

TECHNICAL NOTE

Non-enhanced and Non-gated MR Angiography for Robust Visualization of Peripheral Arteries Using Enhanced Acceleration-selective Arterial Spin Labeling (eAccASL)

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This study aimed to assess the feasibility for applying enhanced acceleration-selective arterial spin labeling (eAccASL) to non-electrocardiogram-gated and non-enhanced peripheral MRA. We compared eAccASL and background suppressed single shot turbo field echo (TFE)-triggered angiography non-contrast-enhanced sequence (BASS TRANCE) required electrocardiographic-gating in eight volunteers and three patients. In the volunteer study, eAccASL demonstrated a comparable arterial visualization compared with BASS TRANCE. In patient observation, the advantages with eAccASL were found in arterial visualization on the collateral vessels and without artifacts affected by arrhythmia events.

Keywords: *magnetic resonance angiography, enhanced acceleration-selective arterial spin labeling, peripheral arteries, non-enhanced, non-gated*

Introduction

The prevalence of peripheral artery disease (PAD) has increased considerably, and some specific tests (e.g., ankle-brachial index, computed tomography angiography) are important to diagnose arterial stenosis or occlusion. In the late 1990's, contrast-enhanced magnetic resonance angiography (MRA) was introduced as peripheral MRA.¹ In recent years, non-contrast-enhanced (NCE) MRA techniques, which do not have a risk of nephrogenic systemic fibrosis, have commonly used to assess PAD. Most NCE MRA techniques such as 3D fresh blood imaging,² and non-subtractive quiescent-interval single shot (QISS)³ require electrocardiography (ECG)-gating. However, there are several limitations which create artifacts in the ECG, such as gradient

switching and arrhythmia, thereby making accurate data collection almost impossible. The use of the ECG gating leads to a relatively long scan time; although MRA techniques without ECG gating based on self-navigation has been reported,⁴ it also requires additional preparation time for ECG setting and an electrocardiogram data set with a well-arranged waveform.

Recent reports have introduced a novel technique with acceleration flow-sensitized dephasing (FSD) to provide NCE peripheral MRA.⁵ FSD-MRA demonstrates the possibility of diagnostic ability in a patient with PAD similar to CE-MRA.⁶ Previous studies with FSD-MRA used the steady-state free-precession (SSFP) sequence^{5,6} with a high contrast of the blood. However, the SSFP sequence may not be suitable at 3T because of increase in off-resonance or banding artifacts. On the other hand, Obara et al.⁷ demonstrated that acceleration-selective arterial spin labeling (AccASL) technique is similar to FSD-MRA for intracranial MRA using a 3T MRI, and also reported an improved sequence with RF pulse optimization, called enhanced AccASL (eAccASL).⁸ Based on these factors, we hypothesized that applying AccASL MRA for peripheral MRA may achieve a highly robust method even without ECG synchronization.

This study aimed to assess the feasibility for applying eAccASL to non-electrocardiogram-gated and non-enhanced peripheral MRA, compared with conventional AccASL (cAccASL) and background suppressed single shot turbo field echo (TFE)-triggered angiography NCE sequence (BASS TRANCE), similar to QISS as reference method.

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Background suppressed single shot TFE-triggered angiography NCE sequence images were acquired in the transverse plane under the following conditions: 2D T₁-TFE, TR = 4.6 ms, TE = 2.2 ms, FA = 25°, *k*-space trajectory = centric ordering, FOV = 400 × 240 mm², voxel size = 1.14 × 1.13 × 3.0 mm³, slice overlap = 0.6 mm, TFE factor = 106 (single shot), SENSE factor (AP) = 2.0, fat suppression = spectral presaturation with inversion recovery, delay time after the saturation pulse for imaging slice = 100 ms, and total acquisition time = 2 min 16 s for a heart rate of 60 beats/min. In addition, phase-contrast (PC) cine MRI was conducted to determine suitable trigger delay time for BASS TRANCE.

