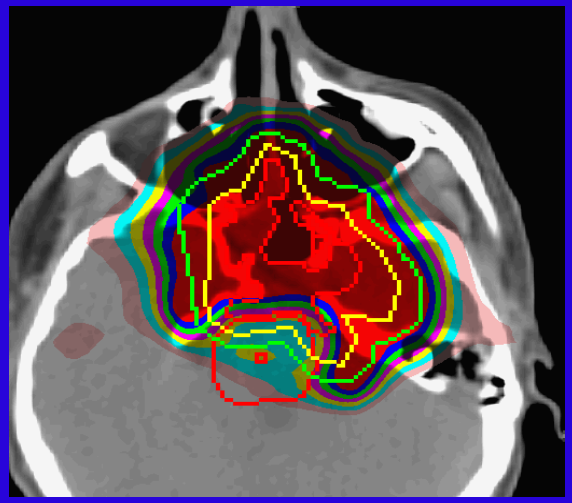
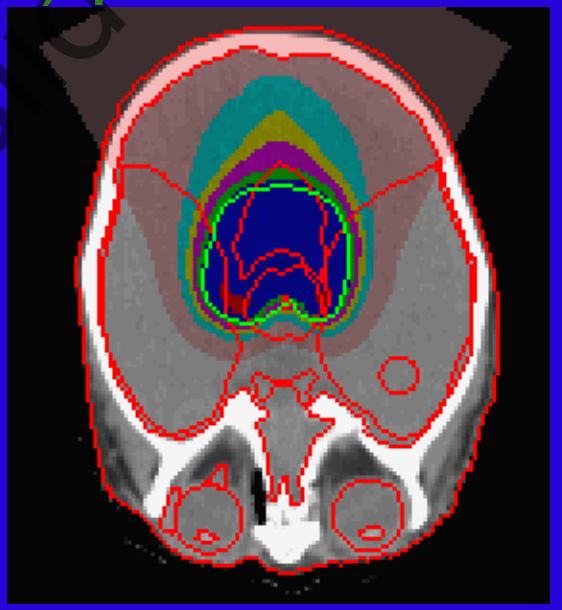
The problem of the patient: Future challenges in particle therapy

Prof Tony Lomax, Paul Scherrer Institute and Department of Physics, ETH Zurich

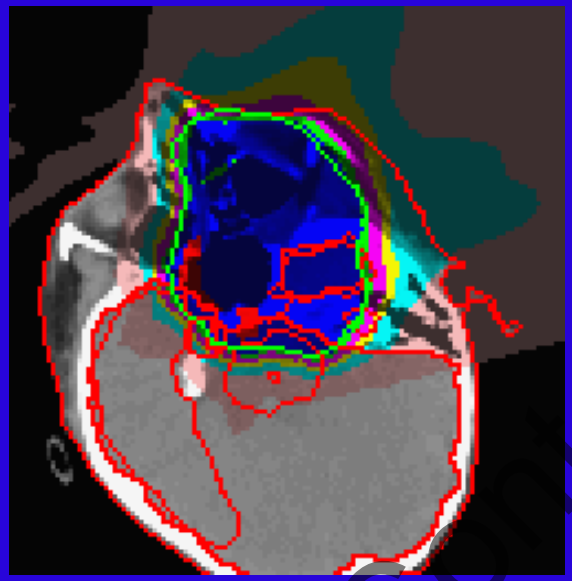
We can do beautiful things with (PBS) protons…



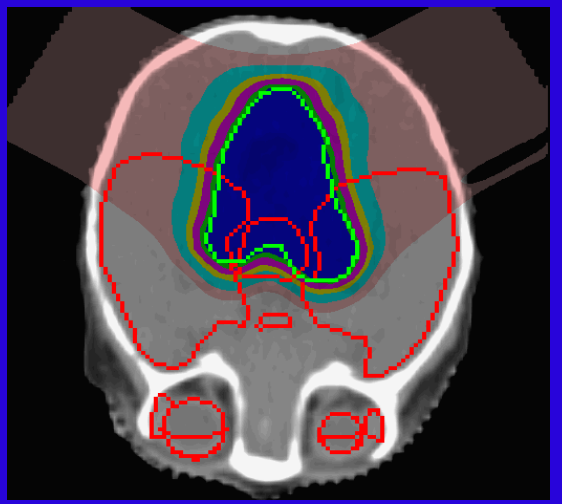
Skull base chordomas
222 Patients
5y Local control: 80%



Ependymomas
50 Patients
5y Local control: 78%

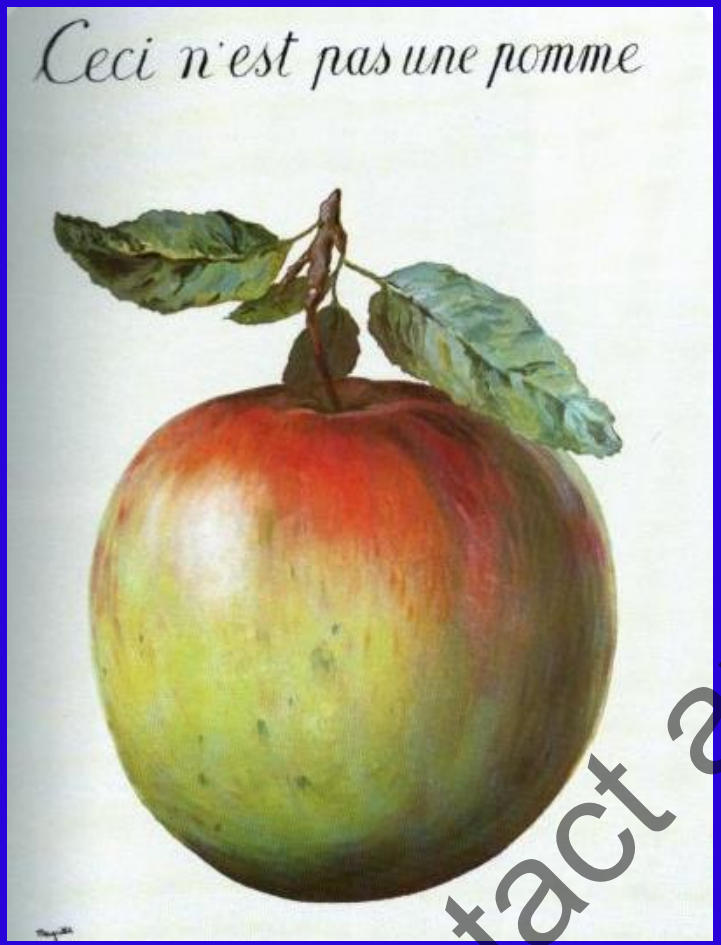


Parameningeal Rhaddomyosarcomas
31 Patients
5y Local control: 73%

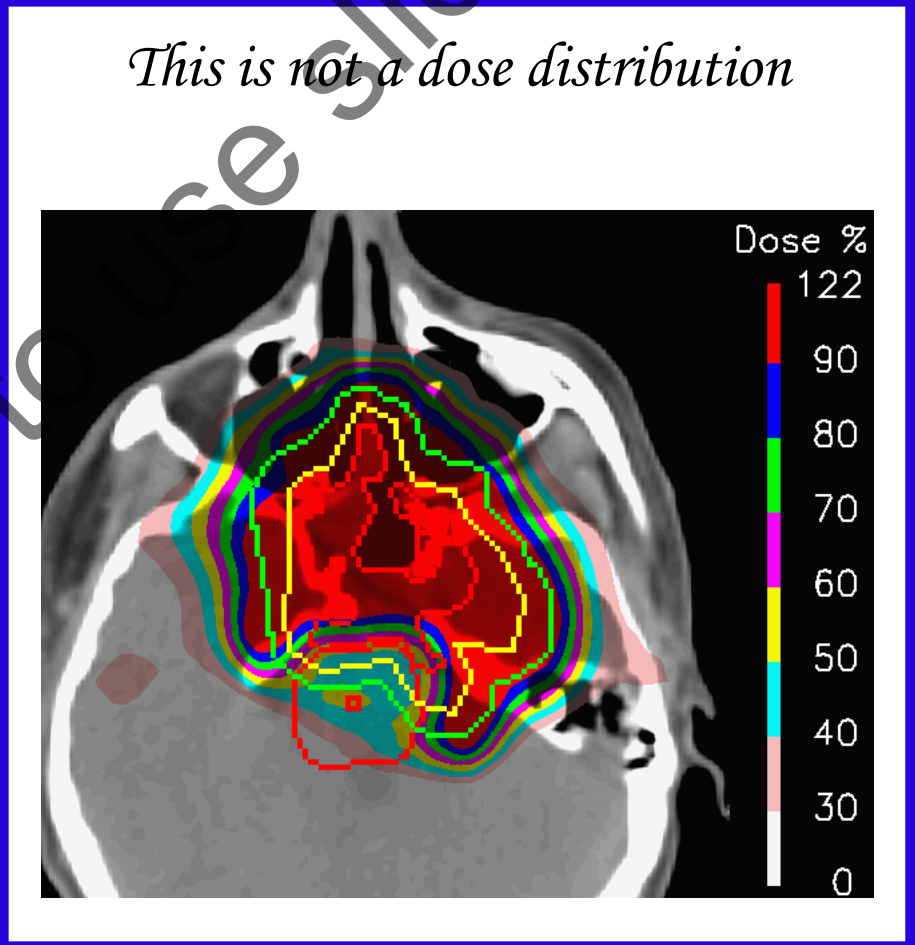


Atypical Teratoid/Rhabdoid
15 Patients
2y Local control: 66%

…but, is what you see what you get?



Rene Magritte 1964



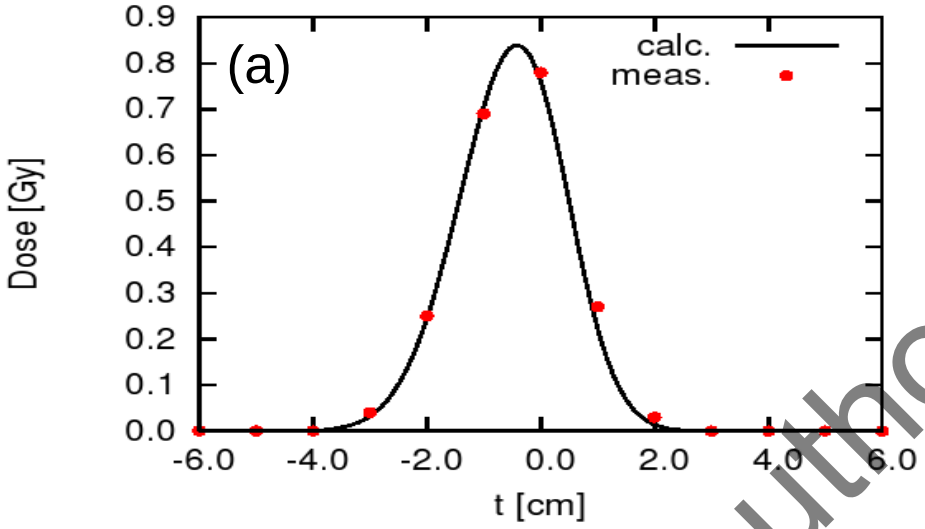
PSIPLAN 2008

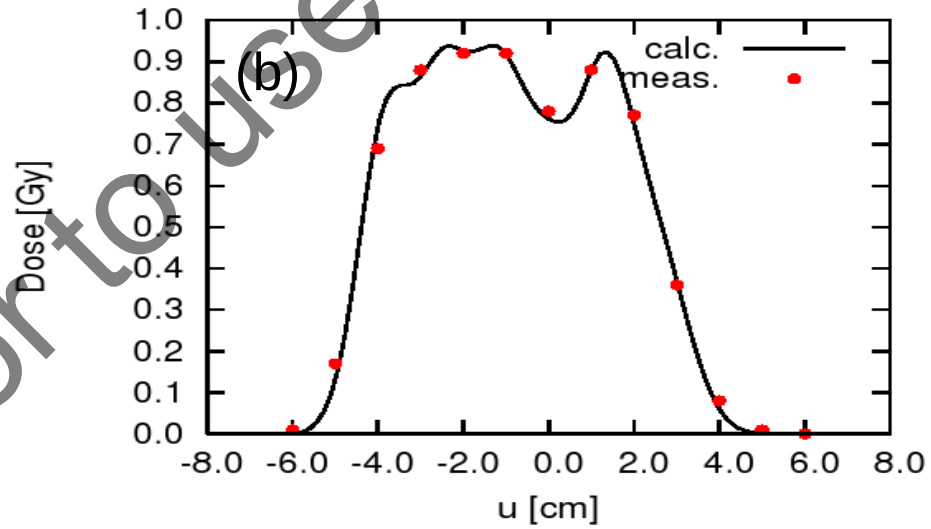
Tasting the apple 1:

The ‘water’ patient

Measuring dose in water

E.g. Measuring patient dose distributions in water





- **Measure with array of 26 pin-point chambers**
- **Spatial error ~ 1mm**
- **Overall dose error ~ 2%**
- **Standard deviation of dose: 0.015 Gy**

Tasting the apple 2:

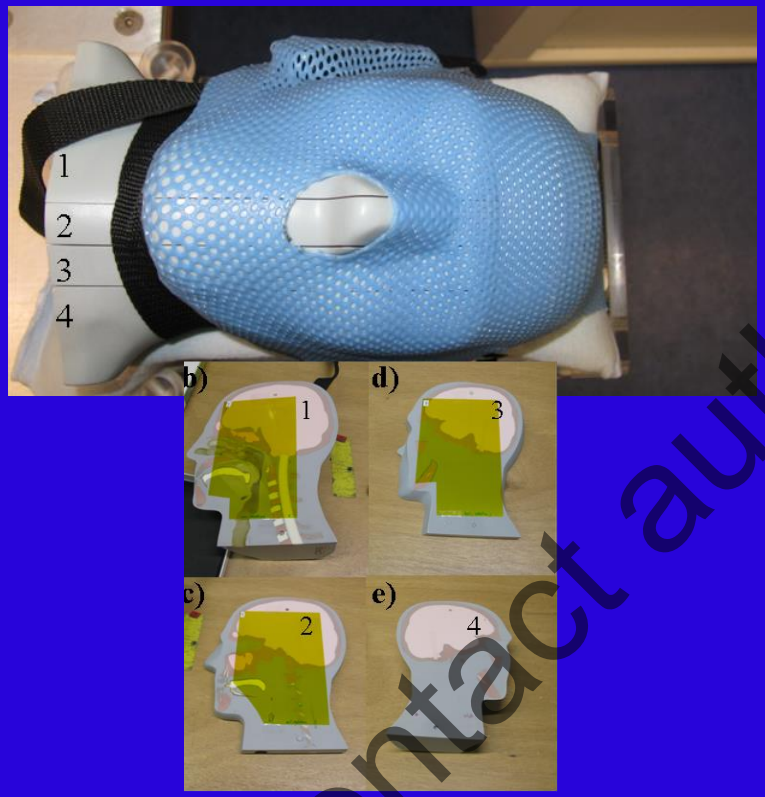
The ‘real’ patient

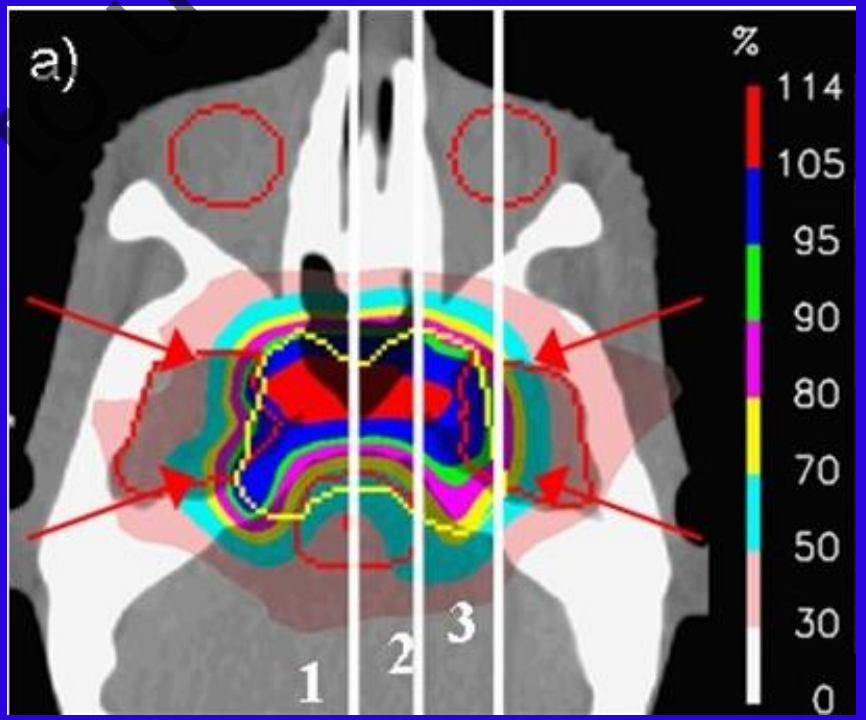
A real patient is not water….

Density (range) effects on protons

How important are these for a ‘real’ (and static) patient?

GafChromic film verification of IMPT plans in an anthropomorphic phantom



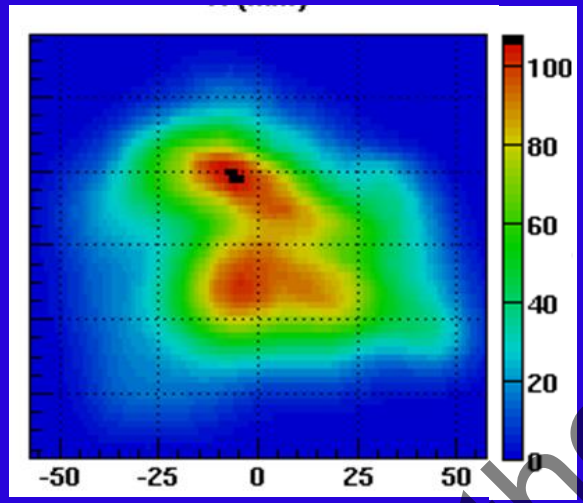


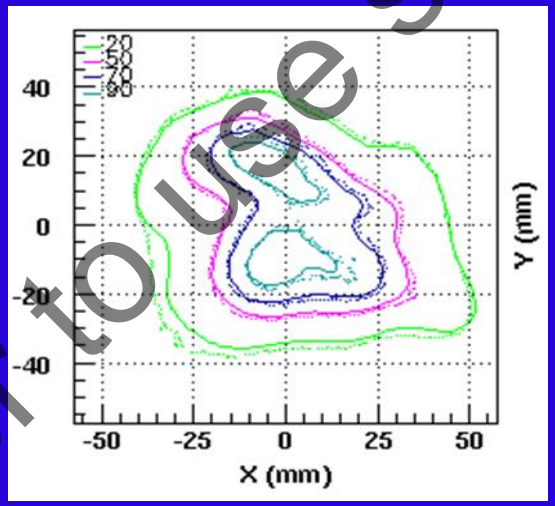
Albertini et al, PMB 56:4415-4431, 2011

Density (range) effects on protons

How important are these for a 'real' (and static) patient?

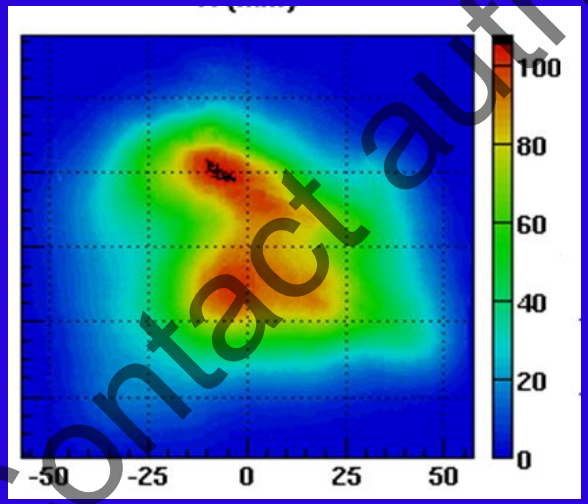
Dose calculation

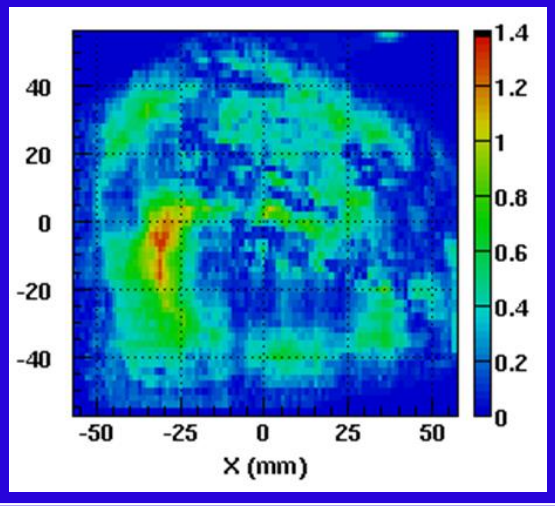




Iso-dose overlay

Measurement





γ analysis (>99% of points agree at 3mm/3%)

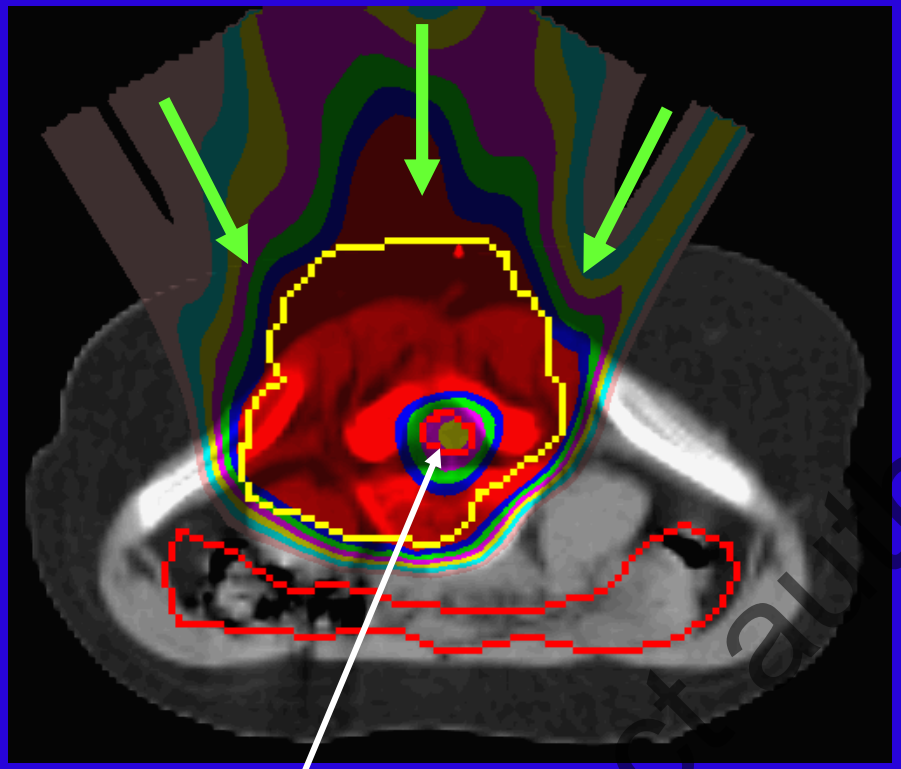
Albertini et al, PMB 56:4415-4431, 2011

Tasting the apple 3:

The changing patient

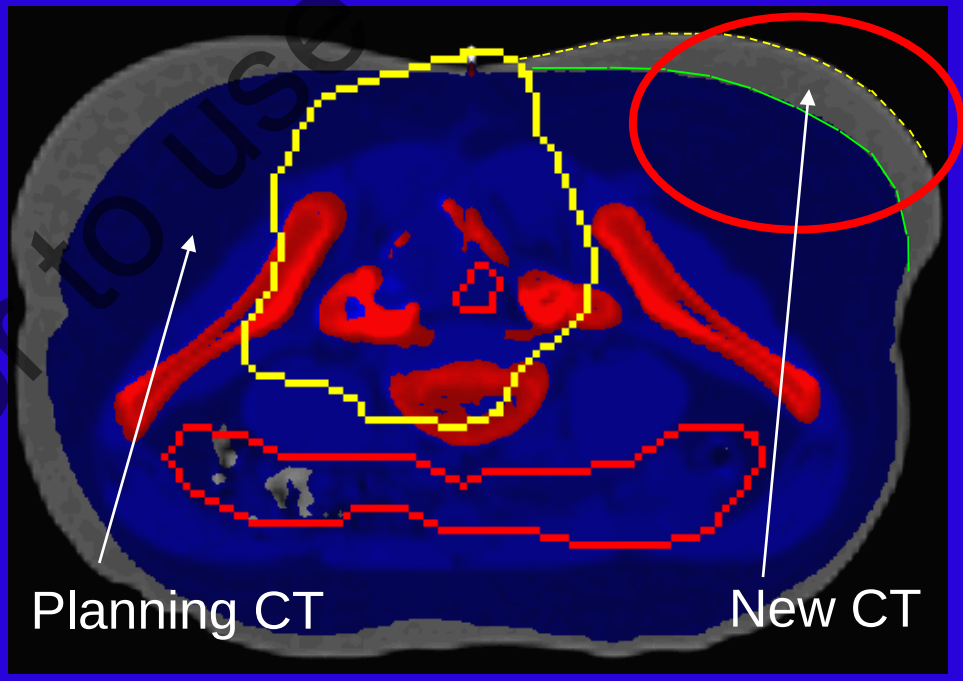
Weight and range changes

3 field IMPT plan to an 8 year old boy



Note, sparing of spinal cord in middle of PTV

During treatment, 1.5kg weight gain was observed



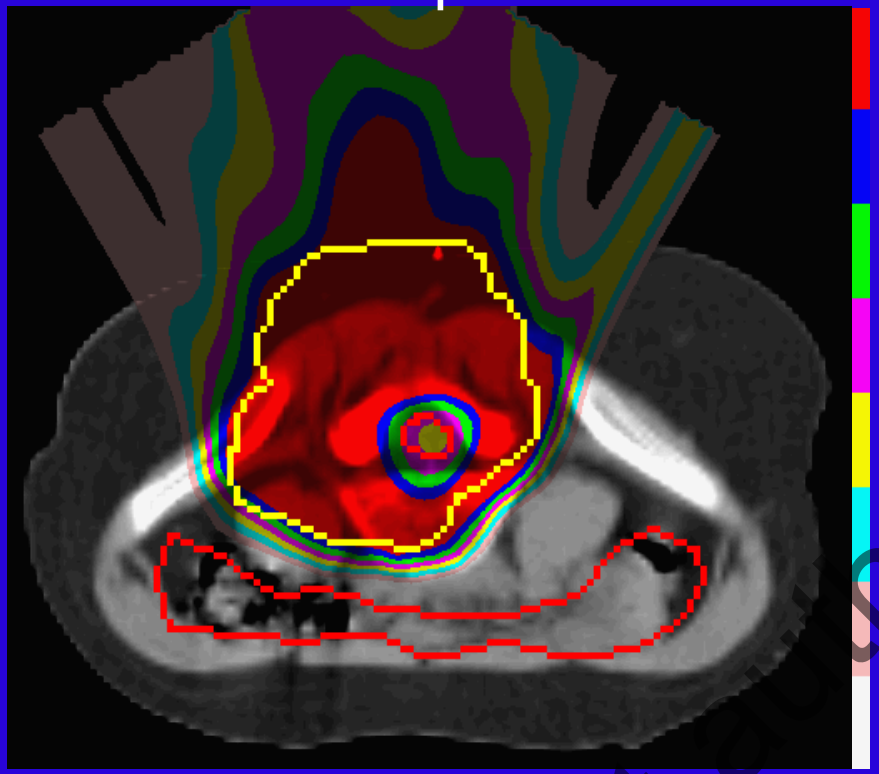
Max range differences:
SC 0.8cm
CTV 1.5cm

Francesca Albertini and Alessandra Bolsi (PSI)

