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Original Article

Image Evaluation of Free-breathing Navigator Echo and Triggered Cardiac-gated Delayed Myocardial Enhancement Magnetic Resonance Imaging in Sedated Infants

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We validated a navigator-echo-triggered sequence that drives magnetization before cardiac-gated inversion recovery T1 turbo field echo acquisition, in the sedated free-breathing pediatric population. Cardiac magnetic resonance imaging was performed on sedated infants with single ventricle. We calculated the signal-to-noise ratios and contrast-to-noise ratios of 2 groups of images obtained using respiratory triggering with and without navigator echo. All images were then visually assessed by 2 observers. The signal-to-noise ratio and the contrast-to-noise ratio were significantly higher with than without navigator echo ($p<0.01$; $p<0.05$). The visual assessment scores were also consistently better with than without navigator echo ($p<0.01$). Free-breathing navigator echo was found to have the advantage of decreasing the motion artifact caused by respiration. Cardiac-gated inversion recovery T1 turbo field echo sequence for free-breathing navigator-echo-triggered respiration allows for the acquisition, in sedated infants, of diagnostic images whose quality exceeds that of the non-navigator-echo-triggered alternative.

Key words: magnetic resonance imaging, navigator echo, inversion recovery T1 turbo field echo, cardiac, infant

Single ventricle is a rare and complicated congenital cyanotic cardiovascular anomaly, accounting for only 2-3% of all congenital heart malformations. A single ventricular patient has one underdeveloped or one functional ventricle [1]. Typically, three surgical operations are required in the first few years of life to sustain infants born with a single functional ventricle [2].

Before each surgery at our hospital, an infant patient undergoes a computed tomography (CT) and magnetic resonance imaging (MRI) examination. These examinations are necessary to diagnose the status of the cardiac system [3]. In patients with risk(s) requiring a high sedation or general anesthesia, or in patients requiring emergent imaging, the cardiac CT (CCT) often represents an excellent, rapid, noninvasive alternative to provide diagnostic information [4-7]. On the other hand, the cardiac MR (CMR) examination is an established modality for the evaluation of congenital heart disease (CHD) [8-12]. Late gadolinium enhancement (LGE) is an optional examination performed for routine examination of CHD. LGE is useful for the histopathological diagnosis of ischemic heart disease, cardiomyopathy, cardiac mass, and regional fibrosis [13, 14]. CMR examinations using LGE are performed for an infant with CHD at our hospital. There are two reasons

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for assessing the contrast enhancement MR examination in this CMR examination: to (1) obtain more information for treating CHD infants, and (2) assess whether myocardial fibrosis and surgical complications are important factors in the selection of future therapeutic outcomes. However, there are many restrictions involved in the examination of an infant with CHD. The sequences and parameters to be used must be determined to be suitable for the infant's body. Moreover, infants have a high heart rate and cannot hold their breath. Their breathing during the scanning of the LGE sequence becomes a motion artifact in the LGE image. The image quality deterioration due to the infant's respiration must be addressed. In the present study, we focused on the use of a navigator-echo-triggered sequence, which is used in the coronary angiography MR examination of infant with Kawasaki disease. The navigator-echo MR imaging technique makes it possible to obtain high-quality images in complete 3D visualization of the main coronary artery and images of the liver and pancreas without blurring [15, 16].

In our study, we validated a navigator-echo-triggered sequence that drives the magnetization before cardiac-gated inversion recovery-T1 turbo field echo (IR-T1TFE) acquisition in a sedated free-breathing pediatric population. We evaluated the usefulness of the combination of electrocardiogram (ECG)-triggered and navigator-echo-triggered sequences in sedated infants.

