From (Particle) Physics to Medical Applications

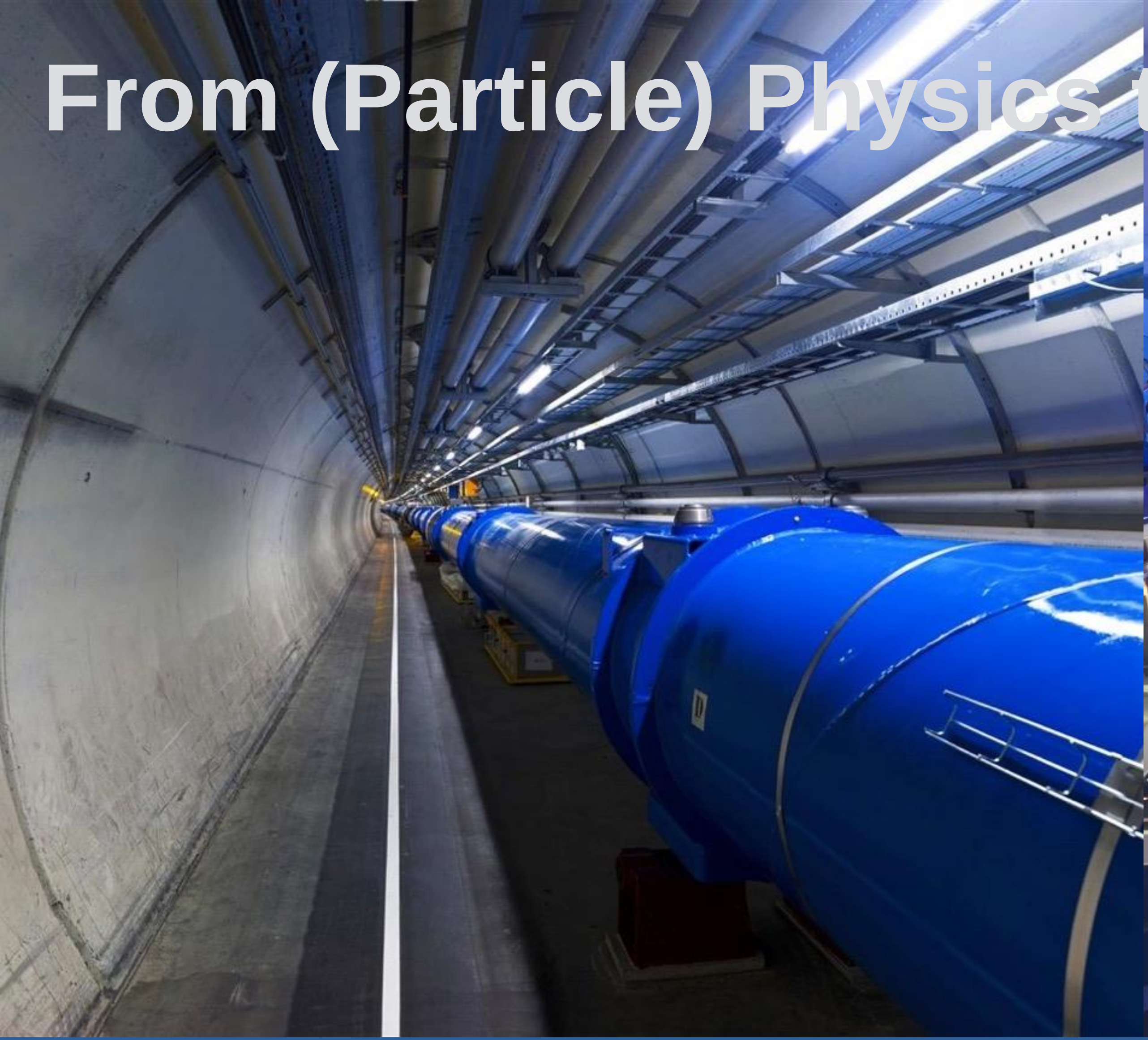


Photo: CNAO treatment room

Manuela Cirilli
Medical Applications Adviser
CERN Knowledge Transfer group

Disclaimer(s) & Acknowledgments

Of course, I had to select the material to be included.
And of course, Physics ≠ HEP (but a lot of HEP here, and a lot of CERN examples).

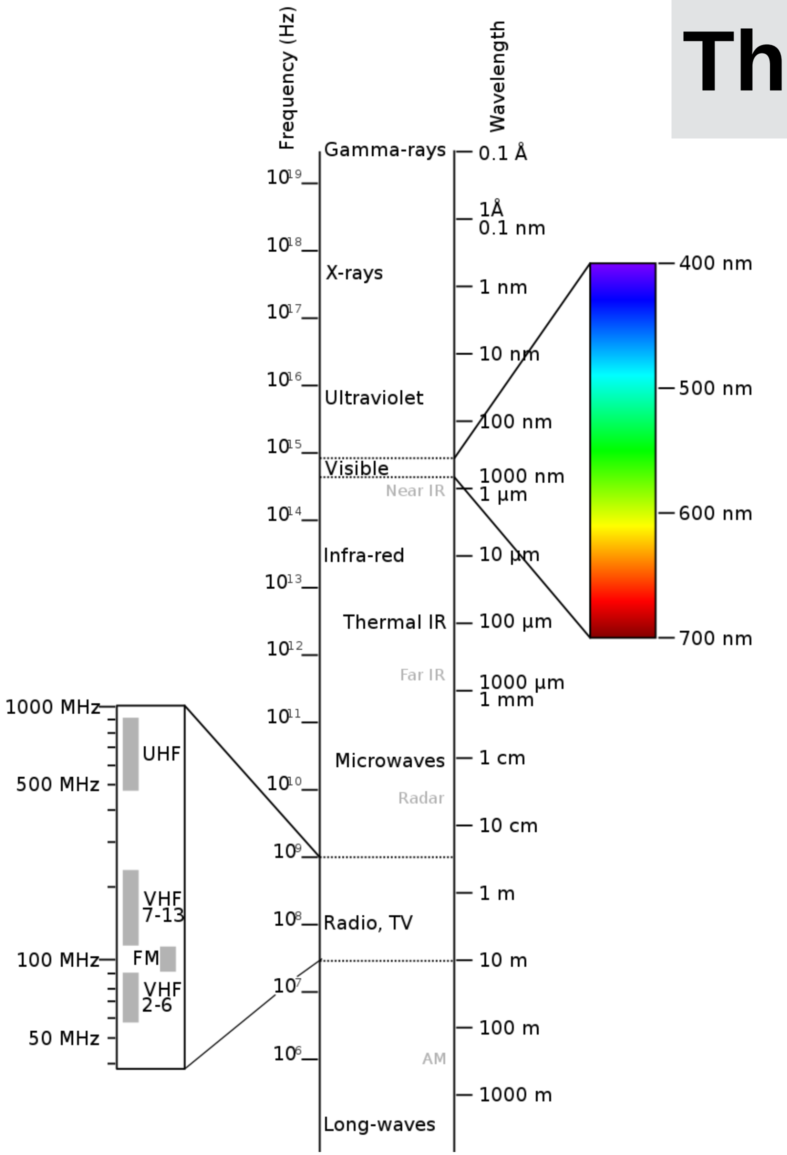
The CERN medical applications-related projects presented in this talk are realized by the CERN scientists and engineers: without their skills, ingenuity, and dedication, there would be no knowledge to transfer! Some names are acknowledged on the respective slides, but there are many more.

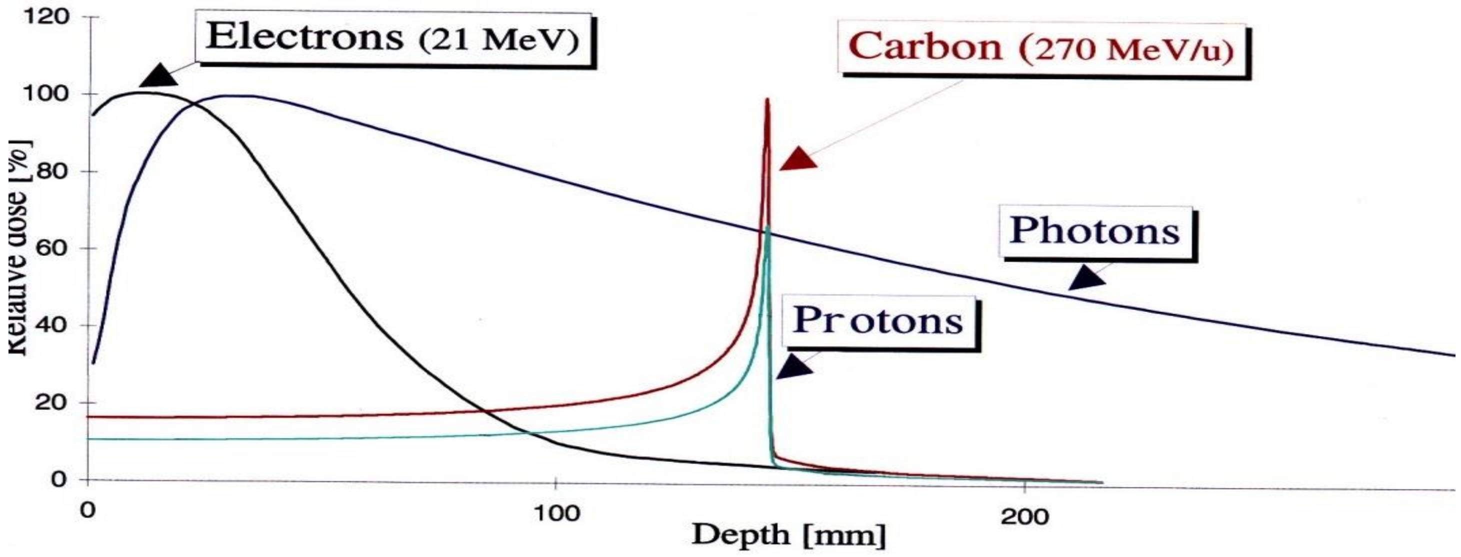
The KT group and myself are privileged to have the opportunity to support these projects in a tailored way, and to help bridge the gap between CERN technologies and society.

Many thanks to all the colleagues from CERN, CNAO, CHUV, GSI, MedAustron, INFN, TERA who have shared their material and wisdom with me; thanks to Ugo Amaldi and Manjit Dosanjh, from whom I first learned about hadron therapy.

I am neither a doctor, nor a medical physicist, nor a technical expert in most of the technologies I present, so let's see how many of your questions I'm able to answer! ☺

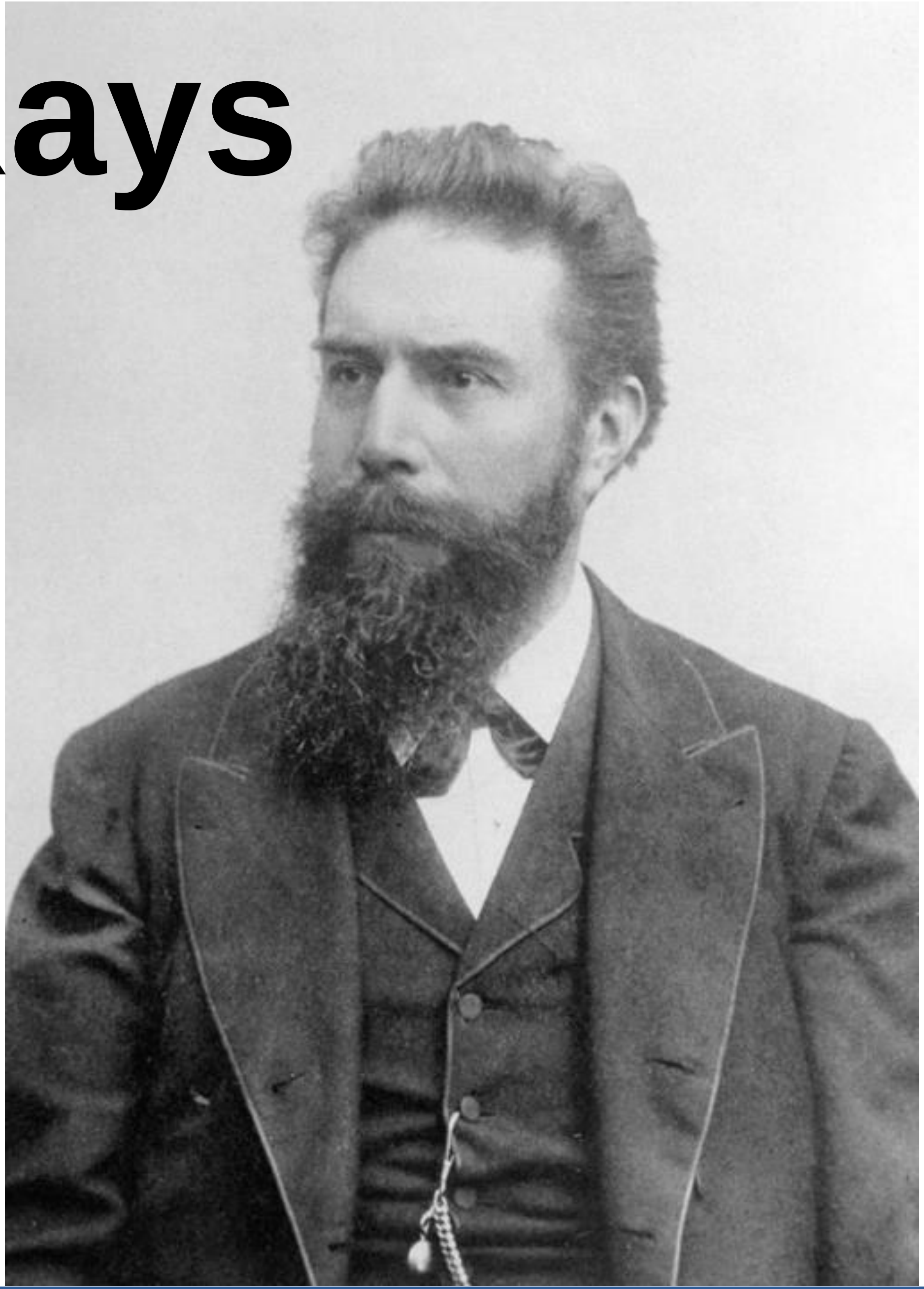
The physics itself

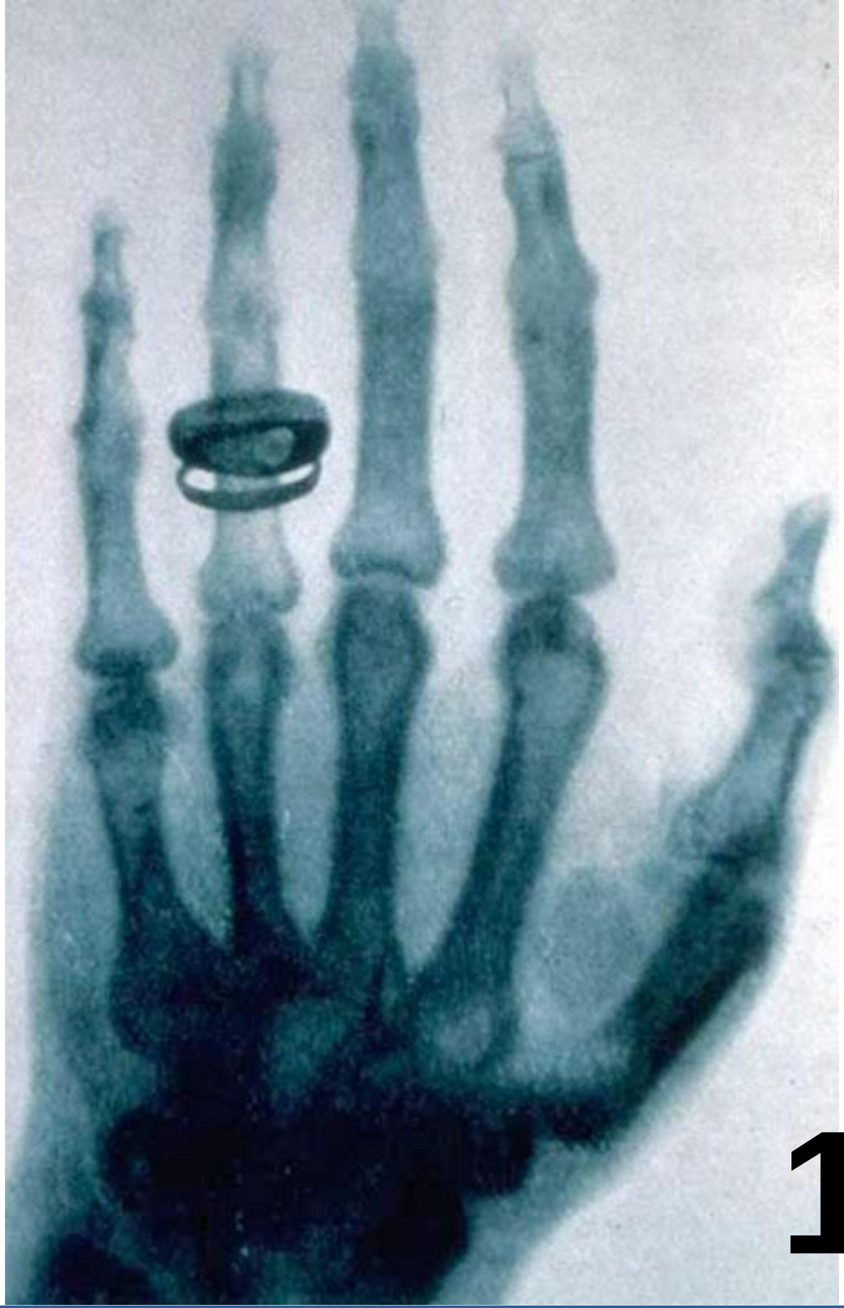




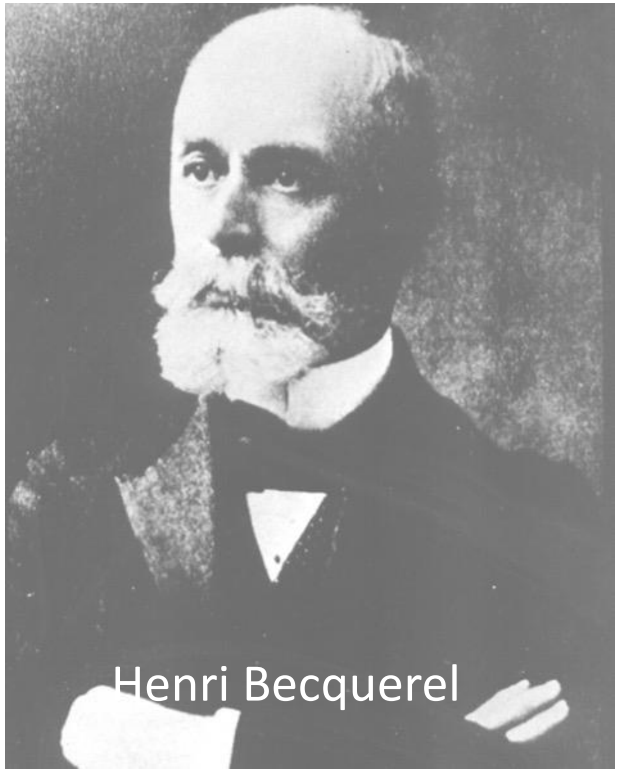
By Original: Penubag Vector: Victor Blacus - Own work based on: Electromagnetic-Spectrum.png,

