Radiotherapy instead of axillary lymph node dissection: evaluation of axillary lymph node dose coverage with whole breast radiotherapy

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ABSTRACT

Background: The purpose of this study was to investigate the dose coverage of sentinel lymph nodes (SLN), level I, II and III axillary volumes from tangent fields for breast cancer patients with positive SLN without axillary dissection.

Materials and methods: In 30 patients with cN0 invasive breast cancer treated with breast conserving surgery and SLN biopsy, the SLN area was intraoperatively marked with a titanium clip. Retrospectively, the SLN area and axillary target volumes were contoured, and three plans [standard tangent fields (sTgF), high tangent fields (HTgF), and sTgF + axillary-supraclavicular field] were generated for each patient. The prescribed dose was standardized to 50 Gy in 2 Gy fractions to the isocenter.

Results: The mean dose with sTgF or HTgF was 33.1 and 49.1 Gy (p = 0.0001) in the SLN area, 25.7 and 45.1 Gy (p < 0.0001) in the volume of level I, 7.2 and 28.9 Gy (p < 0.0001) in the level II and 3.5 and 12.7 Gy (p = 0.0003) in the level III. Adequate therapeutic doses to the level II or III volumes were delivered only with sTgF + axillary-supraclavicular field. The mean dose of ipsilateral lung was the highest with the three-field-technique, 9.9 Gy. SLN area, level I, II or III were completely included in the HTgF with 93.3%, 73.3%, 13.3% and 0%, respectively.

Conclusions: SLN area should be marked by surgical clip and axillary target volumes should be contoured to obtain accurate dose estimations. The use of HTgF improve axillary coverage.

Key words: breast cancer; lymph nodes; lymph node dissection; radiation therapy

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Introduction

Recent clinical trials have shown that axillary lymph node dissection (ALND) provides no outcome benefit to N0 patients with limited sentinel lymph node (SLN) involvement who are treated with breast-conserving surgery (BCS) and whole-breast ± axillary-supraclavicular irra-
Radiation [1, 2]. In the AMAROS trial, the 5-year axillary relapse with ALND or axillary-supraclavicular radiotherapy (RT) in N0 SLN positive patients was 0.43% and 1.19%, respectively [1]. However, the need of level III axillary-supraclavicular RT is unclear for patients with limited SLN involvement [3]. In the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial [2] the cumulative incidence of nodal recurrences at 10 years was 0.5% in the ALND arm and 1.5% in the SLN biopsy alone arm (p = 0.28). The ten-year cumulative locoregional recurrence with ALND or SLN biopsy alone was 6.2% and 5.3%, respectively (p = 0.36). The Saint-Gallen guidelines state that ALND should not be completed in N0 patients with one to two macro-metastases in the SLNs after BCS and tangential field (TgF) RT [4]. The American Society of Clinical Oncology (ASCO) updated guidelines recently concluded that women with one to two metastatic SLNs treated with BCS and TgF RT should not undergo ALND [5]. As the extent of axillary surgery decreases, the radiation dose to the axillary volumes becomes important for therapy planning. In the ACOSOG Z0011 trial dose distribution in the axillary volumes were not reported in the initial publication. Jagsi et al. [6] recently analysed RT dose coverage of ALN of that trial. Most patients treated in Z0011 trial received tangential RT alone, and some received no RT at all. Some patients received directed nodal RT via a third field. They concluded that further research is necessary to determine the optimal RT approach in patients with low-volume axillary disease treated with SLN dissection alone. The purpose of this study was to evaluate the dose distribution in the axillary volumes and critical organs using different field arrangements after BCS and SLN biopsy: standard tangent fields (STgF) ± axillary-supraclavicular field (ASF), and high tangent fields (HTgF) alone. The dose to SLN biopsy area, as determined intraoperatively by surgical clip, was also studied.