Patients and Methods

Patient selection. The approval (1610-562) of our hospital's ethics committee was obtained before this retrospective study was begun. The LGE examination was performed as part of clinical trial on sedated infants with a single ventricle. The data analyzed in the present study were collected from 76 LGE examinations performed on 33 patients with a single ventricle (15 females, 18 males; mean ± SD age, 2.3 ± 1.4 years; range, 0-5 years) from November 2013 to October 2014. Several patients who underwent multiple LGE examination were included. The LGE examinations were part of preoperative, postoperative and follow-up care. Written informed consent was obtained from the parents of each child, permitting them to participate in the clinical trial and allowing the anonymous use of the eliminated data for research purposes. Our study population excluded infants who discontinued the examination and could not be examined according to the clinical trial protocol.

CMR examination in sedated infants. It was necessary to sedate each patient for the LGE examination to inhibit body motion.

Imaging was performed using a 1.5-T MR scanner (Achieva 1.5T, Philips Medical Systems, Amsterdam, The Netherlands). The SENSE Flex-M coil (4-channel coil, Philips Medical Systems) was chosen as a cardiac coil for its high versatility and ability to adhere to the infant's body [16]. One coil was set on the patient's chest and the other coil was set on his or her back.

The entire LGE examination protocol is shown in Fig. 1. Gadoteridol (Gd-HP-D03A, ProHance; Bracco Diagnostics Inc., Milan, Italy) was used at the dosage of 0.4 mL/kg, as the contrast medium. The contrast media was injected before the inversion time (TI) scout imaging (Look-Locker) sequence was scanned. The IR-T1TFE sequence, here termed the "early image," was scanned immediately after measuring the TI value from the Look-Locker sequence. A second Look-Locker sequence was scanned 7 min after contrast media injection was completed. Similarly, the IR-T1TFE sequence LGE imaging was scanned immediately after the TI value was measured. At the end of the examination, IR-T1TFE sequence was scanned without navigator echo. The total LGE examination time was approx. 1 h.

LGE sequences (IR-T1TFE). In this study, respiratory synchronization was appended to the LGE sequence. The details of the IR-T1TFE sequence and parameters are given in Table 1. The IR-T1TFE sequence was scanned in the ventricle short axis (SA) direction. For the subjects of this study, we employed a slice thickness of 4 mm, and a field of view (FOV) of 200 mm. We opted against the use of sensitivity encoding (SENSE), because of the parallel imaging factor, favoring image clarity instead [17, 18]. The TI in each sequence was changed to make the myocardium the null point. The null point plus 50 msec was chosen as the TI, which the ECG triggered in the navigator-echo-triggered sequence, whereas the ECG-only-triggered sequence began at plus 70 msec. The R-R window in which systolic phase images are acquired represents the point when the heart is temporarily at rest. For our subjects, the navigator echo voxel was set at a length of 60 mm, and the gating window was set at a width of 5 mm. A vertical navigator through the dome of the right hemidiaphragm was planned using coronal and

