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Technical feasibility of delivering a simultaneous integrated boost in partial breast irradiation

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ABSTRACT

Feasibility of volumetric modulated arc therapy (VMAT) for partial breast irradiation (PBI) with simultaneous integrated boost (SIB) to tumour bed was investigated. Four plans were created for 10 patients: 30 Gy/5 fractions, 26 Gy/5 fractions with 30 Gy SIB, 40.05 Gy/15 fractions, and 40.05 Gy/15 fractions with 48 Gy SIB. SIB in the 5 fraction arm had reduced ipsilateral breast dose relative to uniform dose. SIB in the 15 fraction arm had noninferior conformity compared to uniform dose. Addition of SIB did not increase other organ-at-risk doses or plan complexity. VMAT PBI with SIB was feasible for both fractionation regimens.

1. Introduction

Standard of care for early-stage breast cancer patients following breast-conserving surgery includes both partial breast irradiation (PBI) [1–4], and whole breast irradiation (WBI) with a simultaneous integrated boost (SIB) to the tumour bed [5,6]. The recently published ASTRO Clinical Practice Guidelines provide detailed analysis of the phase III evidence for PBI in the context of early-stage invasive breast cancer, and provide expert opinion for its use in ductal carcinoma in situ (DCIS) [7]. Two fractionation regimens were strongly recommended: 30 Gy in 5 fractions over 2 weeks (non-consecutive days), or 40.05 Gy in 15 fractions over 3 weeks. PBI was recommended for patients aged ≥40 years with low-intermediate/grade 1–2 DCIS or invasive disease (respectively), with consideration extended to grade 3 disease in both phenotypes. Many of these patients (for example, aged ≤50 years) would also be recommended tumour bed boost in the context of WBI [8]. Therefore, PBI with SIB may represent the next step in the advancement of treatment for these patients, offering a combination of the control benefits of a tumour bed boost with the toxicity benefits of PBI.

Achieving SIB in a partial breast volume may be technically challenging due to needs of both conformity of the lower dose level to the partial breast volume, and an in-field dose gradient to produce the boost to the (potentially small) tumour bed. The use of volumetric modulated arc therapy (VMAT) for PBI has been investigated in prospective studies, with promisingly low rates of early toxicity indicating this is a viable treatment approach [9,10]. Previous planning studies in WBI have found SIB is achievable with either intensity-modulated radiation therapy (IMRT) or VMAT, however, VMAT consistently produced plans with fewer monitor units (MU) and hence has a treatment time benefit [11,12]. In some WBI planning studies, VMAT planning was not recommended due to the additional dose to surrounding OARs (with respect to tangential IMRT) despite achieving adequate target coverage [13,14]. In this work, we explore the technical feasibility of using VMAT to deliver PBI with SIB for both 5 and 15 fraction regimens. In the 5 fraction regimen, an SIB prescription of 26 Gy to the partial breast and 30 Gy to the tumour bed was investigated. In the 15 fraction regimen, an SIB prescription of 40.05 Gy to the partial breast and 48 Gy to the tumour was investigated.

2. Materials and Methods

2.1. Demographics

The 10 most recently treated PBI patients at our institution were selected for the study. Previous treatment plans were IMRT (30 Gy in 5 fractions). Four VMAT plans were created on the original planning CT for each patient in the Eclipse treatment planning system (TPS) v16.1, using a Varian True Beam with Millennium 120 multi-leaf collimator

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(MLC) beam model, and the AcurosXB dose to medium calculation algorithm (Varian Medical Systems, Palo Alto USA). All plans were created by the same qualified radiation therapist (RTT), and checked by a senior RTT and physicist following institutional practice. For each fractionation regimen, both the ASTRO-recommended uniform dose plans were compared to the proposed SIB prescriptions. The study was approved by our institution's ethics review board (project number 17_95R).