X-Rays



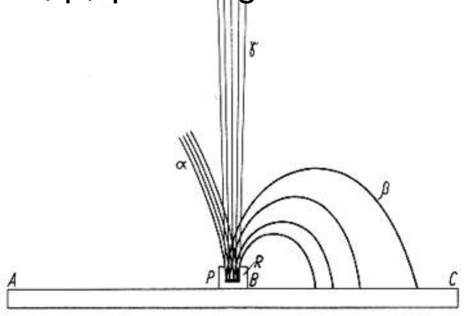


1895

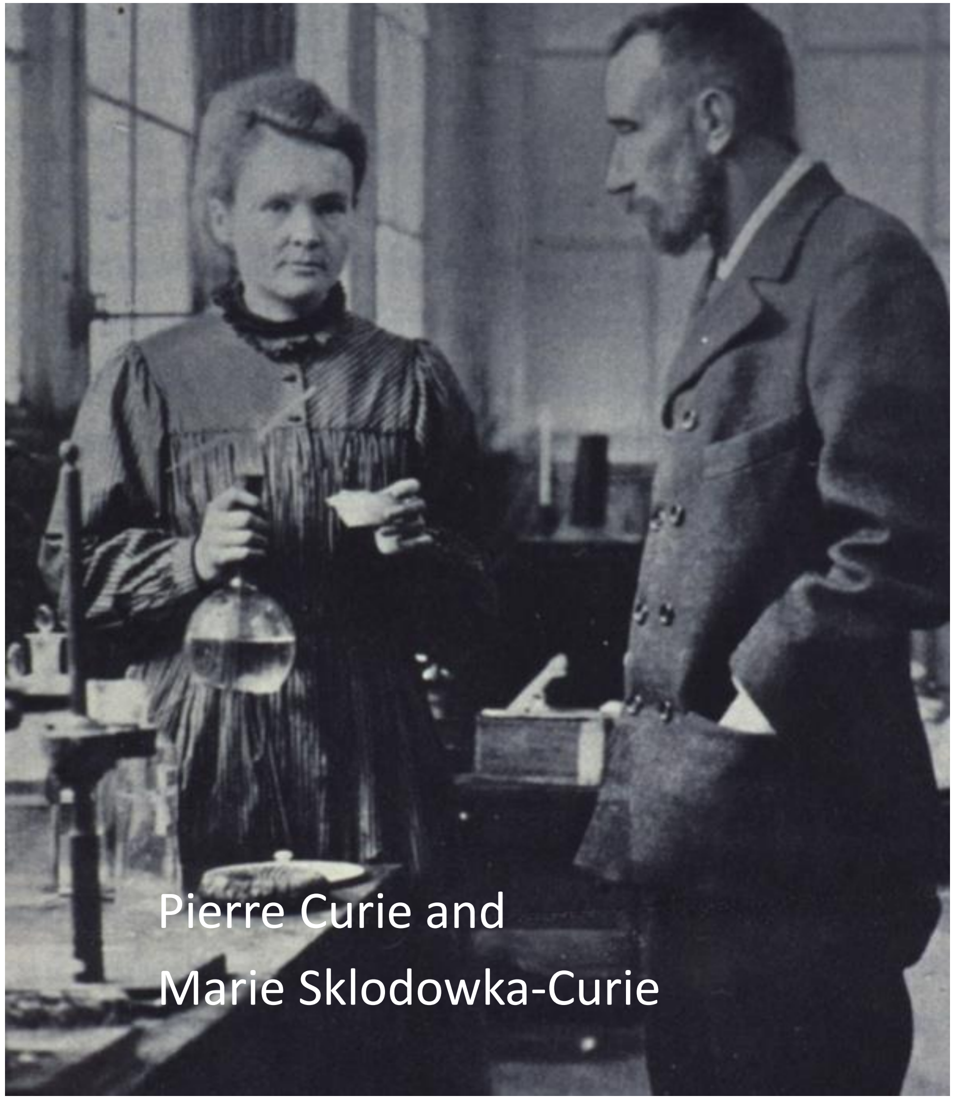


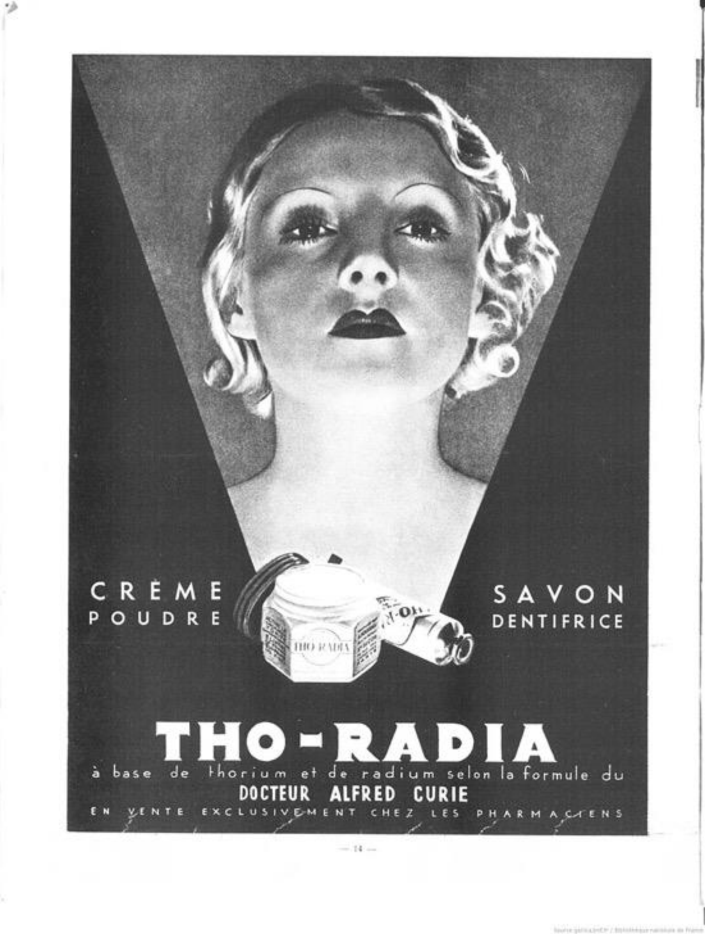
1896: accidental discovery of natural radioactivity

Mme. Curie thesis – 1904
α, β, γ in magnetic field



1898: by studying the strange uranium rays, they soon discovered polonium, thorium, radium

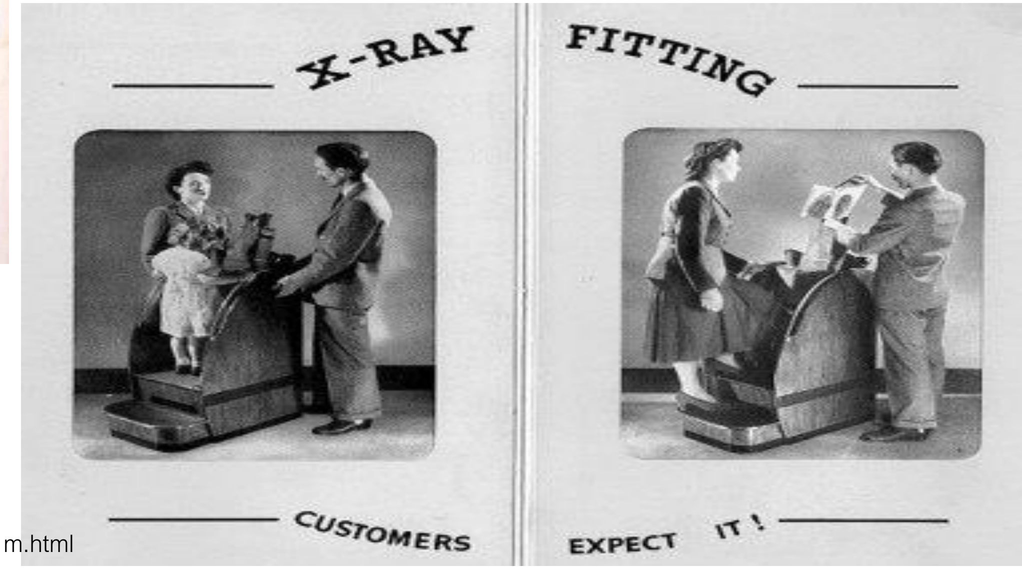




Par Cinémagazine, 14 février 1935 — https://gallica.bnf.fr/ark:/12148/bpt6k2000628h, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=97956453

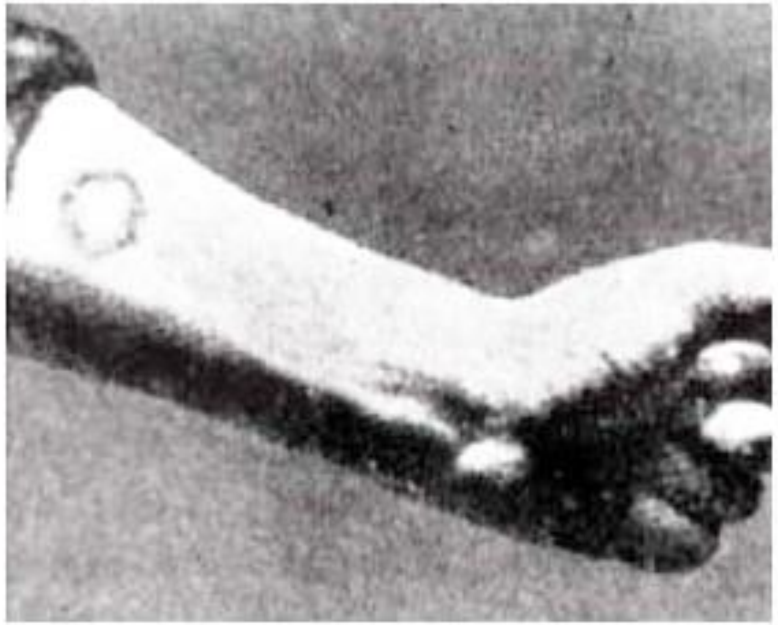
Par Radior cosmetics — sitead New York Tribune Magazine, page 12, Domaine public, https://commons.wikimedia.org/w/index.php?curid=35047170

Par Sam LaRussa from United States of America — Radithor, CC BY-SA 2.0, https://commons.wikimedia.org/w/index.php?curid=57841049



https://www.smh.com.au/national/nsw/from-the-archives-1956-ban-urged-of-x-ray-machines-at-shoe-shops-20210318-p57c1m.html

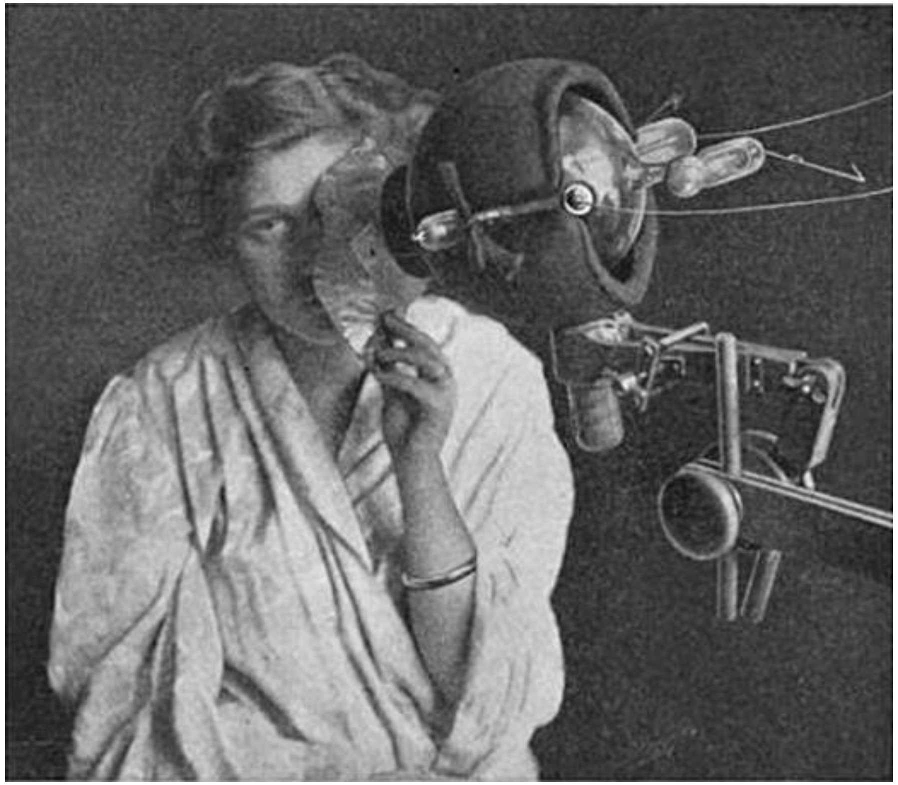
Friedrich Giesel
1852-1927



Burning of Pierre Curie's arm

Pierre Curie
1859-1906

Photo of Pierre Curie's arm, burned by radium salt applied for 10 hours. In 1900, the German dentist Walkhoff noted that radium rays act energetically on the skin in a manner analogous to that of X-rays. This observation was confirmed a few weeks later by the German chemist F. Giesel, with whom Pierre and Marie maintained regular correspondence.



X-ray apparatus used for treatment of epithelioma of the face, 1915.

Small tubes containing radium salts are strapped to a woman's face to treat what was either lupus or rodent ulcer, 1905.

The Nobel Prize in Physics 1944

Photo from the Nobel Foundation archive.

Isidor Isaac Rabi

Prize share: 1/1

The Nobel Prize in Physics 1944 was awarded to Isidor Isaac Rabi "for his resonance method for recording the magnetic properties of atomic nuclei."

The Nobel Prize in Physics 1952

Photo from the Nobel Foundation archive.

Felix Bloch

Prize share: 1/2

Photo from the Nobel Foundation archive.

Edward Mills Purcell

Prize share: 1/2

The Nobel Prize in Physics 1952 was awarded jointly to Felix Bloch and Edward Mills Purcell "for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith."

The Nobel Prize in Physiology or Medicine 2003

Photo from the Nobel Foundation archive.

Paul C. Lauterbur

Prize share: 1/2

Photo from the Nobel Foundation archive.

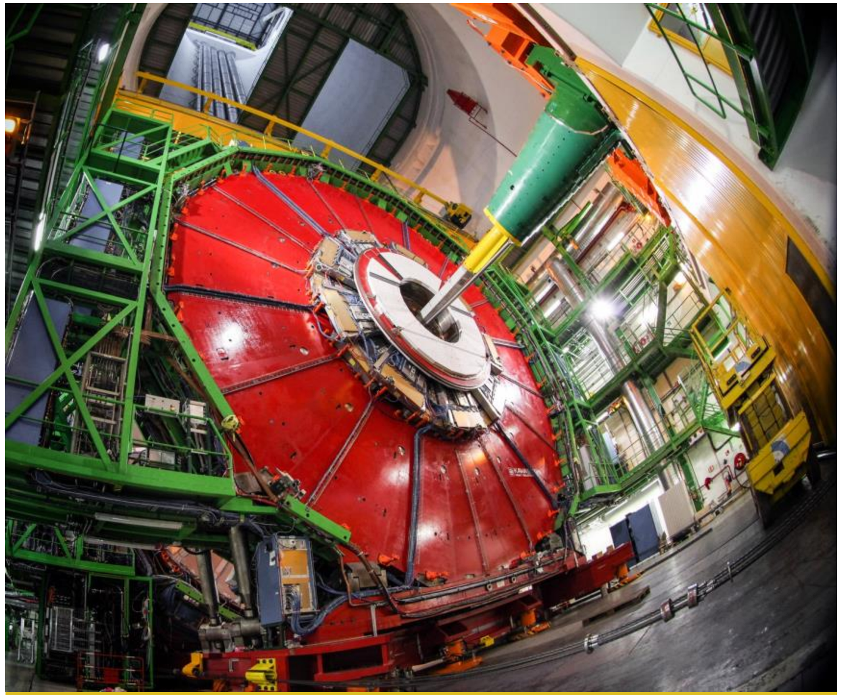
Sir Peter Mansfield

Prize share: 1/2

The Nobel Prize in Physiology or Medicine 2003 was awarded jointly to Paul C. Lauterbur and Sir Peter Mansfield "for their discoveries concerning magnetic resonance imaging."

