Original article

Current practice and short-term outcomes of therapeutic mammaplasty in the international TeaM multicentre prospective cohort study

Rachel L O'Connell[1], Elizabeth Baker[2], Adam Trickey[3], Tim Rattay[4], Lisa Whisker[5], R Douglas Macmillan[5§], Shelley Potter[3,6§] on behalf of the TeaM Steering Group and the Mammary Fold Academic and Research Collaborative*

[1]Department of Breast Surgery, Royal Marsden NHS Foundation Trust, Downs Rd, Sutton SM2 5PT, UK; [2]Department of Breast Surgery, Airedale General Hospital, Skipton Road, Keighley, West Yorkshire, BD20 6TD, UK; [3]Population Health Sciences, Bristol Medical School, Canynge Hall, 39 Whatley Road, Clifton, Bristol BS8 2PS, UK; [4]Leicester Research Cancer, Clinical Sciences Building, University of Leicester, Leicester LE2 2LX, UK; [5]Nottingham Breast Institute, Nottingham University Hospitals NHS Trust, Hucknall Road, Nottingham NG5 1PB, UK; [6]Bristol Breast Care Centre, North Bristol NHS Trust, Southmead Rd, Bristol BS10 5NB UK

[§]RDM and SP are joint senior authors

*Members of the TeaM Steering Group and Mammary Fold Academic and Research Collaborative are PUBMED citable collaborators on this study and are listed at the end of the manuscript

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Corresponding author: Shelley Potter - Bristol Centre for Surgical Research, Population Health Sciences, Bristol Medical School. 2.14 Canynge Hall, Whatley Road, Clifton, Bristol, BS8 2PS.
E-mail Shelley.Potter@bristol.ac.uk, Tel: (+44) 0117 287218

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Abstract

Background: Therapeutic mammaplasty (TM) which combines breast reduction and mastopexy techniques with tumour excision, may extend the boundaries of breast-conserving surgery (BCS) and improve outcomes for patients, but current practice is unknown and high-quality outcome data is lacking. This prospective multicentre cohort study aimed to explore the practice and short-term outcomes of the technique.

Methods: Consecutive patients undergoing TM at participating centres between 1st September,2016 and 30th June,2017 were recruited to the study. Demographic, pre-operative, operative, oncological and complication data were collected. The primary outcome was unplanned re-operation for complications within 30 days of surgery. Secondary outcomes included re-excision rates and time to adjuvant therapy.

Results: Overall 880 patients underwent 899 TM procedures at 50 centres. The most common indications for TM were avoidance of poor cosmetic outcomes associated with standard BCS (n=702, 78.1%) or avoidance of mastectomy (n=379, 42.2%). Wise-pattern skin incisions were the most common (n=429, 47.7%) but a range of incisions and nipple/areola pedicles were used. Immediate contralateral symmetrisation was performed in one-third of cases (n=284, 32.2%). In total, 205 (23.3%) patients experienced a complication but <3%(n=25) required re-operation. Median lesion size was 24.5mm (interquartile range (IQR) 16-38mm). Incomplete excision was seen in 132 cases (14.7%) but only 51 (5.8%) patients ultimately required mastectomy. Median time to adjuvant therapy was 54 days (IQR 42-66).

Conclusion: Therapeutic mammaplasty is a safe and effective alternative to mastectomy or standard BCS. Further work is now required to explore the impact of the technique on quality of life and establish cost-effectiveness.

Introduction

Breast conserving surgery (BCS) with adjuvant radiotherapy is an established treatment for early breast cancer[1 2]. While many women may prefer breast conservation to mastectomy, standard BCS can often result in unacceptable cosmetic outcomes[3 4] which may adversely impact on patient satisfaction and quality of life[5-8].

Therapeutic mammaplasty (TM) describes 'the oncoplastic application of breast reduction and mastopexy techniques to treat selected breast cancers by BCS'[9 10]. These techniques effectively extend the boundaries of traditional BCS by allowing adequate resection of larger tumours in women with medium to large breasts without compromising cosmetic outcome[11-14]; provide an alternative to mastectomy with/without reconstruction in those with ptotic breasts[9 15] and may improve outcomes for women with large breasts in whom standard BCS followed by radiotherapy may be associated with lymphoedema, fibrosis, and chronic pain[16].

Despite the widespread adoption of these techniques into routine practice, there is limited high-quality evidence to support benefits of this approach. TM procedures are more complex than standard BCS with potential resource implications. Although complication rates and oncological safety have been reported in the literature[16-24] the majority of published studies are retrospective single-centre[16 22-24], often single surgeon case-series with limited follow-up. Many are poorly-designed and reported, with inconsistent end-points[25] which limit cross-study comparison and meaningful data synthesis. Several recent systematic reviews[26-34] have highlighted the paucity of high-quality clinical, oncological and cosmetic outcome data and emphasised the urgent need for well-designed prospective studies to establish the indications and outcomes of TM to inform best practice.

Although randomised controlled trials (RCTs) provide the best evidence for the effectiveness of an intervention, RCTs are largely inappropriate in this context. A high-quality prospective multicentre cohort study exploring the practice and outcomes of these techniques is therefore essential to support the safe practice of TM, generate guidelines, guide decision-making, and inform health policy.

The aim of this study was to describe the current practice of TM including indications and techniques used; complication and incomplete tumour excision rates and the impact of TM on the time to delivery of adjuvant therapy. The secondary aims were to identify risk factors associated with complications and incomplete excision and to develop a network of surgeons performing the technique and engage them in the need for evaluation.

Methods

Study design and participants

All breast and plastic surgical units performing TM were invited to participate in this multicentre prospective cohort study through the UK breast and plastic surgical trainee research collaborative network (Mammary Fold Academic and Research Collaborative and the Reconstructive Surgery Trials Network) and the professional associations (Association of Breast Surgery (ABS) and British Association of Plastic, Reconstructive and Aesthetic Surgeons, BAPRAS)[35].

Consecutive female patients undergoing TM at participating units between 1st September 2016 and 30th June 2017 were prospectively recruited to the study. 'Therapeutic mammaplasty' was defined as 'the application of breast reduction or mastopexy techniques, including removal of skin to reduce the skin envelope, to treat invasive or ductal carcinoma in situ (DCIS) using BCS'. Patients undergoing standard BCS not involving reduction of the skin envelope; level one oncoplastic techniques involving glandular remodelling only or BCS with volume replacement techniques such as local perforator, e.g thoracodorsal artery perforator (TDAP), or lateral intercostal artery perforator (LiCAP) flaps or latissimus dorsi mini-flaps were excluded. Also excluded were patients undergoing surgery for benign disease and those undergoing mastectomy with or without immediate breast reconstruction.

