Southern California Chapter
American Association of Physicists in Medicine

Dose Summation

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1/30/2026
2026 AAPM-SCC Mid-Winter Symposium

Introduction

- **Why does dose summation matter?**
  - Re-irradiation is becoming increasingly common due to an aging population and advancements in cancer detection and treatment.
  - Different fractionation: standard fractionation (2 Gy/fx) + hypofractionation (SBRT/SRS)
  - Different modalities: EBRT + brachytherapy
  - Adaptive radiotherapy (ART)
- **Real clinical questions:**
  - “Where is the true hotspot?”
  - “Is this treatment safe?”

Types of Dose Summation

- Plan Summation
- Dose Accumulation
- Biological Dose Accumulation

Plan Summation

- A simple addition of dose distributions from multiple plans.
- Usually done voxel-by-voxel in the same image set or different image sets with rigid image registration.
- Example: Sequential EBRT plan with boost
- Limitations:
  - Ignore anatomical changes
  - No correction for fractionation
  - Physical dose only, not consider the biological effect

Dose Accumulation

- Doses from different plans or fractions are mapped onto a reference image using deformable image registration (DIR).
- The mapped doses are then summed voxel-by-voxel.
- Accounts for anatomical changes (tumor growth/shrinkage, weight gain/loss, organ motion or deformation) and works for different imaging dataset (CT, MRI, CBCT)
- Examples:
  - Re-irradiation, adaptive radiotherapy, staged SRS
- Limitations:
  - Accuracy depends on quality of DIR
  - No correction for fractionation
  - Still physical dose only

Biological Dose Accumulation

- Physical doses are converted to biological doses (such as BED or EQD2).
- The converted biological doses are then summed voxel-by-voxel (with or without DIR).
- Accounts for differences in fractionation, tissue radiosensitivity (α/β ratio), and differences between EBRT and brachytherapy.
- Examples:
  - Re-irradiation (with different fractionation schemes), EBRT + BT
- Limitations:
  - Depends on assumed α/β ratios
  - More uncertainty than physical dose

Dose Summation Workflow

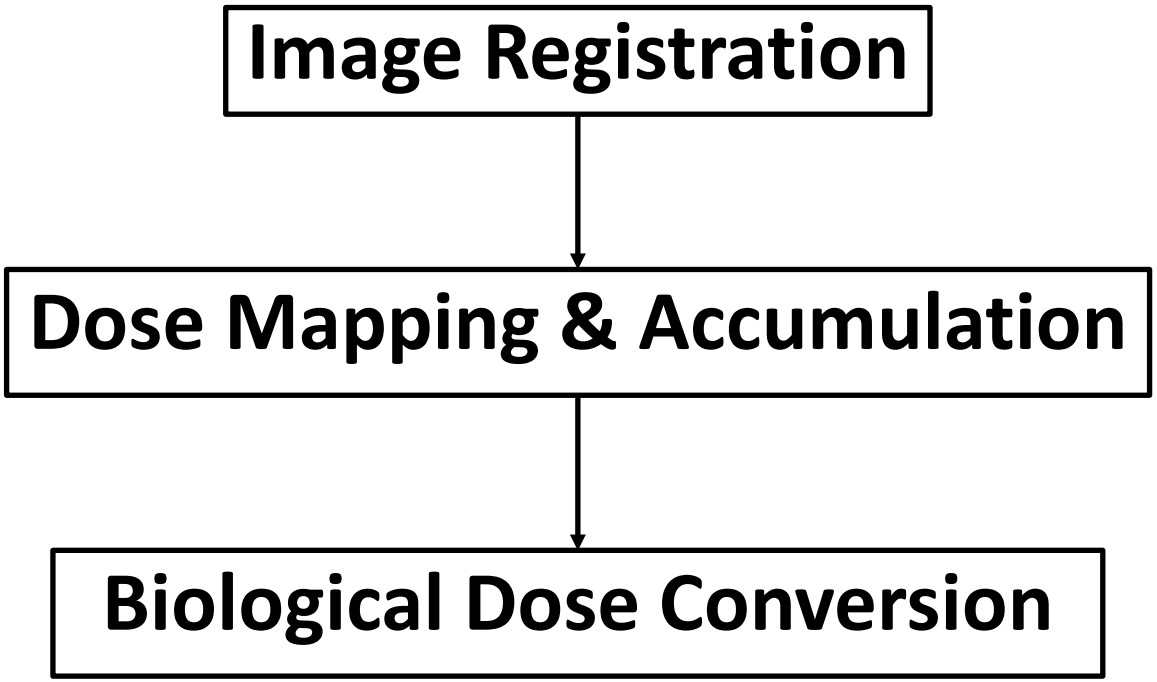
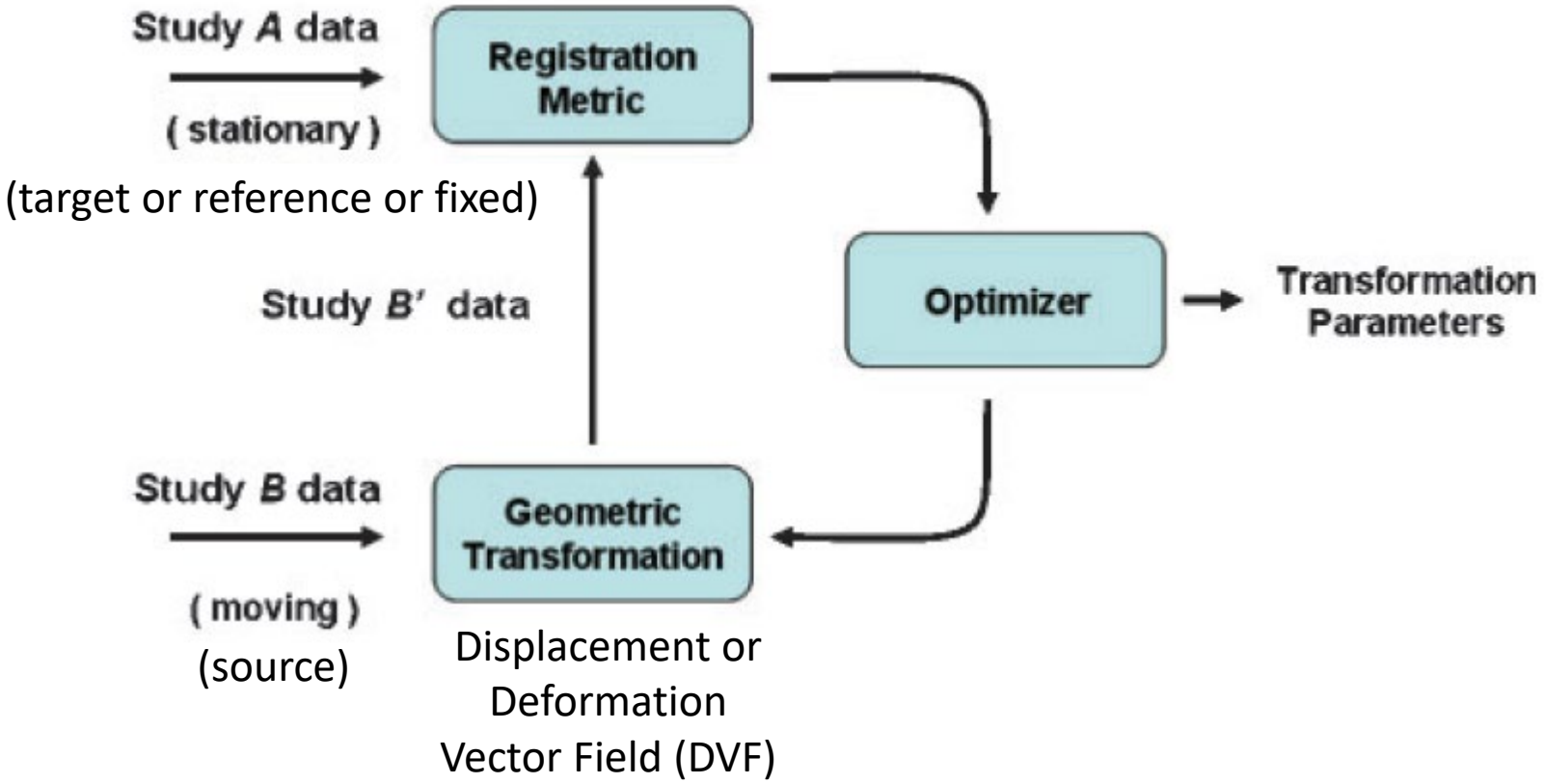


Image Registration

Geometry-Based &
Intensity-Based



Kessler / The British Journal of Radiology, 79 (2006), S99–S108

Image Registration

- **Various image modalities:**
  - CT: for planning with heterogeneity corrections
  - MRI: for enhanced soft-tissue contrast
  - PET: for the physiological information
  - CBCT: for daily image guidance

- **Types of image registration:**
  - Rigid image registration (translations & rotations, 6 DoF)
  - Affine image registration (adds scaling, shearing and plane reflection, 12 DoF)
  - Deformable image registration (DIR; allows spatially varying transformations; B-spline, Demons, biomechanical finite-element models, AI-based deep neural networks)

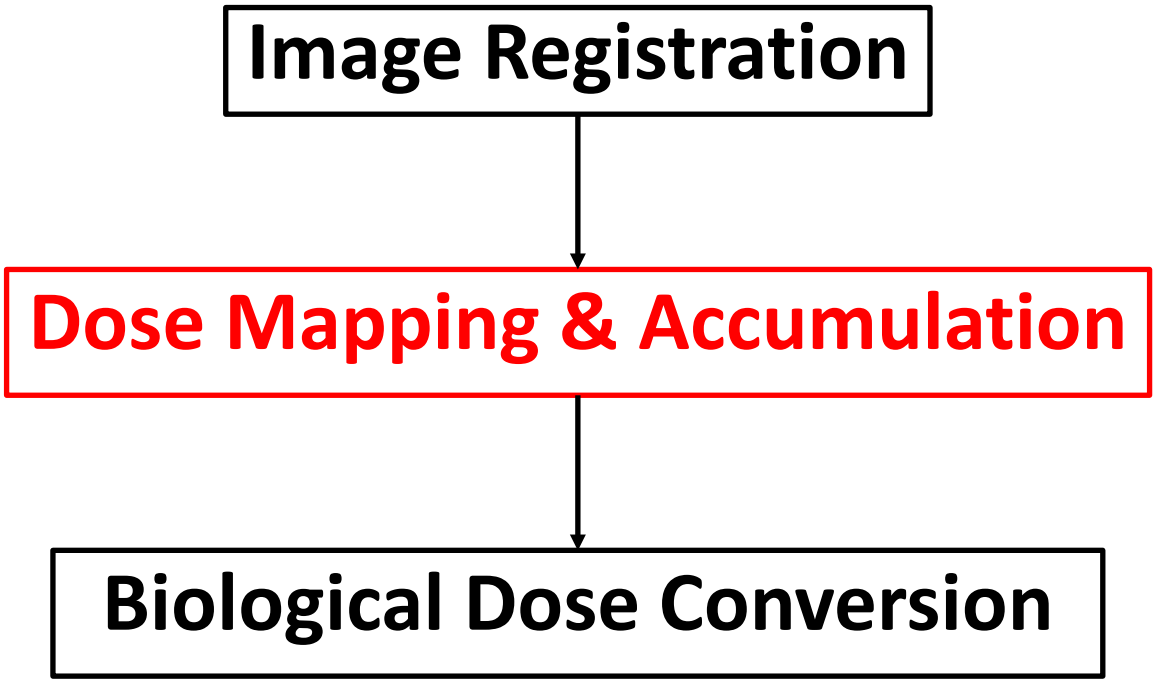
Similarity Metrics

- **Landmark-based**: Distance between points
- **Segmentation-based**: Dice similarity coefficient (DSC) between contours
  - 0: no overlap
  - 1: perfect agreement

$$DSC = \frac{2|A \cap B|}{|A| + |B|}$$

- **Intensity-based**:
  - Sum Squared Difference (SSD)
  - Cross Correlation
  - Mutual Information (useful for registering images from different modalities)
- **Jacobian determinant**
  - >1: volume expansion
  - =1: remain constant
  - >0 and <1: volume reduction
  - <0: indicate an error has occurred

Dose Summation Workflow



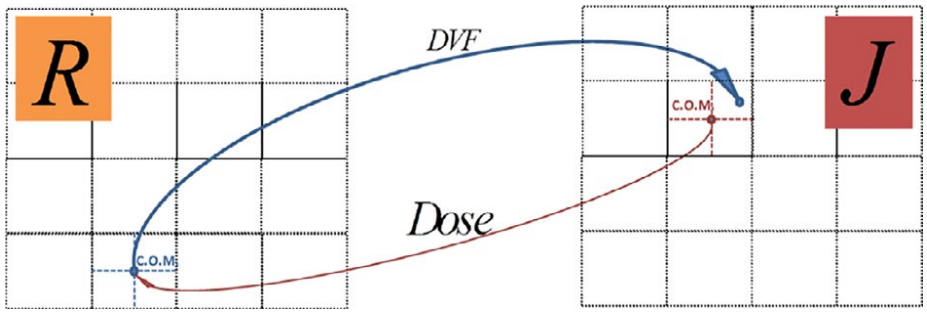
Dose Mapping & Accumulation

- Dose Mapping: the process in which dose from one source image dataset (*S*) is mapped to one target (*T*) or reference dataset, i.e. dose mapping will entail "warping" of the dose based on the DVF between the two image datasets.

