

PROHIBIT-ICH 

Prevention Of Hypertensive Injury to the Brain by
Intensive Treatment in IntraCerebral Haemorrhage

 **UCL**

IMAGING MANUAL

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PROHIBIT-ICH MRI MANUAL VERSION 1 APRIL 2018**Quick Reference Guide**

- **PROHIBIT-ICH:** PREvention Of Hypertensive Injury to the Brain by Intensive Treatment after IntraCerebral Haemorrhage: a pilot randomised trial of home telemetry-guided treatment
- A pilot multi-site randomised controlled trial in approximately 112 adult survivors of spontaneous (SVD-related) ICH
- A 'dummy run' scan is required from all MRI sites. No trial subjects can be scanned until the 'dummy run' scan has been approved.
- MRI visits are scheduled for baseline, month 6 and month 12.
- Scanning protocol (with approx. acquisition time), for all visits, consists of :
 - 3D T1 (5min)
 - 3D FLAIR (5min)
 - DTI (5min)
 - 3D SWI (5min)
 - Axial T2 (2min)

Total: 22 mins

Optional: Arterial Spin labelling (5min)

Total: 27 mins

- MRI scans sent to the MS Centre, UCL Institute of Neurology, London, UK

Section 1: Contact Details

Central MRI Reader Facility Contact Details

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Chief Investigator and Trial Coordinator Contact Details for imaging section of the study

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Section 2 - Introduction and Study Overview

2.1 Background

- Intracerebral hemorrhage (ICH) accounts for 10-15% of all strokes in the Western populations with high mortality, disability, recurrence and socioeconomic burden to society¹⁻³
- Most ICH is caused by cerebral small vessel diseases (SVD): hypertensive arteriopathy and cerebral amyloid angiopathy (CAA)
- Previous studies strongly suggest that intensive and sustained BP lowering could improve secondary prevention of ICH, but there are no current trials to guide the optimum strategy or intensity for BP lowering after ICH.
- Telemetric home BP monitoring is a promising intervention to improve BP control, evaluated previously in Oxford Vascular (OXVASC) Study by the Centrally Observed home telemetric Monitoring of BP to Manage Intensive Treatment (COMMIT) Study.^{4,5}
- Blood pressure control might reduce SVD progression after ICH, which can be monitored by MRI biomarkers, including white matter hyperintensities and cerebral micro-bleeds (CMBs). Use of MRI biomarkers might be useful in demonstrating treatment efficacy in a smaller sample size than clinical outcomes.

1. Wilson D, Adams ME, Robertson F, et al. Investigating intracerebral haemorrhage. *BMJ* 2015;350:h2484.
2. Van Asch CJ, Luitse MJ, Rinkel GJ, et al. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet neurology* 2010;9(2):167-76.
3. Jorgensen HS, Nakayama H, Reith J, et al. Stroke recurrence: predictors, severity, and prognosis. The Copenhagen Stroke Study. *Neurology* 1997;48(4):891-5.
4. U. Fischer, M. Wilson, N.L.M. Paul, L. Bull, S. Welch, L. Tarassenko, P.M. Rothwell. Bluetooth home BP-monitoring in patients with TIA and minor stroke: feasibility and BP control. *Cerebrovasc Dis* 2014;38:137.
5. A Webb, N Lovett, L Li, M Wilson, F Cuthbertson, U Fischer, L Tarrassenko, P M Rothwell. Centrally Observed home telemetric Monitoring of blood pressure to Manage Intensive Treatment (COMMIT) Study: Maximum SBP AND variability on home versus ambulatory monitoring *International Journal of Stroke* 2015. Vol 10 (Suppl. 2); April 2015; 53.

2.2 Study Objectives and Endpoints

The trial will investigate whether intensive lowering of blood pressure (BP) using telemetric home monitoring in survivors of intracerebral haemorrhage (ICH) is feasible, safe and effective in reducing brain injury. If successful this study will be a precursor for a larger definitive trial. Our intervention should allow survivors of ICH to know, understand, and manage their own BP to prevent strokes and cognitive impairment, and improve outcomes.

Primary objectives:

- (i) BP study. Does the use of centralised telemetric home BP monitoring in patients with spontaneous (non-traumatic) ICH achieve a reduction in 3-month BP compared with standard care?
- (ii) Imaging study. Does intensive BP treatment using centralised telemetric home monitoring result in a reduction in progression of small vessel disease (SVD)-related brain injury assessed on MRI (including, but not limited to, white matter hyperintensities (WMH), white matter structural integrity, incident cerebral microbleeds (CMBs), and brain atrophy) compared with standard care?

