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CLINICAL INVESTIGATION **Breast**

POSTMASTECTOMY ELECTRON BEAM CHEST WALL IRRADIATION IN WOMEN WITH BREAST CANCER: A CLINICAL STEP TOWARD CONFORMAL ELECTRON THERAPY

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Purpose: Electron beam radiotherapy of the chest wall with or without lymph node irradiation has been used at the Institut Curie for >20 years. The purpose of this report was to show the latest improvements of our technique developed to avoid hot spots and improve the homogeneity.
Methods and Materials: The study was split into two parts. A new electron irradiation technique was designed and compared with the standard one (dosimetric study). The dose distributions were calculated using our treatment planning software ISIS (Technologie Diffusion). The dose calculation was performed using the same calculation parameters for the new and standard techniques. Next, the early skin toxicity of our new technique was evaluated prospectively in the first 25 patients using Radiation Therapy Oncology Group criteria (clinical study).
Results: The maximal dose found on the five slices was 53.4 ± 1.1 Gy for the new technique and 59.1 ± 2.3 Gy for the standard technique. The hot spots of the standard technique plans were situated at the overlap between the internal mammary chain and chest wall fields. The use of one unique field that included both chest wall and internal mammary chain volumes solved the problem of junction. To date, 25 patients have been treated with the new technique. Of these patients, 12% developed Grade 0, 48% Grade 1, 32% Grade 2, and 8% Grade 3 toxicity.
Conclusions: This report describes an improvement in the standard postmastectomy electron beam technique of the chest wall. This new technique provides improved target homogeneity and conformality compared with the standard technique. This treatment was well tolerated, with a low rate of early toxicity events. © 2007 Elsevier Inc.

Breast cancer, Chest wall irradiation, Postmastectomy radiotherapy with electrons.

INTRODUCTION

The benefit of adjuvant radiotherapy (RT) to the chest wall has been controversial for many years. Recently published data have shown that the RT regimens produced moderate, but definite, reductions, not only in breast cancer mortality, but also overall mortality (1, 2). The benefit of postmastectomy RT, independent of the effects of systemic treatment, was also shown in studies from the Danish Breast Cancer Cooperative Group and the British Columbia study (3–5). However the first meta-analysis report did not find any advantage in overall survival at 10 and 20 years (6). One explanation is the increase of non–breast cancer-related deaths, particularly cardiac disease in relationship to old radiation techniques (7, 8).

Two opposed tangential photon beams is a common technique for postmastectomy RT to the chest wall (9, 10). Electron beam RT of the chest wall is also routinely used (9, 11–15). It has already been shown that this technique yields locoregional control, disease-free survival, and overall survival rates similar to those of standard photon beam RT (15, 16).

Other important problems are the junction of the internal mammary chain (IMC) fields, supraclavicular fields, and the chest wall electron beam field. Computed tomography (CT)-based localization of the IMC has been studied already, and some rules were developed to define the field limits (17).

Electron beam RT to the chest wall, with or without lymph node irradiation, has been used at the Institut Curie for >20 years. The purpose of this study was to report the latest improvements of our technique and to assess the early toxicity.

METHODS AND MATERIALS

For >20 years, electrons have been used for postmastectomy adjuvant irradiation of the chest wall at the Institut Curie, and a few thousand patients have been treated with it. At the Institut Curie, postmastectomy adjuvant irradiation is indicated for lymph node-positive tumors at initial presentation (for patients treated with neoadjuvant chemotherapy, the indication remained even if the histologic examination showed a complete tumor response in the lymph nodes), tumors >40 mm, clinically multiple tumors, and

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vascular invasion in young patients. The prescribed dose has been 50 Gy in 25 fractions to the chest wall and regional lymph nodes (treated by photons for the supraclavicular and axillary regions and a mixed photon-electron technique for the IMC area). No boost is given to the mastectomy scar. The ‘‘new’’ technique is a dosimetric improvement of the ‘‘standard’’ technique, without any change in the treatment volumes (chest wall and lymph node areas) or the prescribed doses. The dose distributions are calculated using our treatment planning software ISIS (Technologie Diffusion, Paris, France). The dose calculation was performed using the same calculation parameters for the new and standard techniques.

