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Breast cancer

Evaluation of organ-specific peripheral doses after 2-dimensional, 3-dimensional and hybrid intensity modulated radiation therapy for breast cancer based on Monte Carlo and convolution/superposition algorithms: Implications for secondary cancer risk assessment

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Background and purpose: To make a comprehensive evaluation of organ-specific out-of-field doses using Monte Carlo (MC) simulations for different breast cancer irradiation techniques and to compare results with a commercial treatment planning system (TPS).

Materials and methods: Three breast radiotherapy techniques using 6MV tangential photon beams were compared: (a) 2DRT (open rectangular fields), (b) 3DCRT (conformal wedged fields), and (c) hybrid IMRT (open conformal + modulated fields). Over 35 organs were contoured in a whole-body CT scan and organ-specific dose distributions were determined with MC and the TPS.

Results: Large differences in out-of-field doses were observed between MC and TPS calculations, even for organs close to the target volume such as the heart, the lungs and the contralateral breast (up to 70% difference). MC simulations showed that a large fraction of the out-of-field dose comes from the out-of-field head scatter fluence (>40%) which is not adequately modeled by the TPS. Based on MC simulations, the 3DCRT technique using external wedges yielded significantly higher doses (up to a factor 4–5 in the pelvis) than the 2DRT and the hybrid IMRT techniques which yielded similar out-of-field doses.

Conclusions: In sharp contrast to popular belief, the IMRT technique investigated here does not increase the out-of-field dose compared to conventional techniques and may offer the most optimal plan. The 3D-CRT technique with external wedges yields the largest out-of-field doses. For accurate out-of-field dose assessment, a commercial TPS should not be used, even for organs near the target volume (contralateral breast, lungs, heart).

Radiation therapy for breast cancer has proven to be an effective treatment to reduce recurrence risk and long-term breast cancer mortality after both breast-conserving surgery and mastectomy [1]. Radiation is however associated with some late adverse effects for long-term survivors of breast cancer [2–4]. Intensity modulated radiation therapy (IMRT) has been shown to improve the dose distribution compared to conventional techniques [5–31] and resulted into a reduction of acute and late deterministic effects in randomized control trials [32–34]. In addition to all the late deterministic effects, breast cancer patients undergoing radiotherapy are also at an increased risk of developing another primary cancer, commonly called "secondary cancer" [35–38]. In sharp contrast to deterministic effects, there is no known dose threshold for cancer induction [39]. In order to assess secondary cancer risk, organ-specific doses need to be determined for both in-field organs as well as remote out-of-field organs which may still receive a considerable amount of radiation through both patient and linac scatter. The widespread use of IMRT has led to concerns regarding secondary cancer risk due to an increased peripheral dose compared to conventional techniques [40]. It is difficult to use epidemiological studies to estimate secondary cancer risk since available data reflect obsolete treatment techniques from 20–30 years ago.

Most studies comparing different treatment techniques with regard to peripheral doses to nearby healthy organs were either based on treatment planning system (TPS) calculations [8,20,23,25,27,28,41] or punctual measurements [9,42–49]. Both approaches have their limitations: while the accuracy of the TPS is typically limited to a couple of centimeters outside the geometrical field edge [50–52], no dose–volume information can be derived from limited point measurements. Out-of-field dosimetry for more remote organs is limited to two recent studies using measurements for obsolete 2D breast radiotherapy techniques exclusively [38,53]. A more detailed and accurate dosimetry of healthy organs following breast radiotherapy is lacking. Since the

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dose-response relationship may be non-linear [54,55] with no known threshold at low doses [39], a sophisticated dose calculation algorithm is required to compute both inhomogeneous dose distribution for complex organ shapes and low doses for remote organs. Therefore Monte Carlo (MC) methods, which are recognized as the most accurate dose calculation algorithm for radiotherapy [56], were chosen for this study.

In this study out-of-field dosimetry for breast radiotherapy was performed for more than 35 organs in a realistic whole-body female phantom using MC methods. We had two objectives: first, we compared peripheral doses between techniques used in current practice such as conformal tangential fields with wedges (3DCRT) and hybrid IMRT combining open and modulated tangents with the older 2D technique using two open tangential beams for both breast and chest wall irradiation. Second, we compared the accuracy of the TPS with MC in the low dose region for healthy organs nearby the PTV based on mean dose and dose volume histogram (DVH) analysis.

Materials and methods

Patient selection

A whole-body CT scan of a breast cancer patient with right breast mastectomy was used for the dose calculation. As only one single patient was used for this study, it was important to assess to what degree this specific patient corresponds to an average female breast cancer patient. The patient weight and height (66 kg and 167 cm) were close to the median values of the female Caucasian population (65 kg and 163.8 cm) [57]. The breast separation (defined by the distance between the midsternal line and the mid-axillary line) was equal to 22.7 cm which is very close to the mean values reported by Lo et al. (22.9 cm) and Smith et al. (22.3 cm) based on 20 patients in each study [10,26]. The volume of the CTV was used as a surrogate of the breast volume. The volume of the intact breast of our patient was equal to 653 cc. The CTV volume from the last 30 breast cancer patients treated at our institution was on average equal to 640 cc (range: 182–1497 cc). In conclusion, the morphological parameters of the selected patient were representative of an average female breast cancer patient.

