Treatment Planning Systems for Proton Therapy

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Optimization of Medical Accelerators school

8th June 2017

Basic radiotherapy physics

- Radiation beams interact with material inside the body causing ionisations which lead to cell DNA damage.
- The radiation dose deposited in the medium is measured in units of Gray.
  - 1 Gray = 1 Joule/kilogramme
- We aim to deposit dose within the tumour to cause the maximum damage, while sparing the surrounding tissue.
- In external beam radiotherapy we…
  - generate a radiation beam,
  - modify it to suit our needs,
  - and (carefully) aim it at the patient

} The basic purpose of treatment planning systems

Rationale for Proton Therapy

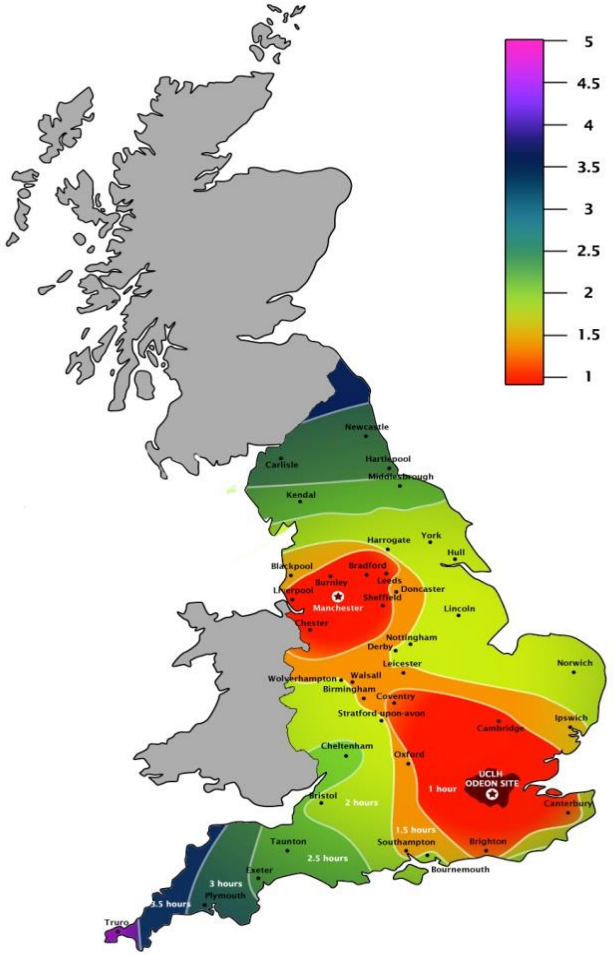
- No exit dose past the target volume being treated
  - **The most important proton property**

- Reduce morbidity (including integral dose & second malignancy)
  - A major motivation in most paediatric indications

- Dose escalation
  - Can increase curative treatment options
  - A major motivation in current adult indications

National Proton Therapy Service

- Two NHS proton developments
  - The Christie (Manchester)
    - Due to open August 2018
  - UCLH (London)
    - Due to open 2020
- Each centre aiming to treat ~750 patients per year.
- Currently referring patients overseas for proton therapy.



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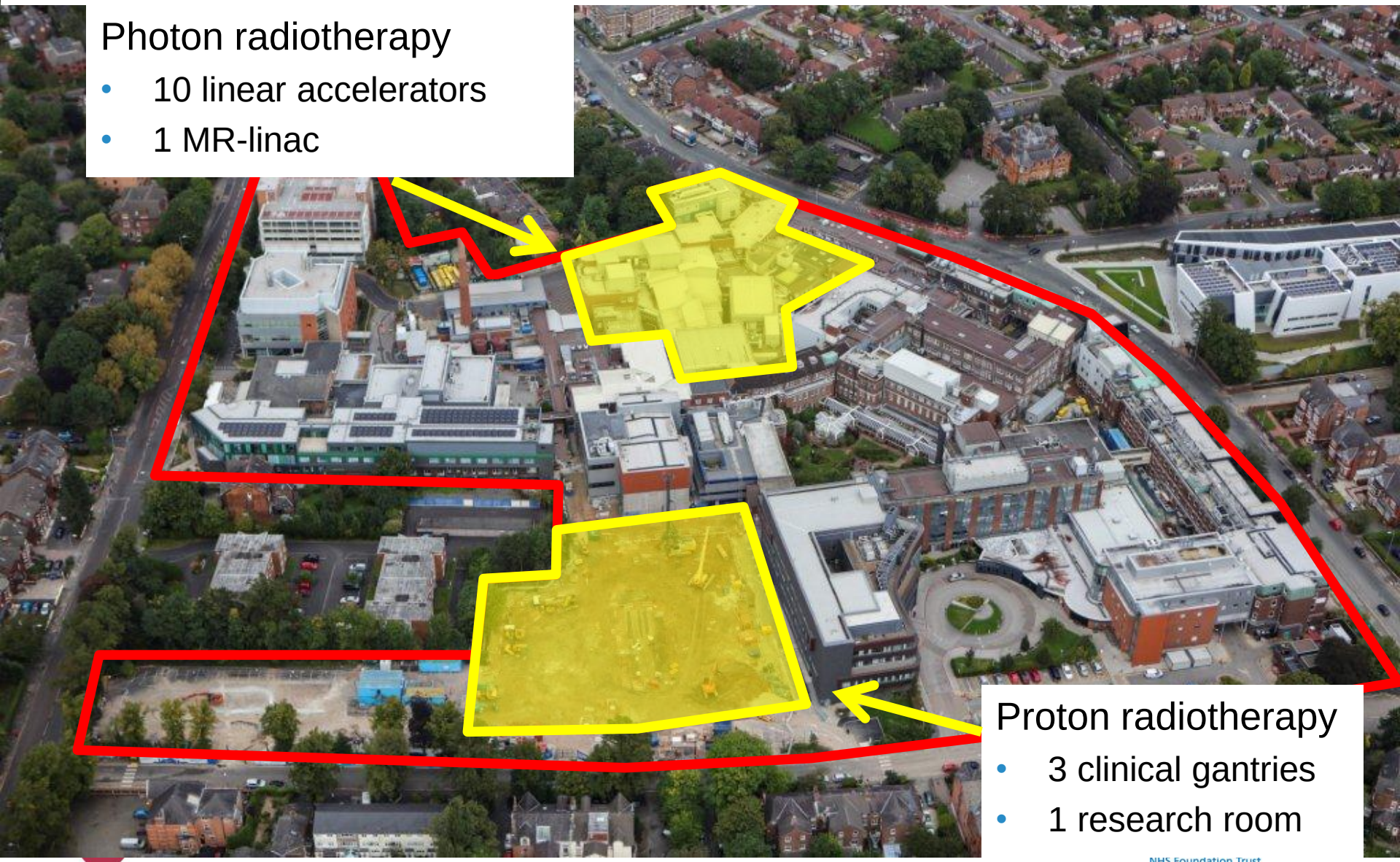
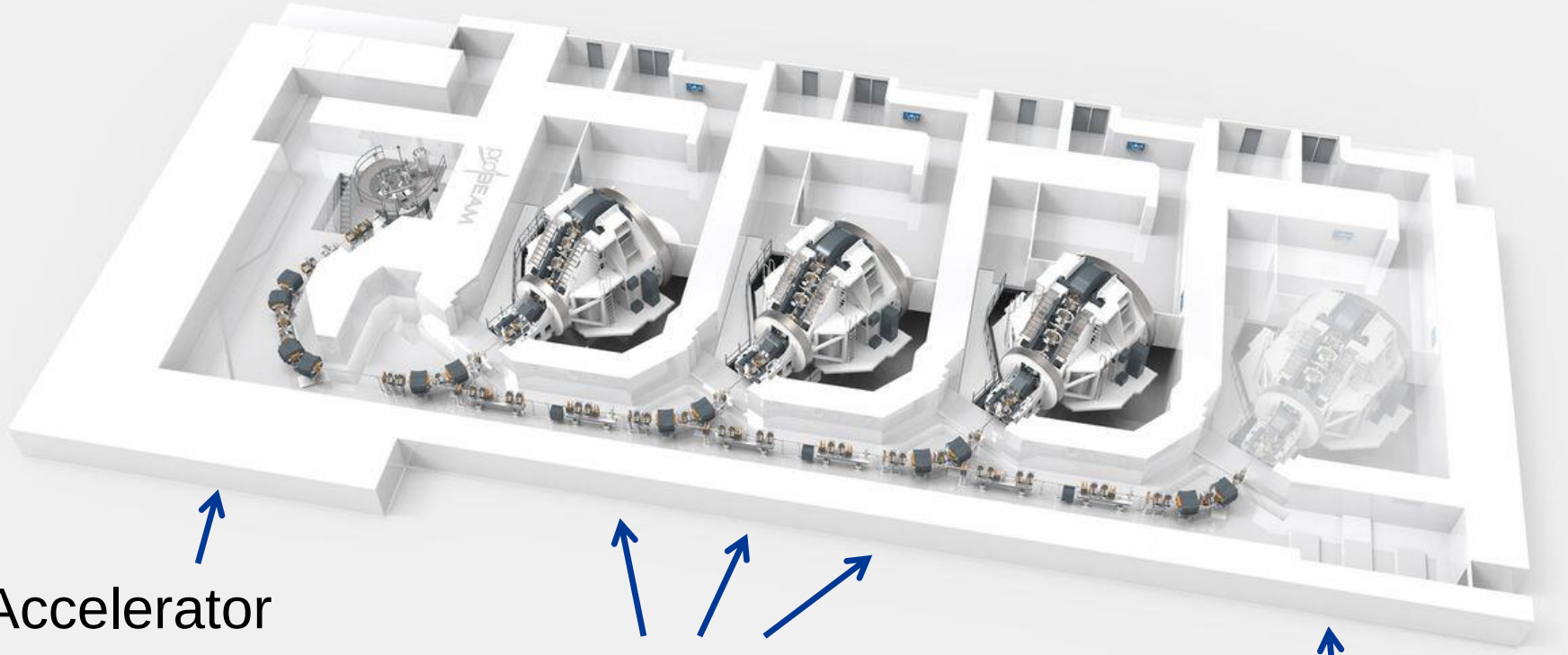
The Christie

(Photo taken early 2016)



Layout of the proton service at the Christie



Accelerator

- Cyclotron
- On schedule for June 2017 delivery

3 treatment rooms

- Varian ProBeam systems
- 360˚ gantries
- Pencil beam scanning

Research room

- For use outside clinical hours

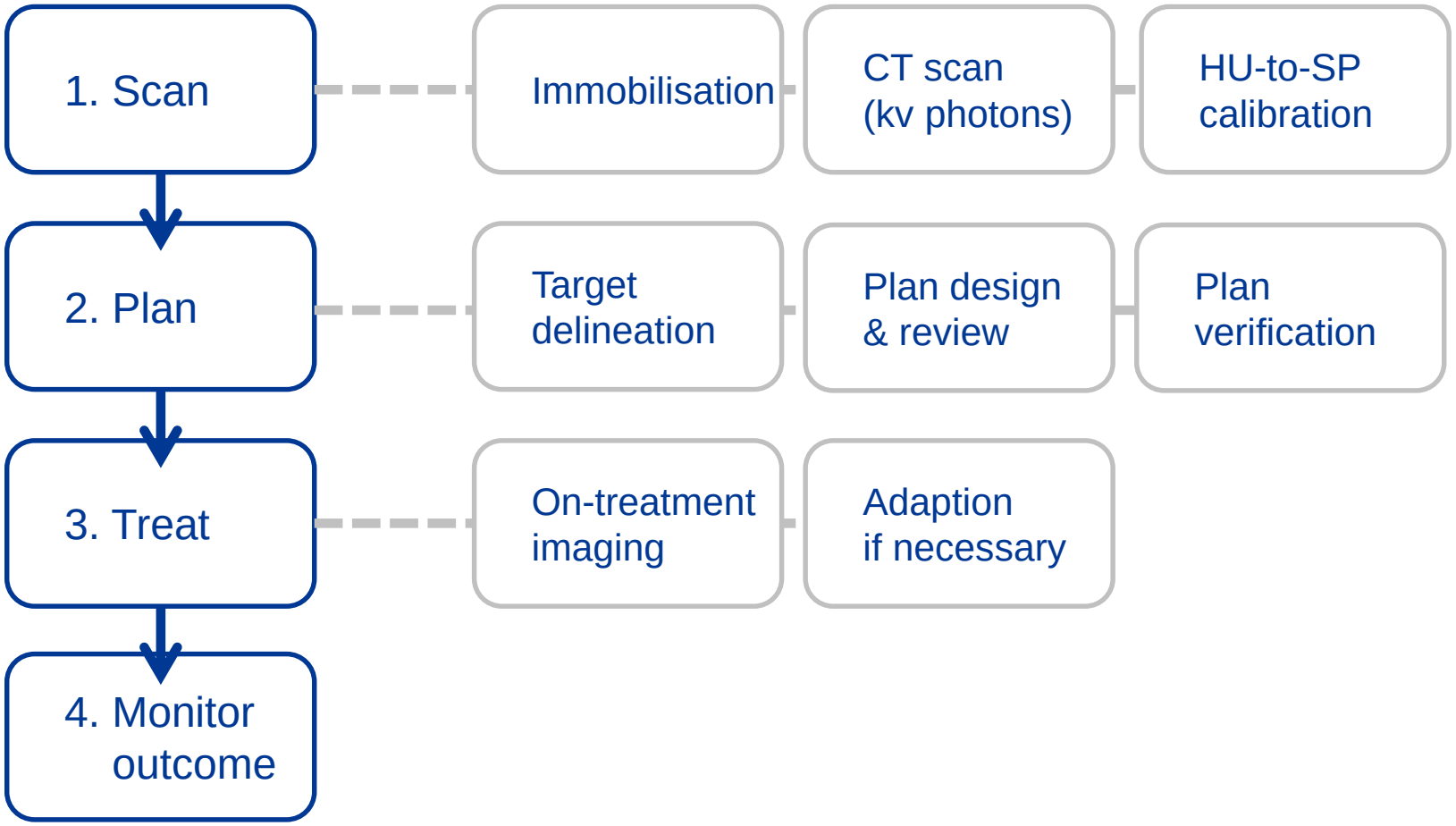
Treatment Planning Systems for proton therapy

- Commercial TPSs:
  - Elekta – XiO
  - Philips - Pinnacle3
  - RaySearch Laboratories – RayStation
  - Varian - Eclipse

v13.7 in use at the Christie

- In-house TPSs:
  - Massachusetts General Hospital – Astroid
  - Paul Scherrer Institut - PSIPlan

The treatment process



1. Scan
2. Plan
3. Treat
4. Monitor outcome

Immobilisation

- The patient is immobilised on the treatment couch.
  - Thermoplastic masks
  - Tattoo dots / semi-permanent skin marks for alignment with in room lasers.
  - Couch tops with adjustable head / arm rests
  - General anaesthetic may be required in small number of cases. (Typically ~ 10% of paediatrics)

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1. Scan
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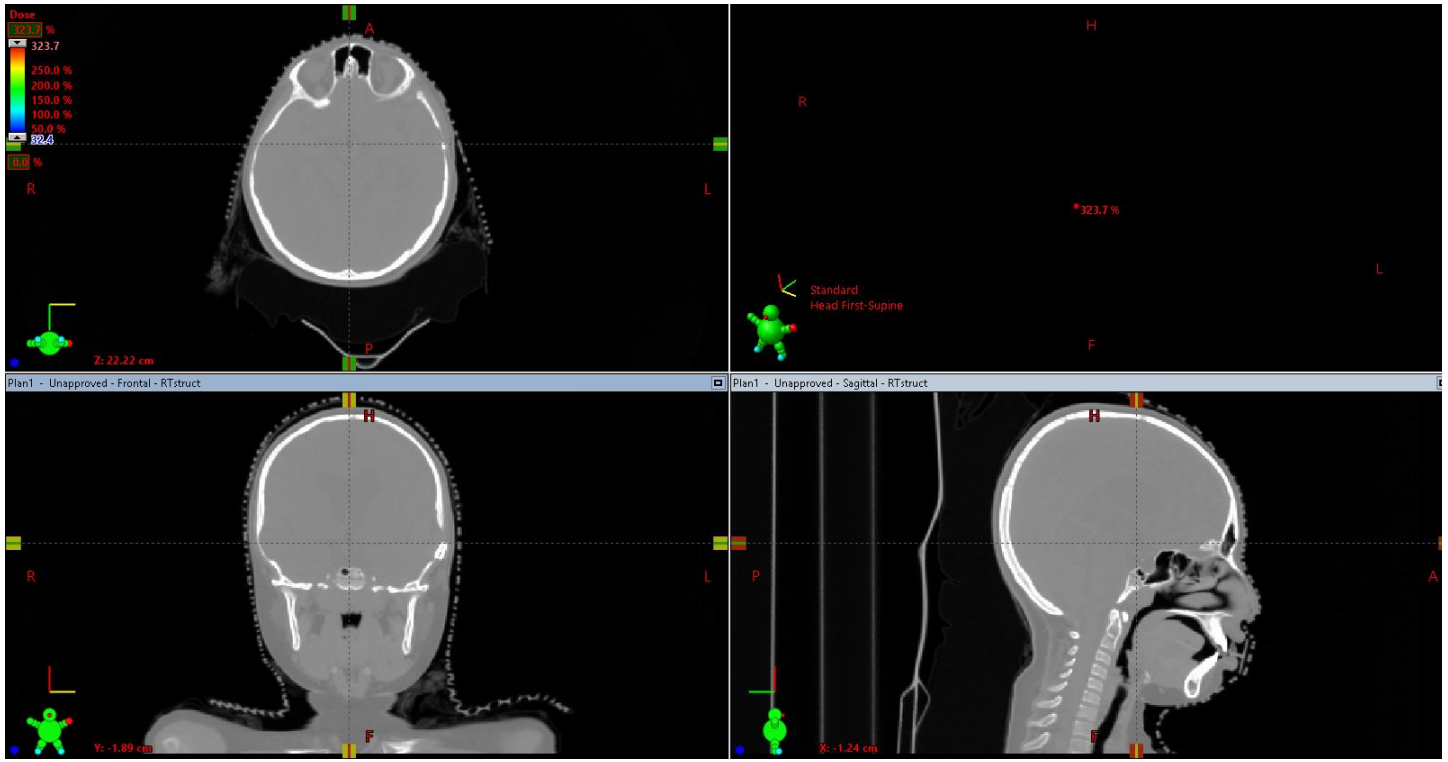
CT scan of patient

- A kV photon CT scan of patient is acquired in the treatment position.
- This is used for:
  - Target/organ delineation
  - Dose calculation.



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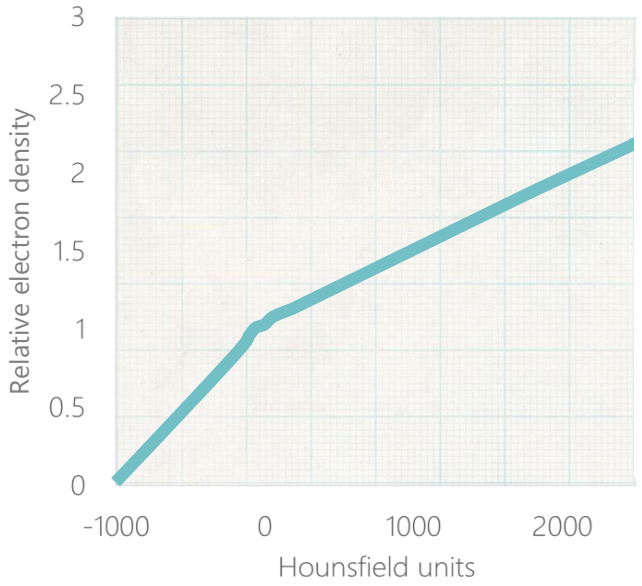
CT calibration: For MV photon therapy

- Photon interactions are primarily with electrons:
  - Photoelectric effect (dominates ~10-25 keV)
  - **Compton scatter** (dominates ~25 keV - 25 MeV)
  - Pair production (dominates ~>25 MeV)
- A calibration mapping Hounsfield Units to **relative electron density** is derived.
- This is then used to calculate dose deposited by the proton beam.



CT calibration: For proton therapy

1. Scan
2. Plan
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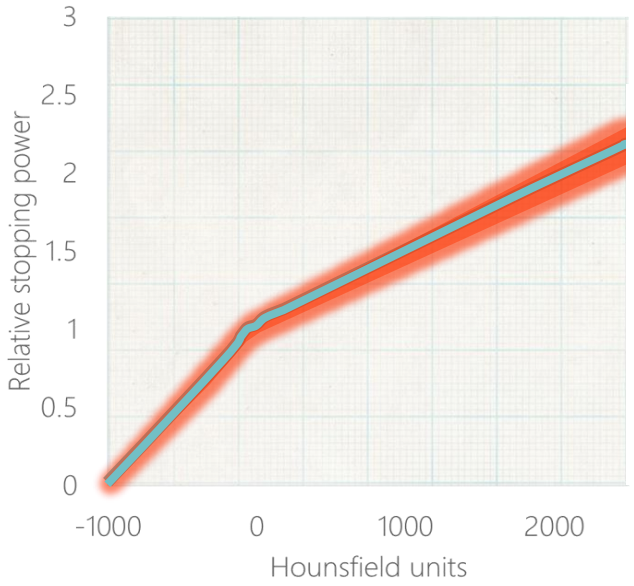
4. Monitor outcome

- Proton interactions are by:
  - Coulomb interactions with orbital electrons
  - Coulomb interactions with nuclei
  - In-/Non- elastic interactions with nuclei
- A calibration mapping Hounsfield Units to **relative proton stopping power** is derived.
  (Stoichiometric method is typically used - see Schneider et al. 1996.)
- This is then used to calculate dose deposited by the proton beam.
- Uncertainty arises because imaging and treatment use different particles.

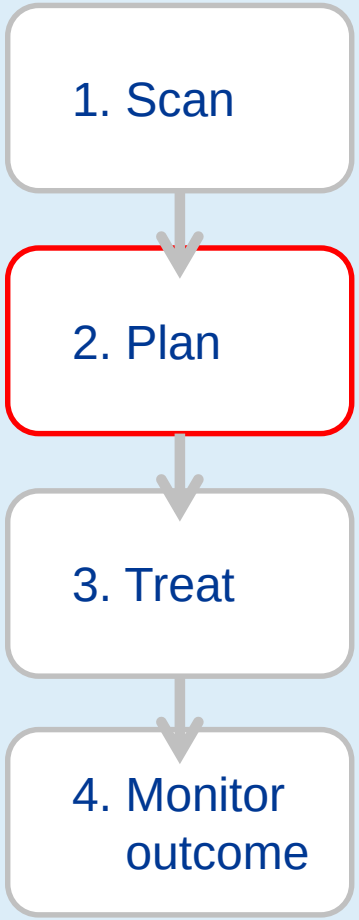


Treatment planning

1. Scan
2. Plan
3. Treat
4. Monitor outcome

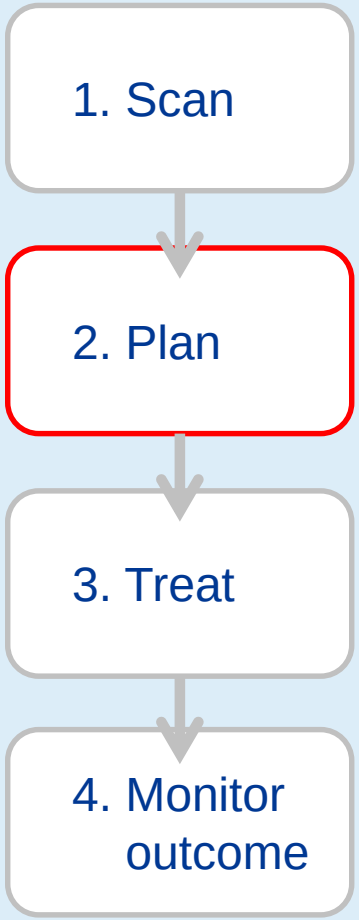
Planning aims

1. To deliver prescribed dose to the target volume
2. To minimise the dose to other tissues



Target definition

There are several classes of target:



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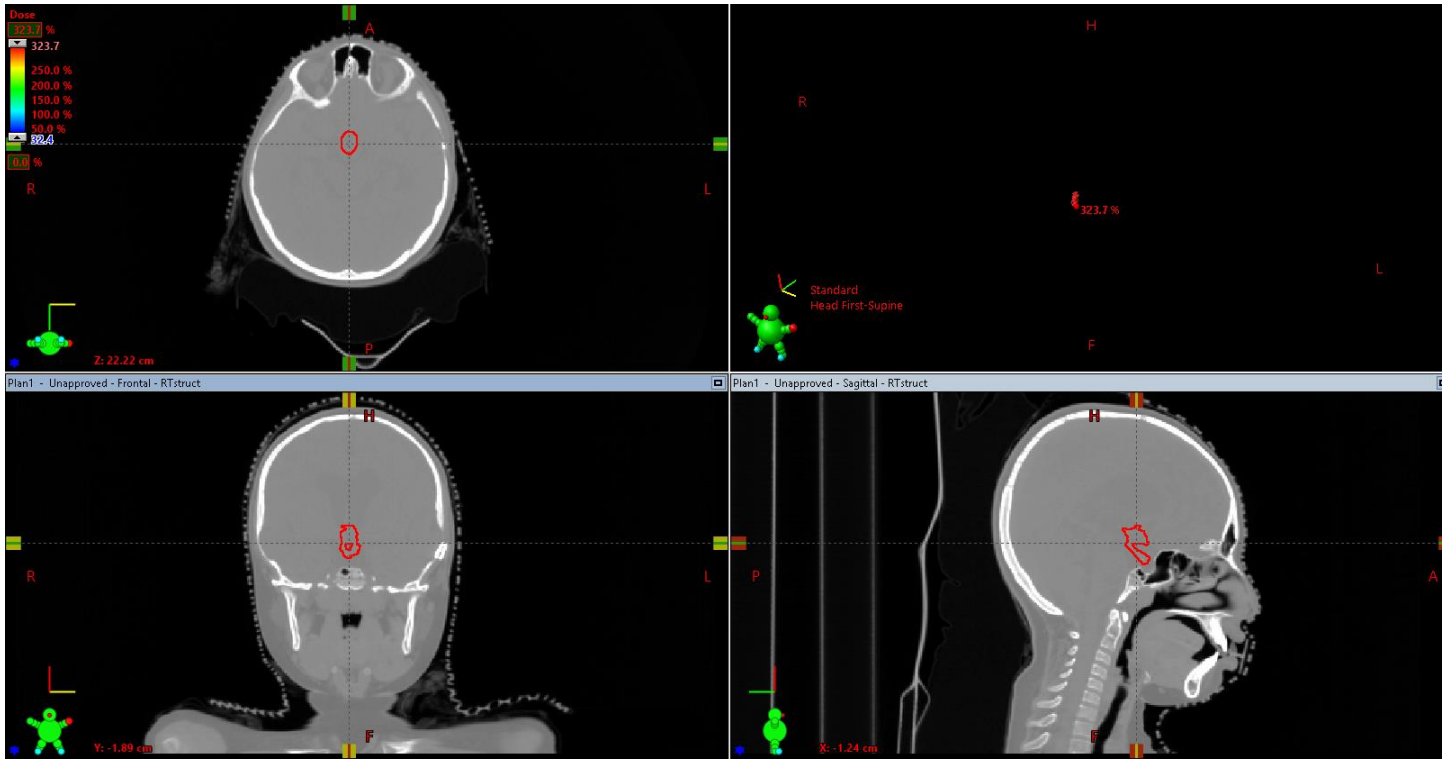
Target definition

There are several classes of target:

GTV – Gross tumour volume
– Defines the visible tumour.



1. Scan
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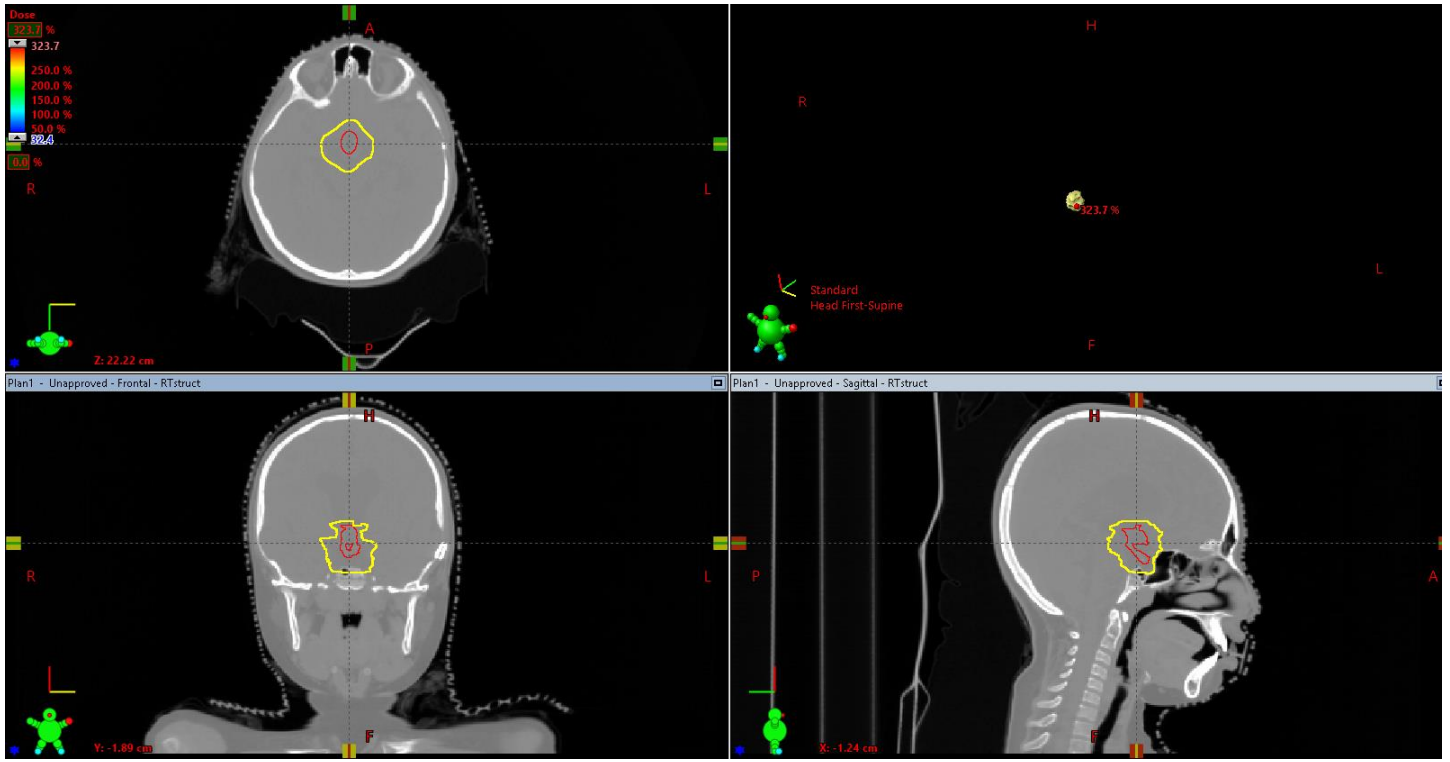
Target definition

There are several classes of target:

CTV
- Clinical target volume
- Defines where there may be tumour cells which are not visible on scans.



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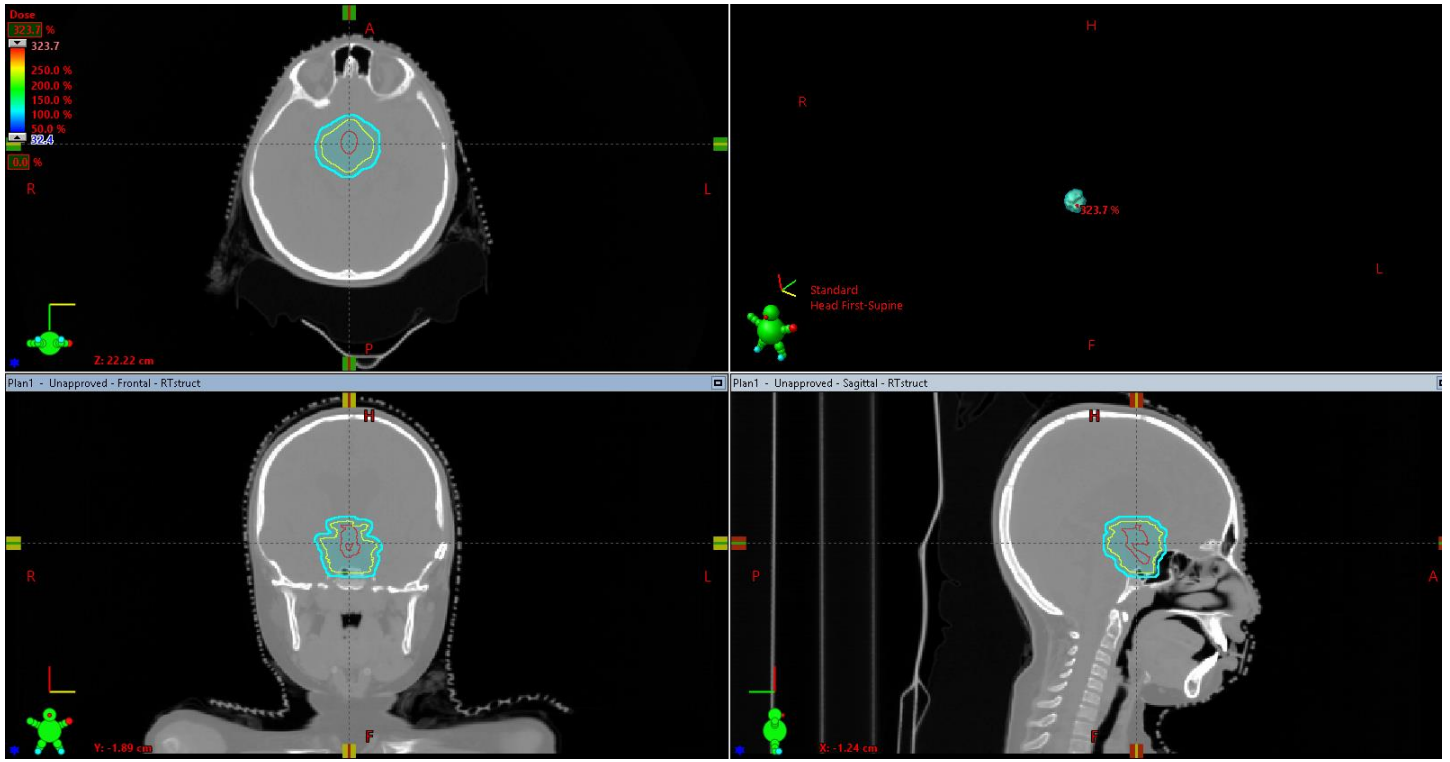
Target definition

There are several classes of target:

PTV
- Planning target volume
- Defines the volume to be treated to ensure coverage of the GTV and CTV.
- For an analysis of appropriate margins, see Van Herk et al (2000)



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Organs-at-risk (OARs)

OARs can be classed as:

Serial
- If part of the organ is damaged then the organ may lose all function.
- E.g. Spinal cord
- Typically limit the max dose to the OAR.

Parallel
- If part of the organ is damaged then the remaining part of the organ may continue to function.
- E.g. Kidneys.
- Typically limit the volume of OAR receiving a given dose.

1. Scan
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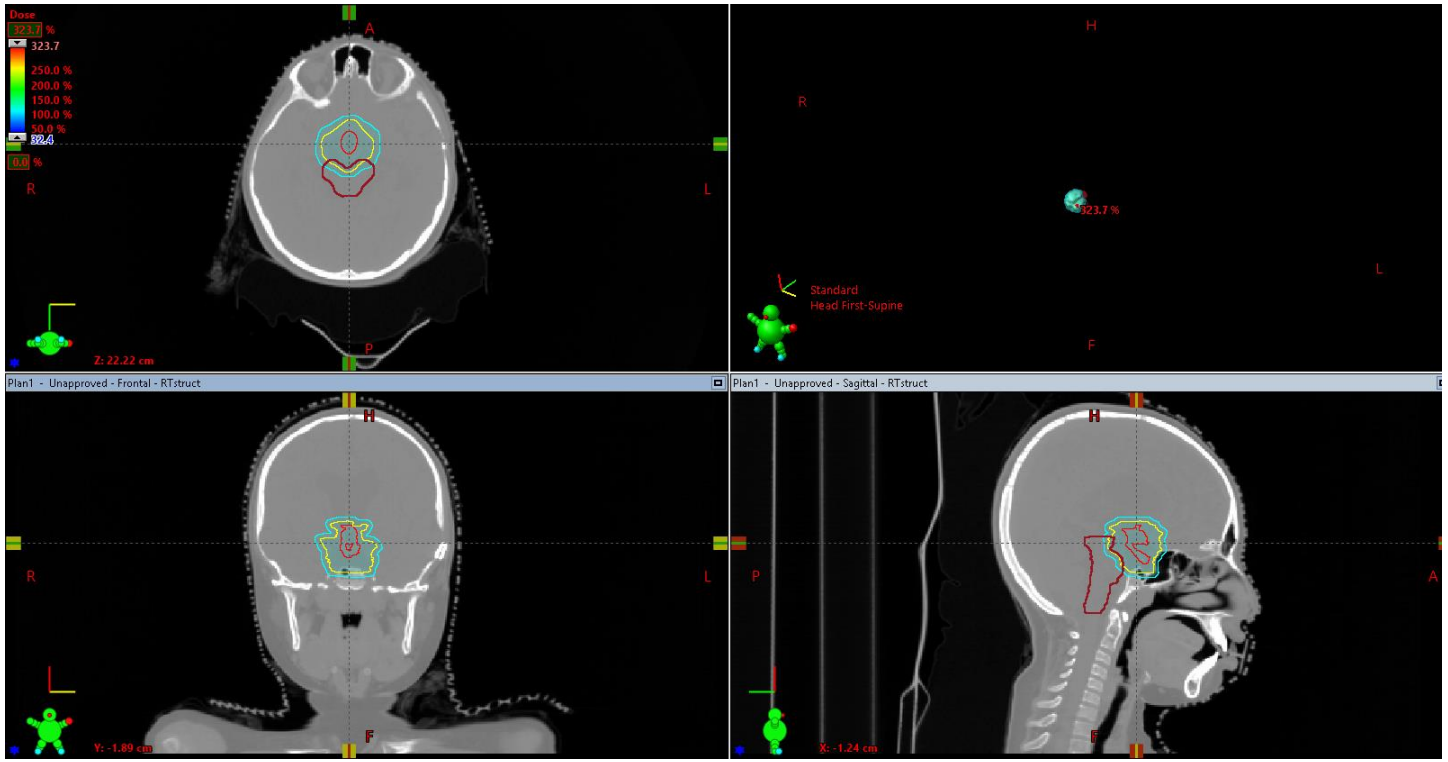
Organs-at-risk (OARs)

Example: Brainstem adjacent to target

- A maximum allowed dose of ~54 Gy is typical



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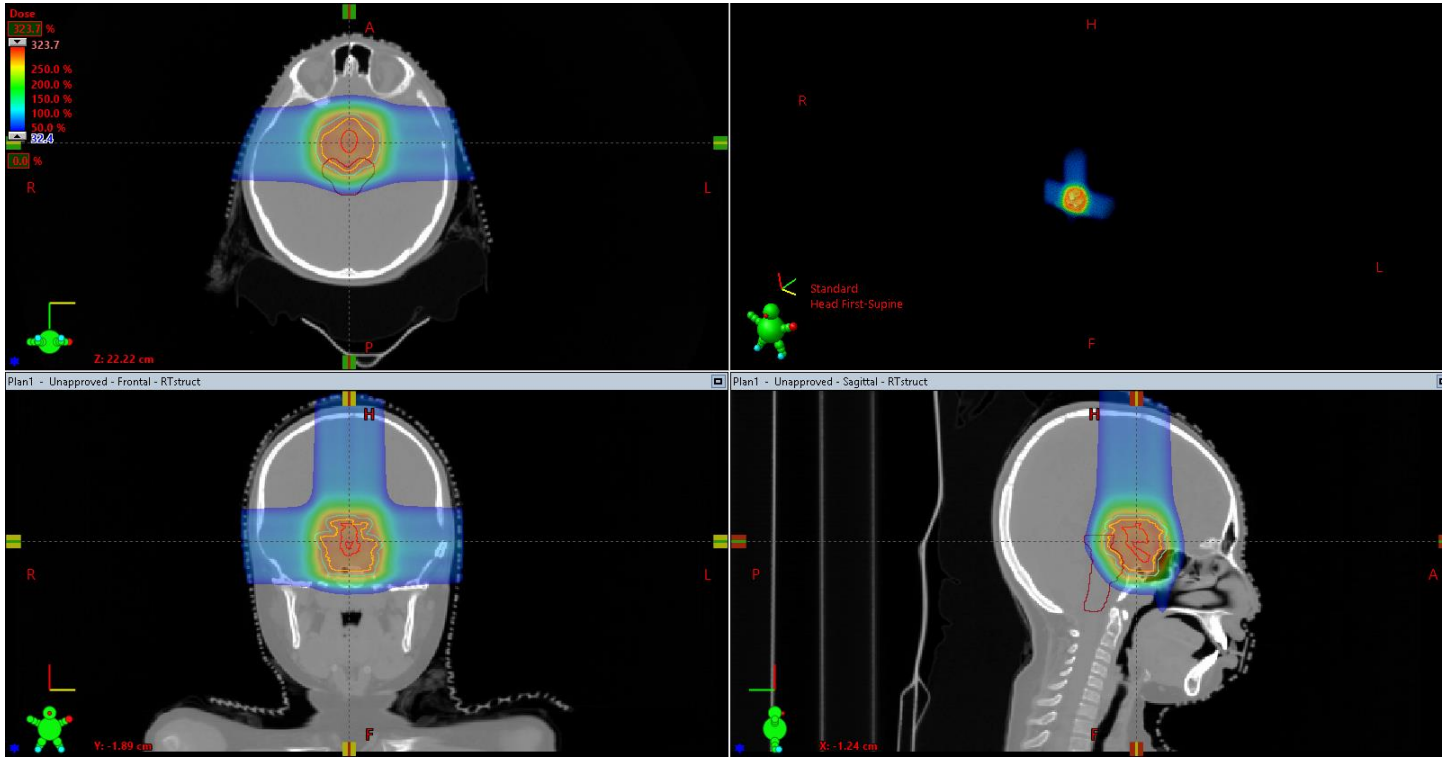
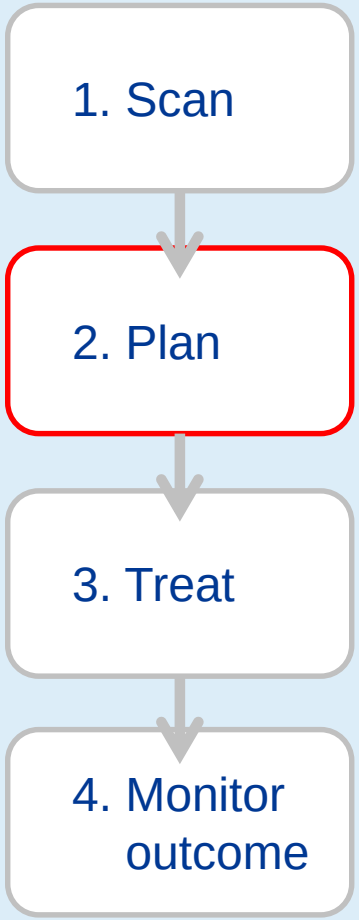
Planning

Example:

- 3 field plan
- Delivers prescribed dose to target
- Dose to adjacent OARs minimised.





Planning technique

- Dependent on:
  - Anatomy of targets and OARs
  - Type of cancer
  - Delivery technology
  - On-treatment imaging technology
  - Treatment planning system features
  - Department protocols

1. Scan
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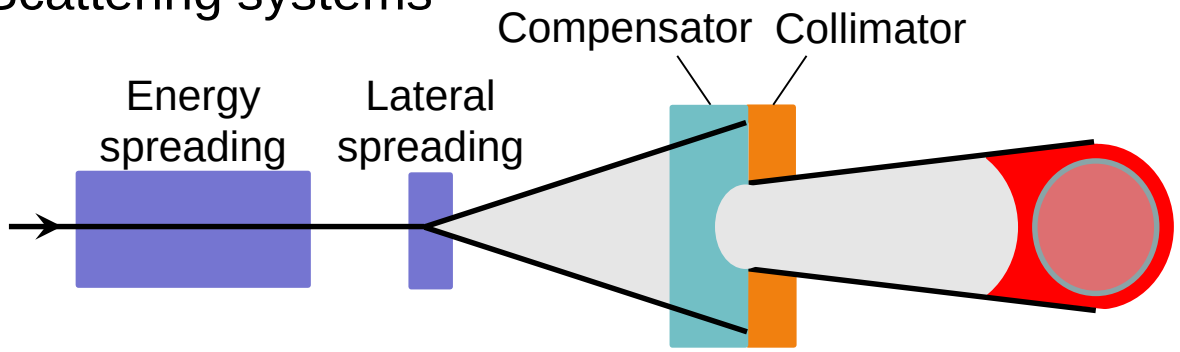
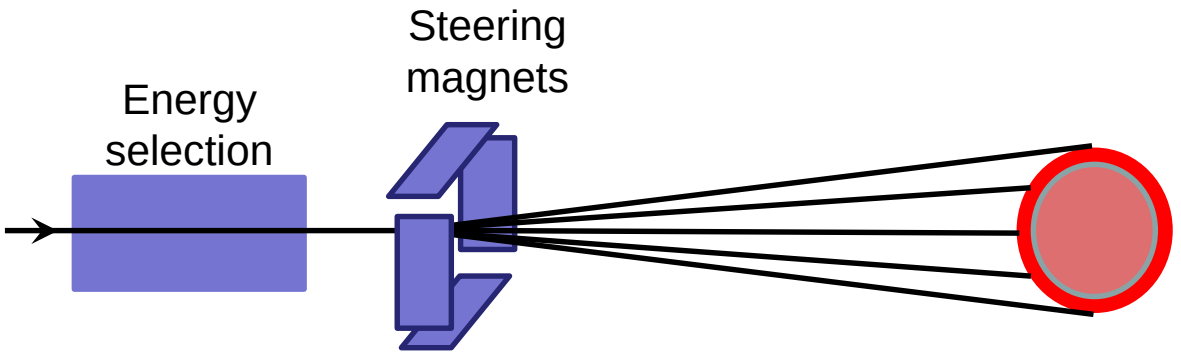
Proton delivery technologies

Scattering systems



Pencil Beam Scanning (PBS) systems



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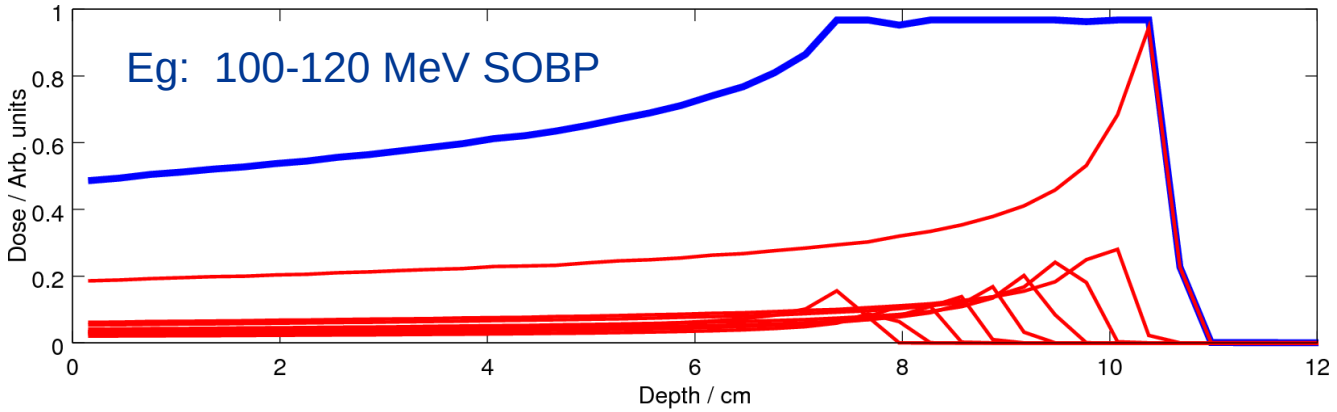
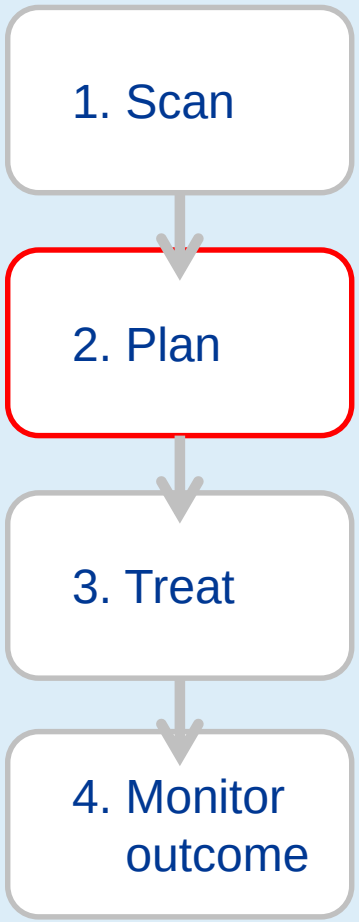
Recap: The Bragg peak

- In 1D, multiple Bragg peaks are added to form a Spread-Out-Bragg-Peak (SOBP)



- Pencil Beam Scanning (PBS) effectively does this in 3D.
- The TPS is used to
  - Determine the spot positions
  - Compute the optimal spot weightings.

PBS planning basics



- Inverse planned
- PTV and OAR objectives
- Discrete beam angles (i.e. not arcs)
- Typically 1-5 fields per plan
  - Mean number of fields is ~2.5
- Beams are not necessarily coplanar

Similar to step-and-shoot photon IMRT

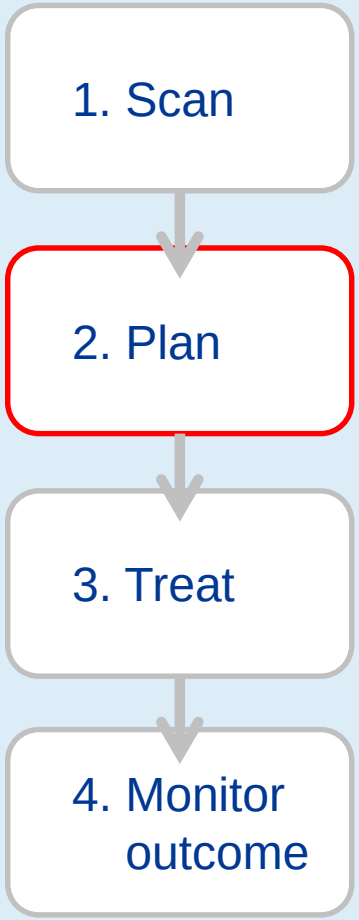
Different from photon IMRT

- Parameters configured during planning:
  - Technique
  - Objectives
  - Beam angles
  - Beam modifiers (range shifters, etc.)
  - Spot positions
  - Spot weights

Defined by the planner

Computed by the optimiser

PBS planning techniques



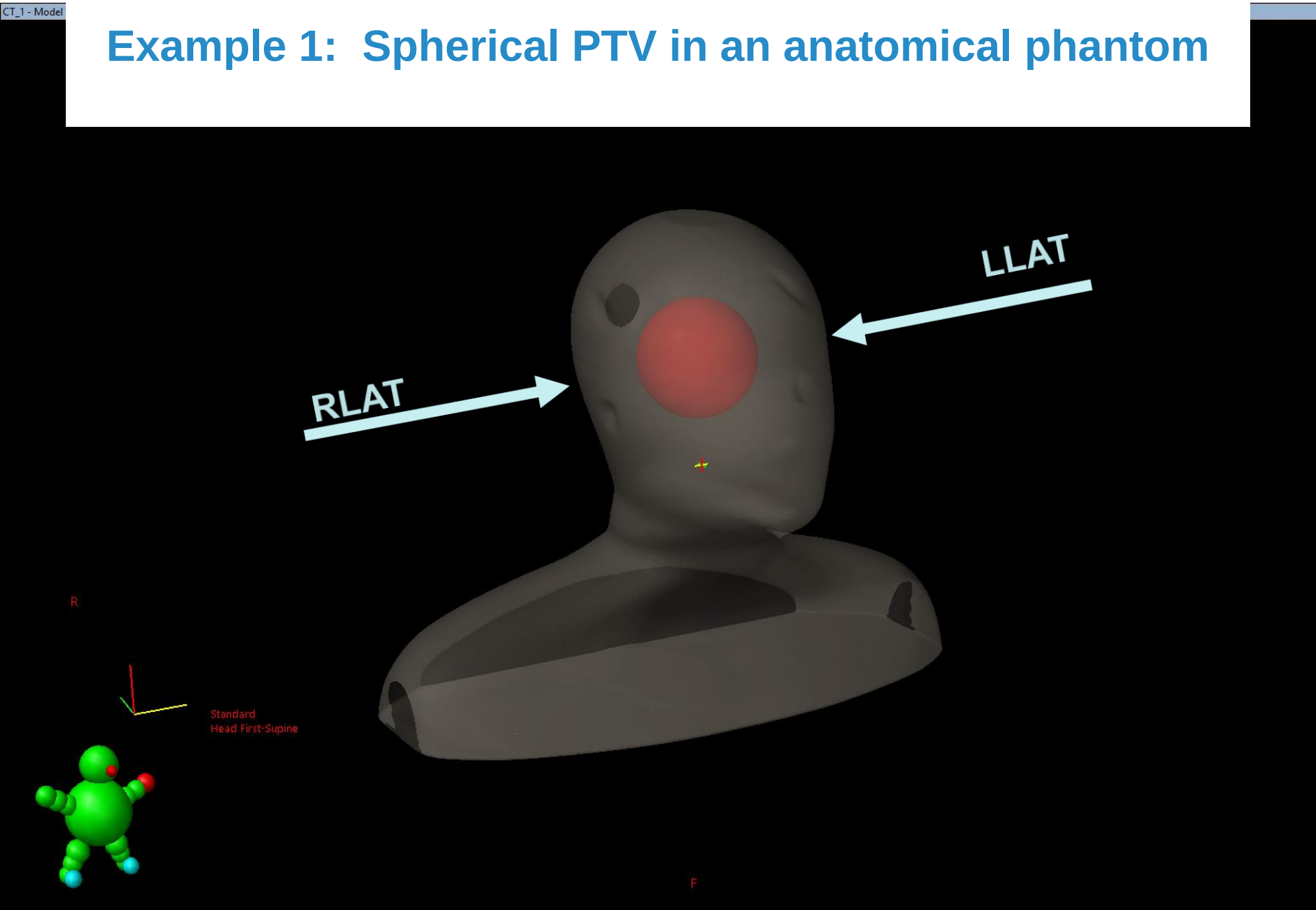
- SFO: Single Field Optimisation

  (or SFUD: Single Field Uniform Dose)

- MFO: Multi Field Optimisation

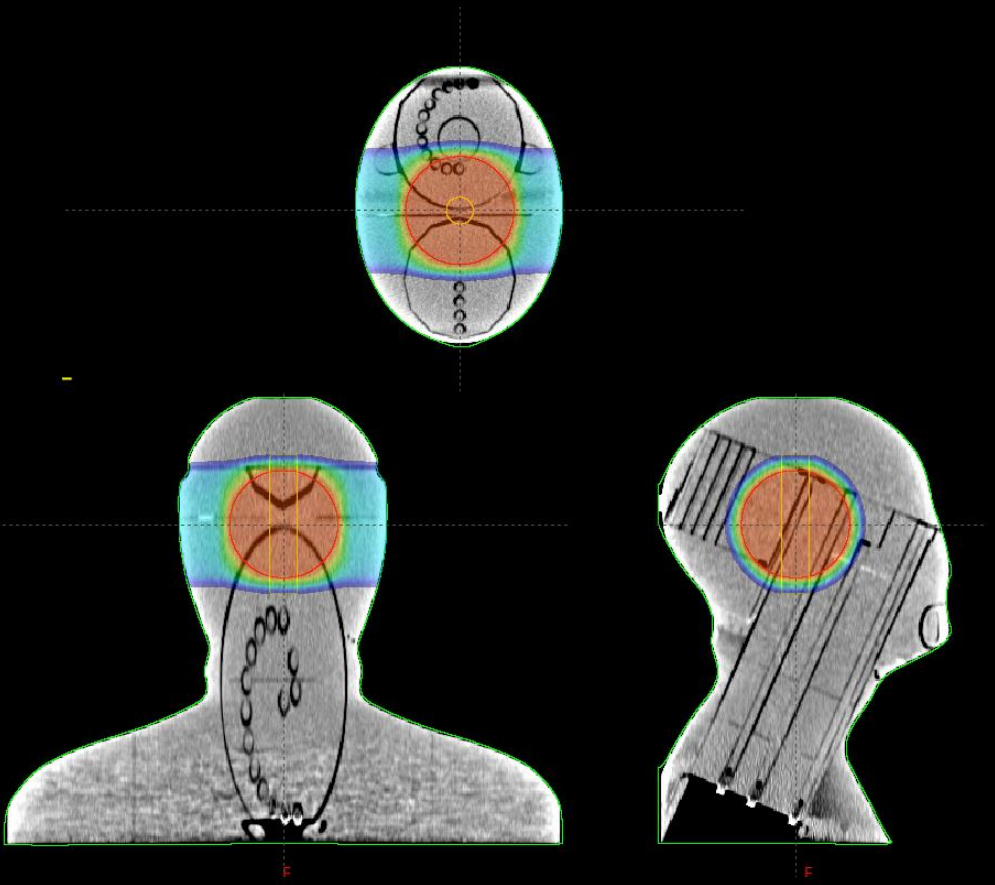
  (or IMPT: Intensity Modulated Proton Therapy)

Example 1: Spherical PTV in an anatomical phantom

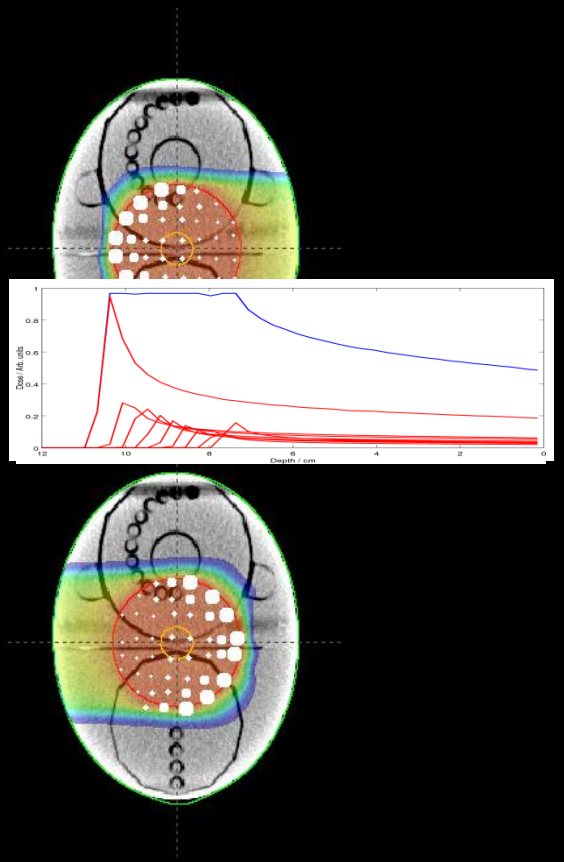


SFO (Single Field Optimisation)

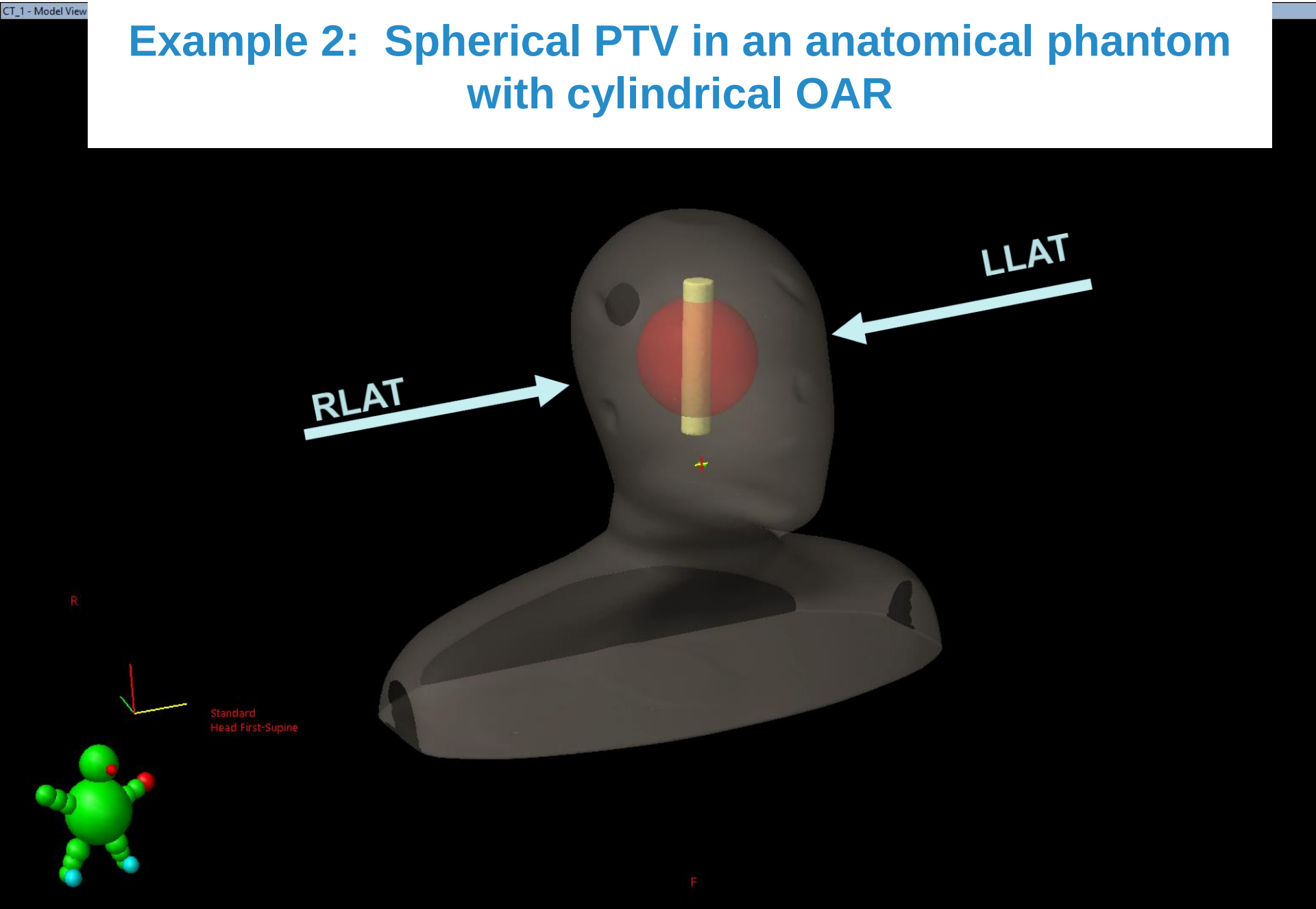
Combined dose



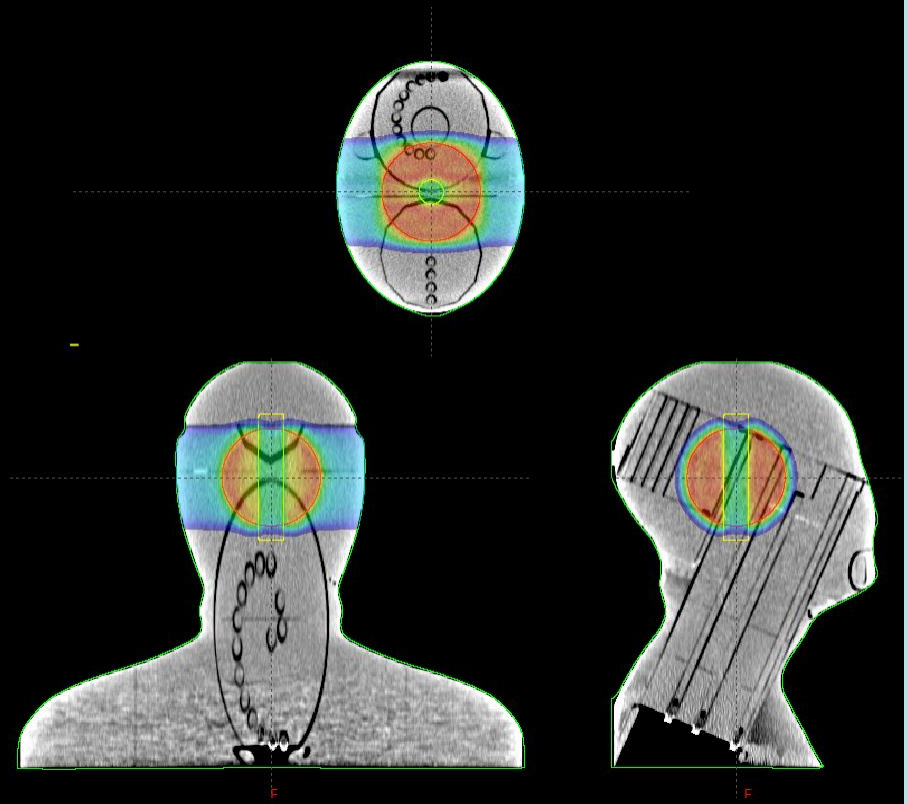
Individual fields



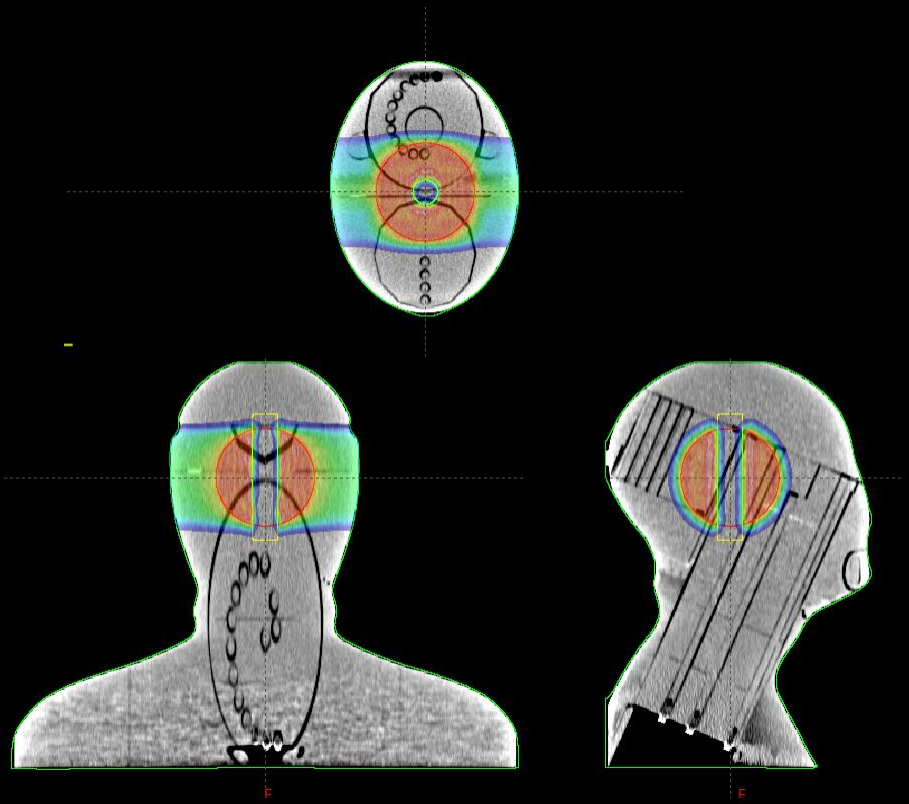
Example 2: Spherical PTV in an anatomical phantom with cylindrical OAR



SFO
(Single Field Optimisation)



MFO
(Multi Field Optimisation)



SFO
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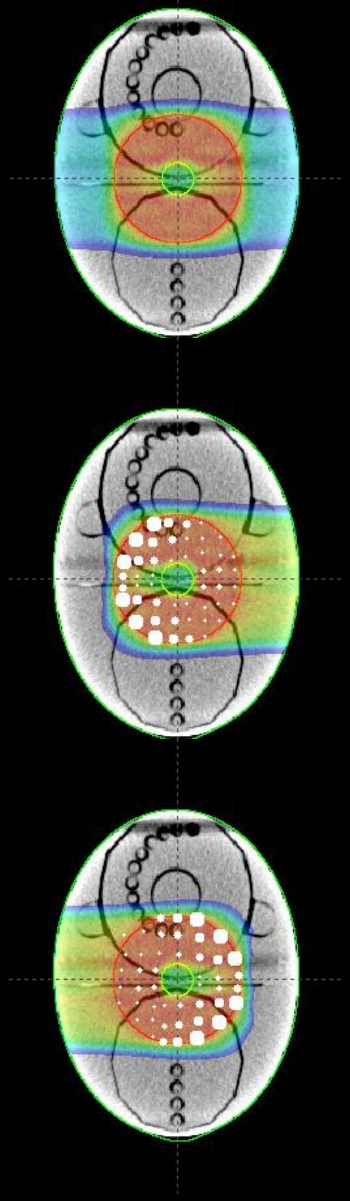
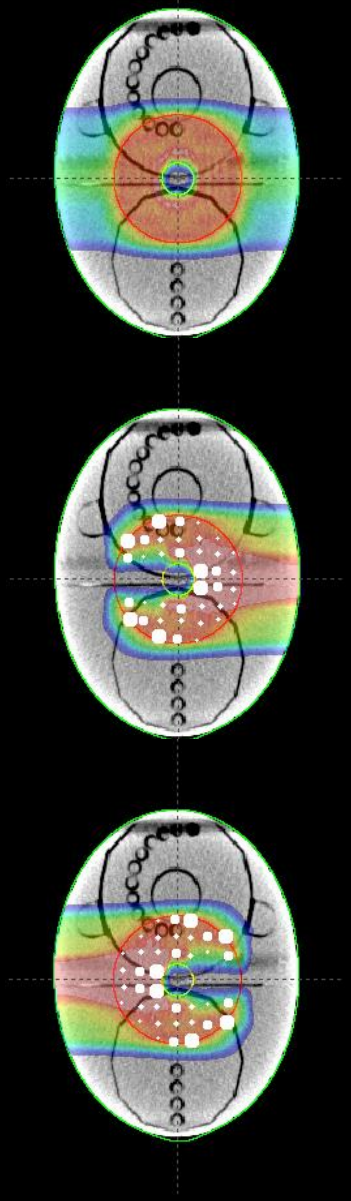
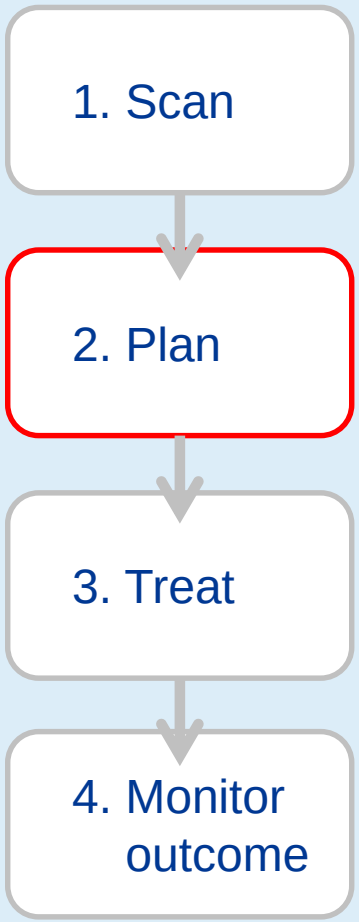


MFO
(Multi Field Optimisation)



Summary: SFO vs. MFO



- Both SFO and MFO are used clinically
- MFO provides more control of the combined dose distribution
  - A uniform dose for each field is not required
  - Only the combined dose distribution must be uniform

→ MFO gives the optimiser more freedom to produce the combined dose in any way it likes.