Study design

The study was split into two parts. A new electron radiation technique was designed and compared with the standard one (dosimetric study). Then, the early skin toxicity of our new technique was evaluated prospectively in the first 25 patients using Radiation Therapy Oncology Group criteria and reported (clinical study) (9).

Treatment planning for Institut Curie standard technique

Since 1990, treatment plans were performed on CT slices (acquired with a simulator CT Varian Ximatron) to be more adapted to the patient’s anatomy. Five CT slices were performed in the chest wall area, from the central axis to 2 cm inside the superior and inferior limits. Because of the unavailability of a large-bore CT scanner in our department, the anatomic data were taken at the simulator CT scanner. This allowed an ideal patient position on an angled breast board, with horizontality of the thorax (which is important for electrons to avoid source-to-skin distance effects) and the patient’s arm at 90° from the craniocaudal direction so that a 30° angled chest wall beam would not intersect either the contralateral breast or the dorsal muscle. When important irregularities of the chest wall were present, more slices were acquired. One CT slice was acquired at the supraclavicular mid-field. The clinical target volume of the chest wall included the breast bed, mastectomy scar with 1–2-cm margins, and IMC and supraclavicular areas. Since 1980, electron beam irradiation was our standard for postmastectomy treatment. The setup facility of a direct en face field was a convincing reason to choose it. The lymph node irradiation at the Institut Curie has been previously described (17). A mixed photon and electron beam in the IMC area was our technique of choice to avoid unnecessary irradiation of the heart, with a ratio of about 20 Gy/30 Gy between the photon and electron doses. The supraclavicular area was irradiated with photons. The patient lay on an angled breast board with an angle of 15–20° to bring the thorax of the patient to a horizontal position. The irradiation consisted of three separate fields: the chest wall, IMC, and supraclavicular field (Fig. 1). The technique used a 30°-angled chest wall beam with a separate anterior IMC field. A gap of 5 mm was systematically used for the junction between the chest wall and the IMC fields and between the chest wall and the supraclavicular fields. A generous 2-cm margin was added to ensure that the target volume would be entirely encompassed in the homogeneous part of the electron beam. To ensure a sufficient skin dose, a 5-mm bolus was systematically used. Electron energy was chosen so that the 95% isodose (47.5 Gy) was situated at the costal wall depth. The energies available on our treatment machine (Saturne 41, Varian) and routinely used for chest wall irradiation were 7.5, 9, and 10.5 MeV. When energy >10.5 MeV was necessary, the patients were treated by photons only or with mixed photons and electrons to avoid late skin complications. For all patients, the treatment plans were optimized and adapted to the individual patient anatomy. The dose distribution in the central axis plane of the chest wall is given in Fig. 2. The 95% isodose (47.5Gy) was situated at the costal wall depth. The skin received a dose of ≥95% of the prescribed dose. To evaluate the dose at the IMC, a dose point (IMC reference point) was positioned at the depth of the lung interface, 3 cm laterally to the medial line, and at the central transverse plane through the IMC target volume, as previously shown in the CT scan study (17). Despite the 5-mm gap between the IMC and chest wall fields, in most cases, an overdosage of >110% (55 Gy) was observed (Fig. 2).

