Universitätsklinikum Hamburg-Eppendorf, Onkologisches Zentrum
Ambulanzzentrum des UKE GmbH, Bereich Strahlentherapie

Symposium on Quantum Science 2025 / Universität Hamburg & Osaka University

Current challenges in radiation therapy

Th. Frenzel

Universitätsklinikum Hamburg-Eppendorf

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Topics

- **Fundamental basics of radiation therapy**
  - Radiation biology
  - Radiation physics
  - Field setup
  - Tumor imaging
- **Flash radiotherapy**

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Fundamental basics of radiation therapy: Biology

- **Cancer is one of the most frequent reasons for death in humans in Germany**
  (https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Gesundheit/Todesursachen/_inhalt.html)
  - 348 312 Heart / blood circulation problems
  - 230 292 Cancer
  - 72 502 Deseases of the respiratory system
- **50% of all cancer patients who are cured received radiotherapy**
- **90% of cancer death are related to metastasis formation and not to the primary tumor**

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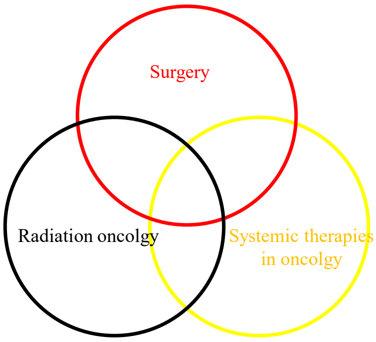
Therapeutic options



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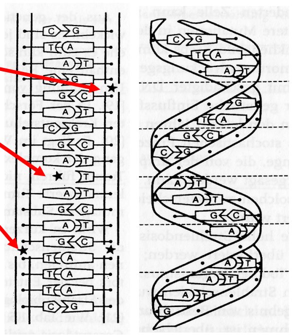
Primary target for radiation therapy is the DNA

- Single-strand break
- Base deletion
- Double-strand break



Enzymes for DNA repair

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Phases of radiation damage

- Physical phase: immediately (ionization)
- Chemical phase: changes in molecules
- Biological phase: early and late responses to radiation therapy

Consequences of radiation damage

- Cell alteration
- Cell death
- Cancer development

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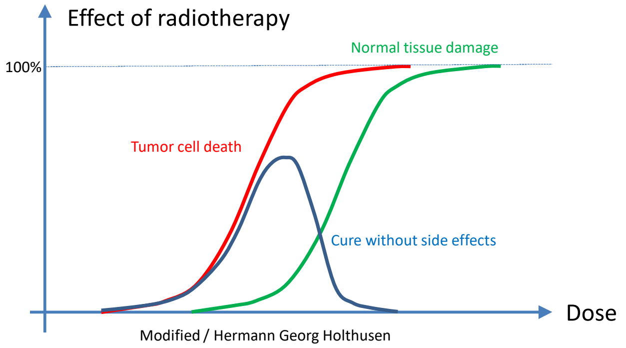
Fundamental problem: Cell alteration



Modified / Hermann Georg Holthusen

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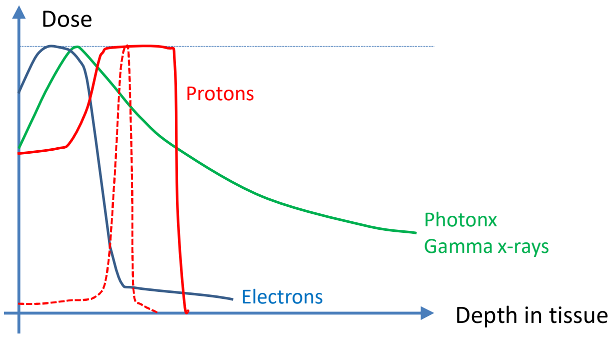
Radiation physics: Depth dose curves



