ISRCTN14323711 https://doi.org/10.1186/ISRCTN14323711

Using artificial intelligence to help doctors and scientists in the lab that studies diseases in the body, in order to use less of a specific testing method called immunohistochemistry and make the work process smoother and more efficient.

Submission date
22/05/2023

Recruitment status
No longer recruiting

Registration date
31/05/2023

Overall study status
Completed

Last Edited
26/05/2023

Condition category
Other

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

Plain English summary of protocol

Background and study aims
In this single-center trial, we aim to investigate an artificial intelligence (AI)-assisted workflow. We investigate whether an AI-assisted workflow reduces expensive immunohistochemistry stains for the detection of cancer cells in lymph nodes in breast cancer patients, and in prostate needle biopsies in patients suspected of prostate cancer. Meanwhile, we maintain current diagnostic safety standards.

Who can participate?
All patients at UMC Utrecht are automatically included

What does the study involve?
Patients' material will be assessed by pathologists conform the 'standard-of-care'-workflow, or in an AI-assisted workflow. Every two weeks, pathologists will (prospectively) assess pathology specimens either with or without AI-assistance.

What are the possible benefits and risks of participating?
Neither benefits or risks are applicable to patients, as we have a diagnostic safety net in place. If no tumor can be seen, we will perform the additional immunohistochemistry, so no tumors will be missed.

Where is the study run from
UMC Utrecht (Netherlands)

When is the study starting and how long is it expected to run for?
January 2022 to December 2023

Who is funding the study?
The Hanarth fund (Netherlands)
Paige (USA)

Who is the main contact?
Paul J van Diest, p.j.vandiest@umcutrecht.nl

Contact information

Type(s)
Principal Investigator

Contact name
Prof Paul van Diest

ORCID ID
https://orcid.org/0000-0003-0658-2745

Contact details
Department of Pathology, PO Box 85500, 3508 GA Utrecht, The Netherlands
Utrecht
Netherlands
3508 GA
+31887556565
p.j.vandiest@umcutrecht.nl

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Clinical implementation of artificial intelligence assistance in pathology workflow

Acronym
CONFIDENT

Study objectives

The number of required immunohistochemistry (IHC) stains used to confirm diagnosis will be reduced in the AI-assisted arm, compared to the standard-of-care arm.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The ethics committee (MREC NedMec) waived the need of official ethical approval, since participants are not subjected to procedures nor are they required to follow rules.

Study design
Single-center interventional non-randomized trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Laboratory

Study type(s)
Diagnostic, Safety, Efficacy

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Reduction of immunohistochemistry used for the diagnosis of lymph node metastases in breast cancer (BCa - CONFIDENT-B), and prostate cancer (PCa - CONFIDENT-P) in prostate needle biopsies.

Interventions
During the study period, all whole slide images (WSI) will be assessed by the same group of pathologists; i.e. two expert urological pathologists for the prostate needle biopsies, and three expert breast pathologists for the lymph node assessment from BCa patients.

For both the CONFIDENT-B and CONFIDENT-P trial, the specific pathology specimens will be assigned to be assessed by a pathologist with or without AI-assistance in a pragmatic (bi-)weekly sequential design. For obvious reasons, allocation concealment and blinding of pathologists and researchers is not applicable.

All eligible specimens of patients will be assigned to either the control group or the intervention group. In the control group, pathologists will assess haematoxylin eosin (HE)-stained WSI of patients digitally, according to the current clinical workflow. For prostate biopsies, IHC is routinely performed on all cases. For BCa lymph nodes, if no metastases or tumour are present, IHC staining will be performed. Additional IHC staining will also be performed by additional request of the pathologist in case of doubt.

