**The impact of radiotherapy on patient-reported outcomes of immediate implant-based breast reconstruction with and without mesh**

Emma Sewart MBBS1, Nicholas L Turner PhD1, Elizabeth J Conroy MSc2, Ramsey I Cutress PhD3, Joanna Skillman MA4, Lisa Whisker MBChB5, Steven Thrush MBBS6, Nicola Barnes PhD7, Chris Holcombe MD8, Shelley Potter PhD1,9 on behalf of the iBRA Steering Group and the Breast Reconstruction Research Collaborative

1Population Health Sciences, Bristol Medical School, Canynge Hall, 39 Whatley Road, Clifton, Bristol, BS8 2PS UK; 2Liverpool Clinical Trials Centre (LCTC), University of Liverpool, Liverpool, L12 2AP UK; 3Faculty of Medicine, Cancer Sciences Unit, University of Southampton, Somers Cancer Research Building, University Hospital Southampton, Tremona Road, Southampton, SO16 6YD, UK; 4Department of Plastic Surgery, University Hospitals Coventry and Warwickshire NHS Trust, Clifford Bridge Road, Coventry, CV2 2DX, UK; 5Nottingham University Hospitals NHS Trust, Hucknall Road, Nottingham, NG5 1PB, UK; 6Breast Unit, Worcester Royal Hospital. Charles Hastings Way, Worcester, WR5 1DD, UK; 7Nightingale Breast Unit, Manchester University NHS Foundation Trust, Southmoor Road, Manchester, M23 9LT, UK; 8Linda McCartney Centre, Royal Liverpool and Broadgreen University Hospital, Prescot Street, Liverpool, L7 8XP, UK; 9Bristol Breast Care Centre, North Bristol NHS Trust, Southmead Road, Bristol, BS10 5NB UK

\*Members of the iBRA Steering Group and Breast Reconstruction Research Collaborative are PUBMED citable collaborators on this study and are listed at the end of the manuscript

This work was funded by an NIHR Research for Patient Benefit Grant (PB-PG-0214-33065), pump-priming funding from the Association of Breast Surgery (ABS) and the British Association of Plastic Reconstructive and Aesthetic Surgeons and a Research Development Award from ABS (2019) and supported by the MRC ConDuCT-II (Collaboration and innovation for Difficult and Complex randomized controlled Trials In Invasive procedures) Hub for Trials Methodology Research (MR/K025643/1) and the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. Shelley Potter is an NIHR Clinician Scientist (CS-2016-16-019). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care

**Corresponding author:** Shelley Potter E-mail: [shelley.potter@bristol.ac.uk](mailto:shelley.potter@bristol.ac.uk)

Bristol Centre for Surgical Research, Population Health Sciences, Bristol Medical School, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, UK Tel: +44(0) 117 9287218

No reprints will be available

**Mini-abstract**

Postmastectomy radiotherapy (PMRT) improves breast cancer outcomes but increases complications following implant-based breast reconstruction (IBBR). This prospective cohort study explored the impact of PMRT on patient-reported outcomes 18-months following IBBR showing worse scores in the PMRT group. These results should be discussed with patients to support informed decision-making for treatment.

**Abstract**

**Objective:** To explore the impact of postmastectomy radiotherapy (PMRT) on patient-reported outcomes (PROs) of implant-based breast reconstruction (IBBR) performed with and without mesh.

**Summary background data:** Post-mastectomy radiotherapy (PMRT) is increasingly given to improve breast cancer outcomes but can adversely impact complications following IBBR. Little, however, is known about the impact of PMRT on the PROs of IBBR, especially when mesh is used.

**Methods:** The iBRA (implant Breast Reconstruction evAluation) prospective cohort study recruited consecutive women undergoing immediate IBBR from 81 UK breast and plastic surgical units. Demographic, operative, oncological and 3-month complication data were collected, and patients consented to receive validated PRO questionnaires at 18-months. The association between IBBR, PMRT and PROs were investigated using mixed-effects regression models adjusted for clinically-relevant confounders and including a random-effect to account for potential clustering by center

**Results:** 1163 women consented to receive 18-month questionnaires of whom 730 (63%) completed it. Patients undergoing PMRT (214 patients) reported worse PROs in three BREAST-Q domains: satisfaction with breasts (-6.27 points, p=0.008,95% confidence interval (CI)[-10.91,-1.63]), satisfaction with outcome (-7.53 points, p=0.002,CI[-12.20,-2.85]) and physical well-being (-6.55 points, p<0.001, CI[-9.43,-3.67]). Overall satisfaction was worse in the PMRT group (OR 0.497, p=0.002, CI [0.32, 0.77]). These effects were not ameliorated by mesh use.

**Conclusions:** PMRT may adversely affect PROs following IBBR irrespective of whether mesh is used. These findings should be discussed with all patients considering IBBR and when indications for PMRT are borderline to enable informed decision-making regarding oncological and reconstructive treatment options.

**Trial registration:** ISRCTN37664281

**Introduction**

Breast cancer is the most common cancer in women worldwide, with a global incidence of 2.09 million cases in 20181. Treatment with curative intent involves surgery, often in combination with systemic treatment and radiotherapy2. Despite improvements in cancer treatment, approximately 40% of all women will receive mastectomy as the surgical management of their disease3. Mastectomy may profoundly impact women’s well-being and immediate breast reconstruction can improve health-related quality of life (HRQL)4,5.