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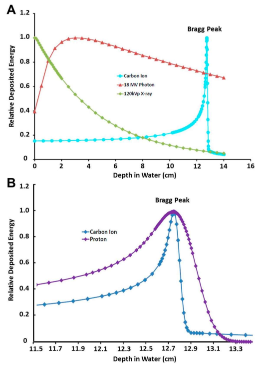
Charged particles in radiotherapy - I



- Increase of energy deposition in a given depth (energy dependent): Bragg peak
- Rapid decrease of energy deposition after Bragg peak
- Nuclear reactions: “dose tail” beyond Bragg peak for heavier particles

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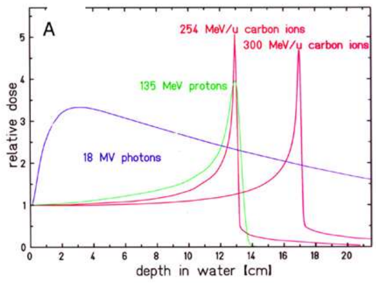
UKE HAMBURG

Energy straggling in radiotherapy



For particles with same range:
C-ions show less straggling than protons → sharper dose gradient after Bragg peak

(BUT: nuclear fragments deposits additional dose after Bragg peak)

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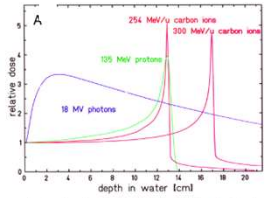
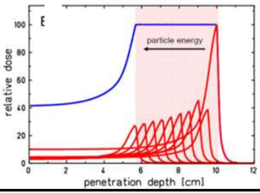
Consequences for radiotherapy- I





Charged particles need to be accelerated to about 150-430 MeV/u to reach depths of 15-30 cm in tissue.

→ $\beta \approx 0.6$-0.7

For clinical applications: need to "expand" Bragg peak → "spread out Bragg peak" (SOBP)

Ratio "plateau to peak" larger for C-ions (← lower "straggling")

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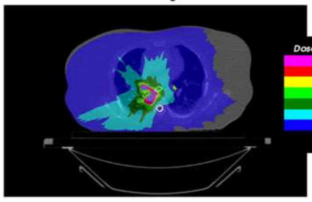
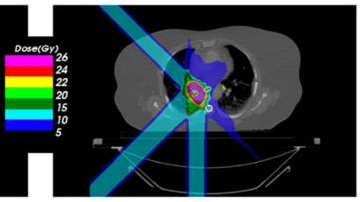
Consequences for radiotherapy- II

X-rays C-ions

Photons must be "cross-fired" from many directions – only a few fields needed when using protons and C-ions

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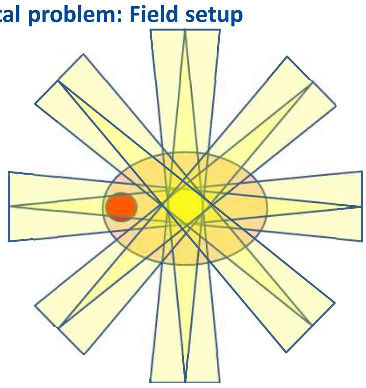
Fundamental problem: Field setup



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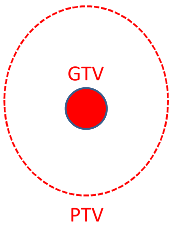
From 3D-konformal radiotherapy to stereotactical treatments

- **Superpositon of multiple fields**
  - Steep dose gradients
- **Small security margins**
  - Goal: PTV = GTV
  - Exact tumor localization
  - Differentiation from healty tissue
  - Motion management
- **„Optimal“ tumor imaging**



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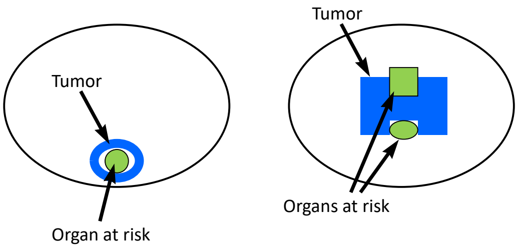
Fundamental problem: Tumor <-> Organs at risk



