Prediction of margin involvement and local recurrence after skin-sparing and simple mastectomy

DOI:

[10.1016/j.ejso.2016.04.055](https://doi.org/10.1016/j.ejso.2016.04.055)

Document Version

Accepted author manuscript

[Link to publication record in Manchester Research Explorer](#)

Citation for published version (APA):

Al-Himdani, S., Timbrell, S., Tan, K., Morris, J., & Bundred, N. J. (2016). Prediction of margin involvement and local recurrence after skin-sparing and simple mastectomy. *European Journal of Surgical Oncology*, 42(7), 935–941. <https://doi.org/10.1016/j.ejso.2016.04.055>

Published in:

European Journal of Surgical Oncology

Citing this paper

Please note that where the full-text provided on Manchester Research Explorer is the Author Accepted Manuscript or Proof version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version.

General rights

Copyright and moral rights for the publications made accessible in the Research Explorer are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Takedown policy

If you believe that this document breaches copyright please refer to the University of Manchester's Takedown Procedures [<http://man.ac.uk/04Y6Bo>] or contact uml.scholarlycommunications@manchester.ac.uk providing relevant details, so we can investigate your claim.

Prediction of margin involvement and local recurrence after skin-sparing and simple mastectomy

S. Al-Himdani^a

S. Timbrell^a

K.T. Tan^a

J. Morris^b

N.J. Bundred^{a,*}

bundredn@manchester.ac.uk

^aDepartment of Academic Breast Surgery, University Hospital of South Manchester NHS Foundation Trust, Manchester, UK

^bDepartment of Medical Statistics, University Hospital of South Manchester NHS Foundation Trust, Manchester, UK

*Corresponding author. University Hospital of South Manchester, Southmoor Road, Manchester, M23 9LT, UK. Tel.: +44 (0)161 291 5861.

Abstract

Skin-sparing mastectomy (SSM) facilitates immediate breast reconstruction. We investigated locoregional recurrence rates after SSM compared with simple mastectomy and the factors predicting oncological failure.

Methods

Patients with early breast cancer that underwent mastectomy between 2000 and 2005 at a single institution were studied to ascertain local and systemic recurrence rates between groups. Kaplan–Meier curves and log-rank test were used to evaluate disease-free survival.

Results

Patients (n = 577) underwent simple mastectomy (80%) or SSM (20%). Median follow up was 80 months. Patients undergoing SSM were of younger average age, less often had involved lymph nodes (22% vs 44%, p < 0.001), more often had DCIS present (79% vs 53%, p < 0.001) and involved margins (29% vs 15%, p = 0.001). Involved surgical margins were associated with large size (p = 0.001). The 8-year local recurrence (LR) rates were 7.9% for SSM and 5% for simple mastectomy respectively (p = 0.35). Predictors of locoregional recurrence were lymph node involvement (HR 8.0, for >4 nodes, p < 0.001) and involved surgical margins (HR 3.3, p = 0.002). In node negative patients, SSM was a predictor of locoregional recurrence (HR 4.8 [1.1, 19.9], p = 0.033).

Conclusion(s)

Delayed reconstruction is more appropriate for node positive early breast cancer after post-mastectomy radiotherapy. Re-excision of involved margins is essential to prevent local recurrence after mastectomy.

Keywords: Breast cancer; Local recurrence; Mastectomy; Breast reconstruction; Surgical margins; DCIS

Introduction

Skin-sparing mastectomy (SSM) with immediate breast reconstruction has become an increasingly popular surgical option amongst both patients and surgeons, advocated in around 25% of patients with early breast cancer and DCIS not amenable to breast conserving surgery.¹ Whilst simple mastectomy consists of removal of the entire breast and overlying skin, SSM involves removal of the nipple-areola complex (NAC) and the entire breast parenchyma whilst preserving the native skin envelope. Patient satisfaction is improved as the preserved skin creates a more naturally appearing cosmetic result.

After SSM, skin flaps often retain glandular breast tissue, thus potentially residual disease. Concerns have been raised about a higher rate of local, regional and systemic recurrence compared with simple mastectomy.^{2,3} Torresan et al.⁴ histologically evaluated skin flaps from 42 patients that were marked for SSM but underwent simple mastectomies. They found residual breast tissue present in 59.5% of patients and residual disease in 9.5%.⁴ Skin flaps of greater than 5 mm thickness were significantly associated with residual breast tissue and disease.⁴ Another evaluation of skin and subcutaneous tissue after 30 simple mastectomies found that 23% (6 out of 30) had skin flap involvement outside the

nipple-areolar complex (NAC).⁵

Skin tethering, large tumour size and perineural infiltration were all significant parameters associated with skin involvement.⁵

Minimising local recurrence is a priority for oncological surgeons as one in every four local recurrences after mastectomy are associated with increased risk of systemic relapse and one extra breast cancer death.⁶ We aimed to determine the factors predicting local recurrence after mastectomy.