Secondary objectives:

- (i) BP study
 1. Is it feasible in a multi-site setting to intensively lower BP using centralised telemetric home BP monitoring for an extended period of time following spontaneous ICH?
 2. Is it safe to intensively lower BP for an extended period of time following spontaneous ICH, or are there adverse responses (including increased progression of cognitive decline)?
 3. Is the intervention acceptable to participants, including measures of quality of life?
- (ii) Imaging study
 1. Does any reduction in recurrent vascular events (including ICH) or progression of cognitive decline on intensive BP treatment correlate with baseline measures of changes in quantitative and structural brain scan markers of small blood vessel health?
 2. Are there any adverse effects on neuroimaging measures (e.g. increased white matter ischaemic injury) associated with intensive BP treatment?

2.3 Study MRI Requirements (Summary)

Two types of MRI studies will be obtained during the course of the study

1. Dummy (test) Scan

Before a site can enrol subjects into this study; a test scan must be submitted for review and approval to the UCL MRI Central Reader Centre, Russell Square, London UK.

2. Routine On-Study Scan

Digital MRI images in DICOM standard will be uploaded to the MRI Central Reader Centre, UCL Russell Square, where they will be analysed and then archived.

Study scans should be performed using the study-specific MRI sequence instructions (see below) at the following time points:

Baseline Visit, Month 12 scans

1. 3D T1
2. 3D FLAIR
3. DTI
4. 3D SWI
5. Axial T2

Optional: Arterial Spin labelling

An archive copy of the local MRI Report **MUST** be kept at the study site in the subjects CRF binder.

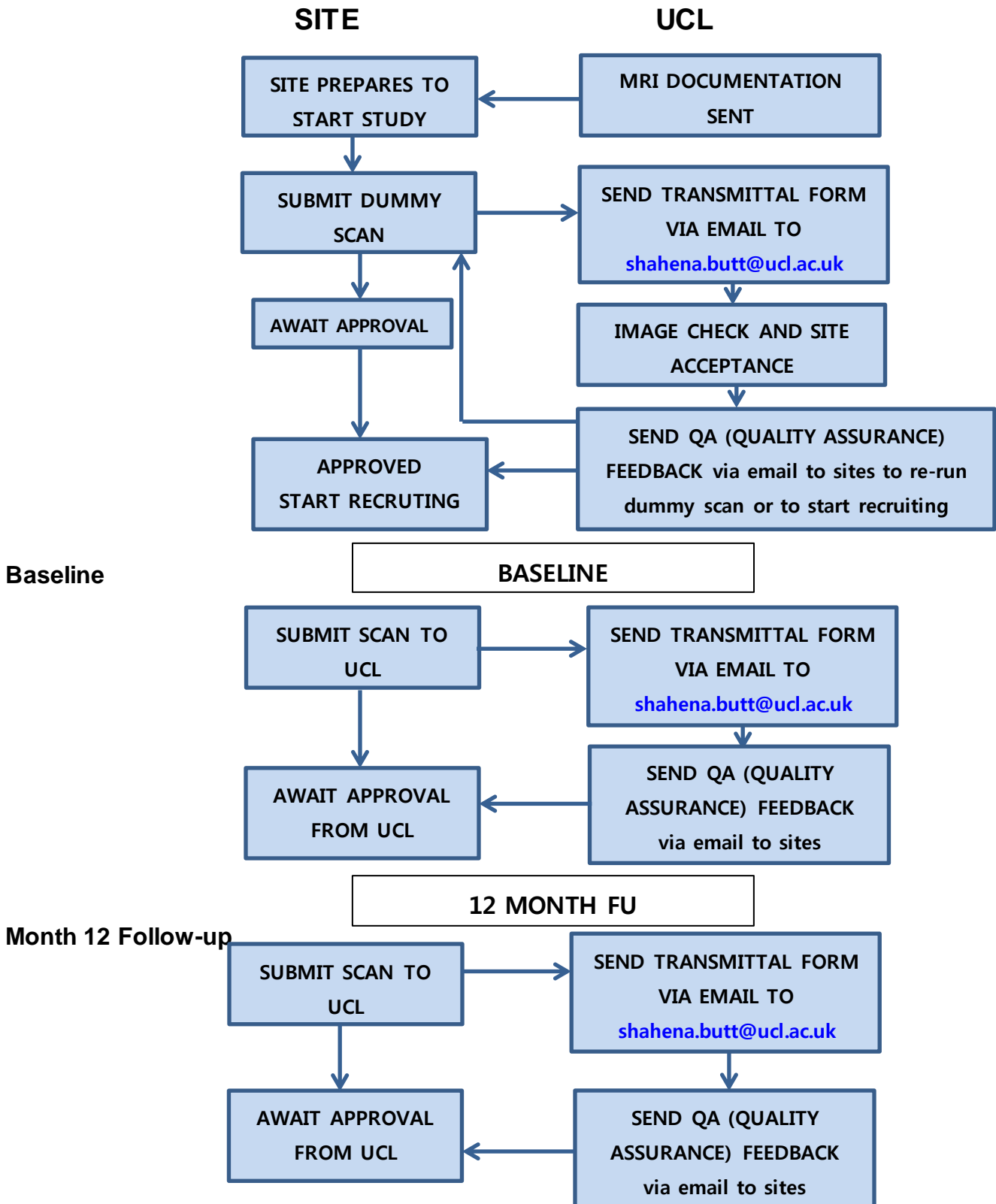
A local archive copy of the MRI data must also be retained at the site for future possible inspection by the sponsor or relevant Regulatory Authorities.

