Journal of BUON **13:** 245-251, 2008
© 2008 *Zerbinis Medical Publications. Printed in Greece*

ORIGINAL ARTICLE

The use of computed tomography in radiotherapy treatment planning for breast cancer. How does conventional radiotherapy planning compare with virtual?

O. Bauduceau[1], M.A. Bollet[2], P. Pons[1], Y.M. Kirova[2], M. Fayolle[1], S. Zervoudis[3], F. Campana[2]

[1]Department of Radiation Oncology, du Val-de-Grace hospital, Paris, France; [2]Department of Radiation Oncology, Institut Curie, Paris, France; [3]Breast Department, "Lito" Private hospital, Athens, Greece

Summary

Purpose: *To compare, in terms of ballistics and dosimetry, a conventional and a virtual simulation in 14 patients without changing the set-up.*

Patients and methods: *14 women with breast cancer were treated with postoperative radiotherapy from October 2003 to November 2004. Whole breast irradiation alone was indicated (50 Gy at International Committee on Radiation Units [ICRU] point in 25 fractions over 5 weeks) with, in some cases, an additional boost of 16 Gy to the tumor bed – that was not taken into account in this study. After CT scan, tangential fields were conventionally simulated using a Mecaserto Phebus-type simulator-CT scan. The planning target volume (PTV) was the clinical target volume (CTV) expanded with an additional margin of 1 cm in all directions but towards the skin. Both the lungs and the heart were delineated as organs at risk. Dosimetries were computed for the two beams arrangements i.e. 2D conventional and 3D virtual.*

Results: *The mean age of 14 women was 51.4 years (range 26-65). Laterality was the left breast for 6 patients and the right for 8. Few differences were noticeable in terms of gantry angles. The 3D medial fields were more medial with a mean of 8 mm (range 0-15). The 3D lateral fields were more posterior with a mean difference of 8 mm (range 0-25). The dosimetry analysis showed that, with regard to conventional simulations, at least 95% of the CTV received in all cases > 95% of the prescribed dose. However, in 8 out of 14 patients (57%), 15% of the PTV received < 95% of the prescribed dose. The ICRU 50 quality criterion that at least 95% of the PTV ($PTV_{95\%}$) should receive at least 95% of the prescribed dose was never met with conventional simulation. In the case of virtual simulation, the ballistics of the treatment were designed to meet the ICRU quality criterion and thus the PTV95% was higher here than with the conventional simulation by a mean of 17.6% ± 9.7%. The percentage of CTV receiving a dose higher than 107% of the prescribed dose was 21.3% ± 12% with conventional and 24% ± 11% with virtual simulation.*

Conclusion: *The high incidence of breast cancer, the essential role of radiotherapy in its treatment and the potential ensuing toxicity explain why so many studies are devoted to the improvements brought to the techniques of this treatment. The virtual planning of the treatment, however, comes up against many difficulties. The countering of the CTV is complex and necessitates a combination of clinical examination and imagery. The choice of margins around the CTV has not been standardised and is largely dependent both on the equipment used and the quality control methods.*

Key words: breast cancer, 2D planning, 3D planning, radiotherapy, virtual simulation

Introduction

The importance of radiotherapy in the treatment of breast cancer operated by breast-conserving surgery has long been proven and has shown a survival benefit in a recent patient-based metaanalysis [1]. Many studies report CT-based dosimetric data from standard 2 opposed tangential fields to the breast [2-4]. They report rather high dose-heterogeneities (more than 10% of breast volume receiving more than 110% of the prescribed dose) due to the volume and shape of the breast. Some showed a correlation between the lung and heart irradiated volumes and the risk of long-term complications [5-10]. The aim of 3D virtual simulation is there-

Correspondence to: Francois Campana, MD. Radiotherapy Department, Institut Curie. 26, Rue d'Ulm, 75005 Paris, France. Tel: +331 44 32 46 32, Fax: +331 44 32 46 16, E-mail: francois.campana@curie.net

Received 05-09-2007; Accepted 13-11-2007

fore to enhance the dose distribution within the target volume, while reducing the volume of normal tissues irradiated. This prospective study aimed to compare, in terms of ballistics and dosimetry, a conventional and a virtual simulation in 14 patients without changing the set-up.

Patients and methods

Fourteen women presenting with breast cancer were treated with postoperative radiotherapy after breast-conserving surgery from October 2003 to November 2004. Whole breast irradiation alone was indicated (50 Gy at ICRU point in 25 fractions over 5 weeks) with, in some cases, an additional boost of 16 Gy to the tumor bed – that was not taken into account in this study.

