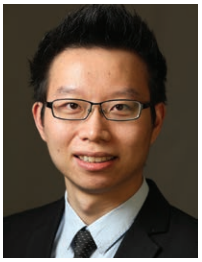

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IMPORTANT ADVANCES IN TECHNOLOGY AND UNIQUE APPLICATIONS TO CARDIOVASCULAR COMPUTED TOMOGRAPHY

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Abstract

For the past decade, multidetector cardiac computed tomography and its main application, coronary computed tomography angiography, have been established as a noninvasive technique for anatomical assessment of coronary arteries. This new era of coronary artery evaluation by coronary computed tomography angiography has arisen from the rapid advancement in computed tomography technology, which has led to massive diagnostic and prognostic clinical studies in various patient populations. This article gives a brief overview of current multidetector cardiac computed tomography systems, developing cardiac computed tomography technologies in both hardware and software fields, innovative radiation exposure reduction measures, multidetector cardiac computed tomography functional studies, and their newer clinical applications beyond coronary computed tomography angiography.

Introduction

For the past decade, multidetector cardiac computed tomography (MDCT) and its main application, coronary computed tomography angiography (CCTA), have been established as a noninvasive technique for anatomical assessment of coronary arteries. According to the 2013 Multimodality Appropriate Use Criteria for the Detection and Risk Assessment of Stable Ischemic Heart Disease, CCTA is a recommended noninvasive testing for diagnostic evaluation of patients suspected of ischemic heart disease.[1] This new era of coronary artery evaluation by CCTA is due mainly to rapid advances in computed tomography (CT) technology that have led to massive diagnostic and prognostic clinical studies in various patient populations. This article offers a brief review of current state-of-the-art MDCT systems, developing cardiac CT technologies, and their newer clinical applications.

Advances in Hardware

Wide-Detector MDCT

Currently, the minimal standard for robust comprehensive cardiac studies is a 64-detector MDCT. Computed tomography systems with more than 64 detectors are considered wide-detector MDCT, including 128-, 256-, and 320-detector scanners. Flagship MDCT models from major manufacturers and their key technologies are summarized in Table 1.[2] At present, the widest z-axis coverage of MDCT is 160 mm (320 detectors x 0.5 mm detector row width) in Aquilion ONE™ (Toshiba Medical Systems Corporation, Ōtawara, Japan). It allows the whole volume of the heart to be scanned axially within a single cardiac cycle. This new system also comes with thinner detector row width (0.5 mm), resulting theoretically in higher spatial resolution. Overall, this new technology makes a “single-beat” image acquisition achievable for patients with low heart rates (< 60 bpm). The single-beat image acquisition is ideal since substantial artifacts can be reduced. In addition, wider coverage also translates into shorter image acquisition times, which in sequence means that a smaller amount of contrast medium is required to obtain optimal scans while still preserving coronary artery enhancement.[3]

The major drawbacks in wide-detector technology include over-ranging and disadvantages associated with cone beam reconstruction. Over-ranging refers to the extra rotation of a gantry at the beginning and end of the actual scan volume, which is required to overcome a cone beam artifact at either end of the scanning volume. This extra radiation exposure is relatively insignificant in conventional MDCT but is more concerning in wide-detector MDCT due to a larger area of radiation source.[4] The second downside of these innovative tools is the substantial increase in radiation-exposed areas that are not used for image reconstruction. Compared to standard narrow-detector MDCT, those with wide detectors have less of the coverage area reconstructed and more of the radiation wasted.[5]

Gantry Rotation Speed and Temporal Resolution

Throughout the evolution of MDCT, gantry rotation speed has increased from 1 s (temporal resolution of 500 ms) in the first helical CT in 1997 to as fast as 270 ms (temporal resolution of 135 ms) in the current Philips Brilliance iCT™ (Koninklijke Philips N.V., Amsterdam, The Netherlands) and Toshiba Aquilion ONE™ systems for single-source scanners. With a dual-source technology, temporal resolution is even further increased to as high as 75 ms (Gantry rotation speed of 285 ms; Siemens Definition Flash, Siemens Healthcare, Forchheim, Germany).

