Physics/Biology of Particle Therapy

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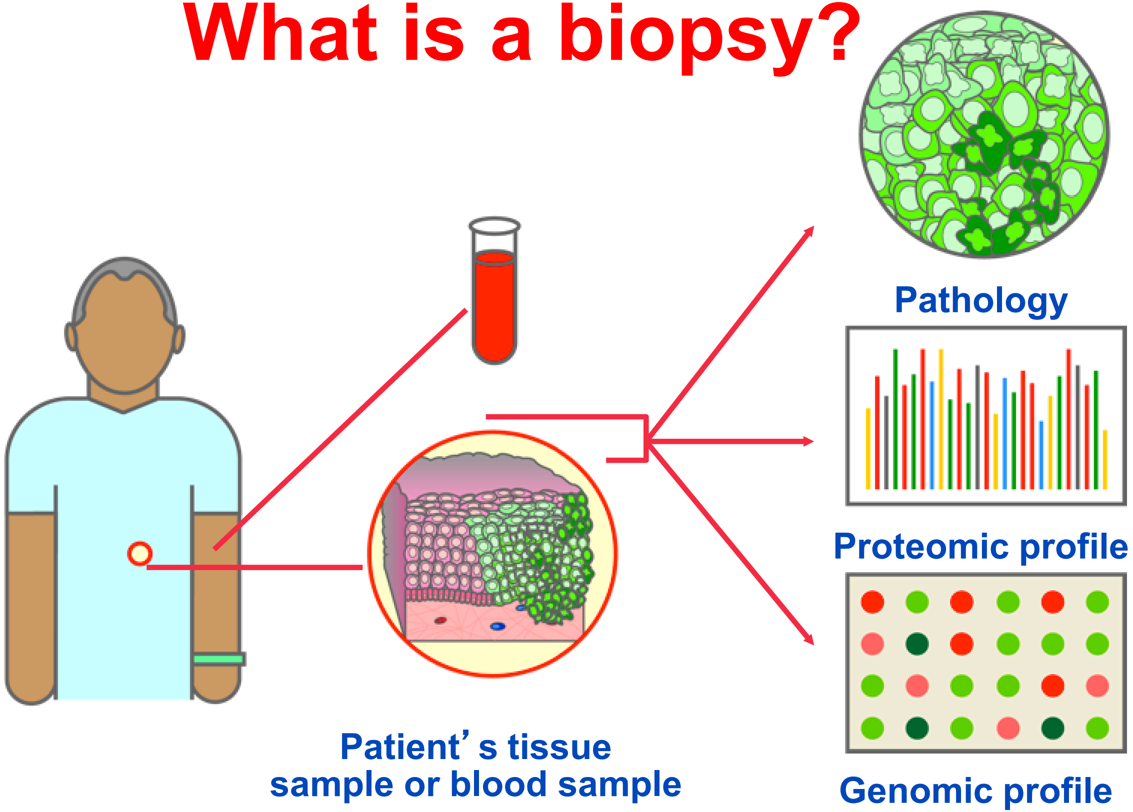
Questions are welcome at any time

How to Treat Cancer ....
With minimal side-effects

- Holy grail of oncology
- Identify characteristics that distinguish tumor cells from normal cells
- Design a Monotherapy that selectively ablates tumor cells

Let‘s start with Biology …

What is a biopsy?



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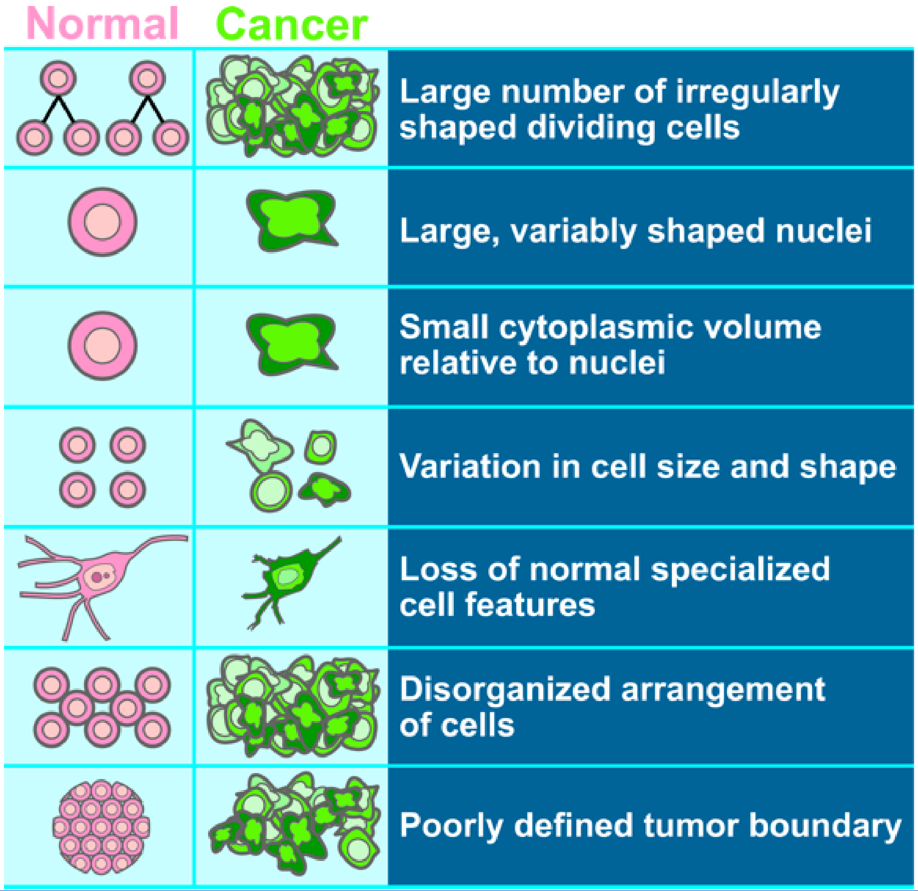
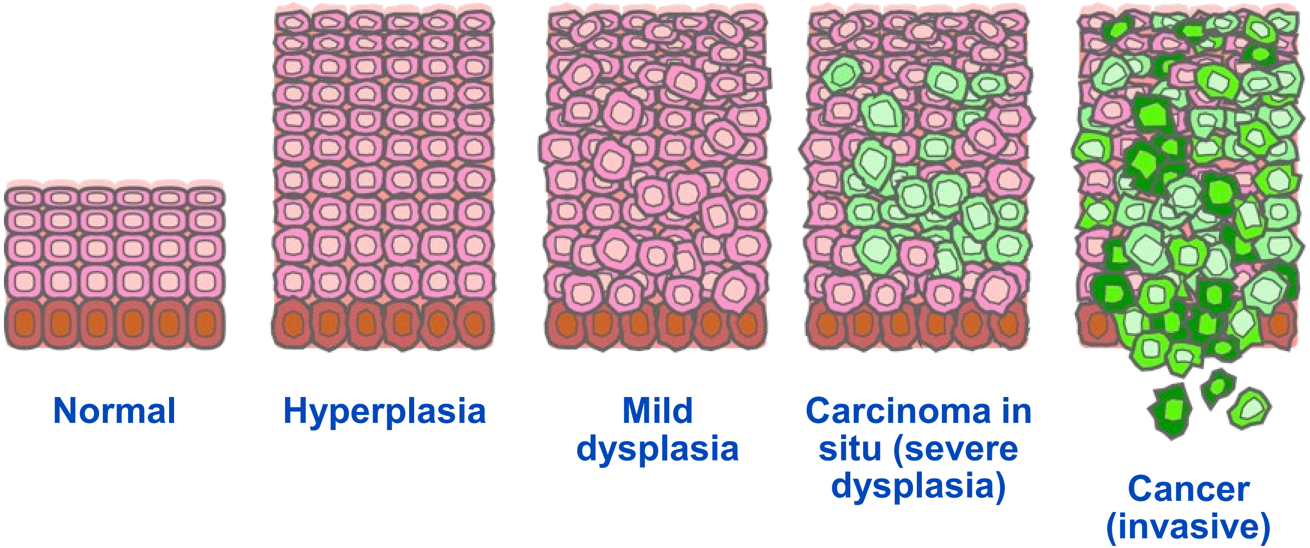
What does a pathologist look for in biopsy tissue?



