

Research Article

Determining the Appropriateness and Acceptability of a Reduced Postradiotherapy Surveillance Practice in Breast Cancer Patients: Results of a Longitudinal Observational Study

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Postradiotherapy surveillance, which aims to detect and treat radiation injury, is important from the patient's perspective, but also from the radiation oncologist's perspective. Unfortunately, patient nonattendance increases over the course of five years. The aim of the study was to investigate the appropriateness and acceptability of reduced versus usual (conventional) postradiotherapy surveillance in breast cancer patients. A total of 192 consecutive patients with curatively irradiated breast cancer from two selected treatment years were included in our study, of whom 65 were offered six (after three months, 12 months, 24 months, 36 months, 48 months, and 60 months) and 127 were offered four follow-up appointments (after three months, 12 months, 36 months, and 60 months). Their patient-, tumour- and treatment-related characteristics were analysed, as well as follow-up events and attendance rates. The reduced four-meeting surveillance practice shows similar results to the traditional six-meeting practice in terms of appropriateness and acceptability, with significantly higher attendance rates at 36 and 60 months ($p = 0.014$ and 0.013 , respectively) when the individual moments are compared on a one-to-one basis. The patient-, tumour-, and treatment-related variables examined did not show an effect on the attendance rate. There was also no significant difference between the two cohorts in the detection of follow-up events (such as recurrence) and late radiation effects. In conclusion, this retrospective study provides scientific support for the trend towards a risk-adjusted, reduced surveillance practice in radiation oncology. In particular, four postradiotherapy follow-up visits seem to be appropriate and accepted in breast cancer patients after curative postoperative breast irradiation. This reduced postradiotherapy surveillance practice has the advantage of saving time for the patient and resources for the healthcare system without compromising quality; it could also improve patient participation. We, therefore, recommend it as an appropriate standard for breast cancer patients.

1. Introduction

The recording of late effects after radiotherapy represents an essential part of the quality of outcome after radiotherapy procedures and is prescribed by law in Germany. To ensure that this responsibility was met, patients were followed up at regular intervals after radiotherapy, usually after three months and then once a year for five years. This surveillance practice, also known as “postradiotherapy follow-up,” is an adjunct to the oncology follow-up care programme that

evaluates and manages late or long-term side effects of cancer treatment [1].

Until now, patients have been called in for follow-up care at fixed intervals after radiotherapy, regardless of their individual risk of late radiation effects, in accordance with the equally rigidly defined oncology follow-up care. Oncological follow-up consists of two parts: aftercare and surveillance. Aftercare aims to detect, manage, and treat the psychosocial and physical consequences of breast cancer (treatment), while surveillance aims to detect locoregional recurrence

(LRR) and second primary breast cancer (SPBC) at an early stage. The latter is supported by two systematic reviews showing that patients with asymptomatic or mammographically detected LRR or SPBC have a better survival rate than patients with symptomatic or clinically detected LRR or SPBC [2]. However, Eijkelboom et al. [2] recently investigated routine and interval detection of locoregional breast cancer recurrence and the risk of subsequent distant metastasis and were able to show that the severity of LRR and the subsequent risk of a distant metastasis (DM) between LRR detected by routine and interval screening did not result in less severe LRR and did not reduce the risk of subsequent DM. This observation fuels the debate about the scope and risk-adapted intensity of oncological follow-up, which, in the UK, for example, includes at least one annual mammography and regular visits with physical examination and medical history [3] but, in some other countries, also includes even denser follow-up schedules with laboratory tests (e.g., tumour markers). On the other hand, there is a lack of evidence on the effectiveness of personalisation, as reported by van Maaren et al. [4]: her review shows that existing interventions to personalise follow-up are scarce (especially for surveillance), vary widely, are not structurally embedded in clinical practice, and do not provide clear evidence of their effectiveness. Against this background, the results of the planned prospective Dutch trial on this topic are awaited with interest.

With regard to radiotherapy, it seems possible to change the appointment practice by extending the examination intervals (currently once a year) and by reducing the number of appointments in cases with a low incidence of late radiation effects; this might also improve patient acceptance of this postradiotherapy follow-up. The German Commission on Radiological Protection has recently approved this option for such patients with a low risk of late radiation effects, as well as in the case of postoperative breast irradiation for breast cancer [1].