Phase-contrast cine MRI was conducted to determine ECG trigger delay times. Parameters of PC cine MRI were as follows: TR = 4.0 ms, TE = 2.4 ms, FA = 10°, FOV = 350 × 300 mm², voxel size = 2.43 × 2.43 × 8.0 mm³, SENSE factor = 2.0, and scan time, approximately 60–100 s depending on heart rate.

Volunteer study

We examined eight healthy volunteers (mean age 26 years; range 22–32 years) by using three MRA sequences: (1) cAccASL, (2) eAccASL, and (3) BASS TRANCE.

In the volunteer study, the signals in the artery and background on three MRA techniques were measured to assess the visualization of arteries. Circular regions of interests (ROIs) were placed at the popliteal artery (Pop.A), anterior tibial artery (ATA), posterior tibial artery (PTA), peroneal artery (Pero.A), and gastrocnemius muscle (GM) for both legs in each maximum intensity projection (MIP) of the subtracted image. ROIs were placed in the middle parts of each artery except for Pop.A. Since the AccASL MRA is based on T₁-TFE, it has the possibility of measurement error by the artifact such as a strong inflow effect. Therefore, we measured the distal parts in Pop.A rather than the proximal or middle parts. ROIs in each volunteer were placed at the same location across the three MRA. Then, the signal intensity ratio (SIR) was calculated as $SIR = S_{artery}/S_{GM}$, where S_{artery} and S_{GM} are the signals in the ROIs in the Pop.A, ATA, PTA, Pero.A, and GM, respectively. Since the venous effect, false stenosis, and arterial depiction were difficult to assess by the placement of ROIs, two radiologists (5 and 6 years of clinical imaging experience) reviewed the MIP of the peripheral MRA as acquired by the three techniques (i.e., cAccASL, eAccASL, and BASS TRANCE) in random order in a blinded manner. The image qualities of major arteries (ATA, PTA, and Pero.A) in left and right legs were independently scored using a four-point scale: 3 = definitely diagnostic in full length; 2 = probably diagnostic in full length; 1 = probably not diagnostic in full length; 0 = not diagnostic. The artifacts, including contamination of veins and B₁ inhomogeneity, were scored for each leg: 3 = no artifact; 2 = minimal; 1 = moderate; 0 = very severe (nondiagnostic).

All statistical analyses were performed using the statistical software package SPSS for Windows, version 25.0 (SPSS, Chicago, IL, USA). The SIRs and each score in three MRA techniques were compared using Friedman's test.

When there was a significant difference, a *post-hoc* test according to the Wilcoxon signed-rank test using Bonferroni correction was performed. A *P*-value <0.05 was considered statistically significant.

Patient's observation

Three clinical patients, one with chronic kidney disease, one underwent hemodialysis with a history of myocardial infarction, and one underwent hemodialysis with atrial fibrillation, underwent peripheral MRA imaging. In the clinical cases, only two techniques (i.e., eAccASL and BASS TRANCE) were scanned due to the time limit in clinical practice. The study protocol was approved by the Institutional Review Boards of participating institutions, and written informed consent was obtained from all participants. In the clinical cases, since the small number of cases (only three patients) did not permit statistical analysis, quantitative and qualitative assessments were not performed.

Results

The volunteer study was summarized as follows. Figure 2 shows the comparison of quantitative assessment acquired by three MRA techniques in the healthy volunteer study. The Friedman tests revealed significant differences among the SIR for the three MRA techniques in almost arteries ($P < 0.05$) except for the pop.A of the right leg. BASS TRANCE MRA had significantly higher SIRs than cAccASL MRA in almost arteries except for Pop.A of the right leg (Pop.A of the left leg, $P = 0.037$; ATA of the right leg, $P = 0.018$; ATA of the left leg, $P = 0.003$; both PTAs, both Pero.As, $P < 0.001$). Regarding below-knee arteries, the SIRs for BASS TRANCE had significantly higher than those for eAccASL (ATA of the right leg, $P = 0.037$; ATA of the left leg, $P = 0.018$; PTA of the left leg, $P = 0.037$; both Pero.As, $P = 0.037$). The SIR on Pop.A of the left leg for eAccASL was significantly higher than that for cAccASL ($P = 0.018$). The eAccASL MRA had a slightly higher mean SIR than cAccASL MRA for all arteries in both legs.