Section 3 - MRI TECHNOLOGISTS INSTRUCTIONS

3.1 GENERAL INTRODUCTION FOR MRI PROCEDURES

1. The preferred method of image transfer to UCL is by direct electronic transfer. All sites will be contacted during the initial site start-up period to discuss the implementation of a direct transfer protocol for scan transfer
2. Prior to starting to scan subjects for the study, you must submit a 'Dummy' or test scan to the MRI Central Reader Centre for evaluation and acceptance. This process will also confirm the sequence parameters you should use for all study scans.
3. All information relating to subject's details will be provided to you by the PI/study coordinator at your site. This information will be used to log the subject in for an MRI Scan.
4. Perform the MRI scan using the agreed upon parameters for your scanner. Parameters for your site will be determined as part of the test scan procedure. Once agreed upon, the finalised MRI parameters for your site will be issued to you on the Scan Parameter Form and should be filed in Section 7 of this manual. These parameters should be used for all study scans.
5. Remember, a subject should only be identified by the Subject Identification Number, date of scan and year of birth. The scan annotation must also include all scan parameters. The information recorded should be consistent with the information provided to you by your site PI/study coordinator.
6. Make a second copy of the MRI scan to be retained at your site for possible future data access (e.g. Regulatory Authority Inspection or routine study monitoring).
7. You should complete a Transmittal Form (attached in this manual) and send this to the UCL via email to shahena.butt@ucl.ac.uk to notify of any scan that has been sent.
8. Following scan evaluation by the Reader Centre, you will receive a quality assurance report (QA Assessment Form) from the co-ordinator via e-mail which will indicate if each scan is acceptable or if problems have been identified. Please file these forms and all other correspondence with UCL.

Section 4 - PROHIBIT-ICH MRI Flow Chart



Section 5 - MRI scanning procedures

5.1 General processes

Subject comfort during the scan is important. Adequate padding and neck support is recognised to be important, but no specific recommendations are made beyond the standard practice at your institution. Please provide ear plugs, eye masks, prism glasses or other items required for subject comfort as routinely used at your institution.

Minimising motion artefact is very important for study scan quality. Use of standard Velcro head straps and foam wedges is recommended. However, other methods of stabilising the head which are used routinely at your institution are acceptable.

The subject must be positioned appropriately so that the mid-line of the brain falls in the middle of the initial sagittal localising sequence. Follow the routine procedures at your institution for your type of scanner for placing subject in the machine and general positioning.

Please refer back to the previous timepoint study scans for study for each subject to enable exact repositioning between scans. This step is essential for the production of comparable scans and to enable effective evaluation by the Reader Centre.

The coil routinely used for research scans should be used. If possible, a high channel array coil (32 or 64 channels) should be used; otherwise an array coil with fewer channels is also acceptable. The coil information should be documented in the MRI Overview Form in Section 10 of the MRI Technologist Manual for future reference. The same coil must be used for all patients throughout the study – this is very important for longitudinal comparability.

Section 6 - MRI scanning procedures – dummy scan

As mentioned earlier, before each MRI centre is accepted into the trial, a test scan needs to be performed. This is often referred to as the “Dummy Scan”. This procedure enables the Central MRI Reading Centre to determine the following:

- Scanner performance is within specification for entry into trial
- The MRI site’s choice of scan sequence parameters give adequate tissue contrast for the purposes of the trial
- The MRI site can provide contiguous slices with adequate signal to noise ratio
- The MRI site is able to produce and transport the electronic data required for the study to the Central MRI Reader Centre at Queen Square

To facilitate the objectives listed above, each MRI site is required to perform an acceptable dummy (or test) scan as listed below **PRIOR** to any study scans being performed.