Demographic, pre-operative planning, operative and oncological data were collected prospectively for all patients as previously described[35]. Recommended adjuvant treatments were identified from post-operative multi-disciplinary team (MDT) meetings and date of commencement of adjuvant treatment from appropriate on-line hospital systems or case-note review. Complications, readmissions and re-operations at 30 days were collected prospectively by clinical review or retrospective review of case-notes in patients

not attending for follow-up. All data were collected by members of the surgical team and managed using REDCap data capture software (http://www.projectredcap.org/)[36 37].

This study was classified as service evaluation/clinical audit by the NHS Health Research Authority Decision Tool (http://www.hra-decisiontools.org.uk/research/index.html) Individual patient consent was not required but each participating centre was required to obtain local clinical governance approvals prior to commencing patient recruitment.

Primary outcomes

The primary outcome was unplanned re-operation for local complications within 30 days of the TM procedure. This included re-operation for any complications of the TM and/or contralateral symmetrising procedure but did not include additional surgery for oncological reasons including the need for re-excision of margins, completion mastectomy or axillary clearance. This outcome was selected based on Quality Criteria (QC) 16 from the Oncoplastic Breast Surgery: Guidelines for best practice[38] which state that less than 5% of patients should require return to theatre for complications following oncoplastic breast surgery. Specific outcomes of interest included; haematoma requiring surgical evacuation; infection requiring surgical drainage or debridement; skin necrosis including the T junction breakdown requiring surgical debridement; nipple necrosis or complete nipple loss requiring surgical debridement and wound dehiscence requiring return to theatre for re-suturing. Full definitions of complications used in the study have been reported previously[35].

Secondary Outcomes

Secondary outcomes reflected current best practice[38] and NICE guidelines[39] and included readmission to hospital, incomplete tumour excision requiring further surgery and time to delivery of adjuvant therapy[35]. Readmission to hospital was defined as any readmission following discharge for local or systemic complications of surgery as defined in the study protocol[35] within 30 days of the index procedure. Incomplete tumour excision was defined as invasive tumour or DCIS at, or close to, the resection margin requiring further surgery (re-excision or margins or completion mastectomy) as defined by local MDT criteria. Re-excision of margins was defined as return to theatre for removal of additional tissue in a second

operation due to one or more involved/positive margins. Completion mastectomy was defined as the complete removal of remaining breast tissue as elected by MDT decision or patient choice. Time to adjuvant therapy was defined as the time in days from the TM (or last oncological surgery, if further surgery was required) to the first adjuvant treatment, i.e. the first dose of chemotherapy or first fraction of radiotherapy.

Data quality assurance

For quality assurance (QA) purposes, the principal investigator at each site was requested to independently validate 5-10% of the data entered from their unit. The validation process involved checking and confirming that all entered data for the selected patients were correct. If concordance between the number of cases submitted on REDCap and those identified independently was <90%, the unit's data was excluded from the final analysis. This was consistent with QA procedures used in other collaborative studies[40].

Statistical analysis

Descriptive summary statistics were calculated for each variable to describe the practice and outcomes of TM. Categorical data were summarised by counts and percentages. Continuous data was summarised by median, interquartile range (IQR) and range.

Univariable logistic regression analysis was used to explore clinico-pathological variables hypothesised to be associated to the outcomes of interest. For complications, these included patient and procedure-related variables, namely age, smoking, body mass index (BMI), diabetes, co-morbidities, American Society of Anesthesiologists (ASA) grade, neoadjuvant chemotherapy, grade and experience of operating surgeon, type of skin incision, unilateral vs bilateral surgery, axillary surgery performed, specimen weight, drain use and duration of surgery. For incomplete excision, variables considered were patient age, neoadjuvant chemotherapy, maximum pre-operative size, pre-operative multifocality and localisation, specimen imaging (yes vs no), invasive disease (vs DCIS), positive nodal status (N0 vs N1/N2), positive HER-2 status, positive ER status, ductal vs lobular invasive disease on post-operative pathology, grade of invasive disease on post-operative pathology, screening (vs symptomatic), and specimen weight. Variables with a p-value <0.1 were carried forward to a multivariable model to identify any independent risk factors for each outcome. P-

values of <0.05 in the multivariable analysis were considered to be strongly associated with the outcome.All univariable and multivariable analyses had standard errors clustered by centre.

Time to adjuvant therapy was calculated for the cohort as a whole and for patients with and without post-operative complications. Kaplan-Meier analyses, univariable Cox survival models (with standard errors clustered by centre), and the log-rank test were then used to determine whether complications impacted on time to delivery of adjuvant therapy.

STATA 15 (STATA, Inc., Texas) was used for all analyses.

Results

Between 1st September 2016 and 30th June 2017, 898 patients were entered onto the REDCap database from 50 units across the United Kingdom (n=48) and Europe (n=2). Of these, eight patients underwent TMs performed outside the study period; five patients received symmetrising reduction surgery only and five records did not provide any details of the patients or surgery performed and were excluded. Some 880 patients and 899 TM procedures were therefore included in the analysis.

Patient demographics

Patient demographics are summarised in Table 1. Median patient age was 56 (range 23-86). Almost 40% (n=344, 39.1%) of study participants were classified as obese (BMI >30), 10% were current smokers and less than 5% (n=38, 4.3%) were diabetic. Approximately 40% (n=363, 41.3%) had at least one co-morbidity. Half of patients (n=454, 51.6%) presented with symptomatic breast lesions and the remainder presented through a breast screening programme. Surgery was the initial cancer treatment for the majority of patients with less than 20% receiving neoadjuvant therapy (n=162, 18.4%) (Table 1).

Pre-operative tumour assessment and treatment planning

Table 2 summarises the pre-operative planning and surgical decision-making for TM. Tumours were a median of 24mm (range 2-120mm) on pre-operative imaging with the majority located in the upper outer quadrant (n= 379, 43.3%) of the breast. Most lesions were invasive cancers (invasive ductal n=605, 68.5%,

invasive lobular n=79, 9.0%) and almost 20% (n=169, 18.8%) were assessed as being multifocal at diagnosis (table 2).

The most common indication for TM was to avoid an anticipated poor cosmetic outcome associated with standard BCS (n=702, 78.1%) but over 40% of patients (n=279, 42.2%) were offered the technique as an alternative to mastectomy. Quality of life benefits and avoidance of the sequelae of radiotherapy in large breasts were less commonly-cited indications (table 2). Two-thirds of patients (n=590, 65.6%) were offered standard BCS as an alternative surgical approach. For the remainder, the only alternative option was mastectomy alone (n=375, 41.7%), or with immediate implant-based (n=270, 30.0%) or autologous (n=231, 25.7%) reconstruction. A third of patients (n=283, 32.2%) were offered contralateral symmetrisation at the time of their TM procedure (table 2).

