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ORIGINAL RESEARCH

Deep Inspiration Breath Hold in Left-Sided Breast Radiotherapy

A Balance Between Side Effects and Costs

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ABSTRACT

BACKGROUND Deep inspiration breath hold (DIBH) is an effective technique for reducing heart exposure during radiotherapy for left-sided breast cancer. Despite its benefits, cost considerations and its impact on workflow remain significant barriers to widespread adoption.

OBJECTIVES This study aimed to assess the cost-effectiveness of DIBH and compare its operational, financial, and clinical outcomes with free breathing (FB) in breast cancer treatment.

METHODS Treatment plans for 100 patients with left-sided breast cancer were generated using both DIBH and FB techniques. Dosimetric data, including the average mean heart dose, were calculated for each technique and used to estimate the cardiotoxicity of radiotherapy. A state-transition microsimulation model based on SCORE2 (Systematic Coronary Risk Evaluation) algorithms projected the effects of DIBH on cardiovascular outcomes and quality-adjusted life-years (QALYs). Costs were calculated from a provider perspective using time-driven activity-based costing, applying a willingness-to-pay threshold of €40,000 for cost-effectiveness assessment. A discrete event simulation model assessed the impacts of DIBH vs FB on throughput and waiting times in the radiotherapy workflow.

RESULTS In the base case scenario, DIBH was associated with an absolute risk reduction of 1.72% (95% CI: 1.67%-1.76%) in total cardiovascular events and 0.69% (95% CI: 0.67%-0.72%) in fatal cardiovascular events over 20 years. Additionally, DIBH was estimated to provide an incremental 0.04 QALYs (95% CI: 0.05-0.05) per left-sided breast cancer patient over the same time period. However, DIBH increased treatment times, reducing maximum achievable throughput by 12.48% (95% CI: 12.36%-12.75%) and increasing costs by €617 per left-sided breast cancer patient (95% CI: €615-€619). The incremental cost-effectiveness ratio was €14,023 per QALY.

CONCLUSIONS Despite time investments, DIBH is cost-effective in the Belgian population. The growing adoption of DIBH may benefit long-term cardiovascular health in breast cancer survivors. (JACC CardioOncol 2024;6:514–525) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Radiotherapy (RT) has been a pillar of the multimodality treatment for breast cancer ever since breast conservation therapy transformed the management of early breast cancer.[1] Landmark clinical studies have demonstrated that RT reduces local recurrence rates by half and breast cancer-specific mortality by approximately one-sixth.[2] However, long-term follow-up studies have highlighted the necessity of balancing these benefits against an increased risk of cardiac morbidity and mortality.[3] RT for breast cancer, especially when targeting the left breast,[4] often results in incidental radiation exposure to the heart, potentially leading to treatment-induced cardiotoxicity. Darby et al[5] showed that the risk of major coronary events increases linearly with the mean dose to the heart at a rate of 7.4% per Gy. This heightened cardiovascular risk can manifest within a few years after exposure and persist for at least 2 decades. Given the absence of a recognized safe lower threshold, any reduction in unintended radiation exposure is advantageous for patients. Efforts should be particularly focused on patients with pre-existing cardiac risk factors because their higher baseline risk results in more substantial absolute increases in risk after RT.

Because of advancements in breast cancer survival, the majority of patients are living longer, at least 1 decade after their diagnosis.[6] Consequently, reducing late iatrogenic side effects has become a primary concern, leading to the development of heart-sparing RT techniques, notably deep inspiration breath hold (DIBH).[7] With DIBH, patients hold their breath during RT, effectively displacing the heart from the radiation field.[8] The superior dosimetric performance of DIBH over free breathing (FB) has been confirmed in a meta-analysis,[9] and the technique is increasingly embraced by the radiation oncology community.[10] However, adoption rates vary across different countries, with some experiencing slower uptake.[11,12] Financial investments and the potential impacts on workflow represent significant barriers to widespread implementation.[13] DIBH necessitates specialized equipment and may require more labor-intensive procedures, potentially affecting treatment duration and patient throughput.[14,15] Moreover, there remains uncertainty regarding whether the dosimetric advantages of DIBH will translate into a meaningful reduction in cardiovascular risk.[16]

A comprehensive evaluation of the benefits and challenges associated with implementing DIBH requires a systematic analysis of its impact on both RT departments and patients. This research aims to provide such an analysis, focusing on assessing the cost-effectiveness of DIBH and comparing its operational outcomes with those of FB during RT.

METHODS

To examine the operational and financial implications of DIBH for RT departments, we integrated data from a time-driven activity-based costing (TD-ABC) study into a discrete event simulation (DES) model of the RT workflow. TD-ABC provides detailed insights into costs, resource consumption, and work times at the patient level,[17] making it well suited for RT analysis.[18] Implementing TD-ABC involves estimating 2 key parameters: the capacity cost rate (CCR), representing the cost of each resource divided by its practical capacity, and the duration of each care activity. These parameters were incorporated into a DES model depicting the care pathway for breast cancer patients within the RT department. DES is a versatile individual-level modeling technique that allows for the representation of patient flow and resource use within health care systems.[19]

A state-transition microsimulation (STMS) model was constructed to estimate the effects of DIBH on quality-adjusted life-years (QALYs). The baseline risk of cardiovascular disease before undergoing RT was assessed using validated SCORE2 (Systematic Coronary Risk Evaluation) and SCORE2-OP (Systematic Coronary Risk Evaluation-Older Persons) algorithms.[20,21] These algorithms address limitations of earlier models[22] and provide more accurate estimations of total cardiovascular disease burden by including both fatal and nonfatal outcomes. To estimate cardiovascular outcomes associated with FB and DIBH, an excess cardiovascular disease rate ratio of 7.4% per Gy was applied to account for the cardiotoxic effect of RT.[5] It is important to note that this study was exempt from institutional ethics review because of its retrospective nature, using data from our internal data bank on quality assurance in treatment planning.

