

# Velocity encoded mitral valve inflow cine: A novel and more reproducible method to determine cardiac rest periods during coronary magnetic resonance angiography

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## Abstract

A high temporal resolution, 4-chamber (4CH) cine is the standard method for determining cardiac rest periods during whole heart coronary magnetic resonance angiography (CMRA). We evaluated the image quality and reproducibility between the 4CH cine method and a novel approach using a velocity encoded mitral valve inflow cine (MVI). The goal of this study was to compare the quality of CMRAs utilizing MVI versus 4CH methods. Sharpness and vessel length for the LCA and RCA using each method were determined using Soap Bubble and two blinded observers independently assessed coronary image quality. Offline analysis on a separate, retrospective cohort (n = 25) was used to compare MVI and 4CH reproducibility. In the prospectively evaluated cohort there was no difference in overall vessel sharpness (4CH vs MVI mean  $\pm$  SD) ( $31.0 \pm 5.5\%$  vs  $30.5 \pm 5.7\%$ ,  $p = .63$ ), LCA vessel sharpness ( $30.0 \pm 5.4\%$  vs  $31.1 \pm 8.2\%$ ,  $p = .44$ ), LCA length ( $4.7 \pm 1.4$  cm vs  $4.6 \pm 1.6$  cm,  $p = .66$ ), RCA vessel sharpness ( $32.1 \pm 6.9\%$  vs  $31.1 \pm 7.7\%$ ,  $p = .55$ ), RCA length ( $5.51 \pm 2.6$  cm vs  $5.95 \pm 2.4$  cm,  $p = .38$ ), or image quality rating (2.66 vs 2.62,  $p = .80$ ) between methods. In the retrospective cohort, the MVI method had 5.4% lower inter-observer variability (95% CI 3.7,7.2%,  $p < .0001$ ) and 3.9% lower intra-observer variability (95% CI 2.4,5.4%,  $p < .0001$ ) than the 4CH method.

MVI is a technically feasible and more reproducible method to determine cardiac rest periods compared to 4CH while preserving vessel sharpness, vessel length & image quality.

## Keywords

CT and MRI, diagnostic testing, cardiology, cardiovascular imaging agents / techniques, diagnostic testing, cardiology, coronary angiography, coronary wall motion

Date received 29 December 2021; Revised 23 February 2022; accepted 24 February 2022

## Objectives

Whole heart coronary magnetic resonance angiography (CMRA) has become an invaluable addition in the evaluation of patients with congenital heart disease (CHD) by providing both detailed cardiac morphology and coronary anatomy.<sup>1–3</sup> Data acquisition is usually performed while the heart is still, during the end-systolic rest period (ESRP) and mid-diastolic rest period (MDRP), to eliminate blurring from cardiac motion. The current reference standard for cardiac rest period determination during CMRA acquisition requires the reading physician to define the cardiac rest periods visually using a high-temporal resolution balanced steady-state free precession (SSFP) 4 chamber (4CH) cine as previously described in the

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literature.<sup>4-7</sup> As a result, an experienced reading physician, specifically trained in the 4CH method is required to determine the cardiac rest periods as they can vary substantially from patient to patient.<sup>8</sup>

Currently, automated detection techniques to determine cardiac rest periods are difficult to use in daily clinical practice as they require off-line analysis with specific software not integrated into commercially available MRI platforms. Studies evaluating cardiac rest period determination by automated detection have not demonstrated significant benefit over real time visual analysis. Some automated methods calculated much shorter shot durations,<sup>9</sup> were unable to accommodate real time changes in heart rate during scanning, or required increased processing time.<sup>10</sup> Sato et al. also recently developed an automated method using the mitral valve, tricuspid valve, and the apex of the heart, but the cardiac rest periods (both MDRP and ESRP) were found to start earlier than that determined by the physicians.<sup>11</sup> Overall, automated detection of cardiac rest periods remains a promising concept, but the application of 4CH and other methods of cardiac rest period determination have not clearly shown to provide any benefit over the current standard 4CH using real time visual analysis.