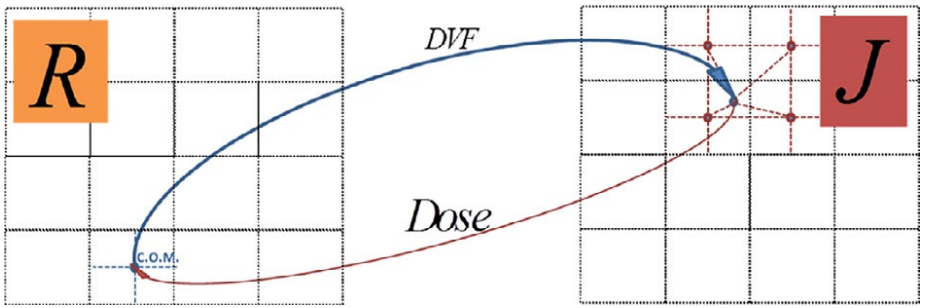
- Dose Accumulation: the process in which dose is summed over multiple "mapped" image datasets to form a composite dose distribution.

Chetty et al. / Semin Radiat Oncol 2019 (29):198–208

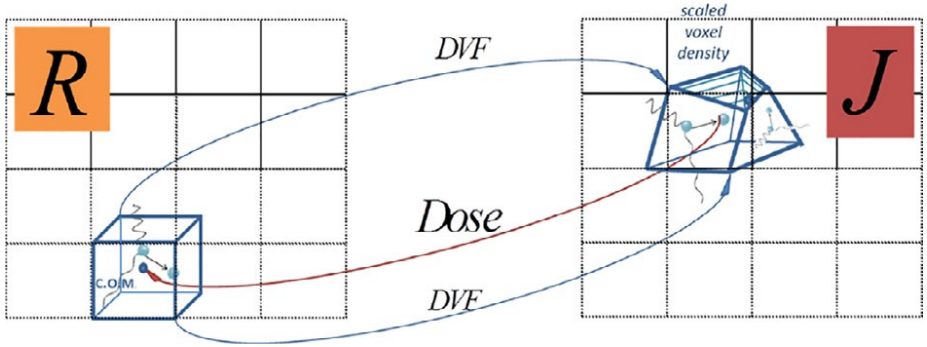
Dose Mapping & Accumulation



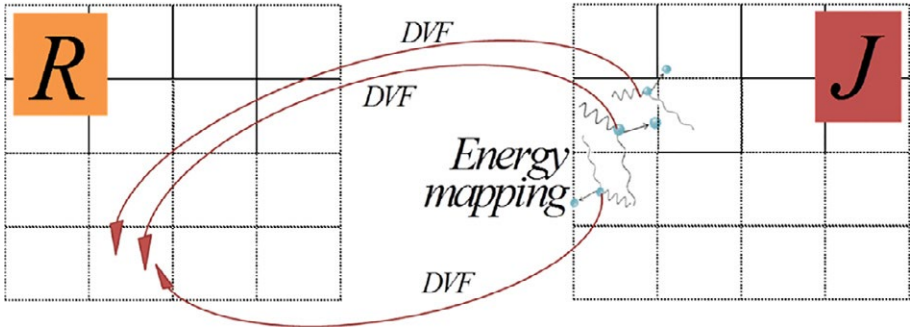
Center-of-Mass (COM) Method



Trilinear Interpolation Method



Direct Voxel Tracking Method



Energy Transfer Method

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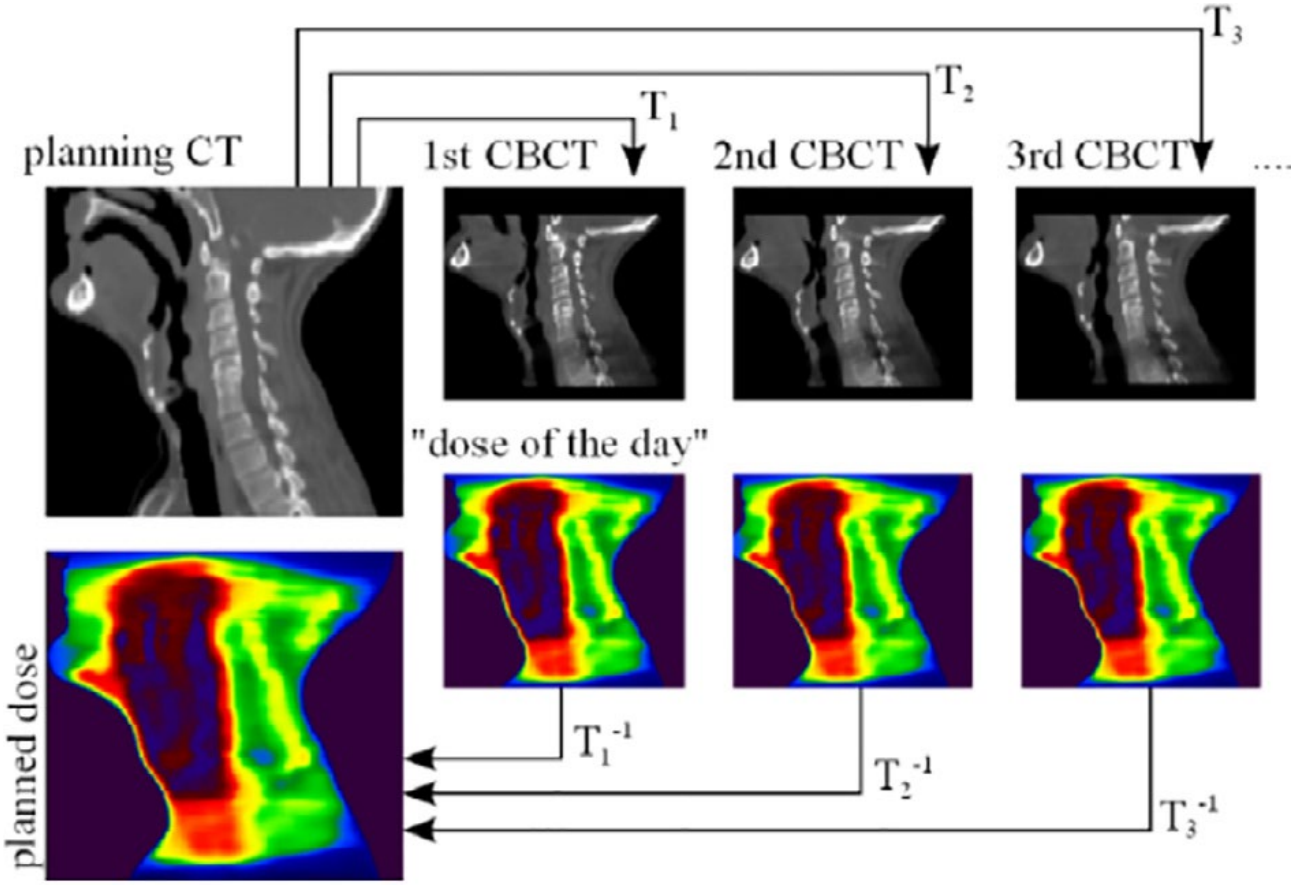
Dose Accumulation Workflow for ART



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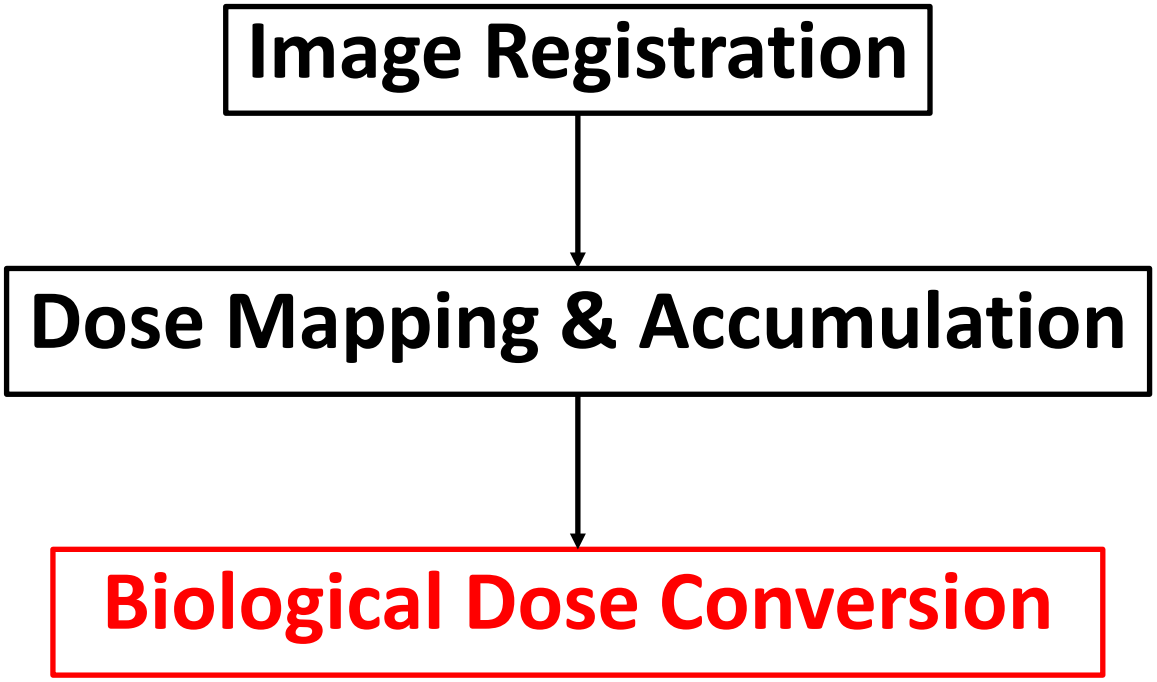
Dose Summation Workflow



Linear Quadratic Model (LQM)

- The most commonly used cell survival curve model
- **Key assumptions:**
  - At least two DNA lesions are required for cell killing (double strand breaks)
  - Lesions can be created by a single ionizing particle creating two strand breaks

$$P = \alpha D$$

  - Lesions can be created by two ionizing particles creating two strand breaks.

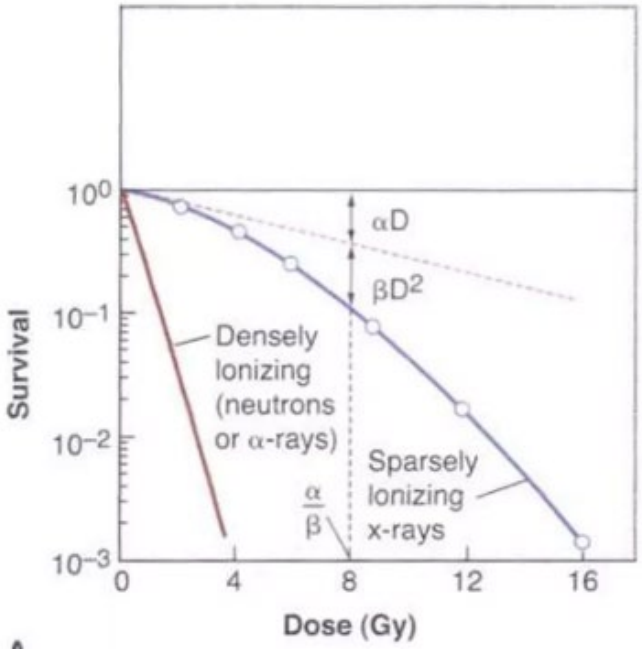
$$P = \beta D^2$$

  - Total probability of killing a cell:

$$P = \alpha D + \beta D^2$$

  - The surviving fraction (S) as a function of dose (D):

$$S(D) = \exp(-\alpha D - \beta D^2)$$



Hall, Radiobiology for the radiologist

α/β Ratio

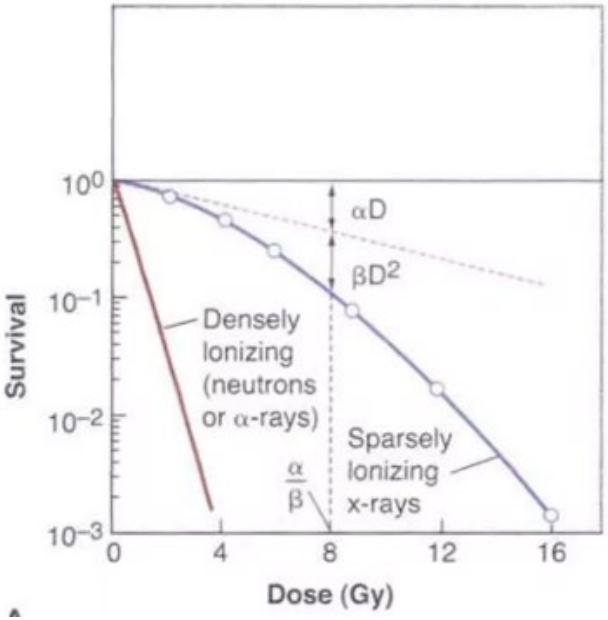
- **α/β Ratio** is the dose at which the linear and quadratic components of cell killing are equal.
- Unit: Gy
- Tumors (non-radioresistant):

  high α/β Ratio of 10
- Prostate tumors:

  low α/β Ratio of 1.5
- Late responding tissues (e.g. CNS, lung, kidney, heart):

  low α/β Ratio of 3
- Early responding tissues (e.g. skin, GI epithelium, hematopoietic cells):

  high α/β Ratio of 10



Hall, Radiobiology for the radiologist

Biologically Effective Dose (BED)

$$\boldsymbol{BED = nd(1 + \frac{d}{\alpha/\beta})}$$

- n: number of fractions
- d: dose per fraction (Gy)
- α/β: alpha-beta ratio for the tumor or organ at risk (OAR)