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3D-conformale radiotherapy

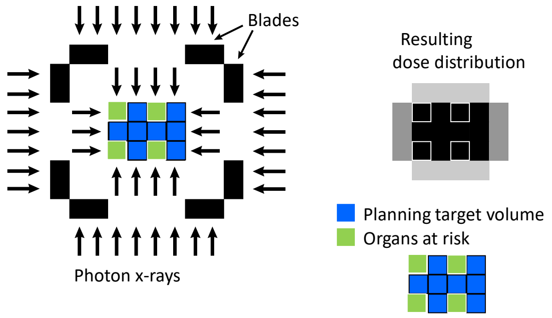

Image modified from: Carol MP. Where we are today. In: Sternick ES (Hrsg.) *The theory and practice of intensity modulated radiation therapy*. Madison: Advanced Medical Publishing, 1997

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Fluenzmodulierte Strahlenbehandlung (IMRT)

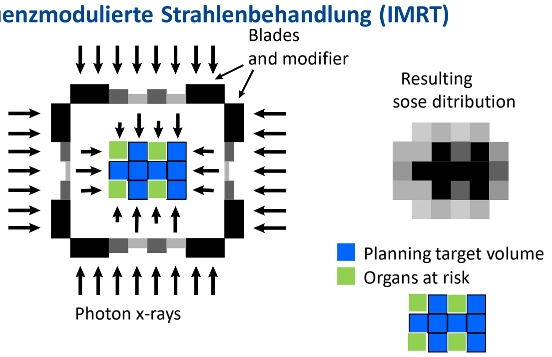

Image modified from: Carol MP. Where we are today. In: Sternick ES (Hrsg.) *The theory and practice of intensity modulated radiation therapy*. Madison: Advanced Medical Publishing, 1997

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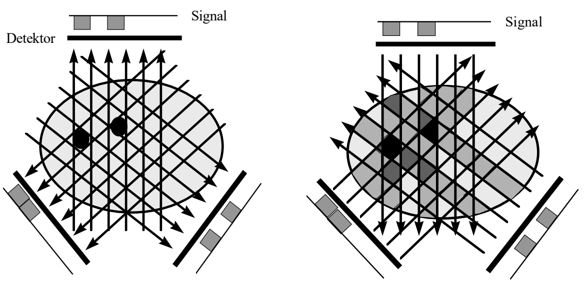
Inverse back projection



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Rosenman. Treatmentplanning for IMRT. In: Sternick ES (Hrsg.) *The theory and practice of intensity modulated radiation therapy*. Madison: Advanced Medical Publishing, 1997

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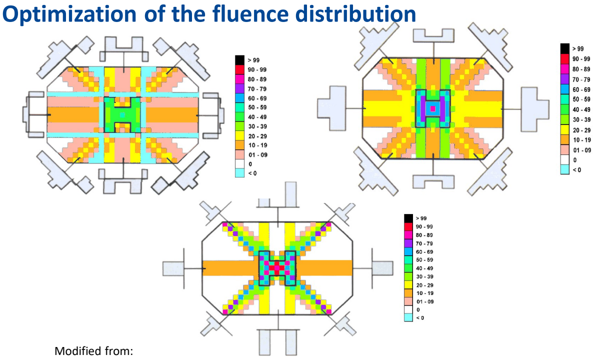
Optimization of the fluence distribution



Modified from:
Rosenman. Treatmentplanning for IMRT. In: Sternick ES (Hrsg.) *The theory and practice of intensity modulated radiation therapy*. Madison: Advanced Medical Publishing, 1997