The technologies

ACCELERATORS



DETECTORS

COMPUTING


sound reproduction
data management
testing satellite components
astronauts' radiation exposure
understanding turbulence
food sterilization
medical implants
homeland security
finding oil, gas, water
geological dating
scientific linux
curing of epoxies and plastics
medical imaging
x-ray diffractometry
spacecraft shielding
radiology
medical equipment sterilization
medical radioisotopes
non-destructive testing
nuclear waste transmutation
ion implantation
rad-hard electronics
shrink wrap
radiotherapy
PET
terrestrial reproduction of space radiation
simulations
optimised irrigation systems
industry 4.0
digital data preservation
drug development
safety
open hardware
www
powering complex biological simulations
industrial control systems
power transmission
analysis of satellite data
treatment planning systems
volcano tomography
space applications
sealing food packages
autonomous vehicles
isotope production
smoke detectors
hadron therapy
cultural heritage
MRI
cleaner air and water
ink curing
cargo screening
computer chips manufacturing
studying the retina
medical dosimetry
material science


Accelerators for America's Future
U.S. DEPARTMENT OF ENERGY
Particle physics – it matters
A forward look at UK research into the building blocks of the Universe and its impact on society
In partnership with
Science & Technology Facilities Council
Accelerating science and innovation
Societal benefits of European research in particle physics
Tools, Techniques, and Technology Connections of Particle Physics
Task force chairs:
Marcel Demarteau
Argonne National Laboratory
Katie Yurkewicz
Fermi National Accelerator Laboratory
U.S. DEPARTMENT OF ENERGY
Office of Science
Accelerators and Beams
TOOLS OF DISCOVERY AND INNOVATION
4th Edition
Published by the Division of Physics of Beams of the American Physical Society
APS physics
APPLICATIONS OF PARTICLE ACCELERATORS IN EUROPE
EuCARD²
Accelerators for Society
Particle accelerators are being applied throughout society. Originally developed for fundamental research, today they are used for a range of applications, from healthcare to manufacturing silicon chips to reducing pollution.
TIARA
From Physics to Daily Life
Applications in Informatics, Energy, and Environment
Edited by Beatrice Bressan
WILEY Blackwell

Over **70 companies and institutes produce accelerators for industrial applications**; these organizations sell more than **1,100 industrial systems per year** — almost twice the number produced for research or medical therapy — at a **market value of $2.2B**.

Over **$1B** of this amount is generated by the sales of accelerators for **ion implantation** into materials — primarily semiconductor devices — whose worldwide value of production is about $300B.

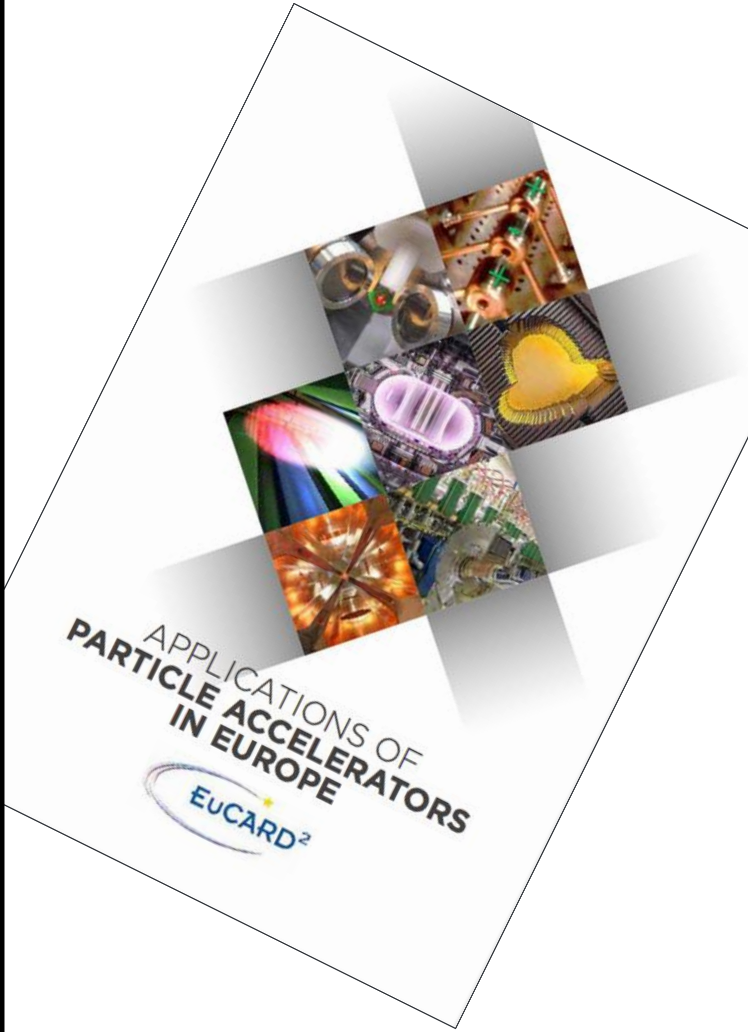
Hamm,R.andHamm,M.(2012).Industrial accelerators and their applications. World Scientific Publishing Co.

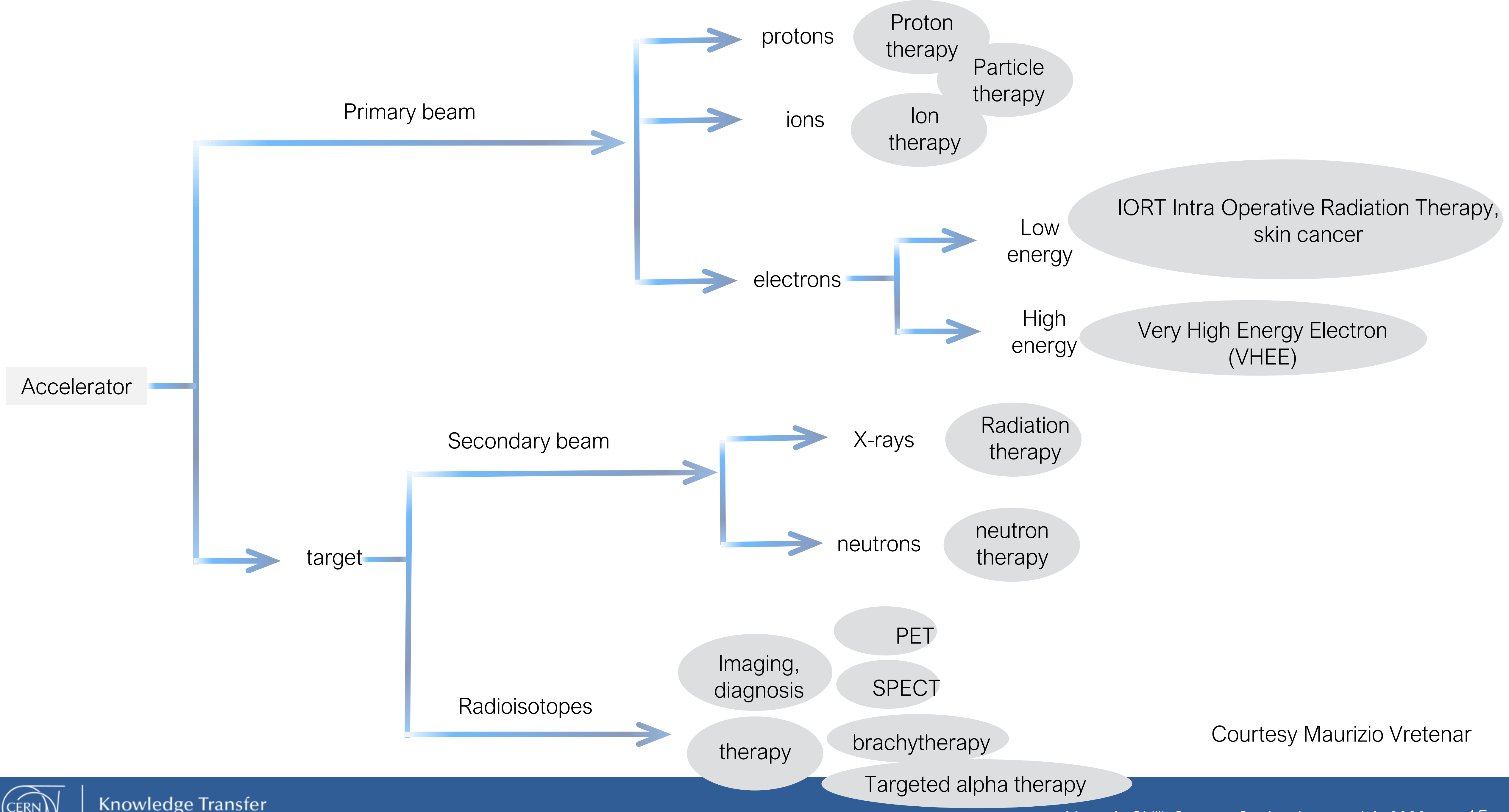
As of 2014 there were **42,200** accelerators worldwide:
27,000 (64%) in industry,
14,000 (33%) for medical purposes
1,200 (3%) for basic research.

These figures exclude electron microscopes and x–ray tubes, and the security and defense industries.

Chernyaev, A. P. and Varzar, S. M. (2014). Particle accelerators in modern world. Physics of Atomic Nuclei, 77(10):1203–1215.

Area	Application	Beam	Accelerator	Beam energy/MeV	Beam current/ mA	Number
Medical	Cancer therapy	e	linac	4-20	10^{-2}	>14000
		p	cyclotron, synchrotron	250	10^{-6}	60
		C	synchrotron	4800	10^{-7}	10
	Radioisotope production	p	cyclotron	8-100	1	1600
Industrial	Ion implantation	B, As, P	electrostatic	< 1	2	>11000
	Ion beam analysis	p, He	electrostatic	<5	10^{-4}	300
	Material processing	e	electrostatic, linac, Rhodatron	≤10	150	7500
	Sterilisation	e	electrostatic, linac, Rhodatron	≤10	10	3000
Security	X-ray screening of cargo	e	linac	4-10	?	100?
	Hydrodynamic testing	e	linear induction	10-20	1000	5
Synchrotron light sources	Biology, medicine, materials science	e	synchrotron, linac	500-10000		70
Neutron scattering	Materials science	p	cyclotron, synchrotron, linac	600-1000	2	4
Energy – fusion	Neutral ion beam heating	d	electrostatic	1	50	10
	Heavy ion inertial fusion	Pb, Cs	Induction linac	8	1000	Under development
	Materials studies	d	linac	40	125	Under development
Energy – fission	Waste burner	p	linac	600-1000	10	Under development
	Thorium fuel amplifier	p	linac	600-1000	10	Under development
Energy – bio-fuel	Bio-fuel production	e	electrostatic	5	10	Under development
Environmental	Water treatment	e	electrostatic	5	10	5
	Flue gas treatment	e	electrostatic	0.7	50	Under development





Courtesy Maurizio Vretenar

Radiotherapy

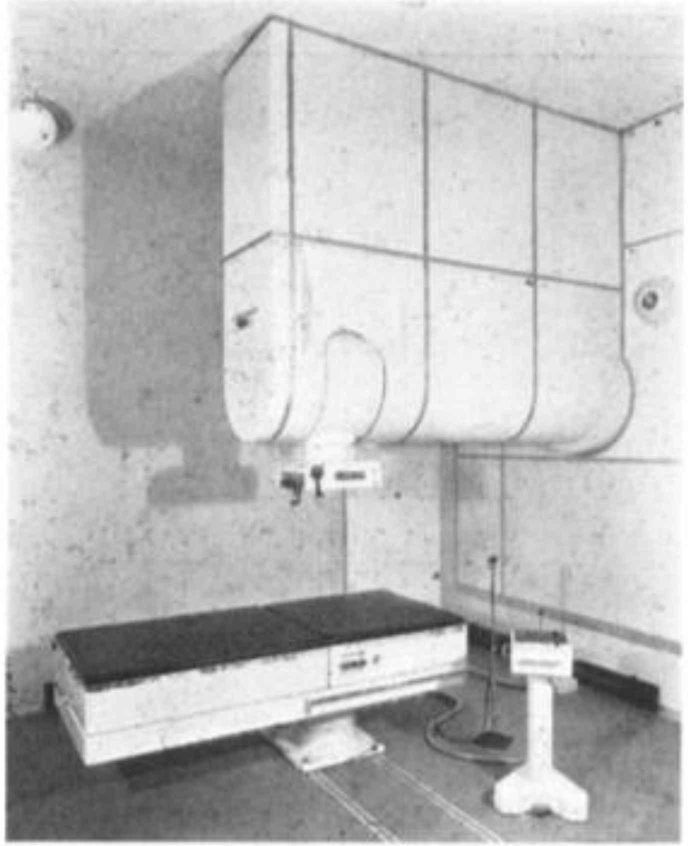
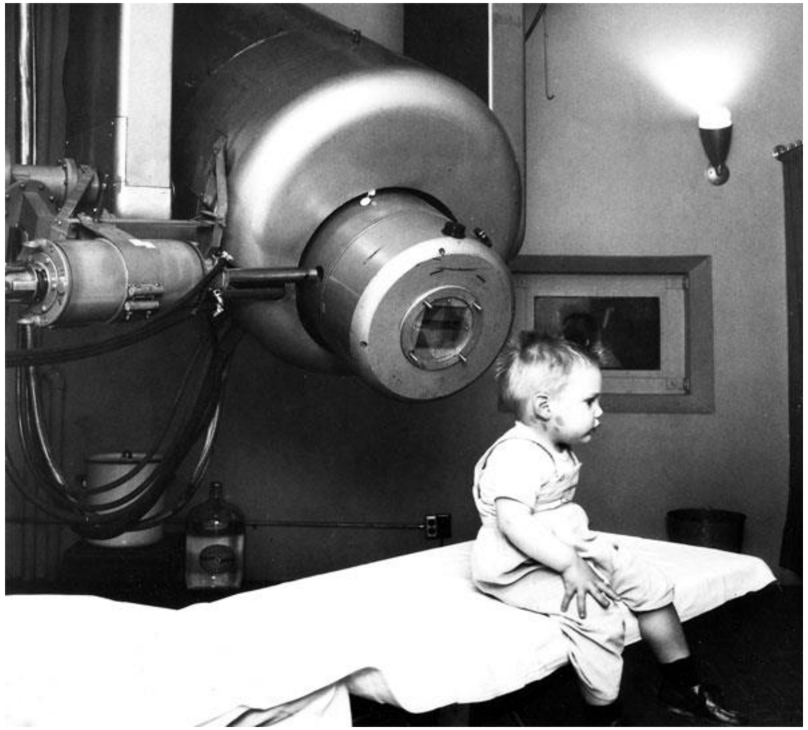


Fig. 1. The 8 MeV linear accelerator (Metropolitan-Vickers) at Hammersmith Hospital with the angle of the roentgen head adjusted to give a beam directed vertically downwards.

1953

P. Howard-Flanders (1954) The Development of the Linear Accelerator as a Clinical Instrument, Acta Radiologica, 41:sup116, 649-655, DOI: 10.3109/00016925409177244



1956: The first patient to receive radiation therapy from the medical linear accelerator at Stanford was a 2-year-old boy.

Approx. date of intro-duction	Model and location	Manufacturer	Beam energy and modality
1953	Hammersmith Hospital, London	Metropolitan-Vickers	8 MV X-rays
1954	St. Bartholomew's Hospital, London	Mullard	15 MeV X-rays and electrons
1954	Christie Hospital, Manchester	Metropolitan-Vickers AEI	4 MV X-ra
1954	Newcastle	Mullard	4 MV X-ra
1955	Stanford	Stanford	5 MV X-ra
1955	Argonne Cancer Hospital, Chicago	Stanford, HVE and Argonne	5–50 M electr
1955	Michael Reese Hospital, Chicago	Stanford. M. Reese and Helene Curtis	45 MeV electr
1962	Newcastle	Vickers Research	4 MV X-ra
1962	Clinac 6	Varian	6 MV X-ray
1965	Mevatron 8	Applied Radiation	6–8 MV X-rays 3–10 MeV electrons
1965	SL-75	Mullard	6–8 MV X-rays 8–10 MeV electrons

Table 1 (*cont.*)

Approx. date of intro-duction	Model and location	Manufacturer	Beam energy and modality
1967	Sagittaire, Paris	CSF	16 MV X-rays 12–32 MeV electrons
1968	Clinac 4	Varian	4 MV X-rays
1969	Mevatron VI & XII	Applied Radiation	6 or 8 MV X-rays 3–11 MeV electrons
1969	LMR-13	Toshiba	8 and 10 MV X-rays 8–13 MeV electrons
1970	Therapi 4	SHM	4 MV X-rays
1970	Clinac 35 Hiroshima	Varian	8 and 25 MV X-rays 7–28 MeV