Operative techniques

Of the 880 patients; 572 (65.6%) underwent a unilateral TM procedure with no simultaneous contralateral surgery; 284 (32.3%) underwent a unilateral TM and simultaneous contralateral symmetrising reduction or mastopexy; 5 (0.6%) underwent a unilateral TM and a contralateral mastectomy with or without immediate reconstruction and 19 (2.2%) underwent bilateral TM procedures. The median operative time was 110.5 minutes (range 39-420 minutes) and the majority of cases (n=771, 85.6%) were performed by a consultant surgeon with significant experience (>25 cases) in performing this technique (table 3). Two-thirds (n=600, 66.6%) of lesions required pre-operative localisation of which 170 (19.3%) involved the use of bracketing wires or equivalent.

A wide range of different surgical approaches and techniques were used (table 3). Wise-pattern skin incisions were the most common (n=429, 48.0%) with peri- or circumareolar approaches (n=232, 25.7%) and vertical scar techniques (n=135, 15.0%) used less frequently. Most TMs preserved the nipple, using a central mound (n=225, 28.1%); inferior (n=204, 25.5%) or superiomedial (n=201, 25.2%) pedicle. Wide local excision specimens had a median weight of 83g (range 6-1515g) and adequacy of tumour excision was confirmed in 90% of cases, most commonly using intra-operative specimen radiography (n=785, 87.3%). Total TM excision weights ranged from 5-2522g with a median of 126.5g and drains were used in

a third (n=296, 32.9%) of cases. Symmetrising reductions were most likely to be performed using a Wise-pattern skin incision (n=232, 81.7%) and a superiomedial (n=112, 39.7%) or inferior (105, 36.6%) nipple pedicle. The median reduction weight was 320g (range 0-2477g) (data not shown). 40% (n=351) patients had their TM procedure as a day case procedure and a quarter (n=232) went home the day following surgery as a 23 hour stay.

Reoperation and readmission for surgical complications

Less than 3% (n=25, 2.8%) patients required re-operation for a complication of their surgery and only 12 (1.4%) patients were readmitted but in total, 205 (23.3%) patients experienced at least one post-operative complication within the first 30 days of surgery. These were generally minor complications which were managed on an outpatient basis and included infections requiring oral antibiotics (n=70, 8.0%) and wound healing problems managed conservatively with dressings (skin necrosis n=77, 8.8%; wound dehiscence n=49, 5.6%) (table 4).

Univariable analyses identified smoking, obesity, ASA grade, surgical experience, Wise-pattern skin incisions, bilateral surgery, specimen weight and the use of drains as risk factors associated with post-operative complications (table 5). Smoking, obesity, higher ASA grade, a less experienced surgeon, and a wise pattern skin incision remained strongly associated with post-operative complications in the multivariable model. Procedure duration was associated with complications in the univariable analysis but only 45% of records contained this variable so this was not included in the multivariable analysis.

Re-excision and completion mastectomy rates

Post-operative oncological data split according to whether resection margins were clear, are summarised in table 6. Incomplete excision according to local criteria was reported in 132 (14.7%) cases. Tumours with positive margins were more likely to be multifocal (59/132, 44.7% vs 133/744, 17.8%) and larger (median 39mm, IQR 25-54mm vs median 23mm, IQR 15-34mm) than those in whom excision margins were clear (table 6). Management of incomplete excision in the study cohort is shown in figure 1. Re-excision of margins was successfully performed in 68 cases giving on overall breast conservation rate of 90.3% (n=812), Completion mastectomy +/- immediate breast reconstruction was required for 43 (n=4.8%)

patients during the study, with a further 8 patients planned for surgery following completion of adjuvant chemotherapy. The completion mastectomy rate was therefore 51/899, 5.7% (figure 1).

Univariable analyses identified maximum pre-operative tumour size, and pre-operative assessment of multifocality as potential risk factors for incomplete excision (table 7). Both variables remained strongly associated with incomplete excision in the multivariable model.

Time to adjuvant therapy

Adjuvant treatment recommendations are summarised in table 8. Adjuvant chemotherapy was recommended for 273 (31.0%) patients of whom 228 (83.5%) accepted treatment and adjuvant radiotherapy was recommended for 794 (90.2%) patients. 811 (92.2%) patients accepted either post-operative chemotherapy and/or radiotherapy and the median time for last oncological surgery to first adjuvant treatment was 54 days (IQR 42-66). There was no significant difference in time to start of adjuvant therapy in patients with and without post-operative complications, OR 0.88 (0.76, 1.03) (p=0.109) (log-rank test p=0.147) (Figure 2).

Discussion

Therapeutic mammaplasty may provide women with a safe alternative to mastectomy or offer improved cosmetic and quality of life outcomes compared with standard BCS, but high-quality evidence to support the safety and effectiveness of the technique is lacking[26 27]. This is the first large prospective multicentre cohort study to assess the current practice and short-term outcomes of the technique and provide 'real world' data from 50 centres regarding complications, rates and management of incomplete excision and impact of TM procedures on delivery of adjuvant therapy.

Although most women are offered TM to avoid poor cosmetic outcomes associated with standard BCS, over 40% of patients are offered TM to avoid mastectomy. As the majority of women receiving TM in this study have high BMIs and comorbidities that may make them unsuitable or high risk for immediate breast reconstruction, the procedure may have particular quality of life benefits in this group. TM appears to be a specialist procedure as it is performed predominantly by consultant surgeons with significant experience of

the technique. Although Wise-pattern mammaplasties were the most common, a wide range of incisions and nipple pedicles were used. The varied techniques encompassed by 'Therapeutic Mammaplasty' mirror the dominant methods of breast reduction surgery but are likely to also reflect tailoring of approach to the tumour and patient as well as surgeon preference and experience. Simultaneous contralateral symmetrising reduction/mastopexy procedures were performed in only a third of patients. Reasons for this were not addressed but may include patient or surgeon preference or local funding issues but given the potential impact that delayed symmetrisation may have on quality of life with little if any improvements in overall symmetry, , these reasons are worthy of further study.

Two thirds of all TM procedures were performed either as a day-case or with a 23 hour stay, consistent with the length of stay required for standard BCS or mastectomy. Major complication rates were low with less than 3% of patients requiring re-operation for a complication of their TM and/or symmetrising procedure, significantly less than the 5% recommended in the Oncoplastic Surgery Guidelines[38]. Complications were associated with smoking, high BMI, Wise-pattern skin incisions, ASA grade and surgical experience but not with contralateral symmetrising surgery.

Median pathological tumour size was 24.5mm but over 20% (n=195) of patients had excisions of lesions >40mm, the traditional maximum size for standard BCS. Over 80% of patients undergoing TM had complete tumour excision as defined by local MDT criteria with a further 7.6% achieving this with one or more margin re-excisions giving an overall breast conservation rate of over 90%. Only 51 (5.7%) patients ultimately required a mastectomy and of these, 20 (39.2%) also had immediate reconstruction. Large pre-operative tumour size and multifocality were the only factors associated with incomplete excision in the multivariable model. This and the rate of re-excision is consistent with other studies of standard breast conserving surgery[41 42], but in these studies, the median tumour size is almost 10mm smaller and the proportion of T2 tumours 25% less than the current study. The implication is that TM can achieve similar rates of complete excision (and completion mastectomy) for large cancers as simple BCS techniques in small cancers.

811 (92.2%) patients required adjuvant chemotherapy and/or radiotherapy and the median time to adjuvant therapy was 54 days. This was not affected by complications and the interval is concordant with that of other studies on different surgical approaches[43]. TM does not therefore affect time to start adjuvant therapy.

The 'real world' outcome data generated from the multicentre TeaM study are remarkably consistent with the complication and re-excision rates reported in other series of oncoplastic surgery in the literature in which TM formed at least part of the oncoplastic approach[27 29 34]. The most recent review of ten large studies reports complication rates ranging between 8.9 and 24.6%[44]. It is not clear whether these rates are per breast or per patient, but our complication rates of 20.1% per breast and 23.3% per patient are broadly comparable. Incomplete excisions were reported in between 5.8 to 18.9% of cases in these studies leading to completion mastectomy rates of between 2.9 and 12.5%[44]. We report incomplete excision in less than 15% of cases and a rate of completion mastectomy of less than 6%. While this is reassuring, such comparisons may not be entirely valid due to the heterogeneity of procedures included in these studies[44] and the lack of consistency of the outcomes assessed[25]. Many studies and subsequently systematic reviews report outcomes of 'oncoplastic breast conservation'. This term is often used to describe a wide range of volume replacement (e.g. LiCAP flaps) and volume displacement techniques and procedures ranging in complexity from a small amount of glandular remodelling to oncoplastic breast reductions often with contralateral symmetrising procedures which are not directly comparable. A number of classification systems have been proposed, most notably Clough's bi-level classification[45], but standard adoption of an agreed terminology is a major barrier to high-quality comparable research[27 46 47]. Recently attempts at standardisation have been proposed but terminology and algorithms for decision-making are complex and the success of this approach is yet to be determined[48]. The agreement regarding the need for standardised outcome assessment including standard definitions of complications and quality of life assessments using validated patient-reported outcome measures however must be a priority if future research in oncoplastic surgery is to be meaningful[47] and the recently developed core outcome set for reconstructive breast surgery is one may by which this may be achieved[49].

This study has provided much needed prospective multicentre evidence for the short-term clinical safety and effectiveness of TM but it has several limitations that require consideration. The main limitation is that this is a short-term clinical study that has not considered the patient-reported, cosmetic and long-term oncological outcomes of the technique. Whilst this is a significant limitation, one of the main aims of the study was to define current practice to inform the design and conduct of a future definitive research study and to develop a network of centres performing TM to participate in the project. Given the uncertainty

regarding patient selection; the techniques used and management of the contralateral breast, this preliminary work was an essential prerequisite to developing a future study which will more accurately reflect current practice. Furthermore, the existing cohort will be used to explore long-term oncological outcomes in a future data-linkage study to provide added value. This study has collected data from 48 centres in the UK and 2 centres in Europe and is the largest prospective cohort of this kind. It is possible that participating units are high-volume highly specialist centres and that the outcomes reported are not representative of those seen at lower volume centres. However, the 48 centres included represent approximately one third of all breast units in the UK[50] and the similarity of the outcomes with the published literature suggests that this is not the case. The observational study design introduces the possibility of a number of forms of bias but several steps were taken to minimise this including publishing the study protocol a priori; providing clear inclusion and exclusion criteria and ensuring participating units recruited consecutive patients; developing standardised outcome definitions and where possible using 'hard' outcomes such as re-operation; margin positivity and treatment start dates which are unambiguous and not open to interpretation. Despite this, we acknowledge that our cohort is heterogenous including a range of procedures and techniques, but this is itself an important finding in terms of informing future studies. Finally, this was a trainee collaborative study, so it is possible that the quality of the data could be questioned. Robust quality assurance processes, however were used and none of the centres were excluded because of concerns regarding data completeness or accuracy. Despite these limitations, therefore, the TeaM study adds significantly to the evidence base in oncoplastic breast surgery, provides much needed data to inform decision-making and will inform future research.

Therapeutic mammaplasty may offer significant benefits to both patients and service providers but further work is needed to robustly define and quantify these benefits to support the ongoing provision of specialist care. TM was offered to over 40% of patients in our study as an alternative to mastectomy and allowing patients to avoid mastectomy may be one specific area where TM may be used to optimal benefit. Recent work comparing the outcomes of patients undergoing TM and those undergoing mastectomy and immediate breast reconstruction suggests that TM may be associated with fewer complications[51] and better body image, function and quality of life than mastectomy and reconstruction[52]. Further work is needed but TM may also be a more cost-effective approach as many of the patients in this cohort would still require post-

mastectomy radiotherapy which may adversely impact the outcomes of immediate reconstruction, especially if implant-based techniques were used[53]. More importantly, many of the patients who would be offered TM including those with co-morbidities and a high BMI would often not be offered immediate reconstruction so the benefits of TM vs. mastectomy alone in these women may be significant. Other groups who may experience particular benefit are those patients with large breasts in whom radiotherapy may result in significant complications[16]. There is ongoing research into how to identify patients at high risk of radiotherapy side-effects using biomarkers and clinical predictors[54]. While this was an indication in less than 20% of our cohort, it may have an increasing role for BCS with increasing BMI (and breast size). Patients may request this form of surgery as awareness of these techniques grows and further work is needed to support this approach and to inform the optimal timing of contralateral symmetrisation when TM procedures are offered. Randomised clinical trials comparing TM with other techniques are largely inappropriate due to patient and surgeon preference and mounting evidence to suggest long-term survival benefits for patients undergoing BCS and radiotherapy compared to mastectomy[55-57]. Well-designed prospective cohort studies incorporating validated patient-reported outcome measures such as the BREAST-Q[58], robust assessments of cosmetic outcome and appropriate health economic assessments may provide the best evidence of effectiveness. This preliminary work will ensure that any future study reflects current practice and addresses issues that are important to patients and the reconstructive community.

