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A clinical protocol for Simultaneous Integrated Boost for proton treatments

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Introduction

- Planning studies for SIB on Head and Neck patients with protons using SFUD technique proved

  - feasibility of dose escalation improving sparing of healthy tissue (given the usually quite large extension of target volumes) [1]

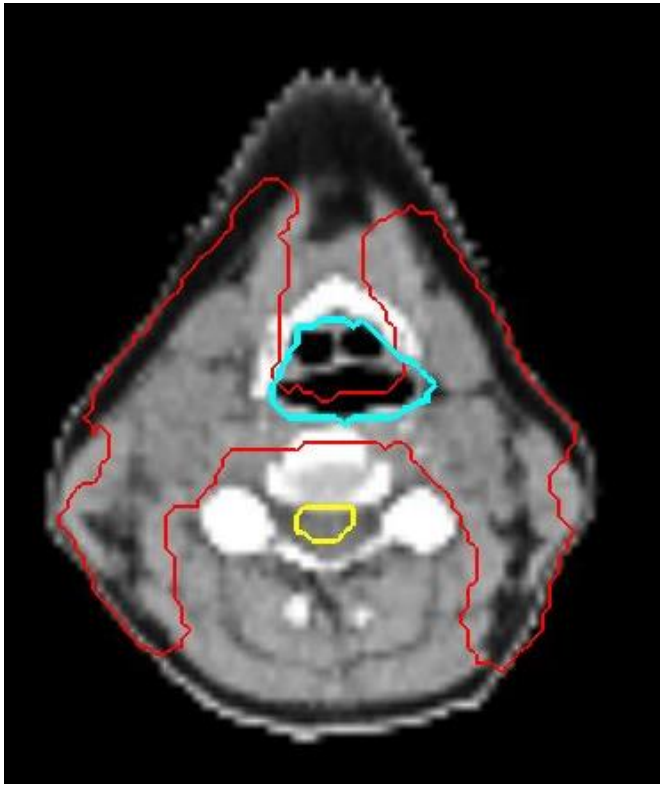
  - more conformal plan compared to sequential SFUD [2]

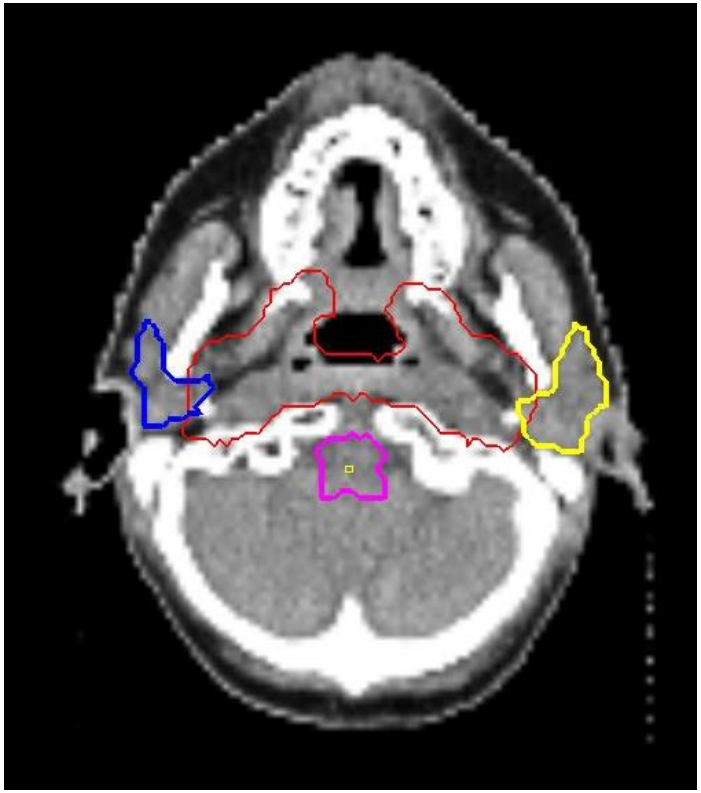
[1] L. Cozzi, A. Bolsi, G. Nicolini, A. Fogliata. The Simultaneous Integrated Boost with proton beams in Head and Neck patients. Z. Med Phys. 14 (2004): 180-188.

[2] X. R. Zhu, F. Poenisch, H. Li et al. A single-field integrated boost treatment planning technique for spot scanning proton therapy. Radiation Oncology 2014, 9:202

Introduction

- Given the complexity of the shape of these targets and the proximity with important OARs, often multiple IMPT series are needed





Introduction

- Goal of the planning study: definition of a clinical protocol for SIB-IMPT on H&N patients
- The challenge with SIB planning is to achieve desired boosting without over-dosage of the ring (PTV1-PTV2)
- What do we need?

- finding out optimization parameters to achieve dose escalation to GTV

- avoid over-boosting in the fraction of elective volume outside GTV (especially to healthy tissue within the ring PTV1-PTV2)

Materials and Methods

- Patients:

- 8 patients originally treated with conventional sequential schedules

- Re-planned with SIB regimen

  -> 1.8 GyRBE * 30 to PTV1 (54 GyRBE)
  -> 2.36 GyRBE * 30 to PTV2 (70.8 GyRBE)

- Based on Phase I study (SIB-IMRT) [3]

- 70.8 Gy (2.36 Gy per fraction) = Maximal Tolerated Dose for acceptable Dose Limiting Toxicity criteria, without changing the standard dose constraints to OARs

[3] Andrew Lauve, M. Morris, R. Schmidt-Ulrich et al. Simultaneous Integrated Boost intensity-modulated Radiotherapy for locally advanced Head-and-Neck squamous cell carcinomas: II-clinical results. Int J Rad Oncol Biol Phys 2004; 60 (2): 374-387.

