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Evaluating the impact of pre-operative versus post-operative radiotherapy in patients undergoing mastectomy with autologous breast reconstruction

Submission date
19/09/2025

Recruitment status
Not yet recruiting

Registration date
24/09/2025

Overall study status
Ongoing

Last Edited
03/10/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Each year in the UK, about 15,000 women undergo mastectomy and lymph node surgery. One in three have breast reconstruction, while others opt for implants or no reconstruction. Many patients also need radiotherapy, which can cause delays to treatment if complications arise after reconstruction, damage to the reconstruction, leading to firmness, shrinkage, unevenness, and discomfort. Because of this, many hospitals avoid immediate reconstruction if radiotherapy is required, leaving women to wait months, with two-thirds never receiving reconstruction at all. Research shows that giving radiotherapy before mastectomy and reconstruction is safe, equally effective for cancer control, and may preserve reconstruction quality. This approach could improve satisfaction with appearance and comfort, reduce treatment delays, and support faster recovery. Ultimately, better reconstruction outcomes can enhance body image, confidence, and overall well-being. This is a large study with 450 patients across 26 NHS hospitals to confirm these early findings. Radiotherapy before mastectomy and reconstruction will be compared to radiotherapy after mastectomy and reconstruction.

Who can participate?
Patients aged over 18 years old who require treatment for breast cancer, involving mastectomy with breast reconstruction and radiotherapy.

What does the study involve?
Women will be randomly allocated to one of two groups. One group will receive radiotherapy to the breast before mastectomy and reconstruction, and the other will receive radiotherapy after mastectomy and reconstruction (standard of care). All women will receive the same number of hospital visits and assessments.
- Baseline Visit - they will be asked to complete 2 questionnaires relating to quality of life. Medical photographs will be taken ahead of their surgery. The photographs will be anonymous and will not contain their face.
- Radiotherapy visits - If they are allocated to have radiotherapy first, it will take place 2-6 weeks

before their breast surgery. If they are having chemotherapy as the first treatment, the radiotherapy will happen 3-6 weeks after completion of chemotherapy. If they are allocated to receive radiotherapy after surgery, it is given when they are medically fit following the operation, usually around 6-8 weeks after. In both groups, the radiation dose will be the same. At the end of treatment, any side effects from the treatment will be recorded.
- Mastectomy - The mastectomy and reconstruction will be performed in the same way regardless of which group participants are in, and will be discussed and planned ahead of time.
-Follow Up Visits - Women will receive follow-up visits with their team several times after their surgery, at around 2 weeks, at 3, 6 and 9 months and at 1 and 2 years. At these visits, they will be monitored for outcomes such as wound healing, status of reconstruction and success in long-term cancer control. They will be asked to complete quality-of-life questionnaires at each visit.

Participants will also be asked for their feedback on how they feel about their breast reconstruction through questionnaires at 3 months, 1 year and 2 years after surgery to find out which group is more satisfied with their breasts and quality of life. Further photos will also be collected in years 1 and 2 to record the cosmetic outcome.

What are the possible benefits and risks of participating?
What are the possible benefits and advantages of taking part?
There are no additional treatment benefits. Regardless of which group they participate in, they will receive radiation therapy and a mastectomy with an immediate breast reconstruction using their own body tissues. There may be some benefits to preoperative radiation, but at this stage, these are unproven, and this is the reason we are conducting this study. Taking part in the study will benefit other patients with a similar condition in the future, particularly regarding breast-related quality of life and accelerating the time between diagnosis and completion of local therapy to the breast.

Preoperative radiation therapy is currently not standard of care, and so the only way to receive this therapy is by participating in this research study and being randomly assigned to the preoperative radiotherapy group.

What are the possible disadvantages and risks of taking part?
Participants may experience some side effects from the radiotherapy, but these are not expected to differ from not taking part in the study.

- Challenges in deciding whether radiotherapy is needed before surgery
Doctors may need to decide whether to treat just the breast or also the nearby lymph nodes. Treating certain lymph nodes is tricky because they’re close to the heart and lungs. If a participant has radiotherapy before surgery, and cancer is later found in these lymph nodes, it can be harder to treat that area again with radiation, but most patients will go on and receive other drug treatments as part of standard management that are known to eliminate any residual cancer cells.
- Additional radiological biopsies, radiation from surgical procedure(s) and/or additional scans
If they have had chemotherapy before radiotherapy, doctors may need to do another biopsy to check if any cancer remains. They might also have extra scans (PET/CT) and a small operation to check lymph nodes. These involve small amounts of radiation, which carries a very low long-term risk.

