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ORIGINAL PAPER

Comparison of Photon with Electron Boost in Treatment of Early Stage Breast Cancer

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Abstract In the treatment of early stage breast cancer breast conserving surgery (BCS) followed by whole breast irradiation (WBI) is a standard method. The impact of the tumor bed boost following WBI is well-defined, but there are various delivery methods. In this study the electron and the photon boost techniques were compared. For 78 early stage breast cancer patients both CT based 3D conformal photon boost and electron boost plans were created. For dosimetric comparison coverage index (CI), external volume index (EI) and conformality index (COIN) were studied. Lung volume receiving a dose of 2 Gy was also reviewed. Seventy-eight patients with 156 plans were compared. The mean tumor bed volume was measured as 61.39 cm^3 the mean tumor bed-skin distance was 3.13 cm. In the case of CI and COIN significant differences were found in favor of the photon boost. In the comparison of EI no significant difference was detected between the two techniques. The mean lung volume receiving 2 Gy were 42.3 and 168.35 cm^3, for photons and electrons respectively. In the adjuvant treatment of early stage breast cancer WBI followed by conformal photon boost showed to be superior to electron boost in focus of the COIN and CI.

Keywords Boost · Breast cancer · Radiotherapy · Photon · Electron

Introduction

Breast conserving surgery followed by whole breast irradiation (WBI) is the gold standard in the treatment of early stage breast cancer. There are several randomized, controlled trial data to demonstrate the local control and survival benefit of this treatment modality [1–3]. The standard irradiation therapy typically includes two tangential fields with a total dose of 50 Gy in 5–6 weeks treatment time with daily treatment, followed by a boost dose to the tumor bed.

The role of the additional tumor bed boost in the local tumor control is evident, in the United State and in Europe the boost is the part of the standard treatment for selected high-risk patients [4, 5]. Usually five to eight fractions are given after the WBI. The delivery method of the tumor bed boost is not standard, direct field electron, conformal photon, intensity modulated radiotherapy (IMRT), interstitial high dose rate afterloading (HDR-AL) are the most common used techniques [6].

For tumor bed definition preoperative mammographical data, surgical clips, CT scans, ultrasound data, postoperative skin scars can be used. Studies have shown that planning target definition for boost irradiation without the use of surgical clips and/or CT were inadequate in 70–80% [7–12].

In our institute for early stage breast cancer patients after the WBI the CT based 3D conformal photon boost therapy has been used since 2003. The purpose of this retrospective study was to compare the 3D conformal photon boost to electron boost in focus of the conformality index (COIN), coverage index (CI) and external volume index (EI).

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Materials and Methods

Patient Characteristics

Between January 2004 and June 2005, 78 early stage (Stage I–II) breast cancer patients were treated in our institute with whole breast irradiation (WBI) after breast conserving surgery (Table 1). 40 patients were classified as Stage I (T1, N0), and 38 as Stage II (T1–T2 with N0–N1 and T3, N0) disease. Staging was based on the classification rules of American Joint Committee on Cancer (AJCC) Staging Manual, Sixth Edition [13].

Treatment Planning

All patients had 3D CT based WBI planning, using Theraplan@ Plus Software (MDS Nordion, 2001). Planning target volumes (PTV) were contoured on axial CT slices (8 mm slice thickness, 5 mm spacing), used routinely in our institute.

For WBI planning two tangential beams were used with the respect of the critical structures (lung, heart, caput humeri, contralateral breast). The total dose of 50.4 Gy in 1.8 Gy fractions was prescribed to a normalization point on the central CT slice 2 cm from the posterior border of the tangent fields, according to ICRU recommendations [14]. If such a defined point was within the lung parenchyma, it was moved anteriorly toward the chest-wall interface.

For the photon boost plans two oblique, wedged fields were applied with the respect of the critical structures. 10 Gy of boost dose was prescribed to the tumor bed, with the minimal coverage of 90% of the target. For photon boost the dose normalization to the maximum dose was chosen instead of normalization to isocentre in order to compare the two methods correctly. All patients in our study received photon boost therapy, and for all of them individual electron boost plans were also made, using the optimal electron field and optimal electron energy—available in our system (14 MeV max energy and fixed electron applicators)—to reach the best tumor bed coverage, with the respect of the lung tissue. For electron boost 90% of the maximum was chosen as prescription isodose line if the resulting coverage index was acceptable, but if this was unacceptable lower percentage was chosen to improve the coverage index.