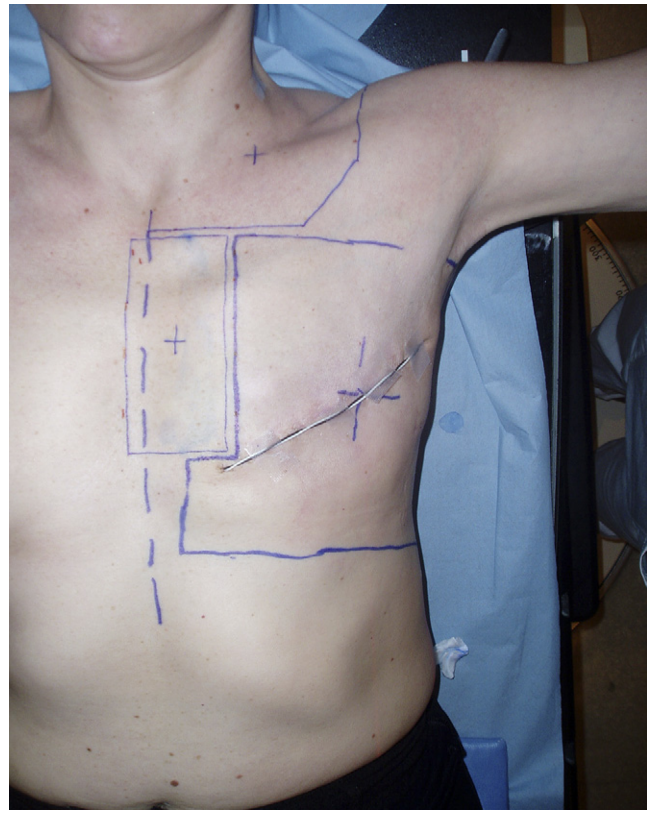

Fig. 1. Patient position and standard postmastectomy fields: chest wall (electrons), internal mammary chain (photons and electrons), and supraclavicular nodes (photons).

Treatment planning for new irradiation technique

A new irradiation technique was recently implemented at our institution after approval from our Board of Radiation Oncology. The

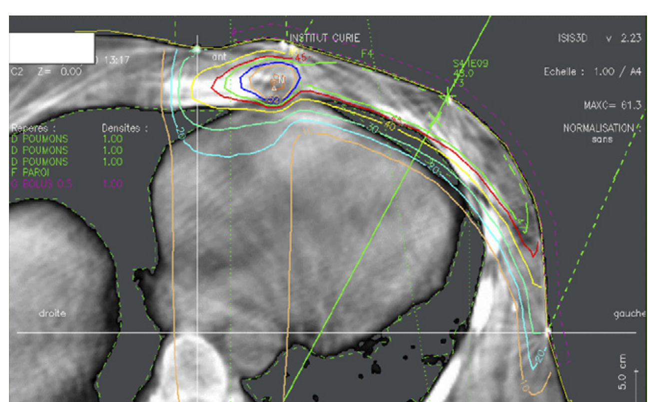

Fig. 2. Standard technique: dose distribution for 50-Gy prescribed total dose.

chest wall and IMC volumes are now included into one unique field at a gantry angle of 20–30° from the vertical. During the simulation, the radiation oncologist determined the clinical volume of the chest wall to be irradiated and also delineated the IMC target volume (Fig. 3). The electron energy was chosen so that the 47.5-Gy isodose was at the costal wall depth when a 5-mm bolus was in place (Fig. 4). Then, the bolus was modified in two dimensions on each of the five chest wall CT slices so that the IMC and chest wall were well covered by the 95% isodose (47.5 Gy).

Because of the beam obliquity and the source-to-skin distance variations, the IMC is often underdosed. In clinical practice, layers of 5-mm silicon (Bolusil) are used as a bolus material. In our standard technique, the IMC was irradiated by a mixed photon-electron field separated from the chest wall field. No bolus was used in this area. During simulation of the new technique (chest wall, including the IMC area), the radiation oncologist delineated the IMC old field. When dosimetrically needed, part of the bolus was removed, corresponding to the size of the old IMC field (Fig. 5). When the IMC reference point received a dose per fraction inferior to 1.8 Gy, part of the bolus was removed from the IMC region, so that the electrons could go deeper into the nodal area (Fig. 5). A boost to the IMC completed the dose to a total of 50 Gy. To better spare the skin when the additional dose was delivered to the IMC, the boost field was delivered with photons (6 MV). It was treated with 0.5-Gy fractions (prescribed at maximal dose), once or twice weekly, depending on the complement dose to be delivered.

In the lateral (external) part of the chest wall, a distance effect is also present. Moreover, the chest wall is always thicker in that region. This leads to an underdosage of the lateral chest wall. To become more conformal, we would also need to boost that portion of the chest wall (18). Our standard technique plans also included the same dosimetric defect. A previous retrospective study (19) showed no recurrences in that area. We, therefore, decided not to complement the dose in that part of the chest wall.