To research the effects of reducing the number of appointments and to compare a reduction with the usual (conventional) postradiotherapy follow-up schedule in patients with breast cancer, we conducted a retrospective longitudinal observational study. The aim of the study was to investigate two selected cohorts of breast cancer patients with different postradiotherapy follow-up schedules over 5 years with respect to follow-up events and late radiation effects as parameters to determine appropriateness and follow-up behaviour measured by attendance rate as a parameter to determine acceptability of the modified postradiotherapy surveillance.

2. Materials and Methods

In our institution, postradiotherapy follow-up was performed six times in five years until 2012 (*schedule A*; i.e., three months (3 M), twelve months (12 M), 2 years (24 M), 3 years (36 M), 4 years (48 M), and for the last time at 5 years (60 M) after completion of radiotherapy). Since 2013, there have only been four postradiotherapy follow-up appointments in five years, with the 24-month and 48-month

appointments being cancelled in particular (*schedule B*; i.e., three months (3 M), twelve months (12 M), 3 years (36 M), and 5 years (60 M) after completion of radiotherapy). The investigation was approved by the Ethics Committee of the Hannover Medical School.

2.1. Study Population. Two cohorts were established for this study: cohort A consisted of all consecutive patients with histologically proven nonmetastatic breast cancer who were treated with curative postoperative breast irradiation in 2011 and who were followed up according to *schedule A*; cohort B consisted of all consecutive patients with histologically proven nonmetastatic breast cancer who were treated with curative postoperative breast irradiation in 2014 and who were followed up according to *schedule B*. To avoid inclusion bias, we excluded patients receiving definitive or palliative breast irradiation, patients participating in clinical trials (due to different follow-up schedules), and patients with insufficient language skills and support-dependent patients.

In both cohorts, following breast-conserving surgery (BCS) or mastectomy, all patients received postoperative whole breast irradiation with tangential fields in the supine position, either normofractionated with a median total dose of 50 Gy in daily fractions of 1.8 to 2.0 Gy, five times a week, or moderately hypofractionated with 15×2.67 Gy according to the British START B trial [5]. If indicated, patients received radiation to supraclavicular lymph nodes (SCRT) normofractionated with a median dose of 45 Gy and/or a sequential normofractionated boost of the tumour region with a median dose of 10 Gy in five fractions. Radiotherapy was delivered using three-dimensional conformal technique (3D-CRT). As an exception to this treatment schedule, five patients in Group A with low-risk breast cancer received intraoperative radiotherapy in a single fraction only in 2011 instead of the standard postoperative whole breast radiotherapy over several weeks. If indicated, patients received additional chemotherapy, either before (neoadjuvant) or after (adjuvant) surgery, and/or additional hormone therapy for hormone receptor-positive breast cancer; the completeness and duration of these drug therapies were not considered in this study.

2.2. Assessments. The assessment and investigation during the postradiotherapy follow-up were carried out exclusively by physicians. Information on patient, tumour, and treatment characteristics was collected from medical records and reports. Postradiotherapy follow-up data included follow-up events (recurrence, metastases, second tumour, death, and late radiation effects) as well as attendance at appointments and were collected from medical records and, in part, from appointment books. Late radiation effects were defined as those occurring at least three months after the completion of radiotherapy and included skin changes, fibrosis, pain, lymphedema, pulmonary sequelae, and cardiac events. Patient contact was not planned as part of this longitudinal study.

The clinical TNM stage was recorded using the standardised tumour/node/metastasis (TNM) classification system (7th edition) [6]. We recorded the initial pretherapeutic

clinical TNM stage if neoadjuvant chemotherapy was performed, i.e., the documented clinical stage before chemotherapy, cN+ was recorded as at least N1. Relevant comorbidities included neurological, cardiac, vascular, rheumatological, psychiatric, nephrological, pulmonary, and previous oncological diseases. Arterial hypertension, mild or moderate hypothyroidism, and skin diseases were considered irrelevant comorbidities.

We classified late radiation effects into mild (grade 1 or 2) and severe (grade 3 or 4) according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 [7] and distinguished between temporary and permanent late radiation effects as follows: late effects that were detectable only at a single follow-up visit (usually at the first visit three months after completion of radiotherapy) were classified as transient. This assumption is also based on the fact that late effects are often not reversible. Those that were detected at least two follow-up visits were classified as permanent late radiation effects. If a patient did not attend, we assumed the worst-case scenario and counted her last visit as the end of compliance; similarly, her reported late radiation effects were always considered permanent.

2.3. Statistical Methods. Patient-, tumour-, and treatment-related data were summarised using descriptive statistics; quantitative variables were expressed as the mean and range. Patient characteristics between the two cohorts were compared by using cross-tables and chi-square tests for continuous and categorical variables, respectively. All p values were two-tailed; $p \leq 0.05$ was considered statistically significant. Participation was measured from the date of the last radiation to the last perceived date of follow-up and censored for tumour recurrence (including metastatic disease), tumour disease (second malignancy), or death. The Kaplan–Meier method and the log-rank test were used to compare the participation rate for the two postradiotherapy follow-up schedules and events leading to discontinuation of treatment. A Cox regression model was used to assess the association of patient-, tumour-, and treatment-related variables with the participation rate. Statistical analyses were performed using SPSS software (IBM SPSS Statistics 26®, Chicago, IL, USA).

3. Results

A total of 192 patients were included in this retrospective observational study. Sixty-five patients from 2011 were included in the cohort A, and 127 patients from 2014 were included in the cohort B. All recorded patient-, tumour- and treatment-related parameters are listed in Table 1.

3.1. Balance of the Postradiotherapy Follow-Up Cohorts. Comparability between the cohorts A and B was demonstrated by the chi-square test, except for the variables T-stage ($p = 0.038$), chemotherapy ($p = 0.049$), and radiotherapy ($p = 0.003$). In the cohort B, there were more T_{is} stage

tumours were included than in the cohort A (A: 5%; B: 13%), resulting in a lower rate of chemotherapy treatment in the cohort B (A: 97%; B: 87%). Five patients in the cohort A received intraoperative radiotherapy (IORT) alone, resulting in a significant p value ($p = 0.003$). If these cases of IORT are excluded from this analysis, the value changes to $p = 0.171$ (p value not significant).

3.2. Analysis of the Follow-Up Events. There was no significant difference between the two cohorts in terms of follow-up events: recurrence, metastasis, second tumour, or death ($p = 0.395$). Three patients in the cohort A (3/65 = 5%) had to discontinue postradiotherapy follow-up, one within the first three months, and ten patients in the cohort B (10/127 = 8%) had to discontinue postradiotherapy follow-up due to one of the above-mentioned follow-up events.

3.3. Analysis of the Late Radiation Effects. In the cohort A, 14 patients out of 57 (25%) attending patients showed late radiation effects 3 months after completion of radiotherapy, while, in the cohort B, 30 out of 118 (25%) patients showed late radiation effects 3 months after completion of radiotherapy ($p = 0.48$). In both cohorts, temporary late effects were only observed at the first follow-up visit (Table 2). In the cohort A, 7/57 (12%) patients and, in the cohort B, 8/118 (7%) patients had temporary late effects ($p = 0.285$). In the cohort A, 7/57 patients (12%) and, in the cohort B, 22/118 patients (19%) developed permanent late effects ($p = 0.361$). Notably, the permanent late effects in both cohorts are not detectable at all follow-up visits due to the loss of some patients. Of the 14 patients from cohort A who attended the last follow-up, one patient had permanent late effects (7%), as did six of the 39 patients in cohort B (15%, $p = 0.435$). All patients with late radiation effects reported here had only mild symptoms. In particular, we found no worsening of late radiation effects when detected in the reduced frequency schedule (cohort B).

3.4. Analysis of Postradiotherapy Follow-Up Behaviour. We chose patient attendance or participation as an objective measure of postradiotherapy follow-up behaviour and found that participation rates declined steadily over the five-year period observed. Of a total of 382 follow-up appointments offered over the five-year period, 208 (54%) were attended in the cohort A, whereas, in the cohort B (reduced follow-up regimen), 332 of 491 (68%) offered appointments were attended. A direct comparison showed that the attendance rates were similar in both cohorts at three months (A: 89%, B: 93%; $p = 0.365$) and twelve months (A: 70%, B: 78%; $p = 0.422$) after completion of radiotherapy. At 36 months, significantly more patients in cohort B participated in the reduced follow-up schedule (A: 48%, B: 63%; $p = 0.014$). This trend was also observed at the final follow-up of 60 months (A: 23%, B: 33%; $p = 0.013$) (Table 3 and Figure 1). However, the log-rank test showed a nonsignificant difference between the two cohorts, with $p = 0.125$ considering the entire observation period.

