*Pediatric Blood & Cancer*

WILEY

Pediatric Blood & Cancer | SIOP International Society of Paediatric Oncology | aspho The American Society of Pediatric Hematology/Oncology

RESEARCH ARTICLE OPEN ACCESS

# Radiotherapy Delivery in Deep Inspiration for Pediatric Patients—Final Results of the Phase II Feasibility Study *TEDDI*

Daniella Elisabet Østergaard[1,2] | Anni Young Lundgaard[1] | Laura Ann Rechner[1] | Danijela Dejanovic[3] | Hanne Krogh Rose[4] | Jolanta Hansen[4] | Leila Vaalavirta[5] | Miia Mokka[6] | Marianne Aznar[7] | Peder Skov Wehner[8] | Lisa Lyngsie Hjalgrim[9] | Maja Vestmø Maraldo[1,2]

[1]Department of Oncology, Copenhagen University Hospital—Rigshospitalet, Copenhagen, Denmark | [2]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark | [3]Department of Nuclear Medicine, Copenhagen University Hospital—Rigshospitalet, Copenhagen, Denmark | [4]Department of Oncology, Aarhus University Hospital, Aarhus, Denmark | [5]Department of Radiation Oncology, Comprehensive Cancer Center, Helsinki University Hospital, Helsinki, Finland | [6]Department of Oncology and Radiotherapy, Turku University Hospital, Turku, Finland | [7]Division of Cancer Sciences, School of Medical Science, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK | [8]Department of Paediatric Haematology and Oncology, H.C. Andersen Children's Hospital, Odense University Hospital, Odense, Denmark | [9]Department of Paediatric Haematology and Oncology, Copenhagen University Hospital—Rigshospitalet, Copenhagen, Denmark

**Correspondence:** Daniella Elisabet Østergaard (daniella.elisabet.oestergaard.01@regionh.dk; daniella.elisabet@gmail.com)

**Received:** 11 September 2025 | **Revised:** 4 December 2025 | **Accepted:** 19 December 2025

**Keywords:** deep-inspirational breath-hold | gating | lymphoma | pediatric cancer | radiotherapy | sarcoma

## Abstract

**Introduction:** The TEDDI trial tested the feasibility and reproducibility of deep-inspiration breath-hold (DIBH) in pediatric patients referred for radiotherapy. This report presents final results, including patient-reported outcomes (PRO) and dosimetric comparison of DIBH and free-breathing (FB).

**Patients and Methods:** Pediatric patients able to perform three sequential breath-holds and potentially requiring thoracic or upper abdominal radiotherapy were recruited. DIBH training was during staging or planning computed tomography (CT) scanning, using external gating with an external marker and visual coaching. Each patient underwent planning CT in both DIBH and FB, generating two radiotherapy plans. DIBH was selected if it resulted in a lower overall dose to organs at risk. At two centers, patients evaluated their DIBH experience during training. Those treated in DIBH also completed three daily questions and extended questionnaires at the start, midpoint, and end of treatment, using yes/no and five-point Likert scales.

**Results:** Twenty-five patients (12 females/13 males, median age 15 years, range: 9–17 years) were enrolled across three centers. Eight received photon radiotherapy, five in DIBH. Of 13 eligible patients, 11 rated DIBH training, with 10 selecting "Really good" or "Good." Patients treated in DIBH reported feeling safe and comfortable. Dosimetric analysis showed clear heart and lung dose reductions with DIBH. FB patients had similar doses across both plans.

**Abbreviations:** CBCT, cone beam computed tomography; CTV, clinical target volume; DIBH, deep-inspirational breath-hold; FB, free breathing; *F*, fractions; Gy, Gray; HL, Hodgkin lymphoma; kV, kilovoltage; MHD, mean heart dose; MLD, mean lung dose; OAR, organs at risk; PET/CT, positron emission tomography/computed tomography; PRO, patient-reported outcomes; TEDDI, radiotherapy delivery in deep inspiration for pediatric patients.

Lisa Lyngsie Hjalgrim and Maja Vestmø Maraldo contributed equally to this work and share last authorship.

**Meeting abstracts**:
D. Østergaard, A. Y. Lundgaard, H. K. Rose, J. Hansen, L. Vaalavirta, M. Mokka, L. L. Hjalgrim, I. R. Vogelius, M. Aznar, M. V. Maraldo, "3425 Dosimetric Results and Patient-Reported Outcomes in TEDDI: Radiotherapy Delivery in Deep Inspiration for Paediatric Patients, a NOPHO Feasibility Study. *Radiation Oncology* 206 (March 2025): S1640–S1642, DOI: 10.1016/S0167-8140(25)01702-5. Mini-Oral, ESTRO Annual Meeting, Vienna, Denmark, May 2025.

**Conclusion:** The TEDDI trial demonstrated the feasibility and safety of DIBH in pediatric radiotherapy. High compliance with the procedure and favorable dosimetric outcomes support the use of DIBH to reduce long-term toxicity risks in this population.

## 1 | Introduction

Pediatric cancer patients are a growing population of long-term survivors at risk. Multiple studies with long-term follow-up have shown an increased mortality and morbidity in survivors of childhood cancer [1]. Second cancers and cardiac late effects after radiotherapy have been examined thoroughly, and minimizing this risk is of great importance [2–4]. Hence, the focus of modern pediatric cancer treatment is to reduce toxicity while maintaining cure rates [5–8]. In adults, deep-inspiration breath-hold (DIBH) has been proven to reduce the radiation dose to organs at risk (OAR) and, in some tumors, DIBH has also been used to reduce the applied margin in radiotherapy planning [9–11]. DIBH with external gating is a simple technique, widely used, and is easily implemented in new patient groups [11–16]. Even though DIBH is used as a standard in adult cancer patients, there has been a reluctance to implement DIBH in paediatric patients [17]. We hypothesized that pediatric patients referred for radiotherapy would benefit from DIBH and, consequently, we initiated the TEDDI (radiotherapy delivery in deep inspiration for pediatric patients) trial (NTC03315546) [18]. The trial protocol [18], the feasibility of pediatric DIBH training [19], as well as the changes seen on PET/CT (positron emission tomography/computed tomography) performed in DIBH [20] have been published previously. In short, the trial aimed to estimate the dosimetric benefit of radiotherapy using DIBH compared to free breathing (FB), to establish patient experience and the compliance of DIBH, and to determine if DIBH is an accurate and reproducible strategy in pediatric patients. Here, we report the final results of the TEDDI trial.

