Dosimetric effect of rotational setup errors in volumetric modulated arc therapy and field-in-field treatment of left-sided breast cancer

Annele Heikkilä, Eeva Boman, Maija Rossi, Antti Vanhanen, Mikko Mankinen, Michiel Postema, Tuomas Koivumäki

Physica Medica 117 (2024) 103203

Contents lists available at ScienceDirect

Physica Medica

journal homepage: www.elsevier.com/locate/ejmp

Technical note

Dosimetric effect of rotational setup errors in volumetric modulated arc therapy and field-in-field treatment of left-sided breast cancer

Annele Heikkilä [a,b,*], Eeva Boman [b,c], Maija Rossi [b,c], Antti Vanhanen [b,c], Mikko Mankinen [d], Michiel Postema [a,e], Tuomas Koivumäki [d]

[a] BioMediTech, Faculty of Medicine and Health Technology, Tampere University, Korkeakoulunkatu 3, 33720 Tampere, Finland
[b] Department of Medical Physics, Tampere University Hospital, P.O. Box 2000, 33521 Tampere, Finland
[c] Department of Oncology, Tampere University Hospital, P.O. Box 2000, 33521 Tampere, Finland
[d] Department of Medical Physics, Central Finland Health Care District, Hoitajantie 3, 40620, Jyväskylä, Finland
[e] School of Electrical and Information Engineering, University of the Witwatersrand, Johannesburg, 1 Jan Smutslaan, 2050 Braamfontein, South Africa

ARTICLE INFO

Keywords:
Breast radiotherapy
Robustness of VMAT
Interfraction positioning errors
DICOM image rotation

ABSTRACT

Setup errors are an important factor in the dosimetric accuracy of radiotherapy delivery. In this study, we investigated how rotational setup errors influence the dose distribution in volumetric modulated arc therapy (VMAT) and tangential field-in-field (FiF) treatment of left-sided breast cancer with supraclavicular lymph node involvement in deep inspiration breath hold. Treatment planning computed tomography images and radiotherapy plans of 20 patients were collected retrospectively for the study. Rotational setup errors up to 3° were simulated by rotating the planning images, and the resulting dosimetric changes were calculated. With rotational setup errors up to 3°, the median decrease of $V_{95\%}$ to clinical target volume was less than 0.8 percentage point in both VMAT and FiF plans. The dose distribution of the heart and left anterior descending artery was more stable with respect to rotations in VMAT plans compared to FiF plans. Correction of ≥ 1° setup errors is recommended due to increased doses to the heart and left anterior descending artery after 1° setup errors.

1. Introduction

Adjuvant radiotherapy after breast-conserving surgery or mastectomy for patients with node-positive disease decreases the probability of cancer recurrence [1,2]. Radiotherapy of breast cancer causes high radiation dose to adjacent normal tissue, which is associated with side effects such as major coronary events and secondary cancer [3,4]. Setup errors during radiotherapy delivery may result in dose inhomogeneity in the treatment target and increase the exposure to organs at risk.

Conventionally, breast irradiation has been delivered using the tangential field-in-field (FiF) technique. At present, volumetric modulated arc therapy (VMAT) is used as an alternative to FiF. VMAT has the advantage of a dose distribution highly conformal to the treatment target, which spares the ipsilateral lung, and, in left-sided treatments, the heart, from high radiation doses [5–9]. However, the low dose volume in VMAT plans is typically larger than in FiF plans [7,9,10].

At present, daily image guidance and six-degrees-of-freedom treatment couches enable correction of setup errors [11–13]. The setup error of a breast radiotherapy patient consists of translational, rotational and deformational variations. In tangential breast radiotherapy, the target dose distribution does not change in a clinically relevant way after systematic 5 mm shifts, 2° rotations or surface-guidance-based intrafractional shifts [14–16]. Two independent groups have reported larger underdosage of target in VMAT plans compared to FiF plans after translational setup errors [15] and combined translational, rotational and deformational setup errors [17]. On the other hand, another group that used the RayStation robust optimisation feature (RaySearch Laboratories, Stockholm, Sweden) observed larger overall dosimetric changes in tangential plans compared to VMAT plans [18]. In [17], the correlation between rotational setup error and PTV coverage was reported to be moderate at highest in VMAT plans, and the dosimetric effect of rotational setup errors on organs at risk was not addressed.

Earlier studies and reports suggest that rotational setup errors have little effect on small or round isosentric targets [19,20]. In treatment of the breast with supraclavicular lymph node involvement, the distance between a point at the edge of PTV and the isocentre may be more than 10 cm, which corresponds to more than 5 mm dislocation of the point after a 3° rotation. Thus, the dosimetric effect of rotations could be different compared to small targets. In addition, the rotations may

* Corresponding author at: BioMediTech, Faculty of Medicine and Health Technology, Tampere University, Korkeakoulunkatu 3, 33720 Tampere, Finland.
E-mail address: annele.heikkila@tuni.fi (A. Heikkilä).

https://doi.org/10.1016/j.ejmp.2023.103203
Received 31 March 2023; Received in revised form 6 October 2023; Accepted 21 December 2023

displace the organs at risk from the original positions, which may have impact on the treatment quality [19].

