Original article

Therapeutic mammaplasty is a safe and effective alternative to mastectomy with or without immediate breast reconstruction

S. Potter[1,2], A. Trickey[1], T. Rattay[3], R. L. O'Connell[4], R. Dave[5], E. Baker[6], L. Whisker[7], J. Skillman[8], M. D. Gardiner[9,10], R. D. Macmillan[7] and C. Holcombe[11], on behalf of the TeaM and iBRA-2 Steering Groups, the Breast Reconstruction Research Collaborative, and the Mammary Fold Academic and Research Collaborative

[1]Population Health Sciences, Bristol Medical School, and [2]Bristol Breast Care Centre, North Bristol NHS Trust, Bristol, [3]Cancer Research Centre, University of Leicester, Leicester Royal Infirmary, Leicester, [4]Royal Marsden NHS Foundation Trust, Sutton, [5]Nightingale Breast Unit, Manchester University NHS Foundation Trust, Manchester, [6]Department of Breast Surgery, Airedale General Hospital, Keighley, [7]Nottingham Breast Institute, Nottingham University Hospitals NHS Trust, Nottingham, [8]Department of Plastic Surgery, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, [9]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Nuffield Orthopaedic Centre, Oxford, [10]Department of Plastic Surgery, Frimley Health NHS Foundation Trust, Slough, and [11]Linda McCartney Centre, Royal Liverpool and Broadgreen University Hospital, Liverpool, UK

Correspondence to: Miss S. Potter, Bristol Centre for Surgical Research, Population Health Sciences, Bristol Medical School, 2.14 Canynge Hall, Whatley Road, Clifton, Bristol BS8 2PS, UK (e-mail: shelley.potter@bristol.ac.uk; @drshelleypotter, @CSR_Bris)

Background: Therapeutic mammaplasty (TM) may be an alternative to mastectomy, but few well designed studies have evaluated the success of this approach or compared the short-term outcomes of TM with mastectomy with or without immediate breast reconstruction (IBR). Data from the national iBRA-2 and TeaM studies were combined to compare the safety and short-term outcomes of TM and mastectomy with or without IBR.

Methods: The subgroup of patients in the TeaM study who underwent TM to avoid mastectomy were identified, and data on demographics, complications, oncology and adjuvant treatment were compared with those of patients undergoing mastectomy with or without IBR in the iBRA-2 study. The primary outcome was the percentage of successful breast-conserving procedures in the TM group. Secondary outcomes included postoperative complications and time to adjuvant therapy.

Results: A total of 2916 patients (TM 376; mastectomy 1532; mastectomy and IBR 1008) were included in the analysis. Patients undergoing TM were more likely to be obese and to have undergone bilateral surgery than those having IBR. However, patients undergoing mastectomy with or without IBR were more likely to experience complications than the TM group (TM: 79, 21·0 per cent; mastectomy: 570, 37·2 per cent; mastectomy and IBR: 359, 35·6 per cent; $P < 0·001$). Breast conservation was possible in 87·0 per cent of patients who had TM, and TM did not delay adjuvant treatment.

Conclusion: TM may allow high-risk patients who would not be candidates for IBR to avoid mastectomy safely. Further work is needed to explore the comparative patient-reported and cosmetic outcomes of the different approaches, and to establish long-term oncological safety.

*Members of the iBRA-2 and TeaM Steering Groups, the Breast Reconstruction Research Collaborative, and the Mammary Fold Academic and Research Collaborative are co-authors of this study and are listed in *Appendix S1* (supporting information)

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Introduction

Breast-conserving surgery (BCS) and adjuvant radiotherapy is the preferred option for many women with breast cancer[1]. Standard BCS may result in poor cosmetic outcome that can adversely influence quality of life[2–6]. Volume of breast tissue resected is a predictor of poor outcome[7,8]. Mastectomy is therefore often recommended for patients with large or multiple tumours, and currently 40 per cent[9] of the 55 000 women[10] diagnosed with breast cancer every year undergo this treatment in the UK. Although national guidelines[11] recommend that immediate breast reconstruction (IBR) should be offered routinely in this group, only one-quarter of women undergoing mastectomy currently receive immediate reconstruction[12,13]. The majority of women thus have a simple mastectomy, which can dramatically influence their psychological well-being[1,14].

Therapeutic mammaplasty (TM) combines wide local excision to remove the cancer with breast reduction and mastopexy techniques to reshape the remaining tissue[15,16]. These techniques can extend the boundaries of BCS by allowing adequate resection of large or multifocal cancers in patients with medium/large or ptotic breasts, without compromising oncological outcomes[17–19]. This may offer women a safe and effective alternative to mastectomy, with or without reconstruction.

There is, however, limited high-quality comparative evidence to support the benefits of TM as an alternative to mastectomy with or without IBR. Single-centre case series[20,21] have suggested that, overall, patients undergoing TM may report better quality of life than those undergoing mastectomy and IBR. There is emerging evidence to suggest that TM may be a cost-effective alternative to mastectomy and immediate implant-based[22] and free-flap[23] reconstruction in a North American setting.

Although these results are promising, there remains a need for high-quality research to establish the benefits of TM as a safe and effective alternative to mastectomy with or without IBR[24]. RCTs are ideally needed, but are not feasible in this context owing to patient and surgeon preference[25–27]. A large-scale multicentre prospective cohort study is therefore required to compare the clinical and patient-reported outcomes of TM *versus* mastectomy, and to establish the cost-effectiveness of the approach. Before such a study can be planned, however, preliminary work is needed to explore what proportion of patients could potentially avoid mastectomy by undergoing a TM procedure and the relative safety of this approach. Two large trainee-led prospective cohort studies have evaluated the short-term outcomes of TM[28] and mastectomy with and without IBR[29] separately. A pooled analysis was undertaken in the present study to evaluate the potential for TM to avoid mastectomy, and to compare the short-term outcomes of the different techniques.

Methods

The methods for the iBRA-2[29,30] and TeaM[28,31] prospective cohort studies have been reported previously. The two studies collected identical data items during an overlapping time interval and 37 centres participated in both studies, supporting the validity of a pooled analysis. In brief, all breast and plastic surgical units performing mastectomy with and without IBR and TM were invited to participate in the iBRA-2 and TeaM studies respectively via the professional associations (Association of Breast Surgery and British Association of Plastic Reconstructive and Aesthetic Surgeons) and the breast and plastic surgery collaborative research networks (Reconstructive Surgery Trials Network and Mammary Fold Academic and Research Collaborative).

Consecutive patients undergoing mastectomy with or without IBR for invasive or preinvasive breast cancer at participating centres between July and December 2016 were recruited prospectively to the iBRA-2 study. Patients undergoing TM, defined as 'the oncoplastic application of breast reduction or mastopexy techniques including removal of skin to reduce the skin envelope to treat invasive or pre-invasive (ductal carcinoma *in situ*; DCIS) breast cancer using breast conserving surgery'[31], at participating centres between 1 September 2016 and 30 June 2017 were recruited to the TeaM study. The surgeon-reported indication for offering TM was recorded prospectively, and only the subgroup of patients offered TM to avoid mastectomy were included in the present study.

Patients in both studies were identified from multidisciplinary team (MDT) meetings; operating diaries and clinics. Demographic and operative data were collected prospectively and oncological data, including adequacy of resection for patients having TM and recommended adjuvant treatments, were obtained from postoperative MDT meetings. The date of first adjuvant treatment was obtained by review of appropriate clinical information systems. Complications, readmissions and reoperations were collected prospectively by clinical or case-note review depending on whether the patient needed to attend for follow-up. REDCap[32] data capture software was used for data collection in both studies.

Both studies were classified as service evaluations according to the National Health Service (NHS) Health Research Authority online decision tool (http://www.hra-decisiontools.org.uk/research/), so ethical approval was

Table 1 Demographics of participants by procedure type

	All patients (*n* = 2916)	Therapeutic mammaplasty (*n* = 376)	Mastectomy only (*n* = 1532)	Mastectomy and immediate breast reconstruction (*n* = 1008)	*P*‡
Age (years)*	57 (48–68; 21–96)	56 (49–65; 29–85)	65 (54–75; 26–96)	50 (44–57; 21–82)	< 0·001§
< 35	100 (3·4)	11 (2·9)	34 (2·2)	55 (5·5)	< 0·001
35–44	370 (12·7)	33 (8·8)	115 (7·5)	222 (22·0)	
45–54	769 (26·4)	114 (30·3)	257 (16·8)	398 (39·5)	
55–64	659 (22·6)	122 (32·4)	320 (20·9)	217 (21·5)	
65–75	580 (19·9)	71 (18·9)	406 (26·5)	103 (10·2)	
> 75	425 (14·6)	23 (6·1)	392 (25·6)	10 (1·0)	
Missing	13 (0·4)	2 (0·5)	8 (0·5)	3 (0·3)	
BMI (kg/m^2)	26·7 (23·4–31; 13·4–80·7)	28·8 (25·0–33·0; 18·3–56·0)	27·3 (23·7–32·2; 13.4–80·7)	25·3 (22·4–28·8; 15·6–61·4)	< 0·001§
Underweight	56 (1·9)	1 (0·3)	33 (2·2)	22 (2·2)	< 0·001
Normal	967 (33·2)	87 (23·1)	445 (29·0)	435 (43·2)	
Overweight	883 (30·3)	114 (30·3)	457 (29·8)	312 (31·0)	
Obese	477 (16·4)	97 (25·8)	252 (16·4)	128 (12·7)	
Severely obese	346 (11·9)	69 (18·4)	221 (14·4)	56 (5·6)	
Missing	187 (6·4)	8 (2·1)	124 (8·1)	55 (5·5)	
Co-morbidities					
Ischaemic heart disease	151 (5·2)	11 (2·9)	133 (8·7)	7 (0·7)	< 0·001
Diabetes	248 (8·5)	16 (4·3)	189 (12·3)	43 (4·3)	< 0·001
Other co-morbidity	1329 (45·6)	143 (38·0)	848 (55·4)	338 (33·5)	< 0·001
Smoking status					0·516
Non-smoker	2097 (71·9)	278 (73·9)	1082 (70·6)	737 (73·1)	
Ex-smoker	452 (15·5)	51 (13·6)	241 (15·7)	160 (15·9)	
Current smoker	316 (10·8)	40 (10·6)	180 (11·7)	96 (9·5)	
Missing	51 (1·7)	7 (1·9)	29 (1·9)	15 (1·5)	
Previous oncological therapy					
Neoadjuvant chemotherapy	478 (16·4)	56 (14·9)	230 (15·0)	192 (19·0)	0·034
Neoadjuvant endocrine therapy	210 (7·2)	24 (6·4)	136 (8·9)	50 (5·0)	< 0·001
ASA fitness grade					< 0·001
I	840 (28·8)	135 (35·9)	333 (21·7)	372 (36·9)	
II	1729 (59·3)	223 (59·3)	906 (59·1)	600 (59·5)	
III	329 (11·3)	16 (4·3)	279 (18·2)	34 (3·4)	
IV	6 (0·2)	0 (0)	6 (0·4)	0 (0·0)	
Missing	12 (0·4)	2 (0·5)	8 (0·5)	2 (0·2)	
Laterality of surgery					< 0·001
Unilateral TM/Mx+/−IBR	2476 (84·9)	241 (64·1)	1427 (93·1)	808 (80·2)	
Bilateral TM/Mx+/−IBR	197 (6·8)	8 (2·1)	71 (4·6)	118 (11·7)	
Unilateral TM/Mx+/−IBR + contralateral symmetrization	217 (7·4)	126 (33·5)	19 (1·2)	72 (7·1)	
Unilateral TM/Mx+/−IBR + contralateral oncological procedure	26 (0·9)	1 (0·3)	15 (1·0)	10 (1·0)	
Axillary surgery†					< 0·001
None	192 (6·6)	65 (17·3)	49 (3·2)	78 (7·7)	
Sentinel node biopsy/axillary sampling	1674 (57·4)	251 (66·8)	871 (56·9)	552 (54·8)	
Axillary lymph node clearance	759 (26·0)	60 (16·0)	506 (33·0)	193 (19·2)	
Missing	291 (10·0)	0 (0)	106 (6·9)	185 (18·4)	