Table 1 Patient characteristics

Characteristics	Number (*n*)
Patients	78
Left side	38
Right side	40
Stage (AJCC classification)	
Stage I (T1, N0)	40
Stage II (T1–T2 with N0–N1 and T3 N0)	38
Tumor site	
Left side	
Upper inner quadrant	8
Upper outer quadrant	27
Lower inner quadrant	0
Lower outer quadrant	2
Central	1
Right side	
Upper inner quadrant	1
Upper outer quadrant)	31
Inferior inner quadrant	5
Inferior outer quadrant	2
Central	1
Surgery	
Excision with SLNB or AXD	72
Excision without SLNB or AXD	6
Reexcision	3
Surgical margin	
Close (4–9 mm)	53
Safe (≥10 mm)	16
Unknown	9
Tumor bed clips	
No clip	18
Single clip	39
Multiple clips (range: 2–7, mean=4)	21
Chemotherapy/hormonal therapy	
Chemotherapy	46
Hormonal therapy	72

SLNB Sentinel lymph node biopsy, *AXD* axillary dissection

Tumor Bed Definition

Placement of the surgical clips in the excision site is accepted as the gold standard. In the cases surgical clips were not implanted, preoperative mammography, ultrasound data, surgical description and postoperative CT scans were used for tumor bed definition. A team of three physicians (two independent radiologists and a radiation oncologist) determined by consensus what was the tumor bed. A 1 cm margin was added to tumor bed with the respect of anatomical structures and pathological data. This volume was defined as planning target volume (PTV). Tumor beds with unknown margin data were contoured as close margin cases. The tumor bed-skin distance was measured as the tumor bed isocenter-skin surface distance.

Plan Comparison

For plan comparison the conformality index (COIN), the coverage index (CI), the external volume index (EI) and the lung volume receiving the dose of 2 Gy were studied.

Coverage Index is the fraction of the planning target volume (PTV) receiving a dose equal to or greater than the reference dose (PTVref/V_{PTV}) [15]. Higher CI ratio means better coverage of the PTV.

External volume index (EI) is the ratio of the normal tissue volume outside the PTV receiving a dose equal to or greater than the reference dose, to the PTV. Lower EI means smaller normal tissue exposure.

The conformality index (COIN) takes into consideration the coverage of the PTV by the reference dose and also the unwanted irradiation of normal tissue outside the PTV. By definition, COIN=c1×c2, where c1=PTVref/V_{PTV} and c2= PTVref/Vref. The PTVref is the volume of the PTV receiving a dose equal to or greater than the reference dose. The V_{PTV} is the volume of the PTV and Vref is the volume receiving a dose equal to or greater than the reference dose. In an ideal case both c1 and c2 are equal to 1 [15].

Statistical Analysis

For evaluating the data, paired *T*-test was used. When comparing the data series, the mean values were confronted in all cases and, during evaluation, a significance level of $p \leq 0.05$ was considered to be a significant difference.

Results

For data acquisition photon plan and electron plan summed dose volume histograms (DVH) and planning CT scans were used (Fig. 1). All data was collected and studied with Microsoft Excel Software (Table 2).

The mean tumor bed volume was measured as 61.39 cm^3 (median: 53.8 cm^3, range: 10–165.3 cm^3, SD: 33.68), the mean tumor bed-skin distance was 3.13 cm (median: 3.22 cm, range: 0.84–4.9 cm, SD: 0.84).

In the case of the coverage index (CI photon mean= 0.97, median: 0.98, range: 0.86–1.00, SD:0.03; CI electron mean=0.77, range: 0.36–1.00, median: 0.79, SD:0.18; $p \leq$ 0.001) and the conformality index (COIN photon mean= 0.34, median: 0.34, range: 0.14–0.6, SD:0.09; COIN electron mean=0.22, median: 0.2, range: 0.05–0.49, SD:0,11; $p \leq 0.001$) significant differences were found in the favor of the photon boost.