In breast radiotherapy, a skin flash margin is commonly used to compensate for respiratory motion, variation in deep inspiration breath hold level and breast deformation [21–23]. The flash margin is effective in compensating the surface dose deficit that could be caused by rotational setup errors. However, a rotational setup error may displace a part of the target outside the PTV inside the body or displace an organ at risk inside the treatment field.

The purpose of this study was to quantify the impact of systematic rotational setup errors on the dose distribution and to determine an intervention tolerance for rotational setup errors in VMAT and FiF treatment of left-sided breast cancer in deep inspiration breath hold. To our knowledge, this is the first systematic evaluation of the effect of rotations on VMAT plans in breast radiotherapy.

2. Materials and methods

Planning computed tomography images and treatment plans of 20 breast cancer patients treated at Central Finland Central Hospital were retrospectively collected for the study. The inclusion criterion was VMAT treatment of left breast with supraclavicular lymph node involvement in deep inspiration breath hold with fractionation scheme of 15 × 2.67 Gy. Ten patients had undergone mastectomy and another ten conservative surgery. The internal mammary lymph nodes (IMLN) were included in the treatment target in 12 patients. A research permit was obtained from Central Finland Health Care District in accordance with local legislation.

The planning computed tomography images were acquired using a Biograph mCT scanner (Siemens Healthineers, Erlangen, Germany) with 2 mm slice thickness and 0.9766 mm pixel spacing in the transverse plane. An Extended Wing Board with U-Grip handles (Civco Radiotherapy, Coralville, Iowa, USA) was used for patient immobilisation. The breath hold level was monitored using Real-time Position Management system (Varian Medical Systems, Palo Alto, California, USA). The breath hold window width was set to 4 mm.

Clinical target volume (CTV) was delineated on the images by radiation oncologists according to ESTRO guideline [24]. Planning target volume (PTV) was created by adding a 5 mm margin to CTV. PTV and CTV were cropped 3 mm from the body outline to exclude the dose build-up region. Henceforth, the terms PTV and CTV refer to the cropped structures. Organs at risk (heart, left anterior descending artery (LAD), lungs, right breast, spinal cord, left brachial plexus, thyroid and left humeral head) were contoured manually and accepted by a radiation oncologist. The treatment plans were generated for a Clinac iX linear accelerator with Millenium 120 multileaf collimator using Eclipse treatment planning system (Varian Medical Systems, Palo Alto, California, USA). The plans were normalised to the mean dose of the PTV.

The clinically used VMAT plans were utilised in this study. The plans were generated by experienced medical physicists and approved by oncologists before treatment. The isocentre was located close to the mass centre of PTV, but near the chest wall. The plans utilised a double partial arc design with arc length of 239°–249°, the start and end gantry angles being 179° and 290°–300°, respectively. 6 MV photon beams were used. Dose calculation was performed with Analytical Anisotropic Algorithm version 13.6 or 15.6 (Varian Medical Systems) with grid size of 2.5 mm. Photon Optimizer algorithm (Varian Medical Systems) was used for plan optimisation.

FiF plans were created for comparison by an experienced medical physicist following the clinical guidelines at our department. The isocentre was located between the breast and supraclavicular lymph nodes with median distance of 4.6 cm (range 2.0–6.8 cm) cranially from the isocentre of the VMAT plan. Two 6 MV tangential treatment fields caudal to the isocentre, and three fields cranial to the isocentre – two 6 MV fields with median gantry angles of 50° and 344° and a 18 MV field with median gantry angle of 175° – were used. The gantry angles were chosen so that the overlap of the target and organs-at-risk was minimised in the beam's eye view. Subfields were used to avoid dose maxima and to fill in the areas of dose minima. For two patients, a supplementary field from additional direction was used to ensure adequate dose coverage. Dose calculation was performed with Analytical Anisotropic Algorithm version 15.6 with grid size of 2.5 mm. The plans were not reviewed by oncologists.