2.2. Contouring

Target volumes were contoured following the IMPORT HIGH protocol [6]. The tumour bed (gross target volume – GTV) was defined as the volume enclosed by the surgical markers plus the surgical change of tissue architecture. The boost planning target volume (PTV_Boost) was defined as the GTV plus 5 mm. The clinical target volume (CTV) was created using a 15 mm expansion on the GTV, cropped at the anatomical boundaries of the ipsilateral breast and 5 mm within the patient contour. The partial breast PTV (PTV_Low) was created using a uniform 5 mm expansion on the CTV. Target coverage was assessed on "evaluation" PTV contours (PTV_Eval and Boost_Eval), cropped 5 mm inside the external contour. Patient target volume sizes and locations are summarised in the supplementary materials. Note all left-sided patients were scanned in deep inspiration breath-hold (DIBH) as per institution policy.

2.3. Beam arrangement

Treatment isocentre was positioned central in the GTV. A combination of 6 MV and 10 MV flattening filter-free (FFF) beam energies were used at their maximum dose rates (1400 and 2400 MU/min respectively). All plans employed four short "butterfly" arcs, designed to act as faux-tangential fields from the medial and lateral aspects. Unique non-zero collimator angles were selected for each arc. Fields were arranged by using 60° to 100° arc spans, extended approximately 15° past traditional tangent angles. A 40° to 50° arc separation was maintained between medial and lateral fields. The region of avoidance was optimised on a per patient basis to minimise the dose exiting into the lung and/or heart.

2.4. Dose constraints

The 5 fraction prescription could be considered as a PBI alternative to ongoing studies exploring SIB to the established FAST Forward WBI dose [15,16], or a conservative means of delivering the ASTRO-preferred dose to the tumour bed, whilst minimising the risk of toxicity in light of the mixed outcomes in studies of 30 Gy in 5 consecutive daily fractions [9,17–19]. The 15 fraction prescription could be considered to make use of the IMPORT HIGH tumour bed dose distribution, without treating the entire breast and hence minimise risk of associated toxicities.

Plans were optimised to meet the organ at risk (OAR) constraints outlined in Table 1. In-field dose gradient was achieved in the SIB plans by limiting the $D_{2\%}$ in a structure defined as PTV_Eval minus Boost_Eval (PTV-BoostEval) to the prescription isodose. All plans were normalised to achieve a median dose of 100 % of the prescription dose to the relevant evaluation structure. Uniform dose plans were normalised to the PTV_Eval structure. Boost plans were normalised to the Boost_Eval structure, ensuring 98 % of the PTV_Eval structure remained covered by the 95 % isodose line of the lower dose level. For patients with PTV_Low abutting the external contour, a 4 mm rind of tissue was added to the

Table 1
Summarised dose-volume results of the planning study. Values shown are medians, with range in square brackets. Asterisk indicates statistical significance.