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.; range). †Axillary surgery performed at the time of therapeutic mammaplasty (TM)/mastectomy (Mx) with or without immediate breast reconstruction (IBR) based on preoperative assessment of disease (such as axillary surgery not performed routinely in patients having breast-conserving surgery for ductal carcinoma *in situ*). ‡χ^2 test across procedure groups, except §Kruskal–Wallis test across procedure groups.

Table 2 Postoperative complications by procedure type

	All patients ($n = 2916$)	Therapeutic mammaplasty ($n = 376$)	Mastectomy only ($n = 1532$)	Mastectomy and immediate breast reconstruction ($n = 1008$)	*P**
At least one breast or donor-site complication	1008 (34·6)	79 (21·0)	570 (37·2)	359 (35·6)	< 0·001
Any major complication	229 (7·9)	8 (2·1)	76 (5·0)	145 (14·4)	< 0·001
Unplanned readmission after surgery	188 (6·5)	4 (1·1)	60 (3·9)	124 (12·3)	< 0·001
Reoperation for complications of surgery	133 (4·6)	8 (2·1)	29 (1·9)	96 (9·5)	< 0·001

Values in parentheses are percentages. *χ^2 test across procedure groups.

not required. Each participating centre was required to register the study locally and obtain local governance approvals before entering patients.

Primary and secondary outcomes

Primary and secondary outcomes in iBRA-2 and TeaM were selected based on current best practice[33] and the National Institute for Health and Care Excellence guidelines[11]. Standardized definitions were used across both studies[28,29], allowing meaningful pooling of the data.

The primary outcome for this study was the percentage of patients successfully avoiding mastectomy in the TM group. Secondary outcomes were major and minor complications, and time to adjuvant therapy. Major complications were defined as those requiring readmission or reoperation, and minor complications were those managed conservatively. Time to adjuvant treatment was defined as the interval from the last cancer surgery to the first dose of chemotherapy or first fraction of radiotherapy. Adequate margins were defined in the TeaM study according to local policy[28,31].

Quality assurance

For quality assurance purposes, the lead investigator at each site was asked to identify an individual not previously involved in data collection to validate 5–10 per cent of the data independently. Similar procedures were used in both studies, and were consistent with those used in other collaborative projects[34].

Statistical analysis

Data from patients undergoing mastectomy with and without IBR in the iBRA-2 study, and the subgroup of patients undergoing TM to avoid mastectomy in the TeaM study, were combined to compare the short-term clinical and oncological outcomes of the different procedure types.

Descriptive summary statistics were calculated for each variable for the pooled cohort overall and split by procedure type (TM, mastectomy only, mastectomy and IBR). Categorical data are presented as counts and percentages, and continuous data as median (i.q.r.; range). Data for procedure groups were compared using χ^2 and Kruskal–Wallis tests. Complications and oncological data were summarized by patient and procedure.

Univariable and multivariable logistic regression analyses were used to explore clinicopathological variables hypothesized to be associated with complications based on the literature and expert opinion. These included patient- and procedure-related factors, namely age, BMI, ischaemic heart disease (IHD), diabetes, other co-morbidities, smoking status (non-smoker, ex-smoker or current smoker), neoadjuvant chemotherapy, ASA fitness grade, laterality of surgery to the breast (unilateral *versus* bilateral), axillary surgery (none, sentinel node biopsy or axillary node clearance) and procedure type (TM, mastectomy only, mastectomy and IBR).

Time to adjuvant treatment was calculated for all patients and by procedure type, with adjuvant therapy as the event. Kaplan–Meier analyses, and univariable and multivariable Cox survival models, with time to adjuvant therapy split by procedure type, were created including patient age, BMI, IHD, diabetes, other co-morbidities, smoking status, neoadjuvant chemotherapy, ASA fitness grade, laterality of surgery, and presence of postoperative complications (none, minor or major) as the variables of interest, clustered by centre. The Kaplan–Meier curves were truncated at 150 days when only 14 patients remained in the analysis. Stata® version 15 (StataCorp, College Station, Texas, USA) was used for all analyses.

Results

The TeaM study[28] recruited 376 patients undergoing 385 TM procedures to avoid mastectomy, from 50 centres in the UK and Europe between 1 September 2016 and 30 June

Table 3 Univariable and multivariable logistic regression analysis for any postoperative complication

