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REVIEW

# Secondary cancer risks after breast radiotherapy: A dose-response-based comparative review across modern techniques

## Riesgo de cáncer secundario tras la radioterapia de mama: una revisión comparativa basada en la relación dosis-respuesta entre técnicas modernas

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## ABSTRACT

**Introduction:** even with major progress in radiotherapy for breast cancer, secondary malignancy risks from unintentional radiation exposure to surrounding healthy organs remain a cause of worry, especially in long-term survivors. As survivorship improves, understanding and minimizing these risks is increasingly critical. Evaluating how different techniques impact secondary malignancies can guide safer treatment planning.
**Objective:** the review aimed to identify the optimal radiotherapy techniques and organ-specific dose thresholds associated with secondary cancer risk after breast radiotherapy. The goal was to provide a full dose-risk overview to help in safer and more tailored treatment planning.
**Method:** the study comparatively evaluated organ-specific dose-response relationships and risk thresholds analyzing data from 24 studies published between 2019 and 2024 using PubMed and Google Scholar databases based on excess absolute risk, excess relative risk, and organ-equivalent dose models. Comparative outcome was performed across four radiotherapy techniques: three-dimensional conformal radiotherapy, intensity-modulated radiation therapy, volumetric-modulated arc therapy, and proton therapy including pencil beam scanning.
**Results:** the analysis found that proton therapy and intensity-modulated radiotherapy with deep inspiration breath hold were linked with the lowest risks for organs at risk particularly the heart, lungs, esophagus, and contralateral breast. Younger patients have always higher risk, which emphasizes the need of customized radiotherapy planning.
**Conclusions:** by synthesizing dose–response data and modeling results, it establishes organ-specific risk thresholds and generates technique-based risk profiles. The graphical and tabulated outputs offer practical guidance for treatment planning. Long-term outcome monitoring and patient-specific strategies should be given top priority in future studies.

**Keywords:** Breast Neoplasms; Dose-response Relationship, Radiation; Neoplasms, Second primary Radiotherapy, Adjuvent; Radiotherpy, Intensity-Modulated.

## RESUMEN

**Introducción:** a pesar de los importantes avances en la radioterapia para el cáncer de mama, los riesgos de malignidades secundarias debido a la exposición involuntaria a radiación en órganos sanos circundantes siguen siendo motivo de preocupación, especialmente en sobrevivientes a largo plazo. A medida que mejora la supervivencia, comprender y minimizar estos riesgos se vuelve cada vez más crucial. Evaluar cómo diferentes técnicas influyen en las malignidades secundarias puede orientar una planificación terapéutica

más segura.
**Objetivo:** esta revisión tuvo como objetivo identificar las técnicas de radioterapia óptimas y los umbrales de dosis específicos por órgano asociados con el riesgo de cáncer secundario tras la radioterapia mamaria. El propósito fue ofrecer una visión integral de la relación dosis-riesgo para apoyar una planificación más segura y personalizada.
**Método:** se evaluaron comparativamente las relaciones dosis-respuesta y los umbrales de riesgo específicos por órgano, analizando datos de 24 estudios publicados entre 2019 y 2024, extraídos de las bases de datos PubMed y Google Scholar. Se aplicaron modelos de riesgo absoluto excesivo (EAR), riesgo relativo excesivo (ERR) y dosis equivalente al órgano (OED). Se compararon cuatro técnicas de radioterapia: radioterapia conformacional tridimensional (3D-CRT), radioterapia de intensidad modulada (IMRT), terapia de arco modulada por volumen (VMAT) y protonterapia, incluyendo escaneo por haz de lápiz (PBS).
**Resultados:** el análisis reveló que la protonterapia y la IMRT con inspiración profunda sostenida se asociaron con los menores riesgos para órganos en riesgo, particularmente corazón, pulmones, esófago y mama contralateral. Los pacientes jóvenes mostraron consistentemente un mayor riesgo, lo que resalta la necesidad de una planificación personalizada.
**Conclusiones:** mediante la síntesis de datos de dosis-respuesta y modelos predictivos, este estudio establece umbrales de riesgo por órgano y genera perfiles de riesgo según la técnica. Los resultados gráficos y tabulados ofrecen una guía práctica para la planificación del tratamiento. El seguimiento a largo plazo y las estrategias individualizadas deben ser prioritarios en futuras investigaciones.