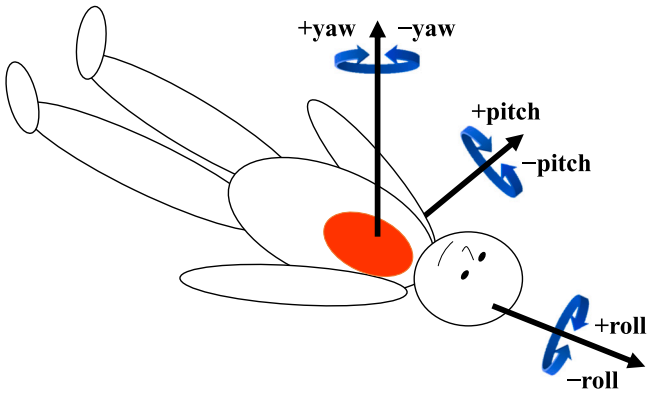


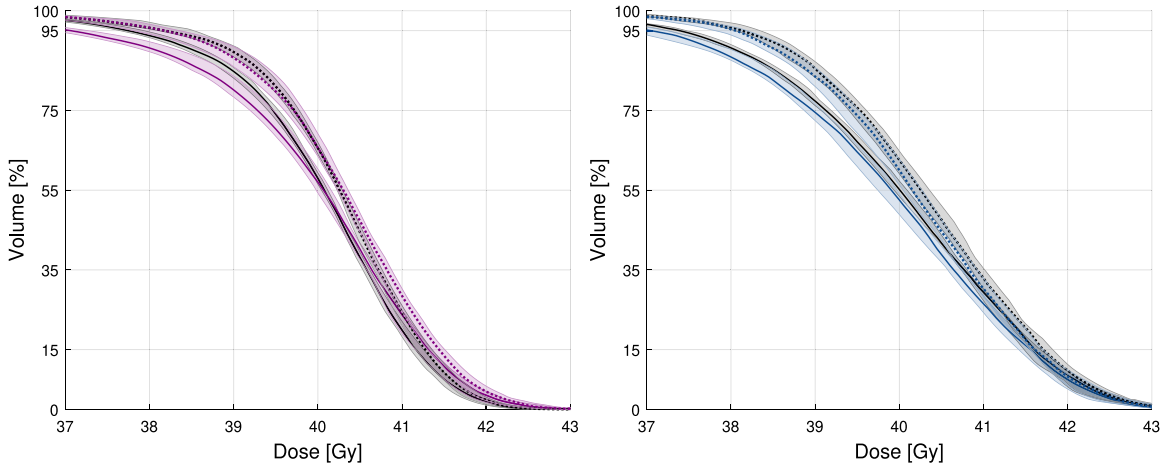
Fig. 1. Rotational setup errors were simulated by rotating the computed tomography images around the axes defined in this figure, following the convention defined by Tudor et al. [26]. The axes cross at the isocentre of the volumetric modulated arc therapy plan. The location of the treatment target is outlined in red. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Both VMAT and FiF plans utilised a flash margin. In VMAT plans, the flash margin was implemented as an 11 mm virtual bolus and 8 mm extension of PTV to the air [25]. In FiF plans, the flash margin was implemented by extending the fields to the air by 3 cm.

Rotational setup errors were simulated by rotating the planning computed tomography images by ±1°, ±2° and ±3° around left–right, posterior-anterior and caudocranial axis (pitch, yaw and roll, respectively) using an in-house developed script in Matlab v. R2020a (The MathWorks, Inc., Natick, Massachusetts, United States). The rotation axes passed through the VMAT treatment isocentre (Fig. 1). The computed tomography images were resampled to 1 mm slice thickness by interpolating pixel values in craniocaudal direction, which resulted in an approximately isotropic image matrix.

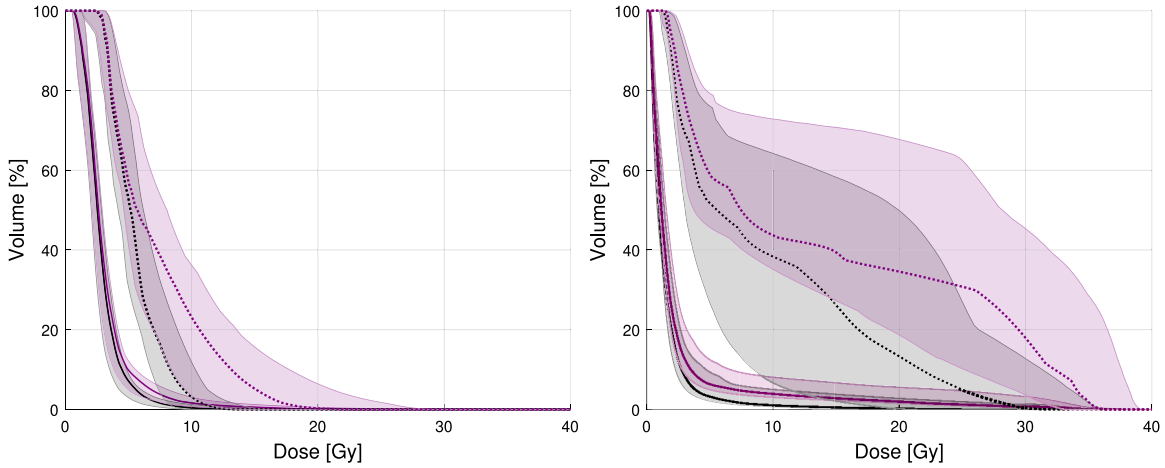
The structure set of the original image was registered and copied to the rotated images in Eclipse. The dose distributions produced by the original VMAT and FiF plans were calculated for the rotated images. For each patient, the same Analytical Anisotropic Algorithm version was used for calculation of dose distribution in rotated images as in the original plan. Differences between the original and rotated dose distributions were quantified by comparing selected dose-volume parameters (Table 2) in original and rotated plans.

Statistical analysis was conducted using SPSS software (v. 26, IBM, Armonk, New York, USA). Shapiro–Wilk test indicated that all parameters were not normally distributed, and thus, non-parametric tests were used. Friedman test was used to detect overall differences between the original and rotated dose distributions. Pairwise differences between the original and rotated dose distributions were analysed using Wilcoxon signed-rank test with exact two-tailed significance. Wilcoxon signed-rank test was also used to compare the change in a parameter value after a given rotation in VMAT plans to the corresponding change in FiF plans. Mann–Whitney U test was used to compare the effect of rotations in the mastectomy patients to the lumpectomy patients and the patients with IMLN involvement to the patients without IMLN involvement.



