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Local recurrence of breast cancer: conventionally fractionated partial external beam re-irradiation with curative intention

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Abstract

Purpose To assess the outcome of breast cancer patients with local recurrence who underwent partial external beam re-irradiation (re-RT) either as part of a second breast-conserving therapy or following mastectomy.

Methods Between 03/2004 and 10/2016, 83 breast cancer patients with local recurrence were treated with surgery followed by re-RT. The re-RT schedules were 45 Gy (1.8 Gy per fraction) administered either to the partial breast ($n=42$) or mastectomy scar ($n=41$). The patients and tumor characteristics predictive of local control, distant control, and survival (overall and breast-cancer specific) were evaluated by univariate and multivariate analyses.

Results The median follow-up was 35 months (range 3–143 months). The median time interval between the first irradiation and re-RT was 117 months (range 16–357 months). The prognostic factors for favorable overall survival rates were younger age ($p=0.045$), lower T-category ($p=0.019$), and N0 category ($p=0.005$). N0 was also superior to N+ with respect to outfield recurrences ($p=<0.001$) and breast cancer-specific survival ($p=0.025$). Acute and late skin toxicity was generally low (<grade 3).

Conclusion Re-RT with 45 Gy (1.8 Gy per fraction) for partial breast or mastectomy scar after the second surgery resulted in high local control rates and tolerable skin toxicity.

Keywords Breast cancer recurrence · Partial re-irradiation · Mastectomy · Breast conserving surgery · External beam radiotherapy

Das lokal begrenzte Brustkrebsrezidiv: konventionell fraktionierte partielle perkutane Rebestrahlung in kurativer Intention

Zusammenfassung

Zielsetzung Das onkologische Ergebnis nach partieller perkutaner Rebestrahlung (Re-RT) bei Brustkrebspatientinnen mit einem Lokalrezidiv nach Mastektomie und/oder nach brusterhaltender Operation zu untersuchen.

Methoden Zwischen 03/2004 und 10/2016 erhielten 83 Patienten postoperativ nach einem Lokalrezidiv des Mammakarzinoms eine perkutane Re-RT. Die Dosierung war 45 Gy (1,8-Gy-Einzeldosis) partiell auf die Brust ($n=42$) oder auf die Mastektomienarbe ($n=41$). Die Patienten- und Tumorcharakteristika wurden univariat und multivariat hinsichtlich lokaler und distanter Kontrolle, als auch auf das Überleben (gesamt- und karzinomspezifisch) untersucht.

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Ergebnisse Die mediane Nachbeobachtungszeit betrug 35 Monate (Spanne 3–143 Monate). Das mediane Intervall zwischen erster Bestrahlung und Re-RT war 117 Monate (Spanne 16–357 Monate). Prognostisch günstig für das Gesamtüberleben waren jüngeres Alter ($p=0{,}045$), kleiner Rezidivtumor ($p=0{,}019$) und kein Lymphknotenbefall ($p=0{,}005$). Patientinnen mit N0-Status hatten im Vergleich zu N+-Patientinnen weniger Rezidive außerhalb des Bestrahlungsfelds ($p=<0{,}001$) und ein besseres brustkrebsspezifisches Überleben ($p=0{,}025$). Grundsätzlich traten überwiegend leichte und moderate (<Grad 3) akute und chronische Hautveränderungen auf.

Schlussfolgerung Die Re-RT mit 45 Gy nach Mastektomie oder brusterhaltender Operation erzielte ein gutes onkologisches Outcome und war zudem gut verträglich.

Schlüsselwörter Brustkrebsrezidiv · Partielle Rebestrahlung · Mastektomie · Brusterhaltende Operation · Perkutane Bestrahlung

Introduction

Treatment of local breast cancer recurrence remains an important challenge for multidisciplinary breast cancer centers. Despite adjuvant radiotherapy, approximately 3–15% of breast cancer patients experience a locoregional recurrence after breast-conserving surgery or mastectomy [1–4]. Most recurrences occur in the ipsilateral breast or chest wall [5].