DES MODEL. TD-ABC analysis. The TD-ABC analysis was conducted at a Belgian academic hospital following the methodology described by Kaplan and Anderson[23] (Supplemental Methods). Briefly stated, the analysis involved creating process maps of all care activities; measuring the time of each process; and estimating the cost, practical

ABBREVIATIONS AND ACRONYMS

CCR = capacity cost rate
CT = computed tomography
DES = discrete event simulation
DIBH = deep inspiration breath hold
FB = free breathing
HF = hypofractionation
ICER = incremental cost-effectiveness ratio
LINAC = linear accelerator
MHD = mean heart dose
RT = radiotherapy
RTT = radiation treatment technician
STMS = state-transition microsimulation
TD-ABC = time-driven activity-based costing
UHF = ultra-hypofractionation
WTP = willingness-to-pay

TABLE 1 Capacity Cost Rates of Resources

Resource	Cost per min (€, 2024)
Physician	1.78
Physicist	0.92
Radiotherapy treatment technician	0.60
Linear accelerator	3.69
DIBH equipment	1.52
Computed tomography scanner	2.52

The capacity cost rate for each resource indicates the cost per unit of time that the resource is available in patient care. Costs are expressed in 2024 euros per minute.

DIBH = deep inspiration breath hold.

capacity, and CCR of the main resources needed for RT treatments. Resource costs for RT treatments were obtained from hospital financial records and subsequently converted into CCRs (Table 1).

Model development. A validated DES model (Supplemental Table 1) of the RT care delivery pathway[24] was used to assess the operational implications of DIBH. The model included patients with both left-sided and right-sided breast cancer. It compared scenarios in which patients with left-sided breast cancer underwent either FB or DIBH, whereas patients with right-sided breast cancer were treated with FB in both scenarios. The effects on operational outcomes were investigated by increasing the yearly patient volume in increments of 250 patients per year and recording key metrics, including the number of patients treated per year and the percentage of patients exceeding clinically relevant waiting time targets. Waiting time targets of 4 weeks and 20 weeks were selected because of their importance for local control and breast cancer-specific survival, respectively.[25]

The model was developed based on process maps (Supplemental Figures 1 and 2) illustrating RT patient flow designed in accordance with the ISPOR-SMDM (International Society for Pharmacoeconomics and Outcomes Research-Society for Medical Decision Making) guidelines[26] and implemented using Simul8 (SIMUL8 Corporation). Extensive verification and external validation (Supplemental Methods), along with face validity confirmed by RT experts, ensured model accuracy. The simulation spanned a period of 1 year, with a 3-month start-up period determined through warm-up analysis. The required number of replications to achieve 95% precision in outcomes was computed using the Simul8 trial calculator. Detailed model parameters and their sources are listed in Supplemental Table 2. Comprehensive sensitivity analyses were conducted to assess the robustness of the model.

TABLE 2 Patient Characteristics and Dosimetric Results

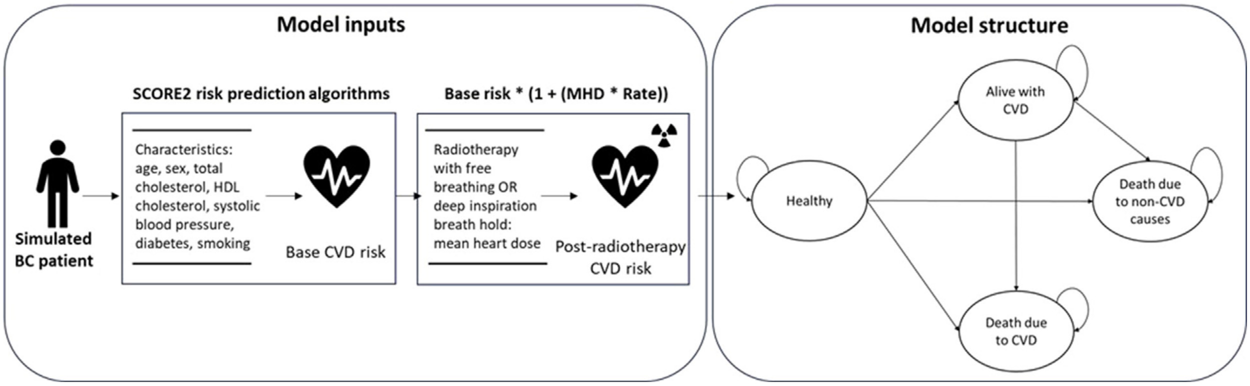
Demographics	
Age, y	58.87 ± 12.03
Female	98
Mean heart dose, Gy	
Deep inspiration breath hold	1.78 ± 1.03
Free breathing	4.33 ± 2.25
Fractionation schedule, Gy	Dose, % of total
5 × 5.2	1
5 × 5.0-6.0	1
5 × 5.0-6.2	5
15 × 2.67	27
15 × 2.8	1
15 × 2.67-3.2	54
15 × 2.67-3.4	1
25 × 2	1
25 × 2-2.4	5
25 × 2-2.6	3
35 × 2 Gy	1

Values are mean ± SD or %. Data presented are based on a sample of 100 left-sided breast cancer patients.

