

Horizon Scanning report No. 6

**Wireless coronary pressure wire for the
measurement of fractional flow reserve**

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Methods

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Limitations

This report is based on information available when the searches were made and does not contain data on subsequent developments or improvements of the evaluated technology. The observations made on effectiveness, safety or cost-effectiveness of the technology evaluated in the report are to be considered temporary.

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Declaration of Conflict of Interest

The authors declare that they will not receive either benefits or harms from the publication of this report. None of the authors have or have held shares, consultancies or personal relationships with any of the producers of the devices assessed in this document.

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Name of the technology/procedure: **Wireless pressure wire for the measurement of fractional flow reserve**

Target population

The target population for Fractional Flow Reserve (FFR) measurement with the pressure wires are patients undergoing coronary angiography to assess the functional significance of a non critical stenosis of the coronary arteries.

Description of the procedure and technology

In recent years there has been technological innovation in the functional assessment of coronary stenosis, based on the use of percutaneous wires fitted with sensors. [Verna E, 2001]. Innovation was necessary in the assessment of intermediate severity stenosis or in the presence of complex morphology, which were difficult to manage with traditional non invasive techniques (ECG and stress echocardiography, angiography, PET, MRI, SPECT MPI) [Verna E, 2001; Siebert U, 2008]. In these cases, quantitative measurements to better define the severity of the stenosis can be a significant decisional support in guiding clinicians in the choice of the most appropriate treatment (angioplasty, aorto-coronary by-pass or pharmacological treatment).

In indicating the entity of a coronary stenosis, the FFR provides a useful indicator as it expresses the ratio between maximal flow in the stenotic vessel and normal maximal flow [De Rosa R, 2009; Kushner FG, 2009]. It is a non-dimensional parameter (expressed with values between 0 and 1 which respectively indicates occluded and healthy vessels) measured by pressure wires (also known as pressure guide-wires) that are similar to those used in angiography. These integrate miniaturised pressure transducers in the terminal section.

The transduced signal is transmitted by wire to an external visualisation system (generally a small dedicated monitor) which enables real time monitoring of the values measured (the FFR, and other parameters too, such as CFR and IMR) [Ng MKC, 2006]. FFR values below 0.75 indicate the presence of a significant myocardial ischemia and suggest the need for treatment with angioplasty. For FFR values greater than or equal to 0.75 the procedure of stenting would not seem indicated as the risk of serious complications (for example myocardial infarction) is low [Pijls NHJ, 2007].

To date the principal innovation in this field is the use of wireless technology to transmit signals from the pressure wire to the visualisation system via a wireless receiver.

The aim of this report is to evaluate this type of technology. The advent of wireless receivers does not imply significant modification in FFR measured during angiography. The pressure wire is inserted via the guide catheter and is positioned under angiographic control beyond the point of

interest. Pharmacological hyperaemia is induced in the patient for a time of some 15 seconds and following different protocols [De Bruyne B, 2008]. The pressure measured by the pressure wire transducer beyond the stenosis is then expressed as a ratio to that acquired via the guide catheter above the stenosis (which coincides with aortic pressure).

This wireless technology does not represent a diagnostic innovation, however it may deliver organizational and management benefits, for the operators and for the hospital, especially in the acquisition and management of the data acquired during FFR measurement.

Clinical importance and burden of disease

Coronary stenosis is a constriction of the vasal lumen generally caused by an atherosclerotic plaque, which reduces blood flow and myocardial oxygen supply. FFR is an indicator for the risk assessment of patients with stenosis [Melikian N, De Bondt P et al. 2010]. It may help to determine the functional significance of a non critical stenosis and provide a precise definition of the coronary damage, and thus in defining the appropriateness of a revascularisation procedure (stent or bypass). The additional use of FFR measurement during angiography procedures was the subject of a multi-centric, randomised, prospective study (FAME study) [Tonino PA, 2009], conducted in the United States on 1,005 patients affected by multivessel coronary artery disease. The study compared the clinical outcomes at 12 months of patients treated with stenting after the measurement of FFR, with patients who had undergone stents after angiography only. The study findings show a significant reduction in the risk of death and heart attack in patients subjected to angiography with FFR measurement compared to those subjected to angiography alone. The possibility of measuring FFR during angiography may direct the therapeutic procedures in a more appropriate way, delivering a significant improvement in the clinical outcome for the patient and reducing the number of stents implanted and consequently the risk associated with the procedure. In Italy there are 242 haemodynamics theatres which host stenting procedures. In 2008, 190,320 stents were implanted (total DES and BMS). Coronary wires were used in only 81 haemodynamics theatres for a total of 1,781 procedures [Giornale Italiano di Cardiologia Invasiva, 2009]. This figure however includes total procedures performed with both pressure and flow wires.

