Dosimetry for Epidemiologic Studies *for* Conventional Radiation Therapy

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DCEG Radiation Epidemiology and Dosimetry Course 2019

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Late Effects Studies in Cancer Survivor Cohorts

- There are unique issues specifically related to radiation therapy (RT) data because these studies are:
  - Multi-institutional
  - Retrospective (often decades after RT)

Late Effects Studies

Require RT doses to the organs/regions in which late effects are observed, but…..

- **Whole body anatomical data are NOT Available**
  - Historic RT used simple 2D planning w/ conventional simulators
  - Even with 3D planning:
    - CT scans only include anatomy close to the treatment area
    - Often only hard-copies of plans are available, which include only selected views of the anatomy

Reconstruct patients' RT fields on age-scaled computational phantoms → organ doses

Retrospective Organ Dose Reconstruction in Radiation Epidemiology Studies

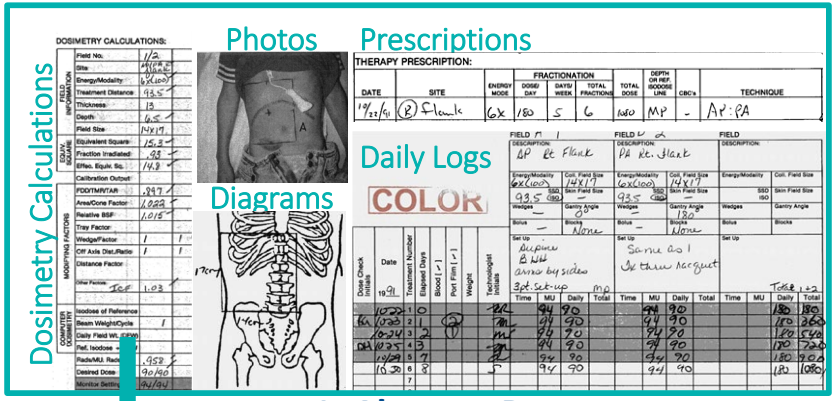
Dose Reconstruction Process

1. Abstract patient's "historic" RT record(s)
2. Scale late effects phantom to age at RT
3. Reconstruct RT fields on age scaled phantom
4. Calculate dose to organs/regions of interest

Repeat process for EACH individual in cohort

N = 10 to > 10,000

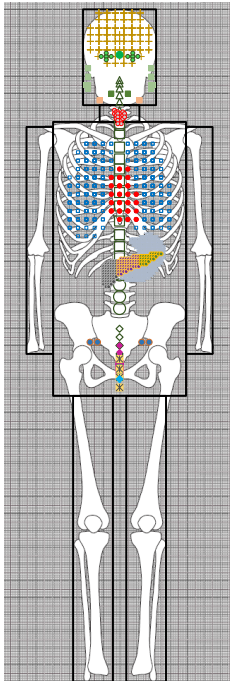
Dose Reconstruction Process



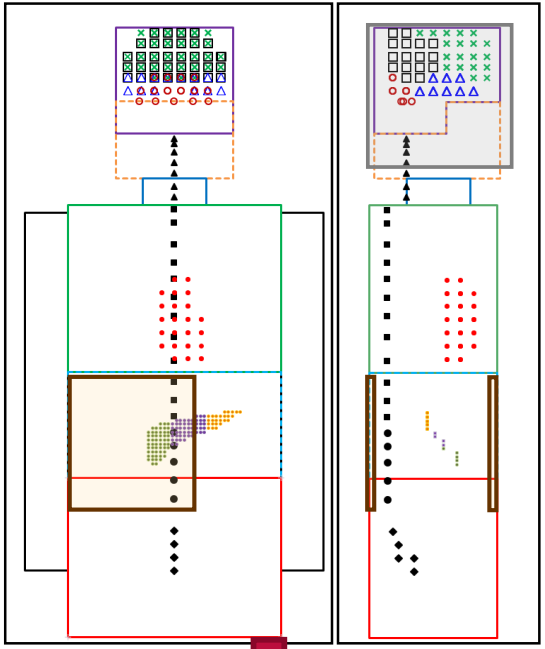
1. Abstract Data

Calculate age at RT from birth date and RT start date (7.3 Years)

2. Scale late effects phantom to age at RT



3. Reconstruct fields on age-scaled phantom



4. Calculate dose to organs of interest

Dose Reconstruction Step 1

Abstract Patients' "Historic" RT Record

RT Record coding, must Look all “Clues”

Experienced Coders are ESSENTIAL

- Details, details, details
- Diagrams, photos, and films are not always consistent with each other
- Daily logs are useful
  - Lots of plans, which was treated, was entire treatment delivered, etc.
  - Blocks get added but not shown in plan, e.g., heart block at 20 Gy
- Some summaries can be as useful as a record
  - May give Rx, energy, location, borders, etc.

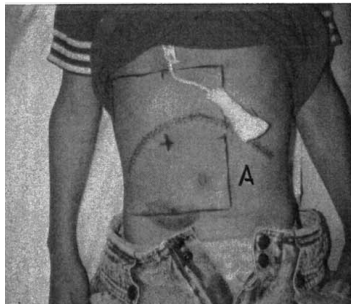
Treatment Record Data (Example)

Dosimetry Calculations

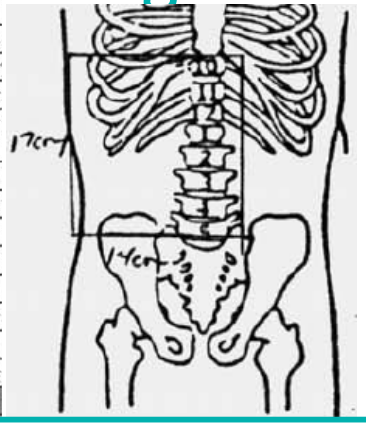
DOSIMETRY CALCULATIONS:

FIELD INFORMATION	Field No.	1/2	
	Site	RT PA flank	
	Energy/Modality	6x(100)	
	Treatment Distance	93.5	
	Thickness	13	
	Depth	6.5	
	Field Size	14x17	
EQUIV. SQUARE	Equivalent Square	15.3	
	Fraction Irradiated	.93	
	Effec. Equiv. Sq.	14.8	
	Calibration Output		
MODIFYING FACTORS	FDD/TMR/TAR	.897	
	Area/Cone Factor	1.022	
	Relative BSF	1.015	
	Tray Factor		
	Wedge/Factor	1	1
	Off Axis Dist./Ratio	1	1
	Distance Factor		
	Other Factors: ICF	1.03	
COMPUTER DOSIMETRY	Isodose of Reference		
	Beam Weight/Cycle	1	
	Daily Field Wt. (DFW)		
	Ref. Isodose ÷ DFW		
	Rads/MU. Rads/Min.	.958	
	Desired Dose	90/90	
	Monitor Setting	94/94	

Photos



Diagrams



Prescriptions

THERAPY PRESCRIPTION:

DATE	SITE	ENERGY MODE	FRACTIONATION DOSE/DAY	FRACTIONATION DAYS/WEEK	FRACTIONATION TOTAL FRACTIONS	TOTAL DOSE	DEPTH OR REF. ISODOSE LINE	CBC's	TECHNIQUE
10/22/91	(R) flank	6x	180	5	6	1080	MP	-	AP:PA

Daily Logs

COLOR

	FIELD 1	FIELD 2	FIELD
DESCRIPTION:	AP Rt Flank	PA Rt. flank	
Energy/Modality	6x(100)	6x(100)	
Coll. Field Size	14x17	14x17	
SSD (ISO)	93.5	93.5	
Skin Field Size	—	—	
Wedges	—	—	
Gantry Angle	0°	180	
Bolus	—	—	
Blocks	None	None	
Set Up	supine B Hdt arms by sides 3pt. set-up mp	Same as 1 thru racquet	

Dose Check Initials	Date 1991	Treatment Number	Elapsed Days	Blood [✓]	Port Film [✓]	Weight	Technologist Initials	Field 1 Time	Field 1 MU	Field 1 Daily	Field 1 Total	Field 2 Time	Field 2 MU	Field 2 Daily	Field 2 Total	Field Time	Field MU	Field Daily	Field Total
	10/22	1	0				RR		94	90			94	90				180	180
BR	10/23	2	1		✓		TM		94	90			94	90				180	360
	10/24	3	2		✓		MF		94	90			94	90				180	540
DH	10/25	4	3				[illegible]		94	90			94	90				180	720
	10/29	5	7				[illegible]		94	90			94	90				180	900
	10/30	6	8				S		94	90			94	90				180	1080
		7																	

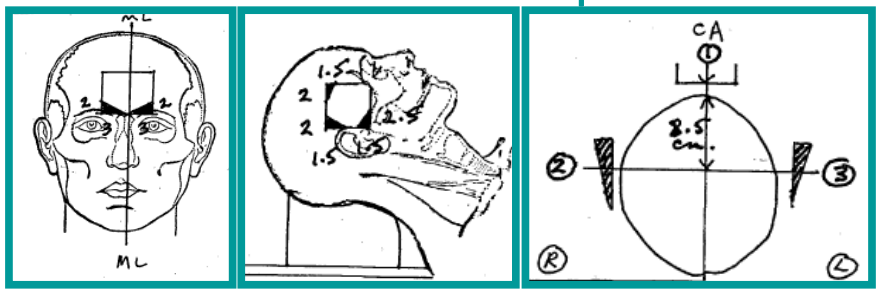
Total 1+2

How useful are the CT data in records?

