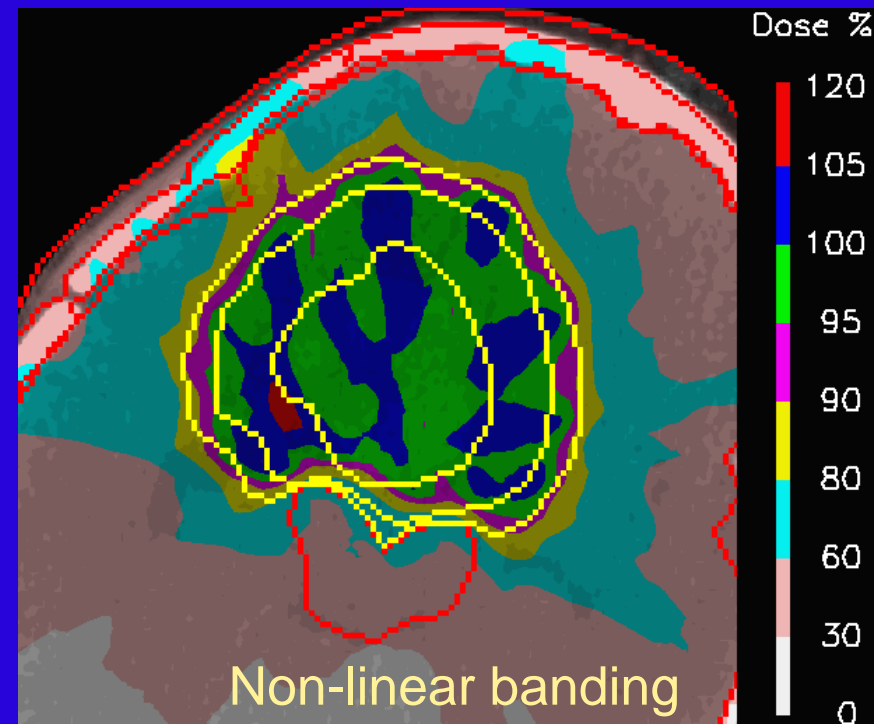
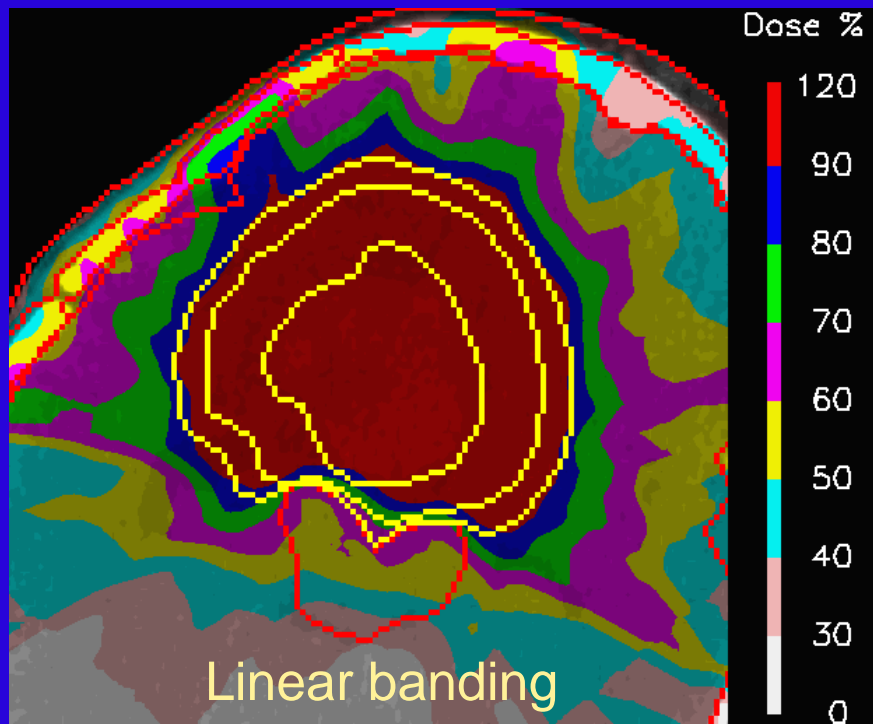
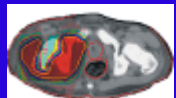


Treatment plan evaluation



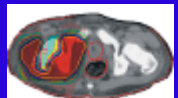
Tony Lomax

Centre for Proton Radiotherapy, Paul Scherrer Institute

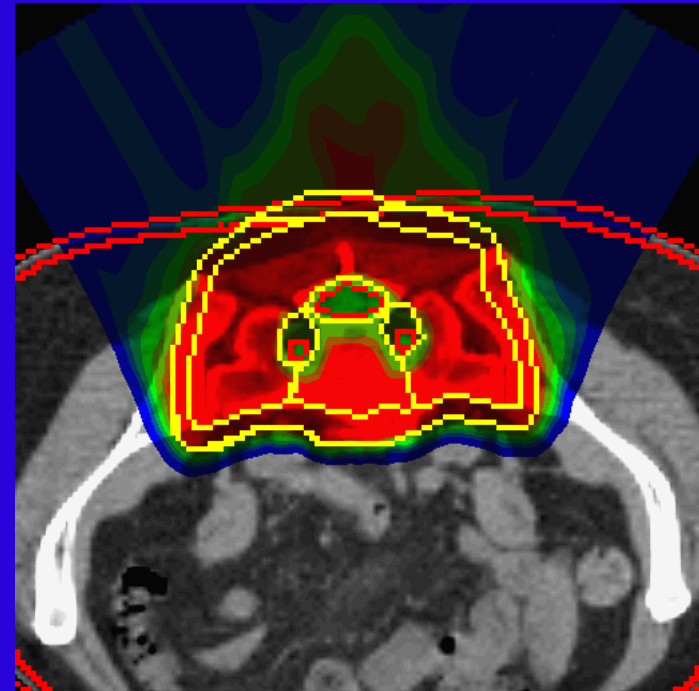
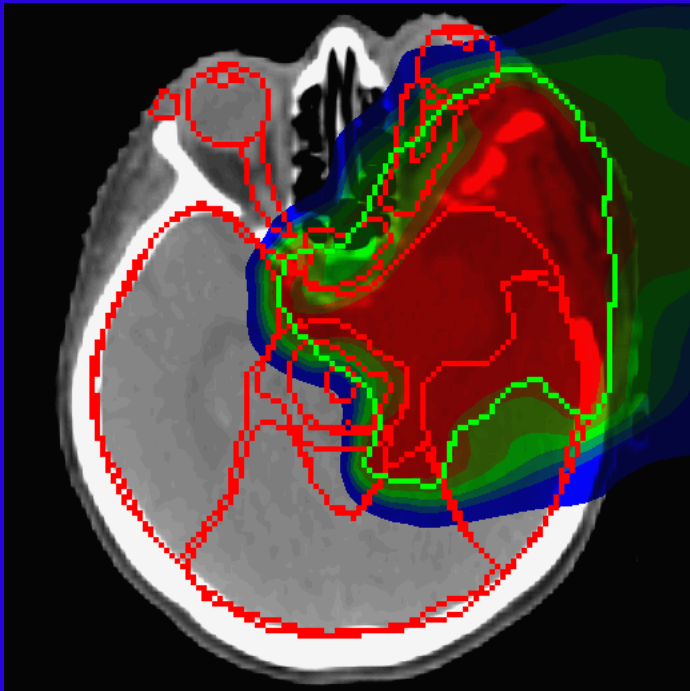


Overview

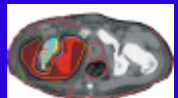
1. Displaying and interpreting dose distributions
2. Scoring and evaluating plans
3. Summary



Example dose distributions

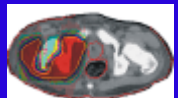


Are they acceptable? What are the risks to the patient? Will they 'cure' the patient?



The display and analysis of dose distributions

1. Displaying dose
2. Dose volume histograms
3. Characterising dose distributions and DVH's



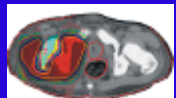
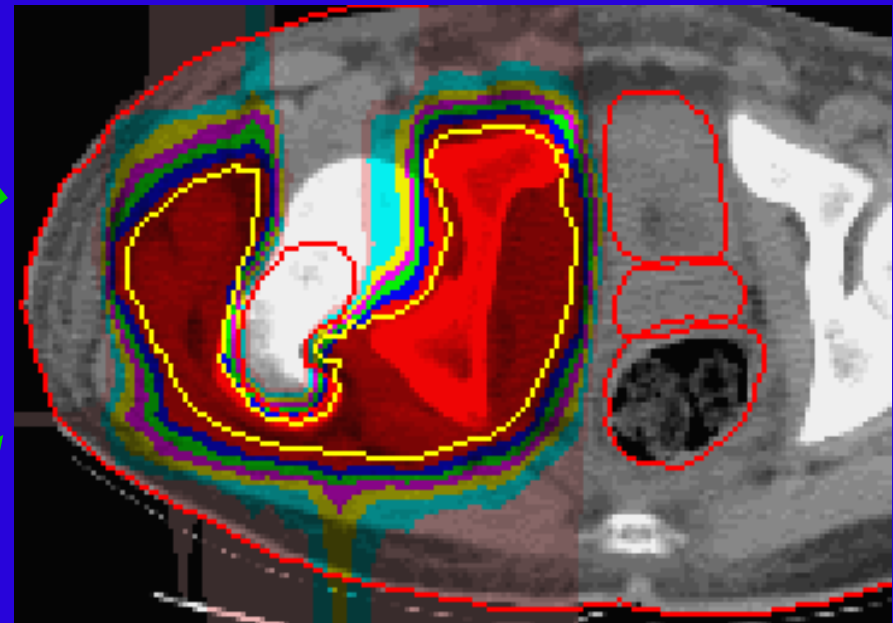
Displaying dose

The dose delivered during a radiation treatment...

...is a 3-d distribution of energy deposited within the patient

The result of a treatment plan....

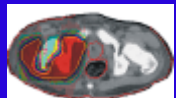
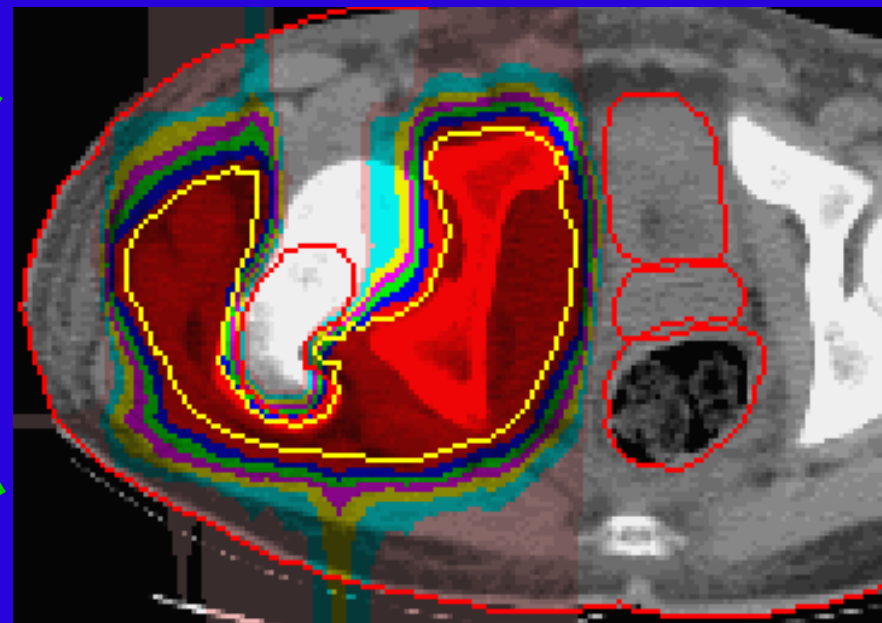
... is a (prediction of the) 3-d distribution of energy deposited within the patient



Displaying dose

The display of a 3-d dose distribution in relation to the target volume and normal structures is the most direct and informative method of assessing a treatment plan.

All other methods of analysing dose distributions are surrogates of this and involve (to a lesser or greater extent) a loss of information.



Methods of displaying dose

1. Iso-dose contours

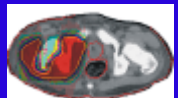
Sets of closed contours linking voxels of equal dose

2. Colour wash

The coding of CT and dose in the same voxel through the modulation of both intensity (CT) and colour (dose)

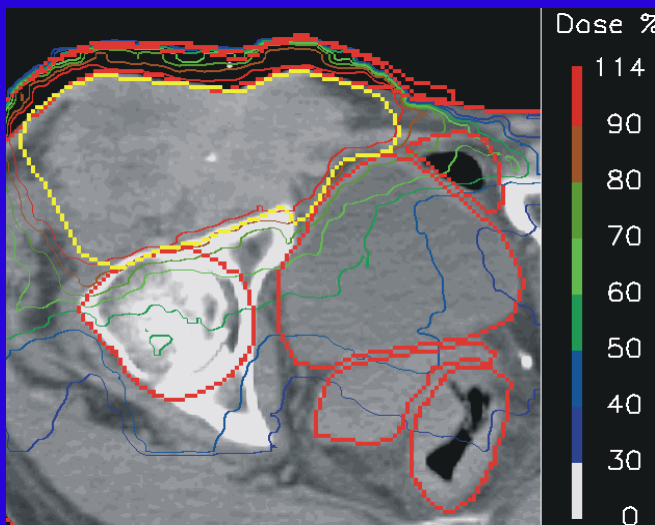
3. Iso-dose surfaces

The shaded surface (pseudo-3d) representation of a particular dose level and selected VOIs.

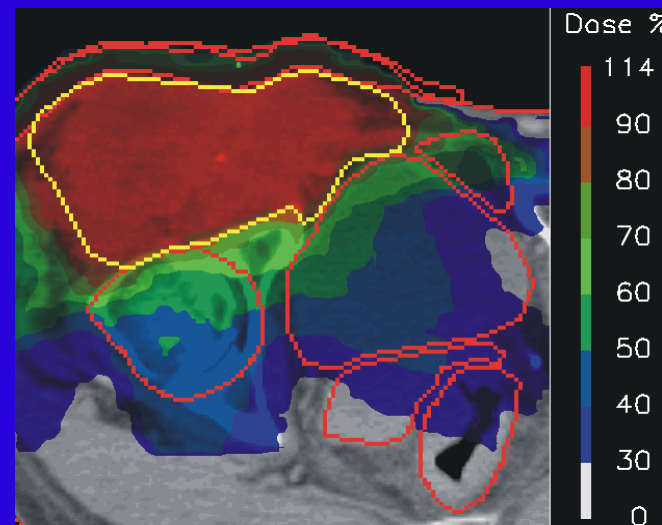


Methods of displaying dose

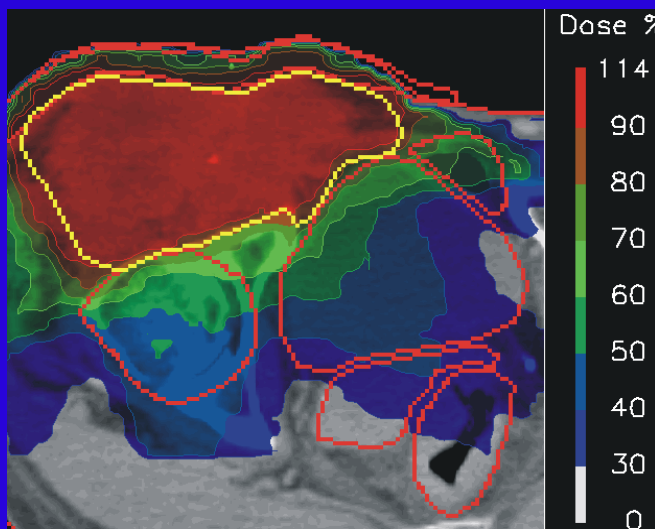
Iso-dose contours



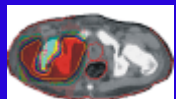
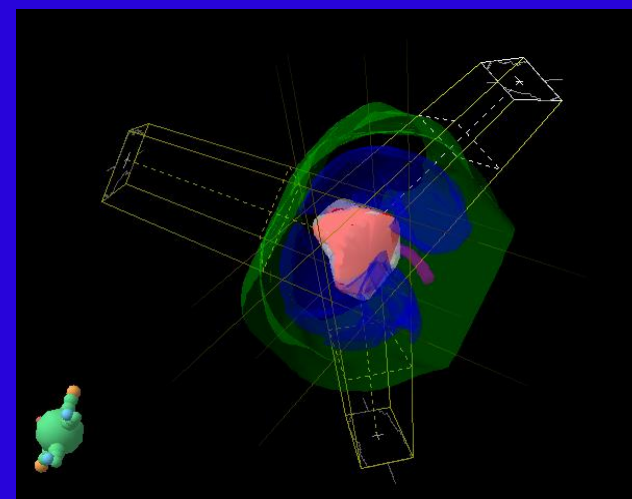
Colour wash



