Practical Approaches to Multiple and Missed Treatments

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ALLIANCE CANCER CARE

DISCLOSURES

NO DISCLOSURES RELATED TO THIS PRESENTATION

ACKNOWLEDGMENTS

AGENDA

- Review a practical approach for missed radiotherapy treatments
  - Discuss the BED parameters
    - α/β (Uncertainty, large vs. small)
    - Timing/Length of the break
  - Strategy
- Discuss “Other” missed treatment situations
  - SBRT
- Commercial Tools
- Dose Accumulations
  - SBRT + conventional treatment
    - EQD_2
- Documentation
- References

Clinical Oncology (2002) **14**: 382–393
doi:10.1053/clon.2002.0111, available online at http://www.idealibrary.com on IDEAL®

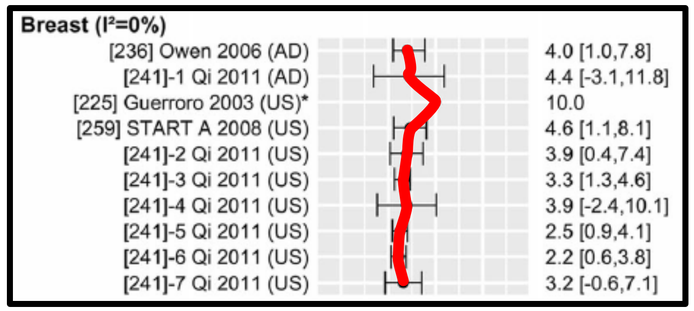
Original Article

Practical Methods for Compensating for Missed Treatment Days in Radiotherapy, with Particular Reference to Head and Neck Schedules

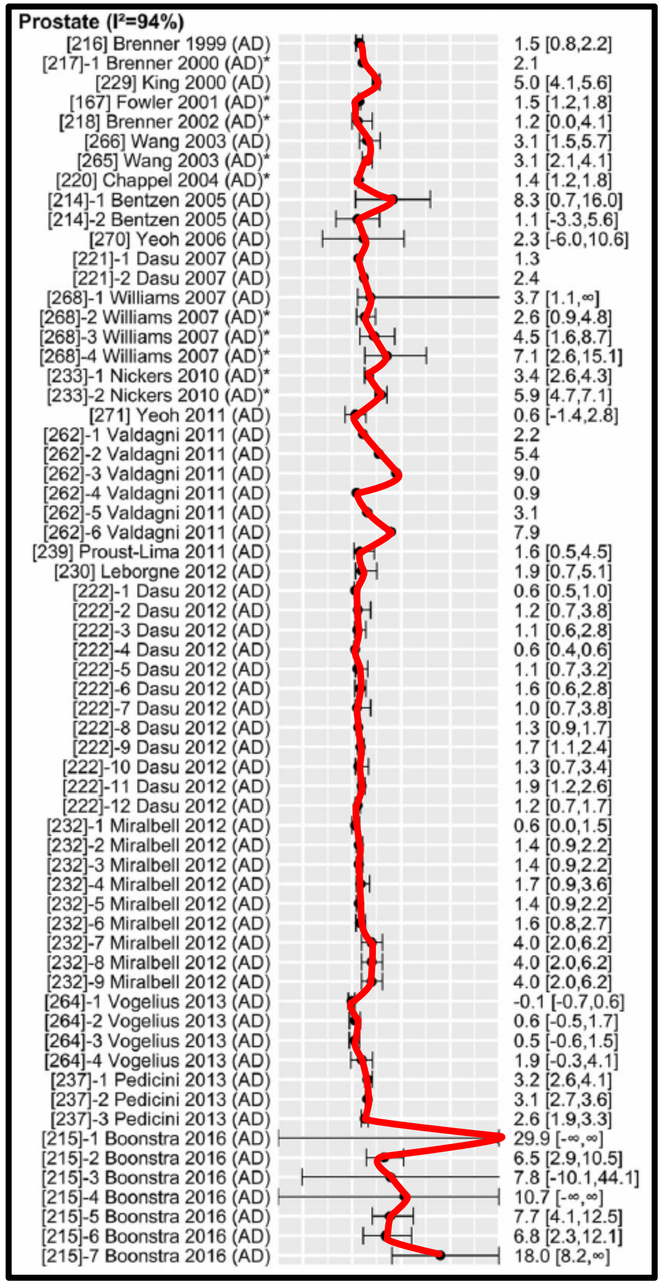
R. G. Dale*, J. H. Hendry†, B. Jones*, A. G. Robertson‡, C. Deehan§, J. A. Sinclair*

