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Safe surgery for multiple breast cancers

Submission date
26/03/2018

Recruitment status
No longer recruiting

Registration date
20/04/2018

Overall study status
Completed

Last Edited
28/06/2022

Condition category
Cancer

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

Plain English Summary

Background and study aims
Current breast imaging methods mean that multiple breast cancers are being diagnosed in many women who are usually offered mastectomy to remove their whole breast with immediate or delayed breast reconstruction. However, these multiple smaller cancers may be treated using breast-saving surgery, called breast-conserving surgery, which is likely to occur currently in about a quarter of women. This breast-saving surgery aims to remove each cancer and to remodel the breast tissue, called a therapeutic mammoplasty. Therapeutic mammoplasty can be used to remove more than one cancer in the breast. Both skin and breast tissue are removed, leaving scars similar to those seen after a standard breast reduction. The aim of this study is to find out if breast-saving surgery is as safe as mastectomy in terms of controlling the rates of a cancer returning in the same breast or armpit, or elsewhere in the body. Currently, surgeons are unsure about the quality of the studies about the long-term safety of breast-saving surgery. However, some studies suggest that breast-saving surgery may be as safe as mastectomy, but there may be a slightly increased 5 and 10-year risk (around 2%) of the cancer returning in the remaining breast tissue. The potential safety of breast-saving surgery also depends on additional treatments of the breast tissue using radiotherapy and chemotherapy and/or endocrine treatments as well as bone strengthening drugs. All of these treatments can work together to kill possible microscopic cancer cells in the breast and reduce the chances of any cancer recurring in the breast. The study will also record women's quality of life, satisfaction with the appearance of their breasts and the costs of the surgery types.

Who can participate?
Women aged over 40 with Multiple Ipsilateral Breast cancer (MIBC)

What does the study involve?
Participants are randomly allocated to undergo either breast-saving surgery or mastectomy (with or without reconstruction). Patients allocated to breast-saving surgery discuss with their surgeon whether it is possible to perform a breast reduction of their other breast either at the same time or at a later time. All women in this group receive radiotherapy to the whole breast plus possible extra doses to some of the lumpectomy sites. Breast surgery combines surgical removal of each breast cancer plus a cosmetic procedure, which occurs whilst they are under a general anaesthetic and takes 4-6 hours. Reduction of the opposite breast may occur 4-10 months later. Patients allocated to mastectomy and breast reconstruction may not require a breast reduction of the other breast. They may also not require radiotherapy except in 30-35%

of women who are recommended for this after their surgery based on all their cancer results. The breast surgery combines surgical removal of the breast plus breast reconstruction either immediate or delayed. Delayed reconstruction occurs 10-12 months later. Other procedures like nipple reconstruction after mastectomy may occur at about 18 months or later. This gives the new breast time to settle into its permanent position. Each patient is followed up for 12 months after treatment. Timings of the follow-up visits are aligned with standard of care practice for this patient population with quality of life questionnaires and clinical photographs completed before and after surgery. Twenty women are also invited to an optional interview at 12 months.

What are the possible benefits and risks of participating?
It is not yet known whether there will be any benefit to the patient by taking part in the study. However, it is hope that the information from the study will benefit women in the future who are diagnosed with multiple breast cancers. This small study will help with the design of a larger national study to include many more women. The risk associated with taking part in this study, for the women in breast saving group, is that one or both of the tumors/lumps may not be completely removed or that the residual tissue may develop cancer in the future. The increased risk of cancer returning is thought to be around 2% compared to mastectomy. In women allocated to breast saving surgery, there may also be about a 10% chance of needing a mastectomy because of cancer margins being positive after one or two attempts at saving the breast. Taking part in the study may have no extra risks over those for mastectomy and breast reconstruction. Both procedures can have some complications but these are not any different from having the surgery outside of the study and their frequencies are described in each treatment information booklet. Information and counselling on the risks of general anesthetic and radiotherapy as well as any possible side effects will be discussed with the patient as part of routine care.

Where is the study run from?
1. Manchester University NHS Foundation Trust (UK)
2. Royal Stoke University Hospital (UK)
3. Queen Alexandra Hospital (UK)
4. Doncaster and Bassetlaw Teaching Hospital (UK)
5. Queen Elizabeth Hospital (UK)
6. East Sussex Healthcare NHS Trust, Eastbourne Hospital/Conquest Hospital (UK)
7. Addenbrookes Hospital (UK)
8. St George's Hospital (UK)
9. New Victoria Hospital Glasgow (UK)
10. Royal Derby Hospital (UK)
11. The Nottingham Breast Institute City Hospital (UK)
12. King's College Hospital (UK)
13. Royal Cornwall Hospital (UK)
14. Royal Surrey County Hospital (UK)
15. York Teaching Hospital (UK)
16. Guy's Hospital (UK)
17. Leeds General Infirmary (UK)
18. John Radcliffe Hospital (UK)
19. Royal Liverpool Hospital (UK)
20. Frimley Park Hospital (UK)
21. Ipswich Hospital (UK)
22. Great Western Hospital (UK)
23. Royal Hampshire County Hospital (UK)
24. Royal Devon and Exeter Hospital (UK)
25. Llandough Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2018 to October 2020

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT03514654

Secondary identifying numbers
37198; 17/0048

Study information

Scientific Title
Can patients with multiple breast cancers in the same breast avoid mastectomy by having multiple lumpectomies to achieve equivalent rates of local breast cancer recurrence? A randomised controlled feasibility study

Acronym
MIAMI

Study hypothesis
Sometimes women have more than one breast cancer in the same breast at the same time. These women are usually offered a mastectomy (removal of that breast) and breast reconstruction. It may be possible to treat these patients by removing each cancer using breast-saving surgery (lumpectomies), used for women with only one breast cancer. Databases show that women who had lumpectomies did well, but they may have been healthier before the surgery than those who had a mastectomy. We need to be sure that lumpectomy is effective, safe, and acceptable for this patient group before making it universally available.

The aim of this study is to evaluate whether a sufficient number of eligible patients can be identified and are willing to accept randomisation of the interventions in question. Recruitment and compliance rates of which will inform the feasibility and design of a larger trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - City & East Research Ethics Committee, 14/03/2018, REC ref: 18/LO/0133

Study design
Randomised; Interventional; Design type: Treatment, Surgery

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Condition
Multiple Ipsilateral Breast cancer

Interventions
This will comprise a multi-centre randomised controlled trial in women with Multiple Ipsilateral Breast cancer (MIBC) requiring surgery. Randomisation will be carried out using an online tool provided by Sealed Envelope, minimised by recruiting centre and multifocal/multicentric disease. Women who provide written informed consent will be randomised in a 1:1 ratio to one of two treatment groups and will be informed of the results after baseline questionnaires are completed. Participants will receive either Therapeutic Mammoplasty (TM) following excision of each cancer focus, or mastectomy (+/- reconstruction). Therapeutic mammoplasty is an operation to remove breast cancer(s) whilst also significantly reducing the size of the breast.

Therapeutic mammoplasty can be used to remove more than one cancer in the breast using separate lumpectomies. Both skin and breast tissue are removed, leaving scars similar to those seen after a standard breast reduction.

Each patient is followed up for 12 months post treatment with a total of 50 patients recruited. Timings of the follow-up visits are aligned with standard of care practice for this patient population with quality of life questionnaires and clinical photographs completed before and after surgery.

Twenty women will also be invited to an optional semi-structured interview at 12 months.

Intervention Type
Procedure/Surgery

Primary outcome measure
Feasibility of a larger trial, assessed using:
1. Numbers of women with more than one cancer in the same breast (MIBC) screened for the trial by 36 months
2. Numbers of eligible women based on trial criteria and suitable for therapeutic mammoplasty by 36 months
3. The proportion of women eligible for the trial who provide written informed consent by 36 months
4. Rate of compliance with allocated treatment and reason for deviation by 36 months

Secondary outcome measures
1. Reasons why patients accept or decline randomisation, assessed from patient-completed Qualitative Study questionnaire
2. Views of clinical staff assessed using qualitative interviews
3. Views of participating patients assessed using qualitative interviews

Overall study start date
01/04/2018

Overall study end date
31/10/2020

Eligibility

Participant inclusion criteria
1. Aged >40 years with MIBC
2. Minimum of two invasive foci of breast cancer
3. Suitable for Therapeutic Mammoplasty
4. Fit for adjuvant therapy
5. Willing and able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
Planned Sample Size: 50; UK Sample Size: 50