- **Why BED is useful?**
  - Compare different fractionation schemes
  - Estimate whether hypofractionation will be more effective or not
  - Help estimate tumor control and normal tissue toxicity

Equivalent Dose in 2 Gy Fractions (EQD2)

- A common application of BED is EQD2.
- EQD2 converts any fractionation scheme into the equivalent total dose if given as 2 Gy per fraction and achieve the same BED.

$$EQD2 = \frac{BED}{1 + \frac{2}{\alpha/\beta}}$$

$$EQD2 = nd\left(\frac{d+\alpha/\beta}{1+\alpha/\beta}\right)$$

- Why EQD2 is useful?
  - 2-Gy fractions are commonly used in historical trials
  - Dose constraints are usually based on 2-Gy fractions
  - Easier for clinical comparison and decision making
  - Commonly used in re-irradiation

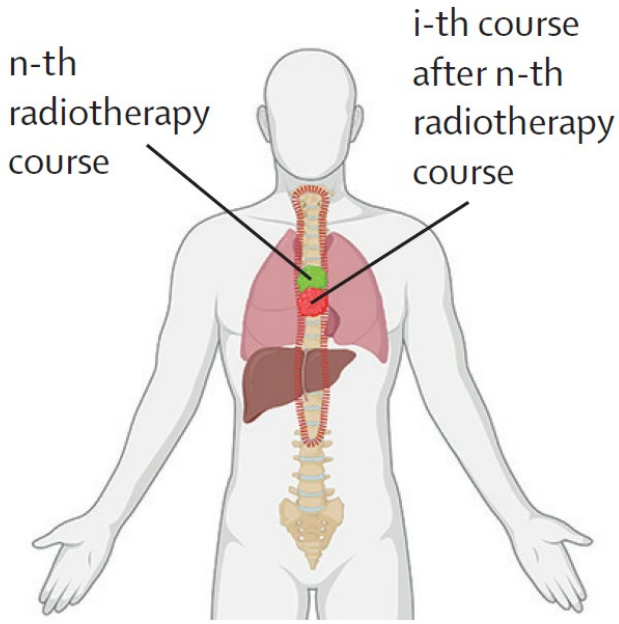
Clinical Cases

- Re-irradiation
- Staged SRS
- EBRT + Brachythearpy (BT)

ESTRO-EORTC Consensus

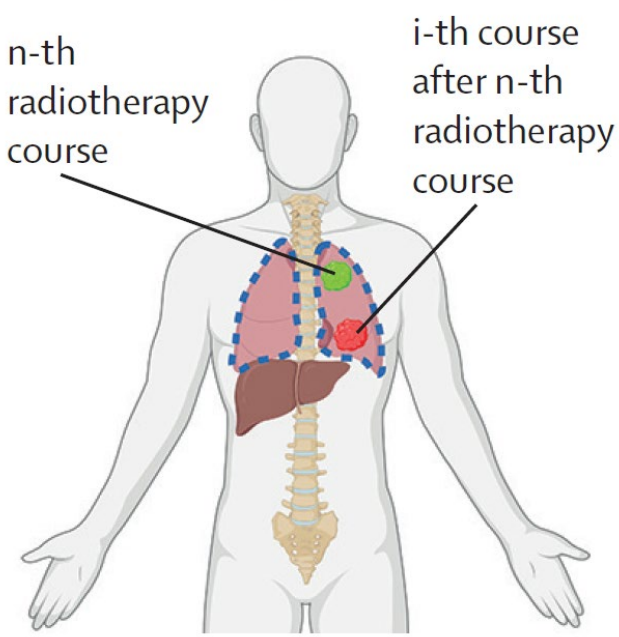
- **Definition of Re-Irradiation**

Type 1



- Overlap of irradiated volumes
- With or without concern for toxicity from cumulative doses

Type 2



- No overlap of irradiated volumes
- Concern for toxicity from cumulative doses

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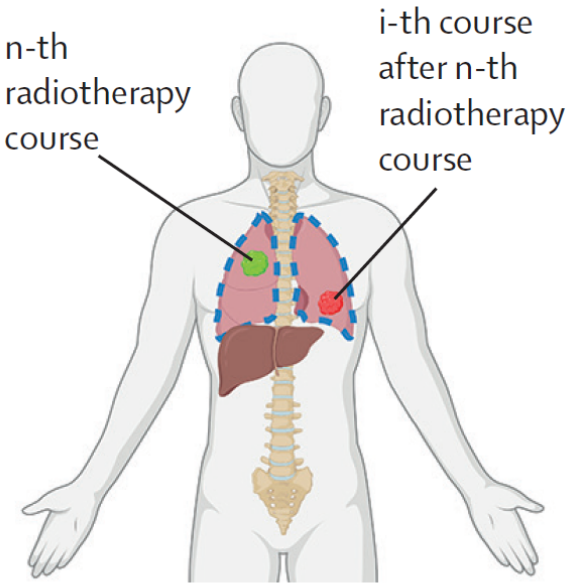
ESTRO-EORTC Consensus

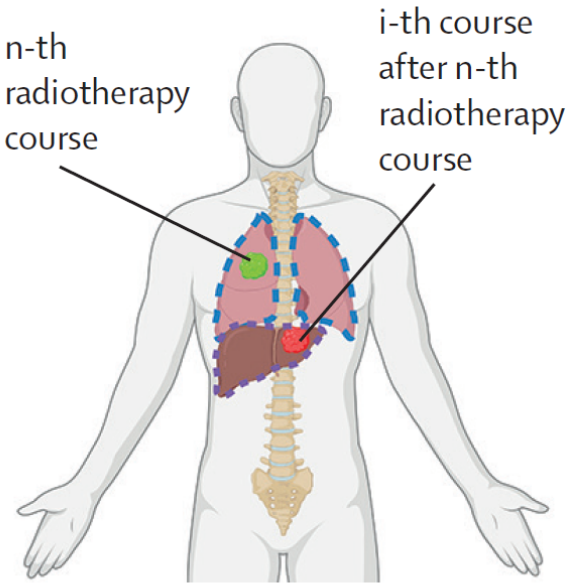
- **Definition of Re-Irradiation**

Repeat organ irradiation



- No overlap of irradiated volumes
- No concern for toxicity from cumulative doses
- Target volumes in the same organ

Repeat irradiation



- No overlap of irradiated volumes
- No concern for toxicity from cumulative doses
- Target volumes in different organs

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ESTRO-EORTC Consensus

- **Reporting Recommendations**

Treatment planning

Required

- Dose prescription and fractionation
- Imaging method for target and organs at risk delineation
- Target and organs at risk definition guideline or protocol
- Dose constraints of organs at risk
- Radiotherapy modality and delivery technique

Recommended

- Biological recalculation of accumulated dose
- Dose calculation algorithm
- Prioritisation of planning objectives

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ESTRO-EORTC Consensus

- **Reporting Recommendations**

Assessment of cumulative doses

Required

- Image registration technique
- Dose summation method (three-dimensional or point doses, physical or biological)
- Radiobiological considerations (such as α/β or tissue recovery)
- Organs at risk cumulative doses

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PHYSICS CONTRIBUTION

Reirradiation Special Medical Physics Consultations: Lessons Learned From Nearly 3000 Courses of Treatment

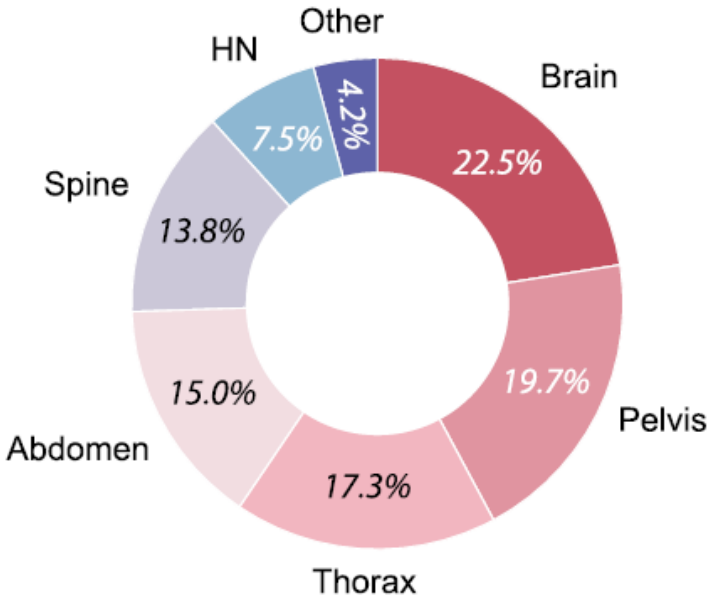
Kelly C. Paradis, PhD,[a] Charles Mayo, PhD,[a] Charles K. Matrosic, PhD,[a] Joann I. Prisciandaro, PhD,[a] Benjamin S. Rosen, PhD,[a] Steven G. Allen, MD, PhD,[a] Alex K. Bryant, MD, MAS,[a] Enid Choi, MD, PhD,[b] Kyle Cuneo, MD,[a] Robert Dess, MD,[a] Alek Dragovic, MD,[a] Joseph R. Evans, MD, PhD,[a] James A. Hayman, MD,[a] Jason Hearn, MD,[a] Elizabeth M. Jaworski, MD,[a] Shruti Jolly, MD, MBA,[a] Michelle M. Kim, MD,[a] Theodore S. Lawrence, MD, PhD,[a] Sean Miller, MD,[a] Grace Sun, MD,[a] Daniel R. Wahl, MD, PhD,[a] Martha M. Matuszak, PhD,[a] and Daniel T. Chang, MD[a]

- U Michigan experience based on ~3000 reirradiation courses
- Standardized workflow for reirradiation special medical physics consultation (SMPC)
- Two dose summation methods

  Rigid Image Registration vs. Point Dose Estimate

Reirradiation SMPC

Body Site Distribution



Distribution of body sites for SMPCs completed June 2023 - May 2024

N = 427

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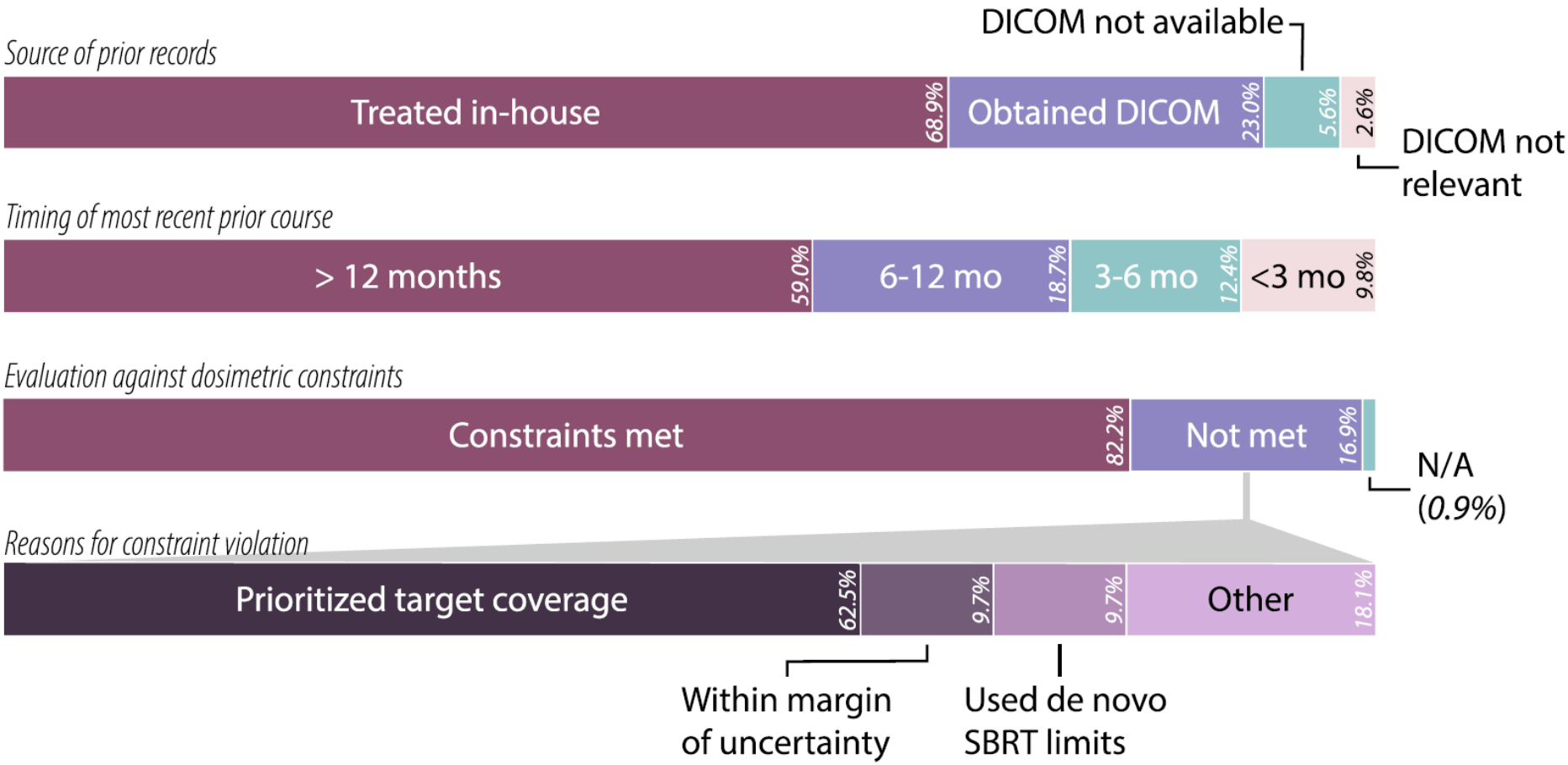
Reirradiation SMPC



