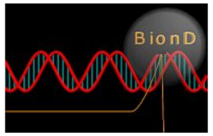
Physics of Charged Particle Therapy

Prof Dr Joao Seco (JS), Dr Paulo Martins (PM), Dr Luca Burigo (LB), Dr Benedikt Kopp (BK), Dr Niklas Wahl (NW), Dr Tim Gehrke (TG)

Research
Research Topics
Cell Biology and Tumor Biology
Functional and Structural Genomics
Cancer Risk Factors and Prevention
Immunology and Cancer
Imaging and Radiooncology
Biomedical Physics in Radiation Oncology
Teaching
DKFZ PhD Program
Research
Staff
Infection, Inflammation and Cancer
Other Units
Research Groups A-Z

Division of Biomedical Physics in Radiation Oncology

Prof. Dr. Joao Seco



Biological effective Ion Dose producing DNA Damage
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Radiation therapy is the most common treatment for cancer, being used in approximately 70% of all cancers either alone or combined with surgery or chemotherapy. It uses high-energy particles or waves, such as x-rays, gamma rays, electron beams, protons, carbon ions, to "kill" or "damage" cancer cells. There is a growing interest in the use of ion-beams (protons, carbon ions) for cancer therapy. The principal benefit of ion-beams are there finite range (or depth) in tissue, known as Bragg peak, where a significant amount of the radiation is deposited at the end of the track where the ions stop. The Bragg peak guarantees that healthy organs distal (deeper) to this peak receive NO radiation, reducing significantly side effects. However, due to treatment planning and beam delivery uncertainties, it is not possible to place accurately the Bragg peak on the distal end of the tumor. Thus, we voluntarily irradiate healthy surrounding organs to guarantee the tumor receives the correct radiation dose. The Bragg peak "uncertainty" reduces the clinical potential of ion-beam radiotherapy, because of the additional radiation given to healthy organs. My Current Research interests are: 1) to develop novel imaging technologies to reduce the Bragg peak positioning "uncertainties" for ion-beam radiotherapy, using Helium beam imaging and prompt gamma spectroscopy. 2) to investigate the mechanism of radiation triggered DNA damage via reactive oxygen species (ROS).

In principle, ion-beam therapy offers a substantial clinical advantage over conventional photon therapy. This is because of the unique Bragg peak depth-dose characteristics, which can be exploited to achieve significant reductions in normal tissue doses proximal and distal to the target volume. These may, in turn, allow escalation of tumor doses and greater sparing of normal tissues, thus potentially improving local control and survival while at the same time reducing toxicity and improving quality of life. In the future, a more widespread use of ion-beam radiotherapy will make it possible to significantly improve cancer survival with minimal side effects. However, in order to take full advantage ion-beam radiotherapy a better control is needed of the Bragg peak within the patient (cancer) and a better understanding of the radiation triggered DNA damage is required. Once we can control very accurately the positioning of the Bragg peak within the cancer to within 1mm, then it will be possible to reduce radiation side-effects, while simultaneously boosting the cancer with more radiation.

Contact

Selected Publications

J Seco, MF Spadea (2015) "Imaging in particle therapy: State of the art and future perspective" Acta Oncologica 54 (9) 1254-1258

J Verburg , J Seco (2014) "Proton range verification through prompt gamma-ray spectroscopy" Physics in Medicine and Biology 60 (3) 7089-7106

J Seco et al (2012) "Treatment of non-small cell lung cancer patients with proton

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Benedikt Kopp
17.45 · Master of Science

Overview

#	Date	Title	Place	Teacher
1	27 April	Course introduction, introduction RT, history of PT	INF 227 / SR 1.404	JS
2	4 May	Introduction to PT		BK
3	11 May	Fundamentals of Interactions of particles in matter	INF 227 / SR 1.404	PM
4	18 May	Monte Carlo particle transport in matter I*		LB
5	25 May	Monte Carlo particle transport in matter II*		LB
6	8 June	Phenomenological interaction models in depth and lateral direction*		NW
7	15 June	Analytical dose calculation algorithms*		NW
8	22 June	Review of Radiobiology for particles & Symbio tutorial*		JS
9	29 June	Review of Particle imaging technology		TG
10	6 July	Application of Particle imaging technology		TG
11	13 July	Introduction to range monitoring in particle therapy		PM
12	20 July	Dose application and treatment planning, matRad tutorial*		NW
13	27 July	Detector and Instrumentation for Range Monitoring	INF 227 / SR 1.404	PM

Course Lecture Room

ONLINE COURSE VIA ZOOM

- Monday, 4-8pm (2hrs theory, 1hr practical)
- Room F.02.082 (2nd Floor)

Learning objectives

- Potential and limitations of heavy charged particle therapy
- Physical processes for the generation and delivery of heavy charged particle beams into patients
- Effects of charged particle beams on biological tissues
- Clinical treatment planning and application of charged particle therapy

Literature

De Laney, Thomas F., and Hanne M. Kooy, eds. *Proton and charged particle radiotherapy*. Lippincott Williams & Wilkins, 2008. (ebook available)

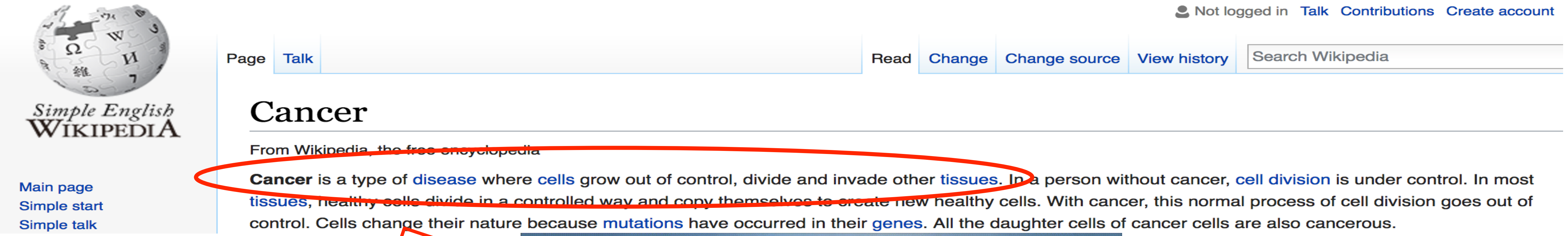
Paganetti, Harald. *Proton therapy physics*. CRC Press, 2011.

Lomax, Tony, ed. *Proton and carbon ion therapy*. CRC Press, 2012.

Seco, Verhaegen, ed. Monte Carlo Techniques in Radiation Therapy. CRC Press, 2013.

Linz, Ute, ed. *Ion Beam Therapy: Fundamentals, Technology, Clinical Applications*. Springer Science & Business Media, 2011. (ebook available)

What is Cancer?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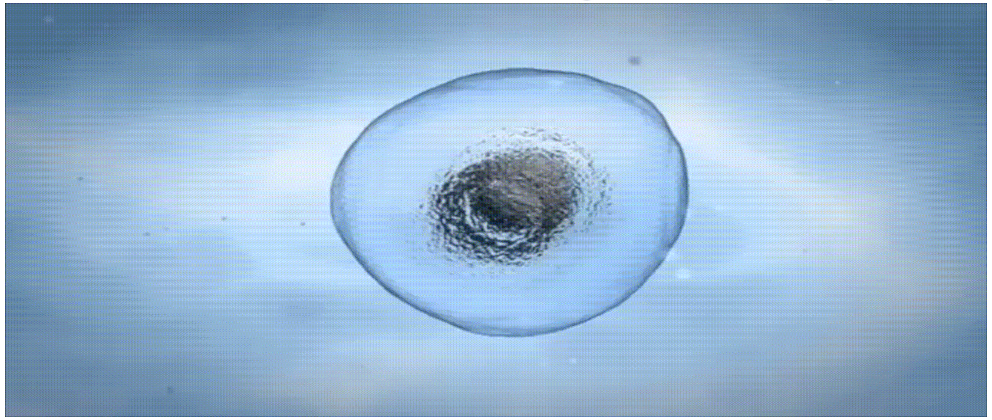
Cancer

From Wikipedia, the free encyclopedia

Cancer is a type of disease where cells grow out of control, divide and invade other tissues. In a person without cancer, cell division is under control. In most tissues, healthy cells divide in a controlled way and copy themselves to create new healthy cells. With cancer, this normal process of cell division goes out of control. Cells change their nature because mutations have occurred in their genes. All the daughter cells of cancer cells are also cancerous.