Materials and Methods

- Planning:

- Planned dose per fraction = 1.8 GyRBE

- 100% dose corresponding to 54.0 GyRBE

- Boosting factor for PTV2 = $\frac{70.8}{54.0}$ = 131%

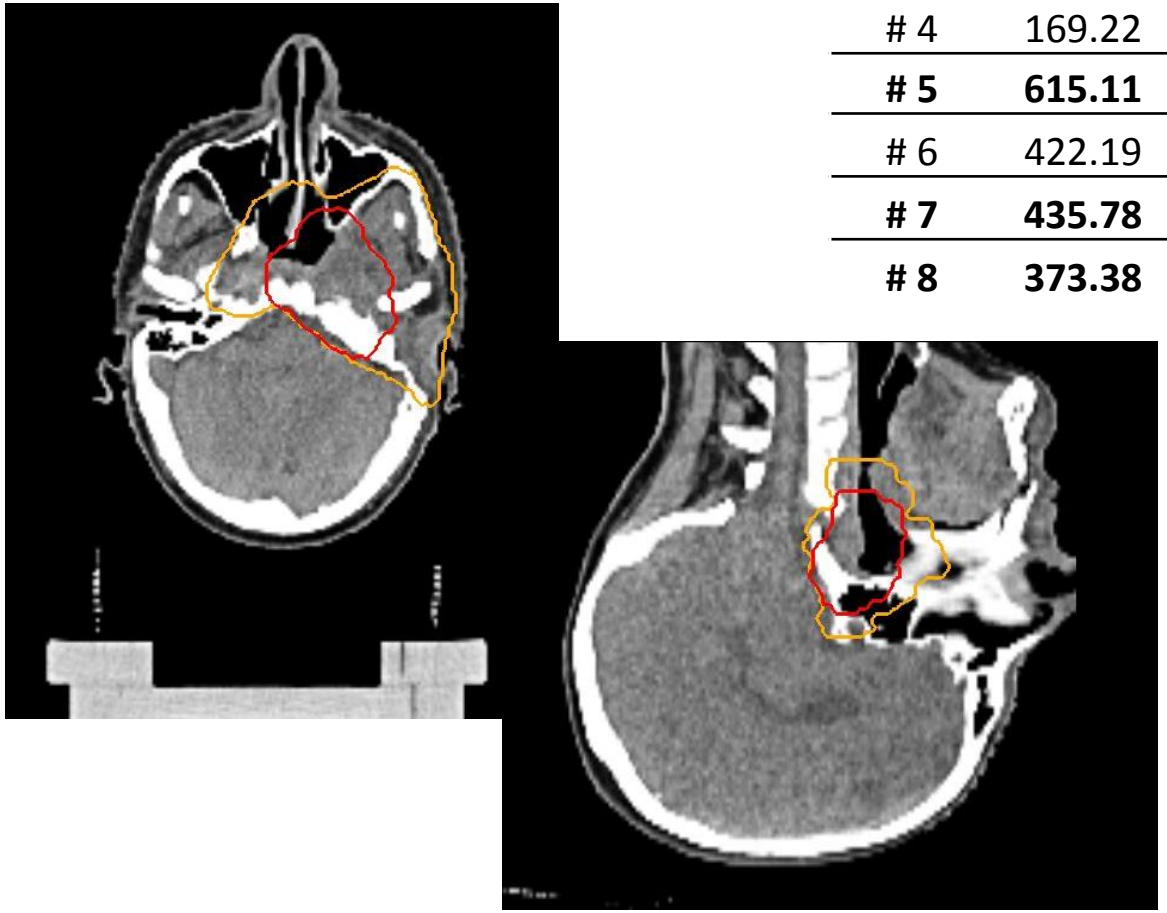
- Dose constraints to the OARs as for the sequential approach

Materials and Methods

- Scenario I: large extension of elective volume (volume PTV2/PTV1 < 40%)

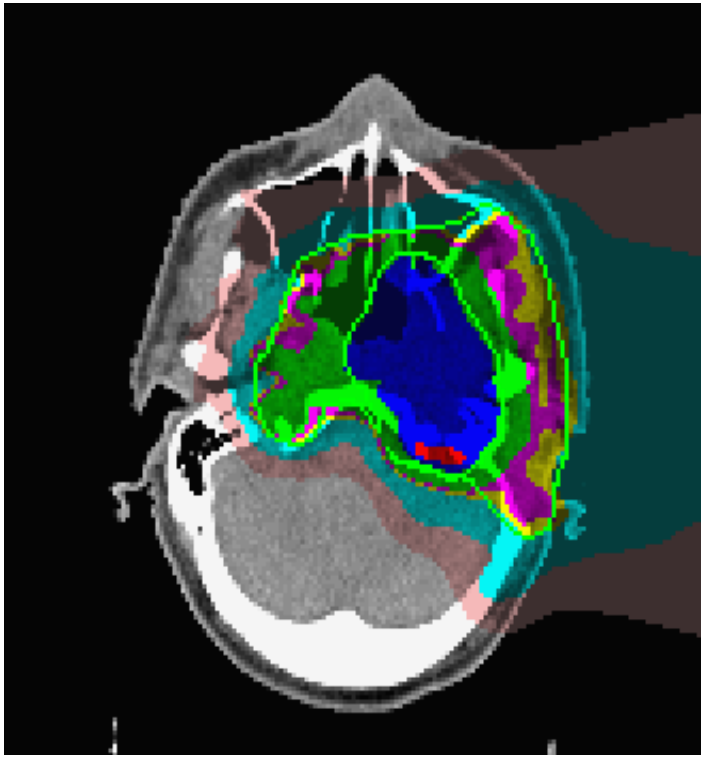
- boosting factor applied to PTV2
- normalization to PTV1-(PTV2+3mm)

Patients	Volume PTV1 [cc]	Volume PTV2 [cc]	Volume GTV [cc]	PTV2/PTV1 [%]
# 1	119.65	56.2	29.22	46.9
# 2	89.08	54.97	21.79	61.7
# 3	105.93	49.24	20.78	46.5
# 4	169.22	93.43	56.443	55.2
# 5	**615.11**	**217.27**	**40.47**	**35.4**
# 6	422.19	217.4	36.77	51.4
# 7	**435.78**	**125.49**	**28.43**	**28.8**
# 8	**373.38**	**100.31**	**46.46**	**26.9**