- **Not very useful….**
- In fact, records for patients that had CT simulations are often *LESS informative* than records for those with conventional simulations

WHY?

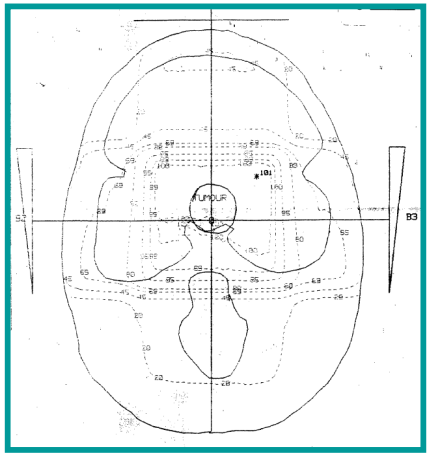
Historic Example



Modern Example

Similar treatment for "modern" record

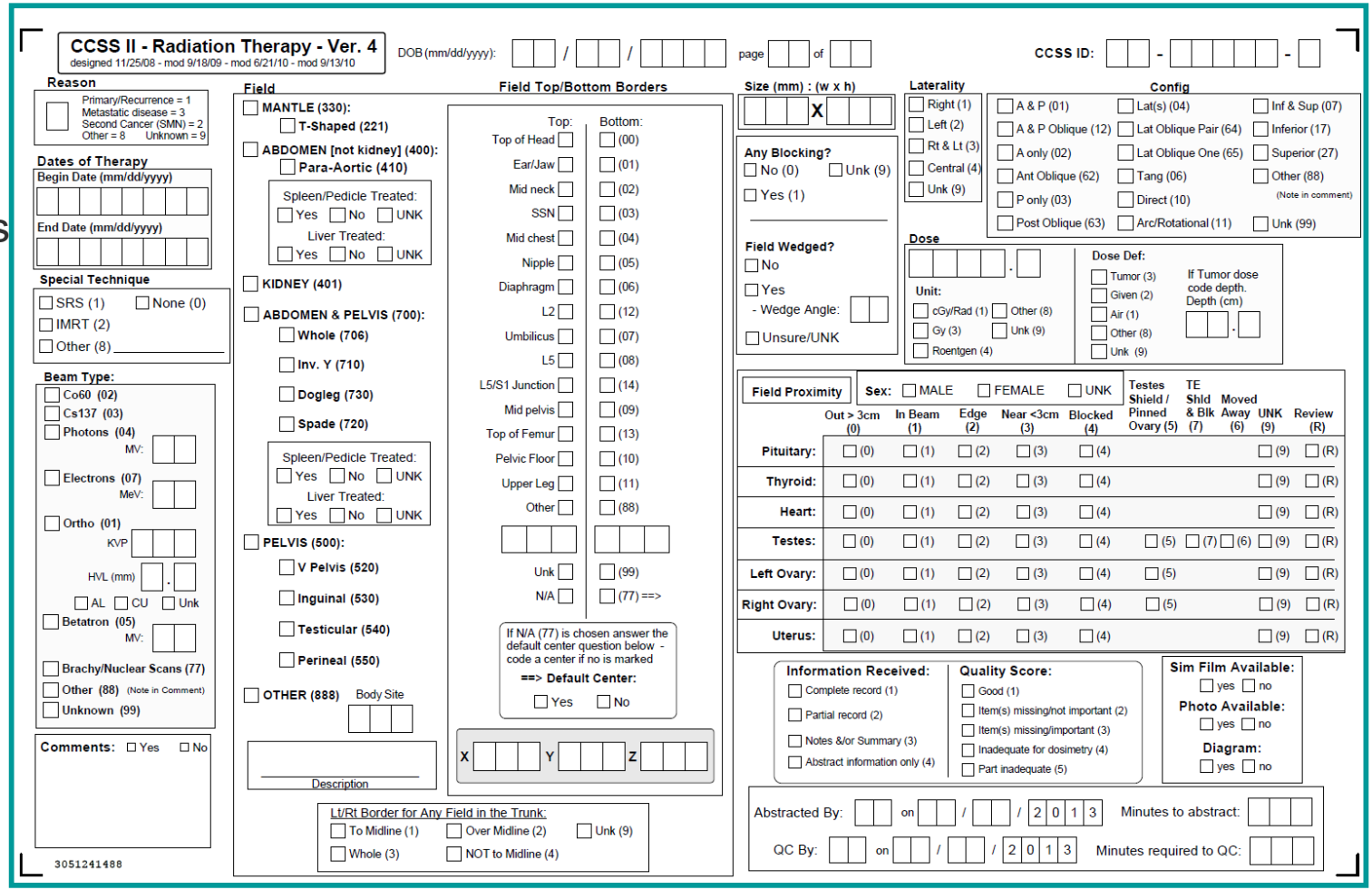
- Black and white isodose lines
- Field borders unknown



Record Abstraction

Pertinent Data Coded

- Treatment Dates
- Date of Birth
- Prescription(s)
- Field Data: orientation, energy, weighting, blocking, modifiers, etc.



CCSS II - Radiation Therapy - Ver. 4

designed 11/25/08 - mod 9/18/09 - mod 6/21/10 - mod 9/13/10

DOB (mm/dd/yyyy): 07 / [redacted] / 1984 page 01 of 01 CCSS ID: [redacted]

Reason

1 — Primary/Recurrence = 1; Metastatic disease = 3; Second Cancer (SMN) = 2; Other = 8; Unknown = 9

Dates of Therapy

Begin Date (mm/dd/yyyy): 10 [redacted] 1991

End Date (mm/dd/yyyy): 10 [redacted] 1991

Special Technique

☐ SRS (1) ☒ None (0)
☐ IMRT (2)
☐ Other (8) _____

Beam Type:

☐ Co60 (02)
☐ Cs137 (03)
☒ Photons (04) MV: 06
☐ Electrons (07) MeV:
☐ Ortho (01) KVP: HVL (mm): . ☐ AL ☐ CU ☐ Unk
☐ Betatron (05) MV:
☐ Brachy/Nuclear Scans (77)
☐ Other (88) (Note in Comment)
☐ Unknown (99)

Comments: ☐ Yes ☒ No

3051261488

Field

☐ MANTLE (330):
☐ T-Shaped (221)
☐ ABDOMEN [not kidney] (400):
☐ Para-Aortic (410)
Spleen/Pedicle Treated: ☐ Yes ☐ No ☐ UNK
Liver Treated: ☐ Yes ☐ No ☐ UNK
☒ KIDNEY (401)
☐ ABDOMEN & PELVIS (700):
☐ Whole (706)
☐ Inv. Y (710)
☐ Dogleg (730)
☐ Spade (720)
Spleen/Pedicle Treated: ☐ Yes ☐ No ☐ UNK
Liver Treated: ☐ Yes ☐ No ☐ UNK
☐ PELVIS (500):
☐ V Pelvis (520)
☐ Inguinal (530)
☐ Testicular (540)
☐ Perineal (550)
☐ OTHER (888) Body Site:

Description: _____

Field Top/Bottom Borders

	Top:	Bottom:
Top of Head	☐	☐ (00)
Ear/Jaw	☐	☐ (01)
Mid neck	☐	☐ (02)
SSN	☐	☐ (03)
Mid chest	☐	☐ (04)
Nipple	☐	☐ (05)
Diaphragm	☒	☐ (06)
L2	☐	☐ (12)
Umbilicus	☐	☐ (07)
L5	☐	☒ (08)
L5/S1 Junction	☐	☐ (14)
Mid pelvis	☐	☐ (09)
Top of Femur	☐	☐ (13)
Pelvic Floor	☐	☐ (10)
Upper Leg	☐	☐ (11)
Other	☐	☐ (88)
Unk	☐	☐ (99)
N/A	☐	☐ (77) ==>

If N/A (77) is chosen answer the default center question below - code a center if no is marked
==> Default Center: ☐ Yes ☐ No

