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Chapter 3

Effects of heart rate, filling and slice thickness on the accuracy of left ventricular volume measurements in a dynamic cardiac phantom using ECG-gated MDCT

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ABSTRACT

Objectives: To assess the effect of heart rate, filling condition and slice thickness on the accuracy of volumetric analysis based on multi-detector-row computed tomography (MDCT) of a cardiac phantom.

Materials and Methods: Retrospective ECG-gated MDCT of a pulsating phantom was performed under different conditions. End-diastolic (EDV) and end-systolic volume (ESV) for different heart rates (60-75/min), filling volumes and reconstructed slice thicknesses (2 and 5 mm) were obtained by 3 observers. Results were analyzed by linear mixed-effects model.

Results: Significant effects on the accuracy were found for heart rate (F-value: 7.3-39.2, p<0.004) and filling condition (F-value: 7.4-55.6, p<0.004), but not for slice thickness. Small relative differences in the assessment of EDV were found (range: –3% to 3%), but there was a trend for overestimation of the ESV (range: -1% to 18%). Underestimation of stroke volume and ejection fraction (range: -1 to -11%) became smaller under conditions of improved temporal resolution and larger EDV. Good interobserver agreement was found (SD < 1.8mL and < 0.5%).

Conclusion: Overall, MDCT allows sufficient and reliable measurements of ventricular volumes and calculation of left ventricle function for clinical applications. Heart rate and filling conditions significantly affect the accuracy of volumetrics as demonstrated in this cardiac phantom. Thicker slices provide similar accuracy as compared to thin slices.
INTRODUCTION

The impact of myocardial damage on the left ventricular (LV) function, expressed as ejection fraction, is of importance for risk stratification, treatment planning, and prognostication in patients with coronary artery disease [1, 2]. Multi-detector-row computed tomography (MDCT) with retrospective ECG-gated cardiac reconstructions has become an established and frequently applied technique for non-invasive 3-dimensional imaging of the coronary arteries [3]. For achieving optimal image quality, MDCT coronary angiography is, in general, performed at heart rates below 70/min. Under the experimental conditions of this study, and for heart rates in the range 60/min-75/min, the temporal resolution of cardiac CT varies between 105-250 ms for typical 4- and 16-MDCT coronary angiography acquisitions, depending on the scanner and the image reconstruction algorithm [4, 5]. MDCT coronary angiography acquisitions provide, in itself, sufficient information for retrospective ECG-gated cardiac reconstruction at any desired phase point. Previous studies have shown that LV function can be assessed from routine coronary 4- and 16-MDCT angiography acquisitions [6-8] that are performed for clinical assessment of the coronary arteries. Accuracy of quantitative assessment of cardiac function however is affected by motion artifacts, particularly in the end systolic phase, since especially during this phase the resulting images are associated with motion artifacts leading to blurring of the LV wall.

For applications in cardiac MDCT, the latest generation of 64-MDCT scanners offers significant shorter scan time and breath-hold compared to 4- and 16-MDCT. However, temporal resolution [9] and spatial resolution of 64-MDCT [10] did not improve substantially compared to 16-MDCT. The current study is therefore also relevant for this range of scanners. Cardiac imaging with CT, and LV volume assessment in particular, may improve with new technological developments such as dual source CT scanners and cone beam CT scanners.