Technical challenges during microsurgical anastomosis.
If the breast reconstruction uses the participant's own tissue, surgeons must connect tiny blood

vessels. Radiation before surgery can make these vessels more fragile, and sometimes they need to be reconnected during the operation. Despite this, previous patients still had 100% successful reconstructions.

- Anxiety in answering sensitive questions in surveys or interviews.

- Pregnancy Radiotherapy can harm an unborn baby, so pregnant women or those planning pregnancy during the study cannot take part.

Where is the study run from?
Imperial College London (UK), in collaboration with Royal Marsden NHS Foundation Trust, UK

When is the study starting and how long is it expected to run for?
March 2025 to June 2031

Who is funding the study?
National Institute for Health and Care Research (NIHR), UK

Who is the main contact?
1. Dr Daniel Leff, d.leff@imperial.ac.uk
2. Ms Puja Jadav (public contact), prada2@imperial.ac.uk

Study website
https://www.imperial.ac.uk/department-surgery-cancer/

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
349225

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 70602, NIHR163836, 172291

Study information

Scientific Title
Pre-operative Radiotherapy And DIEP flAP Reconstruction Trial-II

Acronym
PRADA-II

Study objectives
Primary objective
To investigate whether pre-operative radiation leads to improved 2-year satisfaction with immediate autologous reconstruction compared to post-operative radiation.

Feasibility objective
To assess the feasibility of recruiting a sufficient number of patients, including: (a) the number of sites open and randomising patients, (b) number of patients randomised, (c) mean monthly recruitment, (d) % proportion of patients screened who proceeded to consent, (e) number of locally advanced breast cancers requiring mastectomy that are suitable for autologous reconstruction, and (f) proportion of patients consented who proceeded to be randomised.

Secondary objective
To determine if the pre-operative radiation improves overall health-related quality of life, attenuates treatment times, reduces fat necrosis, and increases pathological complete response rates. Further secondary objectives include recording oncologic outcomes, including local recurrence, distant metastatic spread, disease-free and overall survival.

Process evaluation objective
To identify facilitators and barriers to the implementation of pre-operative radiation, to develop appropriate implementation strategies, and to create an implementation blueprint to support deployment of the pre-operative radiation care pathway, if deemed appropriate.

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 08/09/2025, London - Bromley Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, United Kingdom; +44 (0)207 104 8118; bromley.rec@hra.nhs.uk), ref: 25/LO/0735

Study design
Multicentre randomized (1:1) open-label superiority controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet

See study outputs table

Health condition(s) or problem(s) studied
Breast cancers requiring mastectomy and radiotherapy, and suitable for immediate autologous microvascular breast reconstruction.

Interventions
This is a multicentre, randomised (1:1) controlled trial, comparing pre-operative radiation to post-operative radiation in locally advanced breast cancers requiring mastectomy and autologous reconstruction to test the superiority of the pre-operative radiation pathway with respect to patients' satisfaction with reconstructed breasts at 2 years.

Randomisation: 450 patients will be allocated to the treatment group (1:1) by minimisation, which assigns the next patient to the group that balances the main stratification factors (e.g., age, BMI, and baseline satisfaction with breasts) with high probability (e.g., 75%). This will be generated by a computer algorithm and released after checking patient eligibility and informed consent. This will be implemented by a validated web-based system, "Open Clinica". Once a participant is confirmed to be eligible for randomisation, qualified site staff will register the participant on the system and randomise them. A participant ID will be generated, which must be used to identify participants from this point onward.

Radiotherapy before mastectomy and breast reconstruction (40Gy in 15 fractions over 3 weeks). The clinical target is the breast skin envelope – i.e., the subcutaneous tissues ± the skin, and chest wall with regional lymph nodes, if required.