Otton et al. have previously illustrated the importance of choosing an accurate trigger time and used tissue doppler tracing as a method to clearly identify the cardiac rest phases.<sup>12</sup> In a similar vein, we developed a novel approach using velocity encoded mitral valve inflow cine (MVI) imaging. Utilizing spectral doppler echocardiographic principles, the MVI flow data when represented on a velocity graph represents the early diastolic, passive ventricular filling wave (or "E" wave in spectral doppler echocardiography) and the late diastolic, active ventricular filling wave secondary to atrial contraction (or "A" wave in spectral doppler echocardiography). Using this graph, the cardiac rest phases can be readily determined.<sup>12</sup>

We hypothesized determination of MDRP and ESRP with MVI for CMRA acquisition may be superior to hitherto established visual analysis with a 4CH CINE. Purpose of this study was a systematical analysis of both methods with a comparison of image quality, reproducibility of resting phases and their evaluation time respectively.

## Design

### Study population

Data from consecutive patients who were referred for a clinically indicated Cardiac MRI to include a CMRA at our institution between December 2017 and April 2018 were prospectively reviewed and analyzed. All patients were in sinus rhythm during the procedure. The UT Southwestern Institutional Review Board approved the study and there was a waiver of consent (STU 032016-009).

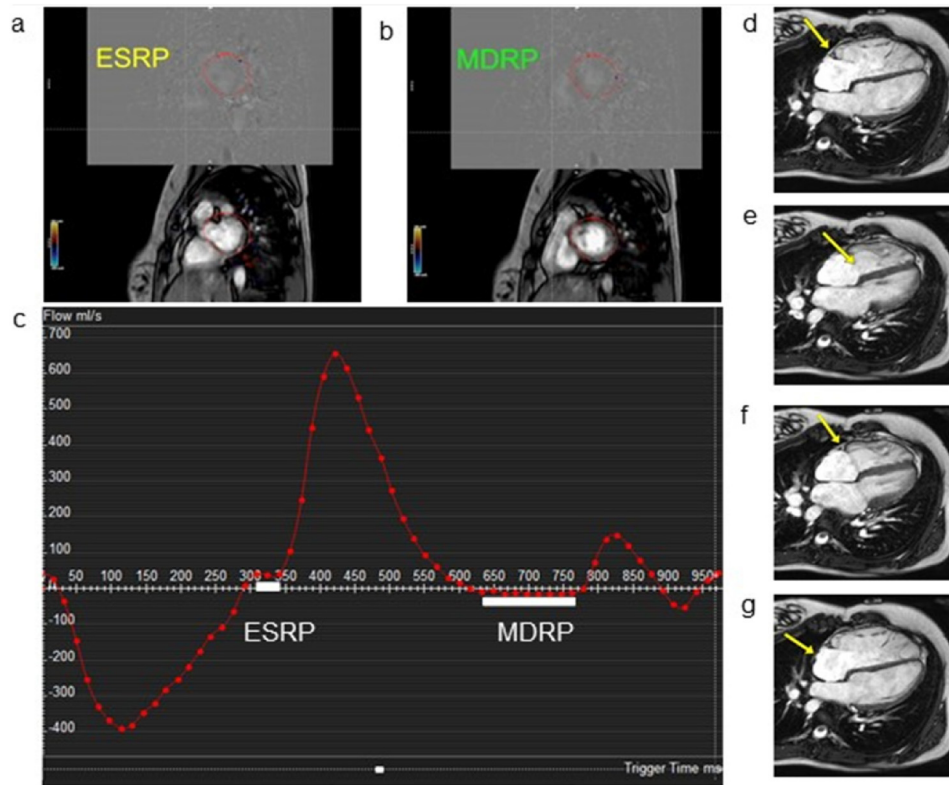
### MRI technique- equipment set up

An Ingenia 1.5 Tesla scanner (Philips, Best, The Netherlands) with the 32-channel phased array digital receiver coil for signal reception was used to obtain the CMRA imaging by an experienced technician.