In patient-based validation studies of LV function assessment with CT, the real end diastolic (EDV) and end systolic volumes (ESV) are unknown. The volumetric measurements presented in these publications are compared to echocardiography [6, 8, 11], cine-ventriculography [4, 12], or magnetic resonance imaging (MRI) [7, 11, 13]. In these studies, the effect of slice thickness, filling condition and heart rate on the accuracy of volume measurements has not been documented. The heart rate and filling conditions of the LV determine the dynamics of the LV. In addition, the degree of blurring of the LV wall and the resulting accuracy of volumetric measurements, depends mainly on rotation time, pitch factor and reconstruction algorithm. By implementing thicker reconstructed slices, shorter reconstruction times and fewer number of images for cardiac MDCT studies may be achieved. An accurate and comprehensive validation could be achieved by using an anthropomorphic phantom with a pulsating ventricle of which the actual EDV and ESV are known. The phantom provides realistic acquisition conditions...
and in the same time an accurate and validated reference for volumetric analysis of the LV. However, only a limited number of phantom studies have been published on the accuracy of (cardiac) functional measurements. Mahnken demonstrated the improving accuracy of volumetric measurements with enhanced temporal resolution, using a simple cylinder as a cardiac model, which may not be an adequate model for the more complex human heart [14]. Utsunomiya used a small three-dimensional cardiac phantom, with which they investigated the accuracy of volumetric measurements of computed tomography. However, the small size of the phantom used for their study does not cover the clinically relevant range of ESV and EDV’s [15]. The aim of the current study was to assess accuracy of ventricular volumetric analysis in a pulsating cardiac phantom in two different reconstruction thicknesses in comparison with actual volumes within a clinically relevant range of the heart rate and filling conditions [4, 5] using 16-MDCT.

MATERIALS AND METHODS

Dynamic cardiac phantom
An anthropomorphic chest phantom with a pulsating left ventricle [16], developed by the Academic Medical Center (AMC), Amsterdam, The Netherlands, was used for this study. The LV volume varies in a sinusoid way at variable heart rates from 60 to 75 cycles per minute, the stroke volume is fixed at 70 ml. The phantom generates an ECG signal that can be fed into the ECG monitor of the MDCT scanner. The LV wall consists of a compartment between an inner and outer silicone membrane with a shape and orientation resembling the human LV. The inner membrane defines the endocardial cavity and LV volume. The cavity between the two silicone membranes (ventricular wall) was filled with 80 mL of water-diluted contrast agent Xenetix ™, (Guerbet, Aulnay S. Bois, France), delivering an attenuation of 160 ± 20 HU (mean ± SD). The intra-ventricular cavity was filled with respectively 120 mL, 160 mL and 190 mL (end-diastolic volume) of water diluted Xenetix ™, delivering an attenuation of 280 ± 20 HU (mean ± SD). The experiment was repeated at 3 heart rates covering a clinically relevant range: 60/min, 67/min and 75/min.

Scan parameters
The imaging of the dynamic phantom was done with a 16-slice MDCT scanner (Aquilion 16, Toshiba Medical Systems, Otawara, Japan). The rotation time was 0.5 seconds and the acquisition configuration was 16 x 0.5 mm. The pitch-factor was 0.25; tube voltage 120 kV and tube current 250 mA.
**MDCT image reconstructions**

A retrospective ECG gated segmental reconstruction algorithm was used to reconstruct two and five mm thick contiguous axial slices (512 x 512 matrix; 240 mm reconstructed field of view). For accurate selection of the end-diastolic and end-systolic phases, 20 phase points were reconstructed (steps of 5%, ranging from 0-95%). Next, short-axis views were created by multi-planar reformatting; this is illustrated in Figure 1.

![Cardiac multiplanar reconstruction displayed at the scanner console](image)

**Figure 1.** **A.** Cardiac multiplanar reconstruction displayed at the scanner console. Short axis reconstruction of the cardiac phantom obtained by multiplanar reformatting. **B.** Horizontal long axis view. **C.** Vertical long axis view. **D.** The control panel, by movements and rotations the multiplanar reformatting are obtained to acquire the horizontal and vertical long axis views and the short axis view.
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The entire LV was presented within 39 slices in the situation of 2 mm reconstructed slice thickness and within 15 slices when using 5 mm reconstructed slice thickness. The applied heart rates of respectively 60/min, 67/min and 75/min correspond with a temporal resolution of 250, 130 and 167 ms respectively. Note that temporal resolution is not proportional to the heart rate which is a complex but well known effect of segmental reconstruction algorithms [17].