Therapeutic mammaplasty is safe and effective and may provide a better alternative to mastectomy or standard BCS for many women. Further work is now needed to establish key patient-reported and longer-term oncological outcomes and demonstrate cost-effectiveness so that this promising technique can become the new standard of care.

Authors' contributions

Conception and design of study EB, TR, AT, SP, RDM; data acquisition RLO'C, TR, EB, SP; data analysis and interpretation AT, RLO'C, LW, SP, RDM. RLO'C wrote the first draft of the manuscript. All authors critically revised the intellectual content and approved the manuscript prior to submission.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Collaborators

The TeaM Steering Group (in alphabetical order) were: Rajgopal Achuthan, Shweta Aggarwal, Elizabeth Baker, Naren Basu, Lisa Brock, Patricia Fairbrother, Matthew D Gardiner, Chris Holcombe, Charlotte Ives, Abhilash Jain, Baek Kim, R Douglas Macmillan, John Murphy, Shelley Potter, Tim Rattay, Dennis Remoundos, Richard Sutton, Adam Trickey, Philip Turton, Kathryn Williams.

Local investigators (alphabetically by centre) and members of the Mammary Fold Academic and Research Collaborative were: **Aberdeen Royal Infirmary, NHS Grampian**: Caitlin MacLeod, Elizabeth Smyth, Ivan Depasquale, Mairi Fuller, Nina Saeed, Yazan Masannat. **Addenbrookes Hospital, Cambridge Universities NHS Foundation Trust:** Amir Tan Mohd-Amin, Amit Agrawal. **Belfast City Hospital, Belfast Health and Social Care Trust:** Gareth Irwin, Sam Sloan, Sigi Refsum, Stuart McIntosh. **Breast Care Centre, North Bristol NHS Trust, Southmead Hospital, Bristol:** Abdulla Ibrahim, Ajay Sahu, Sasirekha Govindarajulu, Simon Cawthorn. **Breast Unit Department. University of Naples "Federico II", Naples, Italy:** Antonello Accurso. **Brighton and Sussex University Hospitals NHS Trust:** Rathi Rathinaezhil. **Castle Hill Hospital, Hull and East Yorkshire Hospitals NHS Trust:** Alex Wilkins, Eiman Khalifa, Kartikae Grover, Penny McManus, Peter Kneeshaw, Tapan Mahapatra. **Chesterfield Royal Hospital NHS Foundation Trust:** Iman Azmy, Julia Massey. **Darent Valley Hospital, Dartford and Gravesham NHS Trust**: Pawel Trapszo, Risha Lane, Seema Seetharam. **Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy:** Nicola Rocco. **East Cheshire NHS Trust:** Chandeena Roshanlall, Jalal Kokan, Khalid Amin. **Edinburgh Breast Unit, Western General Hospital, NHS Lothian:** Alexander Leeper, Dhananjay Kulkarni, JM Dixon, Oliver Young, Talha Saleem. **Forth Valley Royal Hospital, NHS Forth Valley:** Jennifer McIlhenny. **Gartnavel General Hospital, NHS**

Greater Glasgow and Clyde: Andy Malyon, James Mansell, Keith Ogsto, Laszlo Romics. **Glenfield Hospital, University Hospitals of Leicester**: Dimitris Dragoumis, Jaroslaw Krupa, Kalliope Valassiadou, Kelly Lambert, Monika Kaushik, Shelia Shokuhi, Simon Pilgrim, Xiang Wei Jonathan Lee. **Gloucestershire Hospital NHS Foundation Trust:** Asmaa Al-Allak, Clare Fowler, Eleanore Massey, Fiona Court, Richard Hunt, Sarah Vestey. **Good Hope Hospital, Heart of England NHS Foundation Trust:** Haitham Khalil. **Heatherwood and Wexham Park Hospital, Frimley Health NHS Foundation Trust:** Mohsen Elgammal. **Homerton University Hospital NHS Foundation Trust:** Laila Parvanta. **Lincoln County Hospital, United Lincolnshire Hospitals NHS Trust:** A S Sami, Anzors Gvaramadze, Dinesh Thekkinkattil. **Luton and Dunstable University Hospital:** Katharine Kirkpatrick, Ruth James. **Mid Yorkshire Hospitals NHS Trust:** Arish Noshirwani, Tehera Arif, Zbigniew Kryjak. **Milton Keynes University Hospital NHS Foundation Trust:** Amanda Taylor, Farah H Syed, Gazalla Safdar, Kian Chin, Rachel Soulsby. **Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust:** Amanda Thorne, Francesca Guest, Mohammed El-Abbar. **Ninewells Hopsital, NHS Tayside:** D.Alex Munnoch, E.Jane Macaskill, Fiona Hogg, Pauline McGee, Vassilis Pitsinis. **Northern Lincolnshire and Goole NHS Foundation Trust:** Jenny Smith, Sundus Makkiyah, Syed Mustafa. **Nottingham Breast Institute, Nottingham University Hospitals NHS Trust:** Charlene Otieno, Dana Photiou, Douglas Macmillan, Ellie Gutteridge, Fayyaz Mazari, Georgette Oni, Hazem Khout, Jennett Kelsall, Kelly Hallam, Kristjan Asgeirron, Lisa Whisker, Marta D'Auria, Samim Al-zubaidi, Stephen McCulley, Tuabin Rasheed, James Bailey, Lisa Brock, Nazli Muhibullah. **Oxford University Hospitals NHS Foundation Trust:** Alexandra Tenovici, Dionysios-Dennis Remoundos, Nikos Chaidos, Oana Predescu, Pankaj Roy, Rebecca Windle. **Peterborough City Hospital, North West Anglia NHS Foundation Trust:** Elena Popa, Geeta Shetty, Jan Rezulski, Steven Goh, Tholkifl Abdullah. **Pilgrim Hospital Boston, United Lincolnshire Hospitals NHS Trust:** Dinesh Thekkinkattil. **Prince Philip Hospital, Hywel Dda University Health Board:** Saira Khawaja, Sujatha Udayasankar. **Princess Alexandra Hospital NHS Trust:** Sally Tebbal, Veronica Grassi. **Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust:** Adam Talbot, Naren Basu, Jagdeep Singh. **Royal Bolton Hospital, Bolton NHS Foundation Trust:** Amy Smith, Angela Volleamere, Clare Garnsey, Panagiotis Pikoulas. **Royal Devon and Exeter NHS Foundation Trust:** Charlotte Ives, Douglas Ferguson, Rachel Tillett, Sarah Dean, Sisse Olsen. **Royal Hampshire County Hospital,**

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Table 1. Demographics of patients included in the TeaM study