Iso-dose contours and colour wash



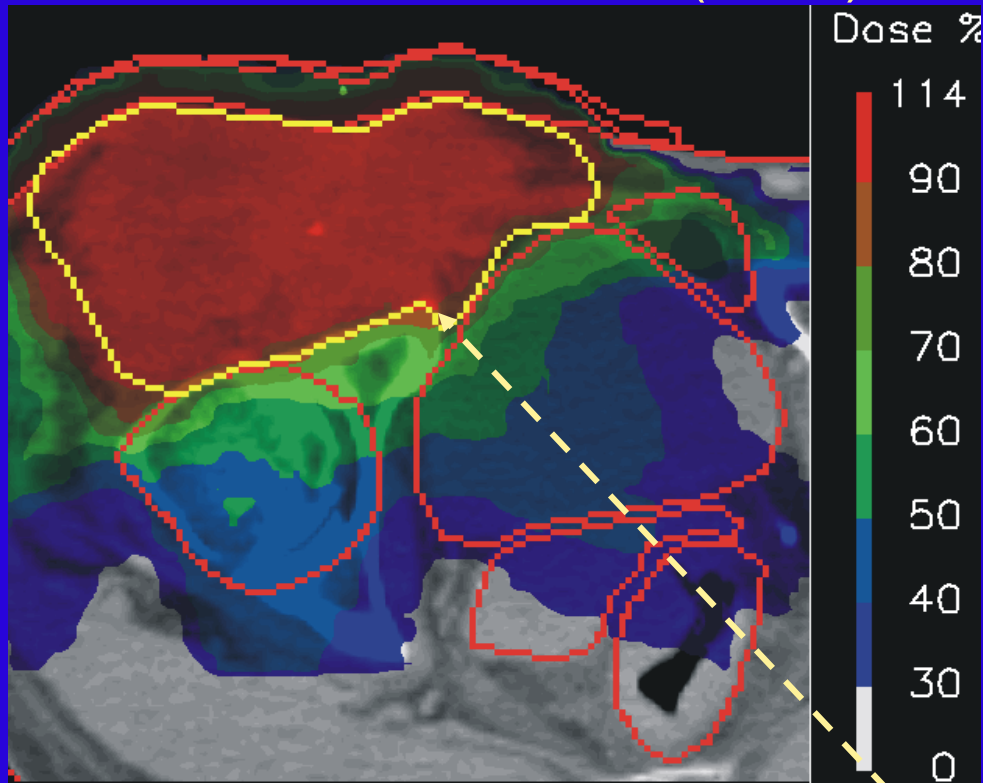
Iso-dose surface



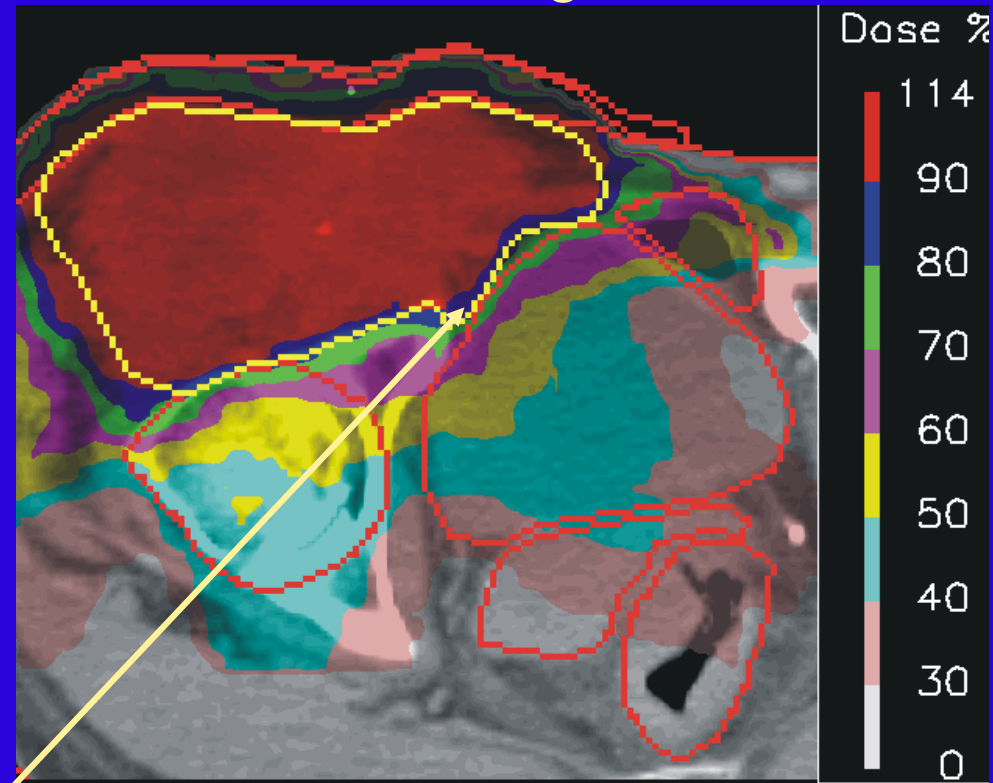
Colour scales

The gradation of colour as a function of dose value

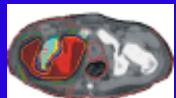
1. Continuous colour (BGR)



2. Contrasting colour



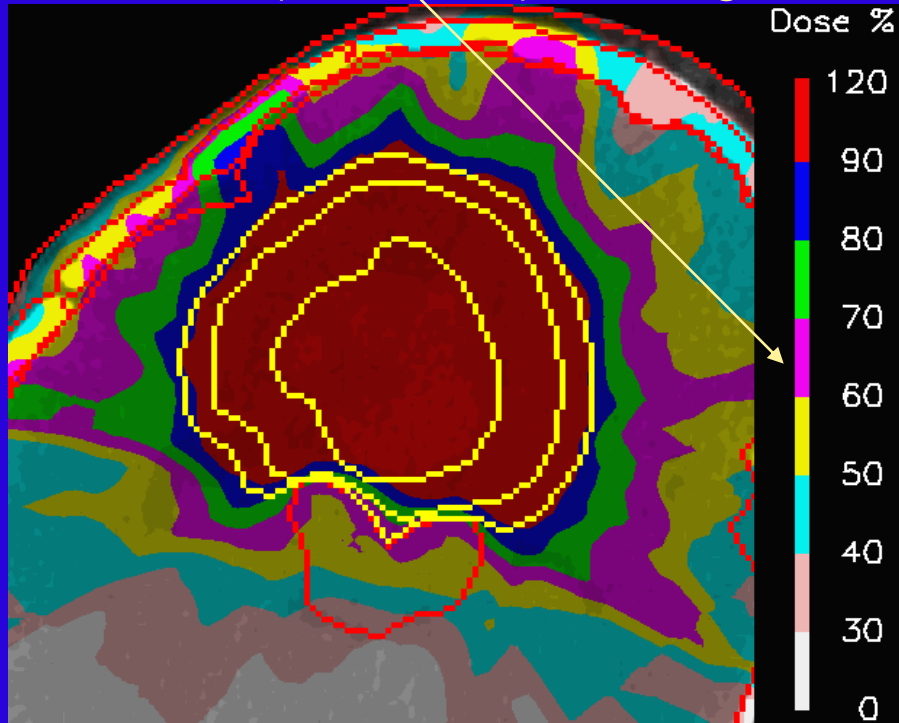
Clearer indication of 'under-dosage' within target volume



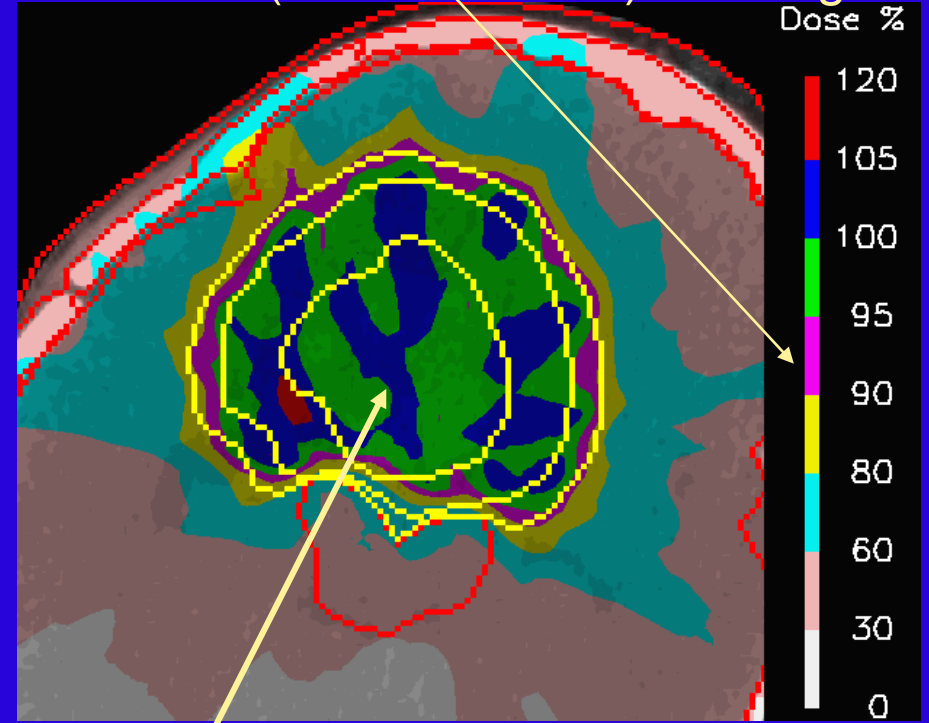
Dose banding

The mapping of dose to colours or contour levels

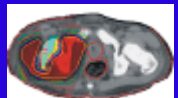
Wide (and linear) banding



Narrow (and non-linear) banding



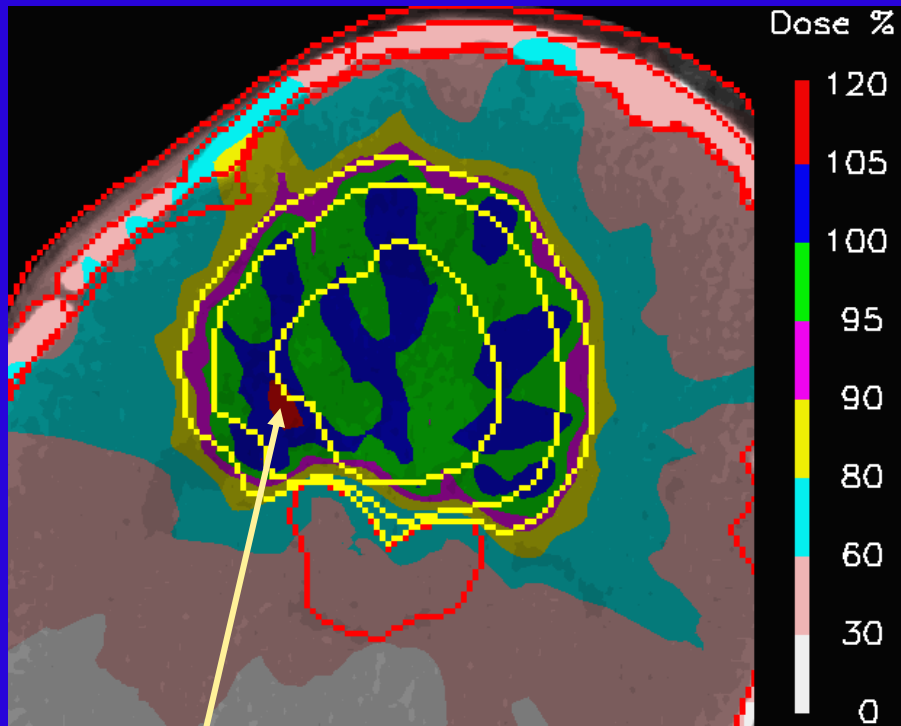
Improved visualisation of dose heterogeneity within PTV



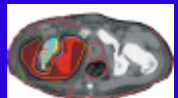
Dose banding

Reasons to be cautious!

1. Accentuated structure due to banding



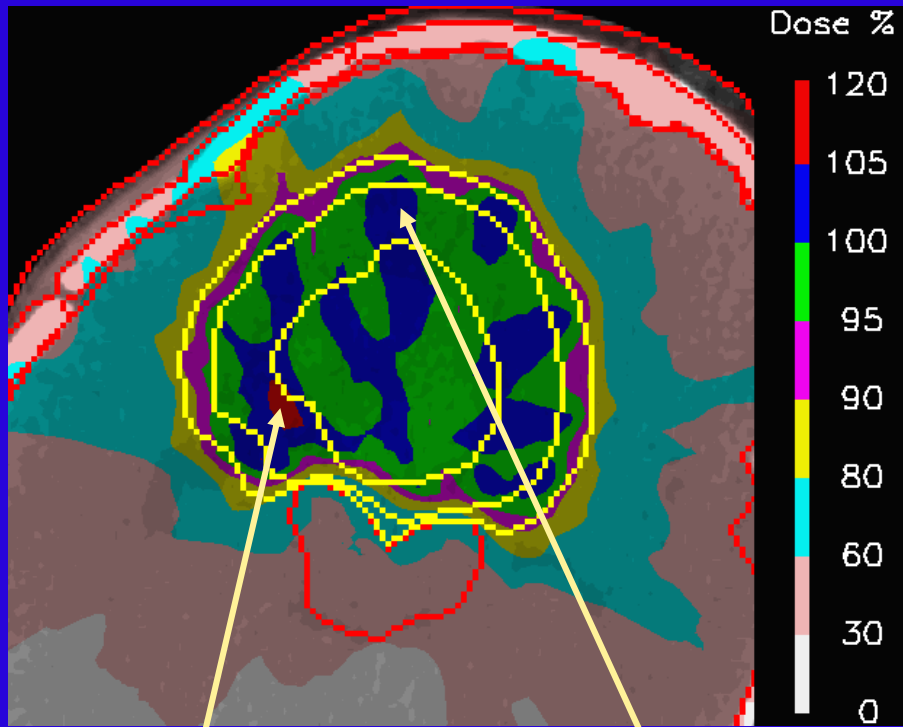
Hot spot?



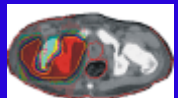
Dose banding

Reasons to be cautious!

1. Accentuated structure due to banding



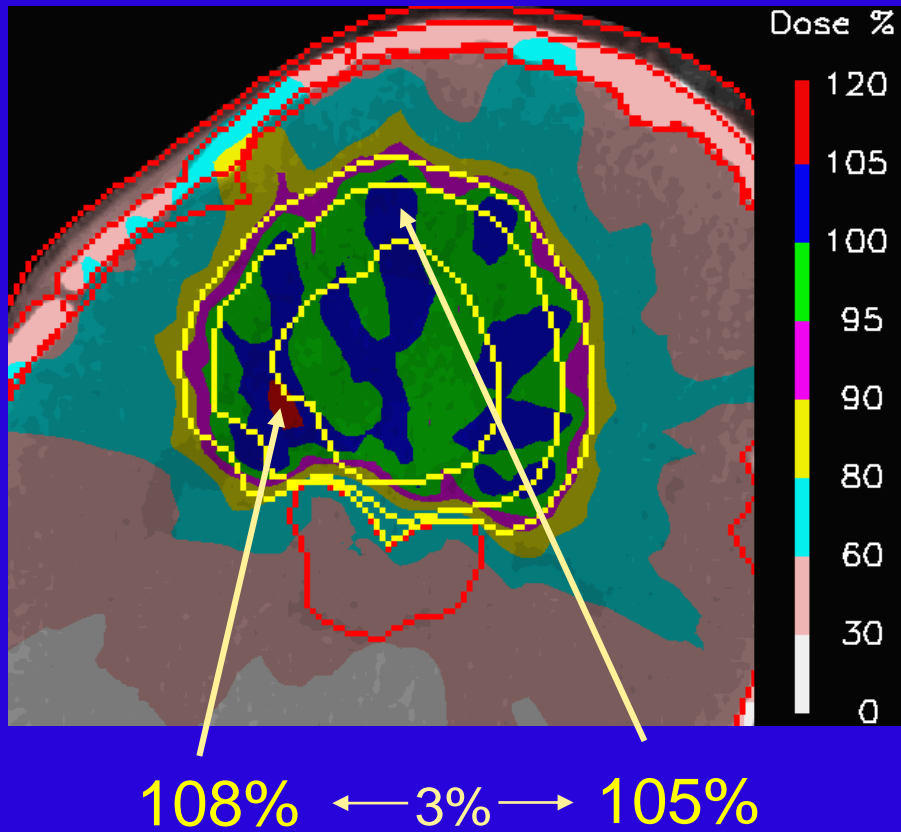
108% ← 3% → 105%



Dose banding

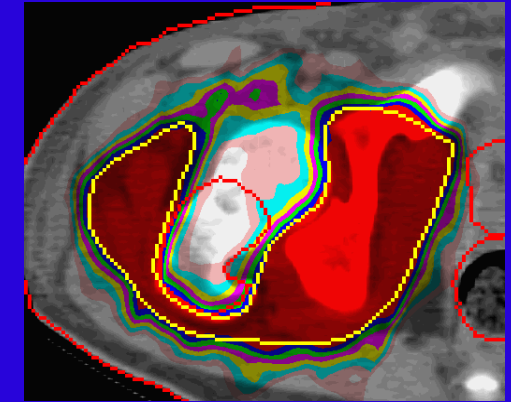
Reasons to be cautious!

1. Accentuated structure due to banding



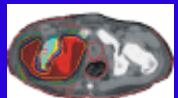
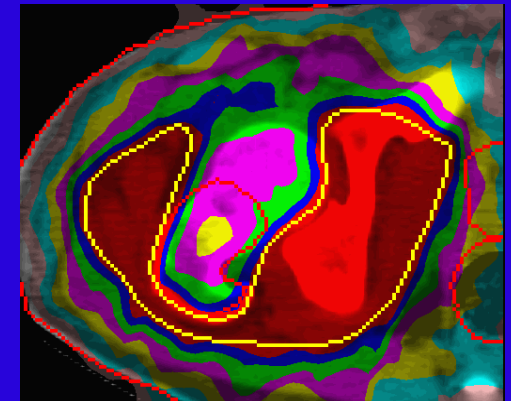
2. 'Hidden' dose

A plan with steep dose gradients...



...a plan with shallow dose gradients

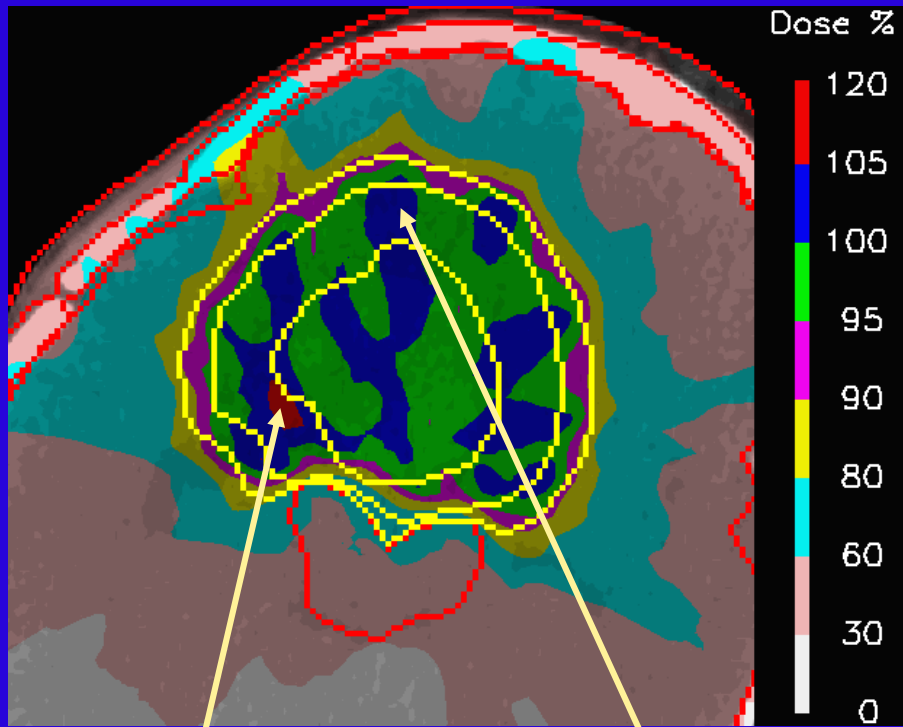
OR...?