**Data analysis**

The end-diastolic and end-systolic short-axis images were analyzed with dedicated cardiac function analysis software (CT-MASS, Medical Imaging Systems, Leiden, The Netherlands). Images with largest and smallest LV volumes, corresponding to end-diastolic and end-systolic phases, were selected from smooth running cine movies. End-diastolic and end-systolic LV endocardial contour borders were drawn manually on every other slice independently by three observers. These observers *(initials will be added)* were blinded to actual volumes. CT-MASS provides appropriate interpolation of contours, so the entire ventricle was covered. The end-diastolic volume (EDV) and end-systolic volume (ESV) were derived by slice summation. From these values, the stroke volume *(SV = EDV - ESV)* and ejection fraction *(EF = SV / EDV)* were calculated.

**Statistical analysis**

The data were analyzed with S-Plus for Windows (version 6.2). Continuous data were expressed as mean (± SD). For all statistical testing, p< 0.05 was considered statistically significant. To compare the calculated EDV, ESV, SV and EF's to the actual values, for the three heart rates and filling conditions (EDV), we fitted linear mixed-effects models to the difference between the actual and observed values, each time adjusting for heart rate and filling condition as fixed effects. Each model corrects for interobserver variability by inclusion of a random observer effect. For both heart rate and filling conditions, we present an F-test, which is a standard testing procedure in analysis of variance modeling to evaluate the basic null hypothesis of no difference (according to heart rate or condition). To facilitate the interpretation of the observed differences, we calculated maximum relative differences of the measured results in comparison to actual values.
RESULTS

Table 1 summarizes the results from the linear mixed modeling analysis. Within the studied range of heart rates (60/min-75/min), left ventricle volumes (120mL-190mL) and reconstructed axial slice thicknesses (2mm-5mm) we found significant effects of heart rate on the accuracy of the volumetric and functional measurements (F-test: 7.3-39.2, p<0.004) and filling conditions (F-test: 7.4-55.6, p<0.004). Resulting overall relative differences in the assessment of EDV were rather small (ranging from −3% to 3%) but there was a trend for overestimation of the ESV, ranging from -1% to 18%. The highest relative overestimation was found, as could be expected, for the smallest filling condition of ESV of 50 mL in combination with the worst temporal resolution (60/min). Despite the highest relative overestimation of 18% for the filling condition of ESV of 50 mL, the maximum absolute difference between the observed and actual ESV in this case was smaller than 10 mL for all ESVs, while the minimum difference in ESV was found for the best temporal resolution of 130 ms (corresponding with heart rate 67/min), and largest filling condition (EDV= 160 mL or 190 mL). The calculated SV and EF underestimated the actual values within a range from −1% to −11%. The smallest difference in EF was also found for the heart rate of 67/min. Relative differences in EF were even smaller than 1% for an EDV filling of 160 mL or 190 mL.

Table 1. Accuracy of MDCT on left ventricular volumetric measurements.

<table>
<thead>
<tr>
<th></th>
<th>Heart rate</th>
<th>Filling condition</th>
<th>Interobserver effects</th>
<th>Relative difference (min., max.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F-value</td>
<td>p-value</td>
<td>F-value</td>
<td>p-value</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td>(S.D.)</td>
</tr>
<tr>
<td>EDV 2mm</td>
<td>0.90</td>
<td>0.42</td>
<td>7.4</td>
<td>0.004</td>
</tr>
<tr>
<td>EDV 5mm</td>
<td>0.39</td>
<td>0.72</td>
<td>21.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>ESV 2mm</td>
<td>7.32</td>
<td>0.004</td>
<td>15.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>ESV 5mm</td>
<td>32.2</td>
<td>0.0001</td>
<td>33.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>SV 2mm</td>
<td>13.2</td>
<td>0.0002</td>
<td>2.5</td>
<td>0.1</td>
</tr>
<tr>
<td>SV 5mm</td>
<td>29.7</td>
<td>0.0001</td>
<td>2.6</td>
<td>0.1</td>
</tr>
<tr>
<td>EF 2mm</td>
<td>15.0</td>
<td>0.0001</td>
<td>33.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>EF 5mm</td>
<td>39.2</td>
<td>0.0001</td>
<td>55.6</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

The calculated end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and ejection fraction (EF) are compared to the actual values and expressed as relative differences. Significant influences of heart rate and filling condition on the accuracy of the measured volumes were found. Note the systematic underestimations of the SV and EF. Nevertheless, the observed relative differences of the volumes are relatively small.