Materials and methods

A retrospective review was conducted of all mastectomies undertaken at the University Hospital of South Manchester for unilateral breast cancer, between 2000 and 2005. All patients' case notes, operation notes and histopathology were reviewed. Demographic information was extracted for each patient. The operation notes and case notes were used to evaluate the exact axillary surgery and/or reconstruction performed. Ethical approval was not required for this local cancer audit in a single hospital unit.

Pathological data was extracted regarding tumour grade, size and type, lymph node status, lymphovascular invasion, tumour stage, margin status, oestrogen receptor (ER) status, Progesterone receptor (PR) status and Human-Epidermal growth factor-2 status (HER-2). Use of neoadjuvant chemotherapy, adjuvant chemotherapy/radiotherapy/hormone therapy was also evaluated.

Follow-up data evaluated included the time to local, regional, systemic recurrence and death. Inflammatory and locally advanced breast cancers were excluded from the study.

Surgical technique

Simple mastectomies or SSMs were undertaken with or without sentinel lymph node biopsy and/or axillary node surgery as deemed clinically appropriate according to the tumour stage and grade. Surgical incisions for SSMs involved a resection of the nipple-areola complex and underlying breast tissue. Scars from biopsies and/or skin overlying superficial tumours were usually resected. SSM was predominantly accompanied by immediate breast reconstruction with the most suitable type of reconstruction determined by the surgeon. Tissue expander reconstruction followed by insertion of a permanent implant, latissimus dorsi flap or a transverse rectus abdominis myocutaneous flap were all used. Decisions regarding the method of treatment were decided at the multi-disciplinary team meetings based on clinical examination, imaging and patient preference.

Follow up and recurrence

Patients were followed up annually by clinical examination of the breast, chest wall and axillary lymph nodes as well as mammography imaging.

If systemic recurrence was suspected, computer tomography (CT) scanning or magnetic resonance imaging (MRI) were utilised to confirm this. Local recurrence included histologically confirmed ipsilateral skin, chest wall and subcutaneous recurrence. Regional recurrence included regional lymph node metastases.

Statistical analysis

Data were analysed using SPSS 19.0 (IBM, Armonk, NY). Features compared between the SSM and simple mastectomy groups included patient demographics, method of detection, histological features and treatment. The students t-test was used to compare continuous variables between the two groups. The chi-squared was used to compare means between categorical variables. Recurrence was evaluated using Kaplan-Meier recurrence curves. The log-rank test was used to compare breast cancer free survival (recurrence) between the two groups. Factors associated with incomplete margins were identified by logistic regression analysis.

Univariate and multivariate Cox proportional hazards regression models were used to calculate predictors of recurrence whilst correcting for any potentially confounding variables. Hazard ratios (HR) were used to estimate the risk of recurrence and death, utilising a 95% confidence interval (CI). Statistical significance was considered when $P \leq 0.05$.

Results

Patient demographics and histological features of tumour

We identified 577 patients that had undergone mastectomy (SSM or simple) for invasive breast cancer (or DCIS) between January 2000 and December 2005 at our institution. Four hundred and sixty two (80%) underwent simple mastectomies whilst 115 (20%) SSM. Table 1 highlights the clinicopathological factor differences between the simple and SSM groups. Patients undergoing SSM were of younger average age compared with those undergoing simple mastectomies. A larger proportion of the simple mastectomies were not screen-detected, had DCIS present and had lymphovascular invasion, compared with those in the SSM group. There was no difference in receptor status between groups.

	Simple (n = 462)	SSM (n = 115)	Comparison of groups
Age (years)	61.6 (22–96)	49.1 (29–69)	P < 0.001 ^a
Symptomatic	314 (68%)	65 (56%)	P = 0.028 ^b
Grade			
0	11 (2%)	2 (2%)	P = 0.12 ^c
1	30 (6%)	7 (6%)	
2	176 (38%)	60 (52%)	
3	245 (53%)	46 (40%)	
Tumour size (n = 548)			
<15 mm	98 (22%)	28 (26%)	P = 0.02 ^c
15–25 mm	141 (32%)	48 (44%)	
>25 mm	201 (45%)	32 (30%)	
No. positive lymph nodes (n = 536)			
0	240 (55%)	79 (78%)	P < 0.001 ^c
1–4	119 (27%)	18 (18%)	
>4	76 (17%)	4 (4%)	
Tumour types			
IDC	323 (70%)	61 (53%)	P = 0.001 ^b
IDC and DCIS	181 (39%)	49 (43%)	P = 0.57 ^b
DCIS (pure)	62 (14%)	41 (36%)	P < 0.001 ^b
ILC	79 (17%)	8 (7%)	P = 0.008 ^b
Margin status (n = 565) Incomplete (≤1 mm)	68 (15%)	33 (29%)	P = 0.001 ^b
Lymphovascular invasion (n = 576)	100 (22%)	14 (12%)	P = 0.031 ^b
ER positive (n = 531)	347 (81%)	87 (85%)	P = 0.37 ^b
PR positive (n = 525)	299 (70%)	78 (78%)	P = 0.16 ^b
Her2 status (n = 158) [3 vs 0,1,2]	33 (26%)	10 (30%)	P = 0.82 ^b
LVI	99 (22%)	14 (12%)	P = 0.03
Sentinel lymph node biopsy (SLNB)	23 (5%)	9 (8%)	P = 0.33 ^b
Axillary node surgery			

