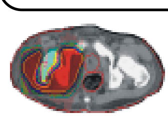
Modern Treatment Planning

INTRODUCTION

Treatment planning is the process of determining the most appropriate way to irradiate the patient

1. Choosing an appropriate patient positioning and immobilisation method so that treatments will be reproducible;
2. Identifying the shape and the location of the tumor and of the neighbouring organs at risk;
3. Selecting a suitable beam arrangement;
4. Evaluating the resulting dose distribution;
5. Calculating the treatment machine setting to deliver the required absolute dose.



PATIENT IMMOBILISATION

Head immobilisation accessories:

- Patients to be treated in the head and neck or brain areas are usually immobilized with a plastic mask which, when heated, can be moulded to the patient's contour.

- The mask is affixed directly onto the treatment couch or to a plastic plate that lies under the patient thereby preventing movement.

PATIENT IMMOBILISATION

Fixations for special treatment techniques:

- Special techniques, such as **stereotactic radiosurgery**, require such high precision that conventional immobilization techniques are inadequate.
- In radiosurgery, a **stereotactic frame** is attached to the patient's skull by means of screws and is used for target localization, patient setup, and patient immobilization during the entire treatment procedure.

Patient data aquisition

First step in the TPS process. It is required for three different purposes:

1. To assess the position and extent of the target volume in relation to the other anatomical structures, particularly the organs at risk;
2. To acquire the data required for accurate computation of the dose distribution (shape and composition of the body);
3. To acquire the information necessary for the acurate set up of the patient (landmarks, reference structures, …);

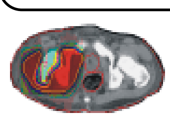
PATIENT DATA ACQUISITION: COMPUTER TOMOGRAPHY

- Enormous technical breakthrough:

  From 2-dim projections CT computes a property of the patient at every point within the the 3D space (resolution < 1 mm)

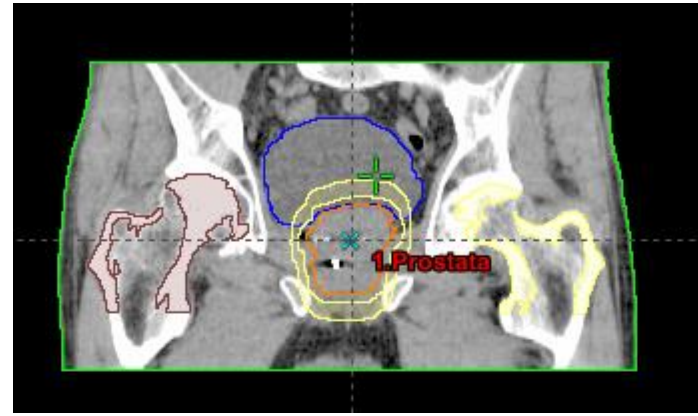
- Measured property:

  Linear x-ray absorption coefficient of the tissue relative to that of water (expressed in Hounsfield units)



COMPUTER TOMOGRAPHY FOR TREATMENT PLANNING

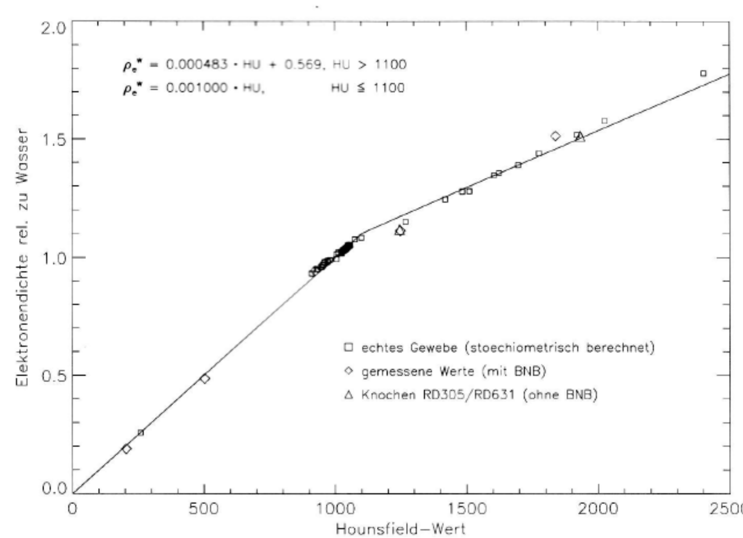
- Definition of targets and OARs



- Basis for dose calculation

  Tissue heterogeneities are considered quantitatively.

  <u>Problem:</u> CT numbers measured at kV energies, patient treated at MV energies!



Target Definition

TARGET DEFINITION: Gross tumor volume

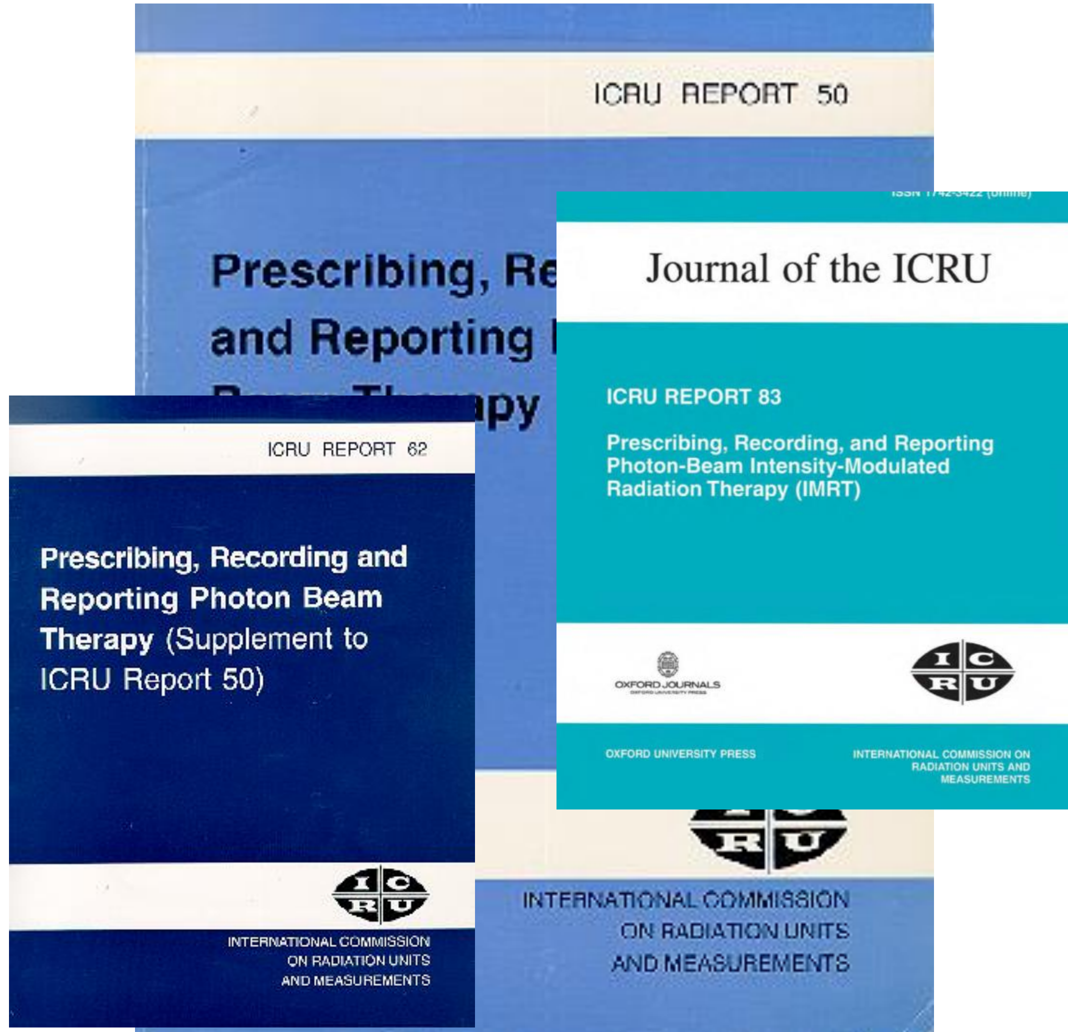
Radiotherapy is a local treatment
(which is complementary to systemic treatments)

Therefore it is an essential part of the
TP-process to:

(a) Define the tumor
(b) Define organs at risk (OAR)

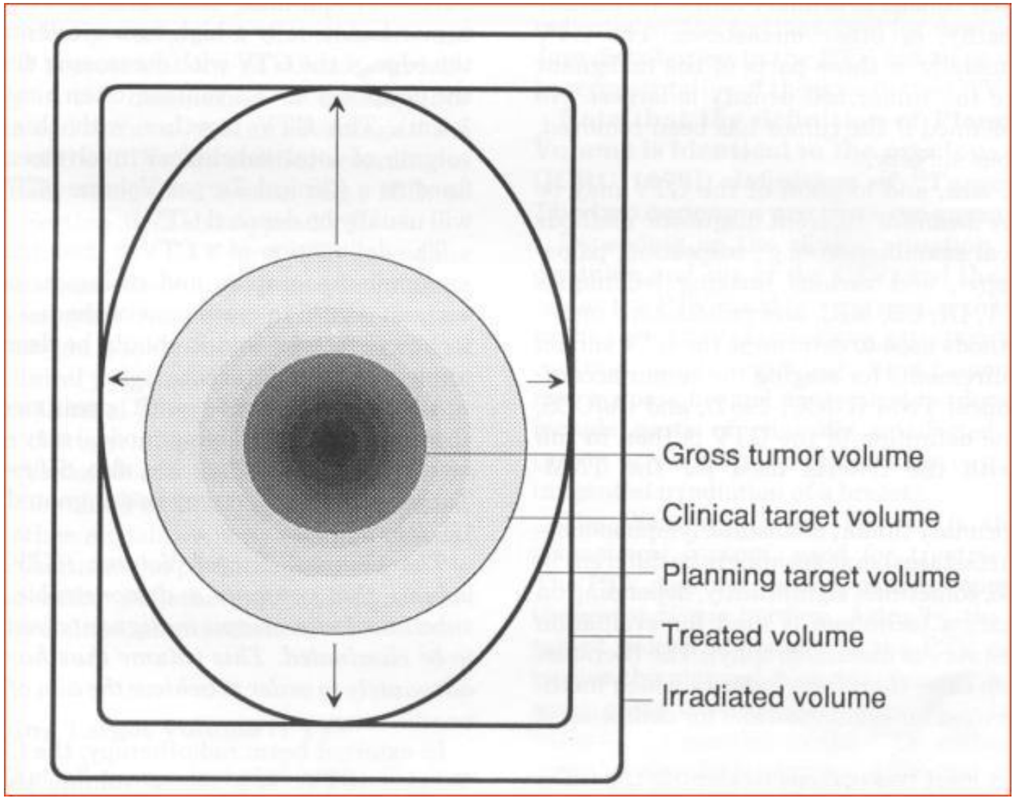
RECOMMENDATIONS BY THE ICRU

- **International Commission on Radiation Units and Measurements**
- **ICRU reports provide guidance on prescribing, recording and reporting**



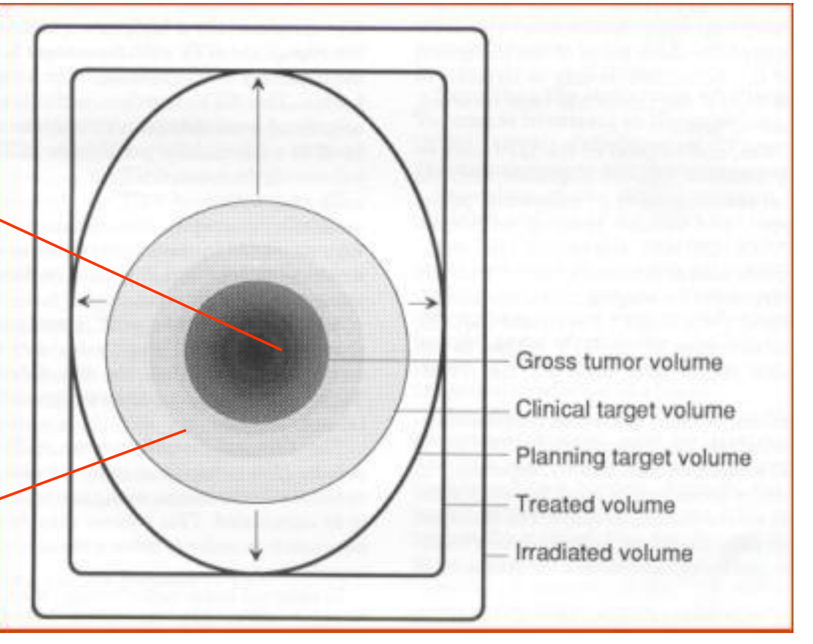
TUMOR RELATED TERMS

- **ICRU report 50**



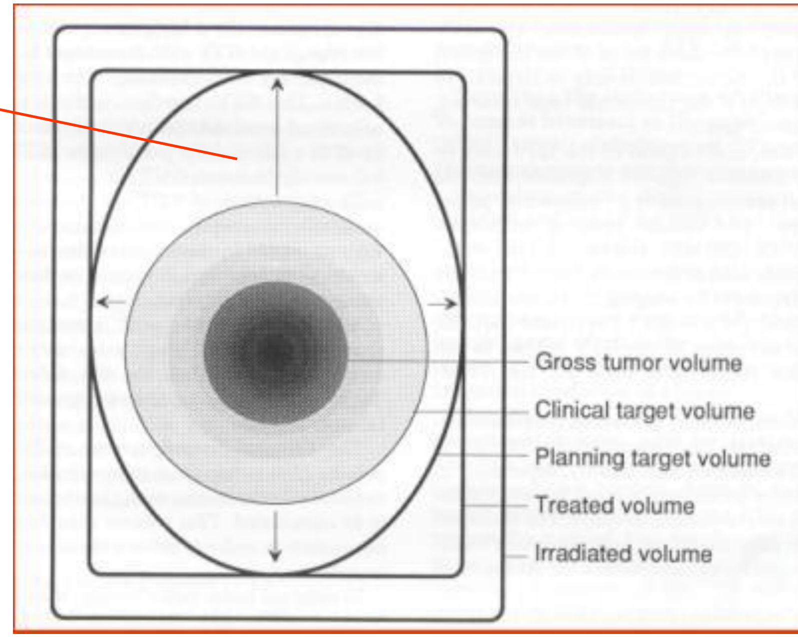
TUMOR RELATED TERMS

- Gross Tumour Volume (GTV) = clinically demonstrated tumour
- Clinical Target Volume (CTV) = GTV + extension for microscopic malignant disease



TUMOR RELATED TERMS

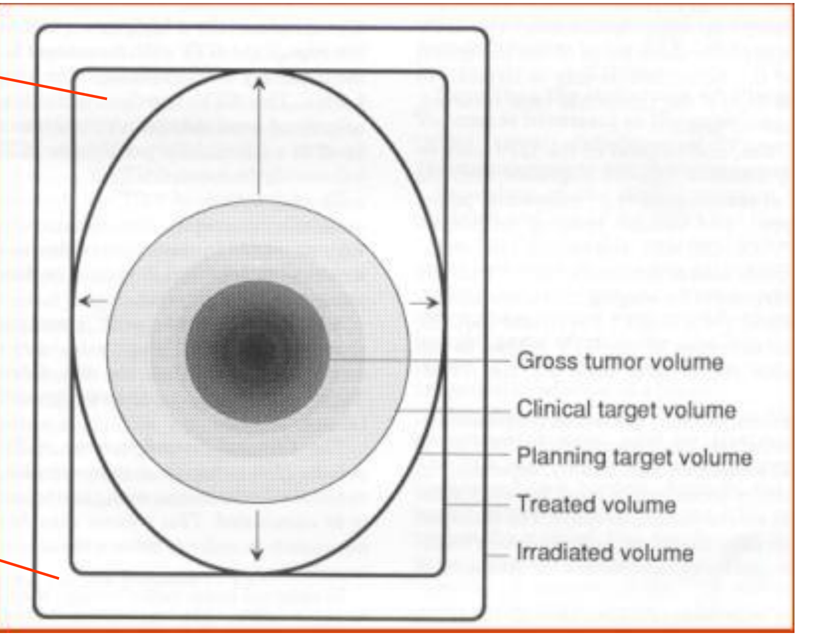
Planning Target Volume (PTV) = volume planned to be treated = CTV + margin for set-up uncertainties and potential of organ movement



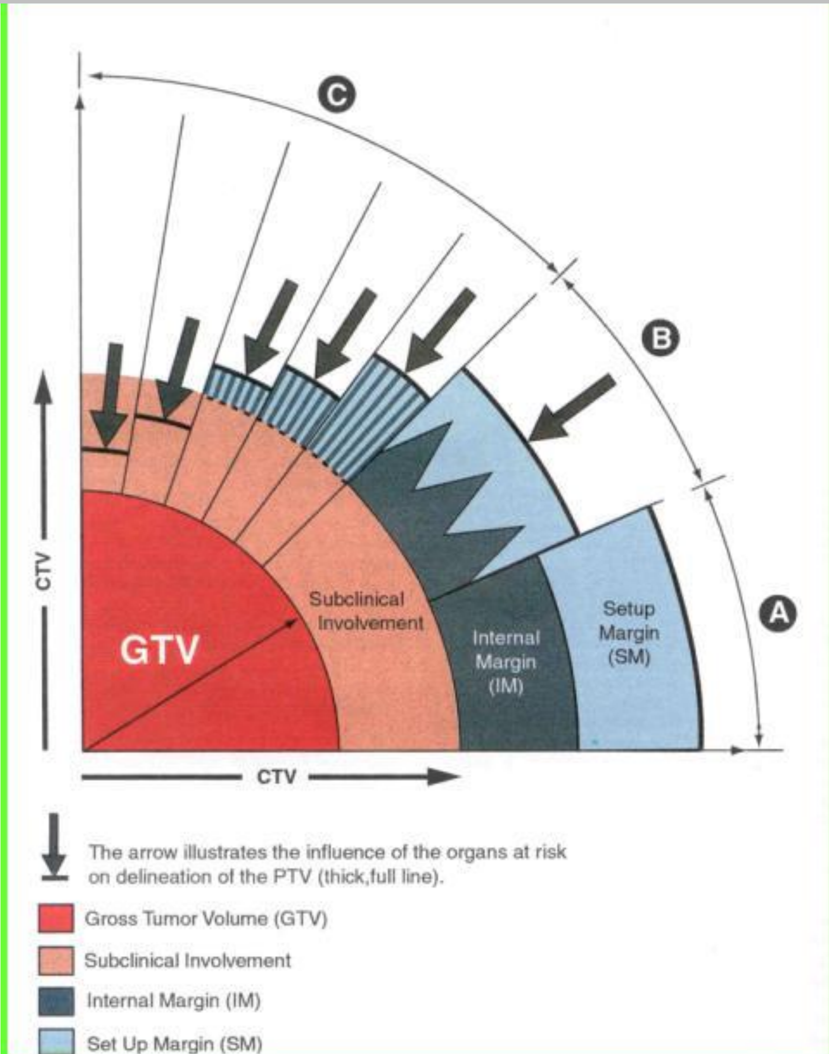
TUMOR RELATED TERMS

Treated Volume = volume that receives dose considered adequate for clinical objective

Irradiated volume = dose considered not negligible for normal tissues



DEFINITIONS FROM ICRU 62



The concept of margins was expanded on by ICRU report 62

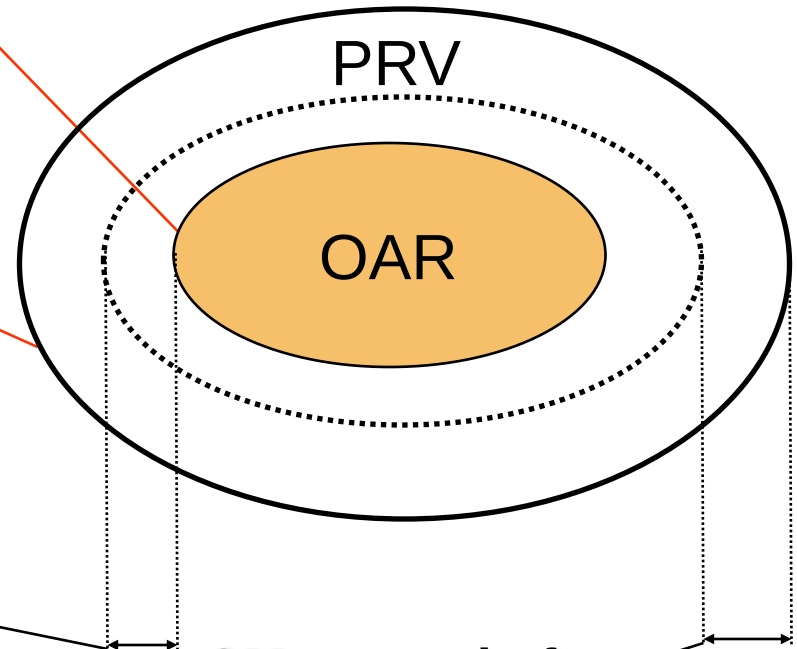
- **Internal margin = due to organ motion**
- **Set-up margin**

The two are often combined as independent uncertainties

NORMAL TISSUE RELATED TERMS

- **Organ at risk (OAR) = any organ of normal tissue which might be imapcted by radiation dose**

