To promote excellency in patient care and innovative proton treatment

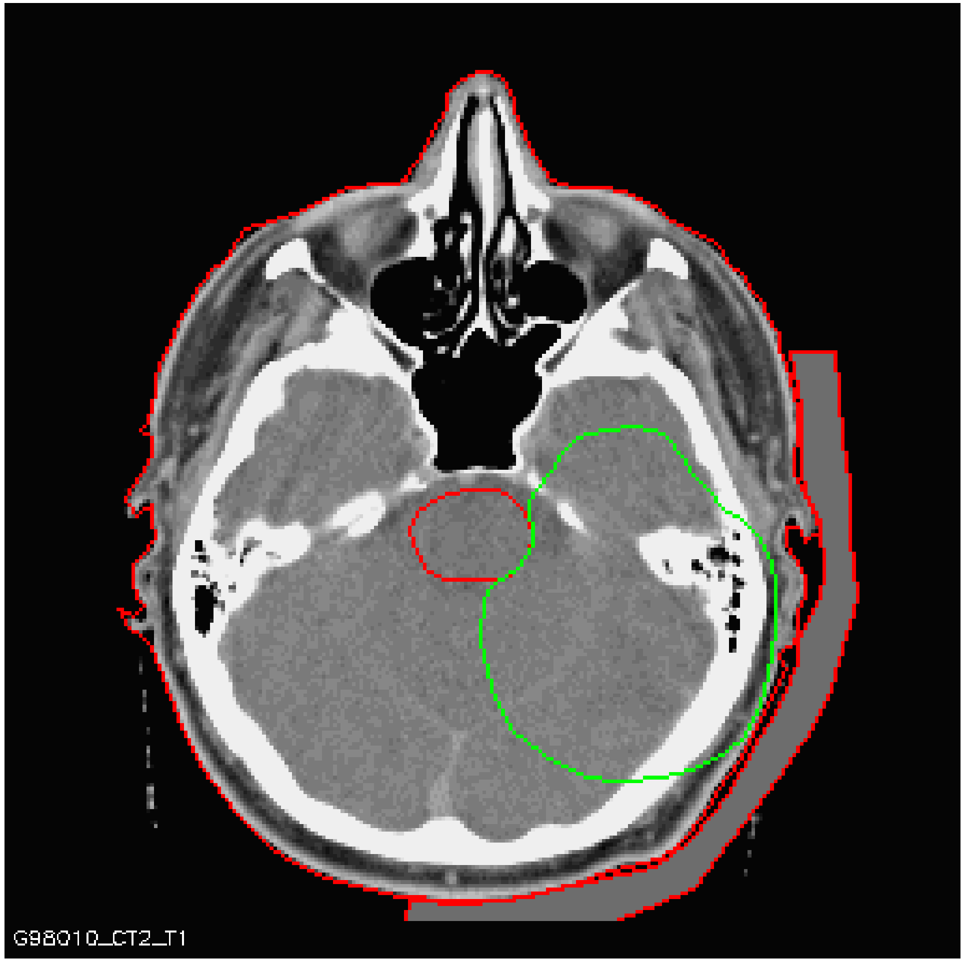
Paul Scherrer Institut
A.Bolsi, F. Albertini, A. J. Lomax

Intensity Modulated Proton Therapy

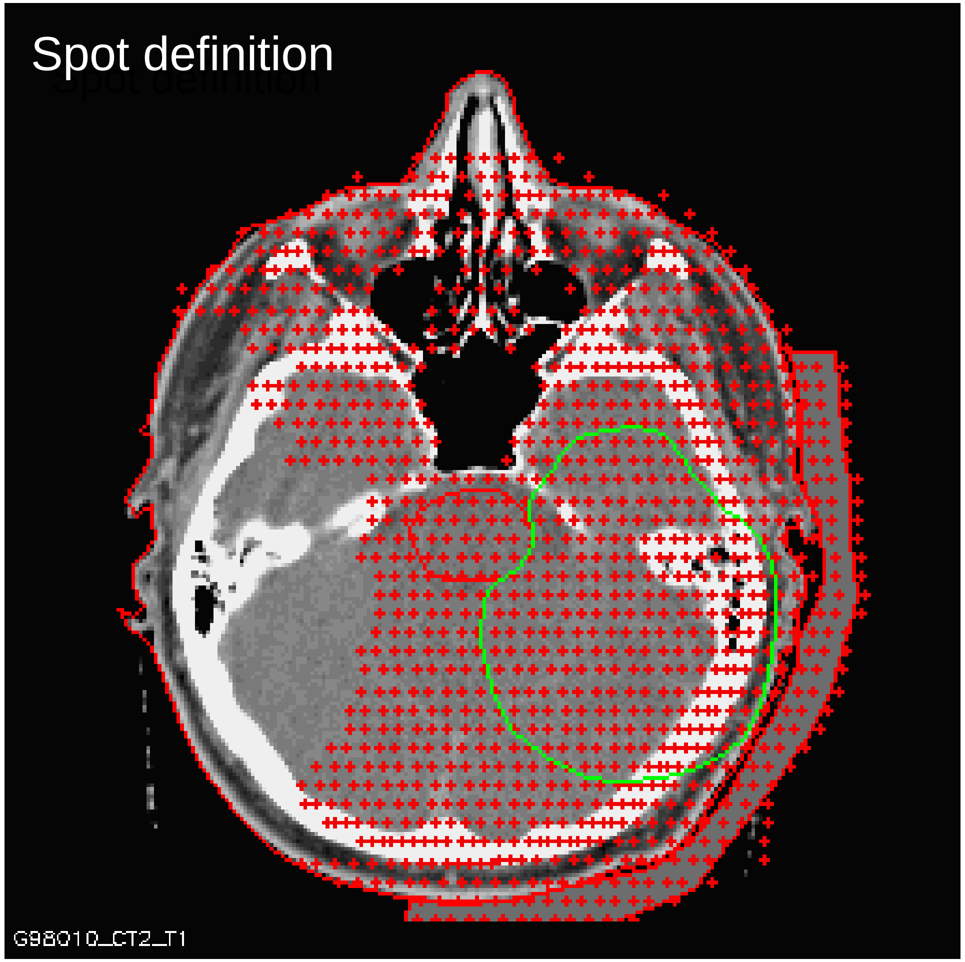
Outlook

1. Introduction (SFUD vs IMPT)
2. Positioning uncertainty
3. Range uncertainty
4. Possible solutions
5. Summary

Optimization process: in practice

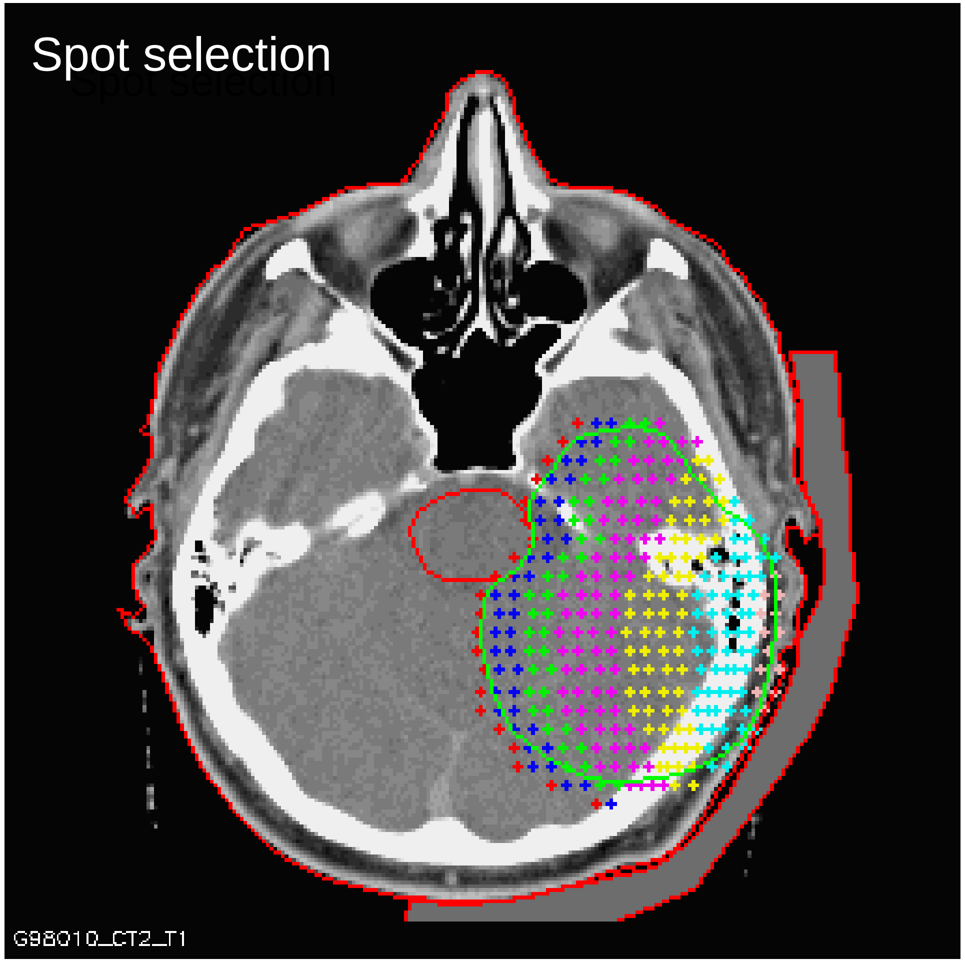


Scheib, ETH Diss 10451, 1993



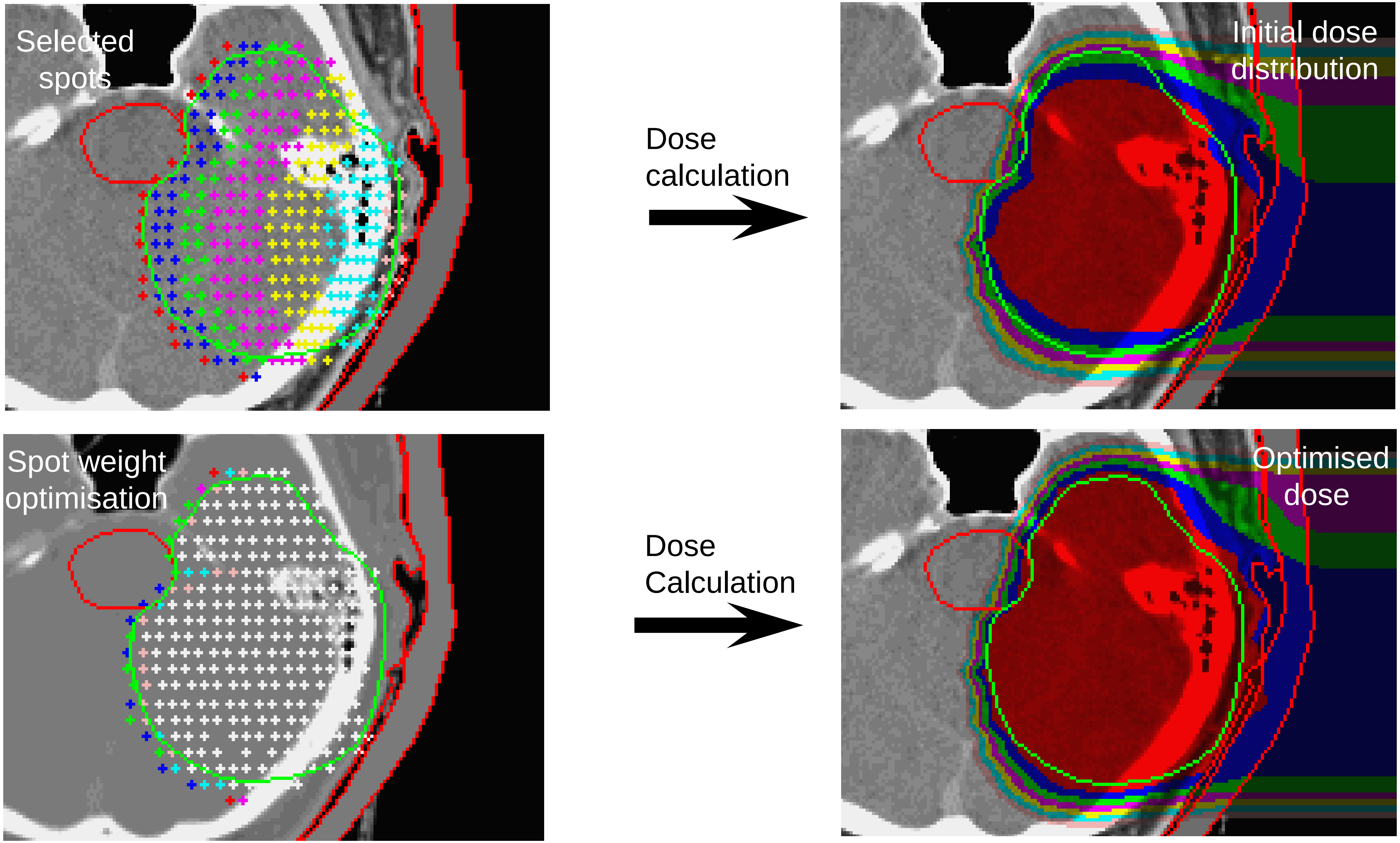
Incident field

Scheib, ETH Diss 10451, 1993



Incident field

Scheib, ETH Diss 10451, 1993


Selected spots
Dose calculation
Initial dose distribution
Spot weight optimisation
Dose Calculation
Optimised dose

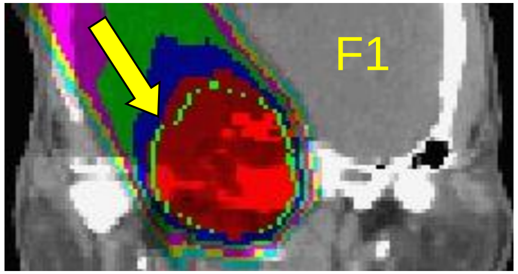
Single field, uniform dose (SFUD*) planning

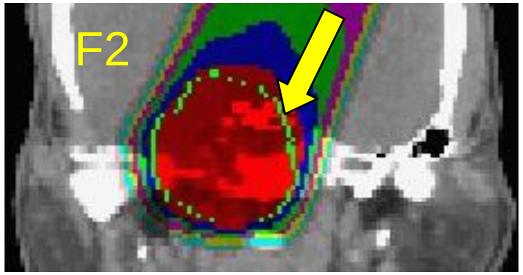
The combination of individually optimized fields, each of which deliver a (more or less) homogenous dose across the target volume

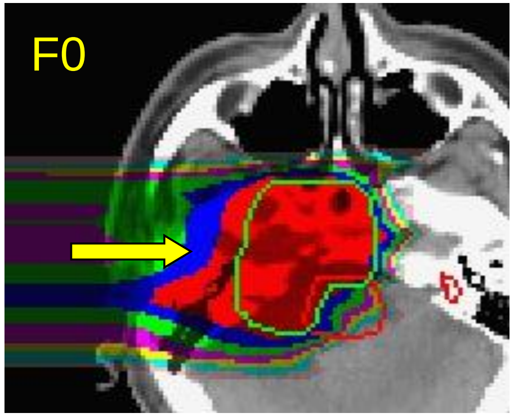
SFUD is the spot scanning equivalent of treating with ‘open’ fields.

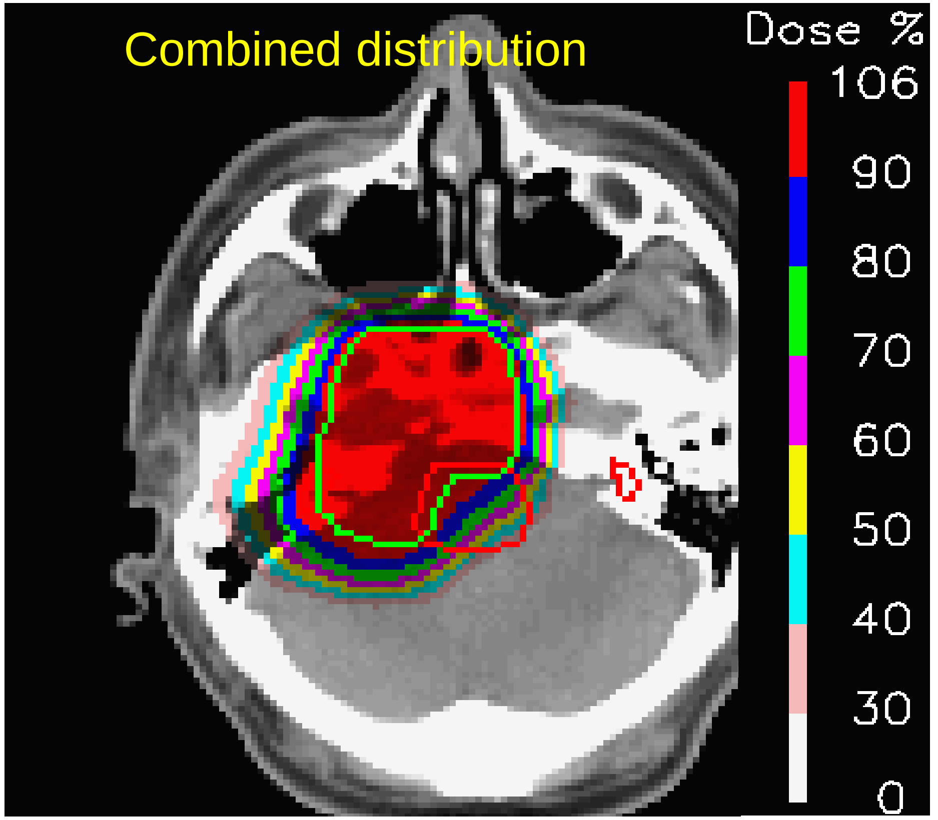
* Lomax AJ (2007) in ‘Proton and charged particle Radiotherapy’, Lippincott, Williams and Wilkins

An example SFUD plan









Note, each individual field is homogenous across the target volume

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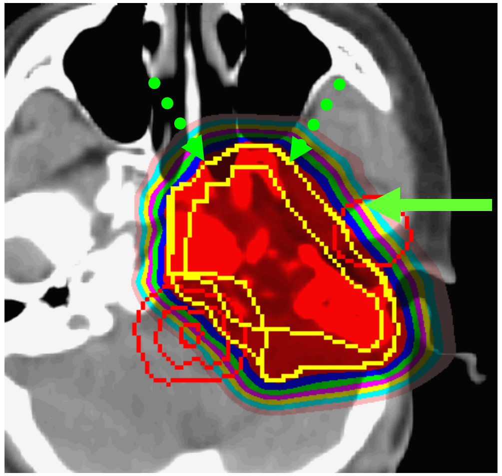
An example SFUD treatment

1st series (0-40 Gy (RBE))

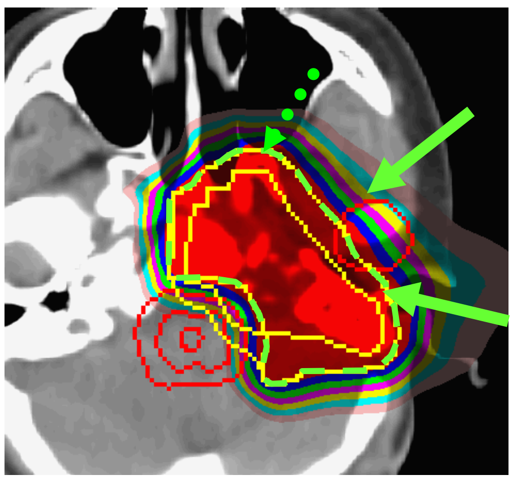
3 field SFUD plan to PTV



+

2nd series (40-74 Gy (RBE))

3 field SFUD plan to ‘TechPTV’



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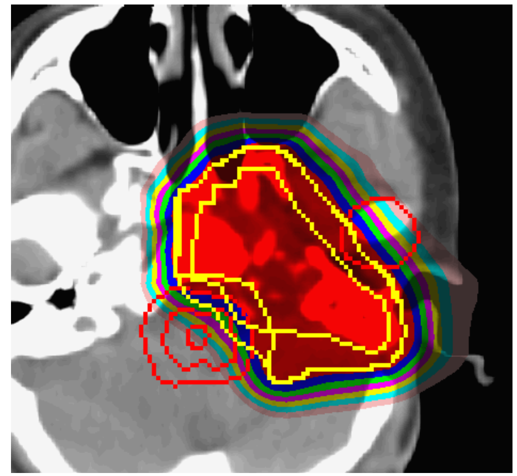

