REVIEW ARTICLE

Deep Inspiration Breath-Hold in the prevention of radiotherapy-induced cardiac injury

Deep Inspiration Breath-Hold *para a prevenção da lesão cardíaca induzida por radioterapia*

Prisley Pereira de Oliveira [1*]
Michel Marcos Dalmedico [2]
Juliana Londero Silva Ávila [1]
Jackson Adriano Canavarro Ribeiro [1]
Paula Karina Hembecker [1]
Sergio Ossamu Ioshii [1]

[1] Pontifícia Universidade Católica do Paraná (PUCPR), Curitiba, PR, Brazil
[2] Universidade Positivo (UP), Curitiba, PR, Brazil

Date of first submission: February 23, 2025
Last received: July 2, 2025
Accepted: July 25, 2025
Associate editor: Ana Paula Cunha Loureiro

***Correspondence:** prisleyoliveiraft1@gmail.com

Abstract

Introduction: Breast-conserving surgery followed by adjuvant radiotherapy remains the gold standard in early-stage breast cancer treatment. However, incidental cardiac irradiation increases the risk of ischemic heart disease, the leading non-malignant cause of death among these patients. **Objective:** To identify evidence-based implications of the Deep Inspiration Breath-Hold (DIBH) technique for preventing cardiac injury associated with adjuvant radiotherapy. **Methods:** A scoping review was conducted in accordance with Joanna Briggs Institute guidelines. The PubMed, LILACS and Web of Science databases were searched for studies reporting the application of DIBH within the context defined by this review. **Results:** Fifteen relevant studies were selected, all assessing DIBH for the prevention of cardiotoxicity secondary to adjuvant radiotherapy. Deep inspiration increases lung volume, expanding the thoracic cavity and displacing the heart to the right and downward, thereby moving the heart out of the radiation field and reducing cardiac exposure. **Conclusion:** The results presented across multiple studies indicate that the use of DIBH in clinical practice consistently reduced cardiac irradiation without compromising target coverage.

Keywords: Breast neoplasms. Adjuvant radiotherapy. Cardiac diseases. Cardiotoxicity. Breath-hold technique.

Resumo

Introdução: *A cirurgia conservadora da mama seguida de radioterapia adjuvante consiste no padrão-ouro de tratamento dos estágios iniciais do câncer de mama. No entanto, a irradiação cardíaca incidental aumenta o risco de doença cardíaca isquêmica, o que representa a principal causa de morte não maligna nestas pacientes.* ***Objetivo:*** *Identificar as implicações, suportadas por evidências, da utilização da técnica* Deep Inspiration Breath-Hold *(DIBH) na prevenção da lesão cardíaca induzida por radioterapia adjuvante.* ***Métodos:*** *Trata-se de uma revisão de escopo baseada nas recomendações do Joanna Briggs Institute. Foram selecionados artigos publicados nas bases PubMed, LILACS e W, que relataram a prática de DIBH, conforme o escopo do presente estudo.* ***Resultados:*** *Foram incluídos quinze estudos relevantes que relataram a utilização de DIBH para a prevenção de cardiotoxicidade secundária à radioterapia adjuvante. Durante a inspiração profunda, a cavidade torácica se expande em função do aumento do volume pulmonar, deslocando o coração para a direita e inferiormente, minimizando o campo de tratamento e afastando o coração do campo de irradiação.* ***Conclusão:*** *Os resultados cumulativos de uma série de estudos apontam que na prática clínica a utilização de DIBH resulta em menor irradiação do coração, sem com-prometer a cobertura do alvo.*

Palavras-chave*: Neoplasias de mama. Radioterapia adjuvante. Cardiopatias. Cardiotoxicidade. Suspensão da respiração.*

Introduction

Breast cancer is the most commonly diagnosed cancer in women worldwide. Globally, there were 2.3 million new cases and 670,000 deaths from female breast cancer in 2022 alone.[1] The majority of cases occur in transitioning countries, where mortality rates are disproportionately higher in women over 50 years old when compared to those in high-income nations.[2]

Key risk factors include genetic predisposition, estrogen exposure (both endogenous and exogenous, including long-term hormone replacement therapy), ionizing radiation, low parity, high breast density, and a history of atypical hyperplasia. A Western-style diet, obesity, and alcohol consumption also contribute to increased incidence.[3,4]

Modern breast cancer treatment is multimodal and combines early detection with locoregional therapies (breast-conserving surgery and radiotherapy), systemic treatments (chemotherapy, hormone therapy), and supportive care. Consequently, patients with breast cancer represent a major survivor population within oncology.[5,6] Treatment selection depends on tumor stage and size, lymph node involvement, molecular subtype, patient clinical status, and other factors.[7,8]

Breast conserving surgery (BCS) followed by whole-breast radiotherapy is considered the gold standard treatment in early-stage disease, defined as invasive carcinoma confined to the breast, with or without regional lymph node involvement, and amenable to surgical excision.[8] BCS involves removing the tumor while preserving the breast.[9,10] More than 80% of patients with breast cancer undergo primary surgery.[11]

To reduce recurrence risk and improve survival outcomes, adjuvant locoregional thoracic radiotherapy is standard after BCS.[12] Combining radiotherapy with surgery is an independent prognostic factor for both breast cancer-specific and overall survival, and for reducing the risk of locoregional recurrence.[13-15]

Despite its therapeutic benefits in breast cancer treatment, radiotherapy exposes healthy tissues to ionizing radiation, in addition to targeting cancer cells.[16] Scatter to adjacent normal tissues is unavoidable, potentially compromising cosmetic results and inducing cardiac and pulmonary toxicity.[17,18]

A major adverse effect of radiotherapy is incidental cardiac radiation, which increases the risk of therapy-related cardiovascular mobility and remains the leading non-malignant cause of death in oncology patients.[19-21] Cardiotoxic manifestations include cardiomyopathy, cardiac fibrosis, coronary artery disease, arrhythmias, and hypertension.[22] Thus, the therapeutic benefits of radiotherapy may be partially offset by adverse cardiovascular outcomes.[23]

Given improvements in long-term breast cancer survival rates, preventing or managing radiation-induced cardiovascular diseases has become a critical challenge in clinical practice, since these late complications can adversely affect patient outcomes, quality of life, and healthcare costs. Accordingly, various preventive strategies have been proposed and implemented, focusing on reducing cardiac exposure to radiation. Against this backdrop, the present study aimed to identify evidence-based implications of the Deep Inspiration Breath-Hold (DIBH) technique for preventing cardiac injury associated with adjuvant radiotherapy.

