Purpose: To quantify the radiation doses received by the heart and coronary arteries from contemporary tangential breast or chest wall radiotherapy.

Methods and Materials: Fifty consecutive patients with left-sided breast cancer and 5 consecutive patients with right-sided breast cancer treated at a large United Kingdom radiotherapy center during the year 2006 were selected. All patients were irradiated with 6- or 8-MV tangential beams to the breast or chest wall. For each dose plan, dose–volume histograms for the heart and left anterior descending (LAD) coronary artery were calculated. For 5 of the left-sided and all 5 right-sided patients, dose–volume histograms for the right and circumflex coronary arteries were also calculated. Detailed spatial assessment of dose to the LAD coronary artery was performed for 3 left-sided patients.

Results: For the 50 patients given left-sided irradiation, the average mean (SD) dose was 2.3 (0.7) Gy to the heart and 7.6 (4.5) Gy to the LAD coronary artery, with the distal LAD receiving the highest doses. The right and circumflex coronary arteries received approximately 2 Gy mean dose. Part of the heart received >20 Gy in 22 left-sided patients (44%). For the 5 patients given right-sided irradiation, average mean doses to all cardiac structures were in the range 1.2 to 2 Gy.

Conclusions: Heart dose from left-tangential radiotherapy has decreased considerably over the past 40 years, but part of the heart still receives >20 Gy for approximately half of left-sided patients. Cardiac dose for right-sided patients was generally from scattered irradiation alone.

Breast radiotherapy, heart disease, long-term effects, coronary artery, contemporary radiotherapy.
the mean percentage volume of the heart receiving 5 Gy, biologically effective dose decreased from 87% for older (1957–1984) radiotherapy to 41% for more recent (1988–1989) radiotherapy (7).

In view of these reductions in cardiac exposure, the cardiac risks of breast radiotherapy are also likely to have decreased over the past few decades. However, given that much of the radiation-induced cardiac death occurs more than a decade after treatment (8), the full risk of recent regimens cannot yet be assessed directly. Nevertheless, some indication of the likely risk can be gained by comparing heart and coronary artery doses for contemporary (2006) patients with doses received by patients irradiated with older regimens (pre-1980s) for which the risks are known.

We used three-dimensional CT-based dosimetry methods to estimate dose and volume irradiated for the heart and the three main coronary arteries in 55 breast cancer patients treated with tangential irradiation in the Yorkshire Cancer Centre, United Kingdom (UK) in 2006.

METHODS AND MATERIALS

Fifty consecutive patients with left-sided breast cancer and 5 consecutive patients with right-sided breast cancer who received adjuvant breast or chest-wall radiotherapy at a large UK radiotherapy center were selected from the CT planning database. Most patients (approximately 75%) had undergone breast-conserving surgery, and the rest had undergone mastectomy for Stage I or II breast cancer followed by tangential pair irradiation in early 2006. The few women who received radiotherapy to the regional lymph nodes were excluded from the study.

All patients were positioned on a breast board with the sternum horizontal to the treatment couch and both arms above the head. The tangential field borders were determined clinically by the attending clinician and marked with radio-opaque wires. The medial border was 1 cm ipsilateral to the mid-line, the superior border was the sternal notch, the inferior border was 1 cm below the infra-mammary fold, and the lateral border was 1 cm outside the lateral palpable border of the breast (or the mid-axillary line for mastectomy patients). Patients were scanned with a wide-bore virtual simulator, with 5-mm slices, from the clavicle to the mid-abdomen. Two 180° opposed isocentric tangential fields were set up according to the clinically determined borders.

Each patient’s radiotherapy was planned such that the dose distribution was optimized on the central slice and was normalized to the International Commission on Radiation Units and Measurements (ICRU) reference point of the breast. Computerized tomography data and treatment parameters were exported to a computerized treatment-planning system (Theraplan Plus; Nucletron UK, Tattenhall, Chester, UK). Beam weights and wedge angles were optimized on the basis of the dose distribution for the central axis plane. All patients were planned with 6-MV photons unless a wide separation between the tangential beams made it impossible to achieve ICRU 50 dose limits on the central slice, in which case 8-MV photons were used. Bolus was used only if there was skin involvement. Field borders were not modified to reduce or avoid cardiac irradiation, and cardiac shielding was not used, in common with many other UK radiotherapy centers at the time. All patients were treated with a tumor dose of 40 Gy to the isocenter in 15 fractions, 5 days per week. The dose distributions were calculated, with full CT density information including lung correction, using the pencil beam algorithm (9, 10).

