A simple clinical method for predicting the benefit of prone vs. supine positioning in reducing heart exposure during left breast radiotherapy

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Radiotherapy is an essential component of the management of early breast cancer. The outcome in most cases is favorable, the majority of the affected patients become long survivors. Breast radiotherapy, however, may increase the risk of non-breast cancer-related morbidity, among which heart diseases rank the first [1,2]. Radiation-induced heart damage clearly depends on the operation of a validated model for the prediction of preferable treatment position during left breast radiotherapy. The benefit of reduced radiation heart exposure in the prone vs. supine position individually differs. In this prospective cohort study, the goal was to develop a simple method for the operation of a validated model for the prediction of preferable treatment position during left breast radiotherapy. Material and methods: In 100 cases, a single CT slice was utilized for the collection of the needed patient-specific data (in addition to body mass index, the distance of the LAD from the chest wall and the area of the heart included in the radiation fields at the middle of the heart in the supine position). Outcome was analyzed in relation to the full CT series acquired in both positions and dosimetric data.

Results: Great consistency was found between the tested and original method regarding sensitivity and specificity. The prioritization of LAD dose, and the use of heart dose and position-specific dose constraints as safety measures ensure sensitivity and specificity values of 82.8% and 87.3%, respectively. In an additional "routine clinical practice" series of 60 patients the new method seemed feasible in routine clinical practice. External testing on a 28-case series indicated similar accuracy.

Conclusion: We consider this simple clinical tool appropriate for assisting individual positioning aiming at maximum heart protection during left breast irradiation.

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Prone positioning was first invented for the irradiation of large-breasted women [23,24]. Indeed, since gravity pulls the breast away from the chest wall, the geometry of a pendulous breast and the tangential irradiation fields gets advantageous in the prone position [12]. Taking the overall population of breast cancer patients, however, prone positioning has such effect in 77–87% of cases only [11,14,15,19]. As a consequence, the position-dependent dose to the LAD or heart also individually differs [11,19,20]. Different approaches exist for selecting the optimal position in left breast cancer cases. Kirby et al. found that a PTV [11,19,20]. As a consequence, the position-dependent dose to the LAD or heart also individually differs [11,19,20]. Different approaches exist for selecting the optimal position in left breast cancer cases. Kirby et al. found that a PTV > 1000 cm³ favors prone positioning [11]. Zhao et al. developed a two-step decision-analysis algorithm that, based on the anatomical features detected on a prone CT series, classified patients prone to radiotherapy or to a second CT in the supine position for comparison [25]. We have demonstrated that a statistical model utilizing 3 anatomical determinants (the body mass index [BMI], the distance of the LAD from the chest wall and the area of the heart included in the radiation fields at the middle of the heart in the supine position) of the patient gives accurate estimates on the benefit of one specific position over the other by means of LAD or heart doses [19]. Here we report on an original method for providing the necessary patient-specific data based on a single CT slice image representing the middle of the heart. In this prospective study, following the validation of the clinical tool, also its routine use has been tested on a separate series of cases.

Patients and methods

The study was approved by the Institutional Review Board of the University of Szeged, and all the enrolled patients gave their written informed consent to participation. Eligible patients needed postoperative left breast radiotherapy.

