# Particle-Beam Therapy

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ENLIGHT Coordinator

IOP PAB Annual Meeting 2020
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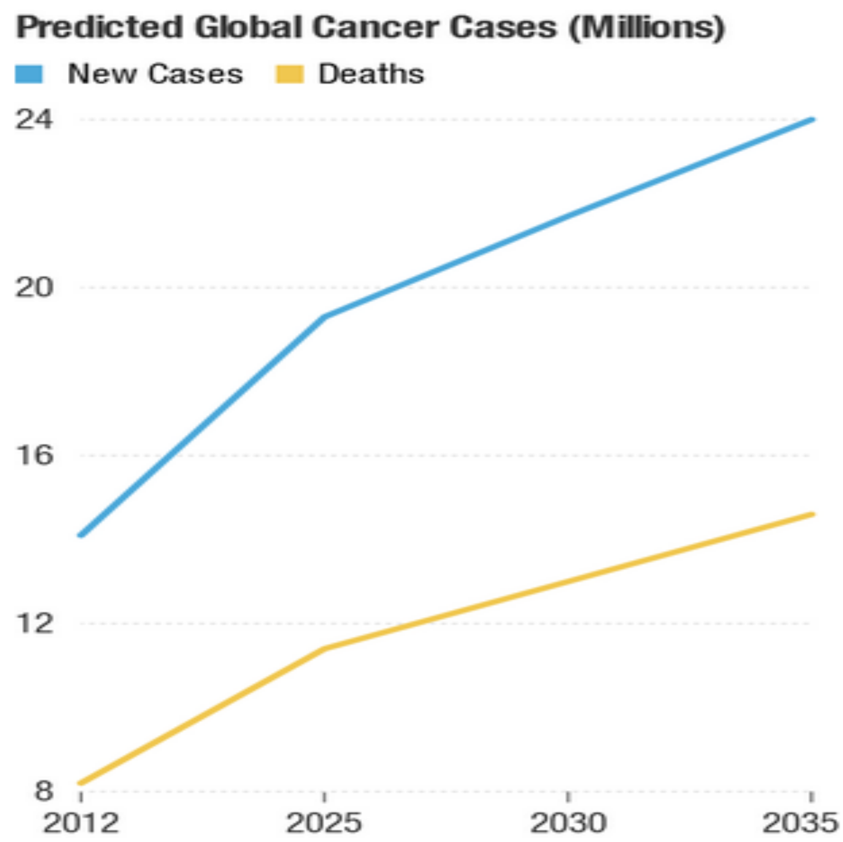
# Cancer is growing global challenge

- Globally **18** million new cases per year diagnosed and **9.6** million deaths in **2018**
- This will increase to **27.5** million new cases per year and **16.3** million deaths by **2040**
- **70% of these deaths** will occur in low-and-middle-income countries (LMICs)




**Radiation therapy is a key tool for treatment for over 50% patients**

# Radiotherapy in 21st Century

## 3 "Cs" of Radiation

**Cure** (about 50% cancer cases are cured)

**Conservative** (non-invasive, fewer side effects)

**Cheap** (about 10% of total cost of cancer on radiation)

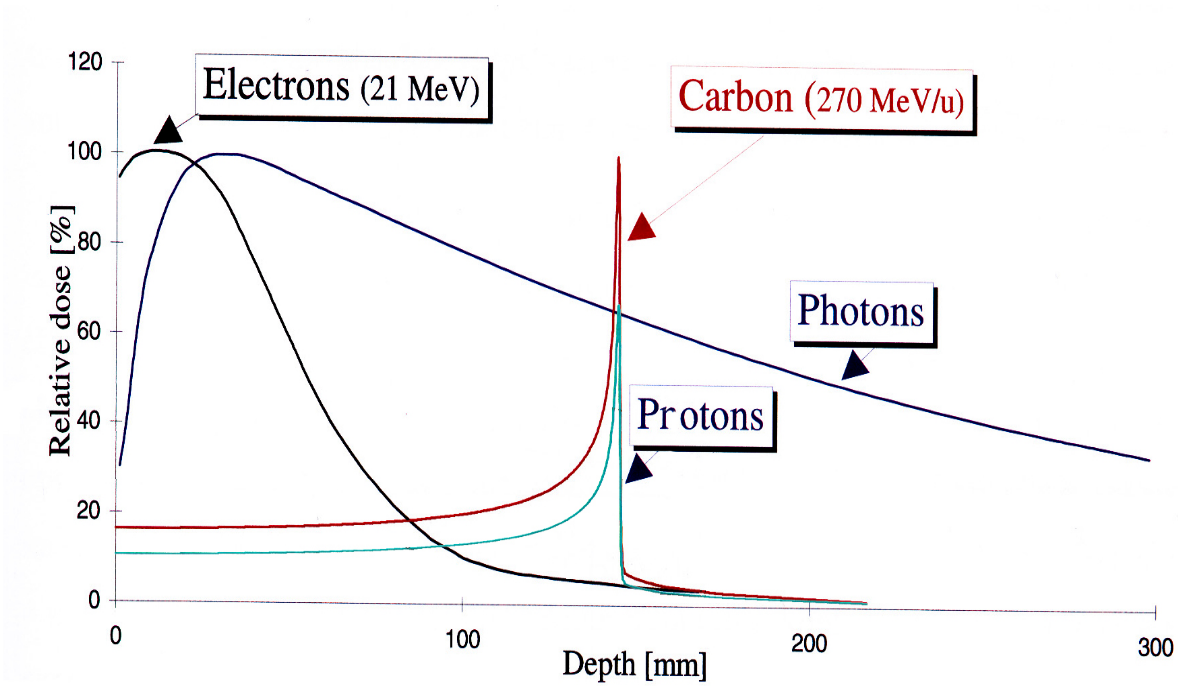
- About 50% patients are treated with RT
- No substitute for RT in the near future
- Number of patients is increasing

**Aims of Radiotherapy:**

- Irradiate tumour with sufficient dose to **stop cancer growth**
- **Avoid complications** and **minimise** damage to surrounding tissue

**Current radiotherapy methods**:

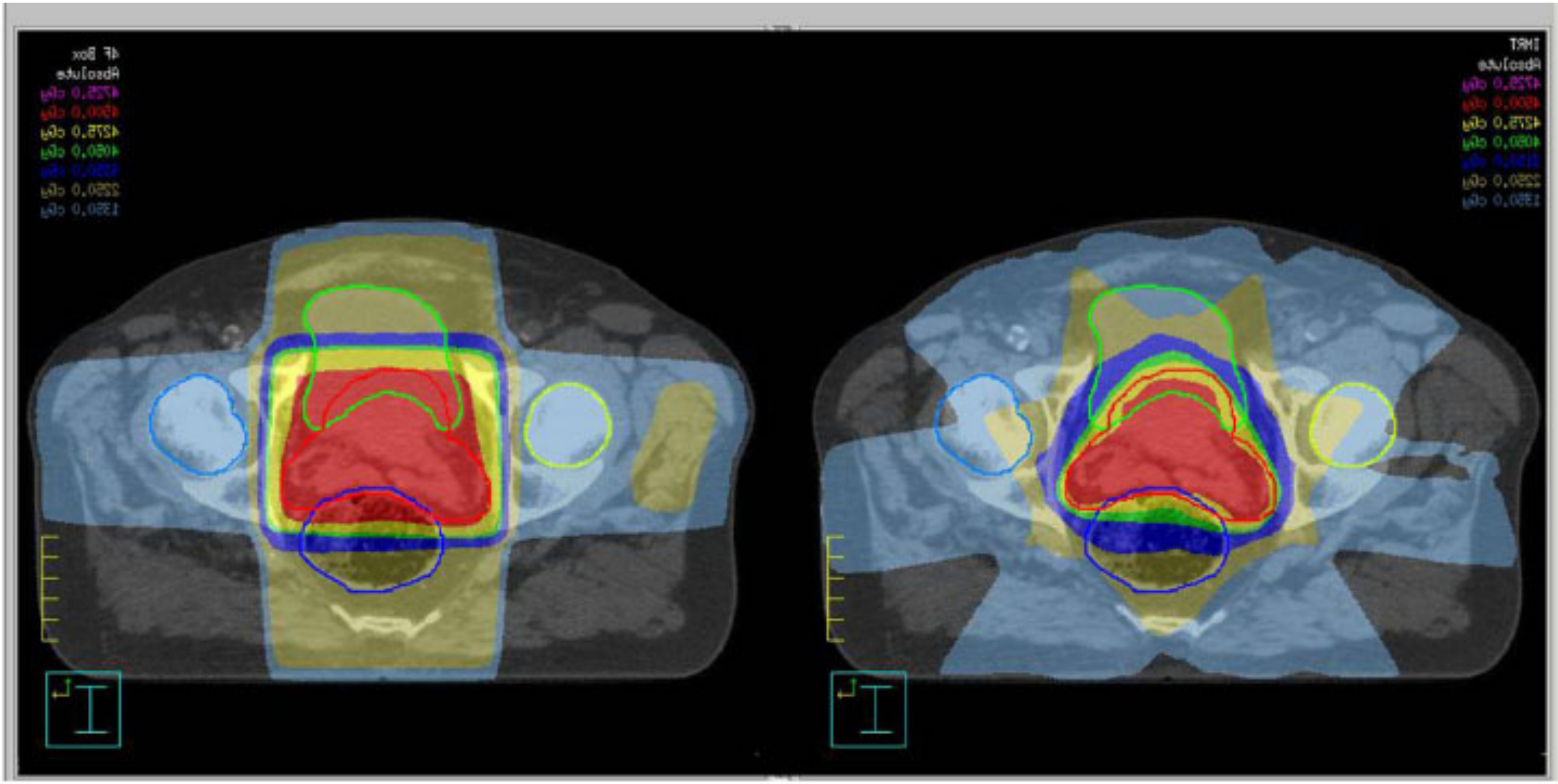
- MV photons
- 5 - 25 MeV electrons
- 50 - 300 MeV/u hadrons



