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Childhood Cancer Survivor Study

Radiation Physics Center 2021 Report

A report from the Childhood Cancer Survivor Study

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THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

Radiation Physics Center Team

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- Our team includes medical physicists and dosimetrists, research data coordinators, computational scientists and programmers, physics technicians, graduate students, and administrative staff
- We have a well-established decades long collaboration with CCSS; Susan Smith, QA Dosimetry Supervisor has worked with CCSS since its inception
- New team members include medical physics graduate students: Constance Owens, Suman Shrestha, and Aashish Gupta

Roles of the Radiation Physics Center

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- Provide input during proposal development regarding level of dosimetry detail needed and/or achievable for planned analyses
- Maintain secure database with scanned indexed copies of the complete RT records from CCSS institutions
- Calculate organ and body-region doses from RT for study participants
- Assist the investigators in understanding and using the RT data in analyses and manuscripts

Radiation Dosimetry Process

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Cohort dosimetry N > 13,000

1. Abstract patients' RT records
2. Reconstruct RT fields on in-house phantom scaled to age at RT
3. Calculate dose to region or organ of interest
4. Quality assurance of computed doses
5. Create output files and documentation
6. Provide data to FH statistics center for distribution to individual investigators (with approved concept proposals)

Dosimetry Completed for All 32 Institutions

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- RT records for institutions 30, 31, and 32 were recently received; to date, we have updated the dosimetry for the following regions and organs:

Organ/Region	Data Reported
Body regions + brain 4 segment	MaxTD, SH, SL
Kidneys (right and left)	D_m
Ovaries (right and left)	D_m
Uterus	D_m
Heart	D_m, V_5, V_{20}
Heart (14) substructures: aorta, arteries, valves, ventricles	D_m

Maximum target dose (maxTD), stray high (SH), stray low (SL), Mean dose (D_m), percent volume ≥ 5 Gy (V_5) and ≥ 20 Gy (V_{20}); Calculation methods described in are described in **Howell *et al.* 2019 and Stovall *et al.* 2006**

Dosimetry Completed for Institutions 1-29

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- Our upcoming projects include updating the following organs' dosimetry to include institutions 30-32
  - Requires detailed coding of field blocking, which is completed on an organ-by-organ basis

Organ	Data Reported
Pancreas (whole)	D_m V_{20}, V_{30}
Pancreas (head, body, tail)	D_m
Pituitary	D_m
Testes	D_m
Thyroid (right and left lobes)	D_m

Mean dose (D_m), percent volume ≥ 20 Gy (V_{20}) and ≥ 30 Gy (V_{30})

Recent and Ongoing Research
Dosimetry Enhancement

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Computational Phantom Enhancement