	5 fractions						15 fractions					
Structure	**Constraint**	**Goal**	**Variation**	**Uniform Dose Median [Range]**	**SIB Median [Range]**	**p-value**	**Constraint**	**Goal**	**Variation**	**Uniform Dose Median [Range]**	**SIB Median [Range]**	**p-value**
Heart	$V_{3\ Gy}$ *[%]*	< 10 %^	–	0 [0, 1.6]	0 [0, 0.8]	0.18	$D_{1\ \%}$ *[Gy]*	< 35 Gy+		1.2 [0.3, 4.4]	1.4 [0.4, 5.5]	0.38
							$D_{5\ \%}$ *[Gy]*	< 17 Gy+	< 20 Gy	0.8 [0.2, 2.1]	0.8 [0.3, 3.2]	0.70
							Mean Dose [Gy]	< 3 Gy	< 5 Gy	0.3 [0.1, 0.7]	0.3 [0.2, 0.8]	0.63
							$V_{13\ Gy}$ *[%]*	< 10 %*	–	0 [0, 0]	0 [0, 0]	NA
Ipsilateral Lung	$V_{10\ Gy}$ *[%]*	< 20 %^	–	0.9 [0, 8.9]	0.4 [0, 7.4]	0.13	$V_{16\ Gy}$ *[%]*	< 15 %**	–	0.3 [0, 6]	0.3 [0, 4.9]	0.61
							Mean Dose [Gy]	< 16 Gy+		1.9 [1.1, 3.7]	1.8 [1, 4.2]	0.70
							$V_{5\ Gy}$ *[%]*	< 50 %	–	10.5 [1.1, 23.4]	10.1 [0.8, 30.6]	1.0
Contralateral Lung	$V_{5\ Gy}$ *[%]*	< 10 %^		0 [0, 0]	0 [0, 0]	NA	$V_{5\ Gy}$ *[%]*	< 10 %	–	0 [0, 0]	0 [0, 1.4]	0.18
							$V_{2.5\ Gy}$ *[%]*	< 15 %*	–	0 [0, 2.4]	0.9 [0, 8.9]	0.03
Contralateral Breast	$D_{1\ cm3}$ *[Gy]*	< 1 Gy^	< 2 Gy^	1.6 [0.8, 2.4]	1.2 [0.9, 1.9]	0.01	$V_{4.1\ Gy}$ *[%]*	< 5 %	–	0 [0, 0.3]	0 [0, 2.6]	0.11
							Mean Dose [Gy]	< 0.5 Gy*	< 1.5 Gy*	0.4 [0.1, 0.6]	0.5 [0.2, 1.1]	<0.01
Ipsilateral Breast	$V_{15\ Gy}$ *[%]*	< 50 %^	< 60 %^	18.9 [11.3, 35]	17 [10.5, 31.5]	<0.01	$V_{40\ Gy}$ *[%]*	< 5 %*		0 [0, 0.2]	0.6 [0.3, 3.5]	<0.01
PTV-BoostEval (SIB only)	$D_{2\ \%}$ *[%]*	< 100 %	< 100 %*	NA	98.1 [97.6, 98.6]	NA	$D_{2\ \%}$ *[%]*	< 100 %	D5% < 100 %*	98 [97.3, 98.4]	NA	NA

* = Constraint taken from IMPORT HIGH protocol.
** = Modified IMPORT HIGH constraint – originally $V_{18\ Gy}$ < 15 %.
+ = Constraint taken from Danish Breast Cancer Group (DBCG) PBI Trial.
^ = Constraint taken from update to APBI-IMRT-FLORENCE Trial.

structure set and assigned to adipose tissue during optimisation. This step was taken to limit hot spots at the skin, arising due to the lack of electronic equilibrium at shallow depths in the target structure. The material assignment was removed for the final dose calculation.

2.5. Plan evaluation

Plan quality was assessed based on the dose constraints in Table 1. Conformity of the dose to the partial breast volume was assessed differently for the two fractionations. In the 5 fraction regimen, conformity was assessed based on the volume of the 27 Gy isodose line in the ipsilateral breast contour. This was motivated by the findings of the FAST-Forward trial, which found increased toxicity in the 27 Gy daily fraction arm relative to the 26 Gy arm [18]. In the 15 fraction regimen, the volume of the 38.05 Gy isodose line (95 % of 40.05 Gy) in the ipsilateral breast contour was assessed, as well as the conformity index taken as the ratio of this isodose line in the patient to the PTV_Eval structure (Patient $V_{38.05\ Gy}$ [cm^3] divided by PTV_Eval $V_{38.05\ Gy}$ [cm^3]).

Patient-specific quality assurance (PSQA) was performed using an ArcCHECK (Sun Nuclear, Melbourne USA) with centrally located CC13 ionisation chamber (IBA Dosimetry GmbH, Schwarzenbruck Germany). Gamma criteria of 3 %/2 mm with a 10 % threshold (normalised to global dose maximum) were applied as per institutional and consensus guidelines [20]. Treatment time and complexity metrics modulation factor (MF – total MU divided by the dose-per-fraction) and average leaf pair opening (ALPO − average distance between moving MLC leaf tips for all control points) were compared between uniform dose and SIB plans.