Scenario analysis. The operational and financial outcomes of RT can be significantly affected by the distribution of fractionation regimens.[24,27] Consequently, the influence of DIBH on these outcomes may vary depending on the applied fractionation schedule. To examine this impact, we used the observed schedule as a base case and systematically adjusted this parameter. In the base case, most patients received moderate hypofractionation (HF), which consists of a 3-week, 15-fraction regimen delivering 39 to 42 Gy. The remainder underwent either conventional fractionation, a 5-week, 25-fraction regimen delivering 50 Gy, or ultrahypofractionation (UHF), a 1-week, 5-fraction regimen delivering 26 to 28 Gy (Supplemental Table 1). To examine the influence of different fractionation schedules, we created 3 additional scenarios: treating all patients with UHF, HF, or conventional fractionation (100% application of each regimen). The results of this scenario analysis are presented in the Supplemental Figures 3 and 4.

STMS MODEL. Patient sample. The patient inclusion criteria comprised individuals who were diagnosed with left-sided breast cancer, underwent treatment using DIBH, and had an FB computed tomography (CT) scan available. A total of 100 consecutive retrospective patients met these criteria. Treatment plans using DIBH and FB techniques were developed for each patient, and the mean heart dose (MHD) was calculated for both techniques (Table 2). Planning was conducted with

FIGURE 1 **State-Transition Microsimulation Model**



The baseline risk of cardiovascular disease is determined using the SCORE2 (Systematic Coronary Risk Evaluation) algorithms, and the risk of cardiovascular disease (CVD) after radiotherapy (RT) is calculated based on the simulated patient's mean heart dose (MHD) using the specified equation. The MHD values are sourced from Supplemental Table 3. The excess CVD rate ratio (Rate) used to account for the cardiotoxic effect of RT is equal to 7.4% per Gy (95% CI: 2.9%-14.5%).[49] The ellipses in the model structure represent the 4 health states within the model. All patients begin the simulation in the healthy state and may transition between states each year based on patient-specific transition probabilities indicated by the arrows. BC = breast cancer; HDL = high-density lipoprotein.

Eclipse v15.6 (Varian) using a hybrid technique that combines tangential fields with surface compensation and a volumetric modulated arc therapy arc for boosting. The anisotropic analytical algorithm calculation algorithm was used for these calculations. The dosimetric data were used to estimate the cardiotoxicity of RT (Supplemental Table 3). Additionally, patient demographics, including age (Supplemental Figure 5) and sex, were recorded and incorporated into the STMS model.

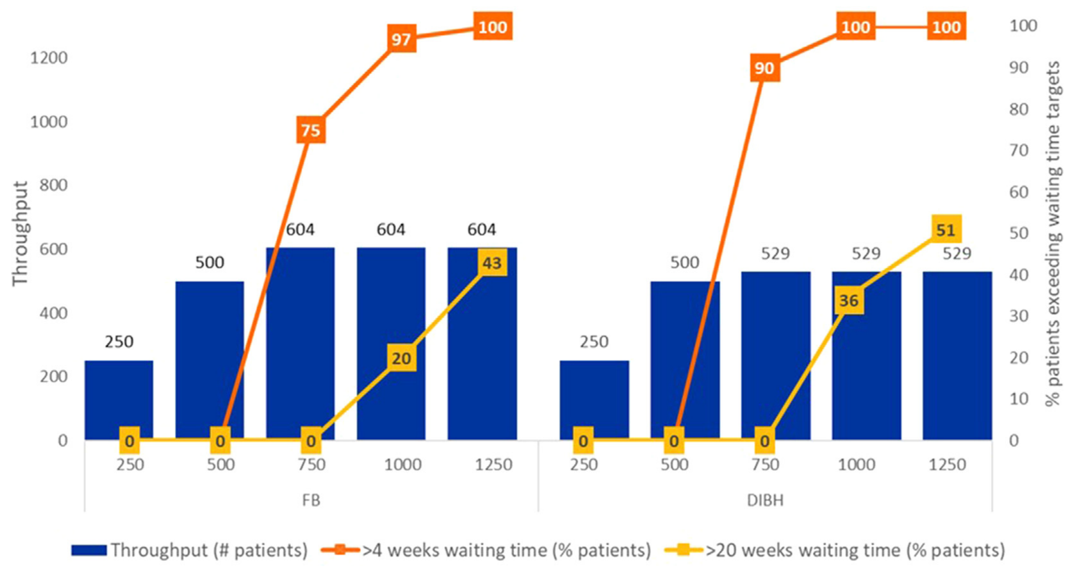
Model development. The model was constructed in accordance with ISPOR-SMDM recommendations[28] and implemented using Simul8. The study compared 2 treatment strategies: RT using DIBH vs FB.

The model is structured around 4 mutually exclusive health states: "healthy" (post-RT), "alive with cardiovascular disease," "death caused by cardiovascular disease," and "death caused by non-cardiovascular disease causes" (**Figure 1**). All patients start in the healthy state and progress through the model based on individual-specific transition probabilities. These transition probabilities as well as state utility values are dynamically updated based on patient attributes throughout the simulation. After a nonfatal cardiovascular disease event, patients transition to the alive with cardiovascular disease state. In the event of a fatal cardiovascular disease occurrence, patients transition directly to the death caused by cardiovascular disease state. Patients who experience a nonfatal cardiovascular disease event remain at risk of recurrent cardiovascular disease events, which can be fatal or nonfatal. Additionally, patients remain at risk of death from other causes, including diseases such as breast cancer.

The model uses a 1-year cycle length and a 20-year time horizon to reflect the known period during which cardiotoxic effects of RT may manifest.[5] The simulation was executed 10,000 times to account for stochastic uncertainty, with results presented as 95% CIs around average model outcomes.

