27.10.2020

ADVANCED ONCOTHERAPY

ADAM an ADVANCED ONCOTHERAPY company

CERN spin-off

Advanced Oncotherapy

Delivering Affordable Proton Therapy

Energy Focused on Saving Lives

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

CERTIFIED ISO 13485

UKAS

Forward Looking Statement

This presentation may contain certain projections and other forward-looking statements with respect to the financial condition, results of operations, businesses and prospects of **Advanced Oncotherapy plc ("AVO", "Advanced Oncotherapy" or the "Company")**. These statements are based on current expectations and involve risk and uncertainty because they relate to events and depend upon circumstances that may or may not occur in the future. There are a number of factors which could cause actual results or developments to differ materially from those expressed or implied by these forward-looking statements. Any of the assumptions underlying these forward-looking statements could prove inaccurate or incorrect and therefore any results contemplated in the forward-looking statements may not actually be achieved. Nothing contained in this presentation should be construed as a profit forecast or profit estimate. Investors or other recipients are cautioned not to place undue reliance on any forward-looking statements contained herein. Advanced Oncotherapy undertakes no obligation to update or revise (publicly or otherwise) any forward-looking statement, whether as a result of new information, future events or other circumstances. Neither this presentation nor any verbal communication shall constitute an invitation or inducement to any person to subscribe for or otherwise acquire securities in Advanced Oncotherapy.

Outlook

- **Advanced Oncotherapy** *10'*
  - Mission and Roadmap
- **My personal experience at Advanced Oncotherapy** *5'*
  - Role and responsibilities
- **Deep dive into Advanced Oncotherapy** *10'*
  - A medical device company
  - Company structure and skills

Outlook

- **Advanced Oncotherapy** *10'*
  - Mission and Roadmap
- **My personal experience at Advanced Oncotherapy** *5'*
  - Role and responsibilities
- **Deep dive into Advanced Oncotherapy** *10'*
  - A medical device company
  - Company structure and skills

Who

- **Advanced Oncotherapy** is a **Medical Device Manufacturing Company** developing a breakthrough proton therapy system**:**

  the LIGHT system

- **AIM listed company**

- **Market capital ~111M£**

- **Operations in**
  - UK, head office in London
    - V&V site at STFC
  - US, Syracuse, NY
  - CH, R&D facility ADAM S.A.

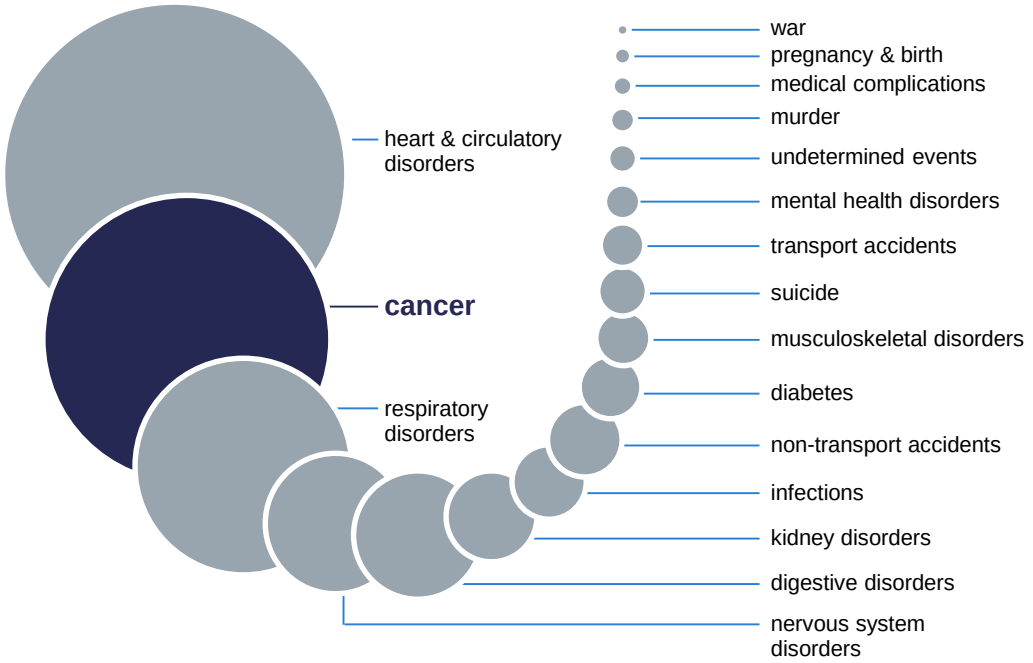
CERN spin-off

LiGHT
Linac for Image Guided Hadron Therapy

https://www.avoplc.com/

Why - Cancer, Second Cause of Death

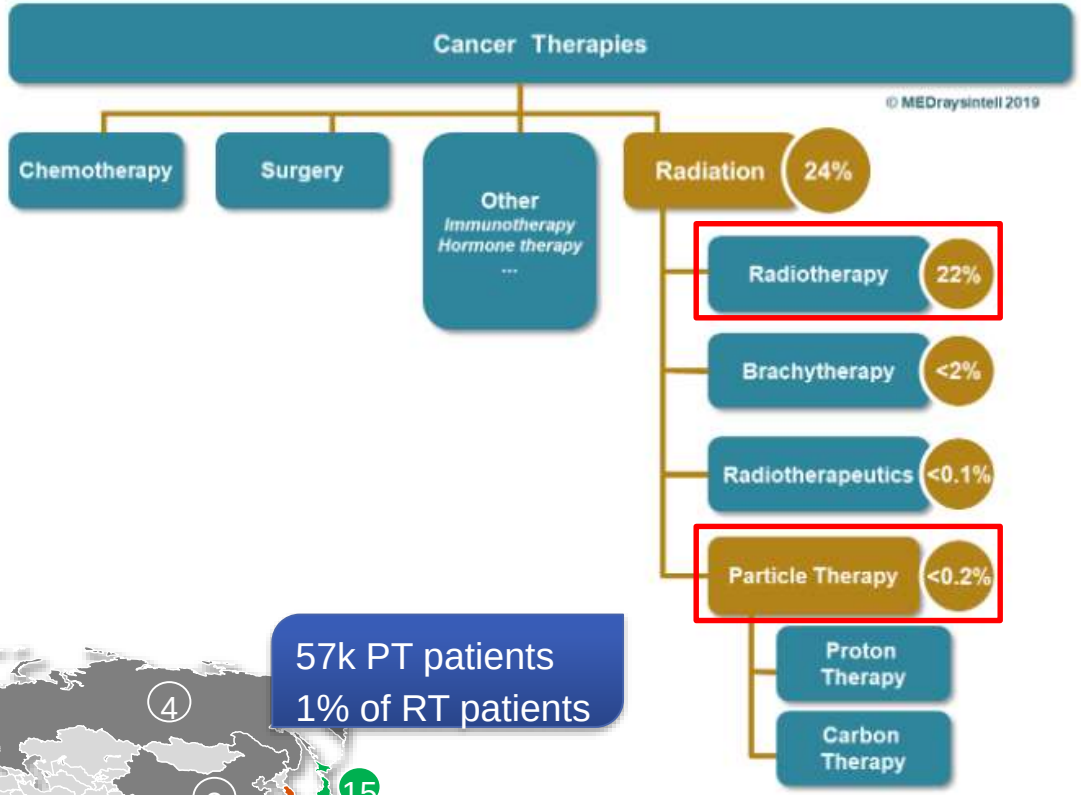
- Cancer is the second leading cause of death globally
- Responsible for an estimated 9.6 million deaths in 2018 – **about 26k people died of cancer every day in 2018!**
- Cancer affects 1 in 2
- Globally, about 1 in 6 deaths is due to cancer