Implant-based breast reconstruction (IBBR) is the most commonly performed reconstructive procedure in both the UK and US6,7. It can achieve good cosmetic results and offers patients a shorter operation and more rapid recovery than autologous alternatives without donor-site morbidity8. Traditionally, IBBR has been a two-stage procedure, involving placement of a subpectoral tissue-expander, sequential expansions with saline to reach the final volume and subsequent replacement of the expander with a permanent implant. However, the introduction of a range of biological (e.g. acellular dermal matrix [ADM]) and synthetic (e.g. titanium-coated polypropylene) meshes has led to the development of single-stage direct-to-implant IBBR techniques. Mesh-assisted sub-pectoral reconstruction involves suturing a mesh between the lower edge of the pectoralis muscle and the chest wall, creating an extended pocket that can accommodate a fixed-volume implant in one procedure9. More recently, pre-pectoral techniques have been introduced. These spare the muscle entirely by wrapping the implant in mesh and placing it on top of the pectoralis muscle10.Whilst new IBBR techniques have become widely adopted into practice, there is a paucity of high-quality evidence to support their safety and effectiveness, particularly in the context of postmastectomy radiotherapy (PMRT)11.

Post-mastectomy radiotherapy (PMRT) improves breast cancer survival and reduces local recurrence12-15, but treatment was traditionally restricted to patients with locally-advanced disease (large tumours and/or significant nodal disease). More recently, evidence has emerged to suggest that PMRT may reduce recurrence and improve long-term survival in intermediate risk patients, in particular those with one to three positive nodes16. Increasing numbers of women are therefore recommended treatment.

The offer of IBBR in the context of anticipated PMRT remains controversial17,18.Radiotherapy may result in skin changes, fibrosis and impaired vascularity and has been shown to be an independent risk-factor for complications following IBBR19. In the longer term, capsular contracture following PMRT is a significant problem leading to pain and deformity that often requires surgery to remove the implant or replace it with autologous tissue20. Using biological mesh to provide implant coverage, however, has been shown to reduce levels of myofibroblasts, fibroblasts, and other markers of inflammation and fibrosis following PMRT21 and there is limited evidence to suggest reduced rates of capsular contracture when biological mesh is used22. This may improve outcomes for patients undergoing surgery but there is little published literature on the impact of PMRT on patient-reported outcomes (PROs) on IBBR, especially in the context of newer mesh-assisted techniques.

A 2017 systematic review found six studies (593 patients) that evaluated patient satisfaction after IBBR and PMRT23. The majority of included studies used non-validated questionnaires and the proportion of satisfied patients varied widely24-29. Four studies (575 patients) used the validated BREAST-Q questionnaire and demonstrated that patients receiving PMRT reported globally worse scores in all domains. None of these studies, however, reported the use of newer single-stage mesh-assisted techniques23. More recently, a prospective multicenter cohort study which included 1604 patients receiving both two-stage and single-stage IBBR reported reduced satisfaction with breasts associated with radiotherapy (224 irradiated patients, 811 non-irradiated) at 1 and 2 years post-operatively19 but did not report details of the direct-to-implant techniques used. Smaller retrospective cross-sectional studies have produced conflicting evidence regarding the impact of PMRT on PROs following IBBR30-32.With the use of both PMRT and IBBR increasing and recent recommendations that reconstruction should be offered to all women, even if PMRT is anticipated2,there is an urgent need for high-quality research to explore the impact of radiotherapy on the outcomes of implant-based procedures to help patients make informed decisions about their reconstructive and oncological options33.

The iBRA (implant Breast Reconstruction evAluation) study is a four-phase study aiming to inform the feasibility, design, and conduct of a future trial in immediate IBBR11. Phase 2, a UK prospective multicenter cohort study, explored the clinical and patient-reported outcomes of different approaches to immediate IBBR with and without mesh.The short-term safety outcomes have been reported elsewhere9. Here we report the 18-month PROs of IBBR in patients undergoing surgery for malignancy to explore the impact of PMRT on patient satisfaction and HRQL and determine whether this is influenced by the use of biological mesh.

**Methods**

***iBRA study design and procedures***

The iBRA study prospectively recruited consecutive women aged 16 years or older undergoing immediate IBBR for malignancy or risk-reduction between Feb 1, 2014 and June 30, 2016. All UK breast or plastic surgical units performing immediate IBBR were invited to participate via the UK Trainee Collaborative Research Network, the Association of Breast Surgery and the British Association of Plastic Reconstructive and Aesthetic Surgeons11.

Patients at participating centers undergoing IBBR using any technique were eligible for inclusion. This included subpectoral reconstructions with and without mesh, and pre-pectoral techniques. Patients were excluded if undergoing delayed reconstruction or receiving an implant in combination with an autologous flap11. Patients undergoing neoadjuvant chemotherapy or endocrine therapy prior to IBBR were eligible for inclusion.

Eligible patients were prospectively identified from clinics, multidisciplinary team (MDT) meetings, and theatre lists. Demographic, operative, oncological and 3-month complication data were collected by the team by clinical or case-note review. Patients who consented to participate in the PROs study were sent electronic or postal questionnaires, according to their preference, at 3- and 18-months after surgery. The 3-month questionnaire focused on satisfaction with information, adjuvant treatment and complications while the 18-month questionnaire included BREAST-Q domains relating to satisfaction with outcome and quality of life. Reminders were sent after 1 month if no response had been received. Data on PMRT were collected by clinical report of treatment recommendations by the MDT and patient self-report at 3 or 18-months. Follow-up was complete in December 2017. Anonymized data were recorded using REDCap, a secure online database11,34.

All patients had skin or nipple-sparing mastectomy with immediate IBBR. Procedural details were recorded but no restrictions were placed on the techniques (e.g. one or two stage; type of implant or expander; types of mesh) used, as this study aimed to explore current practice and inform a future trial11. Reconstructive techniques were categorized for analysis as: standard two-stage submuscular/subfascial, subpectoral with biological mesh, synthetic mesh, or dermal sling, pre-pectoral, and other. Product choice, implant positioning and use of laminar flow, antibiotics and drains were according to local policy or surgeon preference. Adjuvant therapies were as recommended by the multidisciplinary team.

***Study governance and consent to participate***

Ethics approval was not required, as the study was defined as service evaluation by the Health Research Authority (HRA) decision tool (http://www.hra-decisiontools.org.uk/research/). Local audit approval was obtained for each center before commencing study recruitment. Clinical and PRO data were collected as recommended by guidelines for best practice35.