The results of the qualitative assessment for the three MRA techniques are shown in Fig. 3. There was a significant difference in arterial image quality and artifacts among the three techniques ($P < 0.05$). Based on *post-hoc* analyses, arterial image quality of cAccASL was significantly lower than that of eAccASL (ATA of the left leg, $P = 0.04$; both Perp.As, $P = 0.01$; both PTAs, $P < 0.001$) and BASS TRANCE (ATA of the left leg, $P = 0.031$; Perp.A of the right leg, $P = 0.004$; Perp.A of the left leg, $P < 0.001$; PTA of the right leg, $P = 0.002$; PTA of the left leg, $P < 0.001$). However, there was no significant difference between eAccASL and BASS TRANCE in all arterial image quality scores ($P > 0.05$). Artifact scores for cAccASL were significantly lower than eAccASL (the right leg, $P = 0.002$; the left leg, $P = 0.011$) and BASS TRANCE (the right leg, $P = 0.004$; the left leg, $P = 0.024$) on the *post-hoc* analyses.

Figure 4 illustrates representative MRA images of the peripheral artery in volunteer study obtained by three MRA

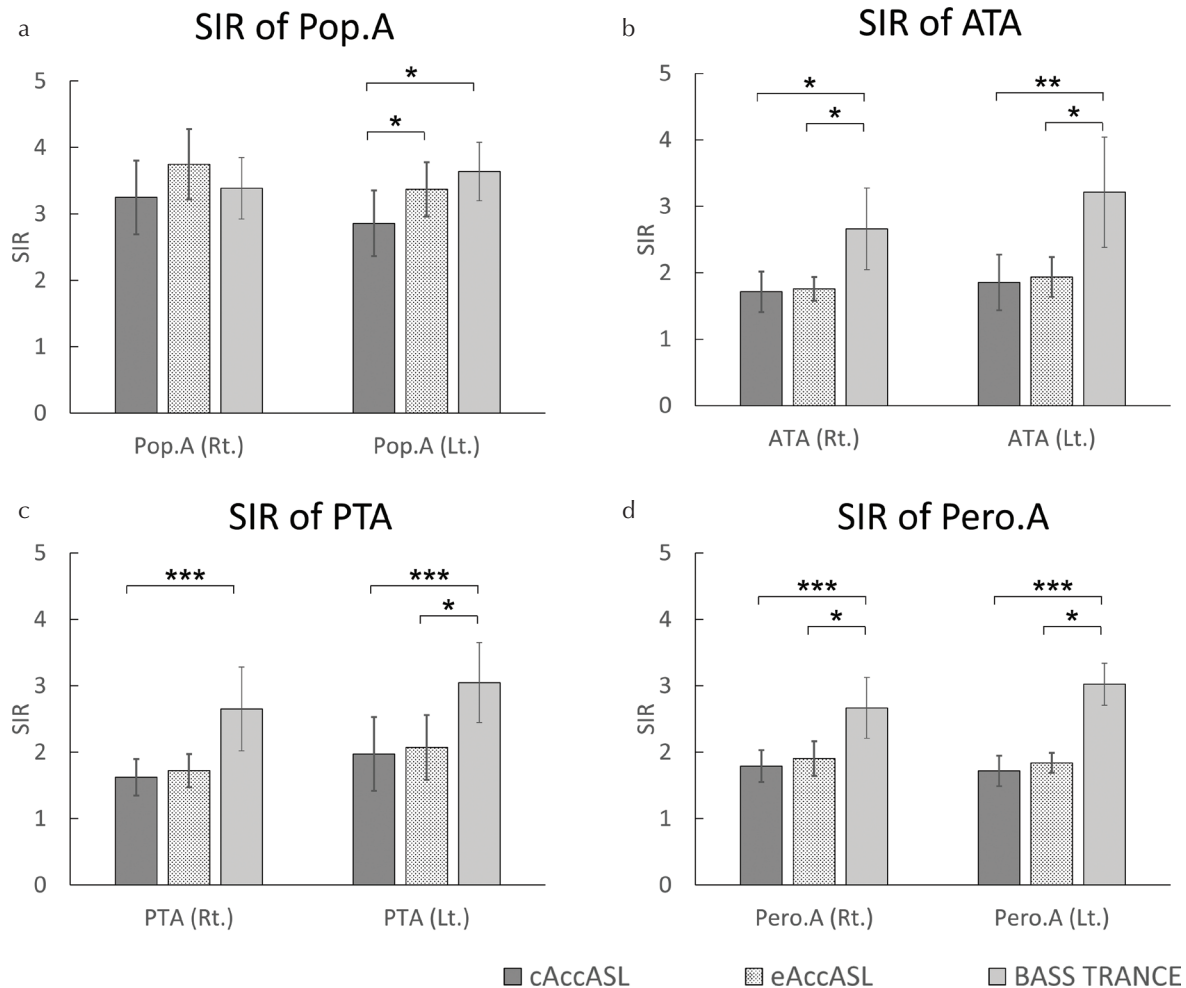


Fig. 2 Calculated SIRs of GM to Pop.A (a), ATA (b), PTA (c), and Pero.A (d) for cAccASL and eAccASL. Significant differences in SIRs were observed for (a) Pop.A of both legs, (c) PTA of the right leg, and (d) Pero.A of the left leg ($*P < 0.05$). The bar graphs show the mean values of SIR. The whiskers indicate one standard deviation. ATA, anterior tibial artery; cAccASL, conventional acceleration-selective arterial spin labeling; eAccASL, enhanced acceleration-selective arterial spin labeling; GM, gastrocnemius muscle; Pero.A, peroneal artery; Pop.A, placed at popliteal artery; PTA, posterior tibial artery; SIR, signal intensity ratio.

techniques. The eAccASL could provide more robust visualization than cAccASL and similar visualization to BASS TRANCE.

The clinical case was summarized as follows. Figure 5 is a comparison of MIP images obtained using eAccASL and BASS TRANCE in three patients. The eAccASL showed the artifact of venous contamination slightly. Although eAccASL was similar to BASS TRANCE in terms of visualizing the peripheral artery, BASS TRANCE was observed as severe stenosis in the part of the femoral artery. The clinical patient in Fig. 5b demonstrates that eAccASL could provide better visualization of the collateral vessels than BASS TRANCE. Focusing on the occlusion point of ATA in the right leg, eAccASL showed the occlusion in the middle part, whereas BASS TRANCE in the original part. The patient with ventricular premature beats is shown in Fig. 5c. Both MRA techniques provided complete visualization of the occlusion of ATA in the right leg. However, arrhythmic events affected the

image quality for BASS TRANCE when the superficial femoral arteries were scanned.

Discussion

The eAccASL MRA was able to visualize the peripheral artery without contrast enhancement and ECG-gating in either volunteers or patients. Preparation of ECG, calibration, and measurement of flow velocity leads to a prolonged examination time with approximately additional 5–10 min. The expedited examination contributes to a quicker MRI scan, thus reducing the pain and suffering during scanning for patients with painful PAD.

Here we assessed SIR values because the differences in signal between the background and blood greatly contribute to the diagnosis of vascular disease. BASS TRANCE MRA showed a higher SIR than the other two MRAs in the area of peripheral arteries from the area of Pop.A. BASS TRANCE

