Radiotherapy and Oncology 106 (2013) 28–32

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Breast cancer

Improved heart, lung and target dose with deep inspiration breath hold in a large clinical series of breast cancer patients

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ARTICLE INFO

Article history:
Received 27 February 2012
Received in revised form 24 September 2012
Accepted 29 October 2012
Available online 28 November 2012

Keywords:
Breast cancer
Deep inspiration breath hold
Heart dose
Target coverage

ABSTRACT

Background and purpose: This study aims at evaluating the effect of deep-inspiration breath hold (DIBH) on target coverage and dose to organs at risk in a large series of breast cancer patients.
Materials and methods: Clinical dose plans for 319 breast cancer patients were evaluated: 144 left-sided patients treated with DIBH and 175 free-breathing (FB) patients (83 left-sided and 92 right-sided). All patients received whole breast irradiation with tangential fields, based on a forward-planned intensity-modulated radiation therapy (IMRT) technique. Dose to heart, ipsi-lateral lung and ipsi-lateral breast were assessed and median values compared between patient groups.
Results: Comparing group median values, DIBH plans show large reductions of dose to the heart compared with left-sided FB plans; V_{20Gy} (relative volume receiving $\geqslant$20 Gy) for the heart is reduced from 7.8% to 2.3% (−70%, $p < 0.0001$), V_{40Gy} from 3.4% to 0.3% (−91%, $p < 0.0001$) and mean dose from 5.2 to 2.7 Gy (−48%, $p < 0.0001$). Lung dose also shows a small reduction in V_{20Gy} ($p < 0.04$), while median target coverage is slightly improved ($p = 0.0002$).
Conclusions: In a large series of clinical patients we find that implementation of DIBH in daily clinical practice results in reduced irradiation of heart and lung, without compromising target coverage.
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Post-operative radiotherapy (RT) for breast cancer patients has been shown to significantly reduce the risk of local recurrence as well as improving long term survival [1,2]. However, irradiating the mammary tissue also causes the ipsi-lateral lung and, in many cases, the heart to receive a non-negligible dose. Convincing evidence of an increased risk of cardiac morbidity following irradiation for left-sided breast cancer exists [3–5], and the use of potentially cardiotoxic chemotherapy may increase this risk [3,6]. The use of modern RT techniques, mainly CT-based conformal, tangential treatment plans, has substantially decreased the incidental irradiation of the heart; however, in anatomically unfavourable cases especially the anterior part of the heart may still receive a considerable dose [7].

As a consequence, a large effort has been made in recent years to develop techniques to reduce the dose to normal tissue (especially heart dose) for patients receiving post-operative RT for breast cancer. The search for an optimal technique which avoids irradiating the heart without compromising target coverage is thus still ongoing.

One method of reduction is deep inspiration breath hold (DIBH). In DIBH, the goal is to achieve the maximum separation of the target area and heart, and irradiation thus takes place only at or near maximum inspiration. This allows a high dose to be delivered to the chest wall and to the breast tissue, while reducing the high dose area of the heart. Several groups have reported a reduction of heart and lung dose when comparing DIBH, as well as other gating techniques, to free breathing [8–11] for smaller number of patients in both dose planning and clinical studies. The focus of those studies has been to quantify the sparing of the heart and lung, and only a single dose planning study [11] also reports details on planning target volume (PTV) coverage for 17 patients.

Following a pilot study, assisted DIBH was introduced in our department as part of the standard radiotherapy treatment for all left-sided breast cancer patients, with the aim of reducing dose to the heart without compromising target coverage. Here we present a retrospective study comparing the first 144 patients treated using DIBH to a control group of free-breathing (FB) patients. Using DIBH we find that group median values show a large reduction in heart dose as well as a reduction in lung dose, combined with a significant increase in PTV coverage.

Methods and materials

DIBH is part of the standard RT treatment for post-operative left-sided breast cancer patients in our department. It was introduced in two steps: from September 2010 for patients aged 60 years or less, and from February 2011 onwards DIBH has been the treatment of choice for all left-sided breast cancer patients.

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0167-8140/$ - see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.radonc.2012.10.016

The present study is based on a retrospective collection of dose volume histograms from the first 144 patients treated with DIBH in our clinic during the period from September 2010 to April 2011. Our standard of comparison consists of two groups: the right-sided and the left-sided breast cancer patients treated in our clinic between March and August 2010. The control groups were selected because the dose planning techniques and criteria were exactly the same as for the DIBH patients, the only difference being the FB planning CT scan. The left-sided control group was used for a direct comparison between the FB and DIBH patients regarding heart, lung and PTV dose. The right-sided control group was used as a reference for the achievable target coverage when heart dose was not a limiting factor.

Treatment plans were based on computed tomography (CT) scans acquired using a 'slow scan' of approximately 25–30 s and encompassing the entire thorax. Contouring of target volumes and organs at risk was performed by experienced oncologists and radiographers following the guidelines published by the Danish Breast Cancer Cooperative Group (DBCG) [12]. Clinical target volume (CTV) of the residual breast included all mammary tissues, as visualized on the CT scan; the contouring was aided by a copper thread placed along the palpated breast tissue prior to the CT scan. For mastectomies the copper thread was placed based on palpation of the contra-lateral breast. The medial border was defined by the edge of the sternum, the dorsal border along the facia of the pectoralis major or by the thoracic wall. PTV was generated by adding a 5 mm isotropic margin to the CTV, allowing for a 5 mm margin to the skin surface. The ipsilateral lung was contoured using a CT lung window. The contoured heart did not include the pericardium or the major vessels.

Patients were treated with 50 Gy in 25 fractions, 1 fraction per day. Planning was performed in Oncentra Masterplan® (Nucletron, an Elekta Company), using a collapsed cone algorithm for dose calculations. All dose plans were based on forward planned IMRT using tangential photon fields, with a combination of 6 and 18 MV beam energies. Plans were optimized for coverage of the PTV with 93–105% of the prescribed dose. For patients where this was indicated, the periclavicular lymph nodes, including the axillary level II and III nodes, were treated using modulated AP/PA fields. For the purpose of this study, however, only dose coverage of the breast CTV and PTV was considered. For right-sided patients the parasternal lymph nodes were included as target where indicated [12].

The relative volume of the lung exposed to $\geqslant$20 Gy (V_{20Gy}) was kept below 25% (35% for patients with periclavicular fields). V_{20Gy} and V_{40Gy} for the heart were kept below 10% and 5%, respectively, according to DBCG guidelines [12]. When necessary, PTV coverage was compromised to conform to normal tissue restrictions. Compromises were made with attention to the tumor bed, marked by surgical clips, to ensure full dose to the high risk quadrant [13].

All DIBH patients were scanned and treated in assisted DIBH using the Active Breathing Coordinator™ (Elekta Oncology System, Crawley, UK, [14]) (ABC) system. Patients underwent a 15–30 min training session prior to CT scanning. The breath hold limit was set to 80% of vital capacity. In order to complete the CT scan and the RT, the ability to maintain a breath hold of >20 s was required. Between 5 and 10 breath holds were needed to complete a single radiotherapy treatment. Based on our initial pilot study, the intra- and interfraction reproducibility of the positioning of the thoracic wall was found to be at least as good as for FB patients. This is in line with the results of other, more extensive studies [15].

Relevant dose metrics were extracted from individual dose plans. To evaluate target coverage, the relative volumes of the CTV and the PTV receiving at least 93% of the prescribed dose ($V_{93\%}$) were found. For the heart, relative V_{20Gy} and V_{40Gy} as well as mean heart dose (D_{mean}) were all calculated; for the ipsilateral lung V_{20Gy} was found. The resulting data were analyzed using standard statistical methods in NCSS (NCSS, LLC. Kaysville, Utah, USA). For each dose metric, median values and ranges were found for each of the three patient groups. Continuous group distributions were compared between groups using the non-parametric Mann–Whitney U test, categorical data using Fisher's exact test, and correlations were analyzed using the Spearman ρ-test. Two-tailed p-values below 0.05 were considered significant.

Results

Main characteristics of the three patient groups can be found in Table 1. In total, 319 patients were included in the analysis, of which 144 were DIBH patients. Left sided breast cancer patients unable to comply with the requirements for DIBH were noted, but not included in the analysis of dose plan metrics; details of this group (20 patients) can be found in Table 2. The two main causes for non-compliance were inability to use the mouthpiece of the ABC equipment and psychological reasons.

The three patient groups did not differ significantly except for median age and median lung volume. There was a small, but significant, correlation between age and breath hold volume ($p = 0.002$) for the DIBH patients, with a reduction of the breath hold volume by 69 mL for each 10 years of age. However, as seen in Fig. 1, the variations in breath hold volume at a given patient age were far larger than this trend. No correlation was found between breath hold volume and V_{20Gy} ($p = 0.5$), V_{40Gy} ($p = 0.6$) or D_{mean} ($p = 0.5$) for the heart or for V_{20Gy} for the lung ($p = 0.6$). Similarly, no correlation with age was found for these parameters.

Table 3 lists the main results of the comparisons of median values of dose metrics for the three patient groups. All evaluated dose metrics for the heart are significantly ($p < 0.0001$) reduced for DIBH patients compared to FB patients: V_{20Gy} is reduced from 7.8% to 2.3% (−70%, $p < 0.0001$), V_{40Gy} is reduced from 3.4% to 0.3% (−91%, $p < 0.0001$) and D_{mean} is reduced from 5.2 to 2.7 Gy (−48%, $p < 0.0001$). Median value of the dose metric for the lung (V_{20Gy}) also shows a smaller but statistically significant reduction. Median PTV $V_{93\%}$ coverage is improved for the DIBH group compared to the FB left-sided patients ($p = 0.0002$). With the use of DIBH median PTV coverage becomes similar to the coverage obtained for the right-sided breast cancer patients ($p = 0.8$).

The proportion of patients with PTV $V_{93\%} < 95\%$ was significantly lower in the DIBH group compared to the FB group (8/144 vs. 14/83, $p = 0.009$), while the proportion in the DIBH group did not differ significantly from the group of right-sided patients (8/144 vs. 2/94, $p = 0.3$).

The results for PTV coverage, heart dose and lung dose remained significant when analysing patients with breast conserving/non-breast conserving operation and periclavicular/no periclavicular irradiation separately (data not shown).

Discussion

The benefits of post-operative RT for breast cancer patients, in terms of reduced risk of recurrence, have been clearly demonstrated, but concurrent heart irradiation leads to an increased risk of heart disease. At the moment, the dose–response relationship for radiation-induced heart disease remains uncertain [3], and thus the best approach seems to be to avoid direct irradiation of the heart altogether [16]. This, on the other hand, will often lead to lower target coverage for left-sided patients [16] and may result in an increased risk of locoregional recurrence [17].

We have found that using DIBH for left-sided breast cancer patients allows for a significant reduction in heart and lung dose while maintaining – or even slightly improving – PTV coverage.