

ECG-gated multidetector-row computed tomography in the assessment of left ventricular function

An accurate quantitative and qualitative assessment of cardiac function is critical for clinical diagnosis, risk stratification, management and prognosis in patients with suspected or documented heart disease. Magnetic resonance, owing to its excellent temporal and spatial resolution, is currently considered a reference standard in the assessment of cardiac function. Multidetector-row computed tomographic scanners, with sub-second rotation times and dedicated cardiac reconstruction algorithms, have shown their ability to acquire high-resolution images suitable for coronary imaging. With retrospective ECG-gating technique, diastolic and systolic images can be produced and analyzed to assess left ventricle functional parameters. The combination of noninvasive coronary artery imaging and assessment of cardiac function with multidetector-row computed tomography is a suitable approach to a conclusive cardiac work-up in patients with suspected coronary artery disease.

KEYWORDS: DSCT ■ image reconstruction ■ left ventricular function ■ MDCT ■ MDCT technique ■ MRI ■ multidetector-row computed tomography

The evaluation of cardiac function can provide important diagnostic and prognostic information in many diseases that have an impact on the performance of the pump activity of the heart. The assessment of cardiac function, in an accurate and reproducible way, is crucial in determining the severity of cardiac impairment and the efficacy of treatment [1]. For several years, investigators have explored different strategies to quantify global and regional cardiac performance using a variety of techniques. With the availability of noninvasive cardiac imaging modalities such as echocardiography and cardiac scintigraphy, assessment of cardiac function became part of routine clinical examination [2]. In particular, for the clinical work-up of patients, echocardiography is still the most used technique to determine left ventricular (LV) volumes [3]. However, its measurements rely on geometric assumptions about ventricular structure. Cardiac MRI provides excellent temporal and spatial resolution, allows image acquisition in any desired plane, and has a high degree of accuracy and reproducibility concerning quantitative measurements. In addition, MRI can be used to measure LV volume, without assumptions regarding LV cavity geometry. Thus, MRI is currently considered a reference standard in assessment of cardiac function [4]. The advent of multidetector computed tomography (MDCT) has provided a new opportunity for cardiac imaging; with submillimetric collimation and a faster gantry

rotation it allows the acquisition of the entire heart volume in a single breath-hold with excellent temporal and spatial resolution. Moreover, data acquisition in spiral MDCT, using a retrospective ECG gating, is continuous and provides information for any phase of the cardiac cycle. Thus, end-systolic and end-diastolic images can be produced to assess ventricular volumes and function. Consequently, MDCT is becoming an attractive option for the assessment of ventricular function, and not only for the evaluation of coronary artery obstruction [5]. This ability to provide both anatomical and functional information may significantly alter future practice within cardiology.

In this article, we aim to discuss the role of MDCT for the evaluation of cardiac function and evaluate its current clinical applications.

Global ventricular volumes & function

Assessment of global ventricular function means measuring the adequacy of the ventricles to eject blood into the vessels. Since the ventricles exhibit a repetitive process of ejection and filling, the filling process must be considered part of the global ventricular performance. In clinical routine, only the ventricular volumes at maximal filling (end diastole) and maximal emptying (end systole) are usually quantified. From these two volumetric parameters, end-diastolic volume (EDV) and end-systolic volume (ESV), all other global functional

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parameters can be deduced. Subtracting the ESV from the EDV provides the stroke volume (SV). The SV divided by the EDV multiplied by 100 gives the ejection fraction (EF) in percent. The EF describes the relative change of EDV to ESV and reflects the global ventricular function: the normal left ventricle ejects 50–70% of the EDV during systolic contraction. The SV multiplied by the heart rate gives the cardiac output. It is evident that the reliability of the deduced global ventricular parameters is only as good as the accuracy by which the EDV and ESV are determined [6]. Another important parameter of global ventricular performance, and an independent predictor of morbidity and mortality from coronary heart disease, is the ventricular or myocardial mass. Myocardial mass can be derived by multiplying the myocardial volume with the myocardial density. The myocardial density is variable, but a value of 1.05 g/cm^3 is often used.