TABLE 1: Patients, tumour, and treatment characteristics of the study population.

Variable		Cohort A (N = 65)	Cohort B (N = 127)	Chi-square test <i>p</i> value
Age, years	Mean (range)	60.23 (27–82)	58.47 (28–84)	0.353
<i>T-stage, n (%)</i>				
	T is	3 (4.6)	17 (13.4)	0.038
	T 1	43 (66.2)	55 (43.3)	
	T 2	14 (21.5)	39 (30.7)	
	T 3	3 (4.6)	12 (9.4)	
	T 4	2 (3.1)	4 (3.1)	
<i>N-stage, n (%)</i>				
	N 0	47 (72.3)	88 (69.3)	0.877
	N 1	14 (21.5)	29 (22.8)	
	≥N 2	4 (6.2)	10 (7.9)	
<i>Surgery, n (%)</i>				
	BCS	61 (93.8)	109 (85.8)	0.099
	Mastectomy	4 (6.2)	18 (14.2)	
<i>Radiotherapy, n (%)</i>				
	CFRT	43 (66.2)	101 (79.5)	0.003
	HFRT	17 (26.2)	26 (20.5)	
	IORT	5 (7.7)	0 (0.0)	
<i>Chemotherapy, n (%)</i>				
	Neoadjuvant	7 (10.8)	18 (14.2)	0.049
	Adjuvant	56 (86.2)	92 (72.4)	
	No	2 (3.1)	17 (13.4)	
<i>Hormone receptor, n (%)</i>				
	Positive	50 (76.9)	107 (84.3)	0.458
	Negative	11 (16.9)	15 (11.8)	
	No information	4 (6.2)	5 (3.9)	
<i>Relevant comorbidities, n (%)</i>				
	Yes	19 (29.2)	39 (30.7)	0.833
	No	46 (70.8)	88 (69.3)	
<i>Nationality, n (%)</i>				
	German	61 (93.8)	110 (86.6)	0.222
	Non-German	1 (1.5)	9 (7.1)	
	No information	3 (4.6)	8 (6.3)	
<i>Employment, n (%)</i>				
	Employed	22 (33.8)	62 (48.8)	0.091
	Unemployed	5 (7.7)	15 (11.8)	
	Retired	19 (29.2)	27 (21.3)	
	No information	19 (29.2)	23 (18.1)	
<i>Familial relationship, n (%)</i>				
	In a relationship	44 (67.7)	78 (61.4)	0.679
	Single	18 (27.7)	41 (32.3)	
	No information	3 (4.6)	8 (6.3)	
<i>Children, n (%)</i>				
	Yes	38 (58.5)	75 (59.1)	0.545
	No	9 (13.8)	24 (18.9)	
	No information	18 (27.7)	28 (22.0)	

BCS, breast-conserving surgery; CFRT, conventionally fractionated radiotherapy; HFRT, hypofractionated radiotherapy; IORT, intraoperative radiotherapy; N and n, number of patients; *after exclusion of the patients with IORT due to statistical imbalance. Bold values represent statistically significant values.

3.5. Analysis of Factors Associated with Nonattendance.

Univariate Cox regression analysis was performed to identify variables influencing the participation rate. Patients without information for a selected individual variable were excluded from the evaluation of that variable. No significant results were found in this univariate analysis (Table 4); therefore, it was not necessary to perform a multivariate Cox regression analysis.

4. Discussion

Due to the increasing number of patients who have become long-term breast cancer survivors, attention has also been focused on the late effects of radiotherapy [8, 9]. Participation in postradiotherapy follow-up helps patients maintain their quality of life by providing information about possible late toxicities and, if necessary, treating late radio-oncological

TABLE 2: Late radiation effects.