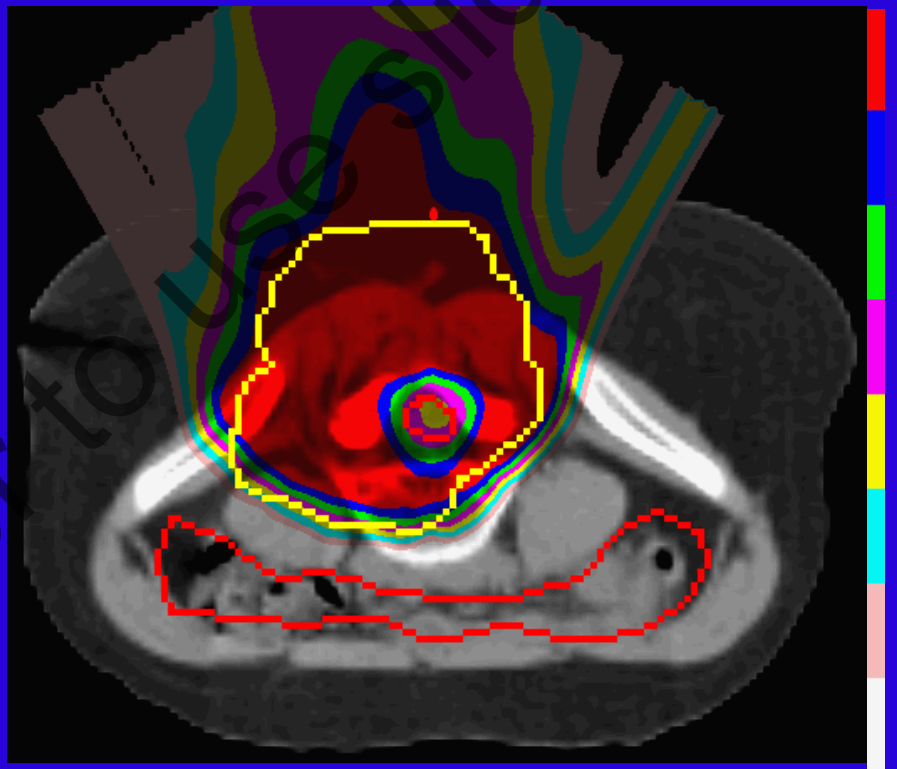
Tony Lomax, ENLIGHT meeting 2015, Krakow

Weight and range changes

Nominal plan



Recalculation on new CT

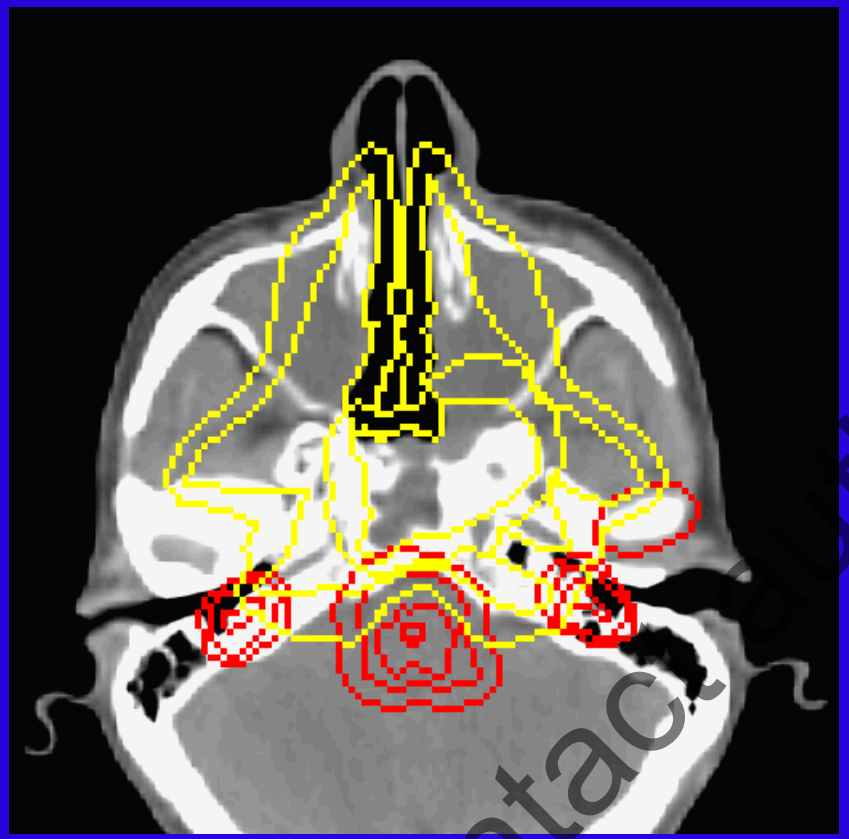


CTV	Mean	V90
Nominal	96.5%	78%
New	95.0%	74%

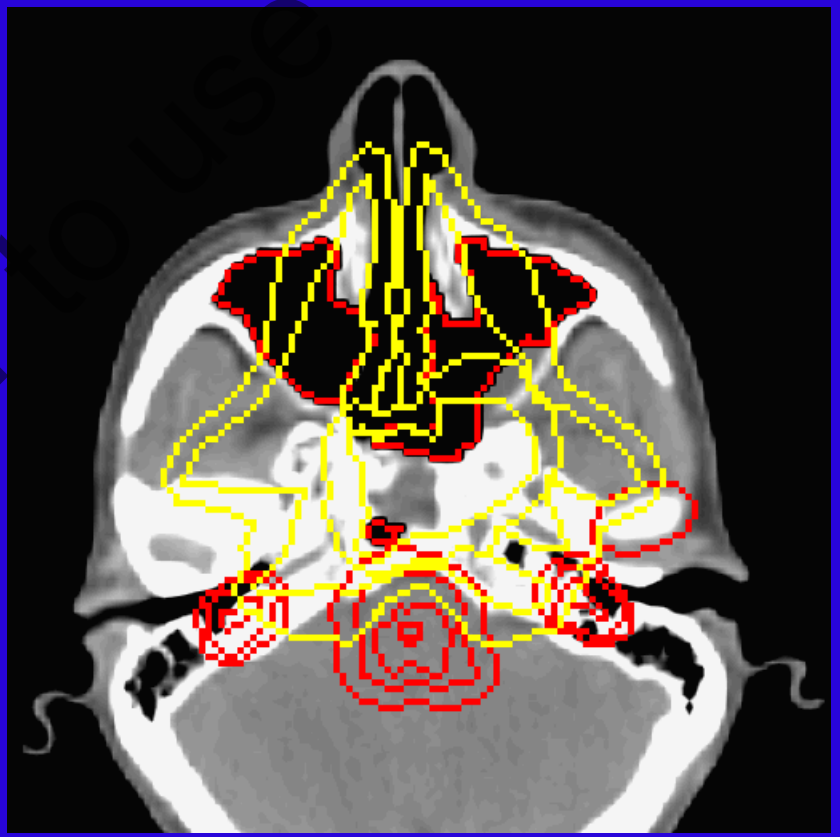
Spinal cord	Mean	Max
Nominal	30.0%	74%
New	28.5%	76%

Cavity filling and range changes

E.g. Skull base Chondrosarcoma



Planning CT



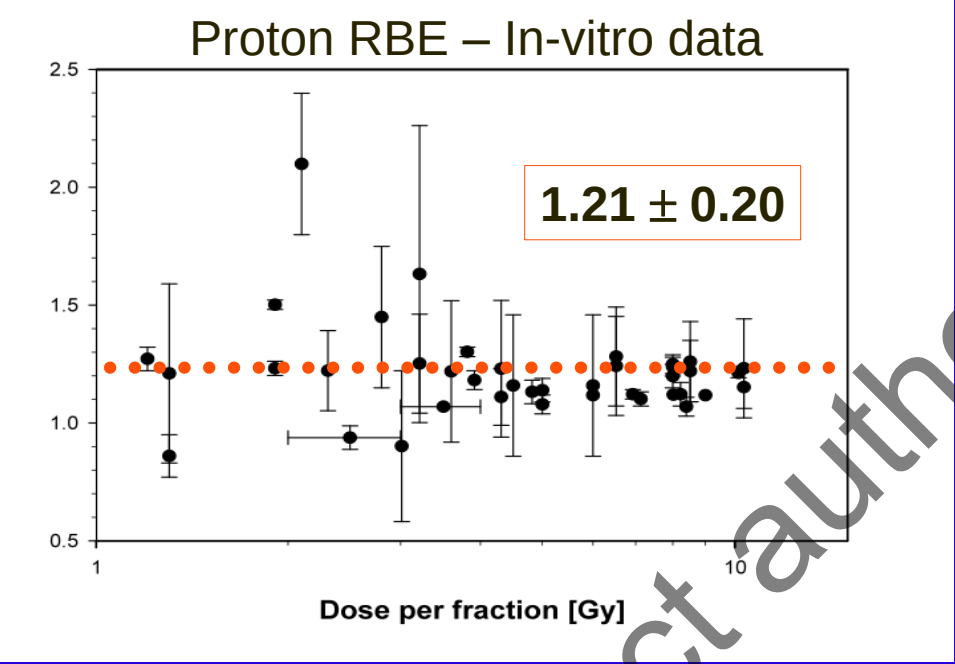
Repeat CT after 2 weeks

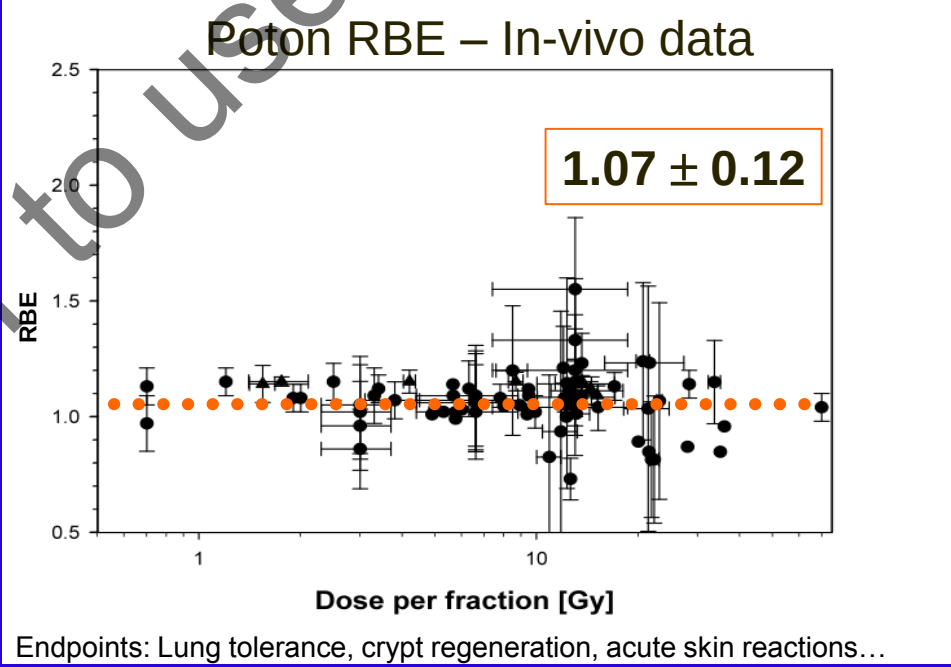
Tasting the apple 4:

The biological patient

(In-vivo) RBE

Review of in-vitro and in-vivo RBE experimental data



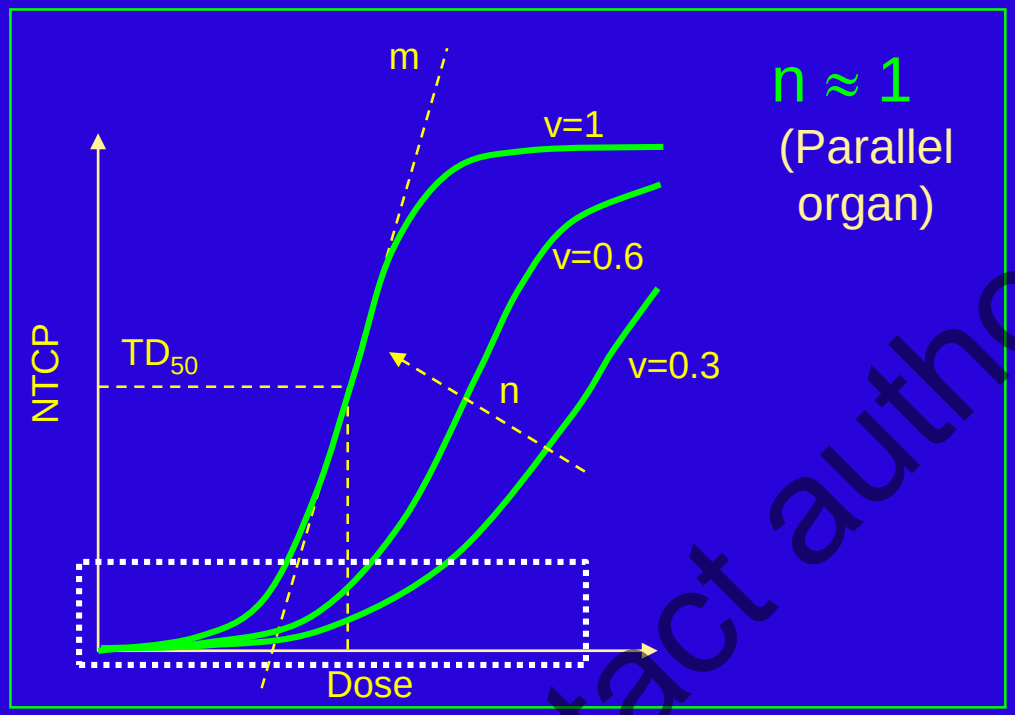


Endpoints: Lung tolerance, crypt regeneration, acute skin reactions…

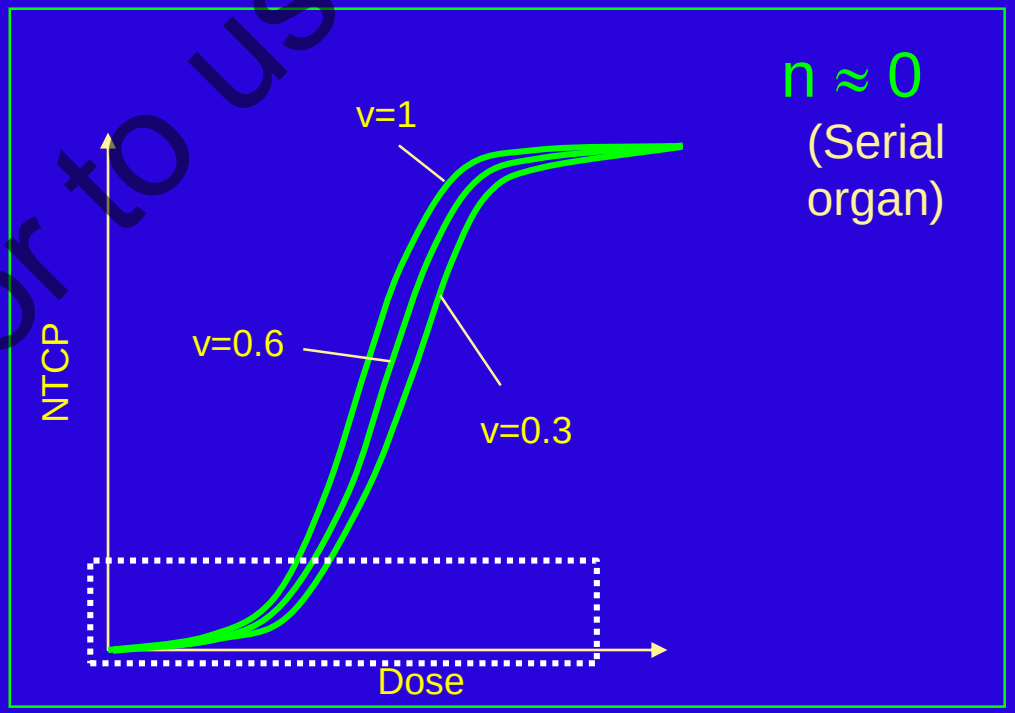
Paganetti *IJROBP*, 2002; 53, 407

Understanding normal tissue response

e.g. The ‘Lyman-Kutcher-Burmann’ model for NTCP



n ≈ 1
(Parallel organ)