(a) Volumetric modulated arc therapy (b) Field-in-field

Fig. 2. The median (25th percentile, 75th percentile) dose-volume histograms (DVHs) of the planning target volume (solid line) and clinical target volume (dotted line) in volumetric modulated arc therapy plans (a) and field-in-field plans (b). The original DVH (black line) and the DVH after the rotation that caused the largest change in target coverage are plotted. Purple line indicates rotation by 3° (–pitch) and yale blue line rotation by 3° (–yaw). The dose axis is delimited to 37–43 Gy for readability. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



(a) Volumetric modulated arc therapy (b) Field-in-field

Fig. 3. The median (25th percentile, 75th percentile) dose-volume histograms (DVHs) of the heart (solid line) and left anterior descending artery (dotted line) in volumetric modulated arc therapy plans (a) and field-in-field plans (b). The original DVH (black line) and DVH after the rotation that caused the largest increase in the mean dose to the heart and LAD are plotted. Purple line indicates rotation by 3° (+pitch).

3. Results

The dose volume parameters of original plans are presented in Table 1.

Statistically significant ($p < 0.05$) overall differences between the original dose distribution and dose distributions calculated for rotated images were found in all dose-volume parameters in both VMAT and FiF plans. In this section, some of the results are reported in the form "median change in the parameter value was $< a$ after α rotations" for conciseness. This means that the highest median change in the parameter value occurring after α [°] rotation in any of the six directions (Fig. 1) was less than a. The change in each parameter value after each rotation is shown in detail in the supplementary material.

The changes in PTV and CTV dose volume histograms are presented in Fig. 2. In VMAT plans, median decrease in PTV $V_{95\%}$ was <3.2 percentage points after 3° rotations. In FiF plans, the median decrease in PTV $V_{95\%}$ was <2.1 percentage points after 3° rotations. In CTV $V_{95\%}$, the median decrease after 3° rotations was <0.8 percentage points in both VMAT and FiF plans.

Median decrease in $D_{\text{min}}(1\ \text{cm}^3)$ to PTV was at maximum −6.48 Gy in VMAT plans and −11.87 Gy in FiF plans after 3° rotations. In $D_{\text{min}}(1\ \text{cm}^3)$ to CTV, the median decrease after 3° rotations was <0.5 Gy in both VMAT and FiF plans. In $D_{\text{max}}(1\ \text{cm}^3)$ to PTV and CTV, the median increase after 3° rotations was <0.4 Gy in both VMAT and FiF plans.

The rotations that caused >1 Gy or >5 percentage points increase in the organ at risk dose volume parameters are summarised in Table 2.

The dosimetric effect of rotations on heart and LAD is presented in Fig. 3. The largest increase in heart and LAD dose volume parameters was observed after rotations in +pitch direction. The absolute increase in heart and LAD dose volume parameters was lower in VMAT plans compared to FiF plans ($p < 0.05$) or not statistically different depending on the direction of the rotation. In $D_{\text{max}}(1\ \text{cm}^3)$ to heart, 1° and 3° rotations caused median increase up to 1.45 Gy and 5.94 Gy in VMAT plans and up to 2.94 Gy and 5.44 Gy in FiF plans. In mean dose to LAD, 1° and 3° rotations caused median increase up to 0.38 Gy and 1.80 Gy in VMAT plans and up to 1.56 Gy and 4.95 Gy in FiF plans. The dose tolerance of $V_{15\text{Gy}} < 10\%$ [27] was originally exceeded in 1 VMAT plan

Table 1
The dose-volume parameter values of the original volumetric modulated arc therapy (VMAT) and field-in-field (FiF) plans. Values are presented as median (25th percentile, 75th percentile) of 20 plans.

Structure	Parameter	VMAT	FiF
Planning target volume	$V_{95\%}$ (%)	93.50(92.96, 94.43)*	90.25(89.96, 91.06)
	D_{min}(1 cm^3) (Gy)	34.21(33.97, 34.72)*	33.00(31.92, 33.70)
	D_{max}(1 cm^3) (Gy)	42.65(42.41, 42.90)*	43.47(43.32, 43.57)
Clinical target volume	$V_{95\%}$ (%)	95.54(95.23, 96.90)	95.60(95.01, 96.78)
	D_{min}(1 cm^3) (Gy)	35.06(34.78, 35.57)	35.08(34.33, 35.62)
	D_{max}(1 cm^3) (Gy)	42.62(42.39, 42.82)*	43.45(43.35, 43.54)
Heart	Mean (Gy)	2.84(2.29, 3.26)*	1.56(1.30, 2.99)
	D_{max}(1 cm^3) (Gy)	11.58(8.85, 16.70)*	25.43(16.74, 33.88)
Left anterior descending artery	Mean (Gy)	5.35(4.36, 6.69)*	10.25(4.38, 16.49)
	V_{15Gy} (%)	0.00(0.00, 0.33)*	26.14(2.28, 58.23)
	D_{max}(1 cm^3) (Gy)	7.17(6.07, 9.71)*	16.53(5.97, 29.64)
Left lung	Mean (Gy)	9.61(8.87, 10.33)*	11.35(9.38, 13.35)
	V_{5Gy} (%)	51.66(46.17, 58.29)*	44.06(38.89, 48.76)
	V_{20Gy} (%)	16.40(14.21, 18.66)*	25.83(20.64, 31.54)
Right lung	Mean (Gy)	2.14(1.51, 2.74)*	0.58(0.49, 0.80)
Right breast	Mean (Gy)	4.17(3.54, 5.72)*	1.34(0.49, 1.92)
	V_{2Gy} (%)	72.21(49.88, 84.03)*	8.92(2.88, 13.72)
Spinal cord	D_{max}(1 cm^3) (Gy)	15.55(11.89, 17.52)*	10.73(9.91, 11.87)
Brachial plexus	D_{max}(1 cm^3) (Gy)	40.81(40.45, 41.04)	40.73(39.91, 41.27)
Thyroid	Mean (Gy)	16.27(14.24, 18.45)	16.72(12.90, 19.26)
Left humeral head	V_{15Gy} (%)	16.14(2.76, 30.15)	12.74(2.57, 21.21)

