Cambridge University Hospitals NHS
NHS Foundation Trust

Incorporating and Managing Uncertainties in PBT

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Making a difference for patients

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Introduction

Our Goal

100% dose to the target, zero dose to normal tissue

Our Reality

OPTIMISATION

Our Question

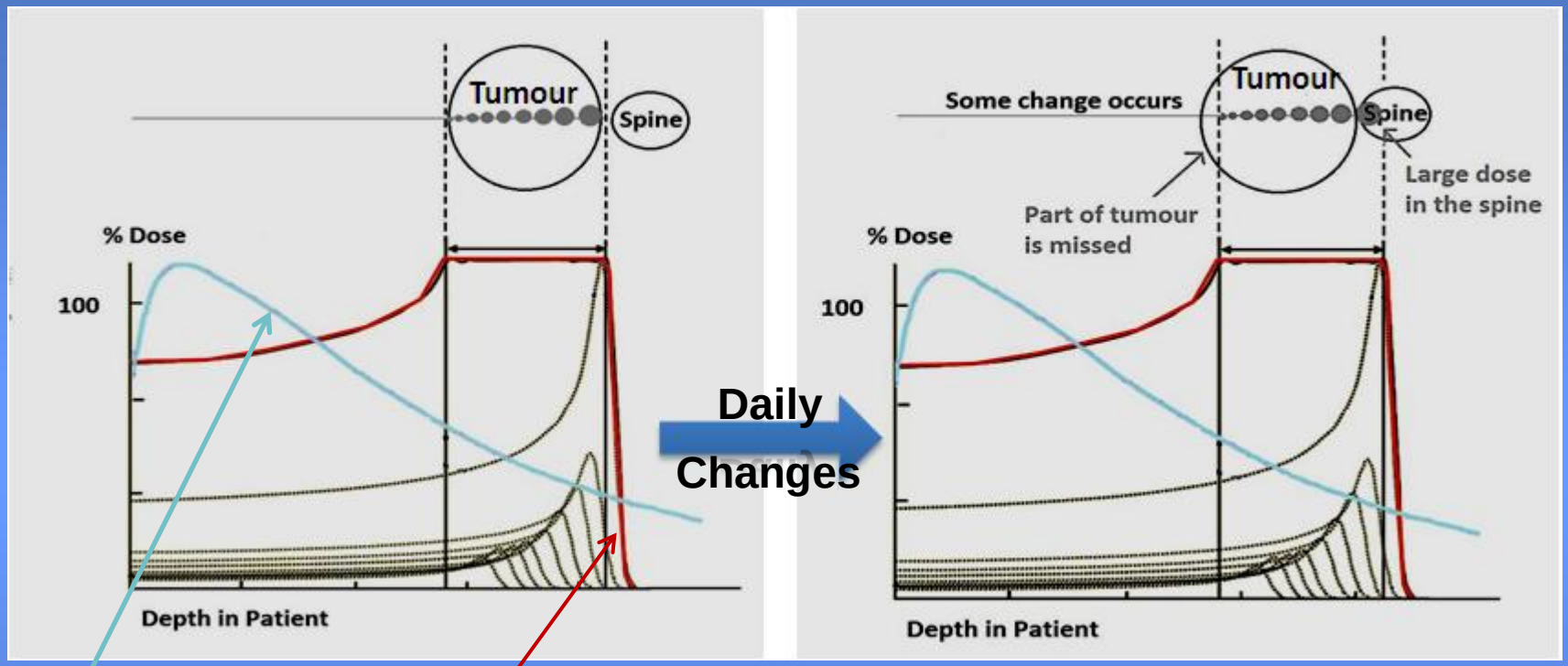
How can we ensure plan robustness
and plan conformality in PBT?