X ___ Y ___ Z ___

Lt/Rt Border for Any Field in the Trunk:
☐ To Midline (1) ☒ Over Midline (2) ☐ Unk (9)
☐ Whole (3) ☐ NOT to Midline (4)

Size (mm) : (w x h)

140 X 170

Any Blocking?
☒ No (0) ☐ Unk (9)
☐ Yes (1)

Field Wedged?
☒ No
☐ Yes
- Wedge Angle:
☐ Unsure/UNK

Laterality
☒ Right (1)
☐ Left (2)
☐ Rt & Lt (3)
☐ Central (4)
☐ Unk (9)

Config

☒ A & P (01)	☐ Lat(s) (04)	☐ Inf & Sup (07)
☐ A & P Oblique (12)	☐ Lat Oblique Pair (64)	☐ Inferior (17)
☐ A only (02)	☐ Lat Oblique One (65)	☐ Superior (27)
☐ Ant Oblique (62)	☐ Tang (06)	☐ Other (88) (Note in comment)
☐ P only (03)	☐ Direct (10)	
☐ Post Oblique (63)	☐ Arc/Rotational (11)	☐ Unk (99)

Dose

1080.0

Unit: ☒ cGy/Rad (1) ☐ Other (8) ☐ Gy (3) ☐ Unk (9) ☐ Roentgen (4)

Dose Def:
☒ Tumor (3)
☐ Given (2)
☐ Air (1)
☐ Other (8)
☐ Unk (9)

If Tumor dose code depth. Depth (cm): 06.5

Field Proximity

Sex: ☒ MALE ☐ FEMALE ☐ UNK

	Out > 3cm (0)	In Beam (1)	Edge (2)	Near <3cm (3)	Blocked (4)	Testes Shield / Pinned Ovary (5)	TE Shld & Blk (7)	Moved Away (6)	UNK (9)	Review (R)
Pituitary:	☒ (0)	☐ (1)	☐ (2)	☐ (3)	☐ (4)				☐ (9)	☐ (R)
Thyroid:	☒ (0)	☐ (1)	☐ (2)	☐ (3)	☐ (4)				☐ (9)	☐ (R)
Heart:	☐ (0)	☐ (1)	☐ (2)	☒ (3)	☐ (4)				☐ (9)	☐ (R)
Testes:	☒ (0)	☐ (1)	☐ (2)	☐ (3)	☐ (4)	☐ (5)	☐ (7)	☐ (6)	☐ (9)	☐ (R)
Left Ovary:	☐ (0)	☐ (1)	☐ (2)	☐ (3)	☐ (4)	☐ (5)			☐ (9)	☐ (R)
Right Ovary:	☐ (0)	☐ (1)	☐ (2)	☐ (3)	☐ (4)	☐ (5)			☐ (9)	☐ (R)
Uterus:	☐ (0)	☐ (1)	☐ (2)	☐ (3)	☐ (4)				☐ (9)	☐ (R)

Information Received:
☒ Complete record (1)
☐ Partial record (2)
☐ Notes &/or Summary (3)
☐ Abstract information only (4)

Quality Score:
☒ Good (1)
☐ Item(s) missing/not important (2)
☐ Item(s) missing/important (3)
☐ Inadequate for dosimetry (4)
☐ Part inadequate (5)

Sim Film Available: ☐ yes ☒ no
Photo Available: ☒ yes ☐ no
Diagram: ☒ yes ☐ no

Abstracted By: 20 on 09 / 26 / 2013 Minutes to abstract: 010

QC By: 16 on 03 / 11 / 2014 Minutes required to QC: 004

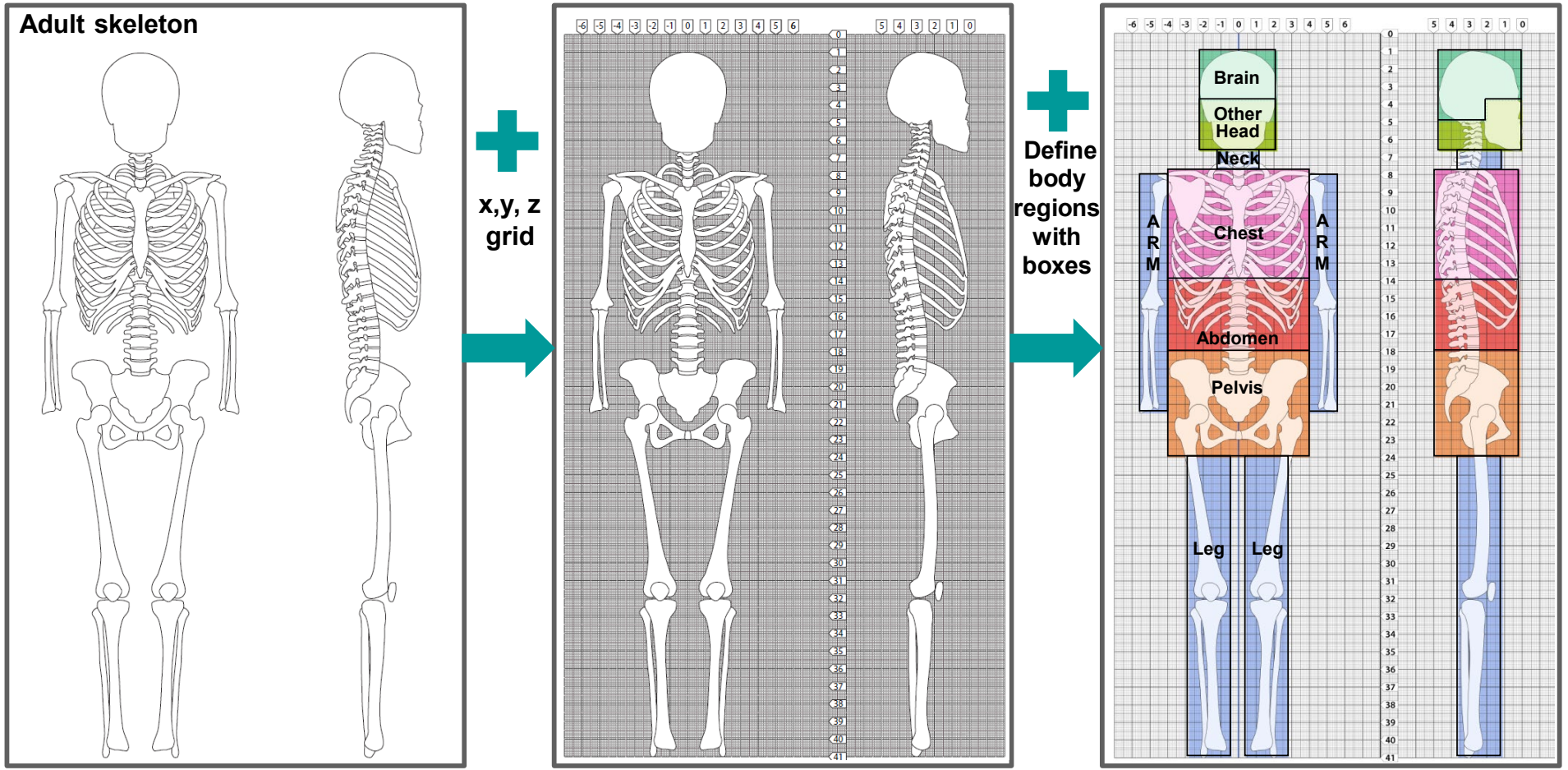
Dose Reconstruction Step 2

Scale Late Effects Phantom to Age at RT

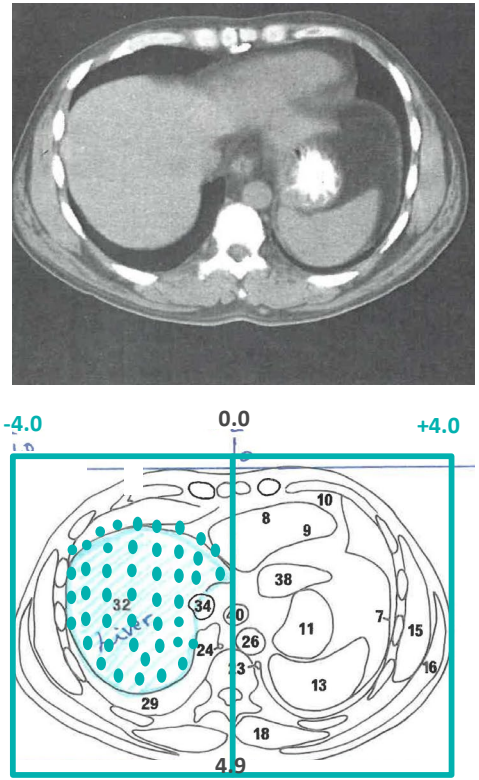
Phantoms

- Phantoms are used as patients' surrogates because actual patient anatomy data do not exist/not available.