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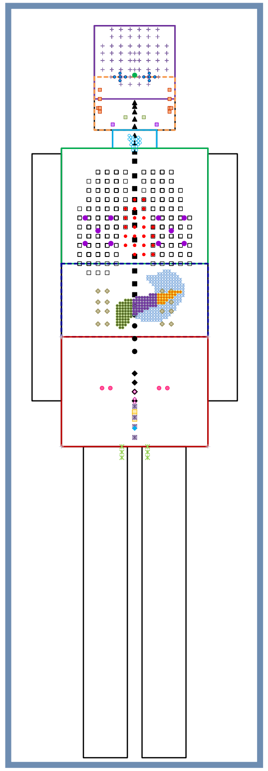
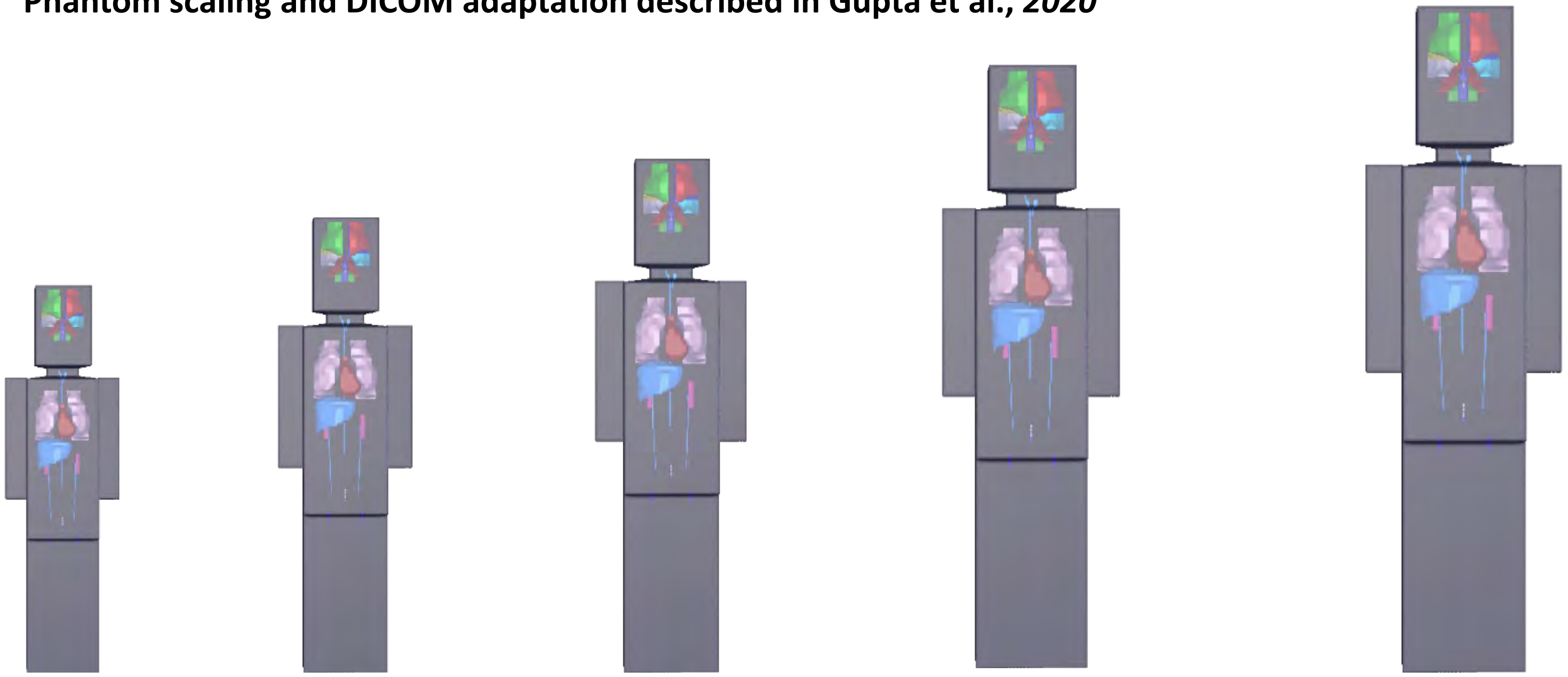
- For more than two decades, we have used an age-scalable computational phantom (modeled on FORTRAN) whose organs are represented by 3D grids of points
- We recently updated our phantom to DICOM format, allowing it to be used and scaled within a commercial RT treatment planning system





