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VENTRICULAR FUNCTION

Relationship of Number of Phases per Cardiac Cycle and Accuracy of Measurement of Left Ventricular Volumes, Ejection Fraction, and Mass

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ABSTRACT

In cine cardiac magnetic resonance imaging (MRI) studies, for any preset imaging parameters the number of phases per cardiac cycle for a single slice is proportional to breath-hold duration. We investigated the relationship between the accuracy of measurement of left ventricular (LV) end-diastolic and end-systolic volumes (EDV and ESV, respectively), mass and ejection fraction (EF), and the number of phases acquired per cardiac cycle. Twelve adult volunteers underwent cardiac MRI and five complete LV functional studies were obtained with 8, 11, 14, 17, and 20 phases per cardiac cycle. We calculated LV volumes, EF, and mass for each acquisition, and compared them using the 20-phase acquisition as the reference standard. The scan duration was proportional to the number of phases acquired. There was a systematic underestimation of LV, EDV, and EF, with decreasing number of phases. Differences from the reference standard became significant for the 8-phase acquisition ($p<0.05$). Subgroup analysis showed that only those with slower heart rates (<65/min) had significant differences in EDV, but not in EF, for the 8-phase acquisition. For those with faster heart rates, no differences were detected between the different acquisitions. There were no significant differences between all acquisitions for the LV ESV and mass. We conclude that at least 11 phases per cardiac cycle are needed to maintain accuracy for cine cardiac MRI studies. Decreasing the number of phases per cardiac cycle beyond this cutoff may introduce significant error of measurement, particularly

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for the left ventricular EDV and EF and especially for those with bradycardia, and should be avoided.

Key Words: Cardiac magnetic resonance; Temporal resolution; Number of phases; Function; Heart.

INTRODUCTION

Cardiac magnetic resonance imaging (MRI) is established as the gold standard for measuring left ventricular (LV) volumes, ejection fraction (EF), and mass (Higgins and Sakuma, 1996; Semelka et al., 1990). For functional cardiac studies image acquisition is typically performed during breath holding (Atkinson and Edelman, 1991), and imaging parameters are adjusted to achieve a combined high spatial and temporal resolution. However, for any given spatial resolution and imaging parameters, any increase in temporal resolution (i.e., the acquisition of more phases per cardiac cycle) comes at the expense of longer breath-holding times, since more cardiac cycles are needed to collect the necessary data for each phase. This principle applies to any acquisition scheme, including parallel imaging [e.g., SMASH (Sodickson and Manning, 1997) and SENSE (Pruessmann et al., 1999)].

Older patients and those with cardiac or respiratory diseases are unable to sustain prolonged breath holding (Gay et al., 1994). Thus, to make cardiac MRI applicable to even these patient groups, it is frequently needed to decrease the number of phases to achieve short breath holds. By doing so, end-diastole and end-systole may not be accurately represented, and thus measurements of LV end-diastolic volume (EDV), end-systolic volume (ESV), EF and mass may be inaccurate.

In a recent study by Miller et al. (2002), the influence of spatial and temporal resolution on the accuracy of measurement of LV functional parameters was investigated. The authors concluded that (for accurate measurements) ''maximal temporal resolution is required'' but no specific recommendations were provided for routine clinical cardiac MRI studies. Accordingly, we examined the relationship between the number of phases acquired per cardiac cycle and accuracy of measurement of LV volumes, EF, and mass with cine cardiac MRI.

MATERIALS AND METHODS

Study Group

Twelve adult volunteers (8 males, age 26–67, mean 38 years) with no known cardiac diseases were included in this study. Exclusion criteria were the presence of pacemakers or implantable defibrillators, cerebral surgical clips, and severe claustrophobia. All subjects were imaged in a single session (<60 min total imaging time). The study was approved by the Institutional Review Board and written informed consent was obtained by all subjects prior to participation.

