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MAJOR PAPER

Single-Breath-Hold Whole-heart Unenhanced Coronary MRA Using Multi-shot Gradient Echo EPI at 3T: Comparison with Free-breathing Turbo-field-echo Coronary MRA on Healthy Volunteers

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Purpose: We investigated the feasibility of single breath hold unenhanced coronary MRA using multi-shot gradient echo planar imaging (MSG-EPI) on a 3T-scanner.

Methods: Fourteen volunteers underwent single breath hold coronary MRA with a MSG-EPI and free-breathing turbo field echo (TFE) coronary MRA at 3T. The acquisition time, signal to noise ratio (SNR), and the contrast of the sequences were compared with the paired *t*-test. Readers evaluated the image contrast, noise, sharpness, artifacts, and the overall image quality.

Results: The acquisition time was 88.1% shorter for MSG-EPI than TFE (24.7 ± 2.5 vs 206.4 ± 23.1 sec, $P < 0.01$). The SNR was significantly higher on MSG-EPI than TFE scans ($P < 0.01$). There was no significant difference in the contrast on MSG-EPI and TFE scans (1.8 ± 0.3 vs 1.9 ± 0.3, $P = 0.24$). There was no significant difference in image contrast, image sharpness, and overall image quality between two scan techniques. The score of image noise and artifact were significantly higher on MSG-EPI than TFE scans ($P < 0.05$).

Conclusion: The single breath hold MSG-EPI sequence is a promising technique for shortening the scan time and for preserving the image quality of unenhanced whole heart coronary MRA on a 3T scanner.

Keywords: *coronary angiography, magnetic resonance imaging, respiration, men*

Introduction

Unenhanced whole-heart coronary MRA is a noninvasive modality for the detection of coronary artery disease.[1,2] Steady-state free precession (SSFP) 1.5T imaging has been widely used for coronary MRA, and its high diagnostic accuracy for the detection of significant coronary arterial disease (CAD) has been reported.[3,4] In addition, previous report suggested the usefulness of single breath hold unenhanced coronary MRA with turbo field echo (TFE) technique.[5] They reported that the single-breath hold technique can shorten the total scan time and reduce the influence of respiratory motion. On the other hand, this sequence suffers from sensitivity to B0 inhomogeneity at 3T MRI.[6] Consequently, the gradient echo sequence with the T_2 preparation (T_2-prep) pulse has been used generally for coronary MRA at 3T MRI. However, the signal to noise ratio (SNR) of TFE with the T_2-prep pulse tends to be lower than of SSFP[6] and the acceleration factor of parallel imaging cannot be easily increased at 3T unenhanced coronary MRA, and there were only a few reports about the usefulness of single breath hold unenhanced coronary MRA at 3T MRI.[5,7,8]

Single shot echo planar imaging (EPI) is a kind of gradient echo- and the fastest acquisition method currently available for clinical MRI (less than 100 ms/slice), however, it is sensitive to off-resonance artifacts and its spatial resolution is limited.[9] Multi-shot gradient (MSG)-EPI[10,11] is a hybrid technique that combines TFE- and EPI scanning without a radiofrequency (RF) refocusing pulse; its scanning speed and artifacts are intermediate. Some studies suggested

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that it can be used for coronary MRA.[12,13] However, its most serious limitation is the low SNR without contrast media.[11,14] To overcome this problem, previous reports used only one RF excitations per heart-beat with a high flip angle.[12,13] However, while this approach increased the SNR it prolonged the scan time and undermined the advantage of MSG-EPI. Therefore, this sequence has not been widely used for unenhanced coronary MRA. Recent 3T MRI systems may overcome the disadvantages of MSG-EPI at unenhanced coronary MRA. Theoretically, the SNR is proportional to the static field strength. This implies that the SNR on 3T- is twice as good as on 1.5T MRI scans.[15] Multi-source RF transmission with patient-adaptive local RF shimming facilitates uniform RF shimming at 3T cardiac MRI.[16] This technique improves B1 homogeneity, and it can increase the image contrast by applying a T_2-prep pulse with high-power refocusing pulses.[17] We posited that these advantages might increase the SNR and enable us to use MSG-EPI for unenhanced coronary MRA.