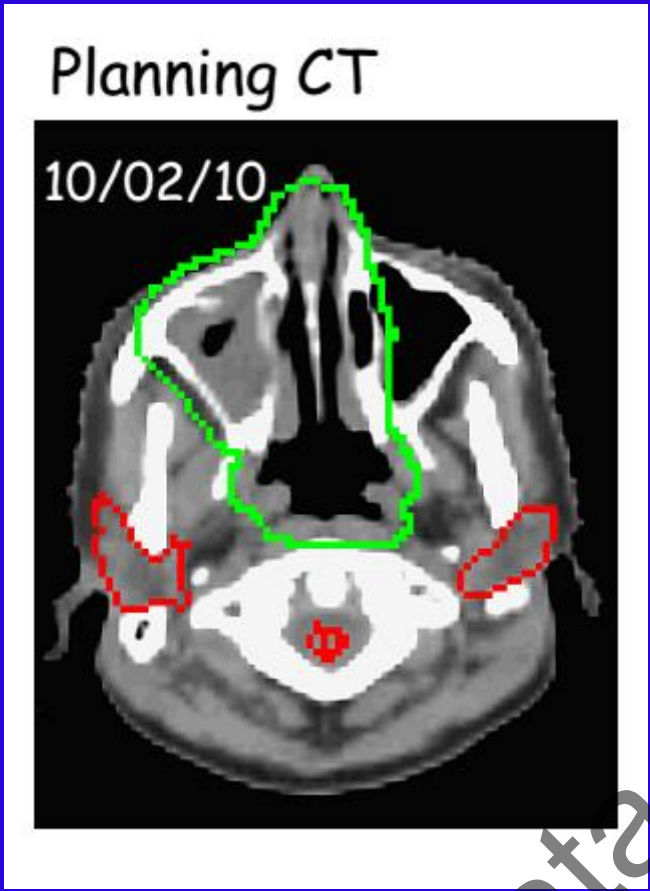


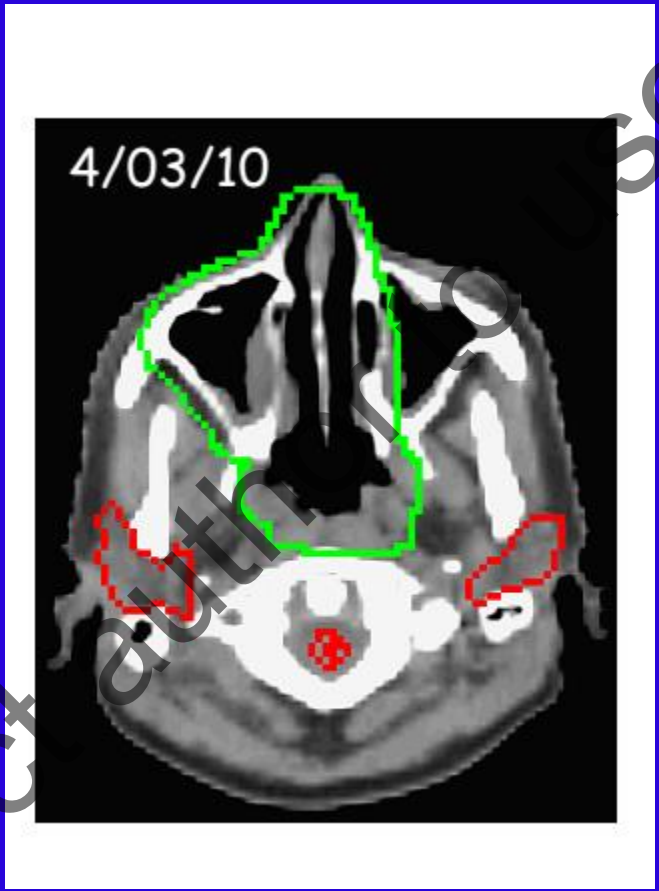
n ≈ 0
(Serial organ)

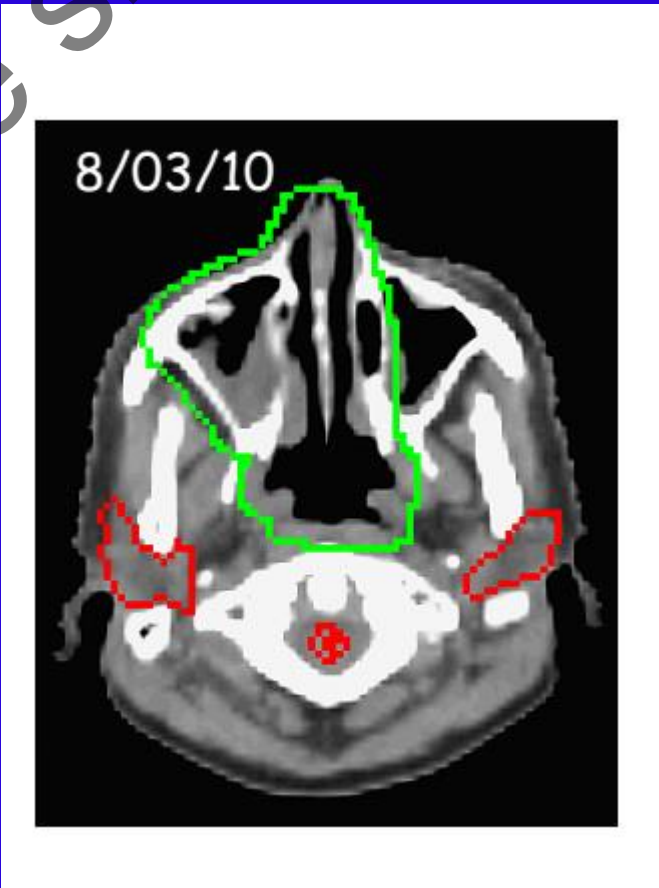
Preserving the apple 1:

Adaptive therapy

The need for adapted proton therapy

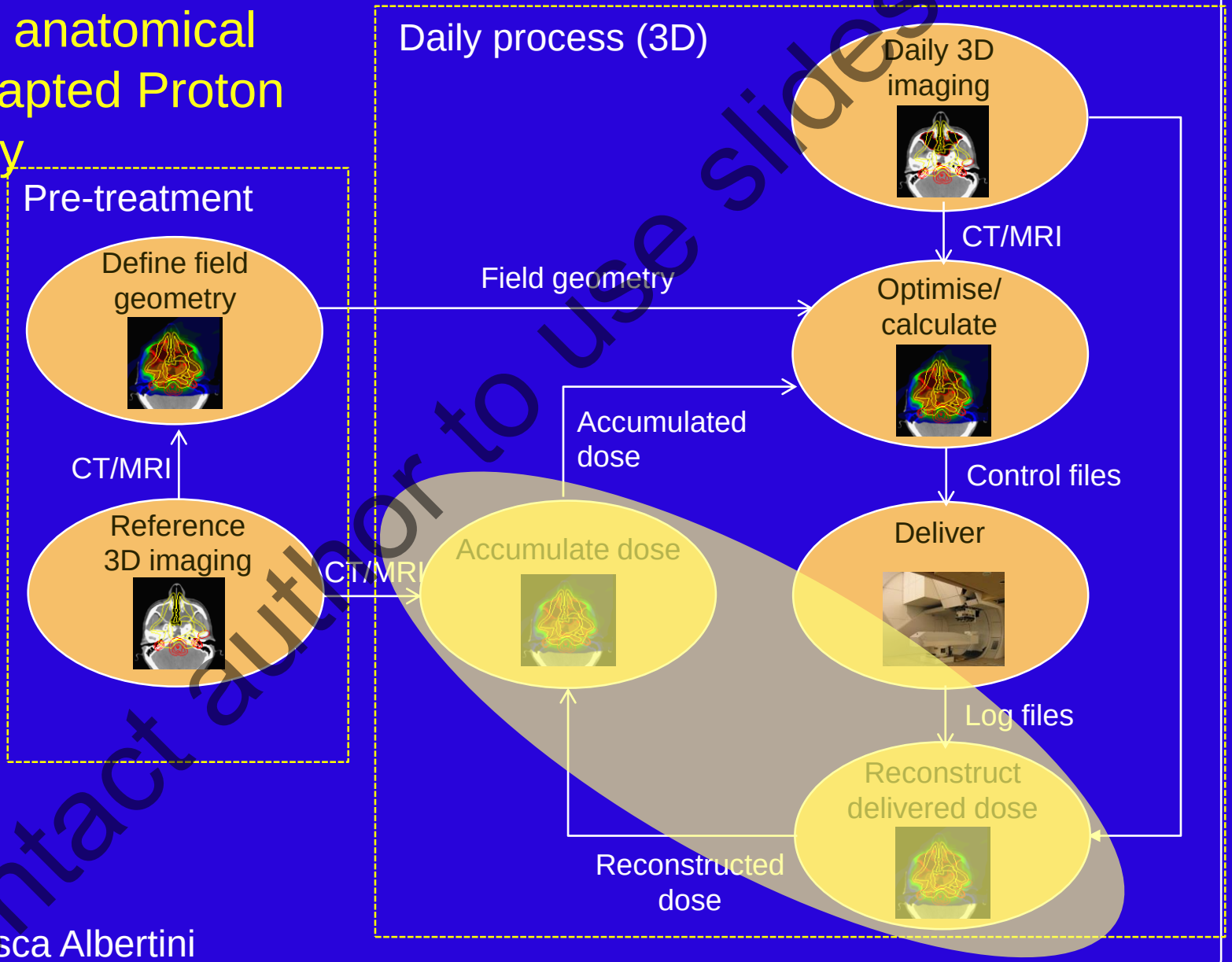






Francesca Albertini and Alessandra Bolsi

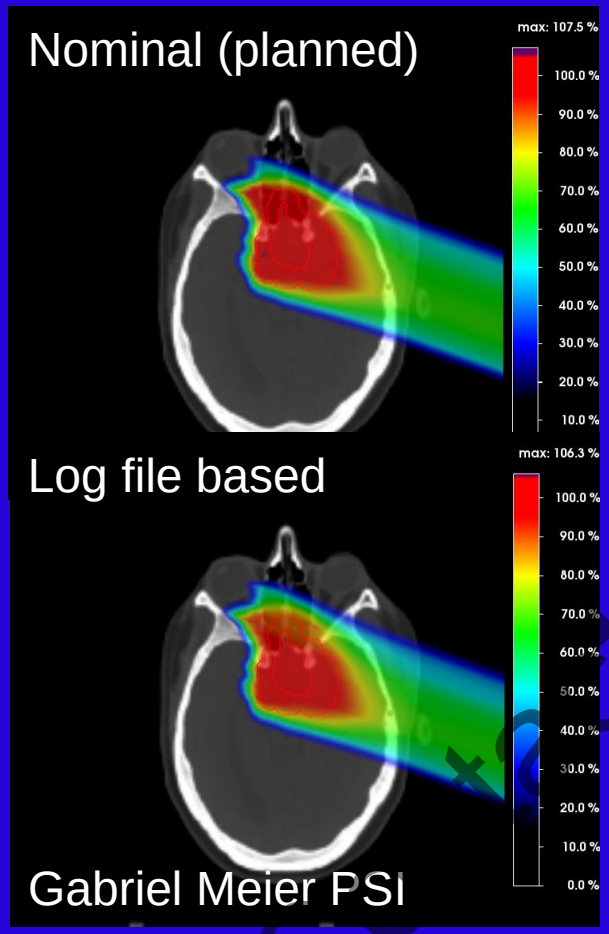
Dealing with daily anatomical changes : Daily Adapted Proton Therapy