Outline of the study

First, a single CT slice image at the middle of the heart (reference plane, $P_{ref}$) was acquired with the help of an AP scout view in the supine position (Fig. 1A). On that CT scan, the shortest distance between the anterior surface of the LAD and the chest wall ($D_{med}$) and the area of the heart ($A_{heart}$) included in the radiation fields were measured after placing a straight line between the border of the ipsilateral latissimus dorsi muscle and the lateral edge of the sternum (Fig. 1B); these data (representing the topography of the heart) were introduced to the calculator together with the patient’s BMI (which correlated with the volumes of the breast and heart) as previously described in detail [19]. The calculator based on a validated statistical model provided the estimated LAD and heart dose differences in the prone vs. supine position of the individual patient. In the first validation set of 100 patients, CT series were acquired in both the supine position and prone position. Conformal radiation treatment plans were generated in both positions using conventional 6 MV tangential photon fields set up isocentrically and median 2 (1–3) individually weighted 6/15 MV segmental fields superimposed on the tangential fields using a multileaf collimator as described [18,19]. Wedges were used in almost all supine radiation plans. A mean dose to the PTV of 50 Gy (25 fractions) and a uniform distribution (−5% +7%) of the prescribed dose to 95% of the PTV, were aimed at. The consistency of all contouring activities had been ensured by a chief radiation oncologist (ZK) and an experienced radiologist (AC) [26]. Equivalent heart and LAD volume contouring in either setup was ensured by one author (ZK). In the next “routine clinical practice” set of 60 patients, the acquisition of a single series of CT images according to the suggestion of the calculator was aimed at, and a second CT series was taken only if any of the dose constraints approved for the specific position were not reached in the position suggested by the calculator. In this series of patients’ dose constraints were specified on the basis of previously recorded data. The upper range limits of the 90% percentile of dosimetry data in the preferred position were the following: mean LAD dose [$MD_{LAD}$]: 12.9 Gy and 12.5 Gy, $V_{25Gy,heart}$: 2.4% and 4.7%, in the prone position and supine position, respectively. In true discordant cases, our strategy for selecting treatment position was to consider the LAD dose as a primary decisive factor.

In the validation set, data on LAD and heart dose differences between the two treatment positions were extracted from the planning system and estimated by the calculator, whereas in the “routine clinical practice” series only the estimated dose differences were available. Analyses were performed on 1. the equivalence of the $P_{ref}$ with the median plane of the full series of CT scans acquired in the supine position ($P_{med}$) and 2. the effect of plane miss on the patient-related determinants and choice of preferable position. The sensitivity and specificity of this simple clinical method were evaluated based on the dosimetry data obtained using the topogram for selecting the position ($n = 100$). In the “routine clinical practice” series, the acceptability of the position as predicted by the calculator, the LAD and heart doses achieved without taking 2 CT series, and the need of performing a second CT series and changing position or irradiation technique were analyzed.

External testing

The supine and prone CT series and supine topogram of patients included in the study “Individualized positioning for maximum heart and index breast protection during breast irradiation: comparative study between Prone and Supine (Approval: 26/09/2013, B707201318246) were retrospectively used for independent testing. The protocol of patient positioning, delineation and radiation treatment planning has been described [27].

First, $P_{ref}$ was selected on the topogram. Then, the predictors $BMI, D_{med}, A_{heart}$ as measured in $P_{ref}$ were introduced to the calculator. As a second step, $D_{med}, A_{heart}$ were also measured in $P_{med}$, LAD and heart dose differences between the two treatment positions extracted from the planning system and estimated by the calculator were analyzed. Finally, the correctness of $P_{ref}$ was evaluated.

Statistical methods

The calculator had been developed based on linear regression models utilizing the patients’ anatomical features, with $\Delta MD_{LAD}$ and $\Delta V_{25Gy,heart}$ as dependent variables [19]. With a single cut-off point, a case was classified to prone positioning when the predicted value exceeded that value. Thresholds were optimized based on sensitivity and specificity as calculated from previous
Next, the concordance of calculator-predicted treatment position based on $\Delta D_{\text{LAD}}$ vs. $\Delta V_{25Gy,\text{heart}}$ and the need for intervention were analyzed in the validation set. In 28 supine-predicted cases and 64 prone-predicted cases, the same treatment position was suggested by both methods (Table 3). Among the 28 supine-predicted cases in 2, the radiotherapy plan revealed that $D_{\text{LAD}}$ exceeded the dose constraint of 12.9 Gy; only 1 could be improved by changing the treatment position. Among the 64 prone-predicted cases in 8, the $D_{\text{LAD}}$ exceeded the dose constraint of 12.9 Gy; only 3 plans could be improved by applying the supine position. Among the discordant cases, $\Delta D_{\text{LAD}}$ suggested prone position in 3 and supine position in 5 cases; in both groups in a single case each could the LAD dose be improved by changing the treatment position. In altogether 7 cases, a different intervention (IMRT) had to be applied (Table 3).