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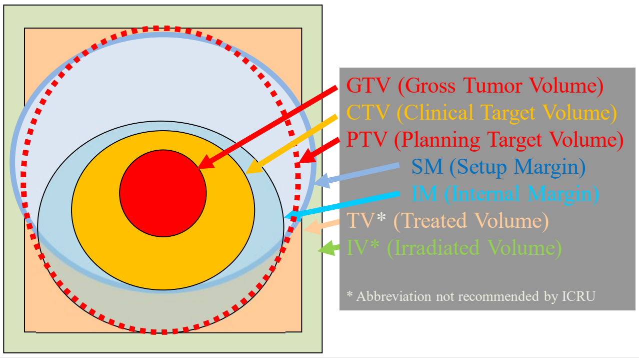
Tumor imaging: Target volume delineation



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Problems in tumor imaging

- **Spatial resolution: Single tumor cells not visible**
  - Microscopic spread enhances the target volume
- **Soft tissue contrast**
  - „Border“ between healthy tissue and tumor tissue
- **Organ movement**
  - E.g. respiration, bladder and rectum filling
- **Tumor changes during therapy**

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Imaging options at clinical accelerators (Varian TrueBeam STX powered by Novalis)

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Automated positioning control

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6D treatment coach

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BrainLab ExacTrac

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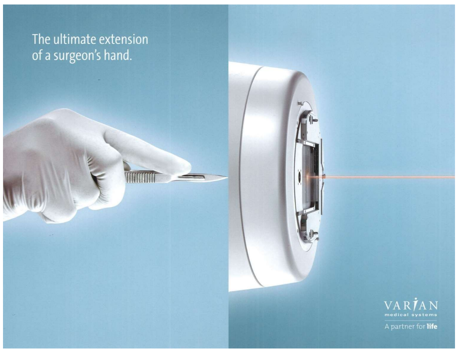
Beam shaping within 1 mm accuracy



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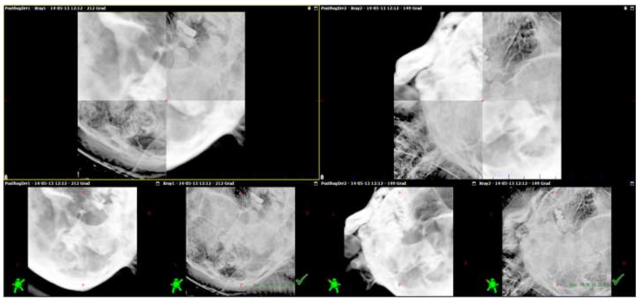
Example: Brain tumors / metastases



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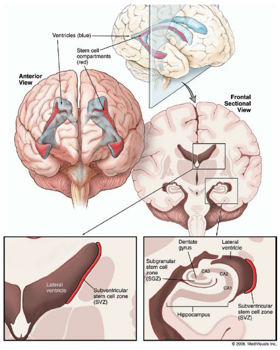
Saving neuronal stem cells



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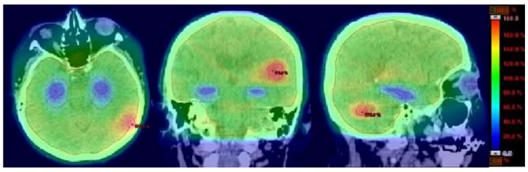
Hippocampal dose reduction



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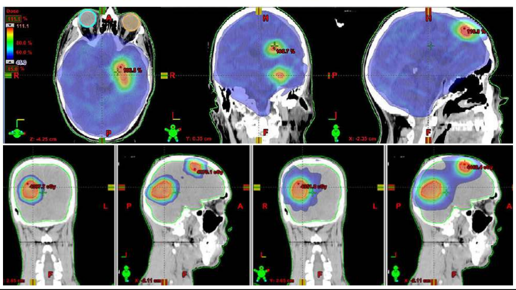
Simultaneously integrated boost

WHOLE-BRAIN RADIOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST TO MULTIPLE BRAIN METASTASES USING VOLUMETRIC MODULATED ARC THERAPY

FRANK J. LAGERWAARD, M.D., PH.D., ELLES A. P. VAN DER HOORN, WILKO F. A. R. VERBAKEL, PH.D., CORNELIS J. A. HAASBEEK, M.D., BEN J. SLOTMAN, M.D., PH.D., AND SURESH SENAN, M.R.C.P., F.R.C.R., PH.D.