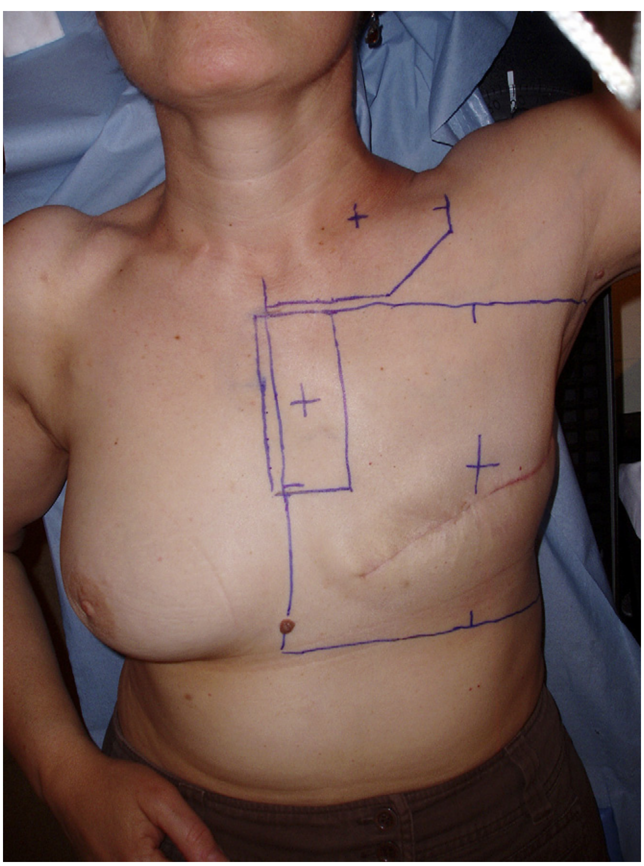

Fig. 3. Postmastectomy fields for new technique: chest wall (electrons), internal mammary chain (electrons and photon boost), and supraclavicular nodes (photons).

When the reference isodose (47.5 Gy) entered into the ipsilateral lung, a second layer of 0.5-cm bolus material was placed on each CT slice, as needed. The bolus was prepared by the dosimetrist. When two layers of bolus were needed to protect the lung, a beam's eye view showing the projection of the bolus layers was used for bolus confection. The transversal and sagittal laser positions were marked on the patient's skin and on each of the bolus layers to ensure reproducible positioning at every fraction (Fig. 6). Because a steep edge of the bolus produces hot and cold spots in the subcutaneous area beneath it, the bolus edges were beveled at the workshop.

Dosimetric comparisons with standard technique

The dosimetry study included the first 25 patients treated with the new technique. To evaluate the dosimetric advantages of this technique, we performed a second treatment plan for each patient using the standard technique. For each treatment plan (standard and new techniques), we have reported the maximal dose in the treated volume; the dose received at the IMC reference point; the depth of the 20-Gy isodose, measured from the posterior border of the sternum, on the medial plane, and in the central axis slice; the depth of the 20-Gy isodose, measured from the posterior border of the sternum, laterally to the sternum, at its ipsilateral edge, and in the central axis slice; and the maximal depth of the 40-Gy isodose in the ipsilateral lung in the central axis slice.

Prospective clinical study

The data of all patients treated with the new technique were prospectively recorded, and early toxicity was assessed weekly according to the Radiation Therapy Oncology Group classification (9). The Radiation Therapy Oncology Group grades were as follows: Grade 0, no skin reaction; Grade 1, follicular, faint, or dull erythema, epilation, dry desquamation, and decreased sweating; Grade 2, tender or bright erythema, patchy moist desquamation, and moderate edema; Grade 3, confluent, moist desquamation other than skin