2.6. Statistics

OAR doses between uniform dose and SIB plans were statistically compared using a Wilcoxon signed-rank test.

3. Results

All OAR objectives were met in the 5 fraction SIB plans. In the uniform dose plans, the two left-sided upper-inner quadrant targets were not able to meet the contralateral breast constraint of $D_{1\ cm3} < 2$ Gy. The SIB plans had slightly reduced contralateral breast $D_{1\ cm3}$ ($p = 0.01$) and ipsilateral breast $V_{15\ Gy}$ ($p < 0.01$) (see Table 1).

In the 15 fraction plans, the ideal constraint for the contralateral breast mean dose (0.5 Gy) was challenging to meet. 50 % of SIB plans and 40 % of uniform dose plans exceeded this goal, however none exceeded the acceptable variation of 2 Gy. The SIB plans produced small increases in some OAR metrics relative to the uniform dose plans (Table 1), but all plans met the constraints.

All SIB plans met the coverage requirement (PTV_Eval $D_{98\%} > 95$ %) for the partial breast volume after normalisation. Median PTV_Eval $D_{98\%}$ was 25.7 Gy (98.7 % of 26 Gy) for the 5 fraction plans, and 39.6 Gy (98.8 % of 40.05 Gy) for the 15 fraction plans. Ipsilateral breast $V_{27\ Gy}$ was reduced in the 5 fraction SIB plans relative to the uniform dose plans (SIB median $V_{27\ Gy} = 0$ %, uniform = 2.9 %, $p < 0.01$). Ipsilateral breast $V_{38.05\ Gy}$ was comparable between both plan types for the 15 fraction regimen, with SIB plans resulting in a median 1 % increase in this conformity metric (SIB median $V_{38.05\ Gy} = 1.9$ %, uniform = 0.9 %, $p = 0.06$). The conformity index correspondingly increased slightly from a median of 1.1 in the uniform dose plans, to 1.2 in the SIB plans.

PSQA and plan complexity results are summarised in Table 2. All results were within institutional tolerances, with median gamma passing rate of 99.9 % (tolerance >95 %) and point dose difference of 1.2 % (tolerance ± 3 %). SIB plans had lower MF than uniform dose in both fractionation regimes. SIB ALPO was slightly decreased in the 5 fraction SIB plans, but was equivalent in the 15 fraction plans. Treatment times were comparable for all plans.

Table 2
Summary of PSQA results, plan complexity metrics and treatment times. Values shown are medians, with range in square brackets. Positive CC13 dose difference indicates measurement is higher than plan.

	5 fractions		15 fractions	
	Uniform Dose	**SIB**	**Uniform Dose**	**SIB**
3 %/2 mm Gamma passing rate [%]	100 [99.7, 100]	100 [97.9, 100]	99.7 [99.0, 100]	99.8 [99.6, 100]
CC13 dose difference [%]	1.1 [0.3, 2.2]	1.2 [0.5, 1.6]	1.3 [0.6, 1.6]	1.1 [-0.2, 1.5]
Per field delivery time [s]	15.3 [10.2, 20.9]	15 [10.1, 18.9]	15 [10, 18.8]	15 [10, 18.8]
Total delivery time [s]	57.4 [52.4, 73.4]	56.1 [50.6, 70.4]	55.1 [50, 69.3]	55 [50, 69.3]
Modulation factor [MU/cGy]	1.65 [1.35, 2.15]	1.5 [1.3, 1.88]	1.68 [1.53, 2.14]	1.48 [1.38, 1.88]
Average leaf pair opening [mm]	50.5 [29.5, 58.8]	46.5 [31.5, 57.8]	45.6 [29.7, 57.3]	45.9 [29.5, 54.8]

4. Discussion

Achieving SIB in the tumour bed whilst maintaining a conformal dose distribution to the larger partial breast volume was possible with partial VMAT arcs. In the 5 fraction plans, the boost allowed dose at the periphery of the partial breast volume to be de-escalated, reflected in reduced contralateral and ipsilateral breast doses. In the 15 fraction plans, the dose was escalated without substantially worsening the conformity or OAR dose-volume metrics.