The next generation of MDCT systems from major manufacturers are undergoing development and the U.S. Food and Drug Administration approval process. These include the GE Revolution CT™ (GE Healthcare, Milwaukee, WI), which will feature a wider z-axis coverage and gantry rotation speed up to 0.20 s to allow single-beat image acquisition,[6] and Siemens SOMATOM Force™ (Siemens AG, Erlangen, Germany), which highlights extremely high temporal (66 ms) and spatial (0.24 mm) resolution with wider z-axis coverage so the whole chest can be

Manufacturers/Models	Number of slices	Slice thickness (mm)	z-axis coverage (mm)	Spatial resolution* (mm)	Gantry rotation speed (second)	Temporal resolution (ms)	Iterative reconstruction software
GE Discovery CT750HD™	64	0.625	40	0.23	0.35	175	Veo™
Philips Brilliance iCT™	256†	0.625	80	0.4	0.27	135	iDose™
Siemens Definition Flash™	128†	0.6	38	0.3	0.28	75	SAFIRE™
Toshiba Aquilion ONE™	320	0.5	160	0.3	0.275	135	AIDR 3D™

* claimed by manufacturers
† number of slices is doubled with z-axis dynamic focal spot

Table 1. Flagship multidetector cardiac computed tomography models from major manufacturers.[5]

imaged in a second in a Turbo Flash spiral™ mode, eliminating the need to breath hold.[7] These new technologies need to be validated clinically when they become available.

New Detector Material and Circuit – Improved Spatial Resolution

The traditional detector in MDCT uses solid-state ceramic scintillators to convert X-rays into visible light. A photodiode array then converts the visible light into an analog electric current that is then transformed into a digital signal for image reconstruction. Each subunit in a detector system functions separately on different electric boards that are connected together. The latest detector system (Stellar Detector™, Siemens AG, Erlangen, Germany) has combined all subunits into one fully integrated detector system in a single electric board. The manufacturer claims that this new detector allows increased spatial resolution from reduced detector row width and improved image quality from reduced electric noise at the same kilovolt of X-ray tube energy.[8]

Researchers are exploring alternative approaches to increasing spatial resolution. As a result, a garnet-based substance is emerging as one of the breakthrough advances in detector technology. It has recently been used in the Gemstone™ detector from GE Healthcare. Compared to a conventional ceramic (Gd_2O_2S) scintillator, the garnet-based detector has 100-times faster decay time (faster rate of light being emitted after the detector is excited) and 75% shorter afterglow (shorter time needed for the material to be ready for the next excitation).[9] Overall, these properties translate into improved spatial resolution and reduced image noise due to increased data sampling per gantry rotation, which is conventionally limited by the properties of the ceramic material. This "high definition" advantage has been applied to various settings, including CT imaging of coronary artery stents that is often limited due to artifacts and noise. The garnet-based detector also has been shown to provide enhanced detection of intrastent area and diameter compared to a conventional detector.[10] In addition, it can acquire multiple energy levels from an X-ray tube simultaneously, making it compatible with dual-energy CT (DECT) as well.

Dual-Source Computed Tomography

Available in 2005,[11] dual-source CT (DSCT) creates two datasets simultaneously from two source-detector units, significantly improving temporal resolution of images by decreasing the imaging time in half compared to single-source CT. One of the drawbacks of DSCT is increased crosstalk artifact between the individual detector channels, which might lead to reduced delineation of the lower density plaque and therefore inaccurate quantification of the residual vessel lumen. However, image noise can be reduced with an integrated circuit detector and advanced image reconstruction algorithms.[12] With the Siemens Flash Spiral™ mode, this system also allows single-beat image acquisition at a reduced radiation dose compared to a conventional single-source CT.[13]

Dual-Energy Computed Tomography

Technically, DECT currently can be achieved by two approaches. With the first approach, two X-ray energy levels can be produced from two X-ray sources in DSCT systems, where one X-ray tube constantly uses 100-kV energy and another generates 140-kV energy. The second approach requires only a single X-ray tube but with rapid (< 25 ms) kV switching of the tube. This technology has been applied primarily to myocardial perfusion CT studies, where enhancement of myocardium necessitates robust delineation power, and has also been investigated to a lesser extent in CCTA. Dual-energy CT has shown to be useful in differentiating calcified atherosclerotic plaques from those with lipid-rich composition but not from those with a thin fibrous cap, which is one of the features of vulnerable plaque.[14] Philips Healthcare is developing a newer generation of spectral CT that it claims will use an innovative yttrium aluminum garnet-based spectral detector for excellent element discrimination power.[15]

