FULL PROTOCOL TITLE OF THE STUDY

A mixed methods study to assess the clinical effectiveness and acceptability of qER artificial intelligence software to prioritise CT Head interpretation.

SHORT STUDY TITLE and ACRONYM

Assess the Clinical Effectiveness in Prioritising CT Heads (ACCEPT)

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PROTOCOL VERSION NUMBER AND DATE

Version Stage	Versions No	Version Date	Protocol updated & finalised by;	Detail the key protocol update
First	0.2	11/01/2023	Mr Haris Shuaib	Template update
Second	0.3	29/01/2023	Mr Haris Shuaib	Edits in response to sponsor review
Third	0.4	08/02/2023	Mr Haris Shuaib	Edits in response of sponsor review – addition of data flow diagram
Final	1.0	05/04/2023	Mr Haris Shuaib	Finalisation of Protocol with accepted changes.

SIGNATURE PAGE

The Chief Investigator and the R&D (sponsor office) have reviewed this protocol. The investigators agree to perform the investigations and to abide by this protocol.

The investigator agrees to conduct the trial in compliance with the approved protocol, EU GCP, the UK Data Protection Act (2018), the Trust Information Governance Policy (or other local equivalent), the UK policy Framework for Health and Social Care research, the Sponsor's SOPs, and other regulatory requirements as amended.

Chief investigator

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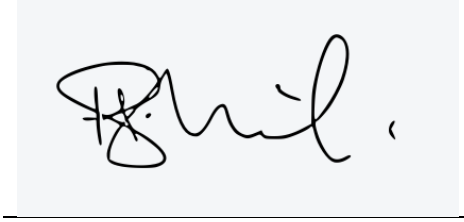

Signature	Date
	12/01/2023

This Protocol template is intended for use with UK sites only.

CONTENTS

1 LIST OF ABBREVIATIONS AND DEFINITIONS

AI	Artificial intelligence
AUC	Area under the receiver operating characteristics curve
CE	Conformité Européenne
CI	Chief investigator
CIP	Clinical investigation plan
CNN	Convolutional neural network
CNORIS	Clinical negligence and other risks indemnity scheme
CRF	Case report form
CRN	Clinical research network
CT	Computed tomography
CTU	Clinical trials unit
CQC	Care Quality Commission
DICOM	Digital imaging and communications in medicine
DMC	Data management committee
DPIA	Data protection impact assessment
ED	Emergency department
EPR	Electronic patient record
FDA	(US) Food and Drug Administration
GCP	Good clinical practice
GDPR	General data protection regulation
GSTT	Guy's and St Thomas' Trust
HL7	Health level seven
HSCN	Health and social care network
ICF	Informed consent form
IMP	Investigational medical product
ISO	International Organisation for Standardisation

ISRCTN	International standard randomised control trial number
LPAC	Local privacy advisory committee
MHRA	Medicines and Healthcare Regulatory Authority
NCCT	Non-Contrast Computed Tomography
NHSGGC	National Health Service Greater Glasgow and Clyde
NICE	The National Institute for Health and Care Excellence
PACS	Picture archiving and communication system
PPI	Patient and Public Involvement
QALY	Quality-adjusted life-year
QEUH	Queen Elizabeth University Hospital
REC	Research ethics committee
RIS	Radiology information system
SAE	Serious adverse event
SADE	Serious adverse device effect
SaMD	Software as a medical device
SMG	Study management group
SOP	Standard operating procedure
SSP	System security policy
SWAN	Scottish wide area network
TFA	Theoretical framework of acceptability
TMG	Trial management group
TSC	Trial steering committee
VPN	Virtual private network

2 SUMMARY/SYNOPSIS

Title	A mixed methods study to assess the clinical effectiveness and acceptability of qER artificial intelligence software to prioritise CT Head interpretation
Protocol Short Title/Acronym	Assess the Clinical Effectiveness in Prioritising CT Heads (ACCEPT)
IRAS Number	313507
REC Reference	**TO BE COMPLETED BEFORE SUBMISSION**
EDGE reference	141791
Study Duration	14 months
Health condition(s) or problem(s) studied	Radiological Turn-around-time (TAT) of Head-NCCT scan reporting
Primary objective	To assess if qER (an artificial intelligence-based prioritisation software for non-contrast CT (NCCT) head scans) tool-based reporting and triage significantly reduces report turnaround time (TAT) of prioritised NCCT head scans for patients attending the emergency department.
Secondary objective (s)	• To assess utility of qER to support emergency department pathways for patients requiring NCCT head and radiology reporting workflow. • To assess the safety of qER at identifying patients with critical findings on NCCT heads. • To evaluate the technical performance of qER. • To conduct a Heath Economic, cost utility analysis of qER.
End of study definition	The end of the study is defined as the end of the 28 days follow-up of the last patient undergoing CT within study period. Final data analysis shall follow this.
Number of Participants	About 16,800 Head-NCCT scans from patients presenting to ED department during the study period.
Study Type	Observational
Human Tissue Samples (if applicable)	Not applicable
Data collected/storage (if applicable)	Data will be collected and stored only within the internal participating sites

3 INTRODUCTION

3.1 Rationale

Emergency Department CT Head Pathway – meeting a need.

A non-contrast head CT (NCCT) is the first line imaging investigation for patients presenting to the emergency department (ED) for a variety of indications including, head injuries, non-traumatic intracranial haemorrhage and strokes. These scans are predominantly interpreted by a radiologist to guide management. Prompt diagnosis results in earlier treatment, reducing brain injury, mortality and illness[1]. Rising ED attendances and concurrent radiologist shortage have resulted in increased wait times and workload[2,3]. This has inadvertently led to higher demands for shorter report turnaround time in an effort to streamline throughput and decrease healthcare expenditures. Furthermore, for time-critical diagnoses like head injuries and strokes, an artificial intelligence (AI) tool which prioritises certain patients' NCCTs for earlier attention, could improve triage and improve patient outcome. Therefore, integrating such a tool in the radiologist workflow could allow for more rapid diagnosis and reporting of these critical conditions, enhancing the triage of patient the appropriate level of care.

The pressures on radiology departments

Diagnostic imaging plays a critical role in the management of ED patients and delays related to imaging are associated with longer hospital stays. As demand for acute care has risen and imaging equipment becomes more readily available, there has been a sustained rise in the demand for acute imaging. An independent review of the NHS England diagnostic service conducted by Sir Mike Richards has recommended doubling the number of scanners to reduce delays[4].

Currently, most scans are interpreted by radiologists, but the Royal College of Radiologists (RCR) are predicting a shortage of 2000 NHS radiologists by 2023[5]. Image reporting turnaround times are now a major bottleneck for EDs. An RCR national audit showed <50% of ED patients receive their scan reports within the recommended time[6] and only 2% of radiology departments can fulfil their reporting requirements within contracted hours.

AI – the opportunity

The potential applications of AI in radiology go well beyond image analysis for diagnostic and prognostic opportunities. It is becoming increasingly clear that AI algorithms have the potential to improve productivity, operational efficiency, and accuracy in diagnostic radiology. AI tools are being developed to aide diagnosis and enhance processes at multiple point in the radiology workflow including: (a) protocolling the prioritised scan, (b) clinical decision support systems for detection of critical findings, (c) worklist priority adjustment via AI results, and (d) reducing turnaround time through worklist prioritisation and semiautomated structures reporting. The adoption of AI tools is dependent on the demonstration of a tangible effect on patient care and improvement in radiologist workflow. Thus, in this study, we aim to assess whether real-world implementation of an AI tool which augments (b), (c) and (d) of the imaging life cycle would affect turnaround times.

qER

qER, a CE Class II approved medical software device, detects, and localizes the presence of six target abnormalities - intracranial haemorrhage, cranial fracture, midline shift, mass effect, atrophy and hypodensities suggestive of infarcts in non-contrast Head-CT scans[7]. A priority status is assigned if any one of the target abnormalities (intracranial haemorrhage, cranial fracture, midline shift or mass effect) is detected by the software, and the user will be able to view a single summary slice listing all the target abnormalities found by qER on the CT scan followed by all slices in scan with the overlay of above abnormalities localization. Alternately, if none of the target abnormalities are detected, the output will indicate that the software has analysed the image and identified no critical findings. qER reports are intended to support certified radiologists and/or licensed medical practitioners for clinical decision making. It is a support tool and, when used with original scans, can assist the clinician to improve efficiency, accuracy, and turnaround time in reading head CTs. It is not to be used to provide medical advice, determine treatment plan, or recommend a course of action to the patient.

3.2 Study hypothesis

Implementation of the qER product will reduce time to reporting of prioritised NCCT head findings requested through the Emergency Department and improve radiology reporting workflow, enabling improved Emergency Department clinical pathways for patients requiring NCCT imaging.

4 PATIENT AND PUBLIC INVOLVEMENT

Patient representatives and groups have contributed to protocol writing and will continue to be integral members of the team for wider dissemination. PPI leads will also be part of the Trial Management Group (TMG).

5 TRIAL OBJECTIVES AND PURPOSE

The purpose of this research is to test the hypothesis that implementation of the qER product in Emergency Department will reduce time to reporting of critical NCCT head findings requested through the Emergency Department and improve radiology reporting workflow, enabling improved Emergency Department clinical pathways for patients requiring NCCT imaging.

5.1 Definition of Terms

For the purpose of this study, there are custom terms specific to the qER device which are used throughout this document. The table below lists these terms and the corresponding definitions.

Term	Definition
Target abnormality	This refers to the list of all target abnormalities that qER can detect in a Head NCCT scan. These are: • Intracranial haemorrhage • Midline shift • Mass effect • Cranial fracture • Atrophy • Hypodensities suggestive of infarct
qER prioritised findings	A subset of target abnormalities which when identified in a Head NCCT scan by qER will lead to the prioritisation of such scans in the radiology worklist. • Intracranial haemorrhage • Midline shift • Mass effect • Cranial fracture
qER non-prioritised findings	A subset of target abnormalities which are detected by qER but not in the list of qER-prioritized findings: • Atrophy • Hypodensities suggestive of infarct These scans will not get prioritized in the radiology worklist for interpretation by the Trust radiologist but will still be available for interpretation in the worklist in a non-prioritized manner.
qER no findings	Any Head NCCT scans where none of the target abnormalities are identified by qER will be classified as scans where no qER findings are identified
qER not interpreted	Head NCCT scans which were not processed by qER and thus have no AI outputs

5.2 Primary Objective

To assess if qER (an artificial intelligence-based prioritisation software for Head-NCCT scan findings) tool-based reporting and triage significantly reduces report turnaround time (TAT) of prioritised NCCT head scans for patients attending the emergency department.