Transition probabilities. The baseline total 10-year risk of first-onset cardiovascular disease was calculated using the SCORE2 risk prediction algorithms (Supplemental Figures 6 and 7; Supplemental Table 4). Subsequently, the formula shown in **Figure 1** was applied to calculate the 10-year risk of cardiovascular disease after RT (Supplemental Figure 8), which was then converted into 1-year event probabilities (Supplemental Figure 9).[29] Age and sex data were obtained from the patient sample, whereas other required inputs for the SCORE2 algorithms were acquired from the Belgian Health Examination Survey[30] (Supplemental Figure 5 and Supplemental Table 5). The main outcome of the SCORE2 algorithms provides a composite of fatal and nonfatal cardiovascular disease events. Given that the ratio of fatal cardiovascular disease to total cardiovascular disease varies significantly by age and sex,[31] cardiovascular disease mortality rates were derived using age- and sex-specific ratios (Supplemental Table 6). Additional details regarding the calculation for the risk of cardiovascular disease can be found in the Supplemental Methods.

FIGURE 2 **Throughput and Percentage of Patients Exceeding Waiting Time Targets (Base Case)**



The bars indicate the achieved throughput (the total number of patients treated per year). The lines represent the percentage of patients exceeding the 4-week (shown in orange) and 20-week (shown in yellow) waiting time target. The results reflect trial averages. DIBH = deep inspiration breath hold; FB = free breathing.

Survivors of cardiovascular disease events are at an increased risk of subsequent events,[32] necessitating the inclusion of recurrence in the model. The EUROASPIRE (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) Risk model[33] was used to estimate the 1-year risk of recurrent fatal or nonfatal cardiovascular disease events (Supplemental Table 7). Lastly, age-specific probabilities of death from other causes were derived from a recent population-based analysis[34] (Supplemental Table 8).

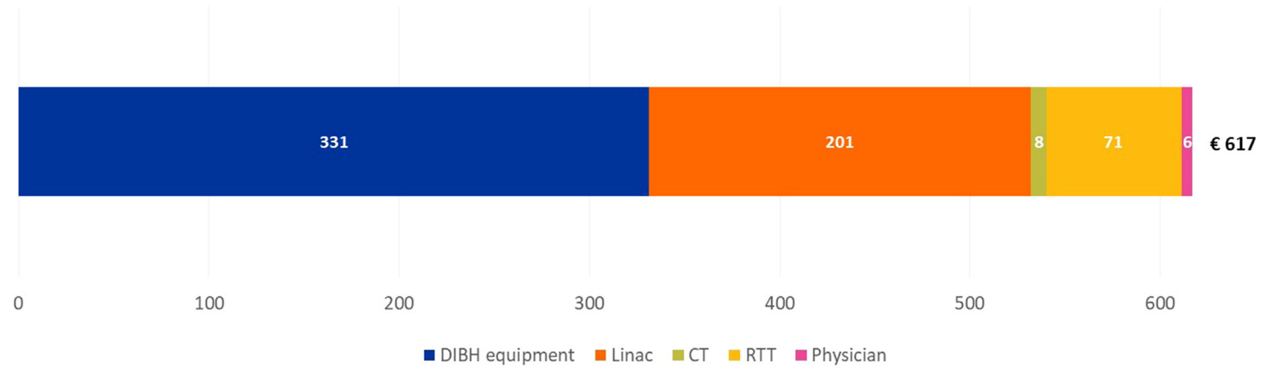
Utilities. Breast cancer survivors demonstrate a comparable overall health-related quality of life with their age-matched counterparts in the general population.[35] Therefore, utility values for the healthy state were obtained from a recent representative survey of the Belgian population[36] (Supplemental Table 9). Nonfatal cardiovascular disease events can have a lasting impact on health-related quality of life with effects that vary over time. Utility decrements based on the time since the event were obtained from a prospective longitudinal study and applied to the alive with cardiovascular disease state[37] (Supplemental Table 10). Both death states were assigned a utility value of 0 to reflect the absence of quality of life.

Study outcomes. The primary outcome of this study was to quantify the QALYs gained through the use of DIBH. Consistent with Belgian national guidelines, QALYs were discounted at a rate of 1.5% per annum.[38] The secondary outcomes included assessing absolute risk reductions in both nonfatal and fatal cardiovascular disease events. Additionally, the number needed to treat was calculated as the inverse of the absolute risk reductions. To assess the cost-effectiveness of DIBH, a willingness-to-pay (WTP) threshold of €40,000 was applied, aligning with common Belgian practice.[39] In the Supplemental Methods, we explore the generalizability of our findings across diverse health care markets by examining various pertinent WTP thresholds and presenting a comprehensive overview of the conducted sensitivity analyses (Supplemental Table 11 and 12).

RESULTS

OPERATIONAL OUTCOMES. In the RT department under study, DIBH was implemented during treatment after a simulation phase. Consequently, the use of DIBH resulted in extended durations of these treatment phases and increased the workload for the necessary resources. Specifically, DIBH led to person-hours of 1.97 (95% CI: 1.90-2.03) for radiation treatment technicians (RTTs) and 0.06 (95% CI: 0.04-0.07) for physicians. Additionally, there were extra

FIGURE 3 Mean Additional Cost of DIBH (Base Case)



This figure illustrates the average additional cost of radiotherapy with deep inspiration breath hold (DIBH) compared to free breathing for left-sided breast cancer patients. The total additional cost per patient is presented to the right of each bar in the chart, with the contribution of each resource detailed within the bars. Results reflect trial averages. CT = computed tomography; DIBH = deep inspiration breath hold; Linac = linear accelerator; RTT = radiation treatment technician.

productive machine-hours of 0.46 (95% CI: 0.43-0.49) for the linear accelerator (LINAC) and 0.053 (95% CI: 0.05-0.06) for the CT scanner.