Products, manufacturers, distributors and approval

The emerging technology identified is Aeris, produced by St. Jude Medical Inc. and marketed by St. Jude Medical Italia S.p.A. The components of the system are:

- a coronary guide-wire (PressureWire® Aeris), which integrates the pressure sensor and the wireless transmitter;
- a signal receiver (PressureWire® Receiver), connected to the theatre polygraph which acquires and converts the signal received via radio from the guide-wire.

The technology enables measurement of the FFR, and its principal elements (sensors, materials, etc.) are those already used by the PressurWire® Certus system (St. Jude Medical) on the market

since 2004. With the new technology the measurements obtained during the procedure can be directly displayed on the monitors of the theatre polygraph system, transmitting them via wireless and enabling their management (archiving, transmission, etc.) together with the angiographic images and other parameters acquired. The Aeris system received the CE mark in September 2009 and was cleared by the FDA in 2008. The manufacturer (St. Jude Medical) declares full compatibility with polygraph systems from the following manufacturers: GE Healthcare, Mennen Medical, McKesson and Siemens. The software update required for integration is provided by the single polygraph manufacturers. The latest versions of polygraphs on the market are equipped with the specific software and do not require further update.

Manufacturers	Distributors	CE Mark	RDM	FDA
St. Jude Medical, Inc.	St. Jude Medical Italia S.p.A.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

Setting

Wireless FFR measurement must be utilised in a hospital context where there are haemodynamics theatres equipped with angiography.

<input type="checkbox"/> Home	<input checked="" type="checkbox"/> Hospital	<input type="checkbox"/> Out Patients
<input type="checkbox"/> Accident and Emergency	<input type="checkbox"/> Other:	

Roll out in Italy

Marketing of the Aeris system began in Italy in March 2010. To date (May 2010) the system is used only in one health facility located in the Marche region. Other Italian facilities are at the negotiating phase and are updating theatre polygraph software for the adoption of the new technology.

<input type="checkbox"/> Pre-marketing	<input checked="" type="checkbox"/> On the market for 1-6 months	<input type="checkbox"/> On the market for 7-12 months
<input type="checkbox"/> On the market for more than 12 months	<input type="checkbox"/> Not identified	

Comparators

The comparators for wireless coronary pressure wires are the traditional (non wireless) technologies with the ability to measure FFR in patients subjected to angiography procedures:

- Systems consisting of pressure wires and dedicated monitor:
 - PressureWire® Certus with RADIANalyzer® Xpress monitor (St. Jude Medical);
 - PrimeWire® with ComboMap® monitor (Volcano Corporation);
- Integrated systems combining pressure and flow wires and intra-coronary ultrasonography in a single acquisition and display system:
 - s5™i IVUS System (Volcano Corporation).

Effectiveness and safety

Wireless coronary pressure wires do not produce diagnostic improvements compared to traditional technologies. The additional value of this technology must be assessed on the basis of its potential ability to improve the procedure and the management of the patients compared with traditional FFR measurement systems.

A search of the literature on the use of the wireless system was conducted on the EuroScan and CRD databases (DARE & HTA), to identify Horizon Scanning (HS) reports and Rapid Health Technology Assessments, published in Italian and English. This search found no relevant documents.

The search of the literature was performed looking for clinical studies published in English and Italian from 2008 in the main databases: Medline (6 May 2010), Cochrane Library (7 May 2010) and Embase (7 May 2010). The inclusion criteria for the studies were *in vivo* studies of coronary heart disease patients subjected to FFR measurement procedures for the functional assessment of intermediate stenosis with the Aeris system. The comparators for wireless coronary pressure wires are the traditional (non wireless) technologies. No studies assessing the new technology were found.

As the technology was only recently introduced to the market, the manufacturer (St. Jude Medical) was consulted to identify evidence from “grey literature” (registers, presentations, posters, unpublished pre-marketing studies, etc.). The manufacturer declared that to date only marketing activities are underway for technical evaluation of the technology by health operators.