5.3 Secondary Objectives

- To assess utility of qER to support emergency department pathways for patients requiring NCCT head and radiology reporting workflow.
- To assess the safety of qER at identifying patients with critical findings on NCCT heads
- To evaluate the technical performance of qER
- To conduct a Heath Economic, cost utility analysis of qER.

6 STUDY DESIGN & FLOWCHART

6.1 Study Design

6.1.1 Summary

A multi-centre stepped wedged cluster randomised study (Figure 1) will be conducted in 4 NHS hospitals over a 13-month period. Hospitals will be identified and initiated into the qER solution with a 30-day implementation period. The order in which sites will receive the qER intervention will be determined by computer-based randomisation. The stepped wedge design allows delivery of the intervention at an organisational level with evaluation of outcome measures at a patient level. Structuring the implementation through a staged activation in a random order provides important methodological advantages for both qualitative and quantitative elements of the study. The design allows control of adoption bias and adjust for time-based changes in the background patient characteristics at a patient level.

Figure 1: illustration of site initiation within the stepped-wedge design. Each square block represents a duration of 1 month.

6.1.1.1 Pre-Implementation

During the pre-implementation phase, data will be collected to support the primary and secondary outcomes as this will constitute the baseline data for analysis.

6.1.1.2 Implementation

The thresholds for detecting target abnormalities will be adjusted, if necessary, during the implementation phase as per the deployment SOP for qER. Data from this implementation phase will not be used for analysis of primary and secondary outcomes pertaining to the utility of qER.

6.1.1.3 Post-Implementation

The implementation of new healthcare practices and the adoption of AI technologies is not linear. Study design and the elements of the study will enable evaluation of broadly the performance of the AI technology, acceptability, and the economic costs of adoption.

This randomised stepped wedge healthcare service delivery study to assess the clinical effectiveness of qER to prioritise patients reporting of NCCT scans that have prioritised findings (identified from AI analysis of a CT). The study will have an unaided (without qER

implemented) and aided phase (with qER implemented). During the unaided phase the reporting of CT will follow the same workflow as in the current standard of care (i.e., the images/cases will appear in the RIS chronologically and the radiologist either follows this order or prioritise some cases based on communication from ED). When the radiologist clicks a case in RIS, a secondary capture of qER along with the original images will be available in PACS.

During the post-implementation phase there will be a notification (prioritised flag) in RIS. The order of the cases in RIS will not be altered. When the radiologist clicks a case in RIS, a secondary capture of qER along with the original images will be available in PACS. This secondary capture will have contour showing the algorithm's attention point. The radiologist can choose to agree with qER findings as it or modify or ignore it according to their clinical judgement, writing and signing off the report. For scans which were not processed by qER the radiologist can prioritise and report as per the standard of care.

For the purposes of technical evaluation of qER, the scans taken during the aided phase will be divided into four categories:

- Scans with qER prioritised findings (prioritised pathway)
- Scans with qER non-prioritised findings (qER non-prioritised pathway)
- Scans not flagged as having no qER findings (qER no finding pathway), and
- Not interpreted (scans not processed by qER, Not interpreted pathway)

In the qER prioritised, qER non-prioritised and qER no finding pathway, all cases where the radiologist did not agree with qER findings will be sent for ground truthing (2+1 method, Figure 2). A random sample of 500 scans will also be sent for ground-truthing process for the purpose of technical evaluation.

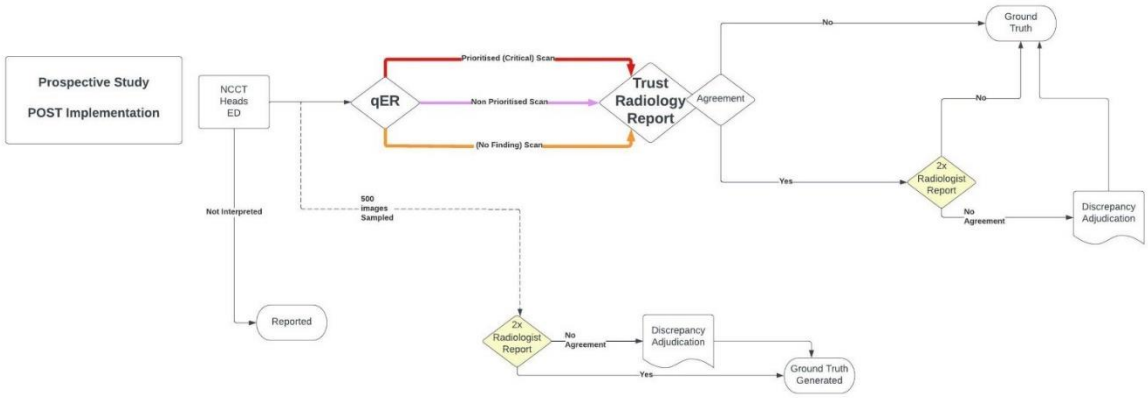

Figure 2: Post-implementation workflow

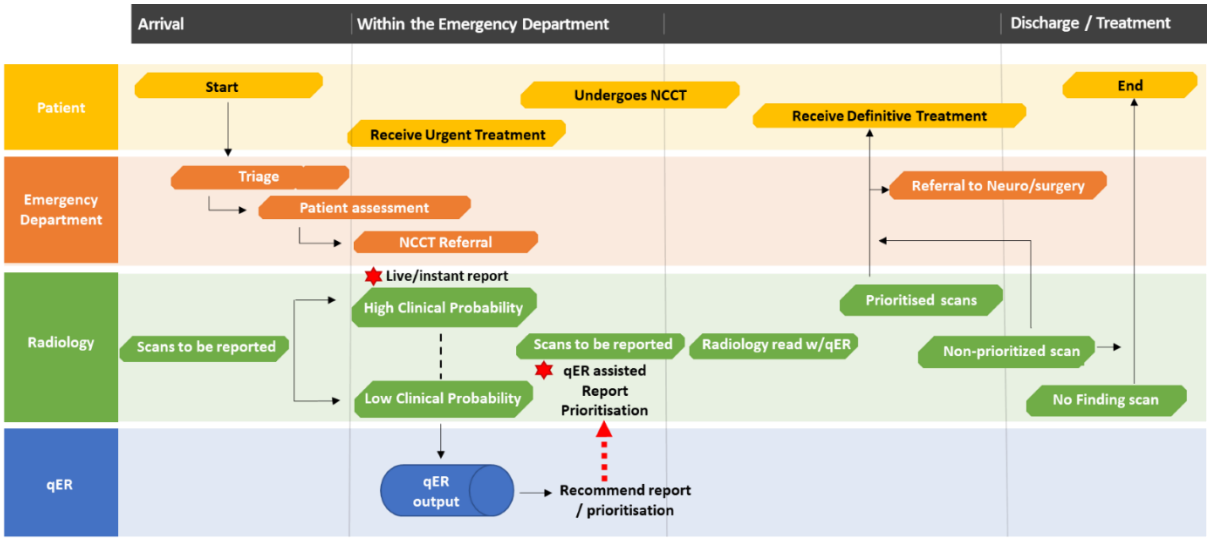

Figure 3: Example of current and proposed pathways for patients undergoing Head-NCCT scans from the Emergency Department.

"qER finding" workflow.

This will involve scans where qER identifies one or more of the target abnormalities which includes prioritised and non-prioritised findings. qER offers the opportunity to optimise NCCT finding detection. The study will integrate qER into ED clinical pathways (Figure 3). Images from ED pathway will be interpreted by qER and those identified to having the presence of any one or more of the prioritised findings will be flagged to radiologist for 'prioritised' reporting (allocated to duty radiologist). Along with the prioritised flag, radiologists can be provided with a secondary DICOM series with a contour that outlines the abnormality identified by qER. Following review, a radiology report will be generated and prioritised findings communicated to the ED clinician through existing escalation pathways. For scans where only non-prioritised finding have been detected by qER, they will also be flagged appropriately so that the reporting radiologist is informed of the same.

"No qER findings" workflow

qER also supports the workflow by ruling out target abnormalities. All images identified as absence of finding will be reviewed and reports verified.

6.1.2 Hospital Sites

Participating hospitals must undertake a significant number (3000) of NCCT Head within the Emergency Department per annum. Specialty leads from radiology and Emergency Department will be identified with support from their NHS Trust/Board to participate in the deployment of qER. Hospitals that have already deployed qER or similar AI-enhanced NCCT head will be excluded. Sites were identified that provide good representation of potential heterogeneity (geographical, population, ethnicity, population age).

An independent statistician will perform a computerised randomisation of the clusters and keep randomisation records prior to the beginning of the data collection. Simple randomisation will be used to randomise one trust to receive the intervention in each of the

time periods. Local investigators will be notified ~6 weeks in advance of activation qER tool at their hospital.

6.2 Primary Outcome Measure

Time taken to report NCCT head from acquisition for patients with prioritised findings in Emergency Department compared to standard of care.

6.3 Secondary Outcome Measures

Utility of qER compared to standard of care:

- Time taken from acquisition to report NCCT head for patients without prioritised findings in Emergency Department
- Time taken from acquisition to report completed for patients with absence of findings on NCCT head scans in Emergency Department
- To assess impact of qER on radiology reporting workflow on other requests for CT scans
- To assess impact of teleradiology on qER supported reporting
- Time to diagnosis from CT acquisition.
- Time to referral from CT acquisition.
- Time to initiation of treatment from CT acquisition for prioritised scans.
- Death within 28 days of NCCT head acquisition
- Percentage of NCCT heads that qER classifies as prioritised and absence of findings.
- Percentage of qER non prioritised scans that radiologist identified as having prioritised finding
- Percentage of qER non prioritised but identified by radiologist as absence of finding.

Technical Evaluation of product performance:

- Sensitivity, specificity, positive and negative predictive values of qER in detecting scans with prioritized findings overall and also stratified by all 6 target abnormalities.
- Percentage of CT scans that could not be processed by qER due to technical factors.

Safety of qER:

- To assess the safety of qER of identifying patients with no prioritised findings identified on NCCT head.
- Percentage of patient NCCT Head reported incorrectly as qER non prioritised.
- Time from acquisition to reporting of CT Chest Abdo Pelvis (CAP) and Pulmonary Angiograms (CTPA) within the trust.

Health economic assessment:

- Compare costs and health benefits between pre and post implementation of qER, including cost evaluation of fully automatic diagnosis of high confidence normal triage.