	Univariable analysis			Multivariable analysis ($n = 2313$)	
	Proportion with postoperative complication*	Odds ratio†	*P*	Odds ratio†	*P*
Procedure type	1008 of 2893 (34·8)				
Therapeutic mammaplasty	79 of 376 (21·0)	0·44 (0·31, 0·63)	< 0·001	0·46 (0·30, 0·71)	< 0·001
Mastectomy only	570 of 1517 (37·6)	1·00 (reference)		1·00 (reference)	
Mastectomy and immediate breast reconstruction	359 of 1000 (35·9)	0·93 (0·74, 1·17)	0·535	1·28 (0·95, 1·72)	0·109
Age	1005 of 2880 (34·9)	1·01 (1·01, 1·02)	< 0·001	1·01 (1·01, 1·02)	0·002
BMI	947 of 2707 (35·0)				
Underweight	16 of 55 (29)	1·04 (0·56, 1·93)	0·911	0·85 (0·53, 1·37)	0·497
Normal weight	272 of 959 (28·4)	1·00 (reference)		1·00 (reference)	
Overweight	315 of 874 (36·0)	1·42 (1·15, 1·77)	0·001	1·27 (0·98, 1·65)	0·076
Obese	199 of 476 (41·8)	1·81 (1·44, 2·29)	< 0·001	1·77 (1·33, 2·34)	< 0·001
Severely obese	145 of 343 (42·3)	1·85 (1·37, 2·50)	< 0·001	1·74 (1·17, 2·58)	0·006
Co-morbidities					
Ischaemic heart disease	1001 of 2868 (34·9)				
No	937 of 2719 (34·5)	1·00 (reference)		1·00 (reference)	
Yes	64 of 149 (43·0)	1·43 (1·00, 2·04)	0·048	1·06 (0·70, 1·61)	0·785
Diabetes	986 of 2829 (34·9)				
No	874 of 2583 (33·8)	1·00 (reference)		1·00 (reference)	
Yes	112 of 246 (45·5)	1·63 (1·27, 2·11)	< 0·001	1·09 (0·79, 1·50)	0·598
Other	1003 of 2874 (34·9)				
No	468 of 1550 (30·2)	1·00 (reference)		1·00 (reference)	
Yes	535 of 1324 (40·4)	1·57 (1·29, 1·90)	< 0·001	1·32 (1·04, 1·66)	0·022
Smoking status	993 of 2843 (34·9)				
Non-smoker	689 of 2078 (33·2)	1·00 (reference)		1·00 (reference)	
Ex-smoker	184 of 450 (40·9)	1·39 (1·13, 1·72)	0·002	1·29 (1·02, 1·63)	0·031
Current smoker	120 of 315 (38·1)	1·24 (0·99, 1·56)	0·066	1·43 (1·11, 1·83)	0·005
Neoadjuvant chemotherapy	1002 of 2872 (34·9)				
No	153 of 475 (32·2)	1·00 (reference)		1·00 (reference)	
Yes	849 of 2397 (35·4)	0·87 (0·68, 1·11)	0·254	0·82 (0·61, 1·10)	0·179
ASA fitness grade	1005 of 2881 (34·9)				
I	238 of 837 (28·4)	1·00 (reference)		1·00 (reference)	
II	624 of 1710 (36·5)	1·45 (1·20, 1·74)	< 0·001	1·07 (0·83, 1·37)	0·600
III	140 of 328 (42·7)	1·87 (1·44, 2·45)	< 0·001	1·03 (0·70, 1·54)	0·867
IV	3 of 6 (50)	2·52 (0·50, 12·72)	0·264	0·96 (0·16, 5·80)	0·962
Bilateral surgery	1008 of 2893 (34·8)				
No	843 of 2455 (34·3)	1·00 (reference)		1·00 (reference)	
Yes	165 of 438 (37·7)	1·16 (0·88, 1·52)	0·301	1·54 (1·18, 2·01)	0·001
Axillary surgery	909 of 2604 (34·9)				
None	51 of 192 (26·6)	1·00 (reference)		1·00 (reference)	
Sentinel node biopsy/axillary sampling	548 of 1661 (33·0)	1·36 (0·91, 2·03)	0·130	1·13 (0·74, 1·71)	0·480
Axillary clearance	310 of 751 (41·3)	1·94 (1·26, 3·01)	0·003	1·69 (1·04, 2·74)	0·033

Values in parentheses are *percentages and †95 per cent confidence intervals.

2017. The iBRA-2 study[29] recruited 2540 patients undergoing mastectomy with (1008) or without (1532) IBR from 76 centres between 1 July and 31 December 2016. Of the 1008 patients receiving IBR, 675 had 773 implant-based reconstructions, 105 received 106 pedicled flaps and 228 patients underwent 247 free-flap reconstructions. Data from these cohorts were pooled and 2916 patients were included in the combined analysis.

Patient demographics

Patient demographics are summarized by procedure type in *Table 1*. Patients undergoing TM were older than those

Table 4 Univariable and multivariable logistic regression analysis for major complications