- **Planning risk volume (PRV) = OAR + IM + SM**



- **IM = margin for expected physiological movements and size variation**

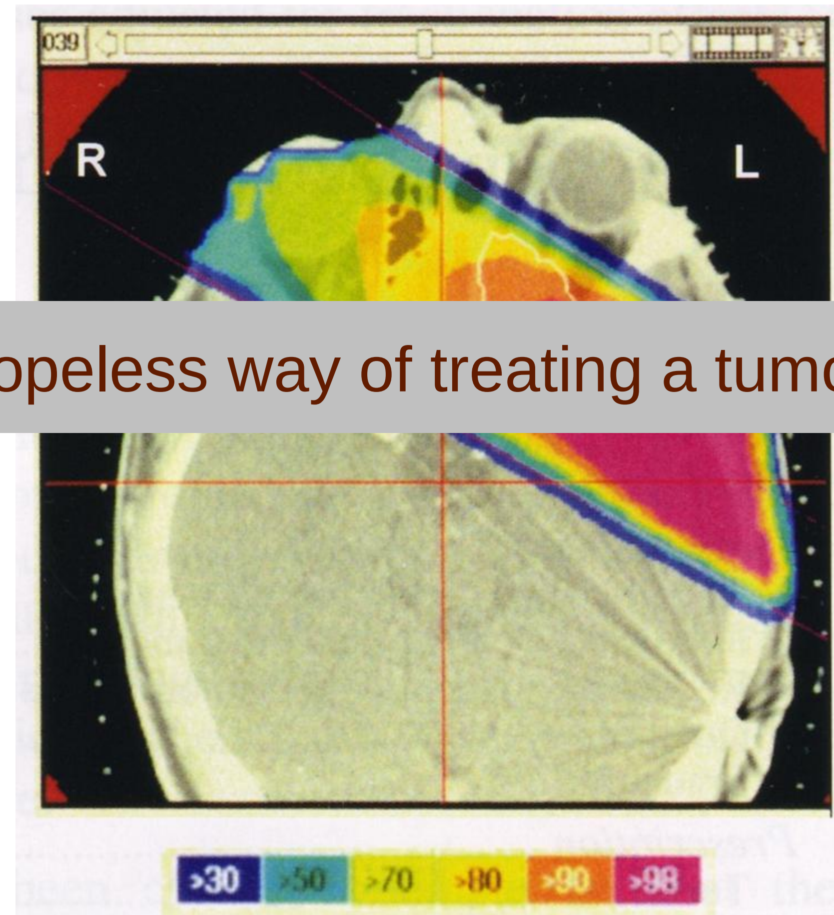
- **SM = margin for uncertainties in patient positioning and beam alignment**

Designing a treatment plan

INTRODUCTION

Application of one treatment beam to a patient:

- Proximal dose is higher than tumor dose
- Beam exits through the eye



Hopeless way of treating a tumor

INTRODUCTION

Solution:

- Tumor cannot be treated using ONE single photon beam
- Use multiple cross-firing beams that concentrate dose within the target
- A treatment plan is the *set* of cross-firing beams and their *weights*

REQUIREMENTS ON THE OVERALL TREATMENT

The clinician must specify the:

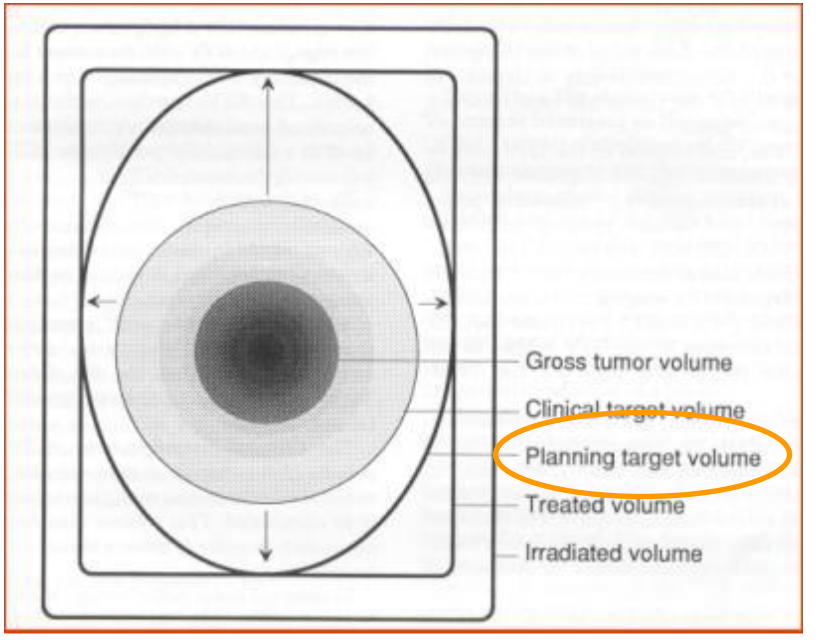
- Fractionation scheme
- Prescription dose

	Physician's Intent
Prescription ID	1.1
Predecessor ID	
Status	Reviewed
Patient Orientation	
Volume (Site)	Breast, Left
Treatment Type	3D-Planung
Energy Mode	
Depth	
Prescribed %	
Prescribed Dose / Fraction [Gy]	2.000
Planned Dose / Fraction [Gy]	
Planned No. Fractions	30
Fractions per Week	5
Fractions per Day	1
Delivered Dose to Date [Gy] +	
Delivered No. Fractions to Date	
Remaining Dose [Gy] +	
Remaining No. Fractions	
Planned Total Dose [Gy] =	60.000
Note	1.Serie bis 50 Gy, dann Boost bis 60 Gy
Entered By	kati
Entered Date	28.01.2008 11:24:28
Reviewed By	kschneider
Reviewed Date	28.01.2008 15:09:58
Create Plan...	Create Plan...
Treat Approved By	
Treat Approved Date	

REQUIREMENTS REGARDING THE TUMOR

Tumor dose is prescribed to the PTV:

- Point-Dose prescription
- Dose homogeneity

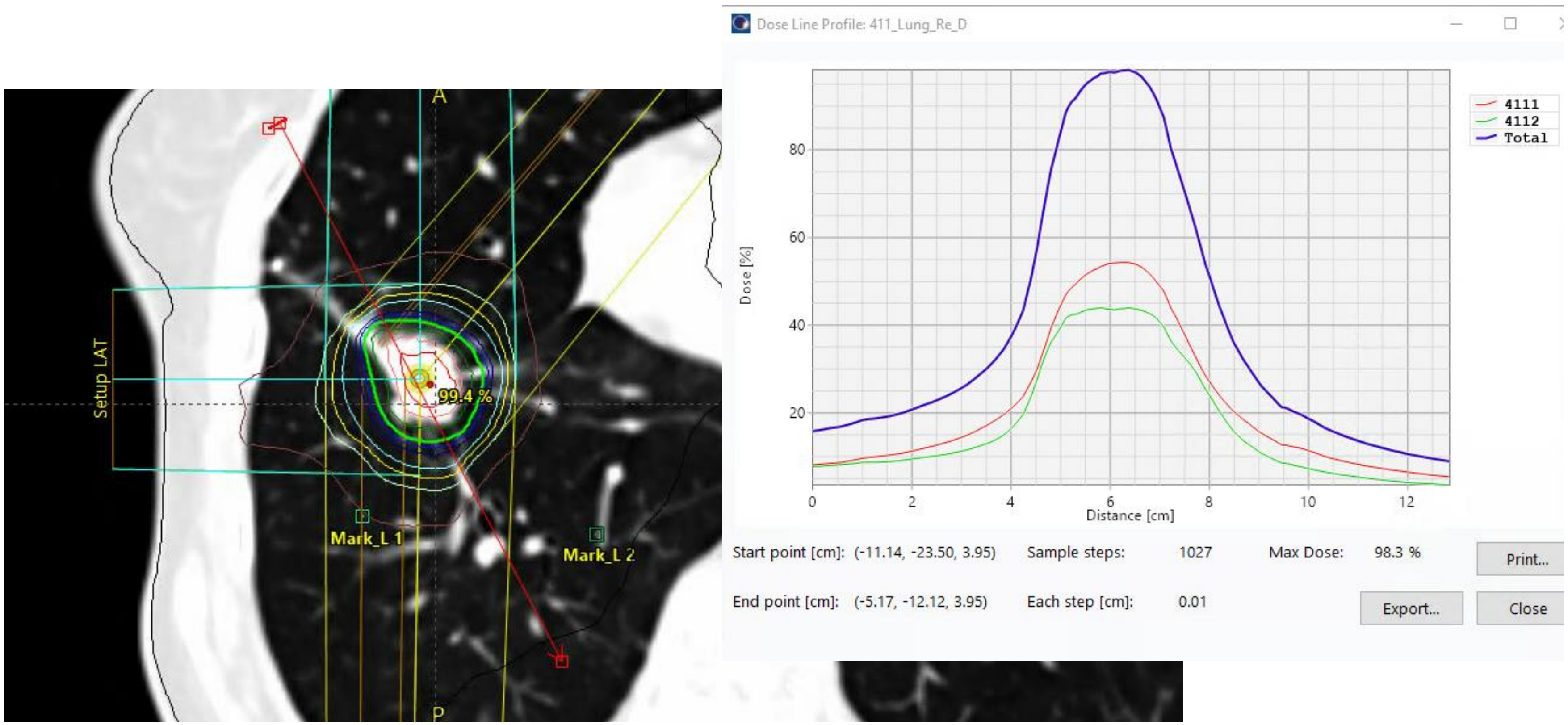


ICRU recommendations:

$95\% < Dose_{pres} < 107\%$

Prescribing dose in sterotactic RT

Dose profile is Gaussian shaped:



Prescribing dose in sterotactic RT

Conformity and prescription depends:

- machine
- filters used
- size of MLC/collimators
- SSD
- ....

Isodose Prescription:

$50\% < Dose_{pres} < 90\%$

Dose evaluation in sterotactic RT

Course ID: 4 Plan ID: 411_Lung_Re_D Target Volume ID: 41_PTV_UL_R

Approval Status: TreatmentApproved Modification by: radonk\jb Modification Date/Time: 16.08.2024 16:56:13

Evaluation by: Uwe Schneider Evaluation Date/Time: 30.09.2024 12:20:43

Plan Summary

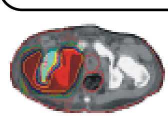
Course ID	Plan ID	Plan Type	Original Target Volume ID	Presc. %	Dose / Fraction	Number of Fractior
4	411_Lung_Re_D	External Beam	41_PTV_UL_R	70.00 %	10.00 Gy	5

☑ Lung Plan ☐ Intracranial / SRS Plan

Plan Details

Target Volume ID	**41_PTV_UL_R**	Target Volume ccm:	7.55 ccm
Prescription Percentage:	70.00 %		
Target Min Dose:	86.34 % 43.17 Gy		
V100% / PTV V100%:	1.22	Target 99% Coverage	95.50 %
NCI:	1.27	MGI:	5.76
PTV V100% PD:	96.55 %		
		Lunge Auswertung	
Lung-GTV V20:	1.29 %	Max Dose 2 cm:	24.31 Gy
Bermerkungen:			

Verwendete Auswertungskriterien für SBRT Pläne für Lunge Zielvolumina, mit Volumina = 7.55, ccm
Prescription Isodose von 60% bis 90%
PTV V100%PD >= 95%, D at 99% of PTV >= 90%
V100%/PTVV100% Target <= 1.2, Tolerance < 1.25, Minor Deviation 1.25 - 1.4
NCI optimal < 1.2, zwingend < 1.5
MGI (V50%/PTVV100% Target <= 7, Tolerance <= 9, Minor Deviation 9 - 11
Lung-GTV V20 (%) < 5%
Max dose > 2 cm < 35.8 Gy



Dose evaluation in sterotactic RT

Application of the LQ-model is questionable:

Radiotherapie Hirslanden   HIRSLANDEN

Eigentum von: Radiotherapie Hirslanden AG, 5001 Aarau   RL.34.001

Tabelle 1. Dosisgrenzwerte für gesundes Gewebe und Organe

Organ / Gewerbe	5 Fraktionen		3 Fraktionen		1 Fraktion		Kommentare und Bemerkungen	Endpoint >= Grade 3 Complication if not commented differently / comments	Reference
	Optimal	Mandatory	Optimal	Mandatory	Optimal	Mandatory			
Hirnstamm	D_0.035cm^3 < 23Gy	D0.035cm^3 < 31Gy D0.5cm^3 < 23Gy	D0.035cm^3 < 18Gy	D0.035cm^3 < 23.1Gy D0.5cm^3 < 15.9Gy	D0.1cm^3 < 10Gy	D0.035cm^3 < 15Gy D0.5cm^3 < 10Gy		Grade 3+ cranial neuropathy	UK SABR [15], Timmer. 2022 [13]
						Dmax < 12.5Gy	risk rate <5%	Grade 3+ cranial neuropathy	Mayo et al. [12]
Gehirn zus. mit GTV		V29Gy < 20cm^3		V23Gy < 20cm^3		V14Gy < 20cm^3	Prior whole brain RT appears to not markedly increase risks in most reports (with the exception of brainstem). However, repeat SRS/fSRS to the same area has been associated with markedly increased risks. [4]	3.4% risk of Grade 3 Toxicity (Necrosis)	HyTEC Brain 2020 [4]
						V14Gy < 10cm^3		0.8% risk of Grade 3 Toxicity (Necrosis)	
						V14Gy < 5cm^3		0.4% risk of Grade 3 Toxicity (Necrosis)	
						V12Gy < 5cm^3		10% risk of radionecrosis	
						V12Gy < 10cm^3		15% risk of radionecrosis	
		V24Gy < 20cm^3		V20Gy < 20cm^3				<10% risk of any necrosis or edema, and <4% risk of radionecrosis requiring resection	
		V24Gy < 30cm^3		V20Gy < 30cm^3				<20% risk of any necrosis or edema, and <4% risk of radionecrosis requiring resection	
Sehbahnen (Optic tract) und Chiasma	D0.035cm^3 < 22.5Gy	D0.035cm^3 < 25Gy D0.2cm^3 < 23Gy	D0.035cm^3 < 15Gy	D0.035cm^3 < 20Gy D0.2cm^3 < 15.3Gy	D0.035cm^3 < 8Gy	D0.035cm^3 < 10Gy D0.2cm^3 < 8Gy	Prior RT exposure of the optic pathway (either whole brain RT or SRS/fSRS) appears to markedly increase risks [6]	<1% risk of Grade 3+ optic neuropathy, Grade 3+ optic neuritis	UK SABR [15], HyTEC Optic Pathways 2017 [6], AAPM [1], Timmer. 2022 [13]
Orbita					D0.1cm^3 < 8Gy			Retinopathy	UK SABR [15]
Retina		Dmax < 5Gy		Dmax < 5Gy		Dmax < 5Gy		Retinopathy	Grimm et al [5]

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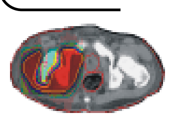


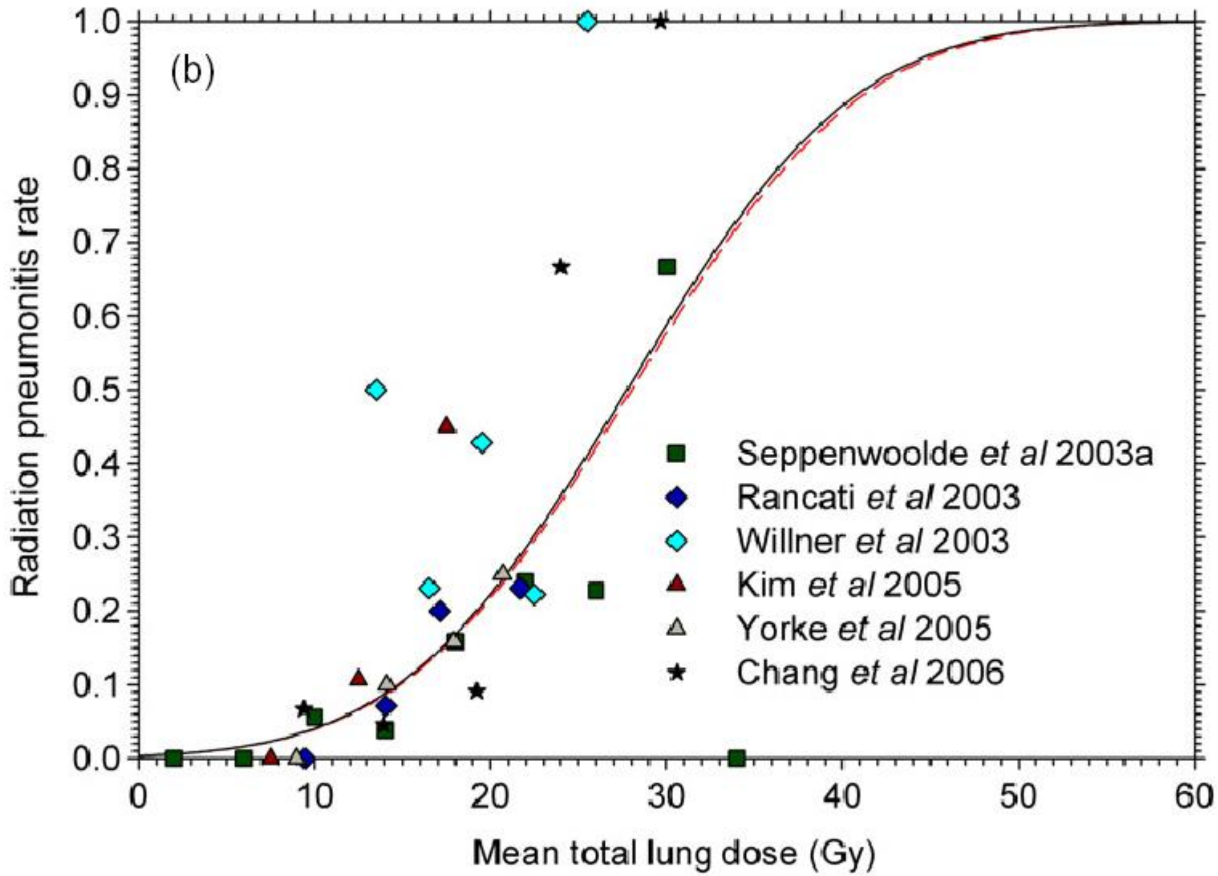
REQUIREMENTS REGARDING THE NORMAL TISSUES (OAR)

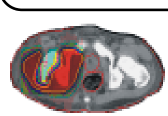
Requirements on OARs are stated as constraints:

- Constraints on dose and volume:
  "no more than 1/3 of the kidney may receive more than 60 Gy"
- Biological constraints:
  "the normal tissue complication probability (NTCP) for pneumonitis of the lung should not exceed 1 %"
- Constraints on dose fraction:
  "the maximum dose per fraction delivered to the optic nerve may not exceed 1.5 Gy"

REQUIREMENTS REGARDING THE NORMAL TISSUES (OAR)

Radiation pneumonitis as a function of mean lung dose





TRADEOFFS

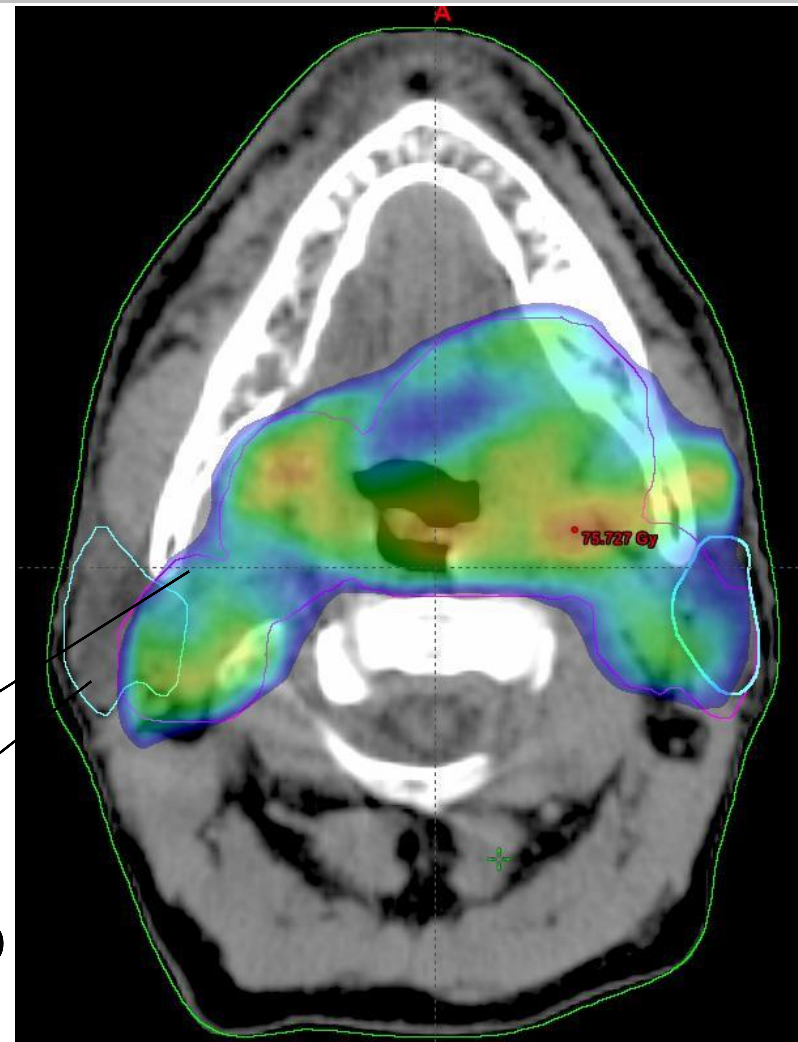
Usually no treatment approach can meet all planning aims.

↓

This will result in tradeoffs amongst target volume and normal tissue aims.

Example:

- treatment of the total PTV up to 70 Gy
- sparing of parotis (mean 26 Gy)



REPRESENTATION OF DOSE

One cannot discuss the design of a treatment plan until having discussed the tools for inspecting one.