Materials and methods

This study included 30 women with clinically N0 invasive breast cancer who have undergone breast conserving surgery (BCS) and SLN biopsy between November 2015 and June 2017. During surgery, SLN area had been marked with a titanium clip. Following BCS all patients had 3D-conformal RT. During CT simulation the patients were positioned supine and immobilized with both arms raised above the head using a breast board. CT images with 5 mm slice thickness were obtained. The breast irradiation was planned with two opposing tangential fields with 6 MV photons. Standard tangential field margins were determined by palpation of the breast parenchyma with the addition of 1–2 cm margin in all directions. The superior borders of these fields intended to treat the breast only, without regard to nodal coverage. Approximately 2 cm (≤ 3 cm) of lung section was included in the posterior border of the field. In patients with SLN macro metastases, supraclavicular fossa field was also used to deliver an effective dose to the axillary apex and clavicular fossa. The supraclavicular fossa field was matched to the whole breast tangential fields. Patient and treatment characteristics are shown in Table 1. All procedures were carried out in compliance with the Declaration of Helsinki and conformed to the ethical standards of human experiments in our country, and all patients pro-

Table 1. Patient and treatment characteristics (n = 30)

| Mean age, years (range) | 60 (42–79) |
|------------------------|------------|
| Pathological tumor classification | |
| T1a                    | 2          |
| T1b                    | 13         |
| T1c                    | 11         |
| T2                     | 4          |
| Sentinel lymph node status | |
| pN0                    | 25         |
| pN1mic                 | 1          |
| pN1a                   | 4          |
| Estrogen receptor (ER) status | |
| ER-positive            | 28         |
| ER-negative            | 2          |
| Histologic grade       | |
| Grade I                | 14         |
| Grade II               | 13         |
| Grade III              | 3          |
| Radiotherapy parameter | |
| Standard fractionation (25 × 2 Gy) | 9          |
| Hypo-fractionation (15 × 2.67 Gy)* | 21         |
| With boost (10–18 Gy, 2 Gy/fraction) | 9          |
| Without boost          | 21         |

*for the study, treatments of all patients were planned with standard fractionation (25 × 2 Gy)
vided written informed consent before the treat-
ment. RT was given according to our institutional
protocol, and retrospectively, for the purpose of
this study, three plans were generated for each pa-
tient using the same CT data: irradiation via STgF,
HTgF, and STgF + ASF. Axillary nodal volumes
(SLN clip area, Level I, II and III) and organs at risk
(heart and lung) were contoured using the Radia-
tion Therapy Oncology Group (RTOG) contouring
atlas [7]. The planning target volume was defined
as the CTV (clinical target volume) plus a 5-mm
expansion in all directions limiting to 5 mm below
the external skin surface.

For analyses, STgF was defined with the superior
border set at 2 cm below the humeral head, whereas
HTgF consisted of a superior border placed
at the inferior edge of the humeral head [8]. In
the HTgF technique the field was also adjusted wid-
er than the traditional standard field in the posteri-
or direction to ensure inclusion of the axillary vol-
umes, but the use of a wider field is limited by lung
radiation dose constraint. The SLN clip area was
defined as a volume of CTV with a 5 mm diameter
surrounding the clip. For the purpose of the study,
for all patients the prescribed dose to whole breast
and axillary-supraclavicular fossa was standardized
to 50 Gy in 2 Gy fractions in the isocenter. Mean
doses were calculated to characterize the doses to
the axillary volumes, heart (left-sided breast can-
er only) and ipsilateral lung. Geometric cover-
age of the axillary volumes was classified according
to the tangential field — planning target volumes
(SLN biopsy area, level I, II and III) overlap: 100%
overlap (complete coverage), < 100% overlap (par-
tial coverage), 0% overlap (no coverage, target is
out of field). Examples of coverage with a standard
or a high tangent field are given in Figure 1. All
comparisons of the mean doses were made using
two-sided paired t-tests. The level of statistical sig-
nificance was set at p < 0.05.

Results

The median number of removed SLNs was 2
(range 1–5). The mean volumes of level I, II or
III were 45.34 cm³ (range, 21.19–92.10 cm³),
13.10 cm³ (range, 5.79–39.01 cm³) and 6.86 cm³
(range, 2.60–15.18 cm³), respectively. The SLN
clip was below the level I volume in 1 case (3.3%),
in the Level I volume in 28 cases (93.3%), and in
the level II volume in 1 case (3.3%). The SLN most
caudal or cranial position was located 5 cm be-
The types and rates of geometric coverage for axillary volumes by tangential fields in patients are shown in Table 2. On simulation films, the rate of complete coverage for level I by HTgF or STgF was 73.3% and 6.7%, respectively (p < 0.0001). The rate of complete coverage with HTgF for level II or level III was 13.3% and 0.0%, respectively. Additionally, the rate of complete coverage for SLN clip area (SLNa) by HTgF or STgF was 93.3% and 53.3%, respectively (p < 0.0001). The HTgF was adjusted wider in 14 cases to improve coverage of Level I volume.