Full treatment

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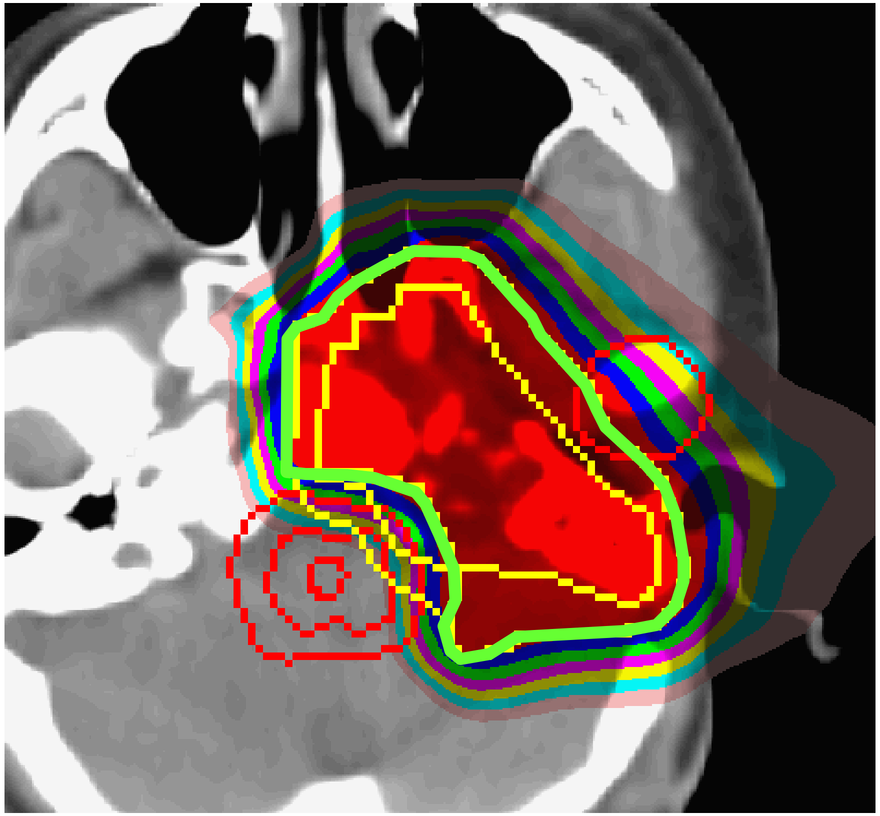
The TechPTV or ‘Virtual 3d block’



In order to carve-out dose to neighbouring critical structures, need to be able to ‘block’ out dose

Modified target volume used to define ‘Virtual 3d blocks’

Currently, such volumes are defined manually on a slice-by-slice basis

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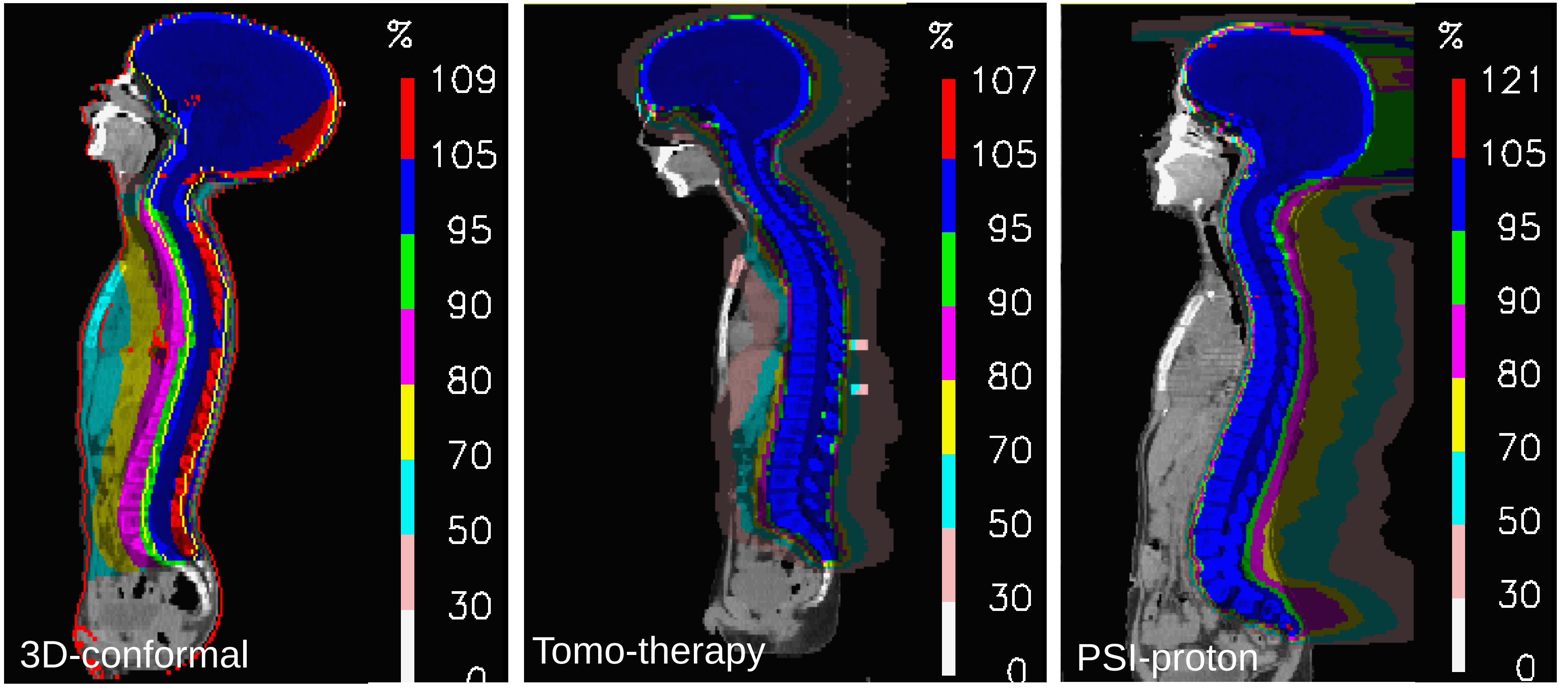
Example of SFUD plans delivered at PSI

Pediatric Proton Therapy: craniospinal axes irradiation



Newhauser et al. The risk of developing a second cancer after receiving craniospinal proton irradiation.PMB 2009

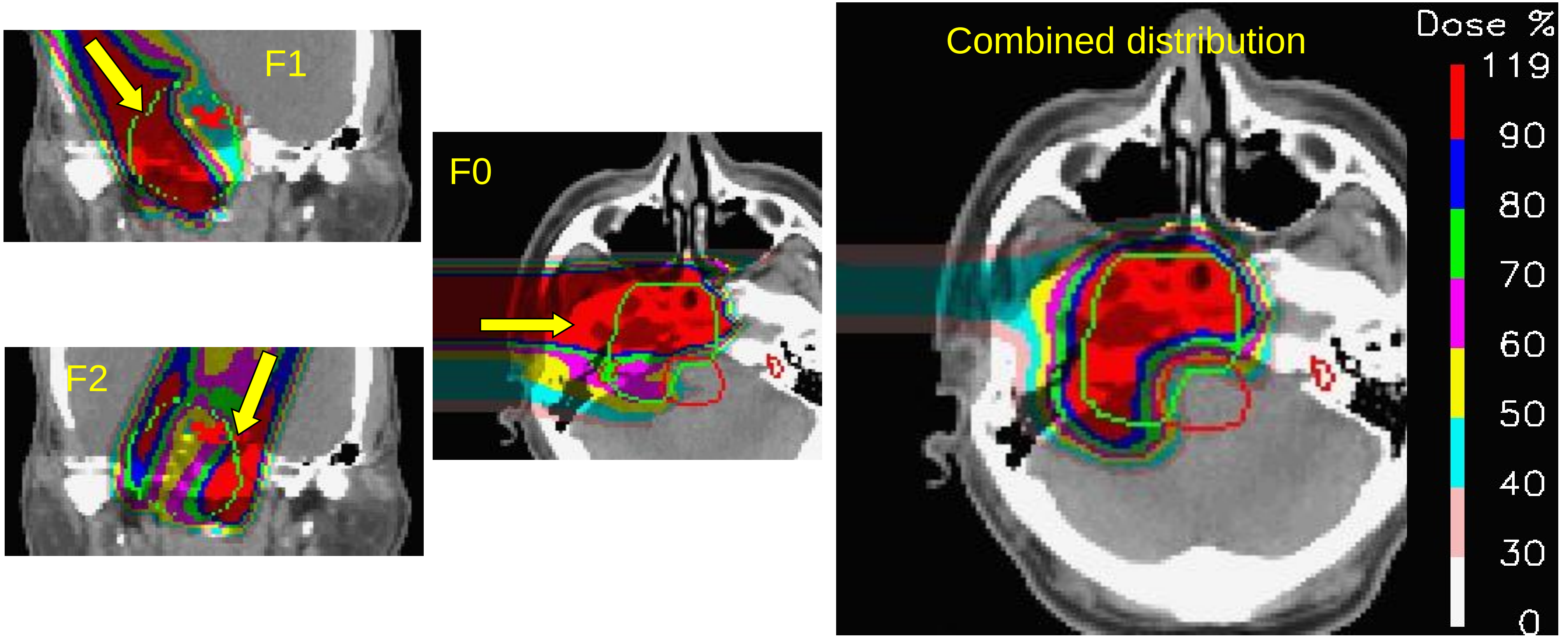
Intensity Modulated Proton Therapy (IMPT*)

The simultaneous optimisation of all Bragg peaks from all fields (with or without additional dose constraints to neighbouring critical structures)

IMPT is the spot scanning equivalent of IMRT (and field patching for passive scattering proton therapy).

***Lomax PMB 1999**

An example IMPT plan



Note, each individual field is highly in-homogenous (in dose) across the target volume (c.f. SFUD plans)

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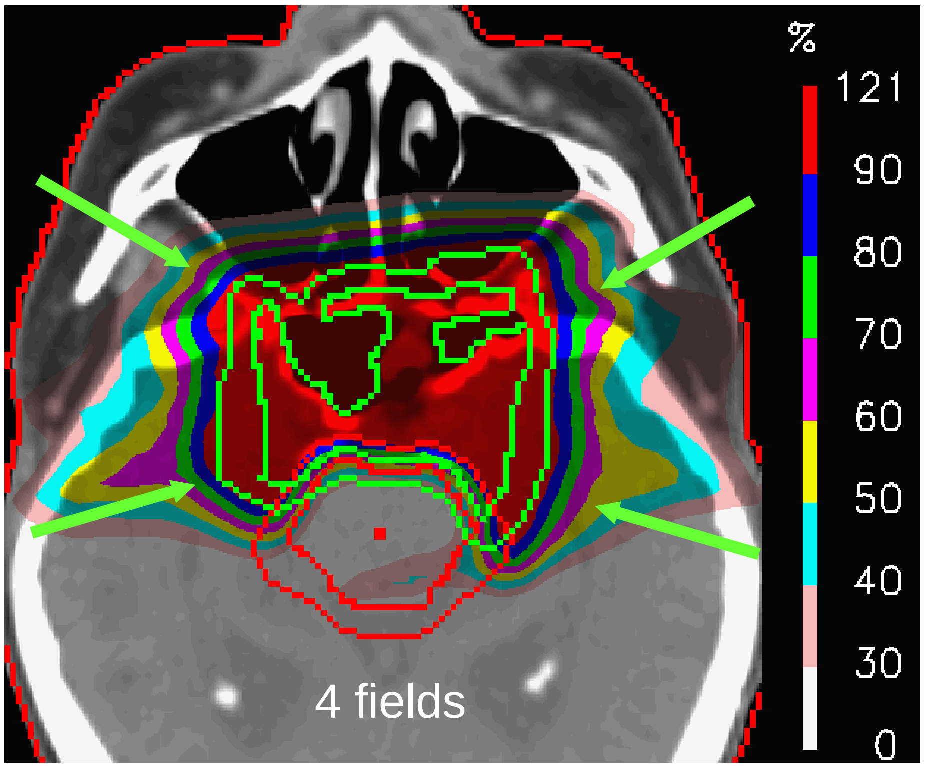
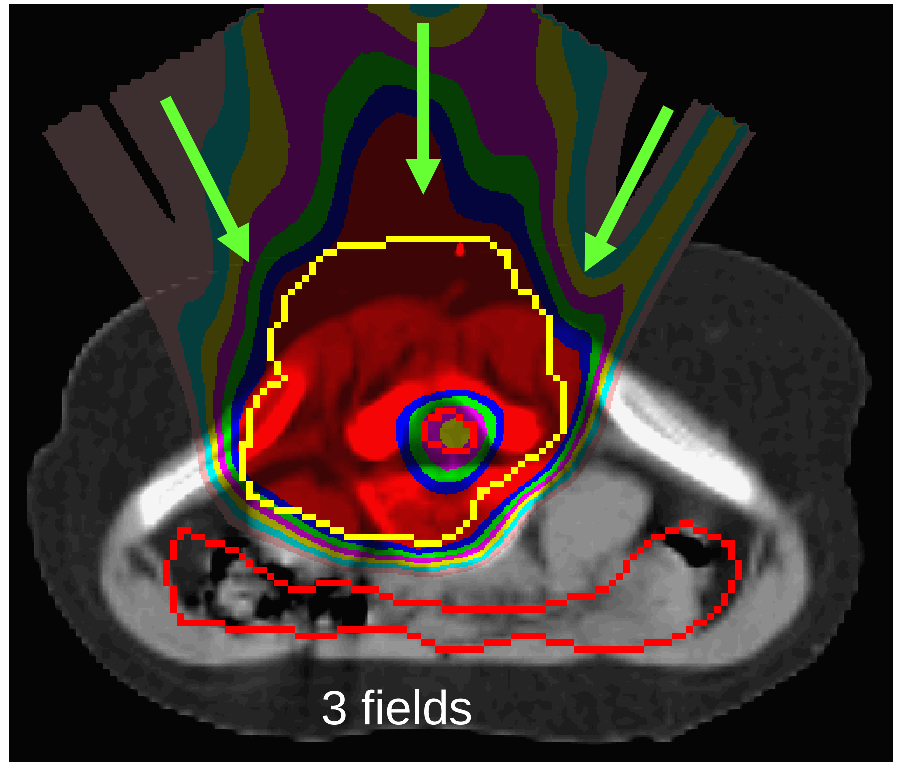
Example clinical IMPT plans delivered at PSI

Skull-base chordoma



3 field IMPT plan to an 8 year old boy



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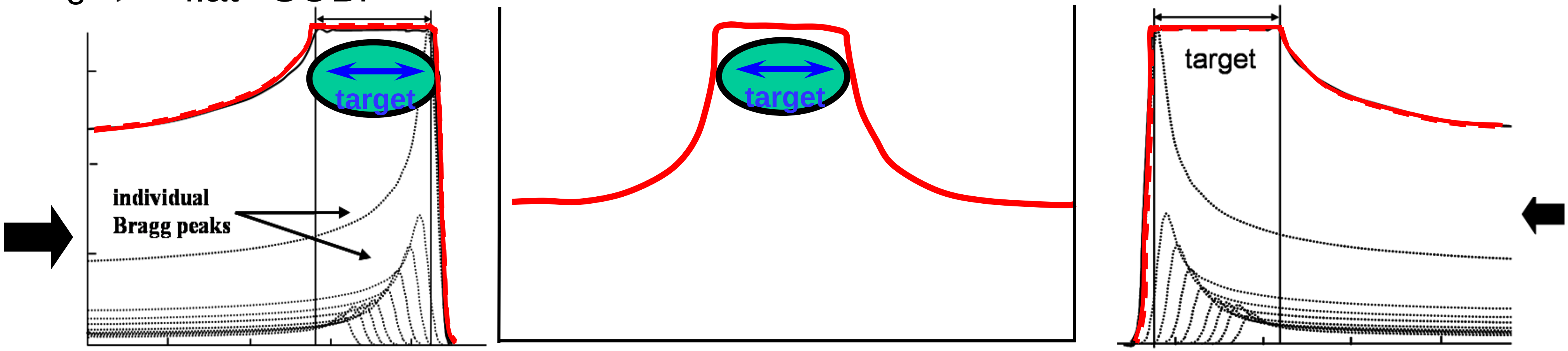
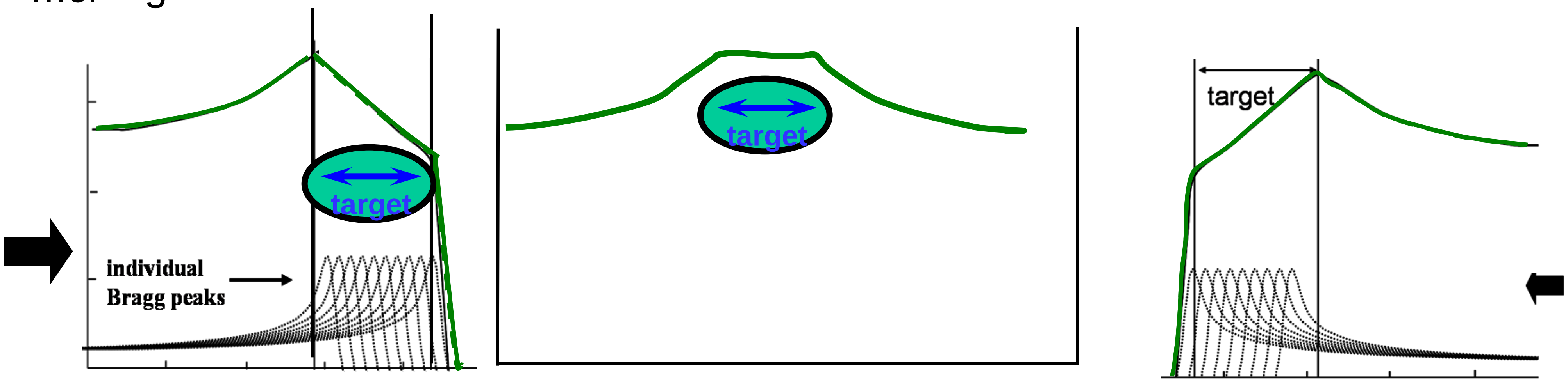
There's more than one way to optimize an IMPT plan…

E.g., "flat" SOBP



…or "gradient" SOBP

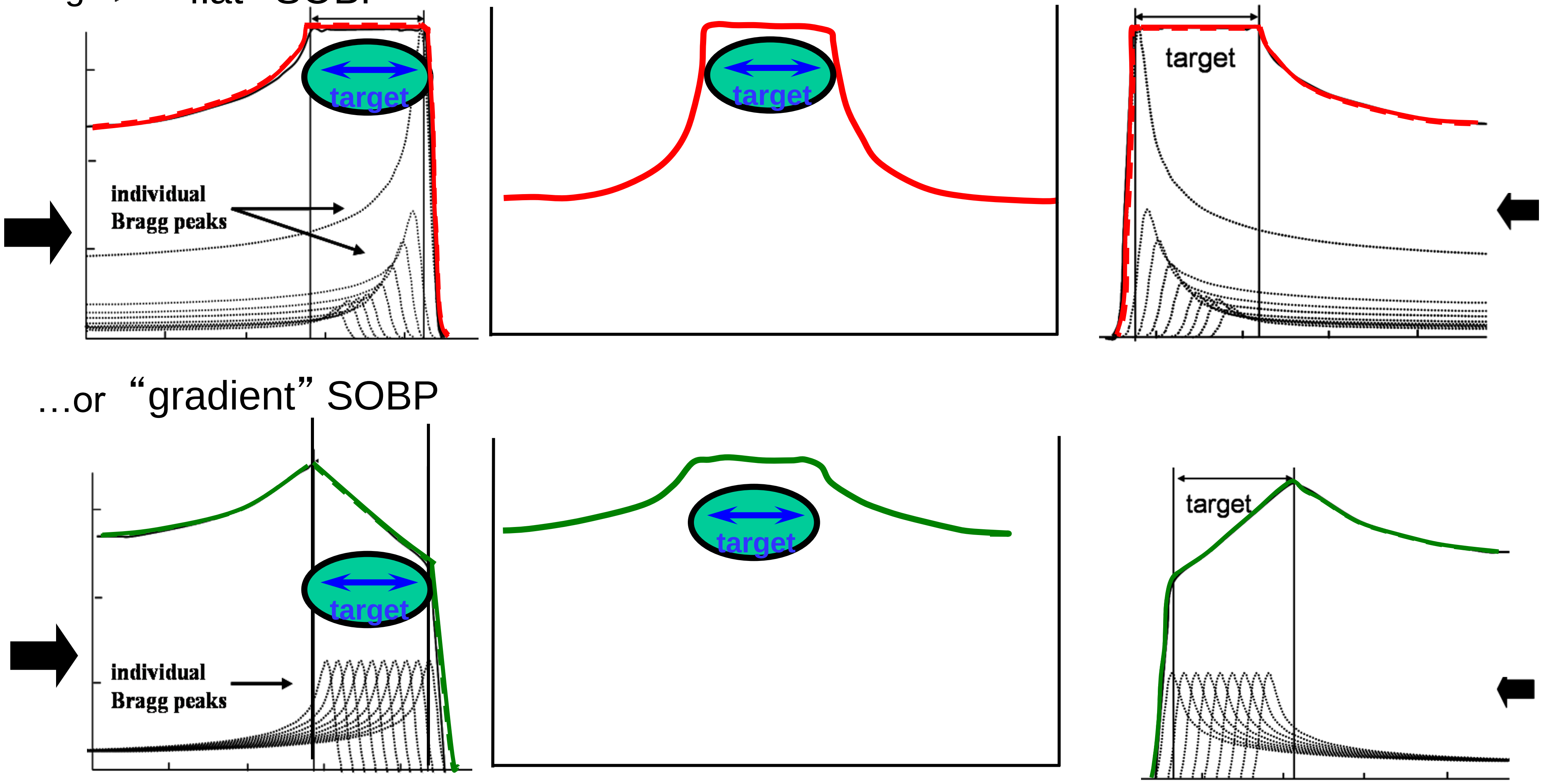


Albertini IJROBP 2007 & PMB 2010

There's more than one way to optimize an IMPT plan …(ex. 1)