In the intervention group, pathologists will assess the HE-specimens digitally with the outcome of the algorithm provided in their first assessment of the specimen. For PCa, they will use the CE-IVD certified Paige Prostate Suite algorithms for tumor detection and tumor volume percentage calculations. For BCa, pathologists will use the CE-IVD certified Metastasis Detection App by Visiopharm. AI analysis of the WSI will be performed right after scanning to avoid delays in the clinical workflow. If the AI-assisted pathologist does not detect metastases or tumours on the HE slide, routine additional IHC staining will be performed by P503S/p63/CK HMW for PCa and CAM5.2 for BCa, to ensure no metastases or tumours are missed. Pathologists can always request an additional IHC-stain if they feel they need this to make an adequate diagnosis.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Paige Prostate Suite and Metastasis Detection App by Visiopharm

Primary outcome measure
Relative risk of IHC-use per detected case of SN-metastases and risk of IHC-use per detected tumor in prostate needle biopies (case- and slide-level) measured using number of spent resources, i.e. the number of IHC-stains performed in both groups, measured after the single visit

Secondary outcome measures
1. Sensitivity and negative-predictive value of the AI-assisted pathologist. We use the assessment of the pathologist on immunohistochemistry stained slides as a reference standard. These slides are always performed in cases where the pathologist is in doubt, or where they think the slides are benign. Obvious malignant cases are spared an IHC staining (as our hypothesis is that these obvious malignant cases will be higher in the AI-assisted arm than in the standard of care-arm).
2. Differences in mean reading time per H&E-slide and per case between study arms, measured during the primary WSI assessment.
3. The number of IHC stains that may have been omitted after AI-implementation by analyzing standalone performances of the AI on the standard-of-care arm retrospectively
4. Pathologists' evaluation by a questionnaire on the AI-assisted work process after ending of the study enrollment.
5. Stand-alone performance of the algorithm. We measure sensitivity and negative-predictive value using the pathologists' assessment as a ground truth (with or without IHC, as specified above), performed retrospectively on the control-arm as well as on the AI-assisted arm. Specificity and positive predictive value cannot be calculated because of the study design and are therefore not incorporated in the stand-alone performance nor in the AI-assisted pathologists' performance.
6. Difference in diagnostic confidence of the pathologists between the study arms, measured on a 5-Likert scale during the primary WSI assessment.

Sensitivity and specificity analyses of the algorithm itself have already been well documented, and is therefore outside the scope of the paper, as we focus on the combination of pathologist and AI to explore cost savings.

Overall study start date
01/01/2022

Completion date
31/12/2023

Eligibility

Key inclusion criteria
Health professionals:
1.1. PCa: dedicated uropathologists
1.2. BCa: dedicated breast pathologists

Patients:
1.1. PCa: adult males of any age undergoing prostate needle biopsies at the investigation site will be enrolled in the study and have their diagnosis determined in a prospective, consecutive manner.
1.2. BCa: adult females or males of any age with breast cancer as primary malignancy whose SN-specimen is assessed at the investigation site will be enrolled in the study and have their diagnosis determined in a prospective, consecutive manner.
2. All specimens that are H&E-stained and glass or film cover-slipped will be evaluated. Adjacent unstained slides will available for IHC staining.
3. The WSIs fulfill the quality checks described in the scanner manufacturer's Instruction for Use and general clinical practice.
4. No diagnostic markings and patient identifiable markings are visible on the slides.

Participant type(s)
Patient, Health professional

Age group
Adult

Sex
Both

Target number of participants
PCa: 80 BCa: 180

Key exclusion criteria
1. Patients who were referred for a second opinion
2. Patients that have opted out of all medical research
3. Cases in which the associated IHC-stained slides are unavailable/cannot be generated
4. Cases not meeting defined quality criteria for digital clinical primary diagnosis evaluation

Date of first enrolment

19/09/2022

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
Netherlands

Study participating centre
University Medical Center Utrecht
Department of Pathology
PO Box 85500
Utrecht
Netherlands
3508 GA

Sponsor information

Organisation
University Medical Center Utrecht

Sponsor details
Heidelberglaan 100
Utrecht
Netherlands
3584 CX
+31 887556565
R.A.W.vanLier-2@umcutrecht.nl

Sponsor type
Hospital/treatment centre

Website
http://www.umcutrecht.nl/nl/

ROR
https://ror.org/0575yy874

Funder(s)

Funder type

Not defined

Funder Name
Hanarth Fonds

Alternative Name(s)
Hanarth Foundation, Hanarth Fund, Hanarth Funds Foundation, Stichting Hanarth Fonds

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Netherlands

Funder Name
Paige

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal.

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date