

Irradiation with standard tangential breast fields in patients treated with conservative surgery and sentinel node biopsy: using a three-dimensional tool to evaluate the first level coverage of the axillary nodes

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Abstract. Recent data show that axillary coverage can be obtained, but only through a selective CT-based treatment planning, as standard tangential fields are inadequate to deliver therapeutic doses. Currently, the replacement of axillary dissection with new techniques, such as sentinel node (SN) biopsy, makes it necessary to re-address the question about the real role of axillary irradiation, complicated by the differences in the anatomy of dissected and undissected axillary regions. The purpose of this paper is the dosimetric analysis of first axillary level coverage in standard irradiation of 15 breast-cancer patients treated with quadrantectomy and SN biopsy (negative finding). During surgery a clip on the site of the SN was positioned, marking the caudal margin of first axillary level. After the breast treatment plan was completed, the first axillary level was contoured on CT scans, from the site of the surgical clip up to the sternal manubrium, for coverage analysis with dose–volume histograms (DVHs) and three-dimensional isodose visualization. The maximum dose mean ranged from 5% to 80% of the prescribed dose (mean value 48.7%). The mean total dose received by the volume of interest was lower than 40 Gy in all but one patient. No patient had total irradiation of first nodal level; only one patient had 35% of the volume enclosed in the 100% isodose. Our analysis lead to the conclusion that therapeutic doses are not really delivered to first level axillary level nodes by a standard tangential field technique, and that specific treatment planning and beam arrangement are required when adequate coverage is necessary.

Adjuvant radiation therapy significantly decreases the incidence of local recurrences in women treated with breast-conserving surgery for early stage breast cancer [1, 2]. The standard clinical approach for patients with none or minimal involvement of regional lymph nodes still uses tangential photons fields to irradiate the whole residual breast parenchyma. Partial breast irradiation, limited to the tumour bed, is still under evaluation and will probably be indicated in selected subgroup of patients not yet reproducibly identified [3–5].

It was generally thought that tangential fields included the lowest part of axilla [6, 7] but there has been no clear demonstration of a coverage of this area by an adequate dose. The role of tangential chest irradiation in eradicating microscopic nodal disease reported in different papers [8, 9] is still unclear. Recent data show that the axillary coverage can be obtained, but only through a selective CT based treatment planning and a three-dimensional (3D) reconstruction of the target volumes, as the standard tangential fields usually fail to deliver therapeutic doses to any of the three axillary levels [10–13]. The coverage of the nodal area with the two-portal tangential irradiation technique can be strongly dependent on different factors, including anatomy

of the patient, treatment position (use of the breast board), beam (blocks, wedges) and gantry (angles) arrangement.

Currently, the replacement of the routine axillary dissection with the introduction of new techniques for the examination of the axilla, such as sentinel node (SN) biopsy, makes it necessary to re-address the question of the real role of axillary irradiation, complicated by the differences in the anatomy of dissected and undissected axillary regions [14].

Material and methods

We analysed the treatment plans of 15 consecutive patients with invasive breast cancer (maximum tumour diameter 25 mm) treated with quadrantectomy and SN biopsy (negative finding).

Lymphoscintigraphy

The day before surgery, 5–10 MBq of technetium-99m-labelled human albumin colloidal particles was administered subdermally immediately above the breast lesion. More details on the technique are reported in previous literature [15].

Surgical procedures

A small incision was made over the area previously marked in the regional lymphatic drainage basin, and the

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area explored with a gamma-detecting probe (GDP). Once the SN was identified a metallic clip was placed in its site marking the caudal margin of first axillary level.

Radiation therapy simulation

According to our current practices, the patients were lying supine on a tilted breast board (angles from 15° to 30°) placed on the simulator couch. Alignment along the longitudinal axis was ensured using a sagittal laser and fluoroscopy. The ipsilateral arm was extended above with the hand behind the head, at an angle of between 60° and 45° to the body axis. A polyurethane foam cast was used both for the CT scan and the treatment. The reference system was taken as the mid-sternal line and a plane at 90° to this passing through the ipsilateral nipple. In order to assist the set-up for the CT imaging study, radio-opaque markers were placed on the skin at the intersection of the two axes and over the tip of the xiphoid process; metal threads were also positioned along the mid-axillary lines on both sides in such a way as to be parallel to the long axis of the simulator couch. The extension of the clinical target volume (CTV), represented by the whole gland, was first clinically defined for each patient. The superior, inferior, medial and lateral margins of the breast were detected by palpation and metallic marks were used to identify them. On average, the upper margin of the portals has usually placed at the head of the clavicle, the medial margin at less than 1 cm over the meadline, the lateral margin near the midaxillary line, and the inferior margin was drawn 1–2 cm below the inframammary fold.

A spiral CT scan (CT ProSpeed, GE Medical Systems) with 3 mm thickness and 10 mm sections was then performed, in quiet respiration, from the supraclavicular fossa to 1–2 cm below the inframammary fold. The breast CTV was outlined on each of the selected CT images. The planning target volume (PTV) was manually shaped applying from 1 cm to 1.5 cm margin to the CTV. The dimensions, the orientation of the two opposed, non parallel 6 MV tangential fields, and the characteristic of the wedge filters were defined on the treatment planning system (TPS) (Cadplan; Varian). The deep alignment of beams was used to minimize lung involvement and no collimator rotation was needed because of the breast board. The 100% tumour dose was specified at the isocentre (ICRU point). A correction factor for lung was also used to calculate the dose distribution.

Anatomical definition of the axilla

The nodal areas were identified and contoured on CT images after the preparation of the conventional breast treatment plan. The first axillary level was contoured from the site of the surgical clip up to the sternal manubrium, for the analysis of its coverage with dose–volume histograms (DVHs) and 3D isodose visualization.

Radiation therapy treatment

All patients received whole breast irradiation, 50 Gy delivered in 25 fractions are 5 weeks, and a 10 Gy boost to the tumour bed was given by a direct electron field. Seven patients were treated with a breast board angle of 15° and

eight with 30°. Nine patients were treated for superior quadrant lesions while the other six had tumours in the lower part of the breast.

Results

The mean volume of the first axillary level was 28.9 cm³, ranging from 14.5 cm³ to 58.6 cm³ with a standard deviation (SD ± 13 cm³). The mean value of the maximum dose detected in the analysed region was 94.3% of the dose prescribed to the breast (SD ± 12.9%), ranging from 55% to 105%. The mean doses delivered ranged from 5% to 80% of the prescribed dose, with a mean value of 48.7% (SD ± 21.5%). The mean total dose received was lower than 40 Gy in all but one patient, as shown in Figure 1. Minimum doses inside the volume ranged from 0 to 10% of the prescribed dose, with a mean value of 3.3% (SD ± 3.1%). No patient had total irradiation of the first nodal level and only one patient had 35% of the volume enclosed in the 100% isodose. The percentages of first axillary level volume enclosed in the 80% and 100% isodose are shown in Figure 2. The mean volume of the first axillary level receiving at least 80% of the prescribed dose was 30.7%, ranging from 0 to 70% (SD ± 22.4%); the volume encompassed by 100% isodose was even smaller: a mean value of 2.5%, ranging from 0 to 35% (SD ± 9%). Figure 3 shows the DVHs of the first axillary level for all patients, while in Figure 4 the minimum, maximum and mean DVHs are plotted. These DVHs are obtained by calculating for each dose, the minimum, maximum and the mean values, respectively, of all the observed data. Higher doses of radiation to the lowest part of the axilla were related to a low angle of the breast board, as shown in Table 1, but no statistical significance was detected. The site of the primary lesion did not significantly affect the axillary irradiated volume (Table 2).

Discussion

External beam radiotherapy using standard tangential fields after conservative surgery is the current approach in managing early stage breast cancer [1, 2]. The role of this technique in local control of breast cancer is unquestionable [16]. On the other hand, its effectiveness in reducing axillary recurrence rate is controversial although some

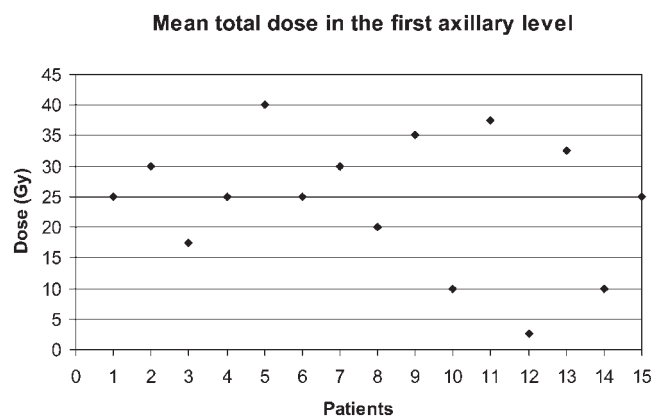


Figure 1. Mean total doses absorbed in the first axillary level, with standard therapy of 50 Gy, in 2 Gy fractions.

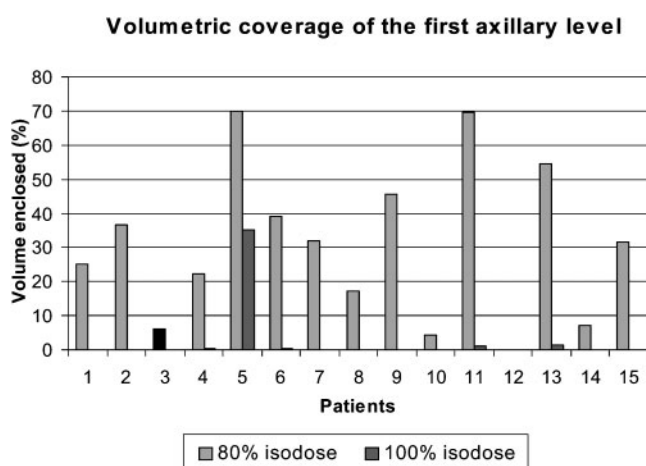


Figure 2. Volumetric coverage of the first axillary level.

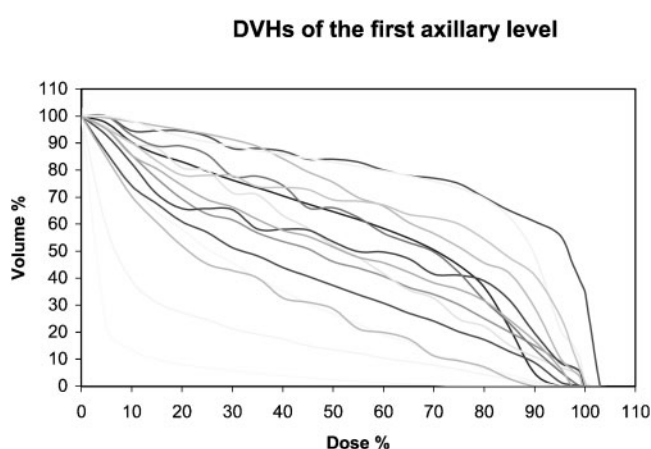


Figure 3. Dose-volume histograms (DVHs) of the first axillary level for all patients.

clinical data show that breast tangential irradiation also resulted in better axillary local control [8, 9]. X-ray simulation film based analysis shows that first axillary levels could be included in the standard tangential fields, although not expressly included in the PTV of breast irradiation [6, 7]. It is commonly thought that the lower part of the axilla often gets a significant dose of radiation that could have a tumoricidal effect. A recent analysis, based on CT scanning and 3D reconstruction, seems to