Your dummy scan will be reviewed by UCL after which you will be sent a **QA Assessment Feedback** telling you whether the scan is acceptable. You may be asked to resubmit a dummy scan to achieve acceptability, or the QA Assessment Feedback may make some recommendations for future scans.

When your dummy (or test) scan has been approved, you will be notified with an approval email by UCL that will confirm whether the MRI scan sequence parameters used for your centre are acceptable. These approved parameters **must** be used by your centre throughout the study for all scans.

ANY FUTURE DEVIATION FROM THESE APPROVED SCAN PARAMETERS MAY RESULT IN THE REQUIREMENT TO RECALL THE STUDY SUBJECT AND PERFORM A REPEAT MRI EXAMINATION.

It is therefore strongly advised that you store/save the approved scan protocol for the study on your scanner to avoid any mistakes being made when performing ‘on study’ MRI examinations for the trial.

6.1 Performing the Scan

It is the responsibility of the Principal Investigator (PI) and/or Study Coordinator (SC) at your site to arrange for a **suitable subject or normal volunteer** to be available for the 'dummy run' scan.

6.2 Guideline scan

1. Position the subject and perform 'localiser' scans in order to align the transverse slices for all scans to run parallel to the inferior points of the corpus callosum (see image below). We recommend that you use axial, coronal and sagittal planning scans to optimally position the subject



2. For all sequences, plan the scan to achieve as full converge of the entire brain as possible.

6.3 Guide tables with scan parameters for use in dummy run scan

The following table (section 7) contains a guide to the scan parameters to be used for the 'dummy run scan'. As parameters can change depending on scanner model and software level, some values are given as approximations.

7.0 Guide tables with scan parameters for the MRI scan

PROHIBIT-ICH PARAMETERS GUIDE FOR GE 3T						
BRAIN	3D T1	3D FLAIR	DTI	3D SWI	Axial T2	ASL (opt)
slice orientation	Sagittal	Sagittal	Axial	Ob axial	Axial	Axial
TR (ms)	-	5000	8000	31	4000	-
TI (ms)	400	1540	-	-	-	2025
TE (ms)	Min Full	152	76.6	25	80	-
Number slices	200	192	80	48	44	-
slice thickness (mm)	1.2	1	2	3	4	4
slice gap (mm)	0	0	0	0	0	0
Field of View (cm)	27	25.6	22.4	25	24	24
Image matrix acquisition (frequency x phase)	256x256	256x240	112x112	384x384	256x256	512x8
Image matrix recon (frequency x phase)	256x256	256x240	112x112	384x384	256x256	512x8
Frequency encoding	S/I	S/I	R/L	R/L	A/P	R/L
Phase encoding	A/P	A/P	A/P	A/P	R/L	A/P
number of averages (excitations)	1	1	32 b=1000 4 b=0	1	1	3
Flip angle	11	-		15	150	-

PROHIBIT-ICH PARAMETERS GUIDE FOR PHILIPS 3T						
BRAIN	3D T1	3D FLAIR	DTI	3D SWI	Axial T2	ASL (opt)
slice orientation	Sagittal	Sagittal	Axial	Axial	Axial	Axial
TR (ms)	6.8	5000	7500	28	3000	4800
TI (ms)	824	1650	-	-	-	2025
TE (ms)	3.1	395	91	25	80	10
Number slices	170	192	60	60	45	36
slice thickness (mm)	1.2	1	2	2	3	4.5
slice gap (mm)	0	0	0	0	4	0
Field of View (cm)	270x252	256x256	224x224	220x182	238x238	220x220
Image matrix acquisition (frequency x phase)	244x227	256x256	112x112	368x303	256x255	64x61
Image matrix recon (frequency x phase)	256x238	256x256	112x112	384x316	256x255	64x64
Frequency encoding	S/I	S/I	R/L	A/P	A/P	R/L
Phase encoding	A/P	A/P	A/P	R/L	R/L	A/P
number of averages (excitations)	1	1	32 b=1000 4 b=0	1	1	30
Flip angle	9	-	-	15	90/120	90