* Statistically significant difference between VMAT and FiF plans ($p < 0.05$).
Abbreviations: V_{XGy} = the percentage volume receiving X Gy dose, $V_{Y\%}$ = the percentage volume receiving Y % of the prescribed dose, $D_{max/min}(Z)$ = the minimum/maximum dose received by the volume Z that received the highest/lowest dose.

and 11 FiF plans out of 20. After 3° (+pitch), the limit was exceeded in 8 VMAT plans and 17 FiF plans. In D_{max}(1 cm^3) to LAD, 1° and 3° rotations caused median increase up to 0.57 Gy and 2.53 Gy in VMAT plans and up to 1.35 Gy and 6.04 Gy in FiF plans.

In most parameters, either the difference between patient groups (mastectomy vs lumpectomy, with IMLN involvement vs without IMLN involvement) was not statistically significant or the difference between group medians was <1 Gy/5 percentage points or the change from original plan was <1 Gy/5 percentage points in both patient groups. The only exceptions were D_{min}(1 cm^3) to PTV and mean dose to LAD. Lumpectomy patients experienced >1 Gy higher median decrease in D_{min}(1 cm^3) to PTV than mastectomy patients after ≥2° (–pitch) and ≥1° (+roll) in VMAT plans. Mastectomy patients experienced >1 Gy higher median increase in mean dose to LAD than lumpectomy patients after ≥1° (+pitch) and ≥2° (+yaw) in FiF plans.

4. Discussion

In this study, VMAT plans had improved PTV coverage, reduced maximum dose to the heart and LAD, reduced V_{20Gy} to left lung and increased doses to right lung and breast compared to FiF plans, which is consistent with previous studies comparing FiF and VMAT plans [6–9]. VMAT plans generally have longer beam delivery times than FiF plans [9], which leads to longer breath hold times. Thus, FiF plans might be more suitable for patients who struggle with long breath holds.

The median changes in $V_{95\%}$ and D_{min}(1 cm^3) to CTV were limited to 0.8 percentage points and 0.5 Gy, respectively, in both VMAT and FiF plans. This suggests that the 5 mm PTV margin is sufficient to cover the effect of systematic rotational setup errors up to 3°. However, since PTV D_{min}(1 cm^3) was reduced by up to –6.48 Gy in VMAT plans and –11.87 Gy in FiF plans after 3° rotations, the margin might not be enough to ensure adequate CTV coverage if other uncertainties, such as breast deformation, were present in addition to the rotational setup error. In [15], translational setup errors of 5–10 mm had a more significant effect on the CTV coverage in VMAT plans than rotational setup errors in our study. This may be partially explained by their use of a 3 mm PTV margin.

In our study, PTV $V_{95\%}$ was statistically more robust towards patient rotations in FiF plans compared to VMAT plans. However, we consider the difference clinically negligible, because the median decrease in PTV $V_{95\%}$ in both VMAT and FiF plans was <3.2 percentage points after any rotation, and because the original VMAT plans had 3.25 percentage points higher median PTV $V_{95\%}$ than FiF plans. One research group reported that interfractional translational setup errors had a greater effect on PTV coverage of FiF plans compared to VMAT plans utilising the Raystation robust optimisation feature [18]. On the other hand, another group reported that translational setup errors had a greater impact on target coverage of VMAT plans [15], which is similar to our results.

A recent study showed that the dose distribution to LAD is sensitive to setup errors in breath-hold radiotherapy utilising FiF due to the proximity of the steep dose gradient [16]. In our study, rotational deviations caused larger changes in the dose distribution of heart and LAD in FiF plans compared to VMAT plans. One research group found a significant association between LAD V_{15Gy} >10% and major adverse cardiac events and all-cause mortality in people who had received radiotherapy for non-small cell lung cancer [27]. In our study, rotations in +pitch direction considerably increased the number of plans in which the limit was exceeded. Thus, systematic rotational deviations could contribute to increased risk of major adverse cardiac events in treatment of left-sided breast cancer even if the value of LAD V_{15Gy} was less than 10% in the original treatment plan.

The results indicate that small organs at risk, such as LAD, thyroid and left humeral head, experience larger absolute dosimetric effect of rotational setup deviations than larger organs, such as heart and lungs. It has been previously reported that the dosimetric effect of rotational setup error on a structure is associated with the size and shape of the structure in radiotherapy treatment of multiple brain metastases [28,29] and prostate [30]. Long cylindrical targets may be sensitive to rotational setup errors. In [31], increasing target dose deviation was observed with increasing pitch in treatment of nasopharyngeal carcinoma and esophageal cancer, however, the mean deviation was

Table 2
Rotations that caused larger than 1 Gy or 5 percentage points median increase in the respective organ at risk dose volume parameter in volumetric modulated arc therapy (VMAT) and field-in-field (FiF) plans. A dash (–) indicates that the median dosimetric increase did not exceed 1 Gy or 5 percentage points after any rotational setup error.

