Potential Clinical Utility of a Free-Breathing Cardiac Magnetic Resonance Imaging Protocol at 3T

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Abstract

Background It is hard for patients with impaired breath-holding (BH) capacity to receive conventional cardiac magnetic resonance (CCMR) imaging.

Purpose To explore the clinical utility of a free-breathing (FB) CMR (FCMR) imaging protocol at 3.0T.

Methods 54 selected patients with suspected heart disease were prospectively enrolled. A total of 30 patients with good BH underwent CCMR protocols first and then FCMR imaging protocols. For other 24 patients with bad BH, CCMR protocols were aborted due to limited BH capacity of patients that led to non-diagnostic image quality (IQ), and the study was finished with FCMR protocols. CCMR included segmented cine and late gadolinium enhancement (LGE) images acquired under BH. FCMR included compressed sensing (CS) accelerated, single-shot cine and motion-corrected (MOCO) single-shot LGE images acquired under FB. IQ of both protocols was evaluated based on a five-point Likert scale. The imaging time, the left ventricular function(LVF), scar presence/absence, and IQ were compared between CCMR and FCMR protocols.

Results The acquisition times of the FB-CS-cine SAX (25 ± 5 s), FB-CS-cine LAX(8 ± 2 s), and FB-MOCO-LGE SAX (120 ± 19 s), FB-MOCO-LGE LAX(37 ± 6 s) were significantly shorter than these with BH-cine SAX (240 ± 13 s), BH-cine LAX (75 ± 16 s) and BH-LGE SAX(331 ± 29 s), BH-LGE LAX(100 ± 9 s) respectively (all $P < 0.001$). For 30 patients that finished both CCMR and FCMR protocols, it was shown that IQ in FB-CS-cine is lower than BH-cine [4 (3-4) vs. 5 (4-5) , $P < 0.001$], however FB-MOCO-LGE is better than BH-LGE [5 (4-5) vs. 3 (3-4), $P < 0.001$]. No significant differences were found in LVF, and LGE presence(all $P > 0.05$). The 24 patients with limited BH capabilities had inconclusive results with the CCMR protocol, but definitive diagnoses were made with the FCMR protocol.

Conclusions FCMR could be used as an alternative scanning protocol in patients with BH impairments, making CMR imaging more widely available also for vulnerable patients.

Introduction

Cardiovascular magnetic resonance (CMR) imaging has become an essential tool for the non-invasive examination of the heart. It has been used for the diagnosis, risk stratification, and prognosis of cardiac diseases [1, 2]. Cine and late gadolinium enhancement (LGE) imaging are routinely included in the conventional cardiovascular magnetic resonance (CCMR) protocols in our center. Data acquisitions are typically performed with breath-holding (BH). While they work well in patients that are capable of holding their breath during image acquisition, such CCMR protocols remain challenging in patients with compromised BH capacities. In addition, the relatively long imaging time hinders the efficiency and throughput at a busy medical center like ours where there is a need to scan over 30 cardiac patients per MRI system per day.

Real-time compressed sensing (CS) cine has been proved to be able to obtain high-quality images for evaluating cardiac function [3–7]. Motion corrected (MOCO) single-shot LGE imaging techniques can also produce high-quality images without BH to detect fibrotic myocardial scars [8–9]. The novelty in this work is that both methods (CS cine and MOCO-LGE) are incorporated for a comprehensive FB CMR study. The feasibility and potential clinical utility of the proposed protocol were evaluated in patients that were unable to hold their breath during CMR imaging.

Materials And Methods

Subject enrollment

After the institutional review board approval was granted, adult patients scheduled for CCMR imaging were prospectively recruited for this study. The inclusion criteria were as follows: in-patient at our hospital scheduled for contrast-enhanced CMR examination, a glomerular filtration rate of ≥ 30 mL/min per 1.7m^2 , and no contraindications for CMR imaging. All patients who received FCMR protocols signed informed consent.