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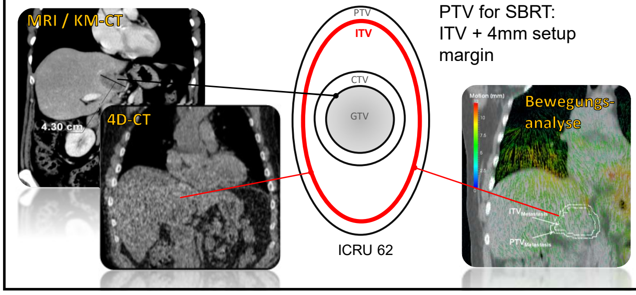
Organ motion management for liver metastases

- Example: 61 years old woman with solitary metastas (surgery no option)
- 3 gold markers surrounding the liver leasion
- 4D CT-Scan for analysis of organ motion



PTV for SBRT:
ITV + 4mm setup margin

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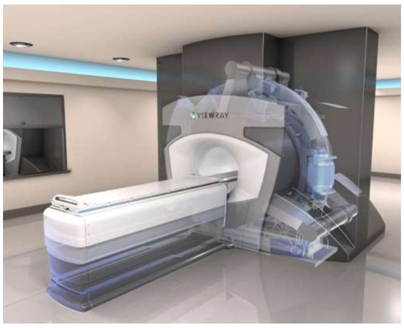
MR guided radiotherapy (ViewRay)



Quelle: www.viewray.com

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MR guided treatment planning

Quelle: www.viewray.com

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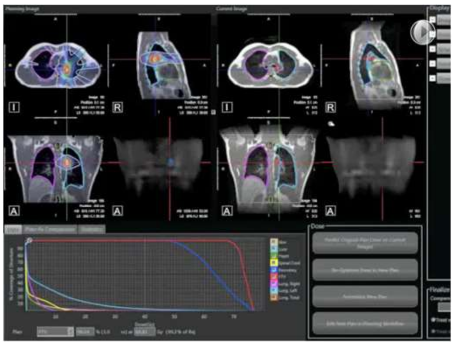
MR guided treatment planning



Quelle: www.viewray.com

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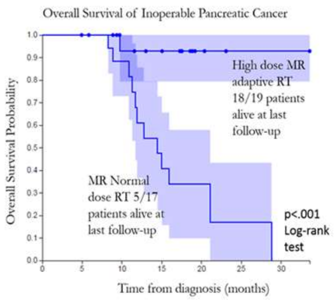
Extremely Preliminary ~Phase I Data

SITEMAN CANCER CENTER



Barnes-Jewish Hospital • Washington University School of Medicine • National Cancer Institute • National Comprehensive Cancer Network

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Topics

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  - Field setup
  - Tumor imaging
- **Flash radiotherapy**

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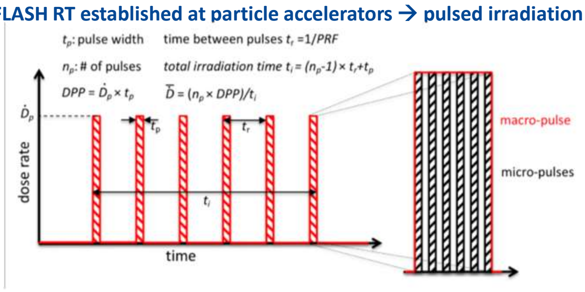
Ultra-high dose rate vs. conventional radiotherapy
FLASH RT established at particle accelerators → pulsed irradiation