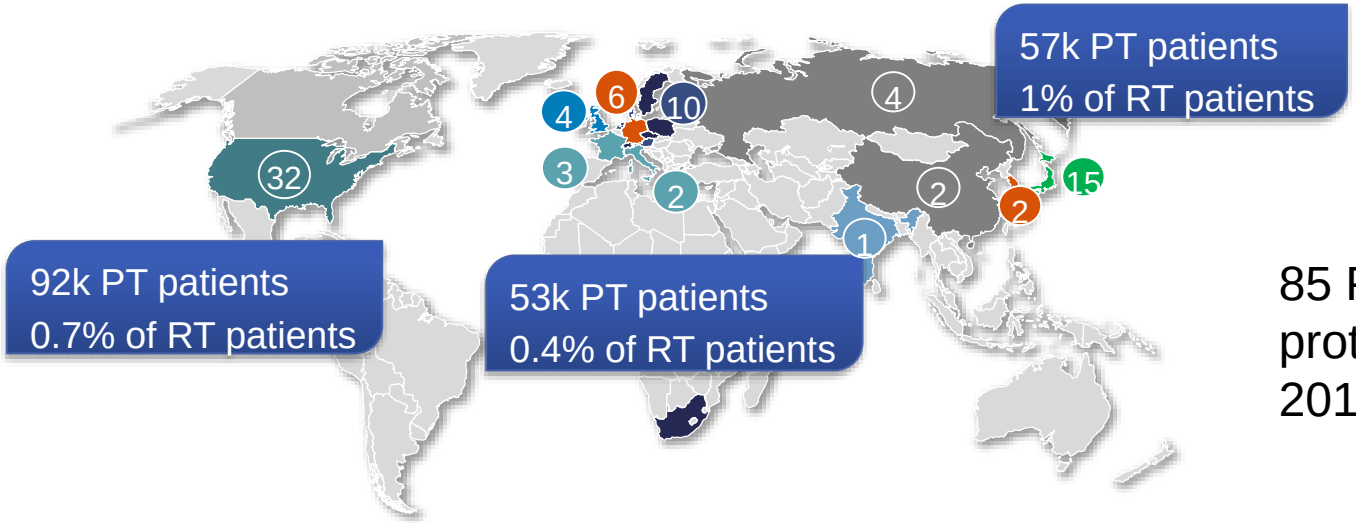


Source: IHME, Global Burden of Disease (GBD)

How – cancer treatment techniques

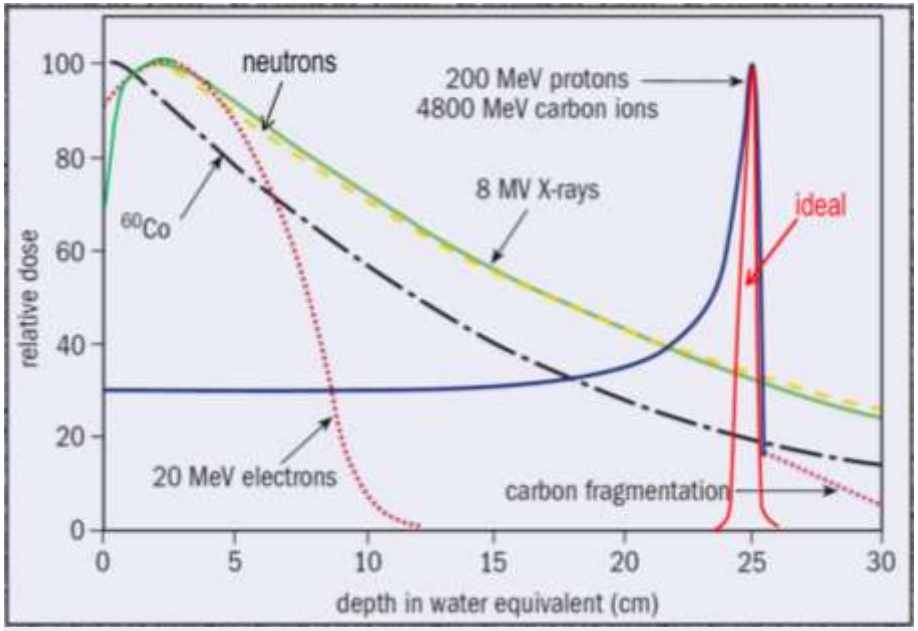
- **Surgery**
- **Radiation Therapy**
  - External beam
  - Brachytherapy
- **Chemotherapy**
- **Immunotherapy**
- **Targeted Therapy**
- **Hormon Therapy**
- **Stem Cell Transplant**
- **Precision Medicine**





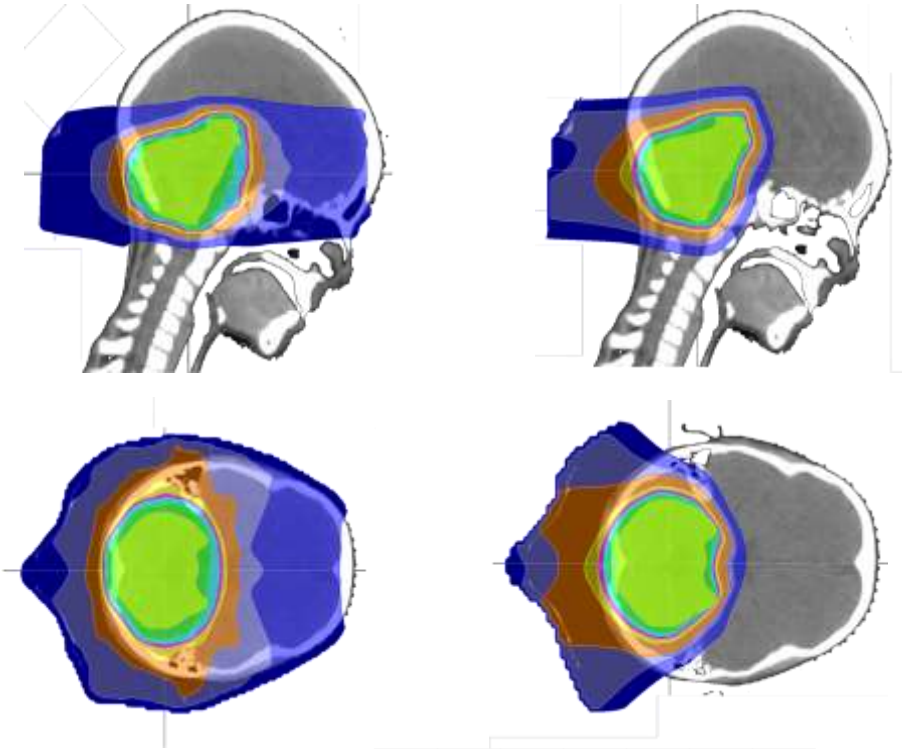
85 PT operational proton facilities in 2019

Clinical benefits - Radiotherapy vs Protontherapy



Distribution of deposited dose in tissue is different for each type of particle.