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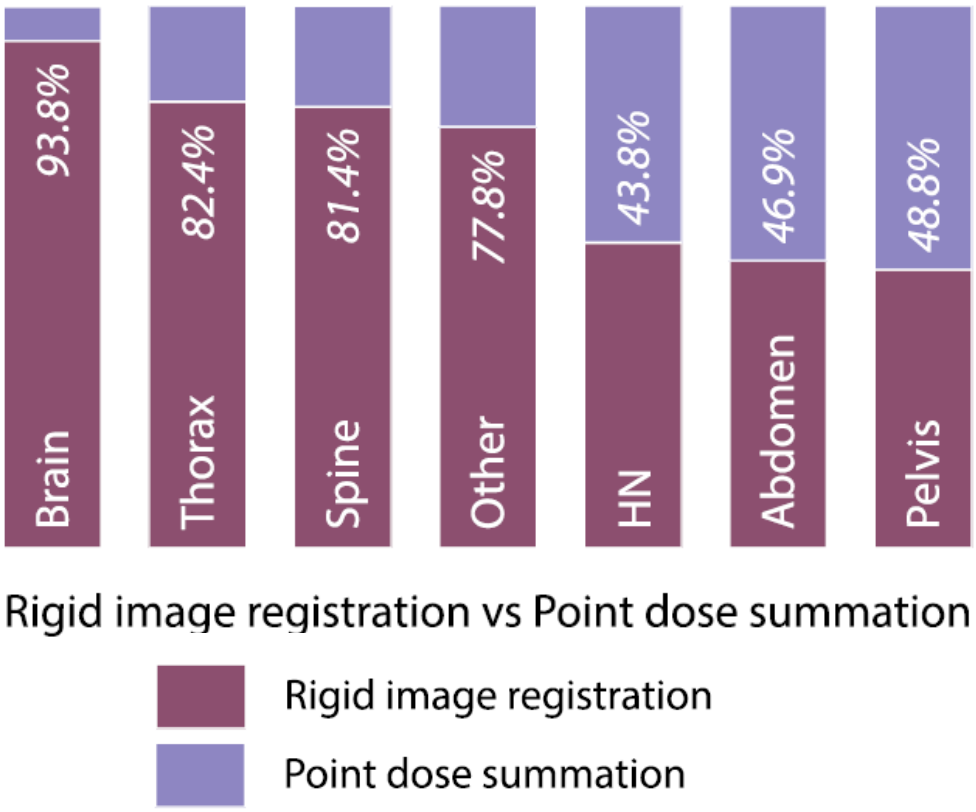
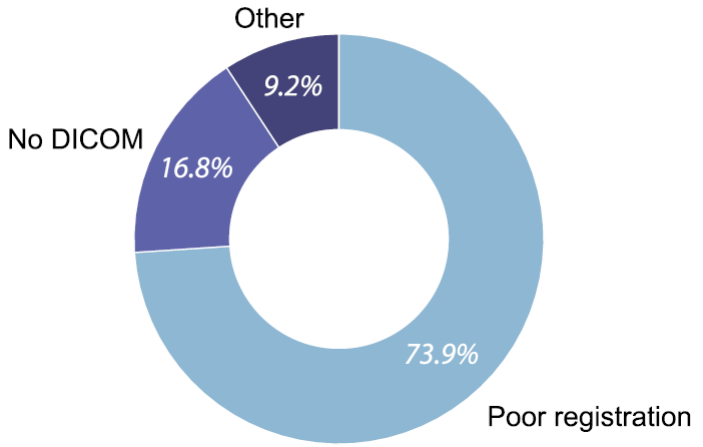
Rigid Image Registration vs Point Dose Summation





- **Deformation of bowel, colon, bladder, thorax**
- **Changes in patient positioning (e.g. neck/spine flexion, supine vs prone, arms up vs. arms down**
- **Brachy applicator**

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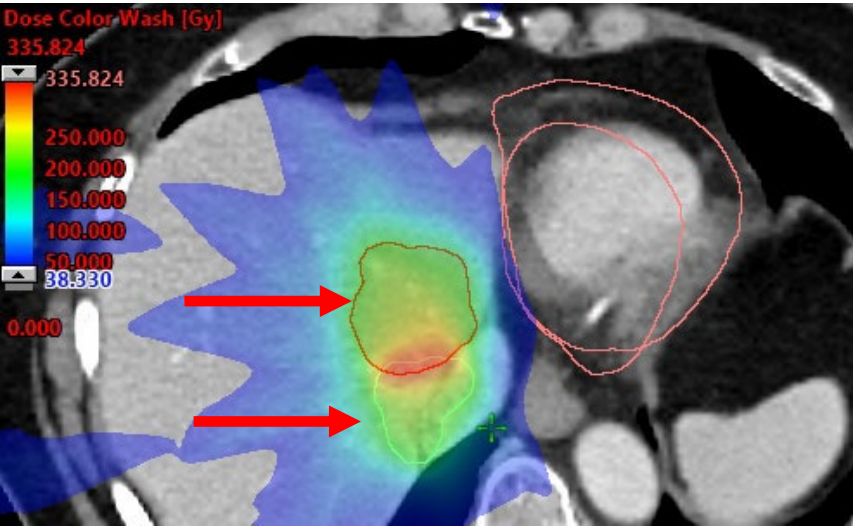
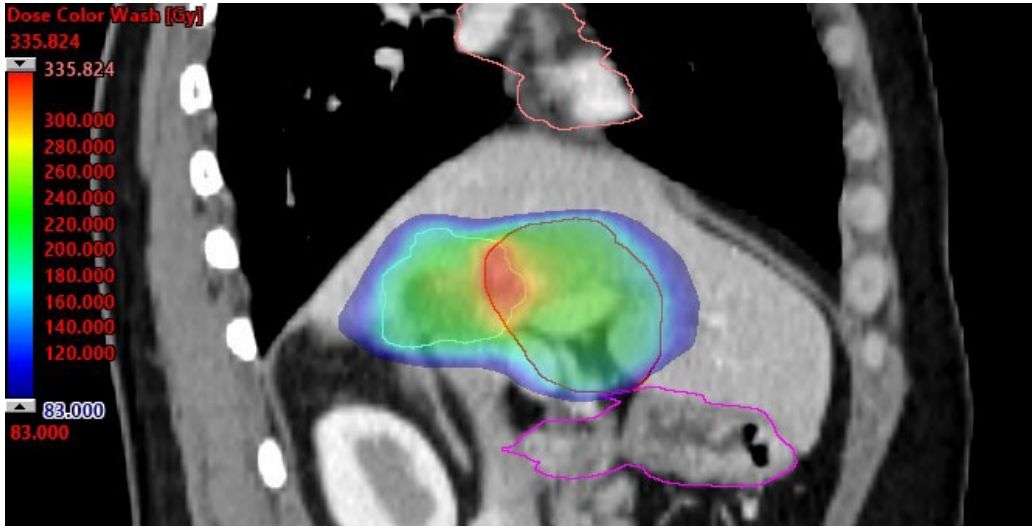
Image Registration-based vs Point Dose Cumulative Dose Estimation

- Prior plan: 50 Gy in 5 fx to liver metastasis
- Current plan: 50 Gy in 5 fx
- Time elapsed: 11 months
- Recovery factor: none
- Rigid registration focused on the high-dose areas
- EQD2Gy (α/β = 2.5 Gy)





Red: Prior target; Green: Current target; Pink: Heart; Magenta: Duodenum

Image Registration-Based vs Point Dose Cumulative Dose Estimation

Table S1: Heart and duodenum metrics for individual and composite plans.

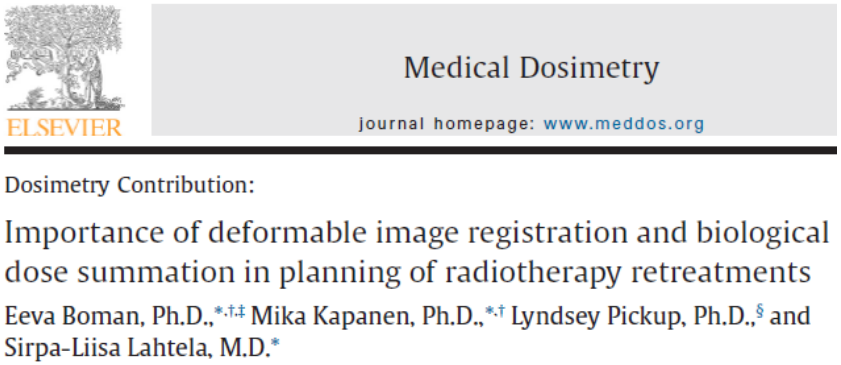
Metric	Plan 1	Plan 2	Registration-based sum	Point dose sum	
Heart					
D0.1cc[Gy]	19.6	13.2	33.2	32.8	-1.2%
D0.1cc[EQD2Gy]	28.0	15.1	45.3	43.1	-4.9%
Duodenum					
D0.1cc[Gy]	9.1	3.4	38.8	12.5	-67.8%
D0.1cc[EQD2Gy]	8.7	2.4	83.2	11.1	-86.7%

- Heart:
  - Registered well and received high dose to the same area
  - A point dose summation of near-maximum doses is very similar to a registration-based cumulative dose calculation.
- Duodenum:
  - Did not register well and received a relatively low dose from both plans
  - The prior high dose region is mapped into a region where the current duodenum is located, leading incorrect cumulative dose (83.2 EQD2Gy).

We have compared Rigid Image Registration vs Point Dose Estimate.

How about Deformable Image Registration (DIR)?