## 2 | Materials and Methods

### 2.1 | Patients

We planned to accrue 25 pediatric patients, aged 5–17 years, with the ability to perform three sequential breath-holds of 20 s each, who might be referred for radiotherapy of the thorax/upper abdomen, irrespective of cancer type. Patients were recruited within the Nordic Society of Pediatric Hematology and Oncology network.

### 2.2 | DIBH Training

Patients were trained for DIBH at the time of staging (if there was a potential later radiotherapy indication) or planning computed tomography (CT) scanning as previously detailed [19]. Briefly, the DIBH was voluntary and monitored with the Real-Time Position Management System from Varian Medical Systems, a noninvasive system with a box placed on the xiphoid process of the sternum. A visual feedback system on a screen was used to aid the reproducibility of the DIBH level. The width of the gating window was set to 2.5–3.5 mm.

### 2.3 | Patient-Reported Outcomes

Patient-reported outcomes (PRO) were collected at two centers following DIBH training and during radiotherapy treatment.

Patients who underwent DIBH training were asked to evaluate their experience and the training instructions immediately after their training session (= DIBH training cohort). The evaluation consisted of a brief questionnaire of eight questions.

Patients selected for radiotherapy in DIBH (= radiotherapy cohort) were asked to evaluate their experience with DIBH during treatment. This included three daily questions, and an extended questionnaire (eight questions) administered at start-, mid-, and end-of-treatment.

Responses were captured using either yes/no options or a five-point Likert scale (e.g., Agree/Somewhat agree/Neither agree nor disagree/Somewhat disagree/Disagree; Really good/Good/Neither bad nor good/Bad/Really bad). Complete questionnaires are provided in the Supporting Information (Supplementary Tables S1–S6).

### 2.4 | Treatment Planning and Dose to Organs at Risk

All patients who were referred for radiotherapy had planning CT scans done in both DIBH and FB for comparative dose planning. Lymphoma patients also had their pre-chemotherapy positron emission tomography (PET)/CT in both DIBH and FB. Coverage of the clinical target volume (CTV) had the highest priority, followed by the dose to OAR (heart, lungs, female breasts, esophagus, and thyroid) [18]. Treatment delivered in DIBH was only chosen if it was superior to the FB treatment plan. Treatment position was supine with arms raised above the head, with relevant immobilization devices on a chest-board (this is standard and matches the setup for PET/CT). Setup verification was done with a daily cone beam CT (CBCT). If the treatment was delivered in DIBH, position verification was also performed in DIBH to verify the level of inspiration. Choice of treatment delivery was made at the discretion of the treating physician. Dose in gray (Gy) and fractionation ($F$) were determined by the treatment protocol of the individual patient, as per international guidelines. Here, we report the dose metrics: mean dose to the heart (MHD) and lungs (MLD), the heart and lung volume receiving 20 and 5 Gy (V20 and V5), respectively, and mean dose to the thyroid, esophagus, and female breasts.

## 2.5 | Ethical Considerations

The TEDDI trial was approved by the Danish Ethical Committee (H-16035870) and by the Danish Data Protection Agency (2012-58-0004), as well as the Finnish Ethical Committee (HUS/60/2018) and Finnish Data Protection Agency (T06/010/18).

# 3 | Results

## 3.1 | Patients

The TEDDI trial was open nationwide in Denmark and at one center in Finland. A total of 25 patients were enrolled, with an even gender distribution (12 females/13 males). The median age at accrual was 15 years (range: 9–17 years). Most patients were diagnosed with lymphoma; however, two patients had sarcoma. Eight out of 25 accrued patients were referred for photon radiotherapy; see Table 1 for patient characteristics and details of radiotherapy (a consort diagram available in Figure S1).

**TABLE 1** | Patient characteristics.

| | DIBH training cohort ($N = 25$) | Radiotherapy cohort ($N = 8$) |
|---|---|---|
| Age in years (range) | 15 (9–17) | 15 (14–16) |
| Gender | | |
| Female | 12 (48%) | 5 (63%) |
| Male | 13 (52%) | 3 (37%) |
| Diagnosis | | |
| Hodgkin lymphoma | 22 (88%) | 6 (75%) |
| Non-Hodgkin lymphoma | 1 (4%) | – |
| Ewing sarcoma | 1 (4%) | 1 (13%) |
| Synovial sarcoma | 1 (4%) | 1 (13%) |
| No. of patients irradiated[a] | 8 (32%) | |
| No. of patients irradiated with DIBH | | |
| Yes/No | | 5 (63%)/3 (38%) |
| No. of days from chemo to first day of radiotherapy | | 23 (9–33) |
| Type of treatment plan *(all were treated with photon)* | | |
| 3DCRT | | 2 (26%) |
| IMRT | | 3 (38%) |
| VMAT | | 3 (38%) |
| IGRT modality | | |
| Daily CBCT | | 7 (88%) |
| Daily kV pair | | 1 (13%) |

Abbreviations: 3DCRT, three-dimensional conventional radiotherapy; CBCT, cone beam computed tomography; DIBH, deep-inspirational breath-hold; IGRT, image-guided radiotherapy; IMRT, intensity-modulated radiotherapy; kV, kilovoltage; No., number; VMAT, volumetric modulated arc therapy.

[a]One extra patient (male) was referred for proton therapy in free breathing (FB). The patient was excluded from further comparison analysis and is not included in the radiotherapy cohort.

## 3.2 | Patient-Reported Outcomes

### 3.2.1 | The DIBH Training Cohort

All patients in the DIBH training cohort could perform a stable and reproducible DIBH after training. Evaluation of the DIBH training was done by 11 (of 13 possible) patients at one center. In general, the training was rated as either "Really good" or "Good"; none found it "Bad" or "Really bad." Only one out of 11 patients found it "Somewhat hard" to lie still (age 15 years), and one found the instructions "Somewhat difficult" to understand (not the same patient). Most patients found the visual screen helpful; although two patients did not find the feedback screen to be of any help, and one patient only found it "Somewhat helpful." Two patients suggested that the feedback system should have a timer. Overall, the training was positively evaluated by all patients, cf. Figure 1.

