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Optical coherence tomography (OCT) to evaluate the microstructure of vulnerable atherosclerotic plaques

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Methods

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For further information contained in this report please contact:
Agenas – Agenzia nazionale per i servizi sanitari regionali
Sezione Iss – Innovazione, sperimentazione e sviluppo
Via Puglie, 23 - 00187 Roma
e-mail: hta@agenas.it

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.

Authors

This HS report was prepared by:

Simona Paone

Mirella Corio

Eliana Ferroni

Emilio Chiarolla

Tom Jefferson

Marina Cerbo

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: **Optical coherence technology (OCT) to evaluate the microstructure of vulnerable atherosclerotic plaques**

Target population

Optical coherence tomography (OCT) is indicated for all patients with medium-high cardiovascular risk (levels IV-VI according to the Cardiovascular Risk Chart prepared and published by the Italian National Institute of Health [Heart project]) undergoing coronary angiography.

Description of the procedure and technology

OCT is an invasive imaging technique based on the use of a beam of light and its reflection by the structures which it encounters [Prati F, 2003]. The system compares the propagation frequencies of the light echo reflected by the tissue with those for the same beam of light reflected from a mirror of reference placed at a known distance. This technology reaches a definition of about 10-20 µm that represents a resolution 20 times superior to intravascular echography (IVUS) and the other non invasive diagnostics such as computerised tomography (CT), magnetic resonance (MR) and scintigraphy [Matter C, 2009]. The new generation of OCT (Fourier-domain, FD-OCT), compared to previous systems (Time-domain OCT), produces faster frequency of image sampling without compromising quality. Further, the new FD-OCT technology enables the acquisition of longitudinal and transverse sequences of a longer tract of the coronaries at greater pull back speed [Gonzalo N, 2010]. Another important skill of the new generation system is the ability to scan vessels of greater diameter (lumen > 4 mm). There are no differences from the traditional systems in axial, lateral and tissue penetration depth resolution parameters,. Finally, as red blood cells create interference with the light signal in the process of image acquisition, earlier systems used an obstructive balloon to temporarily interrupt the blood flow, while the latest generation technology applies a non occlusive technique which provides the injection of washing isomolar solution (flushing technique) [Barlis P, 2008].

FD-OCT technology is used during angiography procedures. A catheter is inserted by femoral artery until it reaches the coronaries, below the section of interest. The procedure is then activated in pull back acquiring the images in approximately 2 seconds. This report only assesses the latest FD-OCT technology.

Clinical importance and burden of disease

Atherosclerosis is a chronic, inflammatory and multifactorial disease which affects the arteries causing very serious pathologies such as angina pectoris, acute myocardial infarction, stroke and sudden death. In 2007 in Italy (the latest year for which data are available) 37,712 males and 37,407 females died from ischemic heart diseases (codes ICD-9-CM 120-125) [Istat. Causes of death. 2010].

Anatomically the typical atherosclerotic lesion is represented by the plaque, which is a thickening of the innermost stratum of the arteries (the intima) mainly due to accumulation of lipid material and proliferation of the connective tissue.

Plaque rupture causes approx. 75% of coronary thrombi, leading to myocardial infarction and/or death [Eijgelaar WJ, 2009].

The tendency of atherosclerotic plaques to rupture is affected by the thickness of the fibrous cap: the greater the thickness, the lower the probability of plaque ulceration. Other factors are the dimension of the lipid core and its composition. Atherosclerotic plaques consisting of at least 40% lipid tissue are at greatest risk of rupture [Davies MJ, 1993; Davies MJ,1994].

Inflammation also plays a major role, and the marked local infiltration of macrophages (immune response cells) is the cause of thinning of the fibrous cap [Davies MJ,1994]. The histological characteristics of vulnerable plaques are principally represented by a thin fibrous cap < 65 µm, made by a lipid pool (at least 40%) and the presence of active macrophages proximal to the cap.

The possibility of undertaking a thorough study of the components of atherosclerotic plaques through the use of intra-coronary probes would allow the identification of an additional prognostic factor for planning an appropriate diagnostic-therapeutic clinical pathway in patients at medium-high cardiovascular risk.

Products, manufacturers, distributors and approval.

