Master of Public Health

Master International de Santé Publique

EVASCAN

Cost evaluation of Computed Tomography Coronary Angiography for patients with suspected or stable heart disease

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MPH (M2) 2011

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Abstract

Purpose

The aim of this study was to evaluate the costs of a diagnostic strategy including Computed Tomography Coronary Angiography (CTCA) in comparison with conventional Coronary Angiography (CA) in a sub-group of patients of a French multi-centre trial (EVASCAN). The primary clinical objective of EVASCAN was to assess the diagnostic accuracy of CTCA versus CA in a large population of stable patients with suspected or known coronary artery disease (CAD).

Methods

All patients in the study underwent CTCA followed by CA. A total of 1 062 patients, enrolled in 40 French centres between June 2006 and May 2008, were included in the evaluation. A micro-costing method was employed to estimate the real cost of CTCA from the hospital's perspective. The cost of CA was taken from the 2008 National Cost Study. [1]

Results

The average cost for each CTCA is 179,67 euros based on the use of a 64 slice CT scanner active for ten hours per day.

For patients with a positive CTCA test for significant CAD (>50% luminal stenosis) followed by CA, the average cost of diagnosis is 2,843 euros. Based on a sensitivity of 86% CI_{95} (78 - 92) and a specificity of 55% CI_{95} (47 - 62) of CTCA in the intermediate risk group, an incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and accuracy of two strategies: CA for all patients versus CTCA as triage followed by CA when necessary for intermediate risk patients. The ICER for each additional correctly classified patient of CA over the triage strategy is estimated to be 14 304 euros in the EVASCAN population.

Conclusion

A strategy of CTCA in the intermediate risk group as a first line diagnostic test for CAD with conventional CA in second line would significantly cut costs and correctly classify 96% of all patients in the population studied. Medium-term and long-term outcomes need to be evaluated in patients with coronary stenosis potentially misclassified by CTCA due to false negative examinations.

Keywords

Coronary Angiography, Computed Tomography Coronary Angiography, Cost, Cost Effectiveness, Coronary Artery Disease, Imaging, Stenosis.

[1] **Number format:** for the **quantities** in this study, decimal marks (radix points) are indicated by a comma as per ISO international standards, and thousands are generally delimited by a space.

French summary

Evaluation médico-économique du scanner multi-coupe des artères coronaires dans l'exploration des coronaropathies supposées ou connues mais stables

Objectif

Le but de cette étude est de comparer l'efficacité et le coût de la stratégie diagnostique de l'Angiogram Coronaire (AC) classique, avec le Scanner Coronaire Multi-coupe (Coroscan) dans une population de patients stables ressentant des douleurs thoraciques évoquant une coronaropathie et chez lesquels une coronarographie est nécessaire.

Méthodes

Entre juin 2006 et mai 2008, 1 062 patients étaient recrutés dans 40 centres Français. Chaque patient a eu un Coroscan suivi par un AC. Le coût moyen du Coroscan du point du vue hôpital a été estimé avec une méthode de micro-costing. Le coût de l'AC a été déduit de l'Etude Nationale des Couts 2008.

Résultats

Le coût moyen pour effectuer un Coroscan avec un scanner 64 barrettes est 179,67 euros. Le ratio coût-efficacité incrémental pour chaque patient bien classé d'AC par rapport au Coroscan est 14 304 euros.

Conclusion

Pour les patients avec risque intermédiaire des maladies coronaires, une stratégie de Coroscan en première ligne suivi par AC réduirait les coûts diagnostiques et classifierait correctement 96% des patients (tous risques). Le coût-efficacité à moyen ou long terme devra être évalué pour ces patients mal classés.

List of acronyms

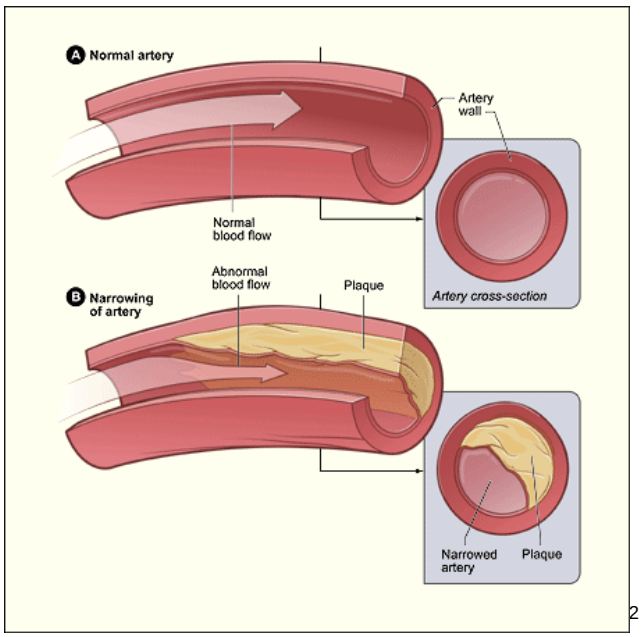
ACCF	American College of Cardiology Foundation
AGEPS	Agence Générale des Equipements et Produits de Santé (*AP-HP central purchasing service*)
AHA	American Heart Association
ALARA	As Low As Reasonably Achievable
AP-HP	Assistance Publique - Hôpitaux de Paris *(Paris University Hospitals)*
ARHIF	Hospitalisation Regional Agency Ile de France region (*Agence régionale de l'hospitalisation de l'Ile-de-France*)
ASN	Autorité de Sûreté Nucleaire *(French Nuclear Safety Authority)*
BEIR	Biological Effects of Ionising Radiations
CAC	Coronary Artery Calcium Scoring
CAD	Coronary Artery Disease
CCAM	Classification Commune des Actes Médicaux *(Social Security Medical Act Classification)*
CD ROM	Compact Disc Read Only Memory
CE	Cost Effectiveness
CI	Confidence Interval
CRF	Case Report Form
CTCA	Computed Tomography Coronary Angiograph
DRG	Diagnostic Related Groups
ECG	Electrocardiogram
EMI	Electrical and Music Industries
ENC	Etude National des Coûts *(French Hospital Cost Database)*
ESC	European Society of Cardiology
EVASCAN	Medical **Eva**luation of **Scan**ner in Coronary Syndrome
FNMR	Federation Nationale des Medecins Radiologues *(National Federation of Doctors in Radiology)*
IAEA	International Atomic Energy Agency
ICD	International Classification of Diseases
ICER	Incremental Cost Effectiveness Ratio
ICRP	International Commission on Radiological Protection
INSEE	Institut National de la Statistique et des Etudes Economiques *(French Institute of Statistical and Economical Studies)*
IPC	Indice des Prix à la Consommation *(Inflation - Consumer Index)*
LNT	Linear No Threshold
MI	Myocardial Infarction
MPS	Myocardial Perfusion
mSv	milli Silvert
NCRPM	National Council of Radiation Protection and Measurement (USA)
NICE	National Institute for Health and Clinical Excellence (UK)
OECD	Organisation for Economic Co-operation and Development
PACS	Picture Archiving and Communication System
QALY	Quality Adjusted Life Years
RTT	Réduction du Temps de Travail *(35 hour week)*
SaaS	Software as a Service
SCAI	Society of Cardiac Angiography and Interventions
SPECT	Single Photon Emission Computed Tomography
STIC	Soutien aux Techniques Innovantes Coûteuses *(Support for costly and innovative techniques in the French hospital setting)*
UGAP	Union Groupement Achat Publique *(Public Services Purchasing Organisation)*
UNCAM	Union Nationale des Caisses d'Assurance Maladie *(National Union of Health Insurance Funds)*

Introduction and background

Coronary Artery Disease

Coronary Artery Disease (CAD) occurs when the coronary arteries become partially blocked causing a narrowing or blockage of the arteries due to atherosclerosis - an accumulation of fatty materials on the inner linings of arteries. Figure 1 shows a normal artery with normal blood flow (example A) and an artery containing plaque build-up (example B).

Figure 1 - Normal artery and artery with stenosis



[2]

CAD is a subsection of the International Classification of Diseases (ICD) section IX, Diseases of the Circulatory System. This blockage, known as *stenosis*, limits the flow of blood from the coronary arteries, which are the major arteries supplying oxygen-rich blood to the heart. If the arteries are unable to expand, for example when the heart is working harder and needs more oxygen, the heart is deprived of oxygen, which leads to the condition myocardial ischemia. When this happens, chest pain or pressure, called angina or angina pectoris, often occurs. This is the most common symptom of CAD. The prevalence of stable angina in France was estimated to be 2 million in 2004. (Meurin & Piot, 2004) A diagnosis of angina can have a significant impact on the patient's level of functioning. In one survey, angina patients scored their general health as twice as poor as those who had had a stroke (Lyons, Lo, & Littlepage, 1994). However, not all CAD is symptomatic, and thus not all people with coronary artery stenosis will have symptoms. This study focuses on stenosis as the major cause of myocardial ischemia, and does not consider the patients with objective evidence of myocardial ischemia but with no apparent structural abnormality of the arteries.

[2] *Diagram courtesy of the United States Department of Health and Human Services.*

Atheroma promotes platelet aggregation and thrombus formation that can cause a blockage cutting off the flow of blood. The result is myocardial infarction (MI), when a number of the heart cells die. Whilst a regularly quoted estimate of MI incidence in France is 120 000 cases per year it was estimated to be between 60 000 and 100 000 from registry data (Danchin, Demichelli, & Cambou, 2003). This estimation includes MI preceded by no symptoms as well as acute angina. EVASCAN focuses on stable or suspected heart disease, but this incidence estimate is cited so as to give an idea of the order of magnitude of severe events associated with ischemia. Conversely, 9-31% of women and 4-14% of men with acute myocardial infarction have normal coronary arteries or non-significant coronary disease (Aldrovandi, et al., 2008). Conditions causing chest pain such as angina have a potentially poor prognosis, so prompt and accurate diagnosis is crucial.

Conventional Coronary Angiography

Coronary Angiography (CA) or Coronarography is an X-ray of the coronary arteries. The CA technique is defined by the American Heart Association (AHA) as "..the two dimensional radiographic visualisation of the coronary vessels after injection of radiopaque contrast". After a local anaesthesia, a catheter is inserted into a blood vessel usually in the femoral artery (groin area) or radial artery (the wrist). The tip of the tube is positioned either in the heart or at the beginning of the arteries supplying the heart, and contrast agent is injected. Contrast agent is a substance that stops the passage of X-rays and is used to outline the interior of hollow organs, such as heart chambers and blood vessels in X-ray or fluoroscopic pictures called angiograms. The angiogram produced by CA is a two-dimensional view of the coronary. As well as its diagnostic value, CA has a therapeutic value with the possibility to proceed directly to angioplasty and stent placement.

Conventional catheter Coronary Angiography (CA) is regarded as the gold standard for the diagnosis of coronary stenosis and for the purpose of this study is considered to have 100% diagnostic accuracy. However, this is an invasive and painful procedure which usually requires hospitalisation. There are numerous undesirable events associated with CA such as renal complications, allergic reactions to the contrast agent, bleeding, vascular complications, cerebrovascular accident (stroke), MI, and perforation of the heart chamber. A 1990 survey by the Society of Cardiac Angiography and Interventions (SCAI) indicated that the total risk of all major complications from CA is <2% (Noto, et al., 1991) and it has a 0,05% in-lab mortality rate (Lloyd-Jones, et al., 2009). Certain patient groups are at higher risk. For example, age is a predictor of major complications of CA. The number of CA carried out in France continues to grow. In 1991 it was estimated that 131 000 CA were carried out and by 2006 this number had risen to 272 000. (Blanchard, 2007). It is not possible to ascertain which proportion of these examinations corresponded to the population of chronic or suspected CAD. In addition, since CTCA has been introduced over this period, it is not possible to know which of these patients may have had a CTCA prior to the CA. This makes a precise budgetary impact report difficult to execute.

Computed Tomography Coronary Angiography CTCA

The first practical implementation of X-ray computed tomography (CT), a medical imaging method employing computer processing tomography, was developed in 1973 by British electronics engineer Godfrey Hounsfield and has revolutionised diagnostic medicine. Hounsfield developed this technology at EMI, a record and electronic components company. First known as the EMI scanner, it later became known as the CAT or CT scanner.

The earliest CT scanner technology generated a three-dimensional image of the inside of an object from a large series of two-dimensional X-ray images taken around a single axis of rotation. Originally the images generated were in the axial or transverse plane, orthogonal to the longitudinal axis (z-axis) of the body, but more modern scanners allow this volume of data to be reformatted in various planes. The 1990s saw a change from slice-by-slice imaging to spiral volume imaging via continuous scanning along the patient's z-axis and using slip ring technology. At the end of the 1990s the "slice race" began: CT scanners had typically one row or two rows of detectors until 1998 when the four slice detector was introduced. At the beginning of the new millennium, more rows were added to the detector arrays and accordingly more image slices were acquired simultaneously. With the exception of studies that only assess coronary calcium, multi-detector CT technology prior to 64-slice systems are now be considered inadequate for cardiac imaging due to the low spatial and temporal resolution.