Therefore, we hypothesized that MSG-EPI can drastically shorten the scan time and enable us to perform the single-breath-hold unenhanced coronary MRA with comparable image quality compared with free breathing TFE coronary MRA. However, to our knowledge, there are no reports on single-breath-hold unenhanced whole heart coronary MRA with MSG-EPI at 3T MRI.

We investigated the feasibility of using the single-breath-hold MSG-EPI sequence for three dimensional (3D) unenhanced whole-heart MRA on a 3T MRI scanner in healthy volunteers.

Materials and Methods

Subjects

This prospective study received institutional review board approval; prior informed consent to participate was obtained from 15 healthy male volunteers. All underwent imaging consecutively between November and December 2015. The data from one volunteer were subsequently excluded due to severe motion artifact and a high variation in the heart rate (60–90 beats/min). The age of the 14 included volunteers ranged from 25 to 46 years (mean 31.4 ± 6.8); their heart rate from 49 to 75 beats (mean 63.1 ± 7.3) per minute, and their body weight from 52 to 87 kg (mean 64.5 ± 9.9).

MR angiography acquisition

All subjects underwent imaging on a 3T MRI scanner (Ingenia-CX, Philips Medical Systems, Tokyo, Japan) using a 16-element phased-array direct digital RF receiver coil and vector electrocardiographic gating.[18] A multi-slice gradient echo (TR = 2.6 ms, TE = 1.27 ms, α = 20°) 3D scout scan was acquired in three orthogonal orientations to determine the volume for whole-heart imaging. Then an axial Electrocardiogram (ECG) triggered, segmented SSFP cine image series (TR = 2.6 ms, TE = 1.28 ms, α = 45°, temporal resolution 10 ms) was acquired during a single breath-hold at the level of the proximal-to-mid right coronary artery (RCA) to visually identify the most quiescent period in the cardiac cycle. It was used to set the trigger delay and the short duration.

Using the visually identified trigger delay, we performed 3D whole-heart MRA with MSG-EPI and TFE. We acquired images with MSG-EPI and TFE during the diastolic phase of the cardiac cycle. No contrast agents were injected. A T_2-prep pulse (TE = 50 ms) constructed with four refocusing pulses was applied to increase the contrast of natural T_2 differences between blood and the myocardium. Spectrally selective fat saturation was used to enhance the endogenous image contrast between the coronary blood pool and surrounding fat.

The schematics of the 3D TFE and the single breath hold MSG-EPI sequence are shown in Fig. 1. The MSG-EPI sequence is similar to single shot gradient-type EPI, except that rather than sampling the k-space completely with one shot, several acquisitions are used. With the MSG-EPI sequence, many

