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Assessment of the performance of a deep learning system at identifying breast cancer on screening mammograms using de-identified historic data.

Submission date
06/03/2019

Recruitment status
No longer recruiting

Registration date
20/03/2019

Overall study status
Completed

Last Edited
07/04/2025

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Current plain English summary as of 25/05/2021:
Background and study aims:
Breast cancer is a leading cause of cancer-related mortality among women worldwide, accounting for approximately 600,000 deaths annually.

There is a need for rigorous large-scale studies to assess the performance of AI for mammography in double reading. This should be done on diverse cohorts of women across multiple screening sites and programmes, and on unenriched data representative of a true screening population.

The aim of this study is to evaluate the ability of a novel AI system to act as a reliable independent reader in a double reading workflow, as well as demonstrating its standalone performance compared to the historical results.

Who can participate?
Being a retrospective study, no participants are directly involved in the study, and there will be no effect or change to any participant's care. The study will evaluate the AI system based on its analysis of historical, de-identified cases from study sites where outcomes data (e.g. biopsy, histopathology results, follow-up information) is also collected.

What does the study involve?
Eligible cases will be presented to the AI system for analysis.

What are the possible benefits and risks of participating?
No benefits or risks of participating are anticipated.

Where is the study run from?
Selected study sites in the UK and Hungary

When is the study starting and how long is it expected to run for?
From September 2018 to January 2021

Who is funding the study?
1. Innovate UK (UK)
2. Kheiron Medical Technologies (UK)

Who is the main contact?
Dr. Annie Ng
annie@kheironmed.com

Previous plain English summary:
Background and study aims
Breast cancer is one of the most frequently occurring cancer types in women worldwide. Breast screening is considered to be the world-wide gold standard for early detection and control of breast cancer. Mammography reading for breast screening is known to be a laboriously repetitive and meticulous task, and many sites struggle to meet required performance targets (NHS, EU), Radiologists currently have no effective practical support tools for reading mammography images; however, with the application of leading-edge deep learning techniques, the sponsor has developed software for the accurate analysis of mammograms to support the diagnosis of breast cancer.
This study aims to calibrate and validate the software's performance on retrospective (historic) data from NHS trusts and mammography units. By doing this study, we will learn how effective and generalisable the software can be in supporting radiologists in breast screening in the UK.

Who can participate?
Being a retrospective study, no patients will be directly involved in the study, and there will be no effect or change to any patient's care. The study will evaluate the software based on its analysis of validated de-identified historical cases from investigational sites where the outcomes (i.e. biopsy results, normal follow-up) are already known.

What does the study involve?
Historic data from NHS trusts and mammography units will be fed into the software to test functionality and performance.

What are the possible benefits and risks of participating?
Not applicable

Where is the study run from?
Kheiron Medical Technologies, London

When is the study starting and how long is it expected to run for?
September 2018 to October 2020 (updated 24/02/2021, previously: July 2020)

Who is funding the study?
1. Innovate UK
2. Kheiron Medical Technologies

Who is the main contact?
Dr Annie Ng
annie@kheironmed.com

Contact information

Type(s)
Scientific

Contact name
Dr Annie Ng

Contact details
Kheiron Medical Technologies
London
United Kingdom
EC1V 9BG
+44 (0)7379467701
annie@kheironmed.com

Type(s)
Scientific

Contact name
Dr Nisha Sharma

Contact details
Leeds Teaching Hospital NHS Trust
Leeds
United Kingdom
LS9 7TF
0113 243 3144
nisha.sharma2@nhs.net

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
AUX-07-2018-KMT

Study information

Scientific Title
A retrospective multi-centre clinical investigation of a novel medical technology solution in the assessment of mammography images

Study objectives
Current study hypothesis as of 25/05/2021:
The purpose of the study is to evaluate the performance of a novel AI system in detecting breast cancer. The study aims to evaluate the AI system's ability to act as a reliable independent reader in a double reading workflow, as well as demonstrating its standalone performance compared to the historical results.

Previous study hypothesis:
The purpose of the study is to calibrate and validate a deep learning software system that provides breast radiologists with recall decision support in a breast screening setting. The performance of this software in supporting recall decisions in breast screening is validated on retrospective data from multiple sites from a cohort of women who have undergone routine mammographic screening for breast cancer and have sufficient follow-up imaging or biopsy data.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Current ethics approval as of 25/05/2021:
1. Approved 03/10/2018, HRA and Health and Care Research Wales (HCRW) (Castle Bridge 4, 15-19 Cowbridge Rd E, Cardiff CF11 9AB; 029 2023 0457; hra.approval@nhs.net), Ref: 19/HRA/0376
2. Approved 03/07/2018, ETT--TUKEB Medical Research Council, Scientific and Research Ethics Committee, Hungary (1051 Budapest, Széchenyi István tér 7-8; (+36 1) 795-1197; tukeb@emmi.gov.hu), ref: OGYÉI/46651-4/2020

Previous ethics approval:
Approved 03/10/2018, HRA and Health and Care Research Wales (HCRW) (Castle Bridge 4, 15-19 Cowbridge Rd E, Cardiff CF11 9AB; 029 2023 0457; hra.approval@nhs.net), Ref: 19/HRA/0376

Study design
Multi-national multi-site retrospective study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
None available

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

Interventions

The intervention is the sponsor's deep learning software, assessed on de-identified randomised retrospective breast screening cases and outcomes. Comparison is made against the control arm of existing reference outcomes within the retrospective dataset where the deep learning software was not in use.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
-

Primary outcome measure
Current primary outcome measure as of 25/05/2021:
Standalone sensitivity and specificity performance of the AI system.