Patients were approached for written consent to receive questionnaires by members of the clinical team either in clinic or during their hospital stay, according to local study team preference. This was consistent with the methodology used in the UK National Mastectomy and Breast Reconstruction Audit (NMBRA)36.Where consent was obtained, patient contact details were sent securely to the coordinating center and questionnaires distributed centrally to optimize compliance, allow accurate follow-up and minimize missing data11.

***Patient population***

Women from the iBRA cohort who underwent at least one procedure for malignancy (invasive breast cancer or ductal carcinoma in situ) and returned the 18-month questionnaire were eligible for inclusion in this analysis. Excluded were patients who underwent exclusively risk-reducing surgery and those for whom PMRT or PRO data were unavailable.

***Outcomes***

This study reports the 18-month PROs of IBBR with and without PMRT in patients undergoing surgery for malignancy in the iBRA study.

PROs were assessed using the validated BREAST-Q Post-Operative Reconstructive module (version 1). The BREAST-Q is a validated questionnaire robustly developed using Rasch methodology for use in a breast reconstruction population and includes six domains: satisfaction with breasts; satisfaction with outcome; physical, psychosocial and sexual well-being37,38. This was selected as it assessed key PRO domains included in the reconstructive breast surgery core outcomes set39. The 18-month questionnaire also included a single-item assessment of overall satisfaction outcome on a five-point Likert scale; excellent, very good, good, fair and poor, as per the NMBRA36.

***Statistical analysis***

Patients were categorized as having received PMRT (RT group) or not (non-RT group). Patients who reported in either the 3-month and/or 18-month questionnaire has having received PMRT were included in the RT group. If no patient-reported information was available on radiotherapy, patients were classified based on adjuvant therapies recommended at MDT.

Simple summary statistics were used to describe patient demographics, procedures performed to the breast and axilla; postoperative oncological data and MDT decision-making, 3-month complications and 18-month PROs across the patient groups (responders vs. non-responders and +/-PMRT). Categorical data were summarized by counts and percentages, and continuous data by median, upper and lower quartiles, and range. The characteristics of patients receiving/not receiving PMRT who completed the questionnaire were compared using t-tests and chi-squared tests for continuous and categorical variables respectively.

Questionnaire responses for the BREAST-Q domains were summed and transformed according to the developers’ instructions using the specifically designed Q-Score software40. This generated a score from 0 to 100 for each domain where higher scores indicate greater patient satisfaction or HRQL37. BREAST-Q scores were treated as continuous variables. For the purpose of analysis, the single-item overall outcome score was dichotomized into ‘excellent/very good’ and ‘good/fair/poor’.

The effect of radiotherapy on each outcome domain was explored using multivariable mixed-effects linear and logistic regression models, including a random effect to account for potential clustering by center. Models were adjusted for clinically-relevant confounders identified by the study steering group based on the literature and clinical expertise. These confounders were: age, body mass index (BMI), smoking status, ASA (American Society of Anesthesiologists) grade, bilateral surgery, nipple-sparing versus other mastectomy types, reconstructive technique (standard two-stage submuscular/subfascial, subpectoral with biological mesh, synthetic mesh, or dermal sling, pre-pectoral, and other), 3-month complications (infection, implant loss, readmission or reoperation), axillary surgery and adjuvant chemotherapy and endocrine therapy. A complete case analysis was undertaken, and robust residual estimates were used to ensure the assumptions of the regression models were not violated. The action of biological mesh as an effect modifier in the regression models was checked using an interaction term.

This study was registered (ISRCTN37664281) and is reported according to STROBE guidelines41.The protocol was published in 201611 and short-term outcomes published in 20199.

**Results**

The iBRA study recruited 2108 patients from 81 centers between February 1, 2014, and June 30, 2016, of whom 1693 (80%) underwent surgery for malignancy. The remaining 415 (20%) who underwent exclusively risk-reducing surgery were excluded from the analysis. A further 56 (3%) patients were excluded as they had no information regarding PMRT. 1164 (71%) of the remaining 1637 eligible patients consented to participate in the PROs study and 730 (63%) returned the 18-month questionnaire (figure 1).

Patients consenting to receive PRO questionnaires were demographically representative of the cohort of patients with malignancy (Appendix 1). However, patients returning the questionnaires were older (median 51.5, interquartile range [IQR] 46-60 vs. 49, IQR 43-57) and were less likely to smoke (n=58, 8% vs n=65, 15%) or have experienced major complications in particular implant loss at 3-months (n=39, 5% vs n=62, 14%) than non-responders. Full cohort demographic details by PRO status and PMRT group are summarized in Appendix 2.

*Participant demographics*

Of the 730 patients completing the 18-month questionnaire, 214 (29%) patients were included in the PMRT group; 203 patients who self-reported receipt of radiotherapy at either 3 or 18-months and 11 patients who did not complete the adjuvant treatment sections of the questionnaires but were recommended radiotherapy by the MDT and therefore considered to have received it. 516 patients (71%) were not recommended radiotherapy and did not report having received treatment so were included in the non-RT group.

Patients who received PMRT were younger than those who did not, but there was no evidence of a difference in BMI or smoking status between the groups (table 1). Patients receiving PMRT were more likely to undergo an axillary node clearance (ANC) at the time of reconstruction than patients not undergoing PMRT, but there were no differences regarding the planned type of reconstruction (single vs two-stage); technique (use or type of mesh); type of prosthesis (tissue expander vs fixed volume implant) or percentage of patients undergoing bilateral surgery. Three-month complication rates were similar between the groups (table 2). Patients who underwent PMRT were more likely to have received neoadjuvant chemotherapy, have grade 3 cancers, larger tumours and involved lymph nodes (table 3).