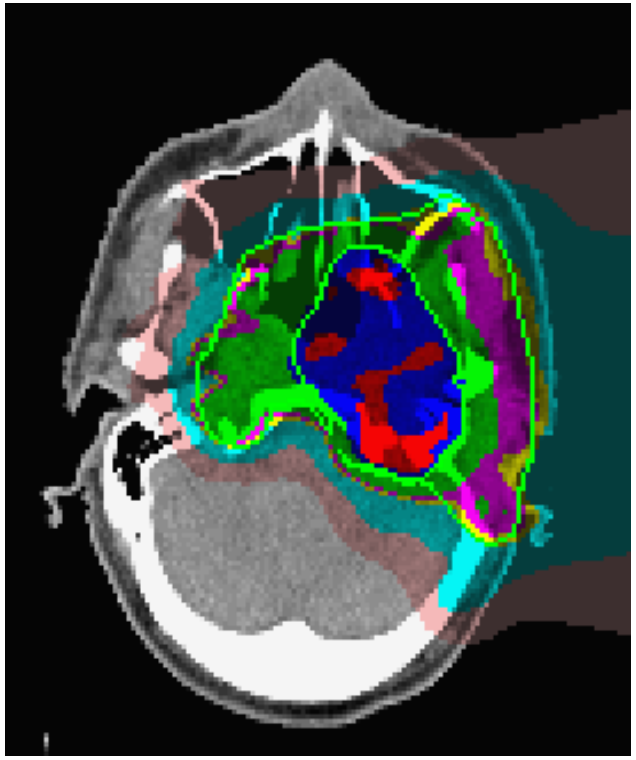


Materials and Methods

- Normalization to PTV1-PTV2



- Normalization to PTV1-(PTV2+3mm)



90% of 54GyRBE

Materials and Methods

- Scenario II: extension of PTV1 similar to PTV2

- higher boosting factor applied to GTV
- normalization to PTV1-PTV2

Patients	Volume PTV1 [cc]	Volume PTV2 [cc]	Volume GTV [cc]	PTV2/PTV1 [%]
# 1	119.65	56.2	29.22	46.9
# 2	89.08	54.97	21.79	61.7
# 3	105.93	49.24	20.78	46.5
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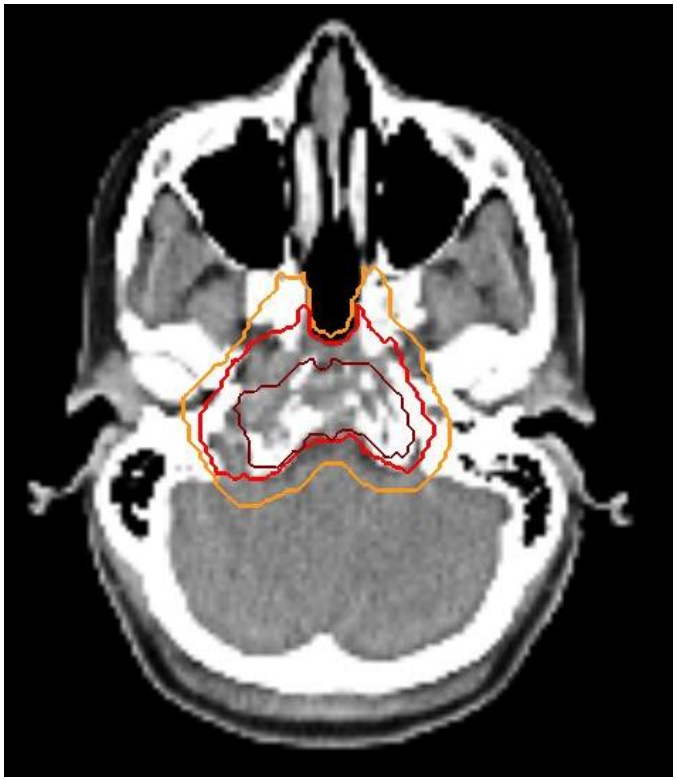
PTV1
PTV2
GTV

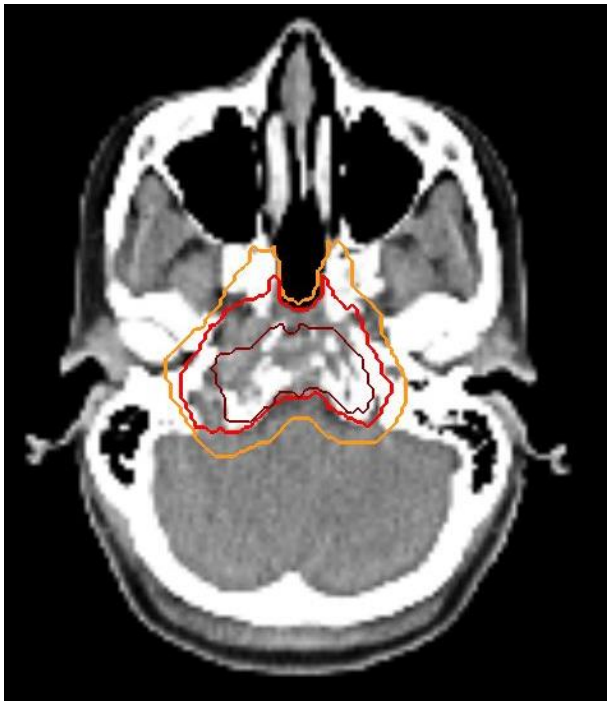


Results

- Choice of boost volume and boosting factor to achieve optimal quality and conformity of the SIB plans depend on different extension of PTV1 compared to PTV2

- more similar volumes -> more difficult to obtain dose gradient avoiding over-boosting
  -> higher boosting factor and smaller boosting volume (GTV)