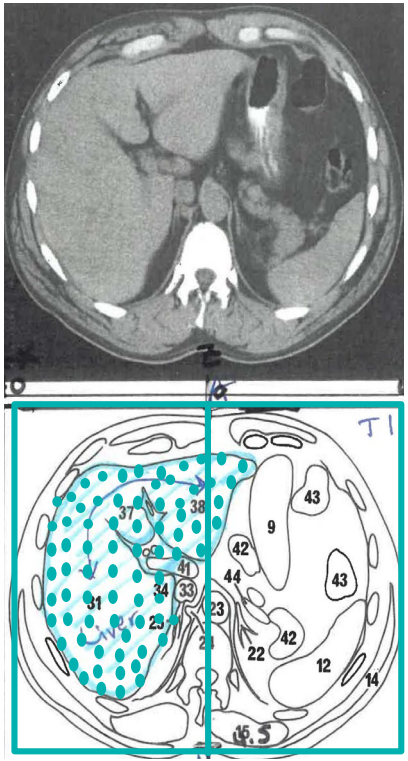
Creating a Generic Adult Phantom



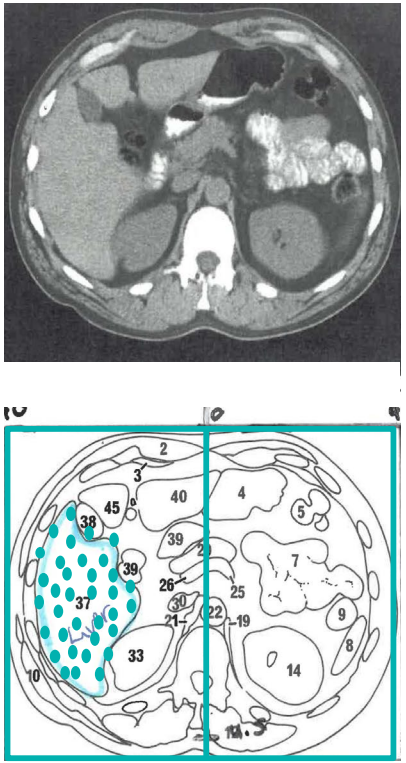
Organs Added to Generic Phantom (Slice by Slice)



Axial at Y = T10



Axial at Y = T11



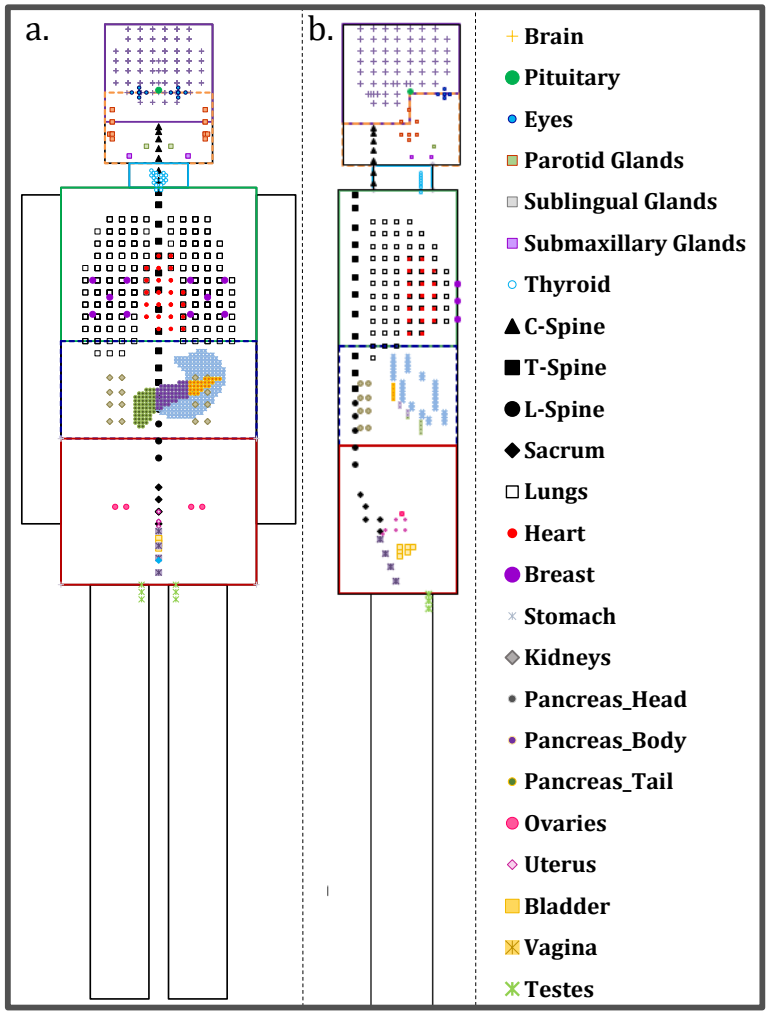
Axial at Y = T12

Full Organ defined with Interpolation

- Each organ point has unique, x, y, z coordinate defined in master phantom coordinate system.

Phantom Organs

- Organ Definition
  - Grid of points (x, y, z)
  - Grid can be moved
  - Grid resolution can be ⇧ or ⇩
- Organ positions
  - Defined using anatomy atlases based on bony anatomy and proximity to other organs (reviewed by MD collaborators)
- Organ Substructures
  - Can be divided into components, e.g., pancreas: head, body, tail



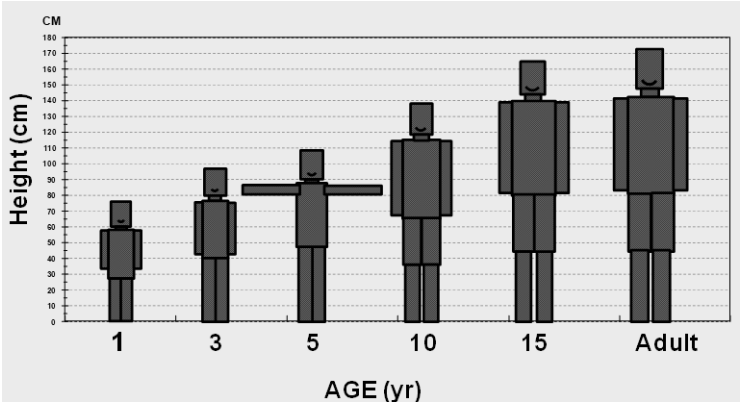
Phantom Scaled to Age at RT

- Childhood cancer survivors' ages at RT range from infant to adult
- Necessary apply scaling functions to adapt the adult phantom to any AGE

Why not BMI or height based scaling?

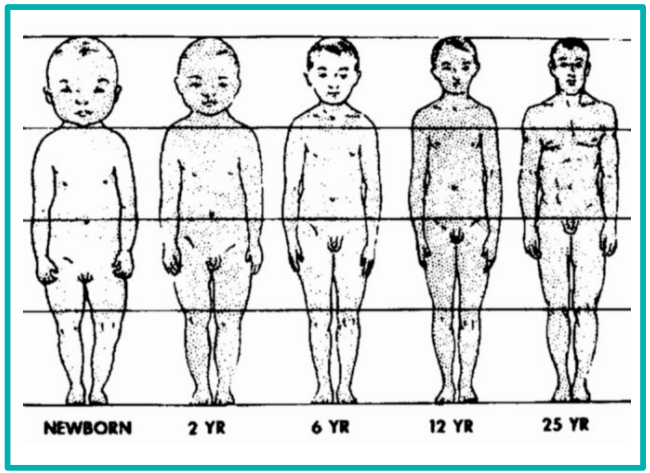
Height/weight are rarely in RT chart!