Methods

This scoping review was conducted in accordance with the Joanna Briggs Institute guidelines (JBI Manual for Evidence Synthesis: Chapter 11: Scoping Reviews).[24] Scoping reviews are designed to address broad research questions, provide comprehensive and in-depth analyses of existing studies, evaluate emerging evidence, and offer a solid foundation for future research. They also enable the systematic identification, examination, and organization of concepts or characteristics within a wide field of knowledge.

The methodology comprises five stages: 1) developing the research question; 2) identifying relevant studies; 3) study selection; 4) data charting; and 5) collecting, summarizing, and reporting results.

The review was guided by the following research question: What is the current evidence regarding the benefits of the DIBH technique in preventing radiotherapy-induced cardiac injury in women with breast cancer?

A systematic search was performed in PubMed/MEDLINE (National Library of Medicine); LILACS (Latin-American and Caribbean Health Sciences Literature) and Web of Science (Clarivate Analytics). A manual search of the grey literature was also conducted using Google Scholar, the U.S. National Library of Medicine, OpenGrey, and Grey Literature Report.

The search strategy combined the following descriptors: ("Deep Inspiration Breath-Hold" OR DIBH) AND ("Breast Cancer" OR " Breast Neoplasms") AND ("Radiation-Induced Heart Disease" OR "Radiation-induced Cardiovascular Disease" OR "Radiation-Associated Cardiovascular Dysfunction").

Inclusion criteria were full-text articles published in Portuguese, Spanish, or English, between 2019 and 2024, reporting the use of DIBH in women diagnosed with breast cancer (right or left) undergoing adjuvant therapy.

To prioritize studies according to evidence quality, the categorization proposed by Fineout-Overholt et al.[25] was applied: 1 – systematic reviews, meta-analyses, or clinical guidelines based on systematic reviews of randomized controlled trials; 2 – randomized controlled trials; 3 – well-designed clinical trials without randomization (quasi-experimental); 4 – cohort and/or case-control studies; 5 – systematic reviews of qualitative studies; 6 – evidence from a single descriptive or qualitative study; 7 – expert opinion or committee consensus.[25]

All retrieved studies were independently screened for eligibility by two reviewers, in two stages: (i) assessment of titles and abstracts; (ii) full-text review of the selected studies, with exclusion reasons documented. For each included study, both reviewers extracted qualitative information (authors, year of publication, journal) and clinical data (study characteristics, main outcomes, and reported adverse effects). Extracted data were organized and synthesized narratively.

Results and discussion

The search strategy identified 97 relevant studies, of which 15 met the inclusion criteria and were incorporated into the qualitative synthesis (Figure 1). A summary of the qualitative findings is presented in Tables 1 and 2.

This review highlights several key findings: (I) DIBH reduces radiation exposure to organs at risk (OAR) in patients with both left- and right-sided breast cancer; (II) it achieves significant dosimetric reductions (Gy) compared with free breathing (FB); (III) target coverage remains uncompromised; (IV) benefits are more pronounced in selected patients; and (V) preparatory physical conditioning can further enhance outcomes.

Breast radiotherapy, particularly for left-sided disease, is associated with an increased risk of long-term cardiac comorbidities.[26,27] Exposure of a significant volume of the heart to high-dose irradiation can damage nearly all its structural components, including the pericardium, myocardium, valves, coronary arteries, capillaries, and conduction system. The latency of these effects ranges from months, in the case of subclinical changes such as pericarditis, to decades, as in the development of coronary artery disease or myocardial infarction.[28,29]

Evidence from observational studies indicates that the radiation dose, volume of the irradiated myocardium, and delivery technique influence the likelihood and severity of cardiac toxicity. Among these, the volume of irradiated heart tissue is a major determinant.[30] Importantly, the risk of ischemic heart disease increases proportionally with the mean heart dose.[29,31]