Phantom scaling and DICOM adaptation described in Gupta et al., *2020*

Development of Enhanced Heart Model

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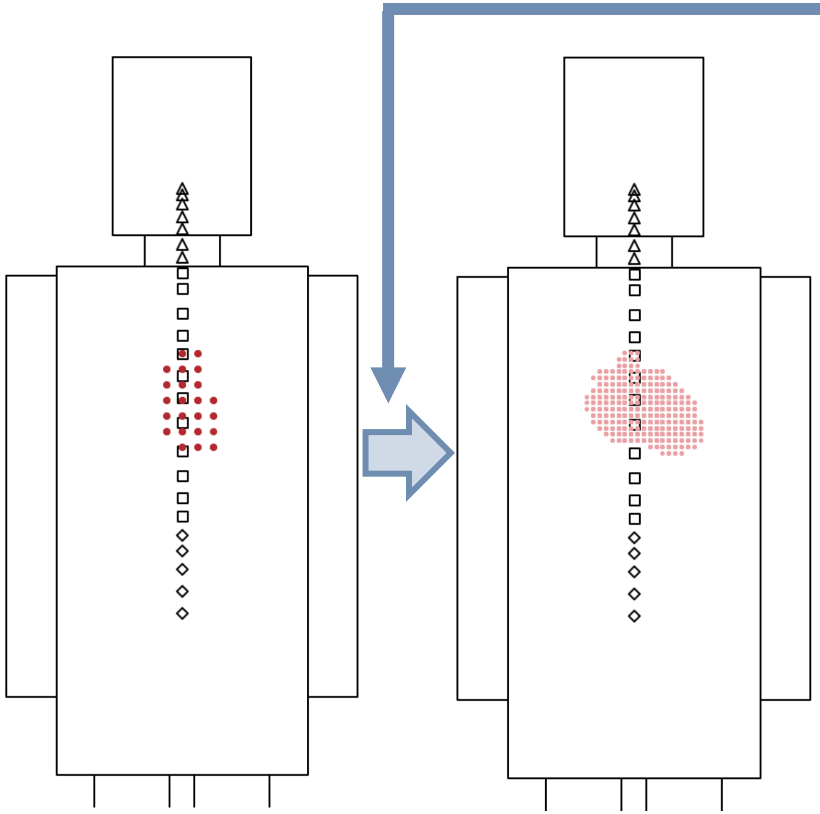
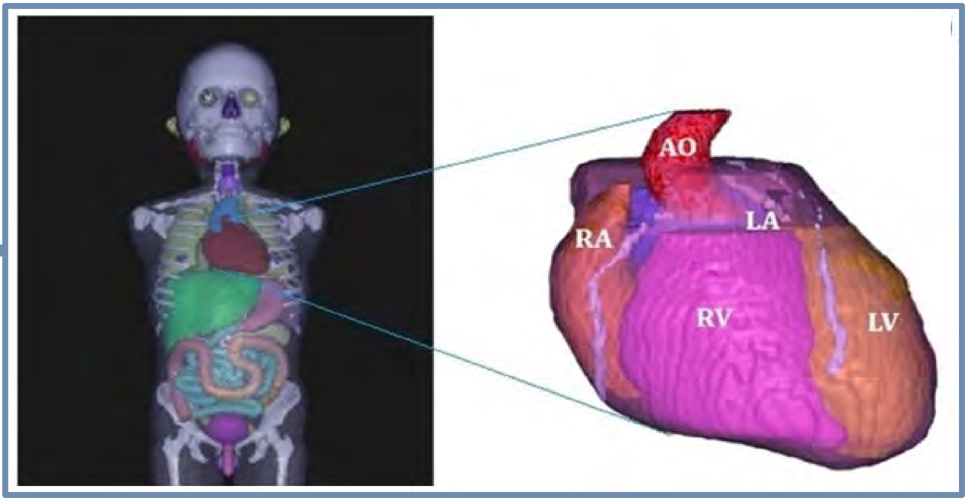
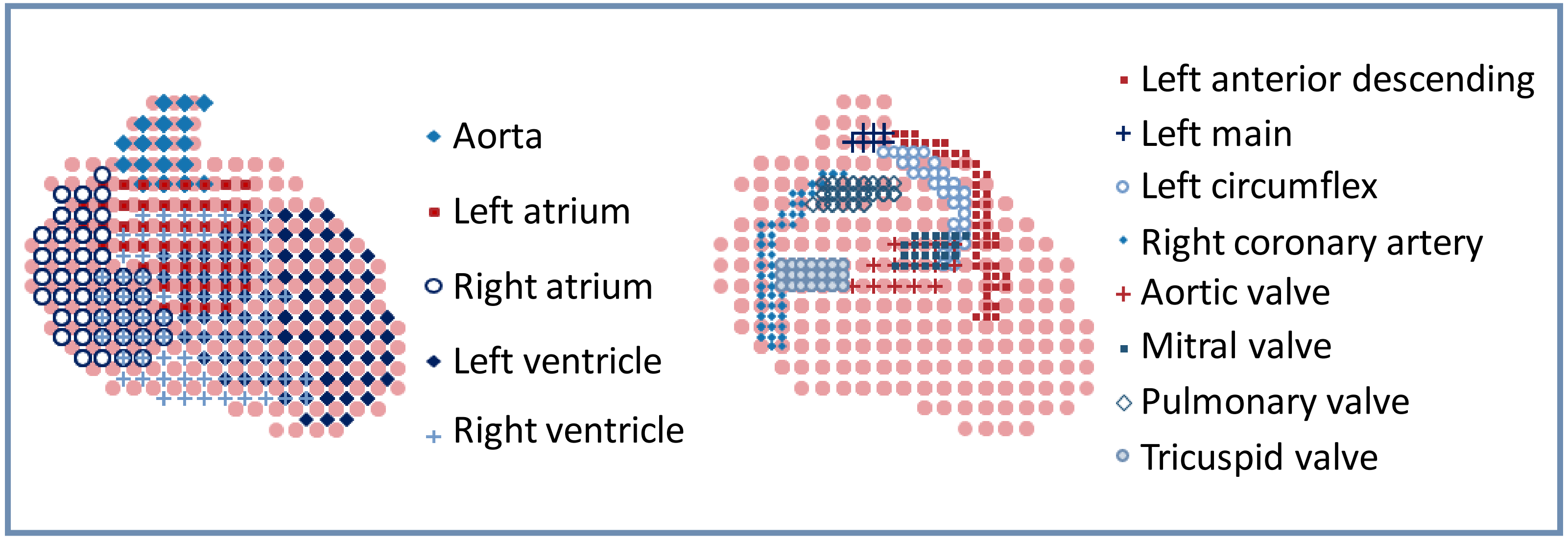
- Enhanced the heart model in our in-house phantom based on the UF/NCI phantom