## 3.3 | The Radiotherapy Cohort

PRO collection during radiotherapy was done for all five patients treated in DIBH. The short daily questionnaire demonstrated that the children overall felt safe during treatment. DIBH was not difficult to perform, and the patients did not tire from performing DIBH, although many were tired on a single day during treatment. One patient, however, was tired every day except two. The results of the extended questionnaire supported this and showed that the children felt comfortable with DIBH, had no trouble performing DIBH, and felt safe and confident with the staff. Also, three out of five felt that DIBH distracted them from feeling anxious during treatments (details shown in Figure 2).

## 3.4 | Dosimetric Analysis

The differences in dose estimates for the heart and lung with DIBH and FB, respectively, are illustrated in Figure 3. Among patients treated with DIBH, there was a clear dosimetric benefit regarding both the mean dose and low-dose exposure (V5) to the heart and lungs, respectively. Interestingly, for patients treated in FB, adopting a DIBH plan would not have been detrimental, as heart and lung doses overall were comparable between the two plans. It is important to note that an FB plan was chosen for these patients because DIBH was considered experimental at the time.

Doses to the thyroid, esophagus, and female breasts were also evaluated. The differences in dose estimates for these structures between the two dose plans are shown in Figure 4. A clear dosimetric benefit was observed for the esophagus among patients treated with DIBH, and a similar pattern was noted for the thyroid, except in the case of one patient. Of note, these patients also experienced a dosimetric benefit from DIBH in terms of MHD and MLD.

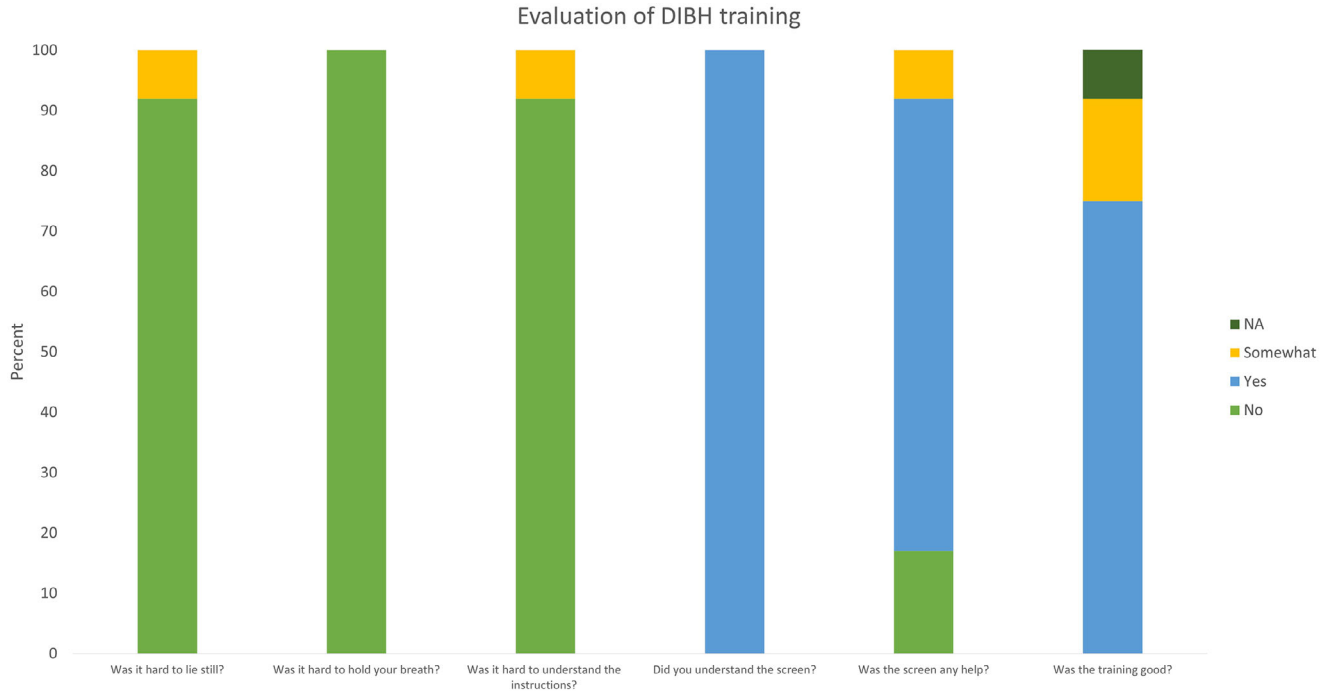


**FIGURE 1** | The histogram shows the distribution of answers from the evaluation of deep-inspiration breath-hold (DIBH) training in percentage (total number of replies = 11 patients). Answers "No" to questions are visualized as green, "Yes" as blue, and "Somewhat" as yellow. Most found DIBH and the instructions easy and the screen understandable, as well as helpful.