# Radiation Therapy Today

- Key radiation therapy delivery systems
  - Cobalt 60 machines
  - Linear accelerators (Linacs)
  - Brachytherapy
  - Image-guided radiotherapy (IGRT); MR-guided etc.
  - Particle therapy (proton and carbon, other ions)
  - FLASH therapy

# Improved Delivery

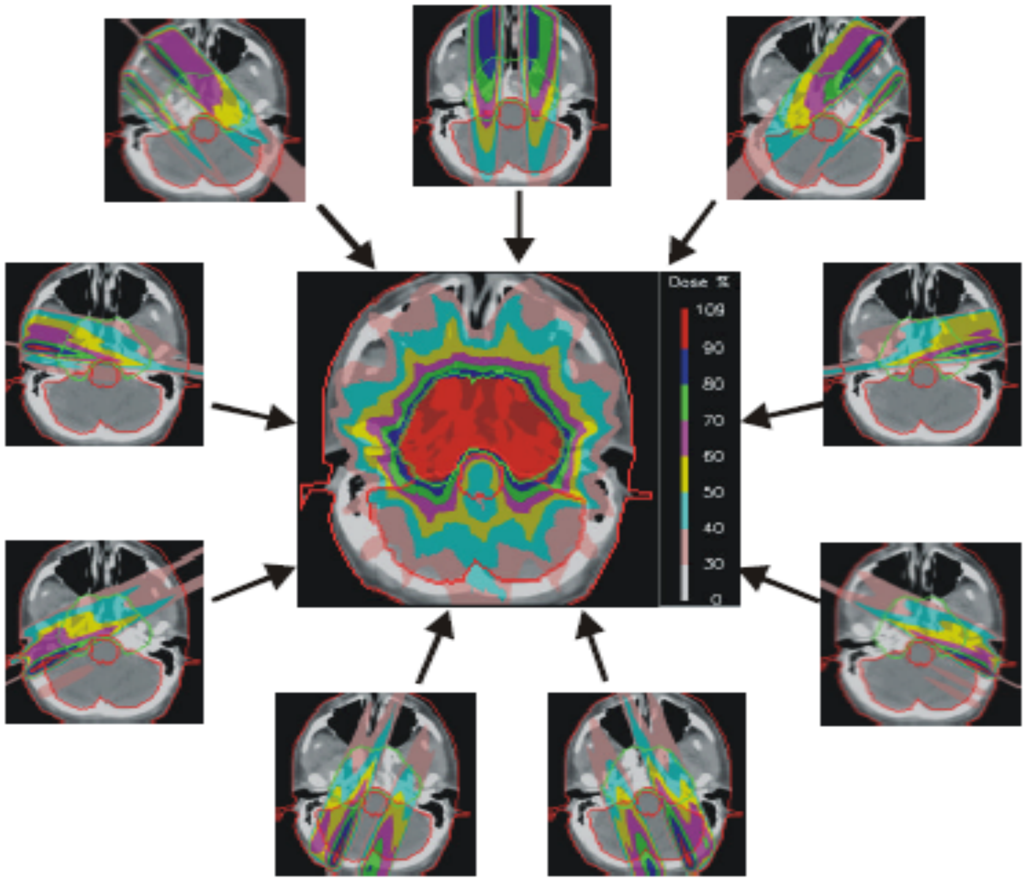


1990s: 4 constant intensity fields

Current state of RT: Intensity Modulated Radiotherapy (IMRT) – Multiple converging field with planar (2D) intensity variations

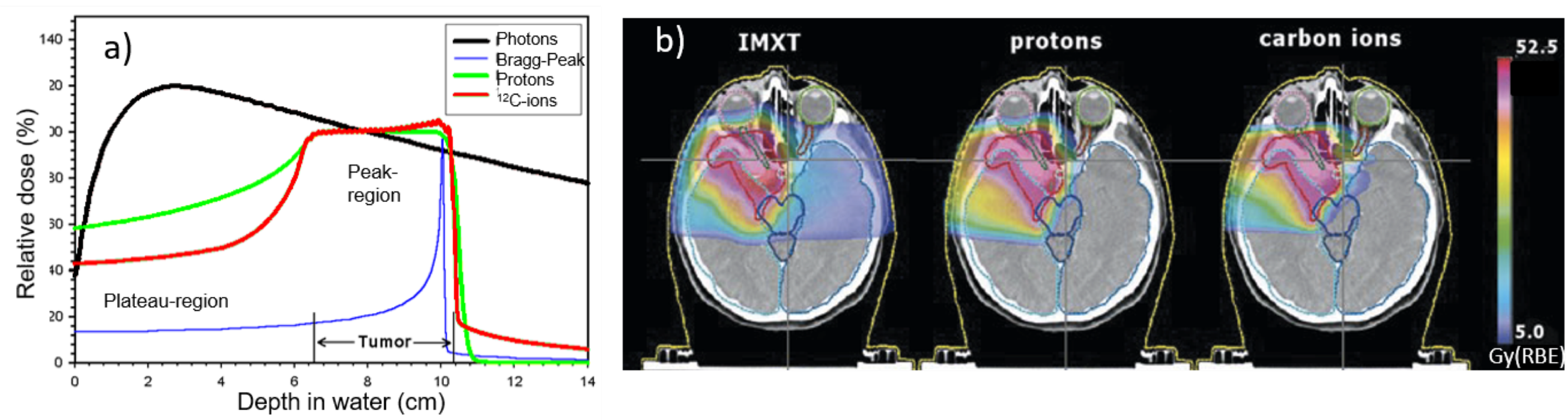
# Intensity Modulated Radiation Therapy

9 NON-UNIFORM FIELDS




PSI

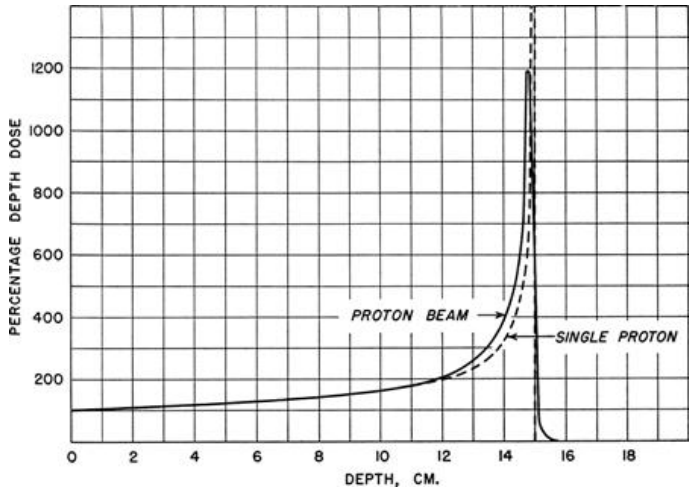
# Why Particle/Hadron Therapy?



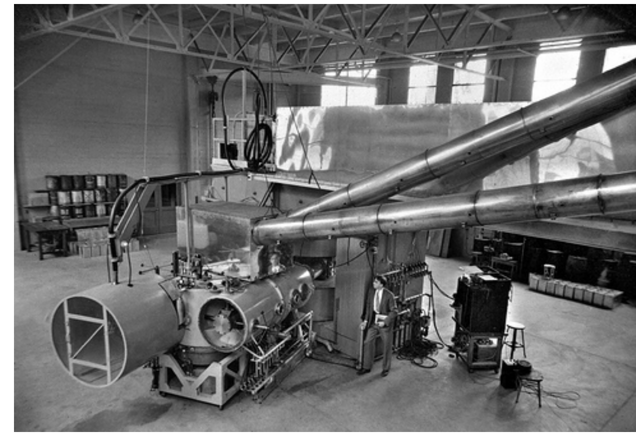

Depth dose profiles in water (a) and treatment plans (b) comparing photons, delivered with the most advanced intensity modulation RT (IMXT), and state-of-the-art scanned protons and $^{12}C$ ions, showing the increased tumour-dose conformity of ion therapy due to the characteristic Bragg peak (a).

