ULTROMICS™

PROTEUS FAQs

1. Background on PROTEUS Study?

A Prospective randomised controlled Trial Evaluating the Use of artificial intelligence in Stress echocardiography.
Phase III trial
Funded by NHSx Artificial Intelligence in Health and Care Award
Main objective - Investigate if EchoGo plus standard care is non-inferior to standard care alone in predicting the risk of cardiovascular disease following stress echocardiogram (SE).

2. Trial Participants and inclusion/Exclusion criteria

Adult patients referred for a stress echocardiogram to investigate CAD in participating NHS units in England.

Inclusion Criteria

1. Able and willing to give informed consent
2. Male or female, ≥18 years of age at study entry
3. Referred for clinically indicated stress echocardiogram to assess inducible ischaemia

Exclusion Criteria

1. Pacemaker
2. More than moderate valvular heart disease present
3. Left ventricular outflow tract obstruction defined as a gradient > 30mmHg (fixed or dynamic; supravalvular, valvular or sub-valvular)
4. Significant co-morbidities (e.g. cancer) with an expected life-expectancy of under 12 months in the investigator's opinion
5. Previous coronary artery bypass graft or other cardiac surgery
6. Congenital or inherited myocardial disease

3. The PROTEUS team

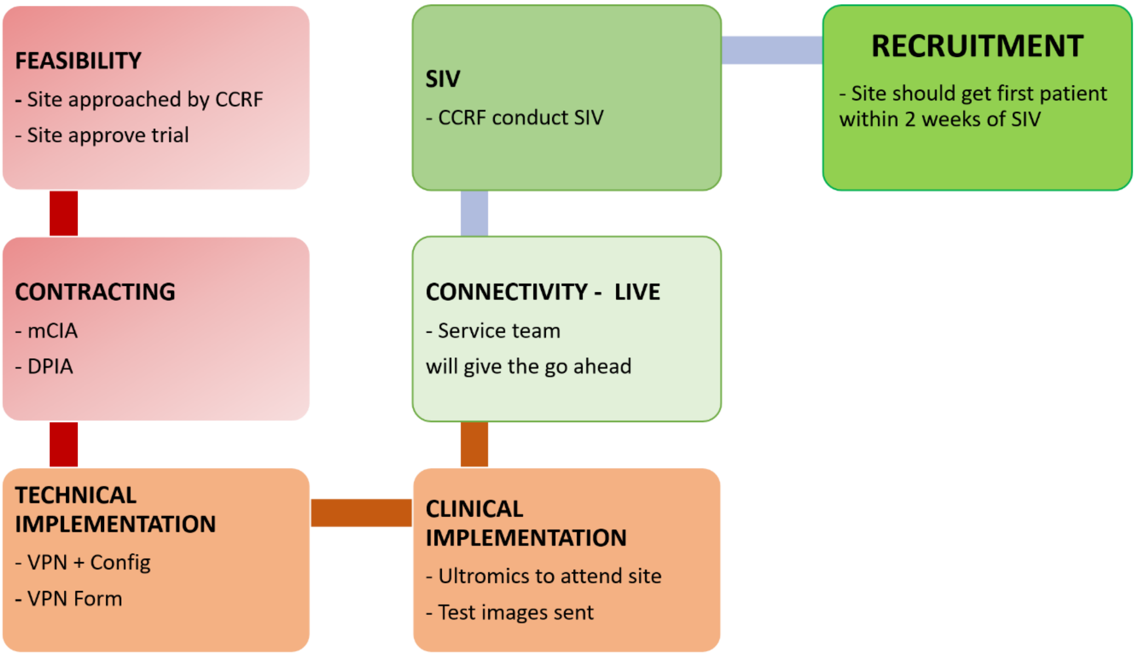
PROTEUS team:

- Casey Johnson – CCRF clinical project manager
- Natalie – CCRF clinical project manager
- Reema Kainth – DPIA Support
- Samantha Thulborn – Ultromics clinical project manager
- Dikla Hamlet – Service PMO manager – Connectivity project manager for PROTEUS
- Zahra Ahmad – Clinical applications lead – Liaise with site about image quality
- Mariam Solomon – Clinical applications specialist - Liaise with site about image quality

Contact the PROTEUS Study Team:

- proteus.trial@cardiov.ox.ac.uk

4. Process for site set-up



5. Recruitment targets and timeframe

Target Recruitment Per Site: 80-120 Patients
4 months recruitment (estimate) + 6 month follow up

6. Site reimbursement

Per site = £1,840.80
Per participant = £33 (control), £80.94 (intervention)
Qualitative Workstream depending on staff participation = £232.20

7. Is PROTEUS on the NIHR portfolio?

This trial is on the CRN portfolio, so CRN support is available for sites.

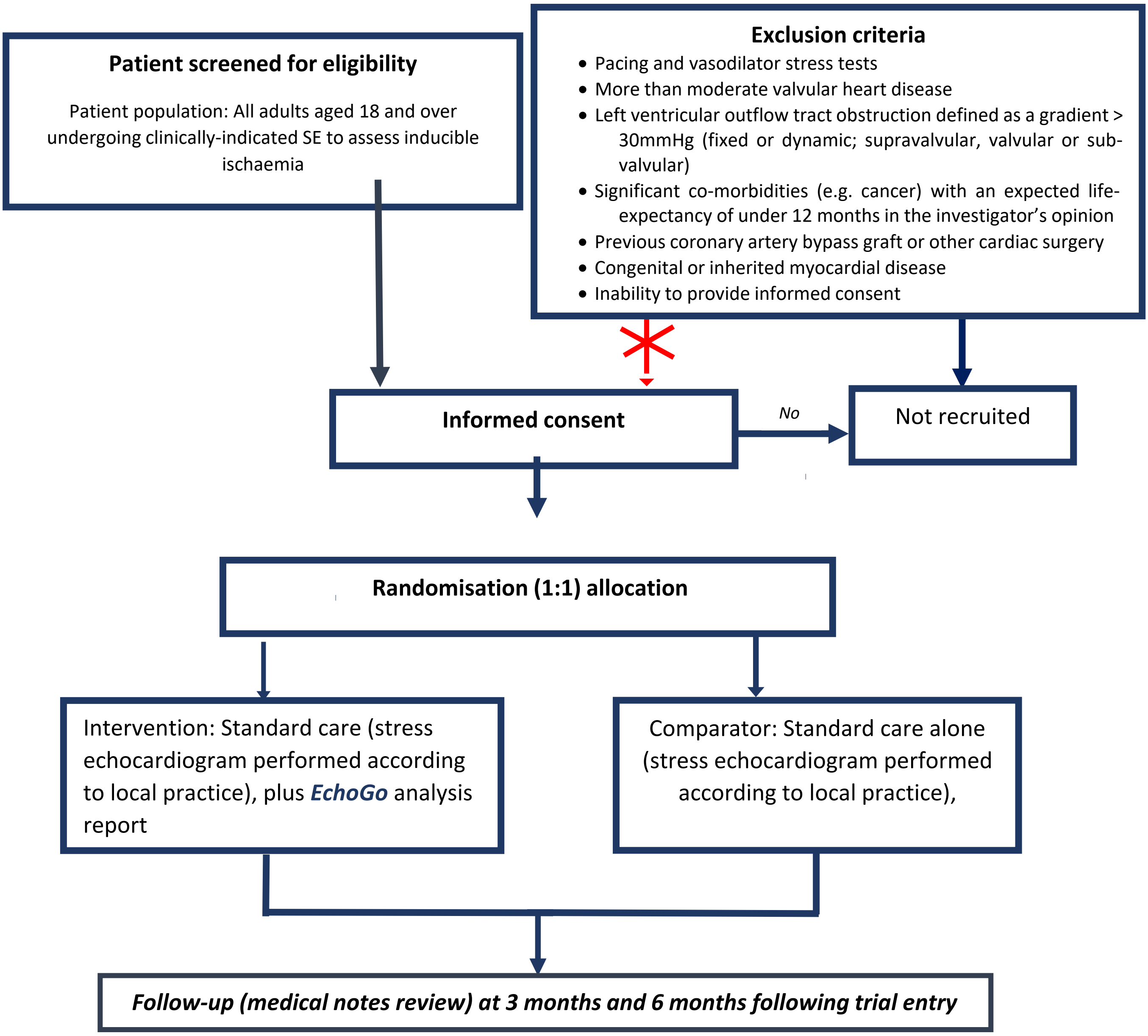
8. Is this study classed as commercial or non-commercial?

The letter of confirmation of funding from NHSx states to consider the trial as non-commercial for funding purposes.

9. DPIA – Who's responsibility is it?

Assessment of the need for, and the completion of a DIPA is the NHS Trust's responsibility. The Sponsor will provide assistance with completion of the sections of the DPIA that relate to the AI technology deployment as they have expert knowledge in this area. Sites should use the Sponsor provided extracted DPIA to populate the local Trust DPIA template. The site can then forward their draft DPIA to Ultromics highlighting sections they may require support with completing. Ulltromics will make every effort to help sites and may refer queries to the NHSx IG lead if appropriate. Ultromics do not take responsibility for or share responsibility with sites for completion of a DPIA.

10. Recruitment pathway



11. Trial procedures

Procedure	Pre-trial entry (day – 0)	Baseline (day 0)	3 months (day 92)	6 months (day 183)
Screening	X	X		
Informed consent	X	X		
Randomisation (trial entry)		X		
Baseline data collection		X		
Stress Echocardiogram		X		
EchoGo report review (intervention arm only)		X		
Outcome data collection (medical notes review)		X	X	X
SAQ-7, EQ-5D-5L (patient reported questionnaire)		X	X	X
Serious Adverse Event data collection		X	X	X

12. GCP training, when is it required?

The principal investigator (PI) and lead research nurse (or person taking informed consent) at site must provide a signed and dated CV and GCP certificate to be filed in ISF.
All on the delegation log must provide a signed and dated CV.
Additional personnel GCP certificates is at the site's discretion.

13. Delegation log

Anyone undertaking a study related activity must be listed on the delegation log. The PI at site must sign the delegation log to confirm that the person undertaking the study task is suitably qualified. The delegation log must be updated if there is any change to the staffing at site, throughout the study.

14. Data entry and randomisation

Data entry and randomisation is via castor. There are 9 forms to complete over the course of the trial per participant.

15. Does baseline data need to be entered into CRF before echo is sent

Once the patient has been consented and recruited into the PROTEUS study, baseline data should be entered into the eDC/CASTOR database as soon as is practical. Entering this data into CASTOR is not a prerequisite for the SE images to be forwarded to Ultromics for processing by the AI tool EchoGo Pro. However, some baseline data must be entered as part of the randomisation process in order to receive a study allocation 'control' or 'intervention' for each participant (Gender, age and CAD diagnosis). The site will need to be aware of each participant's study arm allocation before submitting SE images.

16. Stress Echo image views required

Key views needed to allow processing - A2C, A4C and SAX at rest and peak

17. EchoGo Pro report

This is a binary report – Either suggestive of a higher possibility of significant CAD or suggestive of a lower possibility of significant CAD.

18. EchoGo Pro rejection

Report may not be able to be generated for the following reasons:

a. Unable to fully assess the LV border delineation
b. Incorrect labelling of anatomical view(s)
c. Required image(s) missing from data set
d. Corrupt data set
e. Other – will be specified

19. Masking in the clinical decision - At site the referring clinician who requested the SE is responsible for the clinical decision following the report, are we able to share the echo pro report with them

The EchoGo Pro generated report can be shared with the referring clinician if this individual is responsible for making treatment decisions immediately following the SE examination as part of standard practice at the site. The masking aims to avoid anyone who does not need access to the report having sight of it and being influenced by the contents. If a patient is referred for further investigation or treatment following the SE the report should not be routinely shared with this clinician.

20. What if the report contradicts the original clinical assessment?

Decisions regarding the treatment for any individual patient always remains the responsibility of the treating clinician. The report generated by the EchoGo Pro AI system is a diagnostic aid which can be used at the treating clinician's discretion.

21. Qualitative sub-study?

An additional study to assess the impact of the implementation of the EchoGo Platform into the NHS patient care pathway will also take place.
Up to 2 staff members from each Trust will be asked to take part in a qualitative interview (45 minutes, online).
The aim of this study is to build up a rich, detailed understanding of participant experiences in this context, and allow for the identification of any barriers and facilitators to the uptake of EchoGo Pro into NHS workflows and the care pathway.

22. Invoicing for site reimbursement

Please email your finance details to PROTEUS Trial proteus.trial@cardiov.ox.ac.uk.
Invoicing will take place according to the payment schedule.

23. Who is the PROTEUS primary point of contact?

proteus.trial@cardiov.ox.ac.uk

24. Product support once a site is recruiting?

Support@Ultromics.com

25. Severe Adverse Events

SAEs should be reported immediately via email and castor. Please follow the working instructions provided.