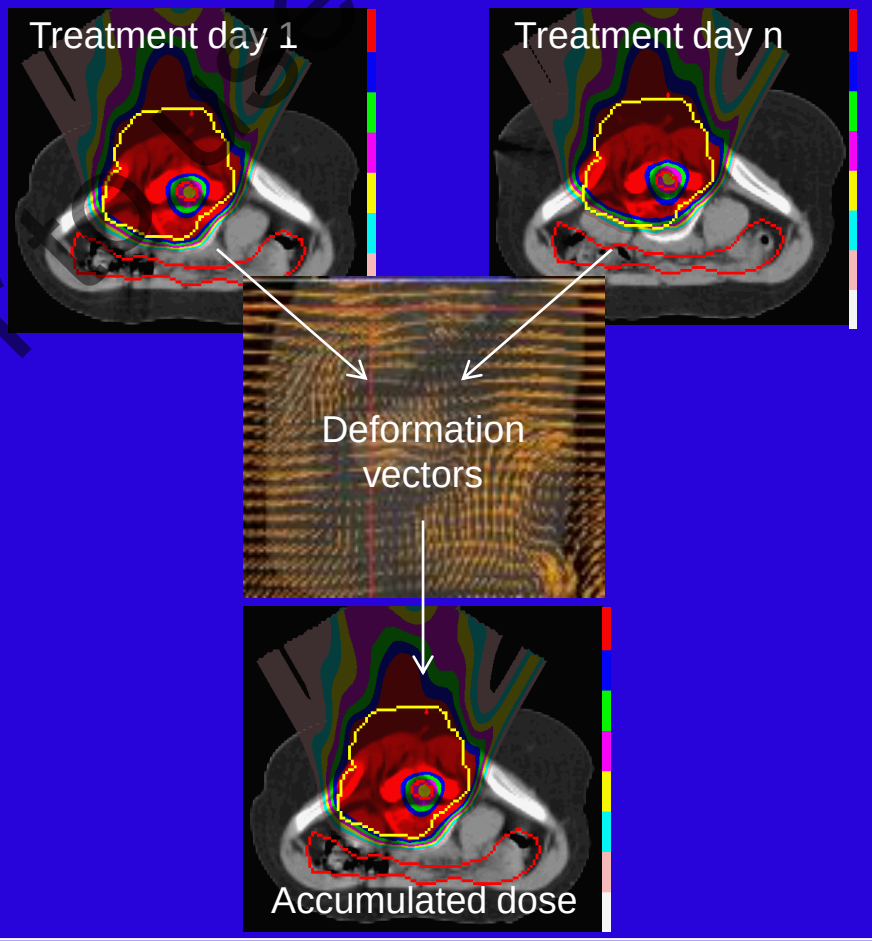
Tony Lomax and Francesca Albertini

Accurate estimates of delivered dose through DAPT

Dose reconstruction



Dose accumulation

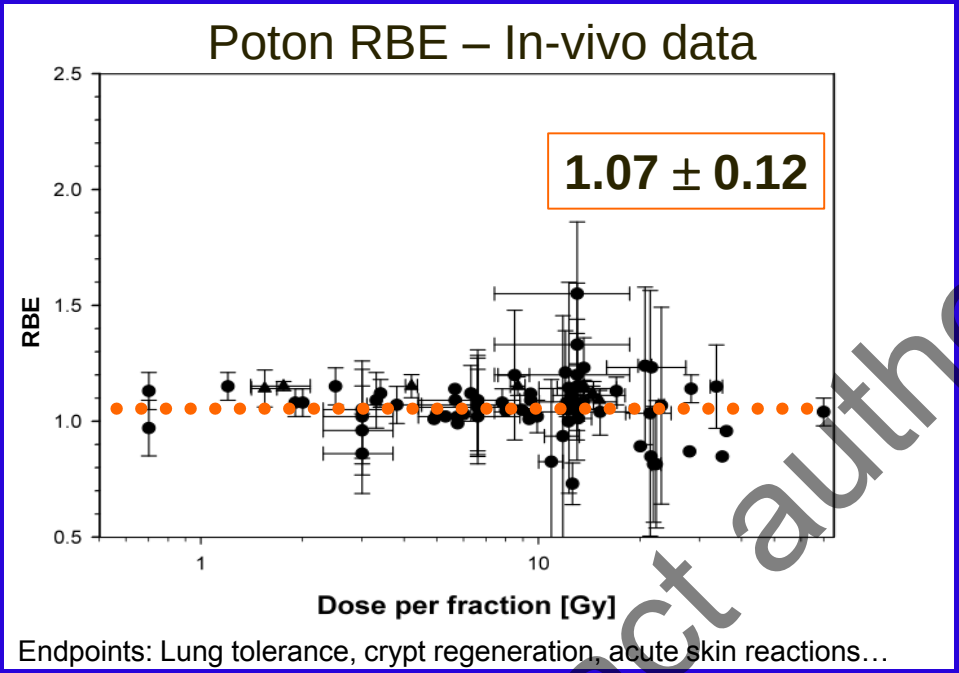


Preserving the apple 2:

Understanding biological response

Understanding (In-vivo) RBE?

Review of in-vitro and in-vivo RBE experimental data



Endpoints: Lung tolerance, crypt regeneration, acute skin reactions…

RBE is dependent on:

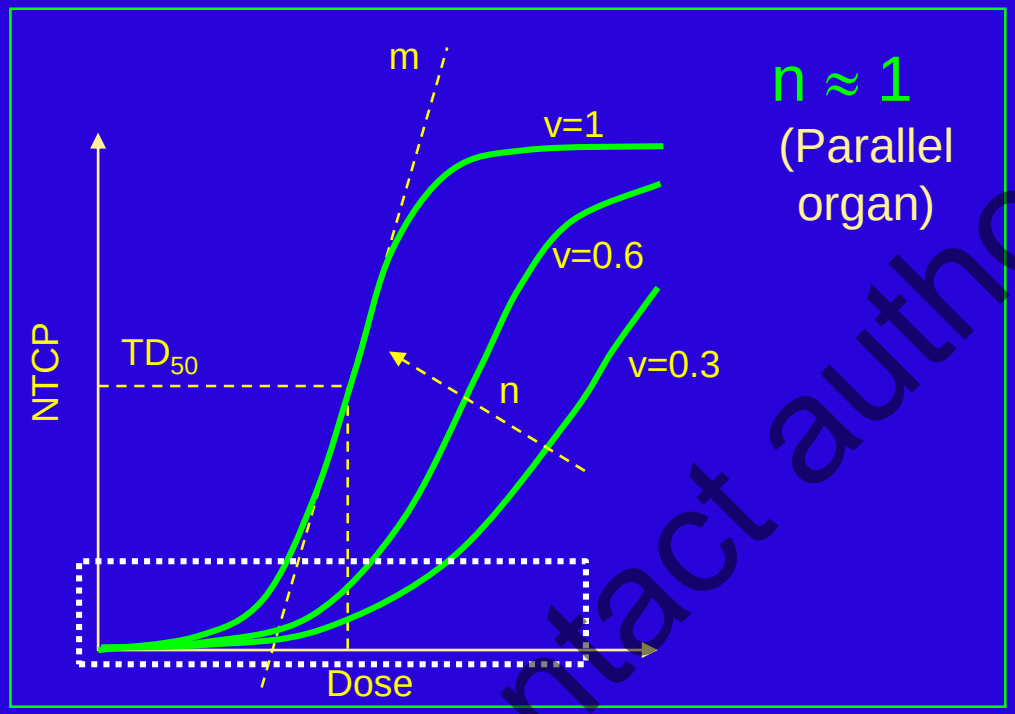
- Organism (mouse/human)
- Tissue/organ type
- End point/complication
- Energy/LET
- Dose
- Dose rate
- …

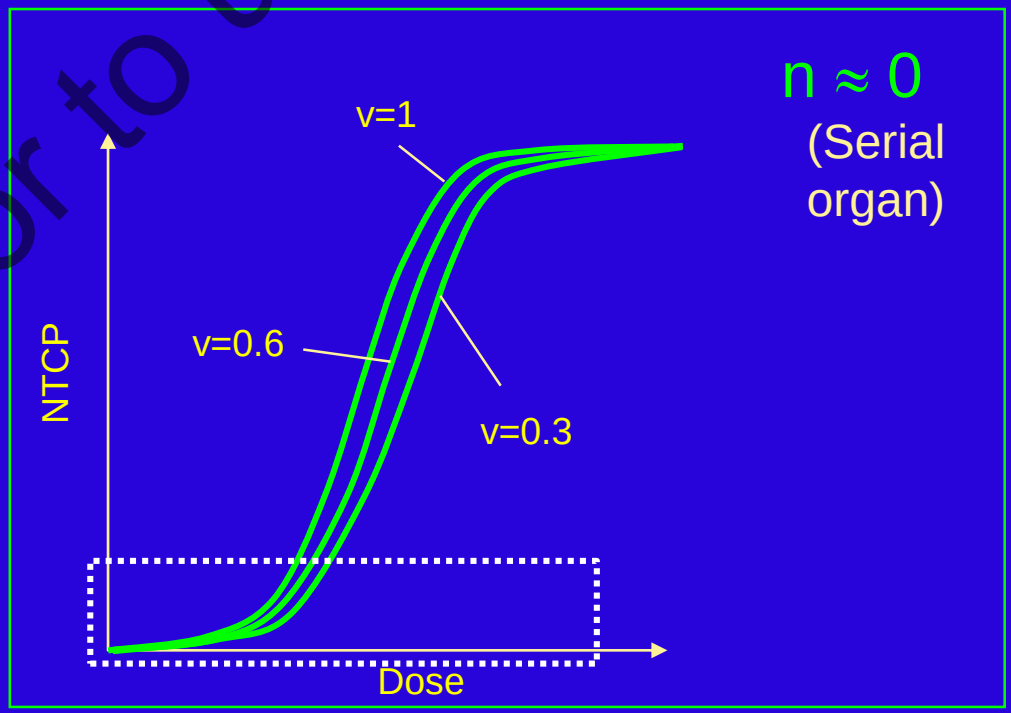
Paganetti *IJROBP*, 2002; 53, 407

Understanding (In-vivo) RBE?

… but is also complicated by tissue architecture

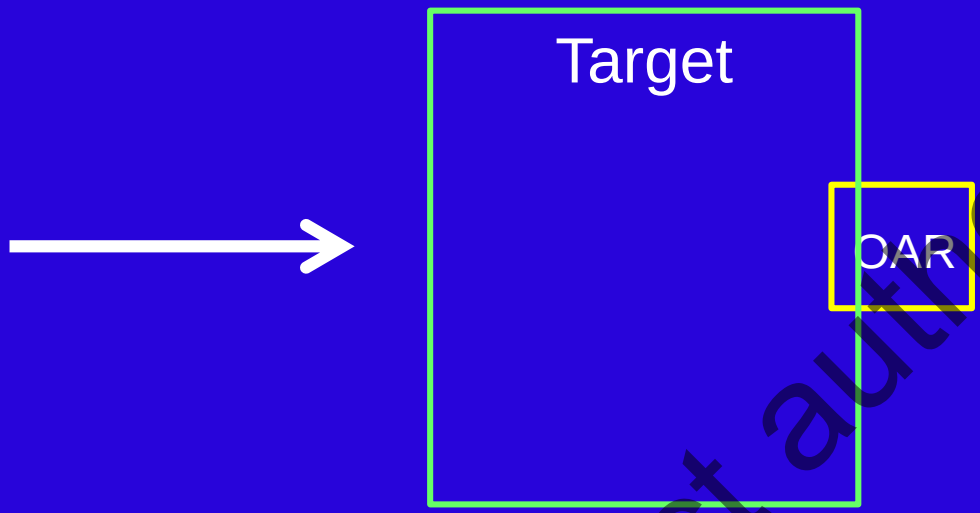
e.g. The ‘Lyman-Kutcher-Burmann’ model for NTCP





Understanding (In-vivo) RBE?

A thought experiment..



Understanding (In-vivo) RBE?

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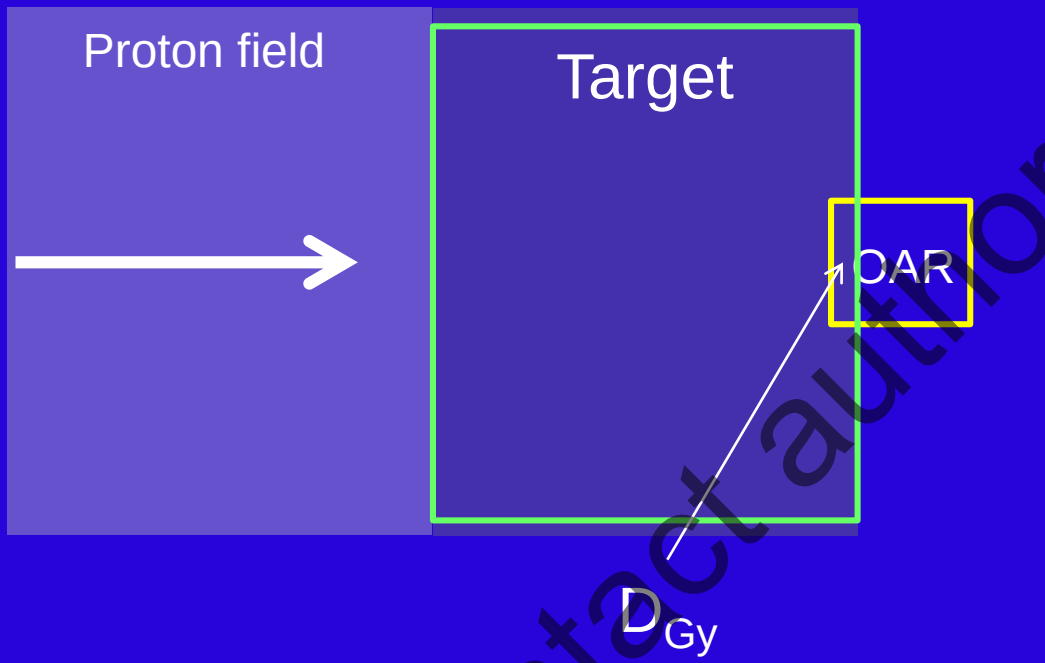

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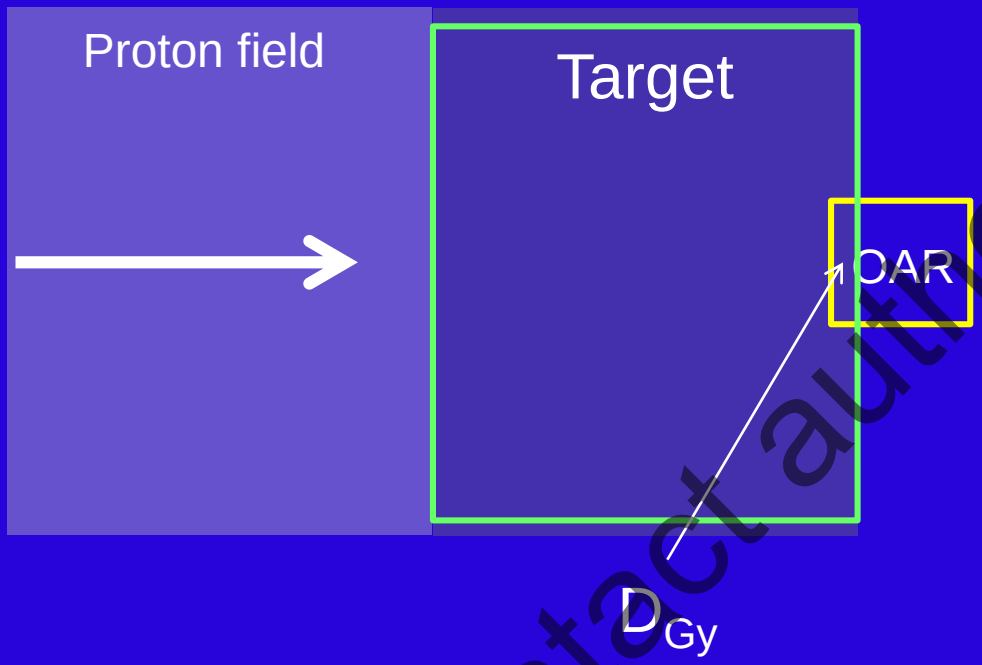

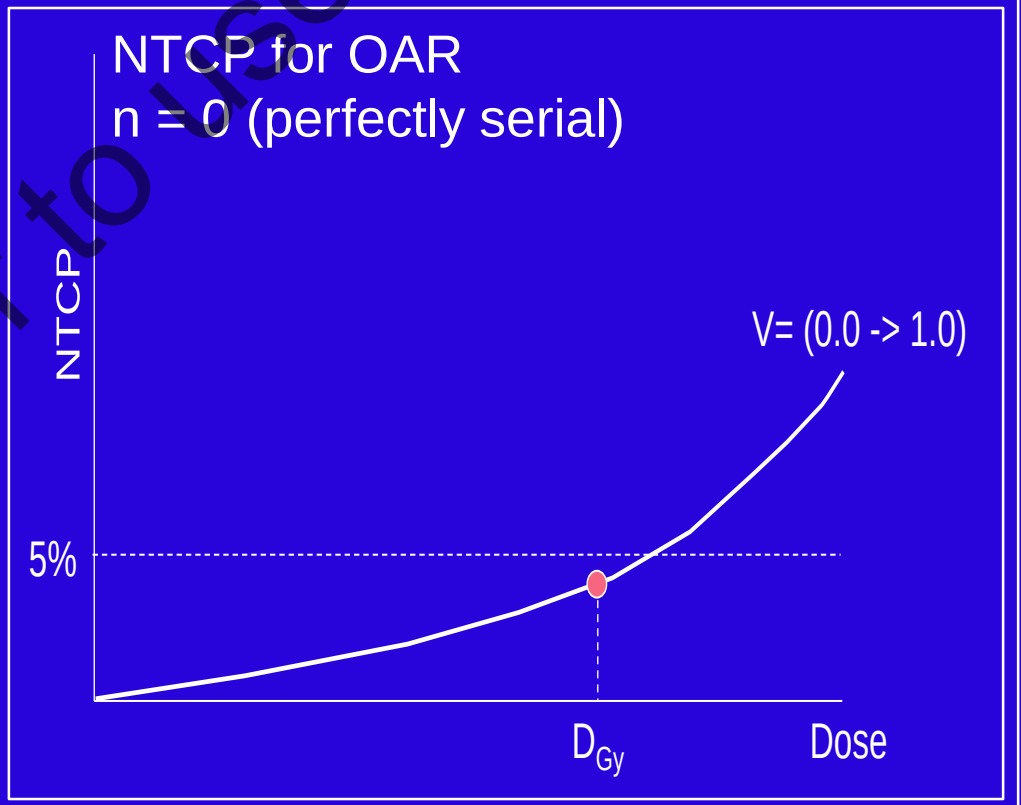

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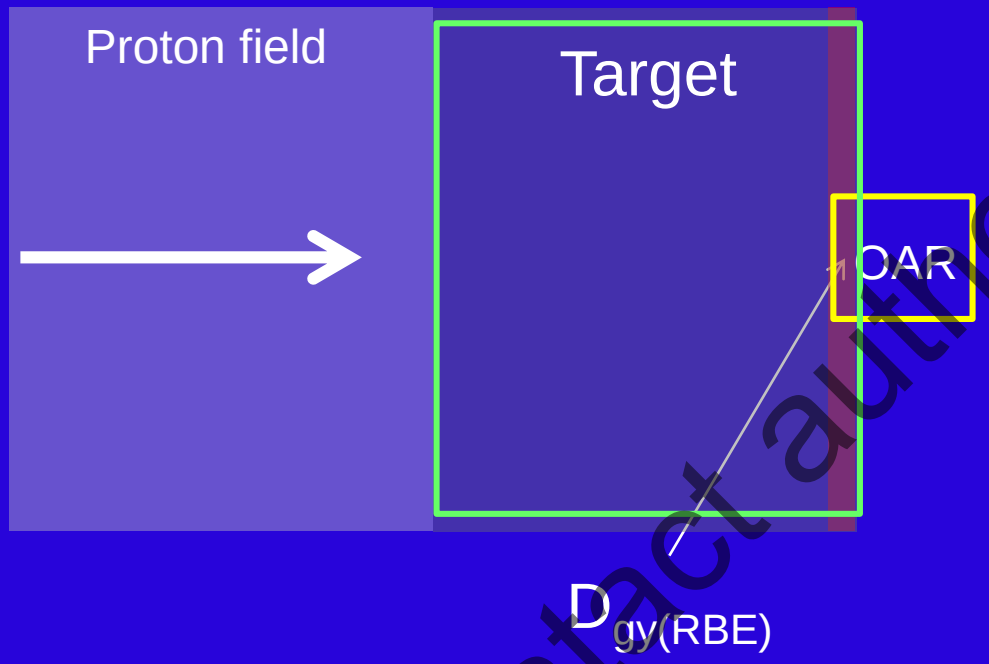

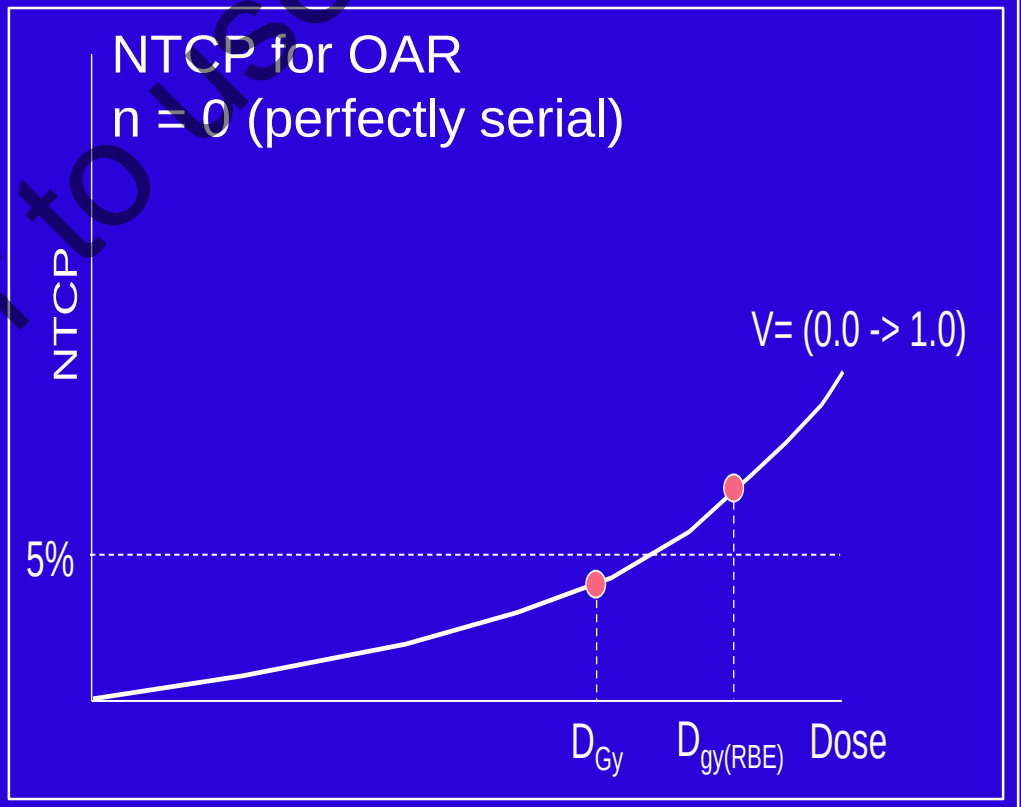

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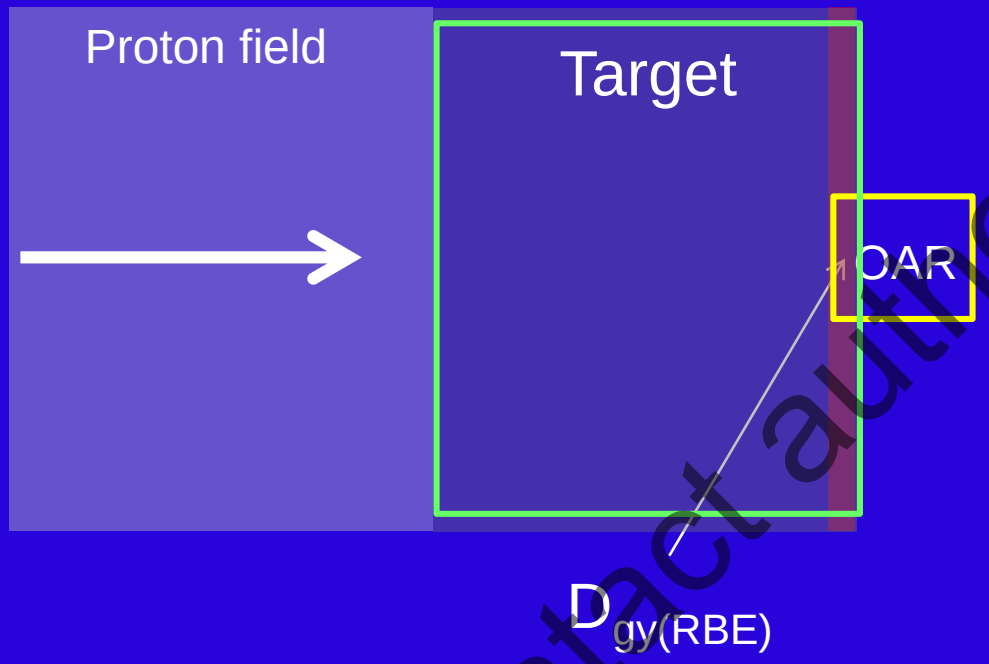

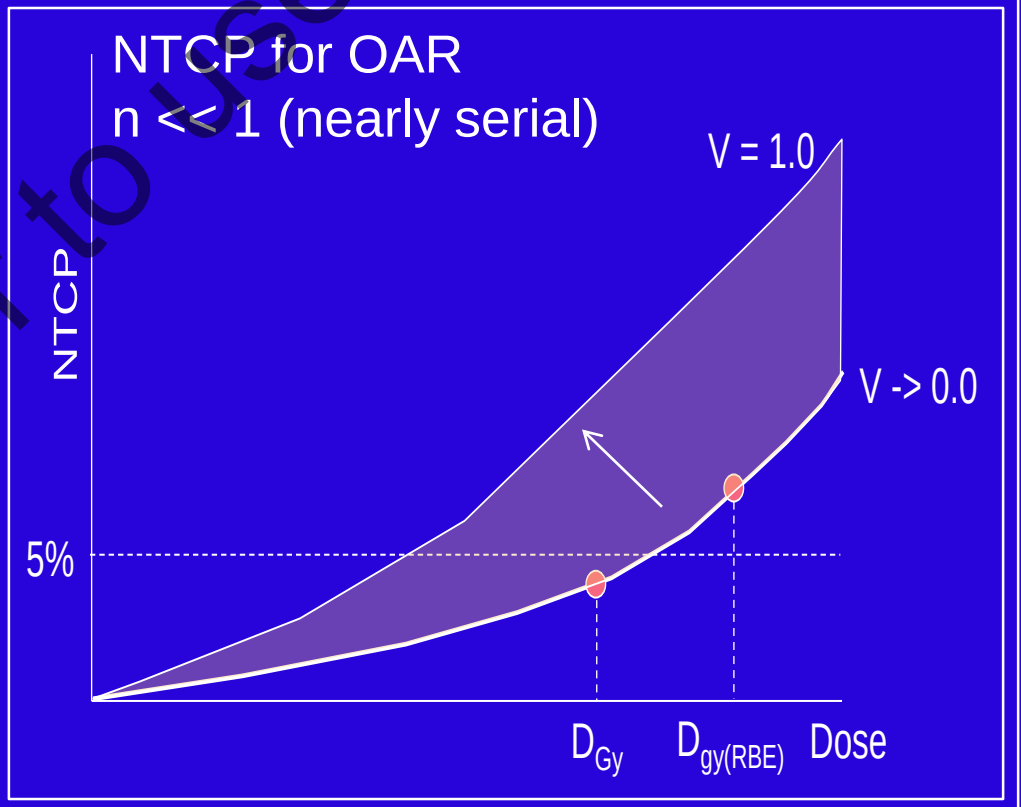

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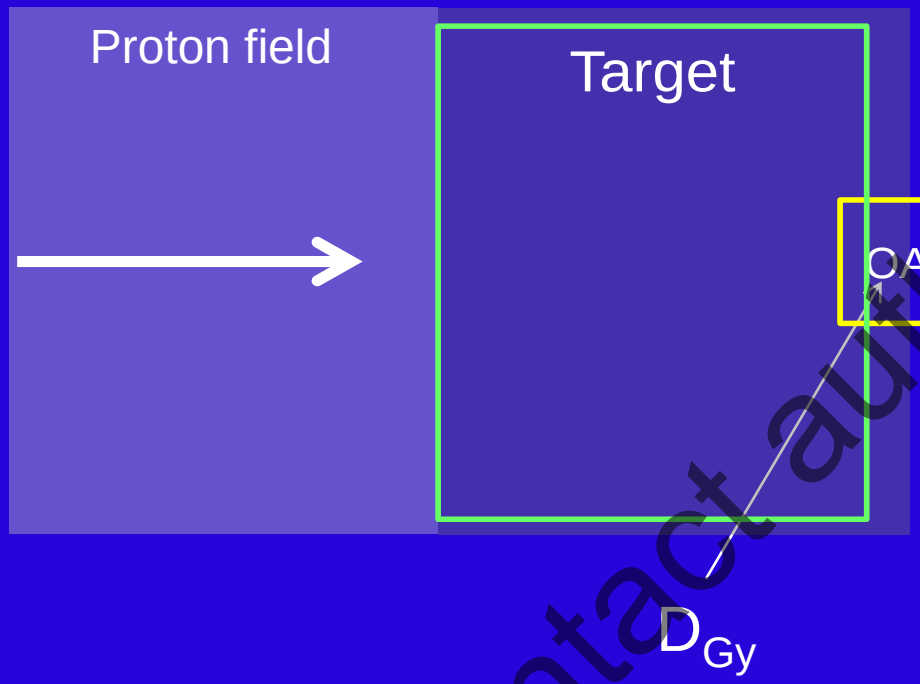