The dose distribution includes:

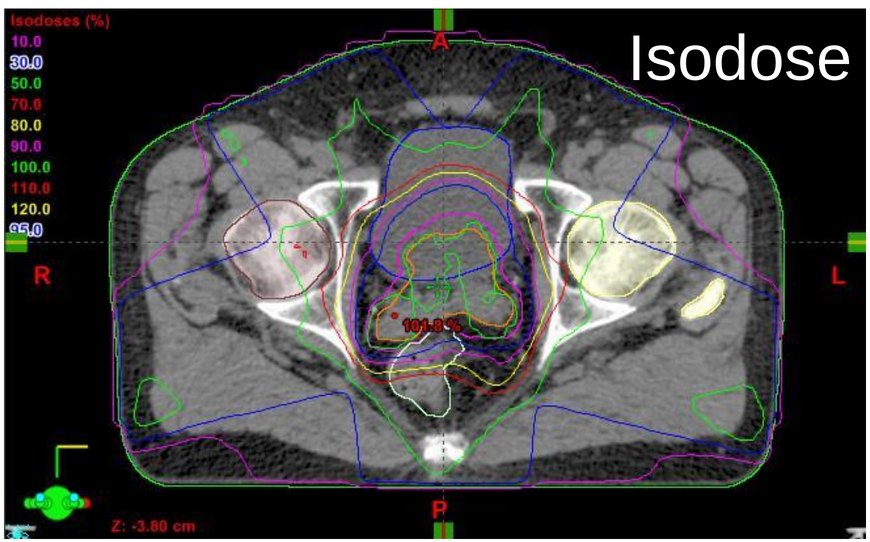
- The dose from a plan in all 3D-directions
- Anatomical information from one or more imaging studies
- Anatomical information from structure delineation

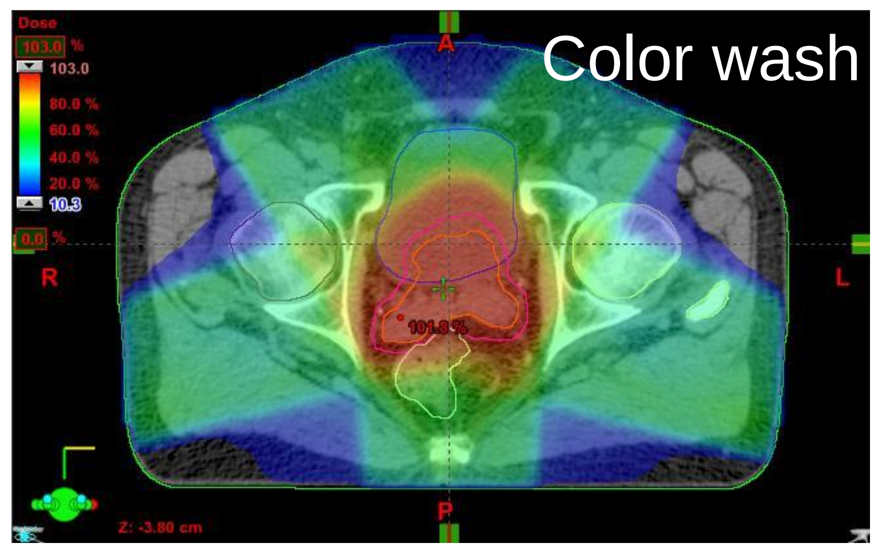
….. and including variations of these data in time

2D DOSE DISTRIBUTIONS

Dose and anatomy are superimposed:

- Anatomic information is represented by image intensity
- Overlay of the outlines of the delineated structures
- Dose display as isodoses (lines of constant dose) or color wash (dose is related to color)

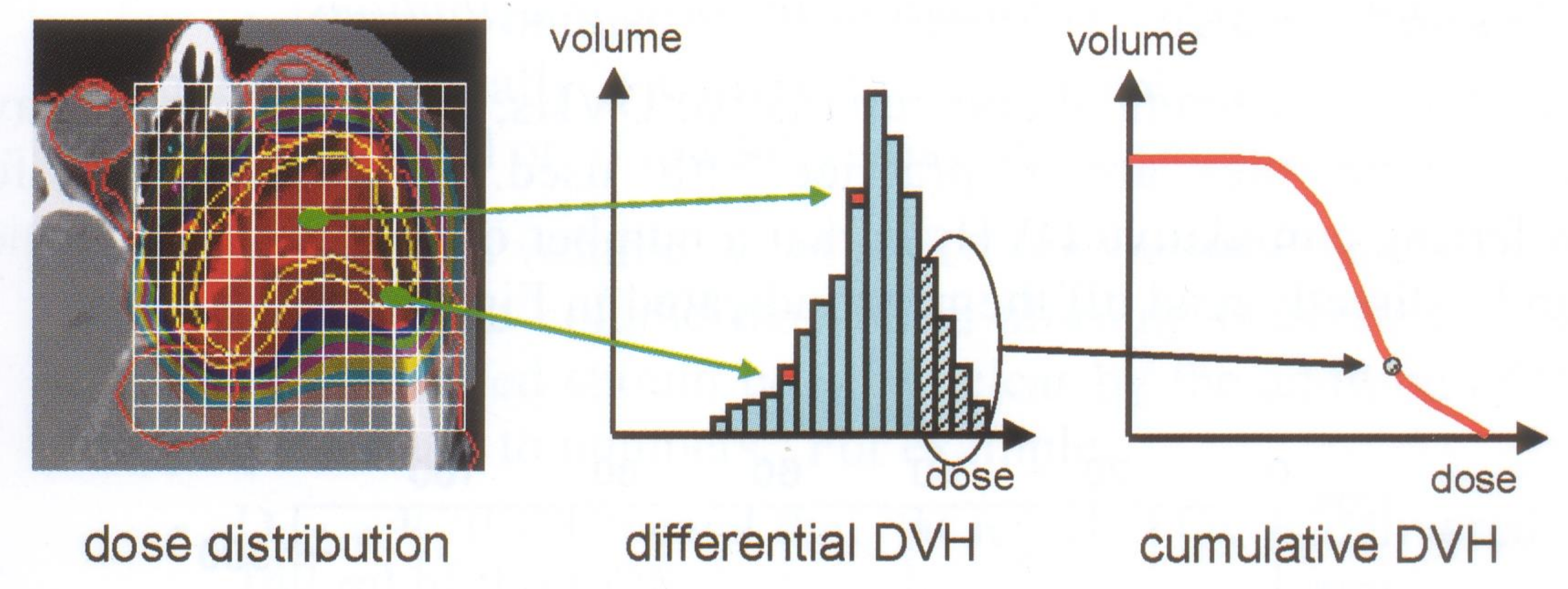




1D DOSE DISTRIBUTIONS

Dose-Volume histogram:

Frequency distribution of dose within a VOI



Attention: spatial information of dose is lost

PRELIMINARIES OF TREATMENT PLANNING

<u>We have been taken care of:</u>

- Imaging studies
- Volumes of interest
- We know how a single photon beam is constructed
- We know how to display dose distributions

….. Let's start

APPROACHES OF TREATMENT PLANNING

Manual planning:

- Plan is iteratively improved
- Review of a large number of computed parameters (“expert inspection”)
- Subjective process

Computer-driven planning:

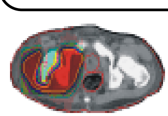
- Decision about the quality of a plan is made by the computer
- Usually used in intensity-modulated radiotherapy

PLANNING BY HAND

Partial list of variables to optimize plan:

- type of therapy
- type of radiation
- the location of the patient the tumor and OARs
- the number of beams
- the angulation and aiming point of each beam
- the shape of each beam
- the weight and intensity profile of each beam

The choice of theses variables is the heart of the planning process



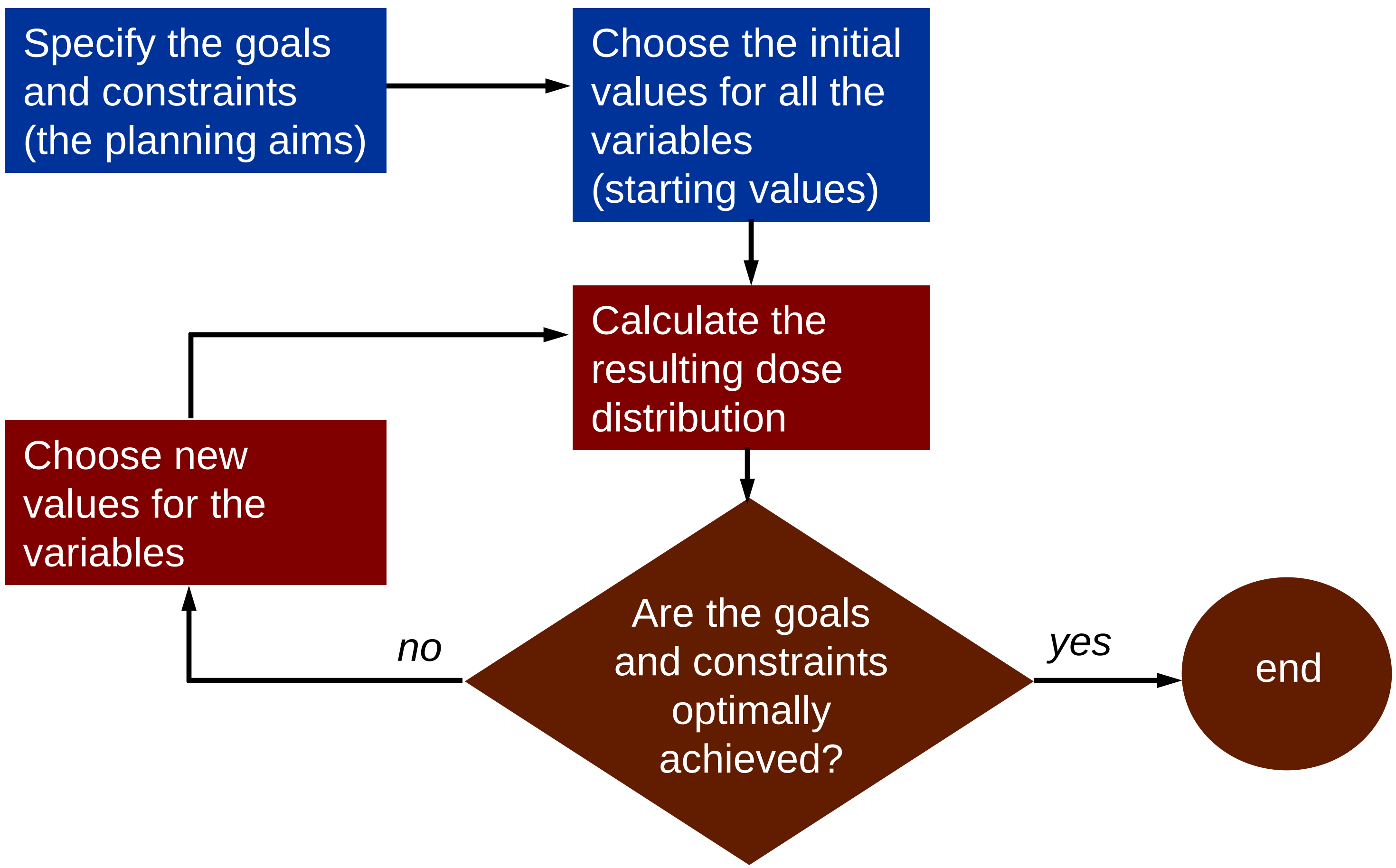
PLANNING BY HAND

On what is the choice of plan variables based on?

- Plans used previously for similar cases
- Rules of thumb as how to set combinations of plan parameter
- Fast calculation engine to calculate interactively the dose distribution
- Display of that dose distribution
- Calculation of dose statistics
- Iteration of the process to arrive at the best plan
- EXPERIENCE

PLANNING BY HAND

Flow chart for manual planning:



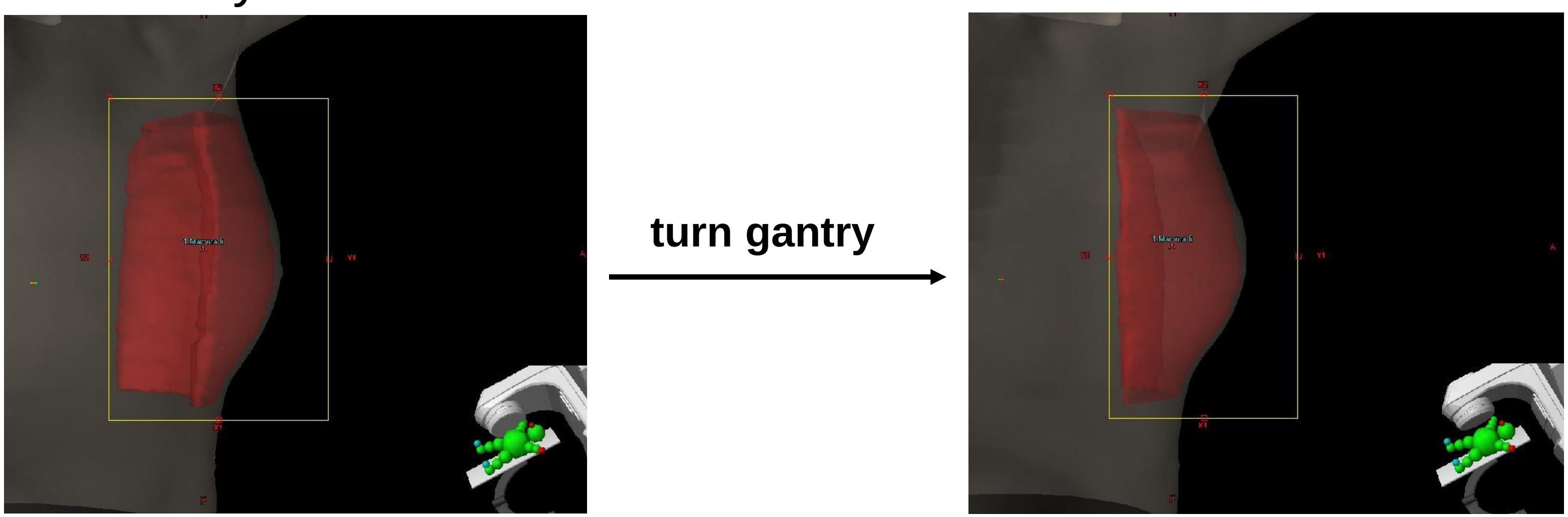
CHOICE OF RADIATION MODALITY AND BEAM ENERGY

	advantages	*disadvantages*
photons	• **widely available** • **good skin sparing**	• **higher entrance dose than tumor dose** • **high dose through patient up to exit surface**
electrons	• **finite penetration, thus sparing tissues distal to the target volume** • **very slight skin sparing**	• **broad penumbra due to scattering** • **only suitable for quite shallow targets due to shallow fall-off of the distal dose at higher energies**
protons	• **virtually no dose distal to the target volume** • **somewhat reduced entrance dose proximal to the target**	• **management of inhomogeneities is not trivial** • **penumbra becomes substantial at large depth** • **no skin sparing** • **limited availability**

CHOICE OF BEAM DIRECTION

Useful approach for direction selection:
Beams-Eye-View (BEV):

- Perspective view of the patient's delineated anatomy as seen from the viewpoint of the radiation source
- Change in beam direction changes display
- Shows the spatial relationship between target and the delineated anatomy

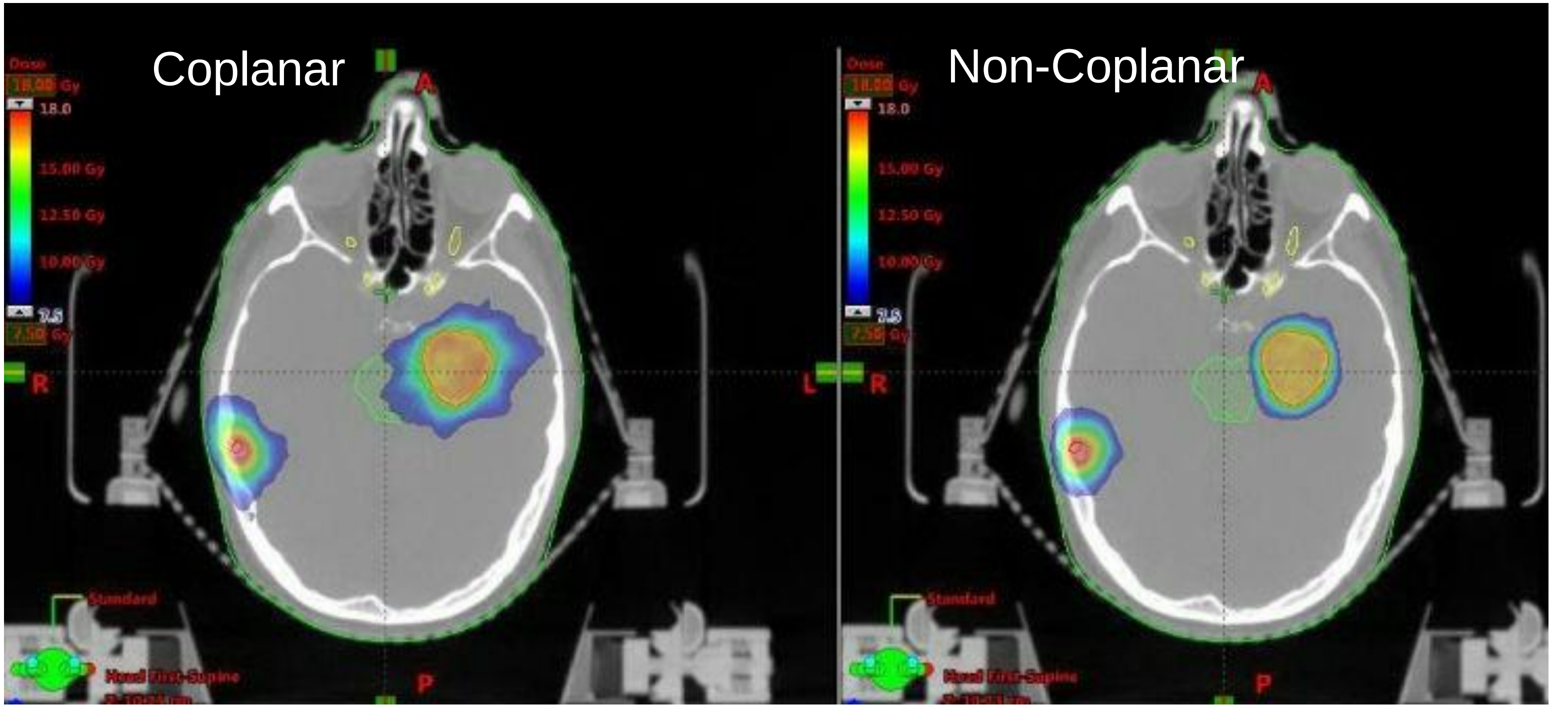


CHOICE OF BEAM DIRECTION

- Frequently the geometry of the target and the OARs will suggest a particular approach
- Not all beams can avoid all OARs; particular OARs are included in one or more beams: dose < constraints
- Linacs rotate around a central point: *isocenter*
- beam lies in a plane perpendicular to the axis of the gantry’s rotation

CHOICE OF BEAM DIRECTION: NON-COPLANAR BEAMS

- Patient couch can rotate around the isocenter
- Is rarely used for geometrical reasons (patient is a “cylinder”)
- Mostly used in head and neck treatments



DESIGN OF FIELD SHAPE

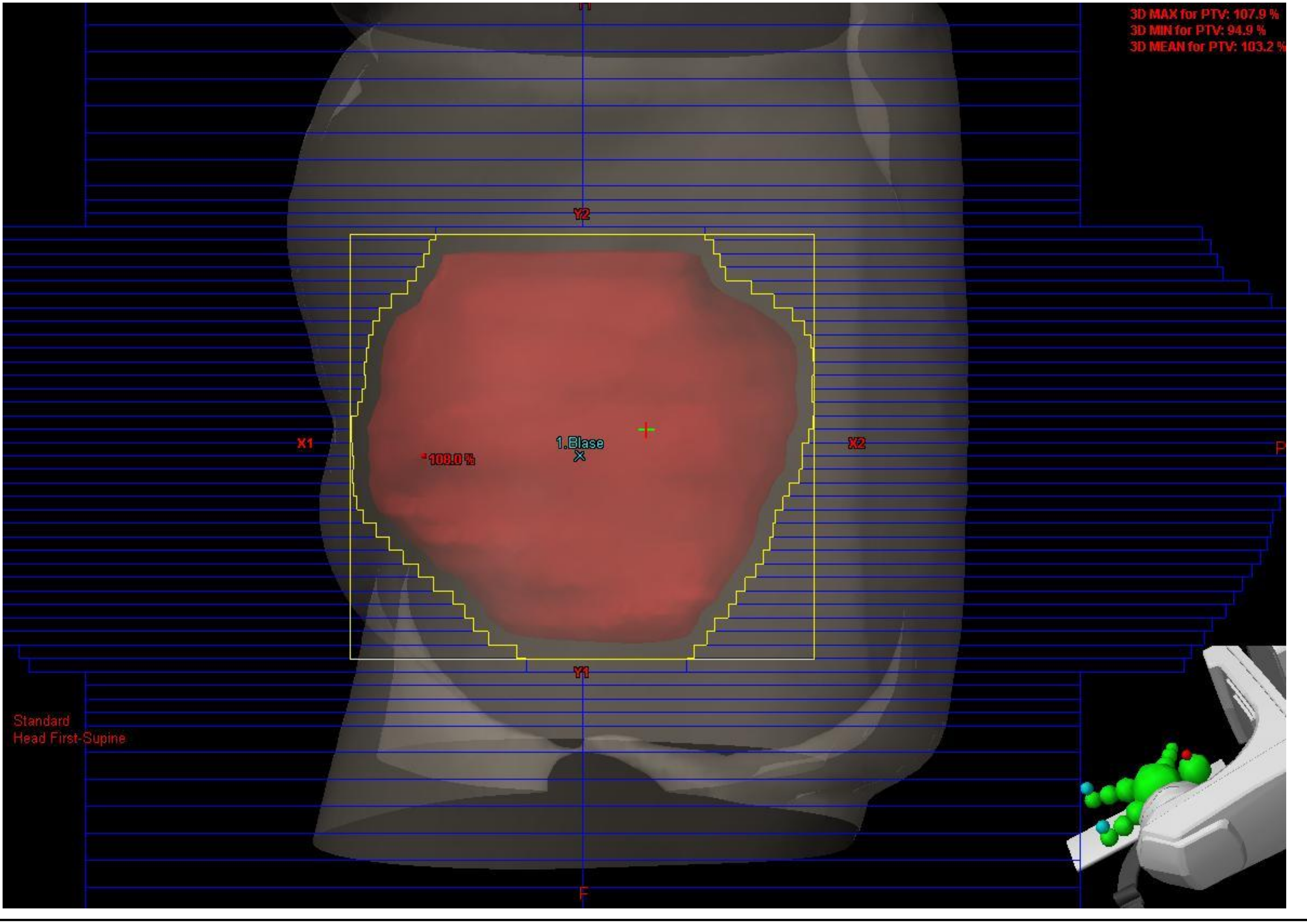
Goal:

- Cover the entire CTV
- Do this with adequate margins (PTV) to take care of patient and organ motion, setup errors and penumbra
- Avoid OARs or minimize volume of OARs that is covered by the beam

Use Beams-Eye-View (BEV):

- Setting the collimator
- Setting the jaws (size of the rectangular field)
- Design of blocks or MLC-settings

DESIGN OF FIELD SHAPE

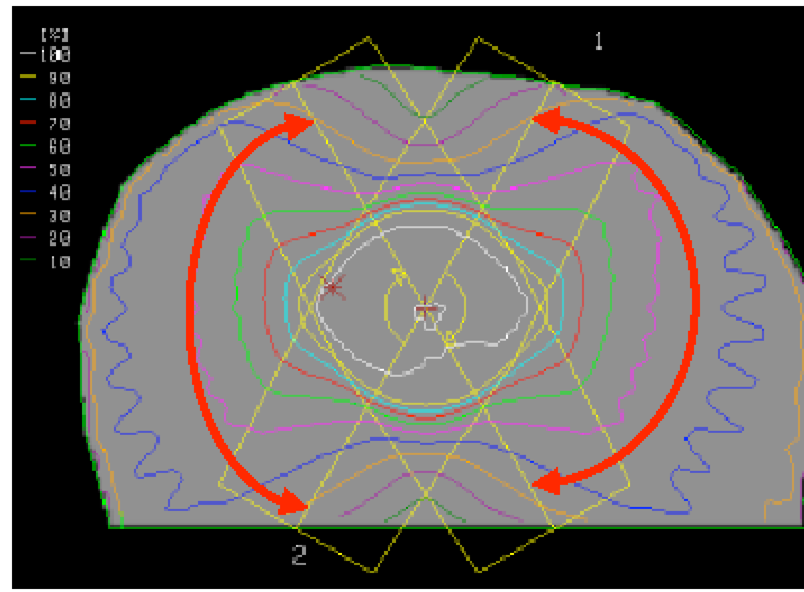


NUMBER OF BEAMS

Generally the choice of number of beams depends on the patient's individual geometry!

