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Development of a low-dose mammography technique to calculate women's breast density to aid breast cancer risk assessment

Submission date
28/01/2021

Recruitment status
Suspended

Registration date
02/11/2021

Overall study status
Completed

Last Edited
15/03/2022

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Breast cancer (BC) is the commonest cause of death in young women. Breast screening (using an X-ray test called a mammogram) in women aged 35 to 45, at increased risk due to their family history, has been shown to improve survival. However, 80% of women who develop BC do not have a family history.

Previous studies have shown that one of the strongest risk factors for BC development is a high mammographic density (MD) seen on a mammogram. Full-field digital mammography (FFDM) can be used to assess MD, however, it is not recommended for screening the population for BC in those younger than 40 years of age due to the concerns about the use of ionising radiation. Safe and accurate methods to quantify MD in young women are needed to improve risk prediction and identify BC earlier, and improve survival.

This study aims to develop a low dose mammogram, with quantification of density using artificial intelligence, to assess young women for their risk of developing BC.

Who can participate?
Women aged between 30 and 45 years with a moderate to high risk of developing breast cancer

What does the study involve?
Eligible participants attending The Nightingale Centre will be recruited. Participants will undergo standard FFDM of the right breast, however, they will also receive a mammogram dose reduced by 90% to generate a low dose (LD) mammogram. During this process, the breast will be held between two plates and this will be repeated for multiple viewpoints (top-down and from the side). The left breast screening will proceed as normal. It is estimated that the additional screening will take 1-2 minutes only at each viewpoint. The study team will use deep machine learning methods to define the relationship between standard FFDM views and their low dose counterparts and determine which viewpoint provides the best correlation to be taken forward to the next stage of the research.

What are the possible benefits and risks of participating?
There will not be any benefits for those participating in this study.

There is an additional radiation dose delivered to each participant in the study. The total radiation dose involved in the study based on an average-sized woman is estimated as 3.2 mGy mean glandular dose. Nearly all of this (3.0mGy) is standard of care and is received in the regular mammogram. There is a very small additional dose of radiation delivered as part of the study. For an average-sized 30-year-old woman this dose will lead to an additional risk of developing cancer of about 1 in 500,000. This is considered as a 'minimal risk', equivalent to about 3 days natural background radiation.

The more prolonged compressions of the breast may cause some additional discomfort.

Where is the study run from?
Manchester University NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
From May 2019 to March 2024

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Dr Sacha Howell
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
253482

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 40945, IRAS 253482, B00394

Study information

Scientific Title
Technical development of Automated Low Dose Risk Assessment Mammography (ALDRAM) in women attending for mammography through a family history clinic

Acronym
ALDRAM

Study objectives
Can an automated, low dose technique be developed to provide an accurate assessment of mammographic density in women aged 30 to 45 years?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/02/2019, North West - Preston Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester M1 3DZ; +44 (0)2071048234; preston.rec@hra.nhs.uk), ref: 19/NW/0037

Study design
Single-site, single-arm non-randomized pilot study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet

Not available in web format. Please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Risk assessment of young women for breast cancer using automated low dose risk assessment mammography

Interventions
Participants will be approached for participation at the Breast Cancer Family History, Risk and Prevention Clinic at Wythenshawe Hospital. If a participant agrees to take part in this study, they will be asked to sign a consent form when they attend for a routine mammogram with the Family History Clinic. The radiographer will then start the process of performing the mammogram. Normally, two x-rays of each breast are performed at different angles (4 images in total), known as CC (craniocaudal) and MLO (mediolateral oblique) views. A CC view is performed on the right breast and then the same on the left before the MLO views are performed, again first on the right breast and then on the left. The radiographer will position the participant's right breast in the mammogram machine and will perform the first cc view completely as normal. The breast will then stay compressed whilst the dose level is turned down manually and a second much lower dose x-ray is taken. We estimate that this extra x-ray will take 1-2 min.
The left CC view will then be taken in entirely the usual way, without any additional lower dose x-rays. After that, the right breast will be repositioned for the MLO view and again an extra lower dose x-ray will be taken. The left MLO view will then be taken in entirely the usual way, concluding the mammogram and participation in the study – there is no additional follow-up required.

Intervention Type
Procedure/Surgery

Primary outcome measure
Correlation between Mammographic density assessed as predicted VAS (visual assessment score) on the full dose and low dose mammograms measured using an artificial intelligence-driven algorithm for automated measurement on Full Field Digital Mammography (FFDM) and low dose counterpart from the raw mammography image files at a single time point

Secondary outcome measures
1. To refine machine learning methods for ALDRAM vs FFDM using mammogram files collected at a single timepoint. The files will be analysed to give a predicted Visual Assessment Score (pVAS), a machine learning derived method for assessing breast density, calculated from FFDM and low dose image data and determine the correlation between the two across the whole study population and in subgroups based on age (30-34; 35-39; and 40-44).
2. To determine the view (CC versus MLO versus both) to take forward in a prospective clinical cohort if the approach is successful, using mammogram files collected at a single timepoint. Correlations of the averaged pVAS values from the four FFDM exposures (this is the standard for density analysis) and the individual CC and MLO and the averaged CC and MLO exposures from ALDRAM will be performed. This will be used to determine the best correlation and root mean squared error values and will determine which approach to take forward to subsequent studies.

Overall study start date
01/05/2019

Completion date

21/03/2024

Eligibility

Key inclusion criteria
1. Women aged between 30 and 45 years
2. Moderate to high risk of developing breast cancer
3. Capable of providing informed consent to a participant information sheet written in English

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Female

Target number of participants
600

Key exclusion criteria
1. Prior breast cancer
2. Prior breast augmentation or reduction (this does not include those who have had breast surgery for a benign condition)
3. Participation in the TARA-Prev study which included an additional mammogram and thus radiation dose

Date of first enrolment
28/03/2019

Date of final enrolment
31/07/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Manchester University NHS Foundation Trust
The Nightingale Centre
Southmoor Road
Wythenshawe Hospital

Manchester
United Kingdom
M23 9LT

Sponsor information

Organisation
Manchester University NHS Foundation Trust

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
https://mft.nhs.uk/

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The study data will be presented at national and international conferences and published in a peer reviewed journal. As this is a technical development study the participants will not be informed of the study results.
The protocol and PIS are available on request to the CI. The protocol will be provided as supplementary information in publications of the research study results.

Intention to publish date
01/04/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. Deidentified data from mammography files will be stored on password-protected University of Manchester computers. No identifiable data will be stored on these computers. Data files cannot be shared as consent has not been obtained for this from participants.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No