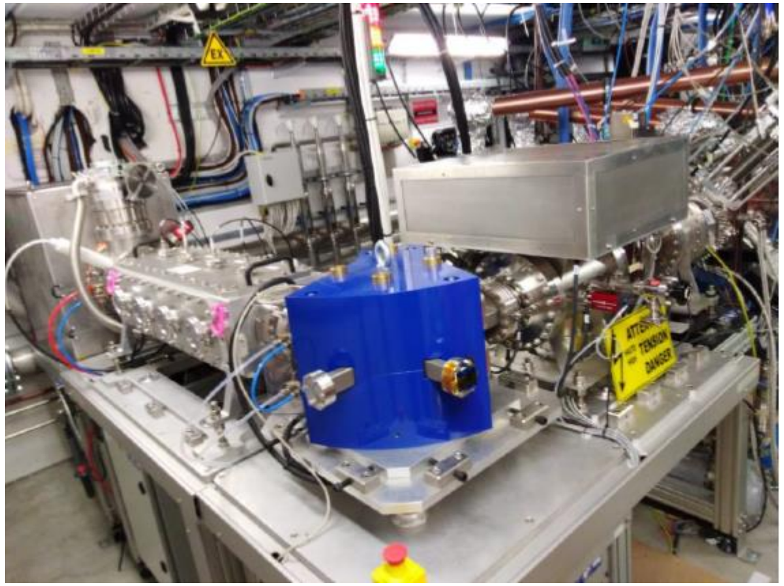
#	Characteristic	Advantages
1	Reduced maintenance	Lower service contract costs, greater availability and higher utilization
2	Cheaper	Lower facility investment costs
3	Lighter	Lower capital and installation costs
4	Smaller	Lower building construction costs
5	Reduced shielding	Lower facility investment costs
6	Reduced activation	Lower decommissioning cost, faster maintenance access time

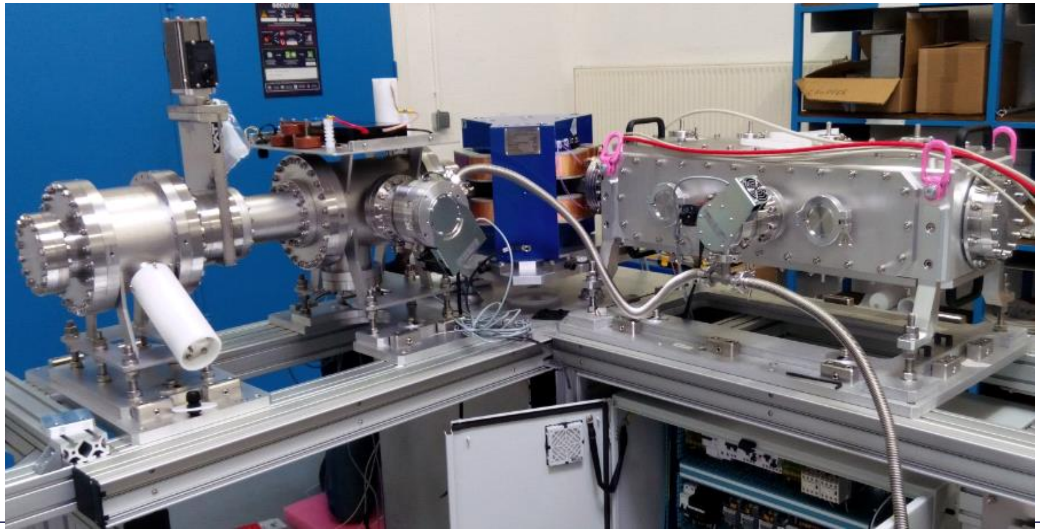
The Emergence of the proton therapy LINAC

e953 Med. Phys. 45 (11), November 2018 0094-2405/2018/45(11)/e953/31

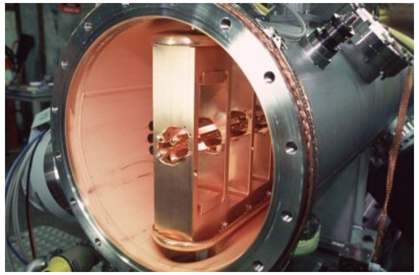
- **Proton source:**
  - MONO 1000 ECRIS
  - RF frequency 2.45 GHz
  - chopped at 200 Hz
  - 300 -1 uA

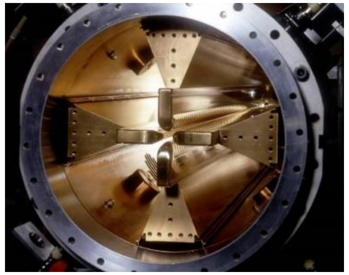




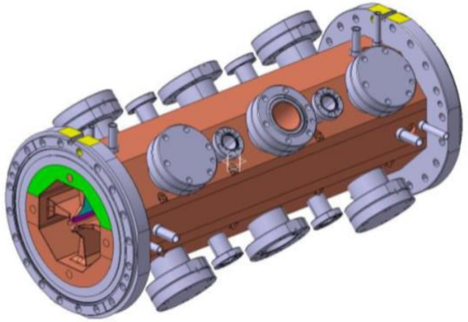


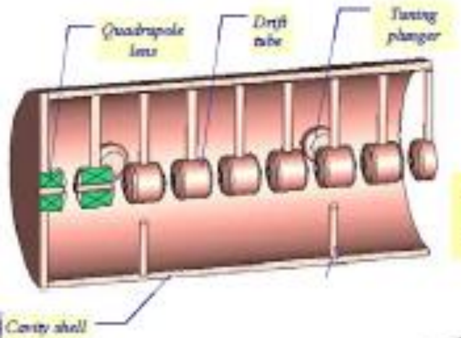
Standing wave normal conducting structures



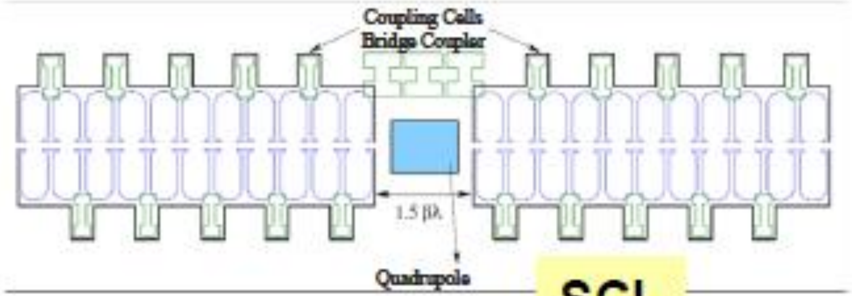


RFQ

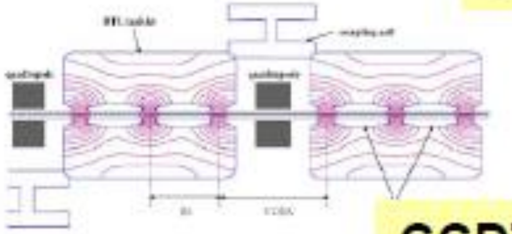




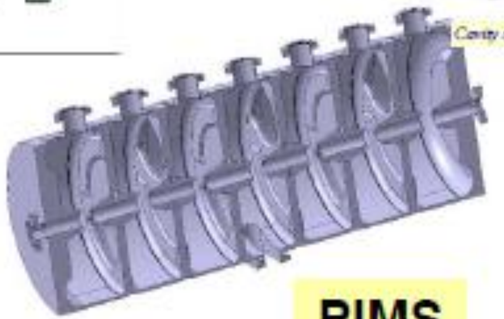
DTL



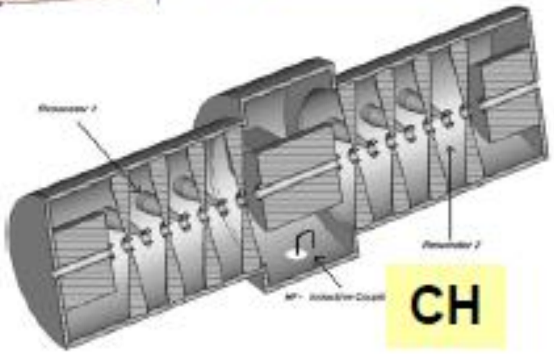
SCL



CCDTL



PIMS

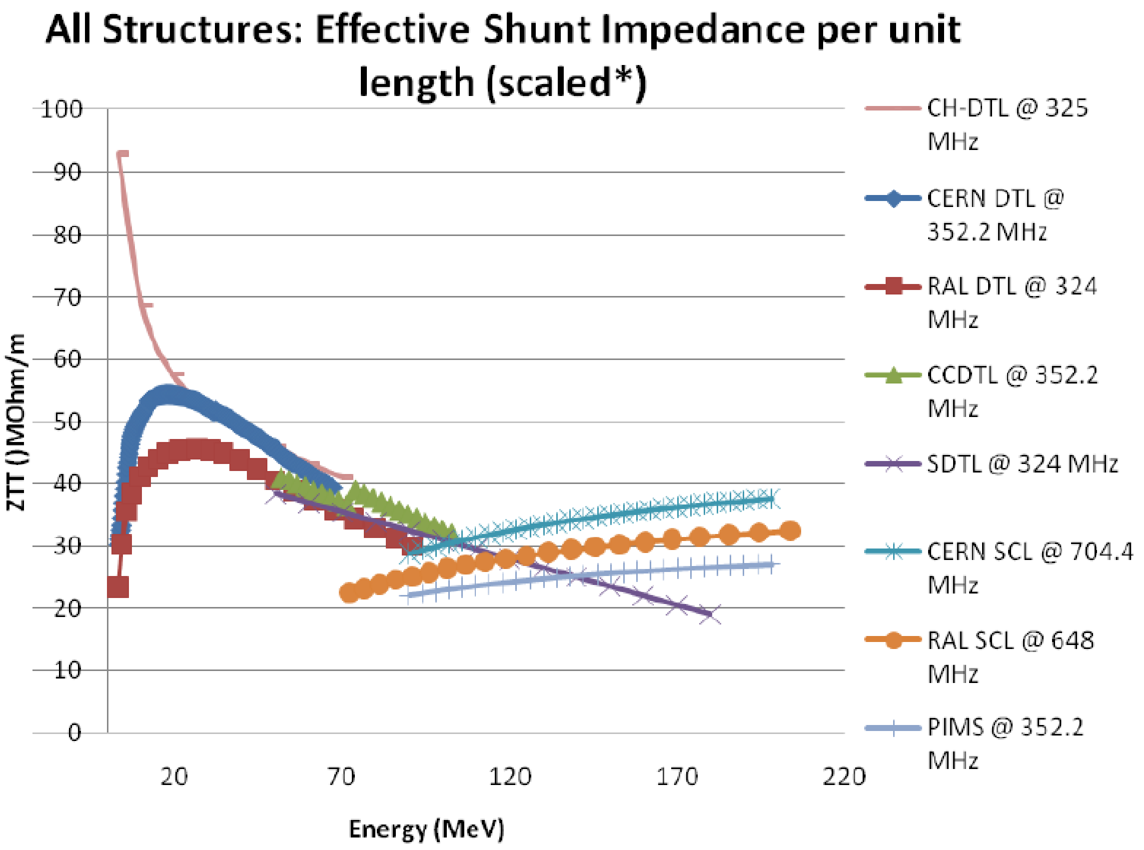


CH

M. Vretenar (CERN), CAS2013

LIGHT Structures Sequence

The accelerating efficiency is strongly dependent on the type of structure used and on the beam energy



For proton linac, several structures are used in sequence to adapt to the increasing particle velocity β

In order of increasing β typical structures are:

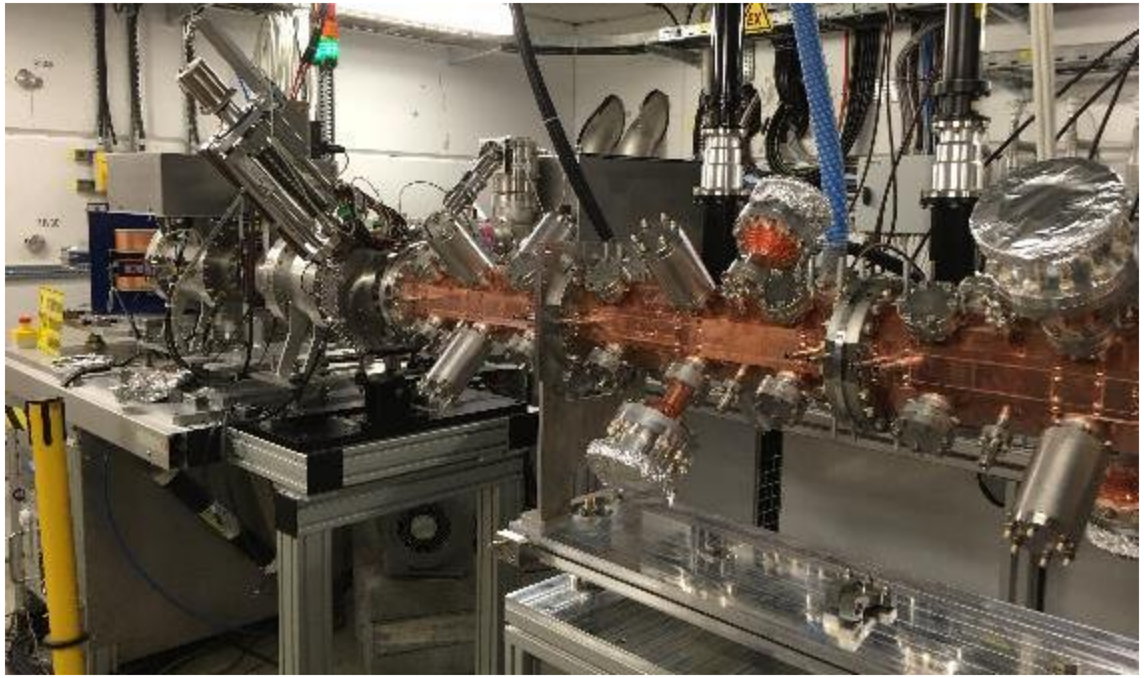
1. RFQ
2. DTL or SCDTL
3. CCL

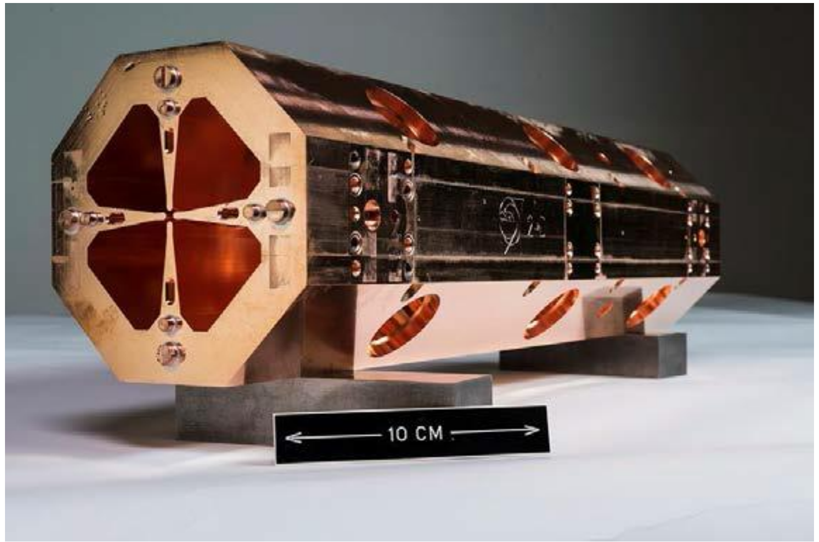
CARE-Report-2008-071-HIPPI (2008)

LIGHT Components

- **High frequency RFQ designed by CERN**
  - 4 vanes type
  - 750 MHz (highest known)
  - 4 modules - 2 m
  - 5 MeV energy gain

Section	RFQ
RF frequency [GHz]	0.749
Energy [MeV]	0.04-5
Length [m]	2

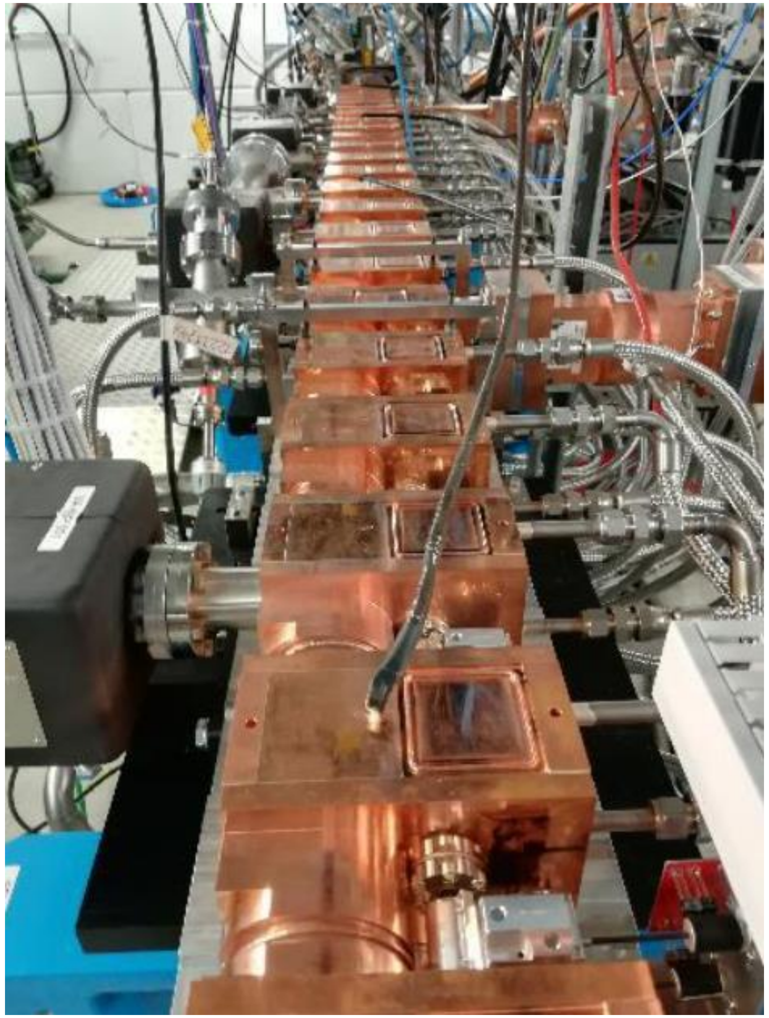




Side Coupled Drift Tube Linac

- **Designed by ENEA (Frascati, I)**
- **Manufactured at TSC/VDL**
  - SCDTL3 (TSC)
  - SCDTL1, SCDTL2, SCDTL4 (VDL)

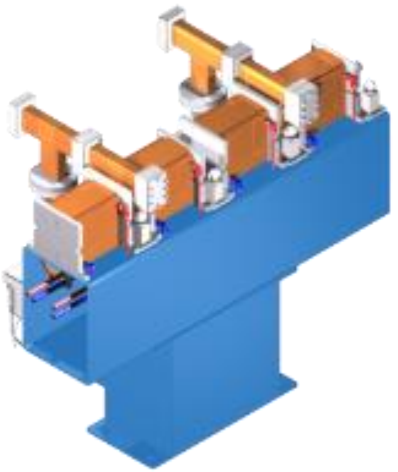
Section	SCDTL
RF frequency [GHz]	2.998
Energy [MeV]	5-37.5
Length [m]	6.2

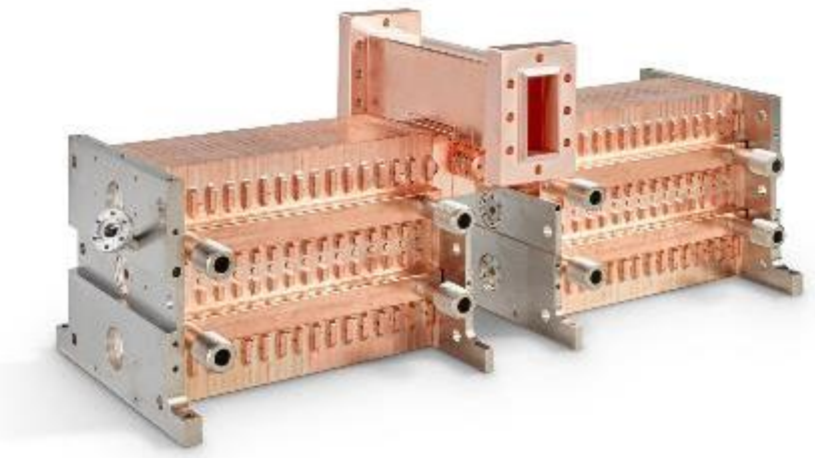


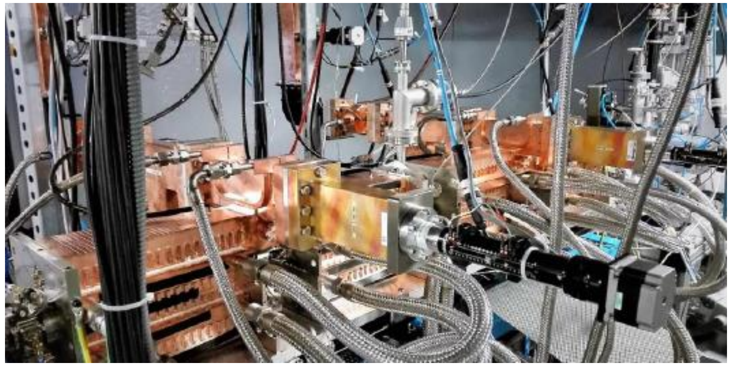
Coupled Cavity Linac

- **Designed by ADAM**
- **Manufactured by VDL**
- **4 modules already in the bunker (conditioned)**
- **CCL1 CCL2 operating**
- **All remaining modules in production**