	Univariable analysis			Multivariable analysis ($n = 2289$)	
	Proportion with major complication*	Odds ratio†	*P*	Odds ratio†	*P*
Procedure type	229 of 2868 (8·0)				
Therapeutic mammaplasty	8 of 376 (2·1)	0·41 (0·20, 0·84)	0·014	0·36 (0·15, 0·85)	0·019
Mastectomy only	76 of 1499 (5·1)	1·00 (reference)		1·00 (reference)	
Mastectomy and immediate breast reconstruction	145 of 993 (14·6)	3·20 (2·20, 4·65)	< 0·001	4·02 (2·23, 7·25)	< 0·001
Age	229 of 2855 (8·0)	0·99 (0·98, 1·00)	0·022	1·01 (0·99, 1·03)	0·172
BMI	216 of 2682 (8·1)				
Underweight	4 of 53 (8)	0·95 (0·27, 3·41)	0·939	1·55 (0·57, 4·25)	0·395
Normal weight	75 of 949 (7·9)	1·00 (reference)		1·00 (reference)	
Overweight	58 of 869 (6·7)	0·83 (0·58, 1·19)	0·315	0·95 (0·64, 1·41)	0·794
Obese	48 of 470 (10·2)	1·33 (0·92, 1·90)	0·125	1·65 (1·05, 2·59)	0·030
Severely obese	31 of 341 (9·1)	1·17 (0·75, 1·82)	0·501	1·67 (0·92, 3·03)	0·093
Co-morbidities					
Ischaemic heart disease	228 of 2844 (8·0)				
No	220 of 2695 (8·2)	1·00 (reference)		1·00 (reference)	
Yes	8 of 149 (5·4)	0·64 (0·34, 1·20)	0·163	0·69 (0·27, 1·72)	0·424
Diabetes	224 of 2804 (8·0)				
No	198 of 2558 (7·7)	1·00 (reference)		1·00 (reference)	
Yes	26 of 246 (10·6)	1·41 (0·91, 2·17)	0·120	1·66 (1·04, 2·64)	0·035
Other	228 of 2849 (8·0)				
No	111 of 1540 (7·2)	1·00 (reference)		1·00 (reference)	
Yes	117 of 1309 (8·9)	1·26 (0·97, 1·65)	0·082	1·43 (1·03, 2·00)	0·035
Smoking status	228 of 2818 (8·1)				
Non-smoker	154 of 2060 (7·5)	1·00 (reference)		1·00 (reference)	
Ex-smoker	41 of 446 (9·2)	1·25 (0·86, 1·82)	0·236	1·16 (0·77, 1·74)	0·482
Current smoker	33 of 312 (10·6)	1·46 (0·96, 2·24)	0·079	1·84 (1·17, 2·89)	0·008
Neoadjuvant chemotherapy	228 of 2848 (8·0)				
No	42 of 470 (8·9)	1·00 (reference)		1·00 (reference)	
Yes	186 of 2378 (7·8)	1·16 (0·75, 1·78)	0·510	1·24 (0·76, 2·02)	0·399
ASA fitness grade	228 of 2856 (8·0)				
I	63 of 835 (7·5)	1·00 (reference)		1·00 (reference)	
II	141 of 1687 (8·4)	1·12 (0·83, 1·50)	0·463	0·87 (0·61, 1·23)	0·428
III	24 of 328 (7·3)	0·97 (0·59, 1·59)	0·896	0·88 (0·47, 1·65)	0·689
IV	0 of 6 (0)	n.a.		n.a.	
Bilateral surgery	229 of 2868 (8·0)				
No	181 of 2433 (7·4)	1·00 (reference)		1·00 (reference)	
Yes	48 of 435 (11·0)	1·54 (1·07, 2·23)	0·021	1·71 (1·14, 2·57)	0·010
Axillary surgery	196 of 2582 (7·6)				
None	11 of 188 (5·9)	1·00 (reference)		1·00 (reference)	
Sentinel node biopsy/axillary sampling	134 of 1650 (8·1)	1·42 (0·83, 2·44)	0·201	1·33 (0·77, 2·27)	0·304
Axillary clearance	51 of 744 (6·9)	1·18 (0·65, 2·15)	0·578	1·08 (0·59, 1·97)	0·801

Values in parentheses are *percentages and †95 per cent confidence intervals. n.a., Not applicable.

having IBR. They also had higher a BMI and were more likely to have undergone simultaneous bilateral surgery than patients in the other groups. Participant demographics are shown by type of reconstruction in *Table S1* (supporting information).

Postoperative complications

Postoperative complications are summarized by procedure type in *Table 2*; details of complications by type of IBR and per breast are available in *Tables S2* and *S3* (supporting information) respectively. The complication rate was

Table 5 Postoperative histology in procedures performed for malignancy

	All procedures performed for cancer (*n* = 2992)	Therapeutic mammaplasty (*n* = 385)	Mastectomy only (*n* = 1564)	Mastectomy and immediate breast reconstruction (*n* = 1043)	*P*‡
Invasive status					< 0·001
DCIS	406 (13·6)	18 (4·7)	141 (9·0)	247 (23·7)	
Invasive disease	2547 (85·1)	361 (93·8)	1413 (90·3)	773 (74·1)	
Not reported	39 (1·3)	6 (1·6)	10 (0·6)	23 (2·2)	
Focality					0·002
Unifocal disease	1998 (66·8)	258 (67·0)	1091 (69·8)	649 (62·2)	
Multifocal disease	956 (32·0)	120 (31·2)	455 (29·1)	381 (36·5)	
Not reported	38 (1·3)	7 (1·8)	18 (1·2)	13 (1·2)	
Grade of invasive disease	*n* = 2547	*n* = 361	*n* = 1413	*n* = 773	< 0·001
1	223 (8·8)	44 (12·2)	98 (6·9)	81 (10·5)	
2	1327 (52·1)	140 (38·8)	759 (53·7)	428 (55·4)	
3	920 (36·1)	120 (33·2)	543 (38·4)	257 (33·2)	
Not reported	77 (3·0)	57 (15·8)	13 (0·9)	7 (0·9)	
Histological type	*n* = 2547	*n* = 361	*n* = 1413	*n* = 773	0·078
Ductal	1783 (70·0)	243 (67·3)	986 (69·8)	554 (71·7)	
Lobular	426 (16·7)	53 (14·7)	246 (17·4)	127 (16·4)	
Mixed/other	326 (12·8)	64 (17·7)	175 (12·4)	87 (11·3)	
Not reported	12 (0·5)	1 (0·3)	6 (0·4)	5 (0·6)	
Invasive tumour size (mm)*	23 (13–36; 0–250)	20 (11–32; 0–155)	25 (15–40; 0–200)	20 (11–30; 0–250)	< 0·001§
Whole tumour size (mm)*	30 (20–50; 0–450)	29 (18–45; 0–145)	32 (20–50; 0–450)	30 (17–50; 0–250)	0·003§
Receptor status†	*n* = 2547	*n* = 361	*n* = 1413	*n* = 773	
Oestrogen receptor					< 0·001
Positive	2017 (79·2)	279 (77·3)	1106 (78·3)	632 (81·8)	
Negative	484 (19·0)	51 (14·1)	298 (21·1)	135 (17·5)	
Unknown	46 (1·8)	31 (8·6)	9 (0·6)	6 (0·8)	
HER-2					< 0·001
Positive	478 (18·8)	56 (15·5)	273 (19·3)	149 (19·3)	
Negative	1947 (76·4)	261 (72·3)	1087 (76·9)	599 (77·5)	
Unknown	122 (4·8)	44 (12·2)	53 (3·8)	25 (3·2)	
Nodal status					
No. of nodes with macrometastasis*	0 (0–1) (0–31)	0 (0–1) (0–18)	0 (0–2) (0–30)	0 (0–1) (0–31)	< 0·001§
N0	1888 (63·1)	225 (58·4)	905 (57·9)	758 (72·7)	< 0·001
N1	984 (32·9)	87 (22·6)	642 (41·1)	255 (24·4)	
Not reported	120 (4·0)	73 (19·0)	17 (1·1)	30 (2·9)	
DCIS	*n* = 406	*n* = 18	*n* = 141	*n* = 247	0·613
Low grade	40 (9·9)	13 (72)	7 (5·0)	20 (8·1)	
Intermediate grade	95 (23·4)	5 (28)	38 (27·0)	52 (21·1)	
High grade	269 (66·3)	0 (0)	95 (67·4)	174 (70·4)	
Not reported	2 (0·5)	0 (0)	1 (0·7)	1 (0·4)	

