ISRCTN13832085 https://doi.org/10.1186/ISRCTN13832085

Comparing x-ray to artificial intelligence guidance in keyhole aortic aneurysm surgery

Submission date	**Recruitment status**	[X] Prospectively registered
22/11/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
03/12/2021	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
01/05/2025	Circulatory System	[X] Record updated in last year

Plain English summary of protocol

Current plain English summary as of 24/01/2022:
An aortic aneurysm is an abnormal swelling of the largest artery of the body, the aorta. As the aneurysm continues to enlarge, there is a risk that it can burst. To prevent this from happening, a device called a stent-graft, which is a metal frame (stent) with a special fabric covering (graft) is introduced within the aorta in a key-hole procedure called endovascular aneurysm repair (EVAR). This is a relatively common procedure with about 5,000 patients undergoing this procedure each year in the UK. The stent-grafts are selected for each patient before the operation using the information from highly detailed three-dimensional (3D) images from a CT scan. However, during the operation, only two-dimensional (2D) X-ray images are used to correctly position the stent-graft, which have less information than the 3D images. Cydar EV is a state-of-the-art software system that uses the 3D images from the CT scan to help select the right sized stent-graft for the patient and joins these images with the 2D X-ray images used during the operation in a process called image fusion. Cydar EV gives the doctor advanced guidance during the operation by using all the benefits of the 3D information. This study will compare operations performed using 2D X-rays (current standard of care) with operations using Cydar EV image guidance. This research will involve 340 patients at ten hospitals across the UK and examine if Cydar EV image guidance makes the operation easier and therefore quicker for the doctors to perform. Patients may benefit from a shorter time under anaesthetic, fewer harmful X-rays and less X-ray dye used during the procedure.

Who can participate?
Patients aged 18 and over who are undergoing endovascular (keyhole) aortic aneurysm repair

What does the study involve?
Participants will be randomly assigned to either one of two groups. One group will undergo the EVAR operation using 2D X-ray imaging alone, this is the standard way this operation is done in the UK. The other group will undergo the operation with their doctor using Cydar EV. During the operation details about the operation will be recorded including radiation dose, time taken and what and how many stents and other equipment is used. Regardless of which group the patients are in, they will have a post-operative CT scan to check the position of the stent as well as an outpatient clinic appointment at 4-12 weeks and 1 year after the stent is inserted. At the time of the operation and at both postoperative clinic appointments they will be given a short

questionnaire asking them questions about their quality of life. This questionnaire takes about 5 minutes to complete and is an addition to the normal practice at their centre; it allows the research team to look at if there are any differences seen between the two groups in this study.

What are the possible benefits and risks of participating?
This research has been funded by the National Institute of Health Research (NIHR) as it is thought that it can benefit both patients and the NHS. Cydar EV, the technology behind this research, has already been shown in smaller studies to roughly halve the radiation exposure to patients and significantly reduce the length of the procedure and the amount of anaesthetic received by patients. It is also possible that the technology may help to place stent-graft more accurately. This research will help to answer if this technology is clinically and cost-effective and can therefore benefit patients and the NHS.
In terms of disadvantages, all patients taking part in this study will have slightly longer clinical appointments (by about 5-10 minutes) to allow time to complete the quality-of-life questionnaire (six brief questions). All patients taking part in the study will have two CT scans after their operation. In the UK, patients will have either one or two CT scans after a similar operation, depending on the hospital and type of stent-graft used for the procedure. This means that a patient may have the same number of CT scans, or one extra scan compared to someone not taking part in this study. These CT scans use ionising radiation to form images of the body. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study is assumed to only add a very small chance of this happening.

