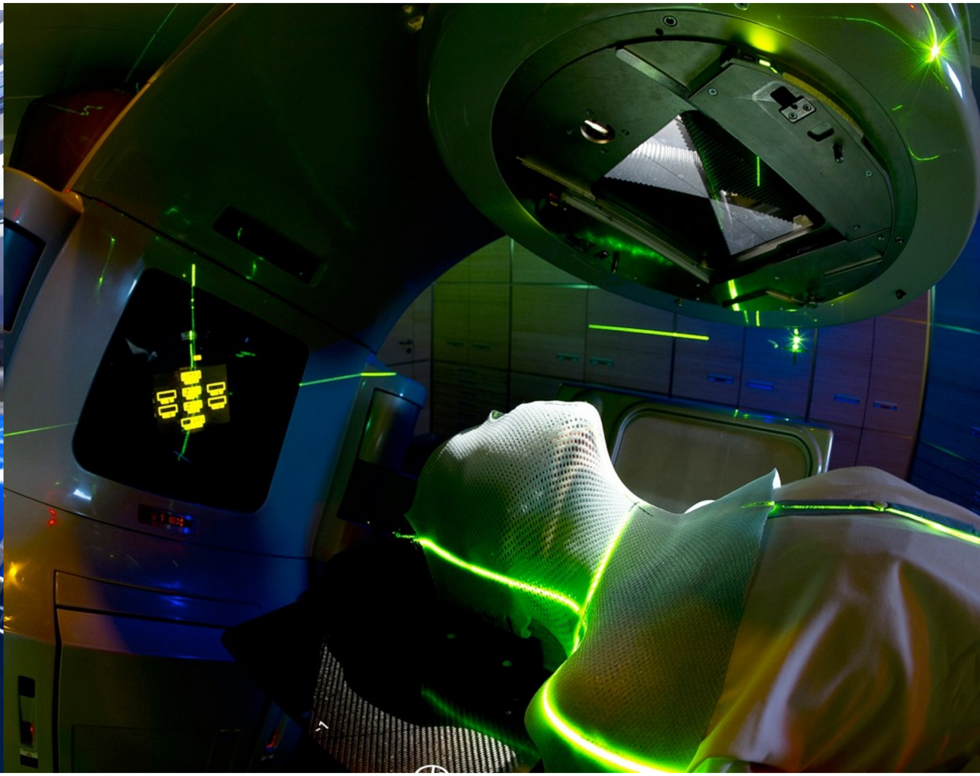
Charged Particle Therapy Overview



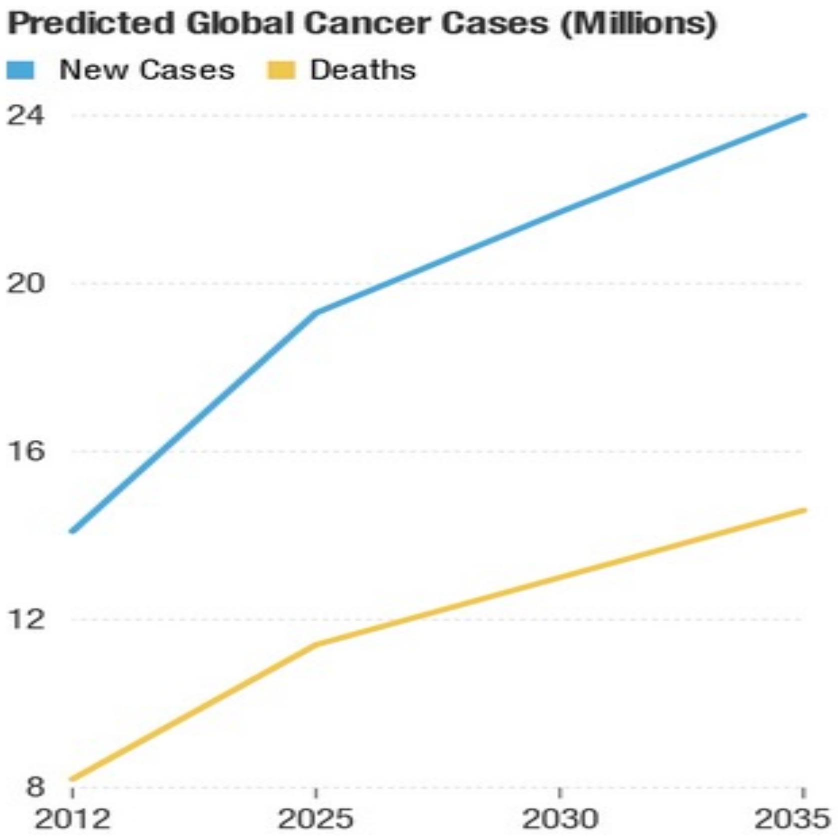
LIP Mini-School on Charged Particle Therapy Applications

Manjit Dosanjh (manjit.dosanjh@cern.ch)
CERN and University of Oxford
ENLIGHT Coordinator

cern.ch/virtual-hadron-therapy-centre

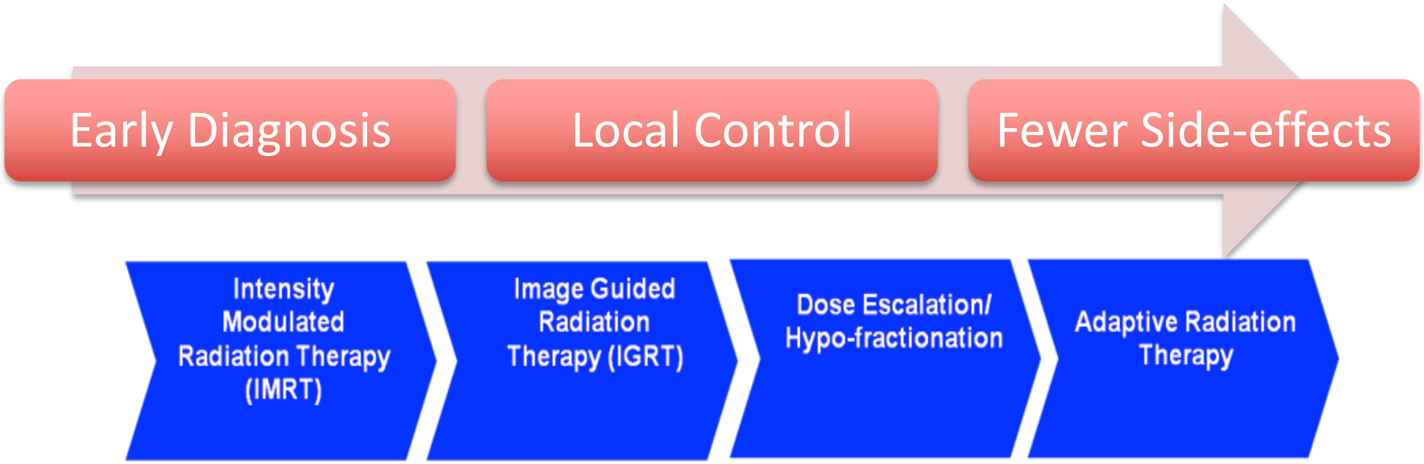
Cancer is growing global challenge

- 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

Improving Cancer Outcomes



- New Technologies
- Advanced radiotherapy
- Radiobiology, Biology, Clinical
- Multi-disciplinary collaboration

The Challenge of Treatment

Ideally one needs to treat:

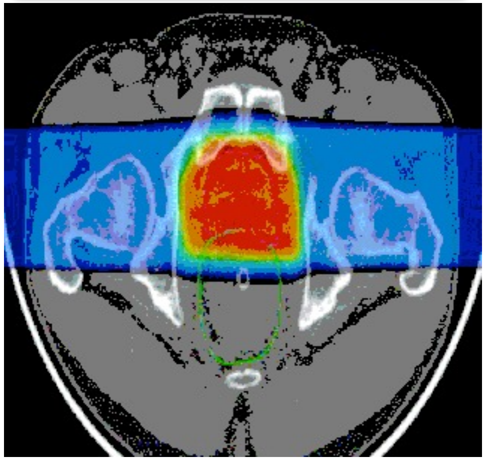
- The tumour
- The whole tumour
- And nothing **BUT** the tumour

Treatment has two important goals to kill the tumour and protect the surrounding normal tissue. Therefore "seeing" in order to know where and precise "delivery" to make sure it goes where it should are key.

Treatment options

Surgery

Radiotherapy



X-ray, IMRT, Brachytherapy, Hadrontherapy

Chemotherapy (+ others)

Hormones; Immunotherapy;
Cell therapy; Genetic treatments; Novel specific targets (genetics..)

AIM:
Survival, Quality of life

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)

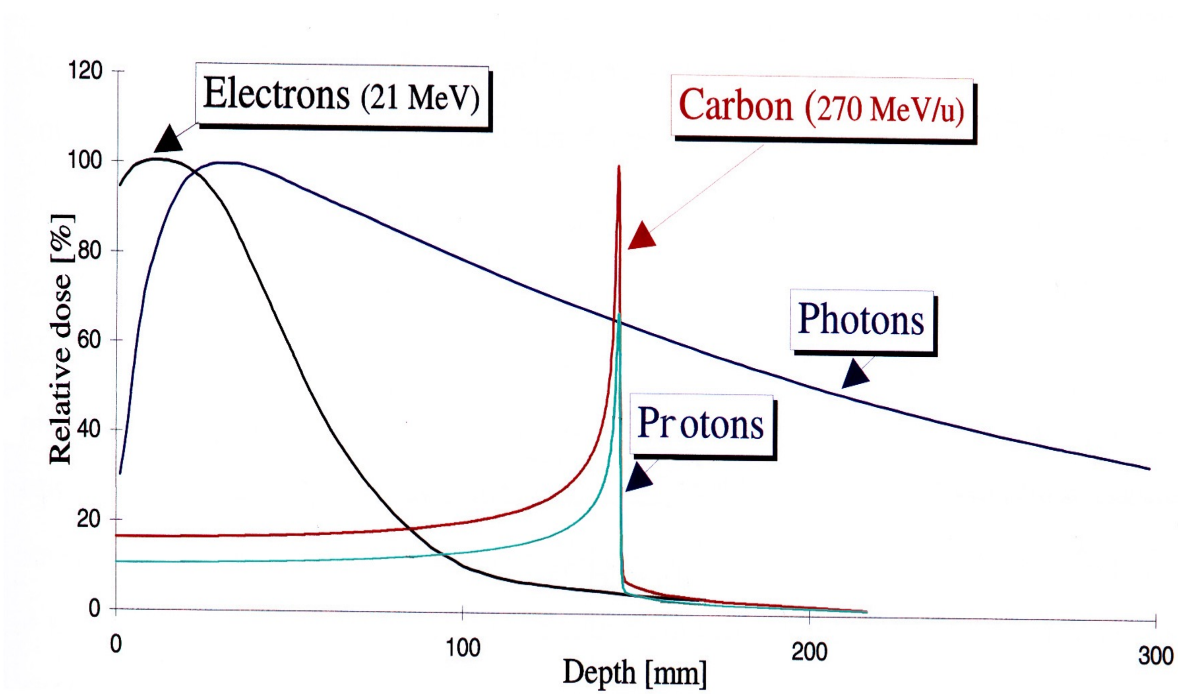
- About 50% patients are treated with RT
- No substitute for RT in the near future
- Number of patients is increasing

Aims of Radiotherapy:

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

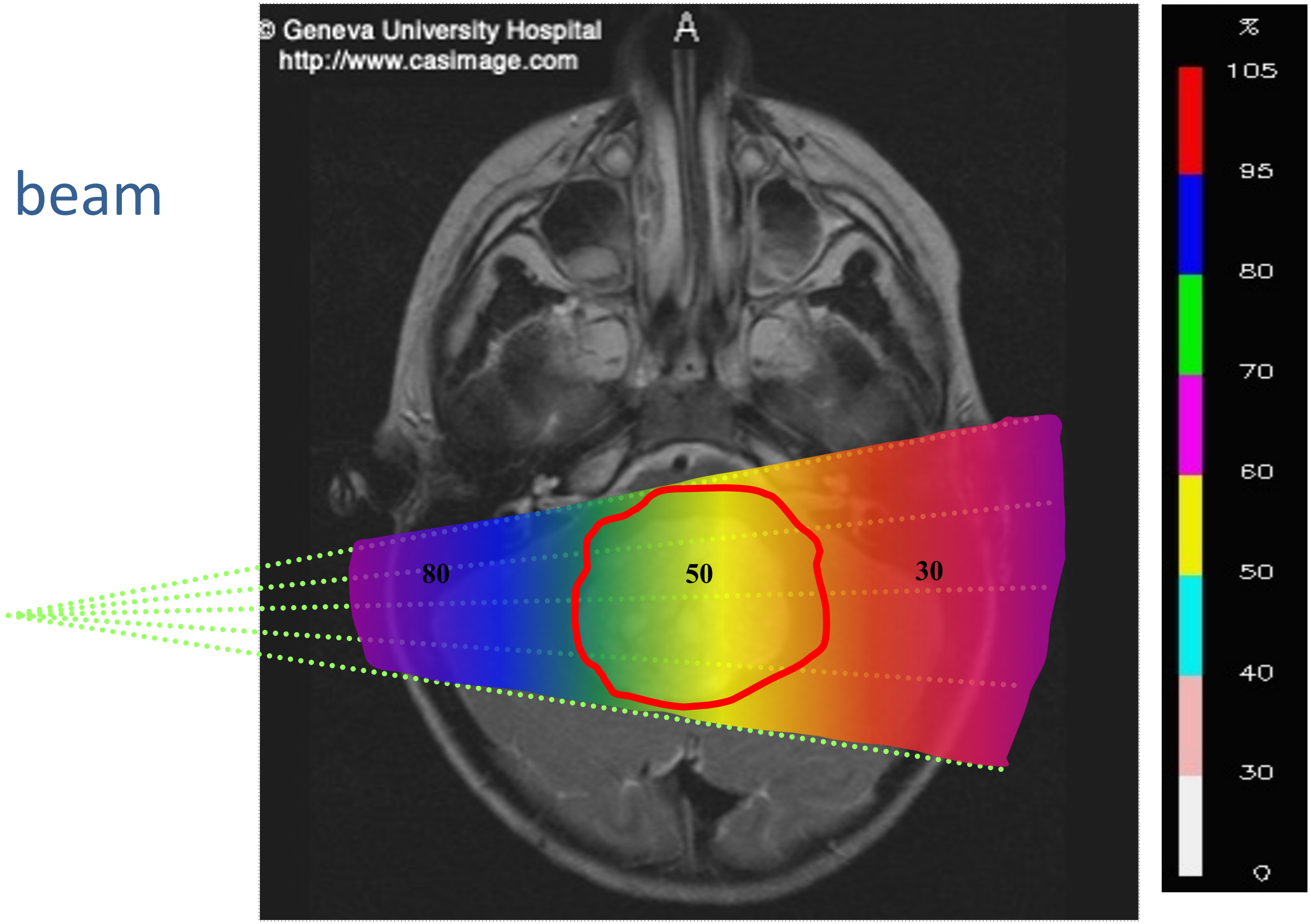
Current radiotherapy methods:

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



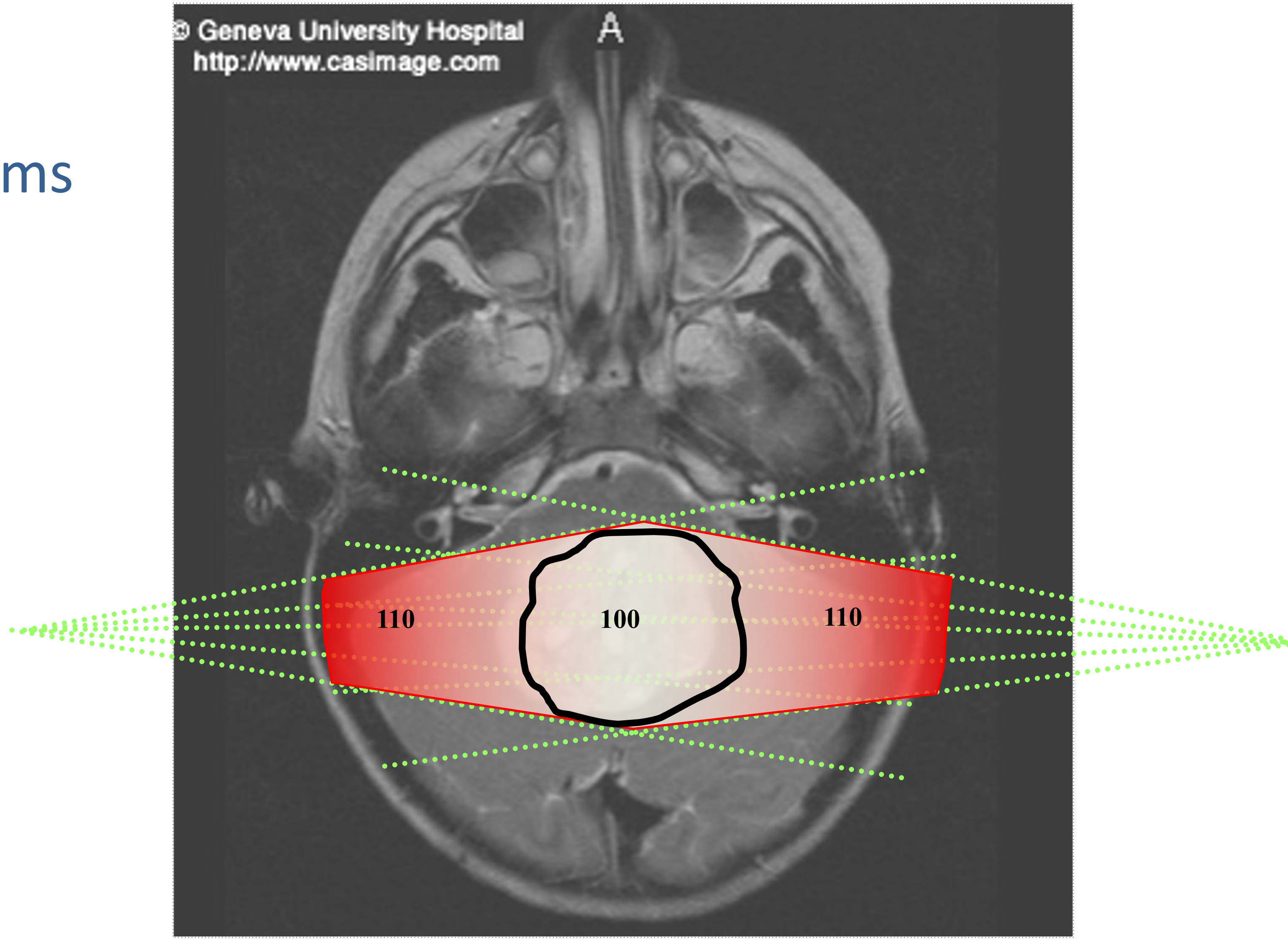
Classical Radiotherapy with X-rays

single beam

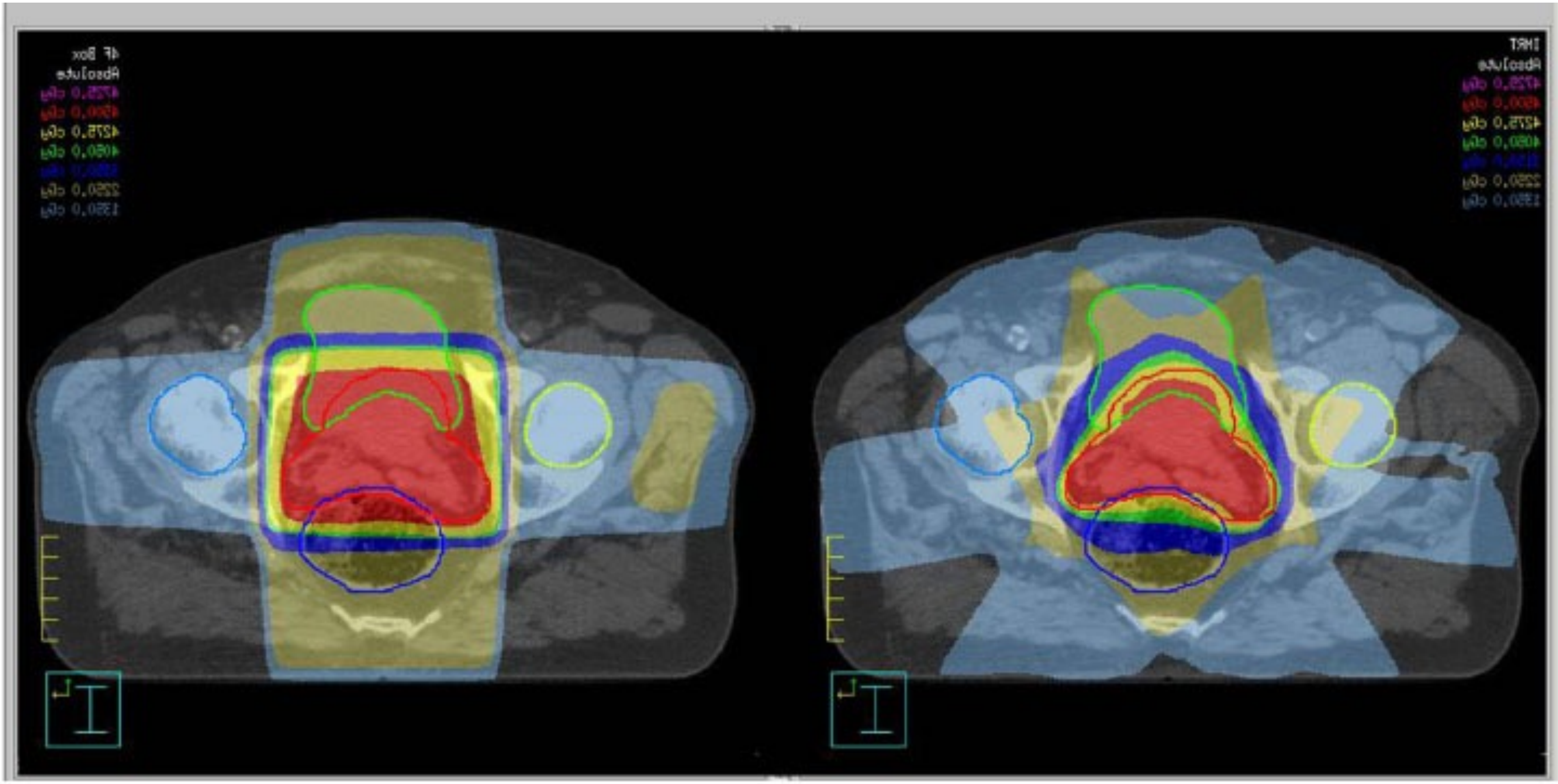


Radiotherapy with X-rays

two beams



Improved Delivery

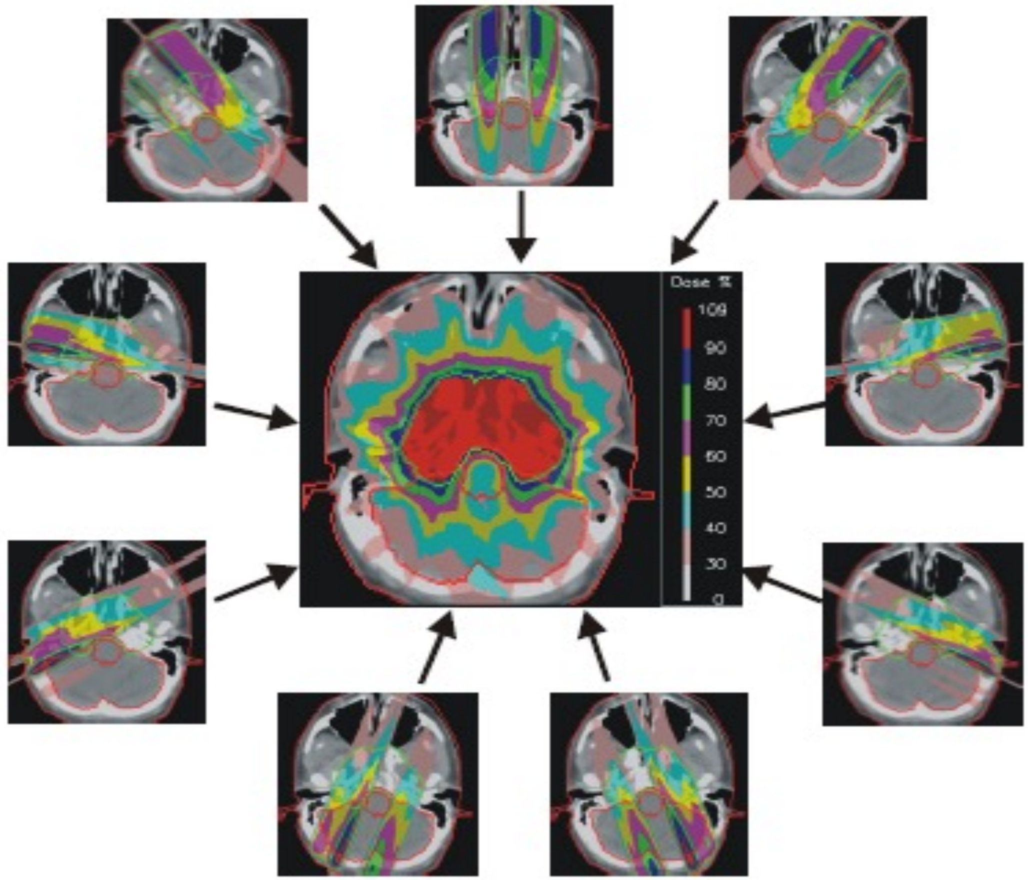


1990s: 4 constant intensity fields

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

Intensity Modulated Radiation Therapy

9 NON-UNIFORM FIELDS



60-75 grays (joule/kg) given in 30-35 fractions (6-7weeks)

to allow healthy tissues to repair:

90% of the tumours are <u>radiosensitive</u>

Advances in Radiation Therapy

In the past two decades due to:

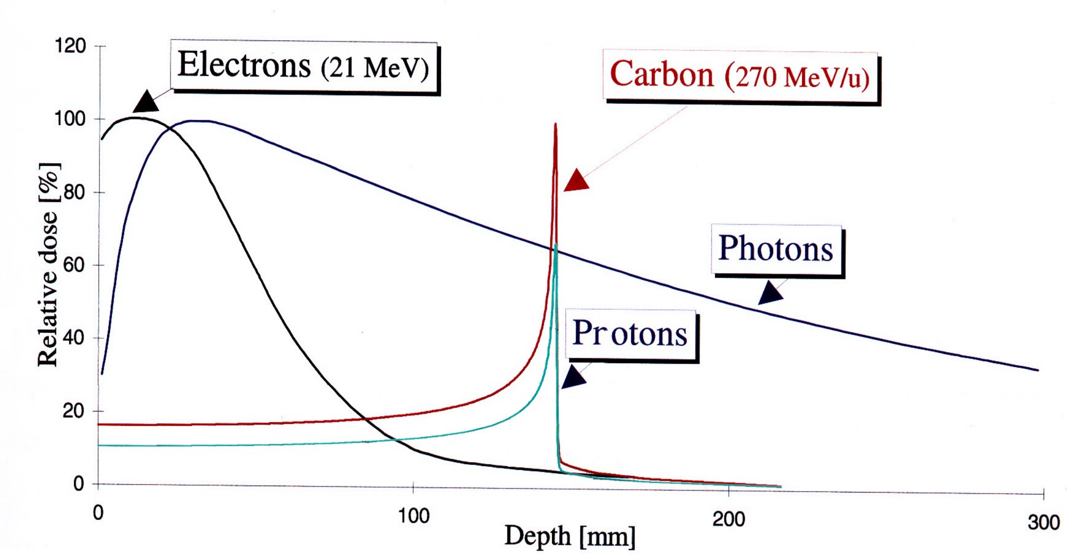
- improvements in imaging modalities, multimodality
- technology, powerful computers and software and delivery systems have enabled:
  - Intensity Modulated Radiotherapy (IMRT),
  - Image Guided Radiotherapy (IGRT),
  - Volumetric Arc Therapy (VMAT) and
  - Stereotactic Body Radiotherapy (SBRT)
  - MRI-guided Linac therapy
- Is Hadron/Particle Therapy the future?
- FLASH??