Heart model **development** and validation described in Shrestha et al., *2020*

Cardiac Substructure Dose Reconstructions

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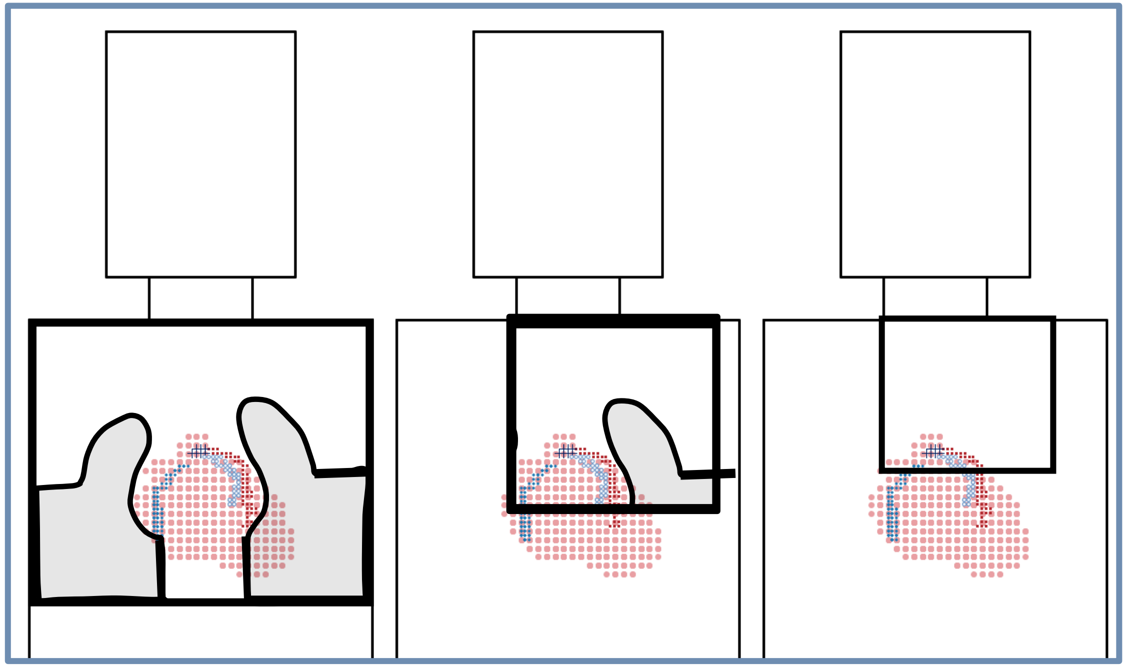
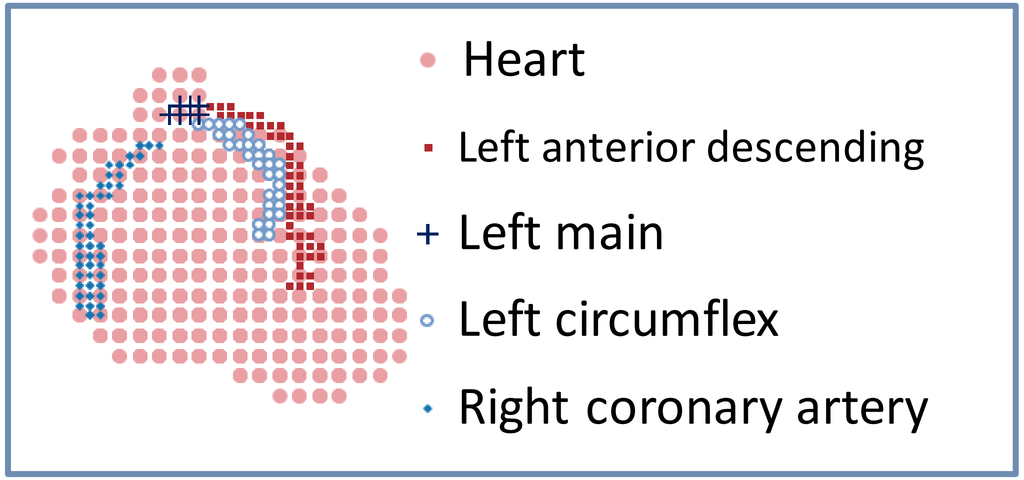
- For each individual (N> 13,000), RT fields were reconstructed on a computational phantom scaled to their age at RT.