Patient demographics	N=880 patients (%)
Age, years (median, IQR, range)	56 (50-65) (23-86)
0-44 years	92 (10.5)
45-54 years	286 (32.5)
55-64 years	274 (31.1)
65-74 years	180 (20.5)
≥75 years	41 (4.7)
Not reported	7 (0.8)
BMI, kg/m^2 (median, IQR, range)	28.3 (25-32.7) (17.0-58.1)
Normal (<25)	200 (22.7)
Overweight (≥25 & <30)	309 (35.1)
Obese (≥30 & <35)	213 (24.2)
Severely obese (>35)	131 (14.9)
Not reported	27 (3.1)
Smoking status	
Non-smoker (never smoked)	642 (73)
Ex-smoker	132 (15)
Current smoker	89 (10.1)

Not reported	17 (1.9)
Co-morbidities	
Diabetes	38 (4.3)
Ischaemic heart disease	25 (2.8)
Current steroid use	13 (1.5)
Other co-morbidities	363 (41.3)
Previous and neoadjuvant cancer therapies	
Previous radiotherapy to the ipsilateral breast	6 (0.7)
Neoadjuvant chemotherapy	104 (11.8)
Neoadjuvant endocrine therapy	54 (6.1)
Neoadjuvant radiotherapy	4 (0.5)
Previous breast surgery, n (%), N=899 breasts	67 (7.5)
American Society of Anesthesiologists (ASA) grade	
Grade 1	295 (33.5)
Grade 2	535 (60.8)
Grade 3	46 (5.2)
Not reported	4 (0.5)
Presentation	
Screening	424 (48.1)
Symptomatic	454 (51.6)
Not reported	2 (0.2)

BMI – body mass index, IQR – interquartile range

Table 2 Pre-operative planning and surgical decision making

	Total TM breasts (n=899) (%)
Predominant location of tumour by quadrant	
Upper outer	379 (42.2)
Upper inner	180 (20.0)
Lower outer	133 (14.8)
Lower inner	109 (12.1)
Central (immediately behind nipple)	75 (8.3)
Not reported	23 (2.6)
Pre-operative assessment of lesion	
DCIS	146 (16.2)
Invasive ductal carcinoma	605 (67.3)
Invasive lobular carcinoma	79 (8.8)
Other	53 (5.9)
Not reported	16 (1.8)
Provisional invasive grade (n=737)	
Grade 1	121
Grade 2	409

Grade 3	192
Provisional grade of DCIS (n=146)	
Low grade	9
Intermediate grade	37
High grade	95
Maximum size of lesion at diagnosis, mm (median, IQR, range)	24 (15-35) (2-120)
Multifocal	169 (18.8)
Surgical decision-making	**Per patient (n=880) (%)**
Contralateral symmetrisation	
Planned simultaneous to TM procedure	283 (31.5)
Planned for a later date	126 (14.0)
To be discussed later	246 (38.5)
Patient declined	65 (7.2)
Not applicable – bilateral disease	38 (4.2)
Not reported	41 (4.6)
Indications for therapeutic mammaplasty[a]	
Large tumour	197 (21.9)
To avoid mastectomy	379 (42.2)
To avoid poor cosmetic outcome associated with standard wide local excision	702 (78.1)
To avoid problems associated with radiotherapy in large breasts	160 (17.8)
Quality of life benefits	250 (27.8)
Other	40 (4.5)
Other treatment options offered[a]	
Standard wide local excision	590 (65.6)
Mastectomy alone	375 (41.7)
Mastectomy with immediate implant reconstruction	270 (30.0)
Mastectomy with immediate autologous reconstruction	231 (25.7)

DCIS – ductal carcinoma in situ; IQR – interquartile range; TM – therapeutic mammaplasty

[a]More than one indication or treatment option could be given per patient

Table 3 Operative data

	N=899, (%)
Duration of the procedure, minutes (median, IQR, range)	110.5 (90-150) (39-420)
Grade of operating surgeon	
Consultant	771 (85.8)
Senior trainee (Oncoplastic Fellow/ST8)	85 (9.5)
Junior trainee (ST7 or below)	16 (1.8)
Associate Specialist/Other	22 (2.4)
Not reported	5 (0.6)
Number of TMs performed using similar technique unsupervised by the operating surgeon	
<5	73 (8.1)
5-10	22 (2.5)
10-25	87 (9.7)
>25	671 (74.6)
Not reported	46 (5.1)
Pre-operative tumour localisation	
Any method	600 (66.7)
Bracketing wires or equivalent	170 (18.9)
Skin incision used	
Wise pattern (inverted T)	429 (47.7)
Peri/circumareolar with skin excision (e.g. round block, Benelli or racquet)	232 (25.8)
Single vertical scar (Le Jour)	135 (15.0)
Grisotti (for central cancers removing nipple-areolar complex, NAC)	16 (1.8)
Melon-slice (horizontal wedge excision +/- NAC excision)	28 (3.1)
Other	55 (6.1)
Not reported	4 (0.4)
Nipple preservation	
On a pedicle	828 (92.1)
As a free nipple graft	10 (1.1)
Nipple not preserved	57 (6.3)
Not reported	4 (0.4)
Pedicle used to preserve nipple (if nipple preserved n=828)	
Superior	81 (9.8)
Superiomedial	201 (24.3)
Medial	21 (2.5)
Inferior	204 (24.6)
Central mound	225 (27.2)
Dual pedicle	45 (5.4)
Other/not reported	51(6.2)
Method of tumour excision	
WLE performed first followed by reduction/mastopexy	378 (42.0)
WLE incorporated in reduction specimen (both performed simultaneously)	520 (57.8)
Not reported	1 (0.1)
Intra-operative confirmation of tumour excision	

None	90 (10.0)
Specimen radiography	785 (87.3)
Other intra-operative assessment method (e.g. frozen section)	19 (2.1)
Not reported	5 (0.6)
Weight of wide local excision, grams (median, IQR, range)	83 (44-173) (6-1545)
Total weight of breast tissue excised, grams (median, IQR, range)	126.5 (50-319) (5-2522)
Method of marking tumour bed	
None	44 (4.9)
Single clip	16 (1.8)
Clips to all margins	836 (93.0)
Not reported	3 (0.3)
Axillary surgery performed	
None	134 (14.9)
Sentinel node biopsy	666 (74.1)
Axillary node clearance	99 (11.0)
Drains used	296 (32.9)
Procedure performed to the contralateral breast (n=880 patients)	
None	562 (63.7)
Contralateral reduction/mastopexy	284 (32.3)
Bilateral therapeutic mammaplasties	19 (2.2)
Mastectomy only	2 (0.2)
Mastectomy and implant reconstruction	2 (0.2)
Mastectomy and autologous reconstruction	1 (0.1)
Not reported	10 (1.1)

IQR – interquartile range, WLE - wide local excision

Table 4. Complications at 30 days per breast and per patient

Complication	Per breast data	
	Therapeutic mammaplasty (N=899) n (%)	**Contralateral reduction/mastopexy (N=284) n (%)**
Seroma requiring aspiration	35 (3.9)	1 (0.4)
Haematoma	**24 (2.3)**	**6 (2.1)**
Managed conservatively	15 (1.7)	2 (0.7)
Requiring surgical evacuation	9 (1)	4 (0.1)
Infection	**64 (7.1)**	**18 (6.3)**
Requiring oral antibiotics	53 (5.9)	17 (6)
Requiring IV antibiotics	6 (0.7)	0
Requiring surgical debridement/drainage	5 (0.6)	1 (0.3)
Skin necrosis, including T junction necrosis	**59 (6.6)**	**22 (7.7)**
Minor – managed conservatively	56 (6.2)	21 (7.4)
Major requiring surgical debridement	3 (0.3)	1 (0.3)
Nipple necrosis	**(n=828)***	**(n=284)***
Minor managed conservatively	8 (1.0)	1 (0.4)
Requiring debridement	2 (0.2)	0 (0.0)
Wound dehiscence	**45 (5.0)**	**9 (3.2)**
Managed conservatively	42 (4.6)	7 (2.5)
Requiring return to theatre	3 (0.3)	2 (0.7)
Any complication	**181 (20.1)**	**42 (14.8)**
	Per patient data (n=880)	
Any surgical complication within 30 days of TM procedure	**205 (23.3)**	
Re-operation for complications within 30 days of TM	**25 (2.8)**	
In hospital complications	**12 (1.3)**	
Reaction to blue dye	2 (0.2)	
Surgical complication[a]	5 (0.6)	
Medical complication[b]	2 (0.2)	
Other	3 (0.3)	
Readmission for complications following discharge within 30 days of surgery[c]	**12 (1.4)**	
Length of stay		
Daycase	351 (39.9)	
23 hour	232 (26.4)	
Inpatient	289 (32.8)	
Not reported	8 (0.9)	

*Denominator is breasts that kept their nipple on a pedicle; [a]Haematomas requiring evacuation, [b]Cardiac arrhythmias
[c]included admission for intravenous antibiotic (n=4); evacuation of haematoma (n=2); debridement of nipple necrosis (n=1); drainage of recurrent seroma (n=1) and recurrent SVTs (n=1)

Table 5. Risk factors for post-operative complications

Variable	Univariable		p-value	Multivariable (N=790, events=185)	p-value
	N (events, %)	Odds Ratio (95% CI)		Odds Ratio (95% CI)	
Age (per year increase)	873 (204, 23%)	1.00 (0.98, 1.01)	0.652		
Current smoker	863 (204, 24%)				
No	774 (171, 22%)	Reference			
Yes	89 (33, 37%)	2.08 (1.35, 3.20)	0.001*	2.32 (1.51, 3.56)	<0.001**
BMI, kg/m^2	853 (201, 24%)				
Normal <25	200 (29, 15%)	Reference		Reference	
Overweight 25-29	309 (68, 22%)	1.66 (1.03, 2.68)	0.037*	1.25 (0.77, 2.04)	0.363
Obese 30-34	213 (63, 30%)	2.48 (1.55, 3.95)	<0.001*	1.73 (1.05, 2.86)	0.033**
Severely obese 35+	131 (41, 31%)	2.69 (1.52, 4.76)	0.001*	1.77 (0.96, 3.27)	0.066
Diabetes	870 (203, 23%)				
No	832 (197, 24%)	Reference			
Yes	38 (6, 16%)	0.60 (0.25, 1.44)	0.254		
Any comorbidities	880 (205, 23%)				
No	490 (106, 22%)	Reference			
Yes	390 (99, 25%)	1.23 (0.92, 1.66)	0.167		
ASA grade	876 (204, 23%)				
Grade 1	295 (50, 17%)	Reference		Reference	
Grade 2	535 (140, 26%)	1.74 (1.25, 2.41)	0.001*	1.45 (1.07, 1.96)	0.018**
Grade 3	46 (14, 30%)	2.14 (1.02, 4.49)	0.043*	1.68 (0.71, 3.98)	0.236
Neoadjuvant chemotherapy	879 (205, 23%)				
No	775 (179, 23%)	Reference			
Yes	104 (26, 25%)	1.11 (0.68, 1.82)	0.681		
Surgeon grade	876 (203, 23%)				
Trainee	121 (34, 28%)	Reference			
Consultant	755 (169, 22%)	0.74 (0.53, 1.04)	0.078		
Surgical experience	866 (201, 23%)				
≤25 similar procedures	103 (32, 31%)	Reference			
>25 similar procedures	763 (169, 22%)	0.63 (0.41, 0.97)	0.034*	0.60 (0.41, 0.88)	0.010**
Skin incision type	876 (204, 23%)				
Other than wise pattern	462 (72, 16%)	Reference			
Wise pattern	414 (132, 32%)	2.54 (1.87, 3.44)	<0.001*	1.90 (1.20, 3.00)	0.006**
Unilateral or bilateral surgery	880 (205, 23%)				
Unilateral TM	577 (107, 19%)	Reference		Reference	
TM + contralateral symmetrisation	284 (89, 31%)	2.00 (1.33, 3.02)	0.001*	1.32 (0.70, 2.47)	0.389
Bilateral TM	19 (9, 47%)	3.95 (1.33, 11.78)	0.014*	3.40 (0.82, 14.10)	0.092
Axillary surgery	880 (205, 23%)				
None	129 (31, 24%)	Reference			
Sentinel node biopsy	653 (146, 22%)	0.91 (0.55, 1.52)	0.720		
Axillary node clearance	98 (28, 29%)	1.26 (0.67, 2.40)	0.473		
Specimen weight (per 10g increase)	842 (196, 23%)	1.01 (1.01, 1.02)	<0.001*	1.00 (1.00, 1.01)	0.612
Drains used	873 (202, 23%)				
No	584 (117, 20%)	Reference			
Yes	289 (85, 29%)	1.66 (1.20, 2.30)	0.002*	1.16 (0.82, 1.64)	0.400
Procedure duration (per extra hour)[a]	400 (93, 23%)	1.74 (1.33, 2.29)	<0.001[a]		

*=p<0.1 therefore put variable put forward to multivariable analysis. **=p<0.05 therefore strong association with having a post-operative complication in the multivariable analysis

[a]Procedure duration is highly significant in the univariate analysis, but given the high level of missing data (n=480), this variable was not carried forward to the multivariable analysis