*Outcomes*

Table 3 summarizes the 18-month PROs for patients undergoing IBBR by receipt of PMRT. The number of responses that were sufficiently complete to be used for analysis were similar for each domain, and percentage responses were similar between the radiotherapy groups, excepting sexual well-being which was an optional scale and had fewer complete responses in the PMRT group (table 4). Median BREAST-Q scores were lower in the PMRT group across all domains. Similar results were observed for the single-item assessment of overall outcome, with fewer patients in the PMRT group considering their reconstruction to be ‘excellent’ or ‘very good’ (table 4).

Mixed-effects linear regression models were used to evaluate the impact of radiotherapy on BREAST-Q scores (table 5). In this analysis, there was evidence that patients receiving PMRT reported lower scores in three of the five BREAST-Q domains: satisfaction with breasts, satisfaction with outcome and physical well-being, but there was no evidence of a difference between groups in scores for sexual or psychosocial well-being. Patients who received radiotherapy were less likely to report an ‘excellent’ or ‘very good’ overall outcome than those who did not (OR 0.497, p=0.002, CI[0.32, 0.77]).

Interaction terms examined the action of biological mesh as an effect modifier in the regression models. There was no evidence that biological mesh modified the association between radiotherapy and satisfaction with breasts (interaction coefficient=3.39, p=0.191, CI[-1.70-8.48]), satisfaction with outcome (interaction coefficient=4.78, p=0.173, CI[-2.09-11.65]), psychosocial well-being (interaction coefficient=4.97, p=0.133, CI[-1.52-11.46]), physical well-being (interaction coefficient=-0.09, p=0.973, CI[-5.01-4.84]) or overall outcome (OR for interaction=1.09, p=0.826, CI[0.52-2.26]). Biological mesh was associated with a reduced impact of radiotherapy on sexual well-being (coefficient=13.37, p=0.001, CI[5.61-21.13]).

**Discussion**

This multicenter prospective cohort study of 730 patients undergoing IBBR with and without mesh demonstrates that women receiving PMRT reported worse PROs at 18-months following surgery in key HRQL domains: satisfaction with breasts, satisfaction with outcome and physical well-being. They were less likely to describe the outcome of their reconstruction as ‘excellent’ or ‘very good’ compared with patients who did not receive PMRT. These effects were not ameliorated by the use of biological mesh and exceed the recently-reported minimum clinically-important difference of 4 points for the BREAST-Q42.Furthermore, the scores reported here are similar to those reported by patients undergoing mastectomy only in the UK NMBRA36. These findings should be discussed with patients considering IBBR in whom PMRT may be indicated or when PMRT recommendations are borderline to help them make informed decisions about their reconstructive and oncological treatment options, bearing in mind that some women may risk a decrease in satisfaction with their reconstruction, rather than undergoing simple mastectomy, which may be the only alternative.

Several studies19 23,30-32,43-46 have evaluated the impact of PMRT on the patient-reported outcomes of IBBR but many of these are small, retrospective and have significant methodological limitations including the use of non-validated PROMs24-29 which cannot reliably be compared between studies23. Furthermore, much of the evidence to date focuses predominantly on traditional two-stage expander-implant IBBR24-26. Evidence regarding the impact of PMRT on newer mesh-assisted-techniques is lacking23. This study provides much needed data to support modern reconstructive practice and suggests that consistent with the findings of previous work, PMRT adversely affects the PROs of IBBR, even if mesh is used.

Although several studies suggest that acellular dermal matrix may reduce capsular contracture following PMRT21,47,the current data do not suggest that this translates into improved PROs when biological mesh is used. Reasons for this are likely complex and may indicate that satisfaction is a multidimensional construct that reflects more than objective measures such as capsular contracture. Additionally, patients in the current study underwent predominantly mesh-assisted subpectoral reconstruction. Further work is now needed to determine if similar results are seen following prepectoral reconstruction as emerging data suggests the effects of PMRT may be less marked when the implant is placed on top of, rather than under the muscle47,48.

This is, to our knowledge, the largest prospective study to explore the impact of PMRT on single-stage IBBR with and without mesh but has limitations. Firstly, it represents an exploratory post-hoc analysis of a subset of patients with malignancy in the iBRA study that was not initially planned and there is the possibility of significant results by chance due to multiple testing. The concordance between the current findings and existing published data19, however, suggests this is unlikely.

In addition, this is an observational study and therefore at risk of potential biases such as confounding. Although there were no obvious demographic differences between patients who consented to receive post-operative questionnaires and those who did not, there were clear differences between the patients who completed the questionnaires and non-responders. Non-responders were more likely to be younger and have experienced major complications at 3-months than those who participated, raising the possibility of response bias which may have impacted the results. Patients who received PMRT were more likely to have more locally-advanced disease than those who were not recommended treatment. Attempts were made to adjust for known confounders such as additional oncological treatments, but the study may still be subject to bias due to subtler differences between the patient groups. As a randomized clinical trial in this context would not be feasible, observational data will provide the best possible evidence of the impact on PMRT on the PROs of IBBR.

The study was pragmatically designed to optimize participation and recruitment, but this limited our ability to optimize data quality and completeness. As a complete case analysis was performed, the number of patients included in the regression models was limited by missing data. There is potential for bias to be introduced due to the missingness and interaction term tests for effect modifiers are likely to be underpowered in this analysis. Future studies should identify key variables for inclusion and use methods to maximize data completion. Finally, this study assessed PROs 18 months post-operatively. While these data are important, the effects of PMRT are likely to evolve over time and longer-term outcomes would ideally be needed to fully evaluate the impact of PMRT.