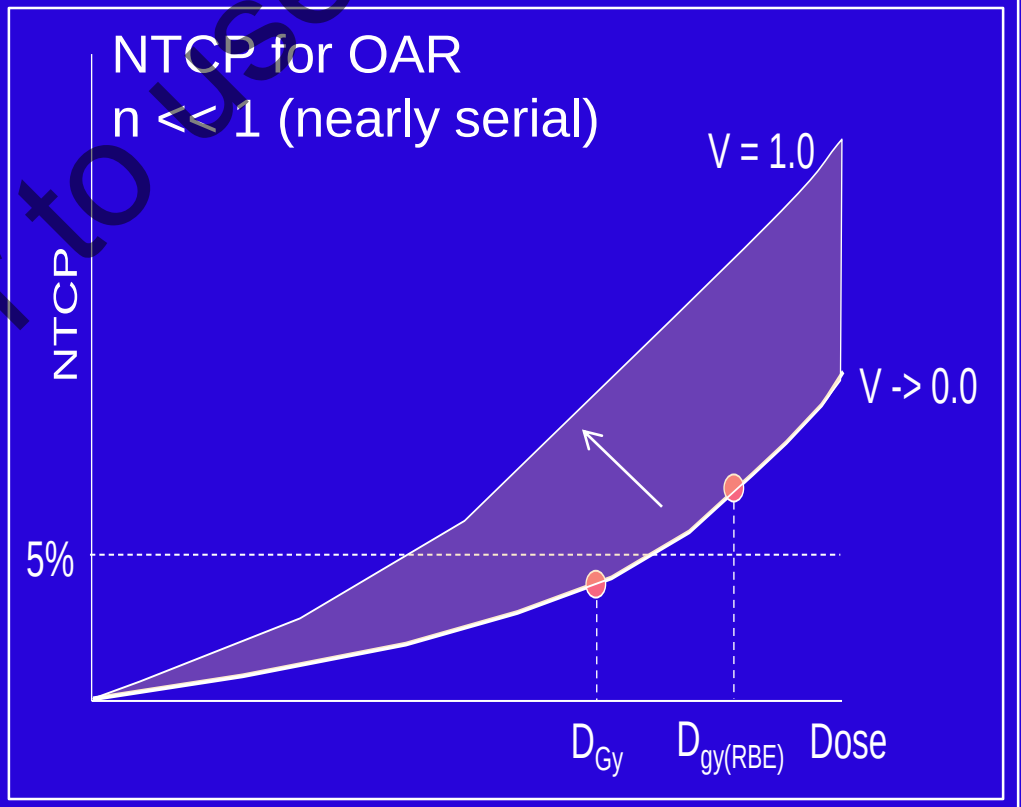

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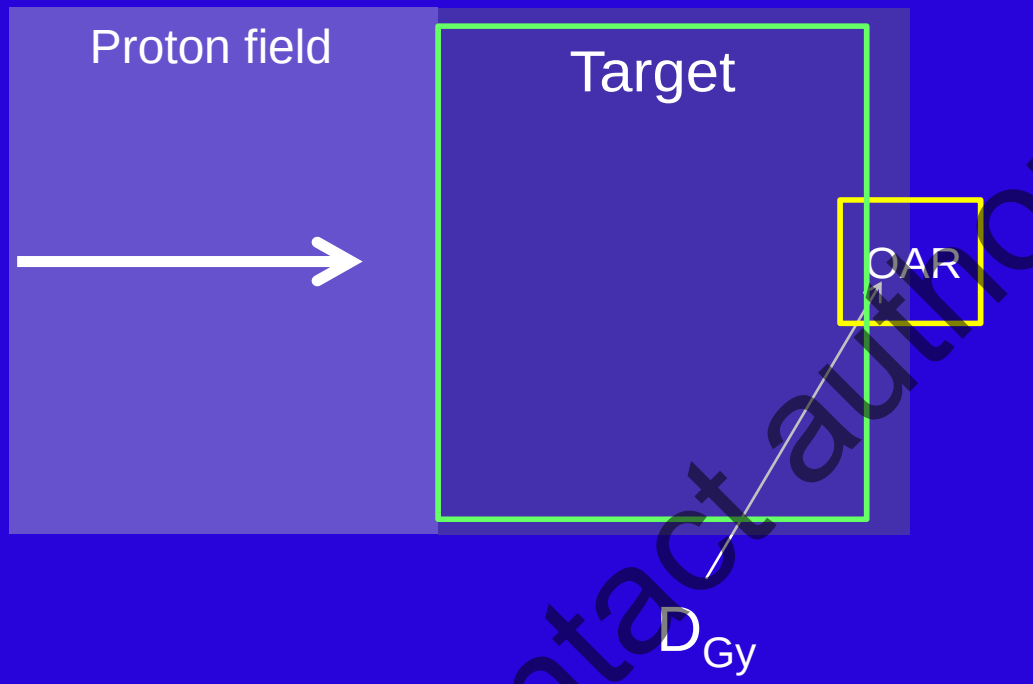
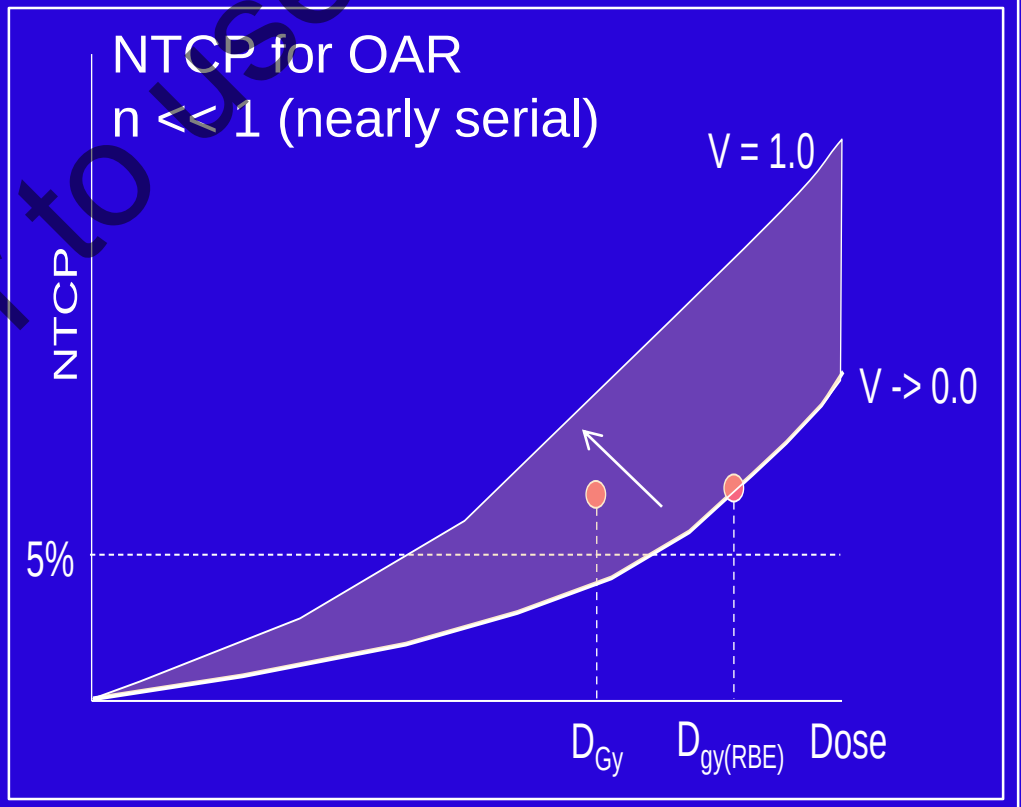
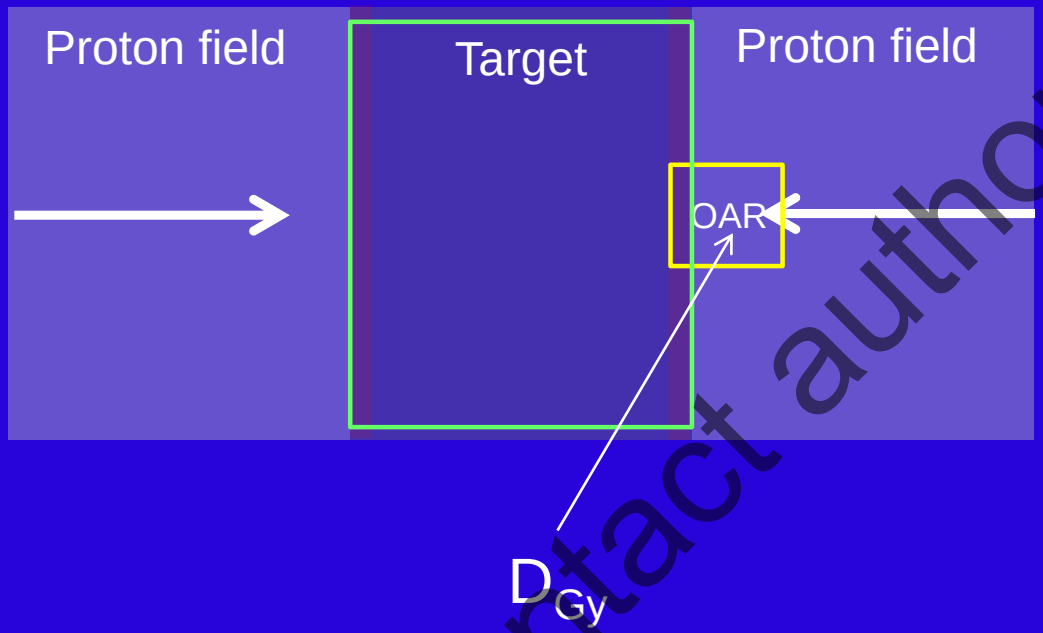
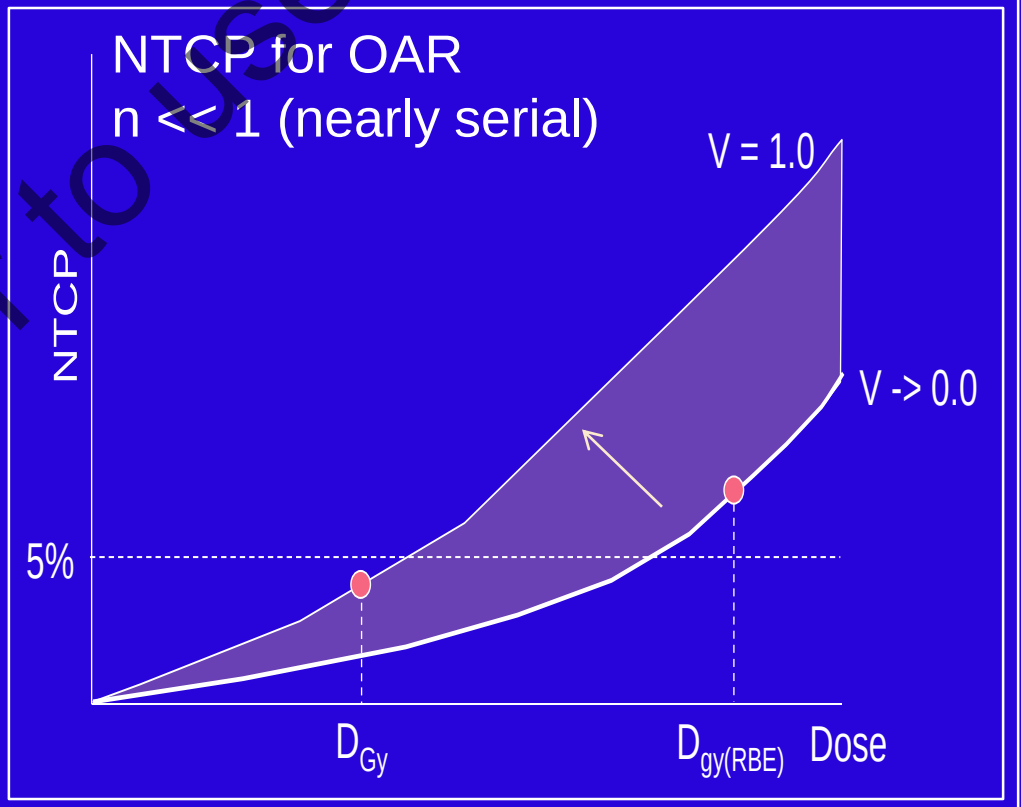




Understanding (In-vivo) RBE?

A thought experiment..





Understanding (In-vivo) RBE?