## 1932 - E. Lawrence First cyclotron

## 1946 – proton therapy proposed by R. Wilson

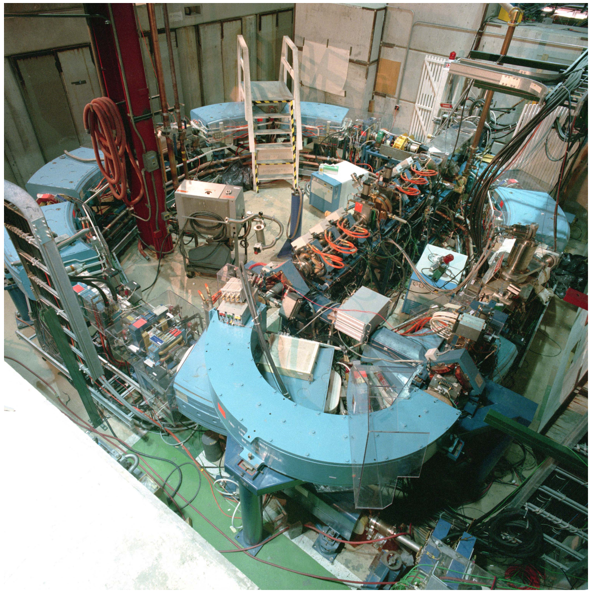



## 1954 – Berkeley treats the first patient



# From physics……..

## 1993- Loma Linda USA (proton)



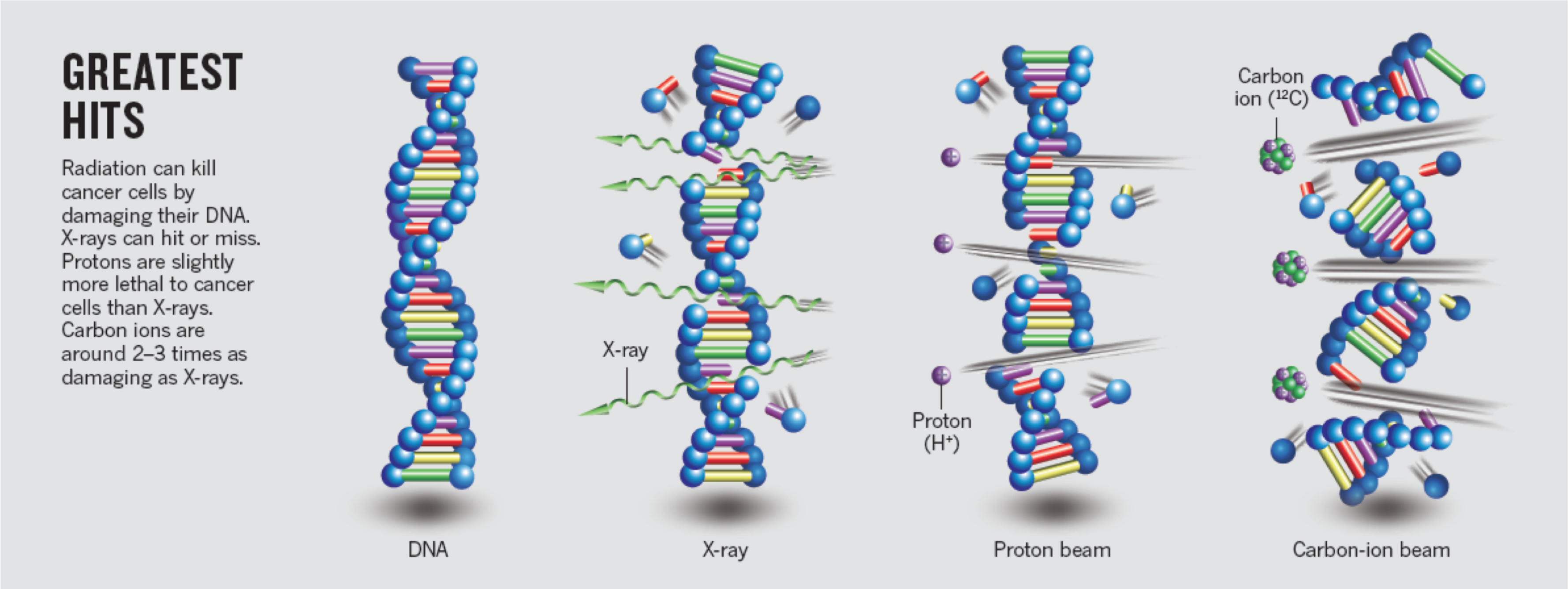
First dedicated clinical facility

## 1994 – HIMAC/NIRS Japan (carbon)

## 1997 – GSI Germany (carbon)

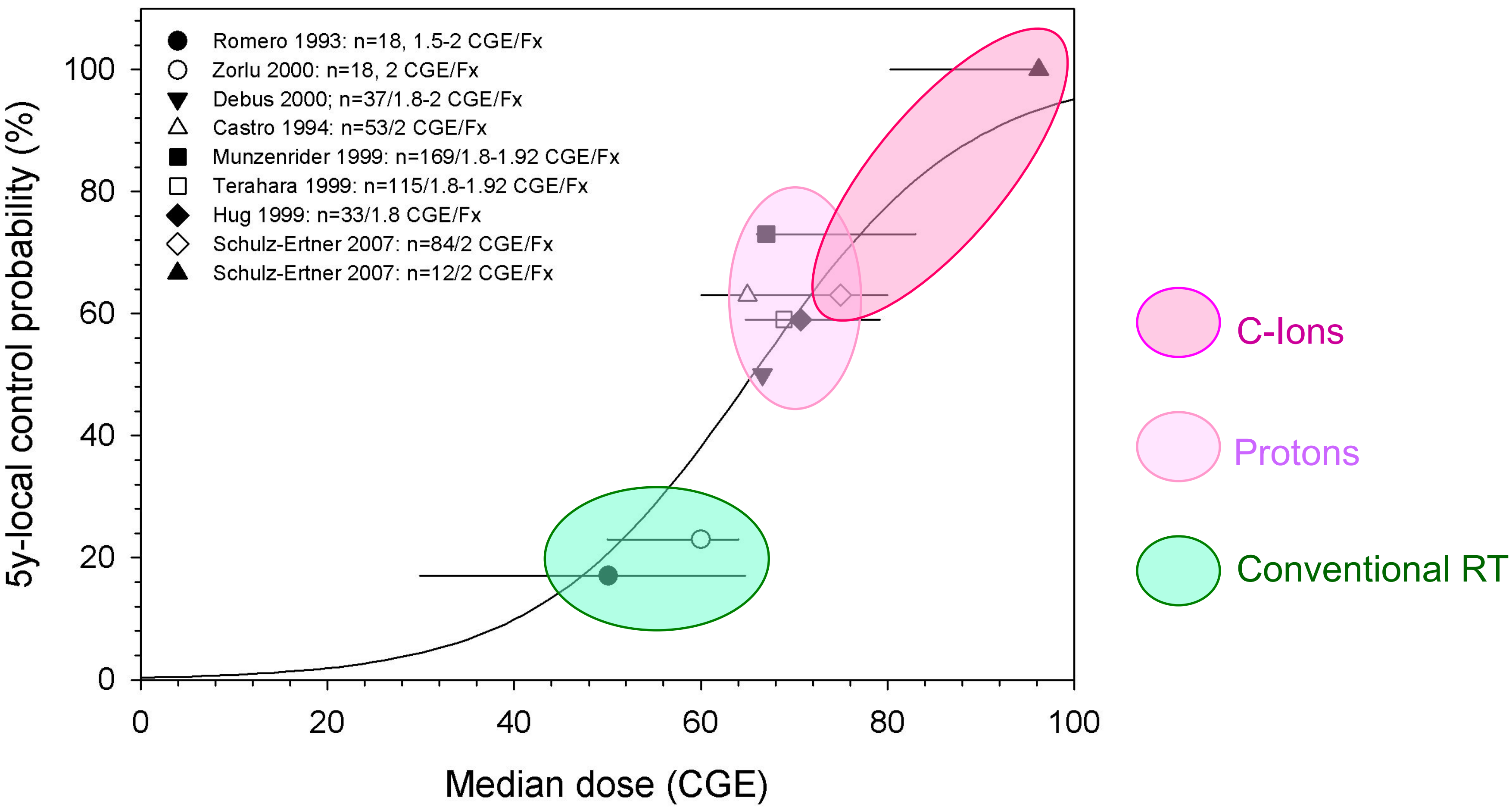
# Three crucial years for PT……..to clinics

