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Review

Technical challenges of coronary CT angiography: Today and tomorrow

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ABSTRACT

Rapid advancements in multidetector row computed tomography (MDCT) are beginning to revolutionise cardiac imaging applications. As a consequence, coronary CT angiography (CTA) is fast emerging as a highly effective, noninvasive imaging technique for the assessment of coronary artery disease (CAD). Technology is improving at a robust pace, which brings with it the benefits of superior spatial and temporal resolution as well as fast volume coverage, achieved through the development of systems with an increased number of detectors and shorter gantry rotation time, as well as the advent of systems equipped with dual-source X-ray tubes. The main power of CTA was thought to lie in its high negative predictive value in excluding coronary disease with a high degree of accuracy in patients with low probability for CAD. However, this rapid progress has meant that we are also adding to the growing list of additional potential applications of CTA that are possible with the technology. The aim of this review is to present an overview of the technical capabilities of cardiac MDCT relating to coronary CTA and other applications, the limitations of current technologies, as well as discuss political perspectives and how to address these in medical practice.

1. Introduction

Coronary artery disease is the leading cause of morbidity and mortality in industrialized countries. Medication, surgical revascularization or percutaneous balloon angioplasty with stenting form the mainstays of therapeutic options. The decision on whether to institute these therapies relies on the evaluation of the coronary artery lumen, provided in the main by direct catheter angiography. With supreme temporal and spatial resolution, invasive coronary angiography provides accurate, reliable, and reproducible evaluation of luminal status for narrowing, stenosis, and occlusion. However, despite it still being the gold standard for assessment, direct angiographic analysis is not without its limitations. In 2004, nearly 1.5 million diagnostic invasive coronary angiograms were performed in the United States alone, with a not insignificant overall complication rate of 3.6% and a procedure-related mortality rate of 0.1% [1]. Conventional catheter angiography also provides only limited information on the presence and type of atherosclerotic plaques not associated with luminal stenosis (i.e., forming a positive remodelling); on plaques that are vulnerable for rupture, eventually leading to thrombosis, occlusion, and myocardial infarction [2–4]. Thus it is obvious that a noninvasive method for visualizing coronary stenosis and plaques that addresses these issues would be cost beneficial, greatly aid diagnosis, and considerably reduces the number of purely diagnostic angiograms and associated morbidity.

Advances in multidetector-row computed tomography (MDCT) of the heart, coupled with the combined benefits of electrocardiogram (ECG) gating, has resulted in tremendous progress in the noninvasive imaging of the cardiovascular system and in particular the coronary vasculature. MDCT technology has been rapidly adopted to generate high-resolution contrast-enhanced angiograms of the heart and coronary arteries [5–8]. Cardiac CT angiography is able to provide information on the chronicity of the atherosclerotic process, the state of the coronary artery wall and allows for plaque characterisation; thus overcoming some of the shortcomings of direct catheter angiography.

The emergence of new diagnostic technologies is often accompanied by the controversy of challenging established methods and techniques. In this regard, coronary CTA is no exception where the debate has centred around its potential role in replacing conventional invasive coronary angiography. One of the major advantages of the latter is the ability to perform therapeutic interventions such as angioplasty and stenting of lesions identified during the same diagnostic procedure. However, recent outcome analysis studies challenge this notion and suggest that therapeutic interventions

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should only be applied to patients with stenoses that result in proven haemodynamically significant alterations [9–11]. This decoupling of diagnostic and therapeutic pathways lends itself very well to less invasive procedures such as coronary CTA in the workup of appropriate patient groups. CTA therefore has a major role to play in reducing the number of unnecessary invasive coronary arteriograms in patients with normal or clinically non-significant coronary artery lesions [8,12,13].

During the course of this review, we aim to discuss the technical aspects of MDCT as applied to cardiac CTA and other applications, the current state of play of the technology, and its limitations. We also tackle the political issues related to the wider adoption of the technology in the practice of cardiological medicine and how these can be addressed.

2. Technical aspects of cardiac CTA

2.1. Spatial and temporal resolution

The demand from cardiac CT is of high spatial resolution, high temporal resolution, and true volume data sets. Thus the aim has been to develop advanced scanners providing super-fast gantry rotation times, submillimetre slice thicknesses and data sets consisting of many hundreds of slices with post-processing allowing isotropic reconstruction in any plane.

High spatial resolution is essential to enable visualization of small arteries and plaques and delineation of complex cardiac anatomy. Coronary arteries are small (1–5 mm). Therefore, in order to detect stenoses, cardiac MDCT scanners need to achieve submillimetre resolution. Not only that, isotropic resolution is the ideal as the resolution is required in 3 dimensions due to the tortuous course of the vessels. Cardiac CTA has a spatial resolution of roughly 0.4 mm, and although it is improving, it is inherently inferior in comparison with invasive coronary angiography (0.1 mm).

High temporal resolution is critical to minimise or eliminate motion artifact associated with the beating heart to make it possible to image the entire heart volume in a single breath-hold. Invasive coronary angiography boasts excellent temporal resolution of just 4–7 ms but in CT imaging of the coronary arteries, cardiac movements are the most important limiting factor. For heart rates of less than 70 bpm, a temporal resolution of less than 250 ms is sufficient for motion-free imaging in diastole, whereas a temporal resolution of 50 ms is needed in systole. With increases in heart rates, better temporal resolution is required [14]. The overall temporal resolution of current cardiac MDCT varies from 100 to 200 ms [15,16]. The most recent scanners are reaching true temporal resolution of between 75 and 83 ms [17,18]. Although the temporal resolution with MDCT depends on several variables related to the intrinsic characteristics of the scanner (gantry rotation time, number of detectors etc.), the utilisation of ECG-gating and the type of synchronization algorithm engaged is of prime importance and an essential component of cardiac CT. ECG-gating and synchronization allows data acquisition and image reconstruction at specific points in the cardiac cycle, optimizing image quality whilst also defining the type of information available to the clinician. There are 2 distinct methods of ECG-gating employed by cardiac CT.