Photon Therapy (X-rays) | **Proton Therapy**



Radiation (Gy): 31 | 29 | 28 | 24 | 15 | 9 | 2

Source: American Society of Clinical Oncology & BCG

Radiation dose must take into account a number of factors:

- the goals of the physician
- the tumor being treated
- the amount of fractionation planned
- the presence of nearby organs
- whether chemotherapy or immunotherapy is being given at the same time

Example:
- Stage I lung cancer: 54 Gy total given over 3 sessions
- Stage III lung cancer: 60 Gy total given over 30 sessions
- Stage I breast cancer: 40 Gy total given over 15 sessions
- Stage IV prostate cancer, spread to the bone: 8 Gy total given over 1 session

Conventional radiotherapy vs protontherapy (PT)

- PT destroys the primary tumour site while **leaving surrounding healthy tissue and organs intact and unharmed**.
- Is a **highly effective treatment** for a wide range of localized tumors in **head and neck area, lung, prostate, bladder, spinal cord, gastro malignancies, ocular tumours, liver, breast, esophagus, rectum, skull base sarcomas, among others**
- Is a **highly preferred** radiation treatment option **for pediatric cases**. Children are susceptible to injury from standard x-ray radiation because their tissues and organs are growing rapidly.

https://youtu.be/MbwG_E3GHBI

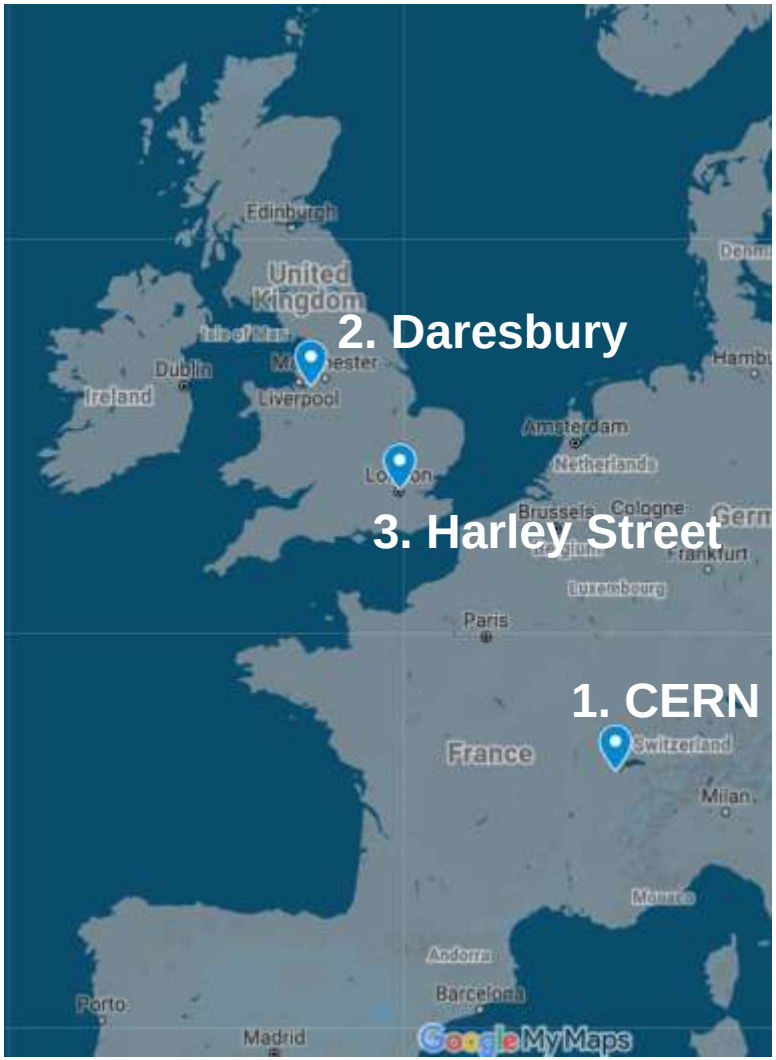
LIGHT project

Milestones:

1. **Technology Validation**
   (Prototype at CERN)

2. **Medical Certification**
   (Verification & Validation at Daresbury)

3. **First commercial product**
   (Harley Street)



LIGHT – Linac technology

The LIGHT accelerator comprises 4 sections: the Proton Injector, the RFQ, the 4 SCDTLs and the CCLs

Active energy modulation
- No absorber and degrader.

Pulsed beam at 200Hz
- Fast intensity and energy modulation
- Image guided hadron therapy.

Pencil beam scanning or 'spot' scanning
Modularity and flexibility

Proton Injector

- **Pantechnik** (at Pt2 bunker)
- **Dreebit** (at DIS)
- **ADAM:** adapt and optimize for variable intensity

Radio Frequency Quadrupole

- **CERN-ADAM** (2013-2015)
- 1st prototype, unique in the world
- Industrialization by **ADAM**

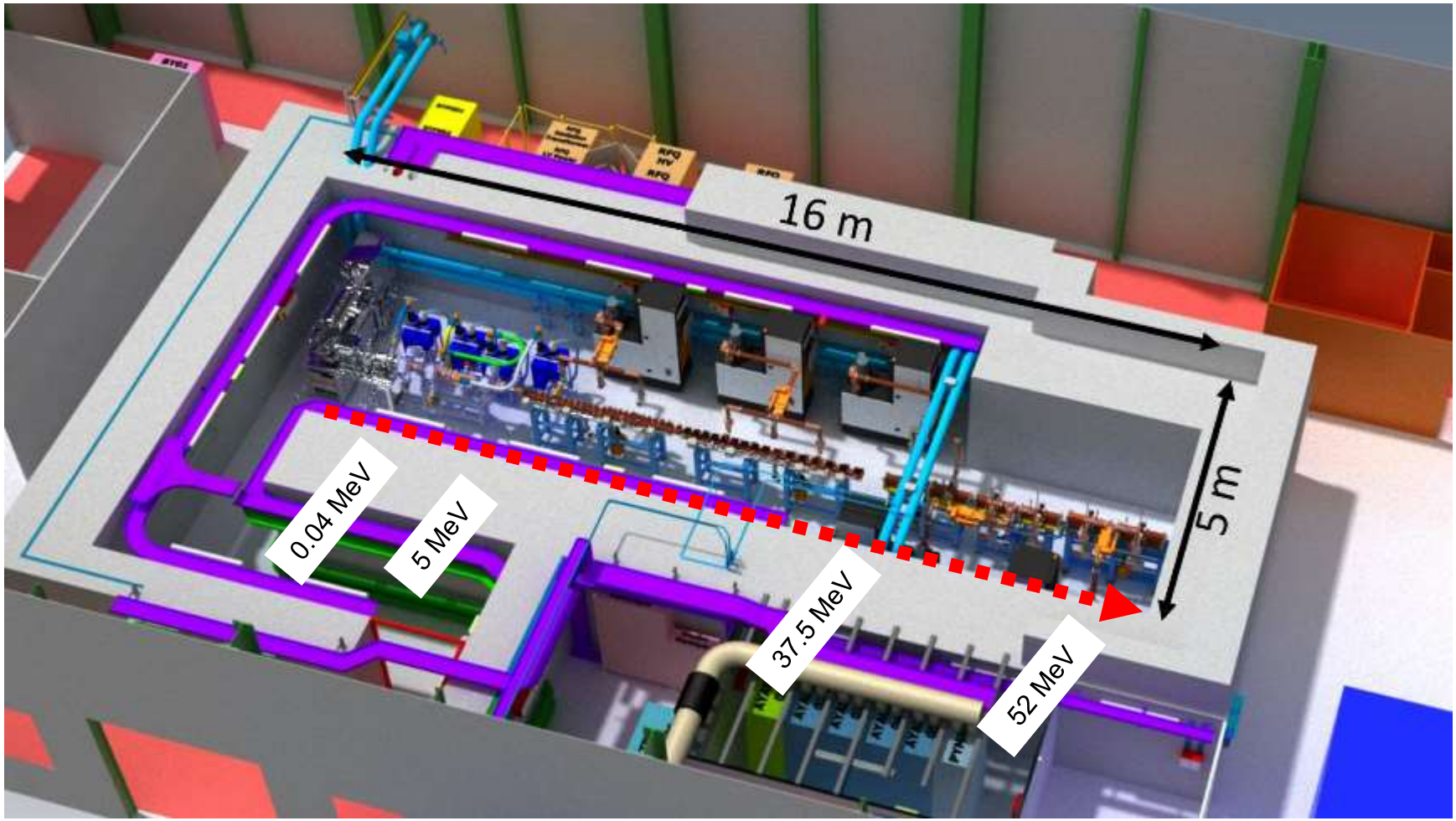
Side Coupled Drift Tube Linac

- **ENEA** concept (Picardi et al. 1996)
- Tested with beam in ENEA Frascati (IMPLART project) since 2011
- Industrialization by **ADAM**
- Mass production by **ADAM**