All steps of the simulations were performed with the patients lying supine on a MED-TEC inclined board (10°-15°) with their ipsilateral arms raised above the head, and shoulder leaning on a dedicated arm-rest. The radiation oncologist first clinically determined the edge of all palpable breast tissues. Then a radiopaque electrical wire was placed on the breast contour, midline, surgical scar and the nipple (Figure 1). A CT scan (Somatom, Siemens, ring diameter = 60 cm) encompassing the whole breast and lungs was then carried out with 5 mm slices. After the CT scan, tangential fields were conventionally simulated using a Mecaserto Phebus-type simulator CT scan (Paris, France). They were designed so that their deep borders passed through lead wires placed 1 cm beyond the medial and lateral edges of the breast and that their width was sufficient to encompass the entire breast with a sufficient margin in all directions. The skin to source distances (SSD) at the central axis of the beams were 100 cm. All images (from simulator and CT scan) and simulation data were then transferred to an Imago/Dosigray (Paris, France) treatment planning system.

CTV was the whole breast. It was delineated on all transverse slices (level: 0 Hounsfield Unit, window: 500 Hounsfield Unit) as the volume comprised between the pectoral muscle and 5 mm below the skin (for dosimetric considerations) within the space outlined by the electrical wire that showed the limits of the palpable breast tissue. The PTV was the CTV expanded with an additional margin of 1 cm in all directions but towards the skin. Both the lungs and the heart were delineated as organs at risk.

Tangential fields were also virtually simulated by means of Beams' Eye Views, i.e. a 3D visualisation of the irradiated volumes. Beams were designed to ensure full coverage of the PTV with an additional 8 mm margin to account for penumbra (and a 1 cm margin around the skin), to avoid irradiation of the contralateral breast and to minimise irradiation of the organs at risk.

Dosimetries were computed for the two beams arrangements i.e. 2D conventional and 3D virtual (Figure 2). The normalisation point was at the intersection of the tangential fields. Beams were 5 MV photons from a SL75/5 Elekta (Stockholm, Sweden) with an integrated

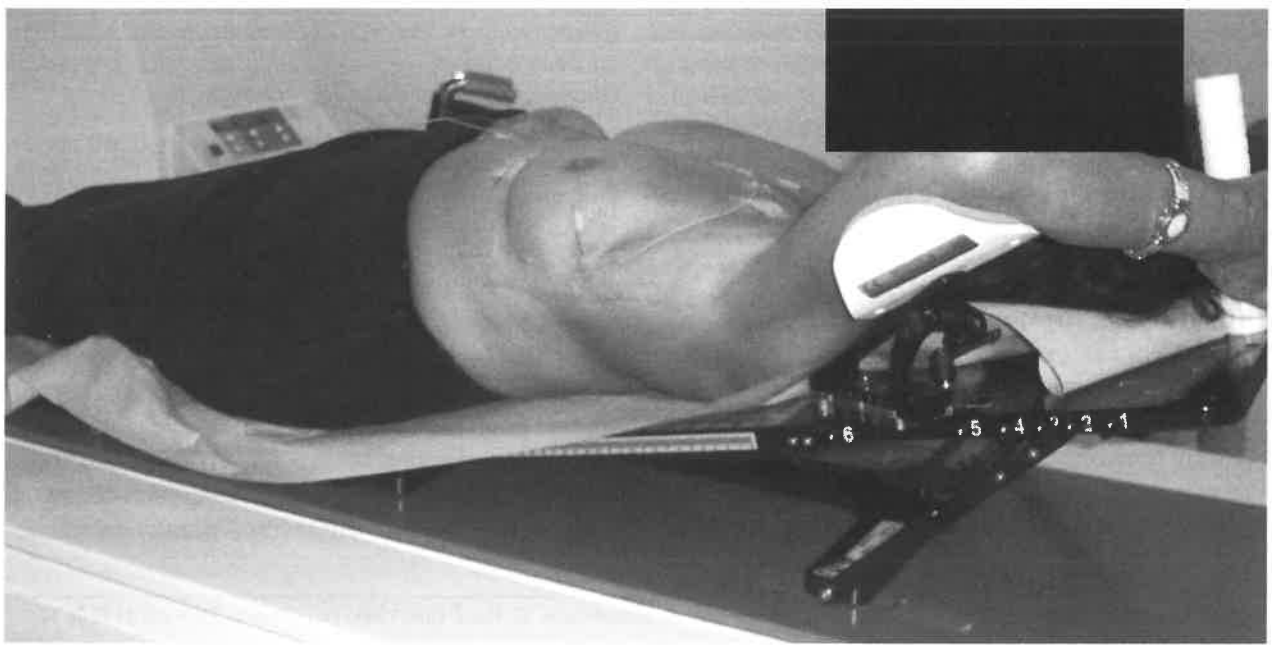


Figure 1. Patient's position and root of the breast and cicatrix visualised with skin markers.