DNA X-rays Protons Carbon ions



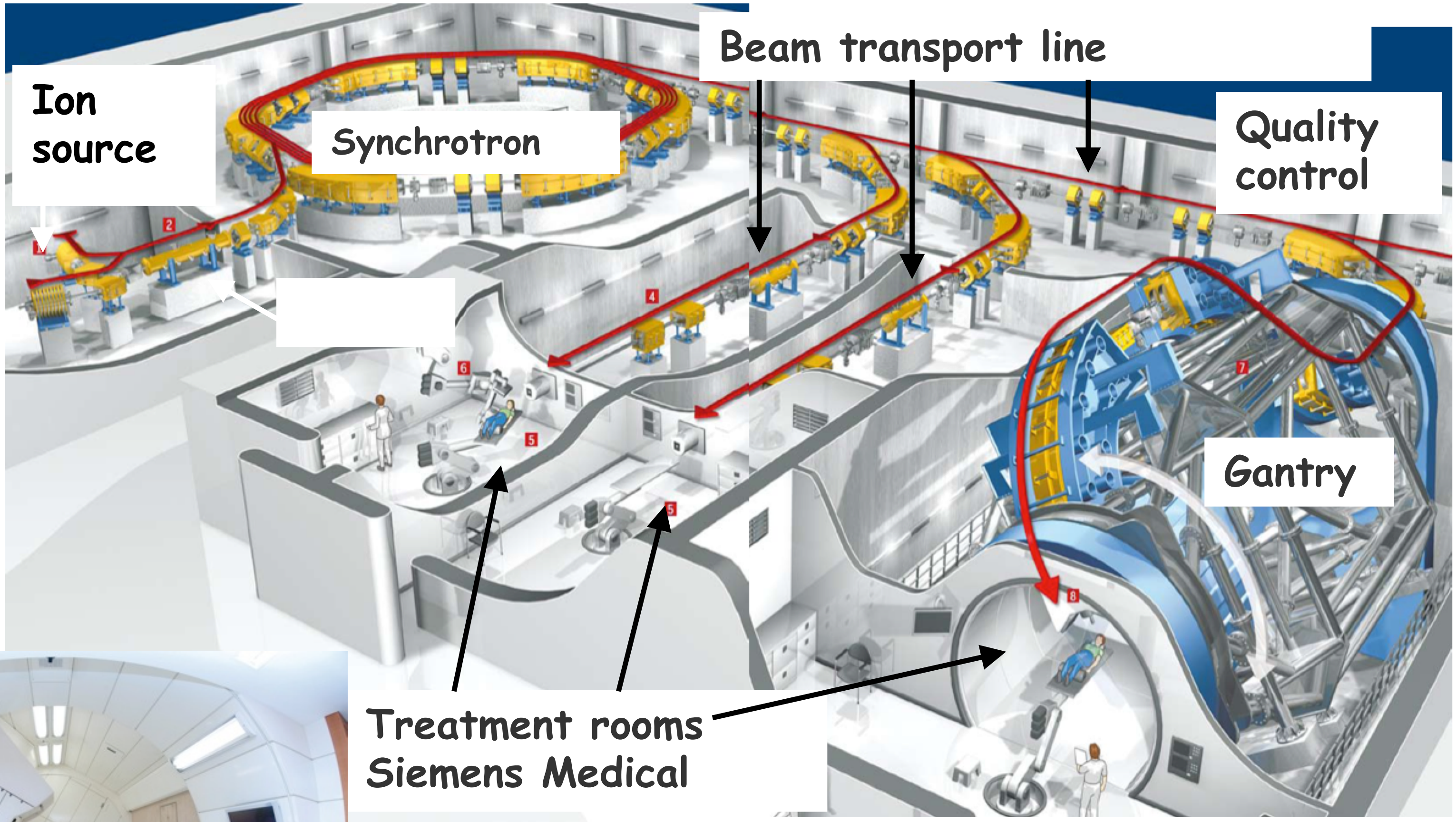

Marx, Nature, 2014

# Tumour Control Rate: Chordomas




*Schulz-Ertner, IJROBP 2007*

# HIT - Heidelberg




Carbon facilities in Europe: first was HIT in Heidelberg – started treating patients in 2009

# Facilities in operation in Europe 2002

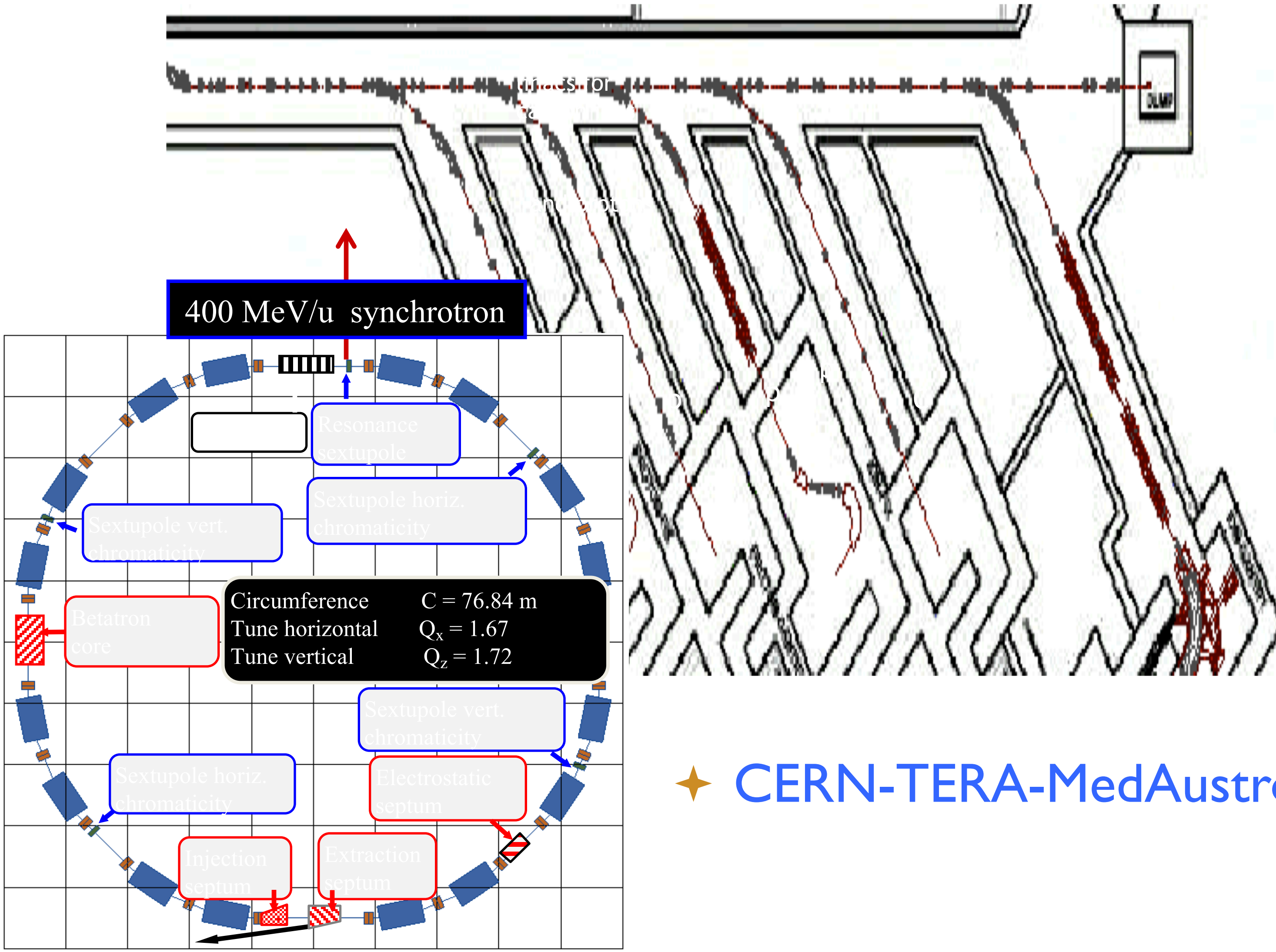
P centres

C-ion centres

Dual-ion centres

Source: PTCOG

# PIMMS at CERN (1996-2000)




- CERN-TERA-MedAustron

# The beginnings of ENLIGHT

- The idea germinated in 2001 after ESTRO- Med-AUSTRON meeting
- In October 2001 the proposal for a Thematic Network was submitted to EC
- ENLIGHT was launched In February 2002 at CERN
- Funded: 1 million Euros in 2002

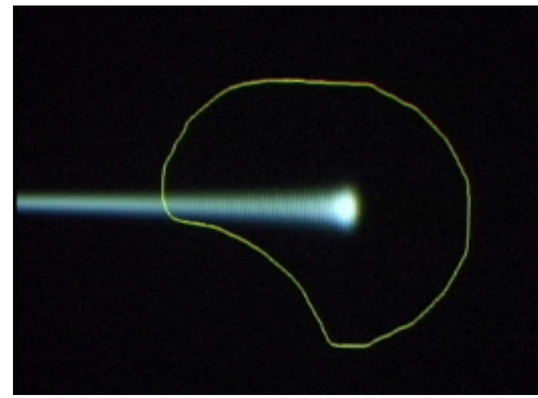
**Driving Force:**
Ugo Amaldi
Jean Pierre Gerard
Germane Heeren

**Organisation:**
Hans Hoffmann
Manjit Dosanjh

ENLIGHT

# European Network for Light Ion Hadron Therapy

- Launched at CERN in 2002, following PIMMS study
- Common **multidisciplinary platform**
- Cancer treatment
- Identify **challenges**
- Share **knowledge** and best practices
- Harmonise data
- Provide **training**, education
- **Innovate** to improve
- Lobby for funding