**Palabras clave:** Neoplasias de la Mama; Relación Dosis-Respuesta a la Radiación; Neoplasias Primarias Múltiples; Radioterapia Adyuvante; Radioterapia de Intensidad Modulada.

## INTRODUCTION

Radiotherapy is an essential component of breast cancer treatment, playing a critical role in attaining locoregional disease control and improving overall survival.[1,2] Advances in radiotherapy techniques like (3DCRT), (IMRT), and (VMAT), all have significantly improved dose conformity while minimizing exposure to healthy tissues.[3]

However, these modern procedures frequently result in greater quantities of normal tissue getting low-to-moderate doses of radiation. This exposure has increased the risk of radiation-induced secondary malignancies.[4,5,6,7,8] As breast cancer survival rates increased, especially among younger women and long-term survivors, the assessment of long-term implications, notably the development of secondary malignancies, have become more important.[9,10,11]

Historically, most previous studies assessing long-term toxicity of breast radiotherapy have focused on a single organ at risk (OAR), such as cardiac events, including ischemic heart disease and pericarditis[12,13] or pulmonary complications like pneumonitis and lung fibrosis.[14,15] However, there is still a significant gap in comprehensive, multi-organ assessments that quantify secondary cancer risks comparing a variety of radiation techniques using robust modeling frameworks.

This review addresses that knowledge gap by providing a thorough synthesis of organ-specific secondary cancer risks across modern radiation modalities and analyzing data derived from contemporary studies (2019-2024) to evaluate organ-specific dose-response relationships for secondary cancers. Quantitative estimations were derived using established models such as Schneider's organ equivalent dose (OED) model,[16] the Biological Effects of Ionizing Radiation (BEIR) VII model,[17] and normal tissue complication probability (NTCP) analyses.

The objective of this study is to compare relative secondary cancer risks associated with different radiotherapy modalities by synthesizing dose-risk data across multiple organs. The aim is to establish clinically relevant dose thresholds that inform safer and personalized radiotherapy planning, especially in high-risk patient categories such as younger patients, left-sided breast cancer cases, and persons with smoking histories.

In conclusion, this review emphasize how important it is to have uniform dosimetry procedures, long-term prospective research, and standardized reporting in order to improve our knowledge of the risks of secondary cancer caused by radiation.

## METHOD

### Search strategy and eligibility criteria

A structured literature search was conducted to identify studies reporting radiation doses to each organ at risk and associated secondary cancer risks after breast cancer radiotherapy. The search included the Google Scholar and PubMed databases due to their strong focus on biomedical literature, along with references of relevant articles. The search spanned publications from 2019 to 2024. The search terms using Medical Subject

Headings (MeSH) “Breast neoplasms”, “Radiotherapy, Adjuvant”, “Neoplasms, Second Primary”, and “Dose-Response Relationship, Radiation”. Free-text terms were added to broaden the scope, including “cardiac toxicity”, “pulmonary toxicity”. To improve comprehensiveness, the research will be extended to include the Scopus database in future updates, given its broader coverage of peer-reviewed literature.

Studies were included if they met the following criteria: (Ⅰ) reported mean or dose-volume metrics for organs at risk; (Ⅱ) provided secondary cancer risk estimates in the form of (EAR), (ERR), odds ratios(OR) or cardiopulmonary toxicity data; (Ⅲ) analyzed modern radiotherapy techniques, specifically 3C-CRT, IMRT, VMAT, or proton therapy; (Ⅳ) inclusion of either clinical data, phantom dosimetry, or application of normal tissue complication probability (NTCP) or risk models; and (Ⅴ) articles published in peer-reviewed journals or presented at major oncology conferences.

Studies that exclusively investigated acute toxicity, local control, cosmetic outcomes, or primary organ complications without evaluating the incidence of radiation-induced secondary malignancies or lacked the detailed dosimetric data and the case reports, the editorial comments, or non-english publications were ineligible for inclusion.

**Data Extraction**

For each study we recorded the reported mean or median organ dose (Dmean), dose-volume metrics (e.g., V20, V25, V30), as well as, (EAR) and (ERR), treatment modality, and the cohort size. The most commonly evaluated OARs were the heart, lungs, contralateral breast, esophagus, thyroid, and liver. A summary of extracted data and study characteristics are detailed in table 1.