- Issues:
  - How do we know the optimiser has picked a safe solution?
  - How sensitive are the plans to uncertainties?

1. Scan
2. Plan
3. Treat
4. Monitor outcome

Range uncertainty

- Protons stop in the patient
- How well do we know exactly <u>where</u> they stop?

→ **'Range uncertainty'**

IOP Publishing — Physics in Medicine and Biology
Phys. Med. Biol. **57** (2012) R99–R117 — doi:10.1088/0031-9155/57/11/R99

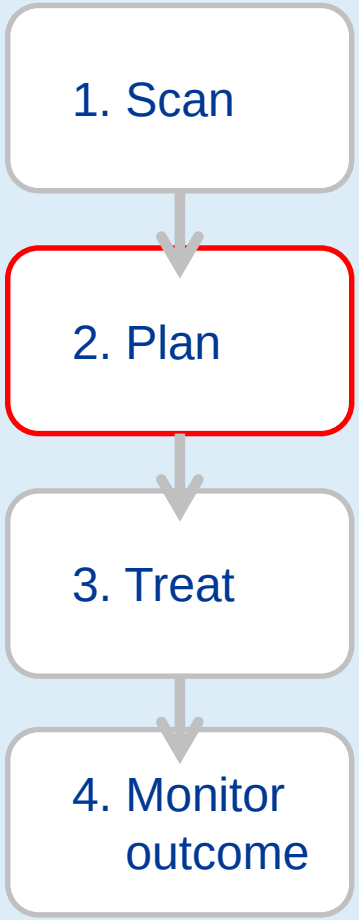
TOPICAL REVIEW

Range uncertainties in proton therapy and the role of Monte Carlo simulations

Harald Paganetti

Total uncertainty: 2.7 - 4.6 % + 1.2 mm

Received 31 October 2011, in final form 21 December 2011
Published 9 May 2012
Online at stacks.iop.org/PMB/57/R99



Clinical sources of range uncertainty

1. CT calibration (and artefacts)
   - Unrelated to patient setup
2. Beam paths passing through inhomogeneities
   - Patient setup
   - Patient motion
   - Gas/liquid in patient cavities
   - etc…
3. Patient anatomy changes from planning scan
   - Weight loss/gain
   - Tumour regression
   - etc…

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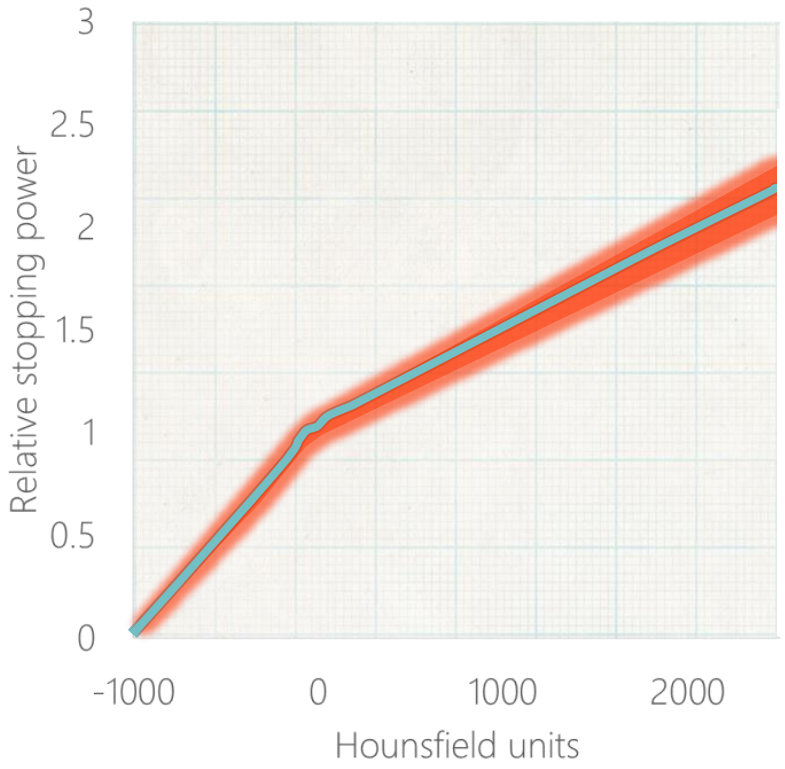
Range uncertainty: 1 – The CT calibration

- Recap: The CT HU-to-stopping power table has an associated uncertainty.

→ This leads to uncertainty in the proton range.



Range uncertainty: 1 – The CT calibration

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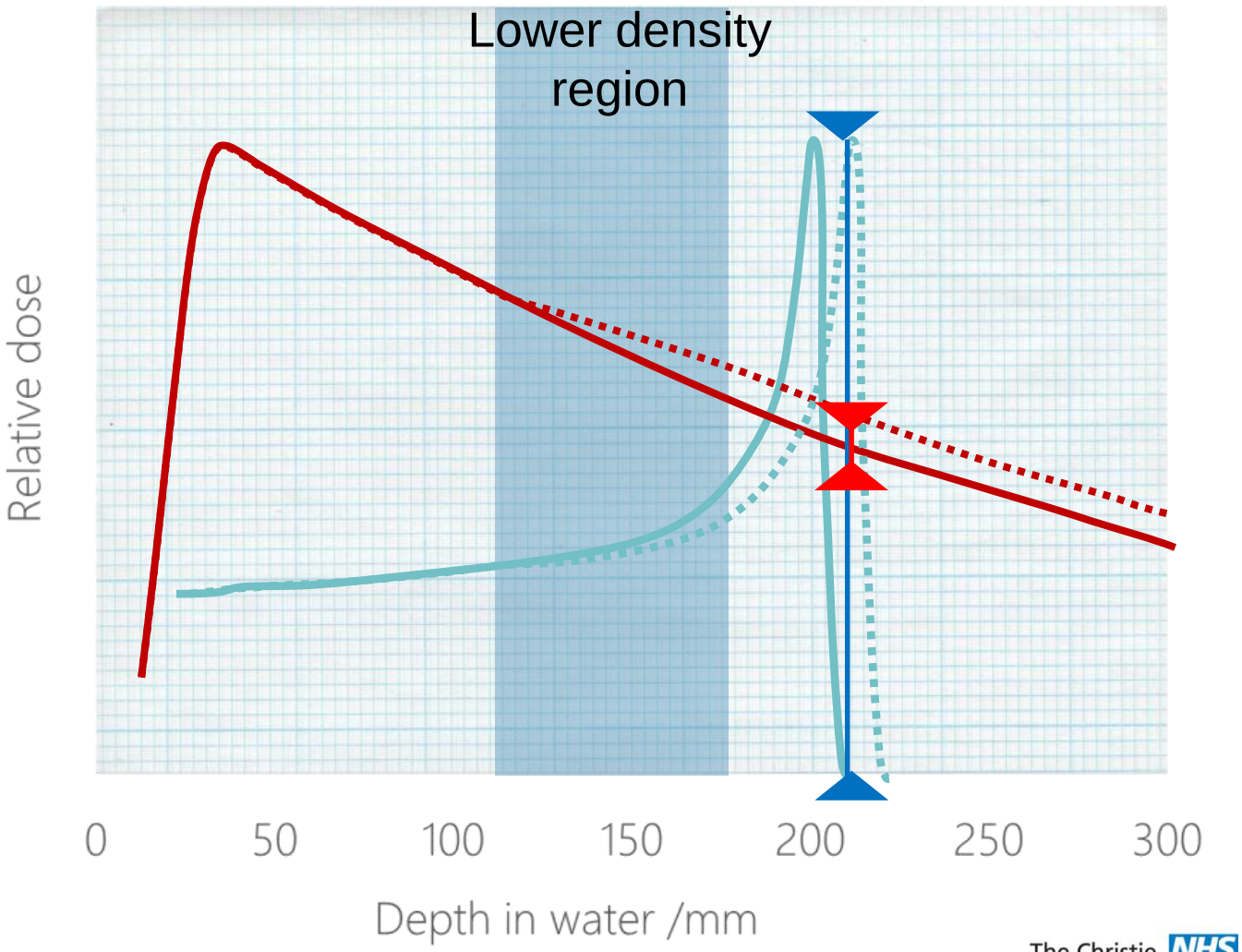

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Range uncertainty: 1 – The CT calibration

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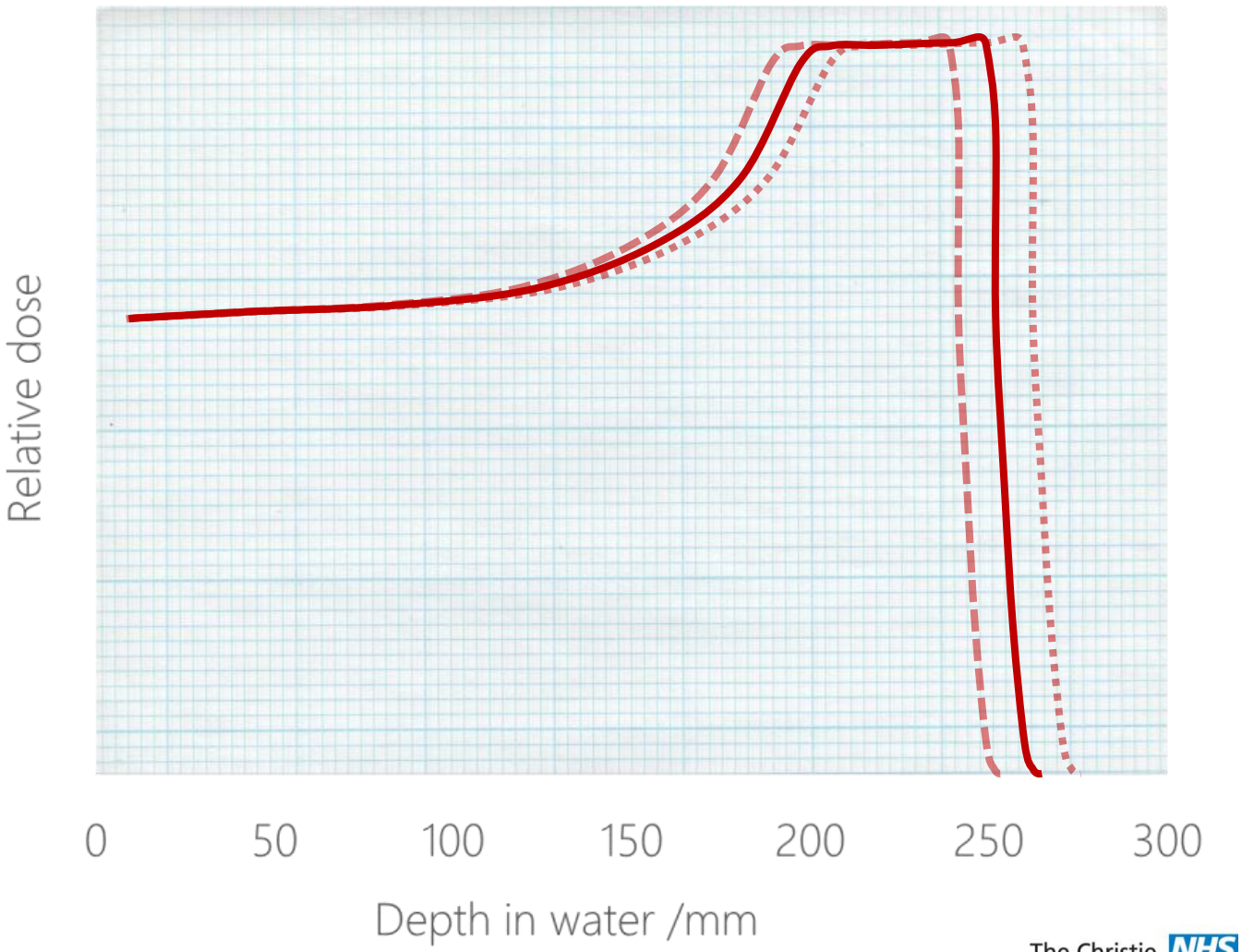

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Range uncertainty: 1 – The CT calibration

1. Scan
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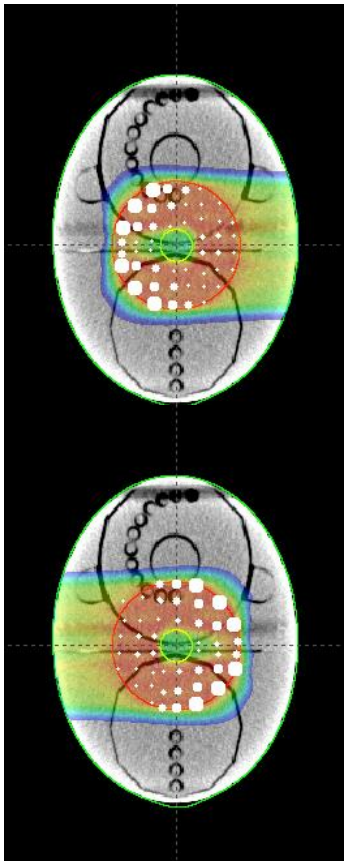
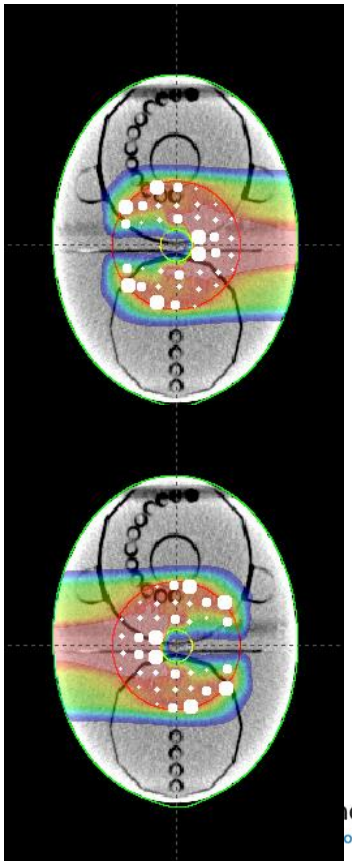
- Return to the previous SFO / MFO plans:
  - What impact could range uncertainty have?

SFO

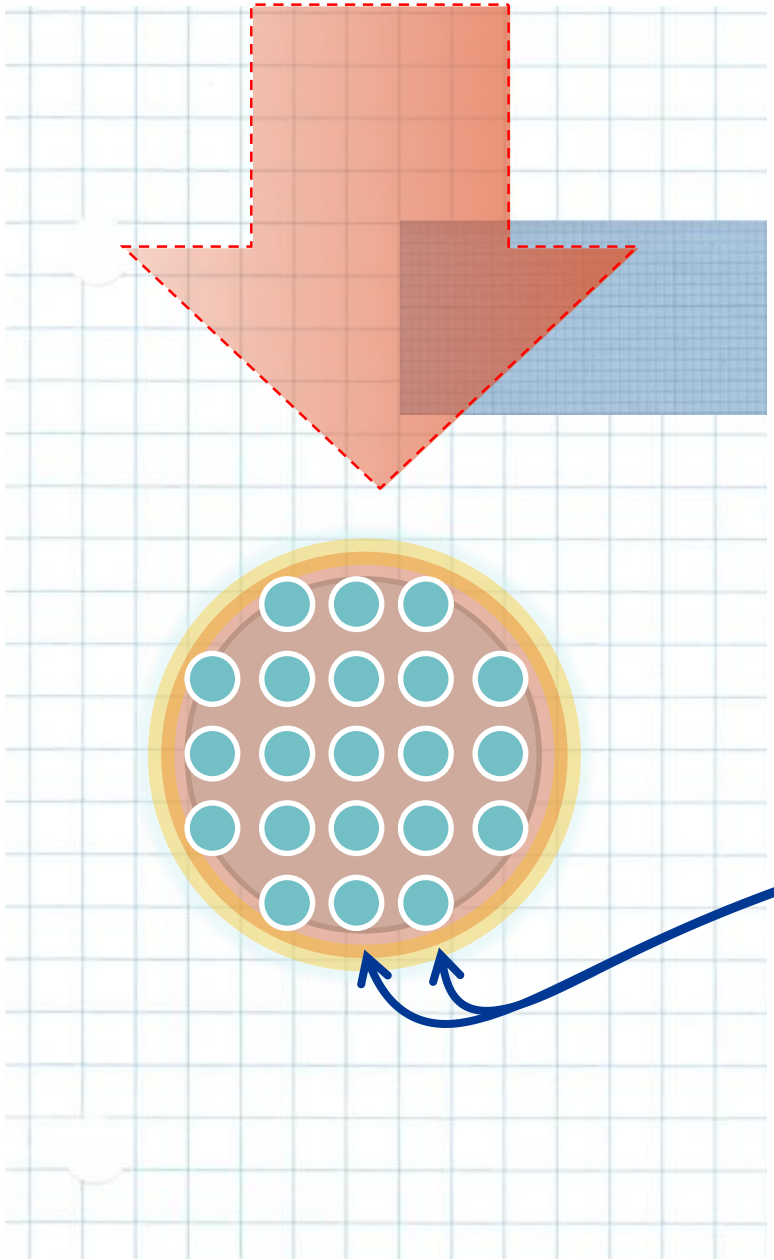


MFO



Range uncertainty: 2 – Inhomogeneities

1. Scan
2. Plan
3. Treat
4. Monitor outcome



- These two spots belong to different energy layers.
- They reach a similar depth because one passes through bone, while the other does not.