The standard of care for patients with locoregional recurrence is a secondary mastectomy, although recently published data suggest that a second breast-conserving surgery (BCS) followed by re-irradiation (re-RT) can be a reasonable option [6]. Regardless of the surgical approach, patients with local breast cancer recurrence might benefit from re-RT. In the past, there have been concerns about the safety and toxicity of re-RT. However, in the last few years, emerging evidence has demonstrated that re-RT can be feasible and safe [7]. Today, a large variety of treatment options and many different dose-fractionation schedules exist, including brachytherapy (BT) [8–11], external beam radiation (EBRT; [12, 13]), and intraoperative radiotherapy (IORT; [14–16]) alone or in combination with hyperthermia (HT; [17–20]). Most previous studies have included special techniques such as BT or HT, which are only available in a limited number of breast cancer centers. Therefore, we report on the effectiveness and safety of a homogenous re-RT schedule of conventionally fractionated EBRT without HT.

Methods

Patient selection

Between 03/2004 and 10/2016, 83 female patients with a histologically confirmed in-field breast cancer recurrence underwent re-RT in two radio-oncological departments in Northern Germany. All cases were discussed and approved in local multidisciplinary tumor boards.

Table 1 summarizes the patient and treatment-related characteristics. Fig. 1 illustrates patient enrollment. The patient data were evaluated retrospectively following the Declaration of Helsinki and the guidelines of the local ethics committee. All patients were initially treated with three-dimensional conformal radiotherapy (3D-CRT) to a mean total dose of 50.9 ± 1.85 Gy to the chest wall ($n=10$, 12%) or to the breast after BCS ($n=73$, 88%). Surgical therapy for recurrence was either re-excision after initial mastectomy ($n=10$, 12%), mastectomy ($n=31$, 50.6%), or BCS ($n=42$, 37.4%). Patients treated with definitive radiotherapy without surgery were excluded from this analysis. A total of 75 (90.4%) patients underwent R0 resection, four underwent R1 resections (4.8%), and one (1.2%) underwent a R2 resection. The resection status was not known in three patients (3.6%). In five (6.0%) patients, M1 statuses (not histologically proven) were based on PET-CT scans (pleural $n=2$, 2.4%; skin $n=1$, 1.2%; bone $n=2$, 2.4%). As all lesions were close to the recurrence site, all lesions were included in the target volume.

Acute and late toxicity were assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 (CTCAE 2010; [21]).

Dose-fractionation concept and target volume of re-irradiation

Re-RT was performed using a 3D conformal technique with 6–15 MV photons after planning computed tomography (CT) in the supine position, Fig. 2 shows an exemplary treatment plan of a partial breast volume treated with dynamic intensity-modulated radiotherapy (IMRT; "rapid arc"). The total dose of re-RT was 45 Gy (single dose: 1.8 Gy). In nine (10.8%) patients, the total dose was escalated to 50.4 Gy. Two (2.4%) patients declined the last fraction due to personal reasons, and not due to toxicity (total doses: 43.2 Gy), and five (6.0%) patients were treated with a total dose of 46 Gy with single doses of 2.0 Gy. The treatment volumes were individualized for each patient. In general, the target volume after mastectomy encompassed

Table 1 Patient- and treatment-related parameters at initial diagnosis and at recurrence