The mean doses delivered to SLNa, to level I, to level II and to level III with HTgF or STgF were 49.1 and 33.1 Gy (p < 0.0001), 45.1 and 25.7 Gy (p < 0.0001), 28.9 and 7.2 Gy (p < 0.0001) and 12.7 and 3.5 Gy (p = 0.0003), respectively. Using the three-field technique, the dose in the SLNa and level I was similar to the dose from HTgF (Tab. 3). The mean doses of critical organs are also shown in Table 3. The mean ipsilateral lung dose with HTgF or STgF was 8 Gy and 6.6 Gy (p < 0.0001). The mean lung dose was the highest with the three-field technique, 9.9 Gy. In the left-sided breast cancer patients (n = 15), the mean heart dose with HTgF or STgF was 4.7 Gy and 3.9 Gy, respectively (p = 0.0083). The mean heart dose with HTgF or STgF + ASF was 4.7 and 4.4 Gy, respectively (p = 0.5783).

The mean doses delivered to the 95% of axillary volumes from STgF or HTgF are shown in Table 4. The use of HTgF increased the doses significantly in all axillary volumes. The V20 (percentage volume received 20 Gy) for the lung with STgF, HTgF or STgF + ASF was 10.9%, 12.7% and 18.3%, respectively. Extended fields significantly increased the volume that received 20% of the prescribed dose (Tab. 4). The V30 (percentage volume received 30 Gy) for the heart with STgF, HTgF or STgF + ASF was 2.57%, 3.1% and 3.87%, respectively. Field ar-

Table 2. Type of coverage of the axillary volumes in percentages (number) of patients by tangent fields

| Coverage         | SLN | Level I         | Level II        | Level III        |
|------------------|-----|-----------------|-----------------|------------------|
|                  | STgF| HTgF            | STgF            | HTgF             |
| Complete         | 53.3 (16) | 93.3 (28)       | 6.7 (2)         | 73.3 (22)        |
| Partial          | 30 (9) | 6.7 (2)         | 73.3 (22)       | 26.7 (8)         |
| None (out of field) | 16.7 (5) | 0 (0)           | 20 (6)          | 0 (0)            |
|                  | STgF| HTgF            | STgF            | HTgF             |
| Complete         | 53.3 (16) | 93.3 (28)       | 6.7 (2)         | 73.3 (22)        |
| Partial          | 30 (9) | 6.7 (2)         | 73.3 (22)       | 26.7 (8)         |
| None (out of field) | 16.7 (5) | 0 (0)           | 20 (6)          | 0 (0)            |

SLN — sentinel lymph node; STgF — standard tangent field; HTgF — high tangent field.

Table 3. Doses in the axillary volumes and critical organs according to the field arrangement

| Regions, organs | STgF + ASF | STgF | HTgF | p-value (STgF vs. HTgF) | p-value (HTgF vs. STgF + ASF) |
|-----------------|------------|------|------|-------------------------|-------------------------------|
| SLNa            | 43.9 (12.8–51.4) | 33.1 (2.4–50.8) | 49.1 (45.1–55.8) | < 0.0001                  | 0.0183                        |
| Level I         | 44.1 (29.0–49.1) | 25.7 (1.7–48.3) | 45.1 (24.1–54.5) | < 0.0001                  | 0.4265                        |
| Level II        | 45.1 (34.5–53.5) | 7.2 (0.9–45.9)  | 28.9 (2.8–48.8)  | < 0.0001                  | < 0.0001                      |
| Level III       | 45.6 (21.7–56.6) | 3.5 (0.6–34.8)  | 12.7 (1.7–45.0)  | 0.0003                    | < 0.0001                      |
| Lung*           | 9.9 (3.4–17.3)   | 6.6 (2.4–12.8)  | 8.0 (3.9–13.3)   | < 0.0001                  | 0.0043                        |
| Heart**         | 4.4 (1.7–10.9)   | 3.9 (1.6–6.2)   | 4.7 (1.9–8.0)    | 0.0083                    | 0.5783                        |

STgF + ASF — standard tangent field + axillary-supraclavicular field; HTgF — high tangent field; SLN — sentinel lymph node area; *ipsilateral lung; **left sided breast cancer.
The correlation between the geometric overlap with high tangent fields and the mean dose or D95 of target volumes was also studied in the cases of 100% overlap. Complete geometric coverage resulted generally in good dose coverage (Tab. 5).