The CT scan was transferred to the VelocityAI version 2.6.2. delineation software (Velocity Medical Solutions, USA) for the organ delineation. Clinical and Planning target volumes (CTV and PTV) were drawn for both the chest wall and the intact breast and over 30 organs at risk were delineated (Fig. 1). Radio-opaque markers were used to define clinically the palpable breast and the chest wall using the contralateral breast to define the superior and inferior limits of the chest wall. The CTV were drawn using radio-opaque markers and the CT images. The CTV were posteriorly limited by the pectoralis muscle. The internal and external extensions of the chest wall CTV were set based on the images of the contralateral breast. The PTV were obtained by adding the following margins to the CTV accordingly with the usual clinical practice at our institution: +5 mm in the left and right direction, +10 mm in the inferior and superior direction, +3 mm in the posterior direction and 0 mm in the anterior direction.

Treatment planning system

All the planning was done using the TPS CMS XiO version 4.60 (Elekta, England). The extent of the calculation volume outside the geometric fields was set to its maximum possible value of 10 cm. Treatment plans were calculated for 6 MV beams of the Siemens Primus linac (Siemens, Germany). All final dose calculations of the treatment plans were done using the superposition algorithm with the calculation grid size set equal to the voxel size used for the MC calculations ($3 \times 3 \times 5$ mm^3).

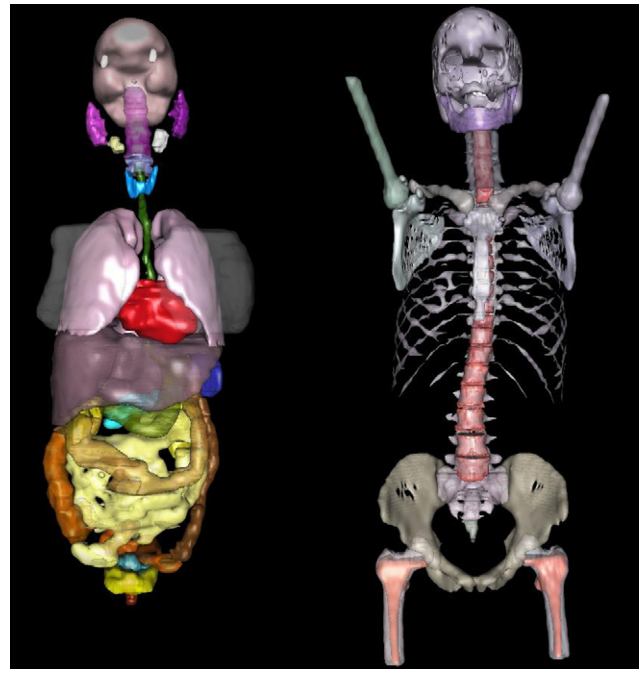

Fig. 1. All delineated organs on the slices of the whole-body CT dataset are represented above in three dimensions.

For both the right chest wall and the left breast, three plans were generated: a 2D plan with two tangential open half-beams, a 3DCRT plan with two wedged beams and a hybrid IMRT plan combining open and modulated tangents.

The 2D plans were created to be representative of the typical field setup used 20 years ago at our institution when no CT-based treatment planning was routinely used. Therefore, the treatment planning was done without using any of the information on internal volumes. Two opposing half-beam tangential fields using asymmetric jaws were setup at a source-skin distance of 100 cm. The borders of the field matched the midsternal line and mid-axillary line posteriorly, the bottom of the clavicular head superiorly and 2 cm below the inframammary fold inferiorly. The anterior borders of the fields were set to have at least a 1 cm air gap above the breast apex. 50 Gy in 25 fractions were delivered at the prescription point set at 1.5 cm from the posterior field border at midseparation.

Both 3DCRT and hybrid IMRT planning were done in isocentric conditions. For the 3DCRT, two wedged tangential beams were set up with the isocenter in the middle of the PTV and the posterior borders of the fields aligned. The wedge angle, the beam weights and the leaf openings were manually adjusted to optimize the target coverage and minimize the dose to the ipsilateral lung using the following parameters: the highest possible homogeneity index (HI) for the PTV (HI = $V_{95\%} - V_{107\%}$, where $V_{x\%}$ refers to the volume receiving more than x% of the prescribed dose), $V_{20Gy} < 15\%$ and $V_{30Gy} < 10\%$ for the ipsilateral lung (V_{xGy} refers to the volume receiving more than x Gy). For the right chest wall plan, the wedge angles for the medial and lateral fields were respectively 30° and 45°. For the left breast plan, wedge angles were set to 30° for both tangent beams. Before the final dose calculation, beams were reweighted in order to have a mean dose of 50 Gy to the PTV.

For the hybrid IMRT plans, the same tangent beams from the 3DCRT were used without wedges and beam weights were set in order to deliver 80% of the prescribed dose to the isocenter. Two additional tangent beams were modulated using the inverse