	Initial diagnosis	Recurrence
Median age at first diagnosis	52 years (range 30–78)	64 years (range 44–83)
Left side	35 (42%)	35 (42%)
Right side	48 (58%)	48 (58%)
Breast-conserving therapy	73 (88%)	42 (51%)
Mastectomy	10 (12%)	41 (49%)
Total dose (single dose: 1.8 or 2.0 Gy)		
54 Gy	18 (22%)	0 (0%)
50/50.4 Gy	61 (74%)	9 (11%)
48 Gy	2 (2%)	0 (0%)
45/46 Gy	2 (2%)	74 (89%)
Boost total dose (single dose: 1.8 or 2.0 Gy)		
10 Gy	14 (17%)	0
4 Gy	1 (1%)	0
6 Gy	2 (2%)	0
14.4 Gy	2 (2%)	0
9 Gy	2 (2%)	0
No boost	62 (75%)	83 (100%)
T status		
DCIS	5 (6%)	0 (0%)
T1	41 (49%)	32 (39%)
T2	31 (37%)	23 (28%)
T3	5 (6%)	5 (6%)
T4	1 (1%)	23 (28%)
N status		
N0	56 (68%)	75 (90%)
N1	26 (31%)	4 (5%)
N2	1 (1%)	3 (4%)
N3	0 (0%)	1 (1%)
Grading		
G1	2 (2%)	2 (2%)
G2	48 (58%)	51 (61%)
G3	28 (34%)	28 (34%)
Not known	5 (6%)	2 (2%)
Resection status		
R0	–	76 (92%)
R1		3 (4%)
R2		1 (1%)
Not known		3 (4%)
Estrogen receptor positive	62 (75%)	61 (73%)
Estrogen receptor negative	18 (22%)	22 (27%)
Not known	3 (4%)	0 (0%)
Progesterone receptor positive	57 (69%)	54 (65%)
Progesterone receptor negative	23 (28%)	29 (35%)
Not known	3 (4%)	0 (0%)
Her2 receptor positive	10 (12%)	5 (6%)
Her2 receptor negative	51 (61%)	16 (19%)
Not known	22 (27%)	62 (75%)

DCIS ductal carcinoma in situ

the scar plus a safety margin of at least 1.0 cm as marked with radiographic contrast agent on planning CT [17]. In the cases of a second BCS, generous margins of at least 1.0 cm to 1.5 cm around the postoperative changes/surgical clips, which represent the boarder of the surgical cavity, were applied to build the clinical target volume (CTV). A 1.0 cm margin around the CTV was used for the planning target volume (PTV). This is almost equivalent to the target volume definition according to RTOG 1014 study protocol: The CTV is defined by uniformly expanding the excision cavity volume by 1.5 cm. The PTV provides a margin around the CTV to compensate for the variability of treatment setup and motion of the breast with breathing (minimum 1.0 cm).

Literature review

A PubMed database research search was performed in November 2017 while applying the following terms: "breast cancer recurrence, re-irradiation", "breast cancer recurrence, reirradiation", "breast cancer, re-irradiation", and "breast cancer, reirradiation". The search revealed 507 results. After the exclusion of duplicates and subjects not fitting the problem according to their titles and abstracts, 34 full papers were evaluated. An additional ten papers were found in the reference sections of the included papers that did not appear in the abovementioned search. After exclusion of palliative settings and case reports/small number analyses, a total number of 17 was included in the review (see Tables 2 and 3).

Statistical analysis

Local control, disease-free survival, and overall survival rates were estimated using the Kaplan–Meier method. The corresponding curves were compared with the log-rank test and univariate analyses. A p-value of <0.05 was considered statistically significant. In cases with significant differences between the curves or a trend toward a difference in outcome ($p \leq 0.08$), additional multivariate Cox regression analyses were performed.

Results

Outcome

The median time from the initial radiotherapy to the recurrence of disease was 117 months (range 16–357 months). The median follow-up after the last day of re-RT was 35 months (range 2–142 months). At the time of analysis, 12 patients (14.5%) presented with second local recurrences after a median time of 21 months (range 10–83 months).

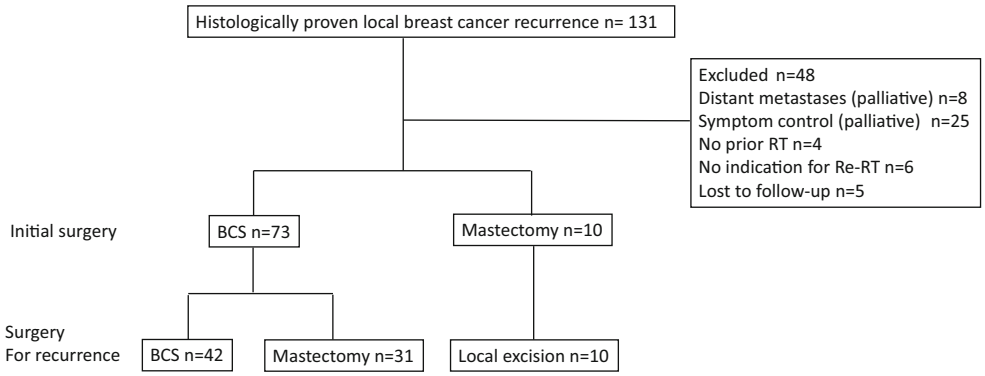


Fig. 1 Consort diagram showing patient selection. *BCS* breast-conserving surgery