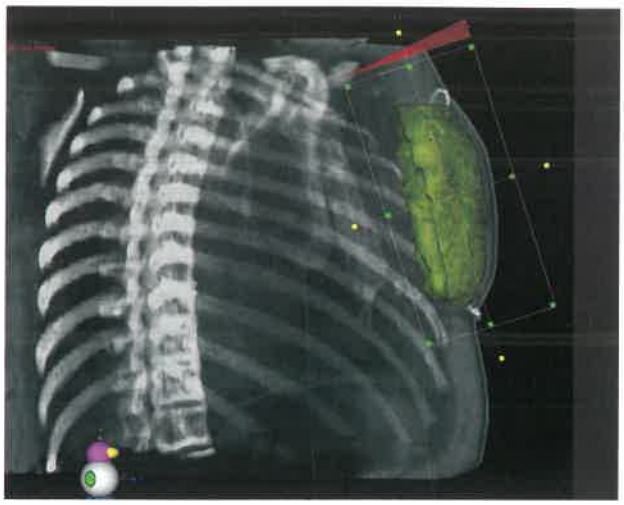


Figure 2. Virtual simulation: the breast is shown in green and the tangential fields are given.

wedge in the transverse plan but no additional multileaf collimator. Dose volume histograms were calculated for all volumes.

Results

The mean age of 14 women was 51.4 years (range 26 - 65). The left breast was involved in 6 patients and the right in 8. Few differences were noticeable in terms of gantry angles. The 3D medial fields were deviated medially with a mean of 8 mm (range 0-15). The 3D lateral fields were deviated posteriorly with a mean difference of 8 mm (range 0-25). The dosimetry analysis with conventional simulation showed that at least 95% of the CTV received in all cases > 95% of the prescribed dose. However, in 8 out of 14 (57%) patients, 15% of the PTV received < 95% of the prescribed dose. The ICRU 50 quality criterion that $PTV_{95\%}$ should receive at least 95% of the prescribed dose was never met with conventional simulation, a modality defined clinically. In virtual simulation, treatment was designed to meet the ICRU quality criterion and thus the $PTV_{95\%}$ was higher here than with the conventional simulation by a mean of 17.6% (±9.7%). The percentage of CTV receiving a dose > 107% of the prescribed dose was 21.3% (±12%) with conventional simulation and 24%±11% with virtual simulation.

Irradiated lung volume

Central lung distance (CLD) is defined as the distance from the posterior field border to the edge of the lung contour at the central axis on the tangential simulation film [9]. Our results showed a correlation between the CLD and the volume of ipsilateral lung receiving > 20 Gy. The latter was higher than 10% for CLD of 2 cm and 21% for 3 cm. Likewise, there was a correlation between the CLD and volume of ipsilateral lung receiving > 30 Gy (data not shown). CLD is thus a simple and effective predictive factor of the percentage of lung irradiation. The percentages of ipsilateral lung receiving > 20 Gy and 30 Gy were respectively 16.4% ± 5.1% and 14.2% ± 4.9% with virtual and 9% ± 2.9% and 7.1% ± 2.7% with conventional simulations.

Irradiated heart volume

Maximum heart diameter (MHD) is defined as the maximum width of heart in the tangential fields, measured from the posterior field border to the most anterior part of the heart [5,8-10]. In our series, 6 patients had cancer of the left breast. Conventional simulation was designed to limit MDH to 1 cm. Virtual simulation, in order to encompass the PTV, generated tangential fields with more heart irradiation. The percentage of heart receiving > 10 Gy was 4.9% ± 2.6% with virtual simulation vs. 1.1% ± 0.7% with conventional simulation.

Conventional simulation

All the figures presented in this study are the result of an optimised dosimetry plan using 3 slices enabling the readjustment of the wedge, taking into account the following criteria: a) at least 95% of the CTV receives 95% of the prescribed dose; b) reduction of the irradiated ipsilateral lung volume; and c) respect of the dose homogeneity (95-107% of the prescribed dose).