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.; range). †Invasive disease only. DCIS, ductal carcinoma *in situ*; HER2, human epidermal growth factor receptor 2. ‡χ^2 test across procedure groups, except §Kruskal–Wallis test across procedure groups.

significantly lower after TM than after mastectomy with or without immediate reconstruction. Only one in five patients undergoing TM (79, 21·0 per cent) experienced a complication, compared with approximately one-third of patients undergoing mastectomy with (359, 35·6 per cent) or without (570, 37·2 per cent) IBR.

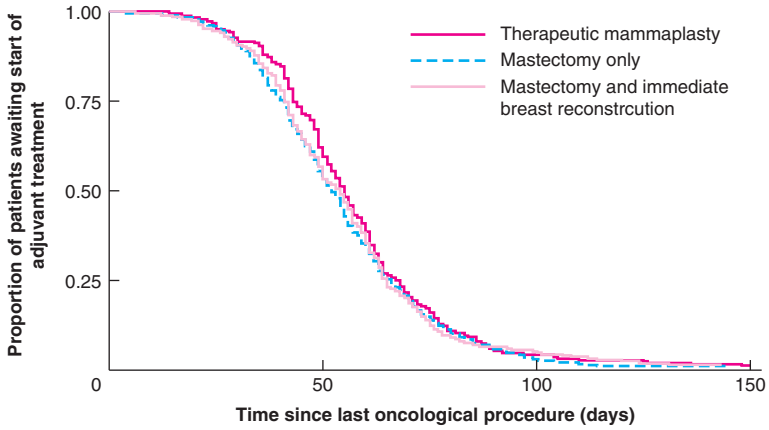
Univariable regression identified age, BMI, IHD, diabetes, having other co-morbidities, being an ex-smoker, ASA grade and having axillary lymph node clearance as risk factors associated with developing a complication. Compared with simple mastectomy without reconstruction, TM was associated with a reduced risk

Table 6 Multidisciplinary team decision-making and time to adjuvant therapy by procedure type

	All patients (n = 2916)	Therapeutic mammaplasty (n = 376)	Mastectomy only (n = 1532)	Mastectomy and immediate breast reconstruction (n = 1008)	P†
Patient accepted adjuvant treatment (either chemotherapy or radiotherapy or both)	1578 (54·1)	343 (91·2)	804 (52·5)	431 (42·8)	< 0·001
Time from last oncological procedure to first adjuvant treatment (days)* (n = 1432)	53 (42–65)	55 (43–67)	52 (41–66)	54 (41–65)	0·085†
Chemotherapy as first adjuvant treatment	719 (50·2)	92 (30·6)	409 (55·4)	218 (55·5)	< 0·001
Time from last oncological procedure to chemotherapy (days)* (n = 719)	47 (37–59)	49 (41–60)	47 (37–59)	47 (37–60)	0·592†
Radiotherapy as first adjuvant treatment	713 (49·8)	209 (69·4)	329 (44·6)	175 (44·5)	< 0·001
Time from last oncological procedure to radiotherapy (days)* (n = 713)	59 (48–72)	57 (48–70)	59 (48–73)	61 (47–73)	0·632†

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). †χ^2 test across procedure groups, except ‡Kruskal–Wallis test across procedure groups.

Fig. 1 Kaplan–Meier analysis of adjuvant treatment by procedure type



No. at risk				
Therapeutic mammaplasty	301	187	13	4
Mastectomy only	738	409	23	5
Mastectomy and immediate breast reconstruction	393	223	21	5

of complications (odds ratio (OR) 0·44, 95 per cent confidence interval 0·31 to 0·63), but immediate reconstruction did not increase the risk (*Table 3*). Age, BMI, other co-morbidities, being an ex-smoker and having axillary lymph node clearance remained strongly associated with complications in the multivariable model, and current smoking, and bilateral surgery were also identified as independent risk factors. Undergoing TM remained strongly associated with a lower risk of complications in the multivariable model (adjusted OR 0·46, 0·30 to 0·71).

Major complications following TM were uncommon, with just eight of 376 patients (2·1 per cent) requiring readmission or reoperation for a complication of surgery. This compared with 76 of 1532 (5·0 per cent) undergoing mastectomy only and 145 of 1008 (14·4 per cent) receiving immediate reconstruction (*Table 2*). Age, undergoing immediate reconstruction and bilateral surgery were associated with major complications in the univariable analysis (*Table 4*). All of these variables, except age, remained strongly associated with major complications in the multivariable model, and smoking, diabetes, having

Table 7 Cox univariable and multivariable survival analyses for adjuvant treatment

