The UK HeartSpare Study (Stage IB): Randomised comparison of the voluntary breath-hold technique and prone treatment in larger-breasted women.

Frederick R. Bartlett, FRCR,^{*} Ruth M. Colgan, ,[†] Ellen M. Donovan, PhD,[†] Helen A. McNair, PhD,^{*} Karen Carr, ,^{*} Philip M. Evans, DPhil,^{†,‡} Clare Griffin, MSc,^{||} Imogen Locke, FRCR,^{*} Joanne S. Haviland,^{||} John R. Yarnold, FRCR,[¶] Anna M. Kirby, FRCR,^{*}

^{*} Department of Radiotherapy, Royal Marsden NHS Foundation Trust, Sutton, UK

[†] Joint Department of Physics, Royal Marsden NHS Foundation Trust and Institute of Cancer Research, Sutton, UK

[‡] Centre for Vision, Speech and Signal Processing, Faculty of Engineering and Physical Sciences, University of Surrey, Guildford, UK ^{||} Clinical Trials and Statistics Unit (ICR-CTSU), Institute of Cancer Research, London, UK

[¶] Division of Radiotherapy and Imaging, Institute of Cancer Research, Sutton, UK

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Corresponding author: Dr Frederick Bartlett FRCR, Department of Academic Radiotherapy, Royal Marsden NHS Foundation Trust, Downs Road, Sutton SM2 5PT, United Kingdom. Telephone: +44 208 661 3169. Fax: +44 208 661 3107. Email: frederick.bartlett@rmh.nhs.uk.

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Conflict of interest: Orfit Industries (Wijnegem, Belgium) loaned the prone breast platforms used in this study.

Summary

The development and implementation of heart-sparing breast radiotherapy techniques is an international priority. This randomised study tested the hypothesis that, in larger-breasted women, heart-sparing radiotherapy is more effective when delivered using a free-breathing prone position than a supine voluntary breath-hold (VBH) technique. Our results showed that heart-sparing was statistically significantly superior with VBH, although cardiac doses were low for both techniques. The results should help radiotherapy centres planning to introduce either of these heart-sparing techniques.

Abstract

Purpose: To compare mean heart and left anterior descending coronary artery (LAD) doses (NTD_{mean}) (Gy) and positional reproducibility in larger-breasted women receiving left breast radiotherapy using supine voluntary deep-inspiratory breath-hold (VBH) and free-breathing prone techniques in a non-blinded randomised-controlled crossover trial.

Methods and materials: Following surgery for early breast cancer, patients with estimated breast volumes $>750\text{cm}^3$ underwent planning-CT scans in supine VBH and free-breathing prone positions. Radiotherapy treatment plans were prepared, and mean heart, LAD, lung and contralateral breast doses were calculated. Patients were randomised to receive one or other technique for fractions 1-7, before switching techniques for fractions 8-15 (40Gy/15 fractions total). Daily electronic portal imaging and alternate-day cone-beam CT (CBCT) imaging were performed. The primary endpoint was the difference in mean LAD NTD_{mean} between VBH and prone techniques. Population systematic (Σ) and random errors (σ) were estimated. Patient comfort, radiographer satisfaction and scanning/treatment times were recorded. Within-patient comparisons between techniques used Wilcoxon signed-rank tests.

Results: Thirty-four patients were recruited from a single centre, with complete dosimetric data available for 28. Mean cardiac doses (Gy) for VBH and prone treatments respectively were: heart NTD_{mean} 0.4 and 0.7 ($p<0.001$) and LAD NTD_{mean} 2.9 and 7.8 ($p<0.001$), and maximum LAD dose 21.0 and 36.8 ($p<0.001$). Clip-based CBCT Σ (VBH and prone) were $\leq 3.0\text{mm}$ and $\leq 6.5\text{mm}$ and $\sigma \leq 3.5\text{mm}$ and $\leq 5.4\text{mm}$. Patients and radiographers preferred VBH ($p<0.001$, $p=0.003$ respectively). Treatment setup and total session times were less with VBH ($p=0.01$, $p=0.002$ respectively), although 'beam on' time was less with prone treatment ($p=0.004$)

Conclusions: In larger-breasted women, supine VBH provides superior cardiac sparing and reproducibility than a free-breathing prone position. VBH is preferred by patients and radiographers and is quicker to deliver than prone treatment.