Abbreviations: S.D. = standard deviation, Rel. difference = relative difference.
The overall interobserver agreement was good (standard deviation <1.8 mL, <0.5% for all measured volumes and EF) and only an insignificant effect was found for selecting the 5 mm thick slices instead of 2 mm thick slices.

In summary, most accurate assessments of EDV, ESV, and SV were achieved at a heart rate 67/min and bigger filling conditions, figure 2 shows, as an example, the temporal resolution dependent underestimation of SV.

![Mean stroke volumes as assessed by three observers for different volume categories](image)

**Figure 2. Mean stroke volumes as assessed by three observers for different volume categories.** Note an underestimation of calculated stroke volume for all volume categories. The smallest deviations correspond with the acquisition with best temporal resolution (TR).

**DISCUSSION**

This study is the first comprehensive validation of assessment of cardiac function with MSCT under controlled and realistic acquisition conditions by using a chest phantom with an insert that accurately mimics the shape and movement of an artificial left ventricle. Postprocessing included all the steps that are performed in routine clinical applications, such as short axis reconstruction and interpolation of contours. This study evaluated the effect of heart rate, LV filling condition and reconstruction thickness on the accuracy of LV volumetric analysis and functional measurements using 16-MDCT.
Effects of heart rate, filling and slice thickness on the accuracy of left ventricular volume measurements in adynamic cardiac phantom using

Significant effects on the accuracy of the volumetric measurements of the phantom were found for heart rate and filling condition, while no effect of reconstruction thickness was found. All volumetric measurements could be accurately reproduced by different observers. Within the clinical relevant range of heart rates (60/min-75/min) and LV filling conditions (120mL-190mL) accurate results were found for the assessment of EDV, whereas measurements are associated with a systematic bias for overestimation of ESV. The measurement of LV volume in the end systolic phase is particular sensitive for motion and the resulting blurring of the LV wall explains the systematic bias (overestimation) in ESV assessment. Impaired myocardial function can be detected with 4- and 16-MDCT, however an underestimation of SV and EF in the range of –1 to –11 % should be taken into account for the studied range of heart rates and filling conditions. No significant effects of reconstruction thickness were found, meaning that reconstruction of 5mm slices is sufficient for accurate global LV function assessment thus reducing reconstruction time as well as the burden on the capacity of the digital archives. This finding is in accordance to other studies which use 5 mm reconstructions [9].

Considerable differences in ESV measurements were found, still, the errors in SV and EF (-1% to -11%) were considered acceptable. Similar differences in ventricular function measurements are also described for validation studies of MDCT relative to MRI in patient populations. Our results of overestimation of ESV and underestimations of SV and EF are in accordance to studies which compared MDCT to MRI in which a bias of -1.5% [11] to -8.5% [17] in left ventricular ejection fraction (LVEF) is found. We found absolute underestimations of LVEF varying within -0.5% and -6.5% (for both 2 mm and 5 mm reconstructions) in comparison to real LVEF, similar to these studies [11, 17]. Recently, rather large mean differences in stroke volume (differences 22 mL [21%]) were reported in a patient based study comparing electron beam computer tomography (EBCT) with MRI [18]. These rather large deviations should probably be explained by uncertainties in the reproducibility of the experiment since similar experimental conditions at both imaging modalities are difficult to achieve in a patient population. The use of a phantom, instead of patients, in our study overcomes this problem.