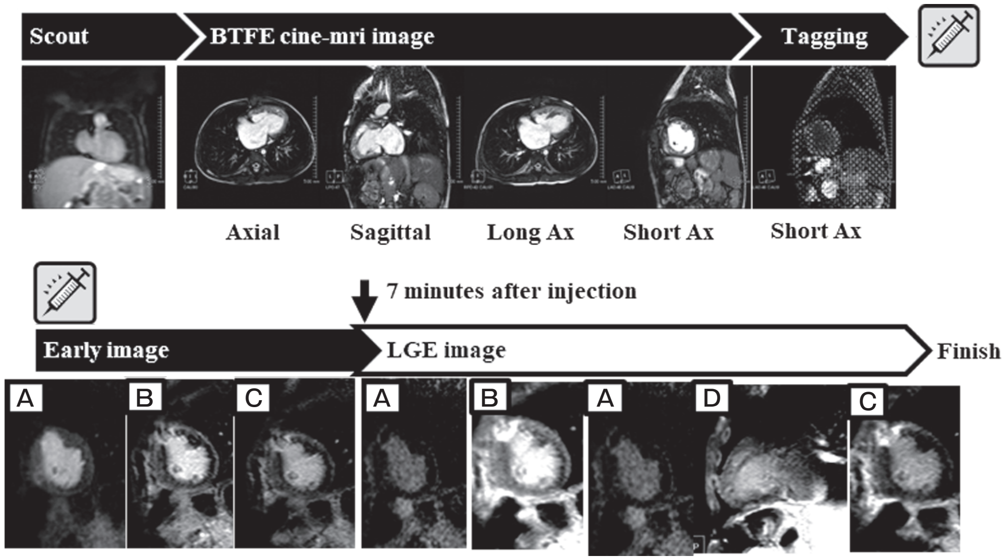

Fig. 1 Timetable of the late gadolinium enhancement (LGE) examination. A, Short axial (Ax) image scanned by Look-Locker sequence; B, Short axial image scanned by the IR-T1TFE with navigator echo sequence; C, Short axial image scanned by the IR-T1TFE without navigator echo sequence; D, Sagittal image scanned by the IR-T1TFE with navigator echo sequence. BTFE, balanced turbo field-echo.

Table 1 IR-T1TFE with navigator echo sequence and parameters

Parameter	
TR	Shortest
TE	Shortest
FA	15°
TFE shots	25 shot
NSA	1 time
Slice thickness	4 mm
Number of slices	16 slice
FOV	200 × 200 mm
Image matrix	320 × 223 pixels
SENSE	Not used
TFE prepulse	Invert
Inversion delay time	Null point + 50 msec
Cardiac synchronization	Trigger
Navigator respiratory compensation	Gate and track

IR-T1TFE, inversion recovery T1 turbo field echo; TR, time to repeat; TE, echo time; TFE, turbo field echo; FA, flip angle; NSA, number of sample (signals) averaged; FOV, field of view; SENSE, sensitivity encoding.

transverse scout images [19]. The sequence without navigator echo was scanned to assist diagnosis.

Image analysis. We evaluated the quality of the images based on the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR), and by visual assessment. The results of these assessments were compared between the images obtained with and without the use of navigator echo for respiratory triggering. We used the standard short-axis LGE images for the image analyses.

We determined and evaluated the SNR values by obtaining the average pixel value from a picture archiving and communication system (PACS) based on the Digital Imaging and Communications in Medicine (DICOM) file image obtained from each pulse sequence (IR-T1TFE with and without navigator echo). The SNR images were evaluated and compared with the use of an Image Processing Workstation (Virtual Place Raijin Plus, AZE, Ltd., Tokyo, Japan). Regions of interest (ROIs) were defined to determine the signal intensity (S) from myocardium (S_M) and the signal intensity from reference tissue, such as that of the ventricle (S_V). Each ROI with an area of 40 mm^2 (approx. 70 pixels) was drawn by one of the study's authors who had 3 years of experience in cardiovascular MRI (R.M.) on IR-T1TFE images about three chosen short-axial planes (Apex: cardiac apex, Base: cardiac base, and Mid: an intermediate position between the cardiac base and apex). These ROIs were placed on the anterior, inferior, and lateral walls, and in the blood pool on each plane. Each location determination and drawing of the ROI were performed by mutual consent between one author (R.M.) and another author who is a special radiologist with > 20 years' experience in cardiovascular MRI (S.S.). The signal intensities of 630 pixels in 9 ROIs were used for the calculation of the SNR about the myocardium. Noise (N) was estimated, along with the associated standard deviation, for each of these ROIs. The SNR was calculated by dividing the signal intensity of the ventricle myocardium by the noise of this tissue. The SNR was therefore defined as follows: $SNR_M = S_M / N_M$.

CNR values were calculated for SNR values using the values of myocardium (SNR_M) and the values of ventricle (SNR_V). The CNR in the single ventricle was defined as follows: $CNR = |SNR_M - SNR_V|$. Just as in the case of the SNR, the final CNR value in each examination was taken as the average value of the three cross-sections measured.