Follow-up	Cohort A	<i>n</i>	<i>N</i>	Cohort B	<i>n</i>	<i>N</i>
3 M, temp/perm/no	14/0/43	57	64**	30/0/88	118	127
12 M, temp/perm/no	0/7/38	45	64	0/22/77	99	127
24 M, temp/perm/no	0/5/31	36	64			
36 M, temp/perm/no	0/4/27	31	64	0/10/66	76	120
48 M, temp/perm/no	0/2/23	25	64			
60 M, temp/perm/no	0/1/13	14	62	0/6/33	39	117
In total, temp/perm/no	7/7/43	208	382	8/22/88	332	491

Temp, temporary; perm, permanent; no, no side effects; M, months after completion of radiotherapy; *n*, attending patients; *N*, available patients; **excluded one patient who has to leave postradiotherapy follow-up within the first three months after completion of radiotherapy.

TABLE 3: Attendance of postradiotherapy follow-up.

Follow-up	Cohort A	<i>N</i>	Cohort B	<i>N</i>	<i>p</i> value
3 M, <i>n</i> (%)	57 (89.1)	64	118 (92.9)	127	0.365
12 M, <i>n</i> (%)	45 (70.3)	64	99 (78.0)	127	0.422
24 M, <i>n</i> (%)	36 (56.3)	64			
36 M, <i>n</i> (%)	31 (48.4)	64	75 (62.5)	120	0.014
48 M, <i>n</i> (%)	25 (39.1)	64			
60 M, <i>n</i> (%)	14 (22.6)	62	39 (33.3)	117	0.013

M, months after completion of radiotherapy; *n*, attending patients; *N*, available patients. Bold values represent statistically significant values.

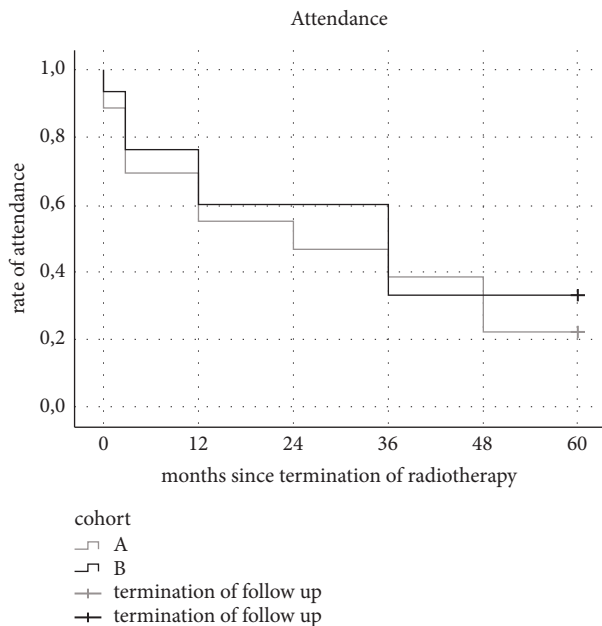


FIGURE 1: Attendance rate* to postradiotherapy follow-up. *For the number at risk, see Table 3.

toxicities in a timely manner to avoid potential adverse health effects [10]. In addition, close contact with patients after radiotherapy provides valuable information for the radiation oncologist to assess the safety of his or her therapeutic approach and maintain quality outcomes [1]. This aspect is becoming increasingly important as radiotherapy procedures are increasingly modulated by different fractionation schemes for individualisation (personalisation) [11–13]. However, the

definition of follow-up intervals after radiotherapy, usually once a year for a period of five years, is historical and requires a certain degree of flexibility. In particular, a reduction in the number of appointments appears to be possible in cases of low incidence of late radiation effects and in the case of curative postoperative breast irradiation for breast cancer [14]. To date, no data on such reduced postradiotherapy follow-up schedules have been reported in the literature.