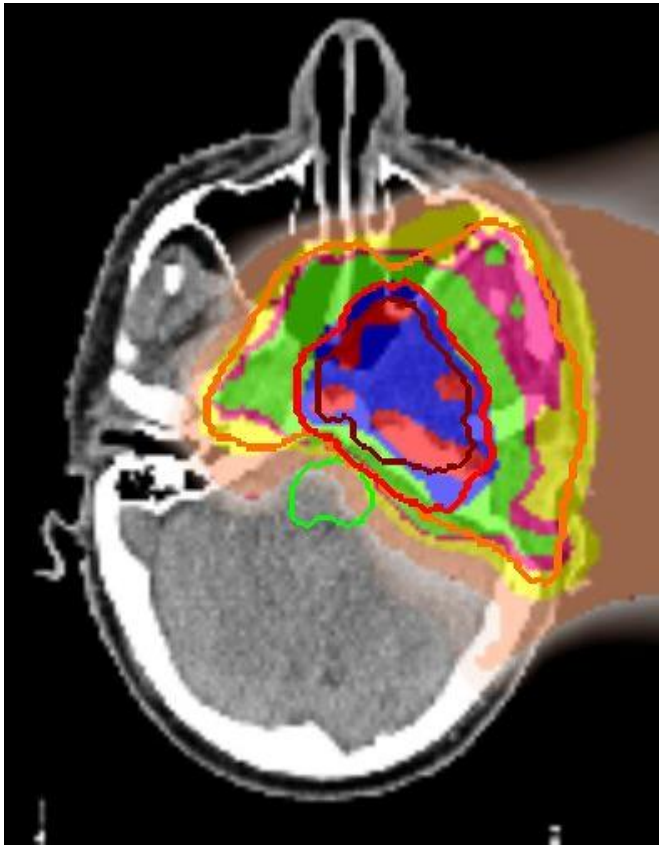
PTV1
PTV2
GTV



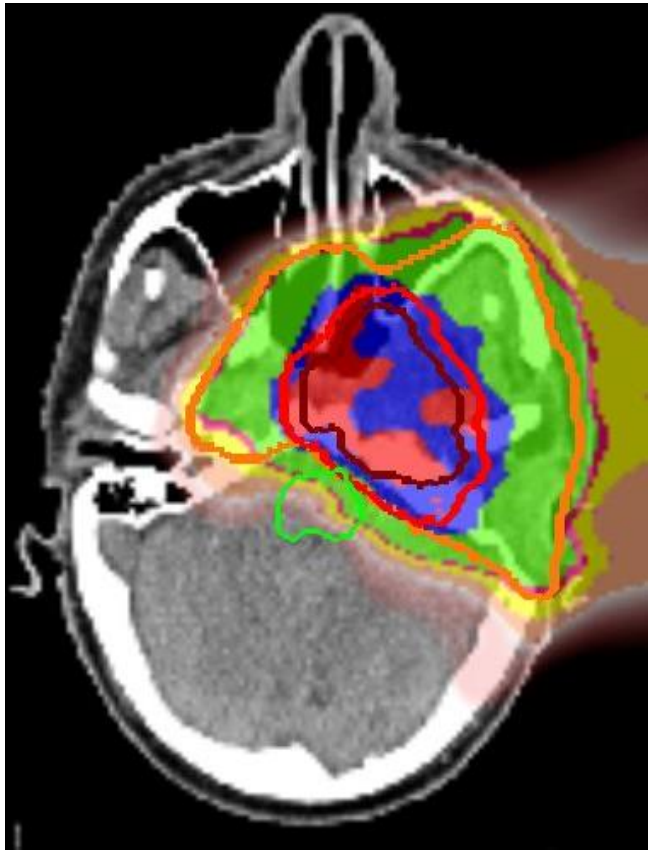
Results

- Plan Comparison with sequential approach

SIB



Sequential (end dose = 74.0 GyRBE)



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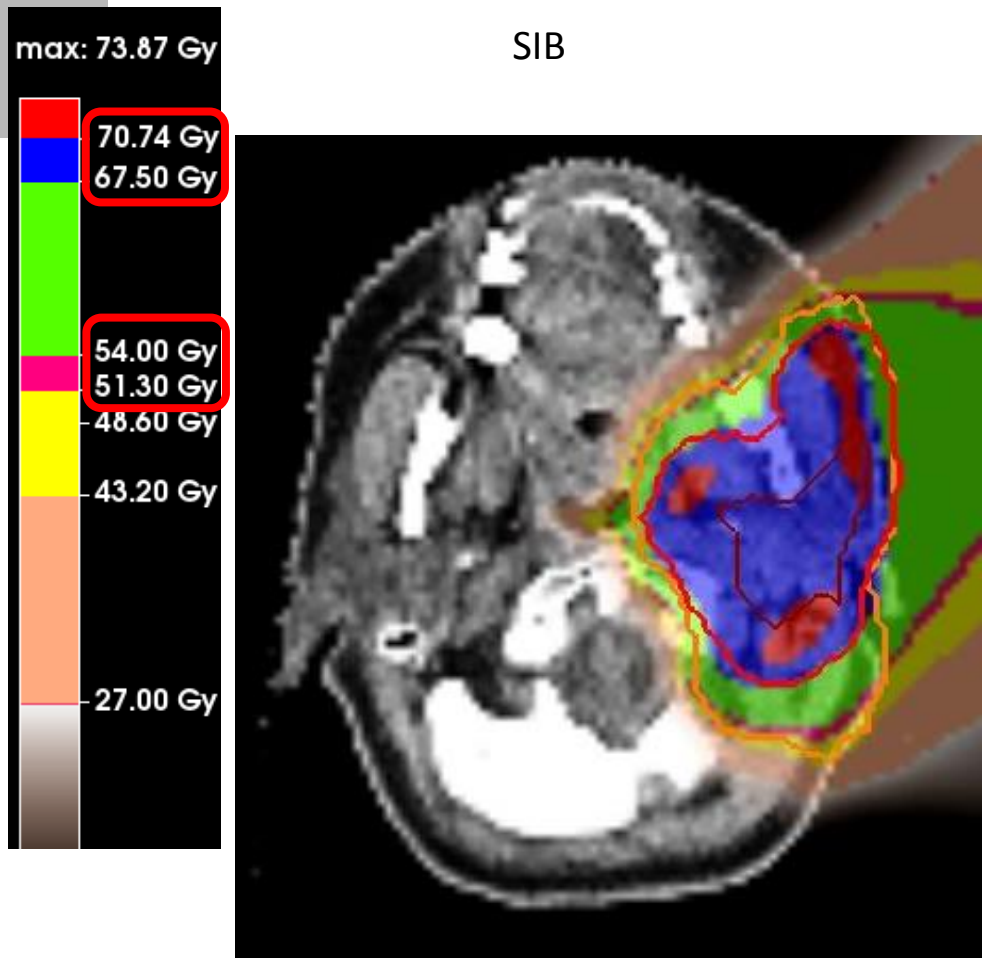
SIB