There is only one FD-OCT system currently on the market. Its brand name is C7XR and it is produced by LightLab Imaging Inc. and had been marketed in Italy since September 2009 by EndoTech S.p.A. The system consists of the following principal units: a console for image acquisition, elaboration and display and a disposable catheter. Its brand name is C7 Dragonfly.

The OCT C7XR is an evolution of previous Time-domain OCT systems, M2x and M3x, also produced by LightLab and still available on the market.

According to the producers' indications, the C7XR system and the C7 Dragonfly catheter should be used in qualitative and quantitative evaluation of the vascular morphology of the coronary arteries, as an adjuvant instrument to traditional type angiography, to provide an image of the vascular lumen and the parietal structures and coronary arteries.

This technology is also recommended in invasive trans-luminal coronary angioplasty procedures for correct stent positioning and in the assessment of its degree of endothelialization [LightLab, Inc. Operating Manual].

The system identified has CE marking since March 2009, but the Food and Drug Administration (FDA) approval has not been given yet..

Another company, Volcano Corporation, is developing an OCT technology [Villard, 2009]. This will be marketed probably in the next few months.

Manufacturers	Distributors	CE Mark	RDM	FDA
LightLab Imaging, Inc.	EndoTech S.p.A.	☑	☑	☐

Setting

This technology is used exclusively in a hospital in an haemodynamics operating theatre equipped with angiography system. However, the number of cases treated and the learning curve are two factors which may affect the maximum number of centres which would employ the technology.

☐ Home	☑ Hospital	☐ Out Patients
☐ Accident and Emergency	☐ Other:	

Roll out in Italy

To date the C7XR is used in 15 centres in Italy. There are, on the other hand, 30 installations of previous models for which there are no information about the clinical applications and actual use for the evaluation of vulnerable atherosclerotic plaques. The distributor foresees the installation of the new model at 40 centres (some replacing the previous models) by the end of September 2010 forecasting 80 installations over the whole 240 haemodynamics in Italy.

☐ Pre-marketing	☐ On the market for 1-6 months	☑ On the market for 7-12 months
☐ On the market for more than 12 months	☐ Not identified	

Comparators

To date OCT is the only intra-coronary technology with the capacity to evaluate vulnerable plaques as the other technologies, both non invasive imaging (CT, MRI, Angiography, SPECT, PET-CT), and invasive imaging (IVUS, IVUS-virtual histology, Angioscopy, Thermography) cannot simultaneously differentiate the histological characteristics of the plaque and measure the microstructures.

Effectiveness and safety

The effectiveness of this technology can be defined as the ability of FD-OCT to display and measure the composition of atherosclerotic plaque accurately and precisely. Safety refers to the association of the execution of a procedure with complications and adverse events.
For identifying Horizon Scanning (HS) reports and Rapid Health Technology Assessments a literature research was carried out on EuroScan and CRD databases (DARE & HTA), published in Italian and English, on the specific topic of the use of FD-OCT in the study of the microstructures of atherosclerotic plaques. No HS report or Rapid HTA was identified.
We looked for the evidence also by searching for studies published in English and Italian from January 1st 2008 (the year before CE marking was obtained) in the major databases: Medline (to January 22th 2010), Cochrane Library (to January 29th 2010) and Embase (to February 22th 2010). The Italian distributor was also consulted to identify pre and post marketing studies. The criteria for inclusion in our report were comparative in vivo studies of patients with medium-high cardiovascular risk undergoing FD-OCT examination with the C7XR system for the study of vulnerable atherosclerotic plaques. The comparators for this technology are both the imaging techniques which analyse at least one of the components of vulnerable atherosclerotic plaques, and the previous OCT systems (still marketed at the date of preparation of this report).
No comparative studies evaluating the diagnostic efficacy or safety in vivo of the model compared to other imaging techniques were identified.
The distributor claims that the risks linked with the procedure via OCT are the same as those for angioplasty.

Potential benefits to patients

The effectiveness of FD-OCT in terms of its capacity to direct patients to the most appropriate therapeutic treatment is not identifiable, as, to date, there are no vulnerable atherosclerotic plaque treatments for which efficacy (the absence or slowdown of the appearance of major acute events) is supported by clinical studies.