Intervention Type
Procedure/Surgery

Primary outcome measure
Patient-reported satisfaction with breasts 2 years after surgery was measured using BREAST-Q at 24 months

Secondary outcome measures
1. Surgical flap and wound complications will be measured using the Breast Reconstruction and Valid Outcomes (BRAVO) study core outcome, as well as cosmesis and QoL, as follows at 3 months, year 1 and year 2:
1.1. Skin necrosis rates measured using the validated SKIN score
1.2. Reconstruction failure rates 2 weeks following surgery
1.3. Post-operative biopsy-proven fat necrosis rates
2. Surgical procedures to improve cosmesis, including rates of contralateral breast procedures, such as symmetrisation mammoplasty/mastopexy and fat grafting measured using data collected from electronic case report forms (eCRF) at one timepoint
3. Oncological outcomes, including pathological complete response (pCR), local recurrence rate, distant metastases, disease-free survival, and overall survival, measured using data collected from patient medical records at one timepoint
4. Radiological outcomes, including rates of radiation toxicity measured using data collected from the reporting system recommended by the Radiation Therapy Oncology Group (RTOG) at 2 years
5. Quality of life (QOL) will be measured using the validated generic health-related QoL EQ-5D-5L questionnaires at baseline, 3, 6, 9, 12 and 24 months post-operatively
Aesthetic evaluation will be measured through the blinded expert panel assessment of

anonymised 2-dimensional photographs taken at 1 year and 2 years after surgery using the validated Visser scale.
6. Treatment journey: pathway times (days) from diagnosis to locoregional therapy and between locoregional therapies (e.g. radiotherapy to surgery, etc), measured using study data at one timepoint
7. The health economic component will consider the joint distribution of cumulative hospital costs and QALYs. The EuroQoL EQ-5D-5L utility score will be used to adjust patient survival times to calculate Quality Adjusted Life Years (QALY), measured using study data at one timepoint

Overall study start date
06/03/2025

Completion date
30/06/2031

Eligibility

Key inclusion criteria
1. Women >= 18 years of age, diagnosed with biopsy-proven, locally advanced breast cancer defined by any of the following (derived from diagnostic imaging) based on the latest guidance from the American Joint Committee on Cancer Staging (2017):
1.1. Tumour (T) stage T3 or T4 and any Nodal (N) stage
1.2. Any T stage, N2 or N3 disease
1.3. T2 and/or N1 disease with additional risk factors for local recurrence, including:
1.3.1. Medial tumour thought to benefit from internal mammary radiation, and/or
1.3.2. Chemoresistant disease (if ER negative and/ or HER-2 positive)
2. In addition:
2.1. Patients must be suitable for autologous reconstruction using microsurgical techniques, including any of the following techniques:
2.2. Deep Inferior Epigastric Perforator Flap (DIEP)
2.3. Transverse Upper Gracilis (TUG) – or variation therein, including Diagonal Upper Gracilis (DUG) or L-Shaped Upper Gracilis (LUG)
2.4. Superior or Inferior Gluteal Artery Perforator Flap (S-GAP or I-GAP, respectively)
2.5. Lumbar perforator flaps
3. Multidisciplinary team recommends mastectomy regardless of response to upfront therapy (if required), either due to tumour size, multicentricity, or multifocality
4. Multidisciplinary team recommends post-mastectomy radiotherapy either due to tumour size or nodal status
5. Patients in whom upfront medical therapy has failed to facilitate breast conservation. The multidisciplinary team must agree that they need radiation after mastectomy, and they must be suitable candidates for microsurgical reconstruction
6. Multidisciplinary team has confirmed that they can define nodal radiation regions to be treated with available information

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 450; UK Sample Size: 450

Key exclusion criteria
1. Pregnancy-associated breast cancer, including women known to be pregnant at diagnosis, patients with a positive pregnancy test at screening, and/or women who are lactating in whom radiation therapy is contraindicated
2. Metastatic disease since breast reconstruction remains controversial in these cases, and would confound survival outcomes. If metastatic disease is discovered after randomisation and prior to protocol interventions, then the participant will be discontinued from protocol interventions. Follow-up information will still be collected, including questionnaires and photos.
3. Biopsy-proven synchronous contralateral breast cancer
4. Inflammatory cancer or skin involvement precluding skin-sparing mastectomy
5. Mastectomy for biopsy confirmed local recurrence after breast conserving surgery since typically these patients have already received whole breast radiation therapy
6. Failed breast-conserving surgery cases, requiring mastectomy to ensure clear resection margins
7. Patients receiving nipple-sparing mastectomy due to attendant risks associated with nipple aerolar vascularity and nipple areolar necrosis
8. Bleeding dyscrasias and anticoagulation, which are relative contraindications to autologous microvascular anastomosis
9. Unable to give informed consent to the trial

Date of first enrolment
30/03/2026

Date of final enrolment
28/02/2029

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Marys Hospital
The Bays
South Wharf Road
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W2 1BL

Study participating centre
The Royal Marsden Hospital
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Sponsor type
University/education

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ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
30/06/2032

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	28/08/2025	23/09/2025	No	Yes