CANCER STEM CELLS



Cancer remains a key public health concern and a burden on the European Union (EU). It is the second largest cause of death in the EU-28, only behind cardiovascular diseases.

More than one quarter of all deaths is due to cancer (26%) and it has been estimated that, in future, 1 in 3 people in the EU will get cancer in their lifetime.

2017 New Cancer Sites

Estimated New Cases

Males			Females		
Prostate	161,360	19%	Breast	252,710	30%
Lung & bronchus	116,990	14%	Lung & bronchus	105,510	12%
Colon & rectum	71,420	9%	Colon & rectum	64,010	8%
Urinary bladder	60,490	7%	Uterine corpus	61,380	7%
Melanoma of the skin	52,170	6%	Thyroid	42,470	5%
Kidney & renal pelvis	40,610	5%	Melanoma of the skin	34,940	4%
Non-Hodgkin lymphoma	40,080	5%	Non-Hodgkin lymphoma	32,160	4%
Leukemia	36,290	4%	Leukemia	25,840	3%
Oral cavity & pharynx	35,720	4%	Pancreas	25,700	3%
Liver & intrahepatic bile duct	29,200	3%	Kidney & renal pelvis	23,380	3%
All Sites	**836,150**	**100%**	**All Sites**	**852,630**	**100%**

2017 Cancer Deaths

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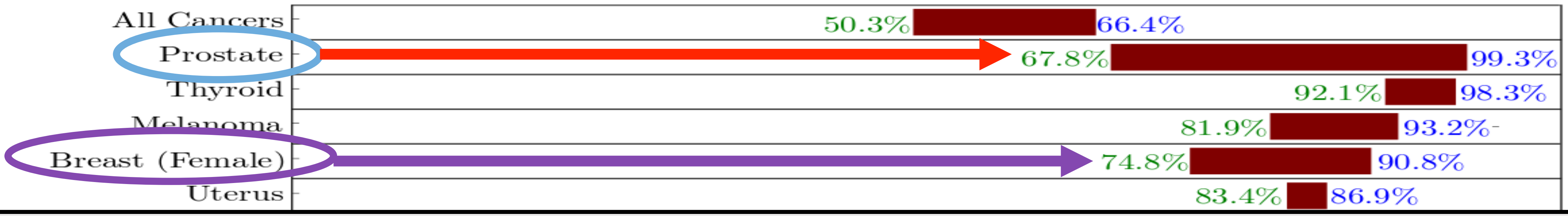
Estimated Deaths

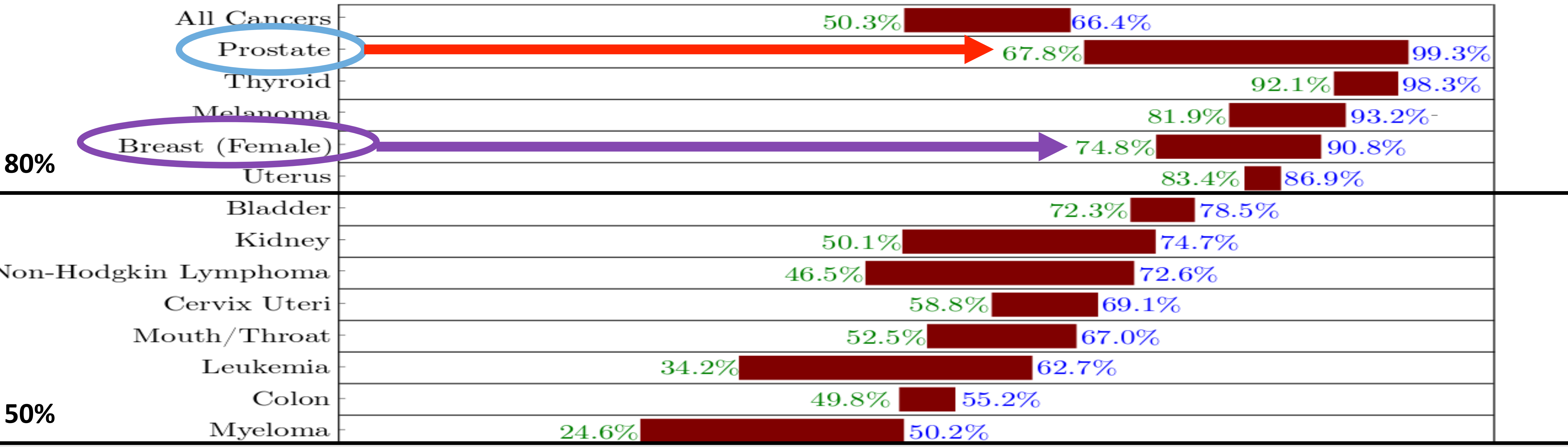
Males			Females		
Lung & bronchus	84,590	27%	Lung & bronchus	71,280	25%
Colon & rectum	27,150	9%	Breast	40,610	14%
Prostate	26,730	8%	Colon & rectum	23,110	8%
Pancreas	22,300	7%	Pancreas	20,790	7%
Liver & intrahepatic bile duct	19,610	6%	Ovary	14,080	5%
Leukemia	14,300	4%	Uterine corpus	10,920	4%
Esophagus	12,720	4%	Leukemia	10,200	4%
Urinary bladder	12,240	4%	Liver & intrahepatic bile duct	9,310	3%
Non-Hodgkin lymphoma	11,450	4%	Non-Hodgkin lymphoma	8,690	3%
Brain & other nervous system	9,620	3%	Brain & other nervous system	7,080	3%
All Sites	**318,420**	**100%**	**All Sites**	**282,500**	**100%**

5-Year Cancer Survival for 1975 and 2016

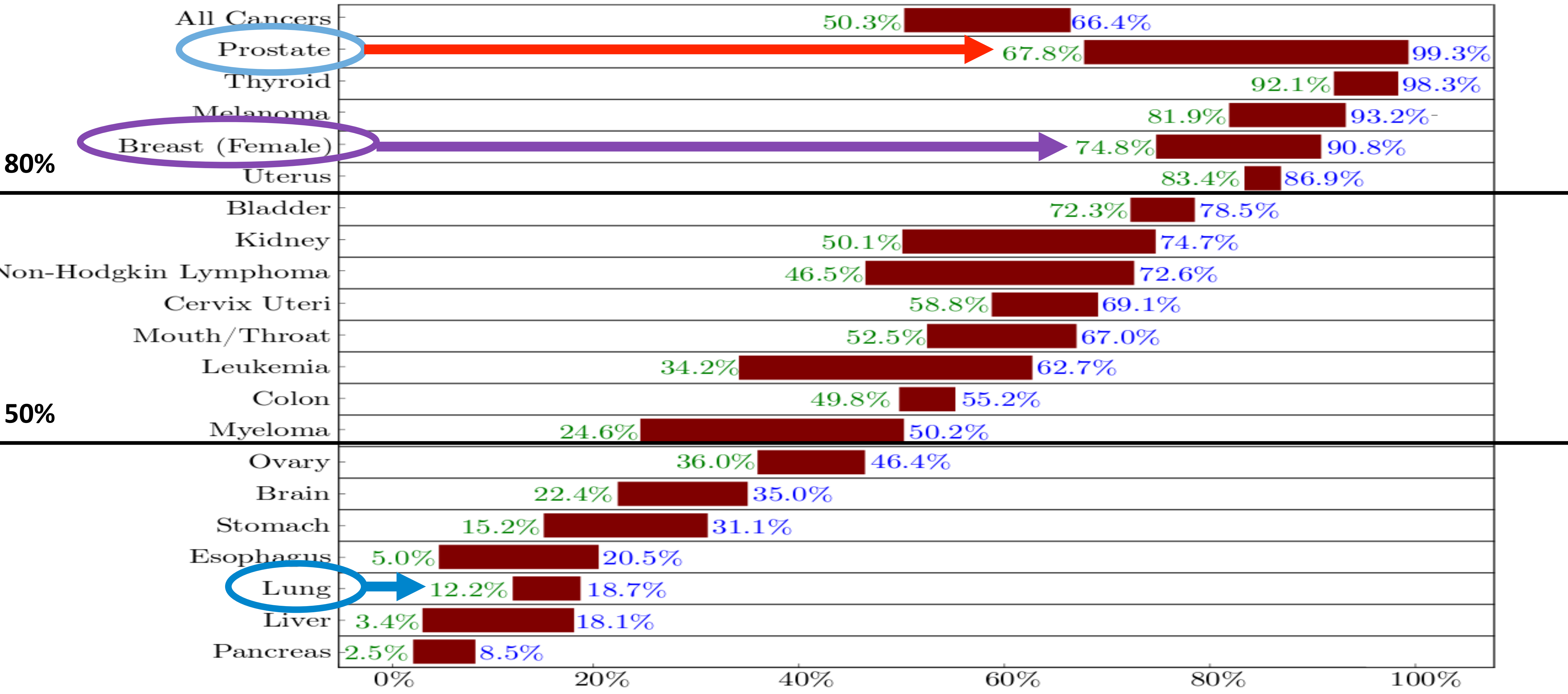


80%

5-Year Cancer Survival for 1975 and 2016



5-Year Cancer Survival for 1975 and 2016



90% of Cancer Patients die from Metastasis

What is Radiation Therapy?

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Radiation therapy

From Wikipedia, the free encyclopedia

"Radiation (medicine)" redirects here. It is not to be confused with Radiation (pain) or Radiology.

Radiation therapy or **radiotherapy**, often abbreviated **RT**, **RTx**, or **XRT**, is therapy using ionizing radiation, generally as part of cancer treatment to control or kill malignant cells and normally delivered by a linear accelerator. Radiation therapy may be curative in a number of types of cancer if they are localized to one area of the body. It may also be used as part of adjuvant therapy, to prevent tumor recurrence after surgery to remove a primary malignant tumor (for example, early stages of breast cancer). Radiation therapy is synergistic with chemotherapy, and has been used before, during, and after chemotherapy in susceptible cancers. The subspecialty of oncology concerned with radiotherapy is called **radiation oncology**.

Radiation therapy is commonly applied to the cancerous tumor because of its ability to control cell growth. Ionizing radiation works by damaging the DNA of cancerous tissue leading to cellular death. To spare normal tissues (such as skin or organs which radiation must pass through to treat the tumor), shaped radiation beams are aimed from several angles of exposure to intersect at the tumor, providing a much larger absorbed dose there than in the surrounding, healthy tissue. Besides the tumour itself, the radiation fields may also include the draining lymph nodes if they are clinically or radiologically involved with tumor, or if there is thought to be a risk of subclinical malignant spread. It is necessary to include a margin of normal tissue around the tumor to allow for uncertainties in

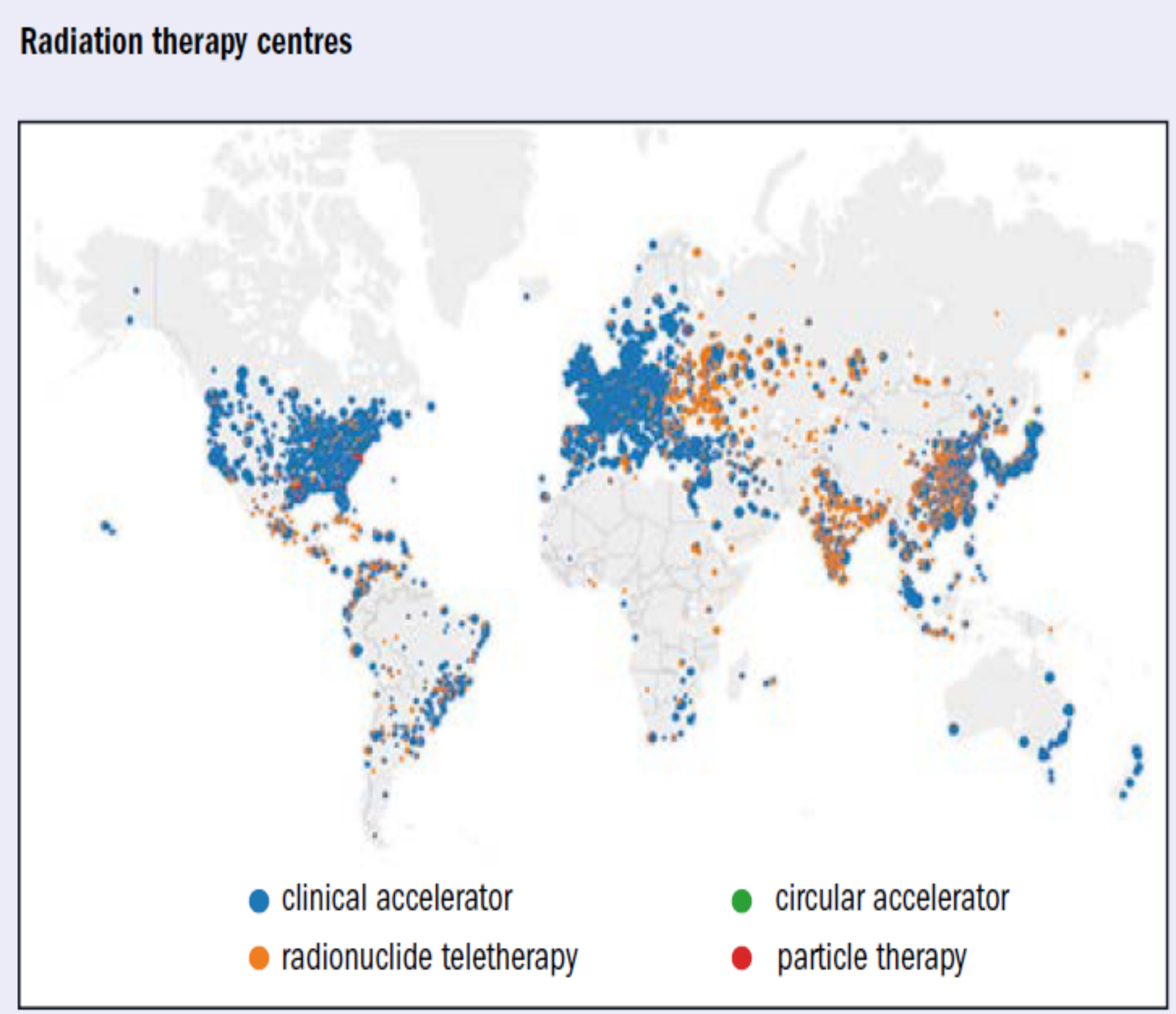
Radiation therapy

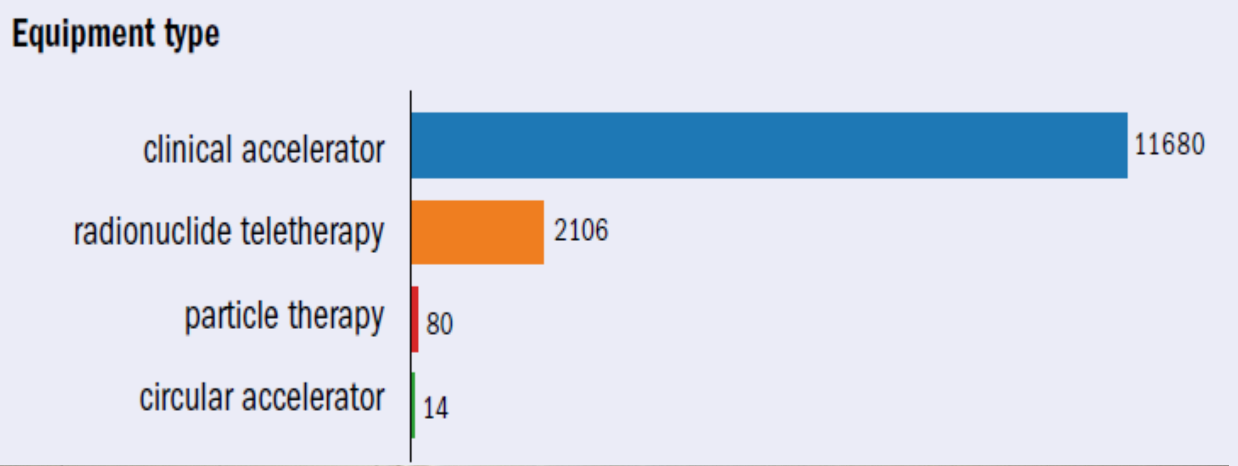
Intervention

Radiation therapy of the pelvis. Lasers and a mould under the legs are used to determine exact position.

Ionizing Radiation Sterilizes Cancer STEM Cells!!!

Worldwide Distribution of Radiation Therapy





Historical overview

- Development of radiation therapy driven by developments in particle therapy
- In parallel improved understanding of radiobiology

Bibliography

1. Linz, Ute, ed. *Ion Beam Therapy: Fundamentals, Technology, Clinical Applications*. Springer Science & Business Media, 2011, Chapter 1.
2. Giap, Huan, and Bosco Giap. "Historical perspective and evolution of charged particle beam therapy." *Translational Cancer Research* 1.3, 2012.
3. "The story of radiology", European Society of Radiology, 2013.
4. Wikipedia

Historical overview 1895

- Systematic studies of x-rays by Wilhelm Röntgen

- Presumably experiments with a wrapped Crookes tube and fluorescent barium platinocyanide screen

Historical overview 1896

- Campbell Swinton investigated biological effects of x-rays without finding any

- Physician John Daniel reported that a child had lost his hair three weeks after one hour exposure to x-rays in order to locate a bullet in his head

  Daniel, J.: Letter, Science 3, 562 (1896)

- Physician Wilhelm Markuse reported dermatological changes in a 17-year-old male that participated in a series of radioscopic experiments

  Markuse, W.: Dermatitis und Alopecie nach Durchstrahlungsversuchen mit Röntgenstrahlen. Deutsche Medizinische Wochenschrift 30, 481 (1896)

- Several physicians use x-rays to treat dermatological diseases

- First basic research with x-ray use for treatment in Vienna by Leopold Freud

Historical overview

1896

- Becquerel discovers natural radioactivity in uranium salts

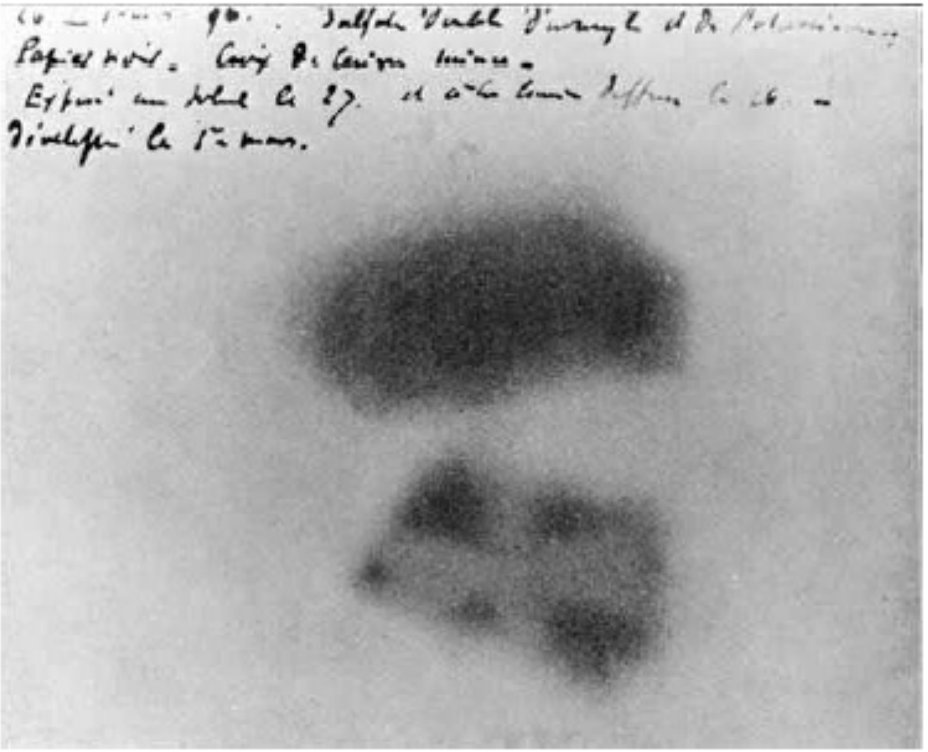


Image of Becquerel's photographic plate which has been fogged by exposure to radiation from a uranium salt. The shadow of a metal cross placed between the plate and the uranium salt is clearly visible.

Historical overview 1897

- Discovery/identification of electron by Sir Joseph John Thomson

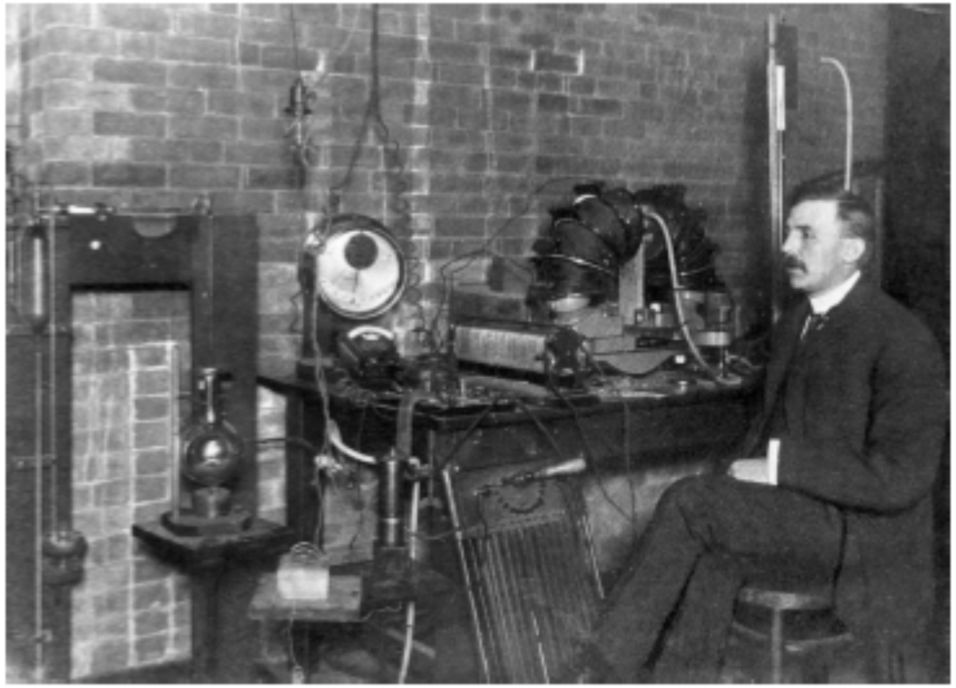
- Experiments with cathode rays emitted by different material in electric field

  - Deflection
  - Higher penetration than expected for atoms
  - Consistent for all materials

→ „Corpuscles“ which are universal, light, charged building blocks of atoms

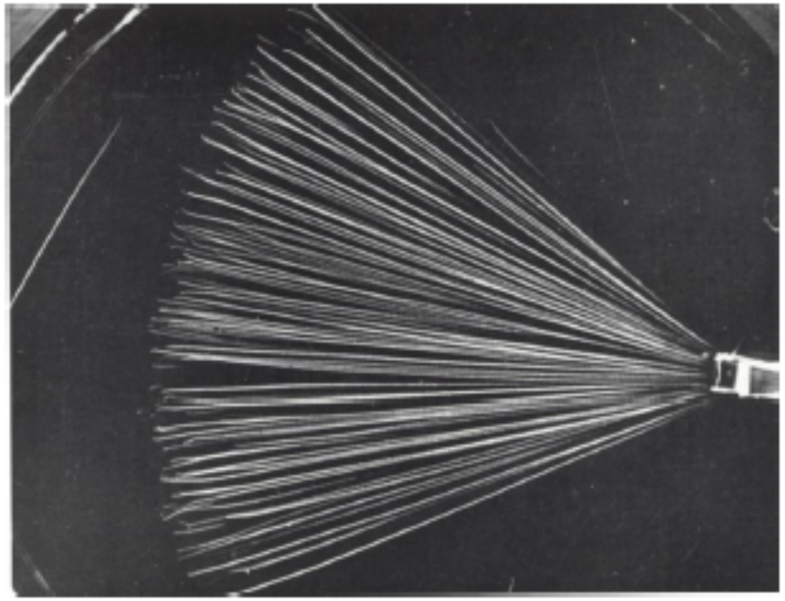
Historical overview 1909-1920

- Ernest Rutherford advances the understanding of the nuclear structure of the atom
- Identification of proton



