Review Article

Breast conserving surgery revisited: a narrative review

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Background and Objective: Breast cancer surgery has seen a reverse evolution particularly over the last decade. There has been a universal acceptance of the fact that tumour biology and response to systemic treatment dictates risk of breast cancer recurrences and not surgical radicalism. The role of surgery has been "risk adapted" over the years to maintain function, contour and body image without compromising on the principles of surgical oncology. In this article we explore the first major transition from radical ablative mastectomies to breast conserving surgery (BCS) as we know it today comparing the different cancer specific and health related outcome measures for BCS and mastectomy.

Methods: We undertook comprehensive search using Ovid Medline from 1946 till May 2021 to identify complete papers published in English, primarily comparing the clinical outcomes of BCS and mastectomy using keywords such as "mastectomy", "breast conserving surgery" to name a few. Particular emphasis was given to data from randomised controlled trials and meta-analyses looking at the safety of breast conserving treatment. The oncological characteristics and results from key studies identified are analysed and summarised in this review.

Conclusions: BCS in conjunction with radiotherapy in appropriately selected cases gives results comparable to mastectomy for overall survival and relapse free survival. Current data suggest that in both node negative and node positive patients, breast conservation therapy (BCT) is a safe option with higher levels of favourable patient related outcomes.

Keywords: Breast conserving surgery (BCS); breast cancer; mastectomy; survival

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Introduction

Globally, breast cancer is the most diagnosed cancer and the leading cause of cancer-related deaths in women. The Surveillance, Epidemiology and End Results (SEER) programme estimates that 281,550 new breast cancers will be diagnosed in 2021 (129.1 per 100,000 women per year), accounting for 14.8% of all new cancers in the United States. In developed countries, approximately 1 in 8 (12.9%) women are likely to develop breast cancer during their lifetime (1). The GLOBOCAN 2018 survey showed that although developing countries had a lower overall incidence, it has been steadily increasing over the years (2).

Surgical management of breast cancer has evolved in the past decades with a reverse evolution, from heroic

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radicality to careful conservatism. In the past, Halsted's radical mastectomy was considered the standard of care for many decades. Although most modern breast surgeons consider it extremely radical, preceding studies assessed even more radical approaches in a desperate attempt to provide a cure and prevent local recurrences (LRs) and distant metastasis (3-5). These extended radical procedures did not show additional benefit and soon fell into disrepute due to the associated morbidity. Bernard Fisher introduced his novel hypothesis that invasive breast cancer is a systemic disease at inception (6). This new school of thought prompted a shift in practice towards a more conservative surgical approach, leading to the initiation of landmark trials like the NSABP B-04 that showed no advantage of radical mastectomy over a more conservative mastectomy (7). This paved the way for even more conservative surgical approaches leading to landmark trials in breast conservation (8,9).

The transition from radical mastectomy to breast conserving surgery (BCS) has been a scientific and systematic de-escalation process validated through several randomised controlled trials (9-16). Offering BCS, where appropriate, was an essential step towards improving the quality of life (QOL) in breast cancer survivors. The rapidly evolving sub-speciality of oncoplastic breast surgery (OPBS) has allowed for even more generous tumour excision volumes while at the same time enhancing the cosmetic appearance of the breast by adopting the aesthetic principles of plastic surgery. The realisation that breast cancer is a heterogeneous disease has led to a multidisciplinary approach to its management where each treatment modality contributes significantly to improved cancer outcomes. Recent advances in medical and radiation oncology have contributed significantly to improved cancer-specific outcomes following BCS by facilitating superior local and systemic control. The remit of surgical management has expanded to include optimal cosmesis and QOL in addition to achieving improved long-term survival and local control.

In this narrative review, we have explored breast conservation from its inception and looked at key trials in literature that enabled this transition from radicality. We have also considered several essential aspects: margins, adjuvant and neoadjuvant treatments, and their impact on survival. We present the following article in accordance with the Narrative Review reporting checklist (available at https://abs.amegroups.com/article/view/10.21037/abs-21-98/rc).

Methodology

Literature search was conducted using Ovid MEDLINE from 1946 to May 2021 combining relevant Keywords and MeSH headings to identify papers published mainly in the English language, primarily comparing BCS and mastectomy clinical outcomes. We gave particular emphasis to outcomes reported from randomised controlled trials and meta-analysis of relevant trials. In addition, the bibliography of these key publications was used to identify further relevant papers to be included in this narrative review.

The transition from mastectomy to breast conservation for invasive breast cancer

Six key randomised trials conducted in the 70s and 80s of the last century, many with long term follow up, showed no difference in overall and disease-free survival between BCS and mastectomy. They established the pivotal role of radiotherapy in decreasing the unacceptable high LR rate after breast conservation (9-12,15,16) (*Table 1*).

Of particular interest is the NSABP B-06, as this key trial reported outcomes of 1,851 women with stage 1 or 2 breast cancer and a tumour diameter of less than 4 cm, randomised to receive either total mastectomy (n=589) lumpectomy alone (n=634) or lumpectomy followed by radiotherapy (n=628). For patients undergoing a lumpectomy, tumours were resected with adequate surrounding normal breast tissue to ensure negative pathological margins. Approximately 10% of patients in the lumpectomy arm had positive margins and subsequently underwent a total mastectomy and received no further treatment. All patients identified with positive axillary nodes on axillary nodal dissection received adjuvant chemotherapy. At 20-year follow-up, the overall cumulative survival was comparable in the conservation and mastectomy arm. The cumulative incidence of death from any cause was 47.7% in women with no lymph node involvement versus 63.3% in women with axillary nodal disease. The conclusion was that lumpectomy and radiotherapy can be considered safe if the tumour resection margins are negative (9).