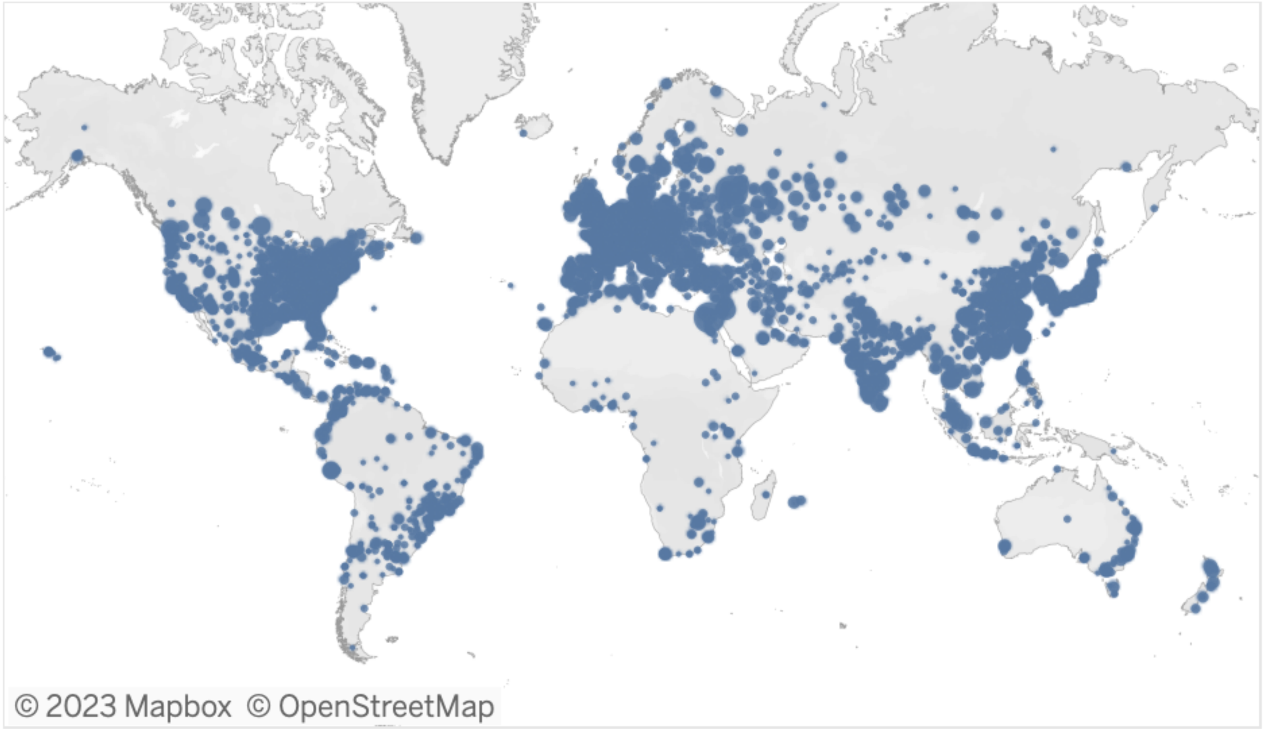
C J Karzmark and N C Pering 1973 *Phys. Med. Biol.* **18** 321

Status of Radiation Therapy Equipment

156 Countries

7687 RT Centres

15130 MV Therapy



Equipment type
(Updated on : 09/03/2023 13:55:27)

MV Therapy	15,130
Brachytherapy	3,336
Light Ion Therapy	107

Equipment per income groups
(Updated on : 09/03/2023 13:55:27)

High income (H)	9,449
Upper middle income (UM)	4,023
Lower middle income (LM)	1,615
Low income (L)	40

IAEA DIRAC Directory of RAdiotherapy Centres

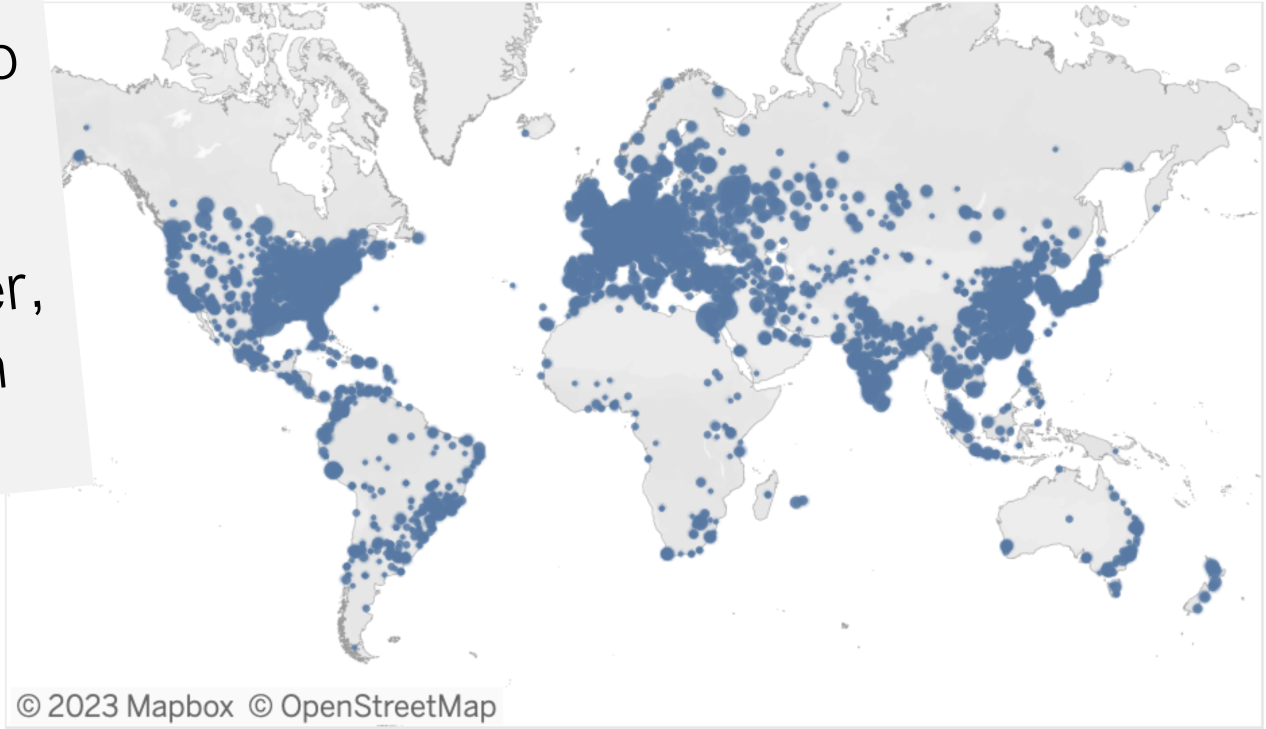
Status of Radiation Therapy Equipment

156 Countries

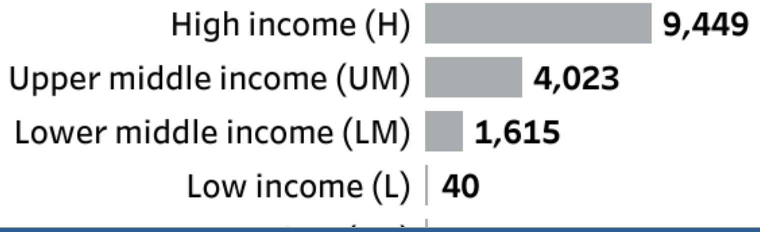
7687 RT Centres

15130 MV Therapy

STELLA (Smart Technologies to Extend Lives with a Linear Accelerator) formed to address the lack of radiotherapy in challenging environments.
Supported by ICEC, UK STFC, Lancaster, Oxford, Daresbury lab, CERN, users in LMICs

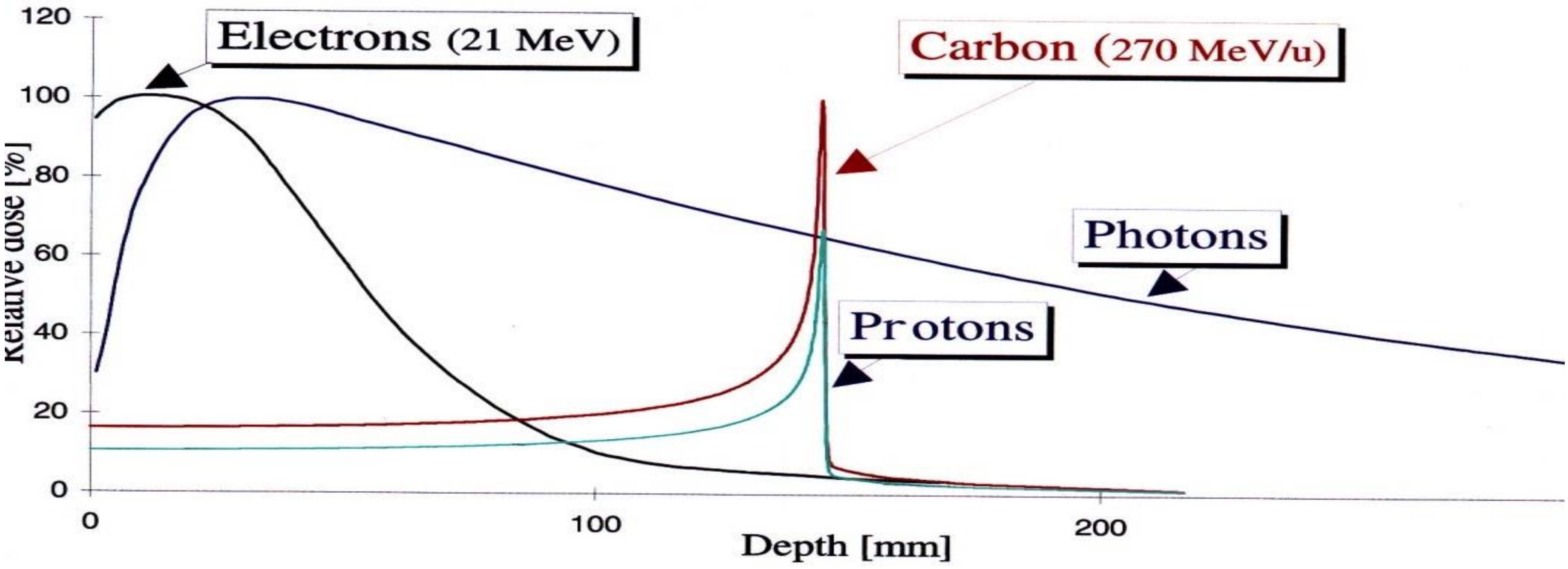


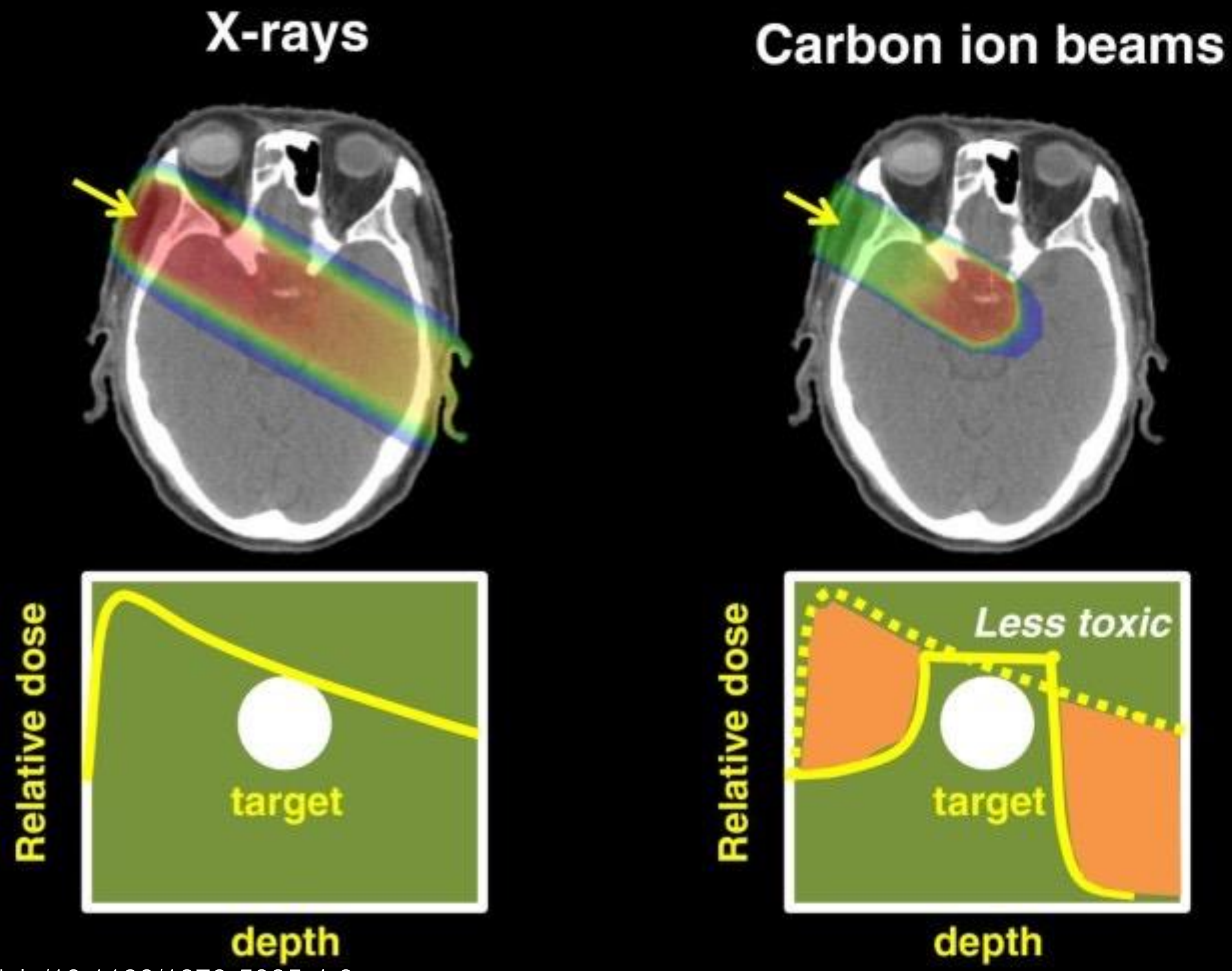
Equipment per income groups
(Updated on : 09/03/2023 13:55:27)



IAEA DIRAC Directory of RAdiotherapy Centres

Protons, ions: hadron therapy, particle therapy, (light, heavy) ion therapy



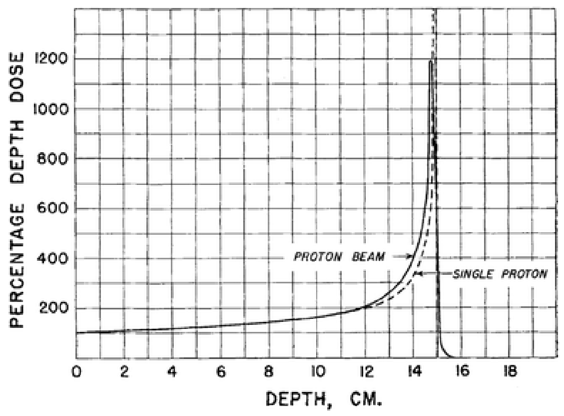


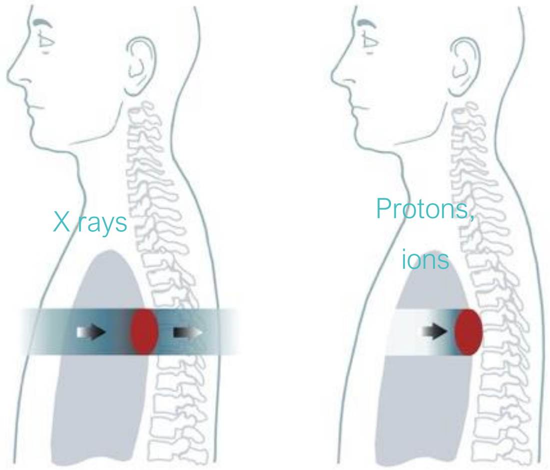
https://link.springer.com/article/10.1186/1878-5085-4-9


X-RAY THERAPY
TREATMENT EXPLAINED
1:17 / 2:44

Berkeley

1931 Invention of cyclotron (Ernest Lawrence)
1946 RR Wilson published his seminal paper on particle therapy
1952 First biological investigation with accelerated nuclei (C Tobias and JH Lawrence)
1954 First therapeutic exposure of humans to protons and alphas (Tobias and JH Lawrence)
1975 Clinical trials with accelerated light ions at LBL (Castro)





Gustav Werner Institute and Theodor Svedberg Laboratory

1949 Synchrocyclotron at the Gustav Werner Institute (Uppsala)
1950s Pre-therapeutic physical experiments with high energy protons (B. Larsson)
1957 First patient treated with proton beam

π^- beam therapy

1935 Yukawa theory on pi meson

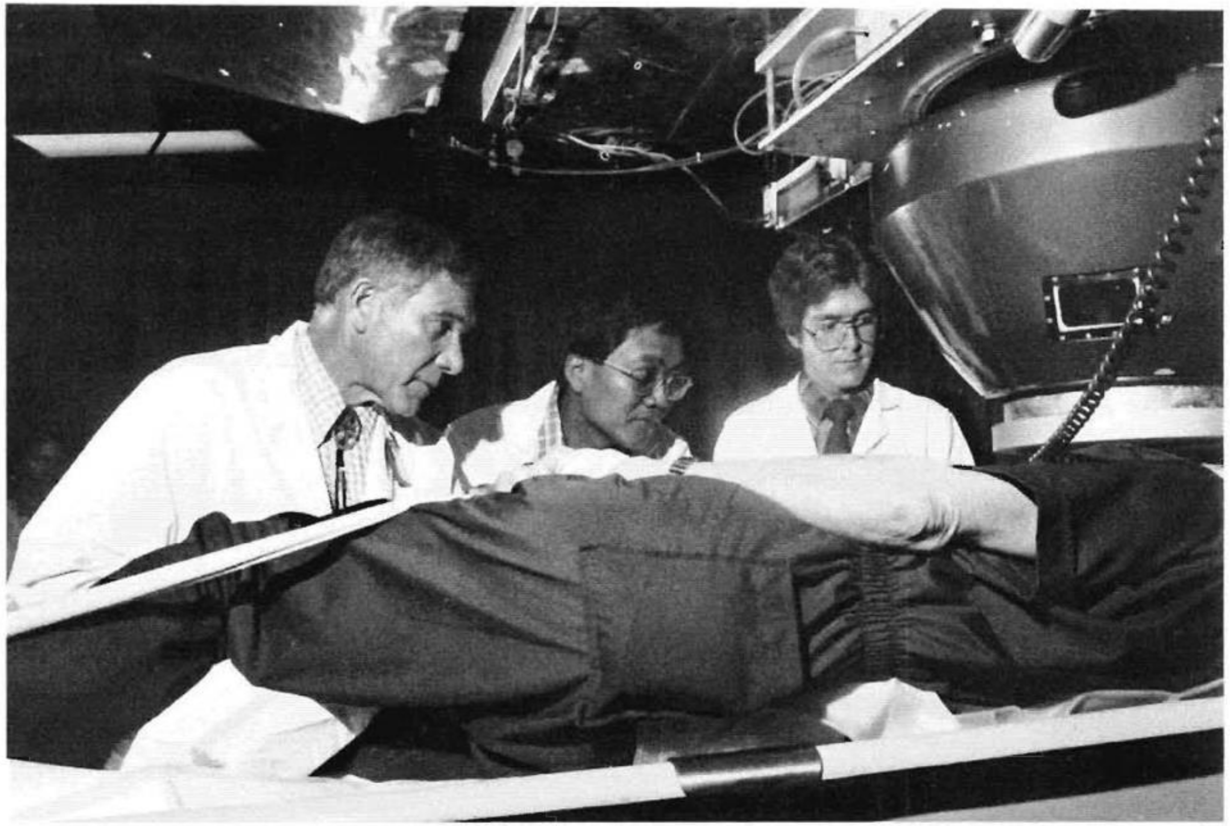
1947 Discovery of pions

1951 Possibility of using negative pions for cancer therapy (Tobias and Richman)

1961 Clinical use of π^- advocated (Fowler and Perkins, Nature 1961)

'70-'80s Clinical trials of negative pions at LAMPF, TRIUMF, PSI and Stanford

William T. Chu
EO Lawrence Berkeley National Laboratory
PTCOG From 1985 to Present and Future