The cardiac dose distributions were calculated with the full three-dimensional CT set. The patient surface was defined by automated density gradient tracking. The organs at risk that were assessed were the heart and coronary arteries. The heart and left anterior descending (LAD) coronary artery were outlined for all patients. In addition, the right and circumflex coronary arteries were outlined for 5 consecutive left-sided patients and for all 5 right-sided patients. The superior limit of the heart included the right and left atria and excluded the pulmonary trunk, ascending aorta, and superior vena cava. The inferior limit of the heart was the caudal border of the myocardium. Because of its short length, the left main coronary artery was assessed with the LAD coronary artery. The CT scans were not contrast enhanced. Therefore, on some CT images it was not possible to visualize the coronary arteries directly, and their location was inferred using visible, reliable, cardiac landmarks (11) as follows: the location of the LAD coronary artery was identified using the course of the anterior interventricular groove. The circumflex coronary artery was contoured from its branch point off the left main coronary artery, and its course was identified using the left atrioventricular groove. The right coronary artery was contoured from its origin above the right cusp of the aortic valve. Its location was identified using the right atrioventricular groove. A radial margin of 1 cm was added to each coronary artery contour to allow for uncertainty in identification of arterial position, respiratory movement, and for the beating movement of the heart. The contours were reviewed and modified, where appropriate, by one of the authors (radiologist J.T.S.).

For each treatment plan, dose–volume histograms (DVHs) for the heart and for the LAD, with a 1-cm radial margin, were generated. For all 5 right-sided and for the first 5 consecutive left-sided patients, DVHs for the right and circumflex coronary arteries, with margin, were also generated. For each organ at risk, mean and maximum doses were assessed for each patient. For each of these quantities the average value over all assessed patients (referred to as “average mean” or “average maximum”) was calculated together with its standard deviation (SD).

Computerized tomographic images of all left-sided patients who received >12 Gy (30% of tumor dose) mean radiation dose to the LAD coronary artery were assessed further to determine which part(s) of the artery received the highest doses. From these, the three CT scans with the least distortion due to movement of the heart were selected. Point dose to the center of the LAD contour was noted on each CT slice. The distances of these point doses from the origin of the LAD (i.e., the branch point of the left main coronary artery into LAD and circumflex coronary arteries) were noted. These doses and distances were used to create a three-dimensional representation of dose to the LAD artery for each of the three CT scans.

RESULTS

Mean dose to the heart and coronary arteries

For left-sided patients the heart was close to the tangential fields, and the average mean (SD) heart dose was 2.3 (0.7) Gy (Table 1, Fig. 1a). In contrast, for the 5 patients who received right-sided irradiation, the heart was distant from the fields. It received scattered dose alone (i.e., dose from radiation outside the radiotherapy beams) (Fig. 1b), and the average mean heart dose was 1.5 (0.2) Gy (Table 1).

For left-sided radiotherapy, the anterior location of the LAD coronary artery in the interventricular groove meant that it was close to or in the fields for most patients
For right-sided radiotherapy the LAD coronary artery was usually more than 7 cm from the fields, and it received 1.6 (0.2) Gy average mean dose from scattered irradiation (Table 1, Fig. 1b). Thus the mean LAD coronary artery dose from left-sided irradiation was approximately five times higher than the dose from right-sided irradiation. The right and circumflex coronary arteries were distant from both left- and right-sided tangential fields and received scattered dose alone (Table 1, Fig. 1).

Cardiac structures that received >20 Gy

For left-sided radiotherapy, the heart received scattered irradiation alone in 28 patients (56%). For the other 22 patients (44%), a small part of the heart was in the radiation fields (i.e., it received >20 Gy) (Figs. 1a and 2). Of these 22 patients, 20 had 1–2% of the heart volume in the fields, and the remaining 2 had >5% of the heart volume in the fields (Fig. 2).

For left-sided radiotherapy, the cardiac structures that received the highest doses were the apex of the left ventricle and the LAD coronary artery (Fig. 1a). For some patients the LAD coronary artery radial margins were outside the volume of the heart. This meant that the LAD coronary artery contour was closer to the fields than the heart was, and it therefore received higher doses than the heart. Average maximum point doses to the heart and LAD coronary artery for left-sided irradiation were 30.7 (10.8) Gy and 35.2 (8.8) Gy, respectively (Table 1). The average volume of the LAD coronary artery included in the field was 13%. There was substantial patient-to-patient variability: for 26% of patients ≤1% of the LAD volume was in the fields, whereas for 58% of patients 2–29% was included, and for 16% of patients ≥30% of the volume was included in the fields (Fig. 2). Average maximum doses to the right and circumflex coronary arteries for left-sided irradiation and to all cardiac structures for right-sided irradiation were <3 Gy and ranged from 1.5 (0.2) for the circumflex coronary artery to 2.6 (0.3) for the heart (Table 1).