"Routine clinical practice" set

In the “routine clinical practice” series of 60 patients, the new method proved feasible. All patients received treatment in the position suggested by the calculator except one, who had to receive a second CT in the other position due to unacceptable LAD dose. The other patients had $D_{\text{LAD}}$ and $V_{25Gy,\text{heart}}$ values well below the predefined dose limits, and these were similar to the values calculated in the validation set (Table 4).

### External testing

In a series of 28 breast cancer patients from Liege, the predictors BMI, $D_{\text{med}}$ and $A_{\text{heart}}$ significantly differed from the same parameters among the patients from Szeged. In 18/28 cases, $P_{\text{ref}}$ was equal or close to $P_{\text{med}}$ ($\leq 6$ mm), while in 10, cases $P_{\text{ref}}$ varied from $P_{\text{med}}$ by 9–16 mm. Comparing the calculator-provided dose differences with the treatment planning data, favorable treatment position was correct in 24/28 (accuracy: 85.7%) and 23/28 (accuracy: 82.1%) cases taking into account the LAD and heart doses.
respectively. Sensitivity and specificity of $D_{MDLAD}$ was 83.3% and 86.4%, respectively, whereas sensitivity and specificity of $D_{V25Gyheart}$ was 100.0% and 80.0%, respectively.

**Discussion**

According to the present study and others [11,14,15,19,20], in about 20% of the cases, prone positioning during left breast radiotherapy increases the dose to the LAD or the heart. To estimate and select the preferable positioning mode, supine CT seems the best approach to consider the patient’s anatomical determinants. We have shown that a single CT scan at the middle of the heart may replace a whole CT series by providing consistent anatomical data thus avoiding extra radiation exposure to the patient and work load to the staff. Based on the outcome of the external implementation of the method on an independent case series, we recommend its use after local testing.

Table 3

<table>
<thead>
<tr>
<th>$\Delta V_{25Gyheart}$</th>
<th>Supine</th>
<th>Prone</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>$MD_{LAD} &gt; 12.5$ Gy</td>
<td>Change position</td>
</tr>
<tr>
<td>Supine</td>
<td>28</td>
<td>2</td>
</tr>
<tr>
<td>Prone</td>
<td>3</td>
<td>2/3</td>
</tr>
</tbody>
</table>

Table 4

<table>
<thead>
<tr>
<th>Treatment position</th>
<th>$n$ (%)</th>
<th>Mean LAD dose (Gy)</th>
<th>$V_{25Gyheart}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation series</td>
<td>Prone</td>
<td>67 (67.0)</td>
<td>6.55</td>
</tr>
<tr>
<td>Supine</td>
<td>33 (33.0)</td>
<td>6.90</td>
<td>3.86</td>
</tr>
<tr>
<td>“Routine clinical practice” series</td>
<td>Prone</td>
<td>47 (78.3)</td>
<td>6.58</td>
</tr>
<tr>
<td>Supine</td>
<td>13 (21.7)</td>
<td>7.35</td>
<td>3.05</td>
</tr>
</tbody>
</table>
Our validated statistical model for predicting the preferable treatment position utilizes 3 specific measures, and seems the most complex predictive tool for this purpose in the literature [19]. In other studies, the in-field heart volume [16,17,25] and most frequently the size of the breast [4,11] have been used for selection. An increased BMI has also been related to larger heart doses [28] or consequential radiation cardiac morbidity [29], but its role in predicting benefit of prone positioning may be refined by the use of other patient-related parameters [19]. We consider the BMI in our calculator as a stable parameter while there is potential uncertainty in the specification of $P_{tr}$ or imprecision in the actual measurement of $D_{median}$ or $A_{heart}$ on a given image. Nevertheless, detailed analysis indicates that accidental imprecision does not significantly influence final prediction (data not shown).

The dose constraints optimized by individual positioning provides additional safety in practice. Despite the lack of full equivalence of the data extracted from the original method vs. the new method, the ultimate consistency still seems to qualify the developed “simple tool” for clinical application.