Comparison of Dose Summation Methods



- **Three dose summation methods:**
  - **Rigid raw sum:** with rigid registration of the planning images and direct dose summing
  - **Deformable raw sum:** with deformable image registration and direct dose summing
  - **Deformable biological sum:** with deformable registration and take into account the dose per fraction in biological manner in certain critical organs

Physical Dose
d1 + d2

Biological Dose
BED1 + BED2

- **Three clinical cases**: head and neck, brain, and mediastinum

E. Boman et al. / Medical Dosimetry 42 (2017) 296–303

Head and Neck (HN)

- C1: 33 fx x 2/1.82/1.64 Gy (66/60/54 Gy) to the left side of tongue
- C2: 25 fx x 2 Gy (50 Gy) to the right side of HN
- Time elapsed: 2 years
- Healing assumption: 25%
- Note: Tumor mass and abnormal neck rigidity
- Medulla: α/β Ratio of 2
- Mandible & Pharynx: α/β Ratio of 3

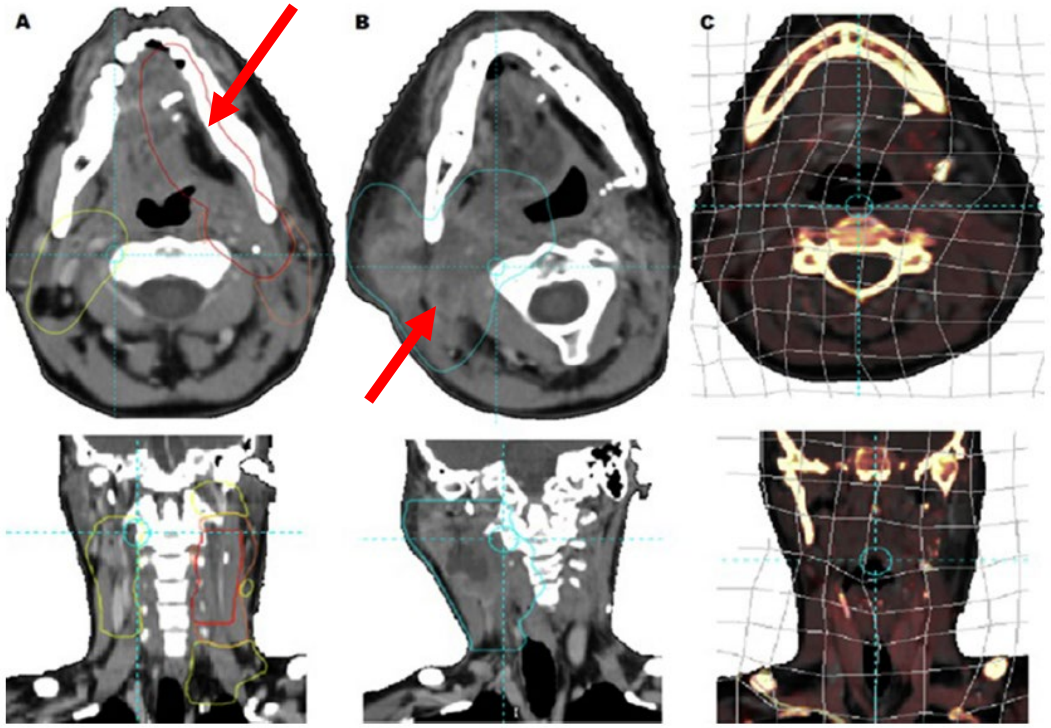


Fig. 1. (A) First planning CT with PTV contours for initial radiotherapy treatment in axial and coronal planes. (B) Second planning CT with new PTV for relapse treatment. (C) Registration deformation grid calculated between the 2 CTs. (Color version of figure is available online.)

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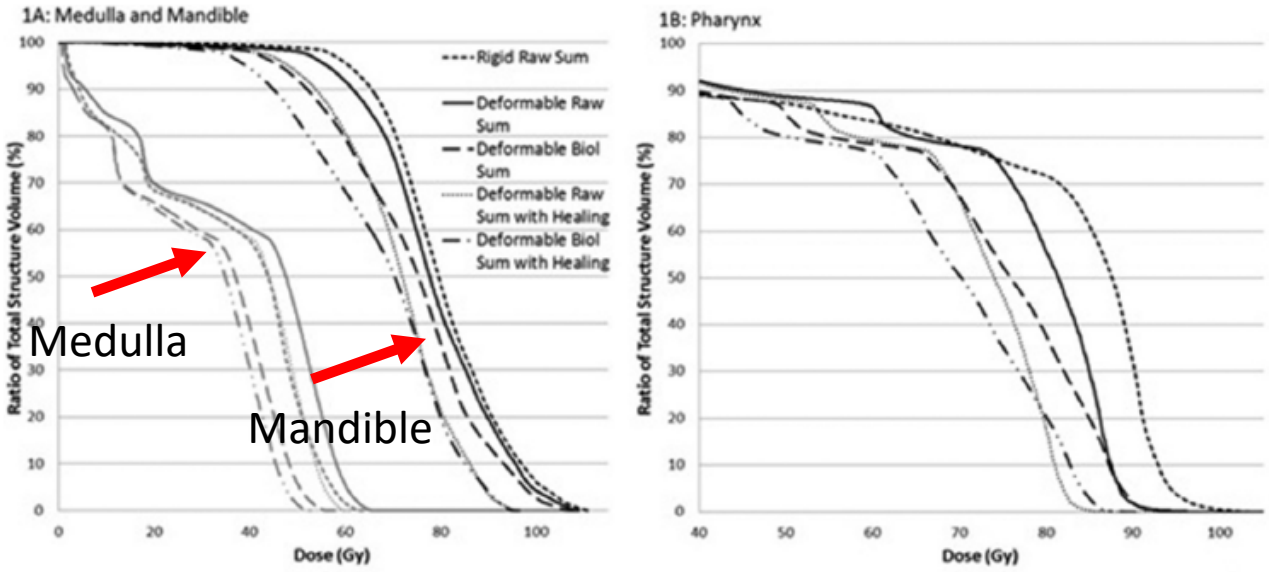
Head and Neck (HN)



Dose parameters D0.1cc, D1cc, and mean dose (Gy) of OARs for different clinical cases obtained from different summation methods

Organ	Rigid raw sum	Deformable raw sum	Deformable biol. sum	Deformable raw sum with healing	Deformable biol. sum with healing
Case I:					
Medulla D0.1cc (Gy)	63	65 (3.7%)	56 (–11.4%)	60 (–5.1%)	52 (–17.3%)
Mandible D0.1cc (Gy)	111	108 (–2.2%)	107 (–3.5%)	95 (–13.8%)	95 (–14.0%)
Pharynx D0.1cc (Gy)	103	97 (–6.5%)	95 (–7.8%)	88 (–15.3%)	89 (–14.0%)
Pharynx mean (Gy)	91	93 (2.4%)	88 (–4.5%)	82 (–10.0%)	79 (–13.9%)

The percentage deviation from the dose parameter of the rigid raw sum is shown in parentheses (%).

Effect of healing

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Brain

- C1: 25 x 1.8 Gy (45 Gy) to PTV1 (red) followed by 8 x 1.8 Gy booster (magenta) (total of 59.4 Gy)
- C2: 33 x 1.8 Gy (59.4 Gy) to PTV2 (orange)
- C3: 20 x 2 Gy (40 Gy) to PTV3 (cyan)
- Time elapsed: 4 yr & 1 yr
- Healing assumption: 25% for C1
- OARs (brainstem & cochlea): α/β Ratio of 3

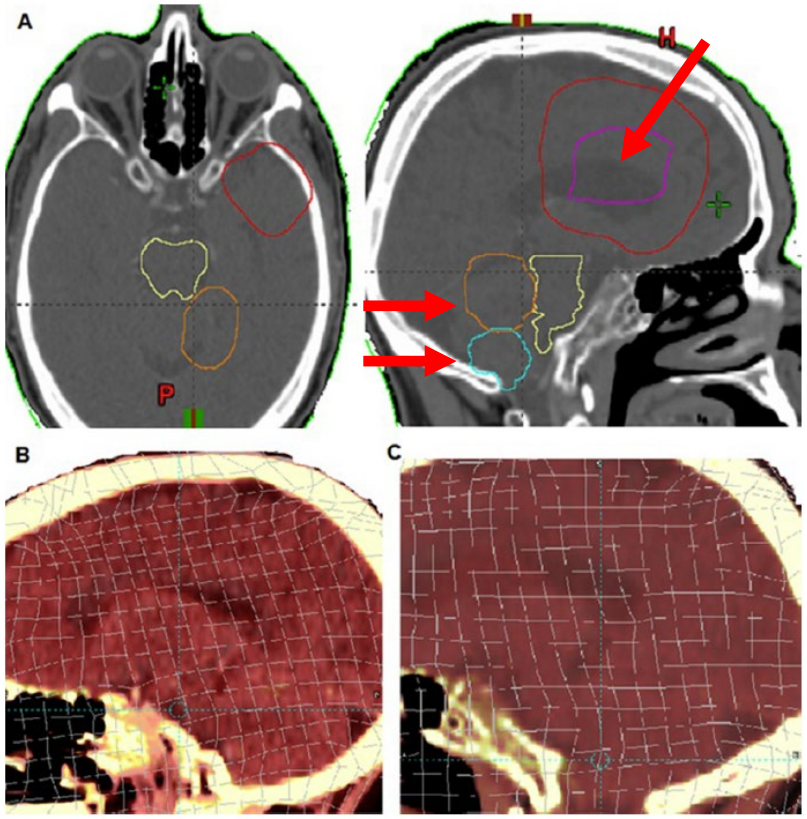

Fig. 2. (A) Last planning CT with all 3 PTVs shown in red or magenta (PTV1/booster), orange (PTV2), and cyan (PTV3). The pons is contoured in yellow. (B) Registration map for first and second treatments. (C) Registration map for the second and third treatments. (Color version of figure is available online.)

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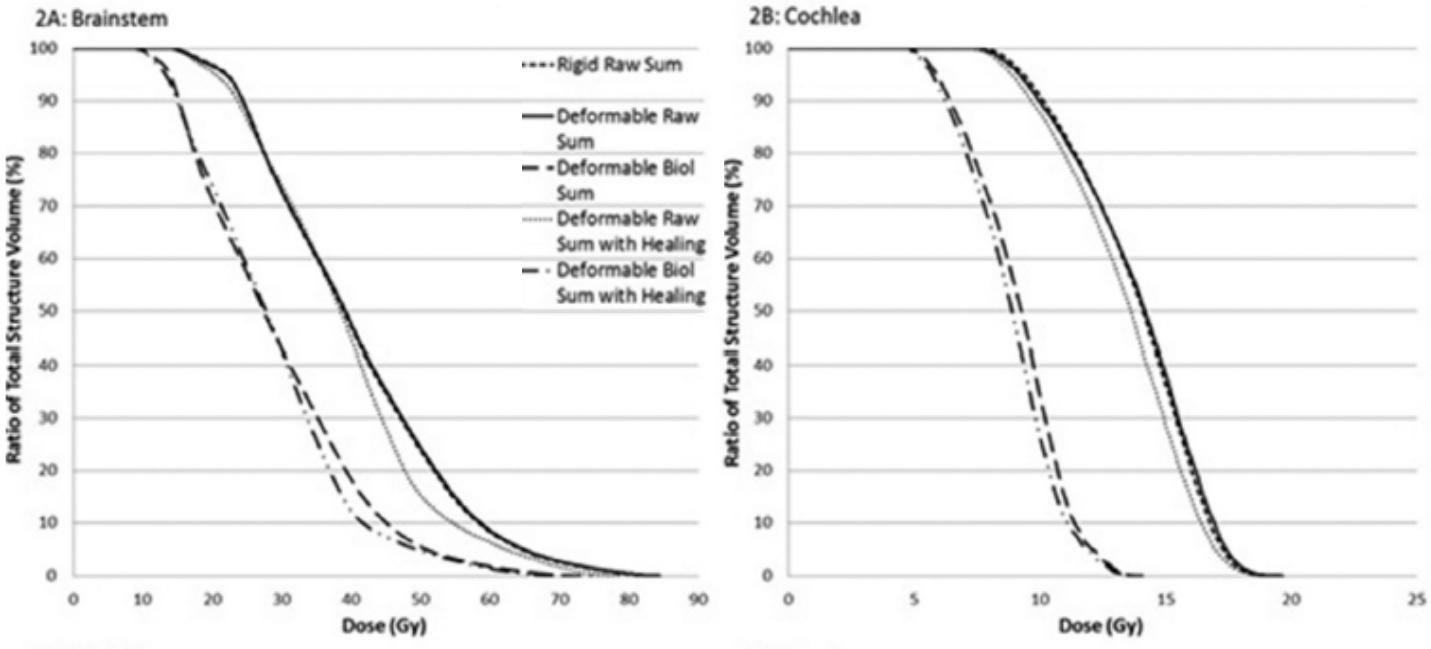
Brain



Dose parameters D0.1cc, D1cc, and mean dose (Gy) of OARs for different clinical cases obtained from different summation methods

Organ	Rigid raw sum	Deformable raw sum	Deformable biol. sum	Deformable raw sum with healing	Deformable biol. sum with healing
Case II:					
Brainstem D0.1cc (Gy)	82	83 (1.2%)	71 (–13.4%)	77 (–6.1%)	68 (–17.1%)
Brainstem D1cc (Gy)	65	65 (0.0%)	51 (–21.5%)	63 (–3.1%)	50 (–23.1%)
Cochlea D0.1cc (Gy)	19	19 (0.0%)	13 (–31.6%)	19 (0.0%)	13 (–31.6%)

Dose/fx <2 Gy

The percentage deviation from the dose parameter of the rigid raw sum is shown in parentheses (%).