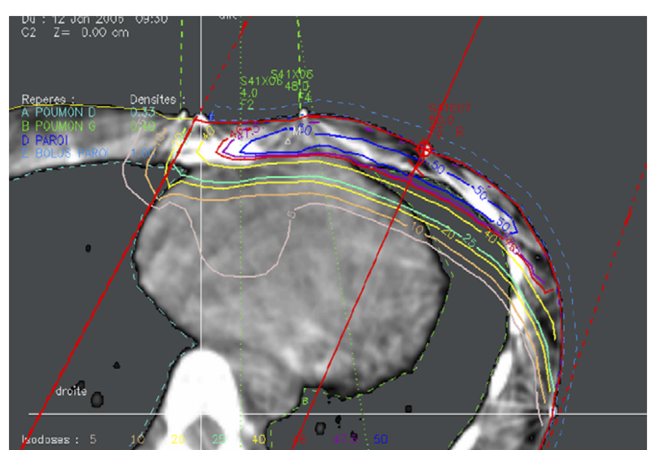

Fig. 4. Dose distribution for 50-Gy prescribed dose using new technique.

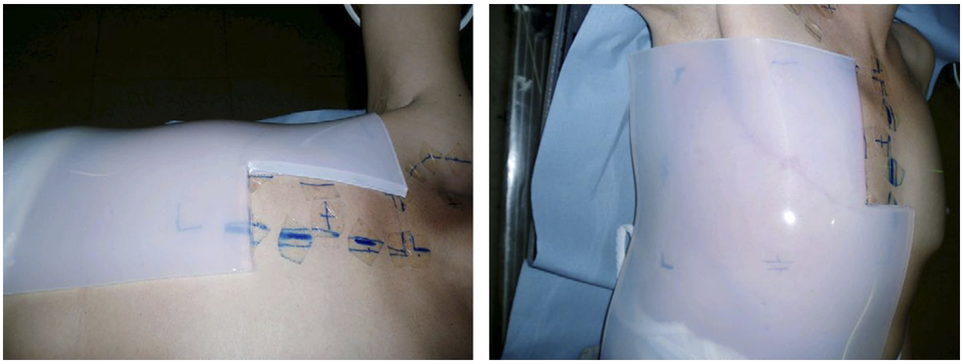

Fig. 5. Bolus shape and positioning: part of bolus removed to obtain better dose distribution in internal mammary chain volume. Missing portion corresponded to internal mammary chain field of standard technique. Edges were beveled to avoid high-dose variations at transition.

folds, and pitting edema; and Grade 4, ulceration, hemorrhage, and necrosis.

RESULTS

Dosimetric study

A chest wall dose of 50 Gy was prescribed for both techniques. In the standard technique, the IMC dose was delivered with photons (20 Gy) and electrons (30 Gy). In the new technique, depending on the conformation of the patient, it was necessary to add a dose of 0–5 Gy to the IMC using a photon boost. Our standard technique used different gantry angles for the IMC and the chest wall. This created hot spots, as shown in Table 1, which summarizes the main dosimetric differences between our new technique and our standard technique.

The maximal dose found on the five slices was 53.4 ± 1.1 Gy for the new technique and 59.1 ± 2.3 Gy for the standard technique. The hot spots of the standard technique plans were situated at the overlap between the IMC and chest wall fields. The mean dose at the IMC reference point was 50 ± 1.8 Gy and 55.2 ± 2.7 Gy for the new and standard plans, respectively. In the medial plane, the 20-Gy isodose was at 0.7 ± 0.3 cm from the sternum with the new technique and 1.4 ± 0.3 cm with the standard plans. At the lateral border of the sternum, the 20-Gy isodose was also deeper in the standard plans. The 40-Gy isodose was at a 1.0 ± 0.3-cm depth in the homolateral lung in the new plans. It was deeper by 0.4 cm (1.4 ± 0.4 cm) in the standard plans.

Clinical prospective study

To date, 25 patients have been treated, studied, and followed. Three patients developed a Grade 0 reaction (12%), 12 (48%) a Grade 1, 8 (32%) a Grade 2, and 2 (8%) a Grade 3 reaction at the end of RT. Two patients underwent concomitant radiochemotherapy, and one of them experienced a Grade 1 and one a Grade 3 reaction. The median radiation dose was 50 Gy (range, 48–52 Gy), and the RT duration was 37 days (range, 36–40 days).