In this talk…

1. Why is plan robustness important in PBT?
2. Sources of range uncertainty
3. Managing uncertainty
4. Pareto surfaces and error doses
5. A new parameter for plan quality
6. Summary



Range Uncertainty



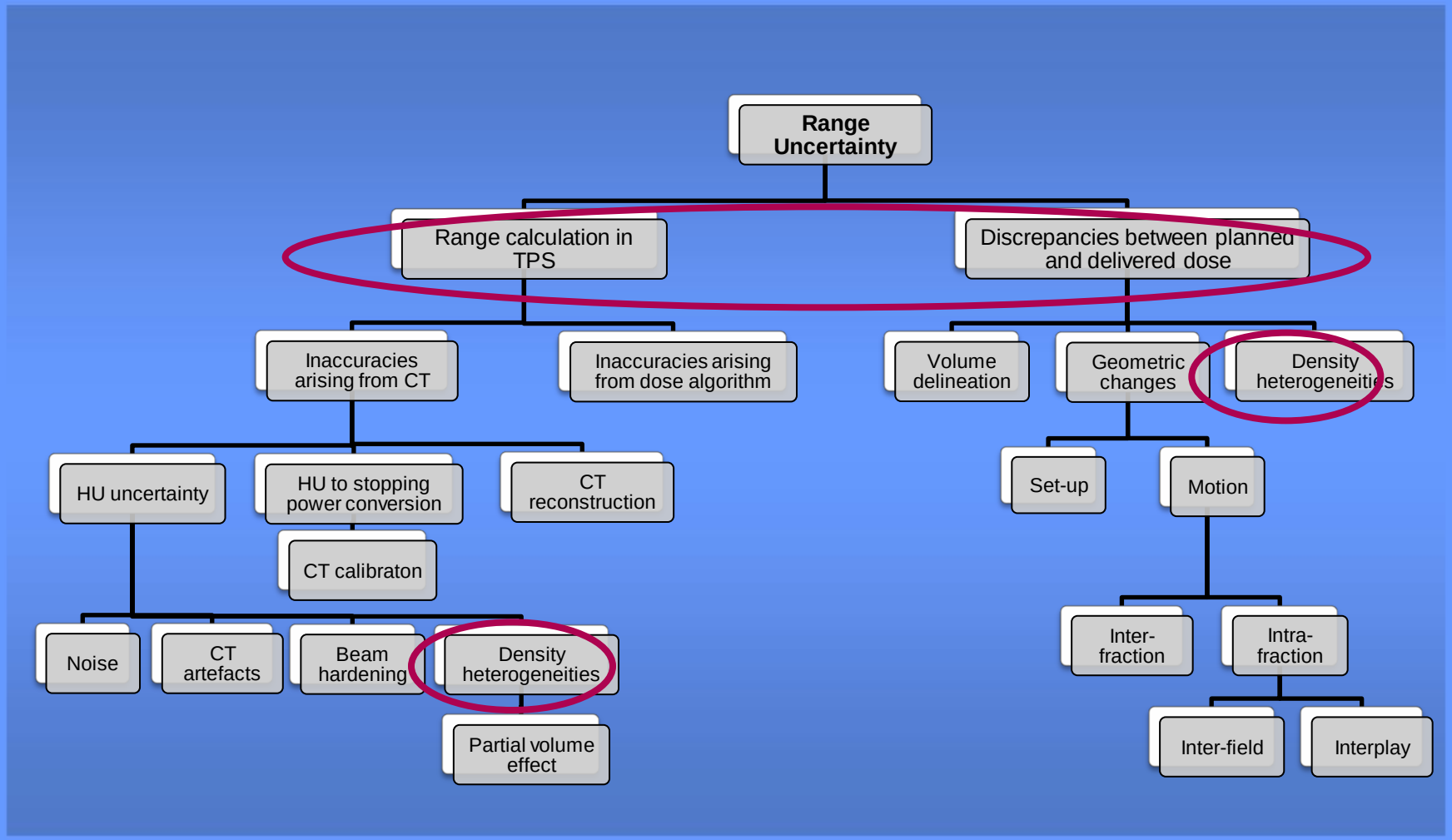
Infinite X-ray fall off

Finite proton range = greater conformity

BUT…
more sensitive to uncertainties

The advantage of finite range can be fully exploited only if the proton range in the patient can be precisely predicted

Sources of Range Uncertainty



McGowan, Burnet, & Lomax, (2013). Treatment planning optimisation in proton therapy. *The British journal of radiology*, *86*(1021), 20120288