- Arc therapy: rotating the beam around the patient (Dynamic Arc)

- Fixed beams:
  - Rarely use one beam, except for superficial tumors
  - Two parallel-opposed beams give a high dose outside the target volume
  - Typically between 3 and 7 beams are chosen

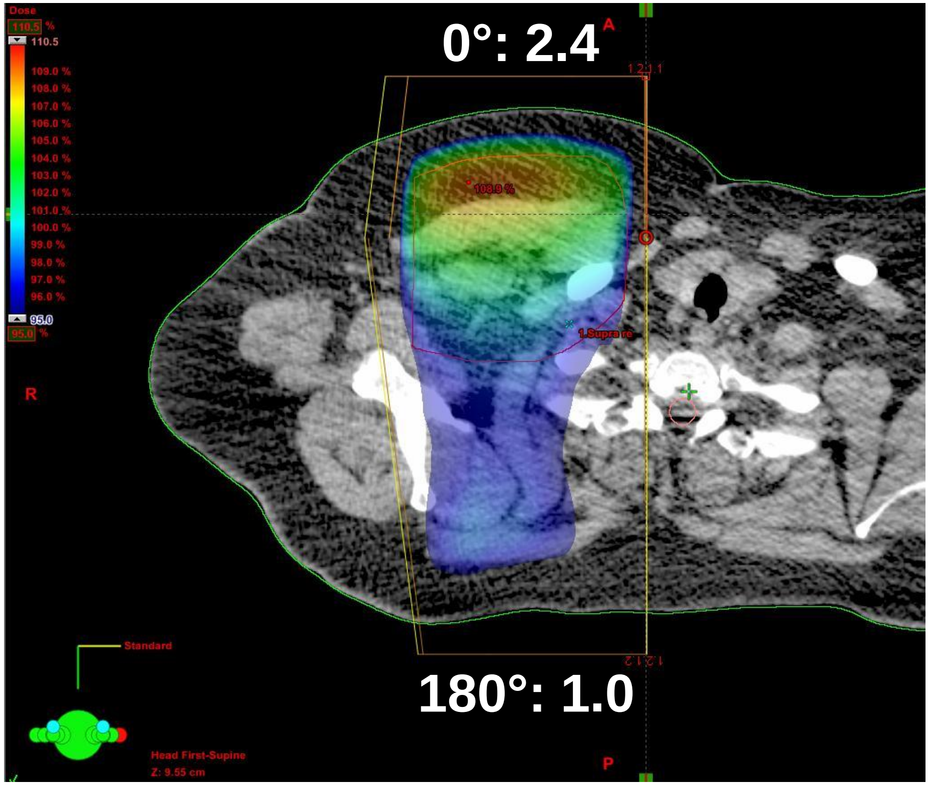


DETERMINATION OF BEAM WEIGHTS

Not all beams
need to be equally weighted = need to deliver the same
dose to the PTV

How is the weighting decided?

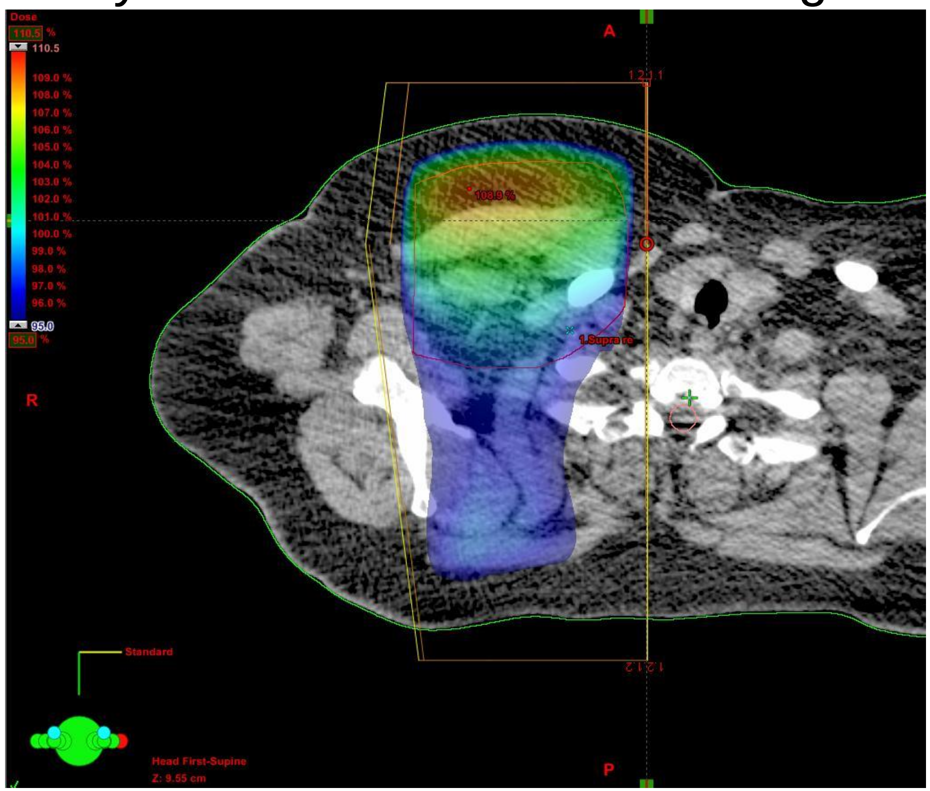
- Experience
- Trial and error
- expert judgement
- Rules of thumb



CENTRAL TENET OF TREATMENT PLANNING

Planner are disposal engineers!

- The planner’s job is to decide how to dispose of the dose that must inevitably be delivered outside the target volume



INTEGRAL DOSE

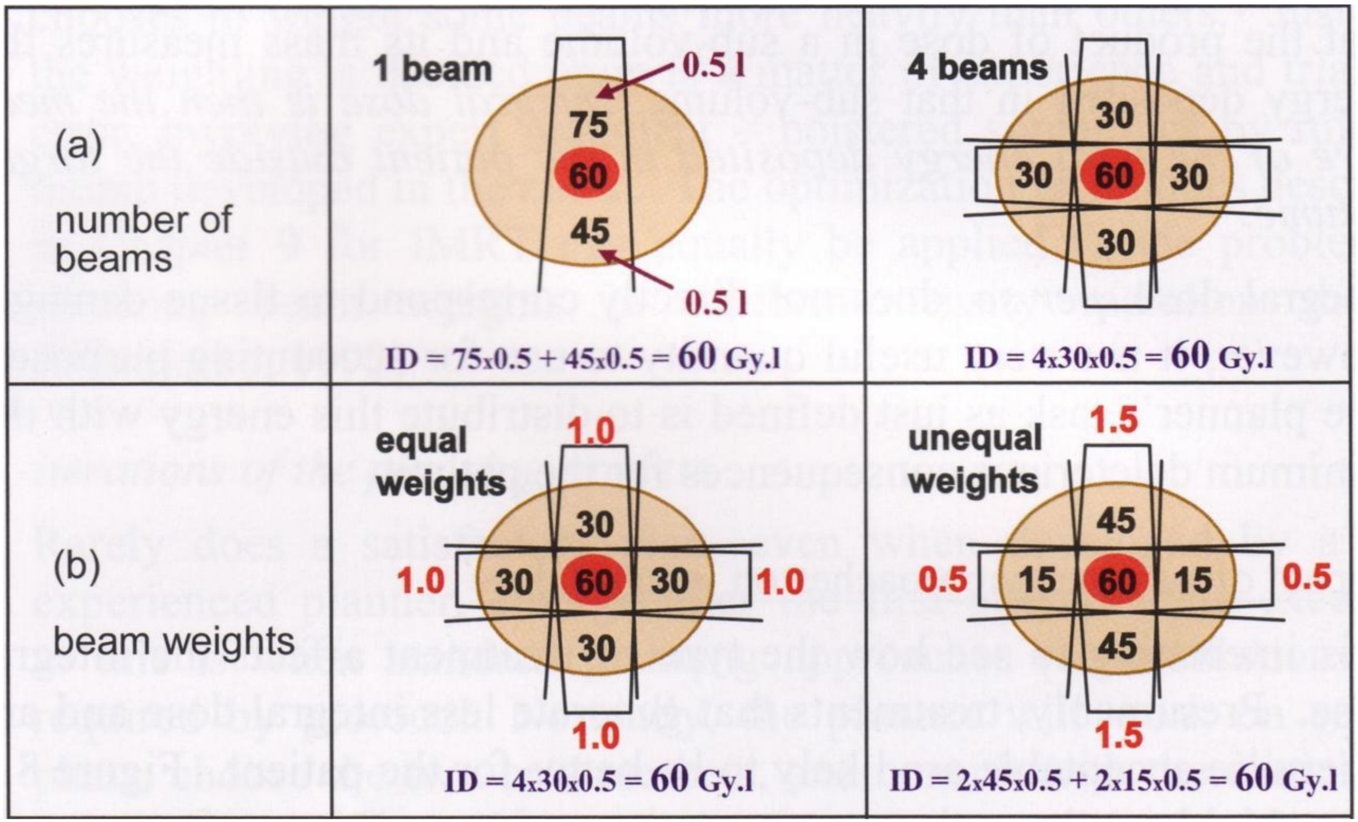
- Dose outside the target volume is a *toxic* substance
- Integral dose is a measure of how much toxic material is involved
- Integral dose is the measure of *total energy* deposited in the patient outside the target volume
- Integral dose does directly correspond to tissue damage

$$I = \sum (D_i \times m_i)$$

Volume outside target

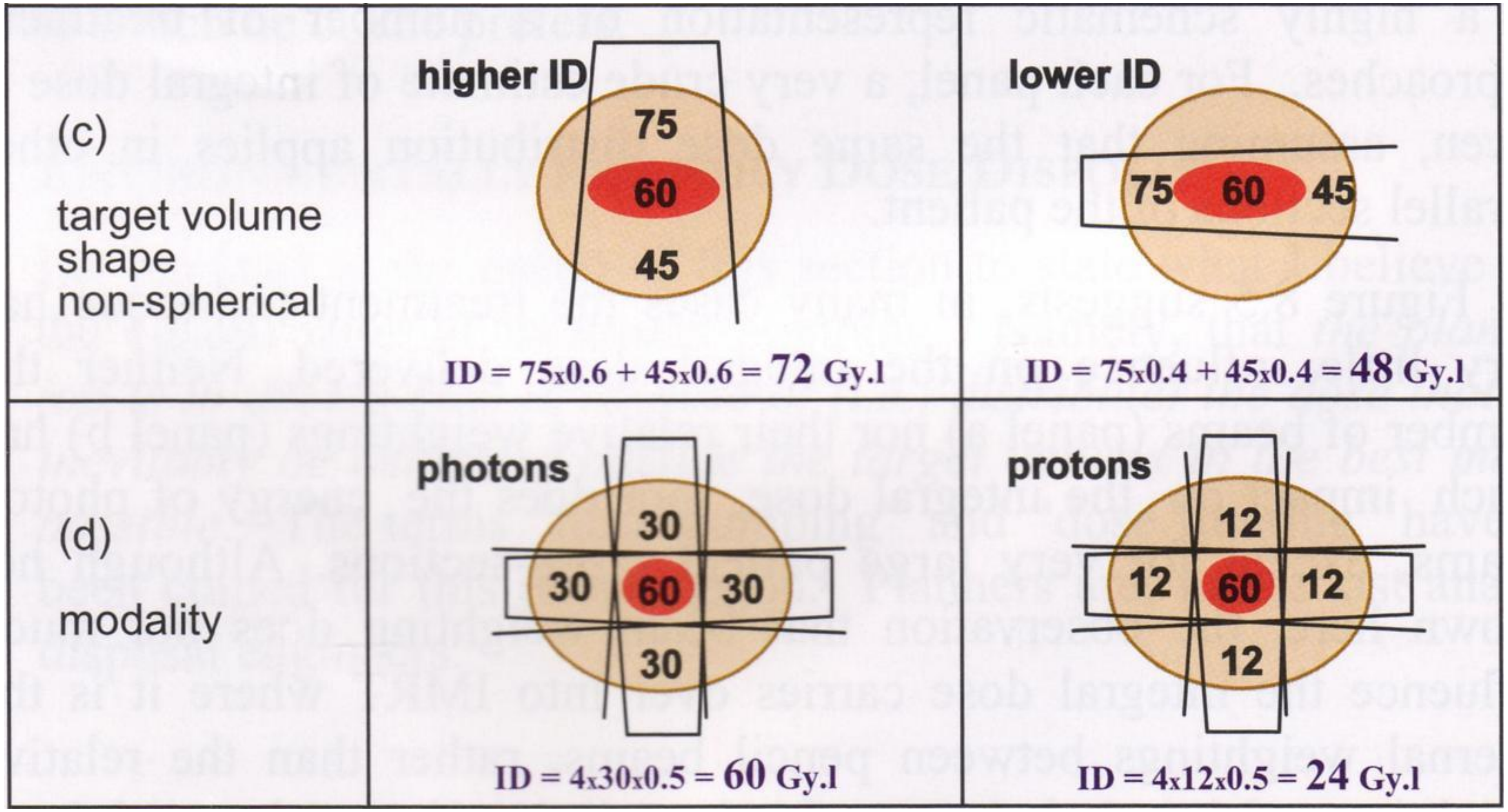
IMPACT OF TREATMENT APPROACHES ON INTEGRAL DOSE

Less integral dose is better for the patient



In many cases treatment technique has little impact on integral dose

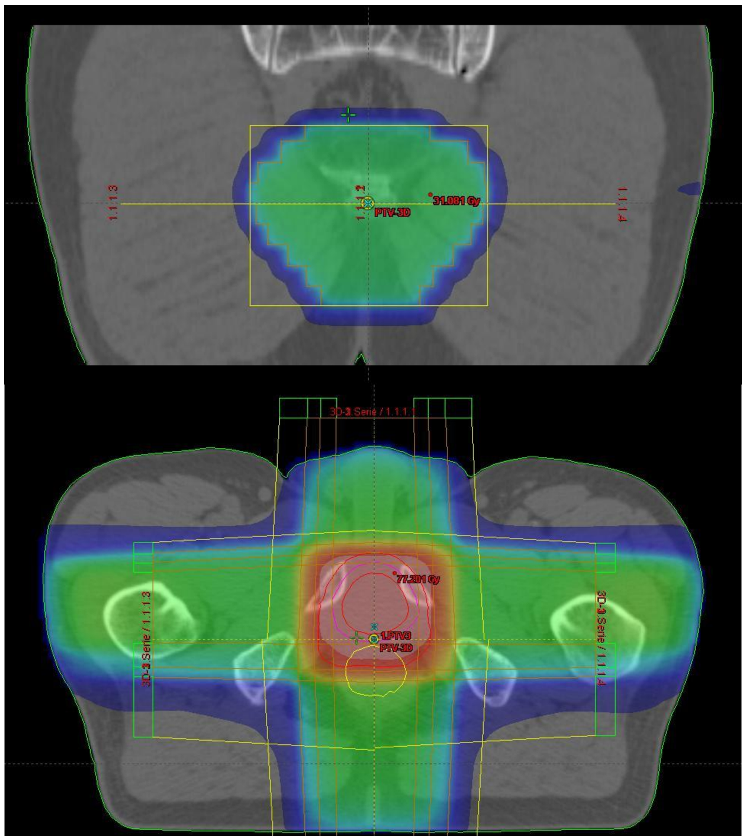
IMPACT OF TREATMENT APPROACHES ON INTEGRAL DOSE



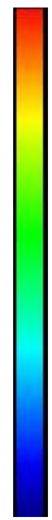
Target shape and radiation modality have biggest impact on integral dose

A LOT TO A LITTLE OR A LITTLE TO A LOT?

Conformal 3D irradiation

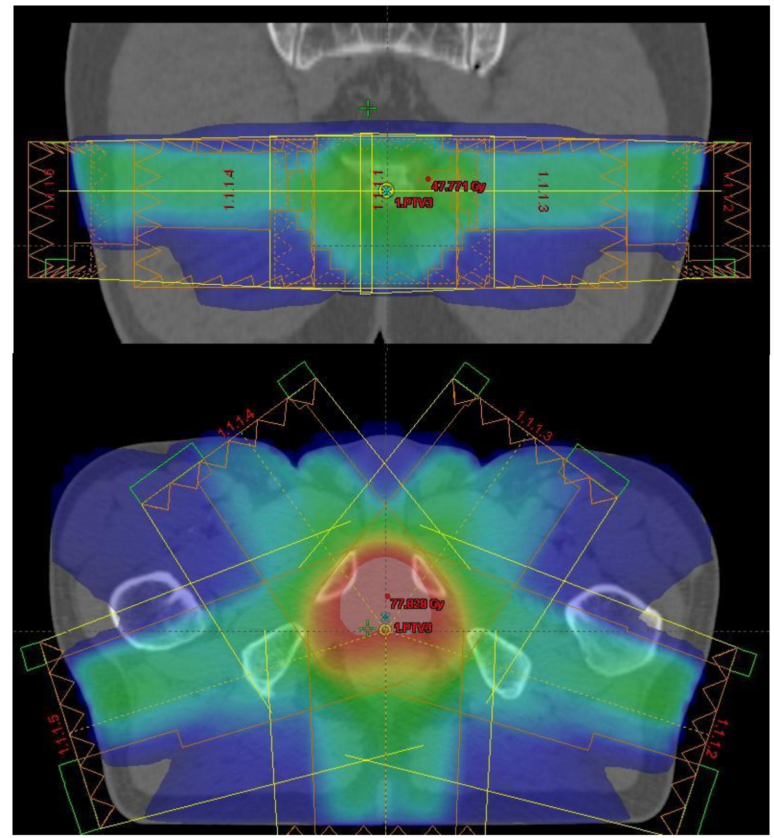


72 Gy



4 Gy

IMRT



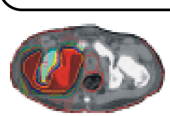
Integral dose is approximately constant

A LOT TO A LITTLE OR A LITTLE TO A LOT?

High dose to a modest volume
or
Low dose to a larger volume
?