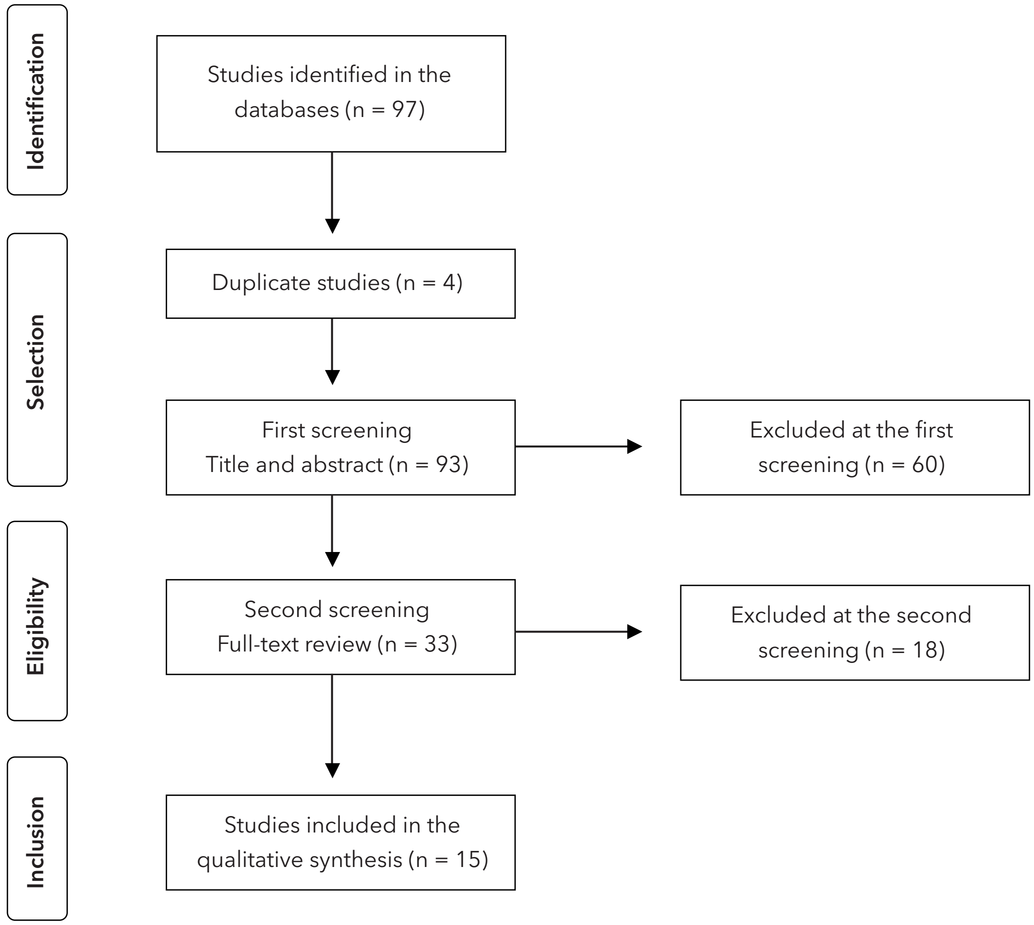

Figure 1 - Flow diagram depicting the identification, screening, exclusion and inclusion of studies.

Table 1 - Narrative synthesis summarizing general characteristics of the studies

Author/Country/Year	Title	Method	Evidence quality
Wolf et al.[56] Germany, 2023	Deep inspiration breath-hold radiation therapy in left-sided breast cancer patients: a single-institution retrospective dosimetric analysis of organs at risk doses	Case series	4
Borgonovo et al.[57] Switzerland, 2022	Deep inspiration breath hold in post-operative radiotherapy for right breast cancer: a retrospective analysis	Case report	4
Stowe et al.[58] United States, 2022	Heart sparing radiotherapy techniques in breast cancer: a focus on deep inspiration breath hold	Literature review	6
Falco et al.[59] Poland, 2021	Deep inspiration breath hold reduces the mean heart dose in left breast cancer radiotherapy	Case series	4
Kalet et al.[60] United States, 2021	The dosimetric benefit of in-advance respiratory training for deep inspiration breath holding is realized during daily treatment in left breast radiotherapy: A comparative retrospective study of serial surface motion tracking	Case series	4
Ferdinand et al.[61] India, 2021	Dosimetric analysis of Deep Inspiratory Breath-hold technique (DIBH) in left-sided breast cancer radiotherapy and evaluation of pre-treatment predictors of cardiac doses for guiding patient selection for DIBH	Case series	4

Table 1 - Narrative synthesis summarizing general characteristics of the studies (continued)

Author/Country/Year	Title	Method	Evidence quality
Reitz et al.[62] Germany, 2020	Stability and reproducibility of 6013 deep inspiration breath--holds in left-sided breast cancer	Case series	4
Simonetto et al.[63] Germany, 2019	Does deep inspiration breath-hold prolong life? Individual risk estimates of ischaemic heart disease after breast cancer radiotherapy. (SAVE-HEART)	Clinical trial	2
Testolin et al.[64] Italy, 2019	Deep inspiration breath-hold intensity modulated radiation therapy in a large clinical series of 239 left-sided breast cancer patients: a dosimetric analysis of organs at risk doses and clinical feasibility from a single center experience	Retrospective study (Case series)	4
Schröder et al.[65] Germany, 2021	Deep inspiration breath-hold for patients with left-sided breast cancer - A one-fits-all approach? A prospective analysis of patient selection using dosimetrical and practical aspects	Case series	4
Zhu et al.[66] China, 2023	Cardiac exposure in left-sided breast cancer patients undergoing deep inspiratory breath hold radiation therapy	Case series	4
Swathi et al.[67] India, 2024	How effective is deep inspiration breath hold in minimizing cardiac doses during hybrid radiotherapy treatment for left-sided breast cancer with comprehensive regional nodes?	Case series	4
Knöchelmann et al.[68] Germany, 2022	Left-sided breast cancer irradiation with deep inspiration breath--hold: changes in heart and lung dose in two periods	Case series	4
Melo[69] Brazil, 2023	Análise comparativa das doses cardíacas recebidas por pacientes com câncer de mama esquerda planejadas com duas formas alternativas de delineamento do CTV da cadeia mamária interna	Case series	4
Leoni et al.[70] Brazil, 2024	Impacto da técnica de retenção do fôlego na dose cardíaca e pulmonar em pacientes submetidos à radioterapia da mama esquerda	Case series	4

Table 2 - Narrative synthesis summarizing the main clinical outcomes

Author/Year	Key findings
Wolf et al. (2023)[56]	In a cohort of 130 patients receiving adjuvant RT with DIBH, the mean heart dose (Dmean) was 1.3 Gy (0.5–3.6) with DIBH versus 2.2 Gy (0.9–8.8) with FB ($p < 0.001$). For the left ventricle, Dmean was 1.5 Gy (0.6–4.5) with DIBH versus 2.8 Gy (1.1–9.5) with FB ($p < 0.001$). All the dosimetric parameters evaluated showed statistically significant dose reductions with DIBH ($p < 0.01$).
Borgonovo et al. (2022)[57]	In 10 patients with right-sided breast cancer, DIBH yielded a mean heart dose of 1.76 Gy versus 2.19 Gy with FB, reducing the radiation dose to the heart, LAD, and liver (in hepatomegaly cases). When correctly applied, patients tolerated the technique well, supporting its effectiveness even in right-sided breast cancer.
Stowe et al. (2022)[58]	DIBH offers a straightforward, non-invasive means of reducing radiation-induced cardiac toxicity in adjuvant breast RT, but not all patients tolerate it or benefit dosimetrically. Implementation should be individualized according to patient tolerance, cost, convenience, and the potential benefit of pre-RT breathing training.
Falco et al. (2021)[59]	DIBH significantly lowered MHD compared with non-gated FB (2.1 vs. 3.48 Gy, $p < 0.0001$) and gated FB (3.28 Gy, $p < 0.0001$). DIBH reduces the mean heart dose when compared to FB techniques (gated or ungated). High-MHD cases (> 4 Gy) declined from 40% in 2014 to 7.9% in 2017, whereas DIBH adoption increased.
Kalet et al. (2021)[60]	Pre-treatment breathing training sustained prolonged DIBH and heart dose reductions throughout RT. It also reduced excessive chest wall excursions, especially in patients with cardiopulmonary disease.
Ferdinand et al. (2021)[61]	In 31 patients with left-sided breast cancer, when compared with FB, DIBH lowered mean heart dose by 39.15% (2.4 Gy vs. 4.01 Gy, $p < 0.001$), maximum LAD dose by 19%, and ipsilateral mean lung dose by 9.9% ($p = 0.036$). DIBH significantly reduces radiations doses to OAR and is recommended for all left-sided cases.
Reitz et al. (2020)[62]	In 103 patients with left-sided breast cancer, optical surface scanning ensured stable, reproducible DIBH across and within fractions in routine clinical practice.