Range calculation in the TPS

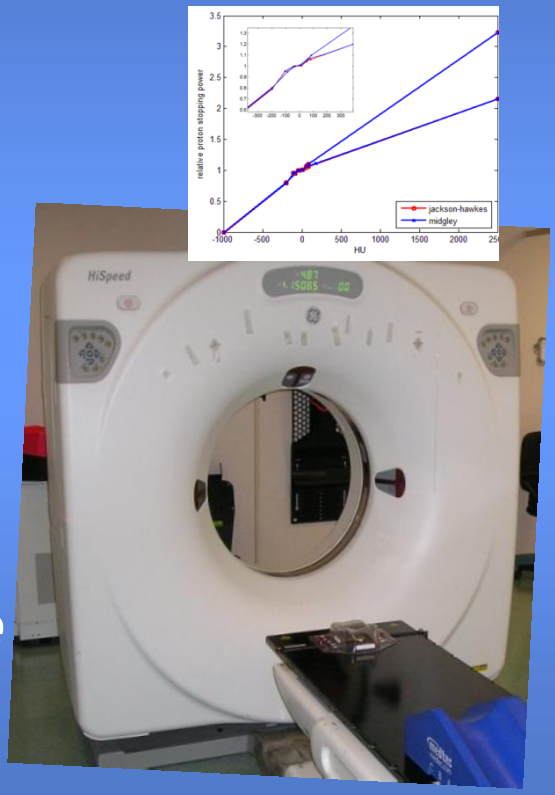
Inaccuracies arising from the dose calculation algorithm

- Analytical Vs. Monte Carlo

Inaccuracies arising from the planning CT

- HU conversion < ±1%
- Noise < ±1%
- Beam hardening ± 1.8% and ± 1.1% for bone and soft tissue.

Allow for an uncertainty in HU value of ±3% used



Espana, Paganetti. The impact of uncertainties in the CT conversion algorithm when predicting proton beam ranges in patients from dose and PET-activity distributions. Phys Med Biol 2010

Schaffner, Pedroni The precision of proton range calculations in proton radiotherapy treatment planning: experimental verification of the relationship between CT-HU and proton stopping power. Phys Med Biol 1998

Discrepancies between planning dose and delivered dose

Geometric changes include… Set-up & Motion

Motion can result in density changes

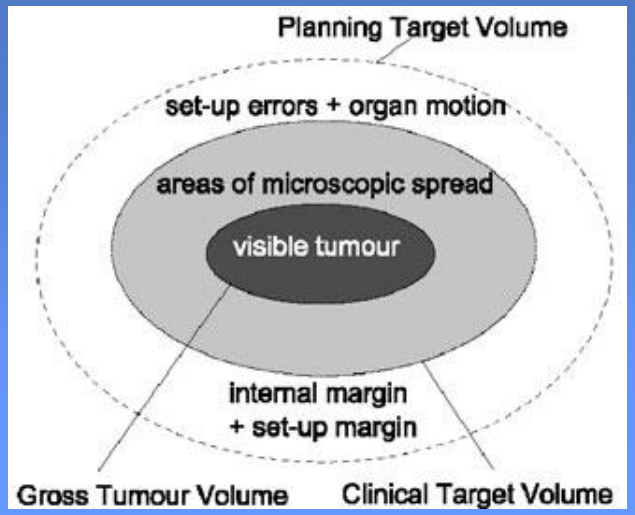
- Inter-fraction (between #s)
- Intra-fraction (within the #)
    - Inter & intra- field (between & within the field)
    - Interplay (In IMPT patient motions has frequency near the scanned beam frequency)

- Lomax[1] reported that, for a 5mm shift in the dose distribution, an under-dosage of up to 20% can occur in the CTV

1. Lomax A. Intensity modulated proton therapy and its sensitivity to treatment uncertainties 2: the potential effects of inter-fraction and inter-field motions. Phys Med Biol 2008;53:1043–56.

Margins

Lambert[1] *et al* took the ICRU 50 recommendations for PTV dose homogeneity of 95–107% as threshold. In extreme cases up to 100% of the target volume received doses below those recommended and with a minimum dose as low as 34% of the prescribed dose.



- These results were backed up by simulations carried out by Grozinger[2] and experimental work by Bert[3].
- Bert[3] carried out the first patient simulation that confirmed under-dosage using 4DCT lung data. Despite using margins that consider the effect of the changing radiobiological path-length, adequate CTV coverage could not be achieved.

1. Lambert *et al*, Intrafractional motion during proton beam scanning. Phys Med Biol 2005
2. Grozinger *et al*, Simulations to design an online motion compensation system for scanned particle beams. Phys Med Biol 2006
3. Bert *et al*. Quantification of interplay effects of scanned particle beams and moving targets. Phys Med Biol 2008.