2.2. Retrospective ECG-gating

In current practice, the vast majority of cardiac CT examinations are performed on MDCT scanners with retrospective ECG-gating. As the name suggests, there is continuous spiral CT acquisition centred over the heart synchronized with simultaneous ECG recording, and data acquisition during all cardiac phases (Fig. 1).

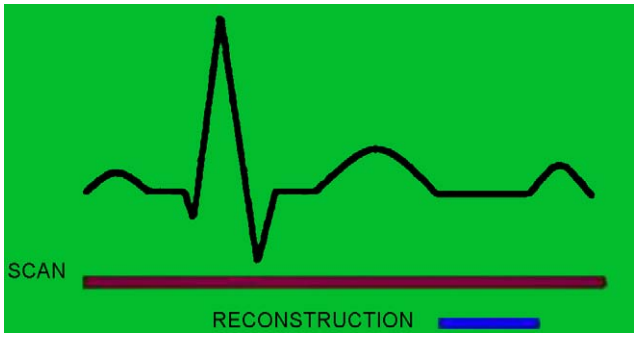

Fig. 1. Retrospective cardiac gating.

This then allows for subsequent retrospective image reconstruction in any given phase of the cardiac cycle. Data may be taken from a specific point in the cardiac cycle in order to generate an image during diastole or to select data from a different point in the cardiac cycle to generate an image during systole. This is beneficial as individual coronary arteries are optimally visualized in different phases of the cardiac cycle, particularly at higher heart rates. Accordingly, the right coronary artery (RCA) is better visualised in late systole, whereas other coronary arteries are best seen in diastole [19]. Multisector reconstruction algorithms have tried to improve temporal resolution further where X-ray projections of more than heartbeat are used to reconstruct an image. This does however require absolutely consistent data from two or more heartbeats. Retrospective gating also enables an evaluation of cardiac function. MDCT has been successfully been validated for the quantification of right ventricular (RV) and left ventricular (LV) function [20] and has been proved to be in excellent agreement with echocardiographic [21] and MR assessment of global ventricular function [22,23]. In addition, as reconstruction is possible throughout the cardiac cycle, retrospective gating can identify potential regional function and wall motion abnormalities. Measurements of regional LV function with MDCT are based on the assessment of systolic thickening by use of the 17-segment model proposed by the American Heart Association as in accordance with other cardiac imaging modalities. Qualitative assessment of regional LV function can be visually assessed by the change in wall thickness and the systolic thickening by use of cine loop displays of multiple cardiac phases (5–95% phases). MDCT determined regional LV function has been shown to correlate well with cardiac MRI [24,25] and echocardiography [26–28]. It must be borne in mind, however, that all of these functional analyses come at the expense of longer post-processing times.

Retrospective gating is heavily reliant on the patient being in normal sinus rhythm with a stable R–R interval during the scanning process. Arrhythmias can lead to data acquisition during an undesirable phase of the cardiac cycle and unless a very low pitch is used (approximately 0.2–0.4), omitting such data could result in significant coverage gaps. The reliance on such a very low pitch to avoid gaps in anatomic coverage is a limitation of retrospective gating methods. This means that each anatomic area of the heart may be scanned several times during data acquisition, which results in higher radiation dose. The entire cardiac cycle is imaged as the patient moves continuously through the gantry—receiving an X-ray dose of between 12 and 20 mSv along the way. The desire to minimize radiation dose, and the realization that the majority of useful information is acquired in diastole, led to the development of ECG modulation methods. This is where a lower tube current (mAs) is applied during the systolic phase. This results in an approximate 30–40% reduction in overall radiation dose.

Fig. 2. Prospective ECG-gating.

2.3. Prospective ECG-gating: step-and-shoot methods

Coronary CTA was initially performed on early generation non-helical conventional scanners with limited numbers of detectors, which employed prospective gating or "step-and-shoot" methods. These yielded relatively poor results due to insufficient temporal resolution which restricted use in patients with high or irregular heart rates, despite the use of beta-blockers. However, high radiation doses associated with retrospective gating was a key factor in prompting reconsideration of prospective ECG triggering, where scanning and reconstruction are only performed during late diastole (Fig. 2).

Traditional step-and-shoot methods used a fixed delay after the R-wave peak to determine when to turn the tube current on and there was considerable interest in determining the optimal phase for single phase scanning. Gutstein first assessed the single best %-phase for reconstruction of data using retrospectively ECG-gated CT [29]. Then, they tested this phase (70% of the R–R interval) with prospective ECG-gating and concluded it could be successful. Leschka et al. [30] also attempted to determine the optimal %-phase for reconstruction and also chose the 70%-phase as the single phase for prospective ECG-gating.

There has been sizeable effort in trying to modify prospective triggering to overcome the limitations of earlier versions. Several important improvements have been made to enhance image quality. The first of these is the introduction of an adaptive scan delay to obtain an optimally timed acquisition. Instead of a fixed delay, *Multiphase Adaptive Prospectively Gated Axial CT* starts with an adaptive delay to determine where in the cardiac cycle the acquisition will take place. The adaptive delay is a function of multiple prior cardiac cycles and changes from beat to beat. In patients with a steady R–R interval, there may be no significant differences between an adaptive delay and fixed delay. However, in patients with shortening of the R–R interval, the scan will be triggered on the basis of multiple previous R–R intervals, which is more likely to result in an optimally timed acquisition.