The implementation of DIBH resulted in increased work time, leading to a decrease of 12.48% (95% CI: 12.36%-12.75%) in maximum achievable throughput. **Figure 2** displays the achieved throughput across varying levels of patient volume. The demands imposed by DIBH on resources suggest that a higher percentage of patients exceed waiting time targets when patient volume is high. Notably, throughput and waiting times are influenced by the adopted fractionation schedule. Supplemental Figure 3 demonstrates that a 100% application of UHF yields the highest throughput with no excessive delays observed under this schedule.

COSTS. The mean cost per left-sided breast cancer patient increased by €617 (95% CI: €615-€619) because of the capital investment required for implementing DIBH and the higher use of the LINAC, CT scanner, and RTTs (**Figure 3**). Sensitivity analysis results are depicted in tornado diagrams in **Figure 4**.

The cost difference between FB and DIBH varies with the fractionation schedule applied (Supplemental Figure 4). Specifically, the smallest cost difference occurs with UHF for all patients, whereas the largest difference is observed with a 100% application of conventional fractionation. This trend reflects the impact of fractionation on treatment duration and resource use, particularly for RTTs, LINAC, and DIBH equipment.

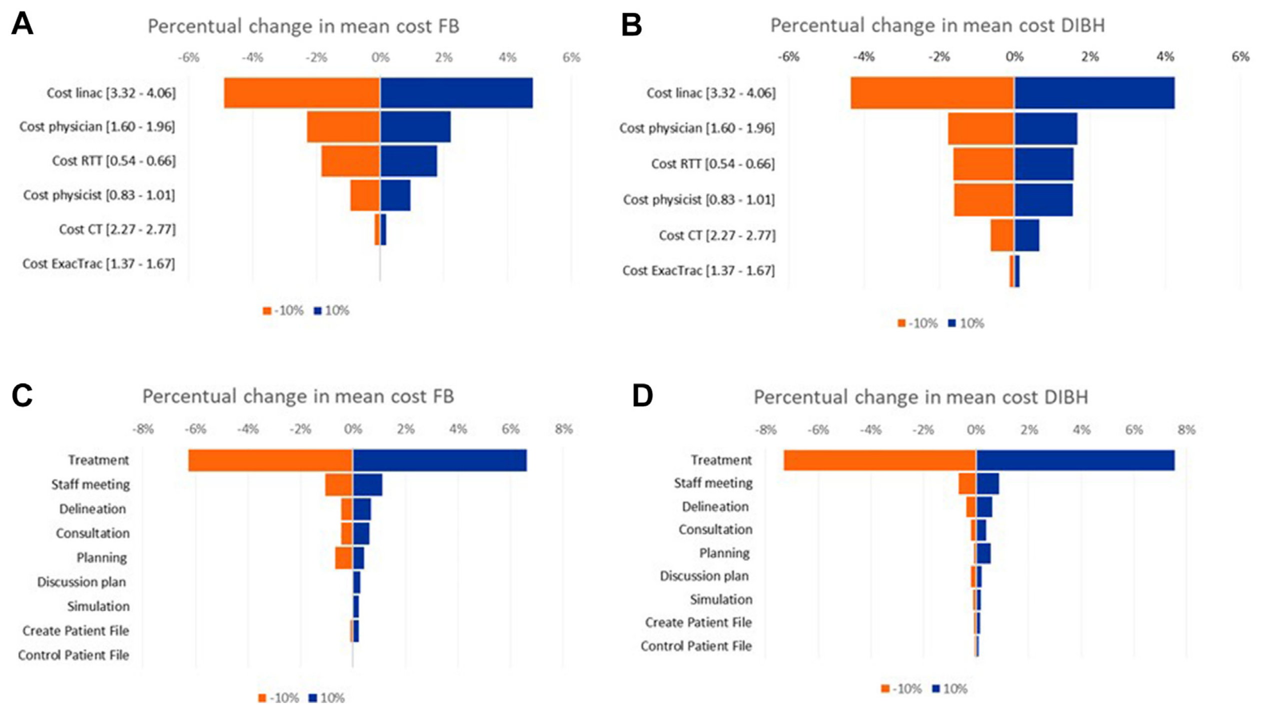
DOSIMETRIC AND CLINICAL OUTCOMES. Dosimetric results revealed a significant difference in MHD between DIBH and FB treatment plans ($P < 0.001$), with DIBH demonstrating an average reduction of 2.55 Gy in MHD compared to FB (95% CI: 2.25-2.85) (**Table 2**) (Supplemental Table 13).

In the base case, the application of DIBH led to an additional 0.04 QALYs (95% CI: 0.04-0.05) per left-sided breast cancer patient over 20 years, yielding an incremental cost-effectiveness ratio (ICER) of €14,023 per QALY (€617 per 0.04 QALYs). Deterministic sensitivity analysis results are depicted in a tornado diagram (**Figure 5**), whereas probabilistic sensitivity analysis outcomes are illustrated in a cost-effectiveness plane (**Figure 6**) and a cost-effectiveness acceptability curve (**Figure 7**).

The average relative risk reduction because of DIBH was 12.27% (95% CI: 11.97%-12.57%) for total cardiovascular disease and 11.30% (95% CI: 10.86%-11.74%) for fatal cardiovascular disease. Additionally, the average absolute risk reduction was 1.72% (95% CI: 1.67%-1.76%) for total cardiovascular disease and 0.69% (95% CI: 0.67%-0.72%) for fatal cardiovascular disease. Expressed in terms of numbers needed to treat, 58 patients (95% CI: 57-60 patients) must receive DIBH to prevent 1 cardiovascular event (fatal or nonfatal), and 144 patients (95% CI: 138-150 patients) must receive DIBH to prevent 1 cardiovascular death.

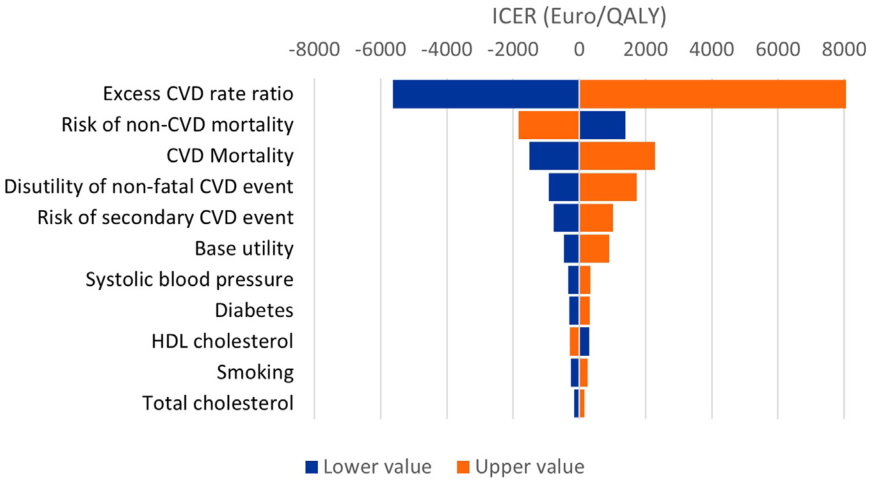
DIBH conferred greater benefits in patients with a higher baseline risk of cardiovascular disease (**Table 3**). In this patient sample, the average total risk of cardiovascular disease before undergoing RT was

FIGURE 4 **Tornado Diagrams of Discrete Event Simulation Model**



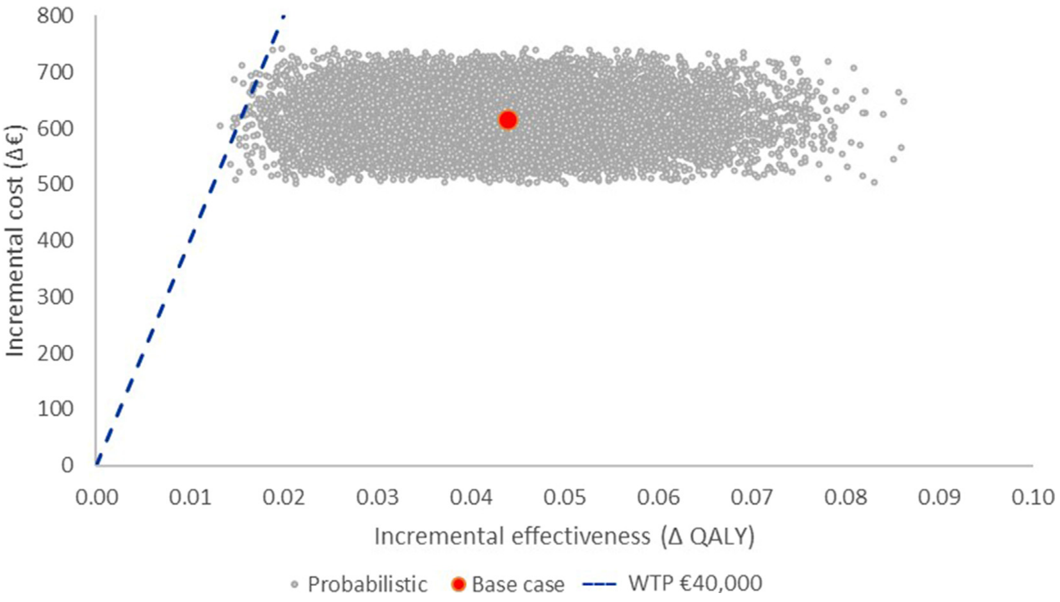
Resource costs (**Table 1**) and time parameters (Supplemental Table 1) were adjusted by −10% and +10%, and the resulting percentual change in the average per patient cost for FB and DIBH was recorded. Results for changes in costs parameters are shown in A and B, and results for changes in time parameters are shown in C and D. Costs are expressed in 2024 euros. Results reflect trial averages. Abbreviations as in **Figures 2 and 3**.

FIGURE 5 **Tornado Diagram of State-Transition Microsimulation Model**



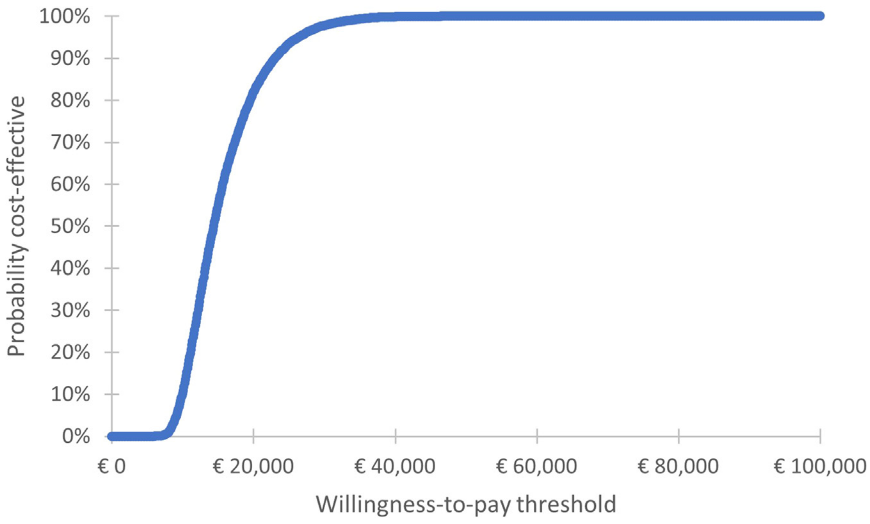
The diagram gives the change in the mean incremental cost-effectiveness ratio (ICER) of DIBH vs FB. Parameters were varied within a 95% CI range derived from the literature, with adjustments of ±30% from the base case for parameters without available CIs. The results reflect trial averages. Base case values and parameter ranges are provided in the Supplemental Methods. QALY = quality-adjusted life-year; other abbreviations as in **Figures 1 and 2**.