Structure	Parameter	VMAT	FiF
Heart	Mean (Gy)	–	–
	D_{max}(1 cm^3) (Gy)	≥1° (+pitch) 3° (+yaw) ≥2° (–roll)	≥1° (+pitch) ≥1° (+yaw) ≥2° (–roll)
Left anterior descending artery	Mean (Gy)	3° (+pitch)	≥1° (+pitch) ≥1° (+yaw) 3° (–roll)
	V_{15Gy} (%)	3° (+pitch)	≥1° (+pitch) ≥1° (+yaw) ≥1° (–roll)
	D_{max}(1 cm^3) (Gy)	≥2° (+pitch)	≥1° (+pitch) ≥2° (+yaw) 3° (–roll)
Left lung	Mean (Gy)	–	–
	V_{5Gy} (%)	–	–
	V_{20Gy} (%)	–	–
Right lung	Mean (Gy)	–	–
Right breast	Mean (Gy)	–	–
	V_{2Gy} (%)	3° (–roll)	–
Spinal cord	D_{max}(1 cm^3) (Gy)	–	≥2° (+roll)
Brachial plexus	D_{max}(1 cm^3) (Gy)	–	–
Thyroid	Mean (Gy)	≥2° (–yaw) 3° (+roll)	3° (+roll)
Left humeral head	V_{15Gy} (%)	≥2° (+pitch)	3° (+pitch)

Abbreviations: V_{XGy} = the percentage volume receiving X Gy dose, $D_{max/min}(Z)$ = the minimum/maximum dose received by the volume Z that received the highest/lowest dose.

at maximum 2% after pitch 3°. Significant increase in organ at risk doses was reported after pitch 1.5°. Thus, correction of pitch ≥1.5° was recommended. Our study supports these findings of the earlier studies and quantifies the magnitude of the dosimetric effect in breast radiotherapy.

To determine the intervention tolerance for rotational setup errors, we defined limits for clinically relevant dosimetric change based on limits used in similar studies [14,29] and our experience. We considered a change clinically relevant if the change was statistically significant and the median absolute change was more than 5 percentage points, 2 Gy for a target dose-volume parameter or 1 Gy for a normal tissue dose-volume parameter. We did not consider favourable dosimetric changes clinically relevant, even if they were relevant in magnitude.

The only clinically relevant dosimetric change in VMAT plans after 1° setup error was +1.45 Gy median change in D_{max}(1 cm^3) to the heart after 1° (+pitch). In FiF plans, 1° rotational setup errors had a clinically relevant dosimetric effect on D_{max}(1 cm^3) to the heart and mean dose, V_{15Gy} and D_{max}(1 cm^3) to LAD. Setup errors of 2° and 3° had clinically relevant dosimetric effect on D_{min}(1 cm^3) to PTV and several normal tissue dose volume parameters in both VMAT and FiF plans. The correction of rotational setup errors ≥1° is recommended because it is seen to improve the dose distribution of the heart and LAD in both VMAT and FiF treatment of breast and supraclavicular lymph nodes. The effect of rotations below 1° cannot be inferred from this study.

We hypothesised that mastectomy and IMLN inclusion would make the dose distribution more susceptible to rotational setup errors due to the narrow and complex shaped target volume. However, the differences between patient groups were negligible in majority of dose volume parameters. Thus, different guidelines for intervention tolerance in different patient groups cannot be recommended based on this study. However, the sample size per patient group was limited, so larger samples might be needed for definitive recommendations.

When radiotherapy is given in free breathing, the heart is located close to the chest wall. In worst case, PTV overlaps with the heart. Thus, rotational setup errors might cause larger excess dose to the heart and LAD in patients treated in free breathing compared to patients treated in deep inspiration breath hold as in our study. In right-sided breast radiotherapy, the heart is located further away from the target volume than in left-sided breast radiotherapy. Thus, the heart might be better spared from high radiation dose after setup errors in right-sided breast radiotherapy.

In this study, the rotation axes were selected so that they passed through the VMAT isocentre to replicate the patient positioning errors in actual treatment in which the positioning is typically based on central PTV location. The choice of common rotation axes also enabled comparison between VMAT and FiF plans.

Different approaches are used to create VMAT plans for breast radiotherapy [8,32], which may lead to variations in plans between different clinics and planners. In our study, VMAT plans were generated by multiple physicists according to our clinical protocol and approved by oncologists. The planners were allowed to modify the optimisation constraints as long as the planning goals (Supplementary material, Table 1) were followed. Thus, slight inter-planner differences, such as variation in the dose gradient around PTV, may exist in VMAT plans. FiF plans were generated by one physicist following the established guidelines of our clinic, eliminating the inter-planner differences.

The dosimetric effect of patient deformation or direct translational setup error were not considered in this study, which only evaluated the dosimetric effect of a six-degrees-of-freedom couch in breast radiotherapy. For the authors' knowledge, the dosimetric effect of six-degrees-of-freedom couch has not been studied earlier for breast radiotherapy using VMAT. Our study also included evaluation of the effect of rotations on a comprehensive set of organs at risk and comparison of mastectomy and lumpectomy patients and comparison of patients with and without IMLN involvement. The effect of translational setup errors has been addressed in [15] and the effect of deformational setup errors in [17].