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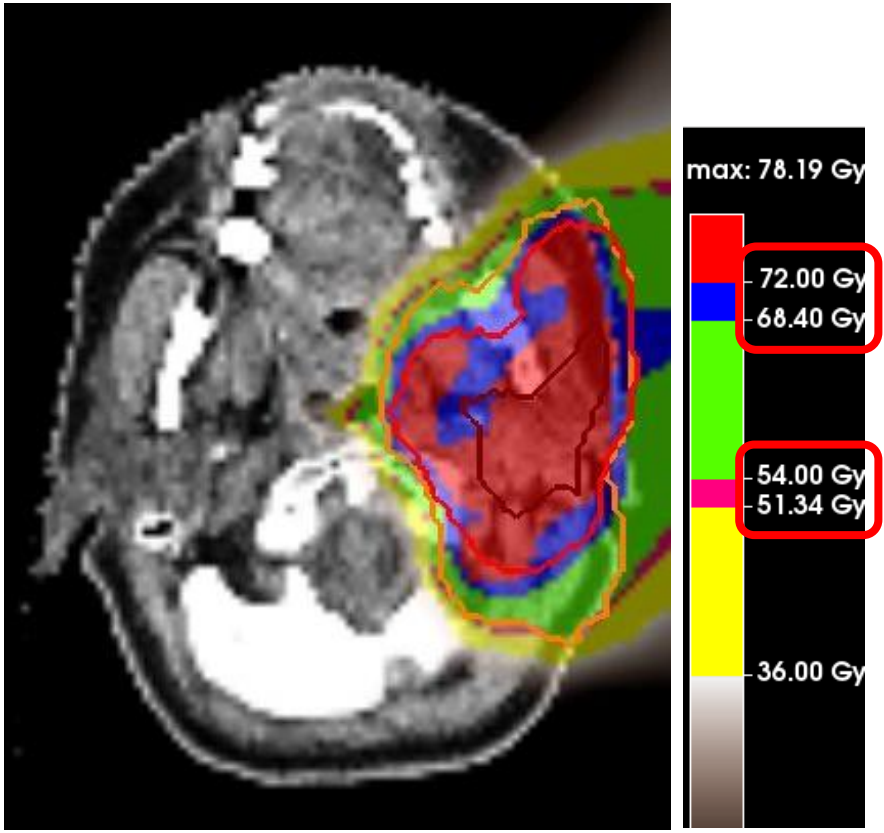
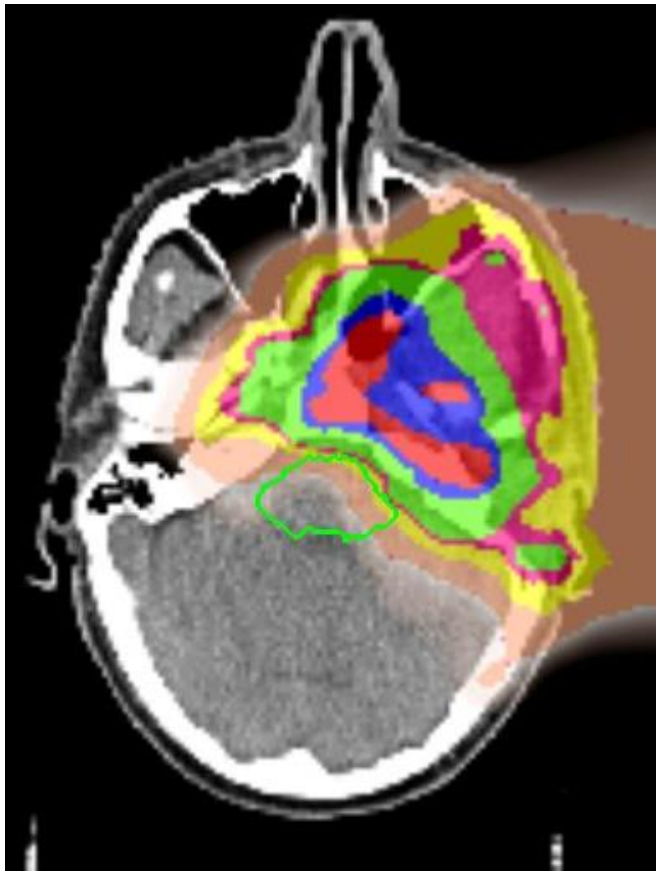