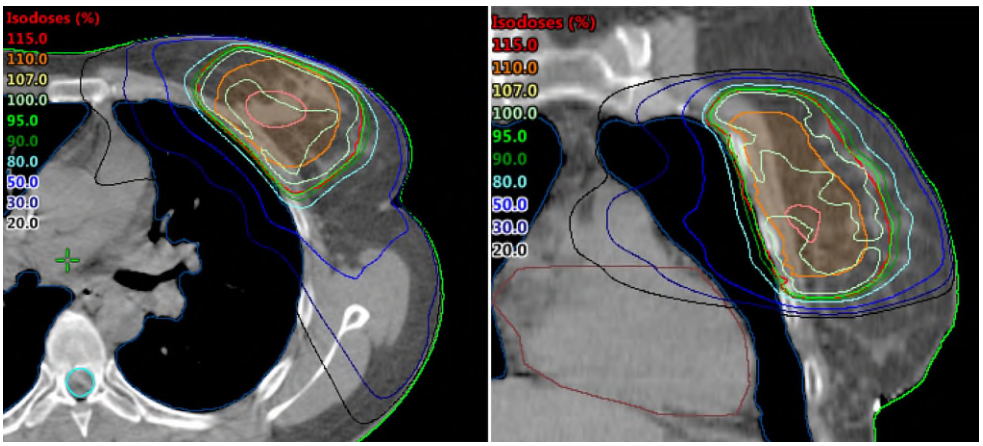


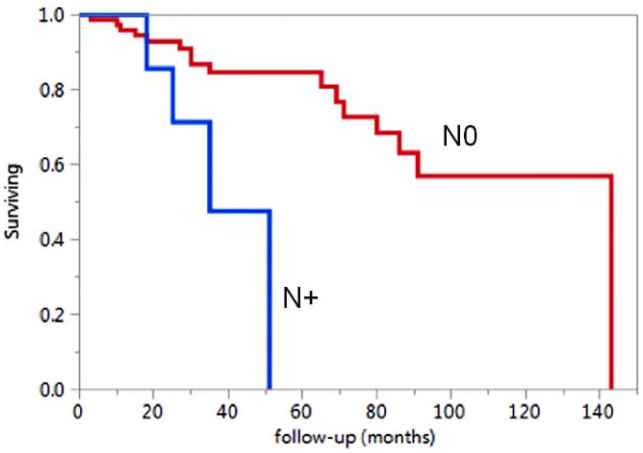
Fig. 2 Exemplary re-irradiation (Re-RT) plan after a second breast-conserving surgery (BCS) with dynamic IMRT (intensity-modulated radiotherapy; rapid arc) in the axial and coronary planes

In all, 23 patients developed an outfield recurrence (multiple [$n=7$], hepatic [$n=1$], cerebral [$n=2$], pulmonary [$n=5$], bone [$n=2$], axillary [$n=2$], contralateral breast [$n=2$], skin [$n=2$]) after a median time of 16 months (range 2–100 months). Of those, five patients showed synchronous local and distal failures. The overall survival and breast cancer-specific survivals were 76% and 84%, respectively.

Different parameters, such as tumor site (left vs. right), age (<65 years vs. ≥65 years), type of surgery (breast conserving vs. mastectomy), T category (T1–2 vs. T3–4) N category (N0 vs. N+), grading (G1-2 vs. G3), hormone receptor (estrogen [ER] and progesterone [PR] positive vs. negative), Her2 status (positive vs. negative), Ki67 (≤30% vs. >30%) and resection status (R0 vs. R1/2) were analyzed for differences in local control and distant control, as well as disease-specific and overall survival.

The prognostic factors for favorable overall survival included younger age ($p=0.045$), lower T category ($p=0.019$) and N0 category ($p=0.005$) in the univariate analysis (Figs. 3, 4 and 5). Nodal status remained significant in the multivariate analysis ($p=0.022$).