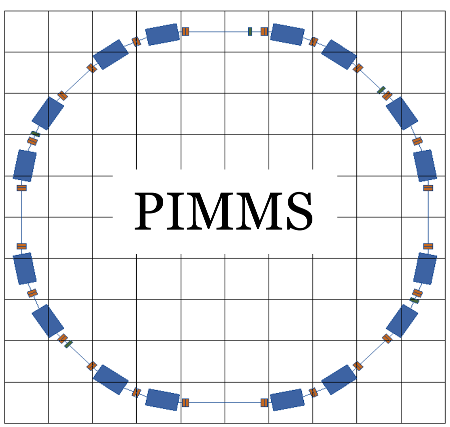


# PIMMS study at CERN (1996-2000)

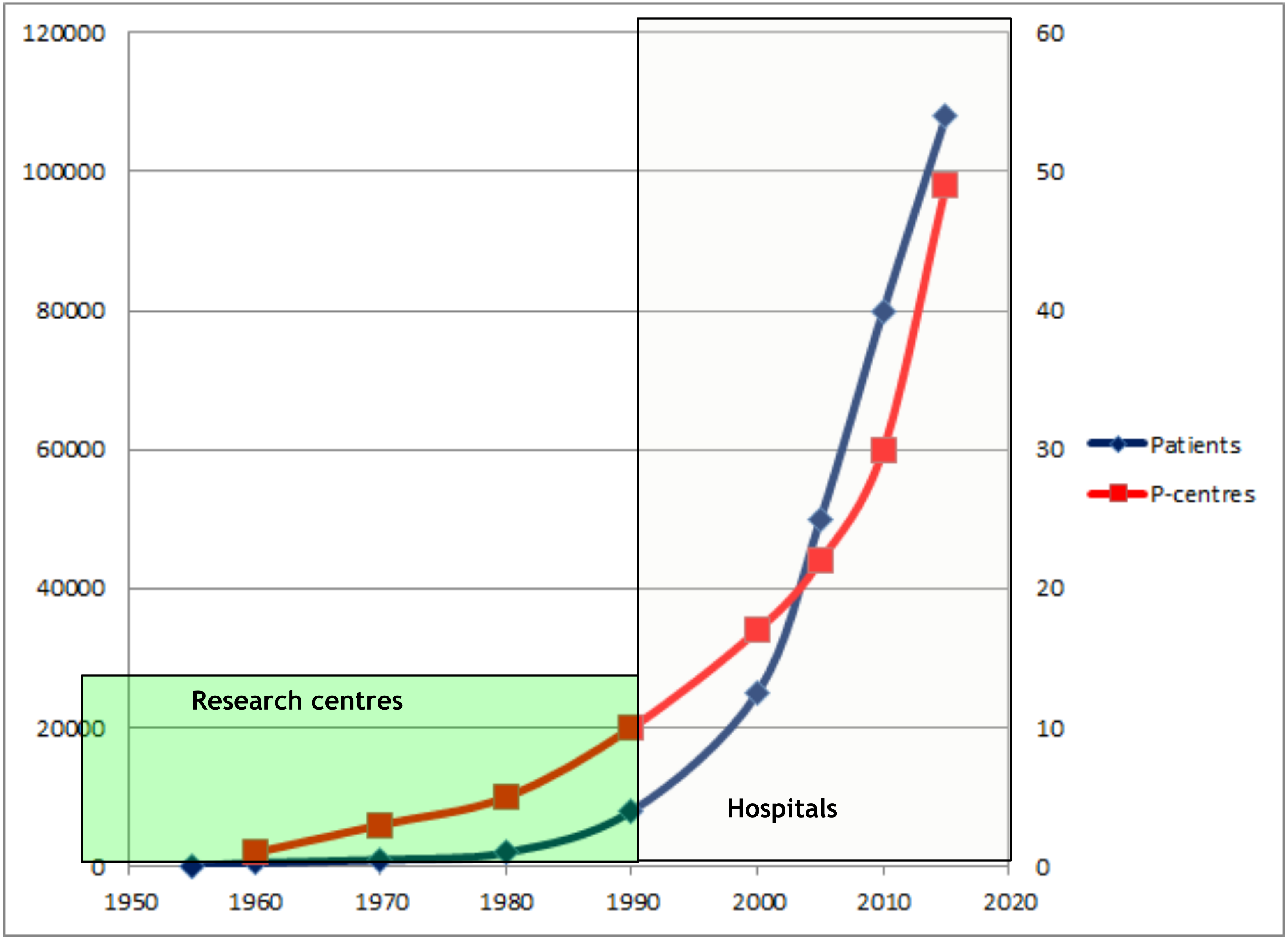

Treatment , CNAO, Italy
2011

MedAustron, Austria 2016

1996-2000
PIMMS study

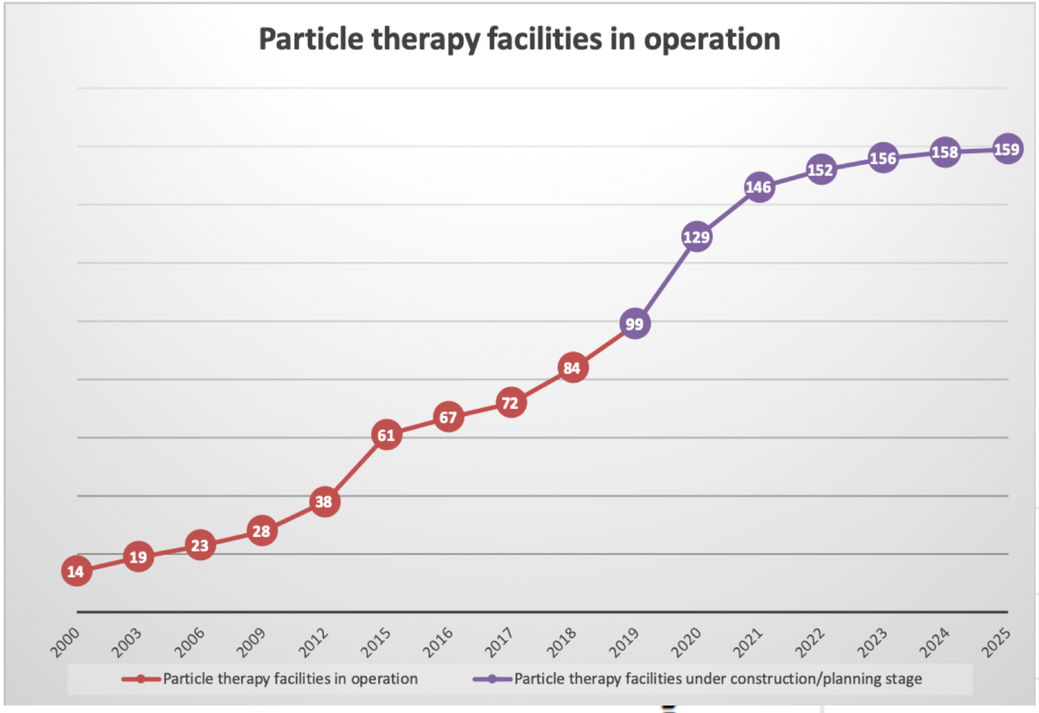


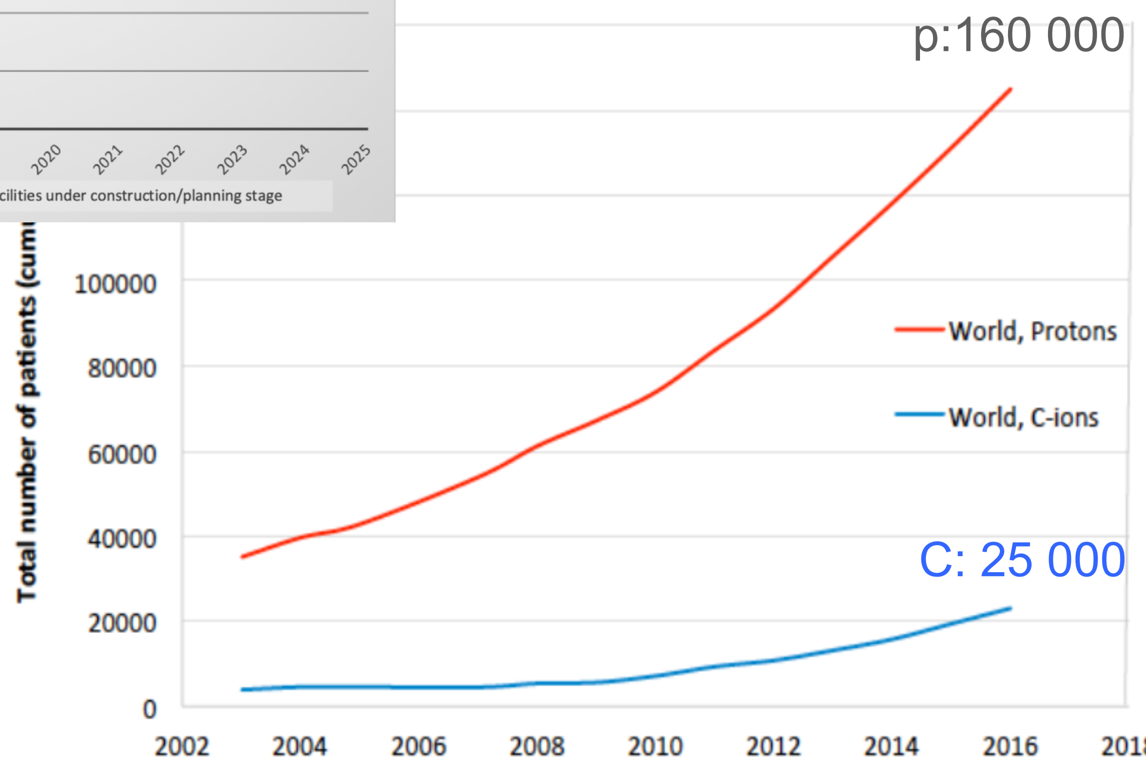

## [Data from www.ptcog.ch]



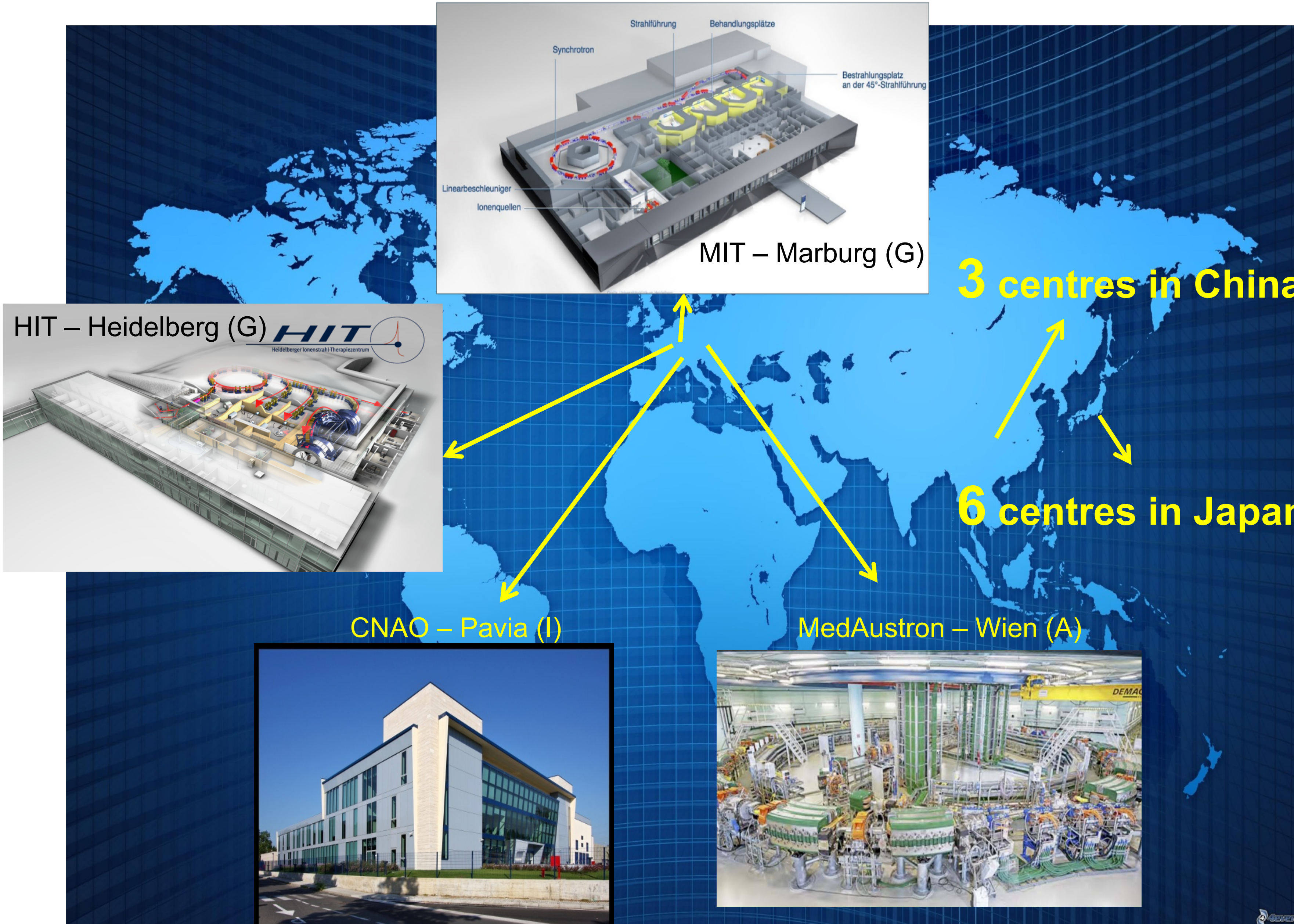
# Facilities in operation in Europe 2020