Minor effect of healing

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Mediastinum

- C1: 5 x 4 Gy (20 Gy) to PTV1 (orange) in the mediastinum
- C2: 10 x 3 Gy (30 Gy) to PTV2 (red) in the HN
- Time elapsed: a few months
- Healing assumption: No
- Note: arm-up in C1 & arm-down in C2
- OARs (medulla & esophagus): α/β Ratio of 3

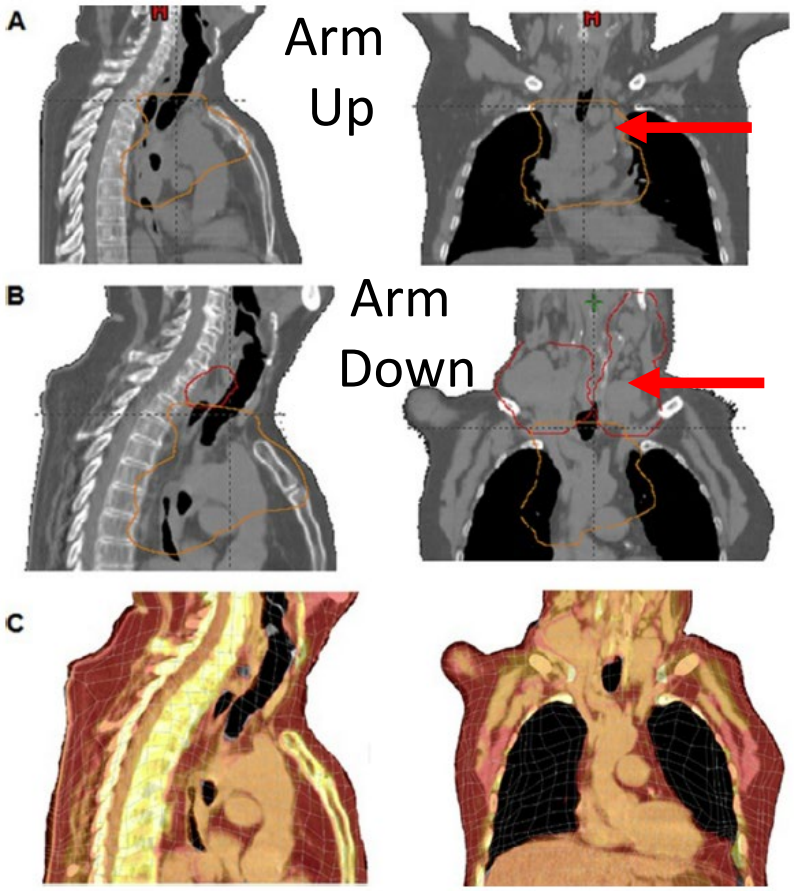

Fig. 3. (A) First planning CT with PTV in mediastinum (orange) in the sagittal and coronal planes. (B) Second planning CT with new PTV in the upper region (red), and the previous mediastinum PTV (orange). (C) Registration deformation grid calculated between the 2 CTs shows several anatomic deformations. (Color version of figure is available online.)

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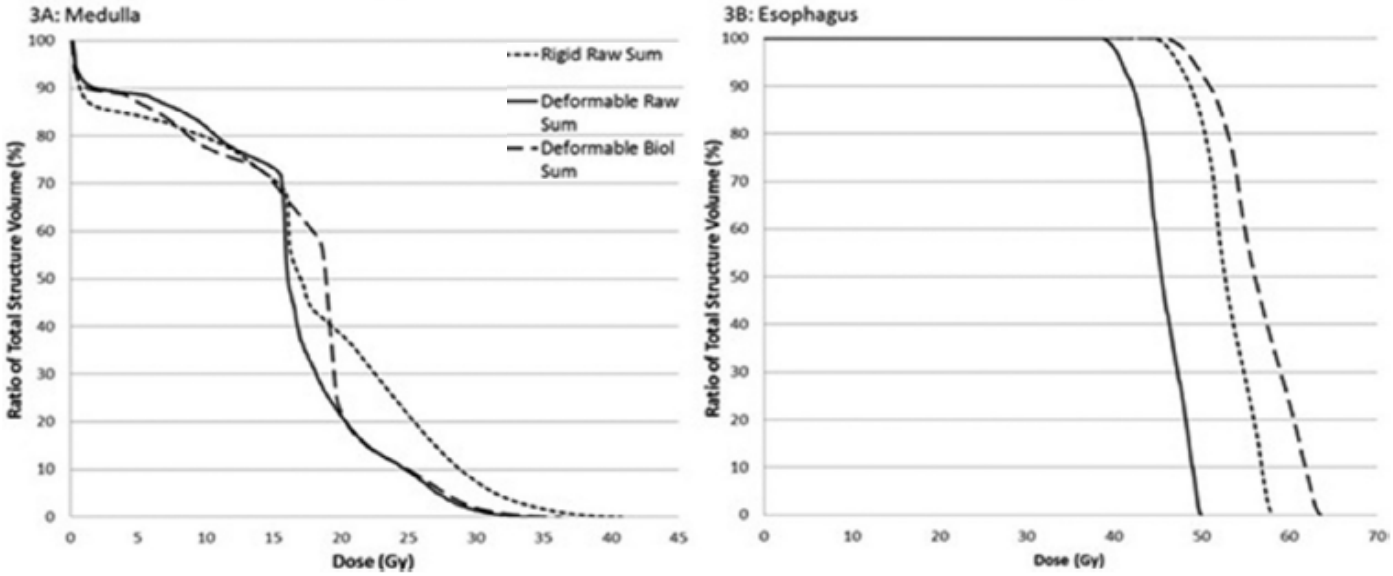
Mediastinum



Dose parameters D0.1cc, D1cc, and mean dose (Gy) of OARs for different clinical cases obtained from different summation methods

Organ	Rigid raw sum	Deformable raw sum	Deformable biol. sum	Deformable raw sum with healing	Deformable biol. sum with healing
Case III:					
Medulla D0.1cc (Gy)	39	33 (–15.4%)	35 (–10.3%)	–	–
Esophagus D0.1cc (Gy)	58	50 (–13.8%)	63 (8.6%)	–	–
Esophagus D50% (Gy)	58	50 (–13.8%)	63 (8.6%)	–	–
Esophagus mean (Gy)	53	46 (–13.8%)	56 (6.6%)	–	–

The percentage deviation from the dose parameter of the rigid raw sum is shown in parentheses (%).

Dose/fx >2 Gy

Poor rigid registration

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Clinical Cases

- Re-irradiation
- Staged SRS
- EBRT + Brachythearpy (BT)

BED of Gamma Knife Staged SRS

frontiers | Frontiers in Oncology

ORIGINAL RESEARCH
published: 30 June 2022
doi: 10.3389/fonc.2022.892139

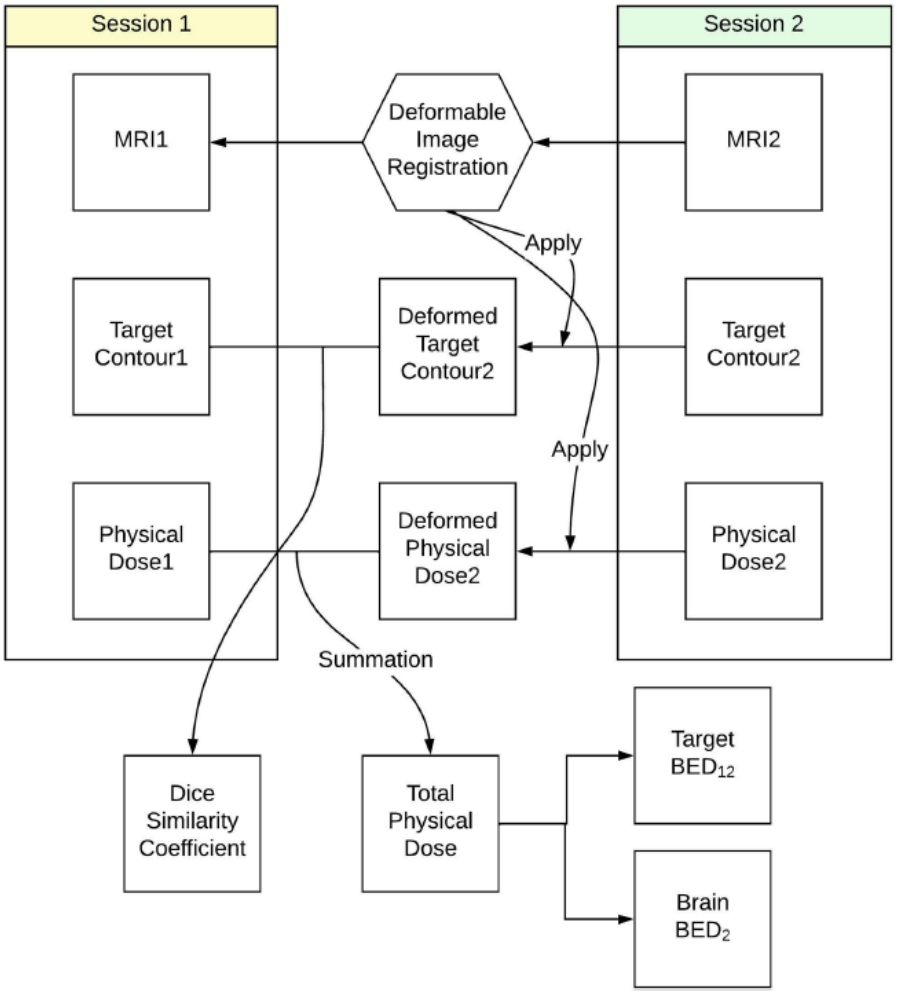
Evaluation of Biological Effective Dose in Gamma Knife Staged Stereotactic Radiosurgery for Large Brain Metastases

Taoran Cui[1], Joseph Weiner[1], Shabbar Danish[2], Anupama Chundury[1], Nisha Ohri[1], Ning Yue[1], Xiao Wang[1] and Ke Nie[1]*

- 12 patients with 24 brain metastases were treated with two sessions of GK staged SRS
- Larger tumor: max diameter > 2 cm or total volume > 4 cc
- Interval: 30.5 d (range: 21-51 d)
- Rx Dose: 13 Gy (range: 13-15 Gy) + 13 Gy (12-13 Gy)
- Relative tumor volume reduction: -52.2% (-81.8% to 4.3%)
- Replanned for single-fraction SRS and hypo-fractionated SRS

T. Cui et al. / Frontiers in Oncology 12 (2022) https://doi.org/10.3389/fonc.2022.892139

Workflow to Calculate BED in Staged SRS



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Formula to Calculate BED in Staged SRS

$$\mathrm{BED}^{i} = D^{i}\left(1 + \frac{D^{i}}{\alpha/\beta}\right)$$

D^{i}: physical dose delivered in the *i*th staged SRS session
α/β: 12 Gy for brain metastases, 2 Gy for normal brain tissue

For tumor: need to consider cell repopulation

$$\mathrm{BED}_{12} = D^{1}\left[1 + \frac{D^{1}}{(\alpha/\beta)_{12}}\right] + D^{2}\left[1 + \frac{D^{2}}{(\alpha/\beta)_{12}}\right] - \frac{\ln 2}{\alpha T_{pot}}\max(0, T - T_{k})$$

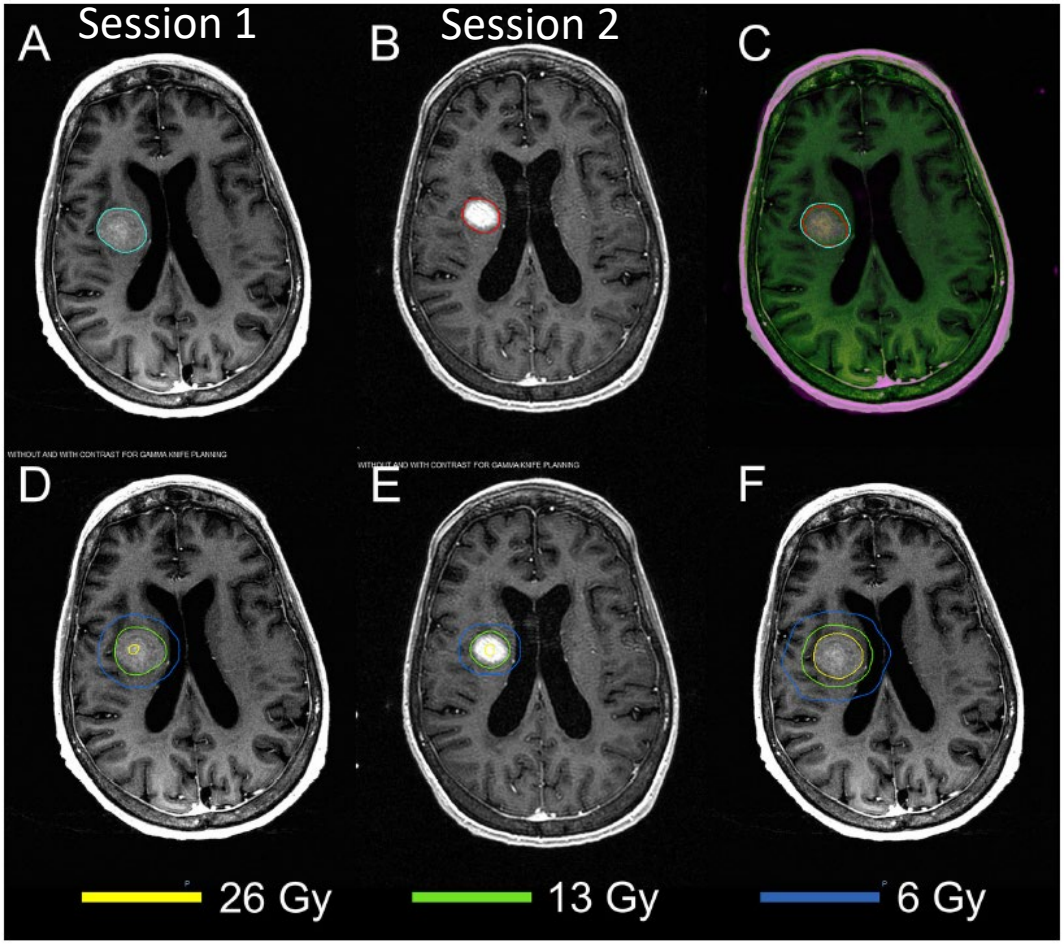
T_{pot}: tumor double time, 3 d
T_{k}: repopulation kick-off time, 28 d
T: interval between sessions, 21-42 d

