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Original Article

Prone vs. supine accelerated partial breast irradiation on an MR-Linac: A planning study

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ABSTRACT

Background and purpose: Accelerated partial breast irradiation (APBI) may benefit from the MR-Linac for target definition, patient setup, and motion monitoring. In this planning study, we investigated whether prone or supine position is dosimetrically beneficial for APBI on an MR-Linac and we evaluated patient comfort.

Materials and methods: Twenty-patients (9 postoperative, 11 preoperative) with a DCIS or breast tumor <3 cm underwent 1.5 T MRI in prone and supine position. The tumor or tumor bed was delineated as GTV and a 2 cm CTV-margin and 0.5 cm PTV-margin were added. 1.5 T MR-Linac treatment plans (5 × 5.2 Gy) with 11 beams were created for both positions in each patient. We evaluated the number of plans that achieved the planning constraints and performed a dosimetric comparison between prone and supine position using the Wilcoxon signed-rank test (p-value <0.01 for significance). Patient experience during scanning was evaluated with a questionnaire.

Results: All 40 plans met the target coverage and OAR constraints, regardless of position. Heart D_{mean} was not significantly different (1.07 vs. 0.79 Gy, p-value: 0.027). V5Gy to the ipsilateral lung (4.4% vs. 9.8% median, p-value 0.009) and estimated delivery time (362 vs. 392 s, p-value: 0.003) were significantly lower for prone position. PTV coverage and dose to other OAR were comparable between positions. The majority of patients (13/20) preferred supine position.

Conclusion: APBI on the MR-Linac is dosimetrically feasible in prone and supine position. Mean heart dose was similar in both positions. Ipsilateral lung V5Gy was lower in prone position.

In recent trials, external beam (accelerated) partial breast irradiation ((A)PBI) was presented as an alternative for whole breast irradiation (WBI) in low-risk breast cancer patients, showing similar local recurrence rates to WBI [1,2]. PBI reduces the irradiated volume and treatment-related toxicity. APBI additionally reduces overall treatment duration, and thus patient burden. Currently, also neoadjuvant APBI is being investigated [3–7] with the aim to further reduce toxicity compared to adjuvant APBI through improved target definition with the tumor still *in situ*. This results in even smaller irradiated volumes [8–10], which might further decrease treatment-induced toxicity.

APBI may benefit from using a hybrid magnetic resonance imaging (MRI)-radiotherapy system, a linear accelerator or ^{60}Co sources combined with an MRI scanner [11–14]. MRI appeared to be important to detect a breast tumor and to define its irregularities [9]. In studies investigating neoadjuvant APBI, MRI is often used for definition of the gross tumor volume (GTV) [3,4,6]. In the adjuvant PBI setting, the benefit of MRI for target delineation is less clear [15–18], but initial clinical experiences on hybrid systems reported benefits for patient setup on the lumpectomy cavity and motion monitoring [19–22].

Because oncological outcomes for low-risk breast cancer patients are excellent, improvements in treatment techniques for breast cancer focus on reducing long-term toxicity. PBI in prone position may reduce dose to organs-at-risk (OAR) compared to PBI in supine position, i.e., reduce the dose to the ipsilateral lung, ipsilateral breast, and heart [23–26]. Yet, increased dose to the heart and contralateral breast compared to supine position have also been reported [24,25]. The limited evidence, evaluated for the conventional linacs, shows heterogenous results on which treatment position is favorable. Charaghvandi et al. have shown that both prone and supine single-fraction PBI are dosimetrically

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feasible on the MR-Linac and suggested that prone position may be favorable for some OAR [27]. However, as the evaluation was performed using two different patient populations for the two positions, the positions could not be directly compared in the same patient.

In this study, we investigated in the same patient whether prone or supine treatment position is dosimetrically beneficial for APBI on a 1.5 T MR-Linac. Additionally, we evaluated patient comfort for both positions.

Methods and materials

Patients

This MR imaging study was approved by the institutional review board of the University Medical Center (UMC) Utrecht (trial number NL56683.041.16). Twenty women (Table 1) diagnosed with a ductal carcinoma in situ (DCIS) or invasive breast cancer gave written informed consent to participate. All women were referred to the radiotherapy department of the UMC Utrecht for preoperative and/or postoperative consultation for adjuvant radiotherapy. Eleven patients participated in this study prior to any treatment and nine patients participated during the adjuvant radiotherapy period after breast-conserving surgery. A tumor >3 cm or large seroma were exclusion criteria. For this planning study, multifocal or node-positive disease were no exclusion criteria. In one preoperative patient with a multifocal tumor, we considered only the largest tumor focus as target.

Patient positioning and imaging

Between July 2017 and February 2020, all patients underwent 1.5 T MRI (Ingenia, Philips, The Netherlands) in supine and prone radiotherapy position (Fig. 1). In supine position, patients were positioned on the ThoraxSupport (MacroMedics, The Netherlands). Supine MRI was acquired with a 16-elements anterior receiver coil, placed on two coil bridges to prevent deformation of the breasts and body contour, and a 16-elements posterior receiver coil located in the scanner table. In prone position, patients were positioned on an in-house developed support with parts provided by Orfit Industries (Belgium). The ipsilateral breast was hanging freely without touching the table top and the contralateral breast was pulled aside and resting on the support. Prone MRI was acquired with the receiver coil in the scanner table, a flexible loop surface coil on each side of the ipsilateral breast, and, when it fitted inside the MRI bore, the anterior receiver coil placed on the back of the patient.

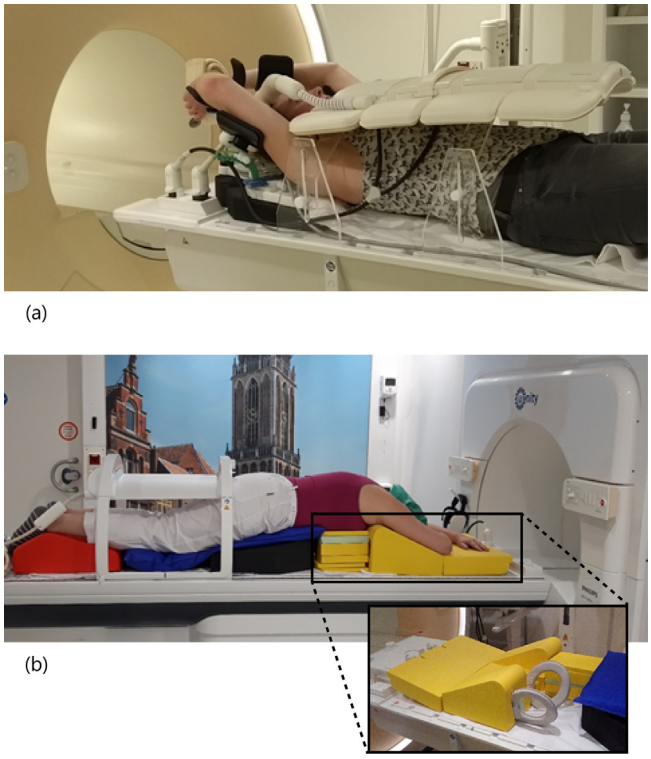

Fig. 1. Setup for MR imaging in supine position (a) and prone position* (b). The inset shows the setup of the flexible loop coils for the ipsilateral breast. *Image (b) shows the MR-Linac and dedicated MR-Linac coil instead of the MRI scanner and receiver coil that were used in the current study. The scanner and coils that were used in both prone and supine position are shown in (a) and the inset in (b).

In both positions, we acquired a 3D T1-weighted (T1w) spoiled gradient echo scan (SPGR) with multi-echo DIXON reconstruction (mDIXON) [28] in all patients and a diffusion-weighted (DW-) MRI with apparent diffusion coefficient map in 17/20 patients. We acquired an additional fast SPGR scan for body contour visualization in ten prone patients for whom the anterior receiver coil did not fit. Scan parameters are presented in appendix A. Median time difference between start of scanning in supine and prone position was 34 minutes (range: 29–52 min), except for three patients in whom the MR images in supine and prone position were acquired on different days (6–13 days apart). Median duration of scanning in each position was 22 min (18–32 min).

Delineations

Delineations were performed using in-house developed software [29]. The gross tumor volumes (GTVs) were delineated by a dedicated breast radiation oncologist (FvdL) on the water-image of the T1w MRI, with co-registered DW-MRI. Co-registered in-phase T1w MRI, fast SPGR scans or clinically acquired planning-CT or non-co-registered diagnostic imaging were consulted when necessary and available. In preoperative patients, the GTV was defined as the visible tumor, and in postoperative patients, the

Table 1
Baseline patient characteristics.

	All (n = 20)
Age (median [range]) (years)	56 (45–72)
BMI (median [range]) (kg/m^2)	24.3 (20.2–36.5)
Timing of MRI	
Preoperative	11 (55%)
Postoperative	9 (45%)
Tumor side	
Left	9 (45%)
Right	11 (55%)
Tumor location	
Lateral	10 (50%)
Medial	4 (20%)
Central	6 (30%)
Tumor stage*	
T0	1 (5%)
Tis	2 (10%)
T1	10 (50%)
T2	7 (35%)
Nodal stage*	
N0	14 (70%)
N1	3 (15%)
N2	1 (5%)
No SNB	2 (10%)

BMI: body mass index; SNB: sentinel node biopsy.
* Tumor stage and nodal stage present cT and cN stage for preoperative patients and pT and pN stage for postoperative patients.

GTV was defined as the tumor bed including seroma and all visible surgical clips. The contours of the ipsilateral and contralateral breast were delineated by several dedicated breast radiation oncologists and a dedicated breast physician assistant. The body contour and OAR (lungs and heart according to the boundaries provided by Feng et al. [30]) were delineated by a researcher (MGK). A skin contour was defined as the first 5 mm below the breast surface with extensions up to 35 mm outside the breast according to Van Heijst et al. [31]. Clinical target volumes (CTVs) were created by 2 cm expansion of the GTVs, excluding the skin and staying inside the ipsilateral breast, and planning target volumes (PTVs) were created by 5 mm expansion of the CTV, excluding the skin, according to Bosma et al. [4]. All final contours were approved by a single dedicated breast radiation oncologist (FvdL).

Treatment planning

Synthetic CTs for dose calculation were created by assigning bulk-density to the body (relative electron density (RED) 1.00), lungs (0.327), ipsilateral breast (RED 0.934), and GTV (RED 0.991). The RED values were taken from the average computed tomography (CT) densities of a previously conducted synthetic CT evaluation [32]. The MRIs, delineations, and assigned densities were imported into the dedicated MR-Linac treatment planning system (TPS; Monaco v5.51.10, Elekta AB, Sweden).

For each scan, we generated an intensity modulated radiotherapy plan with 7 MV beam energy, 11 coplanar beams, and a maximum of 70 segments, in the presence of a 1.5 T magnetic field. In supine position, beam angles were 300°–140° for left-sided breast cancer and 220°–60° for right-sided breast cancer. In prone position, beam angles were 100°–300° for left-sided breast cancer and 60°–260° for right-sided breast cancer. Beam angles were equally spaced, 20°apart. Angles of beams entering through the cryostat pipe (5°–25°) or high-density couch structures were adjusted to avoid these structures. We used a 3 mm^3 isotropic grid size and 3.0% statistical uncertainty per segment for the Monte Carlo-based dose calculation.