PROHIBIT-ICH PARAMETERS GUIDE FOR SIEMENS 3T						
BRAIN	3D T1	3D FLAIR	DTI	3D SWI	Axial T2	ASL (opt)
slice orientation	Sagittal	Sagittal	Axial	Axial	Axial	Axial
TR (ms)	2300	5000	7200	28	4000	4000
TI (ms)	900	1650	-	-	-	2000
TE (ms)	2.95	395	56	25	78	20.26
Number slices	176	192	60	60	47	32
slice thickness (mm)	1.2	1	2	2	3	4.5
slice gap (mm)	0	0	0	0	0	0
Field of View (cm)	270x253	256x256	224x224	220x181	240x217	240x240
Image matrix acquisition (frequency x phase)	256x240	256x256	112x112	384x311	256x232	64x63
Image matrix recon (frequency x phase)	256x240	256x256	112x112	384x311	256x232	64x64
Frequency encoding	S/I	S/I	R/L	A/P	A/P	R/L
Phase encoding	A/P	A/P	A/P	R/L	R/L	A/P
number of averages (excitations)	1	1	32 b=1000 4 b=0	1	1	10
Flip angle	9	-	-	15	150	160

When your dummy (or test) scan has been approved by the imaging team at UCL, you will be provided with an email confirming that the sequence parameters used for the dummy MRI scan are suitable for your centre. These approved parameters must be used by your centre throughout the study for all scans.

Section 8 - Data upload instructions

File preparation:

Ensure your scans are compressed into a zip file before uploading.

Data upload:

Scans from your site should be sent to the Central Reading Facility at UCL by direct image transfer from your scanner or workstation/PC.

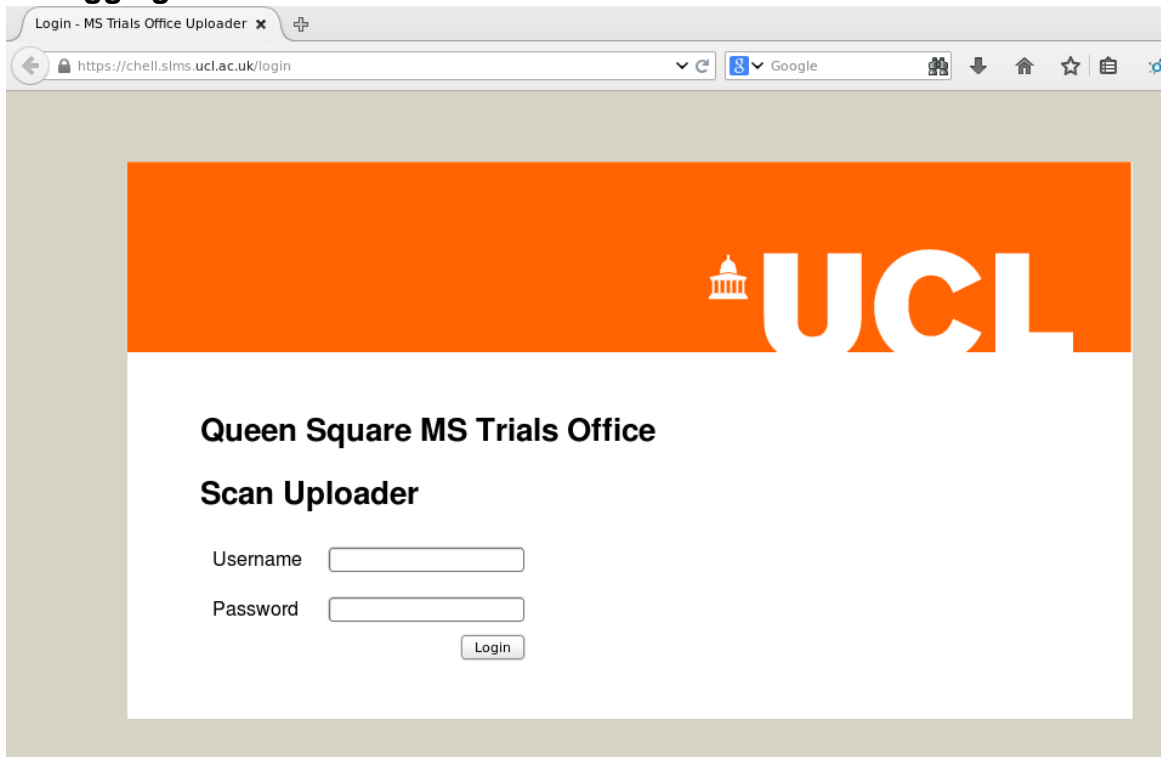
URL: <http://qsmscentre.org.uk>

**We recommend you use web browser: Chrome, Firefox or Microsoft Edge
Internet Explorer 6 and 7 are NOT compatible!**

Web Uploader Guide

This is a guide to sending images to the UCL Stroke Research Centre using the web upload service. To follow these instructions you will need a username and password for the web upload service. If you have not received these please request them by emailing shahena.butt@ucl.ac.uk

1. Logging in



Login - MS Trials Office Uploader x

https://chell.slms.ucl.ac.uk/login

UCL

Queen Square MS Trials Office

Scan Uploader

Username

Password

Login

Figure 1: Login page

The URL for the web upload service is <http://gsmscentre.org.uk>. Most web browsers are compatible with the service but note that Internet Explorer 6 and 7 are *not* compatible.

On connecting you should make sure that you have a secure connection. Your web browser should show a lock symbol in the URL bar and the displayed web address should be <https://chell.sims.ucl.ac.uk/login>. If you're not sure that the connection is secure then you should **not** proceed as your login details and patient data may not be safe.

Once you have made sure you have a secure connection you should enter the username and password you have been provided with and click the login button.

2. Starting an upload

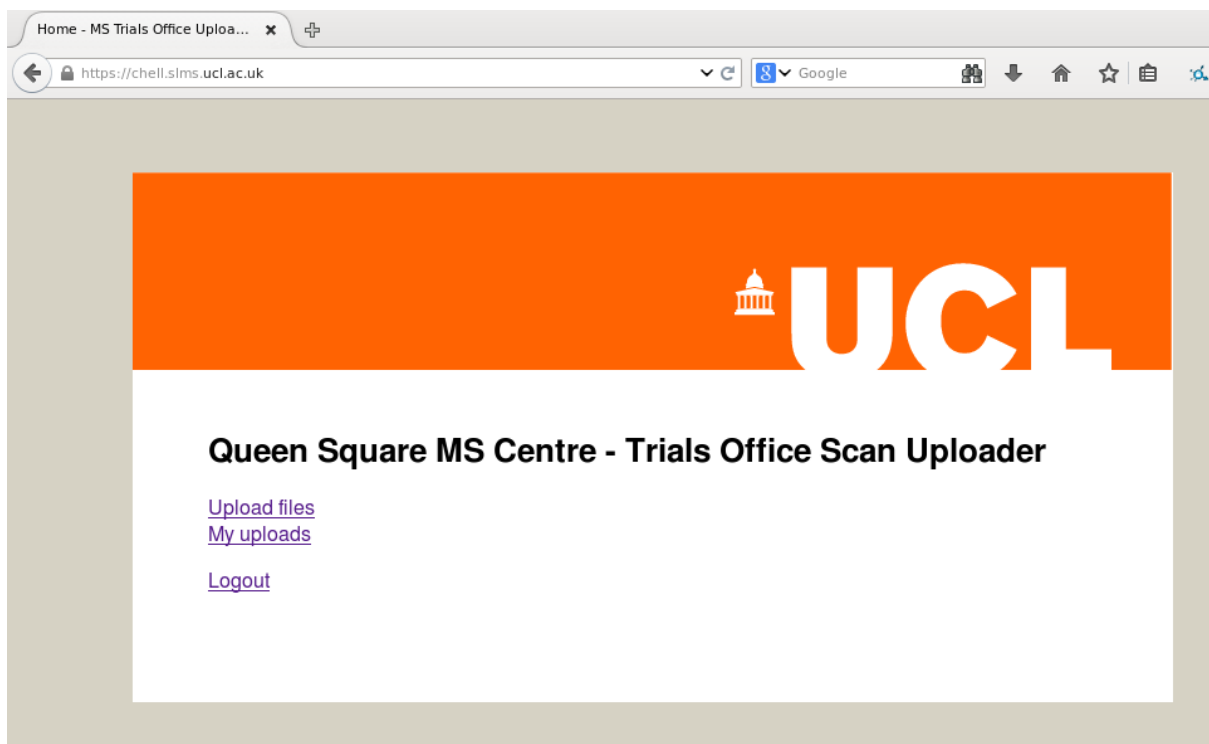


Figure 2: Home page

To begin the upload process click the 'Upload files' link.

3. Scan information

The next step is to enter information about which subject and timepoint you are uploading images for. The following fields must be filled in:

- Site
- Subject number
- Year of birth – ***enter 01/01/ [year of birth]***
- Scan date
- Visit

The comments field can be used for any other information that needs to be provided about the scan.



Upload scans

Upload type

- Patient
 Dummy

Subject

Site

PROHIBIT 00

Subject number

Birth Date

dd / mm / yyyy

Scan

Scan Date

dd / mm / yyyy

Visit

Baseline

Comments

Figure 3: Prepare upload - patient scan

After completing the form please double-check the information you've entered and then scroll down and click the 'Select files' button.

4. Selecting files

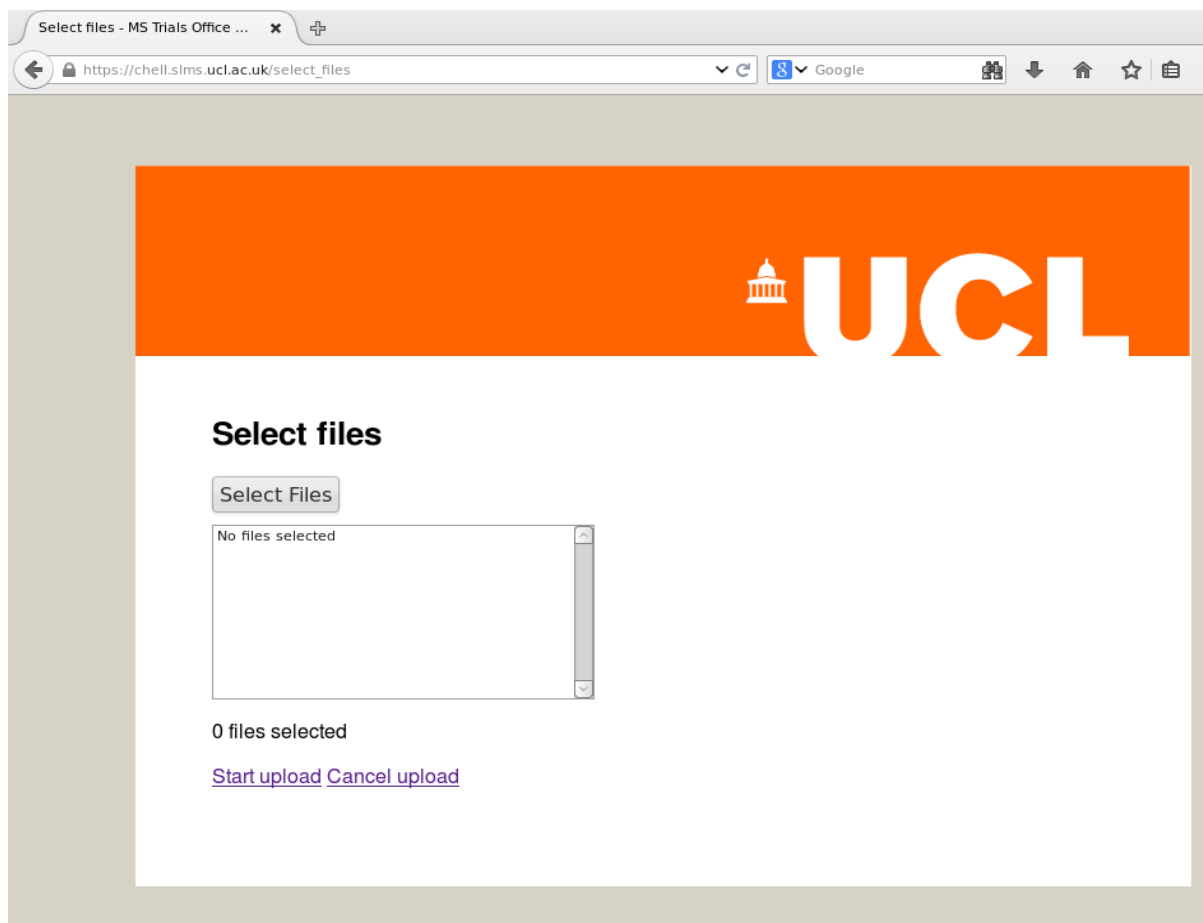


Figure 4: Select files

At this point you need to select the image files that you wish to upload.

We recommend compressing the DICOM image files into a zip format before sending the scans as this reduces the transfer time and assures that all the files are included.

To select files click the 'Select Files' button. Use the file selection window that appears to select your files - you can select multiple files at the same time. When you have selected the files to send, click the 'OK' button and check that the files are now listed in your web browser. Once the correct files are selected, click the 'Start upload' link. A progress bar will be displayed while the images are being transferred.