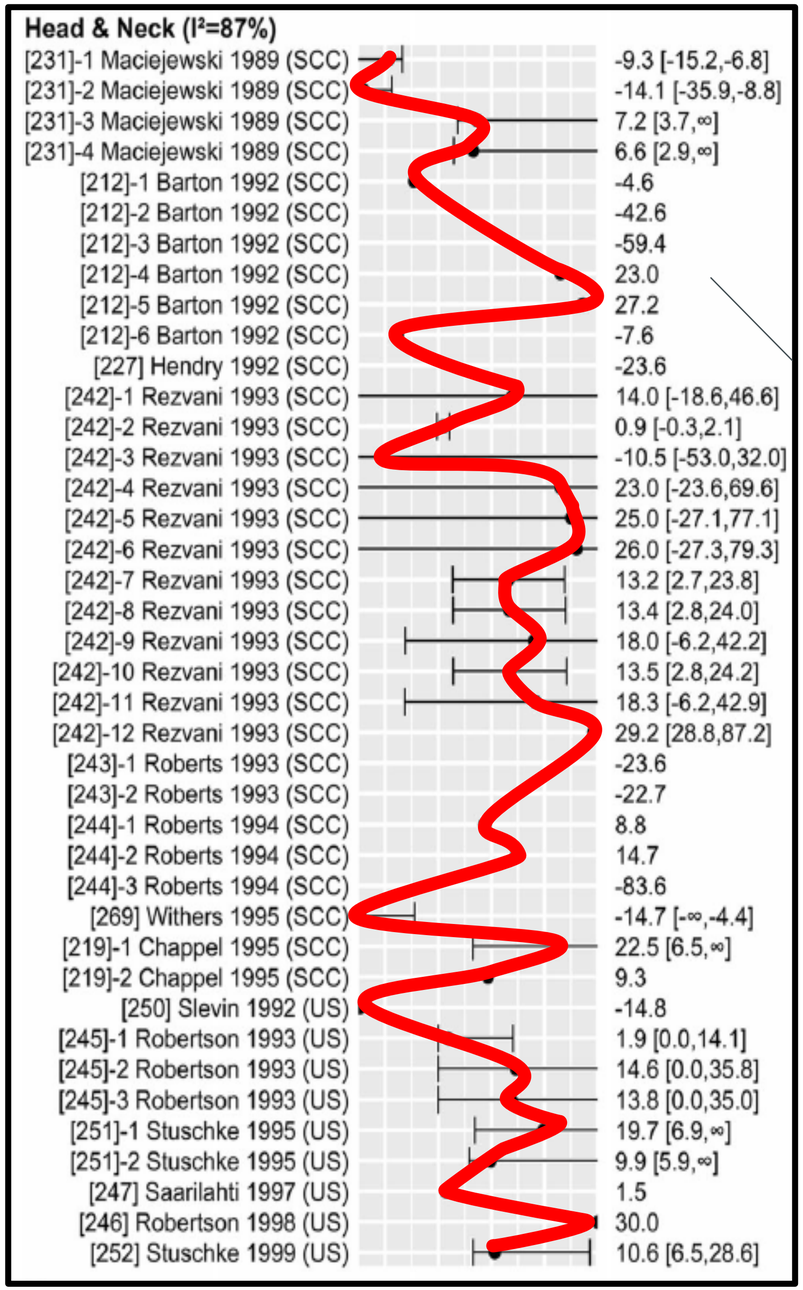
BED FORMALISM

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right]$$



The alfa and beta of tumours: a review of parameters of the linear-quadratic model, derived from clinical radiotherapy studies. Van Leeuwen CM, Oei AL, Crezee J, Bel A, Franken NA, Stalpers LJ, Kok HP. Radiation oncology. 2018 Dec;13(1):1-1.





BED FORMALISM

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right]$$

N (# of fractions)	*d* (dose per fraction)	α/β	*BED* (Gy)
33	2	10	79.2
4	12	10	105.6
33	2	3	110
4	12	3	240

EFFECTIVE DOSE ≠ EQUIVALENT DOSE

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right]$$

$$EQD_2 = \frac{BED}{\left[1 + \frac{2}{\alpha/\beta}\right]}$$

N	d	α/β	BED (Gy)	EQD_2 (Gy)
33	2	10	79.2	66
4	12	10	105.6	88

21 years of Biologically Effective Dose. Fowler JF The British journal of radiology. 2010 Jul;83(991):554-68.

TUMORS REPOPULATE

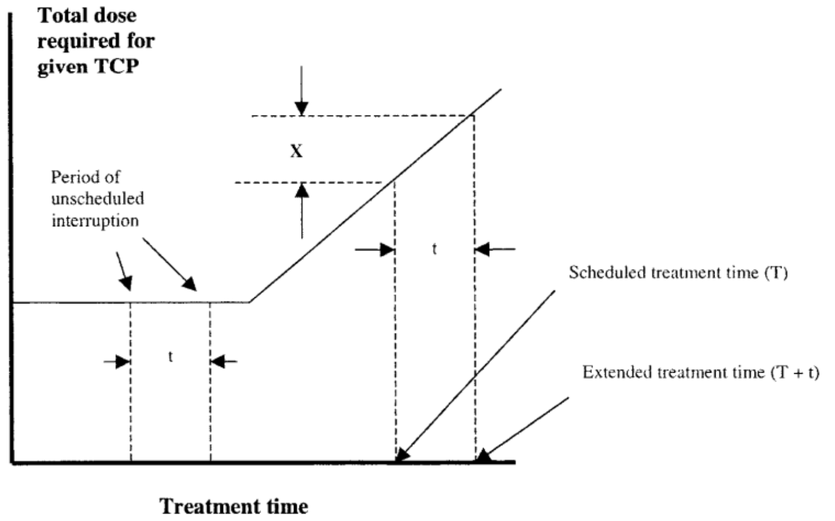
$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right] - K \times \left(T - T_{delay}\right)$$

K = BED equivalent of 1 days repopulation (Gy day $^{-1}$) *(working value of 0.9 suggested)*

T = Overall Treatment Time (days)

T_{delay} = time to onset of significant repopulation (days)

(working value of 28 days suggested)



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BALANCING ACT?

