Radiation Treatment Planning

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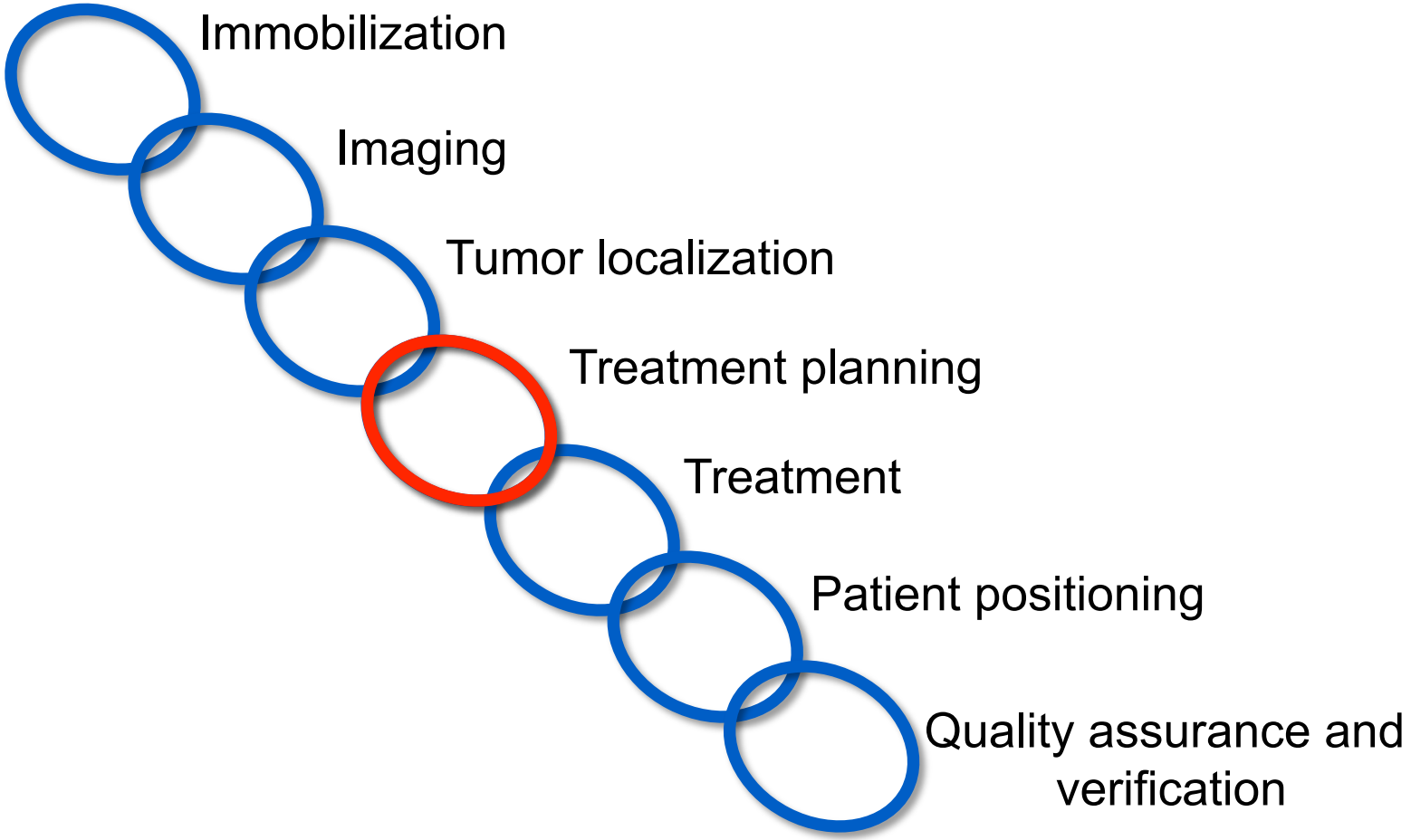
The radiotherapy chain



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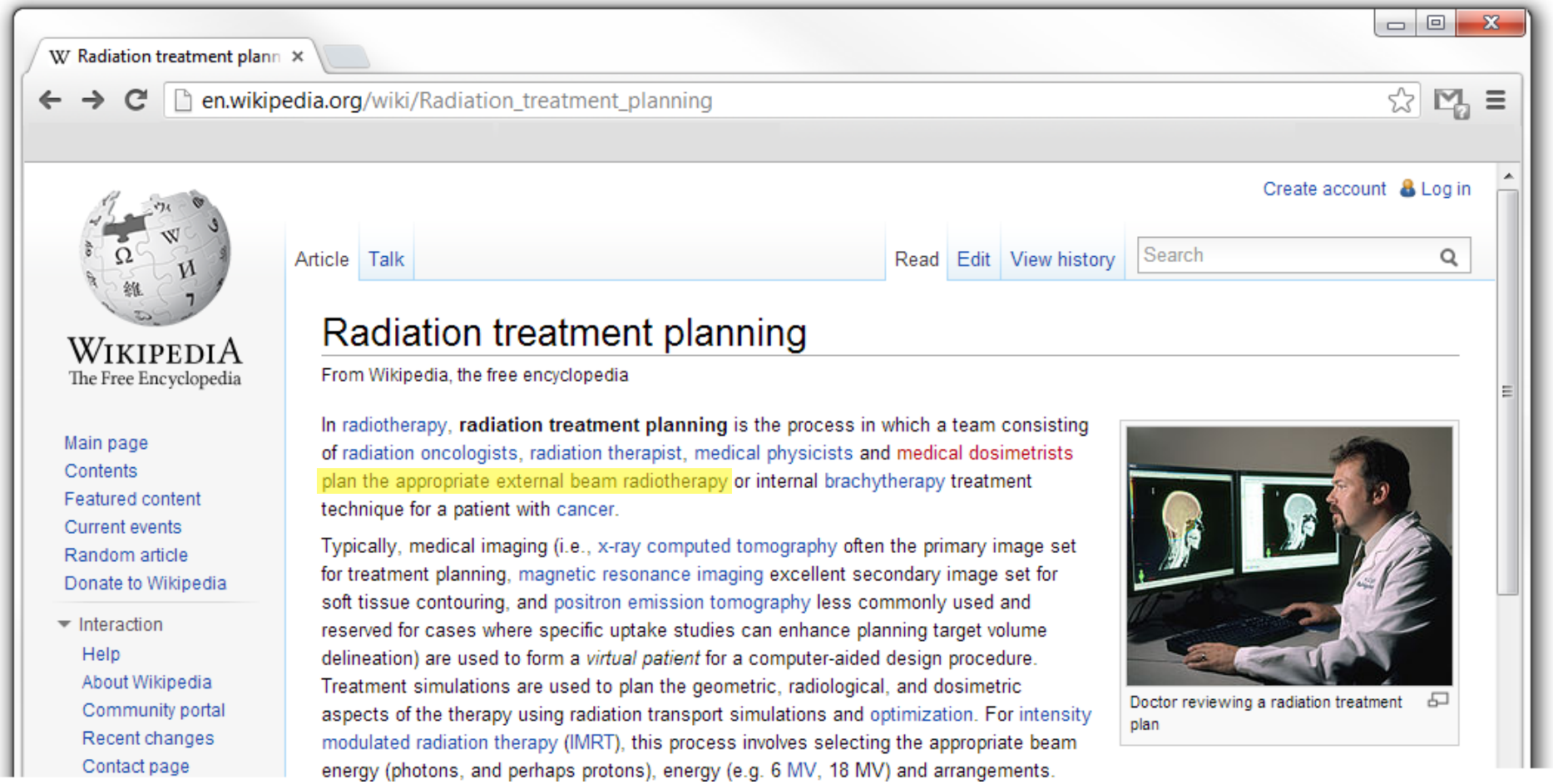
Radiation treatment planning



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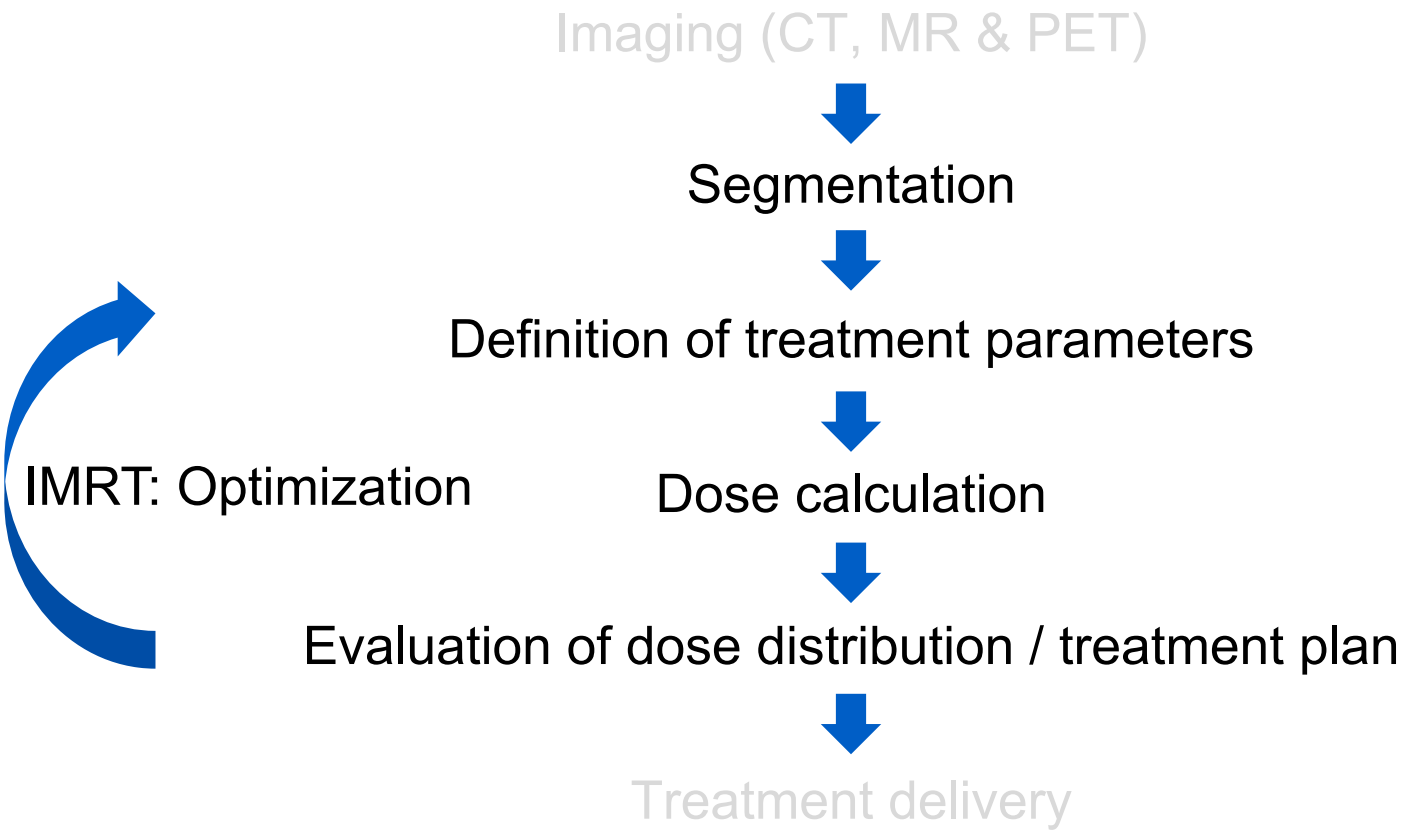
Radiation treatment planning loop



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Outline

- Segmentation
- Dose calculation
- Definition of treatment parameters
- Evaluation of dose distribution / treatment plan
- IMRT & Optimization

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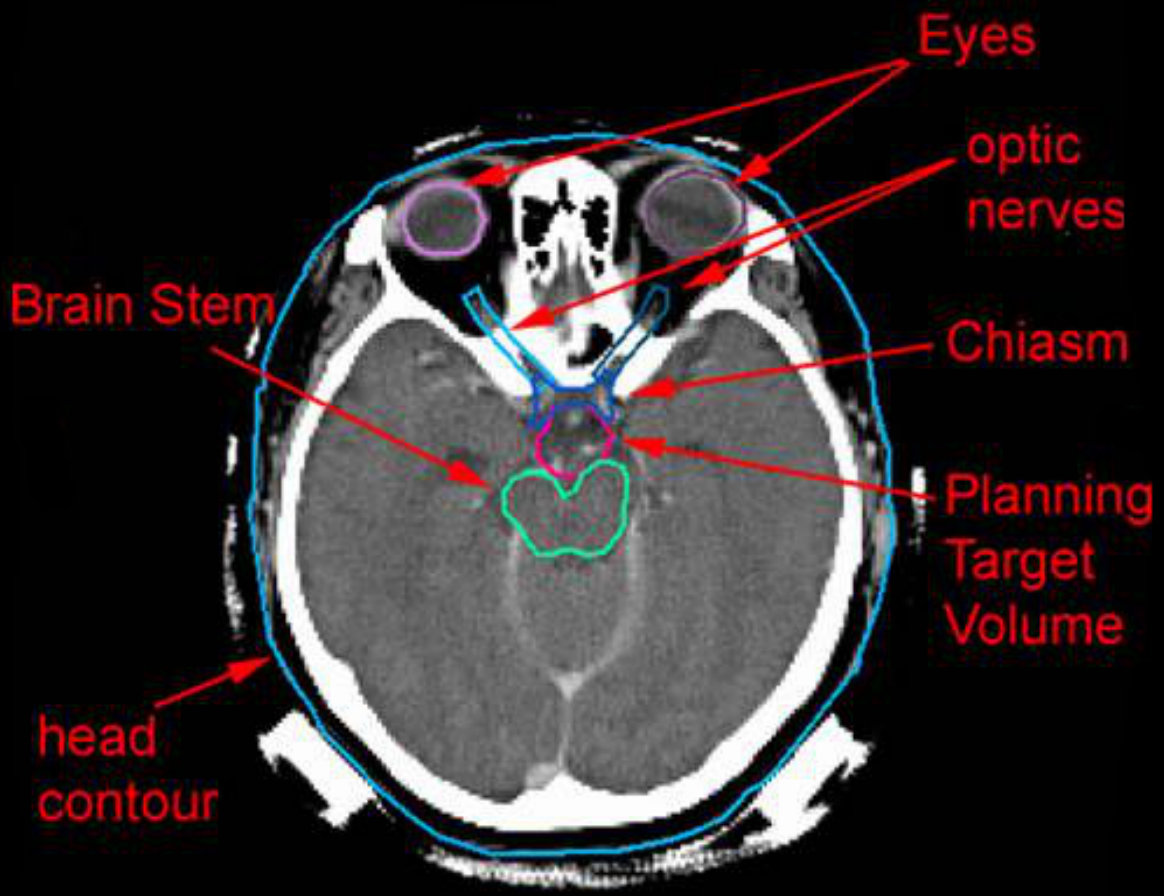
Delineation of target and OAR's



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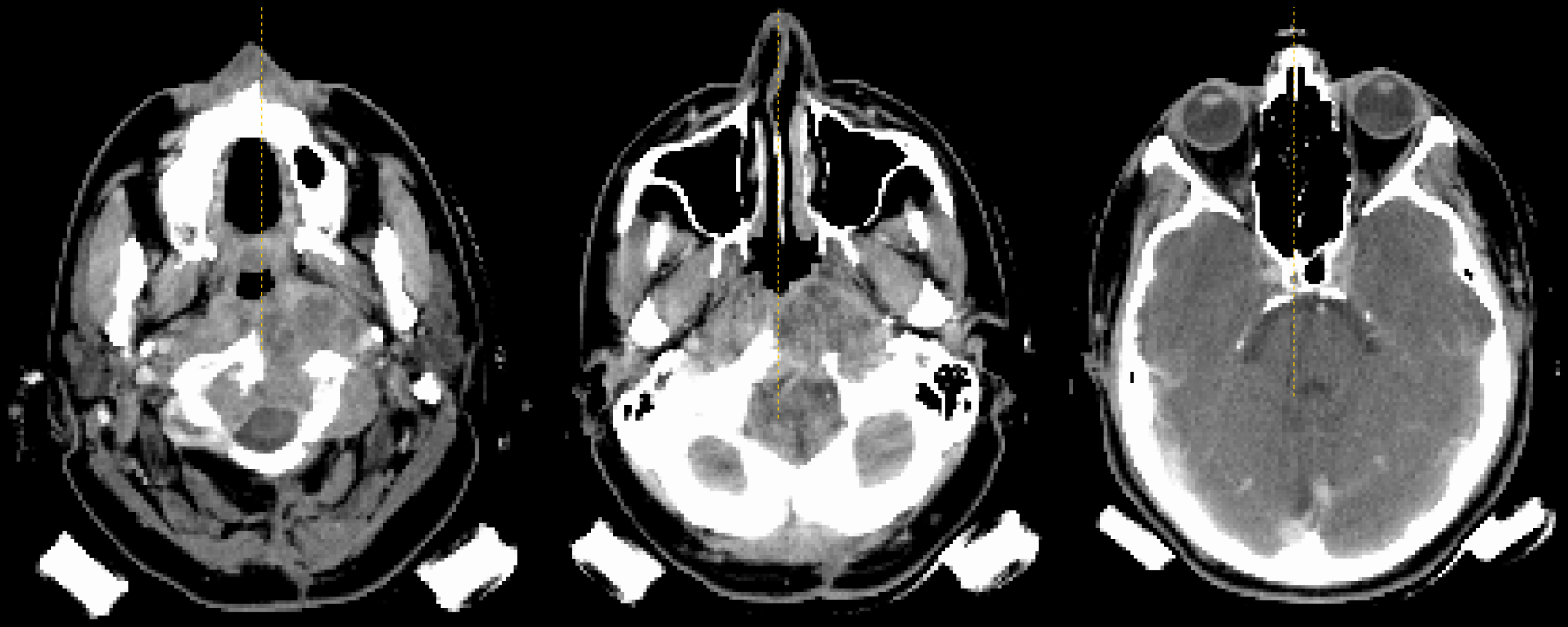
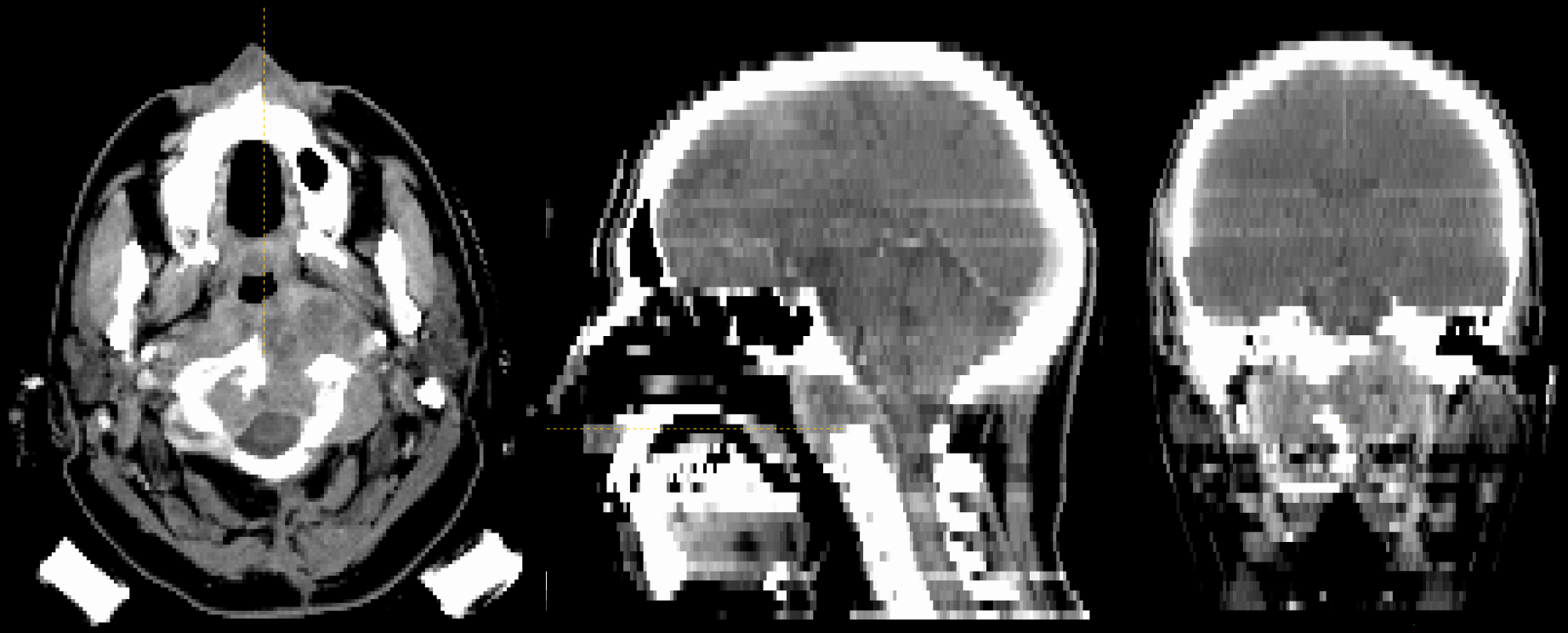
CT images for treatment planning



