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Original article

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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ABSTRACT

Background and purpose: 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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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 morbidities, among which heart diseases rank the first [1,2]. Radiation-induced heart damage clearly depends on the dose exposed to its different structures (3,4). While older radiotherapy practices caused more significant late hazards, heightened awareness and the use of current technical developments make this danger much lower [1,4,5]. Although the application of modern radiotherapy planning and delivery significantly improves the control of radiation dose, in many cases a part of the heart, and especially the left anterior descending artery (LAD) located to its anterior surface still receive a dose sufficient to cause long-term adverse effects. Radiogenic diffuse myocardium damage including microvasculature abnormalities, degenerative cardiomyocyte and interstitial fibrotic changes may be controlled if not extensive, but the damage of the macrovasculature indistinguishable from coronary arteriosclerosis due to other causes more likely lead to a fatal outcome [3,6–8]. The exposure of the heart and the LAD are related [9–11], and irradiation-related cardiac morbidity and mortality are considered to be consequences of late manifesting coronary artery damage. Hence the verification and control of the dose to the LAD, is of prime importance [8,9,11,12].

With the aim of cardiac dose sparing and avoidance, numerous new methods have been developed [4,5]. These include the breath-holding techniques, prone positioning (both operate by separating the heart and the radiation fields), IMRT, proton irradiation or the reduction in the volume to be irradiated, partial breast irradiation (PBI). A significant increase in the number of clinical studies [11–20], and a recent survey on clinical practice [21] suggest that prone positioning has become an alternative of conventional supine positioning in some centers. Prone positioning always provides dramatic reduction in the ipsilateral lung dose, and in many cases significantly reduces heart exposure, too. A potential disadvantage is inferior repositioning accuracy, which may be improved with experience [18] or may be compensated by online daily correction [12,22].

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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 > 1000 cm^3 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 to prone 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, $V_{25Gyheart}$: 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.

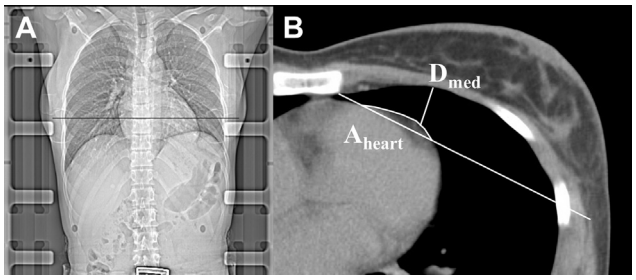

Fig. 1. The simple clinical tool generates patient-specific data to predict the benefit of prone positioning. After selecting the reference plane (P_{ref}) at the middle of the heart on the AP scout view (A), a single CT slice is acquired for the measurement of those determinants (D_{med} and A_{heart}) (B) which operate the calculator to provide estimates of the doses to the LAD or heart.

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 ΔMD_{LAD} and $\Delta V_{25Gyheart}$ 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

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