Coupled Cavity Linac

- **TERA-CERN-INFN** concept (LIBO, 1998-2000)
- Tested **with beam** in Catania in 2002
- Industrial design by **ADAM** (first Unit, 2010)
- Mass production by **ADAM**

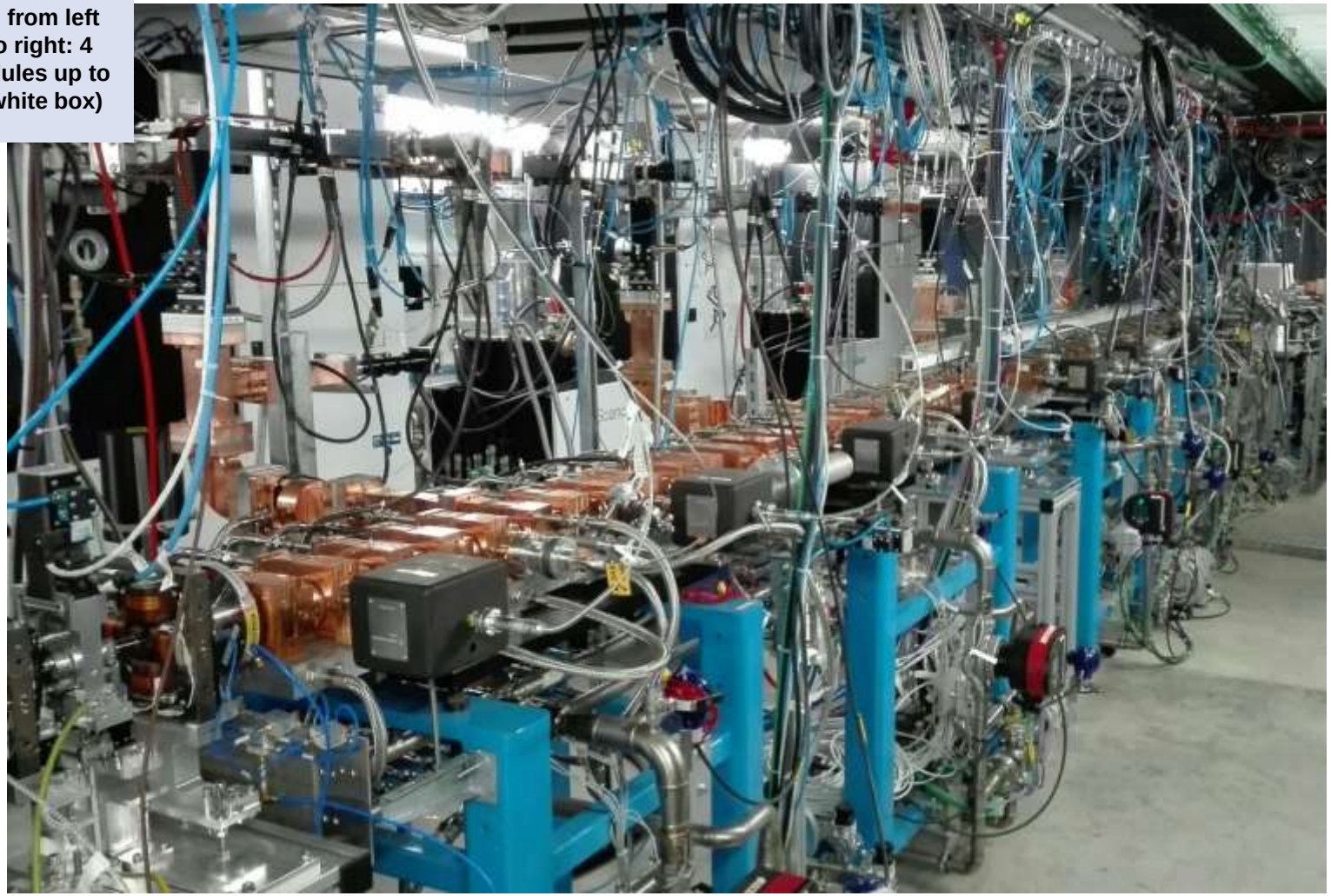
LIGHT Linac Technical Development: P2 bunker (CERN)



Integration:	Source	RFQ	SCDTL1	SCDTL 2	SCDTL3	SCDTL4	CCL1-2
B. energy:	40 keV	5 MeV	7.5 MeV	16 MeV	26.5 MeV	37.5 MeV	52 MeV

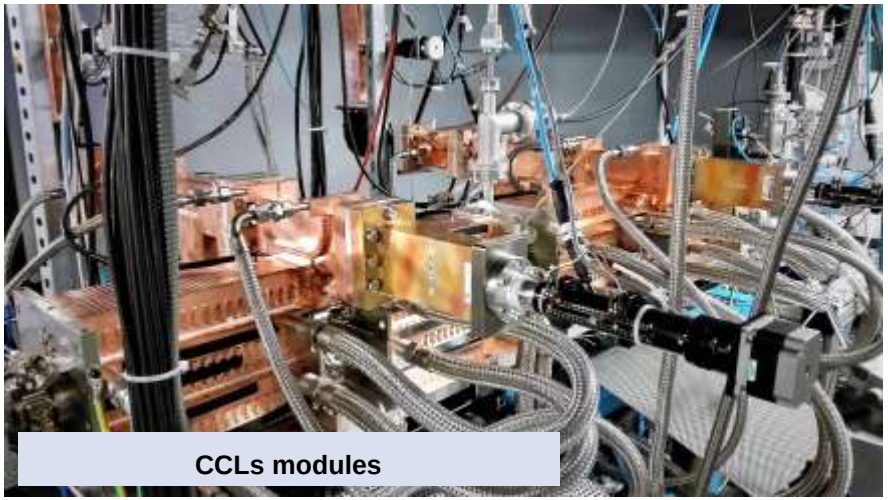
LIGHT Linac Technical Development: P2 bunker (GVA)

P2 bunker - from left (injection) to right: 4 SCDTL modules up to the MLFC (white box)