Tumor

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right] - K \times (T - T_{delay})$$

Normal Tissue

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right]$$

JUST MAKING UP THE BED MIGHT NOT BE ENOUGH…

> “. . . .it is the likelihood of extension to the treatment time, *rather than the gap per se*, which is the main cause for concern when interruptions occur”
>
> **Roger Dale**

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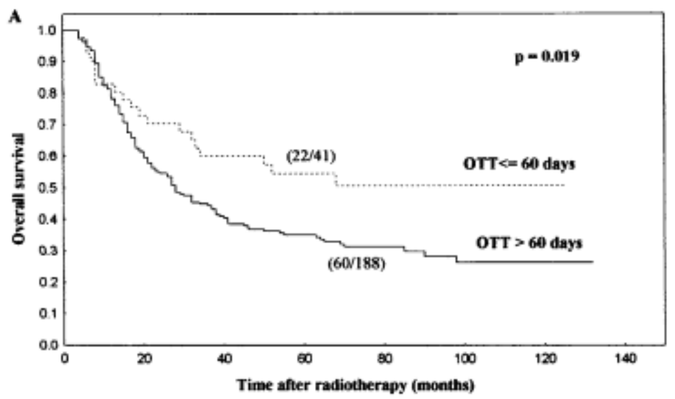
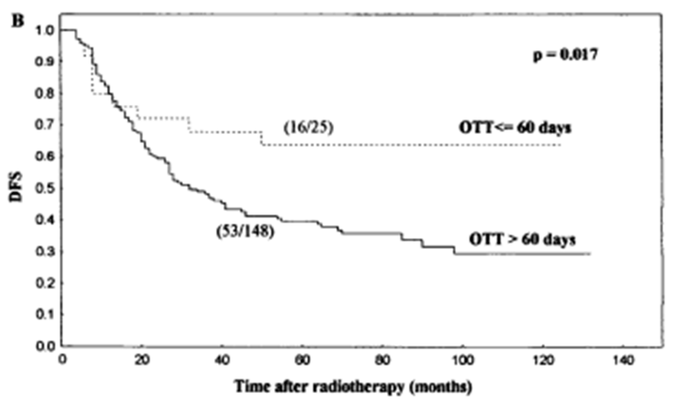
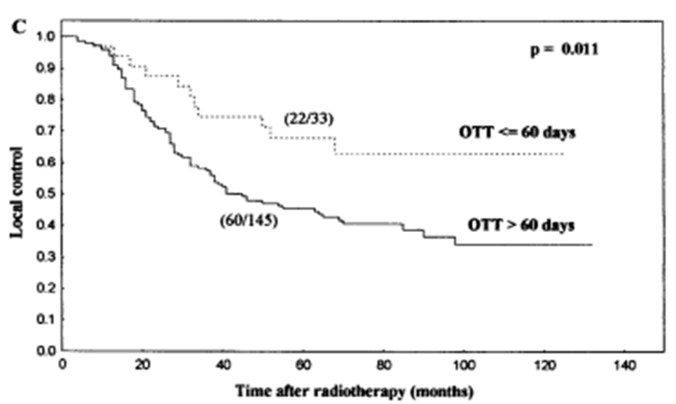
EFFECT OF OVERALL TREATMENT TIME (OTT)







Gasinska A, Fowler JF, Lind BK, Urbanski K. Influence of overall treatment time and radiobiological parameters on biologically effective doses in cervical cancer patients treated with radiation therapy alone. Acta oncologica. 2004 Oct 1;43(7):657-66.

Method	Benefit	Challenge
Treat on weekends	Overall time, fraction size and TI maintained	Might not work if break at end of schedule
Treat BID	Overall time and fraction size maintained	Scheduling. Possible loss of late normal tissue tolerance
↑ fraction size; maintain overall treatment time	Overall time maintained with QD treatments	Not suitable for high dose treatments (SBRT). TI affected. Equivalent tumor BED = ↑ late reactions. Equivalent late reactions = ↓ tumor dose.
Add additional fractions	"some" restoration of BED	TI adversely affected. ↓ tumor control and ↑ late reactions
Add additional fractions; ↑ fraction size	"some" restoration of BED and original Rx schedule	As above
Add additional fractions BID	As above	As above; less effect on TI

Adapted directly from:
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METHODOLOGY

1. Calculate the Tumor and Normal Tissue BEDs for the intended schedule
2. Calculate the Tumor and Normal Tissue BEDs occurring “PRE-GAP”
3. Calculate the difference or “POST-GAP” BEDs aka “Still to Give”
4. Choose your method

www.rcr.ac.uk

Clinical Oncology
The Royal College of Radiologists

The timely delivery of radical radiotherapy: guidelines for the management of unscheduled treatment interruptions

Fourth edition

January 2019

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- Validate
- Explore GAP timing
- Explore α/β differences
- Patient use
  - Weigh trade-offs

Intended Treatment Parameters		
Dose/fraction (Gy)	1.8	←----------ENTER
Number of Treatments:	45	←----------ENTER
Date of Treatment Start:	Jan 17, 2022	←----------ENTER
Original Finish Date:	Mar 18, 2022	←----------Calculated/ENTER
Original overall Tx Time:	60	←----------Calculated
Total Planned Dose (cGy)	8100	←----------Calculated

BED Parameters for Intended Tx	Tumor BED	Normal Tissue (NT) BED
Site	Tumor	General NT
alpha/beta	2.5	3
K Value	0.9	0
Tdelay	28	0
# of Fxs	45	45
dose/fx (Gy)	1.8	1.8
Overal Tx Time	60	60

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right] - K \times (T - T_{delay})$$

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right]$$

Uninterrupted BED		
Tumor BED (Gy) (inc. Repopulation)		NT BED (Gy)
110.5		129.6

Pre - Gap Parameters		
Pre-Gap Tumor BED (Gy) (no-repop)		Pre-Gap NT BED (Gy)
92.9		86.4