The maximal dose to the CTV was calculated using the following: 3 slices (z = 0; Z = +25%; z = −25% of the field size), 5 slices (z = 0; z = +25%; z = −25%; z = +40%; Z= −40% of the field size), and all the CT data. When 3 slices were analysed, despite the optimisation, a maximal dose > 107% was found in 12 (86%) patients, and > 110% in 4 (29%) patients. When 5 slices were analysed, the maximal dose was > 107% in 13 (93%) patients, and > 110% in 12 (86%) patients. The results are given in Figure 3.

When all the CT scan slices were analysed, the maximal dose was > 107% in all the patients and > 110% in 13 (93%) patients. In conclusion, the dosimetry plan using 3 CT scan slices in a conventional simulation did not ensure a sufficiently precise estimation of the overdose zones. A reliable analysis of the dose homogeneity required the use of 5 slices including 2

extreme slices, one +40% and one –40% of the field size. The result obtained by analysis of all the CT scan slices was not superior to the one obtained by a 2D simulation using 5 slices.

Analysis of the dose distribution, based on the CTV gave the following results: 21.3% (range 3.3-48) of the CTV received a dose ≥107% of the prescribed dose and 5.1% (range 0-14.2) a dose ≥110% of the prescribed dose. The percentage of the CTV that received a dose > 110% was linked both to the breast volume (correlation coefficient r= 0.814; Spearman test) and to its thickness at the axis (correlation coefficient r= 0.675; Spearman test). The maximal dose was linked to the breast volume (r = 0.8; Spearman test) and to its thickness at the axis (r = 0.618; Spearman test). Breast thickness at the axis was therefore an easily calculated indicator of the CTV percentage that would receive a dose > 110% of the prescribed dose.

Discussion

This prospective study aimed to compare the advantages and disadvantages of conventional and virtual simulations for a SSD technique of breast irradiation. Fourteen patients were enrolled.

Taking the CTV into consideration, the analysis of the dose volume histograms showed no fundamental differences concerning the dose homogeneity of the 2 simulation techniques.

As shown by Krasin et al. [11] and Zackrisson et al. [12], virtual simulation ensures an irrefutable improvement of the dose distribution to the PTV, since the $PTV_{95\%}$ was, on average, > 17.6% ± 9.7% when compared to conventional simulation. However, the clinical benefit of the virtual technique needs to be confirmed, given the excellent local control already obtained using the conventional technique [13-16]. Moreover, it is not yet possible to confirm whether or not local relapses occur preferably in "under-dosage" zones.

Can the use of virtual planning reduce the volume of irradiated lung? The important role of irradiated lung volume in later complications has been underlined [17,18].

Kong et al. [9] showed that this volume can be calculated by such a simple criterion as the CLD. The mean dose (in Gy) delivered to the ipsilateral lung is roughly equivalent to 4 times the value of the CLD (in cm). The percentage of the ipsilateral lung volume that receives 20 Gy is about 10 times the value of the CLD. Das et al. [5] have even demonstrated that the CLD was a significant indicator for the irradiation of the ipsilateral lung volume. The results of our study are in complete agreement with these publications. In the case of conventional simulation, the CLD needs to be limited to 2.5 cm, even to 2 cm, in order to avoid lung morbidity. In our series, in virtual simulation, the homogeneous irradiation of the PTV, as defined by the CTV plus a margin of 1 cm, always entailed an increase in the irradiated lung volume compared to the conventional simulation. The importance of this volume is due to the margin around the CTV. A means to reduce the lung irradiation would be to use a conformation technique with shields fitted to the PTV contour. Hurkmans et al. [19], in a series of 11 patients, compared 3 irradiation techniques: the conventional technique with tangential fields and no shields, the conformation technique and the modulation of beam intensity technique. The series involved 11 patients. The authors concluded that the normal tissue complication probability (NTCP) for radical pneumonopathies remained low with the conventional technique (0.5%) and no significant reduction was obtained with the conformation technique (0.4%) nor with the modulation of intensity (0.3%).