Due to the major advances in the last 10 years in CT scanning technology, such as multi-detector row systems with electrocardiographic gating and dual source scanners, scan time and image quality have improved, imaging of the heart and coronary arteries has become feasible and Computed Tomography Coronary Angiography (CTCA) has become a wide-spread diagnostic tool for CAD. Two techniques are used to achieve the image of the heart and coronary arteries; retrospective spiral technique and prospective gating. Retrospective spiral technique is the original method that involves a spiral acquisition; it allows assessment of coronary function but results in higher radiation doses. Prospective gating, also known as "step and shoot", acquires data at end-diastole but can only be used in certain patients where functional imaging is not required. The procedure has the advantage of engendering a lower dose of radiation.

In spiral scanning with a 64 slice CT scanner the patient is moved through the gantry during the scan since the detector range only covers up to 4 cm. The increased coverage of a 320 slice scanner (currently the highest coverage available) is 16 cm along the z-axis and this should shorten breath hold times and require a lower number of heart beats to capture the imagery of the whole heart. However, the incremental value of recently introduced CT hardware with 128-, 256-, and 320-slice systems over 64-slice systems has not yet been determined (Mark, et al., 2010).

After the injection of contrast agent, CTCA allows visualisation of the coronary lumen and wall. CTCA image quality depends on many factors such as heart rate, obesity and extent of calcification but in selected patients high accuracy can be achieved. For stenosis detection, CTCA also allows the detection of both calcified and also non-calcified plaque components; plaque characterisation is sometimes possible. CTCA examinations result in a large 4-dimensional (4D) dataset of the heart obtained over the entire cardiac cycle.

Why EVASCAN?

Many publications have reported encouraging results for the diagnostic performance of CTCA for the detection of stenosis in the coronary arteries. However by 2005, the publications available were based on a limited number of patients (50 to 130). The EVASCAN protocol aimed to bridge that gap and was awarded ministerial funding in 2005 with the primary objective of evaluating the diagnostic accuracy of CTCA in comparison with CA.

Under the French ministerial programme Support for costly and innovative techniques in the French hospital setting (*Soutien aux techniques innovantes coûteuses* - STIC) institutions are invited to tender for research project funding. The STIC projects are typically multi-centric and have two main components: to medically validate the innovation and to carry out a costing study or economic evaluation of the technology. The innovations concerned are medical devices (not medication) that have already been approved by the European Union. Projects in oncology are run under the aegis of the National Cancer Institute (*Institut national du cancer* - INCa) while projects in other fields (such as EVASCAN, the subject of this report) are piloted by the French Ministry of Health.

Inclusion of CTCA in the French nomenclature

Despite not being explicitly listed in the list of reimbursed acts by the French National Health Insurance (*Assurance Maladie*), CTCA is frequently used for diagnosis of coronary stenosis. In order to enter the act in the hospital information system and for subsequent reimbursement, the act for a thoracic scan (CCAM version 23 code ECQH010 *Scanographie des vaisseaux du thorax et/ou du cœur [Angioscanner thoracique]*) is used. The current base CCAM rate for reimbursement of a thoracic scan is 25,27 euros, which is then raised by 21,8% to 30,78 euros as the examination requires a radiologist. To this is added the act for the intravenous contrast agent injection, (CCAM version 23 code YYYY467 *Supplément pour injection intraveineuse de produit de contraste au cours d'un examen radiographique ou scanographique)* which is reimbursed at 9,60 euros. In addition, a technical allowance (*forfait technique)* is allotted. This is set by The National Union of Health Insurance Funds (*Union Nationale des Caisses d'Assurance Maladie* - UNCAM) and the National Federation of Doctors in Radiology (*Federation Nationale des Medecins Radiologues* - FNMR) to cover the equipment, maintenance, non-medical personnel, consumables

(excluding contrast agent), management costs, insurance and taxes. The technical allowance is currently fixed at a maximum of 100,51 euros for a specified volume of CT scans of all types of activity (not only CTCA) depending on the type of CT scanner, up to a threshold of between 6 000 and 6 700 acts per year depending on the region in France. Thus for each CTCA a total of 140,89 euros is the maximum amount that can be reimbursed to the hospital. The general opinion amongst the experts, radiologists and cardiologists, is that this reimbursement rate is less than the true cost of a CTCA and is therefore a possible deterrent to widespread use of CTCA, particularly in private care. A disadvantage of using the CCAM code for thoracic scanning is that the number of CTCA actually carried out is not known. In addition, according to the National Audit Office (*Cour des Comptes*), acts carried out for hospitalised patients in the public sector that are bundled in Diagnostic Related Group (DRG) tariffs are not counted at all (Cour des Comptes, 2010).

Current knowledge of the diagnostic accuracy of CTCA

Since the conception of the EVASCAN protocol in 2004, four other studies evaluating diagnostic accuracy have been published: Accuracy (Budoff, et al., 2008), Core 64 (Miller, et al., 2008), Meijboom (Meijboom, et al., 2008), NIMISCAD (Marano, et al., 2009). Main diagnostic accuracy results are shown in Table 1.

Table 1 - Diagnostic accuracy reported from other studies

Study	No. of centres	No. of countries	N	Disease prevalence	Sensitivity	Specificity	PPV	NPV	Strategy for nonevaluable images
Accuracy	16	1	230	25%	95%	83%	64%	99%	Same as most proximal segment
Core 64	9	7	291	56%	85%	90%	91%	93%	Consider normal
Meijboom	3	1	360	68%	99%	64%	86%	97%	Consider as with at least one stenosis
NIMISCAD	20	1	350	58%	73%	93%	93%	73%	Exclude

The exclusion and inclusion criteria vary between the studies. For example, the Accuracy study included adults over the age of 18, whereas the Meijboom study only considered an age range of 50 to 70 years. The differences in population are reflected in the different prevalence rates from 25% to 68%. More details on the difference of exclusion criteria can be found in the Annex Table 23. Importantly, the strategy for classifying patients for whom the image quality was poor (caused by blurring generally because of cardiac motion, artefacts caused by breathing or irregular heartbeat) differed between studies. This negatively impacted the specificity reported since the false positive rate is directly affected by this classification strategy. For the Meijboom study, in cases when it was not possible to evaluate the images, the patient was considered as having at least one stenosis even though the actual presence of stenosis was not visualised, leading to the

lowest specificity reported. Conversely, the NIMISCAD study simply excluded these cases from the analysis thereby not adhering to an “intention to diagnose” policy and resulting in the highest specificity reported. The studies also used different criteria to ascertain the risk level of the different populations. All four studies generally agreed that the sensitivity of the test is good and can be used for ruling out disease.

Whilst there are currently no formal guidelines available in France for the use of CTCA, there is general agreement for the high risk group with a high prevalence of CAD that CA should be the first choice diagnostic tool. In this high risk group, there is reasonable likelihood that the disease is treatable and that patients may be able to have an intervention e.g. angioplasty, at the time of the diagnosis. By proceeding directly to CA without a CTCA triage, these patients would avoid a double dose of contrast agent and an additional radiation dose since even a positive result in this group would probably require diagnostic confirmation via CA.

The appropriateness criteria of the American College of Cardiology indicates that the CTCA is appropriate for the evaluation of chest pain for patients with an intermediate pre-test probability of CA and with an un-interpretable ECG or inability to exercise (Hendel, Kramer, Patel, & Poon, 2006). This recommendation is reflected in the 2010 European Society of Cardiology (ESC) guidelines where the use of CTCA for symptomatic patients with an intermediate pre-test likelihood of CAD is allotted the strength of recommendation Class IIa: the weight of evidence or opinion is in favour of its usefulness or efficacy.

For the low risk group, the prevalence of CAD is so low that too many people would need to be exposed to contrast agent and radiation in order to identify those with stenosis, and the prognosis in this group even for those with stable angina is very good (Hulten, Carbonaro, Petrillo, Mitchell, & Villines, 2011). The American Heart Association published a statement on CTCA in 2006 stating that its use in assessing obstructive disease in symptomatic patients is reasonable but that it should not be used as a screening test in asymptomatic patients.

Slightly different guidelines for the assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin were issued in March 2010 by the United Kingdom National Institute for Health and Clinical Excellence (NICE). These guidelines (NICE, 2010) recommend use of 64-slice (or above) CTCA for the group of patients with an estimated likelihood of CAD of 10-29%. For the intermediate group (30-60%) with a calcium score of less than 400 the guidelines recommend appropriate functional imaging such as myocardial perfusion scintigraphy with single photon emission CT (MPS with SPECT), stress echocardiography or magnetic resonance imaging.

The EVASCAN study

Objectives of the EVASCAN study

The primary objective of the EVASCAN study was to evaluate the diagnostic value of the CTCA in comparison with CA in detecting at least one luminal stenosis >50% in the population of patients with suspected or stable CAD. The patients studied had been referred to a French public or non-profit hospital or centre for a Coronary Angiography. The secondary objectives of the EVASCAN study included the medical-economic evaluation that is the subject of this report. Specifically, the protocol calls for an estimation of the cost of CTCA using a micro-costing method and the total cost of diagnosis for those patients for whom the CTCA would be a replacement of CA and for those for whom it would be an addition.

Materials and methods

Material and methods: clinical study

A total of 1 254 patients over the age of 18 with suspected or stable heart disease necessitating a coronary angiography were enrolled in 40 French centres between June 2006 and May 2008. A total of 192 patients were excluded due to the withdrawal of consent (n=13), deviation from the protocol (n=26) and either the CTCA and/or the CA not being completed (n=153). Each of the remaining 1 062 patients underwent CTCA followed by a CA between 24 and 72 hours later. On average, a 1,7 day gap between the two examinations (standard deviation 0,7 days) was observed. The resulting images from each diagnostic technique were engraved on CD ROM for centralised blind analysis.

The Clinical Research Unit at Hôpital Georges Pompidou was responsible for data management and statistical analysis: evaluation of diagnostic accuracy of CTCA compared to CA for the detection of at least one significant stenosis (>50% luminal stenosis) for the whole EVASCAN population as well as for sub groups classified by CAD risk level using pre-test likelihoods ascertained using the Duke Clinical Score. The Duke Clinical score, developed at the Duke University Medical Center, Durham, North Carolina (Pryor, et al., 1993), ascertains probability of CAD based on age, gender, type of chest pain and risk factors such as smoking, diabetes, and cholesterol levels. It was chosen by the EVASCAN principal investigator who considers that it has superior precision over other algorithms such as the ESC's *HeartScore* or the Framingham cardiac risk score.

Materials and methods: economic study

The EVASCAN protocol requires a cost evaluation from the point of view of the hospital carrying out the examination.

The cost of CA is well known and ascertained from the latest available version (2008) of the French Hospital Cost Database (*Etude nationale des coûts* - ENC). This database consists of data on all hospitalisations in 55 public and private non-profit hospitals. The data for over 2 million hospital stays are collected in the national cost survey which is made available online on the website of the Technical Agency for Hospital Information (*Agence technique de l'information sur l'hospitalisation* - ATIH): www.atih.sante.fr. Aggregated data on average length of stay and associated costs are available. CA almost always requires hospitalisation whereas CTCA for chronic or suspected CAD is generally an outpatient procedure.

The CTCA cost in France was previously unknown and so this study estimates the average cost using a micro-costing method, which is considered the most precise means to evaluate real costs. Health professionals involved in this specialty are interviewed to determine the types of resources involved. The volume of resources used is determined by direct observation of each stage of the diagnostic act and then the unit costs are retrieved from various sources such as the hospital administrators, purchasing departments and manufacturers. As a result, the cost of each component involved in the diagnostic test can be derived. The aim is to estimate the average cost to a hospital of carrying out the test as accurately as possible. In addition, the case report forms (CRF) for each patient include the time required to analyse the images. The main categories of cost and the main sources used in the micro-costing are shown in Table 2.

Table 2 - Types of costs evaluated in the CTCA cost estimation

Type of Cost	Source of information
Fixed Costs	
Hardware (CT scanner, ECG..)	Central Purchasing Department APHP, Manufacturers, Department Administrator
Overheads (heating, laundry..)	Hospital budget information
Variable Costs	
Consumable items (medication, pipettes)	Observations, Department Administrator
Staff time (Doctors in Radiology, technicians…)	Observations (stop watch), CRF data

The patient's travel time and work compensation payments are not accounted for in the micro-costing. In addition, the rental or the real estate financing of the hospital or laboratory building is not included, due to large regional variations in France. Whilst the variable costs can be calculated on a per test basis, the fixed costs have to be distributed between the total number of tests and thus the average cost calculated for any particular hospital will depend on the volume of tests carried out. For all of the hardware, the average maintenance is estimated at 10% per year of the original cost of the machine and the useful clinical life of the hardware is estimated at five years with no resale value.