Range uncertainty: 2 – Inhomogeneities

1. Scan
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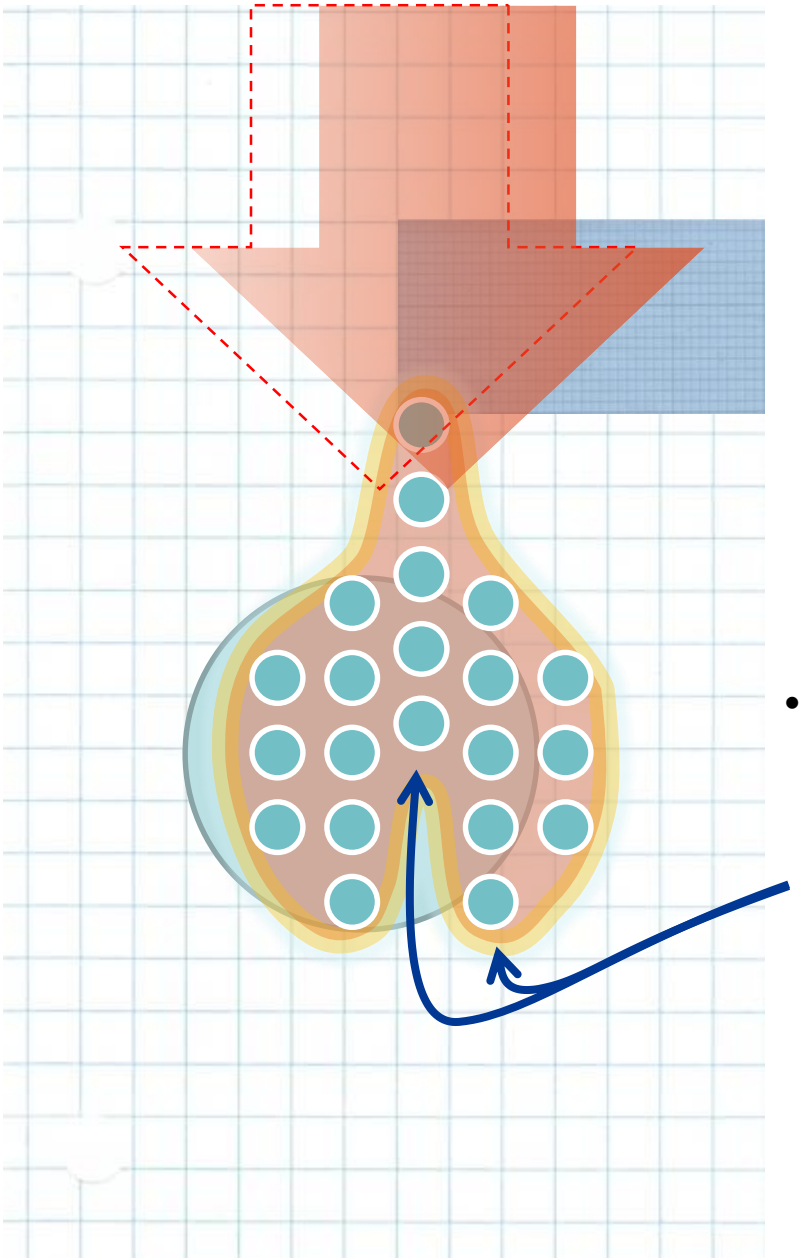
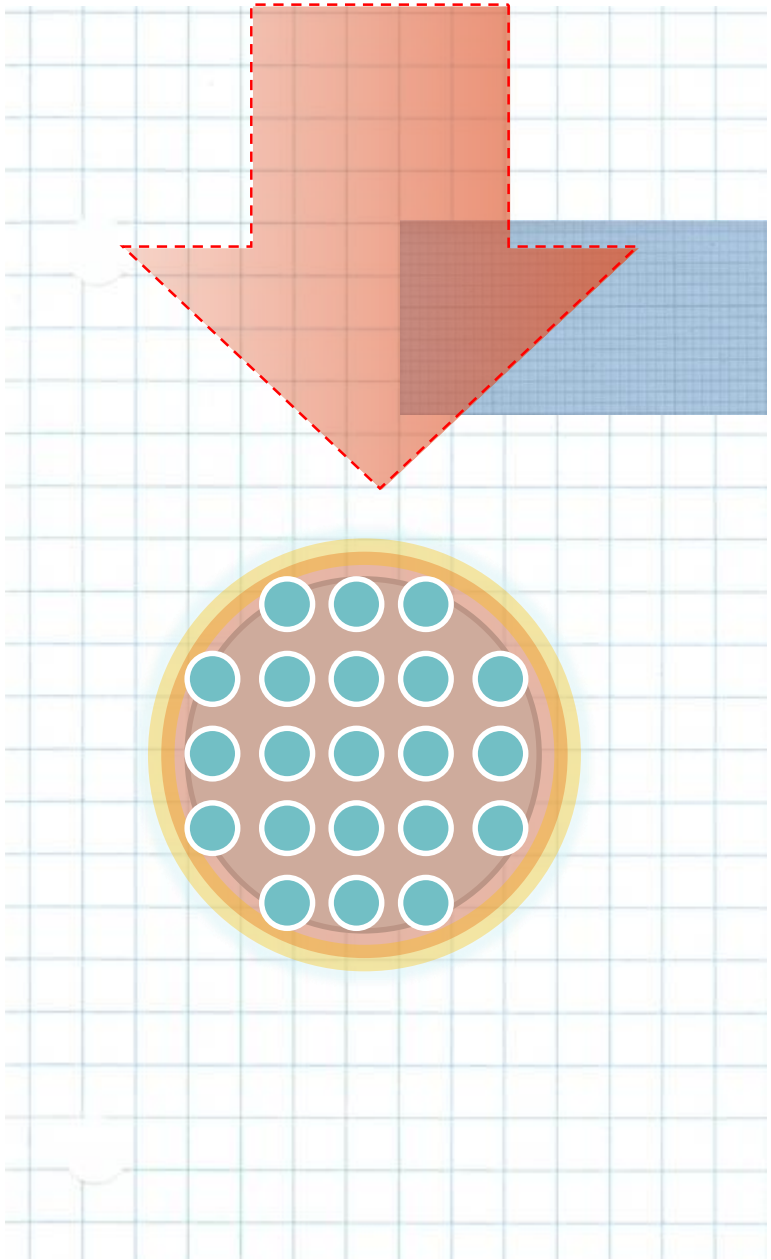
4. Monitor outcome



- A lateral offset in the patient setup means that the two spots no longer reach the same depth, since both now pass through bone.

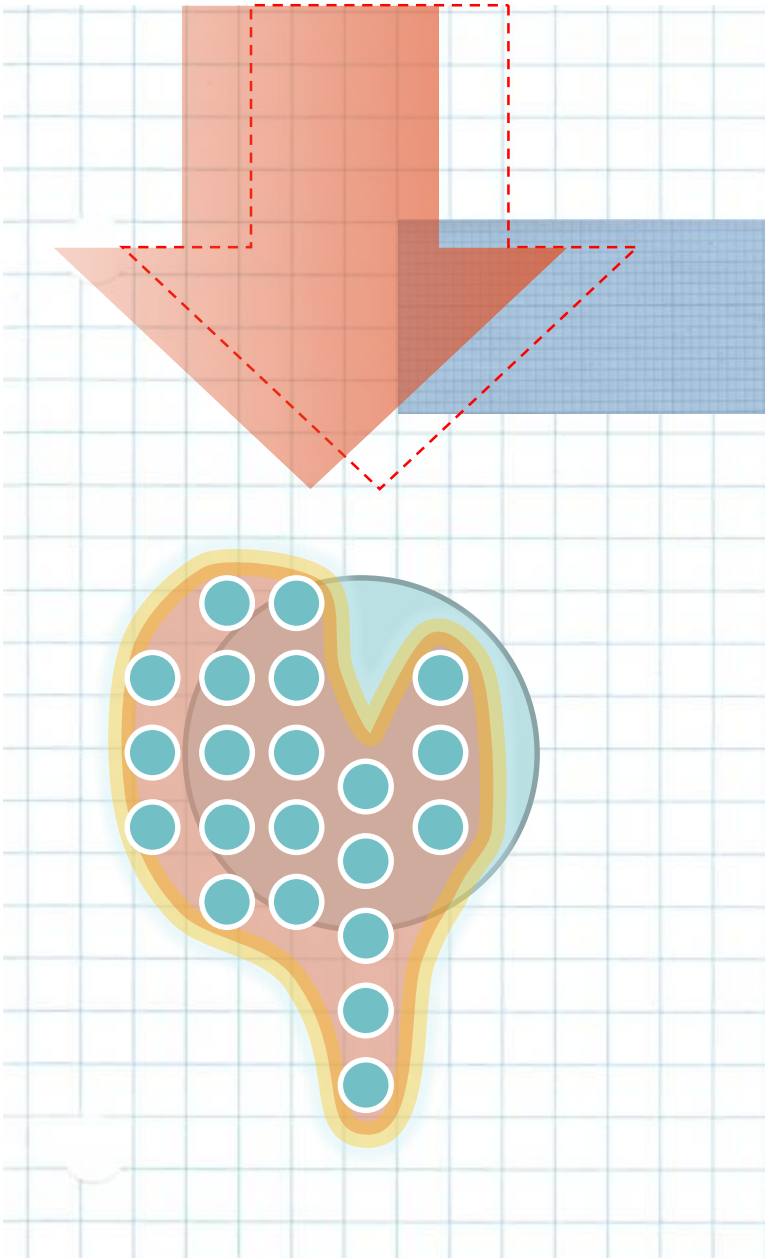
Range uncertainty: 2 – Inhomogeneities

1. Scan
2. Plan
3. Treat
4. Monitor outcome



Range uncertainty: 2 – Inhomogeneities

1. Scan
2. Plan
3. Treat
4. Monitor outcome



Range uncertainty: 2 – Inhomogeneities

1. Scan
2. Plan
3. Treat
4. Monitor outcome

- PBS is more sensitive than photon RT to inhomogeneities

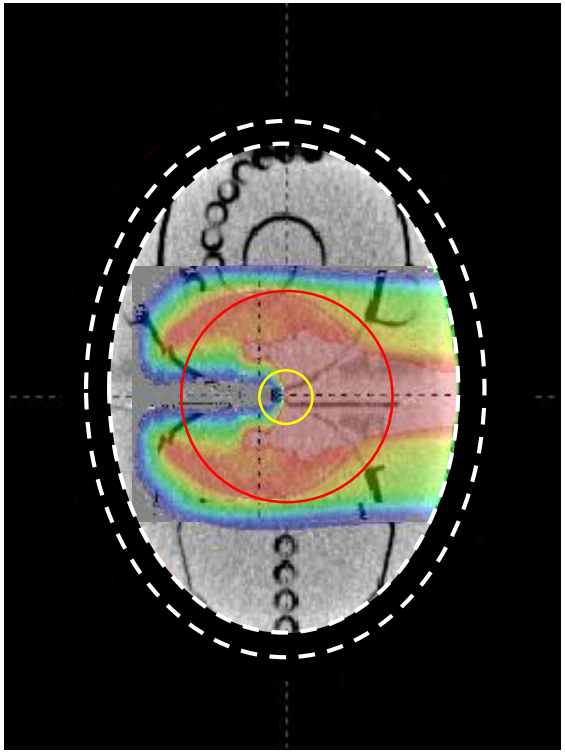
- Potential issues:
  - Beams passing along the edges of inhomogeneities (either low or high density)
  - Cavities which may fill with gas / liquid (eg. Sinuses, bowel)
  - Dense targets in low density surroundings (eg. Lung)
  - Moving targets.

1. Scan
2. Plan
3. Treat
4. Monitor outcome

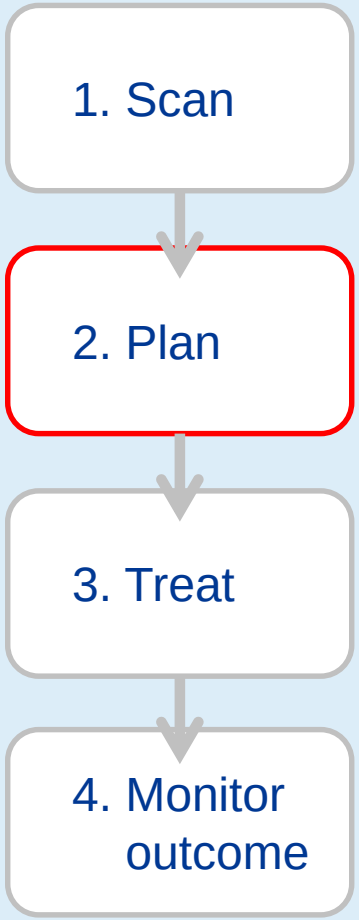
Range uncertainty: 3 – Anatomy changes

- Weight loss example
  - Less tissue between patient surface and the target

  → The dose will overshoot the target



Coping with uncertainties



- PBS plans typically contain 1-5 fields.
- Each field may consist of several 1000 spots.
- There are many ways to weight the spots to achieve the same total dose in the nominal case.

→ There is a high degree of *degeneracy*.

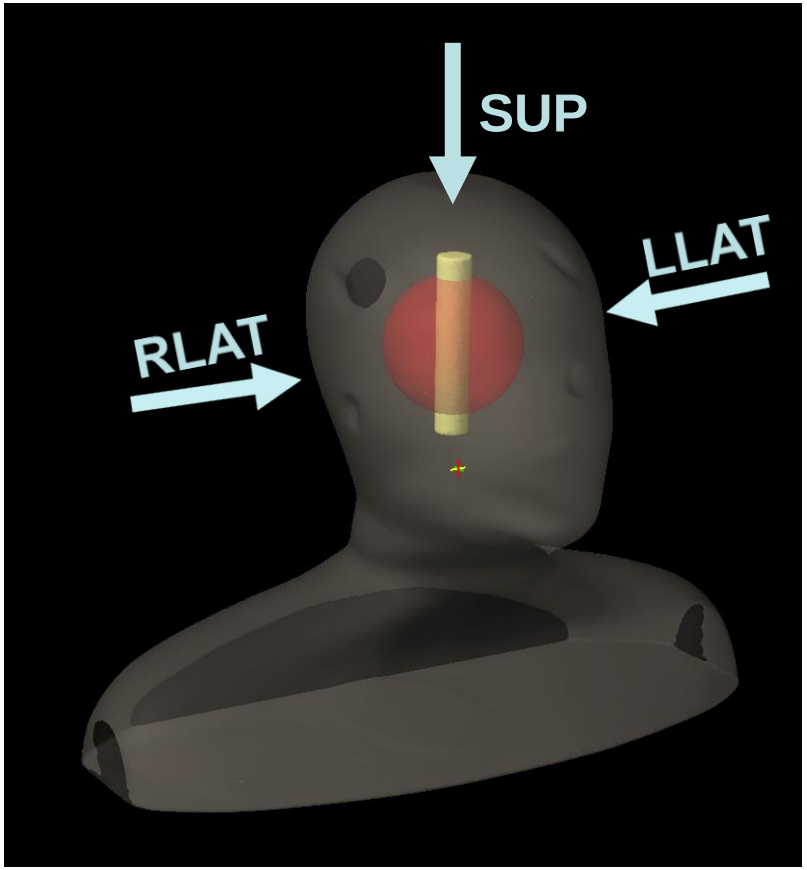
- However, each plan will behave differently under a range of error scenarios (range uncertainty, setup error, etc.)

- A *robust* plan is one which remains within tolerance under possible error scenarios.