Where is the study run from?
King's Trial Unit (UK)

When is the study starting and how long is it expected to run for?
August 2021 to November 2025

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Dr Rachel Clough, rachel.clough@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Rachel Clough

ORCID ID
https://orcid.org/0000-0002-4243-6836

Contact details
Department of Biomedical Engineering
The School of Biomedical Engineering & Imaging Sciences
3rd Floor Lambeth Wing, St Thomas' Hospital

King's College London
London
United Kingdom
SE1 7EH
+44 (0)20 7848 0532
rachel.clough@kcl.ac.uk

Type(s)
Public

Contact name
Dr Izabela Pilecka

ORCID ID
https://orcid.org/0000-0001-7350-4873

Contact details
King’s Clinical Trial Unit
Denmark Hill
De Crespigny Park
London
United Kingdom
SE5 8AF
-
izabela.pilecka@kcl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
280257

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 280257, CPMS 51711

Study information

Scientific Title
A randomised controlled trial to assess the clinical-, technical- and cost-effectiveness of a cloud-based, ARtificially Intelligent image fusion system in comparison to standard treatment to guide endovascular Aortic aneurysm repair (ARIA)

Acronym
ARIA

Study objectives
A randomised controlled trial to assess the clinical, technical and cost-effectiveness of a cloud-based, ARtificially Intelligent image fusion system in comparison to standard treatment to guide endovascular Aortic aneurysm repair (ARIA)

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 10/02/2022, London – South East REC (Barlow House, 3rd Floor, 4 Minshull Street, Manchester , M1 3DZ, United Kingdom; +44 (0)207 104 8120; londonsoutheast.rec@hra.nhs.uk), ref: 22/LO/0081

Study design
Multi-centre open-label two-armed randomized controlled clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Abdominal aortic aneurysm

Interventions
Current intervention as of 24/01/2022:
Participants will be randomised via the KCTU web-based randomisation system. Participants will be randomised to Cydar-EV image fusion for guidance or standard imaging techniques in a ratio of 1:1 post-consent and confirmation of eligibility. The allocation sequence will be generated dynamically using the method of minimisation. Minimisation will be balanced using the following factors:
Surgeon: Surgeons from all sites 01, 02, 03, 04 etc.
Procedure type: 01. Simple | 02. Complex
Procedure urgency: 01. Emergency | 02. Elective

Intervention:
Patients will undergo endovascular aortic aneurysm repair using AI and computer vision (Cydar EV) for planning and surgical guidance, as per instructions for use. Cydar EV provides tools to:
1. Import and visualise CT data
2. Segment and annotate vascular anatomy from CT data
3. Place and edit virtual guidewires and measure lengths on them
4. Make measurements of anatomical structures on planar sections of the CT data
5. Produce an operative plan from measurements and segmentation of preoperative vessel anatomy
6. Overlay planning information such as preoperative vessel anatomy onto live fluoroscopic images, aligned based on the position of anatomical features present in both
7. Non-rigidly transform the visualisation of anatomy when intra-operative vessel deformation is observed
8. Postoperatively review data relating to procedures where the system was used

Comparator:
Patients will undergo endovascular aneurysm repair using standard technology and X-ray fluoroscopy imaging intra-operatively as defined under standard treatment above. The CT imaging for the patients randomised to standard treatment will be uploaded to Cydar EV at the time of randomisation, in case of cross-over.

Intervention delivery:
Procedures will be performed under local, regional or general anaesthesia (likely ratio: 1:1:8). Procedures can be undertaken using either a mobile C-arm in a surgical operating theatre, a dedicated fixed fluoroscopy set, or in a hybrid operating room. Patients may go to the ward, HDU or ITU according to local protocol.

Routine pre-operative CT aortic imaging will be used to determine general suitability for endovascular repair, including assessment of landing zones for fixation and sealing, and procedure type and device selection. After randomisation in all patients the pre-randomisation CT images will be uploaded to Cydar EV.

In the Cydar limb of the trial, Cydar EV will be used to plan the procedure including making appropriate measurements, map creation, procedural annotations, and device selection /verification. At operation, the Cydar equipment will be set up and switched on in theatre prior to ‘knife-to-skin’. The participant's information will have been pre-loaded to the system (according to ‘Cydar EV: Instructions for Use’) and will be available for selection. The machine must be positioned according to surgeon preference. Machine use will be recorded on the Cydar intervention record form. The patient’s information will be loaded on the system anytime up until the day of surgery prior to induction of the anaesthetic.

