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A study looking at the accuracy of using optical coherence tomography angiography at diagnosing an eye condition called neovascular age-related macular degeneration to see if it is just as good as fluorescein angiography

Submission date	**Recruitment status**	[X] Prospectively registered
07/06/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/06/2021	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
03/06/2024	Eye Diseases	[_] Record updated in last year

Plain English summary of protocol

Background and study aims

This is a research study looking at the best way to confirm the presence of an eye condition known as neovascular age-related macular degeneration (nAMD), a common condition that affects the middle part of people's vision. The researchers are especially interested in understanding the best way to look at the back of the eye to get a definite diagnosis.

Neovascular age-related macular degeneration (nAMD) is a common condition that affects the middle part of people's vision.It usually first affects people in their 50s and 60s and diagnosis is usually confirmed by looking at the back of the eye. There are a number of ways of doing this, the most common being a test known as Fluorescein Angiography (FA). FA is labour-intensive, time-consuming and inconvenient for the patient and is not always informative meaning that sometimes another dye test called Indocyanine-Green Angiography (ICGA) is needed.

Newer diagnosis tests are now available. One is called Optical Coherence Tomography (OCT) that quickly scans the back of the eye. The findings of OCT can be confused with other conditions and so to get a definite diagnosis of nAMD it is often used alongside other tests such as FA/ICGA.

Optical Coherence Tomography-Angiography (OCTA) is a more recent technology already available in many NHS Trusts. OCTA is non-invasive and provides a better image of the retina and the blood flow to the back of the eye. This study will see if OCTA is a good enough test to replace FA

Who can participate?

People presenting to secondary care whose treating doctors feel that they may have nAMD in at least one of their eyes after an OCT scan

What does the study involve?

Patients are asked to have two further tests; an OCTA and FA. If the patient decides not to take

part in the study then it is likely that they will have at least one of these other tests to confirm their diagnosis.
The researchers will ask the eye specialists who are looking after the patient to look at the tests and decide whether there is nAMD and how confident they are of this diagnosis. In half of the cases, chosen by chance, the eye specialists will base their diagnosis on OCT and OCTA and in the other half on OCT and FA. The researchers will compare the results of both combinations of tests to see if they are both equally as good for detecting nAMD.
If the patient does decide to take part, and gives their permission, the treating site will produce an anonymised export of each scan, then pseudo-anonymise with a trial number. These images, alongside a brief description of their relevant medical history, will be transferred to specialist software hosted at Moorfields Eye Hospital NHS Foundation Trust. These anonymised scans (the trial number will not be displayed) alongside the clinical information will be presented to doctors based at specialist NHS Reading Centres (The Network of Ophthalmic Reading Centres - NetwORC UK) who will make a diagnosis on the scan and clinical information alone.
By comparing the results of the combination of tests reviewed by their eye care team and by independent eye experts the researchers will be able to decide how good each of these tests is at detecting nAMD.

Are there any risks in taking part?
All procedures have some element of risk associated with them, however low. The main risk in this study is that the dye used in FA imaging may make participants feel unwell, and a very small number of people (1 in 100,000) may be allergic to it. However, as the patient has already been referred with suspected nAMD it is likely that they will undergo the procedure anyway, thus taking part in this study is not associated with any additional risk above standard care.

Where is the study run from?
1. Moorfields NHS Foundation Trust (UK)
2. University of Birmingham's Clinical Trials Unit (BCTU) (UK)

When is the study starting and how long is it expected to run for?
May 2021 to October 2023

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (UK)

Who is the main contact?
Dr Konstantinos Balaskas
k.balaskas@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Konstantinos Balaskas

Contact details
162 City Rd
London

United Kingdom
EC1V 2PD
+44 (0)20 7253 3411
k.balaskas@nhs.net

Type(s)
Scientific

Contact name
Dr William McKinnon

Contact details
Birmingham Clinical Trials Unit
School of Health and Population Sciences
Public Health Building
University of Birmingham
Birmingham
United Kingdom
B15 2TT
+44 (0)121 414 8335
w.mckinnon@bham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
295260

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 295260, BALK1008, HTA - NIHR131432

Study information

Scientific Title
Optical coherence tomography angiography for the detection of neovascular age-related macular degeneration: a comprehensive diagnostic accuracy study

Acronym
ATHENA

Study objectives
ATHENA is a study to see if optical coherence tomography angiography (OCTA) used alongside optical coherence tomography (OCT) is just as good at diagnosing neovascular age-related macular degeneration (nAMD) as the OCT scan used with fluorescein angiography (FA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/01/2022, South Central - Oxford B Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 104 8360; oxfordb.rec@hra.nhs.uk), ref: 21/SC/0412

Study design
Non-inferiority prospective randomized diagnostic accuracy study with an internal pilot to confirm the feasibility of the recruitment plan

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Neovascular age-related macular degeneration (nAMD)

Interventions
Patients presenting to secondary care with suspected nAMD will undergo an OCT. If nAMD is clinically suspected following an OCT, the patient will have two more tests: OCTA and FA.

Patients with clinical (orange nodule, large sub-retinal haemorrhage) and OCT features (high pigment epithelium detachment, double-layer sign, sub-retinal pigment epithelium notch) suggestive of PCV will also undergo ICGA at the same time as FA.