Potential benefits to patients

For the diagnosis and prognosis, compared to traditional systems, wireless coronary pressure wires do not deliver any additional clinical benefit to patients. However, organisational and management benefits may be generated. These may translate into indirect benefits for the patients.

<input type="checkbox"/> Mortality reduction or increased survival	<input type="checkbox"/> Reduction of the morbidity	<input type="checkbox"/> Improved quality of life (patient/users)
<input type="checkbox"/> Improved patient monitoring	<input checked="" type="checkbox"/> Other: Indirect benefits related to the patient management	<input type="checkbox"/> Not identified

Cost of the technology/procedure

The Aeris system is sold at a list price of € 1,350 + VAT for the Aeris PressureWire® (disposable guide-wire) and € 860 + VAT for the PressureWire® Receiver (one off expense).

The cost of the software to integrate the system with the theatre polygraph depends on the contractual conditions specified by the hospital with the polygraph supplier companies (St. Jude Medical declares a maximum cost of € 20,000). Wireless pressure wires can be used exclusively in the presence of compatible polygraphs (GE Healthcare, Mennen Medical, McKesson e Siemens) in the haemodynamics theatre. Thus the calculation of the costs linked with the introduction of the new technology strongly depends on the brand and model of the polygraph installed in the haemodynamic theatre. Table 1 provides an overview of possible alternatives for FFR measurement with pressure wires.

The diagnostic procedure with the use of the Aeris technology and, more in general, the FFR measurement procedure with pressure wires does not currently have a specific reimbursement DRG, but is linked to the diagnostic angioplasty or coronarography procedure. In addition, to date, no extra reimbursement fees for FFR measurement are assigned at national/regional level.

<input type="checkbox"/> Increased costs compared to alternative treatments	<input checked="" type="checkbox"/> Increased costs due to increased demand	<input type="checkbox"/> Increased costs due to the required investments
<input type="checkbox"/> New costs	<input type="checkbox"/> Other:	

Potential structural and organisational impact

Structural impact

The procedure must be performed exclusively in a haemodynamics theatre equipped to perform angiography. The application may also be used in interventional radiology angiography theatres for the measurement of the FFR in peripheral vascular sites. Compared to the traditional systems, the wireless coronary pressure wire has no significant structural impact as it is integrated with the theatre polygraph visualisation system.

<input type="checkbox"/> Increase in requirement of instruments	<input type="checkbox"/> Always be used	<input checked="" type="checkbox"/> Can be used only under specific circumstances
<input type="checkbox"/> Decrease in requirement of instruments	<input type="checkbox"/> Other:	<input type="checkbox"/> Not identified

Organisational impact

The technology analysed may deliver benefits in organisational and management terms, given the absence of wires between the surgical table and the monitor, the use of a visualisation system already in theatre and the integrated management of all the patient data (images, parameters, etc.). These aspects could favour greater acceptance of the technology by health operators and greater facility of interchange of clinical information, thanks to the development of digital health and electronic case histories. Traditional systems in addition require in the theatre system preparation and calibration phase, additional steps which may imply longer set-up times. According to the manufacturer's declarations, a medical operator must perform 2-3 procedures to become acquainted with the new technology (compared with the 5-10 procedures required by non wireless systems).

<input type="checkbox"/> Increase in the number of procedures	<input type="checkbox"/> Re-organisation required	<input checked="" type="checkbox"/> Training required for users
<input type="checkbox"/> Reduction in the number of procedures	<input type="checkbox"/> Other:	<input type="checkbox"/> Not identified

Conclusions

Angiography is the most used procedure to assess coronary stenoses and to select patients for angioplasty procedures. However the limits of this methodology in describing the real morphological complexity of coronary circulation and the potential impact of the stenosis on coronary flow are now evident [Melikian N, Del Furia F et al. 2010]. FFR is considered the "gold standard" index for the evaluation of the functional significance of intermediate stenoses in both single-vessel and multi-vessel coronary disease [De Rosa R, 2009].

A recent HTA report produced by the DIMDI (German Institute of Medical Documentation and Information) [Siebert U, 2008] concluded that FFR measurements should be introduced in clinical routine as the evidence demonstrates that they can support therapeutic choice in patients with single-vessel stenosis [Siebert U, 2008; Pijls NH, 2007]. Promising results were also reported in the FAME study [Tonino PA, 2009] for patients with multi-vessel stenosis.

Despite the evidence available, FFR measurement is not commonly performed in clinical practice. As this parameter can deliver a more rational use of stents with consequent economic and health benefits, further investigation is necessary to analyse the barriers which currently hamper the adoption of the technology, be it wireless-based or not.