The prescribed dose was 26 Gy in 5 fractions [33]. Plans were optimized to meet the following constraints for the PTV: D90% > 95%, D2% < 105%, and D_{mean} of 99–101%. The V26Gy of the ipsilateral breast had to be <30% and the V15Gy <60%. Constraints for the OAR are shown in Table 2.

Plan evaluation and statistical analysis

For both prone and supine position, we evaluated the number of plans meeting the constraints. The conformity of the dose was evaluated by the conformity index $CI_{95\%}$ defined as the 95%-isodose–volume divided by the PTV–volume [34]. We compared the number of segments, number of monitor units (MU) and the

Table 2
Planning constraints and results comparing target volumes, dosimetric parameters and treatment delivery parameters between prone and supine treatment position.

Parameter	Constraint	Supine Median (range)	Prone Median (range)	*p*-Value
Volumes (ml)				
GTV		4.2 (0.8–8.6)	4.0 (0.4–8.3)	0.008*
CTV		103 (34–182)	111 (15–223)	0.040
PTV		161 (61–269)	166 (34–319)	0.070
Ipsilateral breast		927 (210–1622)	960 (224–1628)	<0.001*
PTV coverage				
Mean dose (Gy)	25.74–26.26	25.83 (25.75–26.11)	25.90 (25.76–26.22)	0.019
D98% (Gy)	>24.70	24.90 (24.72–25.31)	24.93 (24.70–25.51)	0.841
D2% (Gy)	<27.30	26.76 (26.44–27.20)	26.83 (26.63–27.30)	0.021
V95%	>98%	99.2% (98.1–99.9%)	99.0% (98.0–100%)	0.823
$CI_{95\%}$	–	1.15 (1.01–1.31)	1.16 (1.03–1.38)	0.898
Dose to OAR				
Ipsilateral breast				
V26Gy	<30%	7.1% (2.6–16.5%)	8.5% (3.3–24.8%)	0.027
V15Gy	<60%	39.3% (15.1–59.6%)	41.0% (18.2–58.9%)	0.349
Ipsilateral lung				
V20Gy	<2%	0.0% (0.0–0.5%)	0.0% (0.0–0.2%)	–
V10Gy	<10%	1.5% (0.1–6.2%)	0.5% (0.0–4.8%)	0.017
V5Gy	<20%	9.8% (3.8–17.9%)	4.4% (0.0–15.4%)	0.009*
Both lungs				
D_{mean} (Gy)	<5	1.25 (0.57–2.10)	1.01 (0.26–1.82)	0.021
Contralateral lung				
V20Gy	<1%	0.0% (0.0–0.0%)	0.0% (0.0–0.0%)	–
V10Gy	<2%	0.0% (0.0–0.0%)	0.0% (0.0–0.0%)	–
V5Gy	<3%	0.0% (0.0–1.8%)	0.0% (0.0–0.0%)	–
Heart				
V20Gy	<1%	0.0% (0.0–0.0%)	0.0% (0.0–0.0%)	–
V10Gy	<2%	0.0% (0.0–0.0%)	0.0% (0.0–0.4%)	–
V5Gy	<5%	0.0% (0.0–2.6%)	0.0% (0.0–4.9%)	–
D_{mean} (Gy)	<2	0.79 (0.22–1.55)	1.07 (0.29–1.82)	0.027
Contralateral breast				
D_{mean}	<1	0.37 (0.15–0.76)	0.53 (0.17–0.77)	0.030
Skin				
D2%	–	24.67 (22.32–25.74)	24.59 (20.68–26.77)	0.985
V80%	–	7.0% (2.8–16.2%)	7.2% (1.9–16.7%)	0.388
Treatment delivery				
Number of segments		69 (66–70)	69 (62–70)	0.405
Number of MU		1705 (1453–2197)	1648 (1159–2044)	0.005*
Estimated delivery time (s)		392 (342–436)	362 (307–431)	0.003*

Parameters with median values of 0 were not statistically tested.
* Statistically significant (*p*-value <0.01).

treatment delivery time as estimated by the TPS. All constraints and parameters were compared between prone and supine position using the non-parametric Wilcoxon signed-rank test (RStudio version 1.0.143, Rstudio Team, USA). To take into account multiple testing, *p*-values <0.01 were considered significant.

Patient experience evaluation

After MR imaging, we asked the patients to complete a questionnaire to evaluate patient experience. Patients indicated if they experienced any pain, discomfort, or anxiety during MRI scanning at a 4-point scale (none; mild; moderate; severe) and indicated their preference for either prone or supine position.

Results

GTV volumes were smaller in prone position, but CTV and PTV volumes were comparable between both positions (Table 2). Median PTV volume was 161 ml (range: 61–269 ml) in supine position and 166 (34–319 ml) in prone position. Ipsilateral breast volume was significantly larger (*p*-value: <0.001) in prone than in supine position: median of 960 ml (224–1628 ml) and 927 ml (210–1622 ml), respectively.

All 40 plans met the target coverage and OAR constraints, regardless of position. Dose distributions and dose–volume histograms (DVH) for three patients are shown in Fig. 2. Dosimetric results are presented in Table 2 and Fig. 3. The volume of the ipsilateral breast receiving 26 Gy was lower in supine compared to prone position: 7.1% vs. 8.5%, but not significant (*p*-value 0.027). The $CI_{95\%}$ was comparable for both positions. The mean dose to the heart and the contralateral breast were lower in supine position than in prone position: 0.79 Gy vs. 1.07 Gy and 0.37 Gy vs. 0.53 Gy respectively, but the differences were not significant (both *p*-values 0.027). V5Gy to the ipsilateral lung was significantly lower in prone position: 9.8% vs. 4.4%, *p*-value 0.009. Mean dose to both lungs (1.25 Gy vs. 1.01 Gy, *p*-value 0.024) was in favor of prone position, but not significant. Dose to the skin was comparable for both positions.