Breast cancer-specific survival was superior for N0 patients compared to N+ patients in the univariate analysis ($p=0.025$) but not in the multivariate analysis.



	0 months	60 months	120 months
N0	n=83	n=70	n=48
	100%	84%	58%
N+	n=83	n=0	n=0
	100%	0%	0%

Fig. 3 Univariate analysis of overall survival for N stage (N0 [*red line*] vs. N+ [*blue line*]), $p=0.005$

Table 2 Outcome of patients treated with repeated breast-conserving surgery and radiotherapy after local recurrence

Study, year	Number of patients	Median follow-up (months)	Median time interval between RT courses (months)	Re-RT technique (total dose)	Local control (%)	Overall survival (%)	Toxicity
Mullen et al., 1996 [12]	16	42–119	31 (10–130)	EBRT, 50 Gy electrons	80	62.5	Persistent pigmentation and fibrosis, no rip fractures or cardiopulmonary damage
Deutsch, 2002 [13]	39	51.5	63 (16–291)	EBRT, 50 Gy electrons	76.9	77.9	No late sequela other than skin pigmentation changes
Resch et al., 2002 [27]	17	59 (20–84)	50 (11–208)	PDR BT 12.5–28 Gy, +EBRT 12–30 Gy, PDR BT only 40.2–50 Gy	76	88.2	No grade 3 fibrosis
Kraus-Tiefenbacher et al., 2007 [14]	15	26 (1–60)	120 (36–300)	IORT, 14.7–20 Gy	100	93	No grade 3 or 4 toxicities
Trombetta et al., 2009 [11]	26	38 (6–75)	–	LDR BT 45–50 Gy, HDR BT 34 Gy	94	100	–
Guix et al., 2010 [8]	36	89 (15–169)	38 (13–61)	BT high dose rate, 30 Gy	89.4	96.7	No grade 3 or 4 toxicities
Kauer-Dorner et al., 2012 [10]	39	57 (±30)	188 (±80)	BT, PDR 50 Gy	93	87	4% grade 3 fibrosis and 13% G3 pain, no grade 4 toxicity
Hannoun-Levi et al., 2013 [9]	217	174 (42–458)	47 (13–124)	BT LDR 46 Gy, PDR 50.4 Gy, HDR 30 Gy	92.8	76.4	11% grade 3/4 complications
Blandino et al., 2017 [15]	30	47 (10–78)	120 (36–600)	IORT, 18 Gy	92.3	91.2	Fibrosis grade 2: 41%, grade 3:21%
Chin et al., 2017 [16]	12	14 (4–25)	216 (2–552)	IORT, 20 Gy	100	91.7	8.3% grade 3 late toxicity
Arthur et al., 2017[a] [14]	55	12	168 (19–332)	EBRT 45 Gy (single dose 1.5 Gy twice daily)	100	100	Grade 1: 64%, grade 2: 7%, grade 3: <2%

BT brachytherapy, *EBRT* external beam radiotherapy, *IORT* intraoperative radiotherapy, *PDR BT* pulsed-dose-rate brachytherapy, *Re-RT* re-irradiation, *LDR BT* low-dose rate brachytherapy, *HDR BT* high-dose rate brachytherapy
[a]prospective study initial results, exclusion: palliative treatments without second surgery and studies <10 patients/case reports

Table 3 Outcome of patients treated with mastectomy and radiotherapy after local recurrence, exclusion: palliative treatments without second surgery and studies <10 patients/case reports

Study, year	Number of patients	Median follow-up (months)	Median time interval between RT courses	Re-RT technique (total dose)	Local control (%)	Overall survival (%)	Toxicity
Oldenborg et al., 2010 [19]	78	64.2	58.4	EBRT (8 × 4 Gy) + HT	65 (5 y)	66	40% grade 3 toxicity
Müller et al., 2011 [18]	42 (30 postoperative)	41 (3–92)	33 (9–400)	EBRT 60 Gy (+HT, $n = 29$)	62 (5 y)	59 (5 y)	Late grade 2: 62% Late grade 3: 19% No grade 4
Linthorst et al., 2013 [17]	198	42	89 (2–523)	28–36 Gy + HT	78 (5 y)	60	Late grade 3/4: 11.9%
Oldenborg et al., 2016 [23]	234	47 (0.6–207)	66 (6–553)	EBRT (8 × 4 Gy) + HT	70 (5 y)	60	7% rib fractures
Auoragh et al., 2016 [20]	18 (10 postoperative)	26.4 (4–108)	64.5 (10–234)	HDR 50Gy (+HT 87%)	56 (5 y)	22 (5 y)	Grade 3:17%
Bakker et al., 2017 [26]	262 (chest wall $n = 211$)	n.a.	n.a.	EBRT 8 × 4 Gy + HT	n.a.	n.a.	26% thermal skin damage