- Different scaling factors for head, neck, trunk, and extremities to account for non-uniform growth

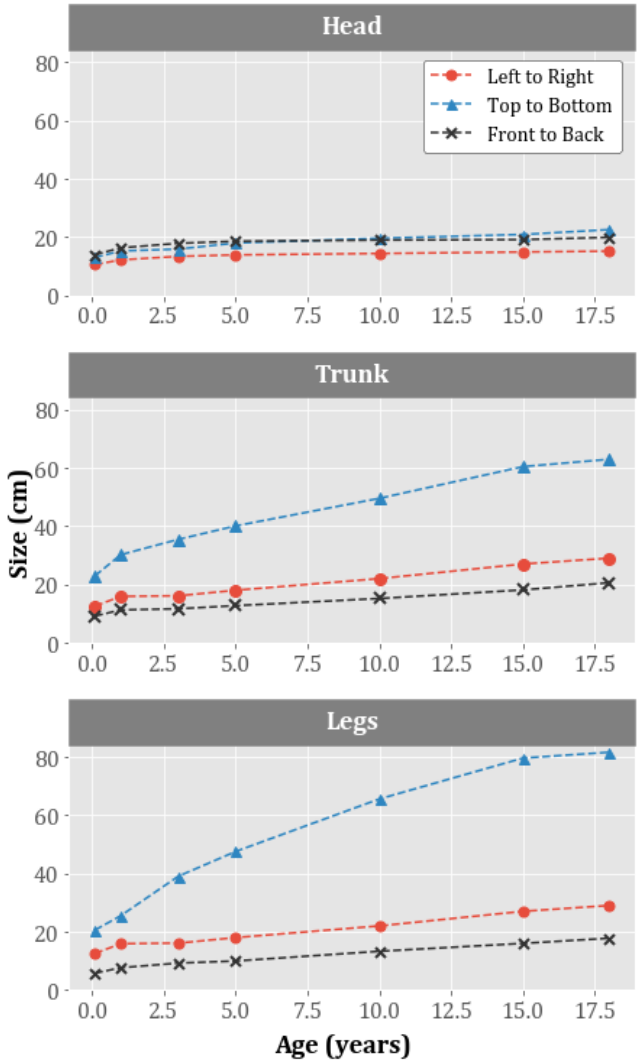


Non-uniform Growth from Infant to Adulthood

- Trunk and extremities grow faster than the head…..
  - Head is 1/4 and 1/7 of total height for infant and adult, respectively



Quantitative data?



Huelke, Donald F. “An Overview of Anatomical Considerations of Infants and Children in the Adult World of Automobile Safety Design.” *Annual Proceedings / Association for the Advancement of Automotive Medicine* vol. 42 (1998): 93–113.

Dose Reconstruction Step 3

Reconstruct RT Fields on Phantom

Wilm's Tumor Example Case

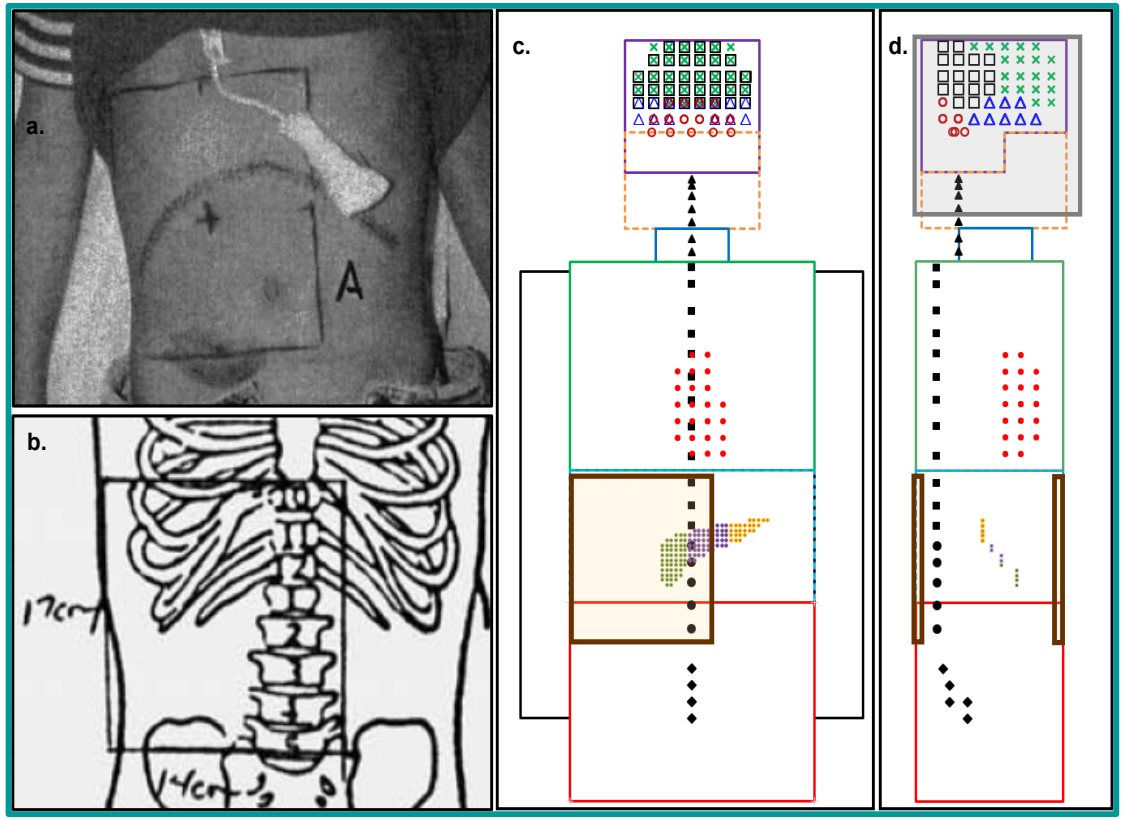
Translation of patient chart data to reconstructed fields on age specific phantom:

a. Photo of RT field outlined on patient's abdomen

b. RT field diagram

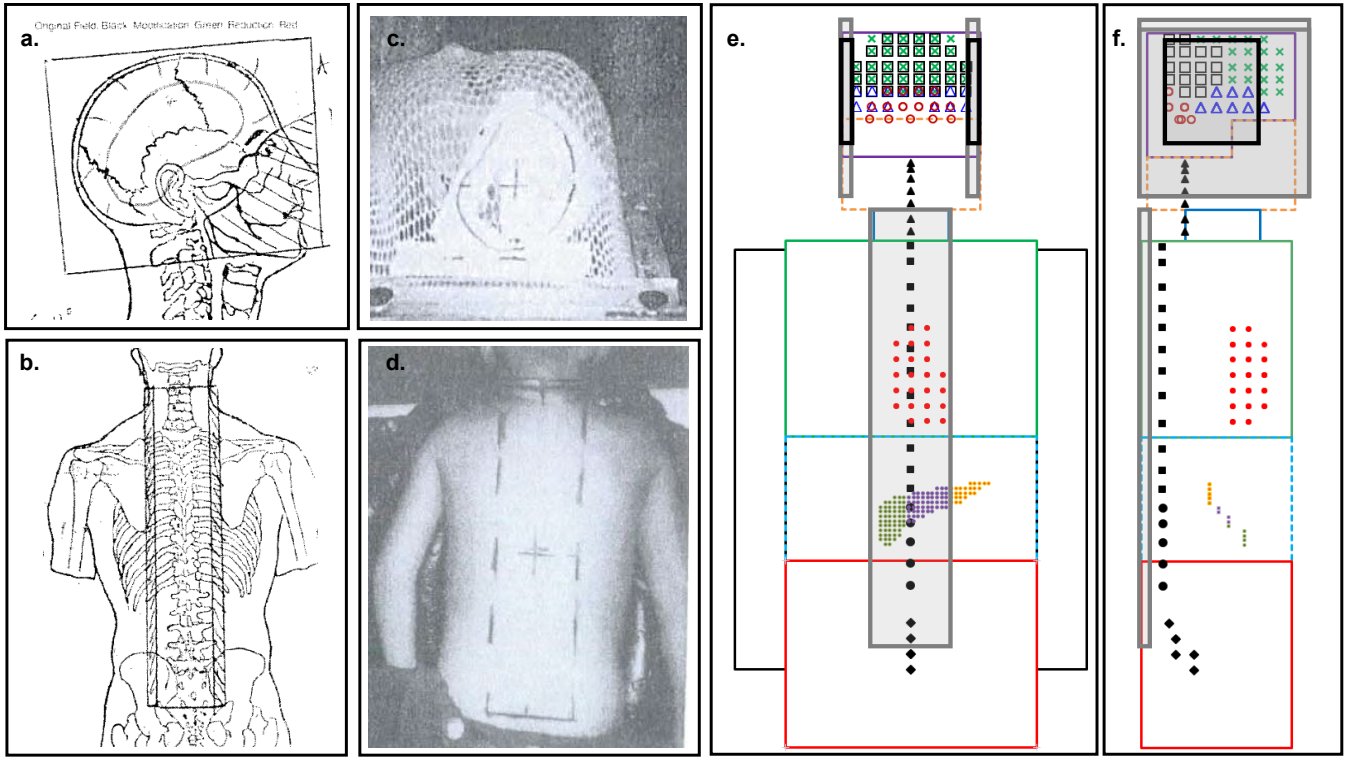
c. Frontal view of phantom showing reconstructed AP field

d. Sagittal view of phantom showing reconstructed AP and PA fields.