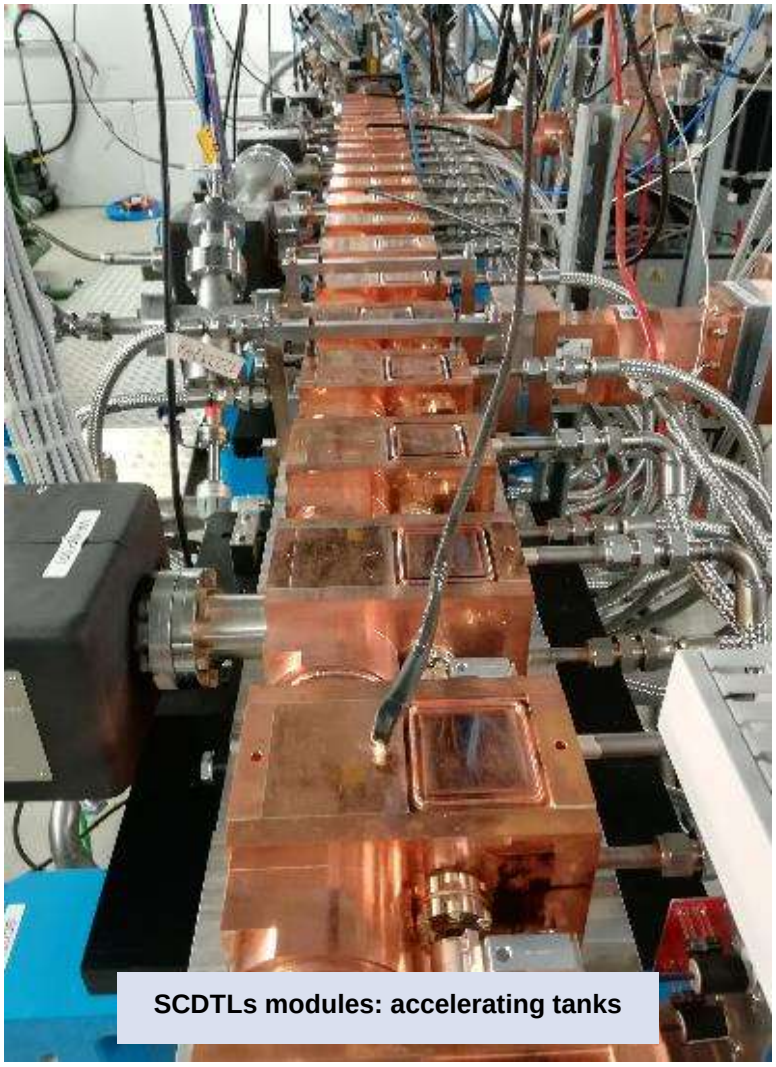


LIGHT Linac Technical Development: P2 bunker (GVA)

RFQ and its coaxial power lines



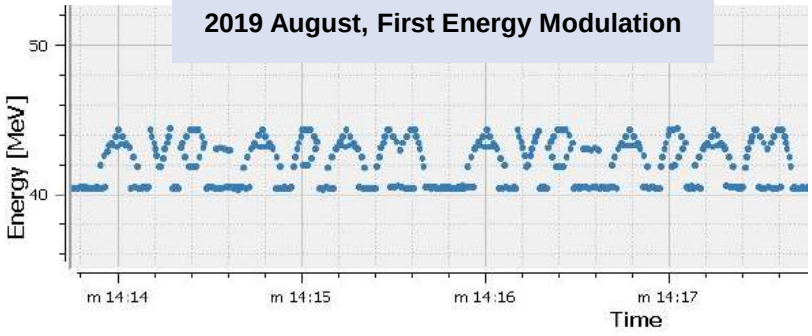
CCLs modules



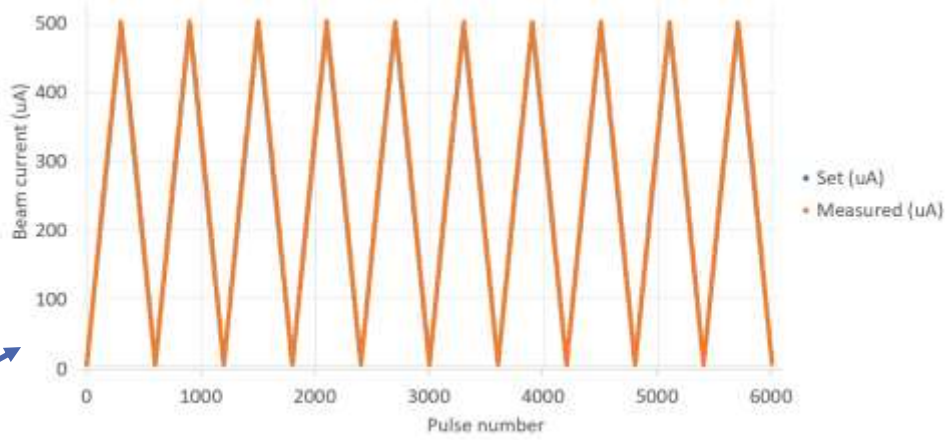
SCDTLs modules: accelerating tanks

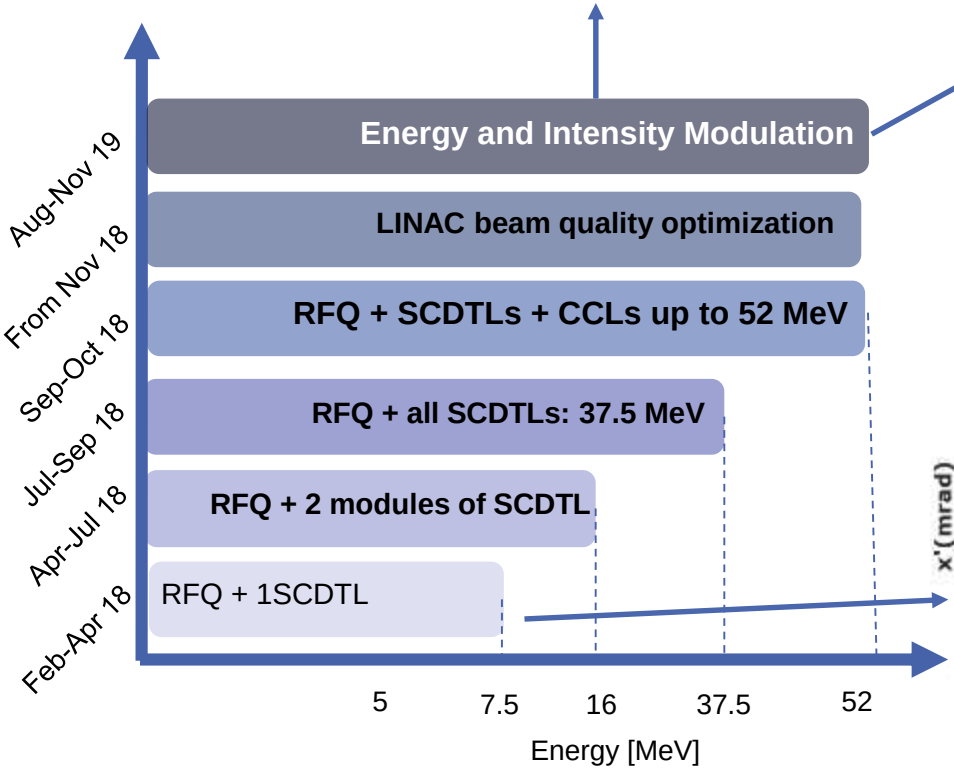
Technology Validation @ CERN

2019 August, First Energy Modulation

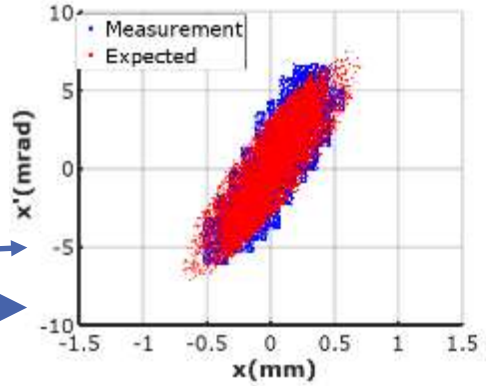


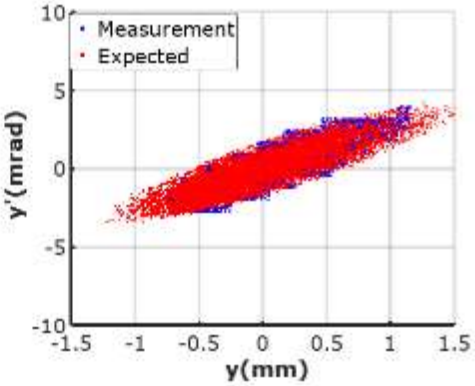
2019 November, First Intensity Modulation