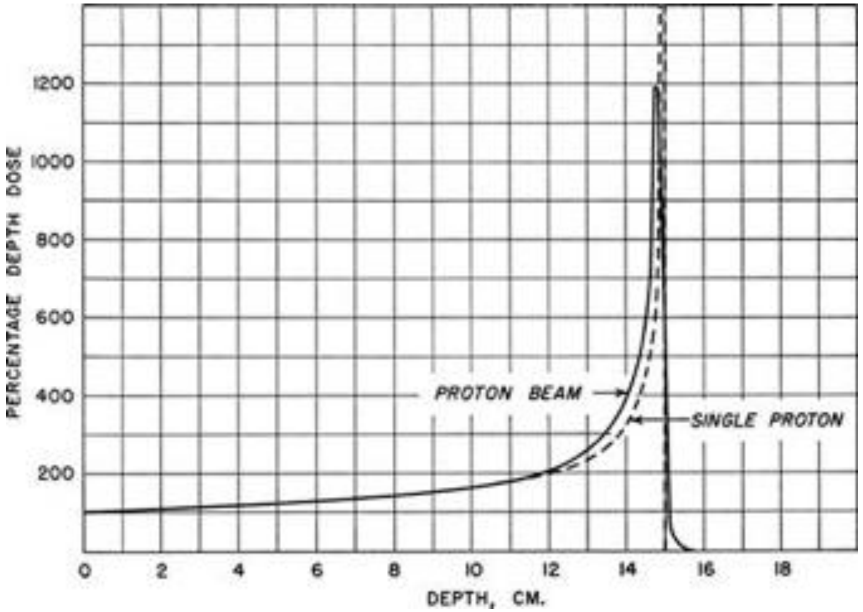


In a pilot experimental program at LAMPF's Biomedical Facility, about 250 patients were treated with negative pions for a variety of advanced deep-seated tumors. Compared to conventional x-ray therapy, pion therapy is expected to provide improved dose localization and biological effectiveness. Shown positioning a patient under the pion radiotherapy beam are (left to right) Dr. Morton Kligerman, former Director of the University of New Mexico's Cancer Research and Treatment Center, a visiting radiotherapist from Japan, and Dr. Steven Bush, formerly of the University of New Mexico. The hardware at the upper right includes a beam collimator, a dose monitor, and a device for changing the penetration depth of the pions.

LAMPF: a dream and a gamble

From physics labs…

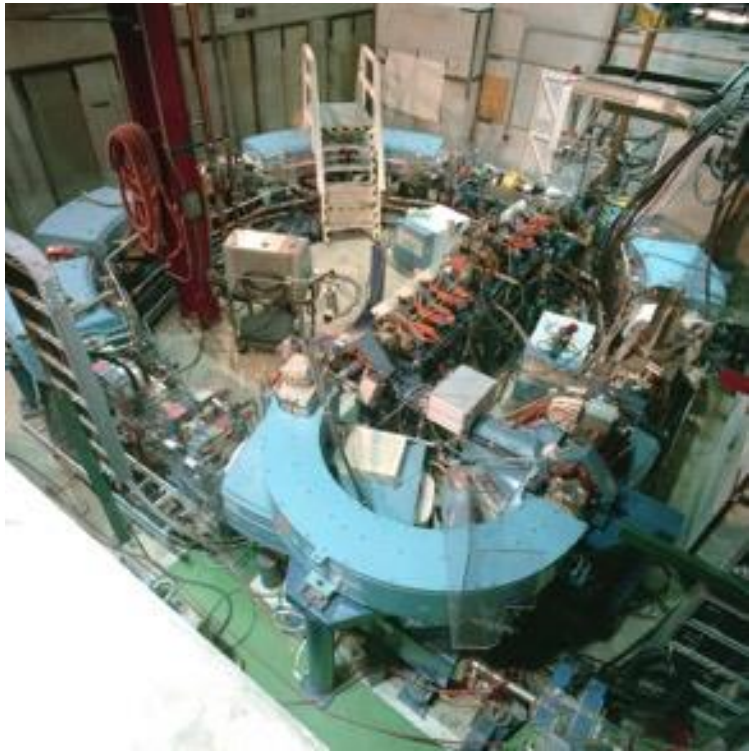
1932 - E. Lawrence
First cyclotron



1946 – proton therapy
proposed by R. Wilson

1954 – Berkeley treats
the first patient

…to clinics



1989
Clatterbridge UK

1990
Loma Linda USA

1994
HIMAC Japan

How to make it better

Image-Guided Radiation Therapy

Intensity-modulated radiation therapy

MRI-guided radiation therapy

Dynamic arc delivery techniques

…

Pioneers in scanned beam delivery

Building Gantry 1 back in the 1990s
(Photo: Paul Scherrer Institute)

1998
Pilot project at GSI
Germany and proposal for HIT facility

Status of Radiation Therapy Equipment

20 Countries

104 RT Centres

107 Light Ion Therapy

Equipment type
(Updated on : 09/03/2023 13:55:27)

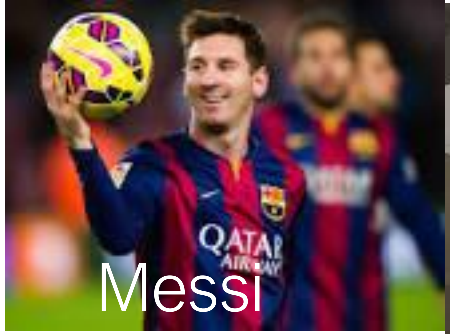
MV Therapy	15,130
Brachytherapy	3,336
Light Ion Therapy	107

Equipment per income groups
(Updated on : 09/03/2023 13:55:27)

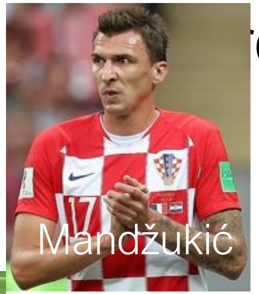
High income (H)	96
Upper middle income (UM)	10
Lower middle income (LM)	1

IAEA DIRAC Directory of RAdiotherapy Centres

200



Multi heavy ions
(protons +
carbon ions)



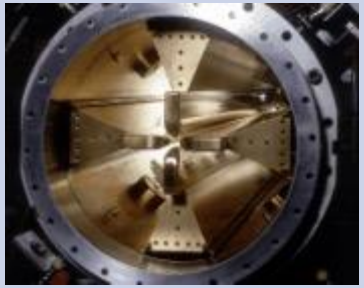
oton multi-room

2

on single-
room

Courtesy
(I'll never thank him enough!)
Marco Durante (GSI)
JENAS 2019
https://indico.ijclab.in2p3.fr/event/5418/timetable/#20191016.detailed

Protons: the LINAC way

1990 RFQ2 200 MHz 0.5 MeV /m Weight :1200kg/m Ext. diametre : ~45 cm	2007 LINAC4 RFQ 352 MHz 1MeV/m Weight : 400kg/m Ext. diametre : 29 cm	2014 HF RFQ 750MHz 2.5MeV/m Weight : 100 kg/m Ext. diametre : 13 cm
		

Compact High-Frequency Radio Frequency Quadrupole (RFQ)

M. Vretenar, A. Dallocchio, V. A. Dimov, M. Garlasché, A. Grudiev, A. M. Lombardi, S. Mathot, E. Montesinos, M. Timmins, “A Compact High-Frequency RFQ for Medical Applications”, in Proc. LINAC2014, Geneva, Switzerland, September 2014

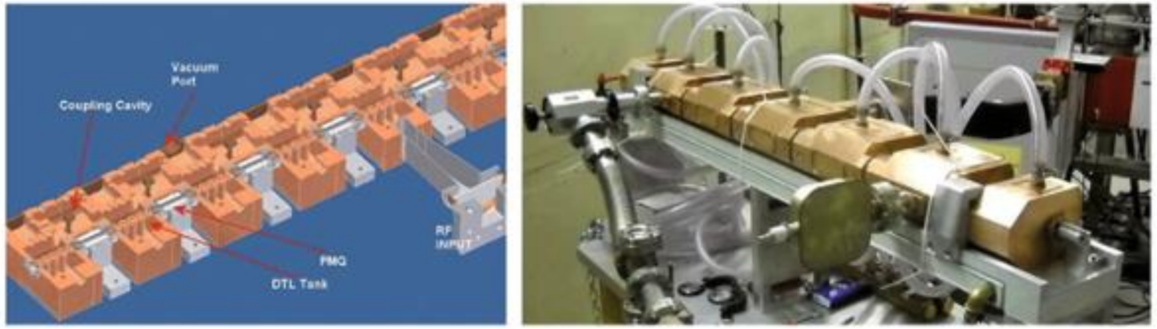
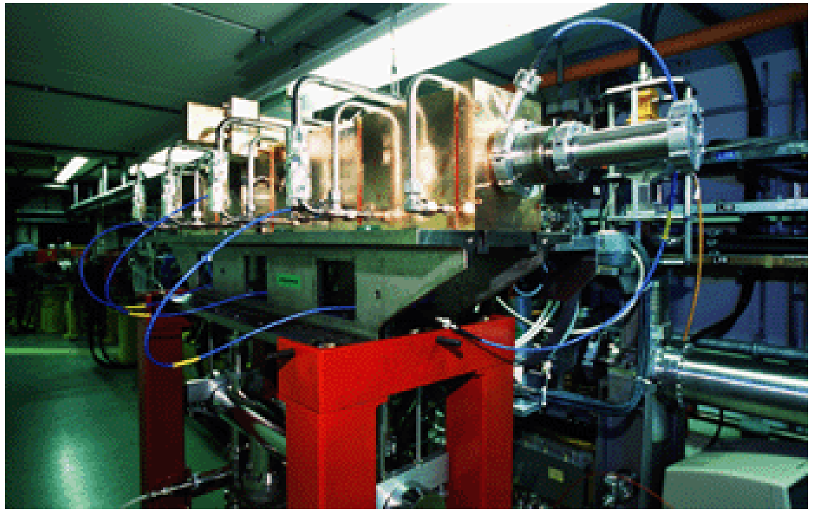


Fig. 4. TOP-IMPLART SCDTL structure: (left) schematic (right) 18–24 MeV booster built for the SPARKLE Company.

TOP IMPLART

C. Ronsivalle, M. Carpanese, C. Marino, G. Messina, L. Picardi, S. Sandri, E. Basile, B. Caccia, D.M. Castelluccio, E. Cisbani, S. Frullani, F. Ghio, V. Macellari, M. Benassi, M. D’Andrea, L. Strigari, The TOP-IMPLART project, Eur. Phys. J. Plus 126: 68 (2011) 1–15, http://dx.doi.org/10.1140/epjp/i2011-11068-x.



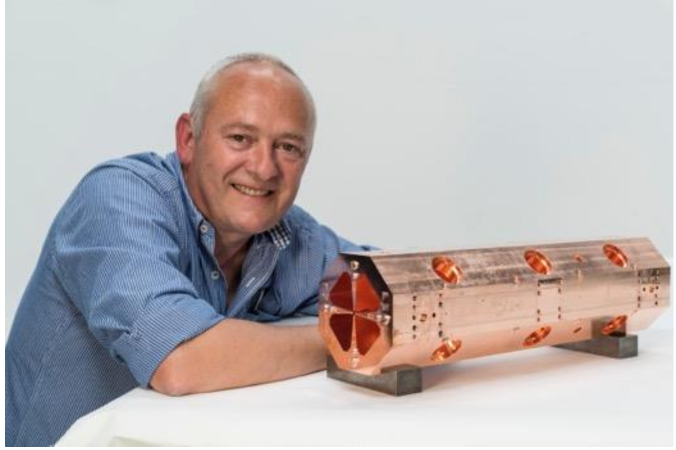
LInac BOoster (LIBO)

U. Amaldi et al., “LIBO-a linac booster for protontherapy: construction and test of a prototype,” Nucl. Instrum. Meth- ods Phys. Res. A, vol. 521, pp. 512-529, 2004.

Toward clinical proton therapy LINACs

The RFQ accelerating structure entirely manufactured by AVO (under CERN licence)
Nominal energy for the full system reached in Sep 2022

ADVANCED ONCOTHERAPY ADAM an ADVANCED ONCOTHERAPY company LiGHT Linac for Image Guided Hadron Therapy



CERN proton therapy RFQ (5 MeV / 2m)

TOP IMPLART under development and construction by ENEA in collaboration with the Italian Institute of Health (ISS) and the Oncological Hospital Regina Elena-IFO.

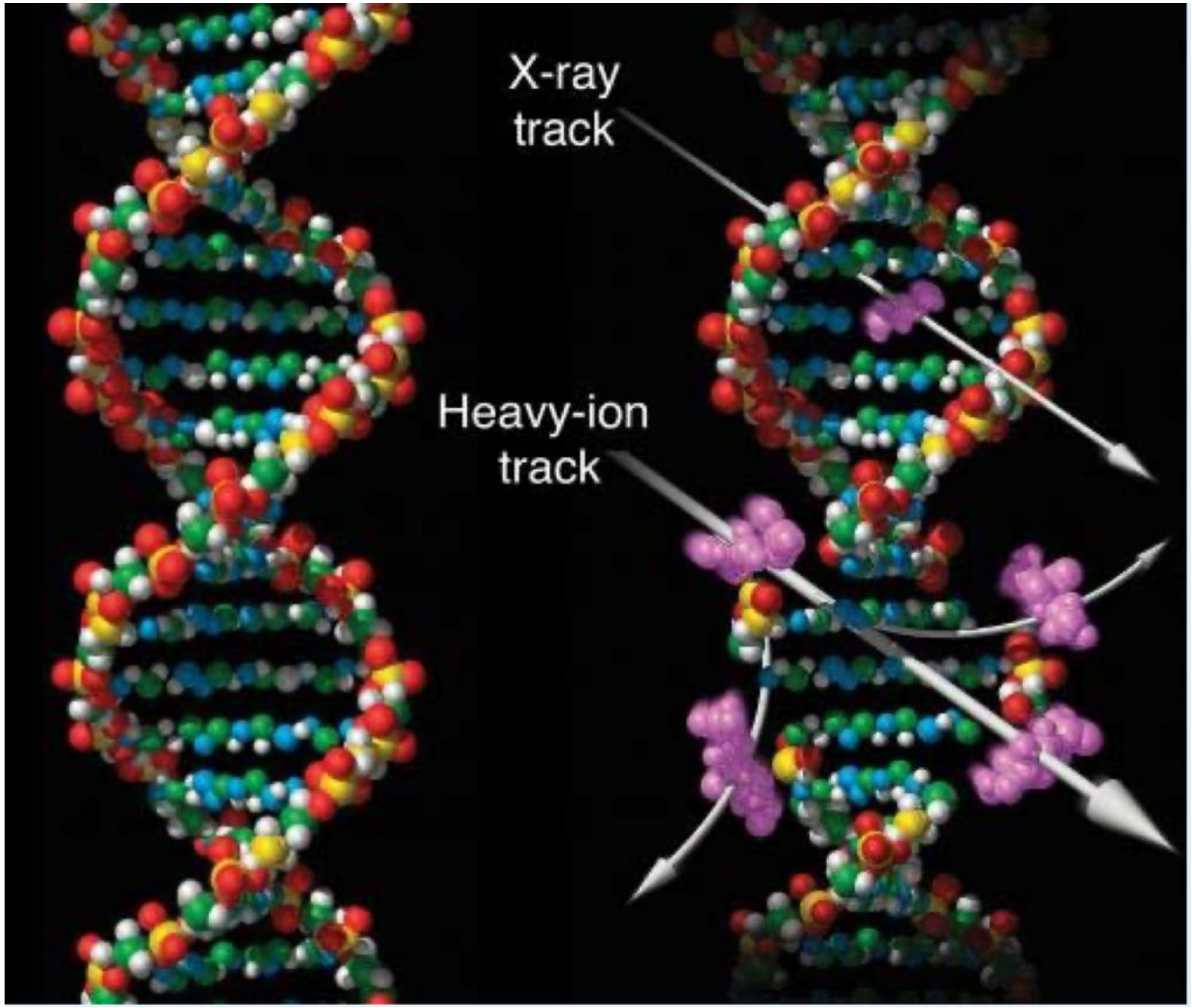
Status in March 2021*: running at 55.5 MeV

