ABSTRACT TO BE SUBMITTED TO ISLCCC 2025

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Title: Development and validation of a principal component analysis statistical shape pediatric/adolescent breast model for dose reconstruction of pre-CT era radiotherapy pediatric patients in long-term outcome studies

Abstract (2,991/3,000 character limit):

Purpose: Prior Childhood Cancer Survivor Study (CCSS) subsequent breast cancer (SBC) dose-response models relied on chest dose as a surrogate for breast dose, lacking the dose-volume metrics needed to optimize radiation therapy (RT). Breast doses were not reconstructed for females ≥12 years due to the absence of a model for developing/developed breasts. We aimed to (1) develop and validate an anatomically realistic pediatric/adolescent population-based breast model, (2) integrate it into an age-scalable phantom, and (3) assess breast dose reconstruction feasibility for CCSS females aged ≥12 years at RT.

Methods: Breast contours were collected from CTs (one reference, 70 training, eight testing) of 79 females (12–21 years) with Hodgkin lymphoma. Principal component analysis statistical shape modeling (PCA-SSM) was performed on training contours to capture population deformations. A population-mean breast model and two alternative shapes were generated and integrated into an age-scalable phantom. Geometric accuracy was assessed using Dice similarity coefficient (DSC), distance-to-agreement (DTA), and Hausdorff distance (HD). Dosimetric accuracy was evaluated by comparing reconstructed whole breast and breast quadrant dose-volume metrics from the PCA models against "ground truth" breast anatomy from the eight test patients CTs. RT was then reconstructed for 663 CCSS females diagnosed 1970-1999 at 31 institutions, aged ≥12 years.

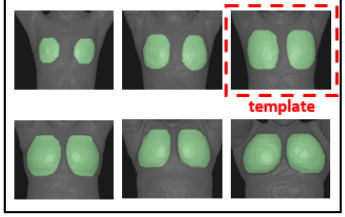
Results: DSC(min-max) was 0.86(0.85–0.88), DTA was 1.46mm(1.21-2.04mm), and 95th HD was 2.44mm(1.98-3.32mm), demonstrating the model's ability to capture anatomical variations. Absolute percent differences for mean breast doses (normalized to prescription dose) between ground truth and mean model (alternative #1, alternative #2) were 2.63%(3.57%, 2.22%). Differences in lower quadrants were within 10% for each model, while upper-inner and upper-outer quadrants showed larger deviations at 16.12%(20.49%, 10.70%) and 10.06%(9.65%, 10.53%), respectively. Dose-volume metric differences (V5–V30) were typically within 5%. Our population-mean model breast doses closely aligned with ground truth doses, validating it as a representative model for pediatric populations. Among 663 CCSS survivors, reconstructed mean (95% CI) breast doses, V5, and V20 were 8.15Gy(7.67-8.59Gy), 35.75%(33.70-37.71%), and 14.25%(13.12-15.31%), respectively. On average, total chest dose overestimated breast dose by a factor of 11.46 (9.42-13.51).

Conclusion: A pediatric/adolescent population-based breast model was developed, validated, and used to reconstruct breast doses for a subset of females in CCSS aged ≥12 years at RT. This PCA-based breast model enables dosimetry for females ≥12 years at RT, which when paired with existing methods for younger girls, will be used to develop novel breast dose-volume-based SBC dose-response models to refine dose-volume constraints for RT planning in newly diagnosed girls/adolescents and guide their survivorship care.

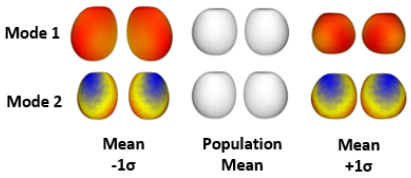
A. PCA-SS Pediatric Breast Model Development and Validation

Model Development

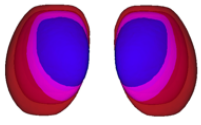
1 Breast Contour Collection



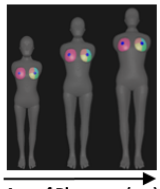
2 Principal Component Analysis



3 Alternative Shape Generation



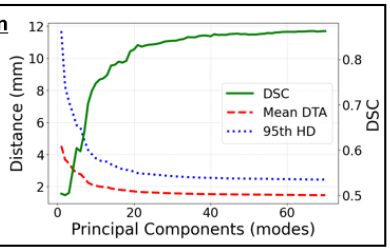
4 Integration with Age-Scalable Phantom



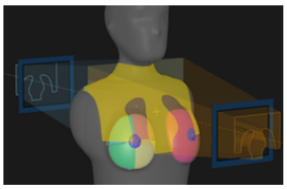
Model Validation

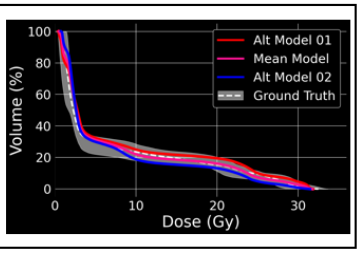
5 Geometric Evaluation

Metric	Mean (Min, Max)
DSC	0.86 (0.85-0.89)
DTA	1.46mm (1.21-2.04)
95th HD	2.44mm (1.98-3.32)



6 Dosimetric Analysis



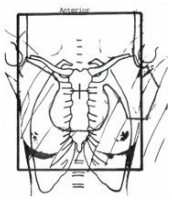


B. Historic Radiotherapy Breast Dose Reconstruction Workflow

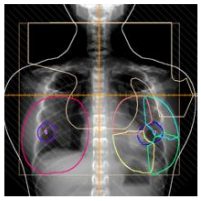
1 Import RT Plan Parameters

- ❑ Prescription Dose
- ❑ Beam Type and Energy
- ❑ Beam Laterality
- ❑ Beam Configuration
- ❑ Field Size

2 Reconstruct patient-specific field blocking on age-matched phantom

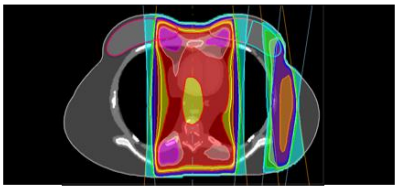


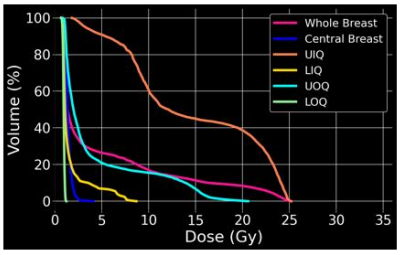
Patient Record



CT-based Phantom

3 Calculate and Export Dose





4 CCSS Reconstructed Dose-Volume Metrics

N Patients	663
Prescribed Dose (Gy)	30.68 (29.88 – 31.48)
Whole Breast	
Mean Dose (Gy)	8.15 (7.67 – 8.59)
V5 (%)	35.75 (33.70 – 37.71)
V10 (%)	26.71 (24.93 – 28.42)
V20 (%)	14.25 (13.12 – 15.31)
Breast Quadrants	
UIQ Mean Dose (Gy)	13.70 (12.98 – 14.36)
LIQ Mean Dose (Gy)	6.79 (6.36 – 7.21)
UOQ Mean Dose (Gy)	10.63 (9.90 – 11.33)
LOQ Mean Dose (Gy)	4.02 (3.57 – 4.43)

Values in parentheses represent 95% confidence interval (CI)

(A) PCA-SS Pediatric Breast Model Development and Validation: (A1) Breast contours from 71 chest CTs (females aged 12–21 years) were collected and pre-processed. One contour was selected as the anatomical template, while the remaining 70 were spatially normalized and deformably registered to it using a symmetric thin-plate spline robust point matching (sTPS-RPM) method. **(A2)** Principal component analysis captured the dominant modes of shape variation, generating **(A3)** a population-mean breast model and two alternative statistical shape models, which were integrated into a pediatric reference computational phantom that can be **(A4)** scaled to any age using an in-house algorithm. All three models were **(A5)** geometrically evaluated, achieving DSC, DTA, and HD values of 0.86, 1.46mm, and 2.44mm, demonstrating their ability to reconstruct global and local shape variations. **(A6)** Dosimetric analysis showed that the mean model accurately captured both anatomical and dose distribution tendencies, with its dose-volume histogram (DVH) closely aligning with the mean DVH of the ground truth, validating it as a robust baseline for dose reconstruction. The alternative models represented realistic anatomical extremes, producing DVHs corresponding to the upper and lower bounds of the ground truth, reflecting variations in breast size and shape.

(B) Historic Radiotherapy Breast Dose Reconstruction Workflow: The process involves **(B1)** importing RT plan parameters from historical records into RayStation using an in-house auto-planning script. **(B2)** Patient photos and diagrams aid in reconstructing patient-specific blocking, after which **(B3)** breast region dose-volume metrics are calculated and exported. **(B4)** To date, we have reconstructed breast dose-volume metrics (population average and 95% CI) for 663 female survivors in the Childhood Cancer Survivor Study diagnosed with eight primary cancers between 1970 and 1999, aged 12–20 years.