

Section for Biomedical Physics
University Hospital for Radiation Oncology

Image-guided radiotherapy for cancer treatment

Recent developments and future innovations

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EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN



Comprehensive
Cancer Center
Tübingen - Stuttgart



**Universitätsklinikum
Tübingen**

Conflicts of Interest

Institutional collaborations with the following companies:

- Elekta AB
- Philips
- Siemens
- PTW Freiburg
- Therapanacea
- Kaiku Health
- Dr. Sennewald
- Brainlab



ZI 736/2-1
PAK 997/1
PAK 997/2



Contents

1. Cancer treatments using radiotherapy
2. Radiotherapy optimization
3. Image-guided radiotherapy: current concepts and technologies
4. Online adaptive image-guided radiotherapy
5. Real-time radiotherapy interventions
6. Functional imaging-/ biology-guided radiotherapy
7. Summary



The role of radiation therapy for cancer treatment

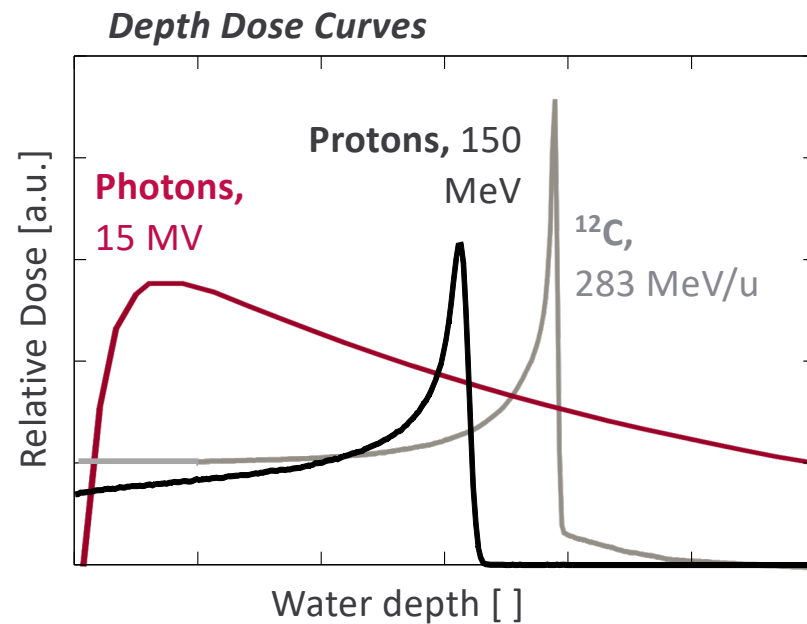
- Approx. 500.000 new cancer diagnosis per year in Germany*
- Three important pillars for the treatment of cancer today
Surgery **Chemotherapy** **Radiotherapy**
- Radiotherapy is involved in >50% of all cancer treatments
 - As primary treatment or in combination with other modalities
- ~50% of all cancer treatments are successful
- > 65% patients with non-curable cancers receive palliative radiotherapy
- Radiotherapy is a localised treatment method



Radiumtherapie 1917

Quelle: www.wikipedia.org

Types of ionizing radiation used for clinical cancer treatments



Electromagnetic radiation

High energy X-Rays ($E \approx 1 - 10 \text{ MeV}$)

Particle radiation

Electrons

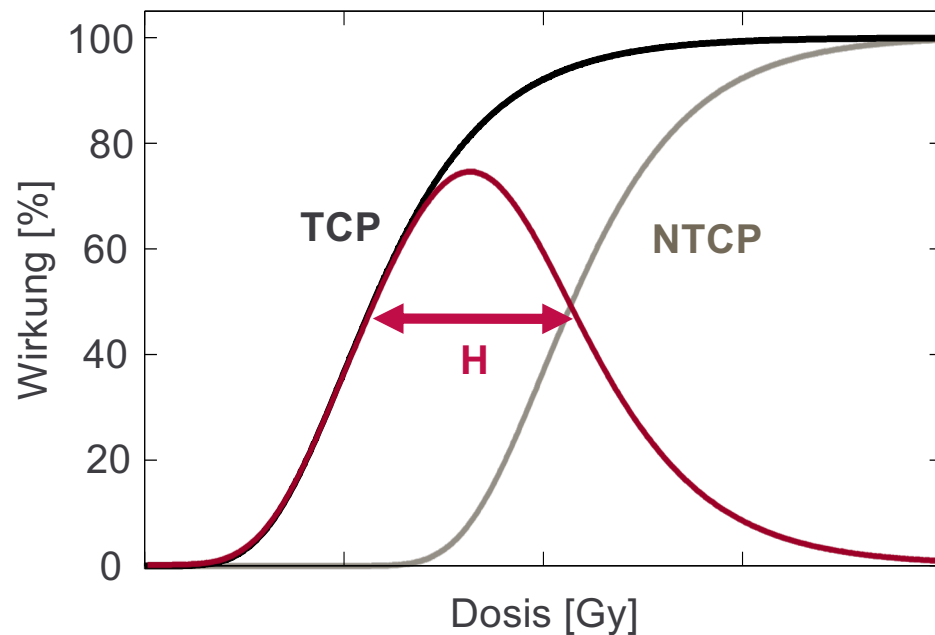
Protons

Ions (He, C)

Neutrons



Dose-response relation of ionizing radiation in cancer treatments



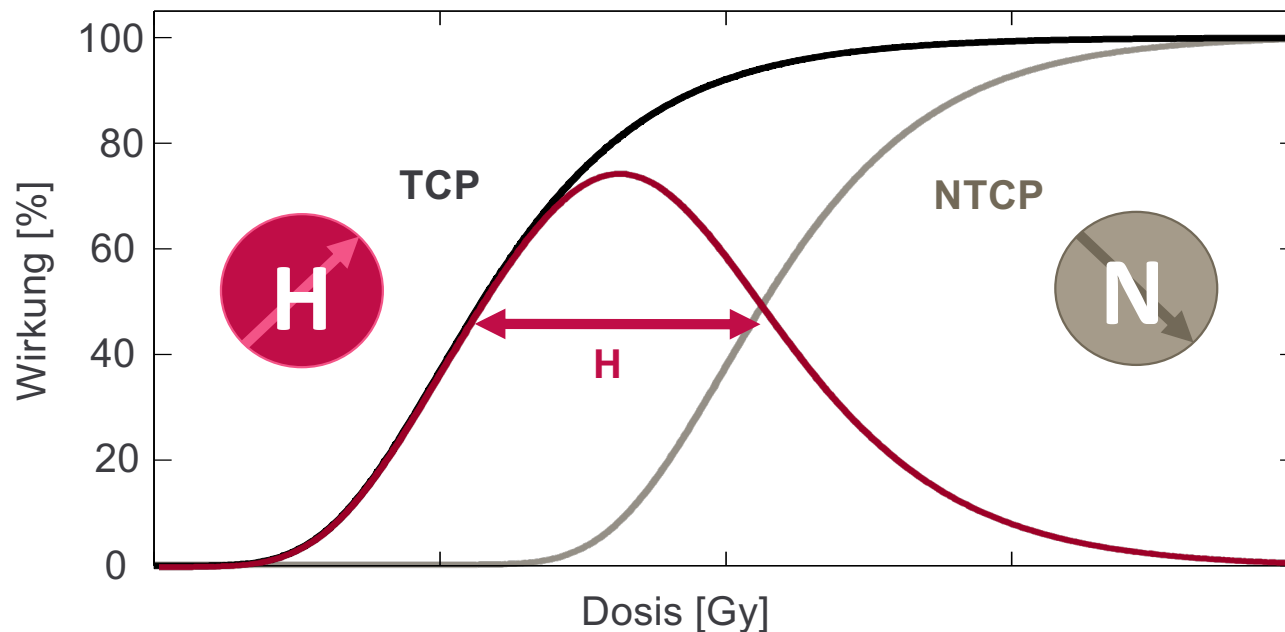
Therapeutic Window:

Optimal dose as $H = TCP \cdot (1 - NTCP)$

- Cell inactivation through radiation:
 - Surviving fraction (SF) of cells after energy dose deposition D:
$$SF = \exp(-\alpha D)$$
- Dose-response relation
 - Tumor control probability (TCP)
$$TCP = \exp(-n \cdot SF)$$
 - Normal tissue complication probability (NTCP)



Dose-response relation of ionizing radiation in cancer treatments



Therapeutic Window:

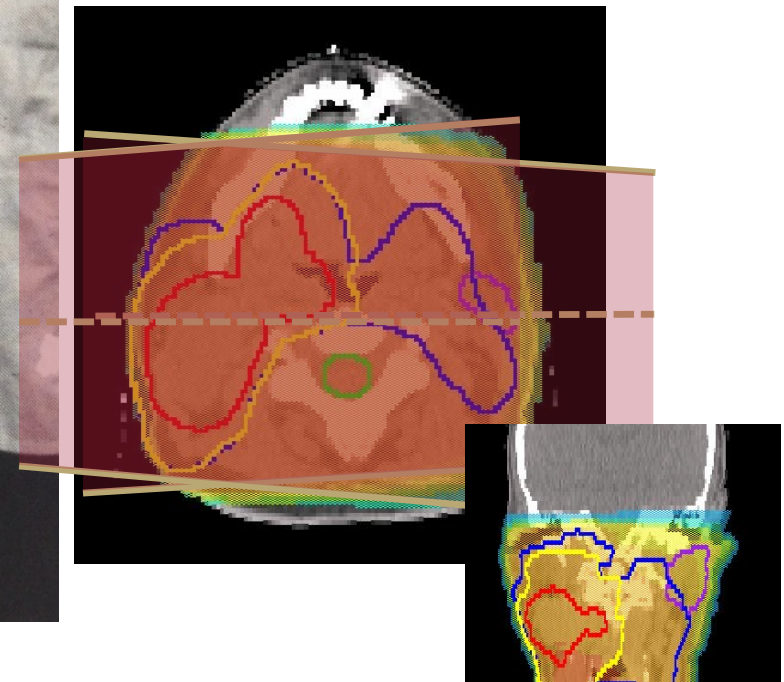
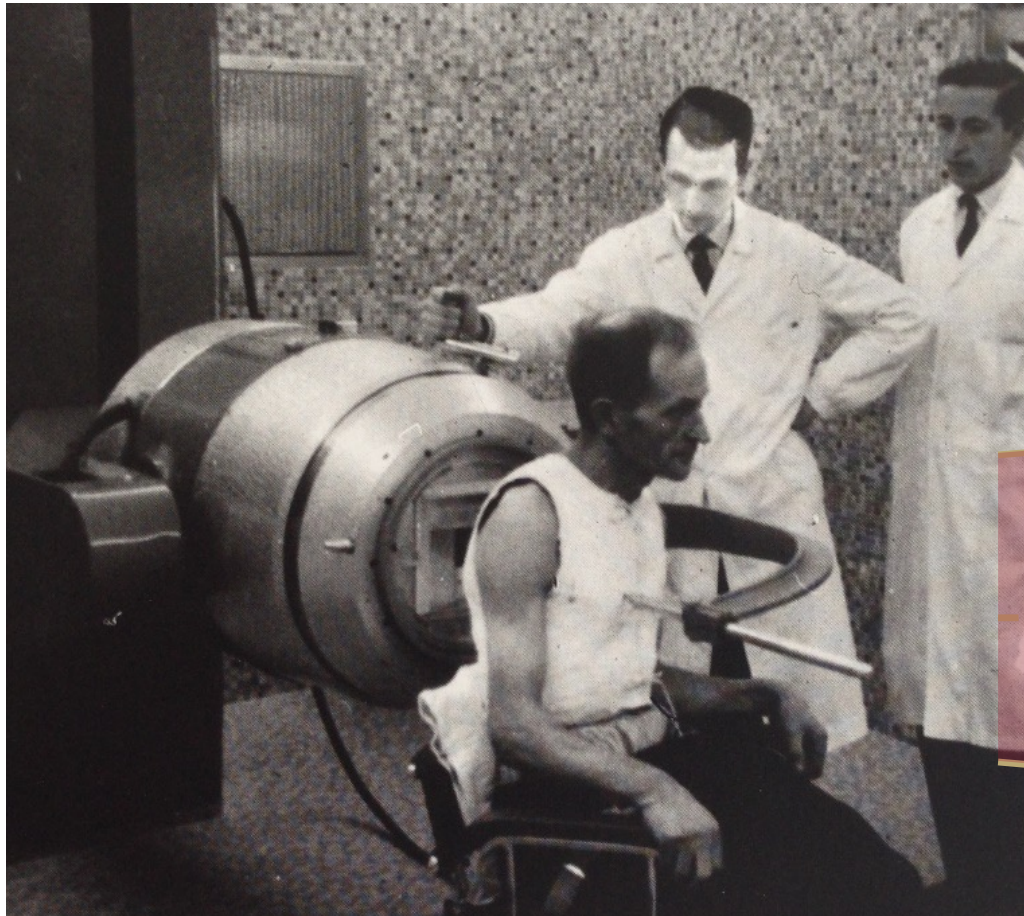
Optimal dose as $H = TCP \cdot (1 - NTCP)$