transversal slices

CT images for treatment planning



transversal

sagittal

coronal

Image registration: CT & MR

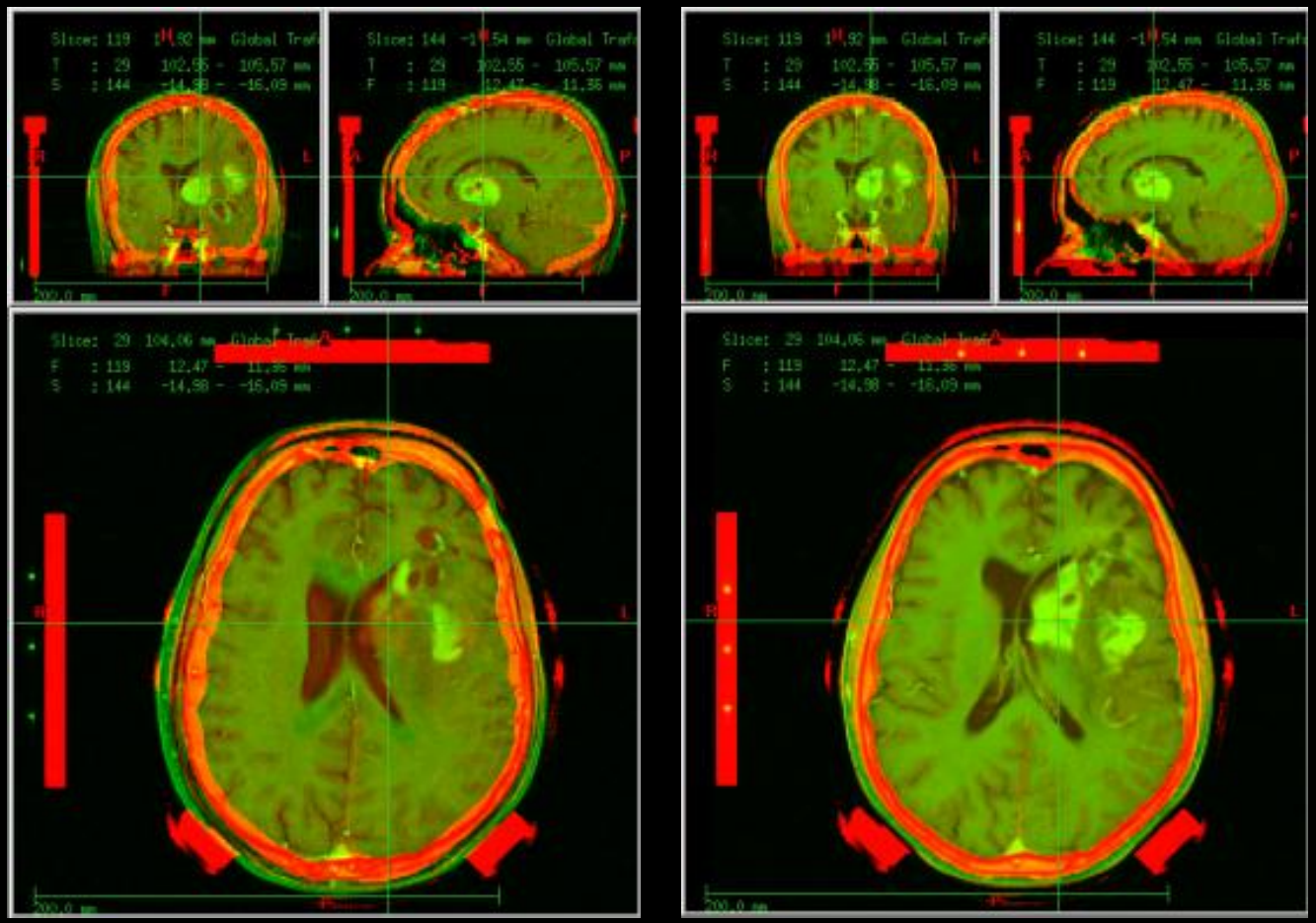


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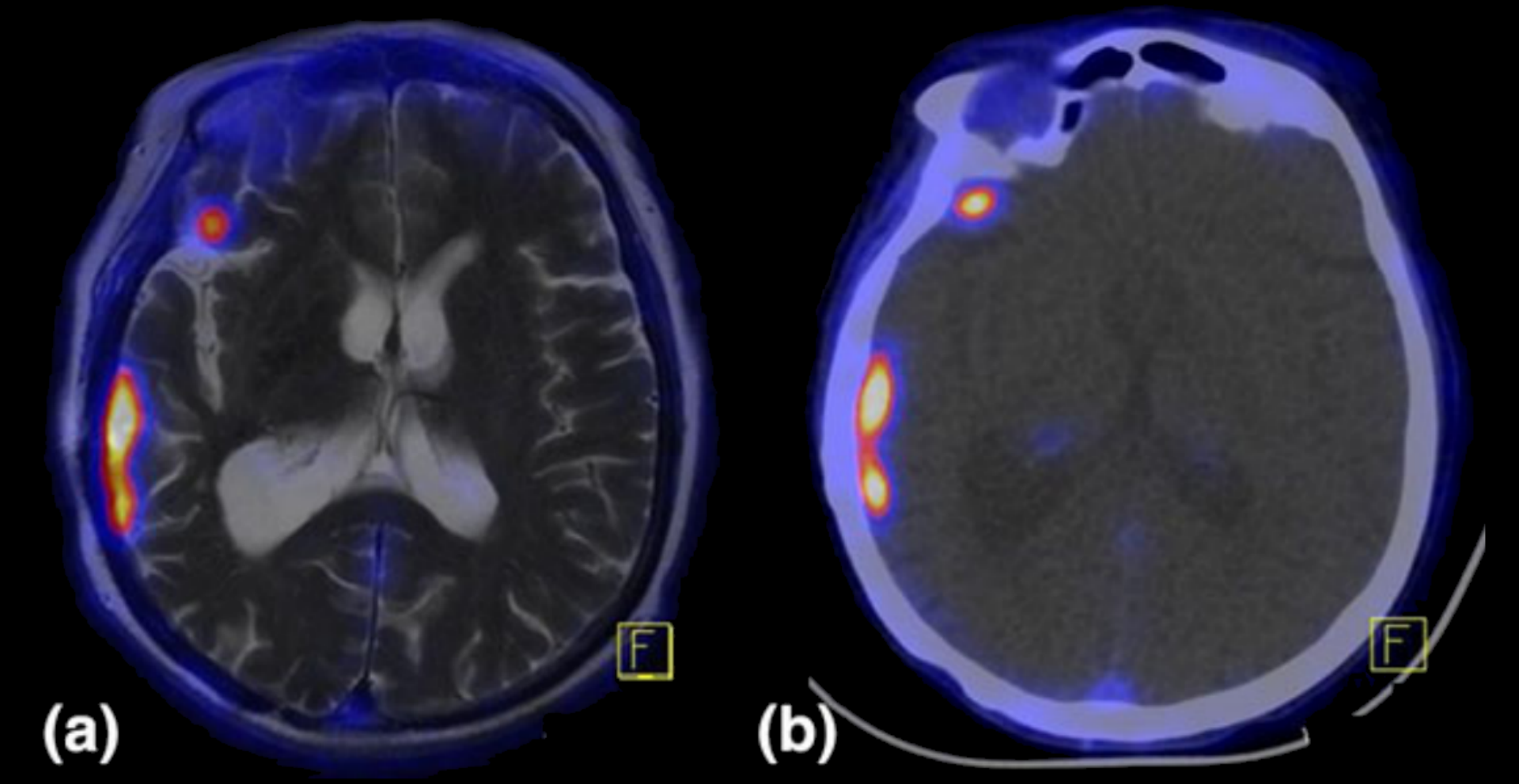
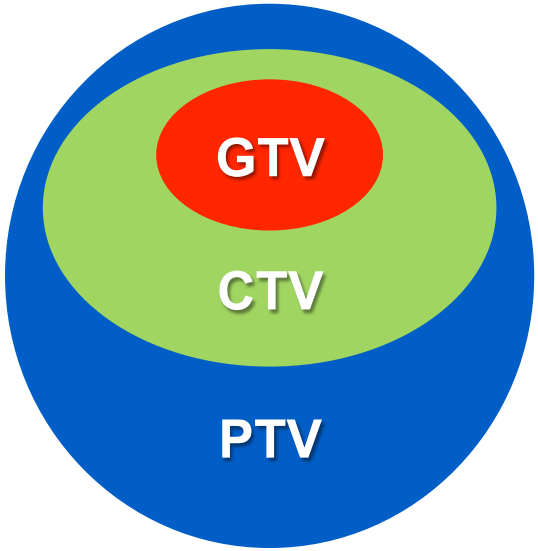
Image registration: PET & MR/CT



D. Thorwarth et al.: Potential role of PET/MRI in radiotherapy treatment planning

Target volume definition



- GTV = Gross tumor volume

  Clinically evident tumor volume as may be visible in diagnositiv images or may be palpable in a clinical examination

- CTV = Clinical target colume

  Covers GTV and margin containing microscsopic spread of tumor cells that is neither palpable nor visible

- PTV = Planning target volume

  Margin to include setup uncertainties, organ motion, organ deformation, and delination uncertainties

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ICRU report 50

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Target volume definition: Radiation Side Effects is Volume Dependent

D. Verellen et al.: Innovations in image guided radiotherapy 2007 Nature Reviews Cancer

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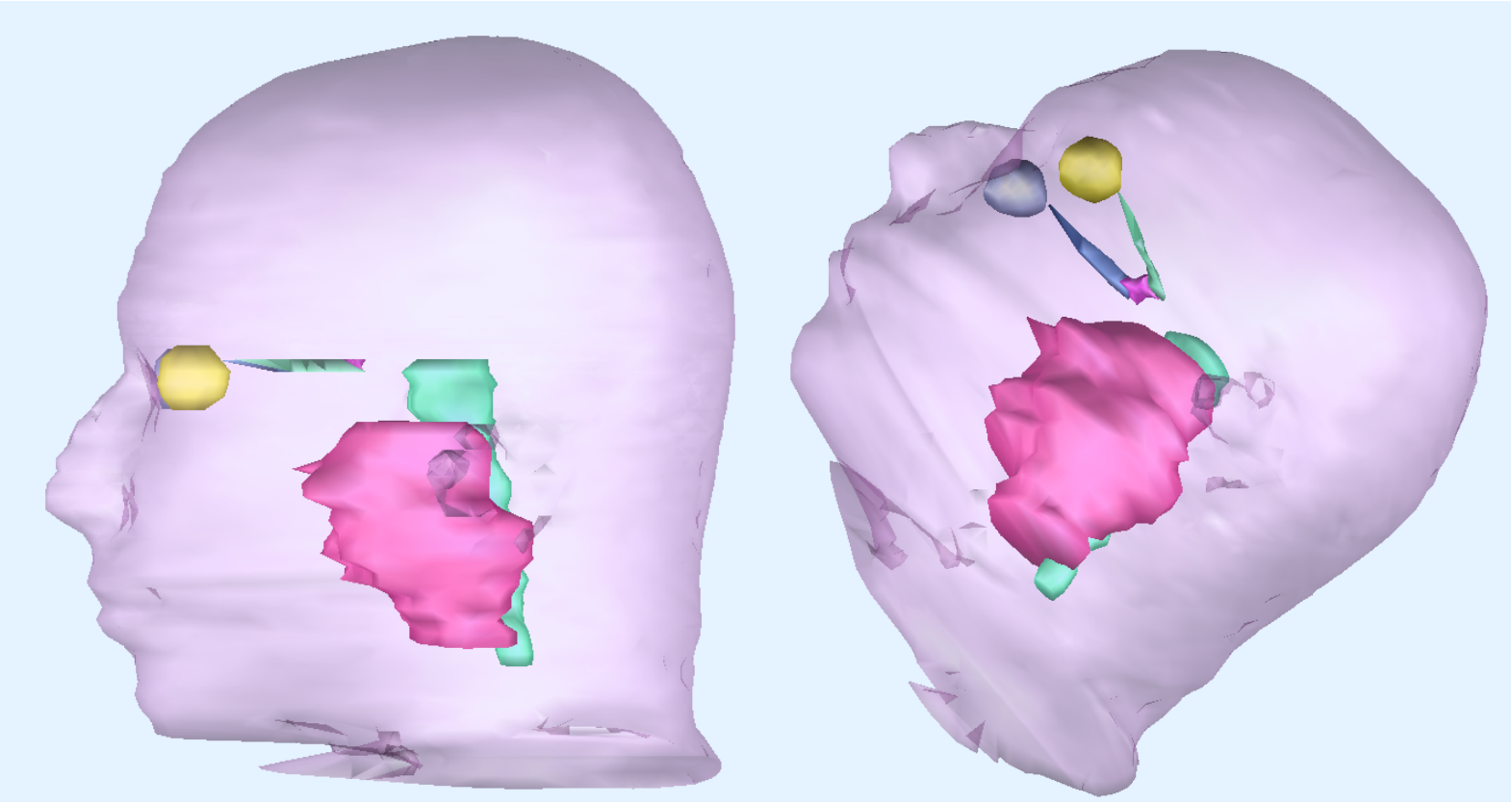
Observer's view

- delineate structures in all CT slices
- build 3D model



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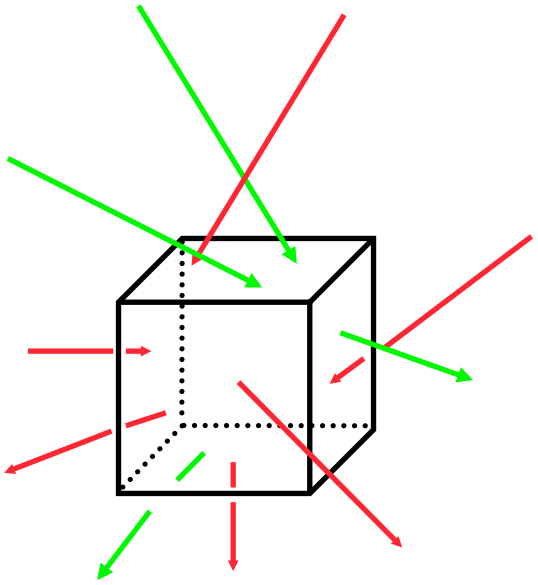
Dose definition

Dose = Divergence of vectorial energy fluence $\mathrm{E}\Phi$ / absorbed Energy per mass

$$D = -\,1/\varrho\ \nabla\cdot(\mathrm{E}\Phi) = \Delta E/\Delta m \quad \text{with} \quad 1\ Gy = 1\ J/kg$$



primary photons
scattered photons
electrons
neutrons, ...

Slide by courtesy of Dr. Simeon Nill

Why do we calculate 3D dose distributions for treatment planning?

- Because we can…

- As a surrogate for cell kill

  → Naive dose concept with evident weak spots

    - Individual radiosensitivity for different cell types (both cancerous and healthy)

    - Other factors: ionization density, dose rate, oxygenation, etc.

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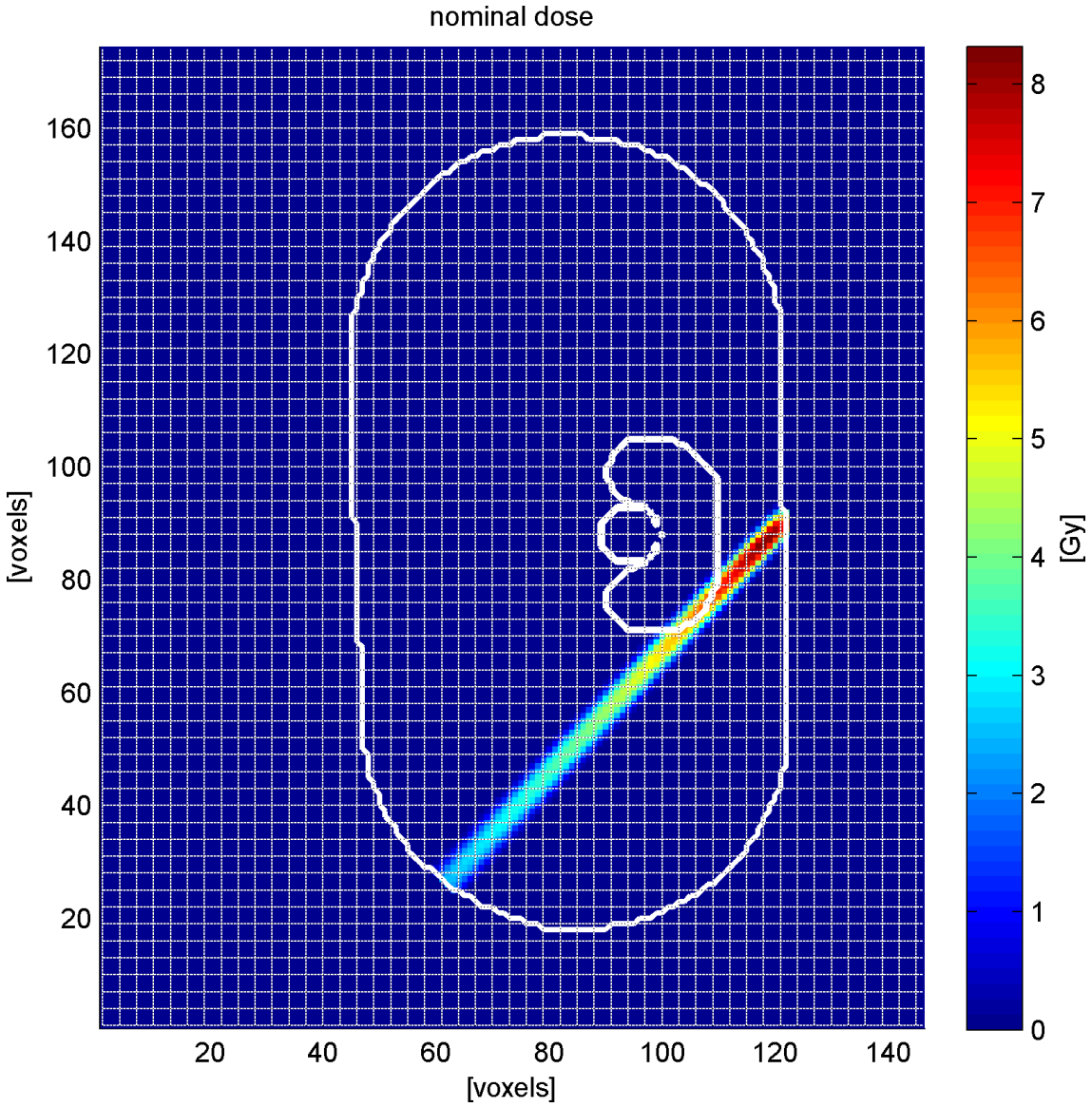
Dose calculation for open fields in water



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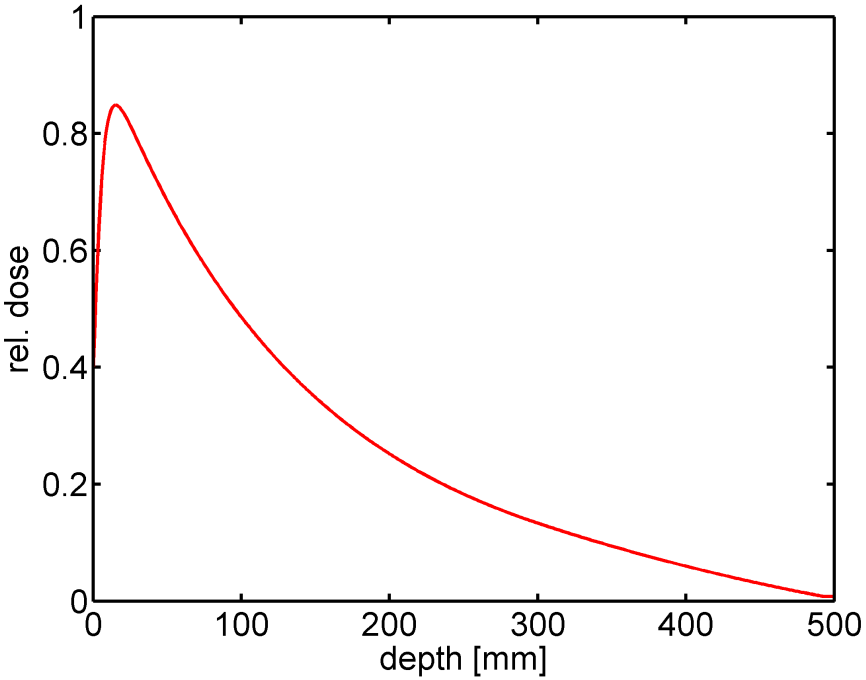
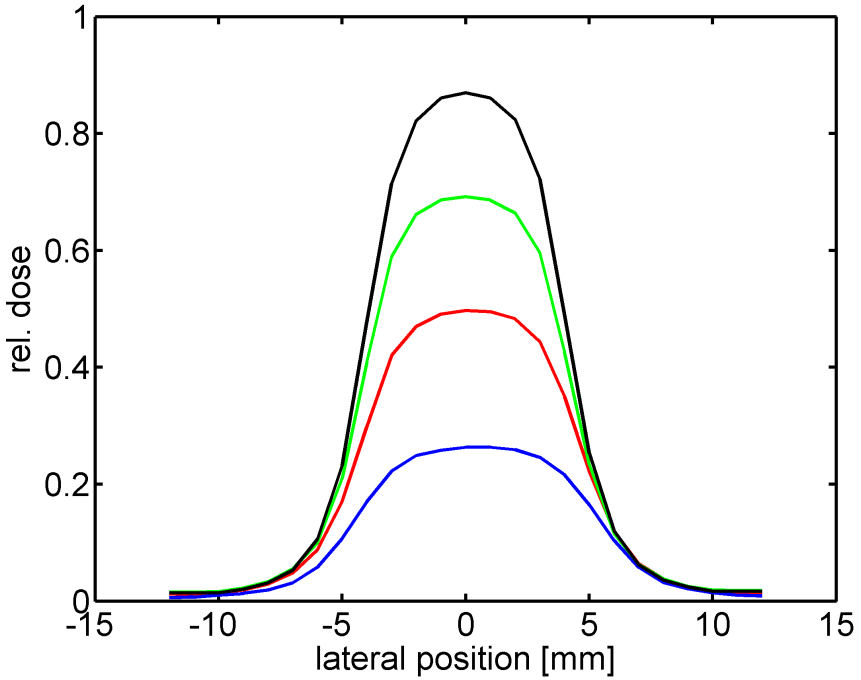
Dose calculation for open fields in water

- Measured depth dose and lateral profiles in water





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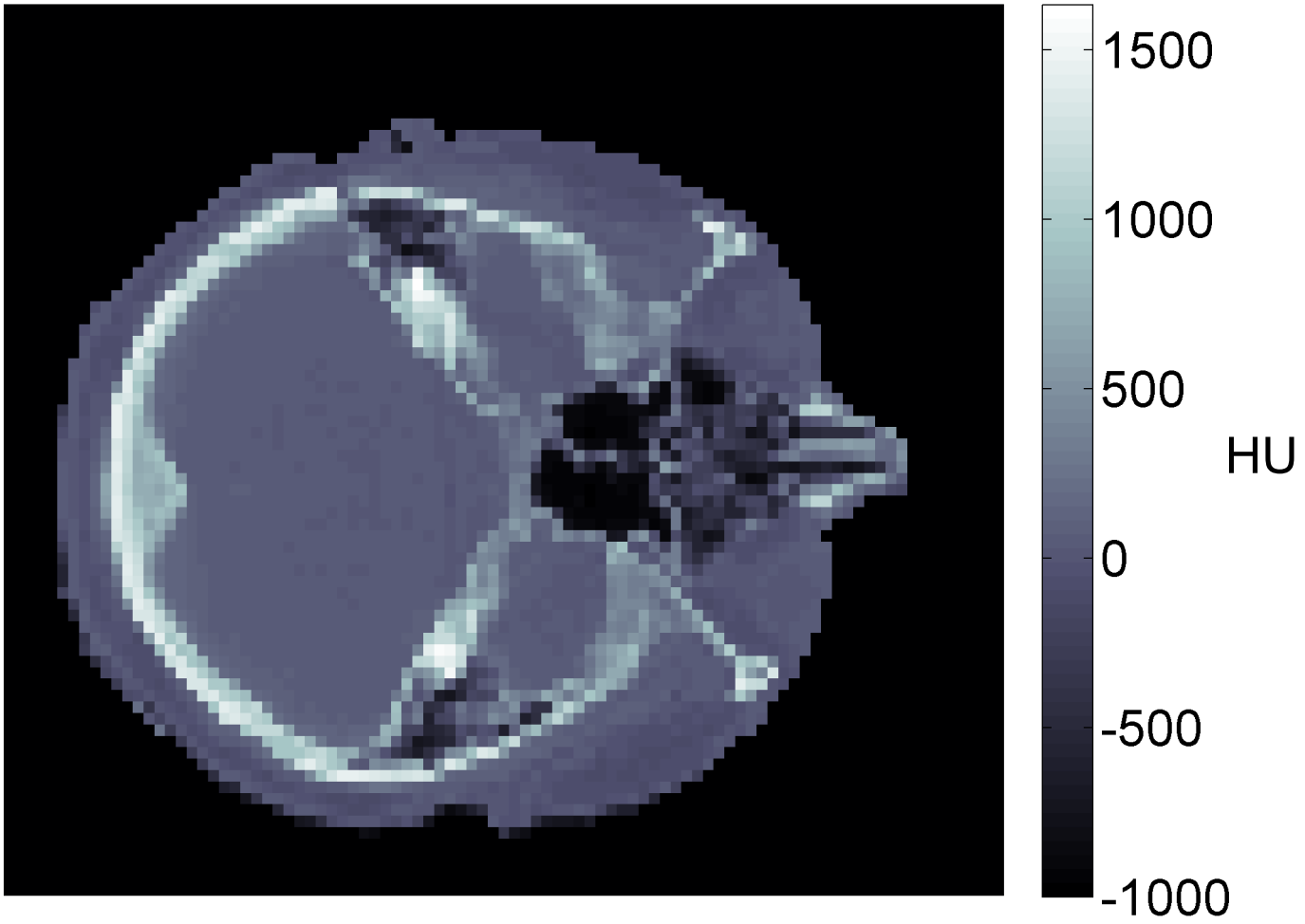
Base data for dose calculation: CT / Hounsfield units



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Base data for dose calculation: Relative electron densities