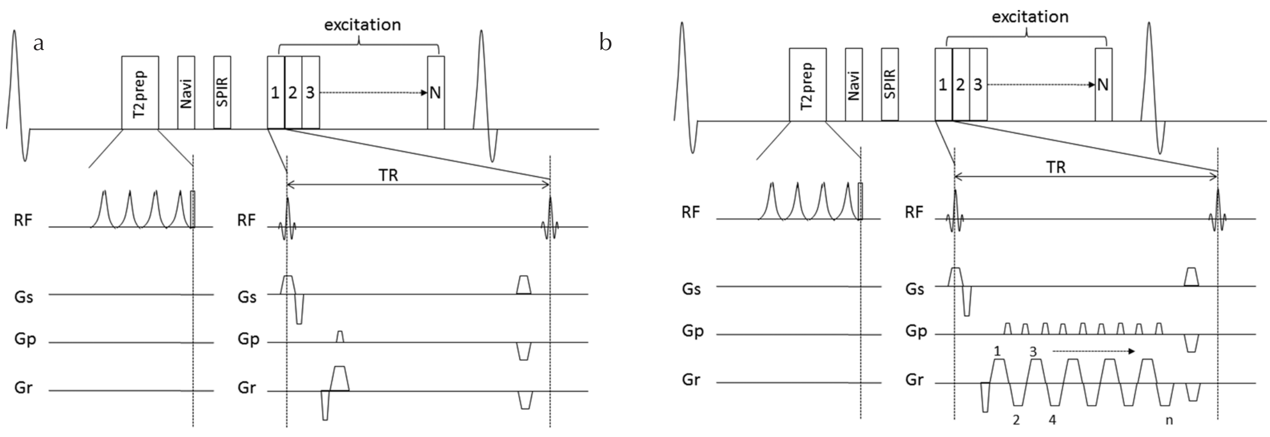

Fig. 1 Pulse sequence scheme. A T_2-prepared (T_2-prep) pulse, fat saturated (SPIR), ECG-triggered, respiratory navigator (Navi)-gated three dimensional (3D) turbo field echo (TFE) (**a**) and multi-shot echo planar imaging (EPI) (**b**) sequence were used for whole-heart coronary MRA. This sequence acquired several n (= EPI factors) echoes per radio-frequency (RF) excitation, and yielded N (= TFE factors) RF excitations per heart beat. As a result, N*n echoes are acquired per heart beat.

Table 1. Magnetic resonance imaging sequences and parameters

	TFE	Multishot-EPI
TR/TE (ms)	2.5 / 1.16	7.7 / 3.2
FOV (mm x mm)	300	300
Matrix	192 × 192	192 × 192
Slice thickness (mm)	1.8 (over contiguous)	1.8 (over contiguous)
Spatial resolution (mm^3)	1.56 × 1.74 × 1.8	1.56 × 1.93 × 1.8
Number slices	140	140
TFE factor	28	18
EPI factor	-	7
Shot duration (msec)	69.8	137.7
Acquisition time (min) (Heart rate 60 beats / min)	3:55	0:26
Flip angle	20	20
Fat suppression	SPIR	SPIR
Half scan	None	0.86
Averages	1	1
SENSE factor	2.2 × 1.2	2.5 × 1.5

EPI, echo-planar imaging; SENSE, sensitivity encoding; TFE, turbo field echo.

signals can be obtained at one RF excitation; however, the signal acquisition time is limited by T_2^* relaxation. The acquisition of many k space lines increases the TE and TR, and results in lowering the SNR and in blurring. Therefore, we used an EPI factor of seven; this setting can yield seven echoes per excitation. The detailed scanning parameters are shown in Table 1.

Quantitative analysis

A board-certified radiologist with 10 years of cardiac MRI experience performed quantitative image analysis on axial images. To minimize bias from single measurements we placed three circular ROI on three different sequential slices and calculated their mean. The mean signal intensity (SI) of the ascending aorta was measured in an ROI placed near the origin of the left main trunk (ROI_{Ao}). Attempts were made to select an ROI of 400 mm^2 in the ascending aorta; this size was large enough to be unaffected by pixel variability and small enough to exclude the vessel wall or perivascular fat. We also recorded the standard deviation (SD_{Ao}) of the attenuation at the ROI_{Ao}. The SNR of the ascending aorta was calculated as SNR = ROI_{Ao}/SD_{Ao}.

To evaluate the contrast between the coronary artery and the cardiac muscle and the SNR of the cardiac muscle we selected the slice level at the center of the left ventricle in each patient. The mean SI in a circular ROI in the RCA was measured (ROI_{RCA}). The ROIs in the RCA were as large as possible and papillary muscles, plaques, and areas of stenosis were carefully avoided. The mean SI in a circular ROI in the interventricular septum was also recorded (ROI_{muscle}) as was the standard deviation (SD_{muscle}) of the attenuation in ROI_{muscle}. These ROIs were also as large as possible and ventricular cavities, vessels, and fat were carefully avoided. The contrast between the RCA and the interventricular septum was calculated as contrast = ROI_{RCA}/ROI_{muscle} and the SNR of the cardiac muscle as SNR = ROI_{muscle}/SD_{muscle}.

Qualitative image analysis

To evaluate the image quality obtained with the different sequences we performed qualitative image analysis on a PACS viewer (View R, version 1.09.15, Yokogawa Electronic, Tokyo, Japan). Two board-certified radiologists with 6 and 12 years of experience with cardiac MRI independently graded the image contrast, noise, sharpness, artifacts, and the overall image quality.