6.4 Technical Evaluation

The technical retrospective study will determine performance of the algorithm in each of the 4 sites. 500 NCCT scans will be identified for analysis from each site for technical evaluation. Sampling will be stratified by age, sex, month of year and target abnormalities.

The use of retrospective images and data has been approved by each site's Caldicott Guardian. In addition, approval for the release of anonymised patient data for research purposes forms part of the ethics application through IRAS.

6.4.1 Objective

- Evaluate performance of qER

6.4.2 Outcome measures

- Sensitivity, specificity, positive and negative predictive values of qER in detecting scans with prioritized findings overall and also stratified by all 6 target abnormalities.
- AUC of qER in detecting presence of 6 target abnormalities

6.5 Health Economic Assessment

6.5.1 Summary

An economic evaluation will be conducted comparing costs and outcomes of a current provision of care in the NHS and one inclusive of qER. qER potentially impacts costs and benefits via two mechanisms: (1) the identification of critical findings can improve radiology reporting times; and (2) the identification of critical findings can support optimisation of patients clinical care, accelerating the treatment and referral pathways, and ultimately better outcomes.

The proposed health economic approach is a cost effectiveness analysis where both the clinical and financial impact of qER will be captured. This approach is chosen in accordance with the guidance in NICE's Evidence Standards Framework (ESF) for digital health interventions (reference). The ESF recommends the development of a cost effectiveness analysis to demonstrate the value of digital health interventions that are deemed to be higher financial risk. qER is categorised as a tier C intervention and is considered to be a high financial risk since the aim is to commission qER on large scale or potential nationwide adoption.

A cost utility model will be developed that allows extrapolation from clinical evaluation endpoints to estimates of incremental costs and quality adjusted life years (QALYs), comparing the use of qER with standard of care. It is likely the model will adopt a lifetime time horizon to capture the potential benefits qER may have on outcomes such as patient survival, surrogates of patient survival and/or long-term disability.

In order to capture such value components in the model, the model requires additional parameter estimates describing prognosis, and the relationship between 'time to treatment initiation' and treatment outcomes, to enable the extrapolation from the endpoints to overall survival (or a surrogate of overall survival), treatment costs and QALYs. The model will only include direct medical costs associated with qER and standard of care as well as implementation and maintenance costs necessary for the integration of qER as outlined in NICE's ESF.

The results of the model will include scenario and sensitivity analysis (both probabilistic and deterministic). These will be founded on alternative variations of parameter utilisation and care pathway design identified through engagement with the clinical advisory team during external validation. For example, a comparison of trusts with the presence of stroke centres and those not.

The following steps will be undertaken to develop the model:

A targeted literature review of previous published health economic studies evaluating head CT.

Using the findings from the evidence review, the appropriate model framework will be chosen for the cost utility model e.g., a Markov model, or decision tree. The model pathway will replicate the current standard of care and capture key therapy area characteristics. The identified model pathway will be tested with key opinion leaders (both clinical and economic).

A further evidence review will be completed to identify any required data that will not be collected in the prospective or retrospective clinical study e.g., health utilities.

A prototype of the economic model will be built in Microsoft Excel, incorporating the agreed data points with a focus upon key outputs of interest. The prototype will be completed in line with the interim results of the prospective and retrospective study to produce early cost effectiveness results. Updates to the model structure may be made to refine the economic value story.

A complete version of the economic model will be produced using results of the clinical trials. Results will be tested with clinical experts as well as an external health economist to the primary modelling team.

The results and version of the model will be documented along with a model quality assurance report.

Methods and results to be presented in a peer-reviewed manuscript suitable for submission to a peer reviewed journal.

6.5.2 Objective

Compare costs and health benefits between pre and post implementation of qER and the associated ratios between the two to examine whether the ratio meets willingness to pay thresholds observed in England (i.e. £20,000 to £30,000 per QALY gained).

6.5.3 Health Economic Data

The data elements that will be used for the analysis of health economic assessment are listed below:

Intervention and comparator

- Numbers of ground truth positive and ground negative cases
- Al false positives, true positives, false negatives, true negatives

- AI output (+/- per disease)
- Radiologist output and/or agreement with AI decision per scan
- Time of admission to ED
- Time (with and without qER) of CT scan
- Time (with and without qER) time to ER physician viewing scan
- Time (with and without qER) to radiologist open scan
- Time (with and without qER) to radiologist report / close scan
- Time (with and without qER) ER physician opens report
- Time (with and without qER) to onwards referral
- Time (with and without qER) to treatment (need specific treatment per speciality pathway e.g. time to embolisation, time to surgery etc)
- Time to AI output delivered to PACS

Resource Use

- Number of head CTs performed out of hours
- Number of head CTs performed in hours
- Definition of in and out of hours per trust
- Reason for the scan (primary suspected diagnosis and/or main symptom)
- Death
- Reattendance to hospital with same presentation
- Transfer to other hospital
- Admission to same hospital, including care pathway
- Clinical diagnosis, including sub-type and severity of (e.g ASPECTS score for stroke, any relevant head trauma scales)
- False negative outcomes (e.g. missed diagnoses and severity)
- False positive outcomes (e.g. misdiagnosis and severity)
- Length of stay and wait in the ED
- Length of stay in hospital / wait to transfer

Costs

- AI implementation, maintenance, training, per scan costs
- Treatment cost per pathway/speciality (to be sourced from published literature)
- ED visit cost (to be sourced from published literature)
- Cost of hospital admission (to be sourced from published literature)
- Cost of hospital transfer (to be sourced from published literature)
- Cost by ward type (to be sourced from published literature)
- Cost of outsourcing CT head reading in and out of hours (to be sourced from published literature)

Utilities

- Will be applied to patient outcomes (values to be sourced from published literature)

6.6 Ground Truth

Both the prospective (stepped wedge) and retrospective (technical evaluation) elements of this study compare the performance of qER against ground truth and

ground truthing is required for confirming which scans contain a prioritised finding and not.

The following **prospective** scenarios (i.e. from the stepped-wedge study) will require independent generation of ground truth by two post-fellowship radiologists (and an arbitrating senior radiologist, where there is interobserver disagreement):

- All images where radiologist disagrees with the qER assessment.

Head-NCCT scans where original reporting radiologist agreed with Qer assessment will not be sent for ground truthing and the original report will be considered as the ground truth for such scans.

All NCCT head images will be reviewed by trust radiologist. Those that the trust radiologist disagrees will require independent generation of ground truth by two post-fellowship radiologists (and an arbitrating senior radiologist, where there is interobserver disagreement).

An image will be presented to ground truth radiologists only after the result has been generated by qER. Images from all sources will be presented in a single list for ground truth generation, so that radiologists cannot identify the source (i.e., whether the ground truth is necessary because there was a discrepancy, or not). All images will be deidentified to ensure the radiologist cannot identify the patient and thereby view the corresponding AI result or seek additional supporting clinical data to make a ground truth decision.

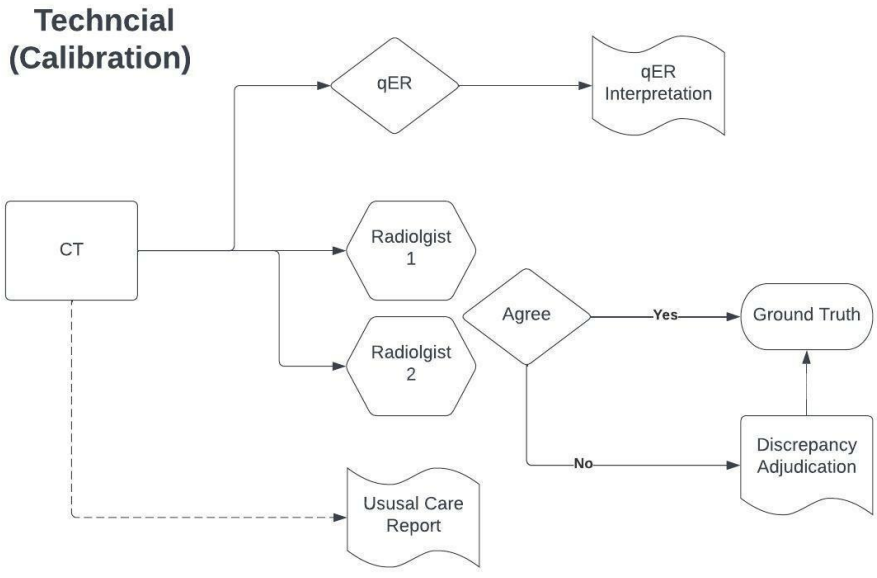

Figure 4: Ground truth for retrospective data.

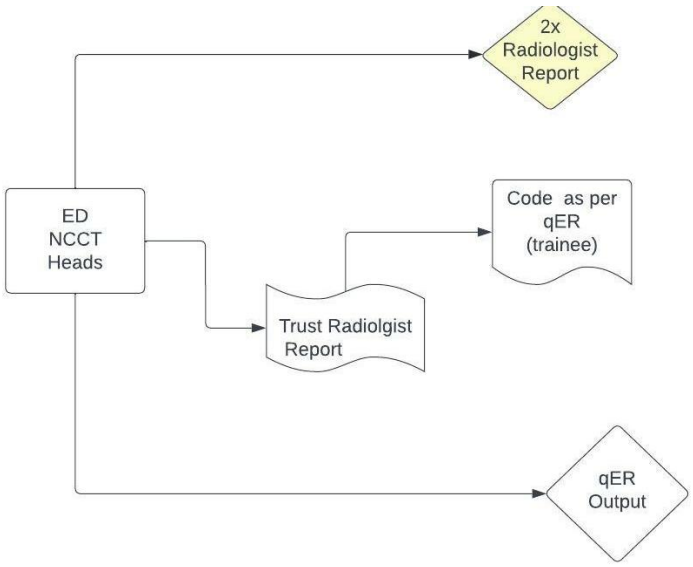

Figure 5: Ground truth for prospective data.

7 PARTICIPANT SELECTION

7.1 Study Population

At each of the four participating sites, we will identify all patients referred through the Emergency Department NCCT requests. Expected number of eligible participants and rationale behind sample sizing are detailed in the 'STATISTICAL CONSIDERATIONS' section.

7.2 Participant inclusion criteria

- Individuals undergoing Head CT scan at the ED / A&E (Accident and Emergency Services).
- Age ≥ 18 years.
- Non-contrast axial CT scan series with consistently spaced axial slices.
- Soft reconstruction kernel covering the complete Brain.
- Maximum slice thickness of 6mm.

7.3 Participant exclusion criteria

- There are no explicit exclusion criteria for qER as all scans in inclusion criteria will be processed by qER. Exclusion criteria are implicit within the inclusion criteria listed above.

8 STUDY PROCEDURES

8.1 Consent

The study intervention is randomised and applied at an institutional level, and therefore individual patient consent is not required. We will not seek individual patient consent.

Data will be captured by the direct care team and anonymised before transfer to central research team at GSTT. Approval for the release of anonymised patient data for research purposes is integral to the ethics application through IRAS.

Under UK GDPR a patient may object to their data being used under certain circumstances. Should a patient involved in this study object to their data being used, then this will be processed by the site's information governance team using local standard operating procedures. If the objection is upheld, then the patient's data will be removed from the study.

qER solution is deployed through individual site agreements with qER, which include a local data processing agreement. Data sharing between sites and GSTT is governed by individual site data sharing agreements.

GP practices in the trust will be notified of the change in pathway through communication with each practice within the trust (GP letter in the Appendix).

Posters will be displayed within each radiology and emergency department detailing the deployment of qER to support radiology reporting (NHS service user/patient poster). Leaflets providing additional detail of the tool will be available on request (supporting patient information leaflet).

A patient co-investigator has reviewed early drafts of this protocol and we are planning on working with PPI groups in London and Oxford to provide further feedback on patient experience.

8.2 Sampling

During the pre-implementation period, data will be gathered on the current clinical pathway. Each site will provide data on volume of images and time periods from referral to acquisition and reporting of NCCT heads. This data collected during pre-implementation period will serve as the baseline data for final study analysis.

8.3 Data Collection

Evaluation sites will periodically collect, clean, link, de-identify and supply data in an agreed format, beginning with baseline data from the pre-implementation phase until the end of the post-implementation phase. The frequency of data collection is subject to change though depending on the feasibility of sites.

A data dictionary will be supplied (example included in the Appendix) that will support fulfilling these requirements from:

Extraction of routinely collected hospital data:

- Referral Data: Age, Sex, date of referral for CT, date of appointment. Where possible ethnicity and deprivation will be captured.

- Radiology Data: Number of referrals, Datetime CT acquired, Datetime CT reported, presence or absence of discordance between qER and reporting radiologist, CT device manufacturer/ type, Usual Care Report
- Clinical Data: Clinical Diagnosis, treatment initiation, referral, including date of death if applicable.
- Follow-up Data: Length of stay ED, Length of stay Hospital, Specialty pathway.
- qER data outputs from qER interpretation
- Changes in treatment pathways after implementation
- Time to diagnosis

Data linkage for follow-up (death within 28 days of Head-NCCT acquisition date) against outcomes will be collected for 28 days.

8.4 National Data opt-out.

If patient has selected National Data opt-out, their data will be excluded from final analysis.

8.5 Follow up Procedures.

Data linkage for follow-up (death within 28 days of Head-NCCT acquisition date) against outcomes will be collected 28 days after the Head-NCCT acquisition date.

9 MEDICAL EQUIPMENT (DEVICES)

qER, a CE Class II approved medical software device, detects, and localizes the presence of six target abnormalities - intracranial haemorrhage, cranial fracture, midline shift, mass effect, atrophy and hypodensities suggestive of infarcts in non-contrast Head-CT scans[7]. It uses pre-trained artificial intelligence algorithms to detect the presence or absence of the target abnormalities in Head-NCCT scans. This device has not been modified for the purpose of this research and will be used within its intended use for this study. The device will be deployed in all the four participating sites for the purpose of this study.

A priority status is assigned if any one of the target abnormalities (intracranial haemorrhage, cranial fracture, midline shift or mass effect) is detected by the software, and the user will be able to view a single summary slice listing all the target abnormalities found by qER on the CT scan followed by all slices in scan with the overlay of above abnormalities localization. Alternately, if none of the target abnormalities are detected, the output will indicate that the software has analysed the image and identified no critical findings. qER reports are intended to support certified radiologists and/or licensed medical practitioners for clinical decision making. It is a support tool and, when used with original scans, can assist the clinician to improve efficiency, accuracy, and turnaround time in reading head CTs. It is not to be used to provide medical advice, determine treatment plan, or recommend a course of action to the patient.

This study has been awarded funding from NHSx AI Award (Award reference: AI_Award02354).

Funding for the study team to deploy and use qER for the study purpose, to perform its analysis of the data gathered from sites, and to produce a final report, is confirmed under the research contract between Qure.ai (manufacturer of qER) and Guys and St Thomas' NHS Foundation Trust.

10 END OF STUDY DEFINITION

The end of the study is defined as the end of the 13th month following the study start date. Final data analysis shall follow this.

11 ASSESSMENT OF SAFETY

11.1 Definitions

Adverse events (AE)	An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether related to the investigational medical device or not. Note 1 to entry: This definition includes events related to the investigational medical device or the comparator. Note 2 to entry: This definition includes events related to the procedures involved. Note 3 to entry: For users or other persons, this definition is restricted to events related to the use of investigational medical devices.
Serious Adverse Event	An adverse event that led to any of the following: a. death, b. serious deterioration in the health of the subject, users or other persons as defined by one or more of the following: 1. a life-threatening illness or injury, or 2. a permanent impairment of a body structure or a body function including chronic diseases, or 3. in-patient or prolonged hospitalisation, or 4. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c. foetal distress, foetal death or a congenital abnormality or birth defect including physical or mental impairment.

	Note 1 to entry: Planned hospitalisation for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.
Serious adverse device event (SADE)	A serious adverse device effect (SADE) is any adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. A SADE may be anticipated or unanticipated.
Unanticipated Serious Adverse Device Effect (USADE)	Unanticipated serious adverse device effect (USADE) is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

Recording and Reporting of Adverse Events

AEs must be recorded, assessed, reported, analysed, and managed in accordance with the Research Governance Framework for Health and Community Care and the study protocol. All AEs must be assessed for seriousness. AEs for this study will be recorded within the patient notes but are not considered reportable.

Recording and Reporting of Serious Adverse Events

Where an SAE requires recording; full details including the nature of the event, start and stop dates, severity, causal relationship to the device and/or trial procedures, and the outcome of the event will be recorded in the patient's medical notes. These events will be monitored and followed up until satisfactory resolution and stabilisation.

Assessment of causality

I.e., does the event have a "reasonable causal relationship" with any trial specific procedures or the investigational device?

The assessment of causality must be carried out by the PI or other medically qualified local investigator.

Assessment of expectedness

If the SAE is considered related to any trial specific procedures or the investigational medical device an assessment should be made of the expectedness i.e., is the SAE a recognised adverse effect of the investigational medical device or a trial procedure.

Reporting to Sponsor

The following events defined as USADEs are considered reportable to the sponsor.

- Any Serious Adverse Event that is considered related to the trial specific procedures, or the medical device(s) that is considered unexpected by the Chief Investigator or their delegate.
- Any device related serious adverse event that led or may have led to one of the following outcomes:
- The death of a patient
- A serious deterioration in the health of a patient.

A serious deterioration in health may include (non-exhaustive):

- Life threatening illness

- Permanent impairment of a body function or permanent damage to a body structure
- A condition necessitating medical/surgical intervention to prevent a) or b)
- Foetal distress or death, or any congenital anomalies or birth defects.

SAEs meeting the above criteria must be reported to the Pharmacovigilance (PV) Office immediately (within 24 hours) using the SAE form for a non CTIMP. The SAE form should be completed and signed by appropriately delegated staff. The form should be e-mailed to the PV Office and a copy placed in the Study Site File.

If all the required information is not available at the time of initial reporting, the CI (or designee) must ensure that any missing information is forwarded to the PV Office as soon as this becomes available. The report should indicate that this information is follow-up information for a previously reported event.

11.2 Ethics Safety Reporting

Reporting of USADEs to the REC and IRIC
The Sponsor will report all USADEs to the ethics committee within 15 days of the PV office becoming aware of the event, via the 'report of serious adverse event form' for non-CTIMPs published on the Health Research Authority web site.

The form will be completed in typescript and signed by the Chief Investigator. The CI or delegate will submit reports relating to the medical device that meets the above criteria to the Incident Reporting and Investigation Centre (IRIC – part of NHS National Services Scotland).

Annual reports to REC
Annual progress reports will be made on the anniversary of the original REC approval.

Once the study has ended, we will declare the end of study to the Research Ethics committee (REC) that gave a favourable opinion within 90 days of the study ending using the appropriate method. This will be followed up with the final report within 12 months of the end of the study.

11.3 Study Management

11.3.1 Trial Steering Committee

No Trial Steering Committee is required for this study.

11.3.2 Trial Management Group

A Trial Management Group (TMG) will convene consisting of the representatives from the Sponsor (GSTT) including the CI, co-investigators, statisticians, PPI leads and the Study Manager (including project managers from each participating Trust). The role of the group is to monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of the trial itself.

11.3.3 Data Monitoring Committee

No Data Monitoring Committee is required for this study.

11.4 Ethics & Regulatory Approvals

Prior to commencing the study, approval will be sought from an appropriate REC. The research will be undertaken in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki. The CI will be responsible for updating the Ethics committee of any new information related to the study.

11.5 Protocol Amendments

Any change in the study protocol will require an amendment. Any proposed protocol amendments will be initiated by the CI following discussion with the sponsor and any required amendment forms will be submitted to the ethics committee and sponsor.

The CI will liaise with study sponsor to determine whether an amendment is non-substantial or substantial. All amended versions of the protocol will be signed by the CI and Sponsor representative.

Before the amended protocol can be implemented favourable opinion/approval must be sought from the original reviewing research ethics committee (REC) and Research and Development (R&D) office.

12 COMPLIANCE AND WITHDRAWAL

12.1 Participant compliance

Not applicable for this study as data is collected only from the existing data records. Specific study participant interviews are not required for the study data collection and there will be no change in standard of care.

12.2 Withdrawal / dropout of participants

If patient has selected National Data opt-out, their data will be excluded from final analysis. Patients who wish to withdraw their data from being used in this research will be removed from analysis prior to anonymisation. Data extracted will be destroyed and the patient withdrawn from this part of the study if requested. The contact information for the research team will be made available to patients through posters and other publications within the department to allow them to express their wish to withdraw their data from the research.

12.3 Protocol Compliance

The CI will monitor any protocol deviations and list them in a deviation log /include a file note in the TMF/Site file where applicable. Significant deviations to the protocol or deviations which are found to frequently recur will be assessed by the CI to see if an amendment to the Protocol is required. These will be reported to the sponsor and action taken through Corrective and preventative Actions (CAPA). The CI and sponsor will be notified immediately of a serious breach, where applicable. The Breach will be reported to the REC Committee with the Sponsor in copy within 7 calendar days of the breach being confirmed as serious.