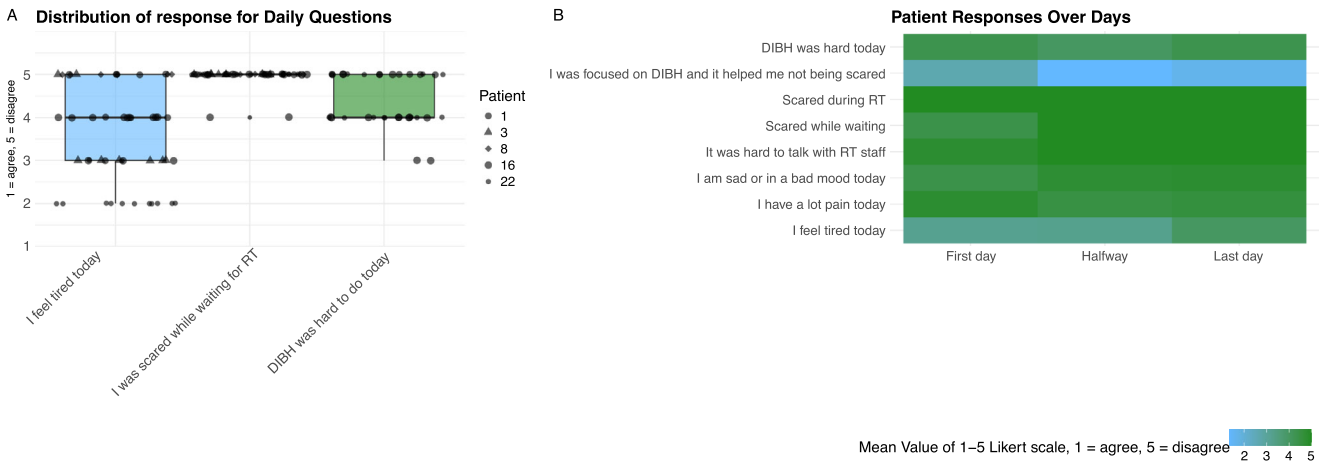


**FIGURE 2** | (A) Boxplot of the total distribution over the whole radiotherapy course for the daily questionnaire (three questions) given to the patients irradiated with deep-inspiration breath-hold (DIBH) (number = 5). Patients are plotted with individual icons. (B) Heatmap of the extended questionnaire answered and the first day, halfway, and the last day during the radiotherapy course. Both questionnaires were answered with a five-point Likert scale from 1 to 5, where 1 = Agree a lot, and 5 = Disagree a lot.

## 4 | Discussion

The TEDDI trial is the first study to systematically evaluate the feasibility of DIBH in a pediatric setting. We used questionnaires and asked the children about their experience of DIBH. Importantly, introducing DIBH both at planning and during treatment did not add further anxiety or uncertainty to the patients, and some even found DIBH to help them focus during their radiotherapy sessions. Furthermore, our comparative dose planning demonstrated that in two-thirds of the patients, radiotherapy in DIBH provided a clear dosimetric benefit. Interestingly, for the patients who were treated in FB, the DIBH plan would not have been detrimental with respect to heart and lung doses.

In our TEDDI pilot study, we reported on the feasibility of DIBH training in both healthy volunteers as well as hospitalized children receiving chemotherapy, focusing on a younger age group (mean age 8.9 years; range: 5–15 years) [19]. We demonstrated that children as young as 5 years old were able to understand the DIBH procedure, and, as in our clinical trial, the children were happy with the training and performing DIBH. Consequently, we argue

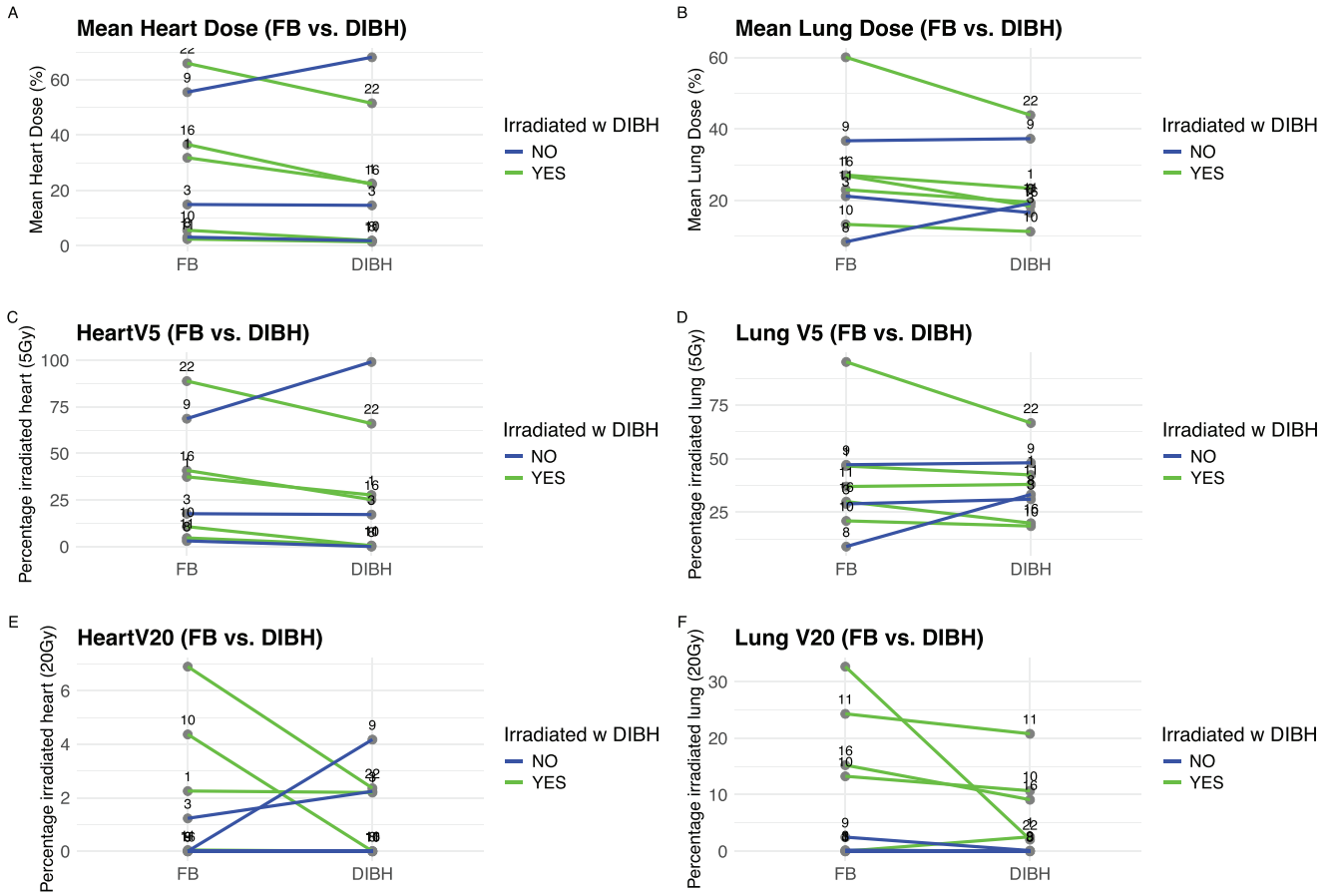


**FIGURE 3** | In all plots, doses in free breathing (FB) are on the left and doses in deep-inspiration breath-hold (DIBH) on the right. Patients who were treated in FB are shown in blue, and DIBH are green, and one line represents one patient. Numbers are patient IDs. (A) Mean heart dose in percentage; (B) mean lung dose in percentage; (C) percentage volume of the heart receiving 5 Gy; (D) percentage volume of the lung receiving 5 Gy; (E) percentage volume of the heart receiving 20 Gy; (F) percentage volume of the lung receiving 20 Gy.

