ISRCTN14341750 https://doi.org/10.1186/ISRCTN14341750

Diagnosis of axillary lymph node status in primary breast cancer without a surgical procedure

Submission date	Recruitment status	[_] Prospectively registered
21/10/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/11/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
22/01/2024	Cancer	

Plain English summary of protocol

Background and study aims
Today, breast cancer is diagnosed at an early stage due to public screening mammography and increased awareness of the disease in the community. As a consequence of early diagnosis, tumor size at time of diagnosis has decreased and the risk of spread to the lymph nodes now affects less than 30% of all breast cancer patients. Despite this, all breast cancer patients undergo a surgical procedure, sentinel lymph node biopsy, to define if axillary lymph nodes are infiltrated by cancer cells. In more than 70% of these patients, there have no cancer infiltration in their axillary lymph nodes and therefore, the procedure has no benefit. Sentinel lymph node biopsy can lead to side-effects such as pain and swelling.
The aim of the study is to evaluate the capacity of patient related and tumor characteristics to determine whether the cancer has spread to the lymph nodes, so that low-risk groups can avoid sentinel node biopsy.

Who can participate?
Patients diagnosed with invasive breast cancer at any age scheduled for primary surgery and without clinically pathological lymph nodes

What does the study involve?
There is no direct involvement for participants. Instead, their medical records and data will be analysed by the study team and they will receive breast cancer treatment as usual.

What are the possible benefits and risks of participating?
As there is no direct involvement of participants and they will receive routine treatment, there are no known benefits or risks to participants taking part in this study.

Where is the study run from?
Skåne University Hospital (Lund and Malmö) (Sweden)

When is the study starting and how long is it expected to run for?
January 2008 to December 2022

Who is funding the study?
1. Lund Univerisity (Sweden)
2. The Swedish Breast Cancer Fund (Sweden)
3. South Swedish Health Care Region (Sweden)
4. Erling Persson Foundation (Sweden)
5. Vetenskapsrådet [Swedish Research Council] (Sweden)

Who is the main contact?
Professor Lisa Rydén
lisa.ryden@med.lu.se

Contact information

Type(s)
Scientific

Contact name
Prof Lisa Rydén

ORCID ID
http://orcid.org/0000-0001-7515-3130

Contact details
Lund University, Medicon Village, Scheleevägen 2,
Lund
Sweden
SE-22381
+46-706720923
lisa.ryden@med.lu.se

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NILS 1.0

Study information

Scientific Title
NILS: Non-Invasive Lymph node Staging

Acronym
NILS

Study objectives

Preoperatively available information on clinicopathological characteristics can aid in predicting nodal status in primary breast cancer

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 15/08/2012, Lund University, ref: 2012/340
2. Approved 07/07/2019, Swedish Ethical Review Authority, ref: 2019-02139
3. Approved 15/02/2021, Swedish Ethical Review Authority, ref: 2021-00174

Study design
Observational prospective cohort study with retrospective estimation of nodal status

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Clinically node-negative primary breast cancer

Interventions
Current intervention as of 31/08/2021:
Patients in this study are undergoing standard diagnostic work-up within the clinical pathway for breast cancer including a clinical examination, mammogram, ultrasound and core biopsy of the tumor before surgery. At time of surgery, they undergo standard procedure according to the multidisciplinary conference and the tumor and axillary nodes are pathologically examined. No extra diagnostic or interventional procedure is undertaken. Logistic regression and artificial neural network models are applied to predict nodal status from clinicopathological data. No follow-up data is extracted as this is an observational diagnostic trial. Separate cohorts will be used for validation of the nomogram and ANN models.

———

Previous intervention:
Patients in this study are undergoing standard diagnostic work-up within the clinical pathway for breast cancer including a clinical examination, mammogram, ultrasound and core biopsy of the tumor before surgery. At time of surgery, they undergo standard procedure according to the multidisciplinary conference and the tumor and axillary nodes are pathologically examined. No extra diagnostic or interventional procedure is undertaken. Logistic regression and artificial

neural network models are applied to predict nodal status from clincopathological data. No follow-up data is extracted as this is an observational diagnostic trial.

Intervention Type
Other

Primary outcome measure
Current primary outcome measure as of 31/08/2021:
Axillary nodal status stratified by stage N0, N1 and N2, determined from pre-operatively available clinicopathological data after surgery compared with the predictive N-status by the algorithms

_____

Previous primary outcome measure:
Axillary nodal status stratified by stage N0, N1 and N2, determined from pre-operatively available clinicopathological data after surgery

Secondary outcome measures
False negative rate with negative predictive value of NPV max to 10% for prediction of N0, determined from sentinel node biopsy data after surgery

Overall study start date
01/01/2008

Completion date
21/12/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 31/08/2021:
1. Invasive breast cancer
2. Clinically and ultrasound node-negative disease
3. Scheduled for primary surgery
4. Female

_____

Previous inclusion criteria:
1. Invasive breast cancer
2. Clinically node-negative disease
3. Scheduled for primary surgery
4. Female

Participant type(s)
Patient

Age group
Adult

Sex

Female

Target number of participants
800 primary cohort, 600 and 22000 in validation cohort

Key exclusion criteria
1. Male
2. Previous ipsilateral breast or axillary surgery
3. Previous neoadjuvant therapy
4. Palpable axillary lymphadenopathy
5. No axillary staging

Date of first enrolment
01/01/2009

Date of final enrolment
21/12/2022

Locations

Countries of recruitment
Sweden

Study participating centre
Skåne University Hospital
Lund and Malmö
Sweden
22185

Sponsor information

Organisation
Lund University

Sponsor details
Medicon Village 406, Scheleevägen 2
Lund
Sweden
223 85

Sponsor type
University/education

Website
www.med.lu.se

ROR
https://ror.org/012a77v79

Funder(s)

Funder type
University/education

Funder Name
Lunds Universitet

Alternative Name(s)
Lund University, Universitas Lundensis, Universitas Gothorum Carolina, Royal Caroline Academy, Regia Academia Carolina, Lund University | Lund, Sweden | LU, Lunds universitet, LU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
South Swedish Health Care Region

Funder Name
Bröstcancerfonden

Funder Name
Familjen Erling Perssons Stiftelse

Funder Name
Vetenskapsrådet

Alternative Name(s)
Swedish Research Council, VR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

Results and Publications

Publication and dissemination plan
A nomogram based on logistic regression data has been published and external validation is ongoing. Data analysis from ANN is finished and a manuscript is pending

Intention to publish date
31/03/2023

Individual participant data (IPD) sharing plan
The datasets analysed during the current study will be available upon request from Lisa Rydén (lisa.ryden@med.lu.se) for baseline characteristics after approval from regulatory authorities responsible of data sharing for Region Skåne. The dataset is kept pseudoanonymised and will be available for any researcher with a documented scientific experience in prediction models of nodal status in order to validate other prediction models generated from their own data. GDPR requires an informed consent to state that data sharing with third party is to be performed and this can be arranged by an opt-out procedure.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Nomogram initial results	01/10/2017		Yes	No
Basic results		02/11/2018	24/04/2019	No	No
Results article	Artificial neural network modeling initial results	21/06/2019	24/06/2019	Yes	No
Other publications	Nomogram validation	01/05/2021	31/08/2021	Yes	No
Results article	Retrospective validation study	16/01/2024	22/01/2024	Yes	No