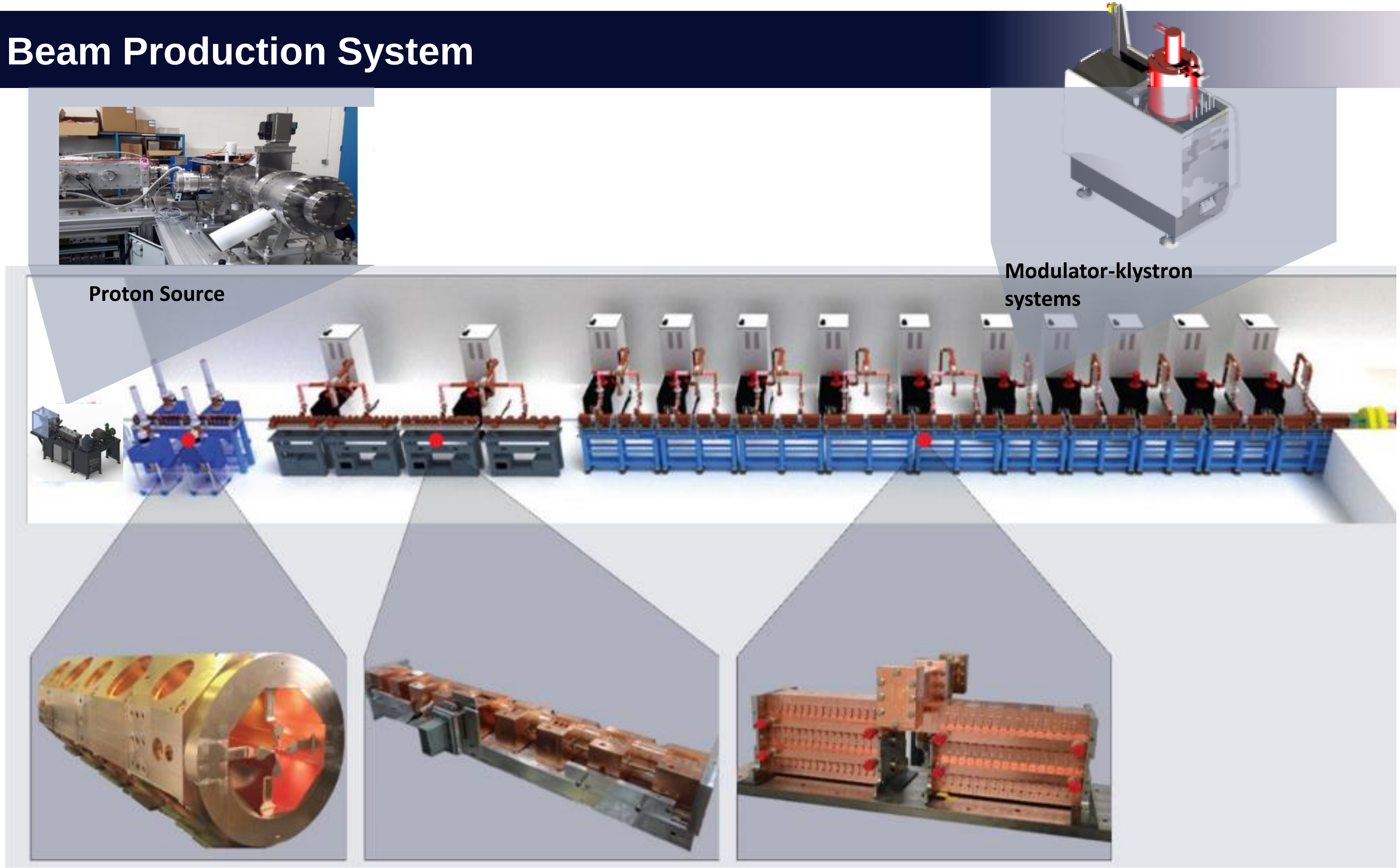
Section	CCL
RF frequency [GHz]	2.998
Energy [MeV]	37.5-230
Length [m]	15.5







LIGHT Beam Production System



Radio Frequency Quadrupole (RFQ)

Side Coupled Drift Tube Linac (SCDTL)

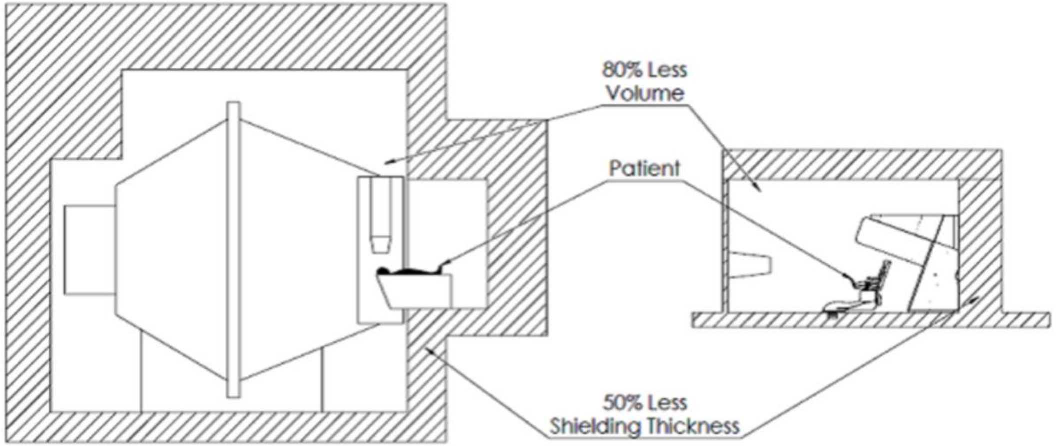
Coupled Cavity Linac (CCL)

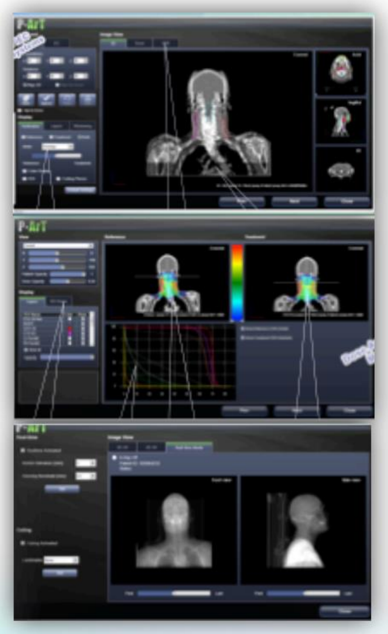
LIGHT features for proton therapy

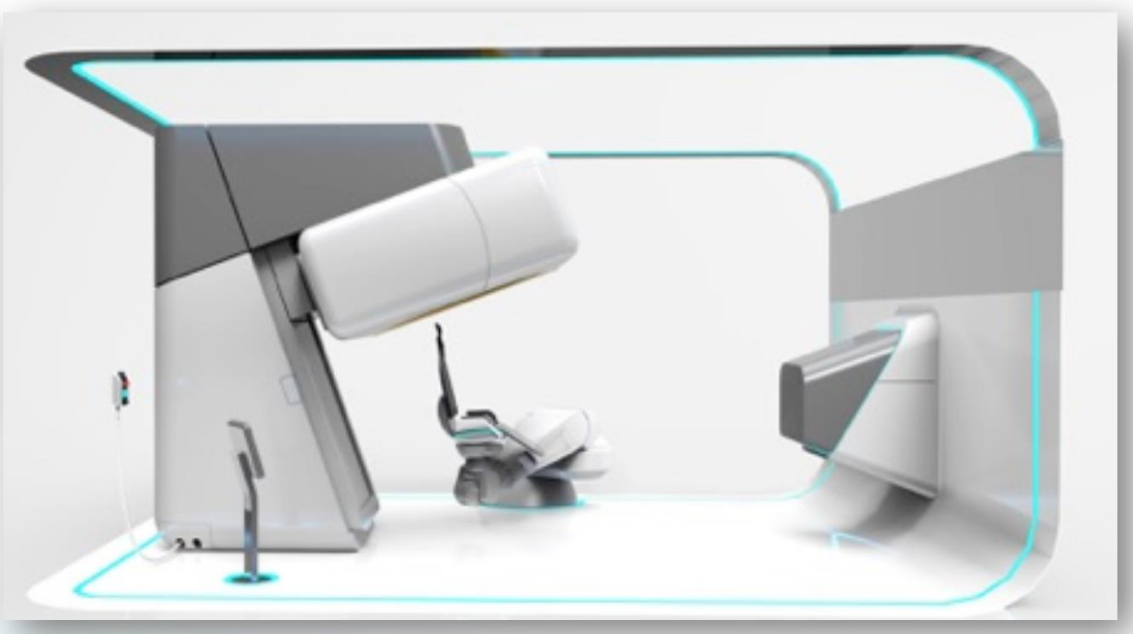
Our intention is to deliver:

- **Active energy modulation** → no absorber and degrader
- **Pulsed beam at 200 Hz** → intensity and energy modulation in 5 ms
- **Small beam emittance** → small magnets aperture
- **Almost no losses!** → reduced shielding