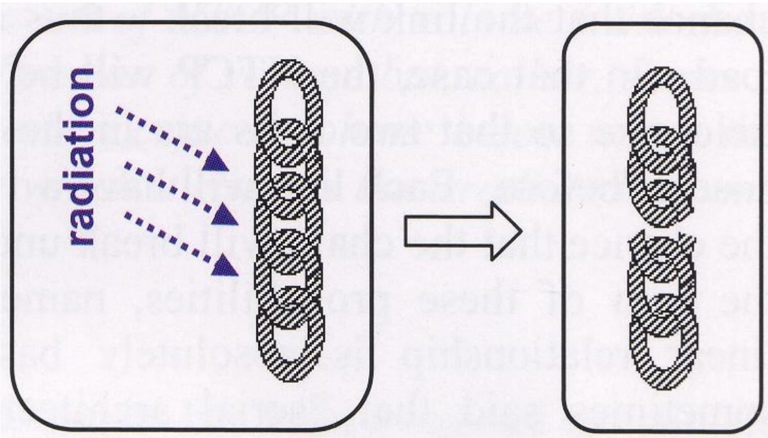
There is no definite answer to this question

Influence of tissue architecture!



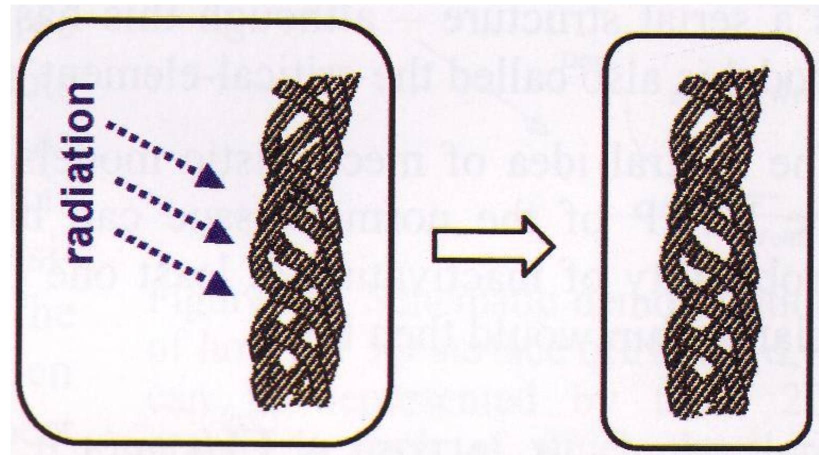
THE INFLUENCE OF TISSUE ARCHITECTURE

serial architecture



an organ has a serial structure if the death of only one functional sub-unit (FSU) is sufficient to cause loss of function of the organ

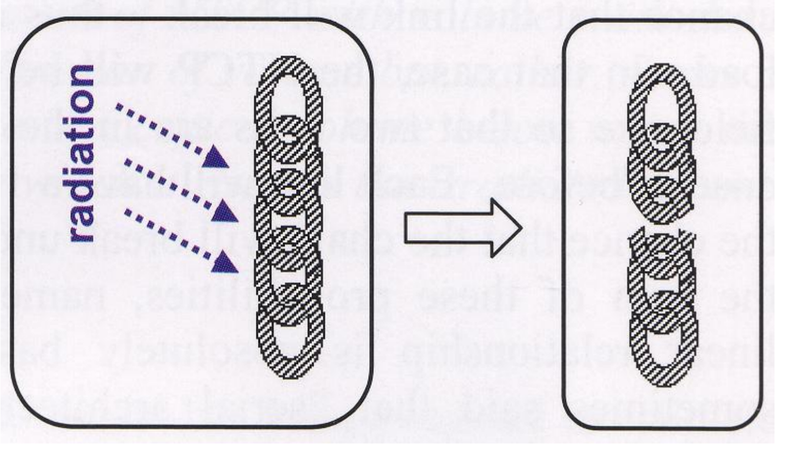
parallel architecture



consists of FSUs each of which performs that the normal tissue is responsible for. Function is lost, when a critical number of FSUs is lost.

THE INFLUENCE OF TISSUE ARCHITECTURE

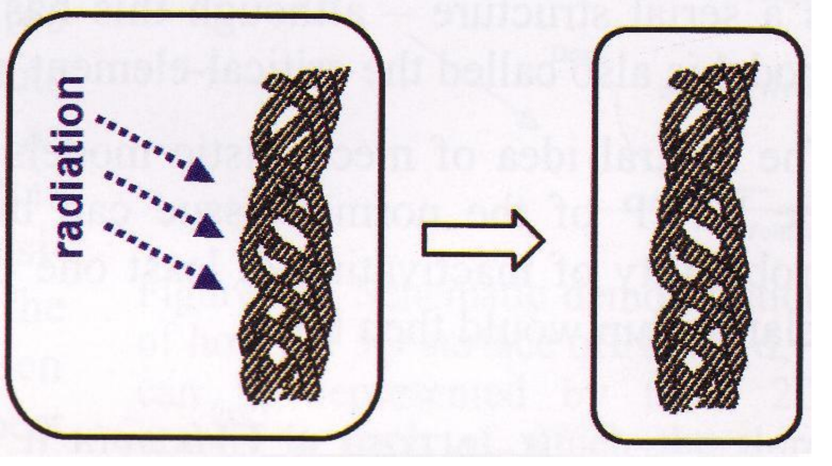
serial architecture



Maximum Dose to the organ is critical:

Strategy:
A little to a lot

parallel architecture



Mean Dose to the organ is critical:

Strategy:
A lot to a little

Intensity Modulated Radio Therapy

IMRT / VMAT

INTRODUCTION

So far we have implicitly assumed that each radiation field is near uniform over its cross section

- 20 years ago Cormack, Brahme and Pedroni had the idea to use non-uniform fields
- Using mathematical techniques, an irradiation scheme using non-uniform beams could be found, which limit dose to normal tissues while delivering the desired dose to the target

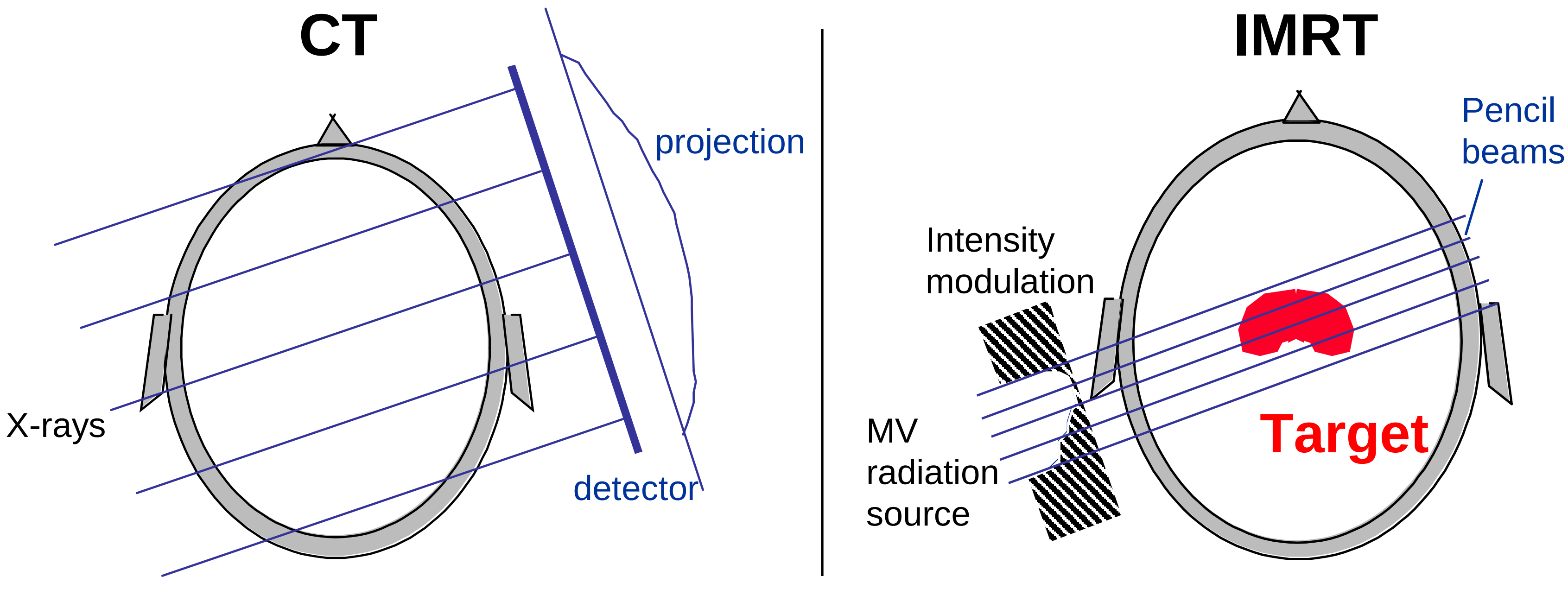
Motivation from CT reconstruction:

From the intensity reduction of x-rays traversing an object one can deduce the internal structure of the object.

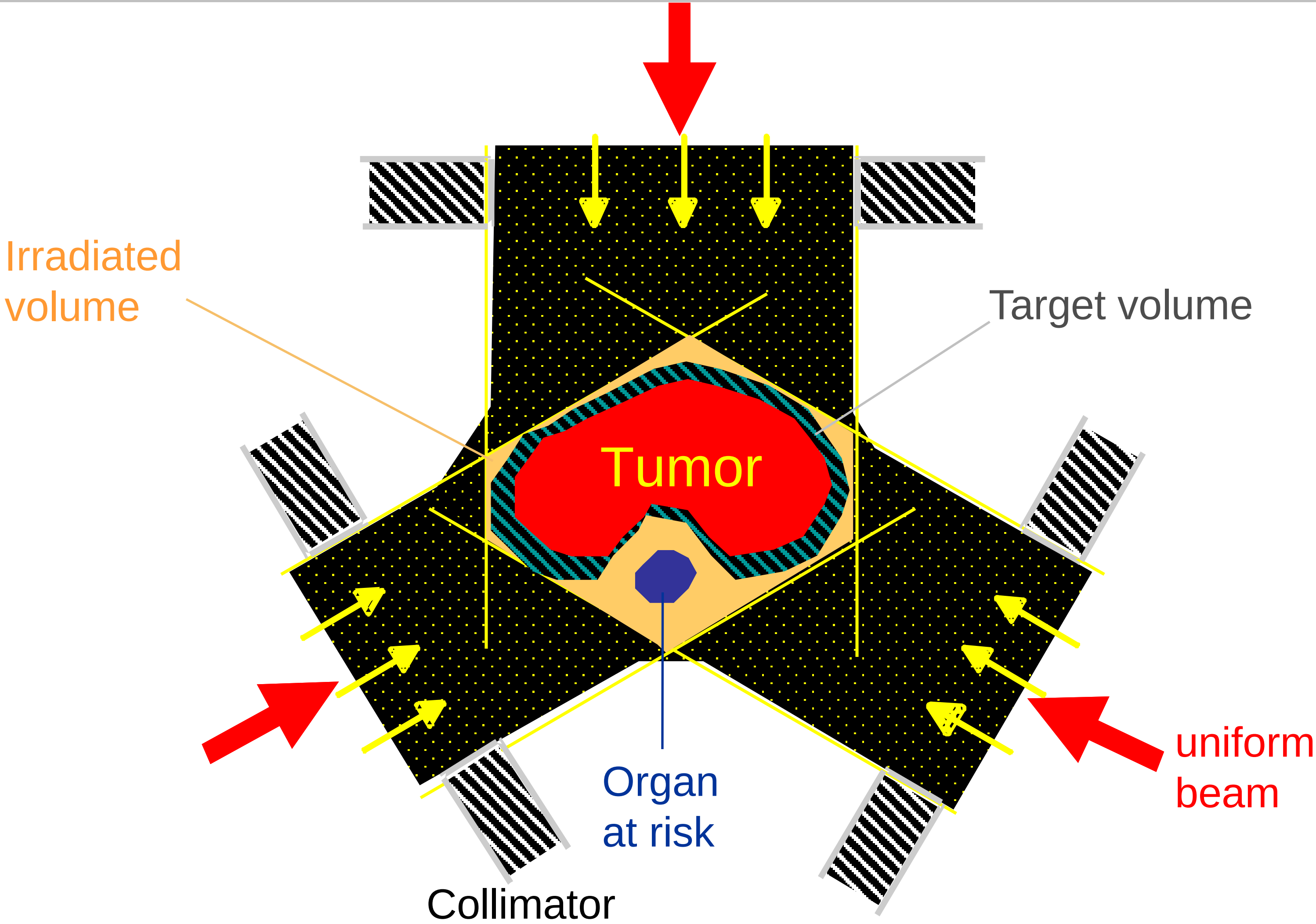
INVERTING COMPUTER TOMOGRAPHY

Calculation of *intensities (pencil beam weights)* that pass through the object an deliver dose

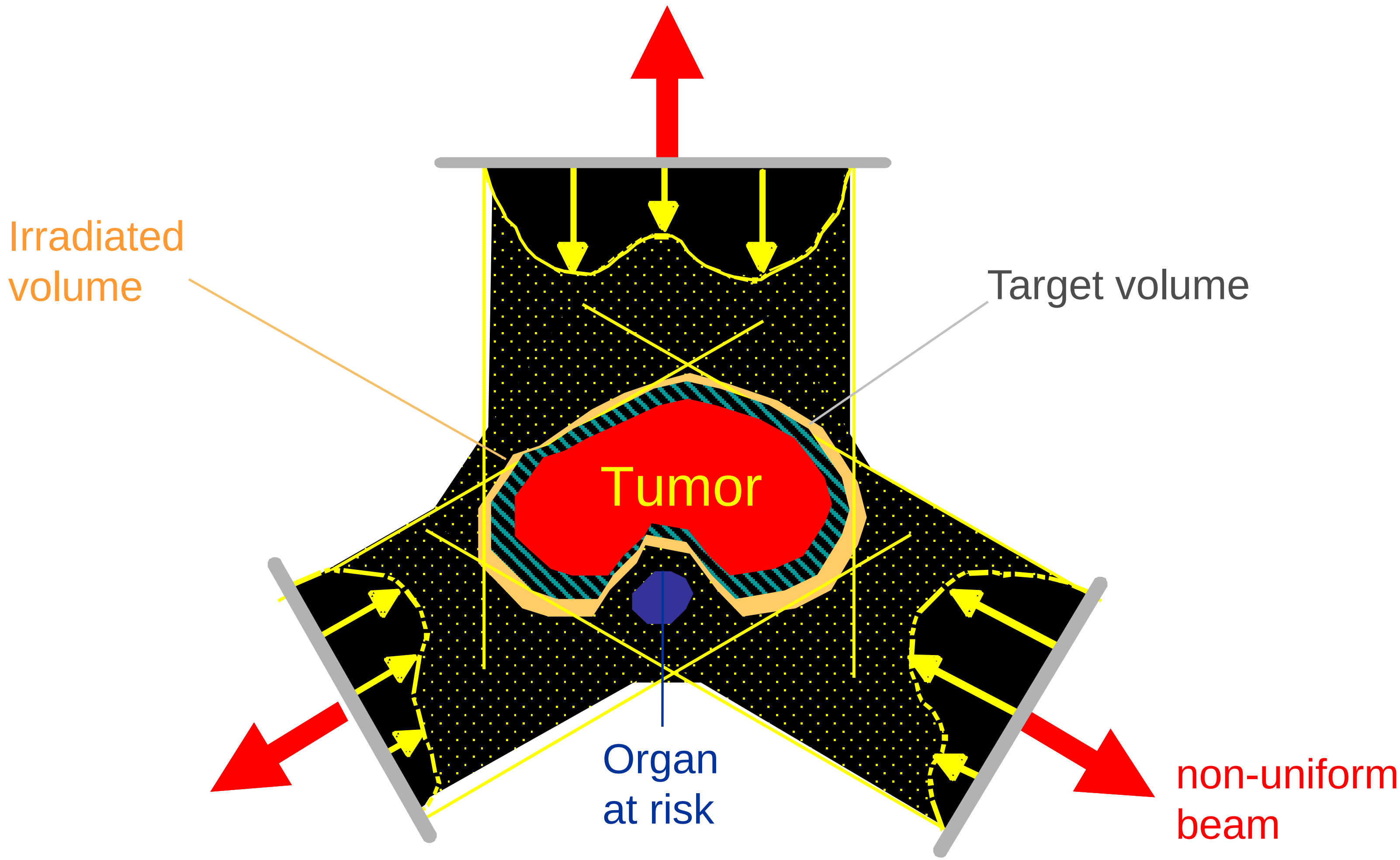
- Highly non-uniform individual fields
- Problem: negative intensities



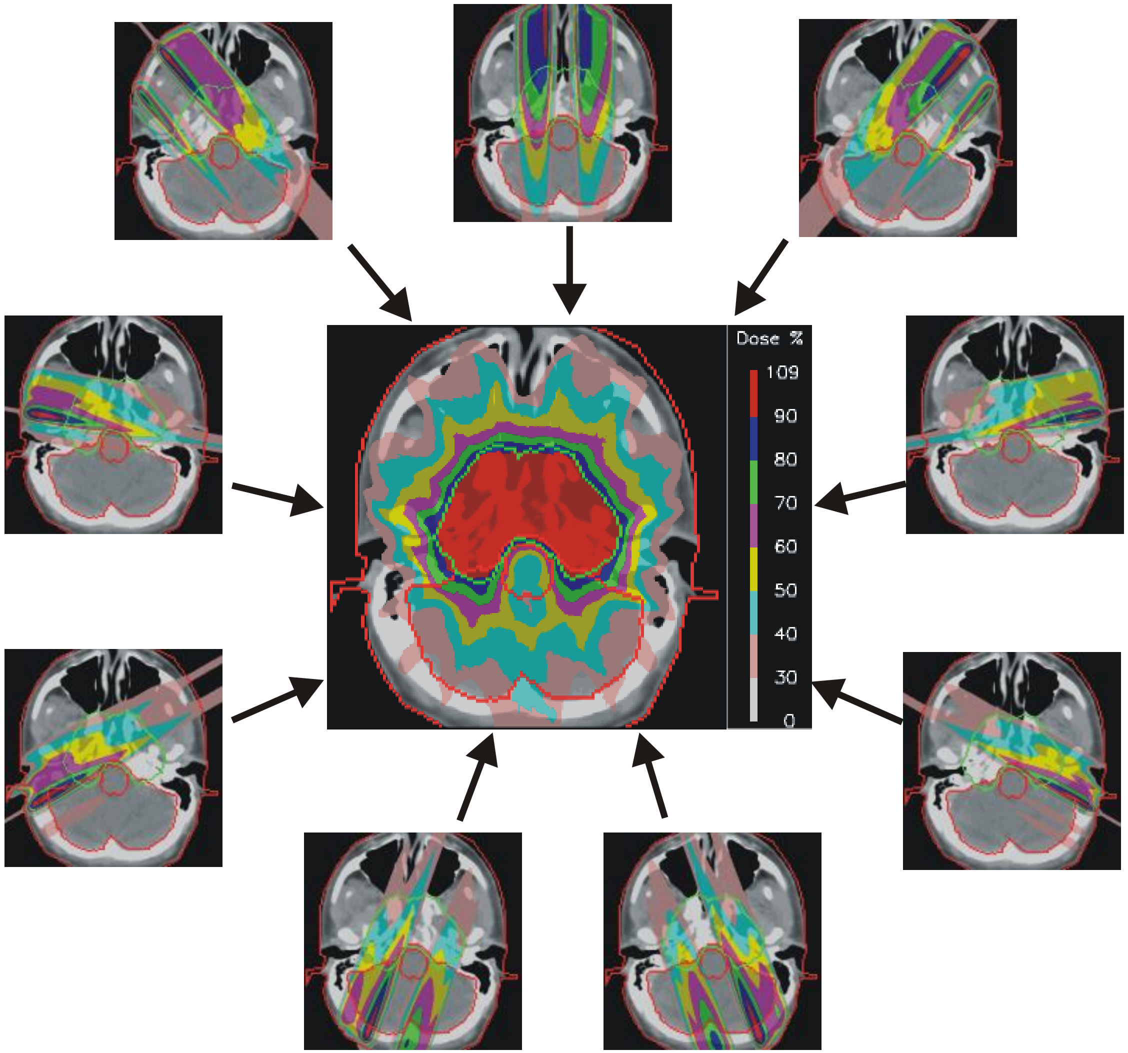
UNIFORM-INTENSITY RADIOTHERAPY CONVEX DOSE DISTRIBUTIONS



NON-UNIFORM-INTENSITY RADIOTHERAPY
CONCAVE DOSE DISTRIBUTIONS



IMRT OF NASOPHARYNGEAL CANCER



ADVANTAGES OF IMRT

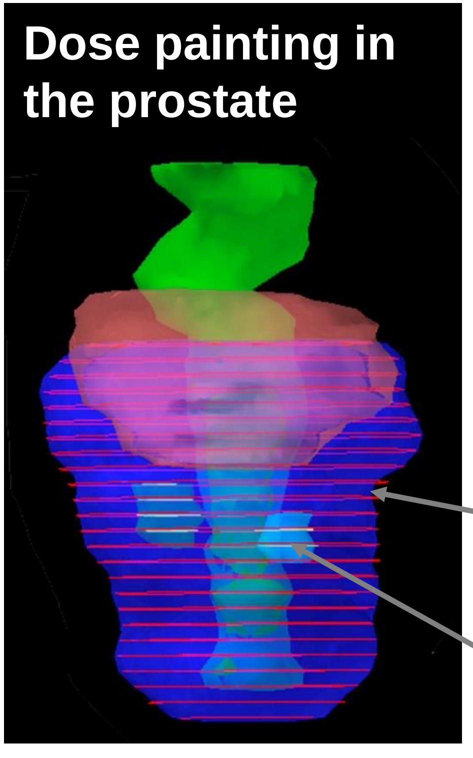
Creation of concave dose distributions:

- Sparing of selected normal tissues (*conformal avoidance*)

Delivery of non-uniform dose distributions to the target:

- Two different target volumes one nested inside the other (*integrated boost*)
- delivering additional dose to sub-regions of the target because they contain more resistant cells *(dose painting)*
- deliver a reduced dose to sub-regions of the target volume because a critical volume runs through it *(dose painting)*

