

Medical Technologies Evaluation Programme

MT 252 - HeartFlow FFRct for the computation of fractional flow reserve from coronary CT angiography

Expert Adviser Questionnaire Responses

Name of Expert Advisers	Job Title	Professional Organisation/ Specialist Society	Nominated by	Ratified
Prof Keith Oldroyd	Consultant Interventional Cardiologist and Director of Research	British Cardiovascular Intervention Society	Sponsor	Yes
Professor Andreas Baumbach	Expert Cardiology Consultant and interventional cardiology specialist	British Cardiovascular Intervention Society	Specialist Society	-
Dr Ronak Rajani	Consultant Cardiologist	British Cardiovascular Society	Sponsor	Yes
Dr Francesca Pugliese	Consultant Radiologist	British Cardiovascular Society	Specialist Society	-
Dr Ian Purcell	Consultant Cardiologist	British Cardiovascular Intervention Society	Specialist Society	-
Prof Nick Curzen	Consultant cardiologist	British Cardiovascular Intervention Society	Specialist Society	-
Dr Rob Henderson	Consultant cardiologist	British Cardiovascular Intervention Society	NICE	Yes
Prof Carl Roobottom	Professor of Radiology	The Royal College of Radiologists	NICE	Expected

YOUR PERSONAL EXPERIENCE (IF ANY) WITH THIS TECHNOLOGY

Question 2: Please indicate your experience with this technology?

Expert Advisers	I have had direct involvement with this	I have referred patients for its use	I manage patients on whom it is used in another part of their care pathway	I would like to use this technology but it is not currently available to me
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Yes	Yes	No	Yes
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	No	No	No	Yes
Dr Ronak Rajani Consultant Cardiologist	Yes	No	Yes	Yes
Dr Francesca Pugliese Consultant Radiologist	No	No	No	Yes
Dr Ian Purcell Consultant Cardiologist	Yes	Yes	Yes	No
Prof Nick Curzen Consultant Cardiologist	Yes	Yes	No	No
Dr Rob Henderson Consultant Cardiologist	No	No	Yes	Yes
Prof Carl Roobottom Professor of Radiology	Yes	No	Yes	Yes
<i>Any Comments?</i>				

Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Blank
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Blank
Dr Ronak Rajani Consultant Cardiologist	My institute, Guy's and St Thomas' NHS Foundation Trust, was selected as the only centre in England for involvement in the last multicentre international trial using FFRct. My involvement with the technology was therefore with the trial. This involved patient recruitment, trial co-ordination and conducting all of the screening and cardiac CT scans. I also have an independent interest in the technology that HeartFlow use for FFRct. Myself and my collaborators at City London University Bioengineering department have reviewed the role of FFRct and its validity. This work has been published in a peer reviewed journal (Rajani et al. EuroIntervention 2013 - Fractional Flow Reserve by Coronary Computed Tomography - Hope or Hype ?). I am the cardiology clinical lead for cardiac computed tomography at Guy's and St Thomas' NHS Foundation Trust with strong academic interests in the UK and also abroad in the field of advanced coronary CTA.
Dr Francesca Pugliese Consultant Radiologist	Blank
Dr Ian Purcell Consultant Cardiologist	My involvement is through a clinical end-point research study of FFRct in clinical practice (Platform study).
Prof Nick Curzen Consultant Cardiologist	Blank
Dr Rob Henderson Consultant Cardiologist	Interested in using technology but this would ideally be in a research setting as current evidence does not support routine use in NHS
Prof Carl Roobottom Professor of Radiology	Blank

Question 3: Have you been involved in any kind of research on this technology? If Yes, please describe?

Expert Advisers	Yes/No	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Yes	Participated in Heartflow NXT trial
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	No	Blank
Dr Ronak Rajani Consultant Cardiologist	Yes	As detailed above. I was involved in the HeartFlow NXT trial as an investigator. This was a multicentre international trial comparing FFRct against the gold standard of invasive FFR in patients with intermediate coronary disease. My role involved patient screening, recruitment, reporting of CT scans and conducting all of the CT scans for the trial. I have also reviewed the literature. My work has been published in peer reviewed journals. I have ongoing collaborations with City London Bioengineering Department who are conducting similar validation trials using computation fluid dynamics. I have also conducted an independent study evaluating the potential economic benefits of incorporating this technology into standard NICE guideline pathways for evaluating patients with stable chest pain. This work is currently under peer review with the International Journal of Cardiology.
Dr Francesca Pugliese Consultant Radiologist	Yes	At this stage, we have been approached to assess the applicability of this method to the routine clinical images acquired in our centre. We have not yet established any research collaboration or project.
Dr Ian Purcell Consultant Cardiologist	Yes	Local PI in on-going PLATFORM study where technology is used to evaluate patients with chset pain.
Prof Nick Curzen Consultant Cardiologist	Yes	Blank
Dr Rob Henderson Consultant Cardiologist	No	Blank
Prof Carl Roobottom Professor of Radiology	Yes	Have been involved with group at Exeter University comparing the complex model used with Heartflow to simpler models created by Exeter

THIS PRODUCT (TECHNOLOGY) AND ITS USE

Question 4: *How would you best describe this technology?*

Expert Advisers	It is a minor variation on existing technologies with little potential for different outcomes and impact	It is a significant modification of an existing technology with real potential for different outcomes and impact	It is thoroughly novel - different in concept and/ or design to any existing
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	No	Yes	No
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	No	Yes	No
Dr Ronak Rajani Consultant Cardiologist	Blank	Blank	Yes
Dr Francesca Pugliese Consultant Radiologist	No	Yes	No
Dr Ian Purcell Consultant Cardiologist	No	Yes	No
Prof Nick Curzen Consultant Cardiologist	No	No	Yes
Dr Rob Henderson Consultant Cardiologist	No	Yes	No
Prof Carl Roobottom Professor of Radiology	No	No	Yes
<i>Any Comments?</i>			

<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Blank</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Blank</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>The technology of HeartFlow is not available elsewhere. It offers potential to provide combined coronary anatomical and functional testing. No other technology at present can provide this. The use of computational fluid dynamics in coronary CTA has not been described before. Heartflow have pioneered the literature in this regard. It is thoroughly novel and the belief by many international experts in the field of coronary CTA is that this technology has potential to revolutionise the evaluation of coronary disease in patients with stable chest pain syndromes.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>The entity of the impact, i.e. the fraction of patients who may have improved benefit out of this, is to be established. It is possible that the 'number needed to treat' is too high to demonstrate benefit.</p>
<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Blank</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>Blank</p>
<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>FFRct is a novel modification of an existing technology (CT coronary angiography)</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>Blank</p>

Question 5: What is the most appropriate use (e.g. clinical indication) for the technology?

Expert Advisers	Comment
<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Patients undergoing CTCA anyway who are found to have disease of uncertain functional significance. ctFFR could remove the need for further non-invasive and invasive assessments.</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Diagnosis of new onset of chest pain</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>The main scenarios where I see this technology being used is for patients with stable chest pain. At present there is widespread heterogeneity in the evaluation of patients who have a low, low-intermediate and intermediate risk of having coronary artery disease. Conventional risk scoring algorithms used to guide further investigations are wholly inadequate, and overestimate the prevalence of coronary disease potentially giving rise to excessive layering of investigations and increased cost to the NHS. Coronary CTA is currently confined to the evaluation of low risk patients. This is primarily since the main evidence base exists for the exclusion of coronary disease. Where coronary CTA is limited is in its positive predictive ability. Coronary CTA is only accurate 44% of the time in predicting significant coronary disease. As a result of this, current guidelines indicate that coronary CTA should be used to exclude coronary disease in low-risk patients and not to confirm it. The HeartFlow technology has the potential to change this paradigm by extending the role of coronary CTA to additional risk groups. It refines and improves the accuracy of detecting significant coronary disease by coronary CTA. The main areas therefore where I see the technology fitting in therefore is in the evaluation of patients with chest pain with a pre-test likelihood of having coronary disease up to 60%. Secondly, in patients with intermediate coronary disease detected by coronary CTA, the technology can also be used to provide better estimation of the stenosis and as to whether it is significant. At present, once coronary disease is detected by coronary CTA, further "functional" tests are often required to establish its significance. The HeartFlow technology in these cases can provide this information without further scans or imaging modalities being required. It uses the same dataset acquired from the CT scan thus permitting functional and anatomical testing within one testing modality. This has hitherto not been possible.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>Intermediate coronary stenoses, or presence of multiple coronary stenoses detected on coronary CTA in patients with (suspected or known) coronary artery disease.</p>

<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Low or intermediate (20-80% risk) coronary artery disease (CAD) risk patients in stable setting to rule out or confirm flow-limiting CAD non-invasively. Better specificity than conventional coronary CT angiography and other imaging modalities which reduces number of false positive scans and reduces number of invasive coronary angiograms in patients without flow-limiting coronary stenoses. Provides both anatomical and physiological coronary data which no other non-invasive test currently achieves.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>It is very early days for FFRCT but the prospect it offers is to allow for anatomical and physiological assessment of the significance of coronary artery disease non-invasively. This is completely novel and if validated would have a major impact on patient care pathways</p>
<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>In patients with evidence of coronary artery disease on CT angiography adjunctive FFRct could potentially help to identify patients that might benefit from invasive coronary angiography (with follow-on revascularisation if indicated). It is unclear how the technology will fit into existing pathways for the investigation of patients with chest pain of suspected cardiac origin (NICE CG95)</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>Invasive fractional flow reserve is considered the new gold standard for decision making regarding percutaneous intervention. It is however invasive and expensive. Computational FFR is a novel non-invasive technology using CT data to obtain similar data using computational modelling. It could potentially be a major technology to assess the haemodynamic significance of coronary stenosis in all patients presenting with chest pain. This is a very common clinical problem.</p>

COMPARATORS (including both products in current routine use and also “competing products”)

Question 6: *Given what you stated is the appropriate indication (clinical scenario) for its use, what are the most appropriate "comparators" for this technology which are in routine current use in the NHS?*

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Invasive coronary angiography with pressure wire assessment; various non-invasive ischaemia tests including SPECT, stress echo, stress perfusion MRI.
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Perfusion MRI
Dr Ronak Rajani Consultant Cardiologist	There is currently no alternative non-invasive estimation of fractional flow reserve. The closest comparators would be alternative methods of assessing the functional significance of coronary disease. These would be myocardial perfusion scintigraphy, stress echocardiography and cardiac MRI perfusion. These are modestly related to invasive fractional flow reserve (considered to be the gold standard assessment of lesion specific ischaemia). FFRct purports itself and compares itself to the goldstandard which is invasive FFR.
Dr Francesca Pugliese Consultant Radiologist	1. Fractional flow reserve during coronary angiography; 2. Non-invasive perfusion imaging (magnetic resonance, nuclear perfusion imaging, dobutamine stress echocardiography); 3. exercise treadmill testing
Dr Ian Purcell Consultant Cardiologist	Conventional CT coronary angiography, myocardial perfusion scanning, stress echo. Invasive coronary angiography with fractional flow reserve study.
Prof Nick Curzen Consultant Cardiologist	It will be compared with existing tests for coronary anatomy (CT angiogram or invasive coronary angiogram) or existing tests for reversible myocardial ischaemia (stress echo/MRI/nuclear medicine or invasive physiological assessment by pressure wire

<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>It is unclear whether FFRct is being proposed as an investigation that would be used in the investigation pathway of patients with chest pain or whether it is being proposed solely as an alternative to invasive measurement of FFR in patients considered to need a pressure wire study. FFRct could potentially be compared with other approaches to the investigation of chest pain - as recommended in CG95 this currently includes clinical assessment followed by a test, as determined by assessment of the likelihood of coronary artery disease. Tests included in this algorithm are: CT calcium score with/without coronary angiography; functional imaging (dobutamine stress echocardiography, myocardial perfusion imaging, MR cardiac perfusion imaging); invasive coronary angiography (with/without invasive measurement of FFR). It is unclear at what point FFRct fits into this algorithm and whether FFRct confers clinical and/or cost advantages over other methods of investigation. If FFRct is being proposed as an alternative method to pressurewire for measurement of FFR it is unclear how patients would be selected and how this would improve the current pathway.</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>Invasive fractional flow reserve. Other non-invasive tests for chest pain (stand alone CT coronary angiography, nuclear medicine and cardiac magnetic resonance imaging [with and without stress testing] and stress echocardiography).</p>

Question 7: "Competing products": Are you aware of any other products which have been introduced with the same purpose as this one?

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Not with CT but several companies and centres are working on deriving FFR from conventional invasive angiography. MEDIS have a product ready to launch.
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	No
Dr Ronak Rajani Consultant Cardiologist	No
Dr Francesca Pugliese Consultant Radiologist	Simplified algorithms are in development with some CT scanner companies
Dr Ian Purcell Consultant Cardiologist	No
Prof Nick Curzen Consultant Cardiologist	No
Dr Rob Henderson Consultant Cardiologist	FFR is conventionally assessed with a pressure wire during invasive coronary arteriography. Moreover, arguments in favour of FFRct may be partly based on evidence supporting the utility of invasive FFR, but this evidence has some important limitations.
Prof Carl Roobottom Professor of Radiology	No. Heart flow have tried to take out a Patent to prevent this.

POSSIBLE BENEFITS FOR PATIENTS

Question 8: *What are the likely additional benefits for patients of using this technology, compared with current practice/comparators?*

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Fewer tests. Fewer "unnecessary" invasive procedures.
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Decision on the need for revascularisation can be made non-invasively. Catheterisation can focus on treatment of significant lesions only
Dr Ronak Rajani Consultant Cardiologist	The potential benefits are a 1) quicker time to diagnosis 2) a more certain diagnosis by coronary CTA 3) A measure that has been proven to be related to prognosis 4) A measure of coronary stenosis that guides appropriateness for stenting 5) less layering of investigations 6) Improved patient pathway.
Dr Francesca Pugliese Consultant Radiologist	More accurate interpretation and reporting of coronary CTA, removing the need of further testing before the decision is taken as to whether or not proceed with angiography
Dr Ian Purcell Consultant Cardiologist	Reduce number of false positive non-invasive test results for CAD. Reduce number of normal invasive coronary angiograms in stable patients. Identify location of flow-limiting coronary disease to plan revascularisation strategy non-invasively. Patients could then proceed directly to planned percutaneous coronary intervention with an accurate assessment of flow-limiting CAD.
Prof Nick Curzen Consultant Cardiologist	A comprehensive assessment of not only the presence and extent of coronary disease (via CT coronary angiography) but also about whether there is a physiological restriction to flow (ie reversible ischaemia). This would be immensely valuable and allow for many more patients to be screened with much less risk
Dr Rob Henderson Consultant Cardiologist	Use of FFRct might potentially avoid the need for invasive investigation, but the efficacy and cost-efficacy of this technology should be demonstrated before it is introduced into routine practice.
Prof Carl Roobottom Professor of Radiology	Safer; non-invasive Quicker; no second procedure Cost; cheaper than invasive FFR but more expensive than competing modalities

Question 8.1: *Is each additional benefit likely to be realised in practice? What are the likely obstacles?*

Expert Advisers	Comment
<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Yes if the cost of ctFFR is realistic. However the need to have the data analysed remotely by a 3rd party is a problem as is the time need for computation.</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Yes</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>The potential obstacles are access of patients to facilities that perform high-quality coronary CTA. The technology does rely on good imaging facilities and image quality where the coronary CTA is of sufficient quality to permit the flow and pressure estimations. In the UK, some centres are more reliant on alternative imaging modalities rather than coronary CTA and have more experience with these. Another potential obstacle will be the acceptance from clinicians that the technique is robust and that the values for FFR_{ct} are robust and can be used to decide future patient management decisions.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>the frequency of the clinical scenarios in which this technology may be required depends on the patterns of use of coronary CTA in the first place, and is to be determined.</p>
<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Heartflow FFR_{ct} still a has false positive rate and will not eliminate need for invasive angiography and physiological testing in stable patients. Significant exclusions because of exacting nature of CT scan data required: atrial fibrillation, BMI>35, cardiac pacemaker etc. This reduces the number of eligible subjects.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>Currently the technology requires clinical validation, some of which is underway, and if validated then generalisability will be an issue to start with, given the need for a supercomputer analysis of individual patient data.</p>
<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>There is currently limited availability of CT coronary angiography across NHS hospitals in England (and the UK).</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>There is a requirement for high quality CT data. The evidence as yet is only from Heartflow sponsored studies so robustness of the technique is unproven.</p>

Question 8.2: How might these benefits be measured? What specific outcome measures would enable assessment of whether additional benefits for patients are being realised?

Expert Advisers	Comment
<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Reduction in costs (resource utilisation). Faster assessment.</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Reduction of normal angiograms</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>These benefits can be measured using a number of metrics. The outcome measures would be 1) time to diagnosis 2) reduction in inappropriate coronary angiograms (reduction in normalcy rate) 3) reduction in inappropriate coronary stenting 4) reduction in number of investigations 5) reduction in clinic appointments.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>mid and long term hard events, saved angiograms, saved further testing, downstream testing and costs</p>
<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Patients undergoing evaluation by FFRct in place of conventional testing would be expected to undergo fewer normal ("unnecessary") angiograms hence less radiation exposure, fewer angiogram related complications, consume less health resource. Clinical end-points should not be inferior: such as rate of myocardial infarction, unscheduled revascularisation.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>Number of patients screened who then do not require other (particularly invasive tests)</p>
<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>FFRct is an investigation for patients with chest pain/angina - benefits might accrue because an investigation pathway utilising FFRct is more effective (at making a diagnosis and determining optimal therapy) and less costly relative to other investigation pathways currently in use (as defined in CG95).</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>Outcome data following patients managed on the basis of non-invasive FFR; do they have similar outcome compared to invasive FFR?</p>

Question 8.3: How good is this evidence for each of these additional benefits?

Expert Advisers	Comment
<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Moderate</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Not yet established</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>To my knowledge there exists 3 economic modelling manuscripts across differing healthcare systems describing some of these potential benefits. These benefits however have not been conclusively demonstrated in a prospective fashion in any study. Most of the data is on economic modelling using retrospectively collected data. The upcoming Platform study will provide prospectively collected multicentre data.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>Minimal</p>
<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Randomised data supporting the accuracy of FFRct in comparison with conventional coronary CT and correlation of FFRct with invasive FFR has been published. Clinical end-point data and strategy comparison data will be available from the PLATFORM study. No randomised clinical end-point study exists.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>There are quite good data regarding the validity of FFRCT versus invasive angiography in a few thousand patients only... more data are on the way</p>
<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>I have little knowledge of this procedure but from the literature available on the Heartflow website it appears that clinical data are limited to studies on a few hundred patients. I doubt that these studies will provide sufficient evidence for any major change to the investigation pathway described in CG95.</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>Outcome data is limited</p>

Question 8.4: Please add any further comment on the claimed benefits of the technology to patients, as you see applicable

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	May be able to predict the outcome of PCI
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Blank
Dr Ronak Rajani Consultant Cardiologist	No additional comments other than the above
Dr Francesca Pugliese Consultant Radiologist	Blank
Dr Ian Purcell Consultant Cardiologist	Blank
Prof Nick Curzen Consultant Cardiologist	Potentially, this is a very important step change in assessment and investigation of patients with coronary disease
Dr Rob Henderson Consultant Cardiologist	Furhter research is likely to be required before this technology can be recommended for routine use in the UK unless there is some additional evidence of which I am currently unaware.
Prof Carl Roobottom Professor of Radiology	The technology may be incorporated into local computer systems in the future to allow more rapid decision making

POSSIBLE BENEFITS FOR THE HEALTHCARE SYSTEM

Question 9: *What are the likely additional benefits for the healthcare system of using this technology, compared with current practice/ comparators?*

Expert Advisers	Comment
<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Overall cost reductions. Could be very useful in hospital without invasive facilities.</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Reduced waiting times for angiography</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>Current practice varies greatly across the UK. The potential benefit would be to provide a more streamlined and consistent approach to evaluating patients with possible coronary disease. Another potential benefit is in that across all cardiac CT centres, the technology would improve the accuracy of cardiac CT thereby reducing the number of additional non-invasive tests required to reach a diagnosis. This would result in the downstream benefits of reduced overall cost and a quicker time to diagnosis. At present the evaluation of chest pain is dependent on what facilities each hospital has. Some utilise exercise treadmill testing, others myocardial perfusion scintigraphy, MRI perfusion and stress echocardiography. Patient testing for coronary disease is thus dependent on their local hospital and the expertise of the individuals performing the test. Coronary CTA on the other hand is potentially possible in almost every hospital in the UK. With FFRct there is potential to remove some of the operator dependent heterogeneity in the reporting of investigations to ensure more reliability in excluding or confirming the presence of coronary disease. The accuracy of FFRct in the trials against the gold standard of invasive FFR is reported to be at the highest level of diagnostic accuracy when compared to alternative measures of assessing significant flow limiting coronary disease. In centres who currently have access to cardiac CTA, the benefits of the technology are that it proposes an extension to the spectrum of patients that can be evaluated with coronary CTA and the removal of the need to refer for additional investigations when disease is detected. It also improves the accuracy of cardiac CTA where coronary disease is detected and thereby reduces unnecessary layering of investigations.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>More rapid diagnosis and decision to treat</p>

<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Streamline cardiac catheter workload by non-invasively identifying patients likely to need revascularisation beforehand. Patients having FFRct would be scheduled for a likely PCI in a PCI centre as the first invasive procedure rather than having an angiogram as a stand-alone procedure or as an angiogram with ad hoc (follow-on) PCI which is not required. Fewer angiograms on patients without flow-limiting CAD.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>Less invasive angiography and less expensive tests for reversible ischaemia</p>
<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>As above - could potentially refine the pathway for investigation of patients with chest pain with greater efficacy/cost-efficacy.</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>It has the potential to be substantially cheaper, quicker and more widely available than invasive FFR</p>

Question 9.1: Is each additional benefit likely to be realised in practice? What are the likely obstacles?

Expert Advisers	Comment
<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>As above</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Yes</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>It is possible that these benefits can be achieved. The likely obstacles will be the adoption of cardiac CT in centres which currently do not have access to this investigation and the appropriate training of individuals to perform coronary CTA. Also centres who use alternative methods of functional testing, have significant expertise in these areas and may be reluctant to use a technology that does not as yet have the same evidence base as their existing techniques. Another clear obstacle is likely to be the issue of removing clinician involvement from the interpretation of the test. The FFRct technology involves transferring the CT data for analysis elsewhere in order that a result can be obtained. Currently physicians report their own imaging investigations and have direct involvement. There may be concerns in relying on a third party on providing a result that guides future patient care.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>patterns of use of diagnostic testing vary according to availability and local expertise</p>
<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Would only be realised as part of a planned restructuring of the chest pain assessment pathway linked with a revascularisation strategy. An obstacle could be that non-PCI cath labs depend on a volume of diagnostic angiography for viability. A truly accurate non-invasive test may render such cath labs obsolete.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>As above</p>
<p>Dr Rob Henderson Consultant Cardiologist</p>	<p>If FFRct is used as an adjunct to CT coronary angiography in selected cases it could improve the management of a small number of patients. Wider application would require review/revision of the current chest pain algorithm (CG95).</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>There is a high probability of realisation.</p>

Question 9.2: *How might these benefits be measured? What specific outcome measures would enable assessment of whether additional benefits for the healthcare system are being realised?*

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	As above
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Reduced waiting times
Dr Ronak Rajani Consultant Cardiologist	The benefits of improving cardiac CT diagnostic accuracy can be measured directly at comparing the number of investigations required to achieve a diagnosis for each individual patient with chest pain. The time to diagnosis. A reduction in the number of false positive non-invasive investigations. A reduction in the number of normal coronary angiograms. A reduction in the number of inappropriate stents implanted for non-significant disease.
Dr Francesca Pugliese Consultant Radiologist	mid and long term outcomes, hard endpoints (not only saved angiograms)
Dr Ian Purcell Consultant Cardiologist	Cost reduction by fewer diagnostic angiograms not linked to a follow-on PCI. Catheter lab time saved for other procedures leading to lower costs.
Prof Nick Curzen Consultant Cardiologist	As above
Dr Rob Henderson Consultant Cardiologist	As above
Prof Carl Roobottom Professor of Radiology	Does the technology result in reduced use of invasive FFR? NHS costings. Outcome data.

Question 9.3: How good is this evidence for each of these additional benefits?

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Moderate
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Not yet established
Dr Ronak Rajani Consultant Cardiologist	The data is largely that indicated in section 8.3. In terms of enhancing the diagnostic accuracy of cardiac CTA. Three multicentre international trials have so far been published showing an enhanced accuracy of coronary CTA in assessing significant coronary disease where FFRct is used. These papers have been all published in leading medical journals. JAMA x 1 and JACC x 2.
Dr Francesca Pugliese Consultant Radiologist	Minimal
Dr Ian Purcell Consultant Cardiologist	None yet. Platform may inform this premise.
Prof Nick Curzen Consultant Cardiologist	As above
Dr Rob Henderson Consultant Cardiologist	As above
Prof Carl Roobottom Professor of Radiology	There is good evidence it is cheaper-does it reduce downstream investigations?

Question 9.4: Please add any further comment on the claimed benefits of the technology to the healthcare system, as you see applicable

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Blank
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Blank
Dr Ronak Rajani Consultant Cardiologist	No further comments
Dr Francesca Pugliese Consultant Radiologist	Blank
Dr Ian Purcell Consultant Cardiologist	Blank
Prof Nick Curzen Consultant Cardiologist	Blank
Dr Rob Henderson Consultant Cardiologist	As above
Prof Carl Roobottom Professor of Radiology	Blank

FACILITIES, TRAINING AND FUNCTIONING

Question 10: *Are there any particular facilities or infrastructure which needs to be in place for the safe and effective use of this technology?*

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Requires very high quality CT imaging
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	CT angiography
Dr Ronak Rajani Consultant Cardiologist	The FFRct can be measured on existing coronary CT datasets. No further facilities or infrastructure would therefore be required in centres that already practice cardiac CT. For centres that do not have cardiac CT capabilities, a cardiac CT capable scanner would be required along with appropriately trained radiographers and clinicians. The technology itself however required no additional facilities or infrastructure.
Dr Francesca Pugliese Consultant Radiologist	Yes, the vendor's core lab
Dr Ian Purcell Consultant Cardiologist	High quality coronary CT scanning
Prof Nick Curzen Consultant Cardiologist	Yes. High quality CT coronary angiography and then the ability to transfer raw data to a core lab at which sophisticated computer modelling is done for each case so that a FFRCT result can be generated and then sent back to the supervising doctor
Dr Rob Henderson Consultant Cardiologist	Widespread availability of CT coronary angiography with access to FFRct for appropriate cases.
Prof Carl Roobottom Professor of Radiology	Ability to upload confidential patient data to company. Payment structures to pay for exams.

Question 11: Is special training required to use this technology safely and effectively?

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Currently the analysis is carried out offline by the vendor
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Yes
Dr Ronak Rajani Consultant Cardiologist	No
Dr Francesca Pugliese Consultant Radiologist	there are restrictions imposed on image quality for the coronary CTA to be processed with this method
Dr Ian Purcell Consultant Cardiologist	Level 2 cardiac CT training sufficient plus a small amount of additional instruction and data review.
Prof Nick Curzen Consultant Cardiologist	Yes
Dr Rob Henderson Consultant Cardiologist	Apart from the process of measurement of FFRct, clinicians will also need to become familiar with the clinical interpretation of FFRct results.
Prof Carl Roobottom Professor of Radiology	It is all performed in-house by Heartflow (at a cost)

Question 12: *Please comment on any issues relating to the functioning, reliability and maintenance of this technology which may be important to consider if it is introduced*

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	As above- requires very high quality CT which may not be generally deliverable
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Needs extra IT involvement
Dr Ronak Rajani Consultant Cardiologist	The technology is dependent on a good quality cardiac CT dataset. However this in effect only means that centres should be conducting cardiac CT according to internationally recommended standards. The reliability is dependent on the company being able to issue results in a timely fashion and having robust IT systems to deal with the flux of analyses.
Dr Francesca Pugliese Consultant Radiologist	the technology depends on a service provided by the vendors, this is not 'in the house' technology
Dr Ian Purcell Consultant Cardiologist	I am not qualified to answer this
Prof Nick Curzen Consultant Cardiologist	As above
Dr Rob Henderson Consultant Cardiologist	My understanding is that the company will require images to be uploaded onto a server for analysis. If the technology is used widely this might have implications for network infrastructure. Patient confidentiality will also need to be considered.
Prof Carl Roobottom Professor of Radiology	Case selection is vital otherwise it could be very expensive.

COSTS

Question 13: *Please provide any comments on the likely cost consequences of introducing this technology. In particular, please comment on the implications of this technology replacing the comparator/s you have described above*

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Potential cost reductions due to less need for other testing
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Not aware of the costs
Dr Ronak Rajani Consultant Cardiologist	There is no cost consequences of introducing the technology immediately. The main costs implications arise from the cost of the analysis and performing the FFRct by the company. On surface value this is greater than all other non-invasive imaging tests. The cost saving anticipated are only from economic modelling of retrospective patient cohorts. The saving in this context are predicted to be as a result of reduced further testing as a result of fewer false positives from coronary CTA, MPS, MRI and DSE. Fewer false positives are anticipated to result in fewer coronary angiograms. The technique also proposes that fewer inappropriate stents would be required thereby introducing a cost saving.
Dr Francesca Pugliese Consultant Radiologist	To be defined
Dr Ian Purcell Consultant Cardiologist	There is a significant cost for each FFRct analysis in addition to the CT itself. The cost saving would be in reducing the amount of normal angiography and the associated costs. A careful cost analysis is required. This is part of the PLATFORM study.
Prof Nick Curzen Consultant Cardiologist	Not a realistic question yet
Dr Rob Henderson Consultant Cardiologist	The technology will require analysis of costs and efficacy of pathways including FFRct (including cost-savings by avoidance of other investigations; impact on rates of 'correct' diagnosis and on therapy, etc.) relative to other possible investigation pathways for patients with chest pain of suspected cardiac origin.
Prof Carl Roobottom Professor of Radiology	It may save money as cheaper than invasive FFR but if case selection is poor it could increase costs.

GENERAL ADVICE BASED ON YOUR SPECIALIST KNOWLEDGE

Question 14: Is there controversy about any aspect of this technology or about the care pathway?

Expert Advisers	Comment
<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Yes</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Validation of results ? /outcome in pts with high calcium score?</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>The main controversial areas are partially detailed above. Physicians are likely to want to decide on what functional test they wish to perform based on their experience and existing knowledge of the literature. The existing modalities have a sizeable historical evidence base to date. Although FFRct purports a higher diagnostic accuracy than these existing imaging modalities, the same body of evidence does not currently exist. Of the three main trials of the technology - of the two multicentre international trials {Defacto and HeartFlow NXT} - one was positive in terms of the endpoints and one was negative. The controversy therefore is that some clinicians believe that further data is required. The other difficulty/controversy is that some clinicians are reluctant to accept that it is possible by mathematical modelling and bioengineering to derive flow and velocity measurements of a coronary artery from a static imaging dataset. This technology however has been used in Industry already for approximately 50 years (Boeing, NASA, Formula 1). The other controversy is the reliance on an independent company providing diagnostics that clinicians would then use to make important patient decisions.</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>Yes</p>
<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>A controversy will be funding. The current funding model pays a tariff for coronary angiography but not for coronary CT scanning. Moving to this non-invasive technology instead of invasive angiography will not be financially sustainable since hospital trusts will lose by not carrying out angiography and will lose again by paying for a CT scan and the additional FFRct analysis.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>Only that some patients will not be suitable for it... but the majority will</p>

Expert Advisers	Comment
Dr Rob Henderson Consultant Cardiologist	Yes - there is controversy about the CG95 pathway as the evidence supporting the pathway has limitations. There is also controversy about the strength of evidence supporting FFRct.
Prof Carl Roobottom Professor of Radiology	Yes-its place is very controversial.

Question 15: If NICE were to develop guidance on this technology, how useful would this be to you and your colleagues?

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Very useful
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Helpful
Dr Ronak Rajani Consultant Cardiologist	The technology of Heartflow is clearly exciting and there is a lot of medical media coverage and exposure to clinicians. Clinical guidance would be very useful at this stage.
Dr Francesca Pugliese Consultant Radiologist	probably useful, but the levels of evidence are not relatively limited to few manufacturer-funded studies
Dr Ian Purcell Consultant Cardiologist	Very useful as this would enable a dialogue to begin with commissioning groups regarding implementation and funding of FFRct. Guidance may identify specific areas where data are lacking and serve as impetus for further studies proving benefit.
Prof Nick Curzen Consultant Cardiologist	Useful but I think it is very early to be considering this
Dr Rob Henderson Consultant Cardiologist	Limited use at this time because access to CT coronary arteriography is restricted. Likely to become more relevant in the future assuming evidence in favour of FFRct accumulates.
Prof Carl Roobottom Professor of Radiology	yes

Question 16: *Do any subgroups of patients need special consideration in relation to the technology (for example, because they have higher levels of ill health, poorer outcomes, problems accessing or using treatments or procedures)? Please explain why*