Dose banding

Reasons to be cautious!

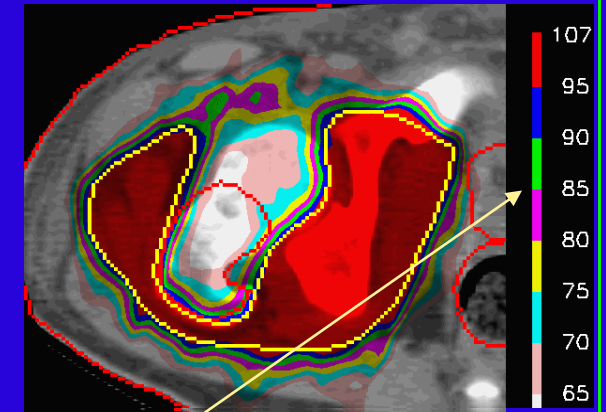
1. Accentuated structure due to banding



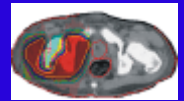
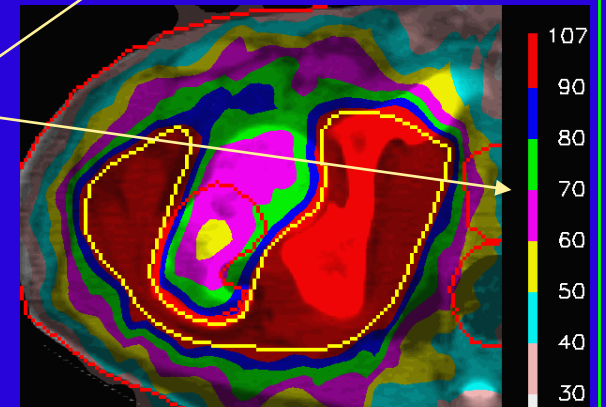
108% ← 3% → 105%

2. 'Hidden' dose

Identical dose distributions

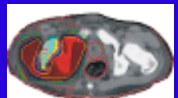


Different dose bandings!



The display and analysis of dose distributions

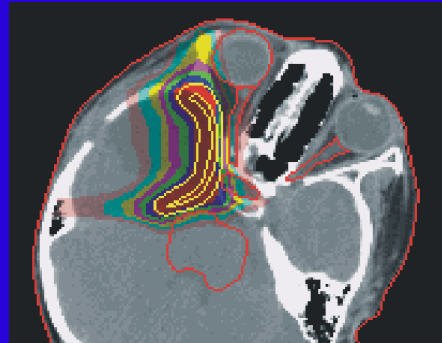
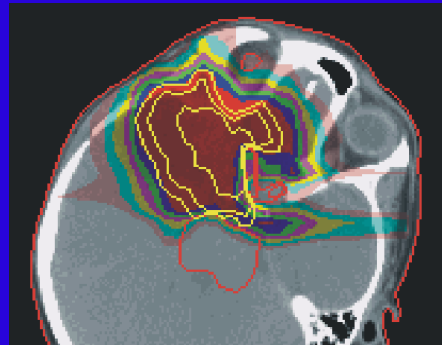
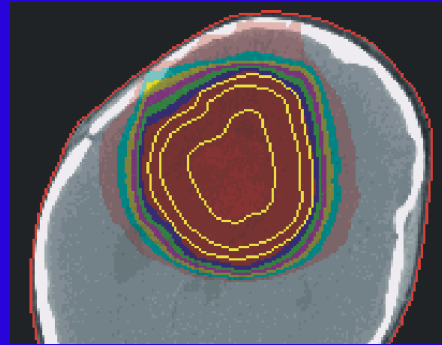
1. Displaying dose
2. Dose volume histograms
3. Characterising dose distributions and DVH's



Dose volume histograms - Why?

Disadvantages of 3-d dose distributions

1. Huge amount of information to assess
2. Difficult to quantify visually
3. Difficult to understand relationship between dose and anatomy in 3-d
4. Dose is itself only a surrogate for clinical outcome (Michael Goitein)

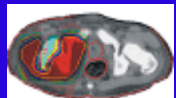


Example 3-d dose distribution

90 CT slices
(>1.5M voxels
within patient
outline)

>500000 voxels with
non-zero dose.

>60000 PTV voxels,
>70000 critical
structure voxels

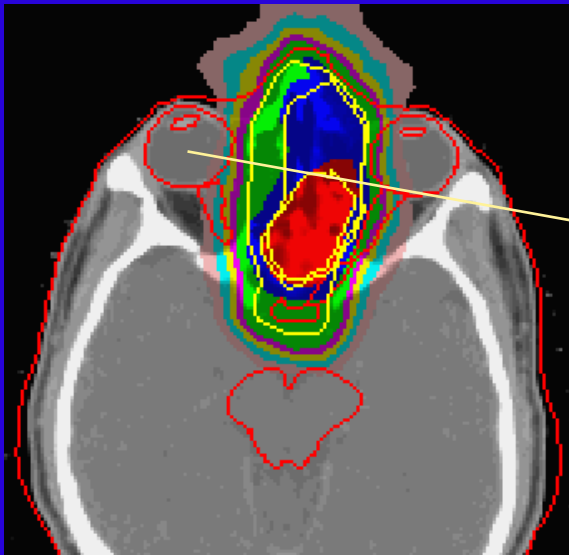


Dose volume histograms (DVH)

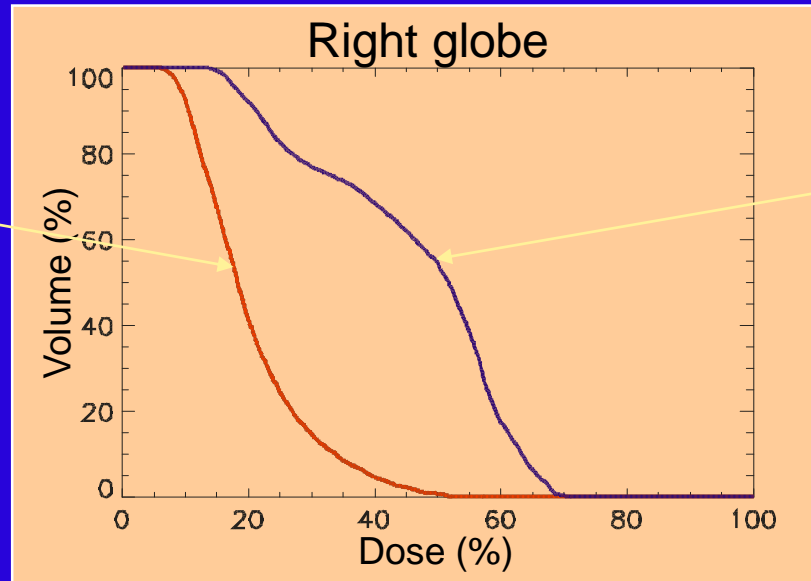
DVHs reduce 3-d dose distributions within a defined volume of interest to simple 1-d curves.

For example...

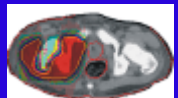
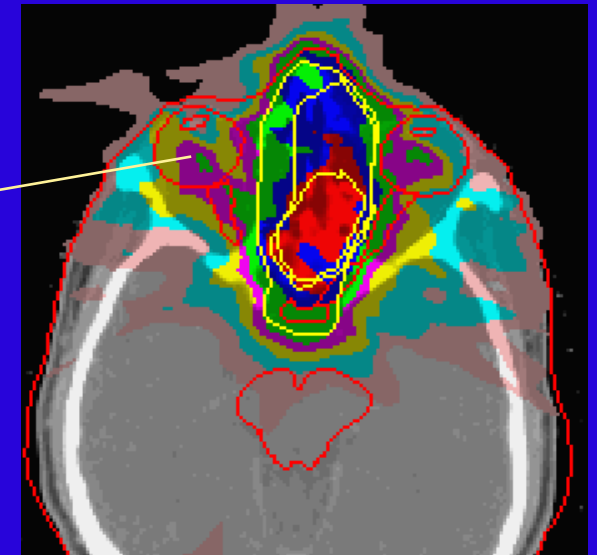
Plan 1



Comparative DVH's

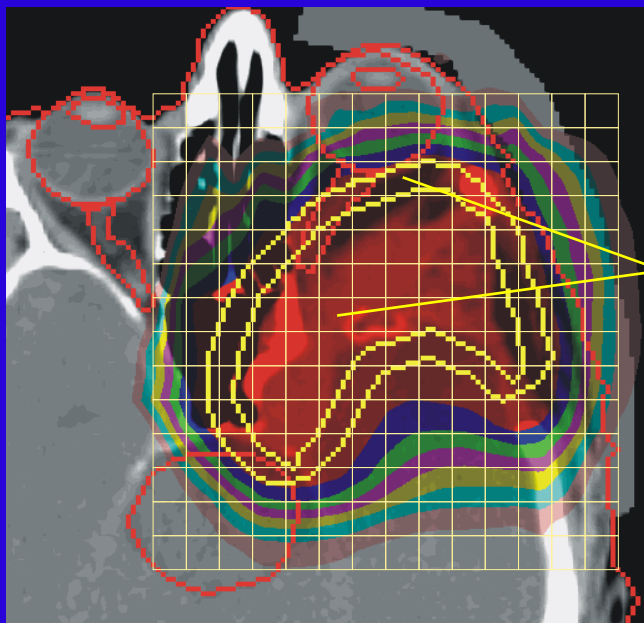


Plan 2

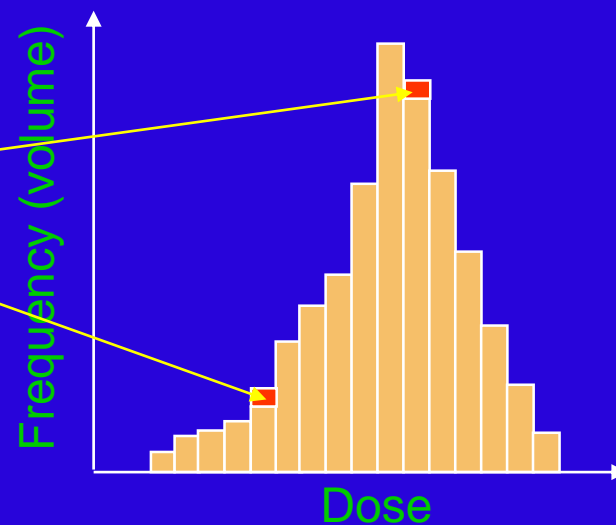


Calculation and interpretation

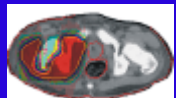
The differential (true) histogram



Dose distribution and defined VOI

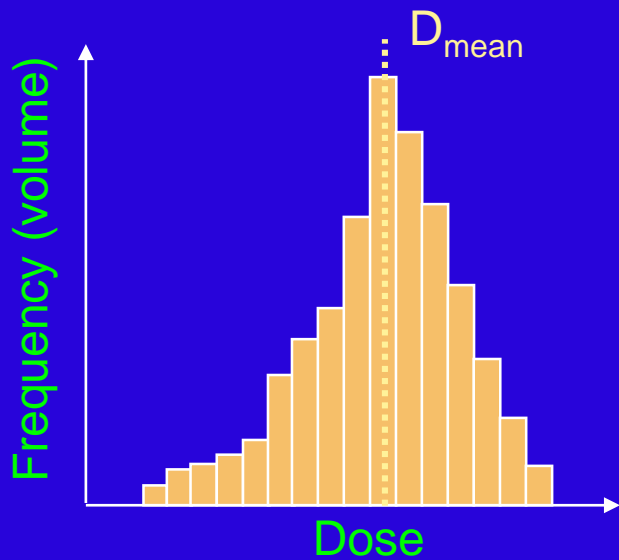


Differential (true) histogram

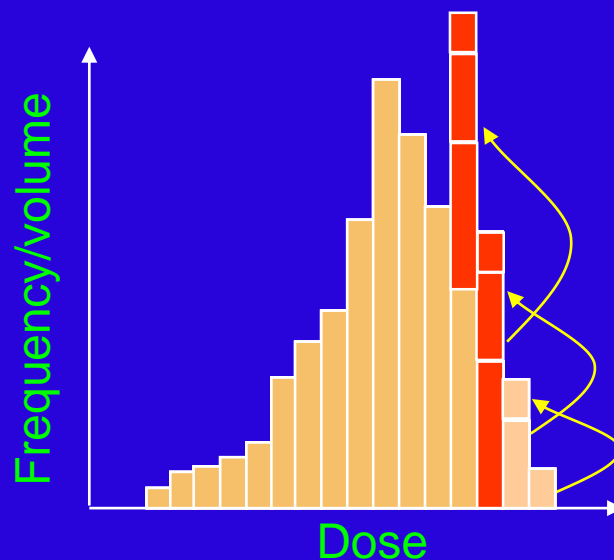


Calculation and interpretation

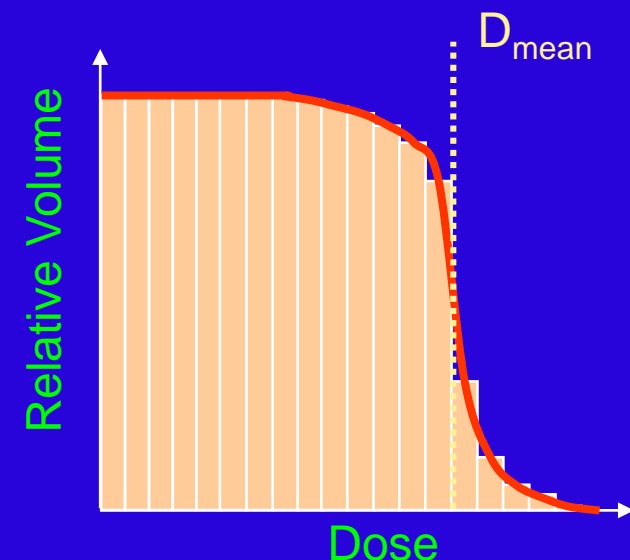
The cumulative dose volume 'histogram'



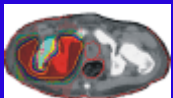
Differential DVH



Bin-by-bin
integration



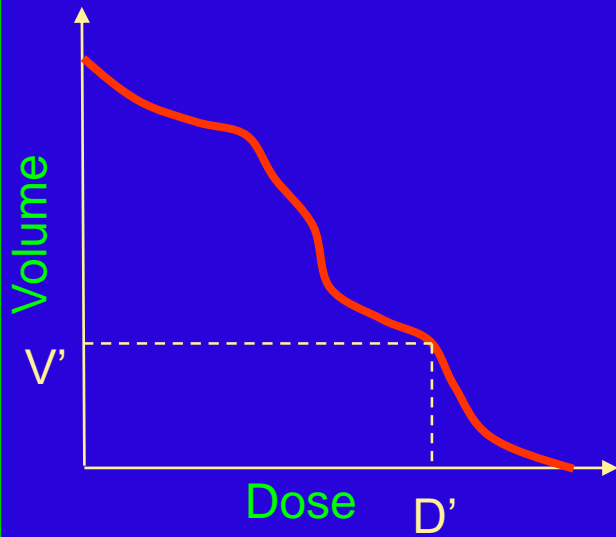
Cumulative DVH



Calculation and interpretation

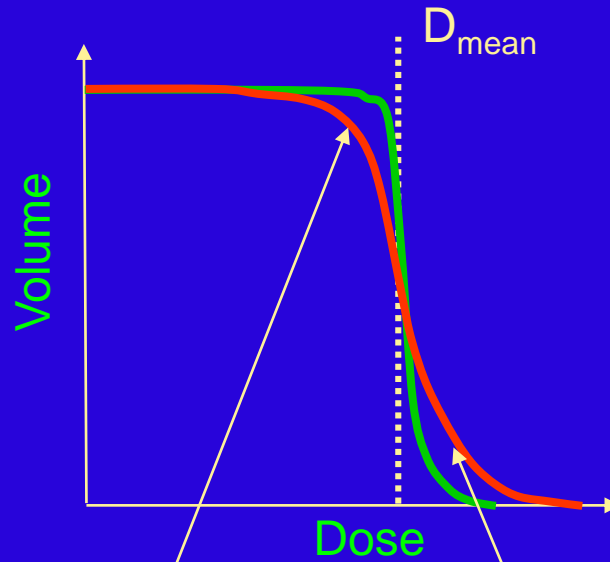
Interpreting cumulative DVHs

For all DVHs

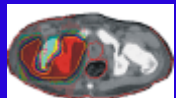
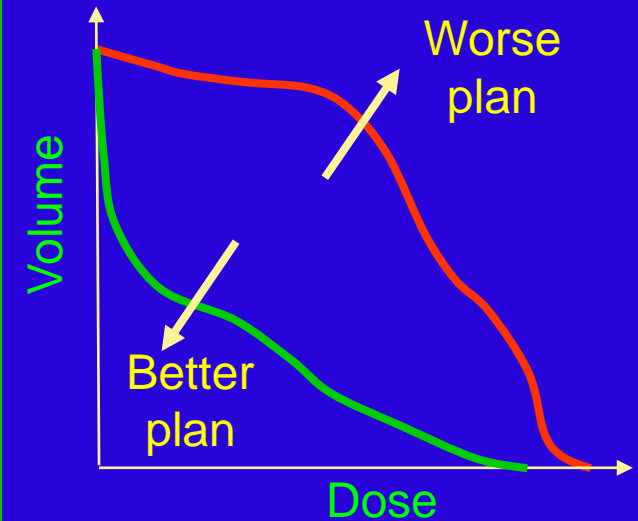