The number of breast cancer survivors is increasing due to improvements in detection and more effective treatments [1]. However, improvements in survival mean more women will live to see the late effects of their cancer treatments. Breast radiotherapy is associated with a 1-2% excess of non-breast cancer mortality, the majority of which is attributable to cardiac disease [2], and recent work has demonstrated a linear, no-threshold relationship between mean heart dose and the risk of subsequent major coronary events (MCE) [3]. It remains unclear which cardiac substructures contribute to the development of MCE, although evidence from myocardial perfusion [4] and coronary angiography [5,6] studies implicates the left anterior descending coronary artery (LAD).

The development and implementation of heart-sparing breast radiotherapy techniques remains an international priority. Breath-holding techniques reduce heart doses [8-11] but have not yet been widely implemented in the UK [2012 Royal College of Radiologists audit] due to resource costs and staff training. A recent UK study (HeartSpare IA) demonstrated a voluntary breath-hold technique to be as effective at heart-sparing and as reproducible as breath-holding treatment with the active breathing coordinator™ (ABC) (Elekta, Crawley, UK) [7]. Additional benefits, including shorter treatment setup times and lower implementation costs, are likely to establish this technique as the standard of care for many left-sided women in the UK. However, there remains a group of larger-breasted women in whom the relative benefits of breath-hold versus prone positioning are unknown. Previous work has shown that, although the prone position moves the heart closer to the chest wall under gravity [8], larger breasts fall further forward, allowing for shallower tangential radiotherapy beam placement [9,10] and therefore significantly reduced cardiac doses in larger-breasted women [11].

This single centre randomised non-blinded crossover study compares cardiac dosimetry for the voluntary breath-hold (VBH) technique with prone positioning in larger-breasted women using a within-patient comparison. We hypothesised that heart-sparing would be superior in the prone

position compared with supine deep-inspiratory breath-hold for a proportion of larger-breasted women.

Methods and materials

This study was approved by the Research and Development Committee and the Research Ethics Committee (ISRCTN XXXXXXXX). Women with left breast cancer who had undergone breast conserving surgery for early stage invasive ductal or lobular carcinoma (pT1-3b N0-1 M0), who required radiotherapy to the breast alone (+/- tumour bed boost) without nodal irradiation, and who had an estimated breast volume of $>750\text{cm}^3$ were approached. All patients were treated at one institution. Randomisation procedures followed those reported by Bartlett *et al.* [7].

Patient positioning and image acquisition

Prior to CT scanning, radio-opaque wire was used to delineate clinically palpable breast tissue with the patient in a standard supine position. The CT-planning session protocol used for the VBH technique has been described by Bartlett *et al* [7]. For prone CT scanning, patients were positioned on an Orfit AIO Solution® prone breast board (ORFIT Industries, Wijnegem, Belgium) (see Figure 1). A marker (tattoo) was placed ipsilaterally in the posterior axillary line and aligned axially with a posterior midline marker using lateral lasers. A second posterior marker was placed 15cm inferior to the primary posterior marker, in line with the sagittal lasers. CT data (Philips Medical Systems, UK) were acquired without contrast for supine VBH and free-breathing prone scans using 3mm slices from C6 to below the diaphragm. Both CT scans were performed in one CT-planning session, with patients dismounting the CT couch between scans. Photographs of patient positioning were taken for both techniques to aid treatment setup. The time taken to complete each planning-CT was recorded, from the time the patient mounted the CT couch to the time at which they dismounted

the couch. After completing both scans, patients were asked to complete validated comfort and acceptability questionnaires and radiographers were asked to complete radiographer satisfaction questionnaires [12].