**Discussion**

The locoregional control benefit of axillary treatment in invasive breast cancer was established first by the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-04 trial, which randomized patients with clinically lymph node-negative disease to 1 of the 3 arms: radical mastectomy, total mastectomy with axillary irradiation, or total mastectomy alone without axillary treatment. Patients with an untreated axilla had a significantly greater risk of regional failure compared with those who either received axillary RT or underwent dissection, although no survival differences were observed between the groups. Surgery and RT were equally efficacious for axillary control. In the NSABP B-04 trial postmastectomy radiotherapy was delivered with the three-field technique, tangent and direct supraclavicular-axillary fields [9]. In the Z0011 trial [2] the whole breast irradiation was delivered with tangent fields and the supraclavicular-axillary field seldom was used. However, the risk of positive axillary nodes left behind is high for cN0 patients, treated only with SLN biopsy. In a randomized study from the National Institute of Oncology Budapest [10] the rate of positive axilla for clinically N0 patients, dissected following positive SLN biopsy, was 38.5%.

In the present study, we evaluated the coverage of axillary volumes and the dose of critical organs using three different RT field arrangements to irradiate clinically node negative breast cancer patients following SLN biopsy and BCS. There are some reports about the doses to the axillary lymph node region from postoperative whole-breast radiation, but the relationship between the SLN location and the whole-breast tangential field has not been sufficiently investigated. In our patients, during surgery the SLN area was marked with a titanium clip which is mandatory for accurate target volumes definition. The SLN clip was below the level I volume in 1 case (3.3%), in the level I volume in 28
cases (93.3%), and in the level II volume in 1 case (3.3%). In a multicenter validation study, the SLNs were found in level I in 89% of the patients [11]. In the study of Wadasaki et al. [12], the SLN locations were detected by SPECT/CT, and at 68 patients (98.5%) the SLNs were located in the level I region. In our cases, the SLN was located in most caudal or cranial position at 5 cm below the clavicle and 1 cm superior to the base of the clavicle, respectively. In the study of Rabinovitch et al., these distances were 6.5 cm and 1.5 cm, respectively [13]. Zunino et al. [14] intended to irradiate the breast only and the SLN clip was covered by the tangent fields in 61% of the cases. In our patients the SLN clip area was completely covered with STgF or HTgF in 53.3% (16/30) and 93.3% (28/30) of the cases. In the study of Belcacemi et al. [15], radiation therapy was planned to treat the breast alone and 38% of the SLN clips were inside the tangent fields. Rabinovitch et al. [13] used STgF and 78% of the SLN clips was completely within the treated breast fields. In the prospective evaluation of Belcacemi et al., SLN biopsy area was completely covered by the TgF in 12 of 25 patients (48%), independently of the TgF size, but HTgF was used only in five patients [8]. In their study, the use of HTgF instead of STgF significantly increased the mean dose of axillary volumes, SLN area: 45 Gy vs. 30 Gy and level I volume: 38 Gy vs. 22 Gy. These results are close to our findings, SLN area: 49 Gy vs. 33 Gy (p < 0.0001) and level I: 45 Gy vs. 26 Gy (p < 0.0001). In another analysis of Belcacemi et al. [15], the mean dose of level I volume with STgF or HTgF was 20 Gy and 33 Gy, respectively (p < 0.0001), but the mean dose of level II volume was only 11 Gy and 4 Gy (p = 0.002). They concluded that the tangential fields can allow only a limited coverage of the axilla. In our patients, the mean dose of level II volume was somewhat higher: with HTgF or STgF 29 Gy and 7 Gy, respectively (p < 0.0001), but the geometric coverage of level II volume by HTgF was complete only in four patients. Aguiar et al. [16] intended to treat only the breast and the mean doses of level I, II or III were 43.9 Gy, 38.6 Gy and 19.5 Gy, respectively. Higher doses were associated with the more voluminous and pendulous breasts. Csenki et al. [17] used only STgF to treat the whole breast and the mean dose of Level I, II or III volumes were 37.7 Gy, 13.8 Gy and 1.6 Gy, respectively. In both studies the conclusion was that axillary coverage with whole breast radiotherapy seems to be insufficient. Mayinger et al. [18] compared helical Tomo Therapy (TT) with 3D conformal conventional tangent field RT. TT improved dose coverage of level I but it was not efficient (TT or 3D conformal RT mean dose: 31.6 Gy and 24.0 Gy, respectively).