Previous primary outcome measure:
Rate of detection of malignancy of the Sponsor’s deep learning software measured using patient notes.

Secondary outcome measures
Current secondary outcome measures as of 25/05/2021:
1. Non-inferiority and superiority testing of the AI system as an independent reader in a double reading workflow compared to national guidelines and historical double reading in terms of recall rate, cancer detection rate, sensitivity, specificity, and interval cancer rate.
2. Comparing the AI system’s standalone performance to the historical first reader.
3. The AI system’s standalone performance in terms of recall rate, cancer detection rate, interval cancer rate, positive predictive value, arbitration rate, and AUC.

Previous secondary outcome measures:
Secondary aims will assess the software's performance (sensitivity, specificity, percent indeterminate) at varying settings as well as measure its recall rate (percentage of screening mammograms recalled for further assessment). Accuracy is measured in terms of sensitivity (true positive rate), specificity (true negative rate) as compared to a defined Reference Standard, plotted onto Receiver Operator Curves, and an Area Under the Curve (AUC) calculated. Recall rate is the rate of positive reported findings in a given sample.

Overall study start date
01/06/2018

Completion date
31/01/2021

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 25/05/2021:
1. Female participants

2. 4-view mammography cases (with exactly one of each: MLO-R, MLO-L, CC-R, CC-L of the four standard views) produced by certified digital mammography hardware and taken for screening purposes

Previous participant inclusion criteria:
1. Female patients
2. Mammography cases for screening purposes, i.e. cases from:
a) patients involved in the national breast screening program (depending on the jurisdiction includes women of age
45-73 who are called for examination via a letter by the national health authorities based on the population database),
and
b) women outside the national breast screening program who decided on their own to participate as per standard of
care
3. Cases with images in DICOM format
4. Cases with images produced by certified digital mammography hardware
5. Cases with one set of all of the 4 standard mammography images (i.e. exactly one of each: MLO-R, MLO-L, CC-R,
CC-L) present (no images missing and no extra images)
6. Cases with available historical outcome information as specified below*:
(Outcome information:
Confirmed positive case: malignancy is confirmed by a decisive biopsy, cytology or histology of the surgical specimen
within 250 days after the time of the image acquisition date.
Confirmed negative case: a negative follow-up result is available at least 34 months after the image acquisition date
(with no malignant operation and no malignancy indication in that period.)
*This inclusion criteria only applies to sensitivity/specificity analysis (not recall rate analysis)

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Female

Target number of participants
Up to 1,000,000

Key exclusion criteria
Current participant exclusion criteria as of 25/05/2021:
1. Male participants
2. Participants from whom any image data is used during training, calibration, or testing for the technology development of the deep learning model
3. Non-original, magnified, or spot-compressed images

Previous participant exclusion criteria:
1. Male patients

2. Images that are non-original images (e.g. post-processed images)
3. Magnified images (in the DICOM file the View Modifier Code Sequence (0054, 0222) has either of the values: R-
102D6, “Magnification” or R-102D7, “Spot compression”)
4. Cases with indication of a breast operation due to malignancy in the past medical history
5. Cases dated after a breast cancer confirmed by biopsy, cytology or histology
6. All patients of whom any image data was used during training, calibration or testing during the technology
development of the deep learning model.
Note: hormone replacement therapy in the past medical history is not an exclusion criterion.

Date of first enrolment
03/10/2018

Date of final enrolment
01/09/2019

Locations

Countries of recruitment
England

Hungary

United Kingdom

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

Study participating centre
Nottingham University Hospitals NHS Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
United Lincolnshire Hospitals NHS Trust
Lincoln County Hospital

Greetwell Road
Lincoln
United Kingdom
LN2 4AX

Study participating centre
MaMMa Klinika Budapest & Mozgó Emlőszűrő Állomás
Kapás u. 22
Budapest
Hungary
1125

Study participating centre
MaMMa Klinika Szekszárd
Szekszárd Béri Balogh Á. u. 9-13
Budapest
Hungary
7100

Study participating centre
MaMMa Klinika Kecskemét
Kecskemét Zrínyi u 38.
Budapest
Hungary
6000

Study participating centre
MaMMa Klinika Szolnok
Szolnok Hősök tere 2-4.
Budapest
Hungary
5000

Sponsor information

Organisation
Kheiron Medical Technologies

Sponsor details

Stylus Building
112-116 Old Street
London
United Kingdom
EC1V 9BG
+44 7379467701
annie@kheironmed.com

Sponsor type
Industry

Website
http://www.kheironmed.com

ROR
https://ror.org/01r3ct535

Funder(s)

Funder type
Government

Funder Name
Innovate UK

Alternative Name(s)
innovateuk

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Kheiron Medical Technologies

Results and Publications

Publication and dissemination plan

Peer reviewed publication is anticipated, alongside academic conference scientific presentations. Results will be submitted to regulatory authorities for the purposes of medical device certification.

Intention to publish date
30/12/2021

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 07/06/2021:
The data generated or analysed during the study cannot be shared at this time due to contractual agreements with study sites.

Previous IPD sharing statement:
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		19/05/2023	22/05/2023	Yes	No
Results article		06/06/2023	07/04/2025	Yes	No