For normal brain: cell repopulation is negligible for late responding tissue

$$\mathrm{BED}_{2} = D^{1}\left[1 + \frac{D^{1}}{(\alpha/\beta)_{2}}\right] + D^{2}\left[1 + \frac{D^{2}}{(\alpha/\beta)_{2}}\right]$$

T. Cui et al. / Frontiers in Oncology 12 (2022) https://doi.org/10.3389/fonc.2022.892139

BED of Gamma Knife Staged SRS



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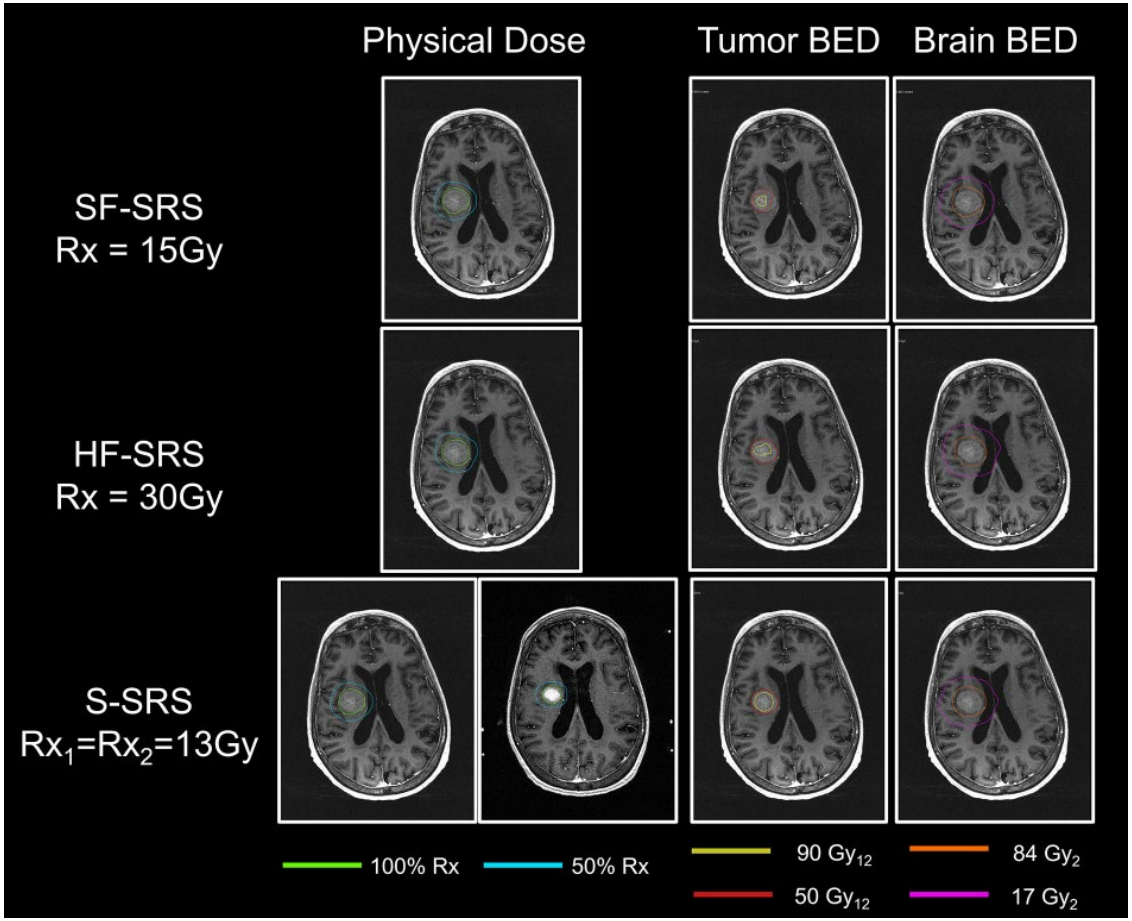
Comparison between Different SRS Techniques

Single-Fraction SRS

Hypo-Fractionated SRS

Staged GK SRS



T. Cui et al. / Frontiers in Oncology 12 (2022) https://doi.org/10.3389/fonc.2022.892139

Comparison between Different SRS Techniques

	Normal Brain V_{84Gy2} (cc)			GTV $BED_{98\%}$ (Gy_{12})		
	SF-SRS	HF-SRS	Staged SRS	SF-SRS	HF-SRS	Staged SRS
Median	28.3	23.6	28.6	35.6	51.4	45.6
Min	4.0	4.03	4.0	27.1	48.8	32.8
Max	80.8	71.0	84.9	47.2	57.3	64.2

- Normal Brain V_{84Gy2} : biologically equivalent to V_{12Gy} assuming α/β of 2 Gy
- GTV $BED_{98\%}$: minimum BED delivered to at least 98% of the tumor

- Better normal brain sparing in the HF-SRS plans than those in the staged SRS plans.
- Higher BED in HF-SRS plans compared to those in the staged SRS plans.

T. Cui et al. / Frontiers in Oncology 12 (2022) https://doi.org/10.3389/fonc.2022.892139

Clinical Cases

- Re-irradiation
- Staged SRS
- EBRT + Brachythearpy (BT)

GYN

ELSEVIER

Brachytherapy 11 (2012) 47–52

BRACHYTHERAPY

American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part II: High-dose-rate brachytherapy

Akila N. Viswanathan[1,*], Sushil Beriwal[2], Jennifer F. De Los Santos[3], D. Jeffrey Demanes[4], David Gaffney[5], Jorgen Hansen[1], Ellen Jones[6], Christian Kirisits[7], Bruce Thomadsen[8], Beth Erickson[9]

Table 1
Examples of regimens frequently used in the United States for tandem and ovoid or tandem and ring brachytherapy

EBRT, dose to ICRU 52 point or median dose in case of IMRT	Fractionation to point A (Gy)	EQD2 (Gy) to the tumor (point A dose with $\alpha/\beta = 10$ Gy)[a]	EQD2 (Gy) with 90% of the target dose to the OAR using $\alpha/\beta = 3$ Gy	EQD2 (Gy) with 70% of the target dose to the OAR using $\alpha/\beta = 3$ Gy
25 × 1.8 Gy	4 × 7 Gy	83.9	90.1	74.2
25 × 1.8 Gy	5 × 6 Gy	84.3	88.6	73.4
25 × 1.8 Gy	6 × 5 Gy	81.8	83.7	70.5
25 × 1.8 Gy	5 × 5.5 Gy	79.8	82.6	69.6

ICRU 52 = International Commission of Radiation Units Report 52; IMRT = intensity modulated radiation therapy; EBRT = external-beam radiotherapy; EQD2 = normalized therapy dose; OAR = organs at risk.

[a] For institutions that use radiographic imaging for treatment planning, these doses (e.g., D_{90}) are recorded at point A. For institutions that use computed tomography or magnetic resonance imaging, these doses are recorded covering the target volume or high-risk clinical target volume.

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Table 2
Dose limits to the target and to the organs at risk

Dose specified to	Radiographs	3D imaging
Point A	5 × 5–6 Gy	Variable
D_{90}		≥80–≤90 Gy EQD2
ICRU point bladder	5 × ≤3.7 Gy	
ICRU point rectum	5 × ≤3.7 Gy	
D_{2cc} bladder		≤90 Gy EQD2
D_{2cc} rectum		≤75 Gy EQD2
D_{2cc} sigmoid		≤75 Gy EQD2

EQD2 = normalized therapy dose; 3D = three dimensional.

Table 3
Examples of potential dose fractionation regimens to consider for template-based HDR interstitial brachytherapy after 45–50.4 Gy of external beam

Dose of EBRT	Brachytherapy dose[a]	EQD2 (Gy) to CTV
45 Gy/25 fractions	3.5 Gy × 9	79.7
	4.25 Gy × 7	79.6
	5 Gy × 5	75.5
50.4 Gy/28 fractions	3 Gy × 9	78.8
	4.5 Gy × 5	76.7

EBRT = external-beam radiotherapy; EQD2 = equivalent dose in 2 Gy/fraction; CTV = clinical target volume; HDR = high-dose-rate.

A.N. Viswanathan et al. / Brachytherapy 11 (2012) 47e52

DVH Parameter Addition

PHYSICAL - BIOLOGICAL DOCUMENTATION OF GYNAECOLOGICAL HDR BT

MRN	Patient Name

EXTERNAL BEAM THERAPY		TUMOUR	OAR
dose per fraction	1.8	D_{iso} [α/β=10Gy]	D_{iso} [α/β=3Gy]
fractions without central shield	25	44.3	43.2
fractions with central shield		0.0	0.0
total dose	**45.0**	**44.3**	**43.2**

BRACHYTHERAPY	F 1	F 2	F 3	F 4	F 5	F 6			
date	7/29/2025	7/31/2025	8/5/2025	8/7/2025			Dose Values in Gy		
physicist									
MR / CT	CT	CT	CT	CT			TOTAL	TOTAL	
applicator(s): type, # needles							BT	BT + EBT	
applicator(s): dimensions									
Plan, remarks							*mean*	*stddev*	
Planning aim for D_{90} CTV_{HR}	6	6	6	6					
planning aim $EQD2_{10}$	8.0	8.0	8.0	8.0	0.0	0.0	32.0	76.3	Gy $EQD2_{10}$

DVH Parameter Addition

							Total BT	Total BT+EBT	
CTV_{HR} [cm^3]	7.9	7.7	12.0	11.7			*9.8*	*2.0*	**cm3**
D_{90}	6.3	6.6	7.0	7.0					
D_{90} $EQD2_{10}$	8.6	9.1	9.9	9.9	0.0	0.0	37.5	**81.7**	**Gy $EQD2_{10}$**
CTV_{IR} [cm^3]	43.2	36.5	38.4	40.4			*39.6*	*2.5*	**cm3**
D_{98}	4.0	3.8	4.5	4.4					
D_{98} $EQD2_{10}$	4.6	4.4	5.5	5.3	0.0	0.0	19.8	**64.1**	**Gy $EQD2_{10}$**
BLADDER [cm^3]	140.6	118.8	182.1	141.9			*145.9*	*22.9*	**cm3**
D_{2cm^3}	3.1	2.8	2.7	3.3					
D_{2cm^3} $EQD2_3$	3.8	3.3	3.0	4.2	0.0	0.0	14.3	**57.5**	**Gy $EQD2_3$**
RECTUM [cm^3]	79.1	59.1	57.2	74.1			*67.4*	*9.4*	**cm3**
D_{2cm^3}	3.9	3.5	3.9	4.0					
D_{2cm^3} $EQD2_3$	5.4	4.5	5.4	5.6	0.0	0.0	20.9	**64.1**	**Gy $EQD2_3$**
SIGMOID [cm^3]	66.8	133.6	54.1	108.1			*90.7*	*31.8*	**cm3**
D_{2cm^3}	1.2	0.6	0.6	0.8					
D_{2cm^3} $EQD2_3$	1.0	0.4	0.4	0.6	0.0	0.0	2.5	**45.7**	**Gy $EQD2_3$**
INTESTINES OR BOWEL [cm^3]	358.5	429.7	149.4	437.6			*343.8*	*116.4*	**cm3**
D_{2cm^3}	1.5	0.7	1.6	0.8					
D_{2cm^3} $EQD2_3$	1.3	0.5	1.5	0.6	0.0	0.0	3.9	**47.1**	**Gy $EQD2_3$**

We have shown DVH Parameter Addition.

Can Deformable Image Registration (DIR) perform better?