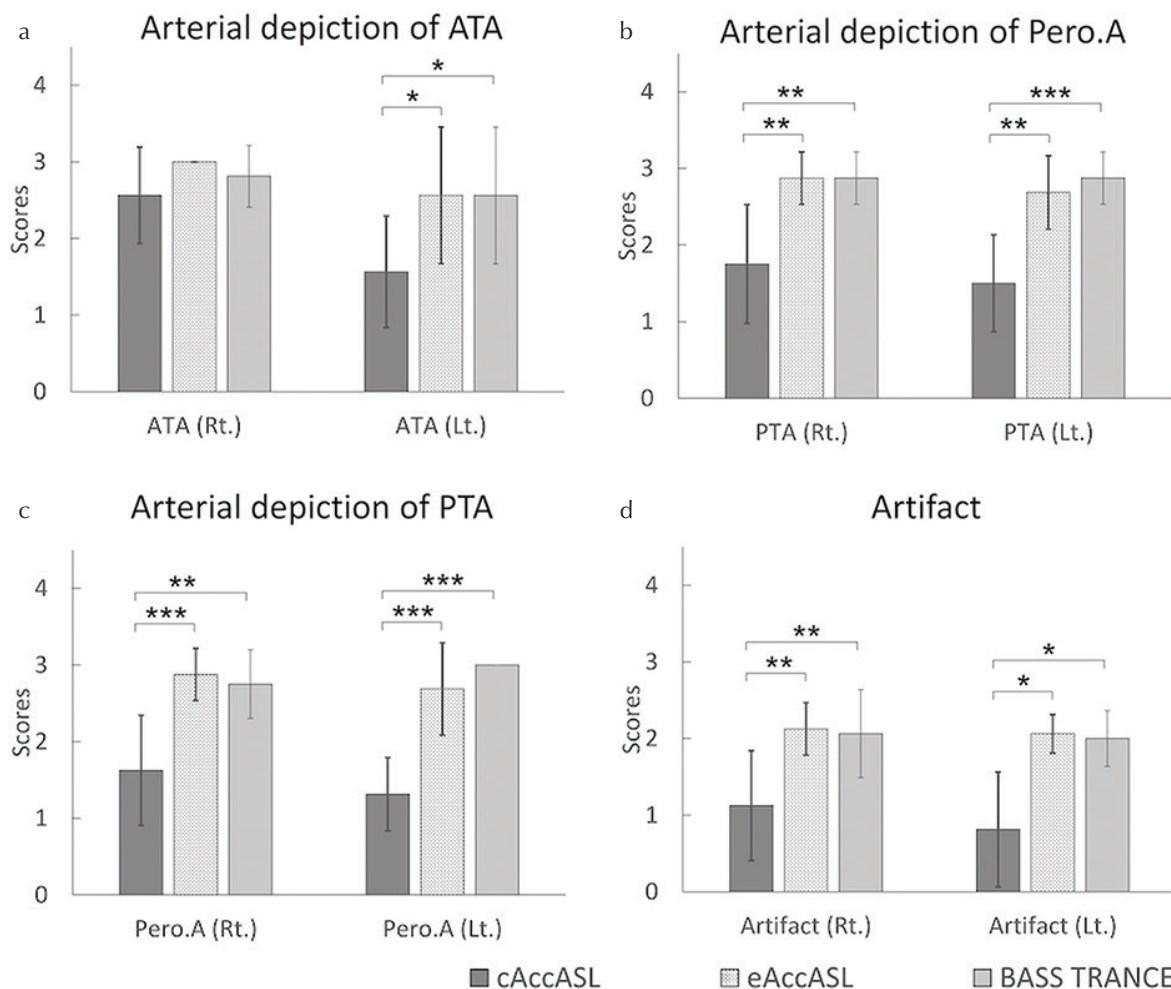


Fig. 3 Comparison of the qualitative assessment of three MRA techniques. Arterial depiction of ATA (a), PTA (b), and Pero.A (c) for each leg. Artifacts including venous contamination and B₁ inhomogeneity (d). Single, double, and triple asterisks indicate significant differences with $P < 0.05$, $P < 0.01$, and $P < 0.001$, respectively. The bar graphs show the mean values of SIR. The whiskers indicate one standard deviation. ATA, anterior tibial artery; cAccASL, conventional acceleration-selective arterial spin labeling; eAccASL, enhanced acceleration-selective arterial spin labeling; Pop.A, placed at popliteal artery; PTA, posterior tibial artery.