		Univariable analysis		Multivariable analysis ($n = 1301$)	
	No. of patients*	Hazard ratio†	*P*	Hazard ratio†	*P*
Procedure type	1432				
Therapeutic mammaplasty	301 (21·0)	0·89 (0·77, 1·02)	0·102	1·06 (0·87, 1·29)	0·548
Mastectomy only	738 (51·5)	1·00 (reference)		1·00 (reference)	
Mastectomy and immediate breast reconstruction	393 (27·4)	0·97 (0·85, 1·10)	0·600	0·96 (0·82, 1·12)	0·571
Postoperative complications	1432				
None	861 (60·1)	1·00 (reference)		1·00 (reference)	
Minor complications	478 (33·4)	0·83 (0·74, 0·93)	0·002	0·85 (0·74, 0·97)	0·017
Major complications	93 (6·5)	0·71 (0·58, 0·87)	0·001	0·63 (0·51, 0·78)	< 0·001
Chemotherapy as first adjuvant treatment	719 (50·2)	1·71 (1·50, 1·94)	< 0·001	2·11 (1·84, 2·41)	< 0·001
Age	1428	1·00 (0·99, 1·00)	0·202	1·01 (1·00, 1·01)	0·043
BMI	1373				
Underweight	29 (2·1)	0·83 (0·64, 1·07)	0·152	0·88 (0·63, 1·22)	0·429
Normal weight	453 (33·0)	1·00 (reference)		1·00 (reference)	
Overweight	447 (32·6)	0·97 (0·85, 1·12)	0·701	0·97 (0·84, 1·13)	0·726
Obese	266 (19·4)	0·73 (0·64, 0·83)	< 0·001	0·75 (0·64, 0·88)	< 0·001
Severely obese	178 (13·0)	0·73 (0·62, 0·86)	< 0·001	0·79 (0·65, 0·95)	0·015
Co-morbidities					
Ischaemic heart disease	1428				
No	1372 (96·1)	1·00 (reference)		1·00 (reference)	
Yes	56 (3·9)	0·69 (0·55, 0·86)	< 0·001	0·78 (0·59, 1·05)	0·100
Diabetes	1403				
No	1290 (91·9)	1·00 (reference)		1·00 (reference)	
Yes	113 (8·1)	0·82 (0·72, 0·94)	0·005	0·97 (0·82, 1·14)	0·718
Other co-morbidity	1422				
No	824 (57·9)	1·00 (reference)		1·00 (reference)	
Yes	598 (42·1)	0·91 (0·80, 1·03)	0·151	0·90 (0·75, 1·09)	0·285
Smoking status	1409				
Non-smoker	1031 (73·2)	1·00 (reference)		1·00 (reference)	
Ex-smoker	204 (14·5)	1·14 (0·98, 1·33)	0·089	1·18 (1·00, 1·40)	0·038
Current smoker	174 (12·3)	0·93 (0·81, 1·07)	0·315	0·92 (0·79, 1·08)	0·326
Neoadjuvant chemotherapy	1421				
No	1083 (76·2)	1·00 (reference)		1·00 (reference)	
Yes	338 (23·8)	1·03 (0·92, 1·15)	0·603	1·56 (1·33, 1·82)	< 0·001
ASA fitness grade	1425				
I	474 (33·3)	1·00 (reference)		1·00 (reference)	
II	823 (57·8)	0·92 (0·81, 1·03)	0·133	1·04 (0·88, 1·21)	0·657
III	126 (8·8)	0·86 (0·70, 1·05)	0·144	1·05 (0·78, 1·43)	0·731
IV	2 (0·1)	0·75 (0·63, 0·89)	0·001	1·29 (0·94, 1·78)	0·119
Bilateral surgery (*versus* none)	232 (16·2)	1·01 (0·86, 1·17)	0·927	1·03 (0·84, 1·26)	0·797

Values in parentheses are *percentages and †95 per cent confidence intervals.

other co-morbidities and BMI were also identified as independent risk factors in this model. IBR (adjusted OR 4·02, 2·23 to 7·25) was the strongest predictor of major complications in the multivariable model. Undergoing TM was associated with a lower risk of experiencing a major complication in both univariable (OR 0·41, 0·20 to 0·84) and multivariable (adjusted OR 0·36, 0·15 to 0·85) models. Univariable and multivariable analysis of risk factors for any and major complications by type of reconstruction are shown in *Table S4* (supporting information).

Oncological outcomes

Postoperative histology by the procedure performed is summarized in *Table 5*. TM was performed less

frequently for pure DCIS than mastectomy with immediate reconstruction. Approximately one-third of all patients (956, 32·0 per cent) had multifocal disease, including those who had TM (120, 31·2 per cent). The median invasive and whole tumour size were similar in the TM and immediate reconstruction groups. Patients undergoing IBR were more likely to be node-negative than those in the other groups.

The 376 patients in the TeaM study underwent 385 TM procedures for cancer. Of these, 305 (79·2 per cent) had clear margins according to local guidelines at the first operation; 71 (18·4 per cent) had involved or close margins and the margin status was unknown in nine (2·3 per cent). In the group with inadequate margins, 30 of 71 (42 per cent) had a successful re-excision and 33 (46 per cent) underwent completion mastectomy. The outcome of the remaining eight patients (11 per cent) was unknown. Overall, 335 of 385 TM procedures (87·0 per cent) resulted in successful breast conservation. Notably, of the 33 patients who required a completion mastectomy, only 11 had IBR within the study interval (*Fig. S1*, supporting information).

Time to adjuvant therapy

Adjuvant therapy was recommended in the majority of patients in the TM group (343, 91·2 per cent) compared with less than half (431, 42·8 per cent) of those undergoing immediate reconstruction (*Table 6*). There was no significant difference in the median time to adjuvant treatment across treatment groups (*Table 6* and *Fig. 1*). Longer time to adjuvant treatment was associated with the development of complications (minor complications: adjusted HR 0·85, 95 per cent c.i. 0·74 to 0·97; major complications: HR 0·63, 0·51 to 0·78) and obesity (HR 0·75, 0·64 to 0·88) in multivariable analysis (*Table 7*). Details of time to adjuvant treatment and risk factors for delay to adjuvant treatment by type of IBR are summarized in *Tables S5* and *S6* (supporting information) respectively.