In our retrospective longitudinal observational study, we compared a four-time appointment with a conventional six-time appointment in the postradiotherapy follow-up after curative postoperative breast irradiation for breast cancer. First, we did not find a significant difference in the detection of the follow-up events of recurrence, metastasis, second tumour, or death, nor did we find a significant difference in the detection of late radiation effects between the two cohorts. The event rates were similar to those reported in other studies [14–16]: 5% in the cohort A and 8% in the cohort B. In contrast, the rate of late radiation effects detected appears to be higher than reported in other studies, probably because of the worst-case scenario of patients dropping out of postradiotherapy follow-up: 12% in the cohort A and 7% in the cohort B for temporary effects, and 12% in the cohort A and 19% in the cohort B for permanent late radiation effects. Timely detection and treatment of follow-up events, such as local recurrence of breast cancer, is primarily the responsibility of the treating (gynaecological) oncologist and is important for optimising survival and minimising the consequences of recurrence. Postradiotherapy follow-up is carried out in parallel with (gynaecological) oncological follow-up, so that delayed documentation of follow-up events is not a problem for radiation oncologists, even with longer follow-up intervals.

Second, analysis of postradiotherapy follow-up behaviour showed a steady decline in attendance rates in both cohorts, falling below the 40% mark at 60 months. At 36 months, significantly more patients participated in the reduced follow-up of cohort B ($p = 0.014$); this trend was also observed at the final follow-up of 60 months ($p = 0.013$). However, the log-rank test showed a non-significant difference between the two cohorts, with a $p = 0.125$ for the entire observation period. However, equivalence in terms of noninferiority can be inferred from the reduced postradiotherapy follow-up schedule.

In this retrospective longitudinal observational study, the noninferiority of a reduced surveillance practice for breast cancer patients after curative postoperative breast irradiation can be assumed. Furthermore, better participation may be expected if the postradiotherapy follow-up schedule is streamlined in cases with a low incidence of late radiation effects, as shown here with the example of breast cancer irradiation. No other variables were found to influence participation behaviour in our study. This is an essential and encouraging result of our work. However, it is important to emphasize that the risk-adjusted reduction in postradiotherapy surveillance is not based on a specific patient risk profile but on the expected frequency and severity of potential radiation late effects. Therefore, attention should be paid to patients with an individualised increased

TABLE 4: Analysis of baseline characteristics for nonattendance—univariate Cox regression analysis.

Univariate Cox regression analysis	Category	<i>p</i> value	HR; 95% CI
Age	Below/above mean	0.876	1.00; 0.98–1.02
T-stage	Tis or T1/>T1	0.399	1.17; 0.82–1.67
N-stage	N0/N1 or ≥N2	0.938	0.98; 0.66–1.47
Surgery	BCS/mastectomy	0.950	1.03; 0.46–2.29
Radiotherapy	CFRT/HFRT or IORT	0.072	1.43; 0.97–2.10
Chemotherapy	Yes/no	0.455	0.80; 0.44–1.45
	Adjuvant/neoadjuvant	0.897	1.04; 0.60–1.78
Hormone receptor	Positive/negative	0.688	0.90; 0.52–1.54
Relevant comorbidities	Yes/no	0.997	1.00; 0.66–1.51
Nationality	German/non-German	0.727	0.85; 0.35–2.09
Employment	Employed/unemployed or retired	0.703	1.08; 0.73–1.60
Familial relationship	In a relationship/single	0.789	0.95; 0.64–1.40
Children	Yes/no	0.220	0.73; 0.44–1.21

BCS, breast-conserving surgery; CFRT, conventionally fractionated radiotherapy; HFRT, hypofractionated radiotherapy; IORT, intraoperative radiotherapy.

sensitivity to radiation, who should be monitored more frequently by the radiation oncologist.

Another point to discuss is the low attendance rate at the end of the postradiotherapy follow-up programme, which should be analysed more closely: failure to attend a follow-up appointment is a risk factor for cancer patients developing unmet needs, according to Harrison et al. [17]. Unmet needs refer to a lack of information, supportive care, and physical or psychological help and can have an impact on relationships or professional fulfilment [17–20]. According to a review by Mirošević et al. [20], breast cancer patients have a higher prevalence of unmet needs than patients with other tumours. Interestingly, there is also evidence to suggest that breast cancer patients who have survived cancer for at least 5 years are less likely to suffer from depression compared to the situation during and shortly after diagnosis and treatment [21]. However, lower participation leads to a lower quality of follow-up care by treating radiation oncologist: for example, fewer patients with late radiation effects can be counselled and treated in a timely manner, or new fractionation regimens may be misjudged in terms of their toxicity. In this case, the data within one year of irradiation are particularly important because of the increased toxicity during this period.