Conclusions from literature

For complex IMPT plans, a simple PTV margin cannot be applied to compensate for range uncertainty

1. How do we ensure the target is robust to range uncertainties?

2. How to record dose to a moving CTV?

How to evaluate plan robustness??

Managing range Uncertainty

- Re-scanning
- Beam Tracking
- Proton margin recipes

- **Robust optimisation**

- **Multi-criteria optimisation**

- **Error-bar dose distribution (ebDD) & error-bar volume histogram (ebVH)**

Robust optimisation

- Unkelbach[1] & Pflugfelder[2] proposed including uncertainties directly into the optimisation algorithm.
- **Probabilistic** – prior knowledge of the probability distribution
- **Worst Case scenario** – 'unphysical' case

- Both led to plans less sensitive to range variations.
- Lateral edge instead of the distal edge to shape the dose distribution
- Adding 'safety margin' to distal end
- ***Sacrifice plan conformality.***

1. Unkelbach J, Chan T, Bortfield T. Accounting for range uncertainties in the optimisation of intensity modulated proton therapy. Phys Med Biol 2007
2. Pflugfelder D, Wilkens JJ, Oelfke U. Worst case optimization: a method to account for uncertainties in the optimiza- tion of intensity modulated proton therapy. Phys Med Biol 2008

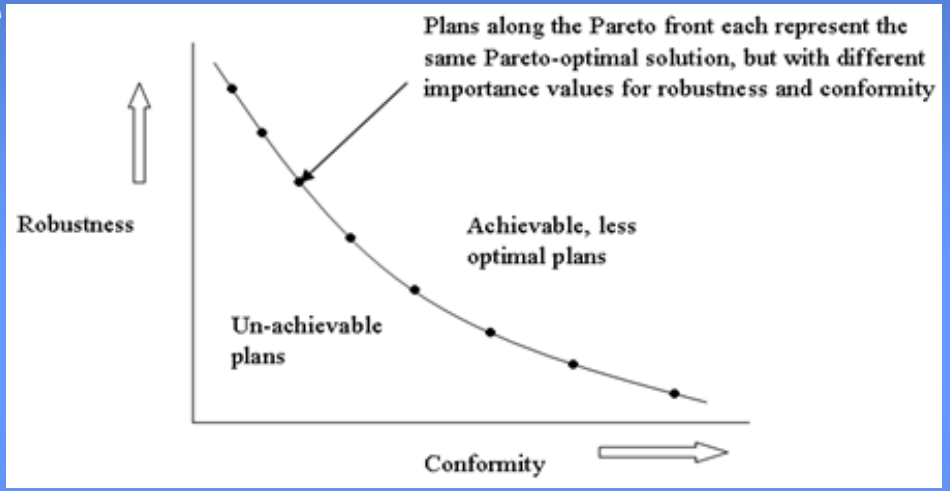
Multi-Criteria Optimisation

Chen *et al* introduced a method of including robustness into a Multiple Objective Pareto/ Multi-Criteria Optimisation (MCO) framework for IMPT

-Overcomes limitations in inverse planning

-Database of a plan rather than a single plan

- Allows planner visualisation of tradeoffs such as conformity Vs. robustness



MCO Vs margins showed similar CTV coverage OAR sparing in the nominal case. When ±3% HU error was included MCO plan remained robust.

The Pareto surface of objectives allows the planner to have greater control in deciding between a robust plan, a conformal plan or somewhere in between.

Chen *et al*. Including robustness in multi-criteria optimization for intensity-modulated proton therapy. Phys Med Biol 2012