Each patient had a standard dual phase, high temporal resolution 4CH cine performed (60 phases, field of view (FOV) was 350 mm, slice thickness 8 mm, acquired voxel size was 2 × 2 mm, echo time (TE) was 1.49 and repetition time (TR) 3.0, Parallel imaging (SENSE factor = 2), Echo train length 9. The cardiac rest periods were determined using the 4CH cine slice as previously described in the literature<sup>4-7,13</sup>: ESRP was defined as starting from cessation of movement of the right coronary artery (RCA) in the right atrioventricular AV groove (i.e. pause in visible contraction of the Right ventricle (RV)) to just before the tricuspid valve opens; and MDRP was defined as starting from the cessation of movement of the RCA at the end of the rapid inflow until the beginning of atrial wall contraction, or atrial systole (Figure 1).

The cardiac rest periods with MVI were determined as follows. First, the standard 2- and 4-chamber cine planes were used to define the mitral valve plane which was aligned to also include part of the left ventricular outflow tract. A velocity-encoded phase contrast cine was obtained in this mitral valve plane (60 phases, Parallel imaging (SENSE factor = 2)), FOV was: 280 mm, slice thickness 8 mm, Acquired Voxel 2 × 2 mm, velocity encoding limit 120 cm/s, Echo train length = 2). On the scanner itself, flow analysis was performed, with the region of interest drawn to include the left ventricular outflow and the entirety of the mitral valve. ESRP was defined as starting at the end of systole immediately after the cessation of flow through the aortic valve and ending with the beginning of flow through the mitral valve. MDRP was defined as starting at the end of rapid ventricular filling and ending at the start of atrial systole when there is no flow across the mitral valve (Figure 1).

Sequential patients undergoing CMRA for clinical purposes were enrolled. In addition to the clinically indicated CMRI sequences chosen by the reading physician, each patient underwent two isotropic dual phase whole heart 3D SSFP CMRAs, as previously described,<sup>14</sup> using prospectively determined cardiac rest periods from either a MVI or 4CH cine. Vessel sharpness and length for both the Left coronary artery (LCA), which included the left anterior descending artery, and Right coronary artery (RCA) were determined in both phases using coronary reformatting software (SoapBubble) for both 3D CMRAs performed on each patient using both the MVI or 4CH method (Figure 2). Vessel sharpness and length in the LCA and RCA in both phases were averaged for each method.<sup>15</sup> Left circumflex branch was not assessed given the variable size and morphology in our pediatric cohort.



**Figure 1.** Cardiac rest period determination by MVI and 4CH methods during CMRA. (a) and (b) represent single frames during a velocity-encoded mitral valve inflow (MVI) cine depicting ESRP and MDRP as viewed by reading physician when there is cessation of blood flow across mitral valve. (c) Graph of blood flow across the mitral valve (y-axis) over time (x-axis). White bars represent cardiac rest periods when there is cessation of blood flow. (d) In a 4CH cine, ESRP begins when the RCA (arrow) stops moving. (e) The end of ESRP is defined by the opening of the tricuspid valve (arrow). (f) After passive ventricular filling in early diastole, the RCA (arrow) movement will pause, representing the beginning of the MDRP. (g) The end of the MDRP occurs once the atrial wall (arrow) contracts indicating the onset of atrial systole. (ESRP: End-systolic rest period; MDRP: Mid-diastolic rest period).