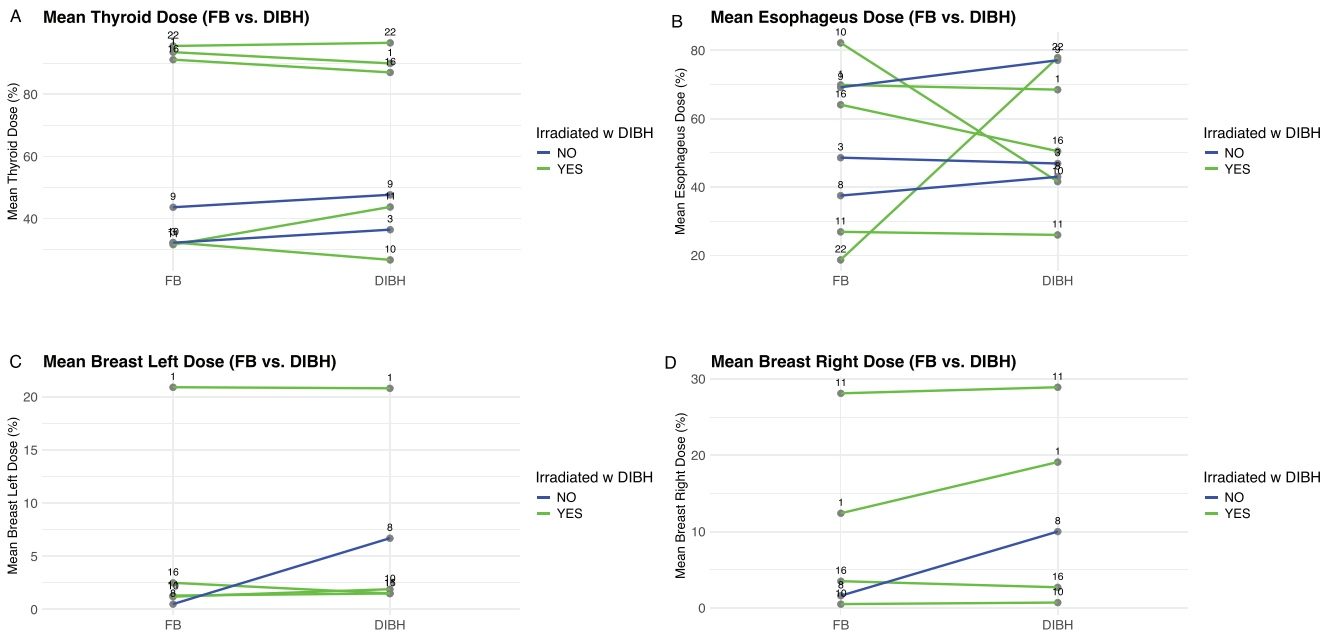


**FIGURE 4** | In all plots, doses in free breathing (FB) are on the left and doses in deep-inspiration breath-hold (DIBH) on the right. Patients who were treated in FB are shown in blue, and DIBH are green, and one line represents one patient. Numbers are patient IDs. (A) Mean thyroid dose in percentage; (B) mean esophagus dose in percentage; (C) mean dose to left breast in percentage (only female patients); (D) mean dose to right breast in percentage (only female patients).

that the feasibility and safety of radiotherapy delivery in DIBH may be extrapolated to younger patients with some degree of certainty. Similarly, setup uncertainties during radiotherapy showed no difference in systematic or random errors between DIBH and FB when using CBCT for patient setup [21]. Consequently, there is no need for increased safety margins in DIBH compared to FB in pediatric patients.

During the TEDDI trial, we faced some challenges in accrual and logistics. While the trial was not diagnosis-specific, as anticipated, most of the enrolled patients were diagnosed with Hodgkin lymphoma (HL). At the time of planning the trial, pediatric patients with HL were treated according to the EuroNet-PHL-C1 protocol [22]. However, with the introduction of the subsequent EuroNet-PHL-C2 trial [23], the use of consolidating radiotherapy diminished considerably [24]. Also, pretreatment PET/CT scans for HL patients were made in both DIBH and FB in TEDDI. This additional step introduced complexity to patient accrual, as the need for consolidating radiotherapy could not be determined until after the patients' post-chemotherapy response assessment [16]. These factors help explain why more patients were trained for DIBH than actually referred for radiotherapy [25, 26]. Detailed analyses on the implications of staging PET/CT in DIBH for radiotherapy planning in pediatric lymphomas have been published previously [20].

Prior to clinical implementation of DIBH in the pediatric setting, we considered a systematic and prospective evaluation prudent due to the fear of a potential added anxiety and treatment time when using DIBH. To the best of our knowledge, there are no other prospective studies investigating the benefit of DIBH in pediatric patients. However, in a retrospective cohort of 12 pediatric patients treated with Active Breathing Control, no significant discomfort, anxiety, or issues were reported during treatment [27], which is in line with our results.

DIBH has been proven to be dose-sparing in several indications in the adult setting [11, 13–15, 28–31]. Minimizing radiation dose to the adjacent OARs is critical to reducing the risk of late effects [1, 32]. In TEDDI, priority was given to heart dose over other OARs, consistent with literature that reports cardiovascular disease as one of the most frequent late effects [1, 33, 34]. Despite the dosimetric benefits, DIBH is not widely implemented for pediatric patients. In a survey amongst pediatric facilities, only 4% (of 50 responders) reported using DIBH, and 36% had no motion management strategies at all [35]. The median age of the cohort was 15 years (range: 14–16 years), representing the typical clinical population eligible for this treatment. Adolescents can follow instructions comparably to young adult cancer patients, who routinely undergo radiotherapy using DIBH, such as those with lymphoma or breast cancer. Given their potential for long-term survival, it is essential to address existing gaps to qualify for radiotherapy.