Volume V' that receives
a dose $\geq D'$

For target DVHs



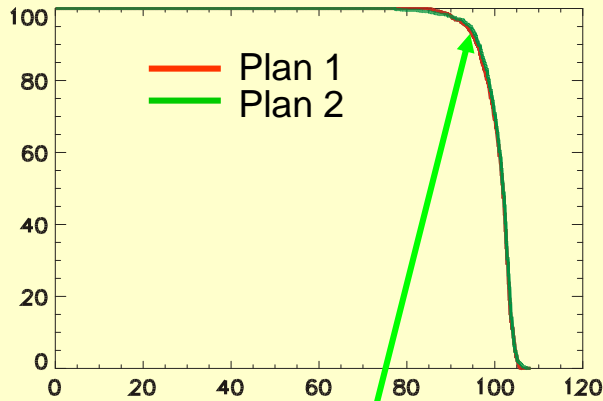
For anatomy DVHs



Problems and pitfalls

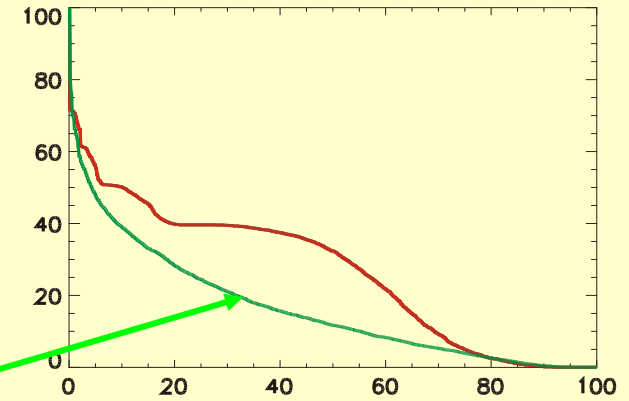
1. DVHs are insensitive to small 'hot' and 'cold' spots

Target volume



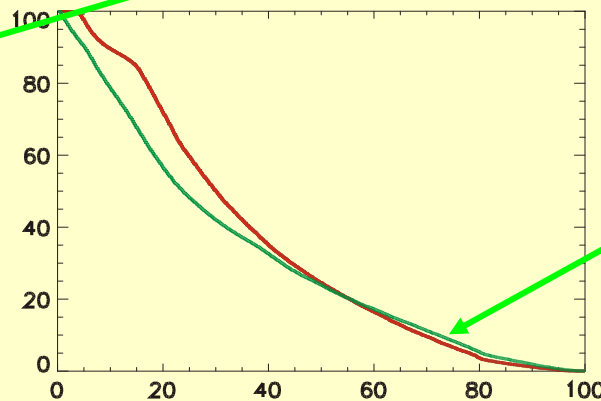
Consider comparative DVHs from two competing plans

Brain stem

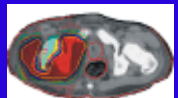


From DVHs, plan 2 appears to be the best....

Posterior fossa

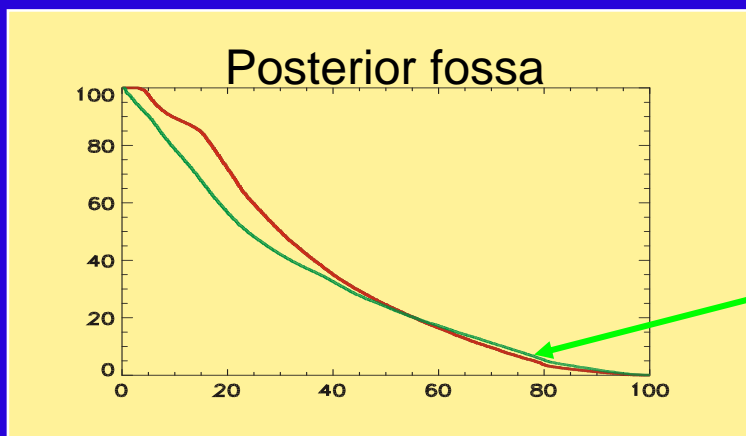
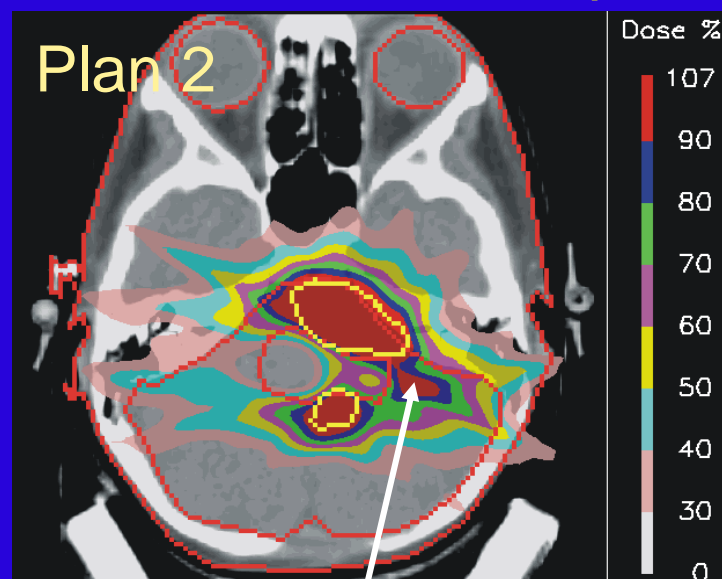
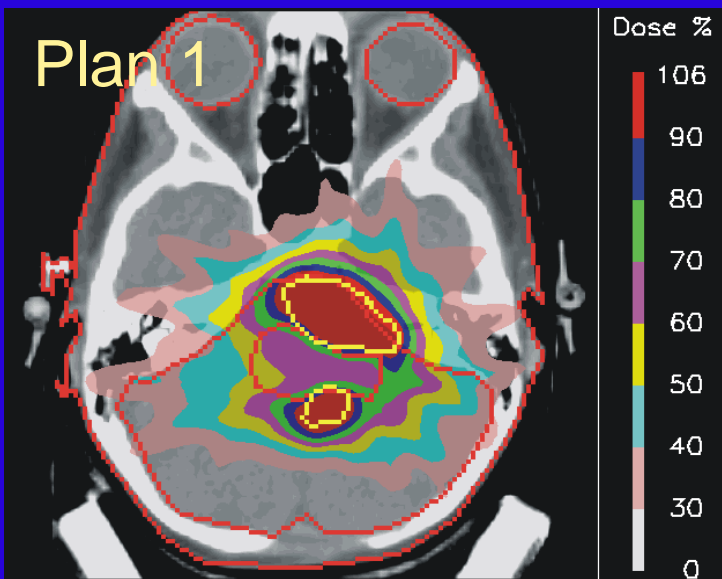


...apart from apparently insignificant increase in high dose to posterior fossa

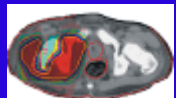


Problems and pitfalls

1. DVHs are insensitive to small 'hot' and 'cold' spots



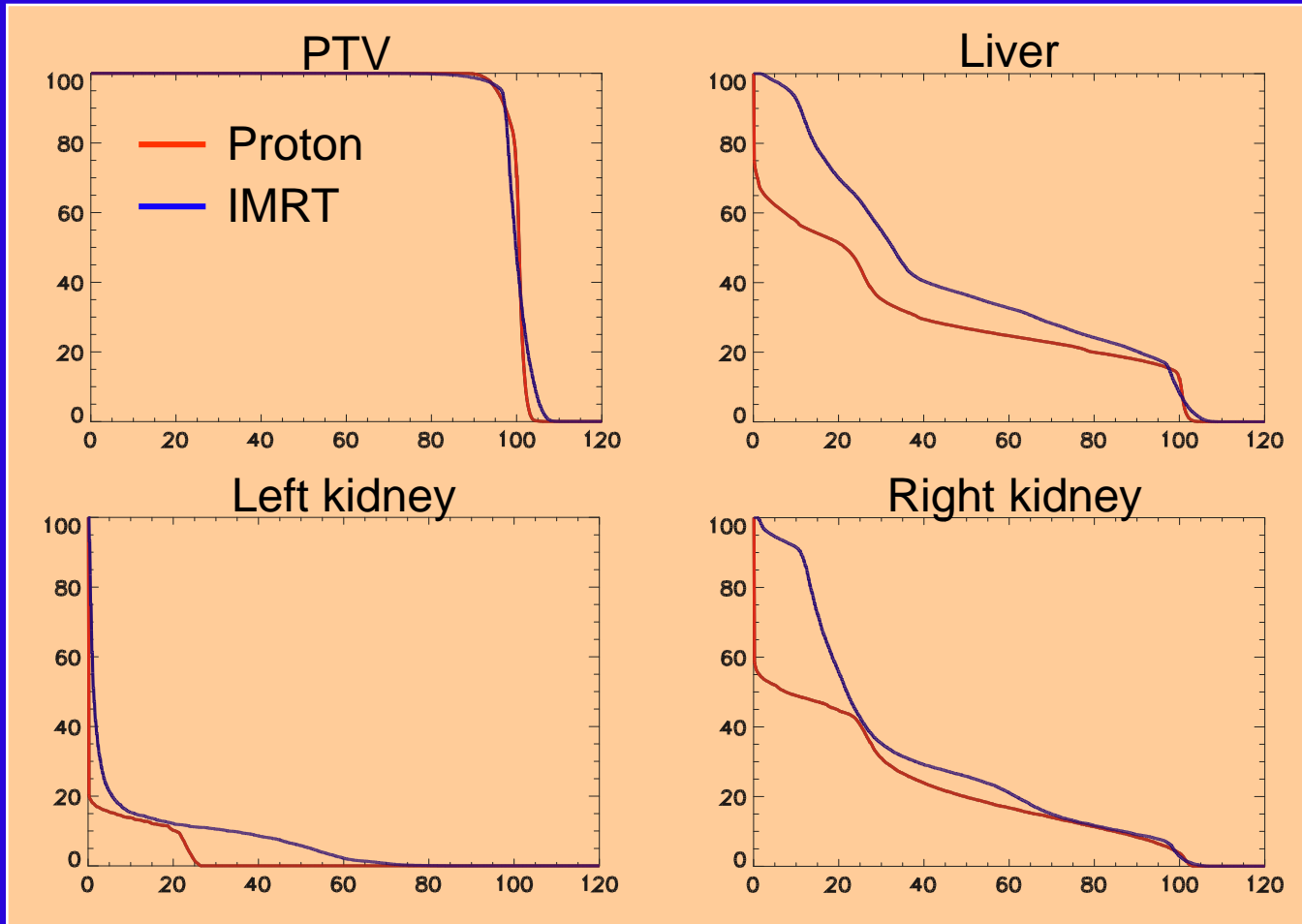
But this increase corresponds to a 105% hot spot in posterior fossa



Problems and pitfalls

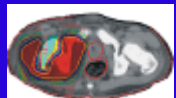
2. DVHs can only be calculated for defined VOIs.

Consider a set of DVHs for a non-coplanar, IMRT plan



From DVHs alone,
the IMRT plan looks
reasonably
favourable in
comparison to the
proton plan

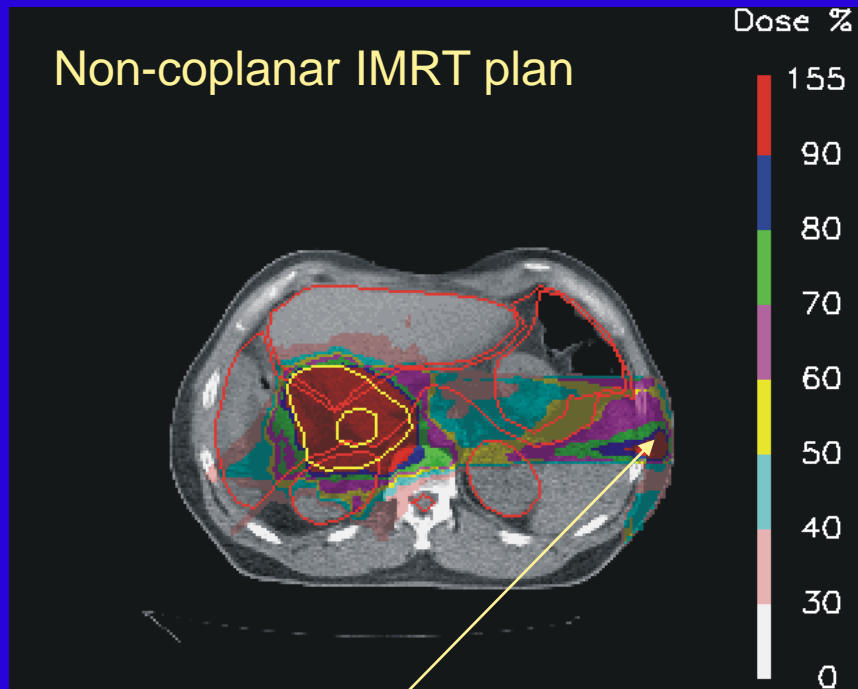
However....



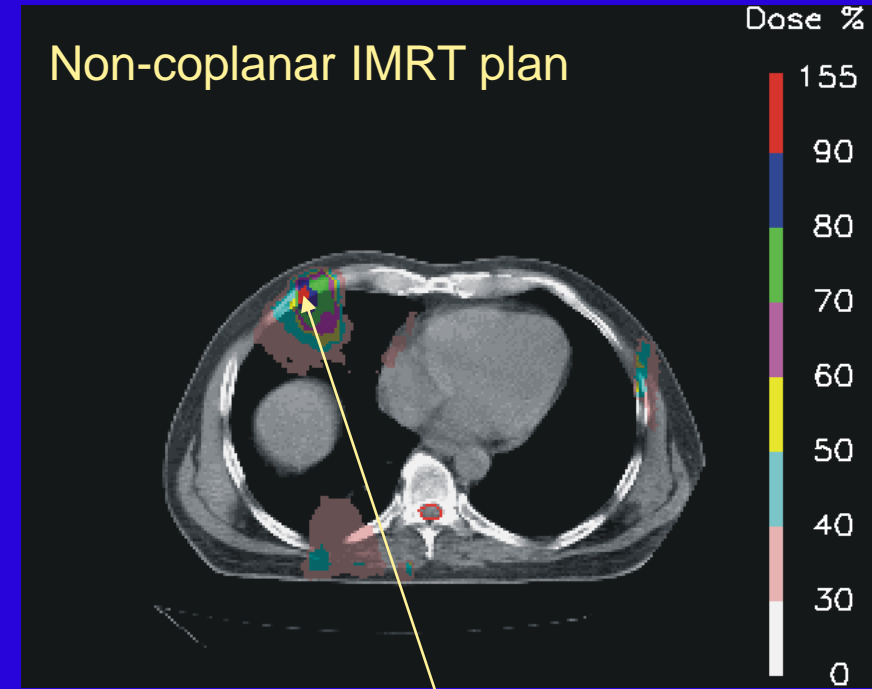
Problems and pitfalls

2. DVHs can only be calculated for defined VOIs.

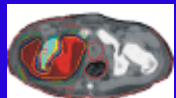
Visual inspection shows the IMRT plan to be unacceptable



>120% hot spot in rib
in target plane

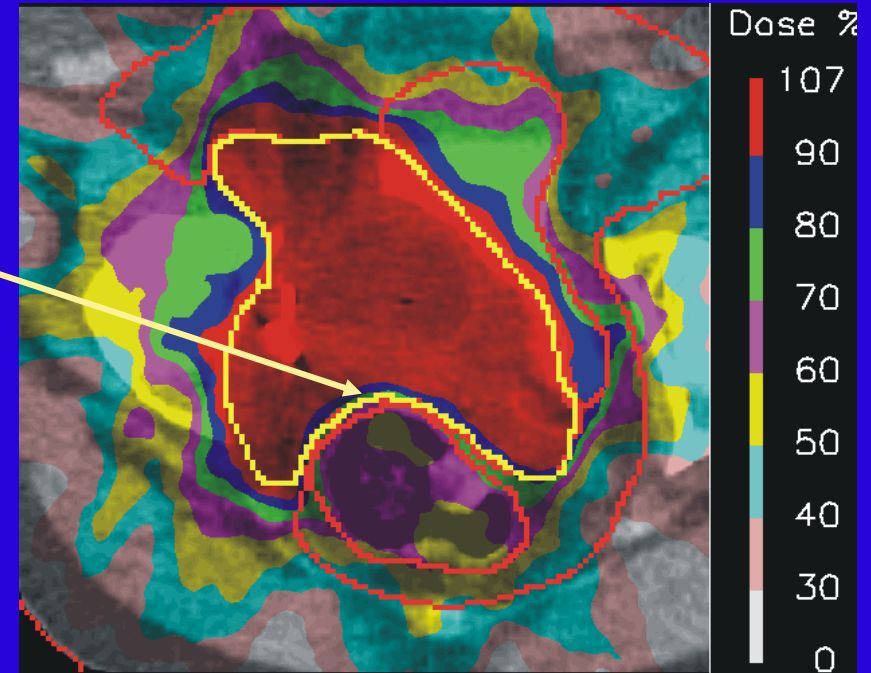
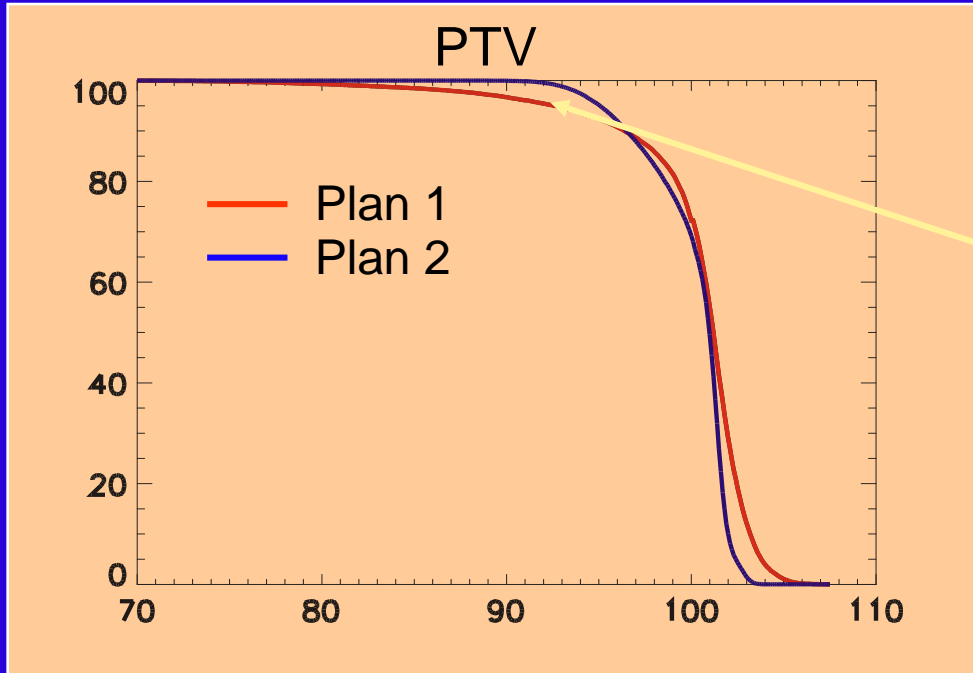


>90% hot spot in rib
out of target plane



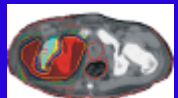
Problems and pitfalls

3. DVHs throw away all spatial information



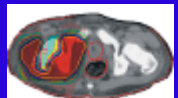
DVH analysis shows clear under-dosage for plan 1, but...