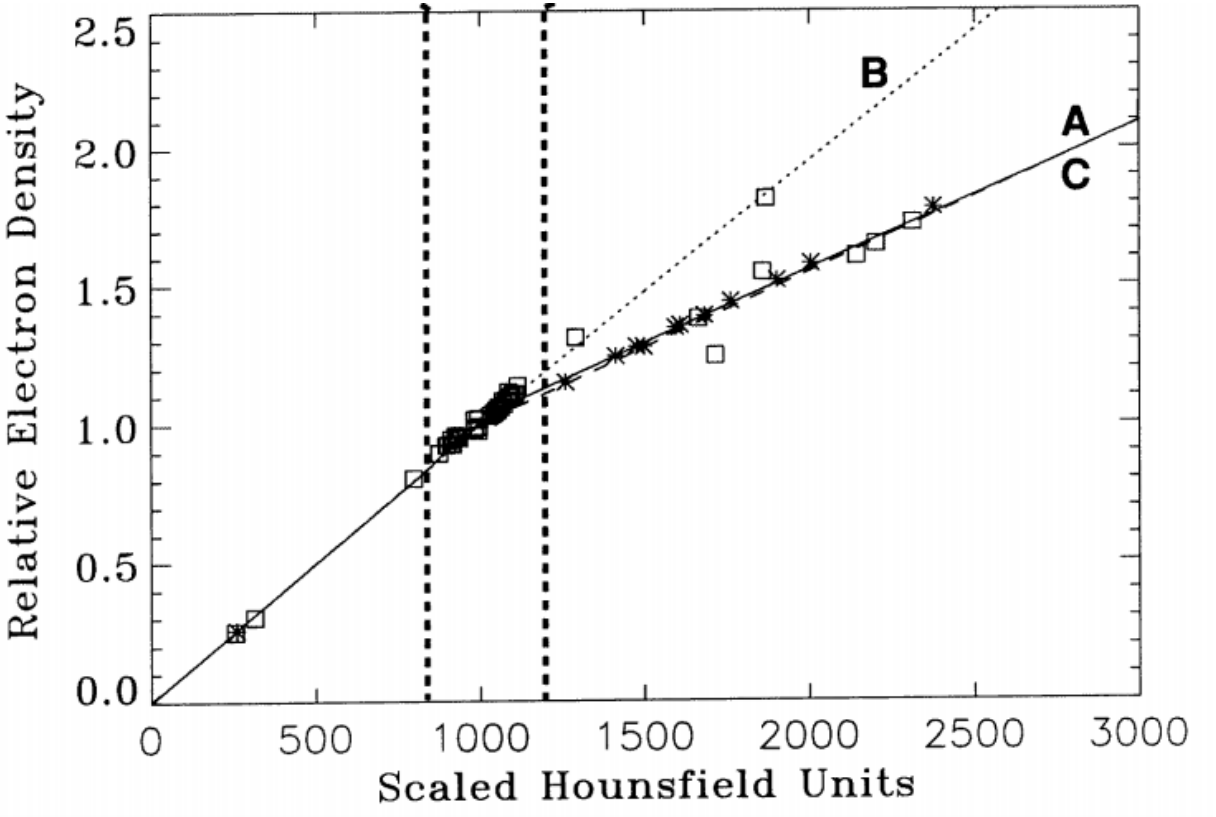
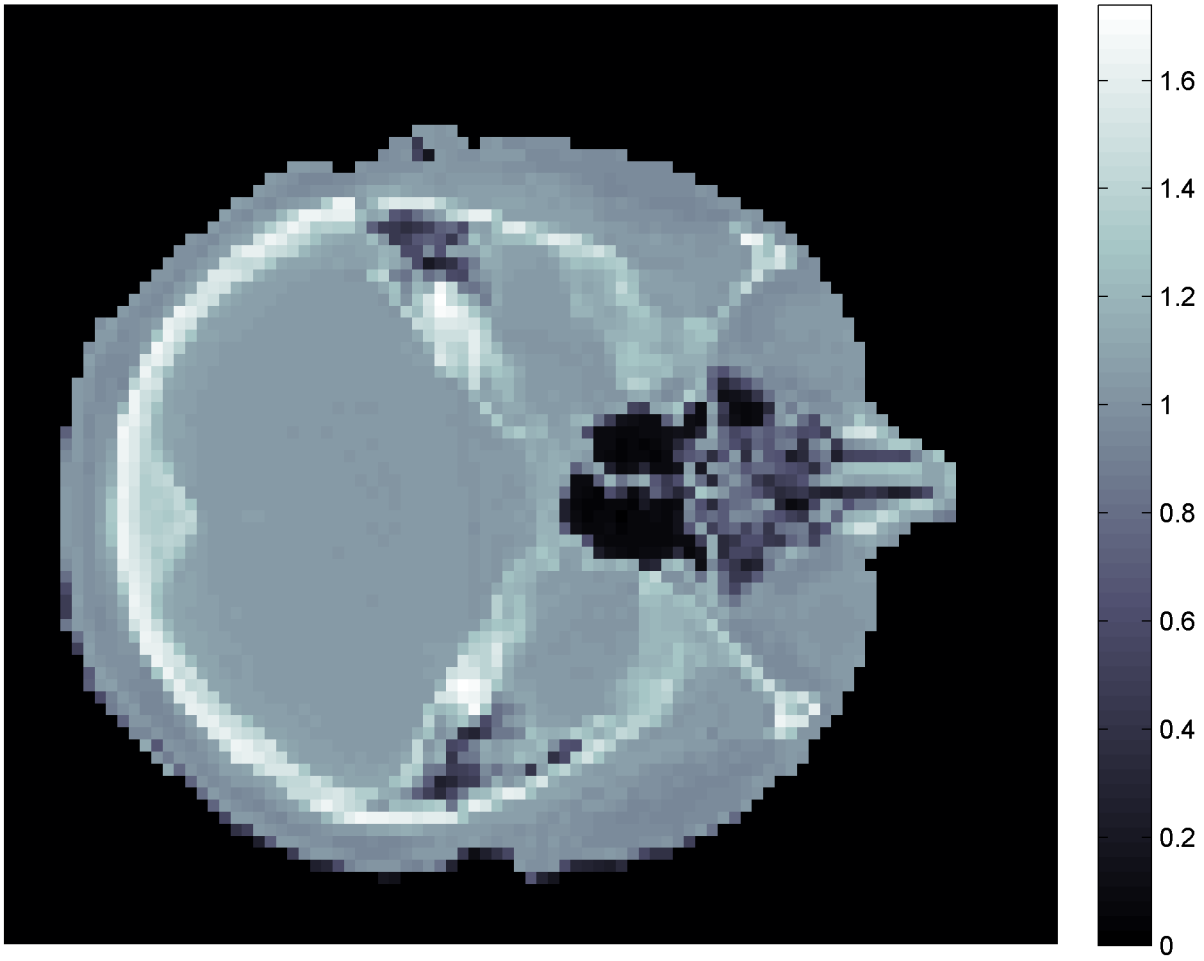


Figure 3. Calibration curves for the transformation of Hounsfield values into relative electron density (ρ_e). The solid line shows the stoichiometric calibration (A) for biological tissues, the dotted line the tissue substitute calibration for Mylar/Melinex/PTFE (B) and the dashed line the tissue substitute calibration for B110/SB5 (C). The squares represent calculations for tissue substitutes and the stars are calculations based on the chemical composition of real tissues. The small plot shows in detail the Hounsfield number range corresponding to soft tissue.

*U Schneider, E Pedroni, A Lomax: The calibration of CT Hounsfield units for radiotherapy treatment planning **1995** PBM 41*

Base data for dose calculation: Relative electron densities



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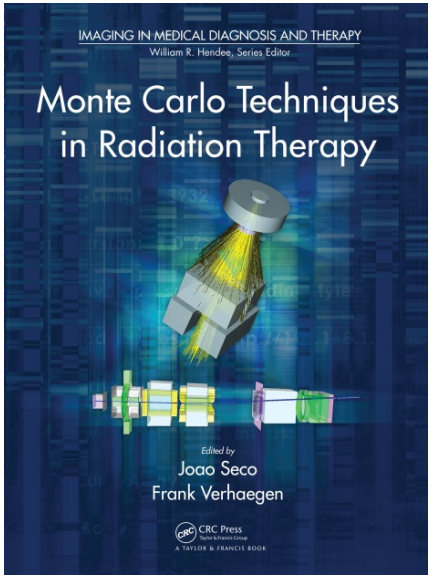
Dose calculation for irregular fields in heterogeneous tissues

- Pencil beam algorithm
- Collapsed cone / convolution super position algorithm
- Monte Carlo algorithm

→ Tradeoff between speed and accuracy



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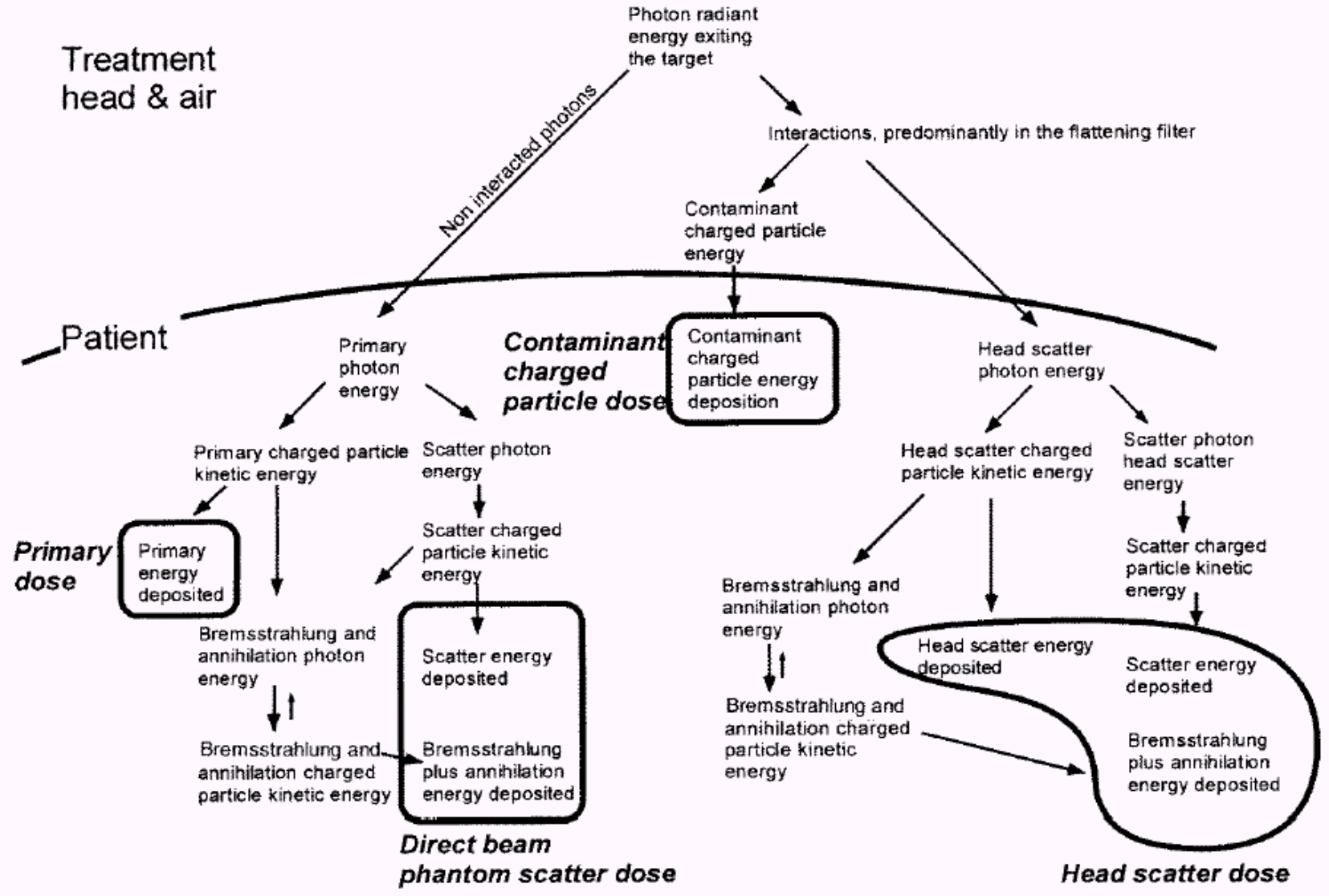
Dose calculation for irregular fields in heterogeneous tissues



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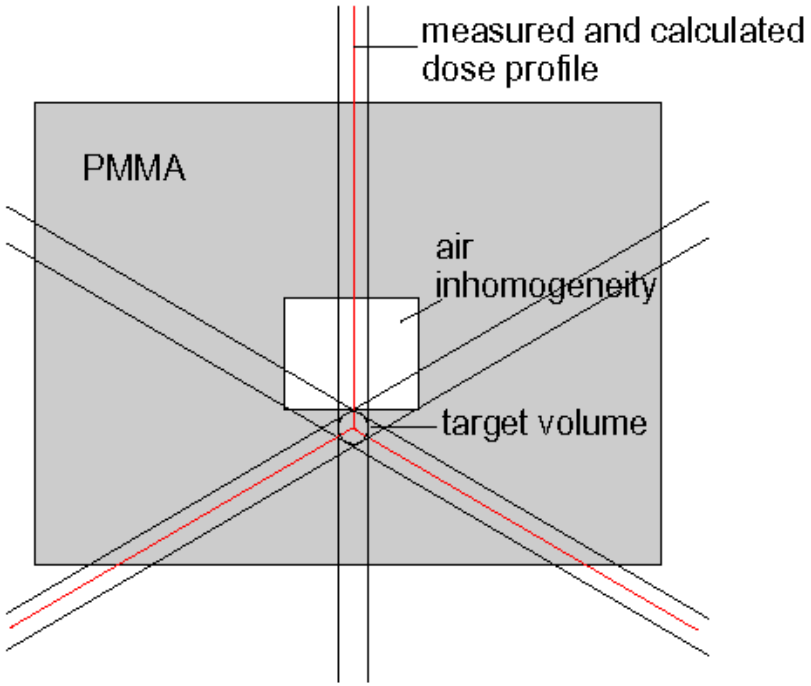
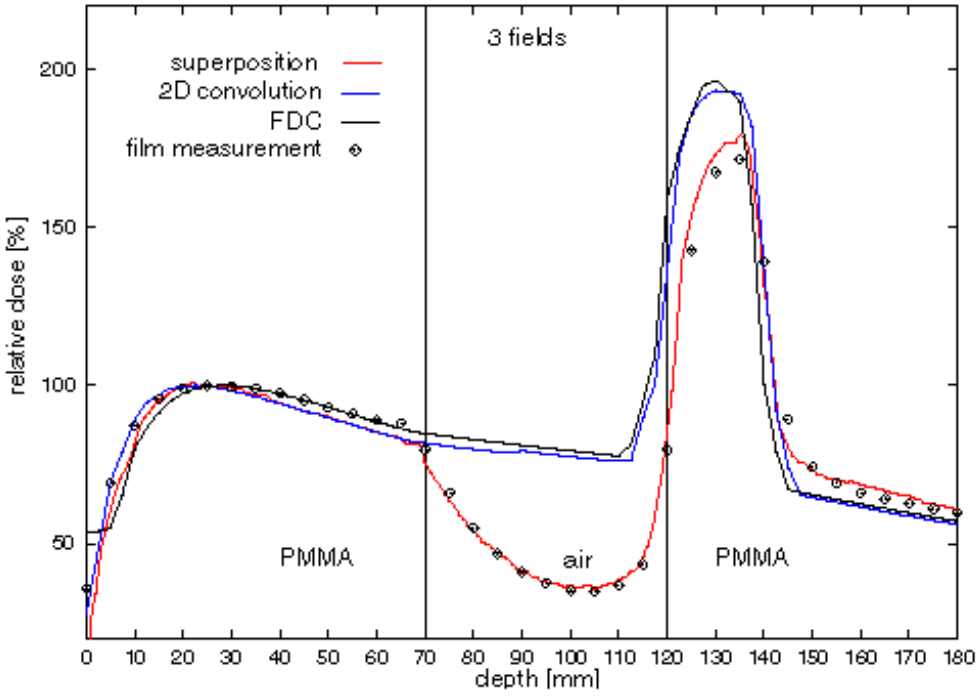
Dose calculation for irregular fields in heterogeneous tissues





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Outline

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- Optimization

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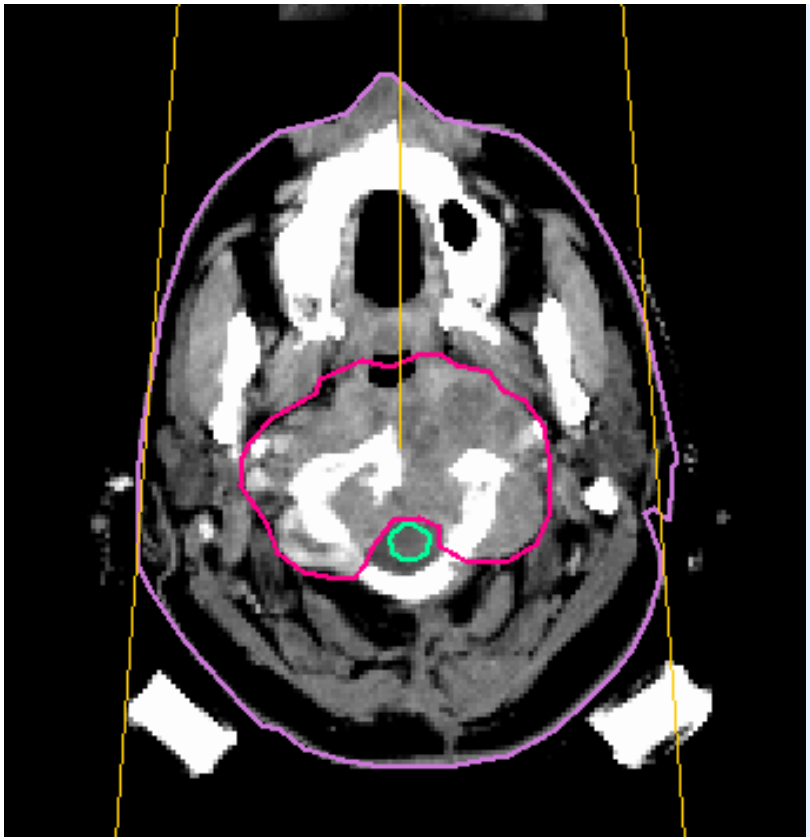
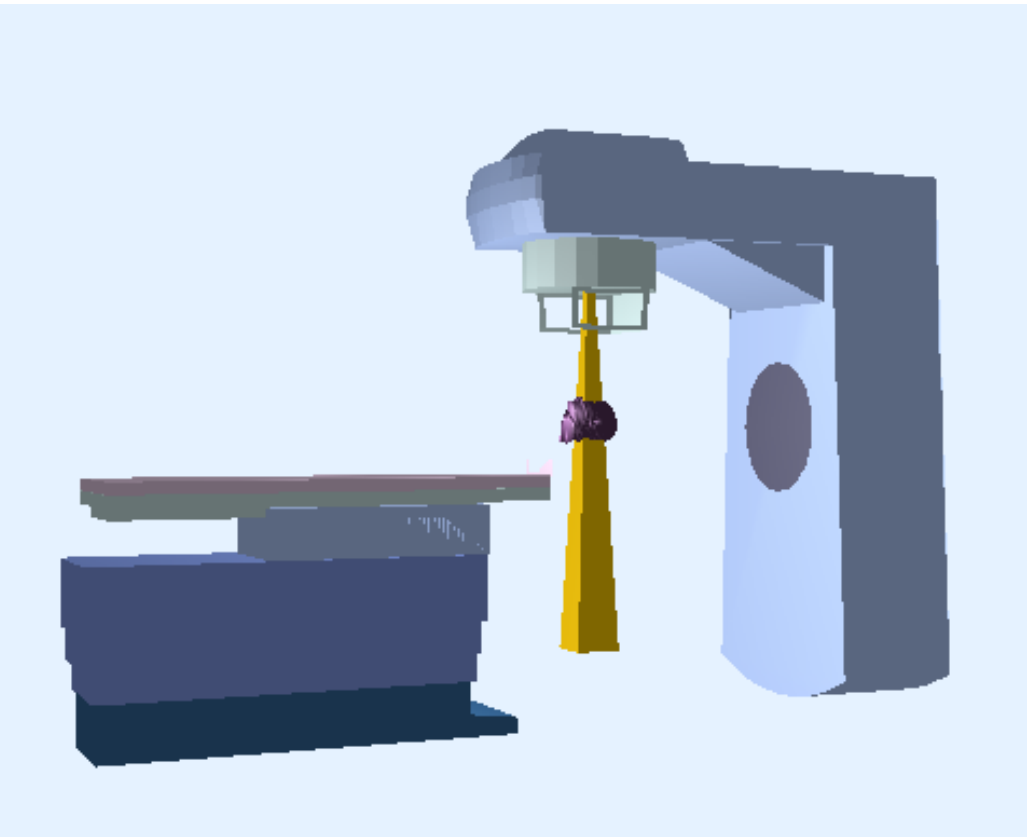
The first beam





Slide by courtesy of Dr. Simeon Nill

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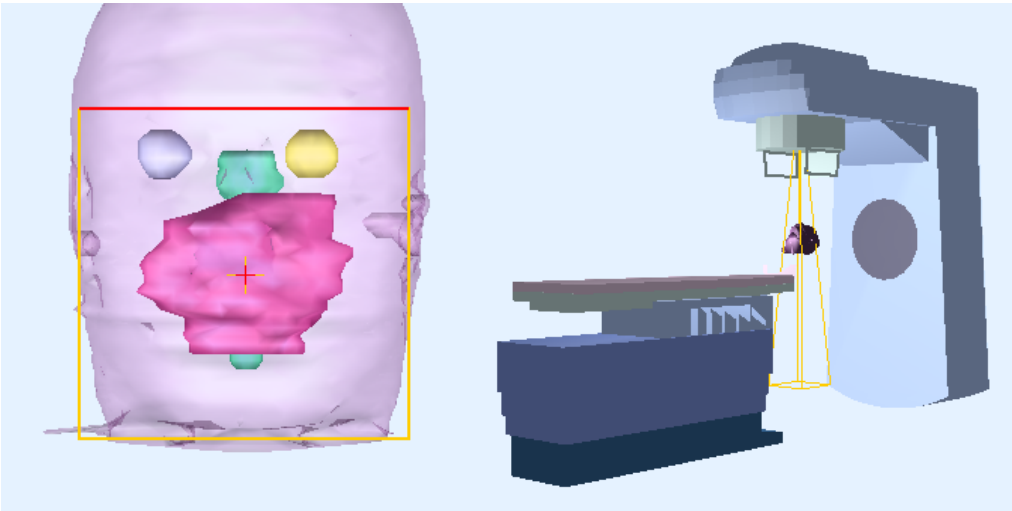
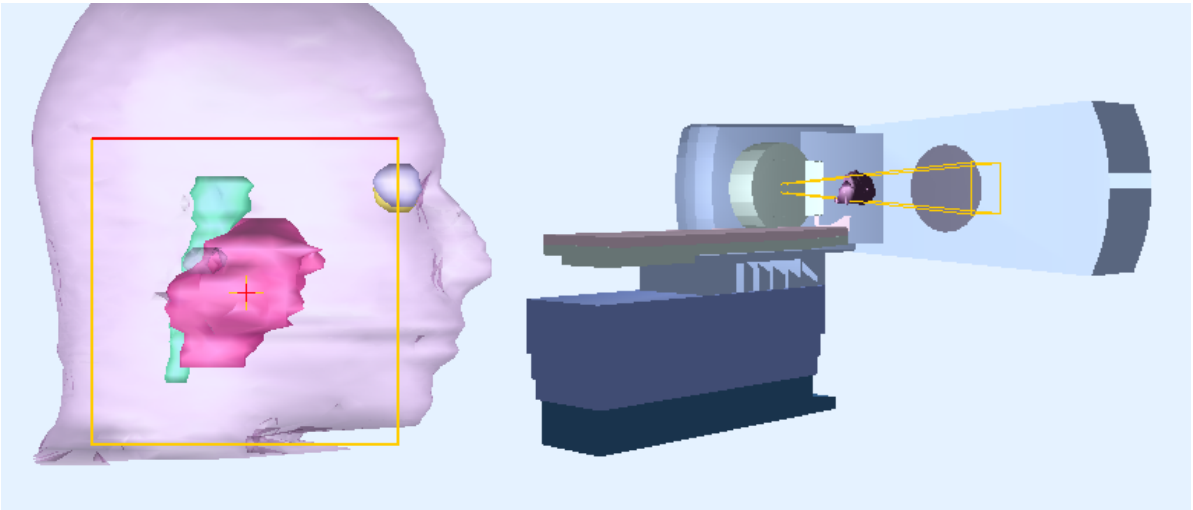
Beam’s eye view