**Table 1. A** detailed breakdown of the included studies

| Author (Year) | Study Type | Sample Size | Technique Used | Organs Evaluated | Key Metrics Evaluated |
|---|---|---|---|---|---|
| Darby et al. (2013) | Case-Control | 2168 | Mixed RT (Historical) | Heart | 7,4 % risk/Gy for major coronary events |
| Lai et al. (2024) | Cohort | 2158 | 3D-CRT | Heart (substructures) | LV V25, LAD dose critical |
| Jacobse et al. (2022) | Case-Control | 366 | Reconstructed 3D | Heart (MI) | 6,4 % ERR/Gy |
| Machado et al. (2021) | Dosimetric | 10 plans × 3 fields | 3D-CRT | Heart, Lung | V15/V25 (heart), Lung V20 |
| Sophie Jacob et al. (2019) | Dosimetric | 104 | 3D-CRT | LAD, LV, RCA | LAD Dmean ~15 Gy |
| Mohamed Errahmani et al. (2022) | Case-Control | 116 | 3D-CRT | Heart, Arrhythmia | RA, LV dose differences (laterality impact) |
| Lorenzen et al. (2020) | Case-Control | 1929 | Photon/Electron | Heart | Excess Odds Ratios for IHD |
| Fredrika Killander (2023) | Randomized Trial Follow-Up | 1187 | 3D-CRT (1991) | Heart, Stroke | MHD ~3 Gy, long-term cardiac mortality |
| Dan Baaken et al. (2022) | Cohort | 1032 | 3D-CRT | Heart | MHD <5 Gy not associated with risk |
| Shima Mahmoudi et al. (2023) | Dosimetric | 450 | VMAT-SIB | Skin, Heart | Toxicity profile, EAR calculation |
| Mohamed Hassan et al. (2021) | Dosimetric | 230 | IMRT vs 3DCRT | Multiple OARs | EAR by dose (lung, heart, thyroid, liver) |
| Haciislamoglu et al. (2019) | Dosimetric | 50 | VMAT vs IMRT | Lung, Breast | EAR threshold trends |
| Quanbin et al. (2020) | Dosimetric | 60 | IMRT/VMAT | Multiple OARs | Organ-specific EAR values |
| Cristoforo et al. (2020) | Modeling | Unknown | Mixed | Multiple | Threshold modeling for risk estimation |
| Duane et al. (2021) | Systematic Review | 112 regimens | 18 Countries | Esophagus | Mean/Max dose ranges |
| Journy et al. (2020) | Case-Control | 252 cases, 488 controls | Historical | Esophagus | Dmedian, V30, SCC risk |
| Qiong Wang et al. (2023) | Dosimetric | Unknown | IMRT | Esophagus | V25–V40 and esophagitis correlation |
| Venessa Figlia et al. (2021) | Modeling | Modeling | Modeling | Heart, Lung | Dmean thresholds for fatal risks |

| | | | | | |
|---|---|---|---|---|---|
| Marc Vogel et al. (2022) | Treatment Planning | 40 plans | 3DCRT + BT vs IMRT | Heart, Lung, Breast | EAR comparison between boost techniques |
| Daniel Karpf et al. (2019) | Dosimetric Planning | 20 patients | t-IMRT vs t-VMAT (DIBH) | Heart, LADCA, Lungs, Contralateral Breast | t-IMRT showed lower mean heart and LADCA dose, lower NTID, V5%, and significantly lower EAR for CL and CB |
| Iga Racka et al. (2023) | Dosimetric Planning | 40 patients | 3D-CRT vs h-IMRT vs h-VMAT (DIBH) | Heart, LAD, LL, RL, RB | h-ARC provided best PTV conformity; h-VMAT increased contralateral OAR dose and projected secondary cancer risk |
| Marie Louise Milo et al. (2021) | Population-Based Cohort | 22 056 RT patients | 3D-CRT (1999–2007 vs 2008–2016 CT-based) | Heart (CAD, Valvular Disease) | Left-sided vs. right-sided IRR 1.44 (non-CT); no laterality risk observed in CT-based RT period |
| Eidmuller et al. (2019) | Treatment planning analysis | 128 patients with early stage-breast cancer | (h-IMRT) 3D-CRT with and without wedges (3D-w/3D+w) | Multiple OARs | IMRT showed the lowest EAR values across all evaluated organs at risk (OARs) |
| Takeshi Takata et al. (2021) | Investigation | japanese female adult designed in 2003 by the National Institute of Information and Communications Technology | WBI with WBI+RNRT | Multiple OARs | RNRT significantly increased both the mean dose and (EAR) across multiple organs, particularly the thyroid, lungs, and stomach |
| Horald Paganetti et al. (2020) | comparison analysis | 34 patients with breast cancer | VMAT and 3DCRT and PBS | Mutiple OARs | PBS was found to be the best modality in both models (S3 and S4) |
| Aime Gloi et al. (2019) | Comparison analysis | 17 conventional (50 Gy) and 13 hypofractionated (42,56 Gy) plans | hypofractionated Vs conventional regimes | Lungs Heart | age-dependent increase in (EAR) for both conventional and hypofractionated radiotherapy |
| Hiltrud Merzenich et al. (2022) | Comparison analysis | 11 982 patients | MRL-PBI vs WBI and CTL-PBI | contralateral breast, lungs, thyroid, and esophagus | MRL-PBI considerably decreased the EAR to the contralateral breast |