While this work demonstrated the feasibility of the planning approach, there are additional technical considerations to ensure the planned dose distribution is delivered accurately, due to the more complex dose distribution (relative to standard PBI). One consideration is the accuracy of targeting the boost volume. Delineating the tumour bed can be challenging if no seroma is present or breast tissue is dense. Multiple surgical clips placed at the boundaries of the excised region may be critical to accurate boost volume contouring [21], and precise matching during image guidance.

Another factor to consider is intra-fraction motion. There is clear evidence for using DIBH to reduce heart/lung doses [22,23], and is the established standard of care for left-sided WBI in many institutions [24,25]. The use of DIBH has been allowed in previous PBI trials without being mandatory [1,4,6,9]. The DBCG recently published a sub-group analysis finding that respiratory gating (predominantly DIBH) resulted in reduced mean heart doses for patients with left upper-quadrant disease, but not in other locations [26]. As it stands, the evidence for the use of DIBH in PBI for the reduction of OAR doses is modest [26,27]. However, the in-field dose gradient of SIB places more impetus on accurate localisation of the boost volume, which may be improved by using respiratory gating [28]. Breath-hold reproducibility and stability may be further improved through patient-specific triaging and selection of preferred approach [29]. Therefore, gating modes not previously considered for WBI (eg − end-exhale breath-hold) may be considered for PBI with SIB as a means of maximising treatment accuracy. Partial VMAT arcs are compatible with breath-hold due to the short per-field delivery times. Previously published PBI VMAT techniques utilised half-arcs which may be sub-optimal from both OAR sparing and treatment time perspectives [9,10]. Efficient dose delivery should be considered alongside motion management to ensure the technique remains accessible to the majority of patients.

In conclusion, PBI with SIB was found feasible for both 5 and 15 fraction regimes, and its efficacy will be tested in a clinical trial at our institution.

Declaration of competing interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Meattini I, Marrazzo L, Saieva C, Desideri I, Scotti V, Simontacchi G, et al. Accelerated partial-breast irradiation compared with whole-breast irradiation for early breast cancer: long-term results of the randomized phase III APBI-IMRT-florence trial. J Clin Oncol 2020;38:4175–83. https://doi.org/10.1200/JCO.20.00650.

[2] Bhattacharya IS, Haviland JS, Kirby AM, Kirwan CC, Hopwood P, Yarnold JR, et al. Patient-reported outcomes over 5 years after whole- Or partial-breast radiotherapy: longitudinal analysis of the import low (CRUK/ 06/003) phase III randomized controlled trial. J Clin Oncol 2019;37:305–17. https://doi.org/10.1200/JCO.18.00982.

[3] Vicini FA, Cecchini RS, White JR, Arthur DW, Julian TB, Rabinovitch RA, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. Lancet 2019;394:2155–64. https://doi.org/10.1016/S0140-6736(19)32514-0.

[4] Offersen BV, Alsner J, Nielsen HM, Jakobsen EH, Nielsen MH, Stenbygaard L, et al. Partial breast irradiation versus whole breast irradiation for early breast cancer patients in a randomized phase III trial: the danish breast cancer group partial breast irradiation trial. J Clin Oncol 2022;40:4189–97. https://doi.org/10.1200/JCO.22.00451.

[5] Chua BH, Link EK, Kunkler IH, Whelan TJ, Westenberg AH, Gruber G, et al. Radiation doses and fractionation schedules in non-low-risk ductal carcinoma in situ in the breast (BIG 3–07/TROG 07.01): a randomised, factorial, multicentre, open-label, phase 3 study. Lancet 2022;400:431–40. https://doi.org/10.1016/S0140-6736(22)01246-6.