Hodgkin lymphoma dose reconstruction example – coronary arteries

- Mantle (full) and two reduced field boosts



- Smaller fractions of heart and coronary arteries in-beam for boost fields



Right Coronary Artery Dose CAD Risk

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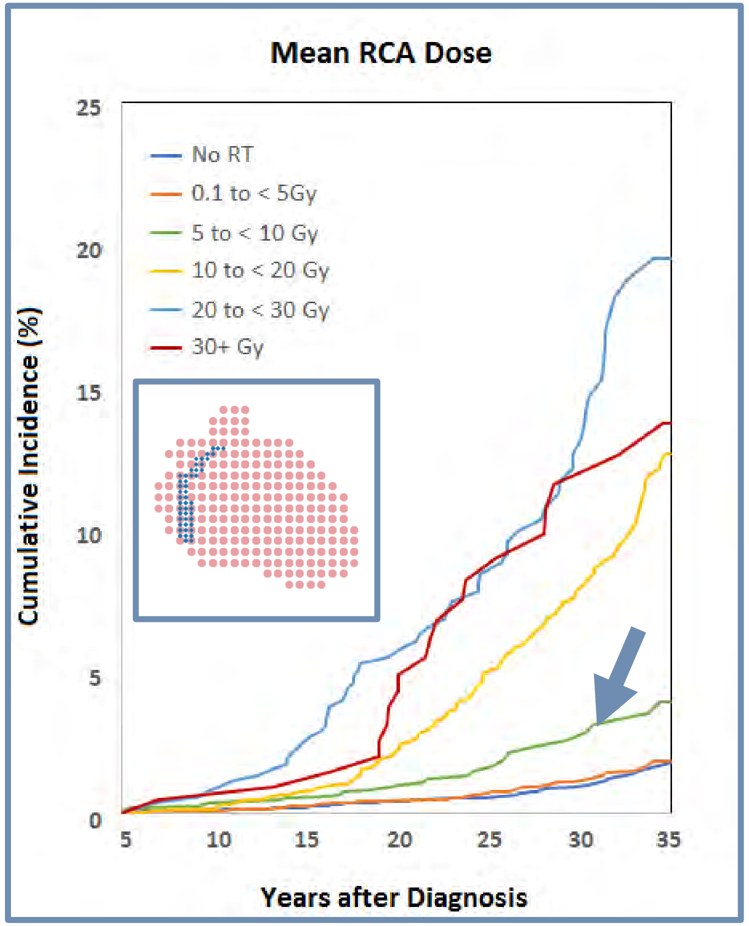
35-year cumulative Incidence (%) and adjusted rate ratios of CAD associated with **right coronary artery** dose