Axillary node clearance (ANC)	393 (85%)	67 (58%)	P < 0.001 ^b
Axillary node sampling (ANS)	30 (7%)	20 (17%)	
None	39 (8%)	28 (24%)	
Breast Reconstruction (Immediate or delayed)	104 (23%)	113 (98%)	P < 0.001 ^b
Staging			
Stage 0	32 (7%)	37 (33%)	P < 0.001
Stage 1	143 (31%)	39 (34%)	
Stage 2	180 (40%)	33 (29%)	
Stage 3	101 (22%)	4 (4%)	
Radiotherapy			
Yes	129 (28%)	12 (11%)	P < 0.001 ^b
No	332 (72%)	101 (89%)	
Adjuvant or Neoadjuvant Chemotherapy (% of chemotherapy) (n = 156)			
Adjuvant	119 (26%)	37 (33%)	P = 0.17 ^b
Neoadjuvant	34 (7%)	4 (3%)	P = 0.21 ^b
Hormone therapy			
Yes	335 (73%)	75 (66%)	P = 0.21 ^b
No	125 (27%)	38 (34%)	
Recurrence ^a			
Locoregional (local)	27 (19)	9 (8)	
Five year	5.6% (4.6%)	5.7% (5.7%)	P = 0.73 ^d
Eight year	6.9% (5.0%)	9.0% (7.9%)	P = 0.35 ^d

^a T-test.

^b Chi-square test.

^c Linear trend.

^d Log⁻Rank test.

Surgical management

Approximately 85% of patients in the simple mastectomy group underwent axillary node clearance (ANC) and 58% in the SSM group (p < 0.001). More patients, 77%, in the simple mastectomy group never underwent reconstruction compared with 2% in the SSM group (p < 0.001) (See [Table 1](#)).

Adjuvant/neoadjuvant therapy

Hormone therapy, radiotherapy and/or chemotherapy (adjuvant or neoadjuvant) were administered to patients depending upon clinical stage and lymph node involvement and receptor status, following discussion at a multidisciplinary team meeting.

Adjuvant radiotherapy was used in 28% of the simple mastectomy patients compared with 11% of the SSM patients (p < 0.001). There were no differences in chemotherapy or endocrine therapy use (either neoadjuvant or adjuvant) between groups.

Local, regional and systemic recurrences

The median overall follow-up was 80 months (range 1~~to~~148 months). The number of patients with local or regional recurrences was 27 for simple mastectomy patients and 9 for SSM ([Table 1](#)). All except one of these recurrences were invasive. All DCIS recurrences after mastectomy for pure DCIS presented as invasive recurrence.

There were 86 systemic recurrences, 74/462 (6%) in the simple mastectomy group and 12/115 (10%) in the SSM group. Of the local recurrences 6/9 (66%) and 14/27 (57%) in the SSM and simple mastectomy groups respectively had no distant metastases.

Kaplan~~Meier~~ survival curves were used to calculate the proportion of patients with loco~~regional~~ recurrence at 5 and 8-year intervals in each of the groups.

In the simple mastectomy group the cumulative recurrence rates were 5.6% and 6.9% at 5 and 8 years respectively whereas in the SSM group, rates were 5.7% and 9.0% at the same time intervals (log~~rank~~ test [p = 0.73]). Local recurrence rates are also given in [Table 1](#).

Predictors of recurrence and survival analysis

Univariate analysis revealed patients with high grade tumours had a 2.61 times greater risk of local recurrence (p = 0.006) ([Table 2](#)). Involved nodes and incomplete margin clearance also increased local recurrence ([Table 2](#)).