There is a cost to spending money in the present, since monetary investment that would be possible by delayed spending yields a real rate of return. Due to this opportunity cost in spending money now to enjoy benefits now rather than in the future, *discounting* is commonly employed to make current costs higher than those occurring in the future. Following standard methodology, this is calculated as follows: if the capital outlay is "K", which is the cost of all of hardware procurement (not maintenance) that is assumed to have all happened at the same time, the annual sum "E" of a period of five years (clinical life of the machine) at a discount rate of "r" is :

$$E = K/(1/(1+r) + 1/(1+r)^2 + 1/(1+r)^3 + 1/(1+r)^4 + 1/(1+r)^5)$$

Values of r in health economic studies generally vary between 0,03 (3%) and 0,05 (5%). In the sensitivity analysis the hardware is discounted over this five year period at rates of 0%, 3% (base case) and 5%. In order to generalise the fixed costs a ratio is calculated as follows :

Machine time of an average CTCA scan / Total annual machine time (saturation)

A number of CTCA must be observed in order to carry out the materials inventory, ascertain the number and type of staff required, assess timings for each part of the process and to collect staff salary information. Four hospitals (three public and one private non-profit) were visited: Hôpital Henri Mondor (*Assistance Public Hôpitaux de Paris* - Paris University Hospitals AP HP) in Creteil, Centre Chirurgical Marie Lannelongue (CCML) in Plessis-Robinson, Hôpital Montfermeil and Hôpital Max Fourestier at Nanterre. The price information was ascertained via the radiology service administrators and information from the AP-HP central purchasing service (*Agence Générale des Equipements et Produits de Santé* - AGEPS). Expert advice from the EVASCAN team and AGEPS was sought to ascertain the machine specification to be used in the costing given the variety of different CT scanners used in France and currently commercially available. In addition, interviews with three of the main CT scanner manufacturers were carried out.

Results

Results: EVASCAN population description

The prevalence of the main CAD risk factors in the EVASCAN population are shown in Table 3.

Table 3 - CAD risk factors in the EVASCAN population

Risk factors	Pecentage of EVASCAN population
Gender (% male)	70%
Hypertension	52%
Smokers	25%
BMI > 30Kg/m2	23%
Diabetes	23%
Average age in years +- SD	61 ± 12

Of the 1 062 patients recruited, 66% had suspected CAD and 33% had stable CAD. This information was not available for the remaining 1%. The EVASCAN population does not include patients with CAD for whom an angioplasty or bypass are thought to be necessary. These patients would have been recommended to undergo CA immediately regardless of risk level ascertainment due to the possibility of being able to proceed directly to the intervention at the time of a CA positive diagnosis.

The prevalence of stenosis in the EVASCAN population was 52,3% The information required to calculate the Duke score was only available for 1 015 members of the EVASCAN population. After risk level calculation using the Duke score, the population was split into three risk level categories: low, intermediate and high as shown in Table 4.

Table 4 - Duke score and CAD prevalence

	Evascan Pop. sorted into this group	Average Duke Score	Prevalence (from CA results)
High Risk of CAD (Duke 71 to 100%)	54% (n=576)	90%	68%
Intermediate Risk of CAD (Duke 31 to 70%)	28% (n=296)	54%	41%
Low Risk of CAD (Duke 0 to 30%)	13% (n=143)	18%	19%
Unknown	*4% (n=47)*	*NA*	*36%*

Employing an accurate method to stratify the patients into risk groups is vital since misclassifying those at high risk into low risk may prevent prescribing the correct therapy. In the high and intermediate risk group, the average Duke score overestimates the actual risk of CAD as demonstrated by a lower actual prevalence as measured by the CA results. Unlike the other risk factors, the BMI did not vary much between risk levels as shown in Table 24 in the Annex.

Results: diagnostic accuracy

EVASCAN endeavours to focus on the real world rather than internal validity. For example, the CT scanners used have different technical specifications as seen in Table 5.

Table 5 - CT scanner types in EVASCAN centres

Type of CT Scanner	N	%
16, 32, 40 slice	280	26%
64 slice	746	70%
Other	29	3%
Not known	7	1%
Total	**1 062**	100%

For the cost estimation, the 64-slice system will be considered the specification necessary to perform CTCA. The results shown in Table 6 are similar to previous studies with the exception of a lower specificity. This is mostly due to the strategy for dealing with poor quality images. In the cases where the images were not interpretable (n=27), the decision was made to consider that the patients had at least one stenosis >50%.

Whilst adversely affecting the reported diagnostic accuracy, this reflects better real world practice where an uncertain CTCA result would probably lead to carrying out a conventional CA. It is known that many factors such as calcification, patient obesity, heart rate and ability to maintain apnoea for several seconds can impact the image quality. For example, the patients with un-interpretable images, the BMI was greater than 30kg/m2 for 33% of them, compared to 23% in the whole population.

Table 6 - Diagnostic accuracy of CTCA by sub-group and for the total EVASCAN population

EVASCAN Results by Risk Level	Sens.	Spec.	PPV	NPV	Accuracy
low risk	85%[66,96]	52% [42,61]	29% [19,40]	94% [85,198]	58%
medium risk	86% [78,92]	55% [47,62]	57% [49,64]	85% [77,91]	68%
high risk	93% [90,95]	49% [42,56]	79% [76,83]	76% [68,84]	79%
Heart Rate < 65bpm	91%[87,94]	52% [47,58]	67% [62,71]	84% [78,89]	72%
Heart Rate > 65bpm	92% [88,95]	51% [43,58]	69% [64,74]	84% [76,90]	73%
Calcium Score <400	86% [79,91]	61% [56,67]	51% [45,58]	90% [85,94]	69%
Calcium Score >400	98% [93,100]	25% [11,45]	82% [74,88]	78% [40,97]	82%
BMI < 30kg/m2	90% [88,93]	54% [48,59]	69% [65,73]	83% [78,88]	73%
BMI >30kg/m2	94% [88,97]	48% [39,57]	65% [58,72]	88% [77,95]	71%
CT scanner < 64 slices	93% [88,97]	54% [46,63]	65% [58,72]	90% [82,96]	73%
CT scanner = 64 slices	91% [88,94]	50% [45,55]	68% [64,72]	83% [77,88]	72%
CT scanner > 64 slices	91% [88,93]	51% [46,56]	68% [64,72]	83% [77,87]	72%
TOTAL Population	91%	52%	67%	84%	72%

The results consolidate current opinion that CTCA is a good tool to rule out disease and the clinical strategy decided by the EVASCAN principal investigator is illustrated in Figure 7 in the Annex.
This strategy (where CTCA positive results are validated by CA) would result in 96% patients (n=971) being correctly classified and 4% (n=44) incorrectly classified (n=1 015). Of these 4% of patients incorrectly classified in our study 61% (n=27) are low risk patients for whom neither CA

nor CTCA would be carried out with the CTCA triage strategy for the intermediate risk group. As previously discussed, these patients, even those with stable angina, have a low risk of adverse cardiac events very similar to that of the general population. The remaining 39% of the incorrectly classified patients (n=17) are those intermediate risk patients with a false negative result from CTCA triage who suffered a relatively high dose of radiation and are at risk for adverse cardiac events.

However, a negative CTCA result does not imply that no treatment is given. These patients would continue to be monitored by their cardiologist for suspected or stable angina, for example with medication. It appears that only the patients who need urgent bypass or angioplasty are really being failed by this strategy of triage. This group of patients (intermediate risk with false negative results at CTCA triage) represents 1,7% of the EVASCAN population (n=17 out of a population of 1015 for whom risk information is available). In the intermediate risk patients who had CAD ascertained by CA, the treatment decision was: 30% medication, 60% angioplasty and 8.3% coronary bypass. However, many studies agree that there is evidence that the extent and severity of CAD defined at CTCA predicts all-cause mortality, whereas patients with a normal CTCA have an excellent prognosis (Bastarrika & Schoepf, 2010).

Integration of CTCA information into clinical practice requires that the results be evaluated in terms of what was known prior to the test and the additional information the test provides. A test's clinical utility can be defined as its ability to identify which patient's post test probability is so low that they do not require further testing and which patients is so high that they should immediately be referred to CA. The positive likelihood ratio of CTCA for the whole EVASCAN population is less than 2, indicating a very slight change from the pre-test probability to the post-test probability for those with stenosis. This implies that a CTCA with a positive result needs to be confirmed by a CA. But as shown in Table 7, and in line with previous studies, the negative likelihood ratio is a little more promising: 0,17. This indicates a moderate change in probability, and the drop in the pre-test probability from 52% to 16% in the event of a negative result is an important indicator for ruling out stenosis.

Table 7 - Pre-test probability based on prevalence for the total EVASCAN population

CTCA results	Pre-test probability	Pre-test odds	Sensitivity	Specificity	Likelihood Ratio	Post-test odds	Post-test probability
Positive :Stenosis >50%	0,52	1,08	91%	52%	1,90	2,05	0,67
Negative: No stenosis					0,17	0,19	0,16

The test's clinical utility by risk group is shown in the Annex in Tables 25 and 26. The positive likelihood ratio never exceeds 2, but is at its maximum in the intermediate group. The negative likelihood ratio improves as the risk of CAD increases. Thus, the probability of stenosis after CTCA with negative results in the low risk group based on a pre-test probability from prevalence data is

6%, in the intermediate group it is 15% and in the high risk group it stands at 23%. The ability of a test such as coronary CTCA to provide incremental diagnostic information that alters management as opposed to simply increasing diagnostic certainty is dependent on the pre-test probability that is ascertained in EVASCAN by the Duke score. Since some of the CAD risk factors are very obvious – sex, weight and age – the mere observation of a patient would change the pre-test probability and could influence the interpretation of the results. Blind analysis of the images eliminated this effect, but does not reflect the real world situation.

Results: CTCA micro-costing

Fixed Costs – Hardware

There are four main manufacturers of CT scanners represented in the EVASCAN study as shown in Table 8.

Table 8 - Scanner manufacturers in the EVASCAN centres

Manufacturer	N	%
General Electric	541	50,9%
Philips	259	24,4%
Siemens	233	21,9%
Toshiba	22	2,1%
Not known	7	0,7%
Total	**1 062**	100%

The hardware inventory and costs are shown in Table 9. For items such as the CT scanners, the prices given by the manufacturers are international. For example, the same catalogue prices are quoted in all parts of the world. Thus catalogue prices are not used in the analysis and will not be shown.

The AGEPS negotiated price was used for the costing of the hardware in the base-case shown above. AGEPS probably gets the best prices available in France and thus they recommend using a lower reduction rate in the micro-costing. This negotiated rate is varied in the sensitivity analysis.

Table 9 - Inventory of hardware CTCA

HARDWARE	Negotiated price inc VAT	Source
CT Scanner + Workstation	840 000 €	AGEPS June 2010 with adjusted reduction rate
Double head injector	19 698 €	AGEPS June 2010 with adjusted reduction rate
CD/DVD engraver - robot	27 201 €	UGAP June 2010
Printer	434 €	Fnac 2010
ECG	2 863 €	AGEPS June 2010 with adjusted reduction rate
Extra workstation	114 334 €	AGEPS June 2010 with adjusted reduction rate
Installation of PACS	100 000 €	ARHIF 2009

The choice of CT scanner used in the costing corresponds to functional configurations for heart scanning but does not include installation costs or other accessories. The CT scanner specification is a 64 slice. An additional workstation (hardware and software) has been added to the configuration since there is usually at least one more workstation used for the post examination image analysis. The injector for the contrast agent corresponds to a model adapted to cardiac scanning with the cardiac gating option. With regards to a Picture Archiving and Communication System (PACS), companies such as Kodak propose a Software as a Service (SaaS) mode using their PACS Carestream at around 1 euro for stocking 1 000 images in each patient's dossier and then 0,50 centimes for each use of the dossier. There is also a project for 90 hospitals in the Ile de France région (*Projet région sans film*) using General Electric and Orange technology that plans to implement a PACS and estimates the cost per patient dossier at 2,17 euros. This does not include the initial set-up fee of roughly 100 000 euros per hospital. In this micro-costing a per exam charge of 2,17 euros has been used in the consumable one-off items category and 100 000 euros has been included in the hardware list that is amortised over 5 years in the base case.

The price of the CD burner tower is the purchase price quoted by the Public Services Purchasing Organisation (*Union Groupement Achat Publique* UGAP) since AGEPS does not have a negotiated purchasing contract (*marché)* for this item. The choice made is for a capacity that burns CDs for the entire production of a Radiology Service and automatically prints on each CD the identity of the patient. The capacity of the CD burner would, in fact, fulfil the needs of a radiology service for all types of imaging, not just CT, but for the purpose of this costing we take the theoretic view of the equipment necessary for a radiology department to carry out CTCA and attribute a cost per act based on CT scanner working at maximum capacity. The price of film to print out images has not been included due to the inclusion of PACS, CD burner and the patient's individual CD. For information, the price of film was estimated at approximately 11 euros per act in 2000 (Blum, 2002). The Electrocardiogram (ECG) is the price for a diagnostic model rather than the basic model.