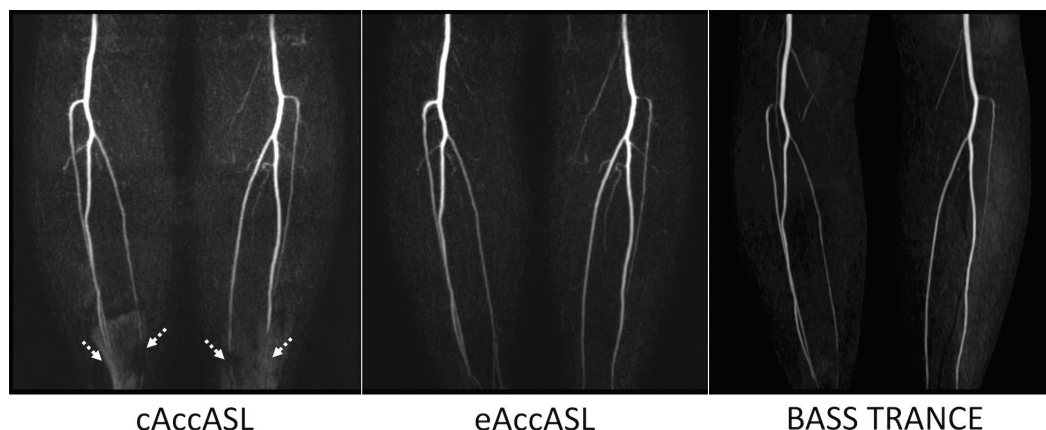


Fig. 4 Representative images of the volunteer for each MRA technique. cAccASL, eAccASL, and BASS TRANCE MRA images are shown, with the MIP image of cAccASL MRA. cAccASL demonstrates inhomogeneous background signal at the lower part in both legs. The broken-line arrows show a specific artifact only observed in cAccASL. BASS TRANCE, background suppressed single shot TFE-triggered angiography non-contrast-enhanced sequence; cAccASL, conventional acceleration-selective arterial spin labeling; eAccASL, enhanced acceleration-selective arterial spin labeling; MRA, magnetic resonance angiography. TFE, turbo field echo.