MR Imaging

Magnetic resonance imaging was performed using a 1.5 T Philips Intera CV MRI scanner (Philips Medical Systems, Best, the Netherlands). A commercially available five-element cardiac phased-array receiver coil was used for signal acquisition. All subjects were imaged supine with 4 electrodes on the anterior left hemithorax to obtain a vectorcardiogram (Fischer et al., 1999) for prospective electrocardiographically (ECG) gated acquisitions.

For each subject, localizing scans were obtained to define the long (2-chamber) axis of the left ventricle. A mid-ventricular short-axis view was then prescribed, and used to plan a four-chamber view. The short axis orientation was then defined accurately, perpendicular to both the two- and four-chamber views. Five complete LV function studies were then acquired in random order, with 20, 17, 14, 11, and 8 cardiac phases per cardiac cycle. The number of phases per cardiac cycle is a parameter that can be a priori defined in our system. Thus, for any preset number of phases acquired, the temporal resolution varies depending on the heart rate (temporal resolution=cycle length/number of phases, where cycle length in ms is 60,000/heart rate), and no interpolation is implemented. Each study consisted of 12 contiguous (gap=0 mm) short-axis slices covering the entire LV (slice thickness 8 mm). One slice was acquired per breath hold in all instances.

The imaging sequence was an ECG-gated two-dimensional (2D) steady-state free-precession (SSFP) breath-hold sequence (TE=1.9 ms, TR=3.9 ms, flip angle 50°), characterized by the application of balanced gradients in all directions. This sequence is less susceptible to artifacts caused by flow and provides substantially enhanced blood-myocardial contrast compared to conventional gradient echo sequences (Plein et al., 2001; Thiele et al., 2001), resulting in improved

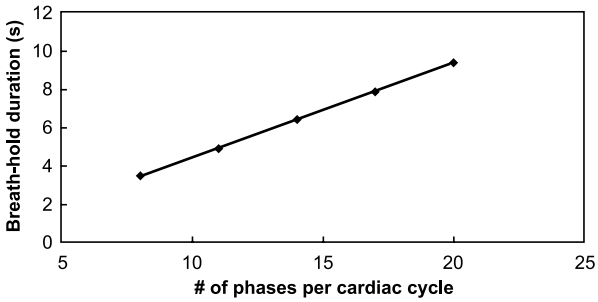

Figure 1. Relationship between number of phases per cardiac cycle and duration of breath holding for each short-axis slice with a SSFP sequence employing SENSE parallel imaging (acceleration factor of 2). The breath-hold times are nominal values for a heart rate of 60 beats per minute.

contour segmentation. A twofold acceleration in data acquisition was achieved by implementing SENSE (Pruessmann et al., 1999) by reducing the number of acquired phase encoding steps by 50%. Since the application of SENSE does not necessitate any change in the order of sampling k-space, its use does not interfere with any of the numerous known contrast mechanisms or acquisition schemes. Thus, with the imaging approach employed in this study, changing the number of phases per cardiac cycle has no effect whatsoever on image quality. Alternative imaging schemes, such as those employing the change of echo train length in segmented data acquisitions, may be limited due to inadvertent variations in image quality.

For all LV studies, the in-plane image spatial resolution was maintained constant (1.5 mm $\times$ 1.9 mm) and only the number of phases acquired per cardiac cycle varied. We assured that for each subject heart rate remained constant for all scans to allow maintaining the same settings for all acquisitions. In cases where the subject's heart rate increased (due to anxiety, fatigue, etc.) we allowed for more time between breath holds, which effectively restored the heart rate to its previous level. Conversely, if the subject's heart rate decreased (due to adjustment in the magnet environment and relaxation), we decreased the between-breath-hold relaxation time, which invariably increased the heart rate to the previous levels.

Image Analysis

Image analysis was performed off line on a dedicated analysis workstation (EasyVision 5, Philips Medical Systems, Best, the Netherlands) by two independent observers (AR, PGD). The number of acquired cardiac phases is readily available during the analysis and thus complete blinding to the acquisition used cannot be achieved. To minimize the possibility for bias, we performed the LV analysis for each acquisition scheme and subject in different sessions, and without knowledge of the quantitative results from other analyses. The Simpson's rule was used to calculate LV volumes, EF and mass. For all tracing, the papillary muscles were included as part of the LV cavity, as previously described (Lorenz et al., 1999).

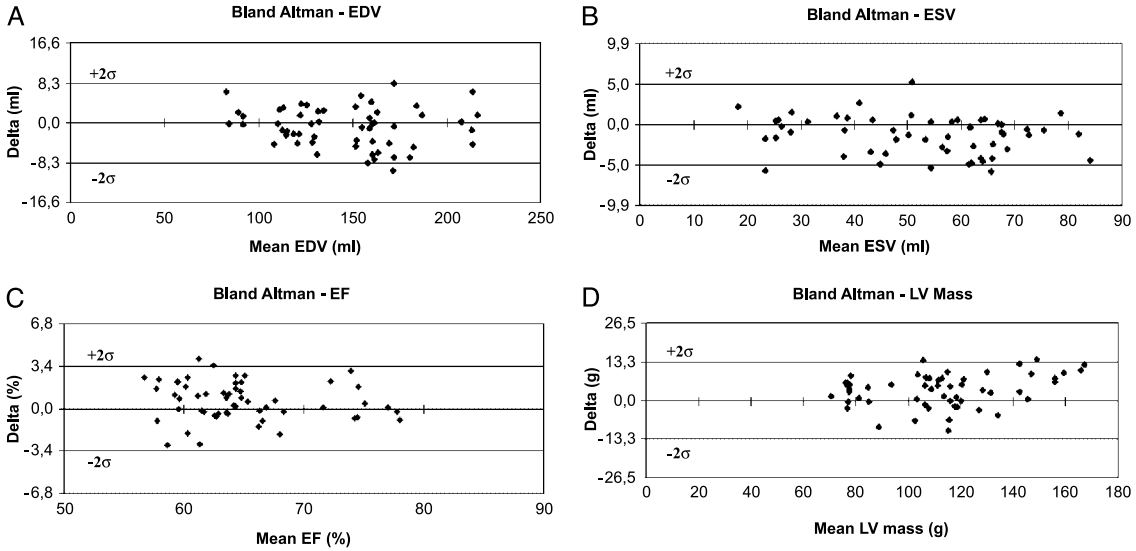

Figure 2. Bland-Altman plots of the interobserver agreement on measurements of (A) left ventricular (LV) end-diastolic volume (EDV), (B) end-systolic volume (ESV), (C) ejection fraction (EF), and (D) mass.

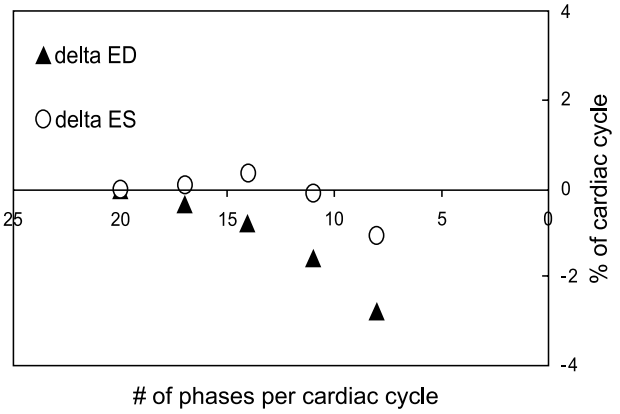

Figure 3. Relative change (delta) of the timing of end-diastole (ED) and end-systole (ES) for acquisitions using 8, 11, 14, and 17 phases per cardiac cycle, compared to a 20-phase acquisition.