Results

- Plan comparison with sequential approach

SIB



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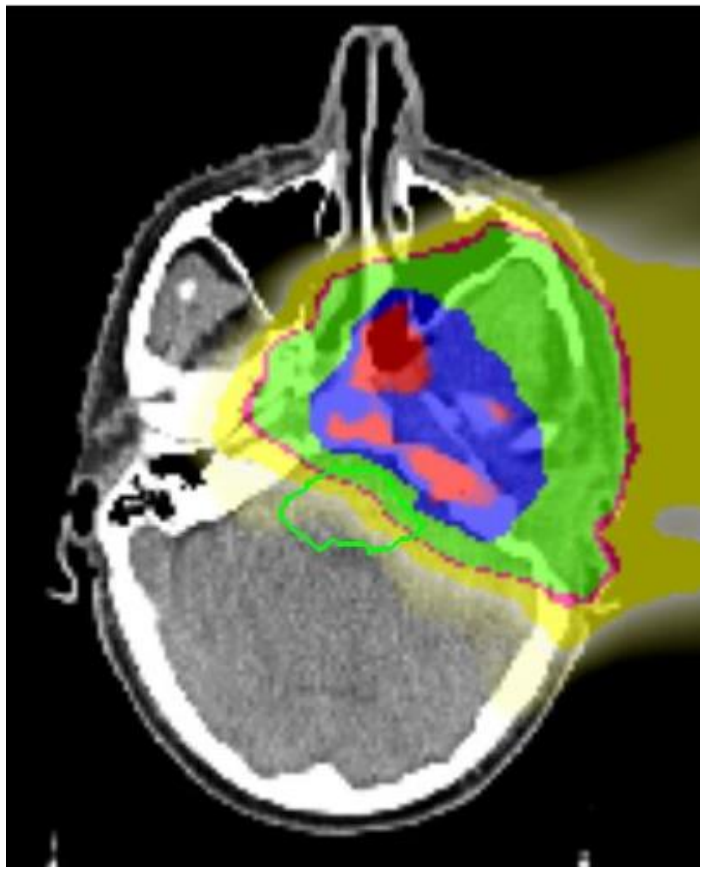
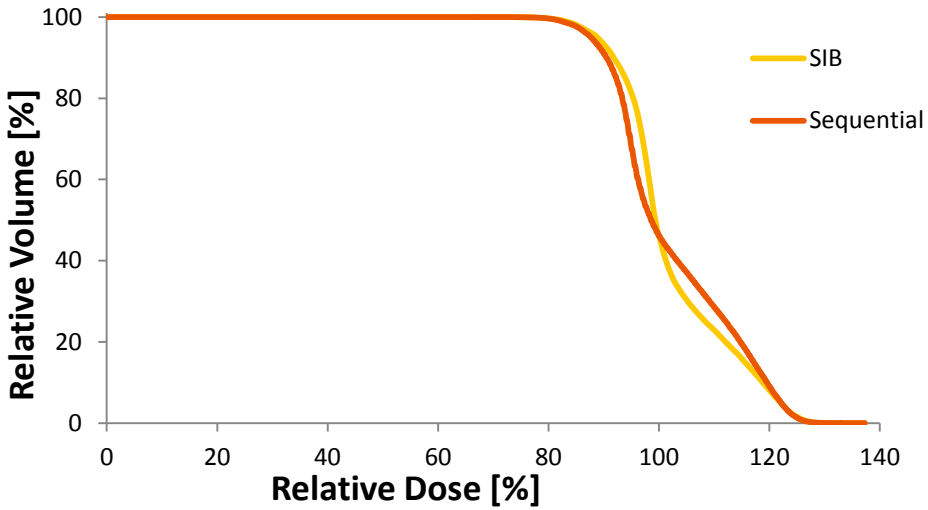


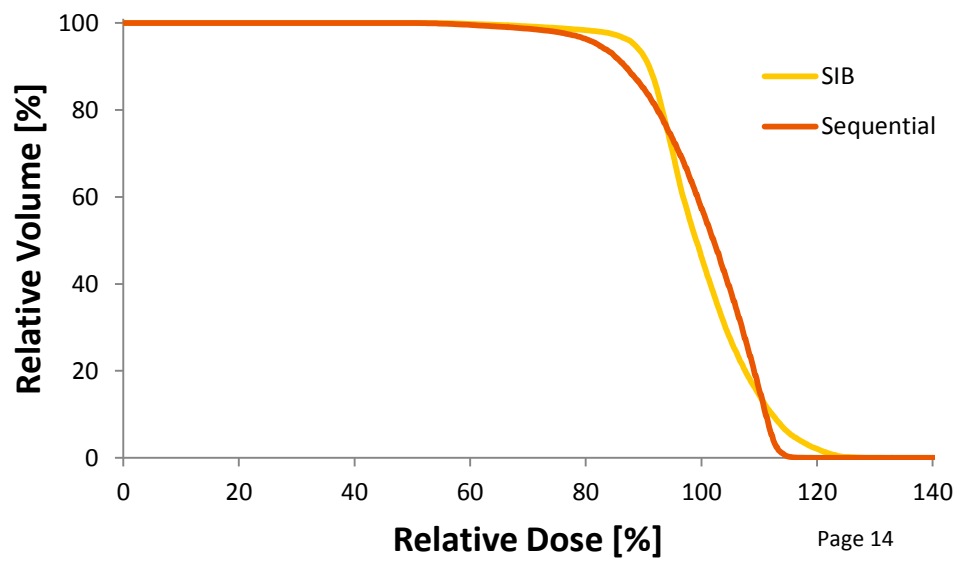
Results

- Plan comparison with sequential approach

PTV1-PTV2 - boost on PTV2



PTV1-PTV2 - boost on GTV



Results

- V95% (PTV1-PTV2) = volume of the ring covered by the 95% of the dose prescribed to the boost

- CI95% Boost = $\frac{Treated\ Volume\ with\ isodose\ 95\%\ of\ prescribed\ dose\ to\ Boost}{Boost\ Volume}$

- Average + Standard Dev
  [min; max]

	Mean Dose PTV1-PTV2 [GyRBE]	V95% (PTV1-PTV2)	Mean Dose Boost [%]	CI95% Boost
SIB	54.68±0.86 [54.00;56.40]	0.58±0.52 [0.00;1.23]	100.15±2.14 [97.90;103.40]	1.14+0.32 [0.87;1.78]
Sequential	64.27±3.46 [58.80;67.50]	25.46±10.79 [11.10;37.26]	100.48±0.48 [99.8;101.2]	2.86+1.97 [1.16;7.19]

Conclusions

- The used optimization parameters for planning H&N patients with proton PBS using SIB-IMPT resulted in dose distributions which guaranteed :

- desired conformity and dose escalation between the elective and the boost volume

- avoid higher fractionation (over-boosting) to OARs within the gradient region

-> OARs sparing was comparable or better with SIB optimization

Conclusions

- The used optimization parameters for planning H&N patients with proton PBS using SIB-IMPT resulted in dose distributions which guaranteed :

- desired conformity and dose escalation between the elective and the boost volume

  - price to pay: loss in homogeneity within the ring PTV1-PTV2

- avoid higher fractionation (over-boosting) to OARs within the gradient region

  -> OARs sparing was comparable or better with SIB optimization

- Approach was transferred to the clinical operation

- definition of internal protocol

- One patient already treated

- no additional early toxicity observed (only the normal mucositis)

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My thanks go to

- Dr. Robert Malyapa
- Alessandra Bolsi
- Daniel Scandurra
- A. J. Lomax
- Dr. D. Weber