Loss to follow-up is a well-known phenomenon in health care, but it is also an underestimated and often neglected health problem [22]. For example, in oncology, Endo et al. [23] investigated the loss to follow-up during active surveillance in 425 patients with stage I seminoma and found that 14% of patients on active surveillance were lost to follow-up in the first two years and 38% in the first five years. In breast cancer patients, Ouyang et al. [24] reported a loss to follow-up rate of 12.9% (198/1536 patients) in the first year and 26.8% (411/1536 patients) in the fifth year after surgery. Santiá et al. [9] reported a similar loss to follow-up rate of 19% (37/194 patients) after the 6th year, which increased to 30% (97/326 patients) after the 16th year. Possible countermeasures include the use of reminder intervention to improve adherence to appointments, such as post-radiotherapy follow-up [9, 22–25]. In a cross-sectional study, Bruns et al. [25] demonstrated that reminder intervention in breast cancer patients resulted in significantly

higher rates of attendance at postradiotherapy follow-up; specifically, he reported an absolute decrease in non-attendance from about 24% to 18% after written (postal) reminders and from about 24% to 9% after telephone reminders. In the future, the development of high-speed Internet and interactive social media text messaging systems may make it easier to reach patients [24, 25].

In this study, we focused on patients with breast cancer because of the large number of women affected. The strength of this study lies in the homogeneous patient population that was followed up under the same conditions after radiotherapy. However, the follow-up examinations in this retrospective study were performed by different investigators at different times. Therefore, the quality of the data collection can only be considered consistent to a limited extent, despite the department's own predefined examination parameters. For this reason, in this study, we only classified late radiation effects into mild and severe and distinguished between temporary and permanent late radiation effects. In our study, no other late radiation effects were observed that were not already present at the first visit three months after completion of radiotherapy. This may be related to the fact that, in both cohorts, permanent late radiation effects were not detectable at all follow-up visits due to discontinuation of some patients and random exit/withdrawal of patients with late radiation effects at post-radiotherapy follow-up. Another possible bias in this study is the time difference, as the two groups of patients were three years apart. We think it is unlikely that this time difference would have affected the results if the treatments were similar and the only major difference between these two groups of women was the follow-up schedule. However, there were some patient and treatment differences between the two groups that may have influenced the conclusions. Other limitations of the study were the retrospective design and possible unrecorded factors leading to patient nonparticipation, which could cause the so-called “confounding bias.” We reduced the likelihood of confounding bias by using a sufficiently long follow-up period and by analysing baseline characteristics between the two cohorts and in relation to participation behaviour. Cox regression analysis showed no evidence that the variables examined affected patient adherence.

5. Conclusions

This retrospective longitudinal observational study has shown that a reduced schedule of four postradiotherapy follow-up visits is appropriate and accepted in breast cancer patients after curative postoperative breast irradiation and thus supports recent activities towards a risk-adapted reduced surveillance practice in radiation oncology. Our statistical analysis was performed to detect a difference between the two cohorts, but the absence of a difference does not automatically indicate noninferiority—so a prospective study with a noninferiority design would ideally be the next step.

A reduced postradiotherapy surveillance practice has the advantage of saving time for the patient and resources for the healthcare system without compromising quality. In addition, better participation can be expected if the post-radiotherapy follow-up schedule is streamlined in the way presented. Where appropriate, the use of reminders in any form should also be considered to increase the participation rate in the follow-up and thus possibly also improve the quality of the results, so that both mild and severe radiation late effects can be reliably detected.

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval

This investigation was performed with the approval of the regional Hannover Medical School Ethics Committee. This article does not contain any studies with human subjects. The research described in the present manuscript was in accordance with both national law and the Helsinki Declaration of 1975 (including its most recently amended version).

Consent

Informed consent was obtained from all individual participants included in the study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Idea was given by FB. Review of the literature was performed by GHH and FB. Conception and design were performed by GHH, ACK, HC, and FB. Acquisition of data was performed by GHH and ACK. Analysis and interpretation of data were performed by GHH and FB. Manuscript draft (including preparation of figures and tables) was performed by GHH and FB. Manuscript revision was performed by GHH, ACK, HC, and FB. All authors read and approved the final manuscript.

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