13 DATA

13.1 Data to be collected:

Evaluation sites will periodically collect, clean, link, de-identify and supply data in an agreed format, beginning with baseline data from the pre-implementation phase until the end of the post-implementation phase. The frequency of data collection is subject to change though depending on the feasibility of sites.

A data dictionary will be supplied (example included in the Appendix) that will support fulfilling these requirements from:

Extraction of routinely collected hospital data:

- Referral Data: Age, Sex, date of referral for CT, date of appointment. Where possible ethnicity and deprivation will be captured.
- Radiology Data: Number of referrals, Datetime CT acquired, Datetime CT reported, presence or absence of discordance between qER and reporting radiologist, CT device manufacturer/ type, Usual Care Report
- Clinical Data: Clinical Diagnosis, treatment initiation, referral, including date of death if applicable.
- Follow-up Data: Length of stay ED, Length of stay Hospital, Specialty pathway.
- qER data outputs from qER interpretation
- Changes in treatment pathways after implementation
- Time to diagnosis

Data linkage for follow-up (death within 28 days of Head-NCCT acquisition date) against outcomes will be collected for 28 days.

Data dictionary is attached as a separate document (Appendix 5).

13.2 Data handling and record keeping

Raw medical data from clinical information systems shall be anonymized using native anonymizing export functions that are available using applications. Where a native anonymizing facility is not available to the researcher, other bespoke methods will be provided depending on the datatype (e.g. DICOM images, JSON files etc.).

13.3 Data sharing

The qER algorithm only analyses the NCCT Images and is done on site. GSTFT will act as the central research team. A clinical research fellow will collect anonymized data from the other sites for the final analysis. This data will be shared by other research sites through a secure KCL repository for the duration of the study in a password-protected database on an encrypted hard drive. This data will not be added to a public/private data repository at the end of the study period.

13.4 Information Governance and Security

Each site will have a data processing agreement (DPA) or equivalent with qER to cover the interpretation of NCCT. Each site, with the assistance of qER, GSTT and other internal stakeholders as appropriate, will produce a Data Protection Impact Assessment (DPIA) and a

System Security Policy (SSP), or local alternatives. These will be substantively similar to the templates in Appendix. A site may require further information governance and security documentation (e.g., imaging governance assessments, etc.), depending upon local operating procedures. We will produce a single 'master' DPIA and separate SSP for the project, which can be amended as necessary for each site.

As Qure.ai are compliant with the ISO27001 information security standard and use a commonly accepted approach to processing patient and personal data within a healthcare environment, we expect that sites will accept their information handling and systems approach.

13.5 Personal Data Breaches

Personal data breaches will be immediately reported to the Sponsor/data controllers and to the Data Protection Officer/IG Department of the site that incurred the breach. The following information will be provided to assess the full risk/impact of the breach: full details as to the nature of the breach, an indication as to the volume of material involved, and the sensitivity of the breach (and any timeframes that apply), steps that have been taken to mitigate the risk (trying to retrieve the data asking third parties to delete information that was sent to them in error).

Sites will additionally follow their Trust incident reporting mechanisms and will document this within their TMF/ISFs in the form of a file note provided by the sponsor with corrective and preventative measures addressed.

The sponsor/data controller will determine whether the breach meets the definition of a serious breach and warrants reporting to the regulators including the ICO.

14 MONITORING AND AUDITING

The Chief Investigator will be responsible for the ongoing management of the study. The Sponsor will monitor and conduct audits on a selection of studies in its clinical research portfolio. Monitoring and auditing will be conducted in accordance with the UK Policy Framework for Health and Social Care and in accordance with the Sponsor's monitoring and audit procedures.

15 STATISTICAL CONSIDERATIONS

15.1 Sample Size

The sample size available for analysis is determined by the number of hospitals taking part in the study and the number of patients coming through the Emergency Department requiring a NCCT during the study period.

The proposed study is a stepped-wedge trial, in which all participating sites will receive the intervention, in a random order, throughout the study period. With 4 participating sites, within a 12-month study period, study sites will receive the intervention in a staggered manner (Figure 1). During the study, each site will have received the intervention at a certain time-point. The specific time point for when the site is will be switched from current standard pathway group to intervention group will be allocated based on randomisation procedure.

Baseline data for all sites prior to the start of the study will be available from electronic records. Follow-up data will be available throughout the study period, including at least 3 months post-intervention at all sites. It is likely that changes in treatment pathways after implementation will take time to reach a steady state, and one of the objectives of any analysis will be to model the transition from the pre-intervention to post-intervention state.

This design has elements of a cluster-randomised trial, and of a before-and-after study. Within each site, there will be sufficient statistical power to detect a 20% change in average outcomes (TAT measure) achieved before and after the implementation of the intervention.

The power estimations were conducted via a simulation approach. The range of conditions for sample size and intraclass correlation coefficient (ICC) were tested. The values of sample sizes tested ranged from 120 to 600 abnormal scans per site per year, while the range of ICC ranged from 0.05 to 0.30. Assuming type I statistical error at the α=0.05 level and the total duration of the study 12months the generalized linear mixed-effect regression model (GLMM) with expected distribution of the outcome variable Gamma the total sample size of 1,680 abnormal scans (35 abnormal per site/month; total yearly per site 420) ensures satisfactory level of statistical power exceeding 80% for detecting reduction in TAT by 20%. The models were estimated for abnormal cases. Assuming that abnormal cases are only ~10% of all CT scans performed at sites it can be expected that the total number of available scans in this study will be 16,800. Simulations were performed in R version v.4.1.0. If the study was conducted in a single hospital, this would not provide definitive evidence. However, if a similar impact is observed across four sites, especially if the time course of changes in multiple outcomes track the implementation of the intervention within each site, then the study will provide compelling evidence of the impact of the intervention. Given the expected amount of data that will be generated as part of the study, then it is expected that there will be good power to detect intervention effects within subgroups of patients, defined by age, sex, deprivation, and final diagnosis.

15.2 Statistical Analysis Plan

To investigate the reduction in TAT (the outcome variable) the multistage data analysis process will be applied in the study. Initial statistical analyses will consist of basic descriptive analyses, and within-site descriptions of changes in outcomes relating to the patient pathway. As a first step also the graphical inspection of the distributions of variables at each site and time points will be conducted. At this stage the shape of the distribution of outcome variable will be assessed. All outlying observations will be detected and checked. In the next step exploratory univariate analyses will be applied. Since the outcome variable is expected to be continuous and highly right-skewed, we are going to apply non-parametric tests Wilcoxon tests to compare the outcome variables between pre- and post-intervention at each site.

In the second step generalized linear mixed-effect regression model (GLMM) will be applied to the data. The assumed structure of the data will be multilevel with measures nested within sites. The specific model to be applied is going to be GLM rather than normal linear regression model since the distribution of the outcome variable is expected to be Gamma (a non-negative continuous values, right skewed). Within our modelling process we will be controlling for study centre, intervention, calendar month, after-hours reporting, individual patient diagnosis

(ground truth indicating bleed, infarct, presence/ absence of midline-shift, mass-effect, and cranial fracture).

The regression coefficients obtained after the model fit will be investigated to find if there is statistically significant reduction in TAT with qER based reporting and triage. Specifically, the applied models will be used to explore the time course of outcomes within sites, in relation to the timing of the implementation of the intervention, allowing for differences between sites, and over time across all sites. Results will be adjusted for individual patient characteristics.

16 PEER REVIEW

The protocol has been reviewed by all investigators including principal investigators from each site, clinical research science team at Qure.ai (manufacturer of qER), study statistician, members of the PPI group and members of trial management group.

17 FINANCING

This study has been awarded funding from NHSx AI Award. Funding for the study team to deploy and use qER for the study purpose, to perform its analysis of the data gathered from sites, and to produce a final report, is confirmed under the research contract between Qure.ai (manufacturer of qER) and Guys and St Thomas' NHS Foundation Trust. Funding for evaluation sites (those contributing data to the study) is allocated from the AI award to the technology provider (Qure.ai).

Award reference number: AI_Award02354.

18 INSURANCE AND INDEMNITY

This study is sponsored by Guy's and St Thomas' NHS Foundation Trust (GSTFT) and indemnity is provided through NHS Resolution's Clinical Negligence Scheme for Trusts (CNST) which provides indemnity for clinical negligence. In the case of negligent harm, health care professionals undertaking clinical trials or studies on volunteers, whether healthy or patients, during their NHS employment are covered by NHS Resolution. In the case of non-negligent harm, legal liability does not arise where a person is harmed but no one has acted negligently. In exceptional circumstances NHS bodies may consider whether an ex-gratia payment could be offered.

19 DATA CONTROLLER

Guy's and St Thomas' NHS Foundation Trust is the Data Controller as defined by UK general data protection legislation (UK GDPR) for this study and as such agrees to comply with the obligations placed on a Data Controller by the UK GDPR. This is not limited to, but includes, being responsible for and able to demonstrate compliance with the principles relating to Processing of Personal Data (Article 5 UK GDPR).

20 REPORTING AND DISSEMINATION

The results from this study will be presented at AI, radiology, and emergency medicine meetings, and published in high-impact peer-reviewed journals in collaboration with all investigators.

Useful reading/websites

Integrated Research Application System (IRAS)
https://www.myresearchproject.org.uk/

Health Research Authority (HRA)
www.hra.nhs.uk

HRA Guidance for Patient Information Sheet and Informed Consent
http://www.hra.nhs.uk/research-community/before-you-apply/participant-information-sheets-and-informed-consent/

CONSORT statement ICH Harmonised Tripartite Guidelines for Good Clinical Practice (1996)
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

Martin Bland et al, Statistical guide for research grant applications
http://www-users.york.ac.uk/~mb55/guide/guide.htm
Includes detailed information and definitions of many aspects required for a research protocol.

Declaration of Helsinki
(http://www.wma.net/en/30publications/10policies/b3/index.html)

21 REFERENCES

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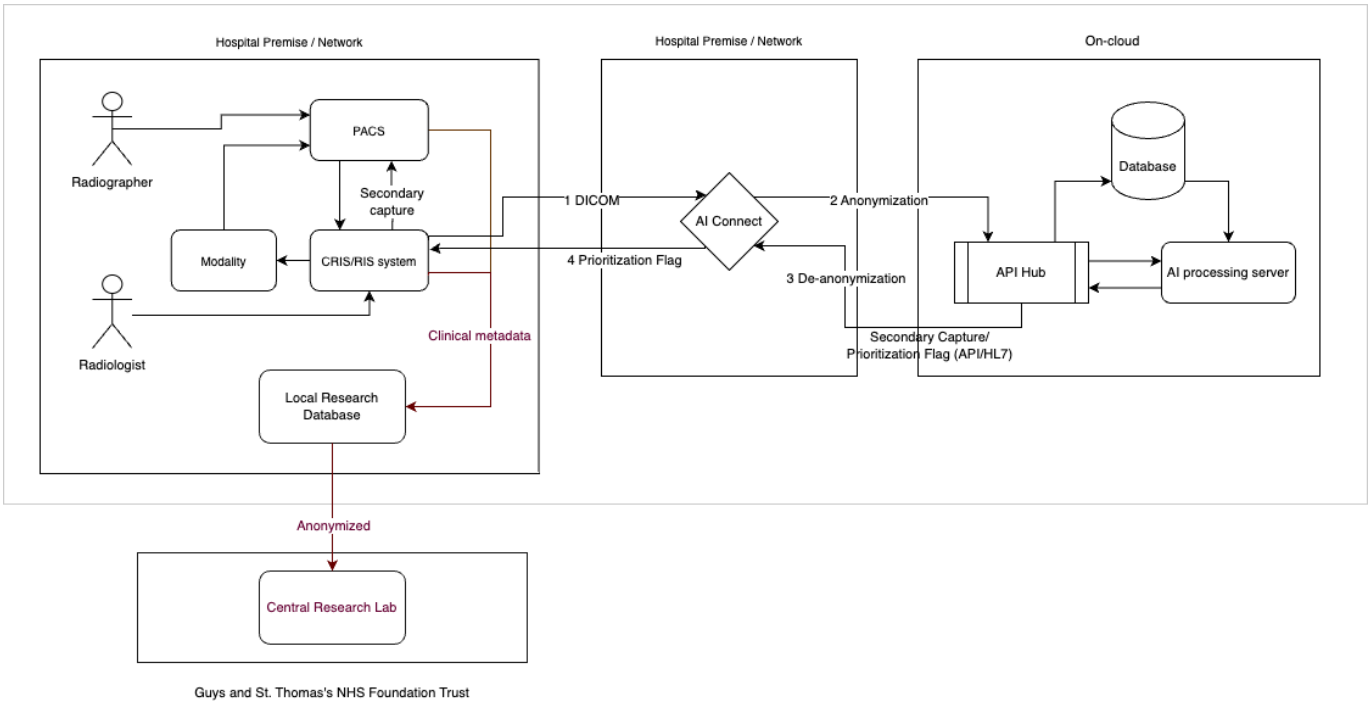
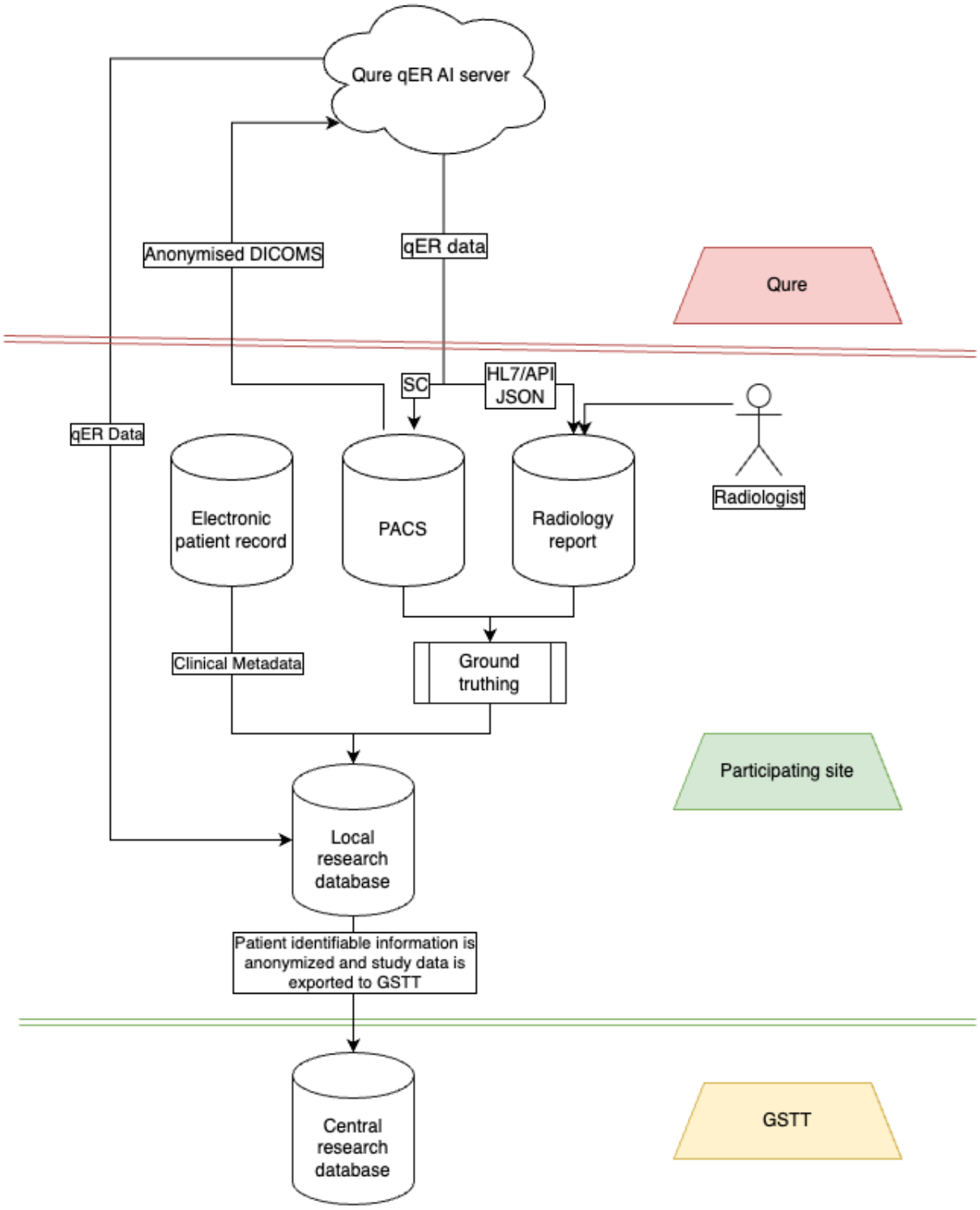
7. Chilamkurthy, S. *et al.* Deep learning algorithms for detection of critical findings in head CT scans: a retrospective study. *Lancet* **392**, 2388–2396 (2018).

APPENDIX 1
DATA FLOW DIAGRAM FOR DATA LEAVING TRUST/SITE PREMISES.

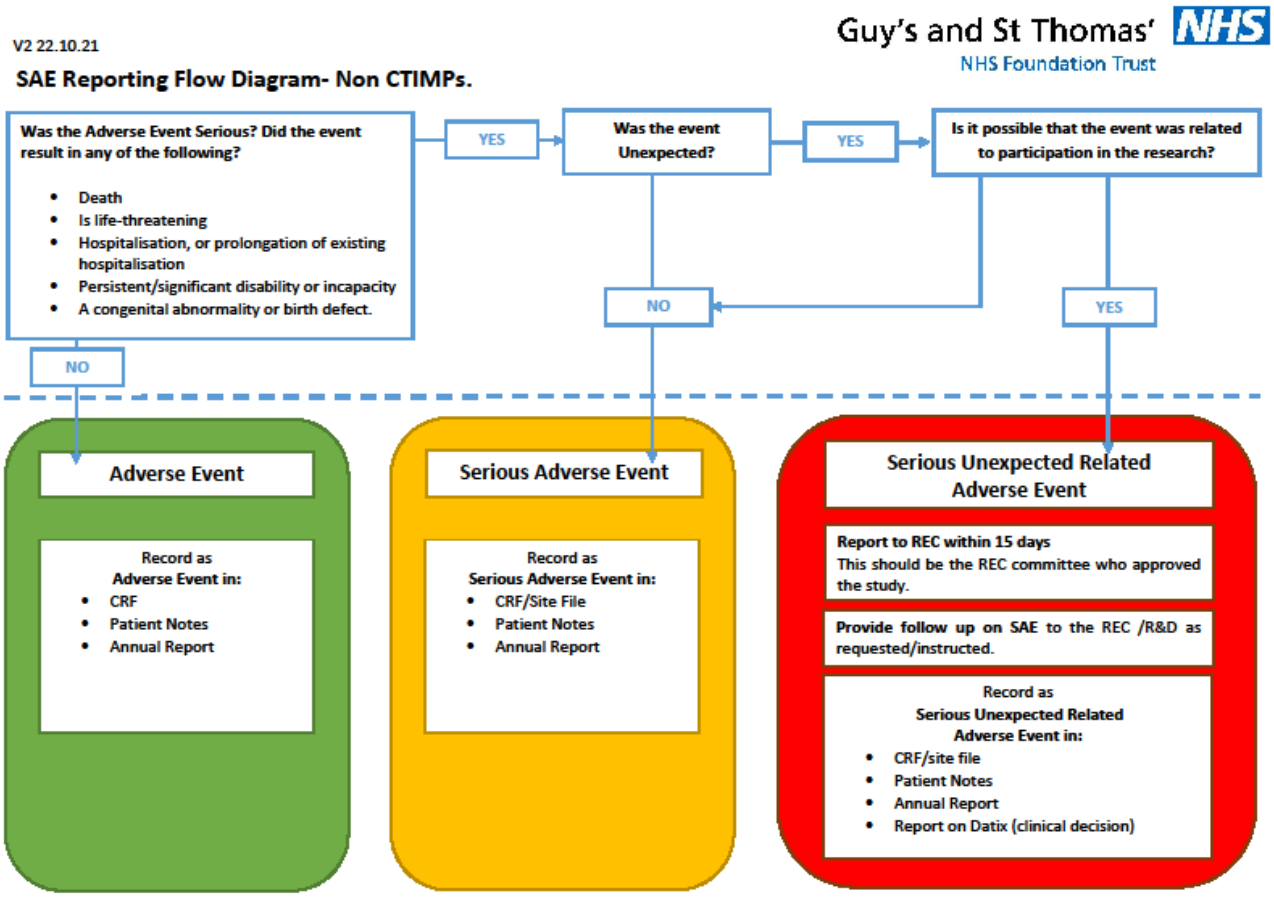
Site collected	Formats	Data items	Stored	Transfer Methods	Locations	Return of data to Sponsor at the end of trial
Hospital	Electronic	anonymous: CRF data, radiologist ground truth assessment	Data will either be entered into eCRF database or sent via encrypted and password-protected Excel files	Web, Email	Data sharing with Guy's & St Thomas' NHS Foundation Trust for analysis.	Compiled/analysed data will be transferred to GSTFT in accordance with their data transfer protocols.




Qure qER AI server
Anonymised DICOMS
qER data
Qure
SC
HL7/API
JSON
qER Data
Electronic patient record
PACS
Radiology report
Radiologist
Clinical Metadata
Ground truthing
Participating site
Local research database
Patient identifiable information is anonymized and study data is exported to GSTT
Central research database
GSTT

APPENDIX 2

SAE Reporting Flow Diagram-Non CTIMPs



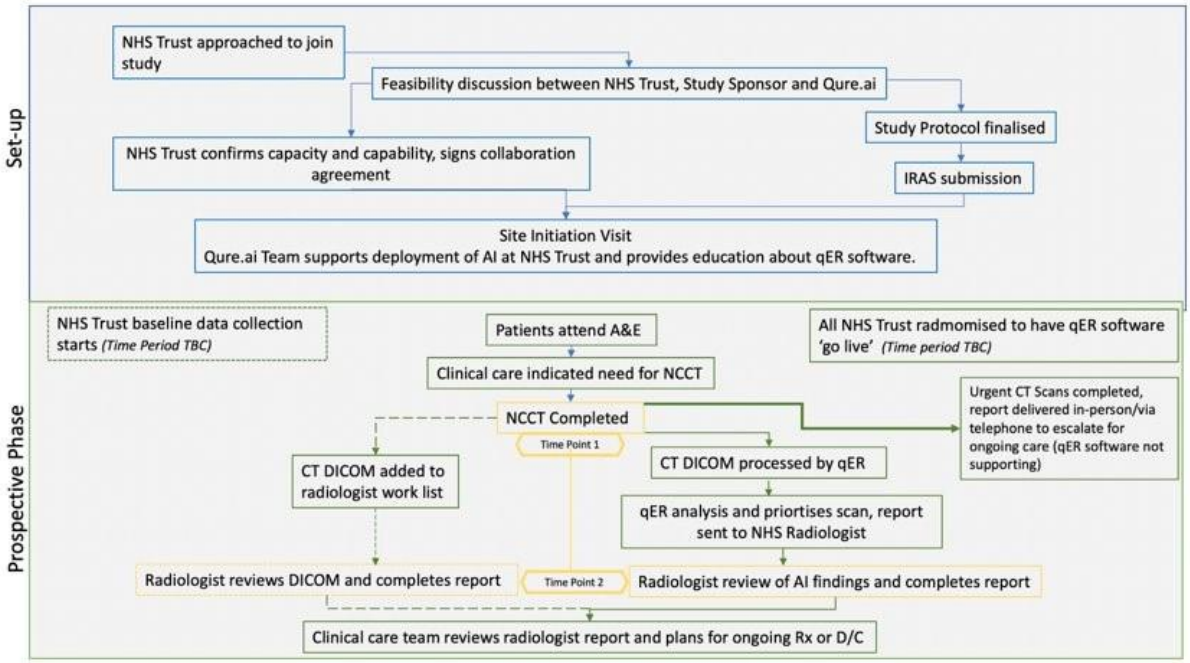
APPENDIX 3

Information with regards to Safety Reporting in Non-CTIMP Research

	Who	When	How	To Whom
SAE (related and unexpected)	Chief Investigator	-Report to Sponsor within 24 hours of learning of the event -Report to the MREC within 15 days of learning of the event	SAE Report form for non-CTIMPs, available from NRES website.	Sponsor and MREC
Urgent Safety Measures	Chief Investigator	Contact the Sponsor and MREC Immediately Within 3 days	By phone Substantial amendment form giving notice in writing setting out the reasons for the urgent safety measures and the plan for future action.	Main REC and Sponsor Main REC with a copy also sent to the sponsor. The MREC will acknowledge this within 30 days of receipt.
Progress Reports	Chief Investigator	Annually (starting 12 months after the date of favourable opinion)	Annual Progress Report Form (non-CTIMPs) available from the NRES website	Main REC with a copy to be sent to the Sponsor
Declaration of the conclusion *or* early termination of the study	Chief Investigator	Within 90 days (conclusion) Within 15 days (early termination) *The end of study should be defined in the protocol*	End of Study Declaration form available from the NRES website	Main REC with a copy to be sent to the sponsor
Summary of final Report	Chief Investigator	Within one year of conclusion of the Research	No Standard Format However, the following Information should be included: Where the study has met its objectives, the main findings and arrangements for publication or dissemination including feedback to participants	Main REC with a copy to be sent to the sponsor

APPENDIX 4

Study Flowchart



APPENDIX 5

Data Dictionary

5.1. Summary

A data dictionary of a study explains exactly what data will be collected by each site and in what format. It explains the record type level (e.g., pre-scan, scan, post-scan, etc.) and attribute level (e.g., patient identifier, age, sex, date of referral, etc.) requirements. It can only be produced after an analysis of the data available at each site, to ensure study-wide consistency.

It will incorporate the following:

- Cohort and data selection criteria
- Source data format
- Data schema (record types along with their attributes, attribute formats, attribute capture requirement and attribute description)

5.2 Cohort and data selection criteria

A common set of cohort and data selection criteria will be developed once the study team has selected the sites and discussed the detailed format and content of their clinical records. The data in each site is likely to differ, especially across regional boundaries (e.g., CDS datasets in England versus SMR datasets in Scotland). The existing clinical protocols are also likely to differ between sites, which influences the way in which data is sequenced, modelled, and stored.

5.3 Source data format

Each site will provide a single file for each record, once every three months (to be defined in consultation with each site). Each file will be in CSV format, with a fixed number of commas separated values, each pertaining to an attribute as defined within the schema for that record type.

The naming convention will be:

<Site ID>_<Batch ID>_<dataset short name>_<version number>.csv

Where:

- 'Site ID' is the number allocated to as site by the study team
- 'Batch ID' is the sequential number indicating the 3-monthly batch that the file relates to (e.g., the first batch is 1, after 3 months the next batch is 2, etc.)
- 'Dataset short name' is the short name for the dataset within the file (e.g., 'patientcore', 'referrals', 'labresults', etc.)
- 'Version number' is used where the same data needs to be sent more than once, perhaps because of quality issues in the previous file. It increments each time a new version of a file is sent.

An example record format for patient demography might be as follows:

<Patient identifier, postcode sector, age, sex, ethnicity>

98740833,ML5 2,63,male,1A

89837748,AB43 6,27,female,5B

The exception will be AI results files and ground truth records, which will be linked and returned as individual json format files within compressed folders. These folders will be named as follows:

<Site ID>_<Batch ID>_<dataset short name>_<version number>.zip

Where:

'Site ID' is the number allocated to a site by the study team

'Batch ID' is the sequential number indicating the 3-monthly batch that the file relates to (e.g., the first batch is 1, after 3 months the next batch is 2, etc.)

'Dataset short name' is the short name for the datasets within the file. It will be 'airesults' for the AI results files and 'gtresults' for the ground truth results files.

'Version number' is used where the same data needs to be sent more than once, perhaps because of quality issues in the previous file. It increments each time a new version of a file is sent.

5.4 Schema

The following record types are to be extracted from routinely collected clinical data or data that is made readily available through the qER platform or from clinical fellow's report after he/she reviews the NHS trust radiology reports.

- Pre-scan
- Scan
- Post-scan
- Ground truth

Limitations of documented schema

- The list of attributes in each of the record types is not a comprehensive list. Additional attributes for study analysis may be **derived** from attributes listed below for each of the four record types during the study analysis phase of the study as applicable.
- The record types and attributes listed below are not the same as short datasets. A subset of attributes within each record type or a combination of attributes between multiple record types may constitute a short dataset depending on the feasibility of data capture. All record types will have one or more unique identifiers which can be used to merge multiple record types or multiple short datasets.

5.4.1 Pre-scan

This record type contains all attributes that are collected before a Head NCCT scan is completed for the patient in the study

	Attribute	Data type	Mandatory	Description	Source
1	Site identifier	Varchar	Yes	The identifier allocated by the study	Assigned

				team to the site which this patient belongs.	
2	Study patient identifier	Varchar	Yes	Unique Identification number given to each patient whose data is being analysed for the study.	Assigned
3	Patient identifier	Varchar	Yes	Unique identifies for a patient (across all sites) - likely to be conflation of site ID and site patient ID.	Assigned
4	Cohort	Varchar	Yes	The reason for having this patient in the cohort	Assigned
5	Date of Birth (DOB)	Date dd.mm.yyyy	Yes	This will determine the age of patient at time of scan	DICOM Meta Data
6	Ethnicity	Varchar	No	The likely race/ethnicity based on self-reported sources, public sources and surname/ethnicity tables.	Site specific electronic patient record
7	Gender	Numeric	Yes	Gender of the patient	DICOM Meta Data
8	Time of arrival to Emergency Department (ED)	Datetime dd.mm.yyyy hh:mm	Yes	The time of patient arrival to the Emergency Department.	Site specific electronic patient record
9	Time of triage in ED	Datetime dd.mm.yyyy hh:mm	Yes	The time of first digitally recorded clinical contact.	Site specific electronic patient record
10	Initial location cared for	Varchar	No	Where the patient was first seen.	Site specific electronic

					patient record
11	Indication for Head CT	Varchar	No	What did the patient present with? List 1 - Trauma; 2 - Altered focal neurology; 3 - Reduced GCS; 4 - Headache; 5 - Seizures; 6 - Other	Radiology Report. RIS - free text.
12	Time of CT Request	Datetime dd.mm.yyyy hh:mm	Yes	Time the clinical team requested the patient to have a head CT scan.	RIS
13	Does NCCT head meet qER inclusion and exclusion criteria?	Binary	Yes	Technical requirements of qER read met.	DICOM Meta Data, qER Log
14	CT Scan Model	Varchar	No	The model of the scanner used to generate images.	DICOM tag
15	CT Scan Manufacturer	Varchar	No	The manufacturer of the scanner uses to generate images.	DICOM tag
16	CT Scan Software Version	Varchar	No	Software version of the CT scan.	DICOM Meta Data

5.4.2 Scan

This record type contains all attributes that are collected during the time when a patient is undergoing a Head NCCT scan and immediately after it to capture the necessary data elements for study analysis. For attributes which are of 'binary' data types, a value of 1 will indicate the presence of that attribute and 0 indicates absence.