E.g. "flat" SOBP

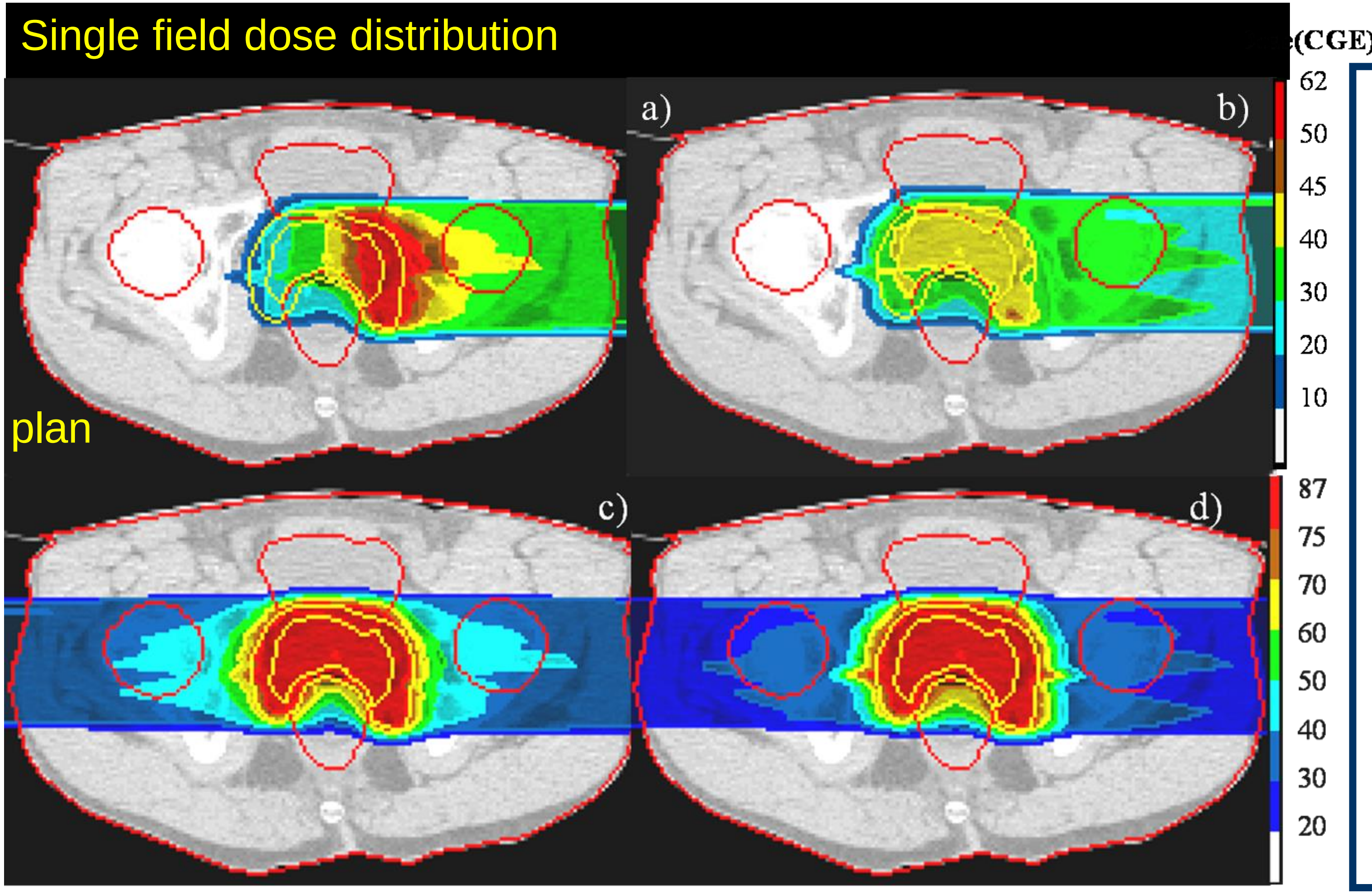
…or "gradient" SOBP



Albertini IJROBP 2007 & PMB 2010

There's more than one way to optimize an IMPT plan…(ex. 1)

'Gradient' SOBP — Flat SOBP



Very similar PTV coverage but with significantly higher dose in entrance region for 'Gradient' SOBP

This can be an 'invisible' consequence of the starting conditions used for the optimization

Albertini, Hug & Lomax 2007, IJROBP

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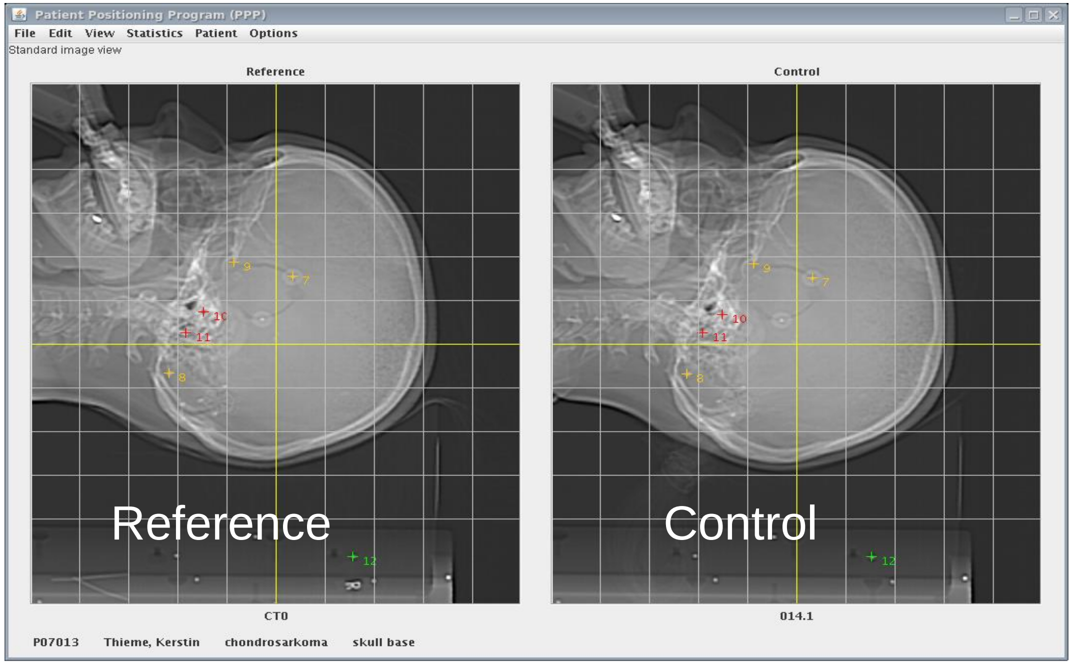
Daily positioning at PSI



Daily pre-treatment positioning at CT

- Horizontal and vertical scouts

  Compared against reference scouts (from treatment planning CT series).

  No axial CT scan acquired

  Online matching of anatomical landmarks

  → Semi-automatically and/or manually

  → Offsets for table coordinates at Gantry (translations only)

  → Linked to Gantry Control System (via PatBase “R&V” interface)

- Software developed in-house (“PPV”)

Bolsi et al IJROBP 2008 *Experiences at the PSI with a remote patient positioning procedure for high-throughput proton radiation therapy*

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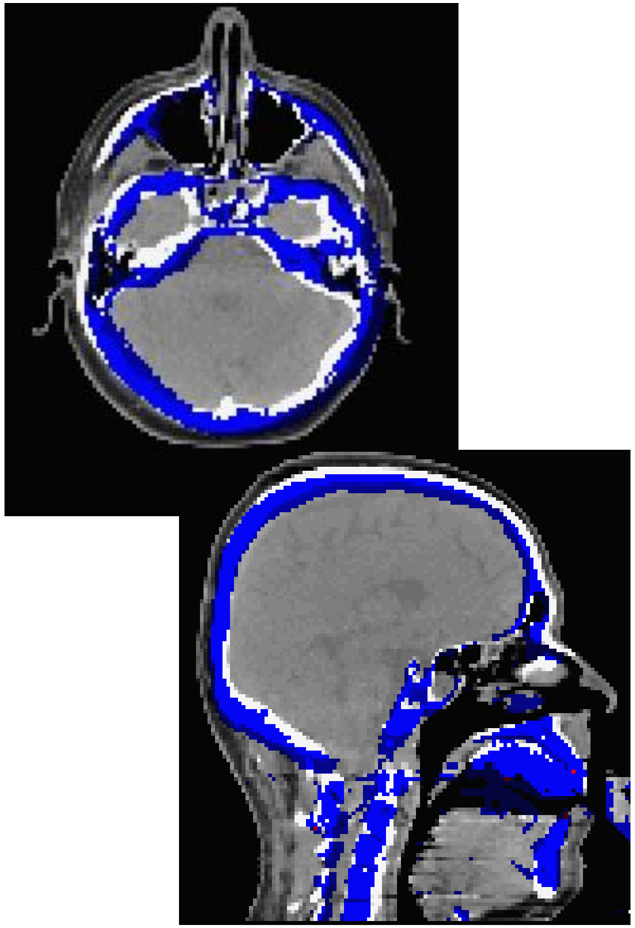
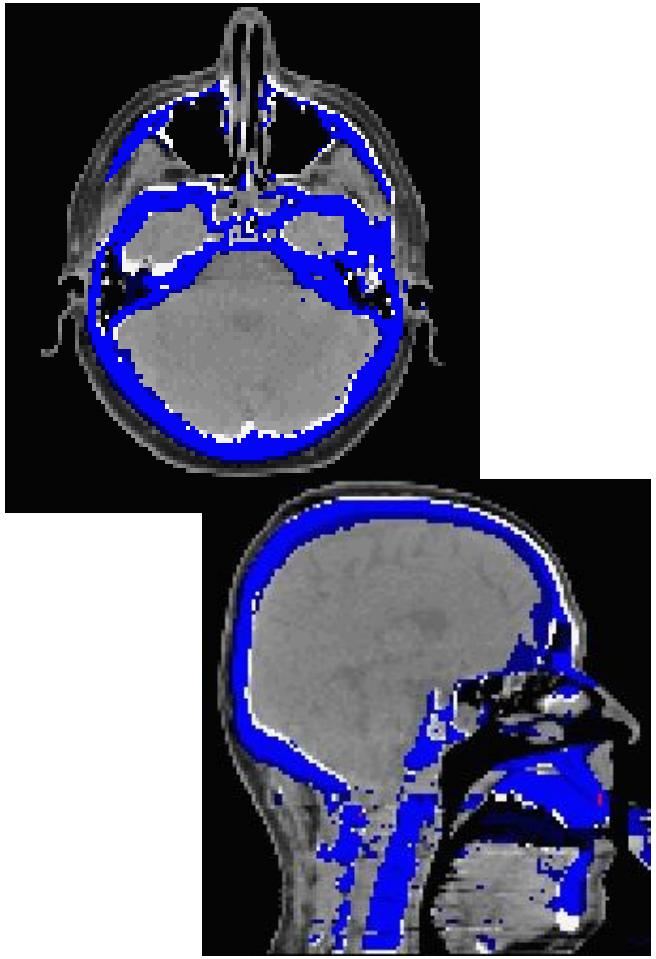
Sensitivity to set-up errors

Uncorrected



Corrected

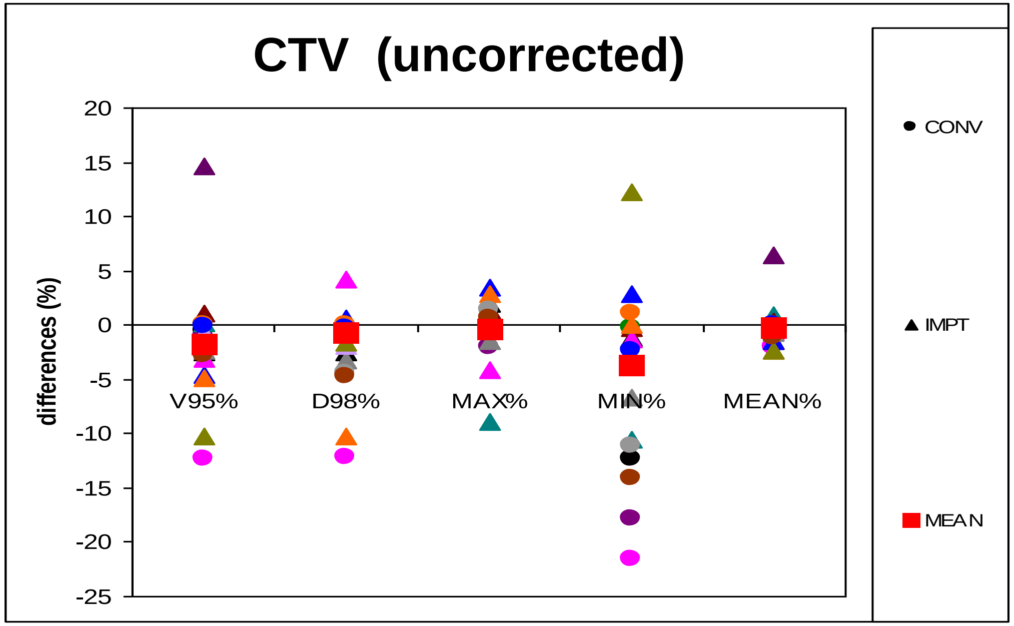


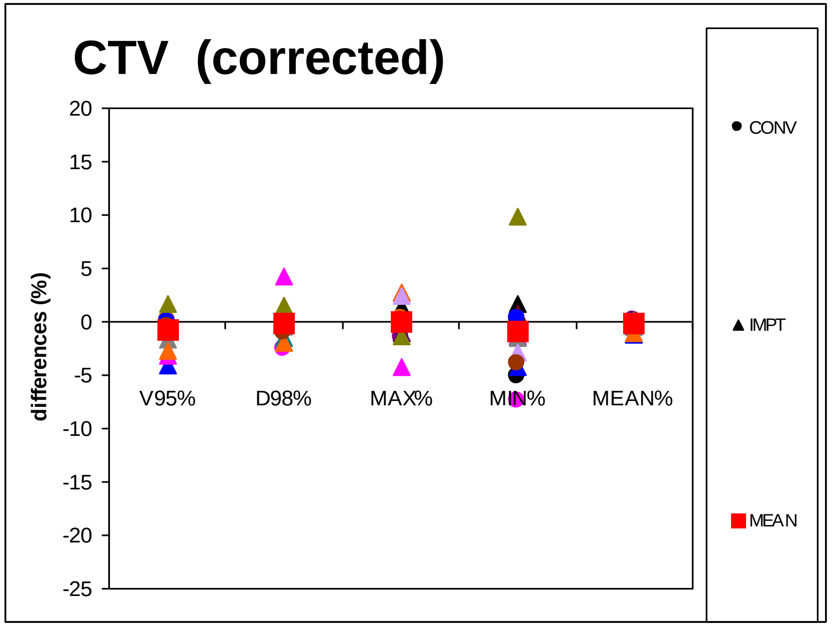
Even when daily imaging is used to correct patient positioning, there are inevitably still residual positioning errors

Alessandra Bolsi & Stefania Comi, PSI/IEO

Sensitivity to set-up errors

- Repeat CT's acquired on 10 skull base patients during treatment
- Doses recalculated on repeat CT's without and with set-up corrections (uncorrected and corrected)





Stefania Comi, PSI/IEO

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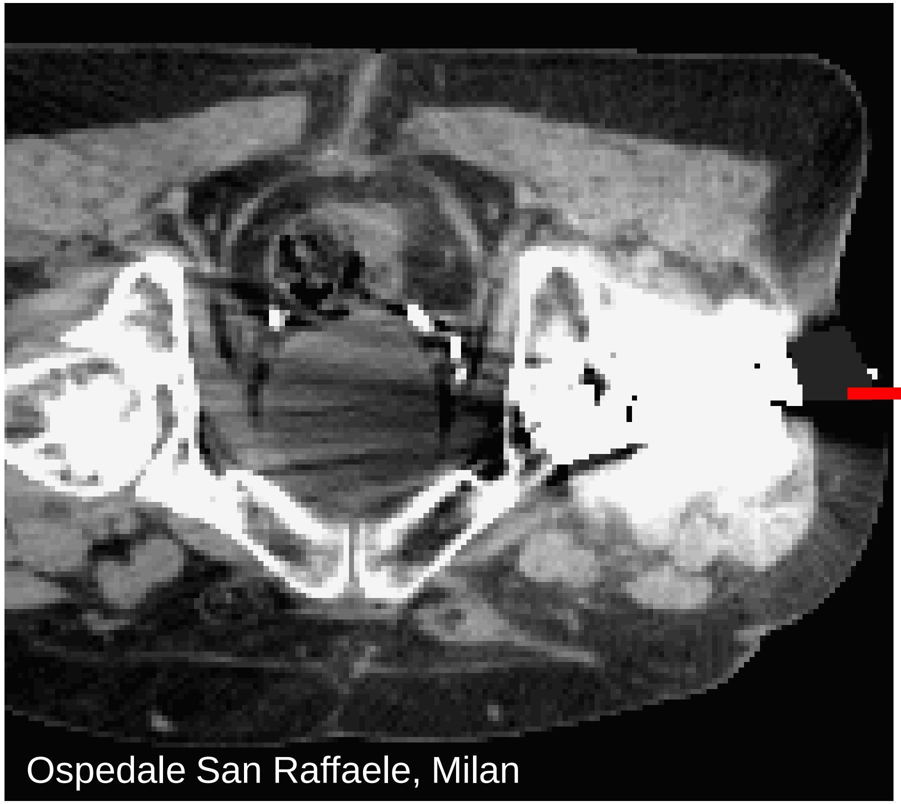
Sources of range uncertainties

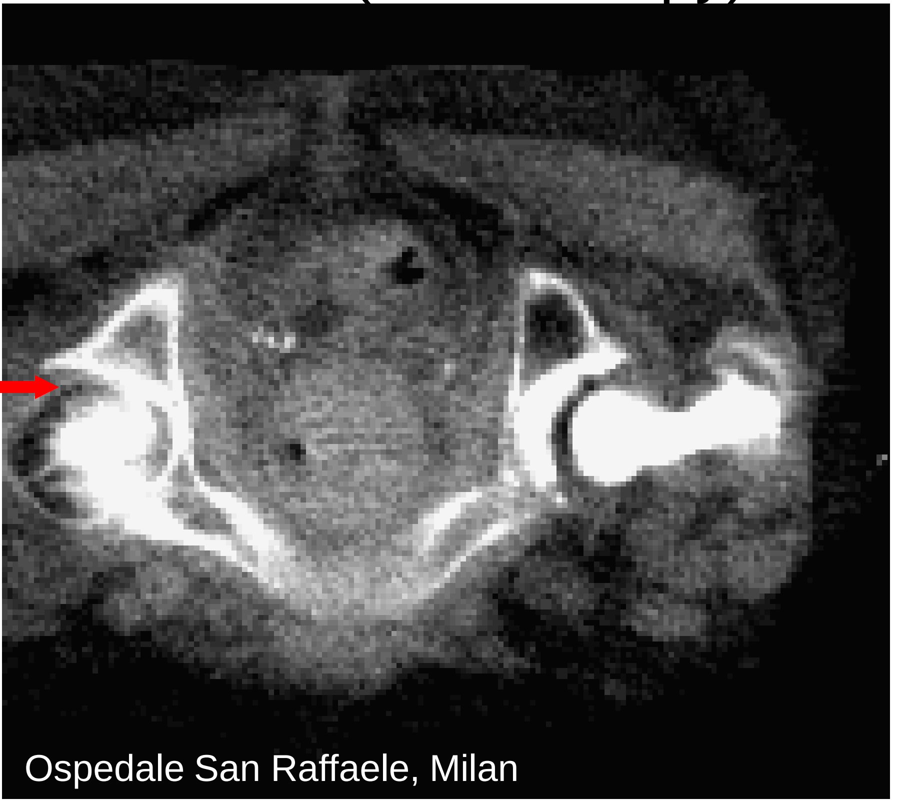
- Limitations of CT data (beam hardening, noise, resolution etc) [Σ ~ 1%]
- Uncertainty in energy dependent RBE [Σ ~ 2%]
- Calibration of CT to stopping power [Σ ~ 1-2%]
- CT artifacts [Σ]
- Variations in patient anatomy [Σ,σ]
- In-homogeneity along the beam path [Σ,σ]
- *Variations in proton beam energy [σ]*
- *Variations in patient positioning [σ]*