When correcting patient position by couch rotations, it is possible that the patient unconsciously compensates the movement of the couch, resulting in tissue displacement with respect to the couch. In [13], a correlation between couch tilt and translational setup error was

observed in lightly fixated patients. In average, a 0.6 mm setup error was caused by each 1° of couch tilt. Thus, it is recommended to check the patient setup after couch tilt by planar kilovoltage or cone-beam computed tomography imaging.

5. Conclusions

This study indicates that the CTV dose distribution is robust towards setup errors up to 3° in both VMAT and FiF treatment of left breast and supraclavicular lymph nodes in deep inspiration breath hold when a 5 mm CTV-PTV margin is used. The dose distribution of the heart and LAD was more robust towards rotations in VMAT plans compared to FiF plans. Small organs, such as LAD, thyroid and left humeral head, experienced larger dosimetric changes than large organs, such as the heart and lungs. An intervention tolerance of 1° is recommended for rotational setup errors due to increased heart and LAD doses after 1° rotations.

Funding

This work was supported by the Support Foundation of Central Finland Central Hospital.

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.

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.ejmp.2023.103203.

References

[1] Early Breast Cancer Trialists' Collaborative Group. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet 2014;383:2127–35. http://dx.doi.org/10.1016/S0140-6736(14)60488-8.

[2] Early Breast Cancer Trialists' Collaborative Group. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials. Lancet 2011;378:1707–16. http://dx.doi.org/10.1016/S0140-6736(11)61629-2.

[3] Shapiro CL, Recht A. Side effects of adjuvant treatment of breast cancer. N Engl J Med 2001;344:1997–2008. http://dx.doi.org/10.1056/NEJM200106283442607.

[4] 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. http://dx.doi.org/10.1056/NEJMoa1209825.

[5] Popescu CC, Olivotto IA, Beckham WA, Ansbacher W, Zavgorodni S, Shaffer R, et al. Volumetric modulated arc therapy improves dosimetry and reduces treatment time compared to conventional intensity-modulated radiotherapy for locoregional radiotherapy of left-sided breast cancer and internal mammary nodes. Int J Radiat Oncol Biol Phys 2010;76:287–95. http://dx.doi.org/10.1016/j.ijrobp.2009.05.038.

[6] Sakumi A, Shiraishi K, Onoe T, Yamamoto K, Haga A, Yoda K, et al. Single-arc volumetric modulated arc therapy planning for left breast cancer and regional nodes. J Radiat Res 2012;53:151–3. http://dx.doi.org/10.1269/jrr.11159.

[7] Osman SOS, Hol S, Poortmans PM, Essers M. Volumetric modulated arc therapy and breath-hold in image-guided locoregional left-sided breast irradiation. Radiother Oncol 2014;112:17–22. http://dx.doi.org/10.1016/j.radonc.2014.04.004.

[8] Virén T, Heikkilä J, Myllyoja K, Koskela K, Lahtinen T, Seppälä J. Tangential volumetric modulated arc therapy technique for left-sided breast cancer radiotherapy. Radiat Oncol 2015;10:79. http://dx.doi.org/10.1186/s13014-015-0392-x.

[9] Koivumäki T, Fogliata A, Zeverino M, Boman E, Sierpowska J, Moeckli R, et al. Dosimetric evaluation of modern radiation therapy techniques for left breast in deep-inspiration breath-hold. Phys Med 2018;45:82–7. http://dx.doi.org/10.1016/j.ejmp.2017.12.009.

[10] Zhang Q, Liu J, Ao N, Yu H, Peng Y, Ou L, et al. Secondary cancer risk after radiation therapy for breast cancer with different radiotherapy techniques. Sci Rep 2020;10:1220. http://dx.doi.org/10.1038/s41598-020-58134-z.

[11] Bujold A, Craig T, Jaffray D, Dawson LA. Image-guided radiotherapy: has it influenced patient outcomes? Semin Radiat Oncol 2012;22:50–61. http://dx.doi.org/10.1016/j.semradonc.2011.09.001.

[12] Zhang Q, Driewer J, Wang S, Li S, Zhu X, Zheng D, et al. Accuracy evaluation of a six-degree-of-freedom couch using cone beam CT and IsoCal phantom with an in-house algorithm. Med Phys 2017;44:3888–98. http://dx.doi.org/10.1002/mp.12342.

[13] Guckenberger M, Meyer J, Wilbert J, Baier K, Sauer O, Flentje M. Precision of image-guided radiotherapy (IGRT) in six degrees of freedom and limitations in clinical practice. Strahlenther Onkol 2007;183:307–13. http://dx.doi.org/10.1007/s00066-007-1695-0.

[14] Harron E, McCallum H, Lambert E, Lee D, Lambert G. Dosimetric effects of setup uncertainties on breast treatment delivery. Med Dosim 2008;33:293–8. http://dx.doi.org/10.1016/j.meddos.2008.01.003.

[15] Zhao Y, Diao P, Zhang D, Wu J, Xin X, Fontanarosa D, et al. Impact of positioning errors on the dosimetry of breath-hold-based volumetric arc modulated and tangential field-in-field left-sided breast treatments. Front Oncol 2020;10:554131. http://dx.doi.org/10.3389/fonc.2020.554131.