The MRI datasets were randomized and the readers were blinded to the acquisition parameters. Using a 4-point subjective scale they independently graded image contrast and overall image quality (1 = unacceptable, 2 = acceptable, 3 = good, 4 = excellent). The image noise and artifacts were similarly recorded as grade 1 (present and unacceptable), grade 2 (present and interfering with the depiction of adjacent structures), grade 3 (present without interfering with the depiction of adjacent structures), and as grade 4 (no noise or artifact). Image sharpness was determined by evaluating the coronary wall sharpness as grade 1 (blurry), grade 2 (poorer than average), grade 3 (better than average), and grade 4 (sharpest). Inter-observer disagreement was settled by consensus.

Statistical analysis

To compare the SNR and contrast of the TFE- and the MSG-EPI sequence, we used the paired *t*-test. The Wilcoxon signed-rank test was employed to perform qualitative MRI image comparisons. Differences of $P < 0.05$ were considered statistically significant. The degree of inter-observer agreement for each qualitative assessment was determined by calculating the kappa value. The scale for the kappa coefficients for inter-observer agreement was: less than 0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = substantial, and 0.81–1.00 = near-perfect. Statistical analyses were with statistical software "R" (R, version 3.2.2; The R Project for Statistical Computing; http://www.r-project.org/).

Results

Figure 2 summarizes the results of our quantitative analyses. The acquisition time was 88.1% shorter for MSG-EPI than TFE (24.7 ± 2.5 vs 206.4 ± 23.1 sec, $P < 0.01$). The SNR of the ascending aorta and the cardiac muscle was significantly higher on MSG-EPI than TFE scans (ascending aorta: 16.3 ± 5.2 vs 11.1 ± 4.0, $P < 0.01$; cardiac muscle: 11.5 ± 3.5 vs 8.3 ± 2.6, $P < 0.01$; respectively). There was