There is growing evidence to suggest that PMRT adversely impacts the early (up to 18-month) PROs of IBBR. These data should be discussed with patients to help them make informed decisions about reconstructive surgery. Further work is now needed to explore whether similar effects are seen with newer prepectoral techniques and to establish if and how PROs change over time. Work is also needed to determine the absolute benefit of PMRT. Current decision making is based on historic data16 and the results of studies such as SUPREMO49 are awaited to determine whether PMRT does improve oncological outcomes in intermediate risk groups in an era of modern systemic treatment. Other novel methods for predicting radiotherapy benefit may also have utility in this group50. Such developments will improve decision-making in the future but currently clear communication of the potential risks and benefits of both IBBR and PMRT are needed to ensure that patients, in partnership with the multidisciplinary healthcare team, make fully-informed decisions regarding their breast cancer treatment and reconstructive options.

**Authors' contributions**

SP, CH, ST, JS, NB, RIC and LW conceived the study; SP, NT and ES planned the analysis; NT and EJC supported ES in undertaking the analysis; all authors contributed to data interpretation. ES and SP wrote the first draft of the manuscript. SP is the guarantor. All authors reviewed and critically revised the manuscript and approved it prior to submission.

**Author access to data**

The authors had full access to the data contained in this manuscript.

**Conflicts of interest, including financial interests, activities, relationships, and affiliations**

The authors have no conflicts of interest to declare.

**Sources of funding and support**

This work was funded by an NIHR Research for Patient Benefit Programme Grant (PB-PG-0214-33065), pump-priming funding from the Association of Breast Surgery and the British Association of Plastic Reconstructive and Aesthetic Surgeons and a Research Development Award from the Association of Breast Surgery (2019). Shelley Potter is an NIHR Clinician Scientist (CS-2016-16-019).

This work was undertaken with the support of the MRC ConDuCT-II (Collaboration and innovation for Difficult and Complex randomized controlled Trials In Invasive procedures) Hub for Trials Methodology Research (MR/K025643/1) and the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

**Role of funder(s)/sponsor(s);**

The funders had no role in the design, conduct or decision to publish the study. No sponsor was required for this study as it was undertaken as a service evaluation.

**Collaborators**

The iBRA steering group and members of the Breast Reconstruction Research Collaborative are PUBMED citable collaborators in this study are were:

**The iBRA Steering Group (in alphabetical order) comprises:** N L P Barnes, J M Blazeby, O A Branford, E J Conroy, R I Cutress, M D Gardiner, C Holcombe, A Jain, K McEvoy, N Mills, S Mylvaganam, S Potter, J M Skillman, E M Teasdale, S Thrush, Z Tolkien, L J Whisker.

**Local investigators (alphabetically by center) and members of the Breast Reconstruction Research Collaborative are PUBMED citable collaborators in this study and were**:

**Airedale General Hospital:** P Christopoulos, V Fung, C Murphy, L Caldon, H Fatayer, E Baker; **Altnagelvin Area Hospital:** R Johnston; **Ashford and St Peters NHS Trust**: R Newton, A Luangsomboon, B Swiech, A Robinson, M Runkel, **Barts Health NHS Trust:** D Zheng, F Tsang, L Johnson, A Peel, S Ledwidge, S Barker, J Hu, V Voynov, G Exarchos, N Jiwa; **Barnsley Hospital NHS Foundation Trust:** OS Olayinka, JR Dicks; **Basingstoke and North Hampshire Hospital:** V Kalles, K Harris; **Bedford Hospital NHS:** N Manoloudakis, H Charfare, F Conroy; **Belfast City Hospital:** G Dobson, S Sloan, G Irwin, L Darragh, S McIntosh, S Refsum, S Dawson; **Blackpool Teaching Hospital NHS Foundation Trust:** I Michalakis, D Debnath, N Geerthan, P Kiruparan; **Bradford Teaching Hospitals NHS Foundation Trust:** S Hignett, E Baker, C Tait, R Linforth, M Salab, K Rigby; **Brighton & Sussex University Hospital NHS Trust:** S Shaheed, F Ugolini, R Rathinaezhil, C Zammit, H Osman, A Chouhan; **Castle Hill Hospital, Hull:** A Wilkins, B Wooler, P Kneeshaw, T K Mahapatra, E Khalifa, K Grover, K Hodgkins, S Harrison, P McManus, E Mallidis, J Robinson, F Langlands; **Chesterfield Royal Hospital:** F Mazari, J Massey, I Azmy, C Hollywood; **Countess of Chester Hospital:** W Hamilton-Burke, H Lennon; C Harding-Mackean; **County Durham and Darlington NHS Trust:** T Collin, J Henton; **Craigavon Area Hospital:** G Irwin, P Mallon; **Diana Princess of Wales Hospital, Grimsby:** J Smith, T Masudi, S Joglekar; **Dorset County Hospital:** K Kennedy, T Graja, C Osborne, R. Sutaria, M Youssef, T Stringfellow; **Dunedin Hospital:** B Smith; **East Lancashire Teaching Hospitals**: A.Topps, M Amanita, S Gawne, J McNicholas, C Thomas, M Khanbhai, R Brindle, N Taheri, R Kuruvilla, M Saleh, F Bux, P Pugh, J Iddon; **East Surrey Hospital:** E J Turner, S Waheed; **Frimley Park Hospital:** D Egbeare, J Stevens, E Mallidis, R Daoud, I Karat, I Laidlaw, H Osman, K Kanesalingam, R Johnson, R Gurung; **Glenfield Hospital Leicester:** K Lambert, S Pilgrim, T Rattay, H Khout, D Appleton, B Vijaynagar, S Bains, M Kaushik, J Krupa; **Great Western Hospital, Swindon:** I Dash, A Chaudry, M Galea, N Coombs; **Homerton Hospital:** S Tayeh, S Darvesh, C Choy, L Parvanta; **Kettering General Hospital:** A Knight, M Wright, G Wilson, S Musa; **King George Hospital, Ilford:** S Saha, S Samlalsingh, A Ogedegbe; **Lancashire Teaching Hospitals – Chorley:** A Topps, N Bishop, G Boland. Z Saidan, B Murthy; **Leighton Hospital:** S Hignett, V Pope **; Lincoln County Hospital:** A Sami, A Giaramadze; **Luton and Dunstable University Hospital:** R James, E Stewart-Parker, K Kirkpatrick, D Ravichandran; **Milton Keynes NHS Trust:** A Taylor, K Chin; **Maidstone and Tumbridge Wells NHS Trust:** M Hashem, R Chalmers, H Devalia, K Cox, S Horn, M Dani, D Akolekar, C Chalmers; **Musgrove Park Hospital, Taunton:** S Potter, A Thorne, S Granger; J Gill, U Hassan, C Ives, T Walker, M Chana; **Nevill Hall Hospital:** V Lefemine, F Soliman; **New Cross Hospital, Wolverhampton:** T Sircar, F Salem, S Mylvaganam, P Matey, G Nagra, S Marla, R Vidya, N Nuru, I Adwan, E Fage, O Al-Jibury; **North Bristol NHS Trust:** S Potter, I Dash, S Cawthorn, J Cook, S Govindarajulu; **North Middlesex University Hospital:** T Gandamihardja; **Nottingham Breast Unit:** L Brock, M Akerlundh, C Otieno, A Halka, R D Macmillan, K Asgeirsson, L Whisker, H Khout, T Rasheed, C Laban, E Gutteridge, S McCulley; **Oxford:** D Remoundos, PJ Roy; **Peterborough City Hospital:** E Popa, Mr Goh, G Shetty; **Poole General Hospital:** S Clark, A Evans; **Prince Phillip Hospital:** S Udayasankar, S Khawaja, Y Sharaiha; **QE2 Welwyn Garden City**: U Walsh, H Deol; **Royal Berkshire Hospital:** N Dunne, B Smith, A Hakim; **Royal Bolton Hospital:** A Volleamere, C Garnsey, C Wright; **Royal Bournemouth Hospital:** E Skene; C Laban, A Iskender, D Perry; **Royal Devon and Exeter NHS Foundation Trust:** D Egbeare, M Wiltsher, R Johnston, D Ferguson; S Olsen, R Tillett, M Youssef; **Royal Glamorgan Hospital:** S Datta, G Patel, C Steventon, R Foulkes, E Vaughan Williams, G Osborn, C Gateley; **Royal Hampshire County Hospital, Winchester:** N Chand, B Zeidan, D Rainsbury, S Laws. L Peiris, K Harris, V Kalles; **Royal Liverpool and Broadgreen University Hospitals:** A Hargreaves, J Henderson, T Kiernan, N Barnes, M Chandrashekar, A Tansley, C Holcombe, G Mitchell, R Little, S Bathla, M Pennick, E De Sousa, W Hamiton-Burke; **Royal Marsden Hospital:** R Di Micco, R O'Connell, V Voynov, A Parvaiz, A Conway, P Barry, G Gui, J Rusby, N Roche, K Ramsey, K Krupa, L Johnson, D Elfadl, F MacNeil, A Peppe, L Soldanova, I Hamo, P Harris, A Augusti, C Constantinou, A R Godden; **Royal Surrey County Hospital:** E Clayton, A Conway, T Irvine, P Partlett, F Pakzad; **Royal United Hospital Bath:** R Shah, I Dash, S Potter, J Mcintosh, R Sutton, N Laurence; **Royal Victoria Infirmary, Newcastle:** L Darragh, J O'Donoghue, S Nicholson, H Cain, N Collis, J Chatterjee, A Critchley, L Caldon; **St. James's University Hospital, Leeds:** B Kim, D Remoundos, J Massey, R Achuthan, C Fenn, F Mazari, C Navin, K Horgan, S McKenzie, P Turton, M Lansdown; **St George's Hospital:** S Tang, Mr Banerjee; **St Marys Hospital, Isle of Wight:** M Jobson; **Salisbury District Hospital:** S Masood, V Brown, G Murphy; **Sheffield Teaching Hospitals NHS Trust:** V Fung, N Dunne, L Wyld. S Kohlhardt, V Chandran, L Maraqa, L Caldon, M Reed, A Ismail; **Southampton:** S Robertson, R Cutress; **Torbay and South Devon NHS Foundation Trust:** C Ives, M Green; **University College Hospital, London:** L Johnson, R Carpenter, J Gattuso, J Franks; **University Hospitals Birmingham:** S Mylvaganam, R Warner, L MacLennan, J Dickson, R Waters, N Basu, S Thomas, S Tadiparthi, S Aggarwal; **University Hospital Coventry and Warwickshire:** A Carbone, J Skillman, T Challoner, S Parker, A Park, A Tomlins, H Khan, E Eltigani, M Kishore, R Nangalia, S Chambers, S Ayaani; **University Hospital Llandough:** C Thomas, R Foulkes, A Hussain, J Iddon, H Sweetland, E Davies, S Tate, S Goyal, A Ghattura, C Zabkiewicz; **University Hospitals North Manchester:** S Narayanan, S Soumian, D Archampong, E Erel; **University Hospitals North Staffordshire:** S Narayanan, S Soumian, V Voynov; **University Hospitals South Manchester:** J Henderson, N Barnes, R Shotton, R Johnson, A Gandhi, J Harvey, C Kirwan, J Murphy, G Byrne, D El Sharief, B Baker, R Chattopadhyay, S Chatterjee, R Irri, Mei Ju Hwang, K Williams; L Barr; **Warrington and Halton Hospitals:** N Sarfraz, P Thawdar; **Warwick Hospital:** M Dakka, H Tafazal, L Jones, D Enver, D Clarke, S Harries; **West Hertfordshire Hospital NHS Trust:** D Cocker, S Monib, L M Lai, S Thomson, K Chong, S Baldota,J Maalo; **Whiston Hospital:** N Barnes, T Kiernan, R Clifford, M Pennick, L Chagla, A Iqbal; **Wirral University Teaching Hospital NHS Foundation Trust:** R Vinayagam, J Lund, M Callaghan, S Poonawalla, K James; **Worcestershire Royal Hospital**: M Tan, R Athwal, M Mullan, S Thrush, R Bright-Thomas, J Taylor, H Tafazal, K McEvoy, M Ahmed; **Yeovil District Hospital:** N Dobner, C Osborne; **York NHS Foundation Trust:** J Piper, E Baker, R Nasr.