Note: DIBH = Deep Inspiration Breath-Hold; Dmean = mean heart dose; FB = free breathing; LAD = left anterior descending artery; MHD = maximum heart displacement; OAR = organs at risk; RT = radiotherapy.

Table 2 - Narrative synthesis summarizing the main clinical outcomes (continued)

Author/Year	Key findings
Simonetto et al. (2019)[63]	In 89 patients with left-sided breast cancer, DIBH reduced the mean heart dose by 35% (IQR: 23-46%) when compared with FB. DIBH should be offered to all patients with left-sided breast cancer. However, the greatest benefits are expected in those with a favorable prognosis, high mean heart dose, or high baseline ischemic heart disease risk.
Testolin et al. (2019)[64]	In 239 patients with left-sided breast cancer, DIBH and IMRT are feasible in daily clinical practice for a high percentage of unselected patients and achieved low OAR doses without compromising target coverage.
Schröder et al. (2021)[65]	In 72 patients selected via predefined criteria, DIBH reduced Dmean Heart by 2.8 Gy and Dmean LAD by 4.2 Gy. From a dosimetric perspective, DIBH is not universally effective for all patients, with the greatest benefits observed in selected patients.
Zhu et al. (2023)[66]	In 67 patients, DIBH reduced mean radiation doses to the heart, LAD, left ventricle (LV), and right ventricle (RV) by 30%, 38.7%, 39.3%, and 34.7%, respectively, compared with FB.
Swathi et al. (2024)[67]	n 15 patients, DIBH improved target coverage ($p < 0.017$) and significantly reduced heart and LAD Dmean values ($p < 0.001$) compared with FB. DIBH significantly reduced radiation doses to the heart and DA in relation to FB.
Knöchelmann et al. (2022)[68]	In 159 patients, DIBH significantly reduced mean heart dose from 2.64 Gy to 1.39 Gy and mean LAD dose from 5.68 Gy to 3.88 Gy (both $p < 0.001$).
Melo (2023)[69]	In 43 patients, DIBH decreased mean heart dose even in patients with extensive nodal irradiation (692 cGy vs 502 cGy - $p < 0.0001$) and lowered left ventricle (1222 cGy vs 857 cGy $p < 0.0001$) and LAD doses (3739 cGy vs 3345 cGy $p = 0.0001$). Simplified protocols may benefit selected patients at centers with high demand and limited resources.
Leoni et al. (2024)[70]	In 64 submitted to left-sided breast RT (2021 to 2023) mean heart dose decreased by 46.13% (±18.06%) and mean LAD dose by 65.86% (±22.21%).

Note: DIBH = Deep Inspiration Breath-Hold; FB = free breathing; IMRT = intensity-modulated radiotherapy; LAD = left anterior descending artery; OAR = organs at risk; RT = radiotherapy.

At present, the only proven strategy to prevent radiation-induced heart disease is to reduce cardiac radiation exposure during left-sided breast radiotherapy.[32,33] This can be achieved through dosimetric optimization methods (partial breast irradiation, intensity-modulated radiotherapy-IMRT, volumetric modulated arc therapy-VMAT) or techniques that physically displace the heart from the treatment field, such as DIBH.[34,35,36] Any measure that lowers cardiac doses is likely to reduce long-term adverse outcomes.[37]

The introduction of evidence-based radiotherapy protocols and the routine use of respiratory control methods implemented in all modern linear accelerators have reduced treatment-related morbidity. In this context, advanced techniques, such as DIBH, have been increasingly incorporated into clinical practice to minimize the risk of cardiac comorbidities.[26,38,39]

DIBH is a well-established heart-sparing approach that can be easily applied in clinical practice and combined with other interventions. By exploiting natural respiratory physiology, this non-invasive technique increases the distance between the heart and the treatment field during radiotherapy.[40] During deep inspiration, the diaphragm flattens and the lungs expand, displacing the heart away from the chest wall, reducing its exposure to radiation,[41] and often leading to significant dose reductions in the left anterior descending artery (LAD). During treatment, patients inhale deeply and hold their breath for 15-30 seconds while the radiation is delivered. By using DIBH, substantial sparing of vulnerable cardiac substructures can be achieved when compared with free breathing techniques.[40-42]

DIBH is based on the principle that active control of breathing reduces both mean heart dose and LAD dose.[40,41] Patients at high cardiovascular risk or with favorable tumor prognosis derive the greatest benefit. The technique significantly lowers doses to OAR and is recommended for all patients receiving radiotherapy for left-sided breast cancer.[43] Its simplicity means that minimal equipment is needed for implementation, such as a laser-based positional guidance system, audiovisual monitoring, and a verification system for patient setup.[43,44]

Meta-analytic data indicate that incorporating DIBH into postoperative radiotherapy for left-sided breast cancer reduces cardiac, LAD, and left lung doses without affecting target coverage compared with control groups. There were no significant differences in target coverage between groups (SMD = 0.03, 95%CI – 0.11 ~ 0.18, p = 0.64).[45]

Similar findings have been reported for right-sided breast cancer. Patients in the DIBH group received significantly lower doses to the heart, liver, and lungs than those in the FB group (heart: SMD = -0.63, 95% CI -0.85 to -0.41; liver: SMD = -1.15, 95% CI -1.91 to -0.38; lungs: SMD = -0.79, 95% CI -1.23 to -0.35; all $p < 0.05$).[46]