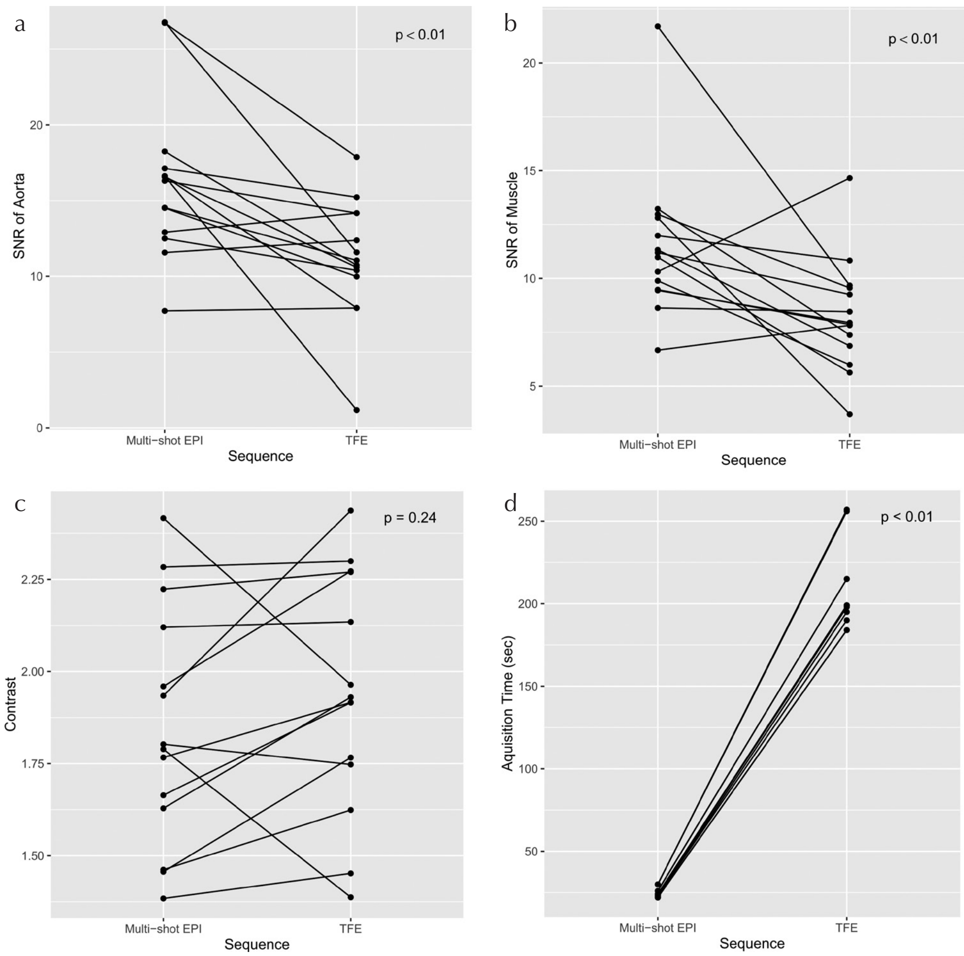

Fig. 2 The signal-to-noise ratio (SNR) of the ascending aorta (**a**) and the cardiac muscle (**b**) were 32% and 25% higher in the multi-shot gradient echo planar imaging (EPI) than the turbo field echo (TFE) (ascending aorta: 16.3 ± 5.2 vs 11.1 ± 4.0, $P < 0.01$; cardiac muscle: 11.5 ± 3.5 vs 8.3 ± 2.6, $P < 0.01$; respectively). There is no significant difference in the contrast of right coronary artery (RCA) and cardiac muscle (**c**) between the multi-shot gradient echo EPI and the TFE (1.8 ± 0.3 vs 1.9 ± 0.3, $P = 0.24$). Acquisition time (**d**) of the single breath hold multi-shot gradient echo EPI was 88.1% lower than that of the TFE (28.7 sec ± 4.3 vs 206.4 sec ± 23.1, $P < 0.01$).

no significant difference in the contrast of the RCA and cardiac muscle between MSG-EPI and TFE scans (1.8 ± 0.3 vs 1.9 ± 0.3, $P = 0.24$).

Table 2 summarizes the results of our qualitative analysis. The qualitative scores for image noise and artifact were significantly higher on MSG-EPI than TFE scans. There were no statistically significant difference in image contrast, image sharpness and overall image quality between MSG-EPI and TFE scans and there was near-perfect or substantial inter-observer agreement with respect to image contrast, noise, sharpness, artifact, and overall image quality (kappa = 0.64, 0.66, 0.86, 0.61 and 0.66, respectively). Representative cases are shown in Figs. 3 and 4.

Table 2. Qualitative analysis

	Multi-shot EPI	TFE	*P* value
Image contrast	3.9 ± 0.4	3.6 ± 0.7	0.24
Image noise	3.6 ± 0.6	3.1 ± 0.5	0.02
Artifact	3.8 ± 0.4	3.3 ± 0.6	0.01
Image sharpness	3.4 ± 0.5	3.7 ± 0.5	0.11
Overall image quality	3.1 ± 0.4	3.4 ± 0.5	0.23

Data are the mean ± standard deviation. TFE, Turbo field echo; EPI, Echo planar imaging.

Discussion

Our study suggests that the single breath hold MSG-EPI sequence yields adequate image quality and drastically reduces the acquisition time compared with the free breathing TFE sequence at unenhanced whole-heart coronary MRA.

A shorter examination time at coronary MRA is desirable; however, fast imaging methods such as parallel imaging are hampered by the low SNR on unenhanced coronary MRA acquired at 3T MRI. Another fast imaging method is the acquisition of multiple echoes per excitation. Representative techniques are the fast spin echo[19] and the EPI sequence.[20] Although these techniques drastically reduce the imaging time, they have significant drawbacks. Each echo is acquired at a different TE; this results in blurring artifacts in the phase-encoding direction due to signal loss in later echoes due to a T_2- or T_2^* decay and the space resolution tends to be low with a limited acquisition time due. These drawbacks are especially severe on EPI sequences because the T_2^*- is much shorter than the T_2