... it needs analysis of the dose distribution to show where.



The display and analysis of dose distributions

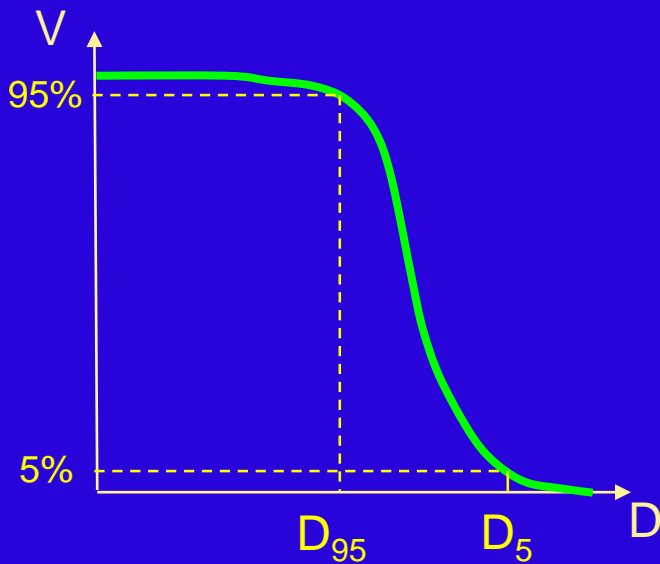
1. Displaying dose
2. Dose volume histograms
3. Characterising dose distributions and DVH's



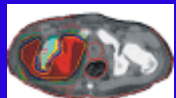
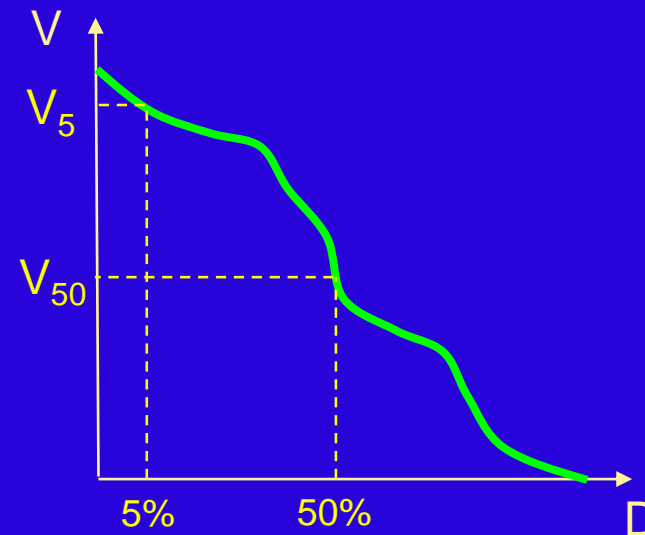
Characterising dose distributions

Common Dose-Volume parameters

D_v – The minimum dose (%/Gy) that volume v (%/ml) of a selected organ receives



V_d – The volume (%/ml) of a selected organ that receives at least dose d (%/Gy)



Characterising dose distributions

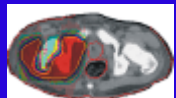
Common Dose-Volume parameters?

Table 1. Various normal tissue doses reported for IMRT breast plans in the literature compared with the results for plans X-E, IMXT1, IMXT2 and P from this work

Dose parameter	Authors and plans										
	Evans <i>et al.</i> (5)	Kestin <i>et al.</i> (7)	Van Asselen <i>et al.</i> (4)	Hong <i>et al.</i> (6)	Li <i>et al.</i> (8) (IMRT)	Li <i>et al.</i> (8) (IMXE)	Smitt <i>et al.</i> (3)	X-E	IMX1	IMX2	P
PTV (breast only)											
Max dose (%)		108.0		112.0	117.0	130		163.0	111.8	129.4	108.0
Min dose (%)					80.0	80.0	45.6	0.0	76.2	47.0	69.6
V95 (%)	95.2	98.0						86.6	96.2	88.1	97.1
V105 (%)	7.2							24.6	3.3	12.5	0.5
D05 (%)				107.0				108.0	105.0	108.0	104.0
D95-D05 (%)			7.6					36.0	10.0	16.0	8.0
Ipsilateral lung											
Mean dose (%)			8.0		25.6	14.3	23.8	33.3	36.3	29.7	25.0
V50 (%)				27.0				28.1	24.4	30.9	22.9
Contralateral lung											
Mean dose (%)				0.7	14.1	2.6	6.0	2.5	24.7	21.3	1.2
Heart											
Max dose (%)					74.6	75.6	73.4	101.0	101.1	99.9	107.6
Mean dose (%)					24.6	10.3	27.8	29.3	32.1	15.8	11.6
D05 (%)				32.0				77.0	76.0	66.0	78.0
Contralateral breast											
Max dose (%)				0.0	62.1	44.8	33.7	2.5	53.7	32.8	2.7
Mean dose (%)				0.0	10.5	2.4	6.0	0.4	11.8	4.1	0.1

Abbreviations: V95 = the volume receiving >95% of the target dose; D05 = the maximum dose to which at least 5% of the volume is irradiated; IMRT = intensity-modulated radiation therapy; PTV = planning target volume.

Lomax et al, IJROBP, 55, 2003, 785-792

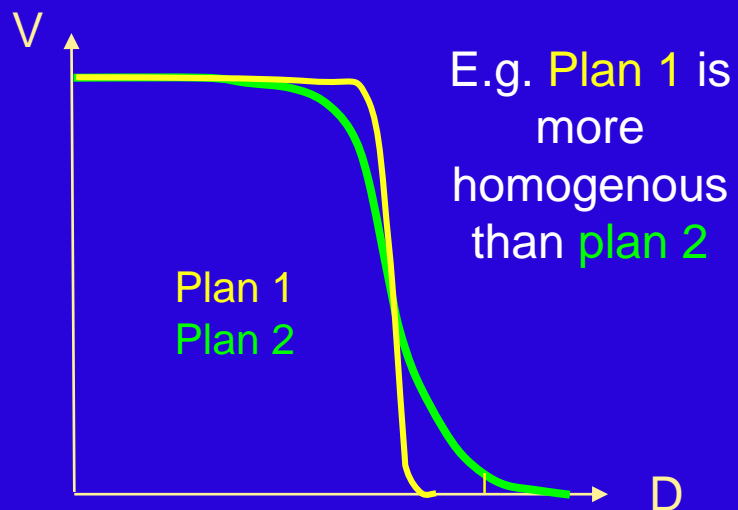


Characterising dose distributions

Homogeneity and conformity indices

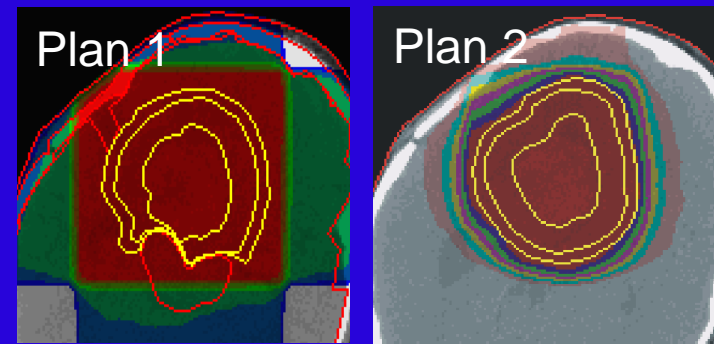
Homogeneity index

A measure of the uniformity of dose across the target volume

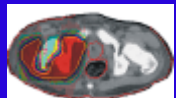


Conformity index

A measure of how the calculated dose conforms to the target volume

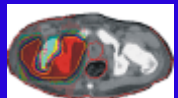


Plan 1 is clearly less 'conformal' than plan 2



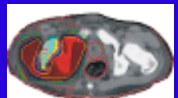
Overview

1. Displaying and interpreting dose distributions
2. Scoring and evaluating plans
3. Summary



Scoring and evaluating plans

1. What is an optimal plan?
2. Biological based scoring



What is an optimal plan? An example

9 intensity-modulated beams, evenly spaced over 360°

3 Target Volumes

Gross volume: 76Gy

Subclinical: 66Gy

Microscopic: 54Gy

Nominal constraints

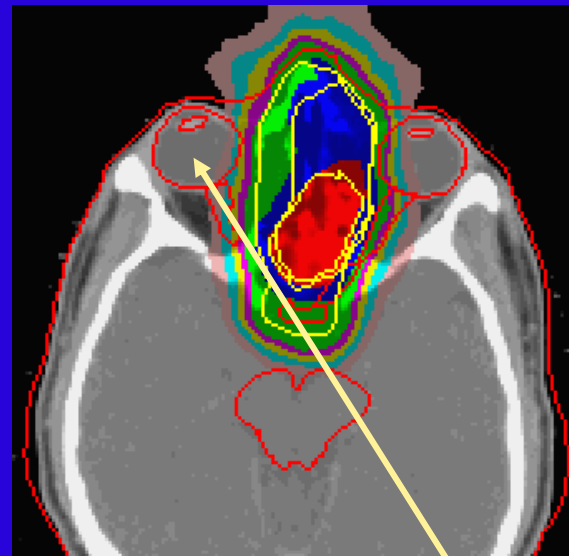
Optic nerves < 56Gy

Brainstem < 53Gy

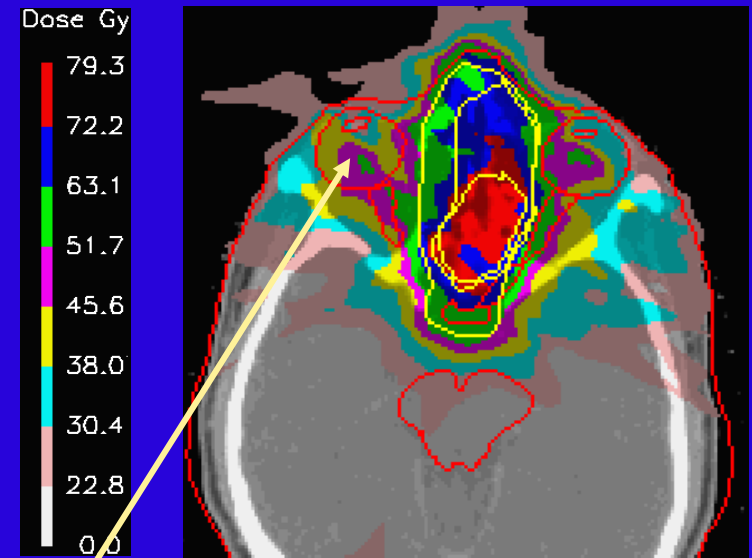
Eyes < 50Gy

Consider a comparison of intensity modulated protons (IMPT) and X-rays (IMXT)...

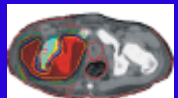
Nominal IMPT



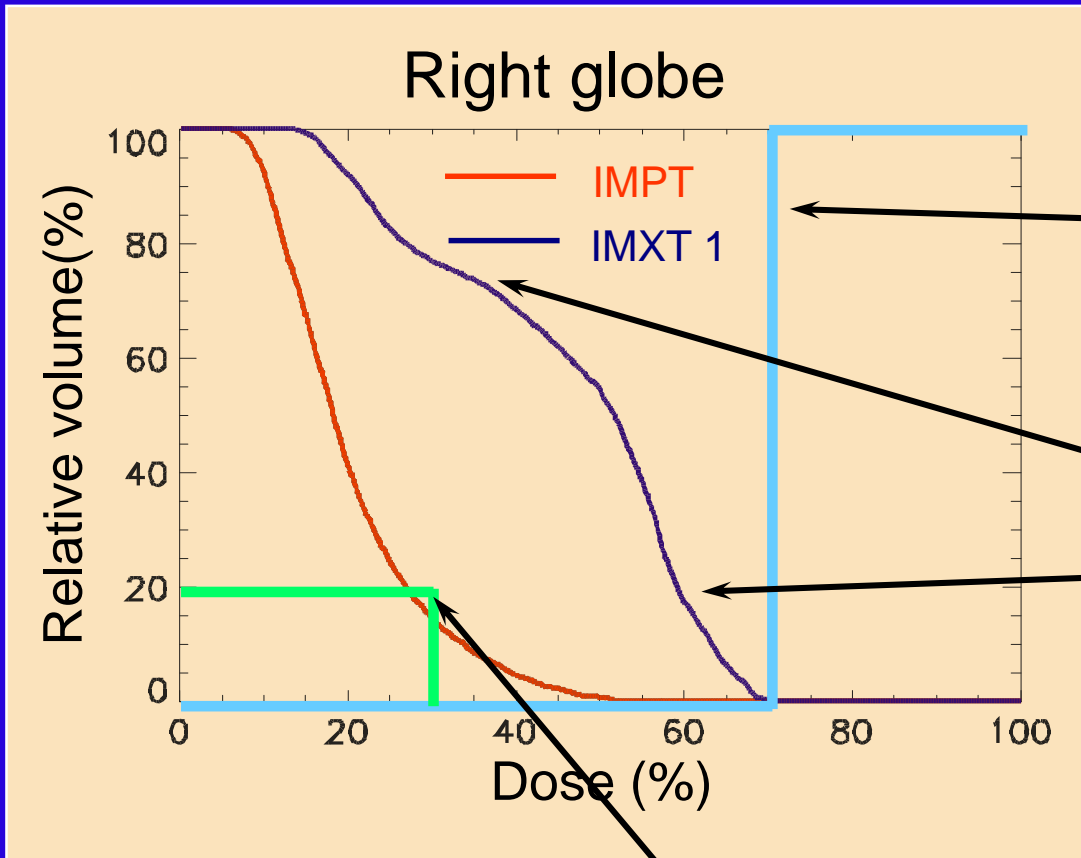
Nominal IMXT



Both plans calculated with exactly the same constraints, but clear differences in doses



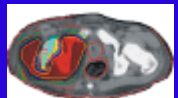
What is an optimal plan? An example



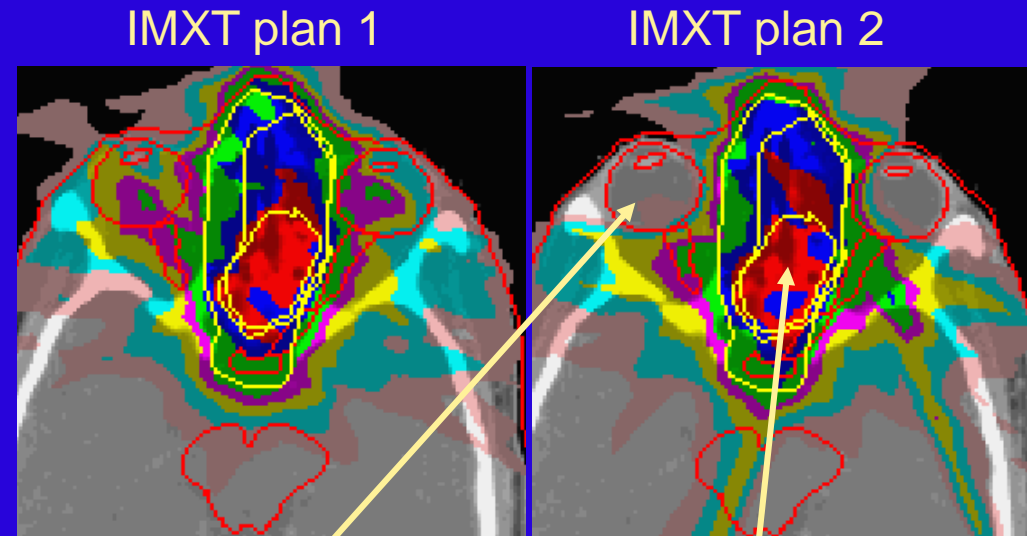
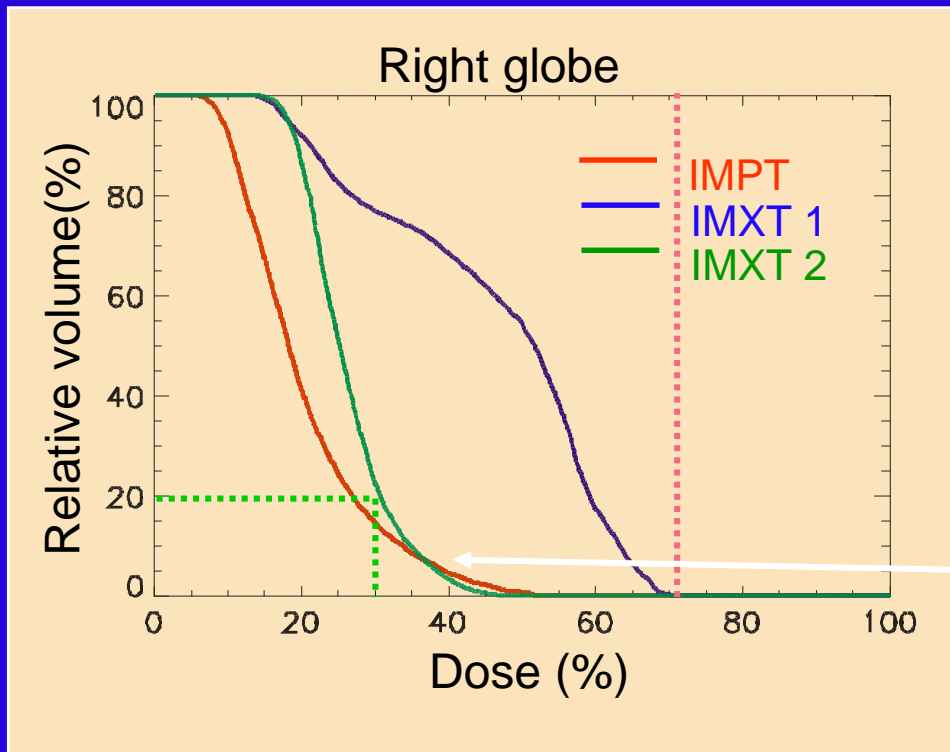
Single dose weighting function

Optimisation makes no attempt to reduce doses below constraint (zero weight)

What happens when we use a dose-volume constraint to attempt to match IMXT DVH to IMPT (nominal) DVH?



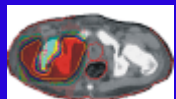
What is an optimal plan? An example



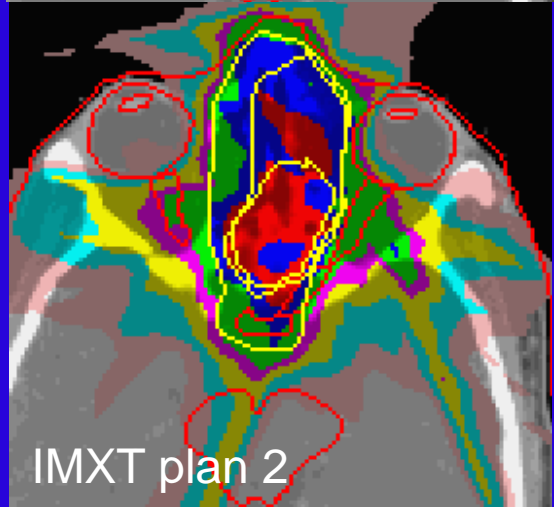
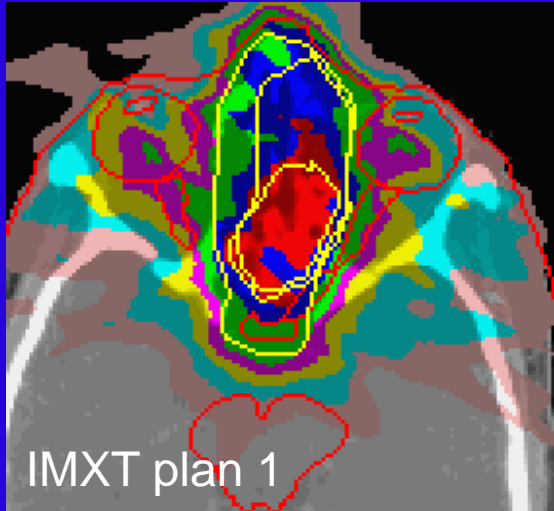
Significantly reduced dose in globe through use of stricter constraint...

..at cost of slightly decreased target homogeneity

The quality of an 'optimised' plan depends on the defined constraints

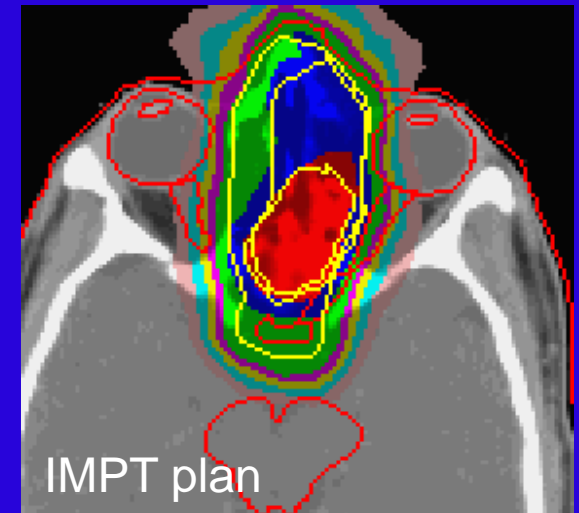


What is an optimal plan? An example



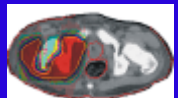
Two 'optimised' X-ray plans, with two quite different dose distributions.

Which is optimal, or even, which is best?



Scoring and evaluating plans

1. What is an optimal plan?
2. Biological based scoring

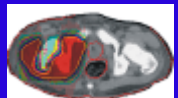


Dose based scoring

The 'gold standard' for assessing and ranking a plan?

Possible score functions

1. Visual assessment of the 3-d dose distribution
2. Visual assessment of DVHs
3. Quantitative analysis of dose distributions (conformity index, homogeneity index, V95 etc)
4. Quantitative analysis of DVHs (max, min, dose-to-volume etc)

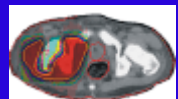
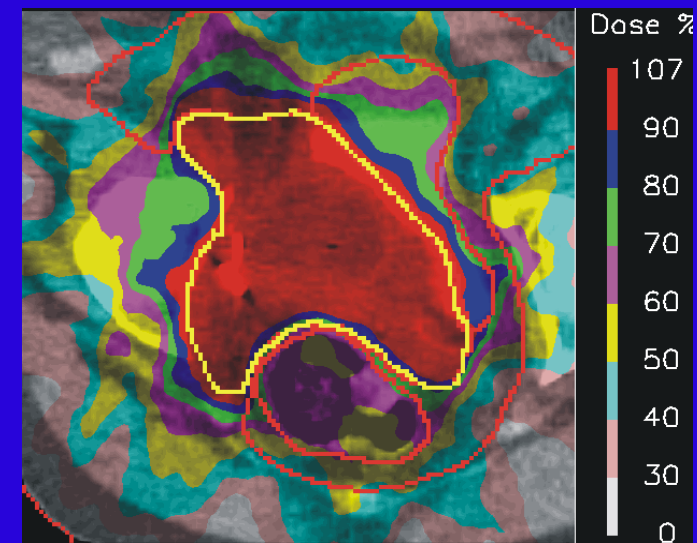
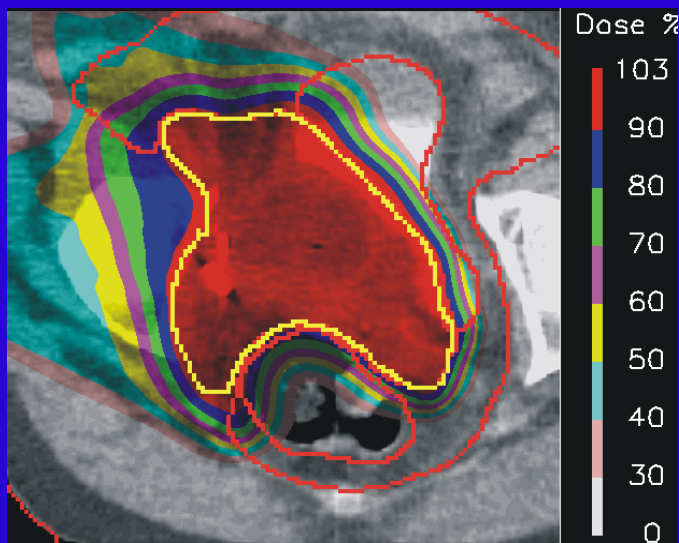


Dose based scoring.

Problems with dose based scoring

Visual assessments
difficult to quantify.

Many, often conflicting
indices required to fully
characterise a plan



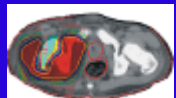
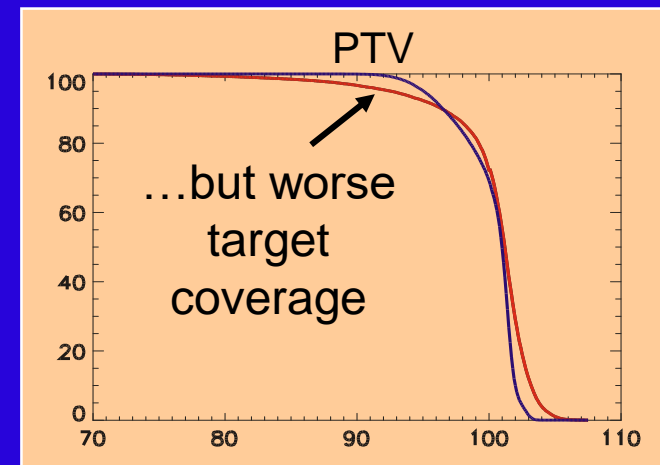
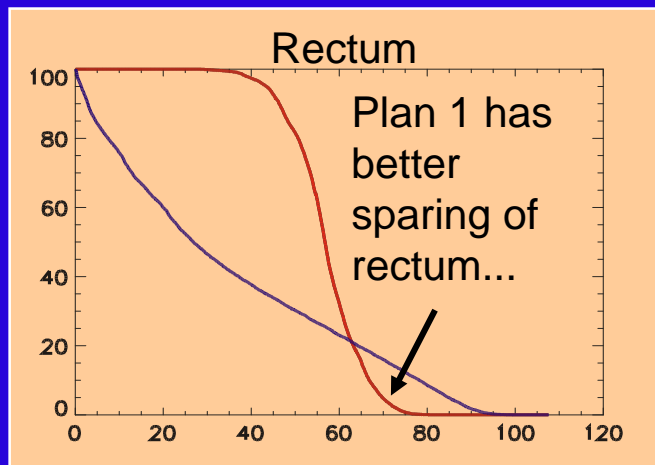
Dose based scoring.

Problems with dose based scoring

Visual assessments
difficult to quantify.

Many, often conflicting
indices required to fully
characterise a plan

E.g.



Dose based scoring.

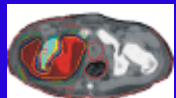
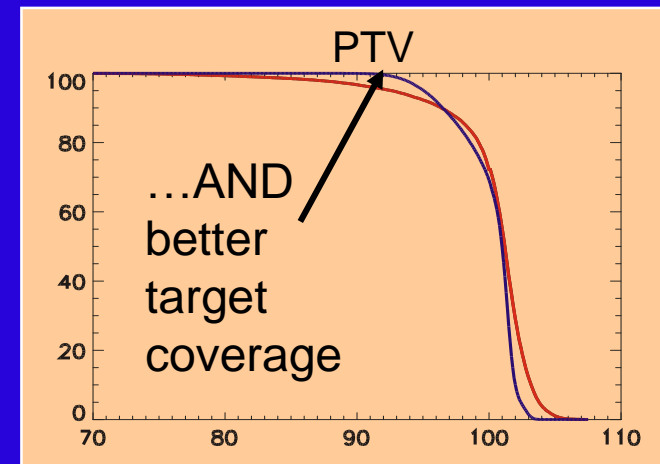
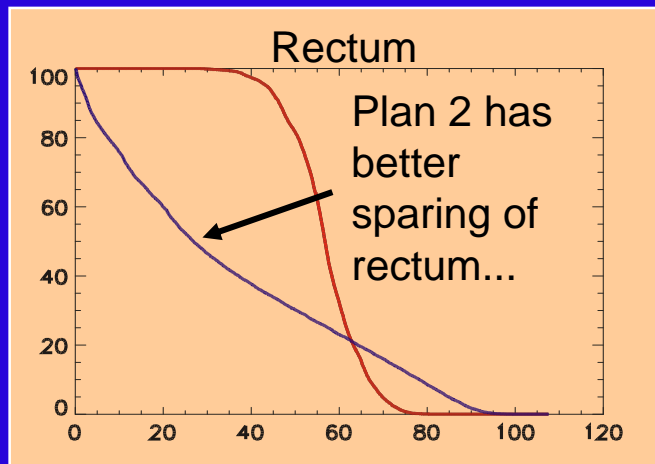
Problems with dose based scoring

Visual assessments
difficult to quantify.

Many, often conflicting
indices required to fully
characterise a plan

Or..

Conflicting indices difficult to resolve
without knowledge of underlying biology

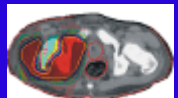


Biological scoring.

Plan scoring based on biological indices

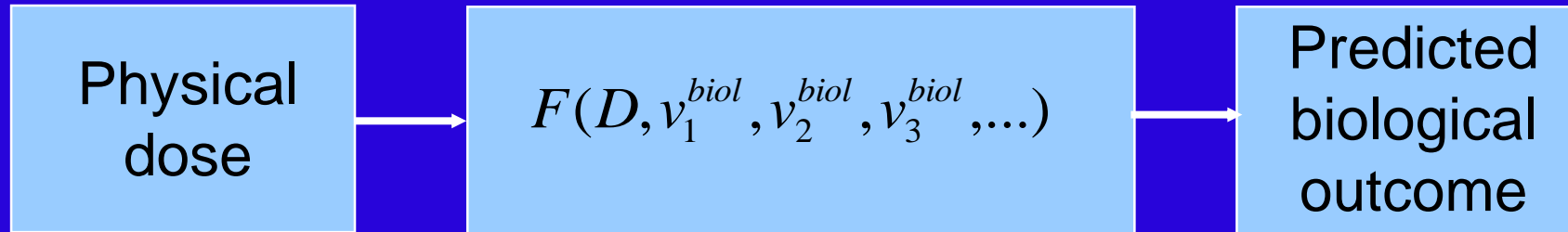
Advantages

1. Clinically relevant scoring function
2. Small number of indices required to characterise plan
3. In theory, can be reduced to single quality figure (weighted combination of tumour control and normal tissue complication probabilities)



Biological models.

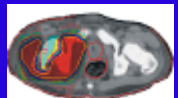
Biological models attempt to transform the physical dose (or DVH) into some biologically relevant end-point. E.g.



Typical biological outcomes

NTCP Normal Tissue Complication
Probability

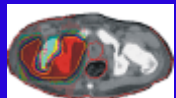
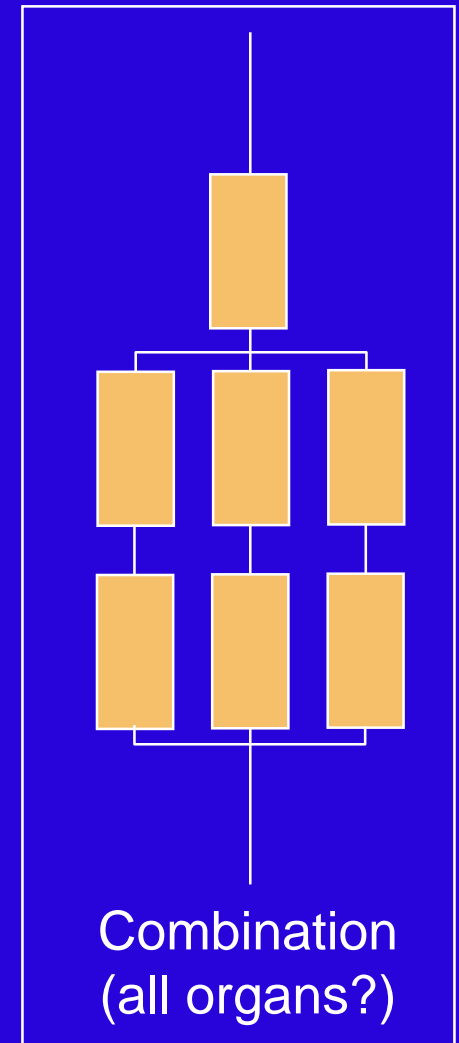
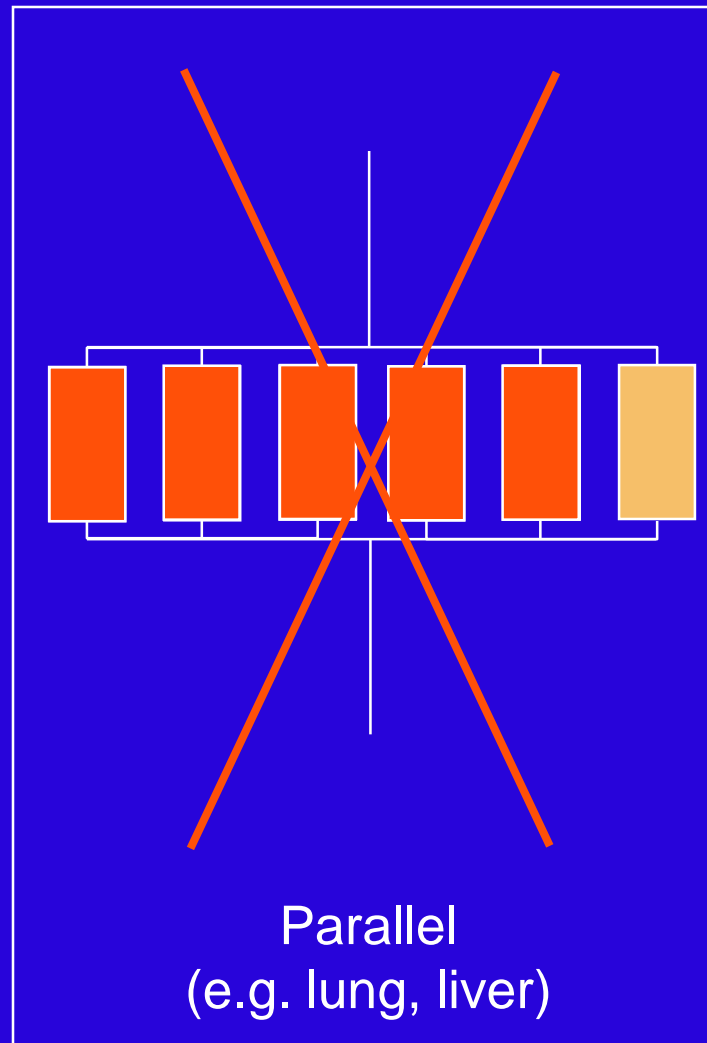
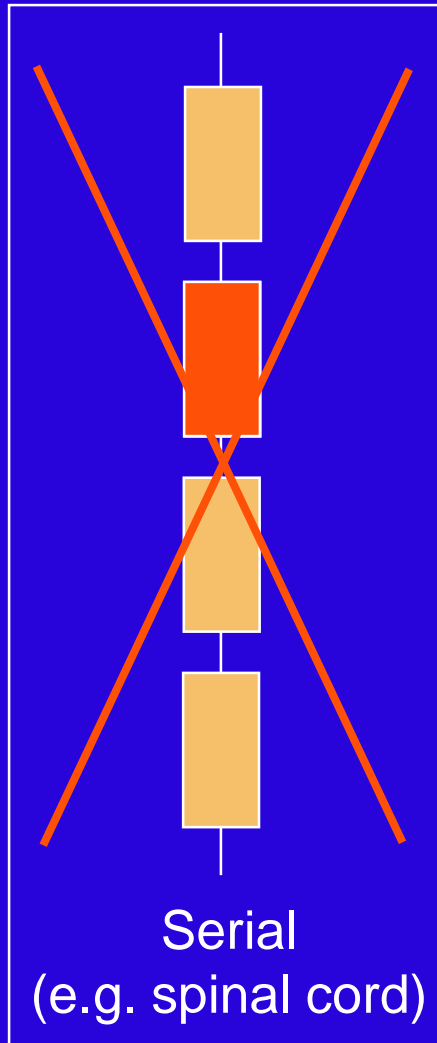
TCP Tumour Control Probability



Biological models.