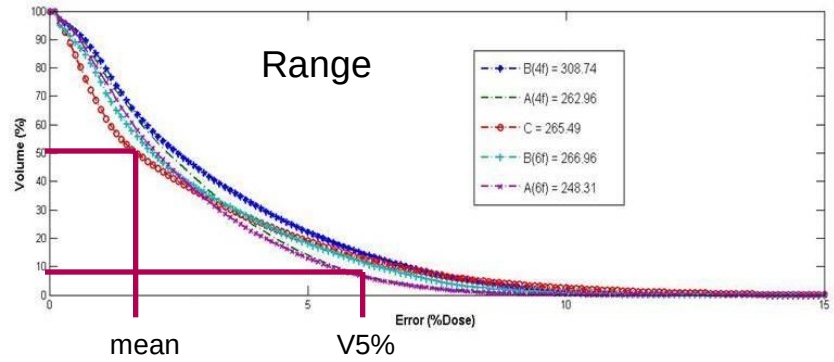
Error-bar Dose Distributions

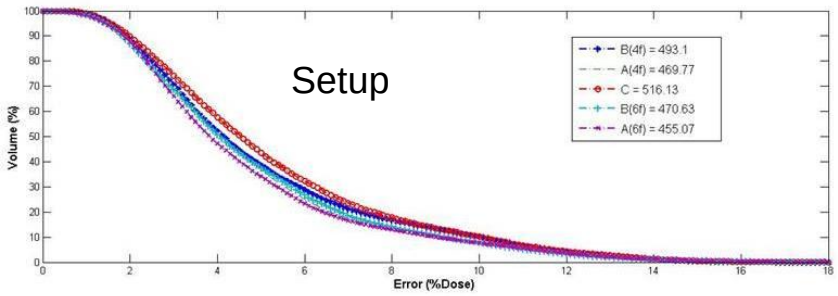
Systematic range uncertainty

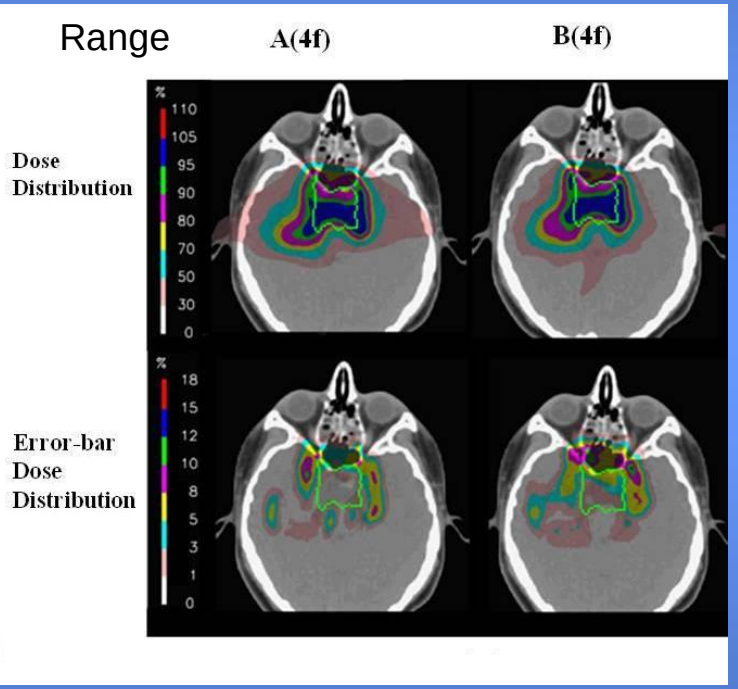
Δdi(sys) = Max(di+HU, di-HU) – Min (di+HU, di-HU)

Random setup uncertainty

Δdi(rand) = Max(di+x, di-y,..., di-z) – Min (di+x, di-y,..., di-z)







Margins can help CTV coverage at the edges of the target, little effect on plan robustness when steep dose gradients exist within the target

Albertini *et al* (2011). Is it necessary to plan with safety margins for actively scanned proton therapy? *Physics in medicine and biology*

Determining Robustness Protocols

- A robust plan is probably the correct way to deal uncertainty.
- Yet it is extremely important to define a threshold between robustness and plan quality.
- Also it is important to establish the adequate level of robustness for each volume.