Range errors are generally systematic!

kV-CT



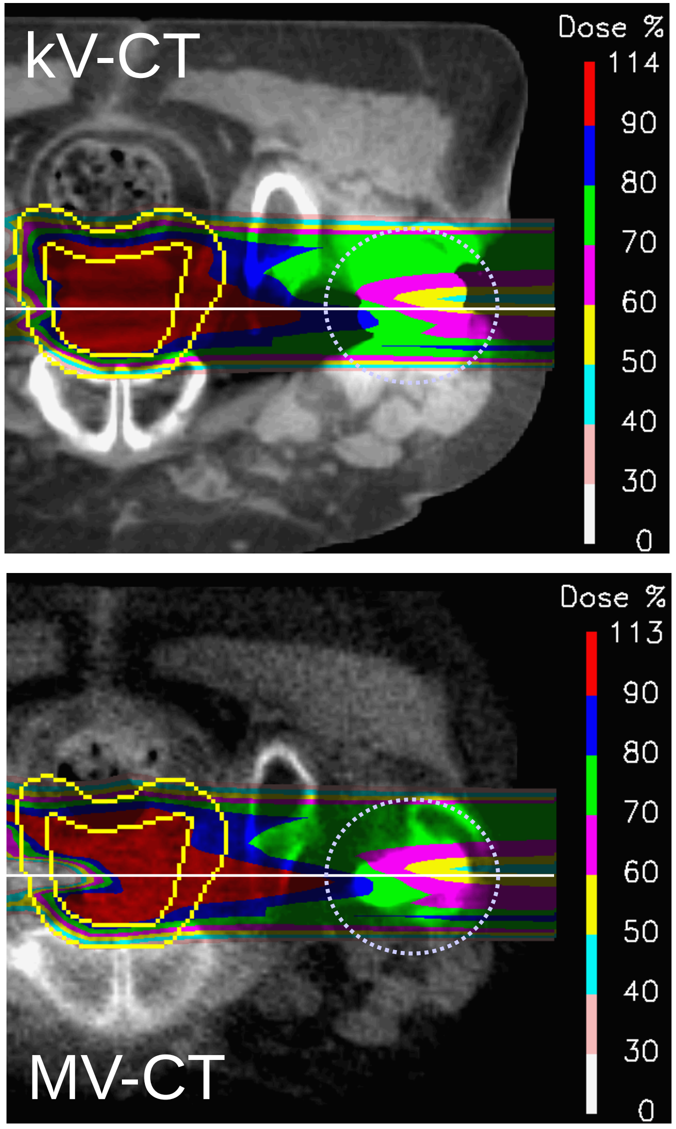
MV-CT (tomotherapy)



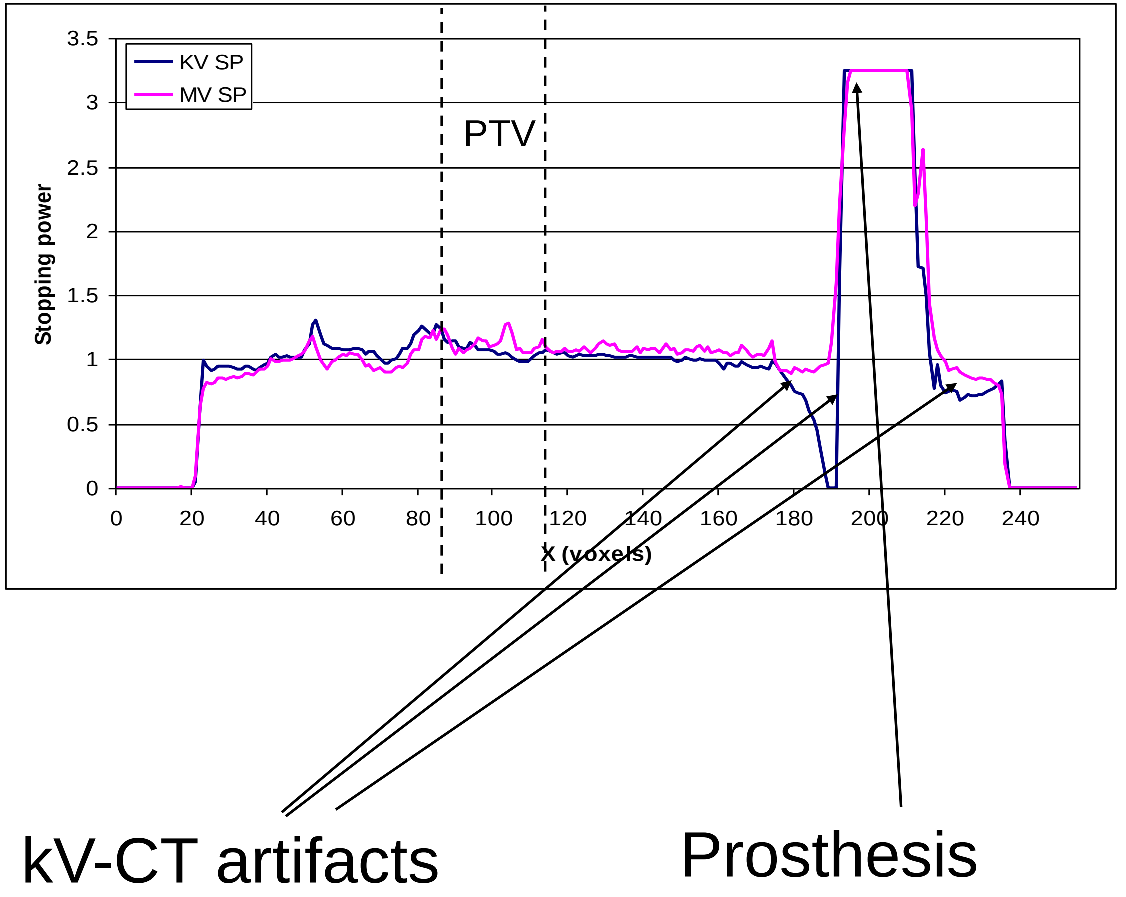
Accuracy of range calculation due to reconstruction artifacts?

No artifacts and linear relationship CT units to proton stopping power

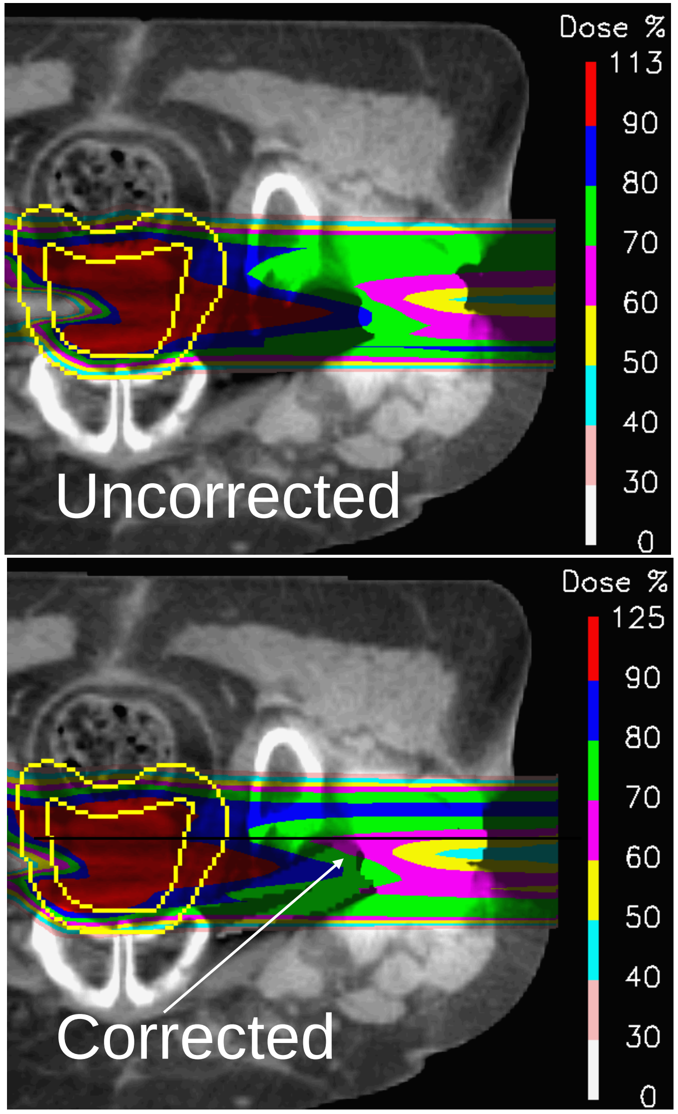
Range uncertainty: 1. CT artifacts

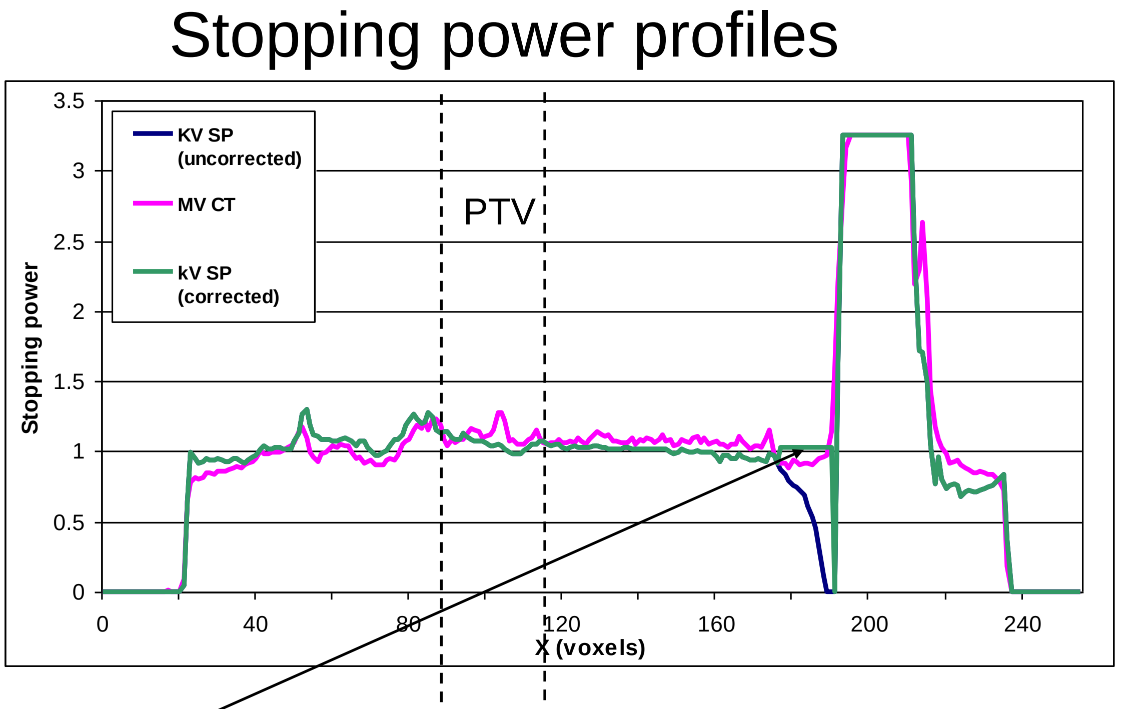


Stopping power profiles



How to deal with them: correct for CT artifacts

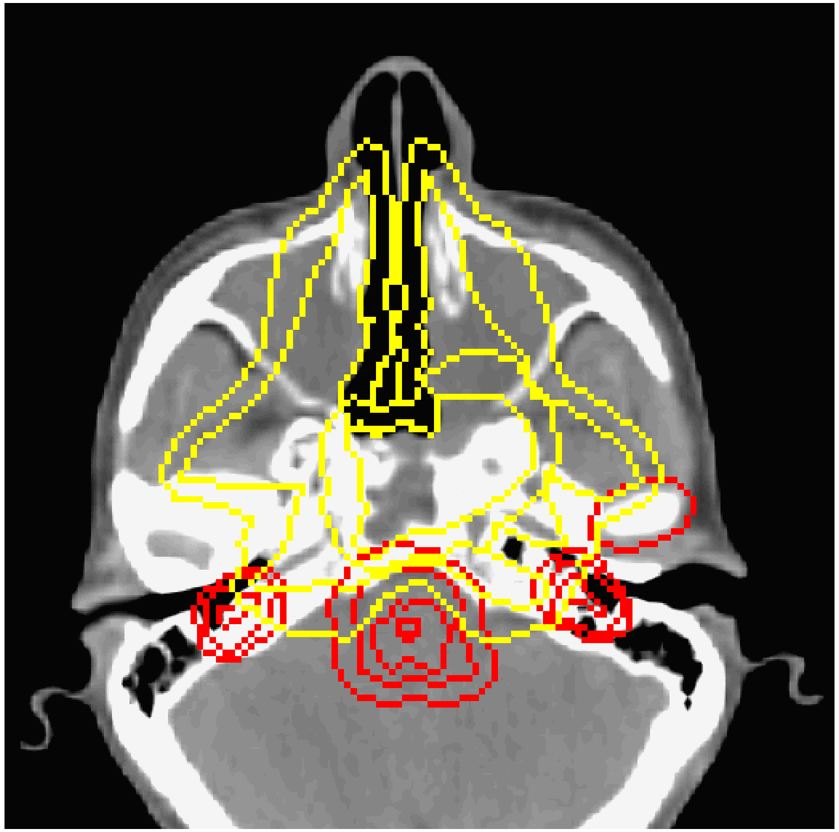




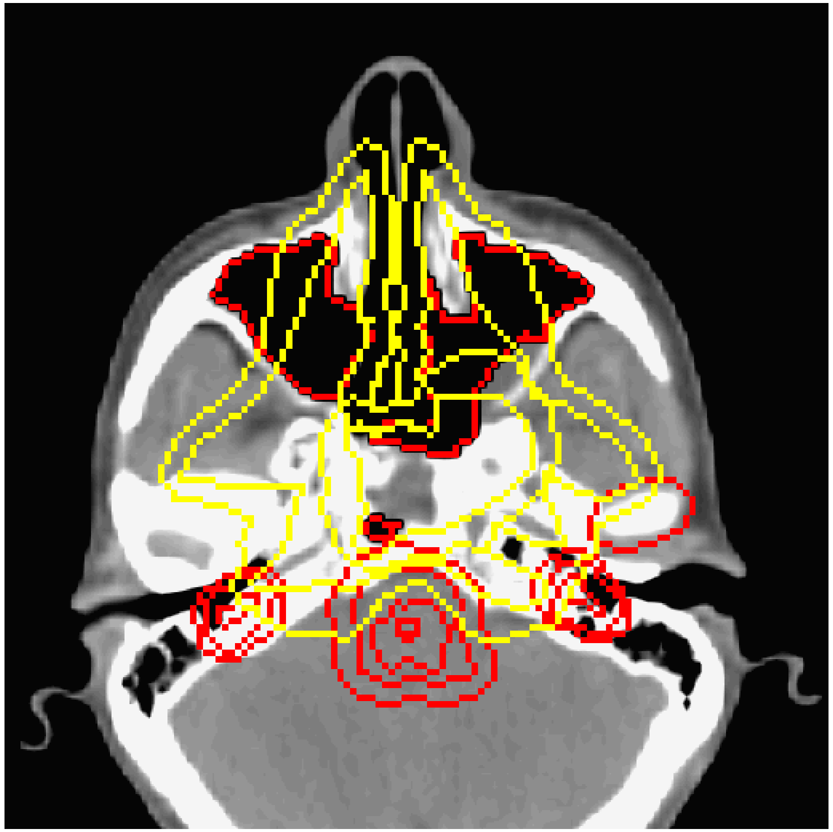
Corrected artifacts improve situation, but inaccuracies in defining artifacts leads to still substantial range problems due to residual artifacts (important for this extreme case!)

Anatomical changes: nasal cavity

Skull base Chondrosarcoma



Planning CT



Repeat CT after 2 weeks

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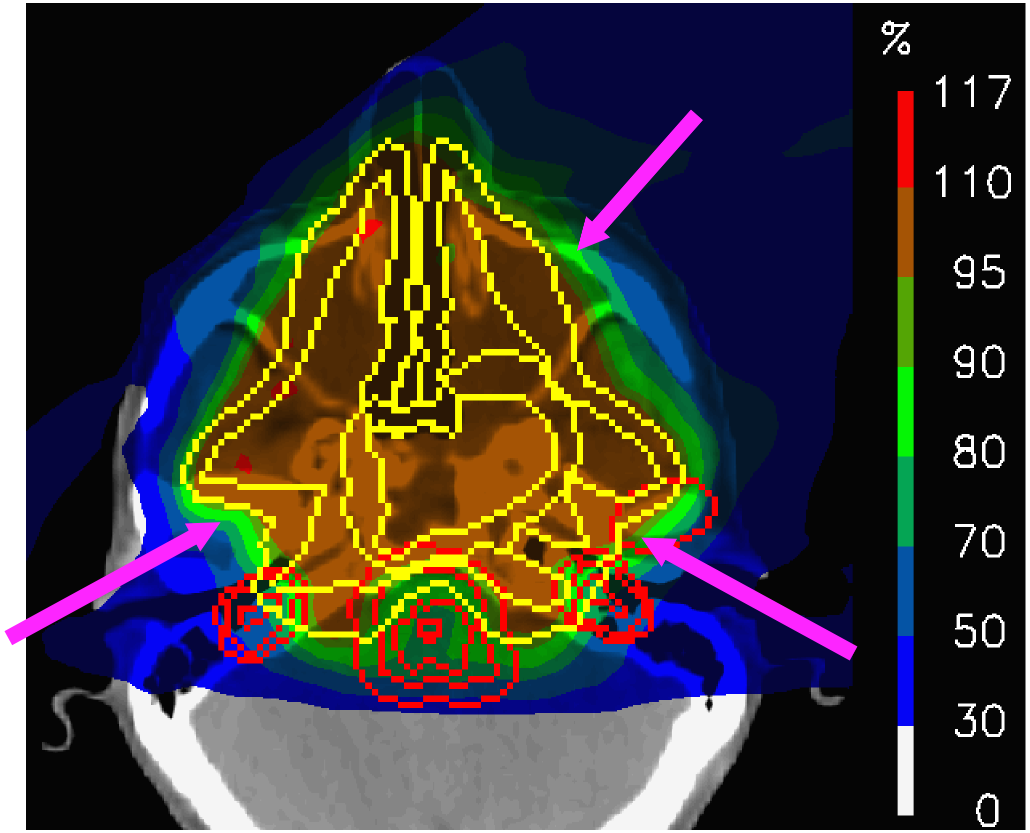
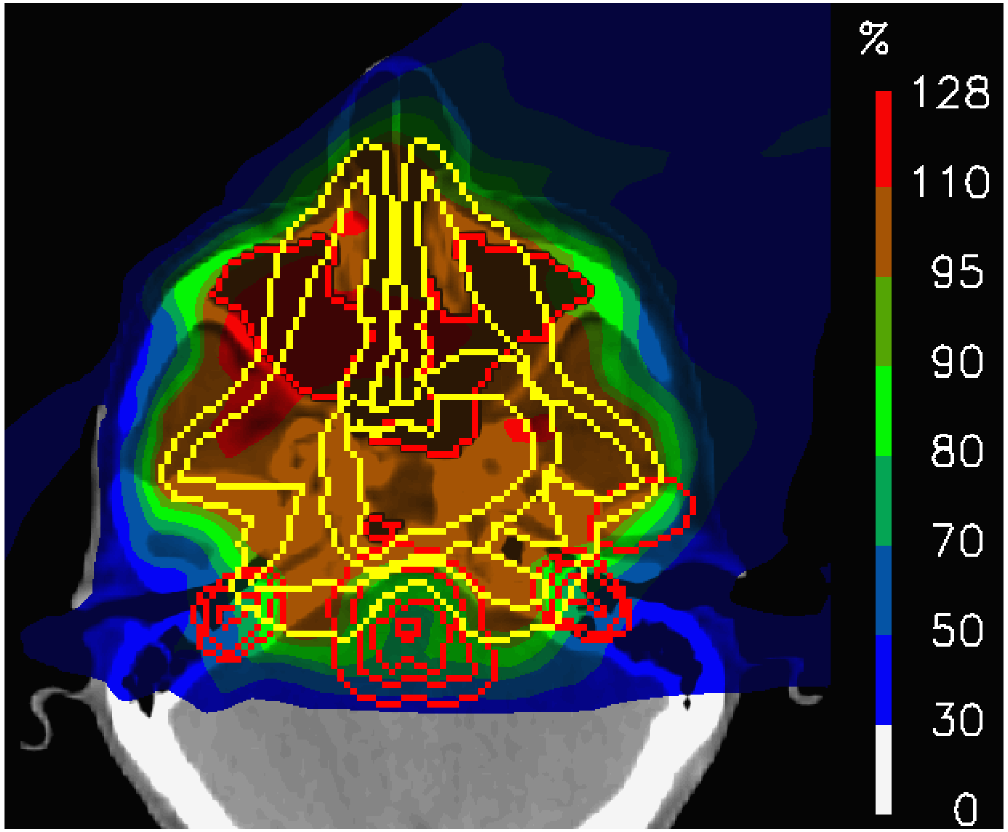
Anatomical changes: nasal cavity