Annual maintenance has been calculated as 10% of original hardware cost, with the exclusion of the costs of installing the PACS. In order to estimate a per patient act cost from the total hardware cost, a ratio of CT usage per patient act was calculated based on a CT scan lasting on average 15 minutes; this is machine time and does not take human intervention or analysis time into consideration. It was also assumed that a CT scanner is available for 10 hours per working day and that there are 251 working days available per year.

Ratio of CT useage = CTCA time expressed in minutes **/**
(CT scanner daily availability in hours*60 minutes*Working Days in year)
= 15/(10 * 60 * 251) = 15 / 1204 80 = **1 / 10 040**

This ratio demonstrates than in a theoretical situation where a CT scanner was dedicated to CTCA, that is, in a 10 hour working day over 251 working days of the year, more than 10 000 patients could undergo a CT scan. In the base-case, the hardware is amortised over 5 years, at a discount rate of 3%. Table 10 shows the results of applying the ratio to the total hardware cost to estimate a hardware cost per act.

Table 10 - Hardware cost per CTCA

Desciption	**Cost**
Total hardware cost	1 104 530 €
Annual cost (amortised over 5 years discounted at 3%)	241 179 €
Annual maintenance cost (10% of hardware cost - PACS)	100 453 €
Total annual cost	341 632 €
Hardware Cost per act (Annual cost *CT ratio)	**34,03 €**

Variable Costs – Consumable Items

The costs for materials used were supplied by the hospital administration staff at two public hospitals and one private non-profit hospital. The contrast agent cost has been included in the costing. However, outpatients would provide the contrast agent and so this cost would not be always be borne by the hospital. The list price of the contrast agent is 84.29 euros, but the SHI reimburses 65% of this so the patient would only have out of pocket charges of 29.50 euros that may be covered by additional health insurance, or *mutuelle.*

Each act uses one of each of the disposable items in Table 11 resulting in a cost 61,51 euros per patient act for the consumable items. The cost of the contrast agent is included in the total.

Table 11 - Consumable items unit cost

CONSUMABLE OR ONE-OFF ITEMS	Price inc VAT	CONSUMABLE OR ONE-OFF ITEMS	Price inc VAT
Double syringe kit for injector	11,40 €	Beta blocker BREVIBLOC	8,30 €
Contrast agent IOMERON 400 mg	29,50 €	Flacon NACL (eg. Trinitine)	0,52 €
PACS image archive	2,17 €	NATISPRAY (trinitine)	3,02 €
Catheter	0,42 €	Folder to contain results and CD	0,60 €
Transparent adhesive film	0,29 €	CD/DVD	1,67 €
Plaster	1,49 €	Paper to print minutes and images	0,80 €
Three way tap for catheter	0,28 €	Single use gloves	0,07 €
Sterile compress	0,08 €	Electrodes	0,06 €
Mini spike	0,60 €	Disposable container - personal items	0,16 €
Syringe 10cc	0,08 €	**Total Cost all Consumables**	**61,51 €**

Variable costs - human resources

The rate per minute for each agent involved is calculated based on 212 working days per year for full time contracts and a 7,5 hour contractual working day for a radiologist and medical secretary and a 10 hour working day for the Doctor in Radiology or executive administrator. No factors were included for lost time due to inefficiency or sickness.

The 212 annual working days is calculated thus :

Week days = 52 weeks of 5 working days per year = 260 days per year

Annual leave = 25 days per year

RTT days (days in lieu of extra hours based on 35 hour week)= 15 days per year

Bank holidays (estimate since changeable in France = 8 days per year

Thus the number of actual working days per fulltime contract = 260 – 25- 15 – 8 = **212 days**.

The total salary cost information is based on AP-HP data supplied by the financial department is shown in Table 12.

Table 12 - Salary information

Staff Time	Salary Cost	Rate per Minute
Radiologist - *manipulateur*	57 710 €	0,60 €
Doctor in Radiology	119 988 €	0,94 €
Medical Secretary	44 243 €	0,46 €
Department Administrator - *cadre*	58 440 €	0,46 €

The analysis time of the resulting images was ascertained primarily from the CRF data with the average time for analysis and interpretation of the CTCA images being 28 minutes, median 25 minutes and standard deviation of 12 minutes. The time for other elements was ascertained through observations in situ. The human resource time summary is shown in Table 13.

Table 13 - Human resource time

Staff Time	Minutes per CTCA	Notes
Radiologist - *manipulateur*	40	Two radiologists work for 20 minutes each
Doctor in Radiology	50	Includes 28 minutes analysis time
Medical Secretary	10	Making appointment and typing up minutes
Department Administrator - *cadre*	5	Stock control and management of the service

Therefore the human resources per CTCA are 78,30 euros as shown in Table 14.

Table 14 - Human resource cost per minute

Staff Time	Rate per Minute	Minutes per CTCA	Cost
Radiologist - *manipulateur*	0,60 €	40	24,20 €
Doctor in Radiology	0,94 €	50	47,17 €
Medical Secretary	0,46 €	10	4,64 €
Department Administrator - *cadre*	0,46 €	5	2,30 €
Total human resource cost per CTCA			**78,30 €**

Fixed costs - overheads

The other costs such as utilities and cleaning charges are notoriously hard to identify and value with certainty. The AP-HP tariffs supplied in 2006 have been applied after updates for inflation using INSEE inflation information (*Indice des prix à la consommation* - IPC) for the 150 m^2 surface area and 3.15 m ceiling height required for a CT scanning service. Laundry, office and computer supplies have been estimated from a general public hospital budget in the Ile de France region.

Table 15 - Cost of utilities

Name of Utility	Cost per unit	Area or Volume	Unit	Service cost per year
Heating	5,59 €	473	m^3	2 639 €
Electricity	8,65 €	150	m^2	1 298 €
Other energy	8,60 €	150	m^2	1 290 €
Water	3,63 €	150	m^2	544 €
Incineration/rubbish	5,29 €	150	m^2	793 €
Cleaning	24,58 €	150	m^2	3 687 €
General services	64,65 €	150	m^2	9 697 €
Security	12,10 €	150	m^2	1 815 €
Total cost per year				**21 763 €**

These fixed utilities costs must be attributed to each CTCA using the same method as for the hardware: Total cost for the service / theoretical number of CTCA per year possible

= 21 763 euros /10 040

= **2,17 euros** per CTCA (base-case 10 hour machine day)

The overheads cost per CTCA is shown in Table 16.

Table 16 - Cost of utilities per CTCA

Description	Cost per CTC	Source
Utilities	2,17 €	APHP based on volume calculated from base-case of 10 hour day saturation of CT scanner
Stamp to send results (250 g package)	2,22 €	La Poste
Telephone charges for 10 minutes	0,78 €	France Telecom
Laundry	0,31 €	Radiology Service Hôpital Montfermeil 2010 (Total annual cost divided by the number of all acts (all types) carried out in the hospital)
Office Supplies	0,10 €	
Computer Supplies	0,11 €	
IT network support (2 PCs on network)	0,16 €	APHP cost for 2 PCs on network divided by CT ratio
TOTAL	**5,84 €**	

Summary of costs

The estimated average cost of a CTCA diagnostic test in the French public or private non-profit hospital setting is 179,67 euros as seen in Table 17.

Table 17 - Total cost of CTCA per patient

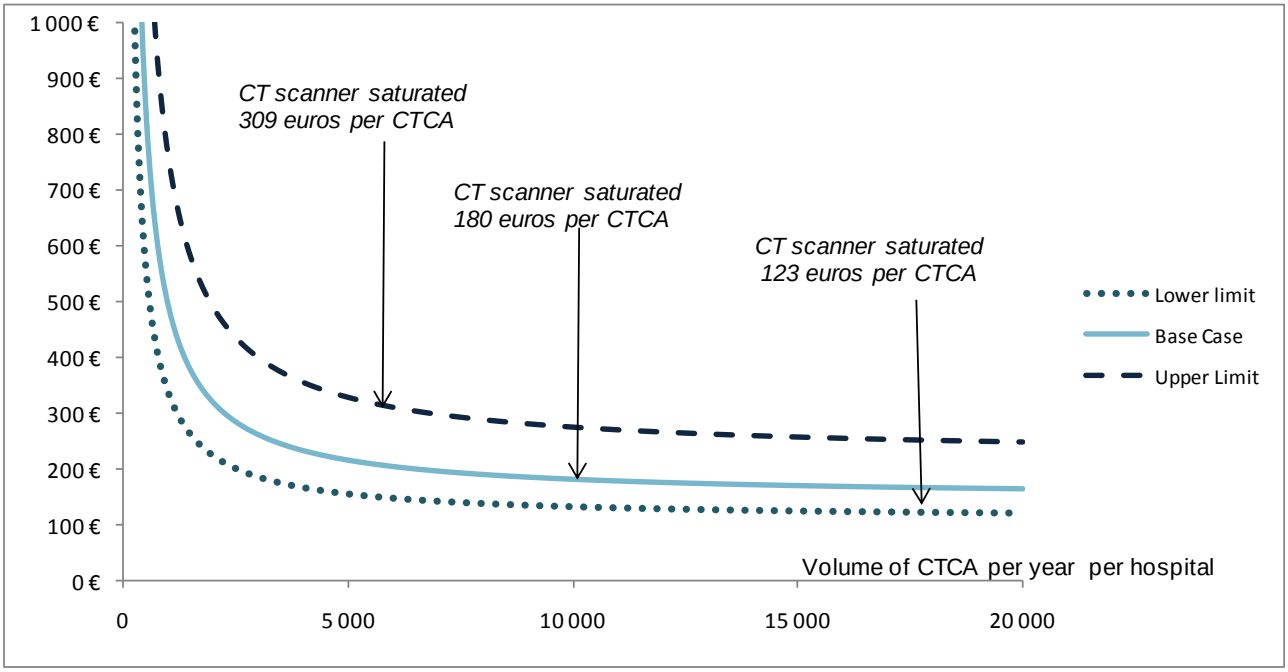
Item	Cost	% of total cost
Hardware including maintenance	34,03 €	19%
Consumables	61,51 €	34%
Time	78,30 €	44%
Other charges	5,84 €	3%
TOT	**179,67 €**	100%

Results: CTCA micro-costing sensitivity analysis

The sensitivity analysis carried out varies a number of the parameters such as salaries, minutes per working day and hardware costs to estimate a lower limit scenario of 123 euros and an upper limit of 309 euros per act. The parameter details used in the sensitivity analysis are shown in Table 27 in the Annex. The hypothesis maintained in all of the estimation includes the notion of a machine operating at maximum capacity depending on length of examination and available machine hours per day. In an emergency setting, the CT scanner could in fact be operational 24 hours per day, but for this study of scheduled CTCA, a maximum machine time of 12 hours per day has been considered.

The true average cost per CTCA depends on the volume of patients examined. However in certain settings the CT scanners are not operating at maximum capacity. Figure 2 demonstrates the variation of average cost per CTCA based on different annual volumes for the 3 scenarios estimated. For a volume greater than 4 000 CTCA per year, the cost curves stabilise with a variation rate of less than 1% for each 100 examinations performed. In a live setting the CT scanner would be used for different pathologies and not just CAD. However, since the average length of any CT scanner examination for outpatients is 15.8 minutes for 80% of the CT acts carried out in France (Appui Santé et Médico-Social, 2010) and given that the length of a CTCA in the base-case is 15 minutes, then we can interpret this graph for all types of CT examinations carried out.

Figure 2- Average cost of CTCA according to annual volume



Results: cost of conventional coronary angiography

The French Hospital Cost Database (*Étude nationale* de *coûts* - ENC) collects financial data from a voluntary or convenience sample of French hospitals and clinics to estimate the average cost of each DRG in France and includes 95% confidence intervals based on a normal distribution.

The French DRG for CA is split into four levels based on the use of resources that is linked to the gravity of the illness of the patient, as well as the length of stay. The level of DRG for the CA in the EVASCAN study was not recorded, although the length of stay was recorded and varied from 0 days (out patients) to 33 days. In the absence of information about the type of patient in the ENC study (chronic CAD, acute CAD, suspected CAD) the weighted average based on the number of hospital stays per level of DRG was calculated as shown in Table 28 in the Annex and is used to estimate the costs for the clinical diagnostic strategy of CTCA triage in the intermediate group as explained above.

The average cost for CA in 2009 is thus estimated to be 2 663 euros (CI 95% 2 166, 3 160 euros).

Results: cost of strategy triage in intermediate risk only

Based on the clinical strategy of neither CTCA nor CA in the low risk group, CTCA triage in the intermediate group and CA in the high risk group, the costs are shown in Table 18 based on the base-case cost deduced for CTCA and the average CA costs deduced from the ENC. Thus the average cost of diagnosing stenosis in the EVASCAN population (n=1 015) for whom risk information is available) is 2 044 euros.

Table 18 - Cost of strategy by risk group

	N	N%		CTCA	CA	Total	Average Cost per patient diagnosis
Low Risk	143	14%	Patients for whom **neither** CCTA **nor** coronarographie should be carried out	0 €	0 €	0 €	0 €
Medium Risk	113	11%	Patients for those the CCTA is a **substitute** (TN + FN)	20 310 €	0 €	20 310 €	180 €
Medium Risk	183	18%	Patients for whom the CCTA is an **addition** (TP + FP)	32 872 €	487 216 €	520 088 €	2 843 €
High Risk	576	57%	**No addition and no substitution**, only coronaragraphy	0 €	1 533 888 €	1 533 888 €	2 663 €
TOT	**1015**	100%		**53 182 €**	**2 021 104 €**	**2 074 286 €**	**2 044 €**

Results: cost effectiveness

The EVASCAN protocol does not ask for a cost effectiveness analysis, and without a budget limit or willingness to pay threshold it is not fully pertinent. Nevertheless, for the purpose of this report an incremental cost effectiveness ratio (ICER) is calculated to combine the costs and accuracies of the two strategies. As described above, the CTCA triage strategy in the intermediate risk group only would lead to 96% of the EVASCAN total population for whom risk level is available (n=1 015) being correctly classified versus 100% with CA. Table 19 calculates the ICER to be 14 304 euros for each additional correct diagnosis that would be attained with a “CA for all” strategy compared to a triage strategy with CCTA that excludes negative CCTA from further testing.

Table 19 - Incremental cost effectiveness analysis

Programme	Total Cost Evascan population	Health Effect N	Health Effect %	Δ Cost	Δ Effect	ICER	Total Rad. mSv	Δ Rad. mSV	Ave. Rad. mSv
New strategy	2 074 286 €	971	96%				**10 907**		**11**
Reference - CA for all risk levels	2 702 945 €	1015	100%	628 659 €	44	**14 304 €**	**7 105**	**-3 802**	**7**

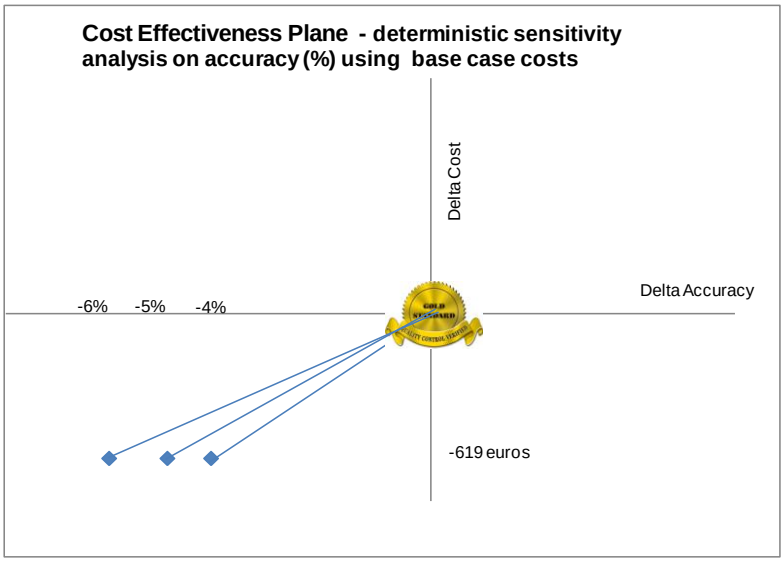
A sensitivity analysis carried out on the ICER calculations using the lower and upper limits of the CTCA sensitivity analysis and the 95% confidence intervals calculated in the ENC, plus binomial 95% confidence intervals for the CTCA sensitivity and specificity gives an lower limit ICER of 8 459 euros and an upper limit of 21 498 euros as shown in Table 20.

Table 20 - ICER sensitivity analysis

Variable	Lower	Base Case/Average	Upper
CTCA cost	309 €	180 €	123 €
Average cost of diagnosis (CTCA triage in intermediate group)	1 719 €	2 044 €	2 383 €
ENC deduced cost of conventional CA	2 166 €	2 663 €	3 160 €
Sensitivity in intermediate group	78%	86%	92%
Specificity in intermediate group	47%	55%	62%
Incorrectly classified patients (n =1015)	54	44	37
Overall accuracy	94,7%	95,7%	96,4%
Δ cost / Δ cases correctly classified	**8 459 €**	**14 304 €**	**21 498 €**

The overall accuracy of the CTCA strategy of 96% is plotted on the CE plane in figure 3 using the base-case micro-costing estimation for CTCA. The gold standard CA always dominates the strategy of CTCA triage in terms of diagnostic accuracy but is on average 619 euros more expensive per patient diagnostic.

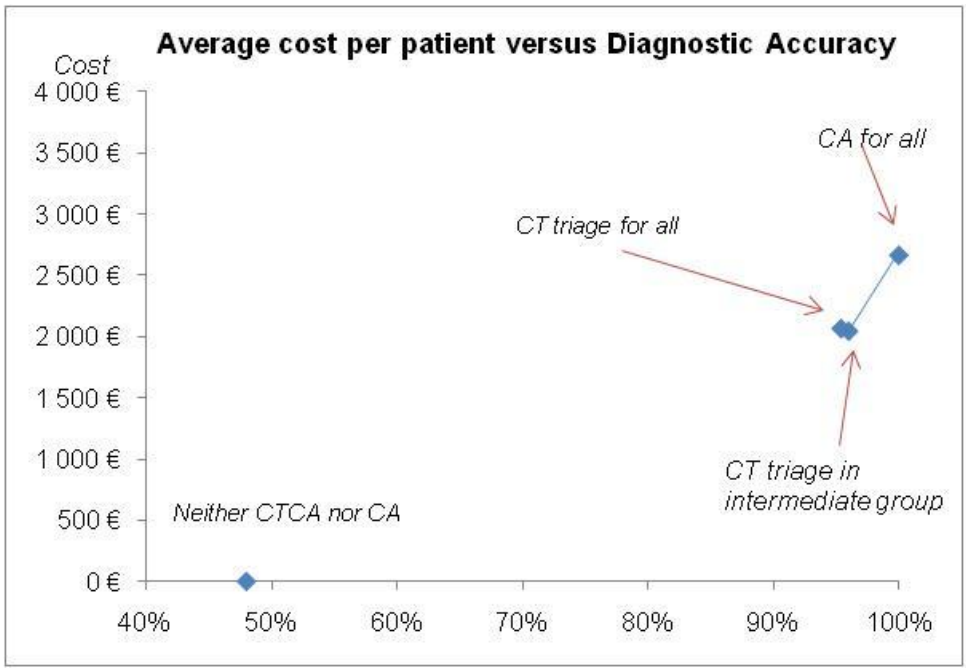
Figure 3 - Cost effectiveness plane –average cost per patient diagnosis versus accuracy



CTCA triage for all risk groups is not supported by the current clinical guidelines. In fact, the cost of CTCA triage for all versus CTCA triage only in the intermediate group have very similar cost per percentage diagnostic accuracy as seen in Figure 4 and Annex Table 29. In such a “CTCA for all” strategy with an average radiation dose of 24 mSv, not all high risk patients would be correctly identified. In the strategy of CTCA triage in the intermediate group, the strategy confirmed by EVASCAN, all high risk patients are correctly identified with an average radiation dose of 11 mSv.

The accuracy of using neither CTCA nor CA is noted for completeness corresponding to the percentage of patients without CAD.

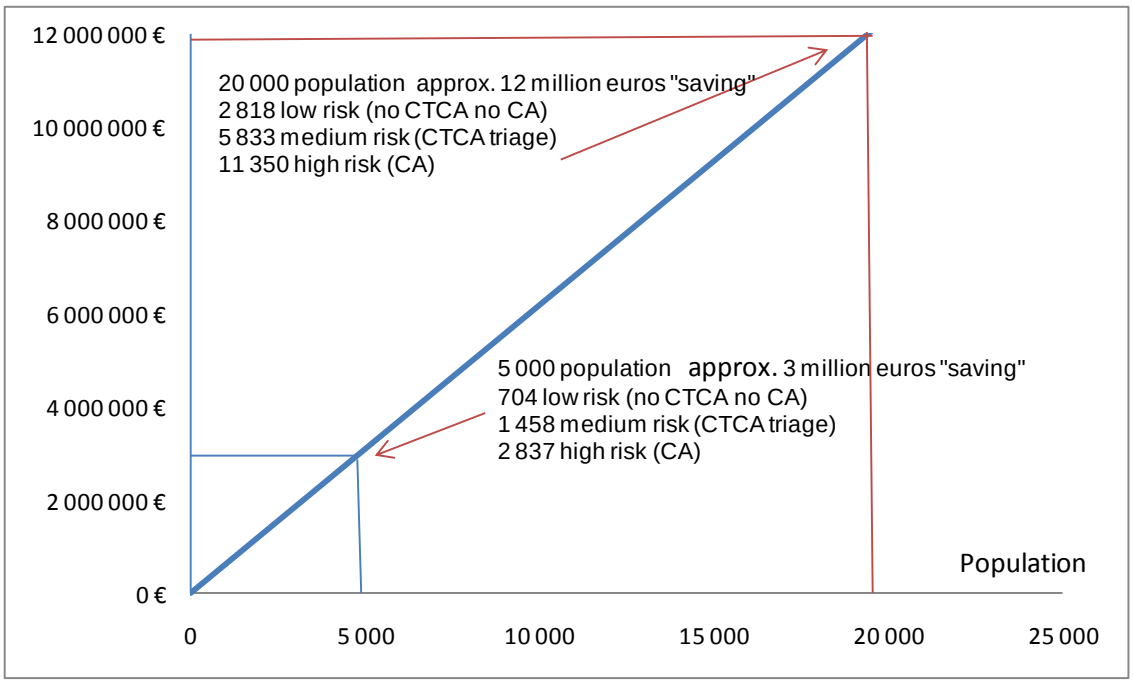
Figure 4 - Average cost per patient plotted against diagnostic accuracy



Results: budget impact

As already mentioned, neither the precise numbers of conventional CA nor the number of CTCA carried out in France are currently known. However, in 2007, 114 469 CT scans of the thorax or coronary arteries (Institut de Veille Sanitaire et Institut de Radioprotection et Sûrété Nucleaire, 2007) were carried out and that approximately 59% of these were carried out in the public sector. As described previously, we do not know the proportion of these examinations which corresponded to CTCA, and we do not know of the 272 000 CA carried out in France in 2006, which of these corresponded to the population of interest. However, if we take a modest hypothesis that 10 000 patients in France correspond to the EVASCAN profile, then we can compare the costs of the strategy of CA for all members of this population versus the costs of the strategy of triage using CTCA in the intermediate group as described above. Thus, for a population of 10 000 patients corresponding to the EVASCAN population, the CTCA triage in the intermediate group strategy would cost less than a CA for all strategy by approximately 6 million euros. The relationship between the size of the population of patients in this category and the related cost “saving” is shown in Figure 5.

Figure 5 - Potential budget impact



Discussion

Radiation exposure

In the USA, where, according to OECD health data, there were 34 CT scanners per million population in 2007, medical exposure to ionising radiation constituted nearly half of the total radiation exposure of the US population from all sources (N.C.R.P., 2009). CT scanning alone contributed 24% to the total radiation exposure. In France at the end of 2009 there were 736 CT scanners installed in France. This corresponds to approximately 11,8 CT scanners per million population, significantly less than the USA. Nevertheless, the rise in radiation doses delivered to patients in medical imaging in France has increased by nearly 50% since 2002 (Autorité de Surété Nucleaire, 2009). This is due to many factors including the rise in numbers of examinations due to improved technology, the rise in number of CT scanners that deliver higher doses than their predecessors and the increase in new types of examination that delivers high doses such as the CTCA and full body scans.

In the past the French Nuclear Safety Authority (*Autorité de sûreté nucléaire* - ASN) has not considered CT scanning as a priority due to the relatively low risk of exposure for the medical staff and doses delivered to patients that are considerably less than therapeutic dose such as for radiotherapy in the treatment of cancers. However, the rapid progression of diagnostic radiation doses in France and internationally has lead the ASN to reinforce their activities in this domain since 2011.

The effective radiation dose of medical imaging techniques is reported in milliSieverts (mSv). The effective dose provides an approximate indicator of potential detriment from ionising radiation and reflects the risk to specific sensitive organs in the body. In particular it allows comparisons of effective dose between different sources of ionising radiation. Background radiation is typically 1 to 3 mSv depending on the location. Between 2002 and 2007 the average effective radiation dose for each member of the French population augmented by 57% and the number of CT scans augmented by 26% in this same period. Thoracic CT scans (CCAM version 23 code ECQH010 *Scanographie des vaisseaux du thorax et/ou du cœur [Angioscanner thoracique]*). account for 20.9% of the total collective radiation dose from medical imaging and 20.8% of the acts.

The average radiation dose received during the CTCA in EVASCAN per patient was 18,9 mSV. Other studies report average effective doses for CTCA of between 5 and 32 mSv with an average value of 16 mSv. For conventional CA, where X-ray technology is also used, effective doses of between 2,0 and 15,8 with an average effective dose of 7 mSv are reported (Mettler, Huda, Yoshizumi, & Mahesh, 2008). The EVASCAN study did not report on the radiation level for conventional CA examinations.

At these low doses of radiation, there is still considerable uncertainty about the overall effects. There is no easy way to differentiate between the effects of medical device radiation, or other "man-made" sources and those from naturally occurring radiation, nor any way to distinguish cancers that occur due to radiation exposure rather than other causes. Thus it is difficult to characterise the effects of ionising radiation at low levels.

At lower doses, the risk of fatal cancer is not precisely known, but it is assumed that there is a direct relationship between dose and risk all the way down to zero. This is known as the linear no-threshold (LNT) theory. For example, at zero dose there is zero risk of harm, and at around 6,000,000 µSv (6 Sv) death is almost certain - a straight line between the two points gives the relationship between dose and risk. LNT assumes that risks (mostly of fatal cancer) observed in populations exposed to high doses of radiation can be extrapolated to the much lower doses for example from diagnostic medical procedures, radiation-worker situations, and other circumstances. Some organisations such as France Academy of Sciences and the American Nuclear Society (Einstein, Henzlova, & Rajagopalan, 2007) believe that the LNT approach overestimates the actual risks at such low doses and some even believe that there is evidence for a threshold for such effects, that is, that there may be a non-zero radiation dose below which there is no increased risk of cancer. The prevailing opinion currently falls on the side of prudence in protection, such that the use of the LNT remains broadly supported. The scientific study of radiation effects at dose lower than 100 mSv, where statistical evidence of increased cancers is practically impossible to detect due to the large number of cancers that occur normally without radiation exposure, continues (OECD Nuclear Energy Agency (NEA), 2007).

One value of the excess of fatal cancer that is widely used is 5 x 10^{-5} per person mSv (N.C.R.P., 1993) (International Commission on Radiological Protection (ICRP), 2007). We do not know the number of CTCA or CA carried out in France, however the number of all types of CT scans in 2008 in France was 130 per 1 000 population. Using the range of values for effective dose of 2 mSv to 20 mSv. for all types of CT scan, the number of annual excess cancer fatalities in France due to all types of CT scanning can be estimated at between approximately 800 and 8 000 as shown in Annex Table 30. Using a different value of fatal cancer risk from the BEIR VII report (National Research Council (USA), 2006) of a 1 in a thousand lifetime risk of fatal cancer for a person exposed to 10mSV, these excess cancer deaths from CT scans (all types) would double to be between 1 616 and 16 156 annually.

However, these excess risk values are average values and do not indicate the differences based on the age of the patient. They can only be used as indicators given that we do not know the distribution of ages and sex levels in France undergoing CT scans. Risk in both men and women lessen with age, a reflection of reduced tissue radio-sensitivity in older adults as well as the long lag time between radiation exposure and development of malignancies, meaning that older adults exposed may die of other causes before developing cancer (Einstein, Henzlova, & Rajagopalan, 2007). Close attention needs to be paid to patient doses, particularly for children.

To determine precisely the health risks at low doses of radiation would require observation of millions of people at higher and lower dose levels and such an epidemiological study would be would be complicated by the absence of a control group which had not been exposed to any radiation. Given the large variety of substances that can cause cancer it is rare to be able to identify with certainty the cause of a particular cancer (IAEA, 2011). However the ICRP and the International Atomic Energy Agency (IAEA) recommend the individual dose must be kept as low as reasonably achievable, (the ALARA principle) and this should be adhered to by the medical community: to achieve the minimum effective radiation dose for pertinent diagnostic information, by using optimal scanning parameters.

The CT manufacturers have developed technical upgrades to limit radiation dose, including prospectively gated step-and-shoot protocols, single-gantry-rotation whole-heart imaging, dual-source scanning, and improved Tube Current Modulation (TCM) algorithms. The TCM algorithm is an ECG guided protocol that minimises radiation dose during part of the cardiac cycle.

Clearly, whilst recognising the utility of medical radiation exposure, it should be evaluated if the annual increase in dose reported is associated to a similar increase in health benefits over time.

Patient preferences and adverse events

The potential to obtain information noninvasively comparable to that provided by invasive coronary angiography has been the major driving force behind the rapid growth and dissemination of cardiac CT imaging. However, as well as financial costs and radiation exposure, patient preferences and adverse events should be considered in making decisions on which tool to use. With respect to patient preference, 59% of patients in the EVASCAN study declared a preference for the non-invasive CTCA, and 15% preferred the conventional CA. For 26% of the cohort the data is either not available or the patient did not express a preference. In the EVASCAN study more adverse events were recorded for the CA examination than CTCA, however, the detail of the adverse events was not always specified as can be seen in Table 21.

Table 21 - Adverse events

Adverse Event	CTCA	CA	Unknown	Total
Sensation of Heat	7	0		7
Nausea	1	2	1	4
Skin redness	1	1	2	4
Skin rash	1		1	2
Transient Ischemic Attack			1	1
Cerebrovascular Accident (stroke)			1	1
Extra Vascular Injection		1	1	2
Exam interrupted		1		1
Not specified	4	25	6	35
Total	**14**	**30**	**13**	**57**

Acceptability of reduced accuracy

The cost effectiveness analysis shows that the CTCA triage strategy is significantly cheaper than CA but brings with it a loss of accuracy. However, it is possible that the reduction in costs could in fact improve overall health outcomes due to the possibility of a more efficient allocation of resources (Nelson, Cohen, Greenberg, Kent, & M., 2009).

Access to CT technology

Notwithstanding guidelines or patient preferences, the choice of diagnostic test will be influenced by the available techniques in the local health setting. The presence or absence of a CT scanner in the local hospital could determine whether or not the patient is referred for CTCA. In 2002 a government directive was issued to ensure coverage of 10 CT scanners per million inhabitants for

the whole of France but with varying regional targets. For example in the Pays de la Loire region the objective was set at 12 scanners per million inhabitants, whilst in the Champagne-Ardenne et Midi Pyrenées regions the objective was set at 18 scanners per million inhabitants. The number of scanners installed in France is shown in Table 22.

Table 22 - Number of CT scanners installed in France from 2001 (OECD Health Data)

Year	Number per million population	Number of CT scanners installed in France
2001	8,9	531
2002	9,7	579
2003	8,3	503
2004	7,4	447
2005	9,8	596
2006	10,0	617
2007	10,3	640
2008	11,0	695
2009	11,8	736

Despite the fact that not all scanners are employed at full capacity, for example 20% of CT scanners in France are operating at 51% of their full capacity, the waiting lists can be very long for an out-patient with over a 15 day wait in 20% of establishments (Appui Santé et Médico-Social, 2010). According to the Health Establishment Annual Statistics (*Statistique annuelle des etablissements de santé)* the wait in the public sector for a CT scan is three times longer than in the private sector despite public hospitals having 55% of the total number of scanners installed in France. Even for hospitalised patients there is an average wait of 3 days for a CT scan.

Of course for specialised examinations such as the CTCA, the necessary qualified personnel must be available. Physicians who interpret these examinations must be able to analyse the image data interactively on a dedicated workstation and combine knowledge of the patient with expertise in coronary anatomy, coronary pathophysiology, and CT image analysis techniques and limitations.

As with all medical devices, technical and medical expertise is at least as important as the technical aspects of the hardware so, even if a hospital has a CT scanner, if a radiologist with the necessary expertise in CTCA is not available, then alternative diagnostic tests would be necessary.

Diagnostic accuracy cut-off point

The objective of EVASCAN was not to evaluate the best cut-off point to determine stenosis. The threshold of 50% stenosis is widely used in CAD diagnosis; after about 50% narrowing, CAD can gradually or suddenly interfere with the pumping and circulation of blood, thereby depriving tissues and organs, including the heart itself, of essential blood and oxygen. If left untreated, this can lead to MI. However the ACCF/AHA guidelines state that stenosis of 50% - 70% may not reduce functional coronary flow as consistently as stenosis > 70%.

Risk level ascertainment

With respect to classifying the risk level of patients, many different methods are available. The Duke Clinical Score used in EVASCAN is based on an American population and so might not be as pertinent to the EVASCAN population as the ESC *HeartScore*. In addition, different studies use different algorithms to test risk and these may not reflect the actual practice of cardiologists, who may use more simple techniques such as definition by age, gender and symptoms (Diamond & Forrester, 1979) or simply their gut feeling. According to the preliminary results of a Canadian study **P**rim**ar**y Care **A**u**di**t of **G**lobal Risk **M**anagement (PARADIGM), two thirds of patients at high risk for cardiovascular events are misclassified (GUPTA, 2010).

Calcium score

Coronary Artery Calcium scoring (CAC) looks for calcifications in the walls of the coronary arteries and measures the results with the Agaston score. It is well established that individuals with Agatston Scores > 400 have a high incidence of obstructive disease. The EVASCAN protocol included CAC as part of the CTCA procedure and since CAC does not require contrast agent it was to be carried out before the contrast agent injection. However, only 53% (n=564) of EVASCAN patients had a calcium score recorded. For these patients, the prevalence of stenosis in the group with calcium score >400 was 78% and the prevalence of stenosis in the group with calcium score <400 was 32%.

Expert opinion from the EVASCAN team underlined that a very high calcium score was correlated with image artefacts and that the patient should proceed to CA immediately. The diagnostic accuracy results corroborate this as shown in Table 6 with a high sensitivity of CTCA for patients with CAC score >400 but a very low specificity. However, since the CT scanner and its facilities would have been reserved for the CTCA scan, and the CAC by CT scanner is not in the CCAM nomenclature, it is unlikely that the Doctor would halt the examination after the CAC was ascertained.

Conclusion

The EVASCAN population is the largest cohort used for a diagnostic accuracy study to date in the population of patients with stable or suspected CAD. The diagnostic accuracy results of EVASCAN support the already numerous articles that conclude that CTCA is good for ruling out disease in the intermediate risk group, particularly for patients who cannot undergo stress tests or who have uncertain results from other diagnostic work-up procedures. CTCA clearly does reduce costs and minimise patient discomfort when used as a triage for diagnosing stenosis. However this study does not measure the medium to long-term outcomes for these patients. One study published in 2009 (Genders, et al., 2009), concluded that CTCA is a cost-saving technique which avoids some unnecessary CA but with a slight detriment in patient outcomes. The study, which was mostly based on modelling data, found that performing CA alone did in fact improve patient outcomes by a small margin; 0.037 QALYs for men and 0,036 QALYs for women.

This report has demonstrated that the hospitals are being reimbursed at an inferior rate to the costs. However, increasing the tariff by introducing a special code in the nomenclature could incite private practices to increase their volume of CTCA and this may not be in the best interests of the patients given the potential for multiple radiation exposure and over-treatment. CTCA requires careful risk assessment of the patient by the Doctor in Cardiology, coupled with expert heart imaging expertise from the Doctor in Radiology.

Thus, CTCA is a useful tool in the diagnostic arsenal for detecting CAD. Used with care by experts for the right patient profile and with consideration for the radiation exposure associated with multiple tests, it is a cost effective tool with good diagnostic accuracy. A unique patient dossier would clearly enable better record keeping of effective dose accumulation. Until a unique patient dosser is available, medical imaging tools should be used prudently. Information on long-term patient outcome is required to fully assess CTCA's place in the diagnostic tool-box for CAD.