Proton therapy also offers the possibility of dose sparing to OAR, which has been found in simulation studies comparing DIBH with either photon or proton treatment [36–41]. However, the precision of DIBH depends on gated 3D-based IGRT, such as respiratory-gated CBCT [42–44], which currently is not available for most proton vendors. This means that while motion uncertainty is minimized with DIBH, position uncertainties are increased due to the lack of gated 3D-IGRT solutions for protons.

In conclusion, the TEDDI trial is the first study to prospectively demonstrate the feasibility and safety of both training and radiotherapy delivery in DIBH in pediatric radiotherapy. Importantly, patients did not report any extra anxiety or stress due to the DIBH procedure. Also, in two-thirds of the patients, there was a dosimetric benefit from using DIBH. Consequently, DIBH should be considered in pediatric radiotherapy to reduce the risk of late effects.


### Acknowledgments

We thank Medical Physicist Mikko Björkqvist (Department of Medical Physics, Turku University Hospital) and Medical Physicist Bob Smulders and head of IT Thomas Carlslund (Department of Oncology, Copenhagen University Hospital) for technical assistance.

### Funding

M.V.M. and D.E.Ø. acknowledge the support of the Danish Child Cancer Foundation (Grant Number 2015–9) and the Danish Cancer Society (Grant Number R150-A10066 and R248-A14714). M.Z. acknowledges the support of the Engineering and Physical Sciences Research Council (Grant Number EP/T028017/1) and of the NIHR Manchester Biomedical Research Centre (NIHR203308).


### Ethics Statement

The TEDDI trial was approved by the Danish Ethical Committee (H-16035870) and by the Danish Data Protection Agency (2012-58-0004), as well as the Finnish Ethical Committee (HUS/60/2018) and Finnish Data Protection Agency (T06/010/18).

### Conflicts of Interest

L.A.R. acknowledges the support of Varian for her research grant. The remaining authors declare no conflicts of interest.

### Data Availability Statement

Research data are not available.

### References


1. J. E. Bates, T. Rancati, H. Keshavarz, et al., "Cardiac Disease in Childhood Cancer Survivors Treated With Radiation Therapy: A PENTEC Comprehensive Review," *International Journal of Radiation Oncology, Biology, Physics* 119, no. 2 (2024): 522–532, https://doi.org/10.1016/j.ijrobp.2023.03.045.

2. T. Gudmundsdottir, T. F. Winther, S. de Fine Licht, et al., "Cardiovascular Disease in Adult Life after Childhood Cancer in Scandinavia: A Population-Based Cohort Study of 32,308 One-Year Survivors," *International Journal of Cancer* 137, no. 5 (2015): 1176–1186, https://doi.org/10.1002/ijc.29468.

3. K. C. Oeffinger, A. C. Mertens, C. A. Sklar, et al., "Chronic Health Conditions in Adult Survivors of Childhood Cancer," *New England Journal of Medicine* 355, no. 15 (2006): 1572–1582, https://doi.org/10.1056/NEJMsa060185.

4. K. Rugbjerg, L. Mellemkjær, J. D. Boice, L. Køber, M. Ewertz, and J. H. Olsen, "Cardiovascular Disease in Survivors of Adolescent and Young Adult Cancer: A Danish Cohort Study, 1943–2009," *JNCI: Journal of the National Cancer Institute* 106, no. 6 (2014): dju110, https://doi.org/10.1093/jnci/dju110.

5. G. Gagliardi, L. S. Constine, V. Moiseenko, et al., "Radiation Dose–Volume Effects in the Heart," *International Journal of Radiation Oncology, Biology, Physics* 76, no. 3 (2010): S77–S85, https://doi.org/10.1016/j.ijrobp.2009.04.093.

6. D. C. Hodgson, M. M. Hudson, and L. S. Constine, "Pediatric Hodgkin Lymphoma: Maximizing Efficacy and Minimizing Toxicity," *Seminars in Radiation Oncology* 17, no. 3 (2007): 230–242, https://doi.org/10.1016/j.semradonc.2007.02.009.

7. L. B. Marks, S. M. Bentzen, J. O. Deasy, et al., "Radiation Dose–Volume Effects in the Lung," *International Journal of Radiation Oncology, Biology, Physics* 76, no. 3 (2010): S70–S76, https://doi.org/10.1016/j.ijrobp.2009.06.091.

8. L. Specht, "Radiotherapy for Hodgkin Lymphoma," *Cancer Journal* 24, no. 5 (2018): 237–243, https://doi.org/10.1097/PPO.0000000000000332.

9. M. C. Aznar, P. Carrasco de fez, S. Corradini, et al., "ESTRO-ACROP Guideline: Recommendations on Implementation of Breath-Hold Techniques in Radiotherapy," *Radiotherapy and Oncology* 185 (2023): 109734, https://doi.org/10.1016/j.radonc.2023.109734.

10. R. Canters, F. Vaassen, I. Lubken, et al., "Radiotherapy for Mediastinal Lymphoma in Breath Hold Using Surface Monitoring and Nasal High Flow Oxygen: Clinical Experiences and Breath Hold Stability," *Radiotherapy and Oncology* 183 (2023): 109594, https://doi.org/10.1016/j.radonc.2023.109594.

11. P. M. Petersen, M. C. Aznar, A. K. Berthelsen, et al., "Prospective Phase II Trial of Image-Guided Radiotherapy in Hodgkin Lymphoma: Benefit of Deep Inspiration Breath-Hold," *Acta Oncologica* 54, no. 1 (2015): 60–66, https://doi.org/10.3109/0284186X.2014.932435.

12. M. Josipovic, G. F. Persson, J. P. Bangsgaard, L. Specht, and M. C. Aznar, "Deep Inspiration Breath-hold Radiotherapy for Lung Cancer: Impact on Image Quality and Registration Uncertainty in Cone Beam CT Image Guidance," *British Journal of Radiology* (2016): 89, no. 1068, https://doi.org/10.1259/bjr.20160544.