Skull base Chondrosarcoma



Nominal plan



Recalculated plan

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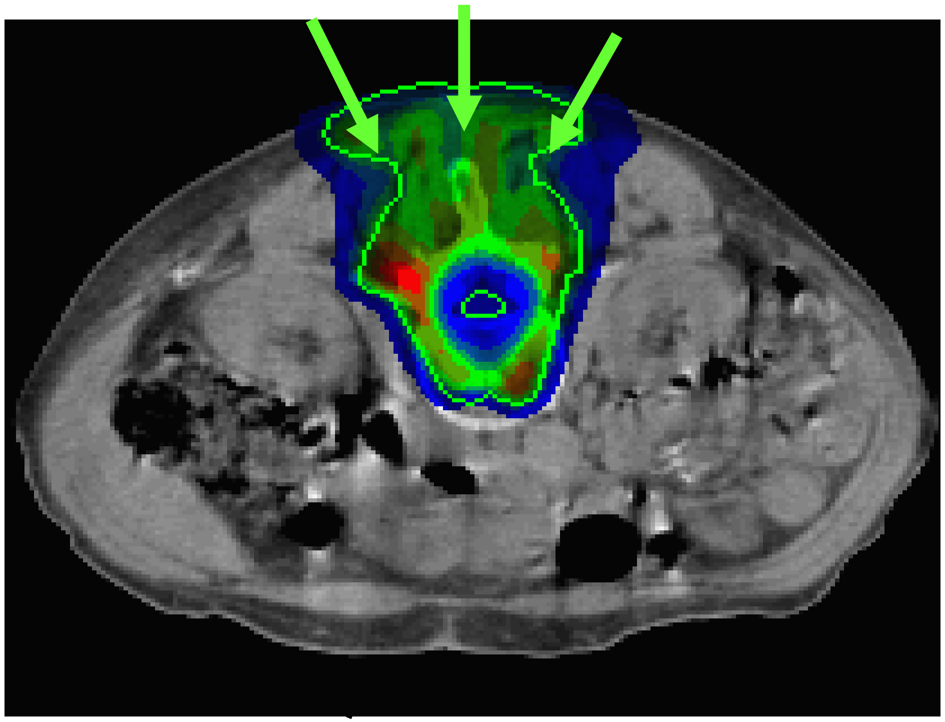
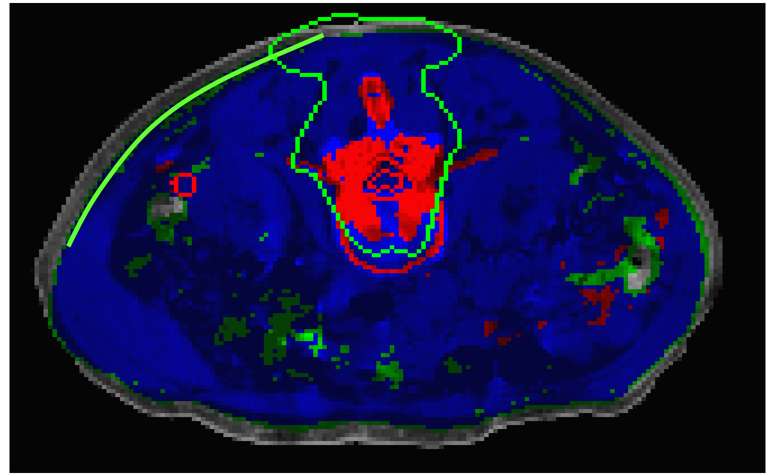
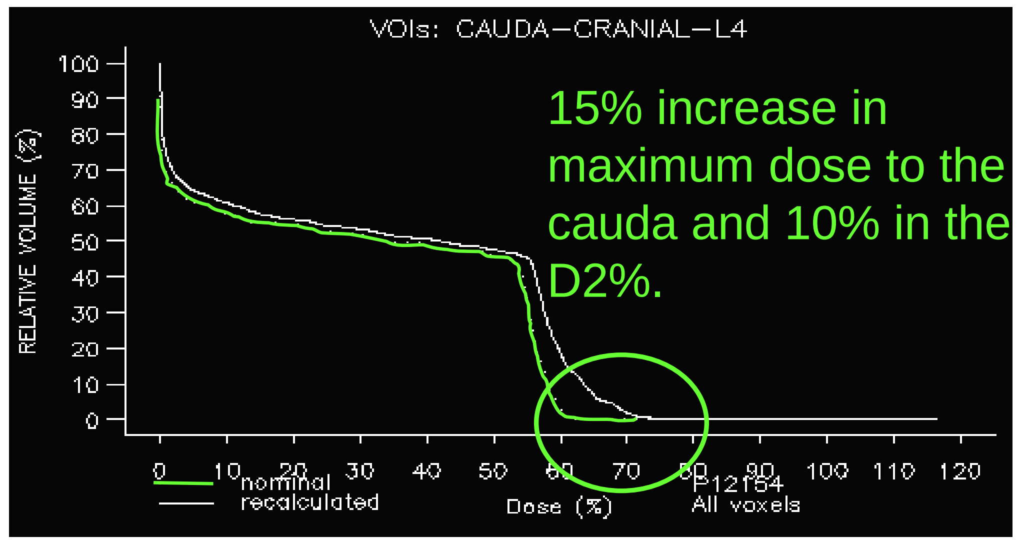
Anatomical changes: weight changes

3 fields IMPT plan, patient lost 1.5 kg



Note, sparing of cauda in middle of PTV





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- patient monitoring (detect range differences as soon as possible – ideally daily)
- adaptive therapy (adapt the plan, as soon as possible – ideally daily)
- robust planning (reduce a-priori the impact of range uncertainties)

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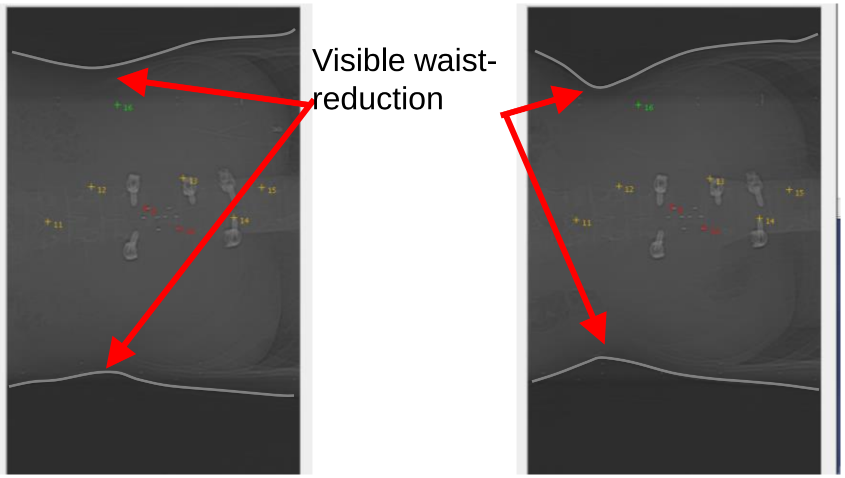
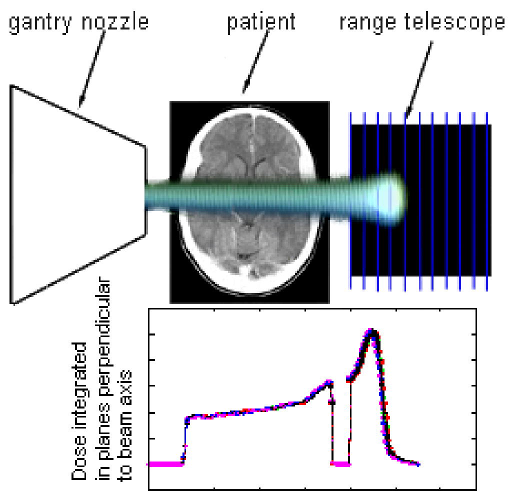
1. Patient monitoring (daily)

Daily X-ray (BEV)

Reference scout 3d fraction



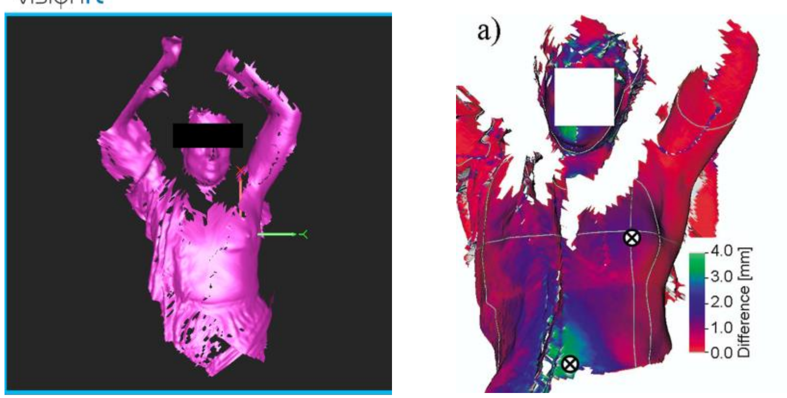
Range probe



Mumot M et al PMB 2010

Surface imaging

visionrt Daily image Difference from the reference



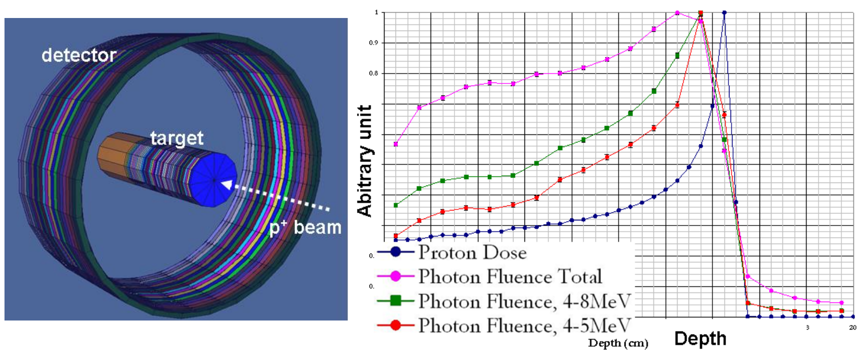
Christoph Bert et al IJROBP 2006

Prompt gamma

$$p + {}^{12}C \rightarrow p' + {}^{12*}C$$

$$ {}^{12*}C \rightarrow {}^{12}C + \gamma_{4.44\,MeV}$$

Calculated dose



Harald Paganetti, MGH Boston

1. Patient monitoring (regularly)

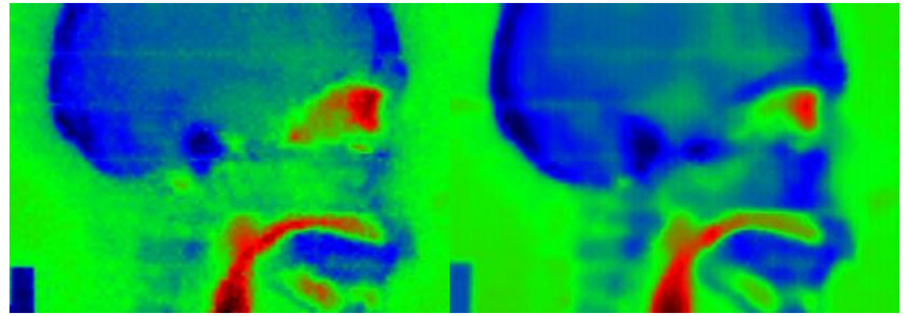
Control CT

Planning CT | control CT

Alessandra Bolsi & Francesca Albertini, PSI

Proton radiography

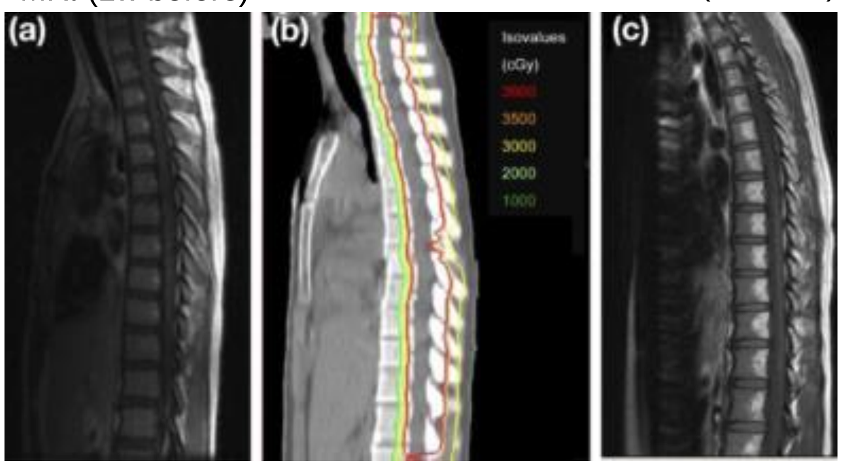
Proton radiograph | Proton DRR



Tourovsky A et al, 2005 PMB

Control MRI

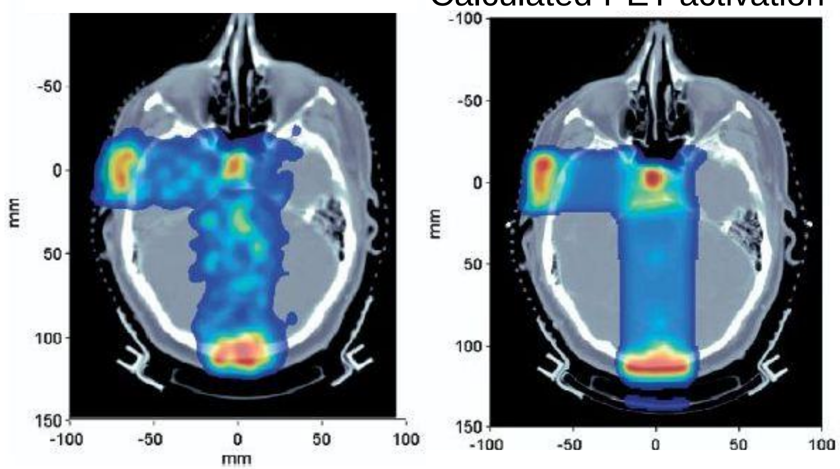
MRI (1w before) | Dose distribution | MRI (1m later)



Krejcarek et al, IJROBP 2007 1;68(3):646-9

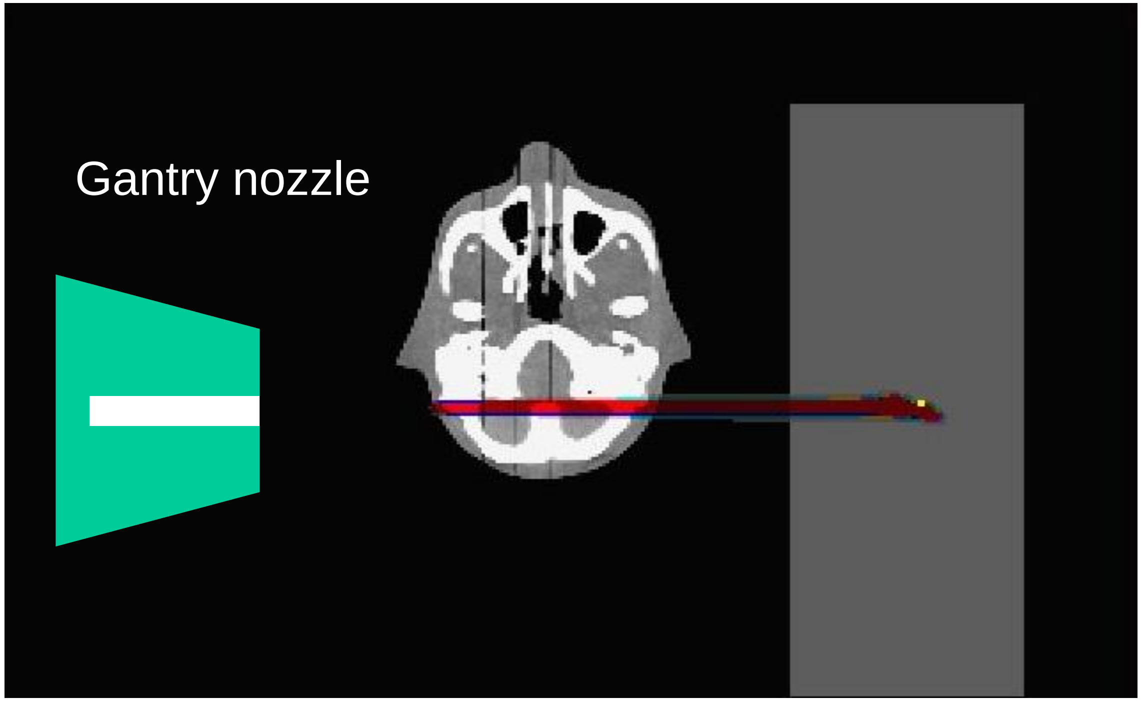
Activation PET

Measured PET activation | Calculated PET activation



Knopf A –Parodi K , IJROBP 2011

Range probe



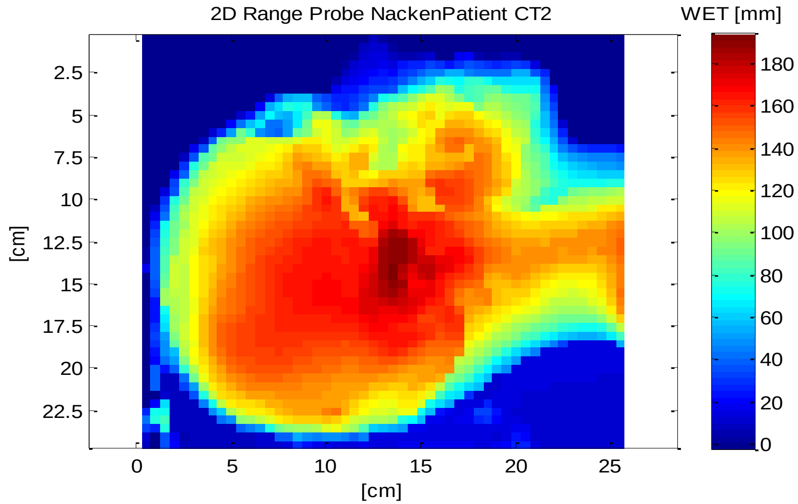
Single pencil beam with going trough the patient

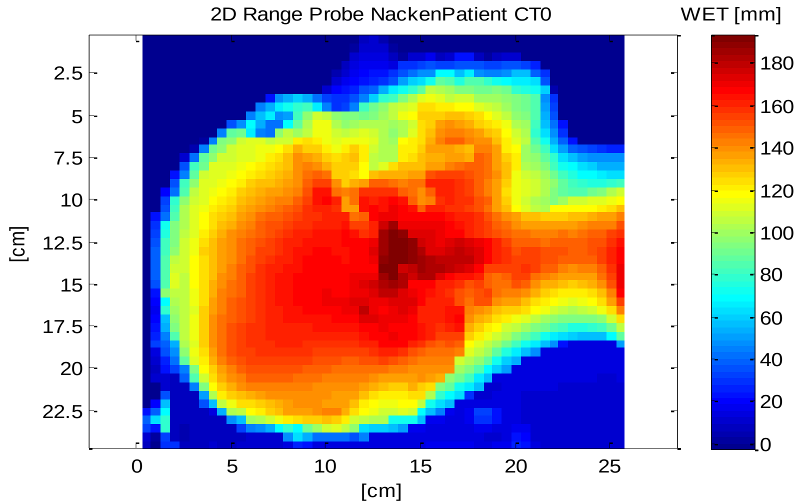
residual range measured in the MLIC

PhD work of Abdel Hammi (PSI)

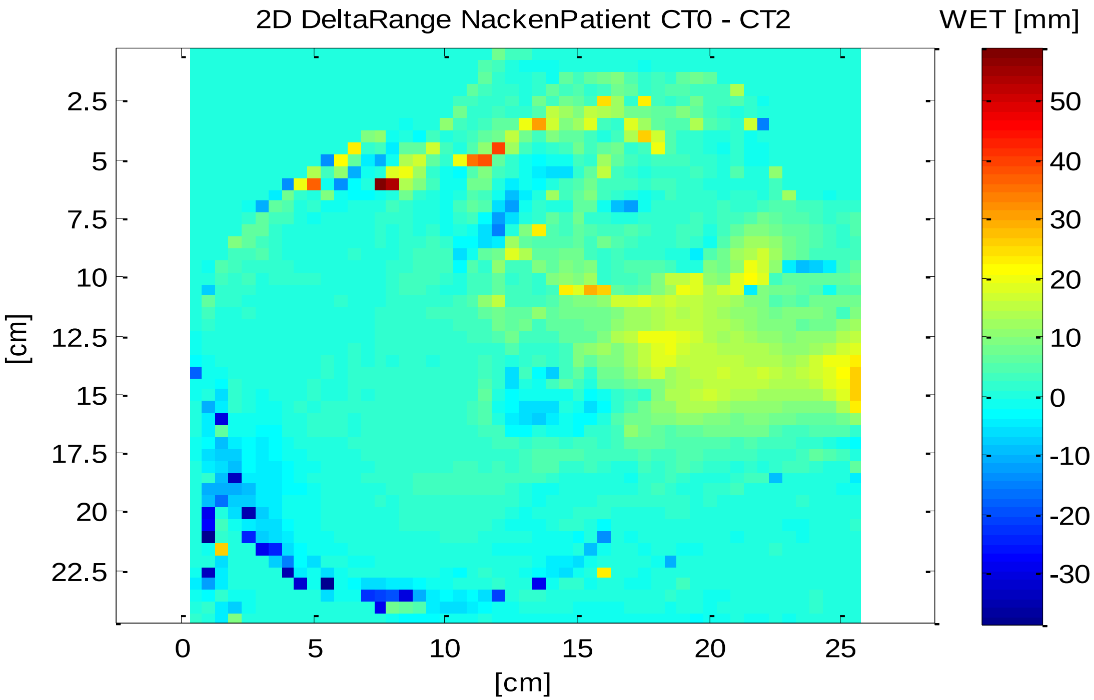
Range probe 2D

2D RP 5x5mm spacing.