Previous intervention:
Participants will be randomised via the KCTU web-based randomisation system. Participants will be randomised to Cydar-EV image fusion for guidance or standard imaging techniques in a ratio of 1:1 post-consent and confirmation of eligibility. The allocation sequence will be generated dynamically using the method of minimisation. Minimisation will be balanced using the following factors:
Surgeon: Surgeons from all sites 01, 02, 03, 04 etc.
Disease extent: 01. AAA | 02. TAAA
Procedure type: 01. Emergency | 02. Elective

Intervention:
Patients will undergo endovascular aortic aneurysm repair using AI and computer vision (Cydar EV) for planning and surgical guidance, as per instructions for use. Cydar EV provides tools to:
1. Import and visualise CT data
2. Segment and annotate vascular anatomy from CT data
3. Place and edit virtual guidewires and measure lengths on them
4. Make measurements of anatomical structures on planar sections of the CT data
5. Produce an operative plan from measurements and segmentation of preoperative vessel anatomy
6. Overlay planning information such as preoperative vessel anatomy onto live fluoroscopic images, aligned based on the position of anatomical features present in both
7. Non-rigidly transform the visualisation of anatomy when intra-operative vessel deformation is observed
8. Postoperatively review data relating to procedures where the system was used

Comparator:
Patients will undergo endovascular aneurysm repair using standard technology and X-ray fluoroscopy imaging intra-operatively as defined under standard treatment above. The CT imaging for the patients randomised to standard treatment will be uploaded to Cydar EV at the time of randomisation, in case of cross-over.

Intervention delivery:
Procedures will be performed under local, regional or general anaesthesia (likely ratio: 1:1:8). Procedures can be undertaken using either a mobile C-arm in a surgical operating theatre, a dedicated fixed fluoroscopy set, or in a hybrid operating room. Patients may go to the ward, HDU or ITU according to local protocol.

Routine pre-operative CT aortic imaging will be used to determine general suitability for endovascular repair, including assessment of landing zones for fixation and sealing, and procedure type and device selection. After randomisation in all patients the pre-randomisation CT images will be uploaded to Cydar EV.

In the Cydar limb of the trial, Cydar EV will be used to plan the procedure including making appropriate measurements, map creation, procedural annotations, and device selection /verification. At operation, the Cydar equipment will be set up and switched on in theatre prior to 'knife-to-skin'. The participant's information will have been pre-loaded to the system (according to 'Cydar EV: Instructions for Use') and will be available for selection. The machine must be positioned according to surgeon preference. Machine use will be recorded on the Cydar intervention record form. The patient's information will be loaded on the system anytime up until the day of surgery prior to induction of the anaesthetic.

Intervention Type
Device

Phase
Phase III

Drug/device/biological/vaccine name(s)
Cydar EV

Primary outcome(s)
Procedure time, measured as the time between insertion of the first wire (after percutaneous access achieved, if applicable) at the beginning of the endovascular procedure to the last frame of the completion angiogram. This will be recorded (in minutes) at the time of the procedure by the local research team.

Key secondary outcome(s))
Current secondary outcome measures as of 24/01/2022:
1. Procedural efficiency:
1.1. Anaesthetic duration – the time between the beginning of induction and the end of emergence. This will be documented at the time of the procedure by the local research team in minutes.
1.2. X-ray dose per procedure – fluoroscopy time (FT) (seconds), dose area product (DAP) (Gy. cm2) and cumulative air kerma (CAK) (mGy) should be recorded and documented at the time of the procedure by the local research team. The imaging system used should also be recorded.
1.3. Contrast dose per procedure – the volume (ml) and concentration (mgI/ml) of the iodinated