**Risk models and dose-response estimation**

Quantitative data extracted from the included studies were transformed into dose-response relationships curves between mean organ dose and secondary cancer risk (EAR). These dose-risk plots were generated using Python for each organ at risk across multiple radiotherapy modalities (3D-CRT, IMRT, VMAT, and proton therapy) to visually clarify at what point (dose) the risk takes off for each OAR and technique. This graphs help propose quantitative organ-specific dose thresholds and guide future consensus of safe planning limits in modern treatment planning, providing a clinically relevant framework for individualized radiotherapy optimization.

In instances where the study did not provide the EAR, we used organ-specific ß-coefficients from Schneider's OED framework [16] to estimate EAR values from reported dose metrics. This ensured consistency in dose-risk interpretation and allowed comparative analysis even in data-limited scenarios.

By bridging treatment planning data with epidemiological observations, the analysis provided visual and tabular risk atlases that support evidence-based dose constraints for critical structures such as the heart, lungs, contralateral breast, and esophagus. This integrative, model-based approach also enabled subgroup-specific insights based on age, laterality, and risk factors, reinforcing the clinical utility of dose-response modeling in secondary cancer risk mitigation.

**Limitations of the Method**

The evaluation considered as a structured comparative analysis rather than a rigorous systematic review due to its limited search scope and lack of preregistration technique. Since majority of the examined publications were treatment-planning studies without patient outcomes, no explicit risk-of-bias technique was used.

## RESULTS

**Search and selection**

The search identified a total of 112 potentially relevant records through PubMed, and Google Scholar

databases, 60 studies were selected for full-text review. Thirty-six were excluded for absence of detailed dosimetric data, insufficient follow-up, lack of organ-specific risk modeling, or published in other language. Six more studies were excluded due to overlapping cohorts or insufficient methodological quality. Ultimately, 18 primary studies were included in the qualitative synthesis, and 6 additional studies were incorporated for supporting dosimetric parameters or risk model calibration, yielding a total of 24 studies used in the final analysis. In total, more than 25 000 breast cancer patients.

**Dose-Response and risk**

Twelve investigations used well-known risk models, such as Schneider's OED, ICRP, and BEIR VII, to offer comprehensive EAR/ERR data for different organs.[13,15,18-26] Proton therapy approaches consistently demonstrated the lowest hazards for the contralateral breast and heart[13,21] techniques had a significant impact on EAR values. VMAT and IMRT without breath-holding were often associated with the greatest ipsilateral lung EAR of 112 per 10,000 person-years. According to multiple studies, EAR values in contralateral organs exceeded 20 indicate that IMRT and VMAT typically enhanced contralateral organ exposure.[15] Lai et al. found that cardiac toxicity was considerably dose-dependent, with LV V25 >4 % serving as a critical threshold.

**Dose and risk comparison by technique**

Techniques that consistently showed lower secondary cancer risks by combining EARs from the heart, ipsilateral lung, esophagus, and contralateral breast showed the following hierarchy:

Proton pencil beam scanning(PBS) = IMRT-DIBH [22,27,28]< FinF[15]< 3D-CRT+brachytherapy[29,30]< Hybrid IMRT[31] < VMAT[24]<VMAT-RNRT[23].

**Organ specific dose-response**

Heart: The pooled (EAR) slope for nine contemporary cohorts was +6,4 % per Gy (95,0 % CI 2,9–14,5 %). (PBS) and tangential IMRT with (DIBH) kept mean heart dose (MHD) less than 2 Gy, while VMAT and nodal field VMAT above 4 Gy; the risk of a major coronary event increased beyond 5 Gy.[26,28,32-39]

Lungs: The absolute EAR at 3,8 Gy was 18 times greater in current smokers than in nonsmokers. Lung Dmean < 10 Gy and EAR < 15/10 000 PY were maintained by PBS, tangential IMRT, and (FinF) plans. It was common for VMAT and RNRT/IMC fields to deliver >12 Gy[15,20,21,23,40]

Contralateral breast: The risk increased sharply above 1 Gy. VMAT and MR guided partial breast irradiation (MRL PBI) had pooled EARs of 21,6 and 5,2, respectively.[22,28] The dose was lowered by 45 % using MRL PBI compared to CBCT guided PBI.

Esophagus: The ratio of excess odds per Gy was 0,071 (95 % CI 0,018–0,206). Squamous cell carcinoma risk was seven times greater in those with a Dmedian ≥ 30 Gy and a V30 > 0 % and above Dmean≥ 3Gy the risk of esophagitis and secondary cancer increases. FinF and Proton kept Dmedian <10 Gy. [18,19,25,41]

Thyroid and liver: EAR increased little over 2 Gy. The hybrid arc plans (HVMAT, HIMRT) attained 2–3 Gy,[42] whereas proton PBS and MRL PBI delivered ≤1 Gy.[40,41]

**Key Modifiers**

*Patient factors*

Smoking significantly raises the chance of developing lung cancer, even when the radiation dose stays constant.

Patient age and organ sensitivity modifie the risk for example, the EAR for contralateral breast cancer at 1 Gy was 42 for a woman treated at age 40 versus 24 at age 70 underscoring age-at-exposure effects.

*Field design*

Internal mammary chain (IMC) irradiation or supraclavicular fields and higher dose-volume metrics add 3 to 6 Gy in organs like the esophagus and heart and lung.[18,43]

*Imaging*

Daily cone-beam computed tomography (CBCT) imagings can double the risk for contralateral breast relative to MRL-PBI.[21]

**Practical planning threshold**

Thresholds varied among studies, the more conservative values were adopted in this atlas which can be used next to the TPS during contouring and optimization. The numbers are the maximum you should strive for.

**Table 2.** Illustrate a comparative dose-risk atlas

| Organ-at-risk | Optimal technique | Risk threshold (mean dose) | Trigger for replanning |
|---|---|---|---|
| Heart (left-sided cases) | IMRT ± DIBH, or PBS if available | 4 Gy | Mean Cardiac Dose > 4–5 Gy should revisit beam angles or use DIBH; every extra 1 Gy increase major cardiac events 7 %.[28,35,36], V25<4 %, V15<5 %[26,37,38] |
| Ipsilateral lung | PBS ≈ FinF < 3DCRT < VMAT/IMRT | 6 Gy (whole), 10 Gy (ipsi) | V5Gy is less prognostic than V20; keep V20<15 %.[19,22,26,40] |
| Contralateral lung | 3DCRT or PBS | 1–1,5Gy | IMRT/VMAT low-dose bath can triple EAR; beware wide arcs.[15,41] |
| Contralateral breast | PBS ≈ 3DCRT + BT boost | 1 Gy (age < 50) | Dose as low as 1 Gy still doubles lifetime risk in young patients.[19,41] |
| Thyroid | Right-sided plans, no RNRT | 0,3–0,5 Gy | Left WBRT + RNRT can spike to 19 Gy; consider shielding/ collar.[41,42] |
| Esophagus / Stomach | 3DCRT without IMC | 2,5–3 Gy | IMC fields or VMAT arcs raise EAR > 1 per 10 000 PY.[18,19,25,41] |
| Liver | Proton or right-sided photon | 2 Gy | Laterality matters right-sided RNRT can push to >2 Gy.[40,41] |

## DISCUSSION

In this review, a structured synthesis of peer-reviewed studies was conducted to assess the relationship between radiation dose and secondary cancer risk across a wide range of organs at risk after breast cancer radiotherapy. Unlike prior studies, which often focused on a small number of organs or techniques, this study used data from planning studies, epidemiological registries, and modeling research to create a comparative dose-risk atlas. The study used existing models, such as (EAR), (ERR), (OED), to identify organ-specific risk thresholds and technique-based risk profiles. This comprehensive and visual framework not only supports evidence-based dose constraints, but it also encourages more personalized, patient-centered radiotherapy planning.

This review emphasized the necessity of radiation technique selection in reducing the likelihood of developing secondary cancers in OAR. Taylor et al.[44] Found similar trends, highlighting that while current procedures give improved conformance, they may unintentionally raise the total integral dose. Findings are consistent with those of Eidemüller et al., who found IMRT as having the lowest (EAR) across critical organs, making it particularly suited for patients with increased baseline risks.[24] Similarly, the finding that proton therapy delivers the most favorable risk profiles confirmed Merzenich et al.'s results about the usefulness of proton treatment and MR-linac in reducing radiation exposure to contralateral structures.[21]

This research emphasizes the need for age, laterality, and comorbidity-specific stratified planning. As discussed by Figlia et al.[32], younger women are more sensitive to contralateral breast irradiation, and Takata and Gloi showed that younger patients have higher lifetime risks that level off in older age.[23,30] Technique-specific outcomes were also discussed by Vogel, who noted that IMRT when used with a simultaneous integrated boost was associated with higher ipsilateral lung EARs than the 3D-CRT with a brachytherapy boost which had a much safer profile.[20] Furthermore, this synthesis confirms the findings by Berrington de González et al. on the significantly elevated risk of esophageal cancer with median doses over 30 Gy, an area that remains underestimated in current planning regimens.[45]

Cardiac exposure is a primary worry. Darby et al.[35] found that each Gy delivered to the heart increased the incidence of coronary events by 7,4 %. Consistent with this, data in this study showed that even moderate mean heart doses can considerably increase long-term cardiac diseases. Smokers have compounded dangers, as noted in Machado[26] and Cristoforo's studies[22] which this study confirmed, notably for pulmonary dose limits.

Unlike previous studies that focused on a few organs, like, Abu-Madyan's work,[46] which compared EARs in only the contralateral breast and lungs this review provides a more comprehensive assessment. By incorporating additional radiosensitive structures such as the heart, Lungs, contralateral breast, esophagus, thyroid, stomach and liver, gained a more comprehensive and practical comprehension of dose-risk relationships. This technique enables a more accurate risk assessment during treatment planning.

Epidemiological evidence clearly supports the necessity of reducing secondary cancer risk in breast cancer survivors. Molina-Montes et al.[47] found a 17 % overall rise in second primary malignancies, with rates reaching 51 % among women under 50. Radiotherapy, in particular, was linked to a 45 % increase in malignancies in high-dose regions and a 9 % increase in contralateral breast cancers.[45] These statistics, supported by Marcheselli et al.[48] highlighted the importance of individualized and risk-aware planning. This analysis directly tackles this issue by converting such data into visual and tabular risk atlases that assist doctors in determining dose

limits for each OAR. This integrative, model-based approach also enabled subgroup-specific insights, which few previous studies provided.

However, some limits exist. Differences in follow-up lengths, patient demographics, and dosimetric reporting across the studies examined limit the generalizability of our findings. Moving forward, long-term prospective trials are required. These should include genetic susceptibility data, use consistent NTCP models, and investigate understudied locations such as the esophagus and liver.

In conclusion, this study contributes to a better knowledge of secondary cancer risk in breast irradiation by providing a systematic, comparative synthesis. By incorporating dose-response modeling with patient-specific factors, it establishes important risk thresholds and recommendations based on evidence which improve both planning safety and personalization.

## CONCLUSION

This review consolidated current evidence on the link between breast radiotherapy and secondary cancer risk across multiple organs at risk. By comparing dose-response graphs, it clarifies how technique selection, anatomy, and patient-specific factors shape long-term outcomes. The study defines risk thresholds and technique-based profiles to support safer, individualized planning. Through integrated modeling and epidemiological insights, it offers practical guidance, with visual and tabular tools aiding in clinical decision-making. It also underscores the importance of minimizing unnecessary exposure, ensuring long-term surveillance, and advancing personalized treatment strategies. Ongoing research is needed to confirm these findings and optimize future radiotherapy approaches.

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