**References**

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424.

2. NICE. Early and locally advanced breast cancer: diagnosis and management NICE guideline [NG101]. <https://www.nice.org.uk/guidance/ng101>. Published 2018. Accessed.

3. Matala CM, McIntosh SA, Purushotham AD. Immediate breast reconstruction after mastectomy for cancer. *Br J Surg.* 2000;87:1455-1472.

4. Harcourt D, Rumsey N. Psychological aspects of breast reconstruction: a review of the literature. *Journal of Advanced Nursing.* 2001;35(4):477-487.

5. Al-Ghazal SK, Sully L, Fallowfield L, Blamey RW. The psychological impact of immediate rather than delayed breast reconstruction. *European Journal of Surgical Oncology.* 2000;26:17-19.

6. Mennie JC, Mohanna PN, O'Donoghue JM, Rainsbury R, Cromwell DA. National trends in immediate and delayed post-mastectomy reconstruction procedures in England: A seven-year population-based cohort study. *Eur J Surg Oncol.* 2017;43(1):52-61.

7. Albornoz CR, Bach PB, Mehrara BJ, et al. A paradigm shift in U.S. Breast reconstruction: increasing implant rates. *Plast Reconstr Surg.* 2013;131(1):15-23.

8. Thiruchelvam PTR, McNeill F, Jallali N, Harris P, Hogben K. Post-mastectomy breast reconstruction. *BMJ.* 2013;347.

9. Potter S, Conroy EJ, Cutress RI, et al. Short-term safety outcomes of mastectomy and immediate implant-based breast reconstruction with and without mesh (iBRA): a multicentre, prospective cohort study. *The Lancet Oncology.* 2019;20(2):254-266.

10. Tasoulis MK, Iqbal FM, Cawthorn S, MacNeill F, Vidya R. Subcutaneous implant breast reconstruction: Time to reconsider? *European Journal of Surgical Oncology (EJSO).* 2017;43(9):1636-1646.

11. Potter S, Conroy E, Williamson P, et al. The iBRA (implant Breast Reconstruction evAluation) Study: Protocol for a prospective multicentre cohort study to inform the feasibility, design and conduct of a pragmatic randomised clinical trial comparing new techniques of implant-based breast reconstruction. . *Pilot and Feasibility Studies.* 2016;in press.

12. Ragaz J, Jackson SM, Le N, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med.* 1997;337(14):956-962.

13. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative Radiotherapy in High-Risk Premenopausal Women with Breast Cancer Who Receive Adjuvant Chemotherapy. *N Engl J Med.* 1997;337(14):949-955.

14. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. *N Engl J Med.* 1997;337(14):949-955.

15. Nielsen HM, Overgaard M, Grau C, Jensen AR, Overgaard J. Study of failure pattern among high-risk breast cancer patients with or without postmastectomy radiotherapy in addition to adjuvant systemic therapy: long-term results from the Danish Breast Cancer Cooperative Group DBCG 82 b and c randomized studies. *J Clin Oncol.* 2006;24(15):2268-2275.

16. Ebctcg. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *The Lancet.* 2014;383(9935):2127-2135.

17. Duxbury PJ, Gandhi A, Kirwan CC, Jain Y, Harvey JR. Current attitudes to breast reconstruction surgery for women at risk of post-mastectomy radiotherapy: A survey of UK breast surgeons. *Breast.* 2015;24(4):502-512.

18. Nava MB, Benson JR, Audretsch W, et al. International multidisciplinary expert panel consensus on breast reconstruction and radiotherapy. *Br J Surg.* 2019;106(10):1327-1340.

19. Jagsi R, Momoh AO, Qi J, et al. Impact of Radiotherapy on Complications and Patient-Reported Outcomes After Breast Reconstruction. *J Natl Cancer Inst.* 2018;110(2).

20. Magill LJ, Robertson FP, Jell G, Mosahebi A, Keshtgar M. Determining the outcomes of post-mastectomy radiation therapy delivered to the definitive implant in patients undergoing one- and two-stage implant-based breast reconstruction: A systematic review and meta-analysis. *J Plast Reconstr Aesthet Surg.* 2017;70(10):1329-1335.

21. Kim IK, Park SO, Chang H, Jin US. Inhibition Mechanism of Acellular Dermal Matrix on Capsule Formation in Expander-Implant Breast Reconstruction After Postmastectomy Radiotherapy. *Ann Surg Oncol.* 2018;25(8):2279-2287.

22. Liu J, Hou J, Li Z, Wang B, Sun J. Efficacy of Acellular Dermal Matrix in Capsular Contracture of Implant-Based Breast Reconstruction: A Single-Arm Meta-analysis. *Aesthetic Plast Surg.* 2020.

23. El-Sabawi B, Ho AL, Sosin M, Patel KM. Patient-centered outcomes of breast reconstruction in the setting of post-mastectomy radiotherapy: A comprehensive review of the literature. *Journal of Plastic, Reconstructive & Aesthetic Surgery.* 2017;70(6):768-780.

24. Cordeiro PG, Pusic AL, Disa JJ, McCormick B, VanZee K. Irradiation after immediate tissue expander/implant breast reconstruction: outcomes, complications, aesthetic results, and satisfaction among 156 patients. *Plastic & Reconstructive Surgery.* 2004;113(3):877-881.

25. Cordeiro PG, Albornoz CR, McCormick B, Hu Q, Van Zee K. The impact of postmastectomy radiotherapy on two-stage implant breast reconstruction: an analysis of long-term surgical outcomes, aesthetic results, and satisfaction over 13 years. *Plast Reconstr Surg.* 2014;134(4):588-595.