Advances in Software

Iterative Reconstruction

In contrast to a traditional filtered back-projection algorithm that uses only some of the whole image data, iterative reconstruction (IR) algorithms employ more image information by simulating the expected measurements based on known CT system parameters and comparing this simulated dataset with the original reconstructed datasets.[16] This new approach improves image quality in each cycle through overall noise reduction while potentially allowing for lower radiation doses.[17,18] Newer generations of IR-based methods are being used by manufacturers as summarized in Table 1 with the same claims of improved image quality through reduced image noise and potentially reduced radiation doses (Figure 1).[18-21]

Motion Correction Algorithm

Motion artifact secondary to cardiac motion is one of the key reasons for uninterpretable coronary artery segments. In addition to current solutions such as heart rate control by medications and hardware technologies that decrease motion artifacts such as DSCT, GE Healthcare has invented Snapshot Freeze™, a software that uses image information from adjacent cardiac phases within a single cardiac cycle to characterize vessel motion information, thereby offsetting any residual coronary artery motion at that

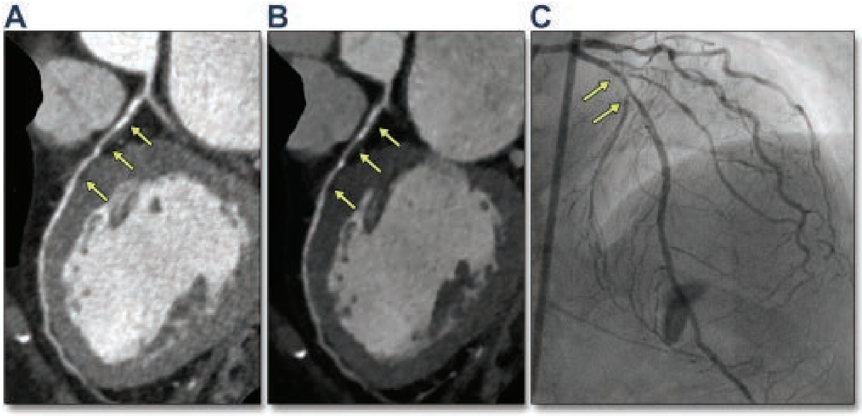

Figure 1. A high-grade coronary artery stenosis detected by coronary computed tomography angiography with (A) filter-back projection, (B) iterative reconstruction, and (C) invasive coronary angiography. The dose-length products were 137 mGy.cm and 63 mGy.cm in filter-back projection and iterative reconstruction, respectively.

phase. This technology has been shown to improve image quality and allow higher image interpretability at a per-segment level compared to standard image reconstruction.[22]

Image Reconstruction in Patients with Arrhythmia

For patients with irregular heart rhythms, CCTA has been a challenge due to motion artifacts and poor image quality from an irregular cardiac cycle. To overcome this obstacle, several technologies are being developed – among them an arrhythmia rejection algorithm and image reconstruction with identical filling. Using a complex arrhythmia detection algorithm and variable data acquisition window, the arrhythmia rejection algorithm reconstruction protocol being developed by Siemens (Siemens Healthcare, Forchheim, Germany) can hold the scan upon encountering an arrhythmia and restart the scan when the arrhythmia ends, allowing precise capture of the desired cardiac cycle phase. Using a different approach, image reconstruction with identical filling is based on the hypothesis that *isovolumetric phases* correlate with the best image quality. Therefore, physiological consideration derived from the left ventricular pressure-volume curve is used to determine the appropriate scanning time and reconstruction. In both image reconstruction protocols, image quality has improved compared to a conventional reconstruction method.[23,24]

Advances in Radiation Exposure Reduction

Due to its increased popularity, CT scan has become the main source of radiation exposure in the United States. Investigations have been ongoing in both the hardware and software realm to address this issue. Recently, data from the PROTECTION I study showed that the average radiation dose from conventional retrospective electrocardiogram-gated CCTA was 11.2 mSv.[25] More recently, high-pitch helical dual-source scanning,[26,27] automatic attenuation for radiation dose optimization,[28,29] and padding reduction[30,31] are emerging as innovative methods to reduce radiation exposure from MDCT.

High-Pitch Helical DSCT

In a conventional single-source scanning system, the pitch (a ratio of CT table movement per gantry rotation to the total X-ray beam width) is limited to no greater than 1.5 mSv (generally 0.2 to 0.3) to guarantee gapless volume coverage.[27] However, with a combination of DSCT, a newer ultrafast-moving examination table, a newer extremely fast gantry system, and a new image reconstruction software, the pitch can be increased up to 3.2 mSv.[26,27] The major benefits of high-pitch DSCT include a diminished radiation dose due to a shortened scanning time, improved temporal resolution, and the capability of single-beat image acquisition that reduces motion artifact. The first-generation SOMATOM Definition Flash™ from Siemens Healthcare consists of two X-ray tube-detector units at an angle offset of 90 degrees. Each detector unit consists of 32 detector rows with 0.6 millimeters width. The pitch of this system is 3.2 and gantry rotation time is 330 ms (temporal resolution is 83 ms). This technology alone with a standard tube potential of 120 kV has been reported to decrease radiation doses down to 1.7 mSv for CCTA, while image quality is maintained with appropriate image acquisition parameters and patient selection.[27] With the second-generation SOMATOM Definition Flash™, which features 2 sources x 64 detector rows (128 slices) x 0.6 millimeters collimation with 75 ms temporal resolution along with tube modulation to 100 kV, the radiation dose could be reduced to less than 1 mSv with excellent image quality (Figure 2).[26]

Automated Attenuation with Tube Potential Modulation

More recently, automated attenuation-based tube potential selection (CARE Dose4D™, Siemens Healthcare, Forchheim, Germany) has been emerging as a novel approach in pursuing the lowest radiation-dose MDCT protocol. Instead of adjusting tube potential according to certain parameters (e.g., body mass index) prior to the scan and constantly using that tube potential throughout the scanning time, this method automatically adjusts energy level in real time as the scan continues. Automatic attenuation-based tube current optimization has been shown to significantly reduce tube current and mean effective radiation dose while preserving image quality.[28,29] With high-pitch helical DSCT and IR technologies, radiation dose could be less than 1 mSv.[29]

Iterative Image Reconstruction

The primary limiting factor in decreasing energy voltage is that it increases image noise artifact, which might interfere with the accuracy of the images. However, by using low-voltage scanning with iterative image reconstruction, image noise can be decreased at the same level of tube voltage selected.[22] Studies have shown that compared to conventional reconstruction method, iterative image reconstruction yielded higher image quality and higher interpretable coronary segments primarily by reducing image noise and increasing contrast-to-noise ratio.[16,18]

Advances in Functional CT

Computed Tomography Perfusion

Currently, computed tomography perfusion (CTP) has been emerging as a complete noninvasive anatomical and functional assessment of coronary artery stenosis. With this technology, coronary artery stenosis with associated perfusion defect during