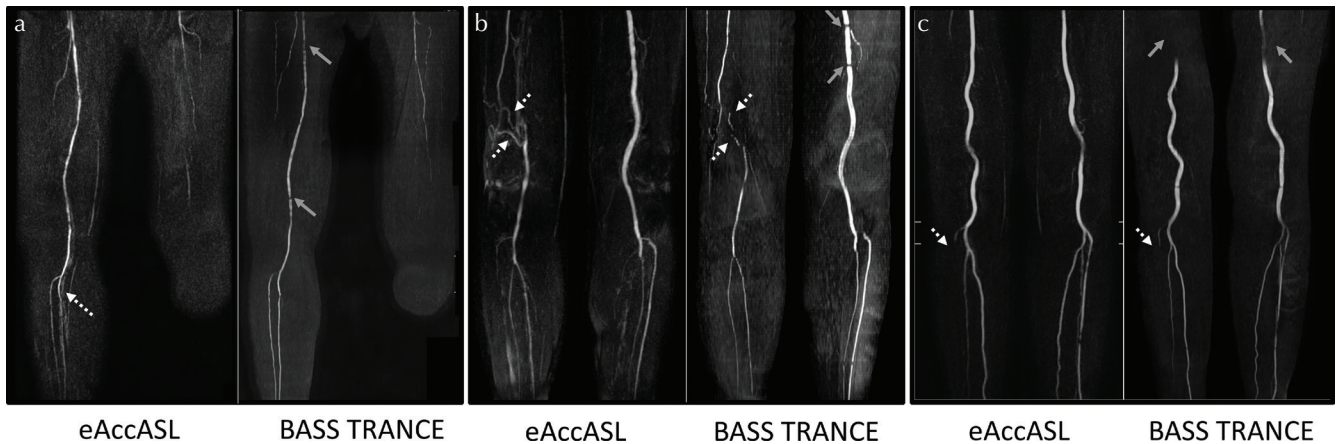


Fig. 5 MIP images of peripheral MRA obtained by eAccASL and BASS TRANCE in two patients with PAD and one with ventricular premature beats. (a) MIP images for the clinical case of a patient with left leg amputation. eAccASL had a slight artifact of venous contamination (a broken-line arrow). BASS TRANCE appeared more severe stenosis compared with eAccASL at the same locations (line arrows). (b) MIP images for the clinical case of a patient with collateral artery formation in the right leg. eAccASL could provide better-formed collateral vessels than BASS TRANCE (broken-line arrows). BASS TRANCE represented false stenosis due to missing trigger events (line arrows). (c) MIP images for the clinical case of a patient with ventricular premature beats. Both MRA techniques provided complete visualization of ATA occlusion in the right leg (broken-line arrows). Arrhythmia events occurred when superficial femoral arteries were scanned with BASS TRANCE, resulting in the visualization of false occlusion (line arrows). ATA, anterior tibial artery; BASS TRANCE, background suppressed single shot TFE-triggered angiography non-contrast-enhanced sequence; eAccASL, enhanced-acceleration-selective arterial spin labeling; MIP, maximum intensity projection; MRA, magnetic resonance angiography; PAD, peripheral artery disease. TFE, turbo field echo.

MRA acquired by 2D sequence can get a higher inflow effect on the peripheral arteries than eAccASL MRA using 3D coronal acquisition. However, because we believe that AccASL MRA allows keeping the SIR for the visibility of the arteries, non-ECG-gating has the advantage of clinical practice. Regarding the SIR for two AccASL techniques, eAccASL technique demonstrated slightly higher mean SIRs than cAccASL; however, the differences between the two AccASL did not approach significance. The addition of the number of 180° pulse in T_2 preparation increases the magnetization transfer (MT) effect causing decrease muscle signal.¹⁰ However, since we measured the signal in the MIP images made from the subtraction image, the MT effect was not able to be assessed clearly. On the other hand, a previous study¹¹ reported that quadruple refocused designs on T_2 preparation more effectively avoid the arterial signal loss by stabilizing B_1 homogeneity and shortening echo space, compared with double refocused designs. This phenomenon may contribute to the slightly higher mean SIRs for eAccASL than those for cAccASL.

The visibility of peripheral artery on the three different approaches for MRA techniques were reviewed by two radiologists. The higher arterial depiction and lower artifact in both eAccASL and BASS TRANCE were objectively substantiated by qualitative assessment in almost all arteries except for the ATA of the right leg, compared with cAccASL. Although the ostium of ATAs was not visually assessed by the radiologists, it was differently observed between eAccASL and BASS TRANCE; it seemed less visualized on BASS TRANCE than eAccASL. Because BASS TRANCE is based on inflow effect, transverse acquisition is susceptible

to blood flow parallel to imaging slice. This might cause a difference in the visibility in the ostium of ATA between these two sequences. The comparison in arterial depiction between cAccASL and eAccASL was more pronounced than SIR results. B_1 and/or B_0 inhomogeneity were optimized with the addition of a pair of refocusing pulses accompanied by phase cycling in the T_2 preparation module (Fig. 4).^{11,12} This optimization of B_0 and/or B_1 inhomogeneity in eAccASL may improve arterial signal loss, leading to good arterial depiction. In addition, the eAccASL MRA showed significantly fewer artifacts than cAccASL. The inhomogeneous signal increase of the background in cAccASL is likely to be caused by the eddy current derived from MSG; it is not expected to be caused by B_0 and/or B_1 inhomogeneity since AccASL MRA is a subtraction image. When the MSG was split in eAccASL MRA, the short gradient duration causes eddy current reduction, whereas the strong gradient strength is assumed to lead to eddy current buildup.¹³ However, based on the results of our experiment, the short gradient duration in relation to cancellation of the eddy current would be expected to have contributed to a greater improvement in signal inhomogeneity than the strong gradient strength. Simulations for the eddy currents effect would be warranted to compare eAccASL and cAccASL more accurately. These results indicate that eAccASL MRA is much more optimized for a 3T scanner than cAccASL MRA.