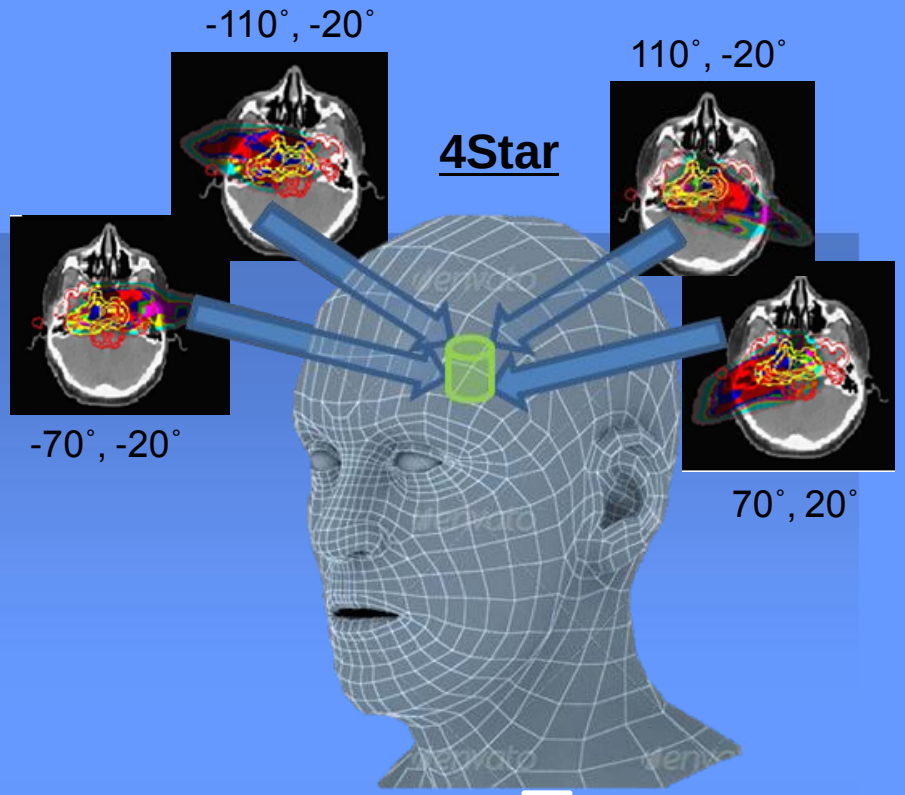
- To be used as an input parameter during the robust optimization process,
- *and* as control parameter during the plan evaluation phase.

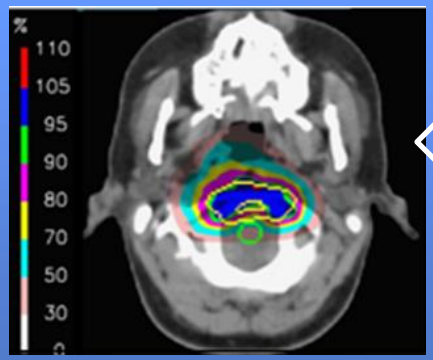
Retrospective Analysis

Aim -To define a robustness protocol site-specific to be used during the clinical plan evaluation process.

- 16 IMPT plans anaylsed using the ebDD to setup and range errors.
- CTV robustness to underdosage
- Brainstem and chiasm robustness to overdosage

- A DATABASE was created that allowed for the indentification of a patient that required greater plan individualisation due to inadeguate robustness.





Final dose distribution

Site specific Robustness DATABASE

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.

The DATABASE idea can be used as an example for other centres to define, for now, their own robustness parameters.

Then in the future, hope to define an adequate level of robustness for each volume that is accepted worldwide, in the same way as dose-volume-constraints to organs-at-risk and prescribed dose to target volumes are generally widely accepted and applied in the different protocols.

Submitted: McGowan & Albertini. Defining robustness protocols: a method to include and evaluate robustness in clinical plans

Summary

1. PBT is sensitive to range uncertainty from both errors in dose calculation and discrepancies between planned and delivered dose.

2. For complex IMPT plans common margin recipes do not allow for plans to meet ICRU recommendations

3. ebDD and robust optimization offer methods of ensuring plan robustness.

4. Multi-objective Pareto optimisation and retrospective analysis offer methods for exploring the trade-off between robustness and conformality and analysing plan quality.

5. Site specific Robustness DATABASE is a solution to define an adequate level of robustness for each volume to aid in planning decisions, to be used directly in the optimisation and to identify patients requiring greater individualisation

Acknowledgments

- Professor Neil Burnet, Addenbrooke's Hospital, Cambridge
- Dr Simon Thomas, Addenbrook's Hospital, Cambridge
- Dr Francesca Albertini, Paul Scherrer Institute, Switzerland
- Professor Tony Lomax, Paul Scherrer Institute, Switzerland

Thank you to the Medical Physics Department at Addenbrooke's Hospital and at PSI