CNS Example Case

Translation of patient chart data to reconstructed fields on age specific phantom



Dose Reconstruction Step 4

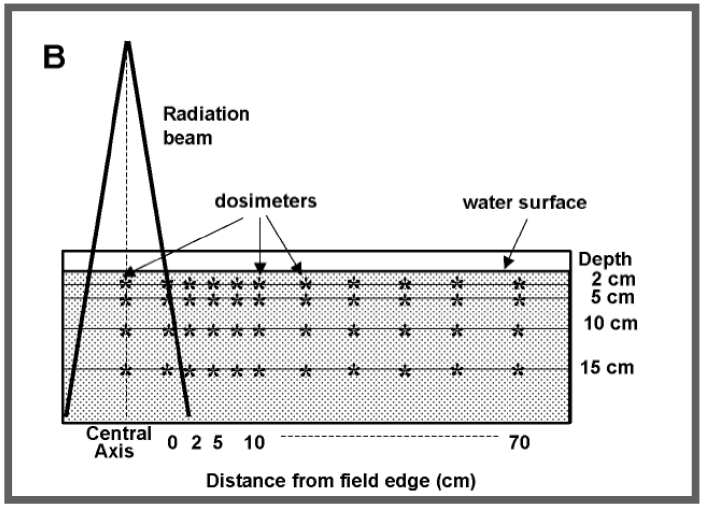
Calculate Dose to Organs/Regions of Interest

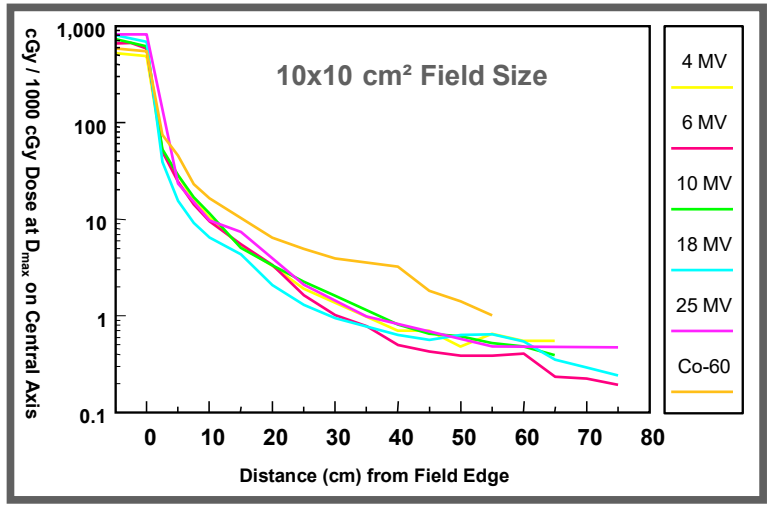
Dose Calculations In-field and Out-of-field

In-beam

- Open
  - BJR-17
- Blocked
  - 10% of in-beam
- Edge
  - 60% of in-beam

- **Out-of-beam: analytical models based on measured data for different beam energies, field sizes, depths**





Levels of Radiation Dosimetry

Different Levels of Radiation Dosimetry

Study Specific Dosimetry Tiers

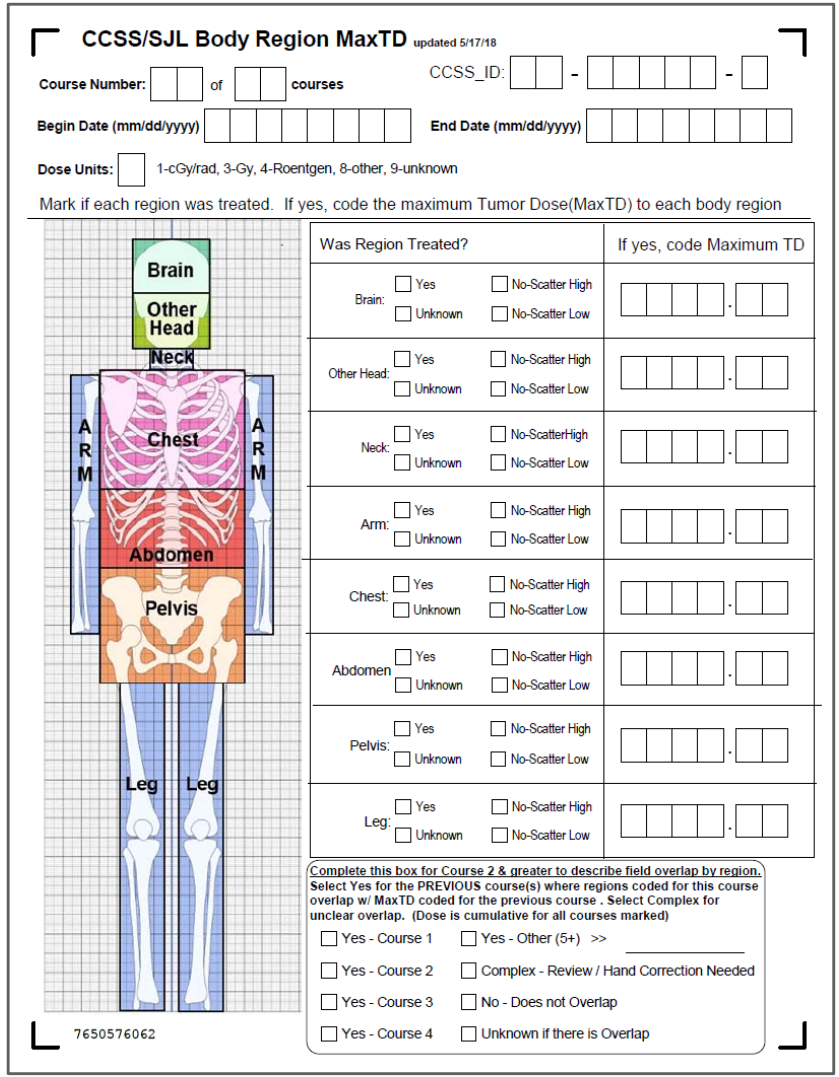
- Y/N RT
- Y/N for specific types of RT, e.g., CSI, TBI, etc.
- Body region maximum tumor dose (maxTD)
- Organ specific doses, e.g., heart, thyroid, gonads, pancreas, etc.
  - Average dose (most common parameter)
  - Average dose to organ parts, e.g., pancreas head, body, tail
  - Percent volume that received ≥ X Gy, e.g., PV_5, PV_{10}, PV_{20}
- Dose to specific site, e.g., second cancer

Whole cohort studies

Case control studies

Body Region Dosimetry

- Standard coding or simplified form
- Simplified Form
  - **Advantages:**
    - Lower cost
    - Less Time
  - **Disadvantage**
    - If want organ doses later, need full coding form
  - 1st pass dosimetry



Body Region Dosimetry

- **In-beam Region**
  - **Maximum treatment dose (MaxTD) to specific body regions taking into account only direct in-beam contributions to that region.**

- **Out-of-beam Regions (2)**
  - **based on distance from in-beam region**

Stray High (SH) Region

- Adjacent to in-beam region
- Doses are 1% to 10% of maxTD

Stray Low (SL) Region

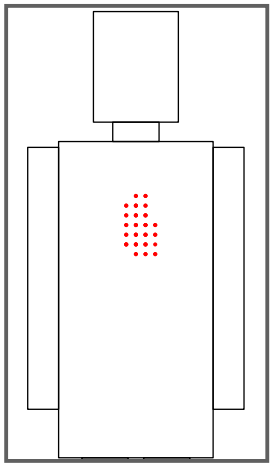
- Not Adjacent to in-beam region
- Doses <1% of maxTD

Organ Dosimetry - Average Dose

- **Mathematical average of dose to all points in the organ.**

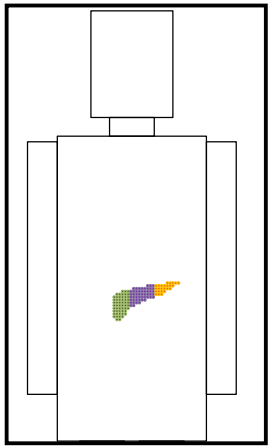
Average Organ dose can be computed for:

Entire Organ: Heart (55 points)



