
Large-Scale Hybrid Reconstruction of Breast Dose In Childhood Cancer Survivors Using Development Stage-Specific Pediatric Breast Models

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Abstract

Purpose: Organ-level breast dosimetry is essential for developing robust dose-response models of subsequent breast cancer (SBC) risk in female childhood cancer survivors. Historically, epidemiologic studies relied on surrogate metrics such as prescription dose due to absence of 3D imaging and dose-volume data in pre-CT radiotherapy. This study demonstrates a large-scale breast dose reconstruction framework that incorporates age-specific pediatric breast models with anatomic phantoms, enabling dose estimation across all stages of breast development.

Methods: A hybrid breast dose reconstruction workflow was applied to 5,747 female survivors from the Childhood Cancer Survivor Study treated between 1970-1999 across eight childhood cancers. Stage-specific population-based breast models were integrated into complementary CT-derived voxelized and analytical computational phantoms to estimate combined in-field and out-of-field dose contributions using treatment parameters from historical radiation records. Reconstructed dose metrics included mean whole-breast and subregion doses and dose-volume metrics.

Results: Breast dose distributions were reconstructed for all survivors spanning infancy through post-pubertal development, with median mean whole-breast doses of 5.6Gy (IQR: 2.0-12.3) following chest-directed radiotherapy (N=2,523) and 0.2Gy (IQR: 0.1-0.4) following non-chest-directed radiotherapy (N=3,224). Among survivors receiving chest-directed radiotherapy, prescription dose systematically overestimated reconstructed breast dose, with median prescription-to-mean whole-breast dose ratios ranging 1-18x across disease sites, and an overall median ratio of 4.8 (IQR: 1.8-12.8). Dose-volume analysis demonstrated substantial partial-volume exposure, with 47.8% (1,205/2523) of survivors receiving >10Gy to >10% of breast volume. Reconstruction of subregion doses further identified localized high-dose exposure, with 11.4% (288/2,523) of survivors having mean whole-breast dose <10Gy while at least one subregion exceeded 10Gy.

Conclusion: This work represents the first large cohort-scale reconstruction of historical pediatric radiotherapy breast dose accounting for breast development while incorporating

breast dose-volume metrics and subregion doses. This framework establishes a critical dosimetric foundation for improved SBC dose-response modeling, survivorship screening strategies, and risk-adapted radiotherapy planning for future pediatric patients.

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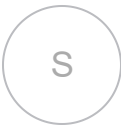
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