The Cmr Imaging Protocol

CCMR and FCMR scans were performed on a 3 Tesla (T) clinical magnetic resonance imaging (MRI) scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany). The system was equipped with an 18-element body array coil and a 32-element spine array coil. Key sequences for the CCMR included: (1) BH-cine imaging with segmented, balanced steady-state free precession (bSSFP) readout; (2) BH-LGE sequence for viability imaging under breath-hold using segmented, fast low-angle shot (FLASH) readout and phase-sensitive inversion recovery (PSIR) reconstruction. The primary FCMR protocols included: (1) Single-shot FB-CS-cine imaging with bSSFP readout, featuring a two-dimensional sparse data sampling and iterative reconstruction (SSIR); and (2) FB-MOCO-LGE employs non-rigid motion-correction and averaging of multiple single-shot SSFP images with PSIR reconstruction [4]. The BH-cine, FB-CS-cine, BH-LGE, and FB-MOCO-LGE protocols comprised separate 2-, 3-, and 4-chamber long-axis (LAX) acquisitions, and a short-axis (SAX) stack covering the entire left ventricle (LV). All scans were started from running BH CCMR protocols and the process was as follows: (1) If a patient could not hold breath which subsequently led to severe imaging artifacts, CCMR protocols were stopped and FCMR protocols were employed to finish the study. (2) In a cohort of 30 patients that CCMR protocols were successfully finished, FCMR protocols were also added to compare image acquisition times, the left ventricular function (LVF), scar presence/absence, and image quality (IQ). Intravenous gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA) contrast agent was administered at a dose of 0.2 ml/kg of body weight. For all exams, the contrast agent was administered to each patient in one injection. The CMR protocol workflows is illustrated in Fig. 1. Detailed information regarding the sequence parameters of both protocols is shown in Table 1. Both protocols were conducted using semi-automated cardiac day optimizing throughput (DOT) engine software including AutoAlign feature to automatically prescribe the

2-, 3-, and 4-chamber views as well as the short axis stack [10]. Scan parameters like trigger delay were automatically adapted to patient physiology such as patient heart rate.

Table 1

Imaging parameters of the late gadolinium enhancement and cine sequences using CCMR and FCMR protocols

Parameter	CCMR		FCMR	
	BH-LGE SAX	BH-cine SAX	FB-MOCO-LGE SAX	FB-CS-cine SAX
Echo time (msec)	1.96	1.41	1.18	1.2
Repetition time (msec)	5.2	3.3	2.9	2.8
Temporal resolution (msec)	-	45.08	-	42.3
Spatial resolution reconstructed (mm ³)	1.4×1.4×8.0	1.7×1.7×8.0	1.4×1.4×8.0	1.7×1.7×8.0
Bandwidth (Hz/pixel)	287	980	1085	910
Slice thickness (mm)	8	8	8	8
Slice gap (mm)	2	2	2	2
No. of slices	6–13	6–13	6–13	6–13
Flip angle (degrees)	20	50	50	50
Breath holds (n)	6–13	6–13	0	0
Mean acquisition time (s)	331 ± 29	240 ± 13	120 ± 19	25 ± 5
ECG mode	prospective triggering	retrospective gating	prospective triggering	adaptive triggering
CCMR, conventional cardiac magnetic resonance; FCMR, free-breathing cardiac magnetic resonance; ECG, Echocardiography. LGE, late gadolinium enhancement; MOCO, motion correction.				

Image analysis

1. Image quality

All FCMR images were transferred to a workstation (cmr42, Version 5.12.1, Circle Cardiovascular Imaging, Calgary, Canada) for evaluations. For those 30 patients where both FCMR and CCMR images were acquired, FCMR and CCMR were randomly assigned to two senior doctors, Reader 1 and Reader 2, both with more than 5 years of experience in CMR reading, for double-blind evaluation respectively. Image quality scores were evaluated based on a five-point Likert score (5 = excellent, 4 = good, 3 = the presence of artifacts but acceptable, 2 = poor, and 1 = nondiagnostic)[6-8].

2. Left ventricular function (LVF)

LVF measurements were assessed with cmr42 software. Endocardial and epicardial contours were automatically delineated on the short-axis cine images using the cmr42 software and manually adjusted as needed [11]. Papillary muscles and trabeculations of the left ventricle (LV) were included in the ventricular cavity volume measurements. Ejection fraction (EF), end-diastolic and end-systolic volumes (EDV and ESV), stroke volume (SV), and LV end-diastolic mass (LVEDM) measurements were accessed from the cine images acquired in both protocols, and the consistency of measurements between both protocols was analyzed by using linear regression analyses and Bland-Altman plots.