Expert Advisers	Comment
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	No
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	No
Dr Ronak Rajani Consultant Cardiologist	No
Dr Francesca Pugliese Consultant Radiologist	possibly, like in patients who are not suitable for other testing
Dr Ian Purcell Consultant Cardiologist	Several patient subgroups may be excluded on purely technical grounds as the scans will be of insufficient quality to yield diagnostic data. Patients who are obese (BMI>35) and patients with heavily calcified CAD, who tend to be older, may not be suitable as the technology currently functions.
Prof Nick Curzen Consultant Cardiologist	Blank
Dr Rob Henderson Consultant Cardiologist	FFRct may have a limited role in patients with severe or diffuse coronary artery disease and this may limit applicability to unselected populations of patients with coronary artery disease
Prof Carl Roobottom Professor of Radiology	Yes. Those with high calcium levels in their coronaries and patients with stents are difficult to analyse with CT and this is likely to effect CFFR performance (data lacking).

CONFLICTS OF INTEREST

Question 18.1: Do you or a member of your family have a personal pecuniary interest? The main examples are as follows:

Expert Advisers	Consultancies or directorships	Fee-paid work	Shareholdings	Expenses and hospitality	Investments	Personal non-pecuniary interest
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	No	No	No	No	No	No
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	No	No	No	No	No	No
Dr Ronak Rajani Consultant Cardiologist	Yes	Yes	No	No	Yes	No
Dr Francesca Pugliese Consultant Radiologist	No	No	No	No	No	No
Dr Ian Purcell Consultant Cardiologist	No	No	No	No	No	No
Prof Nick Curzen Consultant Cardiologist	Yes	Yes	No	No	No	No
Dr Rob Henderson Consultant Cardiologist	Yes	No	No	No	No	Yes
Prof Carl Roobottom Professor of Radiology	No	No	No	No	No	No

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	Blank
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	Blank
Dr Ronak Rajani Consultant Cardiologist	I provide consultancy services to Edwards Lifesciences on aspects of cardiac CT I have unit trust investments in a Global Healthcare Fund (HeartFlow not included) I have no financial relationships with the company HeartFlow who perform the FFRct measurements and have received no funding of any nature. I report cardiac CT scans in the private sector at the European Scanning Centre that offers FFRct as a service.
Dr Francesca Pugliese Consultant Radiologist	Blank
Dr Ian Purcell Consultant Cardiologist	Blank
Prof Nick Curzen Consultant Cardiologist	I have received consultancy speaker fees from Heartflow I am UK PI for the PLATFORM trial which is sponsored by HEARTFLOW I have also received consultancy/speaker fees from Abbott Vascular; Haemonetics; St Jude Medical; Volcano
Dr Rob Henderson Consultant Cardiologist	I am a member of an Advisory Board considering a novel technology for the investigation of patients with acute coronary syndrome for which I receive an honorarium. I am the Honorary Secretary of the British Cardiovascular Society and am a member and former Clinical Standards Lead of the British Cardiovascular Society.
Prof Carl Roobottom Professor of Radiology	Blank

Question 18.2: Do you have a non-personal interest? The main examples are as follows:

Expert Advisers	Fellowships endowed by the healthcare industry	Support by the healthcare industry or NICE that benefits his/her position or department, e.g. grants, sponsorship of posts
Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research	No	Yes
Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist	No	No
Dr Ronak Rajani Consultant Cardiologist	No	No
Dr Francesca Pugliese Consultant Radiologist	No	Yes
Dr Ian Purcell Consultant Cardiologist	No	Yes
Prof Nick Curzen Consultant Cardiologist	No	Yes
Dr Rob Henderson Consultant Cardiologist	No	No
Prof Carl Roobottom Professor of Radiology	No	No

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

<p>Prof Keith Oldroyd Consultant Interventional Cardiologist and Director of Research</p>	<p>Grants from St Jude Medical and Boston Scientific</p>
<p>Professor Andreas Baumbach Expert Cardiology Consultant and interventional cardiology specialist</p>	<p>Blank</p>
<p>Dr Ronak Rajani Consultant Cardiologist</p>	<p>Blank</p>
<p>Dr Francesca Pugliese Consultant Radiologist</p>	<p>Our department has received funding from the Industry to support the post of a post-doctoral researcher for 3 years. The Industry in question is Siemens, and there is no direct conflict relevant to the evaluation of this product. My post is fully funded by Queen Mary University of London with no contribution from Industry.</p>
<p>Dr Ian Purcell Consultant Cardiologist</p>	<p>Only in so far as my hospital directorate, of which I am the clinical director, receives NIHR funding for consultant time and the PLATFORM study is NIHR adopted.</p>
<p>Prof Nick Curzen Consultant Cardiologist</p>	<p>I have received unrestricted research grants from: St Jude Medical; Haemonetics: Medtronic I have received an unrestricted education grant to run a course by Volcano</p>
<p>Prof Carl Roobottom Professor of Radiology</p>	<p>Blank</p>