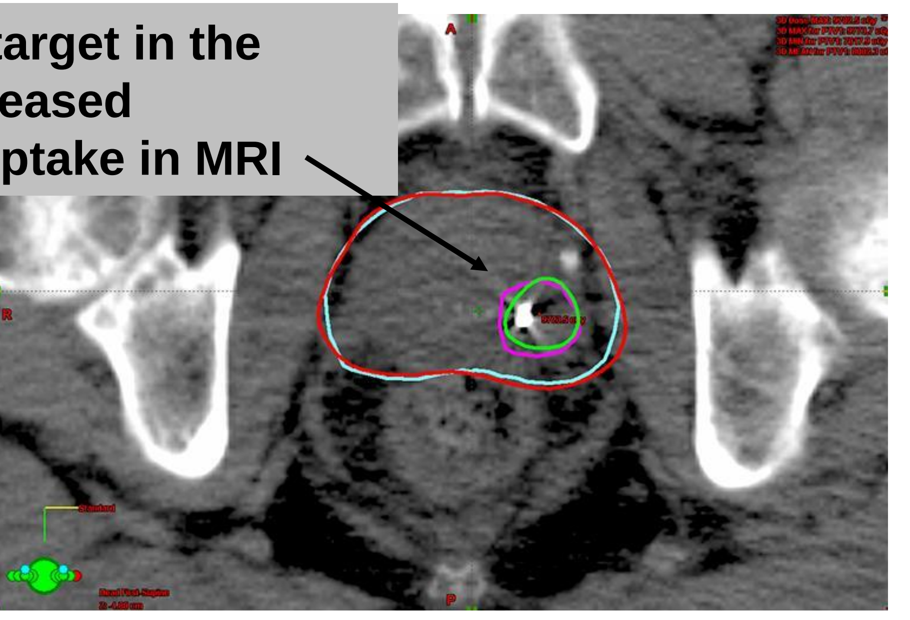
DOSE PAINTING IN TARGET SUBREGIONS



75.6 Gy dose cloud

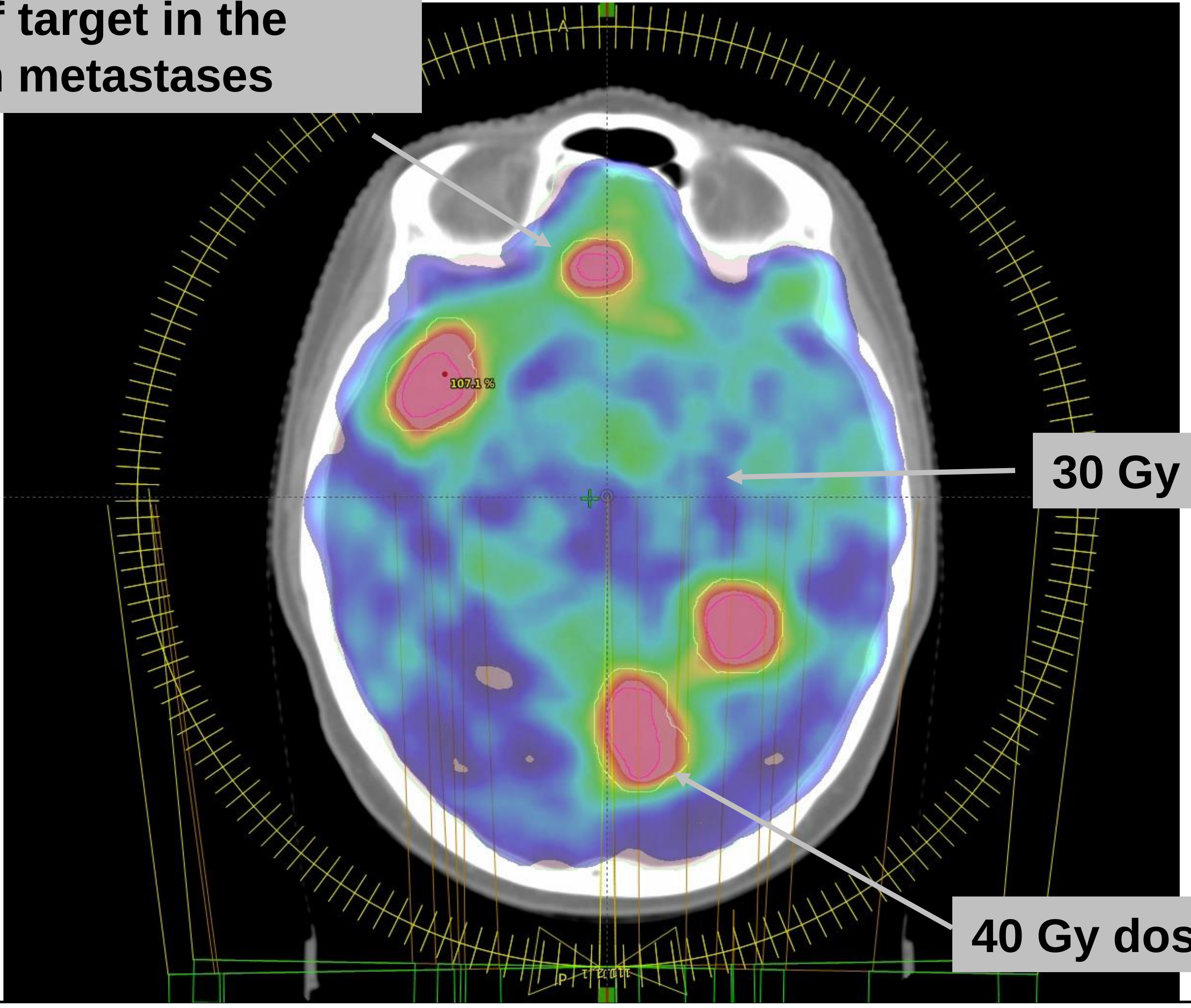
94.5 Gy dose cloud

Definition of target in the target by increased Gadolinium uptake in MRI



DOSE PAINTING IN THE BRAIN

Definition of target in the target: brain metastases



30 Gy dose cloud

40 Gy dose cloud

INVERSE PLANNING OF IMRT

Specify the desired dose distribution

↓

Calculate the treatment variables which would lead to the desired dose distribution

↓

end

Straightforward scheme, but with problems:

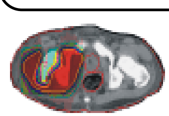
- Negative intensities
- When negative intensities are set to zero there is no room for balancing conflicting goals (TCP ↔ NTCP)

↓

Inverse planning is not used in clinical practice

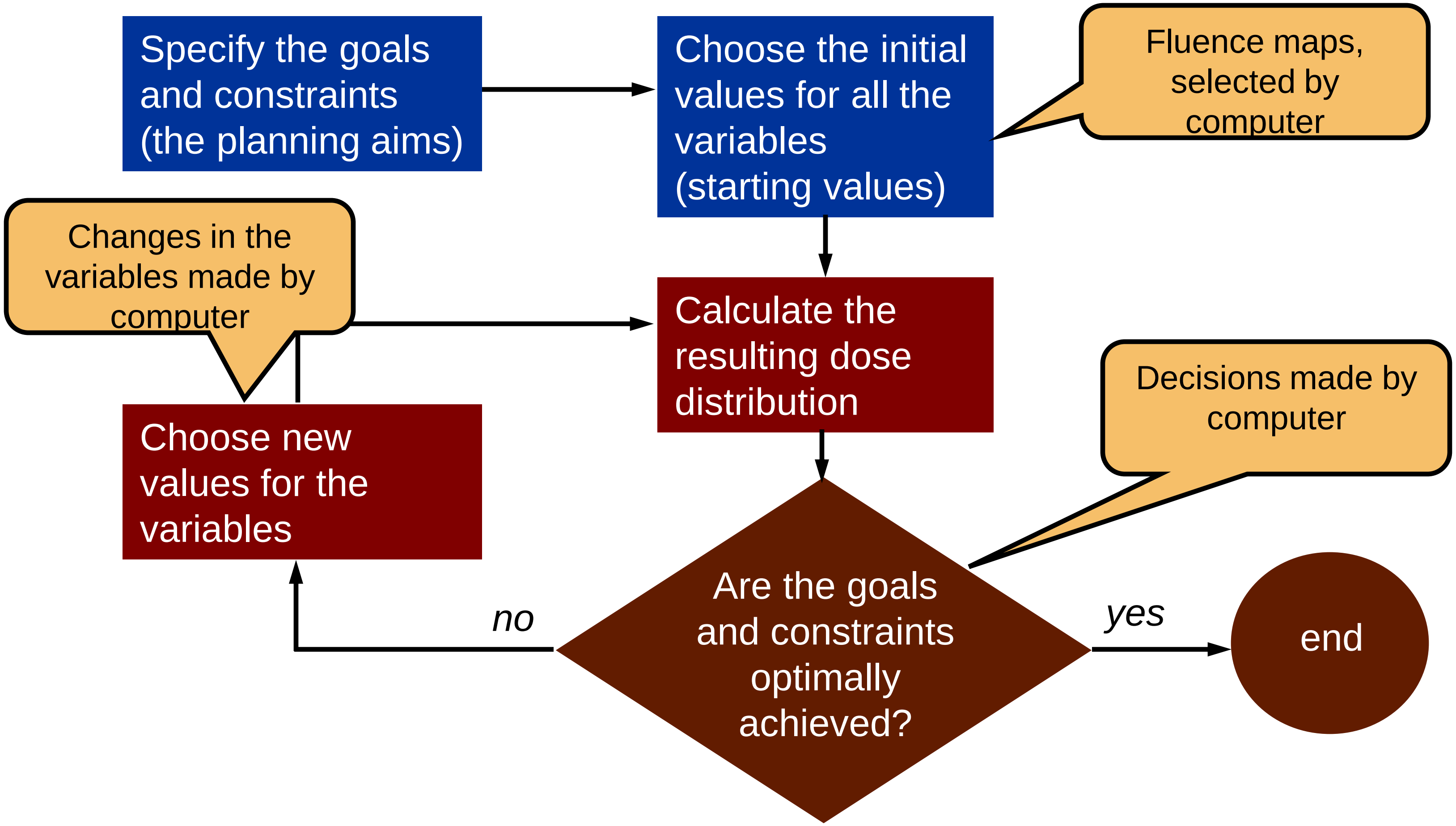
↓

Forward planning of IMRT



FORWARD PLANNING OF IMRT

Flow chart for forward IMRT planning:



FORWARD PLANNING OF IMRT

Two main aspects of planning IMRT:

- Establishing a method for computing a numerical *score*, expressing how well the goals were achieved
  (assign a numerical value to rank plans)
- Conducting a *search* through the space of treatment variables to locate the set of values of those variables that gives the best score
  (6000 variables with 10^{13} choices)

What is usually not included in the score

- Type of radiation
- Energy of radiation
- Number and direction of beams / Arc-angles
- Table rotation (IMRT is usual coplanar)

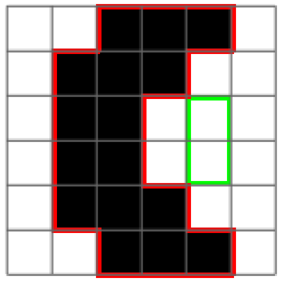
What is usually included in the score

Tumor response:

- The difference between the minimum (mean) target dose and the prescribed dose
- The dose exceeded by 95% of the target volume (cold spots)
- The dose exceeded in 5% of the target volume (hot spots)

Morbidity for each organ at risk:

- The difference between the maximum (mean) OAR dose and its constraint dose
- The difference between the volume of the OAR which receives more than a dose D and the corresponding volume constraint
- integral dose

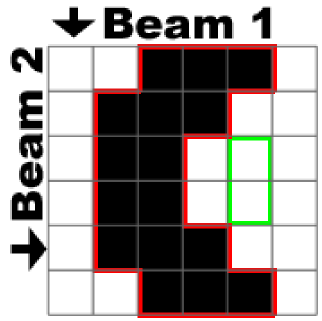


Red: Target
Green: Organ at risk

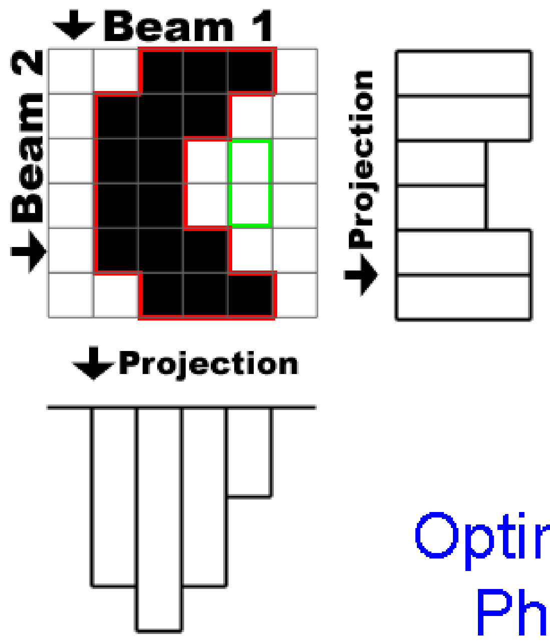
Objective Function:
Mean squared deviation between actual and prescribed dose in the target

Constraint:
Dose in organ at risk < 50 %,
positive intensities

Optimization
Phase 1

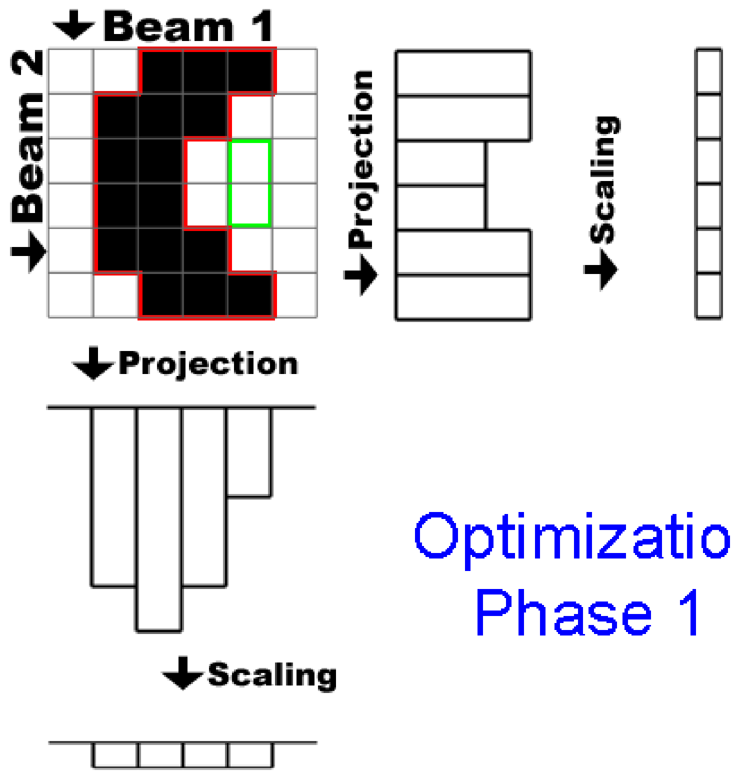


Optimization
Phase 1



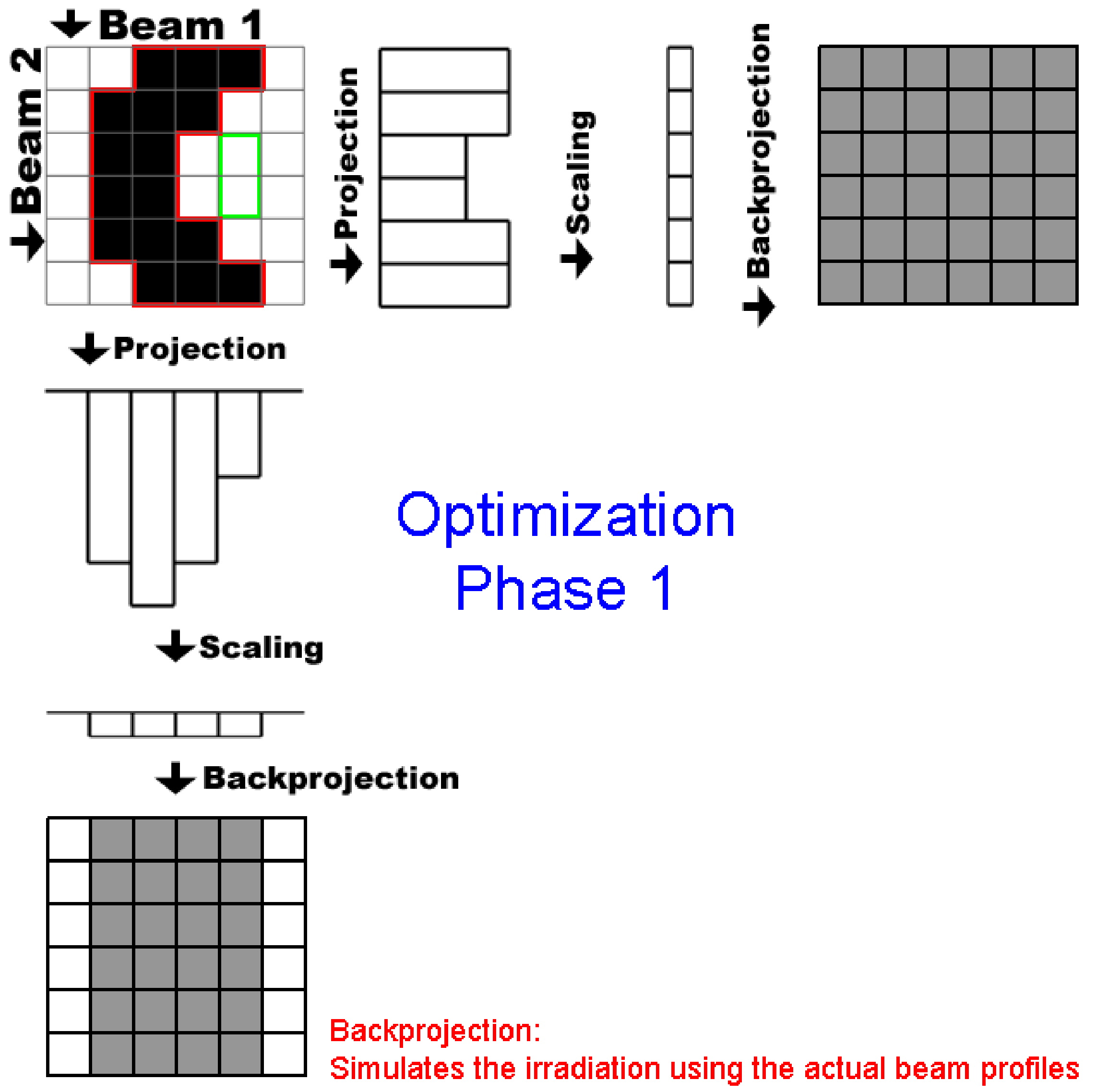
Optimization Phase 1

Projection: Summation of the dose values along the beam direction



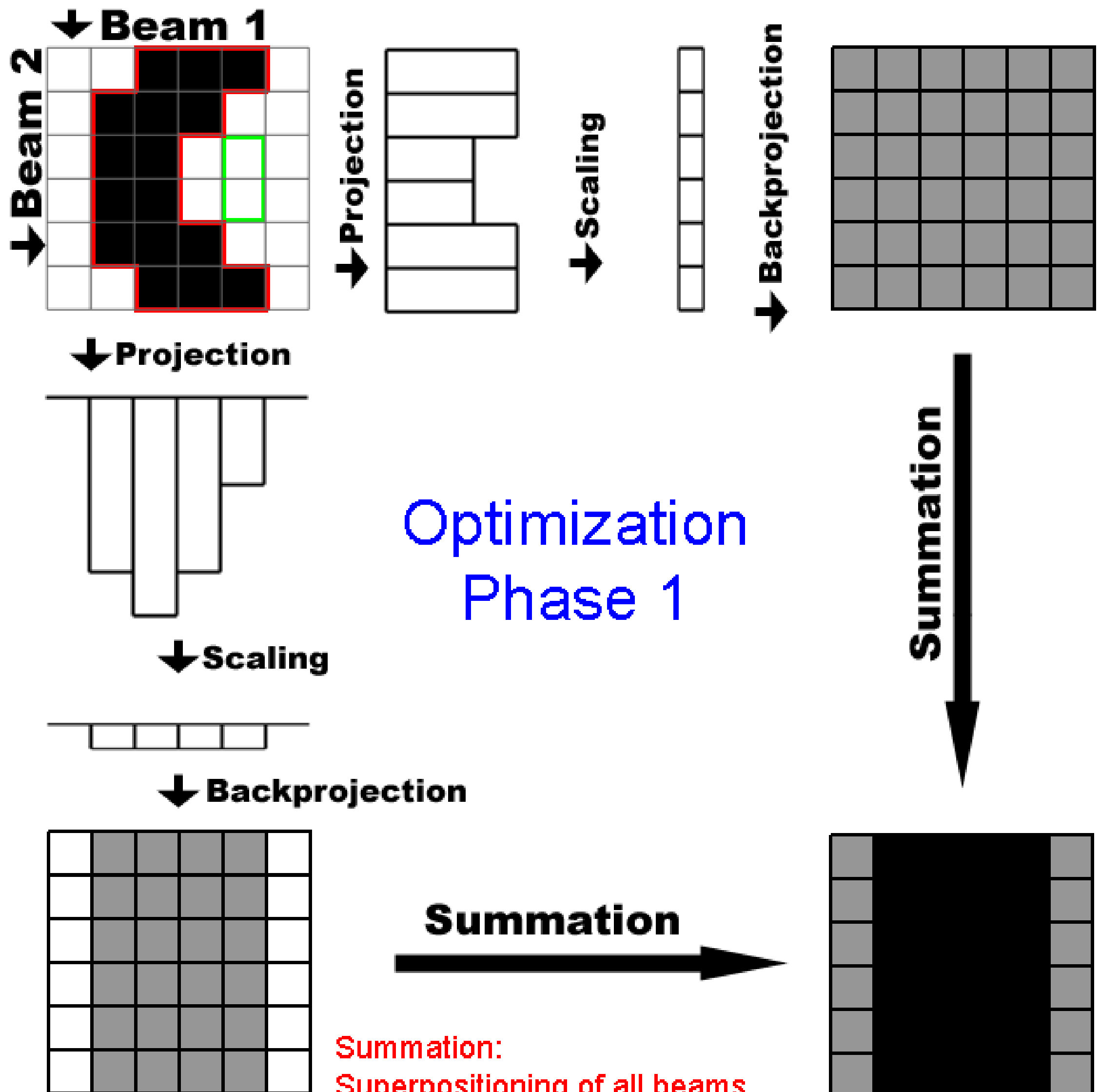
Optimization
Phase 1

Scaling: Division by number of contributing dose elements
and by number of beams



Optimization
Phase 1

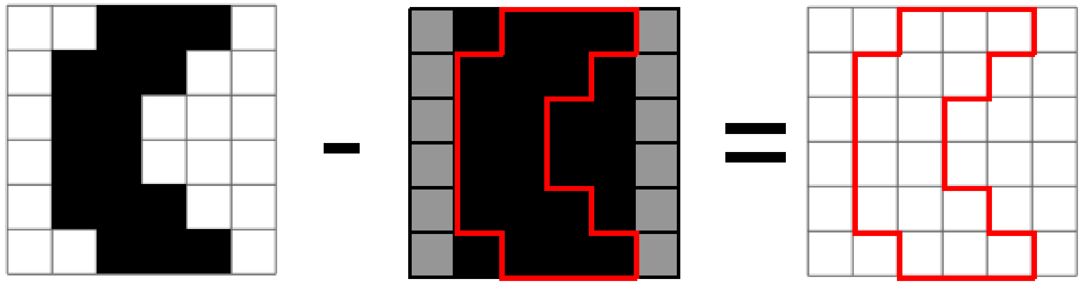
Backprojection:
Simulates the irradiation using the actual beam profiles