contrast material used should be recorded by the local research team at the time of the procedure in minutes.
1.4. Consumable use in the operating theatre for endovascular aortic aneurysm repair – the name of device, unit and quantity used, blood products used; details to be completed by nurse in the operating theatre or research nurse at the time of the procedure using a Source Data Worksheet.
2. Technical success:
2.1. Proximal and distal seal zone at least 10 mm and no evidence of endoleak. This will be documented by the imaging CoreLab team on review of the CT images acquired postoperatively and at 4-12 weeks and at 52 weeks.
3. Patient outcomes:
3.1. Length of ITU/HDU admission – date and time from admission to date and time of discharge from ITU/HDU; documented by the local research team during the time of admission; ITU and HDU admissions should be documented separately
3.2. Postoperative length of hospital stay – date of procedure to date of discharge from hospital (nights); documented by the local research team during the time of admission.
3.3. 30-day mortality – death of the participant within 30 days of the primary procedure; documented by the local research team; to include date of death (dd/mm/yy) and cause.
3.4. Re-intervention – any procedure open surgical or endovascular undertaken within 1 year of the primary endovascular aortic aneurysm repair procedure (binary outcome). The type, timing and number of procedures should also be recorded by the local research team.
3.5. Adverse events – hospitalisation for any reason within 1 year of the primary endovascular aortic aneurysm repair; the type of event should be documented and classified as one of the following: musculoskeletal, urological, neurological, ophthalmological, cardiovascular, gastro-intestinal, hepato-pancreato-biliary, dermatological or other by the local research team, with information captured to understand if linked to re-intervention (section 'i' above). For each hospitalisation the following should also be captured:
3.5.1. Day case, Elective, Non-elective
3.5.2. Length of hospital stay - date of admission to date of discharge (nights)
3.5.3. Length of ITU/HDU admission (if applicable) - date and time from admission to date and time of discharge from ITU/HDU; ITU and HDU admissions should be documented separately
3.6. Quality of life – differences in quality of life between intervention and the comparator group, and changes in quality of life post-surgery will be measured using data from the patient-completed EQ5D-3L instrument. EQ-5D-3L is a validated measure of health-related quality of life, consisting of a five-dimension health status classification system and a separate visual analogue scale. EQ-5D-3L data will be obtained through face-to-face or telephone interview with the participant at baseline, pre-discharge, 4-12 weeks and at 12-months follow up. Patients will complete the questionnaires with the support of the local research team
4. Cost-effectiveness, as assessed by:
4.1. Total resource use and costs assessed over the time horizon of the trial (12-months)
4.2. Quality-Adjusted Life Years (QALYs) - Quality of life will be measured by the EQ-5D-3L instrument as described above at baseline, pre-discharge, 4-12 weeks and at 12-months follow up. In order to be used in the calculation of qualityadjusted life-years (QALYs), the EQ-5D-3L dimension scores will be converted to utilities using the relevant value set for England. Quality-adjusted life-years (QALYs) gained in both groups, over the time horizon of the trial, will be calculated using the area under the curve method.
4.3. Incremental cost per QALY between baseline and 12 month follow-up

Previous secondary outcome measures:
1. Procedural efficiency:
1.1. Anaesthetic duration – the time between the beginning of induction and the end of emergence. This will be documented at the time of the procedure by the local research team in

minutes.
1.2. X-ray dose per procedure – fluoroscopy time (FT) (seconds), dose area product (DAP) (Gy. cm2) and cumulative air kerma (CAK) (mGy) should be recorded and documented at the time of the procedure by the local research team. The imaging system used should also be recorded.
1.3. Contrast dose per procedure – the volume (ml) and concentration (mgI/ml) of the iodinated contrast material used should be recorded by the local research team at the time of the procedure in minutes.
1.4. Consumable use in the operating theatre for endovascular aortic aneurysm repair – the name of device, unit and quantity used, blood products used; details to be completed by nurse in the operating theatre or research nurse at the time of the procedure using a Source Data Worksheet.
2. Technical success:
2.1. Proximal and distal seal zone at least 10 mm and no evidence of endoleak. This will be documented by the imaging CoreLab team on review of the CT images acquired postoperatively and at 6-12 weeks and at 52 weeks.
3. Patient outcomes:
3.1. Length of ITU/HDU admission – date and time from admission to date and time of discharge from ITU/HDU; documented by the local research team during the time of admission; ITU and HDU admissions should be documented separately
3.2. Postoperative length of hospital stay – date of procedure to date of discharge from hospital (nights); documented by the local research team during the time of admission.
3.3. 30-day mortality – death of the participant within 30 days of the primary procedure; documented by the local research team; to include date of death (dd/mm/yy) and cause.
3.4. Re-intervention – any procedure open surgical or endovascular undertaken within 1 year of the primary endovascular aortic aneurysm repair procedure (binary outcome). The type, timing and number of procedures should also be recorded by the local research team.
3.5. Adverse events – hospitalisation for any reason within 1 year of the primary endovascular aortic aneurysm repair; the type of event should be documented and classified as one of the following: musculoskeletal, urological, neurological, ophthalmological, cardiovascular, gastro-intestinal, hepato-pancreato-biliary, dermatological or other by the local research team, with information captured to understand if linked to re-intervention (section ‘i’ above). For each hospitalisation the following should also be captured:
3.5.1. Day case, Elective, Non-elective
3.5.2. Length of hospital stay - date of admission to date of discharge (nights)
3.5.3. Length of ITU/HDU admission (if applicable) - date and time from admission to date and time of discharge from ITU/HDU; ITU and HDU admissions should be documented separately
3.6. Quality of life – differences in quality of life between intervention and the comparator group, and changes in quality of life post-surgery will be measured using data from the patient-completed EQ5D-3L instrument. EQ-5D-3L is a validated measure of health-related quality of life, consisting of a five-dimension health status classification system and a separate visual analogue scale. EQ-5D-3L data will be obtained through face-to-face or telephone interview with the participant at baseline, pre-discharge, 6-12 weeks and at 12-months follow up. Patients will complete the questionnaires with the support of the local research team
4. Cost-effectiveness, as assessed by:
4.1. Total resource use and costs assessed over the time horizon of the trial (12-months)
4.2. Quality-Adjusted Life Years (QALYs) - Quality of life will be measured by the EQ-5D-3L instrument as described above at baseline, pre-discharge, 6-12 weeks and at 12-months follow up. In order to be used in the calculation of qualityadjusted life-years (QALYs), the EQ-5D-3L dimension scores will be converted to utilities using the relevant value set for England. Quality-adjusted life-years (QALYs) gained in both groups, over the time horizon of the trial, will be calculated using the area under the curve method.
4.3. Incremental cost per QALY between baseline and 12 month follow-up