A further improvement in recent scanners is the minor lengthening of the X-ray tube on-time. Conventional step-and-shoot methods simply turned on the tube current for a specified period during diastole and acquired a single data stack. With 'padding' of the tube on-time, the tube is turned on slightly earlier and left on a little later to allow data capture from 10% to 25% of the cardiac cycle on either side of the optimal phase. This provides greater flexibility with prospective ECG-gating by permitting reconstruction in another phase if motion artifact is problematic in one phase. The acquisition of limited multiphase data sets also has the advantage of more optimal visualization of vessel segments with high motion velocities, such as the mid-RCA.

Prospectively gated axial CT has been evaluated recently in a clinical setting [31]. Using a 64-detector row CT scanner, 243 patients underwent cardiac CT; 82 patients using retrospective gating with ECG dose modulation, 40 patients using adaptive prospectively gated axial CT during a learning phase which was disregarded, and 121 clinical patients who also were scanned with prospectively gated axial CT software and were included in the final analysis. Image quality was evaluated for the left main, left anterior descending, left circumflex, and right coronary arteries, using a standard image quality scale [32,33]. The authors concluded that multiphase adaptive prospectively gated axial techniques improved image quality overall as well as for each of the coronary arteries individually. Although image quality was excellent in both groups, there was a small statistically significant difference between the two groups with the prospective methods yielding better results.

2.4. Advances in software

Newer sophisticated reconstruction algorithms allied to prospectively gated axial CT have also led to the enhancement of image quality [34]. Rather than rely on interpolation which leads to image degradation, gated complementary reconstruction algorithms help to correct for the under-sampling of data associated with helical CT examinations by making use of complementary samples from adjacent scans. Some manufacturers have also developed software for automatic selection of best phases for cardiac image reconstruction [35]. Moreover, various software applications allow editing of the reconstruction windows along the ECG trace which is particularly useful in patients with irregular heart rates or premature ventricular contraction.

In addition, softer or lower spatial resolution kernels are used for image reconstruction in an attempt to reduce the image noise that comes as a consequence of the thin-slice profile associated with coronary CTA. Impressive progress has also been made in developing noise reduction filters, to combat problematic image noise especially in obese patients. Although the use of these filters has been assessed in chest and abdomen applications, their role in coronary artery CT still requires evaluation [36].

2.5. Postprocessing

All coronary CTA studies are acquired in ECG-gated dynamic mode where different image sets are obtained at multiple phases of the cardiac cycle. Postprocessing of native axial images is then performed on an independent workstation with retrospective reconstruction. Generally, linear or curved maximum intensity projection (MIP) reformats are most useful for coronary artery imaging. Three-dimensional multiplanar reformats (MPR) are also an essential element of cardiac CT, because transaxial images are off-axis to the axes of the heart and coronary vessels. Postprocessing in volume rendering provides an anatomical overview and is particularly useful in patients with coronary artery bypass grafts for delineating potential complex postoperative anatomy. Dynamic cine sequences of the whole heart can also be generated and oblique reformatted planes obtained along standard anatomical axes. Dynamic cine sequences require the reconstruction of multiple phases. This is particularly true for CT of the cardiac valves and for assessing regional ventricular function (but not for the coronary arteries, where cine-mode views are used on a routine basis. These dynamic cine-mode views can be performed with workstations from all vendors (without exception).

The high spatial resolution of the reconstructed data allow for accurate quantitative assessment of heart anatomy, ventricular volumes and function, ejection fraction and regional wall motion and wall thickening abnormalities [13,19–28,37,38]. There is much exploration in postprocessing software and there are several software applications in use including those for automatic plaque and coronary artery stenosis detection, plaque characterization, and optimal functional analyses. There is currently little data available

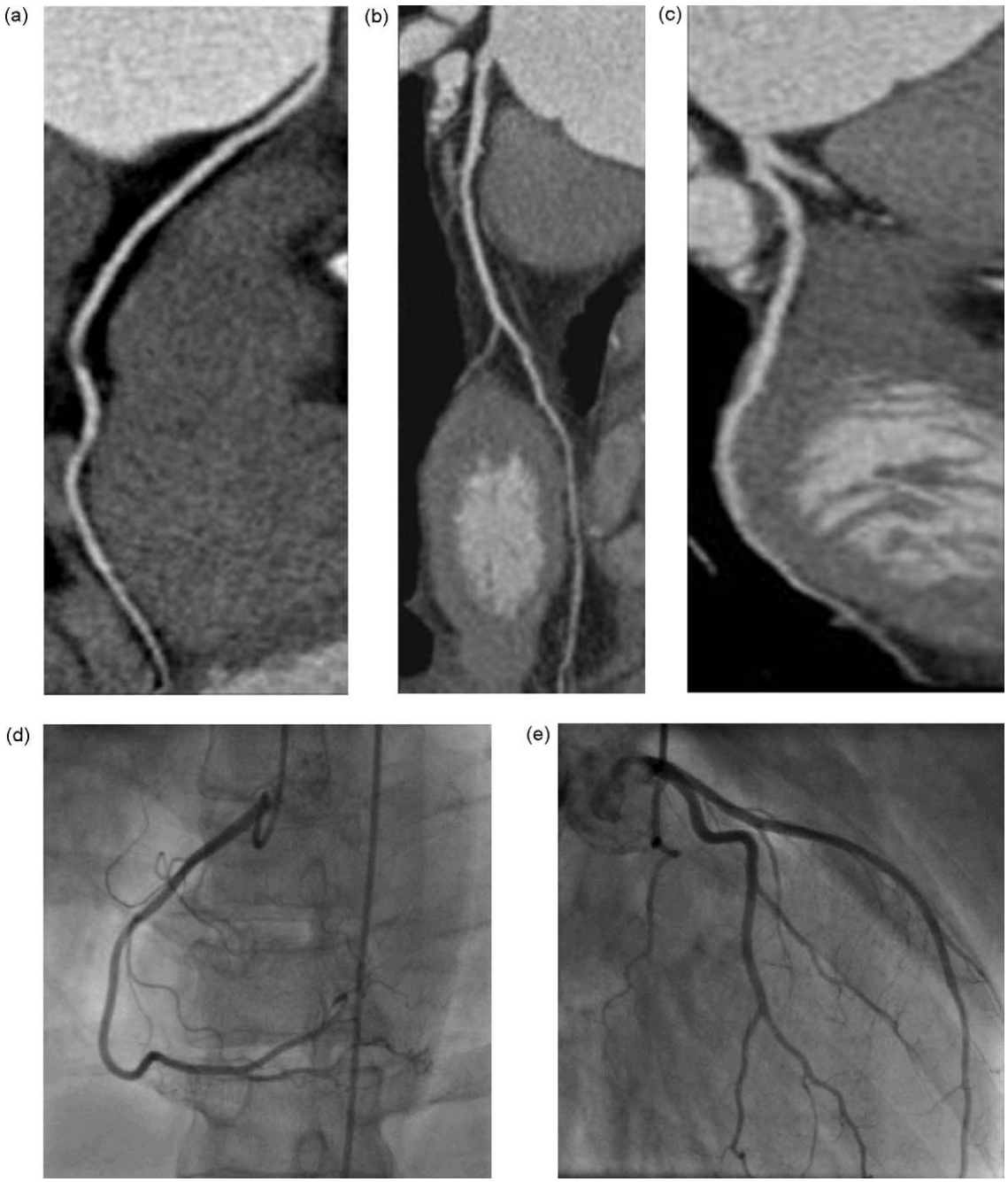

Fig. 3. Normal studies of the coronary arteries as demonstrated by both prospectively ECG-gated 64-section dual-source MDCT and conventional catheter angiography. Curved multiplanar reformations of MDCT coronary angiography data demonstrating (a) normal right coronary artery (RCA), (b) normal left anterior descending artery (LAD) and (c) normal circumflex artery (LCX). (d) Catheter angiographic study confirms a normal left coronary artery (LCA) and LCX and (e) a normal RCA.

on reproducibility and ease of use of these 3D software programs but it is clear to see that they can be extremely useful in routine clinical practice.

2.6. Current status of (single-source) MDCT technology

The biggest advance from earlier scanners to 16-slice MDCT was the improvement in gantry rotation times and hence temporal resolution. This was accompanied by wider longitudinal coverage (because of multiple detector rows), which at a beam pitch of 1:1, increased from 40 mm/s for the 4-slice to 160 mm/s for the 16-slice MDCT scanners, respectively. These improvements led to shorter breath-hold times of around 20 s and better radiation dose efficiency at thinner slice profiles. However, even with 16-slice MDCT, there was a clear need for scanners with wider *z*-axis coverage, faster gantry rotation to reduce scan times, minimize motion artifacts and to enable short breath-hold acquisitions. The advent of 64-slice CT scanners attempted to address these issues. Unfortunately, it was not possible to reduce the gantry rotation speed to lower than 300–350 ms because most MDCT scanners had reached their engineering limits for gravitational forces on the gantry. Producers of 64-slice MDCT therefore increased the number of detector rows for greater *z*-axis coverage, ranging from 32 to 40 mm depending on the manufacturer. One manufacturer developed a 64-slice scanner which used a *z*-axis flying focal spot and double *z*-sampling to generate 64 overlapping slices from a detector configuration of 32×0.6 mm at the fastest gantry rotation time of 330 ms [39]. Regardless of whichever vendor's technology was employed, the

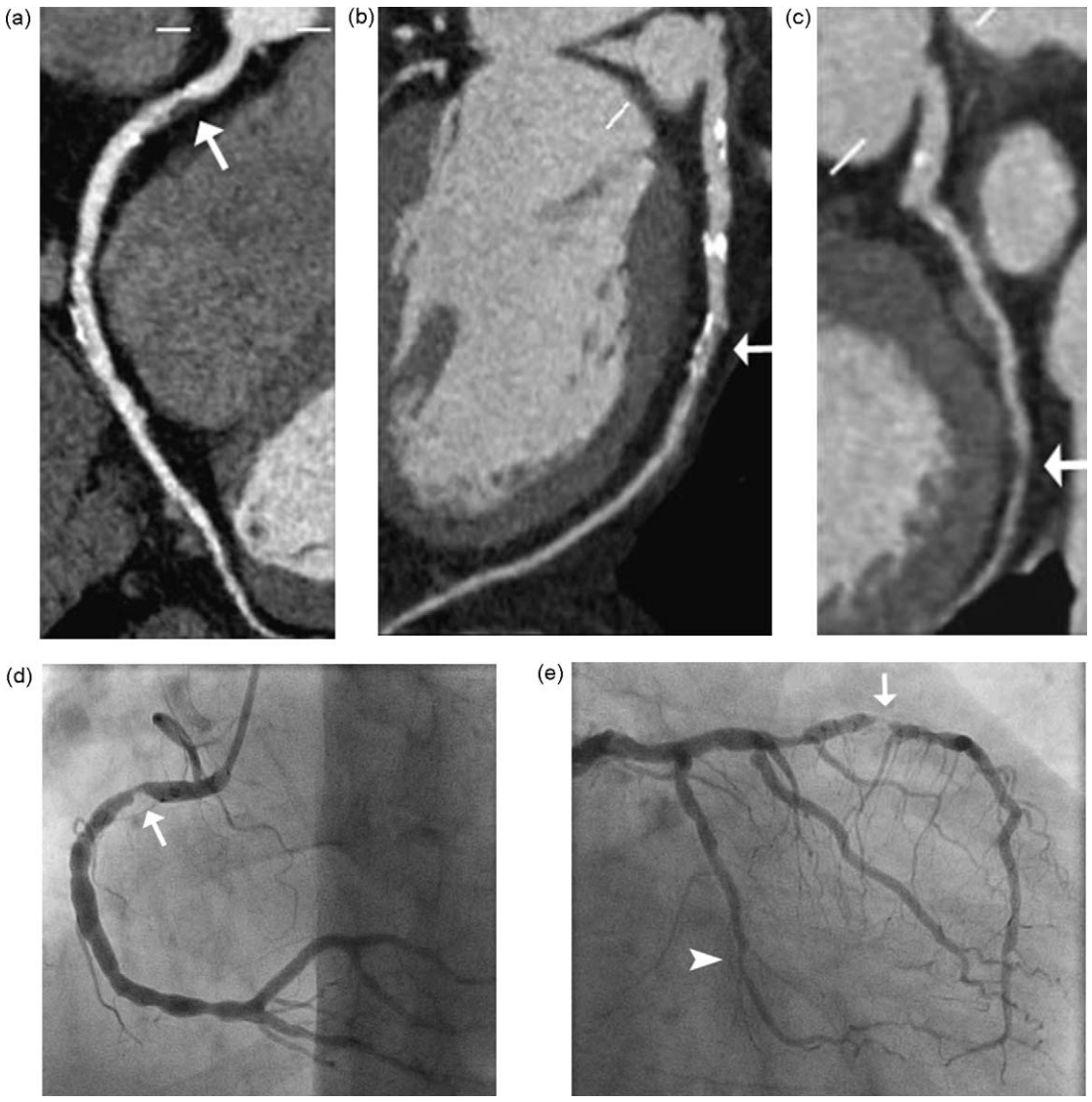

Fig. 4. Abnormal studies of the coronary arteries as demonstrated by retrospectively ECG-gated 64-section dual-source MDCT and correlated with images from conventional catheter angiography. Curved multiplanar reformations of MDCT coronary angiography data demonstrating (a) 80% stenosis in the proximal RCA (arrow), (b) 90% stenosis in the LAD (arrow) and (c) a further stenosis in the LCX (arrow). (d) Catheter angiographic study of diseased left coronary system confirms stenoses in the mid LAD (arrow) and LCX (arrowhead) and (e) a stenosis in the proximal RCA (arrow).

64-slice MDCT scanner brought shorter scan times of 5–10 s compared with 20 s for 16-slice MDCT [40]. Filtered back projection, which still forms the backbone of MDCT image reconstruction, requires data from at least half scan (180° of rotation) in order to maintain sufficient signal-to-noise ratio in the obtained images. For cardiac MDCT on a system with a 400 ms gantry rotation time, an image may be reconstructed from a single cardiac cycle with half-scan data to obtain a temporal resolution of approximately 200 ms, with what is called single segment reconstruction. For a bi-segment reconstruction, a scanner with 400 ms gantry rotation time and half-scan data split over 2 cardiac cycles, will generate a temporal resolution of roughly 100 ms. Depending on the CT manufacturer, a 2–4-segment reconstruction is possible and this multisegmental reconstruction can be useful in improving temporal resolution in cardiac CT studies performed at higher heart rates [41,42]. However, in order to achieve this, the longitudinal position of the heart over successive cardiac cycles should remain as constant as possible. Therefore, multi-segment reconstruction algorithms are prone to artifacts even when slight heart rate variations occur. Furthermore, they require a lower pitch than that of single segment reconstruction algorithms which is undesirably associated with higher radiation dose. Some 64-slice MDCT scanners are able to adapt the pitch to the heart rate, with higher pitch used for rapid heart rates and vice versa.

The aim of 256-slice MDCT was to be the first technology to cover the entire heart in a single gantry rotation with minimal disruption from artifact and stable improved temporal resolution. The 256-slice MDCT has a detector configuration of 256×0.5 mm, 0.5-s gantry rotation time with 12.8-cm z-axis coverage per rotation. Initial phantom studies have shown that there is 72% less radiation dose for chest CT performed with 256-slice CT compared with the 16-slice scanner [43]. However, the 256 slice scanner brings with it no substantial improvement in spatial resolution compared with 64-slice or dual-source MDCT, so it is unclear whether it will aid significantly in the evaluation of coronary arteries with calcification and stents. Meaningful data is awaited and studies will need to show whether the scanner proves to be a useful asset for cardiac evaluation over and above 64-slice and dual-source CT.

In any case, the technology of the latest generation of multi-slice CT scanners has progressed to deliver reliable and reproducible

coronary angiograms in the vast majority of patients [44,45], including clinically obese patients [46] and those with arrhythmias [47]. Large detector arrays are able to acquire images of the whole heart in a single heart beat. They permit faster acquisition multiplane imaging with isotropic voxel technology, thinner slices, and allow single-breath acquisition thus significantly reducing respiratory motion artifact. These scanners have not been available long enough to allow sufficient clinical studies to be performed. The main problem is that coronary CTA is growing at such a rate that by the time sufficient results are obtained, the technology has already evolved in performance, which renders the data obsolete [48–50]. Clearly randomised trial data is needed to validate the accuracy of the technique in identifying and measuring coronary disease compared to conventional coronary angiograms.

2.7. Dual-source MDCT

Dual beam scanners were developed as a novel technology to improve temporal resolution because at a gantry rotation speed of 300–350 ms, MDCT scanners were extremely close to the engineering limit of gravitational forces on the gantry [40,51]. Dual source scanners essentially double the speed of acquisition while maintaining the same spatial resolution [40,52,53]. Two X-ray beams (which may either at the same power or different depending on the manufacturer) and 2 detector arrays rotate simultaneously on the same gantry, which doubles the amount of data acquired per rotation [17]. Both detector arrays allow 64-slice acquisition with double *z*-sampling of data in a single gantry rotation with a spatial resolution of 0.6 mm in the longitudinal direction.

The fastest gantry rotation time for dual-source MDCT is the same as the single source MDCT scanner at approximately 330 ms. The advantage of having a dual X-ray source and 2 sets of detectors is that it enables acquisition of half scan (180°) of data from 2 simultaneously acquired 90° rotations from each X-ray source in the same cardiac cycle and *z*-axis position [54]. This effectively improves the temporal resolution to 83 ms for a single segment reconstruction and less than 50 ms for a bi-segmental reconstruction. This has led most sites to stop the practice of β-blocker administration for slowing the heart rate [52].

Like some newer generation single-source MDCT scanners, dual-source CT scanners are able to automatically adapt pitch to the heart rate [55] but they can also dynamically adapt the pitch over a wider range based on the patient's heart rate. A higher pitch is selected for higher heart rates to enable faster scanning (with concomitant radiation dose reductions) and a lower pitch is selected at lower heart rates.

The use of dual-source CT technology in clinical practice is encouraging (see Figs. 3 and 4). Dual-source CT has been reported to be more accurate for identifying significant coronary artery stenosis than single source MDCT, and enables accurate assessment of coronary artery disease even without heart rate control [56]. Most recently, Siemens has introduced a 2nd generation dual-source CT featuring 2×128 slices and a gantry rotation time of 280 ms providing a temporal resolution of 75 ms. This dual-source CT scanner can achieve gapless *z*-sampling with a pitch as high as 3.4 (so-called *Flash* mode), which enables complete coverage of the heart in a single heart beat in a duration of only 0.6 s. Flash mode (or high-pitch technique) imaging requires heart rates of around 65 bpm and below, which can be achieved through the administration of beta-blockers. If it is not possible to reduce the heart rate to that level or below, the Flash scanner can be operated in the prospective ECG-gating technique for heart rates up to 70 bpm, or up to 100–120 bpm with the retrospective ECG-gating technique. Cardiac CT in the Flash mode is associated with radiation doses of 1 mSv and below. The first clinical study assessing the diagnostic accuracy of high-pitch dual-source CT for the assessment of coronary stenoses concluded that in patients with heart rates ≤60 bpm, MDCT coronary angiography using the Flash technique is associated with high diagnostic accuracy for the assessment of coronary artery stenoses at sub-mSv doses [57].

2.8. Limitations and pitfalls of cardiac MDCT

The three biggest areas of concern for MDCT technology in cardiac applications are motion artifacts from rapid or irregular heart rhythm, blooming artifacts from coronary artery calcium or stent, and radiation dose [58].

2.9. Motion artifacts

Good image quality in ECG-gated 16- or 64-slice CT systems requires relatively low and stable heart rates. Provided there are no contraindications, most authors routinely use oral beta-blockers to reduce heart rate before the CT examination. In those patients already taking beta-blockers routinely, additional beta-blockers are considered if the heart rate still is ≥65 bpm. In almost all studies with 64-slice systems [6,59–63], patients with tachyarrhythmia were excluded. Most patients were either on long-term beta-blockers at the time of the CTA and/or received beta-blockers prior to the CTA. The risk of using beta-blockers in patients with asthma, heart failure, severe aortic stenosis, heart block, or sick sinus syndrome without a permanent pacemaker, should be carefully assessed before taking this step. Some also suggest the use of nitroglycerin sublingually (0.1–0.4 mg, 1–5 min before scanning) to dilate the coronary arteries [60,64,65], however it is generally not preferred as it can potentially cause headache and secondary tachycardia.

The introduction of dual-source CT and its inherent high temporal resolution has certainly reduced the use of β-blockers and may eliminate it entirely. Scheffel et al. [52] have reported high sensitivity, specificity, and negative predictive value of dual-source CT without heart rate control with β-blockers. Similar results were obtained also by other authors employing dual-source CT in larger patient groups [66].

2.10. Calcification

Extensive coronary artery calcification often limits the ability to analyze image data by causing artifacts such as blooming, beam hardening, streaking, scattering, and noise. This applies to either 16-slice [67–69] or 64-slice scanners [6,7,48–51]. Blooming artifacts are probably the most important in terms of cardiac CTA and occur when high density objects, such as coronary artery calcium and small stents (<3 mm), occupy a portion of ≥1 voxel(s) [58]. The effect of these artifacts is to oversize calcified plaques on the CT image [70–72] with subsequent overestimation of luminal narrowing and reciprocal underestimation of residual coronary artery luminal diameter.

One possible way to circumvent the problem, would be to perform an initial unenhanced scan. Although this would avoid suboptimal coronary CTA in patients with severe calcifications [67,69], this is extremely controversial [73]. Although high-spatial resolution algorithms have been shown to decrease the extent of blooming [58], more advanced reconstruction algorithms or iterative reconstruction techniques would need intensive computing power and have not been universally applied to coronary CT [74,75]. As stated above, new dual-energy CT with special edge-enhancing image filters offers a possible solution to the problem of heavily calcified coronary arteries. Dual source scanners enable the separation of high-density calcification from intraluminal iodinated contrast material, thus theoretically providing calcium-free angiograms. It has been suggested that dual-energy CT reduces the overestima-

tion of calcium volume by nearly half [76]. However, at this time, in the clinical setting there is only minor evidence that dual source scanners help in calcified coronary arteries [52]. Scheffel et al. [52] showed that with dual-source scanning in patients with a high calcium load, cardiac CT was still accurate. The interpretation was that the higher temporal resolution at least partly compensates for the artifacts that occur with calcium. The assumption was that part of the blooming artifact is related to motion artifacts and upon reducing these, blooming is also consequently reduced. Obviously, further studies are required to prove the degree of improvement and validate the technology.

2.11. Radiation

Radiation dose of 16-slice CT was estimated to be approximately 9 mSV [77] and around 15 mSv for men and 20 mSv for women for 64-slice CT [55]. These radiation dose values were achieved using retrospective ECG-gating for phase synchronisation. They are clearly a higher effective dosage than is found in conventional coronary angiography (average 7–10 mSv). Several dose-saving strategies such as prospective ECG triggering, X-ray beam filtration, X-ray beam collimation, automatic pitch adaptation, ECG-controlled modulation of the tube current and low kilovoltage [78] have resulted in reduced radiation doses of between 80% at lower heart rates and 50% at higher heart rates. Initial studies on the use of advanced iterative reconstruction techniques for CT images, reveal as much as a 10-fold reduction in the image noise and is clearly another exciting area to possibly apply to cardiac imaging in the future [79,80].

Prospective gated step-and shoot acquisition CT has significantly reduced the exposure dose of coronary CTA way below the dose of a conventional coronary angiogram. Recent publications have shown that by applying this technique and appropriate imaging protocols, accurate images of the coronary arteries can be obtained at doses as low as 1–2 mSv [81,82]. The arrival of 256 or 320 detectors into the workplace will mean that scanners will be able to acquire complete 3-dimensional images of the whole heart in a single rotation, obviating the need for spiral averaging over several multiple heart cycles. This can significantly reduce the dose down to as low as 5 mSv for full dynamic assessment of LV function over the whole heart cycle [83,84].

3. The future

3.1. Flat panel CT

Flat panel detector based volumetric CT (fpVCT) represents an entirely novel CT approach by application of full field flat-panel digital detectors that significantly increase volume coverage with truly isotropic data sampling at high spatial resolution down to approximately 0.2 mm [85–99]. These systems are completely different from their MDCT counterparts in terms of gantry system, x-ray tube, detectors, as well as in other considerations. The potential benefits of superior spatial resolution and volumetric coverage in cardiac applications are self-explanatory. It would allow resolution of smaller distal coronary arteries, significantly less underestimation of in-stent lumen, and enhanced imaging of stents and heavily calcified coronary arteries.

Most studies with fpVCT scanners haven been performed on ex vivo specimens, phantoms, and animals [40]. In any case, the technology is currently limited by poor gantry rotation times (approximately 2 s), which substantially limits its application in cardiac imaging. Inadequate contrast resolution of 5–10 HU (compared with MDCT scanners of 1 HU) is also restrictive. However, the technology certainly merits further research to see whether it can find a niche role in the assessment of coronary artery disease, function, and/or perfusion.

4. Clinical and political challenges of CTCA

There are several questions that need definitive answers before ubiquitous acceptance of noninvasive CT based angiograms in clinical practice. What extra value does CTCA provide? How should the technology be used? What is the clinical niche for this fantastic innovation?

Catheter angiography remains the gold standard for evaluation of the coronary artery lumen. Early noninvasive CT studies with 4-detector scanners reported CTCA sensitivities in detection of significant stenoses of 82–85% and specificities of 76–93%, which increased to approximately 90% and 95% respectively, with 16-slice scanners [67,68–72,100–103]. Studies conducted with 64-slice scanners have further improved mean sensitivities and specificities of 91% and 96%, respectively. These studies have all demonstrated a high negative predictive value (NPV) of CTCA for the detection of significant stenoses with both 16-slice scanners (mean 98%) and 64-slice scanners (mean 97%) [6,7,59–63,67–69,72,100–105]. Further enhancements to scanning technology may improve these percentages further.

Another important issue concerns the repeated demonstration that more than 50% of catheter coronary angiograms performed in Western countries confirm normal coronary arteries. In such cases, patients are exposed to the risks and side effects of an invasive procedure that could be replaced favourably by noninvasive coronary CTCA without compromising accuracy for excluding significant coronary artery disease. The high NPV of CTCA makes it an ideal alternative to invasive coronary angiograms in patients with a low to intermediate pretest probability of coronary artery disease. Invasive coronary angiography studies could be avoided in these select patient populations if CTCA demonstrates normal coronary arteries [61]. These include those with nonspecific chest pain, asymptomatic patients with evidence of ischemia during stress testing, patients with equivocal abnormalities on nuclear imaging, or asymptomatic patients with regional wall motion abnormalities detected by echocardiography or radionuclide ventriculography. The high NPV of CTCA also lends itself well to investigating patients with acute atypical chest pain presenting to emergency department with normal enzymes and ECG. Future prospective studies on these and other patient groups would be helpful in evaluating potential indications.

Ischaemic heart disease in the developed world shows no signs of diminishing in the near future and therefore the focus on resource utilisation is particularly pertinent. Hines et al. have tried to explore this by assessing the impact of the introduction of a 64-detector CT scanner for cardiac applications [106]. The authors found that there was a 21% absolute reduction in the rate of referral to invasive angiography, with no significant change in the percentage of patients undergoing invasive therapeutic procedures. The logical deduction was that CTCA functions well as an effective gatekeeper to the catheterisation laboratory by curtailing unneeded invasive procedures without omitting patients who would benefit from revascularisation. These findings are obviously associated with significant financial implications as it appears the introduction of CT coronary angiography may manage to cut down cost and decrease hospital admission.

The current risk stratification of patients with acute chest pain but non-diagnostic ECG results and normal initial biochemical markers is insufficient. Most analyses agree that compared with the traditional standard of care, integration of CT into the diagnostic algorithm for acute chest pain has potential for reducing time to diagnosis, decreasing the number of unnecessary hospital

admissions, and lowering cost [107–109]. To examine the impact of 64-slice CTCA on clinical decision-making in patients presenting to the ED with possible ischaemic chest pain, Rubinshtein et al. [110] studied 58 consecutive patients with intermediate risk chest pain and no ischaemic electrocardiographic changes or increased biomarker measurements. After standard ED patient assessment, a diagnosis of acute coronary syndrome was made in 41 patients (71%), hospitalization was recommended in 47 (81%), and 32 (55%) were scheduled for an early invasive strategy. After coronary CT, the diagnosis of acute coronary syndrome was revised in 18 of 41 patients (44%; 16 normal MDCT/widely patent stents, 2 alternative diagnoses) and planned hospitalization was cancelled in 21 of 47 patients (45%; 13 normal MDCT/patent stent, 8 minor branch vessel disease), and planned early invasive strategy altered in 25 of 58 patients (43%; unnecessary in 20 of 32, advisable in 5 of 26 others). The effect of CTCA on clinical decisions was greater in the patients without known preceding coronary disease. In 32 patients discharged from the ED, there were no major adverse cardiac events during a 12-month follow-up period. The authors concluded that CTCA was a valuable diagnostic tool in the ED triage of these patients and decreased the need for hospitalization by almost half in this patient cohort.

As the temporal and spatial resolution of CTCA has continued to improve, applications for the technology have also broadened considerably. As well as a more accurate role in stenosis quantification, cardiac CT is beginning to have a role in interventional procedures. CT images with 3D-MPR can be transferred to the catheterisation laboratory prior to intervention for pre-procedure planning and can furnish information on the plaque type, vessel curvature and lesion length. In addition, an increasing number of electrophysiologists are now quite keen to define the relevant anatomy prior to ablation or mapping procedures as one is able to obtain excellent anatomical reconstruction of the area to be ablated. No doubt the future of complex arrhythmia treatment will be found through a combination of CTCA and electrical mapping. Delineation of—sometimes intricate—anatomy is a clear strength of CTCA and it is now the de facto standard for anomalous coronary arteries. These anomalies are seen in 1% of the population [111]. As well as the assessment of coronary arteries [59,68,100,112], cardiac CT has also shown to be useful in the evaluation of the pulmonary veins [113–115], ventricular structure and function [116], the pericardium [117–121] and in patients with valvular [122–124] or congenital heart disease [125].

Myocardial perfusion and viability imaging are certain to become a major application. A new generation of hybrid scanners combining MDCT scanners with positron emission tomography (PET) in a single machine permit simultaneous acquisition of anatomical images from CT and metabolic images from PET scans [116–128]. Fluorodeoxyglucose (FDG) labelled with 18F, is an excellent marker of myocardial viability and allows identification of myocardial infarcts and differentiates scar tissue from viable or hibernating myocardium. In fact, PET scans performed with FDG have become the method of choice for identifying the extent of residual viable myocardium that can benefit from revascularisation and interventions following acute myocardial infarcts. The wider adoption of combined PET/CT techniques in cardiology will lead to better assessment of site, severity and significance of coronary artery lesions prior to therapeutic interventions.

A more controversial application in the use of CTCA is whether the technique could be exploited for large population screening for coronary artery disease. At present, this seems not to be justified, partly because the radiation dose of the first and second generation system remains high, and partly on clinical grounds, where identification of coronary disease in asymptomatic subjects offers no grounds for invasive (or noninvasive) intervention.

The nirvana is the capacity to differentiate "vulnerable" coronary plaques which are inherently at high risk of rupturing and culminating in acute coronary events, from "stable" counterparts. Anticipation of developments of new generation scanners with significantly lower radiation doses with the ability for detailed plaque analysis would certainly generate fervent discussion.

Finally, the prognostic value of CTCA is not definitively established as yet. This is notwithstanding a very recent study by Hadamitzky et al. [129] involving 1256 patients who underwent CTCA for prediction of cardiac events in patients with suspected coronary artery disease, which concluded that CTCA findings are a significant prognostic indicator for the subsequent 18 months. Gopal et al. [130] have also presented findings on the prognostic capabilities of CTCA in a small, single-center, retrospective analysis of 493 symptomatic patients undergoing coronary CTA. It was found that in symptomatic patients with an intermediate likelihood of coronary artery disease referred for CTCA, normal or non-obstructed coronary arteries portends an excellent prognosis. The finding of obstructive disease was found to identify patients at higher risk of subsequent MI, independent of cardiovascular risk factors and coronary artery calcium. Five other studies have shown that the presence of obstructive coronary artery disease by CTCA has prognostic value [131–135]. However, review of these studies raises the question of what are the most appropriate and relevant endpoints. These studies are limited in their analysis of total mortality or coronary revascularisation. The latter cannot in truth be classified as an "outcome" but rather a management decision. Branding revascularisation as an outcome measure is severely biased by the performance of CTCA. Secondly, these studies have not adequately controlled for the full spectrum of relevant covariates such as measured cardiovascular risk variables, functional capacity, cardiovascular risk behaviours, medications and ejection fraction. Future studies assessing CTCA as an "independent" prognostic indication must take into account such factors and focus on definable coronary events such as mortality or MI to establish firm linkage between atherosclerosis on CTCA and subsequent cardiovascular events.

5. Conclusion

CT has emerged as a fundamental imaging method for patients with suspected coronary and cardiac disease. Many studies have demonstrated the high NPV of coronary CTA for significant stenoses in native coronary arteries. Further research is required to demonstrate its efficacy in other patient groups and other applications. The current CTCA technology is still limited by factors such as arrhythmias, motion artifacts from irregular or rapid heart rates, calcium-related artifacts, suboptimal imaging of small coronary stents. CTCA has the potential to become a standard test for plaque quantification by the continuous and rapid improvement of the hardware and software technology. However, tremendous developments in CT technology are gathering pace with newer scanners providing superior fast coverage (single beat scan), better temporal and spatial resolution and dual-energy tissue characterization. In addition, new scanners have brought with them marked reductions in radiation dose and through some very clever software have managed to minimise the effect of arrhythmias and motion artefacts. If improvements in flat panel technology occur at the same pace as MDCT, this may take this further to a significantly higher level.

The solutions to technical and clinical challenges are virtually being achieved by themselves, mainly by the continuous and remarkable improvement of the CTCA technology. It is proving difficult to keep up the rapidity of advancement but there is no doubt an increased number of, as well as more focused, clinical studies are required for validation of cardiac CT as an accurate, evidence-driven application for a multitude of clinical settings.

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