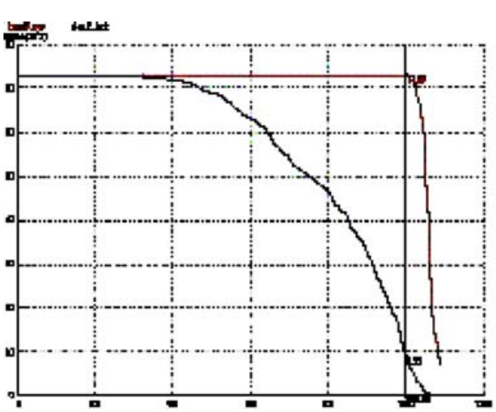

Fig. 1 Summed dose volume histogram (DVH) of a photon (*red line*) and electron (*blue line*) boost plan

In the comparison of external volume indexes (EI) no significant difference was detected in the favor of the photon boost (EI photon mean=2.02, median: 1.79, range: 0.54–6.05, SD: 0.92; EI electron mean=2.31, median: 2.12, range: 0.02–6.19, SD: 1.17; $p=0.167$).

The mean lung volume receiving 2 Gy was measured 42.03 cm^3 (range=0.7–333.4 cm^3, median: 24 cm^3, SD: 55.76) in case of photon, and 168.35 cm^3 (range=0–879 cm^3, median: 132.75, SD: 164.51) in case of electron plans. The difference was significant ($p \leq 0.001$) in favor of the photon boost plans.

Using the tumor bed-skin distance data and coverage indexes, a polinomic based calculation was delivered to demonstrate the relation between tumor bed depth to coverage index in case of electron plans (Fig. 2).

Discussion

In the modern radiotherapy of breast cancer patients, the role of the tumor bed boost is well defined. Randomized, controlled studies have shown the impact of the boost on the local tumor control [4, 5]. The relative reduction in local failure is about 20–50%, reported in various boost studies. In the patient selection women under 40 years of age are routinely recommended to receive tumor bed boost. Big tumor size, close surgical margins, high grade invasive ductal or in situ ductal tumors, high mitotic index, hormone receptor negative tumors or no possible hormonal therapy are additional risk factors for local recurrence [6].

The delivery method of the boost can be various: the main possible techniques are the photon, the electron and the high dose rate afterloading brachytherapy (HDR-AL) boost, either intraoperatively or delayed until after whole-breast irradiation. In focus of local control and side effects the interstitial brachytherapy (BT) compared to external beam techniques, BT seems to be equal or even better in case of deep situated tumors [16, 17]. With the using of the implanted catheters errors originating from breath synchron movements and daily setup can be reduced, and in addition if the catheters are implanted into the tumor bed intra-operatively the most accurate tumor bed definition can be achieved [18]. There are many institutes where direct electron field is used focused on the skin scar for boost irradiation of the tumor bed. Multiple studies have shown the high likelihood of missing the true peri-lumpectomy target volume if clinical localization focusing on the scar is used [7, 8, 19].

The goal of our study was to compare the CT based 3D conformal photon boost to electron boost in the treatment

Table 2 In the cells the mean, the median, the range and the SD values are shown

Characteristic	Photon boost	Electron boost	p value
Mean CI	0.97 (median: 0.98, range: 0.86–1, SD: 0.03)	0.77 (median: 0.79, range: 0.36–1, SD: 0.18)	≤0.001
Mean EI	2.02 (median: 1.79, range: 0.54–6.05, SD: 0.92)	2.31 (median: 2.12, range: 0.02–6.19, SD: 1.17)	0.167
Mean COIN	0.34 (median: 0.34, range: 0.14–0.6, SD:0.09)	0.22 (median: 0.2, range: 0.05–0.49, SD: 0.11)	≤0.001
Mean lung volume 2 Gy (cm^3)	42.03 (median: 24, range: 0.7–333.4, SD: 55.76)	168.35 (median: 132.75, range: 0–879, SD: 164.51)	≤0.001

In case of CI and COIN significant difference were found in favor of photon boost

of early stage breast cancer in focus of coverage index, conformality index and external volume index. These objective indexes were adopted from the studies of Knoos et al., Baltas et al. and Major et al [15, 20, 21].

In tumor bed boost irradiation the tumor bed definition is a very important question. CT scans are useful to localize the postlumpectomy cavity [22, 23], ultrasonography can also be used for it [21], the placement of surgical clips at lumpectomy cavity seems to be the most optimal way to assist tumor bed localization. To date there have been several studies comparing the accuracy of clinical localization to the use of surgical clips. In a number of the early studies no clear definition was given for adequacy of target coverage. In more recent studies, 'adequate' coverage has been variously defined, ranging from surgical clips being within the treatment fields, to requiring inclusion of a margin of up to 2 cm around all clips. Depending on these definitions and the precise method of clinical localization, the accuracy of clinical localization ranged from 26% to 83%. Clinical set up covering the surgical scar with a minimum 1 cm margin in each direction resulted in a 39% rate of adequate coverage, defined as inclusion of all surgical clips with at least a 1 cm margin. Higher rates of adequacy were found when larger clinical margins of up to 4 cm were used, however for many patients this would approximate whole breast irradiation [7–12, 19, 22, 24, 25].