Participant exclusion criteria
1. Neo-adjuvant therapy
2. Women considered high risk by local centre or known to have BRCA1/2 gene mutation
3. Ductal Carcinoma in situ (DCIS) only, and extensive DCIS
4. Bilateral breast cancers
5. Previous breast cancer (invasive or DCIS in either breast)
6. Pregnancy as confirmed on blood tests or ultrasound examination.
7. Metastatic disease.
8. Any previous type of breast radiotherapy
9. Significant other clinical risk factors and co-morbidities at the discretion of the treating clinicians.
10. Previous or concomitant malignancy except adequately treated: non-melanomatous skin cancer; in situ carcinoma of the cervix and in situ melanoma

Recruitment start date
08/06/2018

Recruitment end date
30/04/2020

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Manchester University NHS Foundation Trust
United Kingdom
M23 9QZ

Study participating centre
Royal Stoke University Hospital
United Kingdom
ST4 6QG

Study participating centre
Queen Alexandra Hospital
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Doncaster and Bassetlaw Teaching Hospital
United Kingdom
DN2 5LT

Study participating centre
Queen Elizabeth Hospital
Birmingham
United Kingdom
B15 2TH

Study participating centre
East Sussex Healthcare NHS Trust, Eastbourne Hospital/Conquest Hospital
United Kingdom
BN21 2UD

Study participating centre
Addenbrookes Hospital
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
St George's Hospital
London
United Kingdom
SW17 0QT

Study participating centre

New Victoria Hospital Glasgow
United Kingdom
G42 9LF

Study participating centre
Royal Derby Hospital
United Kingdom
DE22 3NE

Study participating centre
The Nottingham Breast Institute City Hospital
United Kingdom
NG5 1PB

Study participating centre
King's College Hospital
London
United Kingdom
SE5 9RS

Study participating centre
Royal Cornwall Hospital
United Kingdom
TR1 3LQ

Study participating centre
Royal Surrey County Hospital
Guildford
United Kingdom
GU2 7XX

Study participating centre
York Teaching Hospital
United Kingdom
YO31 8HE

Study participating centre

Guy's Hospital
London
United Kingdom
SE1 9RT

Study participating centre
Leeds General Infirmary
United Kingdom
LS1 3EX

Study participating centre
John Radcliffe Hospital
Oxford
United Kingdom
OX3 9DU

Study participating centre
Royal Liverpool Hospital
United Kingdom
L7 8XP

Study participating centre
Frimley Park Hospital
United Kingdom
GU16 7UJ

Study participating centre
Ipswich Hospital
United Kingdom
IP4 5PD

Study participating centre
Great Western Hospital
Swindon
United Kingdom
SN3 6BB

Study participating centre
Royal Hampshire County Hospital
Winchester
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SO22 5DG

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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type

Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: PB-PG-1215-20009

Results and Publications

Publication and dissemination plan
A draft protocol for publication is in process. Planning to submit and publish protocol to open access journal. Planned publication of the results in a high-impact peer reviewed journal.

Intention to publish date
31/10/2021

Individual participant data (IPD) sharing plan
The Surgical & Interventional Trials Unit (SITU) is committed to maximising the use of all trial data to achieve scientific knowledge. To this end, they welcome proposals for collaborative and non-collaborative projects. The MIAMI data sharing policy has been developed to follow a controlled access model for data sharing, which conforms to the MRC Policy on Research Data Sharing. In this model, data is made as freely available as possible while safeguarding the privacy of participants, protecting confidential data and maintaining the reputation of the study and the study and its participants. For general data sharing enquiries, please contact situ.office@ucl.ac.uk. For MIAMI specific requests please contact situ.miami@ucl.ac.uk. Data are available to bona-fide researchers with established scientific record. The data sharing model involves the submission of the Data Sharing Application Form (available from SITU), and the list of variables needed for the project. Please highlight the variables names in the Excel data dictionary (also available from the SITU). Approval for data release can only be considered after each study has published its most latest planned publication, and all requests will be submitted to the appropriate Trial Steering Committee for consideration. Upon approval of the application, applicants will be asked to sign a data sharing agreement. Within two weeks of the receipt of signed data sharing agreement, the data manager will release an anonymised dataset, tailored for this request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Interim results article	Qualitative results	28/02/2022	28/06/2022	Yes	No
HRA research summary			28/06/2023	No	No