Historical overview

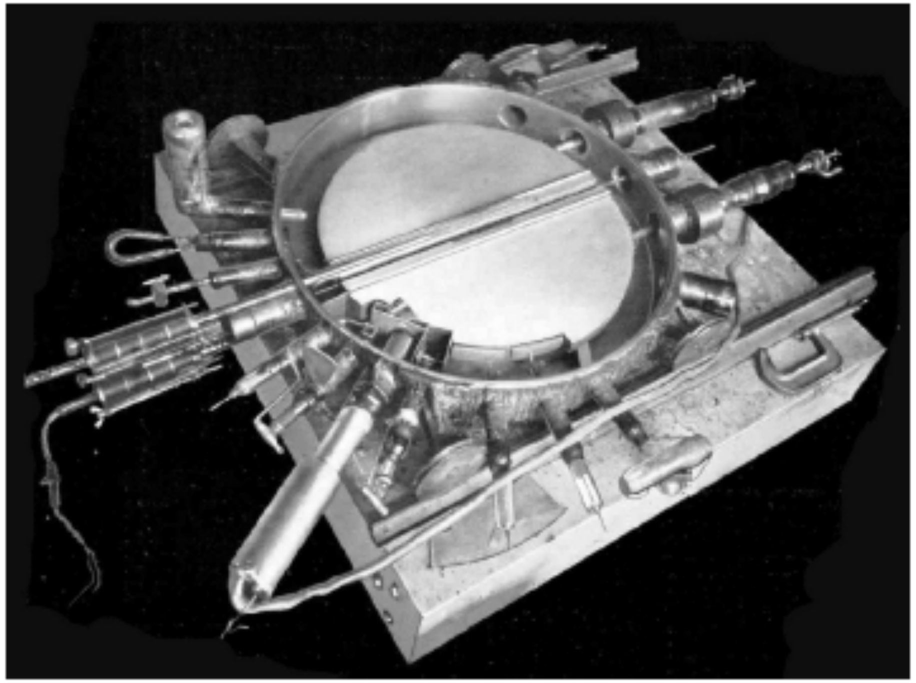
- Alpha particles emitted by polonium in could chamber (1926)



→ Heavy charged particles have a well defined range

Historical overview 1932

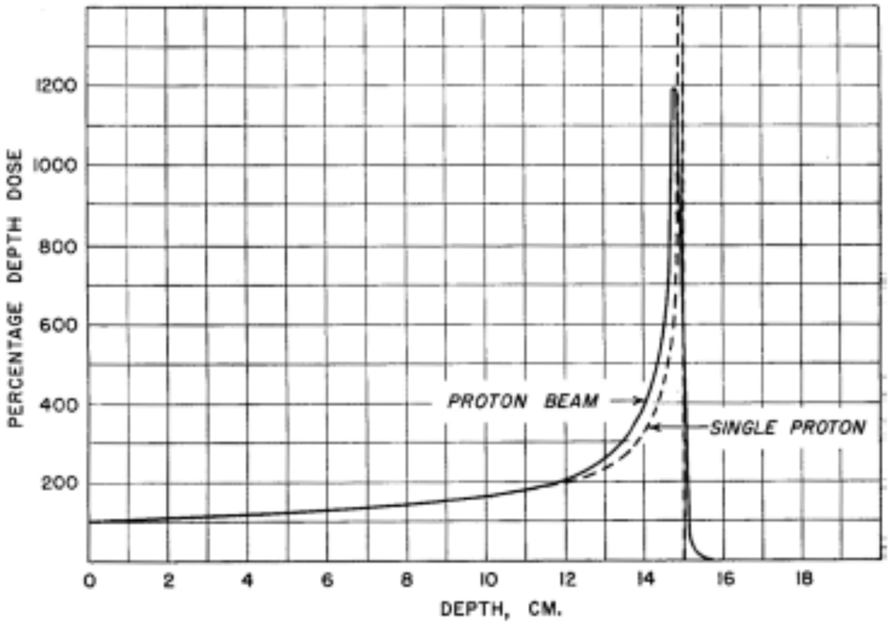
- Ernest O. Lawrence develops the first cyclotron at University of California‘s radiation laboratory



Vacuum chamber of Lawrence‘s 69cm cyclotron in 1932

Historical overview 1946

- Robert R. Wilson suggests use of heavy charged particles for therapeutic use



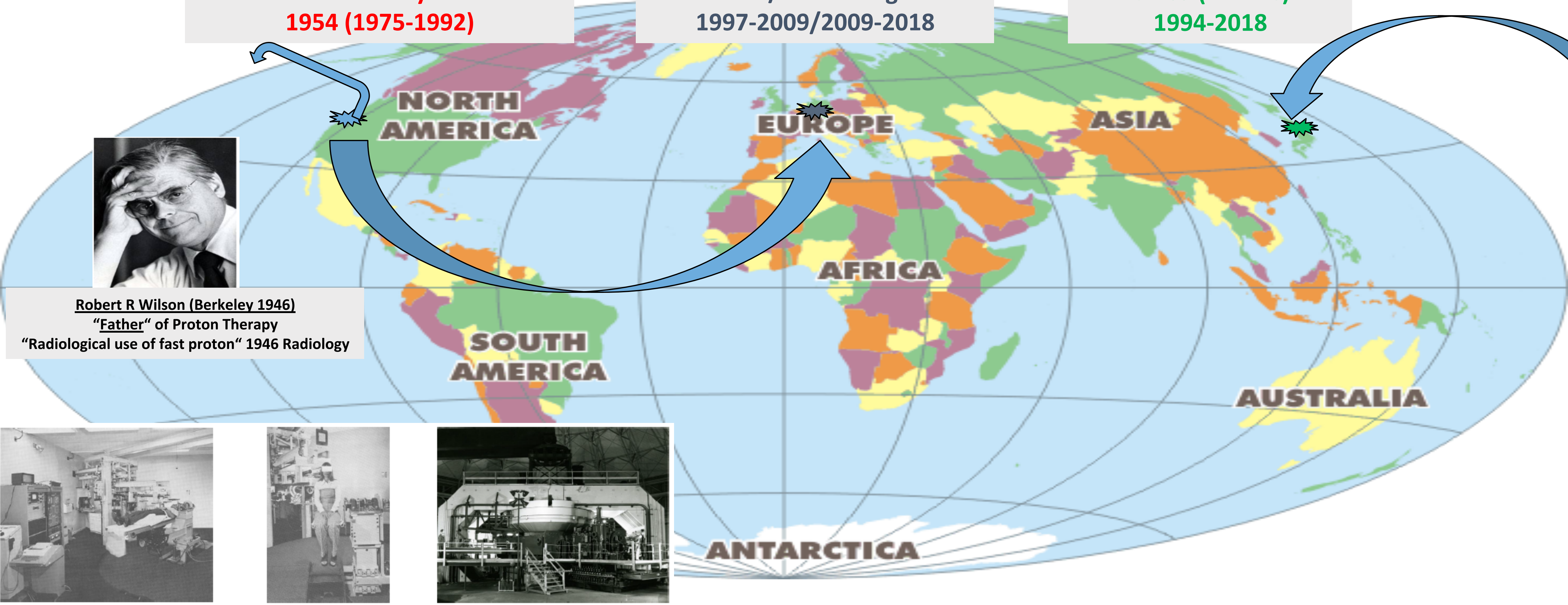
Wilson, Robert R. "Radiological use of fast protons." *Radiology* 47.5 (1946): 487-491.
https://en.wikipedia.org/wiki/Robert_R._Wilson

Carbon (Proton) Beam Therapy

1st Proton (1st Carbon)
Berkeley
1954 (1975-1992)

3rd Carbon
GSI/Heidelberg
1997-2009/2009-2018

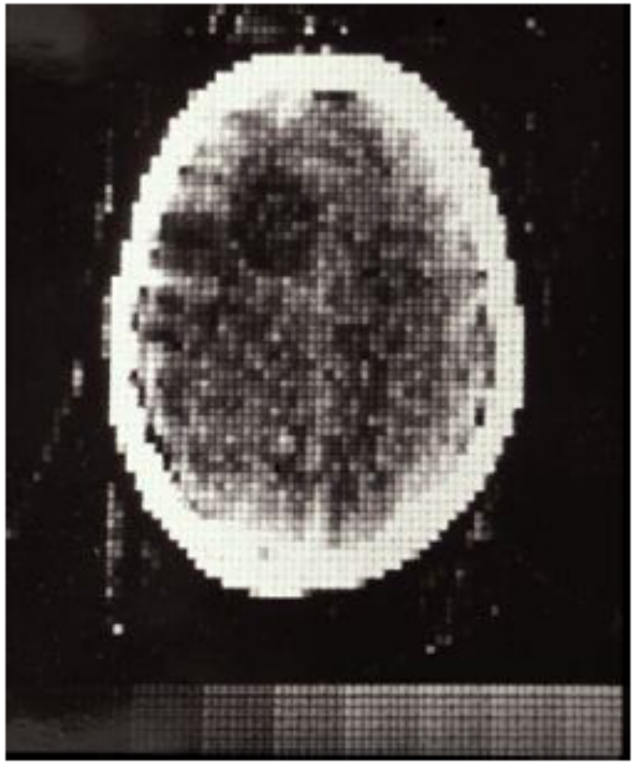
2nd Carbon
Chiba (HIMAC)
1994-2018



Robert R Wilson (Berkeley 1946)
"Father" of Proton Therapy
"Radiological use of fast proton" 1946 Radiology