All models must make some assumptions about tissue architecture

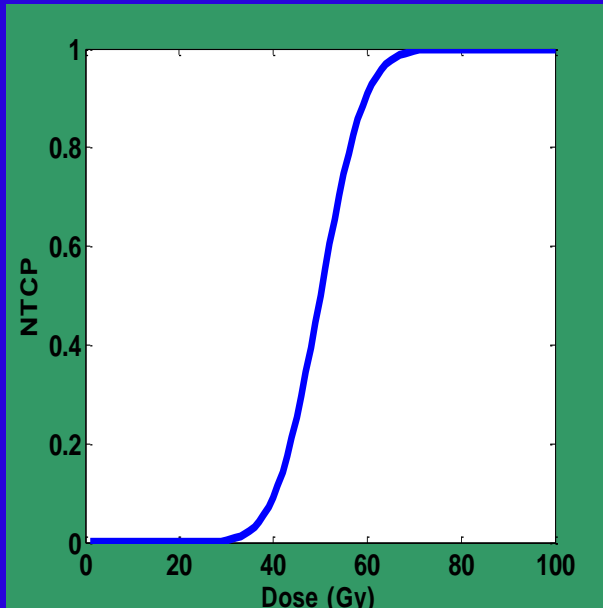
Functional
Sub-unit
(FSU)



Biological models.

E.g. The 'Lyman-Kutcher-Burmann' model for NTCP...

(Lyman LY, Wolbarst B, Int. J. Radiat. Oncol. Biol. Phys, 13:103-109 1987)



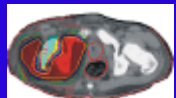
Φ - Probit function

Models the probability of a complication as a sigmoid function

$$NTCP = \Phi(x) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^x \exp(-t^2 / 2) dt$$

Where:

$$x = \frac{D_{eff} - D_{50}}{mD_{50}} \quad \text{and} \quad D_{eff} = \left(\sum_i v_i D_i^{1/n} \right)^n$$



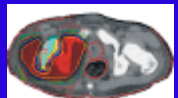
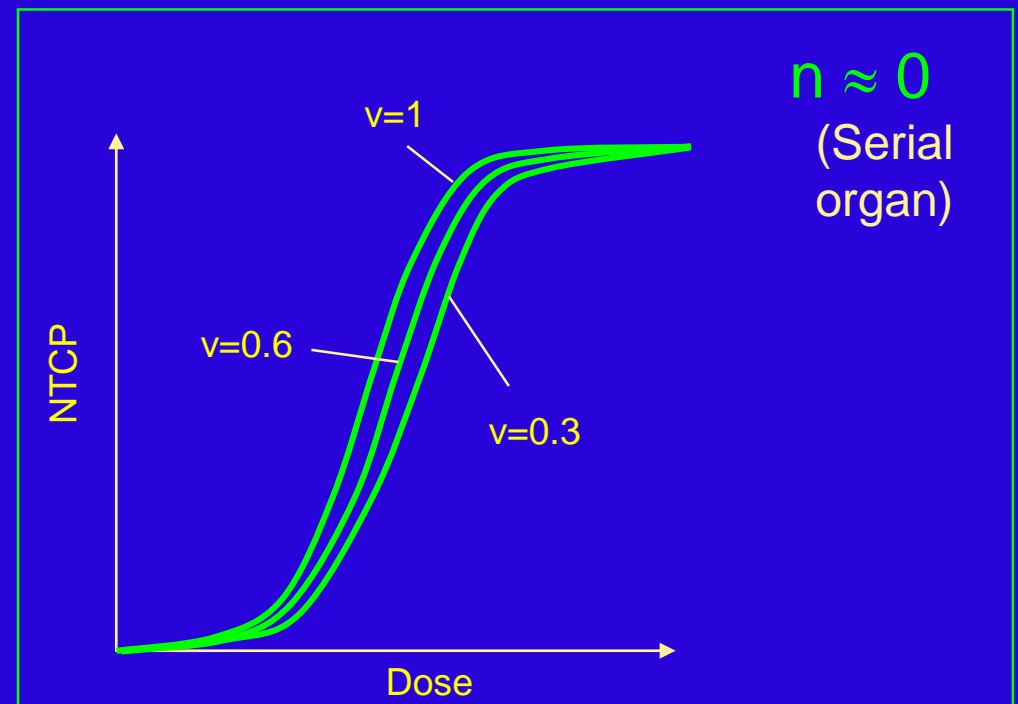
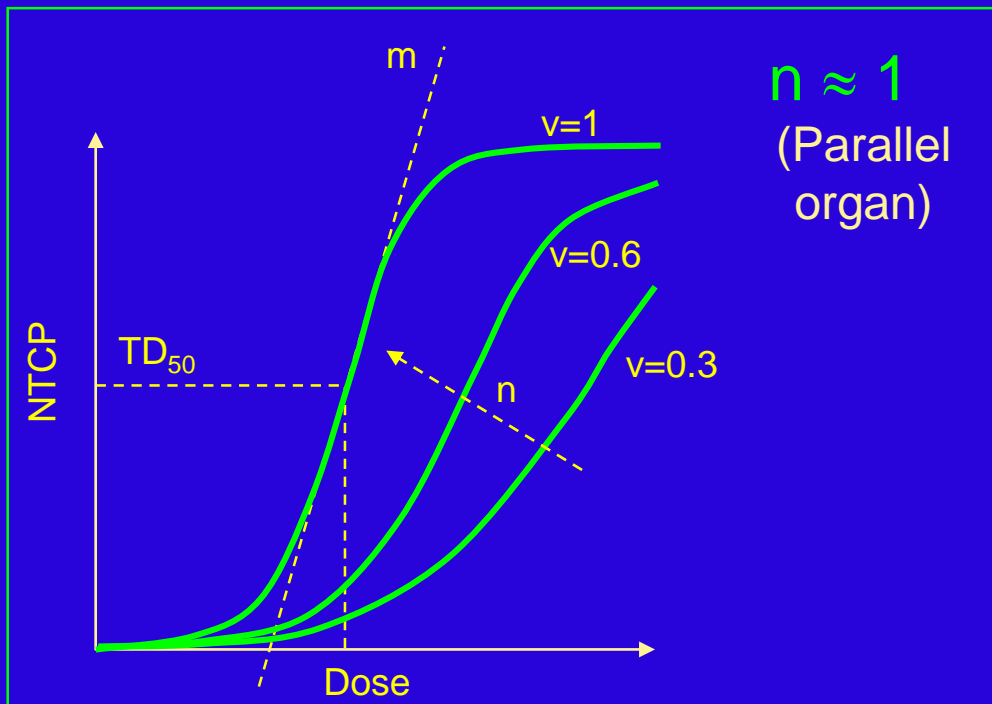
Biological models.

E.g. The 'Lyman-Kutcher-Burmann' model for NTCP...

(Lyman LY, Wolbarst B, Int. J. Radiat. Oncol. Biol. Phys, 13:103-109 1987)

A 3 parameter
'phenomological'
model

- TD_{50} Dose to whole organ resulting in 50% probability of complication
- m Gradient of response curve at TD_{50}
- n 'Volume' parameter



Biological models.

E.G The Equivalent Uniform Dose (EUD) model

(Wu et al, Int. J. Radiat. Oncol. Biol. Phys, 52:224-235, 2002)

$$EUD = \left(\frac{1}{N} \sum_i D_i^a \right)^{\frac{1}{a}}$$

Single parameter model (a) that can be used for both tumours and critical organs

$a = 1$ EUD \equiv mean dose

$|a| \gg 1$ EUD \equiv min/max dose

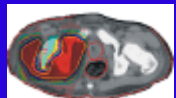
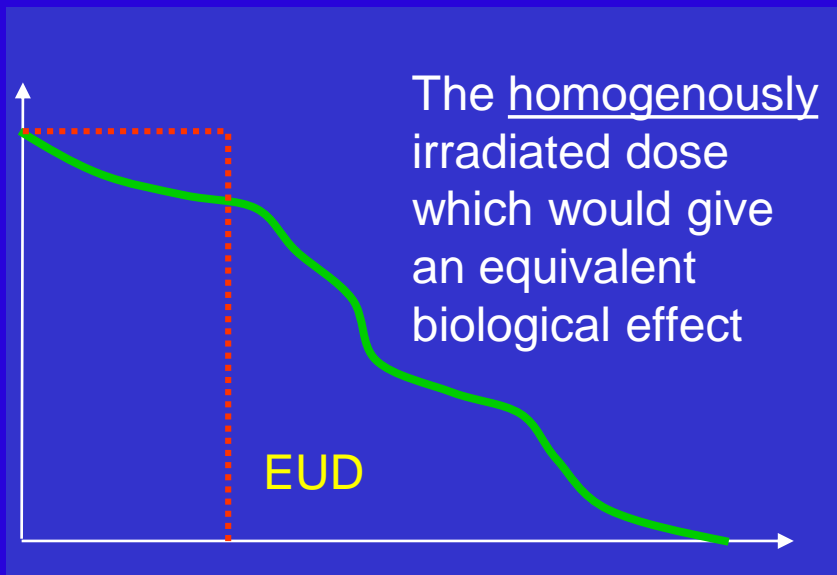
For tumours $\rightarrow a < 0$

For OAR's $\rightarrow a > 0$

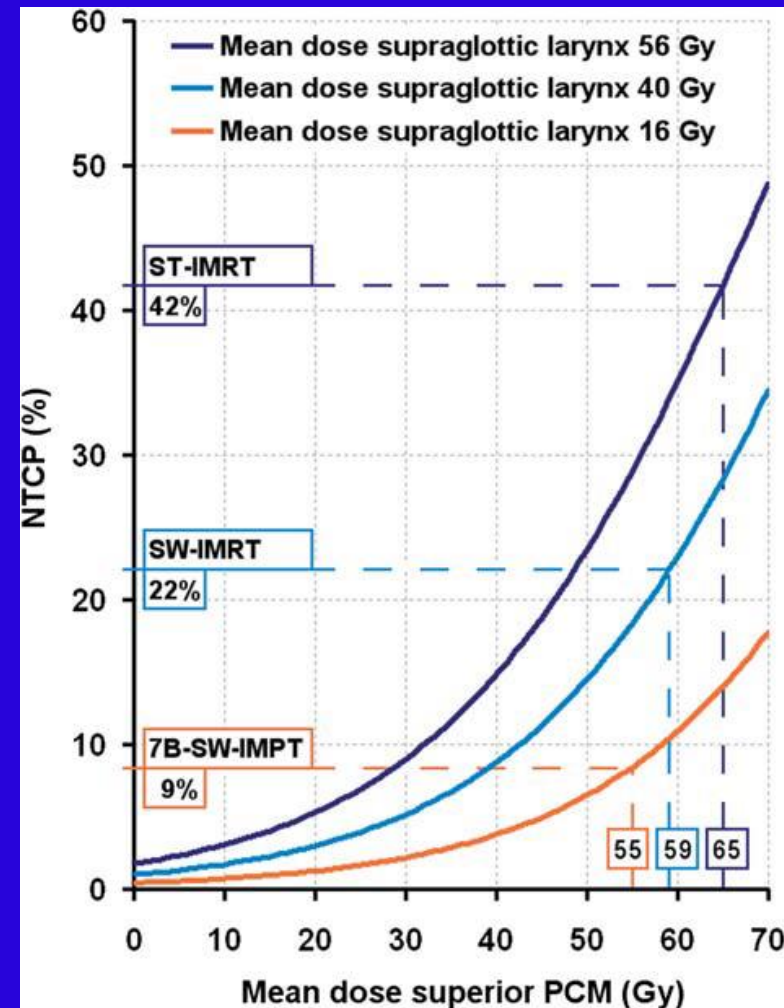
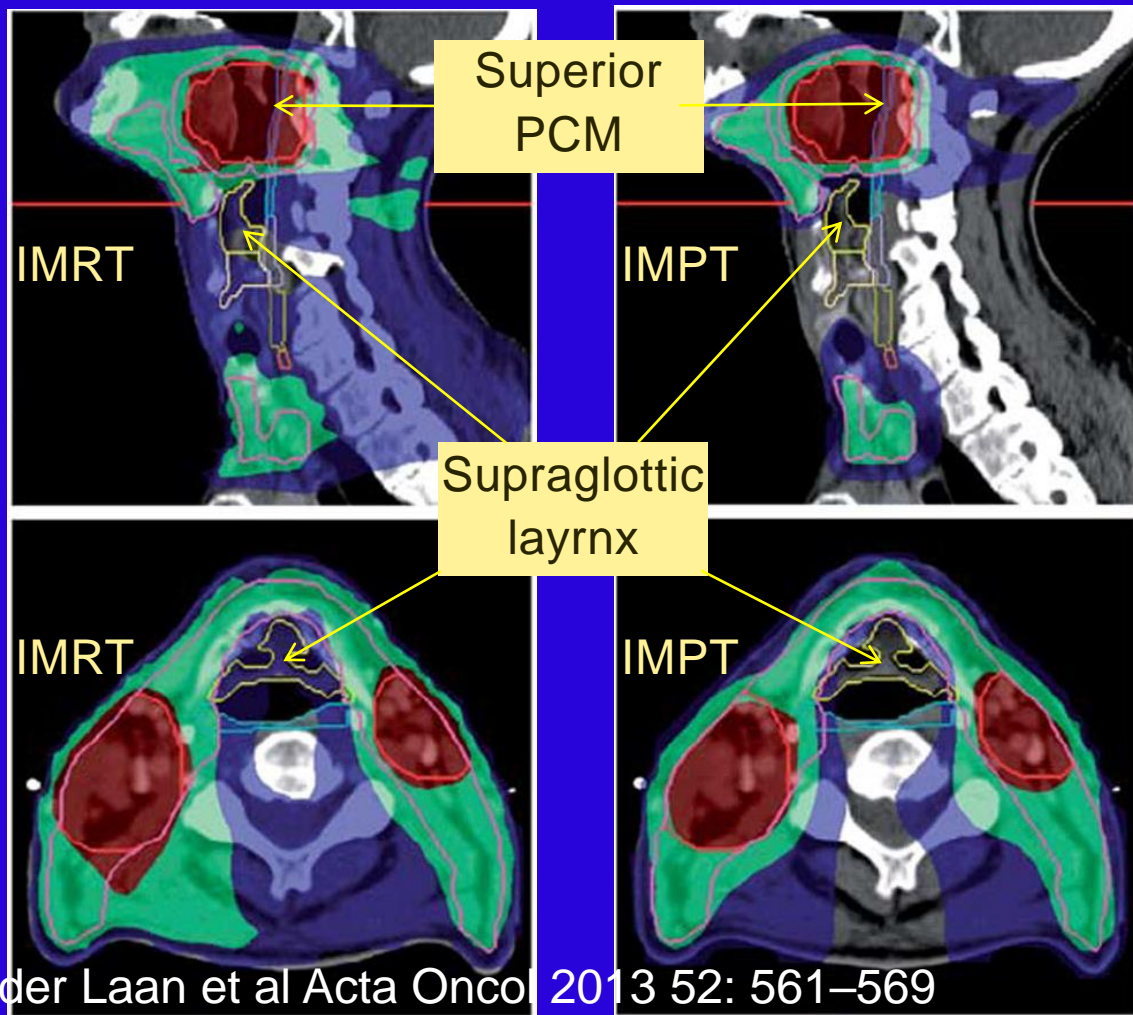
E.g.

