


REVIEW ARTICLE



## Capsular contracture in patients with prior breast augmentation undergoing breast conserving therapy and irradiation

Maja Schjølin Serritzlev<sup>a</sup>, Anne Kathrine Lorentzen<sup>a</sup>, Louise Wichmann Matthiessen<sup>b</sup> and Lisbet Rosenkrantz Hölmich<sup>a</sup> 

<sup>a</sup>Department of Plastic Surgery, Herlev and Gentofte Hospital, University of Copenhagen, Herlev, Denmark; <sup>b</sup>Department of Oncology, Herlev and Gentofte Hospital, University of Copenhagen, Herlev, Denmark

### ABSTRACT

Radiation is considered to be a risk factor for developing capsular contracture in augmented women, but the studies reporting on this subject show conflicting results. In this systematic review we sought to understand the risk of capsular contracture in augmented patients with breast cancer treated with breast conserving surgery and radiotherapy. A search was conducted through PubMed for studies reporting on breast cancer, breast augmentation and radiotherapy, with capsular contracture as our primary outcome. To determine if specific risk factors were significant predictors of the development of capsular contracture, we performed uni- and multivariate analysis. Our search revealed 136 articles, of which 12 were deemed eligible. A total of 237 patients were included in the analysis. Univariate analysis revealed that whole breast irradiation (WBI) was significantly associated with a higher risk of contracture ( $p < .001$ ), compared to treatment with accelerated partial breast irradiation (APBI). A higher radiotherapy dose regimen was also significantly associated with a risk of capsular contracture ( $p < .001$ ). When performing the multivariate analysis only the effect of increasing radiation dose remained significant ( $p < .05$ ). Neither the implant location nor the age of the implant had any significant effect on the development of contracture. In conclusion this review shows that WBI is associated with a higher risk of contracture compared to treatment with APBI. Because of the limitations of the studies included, further studies with larger patient cohorts are needed to establish this correlation and evaluate other potential risk factors.

### ARTICLE HISTORY

Received 13 October 2019  
Revised 20 February 2020  
Accepted 8 April 2020

### KEYWORDS

Breast cancer; breast conserving therapy; irradiation; capsular contracture; augmentation

### Introduction

Breast cancer is the most common type of cancer among women in Europe with more than half a million European women being diagnosed in 2018. It is estimated that one in eight women will develop breast cancer within the age of 85 years [1].

Standard treatment for breast cancer comprises surgery, radiotherapy and/or systemic therapy. Treatment is planned according to several factors including stage, tumor subtype and health status. Depending on the stage and progression of the disease, patients are either offered mastectomy or breast conserving treatment (BCT). BCT involves lumpectomy followed by radiotherapy, which can be delivered as whole breast irradiation (WBI) or as accelerated partial breast irradiation (APBI). Both types of radiation reduce the risk of recurrence, but also cause side effects, such as fibrosis, pain or dyspigmentation [2]. Among women with breast implants, radiotherapy has been pointed out as a risk factor for developing capsular contracture—a complication where a tight fibrous tissue capsule develops around the implant. Development of this capsule can cause pain and a poor cosmetic outcome with distortion of the breast [3]. Contracture is most often graded using the four-grade Baker scale—when classified as grade 1–2, the breast appears normal, but in grade 2 the breast feels harder to palpate. Grade 3 describes moderate contracture with some

distortion, while grade 4 is severe contracture with painful hardening of the breast and obvious distortion [4].

From 2016 to 2017 the total number of breast procedures being performed world-wide increased by 4%, with breast augmentation being the most frequently performed procedure, according to The International Society of Aesthetic Plastic Surgery (ISAPS) [5]. As women with prior augmentation age, a greater number of patients being diagnosed with breast cancer will undoubtedly include previously augmented patients. With this tendency, it is important for surgeons and radiation oncologists to be aware of the side effects of the oncologic treatment and possible complications in augmented women, in order to optimize treatment and patient information.

The literature has shown conflicting results regarding outcomes after BCT and radiotherapy in women with prior augmentation mammoplasty, as some studies state a high rate of capsular contracture and poor cosmetic results [6–9], while others have reported a much lower rate of complications as well as excellent or good cosmetic results [10–19]. The purpose of this study was to review the literature and thereby achieve a more complete understanding of the risk of capsular contracture in patients with prior breast augmentation receiving BCT and radiotherapy. Furthermore, we wished to identify any factors that increase the risk of developing capsular contracture.

## Methods

### Literature search

The search was conducted on 13 February 2019 using PubMed. The database search was carried out using the following terms: “breast cancer” and (“breast implant” or “breast augmentation” or “cosmetic implants” or “augmentation”) and (“radiation” or “irradiation” or “radiotherapy”). We added: not “ALCL” not “lymphoma,” because some articles were about breast implant associated anaplastic large cell lymphoma (ALCL), instead of the subject of interest. We conducted a second search trying to enlarge the number of eligible articles adding the following keywords: [(“breast cancer” OR “breast cancer *in situ*” OR “DCIS”) AND (“breast implant” OR “breast augmentation” OR “implant” OR “implantation” OR “cosmetic breast implantation” OR “cosmetic breast implants” OR “augmentation” OR “mammoplasty”) AND (“radiation” OR “irradiation” OR “radiotherapy” OR “breast conserving therapy” OR “BCT”)]. This did not yield further studies.

We included studies reporting on cosmetic outcome and/or rate of complications in previously augmented patients undergoing BCT and radiotherapy with no restriction on year of publication. We excluded reviews, animal studies, studies written in other languages than English, studies with less than five patients as well as studies that did not report outcome data for the patients in question. Two authors (MS and AKL) screened all titles for eligibility, and subsequently screened abstracts and full text articles. Any disagreements on which articles should be included were settled by discussion with the senior author (LH). References of the included studies and other relevant articles were also examined, and eligible studies included.

### Data extraction

The following data were extracted from the studies: year of publication, number of patients, mean age at diagnosis, time from augmentation to BCT, radiation type, total radiation dose (Gray), dose per fraction, implant location, cosmetic outcome/Baker grade after RT, contracture rate, number of explantations due to complications and mean follow up (Table 1). Furthermore, we calculated equivalent dose in 2 Gy fractions (EQD2) from the data available in the studies. We also extracted specifics about the type of complications reported in each study (Table 2).

To compare biological effects of various radiotherapy regimens we used the linear quadratic formula (EQD2) based on total dose given, dose per fraction and a tissue end point specific constant called  $\alpha/\beta$ . This is instead of looking only at the total dose, which does not take the dose per fraction received into consideration, and this is important for toxicity. We used the EQD2 formula to compare the different radiotherapy regimes used.

Some studies reported cosmetic outcome as a four-grade scale and some capsular contracture using the Baker scale. For comparability, we pooled the cosmetic outcome and Baker Grade into two categories: a “good” vs “poor” result, grouping patients into an “excellent to good/Baker 1–2” group and a “fair-poor/Baker 3–4” group.

### Statistical analysis

We carried out the statistical analyses using IBM SPSS Statistics 25 [21]. We used binary logistic regression to calculate odds ratio (OR) and p-values, which were considered statistically significant when  $p < .05$ . ORs for increasing radiation doses measured as

Table 1. Characteristics of the included studies.

Study	Year	Number of patients	Median/mean age at diagnosis	Time from augmentation to BCT/RT (years)	Radiation type	Total radiotherapy dose (Gray)	Dose per fraction	EQD2**	Implants subglandular	Implants submuscular	Missing data implant location	Grade 1–2 after RT***	Grade 3–4 after RT****	Missing data Baker/cosmesis	Number of capsular contracture	Number of explantations	Follow-up in months
Akhtari [12]	2015	7	61	–	APBI	34	3.4	41.93	–	–	7	6	1	0	0	2	32
Lei [13]	2014	16	50.7	10.7	APBI	38.5	3.85	50.37	1	15	0	15	0	1	0	0	23.9
Kuske [14]	2012	87	52	–	APBI	34	3.4	41.93	–	–	87	72	2	13	10	–	36
Tuli [20]	2006	6	49.2	12.6	WBI	59.7	1.76	57.31	–	–	6	6	0	0	0	0	45
Gray [6]	2004	17	50.7	7	WBI	60.6	1.8	58.58	8	9	0	12	5	0	5	3	36
Karanas [10]	2003	19	48	13.4	WBI	–	–	–	–	–	19	–	–	19	3	3	38
Victor [15]	1998	8	43	–	WBI	60.4	–	–	3	5	0	8	0	0	0	0	32
Mark [8]	1996	21	50	9	WBI	60.04	1.85	58.54	8	13	0	9	12	0	12	7	24
Handel [7]	1996	26	45	7.5	WBI	63.35	1.86	61.87	20	6	0	7	19	0	17	8	39.5
Guenther [19]	1994	20	52	–	WBI	–	2	–	14	6	0	17	3	0	–	1	45.6
Krishnan [16]	1993	5	50	–	WBI	65	–	–	–	–	5	4	1	0	0	–	58
Chu [21]	1992	6	45.3	–	WBI	62	2	62	–	–	6	5	1	0	–	–	43.7
Total		238	49.7	10.24	APBI = 110 pts WBI = 128 pts	62	–	–	54	54	130	161	44	33	47	24	37.8

\*Only augmented patients, reconstructed excluded. \*\*EQD2 = equivalent dose in 2 Gy fractions. \*\*\*Cosmesis/Baker Grade 1–2 after RT = Baker grade 1–2 or good/excellent cosmetic results–physician rated. \*\*\*\*Cosmesis/Baker Grade 3–4 after RT = Baker grade 3–4 or fair/poor cosmetic results–physician rated.

Table 2. Complications.

Study	Year	Number of patients	Follow-up in months	Time to complications	Number with capsular contracture	Number of explantations	Rupture	Leakage	Seroma	Fibrosis	Infection	Erosion	Pain	Tele-angiectasia	Total number of complications
Akthari [12]	2015	7	32	18 months	0	2	1	1	1	1	0	0	0	0	3
Lei [13]	2014	16	23.9	12 weeks–6 months	0	0	0	0	1	1	0	0	0	0	2
Kuske [14]	2012	87	36		10	–	–	–	–	1	–	–	–	6	17
Tuli [20]	2006	6	45		0	0	0	0	0	0	0	0	0	0	0
Gray [6]	2004	17	36		5	3	0	0	0	0	0	0	0	0	5
Karanas [10]	2003	19	38		3	3	1	0	1	0	2	1	2	0	10
Victor [15]	1998	8	32		0	0	0	0	0	0	0	0	0	0	0
Mark [8]	1996	21	18	<11 months	12	7	0	0	0	0	0	0	0	0	12
Handel [7]	1996	26	39.5		17	8	0	0	0	0	0	0	0	0	17
Guenther [19]	1994	20	20	5.6 months	–	1	1	0	0	4	0	0	0	0	5
Krishnan [16]	1993	5	58		0	–	–	–	–	–	–	–	–	–	0
Chu [21]	1992	6	43.7		–	–	–	–	–	–	–	–	–	–	–
TOTAL		238	35.2		47	24	3	1	2	7	2	1	2	6	71

\*Chu et al. [21] did not report on the rate of complications.

EQD2 was calculated per one dose-unit increase and for implant age as one year increase.

We wanted to conduct a formal metaanalysis, but due to the small size and design of the studies included, this was not feasible. Instead, we performed uni- and multivariate analyses. All analyses were performed for the number of individuals for whom the variable in question was available. When performing the multivariate analysis, enough data was obtained to include 172 patients. 65 cases were missing. Only variables which were statistically significant in the univariate analyses were included in the multivariate analysis.

## Results

### Literature search

Our literature search yielded 136 titles. By screening references, we could include three additional studies. After exclusion of irrelevant titles, 30 abstracts were screened for eligibility, leaving 15 articles for full-text screening. The trial flow diagram is shown in Figure 1.

One article met the inclusion criteria, but was excluded: in this study, Kuske et al. [22] followed 250 women for 20 years, and reported that less than 5% experienced new capsular contracture. There was no information on how the assessment of contracture was evaluated, and information regarding mean age, mean follow up, implant types and explantation was not evident in the paper. As the study did not report relevant outcome data, it was excluded. Five other articles were excluded for the reasons given in Figure 1 [20,23–26].

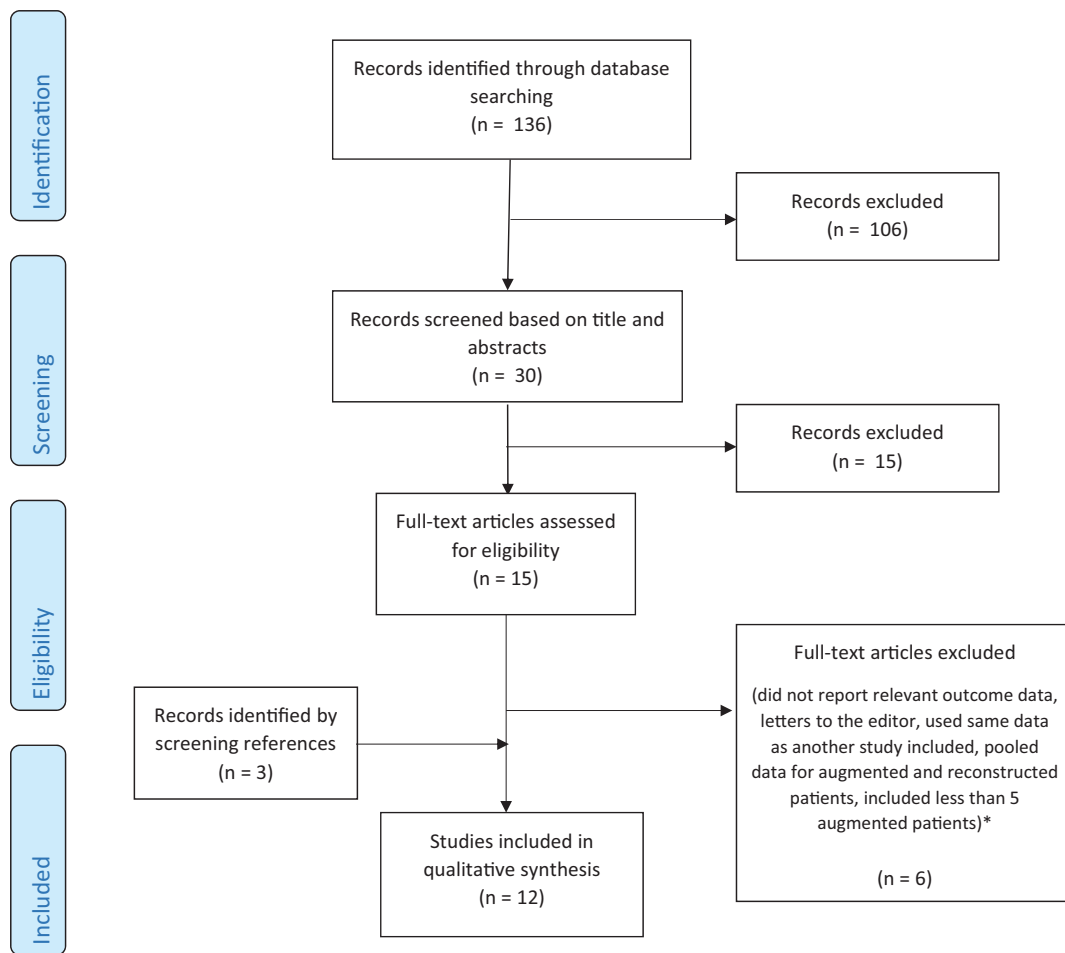
Table 1 lists the characteristics of included studies. The twelve included articles assessed a total of 238 patients with prior augmentation undergoing BCT and radiotherapy. 237 patients were included in the univariate analysis, since one patient was lost to follow-up in the study by Lei et al. [12].

### Outcomes after BCT and radiation therapy (RT)

The outcomes are given in Tables 1 and 2. A total of 47 women out of 212 (22.2%) developed capsular contracture after BCT and radiation therapy. Of 238 patients, 161 (67.6%) had a good cosmetic outcome/Baker Grade 1–2 after RT, while for 44 (18.5%) a poor cosmetic outcome/Baker Grade 3–4 was reported. Data on both cosmesis and Baker Grade was missing for 33 patients.

The studies presented their results with different measures: Three studies [6,7,14] used Baker Classification to define the degree of capsular contracture. Six studies focused on the cosmetic outcome, and used either Harvard breast cosmesis scale [11,13,27], RTOG criteria [12,28] or a four point scoring system [8, 18,19] to evaluate the cosmetic result. Two studies [15,29] assessed the cosmetic outcome by grading the result as excellent, good, fair or poor, but used their own definition or did not define these four categories further. Karanas et al. [9] focused on the rate of complications and did not use any scales or scoring systems.

Only one study [9] reported on BMI. Three studies [8,11,15] reported individual data on patient age, including a total of 33 patients, which was deemed too few to be included in analysis. Three studies [6,7,12] described baseline cosmesis/Baker Grade before radiation therapy (RT), primarily to point out that patients had a favorable cosmetic appearance before RT. Out of 59 patients, 57 (96.6%) had “good results” before RT, whereas 34 out of 58 patients (58.6%) had “good results” after RT. One patient was lost to follow-up [12].



\* References [21-26]

Figure 1. Trial flow diagram. \*References [21–26]

Table 3. Uni- and multivariate analysis.

	Capsular contracture		No capsular contracture		OR (95% CI)	p-Value
	N	(%)	N	(%)		
<b>UNIVARIATE</b>						
<i>Radiation</i>						
WBI (n = 102)	37	(36)	65	(64)		
APBI (n = 109)	10	(9)	99	(91)	0.18 (0.08–0.38)	<.001
EQD2 (n = 172)	43	(25)	129	(75)	1.15 (1.10–1.21)	<.001
<i>Implant location</i>						
Subglandular (n = 38)	23	(61)	15	(39)		
Submuscular (n = 26)	11	(42)	15	(58)	0.48 (0.17–1.32)	.154
Implant age (n = 21)	12	(57)	9	(43)	1.15 (0.94–1.14)	.165
<b>MULTIVARIATE</b>						
WBI (n = 63)	33	(52)	30	(48)		
APBI (n = 109)	10	(9)	99	(91)	0.72 (0.13–3.83)	.68
EQD2 (n = 172)	43	(25)	129	(75)	1.13 (1.03–1.24)	<.05

Table 2 shows the number of complications reported in each study. Complication rates were given for a total of 232 patients. For 6 patients this information was not obtainable, since Chu et al. [19] did not report on the rate of complications. 71 patients (30.6%) developed some type of complication. 24 of 140 patients (17.1%) required revision surgery due to either leakage, rupture, capsular contracture or fibrosis. Fibrosis was defined as Grade 2 or more on RTOG Late Morbidity Scoring Schema or on The National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (CTCAE v. 3) [30].

### Uni- and multivariate analysis

To investigate if implant age, radiation type, implant location, and radiation dose were significant predictors of the development of capsular contracture and the cosmetic outcome, we performed uni- and multivariate analyses with implant age, radiation type, radiation dose (measured in 2 Gy fractions) and implant location as independent and capsular contracture as dependent outcomes, respectively.

The univariate analyses showed that the odds of developing contracture were significantly lower when receiving accelerated

partial breast irradiation (APBI) ( $n=109$ ), compared to whole breast irradiation (WBI) ( $n=102$ ) (OR: 0.18 CI: 0.08–0.38,  $p<.001$ ). Data on contracture was not given for 27 patients, therefore only 211 were included in the analysis (Table 3).

In the univariate analysis, higher radiation doses were significantly associated with a higher risk of capsular contracture (OR: 1.15 CI 1.10–1.21,  $p<.001$ ). There was a lower risk of contracture for implants located submuscularly compared to implants located subglandularly, however, the difference was not statistically significant (OR: 0.48 CI 0.17–1.32,  $p=.154$ ). Capsular contracture was seen in 23 out of 38 patients with subglandular implants (60.5%), and in 11 out of 26 patients with submuscular implants (42.3%). There was also no statistically significant risk associated with increasing implant age (OR: 1.15 CI 0.94–1.14,  $p=.165$ ). Performing multivariate analysis, including type of radiation and radiation dose (in 2Gy fractions), only the effect of increasing radiation dose remained statistically significant (OR: 1.13 CI 1.03–1.24,  $p<.05$ ). Data are presented in Table 3.

## Discussion

### Risk factors for contracture

It has been suggested that higher doses of radiation correlate with a higher rate of contracture. As mentioned before, Handel et al. [6] reported a very high rate of contracture compared to other studies. Seventeen of their patients (65.4%) developed contracture, in contrast Karanas et al. [9] found that only 3 (15.8%) developed contracture, and both Victor et al. [14] and Tuli et al. [29] reported that none of their patients treated with BCT experienced contracture. All of these four studies used WBI. Other articles have pointed out that the fairly high doses of radiation given in the study by Handel et al. may account for the higher rate of contracture. Out of seven patients who got doses lower than 64.8Gy, one (14%) developed contracture, while 16 out of 19 (84%) who got doses of 64.8Gy or higher, experienced contracture. On the other hand, Gray et al. [7] gave all patients the same total doses of 60.6Gy, still 5 patients (29.4%) experienced contracture. Mark et al. [8] found no statistically significant correlation with radiation dose, though there was a trend toward increased contracture with higher doses of radiation. Our results also pointed towards higher odds of contracture with increasing doses (OR: 1.13 CI 1.03–1.24,  $p<.05$ ), but only when using a conversion factor (EQD2) to calculate biological effect of radiation fractions. The largest biological effects of radiation were observed in the studies using WBI instead of APBI.

Surgical technique and the amount of tissue removed have also been identified as possible reasons for poor cosmetic results. Karanas et al. [9] asserted that most women with existing breast implants have small native breast volumes, which can result in a poor cosmetic outcome, when undergoing lumpectomy. Size of implants and surgical experience might also be important factors affecting cosmetic outcome. Wiener et al. [31] examined how incision choice could affect the incidence of capsular contracture, and found that periareolar incision was associated with a higher risk of contracture compared to inframammary incision. They speculated that this could be explained by a higher bacterial load when cutting through large-caliber ducts near the nipple, increasing the risk of bacterial colonization, and potentially increasing the incidence of capsular contracture. When performing a lumpectomy, the placement of the incision will primarily rely on the location of the tumor, but the risk of capsular contracture might increase if the tumor is located near the nipple. Very few articles reported on the incision technique, and therefore we could not

investigate the significance of surgical technique in our dataset. The same applied to implant size and breast volume.

Patients having encapsulation of the implant or any grade of fibrosis before radiation are naturally subject to greater risk of contracture later on. Only three studies [6,7,12] reported on baseline cosmesis/Baker Grade. Halpern et al. [32] did a retrospective study on cosmetic results in reconstructed patients receiving radiation. One of their observations was that patients who had fibrotic changes and encapsulation prior to treatment ended up with poorer cosmetic results. When no fibrotic changes were seen in the study by Halpern et al. radiotherapy did not alter the already favorable cosmetic outcome significantly. Arguably, a high Baker Grade or fibrosis before RT might have been part of the reason why some studies, e.g. Mark et al. [8], experienced such a high rate of contracture compared to other studies—however, this data was not reported.

### WBI vs. APBI

Our analysis initially showed that WBI is associated with a significantly higher risk of capsular contracture compared to APBI. APBI is a localized type of treatment, which targets only a small area of breast tissue and is administered over a shorter period of time. These features minimize the exposure to the surrounding tissue as well as the exposure to the implant, reducing the risk of capsular contracture. Wobb et al. [33] have examined long-term clinical outcomes associated with APBI and WBI, and found that after 10 years there was no difference in recurrence or survival. Several studies support these results [34–37]. However, this method is generally used for selected patients with low-risk cancer. If a woman with prior breast augmentation is otherwise a candidate for APBI, our results indicate that this mode of radiation therapy should be preferred. However, no large studies on this subject have been conducted.