It is estimated, that using STgF, more than 50% of level I and 20% to 30% of level II nodes receive 95% of the prescribed radiation dose. This is dependent on patient anatomy and where the radiation oncologist sets the upper border of TgF [3]. Nagar et al. [19] evaluated 30 patients and the D95 (dose to 95% of volume) received by level I and level II volumes increased from 16.38 Gy and 5.71 Gy for STgF, to 49.38 Gy and 48.08 Gy for HTgF, respectively. The modified tangent fields resulted in a very good dose coverage but the borders of HTgF were not defined exactly. They stated: “Tangent treatment fields were modified to include Ax1 and Ax2 to 95% of the prescribed dose”. In our patients the HTgF was also adjusted wider in 14 cases to improve coverage of level I volume. Therefore, the use of the modified tangent field technique is more exact definition than the high tangent field technique. In the study of Alco et al. [20], HTgF was simulated for 30 patients. The mean D95 for level I or level II was 16.79 Gy and 11.59 Gy, respectively. They concluded, that HTgF do not adequately cover the level I and II axillary lymph node regions. In our study the mean D95 even with HTgF was also insufficient: in level I or level II 29.08 Gy and 11.20 Gy, respectively.

We also studied the geometric coverage of axillary target volumes with tangent breast fields. The geometric coverage was very insufficient with STgF, but the use of HTgF improved the results significantly. The rate of complete coverage of SLNa, level I, II or III volumes was 93.3%, 73.3%, 13.3% and 0%, respectively. Our results show that the complete coverage of level II volume even with modified tangent field is very poor.

Variability in contouring the targets between the institutions is substantial but level II volume shows lower variation. In our patients the mean value of level II volume was 13 cm$^3$ and in the studies using RTOG Atlas, the mean volumes were also under 20 cm$^3$ [16, 17, 20]. Nodal target volume definition in breast cancer radiotherapy using RTOG or European Society for Radiotherapy and Oncol-
ogy (ESTRO) atlas has been debated [21, 22]. We used the RTOG atlas due to the earlier introduction and the available published results. In early breast cancer, ESTRO guidelines have been preferred recently because of the improved coverage of the upper part of the axilla. Independently of the contouring methods, the dose of upper axilla from tangent breast fields is not sufficient.

In the study of Nitche et al. [23] the use of HTgF significantly increased the mean heart dose: STgF or HTgF 3.9 Gy and 4.7 Gy, respectively. In our patients the mean values were also 3.9 Gy and 4.7 Gy (p = 0.0083). In the study of Alco et al. [20] the tangential field was shaping with multi-leaf collimators according to axillary level volumes. This technique increased the mean lung dose significantly, with HTgF or multi-leaf collimators HTgF: 6.5 and 9.6 Gy, respectively (p < 0.0001). In our patients the mean lung dose was 8.0 Gy (range: 3.9–13.3 Gy) with HTgF and the three-field technique further increased the mean lung dose: 9.9 Gy (range: 3.4–17.3 Gy). Using modified tangential irradiation technique, the lateral border of the field is also extended laterally to include the level I and II axillary lymph nodes. Ohashi et al. [24] stated that the deep tangential field increases the lung dose. In our study the use of HTgF also increased significantly the doses to the lung and heart compared with STgF irradiation. At our patients the use of the three-field technique increased both mean lung dose and V20 of the lung compared with HTgF irradiation. In our patients with high risk (three SLNs positive, primary tumor 3–4 cm, lympho-vascular invasion is present, ER negative cancer). Tangent field RT and systemic therapy provide good locoregional control for low risk cN0 patients with 1–2 positive SLN, in spite of the inadequate dose coverage of level I–II regions [2]. In the propensity score matching analysis of BIG02/98 and BCRG005 trials regional nodal irradiation (RNI) did not improve outcomes [25]. However, in these trials RNI was given after ALND and the target volume was the anatomic site of the dissected axillary lymph nodes. Following SLN biopsy without axillary dissection the target volumes are the undissected lymph nodes with risk of metastases.