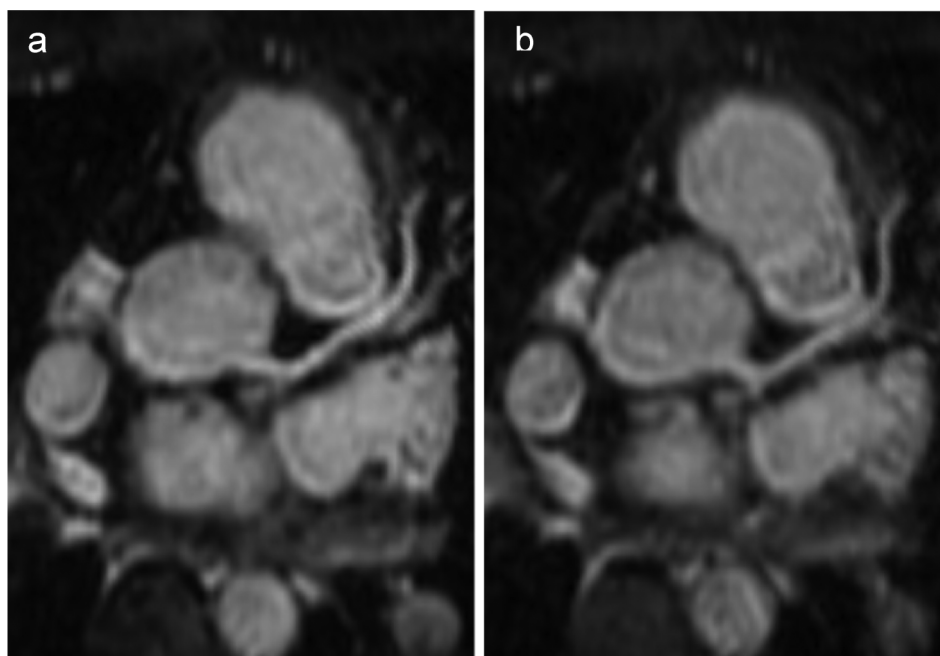
Two observers (GG, TH) independently assessed coronary image quality using scoring system (0–4) as previously described by McConnell et al. with 0 = coronary artery not visible, 1 = coronary artery was visible, 2 = coronary artery was visible with moderately blurred borders, 3 = coronary artery visible with mildly blurred borders, 4 = coronary artery visible with sharp borders) of the MPR image corresponding to the LCA and RCA in diastole and systole for each method. Consensus scoring was utilized when scores between observers differed by 2 or greater.<sup>16</sup>

To assess reproducibility, additional analysis was performed on 25 cardiac MRI studies. Two independent pediatric cardiologists each with >10 years of experience in CMR (GG, TH) then retrospectively determined the ESRP and MDRP using both methods to evaluate reproducibility in this off-line patient cohort. An offline methodology was also chosen to minimize disruption to the clinical workflow and to ensure adequate blinding. Both observers were blinded to patient information, underlying cardiac pathology, the results of the CMRA studies, as well as to each other's results. One observer (TH) evaluated

both methods twice to assess the intra-observer variability. Specifically, for each patient, we computed  $R_{intra} = \Delta_{intra} / m_{intra}$ , where  $\Delta_{intra}$  and  $m_{intra}$  are the difference and average of the two measurements by the same observers using the same method, respectively. To quantify inter-observer variability, we similarly computed  $R_{inter} = \Delta_{inter} / m_{inter}$ , where  $\Delta_{inter}$  and  $m_{inter}$  are the difference and average of measurements by the same observers using two different methods. For the purposes of the study, the images were transferred to an available workstation and retrospectively evaluated and independently scored for image quality.<sup>16</sup>

## Statistical analysis

In the prospective cohort, the parametric variables including the RCA and LCA Vessel sharpness and lengths were compared with paired student t-test and reported as mean  $\pm$  standard deviation. The non-parametric variable of image quality was compared by Wilcoxon matched pairs signed rank test



**Figure 2.** Multiplanar reformatted images from same patient using both techniques. (a) left image and (b) right image are transverse plane reformatted images showing similar image quality of the left coronary artery system utilizing MVI and 4CH techniques on the same patient A:MVI; B:4CH.

In the offline analysis on the retrospective cohort, a linear mixed-effect model was used to compare inter- and intra-observer variability between methods in the retrospective cohort. The dependent variables were  $R_{intra}$  or  $R_{inter}$ . The covariates included methods and measurement sites. Patient random effects were also included to account for within-patient correlation. Inter-observer and intra-observer variability for each method was analyzed. Image quality scoring of the LCA in this cohort was compared by interquartile range.