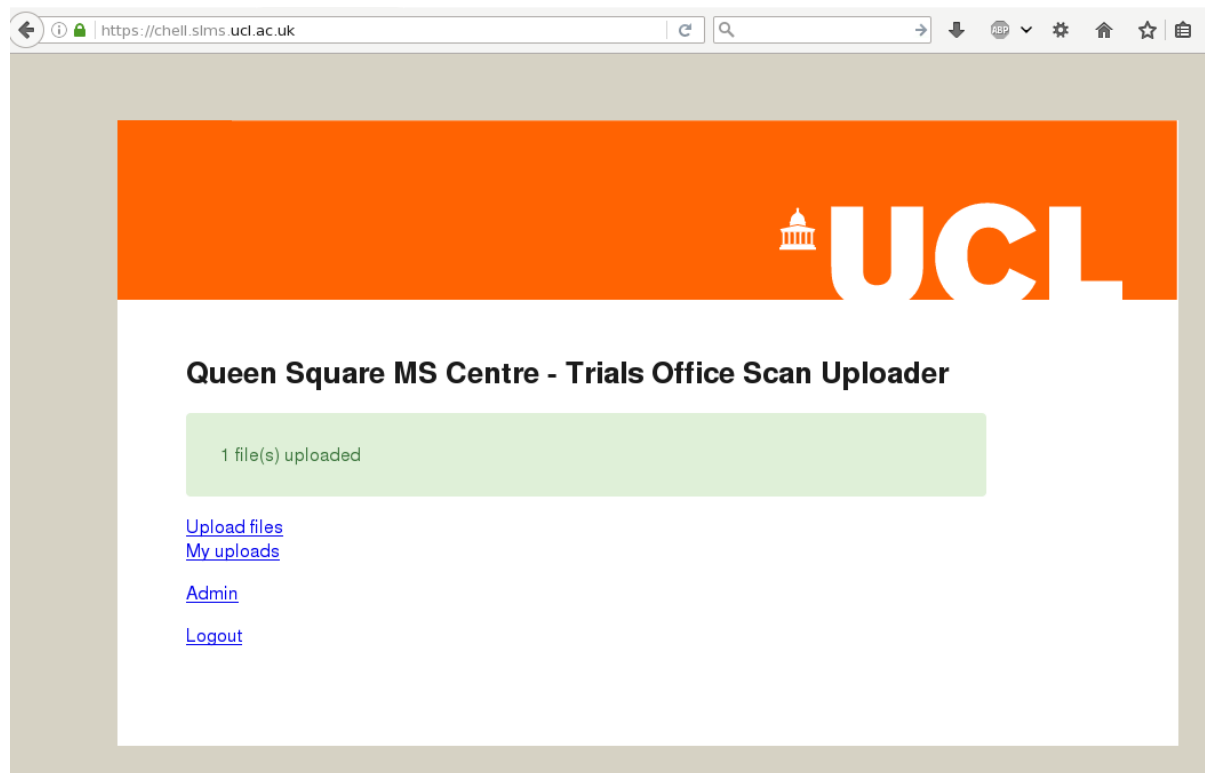


Figure 5: Transfer completed

When the transfer is complete you will be returned to the main page. You should see also a message saying the number of files that have been successfully upload.

After an upload you should use the 'My uploads' link to check that your transfer has been recorded.

Please email now your transmittal form to UCL (shahena.butt@ucl.ac.uk). This would allow the imaging team to run a quality check on the scan promptly.

Example Transmittal form, including Quality Assurance feedback can be found in the appendix below.

This will be sent to you in a separate email also.

APPENDIX 1: TRANSMITTAL FORM

PROHIBIT-ICH TRANSMITTAL FORM

NOTIFICATION OF MRI SCANS SENT TO UCL

Email (shahena.butt@ucl.ac.uk) this form to the PROHIBIT-ICH Trial Office

Senders name:	Site number:
MRI Centre name:	
Date sent:	Sender's phone number/email address:

Details of Scan sent

Subject number	Subject's Birth year (yyyy)	MRI Visit Baseline, month 12	Exam date (dd/mm/yyyy)

Comments:

For UCL MRI core lab use only:

PROHIBIT-ICH MRI QA FEEDBACK

Results of MRI QA Assessment

PASS Adequate image quality. **Scan has been accepted.** No repeat exam necessary

Results of MRI QA Assessment

FAIL Scan has been **rejected** – please see below for **instructions as to action required.**

Upon review of MRI data, the following Data Quality Issues were found:

	3D T1	3D FLAIR	DTI	3D SWI	Axial T2	ASL (opt)
Recall subject and rescan	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resend	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>