First Course Dates (Pre-Gap)		
Initial Fractions Delivered	30	←----------ENTER
Start Date	Jan 17, 2022	←----------ENTER
Last Tx Date	Feb 25, 2022	←----------ENTER
Pre-Gap Duration:	39	←----------Calculated
Dose delivered pre-gap (cGy)	5400	←----------Calculated

BED Gap Parameters		
"Lost" Tumor BED (Gy)	0.0	←----------Calculated
Tumor Repop Factor	28.8	←----------Calculated
Allowable NT BED (Gy)	43.2	←----------Calculated

Second Course Dates (Post-Gap)		
Fractions to be Delivered	15	←----------ENTER
Start Date	Mar 7, 2022	←----------ENTER
Scheduled Last Tx Date	Mar 18, 2022	←----------Calculated/ENTER
Post-Gap Duration:	11	←----------Calculated
Total Duration with Gap	60	←----------Calculated

Change Fractions and/or Dose		
Change in Dose/Fx (Gy)	Change in # of Fxs (2nd Course)	
1.80	16	←----------ENTER
New Total Duration (days)		New Last Tx Date
61		Mar 28, 2022
BED Post-gap Tumor (Gy) (repop)		Post-gap BED NT (Gy)
19.8		46.1
BED Pre + Post Gap Tumor (Gy)		Total BED NT (pre + post gaps) (Gy)
112.7		132.5
New Total Dose Delivered (cGy)		Additional Dose Delivered (cGy)
8280		180

Proposed Dose per fraction to achieve BED at scheduled last treatment		
Dose per Fraction (Gy)	1.80	←----------Calculated
Total Duration (days)		Last Tx Date
60		Mar 18, 2022
BED Post-gap Tumor (Gy) (repop)		Post-gap BED NT (Gy)
17.6		43.2
BED Pre + Post Gap Tumor (Gy)		Total BED NT (pre + post gaps) (Gy)
110.5		129.6
New Total Dose Delivered (cGy)		Additional Dose Delivered (cGy)
8100		0

SBRT MISSED TREATMENTS

- High BED
- Lung α/β uncertainty
  - ~ 4 to 10+
- Conventional strategies not appropriate
- Possibly increase fractionation

Estimation of the α/β ratio of non-small cell lung cancer treated with stereotactic body radiotherapy. Klement RJ, Sonke JJ, Allgäuer M, Andratschke N, Appold S, Belderbos J, Belka C, Dieckmann K, Eich HT, Flentje M, Grills I. Radiotherapy and Oncology. 2020 Jan 1;142:210-6.

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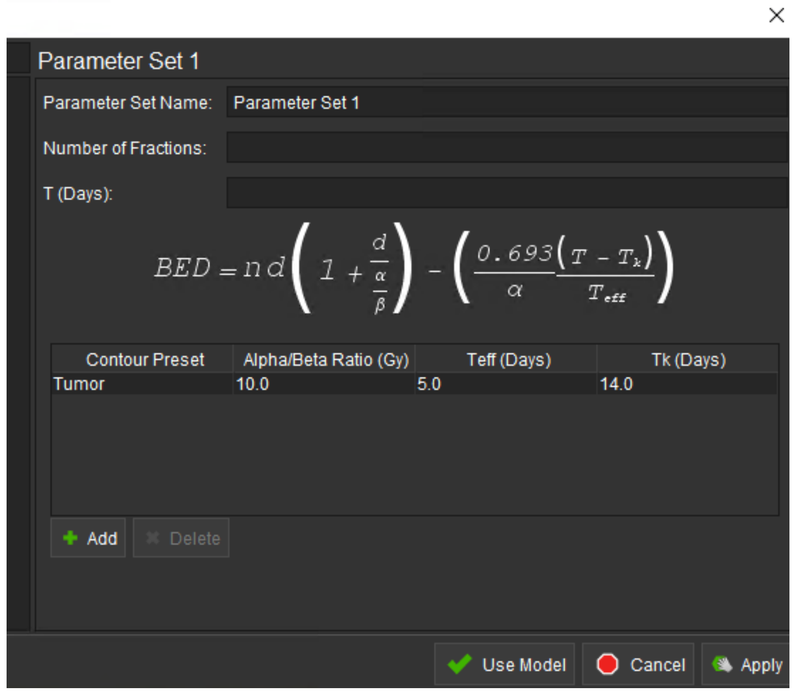
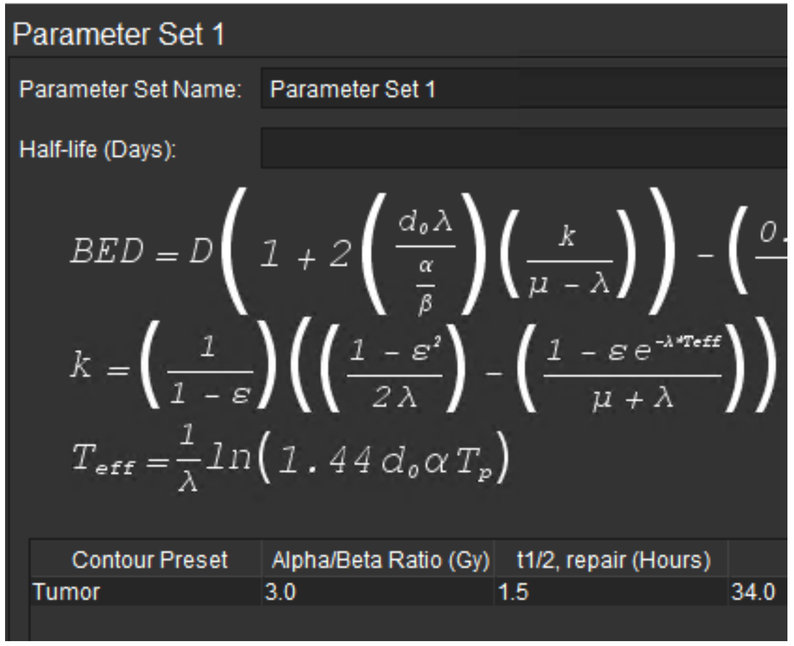
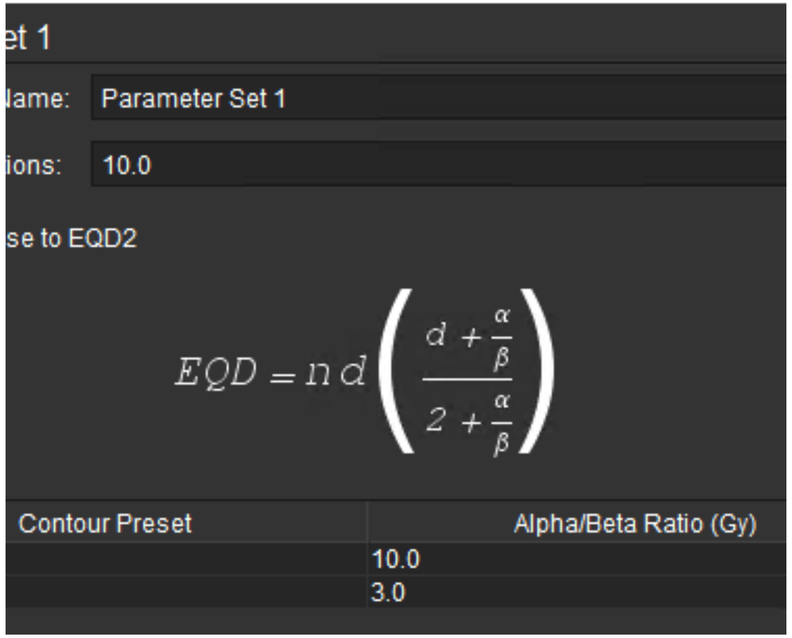