Some more Biology…

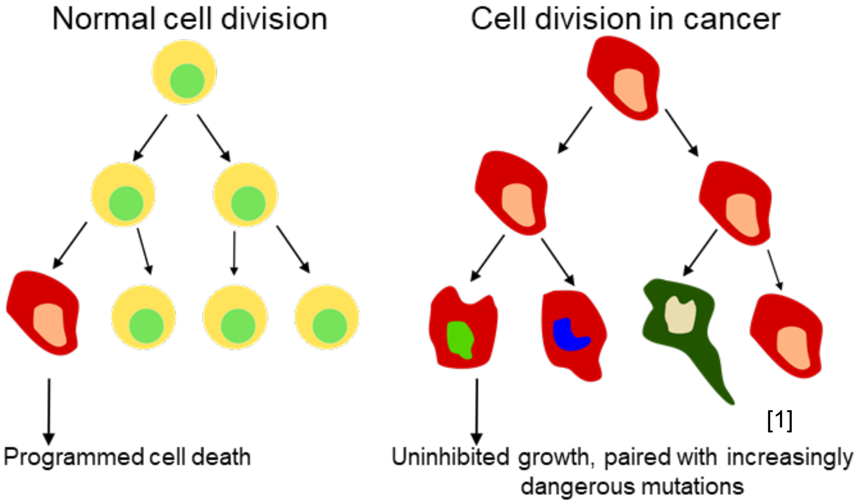
How does Cancer look like under the microscope?



What is Cancer ?

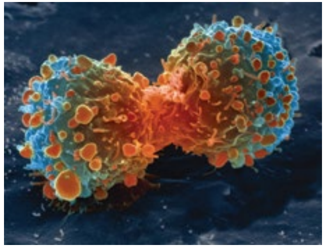
- is uncontrolled cell proliferation and cell rampant growth
- cancer may spread to other parts of the body
- over 100 different types, individual

healthy cells vs. cancer cells



[1]

Cancer cell of a lung tumor during cell proliferation



[2]

Theory of cancer formation:

(random) mutation levers out i.a. programmed cell death
→ cells need to be removed / killed "manually" for treatment

[1] Garak76, Suhadi Jorhaa'ir (https://commons.wikimedia.org/wiki/File:Zellteilung_normal_im_Gegensatz_zu_Krebs.svg), „Zellteilung normal im Gegensatz zu Krebs"
[2] fineartamerica - Lung Cancer Cell Division. - Accessed from https://fineartamerica.com/featured/lung-cancer-cell-division-sem-steve-gschmeissner.html?product=metal-print on 12.02.2021. Lettering was adapted.

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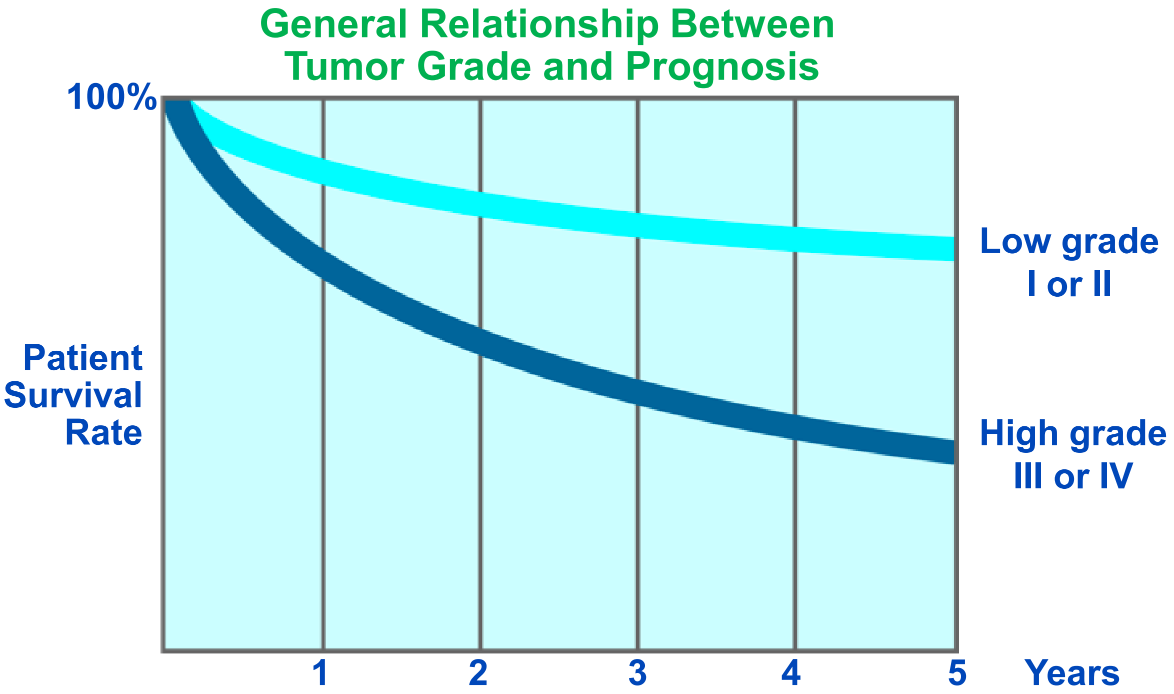
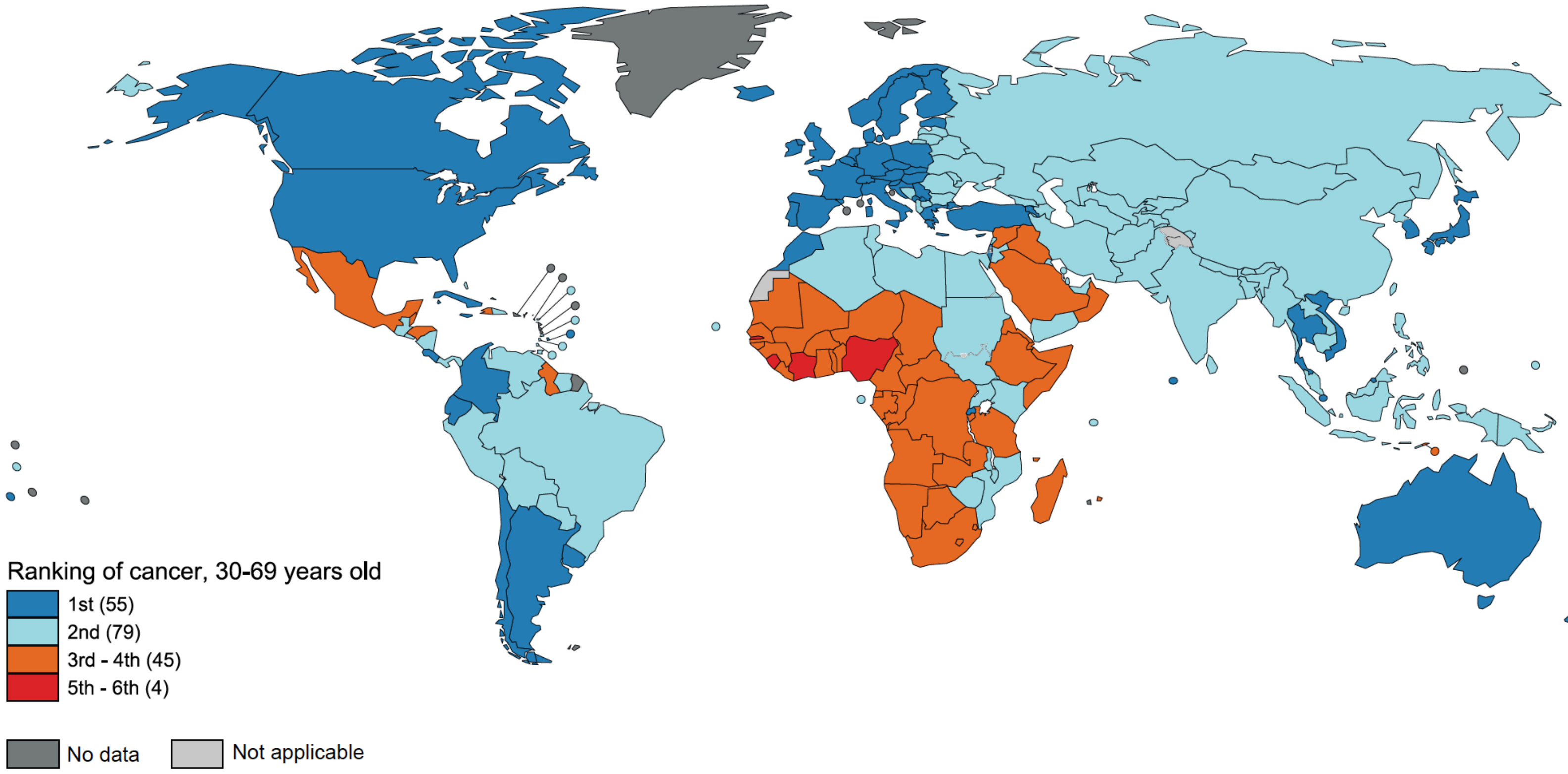
What is the relationship between tumor grade and patient survival?



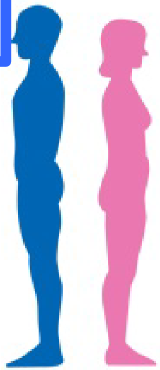
Cancer - incidence



[1] Stewart, B. W. K. P., and Christopher P. Wild. "World cancer report 2014." (2014).
[2] Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries
[3] RKI, Report on cancer in Germany for 2013/2014, cancer registry data
[4] RKI, Report on cancer in Germany for 2015/2016, cancer registry data

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%**

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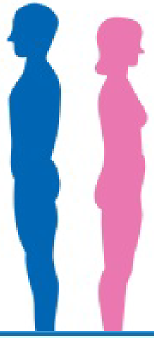
2017 Cancer Deaths

Estimated New Cases



Males			Females		
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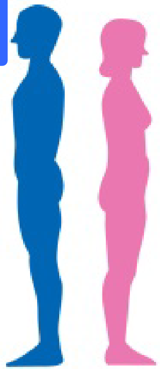
Estimated Deaths



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%**

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Hallmark of Cancer

“Warburg Effect”

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Adequate oxygen

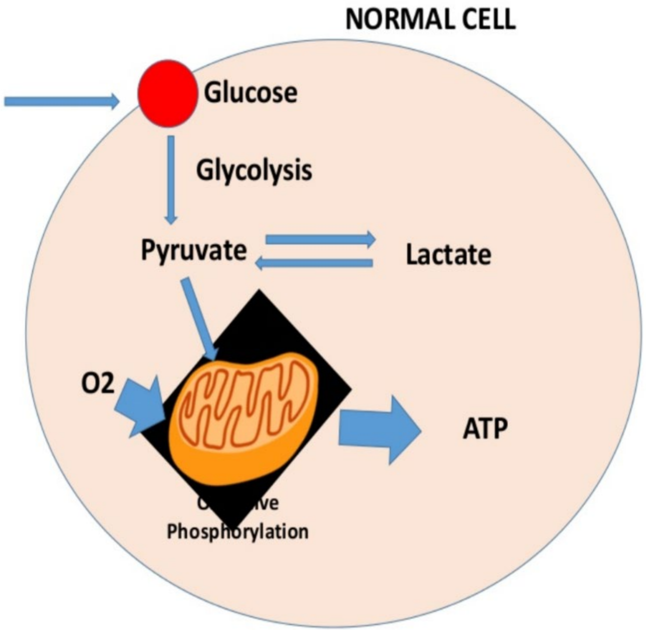
ATP is generated by Oxidative Phosphoryation

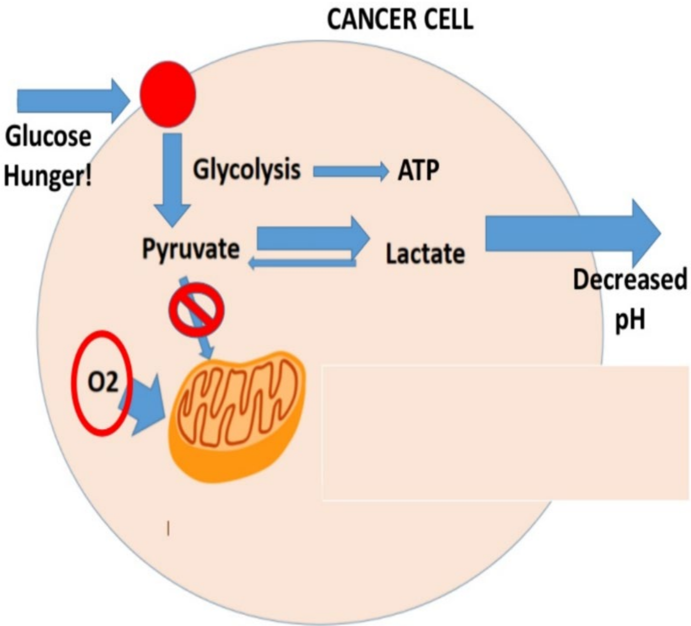
As Oxygen Decreases

Shift from Oxidative phosphorylation to **Glycolysis**

Anaerobic glycolysis

PASTEUR EFFECT





Early 20th Century

Otto Heinrich Warburg
German Physiologist

Observed that cancer cells had increased rates of glycolysis

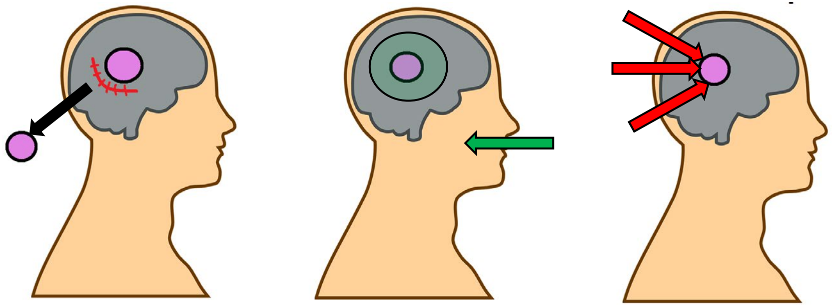
Despite the availability of adequate oxygen levels

Aerobic glycolysis

WARBURG EFFECT

Why do cancer cells activate glycolysis despite the presence of oxygen?

Treatment options



surgery	chemotherapy	radiotherapy
cancer cells are removed	administration of drugs	ionizing radiation

Ionizing radiation:
- External radiotherapy
  - electromagnetic radiation
  - particle radiation
- Internal radiotherapy
  - brachytherapy

Goal:

1. CURE leads survival
2. PALLIATIVE leads better quality of life

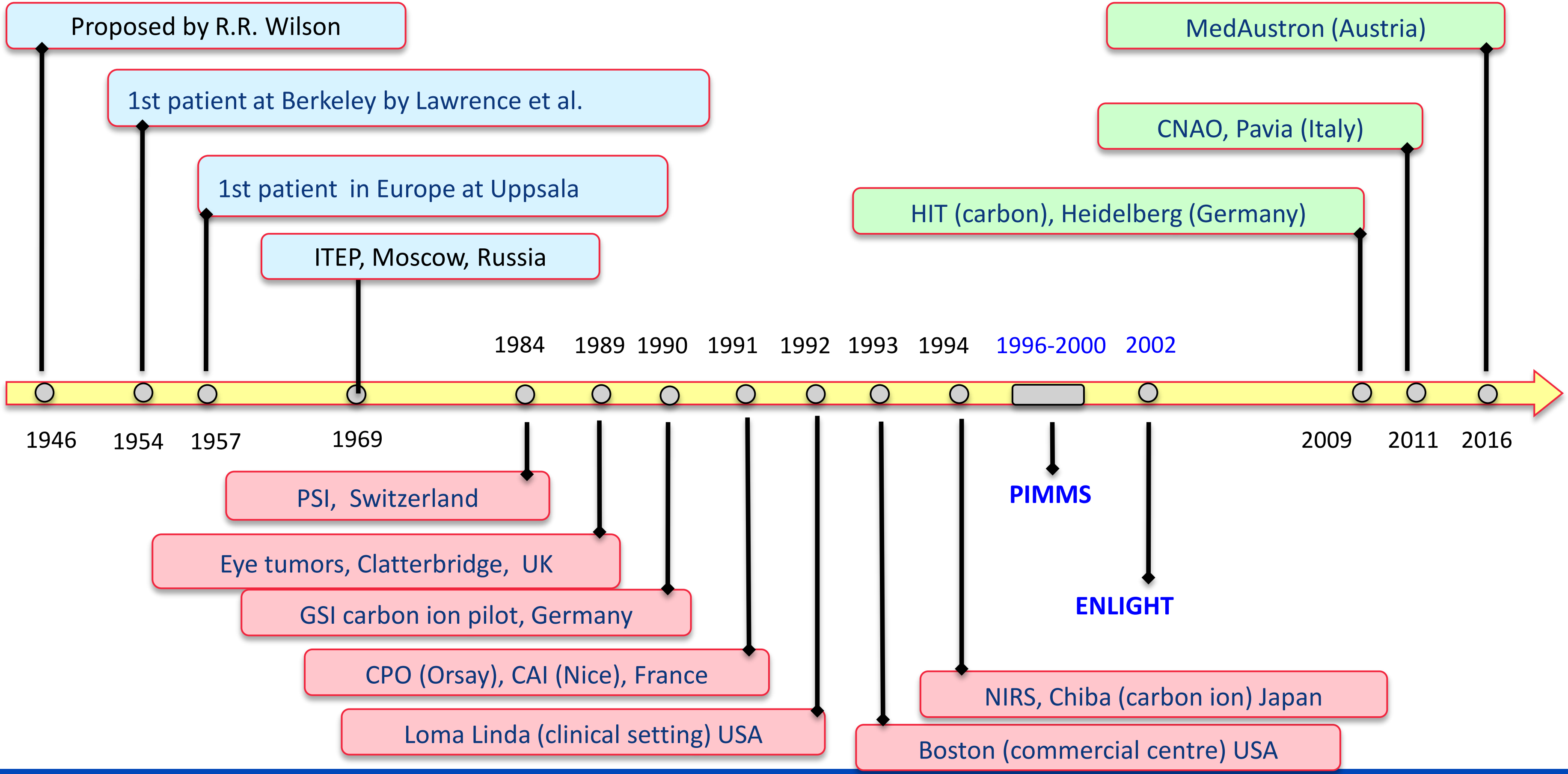
Chances of survival:

60% of all cancer patients survive more than **5** years [1]

- **10**-year prognosis **<1%** pancreatic cancer
- **10**-year prognosis **~84%** prostate cancer

[1] A joint publication of the Robert Koch Institute and the German Cancer Associations (Gesellschaft der epidemiologischen Krebsregister in Deutschland e. V.), 11th issue, 2017, accessed on 20.11.2018

History of particle therapy



Radiation
From Small amounts
to
Large Amounts

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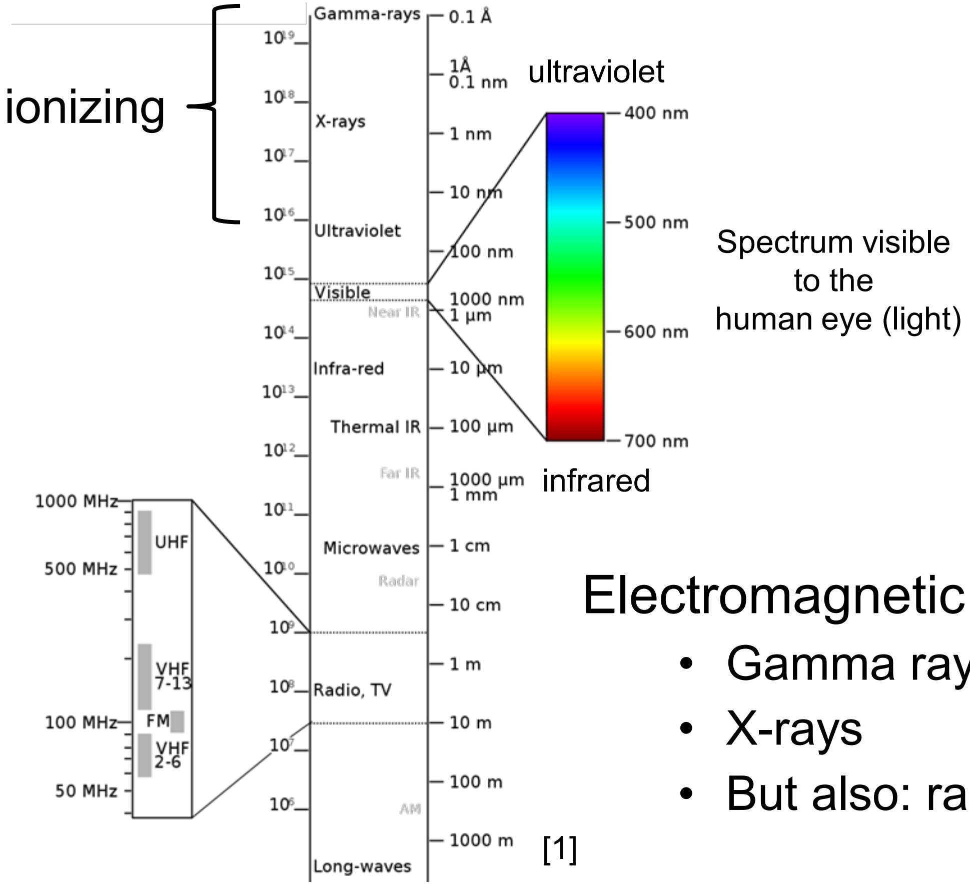
Natural radiation



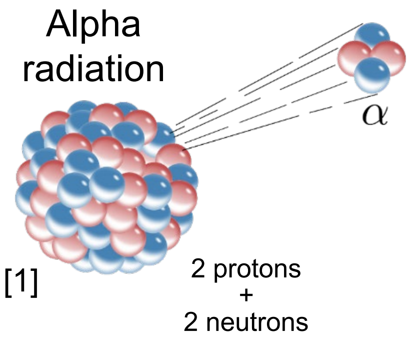
Electromagnetic radiation - **Photons**

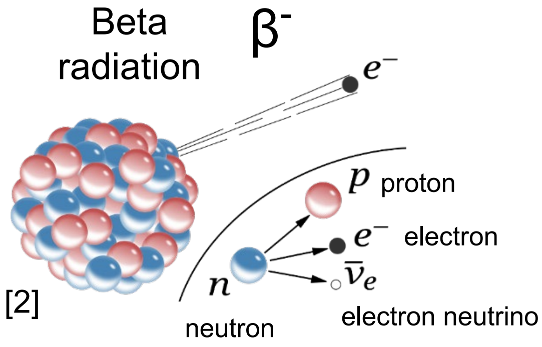
- Gamma rays
- X-rays
- But also: radio, light, microwaves, etc.

[1] !Original: PenubagVector: Victor Blacus (https://commons.wikimedia.org/wiki/File:Electromagnetic-Spectrum.svg), „Electromagnetic-Spectrum“, https://creativecommons.org/licenses/by-sa/3.0/legalcode

Natural radiation

- Particle radiation
  - Alpha radiation – helium nuclei
  - Beta radiation – electrons/positrons
  - Other nuclei/ions (e.g. cosmic radiation)





Types of radioactive decay

Type	Nuclear equation	Representation	Change in mass/atomic numbers
Alpha decay	^A_ZX $^4_2He + ^{A-4}_{Z-2}Y$		A: decrease by 4 Z: decrease by 2
Beta decay	^A_ZX $^0_{-1}e + {}_{Z+1}^{A}Y$		A: unchanged Z: increase by 1
Gamma decay	^A_ZX $^0_0\gamma + ^A_ZY$	γ Excited nuclear state	A: unchanged Z: unchanged
Positron emission	^A_ZX $^0_{+1}e + {}_{Y-1}^{A}Y$		A: unchanged Z: decrease by 1
Electron capture	^A_ZX $^0_{-1}e + {}_{Y-1}^{A}Y$	X-ray	A: unchanged Z: decrease by 1

[3]

[1] Inductiveload (https://commons.wikimedia.org/wiki/File:Alpha_Decay.svg), „Alpha Decay“, marked as public domain, more details on Wikimedia Commons: https://commons.wikimedia.org/wiki/Template:PD-self
[2] Inductiveload (https://commons.wikimedia.org/wiki/File:Beta-minus_Decay.svg), „Beta-minus Decay“, marked as public domain, more details on Wikimedia Commons: https://commons.wikimedia.org/wiki/Template:PD-self
[3] openstax CNX – Radioactive Decay. Accessed from https://cnx.org/contents/IbTLTDQM@1.6:RSq8dk2S@1/Radioactive-Decay on 12.02.2021

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Radiation exposure in everyday life

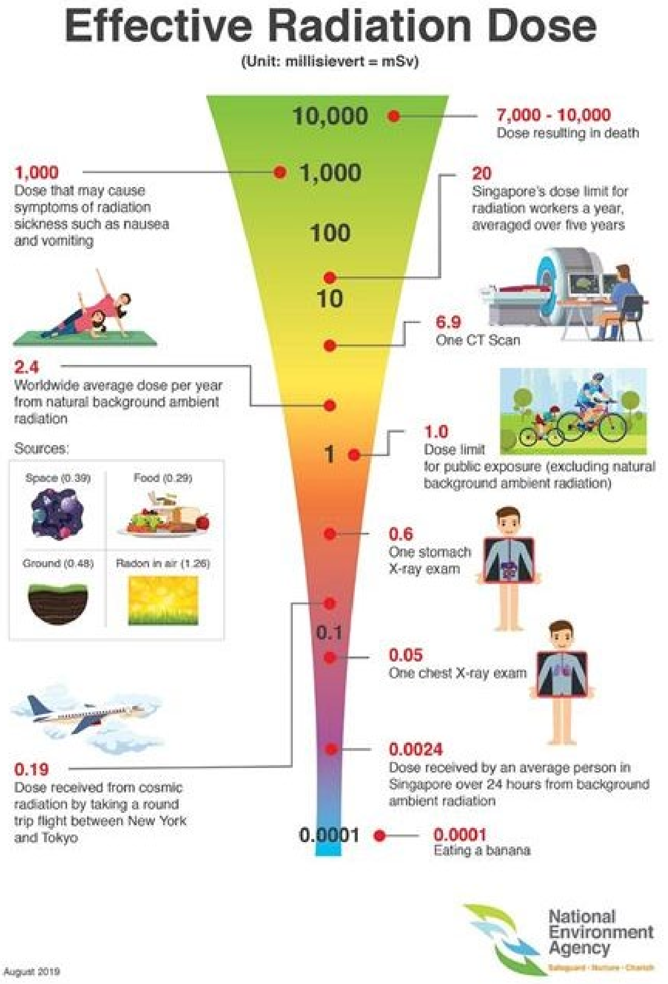
- Generally known: body dose

- given and measured in Sievert
- considers the sensitivity of the respective organ and radiation type
- cosmic and terrestrial radiation
- medical and technical applications
- diverse loads (e.g. flight travels)

Banana equivalent dose:

0.4 gram potassium consists to
0.01% of the radioactive potassium isotope K-40
1000 bananas in 8 hours → 0.1 mSv

Average dose: 4 mSv per year



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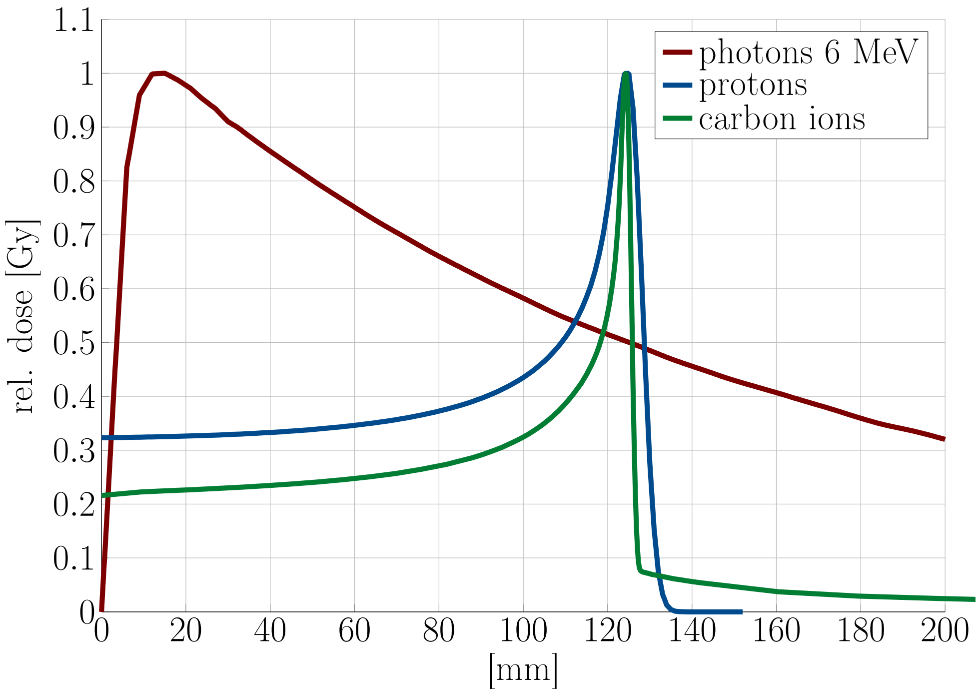
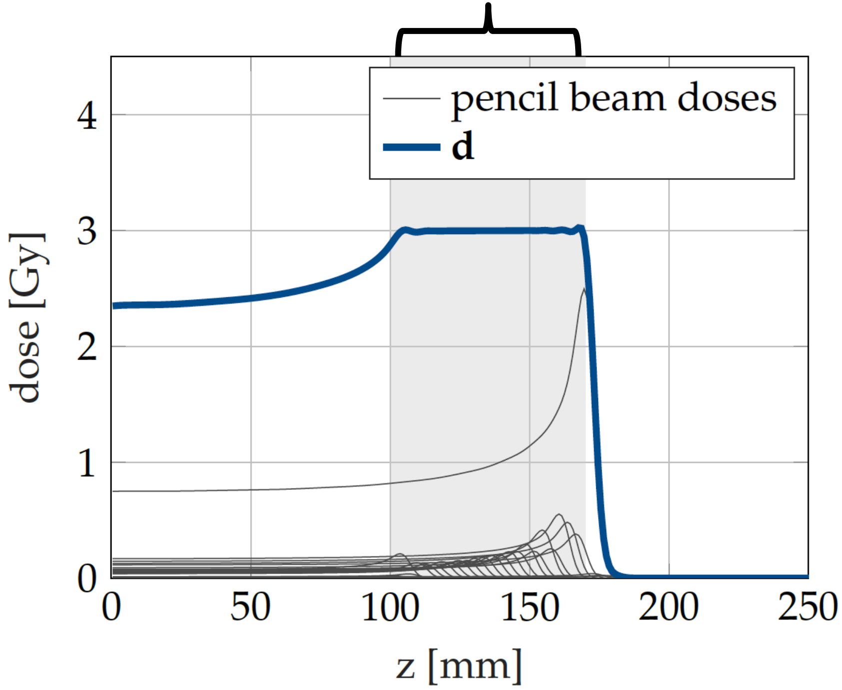
Why bother with particle therapy?



penetration depth

cancerous region



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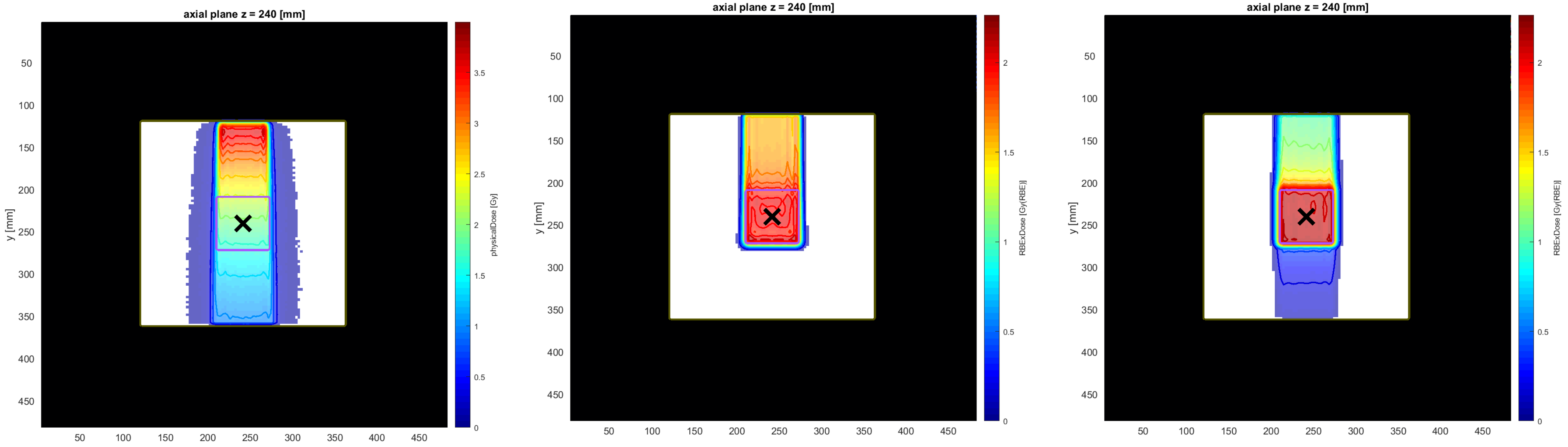
Why bother with particle therapy?

- We always risk damaging healthy tissue “on the way”...

photons

protons

carbon ions



.... but it looks quite good for a particle beam ☺

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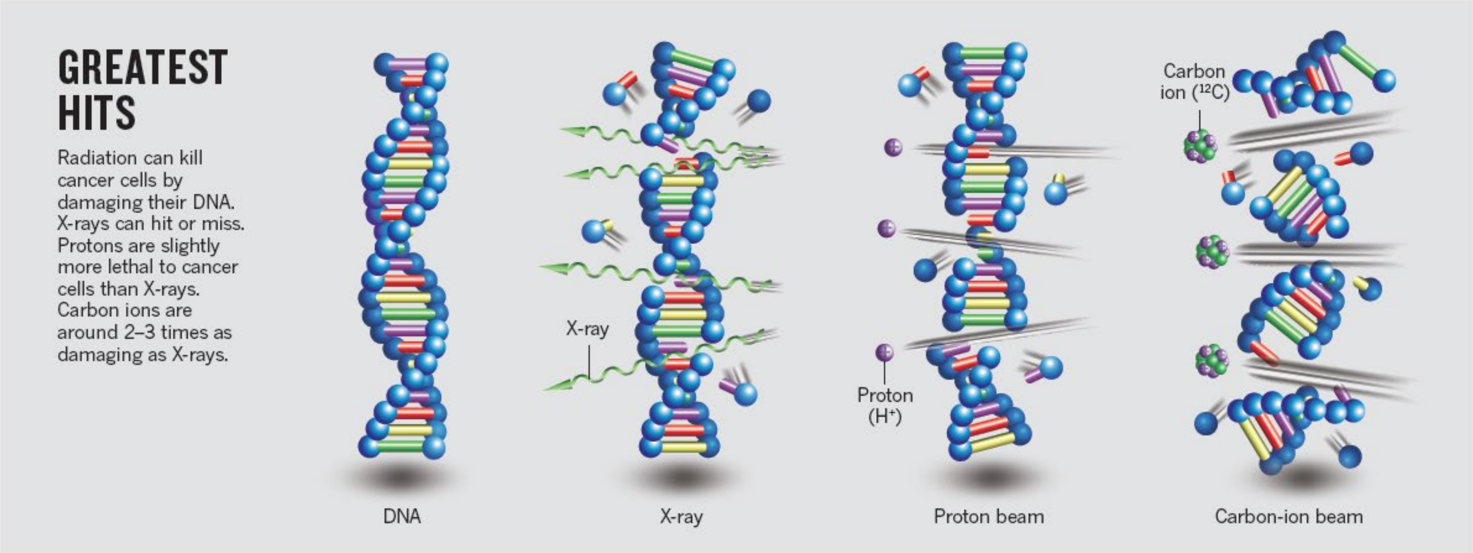
Why bother with carbon ions?

photons protons carbon ions



[1]

- Energy release is **localized** to a varying extent. ^{12}C is 12 times heavier than p^+
- Heavy ions generate locally more severe damage → more difficult to repair

[1] Marx, V. (2014, April 4). Sharp shooters. 508. Nature, p. 137.

Summary

- cancer diseases are characterized by uncontrolled growth of mutated cells
- radiation transfers energy to the tissue in form of elementary physical interactions
  → radiation dose
- energy release ionizes the tissue
  - → breaks down chemical bounds or forms new ones
  - → DNA damage
  - → cell death
- by artificially generating radiation, we can combat cancer cells in a targeted manner
- not without risk for the healthy tissue

→ but high conformity when applying particle beams

- **Questions?**

[1]

GOT IT?

[1] Gage Skidmore from Peoria, AZ, United States of America (https://commons.wikimedia.org/wiki/File:Captain_Jack_Sparrow_(5763467649).jpg), „Captain Jack Sparrow (5763467649)“, https://creativecommons.org/licenses/by-sa/2.0/legalcode

Cancer - incidence

Cancer incidence worldwide

14 million new cases of cancer in **2012** [1]

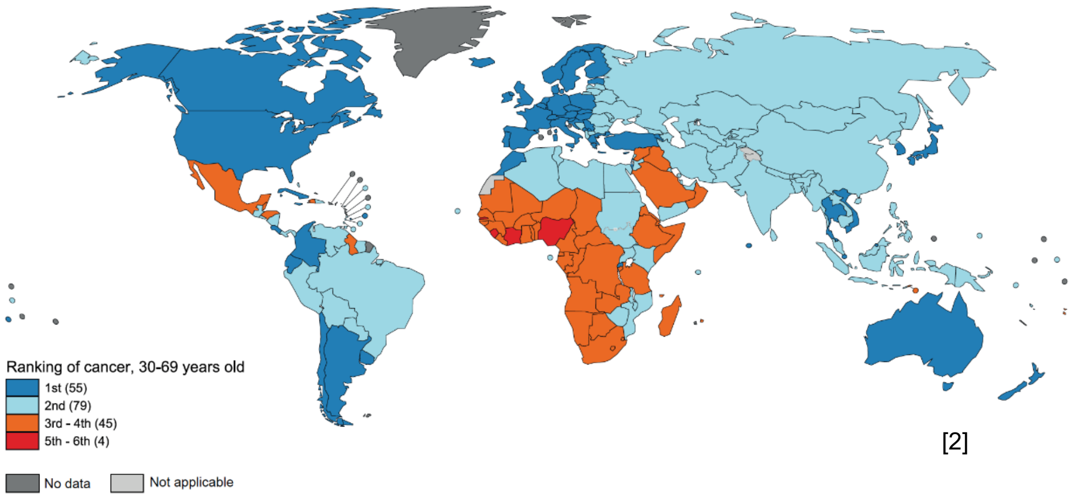
8 million deaths due to cancer in **2012** [1]

19 million new cases of cancer in **2020** [2]

10 million deaths due to cancer in **2020** [2]

2.3 million deaths linked to corona

28.4 million new cases of cancer in **2040** [2]
How many deaths in 2040?



[2]

Dark blue: Cancer is the leading cause of premature death

Cancer incidence national

- **500 000** new cases of cancer in Germany every year [3,4], 2.5 times the population of Mainz
- rising tendency due, among other things, to demographic developments

[1] Stewart, B. W. K. P., and Christopher P. Wild. "World cancer report 2014." (2014).
[2] Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries
[3] RKI, Report on cancer in Germany for 2013/2014, cancer registry data
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