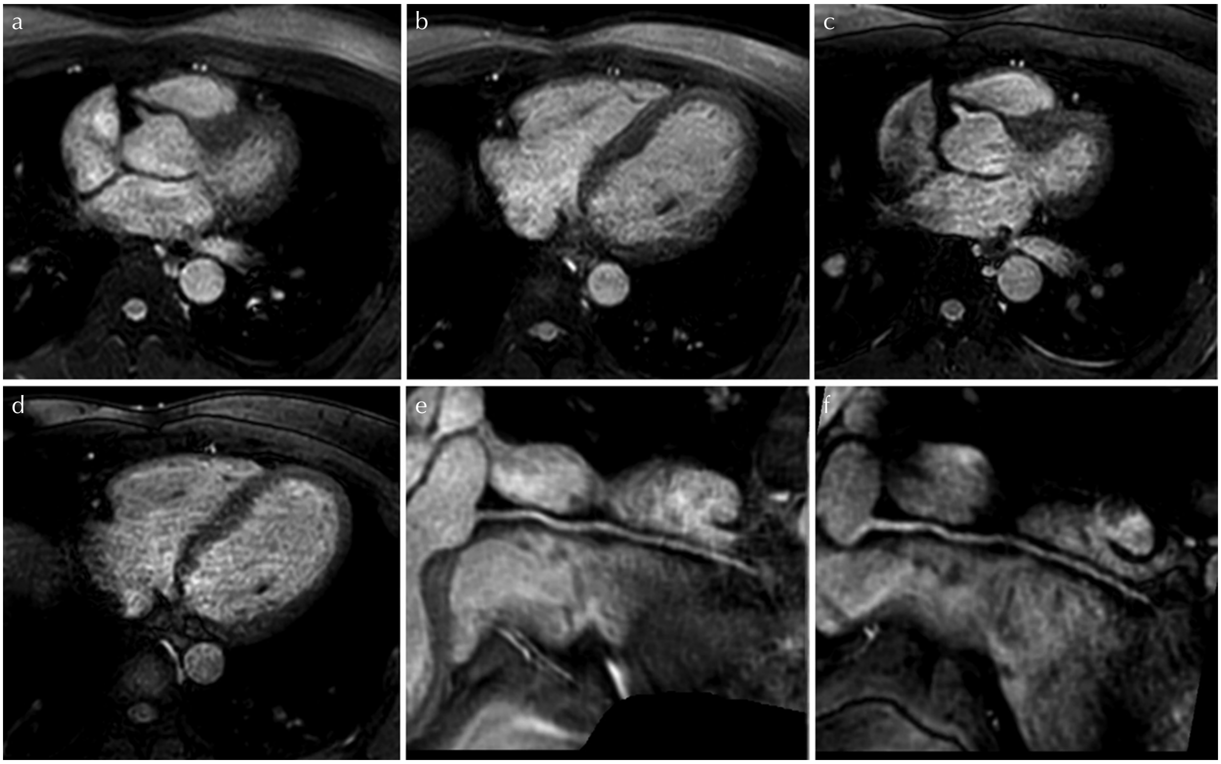

Fig. 3 A 29-year-old volunteer was imaged by single breath hold multi-shot echo planar imaging (EPI) and free breathing turbo field echo (TFE) in 3D whole heart coronary MRA. His heart rate was 50 beats per minute, and scan time 23 sec for multi-shot EPI and 119 sec for TFE. We showed his original image of multi-shot EPI (**a**, **b**), TFE (**c**, **d**), curved multi-planar reconstruction (MPR) of right coronary artery (RCA) image using multi-shot EPI (**e**), and curved MPR of RCA image using TFE (**f**). All coronary branches were successfully depicted with diagnostic image quality with both sequences. There was no significant difference in the image quality between multi-shot-EPI and TFE sequence.