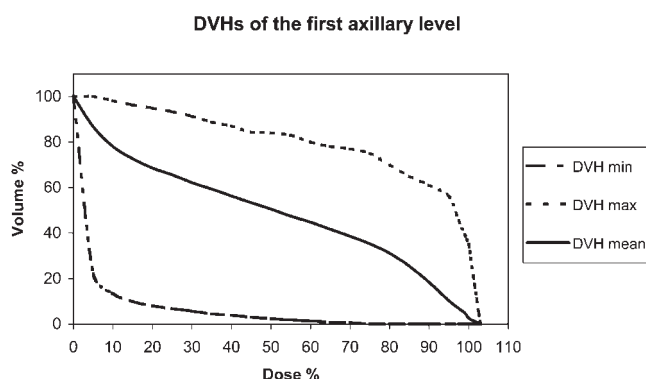


Figure 4. Minimum, maximum and mean dose-volume histograms (DVHs) of the first axillary level.

Table 1. Inclusion of first axillary level in tangential fields for breast cancer

Tilted breast board angle	% Volume in the 80% isodose (Range/Mean)	No. patients
15°	4–69/42	8
30°	0–32/18	7

Table 2. First axillary level inclusion depending on site of the primary lesion

Site of primary lesion	% Volume in the 80% isodose	No. patients
Superior	6–54/30	9
Inferior	0–70/30	5
Midline	70	1



Figure 5. First level axillary lymph nodes contoured on CT slice (arrow) and its relationship to the upper border of planned tangential fields.

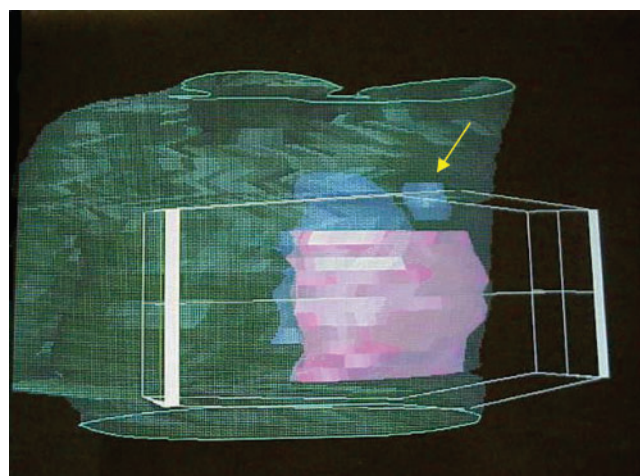


Figure 6. Surface rendered image of tangential portals of a typical patient, showing breast target volume, underlying lung and first axillary node level (arrow). Note that the first level nodes are only partially included within the tangential fields.

demonstrate that effective axillary irradiation through breast tangential fields is not so frequent [12]. The first level nodes were in fact only partially included and more importantly, not at clinically significant doses (Figures 5 and 6). Our work seems to confirm the conclusions of other papers already published [10–13], although the main characteristic of our series was the different management of patients who all had sentinel lymph node biopsy leaving the axilla undissected. As demonstrated also in our cases, only few patients had a consistent dose of radiation to the axilla while most of them received very small doses to part of the volume of interest. The volumes contoured in our patients were smaller than those reported by Krasin et al [12], with a mean value of 28.9 cm^3 (ranging from 4.5 cm^3 to 58.6 cm^3 , $\text{SD} \pm 11.3 \text{ cm}^3$). This may be due to differences in longitudinal definition of first level on the clip marker and the image definition rather than on anatomical landmarks.

While the longitudinal extension of the third axillary level is almost the same with different positions of the arm, location of first and second level is strictly dependent on arm abduction. In patients with a markedly abducted arm (CT scan position) the first axillary level begins at the aortic arch up to the sternal manubrium. Medially and above this lies the second level. The apex of the axilla (third level) is located below the central part of the clavicle, limited posteriorly and inferiorly by the first rib and anteriorly and superiorly by the clavicle itself.