Optimization of the therapeutic window H through **radiation research and innovation**

- **Medical Physics**
- **Radiation Biology**
- **Radiation Oncology**

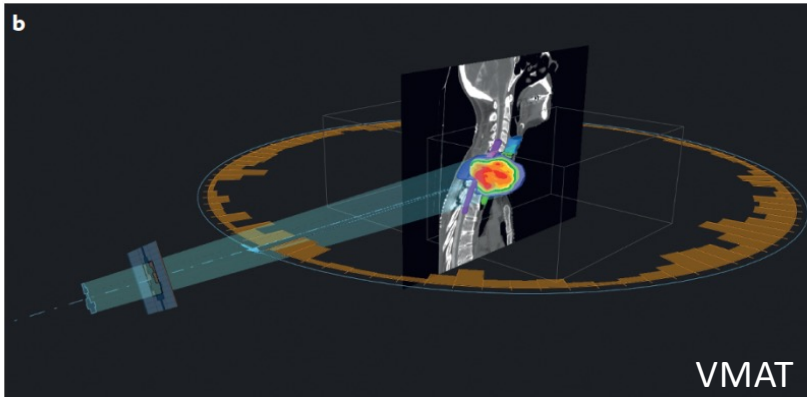
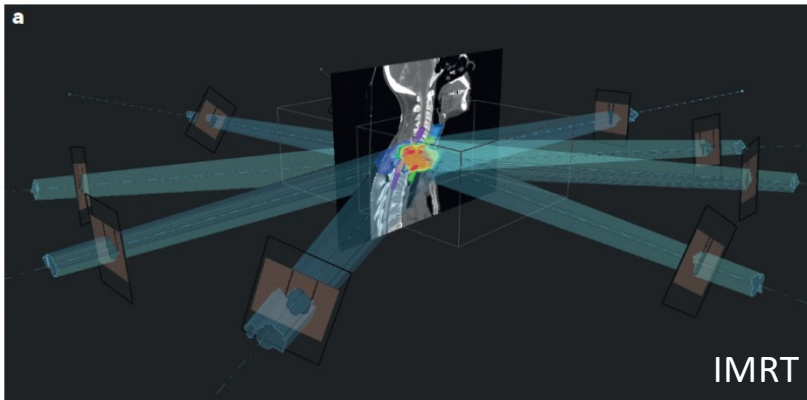


1970er: Medical Linear Accelerators (linacs)



Quelle: ESTRO booklet, three decades of radiotherapy

2000: Intensity Modulated Radiation Therapy (IMRT)

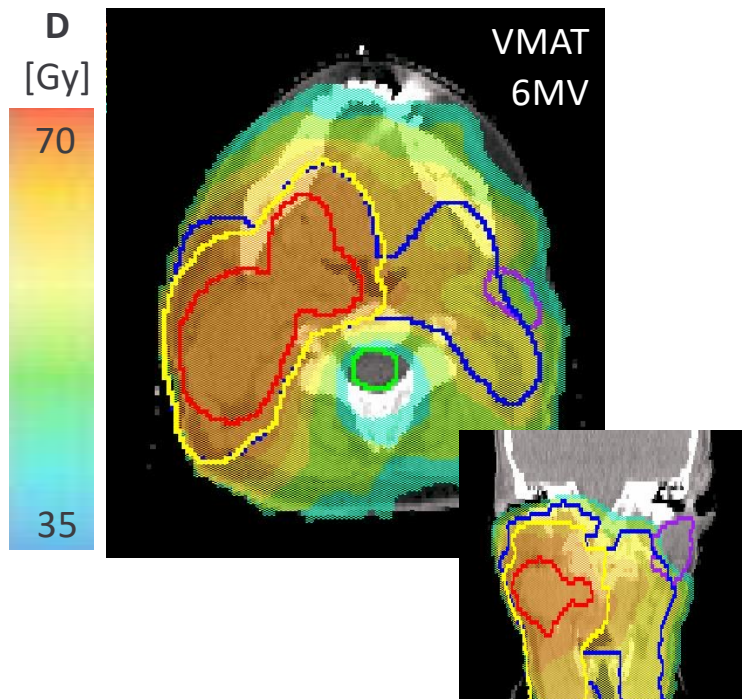


- Technical Innovation: Multi-Leaf Collimator (MLC) for fast and precise collimation of radiation fields
- Computer-assisted identification of radiation field parameters through inverse optimisation
- Accurate definition of tumor volumes through 3D imaging (CT, MRI)
- Verification of patient position in the treatment room

Baumann M et al. Nat Rev Cancer 2016.



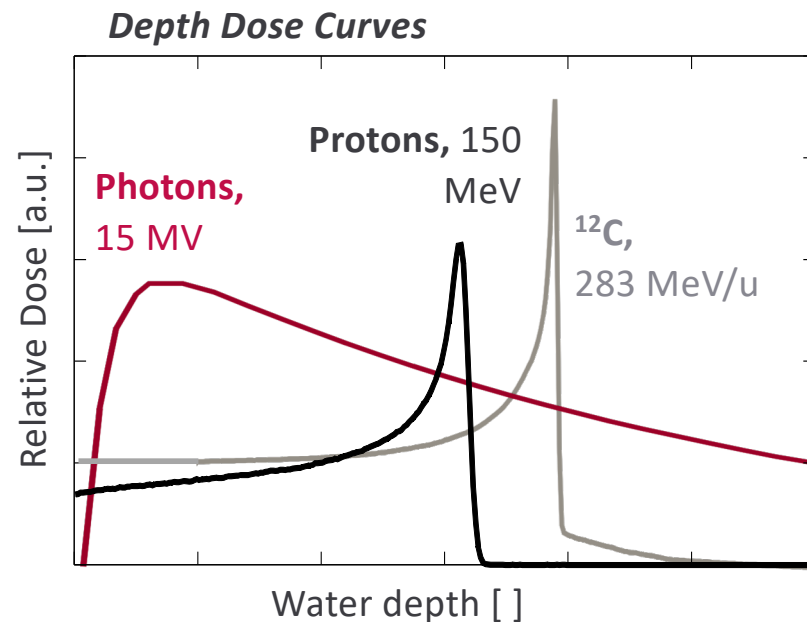
2000: Intensity Modulated Radiation Therapy (IMRT)



- Technical Innovation: Multi-Leaf Collimator (MLC) for fast and precise collimation of radiation fields
- Computer-assisted identification of radiation field parameters through inverse optimisation
- Accurate definition of tumor volumes through 3D imaging (CT, MRI)
- Verification of patient position in the treatment room



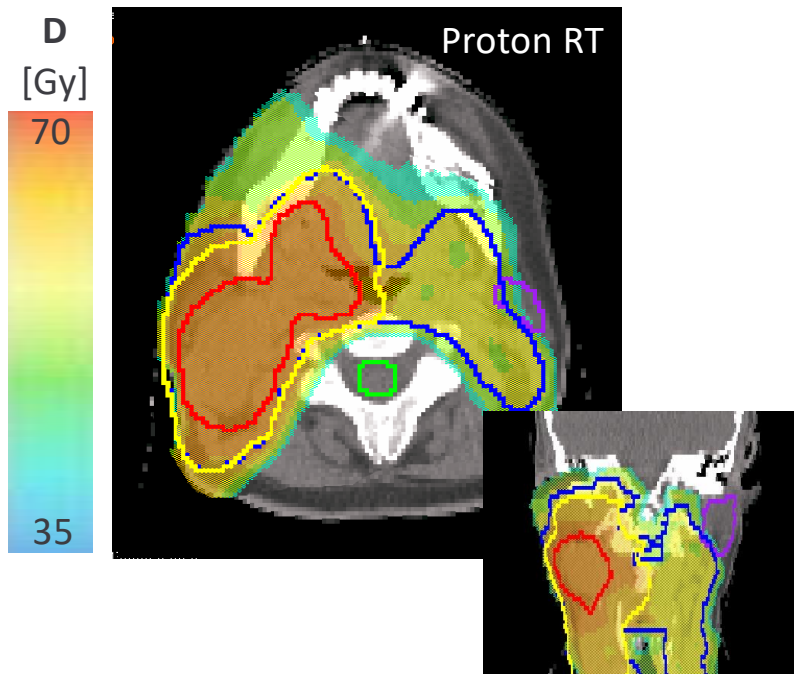
Radiation Therapy using Protons or Ions (He, C)



- High relative energy deposition at the end of the particle range (Bragg-Peak)
- Energy-dependant range
- Higher relative biological effectiveness
- Steep dose gradients
- Reduction in NTCP



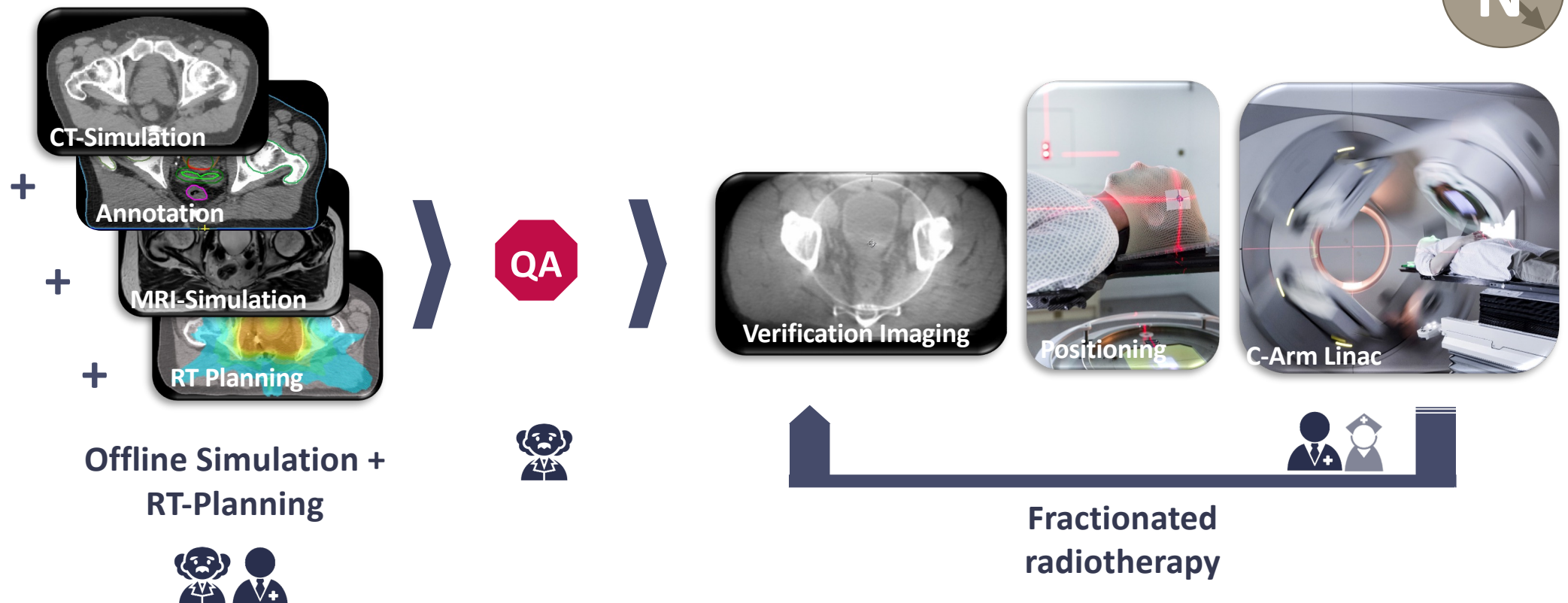
Radiation Therapy using Protons or Ions (He, C)



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- Reduction in NTCP



Image-guided radiotherapy (IGRT)

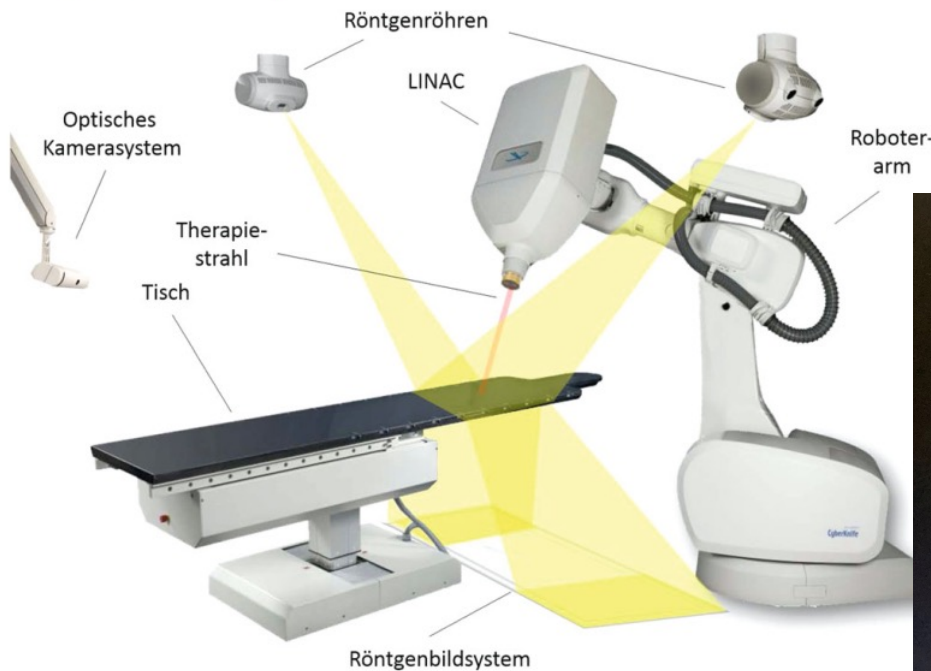


2D-kV image guidance systems

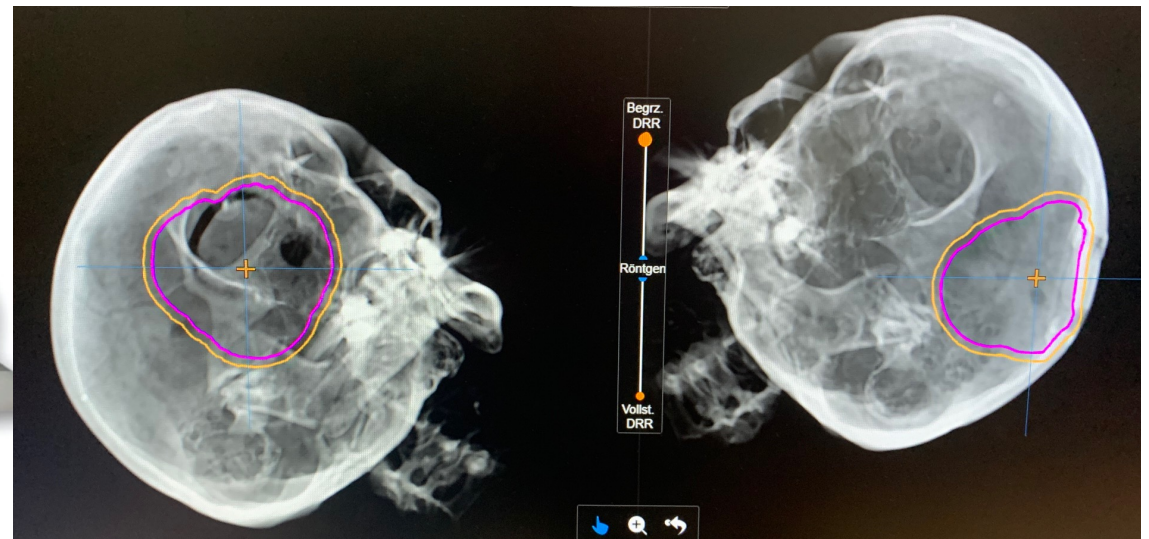
Improving positioning and targeting accuracy in radiotherapy



Stereoscopic X-Ray imaging, 2 fix X-Ray tubes and detector panels



Assumption: Tumor and bony anatomy remain in the same coordinate system.

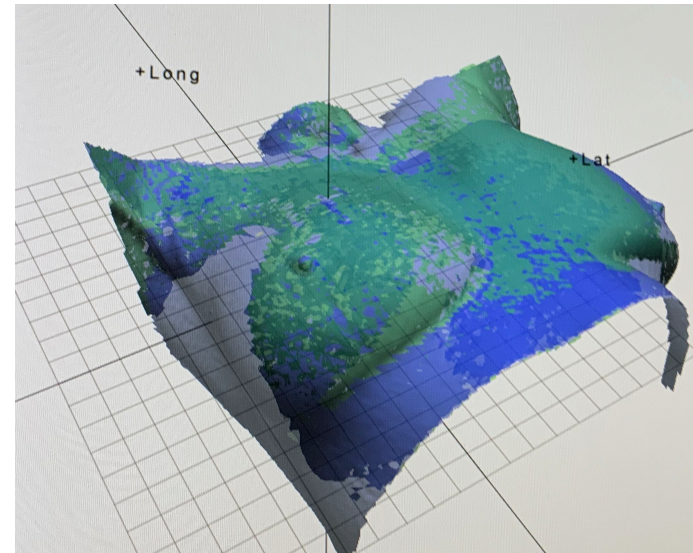
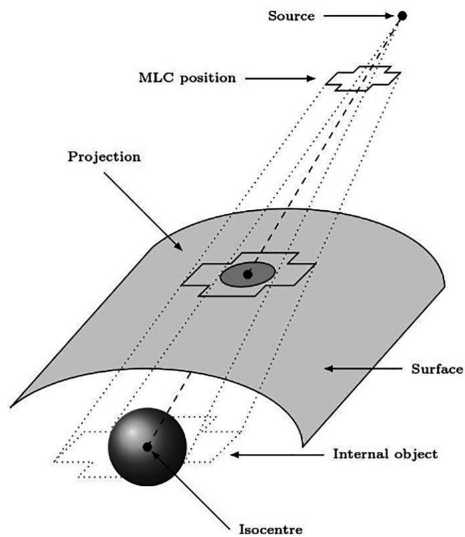


Schlegel W et al. Medizinische Physik. Springer 2018.

2D kV X-Ray for brain RT positioning, Uni Tübingen (03/25)

Surface-guided radiotherapy

- Optical system tracking the patient surface
- No 3D information
- Breathing signal surrogate, biometric patient identification, check of positioning aids



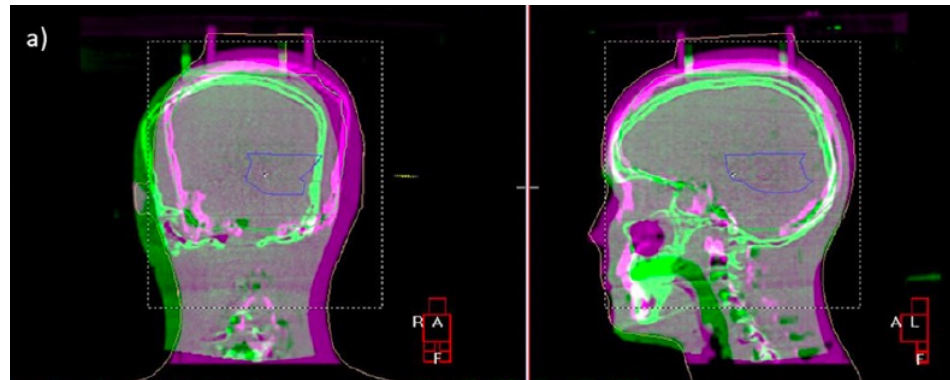
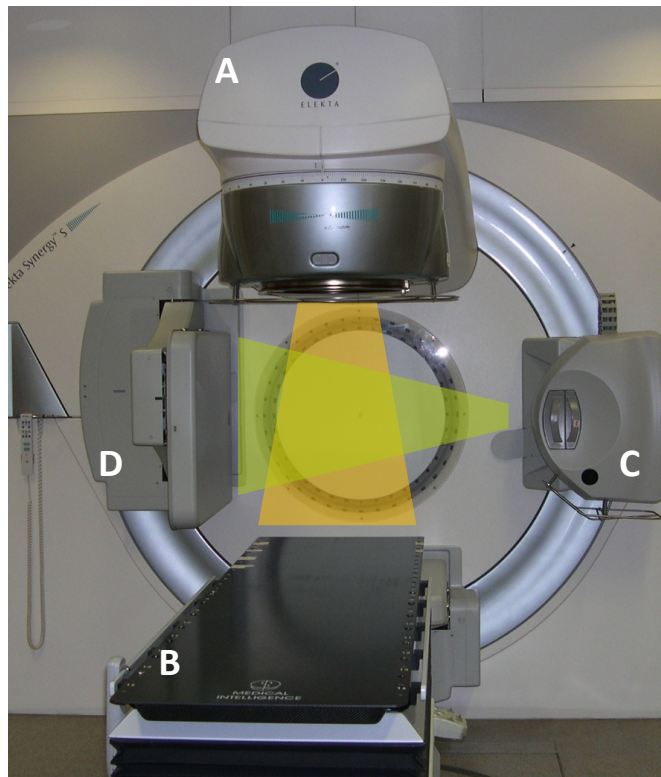
Surface-guidance during breast RT, Uni Tübingen (03/25)



Batista V et al. *Radiother Oncol* 2020;153:43-42.



Image-guided radiotherapy using Cone-Beam Computed Tomography (CB-CT)



Ravindran BP. Image guided radiation therapy. IOP 2022.



CB-CT of a lung cancer patient for radiotherapy positioning, Uni Tübingen (03/25)

IGRT clinical realization

Accelerator head

CB-CT (kV X-Ray rotational)

Detector panels

kV X-Ray sources stationary

Detector panels

Patient couch

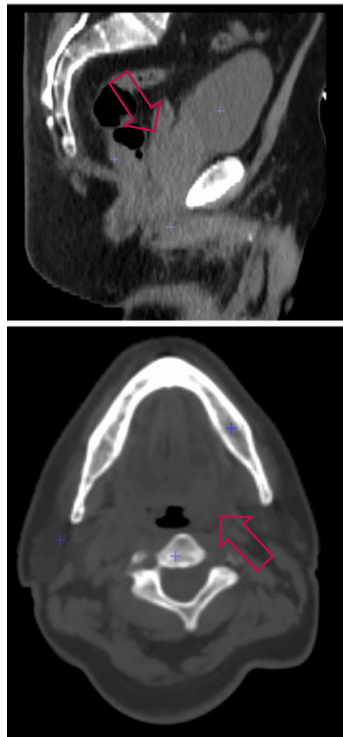
Camera for surface-guided RT



*Clinical IGRT system,
University Hospital
Tübingen (03/25)*



MRI vs. CT for image-guided radiotherapy



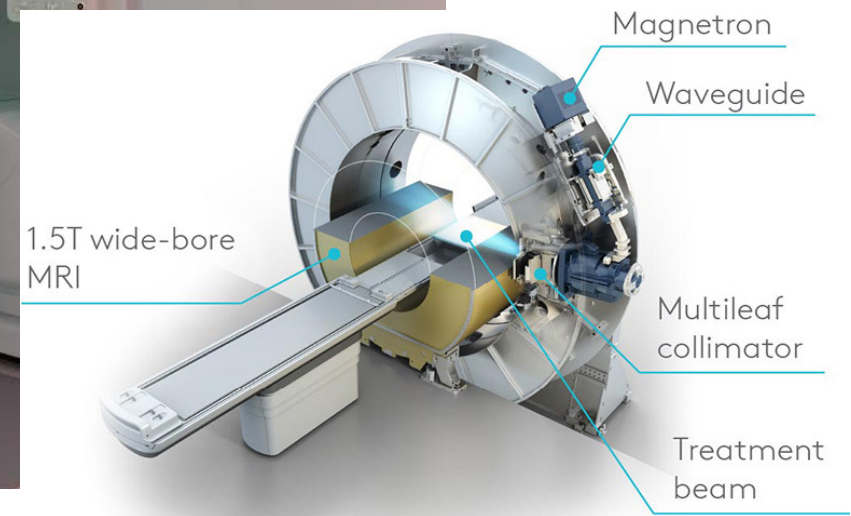
PhD thesis M. Nachbar, University of Tübingen, 2022.



Hybrid MR-Linac systems allow high-quality IGRT



1.5 T MR-Linac (Unity, Elekta AB, Sweden)

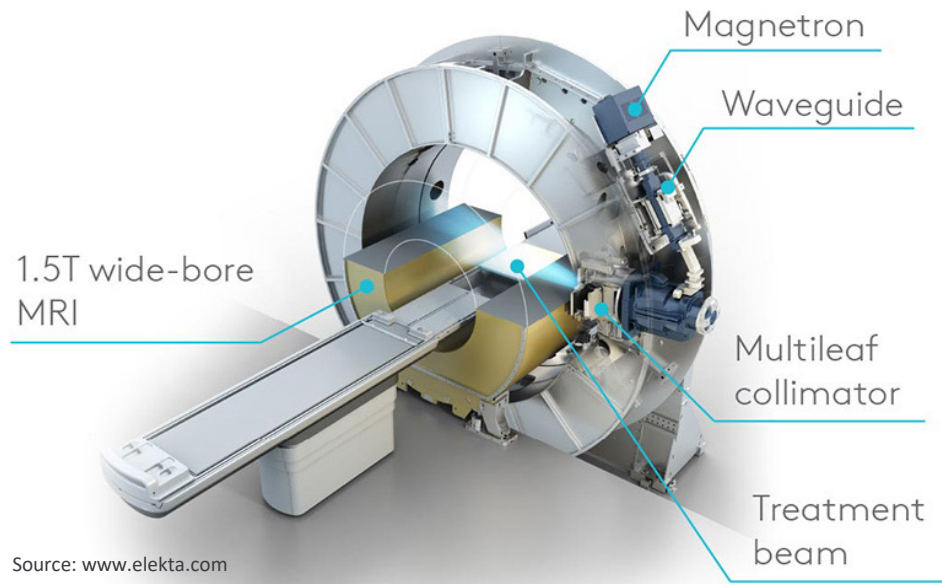


Source: www.elekta.com

Raaijmakers AJ et al. Phys Med Biol 2007.
Legendijk JJ et al. Radiother Oncol 2008.



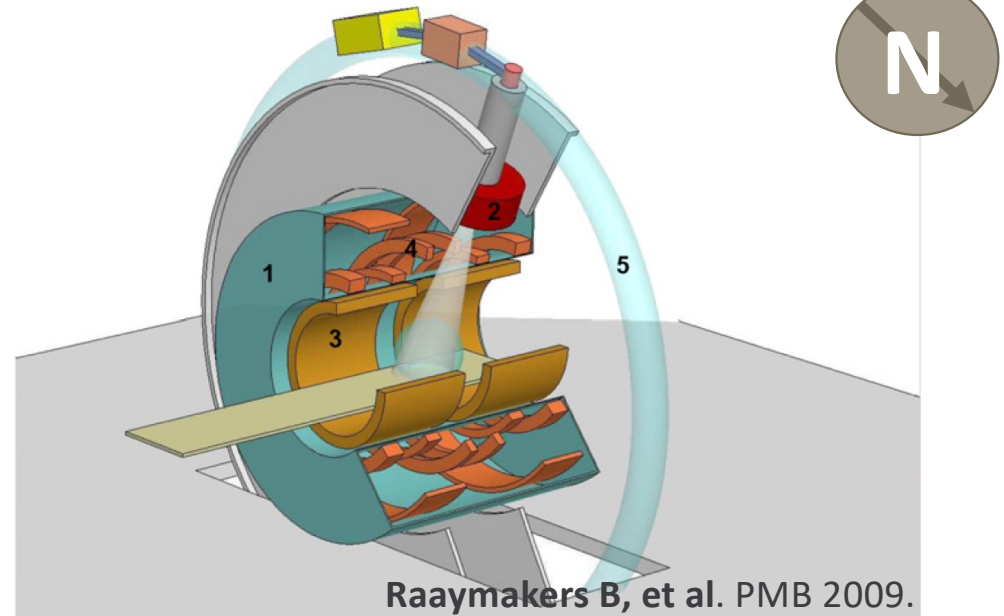
Online adaptive MR-guided RT using the 1.5 T MR-Linac



Technical characteristics

Linac

- $E \approx 7.2$ MV FFF
- FOA = 144.5 cm
- 160 Leafs (cc), width: 7.2 mm
- Max. field size: 22×56 cm²

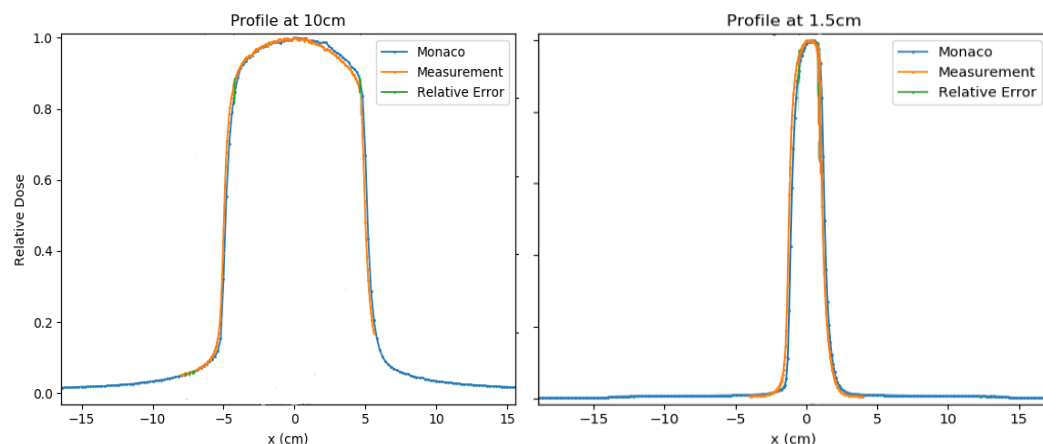


MRI

- $B_0 = 1.5$ T
- T1w, T2w, navigated, diffusion-weighted (DW), ...
- 2D-Cine MRI (8 Hz)
- Radiotransparent MRI-coil
- Bore diameter: 70 cm

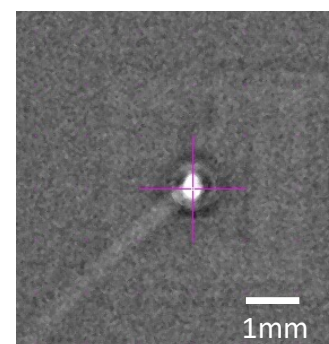
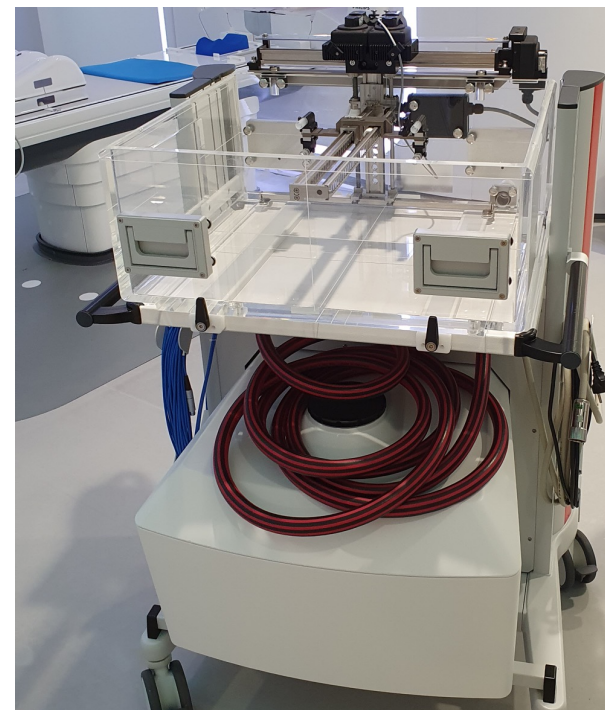


Radiation transport and energy dose deposition in magnetic fields



Dosimetry in B-fields:

- Lorentz force leads to asymmetric fields
- Different detector readings due to Lorentz force (Pojtinger et al. PMB 2018, 2019, 2020)
- Positioning of detectors and equipment in scanner bore / B-field



MV image based
chamber positioning
gantry 0°



High precision IGRT using an 1.5 T MR-Linac

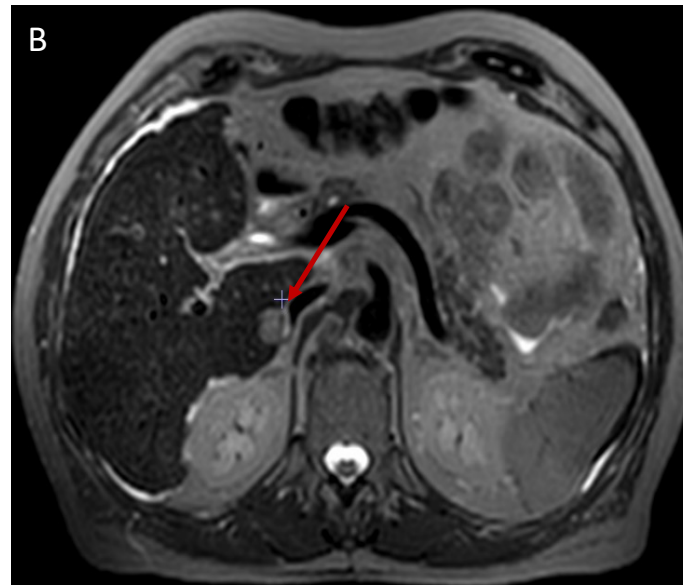
Combination of high resolution soft tissue imaging and med. Linac



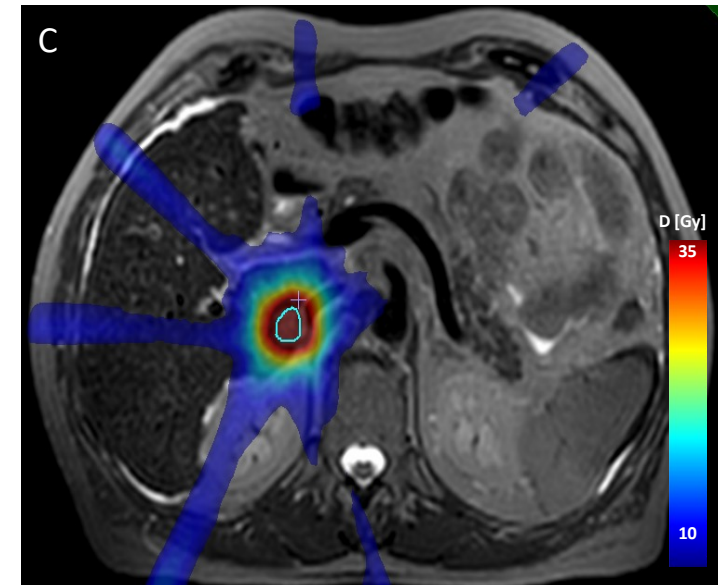
MR-guided high precision-RT of a liver metastasis with the 1.5 T MR-Linac