Table 2 Factors predicting locoregional recurrence after SSM and simple mastectomy. Univariate Cox proportional hazards regression. Figures represent hazard ratios (95% CI); p-values.			
Characteristic	Overall (n = 577)	Simple (n = 466)	SSM (n = 115)
Mastectomy group			
SSM (vs simple)	1.14 (0.53, 2.42) P = 0.74		
Age (years)	0.99 (0.97, 1.02) p = 0.56	1.0 (0.97, 1.03) P = 0.80	0.92 (0.84, 0.99) P = 0.033
Symptomatic (vs screened)	1.31 (0.64, 2.66) P = 0.46	1.84 (0.74, 4.56) P = 0.19	0.63 (0.17, 2.35) P = 0.49
Grade 3	2.61 (1.28, 5.30) P = 0.006	2.44 (1.06, 5.57) P = 0.035	2.98 (0.74, 11.9) P = 0.12
ER positive (n = 531)	0.77 (0.34, 1.77) P = 0.54	0.75 (0.30, 1.86) P = 0.54	0.98 (0.12, 8.13) P = 0.98
PR positive (n = 525)	0.70 (0.34, 1.44) P = 0.34	0.61 (0.28, 1.33) P = 0.21	1.72 (0.21, 14.3) P = 0.62

HER 2 status (n = 158) [3 vs 0,1,2]	0.37 (0.09, 1.63) P = 0.19	0.26 (0.03, 2.02) P = 0.20	0.60 (0.07, 5.43) P = 0.65
Tumour size (n = 548)			
<15 mm 15–25 mm >25 mm	1 1.41 (0.53, 3.75) 1.68 (0.66, 4.27) P = 0.54	1 0.86 (0.29, 2.56) 1.26 (0.48, 3.28) P = 0.69	1 1 1.28 (0.30, 5.34) P = 0.74 ^a
Staging			
Stage 0/1 Stage 2 Stage 3	1 2.12 (0.94, 4.80) 3.79 (1.57, 9.15) P = 0.013	1 4.64 (1.33, 16.1) 7.26 (2.00, 26.4) P = 0.011	1 0.71 (0.14, 3.51) 3.23 (0.39, 26.9) P = 0.45
Lymphovascular invasion	2.66 (1.35, 5.25) P = 0.005	3.26 (1.52, 6.96) P = 0.002	1.02 (0.13, 8.12) P = 0.99
Positive lymph nodes			
0 1–4 >4	1 4.37 (1.83, 10.4) 7.49 (3.01, 18.7) P < 0.001	1 9.41 (2.68, 33) 14.5 (3.98, 53) P < 0.001	1 0.89 (0.10, 7.63) 3.69 (0.43, 31.6) P = 0.47
Any DCIS (pure or with IDC) (n = 571)	0.84 (0.43, 1.61) P = 0.60	0.57 (0.26, 1.23) P = 0.15	^b
Margin status			
Complete Incomplete (≤1 mm)	1 2.92 (1.48, 5.76) P = 0.002	1 2.86 (1.25, 6.56) P = 0.013	1 3.34 (0.90, 12.4) P = 0.072
Margin status by tumour type			
Incomplete (≤1 mm)	6.24 (1.07, 37)	3 2.57	2.87 (0.40, 20.5) P = 0.30

Pure DCIS	P = 0.045	(0.66, 9.94)	2.62 (0.44, 15.7)
DCIS & invasive	2.82	P = 0.17	P = 0.09
Invasive alone	(1.00, 7.92)	2.72	4
	P = 0.050	(0.86, 8.58)	
	2.56	P = 0.09	
	(0.82, 7.96)		
	P = 0.11		

- ^c Only 1 recurrence hence no regression model convergence.
- ^d No recurrence hence no regression model convergence.
- ^a There were no recurrences in the <15 mm subgroup, hence to obtain regression model convergence, the comparison ‘>25’ vs ‘<=15’ was made.
- ^b No regression model convergence as no recurrences in the DCIS group (all 9 recurrences were in the non-DCIS group).

Amongst node negative patients, univariate analysis showed SSM was associated with a higher risk of relapse (despite lower lymphovascular invasion [LVI]) with a HR of 4.8 (1.1–19.9 p = 0.0033).

In the multivariate analysis, the number of involved lymph nodes and involved pathological margins were both strong predictors of overall recurrence (Table 3). Patients with between one and four involved lymph nodes had a 4.6 times higher risk of recurrence and those with greater than four nodes involved had an 8 times higher risk, compared with those with no lymph nodes involved (p < 0.001). Patients with involved margins had a HR 3.28 (95% CI 1.57–6.86) higher risk of recurrence overall compared to those with no margin involvement (Table 3).

Table 3 Factors predicting locoregional recurrence after mastectomy (SSM and simple). Multivariable Cox proportional hazards regression. Figures represent hazard ratios (95% CI); p-values.

Characteristic	Overall hazard ratio
Overall	
Mastectomy type^a	
Simple SSM	1 1.05 (0.43, 2.56) P = 0.91
Positive lymph nodes	
0 1–4 >4	1 4.64 (1.93, 11.2) 7.97 (3.16, 20.1) P < 0.001
Margin status	
Complete Incomplete (≤1 mm)	1 3.28 (1.57, 6.86) P = 0.002
Lymph node negative patients	
Mastectomy type	
Simple SSM	1 4.8 (1.1, 19.9) p = 0.033

^a After adjusting for positive lymph node status and margin status.

Factors predicting margin involvement

In view of the high rate of margin involvement in SSM, we looked at the factors predicting margin involvement in the groups as a whole (Table 4). Large tumour size (>2.5 cm) and SSM was associated with an increased risk of margin involvement; both of which remain significant in multivariate analysis.

Table 4 Logistic regression analysis of factors associated with incomplete margins (≤1 mm). All patients (n = 577).				
	Univariate analysis		Multivariate analysis ^a	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (years)	0.99 (0.97, 1.00)	P = 0.14	—	—
Grade ^b				
0/1	1	P = 0.08	—	—
2	3.12 (0.92, 10.6)			
3	3.85 (1.16, 12.8)			
Tumour size ^b				
<15 mm	1	P = 0.003	1	P = 0.001
15–25 mm	1.82 (0.89, 3.69)		1.75 (0.85, 3.61)	
>25 mm	2.99 (1.54, 5.84)		3.44 (1.74, 6.82)	
DCIS involvement	1.44 (0.92, 2.26)	P = 0.11		
Presenting ^b				
Screened	1	P = 0.18		
Symptomatic	1.38 (0.86, 2.20)			
Operation type ^b				
Simple	1	P = 0.001	1	P < 0.001
SSM	2.33 (1.44, 3.85)		2.83 (1.70, 4.64)	

	3.77)		4.73)	
Tumour size, and operation type were all significantly associated with margin status when considered separately and multivariable analysis showed they were significant independent risk factors for incomplete margins.				
^a Significant independent associations.				

Involved margins were predicted by SSM, HR 2.83 (95% CI 1.7–4.73) and large tumour size HR 3.44 (CI 1.74–6.82). Subsequently, 43% (29 out of 68) with SM and 19% (6 out of 32) with SSM were given post-operative radiotherapy (see [Table 5](#)).

Table 5 Studies comparing local recurrence in SSM compared with simple mastectomy.								
First author	Year of publication	Years covered	Patients		Median follow up (months)		Local recurrence (%)	
			SSM	NSSM	SSM	NSSM	SSM	NSSM
Carlson ¹⁰	1997	1989–1994	327	188	15.6	32.4	4.8	9.5
Kroll ¹¹	1999	1986–1990	114	40	>60	>60	7.0	7.5
Simmons ³	1999	1990–1998	77	154	15.6	32.4	3.9	3.2
Horiguchi ¹²	2001	1993–1999	133	910	66	81	3.8	1.3
Greenway ¹³	2005	1989–2004	225	1022	49	49	7.1	5.4
Howard ^{14,a}	2006	1987–2002	34	395	59	59	0	3.8
Gerber ¹⁵	2009	1994–2000	48	130	101	101	10.4	11.5
Yi ¹⁶	2011	2000–2005	799	1011	53	53	0.6	1.4
^a All patients underwent TRAM flap reconstructions.								

Node negative patients that had undergone SSM had a five-fold higher risk of locoregional recurrence compared with simple mastectomies (p = 0.033) and a seven-fold higher local recurrence rate (p = 0.02 data not shown). Of these patients, 3 recurrences occurred in the 240 simple mastectomies and 5 in the 74 SSMs.

In patients developing local/regional recurrence (n = 36) (see [Table 3](#)), 53% (19/36) had been treated with chemotherapy compared with 32% (172/537) in the patients that did not develop recurrence (Cox's proportional hazards regression; p = 0.013). Approximately 61% (22/36) of the patients that developed local/regional recurrence had undergone adjuvant post-mastectomy radiotherapy, whilst 22% (12/115) of the patients without local/regional recurrence had received radiotherapy (Cox proportional hazards regression; p < 0.001). Patients with local/regional recurrence had a higher rate of distant metastases, 44% (16/36) compared with 10% (68/523) in the patients with no local/regional recurrence (Cox proportional hazards regression; p < 0.001). Finally, mortality was increased following local/regional recurrence at 61% (22/36), compared with 23% (122/541) in the patients with no recurrence (Cox proportional hazards regression; p < 0.001).

Discussion

Higher rates of local recurrence are associated with increased breast cancer death.⁶ It has been estimated that one in every four patients who develop local recurrence after breast cancer treatment subsequently die.⁶ We found increased breast cancer mortality in patients who developed local recurrence. These patients may not have died, had their disease not recurred locally.