Substantial reductions in heart and lung doses are observed with DIBH regardless of the radiotherapy technique used.[43] Compared with FB, DIBH decreases mean heart or LAD dose by over 50%,44 reducing mean heart dose from approximately 5.2 to 2.7.[47,48]

DIBH is a reproducible, stable method for left-breast irradiation that significantly lowers the risk of late cardiac toxicities.[49] It mitigates respiratory-motion effects both during imaging (enhancing planning-phase imaging) and radiotherapy sessions (reducing cardiac and pulmonary exposure).[50] Maintaining reproducibility of the DIBH amplitude is critical, since even minor deviations can substantially alter mean heart dose.[51] Consistent breath-hold duration and precise positioning of the left breast or chest wall are essential between and within radiotherapy to achieve the planned dose distribution.[52,53]

Although DIBH is relatively straightforward, operational challenges remain. Successful implementation requires an experienced clinical team and comprehensive quality procedures covering all stages, from CT simulation to treatment delivery, including patient training, respiratory pattern standardization, minimum breath-hold time, planning margins and setup, imaging technique and frequency, and control during DIBH.[54]

Patient cooperation and adherence, while critical, re-main significant challenges. Not all breast cancer patients can sustain breath-holds long enough to perform DIBH effectively. Patients unsuitable for this technique include those with impaired pulmonary function preventing adequate breath-hold, those unable to complete training during CT simulation or to consistently reproduce breath-holds during treatment, and those for whom DIBH does not provide a dosimetric advantage over free-breathing. Thus, the decision to use DBIH in breast radiotherapy should be individualized.[54]

Moreover, variations in patient instruction and radiotherapy planning can influence the extent of cardiac dose reduction achieved. Further research is needed to assess long-term clinical outcomes associated with different DIBH techniques and refine treatment planning strategies for left breast radiotherapy.[55]

Conclusion

Postoperative radiotherapy for breast cancer, particularly on the left side, exposes a substantial portion of the heart to high radiation doses, leading to long-term cardiovascular effects secondary to cardiotoxicity. Strategies to minimize cardiac radiation exposure are therefore critical for preventing adverse events. Evidence from multiple studies indicates that DIBH effective ly reduces cardiac dose in left-sided breast cancer radiotherapy without compromising target coverage. These findings are also applicable to right-sided breast cancer and other nearby organs at risk. The technique can be readily implemented in oncology radiology departments with minimal additional cost, and patients can undergo respiratory training to maximize performance during treatment sessions.

Nonetheless, there is a continuing need for methodologically robust studies to reinforce the use of DIBH as a routine, evidence-based approach to prevent radiotherapy-induced cardiac injury in women with breast cancer.

Authors' contributions

MMD was responsible for the project design, methodological outline and writing; JACR and JLSA, for the search strategy, selection and evaluation of articles and narrative synthesis; PPO, for data analysis, manuscript standardization and preparation of tables and figures; PKH, for the review and final writing, article curation, and translation; SOI, for supervising and coordinating the project, administrative and financial support.

References

1. Kim J, Harper A, McCormack V, Sung H, Houssami N, Morgan E, et al. Global patterns and trends in breast cancer incidence and mortality across 185 countries. Nat Med. 2025;31(4):1154-62. https://doi.org/10.1038/s41591-025-03502-3

2. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: Global statistics for 2020 and 2040. Breast. 2022;66:15-23. https://doi.org/10.1016/j.breast.2022.08.010

3. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019;30(8):1194-220. https://doi.org/10.1093/annonc/mdz173

4. Lee A, Mavaddat N, Wilcox AN, Cunningham AP, Carver T, Hartley S, et al. BOADICEA: a comprehensive breast cancer risk prediction model incorporating genetic and nongenetic risk factors. Genet Med. 2019;21(8):1708-18. https://doi.org/10.10 38/s41436-018-0406-9

5. Gulati M, Mulvagh SL. The connection between the breast and heart in a woman: Breast cancer and cardiovascular disease. Clin Cardiol. 2018;41(2):253-7. https://doi.org/10.1002/clc.22886

6. Blaes AH, Konety SH. Cardiovascular disease in breast cancer survivors: an important topic in breast cancer survivorship. J Natl Cancer Inst. 2021;113(2):105-6. https://doi.org/10.1093/jnci/djaa097

7. Darapu A, Balakrishnan R, Sebastian P, Hussain MRK, Ravindran P, John S. Is the deep inspiration breath-hold technique superior to the free breathing technique in cardiac and lung sparing while treating both left-sided post-mastectomy chest wall and supraclavicular regions? Case Rep Oncol. 2017;10(1):37-51. https://doi.org/10.1159/000453607

8. Karpf D, Sakka M, Metzger M, Grabenbauer GG. Left breast irradiation with tangential intensity modulated radiotherapy (t-IMRT) versus tangential volumetric modulated arc therapy (t-VMAT): trade-offs between secondary cancer induction risk and optimal target coverage. Radiat Oncol. 2019;14(1):156. https://doi.org/10.1186/s13014-019-1363-4

9. Hadjittofi C, Almalki H, Mirshekar-Syahkal B, Pain S, Zechmeister K, Hussien M. Simple oncoplastic breast defect closure improves long-term cosmetic outcome of breast conserving surgery for breast cancer: A randomised controlled trial. Breast. 2022;65:104-9. https://doi.org/10.1016/j.breast.2022.07.001

10. Leser C, Tan YY, Singer C, Zeillinger R, Fitzal F, Lehrner J, et al. Patient satisfaction after breast cancer surgery: A prospective clinical trial. Wien Klin Wochenschr. 2021;133(1-2):6-13. https://doi.org/10.1007/s00508-020-01730-w

11. Tasoulis MK, Roche N, MacNeill F. Rationalizing breast cancer surgery during the COVID-19 pandemic. Eur J Surg Oncol. 2020;46(6):1192-3. https://doi.org/10.1016/j.ejso.2020.04.049

12. Wei X, Liu M, Ding Y, Li Q, Cheng C, Zong X, et al. Setup errors and effectiveness of Optical Laser 3D Surface imaging system (Sentinel) in postoperative radiotherapy of breast cancer. Sci Rep. 2018;8(1):7270. https://doi.org/10.1038/s41598-018-25644-w