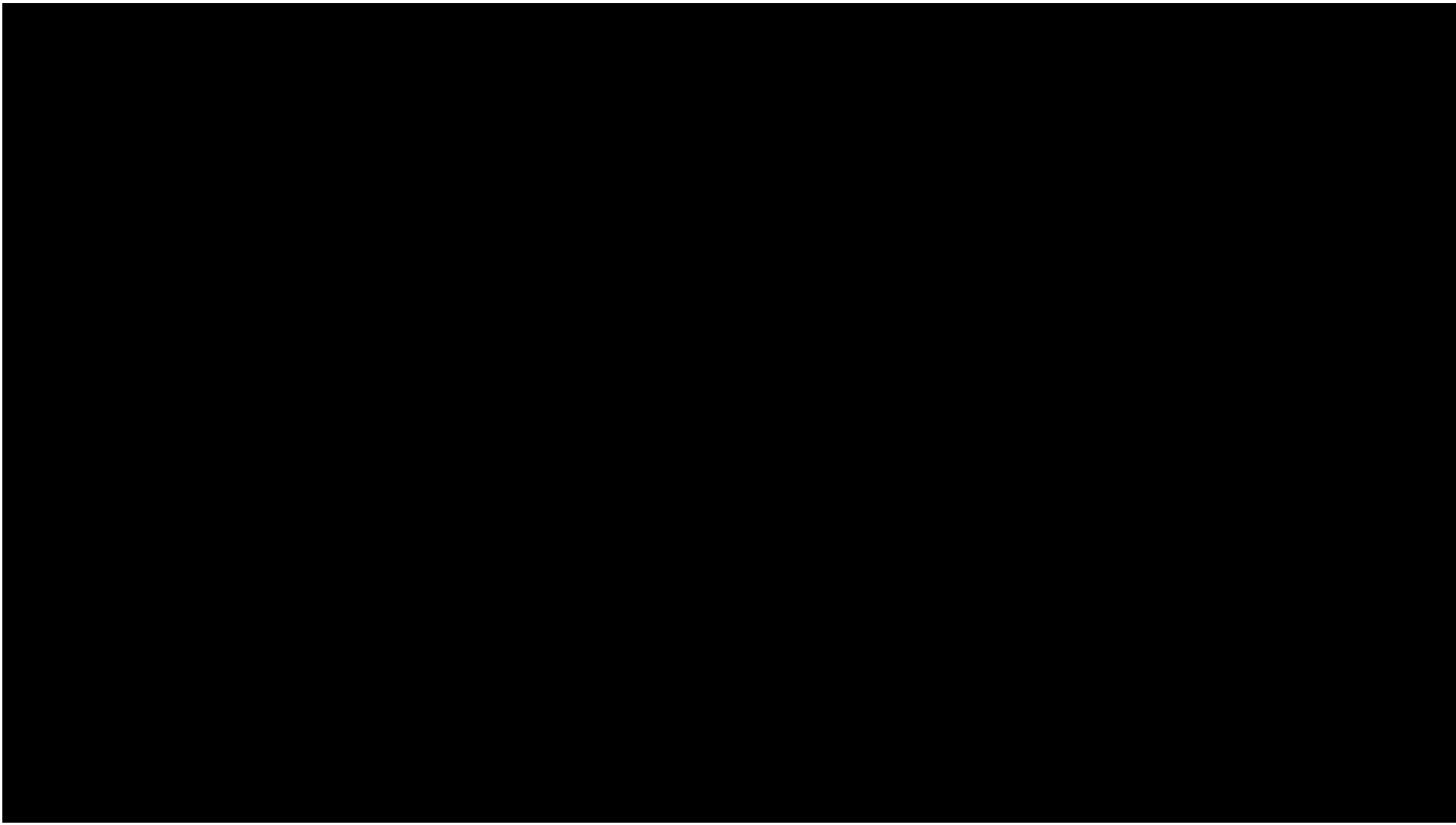


RFQ Beam characterization



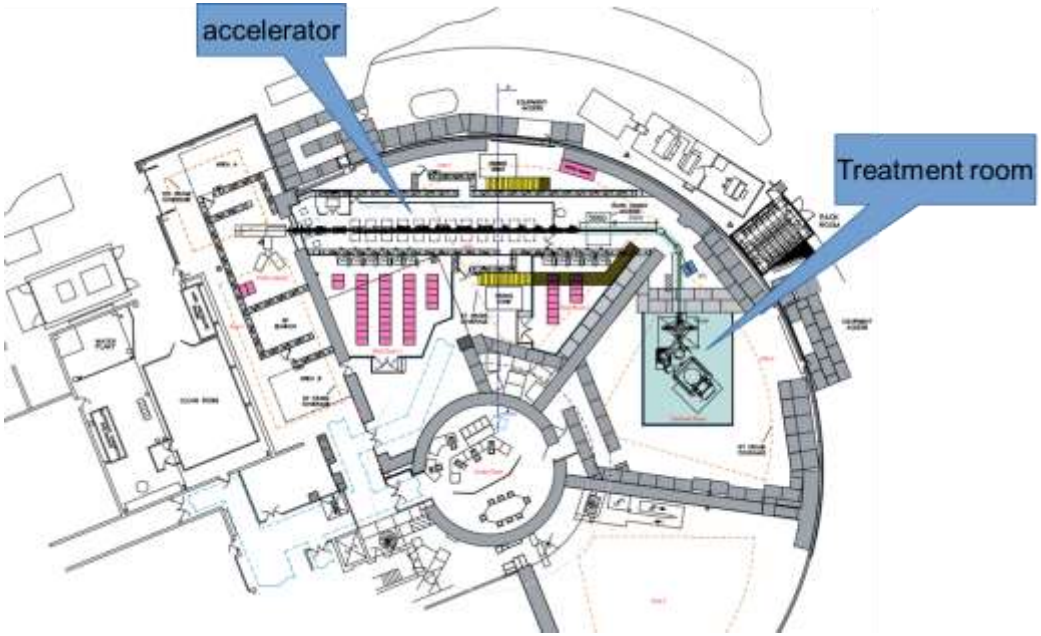


The LIGHT Proton Therapy Solution



Daresbury Integration Site

STFC Daresbury laboratory, Daresbury, Warrington



- **Daresbury Integration Site (DIS):** technical test site in UK
- **End-to-end testing:** Accelerator & Medical technical systems
- After the complete installation and integration → **V&V tests**
- **Partnership with University Hospital Birmingham NHS Foundation Trust ("UHB")** is aimed at treating patients in Daresbury in the context of our certification plan

Hardware for DIS

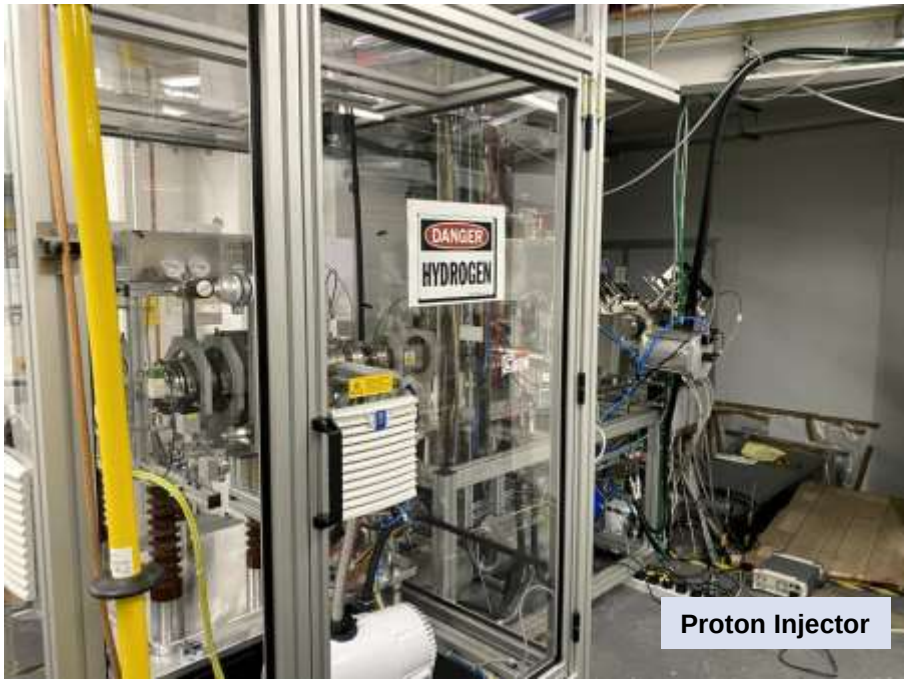
RFQ SAT and tuned at DIS.