Discussion

The results of this large prospective study suggest that TM may allow the majority of women considered suitable for the procedure to avoid mastectomy, and that overall TM is associated with fewer complications than mastectomy and immediate reconstruction. TM may particularly improve outcomes for patients considered high risk (current smokers, those with high BMI) who may not be offered immediate reconstruction because of their risk profile. Reducing the risk of complications after breast cancer surgery is an important consideration as complications have been shown to result in delays to adjuvant therapy[29] that could have an adverse impact on long-term oncological outcomes and compromise survival.

The rate of successful breast conservation in this subset of patients offered TM to avoid mastectomy was higher than may be expected based on previous systematic reviews[35–37], which demonstrated higher completion mastectomy rates in patients with smaller (T1) tumours. Patients in the present study had larger tumours, validating the inclusion criterion that the TM group was offered this option as an alternative to mastectomy. Despite this, the completion mastectomy rate in the present study was less than 10 per cent. This is consistent with previous findings[38] and suggests that TM is a viable option for avoiding mastectomy. Recent retrospective data from a large population-based study[39] suggested that oncoplastic breast conservation may occupy a niche between standard BCS and mastectomy. The present study suggests that it should possibly be promoted as an alternative to mastectomy and reconstruction.

Currently, the recommendation for mastectomy is clearly defined for those with extensive disease. Likewise, the role of breast conservation is clear for those with relatively small disease foci for whom an acceptable cosmetic outcome can be anticipated. There is, however, a widening middle ground in which the extended role of breast conservation offered by oncoplastic surgery can provide an alternative to mastectomy. Patients suitable for TM will have breast ptosis and be accepting of being smaller breasted and, usually, undergoing bilateral surgery. The extended role of breast conservation has been fuelled by neoadjuvant therapy, a better understanding of tumour biology, and increasingly widespread oncoplastic surgical training, with the result that surgeons with an understanding of reduction and mastopexy techniques are more likely to consider and offer these options routinely[40]. Good cosmetic outcomes have been reported[41], and there is emerging data to suggest that avoiding mastectomy and IBR may be associated with improvements in quality of life[20].

At the limits of the spectrum the term 'extreme oncoplasty'[20] has even emerged to describe resections of large tumours (T3), multifocal or multicentric disease for which mastectomy would traditionally have been recommended[42]. Single-centre series[41–43] are generally small but have mostly shown promising results, with low rates of conversion to mastectomy, although long-term oncological outcomes are lacking.

The rate of IBR among patients requiring completion mastectomy after unsuccessful TM was low in the present

study. This may be because they were considered high risk and therefore not good candidates for IBR, but may also reflect the anticipated need for postmastectomy radiotherapy. Evidence suggesting oncological benefits of postmastectomy radiotherapy in patients with one to three positive lymph nodes[44] means that many more patients are now offered treatment. Radiotherapy has been shown to have an adverse impact on both clinical and patient-reported outcomes of immediate breast reconstruction[45], particularly with implants[46]. Despite recent updated national guidance[47], many surgeons would not offer immediate reconstruction if postmastectomy radiotherapy is likely to be required[13]. Avoiding mastectomy may therefore have particular benefits in this group, but work is needed to explore this further.

This study adds to the evidence base supporting the benefits of TM compared with mastectomy, but has limitations. First, this was a pooled analysis of two separate studies and it is not clear to what extent these groups are directly comparable. In particular, although the overall postoperative tumour size and proportion of patients with multifocal disease was similar in the two groups, the authors did not assess how many patients in the iBRA-2 cohort would be technically unsuitable for TM for morphological (for example, small, non-ptotic breasts) or tumour-related (multicentric disease) reasons, or the proportion who would elect to undergo TM to avoid mastectomy. A future prospective study in patients offered all surgical options is therefore needed to compare the outcomes of different operative procedures directly and explore patient decision-making. Only short-term outcomes of TM such as complications and time to adjuvant therapy have been considered in the present study. Although these data are promising, further long-term studies are needed for prospective assessment of oncological safety, particularly of more extreme oncoplastic resections as well as patient-reported and cosmetic outcomes, and cost-effectiveness of TM compared with mastectomy with and without immediate reconstruction in directly comparable patient groups.

A future study directly comparing TM as an alternative to mastectomy with and without IBR in patients with large, multifocal and/or multicentre tumours is the next step in generating the evidence needed to change practice and improve outcomes for patients. Recent experience with the MIAMI feasibility study (ISRCTN17987569)[48] has demonstrated that an RCT in this context is unlikely to be feasible. A well designed multicentre prospective study including validated patient-reported outcomes and a cost-effectiveness analysis is needed, but preliminary work is required to determine whether it is possible to identify and recruit patients to all treatment groups if a fully informed choice is offered, and to establish the optimal study design. A key issue is the selection of an appropriate patient-reported outcome assessment tool. The BREAST-Q[49] includes core breast cancer modules with four subscales (satisfaction with breasts, psychosocial well-being, physical well-being and sexual well-being) for use in patients with breast cancer having BCS and mastectomy with and without immediate reconstruction. The BREAST-Q core module subscales are comparable across procedures but, to date, only one study[50] has used the BCS 'satisfaction with breasts' scale in patients undergoing TM procedures. Work is therefore needed to determine whether it is valid in this group. Qualitative work is also needed to explore patients' decision-making for, and experiences of, different types of surgery and factors influencing their choice. This will provide important information to help inform shared decision-making consultations in the main study and allow patients to make the choice that is right for them.

This study has shown that oncoplastic breast conservation is likely to offer better outcomes than mastectomy with or without breast reconstruction for many women and, together with emerging evidence to support the long-term oncological safety[17,19,51] of oncoplastic breast conservation, adds further support to the use of TM as an alternative to mastectomy. Further work is now needed determine whether TM improves patient-reported outcomes and is cost-effective compared with mastectomy with and without immediate breast reconstruction before definitive recommendations for best practice can be made.

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The protocol papers[30,31] and primary analyses[28,29] for both studies have been published. The combined analysis was not preplanned at the point of primary study design. A pooled analysis was designed by the TeaM steering group before undertaking the primary analysis (December 2017).

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.