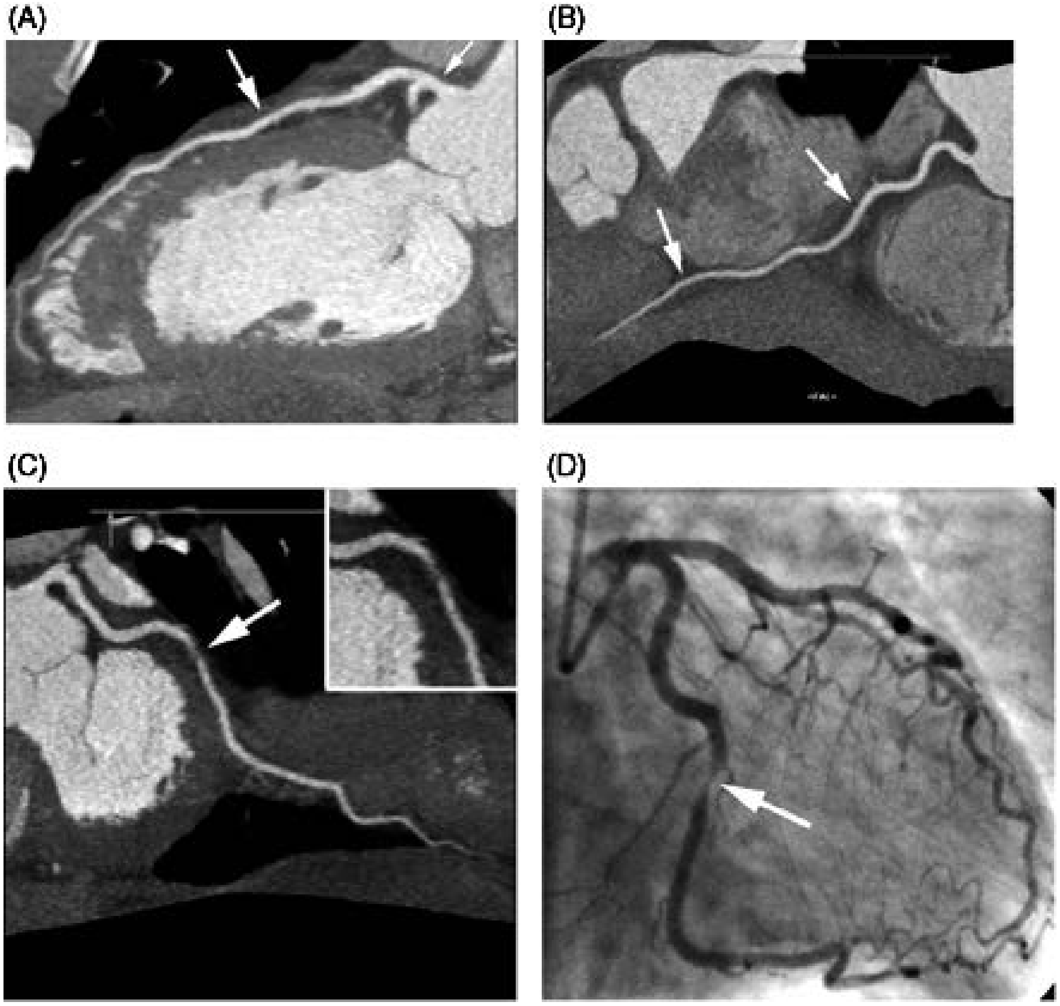

Figure 2. Reconstructed curved multiplanar coronary CT angiographic images using a prospectively ECG-gated high-pitch protocol (pitch 3.2, estimated dose 0.84 mSv) show (A) normal left main artery (small arrow), left anterior descending artery (big arrow), (B) right coronary artery, and (C) high-grade stenosis in left circumflex artery compared to (D) invasive coronary angiography. CT: computed tomography; ECG: electrocardiogram.

stress test can be shown in one combined image series, allowing accurate identification of culprit arteries that cause myocardial ischemia.

CTP can be achieved by either a retrospective or prospective EKG gated approach. Most of the studies to date were performed with wide-detector MDCT or DSCT for higher temporal resolution that is preferred for CTP studies; however, single-source 64-detector MDCT has shown to be feasible as well.[32,33] DECT technology also has been used for CTP to improve depiction power of perfusion defects by assessing changes in iodine distribution within the myocardium.[34]

In CCTA images, ischemic and nonviable myocardium is expressed as a hypoattenuation area reflecting diminished content of contrast medium within that particular myocardium — also known as myocardial blood pool defect. Blood pool defects in both rest and stress images are indicative of infarction. The defects in stress images but not rest images are suggestive of ischemic myocardium. Currently, there have been several CTP image acquisition protocols that vary among institutions. It is unclear whether performing the stress scan first followed by the rest scan yields superior results. The main advantage of obtaining stress images first is that the myocardium is not pre-enhanced during the rest scan, which could potentially result in reduced study accuracy. However, the drawback is controlling heart rate after the stress scan in order to optimally acquire the rest images in a timely fashion. Alternatively, the rest scan can be performed first for CCTA and rest CTP studies to evaluate for coronary artery stenosis and rest myocardial blood pool defect. If something is detected, the stress part of the protocol can be implemented right afterward to functionally examine that particular lesion. The disadvantage of this approach is the potential reduction in sensitivity of the CTP study due to interference of beta blocker, used to lower the patient's heart rate, with the effect of the stress agent.[35] All in all, the optimal protocol for CTP is yet to be defined.