FIGURE 6 **Cost-Effectiveness Plane**



This incremental cost-effectiveness plane shows 10,000 Monte Carlo estimates of the incremental costs and benefits of using DIBH vs FB. DIBH was found to be cost-effective in 99.85% of simulations at a willingness-to-pay (WTP) threshold of €40,000 per QALY. Abbreviations as in **Figures 2 and 5**.

FIGURE 7 **Cost-Effectiveness Acceptability Curve**



This curve represents the probability of deep inspiration breath hold being cost-effective across various WTP thresholds. Each point on the curve indicates the proportion of simulations from the probabilistic sensitivity analysis where DIBH is deemed cost-effective at a specific WTP threshold. Abbreviations as in **Figures 2 and 6**.

TABLE 3 **Estimated Clinical Outcomes**

	QALYs	ARR Total Cardiovascular Disease, %	ARR Fatal Cardiovascular Disease, %	NNT Total Cardiovascular Disease	NNT Fatal Cardiovascular Disease
All patients	0.04 (0.04-0.05)	1.72 (1.67-1.76)	0.69 (0.67-0.72)	58 (57-60)	144 (138-150)
Risk category, %					
Low (71)	0.03 (0.03-0.04)	1.39 (1.34-1.44)	0.39 (0.36-0.41)	72 (70-74)	259 (244-276)
Moderate/high (29)	0.07 (0.06-0.08)	2.51 (2.41-2.61)	1.45 (1.37-1.53)	40 (38-42)	69 (65-73)
Age, %					
30-39 y (6)	0.01 (−0.01 to 0.02)	0.46 (0.37-0.54)	0.03 (0.01-0.06)	220 (187-267)	2,927 (1762-8642)
40-49 y (15)	0.02 (0.01-0.03)	0.81 (0.74-0.89)	0.09 (0.07-0.11)	123 (113-135)	1,084 (870-1346)
50-59 y (28)	0.03 (0.02-0.04)	1.32 (1.25-1.39)	0.30 (0.28-0.33)	76 (72-80)	328 (300-362)
60-69 y (33)	0.06 (0.05-0.06)	2.11 (2.03-2.20)	0.82 (0.77-0.87)	47 (46-49)	122 (115-130)
70-79 y (18)	0.08 (0.07-0.09)	2.77 (2.63-2.91)	1.79 (1.68-1.90)	36 (34-38)	56 (53-60)

Values are median (95% CI). The results reflect trial averages.
ARR = absolute risk reduction; NNT = number needed to treat; QALY = quality-adjusted life year.

4.32% ± 3.36%. According to the risk classification system described in the SCORE2 algorithms,[20,21] the majority of patients had a low baseline total risk of cardiovascular disease (71%). Additionally, clinical benefits were more pronounced in older age groups (**Table 3**).

DISCUSSION

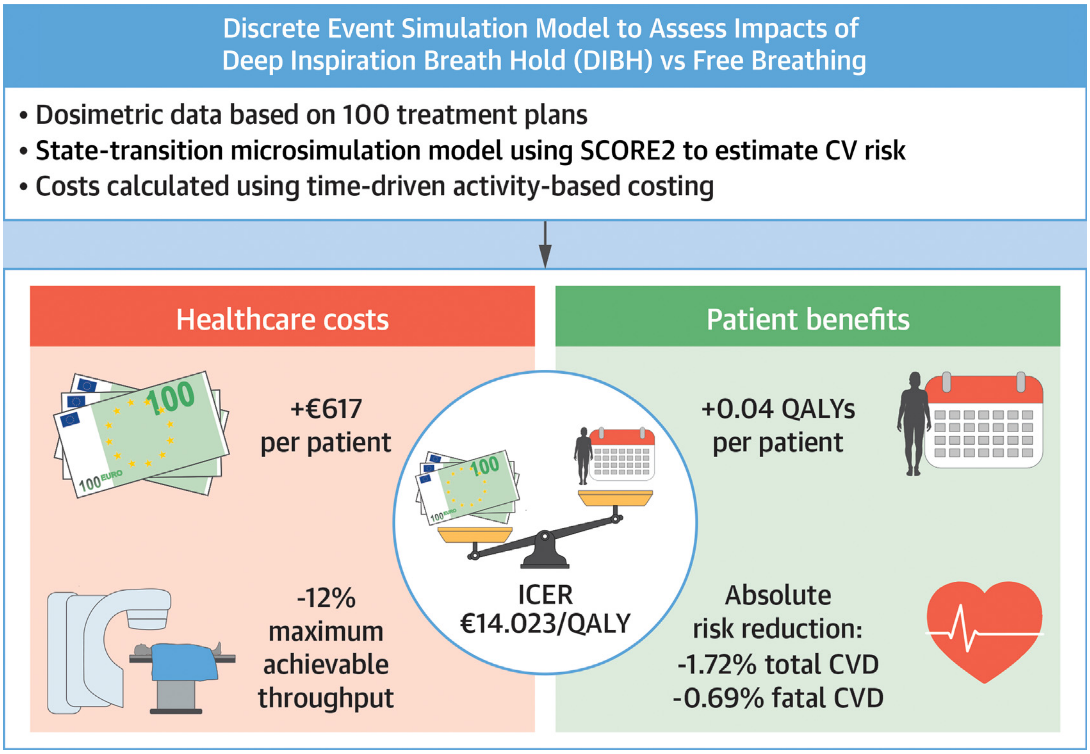
In this study, we systematically investigated the benefits and costs associated with a promising heart-sparing RT technique (**Central Illustration**). Transitioning from FB to DIBH in our patient cohort yielded an ICER of €14,023 per QALY over a 20-year horizon. Considering a WTP threshold of €40,000 per QALY, DIBH emerges as a cost-effective option. Our findings demonstrate that the improved dosimetric performance of DIBH can translate into meaningful clinical benefits, reducing both cardiovascular morbidity and mortality. Specifically, DIBH may improve the long-term health outcomes of breast cancer survivors by enhancing quality of life and extending longevity. Moreover, compared with other RT techniques designed to spare normal tissues such as proton therapy, DIBH is significantly more cost-effective, enhancing its potential as a viable treatment option.[40]