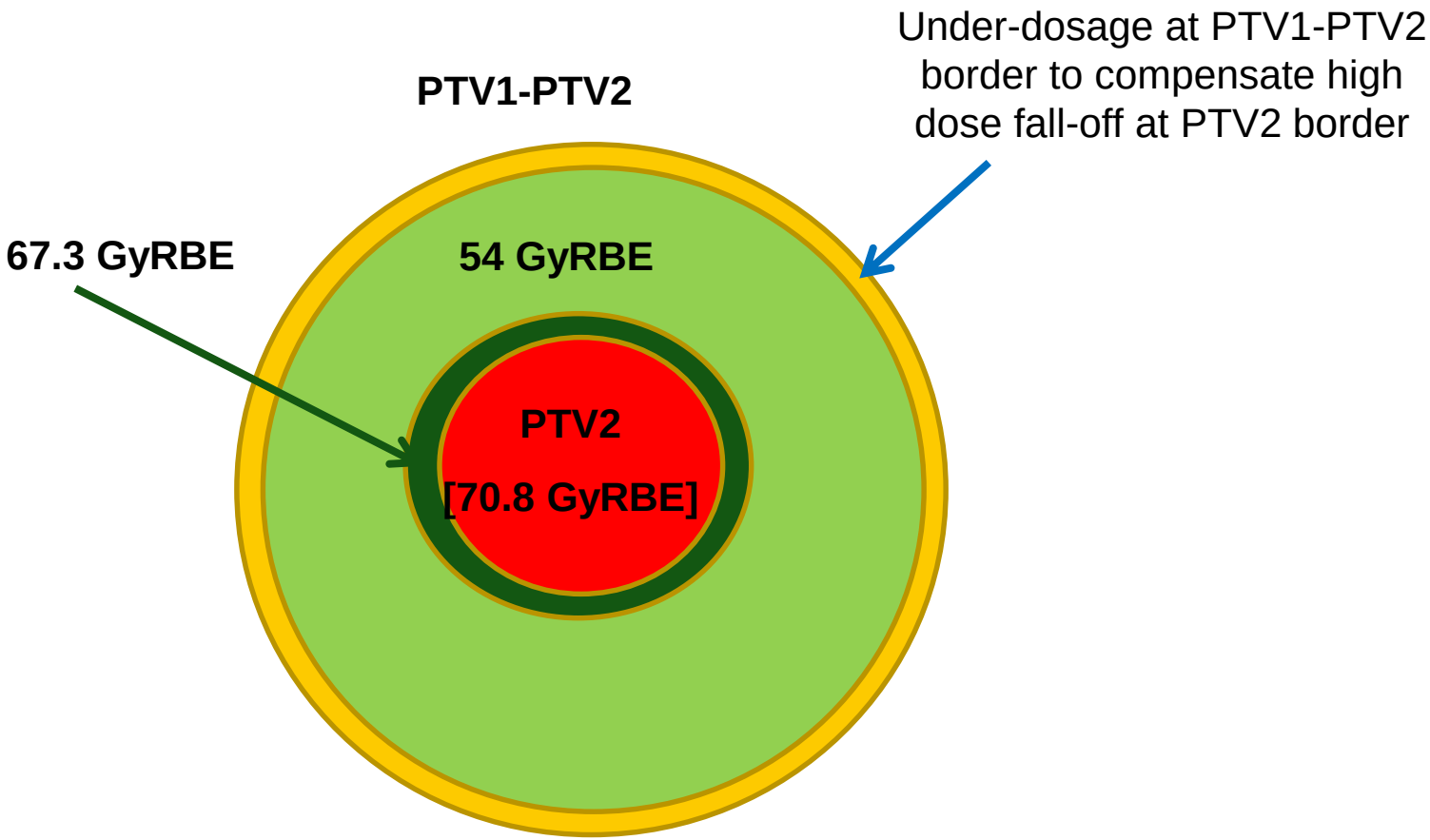
[3] Study from Lauve et al.:

- MTD = maximal dose to GTV that leads to exceed the dose-limiting toxicity criteria in no more than 33.3% of the cases under study

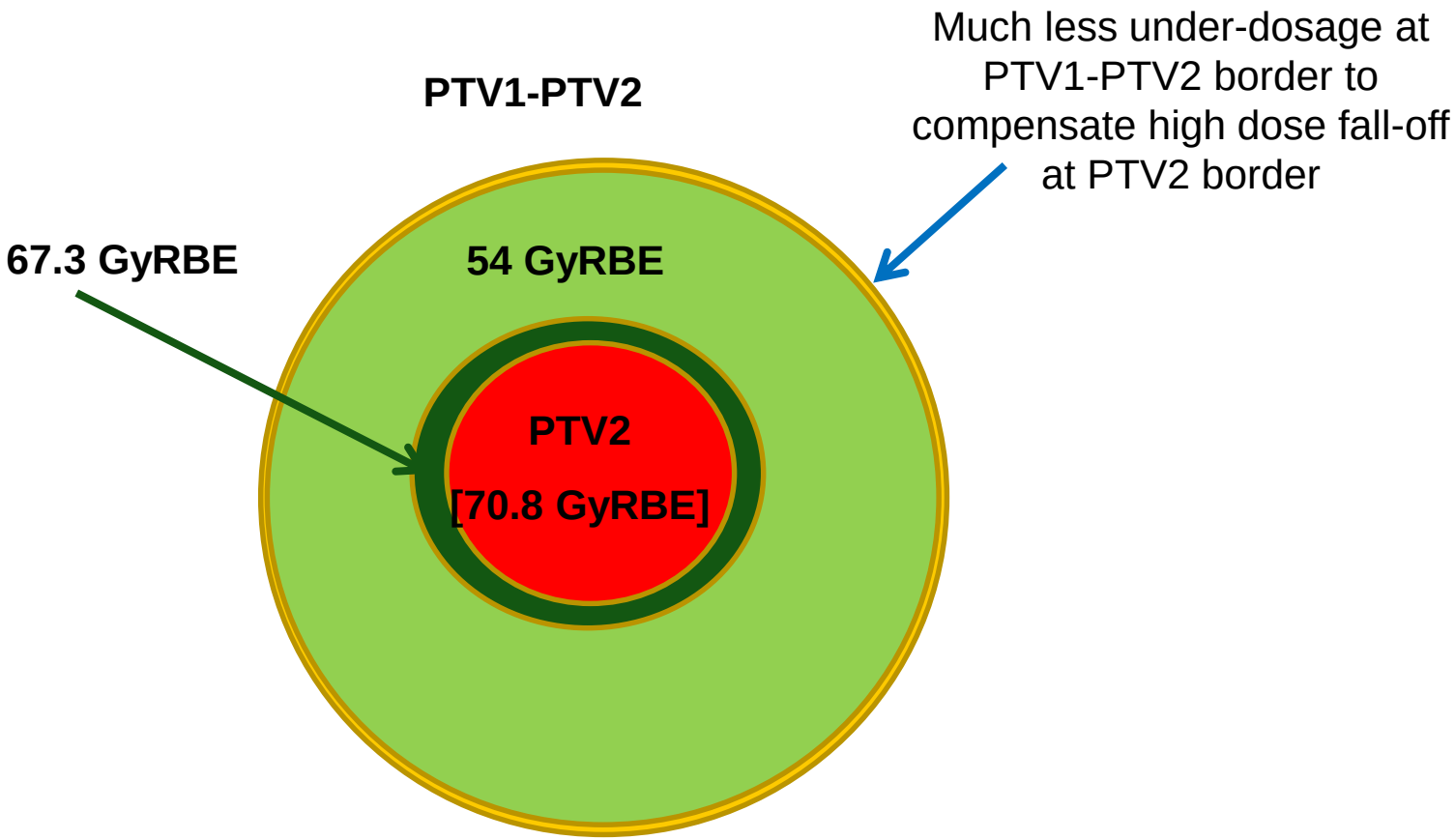
- Dose Limiting Toxicity criteria: any Grade 4 within 90 d from RT, or toxicities requiring either a dose reduction or a treatment break of >5d (toxicity scored using the NCI Common Toxicity Criteria)