The DVHs in Fig. 2 show that advantage of either prone or supine position for dose to OAR differed across patients. The differences may be associated with tumor location inside the breast and the individual patients' anatomy. In patients with a medial tumor (e.g., patient A), we observed a lower dose to the heart in supine position, whereas the most beneficial position to spare the lungs differed across these patients. In some patients with a tumor that moved further away from the chest wall in prone position (e.g., patient B), we observed that prone position was favorable for both the dose to the heart and the lungs. In patients with a lateral tumor (e.g., patient C), we generally observed a lower dose to the heart in supine position and a lower dose to the lungs in prone position, consistent with the results for the full patient population.

The results of the treatment delivery parameters provided by the TPS are shown in Table 2. The number of segments used in the treatment plans was comparable between prone and supine position. Both the number of MUs (median: 1705 vs. 1648, *p*-value 0.005) and the estimated delivery time (median: 392 vs. 362 s, *p*-value 0.003) were significantly lower for the prone position.

Patient experience during scanning is shown in Fig. 4 and was in favor of supine position. For supine position, patients commented on numbness in a leg and on pain, discomfort or cold arms caused by the position of the arms above the head. For prone position, patients commented on an uncomfortable head support, numb or tingling arms, uncomfortable or painful pressure spots on shoulders, sternum, ribs or axilla, or on discomfort caused by the headphones.

Discussion

In this planning study we evaluated whether prone or supine position is dosimetrically beneficial for APBI on an 1.5 T MR-Linac. All treatment plans for both positions met all planning constraints and the dosimetric parameters were comparable for both positions. Only V5Gy to the ipsilateral lung was significantly lower in prone than in supine position, though the constraint was clearly met in both positions. The benefit of prone or supine position for

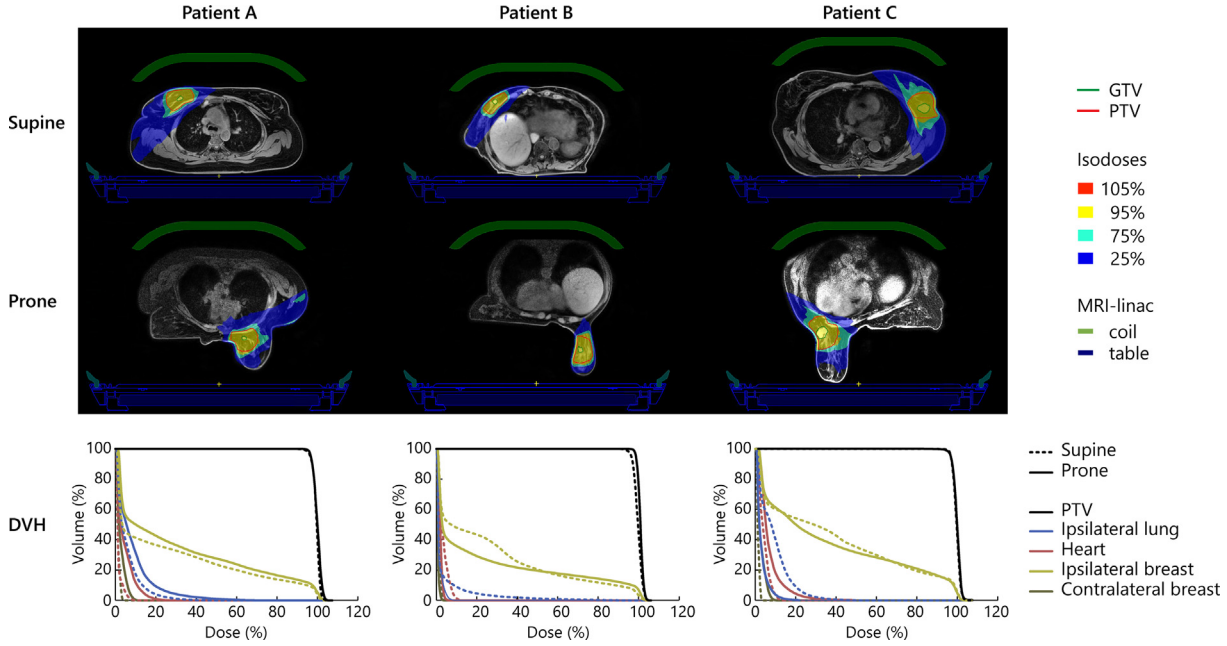

Fig. 2. Dose distributions and DVHs (prone: solid lines; supine: dotted lines) of three different patient examples: (A) a medial tumor close to the chest wall; (B) a central tumor far away from the chest wall in prone position; (C) a lateral tumor close to the chest wall.