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

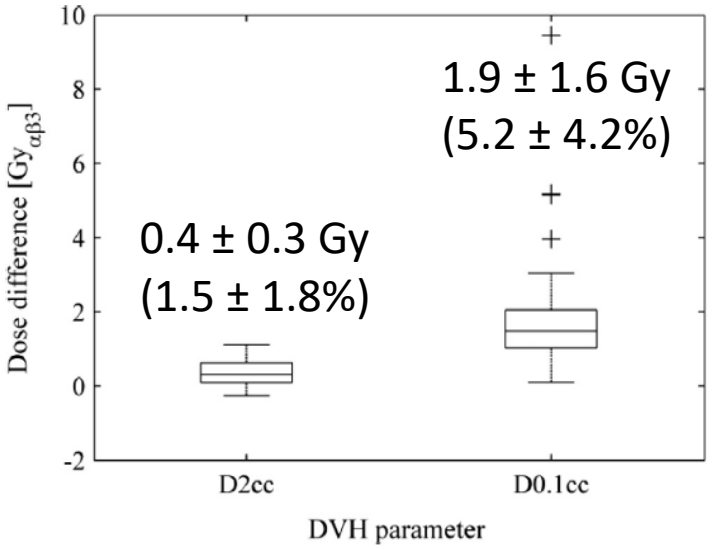
journal homepage: www.thegreenjournal.com

Image guided brachytherapy

Simple DVH parameter addition as compared to deformable registration for bladder dose accumulation in cervix cancer brachytherapy

Else Stougård Andersen [a], Karsten Østergaard Noe [b,c], Thomas Sangild Sørensen [b,d], Søren Kynde Nielsen [a], Lars Fokdal [e], Merete Paludan [e], Jacob Christian Lindegaard [e], Kari Tanderup [a,d,e,*]

- 47 patients with locally advanced cervical cancer
- EBRT + 2 Fx individually planned BT
- DVH parameter addition vs. DIR dose accumulation
- DVH parameter addition provides a good estimate compared to DIR Dose accumulation for bladder D2cc, whereas D0.1cc is less robust.



Radiotherapy and oncology, 2013-04, Vol.107 (1), p.52-57

We have looked at the bladder dose.

How about other OARs such as rectum and sigmoid??

GYN

Journal of Radiation Research, Vol. 62, No. 1, 2021, pp. 155–162
doi: 10.1093/jrr/rraa099
Advance Access Publication: 24 November 2020

Journal of Radiation Research

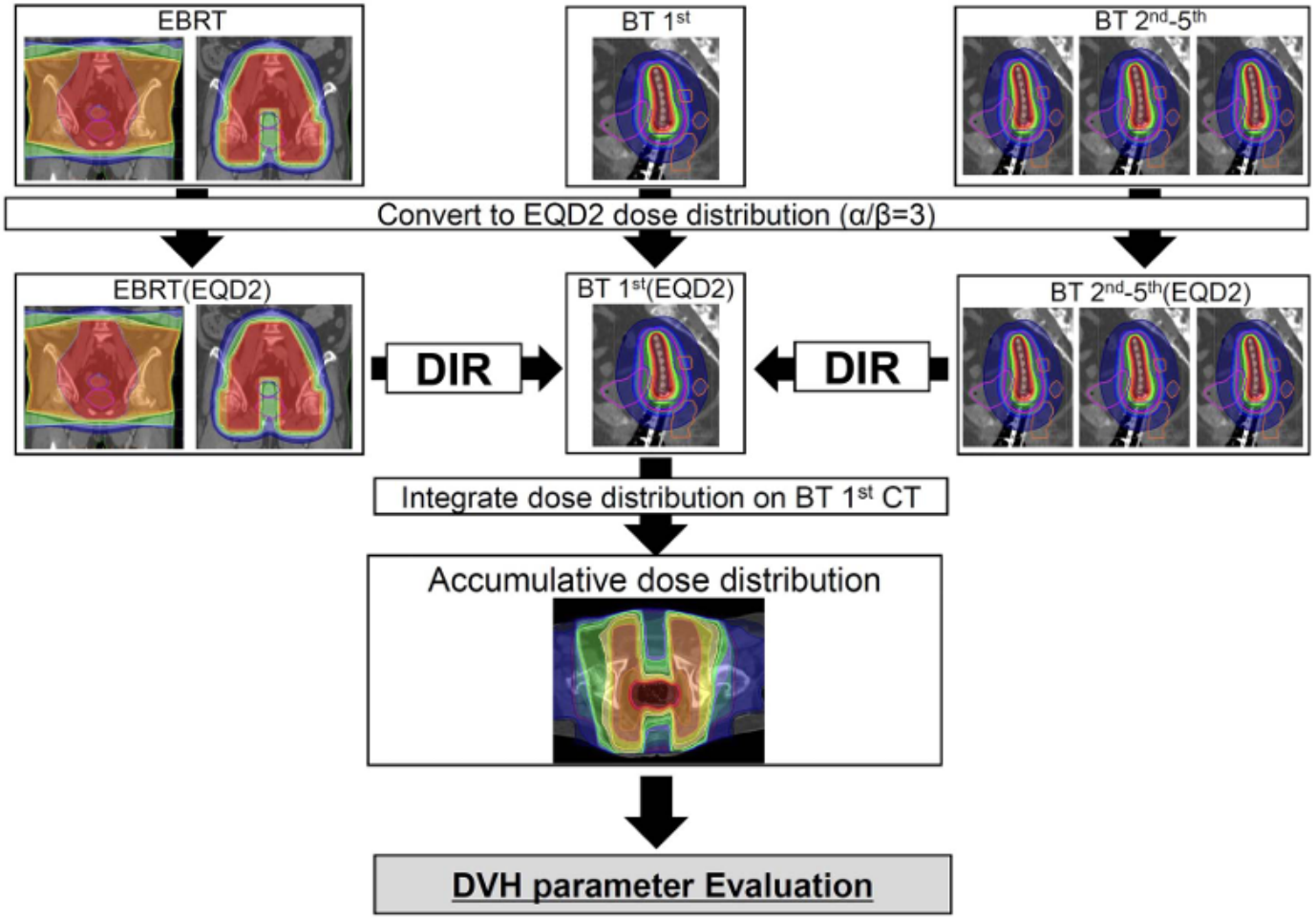
OXFORD

Comparison of predictive performance for toxicity by accumulative dose of DVH parameter addition and DIR addition for cervical cancer patients

Yuya Miyasaka[1,2], Noriyuki Kadoya[1,*], Rei Umezawa[1], Yoshiki Takayama[1,3], Kengo Ito[1], Takaya Yamamoto[1], Shohei Tanaka[1], Suguru Dobashi[4], Ken Takeda[4], Kenji Nemoto[5], Takeo Iwai[2] and Keiichi Jingu[1]

- 59 cervical cancer patients receiving EBRT and BT
- DVH parameter addition vs Full DIR addition vs Partial DIR addition
- Rectum + Sigmoid: D2cc, D1cc, D0.1cc
- Rectum + Sigmoid: V50, V60, V70 Gy (Full DIR addition only)

Dose Summation Workflow



Miyasaka et al. / Journal of Radiation Research, 2021-01, Vol.62 (1), p.155-162

Table 2. The mean value DVH parameters for rectum + sigmoid of all patients

	D_{2cm^3}		D_{1cm^3}		$D_{0.1cm^3}$	
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI
DVH parameter addition	65.7 ± 8.8	(63.5–68.0)	70.7 ± 9.8	(68.1–73.2)	84.3 ± 13.7	(80.7–87.8)
Full DIR addition	68.9 ± 9.2	(66.6–71.3)	72.1 ± 10.5	(69.4–74.8)	81.5 ± 14.0	(77.8–85.1)
Partial DIR addition	61.6 ± 11.3	(58.7–64.6)	66.5 ± 10.8	(63.7–69.3)	75.9 ± 13.5	(72.4–79.4)
	V50 Gy (cm ^{3})		**V60 Gy (cm ^{3})**		**V70 Gy (cm ^{3})**	
	mean ± SD	95% CI	mean ± SD	95% CI	mean ± SD	95% CI
Full DIR addition	37.1 ± 27.2	(30.1–44.2)	15.7 ± 17.1	(11.2–20.2)	3.2 ± 4.5	(2.0–4.4)

Accumulative dose using DIR could be more effective by accumulating not only BT but also all pelvic irradiation using DIR.

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	D_{2cm^3}				
	Toxicity (+)		Toxicity (−)		
	Mean ± SD	95% CI	Mean ± SD	95% CI	*P*-value
DVH parameter addition	65.9 ± 8.4	(61.5–70.9)	65.7 ± 9.0	(62.9–68.5)	0.94
Full DIR addition	73.0 ± 10.6	(67.6–78.5)	67.3 ± 13.3	(64.8–69.8)	*0.04
Partial DIR addition	63.8 ± 9.9	(58.8–68.9)	60.7 ± 11.9	(57.0–64.4)	0.41

	D_{1cm^3}				
	Toxicity (+)		Toxicity (−)		
	Mean ± SD	95% CI	Mean ± SD	95% CI	*P*-value
DVH parameter addition	71.1 ± 9.9	(66.0–76.2)	70.5 ± 9.8	(67.5–73.6)	0.80
Full DIR addition	75.9 ± 12.7	(69.4–82.4)	70.6 ± 9.2	(67.7–73.5)	0.15
Partial DIR addition	68.1 ± 11.0	(62.5–73.7)	65.9 ± 10.8	(62.5–69.3)	0.52

	$D_{0.1cm^3}$				
	Toxicity (+)		Toxicity (−)		
	Mean ± SD	95% CI	Mean ± SD	95% CI	*P*-value
DVH parameter addition	85.5 ± 15.3	(77.6–93.4)	83.8 ± 13.2	(79.7–87.9)	0.76
Full DIR addition	86.5 ± 16.3	(78.1–94.9)	79.4 ± 12.5	(75.5–83.3)	0.13
Partial DIR addition	78.1 ± 15.0	(70.4–85.8)	75.0 ± 12.9	(71.0–79.0)	0.54

Full DIR addition may have the potential to predict toxicity more accurately than the conventional DVH parameter addition.

Full DIR Addition

V50 Gy (cm^3)

Toxicity (+)		Toxicity (−)		
Mean ± SD	95% CI	Mean ± SD	95% CI	*P*-value
33.7 ± 17.8	(24.5–42.9)	38.5 ± 30.2	(29.1–47.9)	0.89

V60 Gy (cm^3)

Toxicity (+)		Toxicity (−)		
Mean ± SD	95% CI	Mean ± SD	95% CI	*P*-value
17.0 ± 11.5	(11.1–22.9)	15.2 ± 19.0	(9.2–21.1)	0.13

V70 Gy (cm^3)

Toxicity (+)		Toxicity (−)		
Mean ± SD	95% CI	Mean ± SD	95% CI	*P*-value
4.5 ± 5.5	(1.7–7.3)	2.7 ± 4.0	(1.4–3.9)	0.08

Full DIR addition may have the potential to predict toxicity more accurately than the conventional DVH parameter addition.

Uncertainty of Dose Summation

- Image registration accuracy (dominant uncertainty)
  - Rigid vs Deformable
- Dose mapping assumptions
  - Interpolation
  - Grid resolution
- Radiobiological parameters
  - Choice of α/β ratio
  - Fractionation differences
  - Recovery factor

Summary

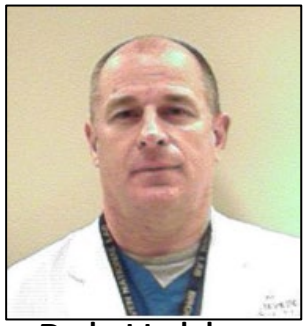
- What dose summation can do:
  - Identify potential cumulative hotspots
  - Support re-irradiation risk assessment
  - Enable comparison across fractionation schemes
  - Inform physicist–physician discussion
  - Help Dr. Jimm Grimm get high quality data for his dose-response models!!!
- What dose summation cannot do:
  - Eliminate uncertainty
  - Predict toxicity on its own
  - Replace clinical judgment

NRG Dose Summation Working Group


Mihaela Rosu


Yixiang Liao


Stanley Benedict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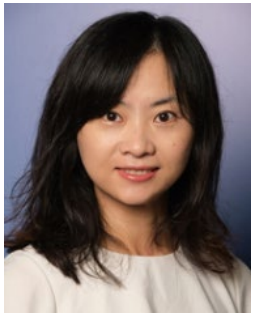
Ying Xiao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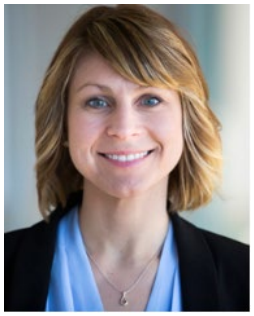
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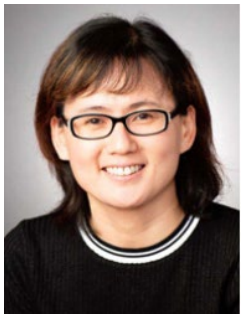
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Zhilei Shen


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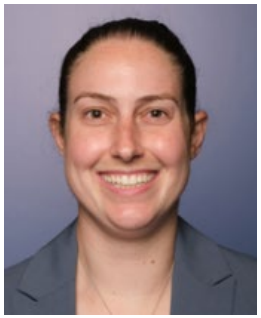
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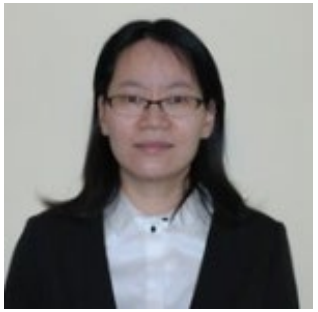
Yang Sheng


Huaizhi Geng


Jennifer Presley