Optimization
Phase 1

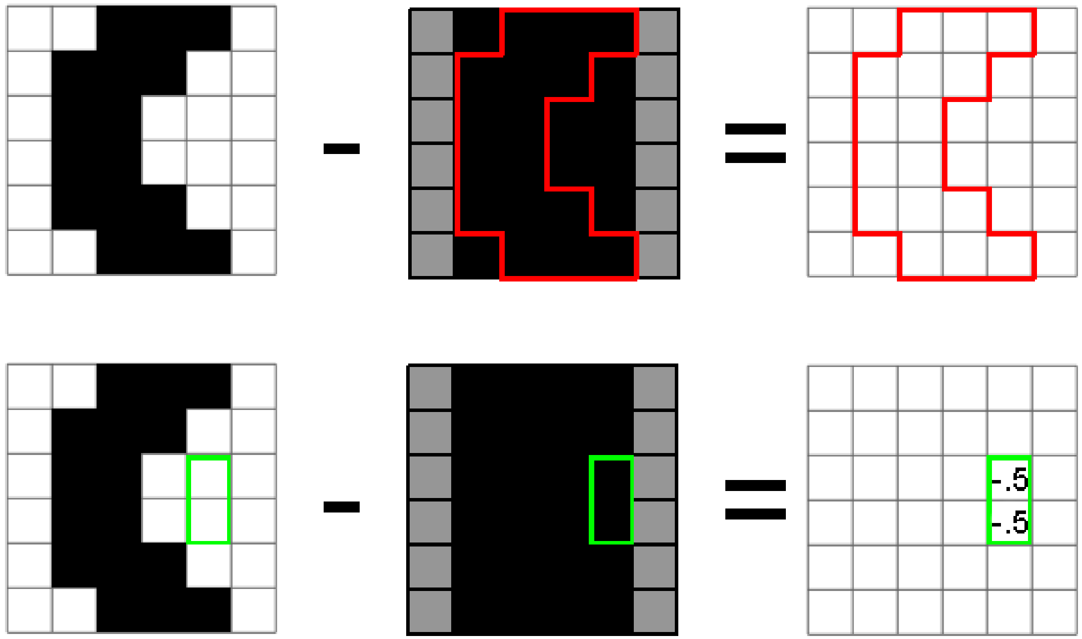
Summation:
Superpositioning of all beams

Evaluation Phase 1



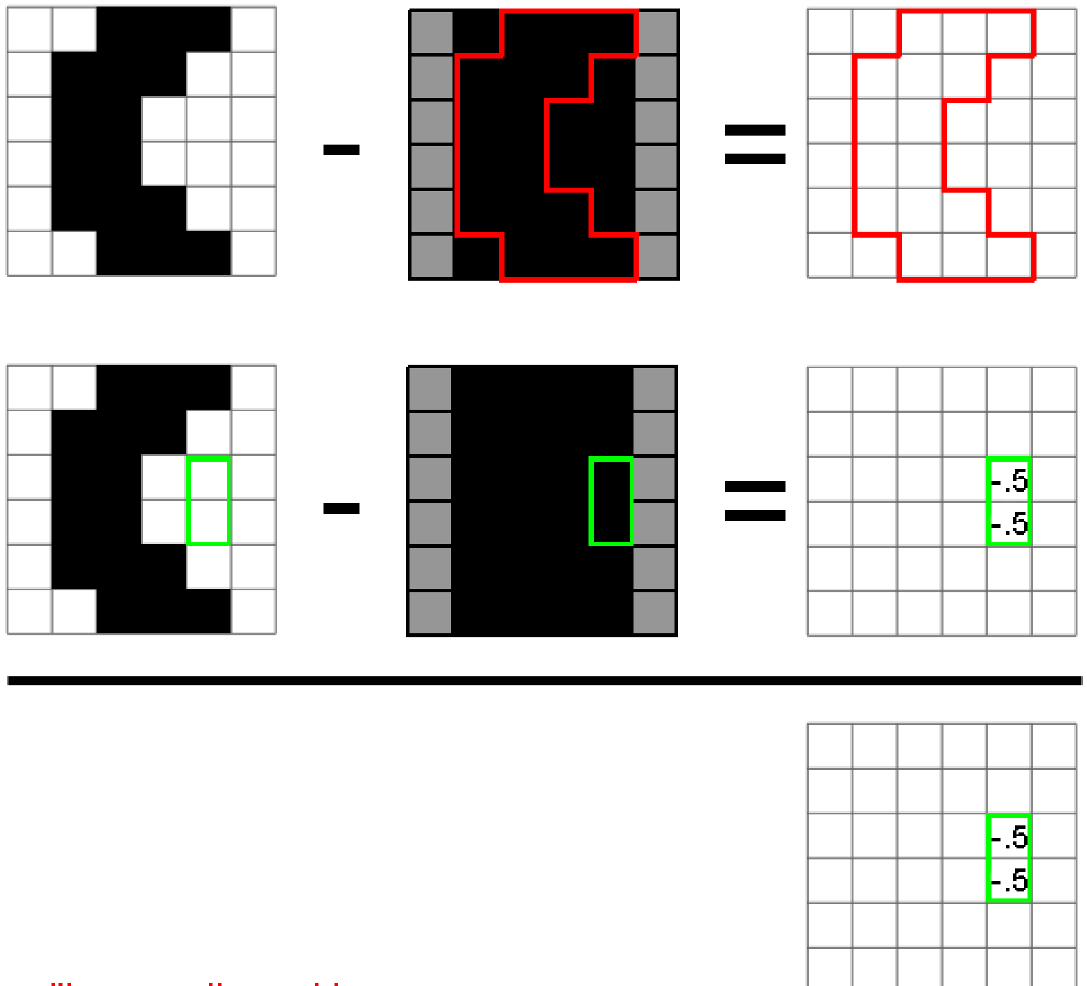
Comparing prescribed and realized dose in the target volume.
In this case there is no difference, therefore no correction necessary.

Evaluation Phase 1

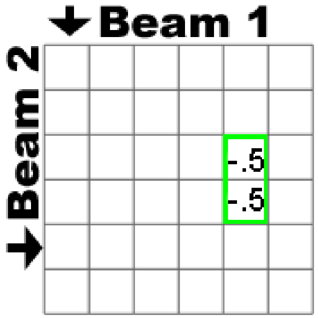


Same for the organ at risk: Here the difference is -0.5.

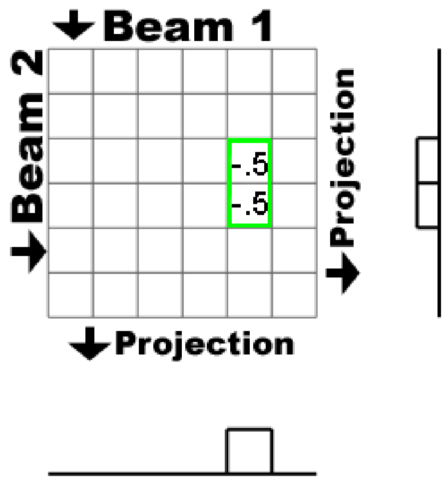
Evaluation Phase 1



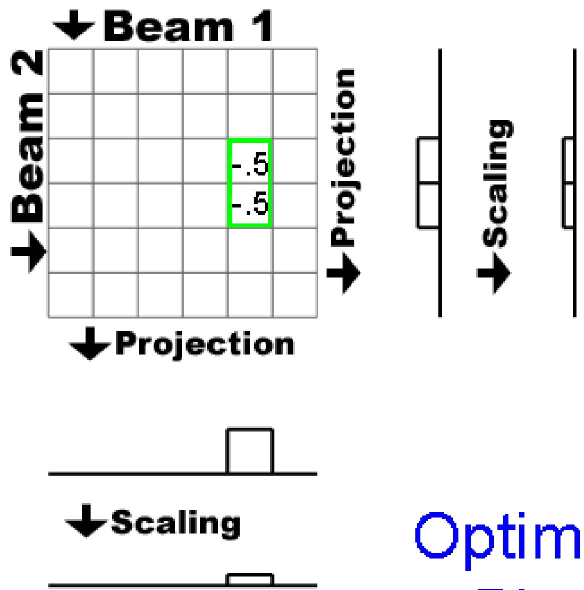
Resulting correction matrix.