BT brachytherapy, *HT* hyperthermia, *EBRT* external beam radiotherapy, *n.a.* not available, *re-RT* re-irradiation, *y* years

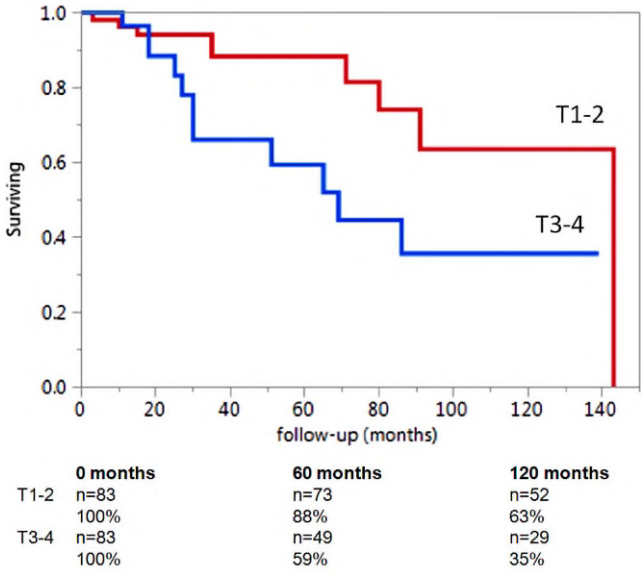


Fig. 4 Univariate analysis of overall survival for T stage (T1-2 [*red line*] vs. T3–4 [*blue line*]), $p = 0.019$

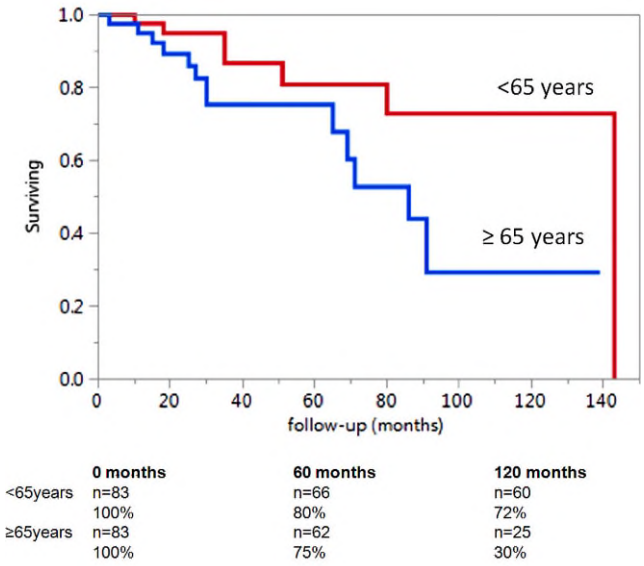


Fig. 5 Univariate analysis of overall survival for different ages (<65 years [*red line*]vs. ≥65 years [*blue line*]) $p = 0.045$

We observed significantly less outfield recurrences for patients following R0-resection ($p = 0.005$ in the univariate but not the multivariate analysis) and N0 status ($p = <0.001$ in the univariate and $p = 0.017$ in the multivariate analysis).

In terms of local control, no significant differences were found for the abovementioned parameters.