13. Sun GY, Wen G, Zhang YJ, Tang Y, Jing H, Wang JY, et al. Radiotherapy plays an important role in improving the survival outcome in patients with T1-2N1M0 breast cancer - A joint analysis of 4262 real world cases from two institutions. BMC Cancer. 2020;20(1):1155. https://doi.org/10.1186/s12885-020-07646-y

14. Early Breast Cancer Trialists' Collaborative Group; McGale P, Taylor C, Correa C, Cutter D, Duane F, Ewertz M, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet. 2014;383(9935):2127-35. https://doi.org/10.1016/s0140-6736(14)60488-8

15. Darby SC, McGale P, Taylor CW, Peto R. Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective cohort study of about 300,000 women in US SEER cancer registries. Lancet Oncol. 2005;6(8):557-65. https://doi.org/10.1016/s1470-2045(05)70251-5

16. Abe JI, Martin JF, Yeh ETH. The future of onco-cardiology: We are not just "side effect hunters". Circ Res. 2016;119(8):896-9. https://doi.org/10.1161/circresaha.116.309573

17. Brownlee Z, Garg R, Listo M, Zavitsanos P, Wazer DE, Huber KE. Late complications of radiation therapy for breast cancer: evolution in techniques and risk over time. Gland Surg. 2018;7(4):371-8. https://doi.org/10.21037/gs.2018.01.05

18. Lee MS, Liu DW, Hung SK, Yu CC, Chi CL, Chiou WY, et al. Emerging challenges of radiation-associated cardiovascular dysfunction (RACVD) in modern radiation oncology: clinical

practice, bench investigation, and multidisciplinary care. Front Cardiovasc Med. 2020;7:16. https://doi.org/10.3389/fcvm.2020.00016

19. Báez-Ferrer N, Izquierdo-Gómez MM, Beyello-Belkasem C, Jorge-Pérez P, García-González MJ, Ferrer-Hita JJ, et al. Long-term radiotherapy-induced cardiac complications: a case report. Am J Case Rep. 2019;20:1182-8. https://doi.org/10.12659/ajcr.917224

20. Dell'Oro M, Giles E, Sharkey A, Borg M, Connell C, Bezak E. A retrospective dosimetric study of radiotherapy patients with left-sided breast cancer; patient selection criteria for deep inspiration breath hold technique. Cancers (Basel). 2019;11(2):259. https://doi.org/10.3390/cancers11020259

21. Ramin C, Schaeffer ML, Zheng Z, Connor AE, Hoffman-Bolton J, Lau B, et al. All-cause and cardiovascular disease mortality among breast cancer survivors in CLUE II, a long-standing community-based cohort. J Natl Cancer Inst. 2021; 113(2):137-45. https://doi.org/10.1093/jnci/djaa096

22. Díaz-Gavela AA, Figueiras-Graillet L, Luis ÁM, Segura JS, Ciérvide R, Del Cerro Peñalver E, et al. Breast radiotherapy-related cardiotoxicity. When, how, why. risk prevention and control strategies. Cancers (Basel). 2021;13(7):1712. https://doi.org/10.3390/cancers13071712

23. Cheng YJ, Nie XY, Ji CC, Lin XX, Liu LJ, Chen XM, et al. Long-term cardiovascular risk after radiotherapy in women with breast cancer. J Am Heart Assoc. 2017;6(5):e005633. https://doi.org/10.1161/jaha.117.005633

24. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil, H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis. JBI; 2020 [cites 2025 Jan 17]. Available from: http://dx.doi.org/10.46658/JBIMES-20-12

25. Fineout-Overholt E, Melnyk BM, Stillwell SB, Williamson KM. Evidence-based practice, step by step: Critical appraisal of the evidence: part III. Am J Nurs. 2010;110(11):43-51. https://doi.org/10.1097/01.naj.0000390523.99066.b5

26. Gaál S, Kahán Z, Paczona V, Kószó R, Drencsényi R, Szabó J, et al. Deep-inspirational breath-hold (DIBH) technique in left-sided breast cancer: various aspects of clinical utility. Radiat Oncol. 2021;16(1):89. https://doi.org/10.1186/s13014-021-01816-3

27. Rudat V, Zhao R, Wang B, Zhang L, Shi Y. Impact of deep inspiration breath hold, surface-guided radiotherapy, and daily CBCT on the organs at risk in breast cancer radiotherapy. Sci Rep. 2024;14(1):27814. https://doi.org/10.1038/s41598-024-77482-8

28. Quintero-Martinez JA, Cordova-Madera SN, Villarraga HR. Radiation-induced heart disease. J Clin Med. 2021;11(1):146. https://doi.org/10.3390/jcm11010146

29. Piroth MD, Baumann R, Budach W, Dunst J, Feyer P, Fietkau R, et al. Heart toxicity from breast cancer radiotherapy: Current findings, assessment, and prevention. Strahlenther Onkol. 2019;195(1):1-12. https://doi.org/10.1007/s00066-018-1378-z

30. Taylor C, McGale P, Brønnum D, Correa C, Cutter D, Duane FK, et al. Cardiac structure injury after radiotherapy for breast cancer: cross-sectional study with individual patient data. J Clin Oncol. 2018;36(22):2288-96. https://doi.org/10.1200/jco.2017.77.6351

31. Zhao F, Shen J, Lu Z, Luo Y, Yao G, Bu L, et al. Abdominal DIBH reduces the cardiac dose even further: a prospective analysis. Radiat Oncol. 2018;13(1):116. https://doi.org/10.1186/s13014-018-1062-6

32. Gaasch A, Schönecker S, Simonetto C, Eidemüller M, Pazos M, Reitz D, et al. Heart sparing radiotherapy in breast cancer: the importance of baseline cardiac risks. Radiat Oncol. 2020;15(1):117. https://doi.org/10.1186/s13014-020-01520-8

33. Siaravas KC, Katsouras CS, Sioka C. Radiation treatment mechanisms of cardiotoxicity: a systematic review. Int J Mol Sci. 2023;24(7):6272. https://doi.org/10.3390/ijms24076272