Mean Dose (Gy)	Cumulative Incidence	95% CI	Rate Ratio	95% CI	P
None	1.8	(1.2 - 2.4)	Ref		
0.1-<5	1.8	(1.3 - 2.3)	1.1	(0.8 - 1.6)	0.48
5-<10	3.9	(2.2 - 5.6)	2.6	(1.6 - 4.1)	<.001
10-<20	12.6	(10.3 - 15.0)	5.3	(3.9 - 7.2)	<.001
20-<30	19.5	(14.5 - 24.5)	8.5	(5.9 - 12.2)	<.001
30+	13.7	(7.9 - 19.5)	5.1	(2.9 - 8.9)	<.001



More on substructure level dose response at 2021 AAPM and ASTRO Annual Meetings by Shrestha et al. and Bates et al., respectively

Development of Colon and Rectum Model

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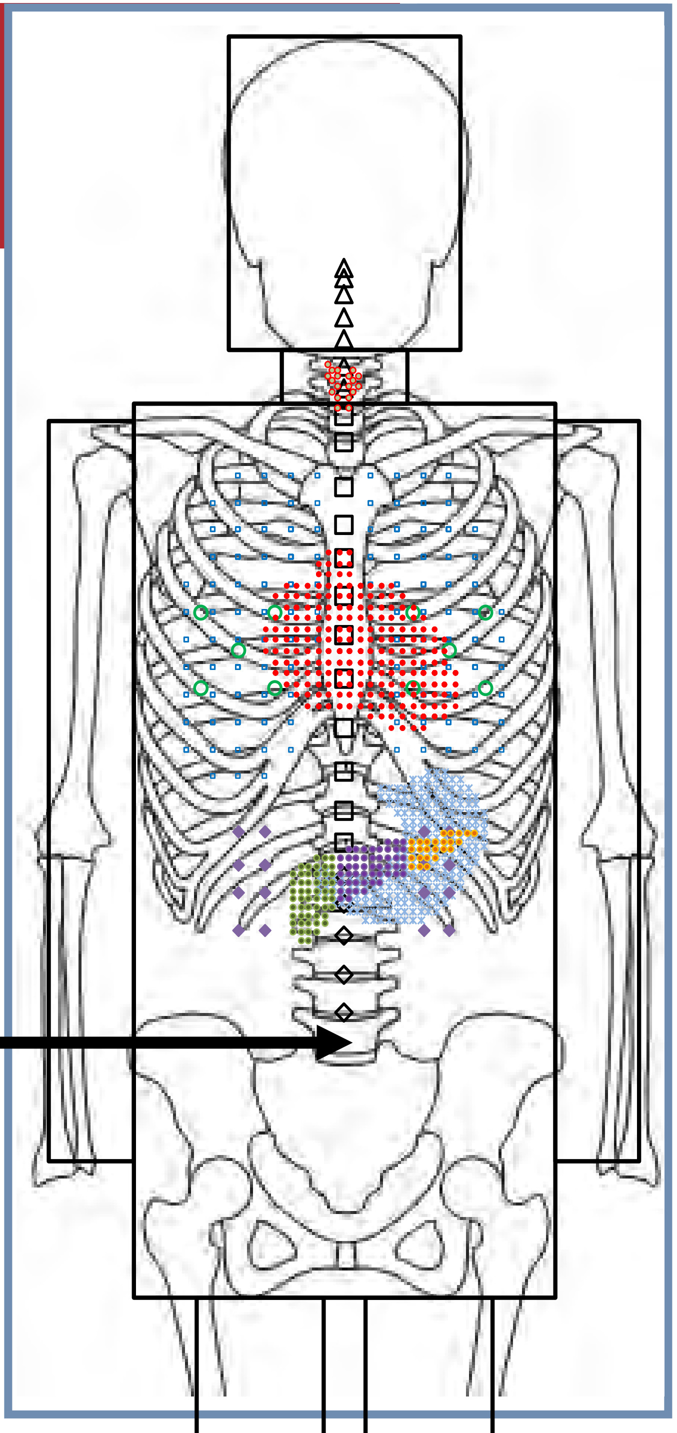
- Wanted to examine associations between colon and rectum doses and subsequent colorectal cancers
  - *But*, our phantom does not have a colon and rectum
  - How to create a single organ model for an organ that has large intra- and inter-patient variation?
- Approach: from a population of pediatric patients, create a population average statistical shape model using principle component analysis (PCA):
  - Video shows deformation modes (or anatomical variations) that were identified by the PCA
  - Video starts from modes those that account for the most anatomical variation to the least anatomical variation