	Attribute	Data type	Mandatory	Description	Source
1	Patient identifier	Varchar	Yes	Unique identifies for a patient (across all sites) - likely to be	Assigned

				conflation of site ID and site patient ID.	
2	SOP instance UID	Varchar	Yes	The unique ID for the image to which the report relates	DICOM Meta Data
3	Accession number	Varchar	Yes	Unique identifier linking the report to a suite of imaging studies	DICOM Meta Data
4	Time of CT Scan Acquisition	Datetime dd.mm.yyyy hh:mm	Yes	The time at which CT scan was completed for the patient	DICOM Meta Data
5	Out of hours scans?	Binary	Yes	Whether the scan was sent for teleradiology reporting (value = 1) or not (value = 0)	qER log/RIS/PACS
6	Time NCCT Brain was received	Datetime dd.mm.yyyy hh:mm	Yes	The time NCCT was received by qER	qER Log
7	Was CT image processed by qER?	Binary	Yes	Did the image meet qER requirements for processing?	qER Log
8	Time qER report received	Datetime dd.mm.yyyy hh:mm	Yes	The time the qER report left the gateway and available for the radiologists to review	qER Log
9	qER probability score for ICH	Numeric	Yes	Probability of the presence of intracranial haemorrhage	qER Log
10	qER ICH	Numeric	Yes	Presence or absence of ICH	qER Log/ qER Report
11	qER probability score for EDH	Numeric	Yes	Probability of the presence of extradural haemorrhage	qER Log

12	qER EDH	Binary	Yes	Presence or absence of EDA	qER Log
13	qER probability score for SDH	Numeric	Yes	Probability of the presence of subdural haemorrhage	qER Log
14	qER SDH	Binary	Yes	Presence or absence of SDH	qER Log
15	qER probability score for SAH	Numeric	Yes	Probability of the presence of subarachnoid haemorrhage	qER Log
16	qER SAH	Binary	Yes	Presence or absence of SAH	qER Log
17	qER probability score for IPH	Numeric	Yes	Probability of the presence of intraparenchymal haemorrhage	qER Log
18	qER IPH	Binary	Yes	Presence or absence of IPH	qER Log
19	qER probability score for IVH	Numeric	Yes	Probability of the presence of intraventricular haemorrhage	qER Log
20	qER IVH	Binary	Yes	Presence or absence of IVH	qER Log
21	qER probability score for MS	Numeric	Yes	Probability of the presence of midline shift	qER Log
22	qER MS	Binary	Yes	Presence or absence of midline shift	qER Log/ qER Report
23	qER probability score for mass effect	Numeric	Yes	Probability of the presence of mass effect	qER Log
24	qER ME	Binary	Yes	Presence or absence of mass effect	qER Log/ qER Report

25	qER probability score for cranial fracture	Numeric	Yes	Probability of the presence of cranial fracture	qER Log
26	qER fracture	Binary	Yes	Presence or absence of cranial fracture	qER Log/ qER Report
27	qER probability score for atrophy	Numeric	Yes	Probability of the presence of atrophy	qER Log
28	qER atrophy	Binary	Yes	Presence or absence of atrophy	qER Log/ qER Report
29	qER probability score for infarct	Numeric	Yes	Probability of the presence of hypodensities suggestive of infarct	qER Log
30	qER Infarct	Binary	Yes	Presence or absence of hypodensities suggestive of infarct	qER Log/ qER Report
31	Time CT Report Generated by radiologist	Datetime dd.mm.yyyy hh:mm	Yes	The time when the final CT report was generated by a radiologist.	RIS/ PACs
32	qER full report of NCCT Brain	Varchar	Yes	Published final qER report	qER log/RIS/PACS
33	qER Scan Category	Integer	Yes	Prioritised or No Finding or Other non-prioritised finding? 1= Prioritised 2 = No finding 3 = Other non-prioritised finding 4 = Not processed	Derived from qER Log/ qER Report

5.4.3 Post-scan

This record type will capture attributes that have occurred after the NHS radiologist final report was available for stakeholders to review including any patient follow-up data that is collected. For

attributes which are of 'binary' data types, a value of 1 will indicate the presence of that attribute and 0 indicates absence.

	Attribute	Data type	Mandatory	Description	Source
1	Patient identifier	Varchar	Yes	Unique identifies for a patient (across all sites) - likely to be conflation of site ID and site patient ID.	Assigned
2	SOP instance UID	Varchar	Yes	The unique ID for the image to which the report relates	DICOM Meta Data
3	Accession number	Varchar	Yes	Unique identifier linking the report to a suite of imaging studies	DICOM Meta Data
4	Rad ICH	Binary	Yes	Radiologist reported presence of Intracranial haemorrhage in the radiology report?	Clinical fellow's report
5	Rad MS	Binary	Yes	Radiologist reported presence midline shift in the radiology report?	Clinical fellow's report
6	Rad ME	Binary	Yes	Radiologist reported presence mass effect in the radiology report?	Clinical fellow's report
7	Rad Fracture	Binary	Yes	Radiologist reported presence cranial/skull fracture in the radiology report?	Clinical fellow's report
8	Rad Atrophy	Binary	Yes	Radiologist reported presence atrophy in the radiology report?	Clinical fellow's report

9	Rad Infarct	Binary	Yes	Radiologist reported presence hypodensities suggestive of infarct in the radiology report?	Clinical fellow's report
10	Rad Other	Binary	Yes	Radiologist reported presence of any other findings other than the six target abnormalities in the radiology report?	Clinical fellow's report
11	Rad Scan Category	Integer	Yes	Prioritised or No Finding or Other non-prioritised finding? 1= Prioritised 2 = No finding 3 = Other non-prioritised finding	Derived from clinical fellow's report
12	Discordance between qER report and NHS Trust radiologist report	Binary	Yes	Is there a discordance between qER report findings and NHS Trust radiologist report? 1 = Yes 0 = No	Derived from clinical fellow's report and qER report
13	Discordance Review Decision: Which AI findings were accepted by the panel?	Varchar	Yes	To capture the agreement between qER and trust radiologist based on specific findings.	Derived from clinical fellow's report and qER report
14	Time of treatment related to head CT findings in ED	Datetime dd.mm.yyyy hh:mm	No	Time of intervention to treat CT Head findings.	Site specific electronic patient record

15	Time of first intervention for critically identified scans	Datetime dd.mm.yyyy hh:mm	No	Time recorded for initial treatment option and/or referral.	Site specific electronic patient record
16	Time of discharge or referral	Datetime dd.mm.yyyy hh:mm	Yes	Electronic discharge point from ED (to ward or home).	Site specific electronic patient record
17	Length of stay in hospital	Numeric	Yes	Length of stay in hospital related to that admission.	Site specific electronic patient record
18	Was the patient enrolled in other clinical trial?	Binary	Yes	Has the patient been recruited to another study? 1 = Yes 0 = No	Site specific electronic patient record
19	If 21 = Yes; Clinical trial number [PLACEHOLDER]	Clinical trial code	Yes	The study ID if the patient is a subject?	Site specific electronic patient record
20	Patient's National Data Opt Out	Binary	Yes	If patient has selected National Data Opt out, their data will be excluded from final analysis. 1= Patient data excluded from analysis 0 = Not excluded	

21	Death within 28 days following discharge	Binary	Yes	Had the patient died within 28 days following discharge from NHS Trust hospital? 1 = Yes 0 = No	Site specific electronic patient record
22	Date of Death	Date dd.mm.yyyy	Yes	If the patient had died within 28 days following discharge from NHS Trust hospital, what is the date of death	Site specific electronic patient record
23	Immediate condition	Varchar	Yes	ICD code relating to the disease or condition directly relating to death	Site specific electronic patient record
24	Contributing condition	Varchar	No	ICD code relating to other significant conditions contributing to the death but not related to the disease or condition causing it	Site specific electronic patient record

5.4.4 Ground truth

This record type will contain attributes that captures the ground truth results for the Head NCCT scans which have findings that are discordant between qER report and NHS trust radiologist report.

	Attribute	Data type	Mandatory	Description	Source
1	Patient identifier	Varchar	Yes	Unique identifies for a patient (across all sites) - likely to be conflation of site ID and site patient ID.	Assigned

2	SOP instance UID	Varchar	Yes	The unique ID for the image to which the report relates	DICOM Meta Data
3	Accession number	Varchar	Yes	Unique identifier linking the report to a suite of imaging studies	DICOM Meta Data
4	Ground truther ID	Varchar	Yes	The unique ID of the person generating ground truth	Assigned
5	Ground truther role	Varchar	Yes	'Adjudicator' if the ground truther is adjudicating a disagreement between two ground truthers, otherwise 'Default ground truther'	Assigned
6	GT ICH	Binary	Yes	Ground truther reported presence of intracranial haemorrhage in the radiology report?	Ground truth report
7	GT MS	Binary	Yes	Ground truther reported presence midline shift in the radiology report?	Ground truth report
8	GT ME	Binary	Yes	Ground truther reported presence mass effect in the radiology report?	Ground truth report
9	GT Fracture	Binary	Yes	Ground truther reported presence cranial/skull fracture in the radiology report?	Ground truth report
10	GT Atrophy	Binary	Yes	Ground truther reported presence atrophy in the radiology report?	Ground truth report

11	GT Infarct	Binary	Yes	Ground truther reported presence hypodensities suggestive of infarct in the radiology report?	Ground truth report
12	GT Other	Binary	Yes	Ground truther reported presence of any other findings other than the six target abnormalities in the radiology report?	Ground truth report
13	GT Scan Category	Integer	Yes	Prioritised or No Finding or Other non-prioritised finding? 1= Prioritised 2 = No finding 3 = Other non-prioritised finding	Derived from ground truth report

APPENDIX 6

GP Letter

qER Evaluation

GP LETTER

Qure.AI qER
CT HEAD Emergency Department Evaluation

For Information

Comms to GPs (or for GP bulletin)

Dear all,

We are shortly going live with a new artificial intelligence solution. The purpose is to support radiology report turnaround time and prioritisation.

The software company is Qure.AI. Currently the project is restricted to patients imaged at participating sites. As part of the project, the AI algorithm will abnormal images with presence of bleeding, fracture, midline shift, mass effect and hypodensities suggestive of infarcts or atrophy. Images will still be reported by a radiologist within the existing clinical pathway.

Please do not hesitate to contact me if you have any questions or concerns about the project. We will be evaluating the impact of the solution on the emergency department CT Head pathway. (*Email address of local site*)

XX
Consultant Radiologist
Hospital XX