All qualitative assessments in the volunteer study demonstrated high quality without significant differences between eAccASL and BASS TRANCE. In three clinical cases, ischemic lesions including occlusion and stenosis were able

to be observed with the use of eAccASL and BASS TRANCE MRA. Assuming that almost the same visualization of the artery can be obtained without ECG-gating, eAccASL MRA is placed on profitable of MRI examination time. Moreover, ECG-gating becomes difficult with a 3T MRI system due to the amplified magneto-hydrodynamic effects.¹⁴ Enhanced T-wave artifacts cause double triggering and poor MRA images. The proposed method also has no concern for arrhythmias, providing robust performance and good throughput.

Several studies have utilized FSD-MRA with ECG-gating.^{5,6} Assuming that no-gating MRA allows for the achievement of arterial visualization depending on setting scan parameters, we used a slightly stronger MSG than that used in a previous study,⁵ as we changed 0.896–0.580m/s². Thus, peripheral arteries were visualized even without ECG synchronization. Although some methods such as self-gating have been reported to resolve the artifact caused by cardiac arrhythmia,⁴ we maintain that eAccASL MRA is the most reasonable method which does not require additional cardiac data.

As shown in Fig. 5, eAccASL MRA showed comparable visibility for the clinical cases of PAD compared with BASS TRANCE. In a patient (Fig. 5a), we observed venous contamination and deteriorated arterial supply but this did not affect diagnostic imaging. If there is no blood flow or very slow flow, a means-added eAccASL MRA with more intense MSG might be effective. Collateral arteries were well depicted in eAccASL MRA (Fig. 5b). However, BASS TRANCE based on 2D axial imaging depending inflow effect was susceptible to blood vessels running parallel to the cross-section. A technique using flow-sensitive dephasing and 3D acquisition seems not to cause such problems. In contrast, for Fig. 5c, there was the heterogeneous signal intensity like observed stenoses in the left ATA with eAccASL MRA. Because the same stenosis was also detected in BASS-TRANCE, both MRAs might show similar detection on straight blood flow. It should be noted that false stenosis due to arrhythmia was observed on BASS TRANCE (Fig. 5b and 5c). Depending on the severity of the proximal arterial stenosis in the both sides, the timing of the bilateral blood flow peak may be different in a patient with severe stenosis. Thus, the low signal band might appear only on the unilateral side but not on the other side, due to missing triggers, as seen in the patient in Fig. 5b. In clinical practice, there is no countermeasure against arrhythmia artifacts in BASS TRANCE, but the proposed eAccASL technique can adjust the AENC value when arterial visualization is poor.

In spite of BASS TRANCE being considered the standard NCE peripheral MRA, one limitation to this study is a lack of comparison with FSD-MRA techniques with ECG gating. Shaida et al.⁶ reported that a velocity-flow-dependent MRA may have better diagnostic in severe PAD; thus, more clinical cases may be needed to assess image quality between gating and non-gating techniques. Another limitation of this study was a lack of the gold standard. As CE-CT and/or digital

subtraction angiography has widely used as the gold standard for PAD diagnosis, future studies should comparatively examine patients with PAD using such methods. Similarly, as a limitation on this clinical case, eAccASL MRA should be assessed compared with contrast-enhanced MRA. Performing the assessment will clearly reveal false stenosis and more.

Conclusion

In conclusion, eAccASL MRA without ECG-gating enabled comparable observation of the peripheral arteries in volunteer study, compared with BASS TRANCE as the standard NCE MRA. The eAccASL MRA would provide sufficient visualization of peripheral arteries even in clinical patients with PAD.

Conflicts of Interest

Two of the authors (M. Obara, Y. Akamine) are employee of Philips Japan. The other authors declare that they have no conflicts of interest.

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