Hadron Therapy

In 1946 Robert Wilson:

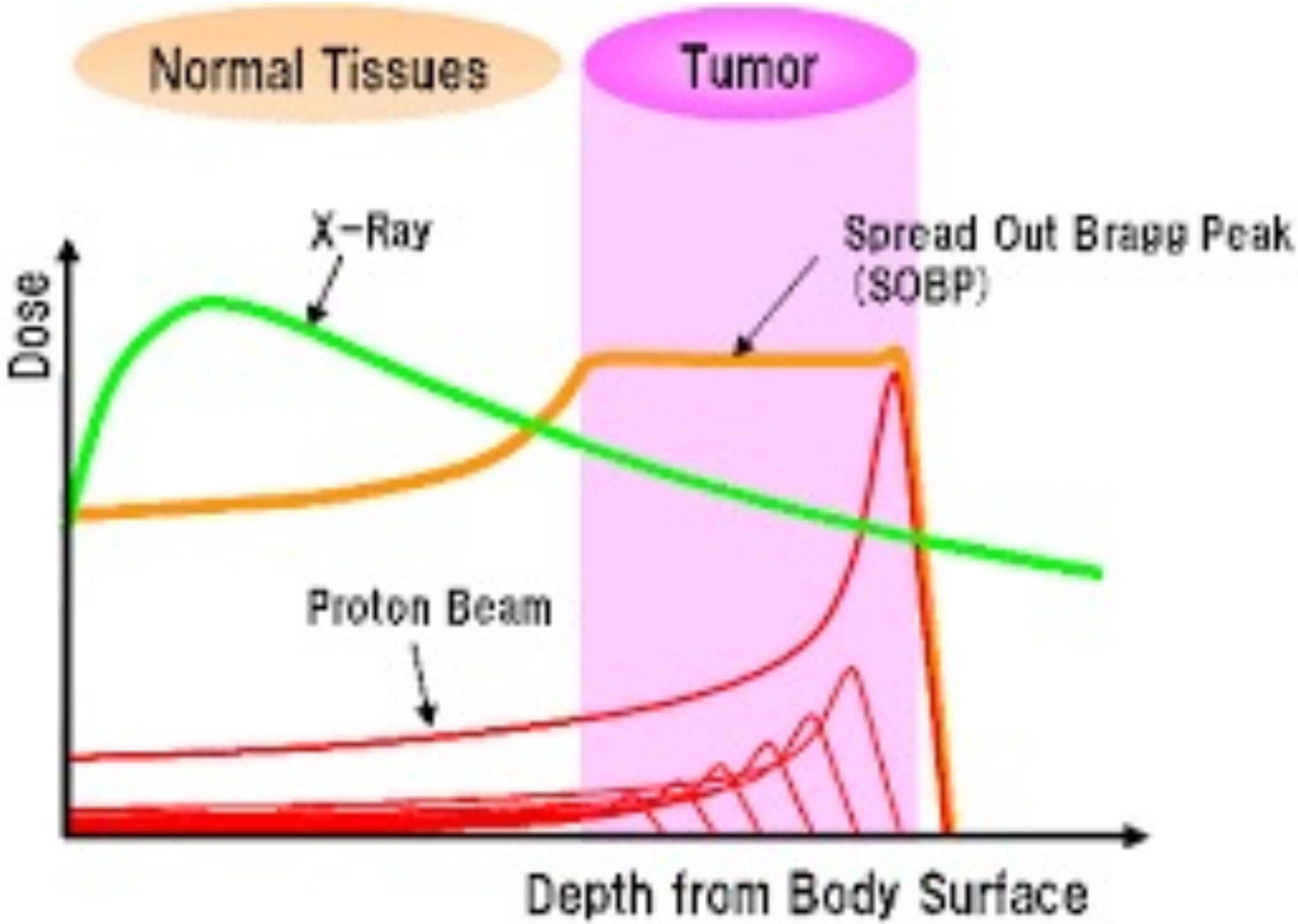
- Protons can be used clinically
- Accelerators are available
- Maximum radiation dose can be placed into the tumour
- Particle therapy provides sparing of normal tissues

- Tumours near critical organs
- Tumours in children
- Radio-resistant tumours

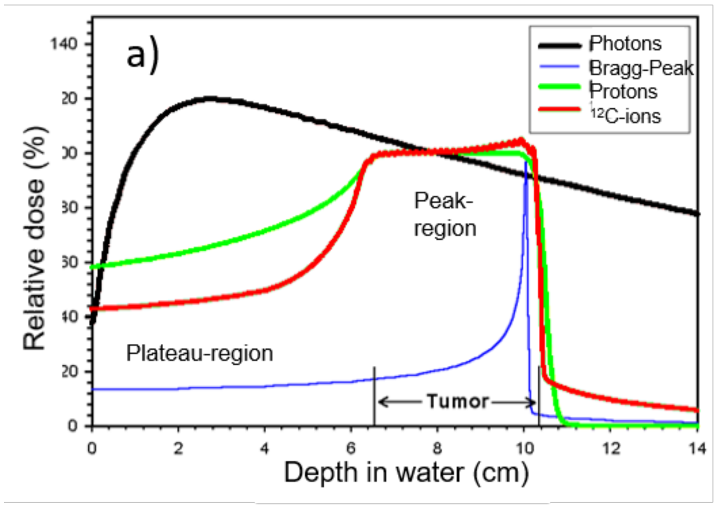


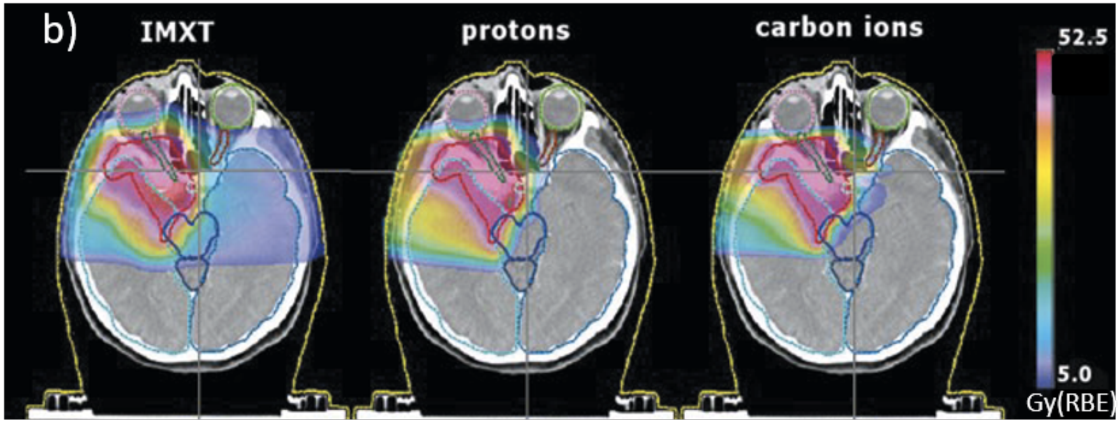
Depth in the body (mm)

Spread Out Bragg-peak targeting the **tumour**



Why Particle/Hadron Therapy?



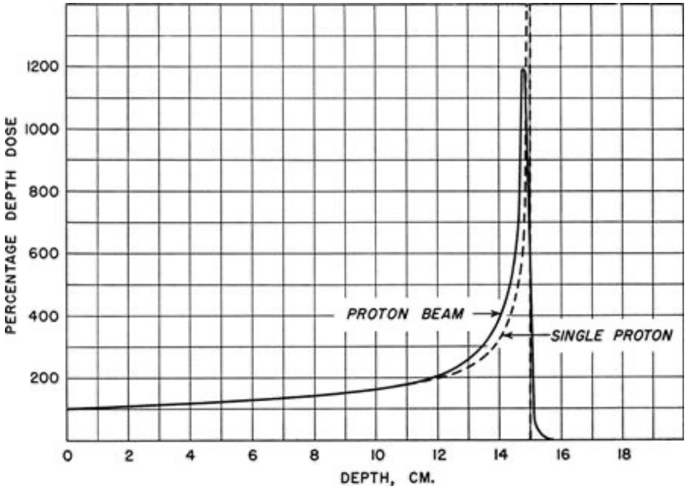


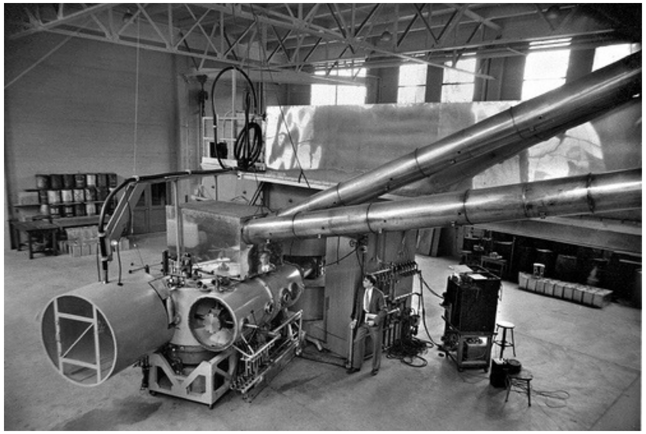
Depth dose profiles in water (a) and treatment plans (b) comparing photons, delivered with the most advanced intensity modulation RT (IMXT), and state-of-the-art scanned protons and ^{12}C ions, showing the increased tumour-dose conformity of ion therapy due to the characteristic Bragg peak (a).

1932 - E. Lawrence First cyclotron

1946 – proton therapy proposed by R. Wilson

1954 – Berkeley treats the first patient





From physics……..

3 crucial years for HT

In the years 1992-1994 the rate of progress changed:

- 1992 at Loma Linda first proton patient
- 1993 MGH (Boston) orders the first commercial protontherapy centre
- 1993 GSI starts the carbon ion ‘pilot project’
- 1994 HIMAC first carbon ion patient

Key Milestones of Hadrontherapy

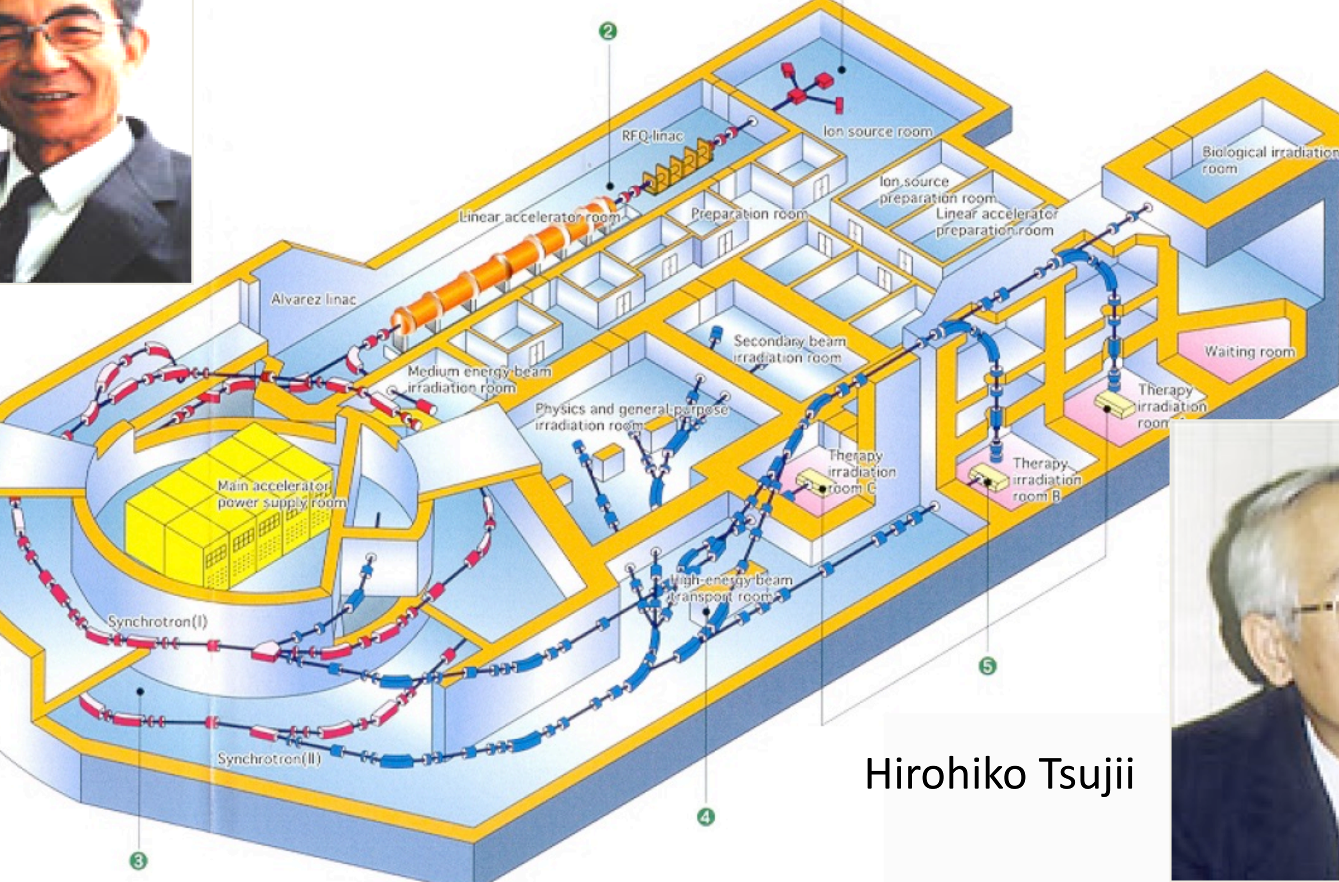
1991 — First hospital based *Proton* facility
Loma Linda University Medical Center, CA, USA

360^0 Gantry

HIMAC in Chiba is the pioneer of carbon therapy

Yasuo Hirao

First patient1994



Hirohiko Tsujii

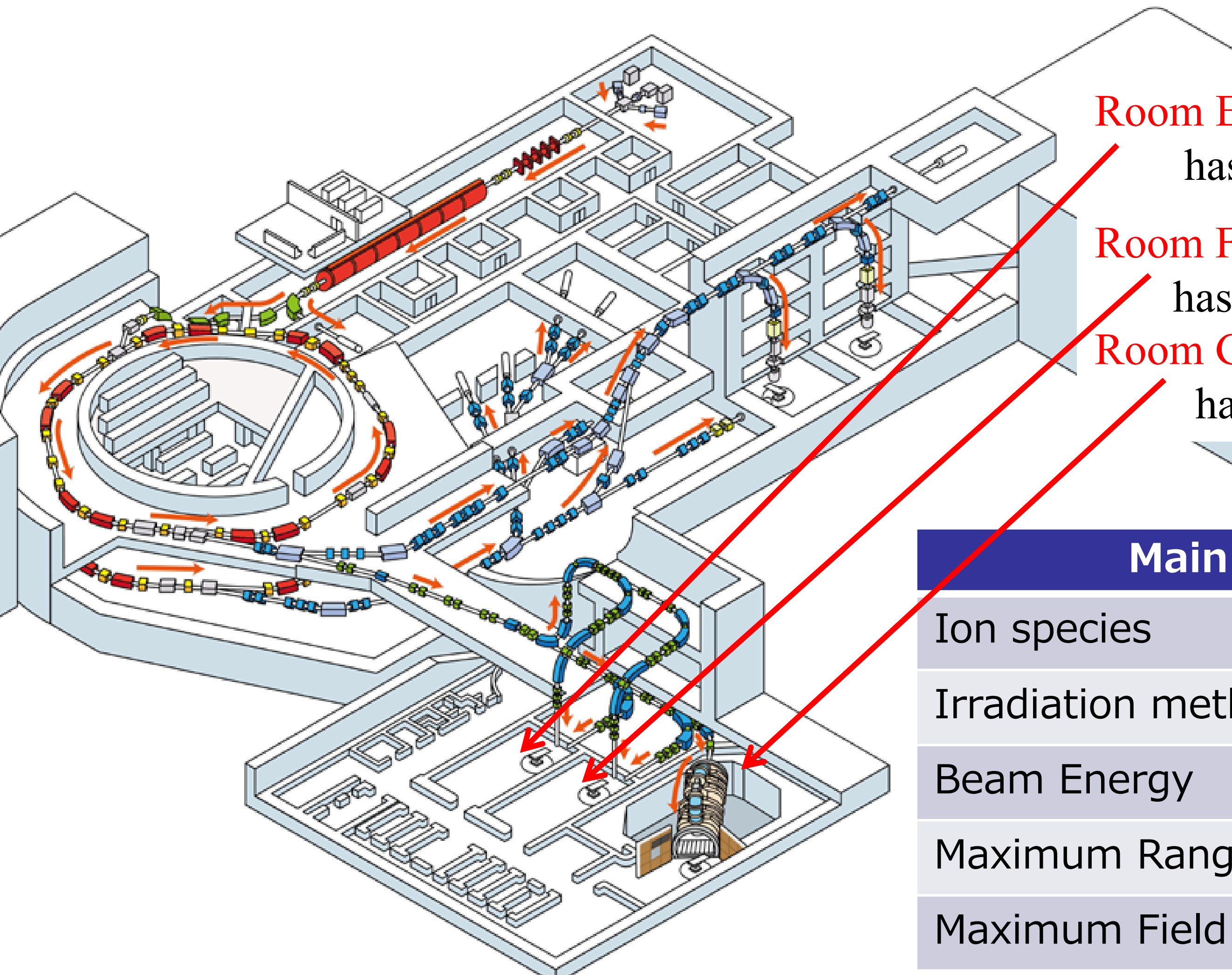
Since the cells do not repair. less fractions are possible

HIMAC: reduced fractions! Even single fraction

NIRS HIMAC

HIMAC and New Facility

First patient: 1994 - So far about 13.000 patients



Room E with H/V scanning ports has been opened since May ’11.

Room F with H/V scanning ports has been opened since Sep ’12.

Room G with rotating gantry has been opened since Apr 2018.

Main specifications	
Ion species	^{12}C
Irradiation method	3D Scanning
Beam Energy	430 MeV/n (max.)
Maximum Range	30cm in water
Maximum Field	22×22 cm^2 (E, F)

(Courtesy K. Noda)

The Darmstadt GSI ‘pilot project’ (1997-2008)

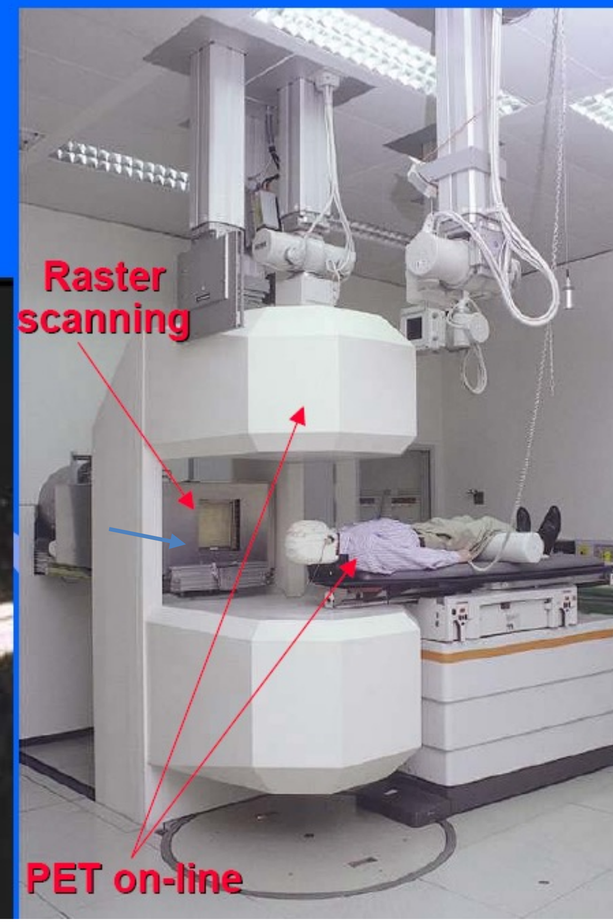
G. Kraft

J. Debus

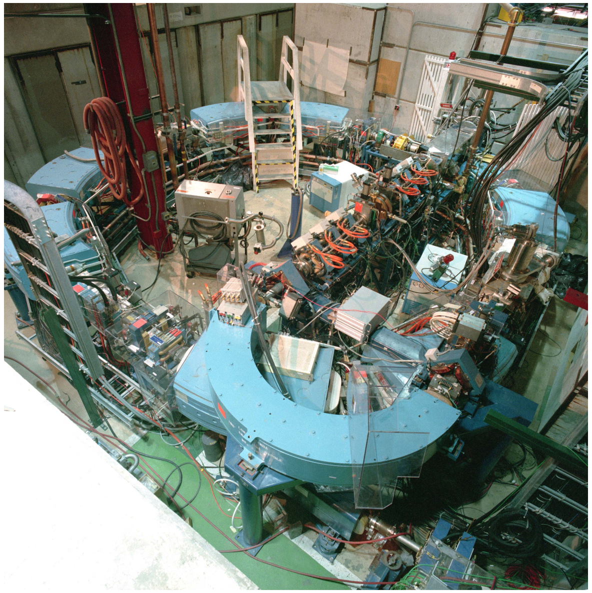
G. Kraft

450 patients treated with carbon ions

J. Debus (Heidelberg Univ.)



1993- Loma Linda USA (proton)



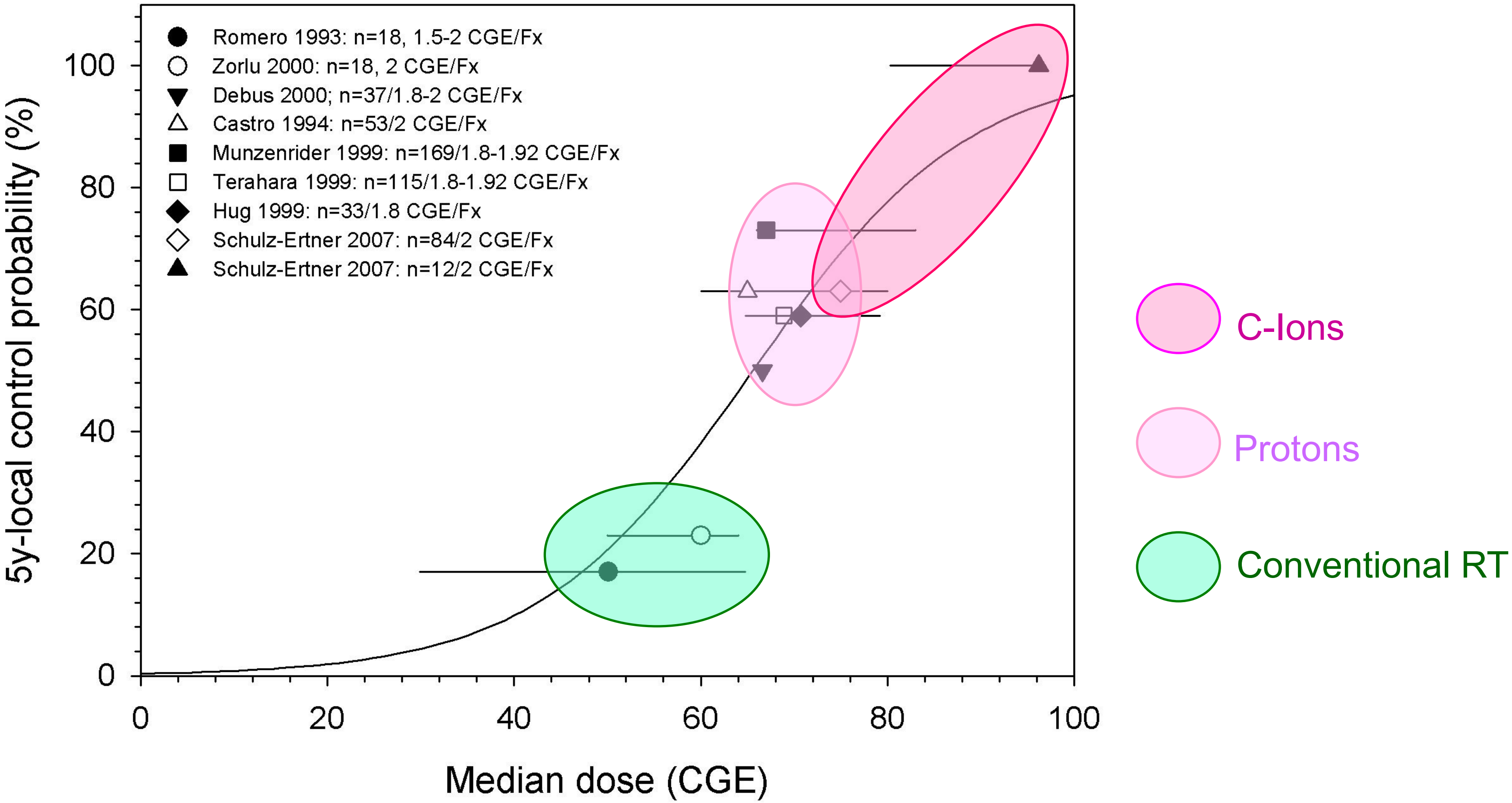
First dedicated clinical facility

1994 – HIMAC/NIRS Japan (carbon)

1997 – GSI Germany (carbon)

Three crucial years for PT……..to clinics

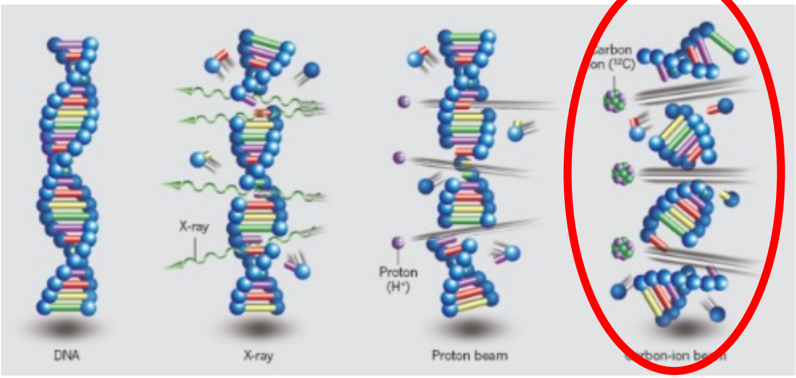
Tumour Control Rate: Chordomas



Schulz-Ertner, IJROBP 2007

Treatment with heavier ions

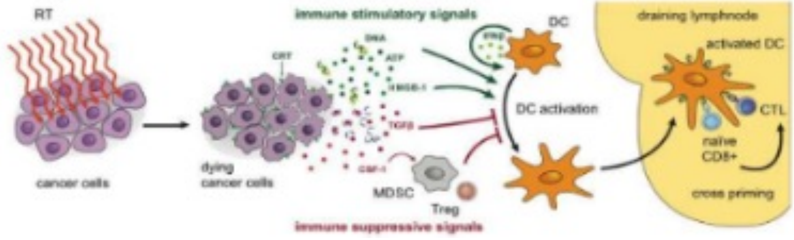
Marx, Nature, 2014



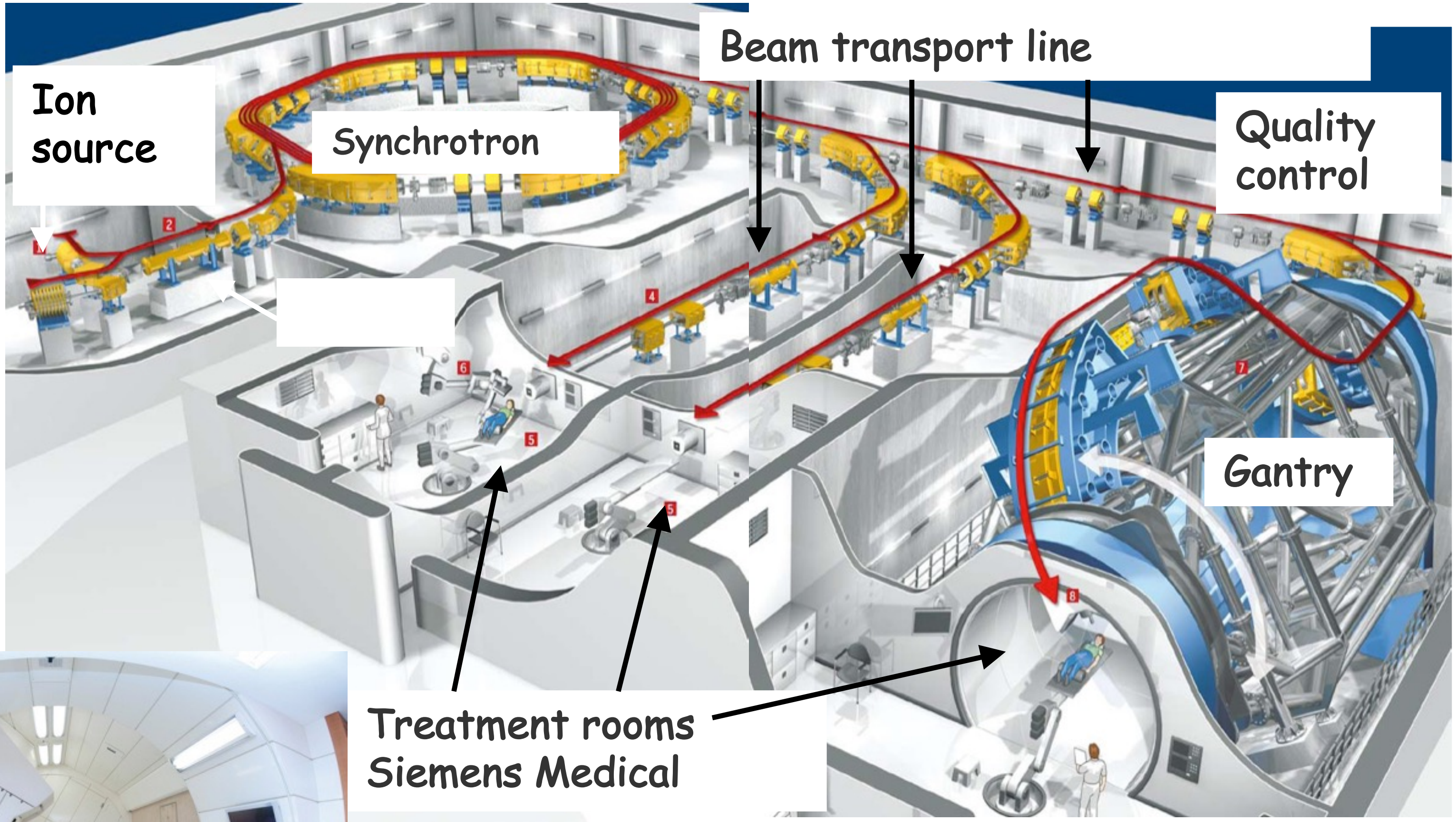
Heavy ions are **more effective than protons or X-rays** in killing cells:

1. Higher energy deposition (and ionisation) per length generates a larger number of double-strand DNA breaks and complex DNA damage that are difficult to repair
2. Energy deposition more precise, with lower straggling and scattering
3. The different damage mechanism makes ions effective on hypoxic radioresistant tumours – around 3% of all RT cases (200-500 cases/year per 10M people).

4. Recent studies show that ion therapy combined with immunotherapy may be successful in treating diffused cancers and metastasis.

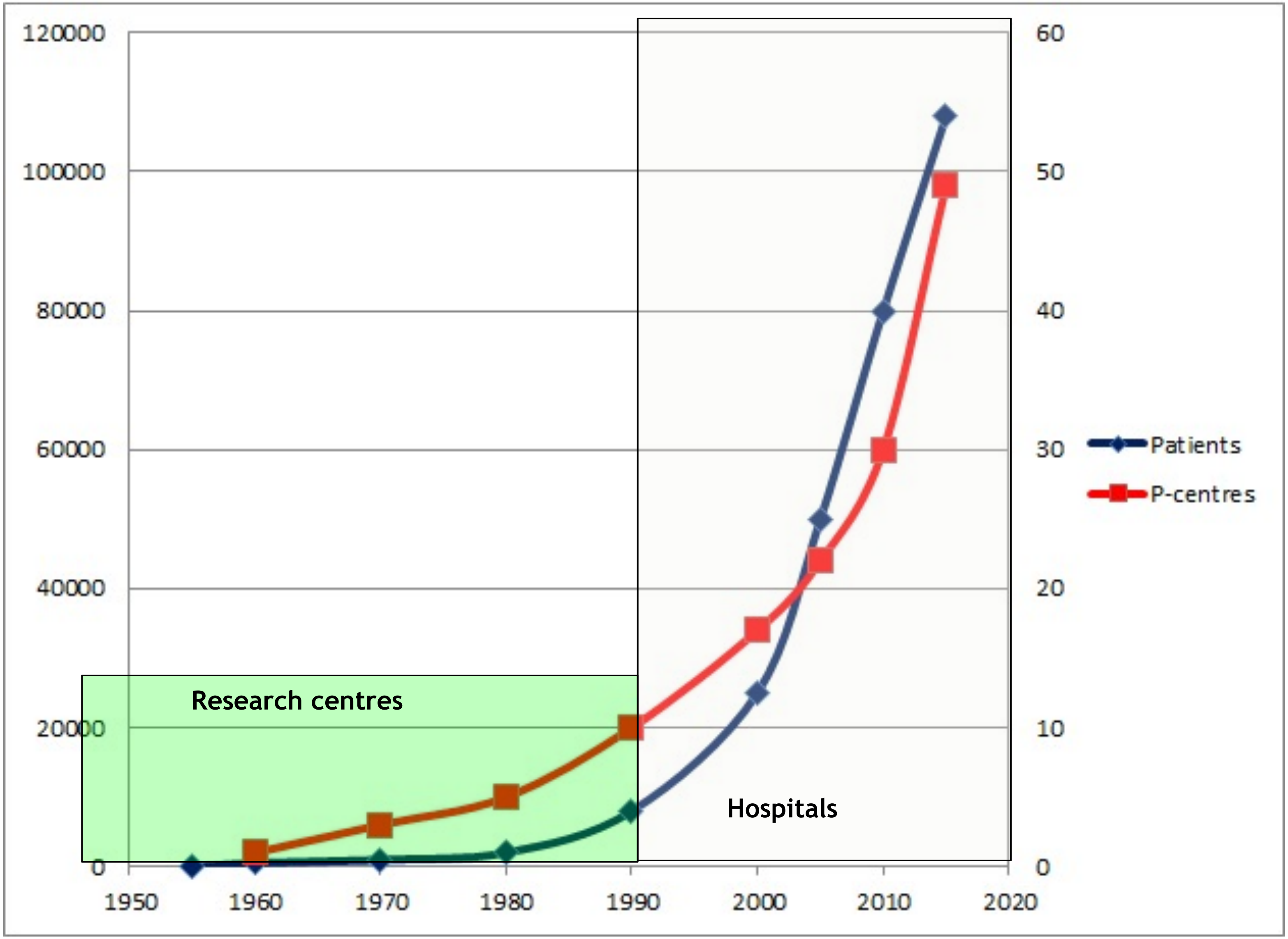


HIT - Heidelberg

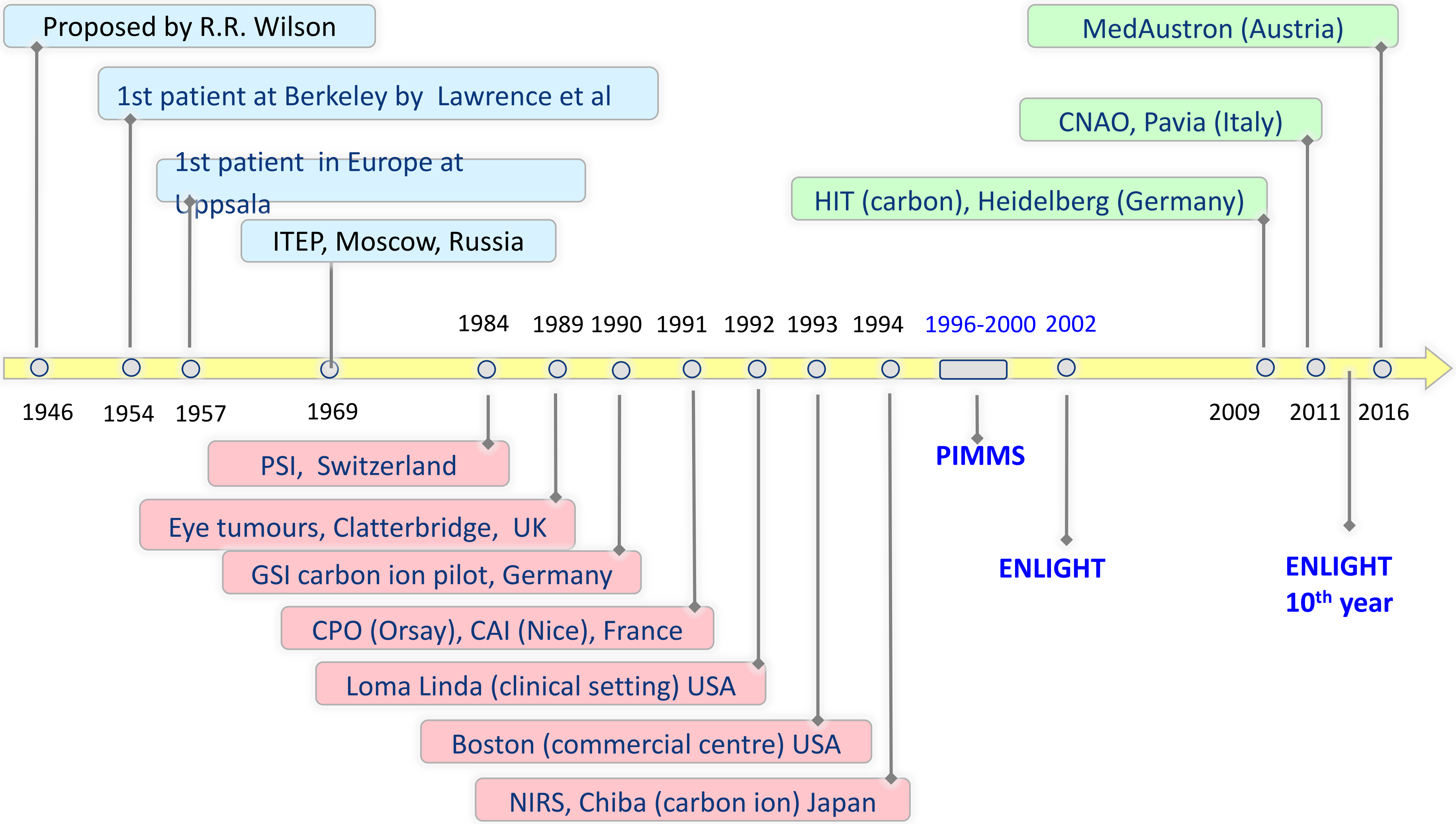


Carbon facilities in Europe: first dual ion clinical facility - started treating patients in 2009

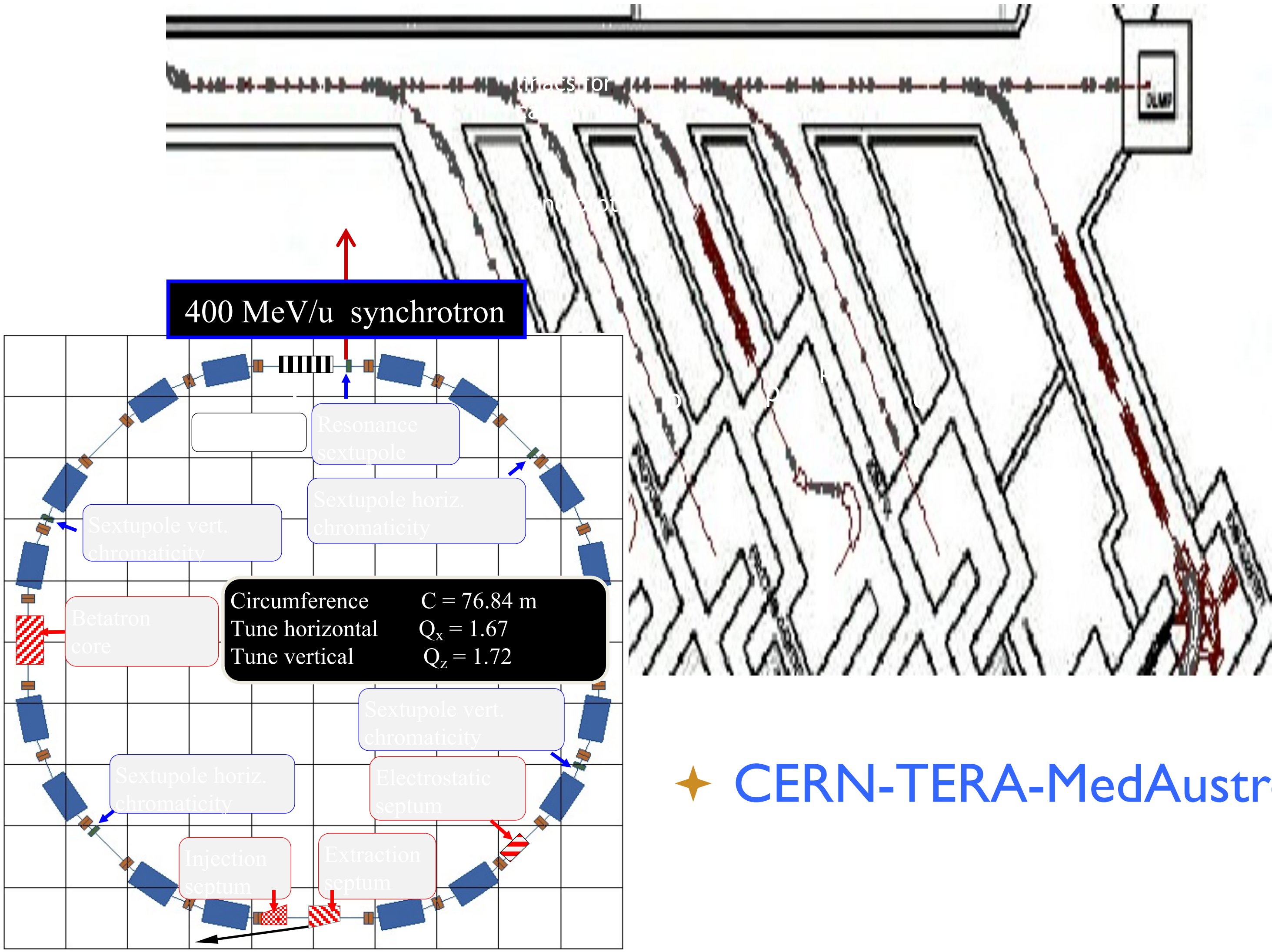
[Data from www.ptcog.ch]



Particle therapy: a short history

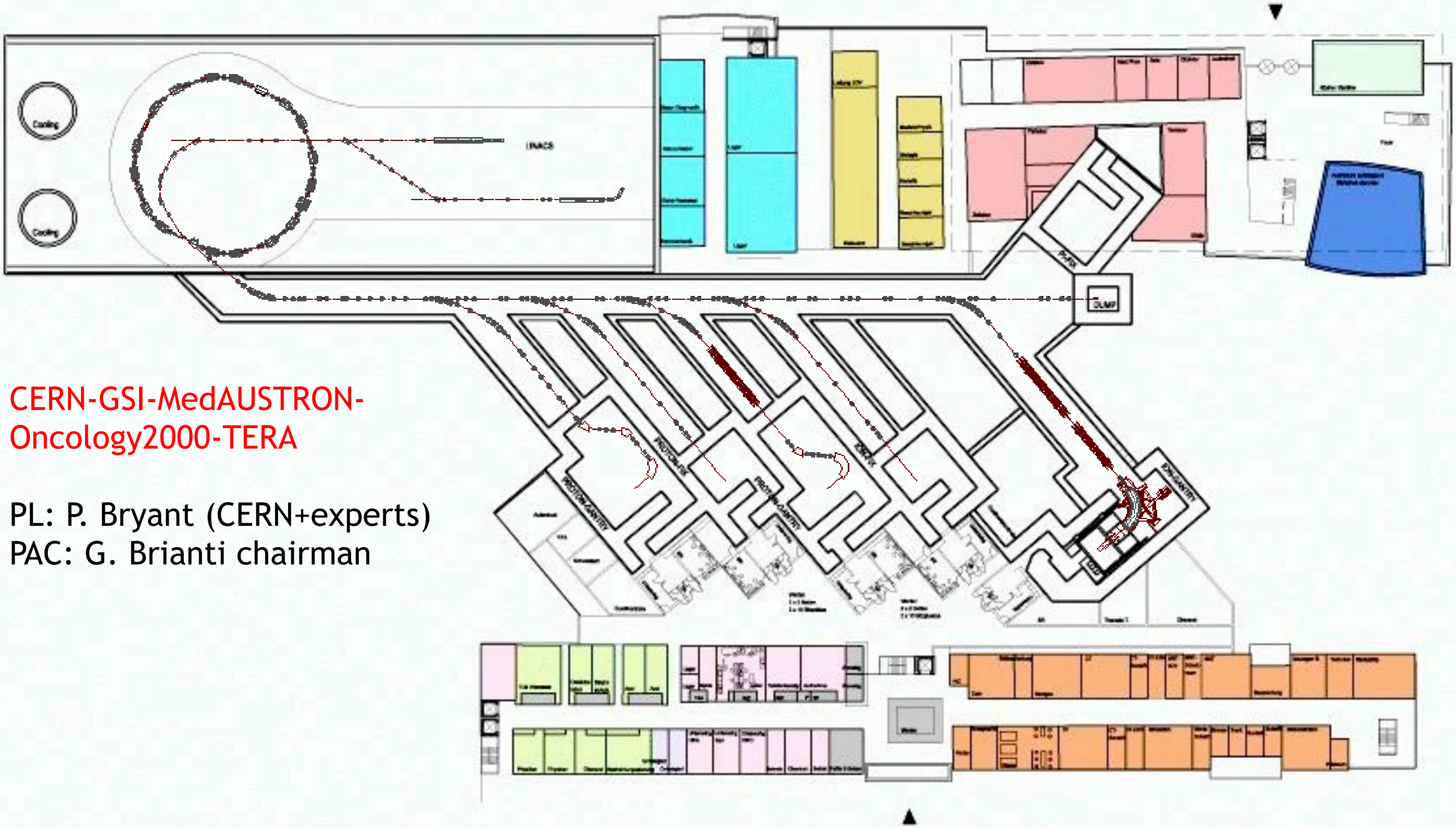


PIMMS at CERN (1996-2000)



✦ CERN-TERA-MedAustron

PIMMS (Proton-Ions Medical Machine Study)



CERN-GSI-MedAUSTRON-Oncology2000-TERA

PL: P. Bryant (CERN+experts)
PAC: G. Brianti chairman

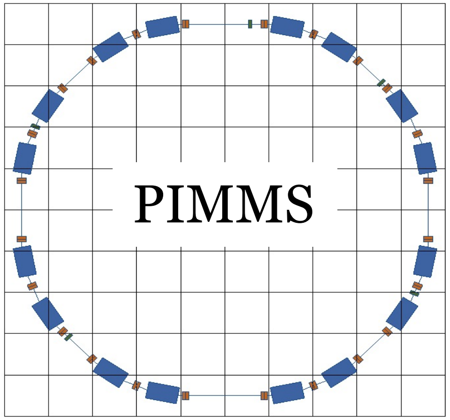
Objective: define the optimal hadrontherapy centre without constraints

PIMMS study at CERN (1996-2000)