Significantly, the benefits of DIBH depend on a patient's cardiovascular disease risk before undergoing RT and age. Patients with a higher baseline risk of cardiovascular disease experience greater reductions in MHD (Supplemental Figure 10), resulting in more substantial gains in QALYs. The relatively low average baseline risk of cardiovascular disease observed in this study explains the relatively modest increase in QALYs observed. Age plays a critical role because of the higher risk of cardiovascular disease and the increased likelihood of fatal outcomes in older individuals.[20,21] Cohort studies underscore the significant cardiovascular mortality risk faced by older breast cancer survivors and individuals with a history of cardiovascular disease, sometimes surpassing breast cancer as the leading cause of death.[41-43] Our model-based analysis suggests that heart-sparing radiation techniques, such as DIBH, could significantly reduce cardiovascular disease risk in high-risk patients and improve their quality-adjusted life expectancy. Given the substantial burden of cardiovascular disease in breast cancer survivors,[44] further clinical research in this area is imperative.

In addition to analyzing the potential cost-effectiveness of DIBH, this study also provides insight into its operational implications. Our results indicate that implementing DIBH is likely to increase resource use, potentially reducing the maximum achievable throughput with existing resources. To avoid a detrimental impact on patient waiting times, RT centers considering DIBH adoption should assess whether their current capacity can accommodate the increased demands associated with this technique.

STUDY LIMITATIONS. The results are based on data from a single academic hospital, cautioning against generalizing these results to populations diverging

CENTRAL ILLUSTRATION The Benefits and Costs of Deep Inspiration Breath Hold in Left-Sided Breast Radiotherapy



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Treating left-sided breast cancer patients with deep inspiration breath hold (DIBH) results in an average gain of 0.04 quality-adjusted life-years (QALYs) attributed to reductions in cardiovascular (CV) morbidity and mortality. Despite necessitating additional time investments from radiotherapy departments, DIBH demonstrates cost-effectiveness. CVD = cardiovascular disease; ICER = incremental cost-effectiveness ratio; SCORE2 = Systematic Coronary Risk Evaluation.

significantly in key parameters from the study population (Supplemental Methods). For example, developing regions often exhibit considerably lower breast cancer survival rates than high-income countries,[45] potentially limiting the benefits of DIBH in such regions. Furthermore, various devices and techniques exist for implementing DIBH,[8] differing in costs and resource demands.

Importantly, the reliability of our results relies on the underlying assumptions of the simulation models and the accuracy of the data used in their construction, as is typical for simulation modeling studies. The baseline risk of cardiovascular disease may have been underestimated because of several factors. First, data on risk factors for cardiovascular disease, such as total cholesterol, were obtained from the general Belgian population,[30] potentially overlooking higher risk factors for cardiovascular disease in breast cancer patients pre-RT than the general population,[46] although this is not consistently observed. Second, breast cancer patients may undergo other potentially cardiotoxic treatments alongside RT.[47] Finally, external validation studies in the Netherlands suggest that SCORE2 algorithms may underpredict the risk of cardiovascular disease in low-risk countries like Belgium.[48]

CONCLUSIONS

This study systematically assessed the benefits and costs of DIBH, a heart-sparing radiation technique. Our results suggest that the application of DIBH is cost-effective in the Belgian population, reducing both cardiovascular morbidity and mortality. However, radiation oncologists must consider the increased demands DIBH places on resources to prevent delays in patient care.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Radiotherapy is a cornerstone of breast cancer treatment but can inadvertently expose the heart to radiation, especially during left breast radiotherapy. Heart-sparing radiotherapy techniques such as deep inspiration breath hold may improve long-term cardiovascular health, particularly benefiting patients with a high baseline risk of cardiovascular disease.

TRANSLATIONAL OUTLOOK: Future research should examine the generalizability of operational and financial implications observed in this study to other radiotherapy departments and assess the applicability of conclusions regarding patient outcomes to diverse breast cancer populations. This model-based analysis suggests that radiotherapy using deep inspiration breath hold, as opposed to free breathing, can improve long-term cardiovascular health in breast cancer patients. Prospective clinical research and data collection will be essential to validate these findings.

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KEY WORDS breast cancer, cost-effectiveness, health economics, medical technology, outcomes, photon therapy, treatment

APPENDIX For an expanded Methods section and supplemental tables and figures, please see the online version of this paper.