3. Late gadolinium enhancement detection

If LGE involves the subendocardial distribution of coronary artery, it can be identified as ischemic LGE type; otherwise, it can be identified as non-ischemic LGE [12,13].

Statistical analyses

Statistical analyses were performed using dedicated SPSS (version 20.0, SPSS Inc., Chicago, USA) and MedCalc10.0 (MedCalc Software, Ostend, Belgium) software. Continuous data were checked for normality using the Shapiro-Wilk test and presented as the mean $\pm$ standard deviation or median (interquartile range, Q1–Q3), and compared using the T test or Mann-Whitney test. Linear regression analyses were used to evaluate the consistency of quantitative data, correlation coefficients were expressed as R², and Bland-Altman plots analyzed LVF biases between the FB-CS-cine and BH-cine images. P <0.05 was considered statistically significant.

Results

1. Patient characteristics

A total of 54 patients who underwent CMR imaging at our hospital were prospectively enrolled for this study. The average age of these patients was 59 ± 16 years, with a male/female ratio of 40/14. Patients with a history of diabetes mellitus, hypertension, hyperlipidemia, hyperhomocysteinemia, smoking were 15%, 25%, 18.1%, 9.7%, and 40.3%, respectively.

For CMR imaging, 30 patients without BH limitations receiving both protocols for comparing the image acquisition times, LVF, scar presence/absence and IQ. For the other 24 patients, 16 of them underwent FCMR directly because they could not carry out the breath-holding. 8 remaining patients started with CCMR protocols, however, CCMR was aborted due to substantial imaging artifacts from suboptimal breath-holding. Scan sessions for these 8 patients were completed by switching to FCMR protocols.

2. Image acquisition times, image quality, left ventricular function assessment, and LGE detection in 30 patients without BH difficulties that underwent both protocols

The total time of the FB-CS-cine SAX (25 ± 5 s), FB-CS-cine LAX (8 ± 2 s), FB-MOCO-LGE SAX (120 ± 19 s), FB-MOCO-LGE LAX (37 ± 6 s) was significantly shorter than that of the BH-cine SAX (340 ± 30 s), BH-cine LAX (75 ± 16 s), BH-LGE SAX (331 ± 29 s), BH-LGE LAX (100 ± 9 s) respectively, (all P-values < 0.001).

IQ was significantly better in the BH-cine images compared to the FB-CS-cine images [5 (4–5) vs. 4 (3–4), $P < 0.001$]. However, IQ was significantly better with FB-MOCO-LGE compared to BH-LGE [5 (4–5) vs. 3 (3–4), $P < 0.001$]. Figure 2 showed images from one patient acquired with both CCMR and FCMR protocols. Excellent image quality was achieved with both methods in this patient who could hold their breath well for CCMR protocols.

The comparison of LVF parameters between BH-cine and FB-CS-cine is as follows: LVEDV(ml) [127 (105.0–185.7) vs. 128 (100.7–175.5), $P = 0.266$], LVESV(ml) [57.5 (34.7–98.2) vs. 55 (34.7–86.7), $P = 0.673$], LVSV(ml) [74.5 (40.7–86.2) vs. 68 (47.2–87.2), $P = 0.398$], LVEDM(g) [154.5 (90.2–192.5) vs. 147.5 (89.3–194.4), $P = 0.611$], LVEF(%) [57 (27.2–70.0) vs. 57 (26.2–70.2), $P = 0.515$]. There was high consistency (R^2 , 0.881–0.981) between BH-cine and FB-CS-cine for LVF evaluations. The Bland-Altman statistical method was used for intergroup bias analysis (Fig. 3). The mean differences in LVF measurements between BH-cine and FB-CS-cine were as follows: LVEDV, 2.1 (95 % CI: -17.0 to 21.2)ml; LVESV, 0.6 (95% CI: -18.7 to 19.9)ml; LVSV, 1.5 (-12.3 to 15.3%)ml; LVEDM, - 3.1 (95% CI: -37.0 to 30.8)g; LVEF, 0.6 (95 % CI: -7.5 to 8.7) % .

The BH-LGE and FB-MOCO-LGE measurements could detect LGEs similarly, including 4 cases with ischemic LGEs, 15 cases with non-ischemic LGEs, and 11 cases with negative results.

3. CMR Findings

Of those 30 patients without BH limitation, only one case was uncertain by CCMR, but was diagnosed as thrombus by FCMR (Fig. 4). No difference was found in another 29 patients. In other 24 patients with inconclusive CCMR results, definitive diagnoses were made with the FCMR protocol in all patients, with positive diagnoses in 20 patients and negative diagnoses in 4 patients. Figures 5–6 show some cases were definitively diagnosed by FCMR protocols.

Discussion

FCMR and CCMR protocols had comparable image quality ratings, left ventricular function assessment, and myocardial scar detection when both protocols were successfully obtained. The total acquisition time of FCMR including FB-CS-cine and FB-MOCO-LGE was significantly shorter than that of the CCMR

including BH-cine and BH-LGE. This finding indicates that the FCMR protocol has feasibility in assessing cardiac function and myocardial viability. Furthermore, our results showed that the FCMR protocols could improve cardiac disease detection in patients with limited BH capabilities.

The CCMR imaging protocol requires multiple breath-holds to provide diagnostic image quality [14, 15]. Generally, each BH takes 8–15 seconds per slice, with an additional pause that lasts 10 seconds before the next breath-hold session. Such repeated BH requirements can be challenging for patients who cannot hold their breath for extended periods. Also, to achieve sufficiently high spatial and/or temporal resolutions during CCMR imaging, segmented k-space data are acquired over multiple heartbeats. Such segmented acquisition is prone to motion artifacts that could lead to repeated scans in case of suboptimal breath-holding. In our clinical setting, a few of the patients were unable to complete the CCMR examinations due to impaired BH capacity. The FCMR protocol not only removes the BH barrier which is particularly important for scanning most vulnerable patients with compromised BH capability, it also improves the scan efficiency. In addition, single-shot readout effectively eliminates breathing motion artifacts in both FB-CS-cine and FB-MOCO-LGE images [14–16]. High quality images were acquired for cine with CS acceleration, the high image quality of the CS technique translated into high agreement for LVF. Also, high quality images were acquired for LGE by combining non-rigid MOCO and averaging of multiple single-shot measurements. High agreement between the BH and FB MOCO technique was also achieved for LGE, with a non significant difference of LGE presence or types.

Our study found that there was no difference in LVF calculation and LGE detection between CCMR and FCMR images obtained from 30 patients without BH impairment, which was consistent with previous studies[3–5, 7–9]. However, the study show that the IQ in FB CS cine is lower than BH cine. We observed that FB-CS-cine scans sometimes lead to a little of image blurring and low spatial resolution. There were some reasons as following [17]. First, FB-CS-cine was susceptibility for fold over artifacts, therefore, the field of view must cover the entire anatomy, and thus, some penalty in spatial resolution may occur in relation to the patient's anatomy. Second, in some scans, flow-related artifacts occurred in the phase-encoding direction during systole because the sparsity in the temporal domain may be limited in anatomic regions of very high flow.

Overall, FCMR imaging leads to consistent images for diagnosis in all patients, regardless of whether they could hold their breath or not. In comparison, the IQ of CCMR depends on the BH capability of a patient during data acquisition. For patients with BH impairment, CCMR images suffer from severe motion artifacts, interfering the radiologist' ability to interpret morphologic cardiac structures, cardiac function calculations, and LGE detection. FCMR obtained consistently good quality images even in patients with compromised BH capabilities. It has been shown to be an effective alternative to CCMR in this study, expanding the application range of CMR imaging.

Limitations

There were several limitations to this study. First, the current study assessed FCMR and CCMR scans in patients with various cardiac diseases, complicating the comparison of the two protocols. Secondly, no advanced MRI sequences, such as mapping, perfusion, and flow quantification were performed in the study since they are not part of the standard CMR protocols at our institution. Thirdly, we have not yet assessed the incremental benefit of T2-weighted short-tau inversion recovery imaging to identify edema because there is no optimized free-breathing sequence available. Finally, the sample size is relatively small, only 24 patients with BH impairment need FCMR as a replacement for CCMR. The encouraging results from this study warrants future study with a larger sample size to demonstrate the clinical utility of free-breathing CMR.

Conclusions

We demonstrated that FCMR imaging could be used as an alternative technique in patients with BH impairment to obtain high-quality images. FCMR significantly shortens the time needed for CMR imaging and resulted in improved image quality. We believe that the FCMR protocol will allow the fast screen of cardiac diseases in clinical practice, with the potential to increase both the throughput and robustness of CMR.