Toxicity

The acute and late side effects were limited to skin reactions, and neither cardiopulmonary events nor rib fractures were observed. Regarding the grade of skin toxicity, re-RT was generally considered well tolerated, i.e., 65.1% ($n = 54$) of the patients presented with acute dermatitis grade 1 and 18.1% ($n = 15$) presented with grade 2. Late skin toxicities of grade 1 and 2 were observed in 22.9% ($n = 19$) and 3.6% ($n = 3$) of the patients, respectively. One patient (1.2%) had a persistent seroma following surgery with a secondary wound infection and skin ulcer (<2 cm), unrelated to re-RT. No grade 3 or 4 acute or chronic toxicities were detected.

Discussion

Local recurrences of breast cancer represent a therapeutic challenge, especially when adjuvant radiotherapy had already been applied [3]. Salvage mastectomy is the standard treatment for local recurrences after BCS resulting in 5-year locoregional and with survival rates of 69–98% and 53–85%, respectively [3, 22]. However, low local control rates of 33% after surgical therapy without radiotherapy have been reported [22]. Similar to the primary situation, prognostic factors indicating a higher risk for a second local recurrence are known also in cases of an in-field recurrence, and re-RT should be considered based on these prognostic factors [3].

Several studies have reported on clinical routine management of re-RT after mastectomy and demonstrated 5-year local control rates of 56–78% [17–20, 23, 24]. Our local control rate of 85.5% after a median follow-up of 35 months compares favorably. This might be due to the inclusion of secondary breast-conserving approaches in our collective in which the tumor stage might have been more favorable. Unfortunately, current studies with re-RT after mastectomy mostly lack information about tumor stages, which makes a direct comparison of the oncologic outcomes impossible. Additionally, some study groups have also included patients who were treated with definitive radiotherapy for recurrence [20]. Without surgery, however, local control rates are known to be very limited, and the treatment intention may be considered palliative [24, 25].

In the abovementioned studies, different treatment regimens were used (summarized in Tables 2 and 3). Apart from Auoragh et al. applying HDR BT [20], EBRT with total doses ranging from 30–60 Gy was mainly used. The most common regimen was hypofractionated EBRT with 8 × 4 Gy [19, 23, 26]. Moreover, most studies combined re-RT with HT (see Table 3).

Apart from mastectomy, BCS followed by re-RT can be a reasonable option for the treatment of locally recurrent breast cancer, especially for patients with unifocal tumors that are limited in size. Additionally, a long interval between the first diagnosis and recurrence may be associated with better results [3]. Because BCS without radiotherapy

after breast cancer recurrence yields local control rates of only 19–38%, re-RT should be mandatory for these patients. In those cases, the largest experience exists with BT. Hannoun-Levi et al. reported a local control rate of 92.8% and an overall survival rate of 76.4% for 217 patients using different types of BT after the second BCS [9]. Other authors have demonstrated comparable results in smaller patient cohorts [8, 10, 11, 27]. Another approach using IORT resulted in 100% local control mainly for T1 tumors after a median follow-up period of 26 months [14]. Two recently published studies confirmed the excellent local control rates for T1 tumors with IORT [15, 16]. However, the availability of BT and IORT is limited to larger centers. Two studies demonstrated the feasibility and safety of a second EBRT with 50 Gy after BCS for recurrence, achieving local control rates of 80% and 76.9% [12, 13]. Our local control rate of 85.5% compares well with older EBRT series [12, 13] and larger BT studies [9]. Recently, Arthur et al. reported on the first-year results of the prospective RTOG 1014 trial using a hyperfractionated re-RT regime of 45 Gy (1.5 Gy per fraction given twice daily). The long-term outcome is pending, but the preliminary data are promising with no local recurrences and little toxicity so far [4].

Two prognostic factors significantly associated with overall survival have already been identified, i.e., the time interval from the initial diagnosis to recurrence and the extent of resection [18]. We did not observe a significantly better overall survival in cases with a long interval between the first diagnosis and recurrence or cases with a microscopically complete (R0) resection. However, we found that the T category, N category and age were significant predictors of overall survival. Additionally, the N category (N0 vs. N+) was significantly associated with distant metastases-free survival and breast cancer-free survival, further highlighting the prognostic importance of lymph node metastases.