Two different approaches are used to obtain the ventricular volumes, function and mass: geometric assumptions and volumetric ventricular quantification.

Geometric assumptions compare the ventricular cavity with a geometrical model. Geometric assumptions are used in planar imaging techniques, such as echocardiography, scintigraphy and contrast ventriculography. They have the advantage of rapidly obtaining ventricular volumes and LV mass, but they are only reliable as long as the geometrical model corresponds to the true ventricular cavity or myocardial wall, which might not be the case in focally diseased ventricles.

Volumetric quantification is based on Simpson's rule. The volume of a complex structure, such as a ventricle, can be quantified by dividing this structure into several smaller, less complex subvolumes. By delineation of the endocardial contours, multiplication of the area by the thickness of the imaging plane and the interslice distance, an addition of these subvolume slices yields the total ventricular volume. Volumetric quantification has the advantage of more reliably quantifying the ventricular volumes and being more easy to reproduce than the geometric assumptions techniques.

LV function

■ Data acquisition & image reconstruction

Cardiac computed tomography (CT) can be performed using both a retrospective ECG-gating or a prospective triggering technique. When retrospective gating is used, the ECG signal is recorded

simultaneously during a spiral CT acquisition. Thus, image reconstruction can be obtained at any desired point throughout the cardiac cycle and the ESV and EDV can be reconstructed to assess ventricular function [6,7]. This acquisition technique is less likely to trigger cardiac arrhythmia. Prospective triggering has historically been used for unenhanced calcium scoring and has recently been proposed for contrast-enhanced coronary imaging owing to the significant dose reduction. This acquisition technique consists of a transverse scan in which x-rays are only turned on during a desired phase of the cardiac cycle. A fundamental requirement for this technique is an accurate prediction of the patient's cardiac cycle and precise synchronization with the x-rays. This technique makes the patient vulnerable to arrhythmia and heart rate variability, and can be performed only in patients with a stable heart rate below 65 beats per min. Furthermore, to evaluate functional parameters, a double trigger needs to be set at end-diastolic and end-systolic phases, which are usually centered at 0 and 30–50% of the cardiac cycle, respectively. To date, this double acquisition can only be performed on a few scanners. Depending on the scanner used, scan time may differ, but the state of the art for coronary assessment requires a submillimeter spatial resolution along the z-axis, and possibly the isotropic voxel; this allows a real 3D reconstruction of images and enables measurements to be made in any desired plane [8]. The most important technical parameter is the temporal resolution (TR); in fact, imaging of the moving heart requires a high TR to achieve an artifact-free display of myocardial contraction over the cardiac cycle. This is possible using new-generation scanners. With four- and 16-slice MDCT systems, the TR achievable was not optimal (250 and 210 ms, respectively) and multisegment reconstruction algorithms were needed [9,10]. Multisegment reconstruction is achieved using small segments of data acquired during two or more cardiac cycles. Multiple segments of data are combined to make the final image at end systole. The resulting TR equals the gantry rotation time divided by $2N$, where N is the number of cycles. However, the z-axis spatial resolution can decrease if there are gaps in the acquired data. The maximum number of cycles typically used is two or three, beyond which image quality falls.

■ Data analysis

To assess EF, a diastolic phase (usually found at 95–0% of RR interval) and a systolic phase (usually found at 30–50% of RR interval) are

necessary, and can be performed by visual analysis of the short-axis images that are reconstructed every 5–10% of the RR interval at a representative mid-ventricular level. LV volumes can then be measured by use of the area–length method (used primarily in echocardiography based on a vertical or horizontal long-axis view), the Simpson method (primarily used in cardiac MRI) or a threshold-based volumetric method (developed in MDCT to take advantage of the high contrast-to-noise ratio between the LV cavity and the myocardium) [11]. Generally, the Simpson method and the threshold-based volumetric method are considered more reliable as they do not rely on geometric assumptions for determination of global LV parameters such as LV volumes or EF. The threshold-based method calculates the EDV and ESV on a pixel-by-pixel basis after appropriate definition of the mitral valve plane and left ventricle, excluding the LV outflow tract (FIGURES 1 & 2). Owing to the complex shape of the heart, the myocardium wall is tilted toward the apex and is not orthogonal to a predetermined study axis; thus, only multiplanar reconstruction images along cardiac axis, long axis, horizontal and vertical axis, and short axis can completely compensate this deviation, providing a precise wall-thickness measurement as well as an evaluation of global and regional function. Most of the recently released software automatically generates these cardiac orientations, shortening the evaluation time, whereas in some cases the manual reformation is needed from the primary axial images [12]. If the planes are not perpendicular to the wall or the cavity, subsequent partial volume effects and obliqueness can introduce a large overestimation of the true dimensions. Once long- and short-axis views are generated, end-diastolic and end-systolic phases can be either automatically or manually individuated, depending on the software in use. Finally, diastolic and systolic LV volumes can be calculated using standard CT software with different approaches. To determine measurements for both global and regional functions, only the end-diastolic and end-systolic phases are used [13]. For the volume analysis, only endocardial LV borders need to be drawn. If LV mass is also needed in order to perform regional quantitative analysis, epicardial borders have to be drawn too. To correctly identify the epicardial border, the opacification of right ventricle cavity is mandatory to obtain a different attenuation compared with the septal myocardium. Thus, a dedicated contrast-medium injection protocol must be applied, such as a dual-flow rate approach or the injection of a mixture of contrast and saline (20%

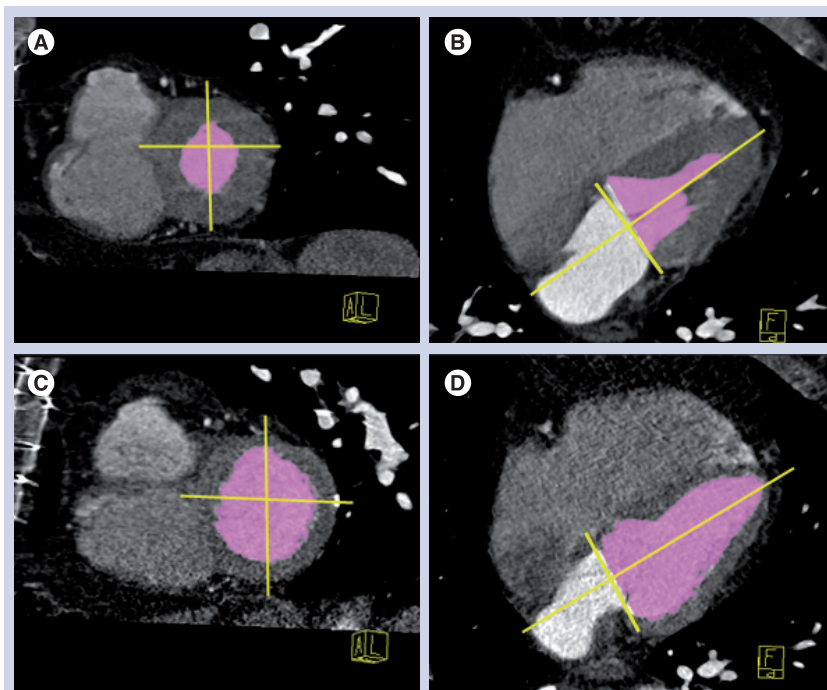


Figure 1. Determination of ejection fraction and left ventricular volumes via a threshold-based method: end-systolic images in (A) short axis and (B) four-chamber views and end-diastolic images in (C) short axis and (D) four-chamber views.

contrast and 80% saline) after the contrast bolus. Endocardial and epicardial contours are either automatically detected by the analysis software or have to be manually traced on systolic and diastolic short-axis image reformations. Software packages for CT that semiautomatically perform ventricular volume and wall-thickness measurements are widely available and help to speed up analysis and reporting, as well as improve reproducibility of results. An accurate definition of the basal slice is desired, because it contains the largest area of the CT image reformations stack; a potential error in LV volumetry might be caused from inadequate slice selection. For the volume calculation, papillary muscles should be excluded from the cavity [14].

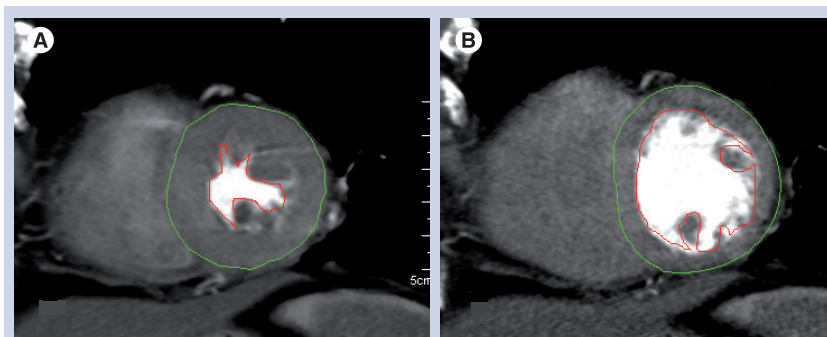


Figure 2. Volumetric and functional analysis based on the endo- and epicardial contours detection in (A) systole and (B) diastole.

For regional function assessment of the left ventricle, there is a need for standardization of imaging modalities to assure that accurate intra- and cross-modality comparisons can be made for patient management and research (cardiac ultrasound, MRI and CT). Measurements of regional LV function are based on the assessment of systolic thickening by use of the 17-segment model proposed by the American Heart Association [15].

Assessment of LV function using MDCT

Since the introduction of CT in the early 1970s, it has remained an ongoing challenge to obtain better spatial resolution and TR in order to acquire more detailed images in less time. Early CT scanners could not attain the acquisition times and the spatial resolution required to generate functional images of the heart. However, the introduction of MDCT in the early 1990s lowered acquisition times and spatial resolution to the range where functional imaging of the heart is feasible [16]. The use of MDCT for the assessment of LV functions has been investigated extensively. Studies using older generation CT showed that function assessment could be performed, but the TR of the four-slice (250 ms) and 16-slice (210 ms) MDCT systems hampered the sensitivity for detection and accurate classification of regional LV wall motion abnormalities. Owing to the limited TR, systolic images, especially those obtained in patients with a higher heart rate, were shown to be of lower quality. Additionally, ESV was overestimated, while EDV was not significantly different. As a result, underestimation of EF was noted in several studies (TABLE 1). More recently, assessments performed on 64-slice MDCT scanners, capable of achieving better TR, demonstrated a significant improvement in the accuracy of MDCT in the evaluation of LV function [17]. Butler *et al.* concluded that 64-slice MDCT could be an alternative for suboptimal echocardiography results [18], and Salem *et al.* found that 64-slice MDCT enabled LV function analysis in patients with regular sinus rhythm [19]. Mahnken *et al.* showed that reliable assessment of LV volumes was also possible at increased heart rates with the introduction of multisegmental image reconstruction algorithms that use data from multiple RR intervals, which allowed the TR of cardiac CT to be improved [20].

Recently, a new CT system equipped with two tubes and corresponding detectors in a 90° geometry has been designed and provides