Glossary

Terminology	Description
Angina	Angina pectoris, commonly known as angina, is severe chest pain due to ischemia (a lack of blood and hence oxygen supply) of the heart muscle, generally due to obstruction or spasm of the coronary arteries. Cramp-like pain that comes and goes, and is made worse by physical effort. It is a sign that the tissue or organ supplied by a narrowed artery is not getting enough blood or oxygen.
Angiography	Medical imaging technique used to visualise the lumen, with particular interest in the arteries, veins and heart chambers. The term is strictly defined as based on projectional radiography - producing 2 dimensional images using X-ray radiation, however the term has been applied to newer vascular imaging techniques such as CTCA and MR angiography.
Angioplasty	Percutaneous Coronary Intervention or Angioplasty is the technique of mechanically widening a narrowed or obstructed blood vessel; typically as a result of atherosclerosis. Using image guidance, an inflatable balloon mounted at the tip of a catheter is inserted through the skin into an artery and advanced to the site of an arterial blockage where the balloon is inflated and deflated. In this process, the balloon expands the artery wall, increasing blood flow through the artery. A stent may be placed at the treatment site to hold the artery open.
Aorta	The aorta is the largest artery in the body, originating from the left ventricle of the heart and bringing oxygenated blood to all parts of the body in the systemic circulation.
Arrhythmia	Irregular heartbeat, abnormal heart rhythm.
Arteriosclerosis	Hardening and thickening of the walls of the arteries. Arteriosclerosis can occur because of fatty deposits on the inner lining of arteries (atherosclerosis), calcification of the wall of the arteries, or thickening of the muscular wall of the arteries from chronically elevated blood pressure
Artherosclerosis or arteriosclerotic vascular disease	Furring of the arteries. Condition in which an artery wall thickens as the result of a build-up of fatty materials such as cholesterol.
As Low As Reasonably Achievable (optimisation)	All doses due to medical exposure for radiological purposes except radio therapeutic procedures shall be kept as low as reasonably achievable (ALARA), consistent with obtaining the required diagnostic information, taking into account economic and social factors.
Atheroma	Atheroma or Atheromatous plaque is an accumulation and swelling in artery walls that is made up of (mostly) macrophage cells, or debris, that contain lipids (cholesterol and fatty acids), calcium and a variable amount of fibrous connective tissue. Atheroma occurs in atherosclerosis. A buildup of white blood cell (sometimes termed fatty, despite absence of adipocytes) deposits within the wall of an artery
Atrial Arrhythmia	An atrial arrhythmia is an abnormality that occurs in one of the two upper chambers of the heart, the left or right atrium.
Bolus	The administration of a medication, drug or other compound that is given to raise its concentration in blood to an effective level. The administration can be given intravenously, by intramuscular, intrathecal or subcutaneous injection.
Calcify	To make or become inflexible and unchanging. To make or become stony or chalky by deposition of calcium salts.
Calcium Score	A number reflecting the degree and extent of calcium deposits in the walls of the coronary arteries, as demonstrated by cardiac computed tomography.
Cardiac Arrest	Stoppage of the heart

Abbrev	Terminology	Description
CRF	Case Report Forms	A Case Report Form (or CRF) is a paper or electronic questionnaire specifically used in clinical trial research. The Case Report Form is the tool used by the sponsor of the clinical trial to collect data from each participating site. All data on each patient participating in a clinical trial are held and/or documented in the CRF, including adverse events.
	Catheter	A tube that can be inserted into a body cavity, duct, or vessel. Catheters thereby allow drainage, administration of fluids or gases, or access by surgical instruments.
	Collimation	The use of metal plates, slots, bars, etc., to confine and direct radiation (e.g. X-rays or gamma-rays) to a specific region and/or to discriminate against radiation from unwanted directions
CTCA	Computed Tomography Cardiac Angiography	Sometimes referred to as CCTA: Cardiac Computed Tomography Angiography. Imaging method that uses a computed tomography scanner to look at the structures and blood vessels of the heart. It produces cross-sectional three dimensional images. (Sometimes known as Coroscan in France).
CT	Computer Tomography	X-ray computed tomography (CT) is a medical imaging method to generate a three-dimensional image of the inside of a patient from a large series of two-dimensional X-ray images taken around a single axis of rotation. CT revolutionised the medical x-ray field with its unprecedented ability to visualize the anatomic structure of the body.
	Contrast agent	Also referred to as contrast material or contrast medium. Any internally administered substance that has a different opacity from soft tissue on radiography or computed tomography
CA	Coronarography /Coronary Angiography	X ray of the coronary arteries. Coronary angiography is defined as the radiographic visualization of the coronary areteries after direct opacification with contrast media.
	Coronary Arteries	Heart's blood vessels
CABG	Coronary Artery Bypass Graft	A surgical procedure performed to relieve angina and reduce the risk of death from coronary artery disease. Arteries or veins from elsewhere in the patient's body are grafted to the coronary arteries to bypass atherosclerotic narrowings and improve the blood supply to the coronary circulation supplying the myocardium (heart muscle).
CAD	Coronary Artery Disease	A condition involving the narrowing of the coronary arteries that carry blood and oxygen to the heart muscle.
CHD	Coronary Heart Disease	Mostly CAD but inlcudes other heart problems such as Vasospasm.
DRG	Diagnostic Related Group	Diagnosis-related group is a system to classify hospital cases into groups, also referred to as DRGs, expected to have similar hospital resource use, originally developed for Medicare as part of the prospective payment system. DRGs are assigned by a "grouper" program based on ICD diagnoses, procedures, age, sex, discharge status, and the presence of complications or comorbidities.
	Diastole	The phase of the heart beat where the heart is completely relaxed and at its largest (opposite: systole). In diastole the heart chambers fill with venous blood that is subsequently ejected in systole.
	Drug Eluding Stents	These stents are coated with a medication that is slowly released to help keep the blood vessel from re-narrowing, a condition called restenosis.
	Effective Dose	Because different tissues and organs have varying sensitivity to radiation exposure, the actual radiation risk to different parts of the body from an x-ray procedure varies. The term effective dose is used when referring to the radiation risk averaged over the entire body. The effective dose accounts for the relative sensitivities of the different tissues exposed. More importantly, it allows for quantification of risk and comparison to more familiar sources of exposure that range from natural background radiation to radiographic medical procedures.
ECG	Electrocardiogram	A test that records the electrical activity of the heart.

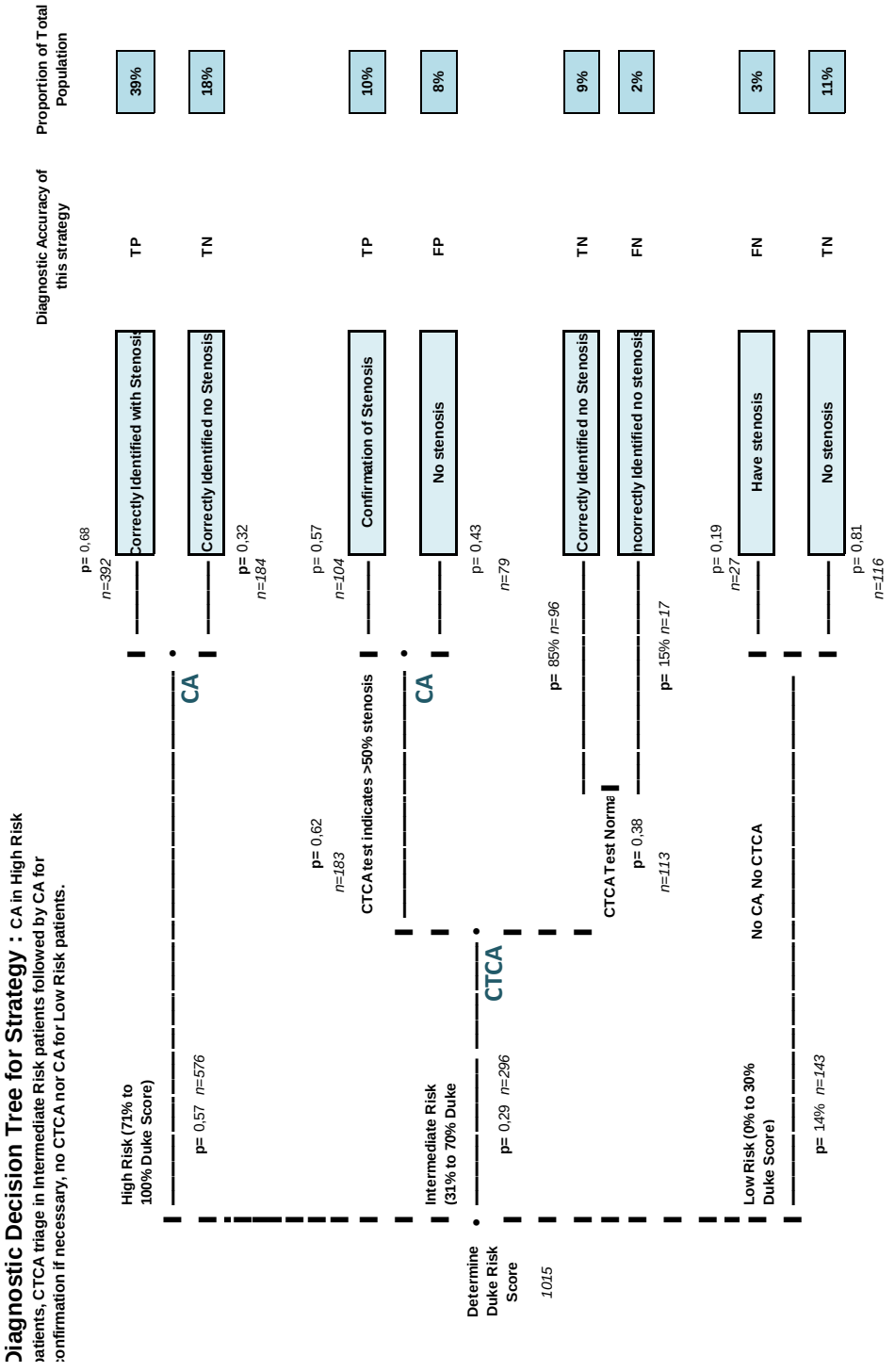
Abbrev	Terminology	Description
ECG gating	Electrocardiogram Gating	By permitting synchronization with the electrocardiogram (ECG), gating enables the user to specify data acquisition and image reconstruction at a specific point in the cardiac cycle, both optimizing image quality and defining the type of information available to the clinician. Gating techniques are used to improve temporal resolution and minimize imaging artifacts aused by cardiac motion.
	Heart Failure	A condition in which a problem with the structure or function of the heart impairs its ability to supply sufficient blood flow to meet the body's needs.
	Hemoglobin	The iron-containing oxygen-transport metalloprotein in the red blood cells of vertebrates.
	Infarction	Death, irreversible damage.
ICD	International Classification of Diseases	The International Statistical Classification of Diseases and Related Health Problems (most commonly known by the abbreviation ICD) published by the World Health Organization (WHO), provides codes to classify diseases and a wide variety of signs, symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or disease. It is used worldwide for morbidity and mortality statistics, reimbursement systems and automated decision support in medicine. This system is designed to promote international comparability in the collection, processing, classification, and presentation of these statistics. The ICD is revised periodically and is currently in its tenth edition.
ICRP	International Commission on Radiological Protection	In 1928, an independent non-governmental body of experts , the International X-ray and Radium Protection Committee was established. It later was renamed the International Commission on Radiological Protection (ICRP). Its purpose is to establish basic principles for, and issue recommendations on, radiation protection.
	Intrastent Restenosis	Stenosis returning when stents are in place.
	Ionising radiation	Today ionising radiation is used in many medical fields. The adjective “ionising” refers to the property of this radiation to eject electrons from an atomic shell; a process called “ionisation”. ionising radiation can be produced in devices like X-ray tubes (radiology) or for higher energies in accelerators (radio-oncology, radiotherapy). In nuclear medicine, the ionising radiation is produced through the decay of radioactive substances.
	Ischemia	Restriction in blood supply, generally due to factors in the blood vessels, with possible resultant damage or dysfunction of tissue.
	Lumen	The inner open space or cavity of a tubular organ, as of a blood vessel or an intestine.
MRA	Magnestic Resonance Angiography	In magnetic resonance angiography (MRA), a powerful magnetic field, radio waves and a computer produce the detailed images. MR angiography does not use ionising radiation .
MI	Myocardial Infarction	Heart Attack - is the interruption of blood supply to part of the heart, causing some heart cells to die.
	Myocardium	Heart muscle - the middle and thickest layer of the heart wall, composed of cardiac muscle
	Myogobline	Primary oxygen-carrying protein of muscle tissues (so you can hold breath). Many other characteristics.
NAO	National Audit Office	The National Audit Office scrutinises public spending on behalf of Parliament. Hold government departments and bodies to account for the way they use public money, thereby safeguarding the interests of taxpayers. Also aims to help public service managers improve performance and service delivery.
	Occlusion	Blockage
	Percutaneous	Surgery carried out through needles, so incision not necessary.
PACS	Picture Archiving and Communication System	A medical imaging technology providing storage and easy access to images.