Does virtual planning reduce the heart volume irradiated? Chronic constrictive pericarditis and myocardial ischemia are the most frequent complications of cardiac irradiations [7,20]. The 2 main factors responsible for these complications are the volume of the irradiated heart and the total dose delivered. Rutqvist et al. [21] have demonstrated the link between cardiac mortality and the dose distribution to the heart. Many authors [6,8,10,22,23] have shown a correlation between the risk of cardiac morbidity and mortality and the heart volume within the tangential fields. This volume can be calculated using a simple parameter: the MHD. Muren et al. [10] showed that cardiac morbidity and mortality could be considerably reduced if the MHD was lower than 1 cm. Hurkmans et al. [8] showed that an MHD of ≥ 2 cm significantly increased the probability of cardiac complications. If the MHD was ≤ 1 cm, the NTCP score was < 1%. Therefore, by limiting the MHD to < 1 cm in conventional simulation, cardiac irradiation toxicity could be avoided. In our series, in virtual simulation, homogeneous irradiation of the PTV could only be obtained by increasing the volume of irradiated heart.

The limits of virtual simulation

Virtual planning necessitates first and foremost the delimitation of the target volumes. The CTV corresponds to the whole breast [24]. The delimitation of this volume is a complex procedure. Anatomical points of reference (below sub-mammary fold, 1st intercostal space, mid-axillary line) are not sufficient [24]; palpation is not a perfect method but, at least, gives rise to a

low degree of error; the visibility of mammary tissue by CT scan is erratic and highly affected by the patient's age [25]. Many authors [26-28] admit the difficulties encountered in attempting to determine the CTV and the ensuing inter and intra-observer variability. Security margins need to be added around the CTV in order to obtain the PTV [29]. Thanks to the development of portal imaging, many authors have shown interest in the reproducibility of tangential beam positioning. Repositioning errors are often due to the support equipment in use. Several studies have shown how insignificant the infraction errors are when using an alpha-cradle system [30-33]. Infraction variations are about 5 mm [34]. In the absence of specific support, the daily use of portal imaging can limit the inter-fraction positioning errors to < 5 mm [35-37]. Breathing movements must be taken into account when determining the CTV margins. Some authors show that using portal imaging for an on-line control reduces the uncertainties linked to the breathing movements [32,38,39]. The breathing-in blocking technique also reduces the respiratory intra-fraction variations (1.4 ± 1.6 mm) [40-42]. In our study, the use of virtual planning ensured a better dose distribution in the PTV; the cardiac and lung volume irradiation was higher though. The use of conformation techniques with optimised shields [19,43] or of intensity modulation [12,44-46] would further improve the dosimetry. These complex techniques need, in addition, experienced teams, functional/purpose-built supports and an extremely rigorous quality control. For the time being, therefore, they cannot be used systematically. We must remind our readers that in our series the irradiation of the CTV is perfectly satisfying whichever simulation technique is used. On the contrary, however, when ballistics determined in a 2D simulation are used, the PTV never receives 95% of the prescribed dose.

Optimisation of conventional simulation

Although the excellent clinical results of conventional mammary irradiation are irrefutable [13-15,47], there is still room for improvement in the dose distribution technique [48].

In our series, the dose heterogeneity and the value of the maximal dose are linked to the breast volume and its axis thickness. This correlation has been found in other series in the literature [2,49]. The importance of the point of prescription position, when analysing the dosimetry, which varies from team to team, must be emphasised [50].

Which is the best way to evaluate the dose homogeneity? Cheng et al. [3] showed that a dosimetric analysis using 3 CT slices was reliable for small breasts. The bigger the breast volume, the bigger number of slices required. In our study, the dosimetric analysis using 3 CT scan slices underestimated the importance of over-dosage zones. Their localisations and areas depend on several parameters: breast volume, shape of the breast and thoracic wall, and angle of the wedge filter used.

Using 5 slices, 2 of which passed at +40% and –40% of the field, enabled us to estimate the overdose as accurately as if using a complete CT scan. Treatment planning using 5 slices ensures an optimal dose distribution (Figure 3). It is not compulsory therefore to make a complete scan once the treatment set-up is in position and especially as it would entail position constraints due to breast size and the diameter of the scanner ring.

In addition, in order to obtain better dose distribution and decrease heart and lung irradiated volumes, alternative techniques can be used for breast irradiation [51].

