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SCIENTIFIC NOTE

Application of retrospective data analysis to clinical protocol design: can the potential benefits of breath-hold techniques for breast radiotherapy be assessed without testing on patients?

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Abstract

The advantages, in terms of heart dose sparing, resulting from using a breath-hold technique when treating supine left breast radiotherapy patients are widely accepted, and increasing numbers of radiotherapy departments are implementing breath-hold techniques. However, due to differences in patient setup and treatment planning protocols between radiotherapy departments, it is important to assess the benefits of using a breath-hold technique within each department, before or during implementation. This study investigated the use of retrospective analysis of past patient treatment plans, as a means to identify the potential for breath-hold techniques to benefit patients. In-house "Treatment and Dose Assessor" code was used to complete a bulk retrospective evaluation of dose-volume metrics for 708 supine and 13 prone breast and chest wall radiotherapy treatments, that were planned using the same clinical protocols, which did not utilise a breath hold technique. For supine patients, results showed statistically significant differences between heart doses from left and right breast treatment plans, in the absence of significant differences between lung doses from left and right breast treatment plans, confirming the potential benefit of using a breath-hold technique for supine left breast radiotherapy patients. Fewer than 1% of the right breast treatment plans showed heart doses high enough to suggest a possible benefit from using a breath-hold technique. Approximately 50% of the prone left breast treatment plans included very low heart doses without intervention, and may therefore have shown no noticeable dosimetric benefit from the use of a breath hold. This study demonstrated the extent of information that can be obtained using retrospective data analysis, before or instead of obtaining multiple CT images of patients and completing a process of dual planning and prospective dose evaluation.

Keywords Radiation therapy · Treatment planning · Dosimetry · Breast cancer

Introduction

Radiotherapy is an effective component of the breast cancer treatment process, capable of decreasing 10 year recurrence rates by approximately 50% compared to surgery alone [1] and significantly reducing breast cancer mortality [1, 2]. Despite this success, concerns about organ at risk (OAR) doses and development of methods to reduce OAR doses remain a focus of breast radiotherapy research [3–7]. In particular, the position of the heart directly posterior to the chest wall on the left side, where the pericardium can be partially irradiated by tangent beams during radiotherapy treatments of the left breast, negatively affecting long-term cardiac outcomes [8, 9], has led to the development of breath-hold techniques that effectively move the heart away from the chest wall and reduce the heart dose [10–14].

Preliminary aspects of this work were presented at the International Conference of Computers in Radiotherapy, London, 2016 and the Engineering and Physical Sciences in Medicine conference, Sydney, 2016. A selection of final results of this work were presented at the IUPESM World Congress on Medical Physics and Biomedical Engineering, Prague, 2018.

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A growing number of clinical radiotherapy departments are implementing breath-hold and respiratory monitoring techniques, when treating patients with left breast cancer [14–17]. Often, this implementation involves prospective dual planning of a cohort of left breast radiotherapy patients, using two computed tomography (CT) images of each patient; one free or shallow breathing CT and one breath-hold CT [10–12, 18–20]. This dual planning assessment, which may be completed before or during breath-hold implementation, provides each local department with an indication of the effectiveness of the intervention, for their particular treatment setup, planning protocol and patient features. The use of dual planning also provides the department with indications of the suitability of their chosen breath-hold, respiratory monitoring and/or bio-feedback systems, in terms of accuracy, consistency, patient comfort and patient compliance.

Local assessments of the relative advantages of using breath-hold techniques during breast radiotherapy are necessitated by the costs (time, equipment and patient discomfort) associated with different techniques [6, 13, 20], which may be offset by the benefits of the treatment (heart dose minimisation, long-term patient health) to varying degrees, depending on local factors.

The achievable organ-at-risk (OAR) sparing during breast radiotherapy can vary between radiotherapy departments, depending on the specific patient setup and treatment planning protocols used [5, 6, 21–23]. For example, for breast radiotherapy patients treated in the prone position, a consistent rotation (roll) around the craniocaudal axis can improve sparing of the contralateral breast, but this requires a modification of the conventional breast board design [21]. For supine patients, a change in treatment planning method from manually optimised forward-planned (field-in-field) intensity modulated radiotherapy (IMRT) using tangent beams to multi-field, inverse-planned IMRT can result in an increase in mean heart dose and mean contralateral breast dose [22], wheras the use of inverse-planning to produce IMRT beams with a conventional tangent arrangement can result in reductions to some lung and heart dose metrics [5]. Even a subtle change in treatment planning protocol, such as systematically adding an extra 1 cm of multi-leaf collimator shielding over the region of the left anterior descending coronary artery, can substantially improve the sparing of cardiac structures, for some patients [6].