26. Anker CJ, Hymas RV, Ahluwalia R, et al. The Effect of Radiation on Complication Rates and Patient Satisfaction in Breast Reconstruction using Temporary Tissue Expanders and Permanent Implants. *Breast J.* 2015;21(3):233-240.

27. Piroth MD, Piroth DM, Pinkawa M, Woodruff SG, Holy R, Eble MJ. Immediate reconstruction with an expander/implant following ablatio mammae because of breast cancer : side effects and cosmetic results after adjuvant chest wall radiotherapy. *Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft [et al].* 2009;185(10):669-674.

28. Cowen D, Gross E, Rouannet P, et al. Immediate post-mastectomy breast reconstruction followed by radiotherapy: risk factors for complications. *Breast Cancer Res Treat.* 2010;121(3):627-634.

29. Jagsi R, Li Y, Morrow M, et al. Patient-reported Quality of Life and Satisfaction With Cosmetic Outcomes After Breast Conservation and Mastectomy With and Without Reconstruction: Results of a Survey of Breast Cancer Survivors. *Ann Surg.* 2015;261(6):1198-1206.

30. Hamann M, Brunnbauer M, Scheithauer H, Hamann U, Braun M, Polcher M. Quality of life in breast cancer patients and surgical results of immediate tissue expander/implant-based breast reconstruction after mastectomy. *Arch Gynecol Obstet.* 2019;300(2):409-420.

31. Devulapalli C, Bello RJ, Moin E, et al. The Effect of Radiation on Quality of Life throughout the Breast Reconstruction Process: A Prospective, Longitudinal Pilot Study of 200 Patients with Long-Term Follow-Up. *Plast Reconstr Surg.* 2018;141(3):579-589.

32. Lagendijk M, van Egdom LSE, van Veen FEE, et al. Patient-Reported Outcome Measures May Add Value in Breast Cancer Surgery. *Ann Surg Oncol.* 2018;25(12):3563-3571.

33. Cutress R, McIntosh S, Potter S, et al. Opportunities and priorities for breast surgical research. *Lancet Oncology.* 2018.

34. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics.* 2009;42(2):377-381.

35. Rainsbury D, Willett A. *Oncoplastic breast reconstruction: guidelines for best practice.* UK2012.

36. Jeevan R, Cromwell DA, Browne JP, et al. Findings of a national comparative audit of mastectomy and breast reconstruction surgery in England. *J Plast Reconstr Aesthet Surg.* 2014;67(10):1333-1344.

37. Pusic A, Klassen A, Scott A, Klok J, ordeiro P G, Cano S. Development of a new patient-reported outcome measure for breast surgery: the BREAST-Q. *Plastic and Reconstructive Surgery.* 2009;124(2):345-353.

38. Cano SJ, Klassen AF, Scott AM, Cordeiro PG, Pusic AL. The BREAST-Q: further validation in independent clinical samples. *Plast Reconstr Surg.* 2012;129(2):293-302.

39. Potter S, Holcombe C, Ward JA, Blazeby JM. Development of a core outcome set for research and audit studies in reconstructive breast surgery. *Br J Surg.* 2015;102(11):1360-1371.

40. QScore. <http://qportfolio.org/score-breast-q-breast-cancer-2/>. Accessed August 21, 2019., 2019.

41. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet.* 2007;370(9596):1453-1457.

42. Voineskos SH, Klassen AF, Cano SJ, Pusic AL, Gibbons CJ. Giving Meaning to Differences in BREAST-Q Scores: Minimal Important Difference for Breast Reconstruction Patients. *Plast Reconstr Surg.* 2019.

43. Eriksson M, Anveden L, Celebioglu F, et al. Radiotherapy in implant-based immediate breast reconstruction: risk factors, surgical outcomes, and patient-reported outcome measures in a large Swedish multicenter cohort. *Breast Cancer Res Treat.* 2013;142(3):591-601.

44. Cordeiro PG, Albornoz CR, McCormick B, et al. What Is the Optimum Timing of Postmastectomy Radiotherapy in Two-Stage Prosthetic Reconstruction: Radiation to the Tissue Expander or Permanent Implant? *Plast Reconstr Surg.* 2015;135(6):1509-1517.

45. Albornoz CR, Matros E, McCarthy CM, et al. Implant breast reconstruction and radiation: a multicenter analysis of long-term health-related quality of life and satisfaction. *Ann Surg Oncol.* 2014;21(7):2159-2164.

46. McCarthy CM, Klassen AF, Cano SJ, et al. Patient satisfaction with postmastectomy breast reconstruction: a comparison of saline and silicone implants. *Cancer.* 2010;116(24):5584-5591.

47. Lardi AM, Ho-Asjoe M, Junge K, Farhadi J. Capsular contracture in implant based breast reconstruction-the effect of porcine acellular dermal matrix. *Gland surgery.* 2017;6(1):49-56.

48. Sinnott CJ, Persing SM, Pronovost M, Hodyl C, McConnell D, Ott Young AJAoSO. Impact of Postmastectomy Radiation Therapy in Prepectoral Versus Subpectoral Implant-Based Breast Reconstruction. 2018;25(10):2899-2908.

49. Kunkler I, Canney P, van Tienhoven G, Russell N, Group obotMSB-STM. Elucidating the role of chest wall irradiation in 'intermediate-risk' breast cancer: the MRC/EORTC SUPREMO Trial. *Clinical Oncology.* 2008;20:31-34.

50. Cui Y, Li B, Pollom EL, Horst KC, Li R. Integrating Radiosensitivity and Immune Gene Signatures for Predicting Benefit of Radiotherapy in Breast Cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research.* 2018;24(19):4754-4762.

**Figure 1*:* Patients included in the 18 month patient reported outcome study**