Completion date
15/11/2025

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 24/01/2022:
1. Clinical diagnosis of abdominal aortic aneurysm (AAA) or thoracoabdominal aortic aneurysm (TAAA) suitable for endovascular treatment, as determined by CT imaging and multidisciplinary review by treating team
2. Fit for endovascular repair as determined by the operating team
3. CT imaging must be in accordance with 'Cydar EV: Instructions for Use' i.e. scans should have the same slice thickness and intervals as the original scan acquisition, must not have any missing slices or discontinuities, must include the pelvis and whole vertebrae including the spinous processes and must not use gantry tilt (this will be done post-consent)
4. Written informed consent (patients lacking capacity or unable to speak English will not be enrolled)
5. Age 18 years and above at the time of consent

Previous participant inclusion criteria:
1. Clinical diagnosis of abdominal aortic aneurysm (AAA) or thoracoabdominal aortic aneurysm (TAAA) suitable for endovascular treatment, as determined by CT imaging and multidisciplinary review by treating team
2. Fit for endovascular repair as determined by the operating team
3. CT imaging must be in accordance with 'Cydar EV: Instructions for Use' i.e. scans should have the same slice thickness and intervals as the original scan acquisition, must not have any missing slices or discontinuities, must include the pelvis and whole vertebrae including the spinous processes and must not use gantry tilt (this will be done post-consent)
4. Written informed consent (patients lacking capacity will not be enrolled)
5. Age 18 years and above at the time of consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
364

Key exclusion criteria

Current participant exclusion criteria as of 24/01/2022:

Patients unable to provide written informed consent

_____

Previous participant exclusion criteria:

Patients with known connective tissue disease

Date of first enrolment
01/02/2022

Date of final enrolment
30/01/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
St Mary's Hospital
The Bays
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton, East Sussex
United Kingdom
BN2 5BE

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Southmead Hospital
Southmead Road
Bristol
United Kingdom
BS10 5NB

Study participating centre
Frimley Park Hospital
Portsmouth Road
Frimley

Camberley
United Kingdom
GU16 7UJ

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Musgrove Park Hospital
Musgrove Park
Taunton
United Kingdom
TA1 5DA

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Organisation
Cydar Medical Ltd

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 current data sharing plans for this study are unknown and will be 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?
Protocol article		25/03/2024	26/03/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet version 1.2	11/11/2025	11/11/2025	No	Yes
Protocol file		10/10/2022	18/04/2023	No	No
Statistical Analysis Plan	version 1.0	30/06/2022	18/04/2023	No	No
Statistical Analysis Plan		30/04/2025	01/05/2025	No	No