Such differences between departmental treatment setup and planning protocols mean that the relative benefits of introducing a substantial intervention such as a breath-hold technique need to be assessed locally, by individual radiotherapy departments. This study provides an example of the use of retrospective data analysis to assess the relative benefits of introducing a breath-hold technique during breast radiotherapy, without using dual planning or other methods to test the intervention on patients. Specifically, a retrospective analysis of treatments planned without breath-hold was undertaken in order to evaluate the need for improvement in cardiac sparing, for patients with cancer of the left or right breast who were treated in the prone or supine position.

This work does not obviate the need to test the suitability of breath-hold techniques and equipment prior to implementation, or the need to assess the ability of each patient to achieve a sufficient breath-hold after implementation. The techniques described in this work should, however, provide guidance for radiotherapy departments struggling with the initial question of whether or not a breath-hold technique or other intervention might be dosimetrically advantageous for their patient cohort. The overall method used in this work should also stand as a useful example for departments needing to investigate the potential dosimetric improvements that may arise from other proposed interventions, for treating other anatomical sites.

Method

The in-house "Treatment and Dose Assessor" (TADA) code [7, 24] was used to complete a bulk retrospective evaluation of dose-volume metrics for 1,137 breast and chest wall radiotherapy treatments planned across five treatment centres operated by one institution between 2013 and 2015. The resulting data were post-processed and filtered to exclude boost treatments and to ensure that only plans with structure names containing the text "ptv", "heart" and "lung" were included [25]. This process resulted in a cohort of 721 cases, for which the DICOM data exported from the treatment planning system contained the information needed to complete this study.

All treatments were planned to conform to the same clinical protocol, using forward-planned (field-in-field) IMRT beams in a conventional tangent arrangement [26, 27]. The planning protocol did not distinguish between left and right breasts. None of the treatment plans utilised a breath-hold technique. Other aspects of the treatment planning process, including planning target volume (PTV) contouring and OAR dose constraints, have been described in a previous retrospective study of 151 treatment plans from the same institution [7].

Of the 721 plans used in this study, 13 cases were identified as involving patients in the prone position, who generally had large breasts that would have fallen laterally to an extent that excessive lung doses would have been delivered if they had been treated supine. While this small proportion of prone patients (1.8% of the total) is similar to the proportion of prone treatments identified in a recent survey of European radiotherapy centres [15], the selection of prone patients within the cohort used for this study should not be regarded as indicative of the selection of prone patients in other radiotherapy departments. All of the prone patients identified in this study were treated by the same three oncologists, while the remaining 14 oncologists who prescribed breast treatments at this organisation [7] used supine positioning only, regardless of patient anatomy.

The 708 supine treatment plans were evaluated in bulk, using statistical techniques. The small number of prone cases allowed the results of the TADA analysis of the prone treatment plans to be qualitatively re-evaluated, on a case-by-case basis.

The TADA analysis of the treatment plans included evaluations of the dose delivered to specific volumes of heart and lung tissue, such as D(98) the dose delivered to 98% of the organ's volume (also known as the near-minimum dose), evaluations of the percentage volume of the heart or lung receiving specific doses, such as V(25) the percentage of the organ's volume receiving a dose of 25 Gy. V(25) was evaluated for the heart, in particular, due to the QUANTEC recommendation that no more than 10% of the heart should receive a dose of 25 Gy, to limit the risk of cardiac mortality 15 years after treatment to less than 1% [28, 29].

Results

Figure 1 summarises the lung doses planned for the prone and supine patients, with data stratified between left and right breast treatments. These results show no significant differences between the lung doses from the left and right breast treatments for patients positioned at each orientation, confirming the conclusion of our 151 patient study [7], that using a breath-hold technique for the left breast treatments would not result in an unacceptable increase in the lung dose.

Figure 2 summarises the results of the heart dose evaluation. There is an obvious difference between the heart doses

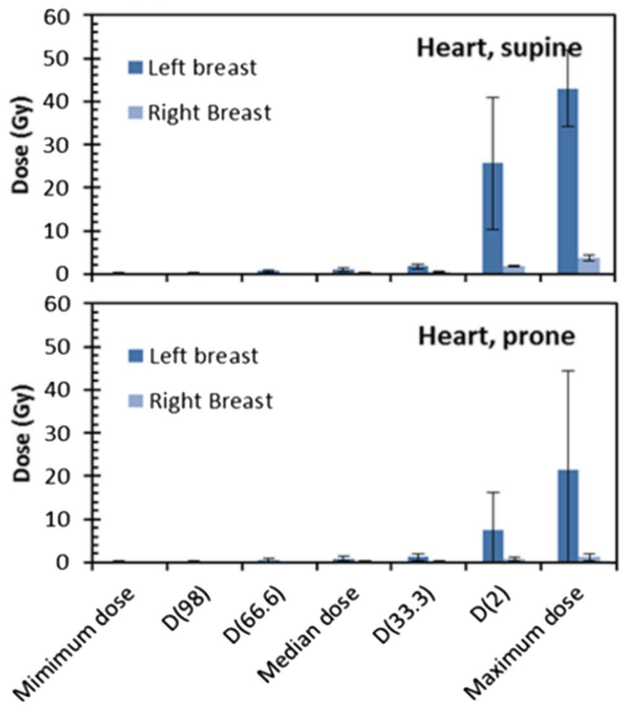

Fig. 2 Summary of clinically relevant heart dose-volume metrics

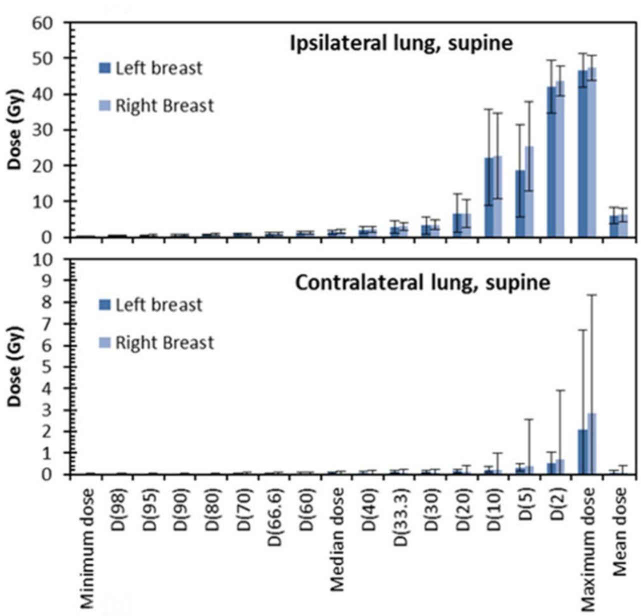

Fig. 1 Summary of clinically relevant lung dose-volume metrics

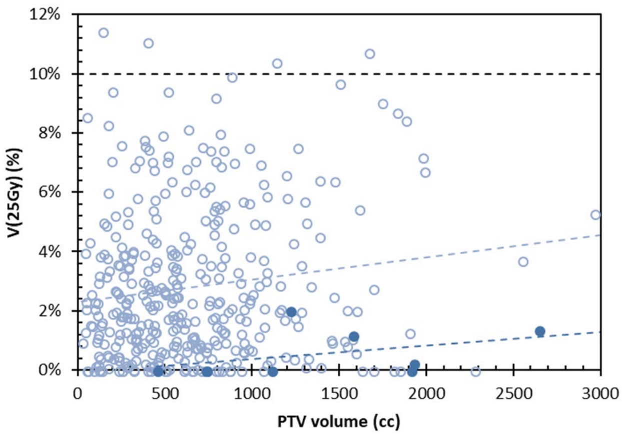

Fig. 3 Percentage volume of heart receiving a planned dose of 25 Gy, from all supine (open plot symbols) and prone (closed plot symbols) left breast treatments. Horizontal dotted line indicates V(25) = 10%. Diagonal dotted lines show linear fits to the data

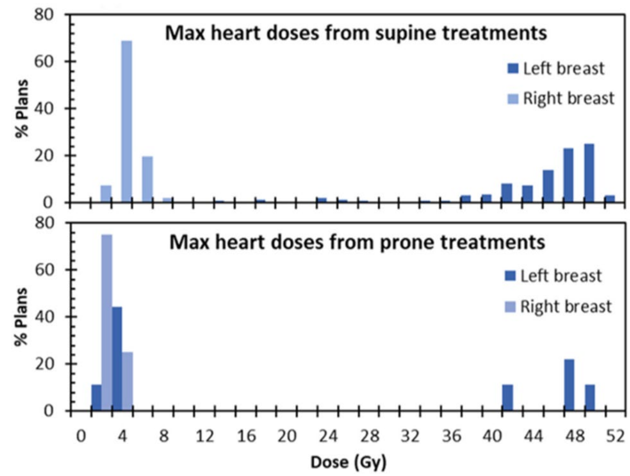

Fig. 4 Maximum heart doses in all prone treatment plans, presented as histograms

from the left and right breast treatments, for the supine patients, confirming the frequent observation that the heart receives substantially higher doses from radiotherapy treatments of supine left breast patients than supine right breast patients, due to anatomical asymmetry [7–11, 13]. For prone treatments, the results in Fig. 2 are more equivocal.