A meta-analysis conducted by Early Breast Cancer Trialists' Collaborative Group (EBCTCG) consisting of 3,100 patients from seven randomised trials reported no difference in the 10-year survival rate comparing BCS to total mastectomy (13). Another meta-analysis by Morris *et al.* included studies comparing BCS and total mastectomy

Table 1 Randomized controlled trials of BCS versus mastectomy in early breast cancer

Trial	Time period	Sample size	Median years of follow-up	T size (cm), inclusion criteria	Margins defined as	RT boost administered	LR		Overall survival		
							BCT (%)	Mastectomy (%)	BCT (%)	Mastectomy (%)	P value
NSABP B-06 (9)	1976–1984	1,851	20	4	Free	No	14	10	46	47	0.57
Milan (16)	1973–1980	701	20	2	–	Yes	9	2	42	41	1.0
NCI (12)	1979–1987	247	18	5	Grossly free	Yes	22	6	59	58	0.67
EORTC (15)	1980–1986	868	10	5	1 cm gross	Yes	20	12	65	66	0.23
Danish (11)	1983–1989	793	20	Any	Grossly free	Yes	NR	NR	58	51	0.24
IGR, Paris (10)	1972–1979	179	15	2	2 cm gross	Yes	9	14	73	65	0.16

BCS, breast conserving surgery; RT, radiation therapy; LR, local recurrence; BCT, breast conservation therapy; NSABP, National Surgical Adjuvant Breast and Bowel Project; NCI, National Cancer Institute; EORTC, European Organization for Research and Treatment of Cancer; IGR, Institute Gustave Roussy; NR, no response.

in early breast cancer, demonstrated a pooled odds ratio (OR) of 0.91 at 10 years. When more than 50% of node-positive patients in both the mastectomy and BCS arms received adjuvant radiation, both arms had similar survival rates. When less than 50% of node-positive patients in both arms received adjuvant nodal radiation, the OR was 0.69, and patients receiving breast conservation therapy (BCT) had a survival advantage (14).

This survival advantage was also seen in a recent prospective cohort study for the Swedish National Cancer Registry that included 48,986 women with T1–2, N0–1 breast cancer, treated outside clinical trials undergoing breast surgery between 2007 and 2018. Three groups were compared: mastectomy without radiation (Mx – RT), mastectomy with radiation (Mx + RT) and BCS with radiation (BCS + RT). At a median follow-up of 6.28 years and after adjustment for covariates notably comorbidities and socio-economic status, overall survival and breast cancer specific survival were significantly worse after Mx – RT [hazard ratio (HR), 1.79; 95% confidence interval (CI): 1.66–1.92 and HR, 1.66; 95% CI: 1.45–1.90, respectively] and Mx + RT (HR, 1.24; 95% CI: 1.13–1.37 and HR, 1.26; 95% CI: 1.08–1.46, respectively) than after BCS + RT. Studies with radiation following BCS have a better long-term outcome than Mx – RT, especially for triple negative breast cancer (TNBC) (17). This better survival with BCS is more likely to be associated with an inherent unavoidable selection bias in most non-randomized reported series. Mastectomy is more likely to be offered to relatively advanced cases with adverse clinical and radiological features. The effect of post-BCS radiation and other adjuvant therapies, especially when compared with mastectomy without indications for adjuvant radiotherapy, may be another possible explanation.

Following the findings of the key initial clinical trials, a gradual change in practice was observed and the SEER data reported an increase in the BCS rate from 23.9% in 1985 to 34.6% in 1989 (18). In 1991, the National Institute of Health (NIH) published a consensus statement acknowledging BCS in conjunction with radiation therapy (RT) as an acceptable treatment for appropriately selected patients with early breast cancer (18,19). Following the NIH Consensus recommendation, the BCS rate increased to 53.4% in women with stage 1 & 2 breast cancers (18,19) and in 2005, the National Cancer Database (NCDB) reported a breast conservation rate of approximately 65%. The contraindications to BCS mainly concern appropriate case selection and the inability to receive adjuvant radiotherapy. A high percentage of patients are suitable for BCS and the adoption of the new OPBS techniques have extended these. However, of late it has been observed that the mastectomy rates seem to be increasing in certain parts of the world for various reasons such as patient choice, surgeon preference, non-availability of RT, RT-related patient anxiety, better reconstruction options, younger age, mutation status and patient anxiety related to their family

history (20).

Factors affecting locoregional recurrence (LRR) rate post BCT

The primary goal of breast conservation is to achieve long term local control with an acceptable risk of LR. A pooled analysis of updated long-term results of all six trials showed that the LRR rate was higher for BCT compared to mastectomy at a median follow-up of approximately 14.6 years (OR, 1.561; 95% CI: 1.289–1.890; P<0.001). The LRR rates varied from 4.6% to 25.6% across the 6 studies (21). However, the mortality rates were no different in the two groups (OR, 1.070; 95% CI: 0.935–1.224; P=0.33). Due to the difference in the definition of "LRR" within the six trials (the NSABP B-06 trial classified supraclavicular recurrence as a LRR, whereas the EORTC trial classified them as a distant recurrence) (9,22) results were calculated for both locoregional and total recurrences separately. Four out of the six trials showed a lower LRR, and three out of four (with total recurrence data) showed a lower total recurrence rate with mastectomy. However, there were variations in surgical procedures among these trials that might have attributed to the heterogeneity for risk LRR. In the Milan study the surgeons performed quadrantectomies while in the Danish and US NCI study wide excision was performed with no gross margin involvement. Another key point to note about the Danish trial was that nearly 248 patients did not follow their randomisation. The trialists excluded these patients from the final analysis, resulting in non-adherence to the principle of intention-to-treat analysis. However, the pooled analysis results did not change even after the exclusion of the Danish study. The most notable finding was that the increase in LRR rates did not translate to a rise in mortality (21).

The high rate of LRR in these studies may be attributed to the era in which they were conducted and factors such as non-uniform reporting of pathological margins, non-availability of modern systemic chemotherapeutic regimes and older radiation techniques with no consistency of tumour bed boost. With the advent of better systemic treatment and radiotherapy protocols, several recent studies have shown a further decrease in the incidence of LRR post BCS with a reported rate of <5% (23,24).

An interplay of several factors contributes to the risk of LR that are either patient-related, tumour-related, or treatment-related factors. Amongst patient-related factors, young age is an independent risk factor for increased LR (25-27). Young age is frequently associated with biologically aggressive cancers that result in higher rates of local relapse. A family history of breast cancer and/or positive germline mutation status confer a higher risk of ipsilateral recurrences and an increased risk of second primaries (28). There are tumour related factors that increase the risk of LRR not only in BCS patients but also for patients with a mastectomy such as tumour size, grade, molecular subtype and disease burden in the axilla. Some features like extensive intraductal component (EIC) was for long considered as an independent risk factor for LR in BCS before routine inking of margins (29). However, recent evidence shows that is not true, provided it is adequately excised (30-33). EIC is an indicator of the potential residual burden of ductal carcinoma in situ (DCIS); however, the need for further re-excision should be gauged based on the extent of DCIS in proximity to the margin and post excision imaging.

A positive resection margin is the most important risk factor associated with a higher rate of LR. Adjuvant radiation with boost and adequate systemic therapy are also of paramount importance in reducing the risk of LR post BCS. Adjuvant chemotherapy and endocrine treatment further decrease the rate of LR. For example, a 66% decrease in LR was observed in patients who received adjuvant hormonal therapy in the NSABP B-13 trial (34). While the node negative, ER negative patients in the NSABP B-13 study, were randomised to receive chemotherapy versus no-treatment and the 8-year recurrence rate in the ipsilateral breast was 2.6% in the chemotherapy arm versus 13.4% in the non-treatment arm.

Margin assessment in BCS for invasive cancer

Involved resection margins is an important factor that contributes to the increased risk of LR as patients with positive surgical margins are at an increased risk of LR varying between 5% and 25% at a median follow up of 5–9 years (31,35-41). Historically, the definition of "an adequate margin/optimal surgical margin" following BCS has always been controversial due to the heterogeneity of results from various studies reported in the literature. For quite some time there was a lack of a clear consensus on adequate margin width, and this was examined by several authors (42-44). It is critical to understand that a negative margin does not rule out residual tumour in the breast but suggests that the residual tumour burden is low enough to be controlled with adjuvant radiotherapy. At the same

time, radiotherapy cannot compensate for inadequate surgery; instead, it serves to sterilise the operative field of microscopic residual disease. The guidelines for adequate margins vary in different parts of the world. They also tend to differ in some guidelines for invasive carcinoma and DCIS due to differences in their patterns of growth and the subsequent adjuvant therapy recommendations, which could potentially impact the risk of LRR (45-47).

NSABP B-06 (9) was one of the prospective randomised trials that defined microscopic margin as "no ink on tumour" and established the safety of BCT in invasive carcinoma. In 2014, "no ink on tumour" was accepted as a negative margin for invasive disease following the consensus guidelines recommended by the Society of Surgical Oncology (SSO) and the American Society for Radiation Oncology (ASTRO) (46). A meta-analysis by Houssami *et al.* looked at the effect of margin status and margin width on ipsilateral breast tumour recurrence (IBTR) in patients with early-stage invasive breast cancer (48). They included 21 studies that identified 1,026 LRs in 14,571 patients, which showed the OR for recurrence was 2.42 (P<0.001) for positive versus negative margins even after they had controlled for the use of tumour bed boost or endocrine therapy. They observed that increasing the width of a negative margin did not reduce the risk of local relapse. They concluded that a negative margin of "no ink on tumour" optimises local control and obtaining a wider margin does not alter outcomes. The National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology, the American Society of Breast Surgeons, and the St. Gallen International Expert Consensus group also accepted this definition (49). Considering the high risk of LR, patients with positive margins should at least undergo a margin revision or then a mastectomy (50).

The publication in 2017 of the national margins audit in the UK showed lots of variation in the different units, many accepting the Association of Breast Surgery (ABS) guidelines (1 mm for both invasive disease and DCIS), while some accepted SSO-ASTRO guidelines ('no ink on tumour' for invasive and 2 mm for DCIS) and some following other guidelines. The re-excision rate was 17.2% across the units and the interesting point was that if all units followed the ABS guidelines the re-excision rate would be 15% and if all followed the SSO-ASTRO this would be 14.8%, so, in essence whatever guidelines you follow the variation in the re-excision rate will be small and not significant (44).

There is no robust data to support the guideline of "no ink on tumour" in patients following neoadjuvant chemotherapy (NACT) but most units will use the same margin policy that they use for post-NACT patients. The expert panel at the 15th St. Gallen's Consensus conference in 2017 voted that "no ink of tumour" would be an acceptable margin in patients undergoing BCS following NACT (49). The majority also voted that a further re-excision of margins need not be undertaken provided the margins of the resection are clear even in cases where the specimen shows multifocal residual cell nests. Wimmer *et al.* retrospectively studied 406 women with invasive breast cancer that underwent BCS following NACT between 1994 and 2014. They concluded that there was no significant difference in LR risk, disease-free survival, or overall survival when comparing close, wide or unknown margins and that the "no ink on tumour" was acceptable following NACT (51).

Role of BCS and margin status in DCIS

Although DCIS has a mortality rate of under 1% after BCT, local control is vital as half of the local relapses are invasive cancers, impacting breast cancer-specific mortality (52). There are no randomised controlled trials that have evaluated the role of breast conservation in DCIS. Most guidelines have accepted wide excision with negative margins as a valid treatment option for localised DCIS based on the data from studies for invasive breast cancer. However, young age, symptoms at presentation, extensive disease, presence of necrosis, margin width and use of adjuvant therapy are all identified as risk factors for LR in patients undergoing BCS for DCIS (53). Margin width and utilisation of adjuvant therapy are modifiable risk factors. The Van Nuys Prognostic Index utilises margin width to risk stratify DCIS (54). The trials conducted to evaluate the benefit of radiotherapy post BCS in DCIS were not designed to assess the association of margin width to LR (53). Hence, there is no guidance on optimal margin width for DCIS. There is a lot of heterogeneity on multiple surveys showing margin width ranging from "no tumour on ink" to >1 cm as acceptable for patients with DCIS treated with BCT. The most widely accepted margin width for DCIS is based on the SSO-ASTRO guidelines which recommends a margin width of 2 mm for DCIS. The recommended margin width for DCIS is more than that in invasive cancer due to the adverse histological features of DCIS, such as the occurrence of skip lesions and multifocality (47).

A meta-analysis including 6,353 women that evaluated the

impact of margin status on LR in women with DCIS treated with BCT (55) reported no additional benefit for margins greater than 2 mm. Subsequently, in 2015, an SSO-ASTRO-ASCO multidisciplinary consensus panel concluded that a 2 mm margin minimises LR risk compared to narrower negative margins. More widely clear margins do not further reduce the risk of LR (47) as demonstrated also in two large single institution studies (55,56) reporting that close margins (<2 mm) were non-inferior to wider negative margins in this cohort of patients. The SSO-ASTRO-ASCO panel took all this evidence into account along with long term favourable outcomes of NSABP trials using no ink on tumour as their margin definition and recognising that minor differences in local control do not impact overall survival in DCIS. Hence, although 2 mm is the desired negative margin, they emphasised that re-excision of margins <2 mm may also be an individualised decision based on the volume of disease near a margin, post excision image findings, the cosmetic impact of re-excision, patient age, tumour size and grade, life expectancy and patient tolerance of risk with accentuation that a negative margin <2 mm is not by itself an indication for mastectomy (53).

In early breast cancer, is BCT a better option than mastectomy?