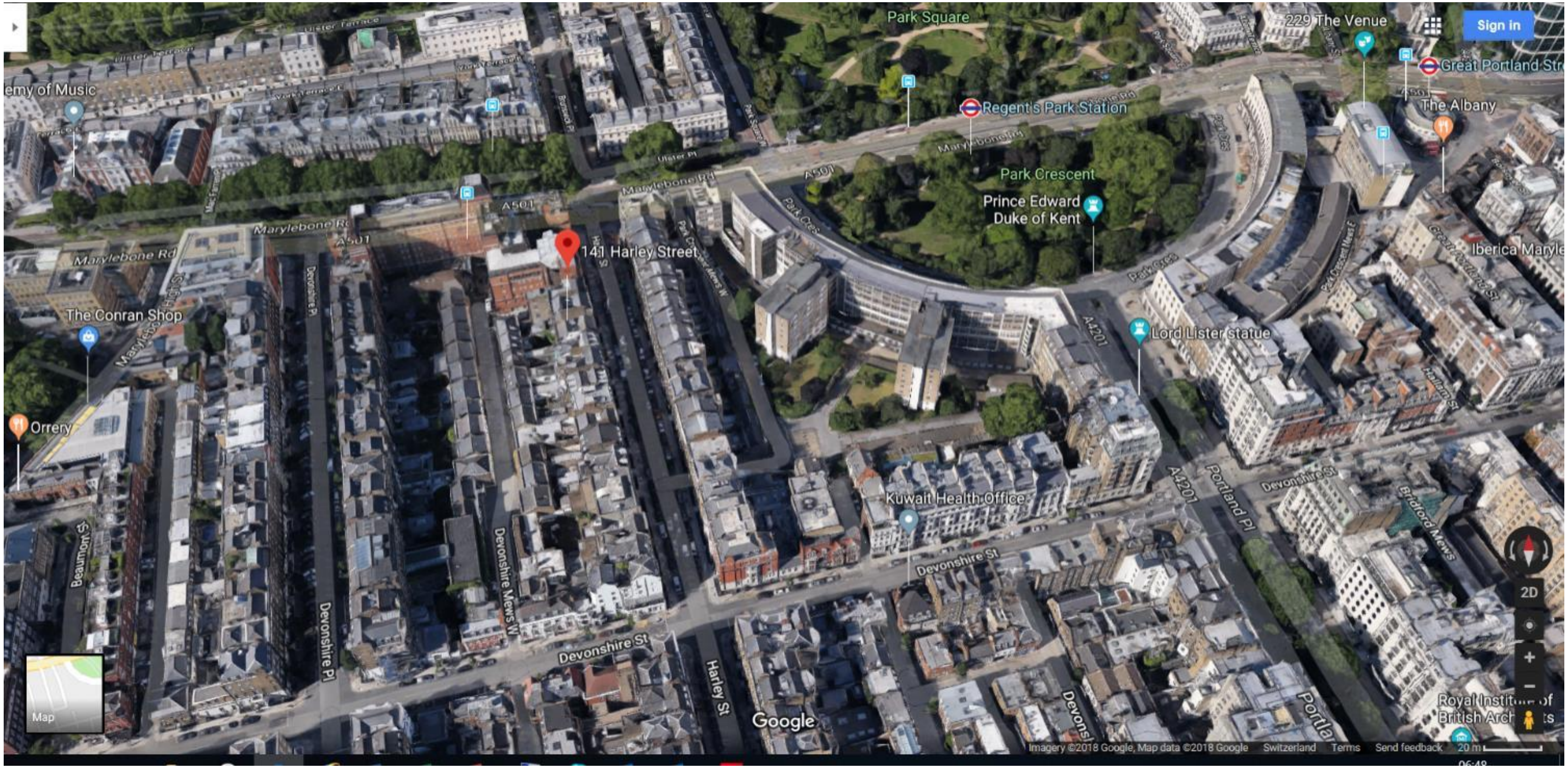
LIGHT Treatment Room







Harley Street Project - London



Harley Street Project - London

Harley Street, London, the First Site Housing LIGHT

141/143 Harley Street
Grade 2 listed buildings

Challenge:
Install and Operate a high energy Proton Therapy Center here

AVO revolutionises Proton Therapy – Size, cost, patient access

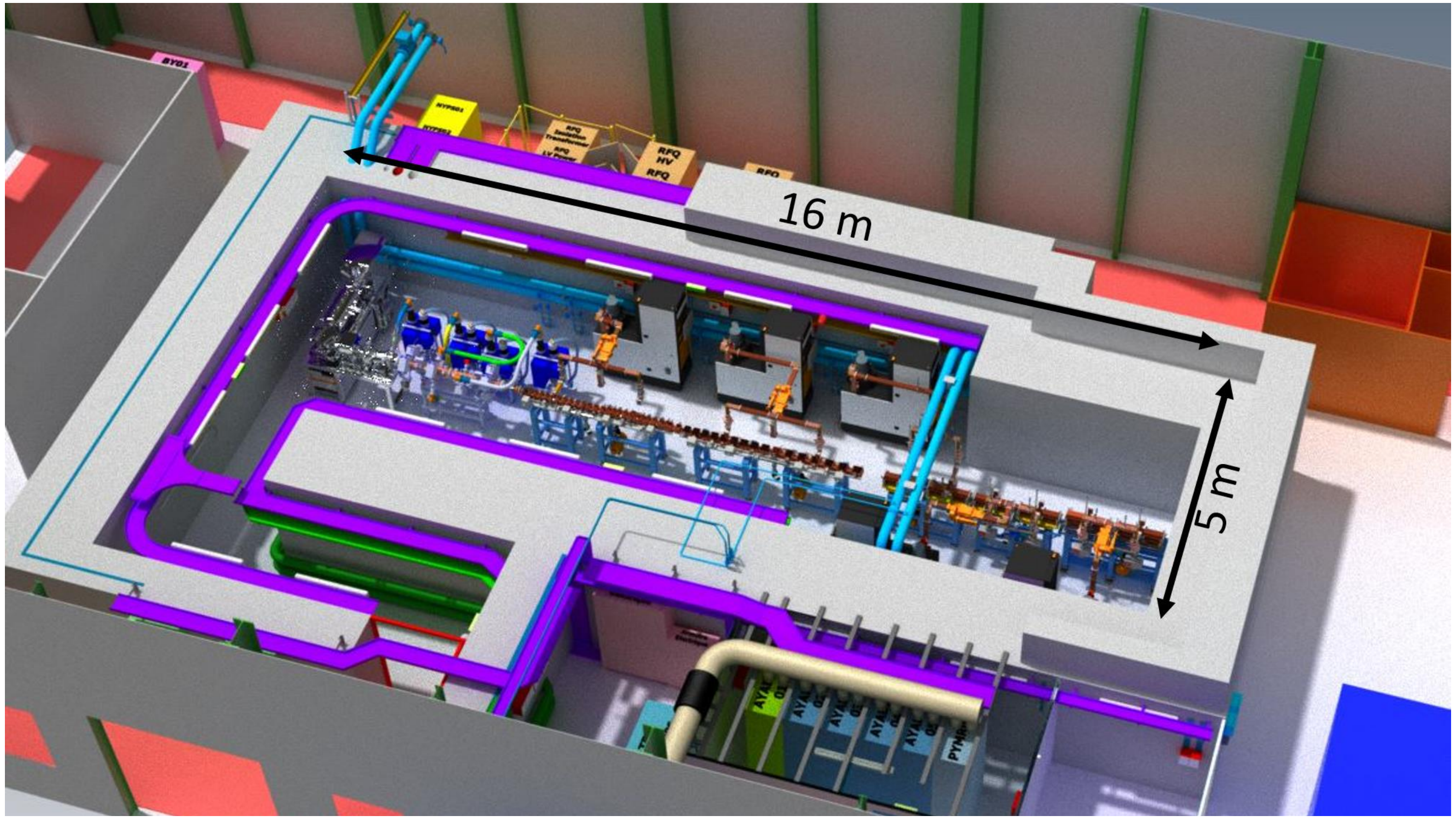
Proton therapy goes slimline

August 2018

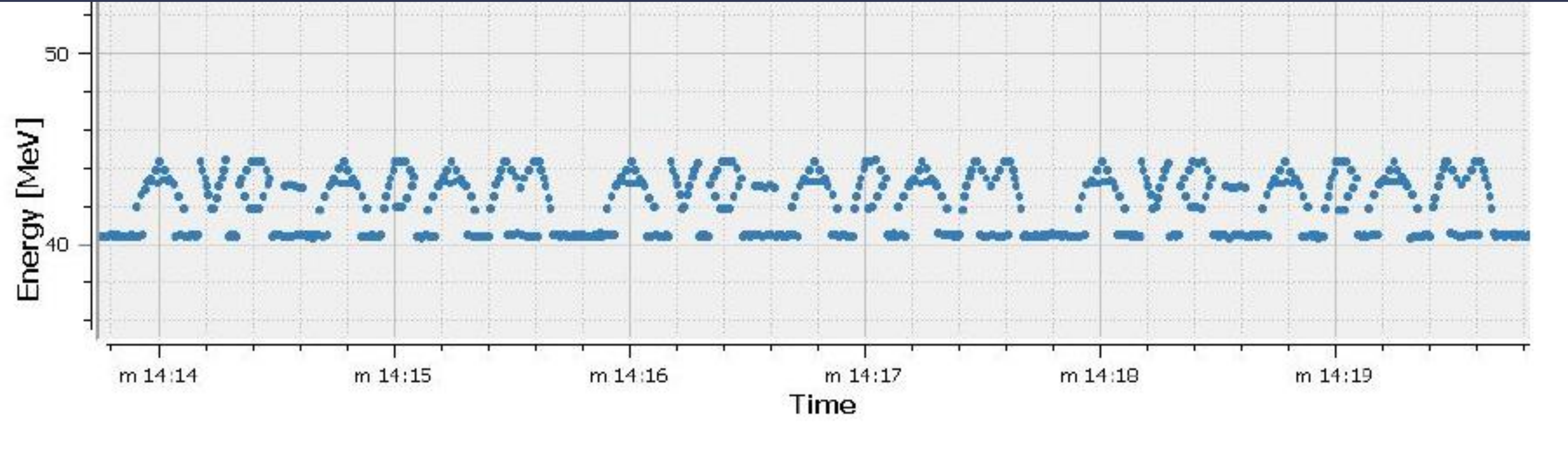
Harley Street, London, the First Site Housing LIGHT

Video

LIGHT Prototype Testing

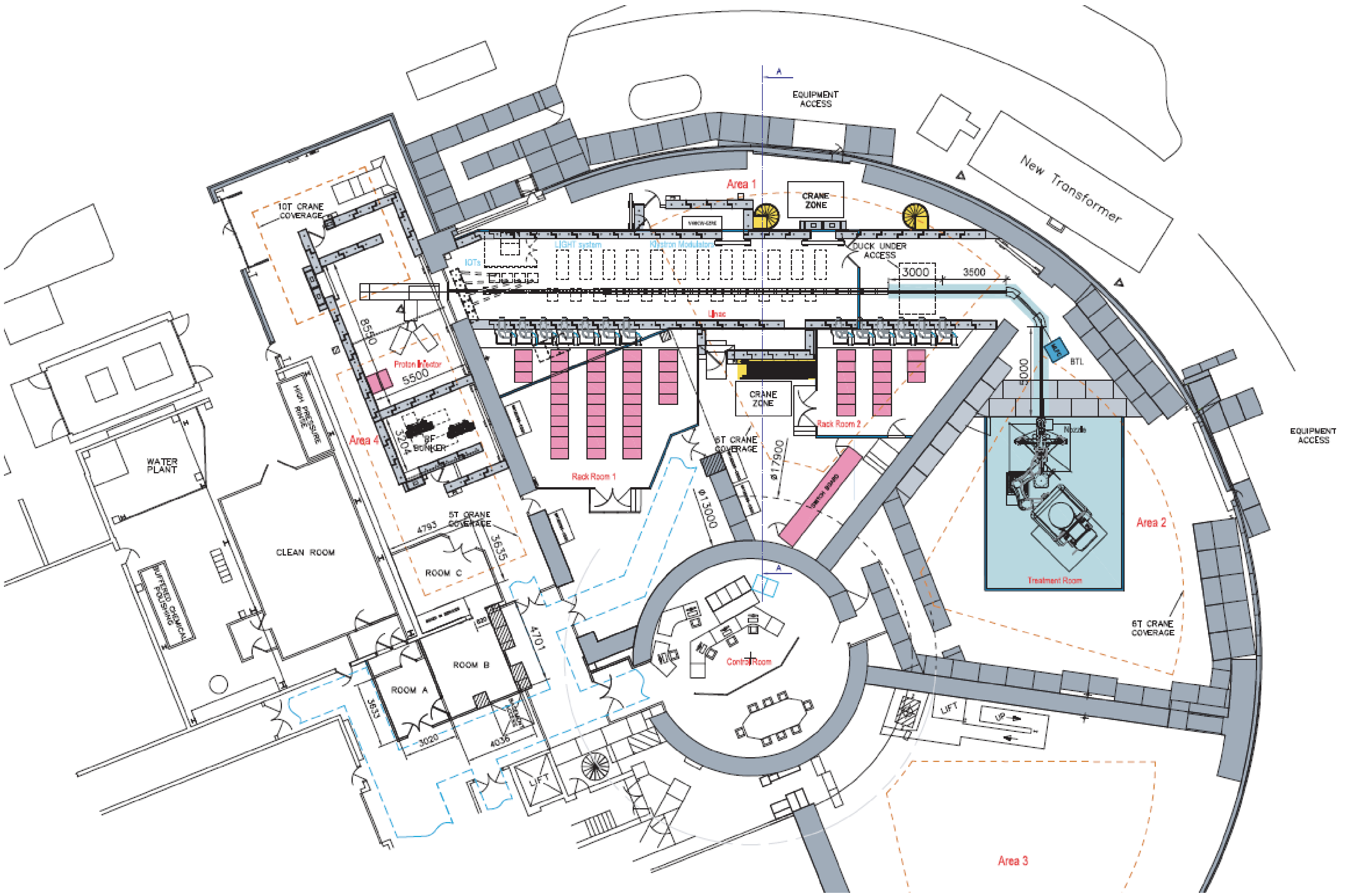


LIGHT Prototype Testing



COMMISSIONING OF LIGHT @ STFC, UK

- UK Science & Technology Facilities Council Partnership
- Daresbury laboratory is the AVO extended testing and assembly site
- Accelerator Science and Technology Centre
- CERN partner
- Cockcroft Institute
- R&D testing, including beam tests, will also continue in Geneva