Higher local recurrence rates might be expected after SSM where thicker breast flaps are used to enable the skin envelope to be preserved but little attention has been paid to this issue and initial reports from SSM have shown varying rates of local recurrence. Subcutaneous mastectomy was associated with higher recurrence rates^{2,7} but more recent meta-analysis has found no significant difference on local recurrence with the increased adjuvant therapies given after breast cancer surgery.^{3,8} This may relate to surgical technique ensuring skin overlying the cancer is sacrificed while still adhering to a skin preserving approach in the majority of cases in the meta-analysis.

Local recurrence rates in previous retrospective studies range from 0.6% to 10.4% in SSM and 1.3% to 11.5% after simple mastectomy (due to varying median follow-up ranging from 15.6 to 101 months).^{3,8}

A meta-analysis involving 1104 SSM and 2635 non-SSM and found recurrence rates in SSM varied from 3.8% to 10.4% whilst after simple mastectomy, rates were 1.7% to 11.5% with no difference between the groups.⁸ This meta-analysis does not necessarily reflect individual patient effects for node positive, negative or DCIS patients, or involved margins. We have clearly shown involved margins should lead to further treatment (usually surgical but potentially

radiotherapy) to clear the margin.

Adjuvant/neoadjuvant therapies which have reduced local recurrence rates internationally to close to 2% were not evaluated in this meta-analysis. The mean follow up period in these studies ranged from 49 to 118 months.^{6,9,10}

Lymph node negative patients are a good prognosis group, potentially cured by surgery alone. Yet, SSM was a predictor of recurrence due to the higher incidence of involved mastectomy margins and the lack of post-mastectomy radiotherapy after SSM. Lymph node negative patients may not receive any further adjuvant therapy, depending also upon the stage of their disease. Unit policy was for all ER positive patients to receive adjuvant endocrine therapy. In the absence of radiotherapy, when residual tissue, disease or DCIS is present, there will be a higher risk of local recurrence.^{11,12} Though several trials have demonstrated that radiotherapy use following mastectomy reduces the rate of local/regional recurrence (in invasive cancer, not DCIS), it has also been shown to adversely affect breast symmetry, increase implant loss and impair long term cosmetic outcome, potentially mitigating the quality of life benefits with reconstruction.^{8,13–15} Complication rates including flap necrosis and capsular contracture with radiotherapy use following autologous breast reconstruction of between 5% and 30% have been reported in the literature and implant loss rate up to 40%.^{11,15}

Local recurrence in most studies is directly related to a close (<1 mm) resection margin and in many UK institutions, re-excision is not standard procedure after mastectomy despite close margins. Indeed Oncoplastic surgery guidelines do not advise on management of involved margins after SSM.^{2,16–18}

Our data indicates that failure to re-excise leads to an unacceptably high local recurrence rate after SSM and we have now changed our practice.

In the US where re-excision occurs regularly with margins involved, the recurrence rate is significantly lower (2–4%); albeit somewhere in the region of 7%–~~10~~10% of patients require further re-excision of breast tissue and skin after SSM.^{6,9}

With the increasing use of oncoplastic surgery, close attention needs to be given to surgical margins and the management of close or involved margins after SSM. Particularly with DCIS, skip lesions over 2 mm away can occur in patients with widespread disease and SSM may be inappropriate.¹⁵ An alternative would be to remove more skin, particularly over the area of DCIS.

In patients with involved margins, the risk of local recurrence is increased and oncological safety compromised if no further surgery is performed. Oncological safety should be prioritised above the aesthetic appearance in these patients. We now ensure clear margins by re-excision of the margins after SSM if necessary, despite potential embarrassment to the Surgeon at explaining the issues to the patient.

Over 90% of all local recurrence after mastectomy occurs before five years have elapsed and late recurrence represents breast tissue left behind.^{3,6}

Cutting thicker mastectomy flaps to avoid skin necrosis increases local recurrence and accounts for the increased rate of late local recurrence seen in the SSM group at eight years.

The diagnostic core needle biopsy site is not routinely re-excised in oncoplastic SSM operations but several reports of local recurrence at the biopsy site have been documented and failure to re-excise the area skin, subjected to biopsy, represents a risk of increasing local recurrence.

Annual National audit of the post-mastectomy local recurrence rate in Holland has reduced the incidence rate across all Dutch hospitals to below 5% at five years¹⁹ and a similar National initiative reporting local recurrence in UK Trusts treating breast cancer is required to address ongoing problems (especially after SSM) with regard to local recurrence. Failure to audit and address these issues will lead to unnecessary breast cancer deaths in the UK.

Careful patient counselling before surgery also needs to address these issues to give full information on the risks of oncological relapse and to consider whether breast conserving surgery is possible, rather than mastectomy for an individual patient.