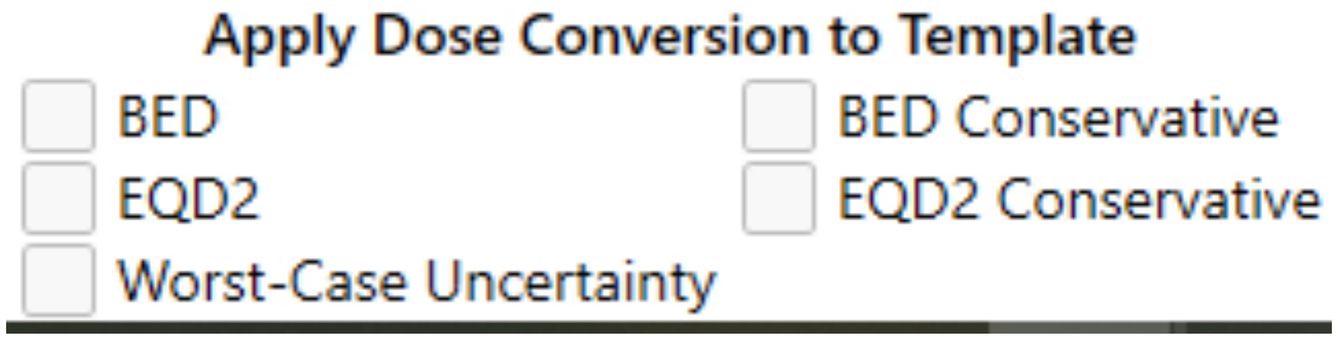


COMMERCIAL TOOLS/ SOLUTIONS

MIMVISTA

COMMERCIAL TOOLS/ SOLUTIONS - RADFORMATION

- Identical Structure Set + Concurrent Treatment
- Same Structure Set + Separate Courses of Treatment (Same Number of Fractions)
- Same Structure Set + Sequential Treatment (Different Number of Fractions)
- Different Structure Sets + Sequential treatment
  - *Re-Binning Method*



WARNING:
Incorrect Use of Phases!