# Centres and patients worldwide



# Multi-ions clinical facilities in the World

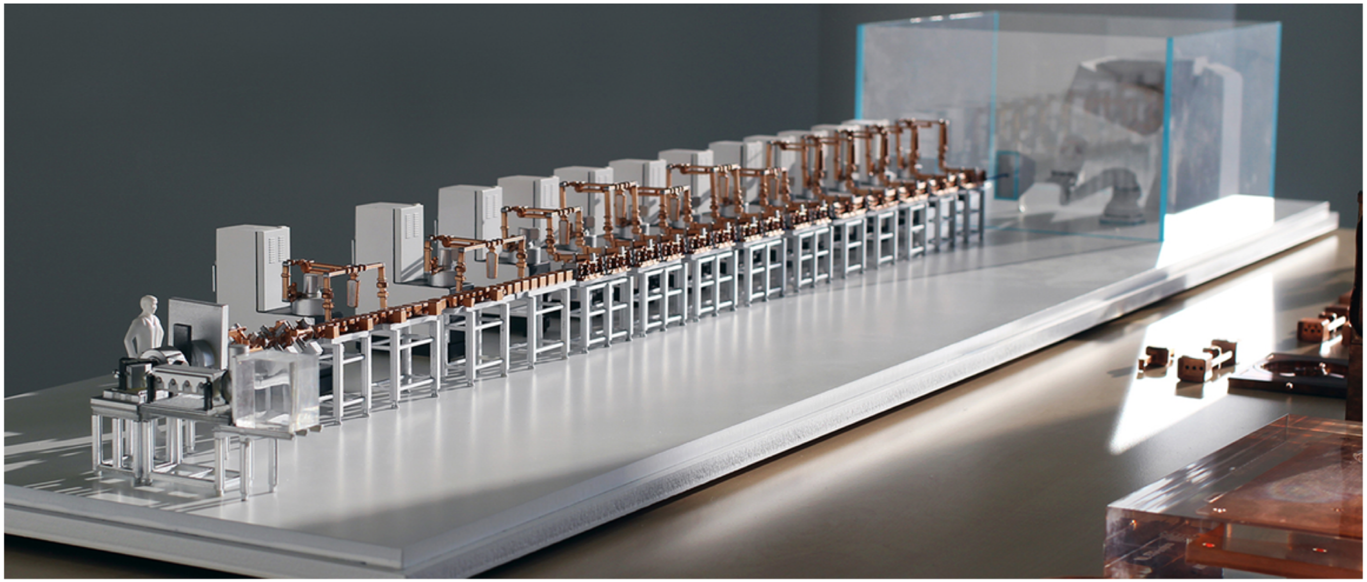


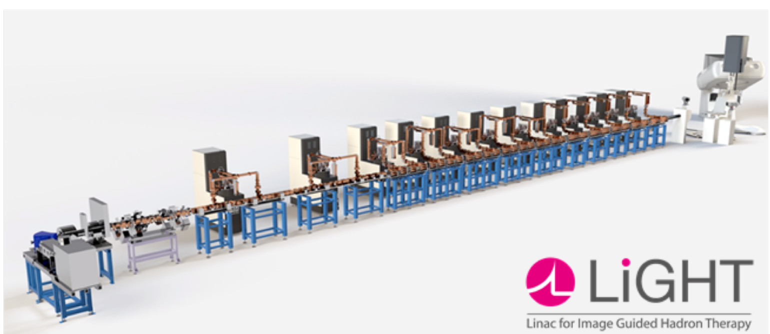
# Much more still needs to be done

- Treat the tumour and only the tumour
  - ⇒ Imaging and dose delivery:  control and monitor the ideal dose to the tumour
  - ⇒ Minimal collateral radiation “outside” the tumour
  - ⇒ Minimal radiation to nearby critical organs
  - ➢ Even if the tumour is moving
- Compact: Fit into a large hospital
  - ⇒ Accelerator:  smaller, simpler, cheaper
  - ⇒ Gantry: compact, cheaper, energy efficient
- Be affordable
  - ✓ Capital cost ?
  - ✓ Operating costs ?
  - ✓ Increased number of treated patients per year ?
- Wish list from community
  - ✓ Improve patient through-put
  - ✓ Increase effectiveness
  - ✓ Decrease cost
- New ideas being explored

# LIGHT system: New Kid on the block

ADVANCED ONCOTHERAPY





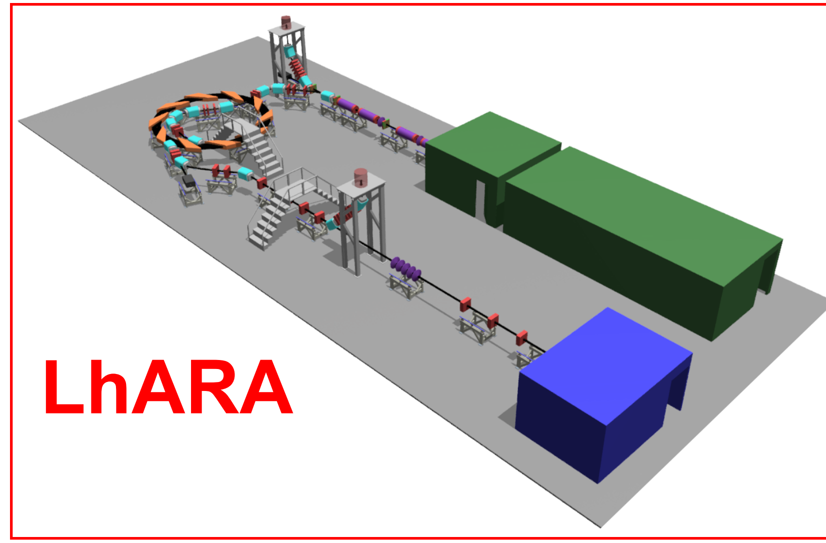

Being assembled at STFC's Daresbury Laboratory

# LhARA: Laser-hybrid Accelerator for Radiobiological Applications (K.Long, ICL)

## A novel, hybrid, approach:

- **High-flux, laser-driven proton/ion source:**
  - Overcome instantaneous dose-rate limitation
- **Delivers protons or ions in very short pulses:**
  - Pulse length 10 – 40 ns
- **Arbitrary pulse structure**
- **Novel plasma-lens capture & focusing**
- **Fast, flexible, efficient acceleration using FFA:**
  - Protons up to 127 MeV p;
  - Ions up to ~33 MeV/u

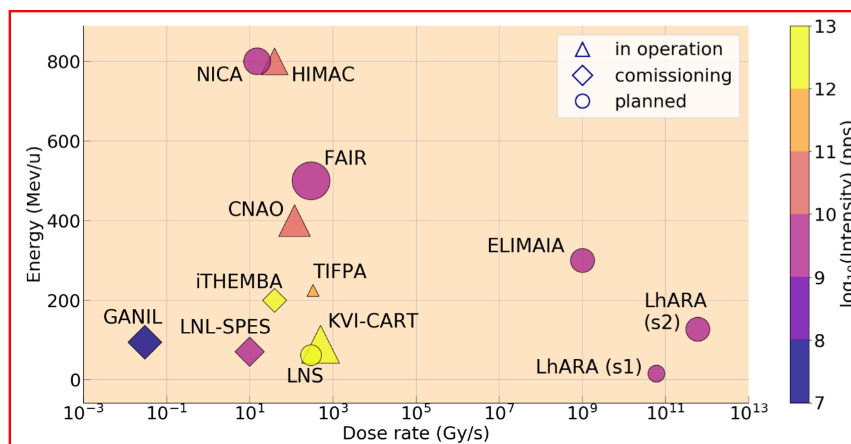
**→ compact, uniquely flexible facility**