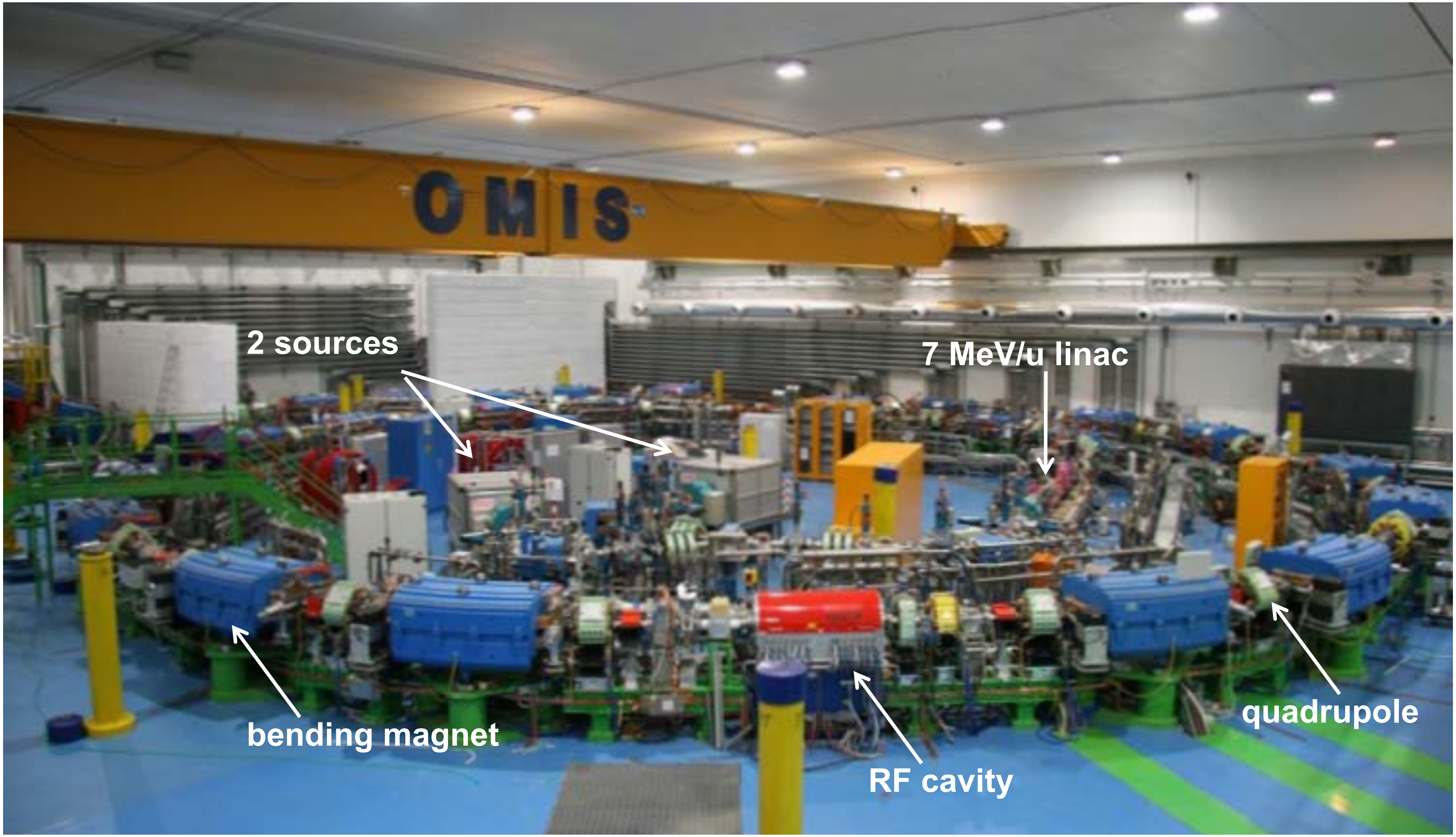
Treatment , CNAO, Italy
2011

MedAustron, Austria 2016

1996-2000
PIMMS study



CNAO: Pavia, Italy

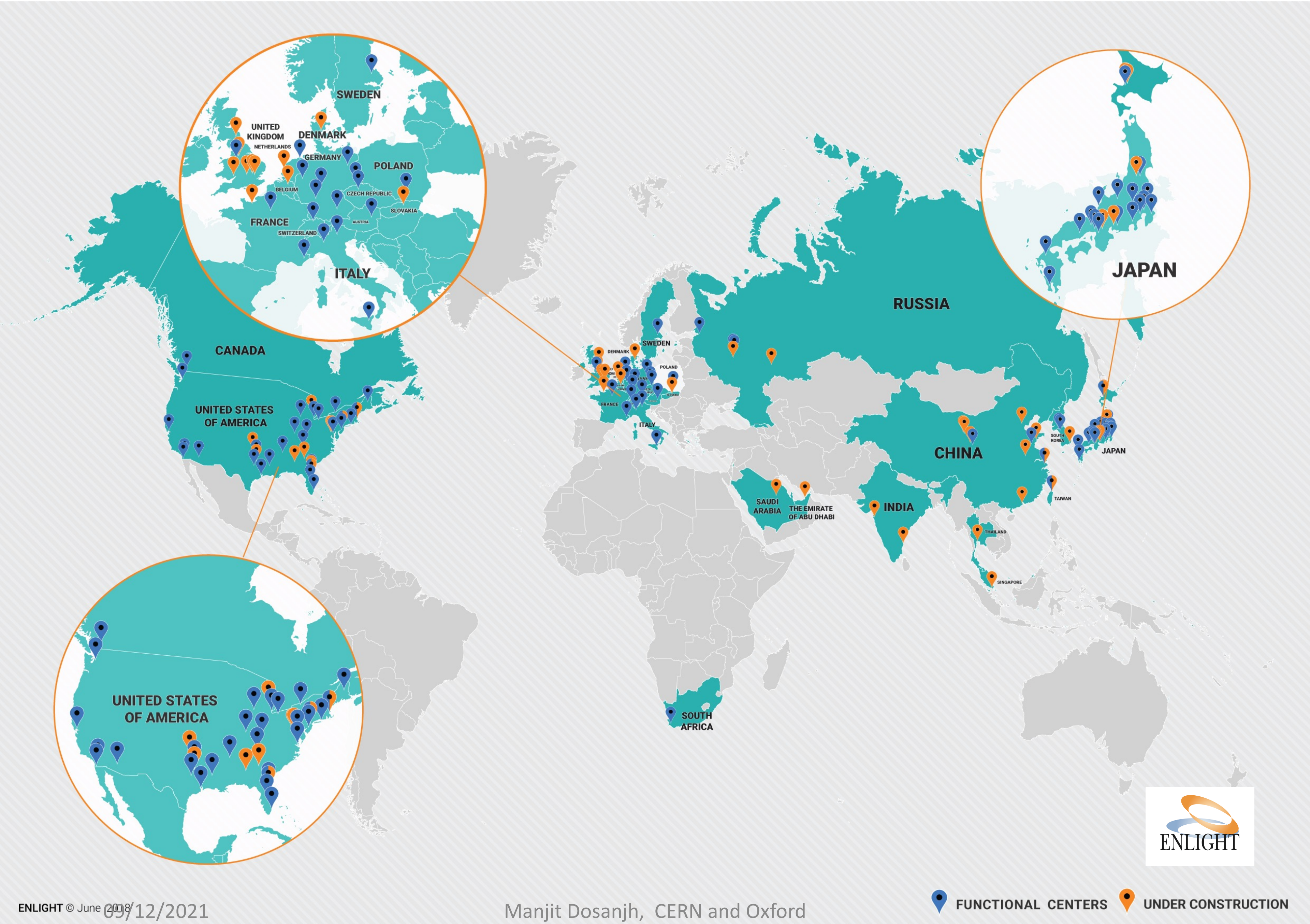


Started treating patients in 2011

MedAUSTRON – collaboration with CERN

Started treating patients December 2016, First carbon in2019

Facilities in operation in Europe 2020


SWEDEN
UNITED KINGDOM
DENMARK
NETHERLANDS
GERMANY
POLAND
BELGIUM
CZECH REPUBLIC
SLOVAKIA
FRANCE
AUSTRIA
SWITZERLAND
ITALY
JAPAN
RUSSIA
CANADA
UNITED STATES OF AMERICA
CHINA
SOUTH KOREA
TAIWAN
SAUDI ARABIA
THE EMIRATE OF ABU DHABI
INDIA
THAILAND
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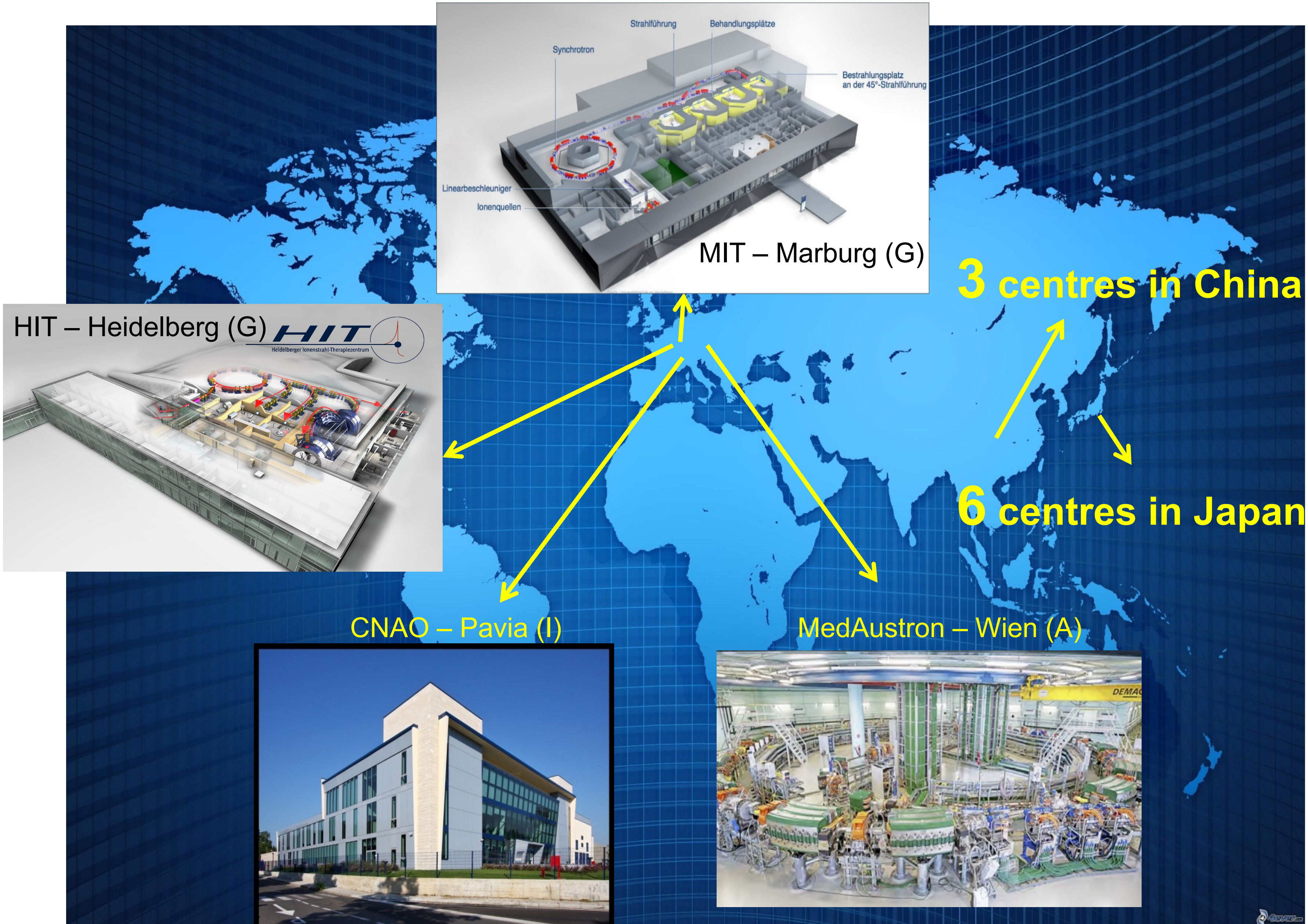
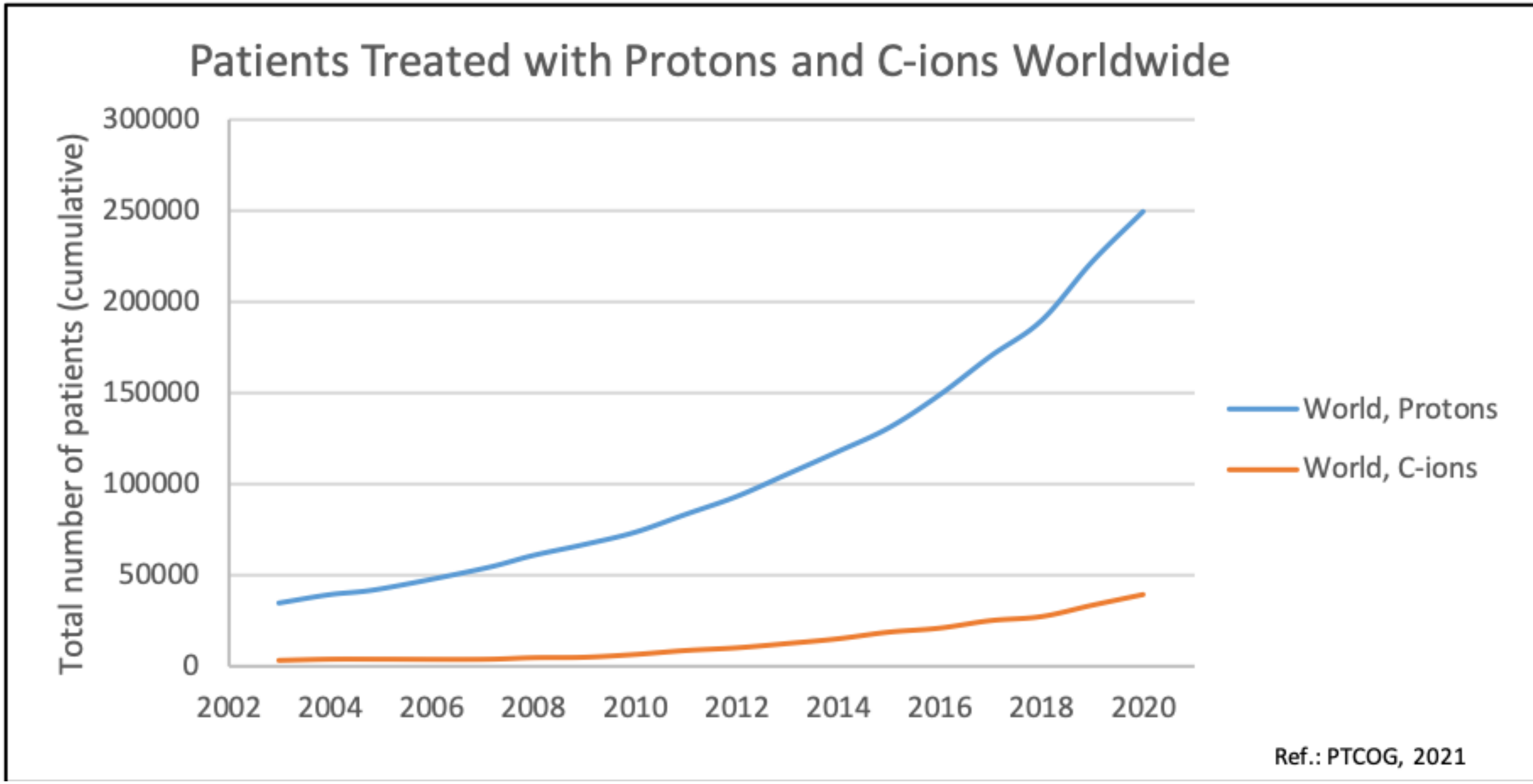
Multi-ions clinical facilities in the World



Patient Numbers

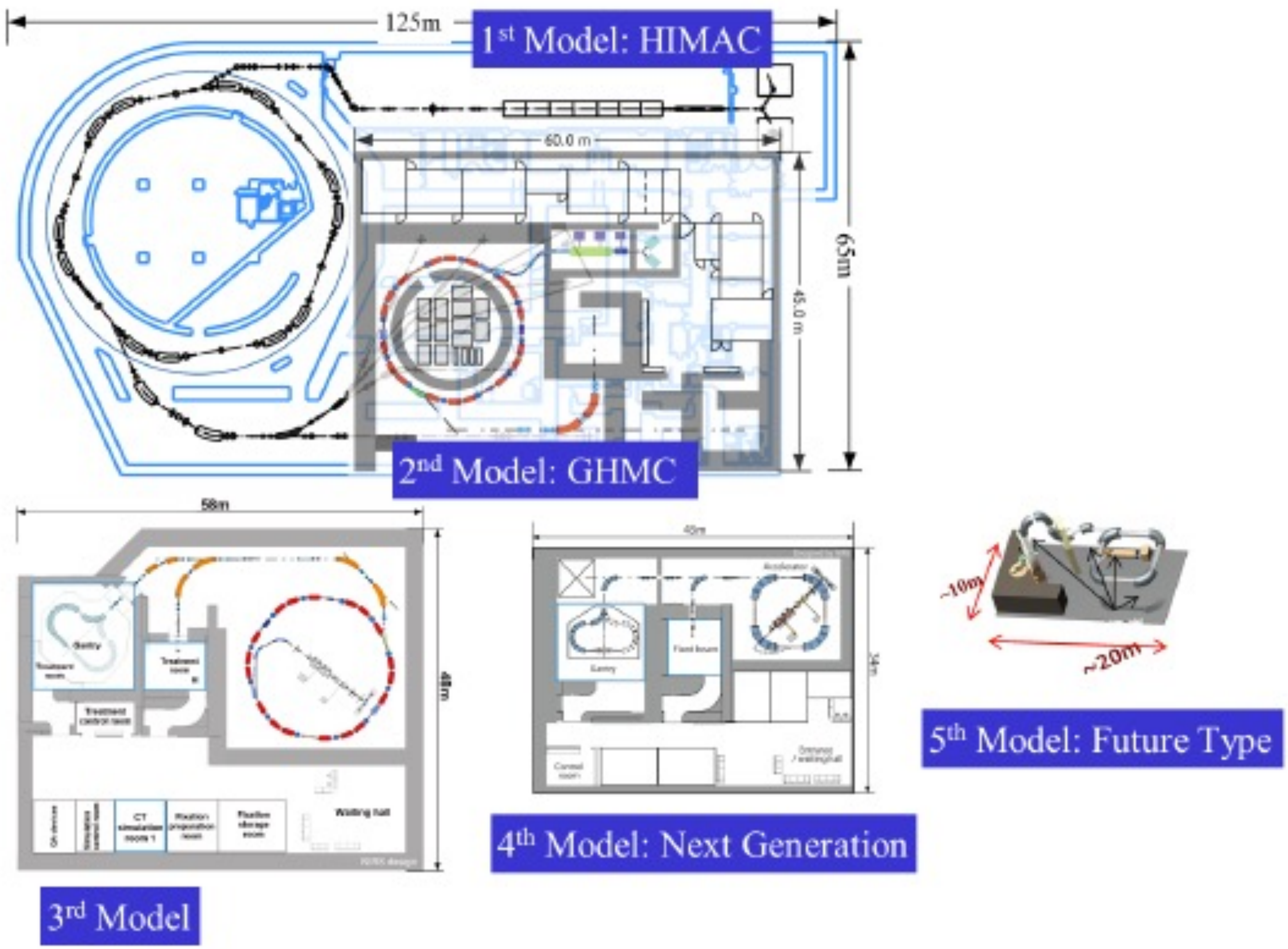


Much more still needs to be done

- 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

New Developments

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.

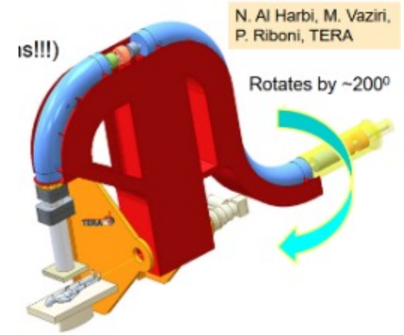
+ Specific requirements for SEEIIST:

- ❑ 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

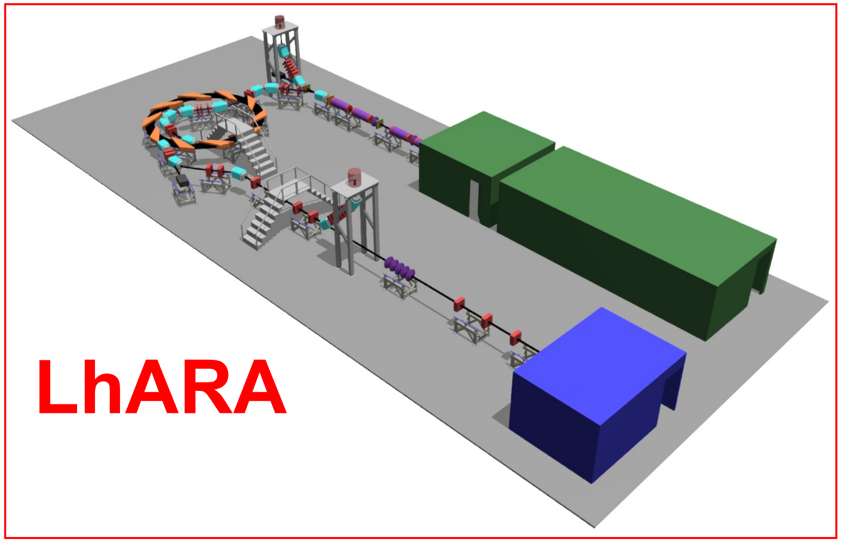
CERN LHC superconducting magnet

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

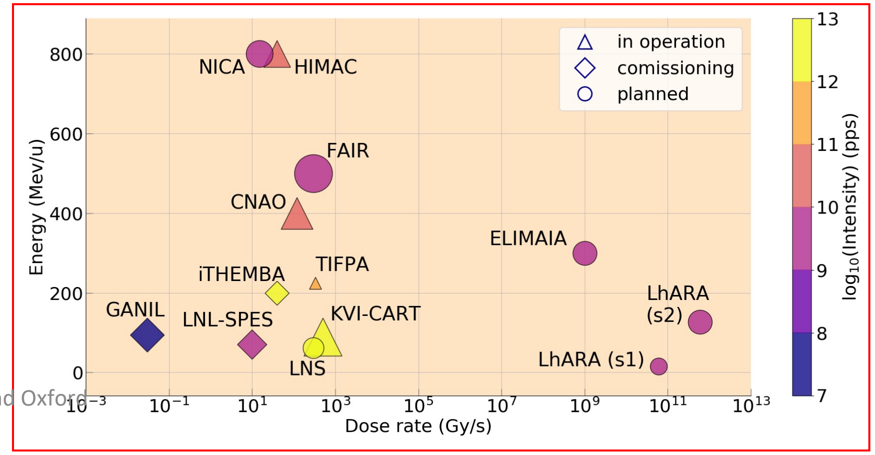


Pre-CDR: CCAP-TN-01; arXiv:2006.00493; submitted to Frontiers in Nuclear Physics, Medical Physics and Imaging

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 Central Laser Facility, Science & Technology Facilities Council ASTeC, Science & Technology Facilities Council ISIS Neutron and Muon Source
Clinical partners: Oncologists, medical/biophysics, providers	Imperial College Healthcare NHS Trust, NHS 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



New Initiatives

South-East European International Institute for Sustainable Technologies (SEEIIST) in the spirit of ‘Science for Peace’

Prof. Herwig Schopper, former Director General of CERN
Dr. Sanja Damjanovic, Minister of Science of Montenegro

positive reception by a number of organizations and institutions

UNESCO · CERN · GSI FAIR · IAEA · ICTP

Why do we need SEEIIST?