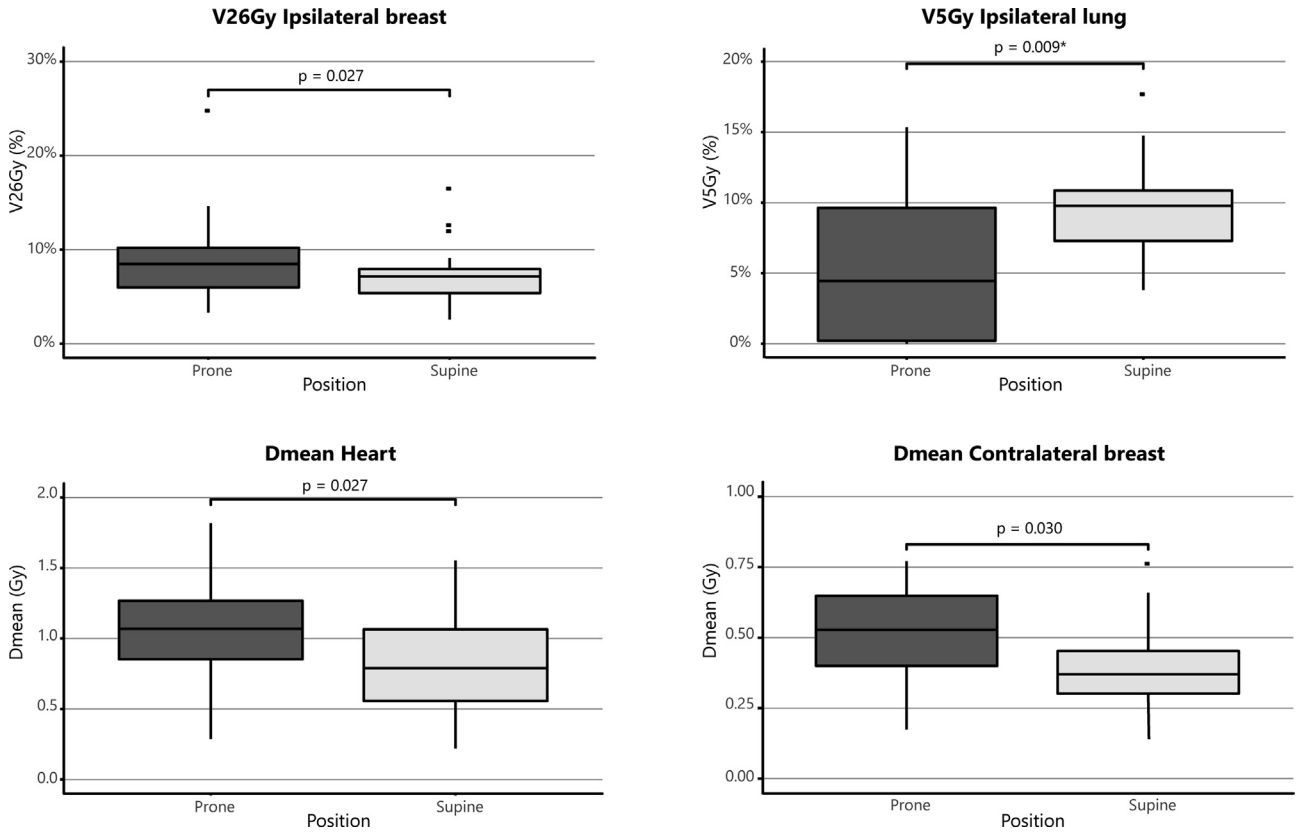

Fig. 3. Boxplots showing V26 Gy to the ipsilateral breast, V5Gy to the ipsilateral lung, and mean dose to the heart and the contralateral breast for prone vs. supine position. Only ipsilateral lung V5Gy was statistically significantly different between both positions ($p < 0.01$).

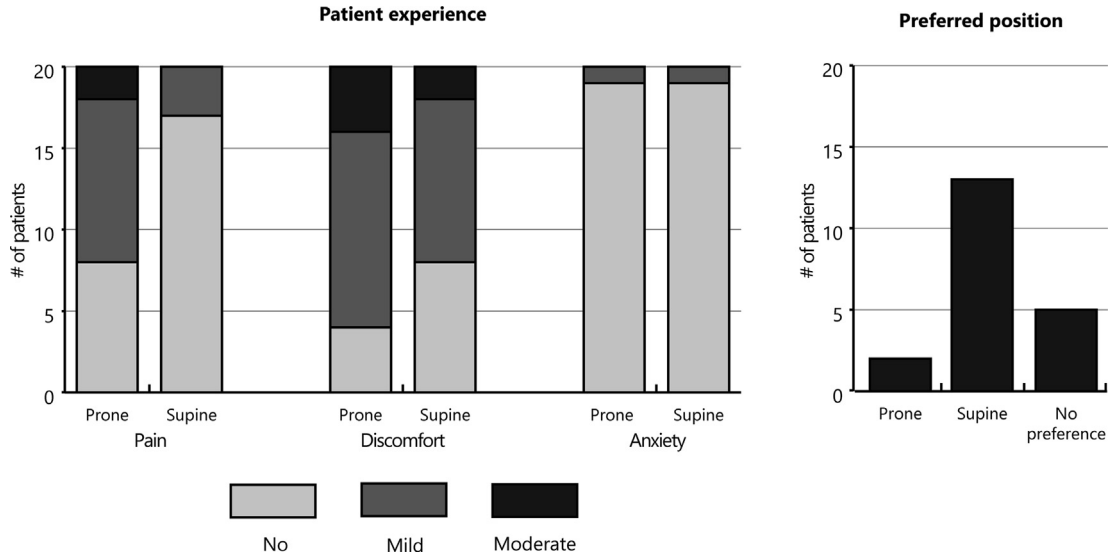

Fig. 4. Answers to the questionnaire evaluating patient experience during scanning.

individual patients is most likely related to multiple factors, such as tumor location inside the breast, distance from the tumor to the chest wall and to the heart in both positions, and breast size. The number of MUs and estimated delivery time were in favor of prone position. The difference in GTV volume was significant, but was considered as clinically not relevant since absolute differences were minimal. Most patients preferred supine position. These results show that APBI on a 1.5 T MR-Linac is dosimetrically feasible in both prone and supine position.