Historical overview 1971

- First patient brain CT scan on October 1 in Atkinson Morley Hospital in Wimbeldon



http://www.impactscan.org

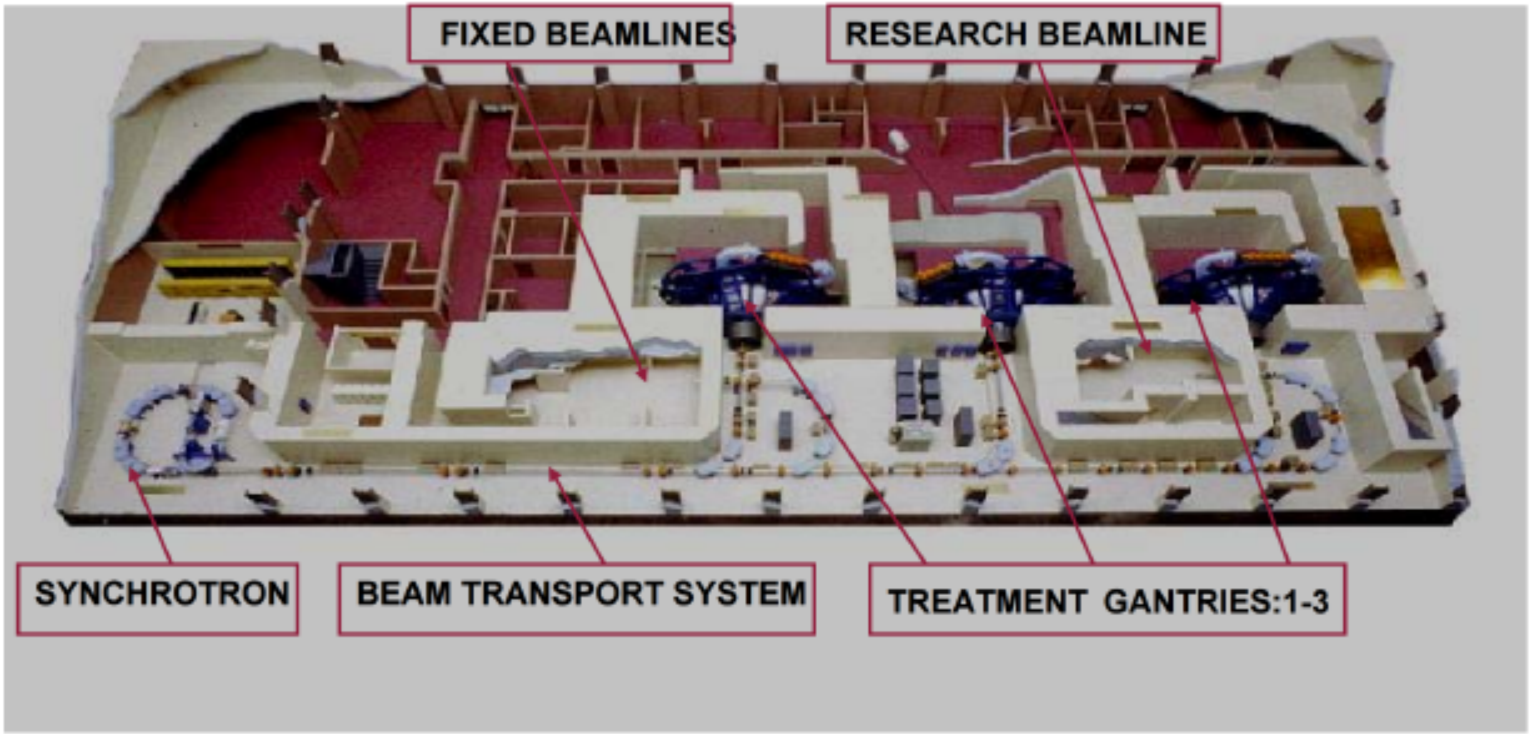
Historical overview

- Early particle therapy facilities

WHERE		WHAT	FIRST	LAST	PATIENT TOTAL	
			PATIENT			
Belgium	Louvain-la-Neuve	p	1991	1993	21	
Canada	Vancouver (TRIUMF)	π^-	1979	1994	367	
Japan	Tsukuba (PMRC, 1)	p	1983	2000	700	
Japan	Chiba	p	1979	Apr-02	145	eyes only
Russia	Dubna (1)	p	1967	1996	124	
Sweden	Uppsala (1)	p	1957	1976	73	
Switzerland	Villigen PSI (SIN-Piotron)	π^-	1980	1993	503	
CA., USA	Berkeley 184	p	1954	1957	30	
CA., USA	Berkeley	He	1957	1992	2054	
CA., USA	Berkeley	ion	1975	1992	433	
IN., USA	Bloomington (MPRI, 1)	p	1993	1999	34	
MA., USA	Harvard	p	1961	2002	9116	
NM., USA	Los Alamos	π^-	1974	1982	230	
					13830	**Total**
				thereof	2054	He
					1100	pions
					433	ions
					10243	protons

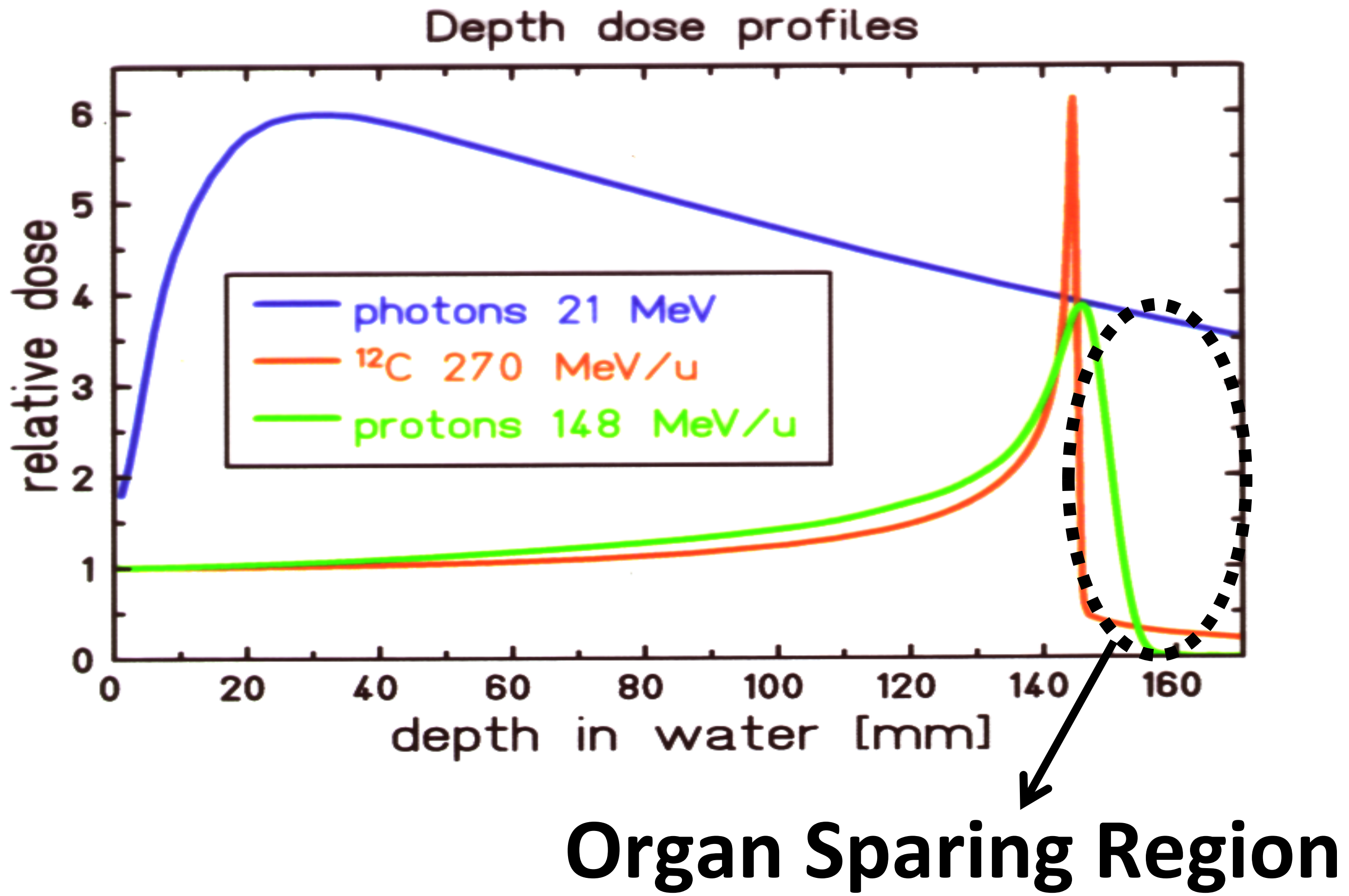
Historical overview 1990

- First hospital based proton therapy facility built in Loma Linda
- Treated more than 18000 patients



Why Particle Therapy?