External use indicated similar accuracy as the originally developed method. Despite the reassuring results on an independent series of patients in a radiotherapy center using a slightly different protocol, the utility of the reported clinical tool could be compromised by the diversity of practice in others. PTV contouring depends on repositioning accuracy and the method of treatment verification. Interfractional differences may be especially large in the prone position [18,30]. Lakosi et al. found population systematic error values of 4.5/3.9/3.3 mm in the lateral/longitudinal/vertical directions, while the random error was 5.4/3.8/2.8 mm [27]. Among our recent breast radiotherapy cases, the population systematic and random error in the lateral/longitudinal/vertical directions was similar in the prone position vs. supine position (3.4/2.3/2.7 mm and 7.8/4.6/6.9 mm, respectively vs. 2.2/3.0/1.6 mm and 6.7/5.5/4.5 mm, respectively). Only some groups study the dose to the coronary arteries [11,12,19,20,31–34]. The outlining of the coronary vessels shows significant inter-observer variation that may jeopardize dose verification in the selected position [35,36]. Different approaches have been tested to improve consistency including the administration of contrast media [35–37]. Lee et al. developed a new protocol to outline the LAD region which included 96% of the LAD volume as delineated by 4 experienced radiation oncologists [37]. Significant impact was made by the implementation of specific guidelines [35–37]. Since the utility of the simple tool might be influenced by several factors, in addition to the use of institutional LAD contouring guidelines and study of inter-observer variation, we consider essential its testing before routine use. In the case of hypofractionated radiotherapy, the model parameters of the calculator should be re-estimated and the dose constraints should be re-defined.

The benefit of positioning prone vs. supine may be discordant by means of LAD and heart doses [11,19,34]. We regard the LAD dose as a surrogate indicator of radiation harm due to its proven role in late cardiac morbidity [3] and because the LAD being situated on the anterior surface of the heart is a sensitive marker of danger if the heart is at all included into radiation. Our strategy for optimization in individual cases is to consider the MD$_{LAD}$ as priority that is usually confirmed by the heart dose (as was true for 92% of cases in our series).

The radiation exposure of the heart may be significantly reduced by the use of respiration-guided techniques including the deep inspiration breath hold (DIBH) technique and respiratory gating. In the UK HeartSpare study, supine DIBH provided superior cardiac sparing than a free-breathing prone position in large-breasted women [12]. Interestingly, the implementation of DIBH in the prone position gave the optimal heart sparing results as compared with that in the supine position or free-breathing [33]. There are some centers that due to resource limitations prioritize high cardiac dose cases for DIBH [38]. Our tool could be used for patients either not amenable for or not having access to DIBH due to patient-specific features (cardiorespiratory problems, lack of compliance) or limited/no resources, respectively.

We think that since a linear, no-threshold association exists between the mean heart dose and coronary events [3], doses to the LAD, right coronary artery or the circumflex artery should be controlled [20]. Nevertheless, the utilization of heart dose–volume data only is a possibility if LAD contouring cannot be afforded. Since good agreement exists between the mean heart dose and $V_{50}^{S()}$ (R prone: 0.98, R supine: 0.99) or MD$_{LAD}$ (R prone and supine: 0.87) in both positions ($p < 0.001$ in all comparisons), here the presented tool could be adapted to practices which adhere to the consideration of the mean heart dose.

In summary, we have demonstrated great consistency of our method based on a validated model for the prediction of treatment position prone vs. supine with less heart exposure during left breast radiotherapy; the simplified tool presented here omits the performance of planning CT in both positions. Based on the results of its external testing, we truly recommend its use in centers that apply prone positioning in routine clinical practice. Due to differences in populations and radiotherapy protocols, local testing is essential.

**Conclusion**

We consider this simple clinical tool useful for assisting individual positioning in routine clinical practice aiming at maximum heart protection during left breast irradiation.

**Conflict of interest**

None declared.

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**References**


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Predictive tool for positioning