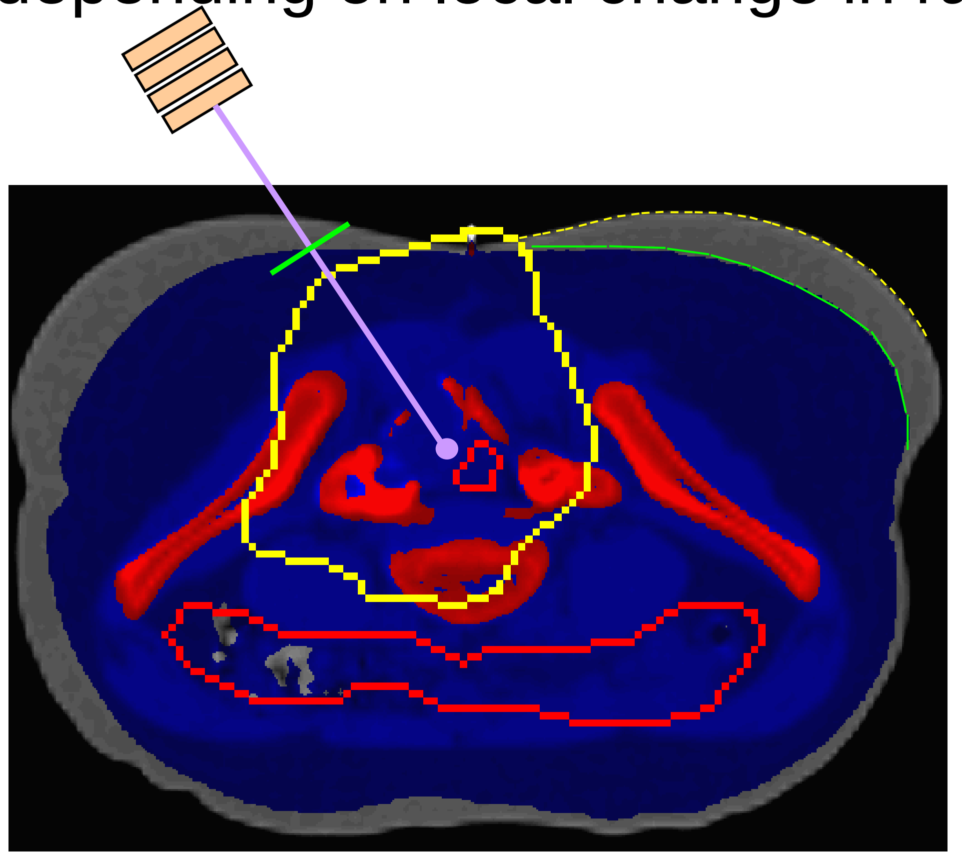
Residual positioning error and anatomical changes



PhD work of Abdel Hammi (PSI)

2. Range adapted therapy

Automatic adaptation of Bragg peak ranges on a spot by spot basis depending on local change in range



A Bolsi, F Albertini, H Pascal and A. Lomax to be submitted

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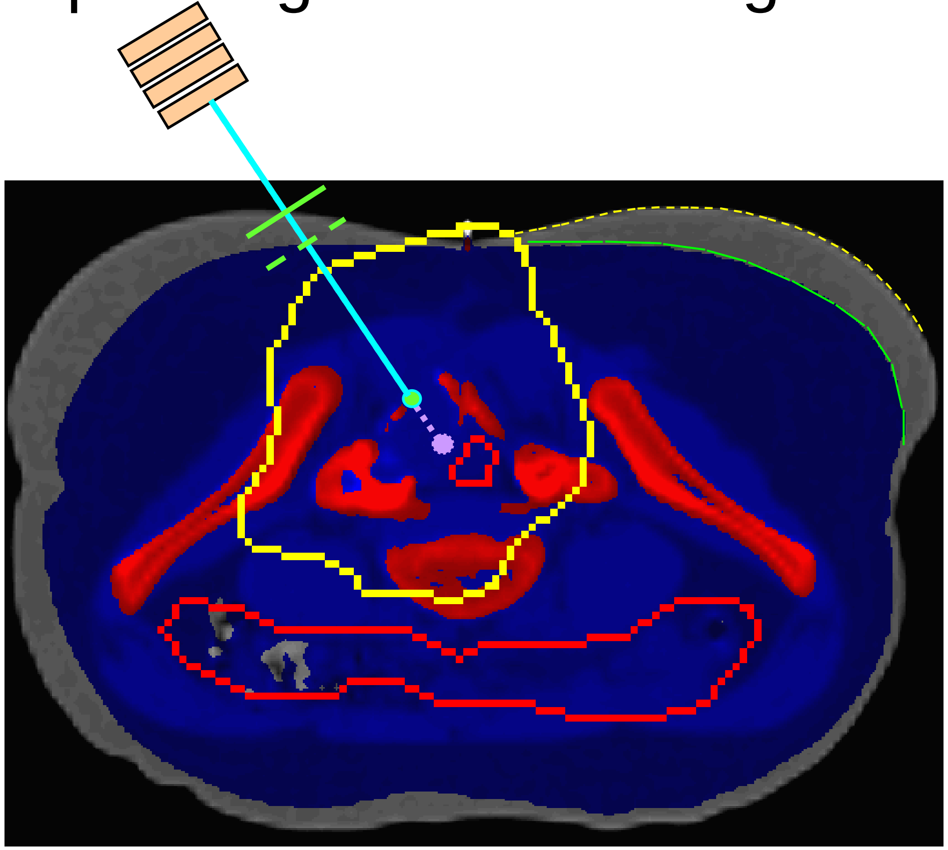

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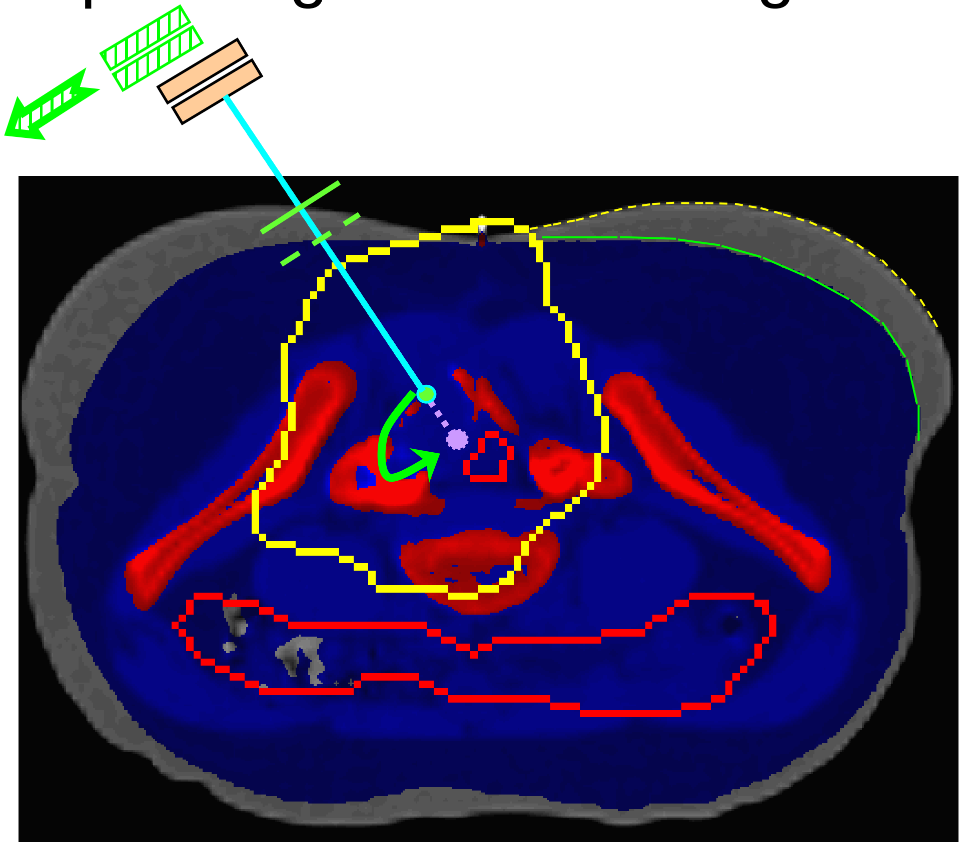

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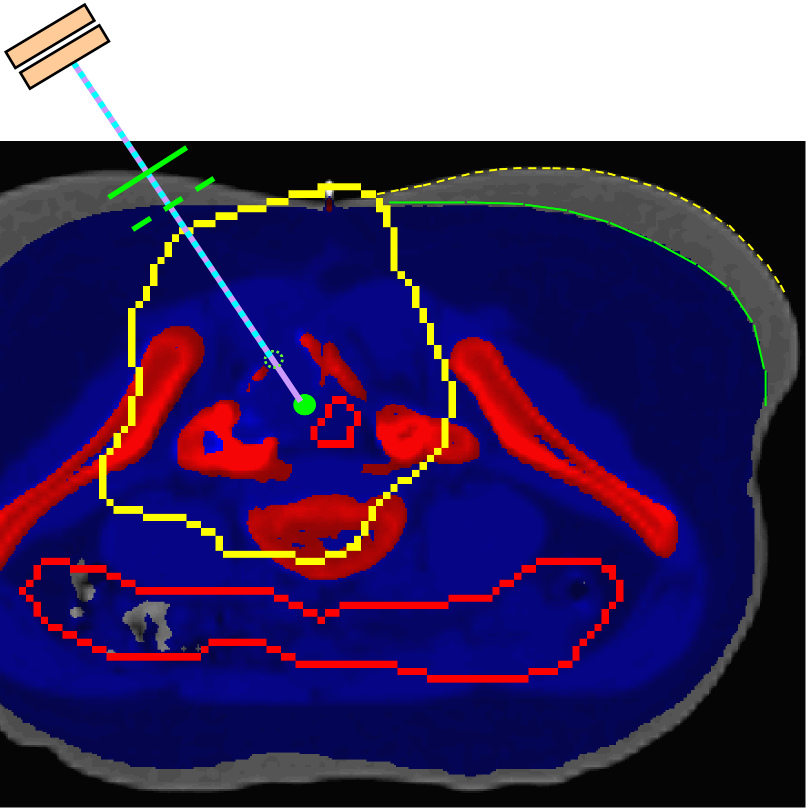

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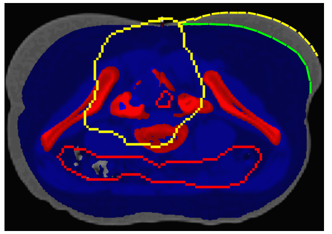
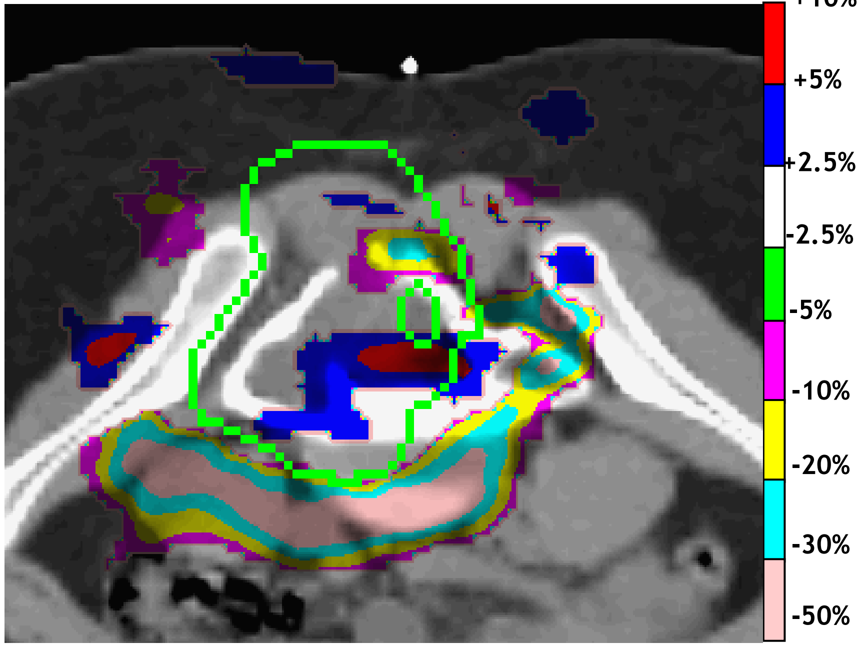
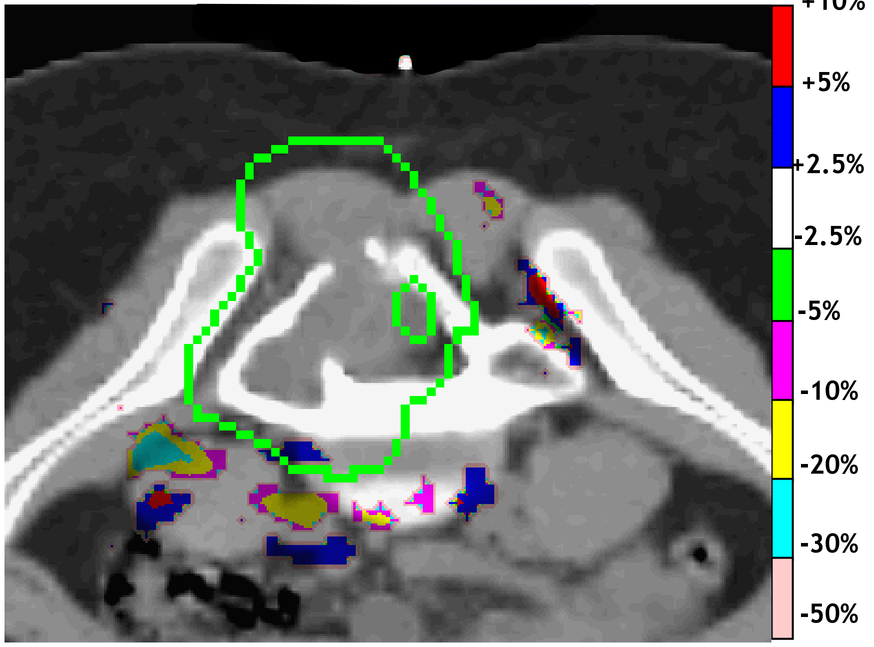


Dose difference: not adapted-nominal



Dose difference: adapted -nominal



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How to minimize the impact of range errors on the dose distribution?

1. automatic incorporation of all the errors (range, set-up) in the optimization process (change of the cost-function)

Unkelbach J et al 2009 Med Phys.
Unkelbach J et al 2007 PMB
Maleike, Flynn (Ex Raysearch)

2. changing the optimization starting condition:
   a. manual selection of beam angles avoiding or penalizing path going through sensitive areas
   b. changing the initial beamlet fluences

Lomax A et al, 2001 Med Phys
Albertini F et al, 2010 PMB
et al, 2010 PMB

Outlook

1. Introduction (SFUD vs IMPT)
2. Positioning uncertainty
3. Range uncertainty
4. Possible solutions
5. Summary

Summary

IMPT is a very powerful technique especially in case of OAR which is included or in proximity of the PTV.

The dose distributions present with steep and very steep dose gradients, which increase the effect of uncertainties typical for proton therapy.

IMPT dose distributions are very sensitive to positioning uncertainties and range uncertainties (e.g. anatomical changes)

There are different methods for compensating those uncertainties:

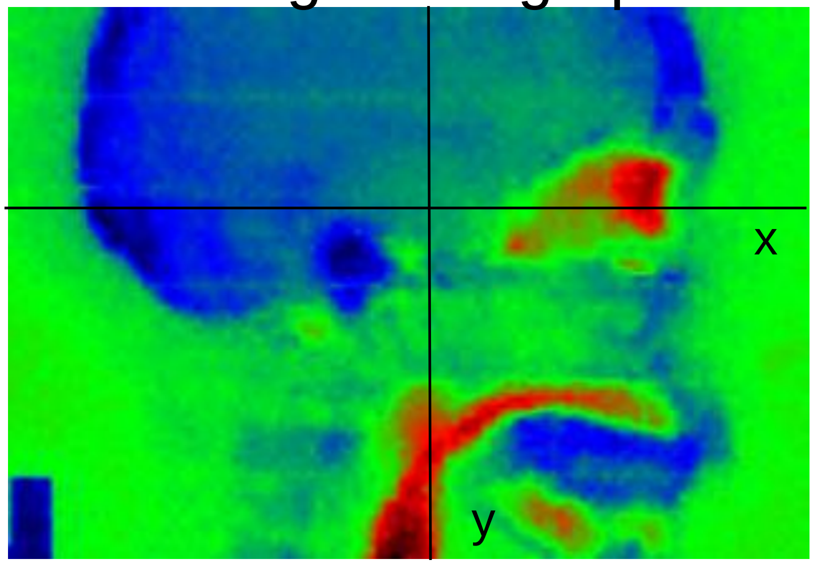
a. Image guidance (proton specific as future development)
b. Robustness
c. Plan adaptation

Those methods can improve the quality of the delivered dose distributions

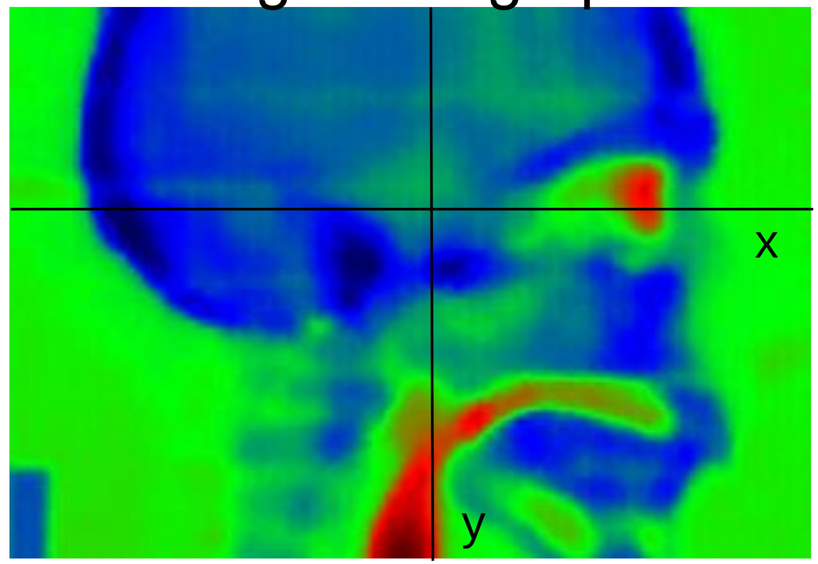
Thank you

Proton radiography

Proton range radiograph



MC 'range radiograph'