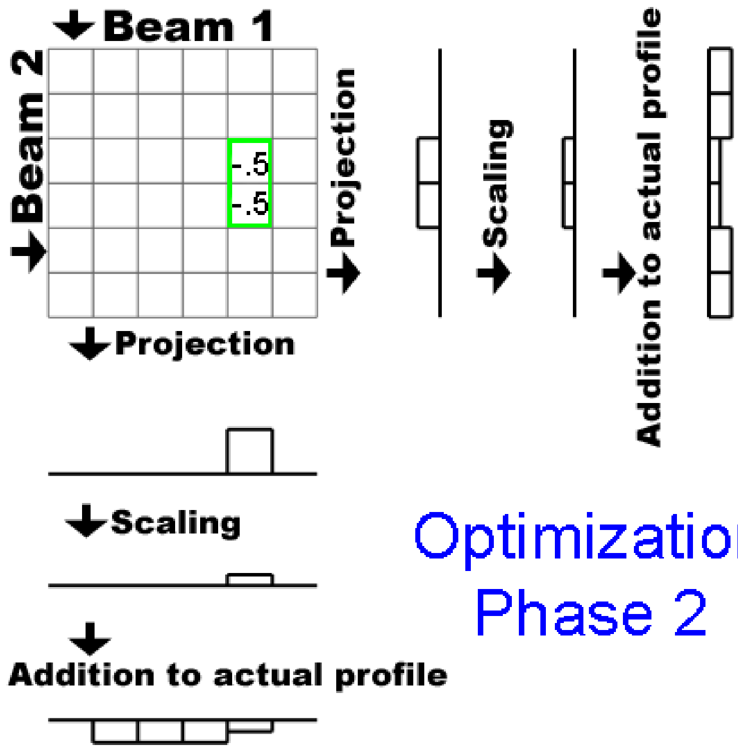
Optimization
Phase 2



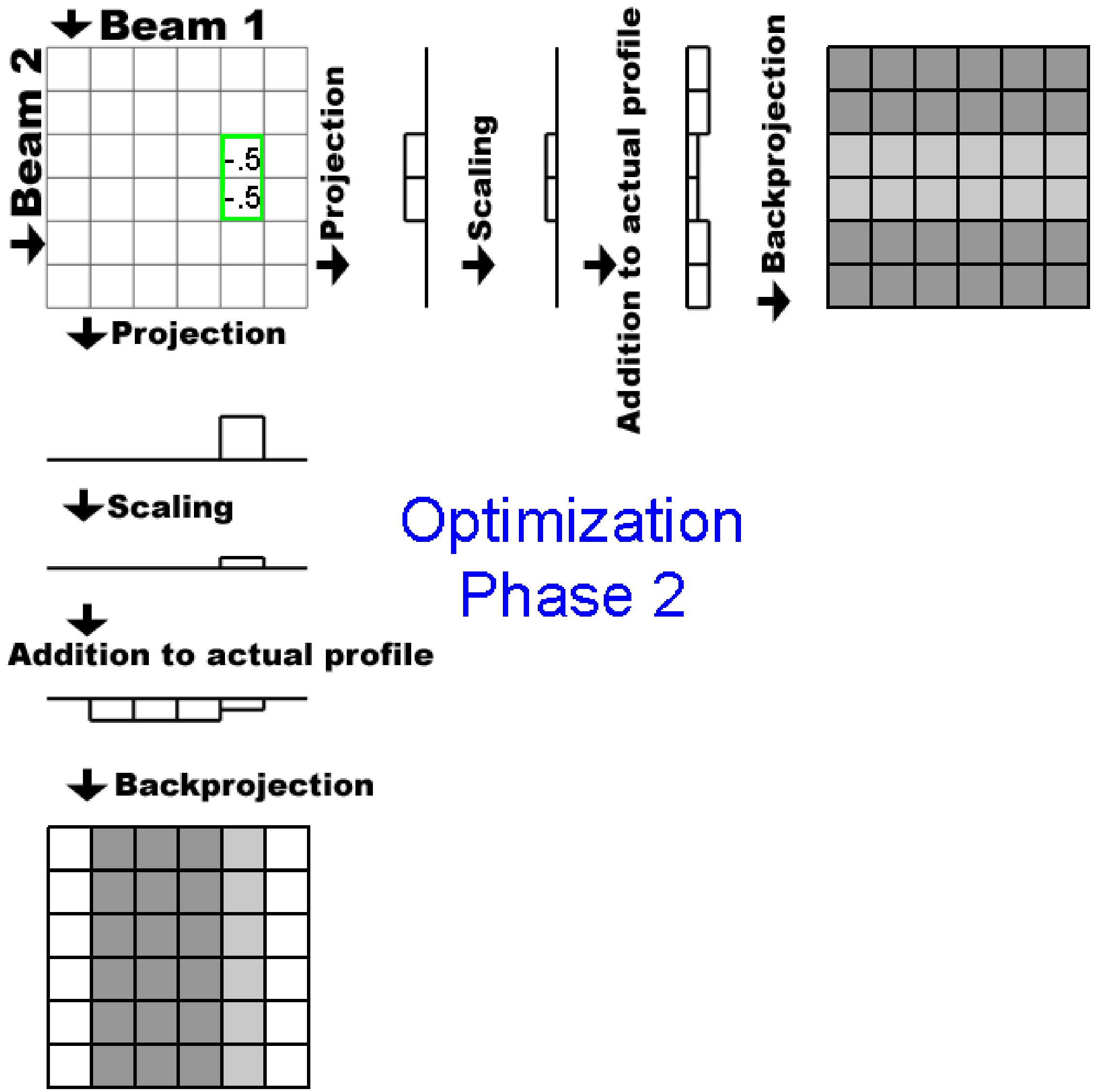
Optimization
Phase 2



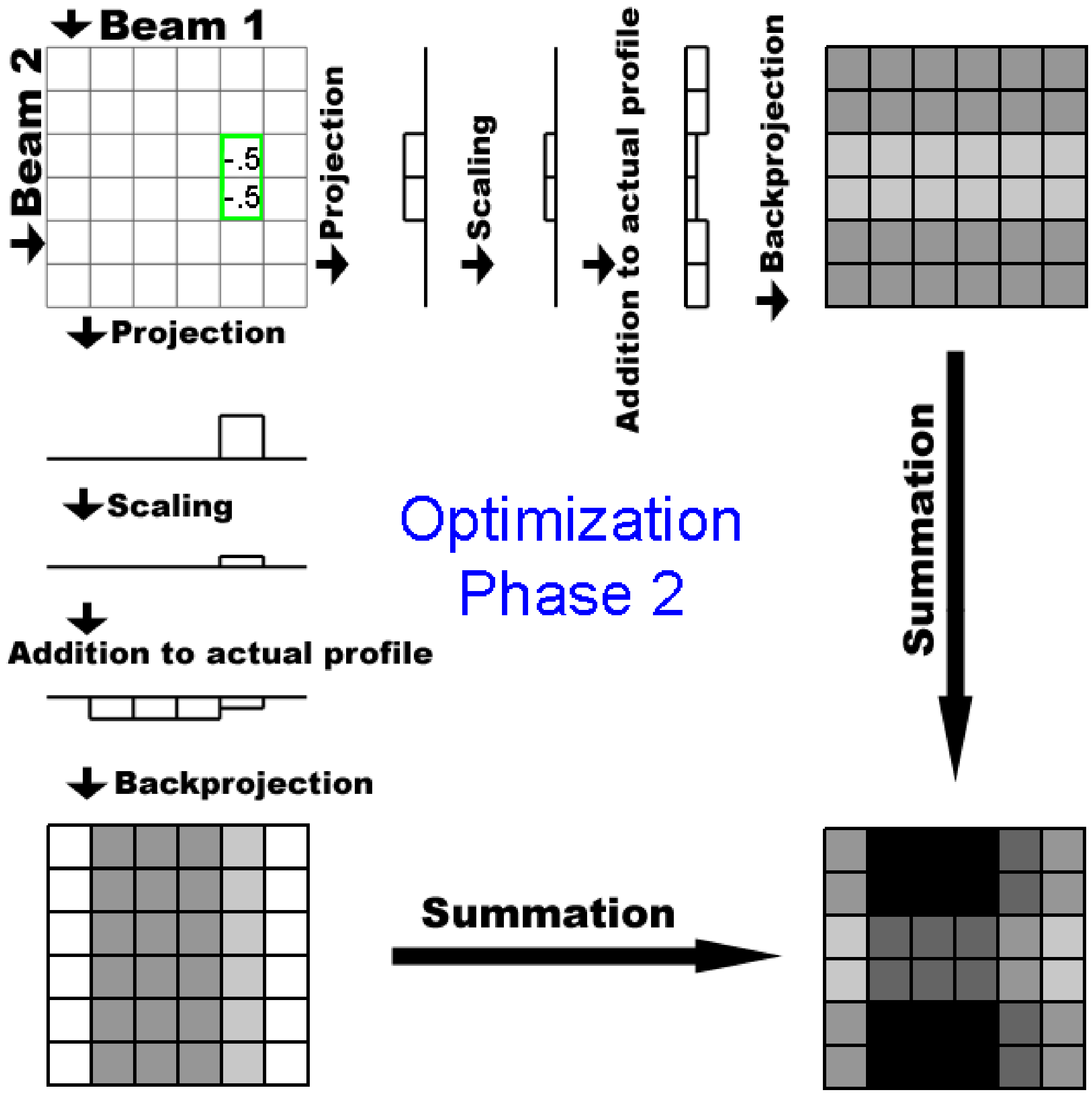
Optimization Phase 2



Optimization Phase 2

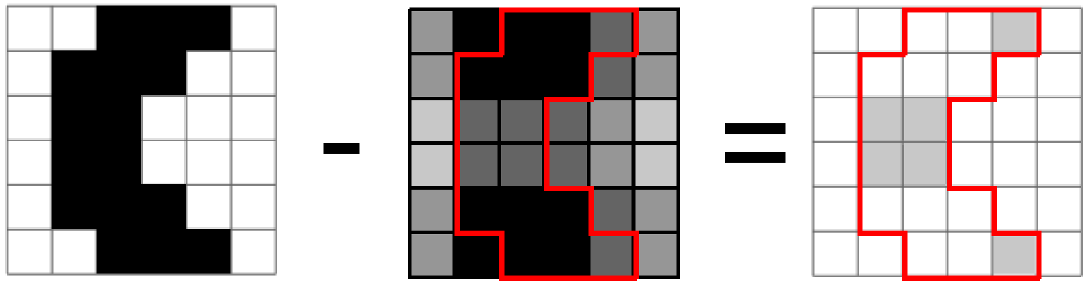


Optimization Phase 2

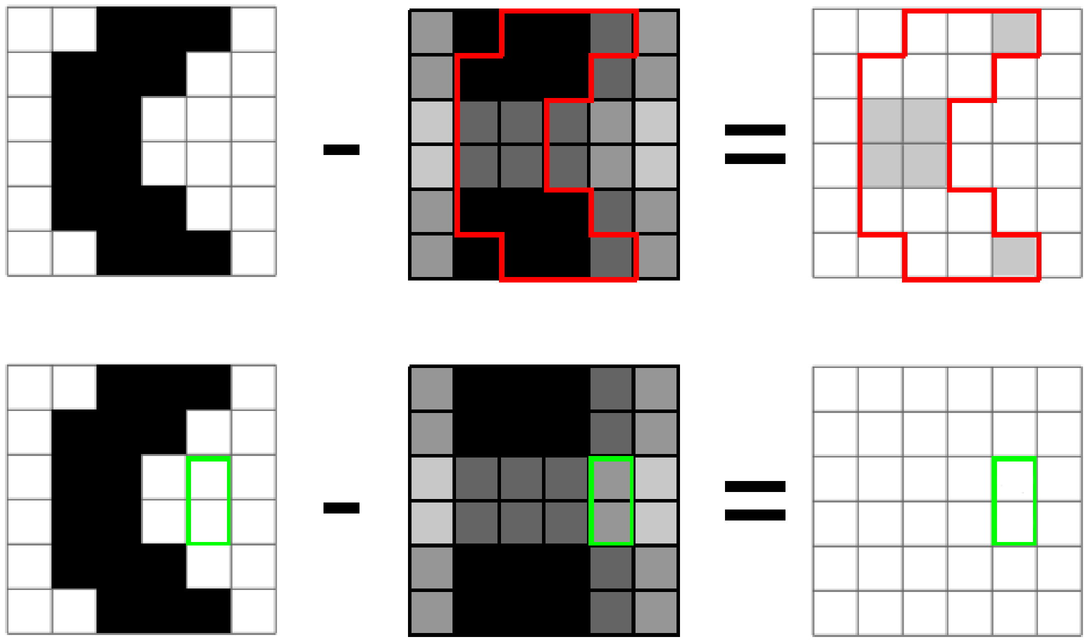


Optimization
Phase 2

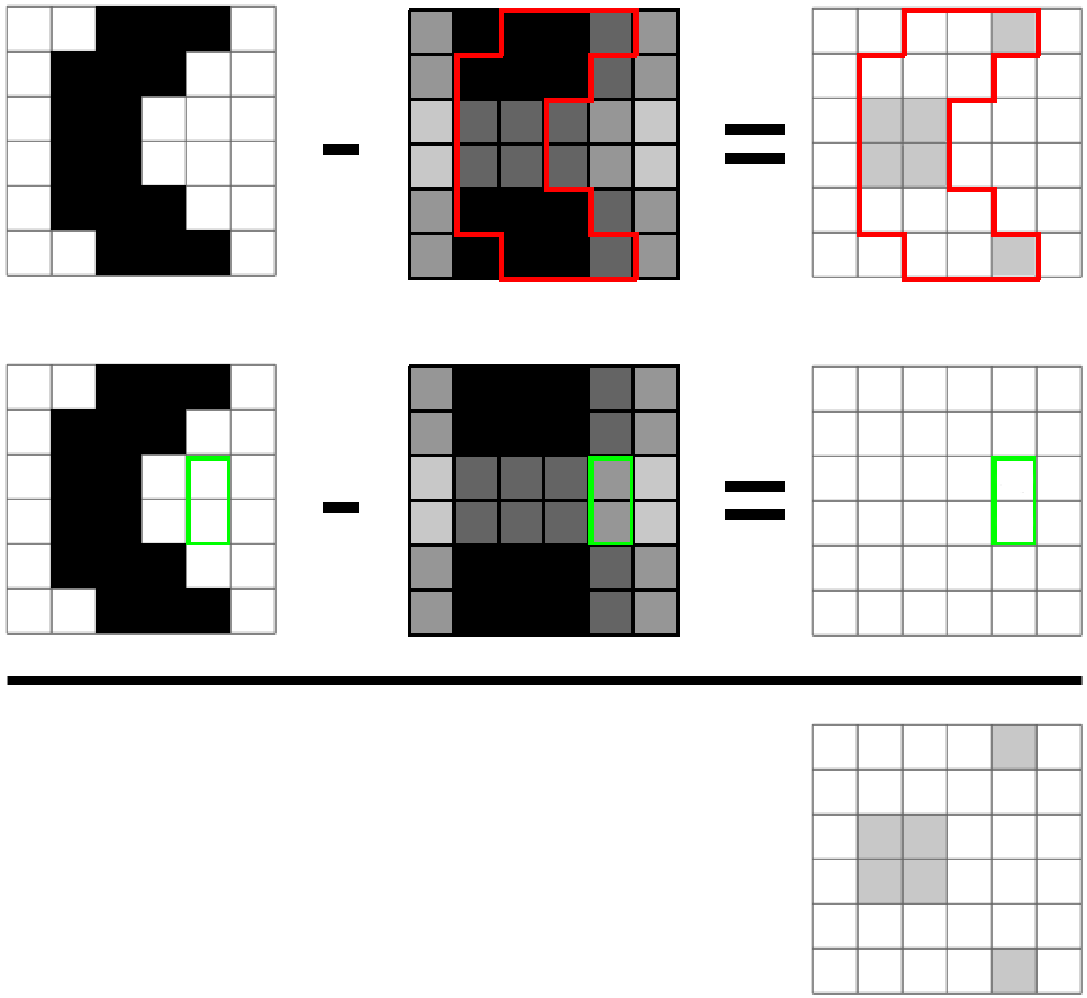
Evaluation Phase 2



Evaluation Phase 2



Evaluation Phase 2

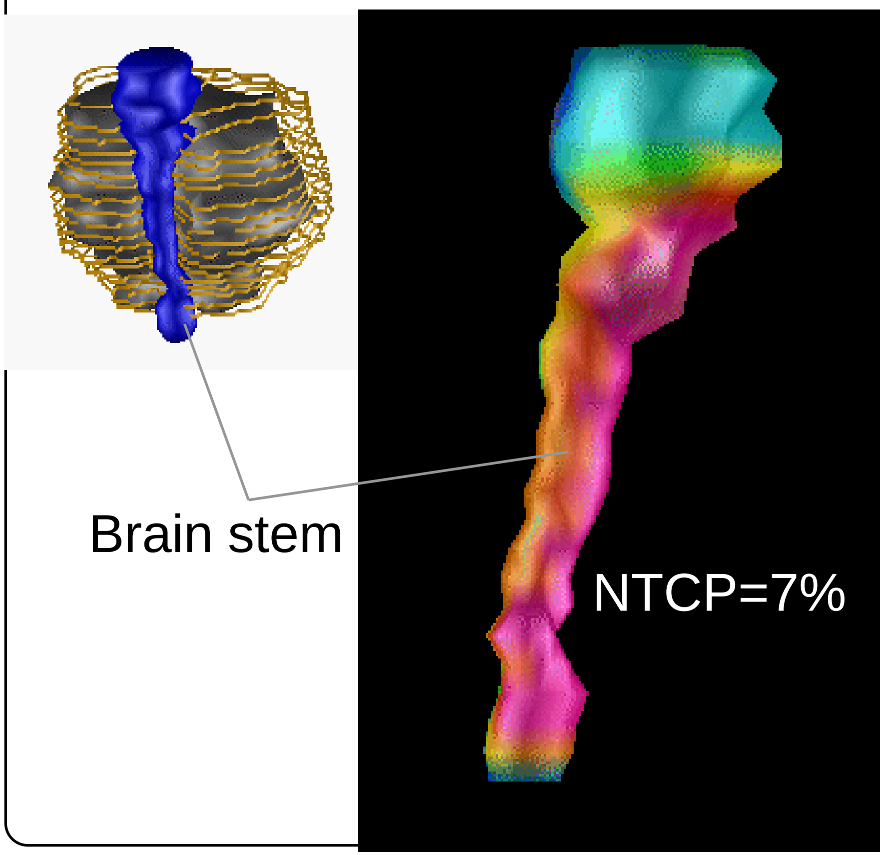


Optimization
Phase 3

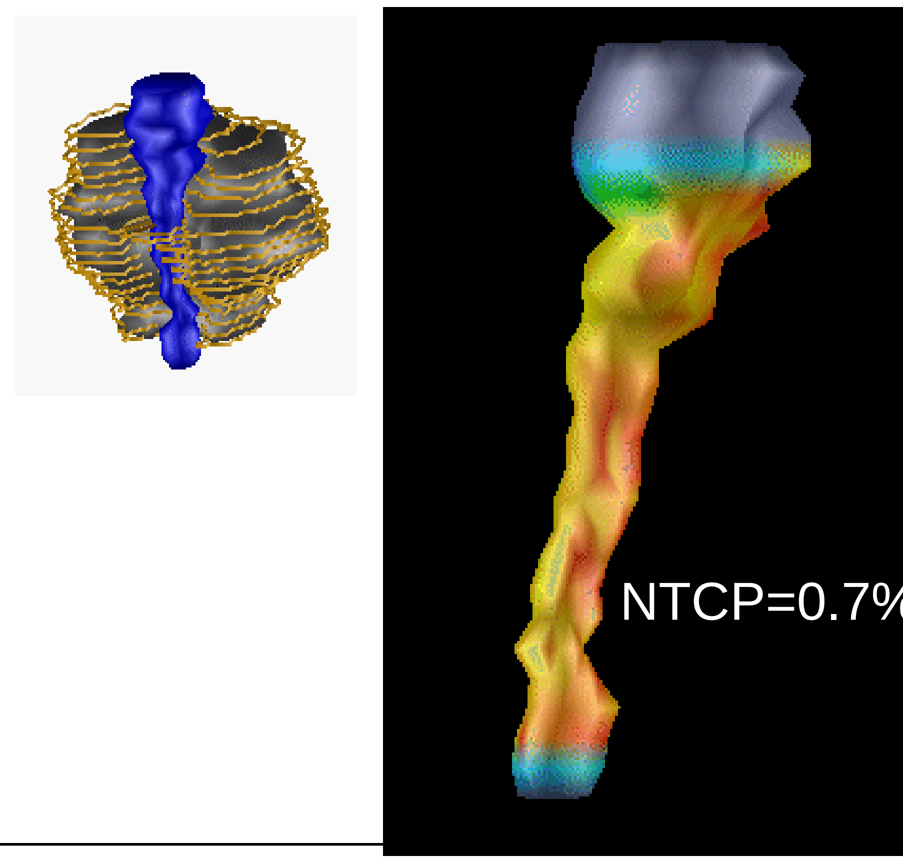
Repeat the steps of evaluation and optimization
until an acceptable treatment plan is found.

IMRT dose distribution: head and neck

3D-conformal
(4 fields)



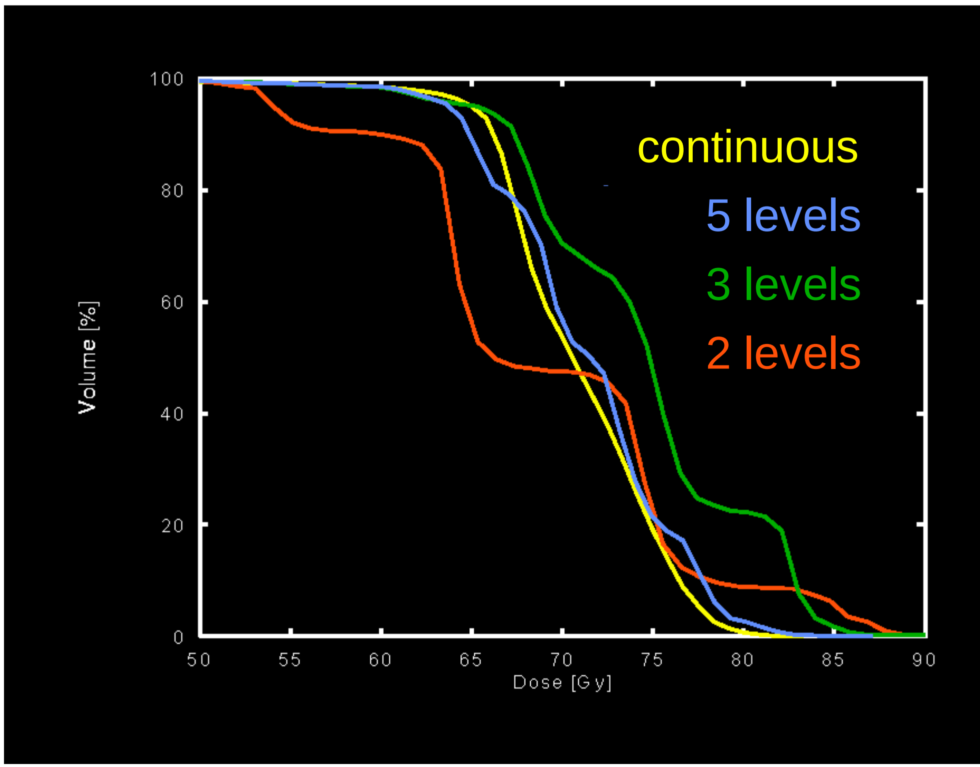
IMRT
(9 fields)



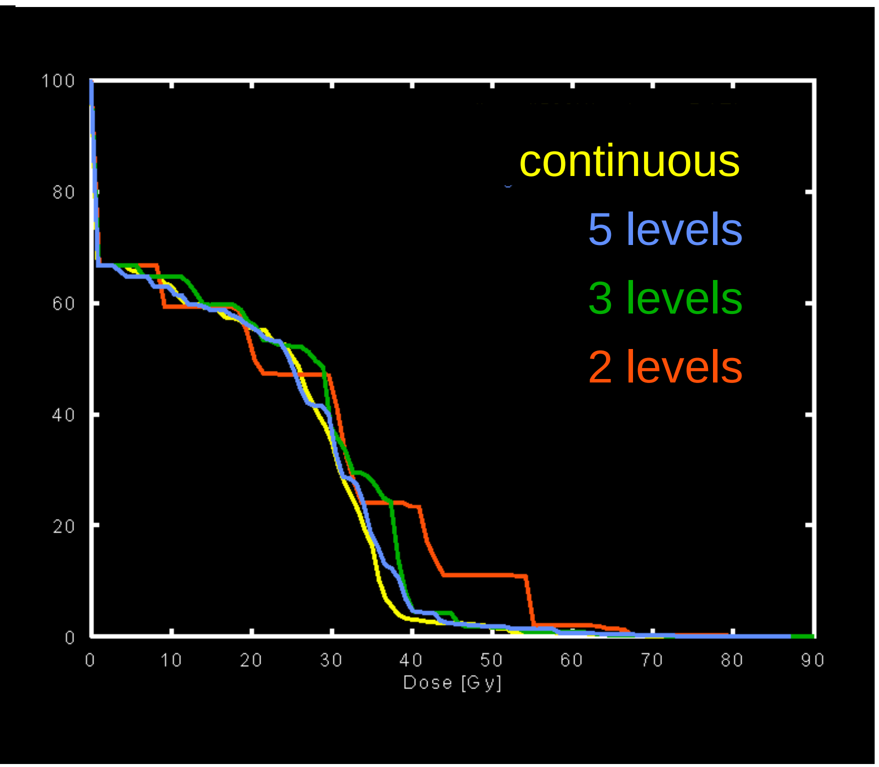
IMRT: number of intensity levels

Example chordoma

Target



Brainstem

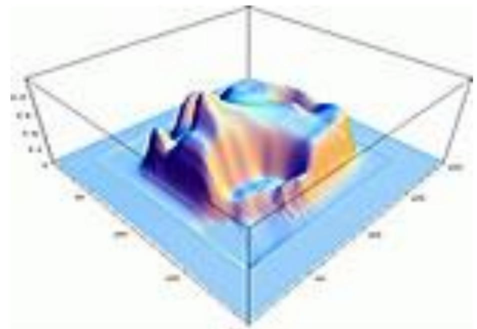


IMRT: number of intensity levels

- About 5 intensity levels per beam are generally sufficient
- This means about 7-8 subfields per beam
- This means about 50-60 subfields in total

REALISATION OF INTENSITY MODULATION

Calculated intensity map:

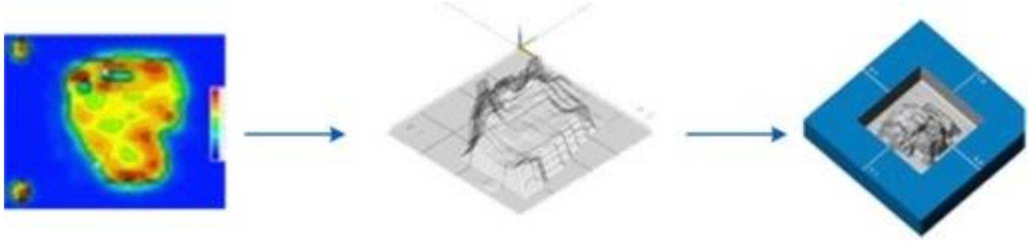


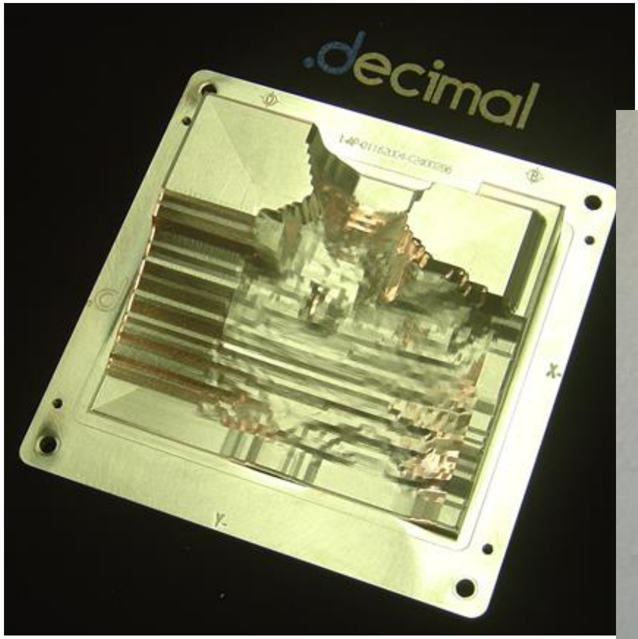
Practical realisation:

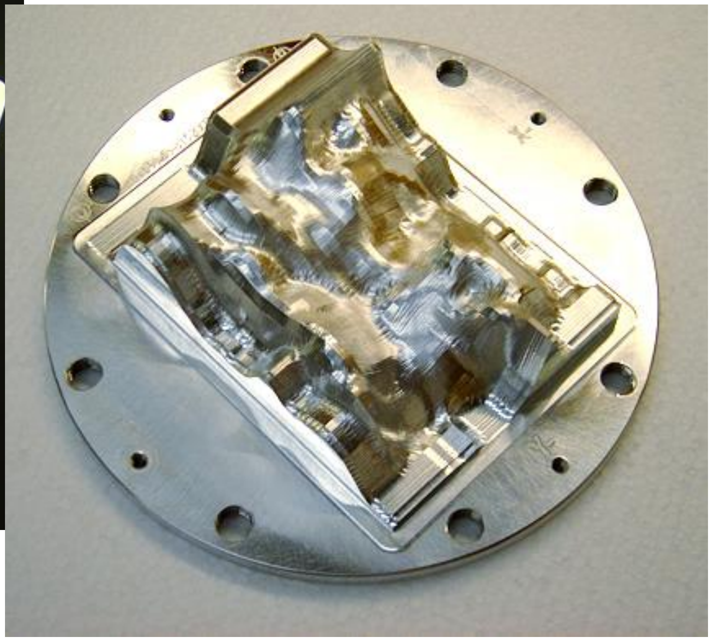
- Metal compensator
- Mutiple-static fields: step-and-shoot technique
- Dynamic multi leaf collimator: DMLC
- (Tomotherapy)
- (Swept pencil beams: Cyberknife etc.)

INTENSITY MODULATION: metal compensator

- Patient specific
- Beam specific

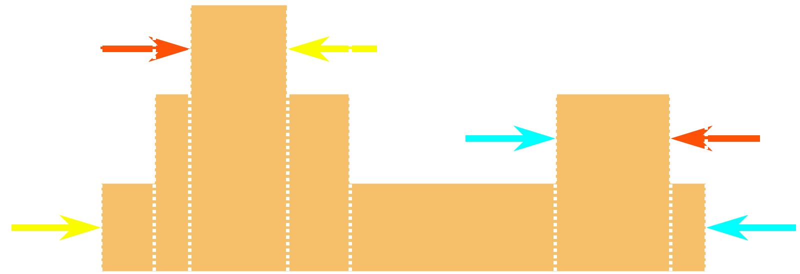




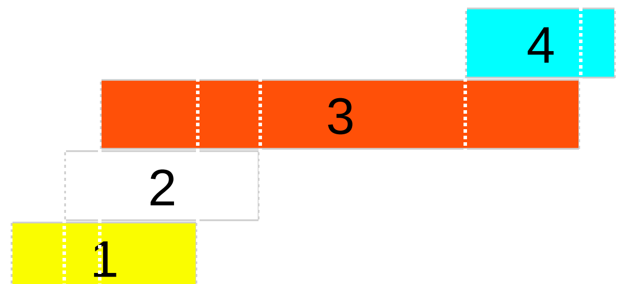


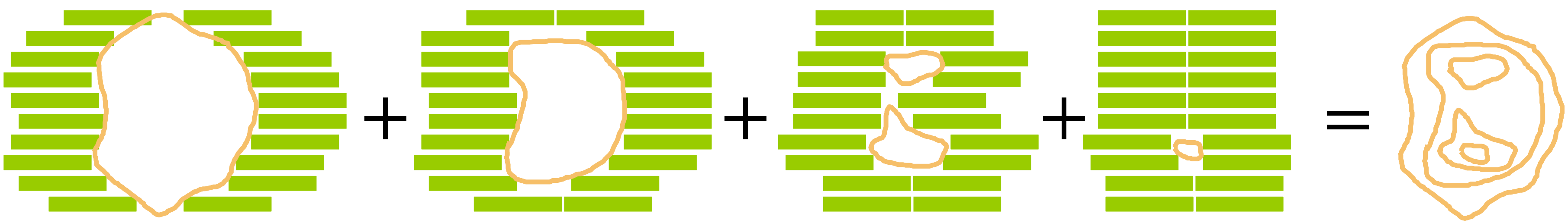
INTENSITY MODULATION: step and shoot

IM-profile



Combination of single fields





INTENSITY MODULATION: DMLC