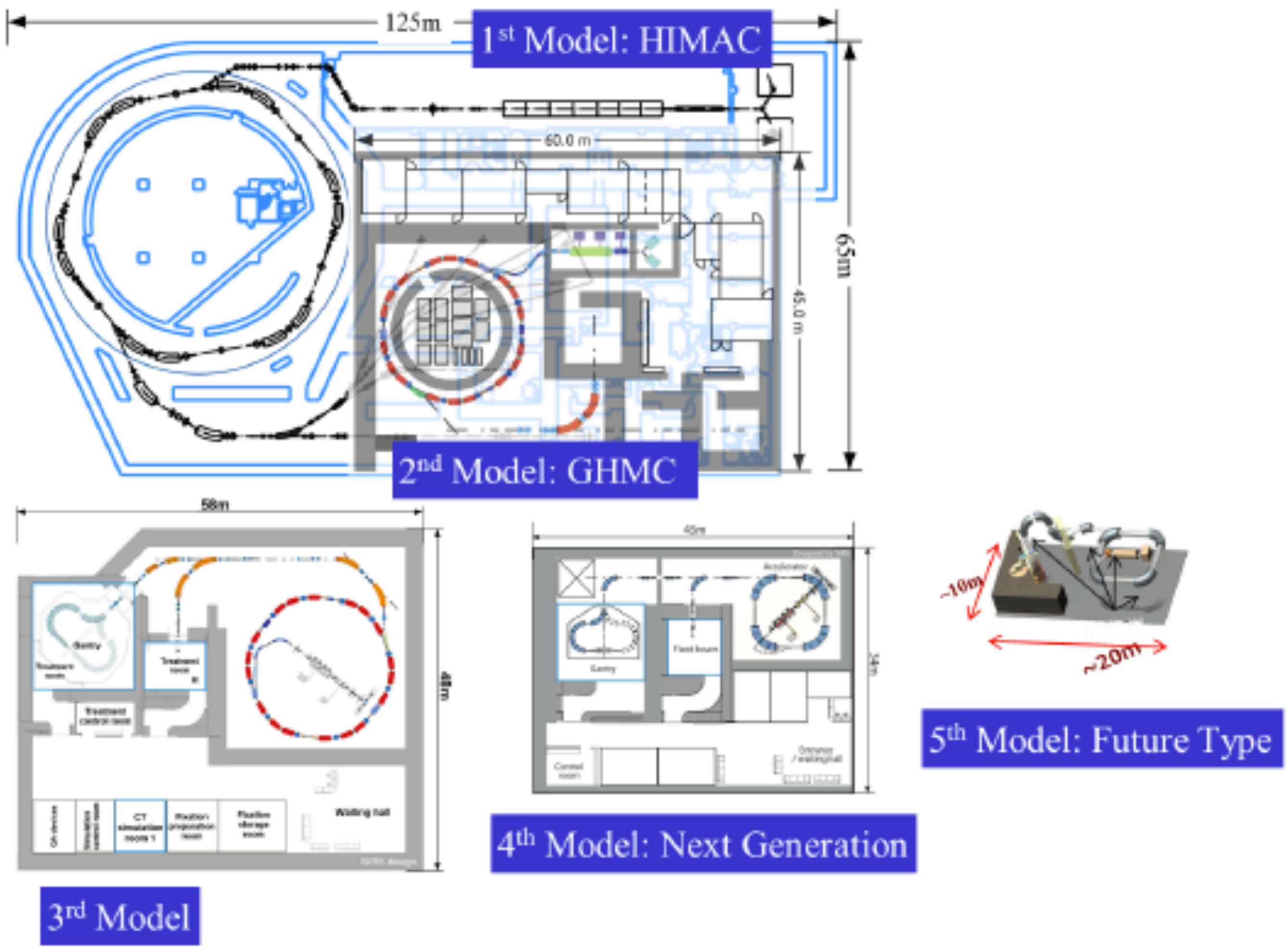

Pre-CDR: CCAP-TN-01; arXiv:2006.00493; submitted to Frontiers in Nuclear Physics, Medical Physics and Imaging

| *The LhARA consortium* | |
|---|---|
| University partners: | Imperial College London; CCAP; University of Liverpool; Manchester 1824 The University of Manchester; Department of Physics; University of Strathclyde Science; Royal Holloway University of London; Queen's University Belfast |
| Accelerator institute partners: | Science & Technology Facilities Council ASTeC; JAI John Adams Institute for Accelerator Science; The Cockcroft Institute of Accelerator Science and Technology |
| Laboratory partners: | Science & Technology Facilities Council Particle Physics Department; Science & Technology Facilities Council ASTeC; Science & Technology Facilities Council Central Laser Facility; Science & Technology Facilities Council ISIS Neutron and Muon Source |
| Clinical partners: Oncologists, medical/biophysics, providers | Imperial College Healthcare NHS Trust; 70 Years of the NHS 1948 - 2018; The Clatterbridge Cancer Centre NHS Foundation Trust |
| Industrial partners: | Maxeler Technologies Maximum Performance Computing; Corerain 鲲云科技; LEO Cancer Care |

+ Brm (Phys, Hosp, Cyclotron), NPL, Surrey, Institut Curie



# Plan of Miniaturizing Machine




Courtesy of Dr. Kojii Noda

# CERN: Beyond PIMMS to NIMMS

## A new accelerator design


Requirements of the ion therapy community, expressed at the Archamps Workshop, June 2018

**1. Concentrate on heavy ions** (Carbon but also Helium, Oxygen, etc.) because proton therapy is now commercial (4 companies offer turn-key facilities) while ions have higher potential for treatment but lower diffusion.

**2. A next generation ion research and therapy accelerator must have:**

- ❑ Lower cost, compared to present;
- ❑ Reduced footprint;
- ❑ Lower running costs;
- ❑ Faster dose delivery with higher beam intensity or pulse rate;
- ❑ A rotating ion gantry;
- ❑ Operation with multiple ions (for therapy and research).

**An innovative design:**

- Can attract a wide support from the scientific community;
- Can increase the exchange SEE-WE and inside SEE thanks to stronger collaboration on scientific and technical issues;
- Can bring modern high technology to the region, with new opportunities for local industry and scientific institutions.

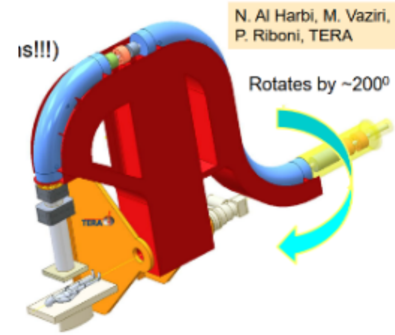
**+ Specific requirements for SEEIIST:**

- ❑ Easy Industrialization
- ❑ Reliability
- ❑ Simple operation
- ❑ Reduced risk
- ❑ Acceptable time to development

# CERN: Beyond PIMMS to NIMMS

## New technologies for future ion therapy accelerators

1. **Improved multiturn injection for higher intensity** 2 x $10^{10}$ ppc, 20 times higher than HIT or CNAO**.**
2. **New linac injector design** at higher intensity, higher energy (10 MeV/u) and higher frequency (325 MHz).
3. **New lattice** with intermediate number of magnets between CNAO (16) and HIT (6).
4. **Combined slow and fast extraction** to test new treatment modalities and to extend the experimental programme.
5. **Superconducting gantry -** different options to be compared for a modern superconducting gantry.
6. **Superconducting accelerator magnets** can bring smaller dimensions and lower cost.



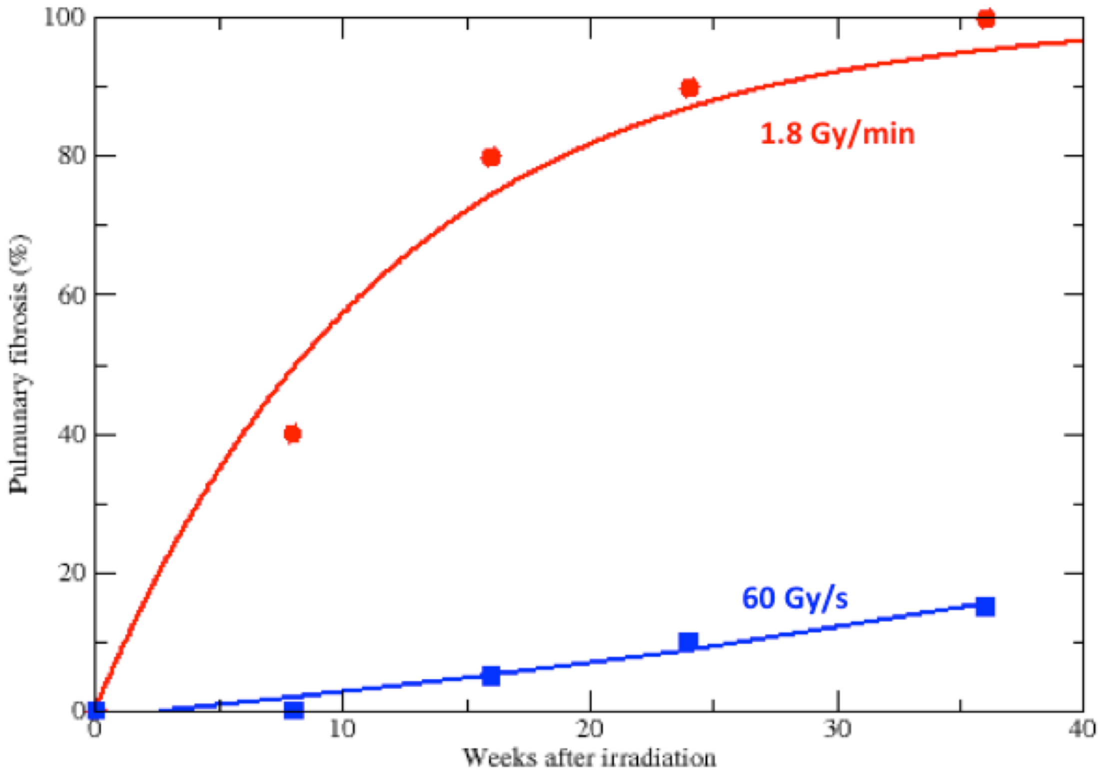

TERA superconducting gantry proposal

CERN LHC superconducting magnet

# SEEIIST Architectural Design

# New modalities  with particles

# FLASH RT with electron




Favaudon *et al., Sci. Transl. Med*. 2014
Reviewed in Durante *et al., Br. J. Radiol*. 2018

