NICE advice

# QAngio XA 3D/QFR imaging software for assessing coronary obstructions

Medtech innovation briefing
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## Summary


- The **technology** described in this briefing is the QAngio XA 3D/QFR imaging software. It is used to assess fractional flow reserve (FFR) non-invasively.
- The **innovative aspects** of the technology are its ability to use invasive coronary angiography (ICA) to measure FFR non-invasively, quickly, on site and without the need for adenosine.
- The intended **place in therapy** would be in people with chest pain of recent onset who are referred for investigative ICA, and in people having a percutaneous coronary intervention (PCI) in which the technology could prevent the need for a pressure wire.
- The **main points from the evidence** summarised in this briefing are from 4 multicentre prospective studies including 568 adults referred for ICA. They show that QAngio XA 3D/QFR shows high correlation with the results from pressure-wire FFR.
- **Key uncertainties** around the evidence or technology are that the evidence is limited but evolving, and it is uncertain how the technology would translate into UK clinical practice given current recommendations in NICE's guideline on chest pain.
- The **cost** of QAngio XA 3D/QFR is £150 to £250 per analysis (excluding VAT). The **resource impact** would be cost saving if the technology avoided the need for invasive investigation and measurement of fractional flow.

## The technology

QAngio XA 3D/QFR (Medis) imaging software is used for the physiologic assessment (quantitative flow ratio; QFR) of coronary artery obstructions. It is designed to be used with all invasive coronary angiography (ICA) systems; biplane or monoplane. It uses 2, 2D X-ray angiographic projections, taken at least 25 degrees apart – and ideally between 35 and 50 degrees apart – to create a 3D-reconstruction of a coronary artery; this shows the QFR values across the artery. QFR is an assessment (by frame count) of the pressure (blood flow velocity) drop over the artery, with a value of 1 representing a normally functioning artery with no pressure drop. A 20% or more drop in blood pressures (QFR value of 0.8 and less) is considered a significant obstruction where revascularisation should be considered. QFR is measured non-invasively without the need for a pressure wire and vasodilator drugs such as adenosine, which increase blood flow.

QAngio XA 3D/QFR software is installed on a laptop or workstation that is connected to the ICA system. The Digital Imaging and Communication in Medicine (DICOM) data from ICA projections are immediately uploaded and viewable on the connected workstation.

### *Innovations*

Unlike current techniques for measuring blood flow across a vessel during ICA – such as fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR) measurements – QFR is measured non-invasively without the need for a pressure wire. Unlike FFR, it does not need vasodilator drugs, such as adenosine, to increase blood flow. The QFR results are processed on site and the company claims that the total time for data acquisition and analysis is about 4 to 5 minutes.

### *Current NHS pathway or current care pathway*

The NICE guideline on chest pain recommends further diagnostic testing for people in whom stable angina cannot be excluded by clinical assessment alone. This includes offering 64-slice or above coronary CT angiography (CCTA) as the first-line diagnostic test when clinical assessment suggests:

- typical or atypical angina **or**
- non-anginal chest pain, but 12-lead resting electrocardiogram (ECG) has been done and shows ST-T changes or Q waves.

Clinicians can ask for subsequent diagnostic tests, dependent on the CCTA results. NICE's guideline on chest pain recommends offering non-invasive functional imaging for myocardial

ischaemia if 64-slice or above CCTA has shown coronary artery disease of uncertain functional significance, or is non-diagnostic. Non-invasive functional imaging includes:

- myocardial perfusion scintigraphy with single-photon emission computed tomography (MPS with SPECT)
- stress echocardiography
- first-pass contrast-enhanced MR perfusion
- MR imaging for stress-induced wall motion abnormalities.

ICA should be offered as a second-line investigation when the results of non-invasive functional imaging are inconclusive.

When ICA is used to determine the presence and severity of coronary stenosis, it may be combined with the invasive measurement of FFR using a pressure wire. Although the NICE guideline on chest pain does not consider FFR, other guidelines (such as those of the European Society of Cardiology and American College of Cardiology) state that lesions with an FFR of 0.80 or less are functionally significant and revascularisation may be considered.

The company has indicated that the technology would be used as a second-line investigation alongside ICA to avoid invasive FFR measurement, and claimed that is could also be used in selection decisions on what interventional device to use (for example, stent).

The NICE medical technologies guidance on HeartFlow FFRCT recommends it as an option in people with stable, recent-onset chest pain and who are offered CCTA as part of the NICE guideline on chest pain.

## *Population, setting and intended user*

The technology would be used by cardiologists in people with chest pain of recent onset during investigative ICA, and in those having a percutaneous coronary intervention (PCI).

## *Costs*

### Technology costs

The first-year cost for the technology is £23,000; this includes unlimited use of the software over that period. In subsequent years payment is on a per-use basis, with each analysis expected to cost

between £150 and £250. The purchase price of the software includes software support and maintenance, usually done remotely from a UK-based support centre. Training is also provided by the company at installation.

The system uses a workstation, which is not included with the purchase of QAngio; the company has indicated, and experts have confirmed, that this is likely to already be in place. Experts have said that in many cases workstations will need to be upgraded or replaced to meet the technical specifications recommended by the company.

### Costs of standard care

The company has said that the cost of an invasive FFR is about £500, with additional costs for adenosine of about £100. Although FFR is recommended by other guideline-producing bodies and appears to be widely used in the NHS, it is not included in the NICE guideline on chest pain.

### *Resource consequences*

QAngio 3D/QFR is not currently used in NHS clinical practice but is being used in research.

QAngio 3D/QFR would represent an additional cost compared with standard ICA. It has the potential to reduce costs if it avoids the need for invasive FFR or PCIs.

The technology is designed to be used alongside existing ICA facilities. However, there are likely to be costs to upgrade or replace IT equipment to ensure that existing ICA centres are capable of running the software.

## Regulatory information

QAngio XA 3D/QFR was CE marked as a class IIa device in 2017.

## Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil

partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

No equality issues were identified.

## Clinical and technical evidence

A literature search was carried out for this briefing in line with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

### *Published evidence*

Four studies involving 568 patients are summarised in this briefing.

Table 1 summarises the clinical evidence as well as its strengths and limitations.

### *Overall assessment of the evidence*

Four studies are summarised in this briefing, but a larger body of evidence was identified mostly consisting of abstracts, technical reports, study protocols, presentations and experimental single-centre cohort studies on pilot devices. Early results from the China arm of the FAVOR II trial (Xu et al. 2017) are reported involving 5 sites and 306 patients, and those from the FAVOR trial (Tu et al. 2016): a pilot for FAVOR II. Rosendale et al. (2017) is presented, which examined the accuracy and reproducibility of 3 methods of quantitative flow ratio (QFR) calculation. Finally, Westra et al. (2018) is summarised, which reports results from the Wire-Free Functional Imaging II study. The reference standard in the reported studies is fractional flow reserve (FFR).

### Table 1 Summary of selected studies

| Tu et al. (2016) | |
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| Study size, design and location | 73 patients (84 vessels).<br>Multicentre prospective observational study involving 8 sites in 7 countries (Belgium, Italy ×2, Netherlands, Germany, China, Japan and US). |

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| Intervention and comparator(s) | QAngio XA 3D/QFR.<br>Reference standard (comparator): pressure-wire derived FFR measured during maximal stable hyperaemia, induced by intravenous adenosine/ adenosine triphosphate infusion. |
| Key outcomes | Mean angiographic percent diameter stenosis (DS%) was 46.1±8.9%; 27 vessels (32%) had FFR ≤0.80. Good agreement with FFR was observed for fQFR, cQFR and aQFR, with mean differences of 0.003±0.068 (p=0.66), 0.001±0.059 (p=0.90) and −0.001±0.065 (p=0.90) respectively. The overall diagnostic accuracy for identifying an FFR of ≤0.80 was 80% (95% CI 71% to 89%), 86% (95% CI 78% to 93%) and 87% (95% CI 80% to 94%) respectively. The area under the ROC was higher for cQFR than fQFR (difference: 0.04; 95% CI 0.01 to 0.08; p<0.01), but did not differ significantly between cQFR and aQFR (difference: 0.01; 95% CI −0.04 to 0.06; p=0.65).<br>The PLR was 4.8, 8.4 and 8.9 for fQFR, cQFR and aQFR, with NLR of 0.4, 0.3 and 0.2 respectively. |
| Strengths and limitations | This is a pilot study with a relatively small study population. None of the centres were in the UK. |
| Van Rosendael et al. (2017) | |
| Study size, design and location | 17 patients, 20 vessels.<br>Single-centre prospective observational study (Netherlands). |
| Intervention and comparator(s) | QAngio XA 3D/QFR.<br>Reference standard (comparator): pressure-wire derived FFR measured during maximal stable hyperaemia, induced by continuous intravenous adenosine (0.14 mg/kg/min). |

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| Key outcomes | Mean difference, standard deviation and 95% limits of agreement (LOA) between invasive FFR and aQFR, cQFR and fQFR for:<br>• observer 1:<br>– aQFR: mean difference ±SD: 0.01±0.04 (95% LOA: −0.07; 0.10)<br>– cQFR: 0.01±0.05 (95% LOA: −0.08; 0.10)<br>– fQFR: 0.01±0.04 (95% LOA: −0.06; 0.08)<br>• observer 2:<br>– aQFR: 0.00±0.03 (95% LOA: −0.06; 0.07)<br>– cQFR: −0.01±0.03 (95% LOA: −0.07; 0.05)<br>– fQFR: 0.00 ± 0.03 (95% LOA: −0.06; 0.05).<br>Between observer reproducibility for aQFR: 0.01±0.04 (95% LOA: −0.07; 0.09), for cQFR: 0.02±0.04 (95% LOA: −0.06; 0.09) and for fQFR: 0.01±0.05 (95% LOA: −0.07; 0.10). |
| Strengths and limitations | Supports other studies showing a high correlation between QFR and FFR. Additionally shows good agreement (reproducibility) between observers. Limited number of patients, 1 of the authors was the chief executive officer (CEO) of Medis and another an employee of Medis. |
| Xu et al. (2017) | |
| Study size, design and location | 306 patients (328 vessels).<br>Prospective multicentre observational study involving 5 sites in China. |
| Intervention and comparator(s) | QFR QCA.<br>Reference standard (comparator): wire-based FFR from QCA. |

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| Key outcomes | Patient-level and vessel-level diagnostic accuracy (defined as accuracy of online QFR [≤0.8 or >0.8] to identify hemodynamically significant coronary stenosis with FFR [≤0.8 or >0.8]) of QFR were 92.4% (95% CI 88.9% to 95.1%) and 92.7% (95% CI 89.3% to 95.3%), that were both significantly higher than the pre-specified target value of 75% (p<0.001). Sensitivity and specificity in identifying hemodynamically significant stenosis were significantly higher for QFR than QCA (sensitivity: 94.6% versus 62.5%, difference: 32.0%, p<0.001; specificity: 91.7% versus 58.1%, difference: 36.1%, p<0.001). Positive predictive value, negative predictive value, PLR and NLR for QFR was 85.5%, 97.1%, 11.4 and 0.06 respectively. Offline analysis showed vessel-level QFR had a high diagnostic accuracy of 93.3% (95% CI 90.0%, 95.7%). |
| Strengths and limitations | Multicentre partially blinded study (QFR, QCA and wire-based FFR were assessed online in blinded fashion during coronary angiography and re-analysed offline at an independent core laboratory) with good patient numbers. Vessels with diameter stenosis below 30% or above 90% were not assessed; 15.6% patients had a previous myocardial infarction, which may have increased the possibility of inaccurate physiology measurements but is reflective of a standard clinical population. |
| Westra et al. (2018) | |
| Study size, design and location | 172 patients (225 lesions).<br>Prospective multicentre observational study involving 2 sites in Denmark. |
| Intervention and comparator(s) | QAngio XA 3D/QFR.<br>Reference standard (comparator): wire-based FFR. |
| Key outcomes | QFR and FFR ≤0.80 were used as the diagnostic cut-off values.<br>Overall sensitivity, specificity, positive predictive value and negative predictive value were 77% (95% CI 66 to 85), 86% (95% CI 79 to 91), 75% (95% CI 65 to 84) and 87% (95% CI 80 to 92) respectively.<br>Mean difference between FFR and QFR was 0.01±0.08. QFR correctly classified 83% of the lesions using FFR. The area under the receiver operating characteristic curve was 0.86 (95% CI 0.81 to 0.91). |
| Strengths and limitations | Multicentre partially blinded study. QFR and FFR were assessed by blinded observers. Vessels with diameter stenosis below 30% or above 90% were not assessed. The study was part-funded by the company. |

Abbreviations: aQFR, measured hyperaemic flow velocity derived from angiography during adenosine-induced hyperaemia; CI, confidence interval; cQFR, modelled hyperaemic flow velocity derived from angiography without drug-induced hyperaemia; FFR, fractional flow reserve; fQFR, fixed empiric hyperaemic flow velocity; LOA, limit of agreement; NLR, negative likelihood ratio; PLR, positive likelihood ratio; QCA, quantitative coronary angiography; QFR, quantitative flow ratio; ROC, receiver operating curve; SD, standard deviation.

### *Recent and ongoing studies*

- Reliability of 3D angio QFR evaluation of non-culprit stenoses in STEMI patients during first acute interventional procedure: comparison with staged procedure FFR (AOStAnnaSS). ClinicalTrials.gov identifier: NCT02998853. Status: Concluded, findings presented at cardiovascular research foundation (US) TCT conference in November 2017, and publications imminent.

## Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Five specialists provided comments, all of whom were aware of the technology or concept, and 1 had used it in a research/demonstration capacity.

### *Level of innovation*

All the specialists considered the technology to be innovative. Two experts noted that similar competing technologies existed and 1 noted that these (fractional flow reserve [FFR] and instantaneous wave-free ratio [iFR]) had an excellent evidence base, and had been widely adopted in the NHS so it potentially had a less compelling case for adoption in the NHS. One considered the technology to be potentially disruptive to the care pathway.

### *Potential patient impact*

The specialists considered that the technology could avoid the need for invasive FFR measurement and the risks associated with the passage of a guide wire, and the side effects associated with adenosine or other vasodilator drugs. One considered it had the potential to improve diagnostic accuracy and avoid further procedures or repeat investigations.

### *Potential system impact*

The specialists considered that the technology could potentially save money and produce system benefits through avoiding invasive measurement of FFR and reducing procedure time, and therefore throughput in ICA. One specialist stated that further evidence was needed on this, and 1 stated that the comparator was important with it likely to save money against invasive coronary angiography (ICA) alone but less certain against FFR and iFR.

### *General comments*

The specialists noted that in addition to potentially replacing FFR and iFR, it could also reduce other functional tests (Echo/MRI/Spect) and FFRCT.

They were split on the appropriateness of NICE guidance. They considered the potential obstacles to adoption, from the cost of the technology to the lack of clinical data, and the widespread belief in FFR as the 'gold standard' assessment.

## Specialist commentators

The following clinicians contributed to this briefing:

- Dr Tom Johnson, consultant cardiologist, Bristol Heart Institute, University Hospitals Bristol NHS Foundation Trust. Has received fees for consultations, speaker engagements, and educational engagements from Abbot vascular, Terumo, Boston Scientific, Europa organisation and Vascular perspectives.
- Professor Andreas Baumbach, chair for device innovation, Barts Heart Centre and Queen Mary University of London. The company is providing him with the technology to do research; he has submitted a trial proposal for the technology with the British Heart Foundation.
- Dr Ian Purcell, consultant interventional cardiologist, Cardiothoracic Centre, Freeman Hospital. Did not declare any interests.
- Dr Robert Henderson, consultant cardiologist, Trent Cardiac Centre, Nottingham University Hospitals NHS Trust. Has received honorarium for participation in an advisory board for Creavo Medical Technology, which is developing a technology to investigate acute chest pain of suspected cardiac origin.
- Dr Jaydeep Sarma, Consultant interventional cardiologist, Manchester University NHS Foundation Trust. Did not declare any interests.

## Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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