A Native planning CT



B Navigated T2-weighted MRI



C Markerless liver SBRT with MR-Linac

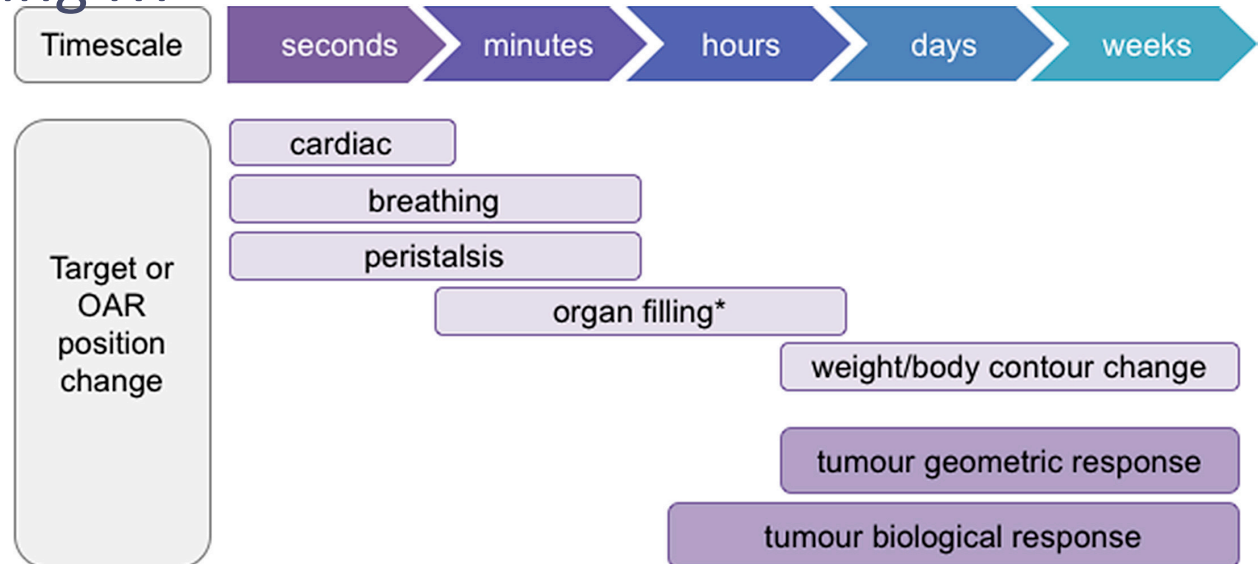


Adaptive Radiotherapy (ART)

- to account for changes during RT

Definition ART:

„A radiation treatment process **where the treatment plan can be modified using a systematic feedback of measurements** (treatment position variation due to beam displacement and target geometric variation) is named ‘adaptive radiation therapy’ (ART).“



Yan D, et al. Phys Med Biol 1997; 42:123–32.

Hunt A, et al. Clin Oncol
2018; 30:711–9.

Adaptive radiotherapy

modification of treatment plans triggered by changes during RT

Changes during RT **measured via Imaging**

- Inter-fraction (z.B. anatomic)
- Intra-fraction (z.B. motion)



Modification of initial RT plans

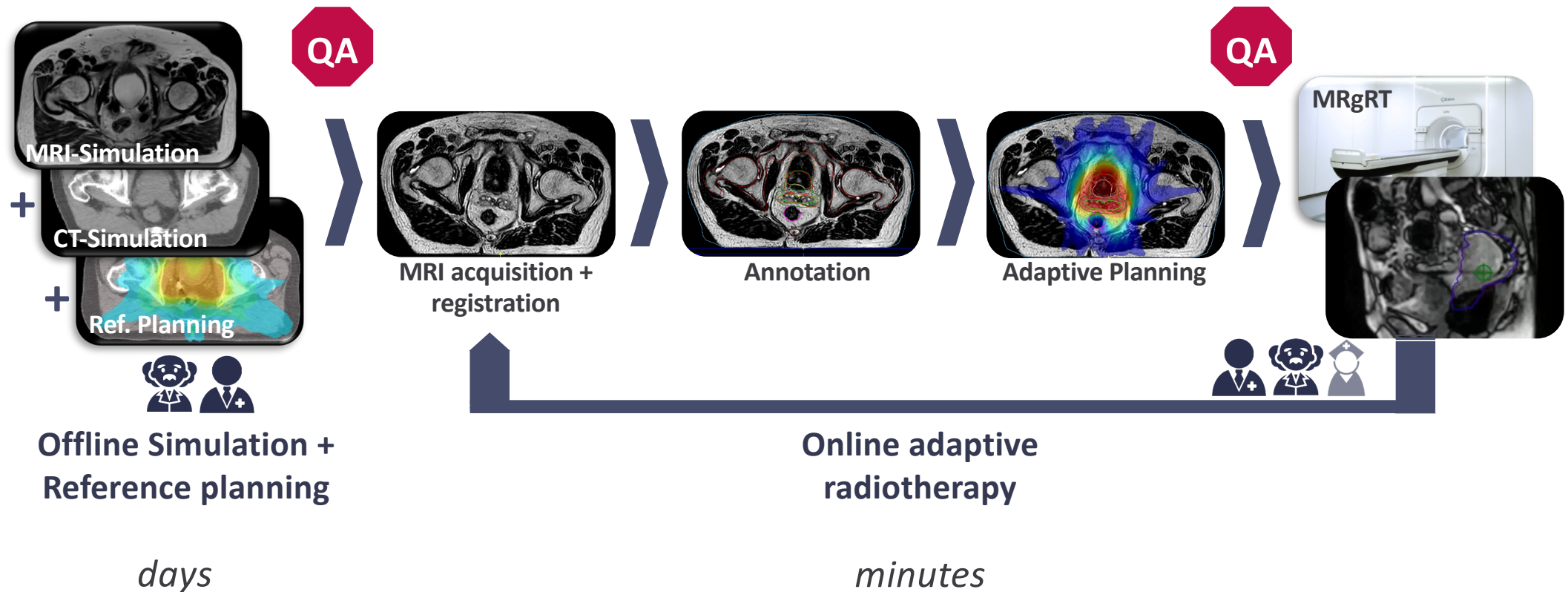
- Geometry/Anatomy (dose distribution)
- Dose / Fractionation scheme
- Gating/ Tracking
- Sequential adaptation of treatment plan

ART-Paradigms:

- Safeguard prescribed dose to initial target volume (TCP),
- Reduction of dose to organs at risk at constant TV dose (decrease NTCP),
- Dose escalation to shrinking tumor (increase TCP),
- Response – adaptive RT (increase TCP).



Workflow online adaptive MR-guided RT

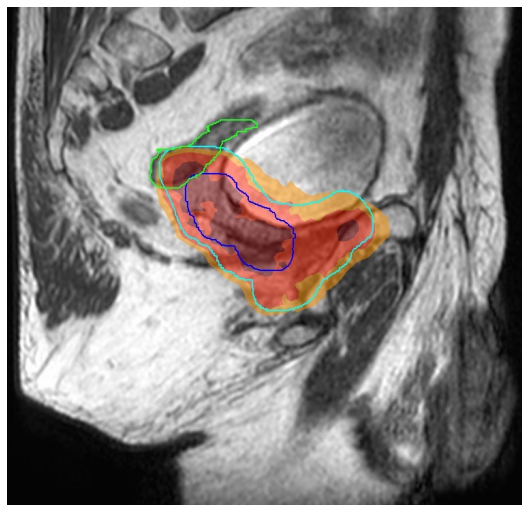
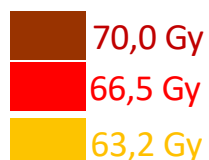


Online adaptive MR-guided RT

Ensuring maximum tolerable doses to mobile organs at risk



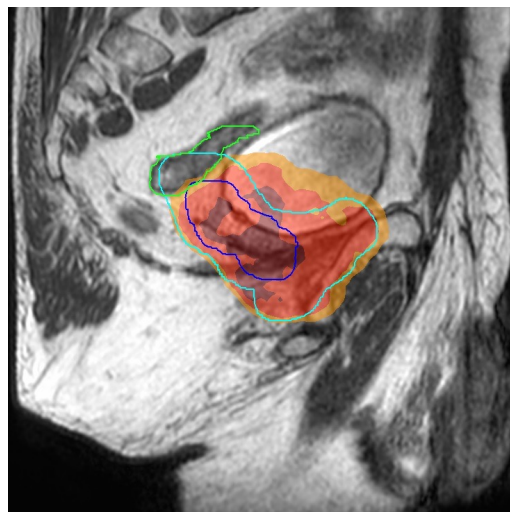
PTV 70
PTV 66,5
Sigmoid



MR-guided RT

Position verification

- Rigid registration of MRI to simulation CT
- Plan optimization on initial structures and CT



MR-adaptive RT

Treatment plan adaptation

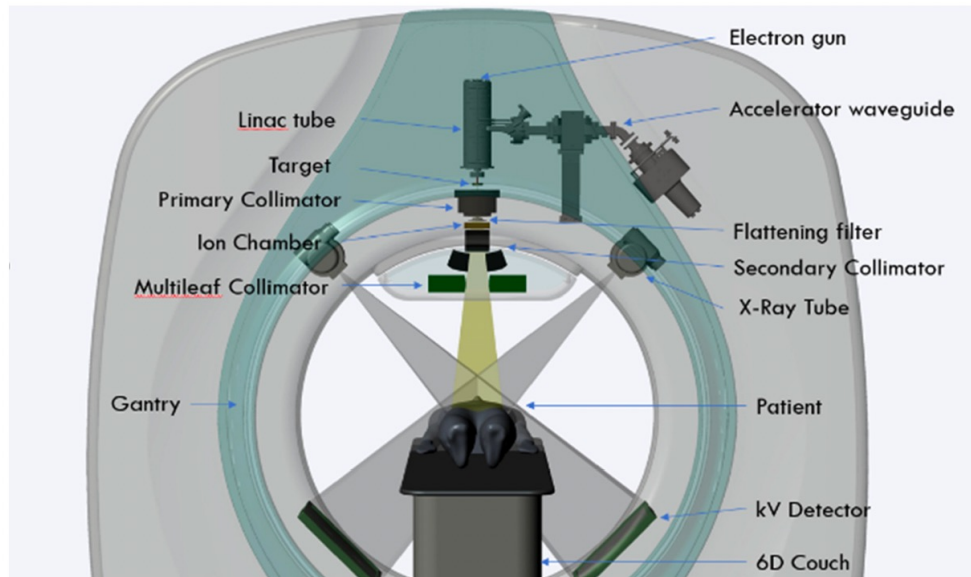
- Deformable registration of MRI to simulation CT
- Propagation of contours to daily MRI
- Adaptive planning on daily MRI / synthetic CT

Winkel D, et al. Clin Transl Radiat Oncol 2019; 18:54–9.

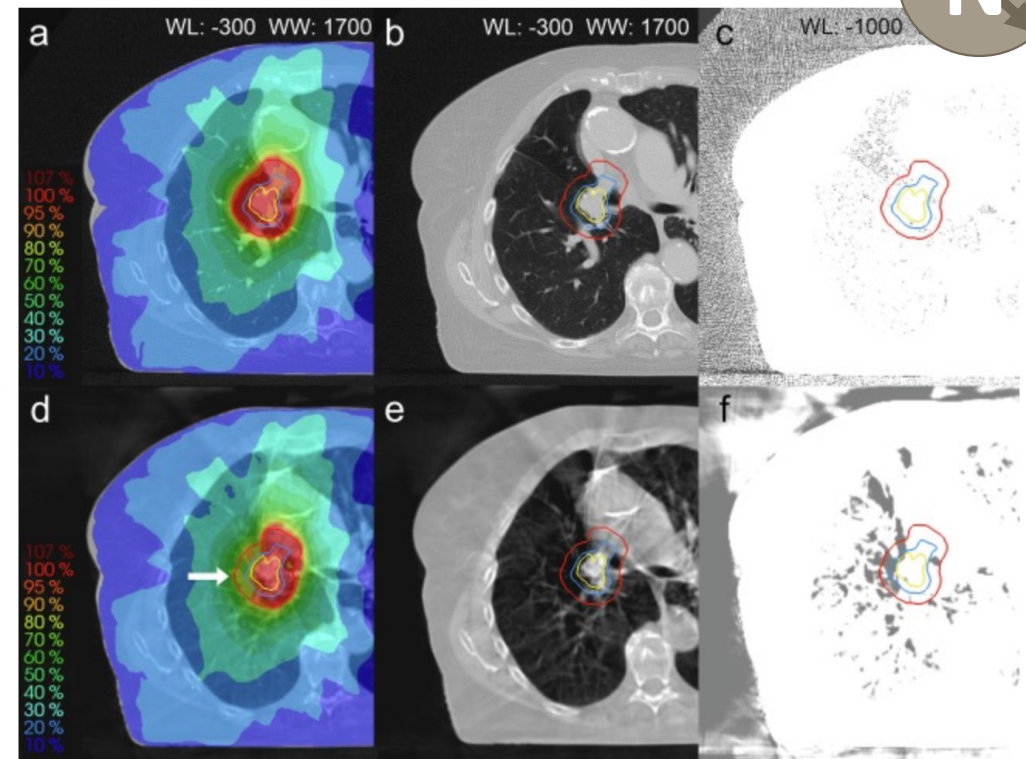


CT-adaptive image guided RT

Hybrid CT-Linac



Ravindran BP. Image guided radiation therapy. IOP 2022.