Science & Technology Facilities Council

New horizons in particle therapy systems

e967 Farr *et al.*: Advanced particle therapy systems e967

8	Faster energy changes	Shorter treatment times, 3D rescanning
9	Faster, more sensitive instrumentation	In order to accommodate some of the desired parameters, one needs better instrumentation.
10	Higher flux	(assuming fast energy changes, scanning, and better instrumentation); shorter treatment times leading to less patient motion and more patients treated per day
11	Smaller spots or collimation	Better conformal avoidance, hypofractionation, SRS, and SBRT, although some may claim the current performance is at a physical limit
12	Variable spot size and shape, faster than currently available	Better conformal avoidance, faster delivery
13	Ions heavier than protons	Radiobiological effectiveness, geometric sparing, hypofractionation, SRS, and SBRT
14	Rapid gantry angle changes	Some claim this may lead to better conformality to targets, better conformal avoidance to organs-at-risk, others claim this is not necessary with optimized scanning techniques
15	Lower input power (green machine)	Lower operating costs

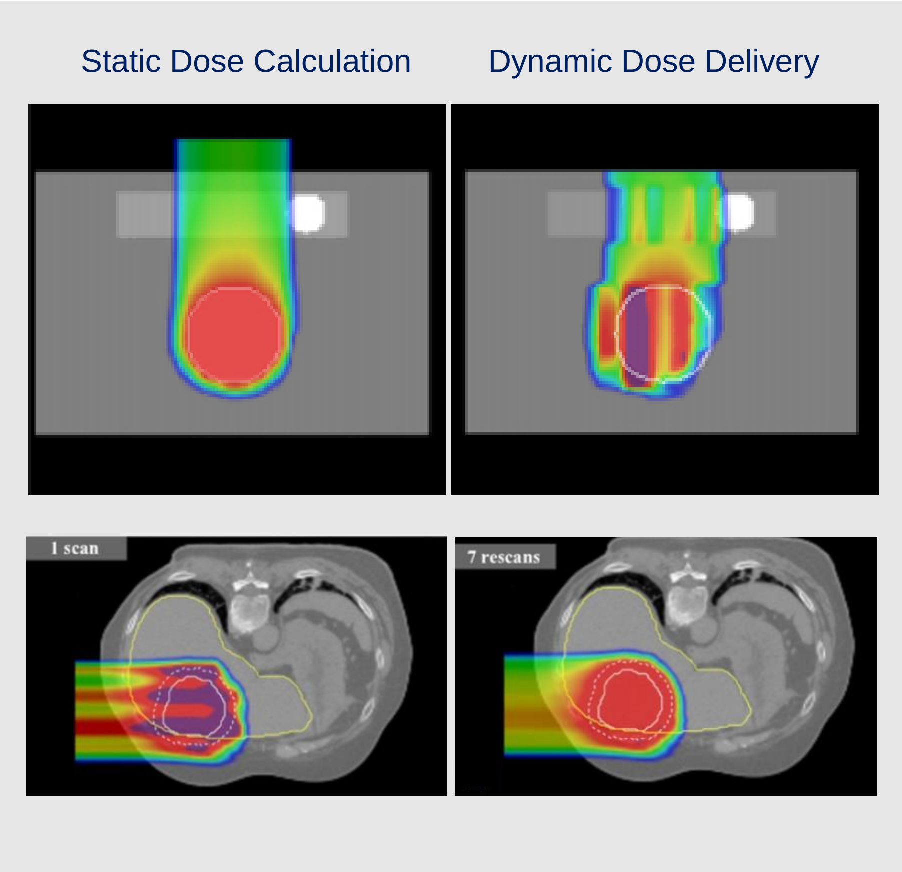
e953 Med. Phys. 45 (11), November 2018 0094-2405/2018/45(11)/e953/31 e953

LIGHT® Delivers Better Medical Outcome

Improved Dose Conformity	• Fast electronic control of beam energy • Fast electronic change spot size • Minibeams	**Better clinical performance**
More Homogeneous Dose Distribution	• The electronic control of beam energy (depth of dose) allows for volumetric repainting and active range control	**More suitable for Pencil Beam Scanning (PBS)**
Higher Dose and Fewer Fractions	• Extreme dose rate available • Available at all energies > 70 MeV	**Enables FLASH**
Adaptive Radiotherapy	• Ideally designed for personalised medicine	**Better quality of life after treatment**

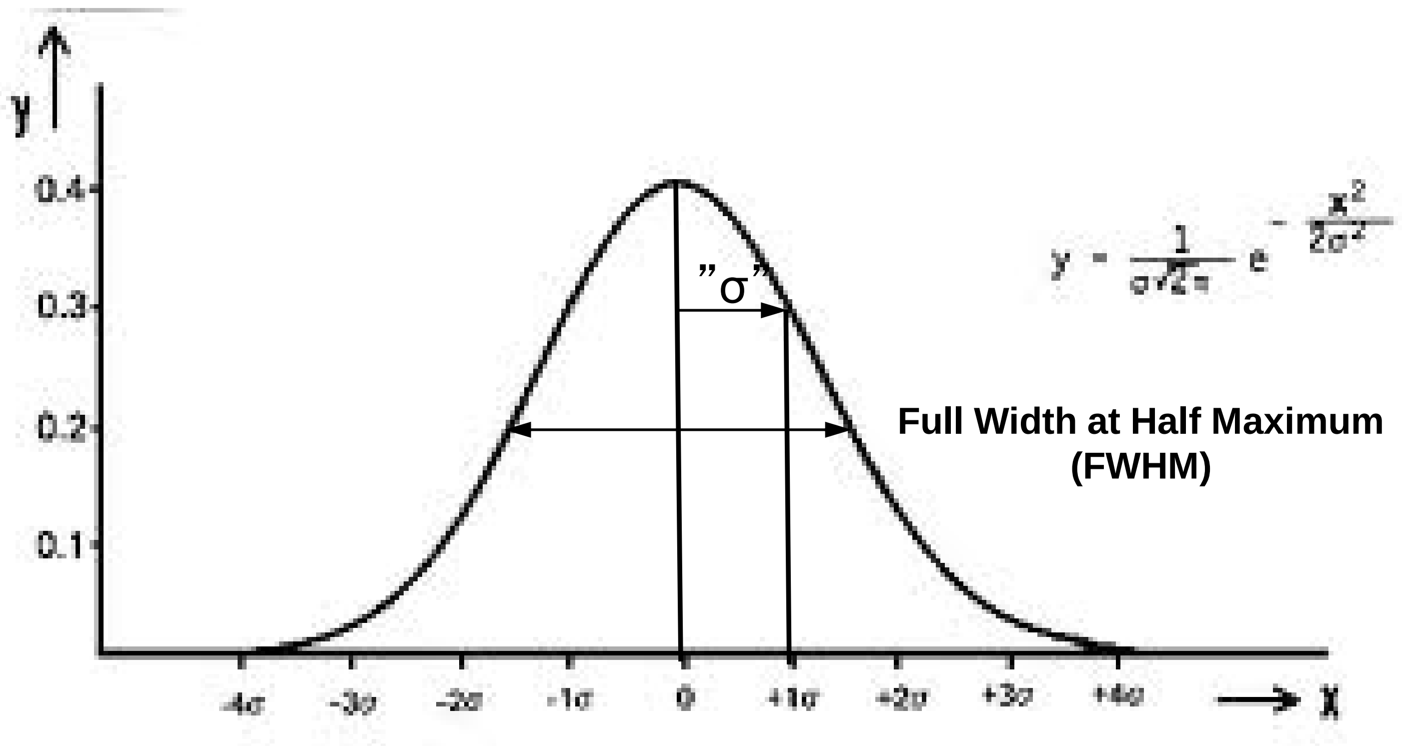
LIGHT®: More Precise Dose Conformity for Moving Targets

- **Current proton systems change energy slowly, resulting in inhomogeneous dose to the tumour, potentially compromising care**
- **LIGHT® is expected to provide volumetric rescanning with fast 5 millisecond energy changes, maximizing the advantage of proton treatment**
- **LIGHT® is expected to improve the accuracy of treating moving targets such as lung and liver and the esophagus**
- **LIGHT® is expected to provide 3D dynamic beam patient target alignment using 5 millisecond active range control**



Sources: "Adequate margin definition for scanned particle therapy in the incidence of intrafractional motion", Antje-Christin Knopf, et al, Physics in Medicine and Biology, Volume 58, Number 17 (2013); "Comparative study of layered and volumetric rescanning for different scanning speeds of proton beam in liver patients", K Bernatowicz, A J Lomax et al, Physics in Medicine and Biology, Volume 58, Number 22 (2013),

Proton Spot Size

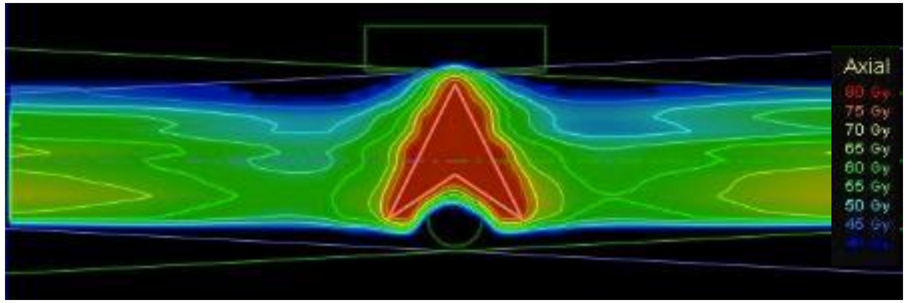


1 FWHM = 2.35 "σ"

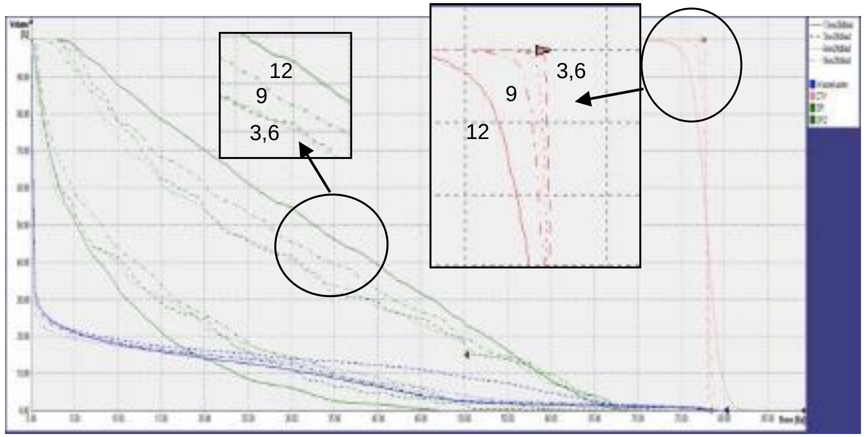
Proton Spot Size

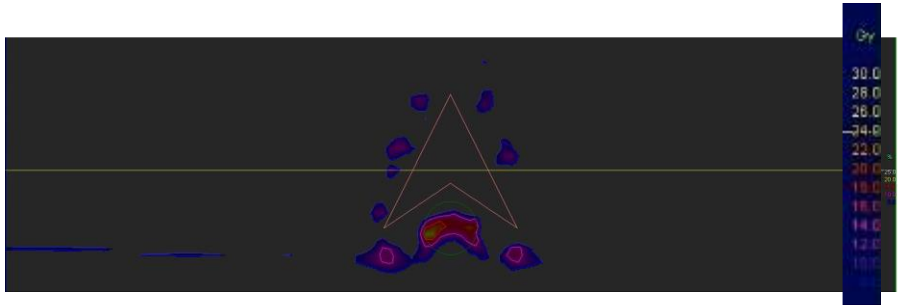
- **The phantom QI's indicated a significant sensitivity to beam size.**
- **A reasonable QI was only achieved by the 3 and 6 mm σ beams.**

	Conformity	OAR Hit	QI
Prostate Phantom			
3mm - 2 Field	1	1.0	1
6mm - 2 Field	2	1.1	2
9mm - 2 Field	5	1.1	5
12mm - 2 Field	17	1.2	14



Highly conformal 3 mm σ plan result



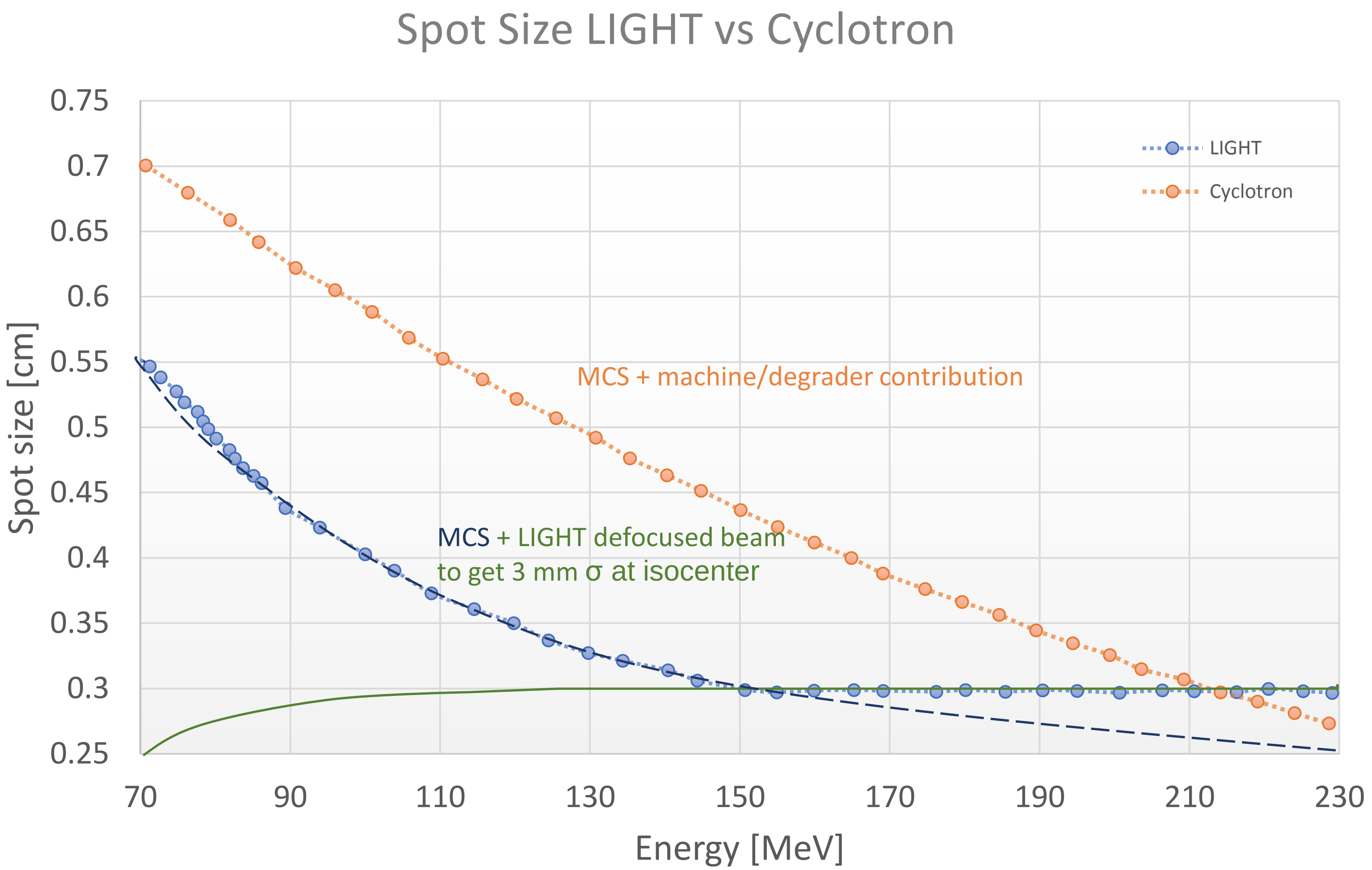


% dose difference between 3 mm and 12 mm σ plans indicating excess dose to the simulated OAR

J. Farr, D. Geismar, A. Kaiser, M. Stuschke, Westdeutsches Protonentherapiezentrum and Universitätsklinikum Essen, "Investigation of the relative conformality and efficiency for a series of different spot sizes in intensity modulated proton therapy," Oral presentation, DEGRO, June 2009, Bremen, Germany.

LIGHT®: More Conformal Dose Distribution – Spot Quality

Deliver Better Medical Outcomes



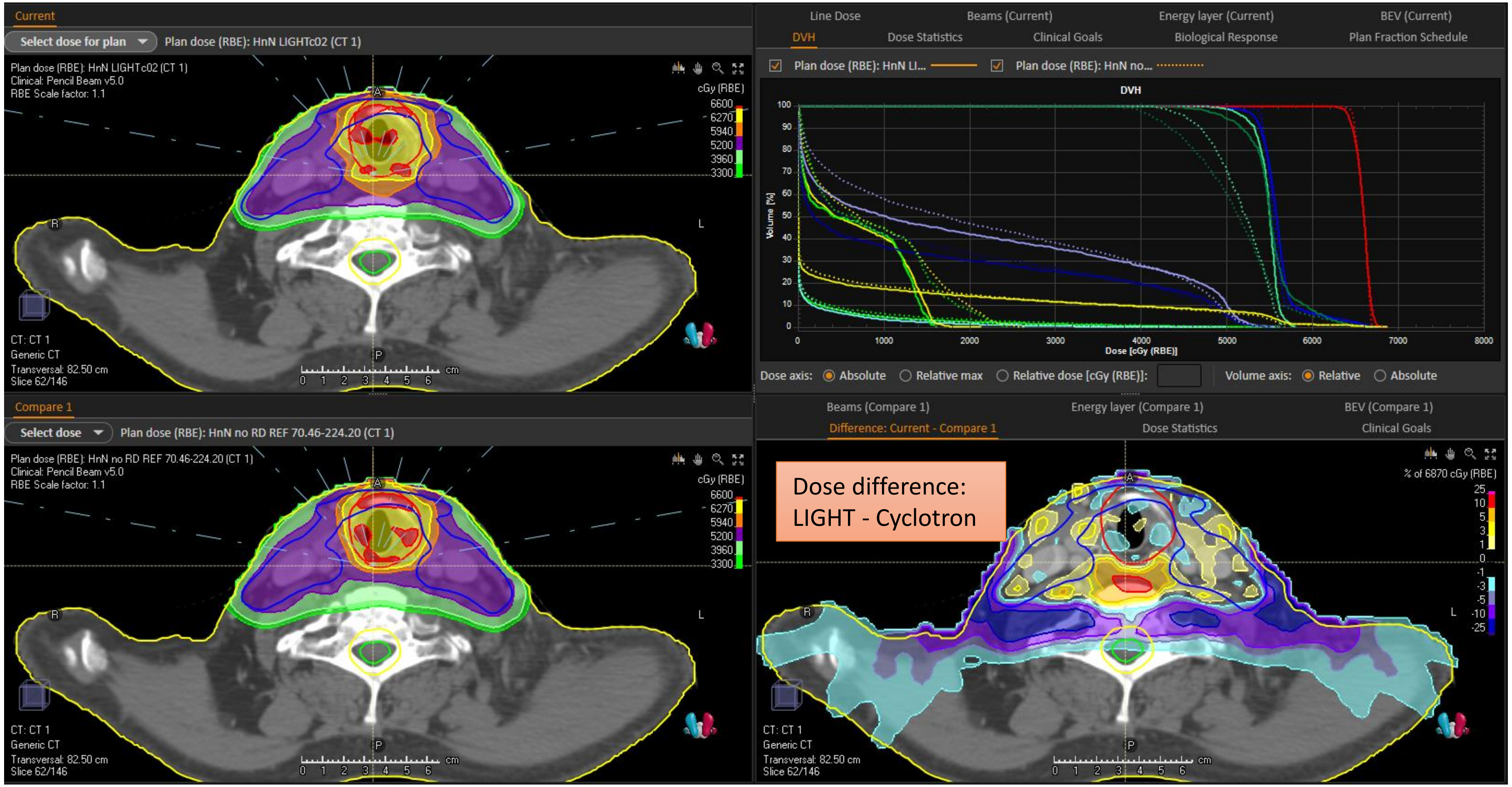
LIGHT can generate very small spot sizes. In order to match standard 3 mm σ at isocenter, the beam is defocused. In contrast, standard machine spot size is dictated by the beam deterioration after passing through the energy degrader.

LIGHT®: More Conformal Dose Distribution – Spot Quality

Deliver Better Medical Outcomes

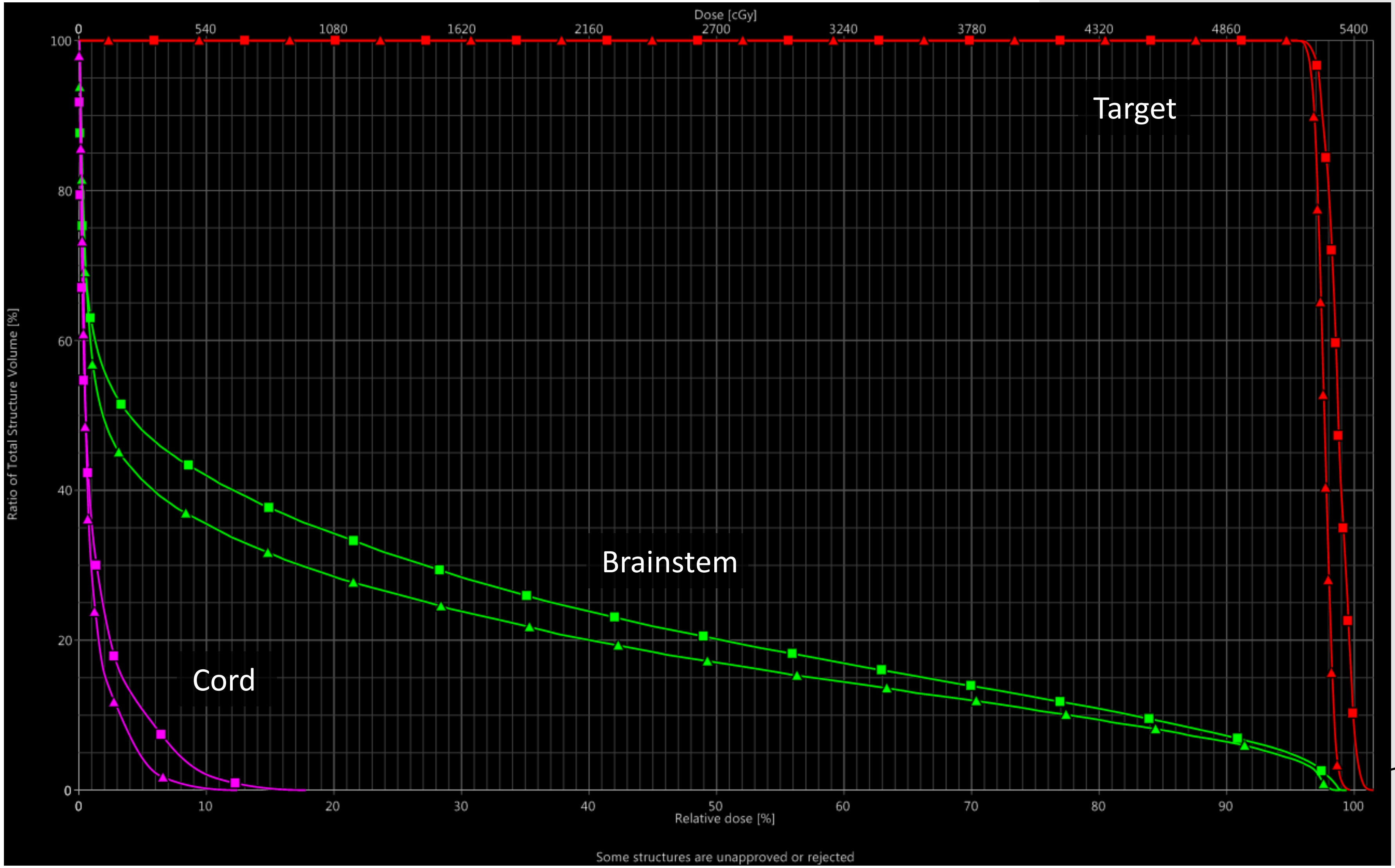
LIGHT

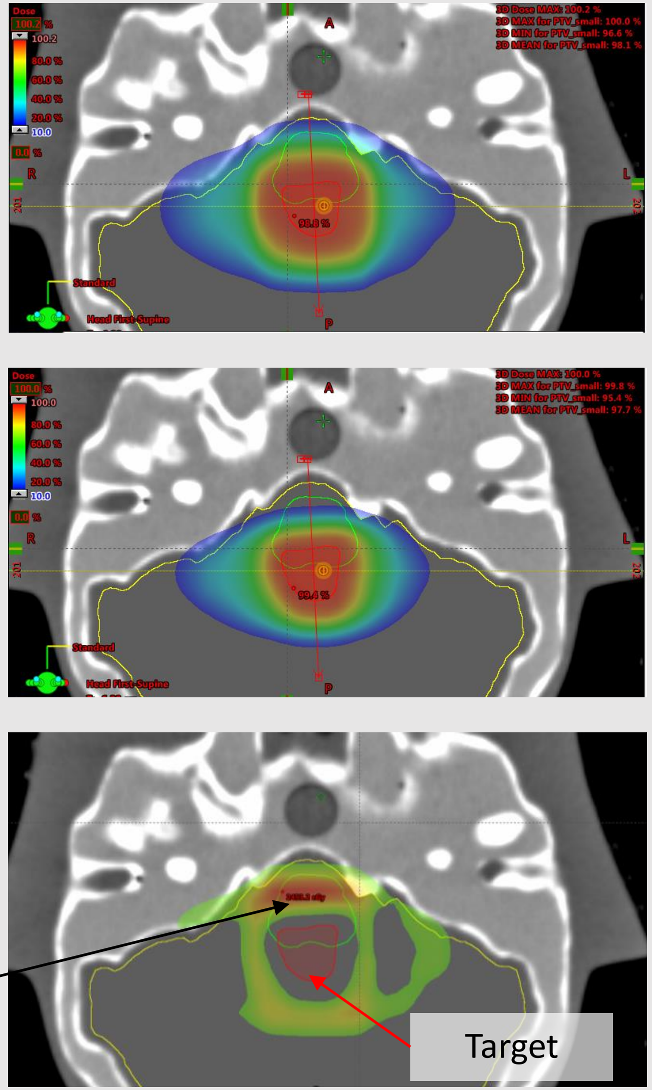
Cyclotron



1) *In draft for ESTRO 2020*

LIGHT®: More Conformal Dose Distribution – Proton Minibeams





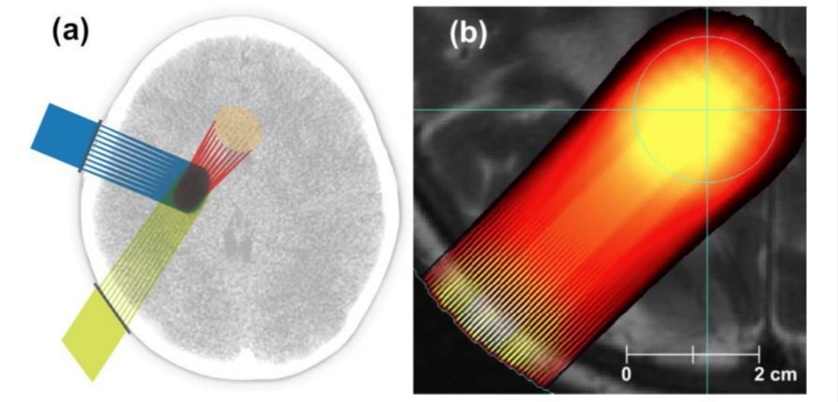
LIGHT®: Higher Dose and Fewer Fractions

- **Hypofractions (large dose fractions) offer advantages:**
  - Fewer total treatments are required
  - Greater patient convenience
  - More patients treated in the facility per year
  - Increased revenue
- **Expected LIGHT® Hypofractionation performance:**
  - Stereotactic Radiosurgery (SRS): Competing with GammaKnife treatments, the AVO partner is investigating SRS conformity with modelled LIGHT® minibeams.
  - Strereotactic Body Radiotherapy (SBRT): Using rapid 3D rescanning and Active Range Control, LIGHT® is designed expected to be a breakthrough proton SBRT platform.
- **In addition, LIGHT® is intended for FLASH treatment and may be uniquely suited to the most effective application of FLASH**

Source: Dilmanian, F. A., et al. (2015). "Minibeam therapy with protons and light ions: physical feasibility and potential to reduce radiation side effects and to facilitate hypofractionation." Int J Radiat Oncol Biol Phys 92(2): 469-474.

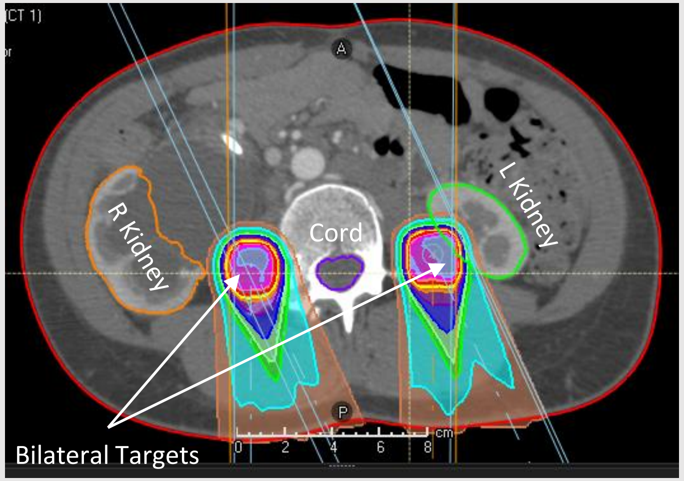
3 proton minibeams delivering SRS

Detail of proton minibeam on a brain MRI SRS target



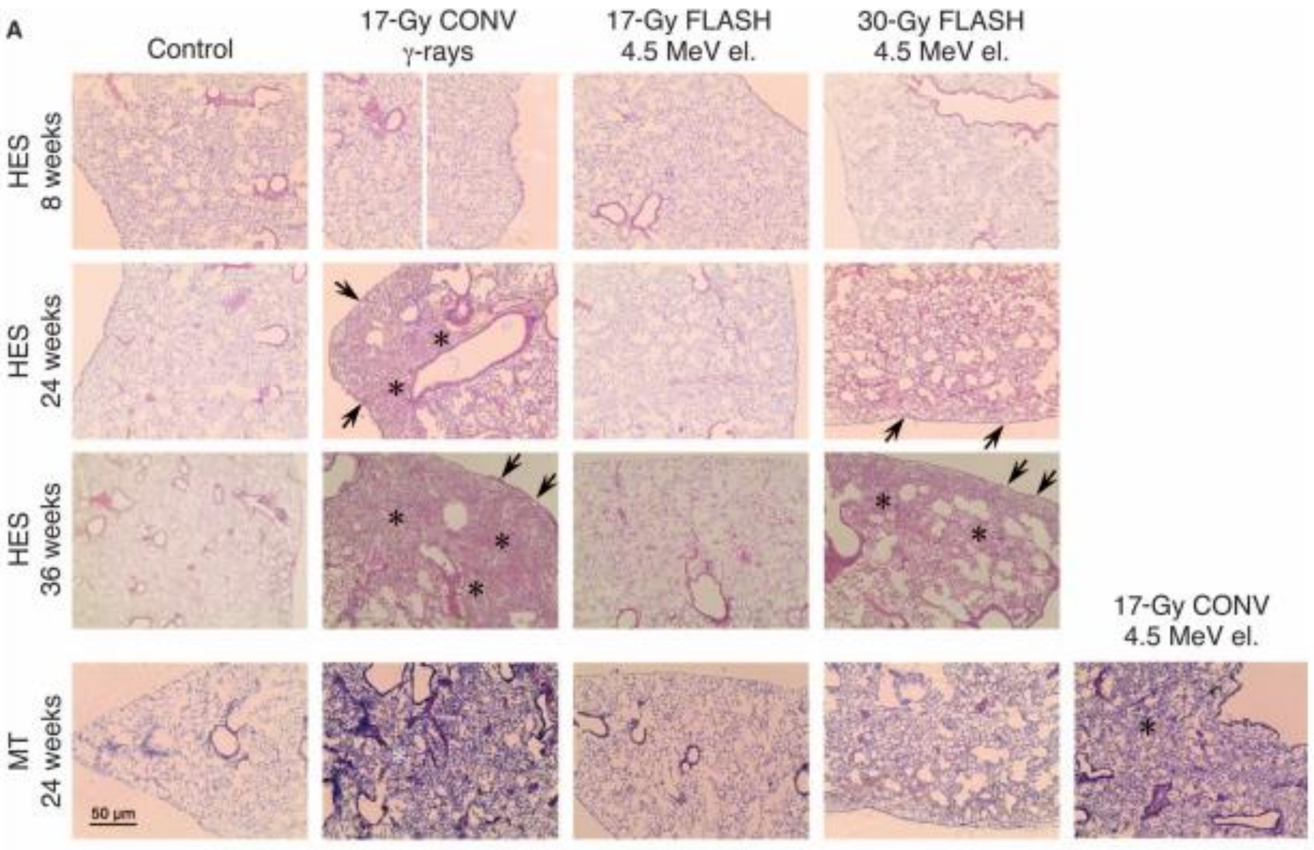
2 proton minibeams delivering SBRT

AVO unpublished



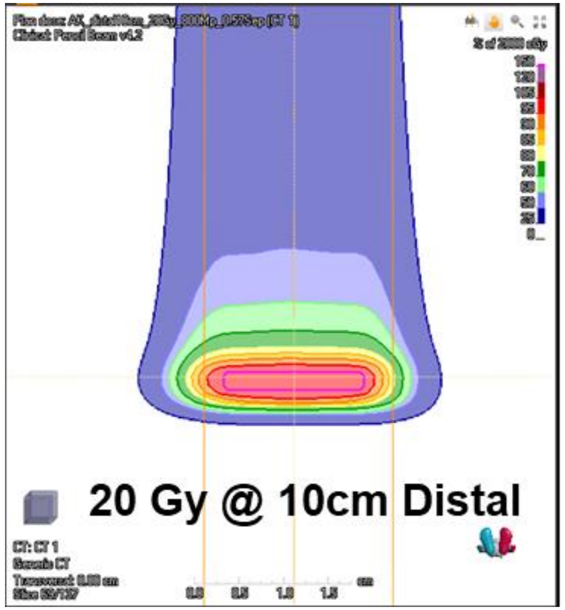
FLASH

- **FLASH involves high dose rates.**
- **Researchers are finding that tumours respond the same to FLASH treatments as they do with regular treatments, but that normal tissues have almost no response to FLASH**
- **Additional protection to normal tissue is provided**
- **Potential major impact on curing more cancer with less toxicity to the patient**



www.ScienceTranslationalMedicine.org 16 July 2014

Proton FLASH



FLASHLIGHT planned irradiation to a 2 cm target cross-section at 10 cm depth in water.

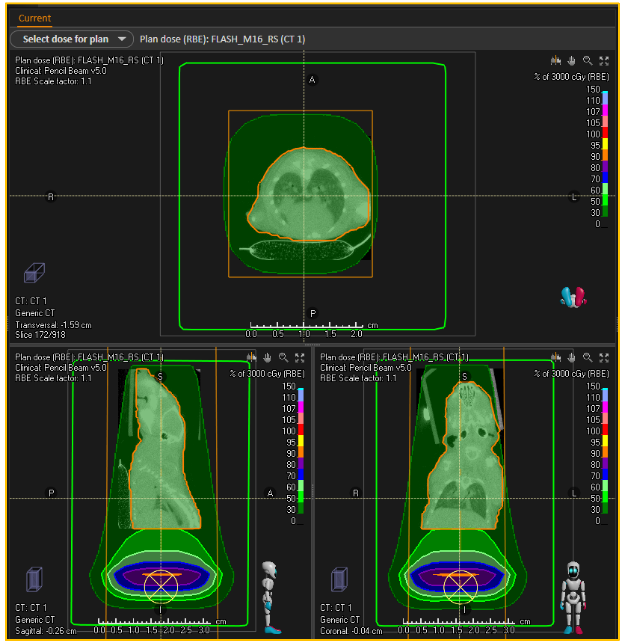
LIGHT intends to provide FLASH treatments and may be uniquely suited to the most effective application of FLASH.

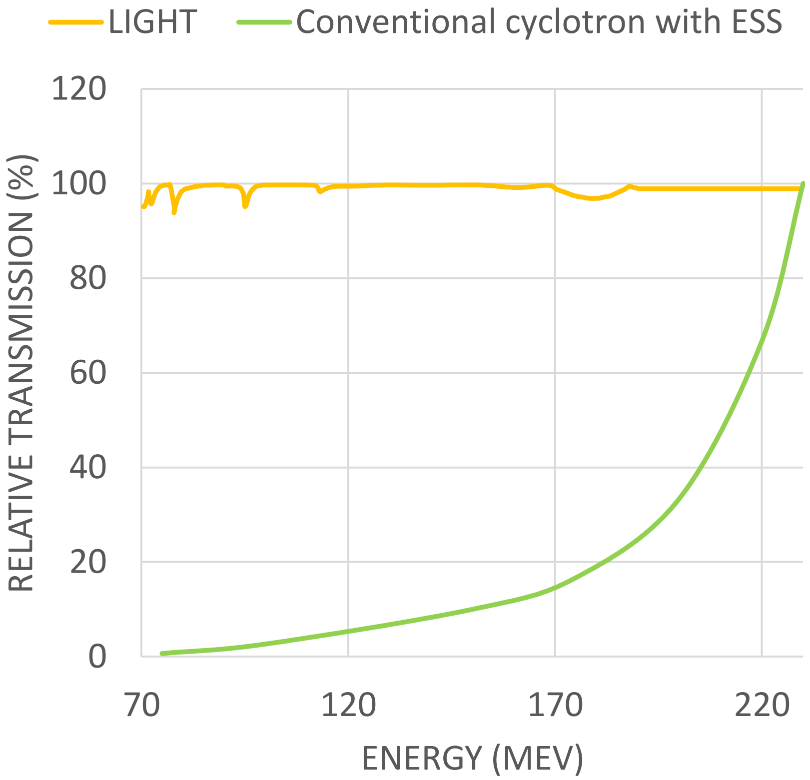
Target	Depth	Dose [Gy]	Machine Max NP per pulse [Mp]	Min spot weight [10^6 NP]	Max spot weight [10^6 NP]	No of layers	Spot spacing [cm]	Snout position [cm]	No of repaintings	Time to deliver [s]	Mean Dose rate [Gy/s]
$2\ cm^2 \times 0.2\ cm$	Depth 0.2 cm	10	200	1.05	190.00	4	0.6	0.2	1	**0.49**	**20.4**
		20	500	17.21	474.98		0.62			**0.49**	**41.3**
		30	800	1.06	759.99		0.59			**0.53**	**57.3**
		40	800	1.56	760.00		0.59			**0.50**	**80.2**
	Depth 10 cm	10	200	4.80	190.00	4	0.5	0.2	1	**0.50**	**20.2**
		20	500	8.62	474.95		0.5			**0.47**	**43.0**
		30	800	2.27	760.00		0.57			**0.42**	**72.3**
		40	800	81.69	760.00		0.57			**0.43**	**93.1**

Proton FLASH

- Cyclotron
- Synchrocyclotron
- Synchrotron?
- Linac
- Scattering?
- Scanning?
- Target size?
- Target depth?

10 Gy FLASH dose distribution of a mouse planned using beam plateau.





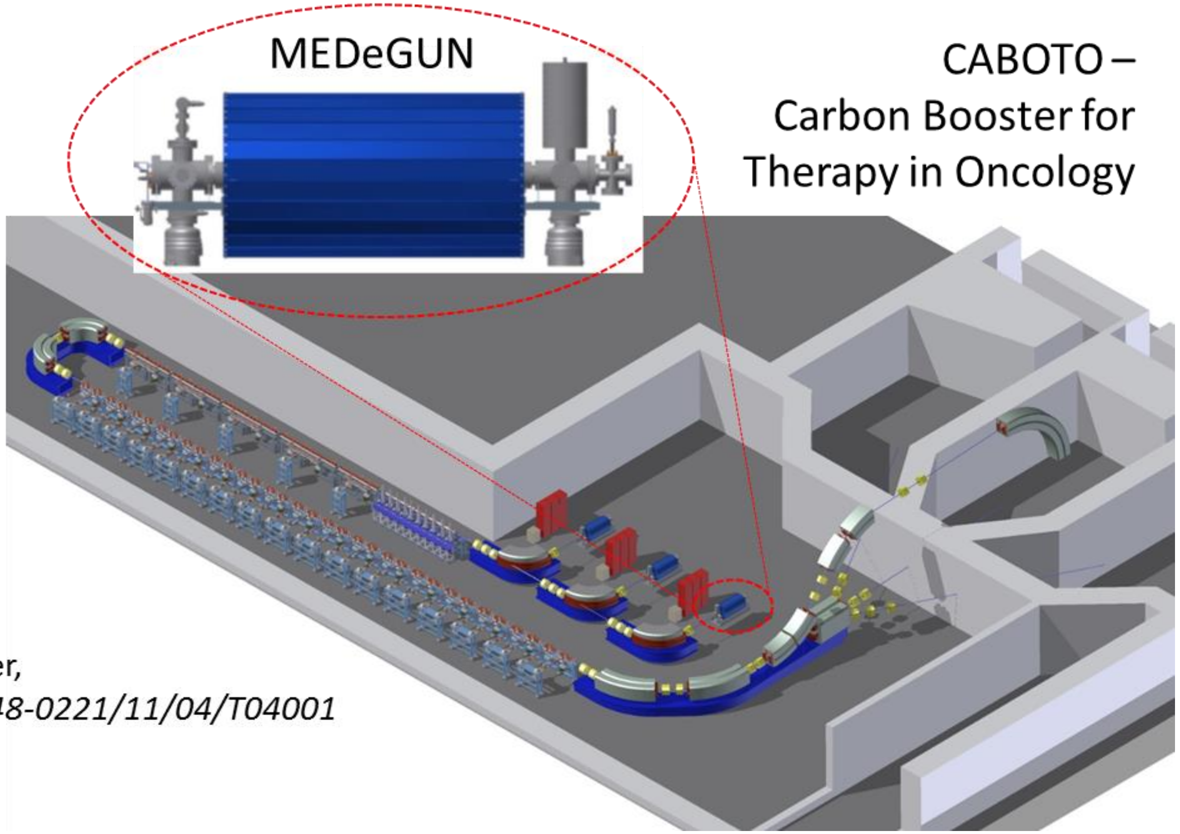
A.M. Kolano, A. Degiovanni, **J. B. Farr**, Applications of Detectors and Accelerators to Medicine (ADAM) SA, Geneva, Switzerland, "Investigation on FLASH therapy using a high frequency linac for protons," ePoster, PTCOG, June, 2019, Manchester, England.

Heavier ions

CERN PIMMS2 Development

- **Multiple ion sources**
- **750 MHz RFQ**
- **High gradient LINAC cavities**
- **High gradient means high RF power: needs efficient low-cost RF power sources.**
- **The linac offers the advantage of pulse-to-pulse energy modulation at high repetition frequency.**

HF-linac requirements:
- **300 – 400 Hz**
- **< 5 μs** pulses
- **10^8 C^{6+}** ions per pulse



* A. Shornikov and F. Wenander,
http://dx.doi.org/10.1088/1748-0221/11/04/T04001

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Dr. Mike Sinclair
Mr. Nicolas Serandour
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