When performing a multivariate analysis, taking into account the effect of both radiation dose measured in 2Gy fractions and type of radiation on the development of contracture, our results no longer showed a significant association between WBI and higher risk of capsular contracture. Among 237 patients included in the analysis, there was only sufficient information on 172 patients covering both radiation dose in 2Gy fractions, type of radiation and rate of capsular contracture. Of the 172 patients included in the multivariate analysis, 63 patients received WBI and 109 patients received APBI, indicating that almost all APBI patients ( $n=110$ ) were included, while more than half of the WBI patients ( $n=128$ ) were excluded from the analysis. This distortion of the groups may probably explain why we could no longer see a significant correlation between WBI and the risk of contracture.

### Subglandular vs. submuscular implant location

Our results showed a tendency towards a lower risk of contracture with submuscular location of the implant compared to subglandularly located implants (OR: 0.48 CI 0.17–1.32), but this correlation was not significant ( $p=.154$ ).

Six articles reported data on implant location, the results of Karanas et al. was left out of Table 1, because they reported the implant location for both reconstructed and augmented patients, and for 22 patients the location was unknown. Implant location was evenly distributed, as 54 patients (50%) had their implants placed subglandularly, and the same number of patients had their implants placed submuscularly. Data was missing on 130 patients. Handel et al., Guenther et al. and Gray et al. [6,7,18] showed

results that pointed towards a worse cosmetic outcome or a higher rate of complications with subglandular implants compared to submuscular implants. Gray et al. reported that four out of eight with subglandular implants developed contracture (50%), while one out of nine (11.1%) with submuscular implants developed contracture. Handel et al. stated that 14 out of 20 patients with subglandular implants developed contracture (70%), while 3 out of 6 (50%) with submuscular implants experienced contracture. Guenther et al. did not report on the rate of contracture, but focused on the cosmetic outcome. When performing the same analysis with excellent/good/Baker 1–2 as our primary outcome instead of contracture, we still did not find any significant difference among the two groups.

Only three studies [6–8,18] reported the location of implants with individual information on who developed contracture. The numbers presented in Table 3 suggest that more patients with subglandular implants (60.5%) developed contracture compared to patients with submuscular implants (42.3%), however, this was not substantiated in the univariate analysis, which might be attributable to the fact that only 64 patients were included in this due to lack of information for the remaining implants. Again, the relatively small sample size may account for the fact that we do not see a significant association.

### Other complications

71 patients (30.6%) developed some kind of complication. There was a big difference between the studies in their way of reporting complications. While some seemed to focus on the more serious complications that required explantation or medication [9,11], others reported only on capsular contracture [6–8], and some did not report any complications at all [14,15,19,29]. The most frequently reported complication was contracture, comprising 66.2% of the total number of complications. No increased risk of any other complication was reported for augmented women having been treated with radiation.

Only a few studies reported the time period between the last treatment with radiotherapy to development of complications. For the ones that did, most complications had appeared within a year. Handel et al. [6] was one of the studies reporting the highest rate of contracture, and stated that the maximum time interval between the onset of contracture and completion of RT was 39.7 weeks, hence less than a year. The majority of the studies had a mean follow-up of at least one year. However, even longer follow-up would have been beneficial, since capsular contracture often develops later on, and with increasing frequency with increasing follow-up time. The Sientra Core Study [38] assessed the safety and effectiveness of Sientra's breast implants in augmented and reconstructed patients, and found that in augmented patients it took 3–4 years for over 50% of all capsular contracture events to occur, supporting the fact that a longer follow-up period might have revealed a higher rate of contracture.

### Limitations

The limitation of this systematic review is mostly related to the heterogeneity of the studies included. The studies did not use the same measures of outcome and had different definitions of both cosmesis and contracture. For most of the studies, aesthetic evaluation was done with non-validated methods. Moreover, the data given on the specific characteristics of each individual participating in the studies were sparse. In several of the studies, data was pooled for reconstructed and augmented patients [9,14,19,29],

which made it difficult to assess only augmented patients treated with BCT. Because data was so sparse and pooled in several of the studies included, we were not able to carry out analysis on several parameters, including implant type, implant size and follow up time. Additionally, most studies included a relatively small number of patients, and hence had to conclude that their study cohort was too small to confirm statistical significance. As mentioned in the methods section, we wanted to conduct a formal metaanalysis, but were not able to do so because of the limitations listed above.

Another important limitation is the risk of publication bias, meaning that the studies which show a given effect will have a stronger probability of being published. This phenomenon could apply both to the studies that reported a higher risk of capsular contracture with the use of WBI [6,8], but also to APBI studies [11–13] that all showed how treatment with partial breast irradiation produces favorable cosmetic outcomes with very few cases of capsular contracture. The more “interesting” articles have a better chance of being published, solely because there is a greater incentive to read them.

Only one article reported both physician-rated and patient-rated cosmesis. Lei et al. [12] reported that all of their patients had good to excellent cosmetic results according to the physician, while after 24 months, only 72.7% agreed with their physician. At this point, five patients were lost to follow-up. Since this is the only study that included both the patient's and the physician's opinions, it is unclear whether this discrepancy might account for some of the good results found in other articles that only assessed the physician's point of view. Though the differences in patient- and physician rated cosmesis may have an impact on the cosmetic result observed, it would not have affected the contracture rate reported in the studies, since this was only assessed by the physician.