ASA – American Society of Anaesthesiologists; BMI – body mass index, TM – therapeutic mammaplasty

Table 6. Post-operative histology and tumour characteristics in therapeutic mammaplasty cases with complete and incomplete excision margins

	Per breast: N=899 (%)*	
Post-operative histology	**Completely excised N=744 (82.8%)**	**Incompletely excised N=132 (14.7%)**
Type of lesion		
Ductal carcinoma in situ	108 (14.5)	24 (18.2)
Invasive ductal carcinoma	512 (68.8)	81 (61.4)
Invasive lobular carcinoma	74 (10.0)	15 (11.4)
Other invasive	46 (6.2)	12 (9.1)
Not reported	4 (0.5)	0 (0.0)
Grade		
Invasive (n=744)		
Grade 1	110 (13.6)	16 (12.1)
Grade 2	302 (40.6)	58 (43.9)
Grade 3	217 (29.2)	32 (24.2)
Not reported	124 (16.7)	26 (19.7)
Ductal carcinoma in situ (DCIS) (n=132)		
Low grade	10 (9.3)	0 (0.0)
Intermediate grade	30 (27.8)	3 (12.5)
High grade	68 (63.0)	21 (87.5)
Multifocal tumour		
No	606 (81.5)	72 (54.5)
Yes	133 (17.8)	59 (44.7)
Not reported	5 (0.7)	1 (0.8)
Size of largest invasive tumour, mm (median, IQR, range)**	18 (10, 26) (0-155)[a]	22 (13, 37) (0-145)[b]
Total size of lesion including DCIS, mm (median, IQR, range)**	23 (15, 34) (0-144)[c]	39 (25, 54) (5-145)[d]
Receptor status* **		
ER positive	565 (75.9)	90 (68.2)
HER-2 positive	108 (14.5)	19 (14.4)
Not reported	71 (9.5)	23 (17.4)
Lymph node status (n=765)		
Number of lymph nodes involved - macrometastases only (median, IQR, range)	0 (0-0) (0-25)	0 (0-0) (0-18)
N0	495 (66.5)	82 (62.1)
N1	77 (10.4)	9 (6.8)

*23 (2.6%) did not have data recorded on whether or not there was complete excision
**Including patients who had a complete pathological response with neoadjuvant chemotherapy; ***Denominator is those with invasive lesions; ER – oestrogen receptor; IQR – interquartile range; MDT – multidisciplinary team
[a]Not reported for 35 [b]Not reported for 11 [c]Not reported for 45 [d]Not reported for 6

Table 7. Risk factors for incomplete excision of tumour according to local MDT criteria

Variable	Univariable			Multivariable (N=859, events=130)	
	N (events, %)	Odds Ratio (95% Confidence Interval)	p-value	Odds Ratio (95% Confidence Interval)	p-value
Age (per year increase)	869 (130, 15%)	0.99 (0.98, 1.01)	0.441		
Neoadjuvant chemotherapy	875 (131, 15%)				
No	774 (121, 16%)	Reference			
Yes	101 (10, 10%)	0.59 (0.27, 1.29)	0.188		
Maximum pre-operative size (as per 5mm increases)	862 (131, 15%)	1.07 (1.02, 1.11)	0.002*	1.06 (1.02, 1.11)	0.009**
Pre-op multifocality	872 (131, 15%)				
No	706 (98, 14%)	Reference		Reference	
Yes	166 (33, 20%)	1.54 (1.08, 2.20)	0.019*	1.48 (1.02, 2.14)	0.038**
Pre-op localisation	865 (131, 15%)				
No	279 (36, 13%)	Reference			
Yes	586 (95, 16%)	1.31 (0.93, 1.82)	0.117		
Specimen imaging	872 (131, 15%)				
No	87 (8, 9%)	Reference			
Yes	785 (123, 16%)	1.83 (0.84, 4.02)	0.129		
Disease type	814 (120, 15%)				
DCIS	132 (24, 18%)	Reference			
Invasive	682 (96, 14%)	0.74 (0.46, 1.18)	0.208		
Positive nodal status	744 (107, 14%)				
N0	577 (82, 14%)	Reference			
N1/N2	167 (25, 15%)	1.06 (0.65, 1.73)	0.806		
Positive HER-2 Status	758 (108, 14%)				
No	127 (19, 15%)	Reference			
Yes	631 (89, 14%)	0.93 (0.55, 1.58)	0.798		
Positive ER Status	784 (112, 14%)				
No	655 (90, 14%)	Reference			
Yes	129 (22, 17%)	1.29 (0.72, 2.31)	0.391		
Ductal vs lobular invasive disease	872 (132, 15%) 725 (105, 14%)				
Ductal	89 (15, 17%)	Reference			
Invasive lobular	58 (12, 21%)	1.20 (0.70, 2.03)	0.506		
Other		1.54 (0.81, 2.92)	0.185		
Grade of invasive disease on post-operative pathology	858 (130, 15%)				
Ductal carcinoma in situ (DCIS)	132 (24, 18%)	1.40 (0.81, 2.43)	0.229		
1	117 (16, 14%)	Reference			
2	360 (58, 16%)	1.21 (0.74, 1.98)	0.442		
3	249 (32, 13%)	0.93 (0.53, 1.63)	0.803		
Presentation type	875 (132, 15%)				
Symptomatic	419 (66, 16%)	Reference			
Screening	456 (66, 14%)	0.91 (0.63, 1.30)	0.592		
Specimen weight (per 10g increase)	840 (126, 15%)	0.99 (0.99, 1.00)	0.274		

*= P<0.1 therefore put variable put forward to multivariable analysis. **=P<0.05 strong association with incomplete excision in the multivariable analysis

Table 8. Multidisciplinary team decision-making and time to adjuvant therapy

Adjuvant treatment recommendations and time to adjuvant therapy	Per patient: N=880 n (%)
Chemotherapy	
Not recommended	509 (57.8)
Chemotherapy recommended	273 (31.0)
Chemotherapy accepted	228 (25.9)
Chemotherapy previously given	78 (9.1)
Missing	20 (2.3)
Radiotherapy	
Not recommended	67 (7.6)
Recommended	794 (90.2)
Already given	2 (0.2)
Missing	17 (1.9)
Adjuvant chemotherapy and/or radiotherapy required	811 (92.2)
Time to first adjuvant therapy (n=695) (days) (median, IQR, range)	54 (42-66) (6-287)
Time to chemotherapy as first adjuvant therapy (n=204) (days) (median, IQR, range)	47 (30-58) (14-237)
Time to radiotherapy as first adjuvant therapy (n=491) (days) (median, IQR, range)	56 (44-69) (6-287)

IQR – interquartile range