EQD2 Template Plan Phases

Plan ID	Recovery Factor	Phase
PriorTx	1	1
CurrentTx	1	1

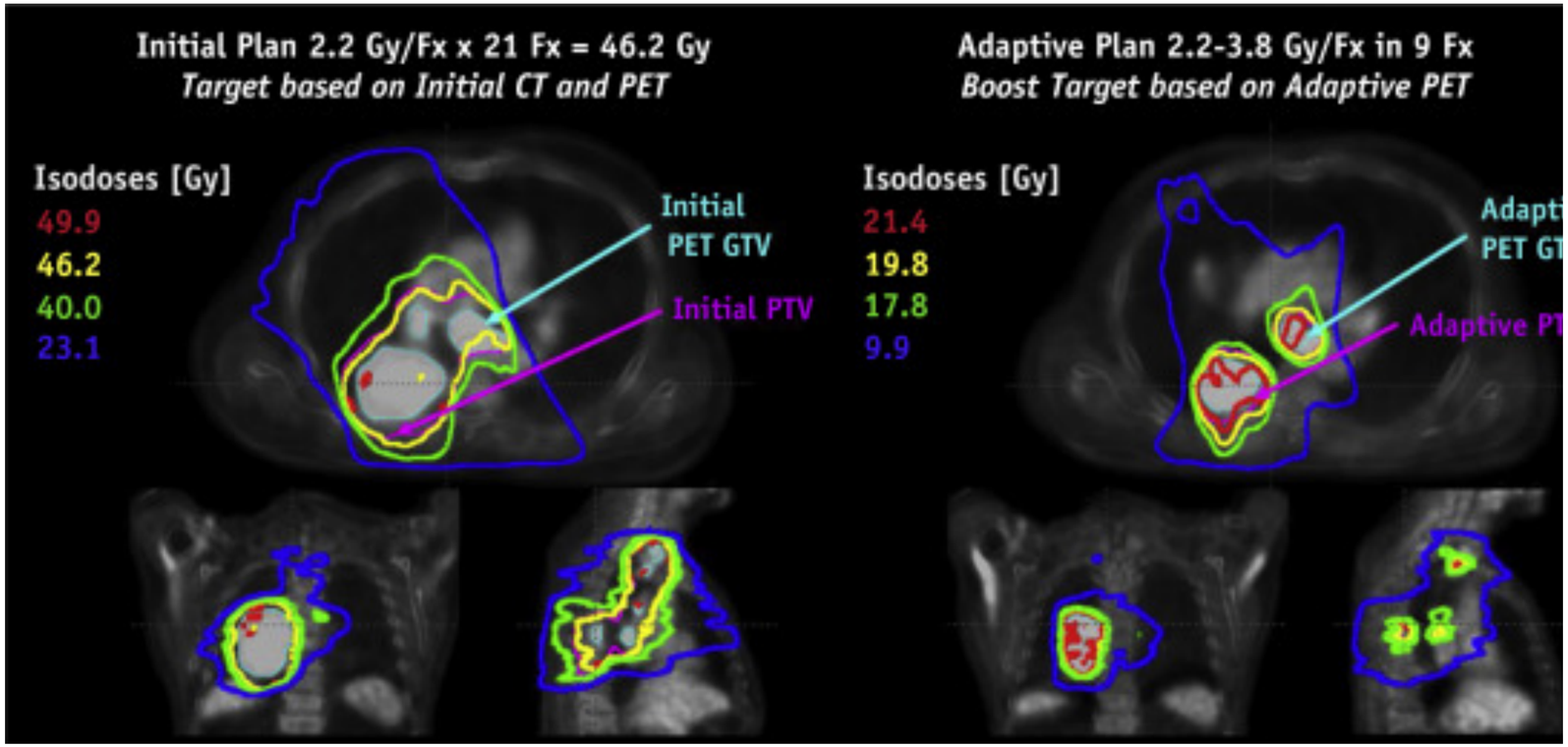
EQD2 Template Constraints

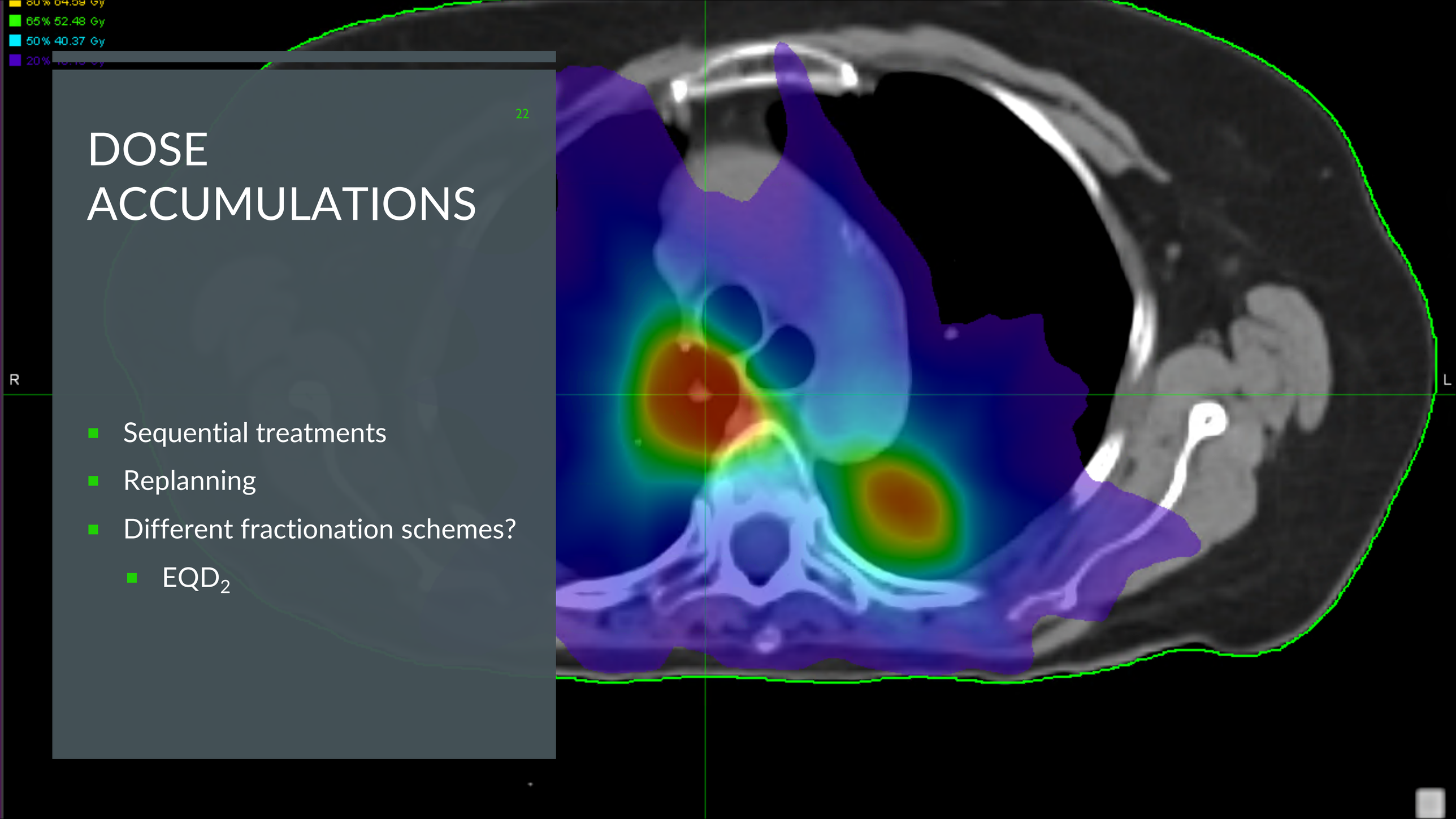
Priority	Structure Template	Structure Plan	Type	Constraint	Goal	PhasesTwo
1	PTV_High	PTV_68	OAR	Max (EQD2 α/β = 10)	cGy	26579.8cGy
2	Rectum	Rectum	OAR	D2cc (EQD2 α/β = 3)	cGy	39171.4cGy
3	Bladder	Bladder_EBRT	OAR	Max (EQD2 α/β = 3)	cGy	48758.3cGy

https://radformation.com/blog/clinical-focus-mastering-bed-and-eqd2-with-clearcheck/

COMMERCIAL TOOLS/ SOLUTIONS

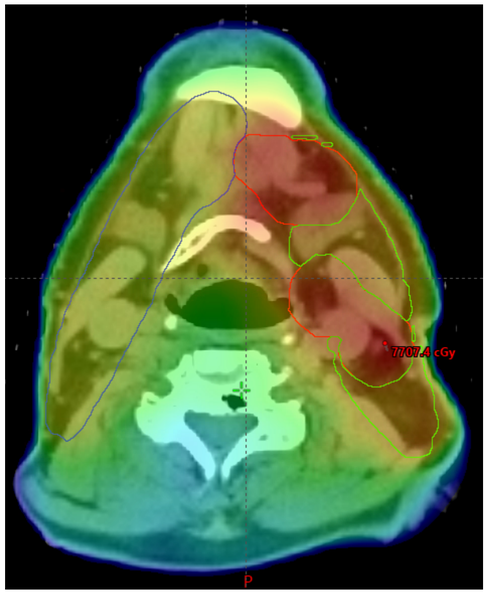
- **Adaptive radiation therapy (ART) strategies and technical considerations: a state of the ART review from NRG oncology.** Glide-Hurst CK, Lee P, Yock AD, Olsen JR, Cao M, Siddiqui F, Parker W, Doemer A, Rong Y, Kishan AU, Benedict SH. International Journal of Radiation Oncology* Biology* Physics. 2021 Mar 15;109(4):1054-75.





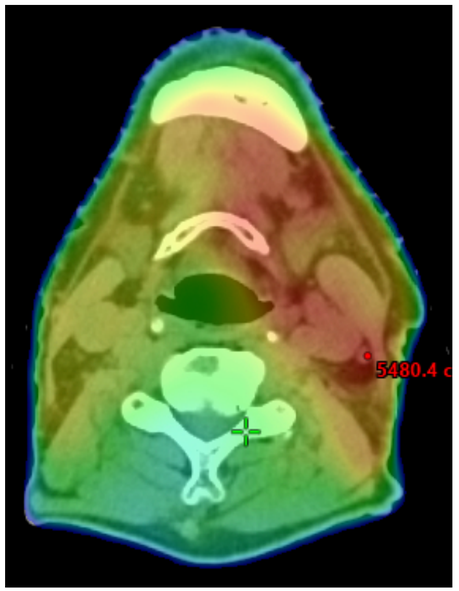
DOSE ACCUMULATIONS

- Sequential treatments
- Replanning
- Different fractionation schemes?
  - EQD_2