Figure 3 shows V(25) for the heart, the percentage of the heart volume receiving a dose of 25 Gy, in all left breast treatment plans. (In the right breast treatment plans, the heart V(25) was equal to zero for more than 99% of the supine cases and 100% of the prone cases.) Data in Fig. 3 show that the QUANTEC recommended heart dose limit of V(25) ≤ 10% [28, 29] is exceeded in none of the prone left breast cases and a small proportion of supine left breast cases. A fit to the data for the supine cases suggests that the volume of heart receiving 25 Gy generally increases with the PTV volume, but this trend is not statistically significant. For the prone cases, there is a change from zero to non-zero values of V(25) as the PTV volume increases above 1200 cc.

The bimodal distribution of heart doses from the prone left breast cases is especially apparent when the maximum heart doses are examined. Figure 4 shows the maximum heart doses from all treatment plans, plotted as histograms. Whereas the maximum heart doses from all right breast treatment plans are consistently low and the maximum heart doses from the supine left breast treatment plans are consistently high (skewed towards the 50 Gy prescription dose), the maximum heart doses from the prone left breast treatment plans are split between low and high. In some cases the maximum heart doses from the prone left breast treatment plans are as low as the maximum heart doses from the right breast treatments, but in other cases the maximum heart doses from the prone left breast treatment plans are close to the 50 Gy prescription dose.

Qualitative re-evaluation of the prone left breast plans provided an explanation for the distribution of the heart doses from these treatments, as shown in Fig. 5. Substantial cardiac sparing was achievable for the prone left breast radiotherapy patients when the PTV was designed to cover breast tissue only. In cases where the chest wall needed to be included and the PTV was extended posteriorly, partial irradiation of the heart became geometrically unavoidable.

Discussion

The consistently low heart doses resulting from the treatments planned for the right breast suggest that heart dose minimisation strategies are likely to be useful for a very small proportion (around 1%) of right breast treatments. Examination of the 3 (out of 361) right breast plans that included heart doses greater than 20 Gy and non-zero heart V(25) values suggested that the partial irradiation of the heart resulted from internal anatomical features (size and location of heart relative to PTV) that could not have been predicted before treatment simulation and planning. While breath-hold techniques may be useful during right breast radiotherapy treatments, to reduce dose to the liver [18] and minimise the dosimetric effects of respiratory motion [19, 30, 31], the results of this study do not support the use of breath-holds to minimise heart dose from right breast radiotherapy, for the cases, setups and planning protocols that produced the data examined in this study.

For supine patients, presence of statistically significant differences between heart doses from left and right breast treatment plans (Fig. 2), in the absence of significant differences between lung doses from left and right breast treatment plans (Fig. 1), confirms the results of our previous

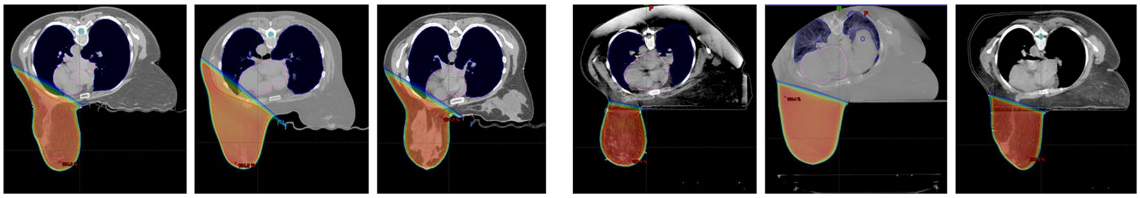

Fig. 5 Examples of planned dose distributions for prone left breast treatments where (left three images) the chest wall is included in the target and (right three images) the chest wall is excluded from the planning target volume and heart tissue is spared

study of 151 cases [7]. The use of breath-hold techniques during left breast radiotherapy treatments, to increase the volume of lung tissue between the heart and the chest wall, and thereby make the irradiated anatomy more similar to that encountered in right breast radiotherapy treatments, could have resulted in increased heart sparing without excessive lung dose, for the cases examined in this study.

The results for the prone patients are more equivocal, but also confirm previous observations [32]. The bimodal distribution of heart dose identified in the treatment plans for prone breast radiotherapy (Fig. 4) is an obvious consequence of the treatment fields overlapping the heart in some cases but not in others, and is similar to the bimodal distribution that can occur in supine left breast treatments with breath-hold, where the heart may move entirely out of the field in some cases but not others. Chino and Marks have reported that "prone positioning causes the heart to be displaced anteriorly within the thorax", with a reduced volume of lung between the heart and the chest wall, so that cardiac sparing may compromise coverage of chest wall or posterior breast tissue [32]. Our retrospective analysis of prone left breast radiotherapy treatment plans supports Chino and Marks' observation, showing that substantial cardiac sparing was achievable for prone left breast radiotherapy patients only when the chest wall was not included in the target (see Figs. 4 and 5).