PT Facilities in operation

Candidate Members for the South-East European International Institute for Sustainable Technologies

Republic of Albania

Bosnia and Herzegovina

Republic of Bulgaria

Republic of Croatia

Hellenic Republic

Kosovo*

FYR of Macedonia

Montenegro

Republic of Serbia

Republic of Slovenia

South-East European International Institute for Sustainable Technologies SEEIIST

Major initiative to create a pan-European facility in South Eastern Europe

Bottom-up led by European Scientists across Europe – building international cooperation

’Science for Peace’, ‘Science Diplomacy’ initiative similar to CERN and SESAME

The Pan-European Dimensions: SEEIIST Cancer Therapy Research Infrastructure Brings an Added Value for Europe

Fighting against cancer

Nuclear medicine as crucial component of future personalised cancer care

Develop advanced cancer therapy with ion beams and isotopes

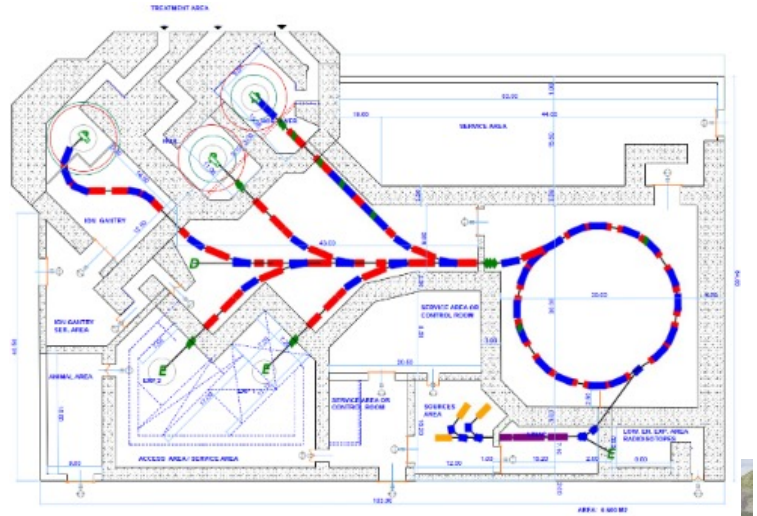
Two Strategic Objectives – One initiative

Building international cooperation and scientific capacity in South East Europe

Advance European integration, reverse brain drain, connect to Europe

New European initiative in ion therapy - SEEIIST

- The **SEEIIST** (South East Europe International Institute for Sustainable Technologies) is a new international partnership aiming at the construction of a new Research Infrastructure for cancer research and therapy in South East Europe (10 member countries).
- SEEIIST is supported by the European Commission, to develop the facility design in collaboration with CERN.
- Goals are to develop a new advanced design and to build international cooperation and scientific capacity in a region that will join EU but is less develop and still divided, in the line of “science for peace”.
- Promoted by H. Schopper, former Director General of CERN, and S. Damjanovic, former Minister of Science of Montenegro.



Accelerator: a large normal-conducting synchrotron
Estimated cost of facility: 240 M€

Goals and Benefits for SEE Region

- more than 40 millions people could benefit from this project
- possibility for education, training and innovation
- more effective cancer treatment using the cutting-edge technologies and innovative treatment options
- participate in clinical trials Europe-wide
- a unique facility in Europe which will have 50% time for fundamental, translational, clinical innovative research
- attractive for external research community: also cheaper research and living costs
- possibility to boost the regional development and create a new generation of young scientists, industry
- mitigate brain-drain - reverse brain in some cases

HITRI plus

Heavy Ion Therapy Research Integration

22 Institutes

(4 CIRT centres, 10 research institutions, 5 universities, 3 SMEs)

14 European Countries

Participant No *	Participant organisation name	Country
1 (Coordinator)	Fondazione Centro Nazionale di Adroterapia Oncologica (CNAO)	IT
2	Bevatech GmbH (BEVA)	DE
3	Commissariat à l'énergie atomique et aux énergies alternatives (CEA)	FR
4	European Organisation for Nuclear Research (CERN)	IEIO
5	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	ES
6	Cosylab Laboratorij za kontrolne systeme dd (CSL)	SI
7	GSI Helmholtzzentrum für Schwerionenforschung GmbH (GSI)	DE
8	Universitätsklinikum Heidelberg (UKHD/HIT)	DE
9	Istituto Nazionale di Fisica Nucleare (INFN)	IT
10	EBG MedAustron GmbH (MEDA)	AT
11	Marburger Ionenstrahl-Therapie Betreibergesellschaft mbH (MIT)	DE
12	Paul Scherrer Institut (PSI)	CH
13	South East European International Institute for Sustainable Technologies (SEEIIST)	CH
14	Universita ta Malta (UM)	MT
15	Philipps-University Marburg (UMR)	DE
16	Uppsala University (UU)	SE
17	Wigner Research Centre for Physics (Wigner RCP)	HU
18	Riga Technical University (RTU)	LV
19	Ss, Cyril and Methodius University in Skopje, Republic of North Macedonia (UKIM)	MK
20	Clinical Centre of Montenegro (CMSM)	ME
21	Sentronis a.d. (SEN)	RS
22	Jožef Stefan Institute (IJS)	SI

HITRI*plus* Objectives

Starting from its basic motivations, the HITRI*plus* Consortium has identified five strategic objectives to be achieved within the Project, aimed at the advancement of ion therapy research with ions heavier than protons.

1. To **integrate, open up** and **broaden** the leading European Research Infrastructure for the treatment of cancer with **beams of ions,** ranging from helium to carbon and to heavier ions.

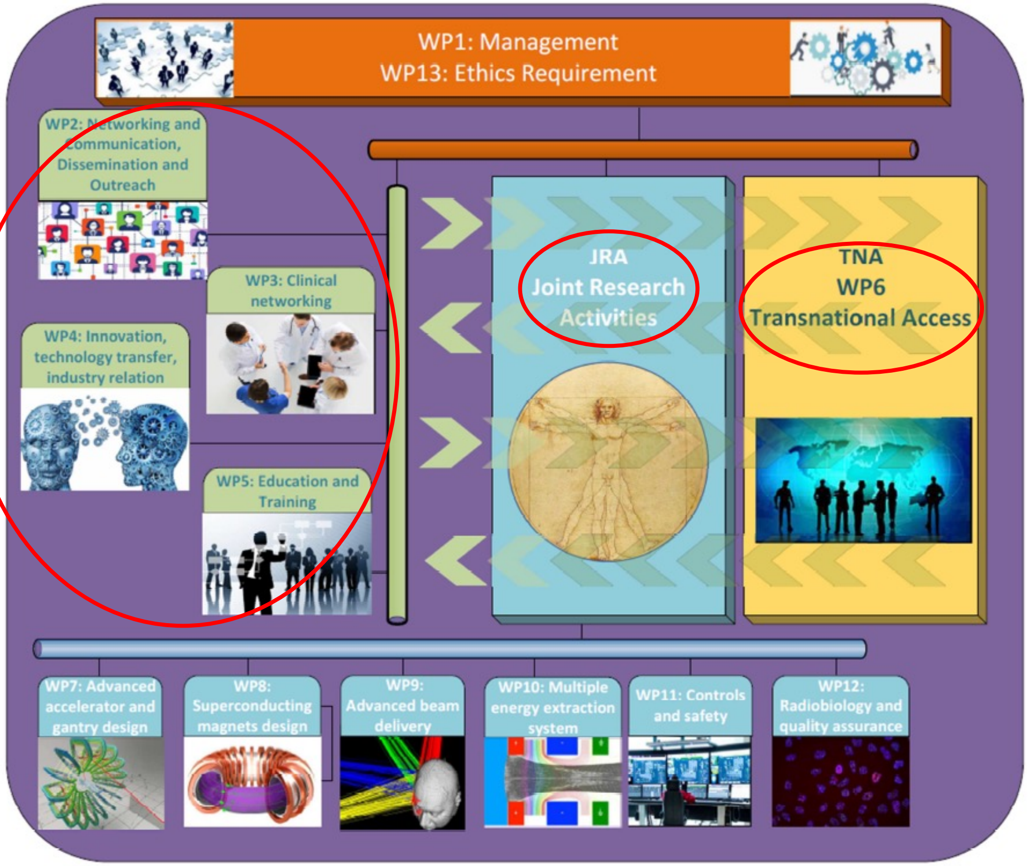
2. To **coordinate and strengthen** the research programmes on heavy ion therapy of different European institutions, by promoting synergies, collaborations, innovation, knowledge transfer, new initiatives and sharing of tools and data.

3. To develop in a joint and coordinated way **novel technologies** to improve the accelerators and their ancillary systems that provide particle beams to this scientific community. These technologies will **improve the present generation** of facilities and will be the **foundation for a next generation** European design for ion therapy facilities.

4. To establish a **European multidisciplinary community** for heavy ion therapy research, aiming at improving treatment strategies and modalities by connecting physics and engineering with medicine, biology and biophysics, and to **extend this community** towards emerging European regions, addressing in particular **new initiatives in South East Europe**.

5. To define the main technical features and the scientific programme of a future **pan-European Research Infrastructure** for medical and radiobiological research with heavy ion beams, to be built in South East Europe or in another European region.

https://www.hitriplus.eu/



Networking Activities: communication, dissemination and outreach, clinical networking, innovation technology transfer and industry relations, education and training; **Transnational Access**: to promote the access to the existing facilities of the research and clinical communities; **Joint Research Activities**: improved accelerator and gantry design, superconducting magnet design, advanced beam delivery, multiple energy extraction system, controls and safety, radiobiological dosimetry and Quality Assurance.

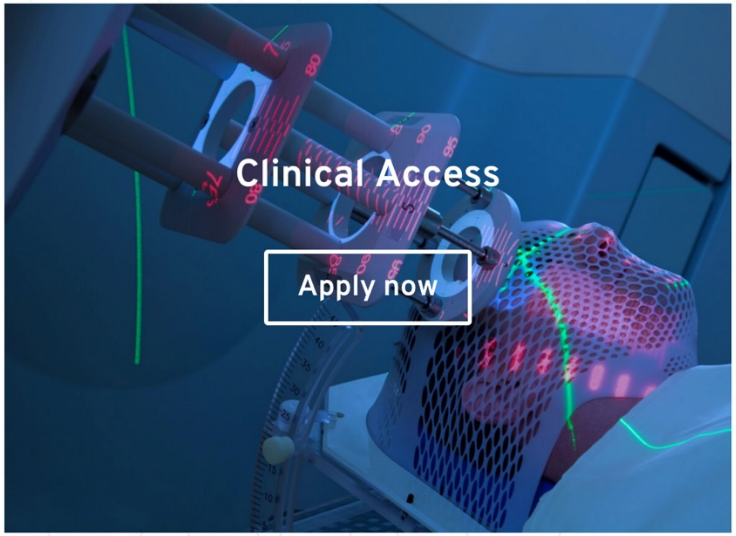
HITRIplus
Heavy Ion Therapy Research Integration

Transnational access opens to Clinical and Research programmes.

www.hitriplus.eu/transnational-access-what-is-ta/

Clinical and Research programmes

Transnational Access opens to scientific community the five European facilities providing ion beams

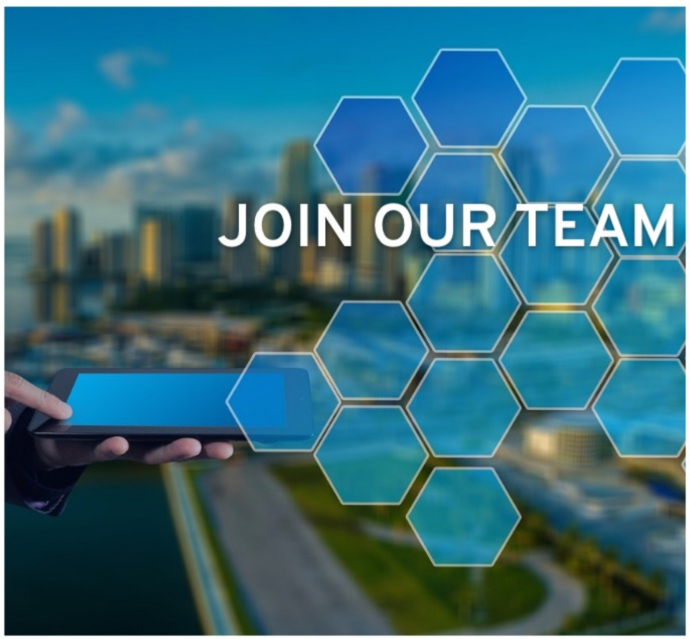


HITRI plus
Heavy Ion Therapy Research Integration

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

For **internship and secondment opportunities**, we have created a form for the application. It is required to upload a CV, that will be directly adressed to UM (Malta University) for application evalutation.

HITRI*plus* internship and secondment opportunities



Name *

Insert your name

Last name *

Insert your last name

Email *

Your email address

Upload CV *

Sfoglia... Nessun file selezionato.

Submit

HITRI plus
Heavy Ion Therapy Research Integration

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- ***Annual meeting***, open, free
- Latest developments in the field
- Oral presentation for winning posters
- <u>Networking</u>
- <u>Collaboration</u>
- Raising awareness at international level
- <u>Special session dedicated to training</u>
- Magazine – ***Highlights***
- **@ENLIGHTNETWORK**

www.cern.ch/enlight