Figure 1 Patient positioned on Orfit AIO Solution® prone breast board (ORFIT Industries, Wijnegem, Belgium)

Target and organ-at-risk delineation

Target and organ-at-risk (OAR) volumes were delineated on both CT scans. The whole breast clinical target volume (WBCTV) was defined using the radio-opaque wire and any additional breast tissue visualised on CT (limited by pectoral fascia and 5mm from skin). The tumour bed was defined using tumour bed clips (inserted at surgery), and included any associated seroma or distortion of breast architecture. A uniform margin of 15mm was added (limited by WBCTV) to form the partial breast CTV (PBCTV). The method for outlining the LAD, heart and lungs follows that of Bartlett *et al.* [7]. The

contralateral breast was also outlined, encompassing any contralateral breast tissue visualised on CT (limited by pectoral fascia and 5mm from skin).

Radiotherapy planning

Tangential fields were applied to encompass WBCTV. Philips Pinnacle 9.2 (Philips Medical Systems, Palo Alto, US) and the collapsed-cone algorithm (0.25x0.25x0.25cm resolution) were used to produce plans such that $\geq 90\%$ of the WBCTV and $\geq 95\%$ of the PBCTV were covered by the 95% isodose [11]. Where required, multileaf collimation (MLC) was used to shield cardiac tissue whilst maintaining target tissue constraints. Segments (field-in-field technique) were used, where necessary, to improve dose homogeneity and all plans fulfilled ICRU 62 criteria (dose variation $\leq +7\%$ and -5% , hotspots $\leq 107\%$) [13]. Patients were prescribed 40Gy in 15 fractions over 3 weeks using 6 and/or 10 MV photons.

Tabular dose-volume histogram (DVH) data was used to derive NTD_{mean} (a biologically weighted mean of total dose to tissue normalised to 2Gy fractions using a standard linear quadratic model [14], $\alpha/\beta=3\text{Gy}$) for LAD, heart, ipsilateral and whole lungs and contralateral breast. In addition, the maximum dose received by the LAD (LAD_{max}) was calculated. Conformity and homogeneity indices were calculated for both techniques using established formulae [13,15].

Radiotherapy delivery

Patients were randomised to receive one treatment technique for fractions 1-7 and the second technique for fractions 8-15. Patient setup for the VBH technique was as described by Bartlett *et al.* [7]. The prone position was reproduced at treatment by aligning tattoos to lasers and using photographs taken at CT-planning to check consistent arm, head and torso positioning. The left

posterior oblique (LPO) field borders were checked using radiotherapy treatment plan measurements and CT skin-rendered views. Visualisation of the right anterior oblique (RAO) field borders was impeded by the prone board structure. Real-time electronic portal images (EPI) were acquired daily and matched on-line to digitally reconstructed radiographs (DRR) on fractions 1-3 and 8-10 using iView software (Elekta, Crawley, UK). Shifts were applied if errors were >5mm in the (u,v)-plane on at least two consecutive days. For study purposes setup errors were measured off-line for every fraction. The LPO was treated first and the RAO treated second.

On-board kV-CT (CBCT) images of the chest were acquired immediately after setup on fractions 1, 3, 5, 7, 8, 10, 12 and 14 using the Elekta Synergy X-ray Volume Imaging System (Elekta, Crawley, UK). CBCT procedures for the supine [16] and prone [11] techniques have been described previously. CBCT data was acquired primarily for study purposes although was used to make isocentre shifts where errors were >5mm in any plane on two or more consecutive days and/or there was insufficient chest wall visible on EPI to make such shifts. Daily CBCT imaging for prone treatment was used where errors were >5mm in opposite directions. CBCT volumes were manually registered to the reference planning-CT, and both chest wall and clip-based matches were performed. The correction reference point was set to the isocentre.

Times at which patients mounted the couch, the radiotherapy beam was switched on and off, and at which patients dismounted the couch, were recorded for every fraction. Patients and radiographers were asked to complete questionnaires on fractions 1, 7, 8 and 15.