Conclusions

For women with SLN positive breast cancer in whom primary RT is used to treat the axilla, the knowledge of the axillary anatomy is necessary for a proper design of the tangential field borders. To understand the impact of that stipulation, it is necessary to understand the anatomic relationship of the axillary lymph nodes to the tangential RT fields used for treatment of the breast. It is important to underline that due to the paradigm shift, the target volumes are the undissected lymph nodes with risk of metastases and not the dissected axilla. Without studying the dose coverage in the accurately contoured axillary target volumes, the unresolved issues (how axillary dose coverage affects endpoints, such as axillary recurrence, locoregional failure, pulmonary toxicity and distant metastasis) cannot be answered. In terms of coverage of SLN region and level I axilla, the use of modified (extended) tangent field instead of the three-field technique, seems to be an appropriate treatment only for selected low risk SLN positive cN0 patients.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Statement of ethics

The paper is exempt from ethical committee approval, because the patients received their treatment according to our clinical protocol, and the treatment planning evaluation was carried out retrospectively.
Author contributions
B.B., J.F., T.M.: substantial contributions to conception and design, drafting of the manuscript, performing statistical calculations; Z.Z., D.M.: revision of radiotherapy planning; C.P., T.M., Z.M., B.D.: critical revision for important intellectual content.

Data availability statement
All data generated or analyzed during this study are stored locally at our institution and are available on request.

References
1. Donker M, van Tienhoven G, Straver ME, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22033 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 2014; 15(12): 1303–1310, doi: 10.1016/S1470-2045(14)70460-7, indexed in PubMed: 25439688.
2. Giuliano AE, Ballman K, McCall L, et al. Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases: Long-term Follow-up From the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 Randomized Trial. Ann Surg. 2016; 264(3): 413–420, doi: 10.1097/SLA.0000000000001863, indexed in PubMed: 27513155.
3. Haafy TG, Hunt KK, Harris JR, et al. Positive sentinel nodes without axillary dissection: implications for the radiation oncologist. J Clin Oncol. 2011; 29(34): 4479–4481, doi: 10.1200/JCO.2011.36.1667, indexed in PubMed: 22042942.
4. Goldhirsch A, Winer EP, Coates AS, et al. Panel members. Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. Ann Oncol. 2013; 24(9): 2206–2223, doi: 10.1093/annonc/mdt303, indexed in PubMed: 23917950.
5. Lyman GH, Temin S, Edge SB, et al. American Society of Clinical Oncology Clinical Practice. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2014; 32(13): 1365–1383, doi: 10.1200/JCO.2013.54.1177, indexed in PubMed: 24663048.
6. Jaggi R, Chaudha M, Moni J, et al. Radiation field design in the ACOSOG Z0011 (Alliance) Trial. J Clin Oncol. 2014; 32(32): 3600–3606, doi: 10.1200/JCO.2014.56.5838, indexed in PubMed: 25139994.
7. White J, Tai A, Arthur D, Buchholz T, MacDonald S, Marks L, et al. Breast Cancer Atlas for Radiation Therapy Planning: Consensus Definition. RTSG website. http://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.
8. Belkacemi Y, Bigorie V, Pan Q, et al. Breast radiotherapy (RT) using tangential fields (TgF): a prospective evaluation of the dose distribution in the sentinel lymph node (SLN) area as determined intraoperatively by clip placement. Ann Surg Oncol. 2014; 21(12): 3758–3765, doi: 10.1245/s10434-014-3966-1, indexed in PubMed: 25096388.
9. Fisher B, Anderson S, Bryant J, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. N Engl J Med. 2002; 347(8): 567–575, doi: 10.1056/NEJMoa020128, indexed in PubMed: 12192016.
10. Sávolt Á, Péley G, Polgár C, et al. Eight-year follow up result of the OTOASOR trial: The Optimal Treatment Of the Axilla - Surgery Or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer: A randomized, single centre, phase III, non-inferiority trial. Eur J Surg Oncol. 2017; 43(4): 672–679, doi: 10.1016/j.ejso.2016.12.011, indexed in PubMed: 28139362.
11. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer—a multicenter validation study. N Engl J Med. 1998; 339(14): 941–946, doi: 10.1056/NEJM199810013391401, indexed in PubMed: 9753708.
12. Wadasaki K, Nishibuchi K. Relationship between sentinel lymph nodes and postoperative tangential fields in early breast cancer, evaluated using SPECT/CT. J Radiat Res. 2015; 56(5): 835–840, doi: 10.1093/jrr/rvv035, indexed in PubMed: 26062810.
13. Rabinovitch R, Ballonoff A, Newman F, et al. Evaluation of breast sentinel lymph node coverage by standard radiation therapy fields. Int J Radiat Oncol Biol Phys. 2008; 70(5): 1468–1471, doi: 10.1016/j.ijrobp.2007.08.064, indexed in PubMed: 17967511.
14. Zunino SB, Garrigo ER, Garello NC, et al. Dose received by the sentinel node volume during tangential radiation therapy to the breast. Radiother Oncol. 2007; 82(3): 329–331, doi: 10.1016/j.radonc.2007.01.003, indexed in PubMed: 17257701.
15. Belkacemi Y, Allab-Pan Q, Bigorie V, et al. The standard tangential fields used for breast irradiation do not allow optimal coverage and dose distribution in axillary levels I-II and the sentinel node area. Ann Oncol. 2013; 24(8): 2023–2028, doi: 10.1093/annonc/mdt151, indexed in PubMed: 23616280.
16. Aguia A, Gomes Pereira H, Azevedo I, et al. Evaluation of axillary dose coverage following whole breast radiotherapy: variation with the breast volume and shape. Radiother Oncol. 2015; 114(1): 22–27, doi: 10.1016/j.radonc.2014.10.005, indexed in PubMed: 25454171.
17. Csenki M, Ujhidy D, Cserháti A, et al. Radiation dose to the nodal regions during prone versus supine breast irradiation. Ther Clin Risk Manag. 2014; 10: 367–372, doi: 10.2147/Tcrm.s59483, indexed in PubMed: 24876782.
18. Mayinger M, Born KJ, Dreher C, et al. Incidental dose distribution to locoregional lymph nodes of breast cancer patients undergoing adjuvant radiotherapy with tomotherapy - is it time to adjust current contouring guidelines to the radiation technique? Radiat Oncol 2019; 14(1): 1:135, doi: 10.1186/s13014-019-1328-7, indexed in PubMed: 31370876.
19. Nagar H, Zhou L, Biritz B, et al. Is there a tradeoff in using modified high tangent field radiation for treating an undissected node-positive axilla? Clin Breast Cancer. 2014; 14(2): 109–113, doi: 10.1016/j.clbc.2013.10.004, indexed in PubMed: 24291379.
20. Alço G, Iğdem SL, Ercan T, et al. Coverage of axillary lymph nodes with high tangential fields in breast radiotherapy.
21. Duma MN. An Update on Regional Nodal Irradiation: Indication, Target Volume Delineation, and Radiotherapy Techniques. Breast Care (Basel). 2020; 15(2): 128–135, doi: 10.1159/000507040, indexed in PubMed: 32398981.