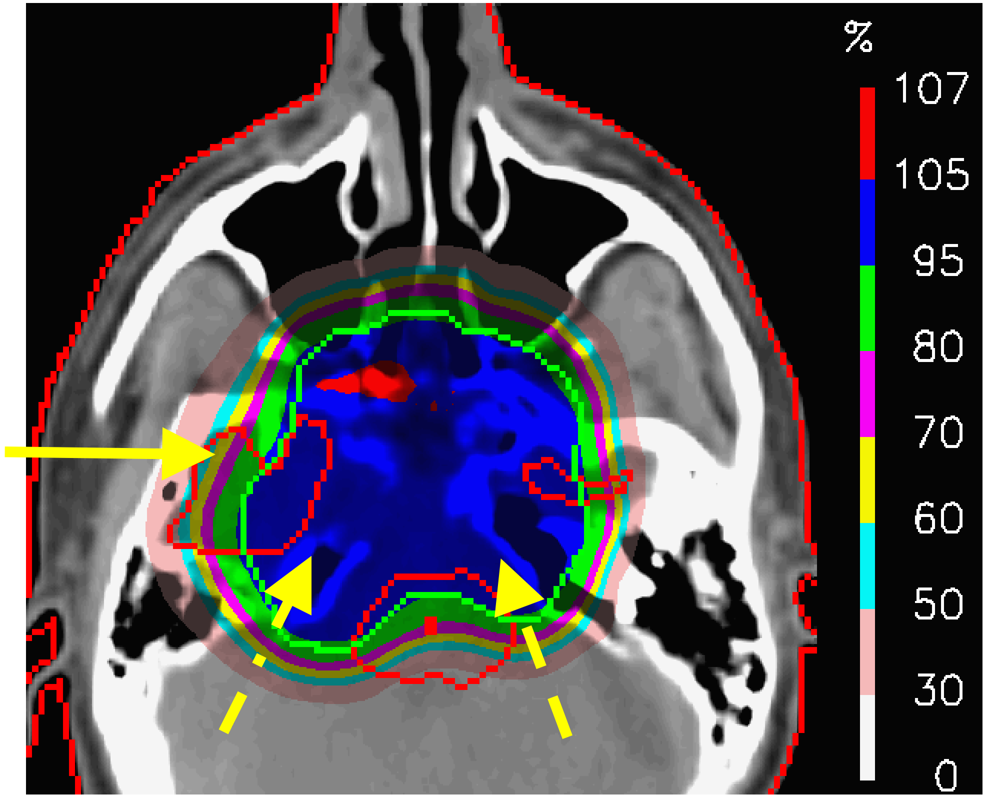
The equivalent of x-ray imaging with protons, where proton range rather than intensity (fluence) is measured

Images courtesy of Uwe Schneider and Alexander Tourovsky (Triemlispital and PSI)

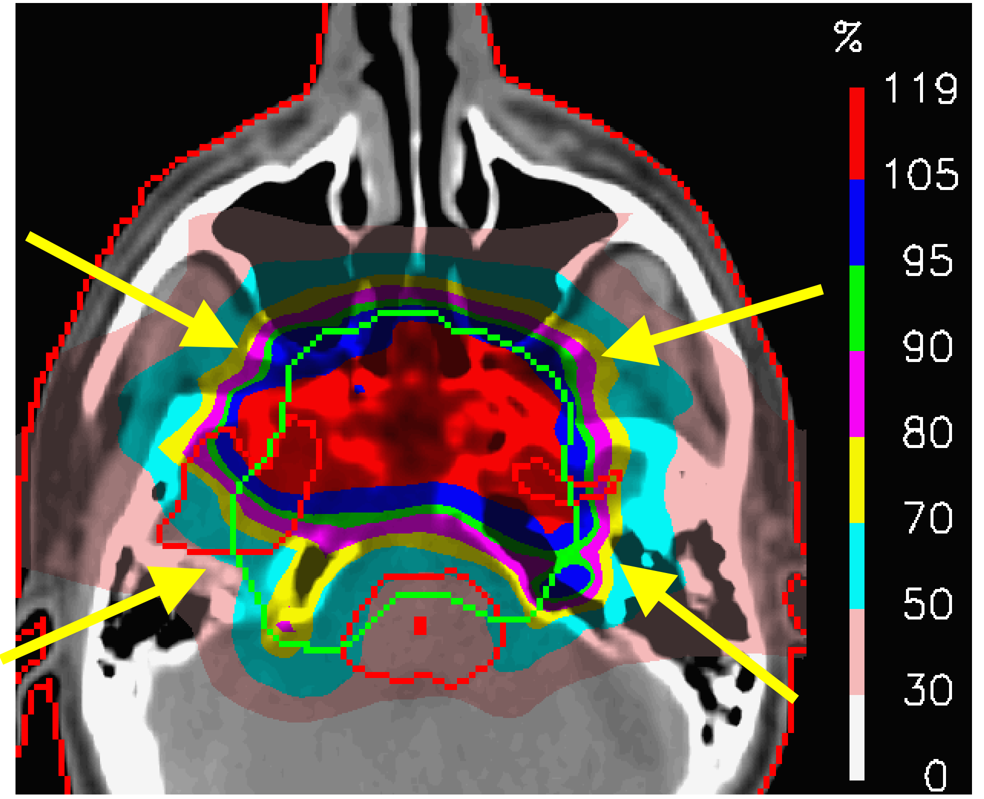
SFUD vs IMPT : which is more robust?

Nominal dose distributions

SFUD



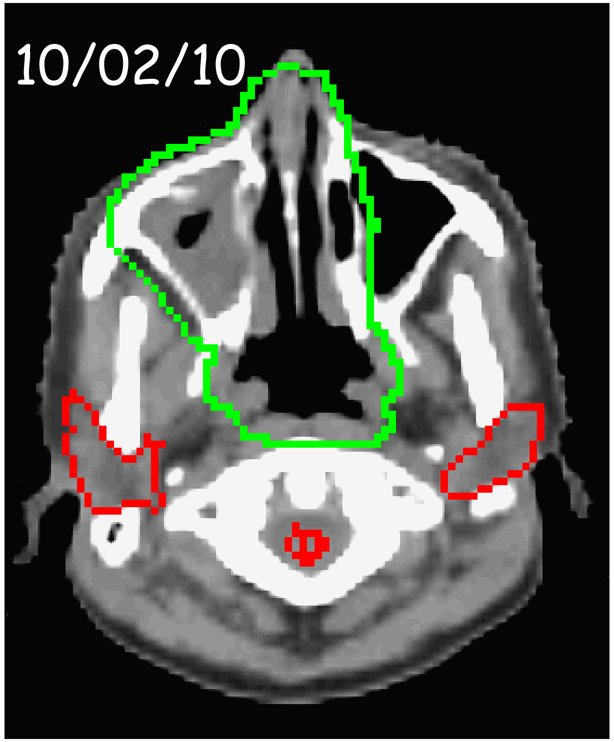
IMPT

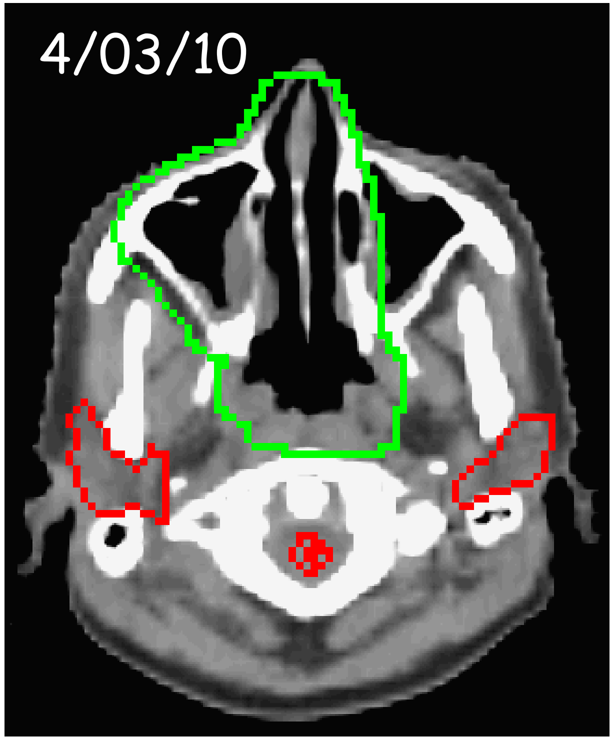


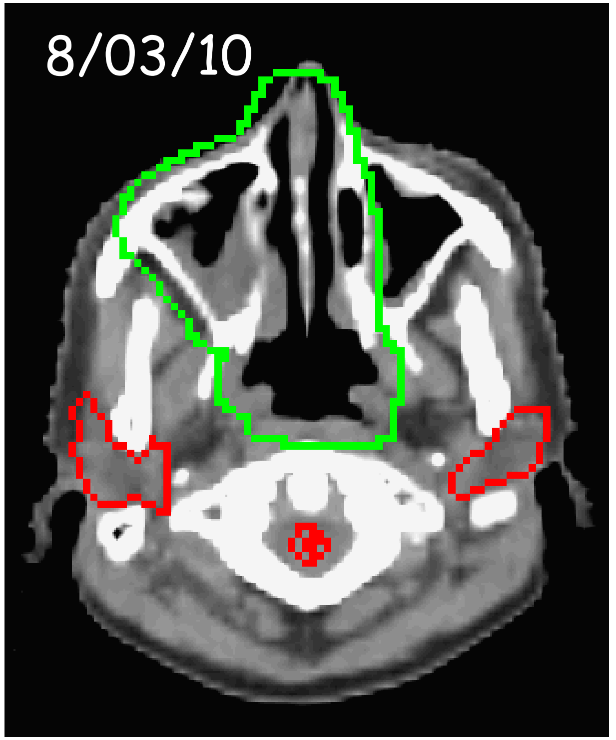
Albertini F et al, 2011 PMB

Range uncertainty: 2. changes in the anatomy (nasal cavity changes)

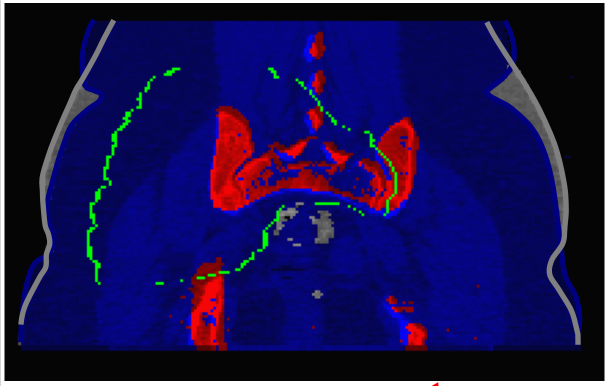
Planning CT







Range uncertainties : robust planning



Range difference 3.6 cm

<u>Option 1</u>: automatic incorporation of all the errors (range, set-up) in the optimization process

ROBUST-OPTIMIZATION process

Unkelbach J et al 2009 Med Phys.
Unkelbach J et al 2007 PMB
Pflugfelder D et al PMB 2008
Fredriksson A et al Med Phys 2011,2012

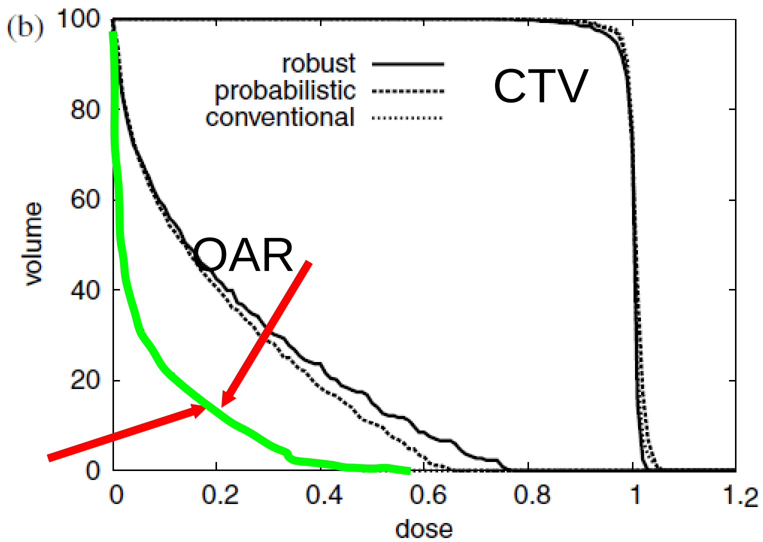
<u>LIMIT (option 1)</u>: only errors defined a-priori are considered in the optimization process

- **what about un-expected errors?**

Critical to define a treshold between robustness and ‚plan quality‘

Threshold between ROBUSTNESS and “nominal” plan quality

Nominal plans



Conventional plan with range errors

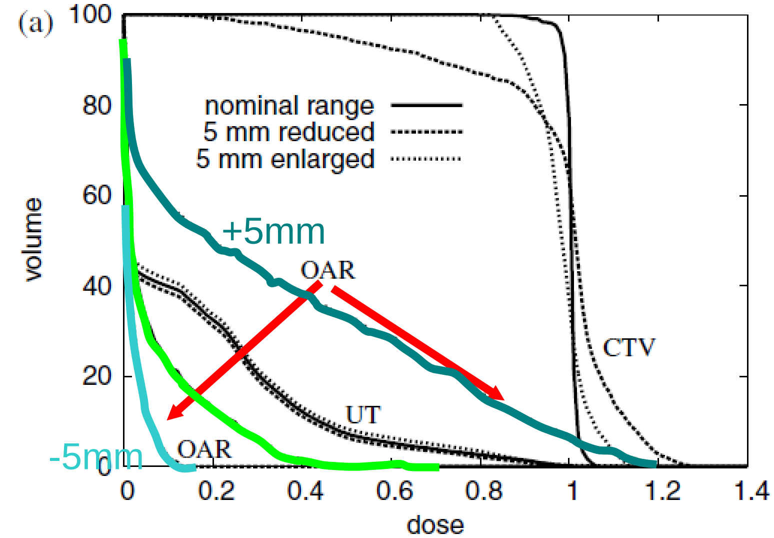
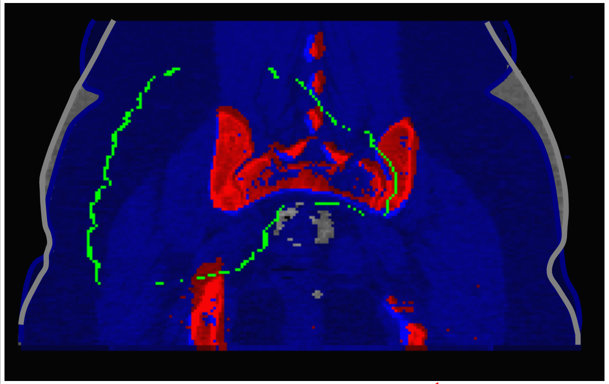


Figure adapted from Unkelbach J, Chan TCY and Bortfeld T (PMB 2007)
“*Accounting for range uncertainties in the optimization of intensity modulated proton therapy*”

Range uncertainties : robust planning



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- **what about un-expected errors?**

Critical to define a treshold between robustness and ‚plan quality'

<u>ADVANTAGE (option 1)</u>: can be automatize and together with a MCO window, the user can navigate through different plans options

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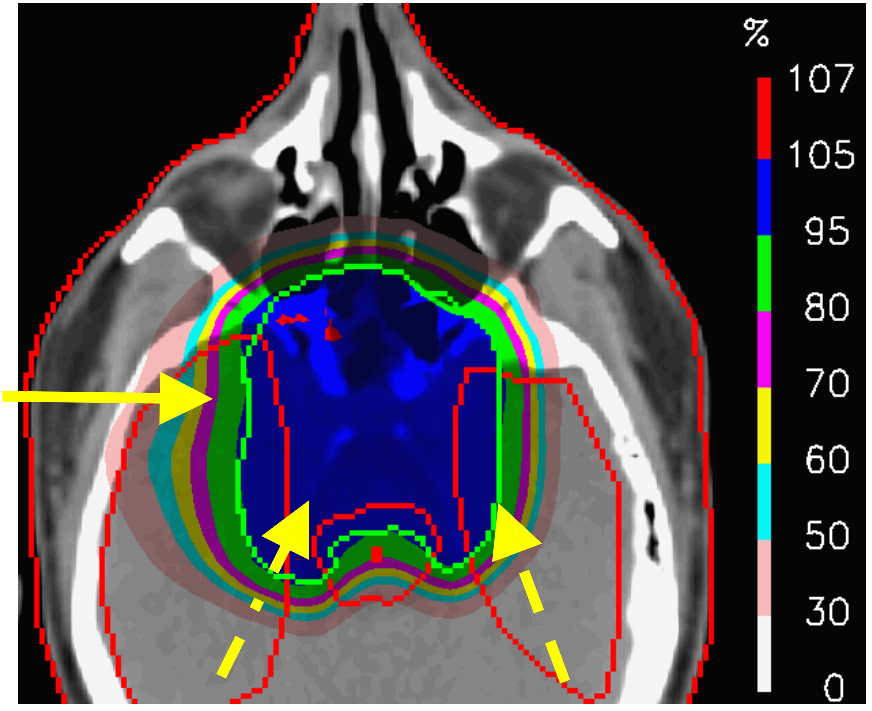
3 field SFUD plan

Nominal dose distribution

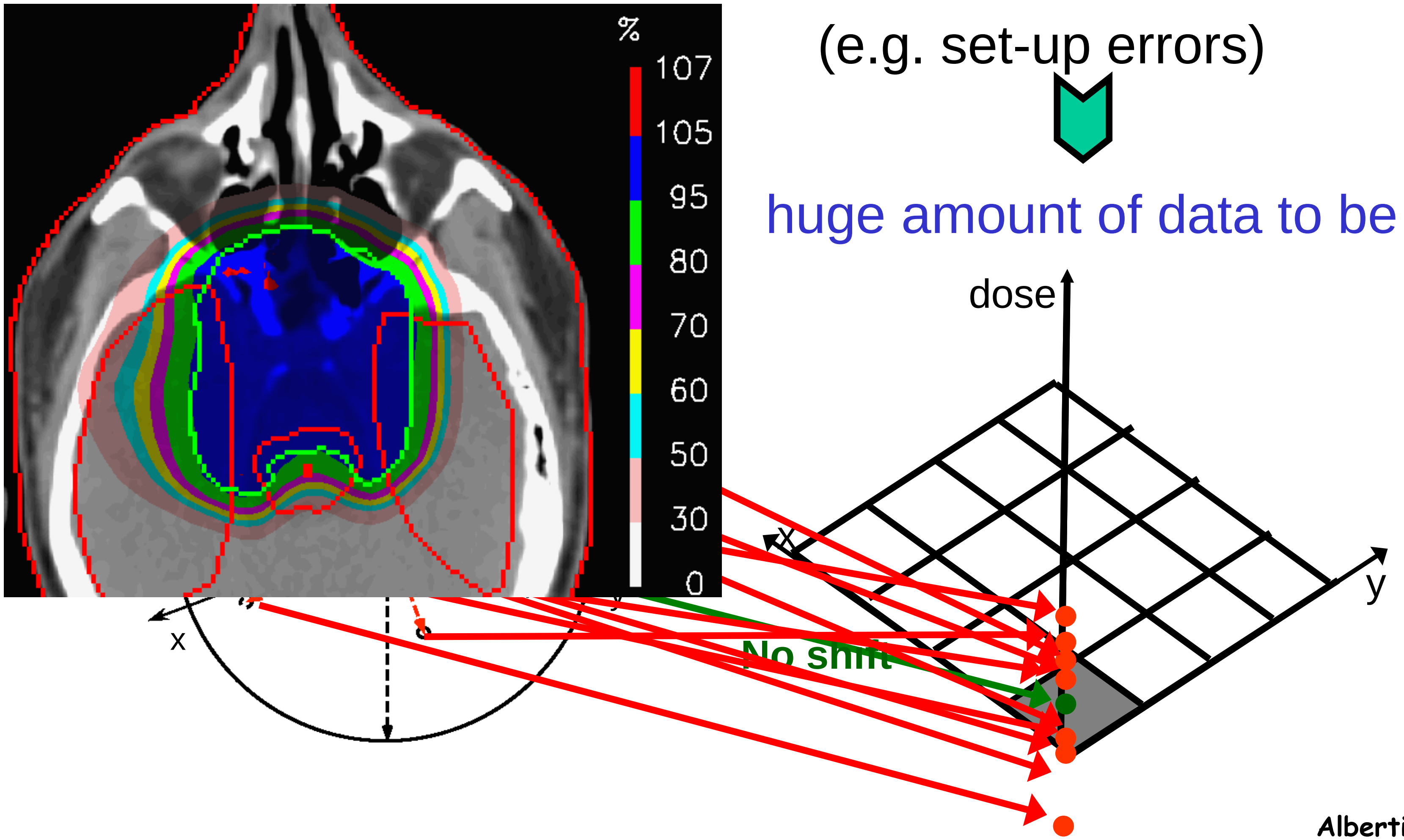


To assess plan robustness:

1. calculate n- 'error' dose distributions (e.g. set-up errors)

Albertini F et al, 2011 PMB

Evaluating uncertainties: max-to-min dose distribution



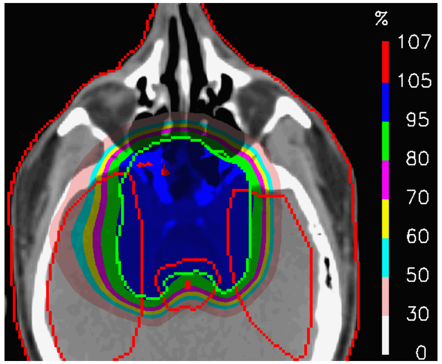
To assess plan robustness:

1. Calculate n- ‘error’ dose distributions (e.g. set-up errors)

huge amount of data to be treated

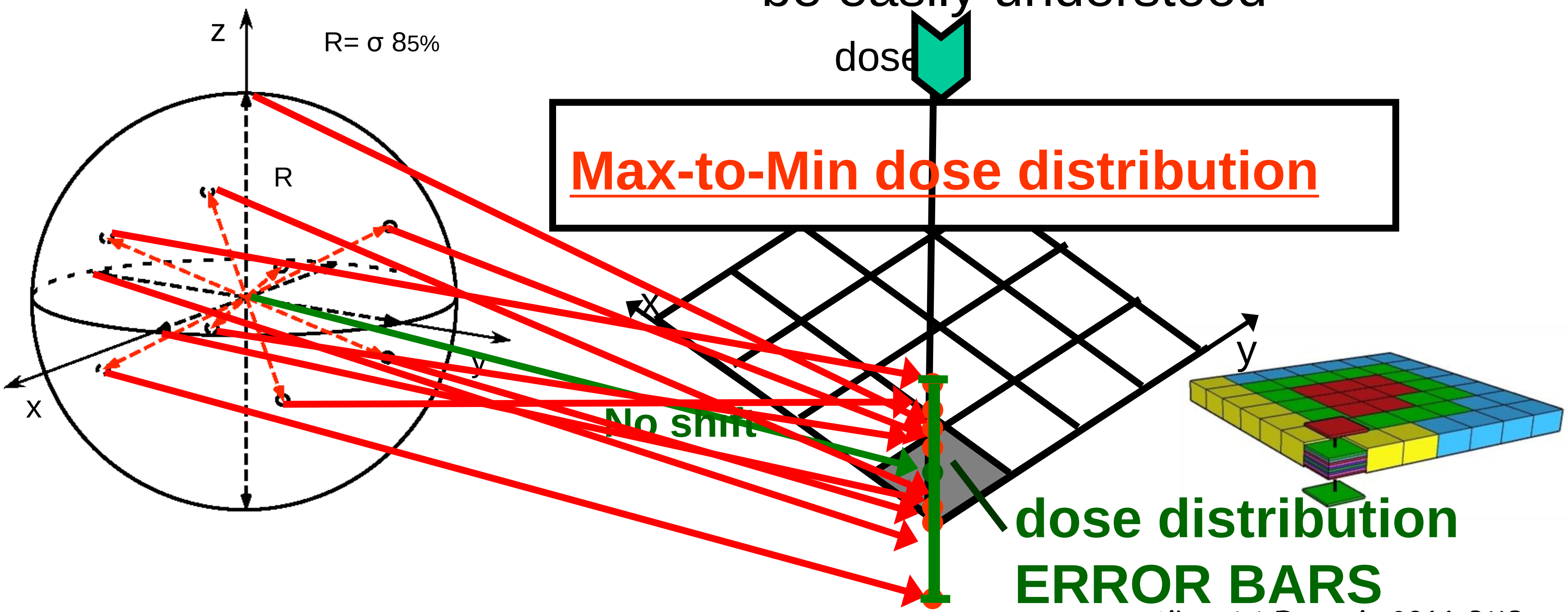
Albertini F et al, 2011 PMB

Evaluating uncertainties: max-to-min dose distribution



To assess plan robustness:

1. calculate n- 'error' dose distributions (e.g. set-up errors)
2. reduce the data so that result can be easily understood

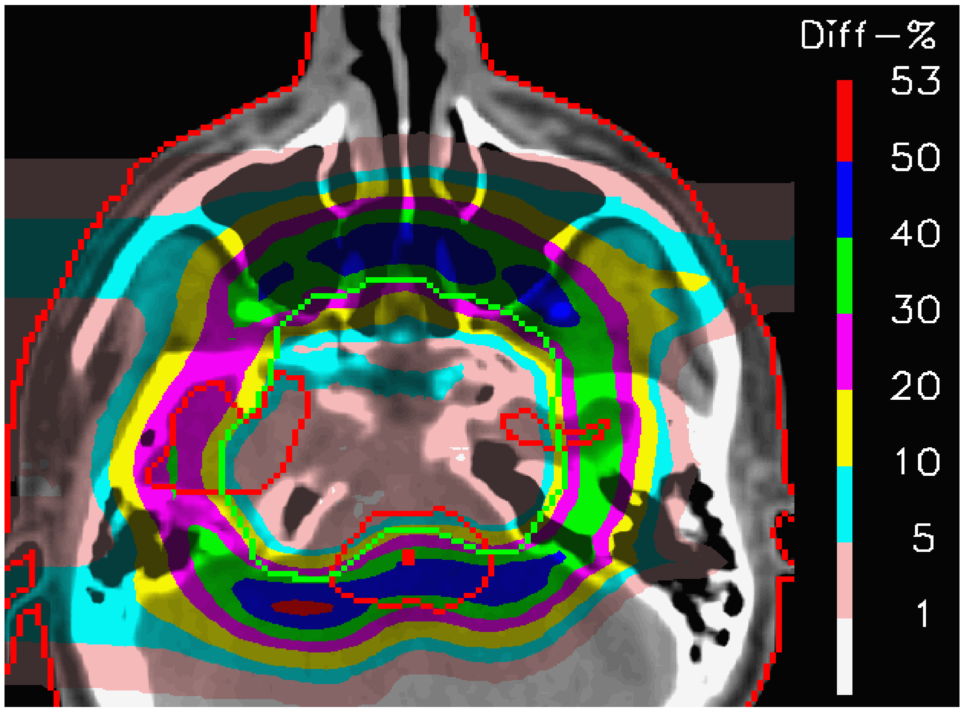


Albertini F et al, 2011 PMB

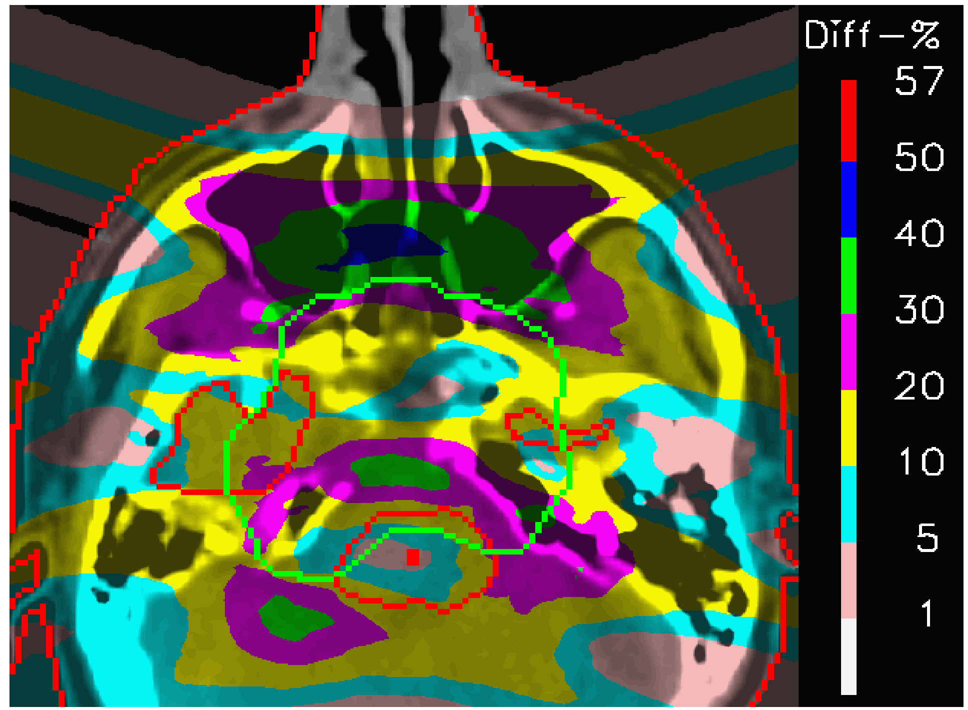
SFUD vs IMPT : which is more robust?

Max-to-Min dose distribution: useful tool to compare 2 plans

SFUD



IMPT

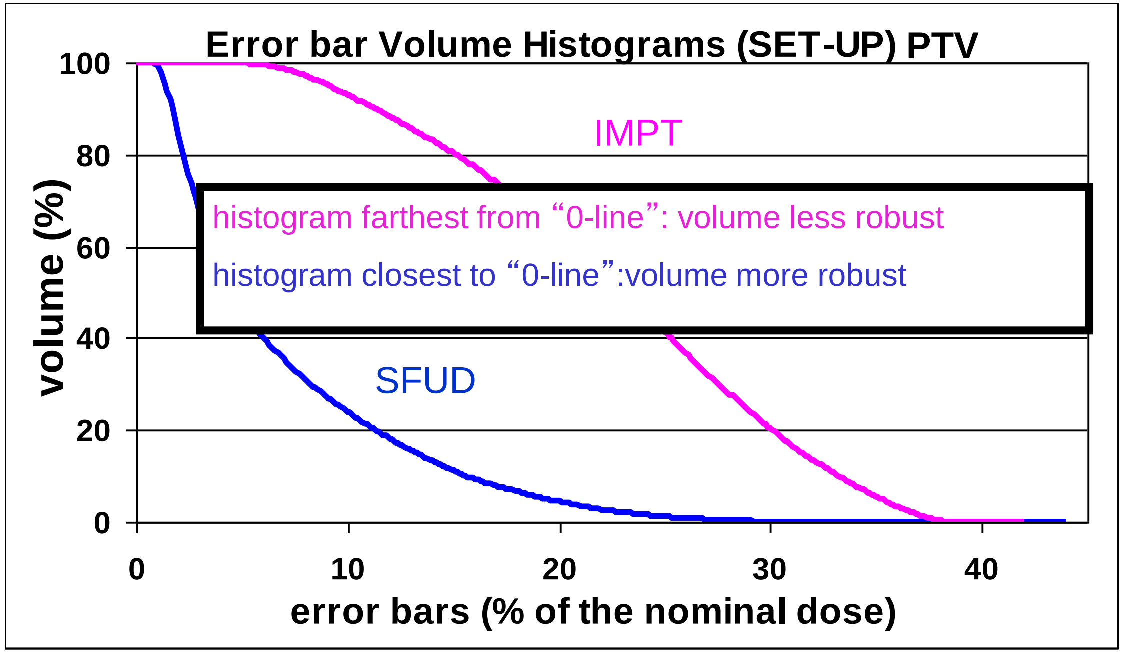


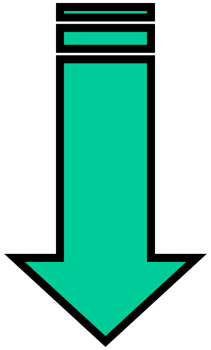
SFUD much more robust in the target area than IMPT (BUT brainstem less robust than for IMPT!)

Albertini F et al, 2011 PMB

From Max-to-min distribution it is possible to extract

Error –Bar Volume Histograms and Metrics

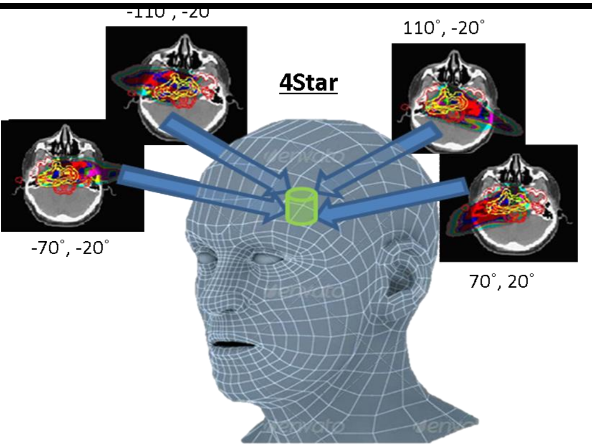




Creation of ‚ plan robustness‘ DATABASE case specific

Evaluating uncertainties: ROBUSTNESS DATABASE

For a standard indication it is necessary to retrospectively analyse the robustness of IMPT/SFUD treatment plans to set-up and/or to range errors (e.g. skull base case)



Example of Robustness DATA-BASE for IMPT plans for skull base

VOI	Mean range	Mean setup	Max range	Max setup
Brainstem	1.75 - 2.2%	4.8 - 7.8%	8.1 - 11.6%	15 - 22%
Chiasm	1 - 2%	6 - 9%	7 - 12.7%	17 - 25%
CTV	1 - 1.2%	8.2 - 15%	2 - 4.5%	13.65 - 18.5%

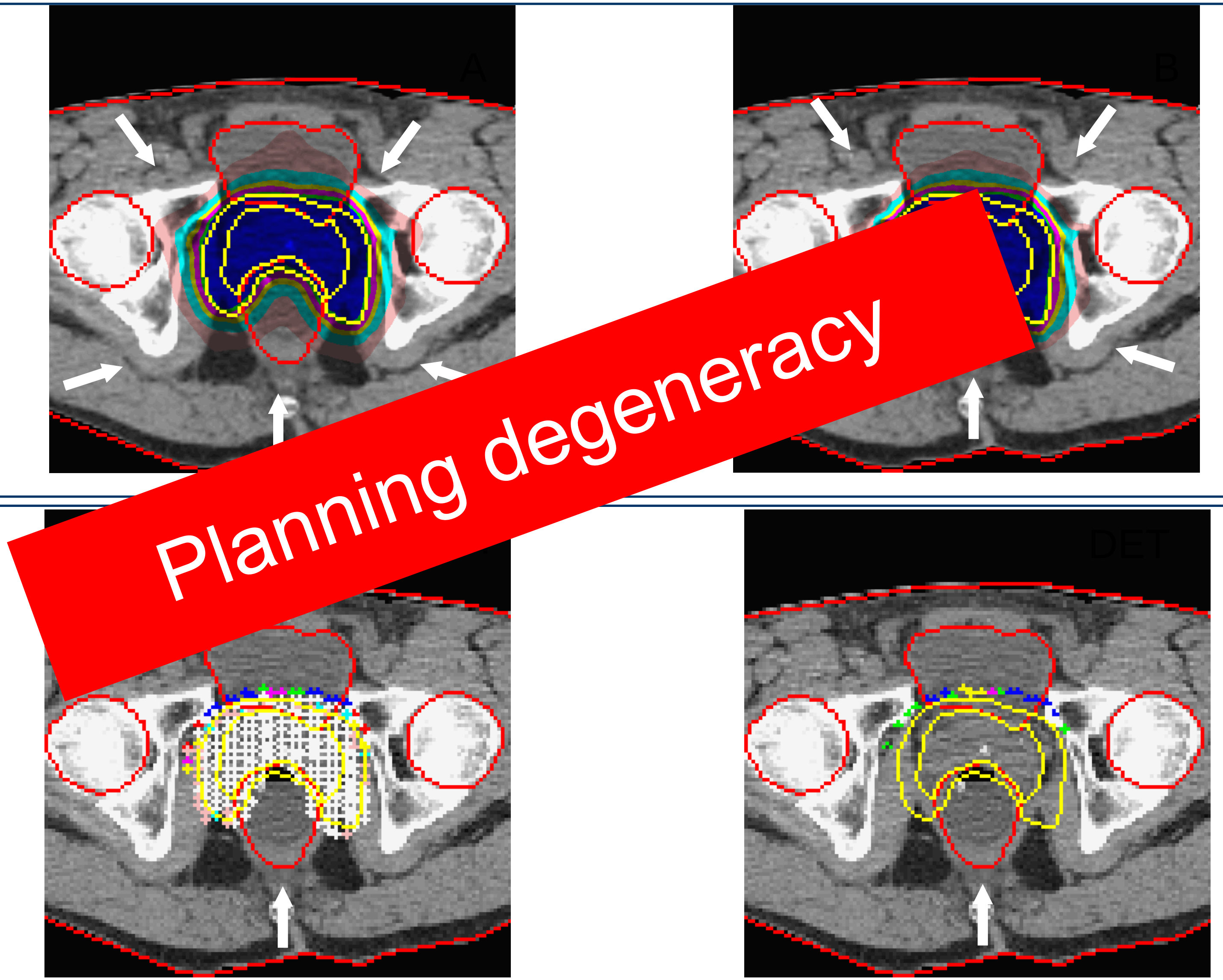
Upper and lower percentage errors as guidelines for the planner for the selection of A NEW PLAN in each VOI based

McGowan S and Albertini F to be submitted

Spot weight degeneracy in IMPT

There's more than one way to optimize an IMPT plan…(ex. 2)

Two examples of 5 field IMPT dose distributions



Corresponding fluences distributions from field 0

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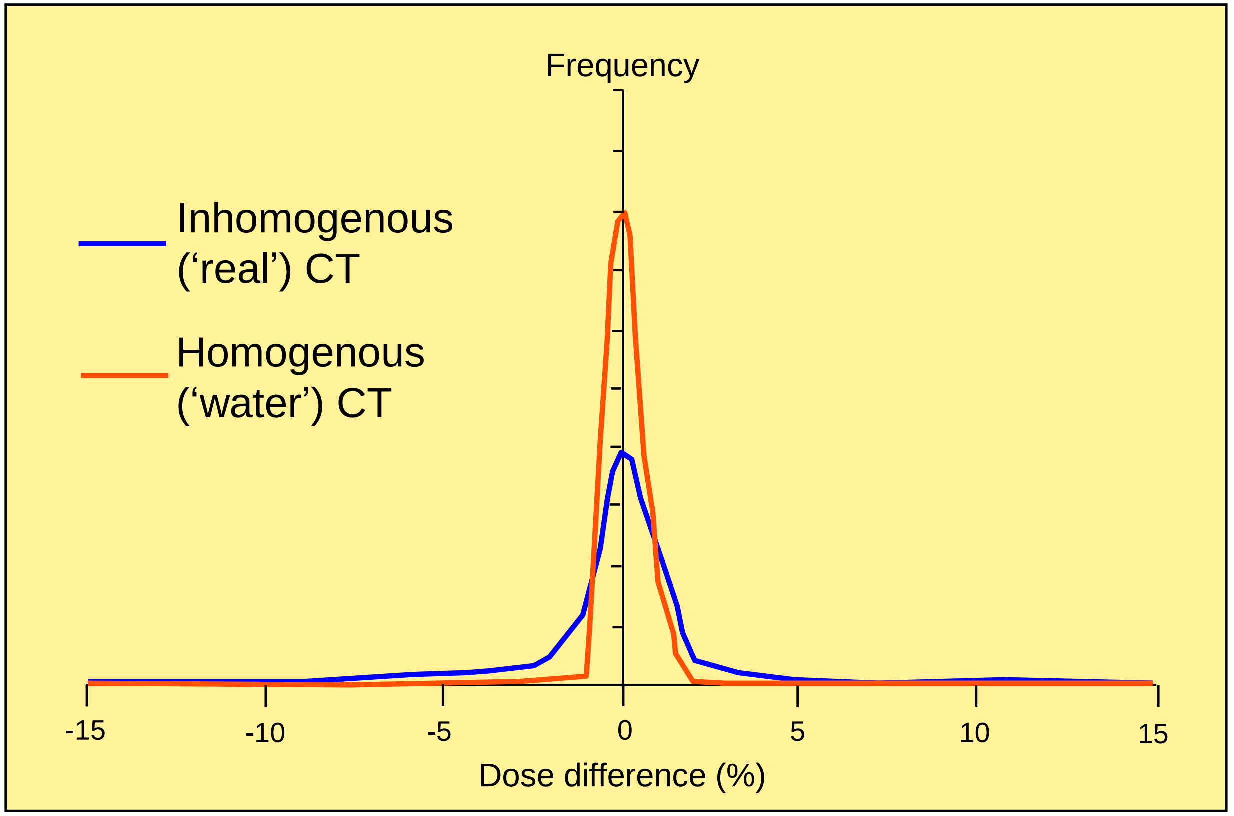
2. Sensitivity to set-up errors

Difference histograms between nominal and recalculated doses on repeat CT

- Dose recalculated on repeated CT after positioning correction (**In-**homogenous)
- Also recalculated on homogenous CT, with all voxels set to water (homogenous)



Alessandra Bolsi & Stefania Comi, PSI/IEO