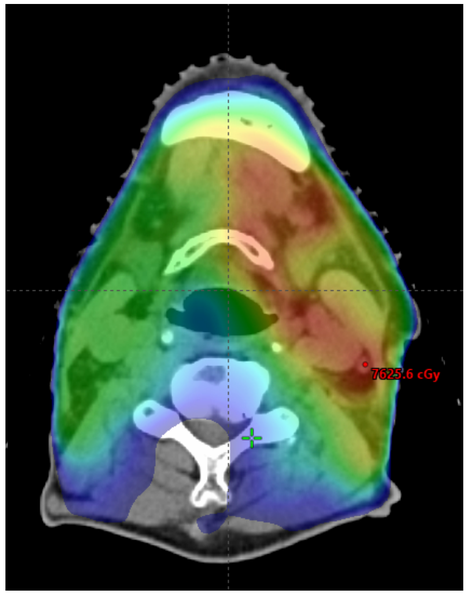


TPS Original Plan

New CT



New CT; Deform Old Dose; TPS



Scale Doses; Accumulate TPS

H&N Definitive Prescriptions

Prescription	Total Dose (cGy)
PTV70	7000
PTV63	6300
PTV56	5600

H&N Definitive Plan Phases

Plan ID	Recovery Factor	Phase
OldDoseNewCT	1	2
RESIM HN	1	1

H&N Definitive Constraints

Structure Template	Structure Plan	Type	Prescription	Constraint	Goal	Plan Sum	Pass/Fail
PTV70	PTV7000	Target	PTV70: 7000cGy	V100% ≥	95%	95.057%	✓
PTV63	PTV6300	Target	PTV63: 6300cGy	**V100% ≥ (BED α/β = 10)**	95%	102.169%	✓
PTV56	PTV5600	Target	PTV56: 5600cGy	**V100% ≥ (BED α/β = 10)**	95%	100.698%	✓
PTV70	PTV7000	Target		Hot Spot Within	7805.8cGy	7805.8cGy	✓
PTV70	PTV7000	Target	PTV70: 7000cGy	D1cc ≤	110-115%	109.463%	✓
SpinalCord	SpinalCord	OAR		D0.035cc ≤	5000cGy	4648.9cGy	✓
Brainstem	Brainstem	OAR		D0.035cc ≤	5400cGy	3685.6cGy	✓
Normal Brain	Brain	OAR		D0.035cc ≤	6000cGy	4372.3cGy	✓
R_Parotid	R_Parotid	OAR		Mean ≤ (Unilateral Whole Gland)	2000cGy	1879.5cGy	✓

DOCUMENTATION

Intended Treatment Parameters		
Dose/fraction (Gy)	1.8	<----------ENTER
Number of Treatments:	45	<----------ENTER
Date of Treatment Start:	Jan 17, 2022	<----------ENTER
Original Finish Date:	Mar 18, 2022	<----------Calculated/ENTER
Original overall Tx Time:	60	<----------Calculated
Total Planned Dose (cGy)	8100	<----------Calculated

BED Parameters for Intended Tx	Tumor BED	Normal Tissue (NT) BED
Site	Tumor	General NT
alpha/beta	2.5	3
K Value	0.9	0
Tdelay	28	0
# of fxs	45	45
dose/fx (Gy)	1.8	1.8
Overal Tx Time	60	60

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right] - K \times (T - T_{delay})$$

$$BED = Nd \times \left[1 + \frac{d}{\alpha/\beta}\right]$$

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BED Gap Parameters

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1.80	16	<----------ENTER
New Total Duration (days)		New Last Tx Date
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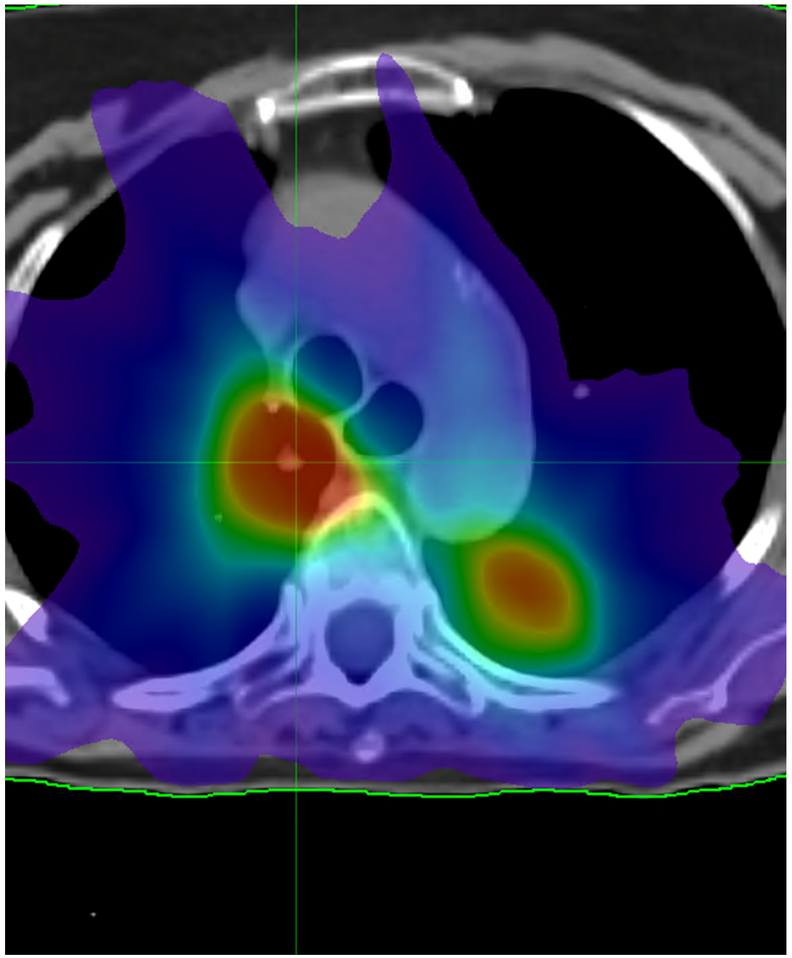

- Special Physics consult?
  - Template?
- What goes in the document?
  - Details!
    - Image (date, number, type, sequence, etc.)
    - Plan(s) info (names, dose, dates, etc.)
    - IMAGES
    - Outline what was done

REFERENCES

- **The timely delivery of radical radiotherapy: guidelines for the management of unscheduled treatment interruptions, fourth edition (2019)** (Accessed January 28, 2022) (Available at: https://www.rcr.ac.uk/publication/timely-delivery-radical-radiotherapy-guidelines-management-unscheduled-treatment)
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