As to wireless pressure wires, since the organisational benefits linked with their use have not been quantified compared to non wireless pressure wires, it is impossible to associate the costs of the technology with the effects its introduction would bring to the health care system.

Given that coronary pressure wires for FFR measurement contribute to the optimisation of the number of stents implanted, this may discourage their use as the extra reimbursement linked with stenting procedure, where present, would make the latter more remunerative (a phenomenon known as cream skimming).

Future prospects

There is a requirement for studies evaluating the economic, clinical and organisational impact of FFR measurement with the wireless system. In the future pressure wires will also have a role in the assessment of stenosis in peripheral vascular circulation.

Table 1: Overview of the possible alternatives for fractional flow reserve (FFR) measurement with pressure wires.

Theatre polygraph	Systems for FFR measurement	Systems available on the market	List price (+ VAT)
Polygraph from any manufacturer	a) Pressure wire and dedicated monitor (non-wireless)	St. Jude Medical: PressureWire® Certus Monitor RADIANalyzer® Xpress Volcano Corporation: PrimeWire® Monitor ComboMap®	€ 1,126 € 15,525 Not declared Not declared
	b) Integrated system *	Volcano: s5™i	Not declared
Polygraph manufactured by: - GE Healthcare - Mennen Medical - McKesson - Siemens <i>(models without specific integration software)</i>	c) Pressure wire and wireless receiver	St. Jude Medical: PressureWire® Aeris PressureWire® Receiver Integration software	€ 1,350 € 860 It depends on the contractual conditions stipulates by the hospital with the polygraph supplier companies (maximum cost of € 20,000)
Polygraph manufactured by: - GE Healthcare - Mennen Medical - McKesson - Siemens <i>(models with specific integration software)</i>	d) Pressure wire and wireless receiver	St. Jude Medical: PressureWire® Aeris PressureWire® Receiver	€ 1,350 € 860

* Non-wireless system combining pressure and flow wires, and intra-coronary ultrasonography with a single acquisition and visualisation system.

Evidence searches

Searches of the databases were executed using the following key words to indicate:

- ***the technology of interest:*** coronary angiography OR angiography, pressure wire OR pressure-wire OR fractional flow reserve OR wireless OR aeris OR guidewire;
- ***the pathology of reference:*** multivessel coronary artery disease OR coronary stenosis OR stenotic coronary lesion OR stenotic artery.

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Glossary

Angiography: Radiological procedure that provides information on the morphology of vessels. Can be performed for diagnostic purposes but is also the basis of therapeutic procedures in interventional radiology. When executed in the coronary arteries is called coronary angiography, and allows the visualization of coronary arteries by introducing a catheter from a main vessel (e.g. a femoral or radial artery) to reach the desired district, and injecting of contrast agent.

Angioplasty: The technique of mechanically widening a narrowed or obstructed blood vessel; typically as a result of atherosclerosis. When performed in coronary arteries is defined coronary angioplasty (also known as percutaneous transluminal coronary angioplasty, PTCA or percutaneous coronary intervention, PCI).

BMS: Bare Metal Stent.

CFR: Coronary Flow Reserve.

CRD: Centre for Reviews and Dissemination.

Cream skimming: Actions aimed to providing a product or a service to only the high-value or low-cost customers of that product or service. In the healthcare sector, the provider tries to select the most profitable patients.

DES: Drug-Eluting Stent.

DIMDI: Deutsches Institut für Medizinische Dokumentation und Information (www.dimdi.de).

DRG: Diagnosis-Related Groups.

ECG: Electrocardiography.

FAME: Fractional Flow Reserve (FFR) vs. Angiography for Multivessel Evaluation.

FDA: Food and Drug Administration.

FFR: Fractional Flow Reserve.

Hyperaemia: Increase of blood flow to an organ or anatomical district.

IMR: Index of Microcirculatory Resistance.

ISS: Italian National Health Institute.

Istat: Italian National Institute of Statistics.

MRI: Magnetic Resonance Imaging.

PET: Positron Emission Tomography.

RDM: Medical device Repertory

(<http://www.salute.gov.it/dispositivi/paginainternasf.jsp?id=499&menu=repertorio>).

SPECT MPI: Single-Photon Emission Computed Tomography Myocardial Perfusion Imaging.

Stenting: Placement of stent.