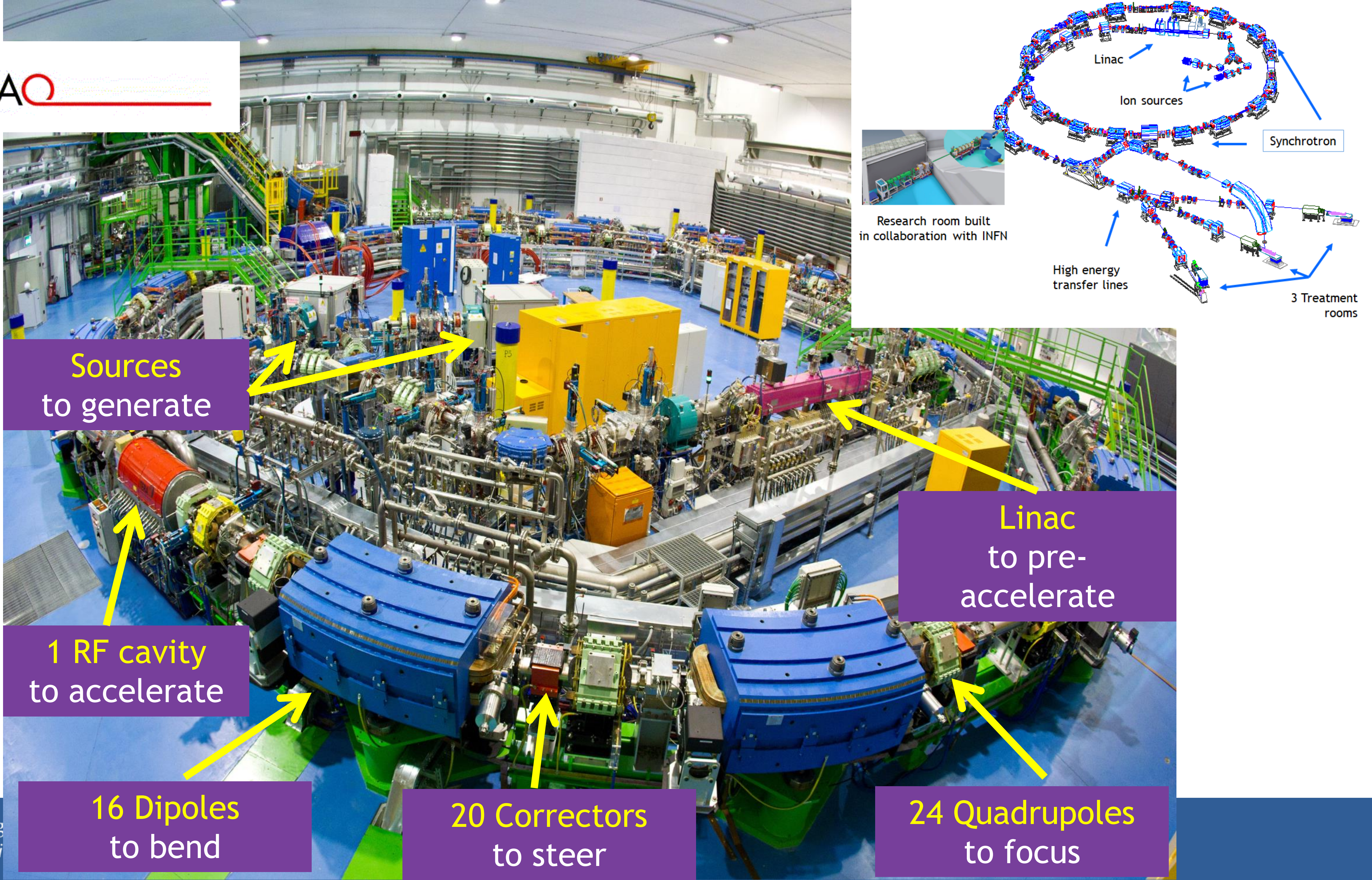
* https://www.accelerators.enea.it/TopImplartStatus&Schedules/index.htm

LinearBeam PROTONS FOR LIFE

ERHA (Enhanced Radiotherapy with Hadrons) is the innovative proton therapy system being developed by LinearBeam for the treatment of tumors.
Collaboration with (among others) ENEA, INFN.

Carbon ions

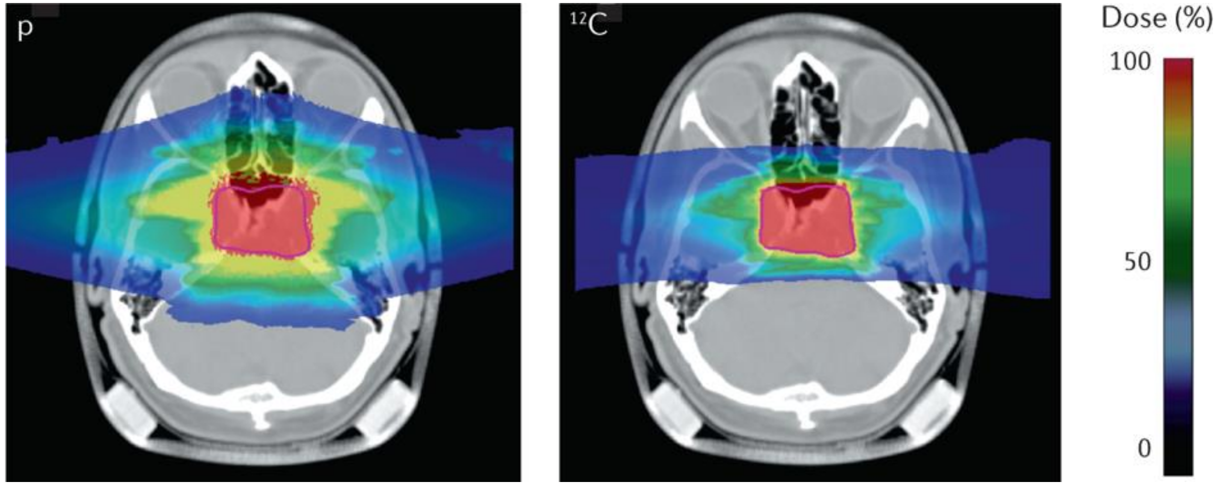




fondazione CNAO
Sources
to generate
1 RF cavity
to accelerate
16 Dipoles
to bend
20 Correctors
to steer
24 Quadrupoles
to focus
Linac
to pre-
accelerate
Linac
Ion sources
Synchrotron
Research room built
in collaboration with INFN
High energy
transfer lines
3 Treatment
rooms

From pioneering rasterscanning & carbon ion pilot project @

440 patiens
1998-2008



The image shows an optimized plan with two opposite fields for a chordoma patient using protons (left) or 12C ions (right).

Since 2009*:
2841 patients with p
3793 patients with C-ion

* Until Dec 2020, source ptcog.ch

From PIMMS @ CERN → TERA

EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH
CERN - PS DIVISION

CERN/PS 2000-007 (DR)

PROTON-ION MEDICAL MACHINE STUDY (PIMMS) PART II

Accelerator Complex Study Group*
supported by the Med-AUSTRON, Onkologie-2000 and the TERA Foundation
and hosted by CERN

ABSTRACT

The Proton-Ion Medical Machine Study (PIMMS) group was formed following an agreement between the Med-AUSTRON (Austria) and the TERA Foundation (Italy) to combine their efforts in the design of a cancer therapy synchrotron capable of accelerating either light ions or protons. CERN agreed to support and host this study in its PS Division. A close collaboration was also set up with GSI (Germany). The study group was later joined by Onkologie-2000 (Czech Republic). Effort was first focused on the theoretical understanding of slow extraction and the techniques required to produce a smooth beam spill for the conformal treatment of complex-shaped tumours with a sub-millimetre accuracy by active scanning with proton and carbon ion beams. Considerations for passive beam spreading were also included for protons. The study has been written in two parts. The more general and theoretical aspects are recorded in Part I and the specific technical design considerations are presented in the present volume, Part II. An accompanying CD-ROM contains supporting publications made by the team and data files for calculations. The PIMMS team started its work in January 1996 in the PS Division and continued for a period of four years.

*Full-time members: L. Badano[1)], M. Benedikt[2)], P.J. Bryant[2)] (Study Leader), M. Crescenti[1)], P. Holy[3)], A. Maier[2)+4)], M. Pullia[1)], S. Reimoser[2)+4)], S. Rossi[1)],
Part-time members: G. Borri[1)], P. Knaus[1)+2)]
Contributors: F. Gramatica[1)], M. Pavlovic[4)], L. Weisser[5)]
1) TERA Foundation, via Puccini. 11, I-28100 Novara.
2) CERN, CH 1211 Geneva-23.
3) Oncology-2000 Foundation, Na Morani 4, CZ-12808 Prague 2.
4) Med-AUSTRON, c/o RIZ, Prof. Dr. Stephan Korenstr.10, A-2700 Wr. Neustadt.
5) Sommer & Partner Architects Berlin (SPB), Hardenbergplatz 2, D-10623 Berlin.

Geneva, Switzerland
May 2000

INFN

fondazione CNAO

MedAustron

Patient treatment at MedAustron

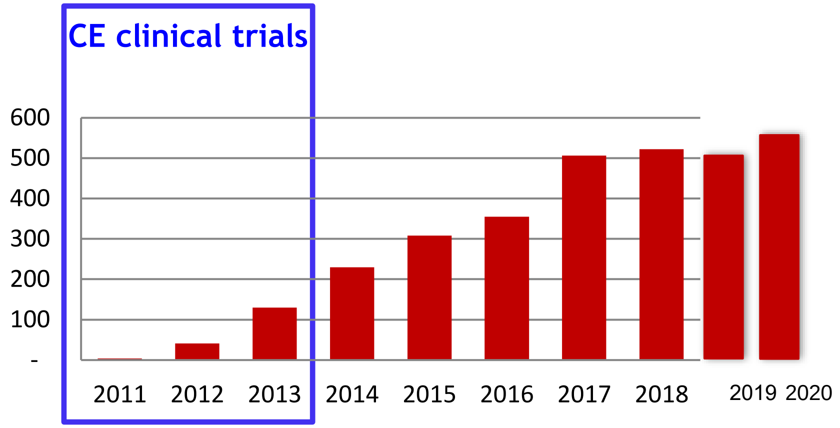
Since 2016:
1174 Patients
30600 Single Fractions

MedAustron

CNS	28%
Head & Neck	20%
Pediatrics	15%
Re-Irradiation	15%
Sarcoma	9%
Skull Base	7%
Prostate	3%
Gastrointestinal (upper)	2%
Gastrointestinal (lower)	<1%
Gynecological Tumors	<1%
Urogenital Tumors	<1%
Breast/Mamma-Ca	<1%

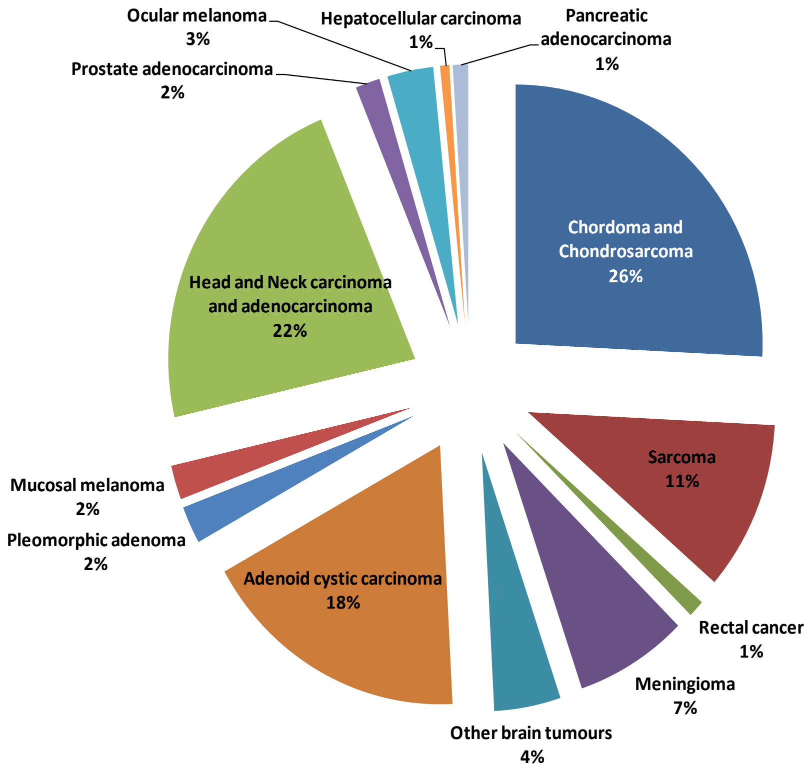
Values October 2021 • values rounded

Patient treatment at CNAO



Patients per year

Since 2011:
3700 Patients
55% C-ions
45% Protons



fondazione CNAO

fondazione CNAO

Non oncological application: ventricular arrhythmia (Collaboration with San Matteo Hospital, Pavia) Published: European Journal of Heart Failure

SCIENTIFIC REPORTS

OPEN

Feasibility Study on Cardiac Arrhythmia Ablation Using High-Energy Heavy Ion Beams

Received: 08 August 2016
Accepted: 09 November 2016
Published: 20 December 2016

H. Immo Lehmann[1,*], Christian Graeff[2,*], Palma Simoniello[2], Anna Constantinescu[2], Mitsuru Takami[1], Patrick Lugenbiel[3], Daniel Richter[2,4], Anna Eichhorn[2], Matthias Prall[2], Robert Kaderka[2], Fine Fiedler[5], Stephan Helmbrecht[5], Claudia Fournier[2], Nadine Erbeldinger[2], Ann-Kathrin Rahm[3], Rasmus Rivinius[3], Dierk Thomas[3], Hugo A. Katus[3], Susan B. Johnson[2], Kay D. Parker[2], Jürgen Debus[6], Samuel J. Asirvatham[1], Christoph Bert[2,4], Marco Durante[2,7] & Douglas L. Packer[1]

› Eur J Heart Fail. 2020 Nov 12. doi: 10.1002/ejhf.2056. Online ahead of print.

The First-in-Man Case of Non-invasive Proton Radiotherapy to Treat Refractory Ventricular Tachycardia in Advanced Heart Failure

Veronica Dusi [1 2], Viviana Vitolo [3], Laura Frigerio [1 4], Rossana Totaro [1 4], Adele Valentini [5], Amelia Barcellini [3], Alfredo Mirandola [3], Giovanni Battista Perego [6], Michela Coccia [2], Alessandra Greco [4], Stefano Ghio [4], Francesca Valvo [3], Gaetano Maria De Ferrari [7], Massimiliano Gnecchi [1 2], Luigi Oltrona Visconti [4], Roberto Rordorf [1 4]

Affiliations + expand

PMID: 33179329 DOI: 10.1002/ejhf.2056

Challenges for next-generation particle-therapy machines

Cost-effective technologies

Reduced footprint

New treatment regimes (e.g. FLASH, microbeams) and fractionation schedules

Multi-ions

Radiobiology research integrated in the facility

Many challenges in common with those for future particle physics facilities. Various initiatives starting/on-going.

KT Seminars

The CERN Next Ion Medical Machine Study: towards a new generation of accelerators for cancer therapy

by Maurizio Vretenar (CERN)

Monday 19 Oct 2020, 14:00 → 16:30 Europe/Z

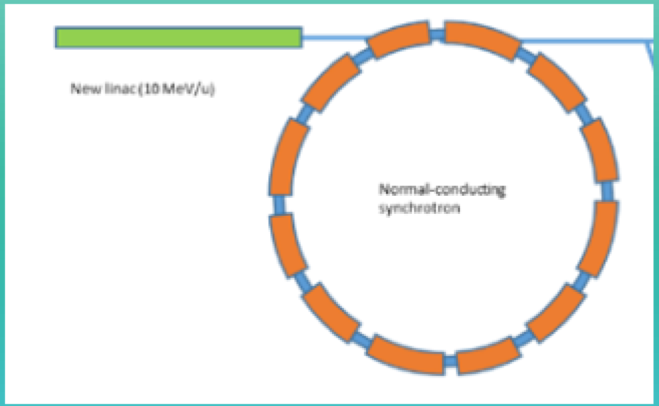
https://indico.cern.ch/event/956260/

Three alternative accelerator designs

Improved synchrotron (warm)

Equipped with several innovative features: multi-turn injection for higher beam intensity, new injector at higher gradient and energy, multiple extraction schemes, multi-ion.

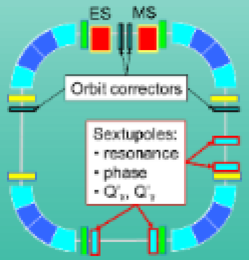
Circumference ~ 75 m



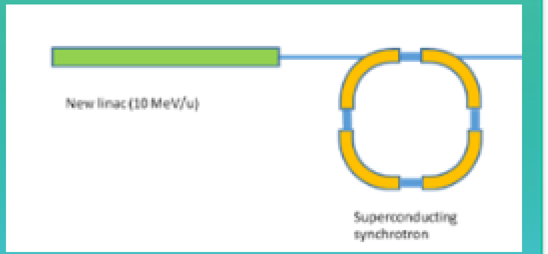
Improved synchrotron (superconducting)

Equipped with the same innovative features as warm, but additionally 90^0 superconducting magnets.

Circumference ~ 27 m



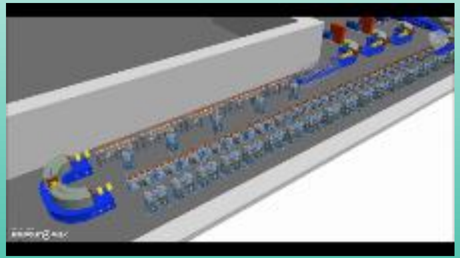
Courtesy: TERA

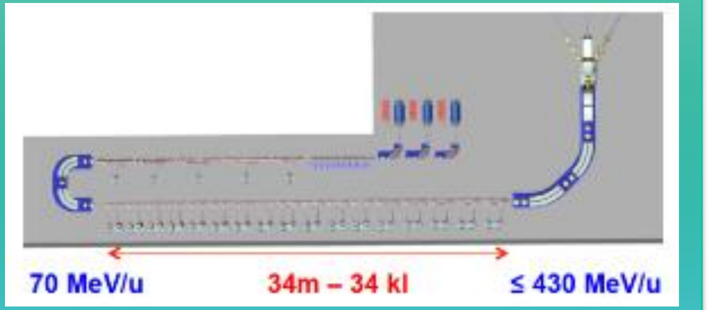


Linear accelerator

Linear sequence of accelerating cells, high pulse frequency.

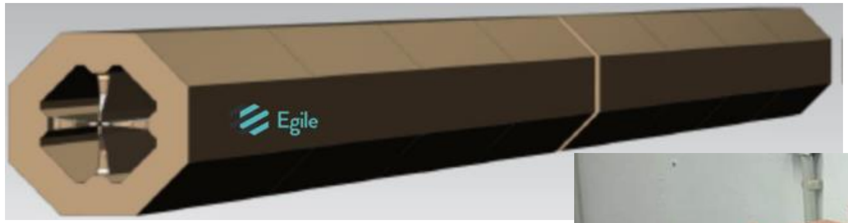
Length ~ 53 m

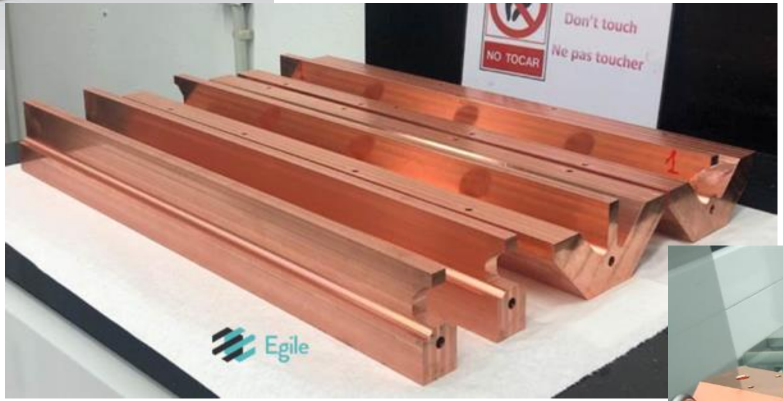


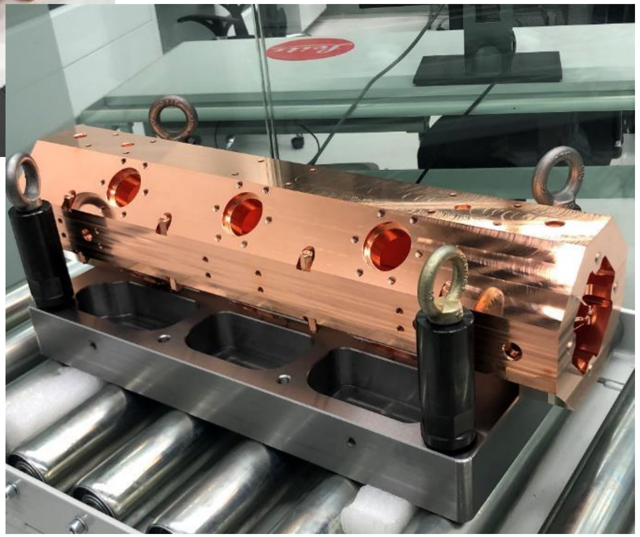


Other options considered as less interesting because of cost and/or required R&D: RC synchrotron, FFAG, SC cyclotron, PWFA

The RFQ for C^{6+} LINAC option







Collaboration CERN-CIEMAT-CDTI-Spanish industry

2.0 m long

750 MHz

Will deliver Carbon (or Helium) at 5 MeV (total energy)

Designed at CERN built in Spanish Industry

R&D on gantries

GaToroid: A Novel Concept for a Superconducting Compact and Lightweight Gantry for Hadron Therapy

Collaboration CNAO-INFN-CERN-MedAustron

Developing enabling technologies for a next-generation compact and lightweight rotating gantry

Protons stop…but where?

(Range uncertainty)

Courtesy Marco Durante

Range monitoring

Dosimetry

Moving organs

Clinical Trials

Combining Heavy-Ion Therapy with Immunotherapy: An Update on Recent Developments

Alexander Helm; Daniel K. Ebner; Walter Tinganelli; Palma Simoniello; Alessandra Bisio; Valentina Marchesano; Marco Durante; Shigeru Yamada; Takashi Shimokawa

Int J Part Ther (2018) 5 (1): 84–93.

https://doi.org/10.14338/IJPT-18-00024.1

Impact of proton therapy on antitumor immune response

Céline Mirjolet, Anaïs Nicol, Emeric Limagne, Carole Mura, Corentin Richard, Véronique Morgand, Marc Rousseau, Romain Boidot, François Ghiringhelli, Georges Noel & Hélène Burckel

Scientific Reports **11**, Article number: 13444 (2021) | Cite this article

FLASH therapy – a growing clinical interest

NATURE May 23, 1959 VOL. 183

Modification of the Oxygen Effect when Bacteria are given Large Pulses of Radiation

D. L. DEWEY
J. W. BOAG

Research Unit in Radiobiology,
British Empire Cancer Campaign,
Mount Vernon Hospital,
Northwood.

> Sci Transl Med. 2014 Jul 16;6(245):245ra93. doi: 10.1126/scitranslmed.3008973.

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon [1], Laura Caplier [2], Virginie Monceau [3], Frédéric Pouzoulet [4], Mano Sayarath [4], Charles Fouillade [4], Marie-France Poupon [4], Isabel Brito [5], Philippe Hupé [6], Jean Bourhis [7], Janet Hall [4], Jean-Jacques Fontaine [2], Marie-Catherine Vozenin [8]

Affiliations + expand

PMID: 25031268 DOI: 10.1126/scitranslmed.3008973

In vitro studies suggested that sub-millisecond pulses of radiation elicit less genomic instability than continuous, protracted irradiation at the same total dose. To determine the potential of ultrahigh dose-rate irradiation in radiotherapy, we investigated lung fibrogenesis in C57BL/6J mice exposed either to short pulses (≤ 500 ms) of radiation delivered at ultrahigh dose rate (≥ 40 Gy/s, FLASH) or to conventional dose-rate irradiation (≤ 0.03 Gy/s, CONV) in single doses. The growth of human HBCx-12A and HEp-2 tumor xenografts in nude mice and syngeneic TC-1 Luc(+) orthotopic lung tumors in C57BL/6J mice was monitored under similar radiation conditions. CONV (15 Gy) triggered lung fibrosis associated with activation of the TGF-β (transforming growth factor-β) cascade, whereas no complications developed after doses of FLASH below 20 Gy for more than 36 weeks after irradiation. FLASH irradiation also spared normal smooth muscle and epithelial cells from acute radiation-induced apoptosis, which could be reinduced by administration of systemic TNF-α (tumor necrosis factor-α) before irradiation. In contrast, FLASH was as efficient as CONV in the repression of tumor growth. Together, these results suggest that FLASH radiotherapy might allow complete eradication of lung tumors and reduce the occurrence and severity of early and late complications affecting normal tissue.

FLASH therapy – a growing clinical interest

Vozenin et al
Clin Cancer Res
2018

Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Original Article

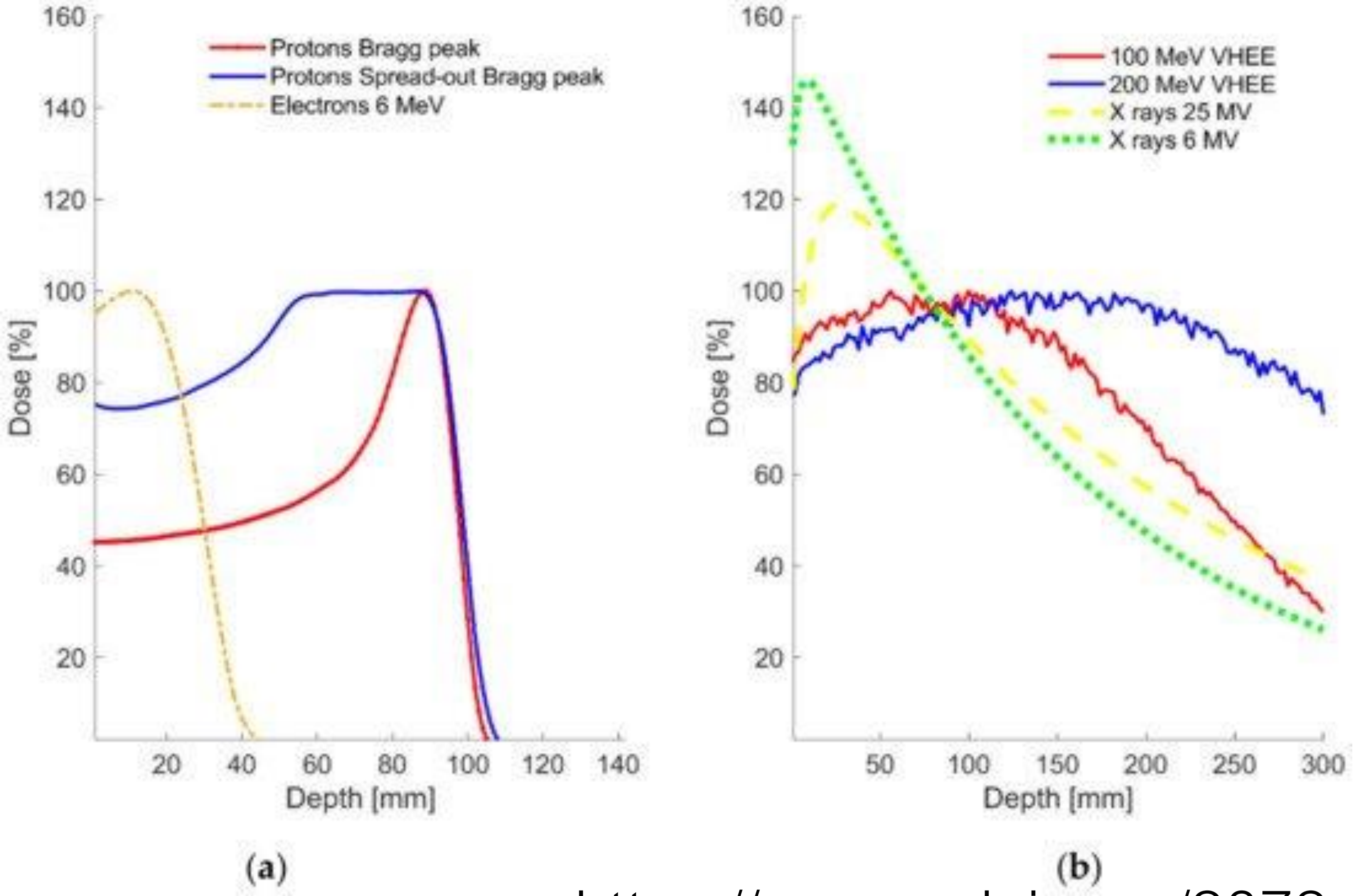
Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis[a,b,*], Wendy Jeanneret Sozzi[a], Patrik Gonçalves Jorge[a,b,c], Olivier Gaide[d], Claude Bailat[c], Fréderic Duclos[a], David Patin[a], Mahmut Ozsahin[a], François Bochud[c], Jean-François Germond[c], Raphaël Moeckli[c,1], Marie-Catherine Vozenin[a,b,1]

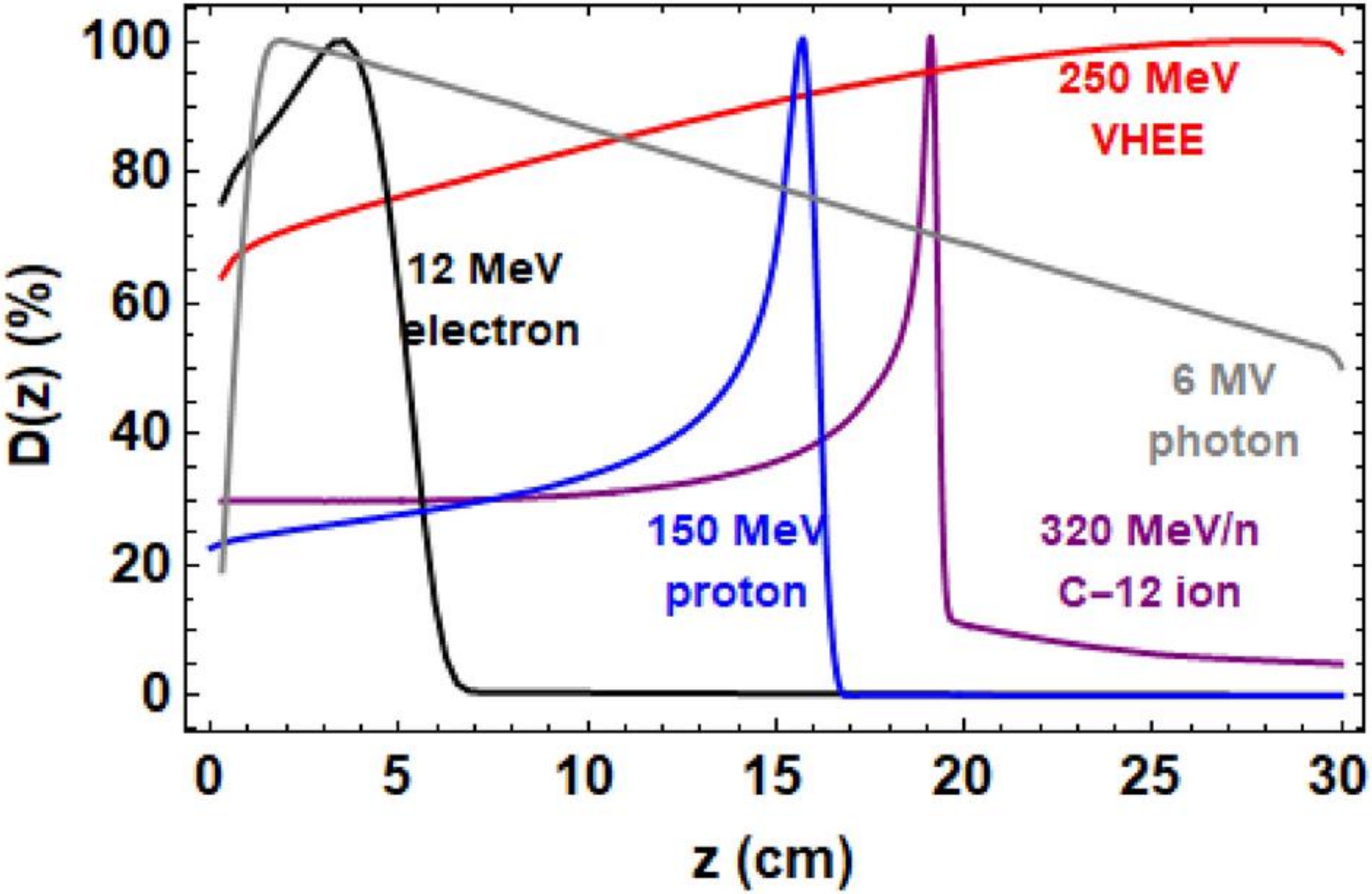
[a] Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; [b] Radiation Oncology Laboratory, Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; [c] Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne; and [d] Department of Dermatology, Lausanne University Hospital and University of Lausanne, Switzerland

Fig. 1. Temporal evolution of the treated lesion: (a) before treatment; the limits of th PTV are delineated in black; (b) at 3 weeks, at the peak of skin reactions (grade 1 epithelitis NCI-CTCAE v 5.0); (c) at 5 months.

First human patient – skin cancer treated with 10 MeV-range electrons



https://www.mdpi.com/2072-6694/13/19/4942/htm



TOPAS-based Monte Carlo simulations of the integrated normalised dose deposited in the plane parallel to the direction of an incident Gaussian beam (σ=4mm). All beams are in the absence of focusing

https://www.nature.com/articles/s41598-021-93276-8#Fig1

Exit Window
Water phantom
Radiosensitive films
YAG screen
Charge monitor
Quadrupole
Camera
VHEE2020
5-7 October 2020
Cherenkov in water

VHEE'17
Very High Energy Electron
Radiotherapy: Medical &
Accelerator Physics Aspects
Towards Machine Realisation
JULY 24 – 26, 2017
COCKCROFT INSTITUTE
Scientific Programme Committee:
Roger M. Jones University of Manchester/Cockcroft Institute, UK– Chair
Colleen DesRosiers Indiana University, USA
Angeles Faus-Golfe IFIC, Spain, and CNRS/LAL, France
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Marcel Van Herk The Christie/Manchester University, UK
Alan Wheelhouse STFC Daresbury Laboratory, UK
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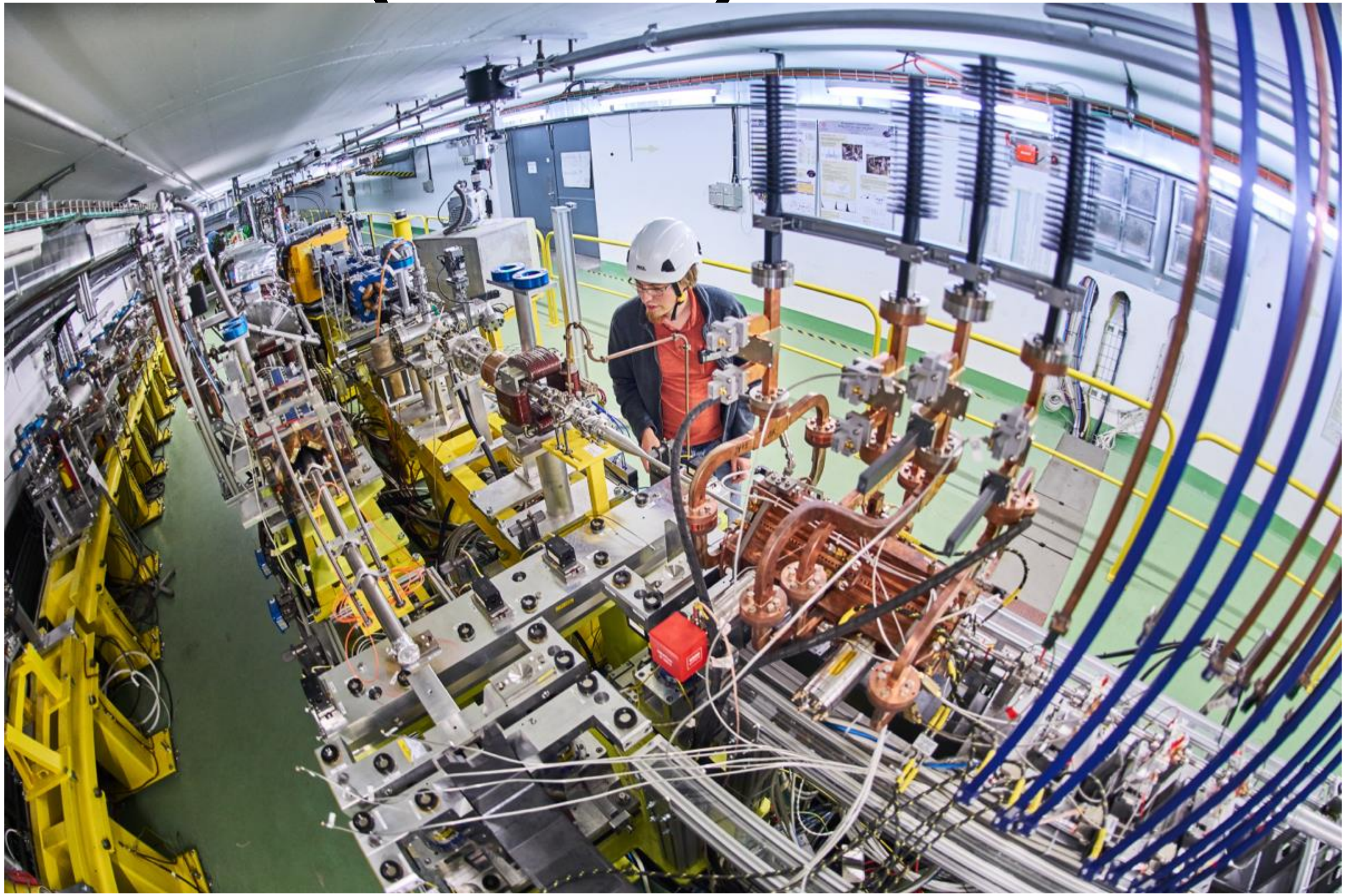
Roger M. Jones University of Manchester/Cockcroft Institute
Nirav Joshi University of Manchester/Cockcroft Institute
Peter McIntosh STFC Daresbury Laboratory
Hywel Owen University of Manchester/Cockcroft Institute
Sue Waller STFC Daresbury Laboratory
This workshop will explore fundamental issues associated with the development of a radiotherapy machine capable of delivering 250 MeV electrons at a high dose. We will explore both the dose delivery aspects, and the potential to realise a radiotherapy machine suitable for patient treatment.
www.cockcroft.ac.uk/events/VHEE17
The Cockcroft Institute
Science & Technology Facilities Council
IOP Institute of Physics Particle Accelerators and Beams Group
EuCARD²

The CERN Linear Electron Accelerator for Research (CLEAR)

CLEAR is a versatile 200 MeV electron linac + a 20m experimental beamline, operated at CERN as a multi-purpose user facility.



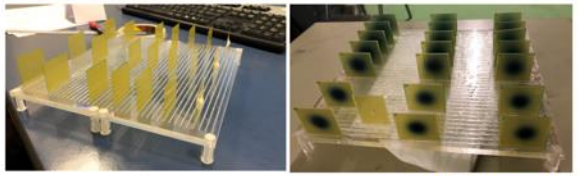
VHEE activities in CLEAR

Calibration of operational medical dosimeters – nonlinear effects with high-dose short pulses

Verification of FLASH effect using biological dosimeters

Experimental verification of dose deposition profiles in water phantoms

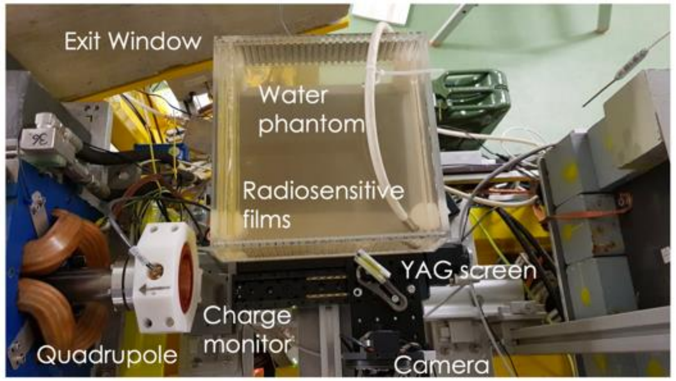
Demonstration of “Bragg-like peak” deposition with focused beams



Films set-up for profile depth dose, CHUV Lausanne
(M.C. Vozenin, C. Bailat, R. Moeckli et al.)

Advance Markus chambers and SRS Array, Oldenburg University and PTW
(B. Poppe, D. Poppinga et al.)

Calorimeter and ROOS chamber, Nat. Phys. Lab. UK
(A. Subiel et al.)



Strathclyde and Manchester

A. Lagdza, R. Jones et al., Influence of heterogeneous media on Very High Energy Electron (VHEE) dose penetration and a Monte Carlo-based comparison with existing radiotherapy modalities, Nuclear Inst. and Meth. in Physics Research, B, 482 (2020) 70-81.

M. McManus, A. Subiel et al., The challenge of ionisation chamber dosimetry in ultra-short pulsed high dose-rate Very High Energy Electron beams, Nature Scientific Reports (2020) 10-9089.

Small, K.L., Henthorn, et al., Evaluating very high energy electron RBE from nanodosimetric pBR322 plasmid DNA damage, Nature Sci. Rep. 11, 3341 (2021).

D. Poppinga et al., VHEE beam dosimetry at CERN Linear Electron Accelerator for Research under ultra-high dose rate conditions, 2021 Biomed. Phys. Eng. Express 7 015012.

Kokurewicz, K., Brunetti, E., Curcio, A. et al. An experimental study of focused very high energy electron beams for radiotherapy, Nature Commun. Phys. 4, 33 (2021).

Table 1. Main parameters for the VHEE sources cited in this document.

Beam Parameters	CLEAR	SPARC	NLCTA
Energy (MeV)	50–220	170	50–120
Bunch charge (pC/shot)	150	60	30
Bunch length rms (ps)	0.1–10	0.87	1
Repetition rate (Hz)	0.8–10	0.1–10	0.1–10
Beam size at water phantom surface (σ mm)	1.2	3.4	2

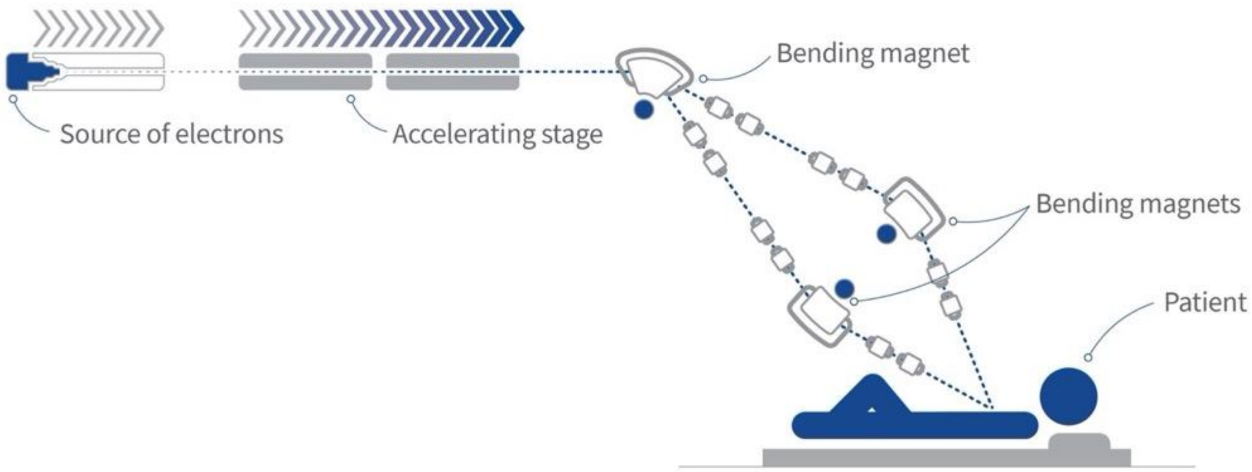
Table 2. List of facilities or accelerators under development for VHEE production.

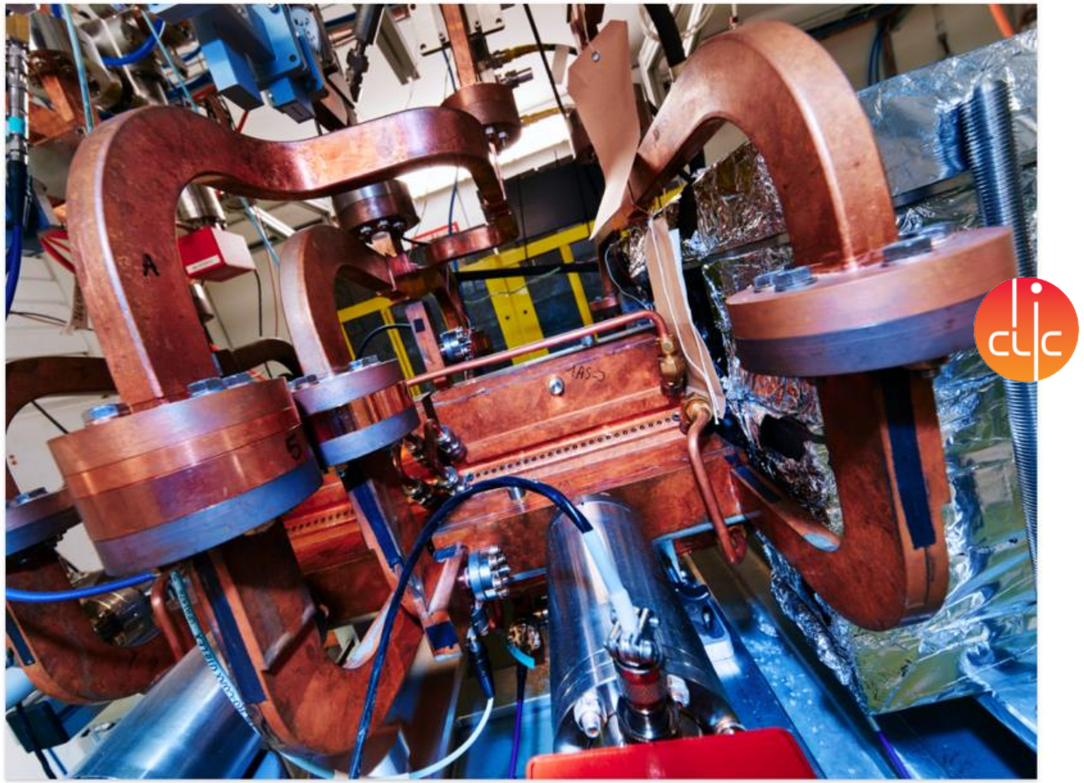
Beam Parameters	PHASER	CLARA	PITZ	Argonne	Tsinghua University
Energy (MeV)	100–200	50 (−250)	20 (−250)	6–63	45 (−350)
Bunch charge (pC/shot)	-	20–100	0.1–5000	$100–10^5$	200
Bunch length rms (ps)	3.10^5	0.3–5	30	0.3	<2
Repetition rate (Hz)	10	10 (−100)	10	0.5–10	5–50

https://www.mdpi.com/2072-6694/13/19/4942/htm

FLASH VHEE therapy

CLIC technology for a FLASH VHEE facility designed by CERN in collaboration with CHUV that will be realized by THERYQ





Close-up of the Compact Linear Collider prototype, on which the electron FLASH design is based (Image: CERN)

An intense beam of electrons is produced in a photoinjector, accelerated to around 100 MeV and then is expanded, shaped and guided to the patient.

The design of this facility is the result of an intense dialogue between groups at CHUV and CERN.

Jean Bourhis from CHUV:
“The clinical need that we have really converges with the technological answer that CERN has.”

The remarkable connection between CLIC technology and FLASH electron therapy

Very intense electron beams
- CLIC – to provide brightness needed for delicate physics experiments
- FLASH – to provide dose fast for biological FLASH effect

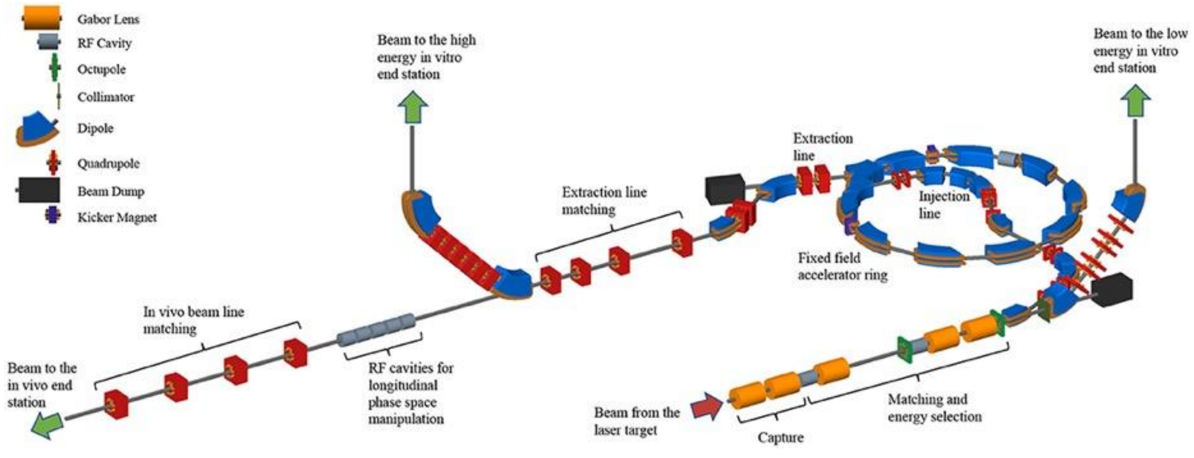
Very precisely controlled electron beams
- CLIC – to reduce the power consumption of the facility
- FLASH – to provide reliable treatment in a clinical setting

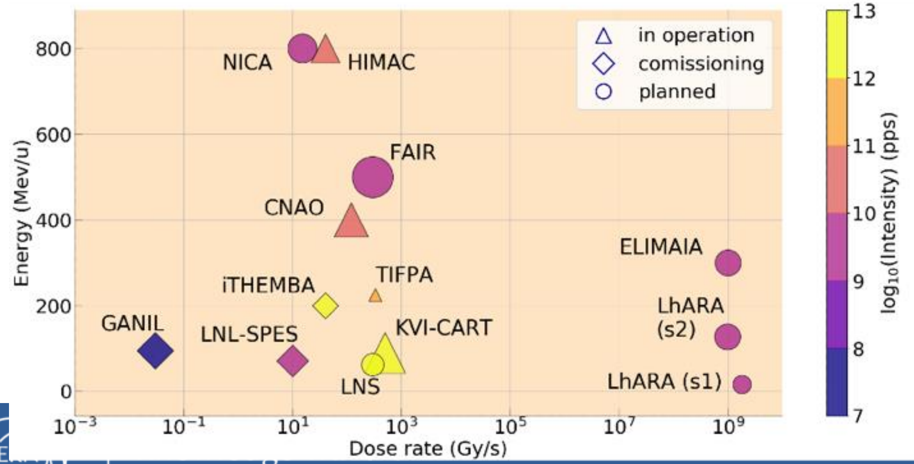
High accelerating gradient (that is high beam energy gain per length)
- CLIC – fit facility in Lac Leman region and limit cost
- FLASH – fit facility on typical hospital campuses and limit cost of treatment

CERN KT Seminar on April 26th, 2021
https://indico.cern.ch/event/975980/

Look even further

Laser-hybrid Accelerator for Radiobiological Applications

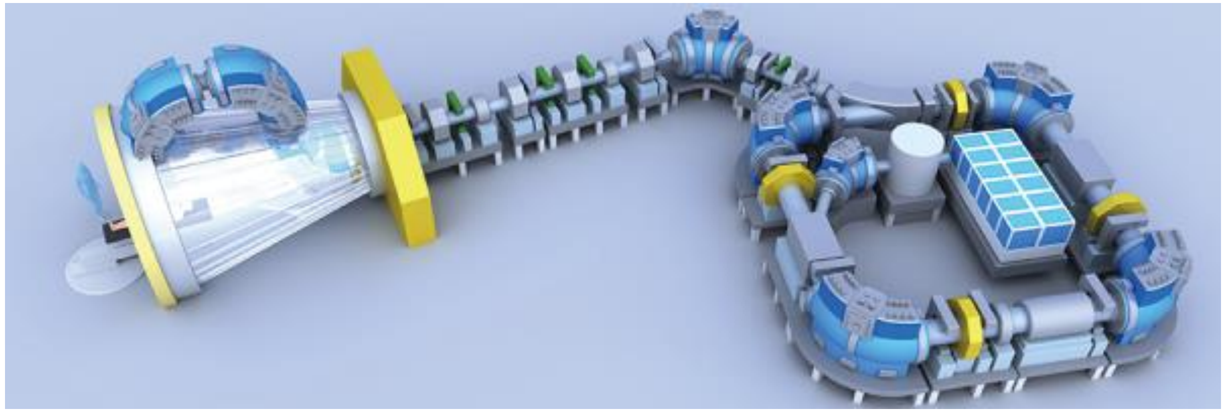




Credit: LhARA Consortium

Quantum Scalpel

National Institutes for Quantum Science and Technology



5th generation facility:

Superconducting synchrotron

Multi-ion irradiation system

Injector with laser acceleration technology

Rotating gantry with HTS magnets

Microsurgery system

End part I

Photo: CNAO treatment room