13. M. Josipovic, G. F. Persson, K. Håkansson, et al., "Deep Inspiration Breath Hold Radiotherapy for Locally Advanced Lung Cancer: Comparison of Different Treatment Techniques on Target Coverage, Lung Dose and Treatment Delivery Time," *Acta Oncologica* 52, no. 7 (2013): 1582–1586, https://doi.org/10.3109/0284186X.2013.813644.

14. S. S. Korreman, A. N. Pedersen, T. J. Nøttrup, L. Specht, and H. Nyström, "Breathing Adapted Radiotherapy for Breast Cancer: Comparison of Free Breathing Gating with the Breath-Hold Technique," *Radiotherapy and Oncology* 76, no. 3 (2005), https://doi.org/10.1016/j.radonc.2005.07.009.

15. H. D. Nissen and A. L. Appelt, "Improved Heart, Lung and Target Dose with Deep Inspiration Breath Hold in a Large Clinical Series of Breast Cancer Patients," *Radiotherapy and Oncology* 106, no. 1 (2013): 28–32, https://doi.org/10.1016/j.radonc.2012.10.016.

16. L. Specht, J. Yahalom, T. Illidge, et al., "Modern Radiation Therapy for Hodgkin Lymphoma: Field and Dose Guidelines From the International Lymphoma Radiation Oncology Group (ILROG)," *International Journal of Radiation Oncology, Biology, Physics* 89, no. 4 (2014): 854–862, https://doi.org/10.1016/j.ijrobp.2013.05.005.

17. M. D. Hall, S. A. Terezakis, J. T. Lucas, et al., "Radiation Therapy Across Pediatric Hodgkin Lymphoma Research Group Protocols: A Report From the Staging, Evaluation, and Response Criteria Harmonization (SEARCH) for Childhood, Adolescent, and Young Adult Hodgkin Lymphoma (CAYAHL) Group," *International Journal of Radiation Oncology, Biology, Physics* 112, no. 2 (2022): 317–334, https://doi.org/10.1016/j.ijrobp.2021.07.1716.

18. A. Y. Lundgaard, L. L. Hjalgrim, L. A. Rechner, et al., "TEDDI: Radiotherapy Delivery in Deep Inspiration for Pediatric Patients—A NOPHO Feasibility Study," *Radiation Oncology* 13, no. 1 (2018): 56, https://doi.org/10.1186/s13014-018-1003-4.

19. A. Y. Lundgaard, M. Josipovic, L. A. Rechner, et al., "The Feasibility of Implementing Deep Inspiration Breath-Hold for Pediatric Radiation Therapy," *International Journal of Radiation Oncology, Biology, Physics* 106, no. 5 (2020): 977–984, https://doi.org/10.1016/j.ijrobp.2019.12.025.

20. A. Y. Lundgaard, D. Dejanovic, A. K. Berthelsen, et al., "Baseline FDG PET/CT in Free Breathing Versus Deep Inspiration Breath-hold for Pediatric Patients With Mediastinal Lymphoma," *Acta Oncologica* 61, no. 2 (2022): 239–246, https://doi.org/10.1080/0284186X.2021.1974554.

21. D. E. Østergaard, L. A. Rechner, A. Y. Lundgaard, et al., "Positioning in Deep Inspiration Breath-Hold Is Comparable to Free Breathing in Paediatric Patients," *Clinical and Translational Radiation Oncology* 53 (2025): 100975, https://doi.org/10.1016/j.ctro.2025.100975.

22. C. Mauz-Körholz, "EuroNET-PHL-C1," NIH, 2007, https://clinicaltrials.gov/study/NCT00433459?term=EuroNet-PHL-C1&rank=2.

23. C. Mauz-Körholz, "EuroNet-PHL-C2," NIH, last updated 2024, https://clinicaltrials.gov/study/NCT02684708?term=EuroNet-PHL-C2&rank=1.

24. S. R. Jhawar, Z. Rivera-Núñez, R. Drachtman, P. D. Cole, B. S. Hoppe, and R. R. Parikh, "Association of Combined Modality Therapy vs Chemotherapy Alone With Overall Survival in Early-Stage Pediatric Hodgkin Lymphoma," *JAMA Oncology* 5, no. 5 (2019): 689, https://doi.org/10.1001/jamaoncol.2018.5911.

25. S. F. Barrington, N. G. Mikhaeel, L. Kostakoglu, et al., "Role of Imaging in the Staging and Response Assessment of Lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group," *Journal of Clinical Oncology* 32, no. 27 (2014): 3048–3058, https://doi.org/10.1200/JCO.2013.53.5229.

26. R. Kluge, L. Kurch, T. Georgi, and M. Metzger, "Current Role of FDG-PET in Pediatric Hodgkin's Lymphoma," *Seminars in Nuclear Medicine* 47, no. 3 (2017): 242–257, https://doi.org/10.1053/j.semnuclmed.2017.01.001.

27. J. Gough, S. Mowat, L. Sellman, K. Robinson, M. Youings, and H. Mandeville, "Institutional Experience of Using Active Breathing Control for Paediatric and Teenage Patients Receiving Thoraco-Abdominal Radiotherapy," *Clinical and Translational Radiation Oncology* 39 (2023): 100575, https://doi.org/10.1016/j.ctro.2022.100575.

28. E. Gogineni, Z. Fellows, W. T. Hrinivich, et al., "Dosimetric Comparison of Breath-Hold and Free-Breathing Techniques in Left-Sided Breast Cancer Patients Treated with Proton Pencil Beam Scanning," *Therapeutic Radiology and Oncology* 7 (2023): 6, https://doi.org/10.21037/tro-22-5.

29. O. A. Houlihan, G. Rangaswamy, M. Dunne, et al., "Deep Inspiration Breath Hold Versus Free Breathing Technique in Mediastinal Radiotherapy for Lymphoma," *BJR|Open* 3, no. 1 (2021): 20200067, https://doi.org/10.1259/bjro.20200067.