Current Research in Colorectal SMN

Next steps

- Integrate and register colorectal model into our in-house phantom
- Dose reconstructions for the CCSS
- Develop dose-response models
- Quantify uncertainties in reconstructed RT dose and their effect on dose-response models

More on colon & rectum model development at 2021 AAPM Annual Meeting by Owens et al.



References

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Methods Publications - Cohort Dosimetry

Stovall, M, Weathers, R, Kasper, C, Smith, SA, Travis, L, Ron, E and Kleinerman, R (2006). "Dose reconstruction for therapeutic and diagnostic radiation exposures: use in epidemiological studies." Radiation Research 166:141-157.

Howell RM, Smith SA, Weathers RE, Kry SF, Stovall M. Adaptations to a generalized radiation dose reconstruction methodology for use in epidemiologic studies: An update from the MD Anderson Late Effect Group. Radiat Res. 192(2):169–188, 9/2019. PMCID: PMC8041091

Gupta AC, Shrestha S, Owens CA, Smith, SA, Qiao Y, Weathers RE, Balter PA, Kry SF, Howell RM. Development of an Age-scalable 3D Computational Phantom in DICOM Standard for Late Effects Studies of Childhood Cancer Survivors. Biomed. Phys. Eng. Express 6(6), https://doi.org/10.1088/2057-1976/ab97a3, 9/2020.

Shrestha S, Gupta AC, Bates JE, Lee C, Owens CA, Hoppe BS, Constine LS, Smith SA, Qiao Y, Weathers RE, Yasui Y, Court LE, Paulino AC, Pinnix CC, Kry SF, Followill DS, Armstrong GT, Howell RM. Development and validation of an age-scalable cardiac model with substructures for dosimetry in late effects studies of childhood cancer survivors. Radiother Oncol. e-Pub 10/2020. PMCID: PMC8132170

Upcoming 2021 Conference Presentations

Shrestha S, Bates JE, Liu Q, Mulrooney DA, Smith SA, Mulrooney D, Gupta A, Owens C, Leisenring WM, Gibson TM, Chow EJ, Oeffinger KC, Robison LL, Armstrong GT, Constine LS, Hoppe B, Lee C, Court L, Kry S, Yasui Y, Howell RM. Impact of Cardiac Substructure Dosimetry on Late Cardiac Risk: A Report from the Childhood Cancer Survivor Study (CCSS). Oral Presentation. American Association of Physicists in Medicine (AAPM) 2021 Annual Meeting, Virtual, 07/2021

Owens C, Rigaud B, Ludmir E, Gupta A, Shrestha S, Paulino A, Peterson C, Kry S, Smith S, Brock K, R. Howell. From Person-Specific to Population-Based Colorectal Models: An Age-Scalable Computational Anatomical Colorectal Model for Radiation Dosimetry in Late Effects Studies of Childhood Cancer Survivors. Oral Presentation. AAPM 2021, Virtual, 07/2021

Bates JE, Shrestha S, Liu Q, Mulrooney DA, Smith SA, Leisenring WM, Gibson TM, Chow EJ, Oeffinger KC, Robison LL, Armstrong GT, Constine LS, Hoppe B, Lee C, Yasui Y, Howell RM. Relationship Between Coronary Artery Radiation Doses and Risk of Late Coronary Artery Disease: A Report From the Childhood Cancer Survivor Study (CCSS). Oral Presentation at American Society for Therapeutic Radiation Oncology 2021 Annual Meeting, Chicago, IL, 10/2021;

Childhood Cancer Survivor Study

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- The Childhood Cancer Survivor Study is an NCI-funded resource (U24 CA55727) to promote and facilitate research among long-term survivors of cancer diagnosed during childhood and adolescence.

- Investigators interested in potential uses of this resource are encouraged to visit:

http://ccss.stjude.org

Thank you