[6] Coles CE, Haviland JS, Kirby AM, Griffin CL, Sydenham MA, Titley JC, et al. Dose-escalated simultaneous integrated boost radiotherapy in early breast cancer (IMPORT HIGH): a multicentre, phase 3, non-inferiority, open-label, randomised controlled trial. Lancet 2023;401:2124–37. https://doi.org/10.1016/S0140-6736(23)00619-0.

[7] Shaitelman SF, Anderson BM, Arthur DW, Bazan JG, Bellon JR, Bradfield L, et al. Partial breast irradiation for patients with early-stage invasive breast cancer or ductal carcinoma in situ: an ASTRO clinical practice guideline. Pract Radiat Oncol 2024;14:112–32. https://doi.org/10.1016/j.prro.2023.11.001.

[8] Smith BD, Bellon JR, Blitzblau R, Freedman G, Haffty B, Hahn C, et al. Radiation therapy for the whole breast: executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Pract Radiat Oncol 2018;8:145–52. https://doi.org/10.1016/j.prro.2018.01.012.

[9] Marrazzo L, Meattini I, Simontacchi G, Livi L, Pallotta S. Updates on the APBI-IMRT-Florence Trial (NCT02104895) technique: from the intensity modulated radiation therapy trial to the volumetric modulated arc therapy clinical practice. Pract Radiat Oncol 2022;13:e28–34. https://doi.org/10.1016/j.prro.2022.05.010.

[10] La Rocca E, Lozza L, D' Ippolito E, Dispinzieri M, Giandini C, Bonfantini F, et al. VMAT partial-breast irradiation: acute toxicity of hypofractionated schedules of 30 Gy in five daily fractions. Clin Transl Oncol 2020;22:1802–8. https://doi.org/10.1007/s12094-020-02319-5.

[11] Aly MMOM, Glatting G, Jahnke L, Wenz F, Abo-Madyan Y. Comparison of breast simultaneous integrated boost (SIB) radiotherapy techniques. Radiat Oncol 2015;10:1–8. https://doi.org/10.1186/s13014-015-0452-2.

[12] Murphy SBD, Drury-Smith H. Which simultaneous-integrated boost (SIB) intensity-modulated radiotherapy (IMRT) technique is dosimetrically superior in the treatment of breast cancer; volumetric-modulated arc therapy (VMAT) or fixed field (ff) IMRT? J Radiother Pract 2017;16:272–9. https://doi.org/10.1017/S1460396917000164.

[13] Wu S, Lai Y, He Z, Zhou Y, Chen S, Dai M, et al. Dosimetric comparison of the simultaneous integrated boost in whole-breast irradiation after breast-conserving surgery: IMRT, IMRT plus an electron boost and VMAT. PLoS One 2015;10:1–11. https://doi.org/10.1371/journal.pone.0120811.

[14] Bi S, Zhu R, Dai Z. Dosimetric and radiobiological comparison of simultaneous integrated boost radiotherapy for early stage right side breast cancer between three techniques: IMRT, hybrid IMRT and hybrid VMAT. Radiat Oncol 2022;17:1–10. https://doi.org/10.1186/s13014-022-02009-2.

[15] Lewis P, Brunt AM, Coles C, Griffin S, Locke I, Roques T. Moving forward fast with FAST-forward. Clin Oncol 2021;33:427–9. https://doi.org/10.1016/j.clon.2021.04.007.

[16] Zanoguera CG, Quintero JG, Artiles AGC, Castell LM, Maturana JEM, Gonzalez IO, et al. Safety and feasibility of simultaneous integrated boost in extreme 1-week hypofractionated radiotherapy for early breast cancer. Int J Radiat Oncol Biol Phys 2022;114:e28. https://doi.org/10.1016/j.ijrobp.2022.07.736.