## Results

The prospective study included 24 patients (mean age 16; range 5 to 52 years) (Table 1). There was no difference in overall vessel sharpness (4CH vs MVI mean  $\pm$  SD) ( $31.04 \pm 5.49\%$  vs  $30.49 \pm 5.74\%$ ,  $p = .63$ ), LCA vessel sharpness ( $30.0 \pm 5.4\%$  vs  $31.1 \pm 8.2\%$ ,  $p = .44$ ), RCA vessel sharpness ( $32.1 \pm 6.9\%$  vs  $31.1 \pm 7.7\%$ ,  $p = .55$ ), RCA vessel length ( $5.51 \pm 2.6$  cm vs  $5.95 \pm 2.4$  cm,  $p = .38$ ), LCA vessel length ( $4.7 \pm 1.4$  cm vs  $4.6 \pm 1.6$  cm,  $p = .66$ ) or image quality rating (2.66 vs 2.62,  $p = .80$ ) (Table 2).

In the retrospective study cohort, we included 25 patients (mean age 14, range 0.8–26 years) (Table 3). The diagnoses varied and included tetralogy of Fallot, hypoplastic left heart syndrome, double outlet right ventricle, hypertrophic cardiomyopathy, coarctation of the aorta, and Marfan syndrome. Results of the linear mixed-effect models showed that inter-observer variability of the MVI

**Table 1.** Demographics.

	CMRA patients (n = 24)
Sex, M/F	11/13
Age (years)*	16 (5–52)
Weight (Kg)**	58.8 $\pm$ 24
General Anesthesia	2
History Of CHD	14

\*median (range); \*\*mean  $\pm$  SD; M: male; F: female; Kg: kilogram; CHD: congenital heart disease.

**Table 2.** Prospective cohort results.

	4CH	MVI	CI	p-value ( $\alpha < .05$ )
Vessel wall sharpness*	31.0% $\pm$ 5.5%	30.5% $\pm$ 5.7%	-1.8%–2.9%	.63
RCA vessel length*	5.5 cm $\pm$ 2.6 cm	6.0 cm $\pm$ 2.3 cm	-1.5–0.6 cm	.38
LCA vessel length*	4.7 cm $\pm$ 1.4 cm	4.6 cm $\pm$ 1.6 cm	-0.5–0.8 cm	.66
Overall Image Quality#	2.7 (1.0–3.9)	2.6 (0.3–3.6)		.80

\*mean  $\pm$  SD; #median (range); RCA: right coronary artery; LCA: left coronary artery.

method was 5.4% lower (95% CI 3.7–7.2%,  $p < .0001$ ) than the 4CH cine view orientation method. The intra-observer variability was 3.9% lower with the MVI

method compared to the 4CH cine view method (95% CI 2.4–5.4%,  $p < .0001$ ). MDRP and ESRP were determined using both methods and recorded. The time needed to determine the rest periods did not differ significantly in this small cohort for both methods (4CH  $57.6 \pm 26.0$  s, MVIPC  $52.5 \pm 36.3$  s,  $p = .4$ ) (Table 4). Image quality scores for LCA were comparable to the published literature (median = 3, IQR 3–4).

## Discussion

The study systematically evaluated two methods for determination of cardiac resting periods for acquisition of dual phase CMRA. We found that the mitral valve inflow method was more reproducible in both inter- and intra-observer variability than the 4CH method. There was no difference in the vessel sharpness, vessel length or image quality of the LCA or RCA between both methods. The time needed to measure the rest periods was similar between both methods as well.