The use of breath holds during breast radiotherapy treatments of patients in the prone position has produced promising results [12]. However, the adoption of a breath hold technique has associated costs [13, 20] and these costs may be increased when breath hold is used in the prone position (prone treatments generally take longer to set up than supine treatments and commercial biofeedback systems are generally designed for use by supine patients [14]). For the prone positioning method and treatment planning protocol that was used to create the treatment plans examined in this study, it is therefore useful to know that adopting a cardiac sparing intervention may be clinically beneficial only in cases where no nodal or chest wall irradiation is prescribed. Furthermore, while the results of this study may justify further investigation of the use of a breath-hold technique when treating prone left breast patients for the institution concerned, this result also suggests that an alternative treatment position (prone with a roll around the cranio-caudal axis, supine with a breath hold, supine with an alternative treatment technique such as volumetric modulated arc therapy, et cetera) may also provide improved cardiac sparing for patients where the left chest wall is included in the target volume.

The above observations may not be generalisable for use by radiotherapy departments that are treating breast radiotherapy cases using different setups and planning protocols than those that produced the data examined in this study. For example, departments that routinely use wide tangent fields for nodal irradiation may observe elevated heart doses from supine right breast treatments that might justify investigation or adoption of a breath-hold technique for right breast patients. The use of different methods or devices for positioning prone patients may have substantial effects on local results and the broad applicability of these results is also limited by the small number of prone cases and the particular patient selection methods used by the doctors involved.

Clearly, there are important aspects of breath hold use that cannot be evaluated via a retrospective evaluation of heart dose in patients treated without a breath hold. This study provides no information on patient compliance or comfort when using the chosen breath hold system, or on the ability of different patients in different positions to hold their breath; these variables can only be assessed through use of the intervention during patient simulation and treatment. Ideally, the analysis described in this study should be followed by a period of patient testing and dual planning, so that the potential improvements in heart dose sparing implied by the retrospective analysis could be evaluated in terms of clinically achievability. Nonetheless, this study provides a demonstration of the level of information that can be obtained using retrospective data analysis, before commencing a process of obtaining multiple CT images of patients for dual planning and prospective dose evaluation.

Conclusions

Due to differences in patient setup and treatment planning protocols between radiotherapy departments, it is important to assess the benefits of using a breath-hold technique during breast radiotherapy treatments within each department, before or during implementation. This study provides an example of the use of retrospective clinical data analysis to investigate the potential for dosimetric improvements, for a cohort of 721 breast radiotherapy cases, and shows that heart dose sparing in these treatment plans varies with patient setup and treated anatomy such that the use of a breath-hold technique (a) is likely to benefit supine left breast patients, (b) may benefit some prone left breast patients, and (c) is likely to have a negligible overall benefit for right breast patients.

Departments considering the implementation of a breath-hold technique (or other heart dose sparing intervention) for use during breast radiotherapy could use a similar process of retrospective data analysis of treatments planned without a breath hold to answer questions such as: What levels of heart dose are our breast radiotherapy patients currently receiving? Under what circumstances (treatment site, patient setup, et cetera) are heart doses already low enough to be acceptable without intervention? Under what circumstances are heart doses high enough to justify intervention, given local constraints? Are there any patient cohorts for whom breath-hold should be implemented immediately, without further testing? Are there any patient cohorts for whom breath-hold should be implemented before/after a period of patient testing via dual planning?

For cohorts where the heart dose is found to be minimal without the intervention, the need for adoption or further evaluation of the intervention may be obviated, whereas for patient cohorts where excessive or undesirable heart doses are identified, the results of this analysis can be used to justify the adoption or further evaluation of the intervention.

This study used heart dose from breast radiotherapy to provide an example of how local treatment planning data can be retrospectively analysed to assess the possible benefits of a proposed change in treatment practice, before the change is introduced or abandoned. Completion of such a process of evaluating existing treatment plans should provide valuable clinical and administrative data, and thereby help to minimise the need to test new interventions on future patients.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval Low-risk ethics approval for retrospective analysis of de-identified patient data was obtained from the Genesis Cancer Care Queensland Research Committee.

Human or animals participants Otherwise, this article does not contain any studies with human participants or animals performed by any of the authors.

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