Researchers have started to publish their initial experience and diagnostic accuracy of CTP over the past few years.[36,37] In the most recent CORE320 trial, the addition of CTP to a standard CCTA study was shown to increase diagnostic accuracy in identifying flow-limiting coronary artery stenosis at a reasonable effective radiation dose (median 8.47 mSv, range 6.63-9.67 mSv).[37] This new advance in cardiac CT will allow physicians to have noninvasive integrated evaluation of the coronary artery with better resolution compared to conventional stress tests (Figure 3).

Noninvasive Fractional Flow Reserve

Advances in image interpretation methods are focused on developing software that automatically measures and compares parameters within acquired images and produces objective interpretational information. Current research has been validating the diagnostic accuracy of these types of software in different clinical settings.[38,39] Noninvasive fractional flow reserve (FFR_{CT}) is a particular example of the technology that is emerging in the research field. Examined in detail over the past few years, FFR_{CT} is a novel computational method to assess functional significance

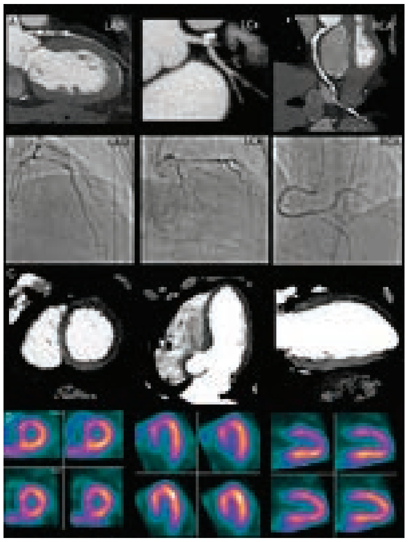

Figure 3. A comparison between anatomical and functional multimodality imaging. (A) Coronary CT angiography, (B) corresponding invasive coronary angiography, (C) a cardiac CT perfusion study, and (D) a corresponding perfusion study using *single-photon emission computed tomography*. CT: computed tomography.

of coronary stenosis by measuring fluid dynamics through the segment of interest.[38,39] This technique does not require any special alterations to the regular CCTA scanning or image acquisition protocol, nor does it require any special pharmacological agent to be given to patients. Using anatomical data obtained from standard CCTA studies, it essentially predicts coronary flow and pressure in response to vasodilators.[40] It has been shown in DISCOVER-FLOW and DeFACTO studies to have higher diagnostic accuracy in detecting obstructive coronary stenosis on conventional CCTA and also have additive diagnostic power to the standard studies.[38,39]

Advances in Structural Heart Evaluation

The main clinical application of MDCT is coronary anatomy evaluation by CCTA. However, given the advantages of MDCT with regard to high image resolution and 3D capability, other practical uses of MDCT include cardiac valve anatomy evaluation, assessment of left atrium and pulmonary vein anatomy for atrial fibrillation catheter ablation procedures, assessment of coronary venous anatomy for cardiac resynchronization therapy, assessment of pacemaker lead location and complications, and evaluation of cardiac morphology in congenital heart diseases. Over the past several years, MDCT has also proven useful in the preprocedural planning of transcatheter aortic valve replacement,[41-43] assessment of prosthetic heart valves,[44-46] evaluation of left ventricular assisted devices,[47] and planning for left atrial appendage occlusion devices.[48]

Conclusion

Given the rapid advances in MDCT technology that have emerged during the past several decades and the prospect of continued development, cardiac computed tomography will be an integrated anatomical and functional high-definition scan with significantly lower radiation exposure. Reduced scanning time and complex image reconstruction algorithms will make CCT less sensitive to rapid heart rate and cardiac arrhythmia, and a multispectral approach will greatly improve differentiation between various cardiac and vascular structures. These collective advances in MDCT should hopefully translate into better evaluation of not only cardiac anatomy and function but also of other anatomical structures, which in turn will improve overall patient care. Coupled with molecular MDCT technologies, a new era of element-targeted scanning is likely to arise.

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