Abbrev	Terminology	Description
	Plaque	A build-up of fat and other substances on the inner wall of a blood vessel. In time, plaque may build up and limit blood flow through the vessel.
	Predictive Factor	Characteristic that identifies subgroups of treated patients with different outcomes/responses
	Prognostic Factor	Identifies subgroups of untreated patients who have different outcomes
QALY	Quality Adjusted Life Years	A measure of disease burden including both the quality and the quantity of life lived. The QALY is based on the number of years of life that would be added by a medical intervention. Each year in perfect health is assigned the value of 1.0 down to a value of 0 for death.
	Radiation dose	The scientific unit of measurement for radiation dose, commonly referred to as effective dose, is the millisievert (mSv). Other radiation dose measurement units include rad, rem, Roentgen, Sievert, and Gray.
	Scintigraphy	Mycardial perfusion scan part of nuclear medecine. the production of two-dimensional images of the distribution of radioactivity in tissues after the internal administration of a radiopharmaceutical imaging agent, the images being obtained by a scintillation camera. Assess regional blood flow and cell viability.
	Sievert	The International System of Units (SI) unit for dose equivalent equal to 1 joule/kilogram. The sievert has replaced the rem; one sievert is equal to 100 rem. One millisievert is equal to 100 millirem.
	Slip Ring Technology	A slip ring is a rotary coupling used to transfer electric current from a stationary unit to a rotating unit.
	Stenosis	An abnormal narrowing in a blood vessel or other tubular organ or structure.
	Stent	A semi-rigid tube-like device used to keep an artery open after angioplasty, to assure the opening of an intact but contracted lumen.
	Stress Test	Treadmill and nuclear stress test (treadmill plus radioative nucleides)
SCD	Sudden Cardiac Death	Sudden cardiac death (SCD) accounts for half of all heart disease deaths in the U.S., but it's not the same as a heart attack. SCD occurs when the heart's electrical system goes haywire, causing it to beat irregularly and dangerously fast. The heart's pumping chambers may quiver instead of pumping blood out to the body.
	Systole	The phase of the heart beat where the heart is maximally contracted (to empty its blood content into the circulation) and at its smallest.
	Tomography	imaging by sections through the use of a penetrating wave
	Triglycerides	High levels of triglycerides in the bloodstream have been linked to atherosclerosis, and, by extension, the risk of heart disease and stroke
	Triple Rule Out	Three main reasons for chest pain can be ruled out : aortic dissectoin, pulmonary embolism, myocardial infarction.
TCM	Tube Current Modulation	The purpose of automatic Tube Current Modulation is to maintain constant image quality regardless of patient attenuation characteristics, thus allowing radiation dose to patients to be reduced.
	Vasospasm	A condition in which blood vessels spasm, leading to vasoconstriction.

Annex

Annex

Figure 6 - Diagnostic Decision Tree



Annex

Table 23 - Exclusion criteria of EVASCAN and the four recent studies

EXCLUSION CRITERIA	CORE 64	MEIJBOOM	ACCURACY	NIMISCAD	EVASCAN
Prenancy, lactation	✔		✔	✔	✔
Contraindication to intravenous contast media	✔	✔	✔	✔	✔
Heart rate > 70 bpm				✔	
Heart rate > 80 bpm	✔				
Resting Heart rate > 100 bpm			✔		
Resting blood pressure <100mm Hg			✔		
Absence of sinus rhythm			✔	✔	✔
NYHA class II to IV				✔	
Previous bypass operation, cardiac surgery	✔	✔	✔	✔	
Persistant arrhthmias, irregular heartbeat		✔	✔		✔
Inability to hold breath 15 s		✔			
Inability to hold breath 20 s					✔
Previous stenting	✔	✔	✔	✔	
Percutaneous coronary intervention within last 6 months	✔		✔		
Creatinine value >2mg/dl				✔	
Creatinine value >1,7 mg/dl			✔		
Creatinine value >1,5 mg/dl or créatine clearance <60ml per minute	✔				✔
Creatinine value >120 µmol/l		✔			
Organ transplantation	✔				
NYA class III or IV heart failure	✔				
Intolerance to beta blockers	✔		✔		
Intolerance to calcium channel blocker, or nitroglycerine			✔		
Multiple myeloma	✔				
Atrial fibrillation	✔				
BMI >40	✔				
Calcium score >600	✔				
Examen iodé dans les 48 heures précédant le scanner					✔

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Table 24 - Risk factors by risk sub-group

Risk factors	Percentage of total population	Low Risk	Intermediate Risk	High Risk
Gender (% male)	70%	27%	56%	89%
Hypertension	52%	41%	49%	56%
Smokers	25%	18%	24%	27%
Average BMI	27	28	27	27
Diabetes	23%	13%	17%	27%
Average age in years +- SD	61	53	59	64
Average Heart Rate	63	65	63	62

Table 25 - Pre-test probability based on prevalence in each risk group

Results by Duke Score group	Pre-test prob.	Pre-test odds	Sens.	Spec.	Likelihood Ratio	Post-test odds	Post-test prob.
High Risk CAD							
Positive :Stenosis >50%	0,68	2,13	93%	49%	1,82	3,88	0,79
Negative: No stenosis					0,14	0,30	0,23
Intermediate Risk CAD							
Positive :Stenosis >50%	0,41	0,69	86%	55%	1,91	1,33	0,57
Negative: No stenosis					0,25	0,18	0,15
Low Risk CAD							
Positive :Stenosis >50%	0,19	0,23	85%	52%	1,77	0,42	0,29
Negative: No stenosis					0,29	0,07	0,06

Table 26 - Pre-test probability based on average Duke score in each group

Results by Duke Score group	Pre-test prob.	Pre-test odds	Sens.	Spec.	Likelihood Ratio	Post-test odds	Post-test prob.
High Risk CAD							
Positive :Stenosis >50%	0,9	9,00	93%	49%	1,82	16,41	0,94
Negative: No stenosis					0,14	1,29	0,56
Intermediate Risk CAD							
Positive :Stenosis >50%	0,54	1,17	86%	55%	1,91	2,24	0,69
Negative: No stenosis					0,25	0,30	0,23
Low Risk CAD							
Positive :Stenosis >50%	0,18	0,22	85%	52%	1,77	0,39	0,28
Negative: No stenosis					0,29	0,06	0,06

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Table 27 - Micro-costing sensitivity analysis

Variable	Lower Limit	Base Case	Upper Limit	Units	Notes
Dr. in Radiology salary	107 989 €	119 988 €	160 211 €	Euros	Upper limit is private not for profit, middle is APHP, lower limit is APHP less 10%
Manipulator's salary	45 109 €	57 710 €	65 288 €	Euros	Upper limit is APHP *cadre sup*, middle is APHP *cadre,* low is local public general hospital
Medical secretary salary	39 294 €	44 243 €	47 572 €	Euros	Upper limit is local public general hospital middle is private not for profit, low is APHP
Department Administrator ("cadre") salary	54 048 €	58 440 €	67 673 €	Euros	Upper limit is private not for profit middle is APHP, low is regional hospital
Dr. in radiology time per year	139 920	127 200	95 400	Minutes worked per year	Upper limit is 7,5 hour day, middle is 10 hour day, low is 11 hour day
Manipulator's time per year	*95 400*	*95 400*	*95 400*		*7,5 hour day in all cases*
Medical secretary time per year	*95 400*	*95 400*	*95 400*		*7,5 hour day in all cases*
Department Administrator ("cadre") time per year	139 920	127 200	95 400	Minutes worked per year	Upper limit is 7,5 hour day, middle is 10 hour day, low is 11 hour day
Dr. in radiology time	38	50	62	Minutes per act	Base case is 28 minutes analysis plus imaging and writing up minutes, +- SD observed in CRF
Manipulator's time	35	40	45	Minutes per act	Estimates based on observations
Medical secretary time	5	10	15	Minutes per act	Estimates based on observations
Department Administrator ("cadre") time	4	5	6	Minutes per act	Estimates based on observations
Dr. in radiology cost per act	29 €	47,17 €	104 €	**Euros**	**Calculated**
Manipulator's cost per act	17 €	24,20 €	31 €	**Euros**	**Calculated**
Medical secretary cost per act	2 €	4,64 €	7 €	**Euros**	**Calculated**
Department Administrator ("cadre") cost per act	2 €	2,30 €	4 €	**Euros**	**Calculated**
Total human resource cost	**49 €**	**78 €**	**147 €**	**Euros**	
Hardware	963 944 €	1 104 530 €	1 354 530 €	Euros	Lower limit is dual power 64 slice (with AGEPS discount), base case dual power 64 slice (with 10% less discount than AGEPS), upper limit is top of the range high definition CT scanner (with AGEPS discount)
Ratio CT	0,0000553	0,0000996	0,0001660		Coefficient to apply to fixed costs to attribute to each CTCA performed
Theoretic number of CTCA per year at saturation	18 072	10 040	6 024		Number of CT scans at saturation
Hardware per year	160 657 €	241 179 €	381 993 €		Total hardware cost/discount rate coefficient
Hardware per year plus maintenance	229 773 €	341 632 €	532 537 €		As a percentage of total cost (excluding PACS)
Discount rate	0%	3%	5%	Percentage	
Discount rate coefficient	6	4,580	3,546		(1/(1+r) + 1/(1+r)2 + 1/(1+r)3 + 1/(1+r)4 + 1/(1+r)5) where r is discount rate
CT scanner active	12	10	8	Hours per day	
Length of scanner time by patient	10	15	20	Minutes	
Maintenance	8%	10%	12%	Percentage	
Hardware life cycle	6	5	4	Years	
Hardware	**13 €**	**34 €**	**88 €**	**Euros per patient act**	
Disposable Materials	**55 €**	**62 €**	**68 €**	**Euros per patient act**	
Environmental/other costs	**5 €**	**6 €**	**6 €**	**Euros per patient act**	
Cost of CTCA	**123 €**	**180 €**	**309 €**		

Annex

Table 28 - Cost of CA deduced from the ENC

Diagnosis Related Group	Number of hospital visits/stays in 2008	Cost Lower limit (CI 95%)	Average Cost	Cost Upper limit (CI 95%)
Conventional Coronary Angiography level 1	16 731	1 508 €	1 834 €	2 160 €
Conventional Coronary Angiography level 2	3 003	3 978 €	4 690 €	5 401 €
Conventional Coronary Angiography level 3	479	7 874 €	8 776 €	9 679 €
Conventional Coronary Angiography level 4	89	13 878 €	15 760 €	17 642 €
Conventional Coronary Angiography out patients	1 680	163 €	1 088 €	2 014 €
Total/weighted average by volume (2008)	**21 982**	**1 931 €**	**2 375 €**	**2 818 €**
Updated for (2009 DREES*)		**2 166 €**	**2 663 €**	**3 160 €**

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**Updated to 2009 figures using National Health Accounts hospital expenditure inflation rates 2008/2009*

**Rates for 2009/2010 not yet available.*

Table 29 - Accuracy, cost and radiation for different strategies

Action	Accuracy	Ave. cost per patient	Ave. Radiation mSv	% of CA for negative results	% high risk with CAD classified as false neg.
Nothing	48%	0 €	0	0	100%
CT for intermediate risk only (neither for low risk and CA for high risk)	96%	2 044 €	11	26%	0%
CT for all triage followed by confirmation CA	95%	2 065 €	24	23%	5%
CA	100%	2 663 €	7	48%	0%

Table 30 - Estimate of excess cancer deaths

Effective Dose mSv	Excess Cancer Deaths France 2008	Source
2	808	
20	8 078	

Number of scans per 1 000	*130*	*OECD 2008*
Population 2008	*62 135 000*	*INSEE*
Excess cancer risk	*0,00005*	*NCRPM*

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Acknowledgements

I would like to thank my professional advisor Professor Isabelle Durand-Zaleski. Without her full support it would not have been possible for me to undertake the MPH. Her encouragement was invaluable.

Much gratitude is due to my friends who had to put up with me groaning about exams. Special thanks to Franck Bilau, Dr. David Dugdale, Dr.Ted Lazo, and Professor Elisabeth Macintyre.

A French Masters in my native language run in Paris felt as if it was tailor-made for me so many thanks to the heads of the programme: Professor Denis Zmirou and Professor Martine Bellanger.

Thanks to the medical corps, administrators, purchasers and the CT manufacturers who helped with the micro-costing – without them this report would have been impossible. In particular:
Elisabeth Aoun (AGEPS), Dr. Michel Cymbalista (Montfermeil Hospital), Roger Delapaule (Toshiba), Catherine Deneux (Centre Chirurgical Marie Lannelongue), Dr. Jean-François Deux (Henri Mondor Hospital), Dr. Franck Digne (Max Fourestier Hospital), Professor Gueret (EVASCAN principal investigator, Henri Mondor Hospital), Philippe GRES (General Electric), Professor Jean-Pierre LAISSY (Bichat Hospital), Jean-Eric Lefèvre (AGEPS), Dr. Jean-François Paul (Centre Chirurgical Marie Lannelongue), Professor Alain Rahmounui (Henri Mondor Hospital), Rémy Raymond (Henri Mondor Hospital), Alain Ygnonin (Siemens).

And last but not least, to my husband Andrew for his unstinting support and to our two lovely sons Benjamin and Sebastian – whilst more interested in Stars Wars or the football results than Public Health, have put up with a distracted mother admirably over the last three years.