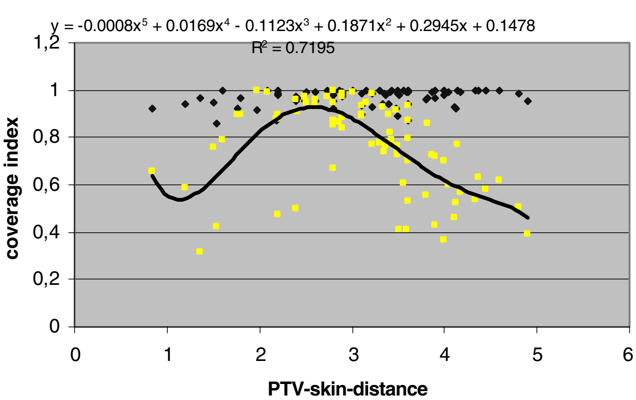

Fig. 2 Tumor bed depth (*x* axis in cm) relation to the coverage indexes (*y* axis) for electron (*yellow points*) and photon (*blue points*), with a polinomic calculated line for electron

A study designed by Smitt et al. found that both the ability to visualize the excision cavity and the cavity size declined over time; results were similar for CT and ultrasound, highlighting the potential for treating excess normal tissues if boosts were planned based on CT scans in the early post-operative period (30 days) [23]. Regine et al. compared both clinical set up and CT planning to surgical clips and found CT planned boosts adequate in 17/17 cases, as compared to 5/17 for clinical set-up [22].

In our study 60/78 patients (76.9%) had surgical clips on the tumor bed, but only 21 (23%) of them had multiple clips. In these cases the number of implanted clips ranged from 2 to 7, the mean number was 4 (Table 1). For the ideal tumor bed marking six clips should be used, marking the tumor bed borders in all directions. Not all of our patients had surgery in clinical centers and due to various reasons not all surgeons use clips. In cases of no surgical clips were present in the tumor bed cavity we used preoperative mammographical and ultrasound data, surgical descriptions and postoperative CT scans for the tumor bed definition.

Our results demonstrate that 3D CT based photon boost irradiation gives better coverage to the tumor bed and higher conformality compared to electron boost. Using the photon boost lower irradiated lung volumes can be achieved (Table 2).

The tumor bed center-skin distance can be identified easily using the planning software measure tool. This data gives a more clear possibility for tumor bed classification. In focus of our results tumor beds with the tumor bed center-skin distance higher than 4 cm, should be treated with conformal photon boost. In case of tumor bed-skin distance 2–4 cm electron boost gives good tumor bed coverage, similar to photon boost. For the superficial targets (tumor bed-skin distance 1–2 cm) photon boost seems to be the better choice (Fig. 2).

Beside the tumor control, in the radiotherapy of breast cancer patients the cosmetic outcome is very important question. The local control is prior to cosmetic outcome, the boost treatment must be given to the patients candidate for tumor bed boost [6]. In the EORTC and Lyon boost studies the cosmetic outcome was significantly better in the no boost group [4, 5]. In our study the mean tumor bed volume was measured as 62.5 cm^3. This volume is lower compared to EORTC “boost-versus-no boost” trial’s photon boost volume (288 cm^3), and on the same level to interstital HDR-AL boost volume (60 cm^3) [26]. In the EORTC study the best cosmetic results were presented in case of HDR-AL boost, using the smallest PTV volumes. The CT based 3D planning allowed us to use well defined and small PTV volumes. Using lower irradiated volumes, better cosmetic outcome can be accepted. Beside the boost method other important factors influences on the cosmetic outcome include tumor location, size of excision, breast size and operative complications [6].

This study was designed to compare the photon boost to electron boost, using objective indices. The clinical follow up of our patients is ongoing, till Jan 1, 2006 no local recurrences were registered. Further follow up planned for the evaluation of the local control, lung toxicity and cosmetic results.

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