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CT coronary angiography at an ultra-low radiation dose (<0.1 mSv): feasible and viable in times of constraint on healthcare costs

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Abstract Computed tomography coronary angiography (CTCA) has reached very high standards both in terms of diagnostic performance and radiation dose reduction. This commentary follows a report on CTCA using less than 0.1 mSv in selected patients. This is an extraordinary accomplishment, both for technology and for medicine. The difficult task is now to implement this tool in clinical practice so it can play the best possible role. CTCA can improve diagnostic pathways, can save money for healthcare systems and could even improve pharmacological therapy. All of this may happen, but it will require the combined effort of all the experienced operators in this field, including the referring clinicians. In times of financial constraint, CTCA may also help to restrict ineffective medical expenses.

Key Points

- *CT coronary angiography provides high diagnostic standards in non-invasive cardiovascular medicine.*
- *It should therefore replace other less effective diagnostic tools.*
- *Inappropriate catheter angiography is costly to healthcare systems.*
- *CTCA could help reduce costs of cardiac investigations by around 33 %.*
- *Low radiation doses in CTCA lead to risk-free individualised pharmacological treatment.*

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Background

In 2009 we witnessed the introduction of sub-millisievert computed tomography coronary angiography (CTCA) [1, 2]. The explosion of evidence concerning the possibility of performing CTCA with a radiation dose below 1 mSv has led to different perspectives and considerations concerning the future of CTCA [1]—not only because a low radiation dose is good for patients, but also because such a development should have an immediate and relevant clinical impact. It was a remarkable achievement following so soon after the initial pioneering experience with 4- and 16-slice CT equipment in 2000 and 2002 [3, 4]. Since then, the clinical impact of CTCA has increased in several countries, and technology has developed further too. In particular we have seen developments in the clinical field concerning the CONFIRM registry, which established the prognostic value of CTCA [5, 6], concerning acute chest pain at low risk in which three large randomised trials established the role of CTCA [7–9], and more recently concerning the promising preliminary data on fractional flow reserve (FFR) performed with CTCA [10, 11]. The total clinical impact was paired with developments in the field of image reconstruction that are referred to as iterative reconstruction algorithms [12–15]. Iterative reconstructions (IR) represent another paradigm shift in CT development. In fact, since the early days, the reconstruction process behind CT images was so expensive in terms of computational power that another algorithm had to be developed: the simpler and much faster filtered back-projection (FBP). We all learned CT with FBP images, mostly thinking about it as the only possible algorithm. Exact reconstructions were always too complex and too difficult to perform.

In 2010 the whole industry started to introduce different iterative reconstruction(IR) algorithms. Each manufacturer followed its own IR strategy to develop something close to exact reconstructions (which in principle should come directly from raw CT data). The limitations remain not in the algorithm but in the time required to generate such images. For the same data set with comparable parameters and state-of-the-art computer power, an iterative reconstruction requires three to ten times more time depending on the depth of iteration. Nevertheless, we are now investigating the potential of second-generation IR algorithms. Cardiac imaging was again the main driver for this development, which ultimately created a benefit for all CT imaging applications.

A new standard for low-dose CTCA

In this issue of *European Radiology* we read the study by Schuhbaeck et al., which provides a new standard for radiation dose delivery in computed tomography coronary angiography (CTCA) [16]. The authors report an average radiation dose of 0.06±0.01 mSv (i.e. DLP=4.6±0.5 mGy*cm; 0.014 conversion factor) in a highly selected population of young patients (mean age=52±14 years) with medium to low body weight (mean body weight=71.5±12.2 kg; mean height=173±7 cm; mean body mass index/BMI=23.9±3.2 kg/m^2), low heart rate ≤60/min and prospectively ECG-triggered high-pitch spiral acquisition mode always performed using 80 kV and 50 mAs. Image reconstruction was always performed with the latest generation of iterative algorithm (SAFIRE). A significant reduction in image noise and significant increase in image quality were reported when comparing IR with FBP. Up to 86.3 % of all segments and 57.1 % of all patients were evaluable considering the 18-segment model from the SCCT. There was no assessment of diagnostic accuracy, and in fact the number of patients enrolled would have been too low for such an assessment. Anyway, as stated by the authors, a major limitation concerns the extremely low prevalence of coronary artery disease. This was a feasibility study on ultra-low radiation dose CTCA that may apply perfectly in coronary artery disease screening settings. With this protocol, the radiation dose is much lower than the usual one for calcium score quantification.

The results are quite impressive in terms of radiation dose levels even if this is just a feasibility study. In 1999, when the first CTCAs were performed, probably no one could have foreseen such a development. It is definitely interesting to see that CTCA can reach a far lower radiation burden than conventional CT imaging. The comparison with other imaging techniques should be reconsidered in the light of the new standard for CTCA. All other CT imaging fields (e.g., neuro, thorax, abdominal, vascular) should follow the lead of cardiac CT in radiation dose reduction strategies.

Radiation dose in CTCA: a complex topic

Most radiologists and cardiologists not directly involved in cardiac CT may ask, how did we get here? Since the early days of CTCA, the radiation dose has been addressed as a major issue [3, 4]. In 1999, the first generation of CT systems with four detector rows showed the capability of assessing the coronary arteries. There were several limitations. One of those limitations was the radiation dose. The relatively low temporal resolution of CT equipment forced the engineers and the operators to develop a spiral acquisition mode with very low pitch. In order to have the flexibility for the reconstruction of the optimal phase of the cardiac cycle (i.e. the one with the fewest residual motion artefacts) several additional phases were acquired, each one with its own radiation burden. This technique is called retrospective ECG gating.

Over the past decade several methods of dose reduction have been introduced (Tables 1 and 2). We will briefly recall them. The first one was *prospective ECG triggered tube current modulation*, which is based on delivering the peak tube current mainly during the phases of the cardiac cycle in which the most static images are expected; it only applies to retrospective ECG gating. The second one is *automatic exposure control*, introduced as a simple hardware/software-driven algorithm able to provide the operator with suggestions concerning the required mAs for a desired signal-to-noise ratio. Lately the algorithm has been hiding in the background of CT platforms to modulate the mAs (and more recently the kV too) for different body parts' absorption on the basis of scout view absorption profiles. The third one was the re-introduction of *prospective ECG triggering* as the main imaging mode. It relies on imaging within a sequential approach in pre-defined phases of the cardiac cycle. It is a means of reducing the radiation dose that is very effective and that requires a low and stable heart rate. The fourth one is *low kV CT imaging*. Low kV (100 kV or even 80 kV instead of the usual 120/130 kV) is very effective in reducing the radiation dose, but requires thin patients. Recently, a fifth method of dose reduction was introduced: *iterative reconstruction*. This is actually a reconstruction algorithm, not an imaging mode. It can be applied to any CT examination, not only cardiac CT. It is based on repeated iterations between final images and raw data in order to approach exact reconstructions. It requires a lot of computational power but can dramatically reduce image noise and increase image sharpness, thereby allowing radiation dose reduction with the same image quality as FBP. The introduction of the latest generation of dual-source CT systems in 2010 allowed a completely new imaging mode, which lies in between spiral and sequential (Figs. 1 and 2). It is called the prospectively ECG-triggered high-pitch spiral mode, and it requires an

Table 1 Radiation dose

Imaging	Philips iCT	GE HD750	Toshiba one	Siemens FLASH
Tubes/sources	1	1	1	2
Slices/rot (detectors)	256 (128)	64	320	256 (128)
Total slice/rot (spiral mode)	256	64	320	256
Slice collimation (mm)	0.625	0.625	0.5	0.6
Tube voltage (kV, range)	80–140	80–140	80–135	80–140
Rotation time (ms)	270	350	350	285
Temporal resolution (ms)	135	175	175	75
Spatial resolution (mm^3)	0.3	0.3	0.3	0.3
X-ray dose (mSv)				
Spiral (full dose)	10–25	10–25	10–25	5–20
Spiral (ECG modulation)	3–8	3–8	3–8	3–8
Prospective (minimum)	1–2	1–2	1–2	1–2
High-pitch spiral	–	–	–	<1

mm millimetres, *kV* kilovolt, *ECG* electrocardiogram

extremely fast (i.e. temporal resolution) CT system. It allows imaging of the heart within one heart beat (i.e. actually one end-diastole) with a very low radiation dose. It requires a very low and stable heart rate.

New developments and good old solutions

Meanwhile, the industry is developing newer exciting hardware and software solutions able to further increase our capabilities for dose reduction in cardiac CT. The aim of all this development is to reduce the radiation dose while preserving the usual diagnostic image quality. Eventually, this approach will lead to a significant increase in image quality with reduced radiation doses.

Table 2 Radiation dose from different imaging techniques

Source	Dose (mSv)
Background radiation (range)	3/year (1–10)
Chest X-ray, two projections (range)	0.1 (0.05–0.24)
Screening chest CT (range)	0.3–1.0
Calcium score	3 (1–12)
CTCA	
PROTECTION I trial (range)	12 (8–20)
64-slice; retrospective ECG	14–18
64-slice; retrospective ECG; tube current modulation	7–9
64-slice; prospective ECG	1.2–5.0
126/320-slice; prospective ECG (narrow window)	1–2
Dual-source; high-pitch spiral mode; 80-100 kV	<1
SPECT Tc^{99} (stress-rest; range)	10–20
CAG	
Diagnostic (range)	7 (2–16)
Interventional-coronary arteries (range)	15 (9–29)
Interventional-radiofrequency ablation (range)	20 (7–57)

The radiation dose numbers are collected from various reports in the literature and should be considered representative values

CTCA computed tomography coronary angiography, *CAG* conventional coronary angiography, *SPECT* single-photon emission computed tomography, *ECG* electrocardiogram, *Tc* technetium, *mSv* milliSievert

New detectors

The whole industry recently introduced or will soon introduce new detector technology. This is a very important hardware component, which allows improvement of the efficiency of photons used for CT imaging. A more sensitive and faster detector would allow use of fewer photons and exploit the potential of all photons. In addition, newer detectors would provide the same signal with less noise.

New reconstruction algorithms

Iterative reconstructions are just the beginning of a new field of development in CT imaging. We should immediately introduce IR into clinical practice and use them to reduce the radiation dose or improve diagnostic image quality in situations in which the diagnosis would normally be very difficult and less reliable. A very easy example in CTCA is the imaging of coronary stents [13]. The introduction of IR determines a consistent improvement in image sharpness, which allows the diagnostic capability in cases of in-stent re-stenosis to be increased. We are now awaiting the third generation of IR algorithms.

The role of beta-blockers

Any resident or radiologist approaching CTCA should understand that the most powerful means of constant