34. Duma MN, Baumann R, Budach W, Dunst J, Feyer P, Fietkau R, et al. Heart-sparing radiotherapy techniques in breast cancer patients: a recommendation of the breast cancer expert panel of the German society of radiation oncology (DEGRO). Strahlenther Onkol. 2019;195(10):861-71. https://doi.org/10.1007/s00066-019-01495-w

35. Buwenge M, Cammelli S, Ammendolia I, Tolento G, Zamagni A, Arcelli A, et al. Intensity modulated radiation therapy for breast cancer: current perspectives. Breast Cancer (Dove Med Press). 2017;9:121-6. https://doi.org/10.2147/bctt.s113025

36. Hussein SH, Kassem L, Adrosy MI, Metwally H. Comparison between breath-hold and the inspiratory phase of free breathing in left breast cancer radiotherapy: target volume coverage and organ sparing. Asian Pac J Cancer Prev. 2025; 26(3):969-75. https://doi.org/10.31557/apjcp.2025.26.3.969

37. Altınok P, Korkmaz L, Altınok A, Beşe N. Were we able to reduce cardiac doses in breast cancer radiotherapy over time? Eur J Breast Health. 2021;17(2):145-9. https://doi.org/10.4274/ejbh.galenos.2021.6148

38. Wang SJ, Zhai YR, Zhang WW, Chen SY, Qin SR, Fang H, et al. Dosimetric benefit and clinical feasibility of deep inspiration breath-hold and volumetric modulated arc therapy-based postmastectomy radiotherapy for left-sided breast cancer. Sci Rep. 2024;14(1):24638. https://doi.org/10.1038/s41598-024-75560-5

39. Corradini S, Alongi F, Andratschke N, Belka C, Boldrini L, Cellini F, et al. MR-guidance in clinical reality: current treatment challenges and future perspectives. Radiat Oncol. 2019; 14(1):92. https://doi.org/10.1186/s13014-019-1308-y

40. De Rose F, De Santis MC, Lucidi S, Colciago RR, Marino L, Cucciarelli F, et al. Dose constraints in breast cancer radiotherapy. A critical review. Radiother Oncol. 2025;202:110591. https://doi.org/10.1016/j.radonc.2024.110591

41. Salvestrini V, Iorio GC, Borghetti P, De Felice F, Greco C, Nardone V, et al. The impact of modern radiotherapy on long-term cardiac sequelae in breast cancer survivor: a focus on deep inspiration breath-hold (DIBH) technique. J Cancer Res Clin Oncol. 2022;148(2):409-17. https://doi.org/10.1007/s00432-021-03875-1

42. Racka I, Majewska K, Winiecki J. Three-dimensional conformal radiotherapy (3D-CRT) vs. volumetric modulated arc therapy (VMAT) in deep inspiration breath-hold (DIBH) technique in left-sided breast cancer patients-comparative analysis of dose distribution and estimation of projected secondary cancer risk. Strahlenther Onkol. 2023;199(1):90-101. https://doi.org/10.1007/s00066-022-01979-2

43. Chen M, Zang S, Yu H, Ning L, Huang H, Bu L, et al. Immobilization-assisted abdominal deep inspiration breath-hold in post-mastectomy radiotherapy of left-sided breast cancer with internal mammary chain coverage. Quant Imaging Med Surg. 2021;11(7):3314-26. https://doi.org/10.21037/qims-20-831

44. Abubakar A, Shaukat SI, Karim NKA, Kassim MZ, Lim SY, Appalanaido GK, et al. Accuracy of a time-of-flight (ToF) imaging system for monitoring deep-inspiration breath-hold radiotherapy (DIBH-RT) for left breast cancer patients. Phys Eng Sci Med. 2023;46(1):339-52. https://doi.org/10.1007/s13246-023-01227-6

45. Lai J, Hu S, Luo Y, Zheng R, Zhu Q, Chen P, et al. Meta-analysis of deep inspiration breath hold (DIBH) versus free breathing (FB) in postoperative radiotherapy for left-side breast cancer. Breast Cancer. 2020;27(2):299-307. https://doi.org/10.1007/s12282-019-01023-9

46. Li Z, Jian C, Li Y, Pan Z, Yang G, Sun X. Clinical benefits of deep inspiration breath-hold in postoperative radiotherapy for right-sided breast cancer: a meta-analysis. BMC Cancer. 2024;24(1):1238. https://doi.org/10.1186/s12885-024-12992-2

47. Nissen HD, Appelt AL. Improved heart, lung and target dose with deep inspiration breath hold in a large clinical series of breast cancer patients. Radiother Oncol. 2013;106(1): 28-32. https://doi.org/10.1016/j.radonc.2012.10.016

48. Mahmoud AA, Sadaka EA, Abouegylah M, Amin SA, Elmansy H, Asal MF, et al. Impact of breath-hold technique on incidence of cardiac events in adjuvant left breast cancer irradiation. J Cancer Res Clin Oncol. 2023;149(9):5853-9. https://doi.org/10.1007/s00432-022-04551-8

49. Smyth LM, Knight KA, Aarons YK, Wasiak J. The cardiac dose-sparing benefits of deep inspiration breath-hold in left breast irradiation: a systematic review. J Med Radiat Sci. 2015;62(1):66-73. https://doi.org/10.1002/jmrs.89

50. Parkes M, Cashmore J, Green S, Clutton-Brock T, Van Dijk I, van Kesteren Z, et al. Defining short and prolonged breath-holds. Br J Radiol. 2020;93(1111):20200191. https://doi.org/10.1259/bjr.20200191

51. Malone C, Fennell L, Folliard T, Kelly C. Using a neural network to predict deviations in mean heart dose during the treatment of left-sided deep inspiration breath hold patients. Phys Med. 2019;65:137-42. https://doi.org/10.1016/j.ejmp.2019.08.014

52. Rudat V, Shi Y, Zhao R, Yu W. Setup margins based on the inter- and intrafractional setup error of left-sided breast cancer radiotherapy using deep inspiration breath-hold technique

(DIBH) and surface guided radiotherapy (SGRT). J Appl Clin Med Phys. 2024;25(6):e14271. https://doi.org/10.1002/acm2.14271