□ Mortality reduction or increased survival	□ Reduction of the morbidity	□ Improved quality of life (patient/user)
□ Improved patient monitoring	□ Other: Improved appropriateness of treatment	☑ Not identified

Cost of the technology / procedure

It is possible to get C7XR system with different packages comprising: purchase console and catheters with a list price indicated by the Italian distributor, deposited at the Chamber of Commerce, respectively of € 150,000.00 + VAT and € 3,000.00 + VAT. The price list (deposited at the Chamber of Commerce) for the previous model M2x is €110,000.00 +VAT; the system uses two catheters: the light guide and the occlusion balloon whose respective prices are €1,700.00 and €1,100.00 + VAT. Another purchasing package is leasing of the console with separate purchase of the catheters. In any case delivery includes some 20 days training and maintenance which, in the case of purchase only covers the warranty period, while with hire it is included in the rental. A final procurement package is free loan of the technology in exchange for the purchase of at least 60-70 catheters per year. In this case, maintenance and training are included in the cost of consumable materials. Diagnostics procedures using this FD-OCT technology does not have a specific DRG but is linked to the angioplasty procedure.

□ Increased costs compared to alternative treatments	□ Increased costs due to increased demand	□ Increased costs due to the required investments
☑ New costs	□ Other:	

Potential structural and organisational impact

Structural impact

This procedure may only be executed in haemodynamics laboratories equipped with angiography facilities. The angiography facility must be of sufficient size to easily host the device, although the latter is of contained size and is easily positioned.

☑ Increase in requirement of instruments	□ Always be used	☑ Can be used only under specific circumstances
□ Decrease in requirement of instruments	□ Other:	□ Not identified

Organisational impact

The FD-OCT procedure extends the duration of the angiography by some 3 minutes. According to the distributor indications, the use of this technology does not require the employment of extra personnel with respect to habitual angiography procedures, although it is necessary to consider a fairly long learning curve for the technology. Indeed, as with other imaging technology, FD-OCT requires continuous exercise in the correct interpretation of the images produced during the examination. A minimum of 15 procedures per year is considered necessary to acquire full autonomy.

☑ Increase in the number of procedures	□ Re-organisation required	☑ Training required for users
□ Reduction in the number of procedures	□ Other:	□ Not identified

Conclusions

FD-OCT technology may be considered emergent in the study of the microstructure of vulnerable atherosclerotic plaques, and is used only experimentally in Italy.

To date, in the absences of comparative studies of the diagnostic efficacy of FD-OCT its effective potential, in terms of the capacity to assess the microstructure of unstable plaques, cannot be assessed.

Also note the absence of indicators (for example evaluation scores) which correlate the characteristics of vulnerable plaques visible with OCT with the risk of major morbid events.

To date, vulnerable plaques can be treated pharmacologically or surgically, yet there is still uncertainty about the degree of correlation between the characteristics of the plaques and atherothrombotic events.

Further, eventual treatment of vulnerable plaque (pharmacological and/or surgical) is still under study and, consequently, the relative benefit to the patient cannot be defined.

In conclusion, there is a need for comparative clinical in vivo studies assessing the diagnostic efficacy of this technology correlated to the therapeutic benefits to the patient, to assess any

advantages of introduction of new models over the previous versions. Finally, currently OCT is mainly used to evaluate the positioning and degree of endothelialization of coronary stents.

Future prospects

As OCT system is to date the only technology able of carrying out a sort of virtual biopsy, its diagnostic value in the evaluation of vulnerable plaques may become significant when evidence on their treatment becomes available.

Evidence searches

Serches were run with the following keywords indicate, respectively, the target pathology and the technology evaluated:

- ***the pathology of reference:*** circulatory system disease, coronary artery disease, Atherosclerosis, atheromas, atherosclerotic plaques, “coronary atherosclerosis” e “cardiovascular disease”, “vulnerable plaque”;
- ***the technology of interest:*** Intravascular imaging, Optical coherence tomography, OCT, C7XR, “atherosclerotic plaque imaging”, C7XR OCT imaging system, OCT imaging system, Fourier domain.

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Glossary

C(A)T: Computerised (Axial) Tomography.

FDA: Food and Drug Administration.

ISS: Italian National Institute of Health.

Istat: Italian National Institute of Statistics.

IVUS: Intravascular ultrasound.

MRI: Magnetic Resonance Imaging

RDM: Medical device Repertory (http://www.salute.gov.it/dispositivi/paginainternasf.jsp?id=499&menu=repertorio).

SPECT: Single Photon Emission Computed Tomography

PET-CT: Positron Emission Tomography - Computed Tomography