Source: Nolan Esplen et al 2020 Phys. Med. Biol. 65 23TR03

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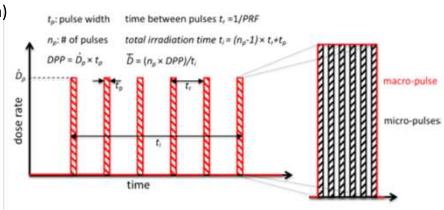
Ultra-high dose rate vs. conventional radiotherapy

Conventional irradiation (e.g., TrueBeam, 6X, 600 MU/min):

$DPP \approx$ 0.3 mGy
$t_p \approx$ 5 µs
$\dot{D}_p = \frac{DPP}{t_p} \approx$ 60 Gy/s
$PRF \approx$ 360 Hz
$\bar{D} \approx$ 0.1 Gy/s (6 Gy/min)



Source: Nolan Esplen et al 2020 Phys. Med. Biol. 65 23TR03

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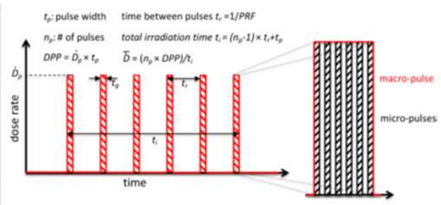
Ultra-high dose rate vs. conventional radiotherapy

UHDR irradiation for FLASH effect:

$DPP > 1$ **Gy**
$t_p \approx$ **1 fs – 1 µs**
$\dot{D}_p$ **> 10^4 Gy/s**
$\bar{D}$ **> 40 Gy/s**



Source: Nolan Esplen et al 2020 Phys. Med. Biol. 65 23TR03

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Rationale ultra-high dose rate (FLASH) radiotherapy

Benefits of UHDR (FLASH) irradiation:

- Kill tumours while providing better protection for normal tissues and preventing side effects → FLASH effect

FLASH effect seems to depend on:

- Dose rate per pulse
- # of pulses & their width
- Frequency
- Total irradiation time

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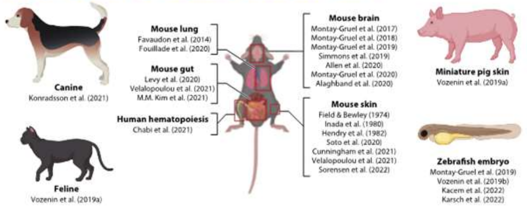
Large evidence of normal tissue sparing



Source: C.L. Limoli & M.-C. Vozenin, Annu. Rev. Cancer Biol. (2023)

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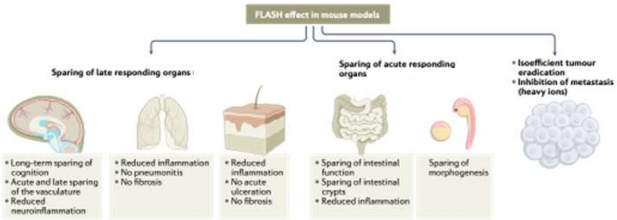
Large evidence of normal tissue sparing



Source: M.-C. Vozenin et al. Nature Reviews Clinical Oncology (2022)

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Ambulanzzentrum des UKE GmbH, Bereich Strahlentherapie

Universitätsklinikum Hamburg-Eppendorf
Ambulanzzentrum des UKE GmbH
Bereich Strahlentherapie
Martinistraße 52
D-20246 Hamburg

Universitätsklinikum Hamburg-Eppendorf
Onkologisches Zentrum
Klinik für Strahlentherapie und Radioonkologie
Labor für Strahlenbiologie
Martinistraße 52
D-20246 Hamburg

Priv.-Doz. Dr. rer. nat. Dr. med. Thorsten Frenzel
Facharzt für Strahlentherapie

Priv.-Doz. Dr. rer. nat. Dr. med. Thorsten Frenzel
Oberarzt und Medizinphysik-Experte

Telefon: +49 (0) 40 7410-54031
Telefax: +49 (0) 40 7410-52846
frenzel@uke.uni-hamburg.de
www.uke.de

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