Conclusion

The high incidence of breast cancer, the essential role of radiotherapy in its treatment and the potential ensuing toxicity explain why so many studies are devoted to the improvements brought to the techniques of this treatment. The virtual planning of the treatment, however, comes up against many difficulties. The countering of the CTV is complex and necessitates a combination of clinical examination and imaging. The choice of margins around the CTV has not been standardised and is largely dependent both on the equipment used and the quality control methods. As the volumes are uncertain, it is difficult to ensure the preservation of organs at risk and at the same time respect the ICRU standards. However, the excellent clinical results obtained using con-

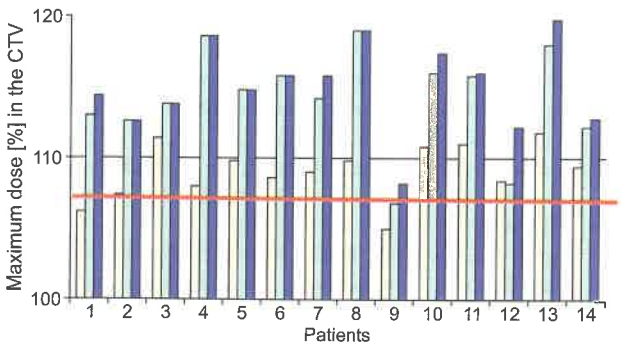


Figure 3. Maximum dose in the CTV: yellow: dosimetry on 3 slices; blue: dosimetry on 5 slices; violet: dosimetry on CT slices.

ventional techniques are proof of the high quality of the treatments and that the simulation of breast fields is also a highly clinical procedure. The notion of PTV in mammary irradiation probably needs to be reconsidered. 2D simulations can be optimised without having recourse to whole scans when in treatment position. The respect of simple geometric parameters (CLD $\leq$ 2 cm and MHD $\leq$ 1 cm) ensures a limitation of cardiac and lung irradiation toxicity. Using 5 CT scan slices makes it possible to choose the angle wedge required to improve the dose homogeneity and to make a reliable estimation of the maximal dose and the extent of the overdose.

Acknowledgements

To all team of breast cancer radiotherapy of the Institut Curie for their precious help.