As discussed above, an earlier pooled analysis of updated data by Jatoi *et al.* in 2005 showed a higher LR rate in four of the six randomised trials, which was also shown in the pooled data. But when looking at the pooled data for mortality there was no significant difference noted (21). Dixon *et al.*, contend that consequent to the availability of better imaging modalities, greater attention to resection margins and better and more effective systemic adjuvant therapies administered in some cases for longer durations, the recurrence rates post BCT are comparable to those of mastectomy in early breast cancer (57). Several large, population-based cohort studies have shown BCT to be superior to mastectomy with respect to breast cancer specific and overall survival, independent of tumour characteristics (17,58-60). A more recent prospective cohort study with a median follow-up of 6.28 years suggests, that conservable node negative patients could potentially benefit from a significantly better breast cancer specific survival were they to undergo BCT as opposed to a mastectomy without radiotherapy. The benefit persists in node positive patients with a lower axillary burden undergoing mastectomy with radiotherapy but is lost in patients with a heavily node positive axilla (17). The better outcome persisted even after adjusting for age, tumour size, tumour grade, year at diagnosis, race, socio-economic status (17,61). Although a smaller proportion of the overall percentage of women affected, there has been some debate about young women <40 years and the increased risk of LR following BCT. Notwithstanding that there have been no randomised controlled trials comparing BCT to mastectomy in this cohort of young women, reported population based and institutional studies have shown no inferiority in overall survival (62). TNBC is deemed to be a more aggressive biological subtype with a higher risk of recurrence, metastasis and lower overall survival that affects typically younger women. Considering these factors, it is vital to maximise local control through risk adapted surgery. A recent SEER based retrospective population study reported that in patients with T1–2N0M0 patients with TNBC, BCT was associated with superior OS and BCSS when compared with mastectomy with or without radiotherapy (63).

Recent studies suggest that the long-held paradigm of the non-inferiority of BCT when compared with mastectomy, needs to change. With the advent of better systemic therapy, targeted therapies, longer endocrine adjuvant manipulation, margin assessment, improved radiotherapy planning and delivery systems the authors suggest that on balance BCT is probably equivalent or in some selected cases even superior to mastectomy in the modern era of multidisciplinary management. The lower complication rate and better QOL following BCT makes BCT a more patient centric option when compared to mastectomy for all patients who are suitable for both surgical options. However, the decision of BCT versus mastectomy is a more complex one and the rising rate of mastectomy and bilateral mastectomy in North America irrespective of BRCA status is a reminder of the same (64). In developing countries, this is confounded by cost of additional radiation and non-availability of radiation centres in smaller cities. Decision aids for shared decision making in this setting may improve decisional conflict as well as BCS rates (65).

BCS post-NACT

There has been a steady increase in the use of NACT in the treatment of breast cancer. This practice initially started with a view to downstaging locally advanced disease prior to surgery. Today it has evolved to down-sizing tumours with an unfavourable tumour to breast volume ratio to facilitate

BCS with a cosmetically acceptable result. Historically, BCS was achieved in up to 25% of cases following NACT (66). The NSABP B-18 study showed that an absolute 8% gain in BCS rate is observed in post-NACT cases. However, the fear of a patchy response to chemotherapy and a slightly increased risk of IBTR makes a reduction in the volume of resection a little difficult to comprehend in such cases.

Since smaller resection volumes are correlated with better cosmetic outcomes, it follows that downsizing with NACT may result in a better QOL. However, there are few prospective studies evaluating patient-related outcome measures. In a systematic review by Volders *et al*. (67), 26 studies were included after screening 1,219 studies, treating 5,379 patients with chemotherapy and 10,110 patients without chemotherapy. The margin positivity rate (2–39.8%), second surgery rate (2–45.4%), specimen excision volume rate (43.2–268 cm^3) showed significant heterogeneity. Only two studies reported on the cosmetic outcomes. The authors concluded that there was no evidence to suggest that preoperative chemotherapy improved surgical outcomes following BCS. This is further confounded by the presumed higher LR rate in BCS post-NACT, as seen in the latest EBCTCG analysis (68). However, it must be stressed the final analysis did include trials where patients did not undergo any surgery following NACT. The rate of LRR is between 4 and 10% across most recent studies of BCT post-NACT (69). In the BrighTNess randomised trial, a 53.2% conversion from BCS ineligibility to BCS eligibility was observed as a part of the secondary outcome analysis (64). However, only around 60% of these patients who were eligible for BCS actually underwent BCS. The decision was largely influenced by the prevailing use of bilateral mastectomy, especially in North America, irrespective of germline BRCA mutation carrier status.

Role of adjuvant radiotherapy

Postoperative whole breast radiation is a critical component of BCT. As mentioned earlier, it is instrumental in eradicating residual occult microscopic disease in the breast. Six randomised trials (9-12,15,16) and two meta-analyses (13,70) have demonstrated the role of lumpectomy with adjuvant radiotherapy in achieving locoregional control and organ preservation while providing survival outcomes that are equivalent to mastectomy. NSABP B-06 (9) is the largest trial with a follow up of 20 years to report a statistically significant decrease in local failure with a trend toward improved disease-free survival in the group that received radiotherapy versus the group that received lumpectomy alone. The lumpectomy plus radiotherapy group also showed no difference in survival compared with the mastectomy group, which was confirmed by the Milan (16), Danish (11) and EORTC trials (15).

Several prospective randomised trials of BCS have been conducted with or without radiotherapy for patients with stage I or II breast cancer. All trials have demonstrated a significant reduction in the risk of IBTR with the addition of radiotherapy at follow up of 5 years or more. The risk of IBTR after 5 years was between 6–39% without radiation compared with 1–14% with radiation (9,71-80) (*Table 2*). After BCS, the omission of radiotherapy is associated with a small but clinically significant increase in breast cancer mortality and decreased overall survival of between 0.5% to 5% within 10 years. The most notable difference was observed in node-positive patients in the Milan quadrantectomy trial (71) with a 10-year overall survival rate of 82% with RT versus 62% without RT. However, a pooled analysis of 15 prospective randomised trials with 9,422 women found the relative risk of mortality to be 1.086 (95% CI: 1.003–1.175), or an 8.6% excess risk of mortality, if radiotherapy was omitted (81). In 2011, the EBCTCG (82) published a meta-analysis of individual patient data for 10,801 from 17 randomised radiotherapy trials versus no radiotherapy after BCS. 8,337 women had pathologically confirmed nodal status as either node-negative (pN0) or node-positive (pN+) disease with a median follow up of 9.5 years, and 25% of women were followed up for more than a decade. In this meta-analysis, six trials were of radiotherapy after lumpectomy and included low-risk and high-risk women (category A, 4,398 women). Four were of radiotherapy after sector resection or quadrantectomy (category B, 2,399 women), and seven more recent trials were of radiotherapy after lumpectomy in low-risk women (category C, 4,004 women). It reported a 10-year risk of any (locoregional or distant) first recurrence to be 19.3% in women who received radiotherapy versus 35% in women who received BCS without radiotherapy, corresponding to an absolute risk reduction of 15.7% (95% CI: 13.7–17.7; P<0.00001) and a 3.8% absolute risk reduction in 15-year risk of breast cancer death from 25.2% to 21.4% (95% CI: 1.6–6.0; P=0.00005). In women with pN0 disease, the absolute recurrence reduction varied according to age, grade, oestrogen-receptor status, tamoxifen use, and extent of surgery, and these characteristics were used to predict large (≥20%), intermediate (10–19%), or lower (<10%) absolute reductions in the 10-year recurrence. The meta-

Table 2 Overall survival and LR rates comparing breast conservation surgery alone to breast conservation surgery and RT

Trial	Sample size	Tumour size (cm)	Tamoxifen (%)	Chemo (%)	Percerntage of LR risk		Follow up (years)
					BCS	BCS + radiotherapy	
British 1996 (78)	418	≤5	If ER positive	If ER negative	35	13	5
Ontario 1996 (73)	837	≤4	0	0	35	11	8
Scottish 1996 (75)	585	≤4	73	26	24.5	5.8	6
Uppsala-Orebro 1999 (72)	381	≤2	0	0	24	8.5	10
Milan 2002 (71)	579	≤2.5	12	17	23.5	5.8	10
NSABP B-06, 2002 (9)	1137	≤4	0	37	39.2	14.3	20
NSABP B-21, 2002 (74)	673	≤1	All	0	16.5	2.8	8
	336	≤1	0	0	–	9.3	–
Canadian 2004 (80)	769	≤5	All	0	7.7	0.6	5
GBCSG 2004 (76)	173	≤2	0	0	29.1*	4.3*	5.9
	174	≤2	All	0	2.5*	3.2*	–
ABCSG 2007 (77)	869	<3	All	0	5.1	0.4	5
CALGB 2013 (79)	636	≤2	All	0	8.5*	1.8*	12

*, crude result. LR, local recurrence; RT, radiation therapy; BCS, breast conservation surgery; NSABP, National Surgical Adjuvant Breast and Bowel Project; GBCSG, German Breast Cancer Study Group; ABCSG, Austrian Breast and Colorectal Cancer study Group; CALGB, Cancer and Leukaemia Group B; ER, estrogen receptor.

analysis concluded that about one breast cancer death was avoided by year 15 for every four recurrences avoided by year 10. The mortality reduction did not differ significantly from this overall relationship in any of the three categories for pN0 or pN+ disease.

Similar to that seen in invasive breast cancer, whole breast radiation reduces the risk of LR after BCS for DCIS (53). However, prognostic indices allow one to choose those low-risk patients with DCIS in whom radiation may be safely avoided. Between 17% and 44% of women with a diagnosis of DCIS are treated by wide excision alone without adjuvant radiotherapy (83). The SEER data for example reported that 31% of women underwent wide excision alone for DCIS between 1988–2011 (83). Several studies showed a significant disparity in the margin width that was adequate to decrease LR in wide excision alone for patients with DCIS (84-90).

Role of tumour bed boost

A tumour bed boost implies an extra dose of radiation applied to cover the primary tumour bed. The rationale behind a boost is to reduce LR that is most observed adjacent to the previous tumour bed site by eliminating remaining microscopic tumour foci. Tumour bed boost remained controversial for many years due to the results of the NSABP B-06 trial (9), which did not incorporate a boost compared to trials that used the boost. In 1997, a French trial (91) that randomised 1,024 patients with a tumour size of 3 cm or less to receive a 10-Gy boost to tumour bed versus no boost reported a statistically significant reduction in LR at 5 years in women receiving a boost (3.6%) compared with women who did not receive a boost (4.5%; P=0.044). The EORTC trial first published its results in 2001 (92) and again in 2007 (93) of 5,318 patients with stage I or II breast cancer and microscopically negative margins with a median follow up of 10.8 years. Patients were randomised to receive 50 Gy of radiation to the whole breast, followed by a 16 Gy boost versus no boost, confirming local control benefit from the addition of a boost. Seventeen-year updated results of the EORTC trial (94), reported that a boost dose of 16 Gy reduced the LR rate from 13.1% to 8.8% at 15 years and from 16.4% to 12% at 20 years (HR, 0.65). This relative risk reduction was seen across all age groups, with the largest absolute benefit (12%) observed in younger patients. A recent Cochrane review (95) of 8,325 women from 5 randomised control trials reported better local control

(HR, 0.64; 95% CI: 0.55–0.75) with tumour bed boost when compared to no boost. However, this did not translate into an overall survival (HR, 1.04; 95% CI: 0.94–1.14) or disease-free survival (HR, 0.94; 95% CI: 0.87–1.02) benefit. There was no difference in late toxicity scored by means of percentage of breast retraction assessment (mean difference, 0.38; 95% CI: –0.18 to 0.93). Cosmesis scored by an expert panel was better for the no boost group (OR, 1.41; 95% CI: 1.07–1.85) but showed no difference when scored by a physician (OR, 1.58; 95% CI: 0.93–2.69).

QOL studies

The multidisciplinary management of breast cancer and early diagnosis driven by screening and breast awareness have significantly improved overall survival rates. With an increasing number of survivors, maintaining a good QOL becomes vital. BCS was introduced to facilitate organ preservation and to move away from more ablative and defeminising surgery. A meta-analysis (96) included six studies comparing the quality-of-life following BCT and mastectomy without reconstruction (2 from Asia-Korea, Taiwan, and 4 from Europe, Turkey, Netherlands, and Germany) EORTC QLQ-BR23 questionnaire. The random effects model showed a statistically significant better QOL in 3 of the 8 aspects of the questionnaire, i.e., in the body image outcome, systemic therapy side effects outcome, and future perspective outcome in patients who underwent BCS compared to those that underwent mastectomy. However, the meta-analysis did not show any difference in QOL aspects such as sexual functioning, sexual enjoyment, upset by hair loss, arm symptoms and breast symptoms. This suggests that QOL with respect to sexual satisfaction is a complex process that is influenced by demographic, biological, psychological, and sociocultural factors. Most systematic reviews (97) report a significant heterogeneity across studies and hence the difficulty in interpreting results.

Conclusions

BCT is a safe treatment modality for patients with early breast cancer without any detriment to long-term oncological outcomes, with acceptable local and regional recurrence rates. Appropriate case selection, achieving adequate resection margins, timely and appropriate adjuvant therapies are crucial to successful outcomes. OPBS, which uses plastic surgical principles to reconstruct partial or total breast defects, is being increasingly preferred as it results in a better QOL and quicker psychosocial rehabilitation of patients.

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Footnote

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References

1. SEER data. Cancer Stat Facts: Female Breast Cancer. 2021. Available online: https://seer.cancer.gov/statfacts/

html/breast.html (Accessed 14th of May 2021 2021).
2. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
3. Halsted WS. I. A Clinical and Histological Study of certain Adenocarcinomata of the Breast: and a Brief Consideration of the Supraclavicular Operation and of the Results of Operations for Cancer of the Breast from 1889 to 1898 at the Johns Hopkins Hospital. Ann Surg 1898;28:557-76.
4. URBAN JA, BAKER HW. Radical mastectomy in continuity with en bloc resection of the internal mammary lymph-node chain; a new procedure for primary operable cancer of the breast. Cancer 1952;5:992-1008.
5. TAYLOR GW, WALLACE RH. Carcinoma of the breast; fifty years experience at the Massachusetts General Hospital. Ann Surg 1950;132:833-43.
6. Fisher B. The surgical dilemma in the primary therapy of invasive breast cancer: a critical appraisal. Curr Probl Surg 1970;1-53.
7. Fisher B, Jeong JH, Anderson S, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. N Engl J Med 2002;347:567-75.
8. Veronesi U. How important is the assessment of resection margins in conservative surgery for breast cancer? Cancer 1994;74:1660-1.
9. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347:1233-41.
10. Arriagada R, Lê MG, Rochard F, et al. Conservative treatment versus mastectomy in early breast cancer: patterns of failure with 15 years of follow-up data. Institut Gustave-Roussy Breast Cancer Group. J Clin Oncol 1996;14:1558-64.
11. Blichert-Toft M, Nielsen M, Düring M, et al. Long-term results of breast conserving surgery vs. mastectomy for early stage invasive breast cancer: 20-year follow-up of the Danish randomized DBCG-82TM protocol. Acta Oncol 2008;47:672-81.
12. Poggi MM, Danforth DN, Sciuto LC, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. Cancer 2003;98:697-702.
13. Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and surgery in early breast cancer. An overview of the randomized trials. N Engl J Med 1995;333:1444-55.
14. Morris AD, Morris RD, Wilson JF, et al. Breast-conserving therapy vs mastectomy in early-stage breast cancer: a meta-analysis of 10-year survival. Cancer J Sci Am 1997;3:6-12.
15. van Dongen JA, Voogd AC, Fentiman IS, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. J Natl Cancer Inst 2000;92:1143-50.
16. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347:1227-32.
17. de Boniface J, Szulkin R, Johansson ALV. Survival After Breast Conservation vs Mastectomy Adjusted for Comorbidity and Socioeconomic Status: A Swedish National 6-Year Follow-up of 48 986 Women. JAMA Surg 2021;156:628-37.
18. Lazovich D, Solomon CC, Thomas DB, et al. Breast conservation therapy in the United States following the 1990 National Institutes of Health Consensus Development Conference on the treatment of patients with early stage invasive breast carcinoma. Cancer 1999;86:628-37.
19. NIH consensus conference. Treatment of early-stage breast cancer. JAMA 1991;265:391-5.
20. Dicks E, Roome R, Chafe J, et al. Factors influencing surgical treatment decisions for breast cancer: a qualitative exploration of surgeon and patient perspectives. Curr Oncol 2019;26:e216-25.
21. Jatoi I, Proschan MA. Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer: a pooled analysis of updated results. Am J Clin Oncol 2005;28:289-94.
22. van Dongen JA, Bartelink H, Fentiman IS, et al. Randomized clinical trial to assess the value of breast-conserving therapy in stage I and II breast cancer, EORTC 10801 trial. J Natl Cancer Inst Monogr 1992;(11):15-8.
23. Zumsteg ZS, Morrow M, Arnold B, et al. Breast-conserving therapy achieves locoregional outcomes comparable to mastectomy in women with T1-2N0 triple-negative breast cancer. Ann Surg Oncol 2013;20:3469-76.
24. Abdulkarim BS, Cuartero J, Hanson J, et al. Increased risk of locoregional recurrence for women with T1-2N0 triple-negative breast cancer treated with modified radical mastectomy without adjuvant radiation therapy