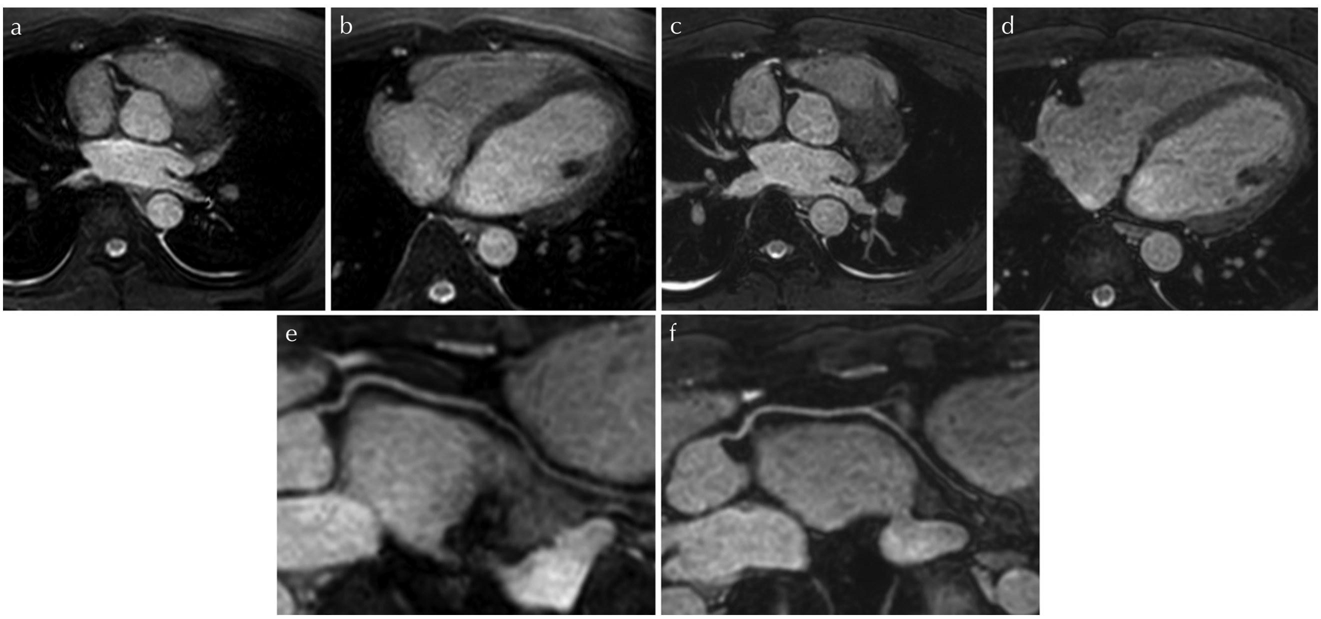

Fig. 4 A 28-year-old volunteer was imaged by single breath hold multi-shot echo planar imaging (EPI) and free breathing turbo field echo (TFE) in 3D whole heart coronary MRA. His heart rate was 65 beats per minute, and scan time 30 sec for multi-shot EPI and 256 sec for TFE. We showed his original image of multi-shot EPI (**a**, **b**), TFE (**c**, **d**), curved multi-planar reconstruction (MPR) of right coronary artery (RCA) image using multi-shot EPI (**e**), and curved MPR of RCA image using TFE (**f**). The image quality was almost same in multi-shot EPI as TFE sequence with extremely short scan duration.

relaxation time due to magnetic field inhomogeneity. In addition, because there are no RF refocusing pulses in the EPI sequence, the spinning protons accumulate phase errors and these results in positioning errors in the phase-encoding direction and significant distortion.

Multi-shot gradient EPI is a type of segmented EPI. It partitions the k-space in the in-plane or through-plane direction based on EPI factors and acquires multiple echoes at one RF excitation. At the same repetition time, the image acquisition time is reduced by the number of the EPI factors. This technique has disadvantages similar to single-shot EPI such as signal loss and blurring artifacts due to the T_2^* decay, a phase error due to the lack of RF refocusing pulses. Certainly in this study, the qualitative scores for image sharpness was higher on TFE scans than MSG-EPI without significant difference (3.7 ± 0.5 vs 3.4 ± 0.5, $P = 0.11$). Therefore, if there is a larger sample size, the qualitative scores for image sharpness might be significantly higher on TFE scans than MSG-EPI.