Statistical methods

The primary endpoint was the difference in mean NTD_{mean} Gy to the LAD between VBH and prone techniques. Secondary endpoints were: comparison of standard deviation in mean LAD NTD_{mean} ; interfraction reproducibility of patient position; difference in NTD_{mean} to ipsilateral, whole lung and

heart; difference in chest wall V20Gy between techniques; interfraction reproducibility of tumour-bed clip position; patient and radiographer satisfaction; time spent in various stages of planning and delivery and cost of techniques. Assuming a 2-sided significance level of 0.05 and standard deviation of the difference in measurements of 6.7%, a sample size of 50 patients (allowing for a 10% drop-out rate) was estimated to provide 83% power in order to detect an absolute difference of 3Gy between the mean LAD NTD_{mean} (primary endpoint) using the two techniques (assuming 0.1 correlation between the two techniques and standard deviations of 5Gy for each technique). During the course of the trial clinicians noted VBH was consistently better than prone at sparing heart tissue and as such an unplanned interim analysis was conducted and reviewed by an independent group (two clinicians and a statistician) after primary endpoint data was available for 27 patients. Following this review, the decision was made to close trial recruitment early following randomisation of 34 patients. The observed standard deviations for the 2 techniques were lower than had been estimated in the original sample size calculation. Therefore, the power of the study remained 83% to detect a 3Gy difference in mean LAD NTD_{mean} despite stopping recruitment early (assuming 4Gy SD for each technique and a 0.1 correlation gave a standard deviation of differences of 5.37).

Q-Q plots and Kolmogorov-Smirnov tests demonstrated that normal tissue dose data were not normally distributed. In view of this, Wilcoxon signed-rank tests were used to compare normal tissue doses between VBH and prone treatments, using each patient as their own control. Wilcoxon signed-rank tests were also used to compare timing data (CT and treatment session times) and the number of segments used for each technique. McNemar's test was used to compare MLC use, beam energies and systematic moves for the VBH and prone techniques. Translational and rotational CBCT registration results were analysed in 3-dimensions for each patient and for both clip-based and chest wall matches. Mean displacements and standard deviations were compared for VBH and prone treatments for each patient. Using the method described by van Herk [17], population mean displacement (M), systematic (Σ) and random (σ) errors were estimated. EPI displacements were analysed for each beam in the (u,v)-plane for every patient (v-direction parallel to craniocaudal axis

and u-direction perpendicular to this) [18]; population M , Σ and σ were estimated. Paired t-tests were used to compare M . Patient comfort and acceptability questionnaires and radiographer satisfaction questionnaires were summarised and analysed as described previously [7].

Statistical analyses were performed using SPSS Statistics Version 21 (IBM, Portsmouth, UK).

Results

Thirty-four patients were randomised between January 2013 and April 2014. Twenty-two (65%) patients completed the study as per protocol, and complete dosimetric data was available for 28 (82%) (see Figure 2 and Appendix e1). 170/229 (74%) planned prone fractions and 221/221 (100%) of planned VBH fractions were completed. The median age of patients recruited was 57 years (range 25-79) and median BMI was 31.2 (range 24.5-38.3). Table e1 shows mean target and OAR volumes for both techniques. Mean WBCTV was similar for both techniques: 1109cm³ (prone) vs 1153cm³ (VBH) and the difference between WBCTV for prone and VBH radiotherapy plans in all patients was <10%. Mean target tissue coverage was ≥95% for both techniques. There was no significant difference in heart, LAD plus 1cm, or contralateral breast volumes between the two techniques. However, both ipsilateral and whole lung volumes were significantly smaller in the prone position (all $p<0.001$).

Figure 2 CONSORT 2010 Flow Diagram for [this study]. More detail on patient protocol breaches is given in Appendix el.

Figure 2

Further information on protocol breaches labelled *, †, †† and || can be found in Appendix el.

All cardiac dose parameters (Gy) were statistically significantly lower with VBH than with prone treatment [95% confidence intervals]: heart NTD_{mean} 0.4 [0.4-0.5] vs 0.7 [0.6-0.7] ($p<0.001$), LAD NTD_{mean} 2.9 [1.8-3.9] vs 7.8 [6.4-9.2] ($p<0.001$), and LAD_{max} 21.0 [15.8-26.2] vs 36.8 [35.2-38.4] ($p<0.001$). Heart NTD_{mean} was lower using VBH than prone treatment in 26/28 (93%) patients, as was LAD NTD_{mean} (27/28, 96%) and LAD_{max} (24/28, 86%). Within-patient comparisons of heart NTD_{mean} for VBH and prone treatments are shown in Figure 3. Ipsilateral and whole lung NTD_{mean} were significantly lower using the prone technique than using VBH: 3.7 [3.4-4.0] vs 0.3 [0.3-0.4] ($p<0.001$) and 1.8 [1.7-2.0] vs 0.2 [0.16-0.24] ($p<0.001$) respectively. Mean contralateral breast dose was significantly lower with VBH than prone treatment: 0.1 [0.07-0.11] vs 0.3 [0.2-0.4] ($p<0.001$).

Figure 3 Hi-Lo chart showing within-patient comparisons of heart NTD_{mean} (Gy) for voluntary breath-hold (VBH) and prone techniques

Conformity indices were statistically significantly closer to one for prone radiotherapy treatment plans (1.13 vs 1.26, $p<0.001$), but there was no difference in homogeneity indices between the two techniques ($p=0.87$). 13/28 (46%) VBH treatment plans used at least one 10MV beam, compared to

2/28 (7%) prone treatment plans ($p=0.001$). MLC was used to shield cardiac tissue in 12/28 (43%) prone treatment plans, compared to 4/28 (14%) VBH plans ($p=0.02$)

Table 1 shows population M, Σ and σ for CBCT clip-based matches. Population M, Σ and σ for CBCT chest wall-based matches and EPI-based matches are shown in Tables e2 and e3 respectively. Displacement errors for prone treatment were consistently greater than for supine VBH irrespective of imaging or matching technique. Prone displacement errors were greatest for CBCT chest wall-based matches. Systematic moves were performed in 11/23 prone treatments and 2/23 VBH treatments ($p=0.01$).

Table 1 Population mean displacement (M), systematic (Σ) and random (σ) translational (mm) and rotational ($^{\circ}$) errors in 3-dimensions for clip-based cone-beam CT versus planning CT matches for voluntary breath-hold (VBH) and prone techniques

		Translational			Rotational		
		VBH	Prone	p	VBH	Prone	p
Right-left (R-L)	M	-0.1	1.5	0.48	1.3	0.0	0.06
	Σ	1.8	5.9		1.2	1.9	
	σ	1.9	5.4		1.5	1.5	
Superior-inferior (S-I)	M	2.0	5.2	0.10	-0.5	-1.0	0.15
	Σ	3.0	6.5		1.4	2.7	
	σ	2.6	4.5		1.1	2.1	
Anterior-posterior (A-P)	M	0.0	-3.1	<u>0.04</u>	-0.2	-1.4	<u>0.02</u>
	Σ	1.8	5.2		1.7	3.5	
	σ	3.5	4.6		1.3	2.3	

Total number of CBCTs: 166

Patients found VBH more comfortable than prone treatment ($p<0.001$) and radiographers found VBH more satisfactory ($p=0.003$) (see Table e4).

Median radiotherapy CT-planning scan and treatment times are shown in Table 2. There was no significant difference between the two techniques in terms of planning-CT session time ($p=0.24$).

Treatment setup and total treatment session times were significantly less with VBH ($p=0.01$, $p=0.002$ respectively), although 'beam on' time was less with prone treatment ($p=0.004$).

Table 2 Median radiotherapy CT-planning session and treatment times for voluntary breath-hold (VBH) and prone techniques with ranges in brackets (minutes).

	VBH	Prone	<i>p</i>
CT-planning session	23 (15-62)	22 (14-48)	0.24
Treatment setup	8 (4-12)	9 (6-16)	0.01
'Beam on' time	5 (4-7)	3 (2-13)	0.004
Leaving treatment room	2 (1-3)	2 (1-4)	0.70
Total treatment time	17 (13-22)	20 (13-49)	0.002

n=30 (CT), 22 (treatment)

Discussion

This randomised crossover study compared supine VBH with free-breathing prone treatment in terms of cardiac doses and setup reproducibility. Our results demonstrate that, in the majority of patients, supine VBH offers better cardiac sparing and a more favourable reproducibility profile than treatment in the prone position.

There was a highly statistically significant difference between techniques for all cardiac dose parameters measured, supporting the superiority (in terms of cardiac-sparing) of supine deep-inspiratory breath-hold over a free-breathing prone technique, and in keeping with published non-randomised data [19]. However, cardiac doses for both techniques were low. Figure 4 shows an example of the relationship between breast and cardiac tissue dosimetry for prone and supine VBH treatments. The prone mean heart NTD_{mean} and mean LAD_{max} doses were lower than those seen in standard free-breathing left breast radiotherapy [20], although confidence intervals overlap. Prone cardiac doses in this study were generally lower than reported in other studies comparing prone and supine treatments [11,21,22]. In keeping with the literature, mean lung doses were also significantly

lower with prone treatment than supine treatment [9,11,23]. Cardiac doses for supine VBH treatment were lower than previously reported by Bartlett *et al.* [7], although confidence intervals for mean LAD_{mean} and mean LAD_{max} doses overlap. A possible reason for this is that MLC use or alteration of beam angles to avoid cardiac tissue is likely to result in relatively less WBCTV coverage compromise in larger- vs smaller-breasted women. Contrary to other published reports [21,24,25], this study demonstrates that it is possible to achieve comparable dose homogeneity for both techniques, but that to do so, more segments are required for supine treatment.

Previous work has found positional reproducibility for prone treatment to be inferior to supine treatment [26], and our results are consistent with this. Reproducibility for supine VBH [7] and prone [26-28] treatment in this study was consistent with published reports. The prone treatment position is difficult to reproduce for a number of reasons, including the instability of breast and subcutaneous tissue, and the fact that target and OAR dosimetry is optimised by rotation of the patient around the superior-inferior axis (towards the treated side). Reproducibility in this study was hindered by the inability to site a contralateral posterior axillary line tattoo due to excess soft tissue, something that was noted in previous work [26]. In line with recommendations from that study, a second midline posterior tattoo was introduced in order to improve reproducibility. However, rotational errors were greatest around the anterior-posterior axis, something which might be improved by increasing the distance between posterior tattoos. Additionally, we used a commercially available prone platform, selected for its comfortable head position and improved arm positioning (no T-bar such as that used in previous work [26]). However, radiographers again found arm position difficult to reproduce, whilst in the absence of a method to encourage arm extension, it was possible for patients to support themselves using their elbows (despite being discouraged from doing so). Subsequently, as patients relax during treatment, the degree of elbow support (and thus patient position) could be expected to vary. Although prone setup errors were greater than for VBH, systematic errors were consistently greater than random errors, suggesting that reproducibility could be improved by implementation of a CBCT-based correction protocol.

Patients generally found treatment in the prone position less comfortable than supine VBH. Patients described finding the headrest uncomfortable (despite the prone platform being selected for its comfortable head position), rib discomfort at the inferior border of the ipsilateral breast aperture and feeling unstable due to tilting. The fact that radiographers found prone treatment less satisfactory than supine VBH reflects the difficulty of patient setup and reproducibility with this technique.

In terms of the amount of time required for each technique, it was anticipated that prone planning-CT session times would be shorter than VBH ones, given that VBH training was included in the VBH CT session. However, this is likely to reflect the additional care that is required to optimise the reproducibility of the prone position at CT-planning compared to supine setup (head comfort, patient rotation, contralateral breast tissue position, avoiding elbow support). Reproducing these positions on treatment accounts for the difference in treatment setup and total treatment session times between the two techniques. Two to three breath-holds were required per treatment beam for VBH, meaning that VBH treatment delivery was longer than for prone treatment.

Only 65% of patients completed the study as per protocol, and the reasons for failure to complete the study can be divided into four categories: (i) failure to meet inclusion criteria, (ii) prone treatment plan issues, (iii) prone equipment shortcomings and (iv) prone setup difficulties (discussed in more detail in Appendix e1). Failure to meet inclusion criteria could have been improved by selecting patients on cup size rather than breast volume, although if, for example, women of D cup or larger were selected, this would have necessitated including some women with smaller breast volumes (ie $<750\text{cm}^3$). In addition, the cross-over design of the study meant that clinicians were able to directly compare VBH and prone treatment plans prior to treatment. Manufacturers are working with consumers to improve prone breast platform comfort and reproducibility, and a system that claims to overcome many of the shortcomings of the platform used in this study has been developed. This study may be criticised for using mean LAD dose as its primary endpoint, as a recent

study demonstrated considerable inter-observer variability in LAD outlining [29]. However, this effect was minimised in our study by the same clinician outlining the LAD for all treatment plans.

Despite demonstrating a clear superiority for supine VBH over free-breathing prone treatment in terms of cardiac sparing and positional reproducibility, there is much to satisfy proponents of either technique in this study; cardiac doses were low for both techniques and reproducibility was, for the majority of women, within tolerance levels used for standard tangential field breast radiotherapy. In addition, continued improvements in prone breast board technology are likely to enhance both patient comfort and reproducibility. However, given the inferior reproducibility and the paucity of visible chest wall on EPI, a CBCT-based correction protocol is indicated for prone treatment. It is hoped that the results of this study will inform the decisions of centres considering implementation of either of these heart-sparing techniques. However, it is expected that in the UK the focus of work will shift to developing the VBH technique further, especially as we anticipate it to be more compatible with complex breast radiotherapy techniques, such as simultaneous integrated boost, arc therapies, and regional nodal treatments.

Conclusion

Our data suggest that, in larger-breasted women, supine VBH treatment is better at sparing cardiac tissues and more reproducible than treatment using a free-breathing prone technique. Patients find VBH more comfortable than the prone position, and radiographers find VBH more satisfactory. Treatment setup and total treatment session times are shorter with VBH.

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Appendix e1: Supplementary information on protocol breaches

* Four patients at treatment planning were found to have WBCTV $<750\text{cm}^3$; for practical reasons, estimation of breast volume in the clinic was based on selecting women of cup size D or above (based on the correlation between cup size and breast volume noted during our previous prone work (Kirby et al)). Cup-size is, however, an imperfect predictor of breast volume. Using cup size rather than breast volume as an inclusion criterion would have prevented these protocol breaches, although would have meant treating patients less likely to benefit from any cardiac-sparing effect of prone treatment as a proportion of self-selected D-cup patients have breast volumes of $<750\text{cm}^3$.

† In two patients, breast tissue touched the CT couch using the standard prone treatment board. An 8cm extension set was available, but the additional height would have presented a very high risk of collision between patient and gantry on-treatment.

†† Three patients were withdrawn due to problems with their prone radiotherapy treatment plans. One patient had a very medial tumour, and adequate tumour bed coverage would have necessitated the addition of a direct anterior beam. Use of an anterior beam would have made assessment of treatment setup position extremely difficult and the attending clinician elected to proceed with the VBH plan whose dosimetry was satisfactory and which only required tangential fields. Two further patients were withdrawn as the attending clinician felt the contralateral breast dose was unacceptably high (although no study-specific contralateral breast dose-volume tolerances were specified). In one patient the contralateral breast NTD_{mean} dose for the prone plan was 14 times greater (0.1 vs 1.4Gy) than the VBH plan, and for the second patient it was 2.5 times greater (0.2 vs 0.5Gy). One patient's tumour bed was very close to the axilla and the second patient had a very medial tumour bed. These cases highlight the difficulty of using prone treatment for very medially- or laterally-located tumour beds.

3 patients were withdrawn due to unacceptable prone setup errors: one was withdrawn on fraction one (errors $>25\text{mm}$ despite multiple setup attempts) and two withdrawn on fraction 3 (errors $>20\text{mm}$ on consecutive days). It was not possible to ascertain the reason(s) for such gross setup errors.

Table e1

Mean patient target and organ-at-risk volumes for voluntary breath-hold (VBH) and prone techniques with standard deviations () and range [] in brackets.

	VBH	Prone	<i>p</i>
WBCTV (cm ³)	1109 (318) [750-1990]	1153 (326) [752-1978]	<u><0.001</u>
PBCTV (cm ³)	138 (77) [41-376]	157 (85) [44-409]	<u>0.002</u>
WBCTV V95% (%)	96 (2) [91-99]	95 (2) [90-99]	0.35
PBCTV V95% (%)	100 (0) [96-100]	100 (0) [97-100]	0.44
Heart volume (cm ³)	558 (86) [435-780]	545 (95) [418-746]	0.12
LAD plus 1cm volume (cm ³)	35.2 (3.0) [29.5-41.4]	34.9 (2.8) [30.2-41.3]	0.17
Ipsilateral lung volume (cm ³)	2119 (436) [1221-2817]	1285 (302) [775-1888]	<u><0.001</u>
Whole lung volume (cm ³)	4473 (919) [2686-5885]	2726 (614) [1690-3872]	<u><0.001</u>
Contralateral breast volume (cm ³)	1104 (295) [718-1784]	1136 (291) [747-1736]	0.26

Table e2

Population mean displacement (M), systematic (Σ) and random (σ) translational (mm) and rotational ($^{\circ}$) errors in 3-dimensions for chest wall-based cone-beam CT versus planning CT matches for voluntary breath-hold (VBH) and prone techniques

		Translational			Rotational		
		VBH	Prone	p	VBH	Prone	p
Right-left (R-L)	M	-0.7	0.8	0.43	1.0	0.1	0.10
	Σ	1.9	6.8		1.3	1.8	
	σ	2.3	6.1		1.1	1.8	
Superior-inferior (S-I)	M	2.8	2.6	0.91	-0.9	-1.2	0.47
	Σ	3.7	8.5		1.5	2.1	
	σ	2.8	8.1		1.2	1.7	
Anterior-posterior (A-P)	M	-0.2	-1.3	0.39	-0.2	-1.8	0.02
	Σ	1.9	4.2		1.5	2.4	
	σ	2.9	4.4		1.0	1.7	

Total number of CBCTs: 166

Table e3

Population mean displacement (M), systematic (Σ) and random (σ) translational (mm) and rotational ($^\circ$) errors for voluntary breath-hold (VBH) and prone techniques measured by electronic portal imaging (EPI).

		Right anterior oblique beam (RAO)			Left posterior oblique beam (LPO)		
		VBH	Prone	p	VBH	Prone	p
u-plane	M	-0.6	2.2	0.96	0.4	-2.0	0.07
	Σ	1.4	4.5		1.8	5.1	
	σ	2.4	4.5		2.1	5.5	
v-plane	M	0.0	2.1	0.95	0.5	3.3	0.41
	Σ	2.6	6.0		3.0	7.2	
	σ	2.1	4.8		2.2	5.5	
Rotation	M	-0.2	0.6	0.03	0.2	0.0	0.58
	Σ	0.8	0.9		0.9	0.7	
	σ	1.0	1.4		0.9	1.8	

Total number of EPIs: 614

Table e4

Median of the differences in patient comfort scores (PCS) and radiographer satisfaction scores (RSS) at CT, first fraction and last fraction

	Patients (n)	<i>p</i>
PCS	< 0 (Prone better)	<0.001
	> 0 (VBH better)	
	0 (no difference)	
RSS	< 0 (VBH better)	0.003
	> 0 (Prone better)	
	0 (no difference)	