30. G. F. Persson, J. Scherman Rydhög, M. Josipovic, et al., "Deep Inspiration Breath-Hold Volumetric Modulated Arc Radiotherapy Decreases Dose to Mediastinal Structures in Locally Advanced Lung Cancer," *Acta Oncologica* 55, no. 8 (2016): 1053–1056, https://doi.org/10.3109/0284186X.2016.1142115.

31. C. Simonetto, M. Eidemüller, A. Gaasch, et al., "Does Deep Inspiration Breath-Hold Prolong Life? Individual Risk Estimates of Ischaemic Heart Disease After Breast Cancer Radiotherapy," *Radiotherapy and Oncology* 131 (2019): 202–207, https://doi.org/10.1016/j.radonc.2018.07.024.

32. N. Bhakta, Q. Liu, K. K. Ness, et al., "The Cumulative Burden of Surviving Childhood Cancer: An Initial Report from the St Jude Lifetime Cohort Study (SJLIFE)," *Lancet* 390, no. 10112 (2017): 2569–2582, https://doi.org/10.1016/S0140-6736(17)31610-0.

33. M. V. Maraldo, N. P. Brodin, M. C. Aznar, et al., "Estimated Risk of Cardiovascular Disease and Secondary Cancers with Modern Highly Conformal Radiotherapy for Early-Stage Mediastinal Hodgkin Lymphoma," *Annals of Oncology* 24, no. 8 (2013): 2113–2118, https://doi.org/10.1093/annonc/mdt156.

34. M. V. Maraldo, M. Jørgensen, N. P. Brodin, et al., "The Impact of Involved Node, Involved Field and Mantle Field Radiotherapy on Estimated Radiation Doses and Risk of Late Effects for Pediatric Patients

with Hodgkin Lymphoma," *Pediatric Blood and Cancer* no. 4 (2014): 61, https://doi.org/10.1002/pbc.24861.

35. D. E. Østergaard, A. Bryce-Atkinson, M. Skaarup, et al., "Paediatric CBCT Protocols for Image-guided Radiotherapy; Outcome of a Survey across SIOP Europe Affiliated Countries and Literature Review," *Radiotherapy and Oncology* 190 (2024): 109963, https://doi.org/10.1016/j.radonc.2023.109963.

36. A. Edvardsson, M. Kügele, S. Alkner, et al., "Comparative Treatment Planning Study for Mediastinal Hodgkin's Lymphoma: Impact on Normal Tissue Dose Using Deep Inspiration Breath Hold Proton and Photon Therapy," *Acta Oncologica* 58, no. 1 (2019): 95–104, https://doi.org/10.1080/0284186X.2018.1512153.

37. A. S. Everett, B. S. Hoppe, D. Louis, et al., "Comparison of Techniques for Involved-Site Radiation Therapy in Patients With Lower Mediastinal Lymphoma," *Practical Radiation Oncology* 9, no. 6 (2019): 426–434, https://doi.org/10.1016/j.prro.2019.05.009.

38. A. C. Moreno, J. R. Gunther, S. Milgrom, et al., "Effect of Deep Inspiration Breath Hold on Normal Tissue Sparing With Intensity Modulated Radiation Therapy Versus Proton Therapy for Mediastinal Lymphoma," *Advances in Radiation Oncology* 5, no. 6 (2020): 1255–1266, https://doi.org/10.1016/j.adro.2020.08.004.

39. L. Rechner, M. V. Maraldo, L. Specht, et al., "Proton Therapy Versus IMRT for Mediastinal Lymphoma With and Without Breath Hold," *International Journal of Radiation Oncology, Biology, Physics* 93, no. 3 (2015): E458–E459, https://doi.org/10.1016/j.ijrobp.2015.07.1717.

40. K. Taparra, S. C. Lester, W. S. Harmsen, et al., "Reducing Heart Dose with Protons and Cardiac Substructure Sparing for Mediastinal Lymphoma Treatment," *International Journal of Particle Therapy* 7, no. 1 (2020): 1–12, https://doi.org/10.14338/IJPT-20-00010.1.

41. Y. D. Tseng, S. M. Maes, G. Kicska, et al., "Comparative Photon and Proton Dosimetry for Patients with Mediastinal Lymphoma in the Era of Monte Carlo Treatment Planning and Variable Relative Biological Effectiveness," *Radiation Oncology* 14, no. 1 (2019): 243, https://doi.org/10.1186/s13014-019-1432-8.

42. T. Alderliesten, J.-J. Sonke, A. Betgen, J. Honnef, C. van Vliet-Vroegindeweij, and P. Remeijer, "Accuracy Evaluation of a 3-Dimensional Surface Imaging System for Guidance in Deep-Inspiration Breath-Hold Radiation Therapy," *International Journal of Radiation Oncology, Biology, Physics* 85, no. 2 (2013): 536–542, https://doi.org/10.1016/j.ijrobp.2012.04.004.

43. A. Betgen, T. Alderliesten, J.-J. Sonke, C. van Vliet-Vroegindeweij, H. Bartelink, and P. Remeijer, "Assessment of Set-Up Variability during Deep Inspiration Breath Hold Radiotherapy for Breast Cancer Patients by 3D-surface Imaging," *Radiotherapy and Oncology* 106, no. 2 (2013): 225–230, https://doi.org/10.1016/j.radonc.2012.12.016.

44. R. Topolnjak, J.-J. Sonke, J. Nijkamp, et al., "Breast Patient Setup Error Assessment: Comparison of Electronic Portal Image Devices and Cone-Beam Computed Tomography Matching Results," *International Journal of Radiation Oncology, Biology, Physics* 78, no. 4 (2010): 1235–1243, https://doi.org/10.1016/j.ijrobp.2009.12.021.

## Supporting Information

Additional supporting information can be found online in the Supporting Information section.

**Figure S1:** CONSORT diagram of patient included in TEDDI. RT: Radiotherapy, RH: Rigshospitalet AUH: Aarhus Univsersity Hospital, OUH Odense University Hospital; PRO: Patient reported outcome. **Table S1:** Inclusion and exclusion criterias. **Table S2:** Scale A. **Table S3:** Scale B. **Table S4:** Evaluation of DIBH training. **Table S5:** Daily questionnaire. **Table S6:** Extended questionnaire (first day, halfway, and last day of radiotherapy course).