"Bragg Peak"

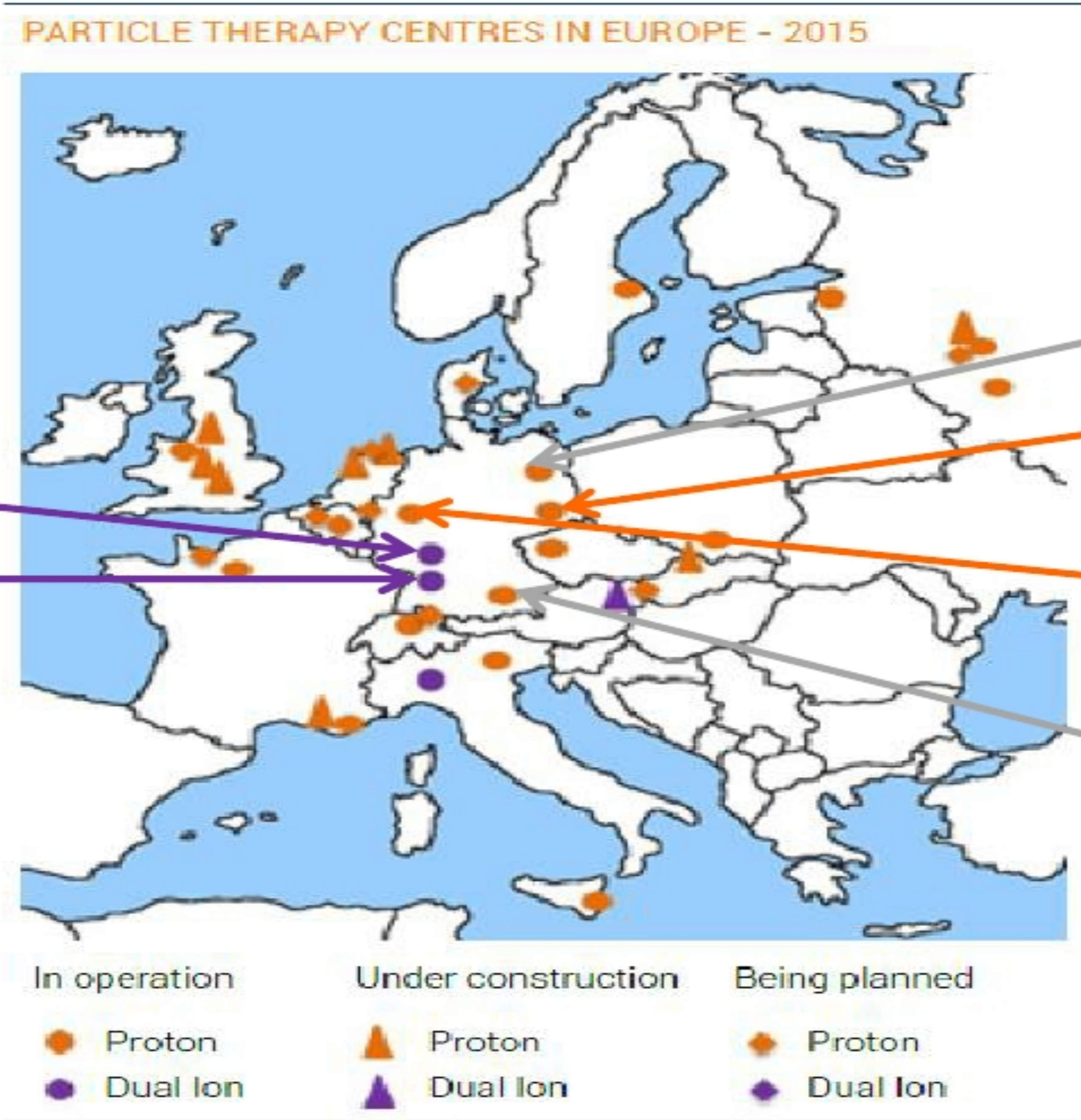


Protons and carbon ions

University Hospital Heidelberg

MIT Marburg

HIT Heidelberg



Protons

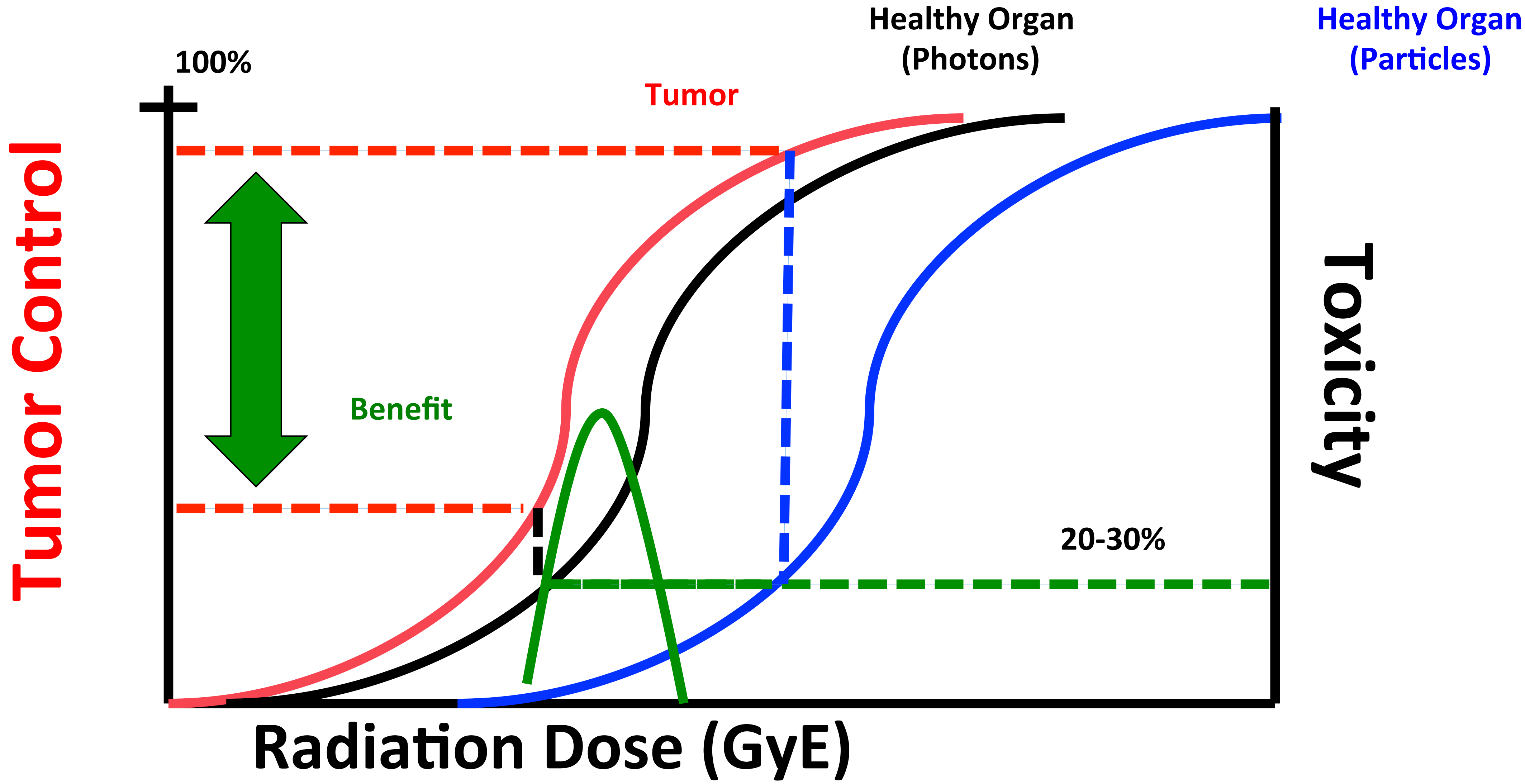
Charité / Helmholtz-Zentrum BerlinProtonen