The dosimetric feasibility of both prone and supine position for APBI on an MR-Linac was previously shown by Charaghvandi et al. [27] and is confirmed by our results. Contrary to Charaghvandi et al., we were able to perform pairwise comparisons between both positions in the same patient. The lower dose to the lung that we found for prone compared to supine position is in line with the results of Charaghvandi et al. [27] and with four studies comparing both treatment positions for conventional linacs [23–26]. Our results regarding the dose to the heart suggested a favor of supine

position, but were not significantly different to prone position. This is contrary to the results of Charaghvandi et al., who suggested a lower V2.8 Gy to the heart in prone position (−3.2%) [27], but similar to the findings of Yu et al. who found a higher D_{mean} (+1.5 and +0.9 Gy) and V5 (+0.1%) to the heart in prone position [25]. Patel et al. and Kirby et al. found no differences for dose to the heart between both positions, though Kirby et al. reported a benefit for cardiac sparing for women with breasts >1000 cm^3 and a disadvantage with breasts ≤1000 cm^3 [23,24]. We could not formally evaluate the effect of breast size due to the limited size of the patient cohort. We visually observed that breast size seemed not related to difference in mean heart dose, while the benefit of prone position regarding lung dose seemed greater with larger breast size. In the end, we can confirm the findings of Charaghvandi et al. that neither prone nor supine position was clearly beneficial for the dose to the heart, skin, ipsilateral breast and contralateral breast. The shorter delivery time we found for prone position was also reported by Charaghvandi et al. [27]. Together with the lower number of MUs in prone position, this is likely due to a shorter pathlength between the beam entry site and the PTV in prone compared to supine position.

A strength of this study is that each patient underwent both prone and supine MRI. Therefore, pairwise comparisons of the dosimetric results could be performed. Additionally, the evaluations were performed using MRI without CT, showing the feasibility of an MR-linac workflow with MRI as sole imaging modality.

This study has some limitations. Firstly, the GTVs were delineated on non-contrast enhanced MRI. In preoperative patients, this made it difficult to visualize the extent of the tumor and distinguish it from glandular breast tissue. Contrast-enhanced MRI is recommended for radiotherapy treatment purposes [35] and contrast administration may be necessary for neoadjuvant APBI on an MR-Linac. *Ex vivo* experiments have shown that MRI contrast agents seemed to remain stable after irradiation [36], but further *in vivo* studies are necessary to evaluate if irradiation after contrast administration is safe. In postoperative patients, the surgical clips used for tumor bed delineation are harder to distinguish on MRI than on CT. Both issues impeded GTV delineation. Secondly, the body contour was not fully captured in the MRI in a few patients in prone position. This was caused by the limited signal-to-noise ratio at the posterior side of the patient (e.g., Fig. 2C) because the anterior receiver coil did not fit inside the MR bore. In these patients, the missing body contour was delineated combining information from different scans acquired in the same session and using interpolation from well-visible parts. Because the beam angle setup was such that no treatment beams entered through the posterior side of the patient in prone position, this has most likely not influenced the results. Thirdly, in four patients a virtual collision error caused by overlap of the body contour and the virtual MR-Linac coil was initially raised by the TPS. The error could be prevented by decreasing the space between the freely hanging breast and the table top to the distance that the breast did just not touch the table top. Though Charaghvandi et al. reported that all their patients would have fit [27], our experience is that MR imaging of larger patients or patients with large breast can be difficult and that often the anterior coil does not fit. These issues clearly illustrate some difficulties for performing prone radiotherapy on the MR-Linac that were also raised previously [14]. Fourthly, the geometric accuracy of the MRI was not taken into account in the current evaluation. Before treating breast cancer patients on the MR-Linac the influence of geometric distortions and necessary corrections should be further evaluated, especially in patients with a lateral tumor in supine position or anterior tumor in either position. Fifthly, the electron streaming effect was not considered. This may affect treatments in both positions, but can be effectively shielded using bolus material [37,38]. Finally, the size of the patient cohort was limited. A larger patient population is necessary to investigate correlations between factors that may determine the benefit of either position for individual patients.

As both positions are dosimetrically feasible, the preference for one of them may be guided by the experience of the treating center, the ease of patient setup, the individual patient's anatomy and tumor location, or preference of the patient. Patient experience in prone position may be improved by further development of the prone patient support using the feedback provided through the questionnaires.

Conclusion

APBI on the MR-Linac is dosimetrically feasible in both prone and supine position. Mean dose to heart was not significantly different between both positions. V5Gy to the ipsilateral lung was the only parameter that differed statistically between prone and supine position, in favor of prone position. The advantage for either supine or prone position depended on the patient anatomy and tumor location in the breast. The majority of the patients preferred supine position over prone position.

Conflicts of interest

The department of radiotherapy of the UMC Utrecht is part of the Elekta MR-Linac Research Consortium. Several authors have received financial support from Elekta for visiting consortium meetings. The funding sources had no role in the preparation, review, or approval of the manuscript, and decision to submit the manuscript for publication.

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Data statement

Participants of this study did not sign informed consent for public sharing of their data, therefore the research data are not available.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2021.11.001.

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] Coles CE, Griffin CL, Kirby AM, Titley J, Agrawal RK, Alhasso A, et al. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. Lancet 2017;390:1048–60. https://doi.org/10.1016/S0140-6736(17)31145-5.

[3] Vasmel JE, Charaghvandi RK, Houweling AC, Philippens MEP, van Asselen B, Vreuls CPH, et al. Tumor response after neoadjuvant magnetic resonance guided single ablative dose partial breast irradiation. Int J Radiat Oncol Biol Phys 2020;106:821–9. https://doi.org/10.1016/j.ijrobp.2019.11.406.