[16] Gnerucci A, Esposito M, Ghirelli A, Pini S, Paoletti L, Barca R, et al. Robustness analysis of surface-guided DIBH left breast radiotherapy: personalized dosimetric effect of real intrafractional motion within the beam gating thresholds [e-pub ahead of print]. Strahlenther Onkol http://dx.doi.org/10.1007/s00066-023-02102-9. [Accessed 1 October 2023].

[17] Rossi M, Boman E, Skyttä T, Haltamo M, Laaksomaa M, Kapanen M. Dosimetric effects of anatomical deformations and positioning errors in VMAT breast radiotherapy. J Appl Clin Med Phys 2018;19:506–16. http://dx.doi.org/10.1002/acm2.12409.

[18] Jensen CA, Roa AMA, Johansen M, Lund JÅ, Frengen J. Robustness of VMAT and 3DCRT plans toward setup errors in radiation therapy of locally advanced left-sided breast cancer with DIBH. Phys Med 2018;45:12–8. http://dx.doi.org/10.1016/j.ejmp.2017.11.019.

[19] The Royal College of Radiologists. On target 2: updated guidance for image-guided radiotherapy. London: The Royal College of Radiologists; 2021.

[20] Manikandan A, Sarkar B, Munshi A, Krishnankutty S, Ganesh T, Mohanti BK, et al. Calculation of set-up margin in frameless stereotactic radiotherapy accounting for translational and rotational patient positing error. J Can Res Ther 2023;19:169–76. http://dx.doi.org/10.4103/jcrt.jcrt_359_21.

[21] Sankar A, Velmurugan J. Different intensity extension methods and their impact on entrance dose in breast radiotherapy: a study. J Med Phys 2009;34:200–5. http://dx.doi.org/10.4103/0971-6203.56079.

[22] Lizondo M, Latorre-Musoll A, Ribas M, Carrasco P, Espinosa N, Coral A, et al. Pseudo skin flash on VMAT in breast radiotherapy: optimization of virtual bolus thickness and HU values. Phys Med 2019;63:56–62. http://dx.doi.org/10.1016/j.ejmp.2019.05.010.

[23] Seppälä J, Vuolukka K, Virén T, Heikkilä J, Honkanen JTJ, Pandey A, et al. Breast deformation during the course of radiotherapy: the need for an additional outer margin. Phys Med 2019;65:1–5. http://dx.doi.org/10.1016/j.ejmp.2019.07.021.

[24] Offersen BV, Boersma LJ, Kirkove C, Hol S, Aznar MC, Sola AB, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. Radiother Oncol 2015;114:3–10. http://dx.doi.org/10.1016/j.radonc.2014.11.030.

[25] Nicolini G, Fogliata A, Clivio A, Vanetti E, Cozzi L. Planning strategies in volumetric modulated arc therapy for breast. Med Phys 2011;38:4025–31. http://dx.doi.org/10.1118/1.3598442.

[26] Tudor GSJ, Bernstein D, Riley S, Rimmer Y, Thomas SJ, van Herk M, et al. Geometric uncertainties in daily online IGRT: refining the CTV-PTV margin for contemporary radiotherapy. London: British Institute of Radiology; 2020.

[27] Atkins KM, Chaunzwa TL, Lamba N, Bitterman DS, Rawal B, Bredfeldt J, et al. Association of left anterior descending coronary artery radiation dose with major adverse cardiac events and mortality in patients with non–small cell lung cancer. JAMA Oncol 2021;7:206–19. http://dx.doi.org/10.1001/jamaoncol.2020.6332.

[28] Selvan KT, Padma G, Revathy MK, Nambi Raj NA, Senthilnathan K, Babu PR. Dosimetric effect of rotational setup errors in single-isocenter volumetric-modulated arc therapy of multiple brain metastases. J Med Phys 2019;44:84–90. http://dx.doi.org/10.4103/jmp.JMP_103_18.

[29] Prentou G, Pappas EP, Logothetis A, Koutsouveli E, Pantelis E, Papagiannis P, et al. Dosimetric impact of rotational errors on the quality of VMAT-SRS for multiple brain metastases: comparison between single- and two-isocenter treatment planning techniques. J Appl Clin Med Phys 2020;21:32–44. http://dx.doi.org/10.1002/acm2.12815.

[30] Chiesa S, Placidi L, Azario L, Mattiucci GC, Greco F, Damiani A, et al. Adaptive optimization by 6 DOF robotic couch in prostate volumetric IMRT treatment: rototranslational shift and dosimetric consequences. J Appl Clin Med Phys 2015;16:35–45. http://dx.doi.org/10.1120/jacmp.v16i5.5525.

[31] Stieb S, Malla M, Graydon S, Riesterer O, Klöck S, Studer G, et al. Dosimetric influence of pitch in patient positioning for radiotherapy of long treatment volumes; the usefulness of six degree of freedom couch. Br J Radiol 2018;91:20170704. http://dx.doi.org/10.1259/bjr.20170704.

[32] Fogliata A, Seppälä J, Reggiori G, Lobefalo F, Palumbo V, De Rose F, et al. Dosimetric trade-offs in breast treatment with VMAT technique. Br J Radiol 2017;90:20160701. http://dx.doi.org/10.1259/bjr.20160701.