The temporal resolution of functional cardiac imaging must be sufficient to isolate the end-diastolic and end-systolic phases of the cardiac cycle. The current study shows that the moderate temporal resolution of cardiac CT leads to systematic underestimation of the SV and EF.

MDCT seems to be a promising technique for non-invasive comprehensive evaluation of coronary arteries and ventricular function, without geometrical assumptions. This has the advantage that one can also assess function of the more complex right ventricle, which is of prognostic importance and can be used in combination with MDCT pulmonary angiography, to facilitate detection of right ventricular dysfunction in depending on pulmonary embolus location [19]. There is considerable variation in performance of different imaging modalities. Utsunomiya
showed for example that MDCT is much more accurate than SPECT [15] and Yamamuro showed that functional analysis with MDCT is more accurate than 2D-echocardiography for cardiac functional analysis [20]. The clinical value of MDCT however, depends not only on the accuracy but also on the application of appropriate normal values. The current systematic bias in assessment of global cardiac function with CT, implies that normal values should be used that are defined specifically for CT and that follow up is performed under similar conditions, especially with regard to imaging technology.

In our study the heart cycle was sampled over 20 phase points, allowing adequate isolation of the appropriate cardiac phase for functional analysis. The LV has its largest volume (i.e. the end-diastolic volume) during the pre-ejection period which is composed of the isovolumetric contraction period plus the electromechanical interval (i.e. the time elapsing from the QRS onset to the beginning of ventricular contraction) [21]. The normal pre-ejection period lasts until about 80-110 ms after the R-wave [22]. Therefore, sampling of the heart cycle within 50 ms after the R-wave is considered adequate for capturing the end-diastolic phase [21]. The smallest end-systolic volume occurs during the isovolumetric relaxation interval. Duration of this relaxation phase varies between 40 and 140 ms measured from the R-wave [22] and therefore sampling of the cardiac cycle should ideally occur within this time frame for optimal isolation of the end-systolic phase [21]. These observations for optimal sampling of the end-systolic and end-diastolic phase explain the observed systematic deviations of the volumes assessed by MDCT, since temporal resolution in our experiments was in the range 130-250 ms thereby exceeding the duration of normal pre-ejection period and the isovolumetric relaxation interval. At 67 bpm (temporal resolution 130 ms) the current study was approaching the nominal EDV, ESV, EF and fixed SV most closely. Overall volumetric measurements have limited biases compared to actual values, however the ESV has a substantial bias towards overestimation in the case that temporal resolution decreases.

We assessed the accuracy of ventricular volumetric analysis for MDCT acquisitions that are associated with a temporal resolution that is representative for common practice in cardiac MDCT (130 - 250 ms) by using 16-MDCT. Within this range our results are also representative for 64-MDCT, because the bottle-neck in cardiac MDCT, moderate temporal resolution, still has not improved substantially with the introduction of 64-MDCT. The accuracy of volumetric analysis will improve for scanners that achieve a temporal resolution better than 130 ms. This can be achieved by implementation of faster rotating x-ray tubes, inclusion of more cardiac cycles in the segmented reconstruction (lower pitch factor), dual source cardiac CT and cone beam CT.
Limitations
This study was an experimental study, in which we used limited repetitions of the conditions we scanned; we have also only the heart rates of common practice, because the heart rate range of our phantom was limited.

Conclusion
At heart rates below 75 beats per minute, MDCT allows sufficient adequate and reliable measurements of ventricular volumes and calculation of left ventricle function for clinical applications, based on a cardiac phantom. While EDV measurements are very accurate, ESV can be overestimated up to 18%, while SV and EF can be underestimated up to 11% (range: -1% to -11%) in comparison to actual values. The accuracy of the measurement depends on heart rate and ventricle filling, while the interobserver agreement is good. A reconstructed slice thickness of 5 mm, instead of 2 mm, can be used with the advantage of shorter reconstruction time, lower storage requirements and faster postprocessing of the functional studies.
**REFERENCE LIST**