[4] Bosma SCJ, Leij F, Vreeswijk S, Maaker Md, Wesseling J, van de Vijver M, et al. Five-year results of the preoperative accelerated partial breast irradiation (PAPBI) trial. Int J Radiat Oncol Biol Phys 2020;106:958–67. https://doi.org/10.1016/j.ijrobp.2019.12.037.

[5] Guidolin K, Yaremko B, Lynn K, Gaede S, Kornecki A, Muscedere G, et al. Stereotactic image-guided neoadjuvant ablative single-dose radiation, then lumpectomy, for early breast cancer: the SIGNAL prospective single-arm trial of single-dose radiation therapy. Curr Oncol 2019;26:334–40. https://doi.org/10.3747/co.26.4479.
[6] Horton JK, Blitzblau RC, Yoo S, Geradts J, Chang Z, Baker JA, et al. Preoperative single-fraction partial breast radiation therapy: A novel phase 1, dose-escalation protocol with radiation response biomarkers. Int J Radiat Oncol 2015;92:846–55. https://doi.org/10.1016/j.ijrobp.2015.03.007.
[7] Nichols E, Kesmodel SB, Bellavance E, Drogula C, Tkaczuk K, Cohen RJ, et al. Preoperative accelerated partial breast irradiation for early-stage breast cancer: preliminary results of a prospective, phase 2 trial. Int J Radiat Oncol Biol Phys 2017;97:747–53. https://doi.org/10.1016/j.ijrobp.2016.11.030.
[8] Palta M, Yoo S, Adamson JD, Prosnitz LR, Horton JK. Preoperative single fraction partial breast radiotherapy for early-stage breast cancer. Int J Radiat Oncol 2012;82:37–42. https://doi.org/10.1016/j.ijrobp.2010.09.041.
[9] den Hartogh MD, Philippens MEP, van Dam IE, Kleynen CE, Tersteeg RJHA, Pijnappel RM, et al. MRI and CT imaging for preoperative target volume delineation in breast-conserving therapy. Radiat Oncol 2014;9:1–9. https://doi.org/10.1186/1748-717X-9-63.
[10] van der Leij F, Elkhuizen PHM, Janssen TM, Poortmans P, van der Sangen M, Scholten AN, et al. Target volume delineation in external beam partial breast irradiation: Less inter-observer variation with preoperative- compared to postoperative delineation. Radiother Oncol 2014;110:467–70. https://doi.org/10.1016/j.radonc.2013.10.033.
[11] Lagendijk JJW, Raaymakers BW, Raaijmakers AJE, Overweg J, Brown KJ, Kerkhof EM, et al. MRI/linac integration. Radiother Oncol 2008;86:25–9. https://doi.org/10.1016/j.radonc.2007.10.034.
[12] Klüter S. Technical design and concept of a 0.35 T MR-Linac. Clin Transl Radiat Oncol 2019;18:98–101. https://doi.org/10.1016/j.ctro.2019.04.007.
[13] Mutic S, Dempsey JF. The ViewRay system: magnetic resonance-guided and controlled radiotherapy. Semin Radiat Oncol 2014;24:196–9. https://doi.org/10.1016/j.semradonc.2014.02.008.
[14] Groot Koerkamp ML, Vasmel JE, Russell NS, Shaitelman SF, Anandadas CN, Currey A, et al. Optimizing MR-guided radiotherapy for breast cancer patients. Front Oncol 2020;10:1–13. https://doi.org/10.3389/fonc.2020.01107.
[15] Mast M, Coerkamp E, Heijenbrok M, Scholten A, Jansen W, Kouwenhoven E, et al. Target volume delineation in breast conserving radiotherapy: are co-registered CT and MR images of added value? Radiat Oncol 2014;9:65. https://doi.org/10.1186/1748-717X-9-65.
[16] Den Hartogh MD, Philippens MEP, Van Dam IE, Kleynen CE, Tersteeg RJHA, Kotte ANTJ, et al. Post-lumpectomy CT-guided tumor bed delineation for breast boost and partial breast irradiation: Can additional pre-and postoperative imaging reduce interobserver variability? Oncol Lett 2015;10:2795–801. 10.3892/ol.2015.3697.
[17] Al-Hammadi N, Caparrotti P, Divakar S, Riyas M, Chandramouli SH, Hammoud R, et al. MRI reduces variation of contouring for boost clinical target volume in breast cancer patients without surgical clips in the tumour bed. Radiol Oncol 2017;51:160–8. 10.1515/raon-2017-0014.
[18] Kirby AM, Yarnold JR, Evans PM, Morgan VA, Schmidt MA, Scurr ED, et al. Tumor bed delineation for partial breast and breast boost radiotherapy planned in the prone position: what does MRI add to X-ray CT localization of titanium clips placed in the excision cavity wall? Int J Radiat Oncol Biol Phys 2009;74:1276–82. https://doi.org/10.1016/j.ijrobp.2009.02.028.
[19] Acharya S, Fischer-Valuck BW, Mazur TR, Curcuru A, Sona K, Kashani R, et al. Magnetic resonance image guided radiation therapy for external beam accelerated partial-breast irradiation: evaluation of delivered dose and intrafractional cavity motion. Int J Radiat Oncol 2016;96:785–92. https://doi.org/10.1016/j.ijrobp.2016.08.006.
[20] Jeon SH, Shin KH, Park S-Y, Kim J-i, Park JM, Kim JH, et al. Seroma change during magnetic resonance imaging-guided partial breast irradiation and its clinical implications. Radiat Oncol 2017;12:103. https://doi.org/10.1186/s13014-017-0843-7.