Conflict of interest

The authors have no conflict of interest to declare.

Funding sources

None.

Uncited reference

²⁰.

References

1

. B.A. Toth and P. Lappert, Modified skin incisions for mastectomy: the need for plastic surgical input in preoperative planning, *Plast Reconstr Surg* **87**, 1991, 1048–1053.

2

. S.A. Robertson, J.E. Rusby and R.I. Cutress, Determinants of optimal mastectomy skin flap thickness, *Br J Surg* **101** (8), 2014, 899–911.

3

. R.M. Simmons, S.K. Fish, L. Gayle, G.S. La Trenta, A. Swistel and P. Christos, Local and distant recurrence rates in skin-sparing mastectomies compared with non-skin-sparing mastectomies, *Ann Surg Oncol* **6**, 1999, 676–681.

4

. R.Z. Torresan, C.C. dos Santos, H. Okamura and M. Alvarenga, Evaluation of residual glandular tissue after skin-sparing mastectomies, *Ann Surg Oncol* **12**, 2005, 1037–1044.

5

. C.M. Ho, C.K. Mak, Y. Lau, W.Y. Cheung, M.C. Chan and W.K. Hung, Skin involvement in invasive breast carcinoma: safety of skin-sparing mastectomy, *Ann Surg Oncol* **10**, 2003, 102–107.

6

. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), P. McGale, C. Taylor, C. Correa, et al., Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: metaanalysis of individual patient data for 8135 women in 22 randomised trials, *Lancet* **383** (9935), 2014, 2127–2135.

7

. B.V. Palmer, K.R. Mannur and W.B. Ross, Subcutaneous mastectomy with immediate reconstruction as treatment for early breast cancer, *Br J Surg* **79** (12), 1992, 1309–1311.

8

. S. Lanitis, P.P. Tekkis, G. Sgourakis, N. Dimopoulos, R. Al Mufti and D.J. Hadjiminias, Comparison of skin-sparing mastectomy versus non-skin-sparing mastectomy for breast cancer: a meta-analysis of observational studies, *Ann Surg* **251**, 2010, 632–639.

9

. J. Shen, J. Ellenhorn, D. Qian, D. Kulber and J. Aronowitz, Skin-sparing mastectomy: a survey based approach to defining standard of care, *Am Surg* **74**, 2008, 902–905.

10

. A. McBride, P. Allen, W. Woodward, et al., Locoregional recurrence risk for patients with T1,2 breast cancer with 1-3 positive lymph nodes treated with mastectomy and systemic treatment, *Int J Radiat Oncol Biol Phys* **89** (2), 2014, 392–398.

11

. K.A. Behranwala, R.S. Dua, G.M. Ross, A. Ward, R. A'Hern and G.P. Gui, The influence of radiotherapy on capsule formation and aesthetic outcome after immediate breast reconstruction using biodimensional anatomical expander implants, *J Plast Reconstr Aesthet Surg* **59**, 2006, 1043–1051.

12

. S.E. Singletary and G.L. Robb, Oncologic safety of skin-sparing mastectomy, *Ann Surg Oncol* **10**, 2003, 95–97.

13

. R. Prabhu, K. Godette, G. Carlson, et al., The impact of skin-sparing mastectomy with immediate reconstruction in patients with Stage III breast cancer treated with neoadjuvant chemotherapy and postmastectomy radiation, *Int J Radiat Oncol Biol Phys* **82**, 2012, e587–e593.

14

. A.V. Tallet, N. Salem, V. Moutardier, et al., Radiotherapy and immediate two-stage breast reconstruction with a tissue expander and implant: complications and aesthetic results, *Int J Radiat Oncol Biol Phys* **57**, 2003, 136–142.

15

. N.P. Rowell, Are mastectomy resection margins of clinical relevance? A systematic review, *Breast* **19**, 2010, 14–22.

16

. D. Cao, T.N. Tsangaris, N. Kouprina, et al., The superficial margin of the skin-sparing mastectomy for breast carcinoma: factors predicting involvement and efficacy of additional margin sampling, *Ann Surg Oncol* **15**, 2008, 1330–1340.

17

. G.W. Carlson, T.M. Styblo, R.H. Lyles, J. Bostwick, D.R. Murray and C.A. Staley, Local recurrence after skin-sparing mastectomy: tumor biology or surgical conservatism?, *Ann Surg Oncol* **10**, 2003, 108–112.

18

. H. Medina-Franco, L.O. Vasconez, R.J. Fix, M.J. Heslin, S.W. Beenken and K.I. Bland, Factors associated with local recurrence after skin-sparing mastectomy and immediate breast reconstruction for invasive breast cancer, *Ann Surg* **235**, 2002, 814–819.

