

# StereoTactic radiotherapy for wet Age-Related macular degeneration (STAR)

<b>Submission date</b> 28/11/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 13/12/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 16/07/2025	<b>Condition category</b> Eye Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Age-related macular degeneration (AMD) is a painless eye condition that leads to loss of central vision. There are two main types of AMD, called dry AMD and wet AMD. Wet AMD is more serious and without treatment, vision can deteriorate within days. This study investigates the use of radiation to treat wet AMD, called stereotactic radiosurgery. The radiation is delivered using a robotically controlled device that projects overlapping beams of radiation onto the macula, the part of the eye that is affected by wet AMD. This study aims to determine if stereotactic radiosurgery can maintain vision and reduce the need for regular injections of ranibizumab (the standard anti-VEGF drug used to treat wet AMD).

### Who can participate?:

Males and females aged 50 years or over with wet AMD requiring anti-VEGF treatment at the time of entry to the study.

### What does the study involve?

Participants will be randomly allocated to receive either radiation (stereotactic radiotherapy) or simulated placebo (sham) treatment. They will be followed up regularly for two years, and then again at the end of three and four years for a safety visit. Participants will also receive injections of ranibizumab (Lucentis) into their eye if their wet AMD is active.

### What are the possible benefits and risks of participating?

The main benefit of stereotactic radiotherapy is that it may reduce the number of eye injections that people require, or in some cases eliminate them entirely. Previous studies have suggested that the patients who will be eligible for the study would obtain a better vision outcome with radiotherapy (with injections as needed) than with injections alone. The main risk of radiation is that it can sometimes damage the healthy tissue in the macula and thereby damage vision. Subtle changes to the macula can sometimes be seen using specialised testing (fluorescein angiography) but in the majority of people this does not affect the vision.

### Where is the study run from?

King's College Hospital (UK).

When is the study starting and how long is it expected to run for?  
Recruitment to the study will begin in December 2014 and continue for approximately 41 months. Each participant will be in the study for 4 years.

Who is funding the study?  
NIHR Efficacy and Mechanism Evaluation Programme (UK).

Who is the main contact?  
Mr Tim Jackson  
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## Contact information

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Scientific

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Public

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## Additional identifiers

## Clinical Trials Information System (CTIS)

Nil known

## Integrated Research Application System (IRAS)

86810

## ClinicalTrials.gov (NCT)

NCT02243878

## Protocol serial number

IRAS 86810

# Study information

## Scientific Title

StereoTactic radiotherapy for wet Age-Related macular degeneration (STAR): a randomised, double-masked, sham-controlled, clinical trial comparing low-voltage X-ray irradiation with as needed ranibizumab to as needed ranibizumab monotherapy

## Acronym

STAR

## Study objectives

The study's primary hypothesis is that the mean number of ranibizumab injections during the first 24 months after randomization will be less in the SRT group than in the sham group. The secondary hypothesis is that participants who undergo SRT will have a non-inferior visual outcome compared with those in the sham group.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

NRES Committee London - City & East, REC ref: 13/LO/1207

## Study design

Randomised double-masked sham-controlled pivotal clinical trial

## Primary study design

Interventional

## Study type(s)

Treatment

## Health condition(s) or problem(s) studied

Retinal disease/age-related macular degeneration

## Interventions

Participants in the treatment arm will receive 16 Gray stereotactic radiotherapy (SRT) with a concomitant injection of ranibizumab.

## Intervention Type

Device

## Phase

Not Applicable

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

Not provided at time of registration

## Primary outcome(s)

The primary outcome is the mean number of ranibizumab injections over 24 months. SRT will be considered superior to sham if the mean number of injections in the SRT group is statistically less than (one-sided  $p < 0.025$ ) the mean in the sham group.

## Key secondary outcome(s)

SRT will be considered non-inferior to sham treatment if the lower bound of the 95% confidence interval for the difference in mean change in ETDRS VA at 24 months, between the SRT and sham groups, is no greater than 5 letters.