References

1. Clarke M, Collins R, Darby S et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2006; 366: 2087-2106.
2. Buchholz TA, Gurgoze E, Bice WS, Prestidge BR. Dosimetric analysis of intact breast irradiation in off-axis planes. Int J Radiat Oncol Biol Phys 1997; 39: 261-267.
3. Cheng CW, Das IJ, Stea B. The effect of the number of computed tomographic slices on dose distributions and evaluation of treatment planning systems for radiation therapy of intact breast. Int J Radiat Oncol Biol Phys 1994; 30: 183-195.
4. Chin LM, Cheng CW, Siddon RL, Rice RK, Mijnheer BJ, Harris JR. Three-dimensional photon dose distributions with and without lung corrections for tangential breast intact treatments. Int J Radiat Oncol Biol Phys 1989; 17: 1327-1335.
5. Das IJ, Cheng EC, Freedman G, Fowble B. Lung and heart dose volume analyses with CT simulator in radiation treatment of breast cancer. Int J Radiat Oncol Biol Phys 1998; 42: 11-19.
6. Gagliardi G, Lax I, Soderstrom S, Gyenes G, Rutqvist LE. Prediction of excess risk of long-term cardiac mortality after radiotherapy of stage I breast cancer. Radiother Oncol 1998; 46: 63-71.
7. Gyenes G, Gagliardi G, Lax I, Fornander T, Rutqvist LE. Evaluation of irradiated heart volumes in stage I breast cancer patients treated with postoperative adjuvant radiotherapy. J Clin Oncol 1997; 15: 1348-1353.
8. Hurkmans CW, Borger JH, Bos LJ et al. Cardiac and lung complication probabilities after breast cancer irradiation. Radiother Oncol 2000; 55: 145-151.
9. Kong FM, Klein EE, Bradley JD et al. The impact of central lung distance, maximal heart distance, and radiation technique on the volumetric dose of the lung and heart for intact breast radiation. Int J Radiat Oncol Biol Phys 2002; 54: 963-971.
10. Muren LP, Maurstad G, Hafslund R, Anker G, Dahl O. Cardiac and pulmonary doses and complication probabilities in standard and conformal tangential irradiation in conservative management of breast cancer. Radiother Oncol 2002; 62: 173-183.
11. Krasin M, McCall A, King S, Olson M, Emami B. Evaluation of a standard breast tangent technique: a dose-volume analysis of tangential irradiation using three-dimensional tools. Int J Radiat Oncol Biol Phys 2000; 47: 327-333.
12. Zackrisson B, Arevarn M, Karlsson M. Optimized MLC-beam arrangements for tangential breast irradiation. Radiother Oncol 2000; 54: 209-212.
13. Gage I, Recht A, Gelman R et al. Long-term outcome following breast-conserving surgery and radiation therapy. Int J Radiat Oncol Biol Phys 1995; 33: 245-251.
14. Clark RM, McCulloch PB, Levine MN et al. Randomized clinical trial to assess the effectiveness of breast irradiation following lumpectomy and axillary dissection for node-negative breast cancer. J Natl Cancer Inst 1992; 84: 683-689.
15. Fowble BL, Solin LJ, Schultz DJ, Goodman RL. Ten year results of conservative surgery and irradiation for stage I and II breast cancer. Int J Radiat Oncol Biol Phys 1991; 21: 269-277.
16. Veronesi U, Banfi A, Salvadori B et al. Breast conservation is the treatment of choice in small breast cancer: long-term results of a randomized trial. Eur J Cancer 1990; 26: 668-670.
17. Emami B, Lyman J, Brown A et al. Tolerance of normal tissue to therapeutic irradiation. Int J Radiat Oncol Biol Phys 1991; 21: 109-122.
18. Hurkmans CW, Saarnak AE, Pieters BR, Borger JH, Bruinvis IA. An improved technique for breast cancer irradiation including the locoregional lymph nodes. Int J Radiat Oncol Biol Phys 2000; 47: 1421-1429.
19. Hurkmans CW, Cho BC, Damen E, Zijp L, Mijnheer BJ. Reduction of cardiac and lung complication probabilities after breast irradiation using conformal radiotherapy with or without intensity modulation. Radiother Oncol 2002; 62: 163-171.
20. Giraud P, Cosset JM. Radiation toxicity to the heart: physiopathology and clinical data. Bull Cancer 2004; 91 (Suppl 3): 147-153.
21. Rutqvist LE, Lax I, Fornander T, Johansson H. Cardiovascular mortality in a randomized trial of adjuvant radiation therapy versus surgery alone in primary breast cancer. Int J Radiat Oncol Biol Phys 1992; 22: 887-896.
22. Hurkmans CW, Borger JH, Giersbergen A, Cho J, Mijnheer BJ. Implementation of a forearm support to reduce the amount of irradiated lung and heart in radiation therapy of the breast. Radiother Oncol 2001; 61: 193-196.
23. Lu HM, Cash E, Chen MH et al. Reduction of cardiac volume in left breast treatment fields by respiratory maneuvers: a CT study. Int J Radiat Oncol Biol Phys 2000; 47: 895-904.
24. Valdagni R, Italia C, Montanaro P, Ciocca M, Morandi G, Salvadori B. Clinical target volume localization using conventional methods (anatomy and palpation) and ultrasonography in early breast cancer post-operative external irradiation. Radiother Oncol 1997; 42: 231-237.
25. Bentel G, Marks LB, Hardenbergh P, Prosnitz L. Variability of the location of internal mammary vessels and glandular breast tissue in breast cancer patients undergoing routine CT-based treatment planning. Int J Radiat Oncol Biol Phys 1999; 44: 1017-1025.
26. Hurkmans CW, Borger JH, Pieters BR, Russell NS, Jansen