In our experience the angle of the breast board did not significantly affect axillary coverage. The better volumetric coverage that was detected in patients with a lower angle seems to be related to the physical characteristics of these patients, four of them being obese with large breasts. The site of primary breast tumour also did not affect nodal coverage, as the entire breast was irradiated in all cases and the breast PTV always defined in the same way. Moreover we did not include in the analysis patients with a primary tumour located in the axillary tail.

The analysis of dose distribution shows that the axillary CTV received a mean total dose of about 25 Gy (delivered in 1 Gy fractions), with a SD of $\pm 21.5 \text{ Gy}$, too low to expect that this could affect local control. Our analysis, as has already been reported, led to the conclusion that therapeutic doses are not delivered to the first level axillary nodes by a standard tangential technique and that specific treatment planning and beam arrangements are required to achieve adequate coverage. It is probable that the reduction in axillary recurrences detected in breast irradiated patients derives from sterilization of skip metastasis, as already proposed by Krasin [12]. It is important to remember that all recent papers are based on patients who had undergone axillary dissection, and currently the surgical approach to the axilla is more often discussed and the role of axillary radiotherapy of increasing interest [14]. In order to ensure an adequate coverage of the axillary volume it will be necessary to overcome the limitation of standard irradiation.

References

- Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, 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;16:1270–1.
- Fisher B, Anderson S, Bryant J, Margolis R, Deutsch M, Fisher E, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;16:1233–41.
- Morrow M, Harris JR, Schnitt SJ. Local control following breast conserving surgery for invasive cancer: results of clinical trials. *J Natl Cancer Inst* 1995;87:1669–73.
- Vicini F, Kini VR, Chen P, et al. Irradiation of the tumor bed alone after lumpectomy in selected patients with early-stage breast cancer treated with breast conserving therapy. *J Surg Oncol* 1999;70:33–40.
- Veronesi U, Orecchia R, Luini A, Gatti G, Intra M, Zurrida S, et al. A preliminary report of intraoperative radiotherapy (IORT) in limited-stage breast cancers that are conservatively treated. *Eur J Cancer* 2001;37:2178–83.
- Wong J, Recht A, Beard C, Busse P, Cady B, Chaffey J, et al. Treatment outcome after tangential radiation therapy without axillary dissection in patients with early-stage breast cancer and clinically negative axillary nodes. *Int J Radiat Oncol Biol Phys* 1997;39:915–20.
- Recht A, Houlihan M. Axillary lymph nodes and breast cancer. *Cancer* 1995;76:1491–512.
- Fisher B, Redmond C, Poisson R, Margolis R, Wolmark N, Wickerham L, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* 1989;320:822–8.
- Ribeiro G, Magee B, Swindell R, Harris M, Banerjee SS. The Christie Hospital breast conservation trial: an update at 8 years from inception. *Clin Oncol* 1993;5:278–83.
- Smitt M, Goffinet D. Utility of three-dimensional planning for axillary node coverage with breast-conserving radiation therapy: early experience. *Radiology* 1999;210:221–6.
- Takeda A, Shigematsu N, Kondo M, Amemiya M, Kawaguchi M, Michinao S, et al. The modified tangential irradiation technique for breast cancer: how to cover the entire axillary region. *Int J Radiat Oncol Biol Phys* 2000;46:815–22.
- 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;47:327–33.
- Ariste C, Chionne F, Marsella A, et al. Evaluation of level I and II axillary nodes included in the standard breast tangential fields and calculation of the administered dose: results of a prospective study. *Int J Radiat Oncol Biol Phys* 2001;51:69–73.
- Schlembach PJ, Buchholz TA, Ross MI, et al. Relationship of sentinel and axillary level I-II lymph nodes to tangential fields used in breast irradiation. *Int J Radiat Oncol Biol Phys* 2001;51:671–8.
- Veronesi U, Paganelli G, Viale G, et al. Sentinel lymph node biopsy and axillary dissection in breast cancer: results in a large series. *J Natl Cancer Inst* 1999;91:368–73.
- Early Breast Cancer Trialists' Collaborative Group. Favorable and unfavorable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomized trials. *Lancet* 2000;355:1757–70.