Statistical Analysis

To adjust for differences in heart rate, the apparent occurrence of end-diastole and end-systole was expressed as a percent of the RR interval (%RR). Inter-observer and intraobserver variabilities for LV EDV, ESV, EF, and mass were computed as the root of the mean squared differences between corresponding observations, divided by the average of all observations. Bland-Altman plots were used to assess inter- and intraobserver agreement. Linear regression analysis was also used to examine the correlation between measurements from the two observers for all parameters. For the calculation of intraobserver variability, the 20-phase acquisition was analyzed twice by both observers and all parameters were measured twice. The average of the four measurements from the 20-phase acquisition (two for each observer) for LV EDV, ESV, EF, and mass was used as the reference (gold) standard. The average of two measurements (one for each observer) was calculated for each subject and each acquisition (8 through 17 phase acquisitions), and the differences from the reference standard were calculated. Differences among groups were compared using a one-way analysis of variance (ANOVA) and Fisher's LSD test for post hoc analysis. Subgroup analysis was performed to evaluate whether the subject's heart rate influenced the accuracy of measurement for all parameters for the various acquisition schemes. The median heart rate was used as a cutoff between the lower and higher heart rates. All comparisons were two-tailed, and a p value of <0.05 was considered as statistically significant.

RESULTS

All subjects were imaged without complications. One subject was excluded from analysis because she failed to sustain reproducible depth of breath holding, resulting in obvious misregistration of images. The subjects' heart rate ranged from 51 to 81 beats per minute. The scan duration per breath hold, adjusted for a heart rate of 60 beats/min, ranged from 4.0 s (for the 8-phase acquisition) to 9.4 s (for the 20-phase acquisition), and correlated well with the number of phases ($R^2=0.99$, $p<0.0001$) (Fig. 1). For a heart rate of 60 beats/min, the various acquisitions would correspond to a temporal resolution of 125 ms (8-phase acquisition), 91 ms (11-phase acquisition), 71 ms (14-phase acquisition), 59 ms (17-phase acquisition) and 50 ms (20-phase acquisition). Similarly, for the same heart rate (60 beats/min), the various sequences would correspond to equal number of frames per second (i.e., the 8-phase acquisition would correspond to 8 frames/s, the 11 phase acquisition would correspond to 11 frames/s, the 14 phase acquisition would correspond to 14 frames/s, etc.).

Intraobserver variability for both observers for the measurement of LV volumes, EF, and mass was <3% for all measurements and ranged from 0.7–2.5%.

Table 1. Mean left ventricular volumes, mass, and ejection fraction (EF) for the study population.

	EDV (ml)	ESV (ml)	EF (%)	Mass (g)	EDV/BSA (ml/m^2)	ESV/BSA (ml/m^2)	Mass/BSA (g/m^2)	EDV/Ht (ml/m)	ESV/Ht (ml/m)	Mass/Ht (g/m)
8 phases	142±37	55±19	63±6	113±27	72±12	27±7	57±8	79±16	30±9	63±12
11 phases	147±37	54±19	65±6	113±28	74±13	27±8	57±9	81±16	30±9	62±13
14 phases	147±36	52±18	66±5	111±26	74±12	26±7	56±7	81±16	29±9	61±11
17 phases	149±36	52±16	66±5	112±26	75±11	26±6	56±7	82±16	28±8	62±11
20 phases	149±35	53±17	65±5	112±25	75±11	27±6	57±6	82±15	29±8	62±11

Indexed values for body surface area (BSA) and height (Ht) are also provided. There were no significant differences in the mean values of all parameters for any of the acquisitions.

Abbreviations: EDV=end-diastolic volume; ESV=end-systolic volume.

Similarly interobserver variability was also low (EDV, 2.0%, ESV, 3.8%, EF, 1.6%, mass, 4.9%, $p<0.001$). Linear regression analysis showed good correlation between the measurements of the two observers ($R^2=0.94-0.99$, $p<0.0001$ for all parameters). Bland-Altman plots for interobserver agreement on measurements of LV EDV, ESV, EF and mass are presented in Fig. 2.