a heart-rate-independent TR of 83 ms. The latter may be further improved by use of a multi-segment reconstruction algorithm and could be as low as 42 ms. There are several data on the diagnostic accuracy of this technique (TABLE 1). In fact, the study by Mahnken *et al.* [21], which used a moving heart phantom, demonstrated a good correlation between dual-source CT (DSCT) and MRI, with no significant differences, which is in accordance to the *in vivo* study by Van der Vleuten *et al.* [22]. The study by Bastarrika *et al.* on transplant patients demonstrated the reliability of LV function quantification in individuals with high heart rates [23]. According to Busch *et al.* [24], the observed nonsignificant differences between functional parameters acquired in DSCT and MRI may be caused by physiological effects due to rapid contrast material injection and the absence of β -blocker medication in CT. In further studies, β -blockers were used to lower the heart rate, which has been postulated to be responsible for reduced EF values in CT examinations. Second, the trend of higher injection rates in CT may cause a stronger inotropic and chronotropic effect and may explain higher values for EF and SV in CT studies compared with values acquired in MRI. An explanation for these differences is the visualization of endocardial borders and the exclusion or inclusion of trabeculae into the LV blood pool. This may explain why there is an underestimation of the systolic volume, while there is an overestimation in diastole, because trabeculae can cause an actual underestimation of EDVs in MRI as they reduce the diameter of the endocardial contour, while the region-growing algorithm counts bright pixels between the trabeculae as blood pool in CT. In systole, the effect should be smaller because the trabeculae lie closely adjacent to each other so that there is only a very small volume between trabeculae. Of course, the depiction of the trabeculae will depend on a high contrast opacification of the ventricular blood pool. Poesken *et al.* suggested that the systematic underestimation of LV volumes by the 3D-segmentation algorithm is explained by a different handling of the papillary muscles: soft-tissue density structures such as the papillary muscles are excluded from the LV volume by attenuation-based segmentation, whereas standard short-axis-based LV function analysis from CT and MRI data sets usually accounts for them as part of the LV cavity [25]. However, Sievers *et al.* demonstrated that systematic subtraction of papillary muscles and trabeculations from LV volume has no significant impact on

Table 1. Principal studies performed with different generations of multidetector computed tomography.

Author (year)	Scanner	Study design	ESV (mean difference between CT and MRI)	EDV (mean difference between CT and MRI)	EF (mean difference between CT and MRI)	Ref.
Juergens <i>et al.</i> (2004)	4-slice MDCT	MDCT vs MRI	-1 ml	-3.2 ml	-7%	[36]
Grude <i>et al.</i> (2003)	4-slice MDCT	MDCT vs MRI	+17 ml	+14 ml	-9%	[37]
Mahnken <i>et al.</i> (2003)	4-slice MDCT	MDCT vs MRI	+0.5 ml	-0.8 ml	-0.9%	[38]
Halliburton (2003)	4-slice MDCT	MDCT vs MRI	-22.4 ml	-35.2 ml	-1.6%	[11]
Heuschmid <i>et al.</i> (2005)	16-slice MDCT	MDCT vs MRI	+8.7 ml	+13.2 ml	-1.4%	[39]
Koch (2004)	16-slice MDCT	MDCT vs MRI	-6.9 ml	-3.2 ml	+3%	[10]
Schlosser <i>et al.</i> (2005)	16-slice MDCT	MDCT vs MRI	+8 ml	+15.5 ml	-1.8%	[40]
Mahnken <i>et al.</i> (2003)	16-slice MDCT	MDCT vs MRI	-0.3 ml	-1 ml	+0%	[41]
Schepis (2006)	64-slice MDCT	MDCT vs SPECT	+9.3 ml	+33.5 ml	+1.1%	[35]
Bastarrika <i>et al.</i> (2008)	DS-MDCT	DSCT vs MRI	+4.9 ml	+16.5 ml	-0.3%	[23]
Puesken (2008)	DS-MDCT	DSCT vs MRI	-8.6 ml	-22.5 ml	-1%	[25]
van der Vleuten <i>et al.</i> (2009)	DS-MDCT	DSCT vs MRI	+3.5 ml	+11 ml	+0.4%	[42]
Busch (2008)	DS-MDCT	DSCT vs MRI	-2.6 ml	+3.7 ml	+3.8%	[24]

CT: Computed tomography; DS: Dual source; DSCT: Dual-source CT; EDV: End-diastolic volume; EF: Ejection fraction; ESV: End-systolic volume; MDCT: Multidetector CT; SPECT: Single photon emission CT.

the reliability of LV EF evaluation [26]. A recent study by Groen *et al.* [27], which compares MRI, 64-slice MDCT and DSCT in assessing functional cardiac parameters of a moving heart phantom, demonstrated that a clinically implemented MRI protocol structurally underestimates functional parameters, EF and cardiac output of a moving heart phantom. A clinical implemented protocol using a 64-slice MDCT underestimates or overestimates these functional parameters depending on the heart rate, and a clinical protocol using DSCT deviates the least from these functional parameters compared with MRI and 64-slice MDCT. De Cecco *et al.* [28] demonstrated *in vivo* an accurate evaluation of functional parameters by DSCT, which was in agreement with data obtained from MRI. However, in this study, the authors underline a tendency to underestimate the EF even if the difference was not statistically significant.