DISCUSSION

Our standard electron irradiation technique has been used for >20 years at the Institut Curie. This study reports on the early evaluation of its improvement. The choice of RT fields has been based on the patterns of local and regional recurrences. Most mastectomy series have demonstrated that >50% of local recurrences develop in the chest wall,

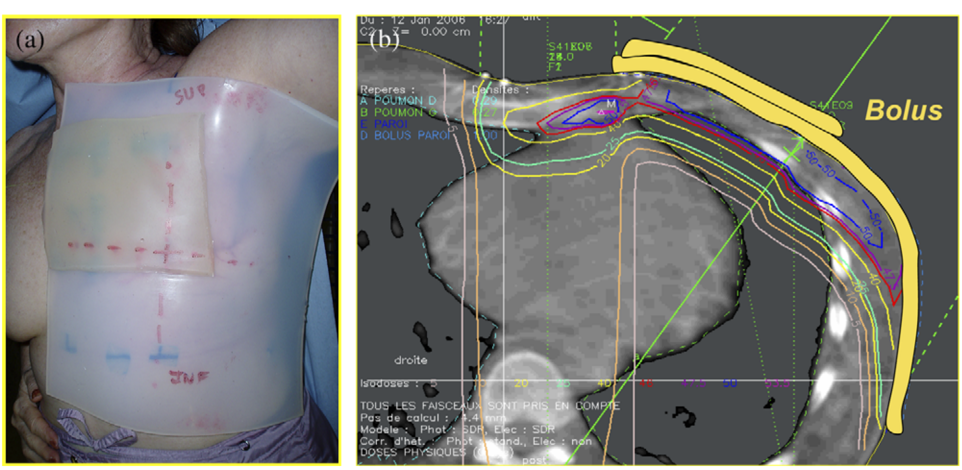

Fig. 6. New technique with two thicknesses of bolus: (a) position and reproducibility and (b) dose distribution.

Table 1. Dosimetric comparison between new and standard techniques executed in 25 patients

Variable	New technique (n = 25)	Standard technique (n = 25)
Maximal dose* (Gy)		
Median	53.3	59.2
Range	52.2–55.4	53.4–62
Mean ± SD	53.4 ± 1.1	59.1 ± 2.3
IMC dose†		
Median	50	55.4
Range	47.5–52.9	49.8–58
Mean ± SD	50 ± 1.8	55.2 ± 2.7
Depth 20-Gy isodose (cm), medial plane‡		
Median	0.6	1.5
Range	0.2–1.3	1–1.8
Mean ± SD	0.7 ± 0.3	1.4 ± 0.3
Depth 20-Gy isodose (cm), parasternal§		
Median	1	1.8
Range	0.3–1.5	1.2–2.2
Mean ± SD	0.9 ± 0.4	1.7 ± 0.3
Depth 40-Gy isodose (cm), lung‖		
Median	0.9	1.2
Range	0.5–1.5	0.9–2.1
Mean ± SD	1.0 ± 0.3	1.4 ± 0.4

Abbreviations: IMC = internal mammary chain; SD = standard deviation.

* Prescribed dose to chest wall, 50 Gy.

† Dose received at IMC reference point.

‡ Distance from posterior border of sternum to 20-Gy isodose curve.

§ Distance from posterior lateral border of sternum to 20-Gy isodose curve.

‖ Maximal depth of 40-Gy isodose curve in lung.

especially in the mastectomy scar, with the second most common site the supraclavicular region (20, 21). It has been shown that advanced disease at presentation and positive lymph nodes after chemotherapy predict for clinically significant rates of locoregional recurrence (22). Therefore, postmastectomy irradiation to the chest wall and supraclavicular region is recommended in patients with four or more positive lymph nodes (23, 24).

It has already been shown that the optimal dose that offers the greatest chance of locoregional control of breast cancer at the lowest cost in locoregional morbidity appears to be 40–60 Gy in 2-Gy fractions (2). Different techniques have been used for irradiation of the chest wall and regional lymph nodes (9, 10). Numerous studies have confirmed that postmastectomy electron beam chest wall irradiation is as effective as photon beam chest wall irradiation for local control and overall survival (11–16). It has also been demonstrated that this technique could be less toxic (16). Our study has confirmed this finding and reported a dosimetric improvement of our standard technique.