[21] Henke LE, Contreras JA, Green OL, Cai B, Kim H, Roach MC, et al. Magnetic resonance image-guided radiotherapy (MRIgRT): A 4. 5-year clinical experience. Clin Oncol 2018;30:720–7. https://doi.org/10.1016/j.clon.2018.08.010.
[22] Nachbar M, Mönnich D, Boeke S, Gani C, Weidner N, Heinrich V, et al. Partial breast irradiation with the 1.5 T MR-Linac: First patient treatment and analysis of electron return and stream effects. Radiother Oncol 2020;145:30–5. https://doi.org/10.1016/j.radonc.2019.11.025.
[23] Patel RR, Becker SJ, Das RK, Mackie TR. A dosimetric comparison of accelerated partial breast irradiation techniques: multicatheter interstitial brachytherapy, three-dimensional conformal radiotherapy, and supine versus prone helical tomotherapy. Int J Radiat Oncol Biol Phys 2007;68:935–42. https://doi.org/10.1016/j.ijrobp.2007.03.005.
[24] Kirby AM, Evans PM, Donovan EM, Convery HM, Haviland JS, Yarnold JR. Prone versus supine positioning for whole and partial-breast radiotherapy: A comparison of non-target tissue dosimetry. Radiother Oncol 2010;96:178–84. https://doi.org/10.1016/j.radonc.2010.05.014.
[25] Yu T, Xu M, Sun T, Shao Q, Zhang YJ, Liu XJ, et al. External-beam partial breast irradiation in a supine versus prone position after breast-conserving surgery for Chinese breast cancer patients. Sci Rep 2018;8:1–8. https://doi.org/10.1038/s41598-018-33741-z.
[26] Brown E, Dundas K, Surjan Y, Miller D, Lim K, Boxer M, et al. The effect of imaging modality (magnetic resonance imaging vs. computed tomography) and patient position (supine vs. prone) on target and organ at risk doses in partial breast irradiation. J Med Radiat Sci 2020:1–10. 10.1002/jmrs.453.
[27] Charaghvandi KR, van't Westeinde T, Yoo S, Houweling AC, Rodrigues A, Verkooijen HM, et al. Single dose partial breast irradiation using an MRI linear accelerator in the supine and prone treatment position. Clin Transl Radiat Oncol 2019;14:1–7. https://doi.org/10.1016/j.ctro.2018.09.001.
[28] Eggers H, Brendel B, Duijndam A, Herigault G. Dual-echo Dixon imaging with flexible choice of echo times. Magn Reson Med 2011;65:96–107. https://doi.org/10.1002/mrm.22578.
[29] Bol GH, Kotte ANTJ, van der Heide UA, Lagendijk JJW. Simultaneous multi-modality ROI delineation in clinical practice. Comput Methods Programs Biomed 2009;96:133–40. https://doi.org/10.1016/j.cmpb.2009.04.008.
[30] Feng M, Moran JM, Koelling T, Chughtai A, Chan JL, Freedman L, et al. Development and validation of a heart atlas to study cardiac exposure to radiation following treatment for breast cancer. Int J Radiat Oncol Biol Phys 2011;79:10–8. https://doi.org/10.1016/j.ijrobp.2009.10.058.
[31] van Heijst TCF, den Hartogh MD, Lagendijk JJW, van den Bongard HJGD, van Asselen B. MR-guided breast radiotherapy: feasibility and magnetic-field impact on skin dose. Phys Med Biol 2013;58:5917–30. https://doi.org/10.1088/0031-9155/58/17/5917.
[32] Groot Koerkamp ML, de Hond YJM, Maspero M, Kontaxis C, Mandija S, Vasmel JE, et al. Synthetic CT for single-fraction neoadjuvant partial breast irradiation on an MRI-linac. Phys Med Biol 2021;66:085010. https://doi.org/10.1088/1361-6560/abf1ba.
[33] 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.
[34] Shaw E, Kline R, Gillin M, Souhami L, Hirschfeld A, Dinapoli R, et al. Radiation therapy oncology group: Radiosurgery quality assurance guidelines. Int J Radiat Oncol Biol Phys 1993;27:1231–9. https://doi.org/10.1016/0360-3016(93)90548-A.
[35] Vasmel JE, Groot Koerkamp ML, Kirby AM, Russell NS, Shaitelman SF, Vesprini D, et al. Consensus on contouring primary breast tumors on MRI in the setting of neoadjuvant partial breast irradiation in trials. Pract Radiat Oncol 2020;10:e466–74. https://doi.org/10.1016/j.prro.2020.03.011.
[36] Wang J, Salzillo T, Jiang Y, Mackeyev Y, David Fuller C, Chung C, et al. Stability of MRI contrast agents in high-energy radiation of a 1.5T MR-Linac. Radiother Oncol 2021;161:55–64. https://doi.org/10.1016/j.radonc.2021.05.023.
[37] Park JM, Shin KH, Kim J-i, Park S-Y, Jeon SH, Choi N, et al. Air–electron stream interactions during magnetic resonance IGRT: Skin irradiation outside the treatment field during accelerated partial breast irradiation. Strahlentherapie Und Onkol 2018;194:50–9. https://doi.org/10.1007/s00066-017-1212-z.
[38] De-Colle C, Nachbar M, Mönnich D, Boeke S, Gani C, Weidner N, et al. Analysis of the electron-stream effect in patients treated with partial breast irradiation using the 1.5 T MR-linear accelerator. Clin Transl Radiat Oncol 2021;27:103–8. https://doi.org/10.1016/j.ctro.2020.12.005.