compared with breast-conserving therapy. J Clin Oncol 2011;29:2852-8.
25. Nixon AJ, Neuberg D, Hayes DF, et al. Relationship of patient age to pathologic features of the tumor and prognosis for patients with stage I or II breast cancer. J Clin Oncol 1994;12:888-94.
26. Gajdos C, Tartter PI, Bleiweiss IJ, et al. Stage 0 to stage III breast cancer in young women. J Am Coll Surg 2000;190:523-9.
27. Kim SH, Simkovich-Heerdt A, Tran KN, et al. Women 35 years of age or younger have higher locoregional relapse rates after undergoing breast conservation therapy. J Am Coll Surg 1998;187:1-8.
28. Davey MG, Davey CM, Ryan ÉJ, et al. Combined breast conservation therapy versus mastectomy for BRCA mutation carriers - A systematic review and meta-analysis. Breast 2021;56:26-34.
29. Harris JR. Breast-conserving therapy as a model for creating new knowledge in clinical oncology. Int J Radiat Oncol Biol Phys 1996;35:641-8.
30. Fisher ER, Sass R, Fisher B, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (protocol 6). II. Relation of local breast recurrence to multicentricity. Cancer 1986;57:1717-24.
31. Anscher MS, Jones P, Prosnitz LR, et al. Local failure and margin status in early-stage breast carcinoma treated with conservation surgery and radiation therapy. Ann Surg 1993;218:22-8.
32. Smitt MC, Nowels KW, Zdeblick MJ, et al. The importance of the lumpectomy surgical margin status in long-term results of breast conservation. Cancer 1995;76:259-67.
33. Hurd TC, Sneige N, Allen PK, et al. Impact of extensive intraductal component on recurrence and survival in patients with stage I or II breast cancer treated with breast conservation therapy. Ann Surg Oncol 1997;4:119-24.
34. Fisher B, Dignam J, Mamounas EP, et al. Sequential methotrexate and fluorouracil for the treatment of node-negative breast cancer patients with estrogen receptor-negative tumors: eight-year results from National Surgical Adjuvant Breast and Bowel Project (NSABP) B-13 and first report of findings from NSABP B-19 comparing methotrexate and fluorouracil with conventional cyclophosphamide, methotrexate, and fluorouracil. J Clin Oncol 1996;14:1982-92.
35. Borger J, Kemperman H, Hart A, et al. Risk factors in breast-conservation therapy. J Clin Oncol 1994;12:653-60.
36. Dewar JA, Arriagada R, Benhamou S, et al. Local relapse and contralateral tumor rates in patients with breast cancer treated with conservative surgery and radiotherapy (Institut Gustave Roussy 1970-1982). IGR Breast Cancer Group. Cancer 1995;76:2260-5.
37. Freedman G, Fowble B, Hanlon A, et al. Patients with early stage invasive cancer with close or positive margins treated with conservative surgery and radiation have an increased risk of breast recurrence that is delayed by adjuvant systemic therapy. Int J Radiat Oncol Biol Phys 1999;44:1005-15.
38. Peterson ME, Schultz DJ, Reynolds C, et al. Outcomes in breast cancer patients relative to margin status after treatment with breast-conserving surgery and radiation therapy: the University of Pennsylvania experience. Int J Radiat Oncol Biol Phys 1999;43:1029-35.
39. Wazer DE, Schmidt-Ullrich RK, Ruthazer R, et al. Factors determining outcome for breast-conserving irradiation with margin-directed dose escalation to the tumor bed. Int J Radiat Oncol Biol Phys 1998;40:851-8.
40. Mirza NQ, Vlastos G, Meric F, et al. Predictors of locoregional recurrence among patients with early-stage breast cancer treated with breast-conserving therapy. Ann Surg Oncol 2002;9:256-65.
41. Park CC, Mitsumori M, Nixon A, et al. Outcome at 8 years after breast-conserving surgery and radiation therapy for invasive breast cancer: influence of margin status and systemic therapy on local recurrence. J Clin Oncol 2000;18:1668-75.
42. Azu M, Abrahamse P, Katz SJ, et al. What is an adequate margin for breast-conserving surgery? Surgeon attitudes and correlates. Ann Surg Oncol 2010;17:558-63.
43. Morrow M, Jagsi R, Alderman AK, et al. Surgeon recommendations and receipt of mastectomy for treatment of breast cancer. JAMA 2009;302:1551-6.
44. Tang SS, Kaptanis S, Haddow JB, et al. Current margin practice and effect on re-excision rates following the publication of the SSO-ASTRO consensus and ABS consensus guidelines: a national prospective study of 2858 women undergoing breast-conserving therapy in the UK and Ireland. Eur J Cancer 2017;84:315-24.
45. Association of Breast Surgery. Margin Width in Breast Conservation Surgery. 2015. Available online: https://associationofbreastsurgery.org.uk/media/64245/final-margins-consensus-statement.pdf (Accessed on the 17th of May 2021).
46. Buchholz TA, Somerfield MR, Griggs JJ, et al. Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: American Society of

Clinical Oncology endorsement of the Society of Surgical Oncology/American Society for Radiation Oncology consensus guideline. J Clin Oncol 2014;32:1502-6.
47. Morrow M, Van Zee KJ, Solin LJ, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Ductal Carcinoma In Situ. Ann Surg Oncol 2016;23:3801-10.
48. Houssami N, Macaskill P, Marinovich ML, et al. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis. Ann Surg Oncol 2014;21:717-30.
49. Curigliano G, Burstein HJ, Winer EP, et al. De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017. Ann Oncol 2017;28:1700-12.
50. Lin J, Lin KJ, Wang YF, et al. Association of surgical margins with local recurrence in patients undergoing breast-conserving surgery after neoadjuvant chemotherapy. BMC Cancer 2020;20:451.
51. Wimmer K, Bolliger M, Bago-Horvath Z, et al. Impact of Surgical Margins in Breast Cancer After Preoperative Systemic Chemotherapy on Local Recurrence and Survival. Ann Surg Oncol 2020;27:1700-7.
52. Narod SA, Iqbal J, Giannakeas V, et al. Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ. JAMA Oncol 2015;1:888-96.
53. Pilewskie M, Morrow M. Margins in breast cancer: How much is enough? Cancer 2018;124:1335-41.
54. Gilleard O, Goodman A, Cooper M, et al. The significance of the Van Nuys prognostic index in the management of ductal carcinoma in situ. World J Surg Oncol 2008;6:61.
55. Marinovich ML, Azizi L, Macaskill P, et al. The Association of Surgical Margins and Local Recurrence in Women with Ductal Carcinoma In Situ Treated with Breast-Conserving Therapy: A Meta-Analysis. Ann Surg Oncol 2016;23:3811-21.
56. Van Zee KJ, Subhedar P, Olcese C, et al. Relationship Between Margin Width and Recurrence of Ductal Carcinoma In Situ: Analysis of 2996 Women Treated With Breast-conserving Surgery for 30 Years. Ann Surg 2015;262:623-31.
57. Dixon JM. Breast conserving surgery: the balance between good cosmesis. In: Dixon JM. editor. A companion to specialist surgical practice: breast surgery. 5th ed. Edinburgh: Elsevier, 2014:51-70.
58. Cao JQ, Olson RA, Tyldesley SK. Comparison of recurrence and survival rates after breast-conserving therapy and mastectomy in young women with breast cancer. Curr Oncol 2013;20:e593-601.
59. Hofvind S, Holen Å, Aas T, et al. Women treated with breast conserving surgery do better than those with mastectomy independent of detection mode, prognostic and predictive tumor characteristics. Eur J Surg Oncol 2015;41:1417-22.
60. Silva E, Tan M. The Impact of Margin Status on Breast Conservation Rates. Ann Surg Oncol 2019;26:3931-8.
61. Johns N, Dixon JM. Should patients with early breast cancer still be offered the choice of breast conserving surgery or mastectomy? Eur J Surg Oncol 2016;42:1636-41.
62. van der Sangen MJ, van de Wiel FM, Poortmans PM, et al. Are breast conservation and mastectomy equally effective in the treatment of young women with early breast cancer? Long-term results of a population-based cohort of 1,451 patients aged ≤ 40 years. Breast Cancer Res Treat 2011;127:207-15.
63. Li H, Chen Y, Wang X, et al. T1-2N0M0 Triple-Negative Breast Cancer Treated With Breast-Conserving Therapy Has Better Survival Compared to Mastectomy: A SEER Population-Based Retrospective Analysis. Clin Breast Cancer 2019;19:e669-82.
64. Golshan M, Loibl S, Wong SM, et al. Breast Conservation After Neoadjuvant Chemotherapy for Triple-Negative Breast Cancer: Surgical Results From the BrighTNess Randomized Clinical Trial. JAMA Surg 2020;155:e195410.
65. Joshi SP, Ramarajan L, Deshpande O, et al. A randomized controlled trial of a self-administered, online decision-aid ("Navya Patient Preference Tool") to reduce decisional conflict in women with early breast cancer. J Clin Oncol 2020;38:abstr 7033.
66. Fisher B, Brown A, Mamounas E, et al. Effect of preoperative chemotherapy on local-regional disease in women with operable breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-18. J Clin Oncol 1997;15:2483-93.
67. Volders JH, Negenborn VL, Spronk PE, et al. Breast-conserving surgery following neoadjuvant therapy-a systematic review on surgical outcomes. Breast Cancer Res Treat 2018;168:1-12.
68. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised

trials. Lancet Oncol 2018;19:27-39.
69. Werutsky G, Untch M, Hanusch C, et al. Locoregional recurrence risk after neoadjuvant chemotherapy: A pooled analysis of nine prospective neoadjuvant breast cancer trials. Eur J Cancer 2020;130:92-101.
70. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;366:2087-106.
71. Veronesi U, Marubini E, Mariani L, et al. Radiotherapy after breast-conserving surgery in small breast carcinoma: long-term results of a randomized trial. Ann Oncol 2001;12:997-1003.
72. Liljegren G, Holmberg L, Bergh J, et al. 10-Year results after sector resection with or without postoperative radiotherapy for stage I breast cancer: a randomized trial. J Clin Oncol 1999;17:2326-33.
73. Clark RM, Whelan T, Levine M, et al. Randomized clinical trial of breast irradiation following lumpectomy and axillary dissection for node-negative breast cancer: an update. Ontario Clinical Oncology Group. J Natl Cancer Inst 1996;88:1659-64.
74. Fisher B, Bryant J, Dignam JJ, et al. Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less. J Clin Oncol 2002;20:4141-9.
75. Forrest AP, Stewart HJ, Everington D, et al. Randomised controlled trial of conservation therapy for breast cancer: 6-year analysis of the Scottish trial. Scottish Cancer Trials Breast Group. Lancet 1996;348:708-13.
76. Winzer KJ, Sauer R, Sauerbrei W, et al. Radiation therapy after breast-conserving surgery; first results of a randomised clinical trial in patients with low risk of recurrence. Eur J Cancer 2004;40:998-1005.
77. Pötter R, Gnant M, Kwasny W, et al. Lumpectomy plus tamoxifen or anastrozole with or without whole breast irradiation in women with favorable early breast cancer. Int J Radiat Oncol Biol Phys 2007;68:334-40.
78. Renton SC, Gazet JC, Ford HT, et al. The importance of the resection margin in conservative surgery for breast cancer. Eur J Surg Oncol 1996;22:17-22.
79. Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol 2013;31:2382-7.
80. Fyles AW, McCready DR, Manchul LA, et al. Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. N Engl J Med 2004;351:963-70.
81. Vinh-Hung V, Verschraegen C. Breast-conserving surgery with or without radiotherapy: pooled-analysis for risks of ipsilateral breast tumor recurrence and mortality. J Natl Cancer Inst 2004;96:115-21.
82. Early Breast Cancer Trialists' Collaborative Group (EBCTCG); Darby S, McGale P, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet 2011;378:1707-16.
83. Smith GL, Smith BD, Haffty BG. Rationalization and regionalization of treatment for ductal carcinoma in situ of the breast. Int J Radiat Oncol Biol Phys 2006;65:1397-403.
84. Silverstein MJ, Lagios MD, Groshen S, et al. The influence of margin width on local control of ductal carcinoma in situ of the breast. N Engl J Med 1999;340:1455-61.
85. Wong JS, Chen YH, Gadd MA, et al. Eight-year update of a prospective study of wide excision alone for small low- or intermediate-grade ductal carcinoma in situ (DCIS). Breast Cancer Res Treat 2014;143:343-50.
86. Macdonald HR, Silverstein MJ, Lee LA, et al. Margin width as the sole determinant of local recurrence after breast conservation in patients with ductal carcinoma in situ of the breast. Am J Surg 2006;192:420-2.
87. Wehner P, Lagios MD, Silverstein MJ. DCIS treated with excision alone using the National Comprehensive Cancer Network (NCCN) guidelines. Ann Surg Oncol 2013;20:3175-9.
88. Solin LJ, Gray R, Hughes LL, et al. Surgical Excision Without Radiation for Ductal Carcinoma in Situ of the Breast: 12-Year Results From the ECOG-ACRIN E5194 Study. J Clin Oncol 2015;33:3938-44.
89. Hughes LL, Wang M, Page DL, et al. Local excision alone without irradiation for ductal carcinoma in situ of the breast: a trial of the Eastern Cooperative Oncology Group. J Clin Oncol 2009;27:5319-24.
90. MacDonald HR, Silverstein MJ, Mabry H, et al. Local control in ductal carcinoma in situ treated by excision alone: incremental benefit of larger margins. Am J Surg 2005;190:521-5.
91. Romestaing P, Lehingue Y, Carrie C, et al. Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. J Clin Oncol 1997;15:963-8.
92. Bartelink H, Horiot JC, Poortmans P, et al. Recurrence

rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. N Engl J Med 2001;345:1378-87.
93. Bartelink H, Horiot JC, Poortmans PM, et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. J Clin Oncol 2007;25:3259-65.
94. Bartelink H, Maingon P, Poortmans P, et al. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. Lancet Oncol 2015;16:47-56. Erratum in: Lancet Oncol 2015;16:e6.
95. Kindts I, Laenen A, Depuydt T, et al. Tumour bed boost radiotherapy for women after breast-conserving surgery. Cochrane Database Syst Rev 2017;11:CD011987.
96. Ng ET, Ang RZ, Tran BX, et al. Comparing Quality of Life in Breast Cancer Patients Who Underwent Mastectomy Versus Breast-Conserving Surgery: A Meta-Analysis. Int J Environ Res Public Health 2019;16:4970.
97. Zehra S, Doyle F, Barry M, et al. Health-related quality of life following breast reconstruction compared to total mastectomy and breast-conserving surgery among breast cancer survivors: a systematic review and meta-analysis. Breast Cancer 2020;27:534-66.

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