SCDTL-01 and 02 under SAT at DIS

Rack room

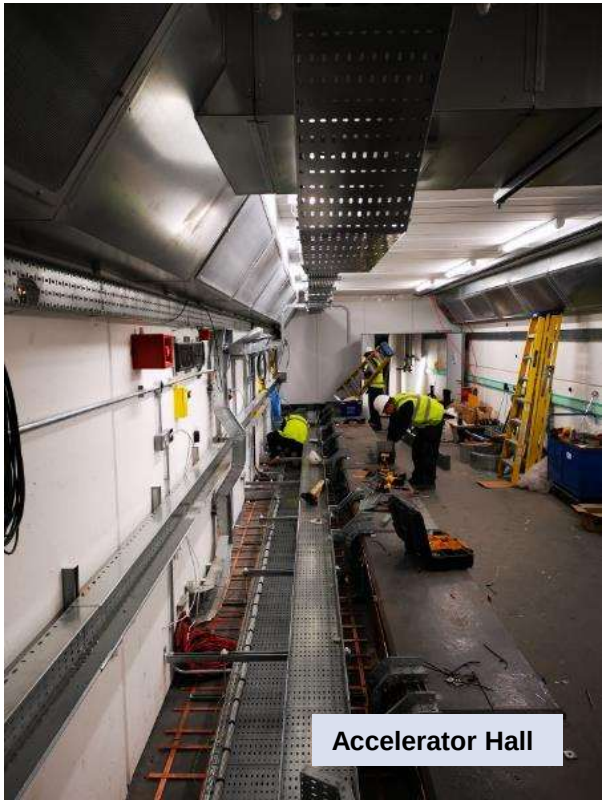
Rack room

Hardware for DIS



Proton Injector


Control Room


Accelerator Hall

Harley Street, London, the First Site Housing LIGHT

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

Harley Street project is the demonstration of the LIGHT integration flexibility thanks to its modularity.

Outlook

- **Advanced Oncotherapy** *10'*
  - Mission and Roadmap
- **My personal experience at Advanced Oncotherapy** *5'*
  - Role and responsibilities
- **Deep dive into Advanced Oncotherapy** *10'*
  - A medical device company
  - Company structure and skills

Personal Details

- **Advanced Oncotherapy, plc, London, UK and Geneva, Switzerland** **2017 –**
  (Deputy Technical Director | Product Manager)

- **Advanced Oncotherapy, plc, London, UK and Geneva, Switzerland** **2014 –**
  (RF Head | People Management | Technical Leader)

- **EPFL, Lausanne, CH - PSI, Villingen, CH – CERN – Geneva, CH** **2011 – 2014**
  (Ph.D. in Acc. Physics – senior engineer)

- **CERN, Geneva, CH** *(senior engineer)* **2008 - 2010**

- **CERN, Geneva, CH** *(junior engineer)* **2007 - 2008**

- **M.Sc. Telecommunication Engineering** **2007**

Outlook

- **Advanced Oncotherapy** *10'*
  - Mission and Roadmap
- **My personal experience at Advanced Oncotherapy** *5'*
  - Role and responsibilities
- **Deep dive into Advanced Oncotherapy** *10'*
  - A medical device company
  - Company structure and skills

Case study: a particle accelerator to treat patients

- **Medical Devices:** products, services, or solutions tat prevent , diagnose, monitor, treat and care for human being by physical means
- **A particle accelerator** design and development is very different when the accelerator is used for **medical purposes vs. fundamental research.**
- Need to prove **safety and effectiveness**, by observing regulations, implementing standards and following guidelines.

The manufacture is the legal responsible body for the medical device.
He is responsible to ensure the device is safe and performs as expected

In EU, the Notified Body, is an organization that has been accredited by a Member State to assess whether a product meets defined requriements.

The particle accelerator: one piece of a puzzle

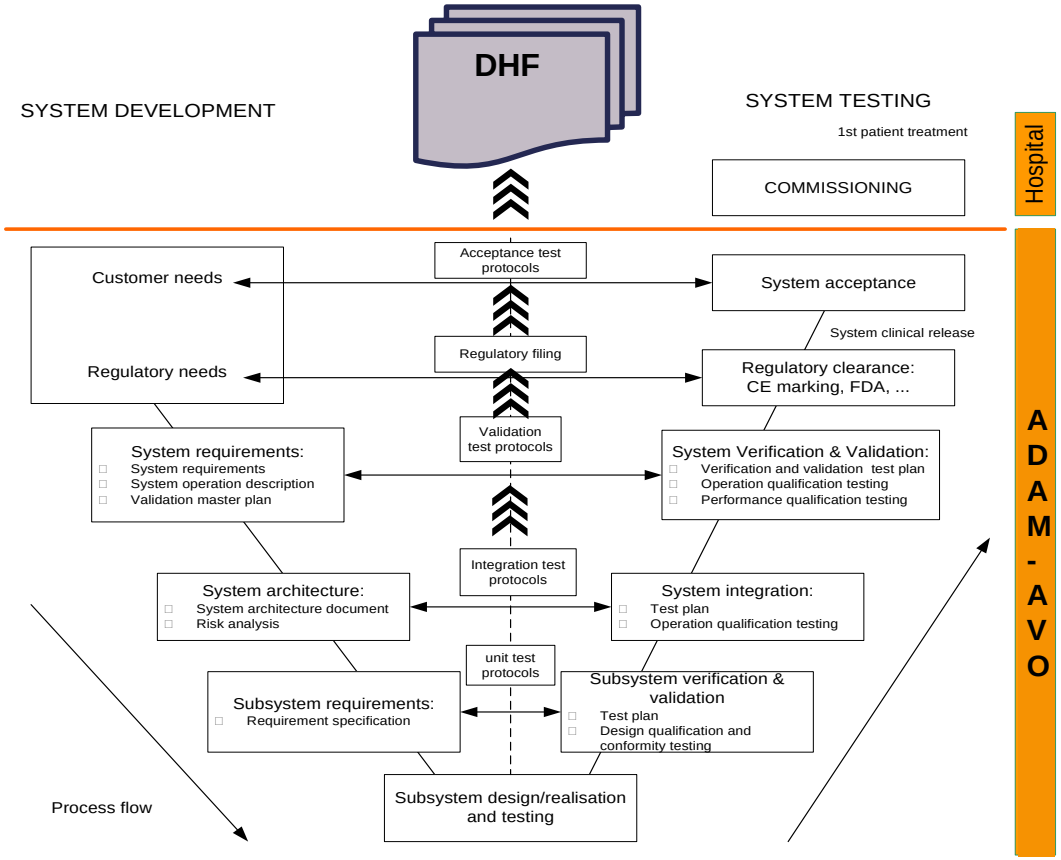
The particle accelerator is only a system among the others: it is responsible for the **beam production.** In addition one needs to measure and control the dose delivery (**dose delivery system**), to accurately position the patient (**patient imaging and positioning system**), to control the operation and execution of the treatment (**treatment planning system**), etc. All together is a medical device.

In order to **meet customer's requirements, meet applicable regulatory requirements,** the company has to put in place a **QMS** (ISO13485) which is an organizational structure to ensure consistent design, development, production, installation and delivery of a medical device that is **safe** and **effective** for its intended use.

QMS – Product Realization

Design History File (DHF): history of the design to ensure it was done according to the regulations.