53. Rajurkar SA, Verma T, Gupta R. Estimation of heart dose in left breast cancer radiotherapy: Assessment of vDIBH feasibility using the supervised machine learning algorithm. J Appl Clin Med Phys. 2025;26(2):e14595. https://doi.org/10.1002/acm2.14595

54. Zheng Y, Liu X, Wang J, Lin R, Liu X, Yuan T, et al. Challenges and benefits of implementing DIBH for breast cancer radiotherapy: Experiences from Guangzhou Concord Cancer Center. Vis Cancer Med. 2023;4:8. https://doi.org/10.1051/vcm/2023005

55. Pang WYC, Yu KS, Loke AY. Cardiac dose comparison of abdominal and thoracic deep inspiration breath hold in adult female with left-sided breast cancer receiving radiation therapy: A systematic review and meta-analysis. Radiography (Lond). 2025;31(1):426-33. https://doi.org/10.1016/j.radi.2024.12.013

56. Wolf J, Stoller S, Lübke J, Rothe T, Serpa M, Scholber J, et al. Deep inspiration breath-hold radiation therapy in left-sided breast cancer patients: a single-institution retrospective dosimetric analysis of organs at risk doses. Strahlenther Onkol. 2023;199(4):379-88. https://doi.org/10.1007/s00066-022-01998-z

57. Borgonovo G, Paulicelli E, Daniele D, Presilla S, Richetti A, Valli M. Deep inspiration breath hold in post-operative radiotherapy for right breast cancer: a retrospective analysis. Rep Pract Oncol Radiother. 2022;27(4):717-23. https://doi.org/10.5603/rpor.a2022.0085

58. Stowe HB, Andruska ND, Reynoso F, Thomas M, Bergom C. Heart sparing radiotherapy techniques in breast cancer: a focus on deep inspiration breath hold. Breast Cancer (Dove Med Press). 2022;14:175-86. https://doi.org/10.2147/bctt.s282799

59. Falco M, Masojć B, Macała A, Łukowiak M, Woźniak P, Malicki J. Deep inspiration breath hold reduces the mean heart dose in left breast cancer radiotherapy. Radiol Oncol. 2021;55(2):212-20. https://doi.org/10.2478/raon-2021-0008

60. Kalet AM, Kim A, Hippe DS, Lo SS, Fang LC, Meyer J, et al. The dosimetric benefit of in-advance respiratory training for deep inspiration breath holding is realized during daily treatment in left breast radiotherapy: A comparative retrospective study of serial surface motion tracking. J Med Imaging Radiat Oncol. 2021;65(3):354-64. https://doi.org/10.1111/1754-9485.13181

61. Ferdinand S, Mondal M, Mallik S, Goswami J, Das S, Manir KS, et al. Dosimetric analysis of Deep Inspiratory Breath-hold technique (DIBH) in left-sided breast cancer radiotherapy and evaluation of pre-treatment predictors of cardiac doses for guiding patient selection for DIBH. Tech Innov Patient Support Radiat Oncol. 2021;17:25-31. https://doi.org/10.1016/j.tipsro.2021.02.006

62. Reitz D, Walter F, Schönecker S, Freislederer P, Pazos M, Niyazi M, et al. Stability and reproducibility of 6013 deep inspiration breath-holds in left-sided breast cancer. Radiat Oncol. 2020;15(1):121. https://doi.org/10.1186/s13014-020-01572-w

63. Simonetto C, Eidemüller M, Gaasch A, Pazos M, Schönecker S, Reitz D, et al. Does deep inspiration breath-hold prolong life? Individual risk estimates of ischaemic heart disease after breast cancer radiotherapy. Radiother Oncol. 2019;131:202-7. https://doi.org/10.1016/j.radonc.2018.07.024

64. Testolin A, Ciccarelli S, Vidano G, Avitabile R, Dusi F, Alongi F. Deep inspiration breath-hold intensity modulated radiation therapy in a large clinical series of 239 left-sided breast cancer patients: a dosimetric analysis of organs at risk doses and clinical feasibility from a single center experience. Br J Radiol. 2019;92(1101):20190150. https://doi.org/10.1259/bjr.20190150

65. Schröder C, Kirschke S, Blank E, Rohrberg S, Förster R, Buchali A. Deep inspiration breath-hold for patients with left-sided breast cancer - A one-fits-all approach? A prospective analysis of patient selection using dosimetrical and practical aspects. Br J Radiol. 2022;95(1135):20210295. https://doi.org/10.1259/bjr.20210295

66. Zhu H, Sun H, Zhang J, Xie Y, Jassem J, Franco P, et al. Cardiac exposure in left-sided breast cancer patients undergoing deep inspiratory breath hold radiation therapy. Gland Surg. 2023;12(5):677-86. https://dx.doi.org/10.21037/gs-23-160

67. Swathi B, Backianathan S, Rafic KM, Joel T, Varghese SS, Patricia S, et al. How effective is deep inspiration breath hold in minimizing cardiac doses during hybrid radiotherapy treatment for left-sided breast cancer with comprehensive regional nodes? Asian Pac J Cancer Prev. 2024;25(9):3301-10. https://doi.org/10.31557/apjcp.2024.25.9.3301

68. Knöchelmann AC, Ceylan N, Bremer M. Left-sided breast cancer irradiation with deep inspiration breath-hold: changes in heart and lung dose in two periods. In Vivo. 2022;36(1): 314-24. https://doi.org/10.21873/invivo.12704

69. Melo MDL. Análise comparativa das doses cardíacas recebidas por pacientes com câncer de mama esquerda planejadas com duas formas alternativas de delineamento do CTV da cadeia mamária interna [tese]. São Paulo: Fundação Antônio Prudente; 2023. https://tinyurl.com/a5tnnysj

70. Leoni ACBP, Alves GAA, Santos FXS, Sbaraini P, Gonzaga AL, Barletta D. Impacto da técnica de retenção do fôlego na dose cardíaca e pulmonar em pacientes submetidos à radioterapia da mama esquerda. Rev Bras Fis Med. 2024;18: 800. https://doi.org/10.29384/rbfm.2024.v18.19849001800

Data Availability Statement

Research data is not available.