- Dose rate >40 Gy/s
- Experiments with electrons in mice show reduced normal tissue toxicity but unmodified tumour control
- This dose rates cannot be achieved with X-rays, but have been reached at proton cyclotrons

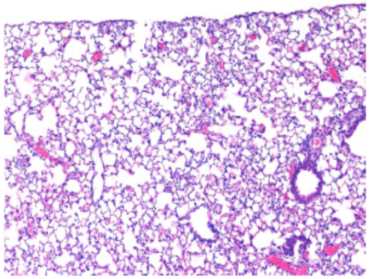
# Varian *FlashForward* Consortium

## Flash resulted in a reduction in radiation induced dermatitis and fibrosis

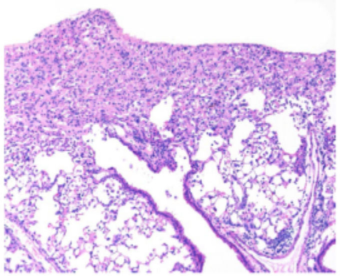
### Normal tissue toxicity studies

**25%** reduction in fibrosis* with FLASH vs. Conventional (17.5 Gy)

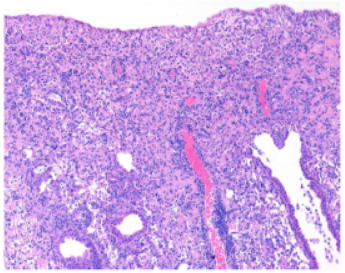
**Control**



**Flash Protons**



**Conventional Protons**



**LUNG FIBROSIS**
**(Graded by independent pathologist, blinded on treatment groups)**

**35%** reduction in dermatitis* with FLASH vs. Conventional (17.5 Gy)

*Average dermatitis scores

**DERMATITIS**

QUEEN'S UNIVERSITY BELFAST | CCRCB CENTRE FOR CANCER RESEARCH AND CELL BIOLOGY varian

# FlashForward™ Consortium

**New York**
Proton Center

**Holland PTC**
Particle Therapy Centre

**Emory**
Proton Therapy Center

**The Christie**
Proton Therapy Centre

**Sylvester Comprehensive Cancer Center**

**University College London**

**University of Maryland**
Dept of Radiation Oncology

**Proton International at UAB**

**Paul Scherrer Institute**

**Cincinnati**
Proton Therapy Center

**Danish Centre**
For Particle Therapy

**Penn Medicine**

**VU Medical Center**
Amsterdam

# Clinical FLASH Protons

- Manufacturers setting up clinical beams

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## Flash Irradiation Delivered in a Proteus®ONE Treatment Room

Proton therapy / 11.06.2019

**Successful Ultra High Dose Rate delivered at Isocenter in IBA's compact proton therapy solution**

Louvain-la-Neuve, Belgium, 11 June 2019 – IBA (Ion Beam Applications SA), the world's leading provider of proton therapy solutions, is pleased to announce the first Flash irradiation in an IBA Proteus®ONE compact gantry treatment room at the Rutherford Cancer Centre Thames Valley in Reading, United Kingdom, on June 8, 2019. This represents another major milestone for IBA and its medical and research partners in their work to lead the development of Flash irradiation.

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## Flash Irradiation Delivered in a Clinical Treatment Room

Proton therapy / 08.03.2019

**Successful Flash Irradiation at Isocenter in IBA's Proteus® Solution Gantry Room**

**Louvain-la-Neuve, Belgium, 8 March 2019 – IBA (Ion Beam Applications SA)**, the world's leading provider of proton therapy solutions, is pleased to announce the first Flash irradiation in an IBA gantry treatment room at the University Medical Centre Groningen (UMCG) in The Netherlands. This achievement represents a major milestone in the work that IBA and its medical and research partners are engaged to bring Flash irradiation to clinical treatment.

# Summary

- **Dose-rate** has a significant impact on radiobiological response
- Recent data has shown that at dose-rates around >40 Gy/s (FLASH Exposures) **normal tissue can be protected**
- An underpinning role for **oxygen dependent chemistry**
- Further studies are needed to fully define the impact of total dose, spatial patterning, total exposure rate and **radiation quality** on response

# Particle therapy + immunotherapy

## Does Heavy Ion Therapy Work Through the Immune System?

Marco Durante, PhD,* David J. Brenner, PhD,† and Silvia C. Formenti, MD‡

**Trento Institute for Fundamental Physics and Applications-National Institute for Nuclear Physics, University of Trento, Trento, Italy; †Center for Radiological Research, Columbia University Medical Center, New York, New York; and ‡Department of Radiation Oncology, Weill Cornell Medical College, New York, New York*

Received Aug 10, 2016, and in revised form Aug 21, 2016. Accepted for publication Aug 25, 2016.

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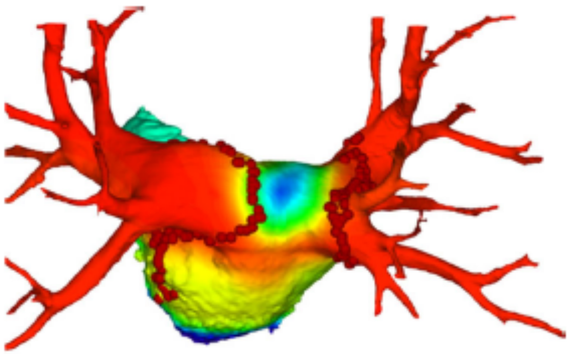
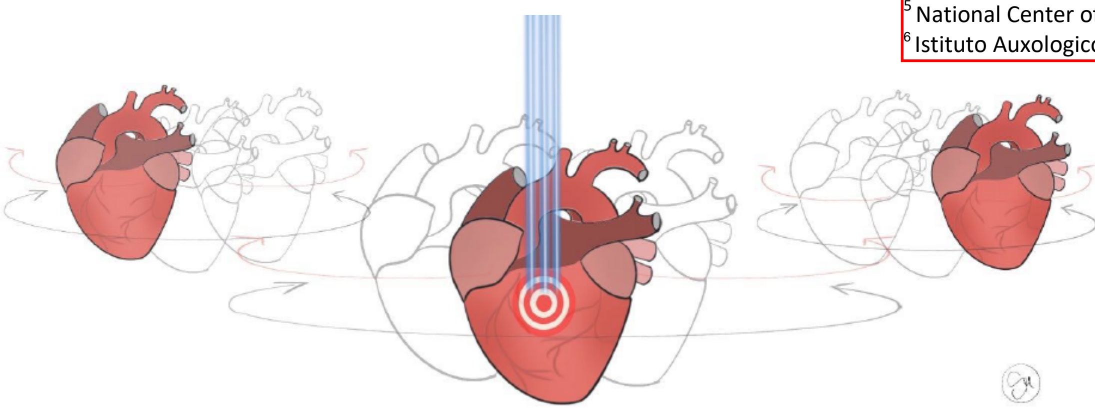
# Non oncological application: ventricular arrhythmia

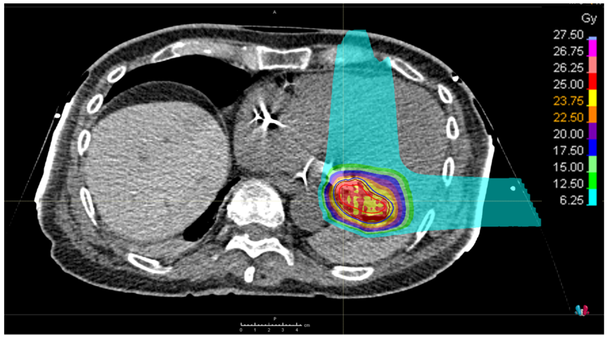




**Non-invasive Proton Radiotherapy for Refractory Ventricular Tachycardia in advanced heart failure: first in-man case.**

Veronica Dusi[1,2], MD, PhD; Viviana Vitolo[5], MD; Laura Frigerio[1,3], MD; Rossana Totaro[1,3], MD; Adele Valentini[4], MD; Amelia Barcellini [5],MD; Alfredo Mirandola[5], PhD; Giovanni Battista Perego[6], MD; Michela Coccia [3], MD , Alessandra Greco[3], MD, Stefano Ghio[3] ,MD, Massimiliano Gnecchi [1,2], MD, PhD; Luigi Oltrona Visconti[3] , MD, Roberto Rordorf[1,3]MD.

[1] Cardiac Intensive Care Unit, Arrhythmia and Electrophysiology and Experimental Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[2]Department of Molecular Medicine, Section of Cardiology, University of Pavia, Pavia, Italy
[3] Department of Cardiology, IRCCS Fondazione Policlinico S. Matteo, Pavia, Italy
[4] Department of Radiology, IRCCS Fondazione Policlinico S. Matteo, Pavia, Italy
[5] National Center of Oncological Hadrontherapy (Fondazione CNAO), Pavia, Italy.
[6] Istituto Auxologico Italiano, Ospedale San Luca, Milan, Italy.



# Where it all started…..

*Thank you for listening*