Patient-to-patient variability in mean dose

Of the cardiac organs considered, patient-to-patient variability in mean dose was greatest for LAD coronary artery dose from left-sided irradiation. The mean LAD dose for 50 left-sided patients varied from 2.4 to 21.2 Gy (SD 4.5) (Table 1, Fig. 3). High LAD dose was associated with high mean heart dose (Fig. 4), and the patient with the highest mean heart dose (4.4 Gy) also had the highest LAD dose (21.3 Gy) (Fig. 3).

Mean heart dose ranged from 1.4 to 4.4 Gy for left-sided irradiation (Fig. 3). There was little variability in mean dose to the right and circumflex coronary arteries for left-sided irradiation or in dose to any cardiac structure for right-sided irradiation (see Table 1 for SDs).

Dose to different parts of the LAD coronary artery

Twelve patients who had left-sided radiotherapy received mean LAD doses of >12 Gy (30% of tumor dose). The 3 patients whose CT scans demonstrated the least motion artefact

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**Table 1. Mean and maximum doses to the heart and three main coronary arteries from tangential pair radiotherapy**

<table>
<thead>
<tr>
<th></th>
<th>Heart</th>
<th>LAD coronary artery</th>
<th>Right coronary artery</th>
<th>Circumflex coronary artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average mean dose (SD)* (Gy)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Left-sided irradiation</td>
<td>2.3 (0.7)</td>
<td>7.6 (4.5)</td>
<td>2.0 (0.3)</td>
<td>1.8 (0.3)</td>
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<td>Right-sided irradiation</td>
<td>1.5 (0.2)</td>
<td>1.6 (0.2)</td>
<td>2.0 (0.3)</td>
<td>1.2 (0.1)</td>
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<tr>
<td>Average maximum dose (SD)* (Gy)</td>
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</tr>
<tr>
<td>Left-sided irradiation</td>
<td>30.7 (10.8)</td>
<td>35.2 (8.8)</td>
<td>2.5 (0.3)</td>
<td>2.4 (0.4)</td>
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<tr>
<td>Right-sided irradiation</td>
<td>2.6 (0.3)</td>
<td>1.9 (0.2)</td>
<td>2.5 (0.4)</td>
<td>1.5 (0.2)</td>
</tr>
</tbody>
</table>

* The mean or maximum organ dose averaged over all patients (50 or 5) for whom the assessment was carried out.

† These values were based on 50 patients, whereas all others were based on 5 patients.

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**Abbreviation:** LAD = left anterior descending.

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Fig. 1. Dose distribution from 6 MV tangential irradiation. The heart is outlined in orange. The coronary arteries are outlined, and a radial margin of 1 cm has been added to each.
were studied in detail. The LAD coronary artery, measured from its origin at the bifurcation of the left main coronary artery to the apex of the left ventricle, varied in length from 8.9 to 10.2 cm (Fig. 5). For all 3 patients the proximal part of the artery (up to 4 cm from its origin) was outside the high-dose region and received <4 Gy (10% of tumor dose). As the LAD descended in the interventricular groove between the apices of the right and left ventricles it extended anteriorly into the tangential beams, and parts of the distal LAD received doses of >30 Gy (75% of tumor dose) (Fig. 5).

**DISCUSSION**

We have quantified dose to the heart and to the three main coronary arteries from adjuvant radiotherapy in 55 breast cancer patients irradiated in a major UK radiotherapy center in the year 2006.

**Strengths and limitations of the study**

Patients for this study were selected consecutively from the CT planning database of the radiotherapy center. Their order on the database should be independent of any of the factors currently known to affect heart dose, for example, surgical procedure, patient anatomy, and the availability of different treatment units. Given this method of selection our sample is likely to be representative of the population of women irradiated at the Yorkshire Cancer Centre in early 2006.

This study assessed heart dose from tangential fields alone and did not consider scar boost or nodal irradiation. For left- or right-sided scar boost irradiation, heart dose is generally <0.3 Gy. For left-sided axillary radiotherapy, heart dose is
approximately 0.4 Gy and less than this for right-sided axillary irradiation (4). Thus for these women, any additional cardiac dose from boost or axillary radiotherapy would have been an order of magnitude lower than the dose from tangential radiotherapy.

Heart dose from left supraclavicular irradiation is also much lower than heart dose from tangential irradiation at approximately 0.6 Gy (for a given dose of 40 Gy) (4) and less than this for right supraclavicular irradiation. There is some geographic variation in its use, but generally the supraclavicular fossa is only irradiated in approximately 10% of adjuvant therapy planning techniques (e.g., intensity-modulated radiotherapy [IMRT]) are routinely used, heart doses are likely to be lower than those in this study.