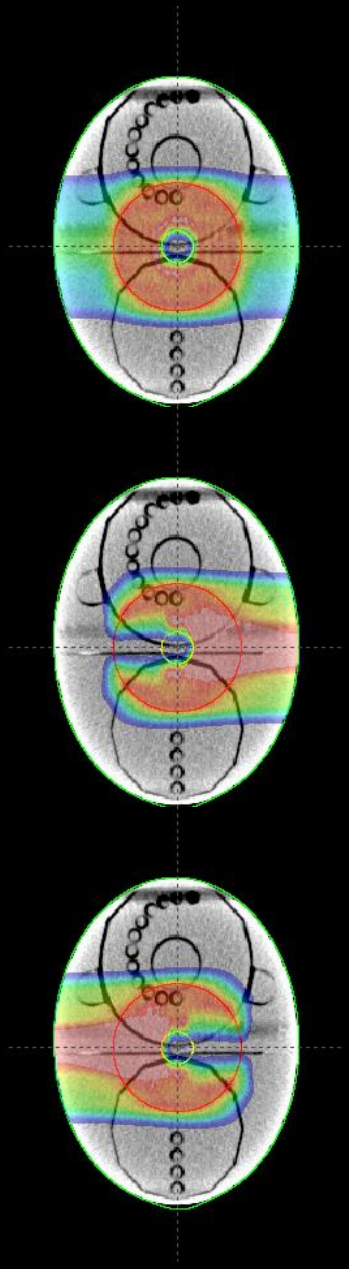
Coping with uncertainties: 1 – Beam directions

1. Scan
2. Plan
3. Treat
4. Monitor outcome

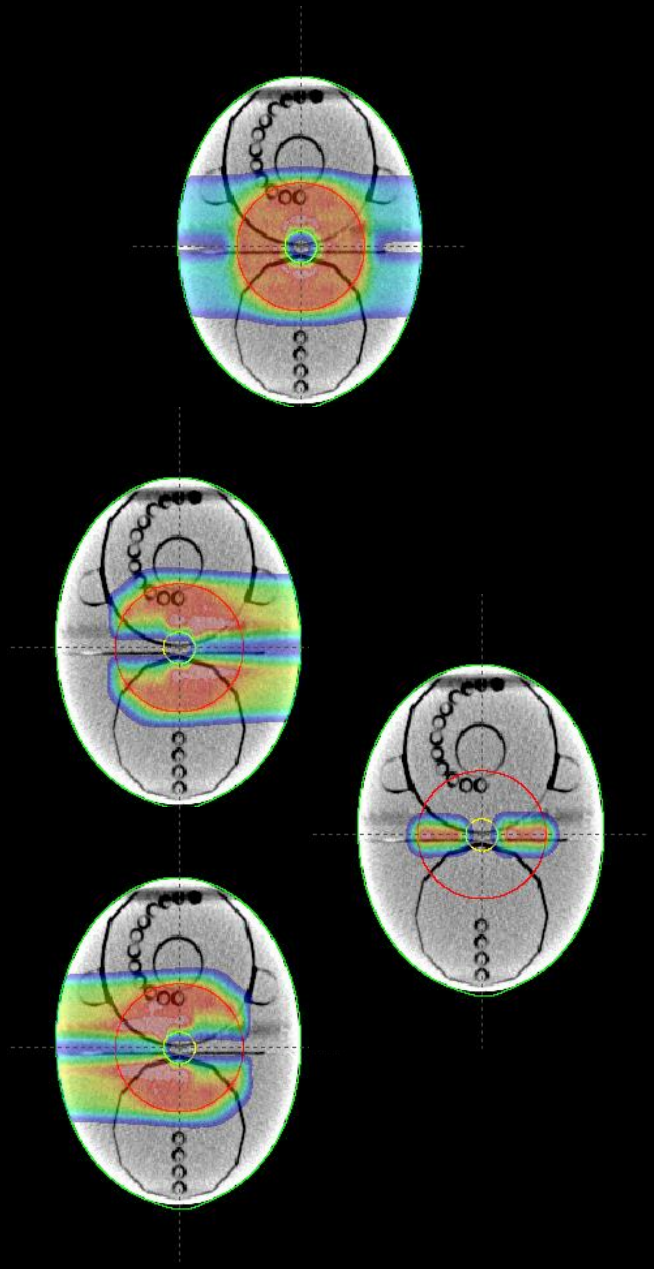
- Avoid beam directions where an OAR is directly behind the target
- Using the lateral edge avoids range uncertainty problems
- Additional fields / patched fields may help.



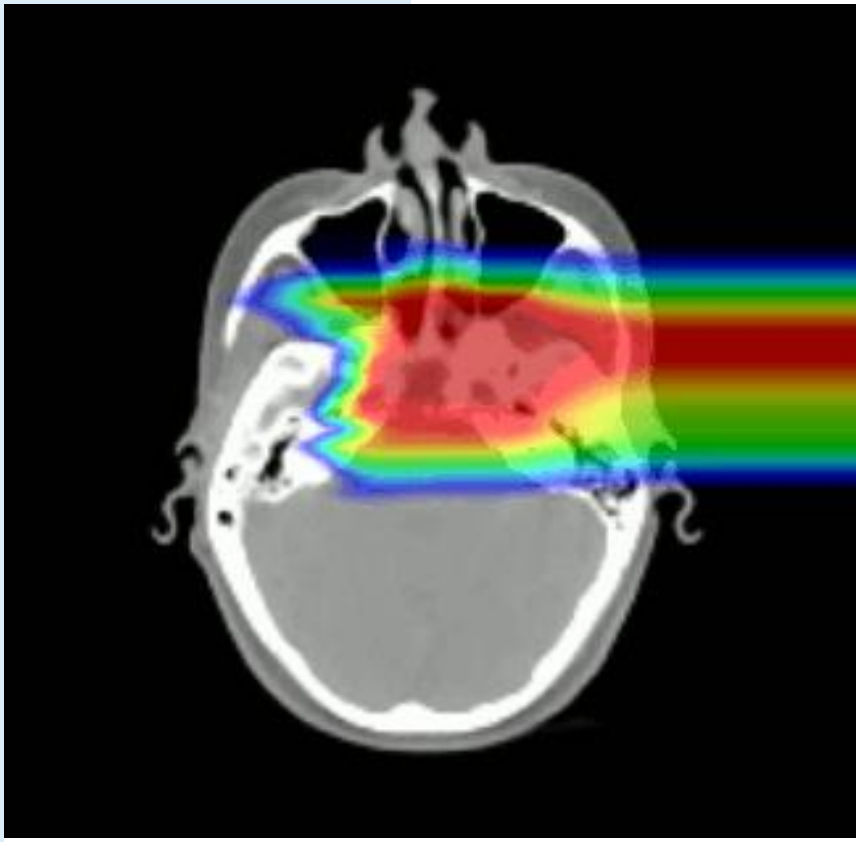
MFO 2-fields



MFO 3-fields



Coping with uncertainties: 2 – Target definitions



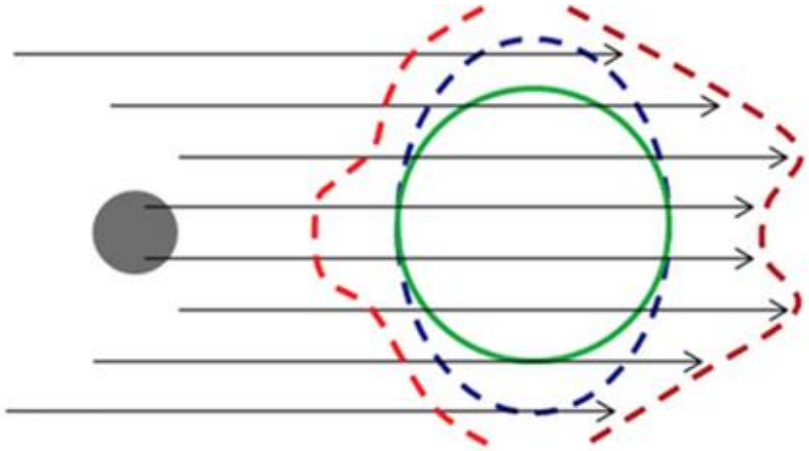
Effect of ± 3mm lateral shift on a proton beam

- Due to the energy dependent range of protons, the proton dose distribution is not well approximated by the **static dose cloud approximation**.
- The effect on the dose distribution depends on:
  - Direction of offset (along or lateral to beam)
  - Heterogeneities in the beam path
- A uniform CTV to PTV expansion does not necessarily ensure good coverage of the CTV.

Coping with uncertainties: 2 – Target definitions

1. Scan
2. Plan
3. Treat
4. Monitor outcome

- One approach is to use **Beam Specific PTVs**
- The CTV to PTV expansion now depends on:
  - Direction (along or lateral to beam)
  - Heterogeneities in the beam path



Park *et al* Int. J. Radiation Oncology Biol. Phys. **82**(2) 2012: e329–e336

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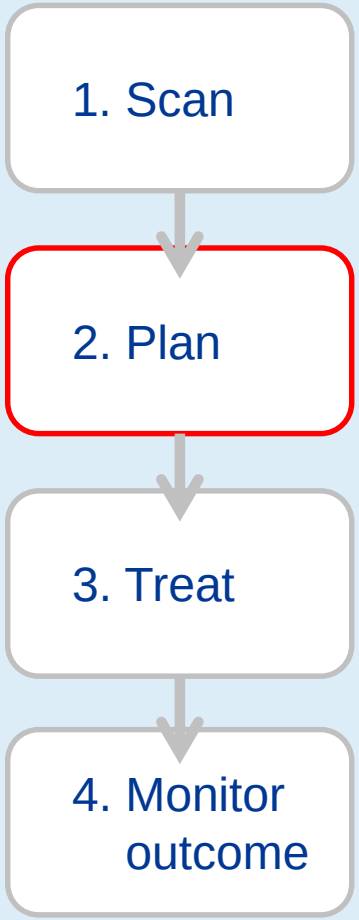
Coping with uncertainties: 3 – Robust optimisation



- Alternatively, the PTV concept can be discarded.
- Instead, the CTV is used for optimisation.
- Information describing the uncertainties (range, setup) is supplied to the optimiser.

- The optimiser looks for a plan which meets the objectives for both:
  - The nominal case
  - A number of error scenarios.

→ Now available in recent commercial TPSs

→ Optimisation is slower than non-robust planning.

Coping with uncertainties:
3 – Robust optimisation example

Conventional IMPT

Robust IMPT

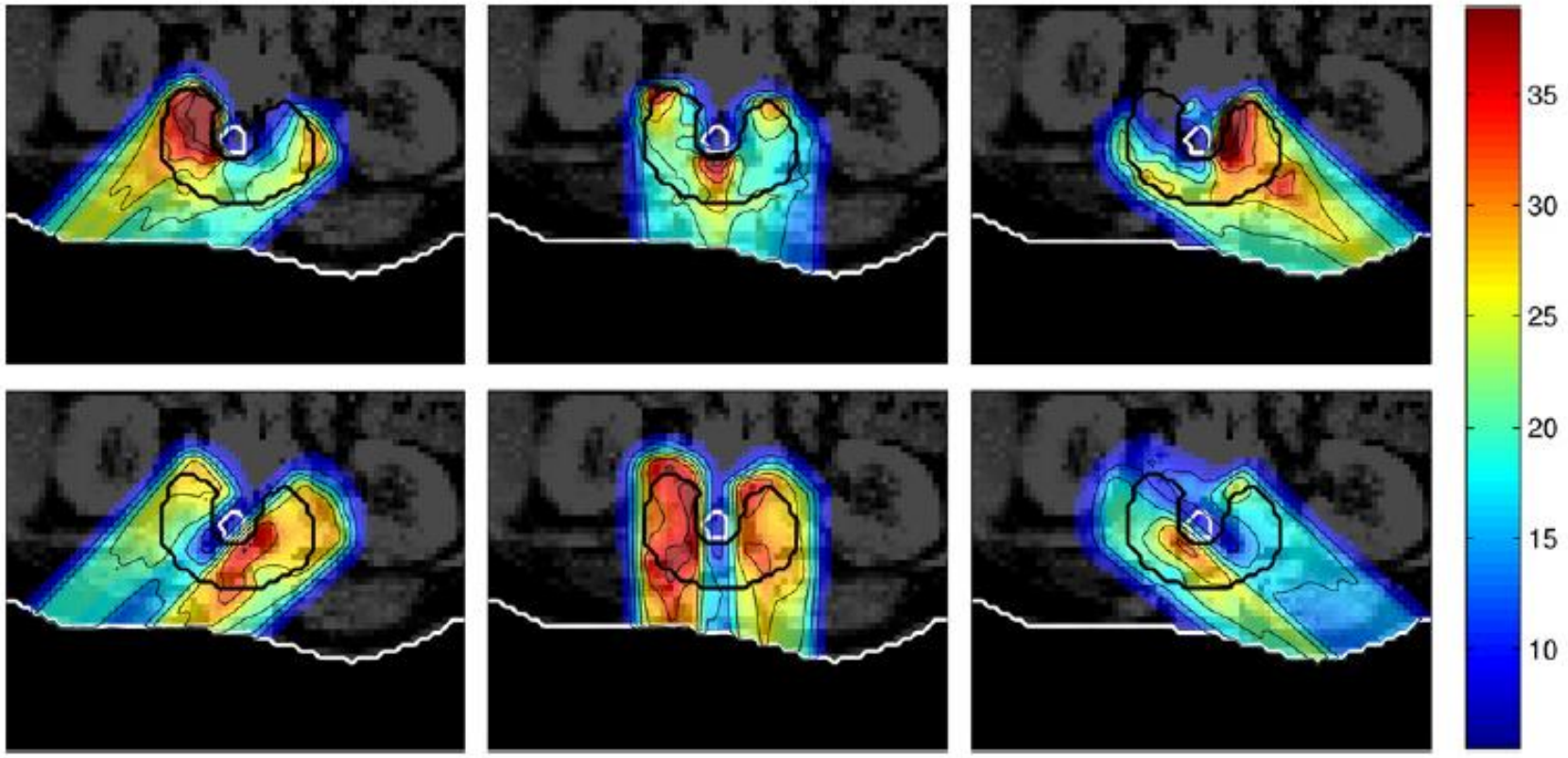


Figure 3. Dose distributions in Gy for the three individual beams for $p_w = 0$ (upper row) and $p_w = 1$ (lower row). Range uncertainties of 5 mm are accounted for.

Pflugfelder *et al.* Phys. Med. Biol. **53** (2008) 1689-1700

Coping with uncertainties: 3 – Robust optimisation example

- The worst case spinal cord dose decreased by ~40 Gy.
- The nominal case spinal cord dose increased by ~10 Gy.
- → **Robustness is a trade-off for plan quality.**

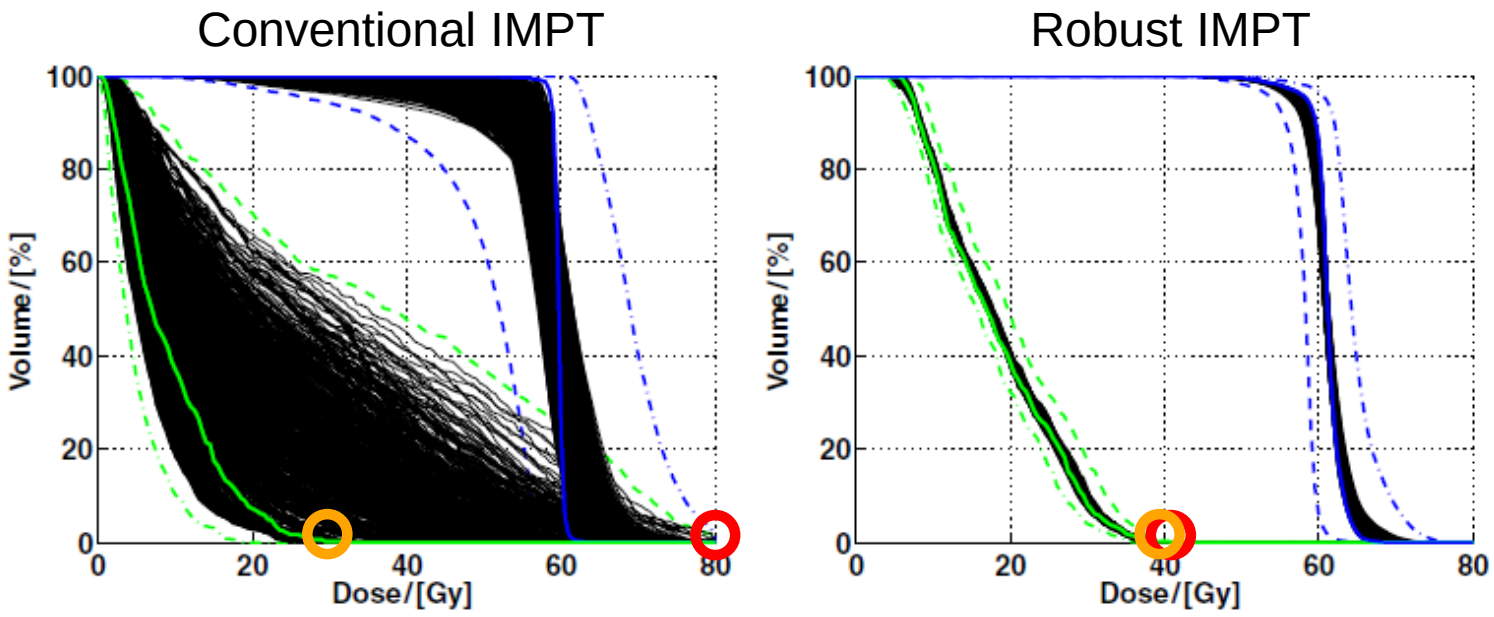


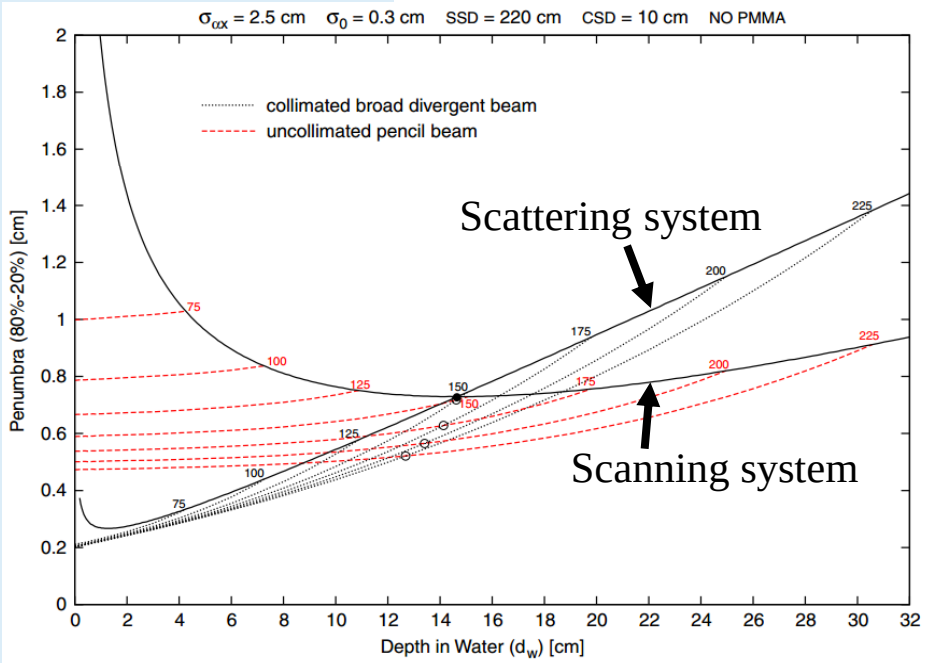
Figure 4. DVH of dose distributions recalculated for 1331 different realizations of the range uncertainties (black lines). Coloured solid lines: DVH for nominal dose distribution. Coloured dashed/chain-dotted lines: worst/best case dose distribution.