### Perspectives to future studies

More elaborate studies are needed to understand the risk of contracture in augmented patients undergoing BCT and radiation. A future study should include a large patient cohort, exclude all reconstructed patients and focus solely on augmented patients. To clearly define any risk factors, it would be necessary to include detailed information on at least the following: BMI, particulars related to radiation treatment including dose, accumulated dose, administration as whole or partial breast radiation, incision technique, age at diagnosis as well as implant position, volume, age and type. Evaluation of fibrosis or Baker Grade before RT should also be assessed, and only by using the Baker scale or other validated grading methods. A long follow-up period should be included. A prospective study of all consecutive patients in a large-volume unit should be aimed for.

### Conclusion

The results of this review show that augmented patients receiving BCT and radiotherapy might have a greater risk of developing capsular contracture, when being treated with whole breast irradiation rather than partial breast irradiation. Furthermore, we found that increasing radiation dose was also associated with a higher risk of capsular contracture. These findings suggest that augmented patients should be informed about the risk of contracture when treated with WBI, but because there are so few articles addressing this subject, future large studies are needed to establish an association and to evaluate other potential risk factors.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

## ORCID

Lisbet Rosenkrantz Hölmich  <http://orcid.org/0000-0002-1983-5222>

## References

- [1] The European Breast Cancer Coalition. Breast Cancer Facts. 2018; [cited 2019 July 1]. Available from: <https://www.euro-padonna.org/breast-cancer-facts/>.
- [2] American Society of Clinical Oncology. Breast Cancer: Types of Treatment. 2018; [cited 2019 July 1]. Available from: <https://www.cancer.net/cancer-types/breast-cancer/types-treatment>.
- [3] Breastcancer.org. Capsular Contracture. 2019; [cited 2019 July 1]. Available from: <https://www.breastcancer.org/treatment/surgery/reconstruction/corrective/capsular-contracture>.
- [4] Stephan P. Capsular Contracture and Breast Implants. 2019; [cited 2019 July 20]. Available from: <https://www.verywell-health.com/capsular-contracture-and-breast-implants-430016>.
- [5] ISAPS. International Survey on Aesthetic/cosmetic procedures performed in 2017; [cited 2019 July 1]. Available from: [https://www.isaps.org/wp-content/uploads/2019/03/ISAPS\\_2017\\_International\\_Study\\_Cosmetic\\_Procedures\\_NEW.pdf](https://www.isaps.org/wp-content/uploads/2019/03/ISAPS_2017_International_Study_Cosmetic_Procedures_NEW.pdf).
- [6] Handel N, Lewinsky B, Jensen JA, et al. Breast conservation therapy after augmentation mammoplasty: is it appropriate? *Plast Reconstr Surg.* 1996;98(7):1216–1224.
- [7] Gray RJ, Forstner-Barthell AW, Pockaj BA, et al. Breast-conserving therapy and sentinel lymph node biopsy are feasible in cancer patients with previous implant breast augmentation. *Am J Surg.* 2004;188(2):122–125.
- [8] Mark RJ, Zimmerman RP, Greif JM. Capsular contracture after lumpectomy and radiation therapy in patients who have undergone uncomplicated bilateral augmentation mammoplasty. *Radiology.* 1996;200(3):621–625.
- [9] Karanas YL, Leong DS, Da Lio A, et al. Surgical treatment of breast cancer in previously augmented patients. *Plast Reconstr Surg.* 2003;111(3):1078–1083. discussion 1084–6.
- [10] Akhtari M, Nitsch PL, Bass BL, et al. Long-term outcome of accelerated partial breast irradiation using a multilumen balloon applicator in a patient with existing breast implants. *Brachytherapy.* 2015;14(2):289–292.
- [11] Akhtari M, Pino R, Scarboro SB, et al. Dosimetric considerations and early clinical experience of accelerated partial breast irradiation using multi-lumen applicators in the setting of breast augmentation. *J Contemp brachyther.* 2015; 6:423–429.
- [12] Lei RY, Leonard CE, Howell KT, et al. External beam accelerated partial breast irradiation yields favorable outcomes in patients with prior breast augmentation. *Front Oncol.* 2014; 4:154.
- [13] Kuske R, Chowdhury R, Snyder M, et al. Accelerated Partial Breast Irradiation for Select Breast Cancers in the Presence of Augmentation. *Int J Radiat Oncol Biol Phys.* 2012;84(3):S87.
- [14] Victor SJ, Brown DM, Horwitz EM, et al. Treatment outcome with radiation therapy after breast augmentation or reconstruction in patients with primary breast carcinoma. *Cancer.* 1998;82(7):1303–1309.
- [15] Krishnan L, Krishnan EC, Wolf CD, et al. Preservation of augmented breasts in patients with breast cancer. *Radiographics.* 1993;13(4):831–839.
- [16] E. Dragun A, T. Sowards K, Matthew Brown C. Breast-conservation surgery and adjuvant multicatheter balloon brachytherapy after augmentation mammoplasty. *Community Oncol.* 2011;8(3):134–136.
- [17] Bloom ES, Kirsner S, Mason BE, et al. Accelerated partial breast irradiation using the strut-adjusted volume implant single-entry hybrid catheter in brachytherapy for breast cancer in the setting of breast augmentation. *Brachytherapy.* 2011;10(3):178–183.
- [18] Guenther JM, Tokita KM, Giuliano AE. Breast-conserving surgery and radiation after augmentation mammoplasty. *Cancer.* 1994;73(10):2613–2618.
- [19] Chu FC, Kaufmann TP, Dawson GA, et al. Radiation therapy of cancer in prosthetically augmented or reconstructed breasts. *Radiology.* 1992;185(2):429–433.
- [20] Miller SH. Therapy for breast cancer after augmentation mammoplasty. *Plast Reconstr Surg.* 1992;89(5):1000–1001.
- [21] IBM Corp. Released. 2017. IBM SPSS Statistics for Windows VA. Armonk, NY: IBM Corp.
- [22] Kuske R. Breast conservation therapy without capsular contracture in young augmented women using interstitial brachytherapy. *J Contemp brachyther.* 2014;2:231–235.
- [23] Ryu J, Yahalom J, Shank B, et al. Radiation therapy after breast augmentation or reconstruction in early or recurrent breast cancer. *Cancer.* 1990;66(5):844–847.
- [24] Molinar VE, Sabbagh MD, Manrique OJ. Management of a late breast implant rupture in the setting of previous radiation. *BMJ case reports.* 2018 Jun 4. 2018.
- [25] Handel N. Conservation therapy for breast cancer following augmentation mammoplasty. *Plast. Reconstr. Surg.* 1999; 104(3):867–869. discussion 870–1.
- [26] Handel N, Lewinsky B, Silverstein MJ, et al. Conservation therapy for breast cancer following augmentation mammoplasty. *Plast Reconstr Surg.* 1991;87(5):873–878.
- [27] Trombetta M, Julian TB, Kim Y, et al. The allegheny general modification of the Harvard Breast Cosmesis Scale for the retreated breast. *Oncology.* 2009;23(11):954–956.
- [28] RTOG Foundation. RTOG/EORTC Late Radiation Morbidity Scoring Schema. 2019; [cited 2019 July 8]. Available from: <https://www.rtog.org/ResearchAssociates/AdverseEventReporting/RTOGEORTCLateRadiationMorbidityScoringSchema.aspx>.
- [29] Tuli R, Flynn RA, Brill KL, et al. Diagnosis, treatment, and management of breast cancer in previously augmented women. *Breast Journal.* 2006;12(4):343–348.
- [30] Common Terminology Criteria for Adverse Events v3.0 (CTCAE). 2006; [cited 2019 July 15]. Available from: [https://ctep.cancer.gov/protocolDevelopment/electronic\\_applications/docs/ctcae3.pdf](https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/ctcae3.pdf).
- [31] Wiener TC. Relationship of incision choice to capsular contracture. *Aesth Plast Surg.* 2008;32(2):303–306.
- [32] Halpern J, McNeese MD, Kroll SS, et al. Irradiation of prosthetically augmented breasts: a retrospective study on toxicity and cosmetic results. *Int J Radiat Oncol Biol Phys.* 1990;18(1):189–191.

- [33] Wobb JL, Shah C, Chen PY, et al. Brachytherapy-based accelerated partial breast irradiation provides equivalent 10-year outcomes to whole breast irradiation: a matched-pair analysis. *Am J Clin Oncol*. 2016;39(5):468–472.
- [34] Shah C, Antonucci JV, Wilkinson JB, et al. Twelve-year clinical outcomes and patterns of failure with accelerated partial breast irradiation versus whole-breast irradiation: results of a matched-pair analysis. *Radiother Oncol*. 2011; 100(2):210–214.
- [35] Livi L, Meattini I, Marrazzo L, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: five-year survival analysis of a phase 3 randomised controlled trial. *Euro J Cancer*. 2015; 51(4):451–463.
- [36] Polgar C, Fodor J, Major T, et al. Breast-conserving therapy with partial or whole breast irradiation: ten-year results of the Budapest randomized trial. *Radiother Oncol*. 2013; 108(2):197–202.
- [37] Strnad V, Ott OJ, Hildebrandt G, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. *Lancet (London, England)*. 2016;387(10015):229–238.
- [38] Stevens WG, Calobrace MB, Alizadeh K, et al. Ten-year core study data for Sientra's food and drug administration-approved round and shaped breast implants with cohesive silicone gel. *Plastic Reconstruc Surg*. 2018;141(4S):7s–19s.