The sampling point of the end-diastole steadily deviated away from the onset of the QRS, as the number of phases per cardiac cycle decreased (Fig. 3). A significant difference from the reference standard was found for acquisitions with 11 and 8 phases (1.6% of cardiac cycle, $p<0.01$% and 2.8% of cardiac cycle, $p<0.02$, respectively). Similarly, the average timing of the phase selected as end-systolic deviated away from the one determined by the 20-phase scan for acquisitions with fewer phases. However, there was no systematic over- or underestimation of the timing of average end-systole for any of the acquisitions. This applied even when the absolute time differences from end-systole were computed for each acquisition (data not shown).

The mean values of all parameters were similar for all acquisitions (Table 1). However, as the number of phases decreased, an underestimation of LV EDV was observed and differences from the reference standard gradually increased (Fig. 4A). These differences

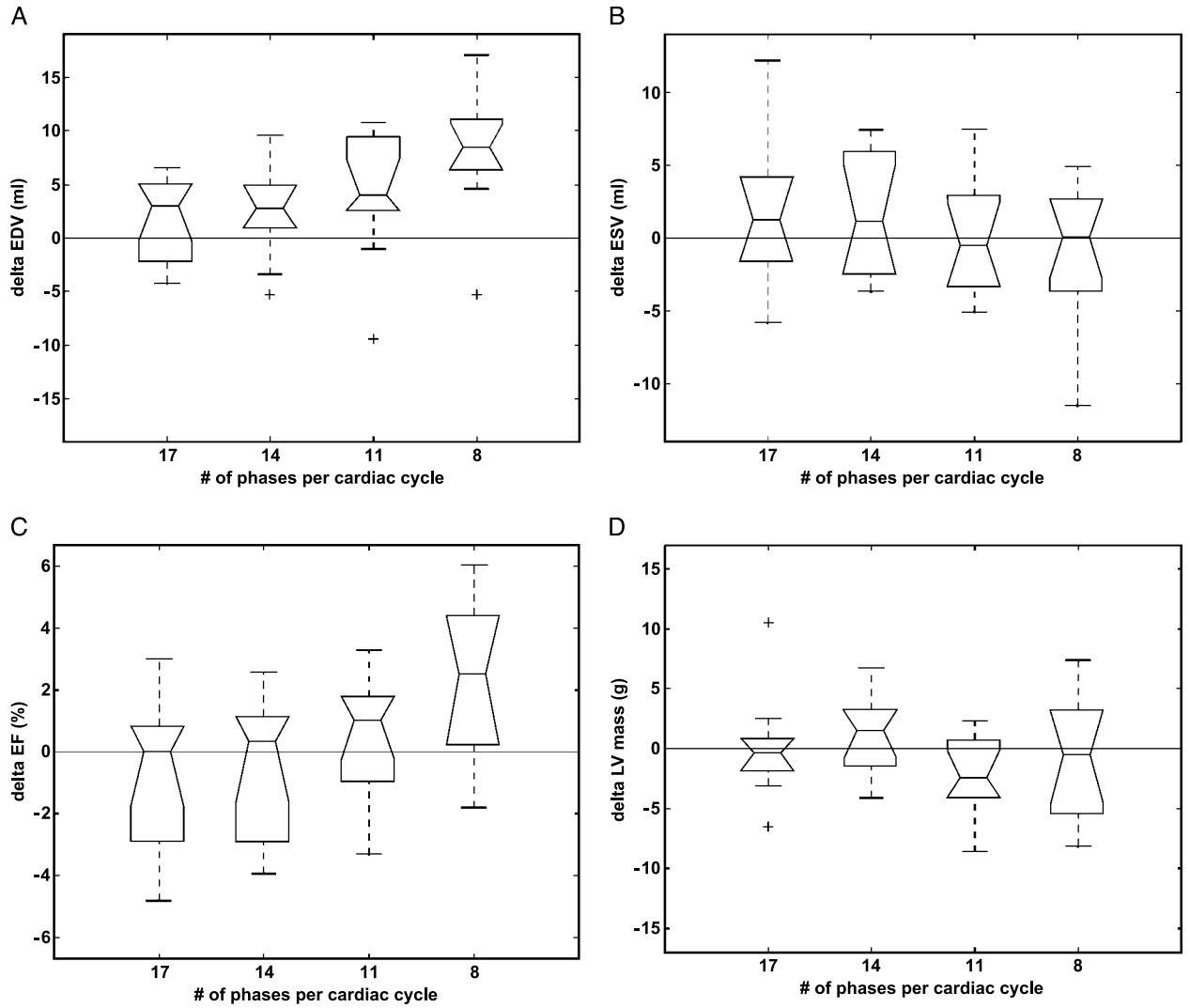

Figure 4. Box plots of the differences of (A) LV EDV measurements (delta EDV); (B) LV ESV measurements (delta ESV); (C) LV EF measurements (delta EF), and (D) LV mass measurements (delta LV mass), for the acquisitions with 8, 11, 14, and 17 phases per cardiac cycle from the 20-phase acquisition. Median differences (mid point), upper and lower quartiles (upper and lower border), range (dotted lines), and outliers (cross) are shown.

became statistically significant for acquisitions with 8 phases per cardiac cycle (5.2% mean difference, $p<0.05$). For ESV there were no significant group differences from the reference standard, even for the 8-phase acquisition (Fig. 4B). As with LV EDV, a tendency to underestimate LV EF with fewer phase acquisitions was observed (Fig. 4C). Differences from the reference standard for LV EF calculations, were found to be significant for the 8-phase acquisition (mean difference 3.8%, $p<0.01$). There were no significant differences between any of the acquisitions for the calculation of LV mass (p=NS for all acquisitions, Fig. 4D).