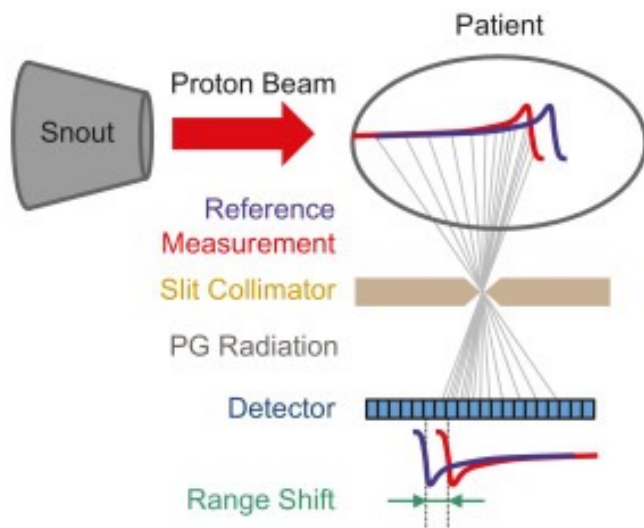
Sijtsema ND, et al. Radiother Oncol 2025; 202:110596.

Online adaptive proton therapy

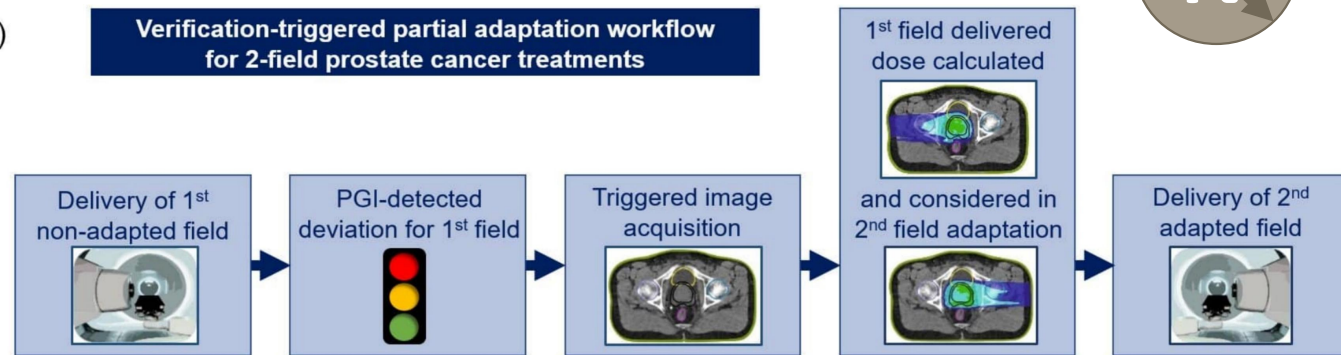
Using direct feedback from prompt gamma imaging



Proton range verification in vivo A)
using **prompt gamma imaging**:



Verification-triggered partial adaptation workflow
for 2-field prostate cancer treatments



B)

Delivery scenario

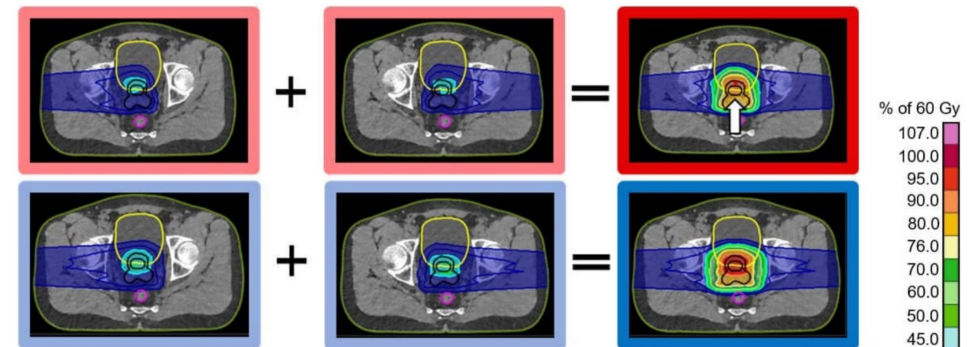
Non-adapted
Initial plan recalculated
on cCT

Fully adapted
Initial plan
re-optimized on cCT

1st field

2nd field

Total dose



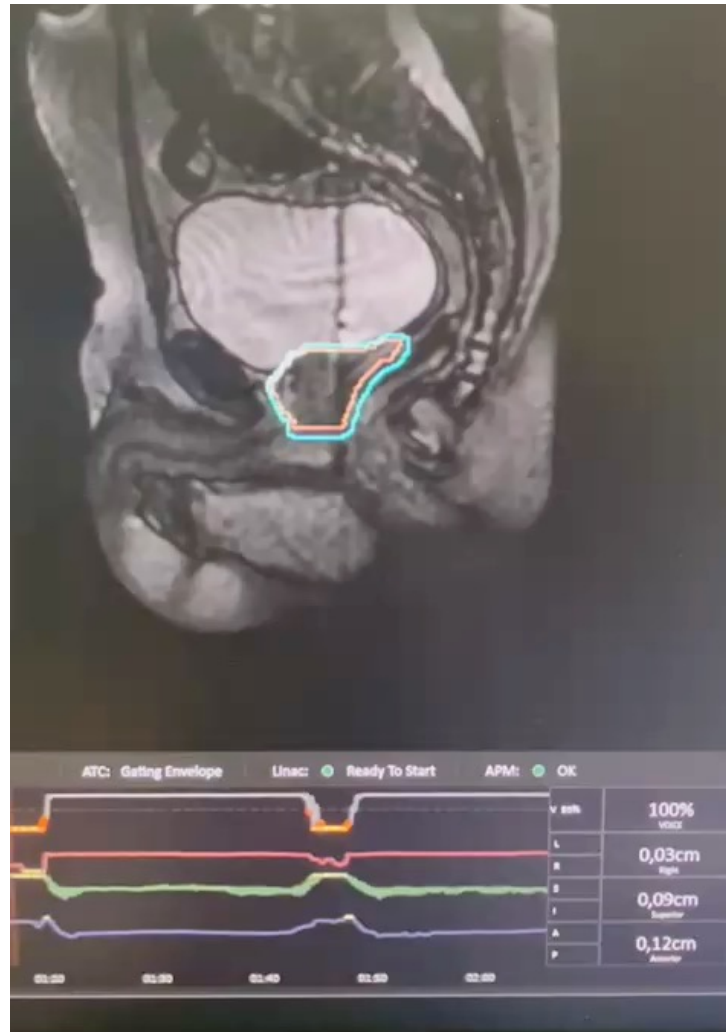
Berthold J, et al. Int J Radiother Oncol Biol Phys 2021.

Gambetta V, et al. Phys Imag Radiat Oncol 2025.

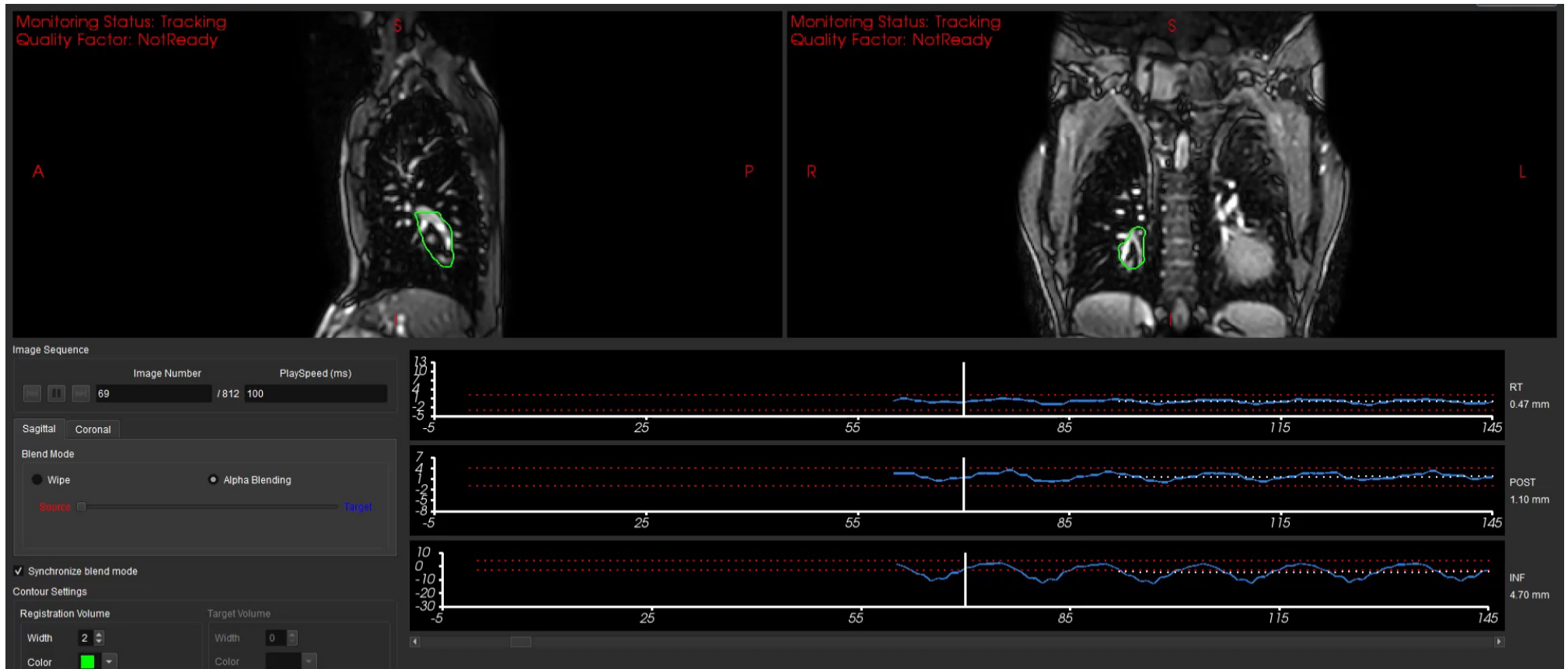
MR-based gating to monitor irregular motion