Our analysis did not show a significant difference in RCA sharpness compared to LCA sharpness despite the RCA having closer proximity to the surface coils.<sup>17</sup> As the cardiac MRI field continues to advance at a rapid pace, variability in MRI techniques and quality across institutions poses a significant challenge. Creating methods such as the MVI which are based upon physiologic principles readily understood by physicians and MRI technicians alike and which require minimal post processing will allow more centers to utilize dual phase cardiac imaging with minimal training and preservation of image quality

between institutions. The 4CH method has been previously validated as a highly reproducible technique for assessment of coronary artery dimensions between two large institutions.<sup>17</sup> Nevertheless, the 4CH method requires both a high-quality image and a reading physician and MRI technician who have extensive experience with this method for it to achieve commensurate image quality in a highly reproducible fashion as previously described.<sup>17</sup> In our opinion, the MVI technique provides a more illustrative graph of the cardiac rest periods, which are largely responsible for the decreased inter- and intra-observer variability demonstrated in our study cohort and produced CMRAs with comparable image quality to the 4CH method. MVI is also an attractive method for cardiac rest period determination as it is based upon phase contrast quantification, which provides an objective measure that lends itself to future automation and integration into available CMRA software. Mitral-aortic continuity allows for easier imaging of inflow-outflow phase-contrast in a single slice, therefore mitral valve inflow plane was used in our study. However, tricuspid valve inflow imaging could be an alternative method. Because the MVI method is based on the assessment of a simple 1D signal, this process can be easily automatized by simple thresholding algorithms. Such software is attractive for its potential to decrease scan time, but also for its theoretical capacity to improve image quality further through real time adjustments in the acquisition window as a patient's heart rate changes and cardiac rest periods vary throughout the sequence. The future aspirations are for a widely available multi-phase CMRA which will allow for reformatting of images in multiple cardiac phases with no need for determination of resting phases prior to CMRA acquisition.<sup>18</sup> As multi-phase CMRA is yet not widely available, our simple method of using MVI provides a practical alternative.

**Table 3.** Demographics.

	CMRA patients (n = 25)
Sex, M/F	8/17
Age (years)*	14 (0.8–26)
Weight (Kg)**	54 ± 21
History of CHD	17

\*median (range); \*\*mean ± SD; M: male; F: female; Kg: kilogram; CHD: congenital heart disease.

**Table 4.** Retrospective cohort for reproducibility calculations.

	4CH Mean ± STDEV	MVI Mean ± STDEV	P-value	Mean Absolute difference (MVI – 4CH) ± STDEV
MDRP1 beginning (msec)	317.21 ± 39.34	308.37 ± 36.40	0.16	35.04 ± 20.73
MDRP2 ending (msec)	399.47 ± 50.01	386.68 ± 47.53	0.11	38.72 ± 39.8
ESRP1 beginning (msec)	596.33 ± 83.41	576.35 ± 63.91	0.10	48.76 ± 37.00
ESRP2 ending (msec)	737.83 ± 157.83	724.85 ± 145.20	0.60	45.88 ± 44.03
Time needed to measure rest periods (MDRP and ESRP) (Sec)	57.6 ± 26.0	52.5 ± 36.3	0.37	

## Limitations

The 3D MRAs were completed predominately towards the end of each patient's CMRI study to ensure that the clinically indicated sequences were obtained. While all patients enrolled completed all clinically indicated sequences, the

research sequences used in our study data may have been adversely impacted by increased patient motion or decreased cooperation resulting in our overall decreased image quality and vessel sharpness compared to previous studies. The study cohort did not include healthy volunteers.

## Conclusions

Mitral valve inflow technique for determination of systolic and diastolic cardiac resting phases for acquisition of CMRA is feasible and has indicated higher reproducibility compared to hitherto established 4CH CINE visual determination. Mitral valve inflow technique may be used for further standardization and automatization of CMRA planning.



## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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## Abbreviations

CMRA	coronary magnetic resonance angiography
CHD	congenital heart disease
4CH	4-chamber
MVI	mitral valve inflow phase contrast
SSFP	steady-state free precession
MDRP	mid-diastolic rest period
RCA	right coronary artery
RV	right ventricle
LAD	left anterior descending artery
ESRP	end-systolic rest period
FOV	field of view
TR	repetition time

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TE	Echo time	ESRP2	end of systolic rest period
IQR	image quality score	MDRP1	beginning of mid-diastolic rest period
ESRP1	beginning of end systolic rest period	MDRP2	end of mid-diastolic rest period