Blue: CTV
Green: Spinal cord

Pflugfelder *et al.* Phys. Med. Biol. **53** (2008) 1689-1700

Beam modifiers: 2 – Collimators

- Lateral spot width is dependent on energy.
- At low energies, especially when using a range-shifter, PBS spot width is greater than for scattered systems.
- Lateral width is important, as it is used in preference to the distal edge next to OARs.



Safai *et al* Phys. Med. Biol. **53** (2008) 1729–1750

- A collimator could potentially sharpen the lateral edge for shallow targets.

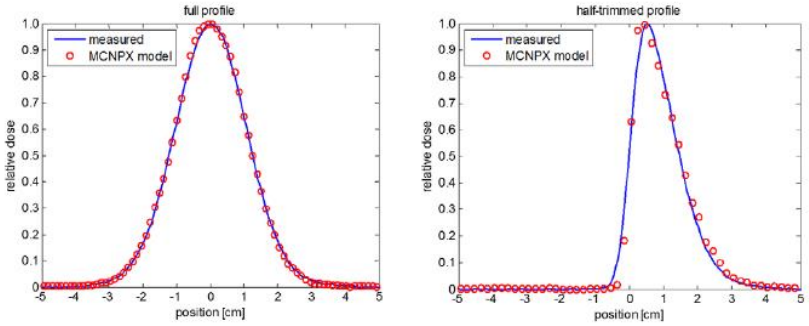
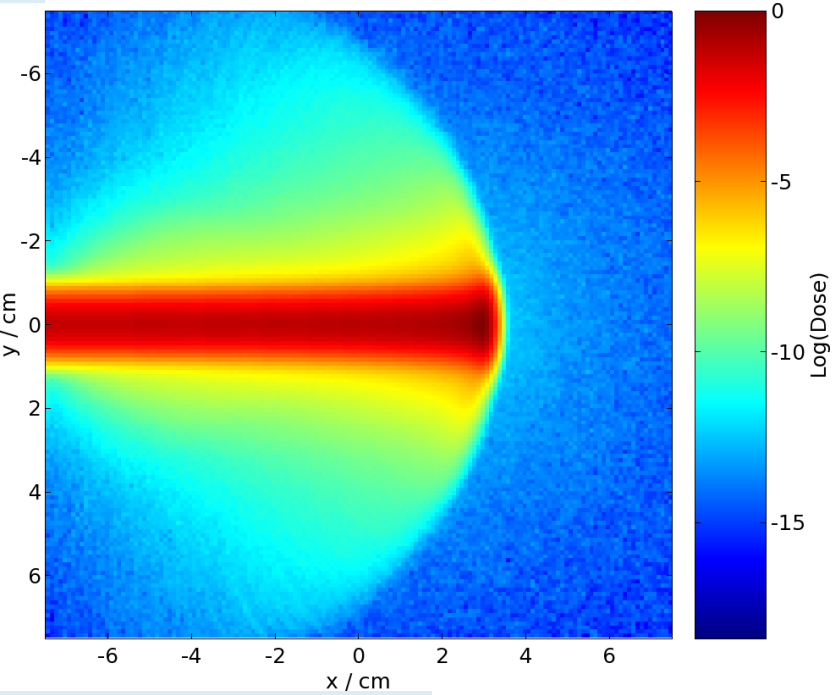


Figure 4. Experimental measurements of an untrimmed and half-trimmed profile to validate the Monte Carlo model.

Hyer et al. Phys. Med. Biol. 59, N187–N196 (2014).

Calculation of absolute dose

120 MeV beam: Logarithmic scale



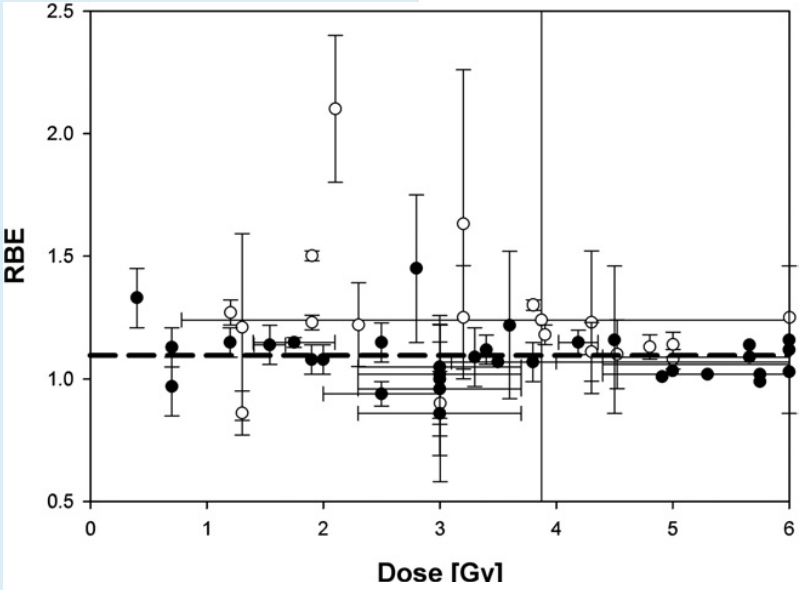
- Lateral shape of spot is usually Gaussian, with σ = ~3-8 mm.
- Nuclear interactions result in a wide, low level halo.
  - < 0.1% of intensity of peak
  - Typically >1000 spots per field

→ Halo significantly affects the dose to the patient.

- Monte-Carlo dose calculations are becoming available in clinical TPSs.
- Plan verification (by physical measurement or independent dose calculation) is necessary before patient treatment.

RBE

- The biological effect due to 1 Gy delivered by protons $\approx 1.1 \times$ The biological effect due to 1 Gy delivered by photons
- i.e. Protons have a relative biological effect (RBE) of ~1.1



Paganetti *et al.* Seminars in radiation oncology 2013;23(2):77-87

- RBE depends on many factors:
  - Tissue type
  - Tissue oxygenation
  - Endpoint (cell survival, toxicity, etc.)
  - Proton energy / Linear energy transfer (LET)
  - …
- An RBE of 1.1 is used clinically, and is intentionally conservative.
- Much research into factors affecting RBE is ongoing.

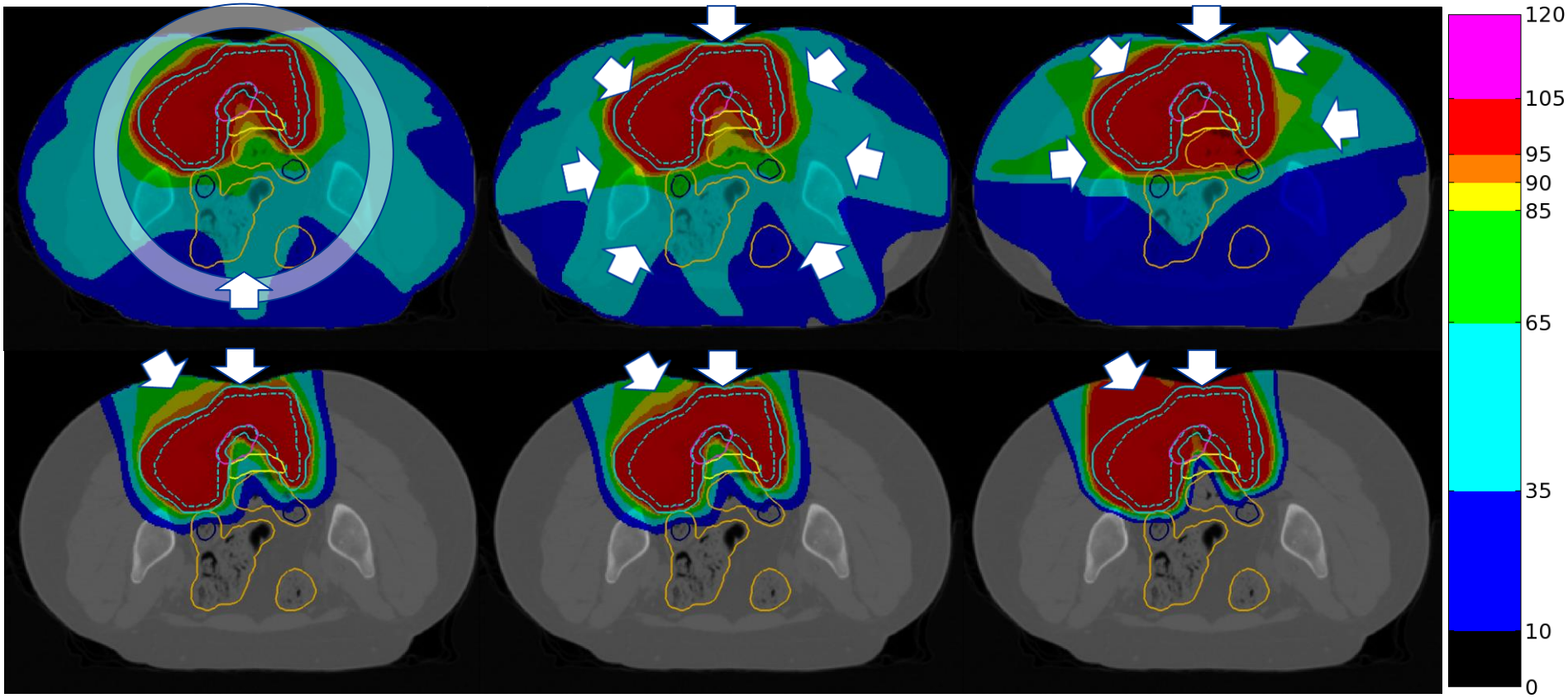
Clinical case example

1. Scan
2. Plan
3. Treat
4. Monitor outcome

Sacrum:

- 13 year old female
- 45 Gy in 25 fractions
- Clinical double scattering plan delivered at UFPTI, Jacksonville (2012)

Sacrum: Dose Distributions



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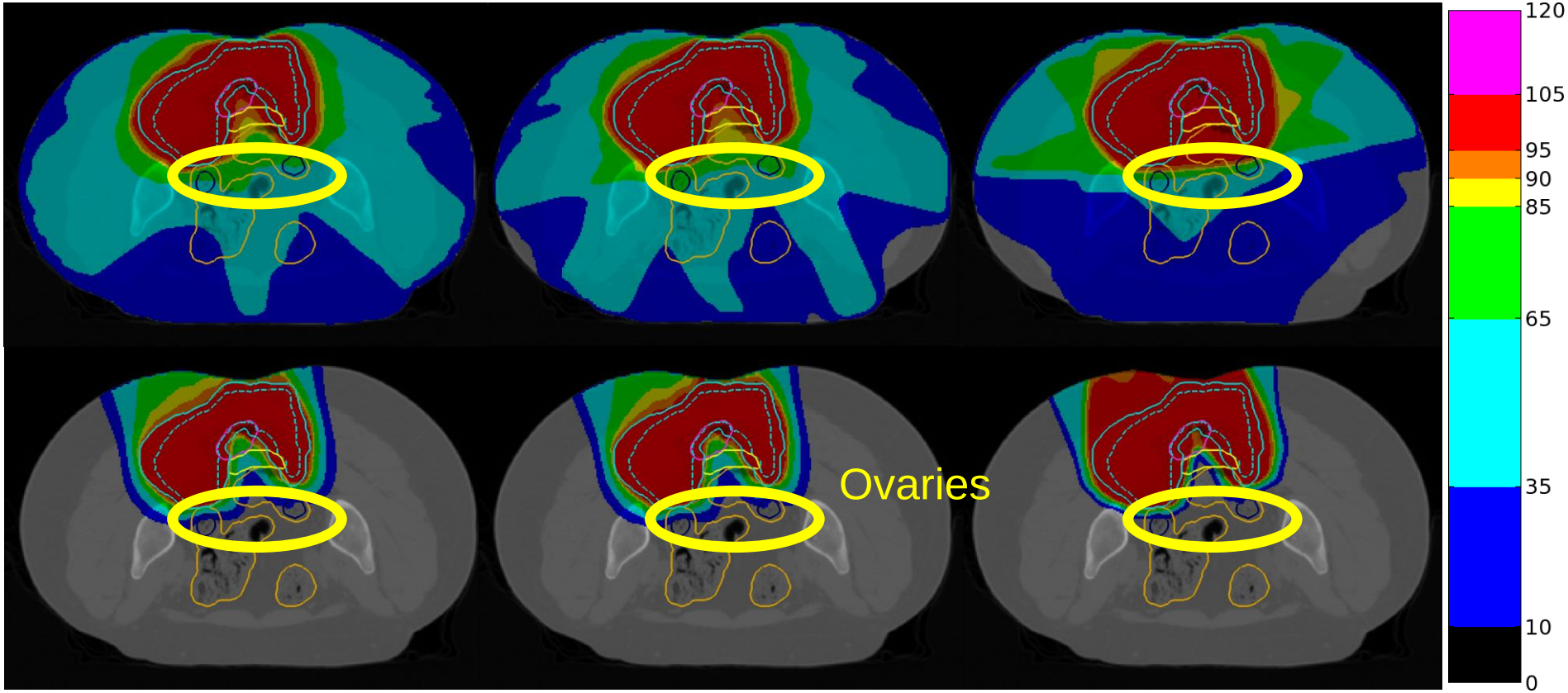
Sacrum: Dose Distributions

VMAT (2 arcs)

IMRT (7 fields)

3D CRT (5 fields)



PBS SFO (2 fields)

PBS MFO (2 fields)

DS (2 fields)

Sacrum: Dose Distributions

VMAT (2 arcs)

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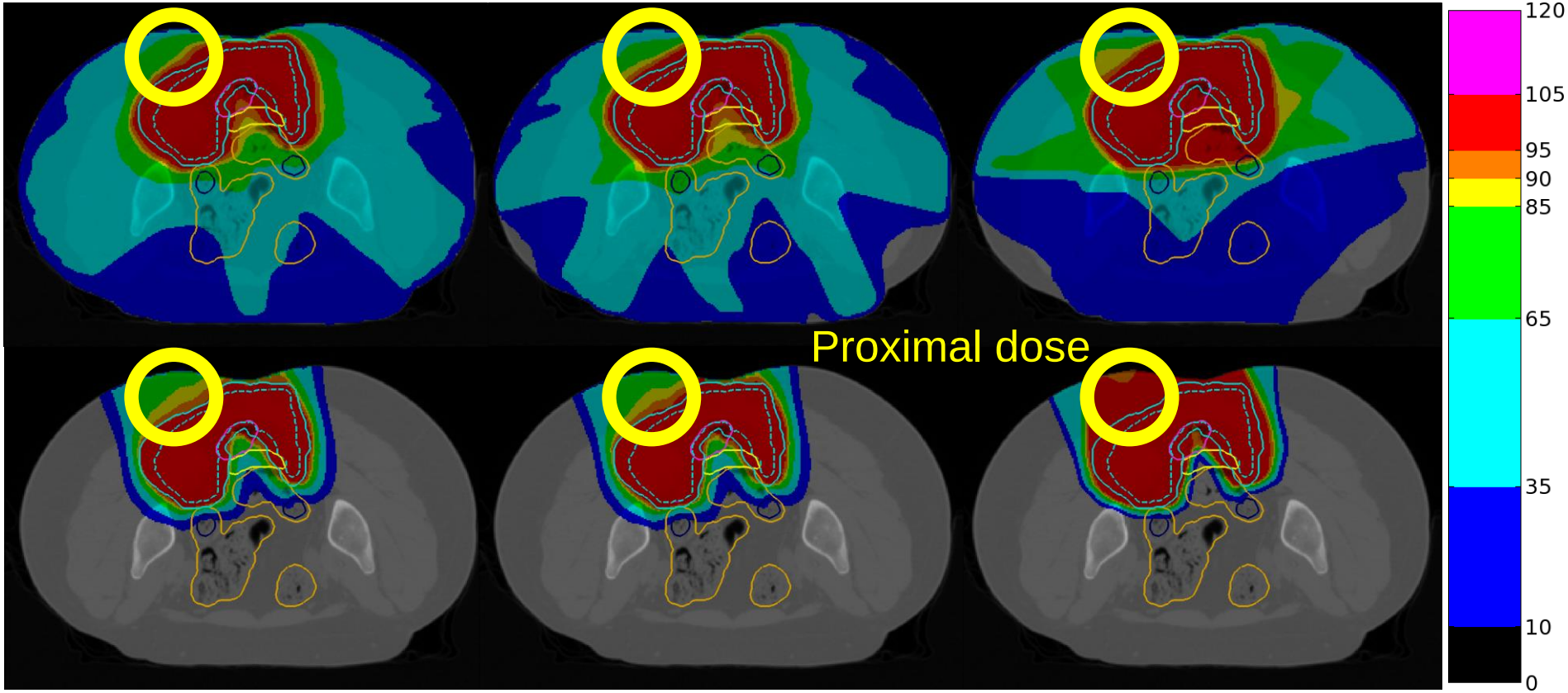
3D CRT (5 fields)



PBS SFO (2 fields)

PBS MFO (2 fields)

DS (2 fields)

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Summary

- Main advantage over photon therapy:
  → Absence of exit dose

- Many possible combinations of beams and spot weights can provide very similar overall dose distributions:
  → High degree of degeneracy

- Several issues need particular care when planning proton therapy
  → CT calibration
  → Robustness (daily setup, range uncertainty, inhomogeneities)
  → RBE

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