22. Loganadane G, Truong PT, Taghian AG, et al. Comparison of Nodal Target Volume Definition in Breast Cancer Radiation Therapy According to RTOG Versus ESTRO Atlases: A Practical Review From the TransAtlantic Radiation Oncology Network (TRONE). Int J Radiat Oncol Biol Phys. 2020; 107(3): 437–448, doi: 10.1016/j.ijrobp.2020.04.012, indexed in PubMed: 32334035.

23. Nitsche M, Temme N, Förster M, et al. Tangential vs. defined radiotherapy in early breast cancer treatment without axillary lymph node dissection: a comparative study. Strahlenther Onkol. 2014; 190(8): 715–721, doi: 10.1007/s00066-014-0681-6, indexed in PubMed: 24838410.

24. Ohashi T, Takeda A, Shigematsu N, et al. Dose distribution analysis of axillary lymph nodes for three-dimensional conformal radiotherapy with a field-in-field technique for breast cancer. Int J Radiat Oncol Biol Phys. 2009; 73(1): 80–87, doi: 10.1016/j.ijrobp.2008.04.003, indexed in PubMed: 18602764.

25. Qi WX, Cao Lu, Xu C, et al. Adjuvant regional nodal irradiation did not improve outcomes in T1-2N1 breast cancer after breast-conserving surgery: A propensity score matching analysis of BIG02/98 and BCIRG005 trials. Breast. 2020; 49: 165–170, doi: 10.1016/j.breast.2019.11.001, indexed in PubMed: 31812892.