Treatment tolerance is a major concern when planning to use re-RT. There is a large variation in the tolerance of re-RT according to the literature. While some study groups report no grade ≥3 toxicities [8, 12–14], others found grade 3 side effects after re-RT in 2–40% [4, 9, 10, 15, 17–20]. Patients with re-RT after mastectomy and additional HT are prone to develop side effects beyond grade 3 (see Tables 2 and 3). In our patients who received re-RT after mastectomy or BCS, we did not observe any differences in tolerance related to the surgical approach. In our cohort, acute and late toxicity did not exceed grade 3. Thus, the presented conventionally fractionated re-RT regime with 45 Gy (1.8 Gy single doses 5 times a week) was considered well tolerated.

In addition to the total dose, the target volume is important regarding the tolerance of re-RT. Compared to the primary situation, treatment volumes are more individualized in the re-RT setting due to repeated surgical procedures. Unfortunately, most study groups did not provide details regarding their target volumes. In case of re-RT after mastectomy, Müller et al. carried out re-RT to the entire chest wall (leading to late grade 3 toxicity in 19%; [18]), while Linthorst et al., who focused on the irradiation of the mastectomy scar, observed a late grade 3 toxicity in 11% of their patients [17]. Oldenborg et al. defined the chest wall or the mastectomy area up to the dorsal axillary fold as the target volume and observed grade 3 toxicity in 40% of their patients [19]. In line with the findings of our study and the observations by Linthorst et al. [17], limiting RT to the mastectomy scar seems to improve tolerance when compared to re-RT of the entire chest wall.

In the case of secondary BCS, no standard target volume has been defined so far. In our cohort, target volumes were individualized for every patient with generous margins around postoperative changes and surgical clips. The volume was generated taking prognostic factors such as tumor size and resection margins into account. Based on the personal radio-oncologist's risk estimation, dose was escalated up to 50.4 Gy in some cases. In case of recurrent N+ situations, no nodal re-irradiation was carried out due to possible injury of the brachial plexus and the risk of lymph edema. The protocol of the prospective RTOG 1014 study provides detailed information on contouring the clinical target volume (CTV) and planning target volume (PTV; [4]). To standardize our target volume concept, we adapted the recently published study protocol of the RTOG 1014 to our clinical routine.

Apart from the target volume itself, the choice of radiation technique is of interest. In case of a secondary BCS, older EBRT series applied 50 Gy using electrons [12, 13]. In their recent study Arthur et al. reported on photon field combinations (with and without electrons) and field-in-field treatment approaches [4]. Most of our patients were treated with electrons or 3D planned photons. However, modern techniques like intensity modulated RT (IMRT) might carry the potential to further spare organs at risk in the recurrence situation. This might be of value in patients with initially large boost volumes close to the chest wall, lung, or heart.

We included both patients treated with mastectomy and those receiving BCS for locally recurrent breast cancer. We feel that this setting closely represents the daily practice where radio-oncologists often face both situations. Our treatment regimen was well tolerated and provided high local control rates for both re-RT after BCS and re-RT after mastectomy. Compared to other RT modalities, e.g., BT, IORT, hyperfractionated EBRT and the addition of HT, our approach is convenient, requires no special equipment, is widely available, and is less labor-intensive than HT and BT.

Limitations

The limitations of our study include the retrospective nature with the known risk of a hidden selection bias. The study is also limited in that we only discussed current knowledge against the background of retrospective data from our daily practice. While our breast cancer cohort consisted of only 83 patients, it is comparable in size to other studies (see Table 3) and contributes to the discussion of treatment of local recurrent breast cancer as it is currently the largest study using a conventionally fractionated EBRT without HT. Thus, in the absence of randomized trials with informative follow-up data and the vast majority of publications on this topic applying either BT, IORT, or additional HT, our study offers a feasible therapeutic approach.

Conclusion

Different treatment approaches for local breast cancer recurrences in previously irradiated patients exist. Our schedule of 45 Gy (1.8 Gy per fraction on five consecutive days per week) for re-RT of the breast or chest wall provided good local control and was well tolerated. Furthermore, since no special equipment is required, this approach is highly practicable for most RT centers.

Conflict of interest S. Janssen, D. Rades, A. Meyer, F. B. Fahlbusch, I. Wildfang, A. Meier, S. Schild, H. Christiansen and C. Henkenberens declare that they have no competing interests.

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