All the images were visually assessed by one radiological technologist (R.M.) and one radiologist (S.S.). Although, the study images had already been used to arrive at diagnoses by radiologists, the results of diagnoses were not provided to the observers beforehand. Fig. 2 shows the images upon which each visual assessment score was based. Image quality was scored as follows: 'poor,' difficult to diagnose with severe motion artifact; 'good,' easy to diagnose but with motion artifact; and 'excellent,' easy to diagnose without motion artifact. On this scale, the grades 'good' and 'excellent' were considered to be of diagnostic quality. Study image scores were discussed by 2 observers before the final grade was given.

Statistical analysis. The Wilcoxon signed rank test was performed to compare the SNR and CNR results of the 2 image groups, *i.e.*, those with and without navigator echo. The Mann-Whitney *U* test was also performed to compare the visual assessment results of the 2 groups. *P*-values ≤ 0.05 were considered significant. All statistical analyses were conducted using R software (R × 64 ver. 3.3.1, R Foundation for Statistical Computing, Vienna, Austria).

Results

SNR. The SNR results are shown in Table 2. The mean ± SD SNR value with navigator echo (21.7 ± 5.4%) was significantly higher than that without navigator echo (18.6 ± 4.7%; $p < 0.01$). The SNR value with navigator echo was also high in each of the slice positions assessed, and was significantly higher than the SNR value without navigator echo at the cardiac apex, mid-

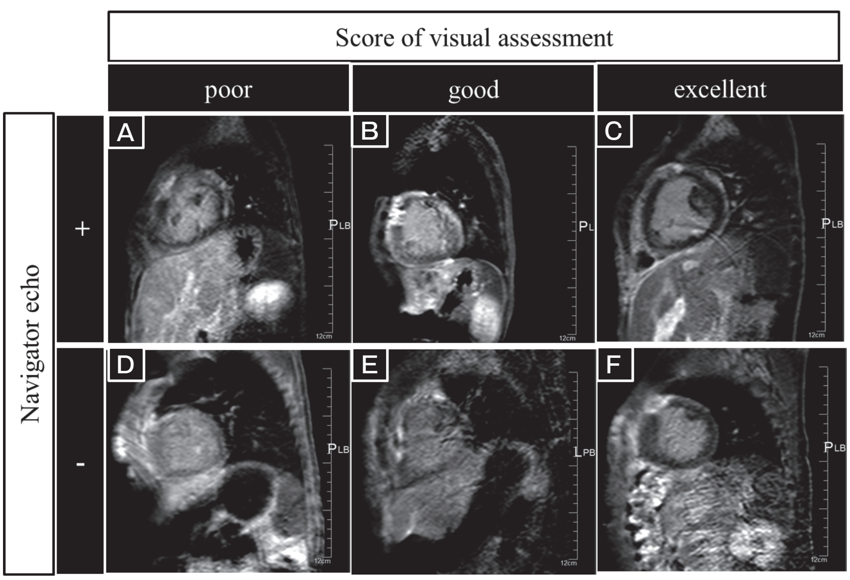

Fig. 2 Clinical images for each visual assessment score in the LGE examinations. The images of the upper lines (A–C) are those scanned by the sequence with navigator echo. The images of the lower lines (D–F) are those scanned without a navigator echo. **A**, A 2-year-old boy's LGE image in which the myocardium shows some movement; **B**, A 7-month-old boy's LGE image scored as 'good' quality. In the contrast between ventricular and myocardial regions, it is worse than 'excellent'-scoring images; **C**, A 2-year-old boy's LGE image in which the myocardium shows clearly; **D**, A 1-year-old boy's LGE image scored as 'poor' quality, chiefly for its poor myocardial contrast; **E**, A 2-year-old girl's LGE image showing slight movement; **F**, A 1-year-old girl's LGE image in which the myocardium is clearly shown.