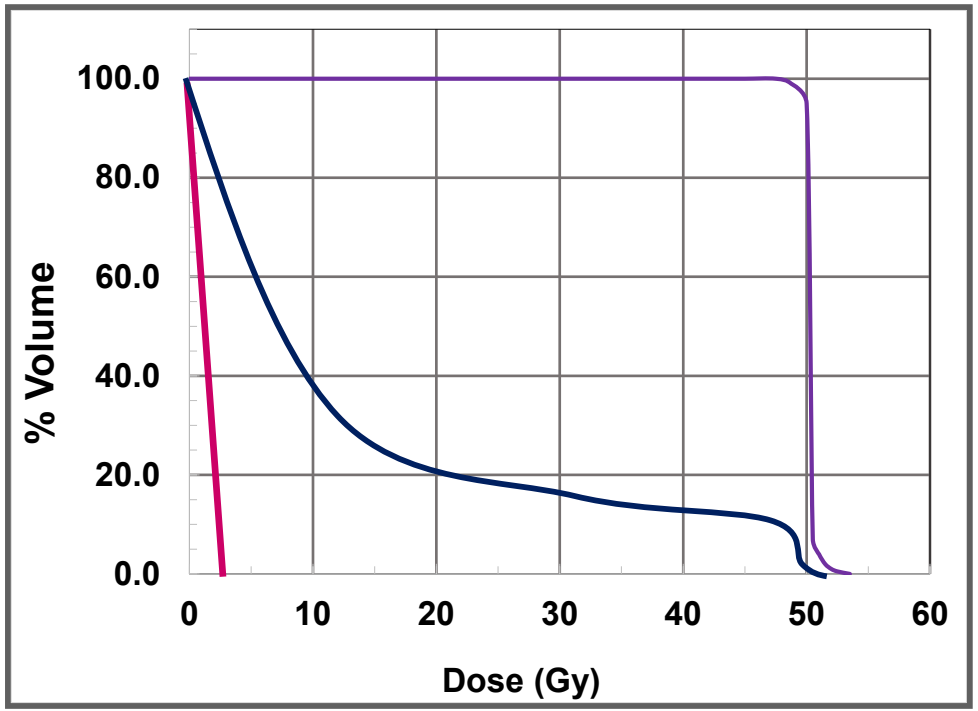
Organ Parts: Pancreas (129 points)

54 head, 50 body, 25 tail



Organ Dosimetry - Dose Volume Metrics

- **Vx: % volume receiving ≥ X Gy**



- **% of points in an organ that receive ≥ "x" dose used to represent Vx.**
  - **Dose is calculated for each point within an organ.**
  - **Points within organs are evenly spaced.**

We calculated Vx data for heart and pancreas for > 13500 individuals overall CCSS cohort (Bates et al. 2019 and Friedman et al. 2019)

Dose Reconstruction

Record Quality and Uncertainty

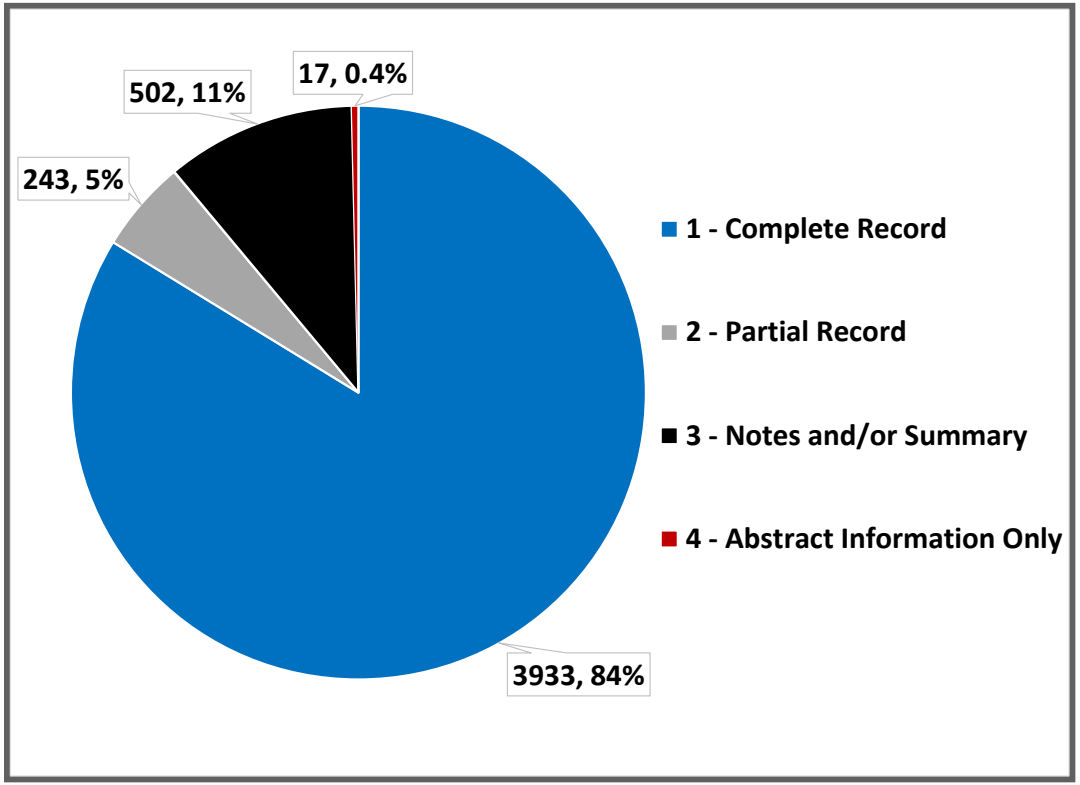
Record Quality Scores

Record “Completeness”

- Did we receive all RT data that were available?

Information Received:

- ☐ Complete record (1)
- ☐ Partial record (2)
- ☐ Notes &/or Summary (3)
- ☐ Abstract information only (4)



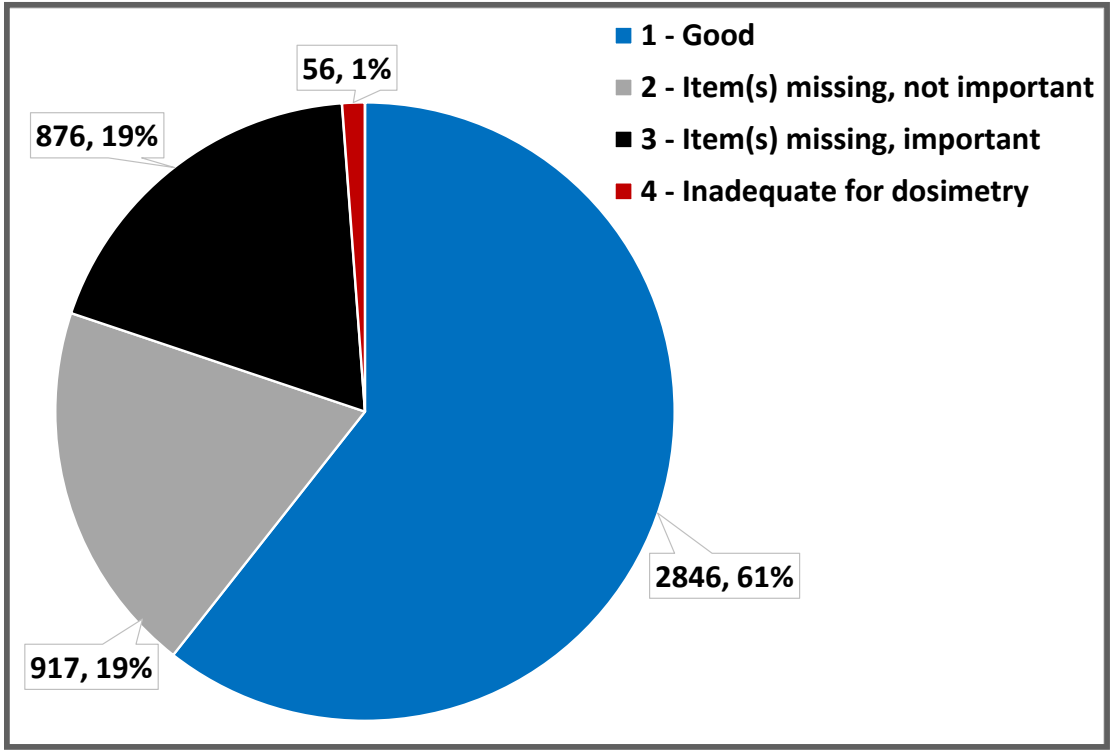
Record Quality Score

Dosimetric “Adequacy”

- Does the missing information matter?