As the median heart rate was 65/min, for subgroup analysis we classified our subjects into those with heart rate $\geq$65/min (N=6) and those with <65/min (N=5). In the lower heart rate group, the LV EDV was significantly different between the various acquisition schemes ($p<0.05$), with only the 8-phase acquisition having lower values than the 20-phase acquisition. In the low heart rate subgroup, there were no significant differences for the ESV, EF, or mass. In the higher heart rate group ($\geq$65/min), there were no differences for any of the parameters between the various acquisition schemes.

DISCUSSION

In the present study we have shown that at least 11 phases are needed in cardiac cine MRI studies to maintain accuracy of measurement of LV volumes, EF, and mass. When fewer phases are obtained using prospectively triggered sequences that evenly distribute the number of phases within the cardiac cycle, the main reason for inaccuracies is the incorrect detection of end-diastole, farther away from the QRS complex. As a result, the LV EDV is underestimated, and this becomes significant with 8-phase acquisitions, when the acquired phases are equally distributed throughout the entire cardiac cycle. End-systole may also be incorrectly detected either before or after the actual end-systole, when a small number of phases is used. As a result, ESV may be overestimated, but on average the effect on the measurement of LV ESV is less prominent and not significant, even with 8-phase acquisitions.

The definition of endocardiac border during systole inherently possesses a greater chance of error due to the difficulty of accurately identifying the contour of the contracted papillary muscles. Indeed, in our study there was slightly greater intraobserver variability for ESV, compared to EDV. The relative independence of ESV to the number of cardiac phases may be in part due to the smaller volume and greater variability of measurement, compared with the EDV. In patients with larger ESV, such as those with cardiomyopathies, ESV inaccuracies due to fewer cardiac phases may become more prominent. This was not examined in our study, as only subjects with no cardiac diseases were included.