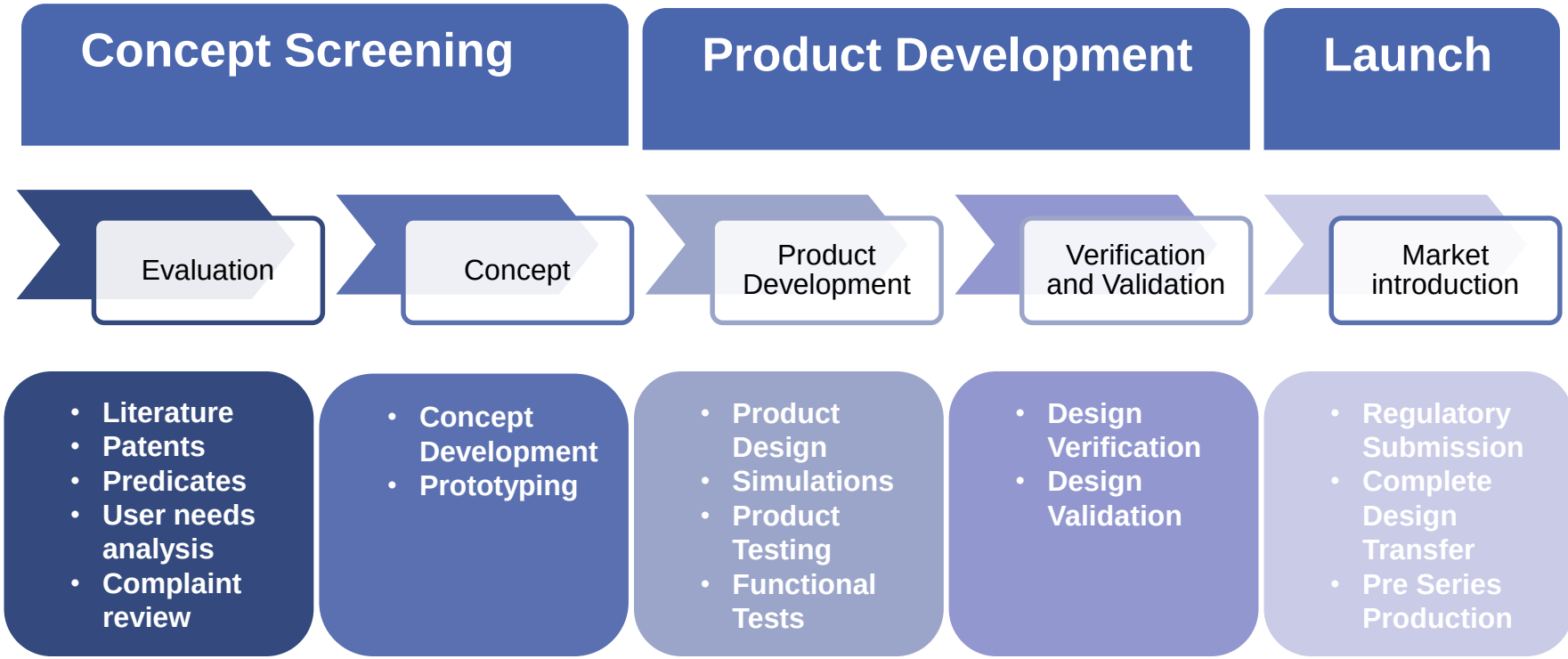
Device Master Record (DMR): to ensure you have all of the necessary items to build, test, package, and service the device.



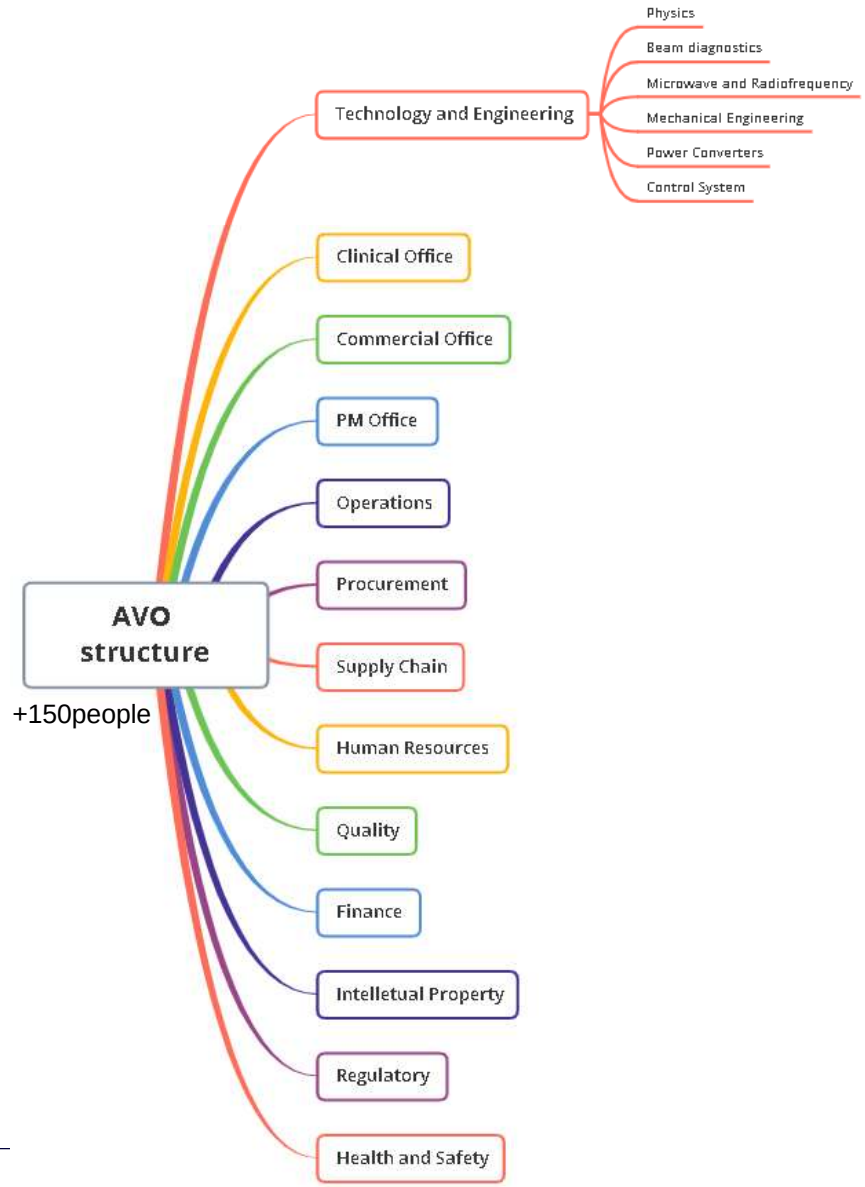
DMR

- ✓ Specs (HW-SW) & Dwgs
- ✓ Production processes specs and methods
- ✓ QA procedures
- ✓ Packaging/labelling specs
- ✓ Installation/Maintenance/Servicing methods

Medical Device Design and Development



Company Structures, Technologies, Software



FLUKA · Altium Designer · redhat · ORACLE · MAD · LTspice · etm · Micro-Research Finland Oy · CST · AUTODESK · C++ · LabVIEW · MATLAB · ANSYS · VHDL · Opera Simulation Software · SIMULIA · python · EPICOR · SIEMENS

Soft skills

ADVANCED ONCOTHERAPY

ADAM
an ADVANCED ONCOTHERAPY company

CERN spin-off

Thank you

https://www.avoplc.com/en-gb/Careers

"The opportunity to work with Advanced Oncotherapy is a shining example of how the public sector can work with industry towards game-changing technologies that will have a huge impact on people's lives"

Prof. Susan Smith,
Head of STFC's Daresbury Laboratory