Prostate carcinoma $a \approx -10$

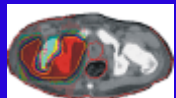
Rectum $a \approx 6$



Biological models. ...or NTCP for dysphagia



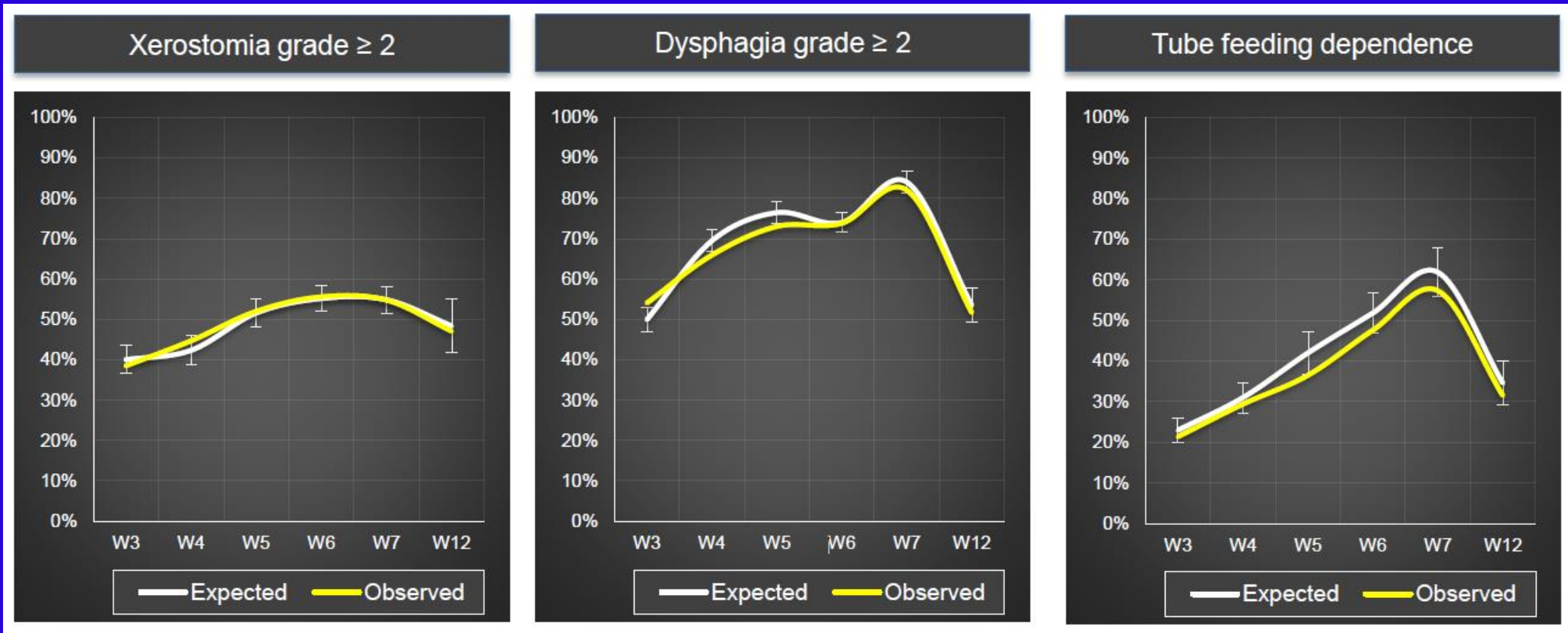
Van der Laan et al Acta Oncol 2013 52: 561–569



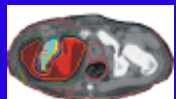
Biological models.

NTCP in practice – Model validation

Predicted and observed toxicity for 126 *photon* patients (VMAT)



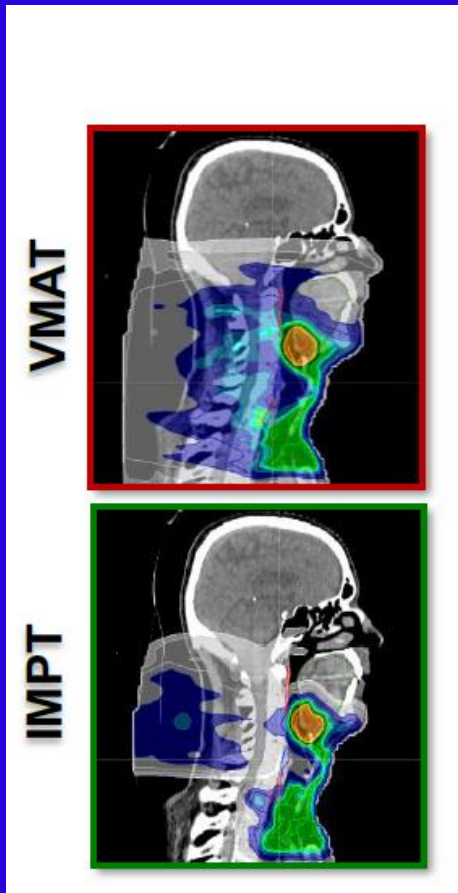
Langendijk, PSI Winterschool 2020



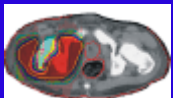
Biological models.

NTCP in practice – Patient selection for proton therapy

Dysphagia NTCP comparison (IMPT vs VMAT)

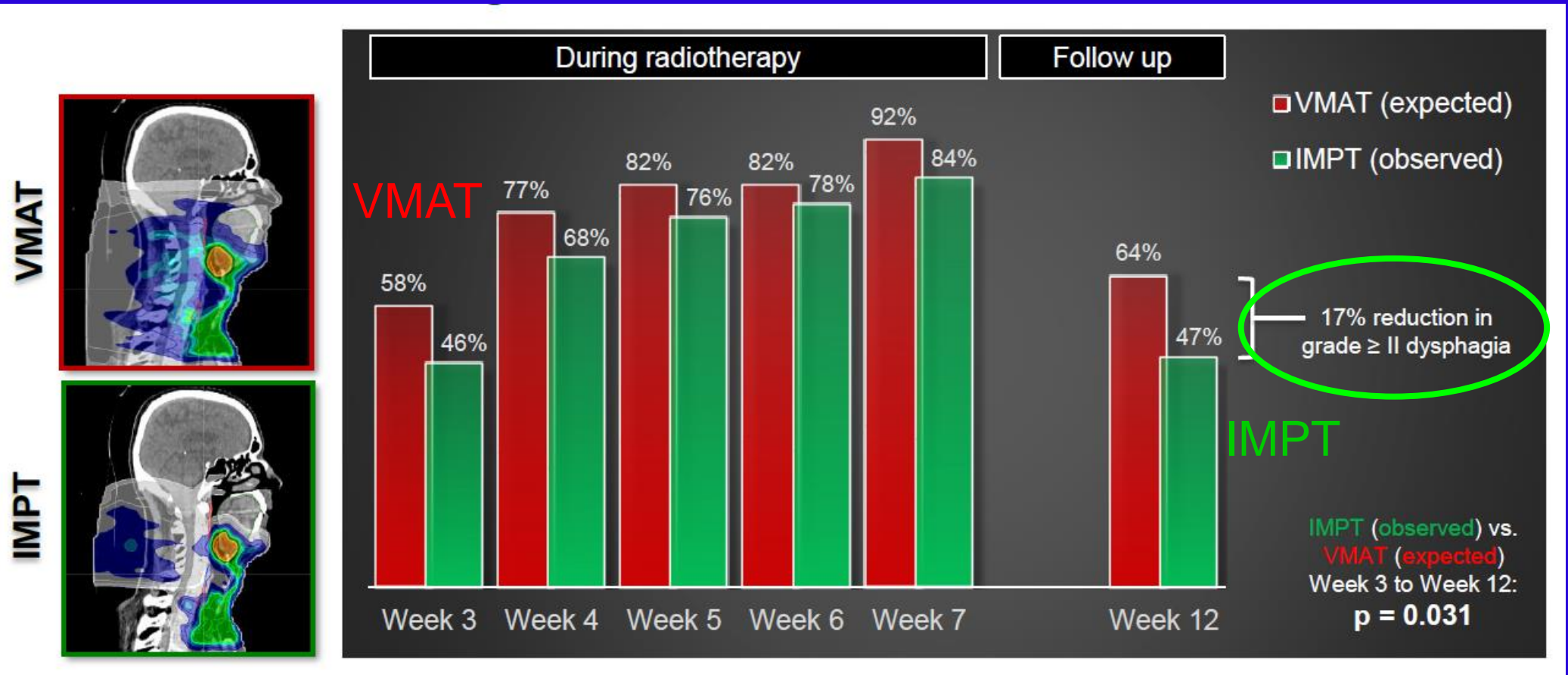


Langendijk, PSI Winterschool 2020

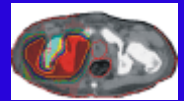


Biological models.

NTCP in practice – Patient selection for proton therapy Dysphagia Observed/NTCP comparison (IMPT vs VMAT)



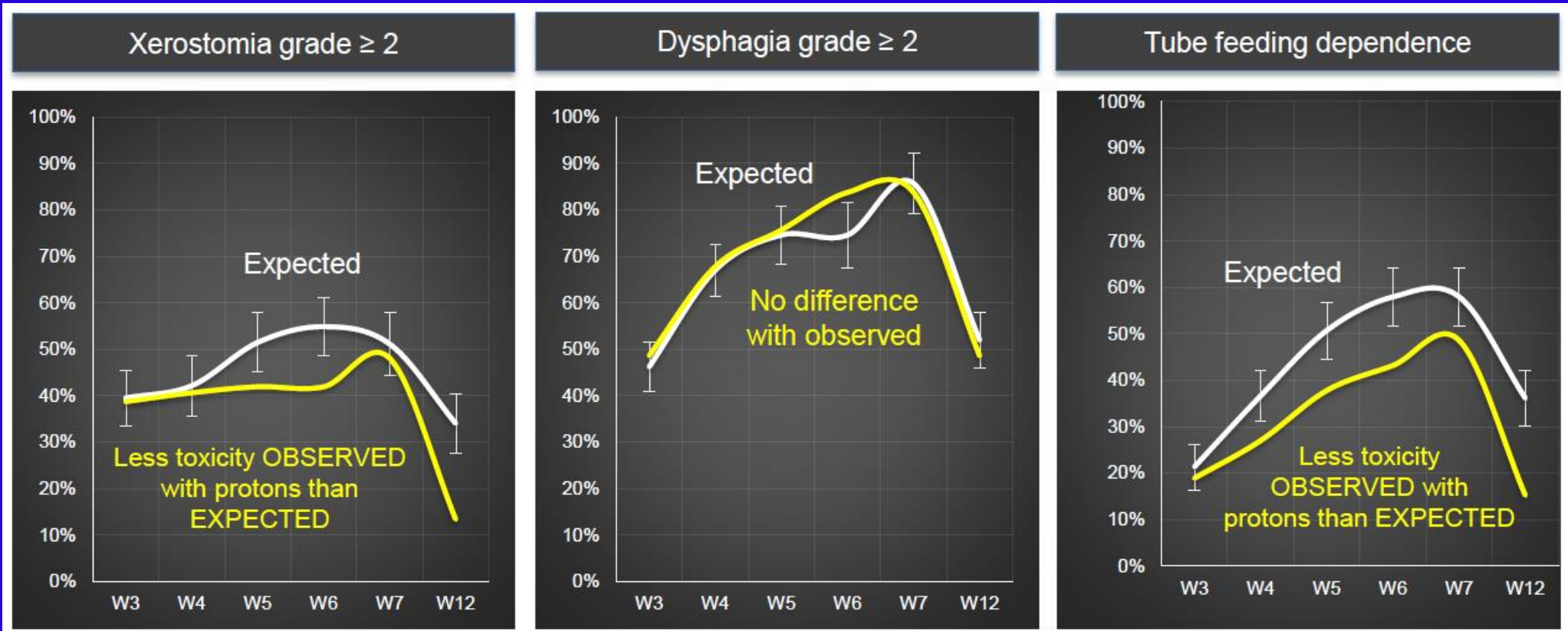
Langendijk, PSI Winterschool 2020



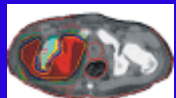
Biological models.

NTCP based patient selection – Does it work?

Predicted and observed toxicities for *proton* patients selected using NTCP



Langendijk, PSI Winterschool 2020

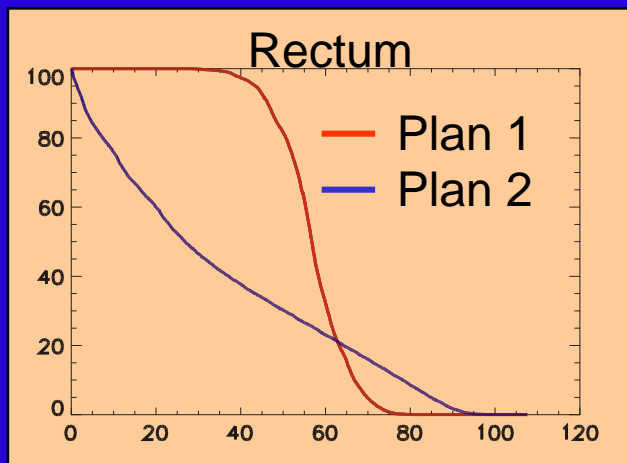


Biological scoring.

Reasons to be cautious.

1. Validity of the biological parameters.

Consider two competing DVHs for the rectum



Apply Lyman's NTCP model with standard volume parameter $n=0.12$ (Emami and Burman)

Plan 1 - 10.4%

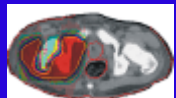
Plan 2 - 24.2%

Apply Lyman's NTCP model with modified volume parameter $n=0.2$

Plan 1 - 8.4%

Plan 2 - 7.1%

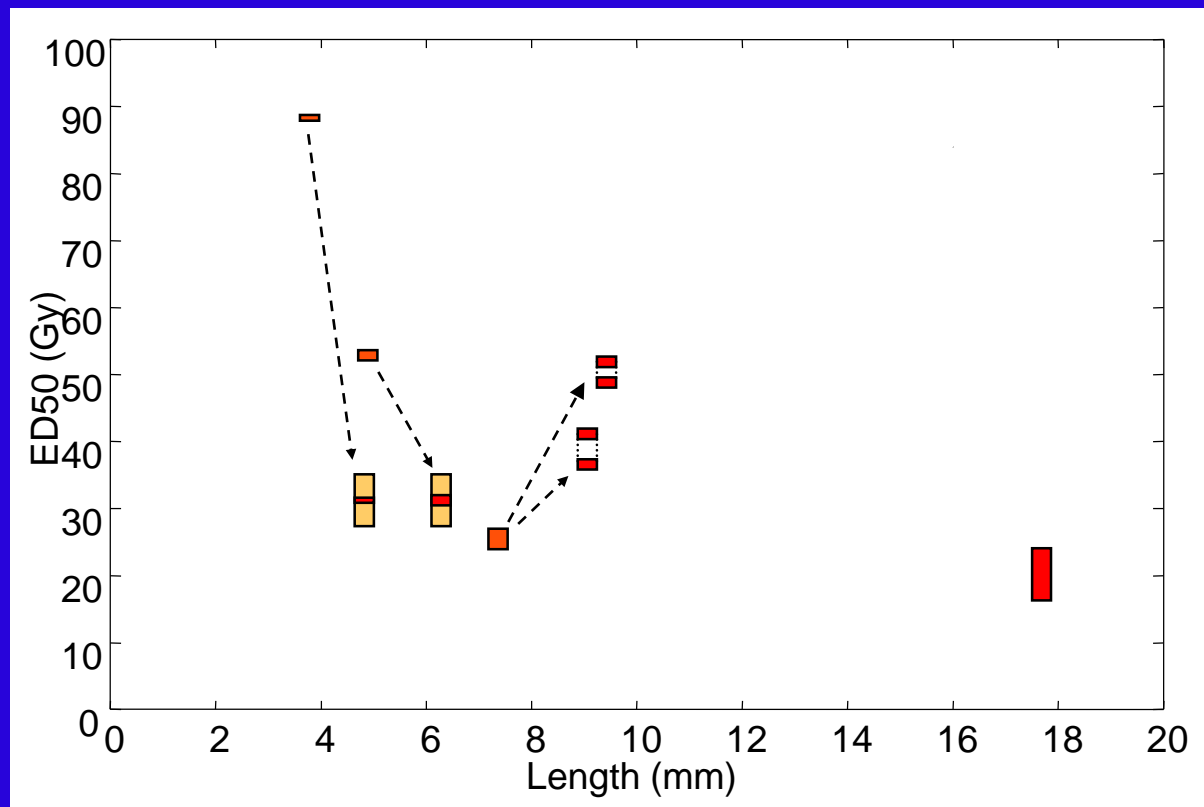
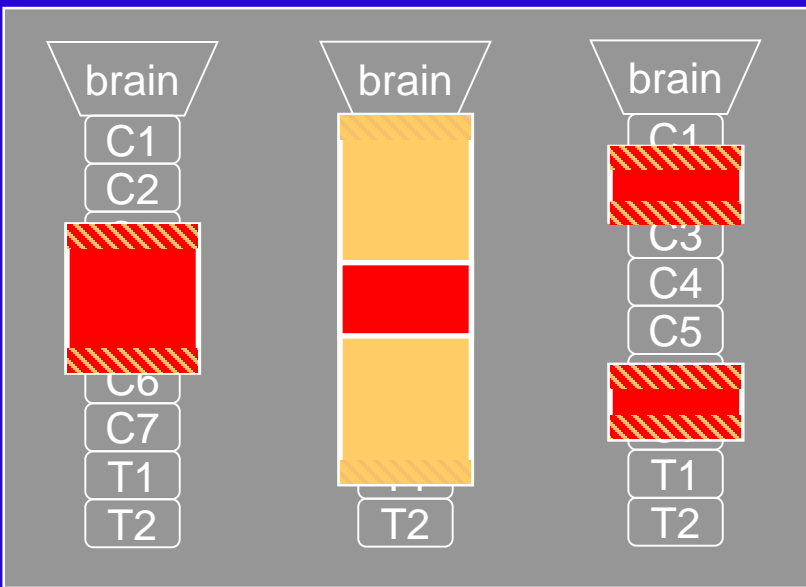
Ranking of plan changes for even a moderate change of a single input parameter



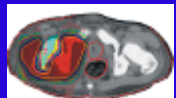
Biological scoring.

Reasons to be cautious.

2. Know your organ – Is the spinal cord serial?

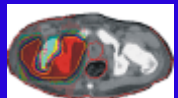


van Luijk et al 2005, IJROBP, 61:892-900



Overview

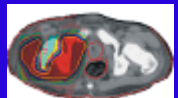
1. Displaying and interpreting dose distributions
2. Scoring and evaluating plans
3. Summary



Summary 1.

Visual assessment of dose distributions

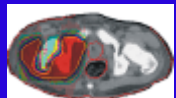
- The most direct and informative representation of a treatment plan available - however....
- 3-D dose distributions are large, cumbersome and difficult to analyse quantitatively
- User interactivity is essential to extract the most information from dose distributions (slice selection/multi slice display, dose banding, dose querying etc).



Summary 2.

Dose volume histograms

- Provide a succinct and quantitative method of representing 3-d dose within selected VOI's - however...
- DVH's should only be used in conjunction with careful visual analysis of 3-d dose distributions
- In particular, care should be taken when analysing large volumes using DVH's
- DVH's should always be assessed in conjunction with dose-volume statistics.



Summary 3.

Plan scoring.

- Dose based assessment is the 'gold standard', but can be difficult to quantify
- Biological scores give succinct results, but must always be interpreted with great caution – interesting research area though!