In half of the cases, chosen by chance, the site clinician will review OCT and then the OCTA and will provide a clinical diagnosis (nAMD: yes/no). In the other half of the cases the site clinician will review the OCT and then the FA and will provide a clinical diagnosis of the presence of nAMD (yes/no) (CD1).

Once they have completed the case response form with CD1 the site clinician will review the remaining third imaging test in each case (FA or OCTA) and will either confirm or change their initial clinical diagnosis of nAMD (yes/no) and will record it on the CRF (CD2).

Comparison of the second treating clinician diagnosis (CD2) with their first clinical diagnosis (CD1) within each arm will provide additional evidence concerning the added value of using a combination of both OCTA and FA in patients with a positive or suspicious OCT.

Treating site staff will pseudo anonymise the scans by means of a trial number and transfer all the images alongside a clinical vignette of relevant medical information to BlueWorks software hosted on servers based at Moorfields Eye Hospital NHS Foundation Trust. Scans with the trial number redacted will be presented to specialist clinicians at specialist NHS reading centres in the UK. The specialist clinicians will make a diagnosis of the presence of nAMD on each scan and accompanying clinical vignette and upload their diagnosis onto the BlueWorks software.

The results of the diagnosis from reviewing the scans at the treating sites, and the reading centres will be transferred to the University of Birmingham where the accuracy of each test will

be assessed, alongside the reliability of using OCTA as a single test for the reliable diagnosis of nAMD.

The health economic impacts of using the various combinations of scans to diagnose nAMD will be undertaken by staff based at the University of Newcastle.

Intervention Type
Other

Primary outcome(s)
The sensitivity and specificity of the index tests, OCTA combined with OCT and FA combined with OCT, for the detection of nAMD in participants with a positive or suspicious OCT at baseline. Sensitivity and specificity are defined respectively as the proportion of participants with nAMD that are correctly identified by the index tests as cases and the proportion of participants without nAMD that are correctly identified by the index tests as non-cases. The index tests are interpreted by clinicians (retinal experts)

Key secondary outcome(s))
1. The sensitivity and specificity of the index tests, OCTA alone and FA alone, for the detection of nAMD in participants with a positive or suspicious OCT at baseline. The positive predictive value (PPV) and negative predictive (NPV) of OCTA alone and FA alone are defined respectively as the proportion of participants with a positive index test result that have nAMD and the proportion of participants with a negative index test result that do not have nAMD. OCTA and FA are interpreted separately by Reading Centre expert graders.
2. The PPV of OCT for detection of nAMD in all patients presenting with suspicion of nAMD at baseline (test interpretation by retinal experts and Reading Centre graders)
3. The difference in sensitivity and difference in specificity of OCT+FA and OCT+FA+OCTA at baseline reviewed by retinal experts within the 'OCT+FA' arm of the study
4. The difference in sensitivity and difference in specificity of OCT+OCTA and OCT+FA+OCTA at baseline reviewed by retinal experts within the 'OCT+OCTA' arm of the study
5. The sensitivity, specificity, PPV and NPV of OCTA, FA, ICGA, alone and in combinations, for detection of PCV in patients with OCT and clinical features suspicious of PCV at baseline
6. Intra- and inter-rater variation in the assessment of OCTA and FA by scans taken at baseline and assessed by Reading Centre graders at a later date
7. Criteria for OCTA-based diagnosis of nAMD determined using a consensus process at baseline
8. Incremental cost per true positive detected and incremental cost per correct diagnosis for nAMD estimated through cost-effectiveness analysis
9. The sensitivity, specificity, PPV and NPV of OCTA for detection of nAMD by lesion type as assessed by Reading Centre expert graders (PCV, type 1-, type 2-, type 3- nAMD) at baseline.
10. The limitations of OCTA use and adverse events summarised descriptively as they occur throughout the study

Completion date
31/10/2023

Eligibility

Key inclusion criteria

1. Patients presenting to secondary/specialist care centres with suspicion of nAMD in the first or second eye
2. Can provide informed consent
3. Have the ability to perform study-specific procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Significant media opacities (cataract, vitreous opacities) that would not allow good quality fundus imaging
2. Diabetic retinopathy of severity worse than mild non-proliferative stage and with any degree of diabetic maculopathy
3. Other causes of choroidal neovascularisation (myopic, angioid streaks, inflammatory, retinal dystrophies, secondary to central serous chorioretinopathy, idiopathic)
4. Inability to undergo dye-based imaging (FA or ICGA) due to history of allergy

Date of first enrolment
10/01/2022

Date of final enrolment
31/03/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Moorfields Eye Hospital NHS Foundation Trust
162 City Rd
London
United Kingdom
EC1V 2PD

Sponsor information

Organisation
Moorfields Eye Hospital NHS Foundation Trust

ROR
https://ror.org/03zaddr67

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Following publication of the findings anonymised datasets generated during and/or analysed during the current study will be available upon request from the ATHENA Trial Management Group and the BCTU Data Sharing Committee in consultation with the Sponsor in line with standard data sharing practices for clinical trial datasets. Applications should be submitted to bctudatashare@contacts.bham.ac.uk. Whilst datasets will be anonymised, consent will be obtained from participants for their data to be shared after the study).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Protocol article		31/05/2024	03/06/2024	Yes	No
HRA research summary			26/07/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes