ISRCTN15109512 https://doi.org/10.1186/ISRCTN15109512

A comparison of 3D mammography with 2D mammography in breast cancer screening

Submission date
13/05/2019

Recruitment status
No longer recruiting

Registration date
07/11/2019

Overall study status
Completed

Last Edited
07/11/2019

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
3D mammography improves the detection of small breast cancers and may decrease the number of women without cancer who are recalled for further tests.
The study compares both the cost and effectiveness of 3D mammography with standard mammography in breast cancer screening. The results of the study will be used to decide whether to use 3D mammography routinely in the National Screening Programme.

The accuracy of two view digital x-ray mammography (2DDM) in breast cancer screening is limited because of superimposition of normal breast structures onto a two dimensional image. Mammography signs of breast cancer may be obscured, particularly in women with dense glandular breast tissue, resulting in delay in diagnosis of cancer. Interval cancer data shows that up to 4000 women per annum (2.88 per 1000 screened) are diagnosed with breast cancer in the interval between screens. Conversely, superimposition of normal tissues may produce features on mammography which are suspicious for cancer and lead to unnecessary recall for further diagnostic tests.

Digital Breast Tomosynthesis (DBT) is an x-ray mammography technique which involves acquiring multiple low dose projection images over a limited angular range (less than 50 degrees). These projection images are reconstructed into a set of images consisting of parallel planes, typically 1mm apart throughout the breast, and provide three dimensional information to the film reader. A synthetic 2D mammogram (S 2D) has been developed using the data from the reconstructed DBT images.

Studies of DBT + 2DDM in screening have shown increased invasive cancer detection rates and lower false positive recall rates. There may be increased costs related to the technology and reading times.

The aim of this trial is to measure the impact and cost-effectiveness of DBT + 2DDM or S 2D in routine screening compared to standard 2DDM.

Who can participate?
Women aged 50-70 years attending for routine breast cancer screening

What does the study involve?
Trial participants who have provided informed consent will be offered either their standard mammography (2D mammography) or their standard mammography and 3D mammography when they come for their routine breast screening appointment

What are the possible benefits and risks of participating?
Having mammograms every 3 years for 20 years very slightly increases the risk of getting cancer over a woman's lifetime, but the benefits of screening and early detection are considered to far outweigh the risks of having the x-ray. If you take part in the trial and have 3D mammography you will receive an additional dose of radiation roughly equivalent to having an extra mammogram. The radiation dose from a mammogram is approximately the same as three months of natural background radiation that we are all exposed to in everyday life

Where is the study run from?
King's College Hospital NHS Foundation Trust, UK

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

Who is funding the study?
Hologic Inc., USA

Who is the main contact?
1. Dr Mike Michell
Michael.michell@nhs.net
2. Ms Mahrufa Choudhury
mahrufa.choudhury@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Michael J Michell

Contact details
King's College Hospital NHS Foundation Trust
Breast Radiology
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS
+44 (0)2032993875
Michael.michell@nhs.net

Type(s)
Scientific

Contact name

Mr Mahrufa Choudhury

Contact details
King's College Hospital NHS Foundation Trust
Breast Radiology
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS
+44 (0)20 3299 6413 Ext 36413
mahrufa.choudhury@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
NCT03733106

Protocol serial number
33373

Study information

Scientific Title
Prospective randomised trial of digital breast tomosynthesis (DBT) plus standard 2D digital mammography (2DDM) or synthetic 2D mammography (S 2D) compared to standard 2D digital mammography in breast cancer screening

Acronym
PROSPECTS

Study objectives
The aim of this trial is to measure the impact and cost-effectiveness of Digital Breast Tomosynthesis (DBT) + two view digital x-ray mammography (2DDM) or synthetic 2D mammogram (S 2D) in routine screening compared to standard 2DDM.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/02/2017, London - Dulwich Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH; +44(0) 20 7972 2561; NRESCommittee.London-Dulwich@nhs.net), ref: 17/LO/0054

Study design
Randomized; Interventional; Design type: Screening, Diagnosis, Imaging

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Breast cancer

Interventions
DBT is a new X-ray mammography technology which overcomes some of the principle disadvantages of 2DDM which are due to tissue superimposition. Studies of screening using DBT in addition to 2DDM in Europe and North America have shown an increase in invasive cancer detection and a decrease in false positive recall rate. This study is designed to measure the impact of DBT on the effectiveness of mammography screening and the cost to the NHS. The proposed trial design is prospective RCT. Potential participants are women aged 50-70 years who are invited for routine screening mammography. The control group will undergo standard 2DDM; the intervention group will undergo DBT + 2DDM. For the intervention group, S 2D images will be generated from the DBT reconstructed images. A total of 100,000 participants are required (50,000 in the control group, 50,000 in the intervention group) in order to demonstrate a significant effect of DBT on interval cancer rates between the two study groups. All cases will be double read. In the intervention group, one read will be DBT+2DDM, one read will be DBT+S 2D.

Recruitment and consent
Clinics available for trial recruitment will be identified by the local screening service and will be randomised to control or intervention by a central online randomisation process. Women invited to the trial clinics will be sent the Participant Information Sheet with the invitation for screening. On arrival for screening, potential trial participants will be asked if they have received the Participant Information Sheet, if they have any questions about the trial, and whether they wish to participate. If the woman wishes to participate, she will be asked to sign a trial consent form. Women who consent to participate will undergo 2DDM (control group) or 2DDM+DBT (intervention group)according to the clinic randomisation process.
Women who decline to participate will be offered standard 2DDM screening.

Mammography reading
The mammograms will be double read. For women in the intervention group, one read will be DBT+2DDM, one read will be DBT+S 2D

Data recording
The results of film reading will be recorded for each film reader on the National Breast Screening Computer System(NBSS) in the normal way. For women who undergo treatment, details of pathology and treatment will be recorded on NBSS. A trial database will be kept and managed with all image data, reader data and outcome data for all participants.

Results and reporting
Cancer detection rates, the pathological characteristics of screen-detected and interval cancers, interval cancer rates, false-positive rates will be collected.
After 18 months, preliminary results of cancer detection and false-positive recall rates will be available. The size and lymph node status of the Grade 2 and Grade 3 invasive cancers in the control and intervention groups will be used to estimate the effect of DBT on breast cancer

mortality compared to standard 2D screening. Later, when interval cancer data becomes available, a more robust estimate of the effect of DBT will be made

Economic evaluation of DBT
We will undertake a detailed study of the cost of screening with 2DDM and with DBT and either S2D or 2DDM. Capital and maintenance costs related to screening technologies will be obtained from the manufacturers or finance departments at the screening centres and amortized appropriately according to predicted lifetime. Staff costs and overheads for screening centres and image reading centres will be derived from centre finance departments. The time taken to record images with each screening modality, and the time to read images will be determined and combined with centre costs to estimate a total cost per mammographic screen for each of the screening centres in the trial.
Costs associated with the follow-up of a positive screen will be determined in consultation with screening centres. Patient costs will be estimated on the basis of typical attendance times valued at average gross wage rate along with estimates of average travel costs. We will undertake a cost-utility analysis of DBT + S2D (or 2DDM) compared to current practice (2DDM). The primary analysis will consider an NHS perspective and include future related costs of screening (diagnosis and treatment of Breast cancer). A societal perspective which includes patient costs of attending screening and follow-up will be examined in a sensitivity analysis. The primary analysis will consider the costs and consequences of Breast screening with either modality over the trial follow-up period. We will estimate the impact on health and treatment costs of cancers detected by predicting treatment costs and mortality according to age and prognostic factors at diagnosis. Mortality will be weighted for quality of life to estimate the Quality Adjusted Life-Years (QALYs) lost to Breast cancer in each arm. A QALY is a measure of health outcomes which combines longevity and quality of life. If overall costs er in the DBT arm the data will be combined to estimate an Incremental Cost-Effectiveness Ratio (ICER) for DBT and allow comparison against accepted thresholds of £20,000 to £30,000 per QALY. The trial data will be
bootstrapped (a resampling technique to quantify the impact of uncertainty in the data) and the results presented as a Cost-Effectiveness Acceptability Curve (CEAC). The CEAC plots the probability an intervention is cost-effective according to the value placed on the health outcome and after allowing for sampling uncertainty.
In addition to this analysis, we will build a simulation model of Breast cancer. The model will utilize data on costs, sensitivity and specificity of each screening modality taken from the trial data along with data from the literature on the natural progression of Breast cancer to estimates costs associated with screening and treatment of Breast cancer and quality-adjusted life-expectancy over women's lifetimes. The model will fully incorporate uncertainty around parameter estimates and the main outputs will be the mean ICER across simulations and the CEAC

Intervention Type
Other

Primary outcome(s)
Cost-effectiveness of breast cancer screening with each method by measuring cancer detection rates, interval cancer rates, size and lymph node status of Grade 2 and 3 invasive cancers at ...

Key secondary outcome(s))
Measured from two to seven years following recruitment start:
1. Impact of screening on screening recall rates, benign biopsy rates at diagnostic assessment and at surgery measured using patient records

2. Effect of screening on patient groups according to breast density, type of screen, age, measured using patient records
3. Develop methods for measuring reader performance with DBT + 2DDM or S2D screening
4. Retrospective reader studies to measure the effect of other screening strategies
5. Patient preferences for breast cancer screening with the two methods measured using a questionnaire at recruitment

Completion date
01/04/2025

Eligibility

Key inclusion criteria
1. Women aged 50-70 years attending for routine breast screening using x-ray mammography
2. Able to provide informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
28/05/2019

Date of final enrolment
28/05/2020

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre

King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Surrey And Sussex Healthcare NHS Trust
East Surrey Hospital
Canada Avenue
Redhill
United Kingdom
RH1 5RH

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
North Bristol NHS Trust
Frenchay Hospital
Bristol
United Kingdom
BS16 1JE

Study participating centre
Barts and the London NHS Trust
The Royal London Hospital
Whitechapel Rd
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Royal Free London NHS FoundationTrust
Royal Free Hospital

Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Breast Test Wales
South East Wales Breast screening Centre
18 Cathedral Road
Cardiff
United Kingdom
CF11 9LJ

Study participating centre
Sandwell and West Birmingham Hospitals NHS Trust
City Hospital
Dudley Road
Birmingham
United Kingdom
B18 7QH

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Industry

Funder Name
Hologic, Inc.

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. Trial participant data will be stored on the national screening computer system (NBSS). Access to data on NBSS is password protected and is in accordance with the regulations and operating procedures within each of the trial sites. Access to trial participant data at the trial sites is limited to those involved in the direct clinical care of trial participants and the local trial data manager. The managers of the Central Trial Database at RSCH will need limited access in order to set up the anonymization process

IPD sharing plan summary

Stored in repository

Study outputs

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