[17] Shaitelman SF, Anderson BM, Arthur DW, Bazan JG, Bellon JR, Bradfield L, et al. Partial breast irradiation for patients with early-stage invasive breast cancer or ductal carcinoma in situ: an ASTRO clinical practice guideline. Pract Radiat Oncol 2023. https://doi.org/10.1016/j.prro.2023.11.001.

[18] Murray Brunt A, Haviland JS, Wheatley DA, Sydenham MA, Alhasso A, Bloomfield DJ, et al. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Lancet 2020;395:1613–26. https://doi.org/10.1016/S0140-6736(20)30932-6.

[19] Kim DH, Theberge V, Provencher S, Yassa M, Kong I, Perera FE, et al. OPAR: a multicenter phase II randomized trial of fractionation schedules for once-a-day accelerated partial breast irradiation (APBI). Int J Radiat Oncol Biol Phys 2021;111:S6. https://doi.org/10.1016/j.ijrobp.2021.07.047.

[20] Miften M, Olch A, Mihailidis D, Moran J, Pawlicki T, Molineu A, et al. Tolerance limits and methodologies for IMRT measurement-based verification QA: Recommendations of AAPM Task Group No. 218. Med Phys 2018;45:e53–83. https://doi.org/10.1002/mp.12810.

[21] Corrao G, Rojas DP, Ciardo D, Fanetti G, Dicuonzo S, Mantovani M, et al. Intra- and inter-observer variability in breast tumour bed contouring and the controversial role of surgical clips. Med Oncol 2019;36:1–8. https://doi.org/10.1007/s12032-019-1273-1.

[22] Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Brønnum D, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med 2013;368:987–98. https://doi.org/10.1056/nejmoa1209825.

[23] Pandeli C, Smyth LML, David S, See AW. Dose reduction to organs at risk with deep-inspiration breath-hold during right breast radiotherapy: a treatment planning study. Radiat Oncol 2019;14:1–10. https://doi.org/10.1186/s13014-019-1430-x.

[24] Anastasi G, Bertholet J, Poulsen P, Roggen T, Garibaldi C, Tilly N, et al. Patterns of practice for adaptive and real-time radiation therapy (POP-ART RT) part I: intra-fraction breathing motion management. Radiother Oncol 2020;153:1–23.

[25] Ball HJ, Santanam L, Senan S, Tanyi JA, van Herk M, Keall PJ. Results from the AAPM Task Group 324 respiratory motion management in radiation oncology survey. J Appl Clin Med Phys 2022;23. https://doi.org/10.1002/acm2.13810.

[26] Høgsbjerg KW, Maae E, Nielsen MH, Stenbygaard L, Pedersen AN, Yates E, et al. Benefit of respiratory gating in the Danish Breast Cancer Group partial breast irradiation trial. Radiother Oncol 2024;194. https://doi.org/10.1016/j.radonc.2024.110195.

[27] Essers M, Osman SOS, Hol S, Donkers T, Poortmans PM. Accelerated partial breast irradiation (APBI): are breath-hold and volumetric radiation therapy techniques useful? Acta Oncol 2014;53:788–94. https://doi.org/10.3109/0284186X.2014.887226.

[28] Carr MA, Gargett M, Stanton C, Zwan B, Byrne HL, Booth JT. A method for beam's eye view breath-hold monitoring during breast volumetric modulated arc therapy. Phys Imaging Radiat Oncol 2023;25:100419. https://doi.org/10.1016/j.phro.2023.100419.

[29] Farrugia B, Knight K, Wright C, Tacey M, Foroudi F, Chao M, et al. A prospective trial demonstrating the benefit of personalized selection of breath-hold technique for upper-abdominal radiation therapy using the active breathing coordinator. Int J Radiat Oncol Biol Phys 2021;111:1289–97. https://doi.org/10.1016/j.ijrobp.2021.08.001.