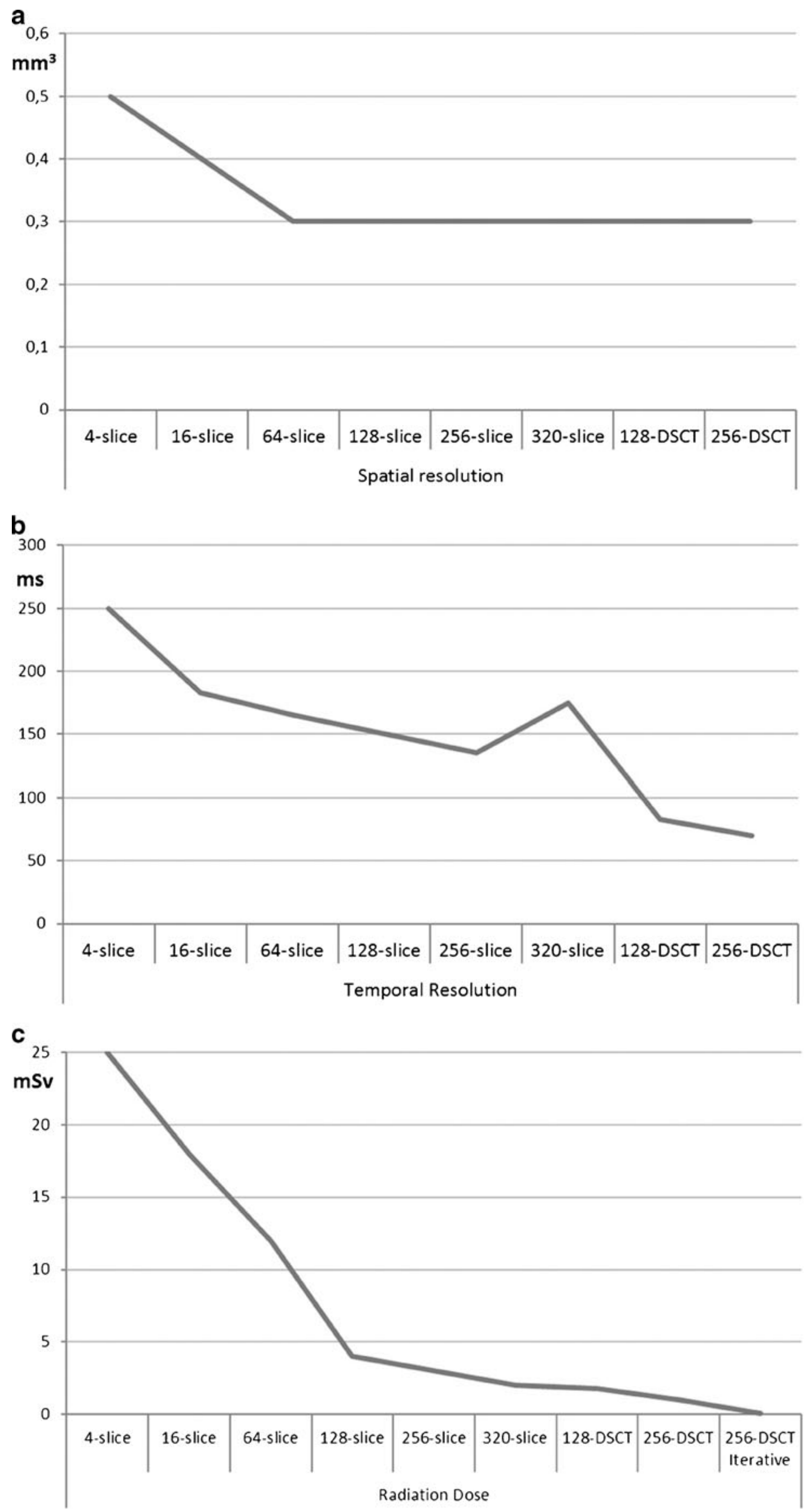

Fig. 1 CT technology development and radiation dose. Simplified view of the development of three main technical features of CT systems from the first generation of multislice equipment to date. Spatial resolution (**a**) was increased in the first steps of development, but later there was only limited improvement. This was mostly due to the constraints in radiation dose control (a thinner detector requires in general a much higher radiation dose). Temporal resolution (**b**) instead showed constant improvement especially with the introduction of dual-source CT systems. The result was that the radiation dose (**c**) was significantly reduced, and this was achieved mainly because of improved temporal resolution. More recently, further improvements have been possible because of kV reduction and iterative reconstructions

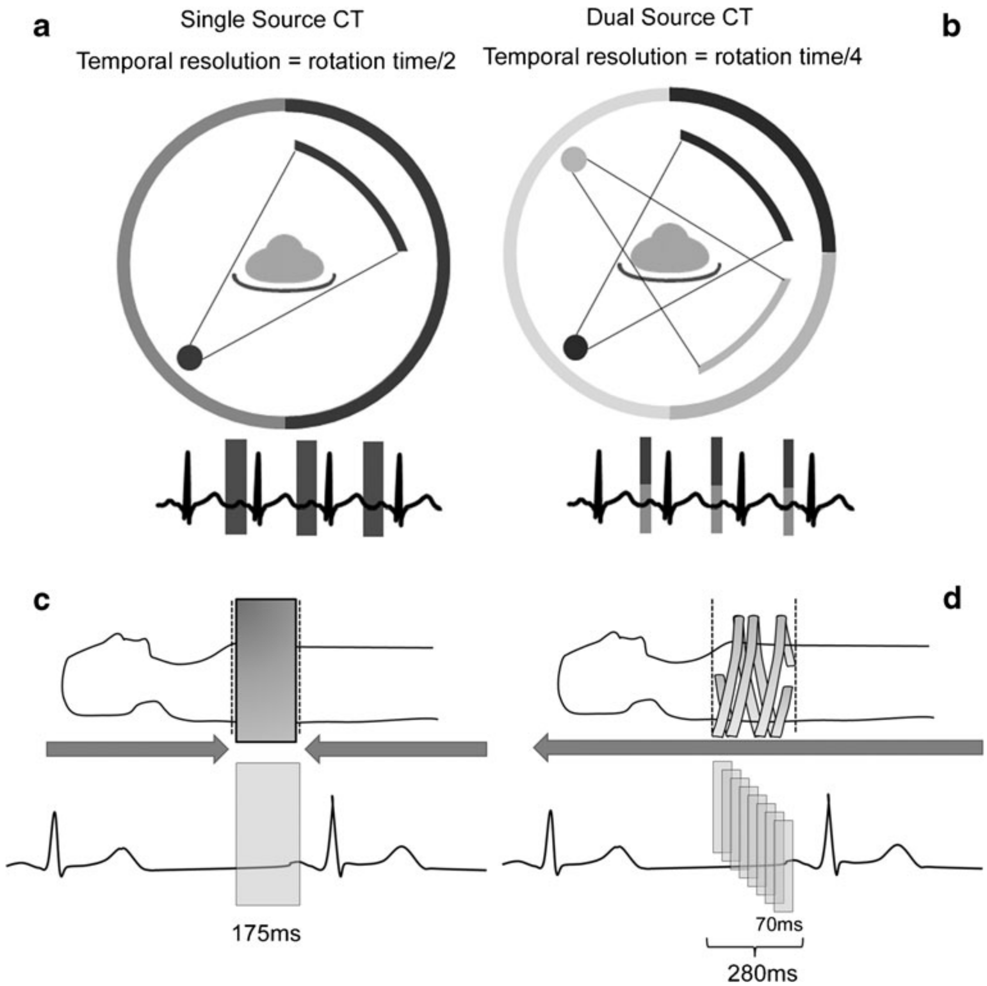

Fig. 2 Main low-dose CT philosophies. Two main CT philosophies concerning low-dose cardiac imaging. There are two approaches to low-dose cardiac CT imaging: the first is based on single-source CT systems (**a**) and the second on dual-source CT systems (**b**). With single-source systems slices are preferably increased (**c**) until the heart can be covered in one heart beat while the table feed is 0. Dual-source systems, instead (**d**), rely mainly on a higher temporal resolution to cover the heart in a single heartbeat with a very high table feed (i.e. high pitch mode)

radiation dose reduction are operator know-how and thorough heart rate control [17]. The latter is normally achieved using beta-blockers. The combined use of beta-blockers and other pharmacological means is the key to robust and reliable CTCA with a low radiation dose (e.g. ivabradine).

Implementation of CTCA in clinical practice: where are we?

CTCA is still underused in Europe (while growing popular in North and South America and Asia), or at least there are several countries and areas in which the implementation of CTCA is not what might be expected based on current evidence and cost-effectiveness. In such countries and areas, the marketing against CTCA is still strong and mainly based on radiation dose issues, lack of functional information and mostly the fact that cardiology is not primarily involved. The cardiological community in some cases keeps discussing the potential of a technique that is revolutionising the approach to cardiovascular medicine instead of adopting it. Currently, the largest ongoing registries and trials on diagnostic imaging in cardiology have been triggered by the introduction of CTCA (i.e. CONFIRM, ISCHEMIA, PROMISE, ACIC/PA, MEDIC, RESCUE, ROMICAT I-II, PROTECTION I-II-III-IV, EISNER, CONSERVE, DISCOVER-FLOW, DeFACTO, CORE64, CorE320, CT-STAT, PRORECAD, DICAD, etc.). Never before has cardiac imaging experienced such attention in terms of scientific debate, growth of evidence and emerging new ideas. The pathophysiology of coronary artery disease (CAD) is going to be addressed in more depth because of the introduction of CTCA. On the other hand, the paradigm shift induced by the introduction of CTCA may also determine a paradigm shift in the field of diagnostic catheter-based coronary angiography (cath).

Healthcare spinoffs: the changing role of diagnostic catheterisation and stress tests

The development of CTCA is challenging the role of catheterisation laboratories worldwide.

It can be argued that too many invasive coronary angiograms are performed that do not lead to revascularisation

(30 % to 60 %) [18–21]. This is a very big issue for several reasons:

(1) It suggests that the diagnostic tests performed before catheter angiography are not good enough for patient selection and stratification; this means that too many patients without significant coronary artery disease are sent for catheter studies and many patients deserving catheter studies are dismissed because of functional test failure.
(2) At least one third of catheterisation laboratories may stop working with a consistent reduction of costs that may reach several hundred million euros/year if we consider countries such as Italy (total number of catheter studies in 2011=~300,000); the reduction in costs could reach billions/year if we consider the whole of Europe, the USA, Brazil, China and India. Of course the costs of computed tomography coronary angiography will have to come from such savings. Furthermore, there is always the danger of increased usage whenever a non-invasive investigation replaces an invasive one.
(3) We need a reliable gatekeeper for catheter angiography and likely revascularisation, which costs less both on a per-patient base and for the entire healthcare system;
(4) Healthcare administrators and authorities should "wake up" and start looking in this direction.

This discussion forms the basis of the largest international multicentre prospective randomised controlled trial ever performed concerning imaging techniques (i.e. the PROMISE study; expected enrolment=10,000 patients). The ideal gatekeeper will probably turn out to be CTCA because of the extremely high rule-out capability.

Stress tests as first-line tools are already being phased out in several countries that were early adopters of CTCA (e.g. North America, Asia). The widely used stress ECG could today be considered one of the most overused/misused tests in cardiology in 2012 [20, 21]. This may appear an exaggerated statement but we know from the literature that in the asymptomatic population and in cases of low-intermediate probability (<50 %) of disease the test has a poor performance. In cases of high and very high pre-test probability (>80 %), it is also useless because the clinician wants to know about the presence and extent of reversible ischaemia, which can only be found using stress imaging (stress echocardiography, stress magnetic resonance and SPECT).

The fact should also be considered that recent evidence shows that, in stable coronary artery disease, percutaneous revascularisation and optimal medical therapy provide basically the same effect [22]. Therefore, the urge to revascularise any slightly stenotic vessel should be limited and accurately assessed for each and every patient.

In conclusion, when we first saw the data on four-slice CTCA in 2000, several people were sceptical (27 % of non-assessable segments) [23]. After a decade, things have developed much further than we could ever have imagined based on those data.

Current data are very promising, and we have reason to believe that we should take steps towards more extensive implementation of CTCA. The breakthrough paper reporting CTCA using less than 0.1 mSv in selected patients [16] provides further impetus for such a recommendation. In addition, as experts in this field, we should be aware of the consequences and the implications of CTCA when applied to real life. If we do not take part in the clinical discussion and take a leading role, this may be damaging to the practice of radiology, to patients and to healthcare in general.

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