Gantry 0°



Gantry -90°



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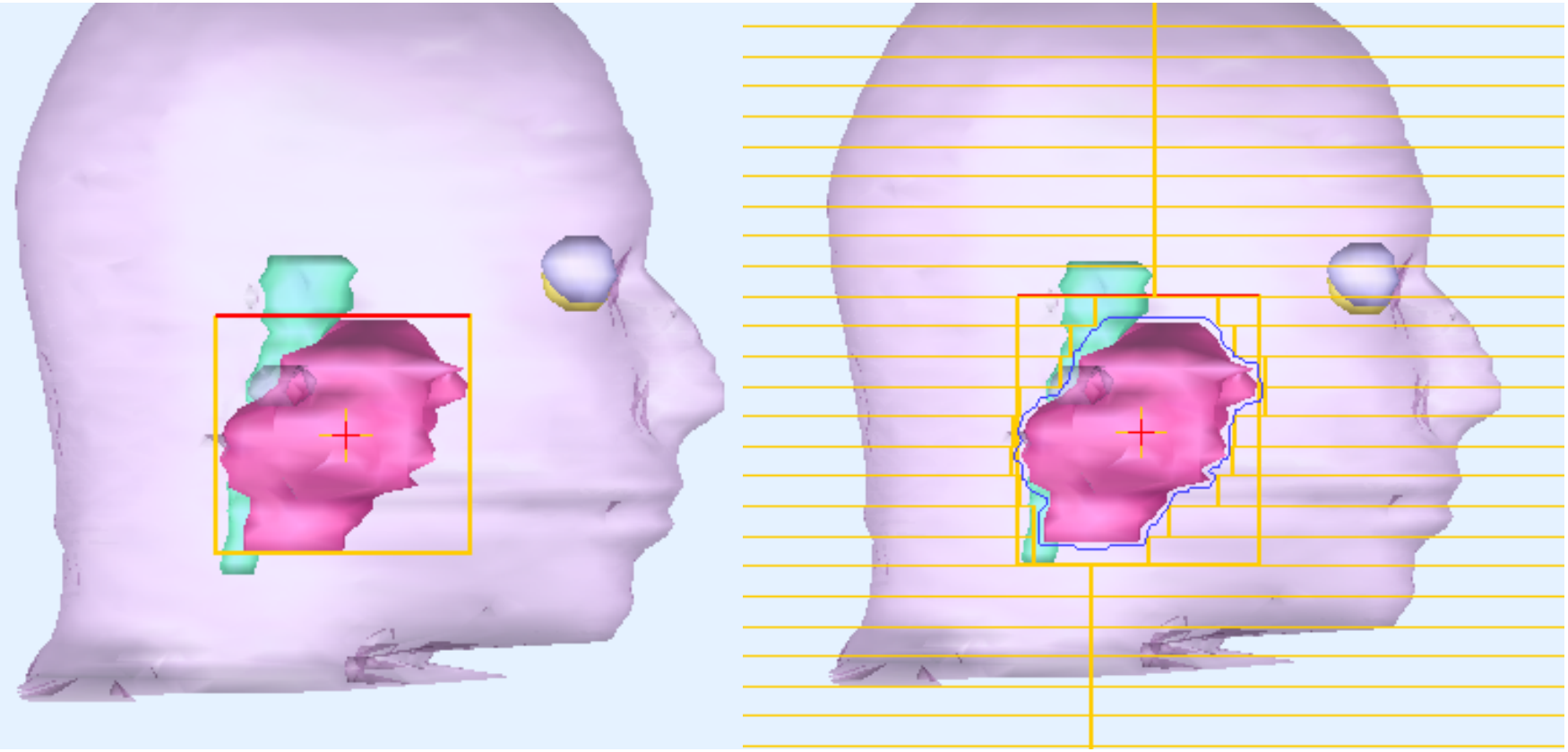
Beam limiting devices



rectangular field

irregular field (MLC)

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Multileaf collimator

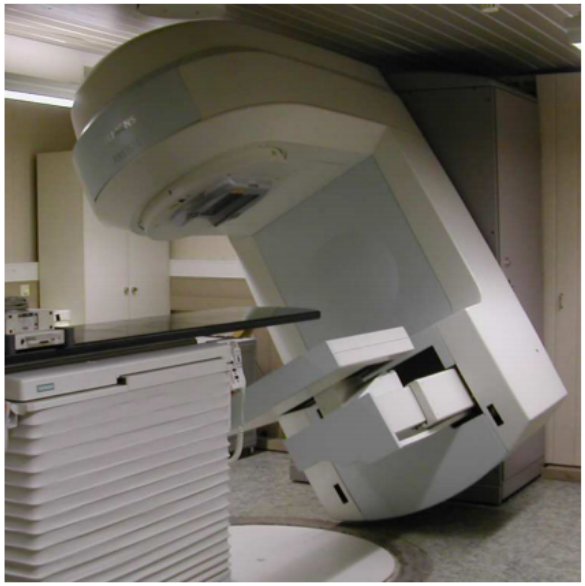


Figure 2.4: *Photograph showing the ARTISTE™, Siemens Healthcare, at the DKFZ. At the lower end of the gantry, an electronic portal imaging device for MV-imaging is shown in its extended position. It can be utilized to monitor the treatment beam.*

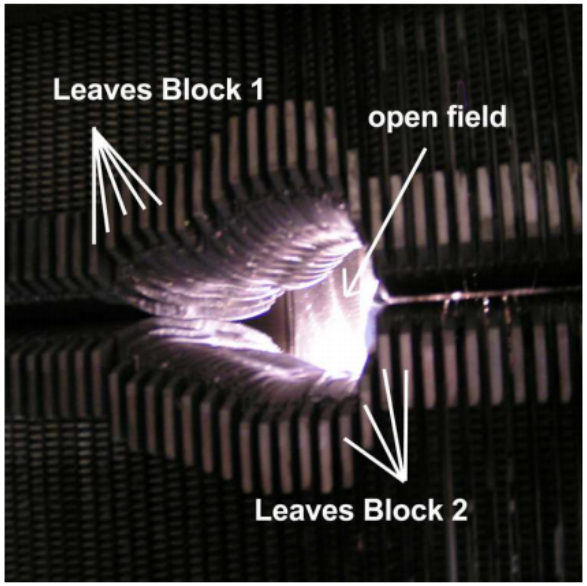
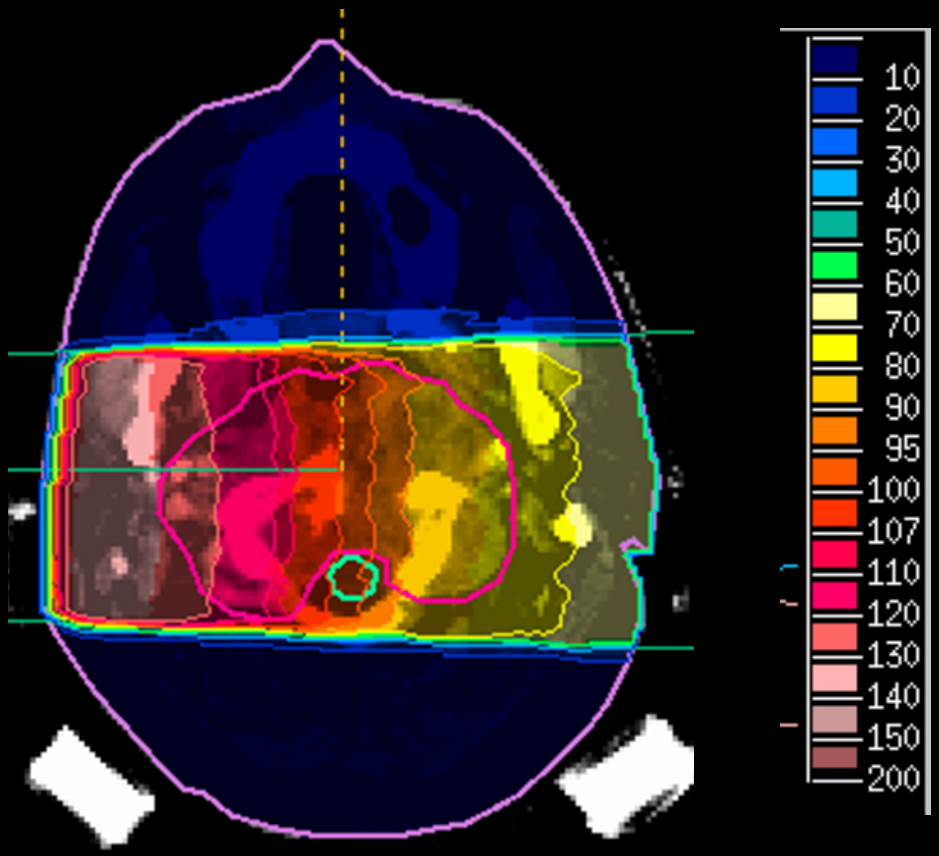


Figure 2.5: *Field shape defined by a MLC. The leaves are moved into the radiation beam to block parts of the beam so that only the planned area is irradiated. In this way, different fluence distributions are deliverable.*

Tacke: Adaptation of High-Precision Radiotherapy to Moving Target Volumes in Real-Time Using Dynamic Multileaf Collimators 2009

Dose distribution for one beam



➔ need more than one beam!!!

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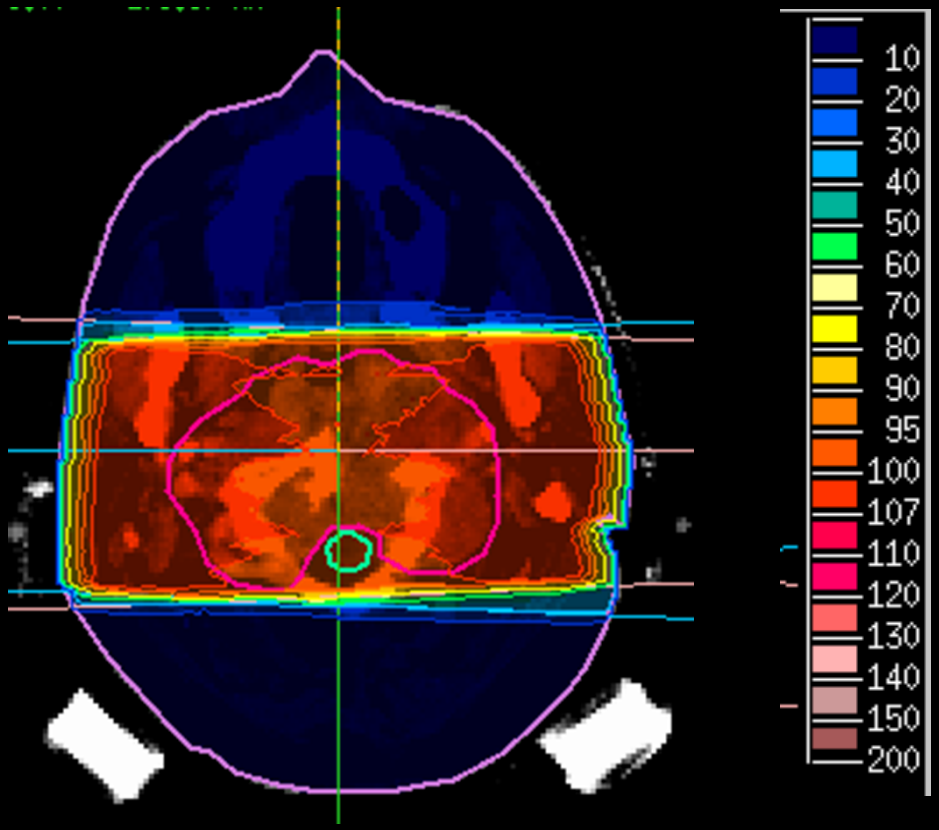
Dose distribution for two beams



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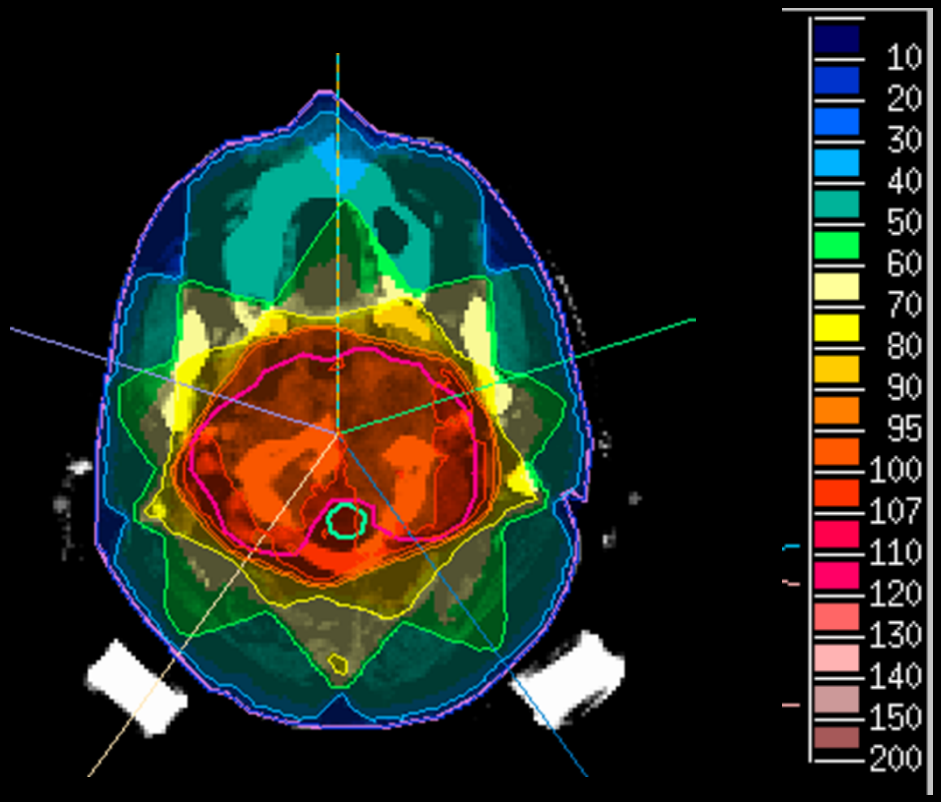
Dose distribution for five conformal beams



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Treatment plan quality indicators

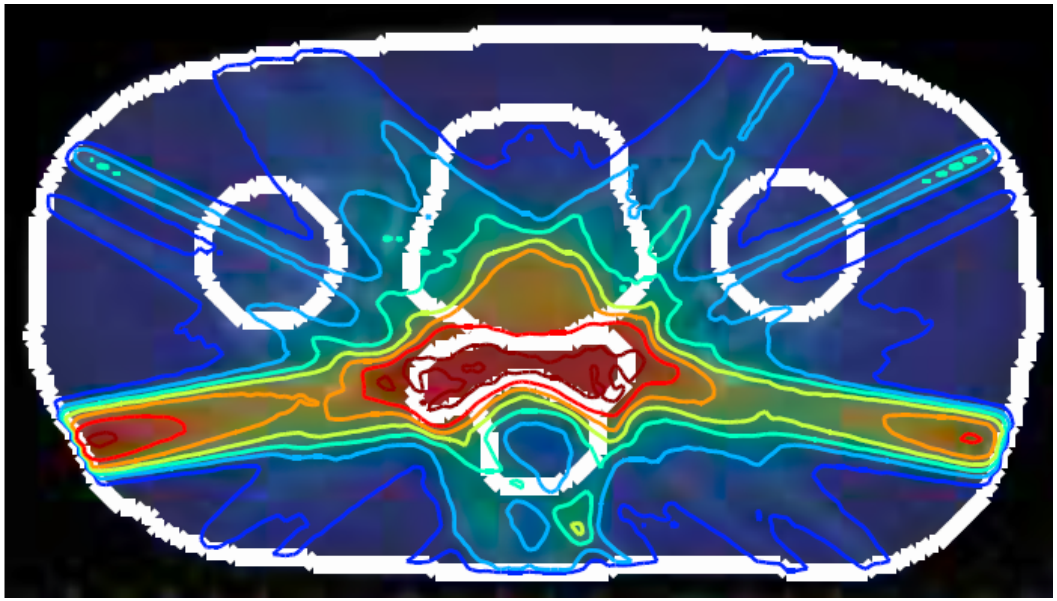
- Inspection of transversal/sagital/frontal 2D dose distributions
  Conformality, hot spots, cold spots

- Homogeneity measures

- Conformity indices
  $Vol_{Target}(D>95\%)/Vol(D>95\%)$

- Dose statistics
  Mean, maximum, minimum dose

- Dose volume histograms
  2D representation of 3D dose distribution



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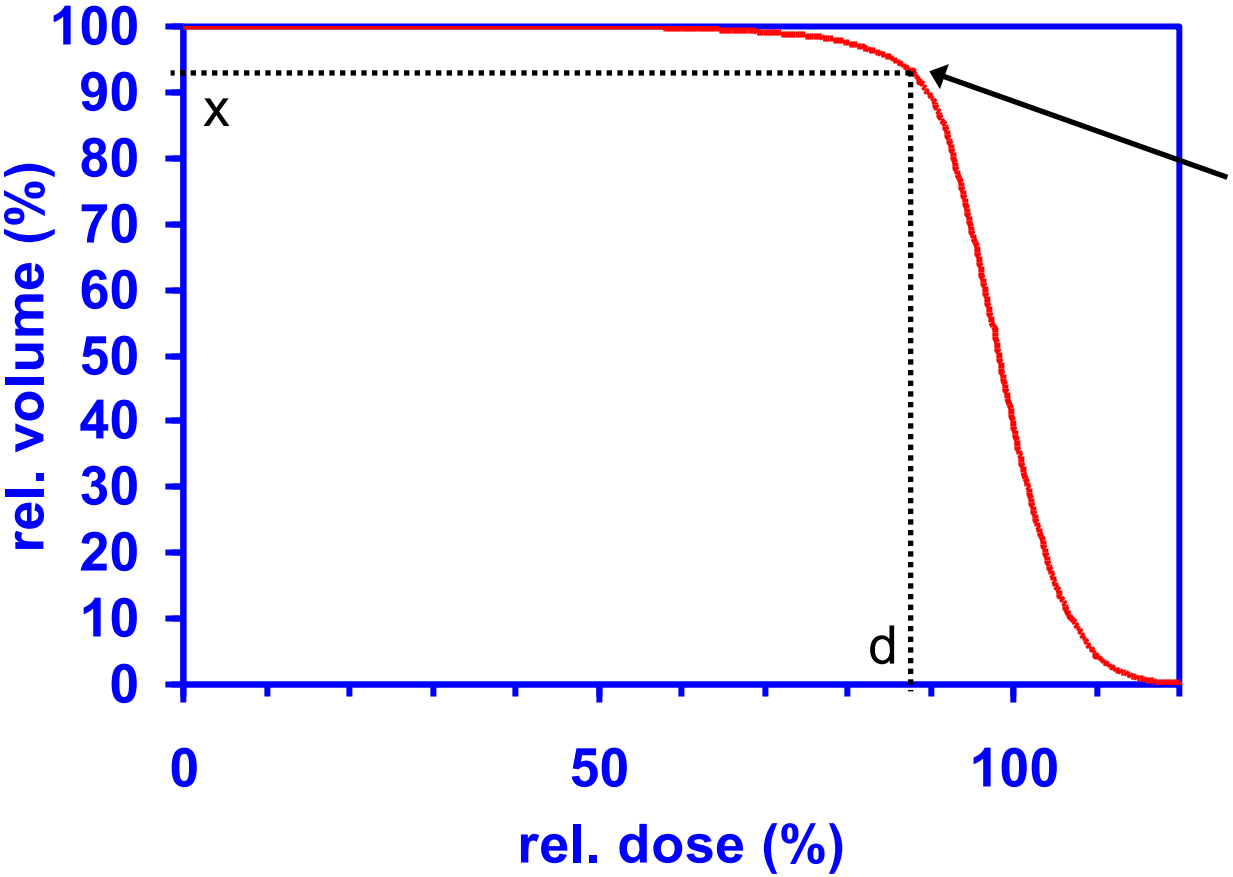
Dose volume histogram



x% of the volume receives at least d% of the prescribed dose

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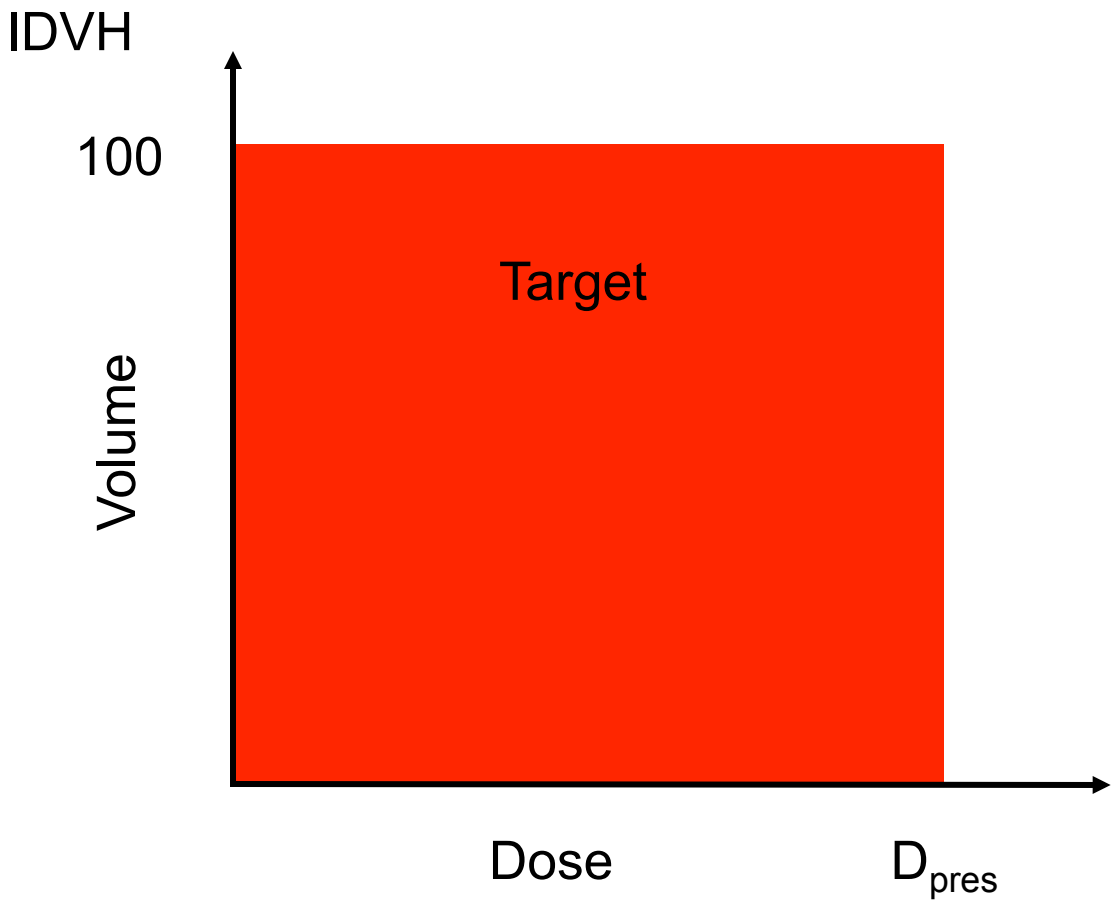
Ideal DVHs - Targets



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Ideal DVHs - OARs

- Tolerance doses
- Irradiated volume
- Tissue organization
  - Assume ‚fictional' functional sub-units of a tissue
  - Their structural organization with respect to a certain functionality of a tissue is assumed to be either:
    a) parallel
    b) serial

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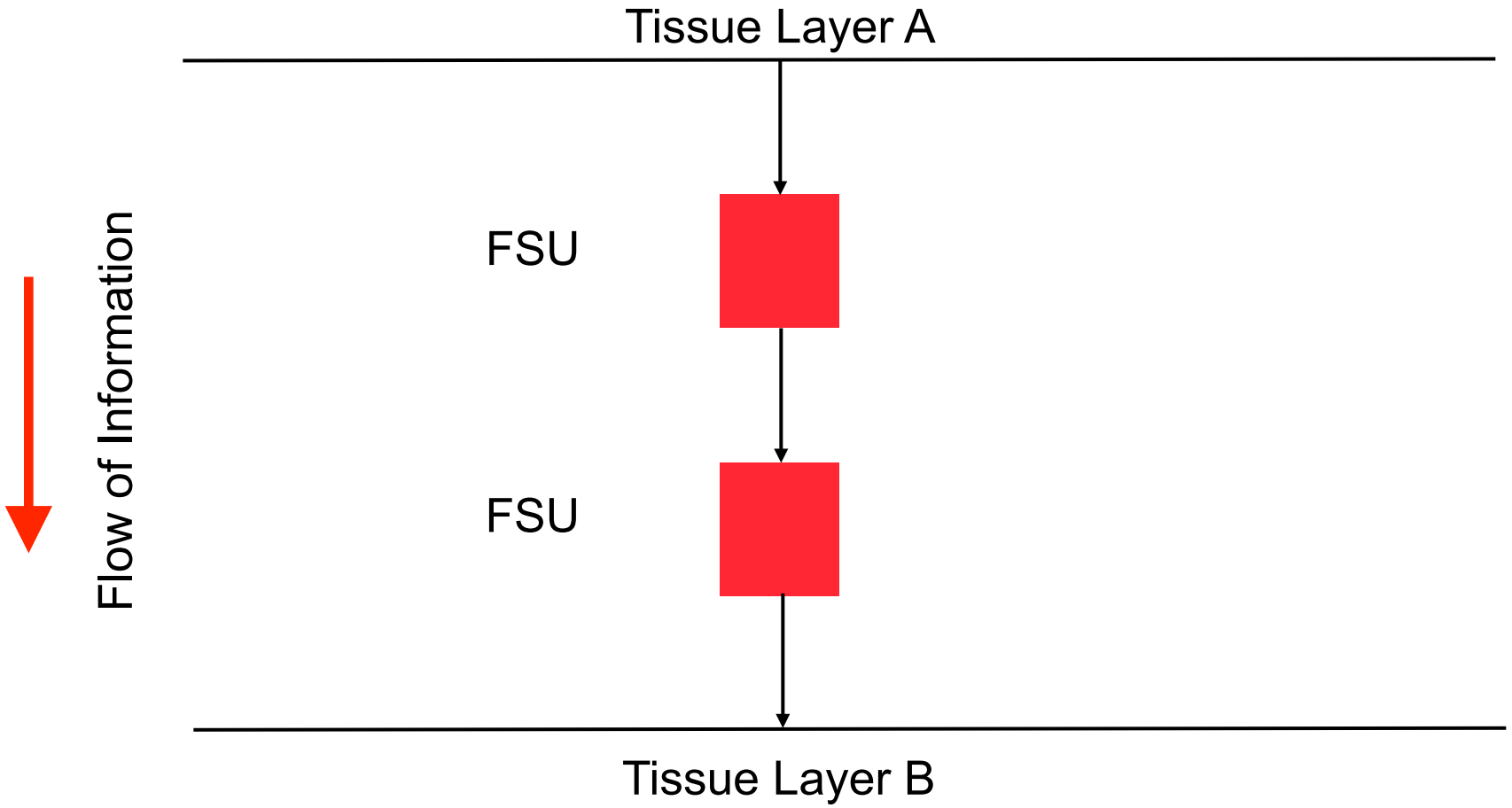
OARs – Functionality – Serial Tissues



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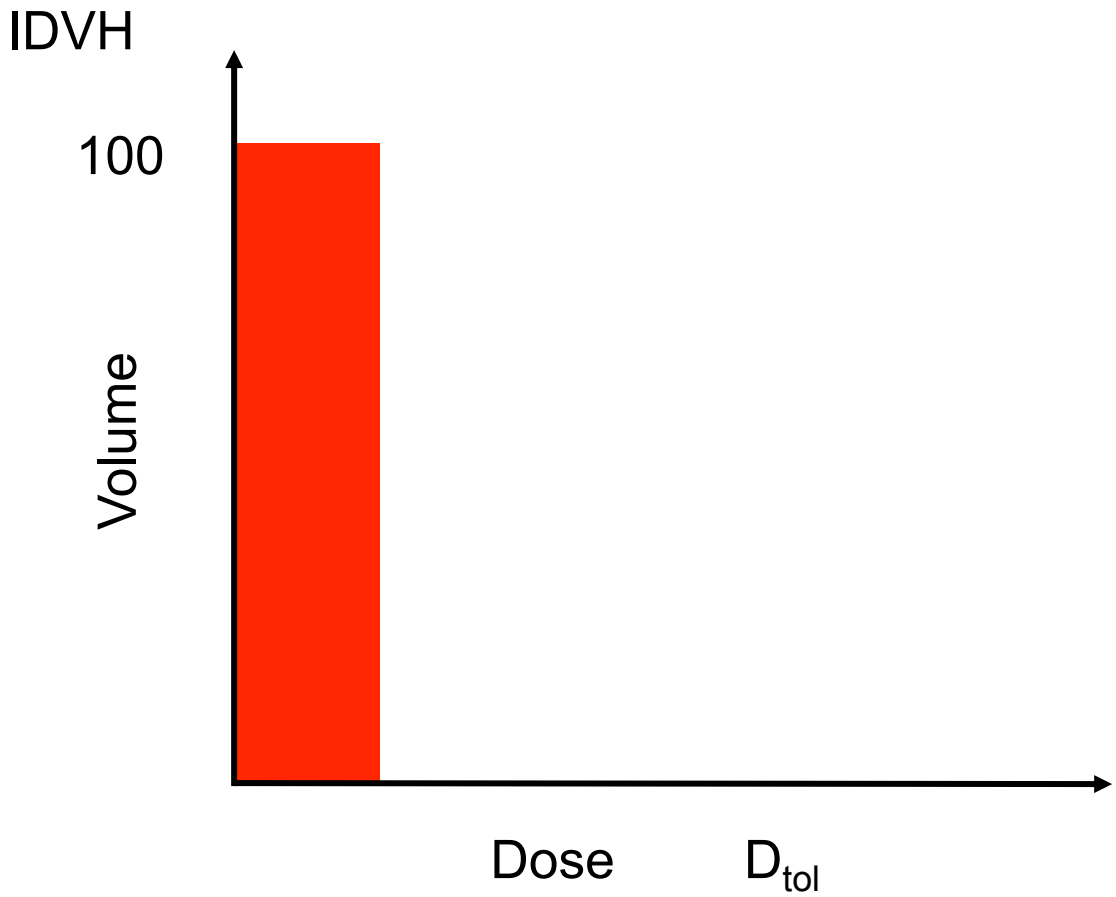
OARs – Serial Tissues - Ideal DVHs



- Functionality determined by tolerance dose of the FSU
- Failure of 1 FSU determines loss of functionality

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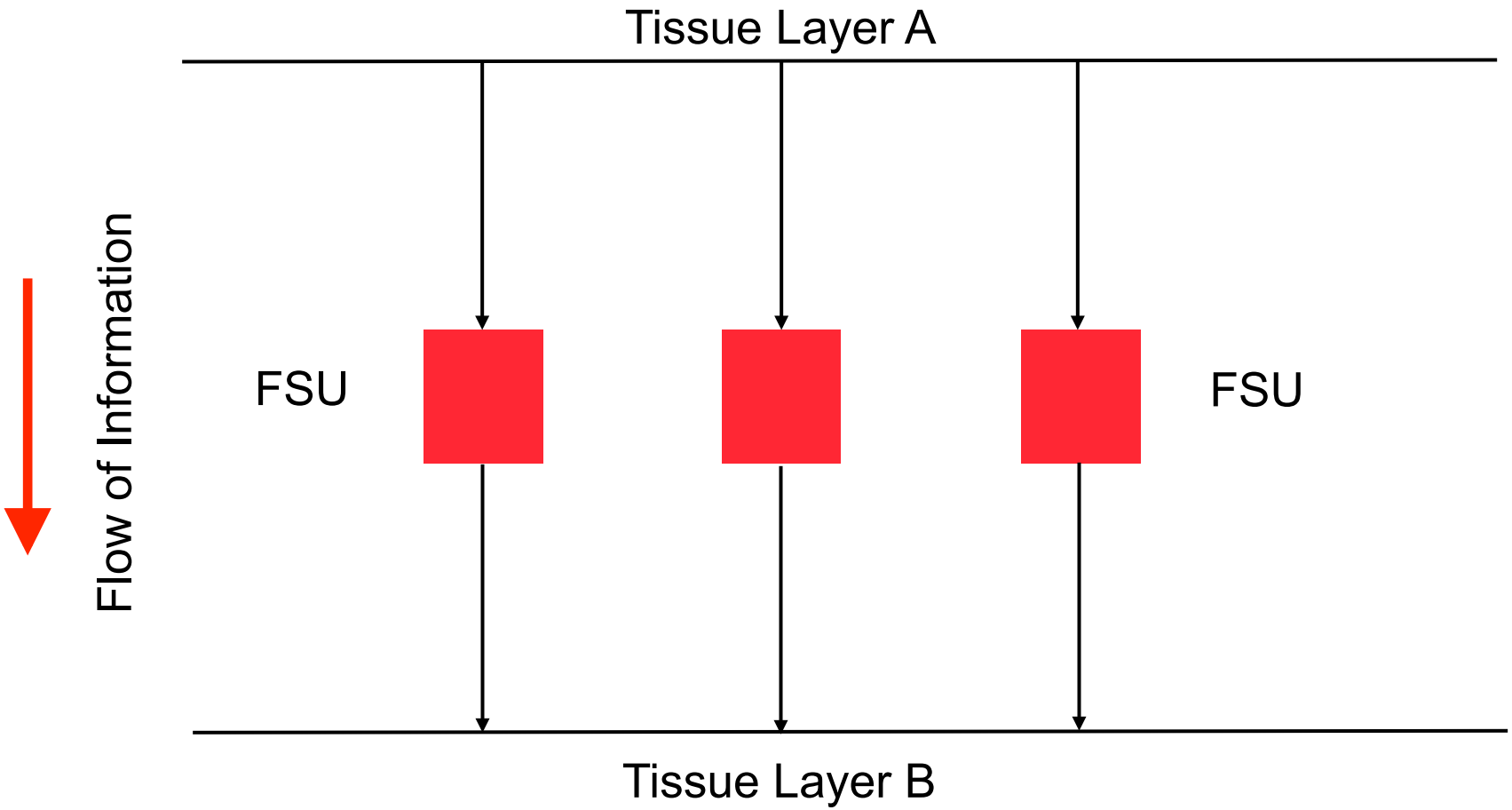
OARs – Functionality – Parallel Tissues



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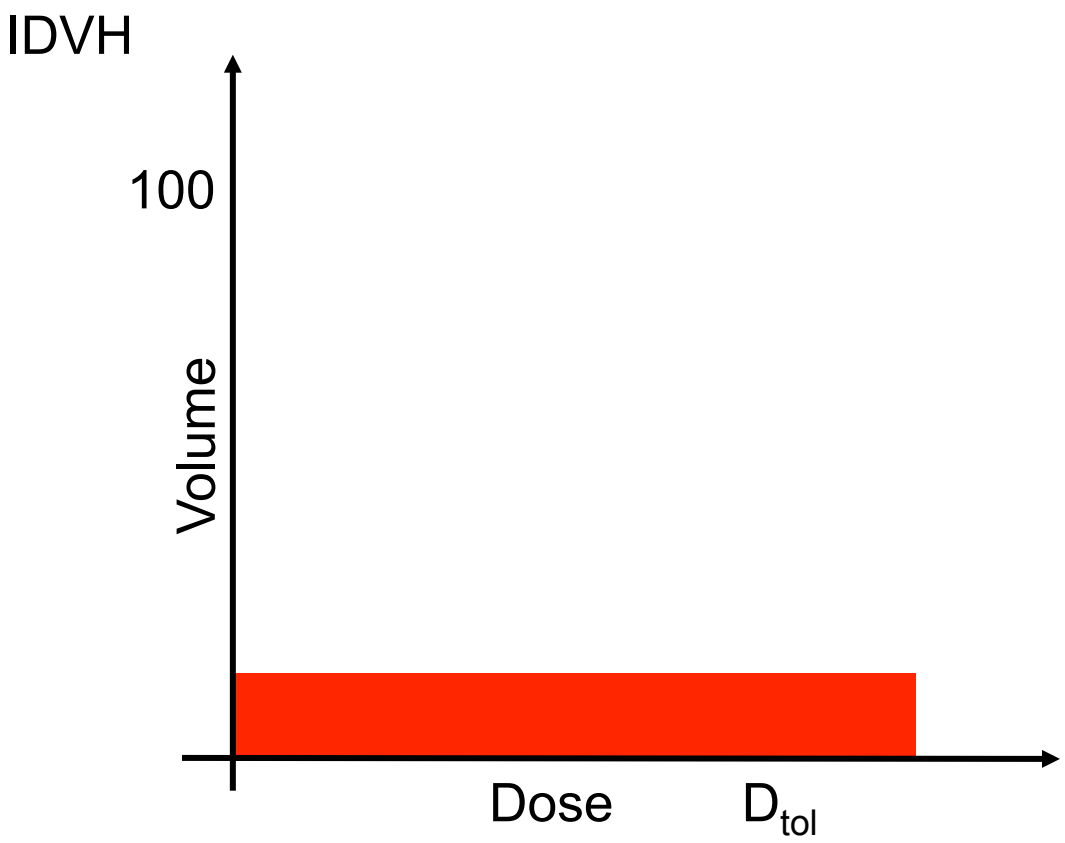
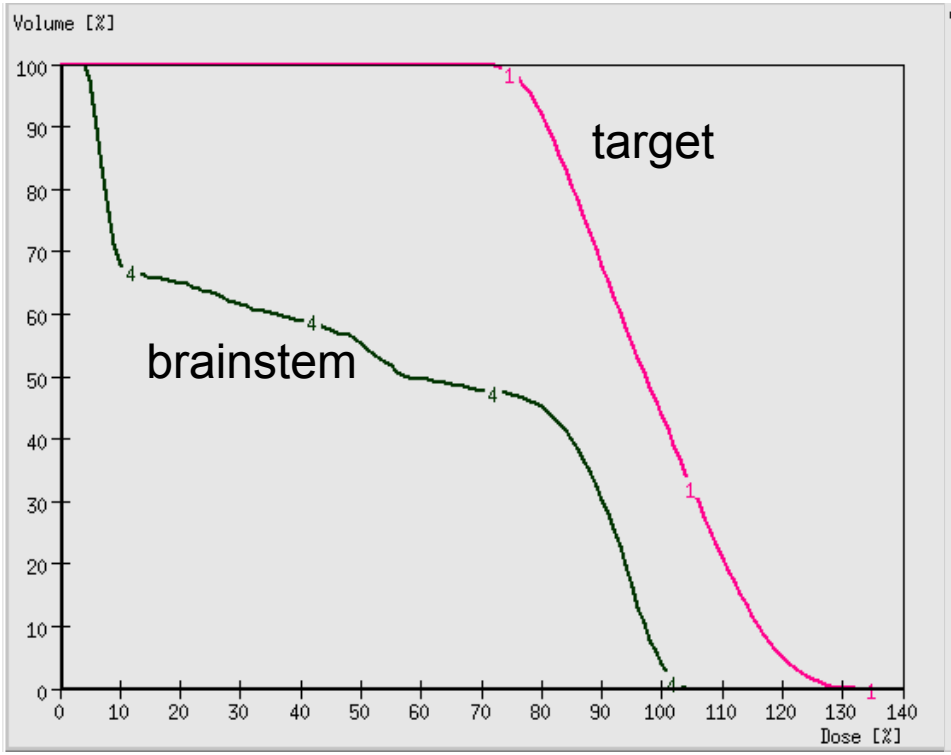
OARs – Parallel Tissues - Ideal DVHs



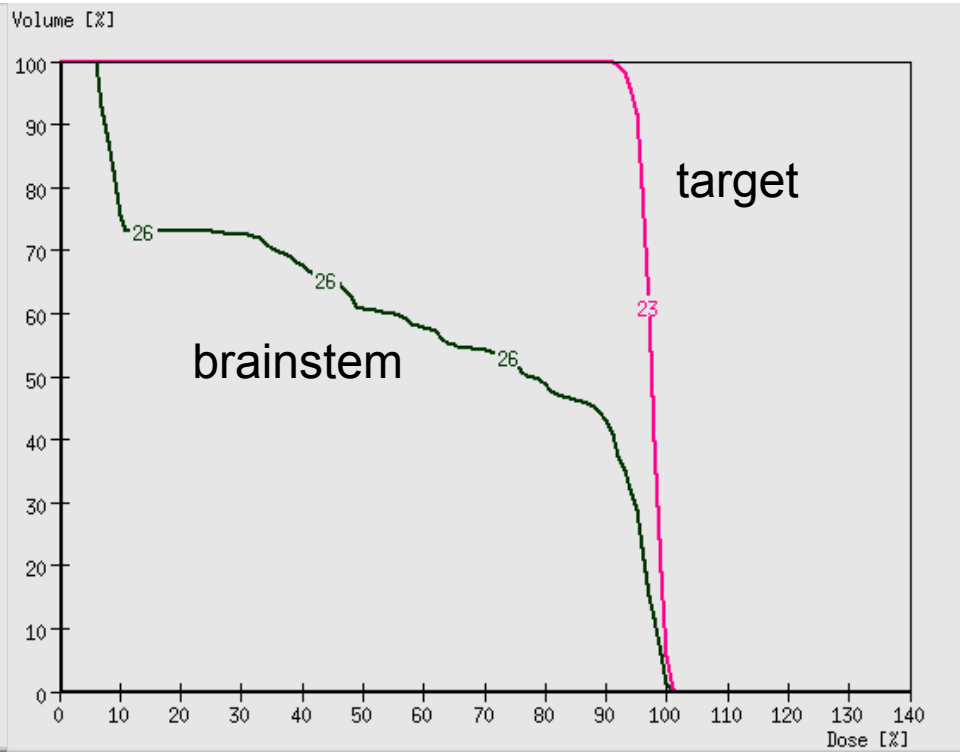
- Functionality determined by tolerance dose of the FSU and the number of inactivated FSUs
- Failure of a large number of FSUs determines loss of functionality

Slide by courtesy of Dr. Simeon Nill

DVH for plan comparison



1 beam



5 beams

Slide by courtesy of Dr. Simeon Nill

QUANTEC

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S10–S19, 2010

0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.07.1754

INTRODUCTORY PAPER

USE OF NORMAL TISSUE COMPLICATION PROBABILITY MODELS IN THE CLINIC

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The Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) review summarizes the currently available three-dimensional dose/volume/outcome data to update and refine the normal tissue dose/volume tolerance guidelines provided by the classic Emami *et al.* paper published in 1991. A "clinician's view" on using the QUANTEC information in a responsible manner is presented along with a description of the most commonly used normal tissue complication probability (NTCP) models. A summary of organ-specific dose/volume/outcome data, based on the QUANTEC reviews, is included. © 2010 Elsevier Inc.

QUANTEC, NTCP.

Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)* (*Continued*)

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
	Bilateral whole parotid glands	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <39	<50	For combined parotid glands (per Fig. 3 in paper) ¶
Pharynx	Pharyngeal constrictors	Whole organ	Symptomatic dysphagia and aspiration	Mean dose <50	<20	Based on Section B4 in paper
Larynx	Whole organ	3D-CRT	Vocal dysfunction	Dmax <66	<20	With chemotherapy, based on single study (see Section A4.2 in paper)
	Whole organ	3D-CRT	Aspiration	Mean dose <50	<30	With chemotherapy, based on single study (see Fig. 1 in paper)
	Whole organ	3D-CRT	Edema	Mean dose <44	<20	Without chemotherapy, based on single study in patients without larynx cancer**
	Whole organ	3D-CRT	Edema	V50 <27%	<20	
Lung	Whole organ	3D-CRT	Symptomatic pneumonitis	V20 ≤ 30%	<20	For combined lung. Gradual dose response
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 7	5	Excludes purposeful whole lung irradiation
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 13	10	
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 20	20	
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 24	30	
	Whole organ	3D-CRT	Symptomatic pneumonitis	Mean dose = 27	40	
Esophagus	Whole organ	3D-CRT	Grade ≥3 acute esophagitis	Mean dose <34	5–20	Based on RTOG and several studies
	Whole organ	3D-CRT	Grade ≥2 acute esophagitis	V35 <50%	<30	A variety of alternate threshold doses have been implicated. Appears to be a dose/volume response
	Whole organ	3D-CRT	Grade ≥2 acute esophagitis	V50 <40%	<30	
	Whole organ	3D-CRT	Grade ≥2 acute esophagitis	V70 <20%	<30	
Heart	Pericardium	3D-CRT	Pericarditis	Mean dose <26	<15	Based on single study
	Pericardium	3D-CRT	Pericarditis	V30 <46%	<15	
	Whole organ	3D-CRT	Long-term cardiac mortality	V25 <10%	<1	Overly safe risk estimate based on model predictions

(*Continued*)

Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)*

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
Brain	Whole organ	3D-CRT	Symptomatic necrosis	Dmax <60	<3	Data at 72 and 90 Gy, extrapolated from BED models
	Whole organ	3D-CRT	Symptomatic necrosis	Dmax = 72	5	
	Whole organ	3D-CRT	Symptomatic necrosis	Dmax = 90	10	
	Whole organ	SRS (single fraction)	Symptomatic necrosis	V12 <5–10 cc	<20	Rapid rise when V12 > 5–10 cc
Brain stem	Whole organ	Whole organ	Permanent cranial neuropathy or necrosis	Dmax <54	<5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	D1–10 cc‖ ≤59	<5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	Dmax <64	<5	Point dose <<1 cc
	Whole organ	SRS (single fraction)	Permanent cranial neuropathy or necrosis	Dmax <12.5	<5	For patients with acoustic tumors
Optic nerve / chiasm	Whole organ	3D-CRT	Optic neuropathy	Dmax <55	<3	Given the small size, 3D CRT is often whole organ‡‡
	Whole organ	3D-CRT	Optic neuropathy	Dmax 55–60	3–7	
	Whole organ	3D-CRT	Optic neuropathy	Dmax >60	>7-20	
	Whole organ	SRS (single fraction)	Optic neuropathy	Dmax <12	<10	
Spinal cord	Partial organ	3D-CRT	Myelopathy	Dmax = 50	0.2	Including full cord cross-section
	Partial organ	3D-CRT	Myelopathy	Dmax = 60	6	
	Partial organ	3D-CRT	Myelopathy	Dmax = 69	50	
	Partial organ	SRS (single fraction)	Myelopathy	Dmax = 13	1	Partial cord cross-section irradiated
	Partial organ	SRS (hypofraction)	Myelopathy	Dmax = 20	1	3 fractions, partial cord cross-section irradiated
Cochlea	Whole organ	3D-CRT	Sensory neural hearing loss	Mean dose ≤45	<30	Mean dose to cochlear, hearing at 4 kHz
	Whole organ	SRS (single fraction)	Sensory neural hearing loss	Prescription dose ≤14	<25	Serviceable hearing
Parotid	Bilateral whole parotid glands	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <25	<20	For combined parotid glands¶
	Unilateral whole parotid gland	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <20	<20	For single parotid gland. At least one parotid gland spared to <20 Gy¶

Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)* (*Continued*)

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
Liver	Whole liver – GTV	3D-CRT or Whole organ	Classic RILD††	Mean dose <30-32	<5	Excluding patients with pre-existing liver disease or hepatocellular carcinoma, as tolerance doses are lower in these patients
	Whole liver – GTV	3D-CRT	Classic RILD	Mean dose <42	<50	
	Whole liver – GTV	3D-CRT or Whole organ	Classic RILD	Mean dose <28	<5	In patients with Child-Pugh A preexisting liver disease or hepatocellular carcinoma, excluding hepatitis B reactivation as an endpoint
	Whole liver – GTV	3D-CRT	Classic RILD	Mean dose <36	<50	
	Whole liver –GTV	SBRT (hypofraction)	Classic RILD	Mean dose <13	<5	3 fractions, for primary liver cancer
				<18	<5	6 fractions, for primary liver cancer
	Whole liver – GTV	SBRT (hypofraction)	Classic RILD	Mean dose <15	<5	3 fractions, for liver metastases
				<20	<5	6 fractions, for liver metastases
	>700 cc of normal liver	SBRT (hypofraction)	Classic RILD	D_{max} <15	<5	Critical volume based, in 3–5 fractions
Kidney	Bilateral whole kidney‡	Bilateral whole organ or 3D-CRT	Clinically relevant renal dysfunction	Mean dose <15–18	<5	
	Bilateral whole kidney‡	Bilateral whole organ	Clinically relevant renal dysfunction	Mean dose <28	<50	
	Bilateral whole kidney‡	3D-CRT	Clinically relevant renal dysfuntction	V12 <55% V20 <32% V23 <30% V28 <20%	<5	For combined kidney
Stomach	Whole organ	Whole organ	Ulceration	D100‖ <45	<7	
Small bowel	Individual small bowel loops	3D-CRT	Grade ≥ 3 acute toxicity§	V15 <120 cc	<10	Volume based on segmentation of the individual loops of bowel, not the entire potential peritoneal space
	Entire potential space within peritoneal cavity	3D-CRT	Grade ≥ 3 acute toxicity§	V45 <195 cc	<10	Volume based on the entire potential space within the peritoneal cavity

(*Continued*)

Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)* (*Continued*)

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
Rectum	Whole organ	3D-CRT	Grade ≥ 2 late rectal toxicity,	V50 <50%	<15	Prostate cancer treatment
			Grade ≥ 3 late rectal toxicity		<10	
	Whole organ	3D-CRT	Grade ≥ 2 late rectal toxicity,	V60 <35%	<15	
			Grade ≥ 3 late rectal toxicity		<10	
	Whole organ	3D-CRT	Grade ≥ 2 late rectal toxicity,	V65 <25%	<15	
			Grade ≥ 3 late rectal toxicity		<10	
	Whole organ	3D-CRT	Grade ≥ 2 late rectal toxicity,	V70 <20%	<15	
			Grade ≥ 3 late rectal toxicity		<10	
	Whole organ	3D-CRT	Grade ≥ 2 late rectal toxicity,	V75 <15%	<15	
			Grade ≥ 3 late rectal toxicity		<10	
Bladder	Whole organ	3D-CRT	Grade ≥ 3 late RTOG	Dmax <65	<6	Bladder cancer treatment. Variations in bladder size/shape/ location during RT hamper ability to generate accurate data
	Whole organ	3D-CRT	Grade ≥3 late RTOG	V65 ≤50 % V70 ≤35 % V75 ≤25 % V80 ≤15 %		Prostate cancer treatment Based on current RTOG 0415 recommendation
Penile bulb	Whole organ	3D-CRT	Severe erectile dysfunction	Mean dose to 95% of gland <50	<35	
	Whole organ	3D-CRT	Severe erectile dysfunction	D90‖ <50	<35	
	Whole organ	3D-CRT	Severe erectile dysfunction	D60-70 <70	<55	

Abbreviations: 3D-CRT = 3-dimensional conformal radiotherapy, SRS = stereotactic radiosurgery, BED = Biologically effective dose, SBRT = stereotactic body radiotherapy, RILD = radiation-induced liver disease, RTOG = Radiation Therapy Oncology Group.

* All data are estimated from the literature summarized in the QUANTEC reviews unless otherwise noted. Clinically, these data should be applied with caution. Clinicians are strongly advised to use the individual QUANTEC articles to check the applicability of these limits to the clinical situation at hand. They largely do not reflect modern IMRT.

† All at standard fractionation (*i.e.,* 1.8–2.0 Gy per daily fraction) unless otherwise noted. Vx is the volume of the organ receiving ≥ x Gy. Dmax = Maximum radiation dose.

‡ Non-TBI.

§ With combined chemotherapy.

‖ Dx = minimum dose received by the "hottest" x% (or x cc's) of the organ.

¶ Severe xerostomia is related to additional factors including the doses to the submandibular glands.

** Estimated by Dr. Eisbruch.

†† Classic Radiation induced liver disease (RILD) involves anicteric hepatomegaly and ascites, typically occurring between 2 weeks and 3 months after therapy. Classic RILD also involves elevated alkaline phosphatase (more than twice the upper limit of normal or baseline value).

‡‡ For optic nerve, the cases of neuropathy in the 55 to 60 Gy range received ≈59 Gy (see optic nerve paper for details). Excludes patients with pituitary tumors where the tolerance may be reduced.

Outline

- Segmentation
- Dose calculation
- Definition of treatment parameters
- Evaluation of dose distribution / treatment plan
- Intensity Modulated RT (IMRT) & Optimization

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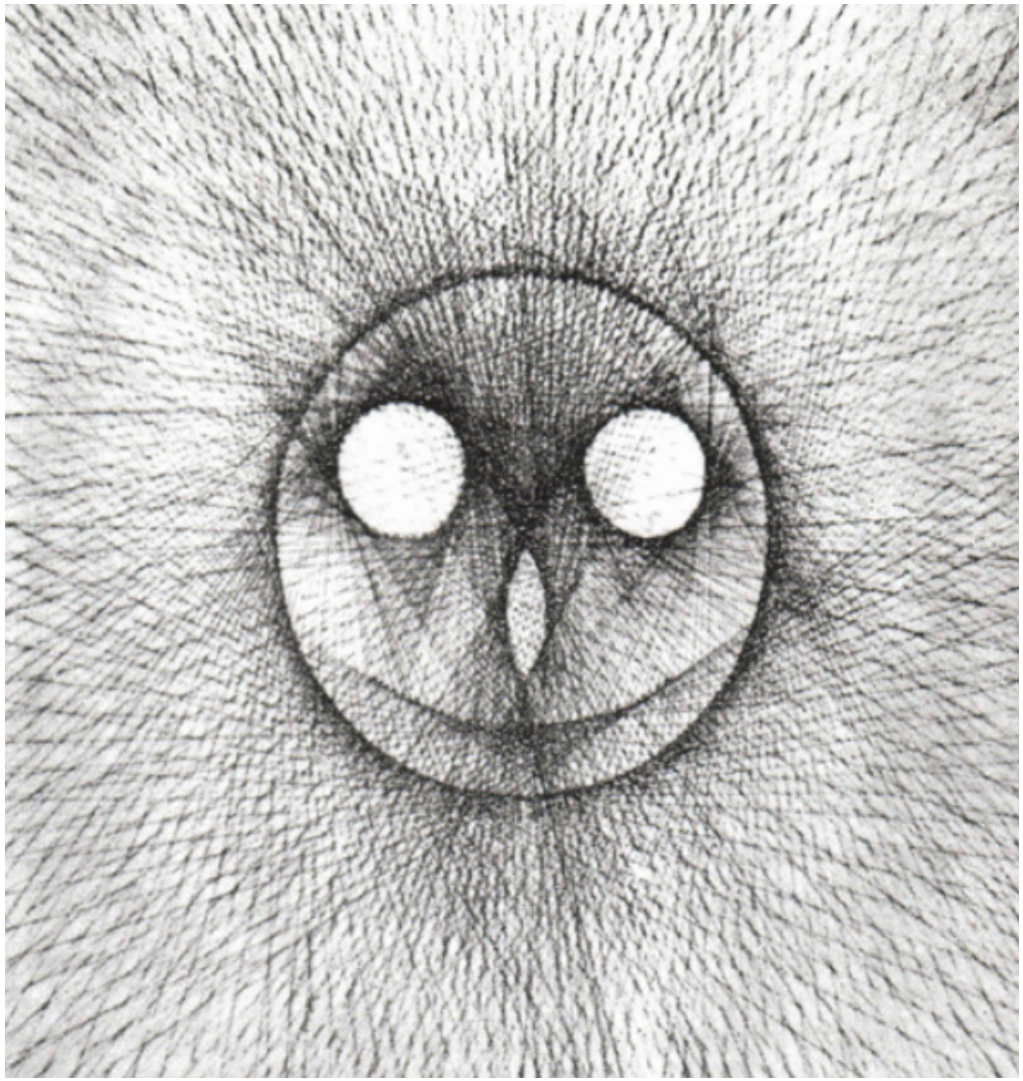
Generating an Image from 360 degrees of linear projections!!



Birkhoff G **1940** *On drawings composed of uniform straight lines* J. Math. Pures Appl. 19 221–36

Radon Transform Principles

- A linear transform
  f(x,y) → g(s,θ)
  - Line integral or "ray-sum"
  - Along a line inclined at angle θ from y-axis and s away from origin

- Fix θ to get a 1-D signal $g_\theta(s)$

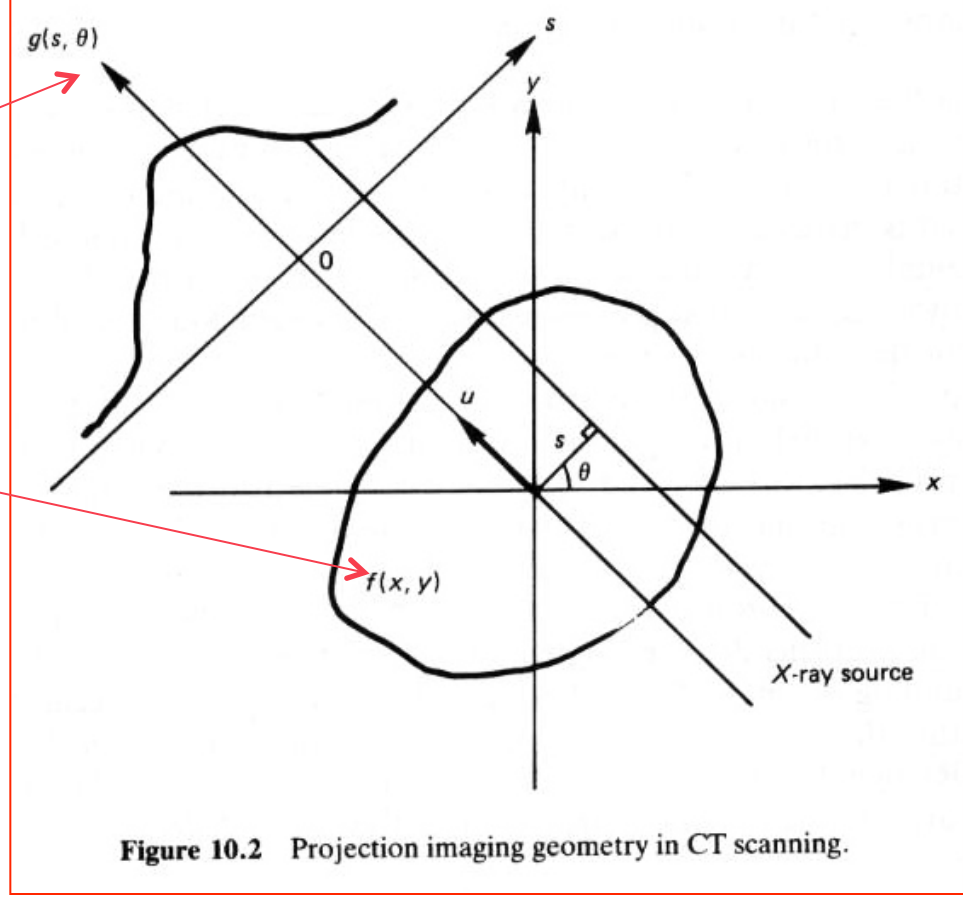


Figure 10.2 Projection imaging geometry in CT scanning.

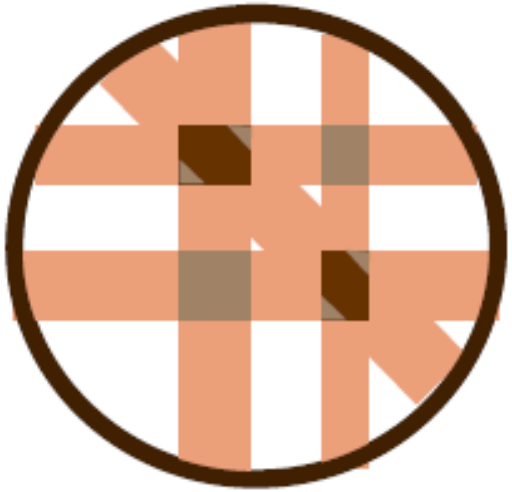
We have now a set of images $g_\theta(s)$ which represent g(s,θ)

$$g(s,\theta) = \int\int_{-\infty}^{+\infty} f(x,y)\delta(x\cos\theta + y\sin\theta - s)dxdy$$

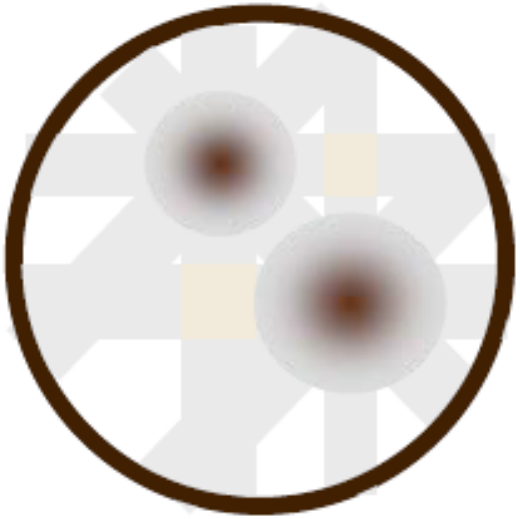
The Radon Transform was introduced in 1917 by Johann Radon

3) Backprojection – Multiple linear projections

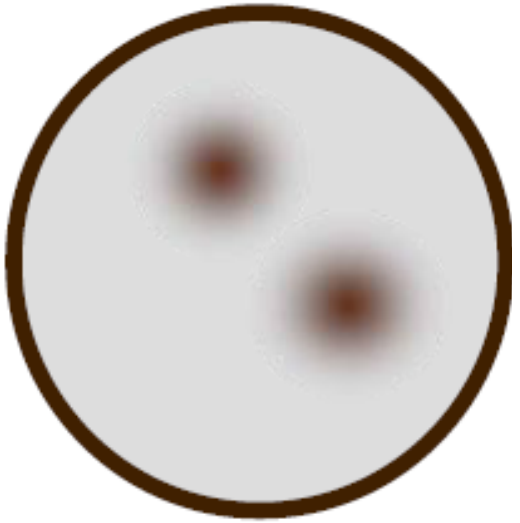
3 projections



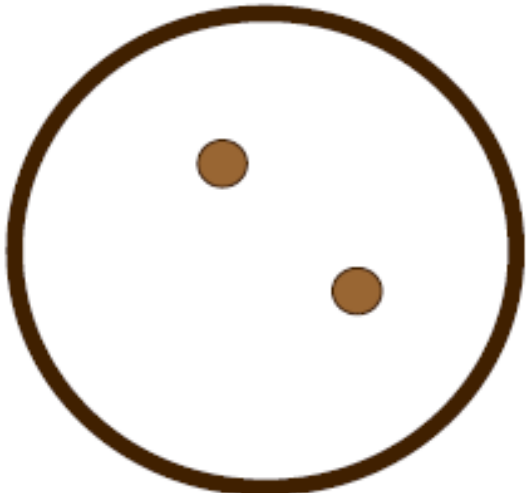
4 projections



many projections



Original object



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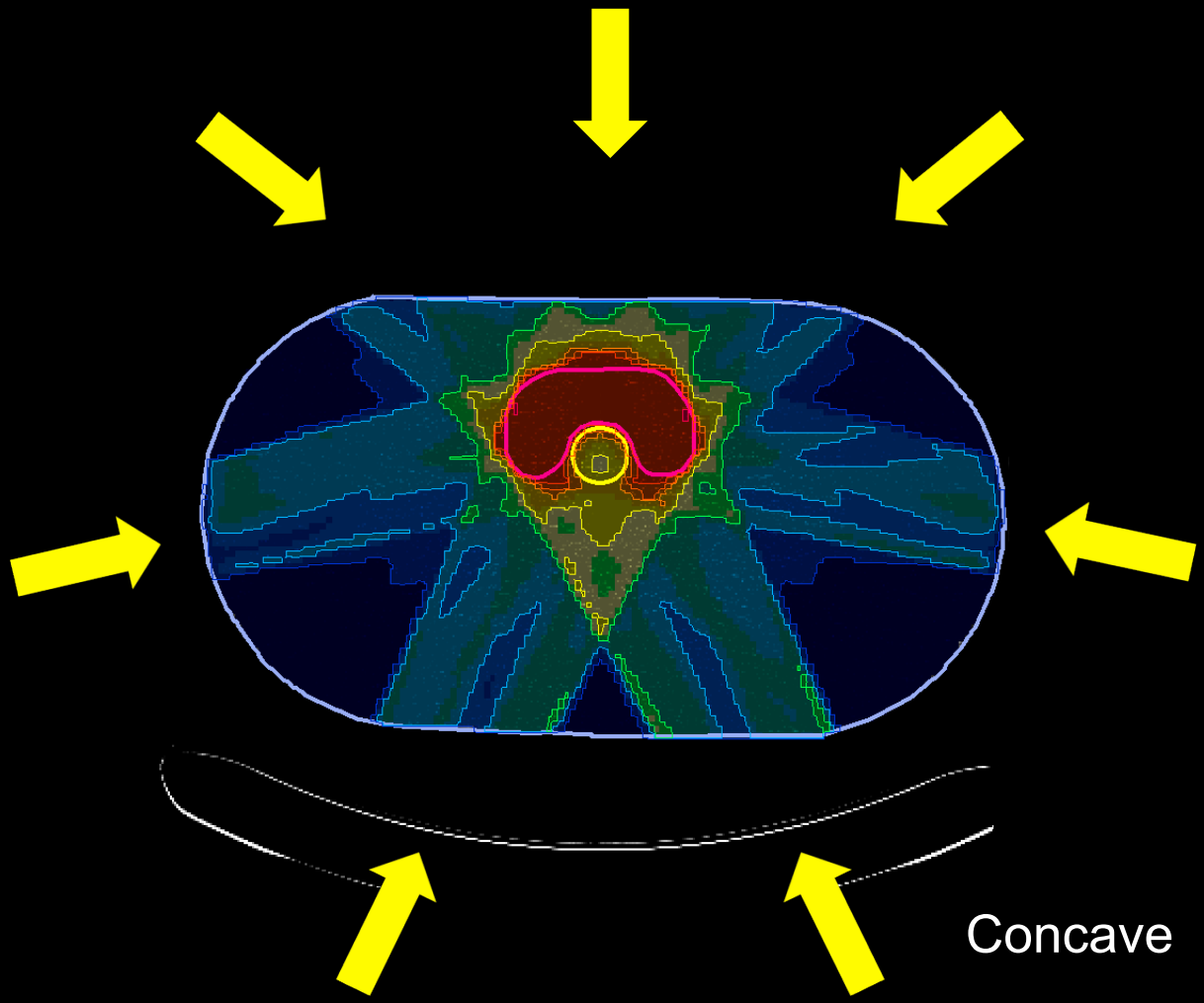
Alan Cormack (Harvard, 1963)

- Alan M. Cormack, physicist (1924-1998) was the first to publish a paper on the reconstruction of tomographic images based on X-ray absorption and proton degradation (J. Appl. Phys. 34, 2722, 1963)
- It took less than 10 years before his idea became reality when the first when Godfrey Hounsfield constructed the first X-ray CT scanner
- Both shared the Nobel Prize for Medicine in 1979

Alan M. Cormack, 1924-1998
Physics Nobel Laureate 1979

The optimization / inverse planning process is closely linked to intensity-modulated radiation therapy

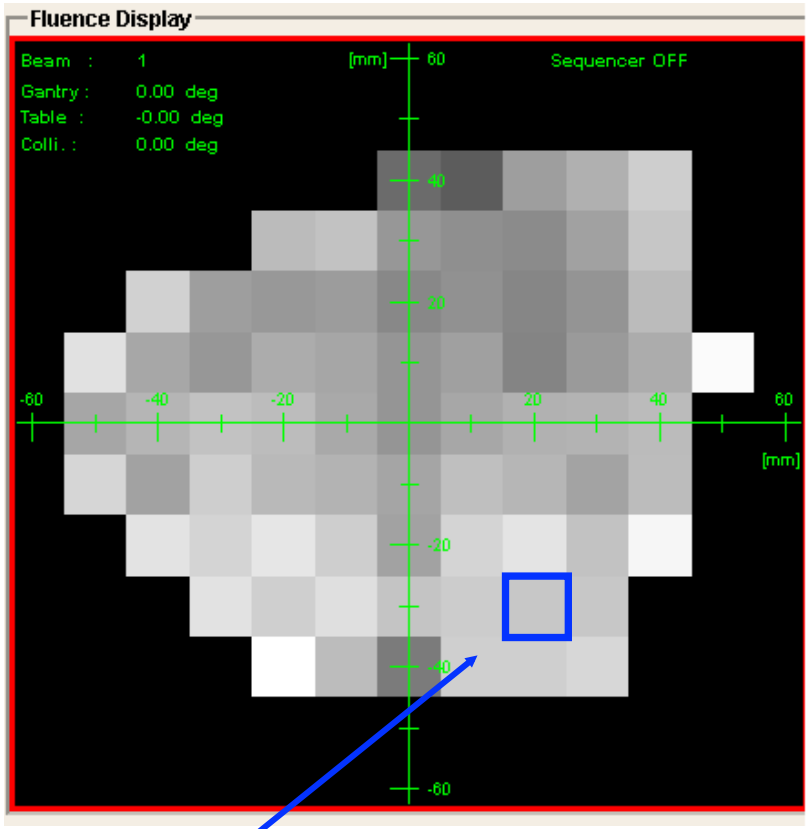


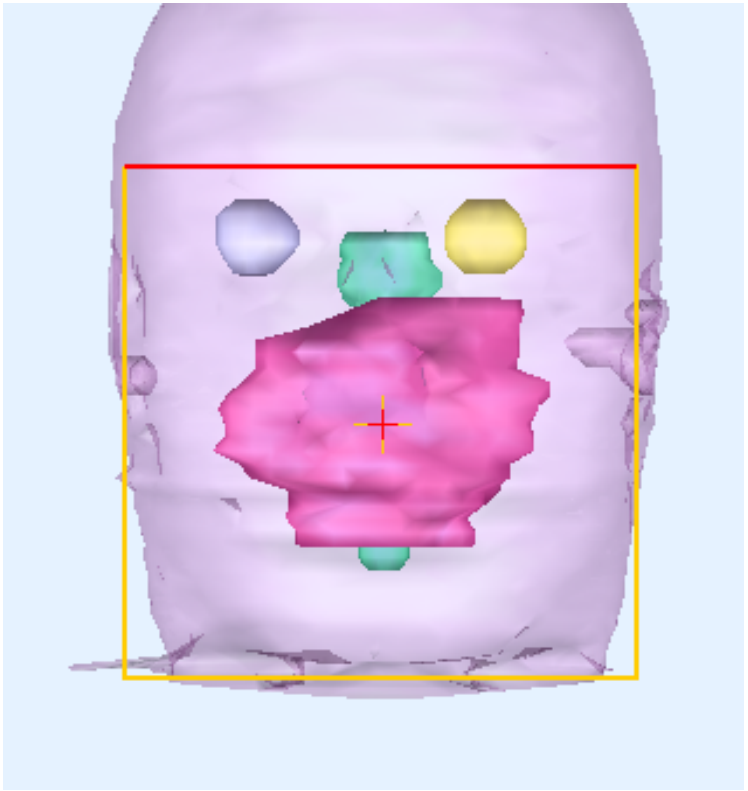
Concave dose distributions

→ Optimization of intensity profiles

Fluence maps

- Divide beam's eye view into bixel
- Assign different fluence weights to each bixel





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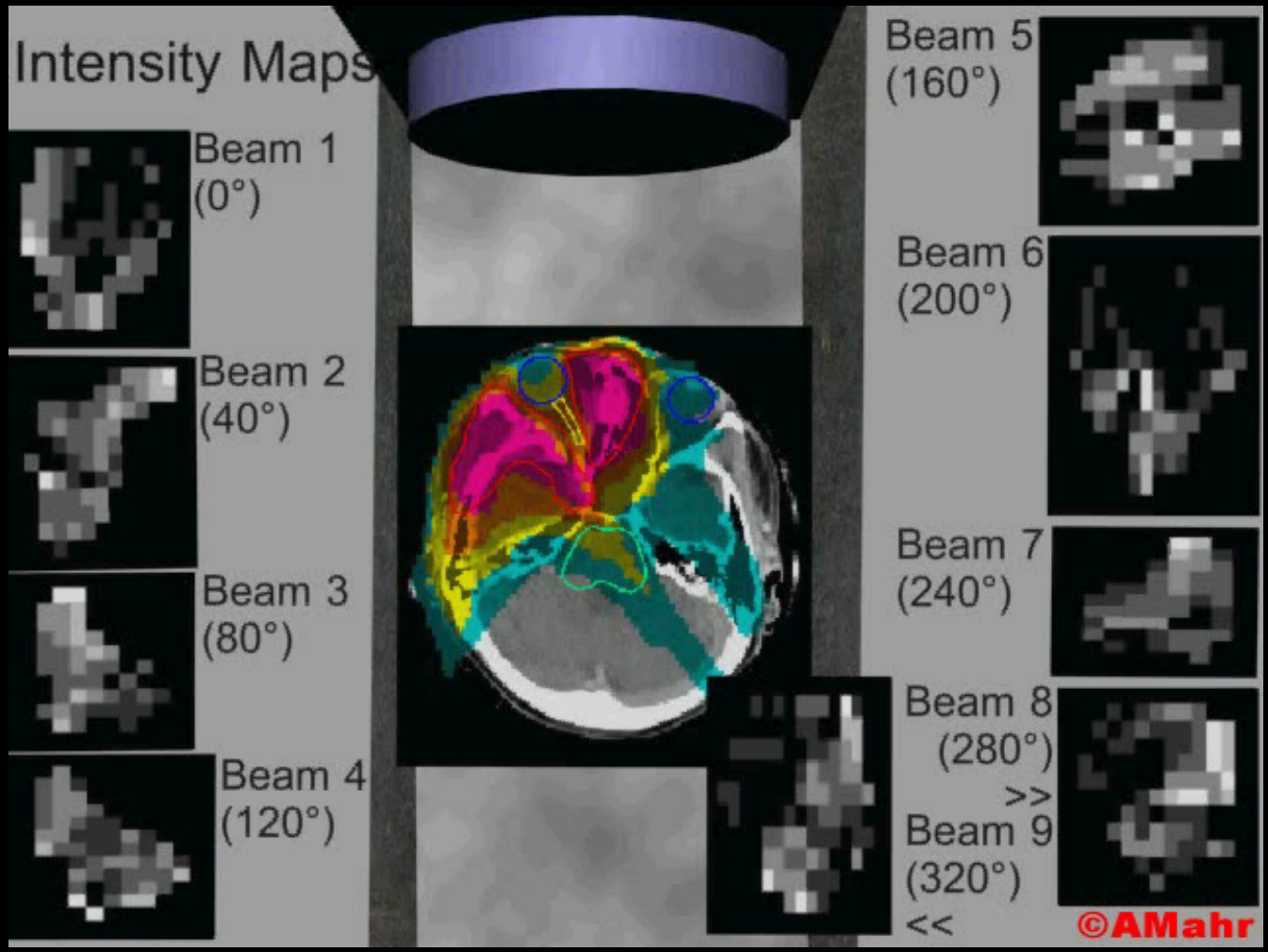
The principle of IMRT



→Two problems

1. How to find the fluences?
2. How to deliver the fluences?

How to find the fluences?

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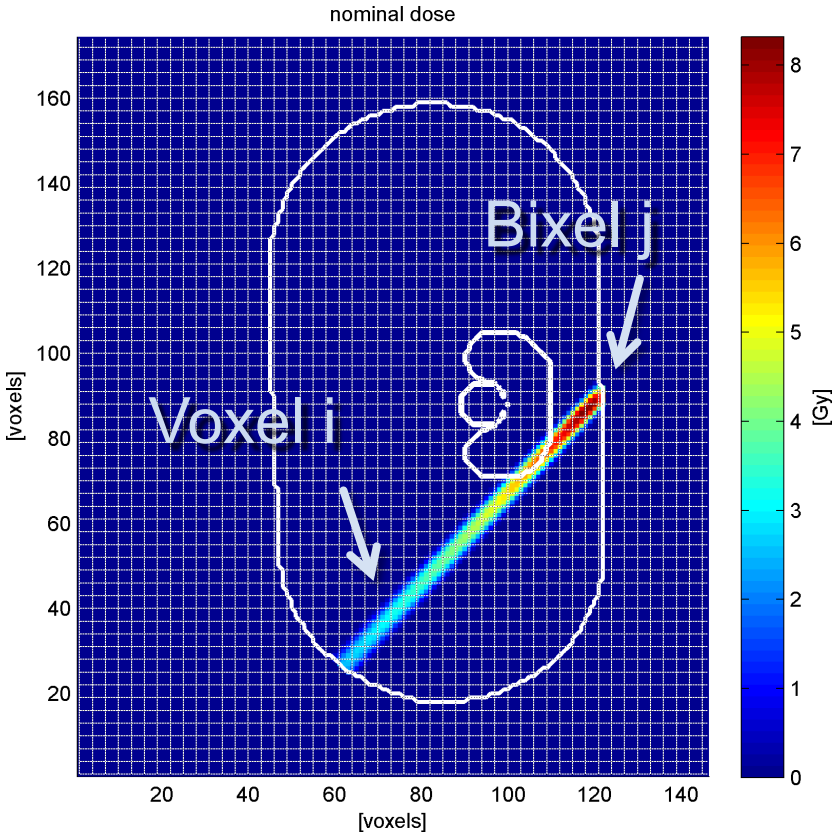
The intensity modulation is found by optimization of a quadratic objective function on a discrete representation of the patient anatomy…

$$F = \sum_{i \in \text{Target}} \left\{ \left[D_i - D_i^{\max} \right]_+^2 + \left[D_i^{\min} - D_i \right]_+^2 \right\}$$

$$\text{where } [x]_+ = \begin{cases} x \text{ for } x > 0 \\ 0 \text{ else.} \end{cases}$$



$$D_i = \sum_j D_{ij} w_j$$

$$w_j \geq 0$$

X-rays ~ 1000 pencil beams
Particles ~ 30000 pencil beams

- Solution with projected L-BFGS

1 run takes ~ 3 min with commercial system

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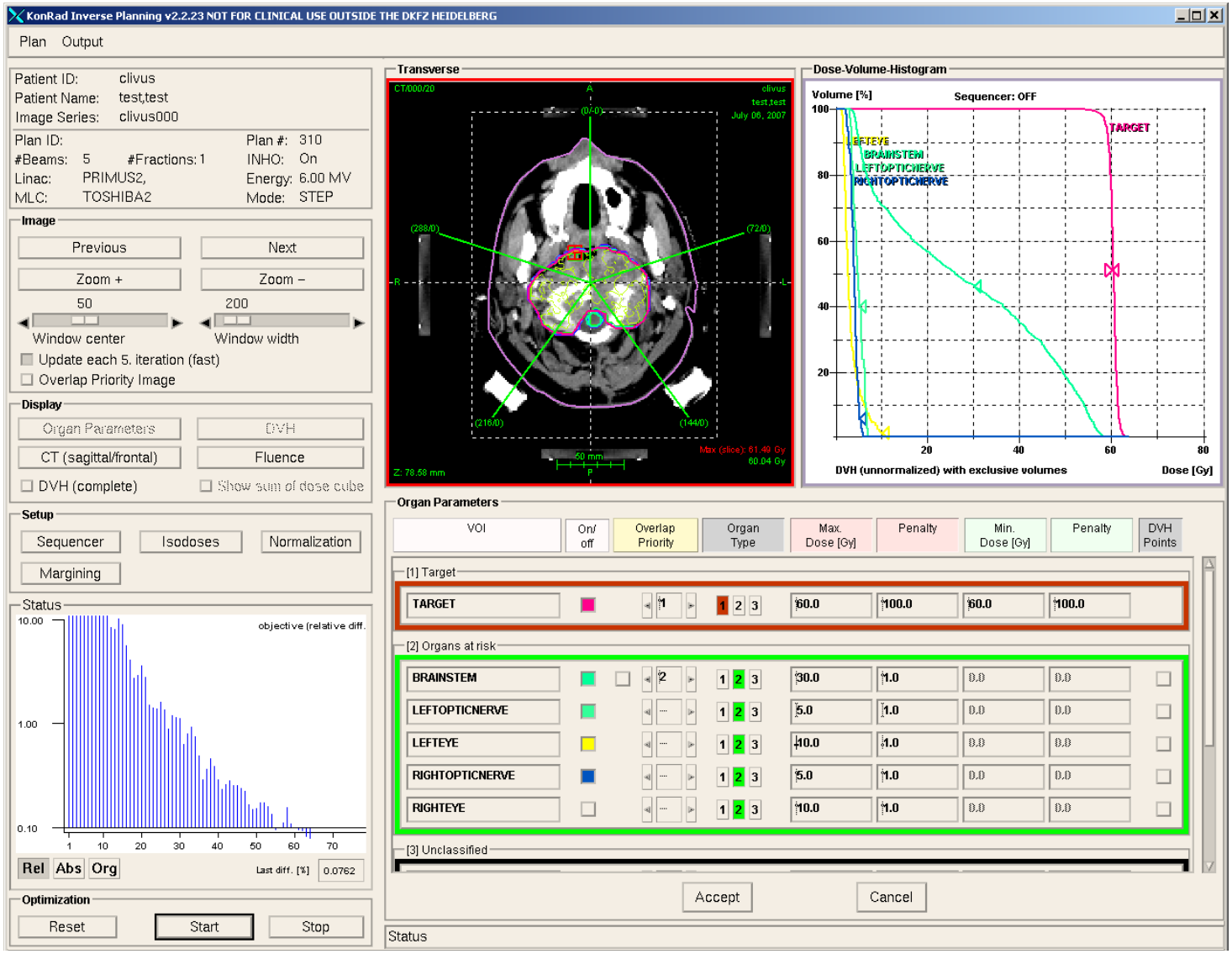
Inverse planning



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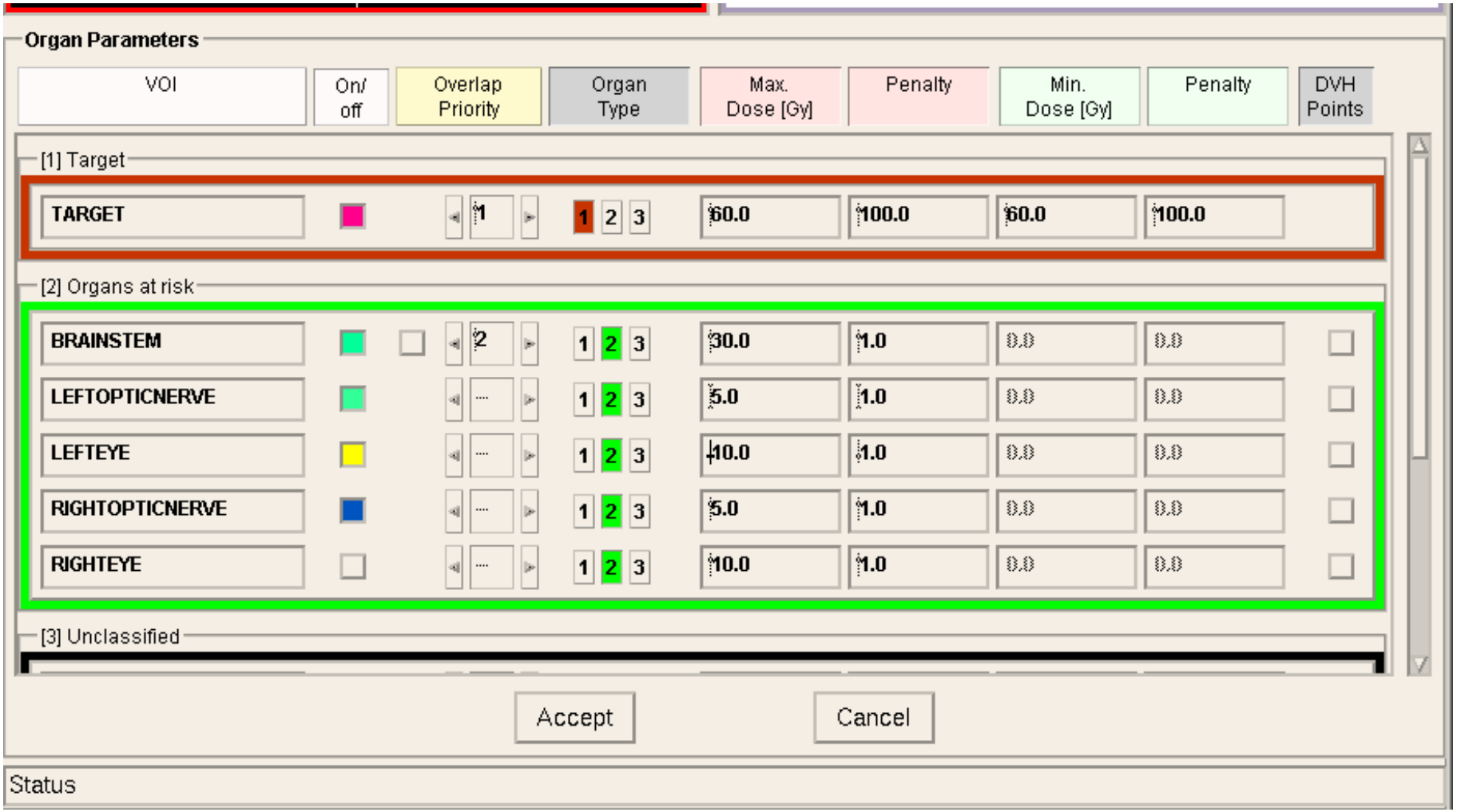
Planning objectives



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How to deliver the fluences?

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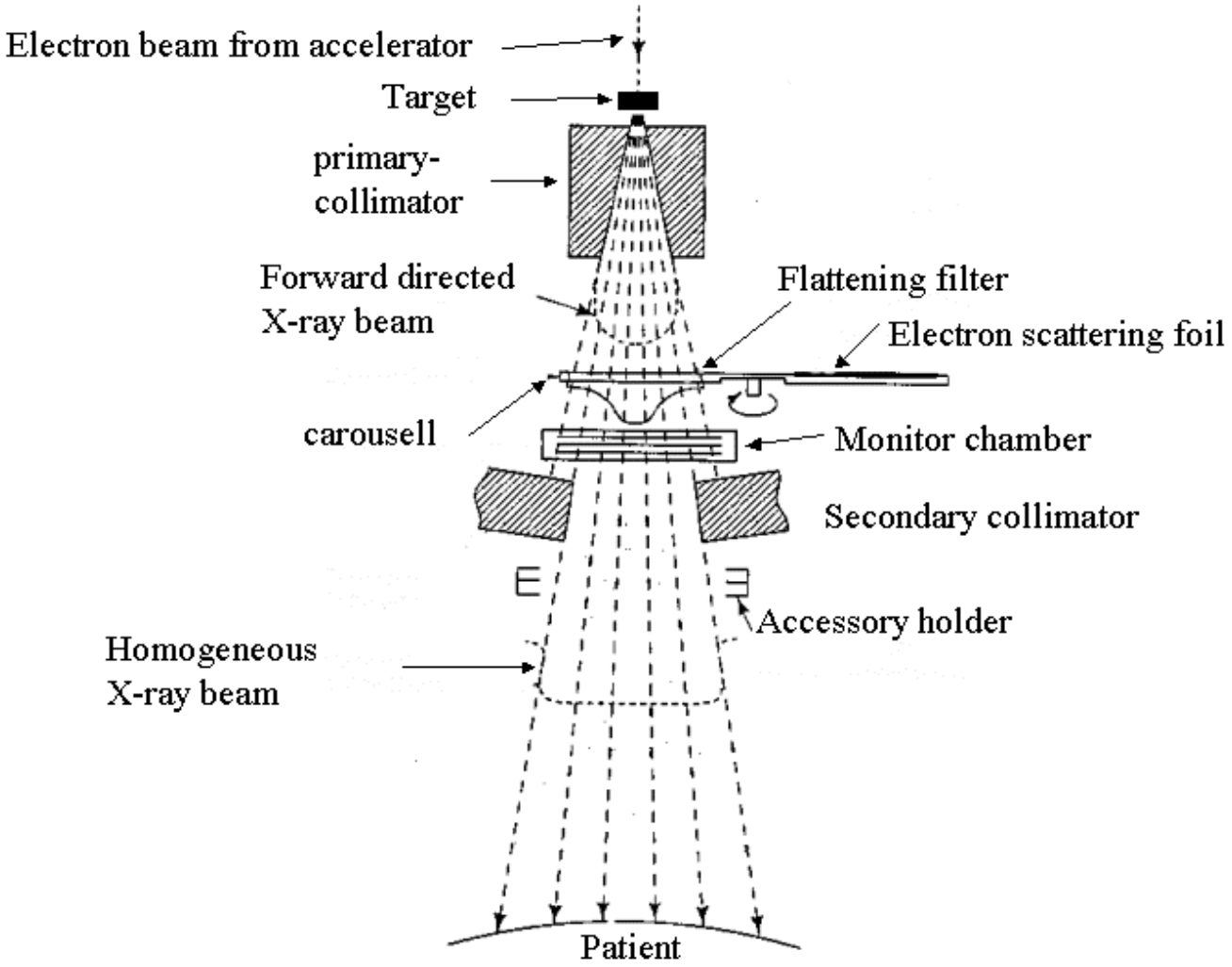
Ein Photonen Linearbeschleuniger – so sieht ihn ein Physiker…



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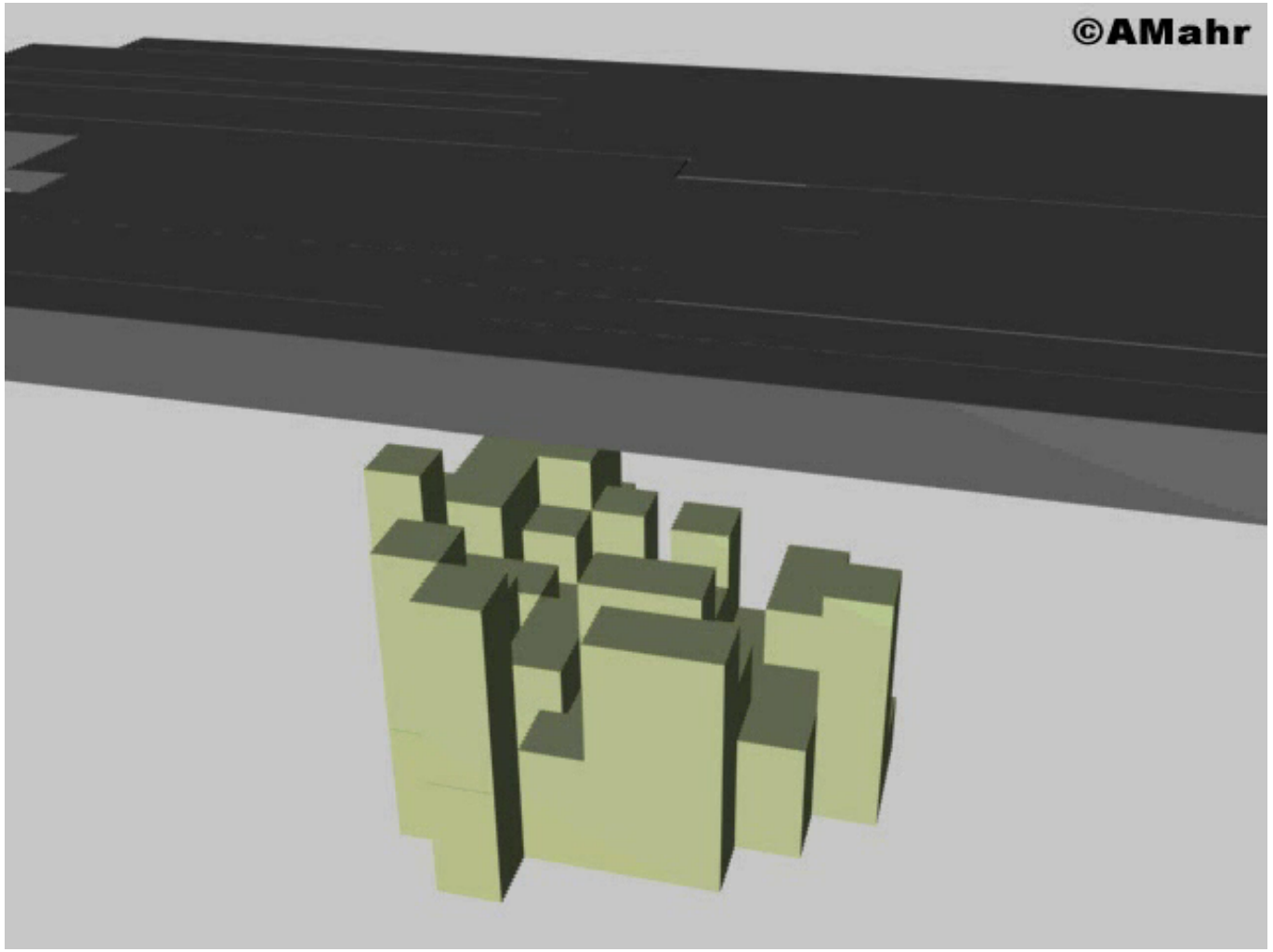
Step-and-shoot delivery



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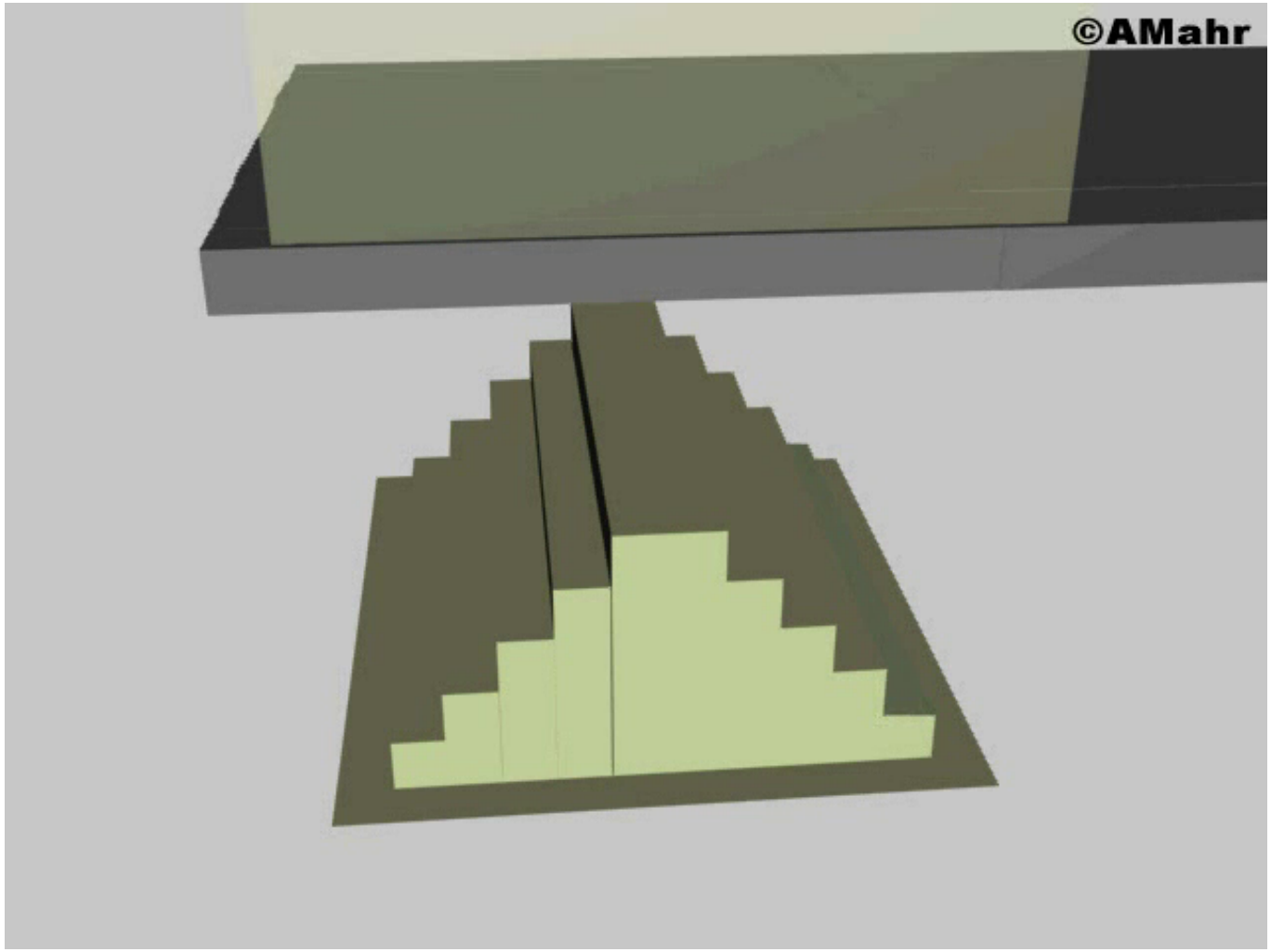
Dynamic IMRT delivery



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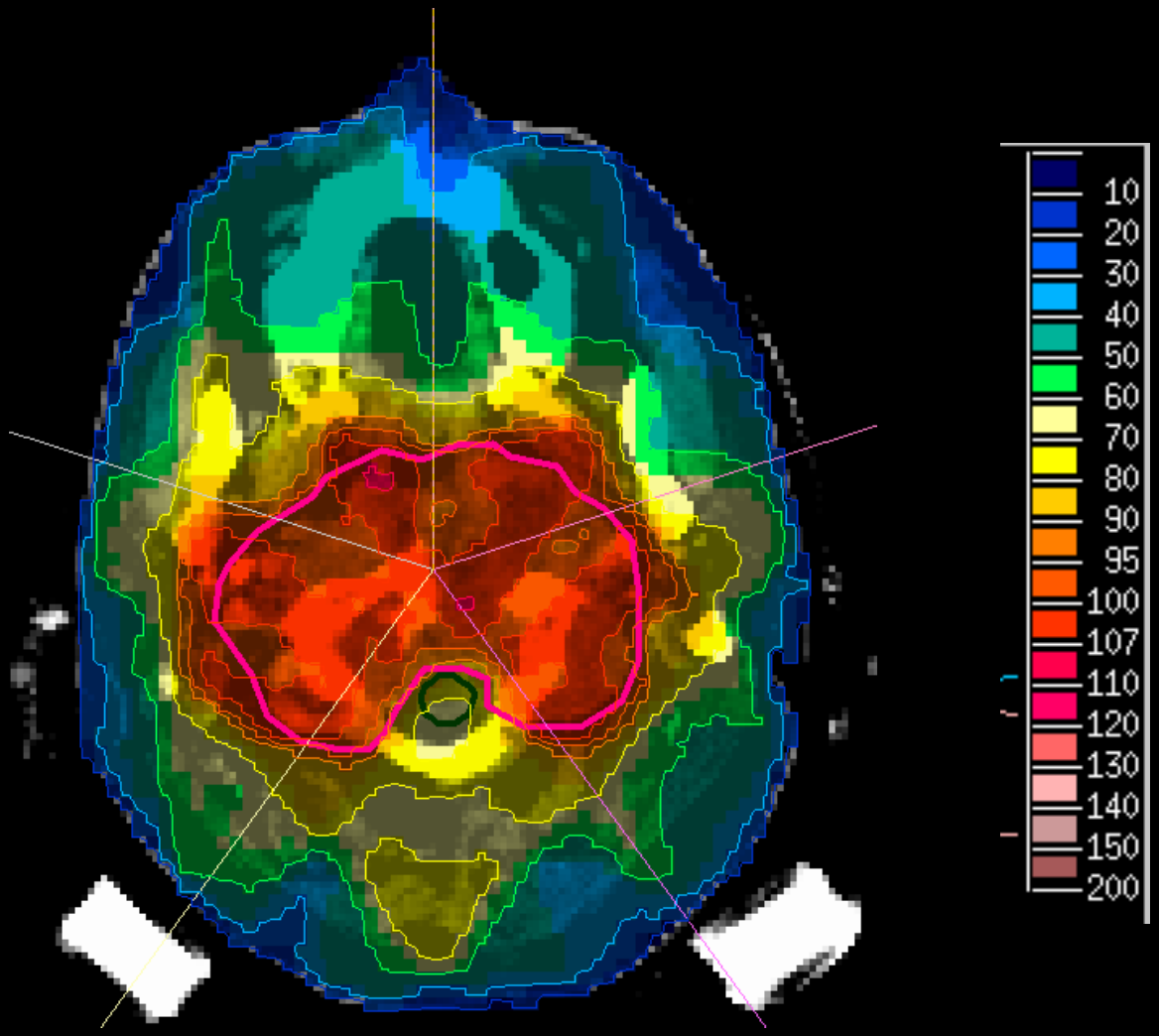
IMRT dose distribution



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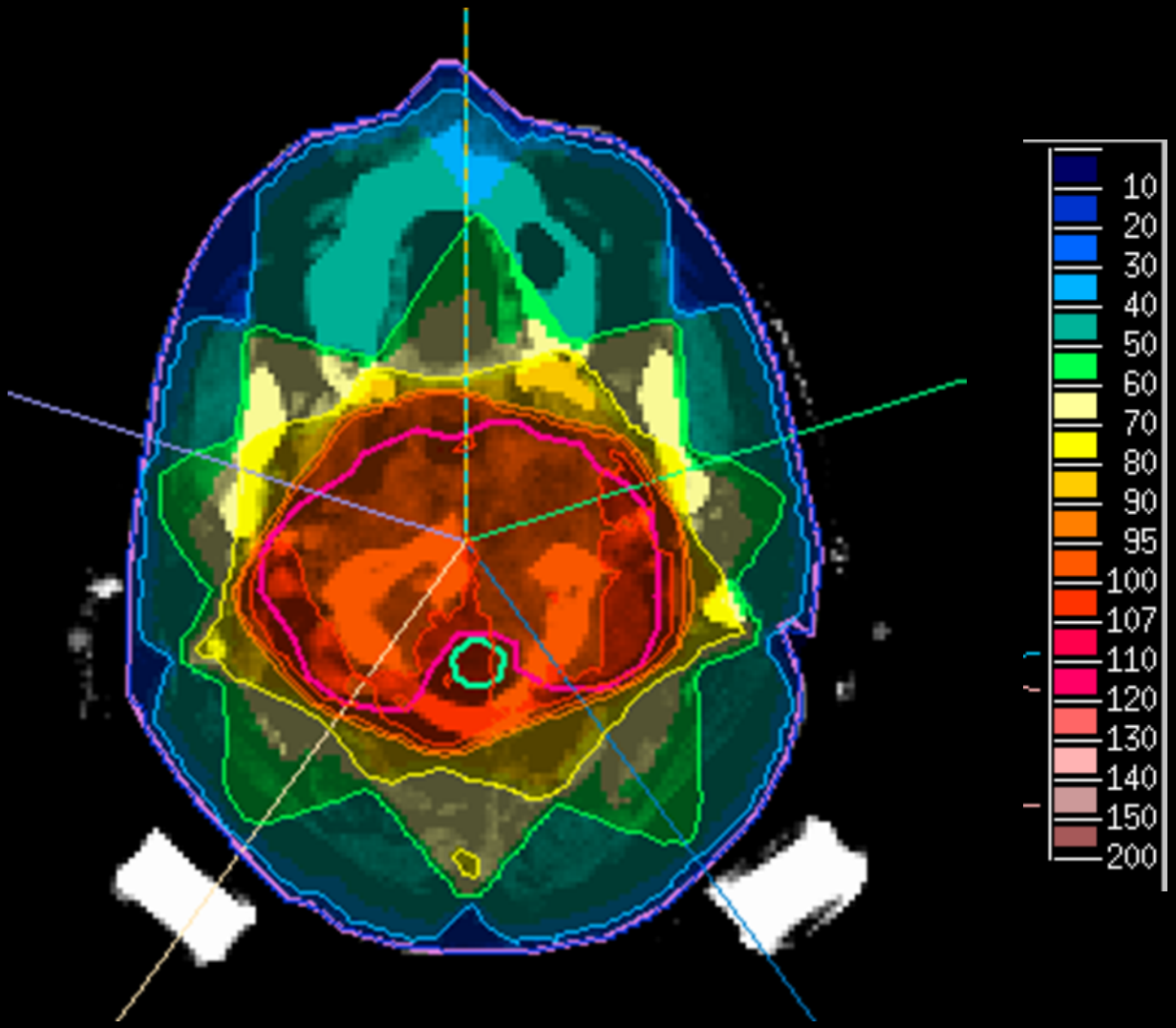
Dose distribution for five conformal beams



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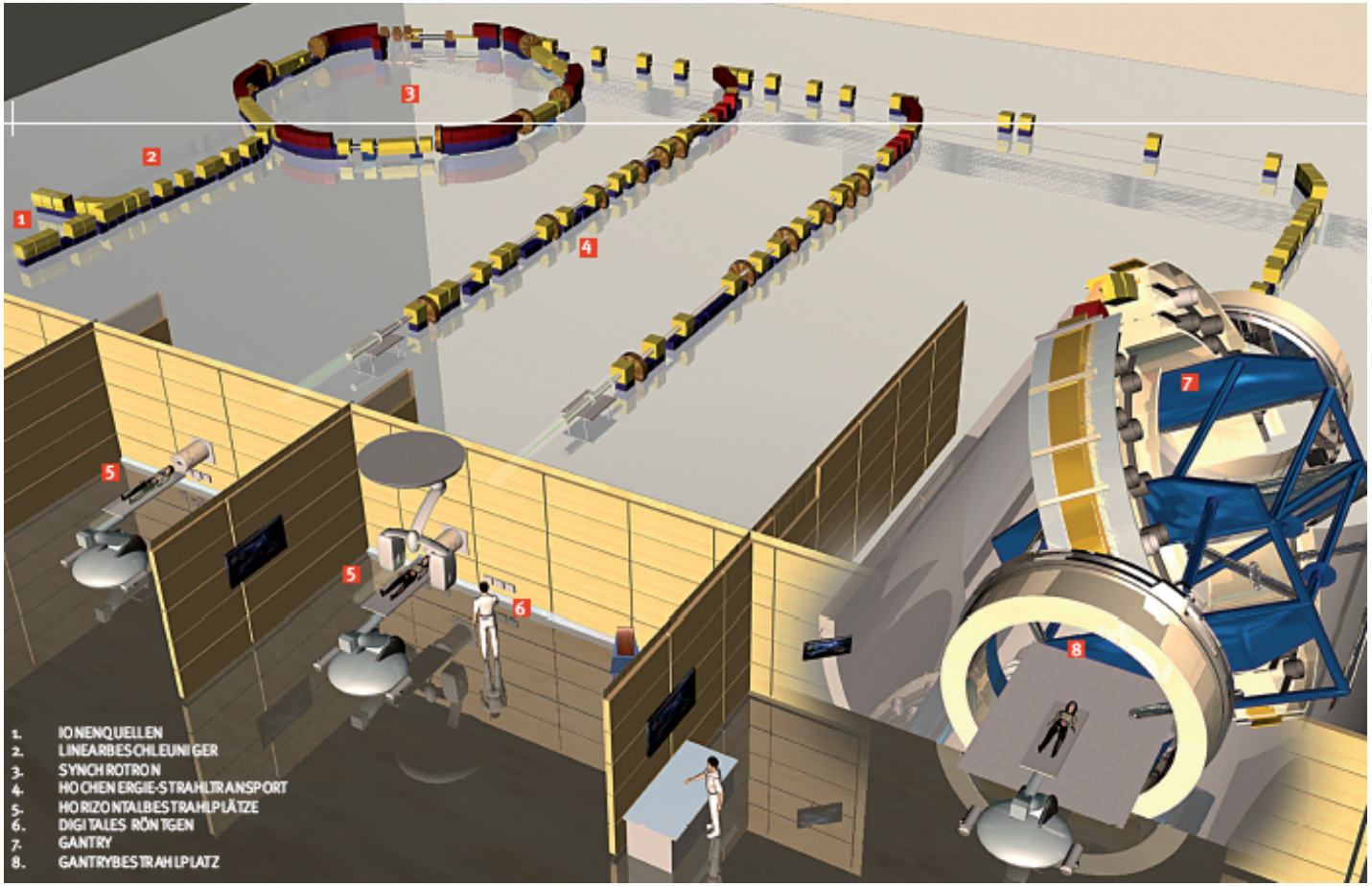
At a glance: particle therapy



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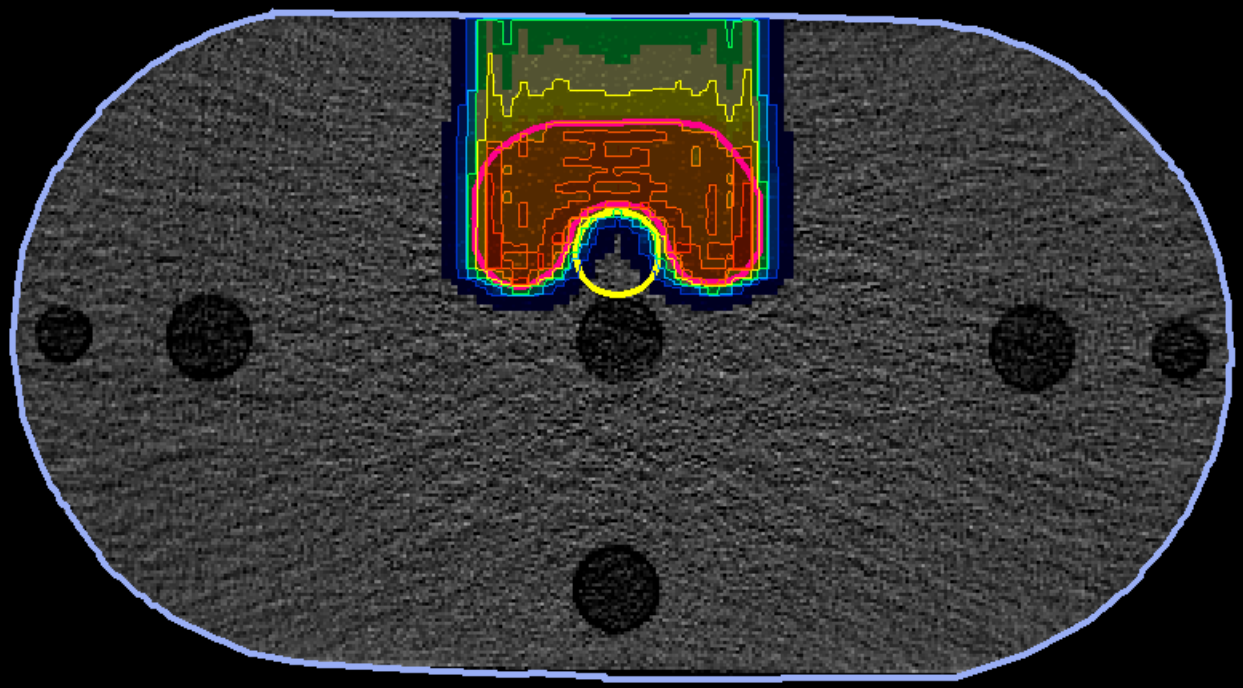
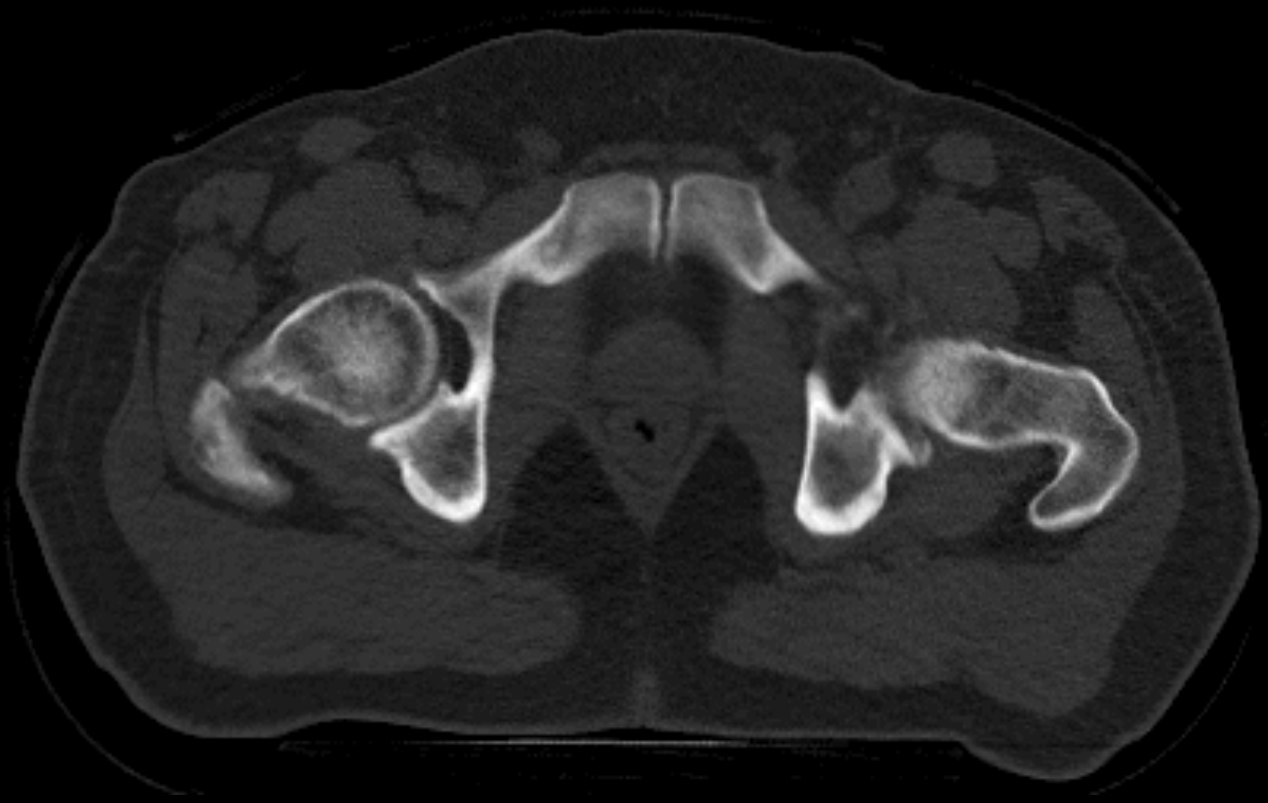
With particle therapy, it is possible to deliver more conformal dose distributions…

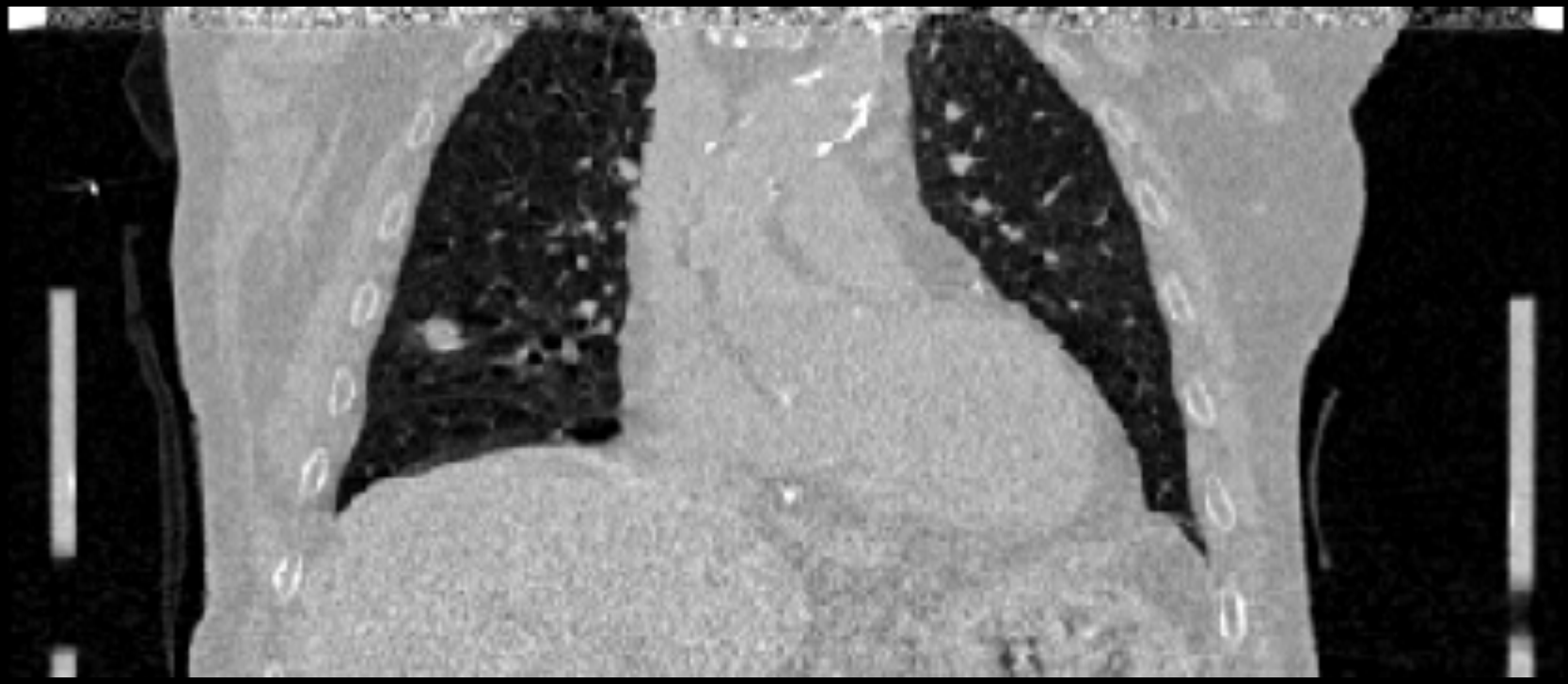


83 MeV/u pencil beam spots with different energies and lateral position

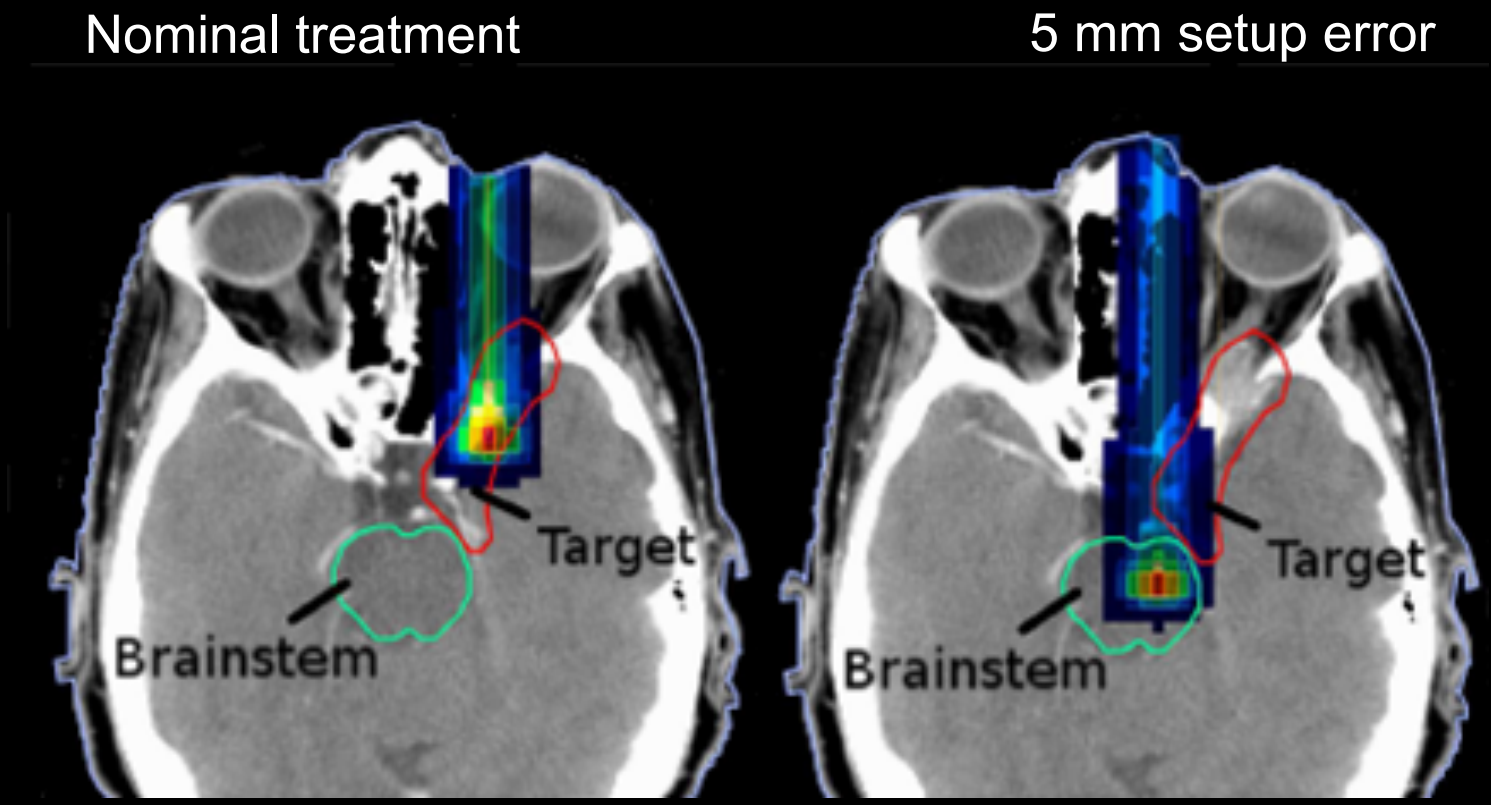
Inter-fractional motion – motion between different days…



Intra-fractional motion – motion during irradiation…



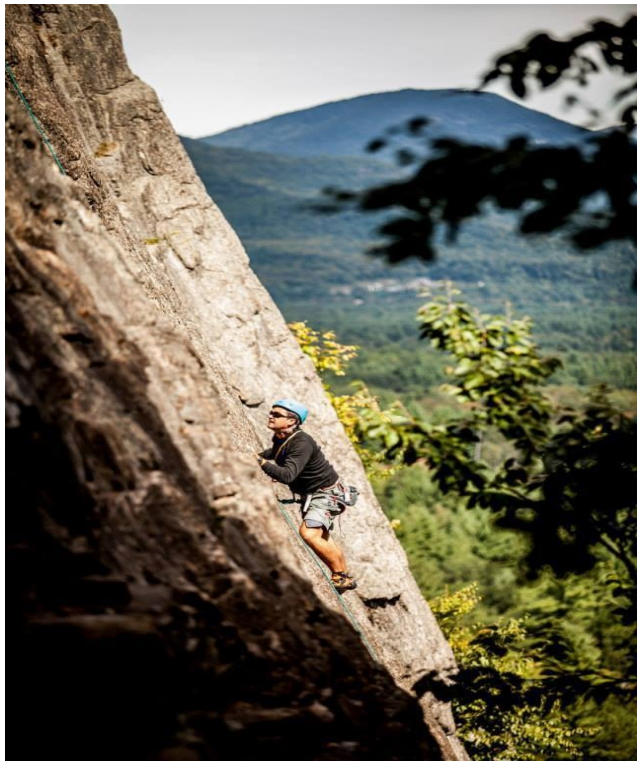
Range and setup uncertainties in particle therapy



Thank You for Your Attention ☺

DKFZ Group

Relaxing!



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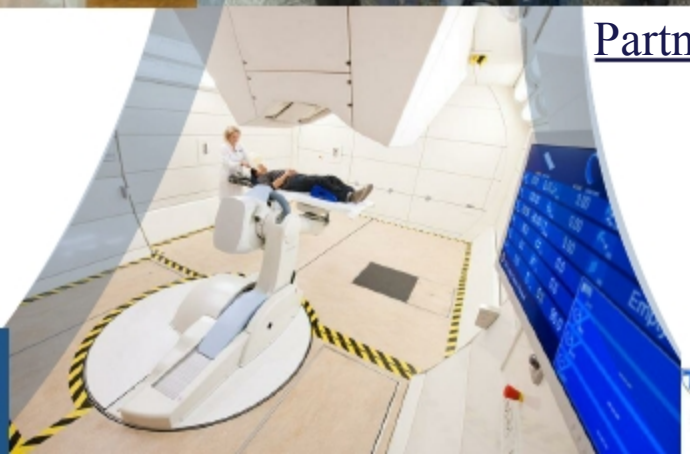
QUESTIONS????

Partners:

HIRO
Heidelberger Institut für Radioonkologie



OncoRay Radiation Research in Oncology

GSI

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