- 'live' imaging during beam-on
- Latency time approx. 200 ms
- 2D planes only

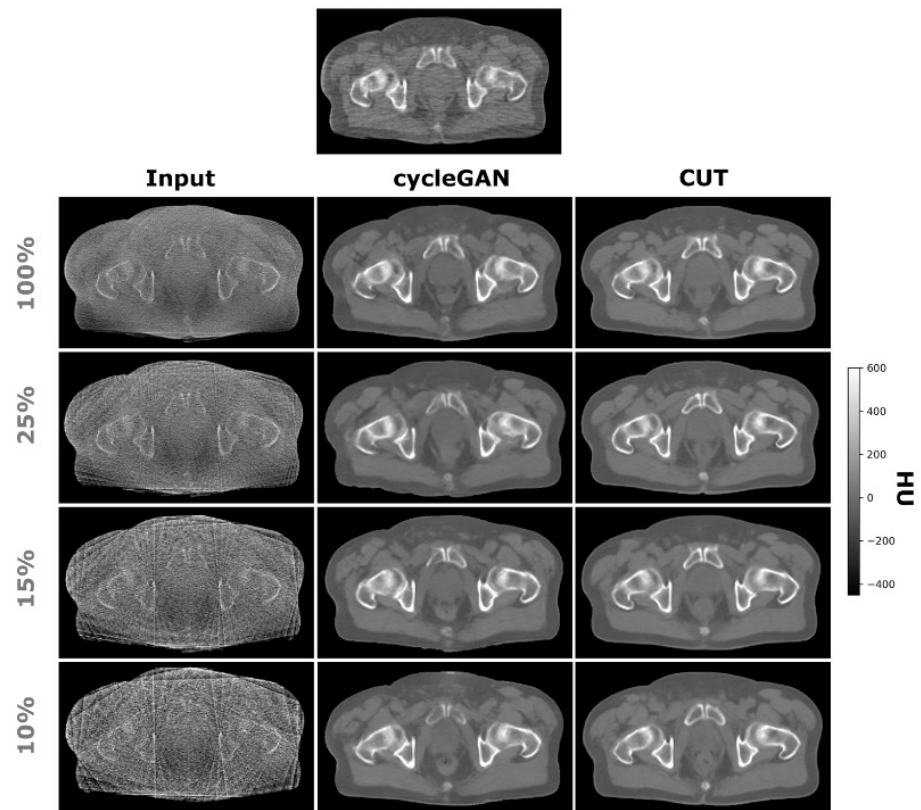


MRI-based gating to compensate for breathing motion



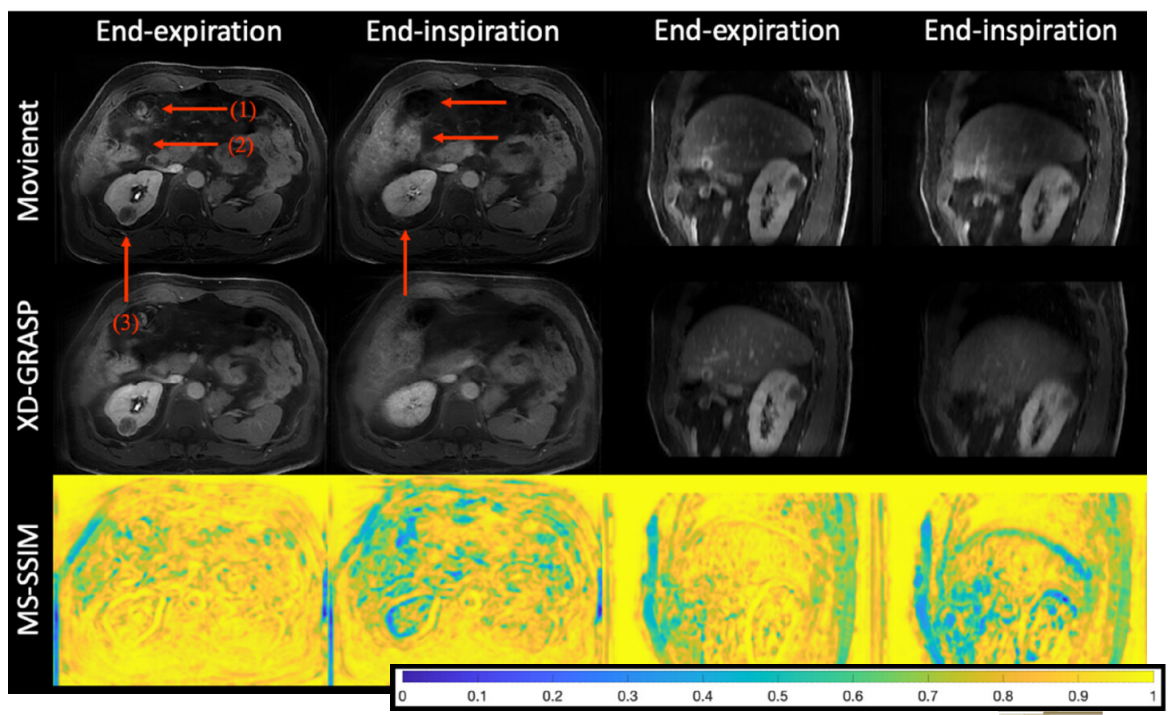
Real-time image reconstruction using artificial intelligence (AI)

CT + AI-Recon: Dose reduction



MRI + AI-Recon: Acceleration

Fast reconstruction (0.7 s) of 4D-MRI:



31 Chan YCI, et al. Phys Imag Radiat Oncol 2024.

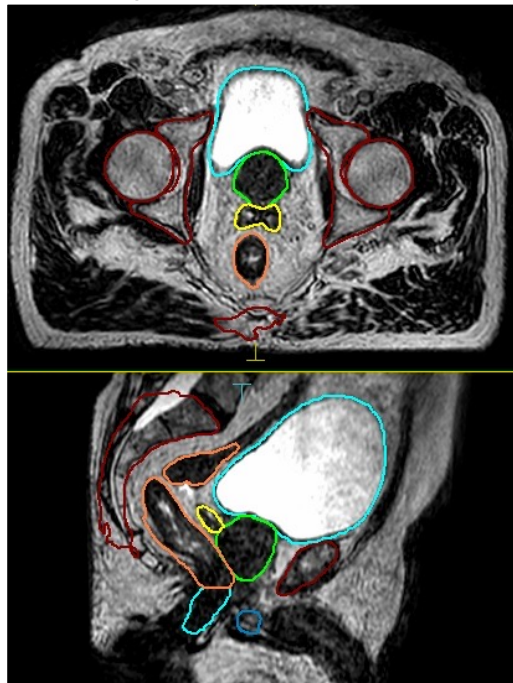
Murray V, et al. Magn Res Med 2024.

Real-time structure segmentation

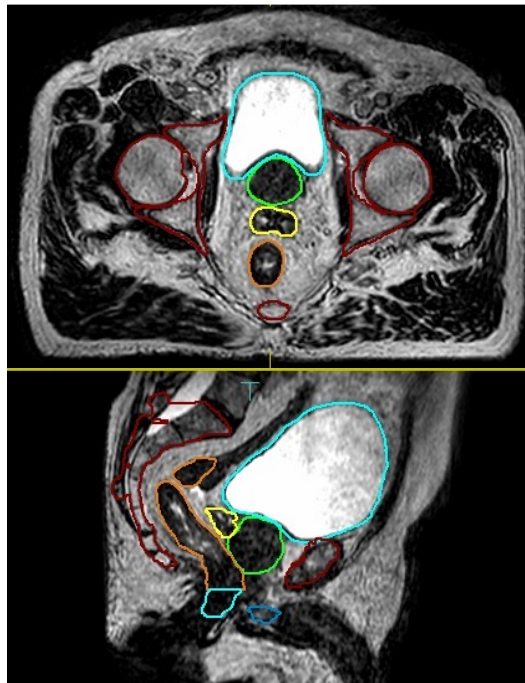
Automation of tumor and organ segmentation for real-time interventions



Expertenkontur

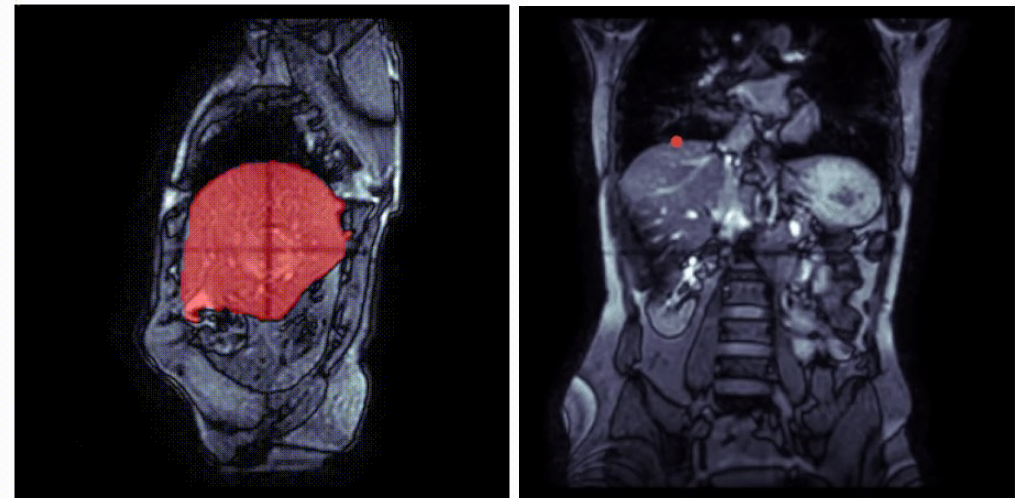


KI-Kontur



Nachbar M, et al. Z Med Phys 2024.

Echtzeit-Detektion von Organen oder anatomischen Landmarken:

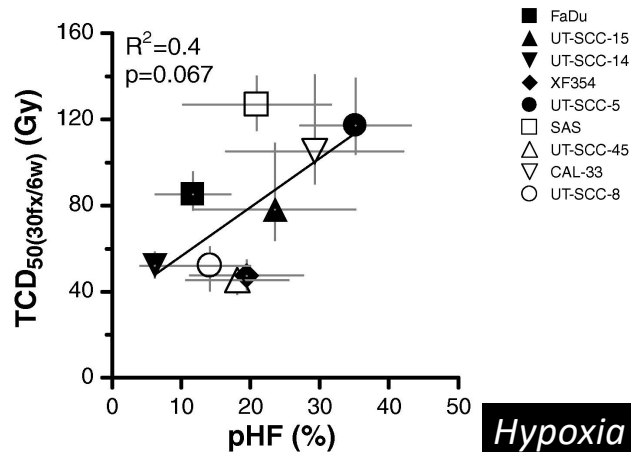


Früh M, et al. Comput Methods Programs Biomed 2022.



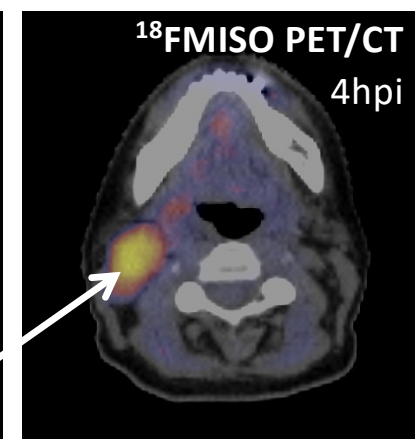
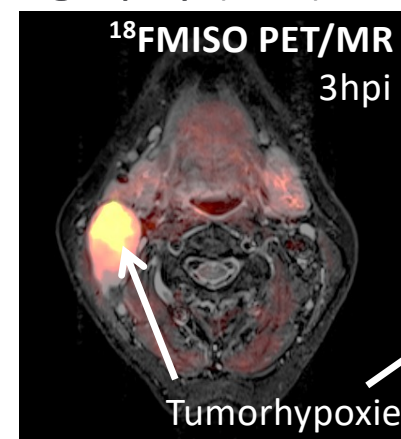
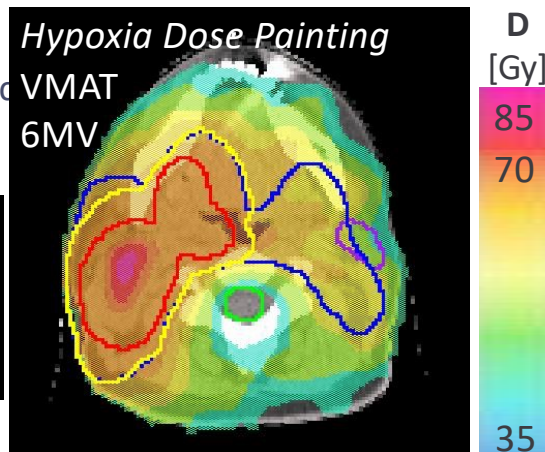
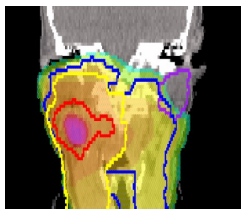
Radiation response:

Tumor hypoxia is a major cause of radiation resistance in tumors



- Resistance level is different from tumor to tumor
- Depends on the level of tumor hypoxia
- Tumor hypoxia can be measured with dedicated positron emission tomography (PET) tracers in vivo:

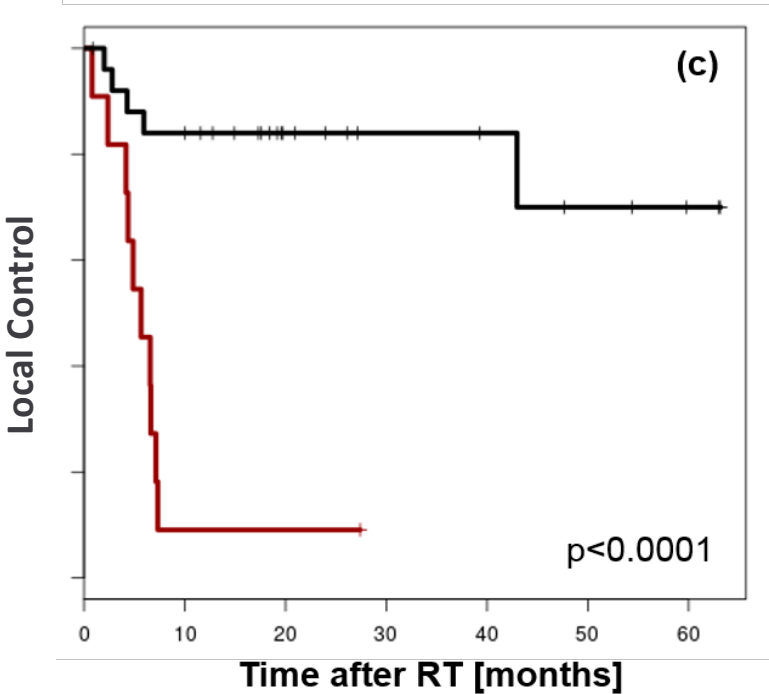
Yaromina A et al. Radiother Oncol



Hypoxia-PET image-guided radiotherapy personalization

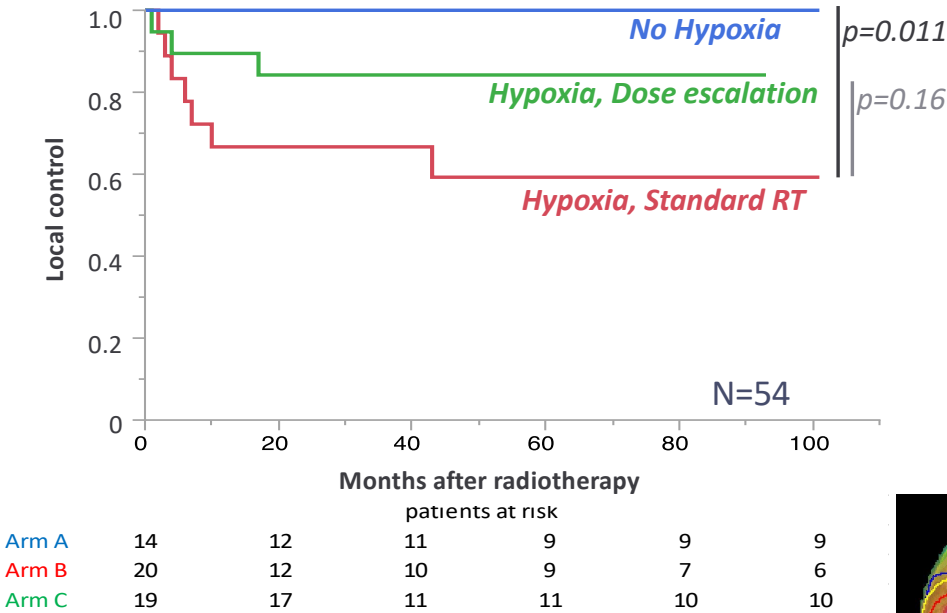


Hypoxia-PET as prognostic biomarker:

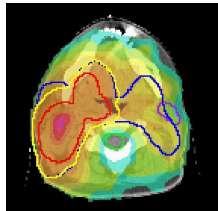


Thorwarth D et al. J Nucl Med 2019.

Clinical Phase II-study in dose escalation based on hypoxia-PET:



Welz S et al. Radiother Oncol 2022.



Imaging of tumor hypoxia using functional MRI

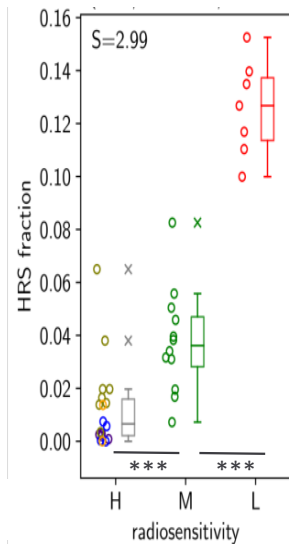
Diffusion-weighted Magnetic Resonance Imaging (DW-MRI)



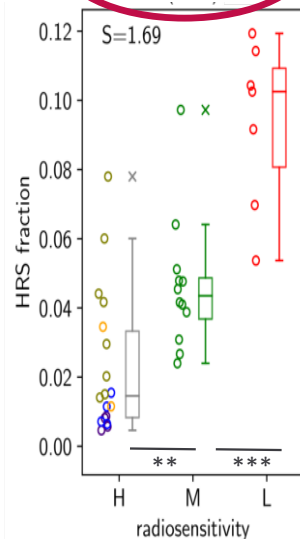
Imaging radiation resistance with hypoxia
PET and/or DW-MRI in small animals

Hypoxia PET + DW-MRI

DW-MRI



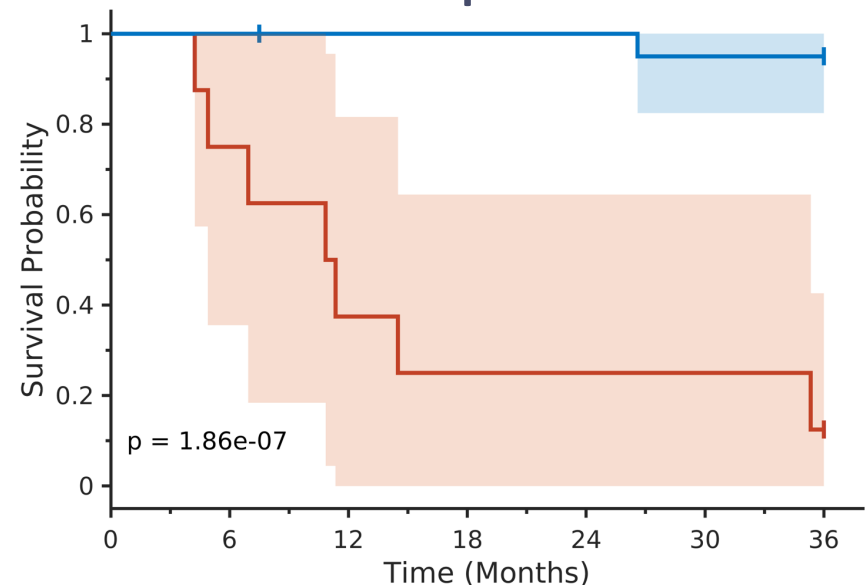
p<0.001



p=0.002

DW-MRI allows to identify patients with
radioresistant tumors:

DW-MRI in patients



Boeke S, Winter RM, et al. EJNMMI 2023.

Winter R, Boeke S, et al. Radiother Oncol 2025.

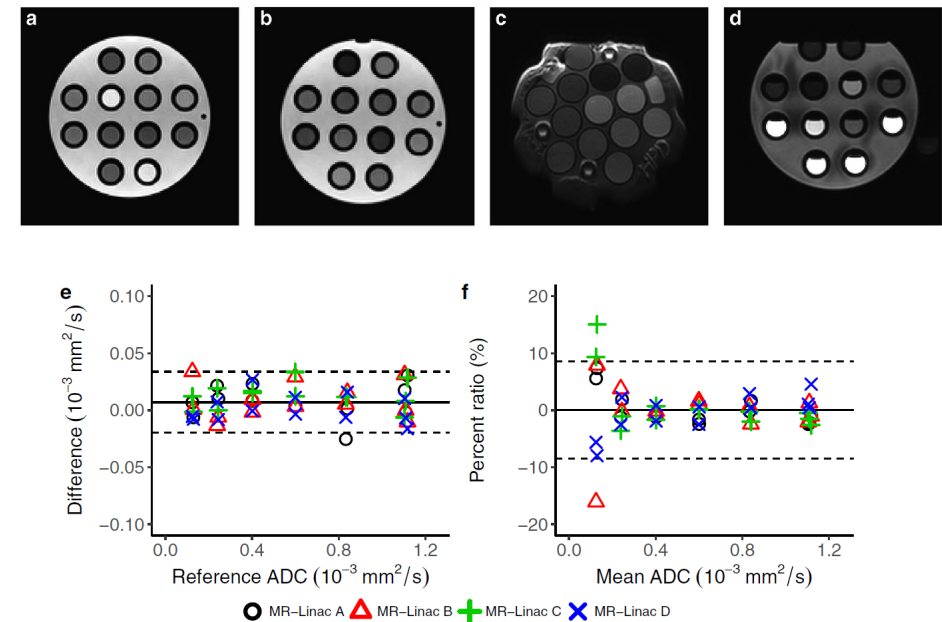


Quantitative MRI using the 1.5 T MR-Linac

Optimizing diffusion weighed imaging for response adaptive IGRT

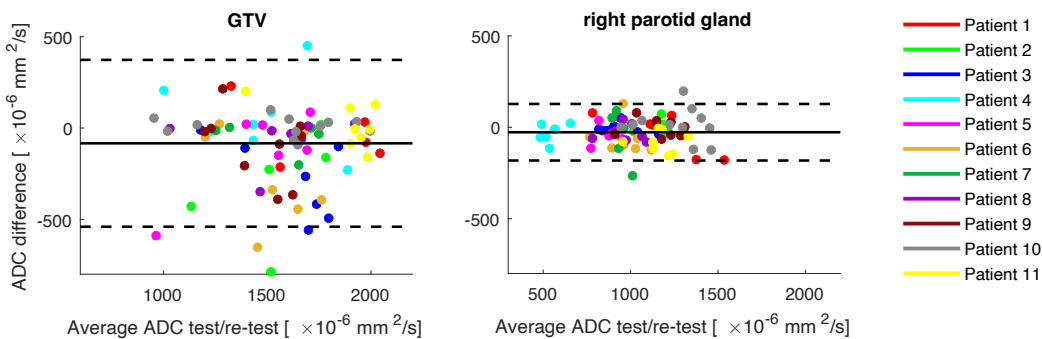


Acquisition of quantitative DW-MRI at the 1.5 T MR-Linac is possible.



Kooreman E, et al. Radiother Oncol 2019; 133:156-62.

Repeatability of DW-MRI in HNC at the 1.5 T MR-Linac is comparable to diagnostic MRI.



Repeatability	Submand	Parotis	GTV	LN
RC ADC [10 ⁻⁶ mm ² /s]	276	146	456,5	310,2
relRC [%]	20,6	14,3	31,3	23,5

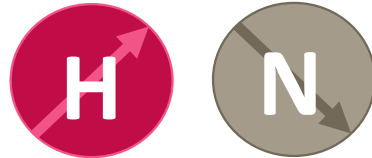
Habrich J, et al. Radiother Oncol 2022; 174:141-8.



Summary

Image-guided radiotherapy to improve cancer treatment IGRT techniques impact daily cancer treatment quality in terms of

- Accurate patient positioning
- Daily radiotherapy adaptation
- Real-time beam gating
- Future challenges:
 - Real-time image-guidance and adaptation
 - Response adaptive radiotherapy through functional image-guided radiotherapy



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Christian La Fougère
Thomas Küstner
Fritz Schick

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Petra van Houdt (Amsterdam, NL)
Faisal Mahmood (Odense, Denmark)
Marielle Philippens (Utrecht, NL)
Johanna Hundvin (Bergen, Norway)
Brigid McDonald (MDACC, USA)
Christian Baumgartner (Luzern, CH)

Section for Biomedical Physics:



European Research Council
Established by the European Commission

EBERHARD KARLS
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TÜBINGEN



Deutsche
Forschungsgemeinschaft



Comprehensive
Cancer Center
Tübingen - Stuttgart



Baden-Württemberg
MINISTERIUM FÜR WISSENSCHAFT, FORSCHUNG UND KUNST



Chancen fördern
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