It is critical for the sampling of end-diastole to be performed as close to the QRS as possible. While retrospective ECG-gating may allow decreasing the initial delay of the first phase from the QRS to a minimum, this is not applicable to prospectively ECG-gated sequences that implement a trigger delay. In a previous study where a prospective navigator slice correction approach was used to compensate for differences of the diaphragmatic (and cardiac) position between serial breath-holds (Chuang et al., 1997), a significant underestimation of the LV EDV was found. This was attributed to the delayed sampling of end-diastole resulting from implementation and analysis of the navigator pulse. Our findings corroborate these findings by Chuang et al. (1997) and extend their significance to nonnavigator imaging.

The LV EF calculation is also sensitive to the number of phases acquired, as it takes into account both EDV and ESV. The underestimation of EDV will invariably tend to decrease the EF, as will the overestimation of ESV. Thus, with an 8-phase acquisition the net effect on the measurement of LV EF was found to be significantly different from the 20-phase acquisition. These data justify the routine sampling of at least 11 phases per cardiac cycle for LV volumetric and EF measurements (Pennell, 2002).

The measurement of LV mass did not vary with the number of phases per cardiac cycle. This is not surprising, because with small time differences in the sampling of end-diastole among acquisitions with different number of phases, only small changes in the appearance of the LV contour (including shape of the papillary muscles and trabeculations within the cavity) are expected. Thus, the measured differences in LV mass between the acquisitions with different number of phases are essentially reflecting the intraobserver reproducibility, as demonstrated in our study.

In a recent study, Miller et al. (2002) reported on the influence of temporal and spatial resolution on the values of LV functional parameters. The authors used a different methodology and analytical approach, examining the effect of different heart phase intervals on the accuracy of measurement of LV parameters. Although no data were provided regarding the association of the number of phases and accuracy of ESV measurement, they suggested that with the exception of LV mass, the

use of maximum temporal resolution (i.e., minimum heart phase interval) is needed to maintain acceptable accuracy. In our study, we addressed the question of temporal resolution in terms of the number of phases per cardiac cycle needed for maintaining accuracy of measurement, in order to provide a clinical yardstick for routine cardiac MRI examinations.

Although our study did not examine many subjects, we were able to show measurable differences in the calculations of LV EDV and EF for acquisitions with less than 11 phases per cardiac cycle. The high interobserver and intraobserver reproducibility of the method demonstrated in our study, similar to previous reports (Miller et al., 2002; Semelka et al., 1990), confirms that conclusions regarding accuracy of the technique can be drawn even with a relatively small number of subjects. A larger group of subjects would possibly increase statistical significance, and might even show significant differences for acquisitions with greater numbers of phases. However, we believe that the percent error from the reference standard would be too small to have clinical significance, even if such a difference could be demonstrated. Finally, it should be noted that the results presented here refer to healthy volunteers and not patients. In the latter case, oversampling of the LV volume curve through the acquisition of a greater number of phases would be required, in order to identify smaller changes that may arise from LV dysfunction (Setser et al., 2000). On the other hand, patients may have higher heart rates. For a fixed number of phases per cardiac cycle, a higher temporal resolution would be achieved for subjects with faster heart rate (shorter cardiac cycle length) than for those with slower heart rates (longer cardiac cycle length). Therefore, for subjects with higher heart rates than those in our study, even fewer than 11 phases per cardiac cycle might be adequate for accurate measurement of left ventricular volumes, mass, and ejection fraction. Indeed, our subgroup analysis demonstrated that the effect of decreasing the number of phases per acquisition, at least for the EDV, is greater for those with slower heart rates. We recognize, however, that our study was not specifically designed to address the accuracy of different approaches at different heart rate levels.

CONCLUSIONS

At least 11 phases per cardiac cycle are adequate to maintain accuracy of measurement of LV volumes, EF, and mass. Decreasing the number of phases per cardiac cycle beyond this cutoff may introduce significant error of measurement, particularly for LV EDV and EF, and should be avoided. Left ventricular mass is the least likely parameter to be affected when fewer phases per cardiac cycle are acquired.

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