University Hospital Dresden

University Hospital Essen/ WPE

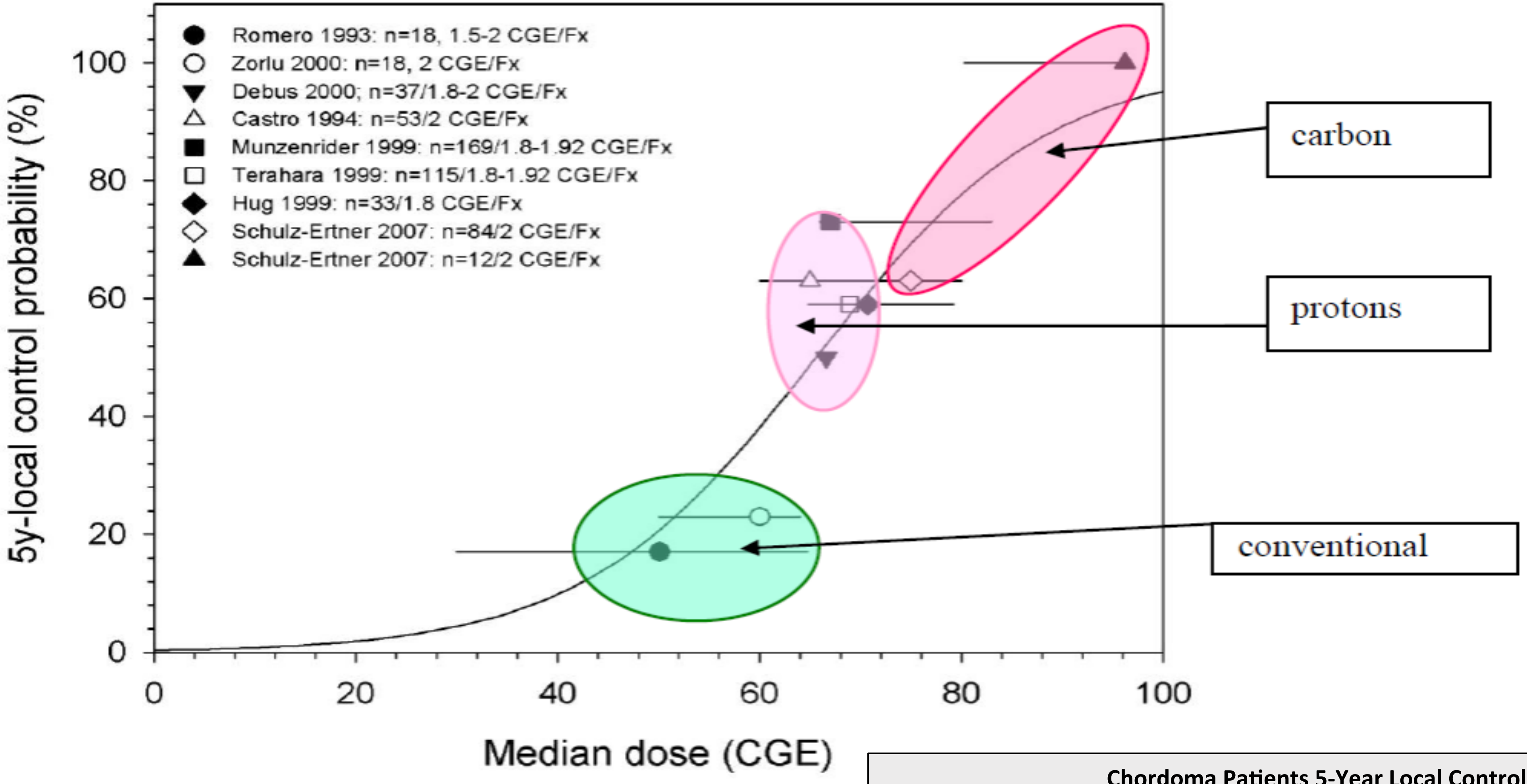
Rinecker Proton Therapy Center RPTC

Advantage of Particle Therapy



Advantage of Particle Therapy

GSI – Darmstadt/Heidelberg Hospital, Germany

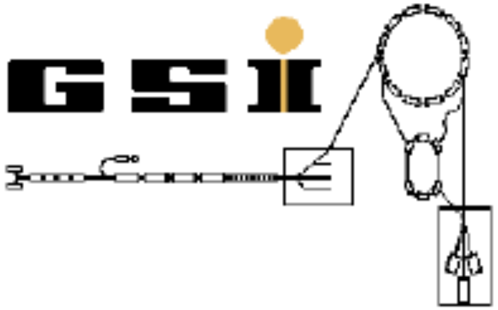


Chordoma Patients 5-Year Local Control
(source: Schulz-Ertner, Int J Radiat Oncol Biol Phys. 2007)

Historical overview

1997-2008

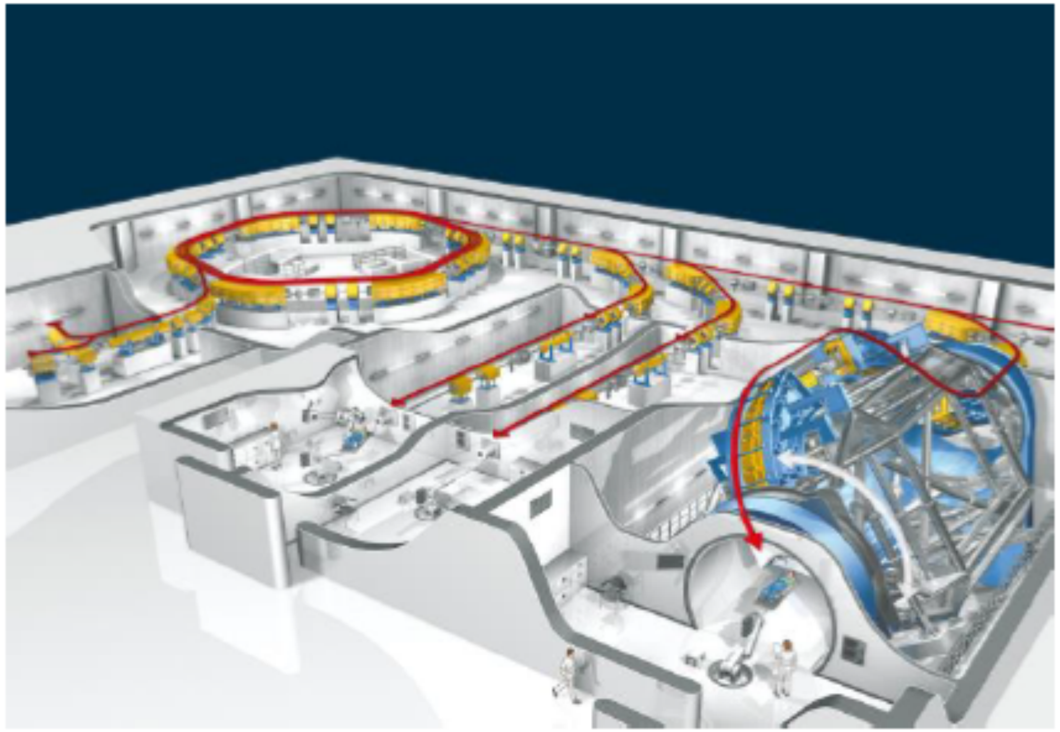
- Carbon ion project @ Gesellschaft für Schwerionenforschungs
- ~435 patients with scanning beam



Material courtesy of Prof. Oliver Jäkel

Historical overview 2009

- Start of clinical operation at Heidelberg Ion-Beam Therapy Center (HIT)



Heavy charged particle therapy patient statistics

	# Patients	Start	End	Notes
Helium	2054	1957	1992	In Berkley only, probably reinitiated in Heidelberg, Vienna
Pions	1100	1974	1994	In Los Alamos, Villingen (PSI), Vancouver (TRIUMF)
Carbon ions	19376	1994	-	First in Chiba
Protons	131240	1954	-	First in Berkley
Other	433	1975	1992	In Berkley only
Total	154203	1954	-	