Quality Score:

- ☐ Good (1)
- ☐ Item(s) missing/not important (2)
- ☐ Item(s) missing/important (3)
- ☐ Inadequate for dosimetry (4)



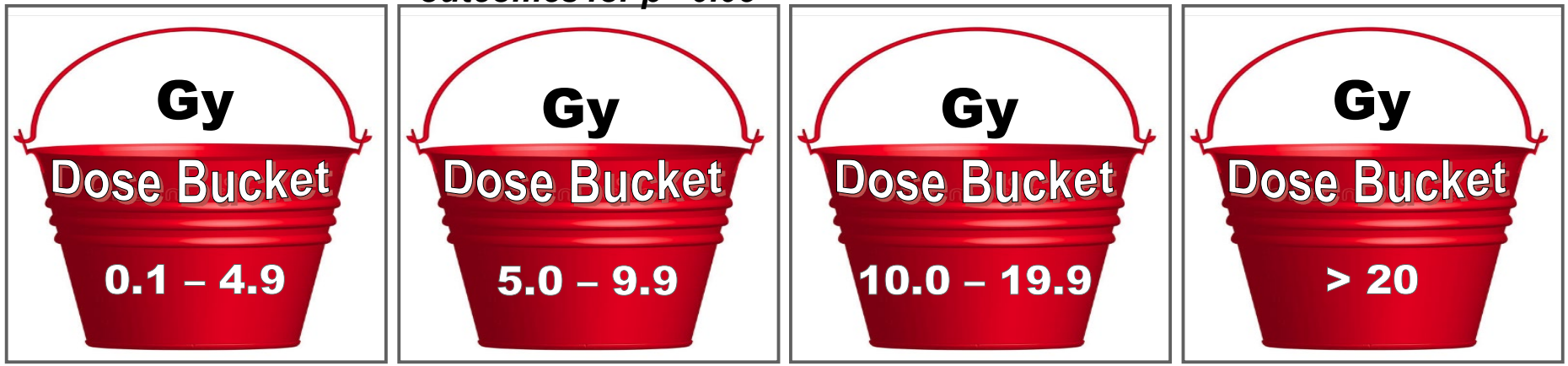
Dosimetric Uncertainty

- Adequate for Dosimetry?
  - The answer is “location” dependent
    - Near Organ: data may be insufficient for organ dosimetry, but acceptable for body-region dosimetry.
    - Data which are insufficient for “near organ” dosimetry may be acceptable for “far organ”
- **Adequate for Dosimetry?**
  - **The answer is “dose bucket” dependent…….**

Dosimetric Uncertainty

Must be considered in the context of the study dose bins!

Not enough outcomes for p< 0.05



Dose Reconstruction for Contemporary RT

- **In-field**
- **Out-of-field**

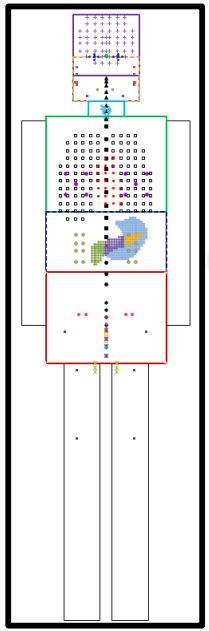
In-field Dosimetry

- Treatments will have been designed in commercial TPS
- Standardized file format: Digital Imaging and Communications in Medicine (DICOM)
- Record collection will include retrieving
  - DICOM images
  - DICOM RT Plan
  - DICOM Dose

Organ doses from DVHs → Organs of interest likely contoured, but if not, can retrospectively contour.

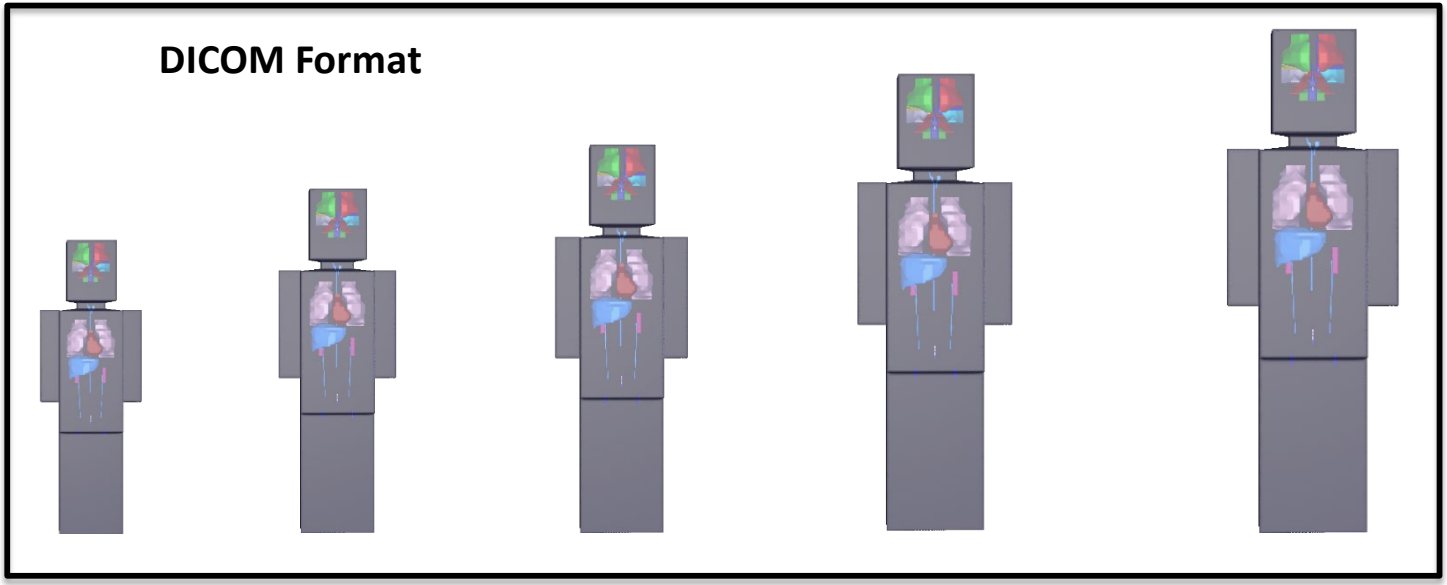
Out-of-field Dosimetry

- MD Anderson Late Effects Phantom has been programmed in DICOM format AND can be scaled to age at RT within commercial TPS….

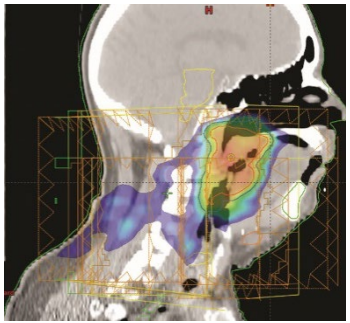


Fortran Format

within TPS



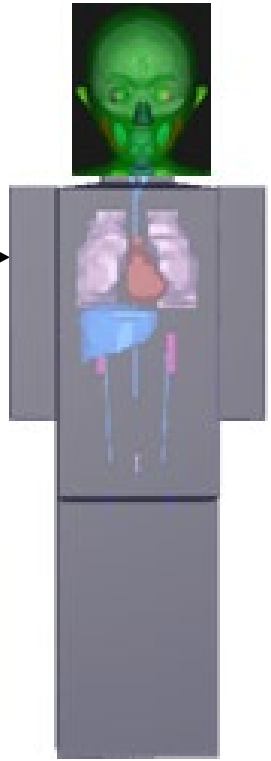
Out-of-field Dosimetry for Contemporary RT



IMRT treatment
CT scan only includes anatomy near RT target volumes

Fuse patient CT to

MD Anderson Late Effects Phantom (scaled to age at RT)



Age scaled phantom

Summary and Conclusions

- Radiation dose reconstructions are an essential component of late effects studies.
- The level of dosimetry that can be done for a study is dependent on the quality of data in the records.
- Important questions can be answered with body-region dosimetry.
- Organ-specific doses are important for establishing dose response models, but the dosimetry for individual studies should be considered in the context of other sources of uncertainty.
- New Dosimetry methods will be needed for patients treated with contemporary RT (IMRT, VMAT, proton therapy, etc).

Review Question

In retrospective radiation epidemiology studies, why are computational phantoms used instead of patient CT data?

a. Majority of Patients did not have CT planning

b. Planning CT data could not be de-archived

c. Planning CT is available, but only included anatomy near treatment site

d. All of the above

Review Question Answer

In retrospective radiation epidemiology studies, why are computational phantoms used instead of patient CT data?

a. Majority of Patients did not have CT planning

b. Planning CT data could not be de-archived

c. Planning CT is available, but only included anatomy near treatment site

d. All of the above

Review Question

Regarding computational phantoms for retrospective dosimetry, which statement is true?

a. Phantom size is not scaled, a standardized phantom is used for all individuals

b. Phantom size is scaled to age at time of RT with all body regions uniformly scaled

c. Phantom size is scaled to age at RT and accounts for non-uniform body growth

d. Phantom size is non-uniformly scaled to age at which late effect was diagnosed

Review Question Answer

Regarding computational phantoms for retrospective dosimetry, which statement is true?

a. Phantom size is not scaled, a standardized phantom is used for all individuals

b. Phantom size is scaled to age at time of RT with all body regions uniformly scaled

c. **Phantom size is scaled to age at RT and accounts for non-uniform body growth**

d. Phantom size is non-uniformly scaled to age at which late effect was diagnosed

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- Late Effects Group Founder
- > 300 publications

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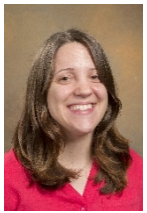

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Thank You

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