EP, Mijnheer BJ. Variability in target volume delineation on CT scans of the breast. Int J Radiat Oncol Biol Phys 2001; 50: 1366-1372.
27. Pitkanen MA, Holli KA, Ojala AT, Laippala P. Quality assurance in radiotherapy of breast cancer - variability in planning target volume delineation. Acta Oncol 2001; 40: 50-55.
28. Severin D, Connors S, Thompson H, Rathee S, Stavrev P, Hanson J. Breast radiotherapy with inclusion of internal mammary nodes: a comparison of techniques with three-dimensional planning. Int J Radiat Oncol Biol Phys 2003; 55: 633-644.
29. Hurkmans CW, Remeijer P, Lebesque JV, Mijnheer BJ. Set-up verification using portal imaging; review of current clinical practice. Radiother Oncol 2001; 58: 105-120.
30. Bohmer D, Feyer P, Harder C et al. Verification of set-up deviations in patients with breast cancer using portal imaging in clinical practice. Strahlenther Onkol 1998; 174 (Suppl 2): 36-39.
31. Carter DL, Marks LB, Bentel GC. Impact of setup variability on incidental lung irradiation during tangential breast treatment. Int J Radiat Oncol Biol Phys 1997; 38: 109-115.
32. Creutzberg CL, Althof VG, Huizenga H, Visser AG, Levendag PC. Quality assurance using portal imaging: the accuracy of patient positioning in irradiation of breast cancer. Int J Radiat Oncol Biol Phys 1993; 25: 529-539.
33. Fein DA, McGee KP, Schultheiss TE, Fowble BL, Hanks GE. Intra- and interfractional reproducibility of tangential breast fields: a prospective on-line portal imaging study. Int J Radiat Oncol Biol Phys 1996; 34: 733-740.
34. Baroni G, Garibaldi C, Scabini M et al. Dosimetric effects within target and organs at risk of interfractional patient mispositioning in left breast cancer radiotherapy. Int J Radiat Oncol Biol Phys 2004; 59: 861-871.
35. Kron T, Lee C, Perera F, Yu E. Evaluation of intra- and interfraction motion in breast radiotherapy using electronic portal cine imaging. Technol Cancer Res Treat 2004; 3: 443-449.
36. Lirette A, Pouliot J, Aubin M, Larochelle M. The role of electronic portal imaging in tangential breast irradiation: a prospective study. Radiother Oncol 1995; 37: 241-245.
37. Mitine C, Dutreix A, van der Schueren E. Tangential breast irradiation: influence of technique of set-up on transfer errors and reproducibility. Radiother Oncol 1991; 22: 308-310.
38. Frazier RC, Vicini FA, Sharpe MB et al. Impact of breathing motion on whole breast radiotherapy: a dosimetric analysis using active breathing control. Int J Radiat Oncol Biol Phys 2004; 58: 1041-1047.
39. van Tienhoven G, Lanson JH, Crabeels D, Heukelom S, Mijnheer BJ. Accuracy in tangential breast treatment set-up: a portal imaging study. Radiother Oncol 1991; 22: 317-322.
40. Pedersen AN, Korreman S, Nystrom H, Specht L. Breathing adapted radiotherapy of breast cancer: reduction of cardiac and pulmonary doses using voluntary inspiration breath-hold. Radiother Oncol 2004; 72: 53-60.
41. Remouchamps VM, Letts N, Yan D et al. Three-dimensional evaluation of intra- and interfraction immobilization of lung and chest wall using active breathing control: a reproducibility study with breast cancer patients. Int J Radiat Oncol Biol Phys 2003; 57: 968-978.
42. Remouchamps VM, Vicini FA, Sharpe MB, Kestin LL, Martinez AA, Wong JW. Significant reductions in heart and lung doses using deep inspiration breath hold with active breathing control and intensity-modulated radiation therapy for patients treated with locoregional breast irradiation. Int J Radiat Oncol Biol Phys 2003; 55: 392-406.
43. Baglan KL, Sharpe MB, Jaffray D et al. Accelerated partial breast irradiation using 3D conformal radiation therapy (3D-CRT). Int J Radiat Oncol Biol Phys 2003; 55: 302-311.
44. Lomax AJ, Cella L, Weber D, Kurtz JM, Miralbell R. Potential role of intensity-modulated photons and protons in the treatment of the breast and regional nodes. Int J Radiat Oncol Biol Phys 2003; 55: 785-792.
45. van Asselen B, Raaijmakers CP, Hofman P, Lagendijk JJ. An improved breast irradiation technique using three-dimensional geometrical information and intensity modulation. Radiother Oncol 2001; 58: 341-347.
46. Vicini FA, Sharpe M, Kestin L et al. Optimizing breast cancer treatment efficacy with intensity-modulated radiotherapy. Int J Radiat Oncol Biol Phys 2002; 54: 1336-1344.
47. Veronesi U, Cascinelli N, Mariani L et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002; 347: 1227-1232.
48. Aref A, Thornton D, Youssef E et al. Dosimetric improvements following 3D planning of tangential breast irradiation. Int J Radiat Oncol Biol Phys 2000; 48: 1569-1574.
49. Neal AJ, Torr M, Helyer S, Yarnold JR. Correlation of breast dose heterogeneity with breast size using 3D CT planning and dose-volume histograms. Radiother Oncol 1995; 34: 210-218.
50. Das IJ, Cheng CW, Fein DA, Fowble B. Patterns of dose variability in radiation prescription of breast cancer. Radiother Oncol 1997; 44: 83-89.
51. Campana F, Kirova YM, Rosenwald JC et al. Breast radiotherapy in the lateral decubitus position – a technique to prevent lung and heart irradiation. Int J Radiat Oncol Biol Phys 2005; 61: 1348-1354.