Table 2 Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR)

Heart measurement position	SNR			CNR		
	ECG, NE	ECG	*p*-value	ECG, NE	ECG	*p*-value
Average of three positions	21.7 ± 5.4	18.6 ± 4.7	< 0.01	16.9 ± 7.1	13.7 ± 8.1	< 0.05
Base	21.6 ± 9.2	17.8 ± 5.9	< 0.05	17.4 ± 10.5	13.9 ± 12.6	0.08
Mid	20.8 ± 8.9	17.8 ± 6.9	< 0.05	17.0 ± 12.8	14.3 ± 9.9	0.36
Apex	22.4 ± 9.4	19.6 ± 6.8	< 0.05	16.0 ± 12.0	12.8 ± 10.4	0.24

ECG, NE, electrocardiogram-triggered and navigator-echo-triggered; ECG, electrocardiogram-triggered without navigator-echo-triggered. Statistical analysis: Wilcoxon signed rank test.

Table 3 Visual assessment scores

		No. of examinations (%)	
		ECG, NE	ECG
Visual assessment score	Poor	11 (14)	18 (24)
	Good	37 (49)	46 (61)
	Excellent	28 (37)	12 (16)
p-value		< 0.01	

The visual assessment scores associated with the navigator echo triggered sequence images were significantly higher than those obtained without navigator echo ($p < 0.01$). Statistical analysis: Mann-Whitney *U* test.

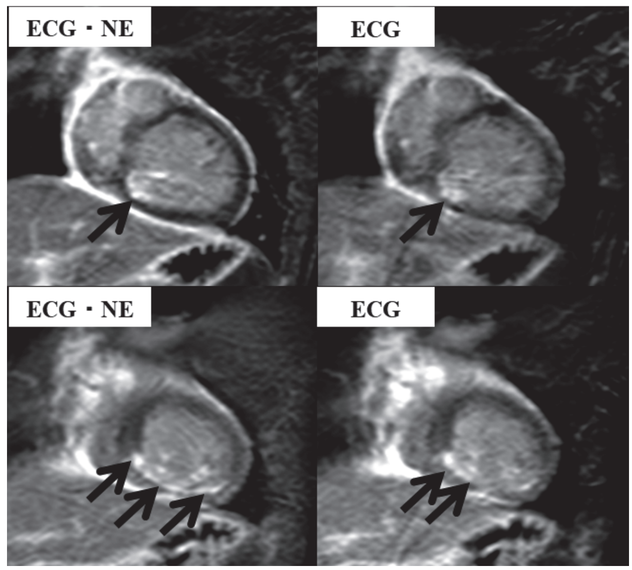

Fig. 3 Comparison of image quality and the appearance of the contrast-enhanced area in an 11-month-old boy's LGE images. The left images were scanned by the sequence with navigator echo. The right images were scanned without navigator echo. The right and left images are at the same slice position. Arrows (→) indicate the enhancement areas in the left images are clear and inform the diagnosis of regional fibrosis.

dle, and base locations ($p < 0.05$).

CNR. The CNR results are shown in Table 2. The CNR value with navigator echo (16.9 ± 7.1%) were significantly higher than those obtained without navigator echo (13.7 ± 8.1%; $p < 0.05$). In each cardiac position assessed, the CNR value with navigator echo was higher than that obtained without navigator echo.

Visual assessment. The results of the visual assessment are summarized in Table 3. The visual assessment scores with navigator echo was consistently significantly better than those without navigator echo ($p < 0.01$). In a within-subject comparison, the visual assessment scores achieved with the navigator echo sequence in 25 examinations were better than those achieved without navigator echo. Indeed, in 16 examinations that were designated as being of 'good' quality in the sequence without navigator echo, the scores were raised to the designation of 'excellent' in the sequence with navigator echo. The sequence with navigator echo provided 'good' or 'excellent' images with a probability of 86% or more. Fig. 3 provides clinical images (left-side images using navigator echo) of an 11-month-old boy with CHD: clearer enhanced myocardium is observed and can be used to verify how the myocardium is enhanced. The density of this area is higher and the enhanced myocardium clearer than on the right side. The advantages of delayed enhancement and navigator echo are thus demonstrated.

Discussion

The respiratory motion artifact in CMR examination using LGE of infants who are sedated causes severe image deterioration. We focused on the navigator echo which is operated under free breathing and conducted a clinical study to reduce this artifact. An SNR and CNR evaluation and visual assessment were performed on 76 LGE images performed on 33 infants. In the measurements of SNR and CNR by MR signal intensities, we paid attention to the setting of the ROIs in order to maintain the accuracy of the analysis because the myocardium of an infant is very thin; the average thickness of the myocardium in the 76 examinations in this study was 4 mm. Therefore, the SNR and CNR values were calculated with the signal intensities of 630 pixels in 9 ROIs on three cross-sections. We concluded that a sufficient number of samples was secured for significance testing. The results showed the effectiveness of navigator echo. The image quality was also scored in visual assessments, and the navigator echo was shown to provide high score images in these assessments. Our present results demonstrated the usefulness of the navigator echo trigger sequence.

Infants breathe 40 to 60 breaths per min, and infants with cyanosis have increased breathing frequency. The motion artifact that occurs due to this respiration reduces the image quality of MR images. Because the navigator echo always detects the diaphragm signal, the cardiac signal could be acquired at the same diaphragm position and motion artifact could be decreased.

With respect to visual assessment, in the navigator echo sequence, the proportion of the images in our study with an 'excellent' score was 37%, which is far higher than the images obtained with the sequence without navigator echo (16%). This result shows the overwhelming usefulness of navigator echo. If the image quality level at which the diagnosis is easily obtained is set as the 'good' grade or higher, it may be the use of nonuse the navigator echo. The sequence with navigator echo provided 'good' and 'excellent' images with a probability of 86%, whereas the sequence without navigator echo provided these images with a probability of 77%. The difference is only 9%, but is considered to be meaningful for infants. However, since the use of the navigator echo extended the scanning time, we were concerned that the signal intensity of the myocardium would be recovered. Even if the scanning time was extended, myocardial signal reduction was not observed at an extent great enough to interfere with the diagnosis of fibrosis. When diagnosing with LGE images, it is important that the shape of the myocardium and the contrast-enhanced area are clear within the image. In the Fig. 3, the images with navigator echo showed a clear shape of the myocardium, and enhanced areas were observed sharply (as shown by arrows). Therefore, the LGE image with navigator echo had high spatial resolution due to the reduction of motion artifact. However, since 'poor'-scoring images were obtained in 14% of the examinations, the cause of this reduced quality must be considered. In these images, the myocardium was blurred or the contrast between the ventricle and myocardium was low, and the diagnosis of fibrosis was difficult. For the benefit of clinicians and researcher conducting similar work, we mention the location of navigator echo and the adjustment of the inversion delay time. Normally, the location of navigator echo should be where the diaphragm moves most. If the diaphragm does not move considerably, it is desirable to move the navigator echo to another location, such as the ventricle as in the study described by Michael *et al.* [20]. When the heart rate is low (below 80 bpm) and thus respiratory motion is slow, the scanning time is extended. In such cases, it is better to set the inversion delay time to the null point plus 50 msec or more.

The present study was limited by its retrospective design, small sample, low number of observers involved in the visual assessment, and the scoring of the visual assessment (graded as simply poor, good, or excellent because it was difficult to decide on the evaluation criteria). Many factors influence the results of the visual examination of an LGE image, including contrast between myocardium and ventricle, the slice orientation, and blurring or enhancement due to arrhythmia, among other factors.

In conclusion, cardiac-gated IR-T1TFE sequence for free breathing and using navigator-echo-triggered respiration allows for the acquisition of clinical images with improved spatial resolution, contributing to the diagnosis of sedated infants.

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