Dosimetric comparisons

At our institution, >1,000 new breast cancer patients are treated every year, about one-third of whom are postmastectomy patients. The challenge was, therefore, to change our technique without involving time-consuming practices for the dosimetrist or therapist. Improvement was needed because our standard technique produced hot spots and was not conformal enough.

As has already been noted, because of the unavailability of a large-bore CT scanner in our department, the anatomic data were preferably taken at the simulator CT. It was shown that a patient's model reconstructed from five slices was comparable to three-dimensional CT acquisition regarding beam placement and dosimetric optimization (25). However, when important irregularities were present in the chest wall, more CT slices were performed.

Our treatment planning software ISIS uses an electron algorithm similar to the primary-scattered radiation concept, originally developed for photon beams (26). It accounts for source-to-skin distance effects throughout the field, as well as penumbra changes in depth. However, heterogeneity corrections are calculated with an equivalent depth method and are, therefore, very inaccurate. For this reason, it was decided in the clinics, that the dose distributions should be shown with no heterogeneity correction, with particular attention to optimizing the dose distribution within the chest wall, choice of energy, and bolus shaping to get the 95% isodose at the costal wall.

The new technique, using one unique electron beam that included both the chest wall and the IMC target volumes, demonstrated a better dose homogeneity. With our standard technique, in which we treated the IMC separately with mixed photons and electrons, we could choose different electron energies for the IMC and the chest wall. With one unique field in the new treatment plans, the depth modulation is performed with a change in bolus thickness (0, 0.5, or 1 cm). Because the change in shape in the craniocaudal direction is well represented by five CT slices, it was possible to design a bolus from the data from our simulator CT slices. The shaping of the bolus associated with the choice of energy by step of 1.5 MeV improves the conformality of the dose distribution. Because the plan is done using five CT slices, the treatment planning time has not noticeably increased; thus, it has been possible to apply these new planning methods to all our mastectomy patients, allowing them to benefit from a more conformal plan adapted to their individual anatomy. Moreover, we have simplified the treatment delivery by suppressing the IMC field, with the boost being delivered at most twice weekly. Standard linear accelerators, other than the Saturne linear accelerators, produce electron energies by steps of 3 MeV. This implies more effort to optimize the plans because of the use of mixed electron energies or a more complex bolus (18, 23, 24). Dose distributions using the five simulator CT slices result in a gain in planning time compared with full CT-based dosimetry. This implies that there is not much variation of contour in the chest wall. A few patients, however, would benefit from a three-dimensional CT scan and a three-dimensional bolus (18). A limitation of our practice is that it was not possible to derive dose–volume histograms of the heart and lung. However, the dose distribution with electrons is strongly dependent on the TPS algorithm (27). To date, we have not used heterogeneity corrections because of the inaccuracy of our calculation model. Efforts were made to get a conformal and homogeneous dose distribution between the skin and costal wall. However, the positions of the 20-Gy and 40-Gy isodoses relative to the sternum and homolateral lung are routinely assessed as warnings to limit unnecessary heart and lung irradiation. The new technique resulted in better sparing of the underlying normal tissue, with the 20-Gy isodose about 0.7 cm shallower in the heart, and the 40-Gy isodose 0.4 cm less deep in the lung. These measurements have been used only as relative measurements to compare the two treatment plans of the same patient.

Another important point is that the early tolerance was similar to that of previously reported findings (19). In the evaluation of the standard technique in a series of 118 patients treated in 1997 at the Institut Curie, we reported Grade 1 early skin reactions in 30 patients (25%), Grade 2 in 75 patients (64%), and Grade 3 in 13 patients (11%).

CONCLUSIONS

This report describes an improvement in the standard postmastectomy electron beam technique of the chest wall. This new technique provides improved target homogeneity and conformality compared with the standard technique. This treatment was well tolerated with a low rate of early toxicity events.

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