Our study suggests that the MSG-EPI sequence holds promise for shortening the examination time without a decrease in the SNR at unenhanced coronary MRA performed on a 3T MRI scanner. The SNR of the EPI sequence tends to be relatively low because the T_2^* decay at a long TE and the wide bandwidth decrease the signal of blood.[20] While we cannot ascertain what maintains the SNR despite the disadvantages of the EPI sequence we think that it may be attributable to the fewer RF excitations per heartbeat of the MSG-EPI sequence. The TFE sequence needs the many RF excitations per heart beat to shorten the scan time because it saturates the blood signal and requires a T_1-shortening contrast agent to maintain the SNR.[21] We applied seven EPI factors under the MSG-EPI protocol; this increased the TR from 2.5 to 10.6 msec. Consequently the number of RF excitations (= TFE factors) was decreased from 28 to 10 at a similar shot duration (multi-shot gradient echo EPI protocol: 69.8 msec, TFE protocol: 84.7 msec). We posit that this suppressed the signal decay due to the frequent RF excitation pulse.

Another important finding was that blurring and off-resonance artifacts on MSG-EPI scans were not a serious problem at unenhanced coronary MRA. Previous report suggested that its sensitivity to flow and cardiac motion is an important disadvantage of MSG-EPI and that the T_2^* decay can be expected to introduce some blurring in the images.[22] We observed neither severe blurring nor artifacts at a relatively small TE (3.5 ms) and TR (10.6 ms) on MSG-EPI scans and this may be a trade-off for increased artifacts on these scans whose shorter imaging time decreases the breathing pattern drifts and heart rate changes that produce motion artifacts.

Previous reports suggested that the clinical use of the single breath hold coronary MRA remains challenging due to small vessel size, interfering signal from fat and myocardium, vessel tortuosity, and physiological motion.[23] To overcome these disadvantages, stringent technics for balancing SNR, spatial resolution, temporal resolution, scan time, vessel contrast, and immunity to physiological motion, must be required. Recent 3T MRI system using TFE sequence can offer adequate SNR in spite of having the short acquisition time of whole-heart coronary MRA because the SNR is proportional to the static field strength.[5] However, the spatial resolution of single breath hold unenhanced coronary MRA with TFE was relatively low[5] (Spatial resolution; 2.00 × 2.00 × 2.00). Additionally, the single breath hold unenhanced coronary MRA with TFE required relatively long time (37.7 ± 5.2 sec, 31 sec to 45 sec).[5] On the other hand, our single breath hold technique using MSG-EPI has advantages of shortening more total scan time and reducing the influence of respiratory motion compared with the previous single breath hold technique using TFE.[5] Indeed, the scan time of single breath hold MSG-EPI sequence was 27% shorter than that of single breath hold TFE sequence which was previously reported (24.7 ± 2.5 vs 37.7 ± 5.2)[5] while yielding higher resolution images (Spatial resolution; 1.56 × 1.93 × 1.8 vs 2.00 × 2.00 × 2.00). The MSG-EPI sequence might be adequate for single breath hold whole heart coronary MRA.

Our study has some limitations. First, as it included only 14 healthy volunteers, we cannot claim that the MSG-EPI sequence yields a non-inferior image quality in patients with suspected coronary disease who tend to manifest breathing pattern drifts and heart rate changes. In addition, we did not evaluate the diagnostic accuracy of MSG-EPI for whole-heart coronary MRA. Further studies are needed to evaluate the diagnostic performance of MSG-EPI in patients with suspected coronary disease. Second, there was a relatively small individual difference in heart rate (mean 63.1 ± 7.3 beats per minute) and body weight (mean 64.5 ± 9.9 kg) between our study volunteers. Therefore, we don't know whether the result is consistent with female subjects, heavy subjects or subjects with tachycardia or not. Lastly, we applied only one parameter for whole-heart coronary MRA. Parameters such as EPI- and TFE factors, the TE of the T_2-prep pulse, and half-Fourier scanning might change the image quality and the scanning time of MSG-EPI. Studies are underway to optimize the MSG-EPI sequence for whole-heart coronary MRA.

Conclusions

In conclusion, the single breath hold MSG-EPI sequence can yield an image quality that is non-inferior to the free breathing gradient echo sequence at unenhanced whole-heart coronary MRA at 3T MRI. This technique is a promising method to reduce the acquisition time of 3D unenhanced whole-heart coronary MRA images.

Conflicts of Interest

Atsushi Takemura and Tomoyuki Okuaki are the employees of Philips Medical Japan. The other coauthors have no conflict of interest.

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