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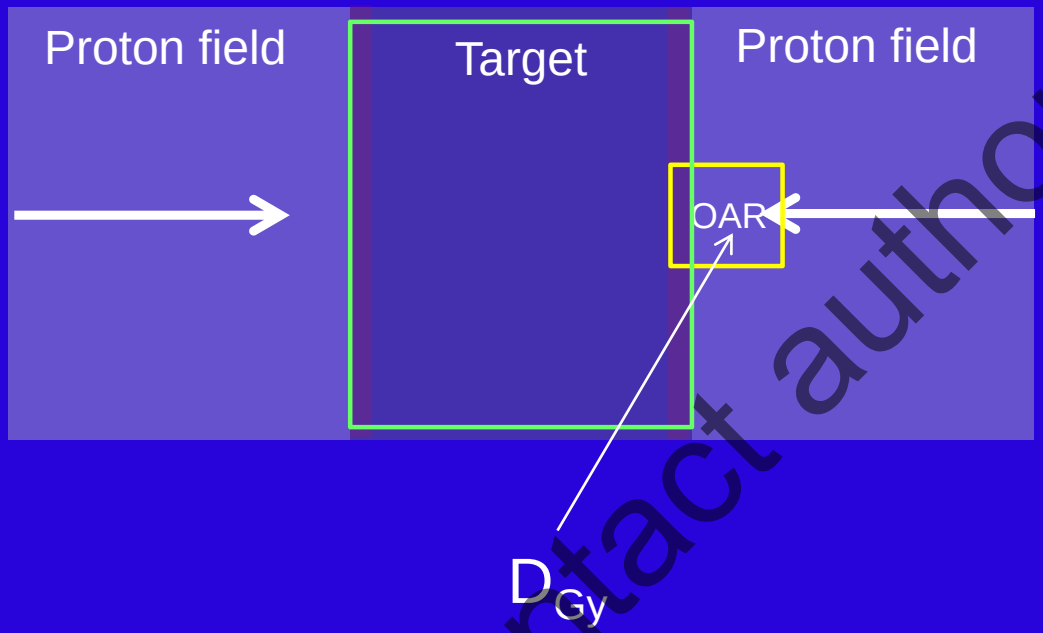
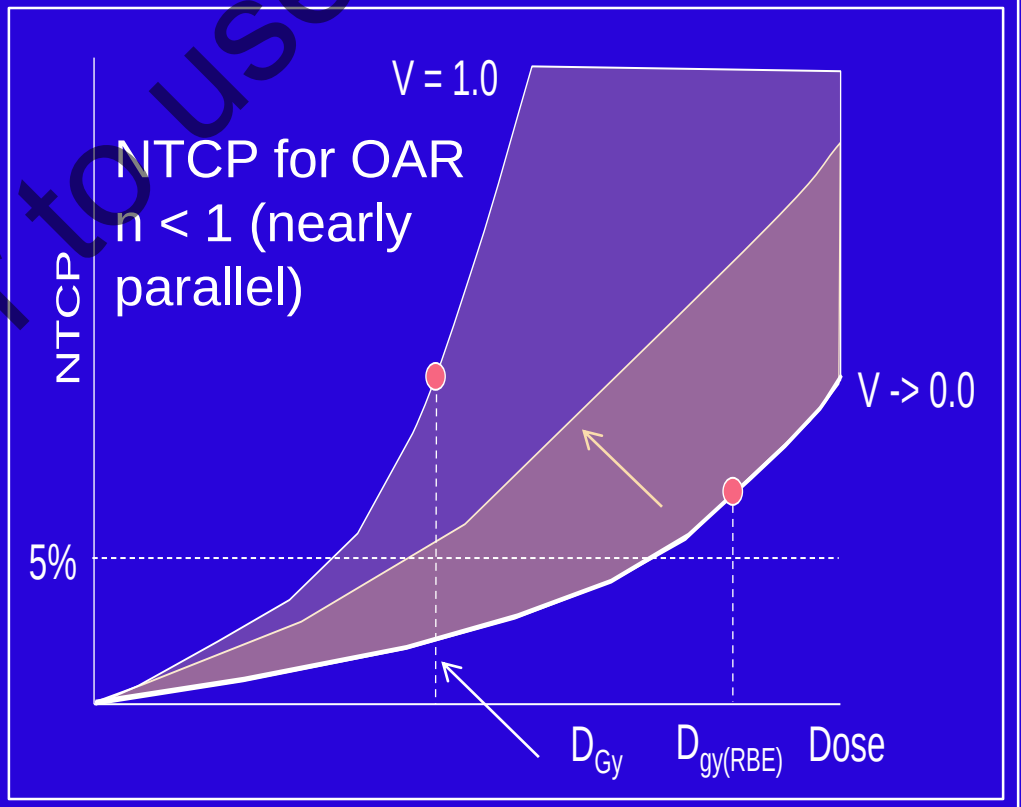
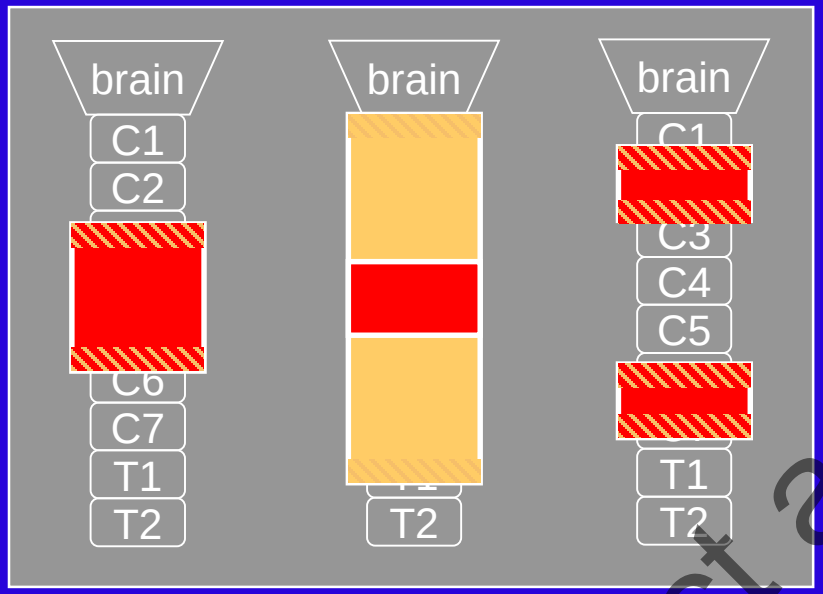
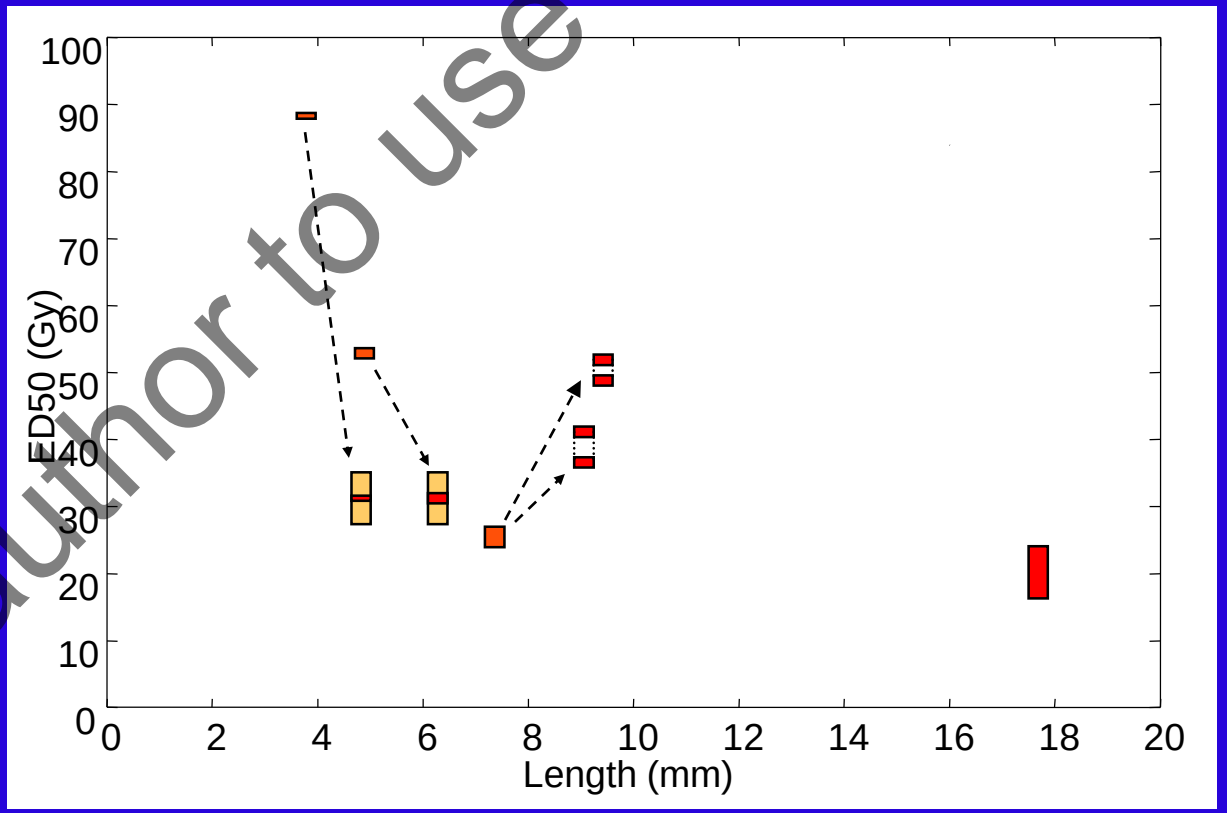




Normal tissue response

In-vivo rat spinal cord irradiations using collimated proton beams

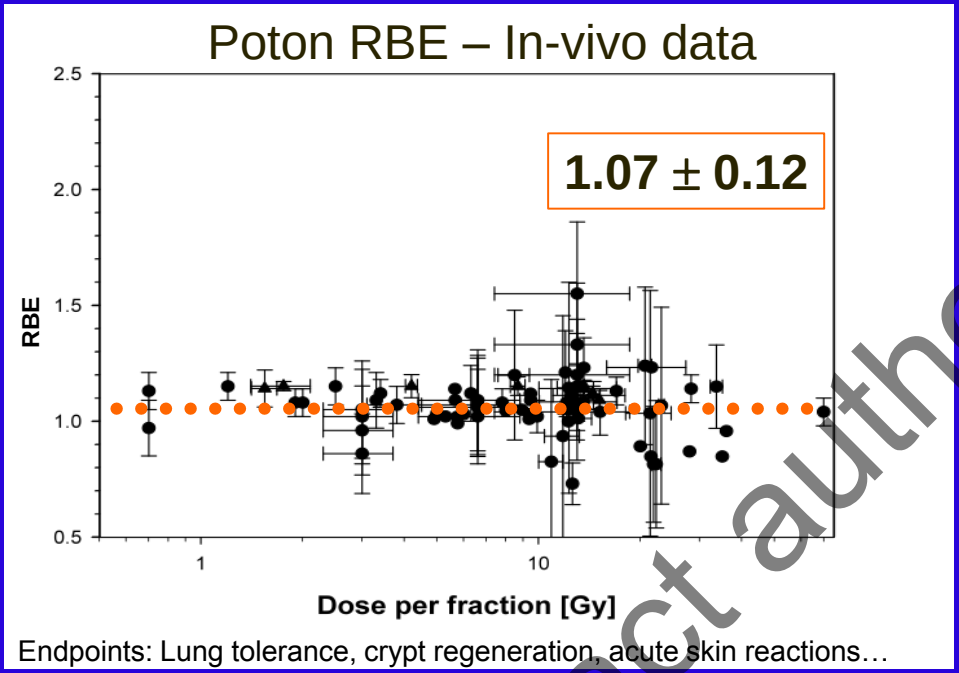




van Luijk et al 2005, IJROBP, 61:892-900

Understanding (In-vivo) RBE?

Review of in-vitro and in-vivo RBE experimental data



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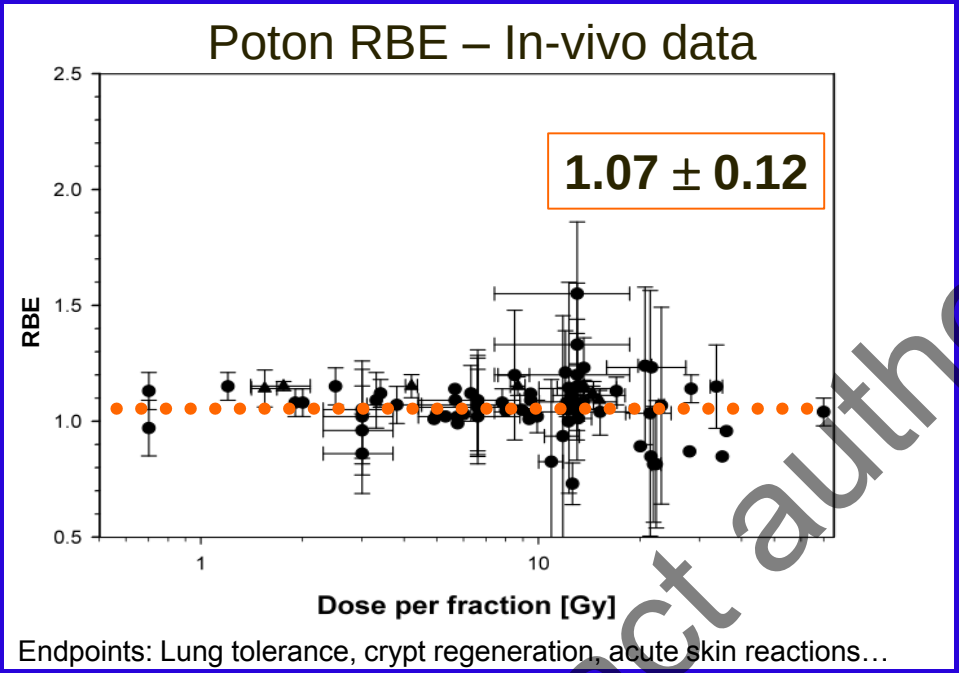
Understanding (In-vivo) RBE?

Review of in-vitro and in-vivo RBE experimental data



Endpoints: Lung tolerance, crypt regeneration, acute skin reactions…

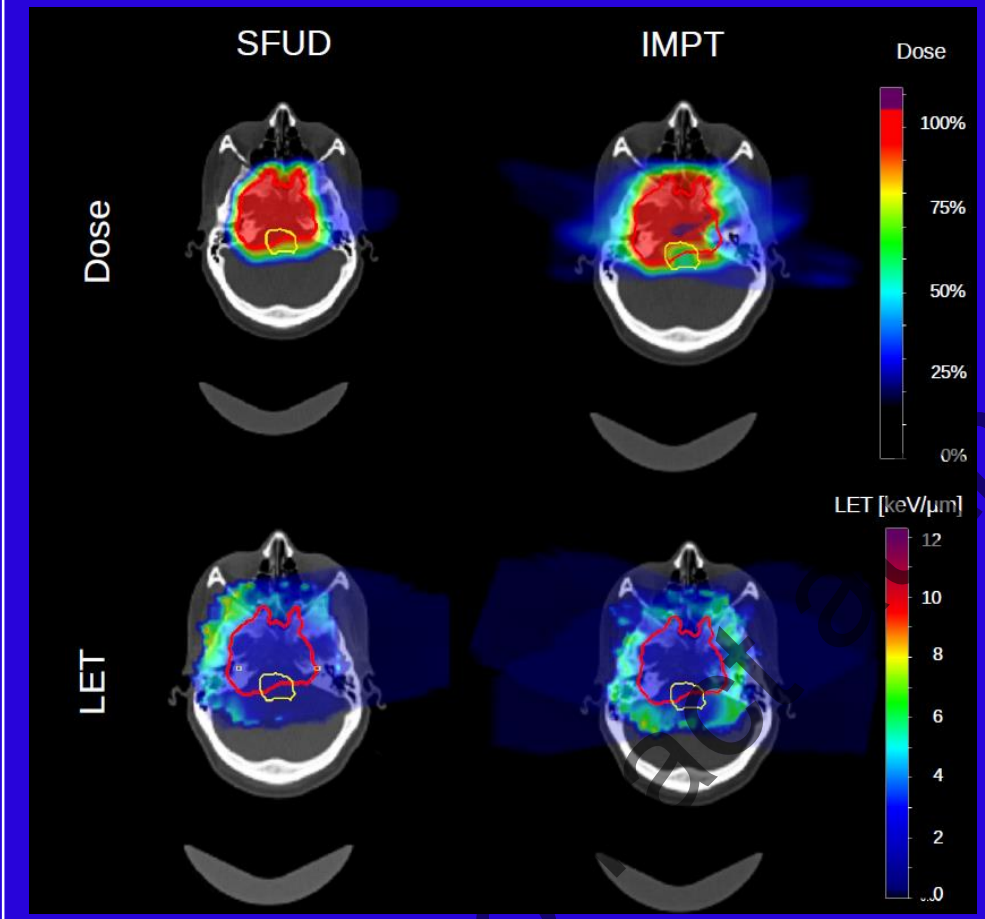
RBE is dependent on:

- Underlying architecture
- Organism (mouse/human)
- Tissue/organ type
- End point/complication
- Energy/LET
- Dose
- Dose rate

} All directly measurable parameters

Paganetti *IJROBP*, 2002; 53, 407

Understanding particle therapy outcomes in terms of verifiable and measurable, biologically relevant parameters



- Analyse outcomes of particle therapy in terms of dose and (e.g.) LET
- Dose and LET are parameters that can be accurately defined and localised
- However, need accurate dose/LET estimates for whole treatment
- Also needs DAPT and accurate dose accumulation…

PAUL SCHERRER INSTITUT PSI

Summary

- PBS proton therapy can be effective and safe
- But all proton therapy is subject to uncertainties,both physical and biological (the “bad apple”?)
- Future challenges in delivery will be aimed at increased imaging and adaption in order to more precisely get what we see
- Based on this, we may begin to undertand the biological aspects to best exploit the power of particles

Thanks for your attention…