- Results: patients irradiated with up to 70.8 Gy (2.36 Gy per fraction), showed only Grade 3 mucositis during the 5th week, as typical for standard RT regimens and remained stable

- Normalization to PTV1-PTV2



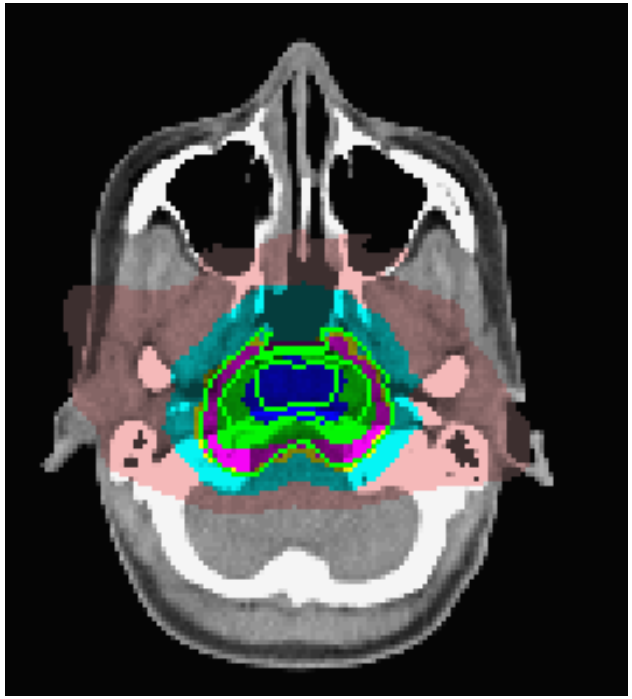
- Normalization to PTV1-(PTV2+3mm)



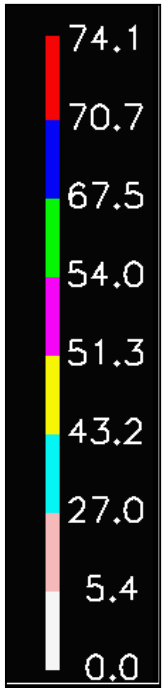
Patients	Volume PTV1 [cc]	Volume PTV2 [cc]	Volume GTV [cc]	PTV2/PTV1 [%]
# 3	105.93	49.24	20.78	46.5

IMPT with boost on PTV2

IMPT with boost on GTV



GyRBE



OAR	Constraint: Dmax [GyRBE]	SIB Dmax [GyRBE]	Sequential Dmax [GyRBE]
Optic Nerves	60.0	46.25±4.90 [39.31; 50.87]	49.48±3.34 [46.27; 54.09]
Chiasm	54	35.67±12.39 [22.36; 51.41]	44.75±13.89 [22.95; 56.09]
Brainstem	64	58.11±6.29 [51.57; 67.12]	61.69±8.46 [45.14; 65.71]
Center of Brainstem	54	40.52±8.83 [29.16; 51.84]	47.65±7.78 [36.89; 54.24]
Spinal Cord	60	46.34±6.96 [36.29; 54.05]	51.2±6.79 [40.77; 59.34]
Cochlea	36	29.58±7.38 [18.86; 35.75]	34.47±1.87 [32.4; 36.31]

Conclusions

how about the biology?

- $\frac{\alpha}{\beta}$ = 15 Gy for H&N (??)

$$BED = n \cdot d \cdot \left(1 + \frac{d}{\frac{\alpha}{\beta}}\right) - \frac{0{,}693}{n \cdot d \cdot \alpha} \cdot \frac{(T - T_k)}{T_{POT}} = 77.3 \text{ GyRBE}$$

- T_{POT} ~ 3 days (potential doubling time)

$$NTD = \frac{BED}{RE_{2(1.8)Gy}}$$

- T_k = 30 days (repopulation time) ??

biological dose

- [3] Study from Lauve et al.:

- $\frac{\alpha}{\beta}$ = 15 Gy for H&N

- T_{POT} = 3 days (potential doubling time)

- T_k = 30 days (repopulation time)

$$\text{BED} = n \cdot d \cdot \left(1 + \frac{d}{\frac{\alpha}{\beta}}\right) - \frac{0{,}693}{n \cdot d \cdot \alpha} \cdot \frac{(T - T_k)}{T_{POT}} = 77.3 \text{ GyRBE}$$

$$\mathbf{NTD} = \frac{\boldsymbol{BED}}{\boldsymbol{RE}_{\mathbf{2(1.8)}\boldsymbol{Gy}}}$$