19

. M. van der Heiden-van der Loo, S. Siesling, M.W. Wouters, T. van Dalen, E.J. Rutgers and P.H. Peeters, The value of ipsilateral breast tumor recurrence as a quality indicator: hospital variation in the Netherlands, *Ann Surg Oncol* 2015, [Epub ahead of print].

20

. J.L. Uriburu, H.D. Vuoto, L. Cogorno, et al., Local recurrence of breast cancer after skin-sparing mastectomy following core needle biopsy: case reports and review of the literature, *Breast J* **12** (3), 2015, 194–198.

Queries and Answers

Query: Please check the inserted keywords, and correct if necessary.

Answer: Satisfied with correction, thank you.

Query: Please note that Table 5 was not cited in the text. Please check that the citation suggested is in the appropriate place, and correct if necessary.

Answer: This table is to be left out of the main manuscript, please. It was included for use as a supplementary table.

Query: The significance symbol P, has been represented by both P and p, and needs to be consistent throughout the article. Please check and amend as necessary.

Answer: Apologies. Please amend to a small 'p' throughout the manuscript.

Query: Please check the ‘Conflict of interest’ and ‘Funding sources’ section, and correct if necessary.

Answer: Both sections are correct, thank you.

Query: Please provide the volume number or issue number or page range or article number for the bibliography in Ref. 19.

Answer: Please update the publication details to Ann Surg Oncol. 2015 Dec;22 Suppl 3:S522-8.

Query: Please check the layout of Tables 1–4, and correct if necessary.

Answer: All appear to be correct, thank you.

Query: Please provide a definition for the significance of bold in the Tables 1 and 2.

Answer: Please remove the 'bolding' and replace with standard text format.

Query: Please note that, figures are not present in the article. Hence, please check the representation of figures in the caption of Tables 1 and 2, and correct if necessary.

Answer: We cannot find any errors in the table captions. Please can you clarify what is meant by this query?

Query: Table footnote ‘c’ and ‘d’ for the Table 2 were provided, but not cited in the table. Please provide a citation for them, and correct as necessary.

Answer: Please remove footnotes C and D.

Query: Please note that the citations present in the first column of Table 5 have not been matched with the author name before that reference citation. Kindly check, and correct if necessary.

Answer: Apologies: Carlson is Reference 17. The other references are as follows (please could these be added to the References?): Kroll SS, Khoo A, Singletary ES, Ames FC, Wang BG, Reece GP, Miller MJ, Evans GRD, Robb GL. (1999) Local recurrence risk after skin-sparing and conventional mastectomy: a 6-year follow-up. *Plastic and Reconstructive Surgery*. 104: 421-425. Horiguchi J, Iino JHY, Takei H, Koibuchi Y, Iijima K, Ikeda F, Morishita Y. (2000) A comparative study of subcutaneous mastectomy with radical mastectomy. *Anticancer Research*. 21: 2963-2967. Greenway RM, Schlossberg L, Dooley WC. (2005) Fifteen-year series of skin-sparing mastectomy for stage 0 to 2 breast cancer. *The American journal of surgery*. 190: 933-938. Howard MA, Polo K, Pusic AL, Cordeiro PG, Hidalgo DA, Mehrara B, Disa JJ. (2006) Breast cancer local recurrence after mastectomy and TRAM flap reconstruction: incidence and treatment options. *Plastic and reconstructive surgery*. 117: 1381-1386. Gerber B, Krause A, Dieterich M, Kundt G, Reimer T. (2009) The oncological safety of skin sparing mastectomy with conservation of the nipple-areola complex and autologous reconstruction: an extended follow-up study. *Annals of surgery*. 249: 461-468. Yi M, Kronowitz SJ, Meric-Bernstam F, Feig BW, Symmans WF, Lucci A, Hunt KK. (2011) Local, regional, and systemic recurrence rates in patients undergoing skin-sparing mastectomy compared with conventional mastectomy. *Cancer*. 117: 916-924.

Query: Uncited reference: This section comprises reference that occur in the reference list but not in the body of the text. Please position each reference in the text or, alternatively, delete it. Any reference not dealt with will be retained in this section. Thank you.

Answer: Please could reference 20 be cited at the end of the sentence 'The diagnostic core needle biopsy site is not routinely re-excised in oncoplastic SSM operations but several reports of local recurrence at the biopsy site have been documented and failure to re-excite the area skin, subjected to biopsy, represents a risk of increasing local recurrence.' (in the Discussion section).

Query: Please confirm that given names and surnames have been identified correctly.

Answer: Yes thank you.

Query: Your article is registered as a regular item and is being processed for inclusion in a regular issue of the journal. If this is NOT correct and your article belongs to a Special Issue/Collection please contact a.chadburn@elsevier.com immediately prior to returning your corrections.

Answer: This is correct, thank you.