Radiotherapy and Oncology 114 (2015) 79–84

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Avoidance of cardiac toxicity

Heart dose reduction by prone deep inspiration breath hold in left-sided breast irradiation

Thomas Mulliez [a,b,*], Liv Veldeman [a], Bruno Speleers [a], Khalil Mahjoubi [b], Vincent Remouchamps [b], Annick Van Greveling [a], Monique Gilsoul [b], Dieter Berwouts [a], Yolande Lievens [a], Rudy Van den Broecke [c], Wilfried De Neve [a]

[a] Department of Radiotherapy, Ghent University Hospital; [b] Department of Radiotherapy, Clinique et Maternité Sainte-Elisabeth, Namur; and [c] Department of Gynaecology, Ghent University Hospital, Belgium

ARTICLE INFO

Article history:
Received 29 May 2014
Received in revised form 14 November 2014
Accepted 23 November 2014
Available online 9 December 2014

Keywords:
Breast
Radiotherapy
Prone position
Supine position
Deep inspiration breath hold

ABSTRACT

Background and purpose: Cardiac disease has been related to heart dose after left-sided breast radiotherapy. This trial evaluates the heart sparing ability and feasibility of deep inspiration breath hold (DIBH) in the prone position for left-sided whole breast irradiation (WBI).

Materials and methods: Twelve patients underwent CT-simulation in supine shallow breathing (SB), supine DIBH, prone SB and prone DIBH. A validation cohort of 38 patients received prone SB and prone DIBH CT-scans; the last 30 patients were accepted for prone DIBH treatment. WBI was planned with a prescription dose of 40.05 Gy.

Results: DIBH was able to reduce ($p < 0.001$) heart dose in both positions, with results for prone DIBH at least as favorable as for supine DIBH. Mean heart dose was lowered from 2.2 Gy for prone SB to 1.3 Gy for prone DIBH ($p < 0.001$), while preserving the lung sparing ability of prone positioning. Moreover prone DIBH nearly consistently reduced mean heart dose to less then 2 Gy, regardless of breast volume. All patients were able to perform the simulation procedure, 28/30 patients were treated with prone DIBH.

Conclusions: This trial demonstrates the ability and feasibility of prone DIBH to acquire optimal heart and lung sparing for left-sided WBI.

A significant overall survival benefit is observed when whole breast irradiation (WBI) is added to breast conserving surgery in the primary treatment of early-stage breast cancer [3]. However, it has also been recognized that breast radiotherapy is associated with an increase in non-breast cancer related deaths [4–8]. Excess radiation-induced mortality is primarily attributed to cardiovascular disease and in early trials the gain in breast cancer specific survival was even offset by the increase in cardiac deaths [5]. Heart and left anterior descending coronary artery (LAD) dose has been related to cardiovascular disease in patients irradiated for left-sided breast cancer [2–6]. Darby et al. [4] demonstrated that rates of major coronary artery events increase linearly by 7.4% (95% confidence interval, 2.9–14.5%) per Gy mean heart dose, with no apparent threshold dose. Long-term epidemiological data also showed that patients who received radiotherapy for breast cancer had an increased risk to develop contralateral breast cancer (1.3% elevated risk after 15-year) and ipsilateral lung cancer (linear increase with 8.5% per Gy (95% confidence interval, 3.1–23.3%)) [6–8]. Radiation techniques have greatly improved in the last decades and extrapolation of these historical data to contemporary techniques might not be completely adequate. However, these publications emphasize the importance of lowering doses to organs at risk (OARs) as low as possible since no safe threshold doses are identified up till now.

The anatomical advantages associated with a shift from supine to prone position – i.e. the breast elongates and falls away from the intra-thoracic region – have been published in pioneering work by the New York University group and the Royal Marsden group of London. Studies comparing supine and prone WBI have demonstrated the ability of prone position to reduce lung volume exposed to radiation [11–15]. A drawback of prone WBI is the gravity-induced anterior displacement of the heart toward the irradiated region [18]. Still, Formenti et al. [12] demonstrated that prone WBI seems to be beneficial for 85% of the patients regarding heart irradiation. However, increased heart doses are of concern in a substantial fraction of patients, especially those with small breast

* Corresponding author at: Department of Radiotherapy, Ghent University Hospital, De Pintelaan 185, 9000 Ghent, Belgium.
E-mail address: thomas.mulliez@uzgent.be (T. Mulliez).

http://dx.doi.org/10.1016/j.radonc.2014.11.038
0167-8140/

volume [9–12]. Irradiation during deep inspiration has been successfully implemented in supine WBI to reduce heart dose without increasing dose to other OARs [19–25]. Deep inspiration breath hold (DIBH) increases the distance between heart and breast compared to normal or shallow breathing (SB). If this effect occurs in prone position, DIBH might further reduce heart dose in the majority of patients and may address the problem of higher heart dose in prone than supine for a specific subgroup of patients.

This manuscript is the first to report on DIBH in prone position for left-sided WBI. The dosimetric results of two studies are reported. The goal of the first study was to explore (1) whether prone DIBH was as effective as supine DIBH in lowering heart dose and (2) whether the reduction in lung dose due to prone positioning was preserved. In this study, further referred to as the explorative study, four techniques were compared in the same patient: supine SB, supine DIBH, prone SB and prone DIBH. The goal of the second study was to validate the results of prone DIBH seen in the first study and to implement the technique in clinical practice. In this study, further referred to as the validation study, prone SB and prone DIBH were compared to investigate whether the dosimetric results of the first study could be reproduced and implemented in clinical practice.

Materials and methods

Patients

In two (consecutive) trials 50 patients were included. They all underwent breast-sparing surgery for left-sided breast cancer and were eligible for WBI according to the multidisciplinary breast cancer board at Clinique et Maternité Sainte-Elisabeth (CMSE), Namur or Ghent University Hospital (GUH), Belgium.

A first CT-simulation and planning study (explorative study) was conducted at CMSE, since they have solid experience in supine DIBH [27]. The goal of the explorative study was to investigate if DIBH could lower heart dose as efficiently in prone as in supine position while keeping its superiority regarding lung dose. Twelve patients received four computed tomography (CT) scans for radiotherapy planning: in supine and prone position, both with and without the DIBH maneuver; and were treated in supine position with the breath hold maneuver if indicated.

Since CMSE has no experience in prone treatment, the second trial (validation trial) was conducted at GUH where the prone position is used as a standard treatment option for WBI [14]. The validation trial aimed at reproducing the dosimetric results of prone DIBH obtained in the explorative trial. The second objective was to investigate the feasibility of prone DIBH treatment. To decrease the radiation burden of four CT simulation scans, the 38 patients of the validation study group received only two planning CT scans: prone SB and prone DIBH. The first 8 patients were part of a learning-phase of the CT-simulation and planning procedure and were treated in prone SB; the last 30 patients were accepted for prone DIBH treatment. Ethics Committee approval of both centers was obtained.

During clinical consultation, the maneuver of the voluntary DIBH was explained, demonstrated and rehearsed as described elsewhere [27]. In brief, patients were educated to execute two "preparatory" deep inspirations before holding their breaths at a level of deep inspiration which they could maintain for 15–20 s. This training took five to ten minutes. At GUH, a figure of the prone setup and an audio-file containing the sequence of the breath hold technique were mailed to the patients for practicing at home. The same audio sequence was used during simulation and treatment. The DIBH maneuver was briefly rehearsed before the start of the simulation procedure.

Simulation procedure

At CMSE, supine positioning was executed on a Breast Step System® (Elekta, Crawley, UK); prone positioning was previously described by Veldeman et al. [16,15] and performed on a prone-lateral Horizon breast board (Civco Medical Solutions, Orange City, Iowa, USA). Both in prone and in supine positions, the breathing cycles were monitored using a Varian Real-time Position Management system (RPM™) positioned at the dorsal side of the thorax. After positioning, the DIBH was rehearsed with audio-coaching using a telecom system. Thorax expansion was visually checked and breathing cycles were documented with the RPM™. When needed, audio instructions were given to patients. First supine SB and supine DIBH CT-acquisition were performed, afterward prone SB and prone DIBH; the CT-acquisition time did not exceed 15–20 s. Neither scan range nor patient position was altered between SB and DIBH.

Figure S1A (supplementary data) shows the workflow during simulation at GUH. A modified prone-lateral breast board fabricated by Orfit Industries (Wijnegem, Belgium) was used for prone positioning [28]; the breathing curves were registered using an emitting and receiving magnetic probe (Respisens magnetic sensors, Nomics, Angleur, Belgium) positioned at the lateral dorsum of the thorax and breast board [17,25].

Planning

Delineation of the target volumes and OARs (heart, LAD, hetero-lateral breast and lungs) was done as reported in previous publications [14,14,15,26]. A two-beam (explorative trial) and two-arc (validation trial) intensity modulated technique was used with a median prescription dose of 40.05 Gy to the whole breast. Plan evaluation for heart, LAD, hetero-lateral breast and ipsilateral lung was performed using mean dose (D_{mean}) and the dose that is exceeded in 2% of the volume as surrogate for maximum dose (D_{max}) [12,26]. Target coverage was evaluated by the dose coverage index i.e. the proportion of the planning target volume for optimization covered by the 95–107% range of 40.05 Gy [28]. For patients to be treated with prone DIBH the beam-on time for each treatment field was computed when the treatment plan was finished. The beam was divided into parts of less than 18 s if the beam-on time exceeded the predefined breath hold limit of 18 s. This duration was empirically chosen in order to avoid shortness of breath during treatment.

Treatment and acute toxicity

Prone DIBH treatment was performed on an Elekta Synergy linear accelerator (Elekta, Crawley, West-Sussex, United Kingdom). If required, a sequential boost was given in four to six fractions according to the department's guidelines. Figure S1B (supplementary data) shows the workflow executed during treatment. Prone positioning was done in SB and vertical, lateral and longitudinal setup errors were corrected on a daily basis using cone beam CT with adapted parameters [29]. The CBCT-scan was not taken in prone DIBH since CT-acquisition takes at least 30 s and might be too long for patients to hold their breath. Afterward, a lateral kV-image was acquired during DIBH and vertical and longitudinal errors were corrected based on the fusion with a DRR generated from the DIBH-scan. The systematic and random setup error for each individual patient was defined as the mean and standard deviation of all shifts in the vertical and longitudinal directions. The population systematic setup error (M) was calculated as the average of all means; the population standard deviation of the systematic setup error (Σ) was computed as the standard deviation of all means; the population random setup error (σ) as the root mean square of all individual standard deviations [30].