Although the TR can be improved with multi-segment reconstruction, leading to better reproducibility in a phantom study [21], it was shown that this technique did not improve results for studies in human subjects. In fact, in a study by Juergens *et al.* [29], the multisegment image reconstruction achieved a significant increase of TR at the expense of spatial resolution causing a deterioration of the slice profile and consecutive

blurring of endocardial borders. Thus, it can be assumed that improved TR without a reduction in spatial volume may allow for a more reliable assessment of global ventricular function.

Conclusion

Since MRI was the first noninvasive technique to provide high-resolution 3D functional images of the heart, it is regarded by many as the current standard of reference for LV function. The main advantage of MRI is its excellent TR without exposing the patient to ionizing radiation. Furthermore, it does not rely on geometrical assumptions for LV function parameters. However, MRI cannot be performed in patients with a pacemaker or cerebral vascular clips for both safety and image-distortion reasons; furthermore, it is expensive and not always available [30]. As an alternative to MRI, MDCT can be used to assess functional parameters of the left ventricle [31]. However, DSCT has a TR more similar to the TR of MRI, and also has a relatively high spatial resolution [32]. A significant reduction in postprocessing time is achieved owing to advanced raw-data reconstruction algorithms, automatic generation of cardiac axis views, automatic determination of end-diastolic and end-systolic phases, and automatic LV myocardial segmentation for regional function

assessment. New software for automatic anatomic tube current modulation is being developed and appears to significantly reduce radiation exposure [33].

In conclusion, over the years, CT has evolved to a point where contemporary multidetector-row systems combined with adequate reconstruction algorithms and postprocessing tools can perform global LV functional assessment. However, for 64-slice MDCT systems with further improved TR, head-to-head comparisons with MRI *in vivo* are not yet available, even if promising results have been published in some studies [26,34,35]. DSCT allows a quick, accurate and global evaluation of the heart, both for functional parameters and coronary artery disease, as demonstrated in several studies. The limitation of this system and MDCT is the tendency to overestimate LV volumes when compared with MRI. There are different explanations, but since the differences are not statistically significant, we can conclude that functional parameters obtained using MDCT are readily interchangeable with those obtained with MRI.

Future perspective

The application of conventional CT to cardiac imaging has long been limited by insufficient TR owing to slow gantry rotation and long total acquisition time, resulting from slow volume

coverage with single-slice imaging. With the development of multidetector technology, cardiac CT is increasingly being used in the diagnosis of coronary artery disease and for cardiac morphology assessment. Furthermore, 64-slice MDCT scanners, capable of achieving better TR, demonstrated a significant improvement in the accuracy of evaluating LV function and is capable of achieving this at faster heart rates with the introduction of multisegmental image-reconstruction algorithms.

The improvement in TR achieved with the dual-source technology increased the accuracy of the evaluation of LV volumes. Newer scanners with even higher TR, owing to faster rotation time and the development of software solutions adapted from MRI or echocardiography, will overcome the current limitations regarding standardized LV function analysis.

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Executive summary

Assessment of left ventricular volumes

- The use of multidetector-row computed tomography (MDCT) for the assessment of left ventricular function has been investigated extensively.
- The most important technical parameter for assessing left ventricular volumes is temporal resolution.
- With four- and 16-slice MDCT systems, the temporal resolution achievable was not optimal and multisegment reconstruction algorithms were needed.
- 64-slice MDCT temporal resolution, including multisegment reconstruction algorithms, enables the assessment of left ventricular function in an accurate and reproducible way.

Future perspective

- The development of dual-source technologies significantly improved the accuracy of the evaluation of left ventricular functional parameters.
- Newer technologies and software developments are needed to achieve the same accuracy in MRI for the evaluation of cardiac function.

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