**Reduction in cardiac doses since the 1970s**

Comparisons of the doses presented in this article with cardiac doses received from different left-tangential radiotherapy regimens used in the past are shown in Table 2. Tumor dose was 40 Gy for the regimen used in 2006 and 50 Gy for the quoted regimens used in the 1970s and 1990s; therefore, results for both mean cardiac dose and percentage of tumor dose delivered to cardiac structures are shown (Table 2). Dose estimates from 1970s and 1990s Swedish left-tangential regimens have been used for comparison with the current estimates because, for these regimens, detailed information concerning both the field parameters and the time period of use have been published (4). Similar regimens were used in other countries during these time periods, so these Swedish cardiac doses are likely to be similar to cardiac doses received elsewhere (21, 22). There have been reductions in both mean heart dose from 13.3 Gy in the 1970s to 2.3 Gy in 2006 and mean percentage of tumor dose received by the heart from 26.6% in the 1970s to 5.8% in 2006 for left-tangential irradiation. Mean doses to all three coronary arteries have also reduced, particularly dose to the LAD coronary artery, which has decreased from 31.8 Gy to 7.6 Gy and from 63.6% to 19.0% of tumor dose. For right-tangential radiotherapy, heart dose has also reduced from 2.3 Gy in the 1970s to 1.5 Gy in 2006 (4). The LAD and circumflex coronary artery doses from right-sided radiotherapy have changed little since the 1970s, whereas right coronary artery dose has decreased from 8.7 Gy to 2.0 Gy (4). The cardiac dose reductions since the 1970s are likely to be due to a number of different factors, including the shift of the medial field border from the contralateral to the ipsilateral side, the use of higher-energy beams (6 or 8 MV rather than 60Co), and the use of CT data for radiotherapy planning. Similar changes have occurred in many different countries, therefore cardiac dose reductions from tangential irradiation are likely to have occurred worldwide.

These dose reductions are likely to have resulted in widespread reductions in cardiac risk over the past 40 years. They probably account for the suggested risk reductions seen when women irradiated for left-sided and for right-sided breast cancer in the United States between 1973 and 2001 are compared (2, 3). In the future, further dose reductions are expected.
owing to the increasing use of advanced radiotherapy techniques, such as IMRT.

Pathogenesis of radiation-induced heart disease

The etiology of the excess cardiac mortality seen years after irradiation is not yet fully understood and is currently being investigated in the SUPREMO (Selective Use of Post-operative Radiotherapy after Mastectomy) trial of postmastectomy radiotherapy. In particular, it is not clear whether myocardial damage or coronary artery damage, or both, are responsible and whether the risk of radiation-induced heart disease is affected by the use of anthracyclines. Damage to the LAD coronary artery is a common cause of non-radiation-induced myocardial infarction (MI) and may also play a role in radiation-induced MI. Left-tangential irradiation tends to deliver a high mean radiation dose to this artery (approximately 8 Gy in this study), with parts of the artery receiving >20 Gy in some patients. The highest doses were received by the distal part of the LAD coronary artery, as also seen in a study by Krueger et al. (2004) (23). The prognosis of non-radiation-induced atherosclerosis is worse for proximal than for distal LAD disease (24, 25). If this were also true of radiation-related coronary artery disease, irradiation of the distal LAD may be less detrimental than irradiation of the proximal part. However, at present the clinical consequences of the high doses received by the distal part of the LAD coronary artery are unknown.

The effect of scattered irradiation

For both left- and right-sided radiotherapy, with use of either standard tangents or IMRT, most of the heart volume receives >1 Gy dose from scattered irradiation (26). This low-dose exposure of the whole heart may contribute to the cardiac damage that leads to excess cardiac mortality. Evidence for this is derived from study of the survivors of the atomic bombings of Hiroshima and Nagasaki, who received mean uniform single cardiac doses of 4 Gy or less (27). There was a significant excess of deaths from heart disease in this cohort, with a linear relationship between dose and cardiac mortality. Excess mortality from heart disease has also been seen in patients who received para-aortic irradiation for testicular cancer, which resulted in approximately 1 Gy scattered irradiation to the heart (28). These studies raise the possibility that doses of approximately 1 to 2 Gy received by the whole heart may contribute to radiation-induced cardiac damage.

CONCLUSIONS

Approximately half of the patients irradiated with left-tangential radiotherapy received doses of ≥20 Gy to a small part of the anterior heart, which usually included the LAD coronary artery. Most of the heart volume, including the right and circumflex coronary arteries, received scattered irradiation alone, and mean heart dose was approximately 2 Gy for left-sided irradiation. For right-sided irradiation, cardiac structures received 1.2 to 2 Gy mean dose. These doses are considerably lower than cardiac doses from the regimens that are now known to have caused excess cardiac mortality, hence their risk is likely to be lower. However, the clinical implications of these doses are as yet unknown.

REFERENCES