Declarations

Funding

None

Competing interests

The authors declare that they have no competing interests.

Code availability

Not applicable

Authors' contributions

KY Wang conceived the study, performed statistical analysis, and drafted the manuscript. XM Bi participated in design of the study, assisted in the interpretation of the results, and helped to revise the manuscript. Michaela Schmidt contributed to the sequence development, implementation on the scanner and helped to revise the manuscript. Jing An participated in the design of the study and coordination and helped to revise the manuscript. Jie Zheng helped to revise the manuscript. Jingliang Cheng assisted in the interpretation of the results and helped to revise the manuscript. Shuman Li and WenBo Zhang quantitatively measured cardiac function, and made the diagnosis respectively. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Approval was obtained from the local ethics committee. The number is 2019-LW-029. All subjects/ legal guardians gave written consent and assent as appropriate.

Consent to participate

Consent for publication

The local ethics committee approved the use of images and content from this study. Consent and assent were signed for all subjects prior to publication.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

Figure 1

The workflow design for the breath-holding (BH) conventional cardiac magnetic resonance imaging (CCMR) protocol and free-breathing cardiac resonance (FCMR) protocol. Abbreviations: HASTE, Half-Fourier-Acquired Single-shot Turbo spin Echo; MOCO, motion-corrected; LGE, late gadolinium enhancement; CS, compressed sensing.

Figure 2

These images show a randomly selected patient that did not have breath-holding (BH) impairment. The free-breathing cardiac magnetic resonance (FCMR) protocols were performed after the conventional cardiovascular magnetic resonance (CCMR) protocols. Both protocols showed excellent image quality that had a 5-point rating. The display of cine-CMR images in both protocols showed that the patient suffers from heart failure with an enlarged left ventricle. The corresponding BH-late gadolinium enhancement (LGE) and motion-corrected (MOCO)-LGE views showed normal in this patient.

Figure 3

Bland-Altman plots for left ventricle (LV) functional parameters in breath-hold cine MRI and free-breathing compressed-sensing cine MRI derived a cohort of 30 patients. A, LV ejection fraction (LVEF); B, LV end-diastolic volume (LVEDV); C, LV end-systolic volume (LVESV); D, LV stroke volume (LVSV); and E, LV end-diastolic myocardial mass (LVEDM). SD = standard deviation.

Figure 4

Images of a patient with an uncertain diagnosis on conventional cardiovascular magnetic resonance (CMR) imaging. A shadow was shown on the 4-chamber breath-holding (BH)-cine (a2) and BH-late gadolinium enhancement (BH-LGE) images (b2); however, it was uncertain that the lesion was an artifact, tumor, or thrombus. On free-breathing cardiac magnetic resonance (FCMR) imaging, an abnormal signal oscillated with the cardiac cycle at FB-CS-cine (a1), and no enhancement was found on motion-corrected (MOCO)-LGE images(b1,c). We, therefore, diagnosed a thrombus, which was confirmed on histopathology(d).

Figure 5

Conventional cardiovascular magnetic resonance (CCMR) imaging was performed first. Free-breathing CMR (FCMR) imaging was performed additionally due to poor image quality on the CCMR images. Obvious artifacts were found on the CCMR imaging, and the image quality was poor. There were no artifacts on FCMR imaging, and the image quality had a 5-point rating. The corresponding breathing hold late gadolinium enhancement (LGE) images demonstrate non-diagnosis (artifact or non-ischemiac LGE).

However, enhancements can be seen in the epicardial sidewall(e2,f2,g2,white arrow), and intramural contrast enhancements are present in the anterior wall (e2,h2,yellow arrow) on free-breathing motion-corrected (MOCO)-LGE images.

Figure 6

Images show a few cases with various cardiac diseases acquired with breath-holding (BH)-LGE (top row) and corresponding motion-corrected (MOCO)-late gadolinium (LGE) (bottom row) acquired under free-breathing. Top row: Pictures (a1–d1) show non-diagnostic BH LGE imaging. Bottom row: corresponding FB-MOCO-LGE images with the following diagnosis: (a2) Negative; (b2) An apical transmural myocardial infarction with a left anterior descending (LAD) distribution; (c2) Hyperenhancement at the junction of the interventricular septum and the right ventricular free wall; (d2) Hyperenhancement involve of the mitral valves and intramural septa.