## Completion date

30/06/2024

## Eligibility

### Key inclusion criteria

Current participant inclusion criteria as of 01/08/2018:

1. Participants must have neovascular AMD in the study eye, for which they have received at least three prior intravitreal injections of either bevacizumab (Avastin), aflibercept (Eylea), ranibizumab (Lucentis) or pegaptanib (Macugen)
2. Participants must have received an anti-VEGF injection in the study eye within 3 months prior to enrolment
3. Participants must require treatment with anti-VEGF therapy at the time of enrolment, due to OCT evidence of subretinal fluid and/or cystoid macular oedema, and have a macular volume that is greater than a pre-defined threshold that varies for each different make of SD-OCT machine
4. Participants must be at least 50 years of age

Previous participant inclusion criteria:

1. Participants must have neovascular AMD in the study eye, for which they have received at least three prior intravitreal injections of either bevacizumab (Avastin), aflibercept (Eylea), ranibizumab (Lucentis) or pegaptanib (Macugen)
2. Participants must have received an anti-VEGF injection in the study eye within 3 months prior to enrolment
3. Participants must require treatment with anti-VEGF therapy at the time of enrolment, due to OCT evidence of subretinal fluid and/or cystoid macular oedema, and a macular volume that is greater than the 95th percentile of normal for the SD-OCT machines used in the investigational sites
4. Participants must be at least 50 years of age

### Participant type(s)

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

411

**Key exclusion criteria**

Current participant exclusion criteria as of 01/08/2018:

1. Disciform scarring that involves the fovea, in the study eye
2. Visual acuity worse than 6/96 (24 ETDRS letters) in the study eye
3. Lesion size greater than 4 mm in greatest linear dimension, or greater than 2 mm from the centre of the fovea to the furthest point on the lesion perimeter
4. An axial length of less than 20 mm, or greater than 26 mm, in the study eye
5. Contraindication or sensitivity to contact lens application, including recurrent corneal erosions, in the study eye
6. Type 1 or Type 2 diabetes mellitus
7. Retinopathy in the study eye
8. Prior or current therapies in the study eye for age-related macular degeneration, other than anti-VEGF agents, including submacular surgery, subfoveal thermal laser photocoagulation, photodynamic therapy (PDT), or transpupillary thermotherapy (TTT)
9. Presence of an intravitreal device in the study eye
10. Previous radiation therapy to the study eye, head or neck with the exception of radio-iodine treatment for hyperthyroidism, epimacular brachytherapy to the non-study eye, or Oraya SRT to the non-study eye
11. Inadequate pupillary dilation or significant media opacities in the study eye, including cataract, which may interfere with visual acuity testing, the clinical evaluation of the posterior segment, or fundus imaging
12. Study eyes with CNV due to causes other than AMD, including presumed ocular histoplasmosis syndrome (POH), angioid streaks, multifocal choroiditis, choroidal rupture, and pathological myopia (greater than 8 Dioptres spherical equivalent). Participants with retinal angiomatous proliferation (RAP) or idiopathic polypoidal choroidal vasculopathy (IPCV) are not excluded
13. Known allergy to intravenous fluorescein, ICG or intravitreal ranibizumab
14. Intraocular surgery or laser-assisted in situ keratomileusis (LASIK) in the study eye within 12 weeks prior to enrolment
15. Prior pars plana vitrectomy in the study eye
16. Current participation in another interventional clinical trial, or participation in such a clinical trial within the last six months
17. Unwilling, unable, or unlikely to return for scheduled follow-up for the duration of the trial
18. Women who are pregnant at the time of radiotherapy

19. Participants with an implantable cardioverter defibrillator (ICD) or pacemaker implant (or any implanted device) where the device labelling specifically contraindicates patients undergoing X-ray
20. Any other condition, which in the judgment of the investigator, would prevent the participant from granting informed consent or completing the study, such as dementia and mental illness (including generalized anxiety disorder and claustrophobia)

Previous participant exclusion criteria:

1. Disciform scarring that involves the fovea, in the study eye
2. Geographic atrophy that involves the fovea, or an area of geographic atrophy that is more than 500 microns in greatest diameter, immediately adjacent to the fovea, in the study eye
3. Visual acuity worse than 6/96 (24 ETDRS letters) in the study eye
4. Lesion size greater than 4 mm in greatest linear dimension, or greater than 2 mm from the centre of the fovea to the furthest point on the lesion perimeter
5. Distance from the center of the fovea to the nearest edge of the optic disc less than 3 mm in the study eye (this distance is confirmed by the Oraya SRT device software immediately prior to treatment)
6. An axial length of less than 20 mm, or greater than 26 mm, in the study eye
7. Contraindication or sensitivity to contact lens application, including recurrent corneal erosions, in the study eye
8. Type 1 or Type 2 diabetes mellitus
9. Retinopathy in the study eye
10. Prior or current therapies in the study eye for age-related macular degeneration, other than anti-VEGF agents, including submacular surgery, subfoveal thermal laser photocoagulation, photodynamic therapy (PDT), or transpupillary thermotherapy (TTT)
11. Presence of an intravitreal device in the study eye
12. Previous radiation therapy to the study eye, head or neck with the exception of radio-iodine treatment for hyperthyroidism, epimacular brachytherapy to the non-study eye, or Oraya SRT to the non-study eye
13. Inadequate pupillary dilation or significant media opacities in the study eye, including cataract, which may interfere with visual acuity testing, the clinical evaluation of the posterior segment, or fundus imaging
14. Likely to need cataract surgery in the study eye within two years of enrolment
15. Study eyes with CNV due to causes other than AMD, including presumed ocular histoplasmosis syndrome (POH), angioid streaks, multifocal choroiditis, choroidal rupture, and pathological myopia (greater than 8 Dioptres spherical equivalent). Participants with retinal angiomatous proliferation (RAP) or idiopathic polypoidal choroidal vasculopathy (IPCV) are not excluded
16. Known allergy to intravenous fluorescein, ICG or intravitreal ranibizumab
17. Intraocular surgery or laser-assisted in situ keratomileusis (LASIK) in the study eye within 12 weeks prior to enrolment
18. Prior pars plana vitrectomy in the study eye
19. Current participation in another interventional clinical trial, or participation in such a clinical trial within the last six months
20. Unwilling, unable, or unlikely to return for scheduled follow-up for the duration of the trial
21. Women who are pregnant at the time of radiotherapy
22. Participants with an implantable cardioverter defibrillator (ICD) or pacemaker implant (or any implanted device) where the device labelling specifically contraindicates patients undergoing X-ray
23. Any other condition, which in the judgment of the investigator, would prevent the participant from granting informed consent or completing the study, such as dementia and mental illness (including generalized anxiety disorder and claustrophobia)

**Date of first enrolment**

01/12/2014

**Date of final enrolment**

31/12/2019

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre****King's College Hospital**

Ophthalmology Department

Normanby Building

Denmark Hill

London

United Kingdom

SE5 9RS

**Study participating centre****University Hospitals Bristol NHS Trust**

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**Study participating centre****Frimley Park Hospital**

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Portsmouth Road

Frimley

Camberley

United Kingdom

GU16 7UJ

**Study participating centre****Maidstone and Tunbridge Wells NHS Trust**

The Maidstone Hospital

Hermitage Lane  
Maidstone  
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ME16 9QQ

**Study participating centre**  
**The Royal Wolverhampton NHS Trust**  
New Cross Hospital  
Wolverhampton Road  
Heath Town  
Wolverhampton  
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**Study participating centre**  
**East Lancashire Hospitals NHS Trust**  
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**Study participating centre**  
**The Sussex Eye Hospital**  
Eastern Road  
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**Study participating centre**  
**William Harvey Hospital**  
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**Study participating centre**  
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Field Heath Road



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**Study participating centre**

**Whipps Cross University Hospital NHS Trust**  
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**Study participating centre**

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NR4 7UY

**Study participating centre**

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**Study participating centre**

**Ophthalmology (calderdale Royal Hospital)**  
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HX3 0PW

**Study participating centre**  
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**Study participating centre**

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**Leighton Hospital**

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CW1 4QJ

**Study participating centre**  
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BA21 4AT

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**Dorset County Hospital**  
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DT1 2JY

**Study participating centre**  
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Huntingdon  
United Kingdom  
PE29 6NT

## **Sponsor information**

### **Organisation**

King's College Hospital NHS Foundation Trust

### **ROR**

<https://ror.org/01n0k5m85>

### **Organisation**

King's College London

## **Funder(s)**

### **Funder type**

Government

## Funder Name

National Institute for Health Research

## Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

United Kingdom

# Results and Publications

## 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

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		11/06/2024	16/07/2025	Yes	No
<a href="#">Protocol article</a>	protocol	24/11/2016		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version 1.9	25/01/2019	01/11/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes